A mathematical framework for evo-devo dynamics

Mauricio González-Forero[a,*], Andy Gardner[a]

[a] *School of Biology, University of St Andrews, Dyers Brae, St Andrews, KY16 9TH, Fife, UK*

Abstract

Natural selection acts on phenotypes constructed over development, which raises the question of how development affects evolution. Classic evolutionary theory indicates that development affects evolution by modulating the genetic covariation upon which selection acts, thus affecting genetic constraints. However, whether genetic constraints are relative, thus diverting adaptation from the direction of steepest fitness ascent, or absolute, thus blocking adaptation in certain directions, remains uncertain. This limits understanding of long-term evolution of developmentally constructed phenotypes. Here we formulate a general tractable mathematical framework that integrates age progression, explicit development (i.e., the construction of the phenotype across life subject to developmental constraints), and evolutionary dynamics, thus describing the evolutionary developmental (evo-devo) dynamics. The framework yields simple equations that can be arranged in a layered structure that we call the evo-devo process, whereby five elementary components generate all equations including those describing genetic covariation and the evo-devo dynamics. The framework recovers evolutionary dynamic equations in gradient form and describes the evolution of genetic covariation from the evolution of gene expression, phenotype, environment, and mutational covariation. This shows that genetic and phenotypic evolution must be followed simultaneously to yield a well-defined description of long-term phenotypic evolution in gradient form, such that evolution described as the climbing of a fitness landscape occurs in geno-phenotype space. Genetic constraints in geno-phenotype space are necessarily absolute because the degrees of freedom of genetic covariation are necessarily limited by genetic space. Thus, the long-term evolutionary dynamics of developed phenotypes is strongly non-standard: (1) evolutionary equilibria are either absent or infinite in number and depend on genetic covariation and hence on development; (2) developmental constraints determine the admissible evolutionary path and hence which evolutionary equilibria are admissible; and (3) evolutionary outcomes occur at admissible evolutionary equilibria, which do not generally occur at fitness landscape peaks in geno-phenotype space, but at peaks in the admissible evolutionary path where "total genetic selection" vanishes if exogenous plastic response vanishes and mutational variation exists in all directions of gene-expression space. Development thus modulates necessarily absolute genetic constraints, and hence it affects evolutionary equilibria, the admissible evolutionary path, and which equilibria are admissible. Our framework provides an alternative method to dynamic optimization (i.e., dynamic programming or optimal control) to identify evolutionary outcomes in models with developmentally dynamic traits. These results show that development has major evolutionary effects.

Keywords:
evolutionary dynamics, developmental constraints, genetic constraints, life history theory, matrix population models, adaptive dynamics

1. Introduction

Natural selection screens phenotypes produced by development, defined as "the process by which genotypes are transformed into phenotypes" (Wolf et al., 2001). Thus, a fundamental evolutionary problem concerns how development affects evolution. Interest in this problem is long-standing (Baldwin 1896, Waddington 1959 p. 399, and Gould and Lewontin 1979) and has steadily increased in recent decades. It has been proposed that developmental constraints (Gould and Lewontin, 1979; Maynard Smith et al., 1985; Brakefield, 2006; Klingenberg, 2010), causal feedbacks among gene expression, phenotype, and environment occurring through development (Lewontin, 1983; Rice, 2011; Hansen, 2013; Laland et al., 2015), and some development-mediated factors (Laland et al., 2014, 2015), namely plasticity (West-Eberhard, 2003), niche construction (Odling-Smee et al., 1996, 2003), extra-genetic inheritance (Baldwin, 1896; Cavalli-Sforza and Feldman, 1981; Boyd and Richerson, 1985; Bonduriansky and Day, 2018), and developmental bias (Arthur, 2004), may all have important evolutionary roles. Understanding how development — including these elements acting individually and together — affects the evolutionary process remains an outstanding challenge (Baldwin, 1896; Waddington, 1959; Müller, 2007; Pigliucci, 2007; Laland et al., 2014, 2015; Galis et al., 2018).

Classic evolutionary theory indicates that development affects evolution by modulating the genetic covariation upon which selection acts. This can be seen as follows. In quantitative genetics, an individual's i-th trait value x_i is written as $x_i = \bar{x}_i + \sum_j \alpha_{ij}(y_j - \bar{y}_j) + e_i$, where the overbar denotes pop-

*Corresponding author:
Email address: mgf3@st-andrews.ac.uk (Mauricio González-Forero)

ulation average, y_j is the individual's gene content at the j-th locus, α_{ij} is the partial regression coefficient of the i-th trait deviation from the average on the deviation from the average of the j-th locus content, and e_i is the residual error (Fisher, 1918; Crow and Kimura, 1970; Falconer and Mackay, 1996; Lynch and Walsh, 1998; Walsh and Lynch, 2018). The quantity α_{ij} is Fisher's additive effect of allelic substitution (his α; see Eq. I of Fisher 1918 and p. 72 of Lynch and Walsh 1998) and is the linear description of development, namely of how genotypes are transformed into phenotypes. In matrix notation, the vector of an individual's trait values is $\mathbf{x} = \bar{\mathbf{x}} + \boldsymbol{\alpha}(\mathbf{y} - \bar{\mathbf{y}}) + \mathbf{e}$, where the matrix $\boldsymbol{\alpha}$ corresponds to what Wagner (1984) calls the developmental matrix (his $\mathbf{B}$). The breeding value of the multivariate phenotype $\mathbf{x}$ is defined as $\mathbf{a_x} \equiv \bar{\mathbf{x}} + \boldsymbol{\alpha}(\mathbf{y} - \bar{\mathbf{y}})$, which does not consider the error term that includes non-linear effects of genes on phenotype. Breeding value thus depends on development via the developmental matrix $\boldsymbol{\alpha}$. The Lande (1979) equation describes the evolutionary change due to selection in the mean multivariate phenotype $\bar{\mathbf{x}}$ as $\Delta\bar{\mathbf{x}} = \mathbf{G}\partial \ln \bar{W}/\partial\bar{\mathbf{x}}$, where the additive genetic covariance matrix is $\mathbf{G} \equiv \mathrm{cov}[\mathbf{a_x}, \mathbf{a_x}] = \boldsymbol{\alpha}\mathrm{cov}[\mathbf{y}, \mathbf{y}]\boldsymbol{\alpha}^{\mathsf{T}}$ (e.g., Wagner 1984), absolute fitness is W, and the selection gradient is $\partial \ln \bar{W}/\partial\bar{\mathbf{x}}$, which points in the direction of steepest increase in mean fitness. An important feature of the Lande equation is that it is in gradient form, so the equation shows that, within the assumptions made, phenotypic evolution by natural selection proceeds as the climbing of a fitness landscape, as first shown by Wright (1937) for frequency change of two alleles in a single locus. Moreover, the Lande equation shows that additive genetic covariation, described by $\mathbf{G}$, may divert evolutionary change from the direction of steepest fitness ascent, and may prevent evolutionary change in some directions if genetic variation in those directions is absent (in which case $\mathbf{G}$ is singular). Since additive genetic covariation depends on development via the developmental matrix $\boldsymbol{\alpha}$, the Lande equation shows that development affects evolution by modulating genetic covariation via $\boldsymbol{\alpha}$ (Charlesworth et al., 1982; Cheverud, 1984; Maynard Smith et al., 1985).

However, this mathematical description might have limited further insight into the evolutionary effects of development, particularly because it lacks two key pieces of information. First, the above description yields a limited understanding of the form of the developmental matrix $\boldsymbol{\alpha}$. The definition of $\boldsymbol{\alpha}$ as a matrix of regression coefficients does not make available a developmentally explicit nor evolutionarily dynamic understanding of $\boldsymbol{\alpha}$, which hinders understanding of how development affects evolution. Although the developmental matrix $\boldsymbol{\alpha}$ has been modelled (Pavlicev and Hansen, 2011) or analysed as unknowable (Martin, 2014), there is a lack of a general theory with an explicit description of the developmental process to unveil the general structure of the developmental matrix $\boldsymbol{\alpha}$.

Second, the description in the second paragraph above gives a very short-term account of the evolutionary process. The Lande equation in the second paragraph strictly describes the evolution of mean traits $\bar{\mathbf{x}}$ but not of mean gene content $\bar{\mathbf{y}}$, that is, it does not describe change in allele frequency; yet, since $\boldsymbol{\alpha}$ is a matrix of regression coefficients calculated for the current population, $\boldsymbol{\alpha}$ depends on the current state of the population including allele frequency $\bar{\mathbf{y}}$. Thus, the Lande equation above describes the dynamics of some traits $\bar{\mathbf{x}}$ as an implicit function of traits $\bar{\mathbf{y}}$ whose dynamics are not described. The equation thus contains fewer dynamic equations (as many as there are traits in $\bar{\mathbf{x}}$) than dynamic variables (as many as there are traits $\bar{\mathbf{x}}$ and loci $\bar{\mathbf{y}}$), so it is underdetermined. Consequently, the Lande equation strictly admits an infinite number of evolutionary trajectories for a given initial condition. Technically, the evolutionary trajectory is ill-defined by the Lande's system (we note that this harsh-sounding term does not mean that the Lande equation is wrong; a common term in this context is "dynamically insufficient" but ill-definition is an older and widespread mathematical notion). The standard approach to this ill-definition is to assume Fisher's infinitesimal model, whereby there is an infinite number of loci such that allele frequency change per locus per generation is negligible (Bulmer, 1971, 1980; Turelli and Barton, 1994; Barton et al., 2017; Hill, 2017). Thus, the Lande equation is said to describe short-term evolution, during which there is negligible allele frequency change per locus (Walsh and Lynch, 2018, pp. 504 and 879). The Lande equation is then supplemented by the Bulmer (1980) equation (Lande and Arnold, 1983, Eq. 12) which describes the dynamics of $\mathbf{G}$ primarily due to change in linkage disequilibrium under the assumption of negligible allele frequency change, thus still to describe short-term evolution (Walsh and Lynch, 2018, p. 553). Typically, the $\mathbf{G}$ matrix is assumed to have reached an equilibrium in such short-term dynamics or to remain constant although this has often been shown not to hold theoretically (Turelli, 1988) and empirically (Björklund et al., 2013). An alternative to the ill-definition of the evolutionary trajectory described by the classic Lande's system would be to consider the vector of gene content $\mathbf{y}$ to be a subvector of the vector of trait values $\mathbf{x}$ (Barfield et al., 2011), although such vector $\mathbf{x}$ does not admit the normality assumption of the Lande equation and doing so does not yield a description of linkage disequilibrium dynamics. Indeed, there appears to be no formal derivation of such extended Lande's system that makes explicit the properties of its associated $\mathbf{G}$-matrix and the dependence of such matrix on development. Overall, understanding how development affects evolution using the classic Lande equation might have been hindered by a lack of a general mechanistic understanding of the developmental matrix $\boldsymbol{\alpha}$ and by the generally ill-defined evolutionary trajectory entailed by the classic Lande's system.

Nevertheless, there has been progress on general mathematical aspects of how development affects evolution on various fronts. Both the classic Lande equation (Lande, 1979) and the classic canonical equation of adaptive dynamics (Dieckmann and Law, 1996) describe the evolutionary dynamics of a multivariate trait in gradient form without an explicit account of development, by considering no explicit age progression or developmental (i.e., dynamic) constraints (there is also an analogous equation for allele frequency change for multiple alleles in a single locus, first incorrectly presented by Wright, 1937 but later corrected by Edwards, 2000 and presented in Lande's form by Walsh and Lynch, 2018, Eq. 5.12a). Various research lines have extended these equations to incorporate different aspects of development. First, one line considers explicit age

progression by implementing age structure, which allows individuals of different ages to coexist and to have age-specific survival and fertility rates. Thus, evolutionary dynamic equations in gradient form for age-structured populations have been derived under quantitative genetics assumptions (Lande, 1982), population genetics assumptions (Charlesworth, 1993, 1994), and adaptive dynamics assumptions (Durinx et al., 2008). An important feature of age-structured models is that the forces of selection decline with age due to demography, in particular due to mortality and fewer remaining reproductive events as age advances (Medawar, 1952; Hamilton, 1966; Caswell, 1978; Caswell and Shyu, 2017). Such age-specific decline in the force of selection does not occur in unstructured models.

Second, another research line in life-history theory has extended age-structured models to consider explicit developmental constraints (Gadgil and Bossert, 1970; Taylor et al., 1974; León, 1976; Schaffer, 1983; Houston et al., 1988; Roff, 1992; Houston and McNamara, 1999; Sydsæter et al., 2008). This line has considered developmentally dynamic models with two types of age-specific traits: genetic traits called control variables, which are under direct genetic control, and developed traits called state variables, which are constructed over life according to developmental constraints, although such literature calls these constraints dynamic. This explicit consideration of developmental constraints in an evolutionary context has mostly assumed that the population is at an evolutionary equilibrium. Thus, this approach identifies evolutionarily stable (or uninvadable) controls and associated states using techniques from dynamic optimization such as optimal control and dynamic programming (Gadgil and Bossert, 1970; Taylor et al., 1974; León, 1976; Schaffer, 1983; Houston et al., 1988; Roff, 1992; Houston and McNamara, 1999). While the assumption of evolutionary equilibrium yields great insight, it does not address the evolutionary dynamics which would provide a richer understanding. Moreover, the relationship of developmental constraints and genetic covariation is not made evident by this approach.

Third, another research line in adaptive dynamics has made it possible to mathematically model the evolutionary developmental (evo-devo) dynamics. By evo-devo dynamics we mean the evolutionary dynamics of genetic traits that modulate the developmental dynamics of developed traits that are constructed over life subject to developmental constraints. A first step in this research line has been to consider function-valued or infinite-dimensional traits, which are genetic traits indexed by a continuous variable (e.g., age) rather than a discrete variable as in the classic Lande equation. Thus, the evolutionary dynamics of univariate function-valued traits (e.g., the gene expression level of a single gene across continuous age) has been described in gradient form by the Lande equation for function-valued traits (Kirkpatrick and Heckman, 1989) and the canonical equation for function-valued traits (Dieckmann et al., 2006). Although function-valued traits may depend on age, they are not subject to developmental constraints describing their developmental dynamics, so the consideration of the evolutionary dynamics of function-valued traits alone does not model the evo-devo dynamics. To our knowledge, Parvinen et al. (2013) were the first to mathematically model what we here call the evo-devo dynamics (but note that there have also been models integrating mathematical modeling of the developmental dynamics and individual-based modeling of the evolutionary dynamics, namely, Salazar-Ciudad and Marín-Riera, 2013). Parvinen et al. (2013) did so by considering the evolutionary dynamics of a univariate function-valued trait (control variable) that modulates the developmental construction of a multivariate developed trait (state variables) subject to explicit developmental constraints (they refer to these as process-mediated models). This approach requires the derivation of the selection gradient of the control variable affecting the state variables, which, as age is measured in continuous time, involves calculating a functional derivative (of invasion fitness; Dieckmann et al., 2006; Parvinen et al., 2013, Eq. 4). Parvinen et al. (2013) noted the lack of a general simplified method to calculate such selection gradient, but they calculated it for specific examples. Metz et al. (2016) illustrate how to calculate such selection gradient using a fitness return argument in a specific example. Using functional derivatives, Avila et al. (2021) derive the selection gradient of a univariate function-valued trait modulating the developmental construction of a univariate developed trait for a broad class of models (where relatives interact and the genetic trait may depend on the developed trait). They obtain a formula for the selection gradient that depends on unknown associated variables (costate variables or shadow values) (Avila et al., 2021, Eqs. 7 and 23), but at evolutionary equilibrium these associated variables can be calculated solving an associated differential equation (their Eq. 32). Despite these advances, the analysis of these models poses substantial technical challenges, by requiring calculation of functional derivatives or differential equations in addition to those describing the developmental dynamics at evolutionary equilibrium. These models have yielded evolutionary dynamic equations in gradient form for genetic traits, but not for developed traits, so they have left unanswered the question of how the evolution of developed traits with explicit developmental constraints proceeds in the fitness landscape. Additionally, these models have not provided a link between developmental constraints and genetic covariation (see Metz 2011; Dieckmann et al. 2006 discuss a link between constraints and genetic covariation in controls, not states).

Fourth, a separate research line in quantitative genetics has considered models without age structure where a set of traits are functions of underlying traits such as gene expression or environmental variables (Wagner, 1984, 1989; Hansen and Wagner, 2001; Rice, 2002; Martin, 2014; Morrissey, 2014, 2015). This dependence of traits on other traits is used by this research line to describe development and the genotype-phenotype map. However, this research line considers no explicit age progression, so it considers implicit rather than explicit developmental (i.e., dynamic) constraints. Thus, this line has not considered the effect of age structure nor explicit developmental constraints (Wagner, 1984, 1989; Hansen and Wagner, 2001; Rice, 2002; Martin, 2014; Morrissey, 2014, 2015). Also, this line has not provided a general and evolutionarily dynamic structure of the developmental matrix, and evolutionary dynamic equations in gradient form yielding a well-defined evolutionary trajectory of

developed traits.

Here we formulate a tractable mathematical framework that integrates age progression (i.e, age structure), explicit developmental constraints, and evolutionary dynamics. The framework describes the evolutionary dynamics of genetic traits and the developmental dynamics of developed traits subject to developmental constraints. It yields expressions describing the evolutionary dynamics in gradient form including for developed traits, so it shows how the climbing of an adaptive topography proceeds for developed traits in a broad class of models. It also describes the structure of the developmental matrix $\boldsymbol{\alpha}$ from mechanistic principles thus relating development to genetic covariation for a broad class of models. The resulting equations yield a well-defined evolutionary trajectory in the sense that the evolutionary dynamics of all variables are described, including the evolutionary dynamics of genetic covariation modulated by development.

We base our framework on adaptive dynamics assumptions (Dieckmann and Law, 1996; Metz et al., 1996; Champagnat, 2006; Durinx et al., 2008). We obtain equations describing the evolutionary dynamics in gradient form of traits $\mathbf{x}$ that arise from a developmental process with explicit developmental constraints occurring as age progresses. Developmental constraints allow the phenotype to be "predisposed" to develop in certain ways, thus allowing for developmental bias. We allow development to depend on the (abiotic) environment, which allows for a mechanistic description of plasticity. We also allow development to depend on the social environment, which allows for a mechanistic description of extra-genetic inheritance and indirect genetic effects (Moore et al., 1997). In turn, we allow the environment faced by each individual to depend on the traits of the individual and of social partners, thus allowing for individual and social niche construction although we do not consider ecological inheritance. We also let the environment depend on processes that are exogenous to the evolving population, such as eutrophication or climate change caused by members of other species, thus allowing for exogenous environmental change. To facilitate analysis, we let population dynamics occur over a short time scale, whereas environmental and evolutionary dynamics occur over a long time scale. Crucially, we measure age in discrete time, which simplifies the mathematics yielding closed-form formulas for otherwise implicitly defined quantities. Our methods use concepts from optimal control (Sydsæter et al., 2008) and integrate tools from adaptive dynamics (Dieckmann and Law, 1996) and matrix population models (Caswell, 2001; Otto and Day, 2007). While we use concepts from optimal control, we do not use optimal control itself and instead derive an alternative method to optimal control that can be used to obtain optimal controls in a broad class of evolutionary models with dynamic constraints. Our approach differs somewhat from standard matrix population models, where the stage (e.g., age and size) of an individual is discrete and described as indices of the population density vector (Caswell, 2001; Caswell et al., 1997; de Vries and Caswell, 2018; Caswell, 2019, Ch. 6); instead, we let the stage of an individual be partly discrete (specifically, age), described as indices in the population density vector, and partly continuous (e.g., size), described as arguments of various functions.

We obtain three sets of main results. First, we derive a multivariate discrete function-valued canonical equation describing the evolutionary dynamics of resident genetic traits $\bar{\mathbf{y}}$ (controls) that modulate the construction of resident developed traits $\bar{\mathbf{x}}$ (states). Such canonical equation depends on the "total selection gradient of controls", for which we derive several formulas that can be easily computed directly with elementary operations. This provides simple expressions to model the evo-devo dynamics in a broad class of models. In particular, these expressions provide an alternative method to dynamic optimization (e.g., dynamic programming or optimal control) to calculate evolutionary equilibria for models with developmentally dynamic traits, both analytically for sufficiently simple models and numerically for more complex ones. Second, we derive equations in gradient form describing the evolutionary dynamics of developed traits $\bar{\mathbf{x}}$ and of the niche-constructed environment. These equations motivate a definition of breeding value and additive genetic covariance matrices under adaptive dynamics assumptions, even though these terms have so far only been defined under quantitative genetics assumptions. These equations also yield formulas for the developmental matrix $\boldsymbol{\alpha}$ for a broad class of models. Analogously to the classic Lande equation, the equation describing the evolutionary dynamics of the developed traits $\bar{\mathbf{x}}$ depends on the genetic traits $\bar{\mathbf{y}}$ and so it yields an ill-defined evolutionary trajectory if the evolutionary dynamics of the genetic traits is not considered. Third, we obtain synthetic equations in gradient form simultaneously describing the evolutionary dynamics of genetic, developed, and environmental traits. These equations provide a well-defined evolutionary trajectory described by an equation in Lande's form, where there are as many evolutionary dynamic equations as evolutionary dynamic variables, which enables one to describe the long-term evolution of developed multivariate phenotypes. Such equations describe the evolutionary dynamics of $\mathbf{G}$ as an emergent property, where genetic traits $\bar{\mathbf{y}}$ play an analogous role to that of allele frequency under quantitative genetics assumptions while linkage disequilibrium is not an issue as we assume clonal reproduction. In this extended Lande's system yielding a well-defined evolutionary trajectory, the associated $\mathbf{G}$-matrix is always singular, which is mathematically trivial, but biologically crucial as it entails that the evolutionary dynamics are strongly non-standard where development plays a major evolutionary role.

While we use terms that have been originally defined under quantitative genetics assumptions, we note that the terms are somewhat different under adaptive dynamics assumptions. In quantitative genetics, a multivariate phenotype and its breeding value are assumed to be normally distributed with arbitrarily large variance. In adaptive dynamics, a monomorphic resident population is subject to invasion (i.e., increase in frequency) of rare mutants that have marginally different trait values from those of the resident. Under adaptive dynamics assumptions, where $\mathbf{y}$ is the vector of genetic trait values of a mutant, the evolutionary dynamics of the resident genetic traits $\bar{\mathbf{y}}$ are given by the canonical equation of adaptive dynamics, namely $\Delta\bar{\mathbf{y}} \approx \kappa \mathrm{cov}[\mathbf{y}, \mathbf{y}] \mathrm{d}\lambda/\mathrm{d}\mathbf{y}|_{\mathbf{y}=\bar{\mathbf{y}}}$ (Dieckmann and Law 1996

and as shown below), where λ is invasion fitness defined as the growth rate of the rare mutant subpopulation. The quantity $\mathrm{d}\lambda/\mathrm{d}\mathbf{y}|_{\mathbf{y}=\bar{\mathbf{y}}}$ is traditionally called the selection gradient although it differs from the notion of selection gradient under quantitative genetics assumptions: for instance, the derivative is taken with respect to individual trait values rather than mean trait values and is evaluated at mean trait values, so the notion of an adaptive topography under adaptive dynamics assumptions is different from that under standard quantitative genetics assumptions (the two notions are much more similar but still not identical assuming marginal variation under quantitative genetics; Iwasa and Pomiankowski, 1991). Analogously, the notions of breeding value and additive genetic variance we obtain here under adaptive dynamics assumptions have differences with the notions under quantitative genetics assumptions. In particular, all variation in genetic traits $\mathbf{y}$ under our adaptive dynamics assumptions is due to mutation in the current evolutionary time step, so we refer to it as mutational variation, whereas variation in gene content $\mathbf{y}$ under quantitative genetics assumptions may stem from any source, so is referred to as standing variation in gene content. Despite this, we define breeding value as the first-order estimate of the developed phenotype from genetic traits, which is the direct analogue of the definition of breeding value under quantitative genetics assumptions. Thus, we use the term breeding value and associated additive genetic covariances to highlight the deep correspondence with the notions in quantitative genetics.

2. Problem statement

We begin by outlining the problem we are interested in before describing the model. We describe each individual by a collection of genetic traits, developed traits, and environmental traits. We envisage each genetic trait as being the expression level of a gene product (Fig. 1). Each gene product may be encoded by one or more loci and has an age-specific expression level. Individuals may be haploid or diploid but reproduction is clonal. We assume that the gene expression level for a given gene product across all ages is entirely specified by the genetic sequence encoding the gene product: we call this "open-loop" gene expression, borrowing terminology from optimal control theory (Sydsæter et al., 2008): this entails that gene expression of a gene product does not depend on the expression of other gene products. In turn, we refer to the developed traits of an individual as her phenotype, which are traits that are indirectly genetically controlled and constructed over her life subject to developmental constraints (note that we restrict the term phenotype to developed traits, such that genetic traits are not part of the phenotype; we do this in an attempt to better capture the vernacular meaning of phenotype). Additionally, environmental traits describe each individual's local environment at each age (e.g., ambient temperature, which the individual may adjust behaviorally such as by roosting in the shade). We assume that the environment faced by an individual at a given age is described by a set of mutually independent variables, which facilitates derivations. We let the phenotype depend on the environment so there can be plasticity, and we let the environment depend on the phenotype and gene expression so there can be niche construction. We will obtain evolutionary dynamic equations in gradient from yielding well-defined evolutionary trajectories by aggregating the various types of traits. We give names to such aggregates for ease of reference. We call the aggregate of gene expression and phenotype the geno-phenotype. We call the aggregate of gene expression, phenotype, and the environment the geno-envo-phenotype.

We use the following notation (Table 1). Each individual can live from age 1 up to a maximum age N_a (this is without loss of generality as N_a can be arbitrarily large). Each individual has a number N_c of genetic traits or control variables, that is, of possible gene products at each age. A mutant individual has a gene expression level y_{ia} for gene product or control variable $i \in \{1,\dots,N_\mathrm{c}\}$ at age $a \in \{1,\dots,N_\mathrm{a}\}$. A mutation may alter gene expression level or may create a new gene product; a mutation altering gene expression alters the value of y_{ia} from a non-baseline (e.g., non-zero) value to another value, whereas a mutation creating a new gene product alters the value of y_{ia} for some i from a baseline (e.g., zero) value to another value. As we assume that gene expression is open-loop, the gene expression level y_{ia} for all $i \in \{1,\dots,N_\mathrm{c}\}$ and all $a \in \{1,\dots,N_\mathrm{a}\}$ is exclusively controlled by the genetic sequence encoding the gene product, and is independent of the gene expression of other gene products, of the phenotype, and of the environment. Additionally, each individual has a number N_s of developed traits or state variables, that is, of phenotypes at each age. A mutant individual has a developed trait value x_{ia} describing her phenotype or state variable $i \in \{1,\dots,N_\mathrm{s}\}$ at age $a \in \{1,\dots,N_\mathrm{a}\}$. Moreover, each individual has a number N_e of environmental variables that describe her environment at each age. A mutant individual faces an environment ϵ_{ia} describing her environmental variable $i \in \{1,\dots,N_\mathrm{e}\}$ at age $a \in \{1,\dots,N_\mathrm{a}\}$.

We use the following notation for collections of these quantities. The gene expression level of the i-th gene product of the mutant across all ages is denoted by the column vector $\mathbf{y}_i = (y_{i1};\dots;y_{iN_\mathrm{a}}) \in \mathbb{R}^{N_\mathrm{a}\times 1}$, where the semicolon indicates a line break, that is, $\mathbf{y}_i = (y_{i1},\dots,y_{iN_\mathrm{a}})^\intercal$. The value of the i-th phenotype of the mutant across all ages is denoted by the column vector $\mathbf{x}_i = (x_{i1};\dots;x_{iN_\mathrm{a}}) \in \mathbb{R}^{N_\mathrm{a}\times 1}$. The value of the i-th environmental variable of the mutant across all ages is denoted by the column vector $\boldsymbol{\epsilon}_i = (\epsilon_{i1};\dots;\epsilon_{iN_\mathrm{a}}) \in \mathbb{R}^{N_\mathrm{a}\times 1}$. The gene expression of the mutant for all gene products across all ages is denoted by the block column vector $\mathbf{y} = (\mathbf{y}_1;\dots;\mathbf{y}_{N_\mathrm{c}}) \in \mathbb{R}^{N_\mathrm{a}N_\mathrm{c}\times 1}$. The multivariate phenotype of the mutant for all developed traits across all ages is denoted by the block column vector $\mathbf{x} = (\mathbf{x}_1;\dots;\mathbf{x}_{N_\mathrm{s}}) \in \mathbb{R}^{N_\mathrm{a}N_\mathrm{s}\times 1}$. The environment faced by the mutant for all environmental variables across all ages is denoted by the block column vector $\boldsymbol{\epsilon} = (\boldsymbol{\epsilon}_1;\dots;\boldsymbol{\epsilon}_{N_\mathrm{s}}) \in \mathbb{R}^{N_\mathrm{a}N_\mathrm{e}\times 1}$. To simultaneously refer to gene expression and phenotype, we denote the geno-phenotype of the mutant individual at age a as $\mathbf{z}_a = (\mathbf{x}_a;\mathbf{y}_a) \in \mathbb{R}^{(N_\mathrm{s}+N_\mathrm{c})\times 1}$, and the geno-phenotype of the mutant across all ages as $\mathbf{z} = (\mathbf{x};\mathbf{y}) \in \mathbb{R}^{N_\mathrm{a}(N_\mathrm{s}+N_\mathrm{c})\times 1}$. Moreover, to simultaneously refer to gene expression, phenotype, and environment, we denote the geno-envo-phenotype of the mutant individual at age a as $\mathbf{m}_a = (\mathbf{z}_a;\boldsymbol{\epsilon}_a) \in \mathbb{R}^{(N_\mathrm{s}+N_\mathrm{c}+N_\mathrm{e})\times 1}$, and the geno-envo-phenotype of the mutant across all ages as

	Gene product 1	Gene product 2
Genetic sequence	... GTAC... or ... GTGC...	... ACGT... or ... ACAT...
Gene product	... Val - Glu - Leu ...	... Thr - Pro - Cys ...
Gene expression level	y_{1a}	y_{2a}

Figure 1: Genetic framing. Depicted are illustrative genetic sequences, gene products, and gene expression levels for two possible gene products. A mutation causes a change in the genetic sequence, which may leave the gene product unchanged while changing its gene expression level, or may change the gene product. If the gene expression level y_{1a} across all ages is fully specified by the genetic sequence encoding the gene product, we say that such gene's expression is "open-loop". If the gene expression y_{1a} depends not only on the genetic sequence of the gene product but also on the expression level of other gene products, and on the individual's phenotype or environment, we say that such gene's expression is closed-loop. As a first approximation, we assume that gene expression is open-loop for all gene products. Even with open-loop gene expression, mutation may tend to simultaneously change the genetic sequences of two gene products, in which case we say that there is mutational covariation between genes. Note that gene product 1 is not equivalent to locus 1: gene product 1 may be produced at several loci and a mutation at locus 1 may change its gene product from 1 to 2.

$\mathbf{m} = (\mathbf{z}; \boldsymbol{\epsilon}) \in \mathbb{R}^{N_\mathrm{a}(N_\mathrm{s}+N_\mathrm{c}+N_\mathrm{e})\times 1}$. We denote resident values analogously with an overbar (e.g., $\bar{\mathbf{z}}$ is the resident geno-phenotype).

The developmental process that constructs the phenotype is as follows (with causal dependencies described in Fig. 2). We assume that an individual's multivariate phenotype at a given age is a function of the gene expression, phenotype, and abiotic and social environment that the individual had at the immediately previous age. Thus, we assume that a mutant's multivariate phenotype at age $a+1$ is given by the developmental constraint

$$\mathbf{x}_{a+1} = \mathbf{g}_a(\mathbf{m}_a, \bar{\mathbf{z}}) \tag{1}$$

for all $a \in \{1, \ldots, N_\mathrm{a} - 1\}$ with initial condition $\mathbf{x}_1 = \bar{\mathbf{x}}_1$ (provided that $N_\mathrm{a} > 1$). The function

$$\mathbf{g}_a(\mathbf{m}_a, \bar{\mathbf{z}}) = (g_{1a}(\mathbf{m}_a, \bar{\mathbf{z}}); \ldots; g_{N_\mathrm{s}a}(\mathbf{m}_a, \bar{\mathbf{z}}))$$

is the developmental map at age a, which we assume is a differentiable function of the individual's geno-envo-phenotype at that age and of the geno-phenotype of the individual's social partners who can be of any age; thus, an individual's development directly depends on the individual's local environment but not directly on the local environment of social partners. The developmental map may be arbitrarily non-linear within those assumptions. The term developmental function can be traced back to Gimelfarb (1982) through Wagner (1984). Developmental constraints such as (1) are standard in life history models, which call such constraints dynamic stemming from the terminology of optimal control theory (Gadgil and Bossert, 1970; Taylor et al., 1974; León, 1976; Schaffer, 1983; Sydsæter et al., 2008). Developmental constraints such as (1) are also standard in physiologically structured models of population dynamics (de Roos, 1997, Eq. 7). For simplicity, we assume that the phenotype $\mathbf{x}_1 = \bar{\mathbf{x}}_1$ at the initial age is constant and does not evolve. This assumption corresponds to the common assumption in life-history models that state variables at the initial age are given (Gadgil and Bossert, 1970; Taylor et al., 1974; León, 1976; Schaffer, 1983; Sydsæter et al., 2008).

Table 1: **Notation summary**

Symbol	Meaning
$\mathbf{x}$	Phenotype (states)
$\mathbf{y}$	Gene expression (controls)
$\mathbf{z}$	Geno-phenotype (states and controls)
$\boldsymbol{\epsilon}$	Environment
$\mathbf{m}$	Geno-envo-phenotype (states, controls, and environment)
N_a	Number of ages
N_s	Number of phenotypes
N_c	Number of possible gene products
N_e	Number of environmental variables
$\mathbf{g}$	Developmental map
$\mathbf{h}$	Environmental map
$\mathbf{n}$	Population density
f	Fertility
p	Survival probability
ℓ	Survivorship
w	Fitness
λ	Invasion fitness
$\mathbf{u}$	Stable age distribution
$\mathbf{v}$	Reproductive value
ϕ	Force of selection on fertility
π	Force of selection on survival
t	Ecological time
τ	Evolutionary time
θ	Socio-devo stabilization time
T	Generation time
$\check{\mathbf{x}}$	Resident phenotype in the context of mutant
$\hat{\mathbf{z}}$	Undeveloped geno-phenotype
$\boldsymbol{\zeta}, \boldsymbol{\xi}$	Arbitrary vectors
$\mathbf{a}_\zeta$	Breeding value of $\boldsymbol{\zeta}$
$\mathbf{b}_\zeta$	Stabilized breeding value of $\boldsymbol{\zeta}$
$\mathbf{G}_\zeta$	Additive genetic covariance matrix of $\boldsymbol{\zeta}$
$\mathbf{H}_\zeta$	Additive socio-genetic cross-covariance matrix of $\boldsymbol{\zeta}$
$\frac{\partial \boldsymbol{\zeta}^\mathsf{T}}{\partial \boldsymbol{\xi}}$	Direct effects of $\boldsymbol{\xi}$ on $\boldsymbol{\zeta}$
$\frac{\delta \boldsymbol{\zeta}^\mathsf{T}}{\delta \boldsymbol{\xi}}$	Semi-total effects of $\boldsymbol{\xi}$ on $\boldsymbol{\zeta}$
$\frac{\mathrm{d}\boldsymbol{\zeta}^\mathsf{T}}{\mathrm{d}\boldsymbol{\xi}}$	Total effects of $\boldsymbol{\xi}$ on $\boldsymbol{\zeta}$
$\frac{\mathrm{s}\boldsymbol{\zeta}^\mathsf{T}}{\mathrm{s}\boldsymbol{\xi}}$	Stabilized effects of $\boldsymbol{\xi}$ on $\boldsymbol{\zeta}$

We describe the environment as follows. We assume that an individual's environment at a given age is a function of the gene expression, phenotype, and social environment of the individual at that age, but also of processes that are not caused by the population considered. Thus, we assume that a mutant's environment at age a is given by the environmental constraint

$$\boldsymbol{\epsilon}_a = \mathbf{h}_a(\mathbf{z}_a, \bar{\mathbf{z}}, \tau) \tag{2}$$

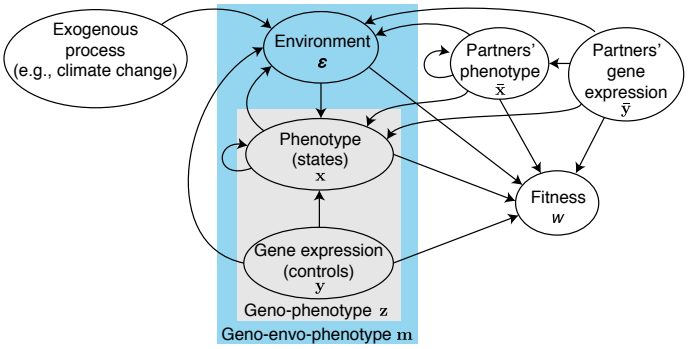

Figure 2: Causal diagram among the framework's components. Variables have age-specific values which are not shown for clarity. The phenotype $\mathbf{x}$ is constructed by a developmental process. Each arrow indicates the direct effect of a variable on another one. A mutant's gene expression may directly affect the phenotype (with the slope quantifying developmental bias from gene expression), environment (niche construction by gene expression), and fitness (direct selection on gene expression). A mutant's phenotype at a given age may directly affect her phenotype at an immediately subsequent age (quantifying developmental bias from the phenotype), thus the direct feedback loop from phenotype to itself. A mutant's phenotype may also directly affect her environment (niche construction by the phenotype) and fitness (direct selection on the phenotype). A mutant's environment may directly affect the phenotype (plasticity) and fitness (environmental sensitivity of selection). Partners' gene expression may directly affect their own phenotype (quantifying developmental bias from gene expression), the mutant's phenotype (indirect genetic effects from gene expression), and the mutant's fitness (social selection on gene expression). Partners' phenotype at a given age may directly affect their own phenotype at an immediately subsequent age (quantifying developmental bias from the phenotype), thus the direct feedback loop. Partners' phenotype at a given age may also directly affect the mutant's phenotype (quantifying indirect genetic effects from the phenotype), the mutant's environment (social niche construction), and the mutant's fitness (social selection on the phenotype). The environment may also be directly influenced by exogenous processes. For simplicity, we assume that controls are open-loop, which means that there is no arrow towards gene expression.

for all $a \in \{1, \ldots, N_{\mathrm{a}}\}$. The function

$$\mathbf{h}_a(\mathbf{z}_a, \bar{\mathbf{z}}, \tau) = (h_{1a}(\mathbf{z}_a, \bar{\mathbf{z}}, \tau); \ldots; h_{N_{\mathrm{e}}a}(\mathbf{z}_a, \bar{\mathbf{z}}, \tau))$$

is the environmental map at age a, which we assume is a differentiable function of the individual's geno-phenotype at that age (e.g., the individual's behavior at a given age may expose it to a particular environment at that age), the geno-phenotype of the individual's social partners who can be of any age (e.g., through social niche construction), and evolutionary time τ due to slow exogenous environmental change. We assume slow exogenous environmental change to enable the resident population to reach carrying capacity to be able to use relatively simple techniques of evolutionary invasion analysis to derive selection gradients. The environmental constraint (2) is a minimalist description of the environment of a specific kind (akin to "feedback functions" used in physiologically structured models to describe the influence of individuals on the environment; de Roos, 1997). A different, perhaps more realistic environmental constraint would be constructive of the form $\boldsymbol{\epsilon}_{a+1} = \mathbf{h}_a(\mathbf{m}_a, \bar{\mathbf{z}}, \tau)$, in which case the only structural difference between an environmental variable and a state variable would be the dependence of the environmental variable on exogenous processes (akin to "feedback loops" used in physiologically structured models to describe the influence of individuals on the environment; de Roos, 1997). We use the minimalist environmental constraint (2) as a first approximation to shorten derivations; our derivations illustrate how to obtain equations with a constructive environmental constraint. With the minimalist environmental constraint in Eq. (2), the environmental variables are mutually independent in that changing one environmental variable at one age does not *directly* change any other environmental variable at any age (i.e., $\partial\epsilon_{kj}/\partial\epsilon_{ia} = 0$ if $i \neq k$ or $a \neq j$). We say that development is social if $\mathrm{d}\mathbf{x}^{\intercal}/\mathrm{d}\bar{\mathbf{z}}|_{\mathbf{y}=\bar{\mathbf{y}}} \neq \mathbf{0}$.

Our aim is to obtain equations describing the evolutionary dynamics of the resident phenotype $\bar{\mathbf{x}}$ subject to the developmental constraint (1) and the environmental constraint (2). The evolutionary dynamics of the phenotype $\bar{\mathbf{x}}$ emerge as an outgrowth of the evolutionary dynamics of gene expression $\bar{\mathbf{y}}$ and of the environment $\bar{\boldsymbol{\epsilon}}$. Indeed, in Appendix A, we provide a short derivation of the canonical equation of adaptive dynamics closely following Dieckmann and Law (1996) although assuming deterministic population dynamics. This equation describes the evolutionary dynamics of resident gene expression as:

$$\frac{\Delta\bar{\mathbf{y}}}{\Delta\tau} \approx \kappa \mathrm{cov}[\mathbf{y}, \mathbf{y}] \left.\frac{\mathrm{d}\lambda}{\mathrm{d}\mathbf{y}}\right|_{\mathbf{y}=\bar{\mathbf{y}}}, \tag{3}$$

where $\lambda = \lambda(\mathbf{m}, \bar{\mathbf{m}})$ is invasion fitness, κ is a non-negative scalar proportional to the mutation rate and the carrying capacity, and $\mathrm{cov}[\mathbf{y}, \mathbf{y}]$ is the mutational covariance matrix (of gene expression). The selection gradient in Eq. (3) involves total derivatives so we call it the *total* selection gradient of gene expression, which measures the effects of gene expression $\mathbf{y}$ on invasion fitness λ across all the paths in Fig. 2. More generally, a total selection gradient is defined in terms of total derivatives and thus measures the total effects of traits on invasion fitness across all the causal paths linking the traits to invasion fitness (Fig. 2) (this corresponds to the notion of "total derivative of fitness" of Caswell 1982, 2001 denoted by him as $\mathrm{d}\lambda$, "total differential" of Charlesworth 1994 denoted by him as $\mathrm{d}r$, "integrated sensitivity" of van Tienderen 1995 denoted by him as IS, and of "extended selection gradient" of Morrissey 2014, 2015 denoted by him as $\boldsymbol{\eta}$). In contrast, Lande's selection gradient is defined in terms of partial derivatives and so measures only the direct effects of traits on fitness (Fig. 2).

The arrangement above describes the evolutionary developmental (evo-devo) dynamics: the evolutionary dynamics of resident gene expression are given by the canonical equation (3), while the concomitant developmental dynamics of the phenotype are given by the developmental (1) and environmental (2) constraints evaluated at resident trait values. To complete the description of the evo-devo dynamics, we obtain simple expressions for the total selection gradient of gene expression. Subsequently, to determine whether the evolution of the resident developed phenotype $\bar{\mathbf{x}}$ can be described as the climbing of a fitness landscape, we additionally derive equations in gradient form describing the evolutionary dynamics of the resident phenotype $\bar{\mathbf{x}}$, environment $\bar{\boldsymbol{\epsilon}}$, geno-phenotype $\bar{\mathbf{z}}$, and geno-envo-phenotype $\bar{\mathbf{m}}$.

Our approach most immediately relates to previous work as follows. Because of the multivariate age structure of $\mathbf{y}$,

Eq. (3) constitutes a canonical equation for multivariate discrete function-valued traits. Dieckmann et al. (2006) derive the canonical equation for univariate continuous function-valued traits. Both Eq. (3) and the canonical equation of Dieckmann et al. (2006) are dynamic equations in gradient form for control variables $\bar{\mathbf{y}}$, but not for state variables $\bar{\mathbf{x}}$, thus leaving unanswered whether and to what extent the evolution of developed traits can be described as the climbing of a fitness landscape. Dieckmann et al. (2006, p. 378) note that the mutational covariance matrix in their canonical equation is singular if and only if the function-valued trait has equality constraints. As their canonical equation describes the evolutionary dynamics in gradient form for control variables, Dieckmann et al.'s (2006) point is that the mutational covariance matrix $\mathrm{cov}[\mathbf{y}, \mathbf{y}]$ is singular if and only if $\mathbf{y}$ has equality constraints. Developmental constraints (1) are equality constraints on state variables $\mathbf{x}$, so Dieckmann et al.'s (2006) point suggests that an analogous singularity would appear in the covariance matrices involved in a canonical equation describing the evolutionary dynamics of state variables in gradient form, although such canonical equation has not been derived (and we will show it to have a different form to that of Eq. 3). Parvinen et al. (2013) and Metz et al. (2016) derive the total selection gradient $\mathrm{d}\lambda/\mathrm{d}\mathbf{y}|_{\mathbf{y}=\bar{\mathbf{y}}}$ for specific models for a univariate continuous function-valued control where λ depends on a multivariate continuous state variable subject to developmental constraints analogous to those in Eq. (1) in continuous age (Parvinen et al's Eq. 2a). Avila et al. (2021) derive $\mathrm{d}\lambda/\mathrm{d}\mathbf{y}|_{\mathbf{y}=\bar{\mathbf{y}}}$ for a broad class of models for a univariate continuous function-valued control where λ depends on a univariate continuous state variable in a group-structured population (their Eqs. 7,23,24); the resulting equation depends on an unknown univariate costate variable, which at evolutionary equilibrium can be calculated by solving an associated differential equation (their Eq. 32). Yet, calculating the selection gradient $\mathrm{d}\lambda/\mathrm{d}\mathbf{y}|_{\mathbf{y}=\bar{\mathbf{y}}}$ when invasion fitness depends on state variables in continuous age remains challenging as functional derivatives, integrals, and associated differential equations must be computed. We circumvent these difficulties by using discrete age, so calculations reduce to basic derivatives and matrix algebra. This enables us to derive simple expressions that can be calculated directly for both the total selection gradient of controls and the evolutionary dynamic equations in gradient form for state variables subject to dynamic constraints.

3. Model

In this section, we describe our methods. A reader interested in first seeing the results may jump straight to section 4.

3.1. Overview

We now provide an overview of our methods. First, we describe the framework's set-up. Second, we explain that social development complicates evolutionary invasion analysis. Third, we derive the mutant invasion dynamics, where we address the complication introduced by social development by adding a phase to the standard separation of time scales in adaptive dynamics. Thus, we divide an evolutionary time step in three phases rather than the usual two of resident population dynamics and mutant invasion dynamics; analogues of such additional phase have been used in modelling the evolution of social learning (Aoki et al., 2012; Kobayashi et al., 2015). Fourth, we obtain a first-order approximation of invasion fitness and use it to derive the canonical equation describing the evolutionary dynamics of gene expression. Fifth, we derive the selection gradient in age structured populations, which we use to calculate the total selection gradient of gene expression. Based on this setting, in Appendices D-L, we derive equations for the total selection gradient of gene expression and for the evolutionary dynamics of the phenotype, environment, geno-phenotype, and geno-envo-phenotype.

3.2. Set up

We base our framework on standard assumptions of adaptive dynamics (Dieckmann and Law, 1996). We consider a large, age-structured, well mixed population of clonally reproducing individuals. The population is finite but, in a departure from Dieckmann and Law (1996), we let the population dynamics be deterministic rather than stochastic for simplicity, so there is no genetic drift. Thus, the only source of stochasticity in our framework is mutation. We separate time scales, so developmental and population dynamics occur over a short discrete ecological timescale t and evolutionary dynamics occur over a long discrete evolutionary timescale τ. Development can be social, which adds a complication to invasion analysis as follows.

3.3. A complication introduced by social development

Social development entails that an individual with resident genotype may develop a non-resident phenotype in the context of the resident phenotype. To see this, consider an individual that has resident gene expression $\bar{\mathbf{y}}$ and that develops in the context of a resident geno-phenotype $\bar{\mathbf{z}} = (\bar{\mathbf{x}}; \bar{\mathbf{y}})$. Using the developmental constraint (1) and writing geno-phenotype in terms of its composing gene expression and phenotype vectors, the phenotype of this individual at age $a + 1$ is given by

$$\bar{\bar{\mathbf{x}}}_{a+1} = \mathbf{g}_a(\bar{\bar{\mathbf{x}}}_a, \bar{\mathbf{y}}_a, \mathbf{h}_a(\bar{\bar{\mathbf{x}}}_a, \bar{\mathbf{y}}_a, \bar{\mathbf{x}}, \bar{\mathbf{y}}, \tau), \bar{\mathbf{x}}, \bar{\mathbf{y}}) \tag{4}$$

for all $a \in \{1, \ldots, N_\mathrm{a} - 1\}$. Such phenotype $\bar{\bar{\mathbf{x}}}$ may be different from the resident phenotype $\bar{\mathbf{x}}$ that is used in the argument of the developmental map in Eq. (4) (an example is given in Section 5.2; see also Kobayashi et al. 2015, Eq. 14 in their Appendix). This possibility introduces a complication since to apply standard invasion analysis, we must have a population with a fixed (expected) resident phenotype. To guarantee this under social development, the resident geno-phenotype must be of a specific kind. Such resident could be achieved by letting the population dynamics of a resident genotype occur until the resident phenotype converges, while convergence of the population dynamics may occur concomitantly or only later. Yet, to simplify the analysis, we separate the dynamics of convergence of the resident phenotype and the dynamics of the resident population. We thus introduce an additional phase to the standard separation of

time scales in adaptive dynamics so that convergence to a single resident geno-envo-phenotype occurs first and then resident population dynamics follow. Such additional phase is a mathematical technique to facilitate analytical treatment and might be justified under somewhat broad conditions. In particular, Aoki et al. (2012, their Appendix A) show that such additional phase is justified in their model of social learning evolution if mutants are rare and social learning dynamics happen faster than allele frequency change; they also show that this additional phase is justified for their particular model if selection is δ-weak. As a first approximation, here we do not formally justify the separation of phenotype convergence and resident population dynamics and simply assume it for simplicity.

3.4. Phases of the evolutionary cycle

3.4.1. Verbal description

To handle the above complication introduced by social development, we partition a unit of evolutionary time in three phases: socio-developmental (socio-devo) stabilization dynamics, resident population dynamics, and resident-mutant population dynamics (Fig. 3).

At the start of the socio-devo stabilization phase of a given evolutionary time τ, the population consists of individuals all having the same resident genotype, phenotype, and environment. A new individual arises which has identical genotype as the resident, but develops a phenotype that may be different from that of the original resident due to social development. This developed phenotype, its genotype, and its environment are set as the new resident. This process is repeated until convergence to what we term a "socio-devo stable" (SDS) resident or until divergence. If development is not social, the resident is trivially SDS so the socio-devo stabilization dynamics phase is unnecessary. If an SDS resident is achieved, the population moves to the next phase; if an SDS resident is not achieved, the analysis stops. We thus study the evolutionary dynamics of SDS geno-envo-phenotypes.

If an SDS resident is achieved, the population moves to the resident population dynamics phase. Because the resident is SDS, an individual with resident gene expression developing in the context of the resident geno-phenotype is guaranteed to develop the resident phenotype (i.e., $\bar{\bar{\mathbf{x}}}_{a+1}$ in Eq. 4 equals $\bar{\mathbf{x}}_{a+1}$ for all $a \in \{1, \ldots, N_\mathrm{a} - 1\}$). Thus, we may proceed with the standard invasion analysis. Hence, in this phase of SDS resident population dynamics, the SDS resident undergoes density dependent population dynamics, which we assume asymptotically converges to a carrying capacity.

Once the SDS resident has achieved carrying capacity, the population moves to the resident-mutant population dynamics phase. At the start of this phase, a random mutant gene expression vector arises in a vanishingly small number of mutants. We assume that mutation of gene expression is unbiased, which means that mutant gene expression is symmetrically distributed around the resident gene expression. We also assume that mutation of gene expression is weak, which means that the variance of mutant gene expression around resident gene expression is marginally small. Weak mutation (Walsh and Lynch, 2018, p. 1003) is also called δ-weak selection (Wild and Traulsen, 2007). We assume that the mutant becomes either lost or fixed in the population (Geritz et al., 2002; Geritz, 2005; Priklopil and Lehmann, 2020), establishing a new resident geno-envo-phenotype.

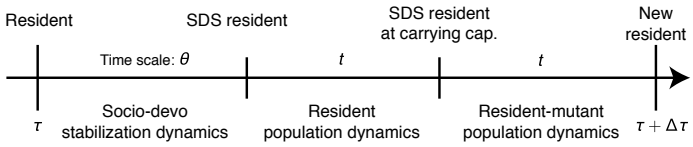

Figure 3: Phases of the evolutionary cycle. Evolutionary time is τ. SDS means socio-devo stable. The socio-devo stabilization dynamics phase is added to the standard separation of timescales in adaptive dynamics, which only consider the other two phases. The socio-devo stabilization dynamics phase is only needed if development is social (i.e., if the developmental map $\mathbf{g}_a$ depends directly or indirectly on social partners' geno-phenotype for some age a).

Repeating this evolutionary cycle generates long term evolutionary dynamics of an SDS geno-envo-phenotype.

3.4.2. Formal description

We now formally describe the three phases in which we partition an evolutionary time step (Fig. 3). We start with the socio-devo stabilization dynamics phase, which yields the notions of socio-devo equilibrium and socio-devo stability.

Socio-devo stabilization dynamics occur as follows. For a resident geno-envo-phenotype $\bar{\mathbf{m}} = (\bar{\mathbf{x}}; \bar{\mathbf{y}}; \boldsymbol{\epsilon})$, a new resident phenotype is obtained from Eq. (4); the resulting phenotype, its gene expression, and the resulting environment are set as the new resident; and this is iterated. To write this formally, let θ denote time for the socio-devo stabilization dynamics (we do not explicitly address how socio-devo time θ relates to ecological time t). During the socio-devo stabilization phase, denote the resident phenotype at socio-devo time θ as $\bar{\mathbf{x}}(\theta)$. Then, using Eq. (4), the resident phenotype at socio-devo time $\theta + 1$ is given by

$$\begin{aligned}&\bar{\mathbf{x}}_{a+1}(\theta+1)\\&= \mathbf{g}_a(\bar{\mathbf{x}}_a(\theta+1), \bar{\mathbf{y}}_a, \mathbf{h}_a(\bar{\mathbf{x}}_a(\theta+1), \bar{\mathbf{y}}_a, \bar{\mathbf{x}}(\theta), \bar{\mathbf{y}}, \tau), \bar{\mathbf{x}}(\theta), \bar{\mathbf{y}}),\end{aligned} \tag{5}$$

for all $a \in \{1, \ldots, N_\mathrm{a} - 1\}$ and with given initial conditions $\bar{\mathbf{x}}(1)$ and $\bar{\mathbf{x}}_1(\theta+1) = \bar{\mathbf{x}}_1$. If $\lim_{\theta\to\infty} \bar{\mathbf{x}}(\theta)$ converges, then this limit, the resident gene expression, and the resulting environment yield a socio-devo stable geno-envo-phenotype as defined below.

We say a geno-envo-phenotype $\bar{\mathbf{m}} = (\bar{\mathbf{x}}; \bar{\mathbf{y}}; \bar{\boldsymbol{\epsilon}})$ is a socio-devo equilibrium if and only if $\bar{\mathbf{x}}$ is produced by development when the individual has such gene expression $\bar{\mathbf{y}}$ and everyone else in the population has that same gene expression, phenotype, and environment; specifically, a socio-devo equilibrium $\bar{\mathbf{m}} = (\bar{\mathbf{x}}; \bar{\mathbf{y}}; \bar{\boldsymbol{\epsilon}})$ satisfies

$$\begin{aligned}\bar{\mathbf{x}}_{a+1} &= \mathbf{g}_a(\bar{\mathbf{x}}_a, \bar{\mathbf{y}}_a, \bar{\boldsymbol{\epsilon}}_a, \bar{\mathbf{x}}, \bar{\mathbf{y}}) \quad \forall a \in \{1, \ldots, N_\mathrm{a} - 1\}, \bar{\mathbf{x}}_1 \text{ fixed},\\ \bar{\boldsymbol{\epsilon}}_a &= \mathbf{h}_a(\bar{\mathbf{x}}_a, \bar{\mathbf{y}}_a, \bar{\mathbf{x}}, \bar{\mathbf{y}}, \tau) \quad \forall a \in \{1, \ldots, N_\mathrm{a}\}.\end{aligned} \tag{6}$$

We assume that there is at least one socio-devo equilibrium for a given developmental map at every evolutionary time τ.

If the resident geno-envo-phenotype is a socio-devo equilibrium, from Eqs. (1), (2), and (6), it follows that evaluation

of the mutant gene expression at the resident gene expression yields resident variables. That is, if $\bar{\mathbf{m}} = (\bar{\mathbf{x}}; \bar{\mathbf{y}}; \bar{\boldsymbol{\epsilon}})$ is a socio-devo equilibrium, then

$$\begin{aligned}\mathbf{x}|_{\mathbf{y}=\bar{\mathbf{y}}} &= \bar{\mathbf{x}}\\ \boldsymbol{\epsilon}|_{\mathbf{y}=\bar{\mathbf{y}}} &= \bar{\boldsymbol{\epsilon}}\\ \mathbf{z}|_{\mathbf{y}=\bar{\mathbf{y}}} &= \bar{\mathbf{z}}\\ \mathbf{m}|_{\mathbf{y}=\bar{\mathbf{y}}} &= \bar{\mathbf{m}}.\end{aligned}$$

More specifically, if the resident geno-envo-phenotype is a socio-devo equilibrium, the resident phenotype at age $a+1$ is given by Eq. (1) evaluating the developmental map at the resident geno-envo-phenotype (i.e., $\bar{\mathbf{x}}_{a+1} = \mathbf{g}_a(\bar{\mathbf{m}}_a, \bar{\mathbf{z}})$), and the resident environment at age a is given by Eq. (2) evaluating the environmental map at the resident geno-phenotype (i.e., $\bar{\boldsymbol{\epsilon}}_a = \mathbf{h}_a(\bar{\mathbf{z}}_a, \bar{\mathbf{z}}, \tau)$).

Now, we say that a geno-envo-phenotype $\bar{\mathbf{m}} = (\bar{\mathbf{x}}; \bar{\mathbf{y}}; \bar{\boldsymbol{\epsilon}})$ is socio-devo stable (SDS) if and only if $\bar{\mathbf{m}}$ is a locally stable socio-devo equilibrium. A socio-devo equilibrium $\bar{\mathbf{m}} = (\bar{\mathbf{x}}; \bar{\mathbf{y}}; \bar{\boldsymbol{\epsilon}})$ is locally stable if and only if a marginally small deviation in the initial phenotype $\bar{\mathbf{x}}(1)$ from the socio-devo equilibrium keeping the same gene expression leads the socio-devo stabilization dynamics to the same equilibrium. Thus, a socio-devo equilibrium $\bar{\mathbf{m}}$ is locally stable if all the eigenvalues of the matrix

$$\left.\frac{\mathrm{d}\mathbf{x}}{\mathrm{d}\bar{\mathbf{x}}^{\intercal}}\right|_{\mathbf{y}=\bar{\mathbf{y}}}$$

have absolute value (or modulus) strictly less than one (Appendices N and O). The requirement that this matrix has such eigenvalues arises naturally in the derivation of the evolutionary dynamics of the resident phenotype $\bar{\mathbf{x}}$ (Appendix I). We assume that there is a unique SDS geno-envo-phenotype for a given developmental map at every evolutionary time τ.

Once the SDS resident is reached (or, more strictly, sufficiently approached) in the socio-devo stabilization phase, we continue to the resident population dynamics phase (Fig. 3). Let the resident geno-envo-phenotype $\bar{\mathbf{m}}$ be SDS. Let $\bar{n}_a(t)$ denote the density of SDS residents of age $a \in \{1, \ldots, N_\mathrm{a}\}$ at ecological time t. The vector of resident density at t is $\bar{\mathbf{n}}(t) = (\bar{n}_1(t), \ldots, \bar{n}_{N_\mathrm{a}}(t))^{\intercal}$. The life cycle is age-structured (Fig. 4). At age a, an SDS resident produces a number $A_{1a}(\bar{\mathbf{m}}_a, \bar{\mathbf{z}}, \bar{\mathbf{n}}(t))$ of offspring and survives to age $a+1$ with probability $A_{a+1,a}(\bar{\mathbf{m}}_a, \bar{\mathbf{z}}, \bar{\mathbf{n}}(t))$ (where we set $A_{N_\mathrm{a}+1,N_\mathrm{a}}(\bar{\mathbf{m}}_a, \bar{\mathbf{z}}, \bar{\mathbf{n}}(t)) = 0$ without loss of generality). The first argument of these two functions is the geno-envo-phenotype of the individual at that age, the second argument is the geno-phenotype of the individual's social partners who can be of any age, and the third argument is density dependence; thus, an individual's fertility and survival directly depend on the individual's local environment (via the first argument $\bar{\mathbf{m}}_a$) but not directly on the local environment of social partners (the second argument $\bar{\mathbf{z}}$ does not include the environment). These expressions for survival and fertility use the assumption that exogenous environmental change is slow so $\bar{\mathbf{m}}$ is constant with respect to the ecological time t. The SDS resident population thus has deterministic dynamics given by

$$\bar{\mathbf{n}}(t+1) = \mathbf{A}(\bar{\mathbf{m}}, \bar{\mathbf{z}}, \bar{\mathbf{n}}(t))\bar{\mathbf{n}}(t), \tag{7}$$

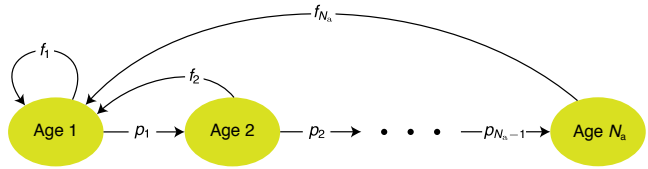

Figure 4: Age-structured life cycle. The vital rates shown are those of rare mutants: a mutant of age a produces f_a offspring and survives to age $a+1$ with probability p_a. See text for the vital rates of the resident.

where $\mathbf{A}(\bar{\mathbf{m}}, \bar{\mathbf{z}}, \bar{\mathbf{n}}(t))$ is a density-dependent Leslie matrix whose entries $A_{ij}(\bar{\mathbf{m}}_j, \bar{\mathbf{z}}, \bar{\mathbf{n}}(t))$ give the age-specific survival probabilities and fertilities of SDS resident individuals; the first argument of $\mathbf{A}(\bar{\mathbf{m}}, \bar{\mathbf{z}}, \bar{\mathbf{n}}(t))$ is the geno-envo-phenotype vector formed by the first argument of $A_{ij}(\bar{\mathbf{m}}_j, \bar{\mathbf{z}}, \bar{\mathbf{n}}(t))$ for all $i, j \in \{1, \ldots, N_\mathrm{a}\}$. We assume that density dependence is such that the population dynamics of the SDS resident (Eq. 7) have a unique stable non-trivial equilibrium $\bar{\mathbf{n}}^*(\bar{\mathbf{m}})$ (a vector of non-negative entries some of which are positive), which solves

$$\bar{\mathbf{n}}^*(\bar{\mathbf{m}}) = \mathbf{A}(\bar{\mathbf{m}}, \bar{\mathbf{z}}, \bar{\mathbf{n}}^*(\bar{\mathbf{m}}))\bar{\mathbf{n}}^*(\bar{\mathbf{m}}). \tag{8}$$

The carrying capacity is given by $\bar{n}^*(\bar{\mathbf{m}}) = \sum_{a=1}^{N_\mathrm{a}} \bar{n}_a^*(\bar{\mathbf{m}})$, which depends on the SDS resident geno-envo-phenotype. We assume that residents in the last age reproduce (i.e., $A_{1N_\mathrm{a}}(\bar{\mathbf{m}}_{N_\mathrm{a}}, \bar{\mathbf{z}}, \bar{\mathbf{n}}(t)) > 0$) and that residents can survive to the last age with non-zero probability (i.e., $A_{a+1,a}(\bar{\mathbf{m}}_a, \bar{\mathbf{z}}, \bar{\mathbf{n}}(t)) > 0$ for all $a \in \{1, \ldots, N_\mathrm{a} - 1\}$); this ensures that $\mathbf{A}(\bar{\mathbf{m}}, \bar{\mathbf{z}}, \bar{\mathbf{n}}^*(\bar{\mathbf{m}}))$ is irreducible (Sternberg, 2010, section 9.4). We further assume that residents of at least two consecutive age classes have non-zero fertility (i.e., $A_{1a}(\bar{\mathbf{m}}_a, \bar{\mathbf{z}}, \bar{\mathbf{n}}(t)) > 0$ and $A_{1,a+1}(\bar{\mathbf{m}}_{a+1}, \bar{\mathbf{z}}, \bar{\mathbf{n}}(t)) > 0$ for some $a \in \{1, \ldots, N_\mathrm{a}-1\}$); this ensures that $\mathbf{A}(\bar{\mathbf{m}}, \bar{\mathbf{z}}, \bar{\mathbf{n}}^*(\bar{\mathbf{m}}))$ is primitive (Sternberg, 2010, section 9.4.1; i.e., raising $\mathbf{A}(\bar{\mathbf{m}}, \bar{\mathbf{z}}, \bar{\mathbf{n}}^*(\bar{\mathbf{m}}))$ to a sufficiently high power yields a matrix whose entries are all positive). Hence, from the Perron-Frobenius theorem (Sternberg, 2010, theorem 9.1.1), it follows that $\mathbf{A}(\bar{\mathbf{m}}, \bar{\mathbf{z}}, \bar{\mathbf{n}}^*(\bar{\mathbf{m}}))$ has an eigenvalue $\bar{\lambda} = 1$ that is strictly greater than the absolute value of any other eigenvalue of the matrix. This $\bar{\lambda}$ describes the asymptotic growth rate of the resident population, as the resident population dynamics equilibrium $\bar{\mathbf{n}}^*(\bar{\mathbf{m}})$ is achieved.

Once the resident population has reached (or, more strictly, sufficiently approached) the equilibrium $\bar{\mathbf{n}}^*(\bar{\mathbf{m}})$, we move on to the resident-mutant population dynamics phase (Fig. 3). After some time inversely proportional to $\mu(\bar{\mathbf{m}})n^*(\bar{\mathbf{m}})$, where $\mu(\bar{\mathbf{m}})$ is the mutation rate, a rare mutant gene expression $\mathbf{y}$ arises, where $\mathbf{y}$ is a realization of a multivariate random variable. A mutant has geno-envo-phenotype $\mathbf{m} = (\mathbf{x}; \mathbf{y}; \boldsymbol{\epsilon})$ where the mutant phenotype $\mathbf{x}$ is given by the developmental constraint (1) and the mutant environment $\boldsymbol{\epsilon}$ is given by the environmental constraint (2).

Let $n_a(t)$ denote the density of mutant individuals of age $a \in \{1, \ldots, N_\mathrm{a}\}$ at ecological time t. The vector of mutant density at t is $\mathbf{n}(t) = (n_1(t), \ldots, n_{N_\mathrm{a}}(t))^{\intercal}$. Given clonal reproduction, the population dynamics of the resident and rare mutant subpopulations are then given by the expanded system

$$\begin{pmatrix}\bar{\mathbf{n}}(t+1)\\ \mathbf{n}(t+1)\end{pmatrix} = \begin{pmatrix}\mathbf{A}(\bar{\mathbf{m}}, \bar{\mathbf{z}}, \bar{\mathbf{n}}(t)) & \mathbf{0}\\ \mathbf{0} & \mathbf{A}(\mathbf{m}, \bar{\mathbf{z}}, \bar{\mathbf{n}}(t))\end{pmatrix}\begin{pmatrix}\bar{\mathbf{n}}(t)\\ \mathbf{n}(t)\end{pmatrix},$$

where the mutant projection matrix $\mathbf{A}(\mathbf{m}, \bar{\mathbf{z}}, \bar{\mathbf{n}}(t))$ is given by evaluating the first argument of $\mathbf{A}(\bar{\mathbf{m}}, \bar{\mathbf{z}}, \bar{\mathbf{n}}(t))$ at the mutant geno-envo-phenotype. Hence, $\mathbf{A}(\mathbf{m}, \bar{\mathbf{z}}, \bar{\mathbf{n}}(t))$ is a density-dependent Leslie matrix whose ij-th entry is $A_{ij}(\mathbf{m}_j, \bar{\mathbf{z}}, \bar{\mathbf{n}}(t))$ that gives either the age-specific survival probability (for $i > 1$) or the age-specific fertility (for $i = 1$) of mutant individuals in the context of the resident. The rare mutant subpopulation thus has population dynamics given by $\mathbf{n}(t+1) = \mathbf{A}(\mathbf{m}, \bar{\mathbf{z}}, \bar{\mathbf{n}}(t))\mathbf{n}(t)$.

The mutant population dynamics around the resident equilibrium $\bar{\mathbf{n}}^*(\bar{\mathbf{m}})$ are to first order of approximation given by

$$\mathbf{n}(t+1) \approx \mathbf{J}\mathbf{n}(t), \tag{9}$$

where the local stability matrix of the mutant (Appendix N) is

$$\mathbf{J} = \left.\frac{\partial \mathbf{A}(\mathbf{m}, \bar{\mathbf{z}}, \bar{\mathbf{n}})\mathbf{n}}{\partial \mathbf{n}^\intercal}\right|_{\mathbf{n}=\mathbf{n}^*} = \left(\left.\frac{\partial}{\partial n_j}\sum_{k=1}^{N_\mathrm{a}} A_{ik}(\mathbf{m}_k, \bar{\mathbf{z}}, \bar{\mathbf{n}})n_k\right|_{\bar{\mathbf{n}}=\bar{\mathbf{n}}^*}\right)$$
$$= \left(A_{ij}(\mathbf{m}_j, \bar{\mathbf{z}}, \bar{\mathbf{n}}^*(\bar{\mathbf{m}}))\right).$$

Explicitly,

$$\mathbf{J} = \begin{pmatrix} f_1 & f_2 & \cdots & f_{N_\mathrm{a}-1} & f_{N_\mathrm{a}} \\ p_1 & 0 & \cdots & 0 & 0 \\ 0 & p_2 & \cdots & 0 & 0 \\ \vdots & \vdots & \ddots & \vdots & \vdots \\ 0 & 0 & \cdots & p_{N_\mathrm{a}-1} & 0 \end{pmatrix}, \tag{10}$$

where we denote the mutant's fertility at age a at the resident population dynamics equilibrium as

$$f_a = f_a(\mathbf{m}_a, \bar{\mathbf{m}}) = A_{1a}(\mathbf{m}_a, \bar{\mathbf{z}}, \bar{\mathbf{n}}^*(\bar{\mathbf{m}})) \tag{11a}$$

and the mutant's survival probability from age a to $a+1$ as

$$p_a = p_a(\mathbf{m}_a, \bar{\mathbf{m}}) = A_{a+1,a}(\mathbf{m}_a, \bar{\mathbf{z}}, \bar{\mathbf{n}}^*(\bar{\mathbf{m}})). \tag{11b}$$

We denote the fertility of a neutral mutant of age a as $f_a^\circ = f_a(\bar{\mathbf{m}}_a, \bar{\mathbf{m}})$ and the survival probability from age a to $a+1$ of a neutral mutant as $p_a^\circ = p_a(\bar{\mathbf{m}}_a, \bar{\mathbf{m}})$, where the superscript $\circ$ denotes evaluation at $\mathbf{y} = \bar{\mathbf{y}}$ (so at $\mathbf{m} = \bar{\mathbf{m}}$ as the resident is a socio-devo equilibrium).

3.5. Evolutionary dynamics of gene expression

We now obtain a first-order approximation of invasion fitness and use it to obtain an equation describing the evolutionary dynamics of gene expression. Invasion fitness is the asymptotic growth rate of the mutant population and it enables the determination of whether the mutant invades the resident population (i.e., whether the mutation increases in frequency) (Otto and Day, 2007). From Eq. (9), the asymptotic population dynamics of the mutant subpopulation around the resident equilibrium are given to first order of approximation by the eigenvalues and eigenvectors of $\mathbf{J}$. As for residents, we assume that mutants in the last age reproduce ($f_{N_\mathrm{a}} > 0$) and that mutants can survive to the last age with non-zero probability (i.e., $p_a > 0$ for all $a \in \{1, \ldots, N_\mathrm{a}-1\}$); so $\mathbf{J}$ is irreducible (Sternberg, 2010, section 9.4). We similarly assume that mutants of at least two consecutive age classes have non-zero fertility (i.e., $f_a > 0$ and $f_{a+1} > 0$ for some $a \in \{1, \ldots, N_\mathrm{a}-1\}$); so $\mathbf{J}$ is primitive (Sternberg, 2010, section 9.4.1; i.e., raising $\mathbf{J}$ to a sufficiently high power yields a matrix whose entries are all positive). Then, from the Perron-Frobenius theorem (Sternberg, 2010, theorem 9.1.1), $\mathbf{J}$ has a real positive eigenvalue $\lambda = \lambda(\mathbf{m}, \bar{\mathbf{m}})$ whose magnitude is strictly larger than that of the other eigenvalues of $\mathbf{J}$. Such leading eigenvalue λ is the asymptotic growth rate of the mutant population around the resident equilibrium, and thus gives the mutant's invasion fitness. Since the population dynamics of rare mutants are locally given by Eq. (9) where $\mathbf{J}$ projects the mutant population to the next ecological time step, the mutant population invades when invasion fitness satisfies $\lambda > 1$.

We consider the evolutionary change in gene expression from the evolutionary time τ, specifically the point at which the socio-devo stable resident is at carrying capacity as marked in Fig. 3, to the evolutionary time $\tau + \Delta\tau$ at which a new socio-devo stable resident is at carrying capacity. The vector $\mathbf{y}$ is a realization of a multivariate random variable $\mathbf{y}$ with probability density $M(\mathbf{y}, \bar{\mathbf{y}})$ called *the mutational distribution* (Dieckmann and Law, 1996), with support in $\mathbb{R}^{N_\mathrm{a}N_\mathrm{c}}$ (abusing notation, we denote a random variable and its realization with the same symbol, as has been common practice—e.g., Lande 1979 and Lynch and Walsh 1998, p. 192). We assume that the mutational distribution is such that (i) the expected mutant gene expression is the resident, $\mathrm{E}[\mathbf{y}] = \bar{\mathbf{y}}$; (ii) mutational variance is marginally small (i.e., selection is δ-weak) such that $0 < \mathrm{E}[\|\mathbf{y} - \bar{\mathbf{y}}\|^2] = \mathrm{tr}(\mathrm{cov}[\mathbf{y}, \mathbf{y}]) = \sum_{i=1}^{N_\mathrm{c}}\sum_{a=1}^{N_\mathrm{a}} \mathrm{E}[(y_{ia} - \bar{y}_{ia})^2] \ll 1$; and (iii) mutation is unbiased, that is, the mutational distribution is symmetric so skewness is $\mathrm{E}[(\mathbf{y} - \bar{\mathbf{y}})(\mathbf{y} - \bar{\mathbf{y}})^\intercal(\mathbf{y} - \bar{\mathbf{y}})] = \mathbf{0}$. Given small mutational variance, Taylor-expanding λ with respect to $\mathbf{y}$ around $\bar{\mathbf{y}}$, invasion fitness is to first order of approximation given by

$$\lambda = 1 + (\mathbf{y} - \bar{\mathbf{y}})^\intercal \left.\frac{\mathrm{d}\lambda}{\mathrm{d}\mathbf{y}}\right|_{\mathbf{y}=\bar{\mathbf{y}}} + O(\|\mathbf{y} - \bar{\mathbf{y}}\|^2), \tag{12}$$

where we use the fact that $\lambda|_{\mathbf{y}=\bar{\mathbf{y}}} = 1$ due to density dependence. A given entry of the operator $\mathrm{d}/\mathrm{d}\mathbf{y}|_{\mathbf{y}=\bar{\mathbf{y}}}$, say $\mathrm{d}/\mathrm{d}y_{ai}|_{\mathbf{y}=\bar{\mathbf{y}}}$, takes the total derivative with respect to y_{ia} while keeping all the other gene expression values y_{jk} constant. Hence, we refer to $\mathrm{d}\lambda/\mathrm{d}\mathbf{y}|_{\mathbf{y}=\bar{\mathbf{y}}}$ as the *total selection gradient of gene expression* $\mathbf{y}$, which takes the total derivative considering both developmental constraints (1) and environmental constraints (2) (Appendix P). Thus, the total selection gradient of gene expression can be interpreted as measuring *total genetic selection*. Since the mutant population invades when $\lambda > 1$ and mutational variances are marginally small (i.e., selection is δ-weak), the mutant population invades if and only if

$$(\mathbf{y} - \bar{\mathbf{y}})^\intercal \left.\frac{\mathrm{d}\lambda}{\mathrm{d}\mathbf{y}}\right|_{\mathbf{y}=\bar{\mathbf{y}}} > 0,$$

to first-order of approximation. The left-hand side of this inequality is the dot product of total genetic selection and the realized mutational effect on gene expression $(\mathbf{y} - \bar{\mathbf{y}})$. The dot product is positive if and only if the absolute value of the smallest angle between two non-zero vectors is smaller than 90 degrees. Hence, to first-order of approximation, the mutant population invades if and only if total genetic selection has a vector

component in the direction of the mutational effect on gene expression.

Using Eq. (12) and closely following Dieckmann and Law (1996), in Appendix A we provide a short derivation showing that the evolutionary dynamics of gene expression are given by the canonical equation of adaptive dynamics:

$$\frac{\Delta\bar{\mathbf{y}}}{\Delta\tau} \approx \kappa \mathbf{G}_{\mathbf{y}} \left.\frac{\mathrm{d}\lambda}{\mathrm{d}\mathbf{y}}\right|_{\mathbf{y}=\bar{\mathbf{y}}}, \tag{13a}$$

where κ is a scalar that is proportional to the mutation rate and carrying capacity, whereas

$$\mathbf{G}_{\mathbf{y}} = \mathrm{cov}[\mathbf{y}, \mathbf{y}] \tag{13b}$$

is equivalently the mutational covariance matrix (of gene expression) and the additive genetic covariance matrix of gene expression under our adaptive dynamics assumptions (cf. Eq. 6.1 of Dieckmann and Law 1996, Eq. 23 of Durinx et al. 2008, p. 332 of Fisher 1922, and Eq. 12 of Morrissey 2015). If the total selection gradient of gene expression is zero, then there is no evolutionary change in the (expected) resident controls to first order of approximation. However, if the total selection gradient of gene expression is zero, mutants may still invade symmetrically around resident controls to second-order of approximation (i.e., $\lambda > 1$ may still hold; Eq. 12), which constitutes evolutionary branching (Geritz et al., 1998; Leimar, 2009; Débarre et al., 2014). Here we will be concerned with describing the evolutionary dynamics to first-order of approximation, so we will treat the approximation in Eq. (13a) as an equality although we keep the approximation symbol to distinguish what is and what is not an approximation.

Owing to the block structure of $\mathbf{y}$, $\mathbf{G}_{\mathbf{y}}$ is a block matrix whose aj-th block entry is the matrix $\mathbf{G}_{\mathbf{y}_a,\mathbf{y}_j} = \mathrm{cov}[\mathbf{y}_a, \mathbf{y}_j]$, which is the mutational or additive genetic cross-covariance matrix between gene expression $\mathbf{y}_a$ at age a and gene expression $\mathbf{y}_j$ at age j. In turn, the ik-th entry of $\mathbf{G}_{\mathbf{y}_a,\mathbf{y}_j}$ is $G_{y_{ia},y_{kj}} = \mathrm{cov}[y_{ia}, y_{kj}]$ which is the mutational or additive genetic covariance between gene expression y_{ia} and gene expression y_{kj}. Since $\mathbf{y} \in \mathbb{R}^{N_\mathrm{a}N_\mathrm{c}\times 1}$, then $\mathbf{G}_{\mathbf{y}} \in \mathbb{R}^{N_\mathrm{a}N_\mathrm{c}\times N_\mathrm{a}N_\mathrm{c}}$.

We will define the additive genetic covariance matrix $\mathbf{G}_{\boldsymbol{\zeta}}$ of a trait vector $\boldsymbol{\zeta}$ once we define breeding value under our adaptive dynamics assumptions. Using a modification of the terminology of Houle (2001) and Klingenberg (2005, 2010), we say that there are no genetic constraints for a vector $\boldsymbol{\zeta}$ if and only if all the eigenvalues of its additive genetic covariance matrix $\mathbf{G}_{\boldsymbol{\zeta}}$ are equal and positive; that there are only relative genetic constraints if and only if $\mathbf{G}_{\boldsymbol{\zeta}}$ has different eigenvalues but all are positive; and that there are absolute genetic constraints if and only if $\mathbf{G}_{\boldsymbol{\zeta}}$ has at least one zero eigenvalue (i.e., $\mathbf{G}_{\boldsymbol{\zeta}}$ is singular). If $\boldsymbol{\zeta} = \mathbf{y}$, we speak of mutational rather than genetic constraints. For example, we say there are absolute mutational constraints if and only if $\mathbf{G}_{\mathbf{y}}$ is singular, in which case there is no mutational variation in some directions of gene expression space. Hence, from Eq. (13a), if there are absolute mutational constraints (i.e., $\mathbf{G}_{\mathbf{y}}$ is singular), the evolutionary dynamics of gene expression can stop (i.e., $\Delta\bar{\mathbf{y}}/\Delta\tau \approx \mathbf{0}$) with a non-zero total selection gradient of gene expression (i.e., $\mathrm{d}\lambda/\mathrm{d}\mathbf{y}|_{\mathbf{y}=\bar{\mathbf{y}}} \neq \mathbf{0}$) (because a homogeneous system $\mathbf{A}\mathbf{x} = \mathbf{0}$ has non-zero solutions $\mathbf{x}$ with $\mathbf{A}$ singular if there is any solution to the system).

As the resident gene expression evolves, the resident phenotype evolves. Specifically, at a given evolutionary time τ, from Eq. (1) the resident phenotype is given by the recurrence equation

$$\bar{\mathbf{x}}_{a+1} = \mathbf{g}_a(\bar{\mathbf{m}}_a, \bar{\mathbf{z}}) \tag{13c}$$

for all $a \in \{1, \ldots, N_\mathrm{a} - 1\}$ with $\bar{\mathbf{x}}_1$ constant, and where the resident environment is given by

$$\bar{\boldsymbol{\epsilon}}_a = \mathbf{h}_a(\bar{\mathbf{z}}_a, \bar{\mathbf{z}}, \tau) \tag{13d}$$

for all $a \in \{1, \ldots, N_\mathrm{a}\}$. Intuitively, the evolutionary dynamics of the phenotype thus occur as an outgrowth of the evolutionary dynamics of gene expression and are modulated by the environmental evolutionary dynamics.

Eq. (13a) describes the evolutionary dynamics of gene expression and Eq. (13c) describes the developmental dynamics of the phenotype, so together Eqs. (13) describe the evo-devo dynamics. To characterize the evo-devo process, we obtain general expressions for the total selection gradient of gene expression and for the evolutionary dynamics of the phenotype, environment, geno-phenotype, and geno-envo-phenotype. To do this, we first re-derive the classical form of the selection gradient in age-structured populations, upon which we build our derivations.

3.6. Selection gradient in age-structured populations

To calculate the evo-devo dynamics given by Eqs. (13), we need to calculate the total selection gradient of gene expression $\mathrm{d}\lambda/\mathrm{d}\mathbf{y}|_{\mathbf{y}=\bar{\mathbf{y}}}$. Since the life cycle is age structured (Eq. 10 and Fig. 4), the total selection gradient of gene expression has the form of the selection gradient in age structured populations, which is well-known but we re-derive it here for ease of reference.

We first use an eigenvalue perturbation theorem to write the selection gradient, which suggests a definition of relative fitness. Let $\bar{\zeta}$ and ζ respectively denote resident and mutant trait values (i.e., $\bar{\zeta}$ is an entry of $\bar{\mathbf{m}}$ and ζ is an entry of $\mathbf{m}$). From a theorem on eigenvalue perturbation (Eq. 9 of Caswell 1978 or Eq. 9.10 of Caswell 2001), the selection gradient of ζ is

$$\begin{aligned}\left.\frac{\partial\lambda}{\partial\zeta}\right|_{\mathbf{y}=\bar{\mathbf{y}}} &= \frac{1}{\mathbf{v}^{\circ\mathsf{T}}\mathbf{u}^\circ}\mathbf{v}^{\circ\mathsf{T}}\left(\left.\frac{\partial\mathbf{J}}{\partial\zeta}\right|_{\mathbf{y}=\bar{\mathbf{y}}}\right)\mathbf{u}^\circ \\ &= \frac{1}{\mathbf{v}^{\circ\mathsf{T}}\mathbf{u}^\circ}\sum_{i=1}^{N_\mathrm{a}}\sum_{j=1}^{N_\mathrm{a}} v_i^\circ\left(\left.\frac{\partial J_{ij}}{\partial\zeta}\right|_{\mathbf{y}=\bar{\mathbf{y}}}\right)u_j^\circ,\end{aligned} \tag{14}$$

where $\mathbf{v}$ and $\mathbf{u}$ are respectively dominant left and right eigenvectors of $\mathbf{J}$ (Eq. 10). The vector $\mathbf{v}$ lists the mutant reproductive values and the vector $\mathbf{u}$ lists the mutant stable age distribution. In turn, $\mathbf{v}^\circ = \mathbf{v}|_{\mathbf{y}=\bar{\mathbf{y}}}$ lists the neutral (mutant) reproductive values and $\mathbf{u}^\circ = \mathbf{u}|_{\mathbf{y}=\bar{\mathbf{y}}}$ lists the neutral (mutant) stable age distribution. Substituting J_{ij} for the entries in Eq. (10) yields

$$\left.\frac{\partial\lambda}{\partial\zeta}\right|_{\mathbf{y}=\bar{\mathbf{y}}} = \frac{1}{\mathbf{v}^{\circ\mathsf{T}}\mathbf{u}^\circ}\sum_{j=1}^{N_\mathrm{a}} u_j^\circ\left(v_1^\circ\left.\frac{\partial f_j}{\partial\zeta}\right|_{\mathbf{y}=\bar{\mathbf{y}}} + v_{j+1}^\circ\left.\frac{\partial p_j}{\partial\zeta}\right|_{\mathbf{y}=\bar{\mathbf{y}}}\right), \tag{15}$$

where we let $v_{N_a+1} = 0$ without loss of generality. Eq. (14) motivates the definition of the relative fitness of a mutant individual per unit of generation time as

$$w = \frac{1}{\mathbf{v}^{\circ\intercal}\mathbf{u}^{\circ}}\mathbf{v}^{\circ\intercal}\mathbf{J}\mathbf{u}^{\circ} = \frac{1}{\mathbf{v}^{\circ\intercal}\mathbf{u}^{\circ}}\sum_{i=1}^{N_a}\sum_{j=1}^{N_a} v_i^{\circ} J_{ij} u_j^{\circ} \tag{16}$$

(cf. Lande, 1982, his Eq. 12c) and of the relative fitness of a mutant individual of age j per unit of generation time as

$$w_j = \frac{1}{\mathbf{v}^{\circ\intercal}\mathbf{u}^{\circ}}\sum_{i=1}^{N_a} v_i^{\circ} J_{ij} u_j^{\circ} = \frac{1}{\mathbf{v}^{\circ\intercal}\mathbf{u}^{\circ}} u_j^{\circ}\left(v_1^{\circ} f_j + v_{j+1}^{\circ} p_j\right). \tag{17}$$

Note, however, that relative fitness w in Eq. (16) is defined here by its property of having the same first derivative as invasion fitness, so it is a first-order approximation of invasion fitness and is not adequate to assess second-order selection, namely, stabilizing or disruptive selection, in particular, evolutionary branching.

We now obtain that relative fitness depends on the forces of selection, which decrease with age. Age-specific relative fitness (Eq. 17) depends on the neutral stable age distribution u_j° and the neutral reproductive value v_{j+1}°, which are well-known quantities but we re-derive them in Appendix B for ease of reference. We obtain that the neutral stable age distribution and neutral reproductive value are

$$u_j^{\circ} = \ell_j^{\circ} u_1^{\circ} \tag{18a}$$

$$v_j^{\circ} = \frac{1}{\ell_j^{\circ}} v_1^{\circ} \sum_{k=j}^{N_a} \ell_k^{\circ} f_k^{\circ}, \tag{18b}$$

for $j \in \{1, \ldots, N_a\}$ and where u_1° and v_1° can take any positive value. The quantity $\ell_j^{\circ} = \prod_{k=1}^{j-1} p_k^{\circ}$ is the survivorship of neutral mutants from age 1 to age j. Hence, the weights on fertility and survival in Eq. (17) are

$$\frac{u_j^{\circ} v_1^{\circ}}{\mathbf{v}^{\circ\intercal}\mathbf{u}^{\circ}} = \frac{1}{T}\ell_j^{\circ} \tag{19a}$$

$$\frac{u_j^{\circ} v_{j+1}^{\circ}}{\mathbf{v}^{\circ\intercal}\mathbf{u}^{\circ}} = \frac{1}{T}\frac{1}{p_j^{\circ}}\sum_{k=j+1}^{N_a} \ell_k^{\circ} f_k^{\circ}, \tag{19b}$$

where generation time is

$$T = \sum_{j=1}^{N_a} j \ell_j^{\circ} f_j^{\circ} \tag{20}$$

(Charlesworth 1994, Eq. 1.47c; Bulmer 1994, Eq. 25, Ch. 25; Bienvenu and Legendre 2015, Eqs. 5 and 12). Eqs. (18) and (19) recover classic equations (Hamilton 1966 and Caswell 1978, his Eqs. 11 and 12). We denote the force of selection on fertility at age j as

$$\phi_j(\bar{\mathbf{m}}) = \ell_j^{\circ} \tag{21a}$$

and the force of selection on survival at age j as

$$\pi_j(\bar{\mathbf{m}}) = \frac{1}{p_j^{\circ}}\sum_{k=j+1}^{N_a} \ell_k^{\circ} f_k^{\circ}, \tag{21b}$$

which are independent of mutant trait values because they are evaluated at the resident trait values. It is easily checked that ϕ_j and π_j decrease with j (respectively, if $p_j^{\circ} < 1$ and $f_{j+1}^{\circ} > 0$ provided that p_j° changes smoothly with age).

We can then obtain a biologically informative expression for the selection gradient in terms relative fitness. Using Eqs. (17), (19), and (21), a mutant's relative fitness at age j is

$$w_j = \frac{1}{T}\left(\phi_j f_j + \pi_j p_j\right), \tag{22}$$

or with explicit arguments using Eq. (11),

$$w_j(\mathbf{m}_j, \bar{\mathbf{m}}) = \frac{1}{T(\bar{\mathbf{m}})}\left[\phi_j(\bar{\mathbf{m}}) f_j(\mathbf{m}_j, \bar{\mathbf{m}}) + \pi_j(\bar{\mathbf{m}}) p_j(\mathbf{m}_j, \bar{\mathbf{m}})\right]. \tag{23}$$

Using Eqs. (16), (17), and (22), a mutant's relative fitness is

$$w = \sum_{j=1}^{N_a} w_j = \frac{1}{T}\sum_{j=1}^{N_a}\left(\phi_j f_j + \pi_j p_j\right), \tag{24}$$

or with explicit arguments,

$$w(\mathbf{m}, \bar{\mathbf{m}}) = \sum_{j=1}^{N_a} w_j(\mathbf{m}_j, \bar{\mathbf{m}}). \tag{25}$$

From Eqs. (14) and (16), the selection gradient entry for trait ζ is

$$\left.\frac{\partial\lambda}{\partial\zeta}\right|_{\mathbf{y}=\bar{\mathbf{y}}} = \left.\frac{\partial w}{\partial\zeta}\right|_{\mathbf{y}=\bar{\mathbf{y}}} = \sum_{j=1}^{N_a}\left.\frac{\partial w_j}{\partial\zeta}\right|_{\mathbf{y}=\bar{\mathbf{y}}}.$$

The same procedure applies for total rather than partial derivatives, so the total selection gradient of ζ is

$$\left.\frac{\mathrm{d}\lambda}{\mathrm{d}\zeta}\right|_{\mathbf{y}=\bar{\mathbf{y}}} = \left.\frac{\mathrm{d}w}{\mathrm{d}\zeta}\right|_{\mathbf{y}=\bar{\mathbf{y}}} = \sum_{j=1}^{N_a}\left.\frac{\mathrm{d}w_j}{\mathrm{d}\zeta}\right|_{\mathbf{y}=\bar{\mathbf{y}}}. \tag{26}$$

It is often useful to write selection gradients in terms of lifetime reproductive success if possible. In Appendix C, we re-derive that the selection gradients can be expressed in terms of expected lifetime reproductive success, as previously known (Bulmer, 1994; Caswell, 2009), because of our assumption that mutants arise when residents are at carrying capacity (Mylius and Diekmann, 1995). For our life cycle, a mutant's expected lifetime reproductive success is

$$R_0 = \sum_{j=1}^{N_a} \ell_j f_j, \tag{27}$$

(Caswell, 2001). In Appendix C, we show that the selection gradient can be written as

$$\left.\frac{\partial\lambda}{\partial\zeta}\right|_{\mathbf{y}=\bar{\mathbf{y}}} = \frac{1}{T}\left.\frac{\partial R_0}{\partial\zeta}\right|_{\mathbf{y}=\bar{\mathbf{y}}}, \tag{28a}$$

and that the total selection gradient can be written as

$$\left.\frac{\mathrm{d}\lambda}{\mathrm{d}\zeta}\right|_{\mathbf{y}=\bar{\mathbf{y}}} = \frac{1}{T}\left.\frac{\mathrm{d}R_0}{\mathrm{d}\zeta}\right|_{\mathbf{y}=\bar{\mathbf{y}}}, \tag{28b}$$

which recover previous equations (Bulmer 1994, Eq. 25 of Ch. 5; and Caswell 2009, Eqs. 58-61).

4. The layers of the evo-devo process

We use the model above to obtain three main results. First, we obtain formulas for the total selection gradient of gene expression and underlying equations. Second, we obtain formulas and underlying equations for the evolutionary dynamics in gradient form for the phenotype and environment, which if considered on their own yield an underdetermined evolutionary system so the evolutionary trajectory is ill-defined. Third, we obtain formulas and underlying equations for the evolutionary dynamics in gradient form for the geno-phenotype and the geno-envo-phenotype, which if considered on their own yield a determined system giving a well-defined evolutionary trajectory. These results provide formulas for genetic covariation and other high-level quantities from low-level mechanistic processes. We term the resulting set of equations the "evo-devo process". The evo-devo process can be arranged in a layered structure, where each layer is formed by components in layers below (Fig. 5). This layered structure helps see how complex interactions between variables involved in genetic covariation are formed by building blocks describing the direct interaction between variables. We thus present the evo-devo process starting from the lowest-level layer up to the highest. The three main results highlighted above are given in the top layers 6 and 7, and the underlying equations are given in the lower level layers 2-5. The derivations of all these equations are provided in the Appendices.

4.1. Layer 1: elementary components

All the components of the evo-devo process can be calculated from five elementary components: the mutational covariance matrix $\mathbf{G}_{\mathbf{y}}$, fertility $f_a(\mathbf{m}_a, \bar{\mathbf{m}})$, survival probability $p_a(\mathbf{m}_a, \bar{\mathbf{m}})$, developmental map $\mathbf{g}_a(\mathbf{m}_a, \bar{\mathbf{z}})$, and environmental map $\mathbf{h}_a(\mathbf{z}_a, \bar{\mathbf{z}}, \tau)$ for all ages a (Fig. 5, Layer 1). Once these elementary components are available, either from purely theoretical models or using empirical data as well, all the remaining layers of the evo-devo process can be computed. These elementary components except for $\mathbf{G}_{\mathbf{y}}$ correspond to the elementary components of physiologically structured models of population dynamics, for which empirical estimation methods exist (de Roos, 1997).

4.2. Layer 2: direct effects

We now write the equations for the next layer, that of the direct-effect matrices which constitute nearly elementary components of the evo-devo process. Direct-effect matrices measure the direct effect that a variable has on another variable, that is, without considering developmental or environmental constraints. Direct-effect matrices capture various effects of age structure, including the declining forces of selection as age advances.

Direct-effect matrices include direct selection gradients, which have the following structure due to age-structure. The *direct selection gradient of the phenotype* or, equivalently, the block column vector of *direct effects of a mutant's phenotype on fitness* is

$$\left.\frac{\partial w}{\partial \mathbf{x}}\right|_{\mathbf{y}=\bar{\mathbf{y}}} \equiv \left.\left(\frac{\partial w}{\partial \mathbf{x}_1}; \cdots ; \frac{\partial w}{\partial \mathbf{x}_{N_\mathrm{a}}}\right)\right|_{\mathbf{y}=\bar{\mathbf{y}}} = \left.\left(\frac{\partial w_1}{\partial \mathbf{x}_1}; \cdots ; \frac{\partial w_{N_\mathrm{a}}}{\partial \mathbf{x}_{N_\mathrm{a}}}\right)\right|_{\mathbf{y}=\bar{\mathbf{y}}} \in \mathbb{R}^{N_\mathrm{a}N_\mathrm{s}\times 1}, \quad \text{(Layer 2, Eq. 1)}$$

which measures direct directional selection on the phenotype. Analogously, Lande's (1979) selection gradient measures direct directional selection under quantitative genetics assumptions. Note that the second line in Layer 2, Eq. 1 takes the derivative of fitness at each age, so from Eq. (23) each block entry in Layer 2, Eq. 1 is weighted by the forces of selection at each age. Thus, the selection gradients in Layer 2, Eq. 1 captures the declining forces of selection in that increasingly rightward block entries have smaller magnitude if survival and fertility effects are of the same magnitude as age increases. Similarly, the *direct selection gradient of gene expression* or, equivalently, the block column vector of *direct effects of a mutant's gene expression on fitness* is

$$\left.\frac{\partial w}{\partial \mathbf{y}}\right|_{\mathbf{y}=\bar{\mathbf{y}}} \equiv \left.\left(\frac{\partial w}{\partial \mathbf{y}_1}; \cdots ; \frac{\partial w}{\partial \mathbf{y}_{N_\mathrm{a}}}\right)\right|_{\mathbf{y}=\bar{\mathbf{y}}} = \left.\left(\frac{\partial w_1}{\partial \mathbf{y}_1}; \cdots ; \frac{\partial w_{N_\mathrm{a}}}{\partial \mathbf{y}_{N_\mathrm{a}}}\right)\right|_{\mathbf{y}=\bar{\mathbf{y}}} \in \mathbb{R}^{N_\mathrm{a}N_\mathrm{c}\times 1}, \quad \text{(Layer 2, Eq. 2)}$$

which measures direct directional selection on gene expression. The *direct selection gradient of the environment* or, equivalently, the block column vector of *direct effects of a mutant's environment on fitness* is

$$\left.\frac{\partial w}{\partial \boldsymbol{\epsilon}}\right|_{\mathbf{y}=\bar{\mathbf{y}}} \equiv \left.\left(\frac{\partial w}{\partial \boldsymbol{\epsilon}_1}; \cdots ; \frac{\partial w}{\partial \boldsymbol{\epsilon}_{N_\mathrm{a}}}\right)\right|_{\mathbf{y}=\bar{\mathbf{y}}} = \left.\left(\frac{\partial w_1}{\partial \boldsymbol{\epsilon}_1}; \cdots ; \frac{\partial w_{N_\mathrm{a}}}{\partial \boldsymbol{\epsilon}_{N_\mathrm{a}}}\right)\right|_{\mathbf{y}=\bar{\mathbf{y}}} \in \mathbb{R}^{N_\mathrm{a}N_\mathrm{e}\times 1}, \quad \text{(Layer 2, Eq. 3)}$$

which measures the environmental sensitivity of selection (Chevin et al., 2010). As for Layer 2, Eq. 1, the selection gradients in Layer 2, Eq. 2 and Layer 2, Eq. 3 capture the declining forces of selection in that increasingly rightward block entries have smaller magnitude if survival and fertility effects are of the same magnitude as age increases.

We use the above definitions to form the direct selection gradients of the geno-phenotype and geno-envo-phenotype. The *direct selection gradient of the geno-phenotype* is

$$\left.\frac{\partial w}{\partial \mathbf{z}}\right|_{\mathbf{y}=\bar{\mathbf{y}}} \equiv \left.\left(\frac{\partial w}{\partial \mathbf{x}}; \frac{\partial w}{\partial \mathbf{y}}\right)\right|_{\mathbf{y}=\bar{\mathbf{y}}} \in \mathbb{R}^{N_\mathrm{a}(N_\mathrm{s}+N_\mathrm{c})\times 1},$$

and the *direct selection gradient of the geno-envo-phenotype* is

$$\left.\frac{\partial w}{\partial \mathbf{m}}\right|_{\mathbf{y}=\bar{\mathbf{y}}} \equiv \left.\left(\frac{\partial w}{\partial \mathbf{x}}; \frac{\partial w}{\partial \mathbf{y}}; \frac{\partial w}{\partial \boldsymbol{\epsilon}}\right)\right|_{\mathbf{y}=\bar{\mathbf{y}}} \in \mathbb{R}^{N_\mathrm{a}(N_\mathrm{s}+N_\mathrm{c}+N_\mathrm{e})\times 1}.$$

Direct-effect matrices also include matrices that measure direct developmental bias. These matrices have specific, sparse structure due to *the arrow of developmental time*: changing a

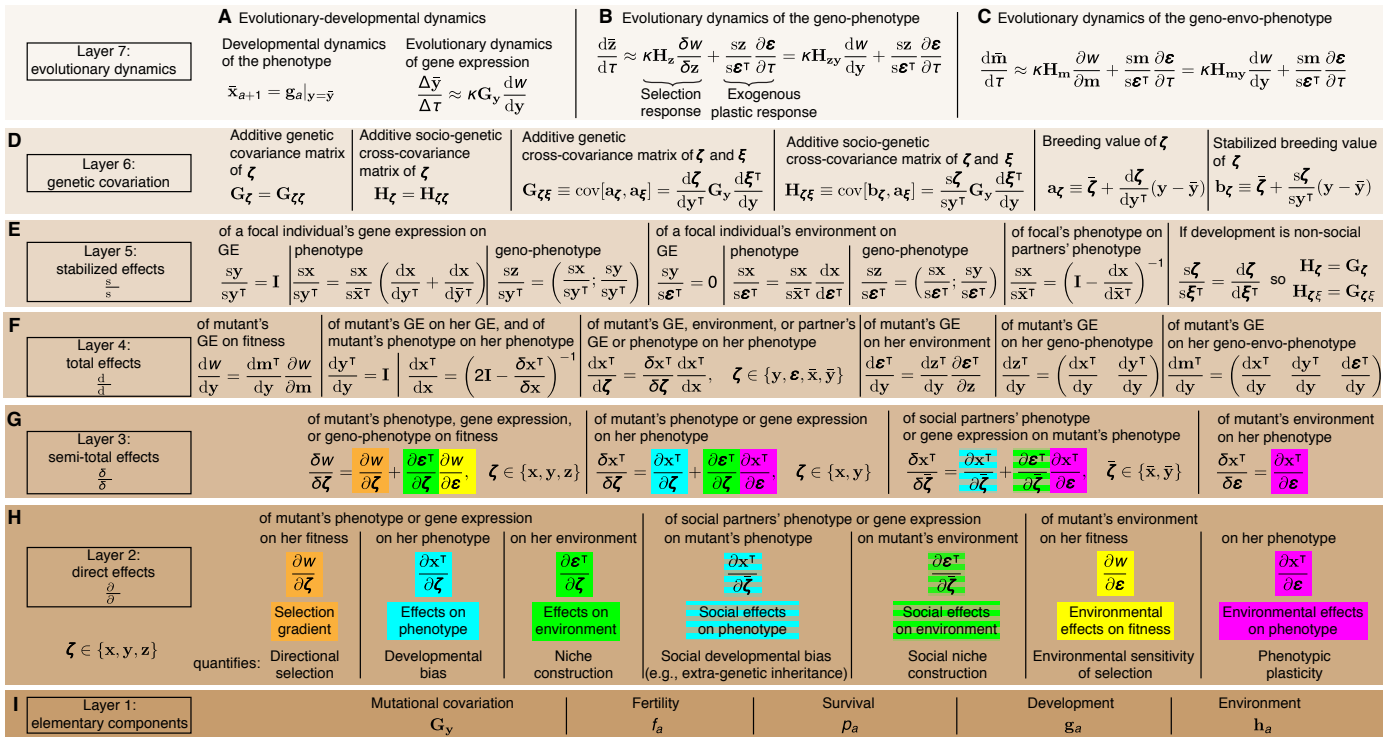

Figure 5: The evo-devo process and its layered structure. Here we summarize the equations composing the evo-devo process arranged in a layered structure. Each layer is formed by components in layers below. Layer 7 describes the evolutionary dynamics as (A) evo-devo dynamics, which implies (B) the evolutionary dynamics of the geno-phenotype, and (C) the evolutionary dynamics of the geno-envo-phenotype. (D) Layer 6 describes genetic covariation. (E) Layer 5 describes stabilized effects (total derivatives after socio-devo stabilization, denoted by s/s). (F) Layer 4 describes total effects (total derivatives before socio-devo stabilization, denoted by d/d, which consider both developmental and environmental constraints). (G) Layer 3 describes semi-total effects (semi-total derivatives, denoted by δ/δ, that is, total derivatives considering environmental but not developmental constraints). (H) Layer 2 describes direct effects (partial derivatives, denoted by ∂/∂, which do not consider any constraints). (I) Layer 1 comprises the elementary components of the evo-devo process that generate all layers above. All derivatives are evaluated at $\mathbf{y} = \bar{\mathbf{y}}$. See text for the equations of direct-effect matrices, which have structure due to age structure. See Fig. 2 and Table 1 for the meaning of symbols. GE: gene expression.

trait at a given age cannot have effects on the developmental past of the individual and only directly affects the developmental present or immediate future. The block matrix of *direct effects of a mutant's phenotype on her phenotype* is

$$\left.\frac{\partial \mathbf{x}^\intercal}{\partial \mathbf{x}}\right|_{\mathbf{y}=\bar{\mathbf{y}}} \equiv \left.\begin{pmatrix} \frac{\partial \mathbf{x}_1^\intercal}{\partial \mathbf{x}_1} & \cdots & \frac{\partial \mathbf{x}_{N_\mathrm{a}}^\intercal}{\partial \mathbf{x}_1} \\ \vdots & \ddots & \vdots \\ \frac{\partial \mathbf{x}_1^\intercal}{\partial \mathbf{x}_{N_\mathrm{a}}} & \cdots & \frac{\partial \mathbf{x}_{N_\mathrm{a}}^\intercal}{\partial \mathbf{x}_{N_\mathrm{a}}} \end{pmatrix}\right|_{\mathbf{y}=\bar{\mathbf{y}}}$$

$$= \left.\begin{pmatrix} \mathbf{I} & \frac{\partial \mathbf{x}_2^\intercal}{\partial \mathbf{x}_1} & \cdots & \mathbf{0} & \mathbf{0} \\ \mathbf{0} & \mathbf{I} & \cdots & \mathbf{0} & \mathbf{0} \\ \vdots & \vdots & \ddots & \vdots & \vdots \\ \mathbf{0} & \mathbf{0} & \cdots & \mathbf{I} & \frac{\partial \mathbf{x}_{N_\mathrm{a}}^\intercal}{\partial \mathbf{x}_{N_\mathrm{a}-1}} \\ \mathbf{0} & \mathbf{0} & \cdots & \mathbf{0} & \mathbf{I} \end{pmatrix}\right|_{\mathbf{y}=\bar{\mathbf{y}}} \quad \text{(Layer 2, Eq. 4a)}$$

$$\in \mathbb{R}^{N_\mathrm{a}N_\mathrm{s} \times N_\mathrm{a}N_\mathrm{s}},$$

which can be understood as measuring direct developmental bias from the phenotype. The equality (Layer 2, Eq. 4a) follows because the direct effects of a mutant's phenotype on her phenotype are only non-zero at the next age (from the developmental constraint in Eq. 1) or when the phenotypes are differentiated with respect to themselves. Analogously, the block matrix of *direct effects of a mutant's gene expression on her phenotype* is

$$\left.\frac{\partial \mathbf{x}^\intercal}{\partial \mathbf{y}}\right|_{\mathbf{y}=\bar{\mathbf{y}}} \equiv \left.\begin{pmatrix} \frac{\partial \mathbf{x}_1^\intercal}{\partial \mathbf{y}_1} & \cdots & \frac{\partial \mathbf{x}_{N_\mathrm{a}}^\intercal}{\partial \mathbf{y}_1} \\ \vdots & \ddots & \vdots \\ \frac{\partial \mathbf{x}_1^\intercal}{\partial \mathbf{y}_{N_\mathrm{a}}} & \cdots & \frac{\partial \mathbf{x}_{N_\mathrm{a}}^\intercal}{\partial \mathbf{y}_{N_\mathrm{a}}} \end{pmatrix}\right|_{\mathbf{y}=\bar{\mathbf{y}}}$$

$$= \left.\begin{pmatrix} \mathbf{0} & \frac{\partial \mathbf{x}_2^\intercal}{\partial \mathbf{y}_1} & \cdots & \mathbf{0} & \mathbf{0} \\ \mathbf{0} & \mathbf{0} & \cdots & \mathbf{0} & \mathbf{0} \\ \vdots & \vdots & \ddots & \vdots & \vdots \\ \mathbf{0} & \mathbf{0} & \cdots & \mathbf{0} & \frac{\partial \mathbf{x}_{N_\mathrm{a}}^\intercal}{\partial \mathbf{y}_{N_\mathrm{a}-1}} \\ \mathbf{0} & \mathbf{0} & \cdots & \mathbf{0} & \mathbf{0} \end{pmatrix}\right|_{\mathbf{y}=\bar{\mathbf{y}}} \quad \text{(Layer 2, Eq. 4b)}$$

$$\in \mathbb{R}^{N_\mathrm{a}N_\mathrm{c} \times N_\mathrm{a}N_\mathrm{s}},$$

which can be understood as measuring direct developmental

bias from gene expression. Note that the main block diagonal is zero.

Direct-effect matrices also include a matrix measuring direct plasticity. Indeed, the block matrix of *direct effects of a mutant's environment on her phenotype* is

$$\left.\frac{\partial \mathbf{x}^\intercal}{\partial \boldsymbol{\epsilon}}\right|_{\mathbf{y}=\bar{\mathbf{y}}} \equiv \left.\begin{pmatrix} \frac{\partial \mathbf{x}_1^\intercal}{\partial \boldsymbol{\epsilon}_1} & \cdots & \frac{\partial \mathbf{x}_{N_\mathrm{a}}^\intercal}{\partial \boldsymbol{\epsilon}_1} \\ \vdots & \ddots & \vdots \\ \frac{\partial \mathbf{x}_1^\intercal}{\partial \boldsymbol{\epsilon}_{N_\mathrm{a}}} & \cdots & \frac{\partial \mathbf{x}_{N_\mathrm{a}}^\intercal}{\partial \boldsymbol{\epsilon}_{N_\mathrm{a}}} \end{pmatrix}\right|_{\mathbf{y}=\bar{\mathbf{y}}}$$

$$= \left.\begin{pmatrix} \mathbf{0} & \frac{\partial \mathbf{x}_2^\intercal}{\partial \boldsymbol{\epsilon}_1} & \cdots & \mathbf{0} & \mathbf{0} \\ \mathbf{0} & \mathbf{0} & \cdots & \mathbf{0} & \mathbf{0} \\ \vdots & \vdots & \ddots & \vdots & \vdots \\ \mathbf{0} & \mathbf{0} & \cdots & \mathbf{0} & \frac{\partial \mathbf{x}_{N_\mathrm{a}}^\intercal}{\partial \boldsymbol{\epsilon}_{N_\mathrm{a}-1}} \\ \mathbf{0} & \mathbf{0} & \cdots & \mathbf{0} & \mathbf{0} \end{pmatrix}\right|_{\mathbf{y}=\bar{\mathbf{y}}} \qquad \text{(Layer 2, Eq. 4c)}$$

$$\in \mathbb{R}^{N_\mathrm{a}N_\mathrm{e}\times N_\mathrm{a}N_\mathrm{s}},$$

which can be understood as measuring the direct plasticity of the phenotype (Noble et al., 2019).

In turn, direct-effect matrices include matrices describing direct niche construction. The block matrix of *direct effects of a mutant's phenotype or gene expression on her environment* is

$$\left.\frac{\partial \boldsymbol{\epsilon}^\intercal}{\partial \boldsymbol{\zeta}}\right|_{\mathbf{y}=\bar{\mathbf{y}}} \equiv \left.\begin{pmatrix} \frac{\partial \boldsymbol{\epsilon}_1^\intercal}{\partial \boldsymbol{\zeta}_1} & \cdots & \frac{\partial \boldsymbol{\epsilon}_{N_\mathrm{a}}^\intercal}{\partial \boldsymbol{\zeta}_1} \\ \vdots & \ddots & \vdots \\ \frac{\partial \boldsymbol{\epsilon}_1^\intercal}{\partial \boldsymbol{\zeta}_{N_\mathrm{a}}} & \cdots & \frac{\partial \boldsymbol{\epsilon}_{N_\mathrm{a}}^\intercal}{\partial \boldsymbol{\zeta}_{N_\mathrm{a}}} \end{pmatrix}\right|_{\mathbf{y}=\bar{\mathbf{y}}}$$

$$= \left.\begin{pmatrix} \frac{\partial \boldsymbol{\epsilon}_1^\intercal}{\partial \boldsymbol{\zeta}_1} & \mathbf{0} & \cdots & \mathbf{0} & \mathbf{0} \\ \mathbf{0} & \frac{\partial \boldsymbol{\epsilon}_2^\intercal}{\partial \boldsymbol{\zeta}_2} & \cdots & \mathbf{0} & \mathbf{0} \\ \vdots & \vdots & \ddots & \vdots & \vdots \\ \mathbf{0} & \mathbf{0} & \cdots & \frac{\partial \boldsymbol{\epsilon}_{N_\mathrm{a}-1}^\intercal}{\partial \boldsymbol{\zeta}_{N_\mathrm{a}-1}} & \mathbf{0} \\ \mathbf{0} & \mathbf{0} & \cdots & \mathbf{0} & \frac{\partial \boldsymbol{\epsilon}_{N_\mathrm{a}}^\intercal}{\partial \boldsymbol{\zeta}_{N_\mathrm{a}}} \end{pmatrix}\right|_{\mathbf{y}=\bar{\mathbf{y}}} \qquad \text{(Layer 2, Eq. 4d)}$$

for $\boldsymbol{\zeta} \in \{\mathbf{x}, \mathbf{y}\}$, which can be understood as measuring direct niche construction by the phenotype or gene expression. The equality (Layer 2, Eq. 4d) follows from the environmental constraint in Eq. (2) since the environment faced by a mutant at a given age is directly affected by the mutant phenotype or gene expression at the same age only (i.e., $\partial \boldsymbol{\epsilon}_j^\intercal / \partial \boldsymbol{\zeta}_a = \mathbf{0}$ for $a \neq j$).

Direct-effect matrices also include matrices describing direct mutual environmental dependence. The block matrix of *direct effects of a mutant's environment on itself* is

$$\left.\frac{\partial \boldsymbol{\epsilon}^\intercal}{\partial \boldsymbol{\epsilon}}\right|_{\mathbf{y}=\bar{\mathbf{y}}} \equiv \left.\begin{pmatrix} \frac{\partial \boldsymbol{\epsilon}_1^\intercal}{\partial \boldsymbol{\epsilon}_1} & \cdots & \frac{\partial \boldsymbol{\epsilon}_{N_\mathrm{a}}^\intercal}{\partial \boldsymbol{\epsilon}_1} \\ \vdots & \ddots & \vdots \\ \frac{\partial \boldsymbol{\epsilon}_1^\intercal}{\partial \boldsymbol{\epsilon}_{N_\mathrm{a}}} & \cdots & \frac{\partial \boldsymbol{\epsilon}_{N_\mathrm{a}}^\intercal}{\partial \boldsymbol{\epsilon}_{N_\mathrm{a}}} \end{pmatrix}\right|_{\mathbf{y}=\bar{\mathbf{y}}}$$

$$= \left.\begin{pmatrix} \frac{\partial \boldsymbol{\epsilon}_1^\intercal}{\partial \boldsymbol{\epsilon}_1} & \mathbf{0} & \cdots & \mathbf{0} & \mathbf{0} \\ \mathbf{0} & \frac{\partial \boldsymbol{\epsilon}_2^\intercal}{\partial \boldsymbol{\epsilon}_2} & \cdots & \mathbf{0} & \mathbf{0} \\ \vdots & \vdots & \ddots & \vdots & \vdots \\ \mathbf{0} & \mathbf{0} & \cdots & \frac{\partial \boldsymbol{\epsilon}_{N_\mathrm{a}-1}^\intercal}{\partial \boldsymbol{\epsilon}_{N_\mathrm{a}-1}} & \mathbf{0} \\ \mathbf{0} & \mathbf{0} & \cdots & \mathbf{0} & \frac{\partial \boldsymbol{\epsilon}_{N_\mathrm{a}}^\intercal}{\partial \boldsymbol{\epsilon}_{N_\mathrm{a}}} \end{pmatrix}\right|_{\mathbf{y}=\bar{\mathbf{y}}}$$

$$= \mathbf{I} \in \mathbb{R}^{N_\mathrm{a}N_\mathrm{e}\times N_\mathrm{a}N_\mathrm{e}}, \qquad \text{(Layer 2, Eq. 5)}$$

which measures direct mutual environmental dependence. The second-to-last equality follows from the environmental constraint (Eq. 2) and the last equality follows from our assumption that environmental variables are mutually independent, so $\partial \boldsymbol{\epsilon}_a^\intercal / \partial \boldsymbol{\epsilon}_a|_{\mathbf{y}=\bar{\mathbf{y}}} = \mathbf{I}$ for all $a \in \{1, \ldots, N_\mathrm{a}\}$. It is conceptually useful to write $\partial \boldsymbol{\epsilon}^\intercal / \partial \boldsymbol{\epsilon}|_{\mathbf{y}=\bar{\mathbf{y}}}$ rather than only $\mathbf{I}$, and we do so throughout.

Additionally, direct-effect matrices include matrices describing direct social developmental bias, which capture effects of extra-genetic inheritance and indirect genetic effects. The block matrix of *direct effects of social partners' phenotype or gene expression on a mutant's phenotype* is

$$\left.\frac{\partial \mathbf{x}^\intercal}{\partial \bar{\boldsymbol{\zeta}}}\right|_{\mathbf{y}=\bar{\mathbf{y}}} \equiv \left.\begin{pmatrix} \frac{\partial \mathbf{x}_1^\intercal}{\partial \bar{\boldsymbol{\zeta}}_1} & \cdots & \frac{\partial \mathbf{x}_{N_\mathrm{a}}^\intercal}{\partial \bar{\boldsymbol{\zeta}}_1} \\ \vdots & \ddots & \vdots \\ \frac{\partial \mathbf{x}_1^\intercal}{\partial \bar{\boldsymbol{\zeta}}_{N_\mathrm{a}}} & \cdots & \frac{\partial \mathbf{x}_{N_\mathrm{a}}^\intercal}{\partial \bar{\boldsymbol{\zeta}}_{N_\mathrm{a}}} \end{pmatrix}\right|_{\mathbf{y}=\bar{\mathbf{y}}}$$

$$= \left.\begin{pmatrix} \mathbf{0} & \frac{\partial \mathbf{x}_2^\intercal}{\partial \bar{\boldsymbol{\zeta}}_1} & \cdots & \frac{\partial \mathbf{x}_{N_\mathrm{a}}^\intercal}{\partial \bar{\boldsymbol{\zeta}}_1} \\ \mathbf{0} & \frac{\partial \mathbf{x}_2^\intercal}{\partial \bar{\boldsymbol{\zeta}}_2} & \cdots & \frac{\partial \mathbf{x}_{N_\mathrm{a}}^\intercal}{\partial \bar{\boldsymbol{\zeta}}_2} \\ \vdots & \vdots & \ddots & \vdots \\ \mathbf{0} & \frac{\partial \mathbf{x}_2^\intercal}{\partial \bar{\boldsymbol{\zeta}}_{N_\mathrm{a}}} & \cdots & \frac{\partial \mathbf{x}_{N_\mathrm{a}}^\intercal}{\partial \bar{\boldsymbol{\zeta}}_{N_\mathrm{a}}} \end{pmatrix}\right|_{\mathbf{y}=\bar{\mathbf{y}}}, \qquad \text{(Layer 2, Eq. 6)}$$

for $\bar{\boldsymbol{\zeta}} \in \{\bar{\mathbf{x}}, \bar{\mathbf{y}}\}$, where the equality follows because the phenotype $\mathbf{x}_1$ at the initial age is constant by assumption. The matrix in Layer 2, Eq. 6 can be understood as measuring direct social developmental bias from either the phenotype or gene expression, including extra-genetic inheritance and indirect genetic effects. This matrix can be less sparse than direct-effect matrices above because the mutant's phenotype can be affected by the phenotype or gene expression of social partners of *any* age.

Direct-effect matrices also include matrices describing direct social niche construction. The block matrix of *direct effects*

of social partners' phenotype or gene expression on a mutant's environment is

$$\left.\frac{\partial \boldsymbol{\epsilon}^{\mathsf{T}}}{\partial \bar{\boldsymbol{\zeta}}}\right|_{\mathbf{y}=\bar{\mathbf{y}}} \equiv \left.\begin{pmatrix} \frac{\partial \boldsymbol{\epsilon}_1^{\mathsf{T}}}{\partial \bar{\boldsymbol{\zeta}}_1} & \cdots & \frac{\partial \boldsymbol{\epsilon}_{N_{\mathrm{a}}}^{\mathsf{T}}}{\partial \bar{\boldsymbol{\zeta}}_1} \\ \vdots & \ddots & \vdots \\ \frac{\partial \boldsymbol{\epsilon}_1^{\mathsf{T}}}{\partial \bar{\boldsymbol{\zeta}}_{N_{\mathrm{a}}}} & \cdots & \frac{\partial \boldsymbol{\epsilon}_{N_{\mathrm{a}}}^{\mathsf{T}}}{\partial \bar{\boldsymbol{\zeta}}_{N_{\mathrm{a}}}} \end{pmatrix}\right|_{\mathbf{y}=\bar{\mathbf{y}}}, \qquad \text{(Layer 2, Eq. 7)}$$

for $\bar{\boldsymbol{\zeta}} \in \{\bar{\mathbf{x}}, \bar{\mathbf{y}}\}$, which can be understood as measuring direct social niche construction by either the phenotype or gene expression. This matrix does not contain any zero entries in general because the mutant's environment at any age can be affected by the phenotype or gene expression of social partners of any age.

We use the above definitions to form direct-effect matrices involving the geno-phenotype. The block matrix of *direct effects of a mutant's geno-phenotype on her geno-phenotype* is

$$\left.\frac{\partial \mathbf{z}^{\mathsf{T}}}{\partial \mathbf{z}}\right|_{\mathbf{y}=\bar{\mathbf{y}}} \equiv \left.\begin{pmatrix} \frac{\partial \mathbf{x}^{\mathsf{T}}}{\partial \mathbf{x}} & \frac{\partial \mathbf{y}^{\mathsf{T}}}{\partial \mathbf{x}} \\ \frac{\partial \mathbf{x}^{\mathsf{T}}}{\partial \mathbf{y}} & \frac{\partial \mathbf{y}^{\mathsf{T}}}{\partial \mathbf{y}} \end{pmatrix}\right|_{\mathbf{y}=\bar{\mathbf{y}}} = \left.\begin{pmatrix} \frac{\partial \mathbf{x}^{\mathsf{T}}}{\partial \mathbf{x}} & \mathbf{0} \\ \frac{\partial \mathbf{x}^{\mathsf{T}}}{\partial \mathbf{y}} & \mathbf{I} \end{pmatrix}\right|_{\mathbf{y}=\bar{\mathbf{y}}} \qquad \text{(Layer 2, Eq. 8)}$$
$$\in \mathbb{R}^{N_{\mathrm{a}}(N_{\mathrm{s}}+N_{\mathrm{c}})\times N_{\mathrm{a}}(N_{\mathrm{s}}+N_{\mathrm{c}})},$$

which measures direct developmental bias of the geno-phenotype, and where the equality follows because gene expression is open-loop by assumption. The block matrix of *direct effects of a mutant's geno-phenotype on her environment* is

$$\left.\frac{\partial \boldsymbol{\epsilon}^{\mathsf{T}}}{\partial \mathbf{z}}\right|_{\mathbf{y}=\bar{\mathbf{y}}} \equiv \left.\left(\frac{\partial \boldsymbol{\epsilon}^{\mathsf{T}}}{\partial \mathbf{x}}; \frac{\partial \boldsymbol{\epsilon}^{\mathsf{T}}}{\partial \mathbf{y}}\right)\right|_{\mathbf{y}=\bar{\mathbf{y}}} \in \mathbb{R}^{N_{\mathrm{a}}(N_{\mathrm{s}}+N_{\mathrm{c}})\times N_{\mathrm{a}}N_{\mathrm{e}}}, \qquad \text{(Layer 2, Eq. 9)}$$

which measures direct niche construction by the geno-phenotype. The block matrix of *direct effects of social partners' geno-phenotypes on a mutant's environment* is

$$\left.\frac{\partial \boldsymbol{\epsilon}^{\mathsf{T}}}{\partial \bar{\mathbf{z}}}\right|_{\mathbf{y}=\bar{\mathbf{y}}} = \left.\left(\frac{\partial \boldsymbol{\epsilon}^{\mathsf{T}}}{\partial \bar{\mathbf{x}}}; \frac{\partial \boldsymbol{\epsilon}^{\mathsf{T}}}{\partial \bar{\mathbf{y}}}\right)\right|_{\mathbf{y}=\bar{\mathbf{y}}} \in \mathbb{R}^{N_{\mathrm{a}}(N_{\mathrm{s}}+N_{\mathrm{c}})\times N_{\mathrm{a}}N_{\mathrm{e}}}, \qquad \text{(Layer 2, Eq. 10)}$$

which measures direct social niche construction by partners' geno-phenotypes. The block matrix of *direct effects of a mutant's environment on her geno-phenotype* is

$$\left.\frac{\partial \mathbf{z}^{\mathsf{T}}}{\partial \boldsymbol{\epsilon}}\right|_{\mathbf{y}=\bar{\mathbf{y}}} \equiv \left.\begin{pmatrix} \frac{\partial \mathbf{x}^{\mathsf{T}}}{\partial \boldsymbol{\epsilon}} & \frac{\partial \mathbf{y}^{\mathsf{T}}}{\partial \boldsymbol{\epsilon}} \end{pmatrix}\right|_{\mathbf{y}=\bar{\mathbf{y}}} = \left.\begin{pmatrix} \frac{\partial \mathbf{x}^{\mathsf{T}}}{\partial \boldsymbol{\epsilon}} & \mathbf{0} \end{pmatrix}\right|_{\mathbf{y}=\bar{\mathbf{y}}} \qquad \text{(Layer 2, Eq. 11)}$$
$$\in \mathbb{R}^{N_{\mathrm{a}}N_{\mathrm{e}}\times N_{\mathrm{a}}(N_{\mathrm{s}}+N_{\mathrm{c}})},$$

which measures the direct plasticity of the geno-phenotype, and where the equality follows because gene expression is open-loop.

We will see that the evolutionary dynamics of the environment depends on a matrix measuring "inclusive" direct niche construction. This matrix is the transpose of the matrix of *direct social effects of a focal individual's geno-phenotype on hers and her partners' environment*

$$\left.\frac{\partial(\boldsymbol{\epsilon}+\check{\boldsymbol{\epsilon}})}{\partial \mathbf{z}^{\mathsf{T}}}\right|_{\mathbf{y}=\bar{\mathbf{y}}} = \left.\left(\frac{\partial \boldsymbol{\epsilon}}{\partial \mathbf{z}^{\mathsf{T}}} + \frac{\partial \boldsymbol{\epsilon}}{\partial \bar{\mathbf{z}}^{\mathsf{T}}}\right)\right|_{\mathbf{y}=\bar{\mathbf{y}}} \in \mathbb{R}^{N_{\mathrm{a}}N_{\mathrm{e}}\times N_{\mathrm{a}}(N_{\mathrm{s}}+N_{\mathrm{c}})}, \qquad \text{(Layer 2, Eq. 12)}$$

where we denote by $\check{\boldsymbol{\epsilon}}$ the environment a resident experiences when she develops in the context of mutants (a donor perspective for the mutant). Thus, this matrix can be interpreted as inclusive direct niche construction by the geno-phenotype. Note that the second term on the right-hand side of Layer 2, Eq. 12 is the direct effects of social partners' geno-phenotypes on a focal mutant (a recipient perspective for the mutant). Thus, inclusive direct niche construction by the geno-phenotype as described by Layer 2, Eq. 12 can be equivalently interpreted either from a donor or a recipient perspective.

4.3. Layer 3: semi-total effects

We now proceed to obtain the equations of the next layer of the evo-devo process, that of semi-total effects. Semi-total-effect matrices measure the total effects that a variable has on another variable considering environmental constraints, without considering developmental constraints (Appendix P). If there are no environmental variables, semi-total effect matrices ($\delta\boldsymbol{\zeta}^{\mathsf{T}}/\delta\boldsymbol{\xi}$) reduce to direct effect matrices ($\partial\boldsymbol{\zeta}^{\mathsf{T}}/\partial\boldsymbol{\xi}$).

Semi-total-effect matrices include semi-total selection gradients, which capture some of the effects of niche construction. The *semi-total selection gradient* of vector $\boldsymbol{\zeta} \in \{\mathbf{x}, \mathbf{y}, \mathbf{z}\}$ is

$$\left.\frac{\delta w}{\delta \boldsymbol{\zeta}}\right|_{\mathbf{y}=\bar{\mathbf{y}}} = \left.\left(\frac{\partial w}{\partial \boldsymbol{\zeta}} + \frac{\partial \boldsymbol{\epsilon}^{\mathsf{T}}}{\partial \boldsymbol{\zeta}}\frac{\partial w}{\partial \boldsymbol{\epsilon}}\right)\right|_{\mathbf{y}=\bar{\mathbf{y}}}. \qquad \text{(Layer 3, Eq. 1)}$$

Thus, the semi-total selection gradient of $\boldsymbol{\zeta}$ depends on direct directional selection on $\boldsymbol{\zeta}$, direct niche construction by $\boldsymbol{\zeta}$, and direct environmental sensitivity of selection, without considering developmental constraints. Consequently, semi-total selection gradients measure semi-total directional selection, which is directional selection in the fitness landscape modified by the interaction of niche construction and environmental sensitivity of selection. In a standard quantitative genetics framework, the semi-total selection gradients correspond to Lande's (1979) selection gradient if the environmental variables are not explicitly included in the analysis.

Semi-total selection on the environment equals directional selection on the environment because we assume environmental variables are mutually independent. The *semi-total selection gradient of the environment* is

$$\left.\frac{\delta w}{\delta \boldsymbol{\epsilon}}\right|_{\mathbf{y}=\bar{\mathbf{y}}} = \left.\left(\frac{\partial \boldsymbol{\epsilon}^{\mathsf{T}}}{\partial \boldsymbol{\epsilon}}\frac{\partial w}{\partial \boldsymbol{\epsilon}}\right)\right|_{\mathbf{y}=\bar{\mathbf{y}}} \in \mathbb{R}^{N_{\mathrm{a}}N_{\mathrm{e}}\times 1}. \qquad \text{(Layer 3, Eq. 2)}$$

Given our assumption that environmental variables are mutually independent, the matrix of direct effects of the environment on itself is the identity matrix. Thus, the semi-total selection gradient of the environment equals the selection gradient of the environment.

Semi-total-effect matrices also include matrices describing semi-total developmental bias, which capture additional effects of niche construction. The block matrix of *semi-total effects of* $\boldsymbol{\zeta} \in \{\mathbf{x}, \mathbf{y}, \bar{\mathbf{x}}, \bar{\mathbf{y}}\}$ *on a mutant's phenotype* is

$$\left.\frac{\delta \mathbf{x}^{\intercal}}{\delta \boldsymbol{\zeta}}\right|_{\mathbf{y}=\bar{\mathbf{y}}} = \left.\left(\frac{\partial \mathbf{x}^{\intercal}}{\partial \boldsymbol{\zeta}} + \frac{\partial \boldsymbol{\epsilon}^{\intercal}}{\partial \boldsymbol{\zeta}} \frac{\partial \mathbf{x}^{\intercal}}{\partial \boldsymbol{\epsilon}}\right)\right|_{\mathbf{y}=\bar{\mathbf{y}}}. \qquad \text{(Layer 3, Eq. 3)}$$

Thus, the semi-total effects of $\boldsymbol{\zeta}$ on the phenotype depend on the direct developmental bias from $\boldsymbol{\zeta}$, direct niche construction by $\boldsymbol{\zeta}$, and the direct plasticity of the phenotype, without considering developmental constraints. Consequently, semi-total effects on the phenotype can be interpreted as measuring semi-total developmental bias, which measures developmental bias in the developmental process modified by the interaction of niche construction and plasticity.

Moreover, semi-total-effect matrices include matrices describing semi-total plasticity of the phenotype, which equals plasticity of the phenotype because environmental variables are mutually independent by assumption. The block matrix of *semi-total effects of a mutant's environment on her phenotype* is

$$\left.\frac{\delta \mathbf{x}^{\intercal}}{\delta \boldsymbol{\epsilon}}\right|_{\mathbf{y}=\bar{\mathbf{y}}} = \left.\frac{\partial \boldsymbol{\epsilon}^{\intercal}}{\partial \boldsymbol{\epsilon}} \frac{\partial \mathbf{x}^{\intercal}}{\partial \boldsymbol{\epsilon}}\right|_{\mathbf{y}=\bar{\mathbf{y}}} \in \mathbb{R}^{N_{\mathrm{a}}N_{\mathrm{e}} \times N_{\mathrm{a}}N_{\mathrm{s}}}. \qquad \text{(Layer 3, Eq. 4)}$$

Given our assumption that environmental variables are mutually independent, the matrix of direct effects of the environment on itself is the identity matrix. Thus, the semi-total plasticity of the phenotype equals the plasticity of the phenotype.

We use the above definitions to form a matrix quantifying the semi-total developmental bias of the geno-phenotype. The block matrix of *semi-total effects of a mutant's geno-phenotype on her geno-phenotype* is

$$\left.\frac{\delta \mathbf{z}^{\intercal}}{\delta \mathbf{z}}\right|_{\mathbf{y}=\bar{\mathbf{y}}} = \left.\left(\frac{\partial \mathbf{z}^{\intercal}}{\partial \mathbf{z}} + \frac{\partial \boldsymbol{\epsilon}^{\intercal}}{\partial \mathbf{z}} \frac{\partial \mathbf{z}^{\intercal}}{\partial \boldsymbol{\epsilon}}\right)\right|_{\mathbf{y}=\bar{\mathbf{y}}} \qquad \text{(Layer 3, Eq. 5)}$$
$$\in \mathbb{R}^{N_{\mathrm{a}}(N_{\mathrm{s}}+N_{\mathrm{c}}) \times N_{\mathrm{a}}(N_{\mathrm{s}}+N_{\mathrm{c}})},$$

which can be interpreted as measuring the semi-total developmental bias of the geno-phenotype. Consequently, the semi-total developmental bias of the geno-phenotype depends on the direct developmental bias of the geno-phenotype, direct niche construction by the geno-phenotype, and direct plasticity of the geno-phenotype.

4.4. Layer 4: total effects

We now move to obtain equations for the next layer of the evo-devo process, that of total-effect matrices. Total-effect matrices measure the total effects of a variable on another one considering both developmental and environmental constraints, but before the effects of social development have stabilized in the population.

The total effects of the phenotype on itself describe the developmental feedback of the phenotype. The block matrix of *total effects of a mutant's phenotype on her phenotype* is

$$\left.\frac{\mathrm{d}\mathbf{x}^{\intercal}}{\mathrm{d}\mathbf{x}}\right|_{\mathbf{y}=\bar{\mathbf{y}}} = \left.\left(2\mathbf{I} - \frac{\delta \mathbf{x}^{\intercal}}{\delta \mathbf{x}}\right)^{-1}\right|_{\mathbf{y}=\bar{\mathbf{y}}} = \sum_{a=1}^{N_{\mathrm{a}}} \left(\frac{\delta \mathbf{x}^{\intercal}}{\delta \mathbf{x}} - \mathbf{I}\right)^{a-1}$$
$$\in \mathbb{R}^{N_{\mathrm{a}}N_{\mathrm{s}} \times N_{\mathrm{a}}N_{\mathrm{s}}}, \qquad \text{(Layer 4, Eq. 1)}$$

which we prove is always invertible (Appendix D, Eq. D15) and where the last equality follows by the geometric series of matrices. This matrix can be interpreted as a lifetime collection of developmentally immediate pulses of semi-total effects of the phenotype on itself. Thus, the total effects of the phenotype on itself describe total developmental bias of the phenotype, or the *developmental feedback* of the phenotype. Developmental feedback may cause major phenotypic effects at subsequent ages, because its block entries involve matrix products:

$$\frac{\mathrm{d}\mathbf{x}_j^{\intercal}}{\mathrm{d}\mathbf{x}_a} = \begin{cases} \overset{\curvearrowright}{\prod_{k=a}^{j-1}} \frac{\delta \mathbf{x}_{k+1}^{\intercal}}{\delta \mathbf{x}_k} = \frac{\delta \mathbf{x}_{a+1}^{\intercal}}{\delta \mathbf{x}_a} \cdots \frac{\delta \mathbf{x}_j^{\intercal}}{\delta \mathbf{x}_{j-1}} & \text{for } j > a \\ \mathbf{I} & \text{for } j = a \\ \mathbf{0} & \text{for } j < a. \end{cases}$$
(Layer 4, Eq. 2)

Since matrix multiplication is not commutative, the $\curvearrowright$ denotes right multiplication. By depending on the semi-total developmental bias from the phenotype, the developmental feedback of the phenotype depends on direct developmental bias from the phenotype, direct niche-construction by the phenotype, and direct plasticity of the phenotype (Layer 3, Eq. 3). Layer 4, Eq. 1 has the same form of an equation for total effects used in path analysis (Greene 1977, p. 380; see also Morrissey 2014, Eq. 2) if $(\delta \mathbf{x}^{\intercal}/\delta \mathbf{x} - \mathbf{I})|_{\mathbf{y}=\bar{\mathbf{y}}}$ is interpreted as a matrix listing the path coefficients of "direct" effects of the phenotype on itself (direct, but without explicitly considering environmental variables).

The total effects of gene expression on the phenotype correspond to Fisher's additive effects of allelic substitution and Wagner's developmental matrix. The block matrix of *total effects of a mutant's gene expression on her phenotype* is given by

$$\left.\frac{\mathrm{d}\mathbf{x}^{\intercal}}{\mathrm{d}\mathbf{y}}\right|_{\mathbf{y}=\bar{\mathbf{y}}} = \left.\left(\frac{\delta \mathbf{x}^{\intercal}}{\delta \mathbf{y}} \frac{\mathrm{d}\mathbf{x}^{\intercal}}{\mathrm{d}\mathbf{x}}\right)\right|_{\mathbf{y}=\bar{\mathbf{y}}} \in \mathbb{R}^{N_{\mathrm{a}}N_{\mathrm{c}} \times N_{\mathrm{a}}N_{\mathrm{s}}}, \qquad \text{(Layer 4, Eq. 3)}$$

which is singular because the developmentally initial phenotype is not affected by gene expression (by our assumption that the initial phenotype is constant) and the developmentally final gene expression does not affect the phenotype (by our assumption that individuals do not survive after the final age; so $\mathrm{d}\mathbf{x}^{\intercal}/\mathrm{d}\mathbf{y}|_{\mathbf{y}=\bar{\mathbf{y}}}$ has rows and columns that are zero; Appendix E, Eq. E16). From Layer 4, Eq. 3, this matrix can be interpreted as involving a developmentally immediate pulse caused by a change in gene expression followed by the triggered developmental feedback of the phenotype. The matrix of total effects of gene expression on the phenotype measures total developmental bias of the phenotype from gene expression. The entries of the matrix of total effects of gene expression on the phenotype are a mechanistic version of Fisher's additive effect of allelic substitution, which he defined as regression coefficients (his α; see Eq. I of Fisher 1918 and p. 72 of Lynch and Walsh 1998). Also, this matrix corresponds to Wagner's (1984, 1989) developmental matrix (his $\mathbf{B}$) (see also Martin 2014), Rice's (2002) rank-1 $\mathbf{D}$ tensor, and Morrissey's (2015) total effect ma-

trix (his $\mathbf{\Phi}$) (interpreting these authors' partial derivatives as total derivatives).

The total effects of the environment on the phenotype measure the total plasticity of the phenotype. The block matrix of *total effects of a mutant's environment on her phenotype* is

$$\left.\frac{\mathrm{d}\mathbf{x}^\intercal}{\mathrm{d}\boldsymbol{\epsilon}}\right|_{\mathbf{y}=\bar{\mathbf{y}}} = \left.\left(\frac{\delta\mathbf{x}^\intercal}{\delta\boldsymbol{\epsilon}}\frac{\mathrm{d}\mathbf{x}^\intercal}{\mathrm{d}\mathbf{x}}\right)\right|_{\mathbf{y}=\bar{\mathbf{y}}} \in \mathbb{R}^{N_\mathrm{a}N_\mathrm{e}\times N_\mathrm{a}N_\mathrm{s}}, \qquad \text{(Layer 4, Eq. 4)}$$

which measures the total plasticity of the phenotype, considering both environmental and developmental constraints. Thus, the total plasticity of the phenotype can be interpreted as a developmentally immediate pulse of plastic change in the phenotype followed by the triggered developmental feedback of the phenotype.

The total effects of social partners' gene expression or phenotype on the phenotype measure the total *social* developmental bias of the phenotype. The block matrix of *total effects of social partners' phenotype or gene expression on a mutant's phenotype* is

$$\left.\frac{\mathrm{d}\mathbf{x}^\intercal}{\mathrm{d}\bar{\boldsymbol{\zeta}}}\right|_{\mathbf{y}=\bar{\mathbf{y}}} = \left.\left(\frac{\delta\mathbf{x}^\intercal}{\delta\bar{\boldsymbol{\zeta}}}\frac{\mathrm{d}\mathbf{x}^\intercal}{\mathrm{d}\mathbf{x}}\right)\right|_{\mathbf{y}=\bar{\mathbf{y}}} \qquad \text{(Layer 4, Eq. 5)}$$

for $\bar{\boldsymbol{\zeta}} \in \{\bar{\mathbf{x}}, \bar{\mathbf{y}}\}$. This matrix can be interpreted as measuring total social developmental bias of the phenotype from phenotype or gene expression, as well as the total effects on the phenotype of extra-genetic inheritance, and as total indirect genetic effects. In particular, the matrix of total social developmental bias of the phenotype from phenotype, $\mathrm{d}\mathbf{x}^\intercal/\mathrm{d}\bar{\mathbf{x}}|_{\mathbf{y}=\bar{\mathbf{y}}}$, is a mechanistic version of the matrix of interaction coefficients in the indirect genetic effects literature (i.e., $\mathbf{\Psi}$ in Eq. 17 of Moore et al. 1997, which is defined as a matrix of regression coefficients). From Layer 4, Eq. 5, the total social developmental bias of the phenotype can be interpreted as a developmentally immediate pulse of phenotype change caused by a change in social partners' traits followed by the triggered developmental feedback of the mutant's phenotype.

The total effects on gene expression are simple since gene expression is open-loop by assumption. The block matrix of *total effects of a mutant's gene expression on itself* is

$$\left.\frac{\mathrm{d}\mathbf{y}^\intercal}{\mathrm{d}\mathbf{y}}\right|_{\mathbf{y}=\bar{\mathbf{y}}} = \mathbf{I} \in \mathbb{R}^{N_\mathrm{a}N_\mathrm{c}\times N_\mathrm{a}N_\mathrm{c}}, \qquad \text{(Layer 4, Eq. 6)}$$

and the block matrix of *total effects of a vector* $\boldsymbol{\zeta} \in \{\mathbf{x}, \boldsymbol{\epsilon}, \bar{\mathbf{x}}, \bar{\mathbf{y}}, \bar{\mathbf{z}}, \bar{\boldsymbol{\epsilon}}, \bar{\mathbf{m}}\}$ *on a mutant's gene expression* is

$$\left.\frac{\mathrm{d}\mathbf{y}^\intercal}{\mathrm{d}\boldsymbol{\zeta}}\right|_{\mathbf{y}=\bar{\mathbf{y}}} = \mathbf{0}.$$

These two equations follow because we assume that gene expression is open-loop (Appendix E, Eq. E13).

We can use some of the previous total-effect matrices to construct the following total-effect matrices involving the geno-phenotype. The block matrix of *total effects of a mutant's phenotype on her geno-phenotype* is

$$\left.\frac{\mathrm{d}\mathbf{z}^\intercal}{\mathrm{d}\mathbf{x}}\right|_{\mathbf{y}=\bar{\mathbf{y}}} \equiv \left.\begin{pmatrix}\frac{\mathrm{d}\mathbf{x}^\intercal}{\mathrm{d}\mathbf{x}} & \frac{\mathrm{d}\mathbf{y}^\intercal}{\mathrm{d}\mathbf{x}}\end{pmatrix}\right|_{\mathbf{y}=\bar{\mathbf{y}}}$$
$$= \left.\begin{pmatrix}\frac{\mathrm{d}\mathbf{x}^\intercal}{\mathrm{d}\mathbf{x}} & \mathbf{0}\end{pmatrix}\right|_{\mathbf{y}=\bar{\mathbf{y}}} \in \mathbb{R}^{N_\mathrm{a}N_\mathrm{s}\times N_\mathrm{a}(N_\mathrm{s}+N_\mathrm{c})}, \qquad \text{(Layer 4, Eq. 7)}$$

measuring total developmental bias of the geno-phenotype from the phenotype. The block matrix of *total effects of gene expression on her geno-phenotype* is

$$\left.\frac{\mathrm{d}\mathbf{z}^\intercal}{\mathrm{d}\mathbf{y}}\right|_{\mathbf{y}=\bar{\mathbf{y}}} \equiv \left.\begin{pmatrix}\frac{\mathrm{d}\mathbf{x}^\intercal}{\mathrm{d}\mathbf{y}} & \frac{\mathrm{d}\mathbf{y}^\intercal}{\mathrm{d}\mathbf{y}}\end{pmatrix}\right|_{\mathbf{y}=\bar{\mathbf{y}}}$$
$$= \left.\begin{pmatrix}\frac{\mathrm{d}\mathbf{x}^\intercal}{\mathrm{d}\mathbf{y}} & \mathbf{I}\end{pmatrix}\right|_{\mathbf{y}=\bar{\mathbf{y}}} \in \mathbb{R}^{N_\mathrm{a}N_\mathrm{c}\times N_\mathrm{a}(N_\mathrm{s}+N_\mathrm{c})}, \qquad \text{(Layer 4, Eq. 8)}$$

measuring total developmental bias of the geno-phenotype from gene expression. This matrix $\mathrm{d}\mathbf{z}^\intercal/\mathrm{d}\mathbf{y}|_{\mathbf{y}=\bar{\mathbf{y}}}$ is singular because any matrix with fewer rows than columns is singular (Horn and Johnson, 2013, p. 14). This singularity will be important when we consider additive genetic covariances. Now, the block matrix of *total effects of a mutant's geno-phenotype on her geno-phenotype* is

$$\left.\frac{\mathrm{d}\mathbf{z}^\intercal}{\mathrm{d}\mathbf{z}}\right|_{\mathbf{y}=\bar{\mathbf{y}}} \equiv \left.\begin{pmatrix}\frac{\mathrm{d}\mathbf{x}^\intercal}{\mathrm{d}\mathbf{x}} & \frac{\mathrm{d}\mathbf{y}^\intercal}{\mathrm{d}\mathbf{x}} \\ \frac{\mathrm{d}\mathbf{x}^\intercal}{\mathrm{d}\mathbf{y}} & \frac{\mathrm{d}\mathbf{y}^\intercal}{\mathrm{d}\mathbf{y}}\end{pmatrix}\right|_{\mathbf{y}=\bar{\mathbf{y}}} = \left.\begin{pmatrix}\frac{\mathrm{d}\mathbf{x}^\intercal}{\mathrm{d}\mathbf{x}} & \mathbf{0} \\ \frac{\mathrm{d}\mathbf{x}^\intercal}{\mathrm{d}\mathbf{y}} & \mathbf{I}\end{pmatrix}\right|_{\mathbf{y}=\bar{\mathbf{y}}}$$
$$= \left.\left(2\mathbf{I} - \frac{\delta\mathbf{z}^\intercal}{\delta\mathbf{z}}\right)^{-1}\right|_{\mathbf{y}=\bar{\mathbf{y}}} = \sum_{a=1}^{N_\mathrm{a}}\left(\frac{\delta\mathbf{z}^\intercal}{\delta\mathbf{z}} - \mathbf{I}\right)^{a-1} \qquad \text{(Layer 4, Eq. 9)}$$
$$\in \mathbb{R}^{N_\mathrm{a}(N_\mathrm{s}+N_\mathrm{c})\times N_\mathrm{a}(N_\mathrm{s}+N_\mathrm{c})},$$

which can be interpreted as measuring the developmental feedback of the geno-phenotype (Appendix G, Eq. G4). Since $\mathrm{d}\mathbf{z}^\intercal/\mathrm{d}\mathbf{z}|_{\mathbf{y}=\bar{\mathbf{y}}}$ is square and block lower triangular, and since $\mathrm{d}\mathbf{x}^\intercal/\mathrm{d}\mathbf{x}|_{\mathbf{y}=\bar{\mathbf{y}}}$ is invertible (Appendix D, Eq. D15), we have that $\mathrm{d}\mathbf{z}^\intercal/\mathrm{d}\mathbf{z}|_{\mathbf{y}=\bar{\mathbf{y}}}$ is invertible.

Moreover, the total effects of the phenotype and gene expression on the environment quantify total niche construction. Total niche construction by the phenotype is quantified by the block matrix of *total effects of a mutant's phenotype on her environment*

$$\left.\frac{\mathrm{d}\boldsymbol{\epsilon}^\intercal}{\mathrm{d}\mathbf{x}}\right|_{\mathbf{y}=\bar{\mathbf{y}}} = \left.\left(\frac{\mathrm{d}\mathbf{x}^\intercal}{\mathrm{d}\mathbf{x}}\frac{\partial\boldsymbol{\epsilon}^\intercal}{\partial\mathbf{x}}\right)\right|_{\mathbf{y}=\bar{\mathbf{y}}}$$
$$= \left.\left(\frac{\mathrm{d}\mathbf{z}^\intercal}{\mathrm{d}\mathbf{x}}\frac{\partial\boldsymbol{\epsilon}^\intercal}{\partial\mathbf{z}}\right)\right|_{\mathbf{y}=\bar{\mathbf{y}}} \in \mathbb{R}^{N_\mathrm{a}N_\mathrm{s}\times N_\mathrm{a}N_\mathrm{e}}, \qquad \text{(Layer 4, Eq. 10)}$$

which can be interpreted as showing that developmental feedback of the phenotype occurs first and then direct niche-constructing effects by the phenotype follow. Similarly, total niche construction by gene expression is quantified by the block matrix of *total effects of a mutant's gene expression on her environment*

$$\left.\frac{\mathrm{d}\boldsymbol{\epsilon}^\intercal}{\mathrm{d}\mathbf{y}}\right|_{\mathbf{y}=\bar{\mathbf{y}}} = \left.\left(\frac{\mathrm{d}\mathbf{x}^\intercal}{\mathrm{d}\mathbf{y}}\frac{\partial\boldsymbol{\epsilon}^\intercal}{\partial\mathbf{x}} + \frac{\partial\boldsymbol{\epsilon}^\intercal}{\partial\mathbf{y}}\right)\right|_{\mathbf{y}=\bar{\mathbf{y}}}$$
$$= \left.\left(\frac{\mathrm{d}\mathbf{z}^\intercal}{\mathrm{d}\mathbf{y}}\frac{\partial\boldsymbol{\epsilon}^\intercal}{\partial\mathbf{z}}\right)\right|_{\mathbf{y}=\bar{\mathbf{y}}} \in \mathbb{R}^{N_\mathrm{a}N_\mathrm{c}\times N_\mathrm{a}N_\mathrm{e}}, \qquad \text{(Layer 4, Eq. 11)}$$

which depends on direct niche construction by gene expression and on total developmental bias of the phenotype from gene expression followed by niche construction by the phenotype. The analogous relationship holds for total niche construction by the geno-phenotype, quantified by the block matrix of *total effects of a mutant's geno-phenotype on her environment*

$$\left.\frac{\mathrm{d}\boldsymbol{\epsilon}^{\mathsf{T}}}{\mathrm{d}\mathbf{z}}\right|_{\mathbf{y}=\bar{\mathbf{y}}} = \left.\left(\frac{\mathrm{d}\mathbf{z}^{\mathsf{T}}}{\mathrm{d}\mathbf{z}}\frac{\partial\boldsymbol{\epsilon}^{\mathsf{T}}}{\partial\mathbf{z}}\right)\right|_{\mathbf{y}=\bar{\mathbf{y}}} \in \mathbb{R}^{N_{\mathrm{a}}(N_{\mathrm{s}}+N_{\mathrm{c}})\times N_{\mathrm{a}}N_{\mathrm{e}}}, \qquad \text{(Layer 4, Eq. 12)}$$

which depends on the developmental feedback of the geno-phenotype and direct niche construction by the geno-phenotype.

The total effects of the environment on itself quantify environmental feedback. The block matrix of *total effects of a mutant's environment on her environment* is

$$\left.\frac{\mathrm{d}\boldsymbol{\epsilon}^{\mathsf{T}}}{\mathrm{d}\boldsymbol{\epsilon}}\right|_{\mathbf{y}=\bar{\mathbf{y}}} = \left.\left(\frac{\partial\boldsymbol{\epsilon}^{\mathsf{T}}}{\partial\boldsymbol{\epsilon}} + \frac{\mathrm{d}\mathbf{x}^{\mathsf{T}}}{\mathrm{d}\boldsymbol{\epsilon}}\frac{\partial\boldsymbol{\epsilon}^{\mathsf{T}}}{\partial\mathbf{x}}\right)\right|_{\mathbf{y}=\bar{\mathbf{y}}} \in \mathbb{R}^{N_{\mathrm{a}}N_{\mathrm{e}}\times N_{\mathrm{a}}N_{\mathrm{e}}}, \qquad \text{(Layer 4, Eq. 13)}$$

which is always invertible (Appendix F, Eq. F5). This matrix can be interpreted as measuring *environmental feedback*, which depends on direct mutual environmental dependence, total plasticity of the phenotype, and direct niche construction by the phenotype.

We can also use some of the following previous total-effect matrices to construct the following total-effect matrices involving the geno-envo-phenotype. The block matrix of *total effects of a mutant's phenotype on her geno-envo-phenotype* is

$$\begin{aligned}\left.\frac{\mathrm{d}\mathbf{m}^{\mathsf{T}}}{\mathrm{d}\mathbf{x}}\right|_{\mathbf{y}=\bar{\mathbf{y}}} &\equiv \left.\begin{pmatrix}\frac{\mathrm{d}\mathbf{x}^{\mathsf{T}}}{\mathrm{d}\mathbf{x}} & \frac{\mathrm{d}\mathbf{y}^{\mathsf{T}}}{\mathrm{d}\mathbf{x}} & \frac{\mathrm{d}\boldsymbol{\epsilon}^{\mathsf{T}}}{\mathrm{d}\mathbf{x}}\end{pmatrix}\right|_{\mathbf{y}=\bar{\mathbf{y}}} \\ &= \left.\begin{pmatrix}\frac{\mathrm{d}\mathbf{x}^{\mathsf{T}}}{\mathrm{d}\mathbf{x}} & \mathbf{0} & \frac{\mathrm{d}\boldsymbol{\epsilon}^{\mathsf{T}}}{\mathrm{d}\mathbf{x}}\end{pmatrix}\right|_{\mathbf{y}=\bar{\mathbf{y}}} \qquad \text{(Layer 4, Eq. 14)} \\ &\in \mathbb{R}^{N_{\mathrm{a}}N_{\mathrm{s}}\times N_{\mathrm{a}}(N_{\mathrm{s}}+N_{\mathrm{c}}+N_{\mathrm{e}})},\end{aligned}$$

measuring total developmental bias of the geno-envo-phenotype from the phenotype. The block matrix of *total effects of a mutant's gene expression on her geno-envo-phenotype* is

$$\begin{aligned}\left.\frac{\mathrm{d}\mathbf{m}^{\mathsf{T}}}{\mathrm{d}\mathbf{y}}\right|_{\mathbf{y}=\bar{\mathbf{y}}} &\equiv \left.\begin{pmatrix}\frac{\mathrm{d}\mathbf{x}^{\mathsf{T}}}{\mathrm{d}\mathbf{y}} & \frac{\mathrm{d}\mathbf{y}^{\mathsf{T}}}{\mathrm{d}\mathbf{y}} & \frac{\mathrm{d}\boldsymbol{\epsilon}^{\mathsf{T}}}{\mathrm{d}\mathbf{y}}\end{pmatrix}\right|_{\mathbf{y}=\bar{\mathbf{y}}} \\ &= \left.\begin{pmatrix}\frac{\mathrm{d}\mathbf{x}^{\mathsf{T}}}{\mathrm{d}\mathbf{y}} & \mathbf{I} & \frac{\mathrm{d}\boldsymbol{\epsilon}^{\mathsf{T}}}{\mathrm{d}\mathbf{y}}\end{pmatrix}\right|_{\mathbf{y}=\bar{\mathbf{y}}} \qquad \text{(Layer 4, Eq. 15)} \\ &\in \mathbb{R}^{N_{\mathrm{a}}N_{\mathrm{c}}\times N_{\mathrm{a}}(N_{\mathrm{s}}+N_{\mathrm{c}}+N_{\mathrm{e}})},\end{aligned}$$

measuring total developmental bias of the geno-envo-phenotype from gene expression, and which is singular because it has fewer rows than columns.

The block matrix of *total effects of a mutant's environment on her geno-envo-phenotype* is

$$\begin{aligned}\left.\frac{\mathrm{d}\mathbf{m}^{\mathsf{T}}}{\mathrm{d}\boldsymbol{\epsilon}}\right|_{\mathbf{y}=\bar{\mathbf{y}}} &= \left.\begin{pmatrix}\frac{\mathrm{d}\mathbf{x}^{\mathsf{T}}}{\mathrm{d}\boldsymbol{\epsilon}} & \frac{\mathrm{d}\mathbf{y}^{\mathsf{T}}}{\mathrm{d}\boldsymbol{\epsilon}} & \frac{\mathrm{d}\boldsymbol{\epsilon}^{\mathsf{T}}}{\mathrm{d}\boldsymbol{\epsilon}}\end{pmatrix}\right|_{\mathbf{y}=\bar{\mathbf{y}}} \\ &= \left.\begin{pmatrix}\frac{\mathrm{d}\mathbf{x}^{\mathsf{T}}}{\mathrm{d}\boldsymbol{\epsilon}} & \mathbf{0} & \frac{\mathrm{d}\boldsymbol{\epsilon}^{\mathsf{T}}}{\mathrm{d}\boldsymbol{\epsilon}}\end{pmatrix}\right|_{\mathbf{y}=\bar{\mathbf{y}}} \qquad \text{(Layer 4, Eq. 16)} \\ &\in \mathbb{R}^{N_{\mathrm{a}}N_{\mathrm{e}}\times N_{\mathrm{a}}(N_{\mathrm{s}}+N_{\mathrm{c}}+N_{\mathrm{e}})},\end{aligned}$$

measuring total plasticity of the geno-envo-phenotype. The block matrix of *total effects of a mutant's geno-phenotype on her geno-envo-phenotype* is

$$\begin{aligned}\left.\frac{\mathrm{d}\mathbf{m}^{\mathsf{T}}}{\mathrm{d}\mathbf{z}}\right|_{\mathbf{y}=\bar{\mathbf{y}}} &\equiv \left.\begin{pmatrix}\frac{\mathrm{d}\mathbf{m}^{\mathsf{T}}}{\mathrm{d}\mathbf{x}} \\ \frac{\mathrm{d}\mathbf{m}^{\mathsf{T}}}{\mathrm{d}\mathbf{y}}\end{pmatrix}\right|_{\mathbf{y}=\bar{\mathbf{y}}} = \left.\begin{pmatrix}\frac{\mathrm{d}\mathbf{x}^{\mathsf{T}}}{\mathrm{d}\mathbf{x}} & \mathbf{0} & \frac{\mathrm{d}\boldsymbol{\epsilon}^{\mathsf{T}}}{\mathrm{d}\mathbf{x}} \\ \frac{\mathrm{d}\mathbf{x}^{\mathsf{T}}}{\mathrm{d}\mathbf{y}} & \mathbf{I} & \frac{\mathrm{d}\boldsymbol{\epsilon}^{\mathsf{T}}}{\mathrm{d}\mathbf{y}}\end{pmatrix}\right|_{\mathbf{y}=\bar{\mathbf{y}}} \qquad \text{(Layer 4, Eq. 17)} \\ &\in \mathbb{R}^{N_{\mathrm{a}}(N_{\mathrm{s}}+N_{\mathrm{c}})\times N_{\mathrm{a}}(N_{\mathrm{s}}+N_{\mathrm{c}}+N_{\mathrm{e}})},\end{aligned}$$

measuring total developmental bias of the geno-envo-phenotype from the geno-phenotype. The block matrix of *total effects of a mutant's geno-envo-phenotype on her geno-envo-phenotype* is

$$\begin{aligned}\left.\frac{\mathrm{d}\mathbf{m}^{\mathsf{T}}}{\mathrm{d}\mathbf{m}}\right|_{\mathbf{y}=\bar{\mathbf{y}}} &= \left.\begin{pmatrix}\frac{\mathrm{d}\mathbf{m}^{\mathsf{T}}}{\mathrm{d}\mathbf{x}} \\ \frac{\mathrm{d}\mathbf{m}^{\mathsf{T}}}{\mathrm{d}\mathbf{y}} \\ \frac{\mathrm{d}\mathbf{m}^{\mathsf{T}}}{\mathrm{d}\boldsymbol{\epsilon}}\end{pmatrix}\right|_{\mathbf{y}=\bar{\mathbf{y}}} = \left.\begin{pmatrix}\frac{\mathrm{d}\mathbf{x}^{\mathsf{T}}}{\mathrm{d}\mathbf{x}} & \mathbf{0} & \frac{\mathrm{d}\boldsymbol{\epsilon}^{\mathsf{T}}}{\mathrm{d}\mathbf{x}} \\ \frac{\mathrm{d}\mathbf{x}^{\mathsf{T}}}{\mathrm{d}\mathbf{y}} & \mathbf{I} & \frac{\mathrm{d}\boldsymbol{\epsilon}^{\mathsf{T}}}{\mathrm{d}\mathbf{y}} \\ \frac{\mathrm{d}\mathbf{x}^{\mathsf{T}}}{\mathrm{d}\boldsymbol{\epsilon}} & \mathbf{0} & \frac{\mathrm{d}\boldsymbol{\epsilon}^{\mathsf{T}}}{\mathrm{d}\boldsymbol{\epsilon}}\end{pmatrix}\right|_{\mathbf{y}=\bar{\mathbf{y}}} \qquad \text{(Layer 4, Eq. 18)} \\ &\in \mathbb{R}^{N_{\mathrm{a}}(N_{\mathrm{s}}+N_{\mathrm{c}}+N_{\mathrm{e}})\times N_{\mathrm{a}}(N_{\mathrm{s}}+N_{\mathrm{c}}+N_{\mathrm{e}})},\end{aligned}$$

measuring developmental feedback of the geno-envo-phenotype, and which we show is invertible (Appendix H). Obtaining a compact form for $\mathrm{d}\mathbf{m}^{\mathsf{T}}/\mathrm{d}\mathbf{m}|_{\mathbf{y}=\bar{\mathbf{y}}}$ analogous to Layer 4, Eq. 9 seemingly needs $(\mathrm{d}\boldsymbol{\epsilon}^{\mathsf{T}}/\mathrm{d}\boldsymbol{\epsilon}|_{\mathbf{y}=\bar{\mathbf{y}}})^{-1}$ which appears to yield relatively complex expressions so we leave this for future analysis.

We will see that the evolutionary dynamics of the phenotype depends on a matrix measuring "inclusive" total developmental bias of the phenotype. This matrix is the transpose of the matrix of *total social effects of a focal individual's gene expression or phenotype on hers and her partners' phenotypes*

$$\left.\frac{\mathrm{d}(\mathbf{x}+\check{\mathbf{x}})}{\mathrm{d}\boldsymbol{\zeta}^{\mathsf{T}}}\right|_{\mathbf{y}=\bar{\mathbf{y}}} = \left.\left(\frac{\mathrm{d}\mathbf{x}}{\mathrm{d}\boldsymbol{\zeta}^{\mathsf{T}}} + \frac{\mathrm{d}\mathbf{x}}{\mathrm{d}\bar{\boldsymbol{\zeta}}^{\mathsf{T}}}\right)\right|_{\mathbf{y}=\bar{\mathbf{y}}}, \qquad \text{(Layer 4, Eq. 19)}$$

for $\boldsymbol{\zeta} \in \{\mathbf{x}, \mathbf{y}\}$ where we denote by $\check{\mathbf{x}}$ the phenotype that a resident develops in the context of mutants (a donor perspective for the mutant). Thus, this matrix can be interpreted as measuring inclusive total developmental bias of the phenotype. Note that the second term on the right-hand side of Layer 4, Eq. 19 is the total effects of social partners' phenotype or gene expression on a focal mutant (a recipient perspective for the mutant). Thus, the inclusive total developmental bias of the phenotype as described by Layer 4, Eq. 19 can be equivalently interpreted either from a donor or a recipient perspective.

Having written expressions for the above total-effect matrices, we can now write the total selection gradients, which measure total directional selection, that is, directional selection considering both developmental and environmental constraints. In other words, while Lande's (1979) selection gradient is the

direct selection gradient measuring the direct effect of a variable on fitness in Fig. 2, total selection gradients measure the effect of a variable on fitness across all paths in Fig. 2 (see also Morrissey 2014). In Appendices D-H, we show that the total selection gradient of vector $\boldsymbol{\zeta} \in \{\mathbf{x}, \mathbf{y}, \mathbf{z}, \boldsymbol{\epsilon}, \mathbf{m}\}$ is

$$\left.\frac{\mathrm{d}w}{\mathrm{d}\boldsymbol{\zeta}}\right|_{\mathbf{y}=\bar{\mathbf{y}}} = \left.\left(\frac{\mathrm{d}\mathbf{m}^{\intercal}}{\mathrm{d}\boldsymbol{\zeta}}\frac{\partial w}{\partial \mathbf{m}}\right)\right|_{\mathbf{y}=\bar{\mathbf{y}}}, \qquad \text{(Layer 4, Eq. 20)}$$

which has the form of the chain rule in matrix notation. Hence, the total selection gradient of $\boldsymbol{\zeta}$ depends on direct directional selection on the geno-envo-phenotype and the total effects of $\boldsymbol{\zeta}$ on the geno-envo-phenotype. Consequently, the total selection gradient of $\boldsymbol{\zeta}$ measures total directional selection on $\boldsymbol{\zeta}$, which is directional selection on the geno-envo-phenotype transformed by the total effects of $\boldsymbol{\zeta}$ on the geno-envo-phenotype considering developmental and environmental constraints. Layer 4, Eq. 20 has the same form of previous expressions by Caswell (e.g., Caswell, 1982, Eq. 4 and Caswell, 2001, Eq. 9.38), except that it is in terms of traits rather than vital rates (i.e, Caswell's equations have the entries of the matrix in Eq. 10 in the place of $\mathbf{m}$). Layer 4, Eq. 20 also recovers the form of Morrissey's (2014) extended selection gradient. Total selection gradients take the following particular forms.

The total selection gradient of the phenotype is

$$\begin{aligned}\left.\frac{\mathrm{d}w}{\mathrm{d}\mathbf{x}}\right|_{\mathbf{y}=\bar{\mathbf{y}}} &= \left.\left(\frac{\mathrm{d}\mathbf{x}^{\intercal}}{\mathrm{d}\mathbf{x}}\frac{\partial w}{\partial \mathbf{x}} + \frac{\mathrm{d}\boldsymbol{\epsilon}^{\intercal}}{\mathrm{d}\mathbf{x}}\frac{\partial w}{\partial \boldsymbol{\epsilon}}\right)\right|_{\mathbf{y}=\bar{\mathbf{y}}} \qquad \text{(Layer 4, Eq. 21)}\\ &= \left.\left(\frac{\mathrm{d}\mathbf{x}^{\intercal}}{\mathrm{d}\mathbf{x}}\frac{\delta w}{\delta \mathbf{x}}\right)\right|_{\mathbf{y}=\bar{\mathbf{y}}}\\ &= \left.\left(\frac{\mathrm{d}\mathbf{z}^{\intercal}}{\mathrm{d}\mathbf{x}}\frac{\delta w}{\delta \mathbf{z}}\right)\right|_{\mathbf{y}=\bar{\mathbf{y}}}\\ &= \left.\left(\frac{\mathrm{d}\mathbf{m}^{\intercal}}{\mathrm{d}\mathbf{x}}\frac{\partial w}{\partial \mathbf{m}}\right)\right|_{\mathbf{y}=\bar{\mathbf{y}}}.\end{aligned}$$

This gradient depends on direct directional selection on the phenotype (Layer 2, Eq. 1) and direct directional selection on the environment (Layer 2, Eq. 3). It also depends on developmental feedback of the phenotype (Layer 4, Eq. 1) and total niche construction by the phenotype, which also depends on developmental feedback of the phenotype (Layer 4, Eq. 10). Consequently, the total selection gradient of the phenotype can be interpreted as measuring total directional selection on the phenotype in the fitness landscape modified by developmental feedback of the phenotype and by the interaction of total niche construction and environmental sensitivity of selection.

The total selection gradient of gene expression is

$$\begin{aligned}\left.\frac{\mathrm{d}w}{\mathrm{d}\mathbf{y}}\right|_{\mathbf{y}=\bar{\mathbf{y}}} &= \left.\left(\frac{\mathrm{d}\mathbf{x}^{\intercal}}{\mathrm{d}\mathbf{y}}\frac{\partial w}{\partial \mathbf{x}} + \frac{\partial w}{\partial \mathbf{y}} + \frac{\mathrm{d}\boldsymbol{\epsilon}^{\intercal}}{\mathrm{d}\mathbf{y}}\frac{\partial w}{\partial \boldsymbol{\epsilon}}\right)\right|_{\mathbf{y}=\bar{\mathbf{y}}} \qquad \text{(Layer 4, Eq. 22)}\\ &= \left.\left(\frac{\mathrm{d}\mathbf{x}^{\intercal}}{\mathrm{d}\mathbf{y}}\frac{\delta w}{\delta \mathbf{x}} + \frac{\delta w}{\delta \mathbf{y}}\right)\right|_{\mathbf{y}=\bar{\mathbf{y}}}\\ &= \left.\left(\frac{\mathrm{d}\mathbf{z}^{\intercal}}{\mathrm{d}\mathbf{y}}\frac{\delta w}{\delta \mathbf{z}}\right)\right|_{\mathbf{y}=\bar{\mathbf{y}}}\\ &= \left.\left(\frac{\mathrm{d}\mathbf{m}^{\intercal}}{\mathrm{d}\mathbf{y}}\frac{\partial w}{\partial \mathbf{m}}\right)\right|_{\mathbf{y}=\bar{\mathbf{y}}}\\ &= \left.\left(\frac{\delta\mathbf{x}^{\intercal}}{\delta \mathbf{y}}\frac{\mathrm{d}w}{\mathrm{d}\mathbf{x}} + \frac{\delta w}{\delta \mathbf{y}}\right)\right|_{\mathbf{y}=\bar{\mathbf{y}}}.\end{aligned}$$

This gradient not only depends on direct directional selection on the phenotype and the environment, but also on direct directional selection on gene expression (Layer 2, Eq. 2). It also depends on Fisher's (1918) additive effects of allelic substitution or Wagner's (1984, 1989) developmental matrix (Layer 4, Eq. 3) and on total niche construction by gene expression, which also depends on the developmental matrix (Layer 4, Eq. 11). Consequently, the total selection gradient of gene expression can be interpreted as measuring total (directional) genetic selection in a fitness landscape modified by the interaction of total developmental bias of the phenotype from gene expression and directional selection on the phenotype and by the interaction of total niche construction by gene expression and environmental sensitivity of selection. In a standard quantitative genetics framework, the total selection gradient of gene expression would correspond to Lande's (1979) selection gradient of gene expression if developed traits and environmental variables were not explicitly included in the analysis. The fifth line of Layer 4, Eq. 22 has the form of previous expressions for the total selection gradient of controls in continuous age in terms of partial derivatives of the Hamiltonian, which lacked closed-form formulas for costate variables (e.g., Day and Taylor 1997, Eq. 4, Day and Taylor 2000, Eq. 6, Avila et al. 2021, Eq. 23), which we provide as formulas for the total selection gradient of states (Layer 4, Eq. 21) (see also Appendix M).

To derive equations describing the evolutionary dynamics of the geno-envo-phenotype, we make use of the total selection gradient of the environment, although such gradient is not necessary to obtain equations describing the evolutionary dynamics of the geno-phenotype. The total selection gradient of the environment is

$$\begin{aligned}\left.\frac{\mathrm{d}w}{\mathrm{d}\boldsymbol{\epsilon}}\right|_{\mathbf{y}=\bar{\mathbf{y}}} &= \left.\left(\frac{\mathrm{d}\mathbf{x}^{\intercal}}{\mathrm{d}\boldsymbol{\epsilon}}\frac{\partial w}{\partial \mathbf{x}} + \frac{\mathrm{d}\boldsymbol{\epsilon}^{\intercal}}{\mathrm{d}\boldsymbol{\epsilon}}\frac{\partial w}{\partial \boldsymbol{\epsilon}}\right)\right|_{\mathbf{y}=\bar{\mathbf{y}}} \qquad \text{(Layer 4, Eq. 23)}\\ &= \left.\left(\frac{\mathrm{d}\mathbf{x}^{\intercal}}{\mathrm{d}\boldsymbol{\epsilon}}\frac{\delta w}{\delta \mathbf{x}} + \frac{\delta w}{\delta \boldsymbol{\epsilon}}\right)\right|_{\mathbf{y}=\bar{\mathbf{y}}}\\ &= \left.\left(\frac{\mathrm{d}\mathbf{m}^{\intercal}}{\mathrm{d}\boldsymbol{\epsilon}}\frac{\partial w}{\partial \mathbf{m}}\right)\right|_{\mathbf{y}=\bar{\mathbf{y}}}\\ &= \left.\left(\frac{\delta\mathbf{x}^{\intercal}}{\delta \boldsymbol{\epsilon}}\frac{\mathrm{d}w}{\mathrm{d}\mathbf{x}} + \frac{\delta w}{\delta \boldsymbol{\epsilon}}\right)\right|_{\mathbf{y}=\bar{\mathbf{y}}}.\end{aligned}$$

This gradient depends on total plasticity of the phenotype and on environmental feedback, which in turn depends on total plasticity of the phenotype and niche construction by the phenotype (Layer 4, Eq. 13). Consequently, the total selection gradient of the environment can be understood as measuring total directional selection on the environment in a fitness landscape modified by environmental feedback and by the interaction of total plasticity of the phenotype and direct directional selection on the phenotype.

We can combine the expressions for the total selection gradients above to obtain the total selection gradient of the geno-phenotype and the geno-envo-phenotype. The total selection gradient of the geno-phenotype is

$$\left.\frac{\mathrm{d}w}{\mathrm{d}\mathbf{z}}\right|_{\mathbf{y}=\bar{\mathbf{y}}} = \left.\left(\frac{\mathrm{d}\mathbf{z}^{\intercal}}{\mathrm{d}\mathbf{z}}\frac{\partial w}{\partial \mathbf{z}} + \frac{\mathrm{d}\boldsymbol{\epsilon}^{\intercal}}{\mathrm{d}\mathbf{z}}\frac{\partial w}{\partial \boldsymbol{\epsilon}}\right)\right|_{\mathbf{y}=\bar{\mathbf{y}}} \qquad \text{(Layer 4, Eq. 24)}$$
$$= \left.\left(\frac{\mathrm{d}\mathbf{z}^{\intercal}}{\mathrm{d}\mathbf{z}}\frac{\delta w}{\delta \mathbf{z}}\right)\right|_{\mathbf{y}=\bar{\mathbf{y}}}$$
$$= \left.\left(\frac{\mathrm{d}\mathbf{m}^{\intercal}}{\mathrm{d}\mathbf{z}}\frac{\partial w}{\partial \mathbf{m}}\right)\right|_{\mathbf{y}=\bar{\mathbf{y}}}.$$

Thus, the total selection gradient of the geno-phenotype can be interpreted as measuring total (directional) geno-phenotypic selection in a fitness landscape modified by developmental feedback of the geno-phenotype and by the interaction of total niche construction by the geno-phenotype and environmental sensitivity of selection. In turn, the total selection gradient of the geno-envo-phenotype is

$$\left.\frac{\mathrm{d}w}{\mathrm{d}\mathbf{m}}\right|_{\mathbf{y}=\bar{\mathbf{y}}} = \left.\left(\frac{\mathrm{d}\mathbf{m}^{\intercal}}{\mathrm{d}\mathbf{m}}\frac{\partial w}{\partial \mathbf{m}}\right)\right|_{\mathbf{y}=\bar{\mathbf{y}}}, \qquad \text{(Layer 4, Eq. 25)}$$

which can be interpreted as measuring total (directional) geno-envo-phenotypic selection in a fitness landscape modified by developmental feedback of the geno-envo-phenotype.

4.5. Layer 5: stabilized effects

We now move on to obtain equations for the next layer of the evo-devo process, that of (socio-devo) stabilized-effect matrices. Stabilized-effect matrices measure the total effects of a variable on another one considering both developmental and environmental constraints, after the effects of social development have stabilized in the population. Stabilized-effect matrices arise in the derivation of the evolutionary dynamics of the phenotype and environment as a result of social development. If development is not social (i.e., $\mathrm{d}\mathbf{x}^{\intercal}/\mathrm{d}\bar{\mathbf{z}}|_{\mathbf{y}=\bar{\mathbf{y}}} = \mathbf{0}$), then all stabilized-effect matrices ($\mathrm{s}\boldsymbol{\zeta}^{\intercal}/\mathrm{s}\boldsymbol{\xi}|_{\mathbf{y}=\bar{\mathbf{y}}}$) reduce to the corresponding total-effect matrices ($\mathrm{d}\boldsymbol{\zeta}^{\intercal}/\mathrm{d}\boldsymbol{\xi}|_{\mathbf{y}=\bar{\mathbf{y}}}$), except one ($\mathrm{s}\mathbf{x}^{\intercal}/\mathrm{s}\bar{\mathbf{x}}|_{\mathbf{y}=\bar{\mathbf{y}}}$) that reduces to the identity matrix.

The stabilized effects of social partners' phenotypes on a focal individual's phenotype measure social feedback. The transpose of the matrix of *stabilized effects of social partners' phenotypes on a focal individual's phenotype* is

$$\left.\frac{\mathrm{s}\mathbf{x}}{\mathrm{s}\bar{\mathbf{x}}^{\intercal}}\right|_{\mathbf{y}=\bar{\mathbf{y}}} = \left(\mathbf{I} - \left.\frac{\mathrm{d}\check{\mathbf{x}}}{\mathrm{d}\mathbf{x}^{\intercal}}\right|_{\mathbf{y}=\bar{\mathbf{y}}}\right)^{-1} = \left(\mathbf{I} - \left.\frac{\mathrm{d}\mathbf{x}}{\mathrm{d}\bar{\mathbf{x}}^{\intercal}}\right|_{\mathbf{y}=\bar{\mathbf{y}}}\right)^{-1}$$
$$= \left.\sum_{\theta=1}^{\infty}\left(\frac{\mathrm{d}\mathbf{x}}{\mathrm{d}\bar{\mathbf{x}}^{\intercal}}\right)^{\theta-1}\right|_{\mathbf{y}=\bar{\mathbf{y}}} \in \mathbb{R}^{N_{\mathrm{a}}N_{\mathrm{s}}\times N_{\mathrm{a}}N_{\mathrm{s}}}, \qquad \text{(Layer 5, Eq. 1)}$$

where the last equality follows by the geometric series of matrices. The matrix $\mathrm{s}\mathbf{x}/\mathrm{s}\bar{\mathbf{x}}^{\intercal}|_{\mathbf{y}=\bar{\mathbf{y}}}$ is invertible by our assumption that all the eigenvalues of $\mathrm{d}\mathbf{x}/\mathrm{d}\bar{\mathbf{x}}^{\intercal}|_{\mathbf{y}=\bar{\mathbf{y}}}$ have absolute value strictly less than one, to guarantee that the resident is socio-devo stable. The matrix $\mathrm{s}\mathbf{x}/\mathrm{s}\bar{\mathbf{x}}^{\intercal}|_{\mathbf{y}=\bar{\mathbf{y}}}$ can be interpreted as as a collection of total effects of social partners' phenotypes on a focal individual's phenotype over socio-devo stabilization (Eq. 5); or vice versa, of a focal individual's phenotype on social partners' phenotypes. Thus, the matrix $\mathrm{s}\mathbf{x}/\mathrm{s}\bar{\mathbf{x}}^{\intercal}|_{\mathbf{y}=\bar{\mathbf{y}}}$ describes *social feedback* arising from social development. This matrix corresponds to an analogous matrix found in the indirect genetic effects literature (Moore et al., 1997, Eq. 19b and subsequent text). If development is not social from the phenotype (i.e., $\mathrm{d}\mathbf{x}^{\intercal}/\mathrm{d}\bar{\mathbf{x}}|_{\mathbf{y}=\bar{\mathbf{y}}} = \mathbf{0}$), then the matrix $\mathrm{s}\mathbf{x}/\mathrm{s}\bar{\mathbf{x}}^{\intercal}|_{\mathbf{y}=\bar{\mathbf{y}}}$ is the identity matrix. This is the only stabilized-effect matrix that does not reduce to the corresponding total-effect matrix when development is not social.

The stabilized effects of a focal individual's phenotype or gene expression on her phenotype measure stabilized developmental bias. We define the transpose of the matrix of *stabilized effects of a focal individual's phenotype or gene expression on her phenotype* as

$$\left.\frac{\mathrm{s}\mathbf{x}}{\mathrm{s}\boldsymbol{\zeta}^{\intercal}}\right|_{\mathbf{y}=\bar{\mathbf{y}}} = \left.\left(\frac{\mathrm{s}\mathbf{x}}{\mathrm{s}\bar{\mathbf{x}}^{\intercal}}\frac{\mathrm{d}(\mathbf{x}+\check{\mathbf{x}})}{\mathrm{d}\boldsymbol{\zeta}^{\intercal}}\right)\right|_{\mathbf{y}=\bar{\mathbf{y}}}, \qquad \text{(Layer 5, Eq. 2a)}$$

for $\boldsymbol{\zeta} \in \{\mathbf{x}, \mathbf{y}\}$. This matrix can be interpreted as measuring stabilized developmental bias of the phenotype from $\boldsymbol{\zeta}$, where a focal individual's gene expression or phenotype first affect the development of her own and social partners' phenotype which then feedback to affect the individual's phenotype. Stabilized developmental bias is "inclusive" in that it includes both the effects of the focal individual on herself and on social partners. If development is not social (i.e., $\mathrm{d}\mathbf{x}^{\intercal}/\mathrm{d}\bar{\mathbf{z}}|_{\mathbf{y}=\bar{\mathbf{y}}} = \mathbf{0}$), then a stabilized developmental bias matrix ($\mathrm{s}\mathbf{x}/\mathrm{s}\boldsymbol{\zeta}^{\intercal}|_{\mathbf{y}=\bar{\mathbf{y}}}$) reduces to the corresponding total developmental bias matrix ($\mathrm{d}\mathbf{x}/\mathrm{d}\boldsymbol{\zeta}^{\intercal}|_{\mathbf{y}=\bar{\mathbf{y}}}$).

The stabilized effects of the environment on the phenotype measure stabilized plasticity. The transpose of the matrix of *stabilized effects of a focal individual's environment on the phenotype* is

$$\left.\frac{\mathrm{s}\mathbf{x}}{\mathrm{s}\boldsymbol{\epsilon}^{\intercal}}\right|_{\mathbf{y}=\bar{\mathbf{y}}} = \left.\left(\frac{\mathrm{s}\mathbf{x}}{\mathrm{s}\bar{\mathbf{x}}^{\intercal}}\frac{\mathrm{d}\mathbf{x}}{\mathrm{d}\boldsymbol{\epsilon}^{\intercal}}\right)\right|_{\mathbf{y}=\bar{\mathbf{y}}} \in \mathbb{R}^{N_{\mathrm{a}}N_{\mathrm{s}}\times N_{\mathrm{a}}N_{\mathrm{e}}}. \qquad \text{(Layer 5, Eq. 2b)}$$

This matrix can be interpreted as measuring stabilized plasticity of the phenotype, where the environment first causes total plasticity in a focal individual and then the focal individual causes stabilized social effects on social partners. Stabilized plasticity does not depend on the inclusive effects of the environment. If development is not social (i.e., $\mathrm{d}\mathbf{x}^{\intercal}/\mathrm{d}\bar{\mathbf{z}}|_{\mathbf{y}=\bar{\mathbf{y}}} = \mathbf{0}$), then stabilized plasticity reduces to total plasticity.

The stabilized effects on gene expression are simple since gene expression is open-loop by assumption. The transpose of the matrix of *stabilized effects of a focal individual's phenotype or environment on gene expression* is

$$\left.\frac{\mathrm{s}\mathbf{y}}{\mathrm{s}\boldsymbol{\zeta}^{\intercal}}\right|_{\mathbf{y}=\bar{\mathbf{y}}} = \left.\frac{\mathrm{d}\mathbf{y}}{\mathrm{d}\boldsymbol{\zeta}^{\intercal}}\right|_{\mathbf{y}=\bar{\mathbf{y}}} = \mathbf{0}, \qquad \text{(Layer 5, Eq. 3a)}$$

for $\boldsymbol{\zeta} \in \{\mathbf{x}, \boldsymbol{\epsilon}\}$. The transpose of the matrix of *stabilized effects of a focal individual's gene expression on gene expression* is

$$\left.\frac{\mathrm{s}\mathbf{y}}{\mathrm{s}\mathbf{y}^{\intercal}}\right|_{\mathbf{y}=\bar{\mathbf{y}}} = \left.\frac{\mathrm{d}\mathbf{y}}{\mathrm{d}\mathbf{y}^{\intercal}}\right|_{\mathbf{y}=\bar{\mathbf{y}}} = \mathbf{I} \quad \in \mathbb{R}^{N_{\mathrm{a}}N_{\mathrm{c}}\times N_{\mathrm{a}}N_{\mathrm{c}}}. \qquad \text{(Layer 5, Eq. 3b)}$$

These two equations follow because gene expression is assumed to be open-loop.

We can use some of the previous stabilized-effect matrices to construct the following stabilized-effect matrices involving the geno-phenotype. The transpose of the matrix of *stabilized effects of a focal individual's gene expression on the geno-phenotype* is

$$\left.\frac{\mathrm{s}\mathbf{z}}{\mathrm{s}\mathbf{y}^{\mathsf{T}}}\right|_{\mathbf{y}=\bar{\mathbf{y}}} \equiv \left.\left(\frac{\mathrm{s}\mathbf{x}}{\mathrm{s}\mathbf{y}^{\mathsf{T}}};\frac{\mathrm{s}\mathbf{y}}{\mathrm{s}\mathbf{y}^{\mathsf{T}}}\right)\right|_{\mathbf{y}=\bar{\mathbf{y}}} \in \mathbb{R}^{N_{\mathrm{a}}(N_{\mathrm{s}}+N_{\mathrm{c}})\times N_{\mathrm{a}}N_{\mathrm{c}}}, \tag{Layer 5, Eq. 4a}$$

measuring stabilized developmental bias of the geno-phenotype from gene expression. The transpose of the matrix of *stabilized effects of a focal individual's environment on the geno-phenotype* is

$$\left.\frac{\mathrm{s}\mathbf{z}}{\mathrm{s}\boldsymbol{\epsilon}^{\mathsf{T}}}\right|_{\mathbf{y}=\bar{\mathbf{y}}} \equiv \left.\left(\frac{\mathrm{s}\mathbf{x}}{\mathrm{s}\boldsymbol{\epsilon}^{\mathsf{T}}};\frac{\mathrm{s}\mathbf{y}}{\mathrm{s}\boldsymbol{\epsilon}^{\mathsf{T}}}\right)\right|_{\mathbf{y}=\bar{\mathbf{y}}} \in \mathbb{R}^{N_{\mathrm{a}}(N_{\mathrm{s}}+N_{\mathrm{c}})\times N_{\mathrm{a}}N_{\mathrm{e}}}, \tag{Layer 5, Eq. 4b}$$

measuring stabilized plasticity of the geno-phenotype. The transpose of the matrix of *stabilized effects of a focal individual's geno-phenotype on the geno-phenotype* is

$$\left.\frac{\mathrm{s}\mathbf{z}}{\mathrm{s}\mathbf{z}^{\mathsf{T}}}\right|_{\mathbf{y}=\bar{\mathbf{y}}} \equiv \left.\begin{pmatrix}\frac{\mathrm{s}\mathbf{x}}{\mathrm{s}\mathbf{x}^{\mathsf{T}}} & \frac{\mathrm{s}\mathbf{x}}{\mathrm{s}\mathbf{y}^{\mathsf{T}}}\\ \frac{\mathrm{s}\mathbf{y}}{\mathrm{s}\mathbf{x}^{\mathsf{T}}} & \frac{\mathrm{s}\mathbf{y}}{\mathrm{s}\mathbf{y}^{\mathsf{T}}}\end{pmatrix}\right|_{\mathbf{y}=\bar{\mathbf{y}}} = \left.\begin{pmatrix}\frac{\mathrm{s}\mathbf{x}}{\mathrm{s}\mathbf{x}^{\mathsf{T}}} & \frac{\mathrm{s}\mathbf{x}}{\mathrm{s}\mathbf{y}^{\mathsf{T}}}\\ \mathbf{0} & \mathbf{I}\end{pmatrix}\right|_{\mathbf{y}=\bar{\mathbf{y}}} \in \mathbb{R}^{N_{\mathrm{a}}(N_{\mathrm{s}}+N_{\mathrm{c}})\times N_{\mathrm{a}}(N_{\mathrm{s}}+N_{\mathrm{c}})}, \tag{Layer 5, Eq. 5}$$

measuring stabilized developmental feedback of the geno-phenotype.

The stabilized effects of the phenotype or gene expression on the environment measure stabilized niche construction. Although the matrix

$$\left.\frac{\mathrm{s}\boldsymbol{\epsilon}}{\mathrm{s}\mathbf{x}^{\mathsf{T}}}\right|_{\mathbf{y}=\bar{\mathbf{y}}}$$

appears in some of the matrices we construct, it is irrelevant as it disappears in the matrix products we encounter. The following matrix does not disappear. The transpose of the matrix of *stabilized effects of a focal individual's gene expression on the environment* is

$$\left.\frac{\mathrm{s}\boldsymbol{\epsilon}}{\mathrm{s}\mathbf{y}^{\mathsf{T}}}\right|_{\mathbf{y}=\bar{\mathbf{y}}} = \left.\left(\frac{\partial(\boldsymbol{\epsilon}+\check{\boldsymbol{\epsilon}})}{\partial\mathbf{z}^{\mathsf{T}}}\frac{\mathrm{s}\mathbf{z}}{\mathrm{s}\mathbf{y}^{\mathsf{T}}}\right)\right|_{\mathbf{y}=\bar{\mathbf{y}}} \in \mathbb{R}^{N_{\mathrm{a}}N_{\mathrm{e}}\times N_{\mathrm{a}}N_{\mathrm{c}}}, \tag{Layer 5, Eq. 6a}$$

which is formed by stabilized developmental bias of the geno-phenotype from gene expression followed by inclusive direct niche construction by the geno-phenotype. This matrix can be interpreted as measuring stabilized niche construction by gene expression. If development is not social (i.e., $\mathrm{d}\mathbf{x}^{\mathsf{T}}/\mathrm{d}\bar{\mathbf{z}}|_{\mathbf{y}=\bar{\mathbf{y}}} = \mathbf{0}$), then stabilized niche construction by gene expression reduces to total niche construction by gene expression (see Layer 4, Eq. 11 and Layer 2, Eq. 12).

The stabilized effects of the environment on itself measure stabilized environmental feedback. The transpose of the matrix of *stabilized effects of a focal individual's environment on the environment* is

$$\left.\frac{\mathrm{s}\boldsymbol{\epsilon}}{\mathrm{s}\boldsymbol{\epsilon}^{\mathsf{T}}}\right|_{\mathbf{y}=\bar{\mathbf{y}}} = \left.\left(\frac{\partial(\boldsymbol{\epsilon}+\check{\boldsymbol{\epsilon}})}{\partial\mathbf{z}^{\mathsf{T}}}\frac{\mathrm{s}\mathbf{z}}{\mathrm{s}\boldsymbol{\epsilon}^{\mathsf{T}}}+\frac{\partial\boldsymbol{\epsilon}}{\partial\boldsymbol{\epsilon}^{\mathsf{T}}}\right)\right|_{\mathbf{y}=\bar{\mathbf{y}}} \in \mathbb{R}^{N_{\mathrm{a}}N_{\mathrm{e}}\times N_{\mathrm{a}}N_{\mathrm{e}}}, \tag{Layer 5, Eq. 6b}$$

which depends on stabilized plasticity of the geno-phenotype, inclusive direct niche construction by the geno-phenotype, and direct mutual environmental dependence.

We can also use some of the following previous stabilized-effect matrices to construct the following stabilized-effect matrices comprising the geno-envo-phenotype. The transpose of the matrix of *stabilized effects of a focal individual's gene expression on the geno-envo-phenotype* is

$$\left.\frac{\mathrm{s}\mathbf{m}}{\mathrm{s}\mathbf{y}^{\mathsf{T}}}\right|_{\mathbf{y}=\bar{\mathbf{y}}} \equiv \left.\left(\frac{\mathrm{s}\mathbf{x}}{\mathrm{s}\mathbf{y}^{\mathsf{T}}};\frac{\mathrm{s}\mathbf{y}}{\mathrm{s}\mathbf{y}^{\mathsf{T}}};\frac{\mathrm{s}\boldsymbol{\epsilon}}{\mathrm{s}\mathbf{y}^{\mathsf{T}}}\right)\right|_{\mathbf{y}=\bar{\mathbf{y}}} \in \mathbb{R}^{N_{\mathrm{a}}(N_{\mathrm{s}}+N_{\mathrm{c}}+N_{\mathrm{e}})\times N_{\mathrm{a}}N_{\mathrm{c}}}, \tag{Layer 5, Eq. 7a}$$

measuring stabilized developmental bias of the geno-envo-phenotype from gene expression. The transpose of the matrix of *stabilized effects of a focal individual's environment on the geno-envo-phenotype* is

$$\left.\frac{\mathrm{s}\mathbf{m}}{\mathrm{s}\boldsymbol{\epsilon}^{\mathsf{T}}}\right|_{\mathbf{y}=\bar{\mathbf{y}}} \equiv \left.\left(\frac{\mathrm{s}\mathbf{x}}{\mathrm{s}\boldsymbol{\epsilon}^{\mathsf{T}}};\frac{\mathrm{s}\mathbf{y}}{\mathrm{s}\boldsymbol{\epsilon}^{\mathsf{T}}};\frac{\mathrm{s}\boldsymbol{\epsilon}}{\mathrm{s}\boldsymbol{\epsilon}^{\mathsf{T}}}\right)\right|_{\mathbf{y}=\bar{\mathbf{y}}} \in \mathbb{R}^{N_{\mathrm{a}}(N_{\mathrm{s}}+N_{\mathrm{c}}+N_{\mathrm{e}})\times N_{\mathrm{a}}N_{\mathrm{e}}}, \tag{Layer 5, Eq. 7b}$$

measuring stabilized plasticity of the geno-envo-phenotype. Finally, the transpose of the matrix of *stabilized effects of a focal individual's geno-envo-phenotype on the geno-envo-phenotype* is

$$\begin{aligned}\left.\frac{\mathrm{s}\mathbf{m}}{\mathrm{s}\mathbf{m}^{\mathsf{T}}}\right|_{\mathbf{y}=\bar{\mathbf{y}}} &\equiv \left.\begin{pmatrix}\frac{\mathrm{s}\mathbf{x}}{\mathrm{s}\mathbf{x}^{\mathsf{T}}} & \frac{\mathrm{s}\mathbf{x}}{\mathrm{s}\mathbf{y}^{\mathsf{T}}} & \frac{\mathrm{s}\mathbf{x}}{\mathrm{s}\boldsymbol{\epsilon}^{\mathsf{T}}}\\ \frac{\mathrm{s}\mathbf{y}}{\mathrm{s}\mathbf{x}^{\mathsf{T}}} & \frac{\mathrm{s}\mathbf{y}}{\mathrm{s}\mathbf{y}^{\mathsf{T}}} & \frac{\mathrm{s}\mathbf{y}}{\mathrm{s}\boldsymbol{\epsilon}^{\mathsf{T}}}\\ \frac{\mathrm{s}\boldsymbol{\epsilon}}{\mathrm{s}\mathbf{x}^{\mathsf{T}}} & \frac{\mathrm{s}\boldsymbol{\epsilon}}{\mathrm{s}\mathbf{y}^{\mathsf{T}}} & \frac{\mathrm{s}\boldsymbol{\epsilon}}{\mathrm{s}\boldsymbol{\epsilon}^{\mathsf{T}}}\end{pmatrix}\right|_{\mathbf{y}=\bar{\mathbf{y}}}\\ &= \left.\begin{pmatrix}\frac{\mathrm{s}\mathbf{x}}{\mathrm{s}\mathbf{x}^{\mathsf{T}}} & \frac{\mathrm{s}\mathbf{x}}{\mathrm{s}\mathbf{y}^{\mathsf{T}}} & \frac{\mathrm{s}\mathbf{x}}{\mathrm{s}\boldsymbol{\epsilon}^{\mathsf{T}}}\\ \mathbf{0} & \mathbf{I} & \mathbf{0}\\ \frac{\mathrm{s}\boldsymbol{\epsilon}}{\mathrm{s}\mathbf{x}^{\mathsf{T}}} & \frac{\mathrm{s}\boldsymbol{\epsilon}}{\mathrm{s}\mathbf{y}^{\mathsf{T}}} & \frac{\mathrm{s}\boldsymbol{\epsilon}}{\mathrm{s}\boldsymbol{\epsilon}^{\mathsf{T}}}\end{pmatrix}\right|_{\mathbf{y}=\bar{\mathbf{y}}} \qquad \text{(Layer 5, Eq. 8)}\\ &\in \mathbb{R}^{N_{\mathrm{a}}(N_{\mathrm{s}}+N_{\mathrm{c}}+N_{\mathrm{e}})\times N_{\mathrm{a}}(N_{\mathrm{s}}+N_{\mathrm{c}}+N_{\mathrm{e}})},\end{aligned}$$

measuring stabilized developmental feedback of the geno-envo-phenotype.

4.6. Layer 6: genetic covariation

We now move to the next layer of the evo-devo process, that of genetic covariation. To present this layer, we first define breeding value under our adaptive dynamics assumptions, which allows us to define additive genetic covariance matrices under our assumptions. Then, we define (socio-devo) stabilized breeding value, which generalizes the notion of breeding

value to consider the effects of social development. Using stabilized breeding value, we define additive socio-genetic cross-covariance matrices, which generalize the notion of additive genetic covariance to consider the effects of social development.

We follow the standard definition of breeding value to define it under our assumptions. The breeding value of a trait is defined under quantitative genetics assumptions as the best linear estimate of the trait from gene content (Lynch and Walsh, 1998; Walsh and Lynch, 2018). Specifically, under quantitative genetics assumptions, the i-th trait value x_i is written as $x_i = \bar{x}_i + \sum_j \alpha_{ij}(y_j - \bar{y}_j) + e_i$, where the overbar denotes population average, y_j is the j-th predictor (gene content in j-th locus), α_{ij} is the partial least-square regression coefficient of $x_i - \bar{x}_i$ vs $y_j - \bar{y}_j$, and e_i is the residual error; the breeding value of x_i is $a_i \equiv \bar{x}_i + \sum_j \alpha_{ij}(y_j - \bar{y}_j)$. Accordingly, we define the breeding value $\mathbf{a}_\zeta$ of a vector $\boldsymbol{\zeta}$ as its first-order estimate with respect to gene expression $\mathbf{y}$ around the resident gene expression $\bar{\mathbf{y}}$:

$$\mathbf{a}_\zeta \equiv \boldsymbol{\zeta}|_{\mathbf{y}=\bar{\mathbf{y}}} + \left.\frac{\mathrm{d}\boldsymbol{\zeta}}{\mathrm{d}\mathbf{y}^\intercal}\right|_{\mathbf{y}=\bar{\mathbf{y}}} (\mathbf{y} - \bar{\mathbf{y}}) = \bar{\boldsymbol{\zeta}} + \left.\frac{\mathrm{d}\boldsymbol{\zeta}}{\mathrm{d}\mathbf{y}^\intercal}\right|_{\mathbf{y}=\bar{\mathbf{y}}} (\mathbf{y} - \bar{\mathbf{y}}). \qquad \text{(Layer 6, Eq. 1)}$$

With this definition, the entries of $\mathrm{d}\boldsymbol{\zeta}/\mathrm{d}\mathbf{y}^\intercal|_{\mathbf{y}=\bar{\mathbf{y}}}$ correspond to Fisher's additive effect of allelic substitution (his α; see Eq. I of Fisher 1918 and p. 72 of Lynch and Walsh 1998). Moreover, such matrix $\mathrm{d}\boldsymbol{\zeta}/\mathrm{d}\mathbf{y}^\intercal|_{\mathbf{y}=\bar{\mathbf{y}}}$ corresponds to Wagner's (1984, 1989) developmental matrix, particularly when $\boldsymbol{\zeta} = \mathbf{x}$ (his $\mathbf{B}$; see Eq. 1 of Wagner 1989).

Our definition of breeding value recovers Fisher's (1918) infinitesimal model under certain conditions, although we do not need to assume the infinitesimal model. According to Fisher's (1918) infinitesimal model, the normalized breeding value excess is normally distributed as the number of loci approaches infinity. Using Layer 6, Eq. 1, we have that the breeding value excess for the i-th entry of $\mathbf{a}_\zeta$ is

$$a_{\zeta_i} - \bar{\zeta}_i = \sum_{k=1}^{N_\mathrm{c}} \sum_{a=1}^{N_\mathrm{a}} \left.\frac{\mathrm{d}\zeta_i}{\mathrm{d}y_{ka}}\right|_{\mathbf{y}=\bar{\mathbf{y}}} (y_{ka} - \bar{y}_{ka}).$$

Let us denote the mutational variance for the k-th gene product at age a by

$$\sigma^2_{ka} = \mathrm{E}[(y_{ka} - \bar{y}_{ka})^2],$$

and let us denote the total mutational variance by

$$s^2_{N_\mathrm{c}N_\mathrm{a}} = \sum_{k=1}^{N_\mathrm{c}} \sum_{a=1}^{N_\mathrm{a}} \sigma^2_{ka}.$$

If the y_{ka} are mutually independent and Lyapunov's condition is satisfied, from the Lyapunov central limit theorem we have that, as either the number of gene products N_c or the number of ages N_a tends to infinity (e.g., by reducing the age bin size), the normalized breeding value excess

$$\frac{1}{s_{N_\mathrm{c}N_\mathrm{a}}}(a_{\zeta_i} - \bar{\zeta}_i)$$

is normally distributed with mean zero and variance 1. Thus, this limit yields Fisher's (1918) infinitesimal model, although we do not need to assume such limit. Our framework thus recovers the infinitesimal model as a particular case, when either N_c or N_a approaches infinity (provided that the y_{ka} are mutually independent and Lyapunov's condition holds).

From our definition of breeding value, we have that the breeding value of gene expression is simply gene expression itself. From Layer 6, Eq. 1, the expected breeding value of vector $\boldsymbol{\zeta}$ is

$$\bar{\mathbf{a}}_\zeta \equiv \mathrm{E}[\mathbf{a}_\zeta] = \bar{\boldsymbol{\zeta}}.$$

In turn, the breeding value of gene expression $\mathbf{y}$ is

$$\mathbf{a}_\mathbf{y} = \bar{\mathbf{y}} + \left.\frac{\mathrm{d}\mathbf{y}}{\mathrm{d}\mathbf{y}^\intercal}\right|_{\mathbf{y}=\bar{\mathbf{y}}} (\mathbf{y} - \bar{\mathbf{y}}) = \bar{\mathbf{y}} + \mathbf{y} - \bar{\mathbf{y}} = \mathbf{y},$$

since $\mathrm{d}\mathbf{y}/\mathrm{d}\mathbf{y}^\intercal|_{\mathbf{y}=\bar{\mathbf{y}}} = \mathbf{I}$ because, by assumption, gene expression does not have developmental constraints and is open-loop (Layer 4, Eq. 6).

We now define additive genetic covariance matrices under our assumptions. The additive genetic variance of a trait is defined under quantitative genetics assumptions as the variance of its breeding value, which is extended to the multivariate case so the additive genetic covariance matrix of a trait vector is the covariance matrix of the traits' breeding values (Lynch and Walsh, 1998; Walsh and Lynch, 2018). Accordingly, we define the additive genetic covariance matrix of a vector $\boldsymbol{\zeta} \in \mathbb{R}^{m\times 1}$ as the covariance matrix of its breeding value:

$$\begin{aligned}
\mathbf{G}_\zeta &\equiv \mathrm{cov}[\mathbf{a}_\zeta, \mathbf{a}_\zeta] \\
&= \mathrm{E}[(\mathbf{a}_\zeta - \bar{\mathbf{a}}_\zeta)(\mathbf{a}_\zeta - \bar{\mathbf{a}}_\zeta)^\intercal] = \mathrm{E}[(\mathbf{a}_\zeta - \bar{\boldsymbol{\zeta}})(\mathbf{a}_\zeta - \bar{\boldsymbol{\zeta}})^\intercal] \\
&= \mathrm{E}\left[\left(\left.\frac{\mathrm{d}\boldsymbol{\zeta}}{\mathrm{d}\mathbf{y}^\intercal}\right|_{\mathbf{y}=\bar{\mathbf{y}}} (\mathbf{y} - \bar{\mathbf{y}})\right)\left(\left.\frac{\mathrm{d}\boldsymbol{\zeta}}{\mathrm{d}\mathbf{y}^\intercal}\right|_{\mathbf{y}=\bar{\mathbf{y}}} (\mathbf{y} - \bar{\mathbf{y}})\right)^\intercal\right] \\
&= \mathrm{E}\left[\left.\frac{\mathrm{d}\boldsymbol{\zeta}}{\mathrm{d}\mathbf{y}^\intercal}\right|_{\mathbf{y}=\bar{\mathbf{y}}} (\mathbf{y} - \bar{\mathbf{y}})(\mathbf{y} - \bar{\mathbf{y}})^\intercal \left.\frac{\mathrm{d}\boldsymbol{\zeta}^\intercal}{\mathrm{d}\mathbf{y}}\right|_{\mathbf{y}=\bar{\mathbf{y}}}\right] \\
&= \left.\frac{\mathrm{d}\boldsymbol{\zeta}}{\mathrm{d}\mathbf{y}^\intercal}\right|_{\mathbf{y}=\bar{\mathbf{y}}} \mathrm{E}\left[(\mathbf{y} - \bar{\mathbf{y}})(\mathbf{y} - \bar{\mathbf{y}})^\intercal\right] \left.\frac{\mathrm{d}\boldsymbol{\zeta}^\intercal}{\mathrm{d}\mathbf{y}}\right|_{\mathbf{y}=\bar{\mathbf{y}}} \\
&= \left.\left(\frac{\mathrm{d}\boldsymbol{\zeta}}{\mathrm{d}\mathbf{y}^\intercal}\mathbf{G}_\mathbf{y}\frac{\mathrm{d}\boldsymbol{\zeta}^\intercal}{\mathrm{d}\mathbf{y}}\right)\right|_{\mathbf{y}=\bar{\mathbf{y}}} \in \mathbb{R}^{m\times m}, \qquad \text{(Layer 6, Eq. 2)}
\end{aligned}$$

where the fourth line follows from the property of the transpose of a product (i.e., $(\mathbf{AB})^\intercal = \mathbf{B}^\intercal\mathbf{A}^\intercal$) and the last line follows since the additive genetic covariance matrix of gene expression $\mathbf{y}$ is

$$\mathbf{G}_\mathbf{y} \equiv \mathrm{cov}[\mathbf{a}_\mathbf{y}, \mathbf{a}_\mathbf{y}] = \mathrm{cov}[\mathbf{y}, \mathbf{y}] \in \mathbb{R}^{N_\mathrm{a}N_\mathrm{c}\times N_\mathrm{a}N_\mathrm{c}}.$$

Layer 6, Eq. 2 corresponds to previous expressions of the additive genetic covariance matrix under quantitative genetics assumptions (see Eq. II of Fisher 1918, Eq. + of Wagner 1984, Eq. 3.5b of Barton and Turelli 1987, and Eq. 4.23b of Lynch and Walsh 1998; see also Eq. 22a of Lande 1980, Eq. 3 of Wagner 1989, and Eq. 9 of Charlesworth 1990). Note $\mathbf{G}_\zeta$ is symmetric.

In some cases, Layer 6, Eq. 2 allows one to immediately determine whether an additive genetic covariance matrix is singular. Indeed, a matrix with fewer rows than columns is always

singular (Horn and Johnson, 2013, section 0.5 second line), and if the product $\mathbf{AB}$ is well-defined and $\mathbf{B}$ is singular, then $\mathbf{AB}$ is singular (this is easily checked to hold). Hence, from Layer 6, Eq. 2 it follows that $\mathbf{G}_\zeta$ is necessarily singular if $\mathrm{d}\boldsymbol{\zeta}^\intercal/\mathrm{d}\mathbf{y}$ has fewer rows than columns, that is, if $\mathbf{y}$ has fewer entries than $\boldsymbol{\zeta}$. Since $\mathbf{y}$ has $N_\mathrm{a}N_\mathrm{c}$ entries and $\boldsymbol{\zeta}$ has m entries, then $\mathbf{G}_\zeta$ is singular if $N_\mathrm{a}N_\mathrm{c} < m$. Moreover, Layer 6, Eq. 2 allows one to immediately identify bounds for the "degrees of freedom" of genetic covariation, that is, for the rank of $\mathbf{G}_\zeta$. Indeed, for a matrix $\mathbf{A} \in \mathbb{R}^{m\times n}$, we have that the rank of $\mathbf{A}$ is at most the smallest value of m and n, that is, $\mathrm{rank}(\mathbf{A}) \leq \min\{m, n\}$ (Horn and Johnson, 2013, section 0.4.5 (a)). Moreover, from the Frobenius inequality (Horn and Johnson, 2013, section 0.4.5 (e)), for a well-defined product $\mathbf{AB}$, we have that $\mathrm{rank}(\mathbf{AB}) \leq \mathrm{rank}(\mathbf{B})$. Therefore, for $\boldsymbol{\zeta} \in \mathbb{R}^{m\times 1}$, we have that

$$\mathrm{rank}(\mathbf{G}_\zeta) \leq \min\{N_\mathrm{a}N_\mathrm{c}, m\}. \qquad \text{(Layer 6, Eq. 3)}$$

Intuitively, this states that the degrees of freedom of genetic covariation are at most given by the lifetime number of gene products (i.e., $N_\mathrm{a}N_\mathrm{c}$). So if there are more traits in $\boldsymbol{\zeta}$ than there are lifetime gene products, then there are fewer degrees of freedom than traits. This point is mathematically trivial and has undoubtedly been clear in the evolutionary literature for decades. However, this point will be biologically crucial because the evolutionary dynamic equations in gradient form that yield a well-defined evolutionary trajectory involve a $\mathbf{G}_\zeta$ whose $\boldsymbol{\zeta}$ necessarily has fewer entries than $\mathbf{y}$. Note also that these points on the singularity and rank of $\mathbf{G}_\zeta$ also hold under quantitative genetics assumptions, where the same structure (Layer 6, Eq. 2) holds, except that $\mathbf{G}_\mathbf{y}$ does not refer to mutational variation but to standing variation in allele frequency. Considering standing variation in $\mathbf{G}_\mathbf{y}$ does not affect the points made in this paragraph.

Now, consider the following slight generalization of the additive genetic covariance matrix. We define the additive genetic cross-covariance matrix between a vector $\boldsymbol{\zeta} \in \mathbb{R}^{m\times 1}$ and a vector $\boldsymbol{\xi} \in \mathbb{R}^{n\times 1}$ as the cross-covariance matrix of their breeding value:

$$\mathbf{G}_{\zeta\xi} \equiv \mathrm{cov}[\mathbf{a}_\zeta, \mathbf{a}_\xi] = \left(\frac{\mathrm{d}\boldsymbol{\zeta}}{\mathrm{d}\mathbf{y}^\intercal}\mathbf{G}_\mathbf{y}\frac{\mathrm{d}\boldsymbol{\xi}^\intercal}{\mathrm{d}\mathbf{y}}\right)\bigg|_{\mathbf{y}=\bar{\mathbf{y}}} \in \mathbb{R}^{m\times n}. \qquad \text{(Layer 6, Eq. 4)}$$

Thus, $\mathbf{G}_{\zeta\zeta} = \mathbf{G}_\zeta$. Note $\mathbf{G}_{\zeta\xi}$ may be rectangular, and if square, asymmetric. Again, from Layer 6, Eq. 4 it follows that $\mathbf{G}_{\zeta\xi}$ is necessarily singular if there are fewer entries in $\mathbf{y}$ than in $\boldsymbol{\xi}$ (i.e., if $N_\mathrm{a}N_\mathrm{c} < n$). Also, for $\boldsymbol{\xi} \in \mathbb{R}^{n\times 1}$, have that

$$\mathrm{rank}(\mathbf{G}_{\zeta\xi}) \leq \min\{N_\mathrm{a}N_\mathrm{c}, n\}.$$

In words, the degrees of freedom of genetic cross-covariation are at most given by the lifetime number of gene products.

The additive genetic covariance matrix of the phenotype takes the following form. Evaluating Layer 6, Eq. 2 at $\boldsymbol{\zeta} = \mathbf{x}$, the additive genetic covariance matrix of the phenotype $\mathbf{x} \in \mathbb{R}^{N_\mathrm{a}N_\mathrm{s}\times 1}$ is

$$\mathbf{G}_\mathbf{x} = \left(\frac{\mathrm{d}\mathbf{x}}{\mathrm{d}\mathbf{y}^\intercal}\mathbf{G}_\mathbf{y}\frac{\mathrm{d}\mathbf{x}^\intercal}{\mathrm{d}\mathbf{y}}\right)\bigg|_{\mathbf{y}=\bar{\mathbf{y}}} \in \mathbb{R}^{N_\mathrm{a}N_\mathrm{s}\times N_\mathrm{a}N_\mathrm{s}}, \qquad \text{(Layer 6, Eq. 5)}$$

which is singular because the developmental matrix $\mathrm{d}\mathbf{x}^\intercal/\mathrm{d}\mathbf{y}|_{\mathbf{y}=\bar{\mathbf{y}}}$ is singular since the initial phenotype is not affected by gene expression and final gene expression does not affect the phenotype (Appendix E, Eq. E16). However, a dynamical system consisting only of evolutionary dynamic equations for the phenotype thus having an associated $\mathbf{G}_\mathbf{x}$-matrix is underdetermined in general because the system has fewer dynamic equations (i.e., the number of entries in $\mathbf{x}$) than dynamic variables (i.e., the number of entries in $(\mathbf{x}; \mathbf{y}; \boldsymbol{\epsilon})$). Indeed, the evolutionary dynamics of the phenotype generally depends on resident gene expression, in particular, because the developmental matrix depends on resident gene expression (Layer 4, Eq. 3; e.g., due to non-linearities in the developmental map involving products between gene expression, or between gene expression and phenotypes, or between gene expression and environmental variables, that is, gene-gene interaction, gene-phenotype interaction, and gene-environment interaction, respectively). Thus, evolutionary dynamic equations of the phenotype alone have either zero or an infinite number of solutions for any given initial condition and are thus unable to identify the evolutionary trajectory followed as the evolutionary trajectory is ill-defined. To have a determined system in gradient form so that the evolutionary trajectory is well-defined, we follow the evolutionary dynamics of both the phenotype and gene expression, that is, of the geno-phenotype, which depends on $\mathbf{G}_\mathbf{z}$ rather than $\mathbf{G}_\mathbf{x}$ alone.

The additive genetic covariance matrix of the geno-phenotype takes the following form. Evaluating Layer 6, Eq. 2 at $\boldsymbol{\zeta} = \mathbf{z}$, the additive genetic covariance matrix of the geno-phenotype $\mathbf{z} \in \mathbb{R}^{N_\mathrm{a}(N_\mathrm{s}+N_\mathrm{c})\times 1}$ is

$$\mathbf{G}_\mathbf{z} = \left(\frac{\mathrm{d}\mathbf{z}}{\mathrm{d}\mathbf{y}^\intercal}\mathbf{G}_\mathbf{y}\frac{\mathrm{d}\mathbf{z}^\intercal}{\mathrm{d}\mathbf{y}}\right)\bigg|_{\mathbf{y}=\bar{\mathbf{y}}} \in \mathbb{R}^{N_\mathrm{a}(N_\mathrm{s}+N_\mathrm{c})\times N_\mathrm{a}(N_\mathrm{s}+N_\mathrm{c})}. \qquad \text{(Layer 6, Eq. 6)}$$

This matrix is necessarily singular because the geno-phenotype $\mathbf{z}$ includes gene expression $\mathbf{y}$ so $\mathrm{d}\mathbf{z}^\intercal/\mathrm{d}\mathbf{y}$ has fewer rows than columns (Layer 4, Eq. 8). From Layer 6, Eq. 3, the rank of $\mathbf{G}_\mathbf{z}$ has an upper bound given by the number of gene products across life (i.e., $N_\mathrm{a}N_\mathrm{c}$), so $\mathbf{G}_\mathbf{z}$ has at least $N_\mathrm{a}N_\mathrm{s}$ eigenvalues that are exactly zero. Thus, $\mathbf{G}_\mathbf{z}$ is singular if there is at least one trait that is developmentally constructed according to the developmental map (Eq. 1) (i.e., if $N_\mathrm{s} > 0$). This is a mathematically trivial singularity, but it is biologically key because it is $\mathbf{G}_\mathbf{z}$ rather than $\mathbf{G}_\mathbf{x}$ that occurs in a determined evolutionary system in gradient form (provided the environment is constant; if the environment is not constant, the relevant matrix is $\mathbf{G}_\mathbf{m}$ which is also always singular if there is at least one phenotype or one environmental variable).

Another way to see the singularity of $\mathbf{G}_\mathbf{z}$ is the following. From Layer 6, Eq. 6, we can write the additive genetic covariance matrix of the geno-phenotype as

$$\mathbf{G}_\mathbf{z} = \begin{pmatrix}\mathbf{G}_\mathbf{zx} & \mathbf{G}_\mathbf{zy}\end{pmatrix},$$

where the additive genetic cross-covariance matrix between $\mathbf{z}$ and $\mathbf{x}$ is

$$\mathbf{G}_\mathbf{zx} = \left(\frac{\mathrm{d}\mathbf{z}}{\mathrm{d}\mathbf{y}^\intercal}\mathbf{G}_\mathbf{y}\frac{\mathrm{d}\mathbf{x}^\intercal}{\mathrm{d}\mathbf{y}}\right)\bigg|_{\mathbf{y}=\bar{\mathbf{y}}} \in \mathbb{R}^{N_\mathrm{a}(N_\mathrm{s}+N_\mathrm{c})\times N_\mathrm{a}N_\mathrm{s}},$$

and the additive genetic cross-covariance matrix between $\mathbf{z}$ and $\mathbf{y}$ is

$$\mathbf{G}_{\mathbf{zy}} = \left(\frac{\mathrm{d}\mathbf{z}}{\mathrm{d}\mathbf{y}^\intercal}\mathbf{G}_{\mathbf{y}}\frac{\mathrm{d}\mathbf{y}^\intercal}{\mathrm{d}\mathbf{y}}\right)\bigg|_{\mathbf{y}=\bar{\mathbf{y}}} \in \mathbb{R}^{N_\mathrm{a}(N_\mathrm{s}+N_\mathrm{c})\times N_\mathrm{a}N_\mathrm{c}}.$$

Thus, using Layer 4, Eq. 6, we have that

$$\mathbf{G}_{\mathbf{zx}} = \mathbf{G}_{\mathbf{zy}}\frac{\mathrm{d}\mathbf{x}^\intercal}{\mathrm{d}\mathbf{y}}\bigg|_{\mathbf{y}=\bar{\mathbf{y}}}. \qquad \text{(Layer 6, Eq. 7)}$$

That is, some columns of $\mathbf{G}_\mathbf{z}$ (i.e., those in $\mathbf{G}_{\mathbf{zx}}$) are linear combinations of other columns of $\mathbf{G}_\mathbf{z}$ (i.e., those in $\mathbf{G}_{\mathbf{zy}}$). Hence, $\mathbf{G}_\mathbf{z}$ is singular.

The additive genetic covariance matrix of the geno-phenotype is singular because the geno-phenotype includes gene expression ("gene content"). The singularity arises because the breeding value of the phenotype is a linear combination of the breeding value of gene expression by definition of breeding value, regardless of whether the phenotype is a linear function of gene expression and regardless of the number of phenotypes or gene products. In quantitative genetics terms, this can be understood as the $\mathbf{G}$-matrix being a function of allele frequencies (which corresponds to our $\bar{\mathbf{y}}$), so a well-defined evolutionary trajectory requires that allele frequencies are part of the dynamic variables considered; consequently, if the geno-phenotypic vector $\bar{\mathbf{z}}$ includes allele frequencies $\bar{\mathbf{y}}$, then $\mathbf{G}$ is necessarily singular since by definition, breeding value under quantitative genetics assumptions is a linear combination of gene content. The singularity of $\mathbf{G}_\mathbf{z}$ implies that if there is only one phenotype and one gene product, with a single age each, then there is a perfect correlation between their breeding values (i.e., their correlation coefficient is 1). This also holds under quantitative genetics assumptions, in which case the breeding value a of a trait x is a linear combination of a single predictor y, so the breeding value a and predictor y are perfectly correlated (i.e., $\mathrm{cov}[a,y]/\sqrt{\mathrm{var}[a]\mathrm{var}[y]} = \mathrm{cov}[\alpha y,y]/\sqrt{\mathrm{var}[\alpha y]\mathrm{var}[y]} = (\alpha/\alpha)\mathrm{cov}[y,y]/\sqrt{\mathrm{var}[y]\mathrm{var}[y]} = 1$). The perfect correlation between a single breeding value and a single predictor arises because, by definition, breeding value excludes residual error e. Note this does not mean that the phenotype and gene expression are linearly related: it is breeding values and gene expression that are linearly related by definition of breeding value (Layer 6, Eq. 1). A standard approach to remove the singularity of an additive genetic covariance matrix is to remove some traits from the analysis (Lande, 1979). To remove the singularity of $\mathbf{G}_\mathbf{z}$ we would need to remove at least either all phenotypes or all gene products from the analysis. However, removing all phenotypes from the analysis prevents analysing phenotypic evolution as the climbing of a fitness landscape whereas removing all gene products from the analysis renders the evolutionary trajectory ill-defined in general because the evolutionary dynamics of some variables is not described. Thus, to analyse a well-defined description of phenotypic evolution as the climbing of a fitness landscape, we must keep the singularity of $\mathbf{G}_\mathbf{z}$.

We now use stabilized-effect matrices (Layer 5) to extend the notion of breeding value (Layer 6, Eq. 1). We define the stabilized breeding value of a vector $\boldsymbol{\zeta}$ as:

$$\mathbf{b}_\zeta \equiv \boldsymbol{\zeta}|_{\mathbf{y}=\bar{\mathbf{y}}} + \frac{\mathrm{s}\boldsymbol{\zeta}}{\mathrm{s}\mathbf{y}^\intercal}\bigg|_{\mathbf{y}=\bar{\mathbf{y}}}(\mathbf{y}-\bar{\mathbf{y}}) = \bar{\boldsymbol{\zeta}} + \frac{\mathrm{s}\boldsymbol{\zeta}}{\mathrm{s}\mathbf{y}^\intercal}\bigg|_{\mathbf{y}=\bar{\mathbf{y}}}(\mathbf{y}-\bar{\mathbf{y}}).$$
(Layer 6, Eq. 8)

Recall that the stabilized-effect matrix $\mathrm{s}\boldsymbol{\xi}/\mathrm{s}\mathbf{y}^\intercal|_{\mathbf{y}=\bar{\mathbf{y}}}$ equals the total-effect matrix $\mathrm{d}\boldsymbol{\xi}/\mathrm{d}\mathbf{y}^\intercal|_{\mathbf{y}=\bar{\mathbf{y}}}$ if development is non-social. Thus, if development is non-social, the stabilized breeding value $\mathbf{b}_\zeta$ equals the breeding value $\mathbf{a}_\zeta$. Also, note that $\mathrm{E}[\mathbf{b}_\zeta] = \bar{\boldsymbol{\zeta}}$.

We extend the notion of additive genetic covariance matrix to include the effects of socio-devo stabilization as follows. We define the *additive socio-genetic cross-covariance matrix of* $\boldsymbol{\zeta} \in \mathbb{R}^{m\times 1}$ as

$$\mathbf{H}_\zeta \equiv \mathrm{cov}[\mathbf{b}_\zeta, \mathbf{a}_\zeta] = \left(\frac{\mathrm{s}\boldsymbol{\zeta}}{\mathrm{s}\mathbf{y}^\intercal}\mathbf{G}_\mathbf{y}\frac{\mathrm{d}\boldsymbol{\zeta}^\intercal}{\mathrm{d}\mathbf{y}}\right)\bigg|_{\mathbf{y}=\bar{\mathbf{y}}} \in \mathbb{R}^{m\times m}.$$
(Layer 6, Eq. 9)

Note $\mathbf{H}_\zeta$ may be asymmetric and its main diagonal entries may be negative (unlike variances). If development is non-social, $\mathbf{H}_\zeta$ equals $\mathbf{G}_\zeta$. As before, $\mathbf{H}_\zeta$ is singular if $\boldsymbol{\zeta}$ has fewer entries than $\mathbf{y}$. Also, for $\boldsymbol{\zeta} \in \mathbb{R}^{m\times 1}$, have that

$$\mathrm{rank}(\mathbf{H}_\zeta) \leq \min\{N_\mathrm{a}N_\mathrm{c}, m\}.$$

That is, the degrees of freedom of socio-genetic covariation are at most also given by the lifetime number of gene products.

Similarly, we generalize this notion and define the *additive socio-genetic cross-covariance matrix between* $\boldsymbol{\zeta} \in \mathbb{R}^{m\times 1}$ *and* $\boldsymbol{\xi} \in \mathbb{R}^{n\times 1}$ as

$$\mathbf{H}_{\zeta\xi} \equiv \mathrm{cov}[\mathbf{b}_\zeta, \mathbf{a}_\xi] = \left(\frac{\mathrm{s}\boldsymbol{\zeta}}{\mathrm{s}\mathbf{y}^\intercal}\mathbf{G}_\mathbf{y}\frac{\mathrm{d}\boldsymbol{\xi}^\intercal}{\mathrm{d}\mathbf{y}}\right)\bigg|_{\mathbf{y}=\bar{\mathbf{y}}} \in \mathbb{R}^{m\times n}.$$
(Layer 6, Eq. 10)

Again, if development is non-social, $\mathbf{H}_{\zeta\xi}$ equals $\mathbf{G}_{\zeta\xi}$. Note $\mathbf{H}_{\zeta\xi}$ may be rectangular and, if square, asymmetric. Also, $\mathbf{H}_{\zeta\xi}$ is singular if $\boldsymbol{\xi}$ has fewer entries than $\mathbf{y}$. For $\boldsymbol{\xi} \in \mathbb{R}^{n\times 1}$, have that

$$\mathrm{rank}(\mathbf{H}_{\zeta\xi}) \leq \min\{N_\mathrm{a}N_\mathrm{c}, n\}.$$

That is, the degrees of freedom of socio-genetic cross-covariation are at most still given by the lifetime number of gene products.

In particular, the additive socio-genetic cross-covariance matrix

$$\mathbf{H}_{\zeta\mathbf{z}} = \left(\frac{\mathrm{s}\boldsymbol{\zeta}}{\mathrm{s}\mathbf{y}^\intercal}\mathbf{G}_\mathbf{y}\frac{\mathrm{d}\mathbf{z}^\intercal}{\mathrm{d}\mathbf{y}}\right)\bigg|_{\mathbf{y}=\bar{\mathbf{y}}} \in \mathbb{R}^{m\times N_\mathrm{a}(N_\mathrm{s}+N_\mathrm{c})} \qquad \text{(Layer 6, Eq. 11)}$$

is singular if there is at least one phenotype (i.e., if $N_\mathrm{s} > 0$). Moreover, $\mathbf{H}_{\zeta\mathbf{z}}$ has at least $N_\mathrm{a}N_\mathrm{s}$ eigenvalues that are exactly zero. Also, the matrix

$$\mathbf{H}_{\zeta\mathbf{m}} = \left(\frac{\mathrm{s}\boldsymbol{\zeta}}{\mathrm{s}\mathbf{y}^\intercal}\mathbf{G}_\mathbf{y}\frac{\mathrm{d}\mathbf{m}^\intercal}{\mathrm{d}\mathbf{y}}\right)\bigg|_{\mathbf{y}=\bar{\mathbf{y}}} \in \mathbb{R}^{m\times(1+N_\mathrm{a})(N_\mathrm{s}+N_\mathrm{c}+N_\mathrm{e})}$$
(Layer 6, Eq. 12)

is singular if there is at least one phenotype or one environmental variable (i.e., if $N_\mathrm{s} > 0$ or $N_\mathrm{e} > 0$). Thus, $\mathbf{H}_{\boldsymbol{\zeta}\mathbf{m}}$ has at least $N_\mathrm{a}(N_\mathrm{s} + N_\mathrm{e})$ eigenvalues that are exactly zero. In contrast, the additive socio-genetic cross-covariance matrix between a vector $\boldsymbol{\zeta} \in \{\mathbf{y}, \mathbf{z}, \mathbf{m}\}$ and gene expression $\mathbf{y}$

$$\mathbf{H}_{\boldsymbol{\zeta}\mathbf{y}} = \left(\frac{\mathrm{s}\boldsymbol{\zeta}}{\mathrm{s}\mathbf{y}^\intercal}\mathbf{G}_\mathbf{y}\right)\bigg|_{\mathbf{y}=\bar{\mathbf{y}}} \in \mathbb{R}^{m\times N_\mathrm{a}N_\mathrm{c}} \qquad \text{(Layer 6, Eq. 13)}$$

is non-singular if $\mathbf{G}_\mathbf{y}$ is non-singular (Appendices J and L). The matrices of additive socio-genetic cross-covariance share various properties with similar generalizations of the $\mathbf{G}$-matrix arising in the indirect genetic effects literature (Kirkpatrick and Lande, 1989; Moore et al., 1997; Townley and Ezard, 2013).

4.7. Layer 7: evolutionary dynamics

Finally, we move to the top layer of the evo-devo process, that of the evolutionary dynamics. This layer contains equations describing the evolutionary dynamics under explicit developmental and environmental constraints. In Appendices A and I-L, we show that the evolutionary dynamics of the phenotype, gene expression, geno-phenotype, environment, and geno-envo-phenotype (i.e., for $\boldsymbol{\zeta} \in \{\mathbf{x}, \mathbf{y}, \mathbf{z}, \boldsymbol{\epsilon}, \mathbf{m}\}$) are given by

$$\frac{\mathrm{d}\bar{\boldsymbol{\zeta}}}{\mathrm{d}\tau} \approx \left(\kappa\mathbf{H}_{\boldsymbol{\zeta}\mathbf{m}}\frac{\partial w}{\partial \mathbf{m}} + \frac{\mathrm{s}\boldsymbol{\zeta}}{\mathrm{s}\boldsymbol{\epsilon}^\intercal}\frac{\partial \boldsymbol{\epsilon}}{\partial \tau}\right)\bigg|_{\mathbf{y}=\bar{\mathbf{y}}}, \qquad \text{(Layer 7, Eq. 1a)}$$

which must satisfy both the developmental constraint

$$\bar{\mathbf{x}}_{a+1} = \mathbf{g}_a(\bar{\mathbf{m}}_a, \bar{\mathbf{z}}) \text{ for all } a \in \{1, \ldots, N_\mathrm{a} - 1\} \text{ with fixed } \bar{\mathbf{x}}_1, \qquad \text{(Layer 7, Eq. 1b)}$$

and the environmental constraint

$$\bar{\boldsymbol{\epsilon}}_a = \mathbf{h}_a(\bar{\mathbf{z}}_a, \bar{\mathbf{z}}, \tau) \text{ for all } a \in \{1, \ldots, N_\mathrm{a}\}. \qquad \text{(Layer 7, Eq. 1c)}$$

If $\boldsymbol{\zeta} = \mathbf{z}$ in Layer 7, Eq. 1a, then the equations in Layers 2-6 guarantee that the developmental constraint is satisfied for all $\tau > \tau_1$ given that it is satisfied at the initial evolutionary time τ_1. If $\boldsymbol{\zeta} = \mathbf{m}$ in Layer 7, Eq. 1a, then the equations in Layers 2-6 guarantee that both the developmental and environmental constraints are satisfied for all $\tau > \tau_1$ given that they are satisfied at the initial evolutionary time τ_1. Both the developmental and environmental constraints can evolve as gene expression, phenotype, and environment evolve and such constraints can involve any family of curves (as long as they are differentiable).

Layer 7, Eq. 1a describes the evolutionary dynamics as consisting of selection response and exogenous plastic response. Layer 7, Eq. 1a contains the term

$$\kappa\mathbf{H}_{\boldsymbol{\zeta}\mathbf{m}}\frac{\partial w}{\partial \mathbf{m}}\bigg|_{\mathbf{y}=\bar{\mathbf{y}}}, \qquad \text{(Layer 7, Eq. 2)}$$

which comprises direct directional selection on the geno-envo-phenotype ($\partial w/\partial \mathbf{m}|_{\mathbf{y}=\bar{\mathbf{y}}}$) and socio-genetic covariation between $\boldsymbol{\zeta}$ and the geno-envo-phenotype ($\mathbf{H}_{\boldsymbol{\zeta}\mathbf{m}}$). Thus, the term in Layer 7, Eq. 2 is the *selection response* of $\boldsymbol{\zeta}$ and is a generalization of Lande's (1979) generalization of the univariate breeder's equation (Lush, 1937; Walsh and Lynch, 2018), although with some differences stemming from our adaptive dynamics assumptions. Additionally, Layer 7, Eq. 1a contains the term

$$\left(\frac{\mathrm{s}\boldsymbol{\zeta}}{\mathrm{s}\boldsymbol{\epsilon}^\intercal}\frac{\partial \boldsymbol{\epsilon}}{\partial \tau}\right)\bigg|_{\mathbf{y}=\bar{\mathbf{y}}}, \qquad \text{(Layer 7, Eq. 3)}$$

which comprises the vector of environmental change due to exogenous causes ($\partial\bar{\boldsymbol{\epsilon}}/\partial\tau$) and the matrix of stabilized plasticity ($\mathrm{s}\boldsymbol{\zeta}/\mathrm{s}\boldsymbol{\epsilon}^\intercal|_{\mathbf{y}=\bar{\mathbf{y}}}$). Thus, the term in Layer 7, Eq. 3 is the *exogenous plastic response* of $\boldsymbol{\zeta}$ and is a generalization of previous expressions (cf. Eq. A3 of Chevin et al. 2010), again with some differences stemming from our adaptive dynamics assumptions. Note that the *endogenous* plastic response of $\boldsymbol{\zeta}$ (i.e., the plastic response due to endogenous environmental change arising from niche construction) is part of both the selection response and the exogenous plastic response (Layers 2-6).

Selection response is relatively incompletely described by direct directional selection on the geno-envo-phenotype. We saw that the matrix $\mathbf{H}_{\boldsymbol{\zeta}\mathbf{m}}$ is always singular if there is at least one phenotype or one environmental variable (Layer 6, Eq. 12). Consequently, evolutionary equilibria of $\boldsymbol{\zeta}$ can invariably occur with persistent direct directional selection on the geno-envo-phenotype, regardless of whether there is exogenous plastic response.

Selection response is also relatively incompletely described by semi-total selection on the geno-phenotype. We can rewrite the selection response, so the evolutionary dynamics of $\boldsymbol{\zeta} \in \{\mathbf{x}, \mathbf{y}, \mathbf{z}, \boldsymbol{\epsilon}, \mathbf{m}\}$ (Layer 7, Eq. 1a) is equivalently given by

$$\frac{\mathrm{d}\bar{\boldsymbol{\zeta}}}{\mathrm{d}\tau} \approx \left(\kappa\mathbf{H}_{\boldsymbol{\zeta}\mathbf{z}}\frac{\delta w}{\delta \mathbf{z}} + \frac{\mathrm{s}\boldsymbol{\zeta}}{\mathrm{s}\boldsymbol{\epsilon}^\intercal}\frac{\partial \boldsymbol{\epsilon}}{\partial \tau}\right)\bigg|_{\mathbf{y}=\bar{\mathbf{y}}}. \qquad \text{(Layer 7, Eq. 4)}$$

This equation now depends on semi-total selection on the geno-phenotype ($\delta w/\delta \mathbf{z}|_{\mathbf{y}=\bar{\mathbf{y}}}$), which measures semi-total directional selection on the geno-phenotype considering environmental constraints (or in a quantitative genetics framework, it is Lande's (1979) selection gradient of the allele frequency and phenotype if environmental variables are not explicitly included in the analysis). We saw that the semi-total selection gradient of the geno-phenotype can be interpreted as pointing in the direction of steepest ascent on the fitness landscape in geno-phenotype space after the landscape is modified by the interaction of direct niche construction and environmental sensitivity of selection (Layer 3, Eq. 1). We also saw that the matrix $\mathbf{H}_{\boldsymbol{\zeta}\mathbf{z}}$ is always singular if there is at least one phenotype (Layer 6, Eq. 11). Consequently, evolutionary equilibria can invariably occur with persistent directional selection on the geno-phenotype after niche construction has modified the geno-phenotype's fitness landscape, regardless of whether there is exogenous plastic response.

In contrast, selection response is relatively completely described by total genetic selection. We can further rewrite selection response, so the evolutionary dynamics of $\boldsymbol{\zeta} \in \{\mathbf{x}, \mathbf{y}, \mathbf{z}, \boldsymbol{\epsilon}, \mathbf{m}\}$ (Layer 7, Eq. 1a) is equivalently given by

$$\frac{\mathrm{d}\bar{\boldsymbol{\zeta}}}{\mathrm{d}\tau} \approx \left(\kappa\mathbf{H}_{\boldsymbol{\zeta}\mathbf{y}}\frac{\mathrm{d}w}{\mathrm{d}\mathbf{y}} + \frac{\mathrm{s}\boldsymbol{\zeta}}{\mathrm{s}\boldsymbol{\epsilon}^\intercal}\frac{\partial \boldsymbol{\epsilon}}{\partial \tau}\right)\bigg|_{\mathbf{y}=\bar{\mathbf{y}}}. \qquad \text{(Layer 7, Eq. 5)}$$

This equation now depends on total genetic selection ($\mathrm{d}w/\mathrm{d}\mathbf{y}|_{\mathbf{y}=\bar{\mathbf{y}}}$), which measures total directional selection on gene expression considering developmental and environmental constraints (or in a quantitative genetics framework, it is Lande's (1979) selection gradient of allele frequency if neither the phenotype nor environmental variables are explicitly included in the analysis). We saw that the total selection gradient of gene expression can be interpreted as pointing in the direction of steepest ascent on the fitness landscape in gene expression space after the landscape is modified by the interaction of total developmental bias from gene expression and directional selection on the phenotype and by the interaction of total niche construction by gene expression and environmental sensitivity of selection (Layer 4, Eq. 22). In contrast to the other arrangements of selection response, in Appendices J and L we show that $\mathbf{H}_{\boldsymbol{\zeta}\mathbf{y}}$ is non-singular for all $\boldsymbol{\zeta} \in \{\mathbf{y}, \mathbf{z}, \mathbf{m}\}$ if $\mathbf{G}_{\mathbf{y}}$ is non-singular (i.e., if there is mutational variation in all directions of gene expression space). Consequently, evolutionary equilibria of gene expression, geno-phenotype, or geno-envo-phenotype can only occur when total genetic selection vanishes if there is mutational variation in all directions of gene expression space and if exogenous plastic response is absent.

Importantly, although Layer 7, Eq. 1a and its equivalents describe the evolutionary dynamics of $\boldsymbol{\zeta}$, such equations are guaranteed to yield a well-defined evolutionary trajectory only for certain $\boldsymbol{\zeta}$. Layer 7, Eq. 1a and its equivalents yield a well-defined evolutionary trajectory if $\boldsymbol{\zeta}$ is gene expression $\mathbf{y}$, the geno-phenotype $\mathbf{z}$, or the geno-envo-phenotype $\mathbf{m}$, provided that the developmental and environmental constrains are satisfied throughout and the five elementary components of the evo-devo process are known (Layer 1, Fig. 5). In contrast, the evolutionary trajectory is ill-defined by Layer 7, Eq. 1a and its equivalents if $\boldsymbol{\zeta}$ is the phenotype $\mathbf{x}$ or the environment $\boldsymbol{\epsilon}$, because the evolution of gene expression is not followed but it generally affects the system.

In particular, the evolutionary trajectory of the phenotype is generally ill-defined if only the evolutionary dynamics of the phenotype are considered. Let us temporarily assume that the following four conditions hold: (1) development is non-social ($\mathrm{d}\mathbf{x}^{\intercal}/\mathrm{d}\bar{\mathbf{z}}|_{\mathbf{y}=\bar{\mathbf{y}}} = \mathbf{0}$), and there is (2) no exogenous plastic response of the phenotype ($[(\mathrm{d}\mathbf{x}/\mathrm{d}\boldsymbol{\epsilon}^{\intercal})(\partial\bar{\boldsymbol{\epsilon}}/\partial\tau)]\,|_{\mathbf{y}=\bar{\mathbf{y}}} = \mathbf{0}$), (3) no semi-total selection on gene expression ($\delta w/\delta\mathbf{y}|_{\mathbf{y}=\bar{\mathbf{y}}} = \mathbf{0}$), and (4) no niche-constructed effects of the phenotype on fitness ($[(\partial\boldsymbol{\epsilon}^{\intercal}/\partial\mathbf{x})(\partial w/\partial\boldsymbol{\epsilon})]\,|_{\mathbf{y}=\bar{\mathbf{y}}} = \mathbf{0}$). Then, the evolutionary dynamics of the phenotype reduces to

$$\frac{\mathrm{d}\bar{\mathbf{x}}}{\mathrm{d}\tau} \approx \kappa\mathbf{G}_{\mathbf{x}}\left.\frac{\partial w}{\partial\mathbf{x}}\right|_{\mathbf{y}=\bar{\mathbf{y}}}. \qquad \text{(Layer 7, Eq. 6)}$$

This recovers the Lande (1979) equation for the phenotype, with some differences due to our adaptive dynamics assumptions. The additive genetic covariance matrix of the phenotype (Layer 6, Eq. 5) in this equation is singular because the developmentally initial phenotype is not affected by gene expression and the developmentally final gene expression does not affect the phenotype (so $\mathrm{d}\mathbf{x}^{\intercal}/\mathrm{d}\mathbf{y}|_{\mathbf{y}=\bar{\mathbf{y}}}$ has rows and columns that are zero; Appendix E, Eq. E16). This singularity might disappear by removing from the analysis the developmentally initial phenotype and final gene expression, provided additional conditions hold. Yet, the key point here is that the evolutionary trajectory of the phenotype is generally ill-defined by the evolutionary dynamics of the phenotype alone because such system depends on resident gene expression whose evolution must also be followed. In particular, setting $\mathrm{d}\bar{\mathbf{x}}/\mathrm{d}\tau = \mathbf{0}$ does not generally imply an evolutionary equilibrium, or evolutionary stasis, but only an evolutionary isocline in the phenotype, that is, a transient lack of evolutionary change in the phenotype. To guarantee a well-defined description of the evolutionary dynamics of the phenotype, we simultaneously consider the evolutionary dynamics of the phenotype and gene expression, that is, the geno-phenotype.

Indeed, the evolutionary trajectory of the geno-phenotype is well-defined if the environment is constant or has no evolutionary effect. Let us now assume that the following three conditions hold: (i) development is non-social ($\mathrm{d}\mathbf{x}^{\intercal}/\mathrm{d}\bar{\mathbf{z}}|_{\mathbf{y}=\bar{\mathbf{y}}} = \mathbf{0}$), and there is (ii) no exogenous plastic response of the phenotype ($[(\mathrm{d}\mathbf{x}/\mathrm{d}\boldsymbol{\epsilon}^{\intercal})(\partial\bar{\boldsymbol{\epsilon}}/\partial\tau)]\,|_{\mathbf{y}=\bar{\mathbf{y}}} = \mathbf{0}$), and (iii) no niche-constructed effects of the geno-phenotype on fitness ($[(\partial\boldsymbol{\epsilon}^{\intercal}/\partial\mathbf{z})(\partial w/\partial\boldsymbol{\epsilon})]\,|_{\mathbf{y}=\bar{\mathbf{y}}} = \mathbf{0}$). Then, the evolutionary dynamics of the geno-phenotype reduces to

$$\frac{\mathrm{d}\bar{\mathbf{z}}}{\mathrm{d}\tau} \approx \kappa\mathbf{G}_{\mathbf{z}}\left.\frac{\partial w}{\partial\mathbf{z}}\right|_{\mathbf{y}=\bar{\mathbf{y}}}. \qquad \text{(Layer 7, Eq. 7)}$$

This recovers the Lande (1979) equation, this time for the geno-phenotype, again with some differences stemming from our adaptive dynamics assumptions. The additive genetic covariance matrix of the geno-phenotype (Layer 6, Eq. 6) in this equation is singular because the geno-phenotype $\mathbf{z}$ includes gene expression $\mathbf{y}$ (so $\mathrm{d}\mathbf{z}^{\intercal}/\mathrm{d}\mathbf{y}$ has fewer rows than columns; Layer 4, Eq. 8). So the degrees of freedom of genetic covariation in geno-phenotype space are at most given by the number of lifetime gene products, so these degrees of freedom are bounded by genetic space in a necessarily larger geno-phenotype space. Thus, $\mathbf{G}_{\mathbf{z}}$ is singular if there is at least one trait that is developmentally constructed according to the developmental map (Layer 7, Eq. 1b). The evolutionary dynamics of the geno-phenotype is now fully determined by Layer 7, Eq. 7 provided that i-iii hold and that the developmental (Layer 7, Eq. 1b) and environmental (Layer 7, Eq. 1c) constraints are met. In such case, setting $\mathrm{d}\bar{\mathbf{z}}/\mathrm{d}\tau = \mathbf{0}$ does imply an evolutionary equilibrium, but this does not imply absence of direct directional selection on the geno-phenotype (i.e., it is possible that $\partial w/\partial\mathbf{z}|_{\mathbf{y}=\bar{\mathbf{y}}} \neq \mathbf{0}$) since $\mathbf{G}_{\mathbf{z}}$ is always singular. Due to this singularity, if there is any evolutionary equilibrium, there is an infinite number of them. Kirkpatrick and Lofsvold (1992) showed that if $\mathbf{G}_{\mathbf{z}}$ is singular and constant, then the evolutionary equilibrium that is achieved depends on the initial conditions. Our results extend the relevance of Kirkpatrick and Lofsvold's (1992) observation by showing that $\mathbf{G}_{\mathbf{z}}$ is always singular and remains so as it evolves. Moreover, since both the developmental (Eq. Layer 7, Eq. 1b) and environmental (Eq. Layer 7, Eq. 1c) constraints must be satisfied throughout the evolutionary process, the developmental and environmental constraints determine the admissible evolutionary trajectory and the admissible evolutionary equilibria if mutational variation exists in all

directions of gene expression space. Therefore, developmental and environmental constraints affect the evolutionary outcome if mutational variation exists in all directions of gene expression space.

Since selection response is relatively completely described by total genetic selection, further insight can be gained by rearranging the Lande equation for the geno-phenotype (Layer 7, Eq. 7) in terms of total genetic selection. Using the rearrangement in Layer 7, Eq. 5 and making the assumptions i-iii in the previous paragraph, the Lande equation in Layer 7, Eq. 7 becomes

$$\frac{\mathrm{d}\bar{\mathbf{z}}}{\mathrm{d}\tau} \approx \kappa \mathbf{H}_{\mathbf{zy}} \left.\frac{\mathrm{d}w}{\mathrm{d}\mathbf{y}}\right|_{\mathbf{y}=\bar{\mathbf{y}}}. \qquad \text{(Layer 7, Eq. 8)}$$

Here, if the mutational covariance matrix $\mathbf{G}_{\mathbf{y}}$ is non-singular, then the socio-genetic cross-covariance matrix between geno-phenotype and gene expression $\mathbf{H}_{\mathbf{zy}}$ is non-singular so evolutionary equilibrium ($\mathrm{d}\bar{\mathbf{z}}/\mathrm{d}\tau = \mathbf{0}$) implies absence of total genetic selection (i.e., $\mathrm{d}w/\mathrm{d}\mathbf{y}|_{\mathbf{y}=\bar{\mathbf{y}}} = \mathbf{0}$) to first order of approximation. Hence, to first order, lack of total genetic selection provides a necessary and sufficient condition for evolutionary equilibria in the absence of exogenous environmental change and of absolute mutational constraints. Consequently, evolutionary equilibria depend on development and niche construction since total genetic selection depends on Wagner's (1984, 1989) developmental matrix and on total niche construction by gene expression (Layer 4, Eq. 22). However, since $\mathrm{d}w/\mathrm{d}\mathbf{y}|_{\mathbf{y}=\bar{\mathbf{y}}} = \mathbf{0}$ has only as many equations as there are lifetime gene products and since not only gene expression but also the phenotype and environmental variables must be determined, then $\mathrm{d}w/\mathrm{d}\mathbf{y}|_{\mathbf{y}=\bar{\mathbf{y}}} = \mathbf{0}$ provides fewer equations than variables to solve for. Hence, absence of total genetic selection still implies an infinite number of evolutionary equilibria. Again, only the subset of evolutionary equilibria that satisfy the developmental (Layer 7, Eq. 1b) and environmental (Layer 7, Eq. 1c) constraints are admissible, and so the number of admissible evolutionary equilibria may be finite. Therefore, admissible evolutionary equilibria have a dual dependence on developmental and environmental constraints: first, by the constraints' influence on total genetic selection and so on evolutionary equilibria; and second, by the constraints' specification of which evolutionary equilibria are admissible.

Because we assume that mutants arise when residents are at carrying capacity, the analogous statements can be made for the evolutionary dynamics of a resident vector in terms of lifetime reproductive success (Eq. 27). Using the relationship between selection gradients in terms of fitness and of expected lifetime reproductive success (Eqs. 28), the evolutionary dynamics of $\boldsymbol{\zeta} \in \{\mathbf{x}, \mathbf{y}, \mathbf{z}, \boldsymbol{\epsilon}, \mathbf{m}\}$ (Layer 7, Eq. 1a) are equivalently given by

$$\begin{aligned}
\frac{\mathrm{d}\bar{\boldsymbol{\zeta}}}{\mathrm{d}\tau} &\approx \left.\left(\kappa \frac{1}{T} \mathbf{H}_{\boldsymbol{\zeta}\mathbf{m}} \frac{\partial R_0}{\partial \mathbf{m}} + \frac{\mathrm{s}\boldsymbol{\zeta}}{\mathrm{s}\boldsymbol{\epsilon}^{\intercal}} \frac{\partial \boldsymbol{\epsilon}}{\partial \tau}\right)\right|_{\mathbf{y}=\bar{\mathbf{y}}} && \text{(Layer 7, Eq. 9a)}\\
&= \left.\left(\kappa \frac{1}{T} \mathbf{H}_{\boldsymbol{\zeta}\mathbf{z}} \frac{\delta R_0}{\delta \mathbf{z}} + \frac{\mathrm{s}\boldsymbol{\zeta}}{\mathrm{s}\boldsymbol{\epsilon}^{\intercal}} \frac{\partial \boldsymbol{\epsilon}}{\partial \tau}\right)\right|_{\mathbf{y}=\bar{\mathbf{y}}} && \text{(Layer 7, Eq. 9b)}\\
&= \left.\left(\kappa \frac{1}{T} \mathbf{H}_{\boldsymbol{\zeta}\mathbf{y}} \frac{\mathrm{d}R_0}{\mathrm{d}\mathbf{y}} + \frac{\mathrm{s}\boldsymbol{\zeta}}{\mathrm{s}\boldsymbol{\epsilon}^{\intercal}} \frac{\partial \boldsymbol{\epsilon}}{\partial \tau}\right)\right|_{\mathbf{y}=\bar{\mathbf{y}}}. && \text{(Layer 7, Eq. 9c)}
\end{aligned}$$

To close, the evolutionary dynamics of the environment can be written in a particular form that is insightful. In Appendix K, we show that the evolutionary dynamics of the environment is given by

$$\frac{\mathrm{d}\bar{\boldsymbol{\epsilon}}}{\mathrm{d}\tau} = \left.\left(\frac{\partial(\boldsymbol{\epsilon} + \check{\boldsymbol{\epsilon}})}{\partial \mathbf{z}^{\intercal}} \frac{\mathrm{d}\bar{\mathbf{z}}}{\mathrm{d}\tau} + \frac{\partial \boldsymbol{\epsilon}}{\partial \tau}\right)\right|_{\mathbf{y}=\bar{\mathbf{y}}}. \qquad \text{(Layer 7, Eq. 10)}$$

Thus, the evolutionary change of the environment comprises "inclusive" endogenous environmental change and exogenous environmental change.

5. Example: allocation to growth vs reproduction

We now provide an example that illustrates some of the points above. In particular, this example shows that our results above enable direct calculation of the evo-devo dynamics and the evolution of **G**-matrices and provide an alternative method to dynamic optimization to identify the evolutionary outcomes under explicit developmental constraints. We first describe the example where development is non-social and then extend the example to make development social.

5.1. Non-social development

We consider the classic life history problem of modeling the evolution of resource allocation to growth vs reproduction (Gadgil and Bossert, 1970; León, 1976; Schaffer, 1983; Stearns, 1992; Roff, 1992; Kozłowski and Teriokhin, 1999). Let there be one state variable (or phenotype), one control variable (or gene product), and no environmental variables. In particular, let x_a be a mutant's state variable at age a (e.g., body size or resources available) and $y_a \in [0, 1]$ be the mutant's resource allocation to state growth at that age. Let mutant survival probability $p_a = p$ be constant, so survivorship is $\ell_a = p^{a-1}$, and let mutant fertility be

$$f_a = d(\bar{\mathbf{z}})(1 - y_a)x_a,$$

where $d(\bar{\mathbf{z}})$ is a positive density dependent scalar that brings the resident population size to carrying capacity. Let the developmental constraint be

$$x_{a+1} = g_a(\mathbf{z}_a, \bar{\mathbf{z}}) = x_a + y_a x_a = (1 + y_a)x_a.$$

This is a simplified form of the classic life history problem of resource allocation to growth vs reproduction in discrete age (Gadgil and Bossert, 1970; León, 1976; Schaffer, 1983; Stearns, 1992; Roff, 1992; Kozłowski and Teriokhin, 1999). If one assumes that evolutionary equilibrium occurs where a pair $(\mathbf{x}^*, \mathbf{y}^*)$ is optimal, this optimal pair can be obtained with dynamic programming or optimal control theory (Sydsæter et al., 2008). Instead, here we illustrate how the evolutionary dynamics of $(\mathbf{x}, \mathbf{y})$ can be analysed with the equations derived in this paper, including identification of an optimal pair $(\mathbf{x}^*, \mathbf{y}^*)$.

Let us calculate the elements of Layers 2-4 that we need to calculate genetic covariation and the evolutionary dynamics. Because there are no environmental variables, semi-total effects

equal direct effects. Also, because development is non-social, stabilized effects equal total effects (except for social feedback, which is simply the identity matrix). Iterating the recurrence given by the developmental constraint yields the state at age a

$$x_a = x_1 \prod_{k=1}^{a-1}(1 + y_k). \qquad \text{(Example, Eq. 1)}$$

To find the density dependent scalar, we note that a resident at carrying capacity satisfies $\sum_{a=1}^{N_a} f_a^\circ \ell_a = 1$ (Eq. B9), which yields

$$d(\bar{\mathbf{z}}) = \frac{1}{\sum_{a=1}^{N_a}(1-\bar{y}_a)\bar{x}_a\ell_a}.$$

Using Eq. (24), the entries of the direct selection gradients are given by

$$\begin{aligned}
\left.\frac{\partial w}{\partial x_a}\right|_{\mathbf{y}=\bar{\mathbf{y}}} &= \sum_{j=1}^{N_a} \left.\frac{\partial w_j}{\partial x_a}\right|_{\mathbf{y}=\bar{\mathbf{y}}} = \left.\frac{\partial w_a}{\partial x_a}\right|_{\mathbf{y}=\bar{\mathbf{y}}} \\
&= \frac{1}{T}\left.\left(\phi_a \frac{\partial f_a}{\partial x_a} + \pi_a \frac{\partial p_a}{\partial x_a}\right)\right|_{\mathbf{y}=\bar{\mathbf{y}}} = \frac{1}{\tilde{T}}\ell_a(1-\bar{y}_a), \\
\left.\frac{\partial w}{\partial y_a}\right|_{\mathbf{y}=\bar{\mathbf{y}}} &= \sum_{j=1}^{N_a} \left.\frac{\partial w_j}{\partial y_a}\right|_{\mathbf{y}=\bar{\mathbf{y}}} = \left.\frac{\partial w_a}{\partial y_a}\right|_{\mathbf{y}=\bar{\mathbf{y}}} \\
&= \frac{1}{T}\left.\left(\phi_a \frac{\partial f_a}{\partial y_a} + \pi_a \frac{\partial p_a}{\partial y_a}\right)\right|_{\mathbf{y}=\bar{\mathbf{y}}} = -\frac{1}{\tilde{T}}\ell_a\bar{x}_a.
\end{aligned} \qquad \text{(Example, Eq. 2)}$$

where the generation time without density dependence is

$$\tilde{T} = \sum_{j=1}^{N_a} j\ell_j(1-\bar{y}_j)\bar{x}_j.$$

Thus, there is always direct selection for increased state and against allocation to growth (except at the boundaries). The entries of the matrices of direct effects on the state (a: row, j: column) are given by

$$\left.\frac{\partial x_j}{\partial x_a}\right|_{\mathbf{y}=\bar{\mathbf{y}}} = \begin{cases} 1+\bar{y}_a & \text{if } j = a+1 \\ 1 & \text{if } j = a \\ 0 & \text{otherwise,} \end{cases}$$

$$\left.\frac{\partial x_j}{\partial y_a}\right|_{\mathbf{y}=\bar{\mathbf{y}}} = \begin{cases} \bar{x}_a & \text{if } j = a+1 \\ 0 & \text{otherwise.} \end{cases}$$

Using Layer 4, Eq. 2 and Eq. (E15), the entries of the matrices of total effects on the state are given by

$$\begin{aligned}
\left.\frac{\mathrm{d}x_j}{\mathrm{d}x_a}\right|_{\mathbf{y}=\bar{\mathbf{y}}} &= \begin{cases} \prod_{k=a}^{j-1} \left.\frac{\partial x_{k+1}}{\partial x_k}\right|_{\mathbf{y}=\bar{\mathbf{y}}} & \text{if } j > a \\ 1 & \text{if } j = a \\ 0 & \text{otherwise} \end{cases} \\
&= \begin{cases} \prod_{k=a}^{j-1}(1+\bar{y}_k) & \text{if } j > a \\ 1 & \text{if } j = a \\ 0 & \text{otherwise,} \end{cases} \\
\left.\frac{\mathrm{d}x_j}{\mathrm{d}y_a}\right|_{\mathbf{y}=\bar{\mathbf{y}}} &= \begin{cases} \left.\left(\frac{\partial x_{a+1}}{\partial y_a}\prod_{k=a+1}^{j-1}\frac{\partial x_{k+1}}{\partial x_k}\right)\right|_{\mathbf{y}=\bar{\mathbf{y}}} & \text{if } j > a+1 \\ \left.\frac{\partial x_{a+1}}{\partial y_a}\right|_{\mathbf{y}=\bar{\mathbf{y}}} & \text{if } j = a+1 \\ 0 & \text{otherwise} \end{cases} \\
&= \begin{cases} \bar{x}_a \prod_{k=a+1}^{j-1}(1+\bar{y}_k) & \text{if } j > a+1 \\ \bar{x}_a & \text{if } j = a+1 \\ 0 & \text{otherwise.} \end{cases}
\end{aligned} \qquad \text{(Example, Eq. 3)}$$

Then, using Layer 4, Eq. 21 and Layer 4, Eq. 22, the entries of the total selection gradients are given by

$$\begin{aligned}
\left.\frac{\mathrm{d}w}{\mathrm{d}x_a}\right|_{\mathbf{y}=\bar{\mathbf{y}}} &= \left.\left(\frac{\mathrm{d}\mathbf{x}^\intercal}{\mathrm{d}x_a}\frac{\partial w}{\partial \mathbf{x}}\right)\right|_{\mathbf{y}=\bar{\mathbf{y}}} = \sum_{j=1}^{N_a}\left.\left(\frac{\mathrm{d}x_j}{\mathrm{d}x_a}\frac{\partial w}{\partial x_j}\right)\right|_{\mathbf{y}=\bar{\mathbf{y}}} \\
&= \left.\left(\frac{\mathrm{d}x_a}{\mathrm{d}x_a}\frac{\partial w}{\partial x_a} + \sum_{j=a+1}^{N_a}\frac{\mathrm{d}x_j}{\mathrm{d}x_a}\frac{\partial w}{\partial x_j}\right)\right|_{\mathbf{y}=\bar{\mathbf{y}}} \\
&= \frac{1}{\tilde{T}}\left[\ell_a(1-\bar{y}_a) + \sum_{j=a+1}^{N_a}\ell_j(1-\bar{y}_j)\prod_{k=a}^{j-1}(1+\bar{y}_k)\right], \\
\left.\frac{\mathrm{d}w}{\mathrm{d}y_a}\right|_{\mathbf{y}=\bar{\mathbf{y}}} &= \left.\left(\frac{\partial w}{\partial y_a} + \frac{\mathrm{d}\mathbf{x}^\intercal}{\mathrm{d}y_a}\frac{\partial w}{\partial \mathbf{x}}\right)\right|_{\mathbf{y}=\bar{\mathbf{y}}} = \left.\left(\frac{\partial w}{\partial y_a} + \sum_{j=1}^{N_a}\frac{\mathrm{d}x_j}{\mathrm{d}y_a}\frac{\partial w}{\partial x_j}\right)\right|_{\mathbf{y}=\bar{\mathbf{y}}} \\
&= \left.\left(\frac{\partial w}{\partial y_a} + \frac{\mathrm{d}x_{a+1}}{\mathrm{d}y_a}\frac{\partial w}{\partial x_{a+1}} + \sum_{j=a+2}^{N_a}\frac{\mathrm{d}x_j}{\mathrm{d}y_a}\frac{\partial w}{\partial x_j}\right)\right|_{\mathbf{y}=\bar{\mathbf{y}}} \\
&= -\frac{1}{\tilde{T}}\ell_a\bar{x}_a + \bar{x}_a\frac{1}{\tilde{T}}\ell_{a+1}(1-\bar{y}_{a+1}) \\
&\quad + \sum_{j=a+2}^{N_a}\bar{x}_a\prod_{k=a+1}^{j-1}(1+\bar{y}_k)\frac{1}{\tilde{T}}\ell_j(1-\bar{y}_j) \\
&= \frac{1}{\tilde{T}}\bar{x}_a\left[-\ell_a + \sum_{j=a+1}^{N_a}\ell_j(1-\bar{y}_j)\prod_{k=a+1}^{j-1}(1+\bar{y}_k)\right],
\end{aligned} \qquad \text{(Example, Eq. 4)}$$

where we use the empty-product notation such that $\prod_{k=a}^{a-1} F_k = 1$ and the empty-sum notation such that $\sum_{k=a}^{a-1} F_k = 0$ for any F_k. There is thus always total selection for increased state, although total selection for allocation to growth may be positive or negative.

Now, using Eqs. (1) and (3), the evo-devo dynamics are given by

$$\begin{aligned}
\frac{\Delta\bar{\mathbf{y}}}{\Delta\tau} &\approx \kappa\mathbf{G}_{\mathbf{y}}\left.\frac{\mathrm{d}w}{\mathrm{d}\mathbf{y}}\right|_{\mathbf{y}=\bar{\mathbf{y}}} \\
\bar{x}_{a+1} &= g_a(\bar{\mathbf{z}}_a, \bar{\mathbf{z}}).
\end{aligned} \qquad \text{(Example, Eq. 5)}$$

Using Layer 7, Eq. 1a, Layer 7, Eq. 4, and Layer 7, Eq. 5, the evolutionary dynamics of the phenotype in the limit as $\Delta\tau \to \infty$ are given by

$$\frac{\mathrm{d}\bar{\mathbf{x}}}{\mathrm{d}\tau} \approx \kappa\mathbf{G}_{\mathbf{xz}}\left.\frac{\partial w}{\partial \mathbf{z}}\right|_{\mathbf{y}=\bar{\mathbf{y}}} = \kappa\mathbf{G}_{\mathbf{xy}}\left.\frac{\mathrm{d}w}{\mathrm{d}\mathbf{y}}\right|_{\mathbf{y}=\bar{\mathbf{y}}}. \qquad \text{(Example, Eq. 6)}$$

Note these are not equations in Lande's form. In particular, the additive genetic-cross covariance matrices involved are not symmetric and the selection gradients are not those of the evolving trait in the left-hand side; Example, Eq. 6 cannot be arranged in Lande's form because controls directly affect fitness (i.e., $\partial w/\partial \mathbf{y}|_{\mathbf{y}=\bar{\mathbf{y}}} \neq \mathbf{0}$; Example, Eq. 2). Importantly, $\mathbf{G_{xz}}$ and $\mathbf{G_{xy}}$ depend on $\bar{\mathbf{y}}$ because of gene-phenotype interaction in development (i.e., the developmental map involves a product $y_a x_a$ such that the total effect of the control on the state depends on the control; Example, Eq. 3); consequently, the evolutionary trajectory of the state (phenotype) is ill-defined by the system in Example, Eq. 6 because the system does not describe the evolution of $\bar{\mathbf{y}}$. In turn, the evolutionary dynamics of the geno-phenotype are given by

$$\frac{\mathrm{d}\bar{\mathbf{z}}}{\mathrm{d}\tau} \approx \kappa \mathbf{G_z} \left.\frac{\partial w}{\partial \mathbf{z}}\right|_{\mathbf{y}=\bar{\mathbf{y}}} = \kappa \mathbf{G_{zy}} \left.\frac{\mathrm{d}w}{\mathrm{d}\mathbf{y}}\right|_{\mathbf{y}=\bar{\mathbf{y}}}. \qquad \text{(Example, Eq. 7)}$$

This system contains dynamic equations for all evolutionarily dynamic variables, namely both $\bar{\mathbf{x}}$ and $\bar{\mathbf{y}}$, so it is determined and the evolutionary trajectory is well-defined. The first equality in Example, Eq. 7 is in Lande's form, but $\mathbf{G_z}$ is always singular. In contrast, the matrix $\mathbf{G_{zy}}$ in the second equality is non-singular if the mutational covariance matrix $\mathbf{G_y}$ is non-singular. Thus, the total selection gradient of controls provides a relatively complete description of the evolutionary process of the geno-phenotype.

Let the entries of the mutational covariance matrix be given by

$$G_{y_a,y_j} = \begin{cases} \gamma \bar{y}_a(1-\bar{y}_a) & \text{if } j = a \\ 0 & \text{otherwise,} \end{cases}$$

where $0 < \gamma \ll 1$ so the assumption of marginally small mutational variance, namely $0 < \mathrm{tr}(\mathbf{G_y}) \ll 1$, holds. Thus, $\mathbf{G_y}$ is diagonal and becomes singular only at the boundaries where the resident control is zero or one. Then, from Example, Eq. 5, the evolutionary equilibria of the control at a given age and their stability are given by the sign of its corresponding total selection gradient.

Let us now find the evolutionary equilibria and their stability for the control. Using Example, Eq. 4, starting from the last age, the total selection on the control at the last age is

$$\left.\frac{\mathrm{d}w}{\mathrm{d}y_{N_\mathrm{a}}}\right|_{\mathbf{y}=\bar{\mathbf{y}}} \propto -\ell_{N_\mathrm{a}},$$

which is always negative so the stable last resident control is

$$\bar{y}^*_{N_\mathrm{a}} = 0. \qquad \text{(Example, Eq. 8a)}$$

That is, no allocation to growth at the last age. Continuing with the second-to-last age, the total selection on the control at this age is

$$\begin{aligned}\left.\frac{\mathrm{d}w}{\mathrm{d}y_{N_\mathrm{a}-1}}\right|_{\mathbf{y}=\bar{\mathbf{y}}} &\propto -\ell_{N_\mathrm{a}-1} + \sum_{j=N_\mathrm{a}}^{N_\mathrm{a}} \ell_j(1-\bar{y}_j) \prod_{k=N_\mathrm{a}}^{j-1}(1+\bar{y}_k) \\ &= -\ell_{N_\mathrm{a}-1} + \ell_{N_\mathrm{a}}(1-\bar{y}_{N_\mathrm{a}}).\end{aligned}$$

Evaluating at the last optimal control (Example, Eq. 8a) and substituting $\ell_a = p^{a-1}$ yields

$$\left.\frac{\mathrm{d}w}{\mathrm{d}y_{N_\mathrm{a}-1}}\right|_{\mathbf{y}=\bar{\mathbf{y}}=\bar{\mathbf{y}}^*} \propto -p^{N_\mathrm{a}-2} + p^{N_\mathrm{a}-1} \propto -1+p,$$

which is negative (assuming $p < 1$) so the stable second-to-last resident control is

$$\bar{y}^*_{N_\mathrm{a}-1} = 0. \qquad \text{(Example, Eq. 8b)}$$

Continuing with the third-to-last age, the total selection on the control at this age is

$$\begin{aligned}\left.\frac{\mathrm{d}w}{\mathrm{d}y_{N_\mathrm{a}-2}}\right|_{\mathbf{y}=\bar{\mathbf{y}}} &\propto -\ell_{N_\mathrm{a}-2} + \sum_{j=N_\mathrm{a}-1}^{N_\mathrm{a}} \ell_j(1-\bar{y}_j) \prod_{k=N_\mathrm{a}-1}^{j-1}(1+\bar{y}_k) \\ &= -\ell_{N_\mathrm{a}-2} + \ell_{N_\mathrm{a}-1}(1-\bar{y}_{N_\mathrm{a}-1}) \\ &\quad + \ell_{N_\mathrm{a}}(1-\bar{y}_{N_\mathrm{a}})(1+\bar{y}_{N_\mathrm{a}-1}).\end{aligned}$$

Evaluating at the last two optimal controls (Example, Eq. 8a and Example, Eq. 8b) and substituting $\ell_a = p^{a-1}$ yields

$$\left.\frac{\mathrm{d}w}{\mathrm{d}y_{N_\mathrm{a}-2}}\right|_{\mathbf{y}=\bar{\mathbf{y}}=\bar{\mathbf{y}}^*} \propto -p^{N_\mathrm{a}-3} + p^{N_\mathrm{a}-2} + p^{N_\mathrm{a}-1} \propto -1+p+p^2,$$

which is positive if

$$p > p^*_{N_\mathrm{a}-2} = \frac{1}{2}(-1+\sqrt{5}) \approx 0.62.$$

So the stable third-to-last resident control is

$$\bar{y}^*_{N_\mathrm{a}-2} = \begin{cases} 0 & \text{if } p < p^*_{N_\mathrm{a}-2} = \frac{1}{2}(-1+\sqrt{5}) \approx 0.62 \\ 1 & \text{if } p > p^*_{N_\mathrm{a}-2} = \frac{1}{2}(-1+\sqrt{5}) \approx 0.62. \end{cases} \qquad \text{(Example, Eq. 8c)}$$

If $p = p^*_{N_\mathrm{a}-2}$, the control at such age is selectively neutral, but we ignore this case as without an evolutionary model for p it is biologically unlikely that survival is and remains at such precise value. Hence, there is no allocation at this age for low survival and full allocation for high survival. Continuing with the fourth-to-last age, the total selection on the control at this age is

$$\begin{aligned}\left.\frac{\mathrm{d}w}{\mathrm{d}y_{N_\mathrm{a}-3}}\right|_{\mathbf{y}=\bar{\mathbf{y}}} &\propto -\ell_{N_\mathrm{a}-3} + \sum_{j=N_\mathrm{a}-2}^{N_\mathrm{a}} \ell_j(1-\bar{y}_j) \prod_{k=N_\mathrm{a}-2}^{j-1}(1+\bar{y}_k) \\ &= -\ell_{N_\mathrm{a}-3} + \ell_{N_\mathrm{a}-2}(1-\bar{y}_{N_\mathrm{a}-2}) \\ &\quad + \ell_{N_\mathrm{a}-1}(1-\bar{y}_{N_\mathrm{a}-1})(1+\bar{y}_{N_\mathrm{a}-2}) \\ &\quad + \ell_{N_\mathrm{a}}(1-\bar{y}_{N_\mathrm{a}})(1+\bar{y}_{N_\mathrm{a}-2})(1+\bar{y}_{N_\mathrm{a}-1}).\end{aligned}$$

Evaluating at the last three optimal controls (Example, Eq. 8a-Example, Eq. 8c) and substituting $\ell_a = p^{a-1}$ yields

$$\begin{aligned}\left.\frac{\mathrm{d}w}{\mathrm{d}y_{N_\mathrm{a}-3}}\right|_{\mathbf{y}=\bar{\mathbf{y}}=\bar{\mathbf{y}}^*} &\propto -p^{N_\mathrm{a}-4} + p^{N_\mathrm{a}-3}(1-y^*_{N_\mathrm{a}-2}) + p^{N_\mathrm{a}-2}(1+y^*_{N_\mathrm{a}-2}) \\ &\quad + p^{N_\mathrm{a}-1}(1+y^*_{N_\mathrm{a}-2})\end{aligned}$$

$$\propto -1 + p(1 - y^*_{N_a-2}) + p^2(1+p)(1 + y^*_{N_a-2}).$$

If $p < p^*_{N_a-2}$, this is

$$\left.\frac{\mathrm{d}w}{\mathrm{d}y_{N_a-3}}\right|_{\mathbf{y}=\bar{\mathbf{y}}=\bar{\mathbf{y}}^*} \propto -1 + p + p^2(1+p),$$

which is positive if

$$p > p^*_{N_a-3} \approx 0.54.$$

If $p > p^*_{N_a-2}$, the gradient is

$$\left.\frac{\mathrm{d}w}{\mathrm{d}y_{N_a-3}}\right|_{\mathbf{y}=\bar{\mathbf{y}}=\bar{\mathbf{y}}^*} \propto -1 + 2p^2(1+p),$$

which is positive if

$$p > \tilde{p}^*_{N_a-3} \approx 0.565.$$

Hence, the stable fourth-to-last resident control is

$$\bar{y}^*_{N_a-3} = \begin{cases} 0 & \text{if } p < p^*_{N_a-3} \approx 0.54 \\ 1 & \text{if } p > p^*_{N_a-3} \approx 0.54, \end{cases} \qquad \text{(Example, Eq. 8d)}$$

for $p \neq p^*_{N_a-2} \approx 0.62$. Again, this is no allocation to growth for low survival, although at this earlier age survival can be smaller for allocation to growth to evolve. Numerical solution for the evo-devo dynamics using Example, Eq. 5 is given in Fig. 6. The associated evolution of the $\mathbf{G_z}$ matrix, plotting Layer 6, Eq. 6, is given in Fig. 7. The code used to generate these figures is in the Supplementary Information.

5.2. Social development

Consider a slight modification of the previous example, so that development is social. Let the mutant fertility be

$$f_a = d(\bar{\mathbf{z}})(1 - y_a)(x_a + q\bar{x}_{a+1}),$$

where the available resource is now given by $x_a + q\bar{x}_{a+1}$, such that an immediately older resident contributes to or scrounges the resource of the focal individual (or the focal learns from the older resident), for some constant q (positive, negative, or zero). Let the developmental constraint be

$$x_{a+1} = g_a(\mathbf{z}_a, \bar{\mathbf{z}}) = x_a + y_a(x_a + q\bar{x}_{a+1}).$$

Note that setting the mutant control to the resident does not necessarily produce a resident state. Indeed, the developed state with resident control is

$$\bar{\bar{x}}_{a+1} = \bar{\bar{x}}_a + \bar{y}_a(\bar{\bar{x}}_a + q\bar{x}_{a+1}).$$

which may not equal the resident state $\bar{x}_{a+1}$. If the resident $\bar{\mathbf{x}}$ is at socio-devo equilibrium $\bar{\mathbf{x}}^{**}$, then the resident satisfies

$$\bar{x}^{**}_{a+1} = \bar{x}^{**}_a + \bar{y}_a(\bar{x}^{**}_a + q\bar{x}^{**}_{a+1}).$$

Solving for $\bar{x}^{**}_{a+1}$ yields the socio-devo equilibrium

$$\bar{x}^{**}_{a+1} = \frac{1 + \bar{y}_a}{1 - q\bar{y}_a}\bar{x}^{**}_a \qquad \text{(Example, Eq. 9)}$$

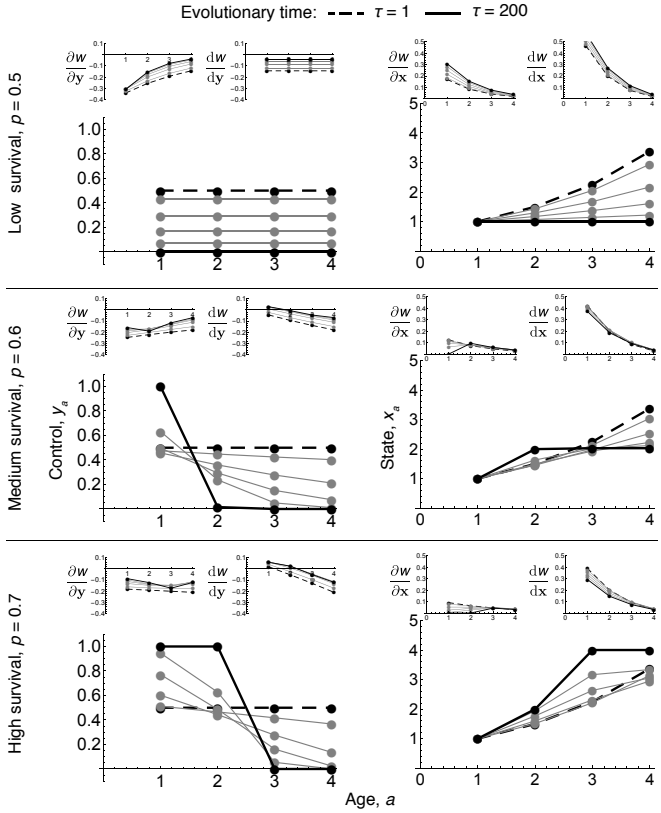

Figure 6: Example. Numerical solution of evolutionary dynamics of the control and associated developmental dynamics of the state. Large plots give the resident control or state vs age over evolutionary time for various p. Small plots give the associated direct and total selection gradients. The evolutionary outcomes match the predictions for the control (Example, Eq. 8) and associated state (Example, Eq. 1). From Eq. (18a), the carrying capacity is $\bar{n}^* = \bar{n}_1 \sum_{a=1}^4 p^{a-1}$, which is constant. We let $\bar{n}_1 = 2/(\mu\gamma)$, so $\kappa = \gamma^{-1}\sum_{a=1}^4 p^{a-1}$.

provided that $1 - q\bar{y}_a \neq 0$. The entries of the matrix of the direct social effects on the state are given by

$$\left.\frac{\partial x_j}{\partial \bar{x}_a}\right|_{\mathbf{y}=\bar{\mathbf{y}}} = \begin{cases} \bar{y}_{a-1}q & \text{if } j = a \\ 0 & \text{otherwise.} \end{cases}$$

Hence, from Eqs. I8 and I9, $\mathrm{d}\mathbf{x}^\intercal/\mathrm{d}\bar{\mathbf{x}}|_{\mathbf{y}=\bar{\mathbf{y}}}$ is upper-triangular, so its eigenvalues are the values in its main diagonal, which are given by $\partial x_a/\partial \bar{x}_a|_{\mathbf{y}=\bar{\mathbf{y}}} = \bar{y}_{a-1}q$. Thus, the eigenvalues of $\mathrm{d}\mathbf{x}^\intercal/\mathrm{d}\bar{\mathbf{x}}|_{\mathbf{y}=\bar{\mathbf{y}}}$ have absolute value strictly less than one if $|q| < 1$, in which case the socio-devo equilibrium in Example, Eq. 9 is socio-devo stable.

Let $\bar{\mathbf{x}}$ denote an SDS resident given by Example, Eq. 9 dropping the ** for simplicity and where $|q| < 1$. Then, the evo-devo dynamics are still given by Example, Eq. 5. Using Layer 7, Eq. 1a, Layer 7, Eq. 4, and Layer 7, Eq. 5, the evolutionary dynamics of the phenotype in the limit as $\Delta\tau \to \infty$ are now given by

$$\frac{\mathrm{d}\bar{\mathbf{x}}}{\mathrm{d}\tau} \approx \kappa\mathbf{H_{xz}}\left.\frac{\partial w}{\partial \mathbf{z}}\right|_{\mathbf{y}=\bar{\mathbf{y}}} = \kappa\mathbf{H_{xy}}\left.\frac{\mathrm{d}w}{\mathrm{d}\mathbf{y}}\right|_{\mathbf{y}=\bar{\mathbf{y}}}. \qquad \text{(Example, Eq. 10)}$$

The evolutionary trajectory is ill-defined by this system as $\mathbf{H_{xz}}$ and $\mathbf{H_{xy}}$ depend on $\bar{\mathbf{y}}$ because of gene-phenotype interaction in

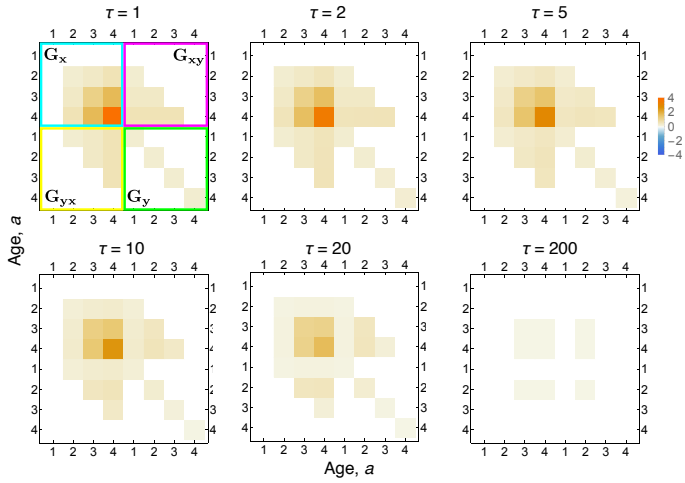

Figure 7: Resulting evolutionary dynamics of the additive genetic covariance matrix $\mathbf{G_z}$. The upper-left quadrant (blue) is the additive genetic covariance matrix $\mathbf{G_x}$ of the phenotype, that is, of the state. For instance, at the initial evolutionary time, the genetic variance for the state is higher at later ages, and the state at age 3 is highly genetically correlated with the state at age 4. As evolutionary time progresses, genetic covariation vanishes as mutational covariation vanishes ($\mathbf{G_y}$ becomes singular) as controls approach their boundary values. $p = 0.7$. The evolutionary times τ shown correspond to those of Fig. 6.

development. In turn, the evolutionary dynamics of the geno-phenotype are given by

$$\frac{\mathrm{d}\bar{\mathbf{z}}}{\mathrm{d}\tau} \approx \kappa \mathbf{H_z} \left.\frac{\partial w}{\partial \mathbf{z}}\right|_{\mathbf{y}=\bar{\mathbf{y}}} = \kappa \mathbf{H_{zy}} \left.\frac{\mathrm{d}w}{\mathrm{d}\mathbf{y}}\right|_{\mathbf{y}=\bar{\mathbf{y}}}. \qquad \text{(Example, Eq. 11)}$$

The evolutionary trajectory is well-defined by this system as it contains dynamic equations for all evolutionary dynamic variables, namely both $\bar{\mathbf{x}}$ and $\bar{\mathbf{y}}$. While $\mathbf{H_z}$ in the first equality is always singular, the matrix $\mathbf{H_{zy}}$ in the second equality is non-singular if the mutational covariance matrix $\mathbf{G_y}$ is non-singular. Thus, the total selection gradient of controls still provides a relatively complete description of the evolutionary process of the geno-phenotype.

We can similarly find that the total selection gradient of the control at age a is

$$\left.\frac{\mathrm{d}w}{\mathrm{d}y_a}\right|_{\mathbf{y}=\bar{\mathbf{y}}} = \frac{1}{\tilde{T}} \bar{x}_a \frac{1+q}{1-q\bar{y}_a} \left[-\ell_a + \sum_{j=a+1}^{N_\mathrm{a}} \ell_j (1-\bar{y}_j) \prod_{k=a+1}^{j-1} (1+\bar{y}_k) \right],$$

where the generation time without density dependence is now

$$\tilde{T} = \sum_{j=1}^{N_\mathrm{a}} j \ell_j (1-\bar{y}_j) \bar{x}_j \frac{1+q}{1-q\bar{y}_j}.$$

This total selection gradient of the control at age a has the same sign as that found in the model for non-social development (Example, Eq. 4). Hence, the stable evolutionary equilibria for controls are still given by Example, Eq. 8. Yet, the associated states, given by Example, Eq. 9, may be different due to social development (Fig. 8). That is, social development here does not affect the evolutionary equilibria, as it does not affect the zeros of the total selection gradient of controls which gives

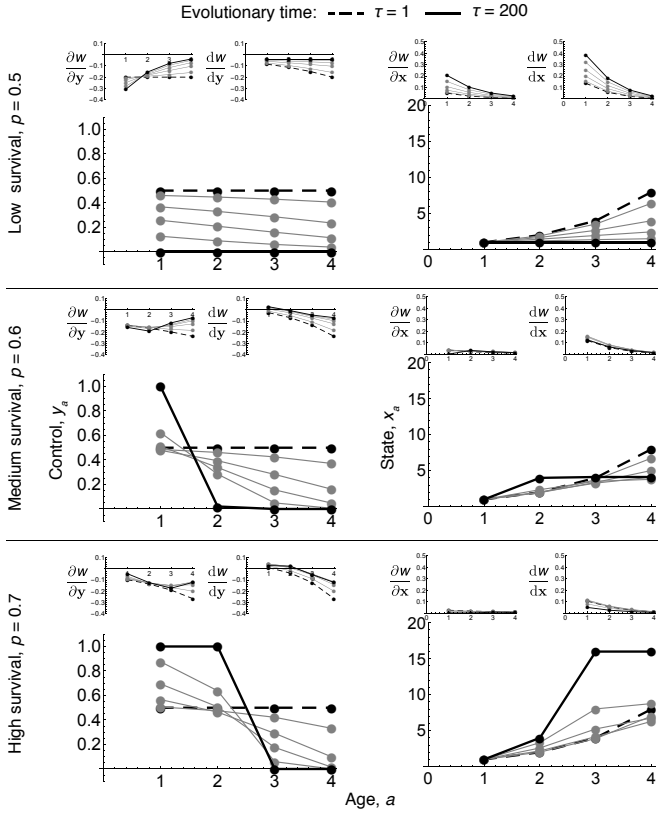

Figure 8: Example with social development. The control evolves to the same values as those with non-social development in Fig. 6. However, the state evolves to much larger values due to social development. Large plots give the resident control or state vs age over evolutionary time for various p. Small plots give the associated direct and total selection gradients. The evolutionary dynamics of the control match the predictions for the control (Example, Eq. 8) and associated state (Example, Eq. 9). κ is as in Fig. 6. $q = 0.5$.

the zeros of the evolutionary dynamics of the geno-phenotype (Example, Eq. 11). Instead, social development affects here the developmental constraint so it affects the admissible evolutionary equilibria of the state. Numerical solution for the evo-devo dynamics using Example, Eq. 5 is given in Fig. 8. For the q chosen, the phenotype evolves to much larger values due to social feedback than with non-social development although gene expression evolves to the same values. The associated evolution of the $\mathbf{H_z}$ matrix, using Layer 6, Eq. 9, is given in Fig. 9. The code used to generate these figures is in the Supplementary Information.

6. Discussion

We have addressed the question of how development affects evolution by formulating a mathematical framework that integrates explicit developmental dynamics into evolutionary dynamics. The framework integrates age progression, explicit developmental constraints according to which the phenotype is constructed across life, and evolutionary dynamics. This framework yields a description of the structure of genetic covariation, including the developmental matrix $\mathrm{d}\mathbf{x}^\intercal/\mathrm{d}\mathbf{y}|_{\mathbf{y}=\bar{\mathbf{y}}}$, from mechanistic processes. The framework also yields a well-defined

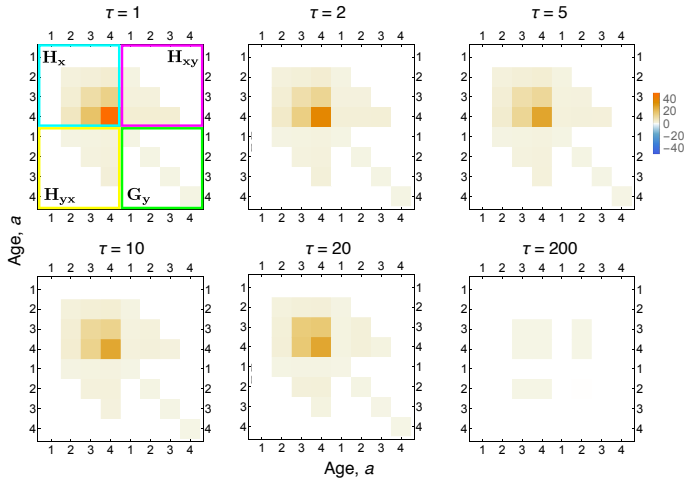

Figure 9: Resulting dynamics of additive socio-genetic covariance matrix $\mathbf{H_z}$. The structure and dynamics of $\mathbf{H_z}$ here are similar to those of $\mathbf{G_z}$ in Fig. 9 but the magnitudes are an order of magnitude larger (compare bar legends). $p = 0.7$, $q = 0.5$. The evolutionary times τ shown correspond to those of Fig. 8.

description of the evolutionary process of developed phenotypes in gradient form, such that their long-term evolution can be described as the climbing of a fitness landscape within the assumptions made. Additionally, this framework provides a tractable method to model the evo-devo dynamics for a broad class of models. Overall, the framework provides a theory of constrained evolutionary dynamics, where the developmental and environmental constraints determine the admissible evolutionary path (Layer 7, Eq. 1).

Previous understanding suggested that development affects evolution by inducing genetic covariation and genetic constraints, although the nature of such constraints had remained uncertain. Our results show that development has major evolutionary effects. First, a well-defined description of phenotypic evolution in gradient form requires that not only phenotypic but also genetic evolution is followed. In such extended description of the evolutionary process in gradient form, the associated **G**-matrix is necessarily singular with a maximum number of degrees of freedom given by the number of lifetime gene products. Consequently, genetic covariation is necessarily absent in as many directions of geno-phenotype space as there are developed traits; thus, there necessarily are absolute genetic constraints in a well-defined evolutionary trajectory for the phenotype along an adaptive topography. Second, since **G** is singular in geno-phenotype space, direct directional selection is insufficient to identify evolutionary equilibria in contrast to common practice. Instead, total genetic selection, which depends on development, is sufficient to identify evolutionary equilibria if there are no absolute mutational constraints and no exogenous plastic response. Third, since **G** is singular in geno-phenotype space, if there is any evolutionary equilibrium and no exogenous plastic response, then there is an infinite number of evolutionary equilibria that depend on development; in addition, development determines the admissible evolutionary trajectory and so the admissible equilibria. The traditional adaptive topography in phenotype space assumes a non-singular **G**-matrix where evolutionary outcomes occur at fitness landscape peaks (i.e., where $\partial w/\partial \mathbf{x}|_{\mathbf{y}=\bar{\mathbf{y}}=\bar{\mathbf{y}}^*} = \mathbf{0}$). Instead, we find that the evolutionary dynamics strongly differ from that representation in that evolutionary outcomes occur at best (i.e., without absolute mutational constraints) at peaks in the admissible evolutionary path determined by development (i.e., where $\mathrm{d}w/\mathrm{d}\mathbf{y}|_{\mathbf{y}=\bar{\mathbf{y}}=\bar{\mathbf{y}}^*} = \mathbf{0}$), and that such path peaks do not typically occur at landscape peaks (so generally $\partial w/\partial \mathbf{z}|_{\mathbf{y}=\bar{\mathbf{y}}=\bar{\mathbf{y}}^*} \neq \mathbf{0}$).

We find that the **G**-matrix is necessarily singular in geno-phenotype space if at least one trait is developmentally constructed according to the developmental map we considered (Layer 7, Eq. 1b). This singularity arises because, to have a well-defined climbing of the adaptive topography for the phenotype, the relevant genetic covariation is in geno-phenotype space whose degrees of freedom are bounded by the number of lifetime gene products. In quantitative genetics terms, this corresponds to genetic covariation in phenotype and allele frequency space being bounded by the number of loci. In quantitative genetics, the evolution of a multivariate phenotype is traditionally followed without simultaneously following allele frequency change. Both in quantitative genetics and in our framework, following phenotypic evolution (i.e., that of developed traits) without simultaneously tracking genetic evolution (i.e., that of gene expression) generally yields an ill-defined evolutionary trajectory. In our framework, the **G**-matrix in phenotype space generally depends on resident gene expression via both the mutational covariance matrix and the developmental matrix. The developmental matrix depends on resident gene expression particularly due to gene-gene interaction, gene-phenotype interaction, and gene-environment interaction (see text below Eq. Layer 6, Eq. 5). The analogous dependence of **G** on allele frequency holds under quantitative genetics assumptions for the same reasons (Turelli, 1988; Service and Rose, 1985), thus requiring consideration of allele frequency as part of the dynamic variables. If, under a quantitative genetics framework, allele frequency were considered as part of the multivariate geno-phenotype in order to render the evolutionary trajectory well-defined in general (within additional assumptions), then the associated **G**-matrix would be necessarily singular, with at least as many zero eigenvalues as there are traits that are not allele frequency. The reason for such singularity is the same we point out here, as the number of degrees of freedom of genetic covariation in phenotypic and genetic space is bounded by the genetic space. In our framework, including gene expression as part of the geno-phenotype trivially enforces singularity of **G** in geno-phenotype space, but crucially such inclusion is needed to guarantee a well-defined description of phenotypic evolution in gradient form. Consequently, lack of selection response in geno-phenotype space generally occurs with persistent direct directional selection in geno-phenotype space. The singularity of **G** in geno-phenotype space persists despite evolution of the developmental map, regardless of the number of gene products or phenotypes provided there is any phenotype, and in the presence of endogenous or exogenous environmental change. The singularity remains if the phenotype directly depends on gene expression (Layer 7, Eq. 1b) so that there is genetic input fed

directly into the phenotype, although the singularity may disappear if every phenotype at every age is exclusively directly genetically encoded: that is, if there are no developed traits but only genetic traits (or in a standard quantitative genetics framework, if only allele frequency change is followed).

The singularity of $\mathbf{G}$ in geno-phenotype space is not due to our adaptive dynamics assumptions. Under quantitative genetics assumptions, the additive genetic covariance matrix of phenotype $\mathbf{x}$ is $\mathbf{G_x} = \boldsymbol{\alpha_x}\text{cov}[\mathbf{y},\mathbf{y}]\boldsymbol{\alpha}_\mathbf{x}^\intercal$ as described in the introduction, where we use $\boldsymbol{\alpha_x}$ to highlight that this $\boldsymbol{\alpha}$ matrix is for the regression coefficients of the phenotype with respect to allele frequency. Under quantitative genetics assumptions, the matrix $\text{cov}[\mathbf{y},\mathbf{y}]$ describes the observed covariance in allele frequency due to any source, so it describes standing covariation in allele frequency. Instead, under our adaptive dynamics assumptions, we recover the same form of $\mathbf{G}$ in phenotype space, but $\text{cov}[\mathbf{y},\mathbf{y}]$ describes the covariance in gene expression only due to mutation at the current evolutionary time step among the possible realised mutations, so it describes (expected) mutational covariation. Regardless of whether $\text{cov}[\mathbf{y},\mathbf{y}]$ describes standing covariation in allele frequency or mutational covariation, the additive genetic covariance matrix in geno-phenotype space $\mathbf{G_z} = \boldsymbol{\alpha_z}\text{cov}[\mathbf{y},\mathbf{y}]\boldsymbol{\alpha}_\mathbf{z}^\intercal$ is always singular because the developmental matrix of the geno-phenotype $\boldsymbol{\alpha_z}$ has fewer rows than columns: that is, the degrees of freedom of $\mathbf{G_z}$ have an upper bound given by the number of loci (or genetic predictors) while the size of $\mathbf{G_z}$ is given by the number of loci and of phenotypes. Thus, whether one considers standing or mutational covariation, the additive genetic covariance matrix of the geno-phenotype is always singular. Eliminating traits from the analysis to render $\mathbf{G_z}$ non-singular as traditionally recommended (Lande, 1979) either renders the gradient system underdetermined and so it yields an ill-defined evolutionary trajectory, or prevents a description of phenotypic evolution as the climbing of a fitness landscape. Thus, a well-defined description of phenotypic evolution in gradient form requires a singular $\mathbf{G}$ matrix.

Extensive research efforts have been devoted to determining the relevance of constraints in adaptive evolution (Arnold, 1992; Hine and Blows, 2006; Hansen and Houle, 2008; Jones et al., 2014; Hine et al., 2014; Engen and Sæther, 2021). Empirical research has found that the smallest eigenvalue of $\mathbf{G}$ in phenotype space is often close to zero (Kirkpatrick and Lofsvold, 1992; Hine and Blows, 2006; McGuigan and Blows, 2007). However, Mezey and Houle (2005) found a non-singular $\mathbf{G}$-matrix for 20 morphological (so, developed) traits in fruit flies; our results suggest $\mathbf{G}$ singularity would still arise in this case if enough traits are included so as to guarantee a well-defined description of the evolutionary process in gradient form (i.e., if allele frequency were included in the analysis as part of the multivariate "geno-phenotype"). Previous theory has offered limited predictions as to when the $\mathbf{G}$-matrix would be singular. These include that more traits render $\mathbf{G}$ more likely to be singular as traits are more likely to be genetically correlated, such as in infinite-dimensional traits (Gomulkiewicz and Kirkpatrick, 1992; Kirkpatrick and Lofsvold, 1992). Suggestions to include gene frequency as part of the trait vector in the classic Lande equation (e.g., Barfield et al., 2011) have been made without noticing that doing so entails that the associated $\mathbf{G}$-matrix is necessarily singular. Kirkpatrick and Lofsvold (1992, p. 962 onwards) showed that, assuming that $\mathbf{G}$ in phenotypic space is singular and constant, then the evolutionary trajectory and equilibria depend on the initial conditions. Our results substantiate Kirkpatrick and Lofsvold's (1992) assumption of singular $\mathbf{G}$ by our observation that $\mathbf{G}$ is always singular in geno-phenotype space to yield a well-defined evolutionary trajectory with a gradient system, even with few traits and evolving $\mathbf{G}$.

Multiple mathematical models have addressed the question of the singularity of $\mathbf{G}$. Recently, simulation work studying the effect of pleiotropy on the structure of the $\mathbf{G}$-matrix found that the smallest eigenvalue of $\mathbf{G}$ is very small but positive (Engen and Sæther, 2021, Tables 3 and 5). Our findings indicate that this model and others (e.g., Wagner, 1984; Barton and Turelli, 1987; Wagner, 1989; Wagner and Mezey, 2000; Martin, 2014; Morrissey, 2014, 2015) would recover $\mathbf{G}$-singularity by considering the geno-phenotype so both allele frequency and phenotype change are part of the gradient system. Other recent simulation work found that a singular $\mathbf{G}$-matrix arising from few segregating alleles still allows the population to reach fitness optima as all directions of phenotype space are eventually available in the long run (Barton, 2017, Fig. 3). Our results indicate that such a model would recover that unconstrained fitness optima in geno-phenotype space are not necessarily achieved by incorporating developmental constraints, which induce convergence to constrained fitness optima that only under certain conditions may coincide with unconstrained fitness optima. Convergence to constrained fitness optima rather than to unconstrained fitness optima still occurs with the fewest number of traits allowed in our framework: two, that is, one gene product and one phenotype with one age each (or in a standard quantitative genetics framework, allele frequency at a single locus and one quantitative trait that is a function of such allele frequency). Such constrained adaptation has substantial implications for biological understanding (see e.g., Kirkpatrick and Lofsvold, 1992; Gomulkiewicz and Kirkpatrick, 1992) and is consistent with empirical observations of lack of selection response in the wild despite selection and genetic variation (Merilä et al., 2001; Hansen and Houle, 2004; Pujol et al., 2018), and of relative lack of stabilizing selection (Kingsolver et al., 2001; Kingsolver and Diamond, 2011).

Our results provide a mechanistic theory of breeding value, thus allowing for insight regarding the structure and evolution of the $\mathbf{G}$-matrix. We have defined breeding value, not in terms of regression coefficients as traditionally done, but in terms of total effect matrices with components mechanistically arising from lower level processes. This yields a mechanistic description of $\mathbf{G}$-matrices in terms of total effects of gene expression, which recover previous results in terms of regression coefficients and random matrices where development is treated as a "black-box" (Fisher, 1918; Wagner, 1984; Barton and Turelli, 1987; Lynch and Walsh, 1998; Martin, 2014; Morrissey, 2014). Matrices of total effects of gene expression correspond to Fisher's (1918) additive effects of allelic substitution (his α) and to Wagner's (1984, 1989) developmental matrix (his $\mathbf{B}$). Wagner (1984, 1989) constructed and analysed evolution-

ary models considering developmental maps, and wrote the **G**-matrix in terms of his developmental matrix to assess its impact on the maintenance of genetic variation. Yet, as is traditionally done, Wagner (1984, 1988, 1989) and Wagner and Mezey (2000) did not simultaneously track the evolution of what we call gene expression and phenotypes, so did not conclude that the associated **G**-matrix is necessarily singular or that the developmental matrix affects evolutionary equilibria. Wagner's (1984, 1989) models have been used to devise models of constrained adaptation in a fitness landscape, borrowing ideas from computer science (Altenberg, 1995, his Fig. 2). This and other models (Houle 1991, his Fig. 2 and Kirkpatrick and Lofsvold 1992, their Fig. 5) have suggested how constrained evolutionary dynamics could proceed although they have lacked a mechanistic theory of breeding value and thus of **G** and its evolutionary dynamics. Other models borrowing ideas from computer science have found that epistasis can cause the evolutionary dynamics to take an exponentially long time to reach fitness peaks (Kaznatcheev, 2019). As the **G**-matrix in geno-phenotype space has at least as many zero eigenvalues as there are lifetime phenotypes (i.e., $N_a N_s$), even if there were infinite time, the population does not necessarily reach a fitness peak in geno-phenotype space, although it may in gene expression space if there are no absolute mutational constraints.

We find that total genetic selection provides more information regarding selection response than direct directional selection or other forms of total selection. Ever since Lande (1979) it has been clear that direct directional selection on the phenotype would be insufficient to identify evolutionary equilibria if the **G**-matrix were singular (Lande, 1979; Via and Lande, 1985; Kirkpatrick and Lofsvold, 1992; Gomulkiewicz and Kirkpatrick, 1992). Evolutionary analysis with singular **G**, including identification of evolutionary equilibria, can be difficult without a mechanistic theory of breeding value and thus of **G**. Our results facilitate evolutionary analysis despite singular **G** and show that evolutionary equilibria occur when total genetic selection vanishes if there are no absolute mutational constraints and no exogenous plastic response. As total genetic selection depends on development rather than exclusively on (unconstrained) selection, and as development determines the admissible evolutionary trajectory along which developmental and environmental constraints are satisfied, our findings show that development has a major evolutionary role.

Total selection gradients correspond to quantities that have received various names. Such gradients correspond to Caswell's (1982, 2001) "total derivative of fitness" (denoted by him as $\mathrm{d}\lambda$), Charlesworth's (1994) "total differential" (of the population's growth rate, denoted by him as $\mathrm{d}r$), van Tienderen's (1995) "integrated sensitivity" (of the population's growth rate, denoted by him as IS), and Morrissey's (2014, 2015) "extended selection gradient" (denoted by him as $\boldsymbol{\eta}$). Total selection gradients measure total directional selection, so in our framework they take into account developmental and environmental constraints. In contrast, Lande's (1979) selection gradients measure direct directional selection, so in our framework's terms they do not consider constraints. We obtained compact expressions for total selection gradients as linear transformations of direct selection gradients, arising from the chain rule in matrix notation (Layer 4, Eq. 20), analogously to previous expressions in terms of vital rates (Caswell, 2001, Eq. 9.38). Our bottom-up approach recovers the top-down approach of Morrissey (2014) who defined the extended selection gradient as $\boldsymbol{\eta} = \boldsymbol{\Phi}\boldsymbol{\beta}$, where $\boldsymbol{\beta}$ is Lande's selection gradient and $\boldsymbol{\Phi}$ is the matrix of total effects of all traits on themselves. Morrissey (2014) used an equation for the total-effect matrix $\boldsymbol{\Phi}$ (his Eq. 2) from path analysis (Greene, 1977, p. 380), which has the form of our matrices describing developmental feedback of the phenotype and the geno-phenotype ($\mathrm{d}\mathbf{x}^\intercal/\mathrm{d}\mathbf{x}|_{\mathbf{y}=\bar{\mathbf{y}}}$ and $\mathrm{d}\mathbf{z}^\intercal/\mathrm{d}\mathbf{z}|_{\mathbf{y}=\bar{\mathbf{y}}}$; Layer 4, Eq. 1 and Layer 4, Eq. 9). Thus, interpreting Morrissey's (2014) $\boldsymbol{\Phi}$ as our $\mathrm{d}\mathbf{x}^\intercal/\mathrm{d}\mathbf{x}|_{\mathbf{y}=\bar{\mathbf{y}}}$ (resp. $\mathrm{d}\mathbf{z}^\intercal/\mathrm{d}\mathbf{z}|_{\mathbf{y}=\bar{\mathbf{y}}}$) and $\boldsymbol{\beta}$ as our $\delta w/\delta\mathbf{x}|_{\mathbf{y}=\bar{\mathbf{y}}}$ (resp. $\delta w/\delta\mathbf{z}|_{\mathbf{y}=\bar{\mathbf{y}}}$) (i.e., Lande's selection gradient of the phenotype or the geno-phenotype if environmental variables are not explicitly included in the analysis), then Layer 4, Eq. 21 (resp. Layer 4, Eq. 24) shows that the extended selection gradient $\boldsymbol{\eta} = \boldsymbol{\Phi}\boldsymbol{\beta}$ corresponds to the total selection gradient of the phenotype $\mathrm{d}w/\mathrm{d}\mathbf{x}|_{\mathbf{y}=\bar{\mathbf{y}}}$ (resp. of the geno-phenotype $\mathrm{d}w/\mathrm{d}\mathbf{z}|_{\mathbf{y}=\bar{\mathbf{y}}}$). We did not show that $\mathrm{d}\mathbf{m}^\intercal/\mathrm{d}\mathbf{m}|_{\mathbf{y}=\bar{\mathbf{y}}}$ has the form of the equation for $\boldsymbol{\Phi}$ provided by Morrissey (2014) (his Eq. 2), but it might indeed hold. If we interpret $\boldsymbol{\Phi}$ as our $\mathrm{d}\mathbf{m}^\intercal/\mathrm{d}\mathbf{m}|_{\mathbf{y}=\bar{\mathbf{y}}}$ and $\boldsymbol{\beta}$ as our $\partial w/\partial\mathbf{m}|_{\mathbf{y}=\bar{\mathbf{y}}}$ (i.e., Lande's selection gradient of the geno-envo-phenotype thus explicitly including environmental variables in the analysis), then Layer 4, Eq. 25 shows that the extended selection gradient $\boldsymbol{\eta} = \boldsymbol{\Phi}\boldsymbol{\beta}$ corresponds to the total selection gradient of the geno-envo-phenotype $\mathrm{d}w/\mathrm{d}\mathbf{m}|_{\mathbf{y}=\bar{\mathbf{y}}}$.

Not all total selection gradients provide a relatively complete description of the selection response. We show in Appendices J (Eq. J4) and L (Eq. L4) that the selection response of the geno-phenotype or the geno-envo-phenotype can respectively be written in terms of the total selection gradients of the geno-phenotype $\mathrm{d}w/\mathrm{d}\mathbf{z}|_{\mathbf{y}=\bar{\mathbf{y}}}$ or the geno-envo-phenotype $\mathrm{d}w/\mathrm{d}\mathbf{m}|_{\mathbf{y}=\bar{\mathbf{y}}}$, but such total selection gradients are insufficient to predict evolutionary equilibria because they are premultiplied by a singular socio-genetic cross-covariance matrix. Also, the selection response of the phenotype can be written in terms of the total selection gradient of the phenotype $\mathrm{d}w/\mathrm{d}\mathbf{x}|_{\mathbf{y}=\bar{\mathbf{y}}}$, but this expression for the selection response has an additional term involving the semi-total selection gradient of gene expression $\delta w/\delta\mathbf{y}|_{\mathbf{y}=\bar{\mathbf{y}}}$, so such total selection gradient is insufficient to predict evolutionary equilibria (even more considering that the evolutionary trajectory following the evolutionary dynamics of the phenotype alone is ill-defined). In contrast, we have shown that the total selection gradient of gene expression $\mathrm{d}w/\mathrm{d}\mathbf{y}|_{\mathbf{y}=\bar{\mathbf{y}}}$ predicts evolutionary equilibria if there are no absolute mutational constraints and no exogenous plastic response. Thus, out of all total selection gradients considered, only total genetic selection provides a relatively complete description of the selection response. Although Morrissey (2015) considers that the total selection gradient of gene expression (his "inputs") and of the phenotype (his "traits") are equal, from the last line of Layer 4, Eq. 22 it follows that the total selection gradients of the phenotype and gene expression are different in general, and only under stringent conditions could they be equal (since $\delta\mathbf{x}^\intercal/\delta\mathbf{y}$ is block superdiagonal due to the arrow of developmental time).

Our results allow for the modelling of evo-devo dynam-

ics in a wide array of settings. First, developmental and environmental constraints (Layer 7, Eq. 1b and Layer 7, Eq. 1c) can mechanistically describe development, gene-gene interaction, and gene-environment interaction, while allowing for arbitrary non-linearities and evolution of the developmental map. Several previous approaches have modelled gene-gene interaction, such as by considering multiplicative gene effects, but general frameworks mechanistically linking gene-gene interaction, gene-environment interaction, developmental dynamics, and evolutionary dynamics have previously remained elusive (Rice, 1990; Hansen and Wagner, 2001; Rice, 2002; Hermisson et al., 2003; Carter et al., 2005; Rice, 2011). A historically dominant yet debated view is that gene-gene interaction has minor evolutionary effects as phenotypic evolution depends on additive rather than epistatic effects to a first-order of approximation, so epistasis would act by influencing a seemingly effectively non-singular $\mathbf{G}$ (Hansen, 2013; Nelson et al., 2013; Paixão and Barton, 2016; Barton, 2017). Our results show that, in geno-phenotype space so the evolutionary trajectory is well-defined by a gradient system, the associated $\mathbf{G}$ is necessarily singular so evolutionary equilibria depend on development and consequently on gene-gene and gene-environment interactions. Hence, gene-gene and gene-environment interaction may well have strong and permanent evolutionary effects (e.g., via developmental feedbacks described by $\mathrm{d}\mathbf{x}^{\mathsf{T}}/\mathrm{d}\mathbf{x}|_{\mathbf{y}=\bar{\mathbf{y}}}$) even by altering the $\mathbf{G}$-matrix alone.

Second, our results allow for the study of long-term evolution of the $\mathbf{G}$-matrix as an emergent property of the evolution of gene expression, phenotype, and environment (i.e., the geno-envo-phenotype). This contrasts with the traditional approach that considers short-term evolution of $\mathbf{G}$ treating it as another dynamic variable under constant allele frequency (Bulmer, 1971; Lande, 1979; Bulmer, 1980; Lande, 1980; Lande and Arnold, 1983; Barton and Turelli, 1987; Turelli, 1988; Gavrilets and Hastings, 1994; Carter et al., 2005; Débarre et al., 2014). Third, our results allow for the study of the effects of developmental bias, biased genetic variation, and modularity (Wagner, 1996; Pavlicev and Hansen, 2011; Pavlicev et al., 2011; Wagner and Zhang, 2011; Pavlicev and Wagner, 2012; Watson et al., 2013). While we have assumed that mutation is unbiased for gene expression, our equations allow for the developmental map to lead to biases in genetic variation for the phenotype. This may lead to modular effects of mutations, whereby altering gene expression of one gene product at a given age tends to affect some phenotypes but not others.

Fourth, our equations facilitate the study of life-history models with dynamic constraints. Life-history models with dynamic constraints have typically assumed evolutionary equilibrium, so they are analysed using dynamic optimization techniques such as dynamic programming and optimal control (e.g., León, 1976; Iwasa and Roughgarden, 1984; Houston and McNamara, 1999; González-Forero et al., 2017; Avila et al., 2021). In recent years, mathematically modelling the evolutionary dynamics of life-history models with dynamic constraints, that is, of what we call the evo-devo dynamics, has been made possible with the canonical equation of adaptive dynamics for function-valued traits (Dieckmann et al., 2006; Parvinen et al., 2013; Metz et al., 2016). However, such an approach poses substantial mathematical challenges by requiring derivation of functional derivatives and solution of associated differential equations for costate variables (Parvinen et al., 2013; Metz et al., 2016; Avila et al., 2021). By using discrete age, we have obtained closed-form equations that facilitate modelling the evo-devo dynamics. By doing so, our framework yields an alternative method to dynamic optimization to analyse a broad class of life-history models with dynamic constraints (see Example).

Fifth, our framework allows for the modelling of the evo-devo dynamics of pattern formation by allowing the implementation of reaction-diffusion equations in *discrete space* in the developmental map, once equations are suitably written (e.g., Eq. 6.1 of Turing, 1952; Tomlin and Axelrod, 2007). Thus, the framework allows one to model and analyse the evo-devo dynamics of existing detailed models of the development of morphology (e.g., Salazar-Ciudad and Jernvall, 2010; Salazar-Ciudad and Marín-Riera, 2013), to the extent that developmental maps can be written in the form of Eq. (1). Sixth, our framework also allows for the mechanistic modelling of adaptive plasticity, for instance, by implementing reinforcement learning or supervised learning in the developmental map (Sutton and Barto, 2018; Paenke et al., 2007). In practice, to use our framework to model the evo-devo dynamics, it may often be simpler to compute the evolutionary dynamics of gene expression and the developmental dynamics of the phenotype (as in Fig. 6), rather than the evolutionary dynamics of the geno-phenotype or geno-envo-phenotype. When this is the case, after solving for the evo-devo dynamics, one can then compute the matrices composing the evolutionary dynamics of the geno-phenotype and geno-envo-phenotype to gain further understanding of the evolutionary factors at play, including the evolution of the $\mathbf{G}$-matrix (as in Fig. 7).

By allowing development to be social, our framework allows for a mechanistic description of extra-genetic inheritance and indirect genetic effects. Extra-genetic inheritance can be described since the phenotype at a given age can be an identical or modified copy of the geno-phenotype of social partners. Thus, social development allows for the modelling of social learning (Sutton and Barto, 2018; Paenke et al., 2007) and epigenetic inheritance (Jablonka et al., 1992; Slatkin, 2009; Day and Bonduriansky, 2011). However, note that in our framework extra-genetic inheritance is insufficient to yield phenotypic evolution that is independent of both genetic evolution and exogenous plastic change (e.g., purely cultural evolution). This is seen by setting mutational covariation and exogenous environmental change to zero (i.e., $\mathbf{G}_{\mathbf{y}} = \mathbf{0}$ and $\partial\bar{\boldsymbol{\epsilon}}/\partial\tau = \mathbf{0}$), which eliminates evolutionary change (i.e., $\mathrm{d}\bar{\mathbf{m}}/\mathrm{d}\tau = \mathbf{0}$). The reason is that although there is extra-genetic *inheritance* in our framework, there is no extra-genetic *variation* because both development is deterministic and we use adaptive dynamics assumptions: without mutation, every SDS resident develops the same phenotype as every other resident. Extensions to consider stochastic development might enable extra-genetic variation and possibly phenotypic evolution that is independent of genetic and exogenously plastic evolution. Note also that we have only considered social interactions among non-relatives,

so our framework at present only allows for social learning or epigenetic inheritance from non-relatives.

Our framework can mechanistically describe indirect genetic effects via social development because the developed phenotype can be mechanistically influenced by the gene expression or phenotype of social partners. Indirect genetic effects mean that a phenotype may be partly or completely caused by genes located in another individual (Moore et al., 1997). Indirect genetic effect approaches model the phenotype considering a linear regression of individual's phenotype on social partner's phenotype (Kirkpatrick and Lande, 1989; Moore et al., 1997; Townley and Ezard, 2013), whereas our approach constructs individual's phenotype from development depending on social partners' gene expression and phenotypes. We found that social development generates social feedback (described by $\mathrm{s}\mathbf{x}/\mathrm{s}\bar{\mathbf{x}}^{\intercal}|_{\mathbf{y}=\bar{\mathbf{y}}}$, Eq. Layer 5, Eq. 1), which closely though not entirely corresponds to social feedback found in the indirect genetic effects literature (Moore et al., 1997, Eq. 19b and subsequent text). The social feedback we obtain depends on total social developmental bias from the phenotype ($\mathrm{d}\mathbf{x}/\mathrm{d}\bar{\mathbf{x}}^{\intercal}|_{\mathbf{y}=\bar{\mathbf{y}}}$, Eq. Layer 4, Eq. 5); analogously, social feedback in the indirect genetic effects literature depends on the matrix of interaction coefficients ($\mathbf{\Psi}$) which contains the regression coefficients of phenotype on social partner's phenotype. Social development leads to a generalization of additive genetic covariance matrices $\mathbf{G} = \mathrm{cov}[\mathbf{a}, \mathbf{a}]$ into additive socio-genetic cross-covariance matrices $\mathbf{H} = \mathrm{cov}[\mathbf{b}, \mathbf{a}]$; similarly, indirect genetic effects involve a generalization of the $\mathbf{G}$-matrix, which includes $\mathbf{C}_{\mathbf{ax}} = \mathrm{cov}[\mathbf{a}, \mathbf{x}]$, namely the cross-covariance matrix between multivariate breeding value and phenotype (Kirkpatrick and Lande, 1989; Moore et al., 1997; Townley and Ezard, 2013). However, there are differences between our results and those in the indirect genetic effects literature. First, social feedback (in the sense of inverse matrices involving $\mathbf{\Psi}$) appears twice in the evolutionary dynamics under indirect genetic effects (see Eqs. 20 and 21 of Moore et al. 1997) while it only appears once in our evolutionary dynamics equations through $\mathrm{s}\mathbf{x}/\mathrm{s}\bar{\mathbf{x}}^{\intercal}|_{\mathbf{y}=\bar{\mathbf{y}}}$ (Eq. Layer 6, Eq. 10). This difference may stem from the assumption in the indirect genetic effects literature that social interactions are reciprocal, while we assume that they are asymmetric in the sense that, since mutants are rare, mutant's development depends on residents but resident's development does not depend on mutants (we thank J. W. McGlothlin for pointing this out). Second, our $\mathbf{H}$ matrices make the evolutionary dynamics equations depend on total social developmental bias from gene expression ($\mathrm{d}\mathbf{x}/\mathrm{d}\bar{\mathbf{y}}^{\intercal}|_{\mathbf{y}=\bar{\mathbf{y}}}$, Eq. Layer 5, Eq. 2a) in a non-feedback manner (specifically, not in an inverse matrix) but this type of dependence does not occur in the evolutionary dynamics under indirect genetic effects (Eqs. 20 and 21 of Moore et al. 1997). This difference might stem from the absence of explicit tracking of allele frequency in the indirect genetic effects literature in keeping with the tradition of quantitative genetics, whereas we explicitly track gene expression. Third, "social selection" (i.e., $\partial w/\partial \bar{\mathbf{z}}$) plays no role in our results consistently with our assumption of a well-mixed population, but social selection plays an important role in the indirect genetic effects literature even if relatedness is zero (McGlothlin et al., 2010, e.g., setting $r = 0$ in their Eq. 10 still leaves an effect of social selection on selection response due to "phenotypic" kin selection).

Our framework offers formalizations to the notions of developmental constraints and developmental bias. The two notions have been often interpreted as equivalents (e.g., Brakefield, 2006), or with a distinction such that constraints entail a negative, prohibiting effect while bias entails a positive, directive effect of development on the generation of phenotypic variation (Uller et al., 2018; Salazar-Ciudad, 2021). We defined developmental constraint as the condition that the phenotype at a given age is a function of the individual's condition at their immediately previous age, which both prohibits certain values of the phenotype and has a "directive" effect on the generation of phenotypic variation. We offered quantification of developmental bias in terms of the slope of the phenotype with respect to itself at subsequent ages. No bias would lead to zero slopes thus to identity matrices (e.g., $\partial\mathbf{x}^{\intercal}/\partial\mathbf{x}|_{\mathbf{y}=\bar{\mathbf{y}}} = \mathbf{I}$ and $\mathrm{d}\mathbf{x}^{\intercal}/\mathrm{d}\mathbf{x}|_{\mathbf{y}=\bar{\mathbf{y}}} = \mathbf{I}$) and deviations from the identity matrix would constitute bias.

Our results clarify the role of several developmental factors previously suggested to be evolutionarily important. We have arranged the evo-devo process in a layered structure, where a given layer is formed by components of layers below (Fig. 5). This layered structure helps see that several developmental factors previously suggested to have important evolutionary effects (Laland et al., 2014) but with little clear connection (Welch, 2017) can be viewed as basic elements of the evolutionary process. Direct-effect matrices (Layer 2) are basic in that they form all the components of the evolutionary dynamics (Layer 7) except mutational covariation and exogenous environmental change. Direct-effect matrices quantify direct (i) directional selection, (ii) developmental bias, (iii) niche construction, (iv) social developmental bias (e.g., extra-genetic inheritance and indirect genetic effects; Moore et al. 1997), (v) social niche construction, (vi) environmental sensitivity of selection (Chevin et al., 2010), and (vii) phenotypic plasticity. These factors variously affect selection and development, thus affecting evolutionary equilibria and the admissible evolutionary trajectory.

Our approach uses discrete rather than continuous age, which substantially simplifies the mathematics. This treatment allows for the derivation of closed-form expressions for what can otherwise be a difficult mathematical challenge if age is continuous (Kirkpatrick and Heckman, 1989; Dieckmann et al., 2006; Parvinen et al., 2013; Metz et al., 2016; Avila et al., 2021). For instance, costate variables are key in dynamic optimization as used in life-history models (Gadgil and Bossert, 1970; León, 1976; Schaffer, 1983; Stearns, 1992; Roff, 1992; Kozłowski and Teriokhin, 1999; Sydsæter et al., 2008), but general closed-form formulas for costate variables were previously unavailable and their calculation often limits the analysis of such models. In Appendix M, we show that our results recover the key elements of Pontryagin's maximum principle, which is the central tool of optimal control theory to solve dynamic optimization problems (Sydsæter et al., 2008). By assuming that there are no environmental variables (hence, no exogenous plastic response), in Appendix M, we show that an admissible locally stable evolutionary equilibrium solves a local, dynamic optimization problem whose solution both "totally" maximises

a mutant's lifetime reproductive success R_0 and "directly" maximises the Hamiltonian of Pontryagin's maximum principle. We show that this Hamiltonian depends on costate variables that are proportional to the total selection gradient of the phenotype at evolutionary equilibrium (Eq. M3), and that the costate variables satisfy the costate equations of Pontryagin's maximum principle. Thus, our approach offers an alternative, equivalent method to optimal control theory to find admissible evolutionary equilibria for the broad class of models considered here. By exploiting the discretization of age, we have obtained various formulas that can be computed directly for the total selection gradient of the phenotype (Layer 4, Eq. 21), so for costate variables, and of their relationship to total genetic selection (fifth line of Layer 4, Eq. 22), thus facilitating analytic and numerical treatment of life-history models with dynamic constraints. Although discretization of age may induce numerical imprecision relative to continuous age (Kirkpatrick and Heckman, 1989), numerical and empirical treatment of continuous age typically involves discretization at one point or another, with continuous curves often achieved by interpolation (e.g., Kirkpatrick et al., 1990). Numerical precision with discrete age may be increased by reducing the age bin size (e.g., to represent months or days rather than years; Caswell, 2001), potentially at a computational cost.

By simplifying the mathematics, our approach yields insight that has been otherwise challenging to gain. Life-history models with dynamic constraints generally find that costate variables are non-zero under optimal controls (Gadgil and Bossert, 1970; Taylor et al., 1974; León, 1976; Schaffer, 1983; Houston et al., 1988; Houston and McNamara, 1999; Sydsæter et al., 2008). This means that there is persistent total selection on the phenotype at evolutionary equilibrium. Our findings clarify that this is to be expected for various reasons including absolute mutational constraints (as in the Example), the occurrence of semi-total effects of controls on fitness, and because of the arrow of developmental time, since gene expression at a given age cannot adjust the phenotype at the same age but only at a later age (i.e., the matrix of semi-total effects of gene expression on the phenotype is singular; Eq. E10). Thus, even when total genetic selection does vanish at equilibrium, it may generally do so with persistent total phenotypic selection (fifth line of Layer 4, Eq. 22). Moreover, life-history models with explicit developmental constraints have found that their predictions can be substantially different from those found without explicit developmental constraints. In particular, with developmental constraints, the outcome of parent-offspring conflict over sex allocation has been found to be that preferred by the mother (Avila et al., 2019), whereas without developmental constraints the outcome has been found to be an intermediate between those preferred by mother and offspring (Reuter and Keller, 2001). Our results show that changing the particular form of the developmental map may induce substantial changes in predictions by influencing total genetic selection and the admissible evolutionary equilibria. In other words, the developmental map is of key evolutionary importance because it modulates absolute socio-genetic constraints (i.e., the **G** or **H** matrices in geno-phenotype space).

We have obtained a term that we refer to as exogenous plastic response, which is the plastic response to exogenous environmental change over an evolutionary time step (Layer 7, Eq. 3). An analogous term occurs in previous equations (Eq. A3 of Chevin et al. 2010). Additionally, our framework considers *endogenous* plastic response due to niche construction (i.e., endogenous environmental change), which affects both the selection response and the exogenous plastic response. Exogenous plastic response affects the evolutionary dynamics even though it is not ultimately caused by change in resident gene expression (or in gene frequency), but by exogenous environmental change. In particular, exogenous plastic response allows for a straightforward form of "plasticity-first" evolution (West-Eberhard, 2003) as follows. At an evolutionary equilibrium where exogenous plastic response is absent, the introduction of exogenous plastic response generally changes socio-genetic covariation or directional selection at a subsequent evolutionary time, thereby inducing selection response. This constitutes a simple form of plasticity-first evolution, whereby plastic change precedes genetic change, although the plastic change may not be adaptive and the induced genetic change may have a different direction to that of the plastic change.

To conclude, we have formulated a framework that synthesizes developmental and evolutionary dynamics yielding a theory of constrained evolutionary dynamics under age structure. This framework shows that development has major evolutionary effects as it affects both evolutionary equilibria and the admissible evolutionary path. Our results provide a tool to chart major territory on how development affects evolution.

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Appendix A. Canonical equation

Here we derive the equation describing the evolutionary dynamics of gene expression. This derivation closely follows that of Dieckmann and Law (1996) except in a few places, particularly in that we consider deterministic population dynamics so the only source of stochasticity in our framework is due to mutation. Denote by $\bar{\mathbf{y}}'(\tau + \Delta\tau)$ a multivariate random variable describing the possible residents at time $\tau + \Delta\tau$ following fixation of mutants arising at time τ. Let this random variable have probability density function $P(\bar{\mathbf{y}}', \tau + \Delta\tau)$ at time $\tau + \Delta\tau$, with support in $\mathbb{R}^{N_a N_c}$. Hence, the expected resident gene expression

at time $\tau + \Delta\tau$ is

$$\mathrm{E}[\bar{\mathbf{y}}'(\tau+\Delta\tau)] = \int_{\mathbb{R}^{N_a N_c}} \bar{\mathbf{y}}' P(\bar{\mathbf{y}}', \tau+\Delta\tau)\mathrm{d}\bar{\mathbf{y}}' \equiv \bar{\mathbf{y}}(\tau+\Delta\tau).$$

The evolutionary change in resident gene expression thus satisfies

$$\begin{aligned}\frac{\Delta\bar{\mathbf{y}}}{\Delta\tau} &= \frac{\mathrm{E}[\bar{\mathbf{y}}'(\tau+\Delta\tau)] - \mathrm{E}[\bar{\mathbf{y}}'(\tau)]}{\Delta\tau} \\ &= \frac{1}{\Delta\tau}\left(\int_{\mathbb{R}^{N_a N_c}} \bar{\mathbf{y}}' P(\bar{\mathbf{y}}', \tau+\Delta\tau)\mathrm{d}\bar{\mathbf{y}}' - \int_{\mathbb{R}^{N_a N_c}} \bar{\mathbf{y}}' P(\bar{\mathbf{y}}', \tau)\mathrm{d}\bar{\mathbf{y}}'\right).\end{aligned}$$

Factorizing yields

$$\begin{aligned}\frac{\Delta\bar{\mathbf{y}}}{\Delta\tau} &= \int_{\mathbb{R}^{N_a N_c}} \bar{\mathbf{y}}' \frac{P(\bar{\mathbf{y}}', \tau+\Delta\tau) - P(\bar{\mathbf{y}}', \tau)}{\Delta\tau}\mathrm{d}\bar{\mathbf{y}}' \\ &= \int_{\mathbb{R}^{N_a N_c}} \bar{\mathbf{y}}' \frac{\Delta P(\bar{\mathbf{y}}', \tau)}{\Delta\tau}\mathrm{d}\bar{\mathbf{y}}'.\end{aligned}$$

Now, the evolutionary change in the distribution of the resident gene expression satisfies the master equation

$$\frac{\Delta P(\bar{\mathbf{y}}', \tau)}{\Delta\tau} = \int_{\mathbb{R}^{N_a N_c}} \left[\omega(\mathbf{y}, \bar{\mathbf{y}}')P(\mathbf{y}, \tau) - \omega(\bar{\mathbf{y}}', \mathbf{y})P(\bar{\mathbf{y}}', \tau)\right]\mathrm{d}\mathbf{y},$$

where $\omega(\mathbf{y}, \bar{\mathbf{y}}')$ is the rate at which a resident $\mathbf{y}$ is replaced by $\bar{\mathbf{y}}'$. Then, the evolutionary change in gene expression is

$$\begin{aligned}\frac{\Delta\bar{\mathbf{y}}}{\Delta\tau} = \int_{\mathbb{R}^{N_a N_c}} \bar{\mathbf{y}}'\Bigg(\int_{\mathbb{R}^{N_a N_c}} &[\omega(\mathbf{y}, \bar{\mathbf{y}}')P(\mathbf{y}, \tau) \\ &- \omega(\bar{\mathbf{y}}', \mathbf{y})P(\bar{\mathbf{y}}', \tau)]\mathrm{d}\mathbf{y}\Bigg)\mathrm{d}\bar{\mathbf{y}}'.\end{aligned}$$

Since the integral is a linear operator, we have

$$\begin{aligned}\frac{\Delta\bar{\mathbf{y}}}{\Delta\tau} &= \int_{\mathbb{R}^{N_a N_c}}\int_{\mathbb{R}^{N_a N_c}} \bar{\mathbf{y}}'\omega(\mathbf{y}, \bar{\mathbf{y}}')P(\mathbf{y}, \tau)\mathrm{d}\mathbf{y}\mathrm{d}\bar{\mathbf{y}}' \\ &\quad - \int_{\mathbb{R}^{N_a N_c}}\int_{\mathbb{R}^{N_a N_c}} \bar{\mathbf{y}}'\omega(\bar{\mathbf{y}}', \mathbf{y})P(\bar{\mathbf{y}}', \tau)\mathrm{d}\mathbf{y}\mathrm{d}\bar{\mathbf{y}}'.\end{aligned}$$

Exchanging $\mathbf{y}$ for $\bar{\mathbf{y}}'$ in the first term since they are dummy variables yields

$$\begin{aligned}\frac{\Delta\bar{\mathbf{y}}}{\Delta\tau} &= \int_{\mathbb{R}^{N_a N_c}}\int_{\mathbb{R}^{N_a N_c}} \mathbf{y}\omega(\bar{\mathbf{y}}', \mathbf{y})P(\bar{\mathbf{y}}', \tau)\mathrm{d}\mathbf{y}\mathrm{d}\bar{\mathbf{y}}' \\ &\quad - \int_{\mathbb{R}^{N_a N_c}}\int_{\mathbb{R}^{N_a N_c}} \bar{\mathbf{y}}'\omega(\bar{\mathbf{y}}', \mathbf{y})P(\bar{\mathbf{y}}', \tau)\mathrm{d}\mathbf{y}\mathrm{d}\bar{\mathbf{y}}'.\end{aligned}$$

Factorizing yields

$$\frac{\Delta\bar{\mathbf{y}}}{\Delta\tau} = \int_{\mathbb{R}^{N_a N_c}}\int_{\mathbb{R}^{N_a N_c}} (\mathbf{y} - \bar{\mathbf{y}}')\omega(\bar{\mathbf{y}}', \mathbf{y})P(\bar{\mathbf{y}}', \tau)\mathrm{d}\mathbf{y}\mathrm{d}\bar{\mathbf{y}}'. \tag{A1}$$

Assuming that invasion implies fixation, we let the rate at which resident $\bar{\mathbf{y}}'$ is replaced by $\mathbf{y}$ be

$$\omega(\bar{\mathbf{y}}', \mathbf{y}) = \delta(\bar{\mathbf{y}}' - \bar{\mathbf{y}})\mu(\bar{\mathbf{m}}')\bar{n}^*(\bar{\mathbf{m}}')\frac{M(\mathbf{y}, \bar{\mathbf{y}}')}{P(\bar{\mathbf{y}}', \tau)}[\lambda(\mathbf{m}, \bar{\mathbf{m}}') - 1] \tag{A2}$$

if $\lambda(\mathbf{m}, \bar{\mathbf{m}}') > 1$ or $\omega(\bar{\mathbf{y}}', \mathbf{y}) = 0$ otherwise. Here $\delta(\cdot)$ is the Dirac delta function, $\mathbf{m}$ is the mutant geno-envo-phenotype arising from $\mathbf{y}$, and $\bar{\mathbf{m}}'$ is the SDS resident geno-envo-phenotype arising from $\bar{\mathbf{y}}'$. This expression for $\omega(\bar{\mathbf{y}}', \mathbf{y})$ can be understood as comprising the probability density $\delta(\bar{\mathbf{y}}' - \bar{\mathbf{y}})$ that the resident $\bar{\mathbf{y}}'$ is $\bar{\mathbf{y}}$, times the rate of appearance of new mutants given by the carrying capacity $\bar{n}^*(\bar{\mathbf{m}}')$ and the mutation rate $\mu(\bar{\mathbf{m}}') \in [0, 1]$, times the conditional probability density $M(\mathbf{y}, \bar{\mathbf{y}}')/P(\bar{\mathbf{y}}', \tau)$ that a mutant is $\mathbf{y}$ given that the resident is $\bar{\mathbf{y}}'$ at time τ, times the rate of substitution $\lambda(\mathbf{m}, \bar{\mathbf{m}}') - 1$ for a mutant $\mathbf{y}$ in the context of resident $\bar{\mathbf{y}}'$. Substituting Eq. (A2) into Eq. (A1) using Eq. (12) yields

$$\begin{aligned}\frac{\Delta\bar{\mathbf{y}}}{\Delta\tau} \approx \int_Q \Bigg\{&(\mathbf{y} - \bar{\mathbf{y}}')\delta(\bar{\mathbf{y}}' - \bar{\mathbf{y}})\mu(\bar{\mathbf{m}}')n^*(\bar{\mathbf{m}}')\frac{M(\mathbf{y}, \bar{\mathbf{y}}')}{P(\bar{\mathbf{y}}', \tau)} \\ &(\mathbf{y} - \bar{\mathbf{y}}')^\intercal \left.\frac{\mathrm{d}\lambda}{\mathrm{d}\mathbf{y}}\right|_{\mathbf{y}=\bar{\mathbf{y}}'} P(\bar{\mathbf{y}}', \tau)\Bigg\}\mathrm{d}\mathbf{y}\mathrm{d}\bar{\mathbf{y}}',\end{aligned}$$

where the integration ranges over the mutant and resident controls that render invasion fitness greater than one, that is,

$$Q = \{(\mathbf{y}, \bar{\mathbf{y}}')|\lambda(\mathbf{m}, \bar{\mathbf{m}}') > 1\}.$$

Cancelling $P(\bar{\mathbf{y}}', \tau)$ produces

$$\begin{aligned}\frac{\Delta\bar{\mathbf{y}}}{\Delta\tau} \approx \int_Q &(\mathbf{y} - \bar{\mathbf{y}}')\delta(\bar{\mathbf{y}}' - \bar{\mathbf{y}})\mu(\bar{\mathbf{m}}')n^*(\bar{\mathbf{m}}')M(\mathbf{y}, \bar{\mathbf{y}}') \\ &(\mathbf{y} - \bar{\mathbf{y}}')^\intercal \left.\frac{\mathrm{d}\lambda}{\mathrm{d}\mathbf{y}}\right|_{\mathbf{y}=\bar{\mathbf{y}}'} \mathrm{d}\mathbf{y}\mathrm{d}\bar{\mathbf{y}}'.\end{aligned}$$

Using the sifting property of the Dirac delta function [i.e., $\int_{\mathbb{R}^n} F(\mathbf{y})\delta(\mathbf{y} - \bar{\mathbf{y}})\mathrm{d}\mathbf{y} = F(\bar{\mathbf{y}})$ for any function $F(\mathbf{y})$ with $\mathbf{y} \in \mathbb{R}^n$] yields

$$\frac{\Delta\bar{\mathbf{y}}}{\Delta\tau} \approx \int_R (\mathbf{y} - \bar{\mathbf{y}})\mu(\bar{\mathbf{m}})n^*(\bar{\mathbf{m}})M(\mathbf{y}, \bar{\mathbf{y}})(\mathbf{y} - \bar{\mathbf{y}})^\intercal \left.\frac{\mathrm{d}\lambda}{\mathrm{d}\mathbf{y}}\right|_{\mathbf{y}=\bar{\mathbf{y}}} \mathrm{d}\mathbf{y},$$

where the integration ranges over the mutant controls that render invasion fitness greater than one, that is,

$$R = \{\mathbf{y}|\lambda(\mathbf{m}, \bar{\mathbf{m}}) > 1\}.$$

Since the integral is a linear operator and because the evaluation at $\mathbf{y} = \bar{\mathbf{y}}$ makes the gradient constant with respect to $\mathbf{y}$, then

$$\frac{\Delta\bar{\mathbf{y}}}{\Delta\tau} \approx \mu(\bar{\mathbf{m}})n^*(\bar{\mathbf{m}})\int_R (\mathbf{y} - \bar{\mathbf{y}})(\mathbf{y} - \bar{\mathbf{y}})^\intercal M(\mathbf{y}, \bar{\mathbf{y}})\mathrm{d}\mathbf{y} \left.\frac{\mathrm{d}\lambda}{\mathrm{d}\mathbf{y}}\right|_{\mathbf{y}=\bar{\mathbf{y}}}.$$

From the assumption that the mutational distribution is symmetric, the above integral is half the value of the corresponding

integral over the control space (this statement is implicitly used by Dieckmann and Law 1996 without proof; we assume it as well without proof), so

$$\frac{\Delta\bar{\mathbf{y}}}{\Delta\tau} \approx \frac{1}{2}\mu(\bar{\mathbf{m}})n^*(\bar{\mathbf{m}}) \int\limits_{\mathbb{R}^{N_a N_c}} (\mathbf{y}-\bar{\mathbf{y}})(\mathbf{y}-\bar{\mathbf{y}})^\intercal M(\mathbf{y},\bar{\mathbf{y}})\mathrm{d}\mathbf{y}\ \frac{\mathrm{d}\lambda}{\mathrm{d}\mathbf{y}}\bigg|_{\mathbf{y}=\bar{\mathbf{y}}}.$$

By definition of covariance matrix, we have

$$\frac{\Delta\bar{\mathbf{y}}}{\Delta\tau} \approx \kappa(\bar{\mathbf{m}})\mathrm{cov}[\mathbf{y},\mathbf{y}]\ \frac{\mathrm{d}\lambda}{\mathrm{d}\mathbf{y}}\bigg|_{\mathbf{y}=\bar{\mathbf{y}}},$$

where

$$\kappa(\bar{\mathbf{m}}) = \frac{1}{2}\mu(\bar{\mathbf{m}})\bar{n}^*(\bar{\mathbf{m}}).$$

The matrix $\mathrm{cov}[\mathbf{y},\mathbf{y}]$ is *the mutational covariance matrix* (of gene expression). This yields Eq. (3), which recovers the canonical equation of adaptive dynamics (cf. Eq. 6.1 of Dieckmann and Law 1996 and Eq. 23 of Durinx et al. 2008).

When deriving the evolutionary dynamics of the resident phenotype $\bar{\mathbf{x}}$, geno-phenotype $\bar{\mathbf{z}}$, and geno-envo-phenotype $\bar{\mathbf{m}}$, we will obtain dynamic equations in terms of additive genetic covariance matrices. In particular, we will see that the mutational covariance matrix $\mathrm{cov}[\mathbf{y},\mathbf{y}]$ that we obtained in the canonical equation (3) equals the additive genetic covariance matrix of gene expression. Indeed, in Layer 6, Eq. 2, we define the *additive genetic covariance matrix* $\mathbf{G}_\zeta$ of a vector $\boldsymbol{\zeta} \in \mathbb{R}^{m\times 1}$ under our adaptive dynamics assumptions, and show that

$$\mathbf{G}_\zeta = \left(\frac{\mathrm{d}\boldsymbol{\zeta}}{\mathrm{d}\mathbf{y}^\intercal}\mathrm{cov}[\mathbf{y},\mathbf{y}]\frac{\mathrm{d}\boldsymbol{\zeta}^\intercal}{\mathrm{d}\mathbf{y}}\right)\bigg|_{\mathbf{y}=\bar{\mathbf{y}}}.$$

In particular, as we will later show that, since gene expression does not have developmental constraints and is open-loop so $\mathrm{d}\mathbf{y}^\intercal/\mathrm{d}\mathbf{y}|_{\mathbf{y}=\bar{\mathbf{y}}} = \mathbf{I}$ (Eq. E13), it follows that the additive genetic covariance matrix of gene expression $\mathbf{G}_\mathbf{y}$ equals the mutational covariance matrix $\mathrm{cov}[\mathbf{y},\mathbf{y}]$. This and Eq. (3) yield Eq. (13a).

Appendix B. Stable age distribution and reproductive values

The mutant stable age distribution and mutant reproductive value are given by dominant left and right eigenvectors $\mathbf{v}$ and $\mathbf{u}$ of the mutant's local stability matrix $\mathbf{J}$ in Eq. (10). That is, $\mathbf{v}$ and $\mathbf{u}$ are defined respectively by $\lambda\mathbf{u} = \mathbf{J}\mathbf{u}$ and $\lambda\mathbf{v}^\intercal = \mathbf{v}^\intercal\mathbf{J}$. Expanding these equations yields

$$\lambda u_1 = \sum_{j=1}^{N_a} f_j u_j \tag{B1a}$$

$$\lambda u_j = p_{j-1}u_{j-1} \quad \text{for } j \in \{2,\dots,N_a\} \tag{B1b}$$

$$\lambda v_j = v_1 f_j + v_{j+1}p_j \quad \text{for } j \in \{1,\dots,N_a\}, \tag{B1c}$$

since $v_{N_a+1} = 0$ without loss of generality. Eqs. (B1b) and (B1c) give the recurrence equations

$$u_j = \lambda^{-1}p_{j-1}u_{j-1}$$

$$v_j = \frac{1}{p_{j-1}}\lambda v_{j-1} - \frac{1}{p_{j-1}}v_1 f_{j-1},$$

for $j \in \{2,\dots,N_a\}$, which iterating yield

$$u_j = \lambda^{-j+1}\ell_j u_1 \tag{B3a}$$

$$v_j = \frac{1}{\ell_j}\lambda^{j-1}v_1 - v_1\sum_{k=1}^{j-1}\frac{\lambda^{j-1-k}}{\ell_j/\ell_k}f_k$$

$$= \frac{1}{\ell_j}\lambda^{j-1}v_1\left(1 - \sum_{k=1}^{j-1}\lambda^{-k}\ell_k f_k\right), \tag{B3b}$$

where $\ell_j = \prod_{k=1}^{j-1} p_k$ is mutant survivorship from age 1 to age j. Eq. (B3b) can be rewritten in the standard form of Fisher's (1927) reproductive value in discrete time using the Euler-Lotka equation as follows. Defining $\ell_1 = 1$ and since $\lambda^0 = 1$, substituting Eq. (B3a) in Eq. (B1a) and dividing both sides of the equation by λu_1 yields

$$1 = \sum_{j=1}^{N_a}\lambda^{-j}\ell_j f_j, \tag{B4}$$

which is the Euler-Lotka equation in discrete time (Charlesworth 1994, Eq. 1.42 and Caswell 2001, Eq. 4.42). Partitioning the sum in Eq. (B4) yields

$$1 - \sum_{j=1}^{m-1}\lambda^{-j}\ell_j f_j = \sum_{j=m}^{N_a}\lambda^{-j}\ell_j f_j, \tag{B5}$$

which substituted in Eq. (B3b) yields

$$v_j = \frac{1}{\ell_j}\lambda^{j-1}v_1\sum_{k=j}^{N_a}\lambda^{-k}\ell_k f_k. \tag{B6}$$

This equation is the standard form of Fisher's (1927) reproductive value in discrete time (Eq. 4.89 of Caswell 2001). Hence, from Eqs. (B3a) and (B6), we obtain the mutant stable age distribution and mutant reproductive value:

$$u_j = \lambda^{-j+1}\ell_j u_1$$

$$v_j = \frac{1}{\ell_j}\lambda^{j-1}v_1\sum_{k=j}^{N_a}\lambda^{-k}\ell_k f_k,$$

for $j \in \{2,\dots,N_a\}$, where u_1 and v_1 can take any positive value. Evaluating at neutrality ($\mathbf{y} = \bar{\mathbf{y}}$), we have that $\lambda^\circ = \lambda|_{\mathbf{y}=\bar{\mathbf{y}}} = 1$, which yields Eqs. (18).

Bienvenu and Legendre (2015) find that generation time can be measured by

$$T = \frac{\mathbf{v}^{\circ\intercal}\mathbf{u}^\circ}{\mathbf{v}^{\circ\intercal}\mathbf{F}^\circ\mathbf{u}^\circ},$$

where we evaluate at resident trait values given our adaptive dynamics assumptions, and where $\mathbf{F}$ is given by Eq. (10) setting all p_j to zero. Using Eq. (B1a), it is easily checked that $\mathbf{v}^{\circ\intercal}\mathbf{F}^\circ\mathbf{u}^\circ = v_1^\circ u_1^\circ$. In turn, we have that the numerator is

$$\mathbf{v}^{\circ\intercal}\mathbf{u}^\circ = \sum_{j=1}^{N_a} v_j^\circ u_j^\circ.$$

Thus, using Eqs. (18) yields

$$T = \frac{\mathbf{v}^{\circ\intercal}\mathbf{u}^{\circ}}{v_1^{\circ}u_1^{\circ}} = \frac{v_1^{\circ}u_1^{\circ} + \sum_{j=2}^{N_\mathrm{a}} v_j^{\circ}u_j^{\circ}}{v_1^{\circ}u_1^{\circ}} = \frac{v_1^{\circ}u_1^{\circ} + v_1^{\circ}u_1^{\circ}\sum_{j=2}^{N_\mathrm{a}}\sum_{k=j}^{N_\mathrm{a}} \ell_k^{\circ}f_k^{\circ}}{v_1^{\circ}u_1^{\circ}} = 1 + \sum_{j=2}^{N_\mathrm{a}}\sum_{k=j}^{N_\mathrm{a}} \ell_k^{\circ}f_k^{\circ}. \tag{B8}$$

We further manipulate this expression to recover a standard expression of generation time (Charlesworth 1994, Eq. 1.47c; Bulmer 1994, Eq. 25, Ch. 25; Bienvenu and Legendre 2015, Eq. 5). Evaluating the Euler-Lotka equation (B4) at the resident expression (so $\lambda|_{\mathbf{y}=\bar{\mathbf{y}}} = 1$), we obtain that a neutral mutant's expected lifetime reproductive success is

$$R_0^{\circ} = \sum_{j=1}^{N_\mathrm{a}} \ell_j^{\circ}f_j^{\circ} = 1. \tag{B9}$$

Therefore, Eq. (B8) is

$$\begin{aligned} T &= 1 + \sum_{j=2}^{N_\mathrm{a}}\sum_{k=j}^{N_\mathrm{a}} \ell_k^{\circ}f_k^{\circ} = R_0^{\circ} + \sum_{j=2}^{N_\mathrm{a}}\sum_{k=j}^{N_\mathrm{a}} \ell_k^{\circ}f_k^{\circ} \\ &= \sum_{j=1}^{N_\mathrm{a}} \ell_j^{\circ}f_j^{\circ} + \sum_{j=2}^{N_\mathrm{a}}\sum_{k=j}^{N_\mathrm{a}} \ell_k^{\circ}f_k^{\circ} \\ &= \ell_1^{\circ}f_1^{\circ} + \sum_{j=2}^{N_\mathrm{a}} \ell_j^{\circ}f_j^{\circ} + \sum_{j=2}^{N_\mathrm{a}}\sum_{k=j}^{N_\mathrm{a}} \ell_k^{\circ}f_k^{\circ} \\ &= \ell_1^{\circ}f_1^{\circ} + \sum_{j=2}^{N_\mathrm{a}}\left(\ell_j^{\circ}f_j^{\circ} + \sum_{k=j}^{N_\mathrm{a}} \ell_k^{\circ}f_k^{\circ}\right). \end{aligned}$$

Expanding the rightmost sum yields

$$T = \ell_1^{\circ}f_1^{\circ} + \sum_{j=2}^{N_\mathrm{a}}\left(\ell_j^{\circ}f_j^{\circ} + \ell_j^{\circ}f_j^{\circ} + \ell_{j+1}^{\circ}f_{j+1}^{\circ} + \cdots + \ell_{N_\mathrm{a}}^{\circ}f_{N_\mathrm{a}}^{\circ}\right)$$

Expanding the remaining sum yields

$$\begin{aligned} T = \ell_1^{\circ}f_1^{\circ} &+ \left(\ell_2^{\circ}f_2^{\circ} + \ell_2^{\circ}f_2^{\circ} + \ell_3^{\circ}f_3^{\circ} + \cdots + \ell_{N_\mathrm{a}}^{\circ}f_{N_\mathrm{a}}^{\circ}\right) \\ &+ \left(\ell_3^{\circ}f_3^{\circ} + \ell_3^{\circ}f_3^{\circ} + \ell_4^{\circ}f_4^{\circ} + \cdots + \ell_{N_\mathrm{a}}^{\circ}f_{N_\mathrm{a}}^{\circ}\right) \\ &+ \cdots \\ &+ \left(\ell_{N_\mathrm{a}-1}^{\circ}f_{N_\mathrm{a}-1}^{\circ} + \ell_{N_\mathrm{a}-1}^{\circ}f_{N_\mathrm{a}-1}^{\circ} + \ell_{N_\mathrm{a}}^{\circ}f_{N_\mathrm{a}}^{\circ}\right) \\ &+ \left(\ell_{N_\mathrm{a}}^{\circ}f_{N_\mathrm{a}}^{\circ} + \ell_{N_\mathrm{a}}^{\circ}f_{N_\mathrm{a}}^{\circ}\right). \end{aligned}$$

Collecting common terms yields

$$\begin{aligned} T &= \ell_1^{\circ}f_1^{\circ} + 2\ell_2^{\circ}f_2^{\circ} + 3\ell_3^{\circ}f_3^{\circ} + 4\ell_4^{\circ}f_4^{\circ} \\ &\quad + \cdots + N_\mathrm{a}\ell_{N_\mathrm{a}}^{\circ}f_{N_\mathrm{a}}^{\circ} \\ &= \sum_{j=1}^{N_\mathrm{a}} j\ell_j^{\circ}f_j^{\circ}, \end{aligned} \tag{B10}$$

which is Eq. (20). This expression recovers a standard measure of generation time (Charlesworth 1994, Eq. 1.47c; Bulmer 1994, Eq. 25, Ch. 25; Bienvenu and Legendre 2015, Eq. 5).

Appendix C. Selection gradient in terms of R_0

Following Hamilton (1966) (see also Eqs. 58-61 in Caswell 2009), we differentiate the Euler-Lotka equation (B4) implicitly with respect to a mutant trait value ζ, which yields

$$0 = \sum_{j=1}^{N_\mathrm{a}}\left(\lambda^{-j}\frac{\partial \ell_j f_j}{\partial \zeta} - j\ell_j f_j \lambda^{-j-1}\frac{\partial \lambda}{\partial \zeta}\right)\bigg|_{\mathbf{y}=\bar{\mathbf{y}}}.$$

Noting that $\lambda|_{\mathbf{y}=\bar{\mathbf{y}}} = 1$ and solving for the selection gradient, we obtain

$$\begin{aligned} \frac{\partial \lambda}{\partial \zeta}\bigg|_{\mathbf{y}=\bar{\mathbf{y}}} &= \frac{1}{\sum_{j=1}^{N_\mathrm{a}} j\ell_j^{\circ}f_j^{\circ}}\sum_{j=1}^{N_\mathrm{a}}\frac{\partial \ell_j f_j}{\partial \zeta}\bigg|_{\mathbf{y}=\bar{\mathbf{y}}} \\ &= \frac{1}{T}\frac{\partial R_0}{\partial \zeta}\bigg|_{\mathbf{y}=\bar{\mathbf{y}}}, \end{aligned} \tag{C1}$$

where we use Eqs. (27) and (B10). This is Eq. (28a). The same procedure using total derivatives yields Eq. (28b).

Appendix D. Total selection gradient of the phenotype

Here we derive the total selection gradient of the phenotype $\mathrm{d}\lambda/\mathrm{d}\mathbf{x}|_{\mathbf{y}=\bar{\mathbf{y}}}$, which is part of and simpler to derive than the total selection gradient of gene expression $\mathrm{d}\lambda/\mathrm{d}\mathbf{y}|_{\mathbf{y}=\bar{\mathbf{y}}}$.

Appendix D.1. Total selection gradient of the phenotype in terms of direct fitness effects

We start by considering the total selection gradient of the i-th phenotype at age a. By this, we mean the total selection gradient of a perturbation of x_{ia} taken as initial condition of the recurrence equation (1) when applied at the ages $\{a, \ldots, n\}$. Consequently, a perturbation in a phenotype at a given age does not affect phenotypes at earlier ages, in short, due to *the arrow of developmental time*. By letting ζ in Eq. (26) be x_{ia}, we have

$$\frac{\mathrm{d}\lambda}{\mathrm{d}x_{ia}}\bigg|_{\mathbf{y}=\bar{\mathbf{y}}} = \frac{\mathrm{d}w}{\mathrm{d}x_{ia}}\bigg|_{\mathbf{y}=\bar{\mathbf{y}}} = \sum_{j=1}^{N_\mathrm{a}}\frac{\mathrm{d}w_j}{\mathrm{d}x_{ia}}\bigg|_{\mathbf{y}=\bar{\mathbf{y}}}. \tag{D1}$$

Note that the total derivatives of a mutant's relative fitness at age j in Eq. (D1) are with respect to the individual's phenotype at possibly another age a. From Eq. (23), we have that a mutant's relative fitness at age j, $w_j(\mathbf{z}_j, \mathbf{h}_j(\mathbf{z}_j, \bar{\mathbf{z}}, \tau), \bar{\mathbf{m}})$, depends on the individual's phenotype at the current age (recall $\mathbf{z}_j = (\mathbf{x}_j; \mathbf{y}_j)$), but from the developmental constraint (1) the phenotype at a given age depends on the phenotype at previous ages. We must then calculate the total derivatives of fitness in Eq. (D1) in terms of direct (i.e., partial) derivatives, thus separating the effects of phenotypes at the current age from those of phenotypes at other ages.

To do this, we start by applying the chain rule, and since we assume that gene expression is open-loop (hence, gene expression does not depend on the phenotype, so $\mathrm{d}\mathbf{y}_j/\mathrm{d}x_{ia} = \mathbf{0}$ for all $i \in \{1, \ldots, N_\mathrm{s}\}$ and all $a, j \in \{1, \ldots, N_\mathrm{a}\}$), we obtain

$$\frac{\mathrm{d}w_j}{\mathrm{d}x_{ia}}\bigg|_{\mathbf{y}=\bar{\mathbf{y}}} = \left(\sum_{k=1}^{N_\mathrm{s}}\frac{\partial w_j}{\partial x_{kj}}\frac{\mathrm{d}x_{kj}}{\mathrm{d}x_{ia}} + \sum_{k=1}^{N_\mathrm{s}}\sum_{r=1}^{N_\mathrm{e}}\frac{\partial w_j}{\partial \epsilon_{rj}}\frac{\partial \epsilon_{rj}}{\partial x_{kj}}\frac{\mathrm{d}x_{kj}}{\mathrm{d}x_{ia}}\right)\bigg|_{\mathbf{y}=\bar{\mathbf{y}}}.$$

Applying matrix calculus notation (Appendix N), this is

$$\left.\frac{\mathrm{d}w_j}{\mathrm{d}x_{ia}}\right|_{\mathbf{y}=\bar{\mathbf{y}}} = \left.\left(\frac{\mathrm{d}\mathbf{x}_j^\intercal}{\mathrm{d}x_{ia}}\frac{\partial w_j}{\partial \mathbf{x}_j} + \sum_{k=1}^{N_\mathrm{s}}\frac{\partial \boldsymbol{\epsilon}_j^\intercal}{\partial x_{kj}}\frac{\partial w_j}{\partial \boldsymbol{\epsilon}_j}\frac{\mathrm{d}x_{kj}}{\mathrm{d}x_{ia}}\right)\right|_{\mathbf{y}=\bar{\mathbf{y}}}.$$

Applying matrix calculus notation again yields

$$\left.\frac{\mathrm{d}w_j}{\mathrm{d}x_{ia}}\right|_{\mathbf{y}=\bar{\mathbf{y}}} = \left.\left(\frac{\mathrm{d}\mathbf{x}_j^\intercal}{\mathrm{d}x_{ia}}\frac{\partial w_j}{\partial \mathbf{x}_j} + \frac{\mathrm{d}\mathbf{x}_j^\intercal}{\mathrm{d}x_{ia}}\frac{\partial \boldsymbol{\epsilon}_j^\intercal}{\partial \mathbf{x}_j}\frac{\partial w_j}{\partial \boldsymbol{\epsilon}_j}\right)\right|_{\mathbf{y}=\bar{\mathbf{y}}}.$$

Factorizing, we have

$$\left.\frac{\mathrm{d}w_j}{\mathrm{d}x_{ia}}\right|_{\mathbf{y}=\bar{\mathbf{y}}} = \left.\left[\frac{\mathrm{d}\mathbf{x}_j^\intercal}{\mathrm{d}x_{ia}}\left(\frac{\partial w_j}{\partial \mathbf{x}_j} + \frac{\partial \boldsymbol{\epsilon}_j^\intercal}{\partial \mathbf{x}_j}\frac{\partial w_j}{\partial \boldsymbol{\epsilon}_j}\right)\right]\right|_{\mathbf{y}=\bar{\mathbf{y}}}. \tag{D2}$$

Eq. (D2) now contains only partial derivatives of age-specific fitness.

We now write Eq. (D2) in terms of partial derivatives of lifetime fitness. Consider the *selection gradient of the phenotype at age j* or, equivalently, the column vector of *direct effects of a mutant's phenotype at age j on fitness* defined as

$$\left.\frac{\partial w}{\partial \mathbf{x}_j}\right|_{\mathbf{y}=\bar{\mathbf{y}}} \equiv \left.\left(\frac{\partial w}{\partial x_{1j}},\ldots,\frac{\partial w}{\partial x_{N_\mathrm{s}j}}\right)^\intercal\right|_{\mathbf{y}=\bar{\mathbf{y}}} \in \mathbb{R}^{N_\mathrm{s}\times 1}.$$

Such selection gradient of the phenotype at age j forms the selection gradient of the phenotype at all ages (Layer 2, Eq. 1). Similarly, the column vector of *direct effects of a mutant's environment at age j on fitness* is

$$\left.\frac{\partial w}{\partial \boldsymbol{\epsilon}_j}\right|_{\mathbf{y}=\bar{\mathbf{y}}} \equiv \left.\left(\frac{\partial w}{\partial \epsilon_{1j}},\ldots,\frac{\partial w}{\partial \epsilon_{N_\mathrm{e}j}}\right)^\intercal\right|_{\mathbf{y}=\bar{\mathbf{y}}} \in \mathbb{R}^{N_\mathrm{e}\times 1},$$

and the matrix of *direct effects of a mutant's phenotype at age j on her environment at age j* is

$$\left.\frac{\partial \boldsymbol{\epsilon}_j^\intercal}{\partial \mathbf{x}_j}\right|_{\mathbf{y}=\bar{\mathbf{y}}} \equiv \left.\begin{pmatrix}\frac{\partial \epsilon_{1j}}{\partial x_{1j}} & \cdots & \frac{\partial \epsilon_{N_\mathrm{e}j}}{\partial x_{1j}}\\ \vdots & \ddots & \vdots\\ \frac{\partial \epsilon_{1j}}{\partial x_{N_\mathrm{s}j}} & \cdots & \frac{\partial \epsilon_{N_\mathrm{e}j}^\intercal}{\partial x_{N_\mathrm{s}j}}\end{pmatrix}\right|_{\mathbf{y}=\bar{\mathbf{y}}} \in \mathbb{R}^{N_\mathrm{s}\times N_\mathrm{e}}.$$

From Eq. (25), w only depends directly on $\mathbf{x}_j$, $\mathbf{y}_j$, and $\boldsymbol{\epsilon}_j$ through w_j. So,

$$\frac{\partial w_j}{\partial \mathbf{x}_j} = \frac{\partial w}{\partial \mathbf{x}_j} \tag{D3a}$$

$$\frac{\partial w_j}{\partial \mathbf{y}_j} = \frac{\partial w}{\partial \mathbf{y}_j} \tag{D3b}$$

$$\frac{\partial w_j}{\partial \boldsymbol{\epsilon}_j} = \frac{\partial w}{\partial \boldsymbol{\epsilon}_j}, \tag{D3c}$$

which substituted in Eq. (D2) yields

$$\left.\frac{\mathrm{d}w_j}{\mathrm{d}x_{ia}}\right|_{\mathbf{y}=\bar{\mathbf{y}}} = \left.\left[\frac{\mathrm{d}\mathbf{x}_j^\intercal}{\mathrm{d}x_{ia}}\left(\frac{\partial w}{\partial \mathbf{x}_j} + \frac{\partial \boldsymbol{\epsilon}_j^\intercal}{\partial \mathbf{x}_j}\frac{\partial w}{\partial \boldsymbol{\epsilon}_j}\right)\right]\right|_{\mathbf{y}=\bar{\mathbf{y}}}$$

$$= \left.\left(\frac{\mathrm{d}\mathbf{x}_j^\intercal}{\mathrm{d}x_{ia}}\frac{\delta w}{\delta \mathbf{x}_j}\right)\right|_{\mathbf{y}=\bar{\mathbf{y}}}, \tag{D4}$$

where the *semi-total selection gradient of the phenotype at age j* or, equivalently, the column vector of *semi-total effects of a mutant's phenotype at age j on fitness* (i.e., the total gradient considering environmental but not developmental constraints) is

$$\left.\frac{\delta w}{\delta \mathbf{x}_j}\right|_{\mathbf{y}=\bar{\mathbf{y}}} = \left.\left(\frac{\partial w}{\partial \mathbf{x}_j} + \frac{\partial \boldsymbol{\epsilon}_j^\intercal}{\partial \mathbf{x}_j}\frac{\partial w}{\partial \boldsymbol{\epsilon}_j}\right)\right|_{\mathbf{y}=\bar{\mathbf{y}}} \in \mathbb{R}^{N_\mathrm{s}\times 1}. \tag{D5}$$

Consider now the semi-total selection gradient of the phenotype at all ages. The block column vector of *semi-total effects of a mutant's phenotype on fitness* is

$$\left.\frac{\delta w}{\delta \mathbf{x}}\right|_{\mathbf{y}=\bar{\mathbf{y}}} \equiv \left.\left(\frac{\delta w}{\delta \mathbf{x}_1};\cdots;\frac{\delta w}{\delta \mathbf{x}_{N_\mathrm{a}}}\right)\right|_{\mathbf{y}=\bar{\mathbf{y}}} \in \mathbb{R}^{N_\mathrm{a}N_\mathrm{s}\times 1}.$$

Using Layer 2, Eq. 4d, we have that

$$\frac{\partial \boldsymbol{\epsilon}^\intercal}{\partial \mathbf{x}}\frac{\partial w}{\partial \boldsymbol{\epsilon}} = \left(\sum_{k=1}^{N_\mathrm{a}}\frac{\partial \boldsymbol{\epsilon}_k^\intercal}{\partial \mathbf{x}_j}\frac{\partial w}{\partial \boldsymbol{\epsilon}_k}\right) = \left(\frac{\partial \boldsymbol{\epsilon}_j^\intercal}{\partial \mathbf{x}_j}\frac{\partial w}{\partial \boldsymbol{\epsilon}_j}\right) \tag{D6}$$

is a block column vector whose j-th entry equals the rightmost term in Eq. (D5). Thus, from (D5), Layer 2, Eq. 1, and (D6), it follows that the semi-total selection gradient of the phenotype is given by Layer 3, Eq. 1.

Now, we write the total selection gradient of x_{ia} in terms of the semi-total selection gradient of the phenotype. Substituting Eq. (D4) in Eq. (D1) yields

$$\left.\frac{\mathrm{d}w}{\mathrm{d}x_{ia}}\right|_{\mathbf{y}=\bar{\mathbf{y}}} = \sum_{j=1}^{N_\mathrm{a}}\left.\left(\frac{\mathrm{d}\mathbf{x}_j^\intercal}{\mathrm{d}x_{ia}}\frac{\delta w}{\delta \mathbf{x}_j}\right)\right|_{\mathbf{y}=\bar{\mathbf{y}}} = \left.\left(\frac{\mathrm{d}\mathbf{x}^\intercal}{\mathrm{d}x_{ia}}\frac{\delta w}{\delta \mathbf{x}}\right)\right|_{\mathbf{y}=\bar{\mathbf{y}}},$$

where we use the block row vector

$$\frac{\mathrm{d}\mathbf{x}^\intercal}{\mathrm{d}x_{ia}} = \left(\frac{\mathrm{d}\mathbf{x}_0^\intercal}{\mathrm{d}x_{ia}},\ldots,\frac{\mathrm{d}\mathbf{x}_{N_\mathrm{a}}^\intercal}{\mathrm{d}x_{ia}}\right) \in \mathbb{R}^{1\times N_\mathrm{a}N_\mathrm{s}}.$$

Therefore, the total selection gradient of all phenotypes across all ages is

$$\left.\frac{\mathrm{d}w}{\mathrm{d}\mathbf{x}}\right|_{\mathbf{y}=\bar{\mathbf{y}}} = \left.\left(\frac{\mathrm{d}\mathbf{x}^\intercal}{\mathrm{d}\mathbf{x}}\frac{\delta w}{\delta \mathbf{x}}\right)\right|_{\mathbf{y}=\bar{\mathbf{y}}} \in \mathbb{R}^{N_\mathrm{a}N_\mathrm{s}\times 1}, \tag{D7}$$

where the semi-total selection gradient of the phenotype is given by Layer 3, Eq. 1 and the block matrix of *total effects of a mutant's phenotype on her phenotype* is

$$\left.\frac{\mathrm{d}\mathbf{x}^\intercal}{\mathrm{d}\mathbf{x}}\right|_{\mathbf{y}=\bar{\mathbf{y}}} \equiv \left.\begin{pmatrix}\frac{\mathrm{d}\mathbf{x}_1^\intercal}{\mathrm{d}\mathbf{x}_1} & \cdots & \frac{\mathrm{d}\mathbf{x}_{N_\mathrm{a}}^\intercal}{\partial \mathbf{x}_1}\\ \vdots & \ddots & \vdots\\ \frac{\mathrm{d}\mathbf{x}_1^\intercal}{\mathrm{d}\mathbf{x}_{N_\mathrm{a}}} & \cdots & \frac{\mathrm{d}\mathbf{x}_{N_\mathrm{a}}^\intercal}{\mathrm{d}\mathbf{x}_{N_\mathrm{a}}}\end{pmatrix}\right|_{\mathbf{y}=\bar{\mathbf{y}}} \in \mathbb{R}^{N_\mathrm{a}N_\mathrm{s}\times N_\mathrm{a}N_\mathrm{s}}.$$

Using Layer 3, Eq. 1, expression (D7) is now in terms of partial derivatives of fitness, partial derivatives of the environment, and total effects of a mutant's phenotype on her phenotype, $\mathrm{d}\mathbf{x}^\intercal/\mathrm{d}\mathbf{x}$, which we now proceed to write in terms of partial derivatives only.

Appendix D.2. Matrix of total effects of a mutant's phenotype on her phenotype

From the developmental constraint (1) for the k-th phenotype at age $j \in \{2,\dots,N_\mathrm{a}\}$ we have that $x_{kj} = g_{k,j-1}(\mathbf{z}_{j-1}, \mathbf{h}_{j-1}(\mathbf{z}_{j-1}, \bar{\mathbf{z}}, \tau), \bar{\mathbf{z}})$, so using the chain rule and since gene expression is open-loop we obtain

$$\left.\frac{\mathrm{d}x_{kj}}{\mathrm{d}x_{ia}}\right|_{\mathbf{y}=\bar{\mathbf{y}}} = \left(\sum_{l=1}^{N_\mathrm{s}} \frac{\partial g_{k,j-1}}{\partial x_{l,j-1}} \frac{\mathrm{d}x_{l,j-1}}{\mathrm{d}x_{ia}} + \sum_{l=1}^{N_\mathrm{s}} \sum_{r=1}^{N_\mathrm{e}} \frac{\partial g_{k,j-1}}{\partial \epsilon_{r,j-1}} \frac{\partial \epsilon_{r,j-1}}{\partial x_{l,j-1}} \frac{\mathrm{d}x_{l,j-1}}{\mathrm{d}x_{ia}}\right)\Bigg|_{\mathbf{y}=\bar{\mathbf{y}}}.$$

Applying matrix calculus notation (Appendix N), this is

$$\left.\frac{\mathrm{d}x_{kj}}{\mathrm{d}x_{ia}}\right|_{\mathbf{y}=\bar{\mathbf{y}}} = \left(\frac{\mathrm{d}\mathbf{x}_{j-1}^\mathsf{T}}{\mathrm{d}x_{ia}} \frac{\partial g_{k,j-1}}{\partial \mathbf{x}_{j-1}} + \sum_{l=1}^{N_\mathrm{s}} \frac{\partial \boldsymbol{\epsilon}_{j-1}^\mathsf{T}}{\partial x_{l,j-1}} \frac{\partial g_{k,j-1}}{\partial \boldsymbol{\epsilon}_{j-1}} \frac{\mathrm{d}x_{l,j-1}}{\mathrm{d}x_{ia}}\right)\Bigg|_{\mathbf{y}=\bar{\mathbf{y}}}.$$

Applying matrix calculus notation again yields

$$\left.\frac{\mathrm{d}x_{kj}}{\mathrm{d}x_{ia}}\right|_{\mathbf{y}=\bar{\mathbf{y}}} = \left(\frac{\mathrm{d}\mathbf{x}_{j-1}^\mathsf{T}}{\mathrm{d}x_{ia}} \frac{\partial g_{k,j-1}}{\partial \mathbf{x}_{j-1}} + \frac{\mathrm{d}\mathbf{x}_{j-1}^\mathsf{T}}{\mathrm{d}x_{ia}} \frac{\partial \boldsymbol{\epsilon}_{j-1}^\mathsf{T}}{\partial \mathbf{x}_{j-1}} \frac{\partial g_{k,j-1}}{\partial \boldsymbol{\epsilon}_{j-1}}\right)\Bigg|_{\mathbf{y}=\bar{\mathbf{y}}}.$$

Factorizing, we have

$$\left.\frac{\mathrm{d}x_{kj}}{\mathrm{d}x_{ia}}\right|_{\mathbf{y}=\bar{\mathbf{y}}} = \left[\frac{\mathrm{d}\mathbf{x}_{j-1}^\mathsf{T}}{\mathrm{d}x_{ia}} \left(\frac{\partial g_{k,j-1}}{\partial \mathbf{x}_{j-1}} + \frac{\partial \boldsymbol{\epsilon}_{j-1}^\mathsf{T}}{\partial \mathbf{x}_{j-1}} \frac{\partial g_{k,j-1}}{\partial \boldsymbol{\epsilon}_{j-1}}\right)\right]\Bigg|_{\mathbf{y}=\bar{\mathbf{y}}}.$$

Rewriting $g_{k,j-1}$ as x_{kj} yields

$$\left.\frac{\mathrm{d}x_{kj}}{\mathrm{d}x_{ia}}\right|_{\mathbf{y}=\bar{\mathbf{y}}} = \left[\frac{\mathrm{d}\mathbf{x}_{j-1}^\mathsf{T}}{\mathrm{d}x_{ia}} \left(\frac{\partial x_{kj}}{\partial \mathbf{x}_{j-1}} + \frac{\partial \boldsymbol{\epsilon}_{j-1}^\mathsf{T}}{\partial \mathbf{x}_{j-1}} \frac{\partial x_{kj}}{\partial \boldsymbol{\epsilon}_{j-1}}\right)\right]\Bigg|_{\mathbf{y}=\bar{\mathbf{y}}}.$$

Hence,

$$\left.\frac{\mathrm{d}\mathbf{x}_{j}^\mathsf{T}}{\mathrm{d}x_{ia}}\right|_{\mathbf{y}=\bar{\mathbf{y}}} = \left[\frac{\mathrm{d}\mathbf{x}_{j-1}^\mathsf{T}}{\mathrm{d}x_{ia}} \left(\frac{\partial \mathbf{x}_{j}^\mathsf{T}}{\partial \mathbf{x}_{j-1}} + \frac{\partial \boldsymbol{\epsilon}_{j-1}^\mathsf{T}}{\partial \mathbf{x}_{j-1}} \frac{\partial \mathbf{x}_{j}^\mathsf{T}}{\partial \boldsymbol{\epsilon}_{j-1}}\right)\right]\Bigg|_{\mathbf{y}=\bar{\mathbf{y}}}, \tag{D8}$$

where we use the matrix of *direct effects of a mutant's phenotype at age j on her phenotype at age $j+1$*

$$\left.\frac{\partial \mathbf{x}_{j+1}^\mathsf{T}}{\partial \mathbf{x}_{j}}\right|_{\mathbf{y}=\bar{\mathbf{y}}} \equiv \left.\begin{pmatrix} \frac{\partial x_{1,j+1}}{\partial x_{1j}} & \cdots & \frac{\partial x_{N_\mathrm{s},j+1}}{\partial x_{1j}} \\ \vdots & \ddots & \vdots \\ \frac{\partial x_{1,j+1}}{\partial x_{N_\mathrm{s}j}} & \cdots & \frac{\partial x_{N_\mathrm{s},j+1}}{\partial x_{N_\mathrm{s}j}} \end{pmatrix}\right|_{\mathbf{y}=\bar{\mathbf{y}}} \in \mathbb{R}^{N_\mathrm{s}\times N_\mathrm{s}},$$

and the matrix of *direct effects of a mutant's environment at age j on her phenotype at age $j+1$*

$$\left.\frac{\partial \mathbf{x}_{j+1}^\mathsf{T}}{\partial \boldsymbol{\epsilon}_{j}}\right|_{\mathbf{y}=\bar{\mathbf{y}}} \equiv \left.\begin{pmatrix} \frac{\partial x_{1,j+1}}{\partial \epsilon_{1j}} & \cdots & \frac{\partial x_{N_\mathrm{s},j+1}}{\partial \epsilon_{1j}} \\ \vdots & \ddots & \vdots \\ \frac{\partial x_{1,j+1}}{\partial \epsilon_{N_\mathrm{e}j}} & \cdots & \frac{\partial x_{N_\mathrm{s},j+1}}{\partial \epsilon_{N_\mathrm{e}j}} \end{pmatrix}\right|_{\mathbf{y}=\bar{\mathbf{y}}} \in \mathbb{R}^{N_\mathrm{e}\times N_\mathrm{s}}.$$

We can write Eq. (D8) more succinctly as

$$\left.\frac{\mathrm{d}\mathbf{x}_{j}^\mathsf{T}}{\mathrm{d}x_{ia}}\right|_{\mathbf{y}=\bar{\mathbf{y}}} = \left.\left(\frac{\mathrm{d}\mathbf{x}_{j-1}^\mathsf{T}}{\mathrm{d}x_{ia}} \frac{\delta \mathbf{x}_{j}^\mathsf{T}}{\delta \mathbf{x}_{j-1}}\right)\right|_{\mathbf{y}=\bar{\mathbf{y}}}, \tag{D9}$$

where we use the matrix of *semi-total effects of a mutant's phenotype at age j on her states at age $j+1$*

$$\left.\frac{\delta \mathbf{x}_{j+1}^\mathsf{T}}{\delta \mathbf{x}_{j}}\right|_{\mathbf{y}=\bar{\mathbf{y}}} = \left.\left(\frac{\partial \mathbf{x}_{j+1}^\mathsf{T}}{\partial \mathbf{x}_{j}} + \frac{\partial \boldsymbol{\epsilon}_{j}^\mathsf{T}}{\partial \mathbf{x}_{j}} \frac{\partial \mathbf{x}_{j+1}^\mathsf{T}}{\partial \boldsymbol{\epsilon}_{j}}\right)\right|_{\mathbf{y}=\bar{\mathbf{y}}} \in \mathbb{R}^{N_\mathrm{s}\times N_\mathrm{s}}. \tag{D10}$$

The block matrix of *semi-total effects a mutant's phenotype on her phenotype* is

$$\begin{aligned} \left.\frac{\delta \mathbf{x}^\mathsf{T}}{\delta \mathbf{x}}\right|_{\mathbf{y}=\bar{\mathbf{y}}} &\equiv \left.\begin{pmatrix} \frac{\delta \mathbf{x}_1^\mathsf{T}}{\delta \mathbf{x}_1} & \cdots & \frac{\delta \mathbf{x}_{N_\mathrm{a}}^\mathsf{T}}{\delta \mathbf{x}_1} \\ \vdots & \ddots & \vdots \\ \frac{\delta \mathbf{x}_1^\mathsf{T}}{\delta \mathbf{x}_{N_\mathrm{a}}} & \cdots & \frac{\delta \mathbf{x}_{N_\mathrm{a}}^\mathsf{T}}{\delta \mathbf{x}_{N_\mathrm{a}}} \end{pmatrix}\right|_{\mathbf{y}=\bar{\mathbf{y}}} \\ &= \left.\begin{pmatrix} \mathbf{I} & \frac{\delta \mathbf{x}_2^\mathsf{T}}{\delta \mathbf{x}_1} & \cdots & \mathbf{0} & \mathbf{0} \\ \mathbf{0} & \mathbf{I} & \cdots & \mathbf{0} & \mathbf{0} \\ \vdots & \vdots & \ddots & \vdots & \vdots \\ \mathbf{0} & \mathbf{0} & \cdots & \mathbf{I} & \frac{\delta \mathbf{x}_{N_\mathrm{a}}^\mathsf{T}}{\delta \mathbf{x}_{N_\mathrm{a}-1}} \\ \mathbf{0} & \mathbf{0} & \cdots & \mathbf{0} & \mathbf{I} \end{pmatrix}\right|_{\mathbf{y}=\bar{\mathbf{y}}} \\ &\in \mathbb{R}^{N_\mathrm{a}N_\mathrm{s}\times N_\mathrm{a}N_\mathrm{s}}. \end{aligned} \tag{D11}$$

The equality (D11) follows because semi-total effects of a mutant's phenotype on her phenotype are only non-zero at the next age (from the developmental constraint in Eq. 1) or when a variable is differentiated with respect to itself. Using Layer 2, Eq. 4d and Layer 2, Eq. 4c, we have that

$$\frac{\partial \boldsymbol{\epsilon}^\mathsf{T}}{\partial \mathbf{x}} \frac{\partial \mathbf{x}^\mathsf{T}}{\partial \boldsymbol{\epsilon}} = \left(\sum_{k=1}^{N_\mathrm{a}} \frac{\partial \boldsymbol{\epsilon}_k^\mathsf{T}}{\partial \mathbf{x}_a} \frac{\partial \mathbf{x}_j^\mathsf{T}}{\partial \boldsymbol{\epsilon}_k}\right) = \left(\begin{cases} \frac{\partial \boldsymbol{\epsilon}_a^\mathsf{T}}{\partial \mathbf{x}_a} \frac{\partial \mathbf{x}_j^\mathsf{T}}{\partial \boldsymbol{\epsilon}_a} & \text{for } j = a+1 \\ \mathbf{0} & \text{for } j \neq a+1 \end{cases}\right), \tag{D12}$$

which equals the rightmost term in Eq. (D10) for $j = a+1$. Thus, from (D10), Layer 2, Eq. 4a, (D11), and (D12), it follows that the block matrix of semi-total effects of a mutant's phenotype on her phenotype satisfies Layer 3, Eq. 3.

Eq. (D9) gives the matrix of total effects of the i-th phenotype of a mutant at age a on her phenotype at age j. Then, it follows that the matrix of total effects of all the phenotypes of a mutant at age a on her phenotype at age j is

$$\left.\frac{\mathrm{d}\mathbf{x}_{j}^\mathsf{T}}{\mathrm{d}\mathbf{x}_{a}}\right|_{\mathbf{y}=\bar{\mathbf{y}}} = \left.\left(\frac{\mathrm{d}\mathbf{x}_{j-1}^\mathsf{T}}{\mathrm{d}\mathbf{x}_{a}} \frac{\delta \mathbf{x}_{j}^\mathsf{T}}{\delta \mathbf{x}_{j-1}}\right)\right|_{\mathbf{y}=\bar{\mathbf{y}}}. \tag{D13}$$

Eq. (D13) is a recurrence equation for $\mathrm{d}\mathbf{x}_j^\mathsf{T}/\mathrm{d}\mathbf{x}_a$ over age $j \in \{2,\dots,N_\mathrm{a}\}$. Because of the arrow of developmental time (due

to the developmental constraint (1)), perturbations in an individual's late phenotype do not affect the individual's early phenotype (i.e., $\mathrm{d}\mathbf{x}_j^\intercal/\mathrm{d}\mathbf{x}_a = \mathbf{0}$ for $j < a$ and $j \in \{1, \ldots, N_\mathrm{a} - 1\}$)[1]. Additionally, from the arrow of developmental time (Eq. 1), a perturbation in an individual's phenotype at a given age does not affect any other of the individual's phenotypes at the *same* age (i.e., $\mathrm{d}\mathbf{x}_a^\intercal/\mathrm{d}\mathbf{x}_a = \mathbf{I}$ where $\mathbf{I}$ is the identity matrix). Hence, expanding the recurrence in Eq. (D13), we obtain for $j \in \{1, \ldots, N_\mathrm{a}\}$ that

$$\left.\frac{\mathrm{d}\mathbf{x}_j^\intercal}{\mathrm{d}\mathbf{x}_a}\right|_{\mathbf{y}=\bar{\mathbf{y}}} = \begin{cases} \left.\left(\frac{\mathrm{d}\mathbf{x}_a^\intercal}{\mathrm{d}\mathbf{x}_a}\frac{\delta\mathbf{x}_{a+1}^\intercal}{\delta\mathbf{x}_a}\cdots\frac{\delta\mathbf{x}_j^\intercal}{\delta\mathbf{x}_{j-1}}\right)\right|_{\mathbf{y}=\bar{\mathbf{y}}} & \text{for } j > a \\ \left.\frac{\mathrm{d}\mathbf{x}_a^\intercal}{\mathrm{d}\mathbf{x}_a}\right|_{\mathbf{y}=\bar{\mathbf{y}}} & \text{for } j = a \\ \mathbf{0} & \text{for } j < a \end{cases} = \begin{cases} \left.\left(\frac{\delta\mathbf{x}_{a+1}^\intercal}{\delta\mathbf{x}_a}\cdots\frac{\delta\mathbf{x}_j^\intercal}{\delta\mathbf{x}_{j-1}}\right)\right|_{\mathbf{y}=\bar{\mathbf{y}}} & \text{for } j > a \\ \mathbf{I} & \text{for } j = a \\ \mathbf{0} & \text{for } j < a. \end{cases} \tag{D14}$$

Thus, the block matrix of *total effects of a mutant's phenotype on her phenotype* is

$$\left.\frac{\mathrm{d}\mathbf{x}^\intercal}{\mathrm{d}\mathbf{x}}\right|_{\mathbf{y}=\bar{\mathbf{y}}} = \left.\begin{pmatrix} \frac{\mathrm{d}\mathbf{x}_1^\intercal}{\mathrm{d}\mathbf{x}_1} & \cdots & \frac{\mathrm{d}\mathbf{x}_{N_\mathrm{a}}^\intercal}{\mathrm{d}\mathbf{x}_1} \\ \vdots & \ddots & \vdots \\ \frac{\mathrm{d}\mathbf{x}_1^\intercal}{\mathrm{d}\mathbf{x}_{N_\mathrm{a}}} & \cdots & \frac{\mathrm{d}\mathbf{x}_{N_\mathrm{a}}^\intercal}{\mathrm{d}\mathbf{x}_{N_\mathrm{a}}} \end{pmatrix}\right|_{\mathbf{y}=\bar{\mathbf{y}}} = \left.\begin{pmatrix} \mathbf{I} & \frac{\mathrm{d}\mathbf{x}_2^\intercal}{\mathrm{d}\mathbf{x}_1} & \cdots & \frac{\mathrm{d}\mathbf{x}_{N_\mathrm{a}-1}^\intercal}{\mathrm{d}\mathbf{x}_1} & \frac{\mathrm{d}\mathbf{x}_{N_\mathrm{a}}^\intercal}{\mathrm{d}\mathbf{x}_1} \\ \mathbf{0} & \mathbf{I} & \cdots & \frac{\mathrm{d}\mathbf{x}_{N_\mathrm{a}-1}^\intercal}{\mathrm{d}\mathbf{x}_2} & \frac{\mathrm{d}\mathbf{x}_{N_\mathrm{a}}^\intercal}{\mathrm{d}\mathbf{x}_2} \\ \vdots & \vdots & \ddots & \vdots & \vdots \\ \mathbf{0} & \mathbf{0} & \cdots & \mathbf{I} & \frac{\mathrm{d}\mathbf{x}_{N_\mathrm{a}}^\intercal}{\mathrm{d}\mathbf{x}_{N_\mathrm{a}-1}} \\ \mathbf{0} & \mathbf{0} & \cdots & \mathbf{0} & \mathbf{I} \end{pmatrix}\right|_{\mathbf{y}=\bar{\mathbf{y}}} \in \mathbb{R}^{N_\mathrm{a}N_\mathrm{s}\times N_\mathrm{a}N_\mathrm{s}}, \tag{D15}$$

which is block upper triangular and its aj-th entry is given by Layer 4, Eq. 2. Eq. (D15) and Layer 4, Eq. 2 write the matrix of total effects of a mutant's phenotype on her phenotype in terms of partial derivatives, given Eq. (D10), as we sought.

From Eq. (D15), it follows that the matrix of total effects of a mutant's phenotype on her phenotype $\mathrm{d}\mathbf{x}^\intercal/\mathrm{d}\mathbf{x}|_{\mathbf{y}=\bar{\mathbf{y}}}$ is invertible. Indeed, since $\mathrm{d}\mathbf{x}^\intercal/\mathrm{d}\mathbf{x}|_{\mathbf{y}=\bar{\mathbf{y}}}$ is square and block upper triangular, then its determinant is

$$\det\left(\left.\frac{\mathrm{d}\mathbf{x}^\intercal}{\mathrm{d}\mathbf{x}}\right|_{\mathbf{y}=\bar{\mathbf{y}}}\right) = \det\left(\left.\frac{\mathrm{d}\mathbf{x}_1^\intercal}{\mathrm{d}\mathbf{x}_1}\right|_{\mathbf{y}=\bar{\mathbf{y}}}\right)\cdots\det\left(\left.\frac{\mathrm{d}\mathbf{x}_{N_\mathrm{a}}^\intercal}{\mathrm{d}\mathbf{x}_{N_\mathrm{a}}}\right|_{\mathbf{y}=\bar{\mathbf{y}}}\right)$$

(Horn and Johnson, 2013, p. 32). Since $\mathrm{d}\mathbf{x}_a^\intercal/\mathrm{d}\mathbf{x}_a|_{\mathbf{y}=\bar{\mathbf{y}}} = \mathbf{I}$, then $\det(\mathrm{d}\mathbf{x}_a^\intercal/\mathrm{d}\mathbf{x}_a|_{\mathbf{y}=\bar{\mathbf{y}}}) = 1$ for all $a \in \{1, \ldots, N_\mathrm{a}\}$. Hence, $\det(\mathrm{d}\mathbf{x}^\intercal/\mathrm{d}\mathbf{x}|_{\mathbf{y}=\bar{\mathbf{y}}}) \neq 0$, so $\mathrm{d}\mathbf{x}^\intercal/\mathrm{d}\mathbf{x}|_{\mathbf{y}=\bar{\mathbf{y}}}$ is invertible.

We now obtain a more compact expression for the matrix of total effects of a mutant's phenotype on her phenotype in terms of partial derivatives. From Eq. (D11), it follows that

$$\left.\frac{\delta\mathbf{x}^\intercal}{\delta\mathbf{x}}\right|_{\mathbf{y}=\bar{\mathbf{y}}} - \mathbf{I} = \left.\begin{pmatrix} \mathbf{0} & \frac{\delta\mathbf{x}_2^\intercal}{\delta\mathbf{x}_1} & \cdots & \mathbf{0} & \mathbf{0} \\ \mathbf{0} & \mathbf{0} & \cdots & \mathbf{0} & \mathbf{0} \\ \vdots & \vdots & \ddots & \vdots & \vdots \\ \mathbf{0} & \mathbf{0} & \cdots & \mathbf{0} & \frac{\delta\mathbf{x}_{N_\mathrm{a}}^\intercal}{\delta\mathbf{x}_{N_\mathrm{a}-1}} \\ \mathbf{0} & \mathbf{0} & \cdots & \mathbf{0} & \mathbf{0} \end{pmatrix}\right|_{\mathbf{y}=\bar{\mathbf{y}}}, \tag{D16}$$

which is block 1-superdiagonal (i.e., only the entries in its first block super diagonal are non-zero). By definition of matrix power, we have that $(\delta\mathbf{x}^\intercal/\delta\mathbf{x} - \mathbf{I})^0 = \mathbf{I}$. Now, from Eq. (D16), we have that

$$\frac{\delta\mathbf{x}^\intercal}{\delta\mathbf{x}} - \mathbf{I} = \left(\begin{cases} \frac{\delta\mathbf{x}_j^\intercal}{\delta\mathbf{x}_a} & \text{if } j = a+1 \\ \mathbf{0} & \text{otherwise} \end{cases}\right).$$

Using Eq. (D16), taking the second power yields

$$\left(\frac{\delta\mathbf{x}^\intercal}{\delta\mathbf{x}} - \mathbf{I}\right)^2 = \left(\frac{\delta\mathbf{x}^\intercal}{\delta\mathbf{x}} - \mathbf{I}\right)\left(\frac{\delta\mathbf{x}^\intercal}{\delta\mathbf{x}} - \mathbf{I}\right) = \left(\begin{cases} \frac{\delta\mathbf{x}_{a+1}^\intercal}{\delta\mathbf{x}_a}\frac{\delta\mathbf{x}_j^\intercal}{\delta\mathbf{x}_{a+1}} & \text{if } j = a+2 \\ \mathbf{0} & \text{otherwise} \end{cases}\right),$$

which is block 2-superdiagonal. This suggests the inductive hypothesis that

$$\left(\frac{\delta\mathbf{x}^\intercal}{\delta\mathbf{x}} - \mathbf{I}\right)^i = \left(\begin{cases} \overset{\curvearrowright}{\prod_{k=a}^{j-1}}\frac{\delta\mathbf{x}_{k+1}^\intercal}{\delta\mathbf{x}_k} & \text{if } j = a+i \\ \mathbf{0} & \text{otherwise} \end{cases}\right) \tag{D17}$$

holds for some $i \in \{0, 1, \ldots\}$, which is a block i-superdiagonal matrix. If this is the case, then we have that

$$\left(\frac{\delta\mathbf{x}^\intercal}{\delta\mathbf{x}} - \mathbf{I}\right)^{i+1} = \left(\frac{\delta\mathbf{x}^\intercal}{\delta\mathbf{x}} - \mathbf{I}\right)^i\left(\frac{\delta\mathbf{x}^\intercal}{\delta\mathbf{x}} - \mathbf{I}\right) = \left(\begin{cases} \overset{\curvearrowright}{\prod_{k=a}^{a+i-1}}\frac{\delta\mathbf{x}_{k+1}^\intercal}{\delta\mathbf{x}_k}\frac{\delta\mathbf{x}_j^\intercal}{\delta\mathbf{x}_{a+i}} & \text{if } j = a+i+1 \\ \mathbf{0} & \text{otherwise} \end{cases}\right) = \left(\begin{cases} \overset{\curvearrowright}{\prod_{k=a}^{j-1}}\frac{\delta\mathbf{x}_{k+1}^\intercal}{\delta\mathbf{x}_k} & \text{if } j = a+i+1 \\ \mathbf{0} & \text{otherwise} \end{cases}\right).$$

[1] More specifically, we take the derivative $\mathrm{d}\mathbf{x}_j^\intercal/\mathrm{d}x_{ia}$ as referring to the effect on $\mathbf{x}_j^\intercal$ of a perturbation of the initial condition $\mathbf{x}_a$ of the difference equation (1) applied at the ages $\{a, \ldots, n\}$. Hence, if $j < a$, $\mathbf{x}_j^\intercal$ is unmodified by a change in the initial condition of (1) applied at the ages $\{a, \ldots, n\}$.

This proves by induction that Eq. (D17) holds for every $i \in \{0, 1, \ldots\}$, which together with Layer 4, Eq. 2 proves that

$$\left(\frac{\delta \mathbf{x}^\intercal}{\delta \mathbf{x}} - \mathbf{I}\right)^i = \left(\begin{cases} \dfrac{\mathrm{d}\mathbf{x}_j^\intercal}{\mathrm{d}\mathbf{x}_a} & \text{if } j = a + i \\ \mathbf{0} & \text{otherwise} \end{cases}\right)$$

holds for all $i \in \{0, 1, \ldots, N_\mathrm{a}\}$. Evaluating this result at various i, note that

$$\left(\frac{\delta \mathbf{x}^\intercal}{\delta \mathbf{x}} - \mathbf{I}\right)^0 = \left(\begin{cases} \dfrac{\mathrm{d}\mathbf{x}_j^\intercal}{\mathrm{d}\mathbf{x}_a} & \text{if } j = a \\ \mathbf{0} & \text{otherwise} \end{cases}\right) = \left(\begin{cases} \mathbf{I} & \text{if } j = a \\ \mathbf{0} & \text{otherwise} \end{cases}\right)$$

is a block matrix of zeros except in its block main diagonal which coincides with the block main diagonal of Eq. (D15). Similarly,

$$\left(\frac{\delta \mathbf{x}^\intercal}{\delta \mathbf{x}} - \mathbf{I}\right)^1 = \left(\begin{cases} \dfrac{\mathrm{d}\mathbf{x}_{a+1}^\intercal}{\mathrm{d}\mathbf{x}_a} & \text{if } j = a + 1 \\ \mathbf{0} & \text{otherwise} \end{cases}\right)$$

is a block matrix of zeros except in its first block super diagonal which coincides with the first block super diagonal of Eq. (D15). Indeed,

$$\left(\frac{\delta \mathbf{x}^\intercal}{\delta \mathbf{x}} - \mathbf{I}\right)^i = \left(\begin{cases} \dfrac{\mathrm{d}\mathbf{x}_{a+i}^\intercal}{\mathrm{d}\mathbf{x}_a} & \text{if } j = a + i \\ \mathbf{0} & \text{otherwise} \end{cases}\right)$$

is a block matrix of zeros except in its i-th block super diagonal which coincides with the i-th block super diagonal of Eq. (D15) for all $i \in \{1, \ldots, N_\mathrm{a} - 1\}$. Therefore, since any non-zero entry of the matrix $(\delta \mathbf{x}^\intercal / \delta \mathbf{x} - \mathbf{I})^i$ corresponds to a zero entry for the matrix $(\delta \mathbf{x}^\intercal / \delta \mathbf{x} - \mathbf{I})^j$ for any $i \neq j$ with $i, j \in \{0, \ldots, N_\mathrm{a} - 1\}$, it follows that

$$\frac{\mathrm{d}\mathbf{x}^\intercal}{\mathrm{d}\mathbf{x}} = \sum_{i=0}^{N_\mathrm{a}-1} \left(\frac{\delta \mathbf{x}^\intercal}{\delta \mathbf{x}} - \mathbf{I}\right)^i. \tag{D18}$$

From the geometric series of matrices we have that

$$\begin{aligned} \sum_{i=0}^{N_\mathrm{a}-1} \left(\frac{\delta \mathbf{x}^\intercal}{\delta \mathbf{x}} - \mathbf{I}\right)^i &= \left[\mathbf{I} - \left(\frac{\delta \mathbf{x}^\intercal}{\delta \mathbf{x}} - \mathbf{I}\right)\right]^{-1} \left[\mathbf{I} - \left(\frac{\delta \mathbf{x}^\intercal}{\delta \mathbf{x}} - \mathbf{I}\right)^{N_\mathrm{a}}\right] \\ &= \left(2\mathbf{I} - \frac{\delta \mathbf{x}^\intercal}{\delta \mathbf{x}}\right)^{-1}. \end{aligned} \tag{D19}$$

The last equality follows because $\delta \mathbf{x}^\intercal / \delta \mathbf{x} - \mathbf{I}$ is strictly block triangular with block dimension N_a and so $\delta \mathbf{x}^\intercal / \delta \mathbf{x} - \mathbf{I}$ is nilpotent with index smaller than or equal to N_a, which implies that $(\delta \mathbf{x}^\intercal / \delta \mathbf{x} - \mathbf{I})^{N_\mathrm{a}} = \mathbf{0}$. From Eq. (D11), the matrix $2\mathbf{I} - \delta \mathbf{x}^\intercal / \delta \mathbf{x}$ is block upper triangular with only identity matrices in its block main diagonal, so all the eigenvalues of $2\mathbf{I} - \delta \mathbf{x}^\intercal / \delta \mathbf{x}$ equal one and the matrix is invertible; thus, the inverse matrix in Eq. (D19) exists. Finally, using Eq. (D19) in (D18) yields Layer 4, Eq. 1, which is a compact expression for the matrix of total effects of a mutant's phenotype on her phenotype in terms of partial derivatives only, once Layer 3, Eq. 3 is used.

Appendix D.3. Conclusion

Appendix D.3.1. Form 1

Using Eqs. (D7) and (Layer 3, Eq. 1) for $\boldsymbol{\zeta} = \mathbf{x}$, we have that the total selection gradient of the phenotype is

$$\left.\frac{\mathrm{d}w}{\mathrm{d}\mathbf{x}}\right|_{\mathbf{y}=\bar{\mathbf{y}}} = \left.\left[\frac{\mathrm{d}\mathbf{x}^\intercal}{\mathrm{d}\mathbf{x}} \left(\frac{\partial w}{\partial \mathbf{x}} + \frac{\partial \boldsymbol{\epsilon}^\intercal}{\partial \mathbf{x}} \frac{\partial w}{\partial \boldsymbol{\epsilon}}\right)\right]\right|_{\mathbf{y}=\bar{\mathbf{y}}}.$$

Thus, using Layer 4, Eq. 10 yields the first line of Layer 4, Eq. 21.

Appendix D.3.2. Form 2

Using Eq. (D7), the total selection gradient of the phenotype is given by the second line of Layer 4, Eq. 21.

Appendix D.3.3. Form 3

Using Eqs. (D7), Layer 3, Eq. 1 for $\boldsymbol{\zeta} = \mathbf{z}$, and Layer 4, Eq. 7, we have that the total selection gradient of the phenotype is given by the third line of Layer 4, Eq. 21, where the *semi-total selection gradient of the geno-phenotype* is

$$\left.\frac{\delta w}{\delta \mathbf{z}}\right|_{\mathbf{y}=\bar{\mathbf{y}}} \equiv \left.\begin{pmatrix} \dfrac{\delta w}{\delta \mathbf{x}} \\ \dfrac{\delta w}{\delta \mathbf{y}} \end{pmatrix}\right|_{\mathbf{y}=\bar{\mathbf{y}}} \in \mathbb{R}^{N_\mathrm{a}(N_\mathrm{s}+N_\mathrm{c})\times 1}. \tag{D20}$$

Appendix D.3.4. Form 4

Finally, using the first line of Layer 4, Eq. 21 and Layer 4, Eq. 14, we obtain the fourth line of Layer 4, Eq. 21.

Appendix E. Total selection gradient of gene expression

Appendix E.1. Total selection gradient of gene expression in terms of direct fitness effects

Here we derive the total selection gradient of gene expression following an analogous procedure to the one used in Appendix D for the total selection gradient of the phenotype. Gene expression of the i-th gene product at age a is y_{ia}, so letting ζ in Eq. (26) be y_{ia}, we have

$$\left.\frac{\mathrm{d}\lambda}{\mathrm{d}y_{ia}}\right|_{\mathbf{y}=\bar{\mathbf{y}}} = \left.\frac{\mathrm{d}w}{\mathrm{d}y_{ia}}\right|_{\mathbf{y}=\bar{\mathbf{y}}} = \sum_{j=1}^{N_\mathrm{a}} \left.\frac{\mathrm{d}w_j}{\mathrm{d}y_{ia}}\right|_{\mathbf{y}=\bar{\mathbf{y}}}. \tag{E1}$$

The total derivatives of a mutant's relative fitness at age j in Eq. (E1) are with respect to the individual's gene expression at possibly another age a. We now seek to express such selection gradient entry in terms of partial derivatives only.

From Eq. (23), we have $w_j(\mathbf{z}_j, \mathbf{h}_j(\mathbf{z}_j, \bar{\mathbf{z}}, \tau), \bar{\mathbf{m}})$ with $\mathbf{z}_j = (\mathbf{x}_j; \mathbf{y}_j)$, so applying the chain rule, we obtain

$$\begin{aligned} \left.\frac{\mathrm{d}w_j}{\mathrm{d}y_{ia}}\right|_{\mathbf{y}=\bar{\mathbf{y}}} = \Bigg(&\sum_{k=1}^{N_\mathrm{s}} \frac{\partial w_j}{\partial x_{kj}} \frac{\mathrm{d}x_{kj}}{\mathrm{d}y_{ia}} + \sum_{k=1}^{N_\mathrm{c}} \frac{\partial w_j}{\partial y_{kj}} \frac{\mathrm{d}y_{kj}}{\mathrm{d}y_{ia}} \\ &+ \sum_{k=1}^{N_\mathrm{s}} \sum_{r=1}^{N_\mathrm{c}} \frac{\partial w_j}{\partial \epsilon_{rj}} \frac{\partial \epsilon_{rj}}{\partial x_{kj}} \frac{\mathrm{d}x_{kj}}{\mathrm{d}y_{ia}} \end{aligned}$$

$$+\sum_{k=1}^{N_c}\sum_{r=1}^{N_e}\frac{\partial w_j}{\partial \epsilon_{rj}}\frac{\partial \epsilon_{rj}}{\partial y_{kj}}\frac{\mathrm{d}y_{kj}}{\mathrm{d}y_{ia}}\Bigg)\Bigg|_{\mathbf{y}=\bar{\mathbf{y}}}.$$

Applying matrix calculus notation (Appendix N), this is

$$\frac{\mathrm{d}w_j}{\mathrm{d}y_{ia}}\Bigg|_{\mathbf{y}=\bar{\mathbf{y}}}=\Bigg(\frac{\mathrm{d}\mathbf{x}_j^\intercal}{\mathrm{d}y_{ia}}\frac{\partial w_j}{\partial \mathbf{x}_j}+\frac{\mathrm{d}\mathbf{y}_j^\intercal}{\mathrm{d}y_{ia}}\frac{\partial w_j}{\partial \mathbf{y}_j}+\sum_{k=1}^{N_s}\frac{\partial \boldsymbol{\epsilon}_j^\intercal}{\partial x_{kj}}\frac{\partial w_j}{\partial \boldsymbol{\epsilon}_j}\frac{\mathrm{d}x_{kj}}{\mathrm{d}y_{ia}}$$
$$+\sum_{k=1}^{N_c}\frac{\partial \boldsymbol{\epsilon}_j^\intercal}{\partial y_{kj}}\frac{\partial w_j}{\partial \boldsymbol{\epsilon}_j}\frac{\mathrm{d}y_{kj}}{\mathrm{d}y_{ia}}\Bigg)\Bigg|_{\mathbf{y}=\bar{\mathbf{y}}}.$$

Applying matrix calculus notation again yields

$$\frac{\mathrm{d}w_j}{\mathrm{d}y_{ia}}\Bigg|_{\mathbf{y}=\bar{\mathbf{y}}}=\Bigg(\frac{\mathrm{d}\mathbf{x}_j^\intercal}{\mathrm{d}y_{ia}}\frac{\partial w_j}{\partial \mathbf{x}_j}+\frac{\mathrm{d}\mathbf{y}_j^\intercal}{\mathrm{d}y_{ia}}\frac{\partial w_j}{\partial \mathbf{y}_j}+\frac{\mathrm{d}\mathbf{x}_j^\intercal}{\mathrm{d}y_{ia}}\frac{\partial \boldsymbol{\epsilon}_j^\intercal}{\partial \mathbf{x}_j}\frac{\partial w_j}{\partial \boldsymbol{\epsilon}_j}$$
$$+\frac{\mathrm{d}\mathbf{y}_j^\intercal}{\mathrm{d}y_{ia}}\frac{\partial \boldsymbol{\epsilon}_j^\intercal}{\partial \mathbf{y}_j}\frac{\partial w_j}{\partial \boldsymbol{\epsilon}_j}\Bigg)\Bigg|_{\mathbf{y}=\bar{\mathbf{y}}}.$$

Factorizing, we have

$$\frac{\mathrm{d}w_j}{\mathrm{d}y_{ia}}\Bigg|_{\mathbf{y}=\bar{\mathbf{y}}}=\Bigg[\frac{\mathrm{d}\mathbf{x}_j^\intercal}{\mathrm{d}y_{ia}}\left(\frac{\partial w_j}{\partial \mathbf{x}_j}+\frac{\partial \boldsymbol{\epsilon}_j^\intercal}{\partial \mathbf{x}_j}\frac{\partial w_j}{\partial \boldsymbol{\epsilon}_j}\right)$$
$$+\frac{\mathrm{d}\mathbf{y}_j^\intercal}{\mathrm{d}y_{ia}}\left(\frac{\partial w_j}{\partial \mathbf{y}_j}+\frac{\partial \boldsymbol{\epsilon}_j^\intercal}{\partial \mathbf{y}_j}\frac{\partial w_j}{\partial \boldsymbol{\epsilon}_j}\right)\Bigg]\Bigg|_{\mathbf{y}=\bar{\mathbf{y}}}. \tag{E2}$$

We now write Eq. (E2) in terms of partial derivatives of lifetime fitness. Consider the *direct selection gradient of gene expression at age j* or, equivalently, the column vector of *direct effects of a mutant's gene expression at age j on fitness*

$$\frac{\partial w}{\partial \mathbf{y}_j}\Bigg|_{\mathbf{y}=\bar{\mathbf{y}}}\equiv\left(\frac{\partial w}{\partial y_{1j}},\dots,\frac{\partial w}{\partial y_{N_c j}}\right)^\intercal\Bigg|_{\mathbf{y}=\bar{\mathbf{y}}}\in\mathbb{R}^{N_c\times 1},$$

and the matrix of *direct effects of a mutant's gene expression at age j on her environment at age j*

$$\frac{\partial \boldsymbol{\epsilon}_j^\intercal}{\partial \mathbf{y}_j}\Bigg|_{\mathbf{y}=\bar{\mathbf{y}}}\equiv\begin{pmatrix}\frac{\partial \epsilon_{1j}}{\partial y_{1j}} & \cdots & \frac{\partial \epsilon_{N_e j}}{\partial y_{1j}}\\ \vdots & \ddots & \vdots\\ \frac{\partial \epsilon_{1j}}{\partial y_{N_c j}} & \cdots & \frac{\partial \epsilon_{N_e j}^\intercal}{\partial y_{N_c j}}\end{pmatrix}\Bigg|_{\mathbf{y}=\bar{\mathbf{y}}}\in\mathbb{R}^{N_c\times N_e}.$$

Using Eqs. (D3) and (D5) in Eq. (E2) yields

$$\frac{\mathrm{d}w_j}{\mathrm{d}y_{ia}}\Bigg|_{\mathbf{y}=\bar{\mathbf{y}}}=\Bigg[\frac{\mathrm{d}\mathbf{x}_j^\intercal}{\mathrm{d}y_{ia}}\left(\frac{\partial w}{\partial \mathbf{x}_j}+\frac{\partial \boldsymbol{\epsilon}_j^\intercal}{\partial \mathbf{x}_j}\frac{\partial w}{\partial \boldsymbol{\epsilon}_j}\right)$$
$$+\frac{\mathrm{d}\mathbf{y}_j^\intercal}{\mathrm{d}y_{ia}}\left(\frac{\partial w}{\partial \mathbf{y}_j}+\frac{\partial \boldsymbol{\epsilon}_j^\intercal}{\partial \mathbf{y}_j}\frac{\partial w}{\partial \boldsymbol{\epsilon}_j}\right)\Bigg]\Bigg|_{\mathbf{y}=\bar{\mathbf{y}}}$$
$$=\left(\frac{\mathrm{d}\mathbf{x}_j^\intercal}{\mathrm{d}y_{ia}}\frac{\delta w}{\delta \mathbf{x}_j}+\frac{\mathrm{d}\mathbf{y}_j^\intercal}{\mathrm{d}y_{ia}}\frac{\delta w}{\delta \mathbf{y}_j}\right)\Bigg|_{\mathbf{y}=\bar{\mathbf{y}}}, \tag{E3}$$

where we use the *semi-total selection gradient of gene expression at age j* or, equivalently, the *semi-total effects of a mutant's gene expression at age j on fitness*

$$\frac{\delta w}{\delta \mathbf{y}_j}\Bigg|_{\mathbf{y}=\bar{\mathbf{y}}}=\left(\frac{\partial w}{\partial \mathbf{y}_j}+\frac{\partial \boldsymbol{\epsilon}_j^\intercal}{\partial \mathbf{y}_j}\frac{\partial w}{\partial \boldsymbol{\epsilon}_j}\right)\Bigg|_{\mathbf{y}=\bar{\mathbf{y}}}\in\mathbb{R}^{N_c\times 1}. \tag{E4}$$

Consider now the semi-total selection gradient of gene expression for all ages. The *semi-total selection gradient of gene expression* or, equivalently, the block column vector of *semi-total effects of a mutant's gene expression on fitness* is

$$\frac{\delta w}{\delta \mathbf{y}}\Bigg|_{\mathbf{y}=\bar{\mathbf{y}}}\equiv\left(\frac{\delta w}{\delta \mathbf{y}_1};\cdots;\frac{\delta w}{\delta \mathbf{y}_{N_a}}\right)\Bigg|_{\mathbf{y}=\bar{\mathbf{y}}}\in\mathbb{R}^{N_a N_c\times 1}.$$

Using Layer 2, Eq. 4d, we have that

$$\frac{\partial \boldsymbol{\epsilon}^\intercal}{\partial \mathbf{y}}\frac{\partial w}{\partial \boldsymbol{\epsilon}}=\left(\sum_{k=1}^{N_a}\frac{\partial \boldsymbol{\epsilon}_k^\intercal}{\partial \mathbf{y}_j}\frac{\partial w}{\partial \boldsymbol{\epsilon}_k}\right)=\left(\frac{\partial \boldsymbol{\epsilon}_j^\intercal}{\partial \mathbf{y}_j}\frac{\partial w}{\partial \boldsymbol{\epsilon}_j}\right) \tag{E5}$$

is a block column vector whose j-th entry is the rightmost term in Eq. (E4). Thus, from (E4), Layer 2, Eq. 2, and (E5), it follows that the semi-total selection gradient of gene expression satisfies Layer 3, Eq. 1.

Now, we write the total selection gradient of y_{ia} in terms of the semi-total selection gradient of gene expression. Substituting Eq. (E3) in Eq. (E1) yields

$$\frac{\mathrm{d}w}{\mathrm{d}y_{ia}}\Bigg|_{\mathbf{y}=\bar{\mathbf{y}}}=\sum_{j=1}^{N_a}\left(\frac{\mathrm{d}\mathbf{x}_j^\intercal}{\mathrm{d}y_{ia}}\frac{\delta w}{\delta \mathbf{x}_j}+\frac{\mathrm{d}\mathbf{y}_j^\intercal}{\mathrm{d}y_{ia}}\frac{\delta w}{\delta \mathbf{y}_j}\right)\Bigg|_{\mathbf{y}=\bar{\mathbf{y}}}$$
$$=\left(\frac{\mathrm{d}\mathbf{x}^\intercal}{\mathrm{d}y_{ia}}\frac{\delta w}{\delta \mathbf{x}}+\frac{\mathrm{d}\mathbf{y}^\intercal}{\mathrm{d}y_{ia}}\frac{\delta w}{\delta \mathbf{y}}\right)\Bigg|_{\mathbf{y}=\bar{\mathbf{y}}},$$

where we use the block row vectors

$$\frac{\mathrm{d}\mathbf{x}^\intercal}{\mathrm{d}y_{ia}}\equiv\left(\frac{\mathrm{d}\mathbf{x}_1^\intercal}{\mathrm{d}y_{ia}},\dots,\frac{\mathrm{d}\mathbf{x}_{N_a}^\intercal}{\mathrm{d}y_{ia}}\right)\in\mathbb{R}^{1\times N_a N_s}$$
$$\frac{\mathrm{d}\mathbf{y}^\intercal}{\mathrm{d}y_{ia}}\equiv\left(\frac{\mathrm{d}\mathbf{y}_1^\intercal}{\mathrm{d}y_{ia}},\dots,\frac{\mathrm{d}\mathbf{y}_{N_a}^\intercal}{\mathrm{d}y_{ia}}\right)\in\mathbb{R}^{1\times N_a N_c}.$$

Therefore, the total selection gradient of gene expression for all gene products across all ages is

$$\frac{\mathrm{d}w}{\mathrm{d}\mathbf{y}}\Bigg|_{\mathbf{y}=\bar{\mathbf{y}}}=\left(\frac{\mathrm{d}\mathbf{x}^\intercal}{\mathrm{d}\mathbf{y}}\frac{\delta w}{\delta \mathbf{x}}+\frac{\mathrm{d}\mathbf{y}^\intercal}{\mathrm{d}\mathbf{y}}\frac{\delta w}{\delta \mathbf{y}}\right)\Bigg|_{\mathbf{y}=\bar{\mathbf{y}}}\in\mathbb{R}^{N_a N_s\times 1}, \tag{E6}$$

where we use the block matrix of *total effects of a mutant's gene expression on her phenotype*

$$\frac{\mathrm{d}\mathbf{x}^\intercal}{\mathrm{d}\mathbf{y}}\Bigg|_{\mathbf{y}=\bar{\mathbf{y}}}\equiv\begin{pmatrix}\frac{\mathrm{d}\mathbf{x}_1^\intercal}{\mathrm{d}\mathbf{y}_1} & \cdots & \frac{\mathrm{d}\mathbf{x}_{N_a}^\intercal}{\partial \mathbf{y}_1}\\ \vdots & \ddots & \vdots\\ \frac{\mathrm{d}\mathbf{x}_1^\intercal}{\mathrm{d}\mathbf{y}_{N_a}} & \cdots & \frac{\mathrm{d}\mathbf{x}_{N_a}^\intercal}{\mathrm{d}\mathbf{y}_{N_a}}\end{pmatrix}\Bigg|_{\mathbf{y}=\bar{\mathbf{y}}}\in\mathbb{R}^{N_a N_c\times N_a N_s},$$

and the block matrix of *total effects of a mutant's gene expression on her gene expression*

$$\frac{\mathrm{d}\mathbf{y}^\intercal}{\mathrm{d}\mathbf{y}}\Bigg|_{\mathbf{y}=\bar{\mathbf{y}}}\equiv\begin{pmatrix}\frac{\mathrm{d}\mathbf{y}_1^\intercal}{\mathrm{d}\mathbf{y}_1} & \cdots & \frac{\mathrm{d}\mathbf{y}_{N_a}^\intercal}{\partial \mathbf{y}_1}\\ \vdots & \ddots & \vdots\\ \frac{\mathrm{d}\mathbf{y}_1^\intercal}{\mathrm{d}\mathbf{y}_{N_a}} & \cdots & \frac{\mathrm{d}\mathbf{y}_{N_a}^\intercal}{\mathrm{d}\mathbf{y}_{N_a}}\end{pmatrix}\Bigg|_{\mathbf{y}=\bar{\mathbf{y}}}\in\mathbb{R}^{N_a N_c\times N_a N_c}.$$

Expression (E6) is now in terms of partial derivatives of fitness, partial derivatives of the environment, total effects of a mutant's gene expression on her phenotype, $\mathrm{d}\mathbf{x}^\intercal/\mathrm{d}\mathbf{y}$, and total effects of a mutant's gene expression on her gene expression, $\mathrm{d}\mathbf{y}^\intercal/\mathrm{d}\mathbf{y}$, once Layer 3, Eq. 1 is used. We now proceed to write $\mathrm{d}\mathbf{x}^\intercal/\mathrm{d}\mathbf{y}$ and $\mathrm{d}\mathbf{y}^\intercal/\mathrm{d}\mathbf{y}$ in terms of partial derivatives only.

Appendix E.2. Matrix of total effects of a mutant's gene expression on her phenotype and her gene expression

From the developmental constraint (1) for the k-th phenotype at age $j \in \{2,\dots,N_\mathrm{a}\}$ we have that $x_{kj} = g_{k,j-1}(\mathbf{z}_{j-1},\mathbf{h}_{j-1}(\mathbf{z}_{j-1},\bar{\mathbf{z}},\tau),\bar{\mathbf{z}})$, so using the chain rule we obtain

$$\left.\frac{\mathrm{d}x_{kj}}{\mathrm{d}y_{ia}}\right|_{\mathbf{y}=\bar{\mathbf{y}}} = \left(\sum_{l=1}^{N_\mathrm{s}} \frac{\partial g_{k,j-1}}{\partial x_{l,j-1}}\frac{\mathrm{d}x_{l,j-1}}{\mathrm{d}y_{ia}} + \sum_{l=1}^{N_\mathrm{c}} \frac{\partial g_{k,j-1}}{\partial y_{l,j-1}}\frac{\mathrm{d}y_{l,j-1}}{\mathrm{d}y_{ia}} + \sum_{l=1}^{N_\mathrm{s}}\sum_{r=1}^{N_\mathrm{e}} \frac{\partial g_{k,j-1}}{\partial \epsilon_{r,j-1}}\frac{\partial \epsilon_{r,j-1}}{\partial x_{l,j-1}}\frac{\mathrm{d}x_{l,j-1}}{\mathrm{d}y_{ia}} + \sum_{l=1}^{N_\mathrm{c}}\sum_{r=1}^{N_\mathrm{e}} \frac{\partial g_{k,j-1}}{\partial \epsilon_{r,j-1}}\frac{\partial \epsilon_{r,j-1}}{\partial y_{l,j-1}}\frac{\mathrm{d}y_{l,j-1}}{\mathrm{d}y_{ia}}\right)\Bigg|_{\mathbf{y}=\bar{\mathbf{y}}}.$$

Applying matrix calculus notation (Appendix N), this is

$$\left.\frac{\mathrm{d}x_{kj}}{\mathrm{d}y_{ia}}\right|_{\mathbf{y}=\bar{\mathbf{y}}} = \left(\frac{\mathrm{d}\mathbf{x}_{j-1}^\intercal}{\mathrm{d}y_{ia}}\frac{\partial g_{k,j-1}}{\partial \mathbf{x}_{j-1}} + \frac{\mathrm{d}\mathbf{y}_{j-1}^\intercal}{\mathrm{d}y_{ia}}\frac{\partial g_{k,j-1}}{\partial \mathbf{y}_{j-1}} + \sum_{l=1}^{N_\mathrm{s}} \frac{\partial \boldsymbol{\epsilon}_{j-1}^\intercal}{\partial x_{l,j-1}}\frac{\partial g_{k,j-1}}{\partial \boldsymbol{\epsilon}_{j-1}}\frac{\mathrm{d}x_{l,j-1}}{\mathrm{d}y_{ia}} + \sum_{l=1}^{N_\mathrm{c}} \frac{\partial \boldsymbol{\epsilon}_{j-1}^\intercal}{\partial y_{l,j-1}}\frac{\partial g_{k,j-1}}{\partial \boldsymbol{\epsilon}_{j-1}}\frac{\mathrm{d}y_{l,j-1}}{\mathrm{d}y_{ia}}\right)\Bigg|_{\mathbf{y}=\bar{\mathbf{y}}}.$$

Applying matrix calculus notation again yields

$$\left.\frac{\mathrm{d}x_{kj}}{\mathrm{d}y_{ia}}\right|_{\mathbf{y}=\bar{\mathbf{y}}} = \left(\frac{\mathrm{d}\mathbf{x}_{j-1}^\intercal}{\mathrm{d}y_{ia}}\frac{\partial g_{k,j-1}}{\partial \mathbf{x}_{j-1}} + \frac{\mathrm{d}\mathbf{y}_{j-1}^\intercal}{\mathrm{d}y_{ia}}\frac{\partial g_{k,j-1}}{\partial \mathbf{y}_{j-1}} + \frac{\mathrm{d}\mathbf{x}_{j-1}^\intercal}{\mathrm{d}y_{ia}}\frac{\partial \boldsymbol{\epsilon}_{j-1}^\intercal}{\partial \mathbf{x}_{j-1}}\frac{\partial g_{k,j-1}}{\partial \boldsymbol{\epsilon}_{j-1}} + \frac{\mathrm{d}\mathbf{y}_{j-1}^\intercal}{\mathrm{d}y_{ia}}\frac{\partial \boldsymbol{\epsilon}_{j-1}^\intercal}{\partial \mathbf{y}_{j-1}}\frac{\partial g_{k,j-1}}{\partial \boldsymbol{\epsilon}_{j-1}}\right)\Bigg|_{\mathbf{y}=\bar{\mathbf{y}}}.$$

Factorizing, we have

$$\left.\frac{\mathrm{d}x_{kj}}{\mathrm{d}y_{ia}}\right|_{\mathbf{y}=\bar{\mathbf{y}}} = \left[\frac{\mathrm{d}\mathbf{x}_{j-1}^\intercal}{\mathrm{d}y_{ia}}\left(\frac{\partial g_{k,j-1}}{\partial \mathbf{x}_{j-1}} + \frac{\partial \boldsymbol{\epsilon}_{j-1}^\intercal}{\partial \mathbf{x}_{j-1}}\frac{\partial g_{k,j-1}}{\partial \boldsymbol{\epsilon}_{j-1}}\right) + \frac{\mathrm{d}\mathbf{y}_{j-1}^\intercal}{\mathrm{d}y_{ia}}\left(\frac{\partial g_{k,j-1}}{\partial \mathbf{y}_{j-1}} + \frac{\partial \boldsymbol{\epsilon}_{j-1}^\intercal}{\partial \mathbf{y}_{j-1}}\frac{\partial g_{k,j-1}}{\partial \boldsymbol{\epsilon}_{j-1}}\right)\right]\Bigg|_{\mathbf{y}=\bar{\mathbf{y}}}.$$

Rewriting $g_{k,j-1}$ as x_{kj} yields

$$\left.\frac{\mathrm{d}x_{kj}}{\mathrm{d}y_{ia}}\right|_{\mathbf{y}=\bar{\mathbf{y}}} = \left[\frac{\mathrm{d}\mathbf{x}_{j-1}^\intercal}{\mathrm{d}y_{ia}}\left(\frac{\partial x_{kj}}{\partial \mathbf{x}_{j-1}} + \frac{\partial \boldsymbol{\epsilon}_{j-1}^\intercal}{\partial \mathbf{x}_{j-1}}\frac{\partial x_{kj}}{\partial \boldsymbol{\epsilon}_{j-1}}\right) + \frac{\mathrm{d}\mathbf{y}_{j-1}^\intercal}{\mathrm{d}y_{ia}}\left(\frac{\partial x_{kj}}{\partial \mathbf{y}_{j-1}} + \frac{\partial \boldsymbol{\epsilon}_{j-1}^\intercal}{\partial \mathbf{y}_{j-1}}\frac{\partial x_{kj}}{\partial \boldsymbol{\epsilon}_{j-1}}\right)\right]\Bigg|_{\mathbf{y}=\bar{\mathbf{y}}}.$$

Hence,

$$\left.\frac{\mathrm{d}\mathbf{x}_j^\intercal}{\mathrm{d}y_{ia}}\right|_{\mathbf{y}=\bar{\mathbf{y}}} = \left[\frac{\mathrm{d}\mathbf{x}_{j-1}^\intercal}{\mathrm{d}y_{ia}}\left(\frac{\partial \mathbf{x}_j^\intercal}{\partial \mathbf{x}_{j-1}} + \frac{\partial \boldsymbol{\epsilon}_{j-1}^\intercal}{\partial \mathbf{x}_{j-1}}\frac{\partial \mathbf{x}_j^\intercal}{\partial \boldsymbol{\epsilon}_{j-1}}\right) + \frac{\mathrm{d}\mathbf{y}_{j-1}^\intercal}{\mathrm{d}y_{ia}}\left(\frac{\partial \mathbf{x}_j^\intercal}{\partial \mathbf{y}_{j-1}} + \frac{\partial \boldsymbol{\epsilon}_{j-1}^\intercal}{\partial \mathbf{y}_{j-1}}\frac{\partial \mathbf{x}_j^\intercal}{\partial \boldsymbol{\epsilon}_{j-1}}\right)\right]\Bigg|_{\mathbf{y}=\bar{\mathbf{y}}}, \tag{E7}$$

where we use the matrix of *direct effects of a mutant's gene expression at age j on her phenotype at age $j+1$*

$$\left.\frac{\partial \mathbf{x}_{j+1}^\intercal}{\partial \mathbf{y}_j}\right|_{\mathbf{y}=\bar{\mathbf{y}}} \equiv \left.\begin{pmatrix} \frac{\partial x_{1,j+1}}{\partial y_{1j}} & \cdots & \frac{\partial x_{N_\mathrm{s},j+1}}{\partial y_{1j}} \\ \vdots & \ddots & \vdots \\ \frac{\partial x_{1,j+1}}{\partial y_{N_\mathrm{c}j}} & \cdots & \frac{\partial x_{N_\mathrm{s},j+1}}{\partial y_{N_\mathrm{c}j}} \end{pmatrix}\right|_{\mathbf{y}=\bar{\mathbf{y}}} \in \mathbb{R}^{N_\mathrm{c}\times N_\mathrm{s}}.$$

We can write Eq. (E7) more succinctly as

$$\left.\frac{\mathrm{d}\mathbf{x}_j^\intercal}{\mathrm{d}y_{ia}}\right|_{\mathbf{y}=\bar{\mathbf{y}}} = \left(\frac{\mathrm{d}\mathbf{x}_{j-1}^\intercal}{\mathrm{d}y_{ia}}\frac{\delta \mathbf{x}_j^\intercal}{\delta \mathbf{x}_{j-1}} + \frac{\mathrm{d}\mathbf{y}_{j-1}^\intercal}{\mathrm{d}y_{ia}}\frac{\delta \mathbf{x}_j^\intercal}{\delta \mathbf{y}_{j-1}}\right)\Bigg|_{\mathbf{y}=\bar{\mathbf{y}}}, \tag{E8}$$

where we use the matrix of *semi-total effects of a mutant's gene expression at age j on her phenotype at age $j+1$*

$$\left.\frac{\delta \mathbf{x}_{j+1}^\intercal}{\delta \mathbf{y}_j}\right|_{\mathbf{y}=\bar{\mathbf{y}}} = \left(\frac{\partial \mathbf{x}_{j+1}^\intercal}{\partial \mathbf{y}_j} + \frac{\partial \boldsymbol{\epsilon}_j^\intercal}{\partial \mathbf{y}_j}\frac{\partial \mathbf{x}_{j+1}^\intercal}{\partial \boldsymbol{\epsilon}_j}\right)\Bigg|_{\mathbf{y}=\bar{\mathbf{y}}} \in \mathbb{R}^{N_\mathrm{c}\times N_\mathrm{s}}. \tag{E9}$$

We also define the corresponding matrix across all ages. Specifically, the block matrix of *semi-total effects of a mutant's gene expression on her phenotype* is

$$\begin{aligned}\left.\frac{\delta \mathbf{x}^\intercal}{\delta \mathbf{y}}\right|_{\mathbf{y}=\bar{\mathbf{y}}} &\equiv \left.\begin{pmatrix} \frac{\delta \mathbf{x}_1^\intercal}{\delta \mathbf{y}_1} & \cdots & \frac{\delta \mathbf{x}_{N_\mathrm{a}}^\intercal}{\delta \mathbf{y}_1} \\ \vdots & \ddots & \vdots \\ \frac{\delta \mathbf{x}_1^\intercal}{\delta \mathbf{y}_{N_\mathrm{a}}} & \cdots & \frac{\delta \mathbf{x}_{N_\mathrm{a}}^\intercal}{\delta \mathbf{y}_{N_\mathrm{a}}} \end{pmatrix}\right|_{\mathbf{y}=\bar{\mathbf{y}}} \\ &= \left.\begin{pmatrix} \mathbf{0} & \frac{\delta \mathbf{x}_2^\intercal}{\delta \mathbf{y}_1} & \cdots & \mathbf{0} & \mathbf{0} \\ \mathbf{0} & \mathbf{0} & \cdots & \mathbf{0} & \mathbf{0} \\ \vdots & \vdots & \ddots & \vdots & \vdots \\ \mathbf{0} & \mathbf{0} & \cdots & \mathbf{0} & \frac{\delta \mathbf{x}_{N_\mathrm{a}}^\intercal}{\delta \mathbf{y}_{N_\mathrm{a}-1}} \\ \mathbf{0} & \mathbf{0} & \cdots & \mathbf{0} & \mathbf{0} \end{pmatrix}\right|_{\mathbf{y}=\bar{\mathbf{y}}} \\ &\in \mathbb{R}^{N_\mathrm{a}N_\mathrm{c}\times N_\mathrm{a}N_\mathrm{s}}.\end{aligned} \tag{E10}$$

The equality (E10) follows because the semi-total effects of a mutant's gene expression on her phenotype are only non-zero at the next age (from the developmental constraint in Eq. 1). Using Layer 2, Eq. 4d and Layer 2, Eq. 4c, we have that

$$\frac{\partial \boldsymbol{\epsilon}^\intercal}{\partial \mathbf{y}}\frac{\partial \mathbf{x}^\intercal}{\partial \boldsymbol{\epsilon}} = \left(\sum_{k=1}^{N_\mathrm{a}} \frac{\partial \boldsymbol{\epsilon}_k^\intercal}{\partial \mathbf{y}_a}\frac{\partial \mathbf{x}_j^\intercal}{\partial \boldsymbol{\epsilon}_k}\right) = \left(\begin{cases} \frac{\partial \boldsymbol{\epsilon}_a^\intercal}{\partial \mathbf{y}_a}\frac{\partial \mathbf{x}_j^\intercal}{\partial \boldsymbol{\epsilon}_a} & \text{for } j = a+1 \\ \mathbf{0} & \text{for } j \neq a+1 \end{cases}\right), \tag{E11}$$

which equals the rightmost term in Eq. (E9) for $j = a+1$. Thus, from Eqs. (E9)–(E11), it follows that the block matrix of semi-total effects of a mutant's gene expression on her phenotype satisfies Layer 3, Eq. 3.

Eq. (E8) gives the matrix of total effects of a mutant's gene expression of the i-th gene product at age a on her phenotype at age j. Then, it follows that the matrix of total effects of a mutant's gene expression for all gene products at age a on her phenotype at age j is

$$\left.\frac{\mathrm{d}\mathbf{x}_j^\intercal}{\mathrm{d}\mathbf{y}_a}\right|_{\mathbf{y}=\bar{\mathbf{y}}} = \left.\left(\frac{\mathrm{d}\mathbf{x}_{j-1}^\intercal}{\mathrm{d}\mathbf{y}_a}\frac{\delta\mathbf{x}_j^\intercal}{\delta\mathbf{x}_{j-1}} + \frac{\mathrm{d}\mathbf{y}_{j-1}^\intercal}{\mathrm{d}\mathbf{y}_a}\frac{\delta\mathbf{x}_j^\intercal}{\delta\mathbf{y}_{j-1}}\right)\right|_{\mathbf{y}=\bar{\mathbf{y}}}. \tag{E12}$$

Eq. (E12) is a recurrence equation for $\mathrm{d}\mathbf{x}_j^\intercal/\mathrm{d}\mathbf{y}_a$ over age $j \in \{2,\dots,N_\mathrm{a}\}$. Since a given entry of the operator $\mathrm{d}/\mathrm{d}\mathbf{y}$ takes the total derivative with respect to a given y_{ia} while keeping all the other gene expression constant and gene expression is open-loop, a perturbation of an individual's gene expression of a given gene product at a given age does not affect the individual's gene expression of other gene products or other ages (i.e., $\mathrm{d}\mathbf{y}_a^\intercal/\mathrm{d}\mathbf{y}_a = \mathbf{I}$ and $\mathrm{d}\mathbf{y}_j^\intercal/\mathrm{d}\mathbf{y}_a = \mathbf{0}$ for $j \neq a$). Thus, the matrix of total effects of a mutant's gene expression on her gene expression is

$$\begin{aligned}\frac{\mathrm{d}\mathbf{y}^\intercal}{\mathrm{d}\mathbf{y}} &= \begin{pmatrix} \frac{\mathrm{d}\mathbf{y}_1^\intercal}{\mathrm{d}\mathbf{y}_1} & \cdots & \frac{\mathrm{d}\mathbf{y}_{N_\mathrm{a}}^\intercal}{\mathrm{d}\mathbf{y}_1} \\ \vdots & \ddots & \vdots \\ \frac{\mathrm{d}\mathbf{y}_1^\intercal}{\mathrm{d}\mathbf{y}_{N_\mathrm{a}}} & \cdots & \frac{\mathrm{d}\mathbf{y}_{N_\mathrm{a}}^\intercal}{\mathrm{d}\mathbf{y}_{N_\mathrm{a}}} \end{pmatrix} = \begin{pmatrix} \mathbf{I} & \mathbf{0} & \cdots & \mathbf{0} & \mathbf{0} \\ \mathbf{0} & \mathbf{I} & \cdots & \mathbf{0} & \mathbf{0} \\ \vdots & \vdots & \ddots & \vdots & \vdots \\ \mathbf{0} & \mathbf{0} & \cdots & \mathbf{I} & \mathbf{0} \\ \mathbf{0} & \mathbf{0} & \cdots & \mathbf{0} & \mathbf{I} \end{pmatrix} \\ &= \mathbf{I} \in \mathbb{R}^{N_\mathrm{a}N_\mathrm{c}\times N_\mathrm{a}N_\mathrm{c}}. \end{aligned} \tag{E13}$$

Moreover, because of the arrow of developmental time (due to the developmental constraint in Eq. 1), perturbations in an individual's late gene expression do not affect the individual's early phenotype (i.e., $\mathrm{d}\mathbf{x}_j^\intercal/\mathrm{d}\mathbf{y}_a = \mathbf{0}$ for $j < a$ and $j \in \{1,\dots,N_\mathrm{a}-1\}$)[2]. Additionally, from the arrow of developmental time (Eq. 1), a perturbation in an individual's gene expression at a given age does not affect any of the individual's phenotypes at the *same* age (i.e., $\mathrm{d}\mathbf{x}_j^\intercal/\mathrm{d}\mathbf{y}_a = \mathbf{0}$ for $j = a$). Consequently, Eq. (E12) for $j \in \{1,\dots,N_\mathrm{a}\}$ reduces to

$$\left.\frac{\mathrm{d}\mathbf{x}_j^\intercal}{\mathrm{d}\mathbf{y}_a}\right|_{\mathbf{y}=\bar{\mathbf{y}}} = \begin{cases} \left.\left(\frac{\mathrm{d}\mathbf{x}_{j-1}^\intercal}{\mathrm{d}\mathbf{y}_a}\frac{\delta\mathbf{x}_j^\intercal}{\delta\mathbf{x}_{j-1}} + \underbrace{\frac{\mathrm{d}\mathbf{y}_{j-1}^\intercal}{\mathrm{d}\mathbf{y}_a}}_{\mathbf{0},\text{ from (E13)}}\frac{\delta\mathbf{x}_j^\intercal}{\delta\mathbf{y}_{j-1}}\right)\right|_{\mathbf{y}=\bar{\mathbf{y}}} & \text{for } j-1 > a \\ \left.\left(\underbrace{\frac{\mathrm{d}\mathbf{x}_{j-1}^\intercal}{\mathrm{d}\mathbf{y}_a}}_{\mathbf{0},\text{ from (1)}}\frac{\delta\mathbf{x}_j^\intercal}{\delta\mathbf{x}_{j-1}} + \underbrace{\frac{\mathrm{d}\mathbf{y}_{j-1}^\intercal}{\mathrm{d}\mathbf{y}_a}}_{\mathbf{I},\text{ from (E13)}}\frac{\delta\mathbf{x}_j^\intercal}{\delta\mathbf{y}_{j-1}}\right)\right|_{\mathbf{y}=\bar{\mathbf{y}}} & \text{for } j-1 = a \\ \left.\left(\underbrace{\frac{\mathrm{d}\mathbf{x}_{j-1}^\intercal}{\mathrm{d}\mathbf{y}_a}}_{\mathbf{0},\text{ from (1)}}\frac{\delta\mathbf{x}_j^\intercal}{\delta\mathbf{x}_{j-1}} + \underbrace{\frac{\mathrm{d}\mathbf{y}_{j-1}^\intercal}{\mathrm{d}\mathbf{y}_a}}_{\mathbf{0},\text{ from (E13)}}\frac{\delta\mathbf{x}_j^\intercal}{\delta\mathbf{y}_{j-1}}\right)\right|_{\mathbf{y}=\bar{\mathbf{y}}} & \text{for } j-1 < a. \end{cases}$$

That is,

$$\left.\frac{\mathrm{d}\mathbf{x}_j^\intercal}{\mathrm{d}\mathbf{y}_a}\right|_{\mathbf{y}=\bar{\mathbf{y}}} = \begin{cases} \left.\left(\frac{\mathrm{d}\mathbf{x}_{j-1}^\intercal}{\mathrm{d}\mathbf{y}_a}\frac{\delta\mathbf{x}_j^\intercal}{\delta\mathbf{x}_{j-1}}\right)\right|_{\mathbf{y}=\bar{\mathbf{y}}} & \text{for } j-1 > a \\ \left.\frac{\delta\mathbf{x}_j^\intercal}{\delta\mathbf{y}_{j-1}}\right|_{\mathbf{y}=\bar{\mathbf{y}}} & \text{for } j-1 = a \\ \mathbf{0} & \text{for } j-1 < a. \end{cases}$$

Expanding this recurrence yields

$$\left.\frac{\mathrm{d}\mathbf{x}_j^\intercal}{\mathrm{d}\mathbf{y}_a}\right|_{\mathbf{y}=\bar{\mathbf{y}}} = \begin{cases} \left.\left(\frac{\mathrm{d}\mathbf{x}_{a+1}^\intercal}{\mathrm{d}\mathbf{y}_a}\frac{\delta\mathbf{x}_{a+2}^\intercal}{\delta\mathbf{x}_{a+1}}\cdots\frac{\delta\mathbf{x}_j^\intercal}{\delta\mathbf{x}_{j-1}}\right)\right|_{\mathbf{y}=\bar{\mathbf{y}}} & \text{for } j-1 > a \\ \left.\frac{\delta\mathbf{x}_{a+1}^\intercal}{\delta\mathbf{y}_a}\right|_{\mathbf{y}=\bar{\mathbf{y}}} & \text{for } j-1 = a \\ \mathbf{0} & \text{for } j-1 < a. \end{cases} \tag{E14}$$

Evaluating Eq. (E14) at $j = a+1$ yields

$$\left.\frac{\mathrm{d}\mathbf{x}_{a+1}^\intercal}{\mathrm{d}\mathbf{y}_a}\right|_{\mathbf{y}=\bar{\mathbf{y}}} = \left.\frac{\delta\mathbf{x}_{a+1}^\intercal}{\delta\mathbf{y}_a}\right|_{\mathbf{y}=\bar{\mathbf{y}}},$$

which substituted back in the top line of Eq. (E14) yields

$$\left.\frac{\mathrm{d}\mathbf{x}_j^\intercal}{\mathrm{d}\mathbf{y}_a}\right|_{\mathbf{y}=\bar{\mathbf{y}}} = \begin{cases} \left.\left(\frac{\delta\mathbf{x}_{a+1}^\intercal}{\delta\mathbf{y}_a}\frac{\delta\mathbf{x}_{a+2}^\intercal}{\delta\mathbf{x}_{a+1}}\cdots\frac{\delta\mathbf{x}_j^\intercal}{\delta\mathbf{x}_{j-1}}\right)\right|_{\mathbf{y}=\bar{\mathbf{y}}} & \text{for } j-1 > a \\ \left.\frac{\delta\mathbf{x}_{a+1}^\intercal}{\delta\mathbf{y}_a}\right|_{\mathbf{y}=\bar{\mathbf{y}}} & \text{for } j-1 = a \\ \mathbf{0} & \text{for } j-1 < a. \end{cases} \tag{E15}$$

Hence, the block matrix of *total effects of a mutant's gene expression on her phenotype* is

$$\left.\frac{\mathrm{d}\mathbf{x}^\intercal}{\mathrm{d}\mathbf{y}}\right|_{\mathbf{y}=\bar{\mathbf{y}}} = \left.\begin{pmatrix} \frac{\mathrm{d}\mathbf{x}_1^\intercal}{\mathrm{d}\mathbf{y}_1} & \cdots & \frac{\mathrm{d}\mathbf{x}_{N_\mathrm{a}}^\intercal}{\mathrm{d}\mathbf{y}_1} \\ \vdots & \ddots & \vdots \\ \frac{\mathrm{d}\mathbf{x}_1^\intercal}{\mathrm{d}\mathbf{y}_{N_\mathrm{a}}} & \cdots & \frac{\mathrm{d}\mathbf{x}_{N_\mathrm{a}}^\intercal}{\mathrm{d}\mathbf{y}_{N_\mathrm{a}}} \end{pmatrix}\right|_{\mathbf{y}=\bar{\mathbf{y}}}$$

[2] Again, we take the derivative $\mathrm{d}\mathbf{x}_j^\intercal/\mathrm{d}y_{ia}$ as referring to the effect on $\mathbf{x}_j^\intercal$ of a perturbation of the initial condition $\mathbf{y}_a$ of the difference equation (1) applied at the ages $\{a,\dots,n\}$. Hence, if $j < a$, $\mathbf{x}_j^\intercal$ is unmodified by a change in the initial condition of (1) applied at the ages $\{a,\dots,n\}$.

$$
= \left.\begin{pmatrix} \mathbf{0} & \frac{\mathrm{d}\mathbf{x}_2^\intercal}{\mathrm{d}\mathbf{y}_1} & \cdots & \frac{\mathrm{d}\mathbf{x}_{N_\mathrm{a}-1}^\intercal}{\mathrm{d}\mathbf{y}_1} & \frac{\mathrm{d}\mathbf{x}_{N_\mathrm{a}}^\intercal}{\mathrm{d}\mathbf{y}_1} \\ \mathbf{0} & \mathbf{0} & \cdots & \frac{\mathrm{d}\mathbf{x}_{N_\mathrm{a}-1}^\intercal}{\mathrm{d}\mathbf{y}_2} & \frac{\mathrm{d}\mathbf{x}_{N_\mathrm{a}}^\intercal}{\mathrm{d}\mathbf{y}_2} \\ \vdots & \vdots & \ddots & \vdots & \vdots \\ \mathbf{0} & \mathbf{0} & \cdots & \mathbf{0} & \frac{\mathrm{d}\mathbf{x}_{N_\mathrm{a}}^\intercal}{\mathrm{d}\mathbf{y}_{N_\mathrm{a}-1}} \\ \mathbf{0} & \mathbf{0} & \cdots & \mathbf{0} & \mathbf{0} \end{pmatrix}\right|_{\mathbf{y}=\bar{\mathbf{y}}} \tag{E16}$$

$$\in \mathbb{R}^{N_\mathrm{a}N_\mathrm{c}\times N_\mathrm{a}N_\mathrm{s}},$$

whose aj-th entry is given by

$$
\begin{aligned}
\frac{\mathrm{d}\mathbf{x}_j^\intercal}{\mathrm{d}\mathbf{y}_a} &= \begin{cases} \frac{\delta\mathbf{x}_{a+1}^\intercal}{\delta\mathbf{y}_a}\frac{\mathrm{d}\mathbf{x}_j^\intercal}{\mathrm{d}\mathbf{x}_{a+1}} & \text{for } j > a \\ \mathbf{0} & \text{for } j \leq a \end{cases} \\
&= \begin{cases} \frac{\delta\mathbf{x}_{a+1}^\intercal}{\delta\mathbf{y}_a}\overset{\curvearrowright}{\prod_{k=a+1}^{j-1}}\frac{\delta\mathbf{x}_{k+1}^\intercal}{\delta\mathbf{x}_k} & \text{for } j > a \\ \mathbf{0} & \text{for } j \leq a \end{cases} \\
&= \begin{cases} \frac{\delta\mathbf{x}_{a+1}^\intercal}{\delta\mathbf{y}_a}\frac{\delta\mathbf{x}_{a+2}^\intercal}{\delta\mathbf{x}_{a+1}}\cdots\frac{\delta\mathbf{x}_j^\intercal}{\delta\mathbf{x}_{j-1}} & \text{for } j > a \\ \mathbf{0} & \text{for } j \leq a, \end{cases}
\end{aligned} \tag{E17}
$$

where we use Layer 4, Eq. 2 and adopt the empty-product convention that

$$\frac{\mathrm{d}\mathbf{x}_{a+1}^\intercal}{\mathrm{d}\mathbf{x}_{a+1}} = \overset{\curvearrowright}{\prod_{k=a+1}^{a}}\frac{\delta\mathbf{x}_{k+1}^\intercal}{\delta\mathbf{x}_k} = \mathbf{I}.$$

Eqs. (E16) and (E17) write the matrix of total effects of a mutant's gene expression on her phenotype in terms of partial derivatives, given Eq. (E9), as we sought.

We now obtain a more compact expression for the matrix of total effects of a mutant's gene expression on her phenotype in terms of partial derivatives. To do this, we note a relationship between the matrix of total effects of a mutant's gene expression on her phenotype with the matrix of total effects of a mutant's phenotype on her phenotype. Note that the aj-th entry of $(\delta\mathbf{x}^\intercal/\delta\mathbf{y})(\mathrm{d}\mathbf{x}^\intercal/\mathrm{d}\mathbf{x})$ is

$$
\begin{aligned}
\left(\frac{\delta\mathbf{x}^\intercal}{\delta\mathbf{y}}\frac{\mathrm{d}\mathbf{x}^\intercal}{\mathrm{d}\mathbf{x}}\right)_{aj} &= \sum_{k=1}^{N_\mathrm{a}}\frac{\delta\mathbf{x}_k^\intercal}{\delta\mathbf{y}_a}\frac{\mathrm{d}\mathbf{x}_j^\intercal}{\mathrm{d}\mathbf{x}_k} \\
&= \frac{\delta\mathbf{x}_{a+1}^\intercal}{\delta\mathbf{y}_a}\frac{\mathrm{d}\mathbf{x}_j^\intercal}{\mathrm{d}\mathbf{x}_{a+1}} \\
&= \frac{\mathrm{d}\mathbf{x}_j^\intercal}{\mathrm{d}\mathbf{y}_a},
\end{aligned}
$$

where we use Eq. (E10) in the second equality and Eq. (E17) in the third equality, noting that $\mathrm{d}\mathbf{x}_j^\intercal/\mathrm{d}\mathbf{x}_{a+1} = \mathbf{0}$ and $\mathrm{d}\mathbf{x}_j^\intercal/\mathrm{d}\mathbf{y}_a = \mathbf{0}$ for $j \leq a$. Hence, Layer 4, Eq. 3 follows, which is a compact expression for the matrix of total effects of a mutant's gene expression on her phenotype in terms of partial derivatives only, once Layer 4, Eq. 1 and Layer 3, Eq. 3 are used.

Appendix E.3. Conclusion

Appendix E.3.1. Form 1

Using Eqs. (E6), (E13), and Layer 3, Eq. 1 for $\boldsymbol{\zeta} \in \{\mathbf{x}, \mathbf{y}\}$, we have that the total selection gradient of gene expression is

$$\left.\frac{\mathrm{d}w}{\mathrm{d}\mathbf{y}}\right|_{\mathbf{y}=\bar{\mathbf{y}}} = \left.\left[\frac{\mathrm{d}\mathbf{x}^\intercal}{\mathrm{d}\mathbf{y}}\left(\frac{\partial w}{\partial\mathbf{x}} + \frac{\partial\boldsymbol{\epsilon}^\intercal}{\partial\mathbf{x}}\frac{\partial w}{\partial\boldsymbol{\epsilon}}\right) + \frac{\partial w}{\partial\mathbf{y}} + \frac{\partial\boldsymbol{\epsilon}^\intercal}{\partial\mathbf{y}}\frac{\partial w}{\partial\boldsymbol{\epsilon}}\right]\right|_{\mathbf{y}=\bar{\mathbf{y}}}.$$

Thus, using Layer 4, Eq. 11 yields the first line of Layer 4, Eq. 22.

Appendix E.3.2. Form 2

Using Eqs. (E6) and (E13), the total selection gradient of gene expression is given by the second line of Layer 4, Eq. 22.

Appendix E.3.3. Form 3

Using Eqs. (E6), (D20), and Layer 4, Eq. 8, we have that the total selection gradient of gene expression is given by the third line of Layer 4, Eq. 22.

Appendix E.3.4. Form 4

Using the first line of Layer 4, Eq. 22 and Layer 4, Eq. 15, we obtain the fourth line of Layer 4, Eq. 22.

Appendix E.3.5. Form 5

Finally, we can rearrange total genetic selection (Layer 4, Eq. 22) in terms of total selection on the phenotype. Using Layer 4, Eq. 3 in the second line of Layer 4, Eq. 22, and then using the second line of Layer 4, Eq. 21, we have that the total selection gradient of gene expression is given by the fifth line of Layer 4, Eq. 22.

Appendix F. Total selection gradient of the environment

Here proceed analogously to derive the total selection gradient of the environment, which allows us to write an equation describing the evolutionary dynamics of the geno-envo-phenotype.

Appendix F.1. Total selection gradient of the environment in terms of direct fitness effects

As before, we start by considering the total selection gradient entry for the i-th environmental variable at age a. By this, we mean the total selection gradient of a perturbation of ϵ_{ia} taken as initial condition of the developmental constraint (1) when applied at the ages $\{a, \ldots, n\}$. Consequently, an environmental perturbation at a given age does not affect the phenotype at earlier ages due to the arrow of developmental time. By letting ζ in Eq. (26) be ϵ_{ia}, we have

$$\left.\frac{\mathrm{d}\lambda}{\mathrm{d}\epsilon_{ia}}\right|_{\mathbf{y}=\bar{\mathbf{y}}} = \left.\frac{\mathrm{d}w}{\mathrm{d}\epsilon_{ia}}\right|_{\mathbf{y}=\bar{\mathbf{y}}} = \sum_{j=1}^{N_\mathrm{a}}\left.\frac{\mathrm{d}w_j}{\mathrm{d}\epsilon_{ia}}\right|_{\mathbf{y}=\bar{\mathbf{y}}}. \tag{F1}$$

The total derivatives of a mutant's relative fitness at age j in Eq. (F1) are with respect to the individual's environmental variables at possibly another age a. We now seek to express such selection gradient in terms of partial derivatives only.

From Eq. (23), we have $w_j(\mathbf{z}_j, \boldsymbol{\epsilon}_j, \bar{\mathbf{m}})$ with $\mathbf{z}_j = (\mathbf{x}_j; \mathbf{y}_j)$, so applying the chain rule and, since we assume that gene expression is open-loop (hence, gene expression does not depend on the environment, so $\mathrm{d}\mathbf{y}_j/\mathrm{d}\epsilon_{ia} = \mathbf{0}$ for all $i \in \{1, \dots, N_\mathrm{s}\}$ and all $a, j \in \{1, \dots, N_\mathrm{a}\}$), we obtain

$$\left.\frac{\mathrm{d}w_j}{\mathrm{d}\epsilon_{ia}}\right|_{\mathbf{y}=\bar{\mathbf{y}}} = \left.\left(\sum_{k=1}^{N_\mathrm{s}} \frac{\partial w_j}{\partial x_{kj}} \frac{\mathrm{d}x_{kj}}{\mathrm{d}\epsilon_{ia}} + \sum_{k=1}^{N_\mathrm{e}} \frac{\partial w_j}{\partial \epsilon_{kj}} \frac{\mathrm{d}\epsilon_{kj}}{\mathrm{d}\epsilon_{ia}}\right)\right|_{\mathbf{y}=\bar{\mathbf{y}}} = \left.\left(\frac{\mathrm{d}\mathbf{x}_j^\mathsf{T}}{\mathrm{d}\epsilon_{ia}} \frac{\partial w_j}{\partial \mathbf{x}_j} + \frac{\mathrm{d}\boldsymbol{\epsilon}_j^\mathsf{T}}{\mathrm{d}\epsilon_{ia}} \frac{\partial w_j}{\partial \boldsymbol{\epsilon}_j}\right)\right|_{\mathbf{y}=\bar{\mathbf{y}}}.$$

In the last equality we applied matrix calculus notation (Appendix N). Using Eq. (D3) we have

$$\left.\frac{\mathrm{d}w_j}{\mathrm{d}\epsilon_{ia}}\right|_{\mathbf{y}=\bar{\mathbf{y}}} = \left.\left(\frac{\mathrm{d}\mathbf{x}_j^\mathsf{T}}{\mathrm{d}\epsilon_{ia}} \frac{\partial w}{\partial \mathbf{x}_j} + \frac{\mathrm{d}\boldsymbol{\epsilon}_j^\mathsf{T}}{\mathrm{d}\epsilon_{ia}} \frac{\partial w}{\partial \boldsymbol{\epsilon}_j}\right)\right|_{\mathbf{y}=\bar{\mathbf{y}}}. \tag{F2}$$

Substituting Eq. (F2) in (F1) yields

$$\left.\frac{\mathrm{d}w}{\mathrm{d}\epsilon_{ia}}\right|_{\mathbf{y}=\bar{\mathbf{y}}} = \sum_{j=1}^{N_\mathrm{a}} \left.\left(\frac{\mathrm{d}\mathbf{x}_j^\mathsf{T}}{\mathrm{d}\epsilon_{ia}} \frac{\partial w}{\partial \mathbf{x}_j} + \frac{\mathrm{d}\boldsymbol{\epsilon}_j^\mathsf{T}}{\mathrm{d}\epsilon_{ia}} \frac{\partial w}{\partial \boldsymbol{\epsilon}_j}\right)\right|_{\mathbf{y}=\bar{\mathbf{y}}} = \left.\left(\frac{\mathrm{d}\mathbf{x}^\mathsf{T}}{\mathrm{d}\epsilon_{ia}} \frac{\partial w}{\partial \mathbf{x}} + \frac{\mathrm{d}\boldsymbol{\epsilon}^\mathsf{T}}{\mathrm{d}\epsilon_{ia}} \frac{\partial w}{\partial \boldsymbol{\epsilon}}\right)\right|_{\mathbf{y}=\bar{\mathbf{y}}}.$$

Therefore, the total selection gradient of all environmental variables across all ages is

$$\left.\frac{\mathrm{d}w}{\mathrm{d}\boldsymbol{\epsilon}}\right|_{\mathbf{y}=\bar{\mathbf{y}}} = \left.\left(\frac{\mathrm{d}\mathbf{x}^\mathsf{T}}{\mathrm{d}\boldsymbol{\epsilon}} \frac{\partial w}{\partial \mathbf{x}} + \frac{\mathrm{d}\boldsymbol{\epsilon}^\mathsf{T}}{\mathrm{d}\boldsymbol{\epsilon}} \frac{\partial w}{\partial \boldsymbol{\epsilon}}\right)\right|_{\mathbf{y}=\bar{\mathbf{y}}} \in \mathbb{R}^{N_\mathrm{a}N_\mathrm{e}\times 1}, \tag{F3}$$

where we use the block matrix of *total effects of a mutant's environment on her phenotype*

$$\left.\frac{\mathrm{d}\mathbf{x}^\mathsf{T}}{\mathrm{d}\boldsymbol{\epsilon}}\right|_{\mathbf{y}=\bar{\mathbf{y}}} \equiv \left.\begin{pmatrix} \frac{\mathrm{d}\mathbf{x}_1^\mathsf{T}}{\mathrm{d}\boldsymbol{\epsilon}_1} & \cdots & \frac{\mathrm{d}\mathbf{x}_{N_\mathrm{a}}^\mathsf{T}}{\partial \boldsymbol{\epsilon}_1} \\ \vdots & \ddots & \vdots \\ \frac{\mathrm{d}\mathbf{x}_1^\mathsf{T}}{\mathrm{d}\boldsymbol{\epsilon}_{N_\mathrm{a}}} & \cdots & \frac{\mathrm{d}\mathbf{x}_{N_\mathrm{a}}^\mathsf{T}}{\mathrm{d}\boldsymbol{\epsilon}_{N_\mathrm{a}}} \end{pmatrix}\right|_{\mathbf{y}=\bar{\mathbf{y}}} \in \mathbb{R}^{N_\mathrm{a}N_\mathrm{s}\times N_\mathrm{a}N_\mathrm{e}}$$

and the block matrix of *total effects of a mutant's environment on her environment*

$$\left.\frac{\mathrm{d}\boldsymbol{\epsilon}^\mathsf{T}}{\mathrm{d}\boldsymbol{\epsilon}}\right|_{\mathbf{y}=\bar{\mathbf{y}}} \equiv \left.\begin{pmatrix} \frac{\mathrm{d}\boldsymbol{\epsilon}_1^\mathsf{T}}{\mathrm{d}\boldsymbol{\epsilon}_1} & \cdots & \frac{\mathrm{d}\boldsymbol{\epsilon}_{N_\mathrm{a}}^\mathsf{T}}{\partial \boldsymbol{\epsilon}_1} \\ \vdots & \ddots & \vdots \\ \frac{\mathrm{d}\boldsymbol{\epsilon}_1^\mathsf{T}}{\mathrm{d}\boldsymbol{\epsilon}_{N_\mathrm{a}}} & \cdots & \frac{\mathrm{d}\boldsymbol{\epsilon}_{N_\mathrm{a}}^\mathsf{T}}{\mathrm{d}\boldsymbol{\epsilon}_{N_\mathrm{a}}} \end{pmatrix}\right|_{\mathbf{y}=\bar{\mathbf{y}}} \in \mathbb{R}^{N_\mathrm{a}N_\mathrm{e}\times N_\mathrm{a}N_\mathrm{e}}.$$

Expression (F3) is now in terms of partial derivatives of fitness, total effects of a mutant's environment on her phenotype, $\mathrm{d}\mathbf{x}^\mathsf{T}/\mathrm{d}\boldsymbol{\epsilon}$, and total effects of a mutant's environment on her environment, $\mathrm{d}\boldsymbol{\epsilon}^\mathsf{T}/\mathrm{d}\boldsymbol{\epsilon}$. We now proceed to write $\mathrm{d}\mathbf{x}^\mathsf{T}/\mathrm{d}\boldsymbol{\epsilon}$ and $\mathrm{d}\boldsymbol{\epsilon}^\mathsf{T}/\mathrm{d}\boldsymbol{\epsilon}$ in terms of partial derivatives only.

Appendix F.2. Matrix of total effects of a mutant's environment on her environment

From the environmental constraint (2) for the k-th environmental variable at age $j \in \{1, \dots, N_\mathrm{a}\}$ we have that $\epsilon_{kj} = h_{kj}(\mathbf{z}_j, \bar{\mathbf{z}}, \tau)$, so using the chain rule since gene expression is open-loop yields

$$\left.\frac{\mathrm{d}\epsilon_{kj}}{\mathrm{d}\epsilon_{ia}}\right|_{\mathbf{y}=\bar{\mathbf{y}}} = \begin{cases} \left.\left(\sum_{l=1}^{N_\mathrm{s}} \frac{\partial h_{kj}}{\partial x_{lj}} \frac{\mathrm{d}x_{lj}}{\mathrm{d}\epsilon_{ia}}\right)\right|_{\mathbf{y}=\bar{\mathbf{y}}} & \text{for } j > a \\ \left.\frac{\partial \epsilon_{kj}}{\partial \epsilon_{ia}}\right|_{\mathbf{y}=\bar{\mathbf{y}}} & \text{for } j = a \\ 0 & \text{for } j < a \end{cases} = \begin{cases} \left.\left(\frac{\mathrm{d}\mathbf{x}_j^\mathsf{T}}{\mathrm{d}\epsilon_{ia}} \frac{\partial \epsilon_{kj}}{\partial \mathbf{x}_j}\right)\right|_{\mathbf{y}=\bar{\mathbf{y}}} & \text{for } j > a \\ \left.\frac{\partial \epsilon_{kj}}{\partial \epsilon_{ia}}\right|_{\mathbf{y}=\bar{\mathbf{y}}} & \text{for } j = a \\ 0 & \text{for } j < a. \end{cases}$$

In the last equality we used matrix calculus notation and rewrote h_{kj} as ϵ_{kj}. Since we assume that environmental variables are mutually independent, we have that $\partial\epsilon_{ka}/\partial\epsilon_{ia} = 1$ if $i = k$ or $\partial\epsilon_{ka}/\partial\epsilon_{ia} = 0$ otherwise; however, we leave the partial derivatives $\partial\epsilon_{ka}/\partial\epsilon_{ia}$ unevaluated as it is conceptually useful. Hence,

$$\left.\frac{\mathrm{d}\boldsymbol{\epsilon}_j^\mathsf{T}}{\mathrm{d}\epsilon_{ia}}\right|_{\mathbf{y}=\bar{\mathbf{y}}} = \begin{cases} \left.\left(\frac{\mathrm{d}\mathbf{x}_j^\mathsf{T}}{\mathrm{d}\epsilon_{ia}} \frac{\partial \boldsymbol{\epsilon}_j^\mathsf{T}}{\partial \mathbf{x}_j}\right)\right|_{\mathbf{y}=\bar{\mathbf{y}}} & \text{for } j > a \\ \left.\frac{\partial \boldsymbol{\epsilon}_j^\mathsf{T}}{\partial \epsilon_{ia}}\right|_{\mathbf{y}=\bar{\mathbf{y}}} & \text{for } j = a \\ \mathbf{0} & \text{for } j < a. \end{cases}$$

Then, the matrix of total effects of a mutant's environment at age a on her environment at age j is

$$\left.\frac{\mathrm{d}\boldsymbol{\epsilon}_j^\mathsf{T}}{\mathrm{d}\boldsymbol{\epsilon}_a}\right|_{\mathbf{y}=\bar{\mathbf{y}}} = \begin{cases} \left.\left(\frac{\mathrm{d}\mathbf{x}_j^\mathsf{T}}{\mathrm{d}\boldsymbol{\epsilon}_a} \frac{\partial \boldsymbol{\epsilon}_j^\mathsf{T}}{\partial \mathbf{x}_j}\right)\right|_{\mathbf{y}=\bar{\mathbf{y}}} & \text{for } j > a \\ \left.\frac{\partial \boldsymbol{\epsilon}_j^\mathsf{T}}{\partial \boldsymbol{\epsilon}_a}\right|_{\mathbf{y}=\bar{\mathbf{y}}} & \text{for } j = a \\ \mathbf{0} & \text{for } j < a. \end{cases} \tag{F4}$$

Hence, the block matrix of *total effects of a mutant's environment on her environment* is

$$\left.\frac{\mathrm{d}\boldsymbol{\epsilon}^\mathsf{T}}{\mathrm{d}\boldsymbol{\epsilon}}\right|_{\mathbf{y}=\bar{\mathbf{y}}} \equiv \left.\begin{pmatrix} \frac{\mathrm{d}\boldsymbol{\epsilon}_1^\mathsf{T}}{\mathrm{d}\boldsymbol{\epsilon}_1} & \cdots & \frac{\mathrm{d}\boldsymbol{\epsilon}_{N_\mathrm{a}}^\mathsf{T}}{\mathrm{d}\boldsymbol{\epsilon}_1} \\ \vdots & \ddots & \vdots \\ \frac{\mathrm{d}\boldsymbol{\epsilon}_1^\mathsf{T}}{\mathrm{d}\boldsymbol{\epsilon}_{N_\mathrm{a}}} & \cdots & \frac{\mathrm{d}\boldsymbol{\epsilon}_{N_\mathrm{a}}^\mathsf{T}}{\mathrm{d}\boldsymbol{\epsilon}_{N_\mathrm{a}}} \end{pmatrix}\right|_{\mathbf{y}=\bar{\mathbf{y}}}$$

$$
= \left.\begin{pmatrix} \frac{\partial \boldsymbol{\epsilon}_1^\intercal}{\partial \boldsymbol{\epsilon}_1} & \frac{\mathrm{d}\boldsymbol{\epsilon}_2^\intercal}{\mathrm{d}\boldsymbol{\epsilon}_1} & \cdots & \frac{\mathrm{d}\boldsymbol{\epsilon}_{N_\mathrm{a}-1}^\intercal}{\mathrm{d}\boldsymbol{\epsilon}_1} & \frac{\mathrm{d}\boldsymbol{\epsilon}_{N_\mathrm{a}}^\intercal}{\mathrm{d}\boldsymbol{\epsilon}_1} \\ \mathbf{0} & \frac{\partial \boldsymbol{\epsilon}_2^\intercal}{\partial \boldsymbol{\epsilon}_2} & \cdots & \frac{\mathrm{d}\boldsymbol{\epsilon}_{N_\mathrm{a}-1}^\intercal}{\mathrm{d}\boldsymbol{\epsilon}_2} & \frac{\mathrm{d}\boldsymbol{\epsilon}_{N_\mathrm{a}}^\intercal}{\mathrm{d}\boldsymbol{\epsilon}_2} \\ \vdots & \vdots & \ddots & \vdots & \vdots \\ \mathbf{0} & \mathbf{0} & \cdots & \frac{\partial \boldsymbol{\epsilon}_{N_\mathrm{a}-1}^\intercal}{\partial \boldsymbol{\epsilon}_{N_\mathrm{a}-1}} & \frac{\mathrm{d}\boldsymbol{\epsilon}_{N_\mathrm{a}}^\intercal}{\mathrm{d}\boldsymbol{\epsilon}_{N_\mathrm{a}-1}} \\ \mathbf{0} & \mathbf{0} & \cdots & \mathbf{0} & \frac{\partial \boldsymbol{\epsilon}_{N_\mathrm{a}}^\intercal}{\partial \boldsymbol{\epsilon}_{N_\mathrm{a}}} \end{pmatrix}\right|_{\mathbf{y}=\bar{\mathbf{y}}} \tag{F5}
$$

$$
\in \mathbb{R}^{N_\mathrm{a}N_\mathrm{e}\times N_\mathrm{a}N_\mathrm{e}}.
$$

Note that the aj-th entry of $(\mathrm{d}\mathbf{x}^\intercal/\mathrm{d}\boldsymbol{\epsilon})(\partial\boldsymbol{\epsilon}^\intercal/\partial\mathbf{x})$ for $j > a$ is

$$
\left(\frac{\mathrm{d}\mathbf{x}^\intercal}{\mathrm{d}\boldsymbol{\epsilon}}\frac{\partial\boldsymbol{\epsilon}^\intercal}{\partial\mathbf{x}}\right)_{aj} = \sum_{k=1}^{N_\mathrm{a}} \frac{\mathrm{d}\mathbf{x}_k^\intercal}{\mathrm{d}\boldsymbol{\epsilon}_a}\frac{\partial\boldsymbol{\epsilon}_j^\intercal}{\partial\mathbf{x}_k} = \frac{\mathrm{d}\mathbf{x}_j^\intercal}{\mathrm{d}\boldsymbol{\epsilon}_a}\frac{\partial\boldsymbol{\epsilon}_j^\intercal}{\partial\mathbf{x}_j},
$$

where we use Layer 2, Eq. 4d in the second equality. Note also that since environmental variables are mutually independent, $\partial\boldsymbol{\epsilon}_j^\intercal/\partial\boldsymbol{\epsilon}_a = \mathbf{0}$ for $j \neq a$ from the environmental constraint (2). Finally, note that because of the arrow of developmental time, $\partial\mathbf{x}_j^\intercal/\partial\boldsymbol{\epsilon}_a = \mathbf{0}$ for $j < a$ due to the developmental constraint (1). Hence, Layer 4, Eq. 13 follows, which is a compact expression for the matrix of total effects of a mutant's environment on itself in terms of partial derivatives and the total effects of a mutant's environment on her phenotype, which we now write in terms of partial derivatives only.

Appendix F.3. Matrix of total effects of a mutant's environment on her phenotype

From the developmental constraint (1) for the k-th phenotype at age $j \in \{2,\ldots,N_\mathrm{a}\}$ we have that $x_{kj} = g_{k,j-1}(\mathbf{z}_{j-1},\boldsymbol{\epsilon}_{j-1},\bar{\mathbf{z}})$, so using the chain rule and since gene expression is open-loop yields

$$
\left.\frac{\mathrm{d}x_{kj}}{\mathrm{d}\epsilon_{ia}}\right|_{\mathbf{y}=\bar{\mathbf{y}}} = \left.\left(\sum_{l=1}^{N_\mathrm{s}}\frac{\partial g_{k,j-1}}{\partial x_{l,j-1}}\frac{\mathrm{d}x_{l,j-1}}{\mathrm{d}\epsilon_{ia}} + \sum_{l=1}^{N_\mathrm{e}}\frac{\partial g_{k,j-1}}{\partial \epsilon_{l,j-1}}\frac{\mathrm{d}\epsilon_{l,j-1}}{\mathrm{d}\epsilon_{ia}}\right)\right|_{\mathbf{y}=\bar{\mathbf{y}}}
$$

$$
= \left.\left(\frac{\mathrm{d}\mathbf{x}_{j-1}^\intercal}{\mathrm{d}\epsilon_{ia}}\frac{\partial x_{kj}}{\partial\mathbf{x}_{j-1}} + \frac{\mathrm{d}\boldsymbol{\epsilon}_{j-1}^\intercal}{\mathrm{d}\epsilon_{ia}}\frac{\partial x_{kj}}{\partial\boldsymbol{\epsilon}_{j-1}}\right)\right|_{\mathbf{y}=\bar{\mathbf{y}}}.
$$

In the last equality we used matrix calculus notation and rewrote $g_{k,j-1}$ as x_{kj}. Hence,

$$
\left.\frac{\mathrm{d}\mathbf{x}_j^\intercal}{\mathrm{d}\epsilon_{ia}}\right|_{\mathbf{y}=\bar{\mathbf{y}}} = \left.\left(\frac{\mathrm{d}\mathbf{x}_{j-1}^\intercal}{\mathrm{d}\epsilon_{ia}}\frac{\partial\mathbf{x}_j^\intercal}{\partial\mathbf{x}_{j-1}} + \frac{\mathrm{d}\boldsymbol{\epsilon}_{j-1}^\intercal}{\mathrm{d}\epsilon_{ia}}\frac{\partial\mathbf{x}_j^\intercal}{\partial\boldsymbol{\epsilon}_{j-1}}\right)\right|_{\mathbf{y}=\bar{\mathbf{y}}}.
$$

Then, the matrix of total effects of a mutant's environment at age a on her phenotype at age j is

$$
\left.\frac{\mathrm{d}\mathbf{x}_j^\intercal}{\mathrm{d}\boldsymbol{\epsilon}_a}\right|_{\mathbf{y}=\bar{\mathbf{y}}} = \left.\left(\frac{\mathrm{d}\mathbf{x}_{j-1}^\intercal}{\mathrm{d}\boldsymbol{\epsilon}_a}\frac{\partial\mathbf{x}_j^\intercal}{\partial\mathbf{x}_{j-1}} + \frac{\mathrm{d}\boldsymbol{\epsilon}_{j-1}^\intercal}{\mathrm{d}\boldsymbol{\epsilon}_a}\frac{\partial\mathbf{x}_j^\intercal}{\partial\boldsymbol{\epsilon}_{j-1}}\right)\right|_{\mathbf{y}=\bar{\mathbf{y}}}.
$$

Using Eq. (F4) yields

$$
\left.\frac{\mathrm{d}\mathbf{x}_j^\intercal}{\mathrm{d}\boldsymbol{\epsilon}_a}\right|_{\mathbf{y}=\bar{\mathbf{y}}} =
$$

$$
\begin{cases}
\left.\left(\frac{\mathrm{d}\mathbf{x}_{j-1}^\intercal}{\mathrm{d}\boldsymbol{\epsilon}_a}\frac{\partial\mathbf{x}_j^\intercal}{\partial\mathbf{x}_{j-1}} + \frac{\mathrm{d}\mathbf{x}_{j-1}^\intercal}{\mathrm{d}\boldsymbol{\epsilon}_a}\frac{\partial\boldsymbol{\epsilon}_{j-1}^\intercal}{\partial\mathbf{x}_{j-1}}\frac{\partial\mathbf{x}_j^\intercal}{\partial\boldsymbol{\epsilon}_{j-1}}\right)\right|_{\mathbf{y}=\bar{\mathbf{y}}} & \text{for } j-1 > a \\
\left.\left(\underbrace{\frac{\mathrm{d}\mathbf{x}_a^\intercal}{\mathrm{d}\boldsymbol{\epsilon}_a}}_{\mathbf{0},\text{ from (1)}}\frac{\partial\mathbf{x}_{a+1}^\intercal}{\partial\mathbf{x}_a} + \frac{\partial\boldsymbol{\epsilon}_a^\intercal}{\partial\boldsymbol{\epsilon}_a}\frac{\partial\mathbf{x}_{a+1}^\intercal}{\partial\boldsymbol{\epsilon}_a}\right)\right|_{\mathbf{y}=\bar{\mathbf{y}}} & \text{for } j-1 = a \\
\left.\left(\underbrace{\frac{\mathrm{d}\mathbf{x}_{j-1}^\intercal}{\mathrm{d}\boldsymbol{\epsilon}_a}}_{\mathbf{0},\text{ from (1)}}\frac{\partial\mathbf{x}_j^\intercal}{\partial\mathbf{x}_{j-1}}\right)\right|_{\mathbf{y}=\bar{\mathbf{y}}} & \text{for } j-1 > a
\end{cases}
$$

$$
= \begin{cases}
\left.\left[\frac{\mathrm{d}\mathbf{x}_{j-1}^\intercal}{\mathrm{d}\boldsymbol{\epsilon}_a}\left(\frac{\partial\mathbf{x}_j^\intercal}{\partial\mathbf{x}_{j-1}} + \frac{\partial\boldsymbol{\epsilon}_{j-1}^\intercal}{\partial\mathbf{x}_{j-1}}\frac{\partial\mathbf{x}_j^\intercal}{\partial\boldsymbol{\epsilon}_{j-1}}\right)\right]\right|_{\mathbf{y}=\bar{\mathbf{y}}} & \text{for } j-1 > a \\
\left.\left(\frac{\partial\boldsymbol{\epsilon}_a^\intercal}{\partial\boldsymbol{\epsilon}_a}\frac{\partial\mathbf{x}_j^\intercal}{\partial\boldsymbol{\epsilon}_{j-1}}\right)\right|_{\mathbf{y}=\bar{\mathbf{y}}} & \text{for } j-1 = a \\
\mathbf{0} & \text{for } j-1 > a.
\end{cases}
$$

Using Eq. (D10), this reduces to

$$
\left.\frac{\mathrm{d}\mathbf{x}_j^\intercal}{\mathrm{d}\boldsymbol{\epsilon}_a}\right|_{\mathbf{y}=\bar{\mathbf{y}}} = \begin{cases}
\left.\left(\frac{\mathrm{d}\mathbf{x}_{j-1}^\intercal}{\mathrm{d}\boldsymbol{\epsilon}_a}\frac{\delta\mathbf{x}_j^\intercal}{\delta\mathbf{x}_{j-1}}\right)\right|_{\mathbf{y}=\bar{\mathbf{y}}} & \text{for } j-1 > a \\
\left.\left(\frac{\partial\boldsymbol{\epsilon}_a^\intercal}{\partial\boldsymbol{\epsilon}_a}\frac{\partial\mathbf{x}_{a+1}^\intercal}{\partial\boldsymbol{\epsilon}_a}\right)\right|_{\mathbf{y}=\bar{\mathbf{y}}} & \text{for } j-1 = a \\
\mathbf{0} & \text{for } j-1 > a.
\end{cases}
$$

Expanding this recurrence yields

$$
\left.\frac{\mathrm{d}\mathbf{x}_j^\intercal}{\mathrm{d}\boldsymbol{\epsilon}_a}\right|_{\mathbf{y}=\bar{\mathbf{y}}} = \begin{cases}
\left.\left(\frac{\mathrm{d}\mathbf{x}_{a+1}^\intercal}{\mathrm{d}\boldsymbol{\epsilon}_a}\frac{\delta\mathbf{x}_{a+2}^\intercal}{\delta\mathbf{x}_{a+1}}\cdots\frac{\delta\mathbf{x}_j^\intercal}{\delta\mathbf{x}_{j-1}}\right)\right|_{\mathbf{y}=\bar{\mathbf{y}}} & \text{for } j-1 > a \\
\left.\left(\frac{\partial\boldsymbol{\epsilon}_a^\intercal}{\partial\boldsymbol{\epsilon}_a}\frac{\partial\mathbf{x}_{a+1}^\intercal}{\partial\boldsymbol{\epsilon}_a}\right)\right|_{\mathbf{y}=\bar{\mathbf{y}}} & \text{for } j-1 = a \\
\mathbf{0} & \text{for } j-1 > a,
\end{cases}
$$

which using Layer 4, Eq. 2 yields

$$
\left.\frac{\mathrm{d}\mathbf{x}_j^\intercal}{\mathrm{d}\boldsymbol{\epsilon}_a}\right|_{\mathbf{y}=\bar{\mathbf{y}}} = \begin{cases}
\left.\left(\frac{\partial\boldsymbol{\epsilon}_a^\intercal}{\partial\boldsymbol{\epsilon}_a}\frac{\partial\mathbf{x}_{a+1}^\intercal}{\partial\boldsymbol{\epsilon}_a}\frac{\mathrm{d}\mathbf{x}_j^\intercal}{\mathrm{d}\mathbf{x}_{a+1}}\right)\right|_{\mathbf{y}=\bar{\mathbf{y}}} & \text{for } j-1 > a \\
\left.\left(\frac{\partial\boldsymbol{\epsilon}_a^\intercal}{\partial\boldsymbol{\epsilon}_a}\frac{\partial\mathbf{x}_{a+1}^\intercal}{\partial\boldsymbol{\epsilon}_a}\right)\right|_{\mathbf{y}=\bar{\mathbf{y}}} & \text{for } j-1 = a \\
\mathbf{0} & \text{for } j-1 > a.
\end{cases} \tag{F6}
$$

It will be useful to denote the matrix of *semi-total effects of a mutant's environment at age j on her phenotype at age j* for $j > 0$ as

$$
\left.\frac{\delta\mathbf{x}_j^\intercal}{\delta\boldsymbol{\epsilon}_{j-1}}\right|_{\mathbf{y}=\bar{\mathbf{y}}} = \left.\frac{\partial\boldsymbol{\epsilon}_{j-1}^\intercal}{\partial\boldsymbol{\epsilon}_{j-1}}\frac{\partial\mathbf{x}_j^\intercal}{\partial\boldsymbol{\epsilon}_{j-1}}\right|_{\mathbf{y}=\bar{\mathbf{y}}} \in \mathbb{R}^{N_\mathrm{e}\times N_\mathrm{s}}. \tag{F7}
$$

The matrix of *direct effects of a mutant's environment on itself* is given by Layer 2, Eq. 5. In turn, the block matrix of *semi-*

total effects of a mutant's environment on her phenotype is

$$\left.\frac{\delta \mathbf{x}^\intercal}{\delta \boldsymbol{\epsilon}}\right|_{\mathbf{y}=\bar{\mathbf{y}}} \equiv \left.\begin{pmatrix} \frac{\delta \mathbf{x}_1^\intercal}{\delta \boldsymbol{\epsilon}_1} & \cdots & \frac{\delta \mathbf{x}_{N_\mathrm{a}}^\intercal}{\delta \boldsymbol{\epsilon}_1} \\ \vdots & \ddots & \vdots \\ \frac{\delta \mathbf{x}_1^\intercal}{\delta \boldsymbol{\epsilon}_{N_\mathrm{a}}} & \cdots & \frac{\delta \mathbf{x}_{N_\mathrm{a}}^\intercal}{\delta \boldsymbol{\epsilon}_{N_\mathrm{a}}} \end{pmatrix}\right|_{\mathbf{y}=\bar{\mathbf{y}}}$$

$$= \left.\begin{pmatrix} \mathbf{0} & \frac{\delta \mathbf{x}_2^\intercal}{\delta \boldsymbol{\epsilon}_1} & \cdots & \mathbf{0} & \mathbf{0} \\ \mathbf{0} & \mathbf{0} & \cdots & \mathbf{0} & \mathbf{0} \\ \vdots & \vdots & \ddots & \vdots & \vdots \\ \mathbf{0} & \mathbf{0} & \cdots & \mathbf{0} & \frac{\delta \mathbf{x}_{N_\mathrm{a}}^\intercal}{\delta \boldsymbol{\epsilon}_{N_\mathrm{a}-1}} \\ \mathbf{0} & \mathbf{0} & \cdots & \mathbf{0} & \mathbf{0} \end{pmatrix}\right|_{\mathbf{y}=\bar{\mathbf{y}}}$$

$$\in \mathbb{R}^{N_\mathrm{a}N_\mathrm{e}\times N_\mathrm{a}N_\mathrm{s}}, \tag{F8}$$

so Layer 3, Eq. 4 follows from Eqs. (F7), Layer 2, Eq. 5, and Layer 2, Eq. 4c.

Using Eq. (F7), Eq. (F6) becomes

$$\left.\frac{\mathrm{d}\mathbf{x}_j^\intercal}{\mathrm{d}\boldsymbol{\epsilon}_a}\right|_{\mathbf{y}=\bar{\mathbf{y}}} = \begin{cases} \left.\left(\frac{\delta \mathbf{x}_{a+1}^\intercal}{\delta \boldsymbol{\epsilon}_a}\frac{\mathrm{d}\mathbf{x}_j^\intercal}{\mathrm{d}\mathbf{x}_{a+1}}\right)\right|_{\mathbf{y}=\bar{\mathbf{y}}} & \text{for } j-1>a \\ \left.\frac{\delta \mathbf{x}_{a+1}^\intercal}{\delta \boldsymbol{\epsilon}_a}\right|_{\mathbf{y}=\bar{\mathbf{y}}} & \text{for } j-1=a \\ \mathbf{0} & \text{for } j-1>a. \end{cases}$$

Note that the aj-th entry of $(\delta\mathbf{x}^\intercal/\delta\boldsymbol{\epsilon})(\mathrm{d}\mathbf{x}^\intercal/\mathrm{d}\mathbf{x})$ is

$$\left(\frac{\delta \mathbf{x}^\intercal}{\delta \boldsymbol{\epsilon}}\right)_{aj} = \sum_{k=1}^{N_\mathrm{a}} \frac{\delta \mathbf{x}_k^\intercal}{\delta \boldsymbol{\epsilon}_a}\frac{\mathrm{d}\mathbf{x}_j^\intercal}{\mathrm{d}\mathbf{x}_k} = \frac{\delta \mathbf{x}_{a+1}^\intercal}{\delta \boldsymbol{\epsilon}_a}\frac{\mathrm{d}\mathbf{x}_j^\intercal}{\mathrm{d}\mathbf{x}_{a+1}} = \frac{\mathrm{d}\mathbf{x}_j^\intercal}{\mathrm{d}\boldsymbol{\epsilon}_a}, \tag{F9}$$

where we use Eq. (F8) in the second equality. Hence, Layer 4, Eq. 4 follows, where the block matrix of *total effects of a mutant's environment on her phenotype* is

$$\left.\frac{\mathrm{d}\mathbf{x}^\intercal}{\mathrm{d}\boldsymbol{\epsilon}}\right|_{\mathbf{y}=\bar{\mathbf{y}}} = \left.\begin{pmatrix} \frac{\mathrm{d}\mathbf{x}_1^\intercal}{\mathrm{d}\boldsymbol{\epsilon}_1} & \cdots & \frac{\mathrm{d}\mathbf{x}_{N_\mathrm{a}}^\intercal}{\mathrm{d}\boldsymbol{\epsilon}_1} \\ \vdots & \ddots & \vdots \\ \frac{\mathrm{d}\mathbf{x}_1^\intercal}{\mathrm{d}\boldsymbol{\epsilon}_{N_\mathrm{a}}} & \cdots & \frac{\mathrm{d}\mathbf{x}_{N_\mathrm{a}}^\intercal}{\mathrm{d}\boldsymbol{\epsilon}_{N_\mathrm{a}}} \end{pmatrix}\right|_{\mathbf{y}=\bar{\mathbf{y}}}$$

$$= \left.\begin{pmatrix} \mathbf{0} & \frac{\mathrm{d}\mathbf{x}_2^\intercal}{\mathrm{d}\boldsymbol{\epsilon}_1} & \cdots & \frac{\mathrm{d}\mathbf{x}_{N_\mathrm{a}-1}^\intercal}{\mathrm{d}\boldsymbol{\epsilon}_1} & \frac{\mathrm{d}\mathbf{x}_{N_\mathrm{a}}^\intercal}{\mathrm{d}\boldsymbol{\epsilon}_1} \\ \mathbf{0} & \mathbf{0} & \cdots & \frac{\mathrm{d}\mathbf{x}_{N_\mathrm{a}-1}^\intercal}{\mathrm{d}\boldsymbol{\epsilon}_2} & \frac{\mathrm{d}\mathbf{x}_{N_\mathrm{a}}^\intercal}{\mathrm{d}\boldsymbol{\epsilon}_2} \\ \vdots & \vdots & \ddots & \vdots & \vdots \\ \mathbf{0} & \mathbf{0} & \cdots & \mathbf{0} & \frac{\mathrm{d}\mathbf{x}_{N_\mathrm{a}}^\intercal}{\mathrm{d}\boldsymbol{\epsilon}_{N_\mathrm{a}-1}} \\ \mathbf{0} & \mathbf{0} & \cdots & \mathbf{0} & \mathbf{0} \end{pmatrix}\right|_{\mathbf{y}=\bar{\mathbf{y}}} \tag{F10}$$

$$\in \mathbb{R}^{N_\mathrm{a}N_\mathrm{e}\times N_\mathrm{a}N_\mathrm{s}}.$$

Layer 4, Eq. 4, (F8), and Layer 4, Eq. 1 write the matrix of total effects of a mutant's environment on her phenotype in terms of partial derivatives. This is a compact expression for the matrix of total effects of a mutant's environment on her phenotype in terms of partial derivatives only.

Appendix F.4. Conclusion

Appendix F.4.1. Form 1

Eq. (F3) gives the total selection gradient of the environment as in the first line of Layer 4, Eq. 23.

Appendix F.4.2. Form 2

Using Eq. (F3) and Layer 4, Eq. 13 yields

$$\left.\frac{\mathrm{d}w}{\mathrm{d}\boldsymbol{\epsilon}}\right|_{\mathbf{y}=\bar{\mathbf{y}}} = \left.\left[\frac{\mathrm{d}\mathbf{x}^\intercal}{\mathrm{d}\boldsymbol{\epsilon}}\frac{\partial w}{\partial \mathbf{x}} + \left(\frac{\partial \boldsymbol{\epsilon}^\intercal}{\partial \boldsymbol{\epsilon}} + \frac{\mathrm{d}\mathbf{x}^\intercal}{\mathrm{d}\boldsymbol{\epsilon}}\frac{\partial \boldsymbol{\epsilon}^\intercal}{\partial \mathbf{x}}\right)\frac{\partial w}{\partial \boldsymbol{\epsilon}}\right]\right|_{\mathbf{y}=\bar{\mathbf{y}}}.$$

Collecting for $\mathrm{d}\mathbf{x}^\intercal/\mathrm{d}\boldsymbol{\epsilon}$ and using Layer 3, Eq. 1 for $\boldsymbol{\zeta} = \mathbf{x}$ as well as Layer 3, Eq. 2, we have that the total selection gradient of the environment is given by the second line of Layer 4, Eq. 23.

Appendix F.4.3. Form 3

Using the first line of Layer 4, Eq. 23 and Layer 4, Eq. 16, we obtain the third line of Layer 4, Eq. 23.

Appendix F.4.4. Form 4

Finally, we can rearrange total selection on the environment in terms of total selection on the phenotype. Using Layer 4, Eq. 4 in the second line of Layer 4, Eq. 23, and then using the second line of Layer 4, Eq. 21, we have that the total selection gradient of the environment is given by the fourth line of Layer 4, Eq. 23.

Appendix G. Total selection gradient of the geno-phenotype

We have that the mutant geno-phenotype is $\mathbf{z} = (\mathbf{x}; \mathbf{y})$. We first define the (direct), semi-total, and total selection gradients of the geno-phenotype and write the total selection gradient of the geno-phenotype in terms of the semi-total selection gradient of the geno-phenotype and of the partial selection gradient of the geno-envo-phenotype.

Appendix G.1. Total selection gradient of the geno-phenotype in terms of direct fitness effects

We have the *selection gradient of the geno-phenotype*

$$\left.\frac{\partial w}{\partial \mathbf{z}}\right|_{\mathbf{y}=\bar{\mathbf{y}}} \equiv \left.\left(\frac{\partial w}{\partial \mathbf{x}}; \frac{\partial w}{\partial \mathbf{y}}\right)\right|_{\mathbf{y}=\bar{\mathbf{y}}} \in \mathbb{R}^{N_\mathrm{a}(N_\mathrm{s}+N_\mathrm{c})\times 1},$$

the *semi-total selection gradient of the geno-phenotype*

$$\left.\frac{\delta w}{\delta \mathbf{z}}\right|_{\mathbf{y}=\bar{\mathbf{y}}} \equiv \left.\left(\frac{\delta w}{\delta \mathbf{x}}; \frac{\delta w}{\delta \mathbf{y}}\right)\right|_{\mathbf{y}=\bar{\mathbf{y}}} \in \mathbb{R}^{N_\mathrm{a}(N_\mathrm{s}+N_\mathrm{c})\times 1},$$

and the *total selection gradient of the geno-phenotype*

$$\left.\frac{\mathrm{d}w}{\mathrm{d}\mathbf{z}}\right|_{\mathbf{y}=\bar{\mathbf{y}}} \equiv \left.\left(\frac{\mathrm{d}w}{\mathrm{d}\mathbf{x}}; \frac{\mathrm{d}w}{\mathrm{d}\mathbf{y}}\right)\right|_{\mathbf{y}=\bar{\mathbf{y}}} \in \mathbb{R}^{N_\mathrm{a}(N_\mathrm{s}+N_\mathrm{c})\times 1}.$$

Now, we write the semi-total selection gradient of the geno-phenotype as a linear combination of the selection gradients of the geno-phenotype and environment. Using Layer 3, Eq. 1 for $\boldsymbol{\zeta} \in \{\mathbf{x}, \mathbf{y}\}$, we have that the semi-total selection gradient of the geno-phenotype is

$$\left.\frac{\delta w}{\delta \mathbf{z}}\right|_{\mathbf{y}=\bar{\mathbf{y}}} \equiv \left.\begin{pmatrix} \frac{\delta w}{\delta \mathbf{x}} \\ \frac{\delta w}{\delta \mathbf{y}} \end{pmatrix}\right|_{\mathbf{y}=\bar{\mathbf{y}}} = \left.\begin{pmatrix} \frac{\partial w}{\partial \mathbf{x}} + \frac{\partial \boldsymbol{\epsilon}^{\mathsf{T}}}{\partial \mathbf{x}} \frac{\partial w}{\partial \boldsymbol{\epsilon}} \\ \frac{\partial w}{\partial \mathbf{y}} + \frac{\partial \boldsymbol{\epsilon}^{\mathsf{T}}}{\partial \mathbf{y}} \frac{\partial w}{\partial \boldsymbol{\epsilon}} \end{pmatrix}\right|_{\mathbf{y}=\bar{\mathbf{y}}}$$
$$= \left.\left[\begin{pmatrix} \frac{\partial w}{\partial \mathbf{x}} \\ \frac{\partial w}{\partial \mathbf{y}} \end{pmatrix} + \begin{pmatrix} \frac{\partial \boldsymbol{\epsilon}^{\mathsf{T}}}{\partial \mathbf{x}} \frac{\partial w}{\partial \boldsymbol{\epsilon}} \\ \frac{\partial \boldsymbol{\epsilon}^{\mathsf{T}}}{\partial \mathbf{y}} \frac{\partial w}{\partial \boldsymbol{\epsilon}} \end{pmatrix}\right]\right|_{\mathbf{y}=\bar{\mathbf{y}}}. \tag{G1}$$

Using Layer 2, Eq. 9, we have that

$$\left.\left(\frac{\partial \boldsymbol{\epsilon}^{\mathsf{T}}}{\partial \mathbf{z}} \frac{\partial w}{\partial \boldsymbol{\epsilon}}\right)\right|_{\mathbf{y}=\bar{\mathbf{y}}} = \left.\left[\begin{pmatrix} \frac{\partial \boldsymbol{\epsilon}^{\mathsf{T}}}{\partial \mathbf{x}} \\ \frac{\partial \boldsymbol{\epsilon}^{\mathsf{T}}}{\partial \mathbf{y}} \end{pmatrix} \frac{\partial w}{\partial \boldsymbol{\epsilon}}\right]\right|_{\mathbf{y}=\bar{\mathbf{y}}} = \left.\begin{pmatrix} \frac{\partial \boldsymbol{\epsilon}^{\mathsf{T}}}{\partial \mathbf{x}} \frac{\partial w}{\partial \boldsymbol{\epsilon}} \\ \frac{\partial \boldsymbol{\epsilon}^{\mathsf{T}}}{\partial \mathbf{y}} \frac{\partial w}{\partial \boldsymbol{\epsilon}} \end{pmatrix}\right|_{\mathbf{y}=\bar{\mathbf{y}}}.$$

Therefore, Eq. (G1) becomes Layer 3, Eq. 1 for $\boldsymbol{\zeta} = \mathbf{z}$.

Appendix G.1.1. Form 2

Now we bring together the total selection gradients of the phenotype and gene expression to write the total selection gradient of the geno-phenotype as a linear transformation of the semi-total selection gradient of the geno-phenotype.

Using the third lines of Layer 4, Eq. 21 and Layer 4, Eq. 22, we have

$$\left.\frac{\mathrm{d}w}{\mathrm{d}\mathbf{z}}\right|_{\mathbf{y}=\bar{\mathbf{y}}} \equiv \left.\begin{pmatrix} \frac{\mathrm{d}w}{\mathrm{d}\mathbf{x}} \\ \frac{\mathrm{d}w}{\mathrm{d}\mathbf{y}} \end{pmatrix}\right|_{\mathbf{y}=\bar{\mathbf{y}}} = \left.\begin{pmatrix} \frac{\mathrm{d}\mathbf{z}^{\mathsf{T}}}{\mathrm{d}\mathbf{x}} \frac{\delta w}{\delta \mathbf{z}} \\ \frac{\mathrm{d}\mathbf{z}^{\mathsf{T}}}{\mathrm{d}\mathbf{y}} \frac{\delta w}{\delta \mathbf{z}} \end{pmatrix}\right|_{\mathbf{y}=\bar{\mathbf{y}}}$$
$$= \left.\left[\begin{pmatrix} \frac{\mathrm{d}\mathbf{z}^{\mathsf{T}}}{\mathrm{d}\mathbf{x}} \\ \frac{\mathrm{d}\mathbf{z}^{\mathsf{T}}}{\mathrm{d}\mathbf{y}} \end{pmatrix} \frac{\delta w}{\delta \mathbf{z}}\right]\right|_{\mathbf{y}=\bar{\mathbf{y}}} = \left.\left(\frac{\mathrm{d}\mathbf{z}^{\mathsf{T}}}{\mathrm{d}\mathbf{z}} \frac{\delta w}{\delta \mathbf{z}}\right)\right|_{\mathbf{y}=\bar{\mathbf{y}}},$$

which is the second line of Layer 4, Eq. 24.

Appendix G.1.2. Form 3

Now we use the expressions of the total selection gradients of the phenotype and gene expression as linear transformations of the geno-envo-phenotype to write the total selection gradient of the geno-phenotype. Using the fourth lines of Layer 4, Eq. 21 and Layer 4, Eq. 22, we have

$$\left.\frac{\mathrm{d}w}{\mathrm{d}\mathbf{z}}\right|_{\mathbf{y}=\bar{\mathbf{y}}} \equiv \left.\begin{pmatrix} \frac{\mathrm{d}w}{\mathrm{d}\mathbf{x}} \\ \frac{\mathrm{d}w}{\mathrm{d}\mathbf{y}} \end{pmatrix}\right|_{\mathbf{y}=\bar{\mathbf{y}}} = \left.\begin{pmatrix} \frac{\mathrm{d}\mathbf{m}^{\mathsf{T}}}{\mathrm{d}\mathbf{x}} \frac{\partial w}{\partial \mathbf{m}} \\ \frac{\mathrm{d}\mathbf{m}^{\mathsf{T}}}{\mathrm{d}\mathbf{y}} \frac{\partial w}{\partial \mathbf{m}} \end{pmatrix}\right|_{\mathbf{y}=\bar{\mathbf{y}}}$$
$$= \left.\left[\begin{pmatrix} \frac{\mathrm{d}\mathbf{m}^{\mathsf{T}}}{\mathrm{d}\mathbf{x}} \\ \frac{\mathrm{d}\mathbf{m}^{\mathsf{T}}}{\mathrm{d}\mathbf{y}} \end{pmatrix} \frac{\partial w}{\partial \mathbf{m}}\right]\right|_{\mathbf{y}=\bar{\mathbf{y}}} = \left.\left(\frac{\mathrm{d}\mathbf{m}^{\mathsf{T}}}{\mathrm{d}\mathbf{z}} \frac{\partial w}{\partial \mathbf{m}}\right)\right|_{\mathbf{y}=\bar{\mathbf{y}}},$$

which is the third line of Layer 4, Eq. 24.

Appendix G.1.3. Form 1

Now, we obtain the total selection gradient of the geno-phenotype as a linear combination of selection gradients of the geno-phenotype and environment. Using Layer 3, Eq. 1 for $\boldsymbol{\zeta} = \mathbf{z}$, the second line of Layer 4, Eq. 24 becomes

$$\left.\frac{\mathrm{d}w}{\mathrm{d}\mathbf{z}}\right|_{\mathbf{y}=\bar{\mathbf{y}}} = \left.\left[\frac{\mathrm{d}\mathbf{z}^{\mathsf{T}}}{\mathrm{d}\mathbf{z}} \left(\frac{\partial w}{\partial \mathbf{z}} + \frac{\partial \boldsymbol{\epsilon}^{\mathsf{T}}}{\partial \mathbf{z}} \frac{\partial w}{\partial \boldsymbol{\epsilon}}\right)\right]\right|_{\mathbf{y}=\bar{\mathbf{y}}}. \tag{G2}$$

We define the block matrix of total effects of a mutant's geno-phenotype on her environment as

$$\left.\frac{\mathrm{d}\boldsymbol{\epsilon}^{\mathsf{T}}}{\mathrm{d}\mathbf{z}}\right|_{\mathbf{y}=\bar{\mathbf{y}}} \equiv \left.\begin{pmatrix} \frac{\mathrm{d}\boldsymbol{\epsilon}^{\mathsf{T}}}{\mathrm{d}\mathbf{x}} \\ \frac{\mathrm{d}\boldsymbol{\epsilon}^{\mathsf{T}}}{\mathrm{d}\mathbf{y}} \end{pmatrix}\right|_{\mathbf{y}=\bar{\mathbf{y}}} \in \mathbb{R}^{N_{\mathrm{a}}(N_{\mathrm{s}}+N_{\mathrm{c}}) \times N_{\mathrm{a}} N_{\mathrm{e}}},$$

which using Layer 4, Eq. 10 and Layer 4, Eq. 11 yields

$$\left.\frac{\mathrm{d}\boldsymbol{\epsilon}^{\mathsf{T}}}{\mathrm{d}\mathbf{z}}\right|_{\mathbf{y}=\bar{\mathbf{y}}} = \left.\begin{pmatrix} \frac{\mathrm{d}\mathbf{z}^{\mathsf{T}}}{\mathrm{d}\mathbf{x}} \frac{\partial \boldsymbol{\epsilon}^{\mathsf{T}}}{\partial \mathbf{z}} \\ \frac{\mathrm{d}\mathbf{z}^{\mathsf{T}}}{\mathrm{d}\mathbf{y}} \frac{\partial \boldsymbol{\epsilon}^{\mathsf{T}}}{\partial \mathbf{z}} \end{pmatrix}\right|_{\mathbf{y}=\bar{\mathbf{y}}} = \left.\left[\begin{pmatrix} \frac{\mathrm{d}\mathbf{z}^{\mathsf{T}}}{\mathrm{d}\mathbf{x}} \\ \frac{\mathrm{d}\mathbf{z}^{\mathsf{T}}}{\mathrm{d}\mathbf{y}} \end{pmatrix} \frac{\partial \boldsymbol{\epsilon}^{\mathsf{T}}}{\partial \mathbf{z}}\right]\right|_{\mathbf{y}=\bar{\mathbf{y}}}$$
$$= \left.\left(\frac{\mathrm{d}\mathbf{z}^{\mathsf{T}}}{\mathrm{d}\mathbf{z}} \frac{\partial \boldsymbol{\epsilon}^{\mathsf{T}}}{\partial \mathbf{z}}\right)\right|_{\mathbf{y}=\bar{\mathbf{y}}},$$

which is Layer 4, Eq. 12, where in the second equality we factorized and in the third equality we used Layer 4, Eq. 9. Using this in Eq. (G2), the first line of Layer 4, Eq. 24 follows.

Appendix G.2. Matrix of total effects of a mutant's geno-phenotype on her geno-phenotype

Here we obtain a compact expression for $\mathrm{d}\mathbf{z}^{\mathsf{T}}/\mathrm{d}\mathbf{z}|_{\mathbf{y}=\bar{\mathbf{y}}}$. Before doing so, let us obtain the block matrix of *semi-total effects of a mutant's geno-phenotype on her geno-phenotype*

$$\frac{\delta \mathbf{z}^{\mathsf{T}}}{\delta \mathbf{z}} \equiv \begin{pmatrix} \frac{\delta \mathbf{x}^{\mathsf{T}}}{\delta \mathbf{x}} & \frac{\delta \mathbf{y}^{\mathsf{T}}}{\delta \mathbf{x}} \\ \frac{\delta \mathbf{x}^{\mathsf{T}}}{\delta \mathbf{y}} & \frac{\delta \mathbf{y}^{\mathsf{T}}}{\delta \mathbf{y}} \end{pmatrix} = \begin{pmatrix} \frac{\delta \mathbf{x}^{\mathsf{T}}}{\delta \mathbf{x}} & \mathbf{0} \\ \frac{\delta \mathbf{x}^{\mathsf{T}}}{\delta \mathbf{y}} & \mathbf{I} \end{pmatrix} \tag{G3}$$
$$\in \mathbb{R}^{N_{\mathrm{a}}(N_{\mathrm{s}}+N_{\mathrm{c}}) \times N_{\mathrm{a}}(N_{\mathrm{s}}+N_{\mathrm{c}})},$$

where the equality follows from the assumption that gene expression is open-loop. Using Layer 2, Eq. 8, Layer 2, Eq. 9, and Layer 2, Eq. 11 we have that

$$\frac{\partial \mathbf{z}^{\mathsf{T}}}{\partial \mathbf{z}} + \frac{\partial \boldsymbol{\epsilon}^{\mathsf{T}}}{\partial \mathbf{z}} \frac{\partial \mathbf{z}^{\mathsf{T}}}{\partial \boldsymbol{\epsilon}} = \begin{pmatrix} \frac{\partial \mathbf{x}^{\mathsf{T}}}{\partial \mathbf{x}} & \mathbf{0} \\ \frac{\partial \mathbf{x}^{\mathsf{T}}}{\partial \mathbf{y}} & \mathbf{I} \end{pmatrix} + \begin{pmatrix} \frac{\partial \boldsymbol{\epsilon}^{\mathsf{T}}}{\partial \mathbf{x}} \\ \frac{\partial \boldsymbol{\epsilon}^{\mathsf{T}}}{\partial \mathbf{y}} \end{pmatrix} \begin{pmatrix} \frac{\partial \mathbf{x}^{\mathsf{T}}}{\partial \boldsymbol{\epsilon}} & \mathbf{0} \end{pmatrix}$$
$$= \begin{pmatrix} \frac{\partial \mathbf{x}^{\mathsf{T}}}{\partial \mathbf{x}} & \mathbf{0} \\ \frac{\partial \mathbf{x}^{\mathsf{T}}}{\partial \mathbf{y}} & \mathbf{I} \end{pmatrix} + \begin{pmatrix} \frac{\partial \boldsymbol{\epsilon}^{\mathsf{T}}}{\partial \mathbf{x}} \frac{\partial \mathbf{x}^{\mathsf{T}}}{\partial \boldsymbol{\epsilon}} & \mathbf{0} \\ \frac{\partial \boldsymbol{\epsilon}^{\mathsf{T}}}{\partial \mathbf{y}} \frac{\partial \mathbf{x}^{\mathsf{T}}}{\partial \boldsymbol{\epsilon}} & \mathbf{0} \end{pmatrix}$$
$$= \begin{pmatrix} \frac{\partial \mathbf{x}^{\mathsf{T}}}{\partial \mathbf{x}} + \frac{\partial \boldsymbol{\epsilon}^{\mathsf{T}}}{\partial \mathbf{x}} \frac{\partial \mathbf{x}^{\mathsf{T}}}{\partial \boldsymbol{\epsilon}} & \mathbf{0} \\ \frac{\partial \mathbf{x}^{\mathsf{T}}}{\partial \mathbf{y}} + \frac{\partial \boldsymbol{\epsilon}^{\mathsf{T}}}{\partial \mathbf{y}} \frac{\partial \mathbf{x}^{\mathsf{T}}}{\partial \boldsymbol{\epsilon}} & \mathbf{I} \end{pmatrix},$$

which equals the right-hand side of Eq. (G3) so Layer 3, Eq. 5 holds.

Now, motivated by Layer 4, Eq. 1 and the equation for total effects in path analysis (Greene, 1977), suppose that

$$\frac{\mathrm{d}\mathbf{z}^\intercal}{\mathrm{d}\mathbf{z}} = (\mathbf{I} - \mathbf{E}_\mathbf{Z})^{-1},$$

for some matrix $\mathbf{E}_\mathbf{Z}$ to be determined. Then,

$$\mathbf{E}_\mathbf{Z} = \mathbf{I} - \left(\frac{\mathrm{d}\mathbf{z}^\intercal}{\mathrm{d}\mathbf{z}}\right)^{-1}. \tag{G4}$$

Using Layer 4, Eq. 9 and a formula for the inverse of a 2×2 block matrix (Horn and Johnson, 2013, Eq. 0.7.3.1), we have

$$\left(\frac{\mathrm{d}\mathbf{z}^\intercal}{\mathrm{d}\mathbf{z}}\right)^{-1} = \begin{pmatrix} \left(\frac{\mathrm{d}\mathbf{x}^\intercal}{\mathrm{d}\mathbf{x}}\right)^{-1} & \mathbf{0} \\ -\frac{\mathrm{d}\mathbf{x}^\intercal}{\mathrm{d}\mathbf{y}}\left(\frac{\mathrm{d}\mathbf{x}^\intercal}{\mathrm{d}\mathbf{x}}\right)^{-1} & \mathbf{I} \end{pmatrix}.$$

Using Layer 4, Eq. 3 yields

$$\left(\frac{\mathrm{d}\mathbf{z}^\intercal}{\mathrm{d}\mathbf{z}}\right)^{-1} = \begin{pmatrix} \left(\frac{\mathrm{d}\mathbf{x}^\intercal}{\mathrm{d}\mathbf{x}}\right)^{-1} & \mathbf{0} \\ -\frac{\delta\mathbf{x}^\intercal}{\delta\mathbf{y}}\frac{\mathrm{d}\mathbf{x}^\intercal}{\mathrm{d}\mathbf{x}}\left(\frac{\mathrm{d}\mathbf{x}^\intercal}{\mathrm{d}\mathbf{x}}\right)^{-1} & \mathbf{I} \end{pmatrix}.$$

Simplifying and using Layer 4, Eq. 1 yields

$$\left(\frac{\mathrm{d}\mathbf{z}^\intercal}{\mathrm{d}\mathbf{z}}\right)^{-1} = \begin{pmatrix} 2\mathbf{I} - \frac{\delta\mathbf{x}^\intercal}{\delta\mathbf{x}} & \mathbf{0} \\ -\frac{\delta\mathbf{x}^\intercal}{\delta\mathbf{y}} & \mathbf{I} \end{pmatrix}.$$

Substituting in Eq. (G4) and simplifying yields

$$\mathbf{E}_\mathbf{Z} = \mathbf{I} - \begin{pmatrix} 2\mathbf{I} - \frac{\delta\mathbf{x}^\intercal}{\delta\mathbf{x}} & \mathbf{0} \\ -\frac{\delta\mathbf{x}^\intercal}{\delta\mathbf{y}} & \mathbf{I} \end{pmatrix} = \begin{pmatrix} -\mathbf{I} + \frac{\delta\mathbf{x}^\intercal}{\delta\mathbf{x}} & \mathbf{0} \\ \frac{\delta\mathbf{x}^\intercal}{\delta\mathbf{y}} & \mathbf{0} \end{pmatrix} = \begin{pmatrix} \frac{\delta\mathbf{x}^\intercal}{\delta\mathbf{x}} & \mathbf{0} \\ \frac{\delta\mathbf{x}^\intercal}{\delta\mathbf{y}} & \mathbf{I} \end{pmatrix} - \mathbf{I}.$$

Hence,

$$\mathbf{E}_\mathbf{Z} = \frac{\delta\mathbf{z}^\intercal}{\delta\mathbf{z}} - \mathbf{I},$$

and so Layer 4, Eq. 9 holds.

Appendix H. Total selection gradient of the geno-envo-phenotype

We have that the mutant geno-envo-phenotype is $\mathbf{m} = (\mathbf{x}; \mathbf{y}; \boldsymbol{\epsilon})$. We now define the (direct), semi-total, and total selection gradients of the geno-envo-phenotype and write the total selection gradient of the geno-envo-phenotype in terms of the partial selection gradient of the geno-envo-phenotype.

We have the *selection gradient of the geno-envo-phenotype*

$$\left.\frac{\partial w}{\partial \mathbf{m}}\right|_{\mathbf{y}=\bar{\mathbf{y}}} \equiv \left.\left(\frac{\partial w}{\partial \mathbf{x}}; \frac{\partial w}{\partial \mathbf{y}}; \frac{\partial w}{\partial \boldsymbol{\epsilon}}\right)\right|_{\mathbf{y}=\bar{\mathbf{y}}} \in \mathbb{R}^{N_\mathrm{a}(N_\mathrm{s}+N_\mathrm{c}+N_\mathrm{e})\times 1},$$

the *semi-total selection gradient of the geno-envo-phenotype*

$$\left.\frac{\delta w}{\delta \mathbf{m}}\right|_{\mathbf{y}=\bar{\mathbf{y}}} = \left.\left(\frac{\delta w}{\delta \mathbf{x}}; \frac{\delta w}{\delta \mathbf{y}}; \frac{\delta w}{\delta \boldsymbol{\epsilon}}\right)\right|_{\mathbf{y}=\bar{\mathbf{y}}} \in \mathbb{R}^{N_\mathrm{a}(N_\mathrm{s}+N_\mathrm{c}+N_\mathrm{e})\times 1},$$

and the *total selection gradient of the geno-envo-phenotype*

$$\left.\frac{\mathrm{d}w}{\mathrm{d}\mathbf{m}}\right|_{\mathbf{y}=\bar{\mathbf{y}}} = \left.\left(\frac{\mathrm{d}w}{\mathrm{d}\mathbf{x}}; \frac{\mathrm{d}w}{\mathrm{d}\mathbf{y}}; \frac{\mathrm{d}w}{\mathrm{d}\boldsymbol{\epsilon}}\right)\right|_{\mathbf{y}=\bar{\mathbf{y}}} \in \mathbb{R}^{N_\mathrm{a}(N_\mathrm{s}+N_\mathrm{c}+N_\mathrm{e})\times 1}.$$

Now we use the expressions of the total selection gradients of the phenotype, gene expression, and environment as linear transformations of the geno-envo-phenotype to write the total selection gradient of the geno-envo-phenotype. Using the fourth lines of Layer 4, Eq. 21 and Layer 4, Eq. 22 and the third line of Layer 4, Eq. 23, we have

$$\begin{aligned}
\left.\frac{\mathrm{d}w}{\mathrm{d}\mathbf{m}}\right|_{\mathbf{y}=\bar{\mathbf{y}}} &\equiv \left.\begin{pmatrix} \frac{\mathrm{d}w}{\mathrm{d}\mathbf{x}} \\ \frac{\mathrm{d}w}{\mathrm{d}\mathbf{y}} \\ \frac{\mathrm{d}w}{\mathrm{d}\boldsymbol{\epsilon}} \end{pmatrix}\right|_{\mathbf{y}=\bar{\mathbf{y}}} = \left.\begin{pmatrix} \frac{\mathrm{d}\mathbf{m}^\intercal}{\mathrm{d}\mathbf{x}}\frac{\partial w}{\partial \mathbf{m}} \\ \frac{\mathrm{d}\mathbf{m}^\intercal}{\mathrm{d}\mathbf{y}}\frac{\partial w}{\partial \mathbf{m}} \\ \frac{\mathrm{d}\mathbf{m}^\intercal}{\mathrm{d}\boldsymbol{\epsilon}}\frac{\partial w}{\partial \mathbf{m}} \end{pmatrix}\right|_{\mathbf{y}=\bar{\mathbf{y}}} \\
&= \left.\left[\begin{pmatrix} \frac{\mathrm{d}\mathbf{m}^\intercal}{\mathrm{d}\mathbf{x}} \\ \frac{\mathrm{d}\mathbf{m}^\intercal}{\mathrm{d}\mathbf{y}} \\ \frac{\mathrm{d}\mathbf{m}^\intercal}{\mathrm{d}\boldsymbol{\epsilon}} \end{pmatrix}\frac{\partial w}{\partial \mathbf{m}}\right]\right|_{\mathbf{y}=\bar{\mathbf{y}}} = \left.\left(\frac{\mathrm{d}\mathbf{m}^\intercal}{\mathrm{d}\mathbf{m}}\frac{\partial w}{\partial \mathbf{m}}\right)\right|_{\mathbf{y}=\bar{\mathbf{y}}},
\end{aligned}$$

which is Layer 4, Eq. 25.

To see that $\mathrm{d}\mathbf{m}^\intercal/\mathrm{d}\mathbf{m}|_{\mathbf{y}=\bar{\mathbf{y}}}$ is non-singular, we factorize it as follows. We define the block matrix of *direct effects of a mutant's geno-envo-phenotype on her geno-envo-phenotype considering environmental constraints without considering developmental constraints* as

$$\left.\frac{\gamma\mathbf{m}^\intercal}{\gamma\mathbf{m}}\right|_{\mathbf{y}=\bar{\mathbf{y}}} = \left.\begin{pmatrix} \mathbf{I} & \mathbf{0} & \frac{\partial\boldsymbol{\epsilon}^\intercal}{\partial\mathbf{x}} \\ \mathbf{0} & \mathbf{I} & \frac{\partial\boldsymbol{\epsilon}^\intercal}{\partial\mathbf{y}} \\ \mathbf{0} & \mathbf{0} & \frac{\partial\boldsymbol{\epsilon}^\intercal}{\partial\boldsymbol{\epsilon}} \end{pmatrix}\right|_{\mathbf{y}=\bar{\mathbf{y}}} \in \mathbb{R}^{N_\mathrm{a}(N_\mathrm{s}+N_\mathrm{c}+N_\mathrm{e})\times N_\mathrm{a}(N_\mathrm{s}+N_\mathrm{c}+N_\mathrm{e})},$$

which is non-singular since it is square, block upper triangular, and $\partial\boldsymbol{\epsilon}^\intercal/\partial\boldsymbol{\epsilon} = \mathbf{I}$ (Layer 2, Eq. 5). We also define the block matrix of *total effects of a mutant's geno-envo-phenotype on her geno-envo-phenotype considering developmental constraints but not selective environmental constraints* as

$$\left.\frac{\beta\mathbf{m}^\intercal}{\beta\mathbf{m}}\right|_{\mathbf{y}=\bar{\mathbf{y}}} = \left.\begin{pmatrix} \frac{\mathrm{d}\mathbf{x}^\intercal}{\mathrm{d}\mathbf{x}} & \mathbf{0} & \mathbf{0} \\ \frac{\mathrm{d}\mathbf{x}^\intercal}{\mathrm{d}\mathbf{y}} & \mathbf{I} & \mathbf{0} \\ \frac{\mathrm{d}\mathbf{x}^\intercal}{\mathrm{d}\boldsymbol{\epsilon}} & \mathbf{0} & \mathbf{I} \end{pmatrix}\right|_{\mathbf{y}=\bar{\mathbf{y}}} \in \mathbb{R}^{N_\mathrm{a}(N_\mathrm{s}+N_\mathrm{c}+N_\mathrm{e})\times N_\mathrm{a}(N_\mathrm{s}+N_\mathrm{c}+N_\mathrm{e})},$$

which is non-singular since it is square, block lower triangular, and $\mathrm{d}\mathbf{x}^\intercal/\mathrm{d}\mathbf{x}$ is non-singular (Eq. D15). Note that

$$\left(\frac{\beta\mathbf{m}^\intercal}{\beta\mathbf{m}}\frac{\gamma\mathbf{m}^\intercal}{\gamma\mathbf{m}}\right)\Bigg|_{\mathbf{y}=\bar{\mathbf{y}}} = \left[\begin{pmatrix}\frac{\mathrm{d}\mathbf{x}^\intercal}{\mathrm{d}\mathbf{x}} & \mathbf{0} & \mathbf{0}\\ \frac{\mathrm{d}\mathbf{x}^\intercal}{\mathrm{d}\mathbf{y}} & \mathbf{I} & \mathbf{0}\\ \frac{\mathrm{d}\mathbf{x}^\intercal}{\mathrm{d}\boldsymbol{\epsilon}} & \mathbf{0} & \mathbf{I}\end{pmatrix}\begin{pmatrix}\mathbf{I} & \mathbf{0} & \frac{\partial\boldsymbol{\epsilon}^\intercal}{\partial\mathbf{x}}\\ \mathbf{0} & \mathbf{I} & \frac{\partial\boldsymbol{\epsilon}^\intercal}{\partial\mathbf{y}}\\ \mathbf{0} & \mathbf{0} & \frac{\partial\boldsymbol{\epsilon}^\intercal}{\partial\boldsymbol{\epsilon}}\end{pmatrix}\right]\Bigg|_{\mathbf{y}=\bar{\mathbf{y}}}$$

$$= \begin{pmatrix}\frac{\mathrm{d}\mathbf{x}^\intercal}{\mathrm{d}\mathbf{x}} & \mathbf{0} & \frac{\mathrm{d}\mathbf{x}^\intercal}{\mathrm{d}\mathbf{x}}\frac{\partial\boldsymbol{\epsilon}^\intercal}{\partial\mathbf{x}}\\ \frac{\mathrm{d}\mathbf{x}^\intercal}{\mathrm{d}\mathbf{y}} & \mathbf{I} & \frac{\mathrm{d}\mathbf{x}^\intercal}{\mathrm{d}\mathbf{y}}\frac{\partial\boldsymbol{\epsilon}^\intercal}{\partial\mathbf{x}}+\frac{\partial\boldsymbol{\epsilon}^\intercal}{\partial\mathbf{y}}\\ \frac{\mathrm{d}\mathbf{x}^\intercal}{\mathrm{d}\boldsymbol{\epsilon}} & \mathbf{0} & \frac{\mathrm{d}\mathbf{x}^\intercal}{\mathrm{d}\boldsymbol{\epsilon}}\frac{\partial\boldsymbol{\epsilon}^\intercal}{\partial\mathbf{x}}+\frac{\partial\boldsymbol{\epsilon}^\intercal}{\partial\boldsymbol{\epsilon}}\end{pmatrix}\Bigg|_{\mathbf{y}=\bar{\mathbf{y}}}$$

$$= \begin{pmatrix}\frac{\mathrm{d}\mathbf{x}^\intercal}{\mathrm{d}\mathbf{x}} & \mathbf{0} & \frac{\mathrm{d}\boldsymbol{\epsilon}^\intercal}{\mathrm{d}\mathbf{x}}\\ \frac{\mathrm{d}\mathbf{x}^\intercal}{\mathrm{d}\mathbf{y}} & \mathbf{I} & \frac{\mathrm{d}\boldsymbol{\epsilon}^\intercal}{\mathrm{d}\mathbf{y}}\\ \frac{\mathrm{d}\mathbf{x}^\intercal}{\mathrm{d}\boldsymbol{\epsilon}} & \mathbf{0} & \frac{\mathrm{d}\boldsymbol{\epsilon}^\intercal}{\mathrm{d}\boldsymbol{\epsilon}}\end{pmatrix}\Bigg|_{\mathbf{y}=\bar{\mathbf{y}}},$$

where the last equality follows from Layer 4, Eq. 10, Layer 4, Eq. 11, and Layer 4, Eq. 13. Using Layer 4, Eq. 18, we thus have that

$$\frac{\mathrm{d}\mathbf{m}^\intercal}{\mathrm{d}\mathbf{m}}\Bigg|_{\mathbf{y}=\bar{\mathbf{y}}} = \left(\frac{\beta\mathbf{m}^\intercal}{\beta\mathbf{m}}\frac{\gamma\mathbf{m}^\intercal}{\gamma\mathbf{m}}\right)\Bigg|_{\mathbf{y}=\bar{\mathbf{y}}}.$$

Hence, $\mathrm{d}\mathbf{m}^\intercal/\mathrm{d}\mathbf{m}|_{\mathbf{y}=\bar{\mathbf{y}}}$ is non-singular since $\beta\mathbf{m}^\intercal/\beta\mathbf{m}|_{\mathbf{y}=\bar{\mathbf{y}}}$ and $\gamma\mathbf{m}^\intercal/\gamma\mathbf{m}|_{\mathbf{y}=\bar{\mathbf{y}}}$ are square and non-singular.

Appendix I. Evolutionary dynamics of the phenotype

Here we derive an equation describing the evolutionary dynamics of the phenotype.

From Eqs. (13) and (26), we have that the evolutionary dynamics of gene expression satisfy the canonical equation

$$\frac{\Delta\bar{\mathbf{y}}}{\Delta\tau} \approx \kappa\mathbf{G}_{\mathbf{y}}\,\frac{\mathrm{d}w}{\mathrm{d}\mathbf{y}}\Bigg|_{\mathbf{y}=\bar{\mathbf{y}}}, \tag{I1}$$

whereas the developmental dynamics of the phenotype satisfy the developmental constraint

$$\bar{\mathbf{x}}_{a+1} = \mathbf{g}_a^\circ,$$

for $a \in \{1,\dots,N_\mathrm{a}-1\}$.

Let $\bar{\mathbf{z}}(\tau)$ be the resident geno-phenotype at evolutionary time τ, specifically at the point where the socio-devo stable resident is at carrying capacity, marked in Fig. 3. The i-th mutant phenotype at age $j+1$ at such evolutionary time τ is $x_{i,j+1} = g_{ij}(\mathbf{z}_j(\tau),\mathbf{h}_j(\mathbf{z}_j(\tau),\bar{\mathbf{z}}(\tau),\tau),\bar{\mathbf{z}}(\tau))$. Then, evolutionary change in the i-th resident phenotype at age $a \in \{2,\dots,N_\mathrm{a}\}$ is

$$\frac{\Delta\bar{x}_{ia}}{\Delta\tau} = \frac{1}{\Delta\tau}\Bigg[g_{i,a-1}\Big(\mathbf{z}_{a-1}(\tau+\Delta\tau),\mathbf{h}_{a-1}(\mathbf{z}_{a-1}(\tau+\Delta\tau),\bar{\mathbf{z}}(\tau+\Delta\tau),\tau+\Delta\tau),\bar{\mathbf{z}}(\tau+\Delta\tau)\Big) - g_{i,a-1}\left(\mathbf{z}_{a-1}(\tau),\mathbf{h}_{a-1}(\mathbf{z}_{a-1}(\tau),\bar{\mathbf{z}}(\tau),\tau),\bar{\mathbf{z}}(\tau)\right)\Bigg]\Bigg|_{\mathbf{y}=\bar{\mathbf{y}}}.$$

Taking the limit as $\Delta\tau \to 0$, this becomes

$$\frac{\mathrm{d}\bar{x}_{ia}}{\mathrm{d}\tau} = \frac{\mathrm{d}g_{i,a-1}(\mathbf{z}_{a-1}(\tau),\mathbf{h}_{a-1}(\mathbf{z}_{a-1}(\tau),\bar{\mathbf{z}}(\tau),\tau),\bar{\mathbf{z}}(\tau))}{\mathrm{d}\tau}\Bigg|_{\mathbf{y}=\bar{\mathbf{y}}}.$$

Applying the chain rule, we obtain

$$\begin{aligned}\frac{\mathrm{d}\bar{x}_{ia}}{\mathrm{d}\tau} =& \Bigg(\sum_{j=1}^{N_\mathrm{s}}\frac{\partial g_{i,a-1}}{\partial x_{j,a-1}}\frac{\mathrm{d}x_{j,a-1}}{\mathrm{d}\tau} + \sum_{j=1}^{N_\mathrm{c}}\frac{\partial g_{i,a-1}}{\partial y_{j,a-1}}\frac{\mathrm{d}y_{j,a-1}}{\mathrm{d}\tau}\\ &+ \sum_{j=1}^{N_\mathrm{s}}\sum_{r=1}^{N_\mathrm{e}}\frac{\partial g_{i,a-1}}{\partial\epsilon_{r,a-1}}\frac{\partial\epsilon_{r,a-1}}{\partial x_{j,a-1}}\frac{\mathrm{d}x_{j,a-1}}{\mathrm{d}\tau} + \sum_{j=1}^{N_\mathrm{c}}\sum_{r=1}^{N_\mathrm{e}}\frac{\partial g_{i,a-1}}{\partial\epsilon_{r,a-1}}\frac{\partial\epsilon_{r,a-1}}{\partial y_{j,a-1}}\frac{\mathrm{d}y_{j,a-1}}{\mathrm{d}\tau}\\ &+ \sum_{k=1}^{N_\mathrm{a}}\sum_{j=1}^{N_\mathrm{s}}\sum_{r=1}^{N_\mathrm{e}}\frac{\partial g_{i,a-1}}{\partial\epsilon_{r,a-1}}\frac{\partial\epsilon_{r,a-1}}{\partial\bar{x}_{jk}}\frac{\mathrm{d}\bar{x}_{jk}}{\mathrm{d}\tau}\\ &+ \sum_{k=1}^{N_\mathrm{a}}\sum_{j=1}^{N_\mathrm{c}}\sum_{r=1}^{N_\mathrm{e}}\frac{\partial g_{i,a-1}}{\partial\epsilon_{r,a-1}}\frac{\partial\epsilon_{r,a-1}}{\partial\bar{y}_{jk}}\frac{\mathrm{d}\bar{y}_{jk}}{\mathrm{d}\tau} + \sum_{r=1}^{N_\mathrm{e}}\frac{\partial g_{i,a-1}}{\partial\epsilon_{r,a-1}}\frac{\partial\epsilon_{r,a-1}}{\partial\tau}\\ &+ \sum_{k=1}^{N_\mathrm{a}}\sum_{j=1}^{N_\mathrm{s}}\frac{\partial g_{i,a-1}}{\partial\bar{x}_{jk}}\frac{\mathrm{d}\bar{x}_{jk}}{\mathrm{d}\tau} + \sum_{k=1}^{N_\mathrm{a}}\sum_{j=1}^{N_\mathrm{c}}\frac{\partial g_{i,a-1}}{\partial\bar{y}_{jk}}\frac{\mathrm{d}\bar{y}_{jk}}{\mathrm{d}\tau}\Bigg)\Bigg|_{\mathbf{y}=\bar{\mathbf{y}}}.\end{aligned}$$

Applying matrix calculus notation (Appendix N), this is

$$\begin{aligned}\frac{\mathrm{d}\bar{x}_{ia}}{\mathrm{d}\tau} =& \Bigg(\frac{\partial g_{i,a-1}}{\partial\mathbf{x}_{a-1}^\intercal}\frac{\mathrm{d}\mathbf{x}_{a-1}}{\mathrm{d}\tau} + \frac{\partial g_{i,a-1}}{\partial\mathbf{y}_{a-1}^\intercal}\frac{\mathrm{d}\mathbf{y}_{a-1}}{\mathrm{d}\tau}\\ &+ \sum_{j=1}^{N_\mathrm{s}}\frac{\partial g_{i,a-1}}{\partial\boldsymbol{\epsilon}_{a-1}^\intercal}\frac{\partial\boldsymbol{\epsilon}_{a-1}}{\partial x_{j,a-1}}\frac{\mathrm{d}x_{j,a-1}}{\mathrm{d}\tau} + \sum_{j=1}^{N_\mathrm{c}}\frac{\partial g_{i,a-1}}{\partial\boldsymbol{\epsilon}_{a-1}^\intercal}\frac{\partial\boldsymbol{\epsilon}_{a-1}}{\partial y_{j,a-1}}\frac{\mathrm{d}y_{j,a-1}}{\mathrm{d}\tau}\\ &+ \sum_{k=1}^{N_\mathrm{a}}\sum_{j=1}^{N_\mathrm{s}}\frac{\partial g_{i,a-1}}{\partial\boldsymbol{\epsilon}_{a-1}^\intercal}\frac{\partial\boldsymbol{\epsilon}_{a-1}}{\partial\bar{x}_{jk}}\frac{\mathrm{d}\bar{x}_{jk}}{\mathrm{d}\tau}\\ &+ \sum_{k=1}^{N_\mathrm{a}}\sum_{j=1}^{N_\mathrm{c}}\frac{\partial g_{i,a-1}}{\partial\boldsymbol{\epsilon}_{a-1}^\intercal}\frac{\partial\boldsymbol{\epsilon}_{a-1}}{\partial\bar{y}_{jk}}\frac{\mathrm{d}\bar{y}_{jk}}{\mathrm{d}\tau} + \frac{\partial g_{i,a-1}}{\partial\boldsymbol{\epsilon}_{a-1}^\intercal}\frac{\partial\boldsymbol{\epsilon}_{a-1}}{\partial\tau}\\ &+ \sum_{k=1}^{N_\mathrm{a}}\frac{\partial g_{i,a-1}}{\partial\bar{\mathbf{x}}_k^\intercal}\frac{\mathrm{d}\bar{\mathbf{x}}_k}{\mathrm{d}\tau} + \sum_{k=1}^{N_\mathrm{a}}\frac{\partial g_{i,a-1}}{\partial\bar{\mathbf{y}}_k^\intercal}\frac{\mathrm{d}\bar{\mathbf{y}}_k}{\mathrm{d}\tau}\Bigg)\Bigg|_{\mathbf{y}=\bar{\mathbf{y}}}.\end{aligned}$$

Applying matrix calculus notation again yields

$$\begin{aligned}\frac{\mathrm{d}\bar{x}_{ia}}{\mathrm{d}\tau} =& \Bigg(\frac{\partial g_{i,a-1}}{\partial\mathbf{x}_{a-1}^\intercal}\frac{\mathrm{d}\mathbf{x}_{a-1}}{\mathrm{d}\tau} + \frac{\partial g_{i,a-1}}{\partial\mathbf{y}_{a-1}^\intercal}\frac{\mathrm{d}\mathbf{y}_{a-1}}{\mathrm{d}\tau}\\ &+ \frac{\partial g_{i,a-1}}{\partial\boldsymbol{\epsilon}_{a-1}^\intercal}\frac{\partial\boldsymbol{\epsilon}_{a-1}}{\partial\mathbf{x}_{a-1}^\intercal}\frac{\mathrm{d}\mathbf{x}_{a-1}}{\mathrm{d}\tau} + \frac{\partial g_{i,a-1}}{\partial\boldsymbol{\epsilon}_{a-1}^\intercal}\frac{\partial\boldsymbol{\epsilon}_{a-1}}{\partial\mathbf{y}_{a-1}^\intercal}\frac{\mathrm{d}\mathbf{y}_{a-1}}{\mathrm{d}\tau}\end{aligned}$$

$$+\frac{\partial g_{i,a-1}}{\partial \boldsymbol{\epsilon}_{a-1}^{\mathsf{T}}}\frac{\partial \boldsymbol{\epsilon}_{a-1}}{\partial \bar{\mathbf{x}}^{\mathsf{T}}}\frac{\mathrm{d}\bar{\mathbf{x}}}{\mathrm{d}\tau}+\frac{\partial g_{i,a-1}}{\partial \boldsymbol{\epsilon}_{a-1}^{\mathsf{T}}}\frac{\partial \boldsymbol{\epsilon}_{a-1}}{\partial \bar{\mathbf{y}}^{\mathsf{T}}}\frac{\mathrm{d}\bar{\mathbf{y}}}{\mathrm{d}\tau}+\frac{\partial g_{i,a-1}}{\partial \boldsymbol{\epsilon}_{a-1}^{\mathsf{T}}}\frac{\partial \boldsymbol{\epsilon}_{a-1}}{\partial \tau}$$
$$+\frac{\partial g_{i,a-1}}{\partial \bar{\mathbf{x}}^{\mathsf{T}}}\frac{\mathrm{d}\bar{\mathbf{x}}}{\mathrm{d}\tau}+\frac{\partial g_{i,a-1}}{\partial \bar{\mathbf{y}}^{\mathsf{T}}}\frac{\mathrm{d}\bar{\mathbf{y}}}{\mathrm{d}\tau}\Bigg)\Bigg|_{\mathbf{y}=\bar{\mathbf{y}}}.$$

Factorizing, we have

$$\frac{\mathrm{d}\bar{x}_{ia}}{\mathrm{d}\tau}=$$
$$\Bigg[\left(\frac{\partial g_{i,a-1}}{\partial \mathbf{x}_{a-1}^{\mathsf{T}}}+\frac{\partial g_{i,a-1}}{\partial \boldsymbol{\epsilon}_{a-1}^{\mathsf{T}}}\frac{\partial \boldsymbol{\epsilon}_{a-1}}{\partial \mathbf{x}_{a-1}^{\mathsf{T}}}\right)\frac{\mathrm{d}\mathbf{x}_{a-1}}{\mathrm{d}\tau}$$
$$+\left(\frac{\partial g_{i,a-1}}{\partial \mathbf{y}_{a-1}^{\mathsf{T}}}+\frac{\partial g_{i,a-1}}{\partial \boldsymbol{\epsilon}_{a-1}^{\mathsf{T}}}\frac{\partial \boldsymbol{\epsilon}_{a-1}}{\partial \mathbf{y}_{a-1}^{\mathsf{T}}}\right)\frac{\mathrm{d}\mathbf{y}_{a-1}}{\mathrm{d}\tau}$$
$$+\left(\frac{\partial g_{i,a-1}}{\partial \bar{\mathbf{x}}^{\mathsf{T}}}+\frac{\partial g_{i,a-1}}{\partial \boldsymbol{\epsilon}_{a-1}^{\mathsf{T}}}\frac{\partial \boldsymbol{\epsilon}_{a-1}}{\partial \bar{\mathbf{x}}^{\mathsf{T}}}\right)\frac{\mathrm{d}\bar{\mathbf{x}}}{\mathrm{d}\tau}$$
$$+\left(\frac{\partial g_{i,a-1}}{\partial \bar{\mathbf{y}}^{\mathsf{T}}}+\frac{\partial g_{i,a-1}}{\partial \boldsymbol{\epsilon}_{a-1}^{\mathsf{T}}}\frac{\partial \boldsymbol{\epsilon}_{a-1}}{\partial \bar{\mathbf{y}}^{\mathsf{T}}}\right)\frac{\mathrm{d}\bar{\mathbf{y}}}{\mathrm{d}\tau}+\frac{\partial g_{i,a-1}}{\partial \boldsymbol{\epsilon}_{a-1}^{\mathsf{T}}}\frac{\partial \boldsymbol{\epsilon}_{a-1}}{\partial \tau}\Bigg]\Bigg|_{\mathbf{y}=\bar{\mathbf{y}}}.$$

Rewriting $g_{i,a-1}$ as x_{ia} yields

$$\frac{\mathrm{d}\bar{x}_{ia}}{\mathrm{d}\tau}=$$
$$\Bigg[\left(\frac{\partial x_{ia}}{\partial \mathbf{x}_{a-1}^{\mathsf{T}}}+\frac{\partial x_{ia}}{\partial \boldsymbol{\epsilon}_{a-1}^{\mathsf{T}}}\frac{\partial \boldsymbol{\epsilon}_{a-1}}{\partial \mathbf{x}_{a-1}^{\mathsf{T}}}\right)\frac{\mathrm{d}\mathbf{x}_{a-1}}{\mathrm{d}\tau}$$
$$+\left(\frac{\partial x_{ia}}{\partial \mathbf{y}_{a-1}^{\mathsf{T}}}+\frac{\partial x_{ia}}{\partial \boldsymbol{\epsilon}_{a-1}^{\mathsf{T}}}\frac{\partial \boldsymbol{\epsilon}_{a-1}}{\partial \mathbf{y}_{a-1}^{\mathsf{T}}}\right)\frac{\mathrm{d}\mathbf{y}_{a-1}}{\mathrm{d}\tau}$$
$$+\left(\frac{\partial x_{ia}}{\partial \bar{\mathbf{x}}^{\mathsf{T}}}+\frac{\partial x_{ia}}{\partial \boldsymbol{\epsilon}_{a-1}^{\mathsf{T}}}\frac{\partial \boldsymbol{\epsilon}_{a-1}}{\partial \bar{\mathbf{x}}^{\mathsf{T}}}\right)\frac{\mathrm{d}\bar{\mathbf{x}}}{\mathrm{d}\tau}$$
$$+\left(\frac{\partial x_{ia}}{\partial \bar{\mathbf{y}}^{\mathsf{T}}}+\frac{\partial x_{ia}}{\partial \boldsymbol{\epsilon}_{a-1}^{\mathsf{T}}}\frac{\partial \boldsymbol{\epsilon}_{a-1}}{\partial \bar{\mathbf{y}}^{\mathsf{T}}}\right)\frac{\mathrm{d}\bar{\mathbf{y}}}{\mathrm{d}\tau}+\frac{\partial x_{ia}}{\partial \boldsymbol{\epsilon}_{a-1}^{\mathsf{T}}}\frac{\partial \boldsymbol{\epsilon}_{a-1}}{\partial \tau}\Bigg]\Bigg|_{\mathbf{y}=\bar{\mathbf{y}}}.$$

Hence, for all resident phenotypes at age $a \in \{2,\dots,N_{\mathrm{a}}\}$, we have

$$\frac{\mathrm{d}\bar{\mathbf{x}}_a}{\mathrm{d}\tau}=\Bigg[\left(\frac{\partial \mathbf{x}_a}{\partial \mathbf{x}_{a-1}^{\mathsf{T}}}+\frac{\partial \mathbf{x}_a}{\partial \boldsymbol{\epsilon}_{a-1}^{\mathsf{T}}}\frac{\partial \boldsymbol{\epsilon}_{a-1}}{\partial \mathbf{x}_{a-1}^{\mathsf{T}}}\right)\frac{\mathrm{d}\mathbf{x}_{a-1}}{\mathrm{d}\tau}$$
$$+\left(\frac{\partial \mathbf{x}_a}{\partial \mathbf{y}_{a-1}^{\mathsf{T}}}+\frac{\partial \mathbf{x}_a}{\partial \boldsymbol{\epsilon}_{a-1}^{\mathsf{T}}}\frac{\partial \boldsymbol{\epsilon}_{a-1}}{\partial \mathbf{y}_{a-1}^{\mathsf{T}}}\right)\frac{\mathrm{d}\mathbf{y}_{a-1}}{\mathrm{d}\tau}$$
$$+\left(\frac{\partial \mathbf{x}_a}{\partial \bar{\mathbf{x}}^{\mathsf{T}}}+\frac{\partial \mathbf{x}_a}{\partial \boldsymbol{\epsilon}_{a-1}^{\mathsf{T}}}\frac{\partial \boldsymbol{\epsilon}_{a-1}}{\partial \bar{\mathbf{x}}^{\mathsf{T}}}\right)\frac{\mathrm{d}\bar{\mathbf{x}}}{\mathrm{d}\tau}$$
$$+\left(\frac{\partial \mathbf{x}_a}{\partial \bar{\mathbf{y}}^{\mathsf{T}}}+\frac{\partial \mathbf{x}_a}{\partial \boldsymbol{\epsilon}_{a-1}^{\mathsf{T}}}\frac{\partial \boldsymbol{\epsilon}_{a-1}}{\partial \bar{\mathbf{y}}^{\mathsf{T}}}\right)\frac{\mathrm{d}\bar{\mathbf{y}}}{\mathrm{d}\tau}+\frac{\partial \mathbf{x}_a}{\partial \boldsymbol{\epsilon}_{a-1}^{\mathsf{T}}}\frac{\partial \boldsymbol{\epsilon}_{a-1}}{\partial \tau}\Bigg]\Bigg|_{\mathbf{y}=\bar{\mathbf{y}}}. \tag{I2}$$

Here we used the following series of definitions. The matrix of *direct effects of social partner's phenotype at age a on the mutant's phenotype at age j* is

$$\left.\frac{\partial \mathbf{x}_j^{\mathsf{T}}}{\partial \bar{\mathbf{x}}_a}\right|_{\mathbf{y}=\bar{\mathbf{y}}}\equiv\left.\begin{pmatrix}\frac{\partial x_{1j}}{\partial \bar{x}_{1a}} & \cdots & \frac{\partial x_{N_{\mathrm{s}}j}}{\partial \bar{x}_{1a}}\\ \vdots & \ddots & \vdots\\ \frac{\partial x_{1j}}{\partial \bar{x}_{N_{\mathrm{s}}a}} & \cdots & \frac{\partial x_{N_{\mathrm{s}}j}}{\partial \bar{x}_{N_{\mathrm{s}}a}}\end{pmatrix}\right|_{\mathbf{y}=\bar{\mathbf{y}}}\in\mathbb{R}^{N_{\mathrm{s}}\times N_{\mathrm{s}}},$$

and the block matrix of direct effects of social partners' phenotype on a mutant's phenotype is given by Layer 2, Eq. 6 with $\bar{\boldsymbol{\zeta}}=\bar{\mathbf{x}}$. The matrix $\partial\mathbf{x}_a^{\mathsf{T}}/\partial\bar{\mathbf{x}}$ is the a-th block column of $\partial\mathbf{x}^{\mathsf{T}}/\partial\bar{\mathbf{x}}$.

Similarly, the matrix of *direct effects of social partners' gene expression at age a on a mutant's phenotype at age j* is

$$\left.\frac{\partial \mathbf{x}_j^{\mathsf{T}}}{\partial \bar{\mathbf{y}}_a}\right|_{\mathbf{y}=\bar{\mathbf{y}}}\equiv\left.\begin{pmatrix}\frac{\partial x_{1j}}{\partial \bar{y}_{1a}} & \cdots & \frac{\partial x_{N_{\mathrm{s}}j}}{\partial \bar{y}_{1a}}\\ \vdots & \ddots & \vdots\\ \frac{\partial x_{1j}}{\partial \bar{y}_{N_{\mathrm{c}}a}} & \cdots & \frac{\partial x_{N_{\mathrm{s}}j}}{\partial \bar{y}_{N_{\mathrm{c}}a}}\end{pmatrix}\right|_{\mathbf{y}=\bar{\mathbf{y}}}\in\mathbb{R}^{N_{\mathrm{c}}\times N_{\mathrm{s}}},$$

and the block matrix of direct effects of social partners' gene expression on a mutant's phenotype is given by Eq. (Layer 2, Eq. 6) with $\bar{\boldsymbol{\zeta}}=\bar{\mathbf{y}}$. The matrix $\partial\mathbf{x}_a^{\mathsf{T}}/\partial\bar{\mathbf{y}}$ is the a-th block column of $\partial\mathbf{x}^{\mathsf{T}}/\partial\bar{\mathbf{y}}$.

In turn, the matrix of *direct effects of social partners' phenotype at age a on a mutant's environment at age j* is

$$\left.\frac{\partial \boldsymbol{\epsilon}_j^{\mathsf{T}}}{\partial \bar{\mathbf{x}}_a}\right|_{\mathbf{y}=\bar{\mathbf{y}}}\equiv\left.\begin{pmatrix}\frac{\partial \epsilon_{1j}}{\partial \bar{x}_{1a}} & \cdots & \frac{\partial \epsilon_{N_{\mathrm{e}}j}}{\partial \bar{x}_{1a}}\\ \vdots & \ddots & \vdots\\ \frac{\partial \epsilon_{1j}}{\partial \bar{x}_{N_{\mathrm{s}}a}} & \cdots & \frac{\partial \epsilon_{N_{\mathrm{e}}j}}{\partial \bar{x}_{N_{\mathrm{s}}a}}\end{pmatrix}\right|_{\mathbf{y}=\bar{\mathbf{y}}}\in\mathbb{R}^{N_{\mathrm{e}}\times N_{\mathrm{s}}},$$

and the block matrix of direct effects of social partners' phenotype on a mutant's environment is given by Layer 2, Eq. 7 with $\bar{\boldsymbol{\zeta}}=\bar{\mathbf{x}}$. The matrix $\partial\boldsymbol{\epsilon}_a^{\mathsf{T}}/\partial\bar{\mathbf{x}}$ is the a-th block column of $\partial\boldsymbol{\epsilon}^{\mathsf{T}}/\partial\bar{\mathbf{x}}$.

Similarly, the matrix of *direct effects of social partners' gene expression at age a on a mutant's environment at age j* is

$$\left.\frac{\partial \boldsymbol{\epsilon}_j^{\mathsf{T}}}{\partial \bar{\mathbf{y}}_a}\right|_{\mathbf{y}=\bar{\mathbf{y}}}\equiv\left.\begin{pmatrix}\frac{\partial \epsilon_{1j}}{\partial \bar{y}_{1a}} & \cdots & \frac{\partial \epsilon_{N_{\mathrm{e}}j}}{\partial \bar{y}_{1a}}\\ \vdots & \ddots & \vdots\\ \frac{\partial \epsilon_{1j}}{\partial \bar{y}_{N_{\mathrm{c}}a}} & \cdots & \frac{\partial \epsilon_{N_{\mathrm{e}}j}}{\partial \bar{y}_{N_{\mathrm{c}}a}}\end{pmatrix}\right|_{\mathbf{y}=\bar{\mathbf{y}}}\in\mathbb{R}^{N_{\mathrm{e}}\times N_{\mathrm{c}}},$$

and the block matrix of *direct effects of social partners' gene expression on a mutant's environment* is given by Layer 2, Eq. 7 with $\bar{\boldsymbol{\zeta}}=\bar{\mathbf{y}}$. The matrix $\partial\boldsymbol{\epsilon}_a^{\mathsf{T}}/\partial\bar{\mathbf{y}}$ is the a-th block column of $\partial\boldsymbol{\epsilon}^{\mathsf{T}}/\partial\bar{\mathbf{y}}$.

Having made these definitions explicit, we now write Eq. (I2) as

$$\frac{\mathrm{d}\bar{\mathbf{x}}_a}{\mathrm{d}\tau}=\Bigg(\frac{\delta\mathbf{x}_a}{\delta\mathbf{x}_{a-1}^{\mathsf{T}}}\frac{\mathrm{d}\mathbf{x}_{a-1}}{\mathrm{d}\tau}+\frac{\delta\mathbf{x}_a}{\delta\mathbf{y}_{a-1}^{\mathsf{T}}}\frac{\mathrm{d}\mathbf{y}_{a-1}}{\mathrm{d}\tau}$$
$$+\frac{\delta\mathbf{x}_a}{\delta\bar{\mathbf{x}}^{\mathsf{T}}}\frac{\mathrm{d}\bar{\mathbf{x}}}{\mathrm{d}\tau}+\frac{\delta\mathbf{x}_a}{\delta\bar{\mathbf{y}}^{\mathsf{T}}}\frac{\mathrm{d}\bar{\mathbf{y}}}{\mathrm{d}\tau}+\frac{\delta\mathbf{x}_a}{\delta\boldsymbol{\epsilon}_{a-1}^{\mathsf{T}}}\frac{\partial\boldsymbol{\epsilon}_{a-1}}{\partial\tau}\Bigg)\Bigg|_{\mathbf{y}=\bar{\mathbf{y}}}, \tag{I3}$$

where we used the transpose of the semi-total effects of a mutant's phenotype and gene expression on her phenotype (Eqs. D10 and E9), and the the matrix of *semi-total effects of social partners' phenotype or gene expression at age a on a mutant's phenotype at age j*

$$\left.\frac{\delta\mathbf{x}_j^{\mathsf{T}}}{\delta\bar{\boldsymbol{\zeta}}_a}\right|_{\mathbf{y}=\bar{\mathbf{y}}}=\begin{cases}\left.\left(\frac{\partial\mathbf{x}_j^{\mathsf{T}}}{\partial\bar{\boldsymbol{\zeta}}_a}+\frac{\partial\boldsymbol{\epsilon}_{j-1}^{\mathsf{T}}}{\partial\bar{\boldsymbol{\zeta}}_a}\frac{\partial\mathbf{x}_j^{\mathsf{T}}}{\partial\boldsymbol{\epsilon}_{j-1}}\right)\right|_{\mathbf{y}=\bar{\mathbf{y}}} & \text{for } j>1\\ \mathbf{0} & \text{for } j=1,\end{cases} \tag{I4}$$

for $\bar{\boldsymbol{\zeta}} \in \{\bar{\mathbf{x}}, \bar{\mathbf{y}}\}$ since the initial phenotype $\mathbf{x}_1$ is constant by assumption. We also define the corresponding matrix of *semi-total effects of social partners' phenotype on a mutant's phenotype* as

$$\left.\frac{\delta \mathbf{x}^\intercal}{\delta \bar{\boldsymbol{\zeta}}}\right|_{\mathbf{y}=\bar{\mathbf{y}}} \equiv \left.\begin{pmatrix} \frac{\delta \mathbf{x}_1^\intercal}{\delta \bar{\boldsymbol{\zeta}}_1} & \cdots & \frac{\delta \mathbf{x}_{N_\mathrm{a}}^\intercal}{\delta \bar{\boldsymbol{\zeta}}_1} \\ \vdots & \ddots & \vdots \\ \frac{\delta \mathbf{x}_1^\intercal}{\delta \bar{\boldsymbol{\zeta}}_{N_\mathrm{a}}} & \cdots & \frac{\delta \mathbf{x}_{N_\mathrm{a}}^\intercal}{\delta \bar{\boldsymbol{\zeta}}_{N_\mathrm{a}}} \end{pmatrix}\right|_{\mathbf{y}=\bar{\mathbf{y}}}$$

$$= \left.\begin{pmatrix} \mathbf{0} & \frac{\delta \mathbf{x}_2^\intercal}{\delta \bar{\boldsymbol{\zeta}}_1} & \cdots & \frac{\delta \mathbf{x}_{N_\mathrm{a}}^\intercal}{\delta \bar{\boldsymbol{\zeta}}_1} \\ \mathbf{0} & \frac{\delta \mathbf{x}_2^\intercal}{\delta \bar{\boldsymbol{\zeta}}_1} & \cdots & \frac{\delta \mathbf{x}_{N_\mathrm{a}}^\intercal}{\delta \bar{\boldsymbol{\zeta}}_1} \\ \vdots & \vdots & \ddots & \vdots \\ \mathbf{0} & \frac{\delta \mathbf{x}_2^\intercal}{\delta \bar{\boldsymbol{\zeta}}_{N_\mathrm{a}}} & \cdots & \frac{\delta \mathbf{x}_{N_\mathrm{a}}^\intercal}{\delta \bar{\boldsymbol{\zeta}}_{N_\mathrm{a}}} \end{pmatrix}\right|_{\mathbf{y}=\bar{\mathbf{y}}}, \tag{I5}$$

for $\bar{\boldsymbol{\zeta}} \in \{\bar{\mathbf{x}}, \bar{\mathbf{y}}\}$. The matrix $\delta \mathbf{x}_a^\intercal / \delta \bar{\boldsymbol{\zeta}}$ is the a-th block column of $\delta \mathbf{x}^\intercal / \delta \bar{\boldsymbol{\zeta}}$. Using Layer 2, Eq. 4c and since the initial phenotype $\mathbf{x}_1$ is constant by assumption, we have that

$$\frac{\partial \boldsymbol{\epsilon}^\intercal}{\partial \bar{\boldsymbol{\zeta}}} \frac{\partial \mathbf{x}^\intercal}{\partial \boldsymbol{\epsilon}} = \left(\sum_{k=1}^{N_\mathrm{a}} \frac{\partial \boldsymbol{\epsilon}_k^\intercal}{\partial \bar{\boldsymbol{\zeta}}_a} \frac{\partial \mathbf{x}_j^\intercal}{\partial \boldsymbol{\epsilon}_k} \right) = \left(\begin{cases} \frac{\partial \boldsymbol{\epsilon}_{j-1}^\intercal}{\partial \bar{\boldsymbol{\zeta}}_a} \frac{\partial \mathbf{x}_j^\intercal}{\partial \boldsymbol{\epsilon}_{j-1}} & \text{for } j > 1 \\ \mathbf{0} & \text{for } j = 1 \end{cases} \right), \tag{I6}$$

for $\bar{\boldsymbol{\zeta}} \in \{\bar{\mathbf{x}}, \bar{\mathbf{y}}\}$, which equals the rightmost terms in Eqs. (I4). Thus, from Eqs. (I4), (I5), and (I6), it follows that the block matrix of semi-total effects of social partners' phenotype or gene expression on a mutant's phenotype satisfies Layer 3, Eq. 3.

Noting that $\delta \mathbf{x}_a / \delta \bar{\mathbf{z}}^\intercal = (\delta \mathbf{x}_a / \delta \bar{\mathbf{x}}^\intercal, \delta \mathbf{x}_a / \delta \bar{\mathbf{y}}^\intercal)$ and that evaluation of $\mathrm{d}\mathbf{z}_a / \mathrm{d}\tau$ and $\partial \boldsymbol{\epsilon}_a / \partial \tau$ at $\mathbf{y} = \bar{\mathbf{y}}$ is $\mathrm{d}\bar{\mathbf{z}}_a / \mathrm{d}\tau$ and $\partial \bar{\boldsymbol{\epsilon}}_a / \partial \tau$ respectively, Eq. (I3) can be written as

$$\frac{\mathrm{d}\bar{\mathbf{x}}_a}{\mathrm{d}\tau} = \left(\frac{\delta \mathbf{x}_a}{\delta \mathbf{x}_{a-1}^\intercal} \frac{\mathrm{d}\bar{\mathbf{x}}_{a-1}}{\mathrm{d}\tau} + \frac{\delta \mathbf{x}_a}{\delta \mathbf{y}_{a-1}^\intercal} \frac{\mathrm{d}\bar{\mathbf{y}}_{a-1}}{\mathrm{d}\tau} + \frac{\delta \mathbf{x}_a}{\delta \bar{\mathbf{z}}^\intercal} \frac{\mathrm{d}\bar{\mathbf{z}}}{\mathrm{d}\tau} + \frac{\delta \mathbf{x}_a}{\delta \boldsymbol{\epsilon}_{a-1}^\intercal} \frac{\partial \bar{\boldsymbol{\epsilon}}_{a-1}}{\partial \tau} \right)\Bigg|_{\mathbf{y}=\bar{\mathbf{y}}},$$

which is a recursion for $\mathrm{d}\bar{\mathbf{x}}_a / \mathrm{d}\tau$ over a. Expanding this recursion two steps yields

$$\begin{aligned} \frac{\mathrm{d}\bar{\mathbf{x}}_a}{\mathrm{d}\tau} = \Bigg\{ & \frac{\delta \mathbf{x}_a}{\delta \mathbf{x}_{a-1}^\intercal} \Bigg[\frac{\delta \mathbf{x}_{a-1}}{\delta \mathbf{x}_{a-2}^\intercal} \Bigg(\frac{\delta \mathbf{x}_{a-2}}{\delta \mathbf{x}_{a-3}^\intercal} \frac{\mathrm{d}\bar{\mathbf{x}}_{a-3}}{\mathrm{d}\tau} + \frac{\delta \mathbf{x}_{a-2}}{\delta \mathbf{y}_{a-3}^\intercal} \frac{\mathrm{d}\bar{\mathbf{y}}_{a-3}}{\mathrm{d}\tau} \\ & + \frac{\delta \mathbf{x}_{a-2}}{\delta \bar{\mathbf{z}}^\intercal} \frac{\mathrm{d}\bar{\mathbf{z}}}{\mathrm{d}\tau} + \frac{\delta \mathbf{x}_{a-2}}{\delta \boldsymbol{\epsilon}_{a-3}^\intercal} \frac{\partial \bar{\boldsymbol{\epsilon}}_{a-3}}{\partial \tau} \Bigg) \\ & + \frac{\delta \mathbf{x}_{a-1}}{\delta \mathbf{y}_{a-1}^\intercal} \frac{\mathrm{d}\bar{\mathbf{y}}_{a-2}}{\mathrm{d}\tau} + \frac{\delta \mathbf{x}_{a-1}}{\delta \bar{\mathbf{z}}^\intercal} \frac{\mathrm{d}\bar{\mathbf{z}}}{\mathrm{d}\tau} + \frac{\delta \mathbf{x}_{a-1}}{\delta \boldsymbol{\epsilon}_{a-2}^\intercal} \frac{\partial \bar{\boldsymbol{\epsilon}}_{a-2}}{\partial \tau} \Bigg] \\ & + \frac{\delta \mathbf{x}_a}{\delta \mathbf{y}_{a-1}^\intercal} \frac{\mathrm{d}\bar{\mathbf{y}}_{a-1}}{\mathrm{d}\tau} + \frac{\delta \mathbf{x}_a}{\delta \bar{\mathbf{z}}^\intercal} \frac{\mathrm{d}\bar{\mathbf{z}}}{\mathrm{d}\tau} + \frac{\delta \mathbf{x}_a}{\delta \boldsymbol{\epsilon}_{a-1}^\intercal} \frac{\partial \bar{\boldsymbol{\epsilon}}_{a-1}}{\partial \tau} \Bigg\}\Bigg|_{\mathbf{y}=\bar{\mathbf{y}}}. \end{aligned}$$

Collecting the derivatives with respect to τ yields

$$\begin{aligned} \frac{\mathrm{d}\bar{\mathbf{x}}_a}{\mathrm{d}\tau} = & \Bigg[\left(\frac{\delta \mathbf{x}_a}{\delta \mathbf{x}_{a-1}^\intercal} \frac{\delta \mathbf{x}_{a-1}}{\delta \mathbf{x}_{a-2}^\intercal} \frac{\delta \mathbf{x}_{a-2}}{\delta \mathbf{x}_{a-3}^\intercal} \right) \frac{\mathrm{d}\bar{\mathbf{x}}_{a-3}}{\mathrm{d}\tau} \\ & + \left(\frac{\delta \mathbf{x}_a}{\delta \mathbf{x}_{a-1}^\intercal} \frac{\delta \mathbf{x}_{a-1}}{\delta \mathbf{x}_{a-2}^\intercal} \frac{\delta \mathbf{x}_{a-2}}{\delta \mathbf{y}_{a-3}^\intercal} \right) \frac{\mathrm{d}\bar{\mathbf{y}}_{a-3}}{\mathrm{d}\tau} \\ & + \left(\frac{\delta \mathbf{x}_a}{\delta \mathbf{x}_{a-1}^\intercal} \frac{\delta \mathbf{x}_{a-1}}{\delta \mathbf{y}_{a-1}^\intercal} \right) \frac{\mathrm{d}\bar{\mathbf{y}}_{a-2}}{\mathrm{d}\tau} + \frac{\delta \mathbf{x}_a}{\delta \mathbf{y}_{a-1}^\intercal} \frac{\mathrm{d}\bar{\mathbf{y}}_{a-1}}{\mathrm{d}\tau} \\ & + \left(\frac{\delta \mathbf{x}_a}{\delta \mathbf{x}_{a-1}^\intercal} \frac{\delta \mathbf{x}_{a-1}}{\delta \mathbf{x}_{a-2}^\intercal} \frac{\delta \mathbf{x}_{a-2}}{\delta \boldsymbol{\epsilon}_{a-3}^\intercal} \right) \frac{\partial \bar{\boldsymbol{\epsilon}}_{a-3}}{\partial \tau} \\ & + \left(\frac{\delta \mathbf{x}_a}{\delta \mathbf{x}_{a-1}^\intercal} \frac{\delta \mathbf{x}_{a-1}}{\delta \boldsymbol{\epsilon}_{a-2}^\intercal} \right) \frac{\partial \bar{\boldsymbol{\epsilon}}_{a-2}}{\partial \tau} + \frac{\delta \mathbf{x}_a}{\delta \boldsymbol{\epsilon}_{a-1}^\intercal} \frac{\partial \bar{\boldsymbol{\epsilon}}_{a-1}}{\partial \tau} \\ & + \left(\frac{\delta \mathbf{x}_a}{\delta \mathbf{x}_{a-1}^\intercal} \frac{\delta \mathbf{x}_{a-1}}{\delta \mathbf{x}_{a-2}^\intercal} \frac{\delta \mathbf{x}_{a-2}}{\delta \bar{\mathbf{z}}^\intercal} + \frac{\delta \mathbf{x}_a}{\delta \mathbf{x}_{a-1}^\intercal} \frac{\delta \mathbf{x}_{a-1}}{\delta \bar{\mathbf{z}}^\intercal} + \frac{\delta \mathbf{x}_a}{\delta \bar{\mathbf{z}}^\intercal} \right) \frac{\mathrm{d}\bar{\mathbf{z}}}{\mathrm{d}\tau} \Bigg]\Bigg|_{\mathbf{y}=\bar{\mathbf{y}}}. \end{aligned}$$

Inspection shows that by expanding the recursion completely and since we assume that initial phenotype does not evolve (i.e., $\mathrm{d}\bar{\mathbf{x}}_1 / \mathrm{d}\tau = \mathbf{0}$), the resulting expression can be succinctly written as

$$\begin{aligned} \frac{\mathrm{d}\bar{\mathbf{x}}_a}{\mathrm{d}\tau} = \Bigg(& \sum_{j=1}^{a-1} \overset{\curvearrowleft}{\prod_{k=j+1}^{a-1}} \frac{\delta \mathbf{x}_{k+1}}{\delta \mathbf{x}_k^\intercal} \frac{\delta \mathbf{x}_{j+1}}{\delta \mathbf{y}_j^\intercal} \frac{\mathrm{d}\bar{\mathbf{y}}_j}{\mathrm{d}\tau} \\ & + \sum_{j=1}^{a-1} \overset{\curvearrowleft}{\prod_{k=j+1}^{a-1}} \frac{\delta \mathbf{x}_{k+1}}{\delta \mathbf{x}_k^\intercal} \frac{\delta \mathbf{x}_{j+1}}{\delta \boldsymbol{\epsilon}_j^\intercal} \frac{\partial \bar{\boldsymbol{\epsilon}}_j}{\partial \tau} \\ & + \sum_{j=1}^{a-1} \overset{\curvearrowleft}{\prod_{k=j+1}^{a-1}} \frac{\delta \mathbf{x}_{k+1}}{\delta \mathbf{x}_k^\intercal} \frac{\delta \mathbf{x}_{j+1}}{\delta \bar{\mathbf{z}}^\intercal} \frac{\mathrm{d}\bar{\mathbf{z}}}{\mathrm{d}\tau} \Bigg)\Bigg|_{\mathbf{y}=\bar{\mathbf{y}}}, \end{aligned}$$

where the $\curvearrowleft$ denotes left multiplication. Note that the products over k are the transpose of the total effects of a mutant's phenotype at age $j+1$ on her phenotype at age a (Layer 4, Eq. 2). Hence,

$$\begin{aligned} \frac{\mathrm{d}\bar{\mathbf{x}}_a}{\mathrm{d}\tau} = \Bigg(& \sum_{j=1}^{a-1} \frac{\mathrm{d}\mathbf{x}_a}{\mathrm{d}\mathbf{x}_{j+1}^\intercal} \frac{\delta \mathbf{x}_{j+1}}{\delta \mathbf{y}_j^\intercal} \frac{\mathrm{d}\bar{\mathbf{y}}_j}{\mathrm{d}\tau} + \sum_{j=1}^{a-1} \frac{\mathrm{d}\mathbf{x}_a}{\mathrm{d}\mathbf{x}_{j+1}^\intercal} \frac{\delta \mathbf{x}_{j+1}}{\delta \boldsymbol{\epsilon}_j^\intercal} \frac{\partial \bar{\boldsymbol{\epsilon}}_j}{\partial \tau} \\ & + \sum_{j=1}^{a-1} \frac{\mathrm{d}\mathbf{x}_a}{\mathrm{d}\mathbf{x}_{j+1}^\intercal} \frac{\delta \mathbf{x}_{j+1}}{\delta \bar{\mathbf{z}}^\intercal} \frac{\mathrm{d}\bar{\mathbf{z}}}{\mathrm{d}\tau} \Bigg)\Bigg|_{\mathbf{y}=\bar{\mathbf{y}}}. \end{aligned} \tag{I7}$$

Before simplifying Eq. (I7), we introduce a series of matrices that are analogous to those already provided, based on Eq. (E17). The matrix of *total effects of social partners' phenotype or gene expression at age a on a mutant's phenotype at age j* is

$$\left.\frac{\mathrm{d}\mathbf{x}_j^\intercal}{\mathrm{d}\bar{\boldsymbol{\zeta}}_a}\right|_{\mathbf{y}=\bar{\mathbf{y}}} = \begin{cases} \left.\sum_{l=1}^{N_\mathrm{a}} \left(\frac{\delta \mathbf{x}_l^\intercal}{\delta \bar{\boldsymbol{\zeta}}_a} \frac{\mathrm{d}\mathbf{x}_j^\intercal}{\mathrm{d}\mathbf{x}_l} \right)\right|_{\mathbf{y}=\bar{\mathbf{y}}} & \text{for } j > 1 \\ \mathbf{0} & \text{for } j = 1, \end{cases} \tag{I8}$$

for $\bar{\boldsymbol{\zeta}} \in \{\bar{\mathbf{x}}, \bar{\mathbf{y}}\}$. The block matrix of *total effects of social partners' phenotype or gene expression on a mutant's phenotype* is

thus

$$\left.\frac{\mathrm{d}\mathbf{x}^{\intercal}}{\mathrm{d}\bar{\zeta}}\right|_{\mathbf{y}=\bar{\mathbf{y}}} \equiv \left.\begin{pmatrix} \frac{\mathrm{d}\mathbf{x}_1^{\intercal}}{\mathrm{d}\bar{\zeta}_1} & \cdots & \frac{\mathrm{d}\mathbf{x}_{N_\mathrm{a}}^{\intercal}}{\mathrm{d}\bar{\zeta}_1} \\ \vdots & \ddots & \vdots \\ \frac{\mathrm{d}\mathbf{x}_1^{\intercal}}{\mathrm{d}\bar{\zeta}_{N_\mathrm{a}}} & \cdots & \frac{\mathrm{d}\mathbf{x}_{N_\mathrm{a}}^{\intercal}}{\mathrm{d}\bar{\zeta}_{N_\mathrm{a}}} \end{pmatrix}\right|_{\mathbf{y}=\bar{\mathbf{y}}}$$

$$= \left.\begin{pmatrix} \mathbf{0} & \frac{\mathrm{d}\mathbf{x}_2^{\intercal}}{\mathrm{d}\bar{\zeta}_1} & \cdots & \frac{\mathrm{d}\mathbf{x}_{N_\mathrm{a}}^{\intercal}}{\mathrm{d}\bar{\zeta}_1} \\ \mathbf{0} & \frac{\mathrm{d}\mathbf{x}_2^{\intercal}}{\mathrm{d}\bar{\zeta}_2} & \cdots & \frac{\mathrm{d}\mathbf{x}_{N_\mathrm{a}}^{\intercal}}{\mathrm{d}\bar{\zeta}_2} \\ \vdots & \vdots & \ddots & \vdots \\ \mathbf{0} & \frac{\mathrm{d}\mathbf{x}_2^{\intercal}}{\mathrm{d}\bar{\zeta}_{N_\mathrm{a}}} & \cdots & \frac{\mathrm{d}\mathbf{x}_{N_\mathrm{a}}^{\intercal}}{\mathrm{d}\bar{\zeta}_{N_\mathrm{a}}} \end{pmatrix}\right|_{\mathbf{y}=\bar{\mathbf{y}}}, \tag{I9}$$

for $\bar{\zeta} \in \{\bar{\mathbf{x}}, \bar{\mathbf{y}}\}$. Then, from Eq. (I8), the block matrix in Eq. (I9) satisfies Layer 4, Eq. 5.

Using Eqs. (E17) and (F9) and given the property of transpose of a product (i.e., $(\mathbf{AB})^{\intercal} = \mathbf{B}^{\intercal}\mathbf{A}^{\intercal}$), Eq. (I7) can be written more succinctly as

$$\frac{\mathrm{d}\bar{\mathbf{x}}_a}{\mathrm{d}\tau} = \left(\sum_{j=1}^{a-1} \frac{\mathrm{d}\mathbf{x}_a}{\mathrm{d}\mathbf{y}_j^{\intercal}} \frac{\mathrm{d}\bar{\mathbf{y}}_j}{\mathrm{d}\tau} + \sum_{j=1}^{a-1} \frac{\mathrm{d}\mathbf{x}_a}{\mathrm{d}\boldsymbol{\epsilon}_j^{\intercal}} \frac{\partial\bar{\boldsymbol{\epsilon}}_j}{\partial\tau} + \sum_{j=1}^{a-1} \frac{\mathrm{d}\mathbf{x}_a}{\mathrm{d}\mathbf{x}_{j+1}^{\intercal}} \frac{\delta\mathbf{x}_{j+1}}{\delta\bar{\mathbf{z}}^{\intercal}} \frac{\mathrm{d}\bar{\mathbf{z}}}{\mathrm{d}\tau}\right)\Bigg|_{\mathbf{y}=\bar{\mathbf{y}}}.$$

Note that from Eq. (E16), we have that $\mathrm{d}\mathbf{x}_a/\mathrm{d}\mathbf{y}_j^{\intercal} = \mathbf{0}$ for $j \geq a$, from Eq. (F10), we have that $\mathrm{d}\mathbf{x}_a/\mathrm{d}\boldsymbol{\epsilon}_j^{\intercal} = \mathbf{0}$ for $j \geq a$, and from Eq. (D15), we have that $\mathrm{d}\mathbf{x}_a/\mathrm{d}\mathbf{x}_{j+1}^{\intercal} = \mathbf{0}$ for $j+1 \geq a$. Hence, the same expression holds extending the upper bounds of the sums to the last possible age:

$$\frac{\mathrm{d}\bar{\mathbf{x}}_a}{\mathrm{d}\tau} = \left(\sum_{j=1}^{N_\mathrm{a}} \frac{\mathrm{d}\mathbf{x}_a}{\mathrm{d}\mathbf{y}_j^{\intercal}} \frac{\mathrm{d}\bar{\mathbf{y}}_j}{\mathrm{d}\tau} + \sum_{j=1}^{N_\mathrm{a}} \frac{\mathrm{d}\mathbf{x}_a}{\mathrm{d}\boldsymbol{\epsilon}_j^{\intercal}} \frac{\partial\bar{\boldsymbol{\epsilon}}_j}{\partial\tau} + \sum_{j=1}^{N_\mathrm{a}-1} \frac{\mathrm{d}\mathbf{x}_a}{\mathrm{d}\mathbf{x}_{j+1}^{\intercal}} \frac{\delta\mathbf{x}_{j+1}}{\delta\bar{\mathbf{z}}^{\intercal}} \frac{\mathrm{d}\bar{\mathbf{z}}}{\mathrm{d}\tau}\right)\Bigg|_{\mathbf{y}=\bar{\mathbf{y}}}.$$

Changing the sum index for the last terms yields

$$\frac{\mathrm{d}\bar{\mathbf{x}}_a}{\mathrm{d}\tau} = \left(\sum_{j=1}^{N_\mathrm{a}} \frac{\mathrm{d}\mathbf{x}_a}{\mathrm{d}\mathbf{y}_j^{\intercal}} \frac{\mathrm{d}\bar{\mathbf{y}}_j}{\mathrm{d}\tau} + \sum_{j=1}^{N_\mathrm{a}} \frac{\mathrm{d}\mathbf{x}_a}{\mathrm{d}\boldsymbol{\epsilon}_j^{\intercal}} \frac{\partial\bar{\boldsymbol{\epsilon}}_j}{\partial\tau} + \sum_{j=2}^{N_\mathrm{a}} \frac{\mathrm{d}\mathbf{x}_a}{\mathrm{d}\mathbf{x}_j^{\intercal}} \frac{\delta\mathbf{x}_j}{\delta\bar{\mathbf{z}}^{\intercal}} \frac{\mathrm{d}\bar{\mathbf{z}}}{\mathrm{d}\tau}\right)\Bigg|_{\mathbf{y}=\bar{\mathbf{y}}}.$$

Expanding the matrix calculus notation for the entries of $\bar{\mathbf{z}}$ in the rightmost term yields

$$\frac{\mathrm{d}\bar{\mathbf{x}}_a}{\mathrm{d}\tau} = \left(\sum_{j=1}^{N_\mathrm{a}} \frac{\mathrm{d}\mathbf{x}_a}{\mathrm{d}\mathbf{y}_j^{\intercal}} \frac{\mathrm{d}\bar{\mathbf{y}}_j}{\mathrm{d}\tau} + \sum_{j=1}^{N_\mathrm{a}} \frac{\mathrm{d}\mathbf{x}_a}{\mathrm{d}\boldsymbol{\epsilon}_j^{\intercal}} \frac{\partial\bar{\boldsymbol{\epsilon}}_j}{\partial\tau} + \sum_{j=2}^{N_\mathrm{a}} \frac{\mathrm{d}\mathbf{x}_a}{\mathrm{d}\mathbf{x}_j^{\intercal}} \frac{\delta\mathbf{x}_j}{\delta\bar{\mathbf{x}}^{\intercal}} \frac{\mathrm{d}\bar{\mathbf{x}}}{\mathrm{d}\tau} + \sum_{j=2}^{N_\mathrm{a}} \frac{\mathrm{d}\mathbf{x}_a}{\mathrm{d}\mathbf{x}_j^{\intercal}} \frac{\delta\mathbf{x}_j}{\delta\bar{\mathbf{y}}^{\intercal}} \frac{\mathrm{d}\bar{\mathbf{y}}}{\mathrm{d}\tau}\right)\Bigg|_{\mathbf{y}=\bar{\mathbf{y}}}.$$

Expanding again the matrix calculus notation for the entries of $\bar{\mathbf{x}}$ and $\bar{\mathbf{y}}$ in the two rightmost terms yields

$$\frac{\mathrm{d}\bar{\mathbf{x}}_a}{\mathrm{d}\tau} = \left(\sum_{j=1}^{N_\mathrm{a}} \frac{\mathrm{d}\mathbf{x}_a}{\mathrm{d}\mathbf{y}_j^{\intercal}} \frac{\mathrm{d}\bar{\mathbf{y}}_j}{\mathrm{d}\tau} + \sum_{j=1}^{N_\mathrm{a}} \frac{\mathrm{d}\mathbf{x}_a}{\mathrm{d}\boldsymbol{\epsilon}_j^{\intercal}} \frac{\partial\bar{\boldsymbol{\epsilon}}_j}{\partial\tau} + \sum_{l=1}^{N_\mathrm{a}}\sum_{j=2}^{N_\mathrm{a}} \frac{\mathrm{d}\mathbf{x}_a}{\mathrm{d}\mathbf{x}_j^{\intercal}} \frac{\delta\mathbf{x}_j}{\delta\bar{\mathbf{x}}_l^{\intercal}} \frac{\mathrm{d}\bar{\mathbf{x}}_l}{\mathrm{d}\tau} + \sum_{l=1}^{N_\mathrm{a}}\sum_{j=2}^{N_\mathrm{a}} \frac{\mathrm{d}\mathbf{x}_a}{\mathrm{d}\mathbf{x}_j^{\intercal}} \frac{\delta\mathbf{x}_j}{\delta\bar{\mathbf{y}}_l^{\intercal}} \frac{\mathrm{d}\bar{\mathbf{y}}_l}{\mathrm{d}\tau}\right)\Bigg|_{\mathbf{y}=\bar{\mathbf{y}}}.$$

Using the transpose of the matrix in Eq. (I8) in the two rightmost terms, noting that $\delta\mathbf{x}_j/\delta\bar{\mathbf{x}}_l^{\intercal} = \mathbf{0}$ and $\delta\mathbf{x}_j/\delta\bar{\mathbf{y}}_l^{\intercal} = \mathbf{0}$ for $j = 1$ (from Eq. I5), yields

$$\frac{\mathrm{d}\bar{\mathbf{x}}_a}{\mathrm{d}\tau} = \left(\sum_{j=1}^{N_\mathrm{a}} \frac{\mathrm{d}\mathbf{x}_a}{\mathrm{d}\mathbf{y}_j^{\intercal}} \frac{\mathrm{d}\bar{\mathbf{y}}_j}{\mathrm{d}\tau} + \sum_{j=1}^{N_\mathrm{a}} \frac{\mathrm{d}\mathbf{x}_a}{\mathrm{d}\boldsymbol{\epsilon}_j^{\intercal}} \frac{\partial\bar{\boldsymbol{\epsilon}}_j}{\partial\tau} + \sum_{l=1}^{N_\mathrm{a}} \frac{\mathrm{d}\mathbf{x}_a}{\mathrm{d}\bar{\mathbf{x}}_l^{\intercal}} \frac{\mathrm{d}\bar{\mathbf{x}}_l}{\mathrm{d}\tau} + \sum_{l=1}^{N_\mathrm{a}} \frac{\mathrm{d}\mathbf{x}_a}{\mathrm{d}\bar{\mathbf{y}}_l^{\intercal}} \frac{\mathrm{d}\bar{\mathbf{y}}_l}{\mathrm{d}\tau}\right)\Bigg|_{\mathbf{y}=\bar{\mathbf{y}}}.$$

Applying matrix calculus notation to each term yields

$$\frac{\mathrm{d}\bar{\mathbf{x}}_a}{\mathrm{d}\tau} = \left(\frac{\mathrm{d}\mathbf{x}_a}{\mathrm{d}\mathbf{y}^{\intercal}} \frac{\mathrm{d}\bar{\mathbf{y}}}{\mathrm{d}\tau} + \frac{\mathrm{d}\mathbf{x}_a}{\mathrm{d}\boldsymbol{\epsilon}^{\intercal}} \frac{\partial\bar{\boldsymbol{\epsilon}}}{\partial\tau} + \frac{\mathrm{d}\mathbf{x}_a}{\mathrm{d}\bar{\mathbf{x}}^{\intercal}} \frac{\mathrm{d}\bar{\mathbf{x}}}{\mathrm{d}\tau} + \frac{\mathrm{d}\mathbf{x}_a}{\mathrm{d}\bar{\mathbf{y}}^{\intercal}} \frac{\mathrm{d}\bar{\mathbf{y}}}{\mathrm{d}\tau}\right)\Bigg|_{\mathbf{y}=\bar{\mathbf{y}}},$$

for $a \in \{2, \ldots, N_\mathrm{a}\}$. Since $\mathrm{d}\bar{\mathbf{x}}_1/\mathrm{d}\tau = \mathbf{0}$, it follows that

$$\frac{\mathrm{d}\bar{\mathbf{x}}}{\mathrm{d}\tau} = \left(\frac{\mathrm{d}\mathbf{x}}{\mathrm{d}\mathbf{y}^{\intercal}} \frac{\mathrm{d}\bar{\mathbf{y}}}{\mathrm{d}\tau} + \frac{\mathrm{d}\mathbf{x}}{\mathrm{d}\boldsymbol{\epsilon}^{\intercal}} \frac{\partial\bar{\boldsymbol{\epsilon}}}{\partial\tau} + \frac{\mathrm{d}\mathbf{x}}{\mathrm{d}\bar{\mathbf{x}}^{\intercal}} \frac{\mathrm{d}\bar{\mathbf{x}}}{\mathrm{d}\tau} + \frac{\mathrm{d}\mathbf{x}}{\mathrm{d}\bar{\mathbf{y}}^{\intercal}} \frac{\mathrm{d}\bar{\mathbf{y}}}{\mathrm{d}\tau}\right)\Bigg|_{\mathbf{y}=\bar{\mathbf{y}}}, \tag{I10}$$

which contains our desired $\mathrm{d}\bar{\mathbf{x}}/\mathrm{d}\tau$ on both sides of the equation.

The matrix premultiplying $\mathrm{d}\bar{\mathbf{x}}/\mathrm{d}\tau$ on the right-hand side of Eq. (I10) is $\mathrm{d}\mathbf{x}/\mathrm{d}\bar{\mathbf{x}}^{\intercal}|_{\mathbf{y}=\bar{\mathbf{y}}}$, which is square. We now make use of our assumption that the absolute value of all the eigenvalues of $\mathrm{d}\mathbf{x}/\mathrm{d}\bar{\mathbf{x}}^{\intercal}|_{\mathbf{y}=\bar{\mathbf{y}}}$ is strictly less than one, which guarantees that the resident geno-phenotype is socio-devo stable (Appendix O). Given this property of $\mathrm{d}\mathbf{x}/\mathrm{d}\bar{\mathbf{x}}^{\intercal}|_{\mathbf{y}=\bar{\mathbf{y}}}$, then $\mathbf{I} - \mathrm{d}\mathbf{x}/\mathrm{d}\bar{\mathbf{x}}^{\intercal}|_{\mathbf{y}=\bar{\mathbf{y}}}$ is invertible. Hence, we can define the transpose of the matrix of *stabilized effects of a focal individual's phenotype on a social partners' phenotype* (second equality of Layer 5, Eq. 1). Thus, solving for $\mathrm{d}\bar{\mathbf{x}}/\mathrm{d}\tau$ in Eq. (I10), we finally obtain an equation describing the evolutionary dynamics of the phenotype

$$\frac{\mathrm{d}\bar{\mathbf{x}}}{\mathrm{d}\tau} = \left[\frac{\mathrm{s}\mathbf{x}}{\mathrm{s}\bar{\mathbf{x}}^{\intercal}}\left(\frac{\mathrm{d}\mathbf{x}}{\mathrm{d}\mathbf{y}^{\intercal}} + \frac{\mathrm{d}\mathbf{x}}{\mathrm{d}\bar{\mathbf{y}}^{\intercal}}\right)\frac{\mathrm{d}\bar{\mathbf{y}}}{\mathrm{d}\tau} + \frac{\mathrm{s}\mathbf{x}}{\mathrm{s}\bar{\mathbf{x}}^{\intercal}} \frac{\mathrm{d}\mathbf{x}}{\mathrm{d}\boldsymbol{\epsilon}^{\intercal}} \frac{\partial\bar{\boldsymbol{\epsilon}}}{\partial\tau}\right]\Bigg|_{\mathbf{y}=\bar{\mathbf{y}}}.$$

Let us momentarily write $\mathbf{x} = \tilde{\mathbf{g}}(\mathbf{y}, \bar{\mathbf{y}})$ for some differentiable function $\tilde{\mathbf{g}}$ to highlight the dependence of a mutant's phenotype $\mathbf{x}$ on her gene expression $\mathbf{y}$ and on the gene expression $\bar{\mathbf{y}}$ of resident social partners. Consider the resident phenotype that develops in the context of mutant gene expression, denoted by $\check{\mathbf{x}} = \tilde{\mathbf{g}}(\bar{\mathbf{y}}, \mathbf{y})$. Hence,

$$\left.\frac{\mathrm{d}\check{\mathbf{x}}}{\mathrm{d}\mathbf{y}^{\intercal}}\right|_{\mathbf{y}=\bar{\mathbf{y}}} = \left.\frac{\mathrm{d}\tilde{\mathbf{g}}(\bar{\mathbf{y}}, \mathbf{y})}{\mathrm{d}\mathbf{y}^{\intercal}}\right|_{\mathbf{y}=\bar{\mathbf{y}}} = \left.\frac{\mathrm{d}\tilde{\mathbf{g}}(\mathbf{y}, \bar{\mathbf{y}})}{\mathrm{d}\bar{\mathbf{y}}^{\intercal}}\right|_{\mathbf{y}=\bar{\mathbf{y}}} = \left.\frac{\mathrm{d}\mathbf{x}}{\mathrm{d}\bar{\mathbf{y}}^{\intercal}}\right|_{\mathbf{y}=\bar{\mathbf{y}}}, \tag{I11}$$

where the second equality follows by exchanging dummy variables. Then, the transpose of the matrix of *total social effects of*

a mutant's gene expression on her and a partner's phenotypes is

$$\left.\frac{\mathrm{d}(\mathbf{x}+\check{\mathbf{x}})}{\mathrm{d}\mathbf{y}^{\mathsf{T}}}\right|_{\mathbf{y}=\bar{\mathbf{y}}} = \left.\left(\frac{\mathrm{d}\mathbf{x}}{\mathrm{d}\mathbf{y}^{\mathsf{T}}}+\frac{\mathrm{d}\check{\mathbf{x}}}{\mathrm{d}\mathbf{y}^{\mathsf{T}}}\right)\right|_{\mathbf{y}=\bar{\mathbf{y}}} = \left.\left(\frac{\mathrm{d}\mathbf{x}}{\mathrm{d}\mathbf{y}^{\mathsf{T}}}+\frac{\mathrm{d}\mathbf{x}}{\mathrm{d}\bar{\mathbf{y}}^{\mathsf{T}}}\right)\right|_{\mathbf{y}=\bar{\mathbf{y}}} \in \mathbb{R}^{N_{\mathrm{a}}N_{\mathrm{s}}\times N_{\mathrm{a}}N_{\mathrm{c}}}. \tag{I12}$$

Similarly, let us momentarily write $\mathbf{x}=\tilde{\tilde{\mathbf{g}}}(\mathbf{x},\bar{\mathbf{x}})$ for some differentiable function $\tilde{\tilde{\mathbf{g}}}$ to highlight the dependence of a mutant's phenotype $\mathbf{x}$ on her (developmentally earlier) phenotype $\mathbf{x}$ and on the phenotype $\bar{\mathbf{x}}$ of resident social partners. Consider the resident phenotype that develops in the context of the mutant phenotype, denoted by $\check{\mathbf{x}}=\tilde{\tilde{\mathbf{g}}}(\bar{\mathbf{x}},\mathbf{x})$. Hence,

$$\left.\frac{\mathrm{d}\check{\mathbf{x}}}{\mathrm{d}\mathbf{x}^{\mathsf{T}}}\right|_{\mathbf{y}=\bar{\mathbf{y}}} = \left.\frac{\mathrm{d}\tilde{\tilde{\mathbf{g}}}(\bar{\mathbf{x}},\mathbf{x})}{\mathrm{d}\mathbf{x}^{\mathsf{T}}}\right|_{\mathbf{y}=\bar{\mathbf{y}}} = \left.\frac{\mathrm{d}\tilde{\tilde{\mathbf{g}}}(\mathbf{x},\bar{\mathbf{x}})}{\mathrm{d}\bar{\mathbf{x}}^{\mathsf{T}}}\right|_{\mathbf{y}=\bar{\mathbf{y}}} = \left.\frac{\mathrm{d}\mathbf{x}}{\mathrm{d}\bar{\mathbf{x}}^{\mathsf{T}}}\right|_{\mathbf{y}=\bar{\mathbf{y}}}, \tag{I13}$$

where the second equality follows by exchanging dummy variables. Then, the transpose of the matrix of *total social effects of a mutant's phenotype on her and a partner's phenotypes* is

$$\left.\frac{\mathrm{d}(\mathbf{x}+\check{\mathbf{x}})}{\mathrm{d}\mathbf{x}^{\mathsf{T}}}\right|_{\mathbf{y}=\bar{\mathbf{y}}} = \left.\left(\frac{\mathrm{d}\mathbf{x}}{\mathrm{d}\mathbf{x}^{\mathsf{T}}}+\frac{\mathrm{d}\check{\mathbf{x}}}{\mathrm{d}\mathbf{x}^{\mathsf{T}}}\right)\right|_{\mathbf{y}=\bar{\mathbf{y}}} = \left.\left(\frac{\mathrm{d}\mathbf{x}}{\mathrm{d}\mathbf{x}^{\mathsf{T}}}+\frac{\mathrm{d}\mathbf{x}}{\mathrm{d}\bar{\mathbf{x}}^{\mathsf{T}}}\right)\right|_{\mathbf{y}=\bar{\mathbf{y}}} \in \mathbb{R}^{N_{\mathrm{a}}N_{\mathrm{s}}\times N_{\mathrm{a}}N_{\mathrm{s}}}. \tag{I14}$$

Thus, from Eq. (I13) and the second equality of Layer 5, Eq. 1, the transpose of the matrix of stabilized effects of a focal individual's phenotype on social partners' phenotype may also be written as

$$\left.\frac{\mathrm{s}\mathbf{x}}{\mathrm{s}\bar{\mathbf{x}}^{\mathsf{T}}}\right|_{\mathbf{y}=\bar{\mathbf{y}}} = \left(\mathbf{I}-\left.\frac{\mathrm{d}\check{\mathbf{x}}}{\mathrm{d}\mathbf{x}^{\mathsf{T}}}\right|_{\mathbf{y}=\bar{\mathbf{y}}}\right)^{-1} = \left.\sum_{\theta=1}^{\infty}\left(\frac{\mathrm{d}\check{\mathbf{x}}}{\mathrm{d}\mathbf{x}^{\mathsf{T}}}\right)^{\theta-1}\right|_{\mathbf{y}=\bar{\mathbf{y}}} \in \mathbb{R}^{N_{\mathrm{a}}N_{\mathrm{s}}\times N_{\mathrm{a}}N_{\mathrm{s}}},$$

where the last equality follows from the geometric series of matrices. This equation is the first and third equalities of Layer 5, Eq. 1.

Therefore, using Layer 5, Eq. 2 and Layer 5, Eq. 2b, the evolutionary dynamics of the phenotype are given by

$$\begin{aligned}\frac{\mathrm{d}\bar{\mathbf{x}}}{\mathrm{d}\tau} &= \left.\left(\frac{\mathrm{s}\mathbf{x}}{\mathrm{s}\bar{\mathbf{x}}^{\mathsf{T}}}\frac{\mathrm{d}(\mathbf{x}+\check{\mathbf{x}})}{\mathrm{d}\mathbf{y}^{\mathsf{T}}}\frac{\mathrm{d}\bar{\mathbf{y}}}{\mathrm{d}\tau}+\frac{\mathrm{s}\mathbf{x}}{\mathrm{s}\bar{\mathbf{x}}^{\mathsf{T}}}\frac{\mathrm{d}\mathbf{x}}{\mathrm{d}\boldsymbol{\epsilon}^{\mathsf{T}}}\frac{\partial\bar{\boldsymbol{\epsilon}}}{\partial\tau}\right)\right|_{\mathbf{y}=\bar{\mathbf{y}}}\\ &\approx \left.\left(\kappa\frac{\mathrm{s}\mathbf{x}}{\mathrm{s}\mathbf{y}^{\mathsf{T}}}\mathbf{G}_{\mathbf{y}}\frac{\mathrm{d}w}{\mathrm{d}\mathbf{y}}+\frac{\mathrm{s}\mathbf{x}}{\mathrm{s}\boldsymbol{\epsilon}^{\mathsf{T}}}\frac{\partial\bar{\boldsymbol{\epsilon}}}{\partial\tau}\right)\right|_{\mathbf{y}=\bar{\mathbf{y}}}\\ &= \left.\left(\kappa\mathbf{H}_{\mathbf{xy}}\frac{\mathrm{d}w}{\mathrm{d}\mathbf{y}}+\frac{\mathrm{s}\mathbf{x}}{\mathrm{s}\boldsymbol{\epsilon}^{\mathsf{T}}}\frac{\partial\bar{\boldsymbol{\epsilon}}}{\partial\tau}\right)\right|_{\mathbf{y}=\bar{\mathbf{y}}},\end{aligned} \tag{I15}$$

where the second line follows by using Eq. (I1) in the limit $\Delta\tau\to 0$, and the third line follows from Layer 6, Eq. 13. The first line of Eq. I15 describing evolutionary change of the phenotype in terms of evolutionary change of gene expression is a generalization of previous equations describing the evolution of a multivariate phenotype in terms of allele frequency change (e.g., the first equation on p. 49 of Engen and Sæther 2021). Eq. (I15) is Layer 7, Eq. 5 for $\boldsymbol{\zeta}=\mathbf{x}$. Using the third line of Layer 4, Eq. 22 and Layer 6, Eq. 11 yields Layer 7, Eq. 4 for $\boldsymbol{\zeta}=\mathbf{x}$, whereas using the fourth line of Layer 4, Eq. 22 and Layer 6, Eq. 12 yields Layer 7, Eq. 1a for $\boldsymbol{\zeta}=\mathbf{x}$.

Appendix J. Evolutionary dynamics of the geno-phenotype

Appendix J.1. In terms of total genetic selection

Here we obtain an equation describing the evolutionary dynamics of the resident geno-phenotype, that is, $\mathrm{d}\bar{\mathbf{z}}/\mathrm{d}\tau$. In this section, we write such an equation in terms of the total genetic selection. Since $\mathrm{d}\bar{\mathbf{z}}/\mathrm{d}\tau=(\mathrm{d}\bar{\mathbf{x}}/\mathrm{d}\tau;\mathrm{d}\bar{\mathbf{y}}/\mathrm{d}\tau)$, from Eqs. (I15) and (13a), we can write the evolutionary dynamics of the resident geno-phenotype $\bar{\mathbf{z}}$ as

$$\frac{\mathrm{d}\bar{\mathbf{z}}}{\mathrm{d}\tau}\approx\left.\left[\kappa\begin{pmatrix}\mathbf{H}_{\mathbf{xy}}\\ \mathbf{G}_{\mathbf{y}}\end{pmatrix}\frac{\mathrm{d}w}{\mathrm{d}\mathbf{y}}+\begin{pmatrix}\frac{\mathrm{s}\mathbf{x}}{\mathrm{s}\boldsymbol{\epsilon}^{\mathsf{T}}}\\ \mathbf{0}\end{pmatrix}\frac{\partial\bar{\boldsymbol{\epsilon}}}{\partial\tau}\right]\right|_{\mathbf{y}=\bar{\mathbf{y}}}. \tag{J1}$$

Using Layer 6, Eq. 13 and Layer 5, Eq. 3, this is

$$\frac{\mathrm{d}\bar{\mathbf{z}}}{\mathrm{d}\tau}\approx\left.\left[\kappa\begin{pmatrix}\frac{\mathrm{s}\mathbf{x}}{\mathrm{s}\mathbf{y}^{\mathsf{T}}}\\ \frac{\mathrm{s}\mathbf{y}}{\mathrm{s}\mathbf{y}^{\mathsf{T}}}\end{pmatrix}\mathbf{G}_{\mathbf{y}}\frac{\mathrm{d}w}{\mathrm{d}\mathbf{y}}+\begin{pmatrix}\frac{\mathrm{s}\mathbf{x}}{\mathrm{s}\boldsymbol{\epsilon}^{\mathsf{T}}}\\ \frac{\mathrm{s}\mathbf{y}}{\mathrm{s}\boldsymbol{\epsilon}^{\mathsf{T}}}\end{pmatrix}\frac{\partial\bar{\boldsymbol{\epsilon}}}{\partial\tau}\right]\right|_{\mathbf{y}=\bar{\mathbf{y}}}.$$

Using Layer 5, Eq. 4, this reduces to

$$\frac{\mathrm{d}\bar{\mathbf{z}}}{\mathrm{d}\tau}\approx\left.\left(\kappa\frac{\mathrm{s}\mathbf{z}}{\mathrm{s}\mathbf{y}^{\mathsf{T}}}\mathbf{G}_{\mathbf{y}}\frac{\mathrm{d}w}{\mathrm{d}\mathbf{y}}+\frac{\mathrm{s}\mathbf{z}}{\mathrm{s}\boldsymbol{\epsilon}^{\mathsf{T}}}\frac{\partial\bar{\boldsymbol{\epsilon}}}{\partial\tau}\right)\right|_{\mathbf{y}=\bar{\mathbf{y}}}.$$

Using Layer 6, Eq. 13 yields Layer 7, Eq. 5 for $\boldsymbol{\zeta}=\mathbf{z}$. Using the third line of Layer 4, Eq. 22 and Layer 6, Eq. 11 yields Layer 7, Eq. 4 for $\boldsymbol{\zeta}=\mathbf{z}$, whereas using the fourth line of Layer 4, Eq. 22 and Layer 6, Eq. 12 yields Layer 7, Eq. 1a for $\boldsymbol{\zeta}=\mathbf{z}$.

In contrast to other arrangements, the premultiplying matrix $\mathbf{H}_{\mathbf{zy}}$ is non-singular if $\mathbf{G}_{\mathbf{y}}$ is non-singular. Indeed, if

$$\left.\frac{\mathrm{s}\mathbf{z}}{\mathrm{s}\mathbf{y}^{\mathsf{T}}}\right|_{\mathbf{y}=\bar{\mathbf{y}}}\mathbf{r}=\mathbf{0}$$

for some vector $\mathbf{r}$, then from Layer 5, Eq. 4a and Layer 5, Eq. 3b we have

$$\left.\begin{pmatrix}\frac{\mathrm{s}\mathbf{x}}{\mathrm{s}\mathbf{y}^{\mathsf{T}}}\\ \mathbf{I}\end{pmatrix}\right|_{\mathbf{y}=\bar{\mathbf{y}}}\mathbf{r}=\mathbf{0}.$$

Doing the multiplication yields

$$\begin{pmatrix}\left.\frac{\mathrm{s}\mathbf{x}}{\mathrm{s}\mathbf{y}^{\mathsf{T}}}\right|_{\mathbf{y}=\bar{\mathbf{y}}}\mathbf{r}\\ \mathbf{r}\end{pmatrix}=\mathbf{0},$$

which implies that $\mathbf{r}=\mathbf{0}$, so $\mathrm{s}\mathbf{z}/\mathrm{s}\mathbf{y}^{\mathsf{T}}|_{\mathbf{y}=\bar{\mathbf{y}}}$ is non-singular. Thus, $\mathbf{H}_{\mathbf{zy}}$ is non-singular if $\mathbf{G}_{\mathbf{y}}$ is non-singular.

Appendix J.2. In terms of total selection on the geno-phenotype

Here we write the evolutionary dynamics of the geno-phenotype in terms of the total selection gradient of the geno-phenotype.

First, using Layer 6, Eq. 2, we define the *additive genetic covariance matrix of the undeveloped geno-phenotype* $\hat{\mathbf{z}} = (\bar{\mathbf{x}}; \mathbf{y})$ as

$$\mathbf{G}_{\hat{\mathbf{z}}} \equiv \mathrm{cov}[\mathbf{a}_{\hat{\mathbf{z}}}, \mathbf{a}_{\hat{\mathbf{z}}}] = \left(\frac{\mathrm{d}\hat{\mathbf{z}}}{\mathrm{d}\mathbf{y}^\intercal}\mathbf{G}_{\mathbf{y}}\frac{\mathrm{d}\hat{\mathbf{z}}^\intercal}{\mathrm{d}\mathbf{y}}\right)\Bigg|_{\mathbf{y}=\bar{\mathbf{y}}} \in \mathbb{R}^{N_{\mathrm{a}}(N_{\mathrm{s}}+N_{\mathrm{c}})\times N_{\mathrm{a}}(N_{\mathrm{s}}+N_{\mathrm{c}})}.$$

By definition of $\hat{\mathbf{z}}$, we have

$$\mathbf{G}_{\hat{\mathbf{z}}} = \left[\begin{pmatrix}\frac{\mathrm{d}\bar{\mathbf{x}}}{\mathrm{d}\mathbf{y}^\intercal}\\ \frac{\mathrm{d}\mathbf{y}}{\mathrm{d}\mathbf{y}^\intercal}\end{pmatrix}\mathbf{G}_{\mathbf{y}}\begin{pmatrix}\frac{\mathrm{d}\bar{\mathbf{x}}^\intercal}{\mathrm{d}\mathbf{y}} & \frac{\mathrm{d}\mathbf{y}^\intercal}{\mathrm{d}\mathbf{y}}\end{pmatrix}\right]\Bigg|_{\mathbf{y}=\bar{\mathbf{y}}}.$$

From Eq. (13c), the resident phenotype is independent of mutant gene expression, so

$$\mathbf{G}_{\hat{\mathbf{z}}} = \left[\begin{pmatrix}\mathbf{0}\\ \mathbf{I}\end{pmatrix}\mathbf{G}_{\mathbf{y}}\begin{pmatrix}\mathbf{0} & \mathbf{I}\end{pmatrix}\right]\Bigg|_{\mathbf{y}=\bar{\mathbf{y}}}.$$

Doing the matrix multiplication yields

$$\mathbf{G}_{\hat{\mathbf{z}}} = \left[\begin{pmatrix}\mathbf{0}\\ \mathbf{I}\end{pmatrix}\begin{pmatrix}\mathbf{0} & \mathbf{G}_{\mathbf{y}}\end{pmatrix}\right]\Bigg|_{\mathbf{y}=\bar{\mathbf{y}}} = \begin{pmatrix}\mathbf{0} & \mathbf{0}\\ \mathbf{0} & \mathbf{G}_{\mathbf{y}}\end{pmatrix}. \tag{J2}$$

The matrix $\mathbf{G}_{\hat{\mathbf{z}}}$ is singular because the undeveloped geno-phenotype includes gene expression (i.e., $\mathrm{d}\hat{\mathbf{z}}^\intercal/\mathrm{d}\mathbf{y}|_{\mathbf{y}=\bar{\mathbf{y}}}$ has fewer rows than columns). For this reason, the matrix $\mathbf{G}_{\hat{\mathbf{z}}}$ would still be singular even if the zero block entries in Eq. (J2) were non-zero (i.e., if $\mathrm{d}\bar{\mathbf{x}}^\intercal/\mathrm{d}\mathbf{y}|_{\mathbf{y}=\bar{\mathbf{y}}} \neq \mathbf{0}$).

Now, we write an alternative factorization of $\mathbf{H}_{\mathbf{z}}$ in terms of $\mathbf{G}_{\hat{\mathbf{z}}}$. Using Layer 4, Eq. 9 and Layer 5, Eq. 5, consider the matrix

$$\left(\frac{\mathrm{s}\mathbf{z}}{\mathrm{s}\mathbf{z}^\intercal}\mathbf{G}_{\hat{\mathbf{z}}}\frac{\mathrm{d}\mathbf{z}^\intercal}{\mathrm{d}\mathbf{z}}\right)\Bigg|_{\mathbf{y}=\bar{\mathbf{y}}} = \left[\begin{pmatrix}\frac{\mathrm{s}\mathbf{x}}{\mathrm{s}\mathbf{x}^\intercal} & \frac{\mathrm{s}\mathbf{x}}{\mathrm{s}\mathbf{y}^\intercal}\\ \mathbf{0} & \mathbf{I}\end{pmatrix}\begin{pmatrix}\mathbf{0} & \mathbf{0}\\ \mathbf{0} & \mathbf{G}_{\mathbf{y}}\end{pmatrix}\begin{pmatrix}\frac{\mathrm{d}\mathbf{x}^\intercal}{\mathrm{d}\mathbf{x}} & \mathbf{0}\\ \frac{\mathrm{d}\mathbf{x}^\intercal}{\mathrm{d}\mathbf{y}} & \mathbf{I}\end{pmatrix}\right]\Bigg|_{\mathbf{y}=\bar{\mathbf{y}}}.$$

Doing the matrix multiplication yields

$$\left(\frac{\mathrm{s}\mathbf{z}}{\mathrm{s}\mathbf{z}^\intercal}\mathbf{G}_{\hat{\mathbf{z}}}\frac{\mathrm{d}\mathbf{z}^\intercal}{\mathrm{d}\mathbf{z}}\right)\Bigg|_{\mathbf{y}=\bar{\mathbf{y}}} = \left[\begin{pmatrix}\frac{\mathrm{s}\mathbf{x}}{\mathrm{s}\mathbf{x}^\intercal} & \frac{\mathrm{s}\mathbf{x}}{\mathrm{s}\mathbf{y}^\intercal}\\ \mathbf{0} & \mathbf{I}\end{pmatrix}\begin{pmatrix}\mathbf{0} & \mathbf{0}\\ \mathbf{G}_{\mathbf{y}}\frac{\mathrm{d}\mathbf{x}^\intercal}{\mathrm{d}\mathbf{y}} & \mathbf{G}_{\mathbf{y}}\end{pmatrix}\right]\Bigg|_{\mathbf{y}=\bar{\mathbf{y}}}$$
$$= \begin{pmatrix}\frac{\mathrm{s}\mathbf{x}}{\mathrm{s}\mathbf{y}^\intercal}\mathbf{G}_{\mathbf{y}}\frac{\mathrm{d}\mathbf{x}^\intercal}{\mathrm{d}\mathbf{y}} & \frac{\mathrm{s}\mathbf{x}}{\mathrm{s}\mathbf{y}^\intercal}\mathbf{G}_{\mathbf{y}}\\ \mathbf{G}_{\mathbf{y}}\frac{\mathrm{d}\mathbf{x}^\intercal}{\mathrm{d}\mathbf{y}} & \mathbf{G}_{\mathbf{y}}\end{pmatrix}\Bigg|_{\mathbf{y}=\bar{\mathbf{y}}}.$$

Using Layer 5, Eq. 3b, we have

$$\left(\frac{\mathrm{s}\mathbf{z}}{\mathrm{s}\mathbf{z}^\intercal}\mathbf{G}_{\hat{\mathbf{z}}}\frac{\mathrm{d}\mathbf{z}^\intercal}{\mathrm{d}\mathbf{z}}\right)\Bigg|_{\mathbf{y}=\bar{\mathbf{y}}} = \begin{pmatrix}\frac{\mathrm{s}\mathbf{x}}{\mathrm{s}\mathbf{y}^\intercal}\mathbf{G}_{\mathbf{y}}\frac{\mathrm{d}\mathbf{x}^\intercal}{\mathrm{d}\mathbf{y}} & \frac{\mathrm{s}\mathbf{x}}{\mathrm{s}\mathbf{y}^\intercal}\mathbf{G}_{\mathbf{y}}\frac{\mathrm{d}\mathbf{y}^\intercal}{\mathrm{d}\mathbf{y}}\\ \frac{\mathrm{s}\mathbf{y}}{\mathrm{s}\mathbf{y}^\intercal}\mathbf{G}_{\mathbf{y}}\frac{\mathrm{d}\mathbf{x}^\intercal}{\mathrm{d}\mathbf{y}} & \frac{\mathrm{s}\mathbf{y}}{\mathrm{s}\mathbf{y}^\intercal}\mathbf{G}_{\mathbf{y}}\frac{\mathrm{d}\mathbf{y}^\intercal}{\mathrm{d}\mathbf{y}}\end{pmatrix}\Bigg|_{\mathbf{y}=\bar{\mathbf{y}}}.$$

Notice that the matrix on the right-hand side is

$$\left(\frac{\mathrm{s}\mathbf{z}}{\mathrm{s}\mathbf{y}^\intercal}\mathbf{G}_{\mathbf{y}}\frac{\mathrm{d}\mathbf{z}^\intercal}{\mathrm{d}\mathbf{y}}\right)\Bigg|_{\mathbf{y}=\bar{\mathbf{y}}} = \mathbf{H}_{\mathbf{z}}.$$

Hence, we obtain an alternative factorization for $\mathbf{H}_{\mathbf{z}}$ as

$$\mathbf{H}_{\mathbf{z}} = \left(\frac{\mathrm{s}\mathbf{z}}{\mathrm{s}\mathbf{z}^\intercal}\mathbf{G}_{\hat{\mathbf{z}}}\frac{\mathrm{d}\mathbf{z}^\intercal}{\mathrm{d}\mathbf{z}}\right)\Bigg|_{\mathbf{y}=\bar{\mathbf{y}}}.$$

Thus, we can write the selection response of the geno-phenotype (in the form of Layer 7, Eq. 4) as

$$\kappa\mathbf{H}_{\mathbf{z}}\frac{\delta w}{\delta\mathbf{z}}\Bigg|_{\mathbf{y}=\bar{\mathbf{y}}} = \kappa\left(\frac{\mathrm{s}\mathbf{z}}{\mathrm{s}\mathbf{z}^\intercal}\mathbf{G}_{\hat{\mathbf{z}}}\frac{\mathrm{d}\mathbf{z}^\intercal}{\mathrm{d}\mathbf{z}}\frac{\delta w}{\delta\mathbf{z}}\right)\Bigg|_{\mathbf{y}=\bar{\mathbf{y}}}.$$

Using the relationship between the total and semi-total selection gradients of the geno-phenotype (second line of Layer 4, Eq. 24), this becomes

$$\kappa\mathbf{H}_{\mathbf{z}}\frac{\delta w}{\delta\mathbf{z}}\Bigg|_{\mathbf{y}=\bar{\mathbf{y}}} = \kappa\left(\frac{\mathrm{s}\mathbf{z}}{\mathrm{s}\mathbf{z}^\intercal}\mathbf{G}_{\hat{\mathbf{z}}}\frac{\mathrm{d}w}{\mathrm{d}\mathbf{z}}\right)\Bigg|_{\mathbf{y}=\bar{\mathbf{y}}}.$$

We can further simplify this equation by noticing the following. Using Layer 6, Eq. 10 and $\hat{\mathbf{z}} = (\bar{\mathbf{x}}; \mathbf{y})$, we have that the *additive socio-genetic cross-covariance matrix of the geno-phenotype and the undeveloped geno-phenotype* is

$$\mathbf{H}_{\mathbf{z}\hat{\mathbf{z}}} = \left(\frac{\mathrm{s}\mathbf{z}}{\mathrm{s}\mathbf{y}^\intercal}\mathbf{G}_{\mathbf{y}}\frac{\mathrm{d}\hat{\mathbf{z}}^\intercal}{\mathrm{d}\mathbf{y}}\right)\Bigg|_{\mathbf{y}=\bar{\mathbf{y}}} \in \mathbb{R}^{N_{\mathrm{a}}(N_{\mathrm{s}}+N_{\mathrm{c}})\times N_{\mathrm{a}}(N_{\mathrm{s}}+N_{\mathrm{c}})}. \tag{J3}$$

Expanding, we have

$$\mathbf{H}_{\mathbf{z}\hat{\mathbf{z}}} = \left[\begin{pmatrix}\frac{\mathrm{s}\mathbf{x}}{\mathrm{s}\mathbf{y}^\intercal}\\ \frac{\mathrm{s}\mathbf{y}}{\mathrm{s}\mathbf{y}^\intercal}\end{pmatrix}\mathbf{G}_{\mathbf{y}}\begin{pmatrix}\frac{\mathrm{d}\bar{\mathbf{x}}^\intercal}{\mathrm{d}\mathbf{y}} & \frac{\mathrm{d}\mathbf{y}^\intercal}{\mathrm{d}\mathbf{y}}\end{pmatrix}\right]\Bigg|_{\mathbf{y}=\bar{\mathbf{y}}}.$$

Using Layer 5, Eq. 3b and since the resident phenotype does not depend on mutant gene expression, then

$$\mathbf{H}_{\mathbf{z}\hat{\mathbf{z}}} = \left[\begin{pmatrix}\frac{\mathrm{s}\mathbf{x}}{\mathrm{s}\mathbf{y}^\intercal}\\ \mathbf{I}\end{pmatrix}\mathbf{G}_{\mathbf{y}}\begin{pmatrix}\mathbf{0} & \mathbf{I}\end{pmatrix}\right]\Bigg|_{\mathbf{y}=\bar{\mathbf{y}}}.$$

Doing the matrix multiplication yields

$$\mathbf{H}_{\mathbf{z}\hat{\mathbf{z}}} = \left[\begin{pmatrix}\frac{\mathrm{s}\mathbf{x}}{\mathrm{s}\mathbf{y}^\intercal}\\ \mathbf{I}\end{pmatrix}\begin{pmatrix}\mathbf{0} & \mathbf{G}_{\mathbf{y}}\end{pmatrix}\right]\Bigg|_{\mathbf{y}=\bar{\mathbf{y}}} = \begin{pmatrix}\mathbf{0} & \frac{\mathrm{s}\mathbf{x}}{\mathrm{s}\mathbf{y}^\intercal}\mathbf{G}_{\mathbf{y}}\\ \mathbf{0} & \mathbf{G}_{\mathbf{y}}\end{pmatrix}\Bigg|_{\mathbf{y}=\bar{\mathbf{y}}}.$$

Notice that the last matrix equals

$$\left(\frac{\mathrm{s}\mathbf{z}}{\mathrm{s}\mathbf{z}^\intercal}\mathbf{G}_{\hat{\mathbf{z}}}\right)\Bigg|_{\mathbf{y}=\bar{\mathbf{y}}}.$$

We can then write the evolutionary dynamics of the resident geno-phenotype $\bar{\mathbf{z}}$ in terms of the total selection gradient of the geno-phenotype as

$$\frac{\mathrm{d}\bar{\mathbf{z}}}{\mathrm{d}\tau} \approx \left(\kappa \mathbf{H}_{\mathbf{z}\hat{\mathbf{z}}} \frac{\mathrm{d}w}{\mathrm{d}\mathbf{z}} + \frac{\mathrm{s}\mathbf{z}}{\mathrm{s}\boldsymbol{\epsilon}^{\intercal}} \frac{\partial \bar{\boldsymbol{\epsilon}}}{\partial \tau}\right)\Bigg|_{\mathbf{y}=\bar{\mathbf{y}}}. \tag{J4}$$

The cross-covariance matrix $\mathbf{H}_{\mathbf{z}\hat{\mathbf{z}}}$ is singular because $\mathrm{d}\hat{\mathbf{z}}^{\intercal}/\mathrm{d}\mathbf{y}|_{\mathbf{y}=\bar{\mathbf{y}}}$ has fewer rows than columns since the undeveloped geno-phenotype includes gene expression. For this reason, $\mathbf{H}_{\mathbf{z}\hat{\mathbf{z}}}$ would still be singular even if the zero block entries in Eq. (J3) were non-zero (i.e., if $\mathrm{d}\bar{\mathbf{x}}^{\intercal}/\mathrm{d}\mathbf{y}|_{\mathbf{y}=\bar{\mathbf{y}}} \neq \mathbf{0}$). Then, evolutionary equilibria of the geno-phenotype do not imply absence of total selection on the geno-phenotype, even if exogenous plastic response is absent.

Appendix K. Evolutionary dynamics of the environment

Appendix K.1. In terms of endogenous and exogenous environmental change

Here we derive an equation describing the evolutionary dynamics of the environment. Let $\bar{\mathbf{z}}(\tau)$ be the resident geno-phenotype at evolutionary time τ, specifically at the point where the socio-devo stable resident is at carrying capacity, marked in Fig. 3. From the environmental constraint (2), the i-th environmental variable experienced by a mutant of age a at such evolutionary time τ is $\epsilon_{ia} = h_{ia}(\mathbf{z}_a(\tau), \bar{\mathbf{z}}(\tau), \tau))$. Then, evolutionary change in the i-th environmental variable experienced by residents at age a is

$$\frac{\Delta\bar{\epsilon}_{ia}}{\Delta\tau} = \frac{1}{\Delta\tau}\Bigg[h_{ia}\left(\mathbf{z}_a(\tau+\Delta\tau), \bar{\mathbf{z}}(\tau+\Delta\tau), \tau+\Delta\tau\right) - h_{ai}\left(\mathbf{z}_a(\tau), \bar{\mathbf{z}}(\tau), \tau\right)\Bigg]\Bigg|_{\mathbf{y}=\bar{\mathbf{y}}}.$$

Taking the limit as $\Delta\tau \to 0$, this becomes

$$\frac{\mathrm{d}\bar{\epsilon}_{ia}}{\mathrm{d}\tau} = \frac{\mathrm{d}h_{ia}(\mathbf{z}_a(\tau), \bar{\mathbf{z}}(\tau), \tau)}{\mathrm{d}\tau}\Bigg|_{\mathbf{y}=\bar{\mathbf{y}}}.$$

Applying the chain rule, we obtain

$$\frac{\mathrm{d}\bar{\epsilon}_{ia}}{\mathrm{d}\tau} = \Bigg(\sum_{j=1}^{N_\mathrm{s}} \frac{\partial h_{ia}}{\partial x_{ja}}\frac{\mathrm{d}x_{ja}}{\mathrm{d}\tau} + \sum_{j=1}^{N_\mathrm{c}} \frac{\partial h_{ia}}{\partial y_{ja}}\frac{\mathrm{d}y_{ja}}{\mathrm{d}\tau} + \sum_{k=0}^{N_\mathrm{a}}\sum_{j=1}^{N_\mathrm{s}} \frac{\partial h_{ia}}{\partial \bar{x}_{jk}}\frac{\mathrm{d}\bar{x}_{jk}}{\mathrm{d}\tau} + \sum_{k=0}^{N_\mathrm{a}}\sum_{j=1}^{N_\mathrm{c}} \frac{\partial h_{ia}}{\partial \bar{y}_{jk}}\frac{\mathrm{d}\bar{y}_{jk}}{\mathrm{d}\tau} + \frac{\partial h_{ia}}{\partial \tau}\Bigg)\Bigg|_{\mathbf{y}=\bar{\mathbf{y}}}.$$

Applying matrix calculus notation, this is

$$\frac{\mathrm{d}\bar{\epsilon}_{ia}}{\mathrm{d}\tau} = \Bigg(\frac{\partial h_{ia}}{\partial \mathbf{x}_a^{\intercal}}\frac{\mathrm{d}\mathbf{x}_a}{\mathrm{d}\tau} + \frac{\partial h_{ia}}{\partial \mathbf{y}_a^{\intercal}}\frac{\mathrm{d}\mathbf{y}_a}{\mathrm{d}\tau} + \sum_{k=0}^{N_\mathrm{a}} \frac{\partial h_{ia}}{\partial \bar{\mathbf{x}}_k^{\intercal}}\frac{\mathrm{d}\bar{\mathbf{x}}_k}{\mathrm{d}\tau} + \sum_{k=0}^{N_\mathrm{a}} \frac{\partial h_{ia}}{\partial \bar{\mathbf{y}}_k^{\intercal}}\frac{\mathrm{d}\bar{\mathbf{y}}_k}{\mathrm{d}\tau} + \frac{\partial h_{ia}}{\partial \tau}\Bigg)\Bigg|_{\mathbf{y}=\bar{\mathbf{y}}}.$$

Applying matrix calculus notation again yields

$$\frac{\mathrm{d}\bar{\epsilon}_{ia}}{\mathrm{d}\tau} = \Bigg(\frac{\partial h_{ia}}{\partial \mathbf{x}_a^{\intercal}}\frac{\mathrm{d}\mathbf{x}_a}{\mathrm{d}\tau} + \frac{\partial h_{ia}}{\partial \mathbf{y}_a^{\intercal}}\frac{\mathrm{d}\mathbf{y}_a}{\mathrm{d}\tau} + \frac{\partial h_{ia}}{\partial \bar{\mathbf{x}}^{\intercal}}\frac{\mathrm{d}\bar{\mathbf{x}}}{\mathrm{d}\tau} + \frac{\partial h_{ia}}{\partial \bar{\mathbf{y}}^{\intercal}}\frac{\mathrm{d}\bar{\mathbf{y}}}{\mathrm{d}\tau} + \frac{\partial h_{ia}}{\partial \tau}\Bigg)\Bigg|_{\mathbf{y}=\bar{\mathbf{y}}}.$$

Rewriting h_{ia} as ϵ_{ia}, we obtain

$$\frac{\mathrm{d}\bar{\epsilon}_{ia}}{\mathrm{d}\tau} = \Bigg(\frac{\partial \epsilon_{ia}}{\partial \mathbf{x}_a^{\intercal}}\frac{\mathrm{d}\mathbf{x}_a}{\mathrm{d}\tau} + \frac{\partial \epsilon_{ia}}{\partial \mathbf{y}_a^{\intercal}}\frac{\mathrm{d}\mathbf{y}_a}{\mathrm{d}\tau} + \frac{\partial \epsilon_{ia}}{\partial \bar{\mathbf{x}}^{\intercal}}\frac{\mathrm{d}\bar{\mathbf{x}}}{\mathrm{d}\tau} + \frac{\partial \epsilon_{ia}}{\partial \bar{\mathbf{y}}^{\intercal}}\frac{\mathrm{d}\bar{\mathbf{y}}}{\mathrm{d}\tau} + \frac{\partial \epsilon_{ia}}{\partial \tau}\Bigg)\Bigg|_{\mathbf{y}=\bar{\mathbf{y}}}.$$

Hence, for all environmental variables at age a, we have

$$\frac{\mathrm{d}\bar{\boldsymbol{\epsilon}}_a}{\mathrm{d}\tau} = \left(\frac{\partial \boldsymbol{\epsilon}_a}{\partial \mathbf{x}_a^{\intercal}}\frac{\mathrm{d}\mathbf{x}_a}{\mathrm{d}\tau} + \frac{\partial \boldsymbol{\epsilon}_a}{\partial \mathbf{y}_a^{\intercal}}\frac{\mathrm{d}\mathbf{y}_a}{\mathrm{d}\tau} + \frac{\partial \boldsymbol{\epsilon}_a}{\partial \bar{\mathbf{x}}^{\intercal}}\frac{\mathrm{d}\bar{\mathbf{x}}}{\mathrm{d}\tau} + \frac{\partial \boldsymbol{\epsilon}_a}{\partial \bar{\mathbf{y}}^{\intercal}}\frac{\mathrm{d}\bar{\mathbf{y}}}{\mathrm{d}\tau} + \frac{\partial \boldsymbol{\epsilon}_a}{\partial \tau}\right)\Bigg|_{\mathbf{y}=\bar{\mathbf{y}}}.$$

Note that evaluation of $\mathrm{d}\mathbf{z}_a/\mathrm{d}\tau$ and $\partial\boldsymbol{\epsilon}_a/\partial\tau$ at $\mathbf{y} = \bar{\mathbf{y}}$ is $\mathrm{d}\bar{\mathbf{z}}_a/\mathrm{d}\tau$ and $\partial\bar{\boldsymbol{\epsilon}}_a/\partial\tau$, respectively. Using Layer 2, Eq. 4d and Layer 2, Eq. 4d yields

$$\frac{\partial \boldsymbol{\epsilon}_a}{\partial \mathbf{x}^{\intercal}}\frac{\mathrm{d}\bar{\mathbf{x}}}{\mathrm{d}\tau} = \sum_{j=1}^{N_\mathrm{a}} \frac{\partial \boldsymbol{\epsilon}_a}{\partial \mathbf{x}_j^{\intercal}}\frac{\mathrm{d}\bar{\mathbf{x}}_j}{\mathrm{d}\tau} = \frac{\partial \boldsymbol{\epsilon}_a}{\partial \mathbf{x}_a^{\intercal}}\frac{\mathrm{d}\bar{\mathbf{x}}_a}{\mathrm{d}\tau}$$

$$\frac{\partial \boldsymbol{\epsilon}_a}{\partial \mathbf{y}^{\intercal}}\frac{\mathrm{d}\bar{\mathbf{y}}}{\mathrm{d}\tau} = \sum_{j=1}^{N_\mathrm{a}} \frac{\partial \boldsymbol{\epsilon}_a}{\partial \mathbf{y}_j^{\intercal}}\frac{\mathrm{d}\bar{\mathbf{y}}_j}{\mathrm{d}\tau} = \frac{\partial \boldsymbol{\epsilon}_a}{\partial \mathbf{y}_a^{\intercal}}\frac{\mathrm{d}\bar{\mathbf{y}}_a}{\mathrm{d}\tau}.$$

Then, we have

$$\frac{\mathrm{d}\bar{\boldsymbol{\epsilon}}_a}{\mathrm{d}\tau} = \left(\frac{\partial \boldsymbol{\epsilon}_a}{\partial \mathbf{x}^{\intercal}}\frac{\mathrm{d}\bar{\mathbf{x}}}{\mathrm{d}\tau} + \frac{\partial \boldsymbol{\epsilon}_a}{\partial \mathbf{y}^{\intercal}}\frac{\mathrm{d}\bar{\mathbf{y}}}{\mathrm{d}\tau} + \frac{\partial \boldsymbol{\epsilon}_a}{\partial \bar{\mathbf{x}}^{\intercal}}\frac{\mathrm{d}\bar{\mathbf{x}}}{\mathrm{d}\tau} + \frac{\partial \boldsymbol{\epsilon}_a}{\partial \bar{\mathbf{y}}^{\intercal}}\frac{\mathrm{d}\bar{\mathbf{y}}}{\mathrm{d}\tau} + \frac{\partial \bar{\boldsymbol{\epsilon}}_a}{\partial \tau}\right)\Bigg|_{\mathbf{y}=\bar{\mathbf{y}}}.$$

Now note that $\partial\boldsymbol{\epsilon}_a/\partial\mathbf{z}^{\intercal} = (\partial\boldsymbol{\epsilon}_a/\partial\mathbf{x}^{\intercal}, \partial\boldsymbol{\epsilon}_a/\partial\mathbf{y}^{\intercal})$, so

$$\frac{\mathrm{d}\bar{\boldsymbol{\epsilon}}_a}{\mathrm{d}\tau} = \left(\frac{\partial \boldsymbol{\epsilon}_a}{\partial \mathbf{z}^{\intercal}}\frac{\mathrm{d}\bar{\mathbf{z}}}{\mathrm{d}\tau} + \frac{\partial \boldsymbol{\epsilon}_a}{\partial \bar{\mathbf{z}}^{\intercal}}\frac{\mathrm{d}\bar{\mathbf{z}}}{\mathrm{d}\tau} + \frac{\partial \bar{\boldsymbol{\epsilon}}_a}{\partial \tau}\right)\Bigg|_{\mathbf{y}=\bar{\mathbf{y}}}.$$

Hence, for all environmental variables over all ages, we have

$$\frac{\mathrm{d}\bar{\boldsymbol{\epsilon}}}{\mathrm{d}\tau} = \left(\frac{\partial \boldsymbol{\epsilon}}{\partial \mathbf{z}^{\intercal}}\frac{\mathrm{d}\bar{\mathbf{z}}}{\mathrm{d}\tau} + \frac{\partial \boldsymbol{\epsilon}}{\partial \bar{\mathbf{z}}^{\intercal}}\frac{\mathrm{d}\bar{\mathbf{z}}}{\mathrm{d}\tau} + \frac{\partial \bar{\boldsymbol{\epsilon}}}{\partial \tau}\right)\Bigg|_{\mathbf{y}=\bar{\mathbf{y}}} = \left[\left(\frac{\partial \boldsymbol{\epsilon}}{\partial \mathbf{z}^{\intercal}} + \frac{\partial \boldsymbol{\epsilon}}{\partial \bar{\mathbf{z}}^{\intercal}}\right)\frac{\mathrm{d}\bar{\mathbf{z}}}{\mathrm{d}\tau} + \frac{\partial \bar{\boldsymbol{\epsilon}}}{\partial \tau}\right]\Bigg|_{\mathbf{y}=\bar{\mathbf{y}}},$$

where we use Layer 2, Eq. 9 and the block matrix of direct effects of social partners' geno-phenotype on a mutant's environment (Layer 2, Eq. 10; see also Layer 2, Eq. 7).

Let us momentarily write $\boldsymbol{\epsilon} = \tilde{\mathbf{h}}(\mathbf{z}, \bar{\mathbf{z}})$ for some differentiable function $\tilde{\mathbf{h}}$ to highlight the dependence of a mutant's environment $\boldsymbol{\epsilon}$ on her geno-phenotype $\mathbf{z}$ and on the geno-phenotype $\bar{\mathbf{z}}$ of resident social partners. Consider the environment a resident experiences when she is in the context of mutants, denoted by $\check{\boldsymbol{\epsilon}} = \tilde{\mathbf{h}}(\bar{\mathbf{z}}, \mathbf{z})$. Hence,

$$\frac{\partial \check{\boldsymbol{\epsilon}}}{\partial \mathbf{z}^{\intercal}}\Bigg|_{\mathbf{y}=\bar{\mathbf{y}}} = \frac{\partial \tilde{\mathbf{h}}(\bar{\mathbf{z}}, \mathbf{z})}{\partial \mathbf{z}^{\intercal}}\Bigg|_{\mathbf{y}=\bar{\mathbf{y}}} = \frac{\partial \tilde{\mathbf{h}}(\mathbf{z}, \bar{\mathbf{z}})}{\partial \bar{\mathbf{z}}^{\intercal}}\Bigg|_{\mathbf{y}=\bar{\mathbf{y}}} = \frac{\partial \boldsymbol{\epsilon}}{\partial \bar{\mathbf{z}}^{\intercal}}\Bigg|_{\mathbf{y}=\bar{\mathbf{y}}}, \tag{K1}$$

where the second equality follows by exchanging dummy variables. Then, the transpose of the matrix of *direct social effects of a mutant's geno-phenotype on her and a partner's environment* is

$$\left.\frac{\partial(\boldsymbol{\epsilon}+\check{\boldsymbol{\epsilon}})}{\partial \mathbf{z}^{\intercal}}\right|_{\mathbf{y}=\bar{\mathbf{y}}} = \left.\left(\frac{\partial \boldsymbol{\epsilon}}{\partial \mathbf{z}^{\intercal}} + \frac{\partial \check{\boldsymbol{\epsilon}}}{\partial \mathbf{z}^{\intercal}}\right)\right|_{\mathbf{y}=\bar{\mathbf{y}}} = \left.\left(\frac{\partial \boldsymbol{\epsilon}}{\partial \mathbf{z}^{\intercal}} + \frac{\partial \boldsymbol{\epsilon}}{\partial \bar{\mathbf{z}}^{\intercal}}\right)\right|_{\mathbf{y}=\bar{\mathbf{y}}} \in \mathbb{R}^{N_{\mathrm{a}}N_{\mathrm{e}}\times N_{\mathrm{a}}(N_{\mathrm{s}}+N_{\mathrm{c}})}. \tag{K2}$$

Similarly, the transpose of the matrix of *direct social effects of a mutant's phenotype on her and a partner's environment* is

$$\left.\frac{\partial(\boldsymbol{\epsilon}+\check{\boldsymbol{\epsilon}})}{\partial \mathbf{x}^{\intercal}}\right|_{\mathbf{y}=\bar{\mathbf{y}}} = \left.\left(\frac{\partial \boldsymbol{\epsilon}}{\partial \mathbf{x}^{\intercal}} + \frac{\partial \check{\boldsymbol{\epsilon}}}{\partial \mathbf{x}^{\intercal}}\right)\right|_{\mathbf{y}=\bar{\mathbf{y}}} = \left.\left(\frac{\partial \boldsymbol{\epsilon}}{\partial \mathbf{x}^{\intercal}} + \frac{\partial \boldsymbol{\epsilon}}{\partial \bar{\mathbf{x}}^{\intercal}}\right)\right|_{\mathbf{y}=\bar{\mathbf{y}}} \in \mathbb{R}^{N_{\mathrm{a}}N_{\mathrm{e}}\times N_{\mathrm{a}}N_{\mathrm{s}}}, \tag{K3}$$

and the transpose of the matrix of *direct social effects of a mutant's gene expression on her and a partner's environment* is

$$\left.\frac{\partial(\boldsymbol{\epsilon}+\check{\boldsymbol{\epsilon}})}{\partial \mathbf{y}^{\intercal}}\right|_{\mathbf{y}=\bar{\mathbf{y}}} = \left.\left(\frac{\partial \boldsymbol{\epsilon}}{\partial \mathbf{y}^{\intercal}} + \frac{\partial \check{\boldsymbol{\epsilon}}}{\partial \mathbf{y}^{\intercal}}\right)\right|_{\mathbf{y}=\bar{\mathbf{y}}} = \left.\left(\frac{\partial \boldsymbol{\epsilon}}{\partial \mathbf{y}^{\intercal}} + \frac{\partial \boldsymbol{\epsilon}}{\partial \bar{\mathbf{y}}^{\intercal}}\right)\right|_{\mathbf{y}=\bar{\mathbf{y}}} \in \mathbb{R}^{N_{\mathrm{a}}N_{\mathrm{e}}\times N_{\mathrm{a}}N_{\mathrm{c}}}. \tag{K4}$$

Consequently, the evolutionary dynamics of the environment are given by Layer 7, Eq. 10.

Appendix K.2. In terms of total genetic selection

Using the expression for the evolutionary dynamics of the geno-phenotype (Layer 7, Eq. 5 for $\boldsymbol{\zeta} = \mathbf{z}$) in that for the environment (Layer 7, Eq. 10) yields

$$\frac{\mathrm{d}\bar{\boldsymbol{\epsilon}}}{\mathrm{d}\tau} \approx \left.\left[\frac{\partial(\boldsymbol{\epsilon}+\check{\boldsymbol{\epsilon}})}{\partial \mathbf{z}^{\intercal}}\left(\kappa \mathbf{H}_{\mathbf{zy}}\frac{\mathrm{d}w}{\mathrm{d}\mathbf{y}} + \frac{\mathrm{s}\mathbf{z}}{\mathrm{s}\boldsymbol{\epsilon}^{\intercal}}\frac{\partial \boldsymbol{\epsilon}}{\partial \tau}\right) + \frac{\partial \boldsymbol{\epsilon}}{\partial \tau}\right]\right|_{\mathbf{y}=\bar{\mathbf{y}}}.$$

Using Layer 6, Eq. 13 for $\boldsymbol{\zeta} = \mathbf{z}$ yields

$$\frac{\mathrm{d}\bar{\boldsymbol{\epsilon}}}{\mathrm{d}\tau} \approx \left.\left[\frac{\partial(\boldsymbol{\epsilon}+\check{\boldsymbol{\epsilon}})}{\partial \mathbf{z}^{\intercal}}\left(\kappa \frac{\mathrm{s}\mathbf{z}}{\mathrm{s}\mathbf{y}^{\intercal}}\mathbf{G}_{\mathbf{y}}\frac{\mathrm{d}w}{\mathrm{d}\mathbf{y}} + \frac{\mathrm{s}\mathbf{z}}{\mathrm{s}\boldsymbol{\epsilon}^{\intercal}}\frac{\partial \boldsymbol{\epsilon}}{\partial \tau}\right) + \frac{\partial \boldsymbol{\epsilon}}{\partial \tau}\right]\right|_{\mathbf{y}=\bar{\mathbf{y}}}.$$

Collecting for $\partial\boldsymbol{\epsilon}/\partial\tau$ and using Layer 5, Eq. 6 yields

$$\frac{\mathrm{d}\bar{\boldsymbol{\epsilon}}}{\mathrm{d}\tau} \approx \left.\left(\kappa \frac{\mathrm{s}\boldsymbol{\epsilon}}{\mathrm{s}\mathbf{y}^{\intercal}}\mathbf{G}_{\mathbf{y}}\frac{\mathrm{d}w}{\mathrm{d}\mathbf{y}} + \frac{\mathrm{s}\boldsymbol{\epsilon}}{\mathrm{s}\boldsymbol{\epsilon}^{\intercal}}\frac{\partial \boldsymbol{\epsilon}}{\partial \tau}\right)\right|_{\mathbf{y}=\bar{\mathbf{y}}}.$$

Using Layer 6, Eq. 13 yields Layer 7, Eq. 5 for $\boldsymbol{\zeta} = \boldsymbol{\epsilon}$. Using the third line of Layer 4, Eq. 22 and Layer 6, Eq. 11 yields Layer 7, Eq. 4 for $\boldsymbol{\zeta} = \boldsymbol{\epsilon}$, whereas using the fourth line of Layer 4, Eq. 22 and Layer 6, Eq. 12 yields Layer 7, Eq. 1a for $\boldsymbol{\zeta} = \boldsymbol{\epsilon}$.

Appendix L. Evolutionary dynamics of the geno-envo-phenotype

Appendix L.1. In terms of total genetic selection

Here we obtain an equation describing the evolutionary dynamics of the resident geno-envo-phenotype, that is, $\mathrm{d}\bar{\mathbf{m}}/\mathrm{d}\tau$. In this section, we write such an equation in terms of total genetic selection. Since $\mathrm{d}\bar{\mathbf{m}}/\mathrm{d}\tau = (\mathrm{d}\bar{\mathbf{x}}/\mathrm{d}\tau; \mathrm{d}\bar{\mathbf{y}}/\mathrm{d}\tau; \mathrm{d}\bar{\boldsymbol{\epsilon}}/\mathrm{d}\tau)$, from (I15), (13a), and Layer 7, Eq. 5 for $\boldsymbol{\zeta} = \boldsymbol{\epsilon}$, we can write the evolutionary dynamics of the resident geno-envo-phenotype $\bar{\mathbf{m}}$ as

$$\frac{\mathrm{d}\bar{\mathbf{m}}}{\mathrm{d}\tau} \approx \left.\left[\kappa \begin{pmatrix}\mathbf{H}_{\mathbf{xy}}\\ \mathbf{G}_{\mathbf{y}}\\ \mathbf{H}_{\boldsymbol{\epsilon}\mathbf{y}}\end{pmatrix}\frac{\mathrm{d}w}{\mathrm{d}\mathbf{y}} + \begin{pmatrix}\frac{\mathrm{s}\mathbf{x}}{\mathrm{s}\boldsymbol{\epsilon}^{\intercal}}\\ \mathbf{0}\\ \frac{\mathrm{s}\boldsymbol{\epsilon}}{\mathrm{s}\boldsymbol{\epsilon}^{\intercal}}\end{pmatrix}\frac{\partial \bar{\boldsymbol{\epsilon}}}{\partial \tau}\right]\right|_{\mathbf{y}=\bar{\mathbf{y}}}. \tag{L1}$$

Using Layer 6, Eq. 10 and Layer 5, Eq. 3, this is

$$\frac{\mathrm{d}\bar{\mathbf{m}}}{\mathrm{d}\tau} \approx \left.\left[\kappa \begin{pmatrix}\frac{\mathrm{s}\mathbf{x}}{\mathrm{s}\mathbf{y}^{\intercal}}\\ \frac{\mathrm{s}\mathbf{y}}{\mathrm{s}\mathbf{y}^{\intercal}}\\ \frac{\mathrm{s}\boldsymbol{\epsilon}}{\mathrm{s}\mathbf{y}^{\intercal}}\end{pmatrix}\mathbf{G}_{\mathbf{y}}\frac{\mathrm{d}w}{\mathrm{d}\mathbf{y}} + \begin{pmatrix}\frac{\mathrm{s}\mathbf{x}}{\mathrm{s}\boldsymbol{\epsilon}^{\intercal}}\\ \frac{\mathrm{s}\mathbf{y}}{\mathrm{s}\boldsymbol{\epsilon}^{\intercal}}\\ \frac{\mathrm{s}\boldsymbol{\epsilon}}{\mathrm{s}\boldsymbol{\epsilon}^{\intercal}}\end{pmatrix}\frac{\partial \bar{\boldsymbol{\epsilon}}}{\partial \tau}\right]\right|_{\mathbf{y}=\bar{\mathbf{y}}}.$$

Using Layer 5, Eq. 7, this reduces to

$$\frac{\mathrm{d}\bar{\mathbf{m}}}{\mathrm{d}\tau} \approx \left.\left(\kappa \frac{\mathrm{s}\mathbf{m}}{\mathrm{s}\mathbf{y}^{\intercal}}\mathbf{G}_{\mathbf{y}}\frac{\mathrm{d}w}{\mathrm{d}\mathbf{y}} + \frac{\mathrm{s}\mathbf{m}}{\mathrm{s}\boldsymbol{\epsilon}^{\intercal}}\frac{\partial \bar{\boldsymbol{\epsilon}}}{\partial \tau}\right)\right|_{\mathbf{y}=\bar{\mathbf{y}}}.$$

Using Layer 6, Eq. 13 yields Layer 7, Eq. 5 for $\boldsymbol{\zeta} = \mathbf{m}$.. Using the third line of Layer 4, Eq. 22 and Layer 6, Eq. 11 yields Layer 7, Eq. 4 for $\boldsymbol{\zeta} = \mathbf{m}$, whereas using the fourth line of Layer 4, Eq. 22 and Layer 6, Eq. 12 yields Layer 7, Eq. 1a for $\boldsymbol{\zeta} = \mathbf{m}$.

In contrast to other arrangements, the premultiplying matrix $\mathbf{H}_{\mathbf{my}}$ is non-singular if $\mathbf{G}_{\mathbf{y}}$ is non-singular. Indeed, if

$$\left.\frac{\mathrm{s}\mathbf{m}}{\mathrm{s}\mathbf{y}^{\intercal}}\right|_{\mathbf{y}=\bar{\mathbf{y}}}\mathbf{r} = \mathbf{0}$$

for some vector $\mathbf{r}$, then from Layer 5, Eq. 7a and Layer 5, Eq. 3b we have

$$\left.\begin{pmatrix}\frac{\mathrm{s}\mathbf{x}}{\mathrm{s}\mathbf{y}^{\intercal}}\\ \mathbf{I}\\ \frac{\mathrm{s}\boldsymbol{\epsilon}}{\mathrm{s}\mathbf{y}^{\intercal}}\end{pmatrix}\right|_{\mathbf{y}=\bar{\mathbf{y}}}\mathbf{r} = \mathbf{0}.$$

Doing the multiplication yields

$$\begin{pmatrix}\left.\frac{\mathrm{s}\mathbf{x}}{\mathrm{s}\mathbf{y}^{\intercal}}\right|_{\mathbf{y}=\bar{\mathbf{y}}}\mathbf{r}\\ \mathbf{r}\\ \left.\frac{\mathrm{s}\boldsymbol{\epsilon}}{\mathrm{s}\mathbf{y}^{\intercal}}\right|_{\mathbf{y}=\bar{\mathbf{y}}}\mathbf{r}\end{pmatrix} = \mathbf{0},$$

which implies that $\mathbf{r} = \mathbf{0}$, so $\mathrm{s}\mathbf{m}/\mathrm{s}\mathbf{y}^{\intercal}|_{\mathbf{y}=\bar{\mathbf{y}}}$ is non-singular. Thus, $\mathbf{H}_{\mathbf{my}}$ is non-singular if $\mathbf{G}_{\mathbf{y}}$ is non-singular.

Appendix L.2. In terms of total selection on the geno-envo-phenotype

Here we write the evolutionary dynamics of the geno-envo-phenotype in terms of the total selection gradient of the geno-envo-phenotype.

First, using Layer 6, Eq. 2, we define the *additive genetic covariance matrix of the undeveloped geno-envo-phenotype* $\hat{\mathbf{m}} = (\bar{\mathbf{x}}; \mathbf{y}; \bar{\boldsymbol{\epsilon}})$ as

$$\mathbf{G}_{\hat{\mathbf{m}}} \equiv \mathrm{cov}[\mathbf{a}_{\hat{\mathbf{m}}}, \mathbf{a}_{\hat{\mathbf{m}}}] = \left.\left(\frac{\mathrm{d}\hat{\mathbf{m}}}{\mathrm{d}\mathbf{y}^{\intercal}}\mathbf{G}_{\mathbf{y}}\frac{\mathrm{d}\hat{\mathbf{m}}^{\intercal}}{\mathrm{d}\mathbf{y}}\right)\right|_{\mathbf{y}=\bar{\mathbf{y}}}$$

$$\in \mathbb{R}^{N_a(N_s+N_c+N_e)\times N_a(N_s+N_c+N_e)}.$$

By definition of $\hat{\mathbf{m}}$, we have

$$\mathbf{G}_{\hat{\mathbf{m}}} = \left[\begin{pmatrix} \frac{\mathrm{d}\bar{\mathbf{x}}}{\mathrm{d}\mathbf{y}^\intercal} \\ \frac{\mathrm{d}\mathbf{y}}{\mathrm{d}\mathbf{y}^\intercal} \\ \frac{\mathrm{d}\bar{\boldsymbol{\epsilon}}}{\mathrm{d}\mathbf{y}^\intercal} \end{pmatrix} \mathbf{G}_{\mathbf{y}} \begin{pmatrix} \frac{\mathrm{d}\bar{\mathbf{x}}^\intercal}{\mathrm{d}\mathbf{y}} & \frac{\mathrm{d}\mathbf{y}^\intercal}{\mathrm{d}\mathbf{y}} & \frac{\mathrm{d}\bar{\boldsymbol{\epsilon}}^\intercal}{\mathrm{d}\mathbf{y}} \end{pmatrix}\right]\Bigg|_{\mathbf{y}=\bar{\mathbf{y}}}.$$

From Eqs. (13c) and (13d), the resident phenotype and environment are independent of mutant gene expression, so

$$\mathbf{G}_{\hat{\mathbf{m}}} = \left[\begin{pmatrix} \mathbf{0} \\ \mathbf{I} \\ \mathbf{0} \end{pmatrix} \mathbf{G}_{\mathbf{y}} \begin{pmatrix} \mathbf{0} & \mathbf{I} & \mathbf{0} \end{pmatrix}\right]\Bigg|_{\mathbf{y}=\bar{\mathbf{y}}}.$$

Doing the matrix multiplication yields

$$\mathbf{G}_{\hat{\mathbf{m}}} = \left[\begin{pmatrix} \mathbf{0} \\ \mathbf{I} \\ \mathbf{0} \end{pmatrix} \begin{pmatrix} \mathbf{0} & \mathbf{G}_{\mathbf{y}} & \mathbf{0} \end{pmatrix}\right]\Bigg|_{\mathbf{y}=\bar{\mathbf{y}}} = \begin{pmatrix} \mathbf{0} & \mathbf{0} & \mathbf{0} \\ \mathbf{0} & \mathbf{G}_{\mathbf{y}} & \mathbf{0} \\ \mathbf{0} & \mathbf{0} & \mathbf{0} \end{pmatrix}. \tag{L2}$$

The matrix $\mathbf{G}_{\hat{\mathbf{m}}}$ is singular because the undeveloped geno-envo-phenotype includes gene expression (i.e., $\mathrm{d}\hat{\mathbf{m}}^\intercal/\mathrm{d}\mathbf{y}|_{\mathbf{y}=\bar{\mathbf{y}}}$ has fewer rows than columns). For this reason, the matrix $\mathbf{G}_{\hat{\mathbf{m}}}$ would still be singular even if the zero block entries in Eq. (L2) were non-zero (i.e., if $\mathrm{d}\bar{\mathbf{x}}^\intercal/\mathrm{d}\mathbf{y}|_{\mathbf{y}=\bar{\mathbf{y}}} \neq \mathbf{0}$ and $\mathrm{d}\bar{\boldsymbol{\epsilon}}^\intercal/\mathrm{d}\mathbf{y}|_{\mathbf{y}=\bar{\mathbf{y}}} \neq \mathbf{0}$).

Now, we write an alternative factorization of $\mathbf{H}_{\mathbf{m}}$ in terms of $\mathbf{G}_{\hat{\mathbf{m}}}$. Using Layer 4, Eq. 18 and Layer 5, Eq. 8, we have

$$\left(\frac{\mathrm{s}\mathbf{m}}{\mathrm{s}\mathbf{m}^\intercal}\mathbf{G}_{\hat{\mathbf{m}}}\frac{\mathrm{d}\mathbf{m}^\intercal}{\mathrm{d}\mathbf{m}}\right)\Bigg|_{\mathbf{y}=\bar{\mathbf{y}}} = \left[\begin{pmatrix} \frac{\mathrm{s}\mathbf{x}}{\mathrm{s}\mathbf{x}^\intercal} & \frac{\mathrm{s}\mathbf{x}}{\mathrm{s}\mathbf{y}^\intercal} & \frac{\mathrm{s}\mathbf{x}}{\mathrm{s}\boldsymbol{\epsilon}^\intercal} \\ \mathbf{0} & \mathbf{I} & \mathbf{0} \\ \frac{\mathrm{s}\boldsymbol{\epsilon}}{\mathrm{s}\mathbf{x}^\intercal} & \frac{\mathrm{s}\boldsymbol{\epsilon}}{\mathrm{s}\mathbf{y}^\intercal} & \frac{\mathrm{s}\boldsymbol{\epsilon}}{\mathrm{s}\boldsymbol{\epsilon}^\intercal} \end{pmatrix} \begin{pmatrix} \mathbf{0} & \mathbf{0} & \mathbf{0} \\ \mathbf{0} & \mathbf{G}_{\mathbf{y}} & \mathbf{0} \\ \mathbf{0} & \mathbf{0} & \mathbf{0} \end{pmatrix} \begin{pmatrix} \frac{\mathrm{d}\mathbf{x}^\intercal}{\mathrm{d}\mathbf{x}} & \mathbf{0} & \frac{\mathrm{d}\boldsymbol{\epsilon}^\intercal}{\mathrm{d}\mathbf{x}} \\ \frac{\mathrm{d}\mathbf{x}^\intercal}{\mathrm{d}\mathbf{y}} & \mathbf{I} & \frac{\mathrm{d}\boldsymbol{\epsilon}^\intercal}{\mathrm{d}\mathbf{y}} \\ \frac{\mathrm{d}\mathbf{x}^\intercal}{\mathrm{d}\boldsymbol{\epsilon}} & \mathbf{0} & \frac{\mathrm{d}\boldsymbol{\epsilon}^\intercal}{\mathrm{d}\boldsymbol{\epsilon}} \end{pmatrix}\right]\Bigg|_{\mathbf{y}=\bar{\mathbf{y}}}.$$

Doing the matrix multiplication yields

$$\begin{aligned}
&\left(\frac{\mathrm{s}\mathbf{m}}{\mathrm{s}\mathbf{m}^\intercal}\mathbf{G}_{\hat{\mathbf{m}}}\frac{\mathrm{d}\mathbf{m}^\intercal}{\mathrm{d}\mathbf{m}}\right)\Bigg|_{\mathbf{y}=\bar{\mathbf{y}}} \\
&= \left[\begin{pmatrix} \frac{\mathrm{s}\mathbf{x}}{\mathrm{s}\mathbf{x}^\intercal} & \frac{\mathrm{s}\mathbf{x}}{\mathrm{s}\mathbf{y}^\intercal} & \frac{\mathrm{s}\mathbf{x}}{\mathrm{s}\boldsymbol{\epsilon}^\intercal} \\ \mathbf{0} & \mathbf{I} & \mathbf{0} \\ \frac{\mathrm{s}\boldsymbol{\epsilon}}{\mathrm{s}\mathbf{x}^\intercal} & \frac{\mathrm{s}\boldsymbol{\epsilon}}{\mathrm{s}\mathbf{y}^\intercal} & \frac{\mathrm{s}\boldsymbol{\epsilon}}{\mathrm{s}\boldsymbol{\epsilon}^\intercal} \end{pmatrix} \begin{pmatrix} \mathbf{0} & \mathbf{0} & \mathbf{0} \\ \mathbf{G}_{\mathbf{y}}\frac{\mathrm{d}\mathbf{x}^\intercal}{\mathrm{d}\mathbf{y}} & \mathbf{G}_{\mathbf{y}} & \mathbf{G}_{\mathbf{y}}\frac{\mathrm{d}\boldsymbol{\epsilon}^\intercal}{\mathrm{d}\mathbf{y}} \\ \mathbf{0} & \mathbf{0} & \mathbf{0} \end{pmatrix}\right]\Bigg|_{\mathbf{y}=\bar{\mathbf{y}}} \\
&= \begin{pmatrix} \frac{\mathrm{s}\mathbf{x}}{\mathrm{s}\mathbf{y}^\intercal}\mathbf{G}_{\mathbf{y}}\frac{\mathrm{d}\mathbf{x}^\intercal}{\mathrm{d}\mathbf{y}} & \frac{\mathrm{s}\mathbf{x}}{\mathrm{s}\mathbf{y}^\intercal}\mathbf{G}_{\mathbf{y}} & \frac{\mathrm{s}\mathbf{x}}{\mathrm{s}\mathbf{y}^\intercal}\mathbf{G}_{\mathbf{y}}\frac{\mathrm{d}\boldsymbol{\epsilon}^\intercal}{\mathrm{d}\mathbf{y}} \\ \mathbf{G}_{\mathbf{y}}\frac{\mathrm{d}\mathbf{x}^\intercal}{\mathrm{d}\mathbf{y}} & \mathbf{G}_{\mathbf{y}} & \mathbf{G}_{\mathbf{y}}\frac{\mathrm{d}\boldsymbol{\epsilon}^\intercal}{\mathrm{d}\mathbf{y}} \\ \frac{\mathrm{s}\boldsymbol{\epsilon}}{\mathrm{s}\mathbf{y}^\intercal}\mathbf{G}_{\mathbf{y}}\frac{\mathrm{d}\mathbf{x}^\intercal}{\mathrm{d}\mathbf{y}} & \frac{\mathrm{s}\boldsymbol{\epsilon}}{\mathrm{s}\mathbf{y}^\intercal}\mathbf{G}_{\mathbf{y}} & \frac{\mathrm{s}\boldsymbol{\epsilon}}{\mathrm{s}\mathbf{y}^\intercal}\mathbf{G}_{\mathbf{y}}\frac{\mathrm{d}\boldsymbol{\epsilon}^\intercal}{\mathrm{d}\mathbf{y}} \end{pmatrix}\Bigg|_{\mathbf{y}=\bar{\mathbf{y}}}
\end{aligned}$$

Using Layer 5, Eq. 3b, we have

$$\begin{aligned}
&\left(\frac{\mathrm{s}\mathbf{m}}{\mathrm{s}\mathbf{m}^\intercal}\mathbf{G}_{\hat{\mathbf{m}}}\frac{\mathrm{d}\mathbf{m}^\intercal}{\mathrm{d}\mathbf{m}}\right)\Bigg|_{\mathbf{y}=\bar{\mathbf{y}}} \\
&= \begin{pmatrix} \frac{\mathrm{s}\mathbf{x}}{\mathrm{s}\mathbf{y}^\intercal}\mathbf{G}_{\mathbf{y}}\frac{\mathrm{d}\mathbf{x}^\intercal}{\mathrm{d}\mathbf{y}} & \frac{\mathrm{s}\mathbf{x}}{\mathrm{s}\mathbf{y}^\intercal}\mathbf{G}_{\mathbf{y}}\frac{\mathrm{d}\mathbf{y}^\intercal}{\mathrm{d}\mathbf{y}} & \frac{\mathrm{s}\mathbf{x}}{\mathrm{s}\mathbf{y}^\intercal}\mathbf{G}_{\mathbf{y}}\frac{\mathrm{d}\boldsymbol{\epsilon}^\intercal}{\mathrm{d}\mathbf{y}} \\ \frac{\mathrm{s}\mathbf{y}}{\mathrm{s}\mathbf{y}^\intercal}\mathbf{G}_{\mathbf{y}}\frac{\mathrm{d}\mathbf{x}^\intercal}{\mathrm{d}\mathbf{y}} & \frac{\mathrm{s}\mathbf{y}}{\mathrm{s}\mathbf{y}^\intercal}\mathbf{G}_{\mathbf{y}}\frac{\mathrm{d}\mathbf{y}^\intercal}{\mathrm{d}\mathbf{y}} & \frac{\mathrm{s}\mathbf{y}}{\mathrm{s}\mathbf{y}^\intercal}\mathbf{G}_{\mathbf{y}}\frac{\mathrm{d}\boldsymbol{\epsilon}^\intercal}{\mathrm{d}\mathbf{y}} \\ \frac{\mathrm{s}\boldsymbol{\epsilon}}{\mathrm{s}\mathbf{y}^\intercal}\mathbf{G}_{\mathbf{y}}\frac{\mathrm{d}\mathbf{x}^\intercal}{\mathrm{d}\mathbf{y}} & \frac{\mathrm{s}\boldsymbol{\epsilon}}{\mathrm{s}\mathbf{y}^\intercal}\mathbf{G}_{\mathbf{y}}\frac{\mathrm{d}\mathbf{y}^\intercal}{\mathrm{d}\mathbf{y}} & \frac{\mathrm{s}\boldsymbol{\epsilon}}{\mathrm{s}\mathbf{y}^\intercal}\mathbf{G}_{\mathbf{y}}\frac{\mathrm{d}\boldsymbol{\epsilon}^\intercal}{\mathrm{d}\mathbf{y}} \end{pmatrix}\Bigg|_{\mathbf{y}=\bar{\mathbf{y}}}
\end{aligned}$$

Notice that the matrix on the right-hand side is

$$\left(\frac{\mathrm{s}\mathbf{m}}{\mathrm{s}\mathbf{y}^\intercal}\mathbf{G}_{\mathbf{y}}\frac{\mathrm{d}\mathbf{m}^\intercal}{\mathrm{d}\mathbf{y}}\right)\Bigg|_{\mathbf{y}=\bar{\mathbf{y}}} = \mathbf{H}_{\mathbf{m}}.$$

Hence, we obtain an alternative factorization for $\mathbf{H}_{\mathbf{m}}$ as

$$\mathbf{H}_{\mathbf{m}} = \left(\frac{\mathrm{s}\mathbf{m}}{\mathrm{s}\mathbf{m}^\intercal}\mathbf{G}_{\hat{\mathbf{m}}}\frac{\mathrm{d}\mathbf{m}^\intercal}{\mathrm{d}\mathbf{m}}\right)\Bigg|_{\mathbf{y}=\bar{\mathbf{y}}}.$$

We can now write the selection response of the geno-envo-phenotype (in the form of Layer 7, Eq. 1a) as

$$\kappa\mathbf{H}_{\mathbf{m}}\frac{\partial w}{\partial \mathbf{m}}\Bigg|_{\mathbf{y}=\bar{\mathbf{y}}} = \kappa\left(\frac{\mathrm{s}\mathbf{m}}{\mathrm{s}\mathbf{m}^\intercal}\mathbf{G}_{\hat{\mathbf{m}}}\frac{\mathrm{d}\mathbf{m}^\intercal}{\mathrm{d}\mathbf{m}}\frac{\partial w}{\partial \mathbf{m}}\right)\Bigg|_{\mathbf{y}=\bar{\mathbf{y}}}.$$

Using the relationship between the total and partial selection gradients of the geno-envo-phenotype (Layer 4, Eq. 25), this becomes

$$\kappa\mathbf{H}_{\mathbf{m}}\frac{\partial w}{\partial \mathbf{m}}\Bigg|_{\mathbf{y}=\bar{\mathbf{y}}} = \kappa\left(\frac{\mathrm{s}\mathbf{m}}{\mathrm{s}\mathbf{m}^\intercal}\mathbf{G}_{\hat{\mathbf{m}}}\frac{\mathrm{d}w}{\mathrm{d}\mathbf{m}}\right)\Bigg|_{\mathbf{y}=\bar{\mathbf{y}}}.$$

We can further simplify this equation by noticing the following. Using Layer 6, Eq. 10 and $\hat{\mathbf{m}} = (\bar{\mathbf{x}}; \mathbf{y}; \bar{\boldsymbol{\epsilon}})$, we have that the *additive socio-genetic cross-covariance matrix of the geno-envo-phenotype and the undeveloped geno-envo-phenotype* is

$$\mathbf{H}_{\mathbf{m}\hat{\mathbf{m}}} = \left(\frac{\mathrm{s}\mathbf{m}}{\mathrm{s}\mathbf{y}^\intercal}\mathbf{G}_{\mathbf{y}}\frac{\mathrm{d}\hat{\mathbf{m}}^\intercal}{\mathrm{d}\mathbf{y}}\right)\Bigg|_{\mathbf{y}=\bar{\mathbf{y}}} \tag{L3}$$
$$\in \mathbb{R}^{N_a(N_s+N_c+N_e)\times N_a(N_s+N_c+N_e)}.$$

Expanding, we have

$$\mathbf{H}_{\mathbf{m}\hat{\mathbf{m}}} = \left[\begin{pmatrix} \frac{\mathrm{s}\mathbf{x}}{\mathrm{s}\mathbf{y}^\intercal} \\ \frac{\mathrm{s}\mathbf{y}}{\mathrm{s}\mathbf{y}^\intercal} \\ \frac{\mathrm{s}\boldsymbol{\epsilon}}{\mathrm{s}\mathbf{y}^\intercal} \end{pmatrix} \mathbf{G}_{\mathbf{y}} \begin{pmatrix} \frac{\mathrm{d}\bar{\mathbf{x}}^\intercal}{\mathrm{d}\mathbf{y}} & \frac{\mathrm{d}\mathbf{y}^\intercal}{\mathrm{d}\mathbf{y}} & \frac{\mathrm{d}\bar{\boldsymbol{\epsilon}}^\intercal}{\mathrm{d}\mathbf{y}} \end{pmatrix}\right]\Bigg|_{\mathbf{y}=\bar{\mathbf{y}}}.$$

Using Layer 5, Eq. 3b and since the resident phenotype and environment do not depend on mutant gene expression, then

$$\mathbf{H}_{\mathbf{m}\hat{\mathbf{m}}} = \left[\begin{pmatrix} \frac{\mathrm{s}\mathbf{x}}{\mathrm{s}\mathbf{y}^\intercal} \\ \mathbf{I} \\ \frac{\mathrm{s}\boldsymbol{\epsilon}}{\mathrm{s}\mathbf{y}^\intercal} \end{pmatrix} \mathbf{G}_{\mathbf{y}} \begin{pmatrix} \mathbf{0} & \mathbf{I} & \mathbf{0} \end{pmatrix}\right]\Bigg|_{\mathbf{y}=\bar{\mathbf{y}}}.$$

Doing the matrix multiplication yields

$$\mathbf{H}_{\mathbf{m}\hat{\mathbf{m}}} = \left[\begin{pmatrix} \frac{\mathrm{s}\mathbf{x}}{\mathrm{s}\mathbf{y}^\intercal} \\ \mathbf{I} \\ \frac{\mathrm{s}\boldsymbol{\epsilon}}{\mathrm{s}\mathbf{y}^\intercal} \end{pmatrix} \begin{pmatrix} \mathbf{0} & \mathbf{G}_\mathbf{y} & \mathbf{0} \end{pmatrix}\right]\Bigg|_{\mathbf{y}=\bar{\mathbf{y}}}$$

$$= \begin{pmatrix} \mathbf{0} & \frac{\mathrm{s}\mathbf{x}}{\mathrm{s}\mathbf{y}^\intercal}\mathbf{G}_\mathbf{y} & \mathbf{0} \\ \mathbf{0} & \mathbf{G}_\mathbf{y} & \mathbf{0} \\ \mathbf{0} & \frac{\mathrm{s}\boldsymbol{\epsilon}}{\mathrm{s}\mathbf{y}^\intercal}\mathbf{G}_\mathbf{y} & \mathbf{0} \end{pmatrix}\Bigg|_{\mathbf{y}=\bar{\mathbf{y}}}.$$

Notice that the last matrix equals

$$\left(\frac{\mathrm{s}\mathbf{m}}{\mathrm{s}\mathbf{m}^\intercal}\mathbf{G}_{\hat{\mathbf{m}}}\right)\Bigg|_{\mathbf{y}=\bar{\mathbf{y}}}.$$

Thus,

$$\mathbf{H}_{\mathbf{m}\hat{\mathbf{m}}} = \left(\frac{\mathrm{s}\mathbf{m}}{\mathrm{s}\mathbf{m}^\intercal}\mathbf{G}_{\hat{\mathbf{m}}}\right)\Bigg|_{\mathbf{y}=\bar{\mathbf{y}}}.$$

We can then write the evolutionary dynamics of the resident geno-envo-phenotype $\bar{\mathbf{m}}$ in terms of the total selection gradient of the geno-envo-phenotype as

$$\frac{\mathrm{d}\bar{\mathbf{m}}}{\mathrm{d}\tau} \approx \left(\kappa\mathbf{H}_{\mathbf{m}\hat{\mathbf{m}}}\frac{\mathrm{d}w}{\mathrm{d}\mathbf{m}} + \frac{\mathrm{s}\mathbf{m}}{\mathrm{s}\boldsymbol{\epsilon}^\intercal}\frac{\partial\bar{\boldsymbol{\epsilon}}}{\partial\tau}\right)\Bigg|_{\mathbf{y}=\bar{\mathbf{y}}}. \tag{L4}$$

The cross-covariance matrix $\mathbf{H}_{\mathbf{m}\hat{\mathbf{m}}}$ is singular because $\mathrm{d}\hat{\mathbf{m}}^\intercal/\mathrm{d}\mathbf{y}|_{\mathbf{y}=\bar{\mathbf{y}}}$ has fewer rows than columns since the undeveloped geno-envo-phenotype includes gene expression. For this reason, $\mathbf{H}_{\mathbf{m}\hat{\mathbf{m}}}$ would still be singular even if the zero block entries in Eq. (L3) were non-zero (i.e., if $\mathrm{d}\bar{\mathbf{x}}^\intercal/\mathrm{d}\mathbf{y}|_{\mathbf{y}=\bar{\mathbf{y}}} \neq \mathbf{0}$ and $\mathrm{d}\bar{\boldsymbol{\epsilon}}^\intercal/\mathrm{d}\mathbf{y}|_{\mathbf{y}=\bar{\mathbf{y}}} \neq \mathbf{0}$). Then, evolutionary equilibria of the geno-envo-phenotype do not imply absence of total selection on the geno-envo-phenotype, even if exogenous plastic response is absent.

Appendix M. Connection to dynamic optimization

Life-history models often consider traits that depend on an underlying variable (e.g., age) together with developmental (or dynamic) constraints. When such a model is simple enough, analytical solution (i.e., identification of evolutionarily stable strategies) is possible using optimal control or dynamic programming methods (Sydsæter et al., 2008). A key tool from optimal control theory that enables finding such analytical solutions (i.e., optimal controls) is Pontryagin's maximum principle. The maximum principle is a theorem that essentially transforms the dynamic optimization problem into a simpler problem of maximizing a function called the Hamiltonian, which depends on control, state, and costate (or adjoint) variables. The problem is then to maximize the Hamiltonian with respect to the controls, while state and costate variables can be found from associated dynamic equations. We now show that our results recover the key elements of Pontryagin's maximum principle.

First, we state the optimization problem. Assume that there are no environmental variables. Let survivorship be a state variable, denoted by $x_{\ell a} = \ell_a$, so it satisfies the developmental constraint $x_{\ell,a+1} = g_{\ell a}(\mathbf{z}_a, \bar{\mathbf{z}}) = x_{\ell a}p_a(\mathbf{z}_a, \bar{\mathbf{z}})$ with initial condition $x_{\ell 1} = \bar{x}_{\ell 1} = 1$. Thus, using Eq. 27, we can write the expected lifetime number of offspring of a mutant with geno-phenotype $\mathbf{z} = (\mathbf{x}; \mathbf{y})$ in the context of a resident with geno-phenotype $\bar{\mathbf{z}} = (\bar{\mathbf{x}}; \bar{\mathbf{y}})$ as

$$R_0(\mathbf{z}, \bar{\mathbf{z}}) = \sum_{a=1}^{N_\mathrm{a}} x_{\ell a} f_a(\mathbf{z}_a, \bar{\mathbf{z}}). \tag{M1a}$$

Consider the optimization problem of finding an optimal pair $\mathbf{z}^* = (\mathbf{x}^*; \mathbf{y}^*)$ such that

$$\mathbf{y}^* \in \arg\max_{\mathbf{y}} R_0(\mathbf{z}, \mathbf{z}^*), \tag{M1b}$$

subject to the dynamic constraint

$$\mathbf{x}_{a+1} = \mathbf{g}_a(\mathbf{z}_a, \bar{\mathbf{z}}), \tag{M1c}$$

for $a \in \{1, \ldots, N_\mathrm{a}\}$, with $\mathbf{x}_1 = \bar{\mathbf{x}}_1$ given and $\mathbf{x}_{N_\mathrm{a}}$ free. Hence, $\mathbf{z}^*$ is a best response to itself under the best response function R_0, where $\mathbf{y}^*$ is an optimal control and $\mathbf{x}^*$ is its associated optimal state. The optimization problem in (M1) is a standard life-history problem generalized to include social interactions. From Layer 7, Eq. 5 for $\boldsymbol{\zeta} = \mathbf{z}$ and Eq. (28b), it follows that since there is no exogenous environmental change, an admissible locally stable evolutionary equilibrium $\mathbf{z}^*$ locally solves the problem (M1).

Second, we define the costate variables and show that they are proportional to the total selection gradient of states evaluated at an admissible locally stable evolutionary equilibrium. The costate variable of the i-th state variable at age a is defined as

$$k_{x_{ia}} \equiv \frac{\mathrm{d}R_0}{\mathrm{d}x_{ia}}\Bigg|_{\mathbf{z}=\bar{\mathbf{z}}=\mathbf{z}^*} \tag{M2}$$

(section 9.6 of Sydsæter et al. 2008). Hence, from Eq. (28b), we have that the costate for the i-th state variable at age a is

$$k_{x_{ia}} = T\,\frac{\mathrm{d}w}{\mathrm{d}x_{ia}}\Bigg|_{\mathbf{z}=\bar{\mathbf{z}}=\mathbf{z}^*}. \tag{M3}$$

That is, costate variables are proportional to the total selection gradient of state variables at an admissible locally stable evolutionary equilibrium $\mathbf{z}^*$. The total selection gradient of states thus generalizes the costate notion to the situation where controls and states are outside of evolutionary equilibrium for the life-history problem of R_0 maximization. We have obtained various equations (Layer 4, Eq. 21) that enable direct calculation of such generalized costates in age structured models with R_0 maximization. Moreover, we have obtained an equation that relates such generalized costates to the evolutionary dynamics (fifth line of Layer 4, Eq. 22). Since we are assuming that there are no environmental variables, semi-total effect matrices reduce to direct effect matrices. Thus, the fifth line of Layer 4,

Eq. 22 shows that such generalized costates affect the evolutionary dynamics indirectly by being transformed by the direct effects of controls on states, $\partial \mathbf{x}^\intercal / \partial \mathbf{y}$.

Third, we show that total maximization of R_0 is equivalent to direct maximization of the Hamiltonian, which is the central feature of Pontryagin's maximum principle. We have that the total selection gradient of controls can be written in terms of the total selection gradients of states (fifth line of Layer 4, Eq. 22), so for the controls at age a we have

$$\left.\frac{\mathrm{d}w}{\mathrm{d}\mathbf{y}_a}\right|_{\mathbf{y}=\bar{\mathbf{y}}} = \left.\left(\frac{\partial \mathbf{x}^\intercal}{\partial \mathbf{y}_a}\frac{\mathrm{d}w}{\mathrm{d}\mathbf{x}} + \frac{\partial w}{\partial \mathbf{y}_a}\right)\right|_{\mathbf{y}=\bar{\mathbf{y}}},$$

where we substituted semi-total derivatives for partial derivatives because we are assuming that there are no environmental variables. Using Eqs. (28) yields

$$\left.\frac{\mathrm{d}R_0}{\mathrm{d}\mathbf{y}_a}\right|_{\mathbf{y}=\bar{\mathbf{y}}} = \left.\left(\frac{\partial \mathbf{x}^\intercal}{\partial \mathbf{y}_a}\frac{\mathrm{d}R_0}{\mathrm{d}\mathbf{x}} + \frac{\partial R_0}{\partial \mathbf{y}_a}\right)\right|_{\mathbf{y}=\bar{\mathbf{y}}}.$$

From Eqs. (E10) and (M1a) given that the partial derivative ignores the dynamic constraint (M1c), it follows that

$$\left.\frac{\mathrm{d}R_0}{\mathrm{d}\mathbf{y}_a}\right|_{\mathbf{y}=\bar{\mathbf{y}}} = \left.\left(\frac{\partial \mathbf{x}_{a+1}^\intercal}{\partial \mathbf{y}_a}\frac{\mathrm{d}R_0}{\mathrm{d}\mathbf{x}_{a+1}} + \frac{\partial (x_{\ell a} f_a)}{\partial \mathbf{y}_a}\right)\right|_{\mathbf{y}=\bar{\mathbf{y}}}.$$

Using Eqs. (M2) and (M1c) and evaluating at optimal controls yields

$$\left.\frac{\mathrm{d}R_0}{\mathrm{d}\mathbf{y}_a}\right|_{\mathbf{y}=\bar{\mathbf{y}}=\mathbf{y}^*} = \left.\left(\frac{\partial \mathbf{g}_a^\intercal}{\partial \mathbf{y}_a}\mathbf{k}_{\mathbf{x}_{a+1}} + \frac{\partial (x_{\ell a} f_a)}{\partial \mathbf{y}_a}\right)\right|_{\mathbf{y}=\bar{\mathbf{y}}=\mathbf{y}^*}.$$

This suggests to define

$$H_a \equiv \mathbf{g}_a^\intercal \mathbf{k}_{\mathbf{x}_{a+1}} + x_{\ell a} f_a, \tag{M4}$$

which recovers the Hamiltonian of Pontryagin's maximum principle in discrete time (section 12.5 of Sydsæter et al. 2008) for the objective function (M1a). Then, the total derivative of controls at a given age equals the partial derivative of the Hamiltonian, when both derivatives are evaluated at optimal controls:

$$\left.\frac{\mathrm{d}R_0}{\mathrm{d}\mathbf{y}_a}\right|_{\mathbf{y}=\bar{\mathbf{y}}=\mathbf{y}^*} = \left.\frac{\partial H_a}{\partial \mathbf{y}_a}\right|_{\mathbf{y}=\bar{\mathbf{y}}=\mathbf{y}^*}.$$

This is the essence of Pontryagin's maximum principle: the signs of the left-hand side derivatives are the same as the signs of the derivatives on the right-hand side, which are simpler to compute (although one must then compute costate variables).

Fourth, we prove that the formulas we found for the costate variables (M2) satisfy the costate equations of Pontryagin's maximum principle for discrete time. Such costate equations are dynamic equations that allow one to calculate the costate variables. Using Layer 4, Eq. 21 and Eqs. (28), we have that

$$\left.\frac{\mathrm{d}R_0}{\mathrm{d}\mathbf{x}_a}\right|_{\mathbf{y}=\bar{\mathbf{y}}} = \left.\left(\frac{\mathrm{d}\mathbf{x}^\intercal}{\mathrm{d}\mathbf{x}_a}\frac{\partial R_0}{\partial \mathbf{x}}\right)\right|_{\mathbf{y}=\bar{\mathbf{y}}}.$$

Expanding the matrix multiplication on the right-hand side, this is

$$\left.\frac{\mathrm{d}R_0}{\mathrm{d}\mathbf{x}_a}\right|_{\mathbf{y}=\bar{\mathbf{y}}} = \left.\left(\sum_{j=1}^{N_\mathrm{a}} \frac{\mathrm{d}\mathbf{x}_j^\intercal}{\mathrm{d}\mathbf{x}_a}\frac{\partial R_0}{\partial \mathbf{x}_j}\right)\right|_{\mathbf{y}=\bar{\mathbf{y}}} = \left.\left(\frac{\partial R_0}{\partial \mathbf{x}_a} + \sum_{j=a+1}^{N_\mathrm{a}} \frac{\mathrm{d}\mathbf{x}_j^\intercal}{\mathrm{d}\mathbf{x}_a}\frac{\partial R_0}{\partial \mathbf{x}_j}\right)\right|_{\mathbf{y}=\bar{\mathbf{y}}},$$

where we used Eq. (D15). Using the expression of the total effect of states on themselves as a product (Layer 4, Eq. 2) yields

$$\left.\frac{\mathrm{d}R_0}{\mathrm{d}\mathbf{x}_a}\right|_{\mathbf{y}=\bar{\mathbf{y}}} = \left.\left(\frac{\partial R_0}{\partial \mathbf{x}_a} + \sum_{j=a+1}^{N_\mathrm{a}} \frac{\partial \mathbf{x}_{a+1}^\intercal}{\partial \mathbf{x}_a}\frac{\mathrm{d}\mathbf{x}_j^\intercal}{\mathrm{d}\mathbf{x}_{a+1}}\frac{\partial R_0}{\partial \mathbf{x}_j}\right)\right|_{\mathbf{y}=\bar{\mathbf{y}}}.$$

Doing the sum over j yields

$$\begin{aligned}\left.\frac{\mathrm{d}R_0}{\mathrm{d}\mathbf{x}_a}\right|_{\mathbf{y}=\bar{\mathbf{y}}} &= \left.\left(\frac{\partial R_0}{\partial \mathbf{x}_a} + \frac{\partial \mathbf{x}_{a+1}^\intercal}{\partial \mathbf{x}_a}\sum_{j=a+1}^{N_\mathrm{a}} \frac{\mathrm{d}\mathbf{x}_j^\intercal}{\mathrm{d}\mathbf{x}_{a+1}}\frac{\partial R_0}{\partial \mathbf{x}_j}\right)\right|_{\mathbf{y}=\bar{\mathbf{y}}} \\ &= \left.\left(\frac{\partial R_0}{\partial \mathbf{x}_a} + \frac{\partial \mathbf{x}_{a+1}^\intercal}{\partial \mathbf{x}_a}\frac{\mathrm{d}\mathbf{x}^\intercal}{\mathrm{d}\mathbf{x}_{a+1}}\frac{\partial R_0}{\partial \mathbf{x}}\right)\right|_{\mathbf{y}=\bar{\mathbf{y}}}.\end{aligned}$$

Using the second line of Layer 4, Eq. 21 and Eqs. (28) again yields

$$\left.\frac{\mathrm{d}R_0}{\mathrm{d}\mathbf{x}_a}\right|_{\mathbf{y}=\bar{\mathbf{y}}} = \left.\left(\frac{\partial R_0}{\partial \mathbf{x}_a} + \frac{\partial \mathbf{x}_{a+1}^\intercal}{\partial \mathbf{x}_a}\frac{\mathrm{d}R_0}{\mathrm{d}\mathbf{x}_{a+1}}\right)\right|_{\mathbf{y}=\bar{\mathbf{y}}}. \tag{M5}$$

This equals the partial derivative of the Hamiltonian with respect to the states at age a. Indeed, using (M4) we have

$$\left.\frac{\partial H_a}{\partial \mathbf{x}_a}\right|_{\mathbf{y}=\bar{\mathbf{y}}} = \left.\left(\frac{\partial \mathbf{x}_{a+1}^\intercal}{\partial \mathbf{x}_a}\frac{\mathrm{d}R_0}{\mathrm{d}\mathbf{x}_{a+1}} + \frac{\partial R_0}{\partial \mathbf{x}_a}\right)\right|_{\mathbf{y}=\bar{\mathbf{y}}}.$$

Substituting this in Eq. (M5) and evaluating at optimal controls yields

$$\mathbf{k}_a = \left.\frac{\partial H_a}{\partial \mathbf{x}_a}\right|_{\mathbf{y}=\bar{\mathbf{y}}=\mathbf{y}^*}.$$

This is the costate equation of the Pontryagin's maximum principle in discrete time (Eq. 4 in section 12.5 of Sydsæter et al. 2008).

Appendix N. Matrix calculus notation

For vectors $\mathbf{a} \in \mathbb{R}^{n\times 1}$ and $\mathbf{b} \in \mathbb{R}^{m\times 1}$, we denote

$$\frac{\partial \mathbf{a}}{\partial \mathbf{b}^\intercal} = \begin{pmatrix} \frac{\partial a_1}{\partial b_1} & \cdots & \frac{\partial a_1}{\partial b_m} \\ \vdots & \ddots & \vdots \\ \frac{\partial a_n}{\partial b_1} & \cdots & \frac{\partial a_n}{\partial b_m} \end{pmatrix} \in \mathbb{R}^{n\times m},$$

so $(\partial \mathbf{a}/\partial \mathbf{b}^\intercal)^\intercal = \partial \mathbf{a}^\intercal / \partial \mathbf{b}$. The same notation applies with total derivatives.

Appendix O. Matrix of socio-devo stability

To see why the matrix

$$\left.\frac{\mathrm{d}\mathbf{x}}{\mathrm{d}\bar{\mathbf{x}}^{\intercal}}\right|_{\mathbf{y}=\bar{\mathbf{y}}}$$

is sufficient to determine socio-devo stability, consider the following. Let $\bar{\mathbf{x}}(\theta+1) = \tilde{\mathbf{g}}(\bar{\mathbf{x}}(\theta))$ denote the solution of iterating Eq. (5) over a, where we highlight only the argument corresponding to the phenotype of social partners. An equilibrium $\bar{\mathbf{x}}^{**}$ of the socio-devo stabilization dynamics satisfies $\bar{\mathbf{x}}^{**} = \tilde{\mathbf{g}}(\bar{\mathbf{x}}^{**})$. Taylor-expanding $\bar{\mathbf{x}}(\theta+1)$ to first-order around $\bar{\mathbf{x}}^{**}$, we have

$$\bar{\mathbf{x}}(\theta+1) = \tilde{\mathbf{g}}(\bar{\mathbf{x}}^{**}) + \left.\frac{\mathrm{d}\tilde{\mathbf{g}}}{\mathrm{d}\bar{\mathbf{x}}^{\intercal}}\right|_{\bar{\mathbf{x}}=\bar{\mathbf{x}}^{**}} (\bar{\mathbf{x}}(\theta) - \bar{\mathbf{x}}^{**}) + O(\|\bar{\mathbf{x}}(\theta) - \bar{\mathbf{x}}^{**}\|^2),$$

where the operator $\mathrm{d}/\mathrm{d}\bar{\mathbf{x}}^{\intercal}$ takes the total derivative to take into account developmental and environmental constraints. Noting that $\mathrm{d}\tilde{\mathbf{g}}/\mathrm{d}\bar{\mathbf{x}}^{\intercal}|_{\bar{\mathbf{x}}=\bar{\mathbf{x}}^{**}} = \mathrm{d}\mathbf{x}/\mathrm{d}\bar{\mathbf{x}}^{\intercal}|_{\mathbf{y}=\bar{\mathbf{y}}}$ since the resident is a socio-devo equilibrium, we have that a perturbation from a socio-devo equilibrium is approximately

$$\bar{\mathbf{x}}(\theta+1) - \tilde{\mathbf{g}}(\bar{\mathbf{x}}^{**}) \approx \left.\frac{\mathrm{d}\mathbf{x}}{\mathrm{d}\bar{\mathbf{x}}^{\intercal}}\right|_{\mathbf{y}=\bar{\mathbf{y}}} (\bar{\mathbf{x}}(\theta) - \bar{\mathbf{x}}^{**}),$$

which asymptotically converges to $\mathbf{0}$ (i.e., $\bar{\mathbf{x}}^{**}$ is locally stable) if all the eigenvalues of the matrix

$$\left.\frac{\mathrm{d}\mathbf{x}}{\mathrm{d}\bar{\mathbf{x}}^{\intercal}}\right|_{\mathbf{y}=\bar{\mathbf{y}}}$$

have absolute value strictly less than one.

Appendix P. Total and semi-total derivatives

Consider a function $f(a, \mathbf{b}, \mathbf{c}) \in \mathbb{R}$ where the vectors $\mathbf{b} \in \mathbb{R}^{n\times 1}$ and $\mathbf{c} \in \mathbb{R}^{m\times 1}$ satisfy the (equality) constraints

$$\mathbf{b} = \mathbf{d}(a)$$
$$\mathbf{c} = \mathbf{e}(a),$$

for some differentiable functions $\mathbf{d}(a) \in \mathbb{R}^{n\times 1}$ and $\mathbf{e}(a) \in \mathbb{R}^{m\times 1}$. From the chain rule, the total derivative of $f(a, \mathbf{b}, \mathbf{c})$ with respect to a is

$$\begin{aligned}\frac{\mathrm{d}f}{\mathrm{d}a} &= \frac{\mathrm{d}f(a, \mathbf{d}(a), \mathbf{e}(a))}{\mathrm{d}a} = \frac{\partial f}{\partial a} + \sum_{i=1}^{n} \frac{\partial f}{\partial b_i}\frac{\mathrm{d}b_i}{\mathrm{d}a} + \sum_{i=1}^{m} \frac{\partial f}{\partial c_i}\frac{\mathrm{d}c_i}{\mathrm{d}a} \\ &= \frac{\partial f}{\partial a} + \frac{\partial f}{\partial \mathbf{b}^{\intercal}}\frac{\mathrm{d}\mathbf{b}}{\mathrm{d}a} + \frac{\partial f}{\partial \mathbf{c}^{\intercal}}\frac{\mathrm{d}\mathbf{c}}{\mathrm{d}a}.\end{aligned}$$

We call the semi-total derivative of $f(a, \mathbf{b}, \mathbf{c})$ with respect to a, considering the constraints on $\mathbf{b}$ without considering the constraints on $\mathbf{c}$, the quantity

$$\frac{\delta f}{\delta a} = \frac{\mathrm{d}f(a, \mathbf{d}(a), \mathbf{c})}{\mathrm{d}a} = \frac{\partial f}{\partial a} + \frac{\partial f}{\partial \mathbf{b}^{\intercal}}\frac{\mathrm{d}\mathbf{b}}{\mathrm{d}a}.$$

We use "derivative-like" notation like this one for various differential operators, motivated by some analogous use by Caswell (2019) (his Eqs. 1.2 and 2.21, which he based on a suggestion by Samuelson 1947).

References

Altenberg, L., 1995. Genome growth and the evolution of the genotype-phenotype map, in: Banzhaf, W., Eeckman, F.H. (Eds.), Evolution and biocomputation. Springer-Verlag. volume 899 of *Lecture Notes in Computer Science*, pp. 205–259.

Aoki, K., Wakano, J.Y., Lehmann, L., 2012. Evolutionarily stable learning schedules and cumulative culture in discrete generation models. Theor. Popul. Biol. 81, 300–309.

Arnold, S.J., 1992. Constraints on phenotypic evolution. Am. Nat. 140, S85–S107.

Arthur, W., 2004. Biased Embryos and Evolution. Cambridge Univ. Press, Cambridge, UK.

Avila, P., Fromhage, L., Lehmann, L., 2019. Sex-allocation conflict and sexual selection throughout the lifespan of eusocial colonies. Evolution 73, 1116–1132.

Avila, P., Priklopil, T., Lehmann, L., 2021. Hamilton's rule, gradual evolution, and the optimal (feedback) control of phenotypically plastic traits. J. Theor. Biol. , 110602.

Baldwin, J.M., 1896. A new factor in evolution. Am. Nat. 30, 441–451.

Barfield, M., Holt, R.D., Gomulkiewicz, R., 2011. Evolution in stage-structured populations. Am. Nat. 177, 397–409.

Barton, N.H., 2017. How does epistasis influence the response to selection? Heredity 118, 96–109.

Barton, N.H., Etheridge, A.M., Véber, A., 2017. The infinitesimal model: definition, derivation, and implications. Theor. Popul. Biol. 118, 50–73.

Barton, N.H., Turelli, M., 1987. Adaptive landscapes, genetic distance and the evolution of quantitative characters. Genet. Res. 49, 157–173.

Bienvenu, F., Legendre, S., 2015. A new approach to the generation time in matrix population models. Am. Nat. 185, 834–843.

Björklund, M., Husby, A., Gustafsson, L., 2013. Rapid and unpredictable changes of the G-matrix in a natural bird population over 25 years. J. Evol. Biol. 26, 1–13.

Bonduriansky, R., Day, T., 2018. Extended Heredity: a new understanding of inheritance and evolution. Princeton Univ. Press, Princeton, NJ, USA.

Boyd, R., Richerson, P.J., 1985. Culture and the Evolutionary Process. The Univ. of Chicago Press, Chicago, IL, USA.

Brakefield, P.M., 2006. Evo-devo and constraints on selection. Trends Ecol. Evol. 21, 362–368.

Bulmer, M., 1994. Theoretical Evolutionary Ecology. Sinauer, Sunderland, MA, USA.

Bulmer, M.G., 1971. The effect of selection on genetic variability. Am. Nat. 105, 201–211.

Bulmer, M.G., 1980. The Mathematical Theory of Quantitative Genetics. Oxford Univ. Press, Oxford, UK.

Carter, A.J.R., Hermisson, J., Hansen, T.F., 2005. The role of epistatic interactions in the response to selection and the evolution of evolvability. Theor. Popul. Biol. 68, 179–196.

Caswell, H., 1978. A general formula for the sensitivity of population growth rate to changes in life history parameters. Theor. Popul. Biol. 14, 215–230.

Caswell, H., 1982. Optimal life histories and the age-specific costs of reproduction. J. Theor. Biol. 98, 519–529.

Caswell, H., 2001. Matrix Population Models. 2nd ed., Sinauer, Sunderland, MA, USA.

Caswell, H., 2009. Stage, age and individual stochasticity in demography. Oikos 118, 1763–1782.

Caswell, H., 2019. Sensitivity Analysis: Matrix Methods in Demography and Ecology. Springer Open, Cham, Switzerland.

Caswell, H., Nisbet, R.M., de Roos, A., Tuljapurkar, S., 1997. Structured-population models: many methods, a few basic concepts, in: Tuljapurkar, S., Caswell, H. (Eds.), Structured-population models in marine, terrestrial, and freshwater systems. Chapman & Hall, New York, NY, USA.

Caswell, H., Shyu, E., 2017. Senescence, selection gradients and mortality. Cambridge Univ. Press, Cambridge, UK. chapter 4. pp. 56–82.

Cavalli-Sforza, L.L., Feldman, M.W., 1981. Cultural Transmission and Evolution. Princeton Univ. Press, Princeton, NJ, USA.

Champagnat, N., 2006. A microscopic interpretation for adaptive dynamics trait substitution sequence models. Stoch. Process. Their Appl. 116, 1127–1160.

Charlesworth, B., 1990. Optimization models, quantitative genetics, and mutation. Evolution 44, 520–538.

Charlesworth, B., 1993. Natural selection on multivariate traits in age-structured populations. Proc. R. Soc. Lond. B 251, 47–52.
Charlesworth, B., 1994. Evolution in age-structured populations. 2nd ed., Cambridge Univ. Press.
Charlesworth, B., Lande, R., Slatkin, M., 1982. A neo-Darwinian commentary on macroevolution. Evolution 36, 474–498.
Cheverud, J.M., 1984. Quantitative genetics and developmental constraints on evolution by selection. J. Theor. Biol. 110, 155–171.
Chevin, L.M., Lande, R., Mace, G.M., 2010. Adaptation, plasticity, and extinction in a changing environment: Towards a predictive theory. PLOS Biology 8, 1–8.
Crow, J.F., Kimura, M., 1970. An Introduction to Population Genetics Theory. Blackburn Press, Caldwell, NJ, USA.
Day, T., Bonduriansky, R., 2011. A unified approach to the evolutionary consequences of genetic and nongenetic inheritance. Am. Nat. 178, E18–E36.
Day, T., Taylor, P.D., 1997. Hamilton's rule meets the Hamiltonian: kin selection on dynamic characters. Proc. R. Soc. Lond. B 264, 639–644.
Day, T., Taylor, P.D., 2000. A generalization of Pontryagin's maximum principle for dynamic evolutionary games among relatives. Theor. Popul. Biol. 57, 339–356.
de Roos, A., 1997. A gentle introduction to physiologically structured population models, in: Tuljapurkar, S. (Ed.), Structured-population models in marine, terrestrial, and freshwater systems. Chapman & Hall, New York, NY, USA, pp. 119–271.
de Vries, C., Caswell, H., 2018. Demography when history matters: construction and analysis of second-order matrix population models. Theor. Ecol. 11, 129–140.
Débarre, F., Nuismer, S.L., Doebeli, M., 2014. Multidimensional (co)evolutionary stability. Am. Nat. 184, 158–171.
Dieckmann, U., Heino, M., Parvinen, K., 2006. The adaptive dynamics of function-valued traits. J. Theor. Biol. 241, 370–389.
Dieckmann, U., Law, R., 1996. The dynamical theory of coevolution: a derivation from stochastic ecological processes. J. Math. Biol. 34, 579–612.
Durinx, M., (Hans) Metz, J.A.J., Meszéna, G., 2008. Adaptive dynamics for physiologically structured population models. J. Math. Biol. 56, 673–742.
Edwards, A.W.F., 2000. Sewall wright's equation $\delta q = (q(1-q)\partial w/\partial q)/2w$. Theor. Popul. Biol. 57, 67–70.
Engen, S., Sæther, B.E., 2021. Structure of the G-matrix in relation to phenotypic contributions to fitness. Theor. Popul. Biol. 138, 43–56.
Falconer, D.S., Mackay, T.F.C., 1996. Introduction to Quantitative Genetics. 4th ed., Pearson Prentice Hall, Harlow, England.
Fisher, R., 1918. XV.—The correlation between relatives on the supposition of Mendelian inheritance. Trans. Roy. Soc. Edinb. 52, 399–433.
Fisher, R.A., 1922. XXI.—On the dominance ratio. Trans. Roy. Soc. Edinb. 42, 321–341.
Fisher, R.A., 1927. The actuarial treatment of official birth records. Eugen. Rev. 19, 103–108.
Gadgil, M., Bossert, W.H., 1970. Life historical consequences of natural selection. Am. Nat. 104, 1–24.
Galis, F., Metz, J.A.J., van Alphen, J.J.M., 2018. Development and evolutionary constraints in animals. Annu. Rev. Ecol. Evol. Syst. 49, 499–522.
Gavrilets, S., Hastings, A., 1994. A quantitative-genetic model for selection on developmental noise. Evolution 48, 1478–1486.
Geritz, S.A.H., 2005. Resident-invader dynamics and the coexistence of similar strategies. J. Math. Biol. 50, 67–82.
Geritz, S.A.H., Gyllenberg, M., Jacobs, F.J.A., Parvinen, K., 2002. Invasion dynamics and attractor inheritance. J. Math. Biol. 44, 548–560.
Geritz, S.A.H., Kisdi, E., Meszéna, G., Metz, J.A.J., 1998. Evolutionarily singular strategies and the adaptive growth and branching of the evolutionary tree. Evol. Ecol. 12, 35–57.
Gimelfarb, A., 1982. Quantitative character dynamics: Gametic model. Theor. Popul. Biol. 22, 324–366.
Gomulkiewicz, R., Kirkpatrick, M., 1992. Quantitative genetics and the evolution of reaction norms. Evolution 46, 390–411.
González-Forero, M., Faulwasser, T., Lehmann, L., 2017. A model for brain life history evolution. PLOS Comp. Biol. 13, e1005380.
Gould, S.J., Lewontin, R.C., 1979. The spandrels of San Marco and the Panglossian paradigm: a critique of the adaptationist programme. Proc. R. Soc. Lond. B 205, 581–598.
Greene, V.L., 1977. An algorithm for total and indirect causal effects. Political Methodology 4, 369–381.
Hamilton, W.D., 1966. The moulding of senescence by natural selection. J. Theor. Biol. 12, 12–45.
Hansen, T.F., 2013. Why epistasis is important for selection and adaptation. Evolution 67, 3501–3511.
Hansen, T.F., Houle, D., 2004. Evolvability, stabilizing selection, and the problem of stasis, in: Pigliucci, M., Preston, K. (Eds.), Phenotypic integration: studying ecology and evolution of complex phenotypes. Oxford Univ. Press. chapter 5.
Hansen, T.F., Houle, D., 2008. Measuring and comparing evolvability and constraint in multivariate characters. J. Evol. Biol. 21, 1201–1219.
Hansen, T.F., Wagner, G.P., 2001. Modeling genetic architecture: a multilinear theory of gene interaction. Theor. Popul. Biol. 59, 61–86.
Hermisson, J., Hansen, T.F., Wagner, G.P., 2003. Epistasis in polygenic traits and the evolution of genetic architecture under stabilizing selection. Am. Nat. 161, 708–734.
Hill, W.G., 2017. "Conversion" of epistatic into additive genetic variance in finite populations and possible impact on long-term selection response. J. Anim. Breed. Genet. 134, 196–201.
Hine, E., Blows, M.W., 2006. Determining the effective dimensionality of the genetic variance-covariance matrix. Genetics 173, 1135–1144.
Hine, E., McGuigan, K., Blows, M.W., 2014. Evolutionary constraints in high-dimensional traits sets. Am. Nat. 184, 119–131.
Horn, R.A., Johnson, C.R., 2013. Matrix Analysis. 2nd ed., Cambridge Univ. Press, New York, NY, USA.
Houle, D., 1991. Genetic covariance of fitness correlates: what genetic correlations are made of and why it matters. Evolution 45, 630–648.
Houle, D., 2001. Characters as the units of evolutionary change, in: Wagner, G.P. (Ed.), The Character Concept in Evolutionary Biology. Academic Press, San Diego, CA, USA, pp. 109–140.
Houston, A., Clark, C., McNamara, J., Mangel, M., 1988. Dynamic models in behavioural and evolutionary ecology. Nature 332, 29–34.
Houston, A.I., McNamara, J.M., 1999. Models of Adaptive Behaviour: an approach based on state. Cambridge Univ. Press.
Iwasa, Y., Pomiankowski, A., 1991. The evolution of costly mate preferences II. The "handicap" principle. Evolution 45, 1431–1442.
Iwasa, Y., Roughgarden, J., 1984. Shoot/root balance of plants: optimal growth of a system with many vegetative organs. Theor. Popul. Biol. 25, 78–105.
Jablonka, E., Lachmann, M., Lamb, M.J., 1992. Evidence, mechanisms and models for the inheritance of acquired characters. J. Theor. Biol. 158, 245–268.
Jones, A.G., Bürger, R., Arnold, S.J., 2014. Epistasis and natural selection shape the mutational architecture of complex traits. Nat. Comm. 5, 3709.
Kaznatcheev, A., 2019. Computational complexity as an ultimate constraint on evolution. Genetics 212, 245–265.
Kingsolver, J.G., Diamond, S.E., 2011. Phenotypic selection in natural populations: What limits directional selection? Am. Nat. 177, 346–357.
Kingsolver, J.G., Hoekstra, H.E., Hoekstra, J.M., Berrigan, D., Vignieri, S.N., Hill, C.E., Hoang, A., Gibert, P., Beerli, P., 2001. The strength of phenotypic selection in natural populations. Am. Nat. 157, 245–261.
Kirkpatrick, M., Heckman, N., 1989. A quantitative genetic model for growth, shape, reaction norms, and other infinite-dimensional characters. J. Math. Biol. 27, 429–450.
Kirkpatrick, M., Lande, R., 1989. The evolution of maternal characters. Evolution 43, 485–503.
Kirkpatrick, M., Lofsvold, D., 1992. Measuring selection and constraint in the evolution of growth. Evolution 46, 954–971.
Kirkpatrick, M., Lofsvold, D., Bulmer, M., 1990. Analysis of inheritance, selection and evolution of growth trajectories. Genetics 124, 979–993.
Klingenberg, C.P., 2005. Variation. Academic Press, Burlington, MA, USA. chapter 11. Developmental constraints, modules, and evolvability. pp. 219–247.
Klingenberg, C.P., 2010. Evolution and development of shape: integrating quantitative approaches. Nat. Rev. Genet. 11, 623–635.
Kobayashi, Y., Wakano, J.Y., Ohtsuki, H., 2015. A paradox of cumulative culture. J. Theor. Biol. 379, 79–88.
Kozłowski, J., Teriokhin, A.T., 1999. Allocation of energy between growth and reproduction: the Pontryagin Maximum Principle solution for the case of age- and season-dependent mortality. Evol. Ecol. Res. 1, 423–441.
Laland, K., Uller, T., Feldman, M., Sterelny, K., Müller, G.B., Moczek, A., Jablonka, E., Odling-Smee, J., 2014. Does evolutionary theory need a rethink? Yes, urgently. Nature 514, 161–164.

Laland, K.N., Uller, T., Feldman, M.W., Sterelny, K., Müller, G.B., Moczek, A., Jablonka, E., Odling-Smee, J., 2015. The extended evolutionary synthesis: its structure, assumptions and predictions. Proc. R. Soc. B 282, 20151019.

Lande, R., 1979. Quantitative genetic analysis of multivariate evolution applied to brain: body size allometry. Evolution 34, 402–416.

Lande, R., 1980. The genetic covariance between characters maintained by pleiotropic mutations. Genetics 94, 203–215.

Lande, R., 1982. A quantitative genetic theory of life history evolution. Ecology 63, 607–615.

Lande, R., Arnold, S.J., 1983. The measurement of selection on correlated characters. Evolution 37, 1210–1226.

Leimar, O., 2009. Multidimensional convergence stability. Evol. Ecol. Res. 11, 191–208.

León, J.A., 1976. Life histories as adaptive strategies. J. Theor. Biol. 60, 301–335.

Lewontin, R.C., 1983. Gene, organism and environment, in: Bendall, D.S. (Ed.), Evolution from molecules to men. Cambridge Univ. Press, Cambridge, UK. chapter 14, pp. 273–285.

Lush, J.L., 1937. Animal Breeding Plans. Iowa State Univ. Press, Ames, IA, USA.

Lynch, M., Walsh, B., 1998. Genetics and Analysis of Quantitative Traits. Sinauer, Sunderland, MA, USA.

Martin, G., 2014. Fisher's geometrical model emerges as a property of complex integrated phenotypic networks. Genetics 197, 237–255.

Maynard Smith, J., Burian, R., Kauffman, S., Alberch, P., Campbell, J., Goodwin, B., Lande, R., Raup, D., Wolpert, L., 1985. Developmental constraints and evolution. Q. Rev. Biol. .

McGlothlin, J.W., Moore, A.J., Wolf, J.B., Brodie III, E.D., 2010. Interacting phenotypes and the evolutionary process. III. Social evolution. Evolution 64, 2558–2574.

McGuigan, K., Blows, M., 2007. The phenotypic and genetic covariance structure of Drosophilid wings. Evolution 61, 902–911.

Medawar, P.B., 1952. An unsolved problem of biology. H. K. Lewis, London, UK.

Merilä, J., Sheldon, B., Kruuk, L., 2001. Explaining stasis: microevolutionary studies in natural populations. Genetica 112, 199–222.

Metz, J., Geritz, S., Meszéna, G., Jacobs, F., van Heerwaarden, J., 1996. Adaptive dynamics, a geometrical study of the consequences of nearly faithful reproduction, in: van Strien, S., Lunel, S.V. (Eds.), Stochastic and spatial structures of dynamical systems. Konink. Nederl. Akad. Wetensch. Verh. Afd. Natuurk. Eerste Reeks, Amsterdam, Netherlands, pp. 183–231.

Metz, J.A.J., 2011. Thoughts on the geometry of meso-evolution: collecting mathematical elements for a postmodern synthesis, in: Chalub, F.A.C.C., Rodrigues, J.F. (Eds.), The Mathematics of Darwin's Legacy. Springer, pp. 193–231.

Metz, J.A.J., Staňková, K., Johansson, J., 2016. The canonical equation of adaptive dynamics for life histories: from fitness-returns to selection gradients and Pontryagin's maximum principle. J. Math. Biol. 72, 1125–1152.

Mezey, J.G., Houle, D., 2005. The dimensionality of genetic variation for wing shape in *Drosophila melanogaster*. Evolution 59, 1027–1038.

Moore, A.J., Brodie III, E.D., Wolf, J.B., 1997. Interacting phenotypes and the evolutionary process: I. direct and indirect genetic effects of social interactions. Evolution 51, 1352–1362.

Morrissey, M.B., 2014. Selection and evolution of causally covarying traits. Evolution 68, 1748–1761.

Morrissey, M.B., 2015. Evolutionary quantitative genetics of nonlinear developmental systems. Evolution 69, 2050–2066.

Müller, G.B., 2007. Evo-devo: extending the evolutionary synthesis. Nat. Rev. Genet. 8, 943–949.

Mylius, S.D., Diekmann, O., 1995. On evolutionarily stable life histories, optimization and the need to be specific about density dependence. Oikos 74, 218–224.

Nelson, R.M., Pettersson, M.E., Carlborg, Ö., 2013. A century after Fisher: time for a new paradigm in quantitative genetics. Trends Genet. 29, 669–676.

Noble, D.W.A., Radersma, R., Uller, T., 2019. Plastic responses to novel environments are biased towards phenotype dimensions with high additive genetic variation. Proc. Natl. Acad. Sci. USA 116, 13452–13461.

Odling-Smee, F.J., Laland, K.N., Feldman, M.W., 1996. Niche construction. Am. Nat. 147, 641–648.

Odling-Smee, F.J., Laland, K.N., Feldman, M.W., 2003. Niche Construction: the neglected process in evolution. Princeton Univ. Press, Princeton, NJ, USA.

Otto, S.P., Day, T., 2007. A Biologist's Guide to Mathematical Models in Ecology and Evolution. Princeton Univ. Press, Woodstock, UK.

Paenke, I., Sendhoff, B., Kawecki, T.J., 2007. Influence of plasticity and learning on evolution under directional selection. Am. Nat. 170, E47–E58.

Paixão, T., Barton, N.H., 2016. The effect of gene interactions on the long-term response to selection. Proc. Natl. Acad. Sci. USA 113, 4422–4427.

Parvinen, K., Heino, M., Dieckmann, U., 2013. Function-valued adaptive dynamics and optimal control theory. J. Math. Biol. 67, 509–533.

Pavlicev, M., Cheverud, J.M., Wagner, G.P., 2011. Evolution of adaptive phenotypic variation patterns by direct selection for evolvability. Proc. R. Soc. B 278, 1903–1912.

Pavlicev, M., Hansen, T.F., 2011. Genotype-phenotype maps maximizing evolvability: modularity revisited. Evol. Biol. 38, 371–389.

Pavlicev, M., Wagner, G.P., 2012. A model of developmental evolution: selection, pleiotropy and compensation. Trends. Ecol. Evol. 27, 316–322.

Pigliucci, M., 2007. Do we need an extended evolutionary synthesis. Evolution 61, 2743–2749.

Priklopil, T., Lehmann, L., 2020. Invasion implies substitution in ecological communities with class-structured populations. Theor. Popul. Biol. 134, 36–52.

Pujol, B., Blanchet, S., Charmantier, A., Danchin, E., Facon, B., Marrot, P., Roux, F., Scotti, I., Teplitsky, C., Thomson, C.E., et al., 2018. The missing response to selection in the wild. Trends Ecol. Evol. 33, 337–346.

Reuter, M., Keller, L., 2001. Sex ratio conflict and worker production in eusocial hymenoptera. Am. Nat. 158, 166–177.

Rice, S.H., 1990. A geometric model for the evolution of development. J. Theor. Biol. 143, 319–342.

Rice, S.H., 2002. A general population genetic theory for the evolution of developmental interactions. Proc. Natl. Acad. Sci. USA 99, 15518–15523.

Rice, S.H., 2011. The place of development in mathematical evolutionary theory. J. Exp. Zool. 314B, 1–9.

Roff, D.A., 1992. The Evolution of Life Histories. Chapman & Hall, New York, NY, USA.

Salazar-Ciudad, I., 2021. Why call it developmental bias when it is just development? Biol. Direct 16, 3.

Salazar-Ciudad, I., Jernvall, J., 2010. A computational model of teeth and the developmental origins of morphological variation. Nature 464, 583–586.

Salazar-Ciudad, I., Marín-Riera, M., 2013. Adaptive dynamics under development-based genotype–phenotype maps. Nature 497, 361–364.

Samuelson, P.A., 1947. Foundations of economic analysis. Harvard Univ. Press, Cambridge, MA, USA.

Schaffer, W.M., 1983. The application of optimal control theory to the general life history problem. Am. Nat. 121, 418–431.

Service, P.M., Rose, M.R., 1985. Genetic covariation among life-history components: the effect of novel environments. Evolution 39, 943–945.

Slatkin, M., 2009. Epigenetic inheritance and the missing heritability problem. Genetics 182, 845–850.

Stearns, S.C., 1992. The Evolution of Life Histories. Oxford University Press, Oxford, UK.

Sternberg, S., 2010. Dynamical Systems. Dover Publications, Inc., Mineola, NY, USA.

Sutton, R.S., Barto, A.G., 2018. Reinforcement Learning: An Introduction. 2nd ed., The MIT Press, Cambridge, Massachusetts, USA.

Sydsæter, K., Hammond, P., Seierstad, A., Strom, A., 2008. Further Mathematics for Economic Analysis. 2nd ed., Prentice Hall.

Taylor, H.M., Gourley, R.S., Lawrence, C.E., Kaplan, R.S., 1974. Natural selection of life history attributes: an analytical approach. Theor. Popul. Biol. 5, 104–122.

Tomlin, C.J., Axelrod, J.D., 2007. Biology by numbers: mathematical modelling in developmental biology. Nat. Rev. Genet. 8, 331–340.

Townley, S., Ezard, T.H.G., 2013. A G matrix analogue to capture the cumulative effects of nongenetic inheritance. J. Evol. Biol. 26, 1234–1243.

Turelli, M., 1988. Phenotypic evolution, constant covariances, and the maintenance of additive variance. Evolution 42, 1342–1347.

Turelli, M., Barton, N.H., 1994. Genetic and statistical analyses of strong selection on polygenic traits: what, me normal? Genetics 138, 913–941.

Turing, A.M., 1952. The chemical basis of morphogenesis. Phil. Trans. R. Soc. Lond. B 237, 37–72.

Uller, T., Moczek, A.P., Watson, R.A., Brakefield, P.M., Laland, K.N., 2018.

Developmental bias and evolution: A regulatory network perspective. Genetics 209, 949–966.
van Tienderen, P.H., 1995. Life cycle trade-offs in matrix population models. Ecology 76, 2482–2489.
Via, S., Lande, R., 1985. Genotype-environment interaction and the evolution of phenotypic plasticity. Evolution 39, 505–522.
Waddington, C.H., 1959. Evolutionary adaptation. Perspect. Biol. Med. 2, 379–401.
Wagner, G.P., 1984. On the eigenvalue distribution of genetic and phenotypic dispersion matrices: Evidence for a nonrandom organization of quantitative character variation. J. Math. Biol. 21, 77–95.
Wagner, G.P., 1988. The influence of variation and of developmental constraints on the rate of multivariate phenotypic evolution. J. Evol. Biol. 1, 45–66.
Wagner, G.P., 1989. Multivariate mutation-selection balance with constrained pleiotropic effects. Genetics 122, 223–234.
Wagner, G.P., 1996. Homologues, natural kinds and the evolution of modularity. Am. Zool. 36, 36–43.
Wagner, G.P., Mezey, J., 2000. Modeling the evolution of genetic architecture: a continuum of alleles models with pairwise $A \times A$ epistasis. J. Theor. Biol. 203, 163–175.
Wagner, G.P., Zhang, J., 2011. The pleiotropic structure of the genotype-phenotype map: the evolvability of complex organisms. Nat. Rev. Genet. 12, 204–213.
Walsh, B., Lynch, M., 2018. Evolution and Selection of Quantitative Traits. Oxford Univ. Press, Oxford, UK.
Watson, R.A., Wagner, G.P., Pavlicev, M., Weinreich, D.M., Mills, R., 2013. The evolution of phenotypic correlations and "developmental memory". Evolution 68, 1124–1138.
Welch, J.J., 2017. What's wrong with evolutionary biology? Biol. Philos. 32, 263–279.
West-Eberhard, M.J., 2003. Developmental Plasticity and Evolution. Oxford Univ. Press, Oxford, UK.
Wild, G., Traulsen, A., 2007. The different limits of weak selection and the evolutionary dynamics of finite populations. J. Theor. Biol. 247, 382–390.
Wolf, J.B., Frankino, W.A., Agrawal, A.F., Brodie III, E.D., Moore, A.J., 2001. Developmental interactions and the constituents of quantitative variation. Evolution 55, 232–245.
Wright, S., 1937. The distribution of gene frequencies in populations. Proc. Natl. Acad. Sci. USA 23, 307–320.