

Supplementary Information for:

How development affects evolution

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1 Long-term phenotypic evolution by extending the Lande equation

While Eq. 3 in the main text describes long-term phenotypic evolution, the classic Lande equation¹ describes short-term phenotypic evolution². The basic reason is that in the classic Lande equation¹ the \mathbf{G} -matrix depends on allele frequency and linkage disequilibrium but the classic Lande equation does not describe change in allele frequency or linkage disequilibrium. The standard approach to address this issue is to assume that each trait is controlled by an arbitrarily large number of loci so in the short term allele frequency change per locus is negligible (i.e., Fisher's infinitesimal model)^{3;2}; then, \mathbf{G} is assumed constant or its evolution is described by the Bulmer equation which considers change in \mathbf{G} due to change in linkage disequilibrium while still assuming negligible allele frequency change^{4;5;2}. However, such an approach allows for the classic Lande equation to describe evolution only in the short term, where allele frequency change per locus remains negligible². In contrast, the extended Lande equation in Eq. 3 in the main text simultaneously describes evolution of gene expression, which plays the role of allele frequency under the framework's assumptions whereas linkage disequilibrium is not an issue as reproduction is assumed to be clonal for simplicity⁶. In turn, the classic canonical equation of adaptive dynamics describes long-term evolution of genetic traits that do not have developmental constraints⁷. Instead, Eq. 3 in the main text describes the evolution of developed traits in the long term given the formulas describing the \mathbf{G}_z -matrix as a function of developed and genetic traits. Eq. 3 in the main text describes the dynamics of all dynamic variables involved (i.e., phenotype and gene expression) so the long-term evolutionary trajectory is well-defined, but consequently the associated \mathbf{G}_z -matrix is always singular. The evolution of genetic covariation \mathbf{G}_z emerges here from the evolution of the geno-phenotype \mathbf{z} under arbitrarily complex gene-gene interactions.

The framework uses adaptive dynamics assumptions⁶, which differ from the quantitative dynamics assumptions of the classic Lande equation. Thus, while the classic \mathbf{G} matrix has the same form of Eq. 5 of the main text (see Eq. II of ref. ⁸, Eq. + of ref. ⁹, Eq. 3.5b of ref. ¹⁰, and Eq. 4.23b of ref. ¹¹; see also Eq. 22a of ref. ¹², Eq. 3 of ref. ¹³, and Eq. 9 of ref. ¹⁴), the covariance matrix $\text{cov}[\mathbf{y}, \mathbf{y}]$ under quantitative genetics assumptions describes covariation in standing allele frequency. In contrast, the \mathbf{G} matrix we use is based on adaptive dynamics

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30 assumptions so the covariance matrix $\text{cov}[\mathbf{y}, \mathbf{y}]$ describes mutational covariation in gene expression, that is, the
 31 covariation in gene expression among possible mutations at the current evolutionary time step (even though
 32 at the current evolutionary time step there is only one realised mutation). This difference in the meaning of
 33 $\text{cov}[\mathbf{y}, \mathbf{y}]$ does not affect any of the points made in the main text.

34 2 Matrix calculus notation

35 In the main text we use the following notation from matrix calculus. The Jacobian of a vector $\mathbf{a} \in \mathbb{R}^{n \times 1}$ with
 36 respect to a vector $\mathbf{b} \in \mathbb{R}^{m \times 1}$ in its standard or transposed form is, respectively,

$$\frac{\partial \mathbf{a}}{\partial \mathbf{b}^\top} = \begin{pmatrix} \frac{\partial a_1}{\partial b_1} & \cdots & \frac{\partial a_1}{\partial b_m} \\ \vdots & \ddots & \vdots \\ \frac{\partial a_n}{\partial b_1} & \cdots & \frac{\partial a_n}{\partial b_m} \end{pmatrix} \in \mathbb{R}^{n \times m} \quad \text{or} \quad \frac{\partial \mathbf{a}^\top}{\partial \mathbf{b}} = \begin{pmatrix} \frac{\partial a_1}{\partial b_1} & \cdots & \frac{\partial a_n}{\partial b_1} \\ \vdots & \ddots & \vdots \\ \frac{\partial a_1}{\partial b_m} & \cdots & \frac{\partial a_n}{\partial b_m} \end{pmatrix} \in \mathbb{R}^{m \times n}.$$

37 The transpose of $\partial \mathbf{a} / \partial \mathbf{b}^\top$ is $(\partial \mathbf{a} / \partial \mathbf{b}^\top)^\top = \partial \mathbf{a}^\top / \partial \mathbf{b}$. The analogous notation applies for total derivatives.

38 3 How development enables negative senescence

39 Here we derive Eq. 13 of the main text. González-Forero and Gardner (Eqs. 13a and 26 of ref.⁶) show that
 40 the evolutionary dynamics of gene expression are given by the canonical equation of adaptive dynamics (cf.
 41 Eq. 6.1 of Dieckmann and Law⁷ and Eq. 23 of Durinx et al.¹⁵):

$$\frac{d\bar{\mathbf{y}}}{d\tau} = \kappa \mathbf{G}_y \left. \frac{dw}{dy} \right|_{\mathbf{y}=\bar{\mathbf{y}}}, \quad (\text{S1a})$$

42 where

$$\mathbf{G}_y = \text{cov}[\mathbf{y}, \mathbf{y}] \quad (\text{S1b})$$

43 is equivalently the mutational covariance matrix (of gene expression) and the additive genetic covariance ma-
 44 trix of gene expression. Due to age structure, a mutant's relative fitness is

$$w = \sum_{j=1}^{N_a} w_j,$$

45 where a mutant's relative fitness at age j is

$$w_j = \frac{1}{T} (\phi_j f_j^\circ + \pi_j p_j^\circ)$$

46 (Eq. 24 of ref.⁶). The superscript \circ denotes evaluation at $\mathbf{y} = \bar{\mathbf{y}}$, so f_j° and p_j° are, respectively, the fertility and
 47 survival probability of a neutral mutant at age j . Generation time is

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

48 (Eq. 20 of ref. ⁶) where the survivorship of neutral mutants is $\ell_j^\circ = \prod_{i=1}^{j-1} p_i^\circ$. The forces of selection on fertility
 49 and survival are, respectively,

$$\begin{aligned}\phi_j &= \ell_j^\circ \\ \pi_j &= \frac{1}{p_j^\circ} \sum_{k=j+1}^{N_a} \ell_k^\circ f_k^\circ,\end{aligned}$$

50 (Eqs. 21 of ref. ⁶). In turn, the total selection gradient of gene expression is

$$\left. \frac{dw}{d\mathbf{y}} \right|_{\mathbf{y}=\bar{\mathbf{y}}} = \left(\frac{\delta w}{\delta \mathbf{y}} + \frac{d\mathbf{x}^\top}{d\mathbf{y}} \frac{\delta w}{\delta \mathbf{x}} \right) \Big|_{\mathbf{y}=\bar{\mathbf{y}}} \quad (\text{S2})$$

51 (Layer 4 Eq. 22 of ref. ⁶).

52 Hence, if gene expression levels are mutationally uncorrelated (i.e., all non-diagonal entries of \mathbf{G}_y are zero),
 53 the evolutionary dynamics of the expression level of the i -th gene product at age a are given by

$$\frac{d\bar{y}_{ia}}{d\tau} = G_{y_{ia}} \left. \frac{dw}{dy_{ia}} \right|_{\mathbf{y}=\bar{\mathbf{y}}}. \quad (\text{S3})$$

54 Since $G_{y_{ia}}$ is a variance, it is non-negative, so the i -th resident gene expression at age a increases over evolu-
 55 tionary time if and only if the total selection gradient of this gene expression is positive, provided that there
 56 is mutational variation for this gene expression at that age. From Eq. (S2), the total selection gradient of gene
 57 expression y_{ia} is

$$\left. \frac{dw}{dy_{ia}} \right|_{\mathbf{y}=\bar{\mathbf{y}}} = \left(\frac{\delta w}{\delta y_{ia}} + \sum_{k=1}^{N_s} \sum_{j=1}^{N_a} \frac{dx_{kj}}{dy_{ia}} \frac{\delta w}{\delta x_{kj}} \right) \Big|_{\mathbf{y}=\bar{\mathbf{y}}} = \left(\frac{\delta w_a}{\delta y_{ia}} + \sum_{k=1}^{N_s} \sum_{j=1}^{N_a} \frac{dx_{kj}}{dy_{ia}} \frac{\delta w_j}{\delta x_{kj}} \right) \Big|_{\mathbf{y}=\bar{\mathbf{y}}}, \quad (\text{S4})$$

58 where the second equality follows because semi-total derivatives do not consider developmental constraints.

59 Let us now see that the forces of selection decrease, or remain constant, with age as has been long estab-
 60 lished ¹⁶⁻¹⁸. The change in the force on fertility with age is

$$\phi_{j+1} - \phi_j = \ell_{j+1}^\circ - \ell_j^\circ = \ell_j^\circ p_j^\circ - \ell_j^\circ = \ell_j^\circ (p_j^\circ - 1) \leq 0,$$

61 where the rightmost inequality follows because p_j° is a probability. Hence, the force on fertility is non-increasing
 62 with age. In turn, the change in the force on survival with age is

$$\begin{aligned}\pi_{j+1} - \pi_j &= \frac{1}{p_{j+1}^\circ} \sum_{k=j+2}^{N_a} \ell_k^\circ f_k^\circ - \frac{1}{p_j^\circ} \sum_{k=j+1}^{N_a} \ell_k^\circ f_k^\circ \\ &= \left(\frac{1}{p_{j+1}^\circ} - \frac{1}{p_j^\circ} \right) \sum_{k=j+2}^{N_a} \ell_k^\circ f_k^\circ - \frac{1}{p_j^\circ} \ell_{j+1}^\circ f_{j+1}^\circ,\end{aligned} \quad (\text{S5})$$

63 which is non-positive if $p_j^\circ \rightarrow p_{j+1}^\circ$ as is the case if the survival probability changes smoothly with age.

64 Now, suppose that gene expression of a given gene product has a deleterious effect $\delta w_a / \delta y_{ia} < 0$ at an
 65 early age a and a pleiotropic, beneficial effect $\delta w_j / \delta x_{kj} > 0$ of similar magnitude at a later age $j > a$ for some
 66 phenotype x_{kj} , but no other fitness effects. Then, semi-total selection is weaker at the later age because of
 67 declining selection forces ($|\delta w_a / \delta y_{ia}| \geq |\delta w_j / \delta x_{kj}|$). Yet, from Eq. (S4) we obtain that such gene's expression
 68 is favoured if its total effect on the phenotype is sufficiently large, that is, if

$$\left(\frac{\delta w_a}{\delta y_{ia}} + \frac{dx_{kj}}{dy_{ia}} \frac{\delta w_j}{\delta x_{kj}} \right) \Big|_{\mathbf{y}=\bar{\mathbf{y}}} > 0.$$

69 In such case, from Eq. (S3), the resident gene expression \bar{y}_{ia} increases if its mutational variance is non-zero.

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