

1 **PERSPECTIVES**

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3 **Rethinking inheritance, yet again: inheritomes, contextomes and dynamic**
4 **phenotypes**

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25

26 **Running title:** *An extended view of inheritance*

27

28 **Key-words:** Extended evolutionary synthesis; non-genetic inheritance; phenotypic variance
29 partitioning; cultural evolution; epigenetics; parental effects.

30

31 **Abstract**

32 In recent years, there have been many calls for an extended evolutionary synthesis, based in part
33 upon growing evidence for non-genetic mechanisms of inheritance i.e. similarities in phenotype
34 between parents and offspring that are not due to shared genes. While there has been an
35 impressive marshalling of evidence for diverse forms of non-genetic inheritance (epigenetic,
36 ecological, behavioural, symbolic), there have been relatively few studies trying to weld the
37 different forms of inheritance into a common conceptual structure, a development that would be
38 important to formalizing elements of the extended evolutionary synthesis. Here, we develop a
39 framework for an extended view of inheritance and introduce some conceptual distinctions that
40 we believe are important to this issue. In this framework, the phenotype is conceived of as a
41 dynamic entity, its state at any point in time resulting from intertwined effects of previous
42 phenotypic state, and of hereditary materials (DNA and otherwise) and environment. We contrast
43 our framework with the standard gene-based view of inheritance, and also discuss our framework
44 in the specific context of recent attempts to accommodate non-genetic inheritance within the
45 framework of classical quantitative genetics and the Price equation. In particular, we believe that
46 the extended view of inheritance and effects on the phenotype developed here is particularly well
47 suited to algorithmic modeling for simulation studies of evolutionary dynamics.

48

49 **Introduction**

50 In recent decades, increasing attention within evolutionary biology is being focused on the issue
51 of non-genetic (i.e. not based on gene sequence variation) inheritance (reviewed at length in
52 Jablonka and Lamb 2005; Pigliucci and Müller 2010). There is increasing evidence for the
53 inheritance of environmentally induced epigenetic states from parents (reviewed in
54 Bonduriansky and Day 2009; Jablonka and Raz 2009), as well as for the passing on of culturally
55 acquired (i.e. learnt) behaviours to offspring and, indeed, other peers, referred to as cultural
56 inheritance or transmission (Cavalli-Sforza and Feldman 1981; Richerson and Boyd 2005;
57 Jablonka and Lamb 2005; El Mouden et al. 2014). The literature in these areas is growing but, as
58 a result of coming from diverse disciplinary backgrounds of inquiry, it is often confusing
59 with regard to terminology and underlying concepts. In this brief essay, we delineate some
60 concepts and conceptual distinctions, and attendant terminology, that we believe may help
61 ameliorate some of the confusion in attempts to bring together various forms of inheritance into a
62 coherent and expanded view of evolutionary dynamics. Much of what we are drawing upon has
63 been said before: what we hope to accomplish is to (a) highlight some specific aspects of present
64 attempts to extend the evolutionary synthesis with regard to extra-genic inheritance where we
65 believe that conceptual clarity is still lacking, and (b) make some suggestions as to how that
66 conceptual clarity can be attained. Given the numerous recent reviews of different aspects on
67 non-genetic inheritance and its evolutionary implications, the list of references is not
68 comprehensive and is somewhat biased towards broad reviews or books wherein leads to most of
69 the primary literature can be found.

70

71 Following the rediscovery of Mendel's laws, the study of heredity gradually narrowed to
72 an almost exclusive focus on genic inheritance, especially after Johanssen's (1911) delineation of
73 the concepts of genotype and phenotype, mirroring the hard dichotomy of germline and soma,
74 laid down by Weissmann (1904), that excluded any possibility of the inheritance of acquired
75 characteristics (discussed in Schwarz 2008). Subsequently, this narrower, Mendelian, version of
76 heredity was what was reconciled with a neo-Darwinian (*sensu* Romanes 1888) emphasis on
77 natural selection as the principal mechanism of adaptive evolution, largely by the work of Fisher
78 (1930), Haldane (1932) and Wright (1932), becoming a major foundation of the Modern
79 Synthesis (Mayr 1992). The importance of genes as explanatory factors in biology got further
80 strengthened following the advent of molecular genetic understanding of DNA structure,
81 replication, expression and regulation. Thus, as heredity was central to the mechanism of natural
82 selection, the narrowing of heredity to genic inheritance naturally led to the gene-centric bias of
83 much modern evolutionary thinking, at least insofar as it pertained to adaptive evolution within
84 populations (i.e. microevolutionary change) (discussed in Gould 2002; Amundson 2005;
85 Bonduriansky 2012).

86

87 While the gene-centric version of microevolutionary theory has been extensively
88 criticized for being limited in scope, especially in the light of ever-increasing evidence for non-
89 genetic inheritance (e.g. Richerson and Boyd 1985; Odling-Smee et al 2003; Jablonka and Lamb
90 2005; Pigliucci and Müller 2010), certain aspects of this theory, we believe, have not received as
91 much attention from critics as they should have. First, in addition to the framework of population
92 genetics in the strict sense, there is also the essentially phenotypic framework of quantitative
93 genetics, arising from Fisher's (1918) seminal paper on the correlations between relatives for

94 polygenic traits following Mendelian inheritance. Interestingly, several critics of the Modern
95 Synthesis ignore the quantitative genetics tradition altogether (e.g. Amundson 2005; Jablonka
96 and Lamb 2005; Laland et al. 2014), although it is considerably more relevant than population
97 genetics is to understanding adaptive evolution. While quantitative genetics did attempt to root
98 its statistical analysis of trait correlations and evolution in Mendelian genetics, its most important
99 insights – the notion of breeding value for fitness and its variance as determinants of adaptive
100 evolutionary responses to fitness differences among individuals – are essentially not dependent
101 on any underlying mechanistic model of inheritance. Indeed, the statistical approach of
102 quantitative genetics, which effectively black-boxed the details of how genotypes affect
103 phenotypes, reached its later, even more generalized, fruition in the Price (1970, 1972) equation
104 that makes no assumption about the pattern of inheritance at all, subsuming it into a correlation
105 of phenotypic values between individuals and immediate descendants. What the results from this
106 statistical tradition clarify is that ultimately what matters in determining the response to a given
107 selective scenario is not so much the genes that pass from parent and offspring but rather their
108 statistical effects on offspring phenotype. This important distinction is rooted in the fact that
109 heredity is ultimately about phenotypic similarity between parents and offspring, even though
110 one major underlying reason for such similarity is the material genes that pass from parent to
111 offspring, albeit subject to the vagaries of mutation, recombination, sex and chance. Thus, what
112 an individual inherits, in terms of a genetic endowment leading to the propensity towards certain
113 phenotypic values, is usually different from what the same individual transmits to its offspring in
114 terms of expected effects on the offspring phenotype. This principle is reflected in the clear
115 distinction between the genotypic value (G) and the breeding value (A) of a trait in quantitative
116 genetics (Falconer and Mackay 1996). This distinction has implications for the development of

117 an extended theory of evolutionary change incorporating varied non-genetic forms of
118 inheritance. There are now some studies that use the framework of quantitative genetics or the
119 Price equation to incorporate non-genetic inheritance into models of evolutionary change
120 (Bonduriansky and Day 2009; Helanterä and Uller 2010; Danchin et al. 2011; Santure and
121 Spencer 2011; El Mouden et al. 2013), and we will discuss them in subsequent sections.

122

123 A second aspect of the gene-centric view of the evolutionary process that we believe has
124 not received much critical attention is the essentially static conception of genotype and
125 phenotype, at least within an individual's lifetime. Even the notion of the genotype-phenotype
126 (G-P) map, which was developed as a reaction to the black-boxing of the details of development
127 in Mendelian genetics (Alberch 1991), is an attempt to define a relationship (a map) linking
128 genotypic space and phenotypic space. Despite the complexity of this relationship, it is
129 nevertheless conceived of as a relationship between two spaces that are static within an
130 individual's lifetime, though not over evolutionary timescales.

131

132 In the next section, we briefly review the standard gene-based view of inheritance,
133 emphasizing some points that we will draw upon in order to develop an extended view of
134 inheritance. The subsequent section will be devoted to incorporating non-genetic inheritance into
135 a conceptual framework of heredity, and the shaping of the phenotype, that will stress the
136 dynamic nature of phenotypes even within the lifetime of an individual. In the final section, we
137 will discuss other studies that have addressed the issue of non-genetic inheritance and its
138 evolutionary implications and highlight similarities and differences between our view and theirs,
139 in particular highlighting conceptual distinctions that we believe are important and have not been

140 drawn earlier. We will also discuss some of the broader implications of the extended view of
141 inheritance developed here.

142

143 **The standard gene-based view of inheritance**

144 Before developing an extended view of inheritance, we briefly reiterate what the standard gene-
145 based model of inheritance is, and how quantitative genetics distinguishes between the genotypic
146 value and breeding value of a trait in an individual. The fundamental components of this view
147 are that information regarding the specification of phenotypes (whether as blueprint or
148 developmental program) is transmitted to offspring from parent(s) via the inheritance of
149 genomes, and that the specification of the phenotype by the genome can be affected by the
150 environment which includes biotic and abiotic components (Fig. 1). Direct environmental effects
151 on the phenotype of an individual (solid dark blue arrow from E to the octagon around P),
152 however, cannot be passed on to that individual's offspring, as only genes are transmitted
153 between generations. We note that, in this view, environment in a broad sense can affect the
154 genome (solid dark orange arrow from E to the circle around G in Fig. 1) by inducing mutations
155 or transpositions, or via horizontal gene transfer from conspecifics or heterospecifics. We will
156 not treat acquisition of genetic material by an individual via horizontal gene transfer as
157 constituting inheritance from the viewpoint of that individual, as it does not involve inherited
158 material acquired at conception via transmission from parent(s). Of course, once acquired by
159 horizontal gene transfer, such genetic material can subsequently be transmitted by that individual
160 to its own offspring, becoming part of their inheritance. We next stress a few specific points
161 about this gene-based view of inheritance that we believe will be relevant to the development of
162 an extended view of inheritance in the next section.

163 (i) Although the organism and its phenotype are central in ecology and evolution because
164 Darwinian fitness typically accrues to the individual as a result of its phenotype and how well it
165 functions in a given environmental context, evolutionary dynamics are often tracked at the
166 genetic level. This is because, at least for typical Mendelian traits, the G-P mapping is simple,
167 and the transmission of genes is amenable to mathematical representation. For more complex
168 polygenic phenotypes, a phenotypic approach (quantitative genetics) is taken, although here too
169 there is often an underlying genetic model (see (iv, vi) below).

170 (ii) The genome plays two distinct roles here: that of a transmissible genome and an expressible
171 genome. During transitions between generations, the genome acts as the transmissible material of
172 heredity, whereas during an individual's lifetime the genome acts as an expressible material that
173 directs the generation of the phenotype. While there is a degree of materialistic continuity to the
174 genome between generations, functionally the expressed genome can vary temporally and
175 spatially within the lifetime and the body of the individual, respectively (see also (v) below).

176 (iii) When an individual reproduces, it typically does not transmit the genome it inherited from
177 its parents. This difference between the inherited and transmitted genomes arises due to (a)
178 changes in the genome due to mutations, transpositions and horizontal gene transfer during the
179 individual's lifetime, and (b) the effects of recombination and meiosis during sexual
180 reproduction.

181 (iv) In the quantitative genetics approach, an individual's phenotypic value for a trait is
182 conceptualized as being made up of a genotypic value and an environmental effect, with the
183 mean environmental effect assumed to be zero. The genotypic value is the expected phenotypic
184 value of individuals of a given genotype exposed to all possible environments (Falconer and
185 Mackay 1996). Thus, there is a material partitioning of *causes* of phenotypic value into a

186 genotypic value and an environmental deviation from it. The genotypic value of an individual is,
187 however, not what the individual transmits in terms of phenotypic value propensity to its
188 offspring. Essentially, in a statistical partitioning of *effects*, the genotypic value is further divided
189 into a transmissible component (the breeding value or additive component) and a non-
190 transmissible component traditionally ascribed to genotype-by-genotype interactions. The
191 breeding value of an individual is a measure of how much the mean phenotypic value of that
192 individual's offspring is expected to differ from the population mean phenotypic value, were that
193 individual to mate at random within the population. In terms of phenotype, the breeding value is
194 what an individual passes on to its offspring, on an average, and it is a function of the
195 individual's genotype as well as the genotypic composition of the population (Falconer and
196 Mackay 1996).

197 (v) Thus, in terms of the phenotype, the transmissible genome of an individual is reflected in its
198 breeding value (which is dependent also on the genotypic composition of the population)
199 whereas its expressible genome is reflected in its genotypic value, which is independent of the
200 populational context.

201 (vi) The partitioning of phenotypic value into breeding value and a non-transmissible
202 component, and the analogous partitioning of phenotypic variance in a population into a variance
203 of breeding values (the so-called additive genetic variance) and a non-transmissible variance are
204 purely phenotypic, reflecting the degree to which phenotypic differences among individuals are
205 transmitted to the next generation. In this sense, quantitative genetics is essentially a phenotypic
206 theory. Under the assumption of a large number of Mendelian genes contributing to phenotypic
207 value, however, corresponding genetic models can also be developed and have been used in
208 quantitative genetics (Falconer and Mackay 1996).

209 (vii) In this standard gene-based view, the phenotype is conceived of as a largely static entity, at
210 least within the individual's lifetime.

211
212 One last point we wish to make before moving on to developing an extended view of
213 inheritance is that the framework of quantitative genetics, simple though it is, can incorporate
214 many biological phenomena that are often mentioned in the extended evolutionary synthesis
215 literature as being beyond the gene-based view. For example, at least from the perspective of
216 *effects* on phenotypic value, an environmental effect and genotype-by-environment interaction
217 reflect phenotypic plasticity and genetic variation for it. Similarly, many types of adaptive niche
218 construction can be conceptualized as a subset of positive genotype-environment covariance.

219

220 **An extended view of inheritance**

221 We now develop an extended view of inheritance that takes cognizance of phenomena like
222 transgenerational epigenetic inheritance, parental effects, ecological inheritance and cultural
223 inheritance. We follow the categorization of Danchin et al. (2011); types of non-genetic
224 inheritance have been categorized differently (e.g. Bonduriansky and Day 2009; Helanterä and
225 Uller 2010), but these differences do not affect the development of our view and we defer their
226 discussion to the next section. We first describe some terms and conceptual distinctions we
227 believe to be helpful in discussing such an extended view of inheritance. Our primary focus
228 throughout remains the phenotype, and the acquisition from, and contribution to, other
229 individuals of effects on the phenotype. Rather than the distinction between vertical, horizontal
230 and oblique transmission (e.g. Bonduriansky and Day 2009; Helanterä and Uller 2010), we
231 believe it is important to distinguish between heritable phenotypic effects acquired as a material

232 endowment at conception and those acquired subsequently in an individual's lifetime.
233 Consequently, we will distinguish, in a manner similar to the gene-based view, between
234 inheritome, phenotype and environment (Fig. 2). In Fig. 2, time runs from top to bottom and, at
235 conception, the focal individual has an inheritome I_1 , inherited from its parent(s) (dashed dark
236 orange arrow at top). The inheritome includes DNA sequence, as well as any epigenetic
237 modifications of DNA/chromatin and cytoplasmic mediators of parental effects. The focal
238 individual also receives a phenotype P_1 as a parental endowment (dashed dark blue arrow at top),
239 comprising, for example, cytoplasmic components and cellular structure. The environment is
240 conceptualized as a dynamic entity encompassing all individuals and the physical and cultural (if
241 applicable) backdrop within which they live. Clearly, though individuals live and die, the
242 environment has a continuity, while subject to changes, that transcends individual lifetimes: it is
243 a superset to the other categories depicted in Fig. 2. When examining inheritance/transmission of
244 phenotypic variations from the point of view of a focal individual (Fig. 2), we refer to its local
245 environment at a given time step i as its contextome at that time step (C_i). We treat the initial
246 phenotype as distinct from the inheritome because, over the course of a lifetime, the phenotype
247 of an individual undergoes vastly more change than its inheritome. For example, the phenotype
248 of a multicellular organism changes much more than the inheritome over the course of
249 developing from a zygote to an adult. The inheritome, on the other hand, does have considerable
250 integrity across the lifetime. We propose that the terms *inherit* and *transmit* be used solely in the
251 context of an inheritome being received from parent(s) and inheritomic components being passed
252 on to offspring, respectively. We propose using the terms *acquire* and *contribute* to refer to the
253 receiving and giving of changes to the inheritome and/or phenotype that occur after conception.
254 Of course, changes to the inheritome that are acquired, in this sense, can subsequently be

255 transmitted and therefore inherited by offspring. We further propose a distinction between
256 *parents* and *peers* in terms of this distinction between inheritance and acquisition. Parents
257 transmit phenotypic effects via the inheritome and, transiently, through the initial phenotype,
258 whereas peers contribute phenotypic effects via the inheritome, phenotype and contextome.
259 Biological parents, therefore, can affect offspring phenotypes both as parents, at conception, and
260 as peers, subsequently. This distinction is similar to Bonduriansky and Day's (2009) use of the
261 term inheritance solely for vertical transmission, and differs from other, broader, usages (e.g.
262 Odling-Smee et al. 2003; Jablonka and Lamb 2005; Helanterä and Uller 2010; Danchin et al.
263 2011). However, our usage is narrower than that of Bonduriansky and Day (2009) because we
264 restrict inheritance to heritable phenotypic effects acquired as a material endowment at
265 conception.

266

267 In Fig. 2, the set of arrows between I_1 , I_2 , P_1 , P_2 , C_1 and C_2 encompasses the various ways
268 in which inheritome, phenotype and contextome affect phenotypes, either directly (arrows
269 impinge upon I, P or C) or in an interacting manner (arrows impinge upon other arrows linking I,
270 P or C). This pattern of potential phenotypic effects of I, P and C is iterated at every time step, as
271 indicated by the dashed grey arrow labeled 'time' connecting I_2 , P_2 , and C_2 to I_n , P_n , and C_n .
272 Within a given time step, the specific expressed inheritome at that time step directs the
273 generation of the phenotype at that time step, also subject to interactions with the contextome at
274 that time step. In contrast to the gene-based view (fig. 1), however, the phenotype is also directly
275 affected by the phenotype in the previous time step in a manner also subject to interactions with
276 the contextome in the previous time step. Moreover, the phenotype can also be affected directly
277 by the contextome in the previous time step. Thus, in this view, the phenotype during the lifetime

278 of an individual is a dynamic flow from P_i to P_{i+1} , mediated by inputs from the inheritome (I_{i+1})
279 and the contextome (C_i and C_{i+1}), which themselves are dynamic flows. Thus, the phenotype
280 initiated at conception undergoes transformation throughout the lifetime of the individual under
281 the joint inputs from its previous state and the also changing inheritome and contextome, and
282 interactions between them, in a manner echoing the 'triple helix' metaphor of Lewontin (2002).

283

284 The inheritome and contextome of the focal individual, in this view, are also
285 conceptualized as flows through time. The inheritome may be altered as a result of its own
286 previous state, and the previous state of the phenotype and contextome, as well as interactions
287 among them (solid dark orange arrows between entities in time steps 1 and 2 in Fig. 2). These
288 changes to the inheritome encompass mutations/transpositions (directed or otherwise), resetting
289 of epigenetic marks on DNA and chromatin, or acquisition of cytoplasmic constituents that may
290 affect offspring phenotypes, mediated by either the physical aspects of the experienced
291 environment, or biological interactions with other individuals. This includes a subset of
292 phenomena included under the label of non-genetic inheritance in the all-encompassing
293 formulations (e.g. Odling-Smee et al. 2003; Jablonka and Lamb 2005; Helanterä and Uller 2010;
294 Danchin et al. 2011). We prefer to treat the remaining mechanisms of non-genetic inheritance,
295 broadly construed, as being changes in the contextome, which is also acquired at conception as a
296 local reflection of the environmental state at that point of time. The contextome of an individual
297 is changing as part of the dynamic change in environment (solid green arrow from C_1 to C_2 in
298 Fig. 2). We note that these changes include modifications to the physical or cultural aspects of
299 the environment due to the effects of phenotypes of other individuals, conspecific or
300 heterospecific (e.g. social interactions, competition, niche construction). In addition, an

301 individual's contextome can be affected by the same individual's phenotype, subject to
302 interactions with the contextome, and the altered contextome, in turn, can exert effects on
303 subsequent phenotypic states (solid green arrow from P_1 to C_2 in Fig. 2). In our view, therefore,
304 we are treating ecological and cultural inheritance (*sensu* Danchin et al. 2011) as being
305 encompassed by the changes to an individual's contextome and not as inheritance in our
306 narrower usage. Of course, changes made to an individual's phenotype by its contextome can
307 lead to phenotypic correlations between parent(s) and offspring, as does inheritance, provided the
308 contextome remains the same for the offspring. This is analogous to genotype-environment
309 covariance in quantitative genetics and we do not believe that it is helpful to label this
310 phenomenon as inheritance, especially since these effects are typically mediated by the
311 phenotypes of many peers that are part of the individual's contextome, rather than by one or two
312 parents.

313

314 During its lifetime, an individual can, in principle, reproduce at any time step. When it
315 does so, it transmits to its offspring inheritomic materials which, in the case of sexual
316 reproduction, together with inheritomic materials transmitted by the other parent, form the
317 inheritome of the newly conceived offspring. The parents also pass on an initial phenotype to
318 offspring which will then undergo changes through the offspring's lifetime. As was the case for
319 genomes (Fig. 1), what is transmitted/passed on is dependent upon the reproducing individual's
320 inheritome/phenotype at that time step but is also different from it (distinction between I_2 and I_2' ,
321 and P_2 and P_2' in Fig. 2). One point of departure from the gene-based view of inheritance here is
322 that the inheritome is more plastic than genomes typically are, since the former are subject to a
323 greater variety of genetic, epigenetic and cytoplasmic changes. Consequently, the source of

324 inheritomic materials to be transmitted to offspring by an individual during reproduction at any
325 time step is likely to vary from time step to time step, in contrast to the germline genome which
326 is assumed to be relatively unchanged through life, barring rare mutations.

327

328 **Discussion**

329 In this final section, we discuss some implications of the extended view of inheritance developed
330 in the preceding section, especially in the context of earlier attempts to formalize theories of non-
331 genetic inheritance. There are two aspects in which our formulation differs from much of the
332 previous work on this theme. The first is our separation of inheritomic and contextomic
333 mediation of phenotypic correlations between parents and offspring, and our restriction of the
334 term inheritance to describe only the former. The second is our emphasis on the inheritome, and
335 especially the phenotype and contextome, as dynamic flows rather than static entities. We will
336 now discuss some implications of these two emphases.

337

338 There are two approaches that have been taken to formalizing the evolutionary
339 consequences of the various types of non-genetic inheritance mechanisms. One is to treat each
340 category – epigenetic inheritance, parental effects, ecological inheritance and cultural inheritance
341 – separately, as is done by Jablonka and Lamb (2005). The other approach is to seek a combined
342 framework within which all forms of non-genetic inheritance can be formalized with regard to
343 their evolutionary implications. This approach has been taken from a quantitative genetics
344 perspective by Bonduriansky and Day (2009) and Danchin et al. (2011), and using the
345 framework of the Price equation by Helanterä and Uller (2010). We note that the important
346 elements of quantitative genetics framework for explaining adaptive evolution can be derived as

347 special cases assuming Mendelian inheritance from the Price equation (Frank 1997).
348 Bonduriansky and Day (2009) treat the change in mean phenotypic value in a population
349 between subsequent generations as being divisible into components due to the change in mean
350 additive genotypic value and in the mean non-genetic component of inheritance. Danchin et al.
351 (2011: Box 4) use a partitioning of variance approach to partition phenotypic variance in the
352 population, V_P , into transmitted genetic variance (V_G in their notation, V_A in standard
353 quantitative genetic notation: Falconer and Mackay 1996), various kinds of transmitted non-
354 genetic variance (V_{TNG}) combining phenotypic variance components variance ascribable to
355 epigenetic, parental, ecological and socio-cultural inheritance, and a non-transmitted component.
356 They propose to call the fraction of phenotypic variance that is transmissible $[(V_A + V_{TNG})/V_P]$
357 the 'inclusive heritability' of a trait (Danchin and Wagner 2010) and suggest that it “quantifies the
358 whole evolutionary potential of a trait and can be seen as the result of both genetic and non-
359 genetic heritability” (Danchin et al. 2011). They further suggest that it may be possible to
360 estimate different components of the transmissible phenotypic variance through extensions to
361 classic breeding experiments that also include multiple environmental contexts thought to play a
362 role in non-genetic inheritance, and by tracking epigenetic changes. It is not clear to us that the
363 kinds of partitionings envisaged by Bonduriansky and Day (2009) and Danchin et al. (2011) will
364 actually be experimentally feasible in the context of ecological and cultural inheritance.

365

366 Helanterä and Uller (2010) fit various types of non-genetic inheritance mechanisms into
367 the Price equation and try to categorize them into clusters based on the effect each type of non-
368 genetic inheritance has on the different terms in the Price equation (Table 1 in Helanterä and
369 Uller 2010). They find that their approach suggests a clustering different from that into genetic,

370 epigenetic, behavioural and symbolic inheritance (Jablonka and Lamb 2005). They find three
371 clusters that group mechanisms of non-genetic inheritance that will be similarly incorporated into
372 a Price equation framework, and these three clusters are differentiated by whether “inheritance”
373 is by “vertical transmission” (parent to offspring), “induction (environmentally determined
374 changes between parents and offspring) or “acquisition” (phenotypes affected by peers or other
375 sources). These three clusters differ in the way they mediate adaptive evolutionary change of
376 phenotypes across generations, with and without classic responses to selection in the sense of the
377 breeder's equation in quantitative genetics (Helanterä and Uller 2010).

378

379 Our position is intermediate between the two approaches described above. We note that,
380 of the three clusters of Helanterä and Uller (2010), the “vertical transmission” case corresponds
381 to inheritomic transmission, while their other two clusters are encompassed in contextomic
382 continuity, coupled with contextome effects on phenotype, in our framework. Similarly, the three
383 terms V_G , V_{TEpi} and V_{PNGE} in the fomulation of Danchin et al. (2011: Box 4), encompassing
384 phenotypic variance due to additive genetic variance, epigenetic variance and parental effect
385 variance, respectively, together correspond to variance due to inheritomic transmission in our
386 framework. What Danchin et al. (2011: Box 4) term transmitted ecological and socio-cultural
387 variation is encompassed in contextomic continuity, coupled with contextome effects on
388 phenotype, in our framework. We believe there is a point to separating inheritomic and
389 contextomic effects on the phenotype, for two reasons. First, their effects on adaptive
390 evolutionary dynamics differ, as shown by Helanterä and Uller (2010). Second, following
391 classical quantitative genetics, if we define phenotypic value as being made up of an inheritomic
392 value plus a contextomic value, then it is clear that we need to separately partition each into a

393 transmissible and non-transmissible component. This is exactly analogous to the partitioning of
394 Bonduriansky and Day (2009: Eqns. 2a,b). The partitioning into a transmissible and non-
395 transmissible component of genotypic value is standard in quantitative genetics. Moreover, there
396 is already considerable work on incorporating epigenetic effects, genomic imprinting and
397 parental effects into quantitative genetics models (Kirkpatrick and Lande 1989; Spencer 2002,
398 2009; Johannes et al. 2008; Tal et al. 2010; Santure and Spencer 2011), suggesting that the
399 partitioning of inheritomic value into transmissible and non-transmissible components is likely to
400 be feasible. It is not clear to us at this time whether a partitioning of contextomic value that is
401 similar in structure to the partitioning for inheritomic value will be possible and, therefore, we
402 believe it might be best to treat it separately. Experimentally, too, we speculate that estimation of
403 the partitioned phenotypic variances due to contextomic and inheritomic effects may require
404 fairly different kinds of designs. A framework analogous to classical quantitative genetics
405 directly suggests possible experimental designs to estimate transmitted versus non-transmitted
406 components on inheritomic variance. For contextomic effects, a completely mechanism free
407 approach like the Price equation may be more suited, with the drawback that it does not lend
408 itself to suggesting designs for experiments.

409
410 Our explicit conceptualization of inheritome, contextome and phenotype as flows in time
411 rather than static entities during an individual's lifetime is another point of departure from many
412 earlier treatments. In particular, this conceptualization suggests that the G-P map metaphor is
413 fundamentally misplaced, as a map is a relation between static entities. In our framework, the
414 inheritome-phenotype map is itself a flow in time and we believe further work is needed to
415 model this relationship more accurately as a dynamic one. One implication of this view of

416 dynamic phenotype is for genome wide association studies (GWAS). It has already been pointed
417 that the problem of “missing heritability” (Maher 2008) is potentially explained if there is a
418 substantial non-genetic component to inheritance in the sense of parent-offspring similarity in
419 phenotype (Danchin et al. 2011). If phenotypes are viewed as changing in time, based largely on
420 previous phenotypic state, modulated by inheritomic and contextomic effects on the phenotype,
421 then it is very likely that, at least for complex traits, the best predictors of phenotypic state
422 maybe previous phenotypic states rather than genotypes. If this speculation is correct, it is a
423 potential explanation for the efficacy of traditional holistic systems of medicine (like Ayurveda
424 in India) in dealing with complex so-called life-style diseases, as these systems try to correlate
425 diseased phenotypic states with a constellation of previous phenotypic states along different trait-
426 axes.

427 Overall, we believe that the framework for an extended view of inheritance that we have
428 developed here provides a good basis for thinking about specific lines of inquiry relating to the
429 conceptual partitioning of inheritomic and contextomic values, as well as related experimental
430 approaches for obtaining estimates of such partitioned effects and variances. We believe this
431 framework can be fruitfully extended to issues like how non-genetic effects on phenotypes, and
432 their inheritance or acquisition, can affect fitness surfaces; this is an issue we have not touched
433 upon here. Finally, we believe that the extended view of inheritance and effects on the phenotype
434 developed here is particularly well suited to algorithmic modeling for simulation studies of
435 evolutionary dynamics along the lines of the extended evolutionary synthesis (Pigliucci and
436 Müller 2010).

437

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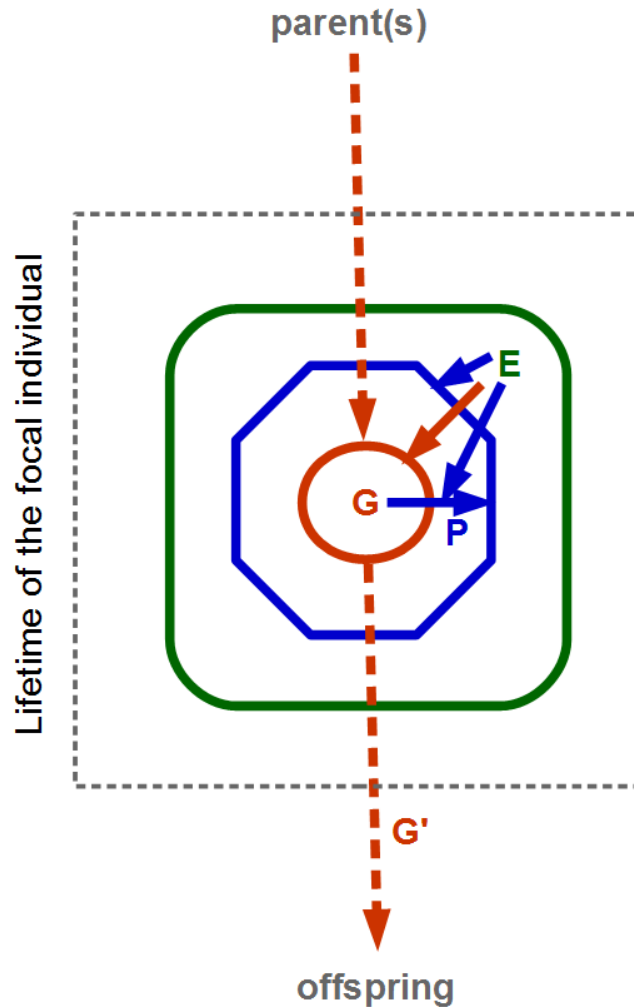
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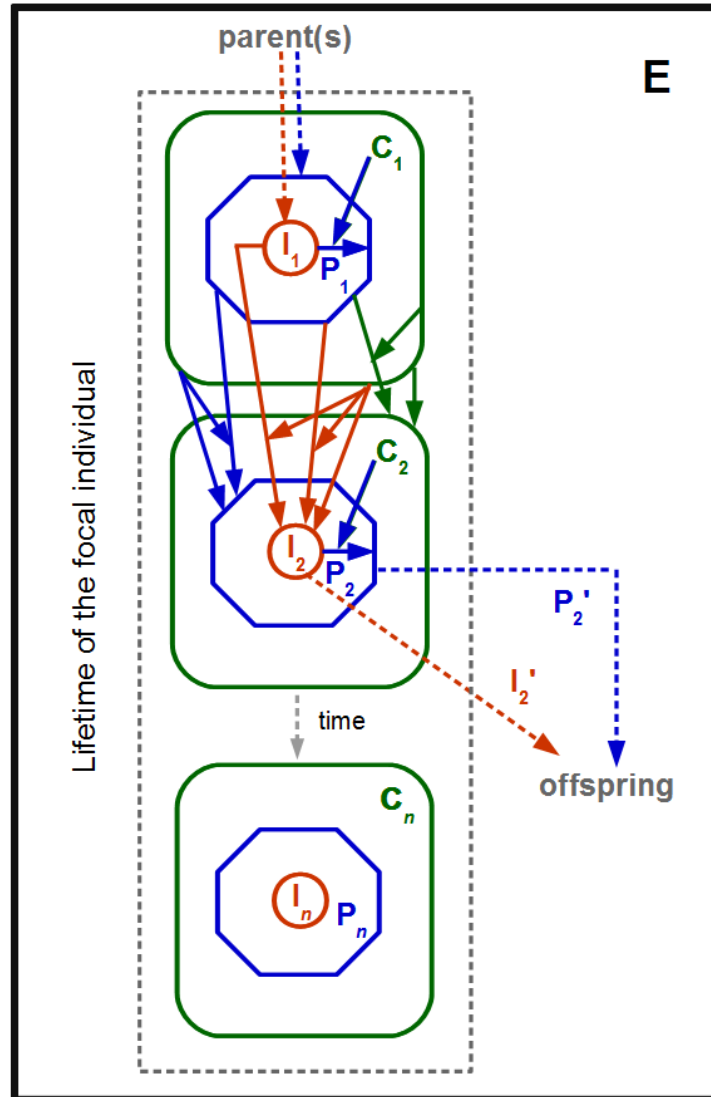
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526



527

528 **Figure 1.** Schematic representation of the relationships between phenotype, genome and
529 environment in the standard gene-based view of inheritance. The focal individual depicted
530 within the gray dashed box has a genome G (dark orange circle) inherited from its parent(s).
531 This genome, when expressed, directs the generation of the phenotype P (dark blue octagon),
532 and the generation of the phenotype is affected by the environment E (green box), which
533 includes both biotic (conspecifics and heterospecifics) and abiotic components. Eventually,
534 the focal individual transmits genomic material G' to its offspring. What is transmitted,
535 however, is not necessarily identical to what was inherited (G), as a result of mutation and
536 horizontal gene transfer (hence the dark orange arrow from E to G), as well as recombination
537 and meiosis. For the focal individual, an interaction between P and E determines its
538 Darwinian fitness. Solid arrows indicate the role of one component affecting the other, or
539 interactions between components, when an arrow from one component impinges upon an
540 arrow connecting two others. Thus, E interacts with G in generating P, and also affects P
541 directly.
542



543

544 **Figure 2.** Schematic representation of the relationships between the phenotype P_i , inheritance I_i
545 and environment E , at different time steps ($i = 1..n$) during the lifetime of the focal individual
546 depicted within the gray dashed box. The environment (solid dark grey box), which includes all
547 individuals (conspecifics and heterospecifics) as well as the physical and cultural backdrop, is a
548 dynamic superset that transcends the lifespan of individuals of various species. It is the sum of
549 all individuals and together with the physical and, for some species, cultural backdrop within
550 which individuals are transiently embedded during their lifespan. In principle the environment
551 changes on a time-scale that is often similar to the lifespans of individuals. Therefore, the
552 effective local environment of a focal individual is referred to as its contextome (C_i at time step
553 i) which changes during an individual's lifetime. Note that the focal individual is in principle a
554 component of every other individual's contextome. At conception (time $i = 1$), the focal
555 individual has an inheritance I_1 , inherited from its parent(s) (dashed dark orange arrow). The
556 inheritance includes DNA sequence, as well as any epigenetic modifications of DNA and
557 cytoplasmic mediators of parental effects. The focal individual also receives a phenotype P_1 as a
558 parental endowment (dashed dark blue arrow); this includes, for example, cytoplasmic

559 components and cellular structure. At conception, the focal individual inhabits and experiences a
560 contextome C_1 . In subsequent time steps (2.. n), the inheritome can change (e.g. from I_1 to I_2).
561 This change in inheritome includes changes due to mutation, transposition, horizontal gene
562 transfer and the acquisition of new epigenetic marks due to phenotype, and hence there are solid
563 dark orange arrows from I_1 , P_1 and C_1 to I_2 . Change in the phenotype from P_1 to P_2 encompasses
564 changes directed at time step 2 by the expressed subset(s) of I_2 , subject to interaction with C_2 ,
565 and also direct effects of and interactions between P_1 and C_1 (dark blue solid arrows). The
566 contextome can also change from C_1 to C_2 , subject to direct effects of and interactions between
567 P_1 and C_1 (green solid arrows). The same set of arrows as between times steps 1 and 2 will apply
568 to every pair of time steps t and $t+1$, till $t = n-1$, indicated by the dotted gray arrow labeled 'time'
569 between time steps 2 and n . At any time step r (ranging from 2 to n), the focal individual may
570 produce offspring, transmitting to them an inheritome I_r' that is typically different from I_r (dashed
571 dark orange arrows leading to offspring), and a phenotype P_r' , determined by, but different from,
572 P_r (dashed dark blue arrows leading to offspring).
573