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FACULTAD DE CIENCIAS EXACTAS Y NATURALES
UNIVERSIDAD DE BUENOS AIRES

1° CUATRIMESTRE 2019

DEBATES ACTUALES:

Teoría Sintética de la Evolución o
Síntesis Extendida?

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Evolutionary biology today and the call for an extended synthesis

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Evolutionary theory has been extended almost continually since the evolutionary synthesis (ES), but except for the much greater importance afforded genetic drift, the principal tenets of the ES have been strongly supported. Adaptations are attributable to the sorting of genetic variation by natural selection, which remains the only known cause of increase in fitness. Mutations are not adaptively directed, but as principal authors of the ES recognized, the material (structural) bases of biochemistry and development affect the variety of phenotypic variations that arise by mutation and recombination. Against this historical background, I analyse major propositions in the movement for an 'extended evolutionary synthesis'. 'Niche construction' is a new label for a wide variety of well-known phenomena, many of which have been extensively studied, but (as with every topic in evolutionary biology) some aspects may have been understudied. There is no reason to consider it a neglected 'process' of evolution. The proposition that phenotypic plasticity may engender new adaptive phenotypes that are later genetically assimilated or accommodated is theoretically plausible; it may be most likely when the new phenotype is not truly novel, but is instead a slight extension of a reaction norm already shaped by natural selection in similar environments. However, evolution in new environments often compensates for maladaptive plastic phenotypic responses. The union of population genetic theory with mechanistic understanding of developmental processes enables more complete understanding by joining ultimate and proximate causation; but the latter does not replace or invalidate the former. Newly discovered molecular phenomena have been easily accommodated in the past by elaborating orthodox evolutionary theory, and it appears that the same holds today for phenomena such as epigenetic inheritance. In several of these areas, empirical evidence is needed to evaluate enthusiastic speculation. Evolutionary theory will continue to be extended, but there is no sign that it requires emendation.

1. Introduction

The current framework of evolutionary theory grew out of the evolutionary synthesis (ES), or the modern synthesis, as Huxley [1] called it. In any discussion of extending or revising current theory, some understanding of the history of the ES and the subsequent development of the subject will be useful. My impression of the history of biology, and of evolutionary biology in particular, is one of generally gradual, rather than paradigm-shaking, development that builds successively on previous accomplishments. For example, soon after the discovery and canonization of Mendel's 'laws' in the earliest twentieth century, the 'law' of independent assortment had to be modified to account for linkage. The 'gene' went from a particulate 'factor' to a trinity of recon, muton and cistron (unit of recombination or mutation or function), thence to a protein-signifying code, and recently to an increasingly ambiguous functional part of a genome. Nevertheless, genetics has not cast out the old to accommodate the revolutionary new. Quite the opposite: classical Mendelian segregation, meiosis, linkage mapping and mutation are still important foundations of today's immensely more complex genetics.

The same holds for the evolutionary theory that has developed since the late 1920s. The ES [2] remains, *mutatis mutandis*, the core of modern evolutionary

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biology. The ES included both the formulation of population genetic theory by Fisher [3], Haldane [4] and Wright [5], and the interpretation of variation within species [6] and of diverse information in zoology [7–9], botany [10] and palaeontology [11].

Since the 1930s and 1940s, there has been a steady incorporation of new information, ranging from phylogeny and field studies of natural selection to evolutionary genomics and the panoply of genetic phenomena that could not have been imagined in the 1940s or even the 1960s—information that has informed (and sometimes been predicted by) a steady expansion of theory. Modern evolutionary biology recognizes and studies transposable elements, exon shuffling and chimeric genes, gene duplication and gene families, whole-genome duplication, *de novo* genes, gene regulatory networks, intragenomic conflict, kin selection, multilevel selection, phenotypic plasticity, maternal effects, morphological integration, evolvability, coevolution and more—some of these being phenomena and concepts unknown or dimly perceived a few decades ago.

Almost all of this amplification of evolutionary biology has been built on the core concepts of the ES, which have held fast with only modest modification. The most important tenets of the ES, I think, are these:

— The basic process of biological evolution is a population-level, not an individual-level, process that entails change not of the individual organism, but of the frequency of heritable variations within populations, from generation to generation. Dobzhansky defined evolution as change of allele frequencies, but some organism-focused evolutionary biologists, such as Rensch, Simpson and Mayr, had a more comprehensive conception of evolution, including phenotypic evolution, speciation and differential proliferation of clades, while recognizing that phenotypic evolution and speciation occur by changes in allele frequencies. When Rensch wrote of 'Evolution above the species level' and Simpson wrote about 'Tempo and mode in evolution', they were not talking about allele frequencies—although they recognized this as the elementary, generation by generation process of change.
— Heredity is based on 'genes', now understood to be DNA or RNA. DNA sequences transmitted in eukaryotes' gametes are not affected by an individual organism's experiences. Cultural inheritance has long been recognized, but insofar as it affects biological evolution, it does so by affecting natural selection. Some authors prefer to limit the term 'inheritance' to genetic transmission. For the sake of using a common language in this discourse, I will use the term 'inclusive inheritance' to include several forms of non-genetic 'inheritance', recognizing that this terminology may be disputed.
— Inherited variation arises by individually infrequent mutations; they are random in that their phenotypic effects, if any, are not directed towards 'need'. 'Random' should always be qualified by 'with respect to'; randomness of mutation has never meant that all possible alterations are equally likely, or that all genes mutate at the same rate, or that rates of mutation are immune from environmental factors (such as radiation and mutagens). Claims of 'directed mutation' have been shown to be groundless [12]. The great majority of mutations that affect fitness are deleterious [13]. Likewise, the direct effects of novel environments are more often harmful than beneficial: that is why they engender natural selection and adaptive change. These facts imply that we should be sceptical of the view that organisms are so constructed as to have well integrated, functional responses to mutations or novel environments (as proposed in [14, p. 2]). Without question, organisms have diverse homeostatic properties that buffer fitness against many environmental or genetic destabilizing events; but the maintenance of function depends on stabilizing or purifying natural selection.
— The frequencies of hereditary variants are altered by mutation (very slightly), gene flow, genetic drift, and natural selection. Directional or positive natural selection is the only known cause of adaptive change. Natural selection is not an agent, but a name for a consistent (biased, non-random) difference in the production of offspring by different classes of reproducing entities. The entities that were the focus of the ES were mostly phenotypically different individual organisms, but they can also be genes (as already recognized by Fisher, Haldane and Wright), populations or species.
— Species of sexually reproducing organisms are reproductively isolated groups of populations that arise by evolutionary divergence of geographically isolated (allopatric) populations. Species evolve gradually, so not all populations can be classified into discrete species. Non-allopatric speciation is now recognized as possible, although its frequency is unknown.
— Large phenotypic changes of the kind that distinguish higher taxa and occur over long periods of time evolve gradually, as Darwin proposed, i.e. by the cumulation of relatively small incremental changes.

It is important to recognize that in population genetics theory, 'mutation' means any new alteration of the hereditary material that is stably transmitted across generations. The discovery of the molecular basis of heredity after the ES led to a greatly amplified understanding of evolutionary process and history, but the core theory of population genetics remained intact. For example, the core theory does not specify whether a mutation is a single base pair substitution, an insertion of a transposable element in a regulatory sequence, a gene duplication or a doubling of the entire genome. The framework of population genetics has incorporated new kinds of mutations, such as transposable elements, as they have been discovered.

Natural selection commonly was, and often still is, thought of as stemming from the ecological environment, but the forgers of the ES were well aware that selection had a far broader basis. Fisher described the evolution by selection of sex ratio, selfing and outcrossing, and he provided a genetic interpretation of Darwin's idea of sexual selection; Wright (who influenced Dobzhansky, who influenced Mayr) emphasized epistasis for fitness, in which prevalent alleles at one locus affect the selective value of alleles at another locus. Schmalhausen described 'internal selection'; mutations can have environment-independent effects on the function of physiological and developmental processes, and in turn on viability and reproduction. A causal account of any instance of selection requires different kinds of data—molecular, behavioural, ecological or other—but showing the existence of selection on a gene locus or a trait requires

only data on components of fitness, such as rates of survival, fecundity or mating success.

Thus, the broad concepts of mutation and natural selection lack material content, in the sense that empirical data are needed to describe real instances of evolution, by identifying the agents of selection and the molecular and developmental basis of phenotypic variants. The conception of causes of evolution embodied in the synthetic theory, i.e. allele frequency change, differs from the 'structuralist' view of the causes of differences in morphology, physiology or behaviour that are commonly envisioned by mechanistic developmental biologists, physiologists or neurobiologists (cf. [15]). A 'structuralist' approach to biology is cast in terms of the physical and chemical features of organisms, such as cell types and organs, and a 'structuralist' explanation of a morphological difference among species would be expressed in terms of signalling cascades, gene regulation and assembly of proteins into features that distinguish cell types [16, pp. 7–38]. A complete account of any evolutionary change in phenotype would combine the two kinds of information: population genetic processes (causes of allele frequency change) together with the specific agents of selection and the structural and developmental basis of the altered phenotype. Part of the great power of the population genetic theory of evolutionary change lies in its generalization across diverse kinds of mutations, selective causes and phenotypic structures.

The leaders of the ES affirmed Darwin's gradualist view of long-term evolution, and rejected the saltationism of Schindewolf, Goldschmidt and others who supposed that higher taxa evolve by macromutations. Still, what might qualify as a 'large' mutational change was and is difficult to specify. Certainly some species differences and polymorphisms map to single loci with discretely different effects; phenomena such as neoteny (e.g. paedomorphic salamanders) were recognized, and nobody seemed to worry that partially paedomorphic salamanders were unknown and functionally unlikely. The 'instantaneous' origin of reproductively isolated species by polyploidy was likewise well known, especially in plants—but the species produced by polyploidy closely resemble the parent species: they are not new higher taxa.

2. Extensions of the evolutionary synthesis

Evolutionary research in the 1950s and 1960s greatly increased information on genetic variation in natural populations, the seeming ubiquity of natural selection and speciation. In the 1960s, efforts to synthesize ecology with evolutionary biology were renewed as 'population biology' [17,18], the beginning of a flourishing field of evolutionary ecology [19]. The development of kin selection theory and the distinction between individual selection and group selection gave rise to fields such as behavioural ecology and life-history theory. The abundant evidence of natural selection and the development of optimality models for characters that almost unquestionably affect fitness may have led to a broadly held view of selection as an almost exclusive factor of evolution. But the all-important role of selection was challenged by interpretations of molecular polymorphism and evolution in neutralist terms [20–22], and the 'neutralist–selectionist' debate ultimately resolved itself into rendering unto Kimura and unto Darwin those provinces of variation that each best explains. In the 1980s and 1990s, the field of molecular evolution grew so massively as to warrant its own society and journal. This expansion was accompanied by the maturation of phylogenetic analysis and its long-deferred integration with the study of evolutionary processes [23–25]. Thus, evolutionary theory has undergone enormous expansion since the ES [26,27], with the neutral theory of molecular evolution its most radical extension.

Nevertheless, there have been undercurrents of discontent with the synthetic theory ever since the ES [28]. For example, *Beyond neo-Darwinism* [29] was a diverse collection of essays by developmental biologists, systematists, ecologists and others whose common characteristic seemed to be only an animus against the prevailing paradigm. Stephen Jay Gould's [30,31] calls for extension of the ES had rather more impact. Gould played a significant role in reviving development as a factor in the evolution of form [32], as well as the role of developmental or genetic constraints. Although Gould flirted with Goldschmidtian saltation, there is still no evidence that single mutations are responsible for the multiple character differences that typify most genera or other higher taxa. However, population geneticists found that many character differences between closely related species appear to be based on fewer gene differences, of larger effect, than previously supposed [33,34]. (Nonetheless, even the effects of a single gene can sometimes be ascribed to complementary effects of several mutations [35].) The model of punctuated equilibria introduced by Eldredge & Gould [36] was a different challenge to gradualism. They claimed that most fossil lineages display rapid shifts (punctuations) between one long-lasting, virtually constant (static) phenotype and another. Following Mayr [37,38] in large part, they postulated that populations cannot readily respond to natural selection because of genetic constraints that may be loosened when a population undergoes a bottleneck associated with founder-effect speciation. This model has been almost universally rejected, but Eldredge and Gould called attention to the important and still not fully explained pattern of stasis, and raised a possible role for speciation in fostering long-term character evolution, which is a topic of ongoing research [39–42]. The controversy unleashed by Eldredge & Gould [36] also contributed to a renaissance of palaeontology, in the form of palaeobiology. Possibly the current calls for an extended synthesis will similarly have some positive effects.

3. Proposed extensions of the evolutionary synthesis

Against this background, I will consider the major themes of the proposed extended evolutionary synthesis (EES), drawing largely on the position paper by Laland *et al*. [14] and the oral presentations at the discussion meeting sponsored by the Royal Society and the British Academy (November 2016). I will consider niche construction, phenotypic plasticity, inclusive inheritance and the role of development in the evolution of form.

3.1. Niche construction

The concept of niche construction emphasizes ways in which organisms actively modify their environment, such as

burrowing by gophers and dam-building by beavers, but the broadest expression of the idea of niche construction is simply, as Lewontin [43, p. 280] wrote, that 'organisms determine what is relevant'. The core idea is that the evolved properties of organisms make some aspects of the environment relevant sources of natural selection, and screen off others, thereby helping to shape and constrain likely paths of the population's evolution. Thus (although Lewontin did not explicate this point), properties of the organism that we think of as proximate mechanisms (e.g. biochemcal capabilities, tolerances, habitat selection, other behaviours of animals) can determine or even constitute Mayr's 'ultimate' (i.e. selective) causes of organisms' characteristics. The proponents of niche construction [44] take this broad view, even if they stress examples in which species (especially of animals such as beavers) actively modify their environment—a theme that has also been developed by Dawkins [45].

I have been a naturalist since boyhood. I think I recognized niche construction even then, because Lewontin's principle is blindingly obvious to any naturalist. Even if a species does not literally construct its environment, like a beaver, it determines its environment by its behaviour and physiology. What is relevant to the life of an aerially foraging swift, to a foliage-gleaning warbler, and to a fish-eating loon (diver) is obviously very different. To a eucalyptus-feeding koala or a larval monarch butterfly that eats only milkweed (*Asclepias*), the defensive compounds of these few plants are highly relevant, but those of hundreds of other plant species in their habitat are not. Likewise, an understory herb experiences a very different environment from an epiphytic bromeliad in the same tropical forest. This principle was obvious to ES figures such as Mayr [46], who emphasized that behaviour (such as habitat choice) often frames selection on morphology and physiology. Jakob von Uexküll's [47] concept of an animal's *Umwelt*—its species-specific perceptual environment—has long been familiar to students of animal behaviour.

In my own research area, the evolution of herbivore–plant associations, the coevolution of behaviour and physiology has been a major topic for modelling and empirical study [48–50]. In simple two-locus models, one locus affects which species of plant an insect chooses; this affects allele frequency dynamics at a second locus that determines fitness on these plants (and vice versa). The evolution of host choice will influence the subsequent evolution of other features, such as coloration that makes the insect cryptic by resembling part of the plant. This coevolution of habitat preference and other features is one of a rather long list of well-studied topics that Odling-Smee *et al*. include under niche construction, which seems to embrace much of behavioural ecology, evolutionary ecology and (by virtue of the many effects of niche construction) community ecology. So the phenomena gathered under the label 'niche construction' are unquestionably important, and have long been the subjects of research, but the inclusiveness of the term 'niche construction' has been cited as 'precisely what weakens the value of the idea', for 'organismal influences on the environment with profoundly different evolutionary impacts are lumped together' [51].

The related notion of 'ecological inheritance' can likewise be criticized because of its imprecision and excessive breadth. Odling-Smee *et al*. [44, p. 45] define ecological inheritance as 'any case in which organisms encounter a modified feature–factor relationship between themselves and their environment where the change in the selective pressures is a consequence of the prior niche construction by parents or other ancestral organisms', including 'the ancestors of other species in their communities'! Their examples include offspring inheritance of their parent's environment (e.g. burrow), occupation of an environment constructed by antecedent generations without reference to kinship, and simple parental care. (For example, because many insects lay eggs on a food plant or other food resource, the offspring 'inherit from their mother the legacy of an appropriate source of larval food' [44, p. 65].)

'Ecological inheritance' must differ profoundly from genetic inheritance if it is not transmitted down ancestor–descendant lineages. The critical distinction is whether or not there is covariance between niche-constructing behaviour and offspring fitness [51,52]. The literature of quantitative genetics has long recognized genotype–environment covariance [53]. Situations in which this is the case, including maternal effects and gene–culture coevolution, have been described by models based in traditional population genetics [54,55].

Niche construction may prove useful if it prompts questions and generates research on familiar aspects of biology (as has research on phenomena such as stasis and sex ratios). So far, studies that identify themselves with niche construction have been mostly theoretical, and mostly addressed to cultural niche construction, especially by humans. But these themes had already been addressed long before the term 'niche construction' was introduced [52], and understudied phenomena are available to anyone who becomes familiar with enough biology (why do haploid chromosome numbers range from one to more than one hundred among insect species?); so associating a study with a term does not in itself show that the term or concept played a critical generative role. A great deal of research, on many topics as I have noted, has long used the concept of niche construction, without using the label.

Odling-Smee *et al*. [44, p. 2] proposed that niche construction 'should be regarded, after natural selection, as a second major participant in evolution', and indeed as a 'core evolutionary process'. In a valuable interchange [56], sceptics point out that niche construction can influence or even cause the evolutionary process of natural selection, but is not itself an evolutionary process, any more than a changing environment is. If niche construction shapes selection, so do the sources of ecological selection, internal selection, and sexual or social selection. The sources of these several forms of selection are not processes. We can identify many evolutionary processes (Red Queen evolution, kin selection, changes in linkage disequilibrium and more), i.e. ongoing series of events that constitute evolutionary change. Are they 'core' evolutionary processes? I do not know what the criterion of a 'core' evolutionary process might be, but none of these seems to be as fundamental and comprehensive as mutation, genetic drift, gene flow and natural selection. Perhaps, a taxonomy of processes would be useful.

Professor Laland also suggests that the value of niche construction is that it provides a different point of view. Whether or not that will prove to be so will depend on whether or not it yields theoretical and empirical research that differs from what would otherwise be pursued [56]. What, exactly, as Gupta *et al*. [52] ask, has been neglected by standard evolutionary theory that niche construction theory proposes to

supply? Will 'niche construction' be merely a label or 'brand' that advertises its advocates' research, or will it be uniquely productive of insight and understanding? So far, no new, general theoretical principles that promise to guide novel empirical research have been articulated by proponents of niche construction.

3.2. The role of phenotypic plasticity in evolution

Phenotypic plasticity refers to the expression of different phenotypic states (together forming a norm of reaction) by a single genotype under different environmental conditions. It takes many forms. It can be reversible, as are many behavioural reactions, physiological acclimation, upregulation or downregulation of an enzyme level, and some morphological states, such as seasonal changes in bird plumages. Or it may be irreversible, as are many alternative morphological phenotypes induced by environmental conditions during development; familiar examples include height in some plants, the solitary versus gregarious phases of plague locusts (*Schistocerca*), and the castes of many eusocial insects. Plastic responses *sensu lato* include many environmentally induced phenotypes that are called developmental defects, such as skeletal aberrations in rickets, but most evolutionary literature is concerned with adaptive plasticity, such as the cases I have cited.

The concept of phenotypic plasticity, if not the term, is about as old as the distinction between genotype and phenotype. I learned about it in an undergraduate genetics course. As a graduate student, I learned that genotype × environment interaction was a staple in quantitative genetics [53,57]. Clausen *et al*. [58] and many other researchers described adaptive plasticity in plants and animals, and the evolution of adaptive reaction norms was a major topic in Schmalhausen's *Factors of evolution* [59]. Biologists agreed that some plastic responses are adaptive, and that others are harmful effects of environment. There is no doubt that plasticity can extend tolerance to some new environments and help prevent population extinction. By the 1990s, a large body of quantitative genetic theory on the evolution of adaptive phenotypic plasticity had been developed [60–63], and a large theoretical and empirical literature on the topic has developed since then. For example, young tiger snakes (*Notechis scutatus*) that are fed larger prey develop longer jaws, and the response is enhanced in an island population that normally feeds on larger prey [64]. This simply shows that reaction norms can evolve by natural selection. There is also an extensive literature on the benefits and costs of phenotypic plasticity. Thus, the phenomenon of phenotypic plasticity is widespread, is very well known and is understood to a considerable degree [65,66].

Under some conditions, the optimal reaction norm is 'flat', i.e. a constitutive (constant) expression of the same phenotype in all normally encountered environments. The evolution of a constant (constitutive) phenotype from an ancestrally more plastic reaction norm often exemplifies what I will refer to as genetic assimilation, following Waddington [67]. Waddington observed that a phenotype that was induced by an environmental stimulus could become constitutive, and be expressed in the normal environment in the absence of the stimulus, after several generations of selection for individuals most prone to exhibit the phenotype when stimulated. He rightly postulated that selection had increased the frequency of alleles that enhanced the reliability and consistency of the new phenotype. Strong evidence for this hypothesis was provided by experiments in which selection yielded no genetic assimilation in inbred stocks that lacked genetic variation [68].

Genetic assimilation of a character state in a plastic reaction norm underlies a controversial hypothesis by Mary Jane West-Eberhard [69] that she calls genetic accommodation because it includes more genetic shaping of characters than in simple genetic assimilation—which, however, is the core of her hypothesis. West-Eberhard proposed that adaptation to a novel environment often proceeds first by inducing a phenotypic response that increases fitness (phenotypic plasticity), followed by allele frequency changes that assimilate and perhaps fine-tune the new character state, so that it becomes a novel, species-typical trait. She stated, provocatively, that 'most phenotypic evolution begins with environmentally initiated phenotypic change… The leading event is a phenotypic change with particular, sometimes extensive, effects on development. Gene-frequency change follows, as a response to the developmental change. In this framework, most adaptive evolution is accommodation of developmental-phenotypic change. Genes are followers, not necessarily leaders, in phenotypic evolution' [69, pp. 157–158] The hypothesis has drawn some favourable attention as an important contribution of development to evolution [70].

West-Eberhard's hypothesis is very similar to what Simpson [71] called the Baldwin effect. Simpson said that the idea does not violate the standard theory of evolution by natural section. Indeed, Lande [72] (also Chevin *et al.* [73]) modelled the role of plasticity and genetic assimilation in adaptation to environmental change, using orthodox quantitative genetics. But Simpson noted that there were few real examples, and doubted they would prove to be common. Should his assessment be revised? Not greatly, at least based on currently available evidence.

West-Eberhard cites many cases in which a species constitutively exhibits a character state that is part of a more variable reaction norm in a related species. In almost none of these examples is there phylogenetic or fossil evidence on the direction of the change, so these tell us only that reaction norms can evolve, an issue not in doubt. Information on the direction of evolution (from plastic to constitutive) has been recognized as an important criterion for testing the hypothesis, and such information is available in a few recent cases which show that genetic assimilation can happen in natural populations [74,75]. For example, montane populations of *Daphnia*, recently faced with introduced fish that more easily detect melanized individuals, have lost a melanization reaction to ultraviolet light [76]. Anadromous marine sticklebacks (*Gasterosteus aculeatus*), when reared under lake-like conditions, display changes in body form that slightly resemble those that have evolved in derived lake-dwelling populations [77]. However, there is a long history of bidirectional gene flow between freshwater and marine populations [78], and the possibility cannot be ruled out that the reaction norm of the marine fishes is affected by alleles derived from freshwater populations. The experimental marine fishes do not show a plastic response of other characters, such as gill raker number, that have also evolved in freshwater populations.

More importantly, the genetically variable reaction norms in a population may or may not be oriented towards the

character state that is optimal in the altered environment [79]. If it is directed towards the optimum, evolution towards and possible genetic fixation of the optimal character state may occur; but as Pigliucci [80, p. 369] (who is sympathetic to West-Eberhard's hypothesis) has noted, the novel environment 'will often not be novel at all, but will be some variant of the sort of environment that has been common in the history of the species'. In this case, the reaction norm has previously been shaped by natural selection acting on genetic variation; genes are 'followers' only to the extent that genetic assimilation or accommodation 'fine-tunes' an adaptation that had already evolved by selection and genetic variation.

Therefore, phenotypic plasticity could be said to truly play a leading role (with genes as followers) if an advantageous phenotype were to be triggered by an environment that really is novel for the species lineage, an environment that its recent ancestors did not experience and which, therefore, had not exerted natural selection. Of course it is possible that a novel environment—a new pesticide, for example—could evoke a developmental effect that happens to improve fitness, just as it is possible that a random DNA mutation improves fitness. But no theory leads us to expect such an effect to be especially likely. On the empirical front, a few candidate instances have been described. Terrestrial tiger snakes that were raised in water for several months swam faster than land-reared siblings [81]; but how does this differ from the performance of trained human athletes? Aside from the lack of inheritance of this phenotypic change, how would one show that this response played a role in the evolution of aquatic species, such as the confamilial sea snakes? Perhaps the best example I have found that fits the Baldwin effect or genetic accommodation is the study by Ledón-Rettig *et al*. [82] of the tadpoles of spadefoot toads in the genus *Spea*. Their diet is commonly algae and detritus, but if tadpoles eat animal prey when young, they develop into a carnivorous morph with very large jaw muscles and a shorter gut. Another genus, *Scaphiopus*, in which the carnivorous morph has never been recorded, feeds entirely on algae and detritus. This is almost surely the ancestral diet, so animal prey is a novel environmental stimulus. Young *Scaphiopus* tadpoles, experimentally fed shrimp, developed a shorter than normal gut (as in *Spea*), a point in favour of West-Eberhard's hypothesis. However, they did not develop the most conspicuous features of *Spea*'s carnivorous morph, the greatly enlarged jaw muscles. The critical evidence, induction of an adaptive plastic response by a truly novel environment (to say nothing of subsequent genetic assimilation and accommodation) is supported by only tenuous evidence at this time.

Moreover, phenotypically plastic reactions to novel environments are often wholly or partly *counteradaptive*. In the well-known phenomenon of countergradient adaptation [83], genetic differences between populations are precisely opposite to the maladaptive direct effects of the different environments the populations inhabit, and compensate for the maladaptive plastic effect [84]. Human acclimation to high altitude improves performance, but at the cost of increased haematocrit, decreased affinity of haemoglobin for oxygen, and hypertensive pulmonary vessels—all features that differ from genetically adapted highland populations [85]. A guppy (*Poecilia reticulata*) population exhibited evidently maladaptive plastic changes in expression of many genes when reared in a novel environment (one that lacked predatory fish); descendants of this population adapted to a predator-free environment by precisely opposite evolutionary changes in gene regulation [86]. Deleterious phenotypic plasticity may be at least as effective in triggering adaptive genetic change as plasticity that enhances fitness [87].

I conclude that the evidence so far does not warrant much enthusiasm for the proposition that plasticity often paves the way for adaptation to novel selection pressures, much less for novel morphological or physiological adaptations. Abundant traditional theory, based in population genetics, describes how reaction norms evolve by selection on genetic variation, and there is abundant evidence of adaptation by natural selection on standing genetic variation [88,89]. Some conditions favour plasticity, some a fixed phenotype. The implication that development has inherent properties that are usually likely to generate new, adaptively directed phenotypes lacks any theoretical—or material, as far I can tell—foundation.

3.3. Inclusive inheritance

Several bases for non-genetic inheritance (meaning here inheritance that is not based on DNA sequence) have long been recognized, including culture, behavioural imprinting, parental environment including some maternal effects, and parental transmission of nucleic acids and diverse chemical compounds. Some, but by no means all, cases of niche construction also qualify [90]. As noted earlier, many of these phenomena have been modelled and empirically studied by evolutionary biologists for several decades [55,91–93], and it is not clear that the EES brings anything new to the topic.

More recently, novel molecular mechanisms of inheritance have proved to be widespread, such as inherited DNA methylation and other epigenetic 'marks'. Some authors have placed a provocative Lamarckian interpretation on certain of these phenomena [94,95], while others have urged that they be viewed as 'interpretive machinery' that can influence gene expression and development, and are inherited along with DNA [96]. These mechanisms can and should be studied, like other organismal and genomic features, in order to determine their evolutionary dynamics and their evolutionary effects. For example, some of these mechanisms can cause traits to continue to evolve after selection has ceased, and can even evolve in a direction opposite to selection [55]. Day & Bonduriansky [96] have developed a general model that they claim applies broadly across the various kinds of non-genetic inheritance, in which a key feature is that phenotypic change across generations can be decoupled from genetic change. Depending on the mechanism, non-genetic inheritance may be more transient (lasting for few generations) or more persistent, but in some cases, even transient inheritance can influence the direction of genetic evolution.

Some inherited epigenetic effects are influenced by environment, and have been described as vindicating Lamarckian inheritance. I think Haig [97] and Dickins & Rahman [98] are likely to be right: they do nothing of the kind. Transgenerational epigenetic inheritance does not intrinsically produce advantageous environmentally induced phenotypes. Epigenetic imprinting, whether inherited or not, can have both benefits and costs, which provide fuel for theoretical and empirical research [99]. Many epigenetic effects are deleterious [100], so population-typical

advantageous instances are best interpreted as the result of natural selection of those genetic variants with epigenetic modification that enhance fitness. The capacity of DNA sites to be marked is genetically variable, and epigenetic variation responds to selection [98,100,101]. Therefore, most instances of adaptive epigenetic variation are best viewed as transgenerationally transmitted adaptive phenotypic plasticity [102,103] that has evolved by mutation and natural selection [104].

That is not to deny the possible importance of such effects in evolution, but the importance has yet to be determined. By contrast to a century's accumulated evidence that variation within and among species is based on genes, there is little evidence, so far, that ecologically adaptive features of whole populations or species have an epigenetic basis [105]. The frequency of certain methylated sites differs among some populations of both plants and animals, and in some instances suggests a correlation with environment [106,107], although in only a few cases have population samples been reared in a common environment, in order to exclude direct environmental induction [108]. By contrast, a massive literature provides evidence that character differences between species are based on DNA sequence differences in genes [109]. Epigenetic transmission seems to last for at most a few dozen generations, and usually much less. The *peloria* variant of the toadflax *Linaria vulgaris* that Linnaeus described (an epigenetically based reversion from a bilaterally symmetrical to a radially symmetrical flower) can be found in populations today, but there is no reason to think there has been transmission of a mutant lineage since the eighteenth century. At this time, 'empirical evidence for epigenetic effects on adaptation has remained elusive' [101]. Charlesworth *et al*. [110], reviewing epigenetic and other sources of inherited variation, conclude that initially puzzling data have been consistent with standard evolutionary theory, and do not provide evidence for directed mutation or the inheritance of acquired characters.

Perhaps epigenetic inheritance will prove to have important effects in evolution, affecting the dynamics and direction of genetic adaptation [100]. However, just as evolutionary biology embraced the discovery of introns, transposable elements, and highly repetitive DNA, and easily adapted traditional population genetic models to describe their evolutionary behaviour, so it will be, I suspect, with epigenetic and other non-genetic inheritance. The basic framework of orthodox evolutionary theory has served well in evolutionary genomics thus far, and will almost certainly do so in this context, too. Evolutionary theory will be extended, just as it has been by other discoveries about genomes, but there is no sign that any of its components will have to be discarded.

3.4. Development and evolution

During and since the ES, relationships between developmental biologists and evolutionary biologists have at times been not entirely comfortable. It is sometimes said that development was excluded from the ES, but there is little ground for this accusation [15,111,112]. In the early twentieth century, experimental embryologists divorced themselves from what they viewed as a descriptive, speculative tradition of evolutionary embryology. The developmental biologist Viktor Hamburger [113] noted that during the period of the ES, books on experimental embryology did not treat evolution; Mayr [114] claimed that developmental biologists 'were not left out of the synthesis…they simply did not want to join'. The split between genetics and embryology, initiated by T. H. Morgan, probably affected the content of the synthetic theory, which built more on genetic than developmental foundations [115]. Nonetheless, development was not entirely ignored, as I note below. (My treatment of this topic draws on a rather lengthy essay on macroevolution [116] that at this time can be downloaded without cost at http://www.springer.com/us/book/9783319150444.)

Whatever the reasons may have been, development was not as effectively assimilated into the ES as it might have been; as many authors have noted, the ES lacked a theory of the origin of phenotypic variation, and especially of phenotypic novelty. One may well wonder what kind of theory could have been developed when the mechanisms of development, and even the molecular nature of genes, were entirely unknown. Experimental embryologists used phenomenological descriptors such as induction and prepattern, just as comparative embryologists had descriptors such as heterochrony and allometry. Kirschner & Gerhardt [117, p. 276] write that the 'Modern Synthesis did not and could not incorporate any understanding of how the phenotype is generated'.

Certainly some evolutionary biologists were sensitive to the significance of development. Huxley contributed an analysis of allometry to the ES, and speculated that it provided a non-adaptive (we might now say pleiotropic) explanation for some exaggerated features. Rensch [8,9] discussed allometry and other developmental phenomena at length, and speculated that parallel evolution, as in the wing patterns of Lepidoptera, may arise from similar genetic and developmental factors. Wright [118,119] provided a polygenic model for threshold traits (and Lande [120,121] later modelled how such traits evolve under natural selection). The idea that development can influence the direction of evolution was fully congenial to the architects of the ES. Mayr [38, pp. 607–610] wrote, in a passage on 'Evolutionary potential and predisposition', that 'Every group of animals is "predisposed" to vary in certain of its structures, and to be amazingly stable in others', and that this is reflected in parallel evolution: 'Only part of these differences can be explained by the differences in selection pressures to which the organisms are exposed; the remainder are due to the developmental and evolutionary limitation set by the organisms' genotype and its epigenetic[1] system…The epigenotype sets severe limits to the phenotypic expression of …mutations; it restricts the phenotypic potential'. Stebbins [10] wrote about evolutionary trends in plants, such as the repeated evolution of fused petals, which he analysed in terms of development: 'while the process of "fusion" is begun by the initiation of a new type of growth center, the degree of union, like that of reduction, is determined chiefly by allometry'. Stebbins [10,122] noted that the evolution of different floral structures constrained the way in which seed number might evolve; for example, by increasing the number of ovules per carpel in lilies (Liliaceae), by the number of carpels per flower in buttercups (Ranunculaceae) and by the number of flowers (florets) in the flowerheads of sunflowers (Asteraceae).

The first steps towards modern developmental biology, such as the Jacob & Monod [123] and the Britten–Davidson [124] models of gene regulation, were featured in textbooks by Dobzhansky *et al*. [125] and myself [126], both of which emphasized that evolutionary changes in gene regulation could underlie morphological evolution. The second edition of my textbook [127] included 14 pages on development and evolution, including discussions of prepatterns, the Turing model of pattern formation, the genetics of segment identity in *Drosophila*, developmental constraints and developmental integration. Today's leading textbooks of evolutionary biology all cover evolutionary developmental biology [128–131]. There are now journals that integrate developmental and evolutionary perspectives. Development is now well integrated into evolutionary thinking.

The rise of modern EDB (evolutionary developmental biology) is a valuable maturation of a dimension of evolutionary biology that has been present all along. It represents a structuralist approach that adds material mechanisms to the theory of allele frequency change [15]. It is part of a broader union of the theory of evolutionary dynamics with mechanistic biology—a conjunction of Mayr's [132] 'ultimate' (evolutionary) explanation with 'proximate' explanation at the level of organisms' structure and function.

These are complementary, not alternative explanations. For instance, one role of EDB may be to demonstrate and clarify the importance of developmental constraints on evolution [133,134]. For example, Brakefield's research group showed that the colours of two spots on the wing of a butterfly species could not be decoupled by artificial selection [135]. This well-known phenomenon is usually referred to as genetic correlation, which is typically ascribed to pleiotropic effects of genes that affect both characters, and is understood to act as a potential constraint on the direction of evolution [39,136,137]. Genetic constraints become developmental constraints when the mechanisms underlying genetic patterns are understood.

Developmental (or genetic) constraints of this kind clearly influence the direction of evolution, just as the direction of my travel is influenced when the police close a road. As the passages I cited from Mayr and Stebbins show, the idea that genetic or developmental 'potential' biases variation and evolution is neither new nor a challenge to traditional theory. Where EDB can provide insight is by identifying mechanistic causes. The demonstration, early in the twentieth century, that some salamanders are paedomorphic because of reduced thyroxin production provided a mechanistic complement to an evolutionary explanation [32]. Alberch & Gale's [138] famous experiment provided a mechanistic understanding of the evolutionary sequence of digit loss in amphibians, following a long history of developmental and genetic studies of the mechanisms and evolution of the reduction and loss of limbs in tetrapods [120]. Likewise, Turing's model provided a possible mechanism for patterns (e.g. the distribution of hairs or coloured spots on an animal [139]), but it did not explain why an animal would evolve spots. If spots do evolve, there must be a physical mechanism for their production and distribution. This proximate mechanism should not be confused with the ultimate explanation.

EDB helps to explain some enigmatic evolutionary changes. For example, the pectoral girdle of turtles lies below the ribs, but above the ribs in all other tetrapods. Recent descriptions of development, together with a key fossil turtle, show how changes in the development of the rib primordia and in the antero-posterior orientation of the ribs enabled this remarkable change [140,141]. EDB addresses interesting and important questions, such as coordinated evolutionary changes in functionally integrated characters [142] and the origin of truly novel characters [16]. But the argument for the importance of EDB need not be weakened by unnecessary claims and speculations. Müller [143] provides a very interesting treatment of morphological evolutionary novelties, such as the turtle carapace and the mammalian patella (knee cap). He describes models of developmental mechanisms that produce changes that result from 'activation–inhibition thresholds in geometrically confined spaces'. That may well be, but he goes on to postulate that the innovation may be produced as a phenotypically plastic effect that is later genetically assimilated. Thus 'genetic evolution, while facilitating innovation, serves a consolidating role rather than a generative one, capturing and routinizing morphogenetic templates'.

I view this as an unnecessary concatenation of speculations. Why is so complex and unsupported a hypothesis needed to explain the origin of the patella, which is formed by existing cellular and molecular processes of osteogenesis in a phylogenetically novel location in the body? Changes in gene regulation are known to trigger expression of entire developmental pathways at different times in development (heterochrony) or different sites in the body (heterotopy). Why not simply suppose genetic variation in sites of gene expression, and natural selection for those particular sites in which novel sesamoid bones prove advantageous? The patella is one of many heterotopic bones (e.g. osteoderms of armadillos) that have clear selective value. There have undoubtedly been many disadvantageous mutations that produced heterotopic bones in places that were decidedly wrong. Simpler explanations are generally preferred over more complex (and vague) hypotheses, unless these are supported by evidence.

The EDB described by some adherents to an EES is oddly different from the research literature that has made the most substantial progress in evolutionary developmental biology. That literature is largely concerned with evolutionary changes in gene regulation, and identifying the nature and causes of changes in *cis*-regulatory regions and trans-regulatory factors [144–146]. To be sure, much of this literature describes what might be called genetic blueprints or algorithms for making organisms, and not the final molecular processes by which tissues and organs are produced. But models of developmental fields and activation thresholds generally do not achieve this level of mechanism either. Some developmental biologists have been downright anti-genetical in the past [147]. A disjunction of developmental process from the genetic-*cum*-environmental specification of development seems unlikely to enhance our understanding of evolution.

4. Core assumptions

Laland *et al*. [14] list six 'core assumptions' that they say differ between the ES and the EES. I will comment on them only briefly, as the preceding discussion addresses most of these points.

(i) *The ES assumes preeminence of natural selection, the EES 'reciprocal causation' owing to developmental bias and niche construction*. No; advocates of the ES have long recognized (as did Darwin himself) that organisms determine, to a considerable extent, the environmental sources of selection, including by modifying their environment, and they recognized a role for developmental (or genetic) biases and constraints that can affect the directions of evolutionary change. But natural selection remains the only process that increases fitness and shapes adaptive characteristics.

(ii) *The ES assumes random genetic variation, the EES non-random variation*. No; it has always been recognized that some phenotypic variants are more likely to arise by mutation (expressed via development) than others. The fact that most mutations that affect fitness are deleterious, and that most novel environments reduce fitness, contradicts the EES claim that developmental systems facilitate well-integrated, functional phenotypic responses to mutation or environmental induction.

(iii) *The ES assumes gradualism, the EES variable rates of change*. Of course, advocates of the ES, beginning with Simpson [11] and Rensch [8], have recognized that rates of evolution are highly variable; evolutionary rates at both the phenotypic and genomic levels have been a focus of extensive research. This passage from Laland *et al.* [14] refers to the supposition in the EES that saltations are possible, and that the ES does not entertain saltations. I have explained that advocates of the ES have always accepted certain kinds of 'large effect' mutations, as in paedomorphosis and polyploidy. There is little or no evidence that saltations occur in evolution via mutations in gene regulation.

(iv) *The ES has a gene-centred perspective, the EES an organism-centred perspective*. A reading of the seminal works of the ES will show that most of the authors had a deep interest in and knowledge of organisms—considerably greater, I venture, than many or even most practicing evolutionary biologists today. I have illustrated this with examples concerning niche construction, developmental processes and constraints. But the founders of the ES recognized that these and other properties of organisms evolve only if they are inherited across generations. Like Darwin, they recognized the common elements of a truly general theory of the evolution of phenotypes—including the phenotypic states that influence subsequent evolution—in variation, inheritance, and natural selection. (We would add genetic drift today.)

(v) *The ES assumes genetic inheritance, the EES inclusive inheritance*. Of course, the ES has always recognized cultural inheritance, but largely ignored it because it was considered taxonomically very restricted. As the prevalence of several widespread molecular mechanisms of inheritance other than by DNA sequence has come to light, evolutionary biology is provided with new phenomena to study and explain. Interesting theory is being developed as a consequence, and it is largely grounded in traditional population genetics. Documenting the frequency and distribution of non-genetic inheritance in natural populations, and its importance for evolved differences among populations and species, will be a task for empirical research.

(vi) *Macroevolution: ES explains by microevolutionary processes, the EES by additional processes such as developmental bias and ecological inheritance*. I have noted that developmental bias is not a new idea, and no evolutionary biologist who studies macroevolution would deny it. The role of ecological inheritance in macroevolution is speculative and unnecessary until shown otherwise.

5. Conclusion

Laland *et al*. [14] add that in the EES, evolution is 'redefined as a transgenerational change in the distribution of heritable traits of a population'. That sounds equivalent to one traditional definition of evolution as change in gene frequencies, except that the EES redefinition would include non-genetic inheritance. Definitions are conventions, so does the definition of evolution matter? Perhaps, the philosophers of science Evelyn Fox Keller and Elizabeth Lloyd [148, pp. 2–3] noted that words 'help to hold worldviews together' and that 'the effort to "control and curtail the power of language" remains a significant feature of scientific activity. The very extent to which scientists…aim at a language of fixed and unambiguous meanings constitutes, in itself, one of the most distinctive features of their enterprise. And even though never quite realizable, this effort to control the vicissitudes of language, like the commitment to objectivity, reaps distinctive cognitive benefits'. Definitions, then, should not be altered lightly.

Are advocates of an EES engaged in an 'effort to control the vicissitudes of language', and to what end? Some of the emphases in the proposed EES, such as niche construction, the supposed pioneering role of phenotypic plasticity in adaptation, and quasi-Lamarckian interpretations of epigenetic inheritance, are reminiscent of the rise of neo-Lamarckism in the early twentieth century, during the 'eclipse of Darwinism'. Bowler [149, p. 258] writes that 'Lamarckism allows life itself to be seen as purposeful and creative. Living things are in charge of their own evolution: they choose their response to each environmental challenge and thus direct evolution by their own efforts. With or without any religious implications, this is certainly a more hopeful vision than that derived from Darwinism. Life becomes an active force in nature, no longer merely responding in a passive manner to environmental pressures'. Welch [28] hears echoes of this theme in current critiques of standard evolutionary theory. He quotes neurobiologist Steven Rose [150] to that effect 'redefining evolution as "a change of gene frequency in a population" is a reductionism too far, depriving living organisms of playing any part in their own destiny', and recalls that Gregory Bateson [151] found in Waddington's genetic assimilation implications 'for the battle between non-moral materialism and the more mystical view of the universe'. I do not think all advocates of an EES are impelled by emotional distaste for the utter lack of purpose and agency in evolution by natural selection, but it may be useful to ask if our views of evolutionary theory are affected by extrascientific values. As Welch [28] notes, 'we do need to explain why ideas are so often hailed as important before they have done much scientific work'.

Some of the emphases in the proposed EES, especially non-genetic inheritance, may prove interesting, if developed both theoretically and empirically. Evolutionary developmental

biology is an exciting field that can join a structuralist approach to the traditional emphasis on genetic variation — but it does not diminish the roles of genetic variation and selection. Modern versions of the Baldwin effect will need considerably more evidence before we can conclude that this kind of effect is important, and there are good reasons to doubt that it is. Overall, I have seen little evidential support for challenges to the basic tenets of the ES.

There have now been many essays on why a new, or supposedly new, viewpoint or approach is warranted. If advocates of an EES are to convince many biologists, they will need to provide empirical support. To remain vital, a field of science requires challengers who aim to topple traditional views; but if it is not to be knocked about and smashed by unruly children (I am thinking of current politics in my country), the science also needs traditionalists. John Maynard Smith [152], one of the most broad-minded of great evolutionary biologists, wrote, 'It is in the nature of science that once a position becomes orthodox it should be subjected to criticism. . .It does not follow that because a position is orthodox, it is wrong'.

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Endnote

[1]Mayr, like Waddington and other biologists until recently, used 'epigenetic' to refer simply to developmental processes, not in its modern molecular sense.

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THE ROYAL SOCIETY PUBLISHING

Why an extended evolutionary synthesis is necessary

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Since the last major theoretical integration in evolutionary biology—the modern synthesis (MS) of the 1940s—the biosciences have made significant advances. The rise of molecular biology and evolutionary developmental biology, the recognition of ecological development, niche construction and multiple inheritance systems, the '-omics' revolution and the science of systems biology, among other developments, have provided a wealth of new knowledge about the factors responsible for evolutionary change. Some of these results are in agreement with the standard theory and others reveal different properties of the evolutionary process. A renewed and extended theoretical synthesis, advocated by several authors in this issue, aims to unite pertinent concepts that emerge from the novel fields with elements of the standard theory. The resulting theoretical framework differs from the latter in its core logic and predictive capacities. Whereas the MS theory and its various amendments concentrate on genetic and adaptive variation in populations, the extended framework emphasizes the role of constructive processes, ecological interactions and systems dynamics in the evolution of organismal complexity as well as its social and cultural conditions. Single-level and unilinear causation is replaced by multilevel and reciprocal causation. Among other consequences, the extended framework overcomes many of the limitations of traditional gene-centric explanation and entails a revised understanding of the role of natural selection in the evolutionary process. All these features stimulate research into new areas of evolutionary biology.

1. Introduction

A century ago, it was noted in the domain of physics that 'concepts that have proven useful in ordering things easily achieve such an authority over us that we forget their earthly origins and accept them as unalterable givens. Thus, they come to be stamped as "necessities of thought", "*a priori* givens", etc. The path of scientific advance is often made impassable for a long time through such errors.' [1]. Evolutionary biology finds itself in a similar situation today. A well-established paradigm that has its roots in a major theoretical integration that took place approximately eight decades ago, traditionally labelled the modern synthesis (MS) or Synthetic Theory, still dominates evolutionary thought today. In the meantime, the biological sciences have progressed extensively. The material basis of inheritance has been unravelled and entire new fields of research have arisen, such as molecular genetics, evolutionary developmental biology and systems biology. In addition, new evolutionarily relevant factors have been described, including non-genetic inheritance, developmental bias, niche construction, genomic evolution and others. Clearly, our understanding of evolution has significantly expanded, and it would be surprising if these empirical and conceptual advances had no theoretical consequences, so that in the midst of a substantial growth of knowledge, the central theory uniting the different fields of biology remained unaltered.

In fact, our theoretical understanding of biological evolution has not remained unaltered. Slight modifications and adjustments to the received theory are recognized even in the most traditional quarters. But in the past decade, without much notice by general audiences, a more wide-ranging debate has arisen from different areas of biology as well as from history and philosophy of science, about whether and in which ways evolutionary theory is affected, challenged or changed by the advances in biology and other fields. As usual in such cases, more conservative perspectives and more progressive ones are in conflict with each other, with differences ranging from minor to intense. A rising number of publications argue for a major revision or even a replacement of the standard theory of evolution [2–14], indicating that this cannot be dismissed as a minority view but rather is a widespread feeling among scientists and philosophers alike. In the present essay, I will concentrate on the arguments and debates triggered by one particular alternative to the standard theory that has become known under the term extended evolutionary synthesis (EES). This proposal for an integration of revised and additional components of evolutionary theory into a coherent explanatory framework, as recently elaborated by Laland *et al*. [15], has caught on as one of the crystallizing points in the ongoing debate. No claim is made that this approach represents the only way of addressing theory revision in biology.

The theory of evolution is the fundamental conceptual framework of biology all scientific explanations of living phenomena must be consistent with. As it does not describe a universal law regarding a single natural phenomenon, such as gravity, but rather the principles of organismal change over time, based on the highly complex inputs and interactions of a multiplicity of different factors, evolutionary theory cannot be expected to remain static but is subject to change in the light of new empirical evidence. This is a normal process of scientific advancement and not a heretical undertaking as it is sometimes perceived to be. Explanations of organismal diversity have changed significantly during pre- and post-Darwinian periods, and it should not come as a surprise that fresh stimuli arise from the new methodologies and the expanded scope of modern biological research. Indeed, a growing number of challenges to the classical model of evolution have emerged over the past few years, such as from evolutionary developmental biology [16], epigenetics [17], physiology [18], genomics [19], ecology [20], plasticity research [21], population genetics [22], regulatory evolution [23], network approaches [14], novelty research [24], behavioural biology [12], microbiology [7] and systems biology [25], further supported by arguments from the cultural [26] and social sciences [27], as well as by philosophical treatments [28–31]. None of these contentions are unscientific, all rest firmly on evolutionary principles and all are backed by substantial empirical evidence.

Sometimes these challenges are met with dogmatic hostility, decrying any criticism of the traditional theoretical edifice as fatuous [32], but more often the defenders of the traditional conception argue that 'all is well' with current evolutionary theory, which they see as having 'co-evolved' together with the methodological and empirical advances that already receive their due in current evolutionary biology [33]. But the repeatedly emphasized fact that innovative evolutionary mechanisms have been mentioned in certain earlier or more recent writings does not mean that the formal structure of evolutionary theory has been adjusted to them. To the contrary, the discrepancies between the current usage of evolutionary concepts and the predictions derived from the classical model have grown. Hence, it will be useful to characterize some of the differences that exist between the MS theory and proposed alternatives.

2. A problem agenda

When attempting to define the issues at stake in the current debate, it is necessary to keep in sight what it is that should be explained by a theory of evolution. Evolutionary biology, as practised today, does not represent a single coherent approach but includes sets of different topics and research programmes. For instance, one may be interested in the patterns of phylogenetic relatedness and the processes of species formation. Here, the emphasis is on reconstructing relationships among organisms and unravelling the principles of the separation and diversification of higher taxonomical clades, as pursued by the field of phylogenetics. Another approach examines genetic and phenotypic variation in populations in order to derive rules of variational change over time, a perspective most elaborately pursued by population genetics and quantitative genetics. Still another approach is the study of the origin of complex organismal features, such as morphological, physiological or behavioural traits, in order to explain the evolution of the processes that generate these features and how—in turn—these processes influence the course of evolution, as investigated by evolutionary developmental biology (evo-devo), systems biology, or the behavioural sciences. Finally, one may study evolution with a view to the origins of mind, language, society and culture, as well as their feedback on biological evolution, as conducted by the fields of cognitive biology, linguistics, anthropology and certain domains of the social sciences.

The vastly different explananda and the progress made in each of these fields must be kept in mind when we examine the tenets of the present theory of evolution. While documenting numerous empirical and theoretical advances, at the level of core assumption most current textbooks on evolution, whether explicitly or implicitly, still offer a theoretical framework that is largely based on the MS of the 1930s and 1940s. Even though it never constituted an encompassing formal synthesis [34], this movement had brought together the basic neo-Darwinian principles of variation, inheritance, differential reproduction and natural selection with Mendelian, experimental and population genetics, as well as with concepts and data addressing the patterns of evolution stemming from the fields of palaeontology, botany and systematics. The formalized core of the MS theory was—and still is—population genetics [35], a mathematical account of gene frequency dynamics in populations of organisms. The empirical basis and key concern of the population genetic approach is the measurement of trait variability in populations, and its intended explananda are adaptive variation, speciation and calculations of fitness. The flurry of fitness landscapes based on ever more nuanced algorithms is indicative of this received approach.

Even though claims have been made that classical evolutionary biology has continuously incorporated aspects from new conceptual domains [33,36], the majority of tenets

and explanations that appear in characterizations of the current theory are still derived from the MS account and its population genetic principles [37]. In a condensed form, these tenets are as follows: (i) all evolutionary explanation requires the study of populations of organisms; (ii) populations contain genetic variation that arises randomly from mutation and recombination; (iii) populations evolve by changes in gene frequency brought about by natural selection, gene flow and drift; (iv) genetic variants generate slight phenotypic effects and the resulting phenotypic variation is gradual and continuous; (v) genetic inheritance alone accounts for the transmission of selectable variation; (vi) new species arise by a prevention of gene flow between populations that evolve differently; (vii) the phenotypic differences that distinguish higher taxa result from the incremental accumulation of genetic variation; (viii) natural selection represents the only directional factor in evolution. For a more extensive description of tenets see Futuyma [37].

As can be noted from the listed principles, current evolutionary theory is predominantly oriented towards a genetic explanation of variation, and, except for some minor semantic modifications, this has not changed over the past seven or eight decades. Whatever lip service is paid to taking into account other factors than those traditionally accepted, we find that the theory, as presented in extant writings, concentrates on a limited set of evolutionary explananda, excluding the majority of those mentioned among the explanatory goals above. The theory performs well with regard to the issues it concentrates on, providing testable and abundantly confirmed predictions on the dynamics of genetic variation in evolving populations, on the gradual variation and adaptation of phenotypic traits, and on certain genetic features of speciation. If the explanation would stop here, no controversy would exist. But it has become habitual in evolutionary biology to take population genetics as the privileged type of explanation of *all* evolutionary phenomena, thereby negating the fact that, on the one hand, not all of its predictions can be confirmed under all circumstances, and, on the other hand, a wealth of evolutionary phenomena remains excluded. For instance, the theory largely avoids the question of how the complex organizations of organismal structure, physiology, development or behaviour—whose variation it describes—actually arise in evolution, and it also provides no adequate means for including factors that are not part of the population genetic framework, such as developmental, systems theoretical, ecological or cultural influences.

Criticisms of the shortcomings of the MS framework have a long history. One of them concerns the profoundly gradualist conception the MS has inherited from the Darwinian account of evolution. Darwin saw slight, incremental and accumulating variation as *the* essential prerequisite without which 'my theory would absolutely break down.' [38] a position already characterized by Huxley in 1901 [39] as an 'unnecessary difficulty.' Subsequently, the perceived necessity of a slow and continuous flux of variation seemed to have been supported by innumerable studies that demonstrate corresponding behaviours of character variation in natural populations or under artificial selection regimes. The notion of slight successive variation was further reinforced by the molecular conception of genetic variation. When mutation of individual genes or even smaller entities of DNA is taken as the predominant source of variation, it seemed inevitable that phenotypic modifications should be small, because larger changes were deemed to be disruptive and unlikely to produce adaptive outcomes. The supposed randomness of genetic variation further contributed to this view. Today, all of these cherished opinions have to be revised, not least in the light of genomics, which evokes a distinctly non-gradualist picture [40]. In addition, it is necessary to realize that all models of gradual variation are based on empirical measurements of precisely this kind of change and to the exclusion of other forms of variation. If cases of gradual variation are chosen and quantified, and theoretical models are derived from them, it should not be unexpected that it is gradual variation that will be explained.

Connected with the gradualist requirement of the MS theory is the deeply entrenched notion of adaptation. Again, we are confronted with a feature of the classical theory that has been criticized repeatedly in the past, both on empirical and theoretical grounds [30,41] but also on the basis of modern results of genetics [22]. Whereas different forms of adaptationism can be discerned, for instance in the British and the American research traditions [30], the notion most frequently encountered is still that of a collection of features that make up the organism, each one individually adapted to performing a function in the way best suited for the organism's survival, a picture that has been described as 'bundles of discrete adaptations.' This view was neither eliminated by Dobzhansky's alternative view, in which he interpreted populations as states of relative adaptedness [30], nor by the demonstration of the frequent occurrence of non-adaptive traits. Already in the late 1970s, Gould & Lewontin [41] described the adherence to pervasive adaptationism as an 'old habit,' but despite extensive learned discussions of the subject that habit has not receded.

Natural selection, the cornerstone of the MS theory so intimately linked to both gradualism and adaptationism, has itself been the subject of a fair share of critical debate. In this case, it is not so much the principle itself that is contested, but the uniqueness of the causal agency that has been ascribed to it. Are all features of biological organisms necessarily the result of natural selection, and is it the only factor in the evolutionary process that provides directionality to organismal change? Numerous authors have challenged the pervasiveness of natural selection as a unique 'force' of evolution, whereas others have questioned whether the individual is the sole and appropriate 'target' of selection or whether other levels of selection at supra- and infra-individual levels also need to be included in selectionist scenarios [42–44]. Again we are confronted with a classical criticism that stood at the centre of multiple debates in the past [42], but the issue is as unresolved as ever.

Finally, it is apparent that nearly all of the relevant predictions that derive from the MS theory are based on genetic principles and gene determinist convictions. Although the long-held belief that genes are the unique determinants of biological form in development and evolution has been challenged by an extensive number of commentators [21,23,45–48], the genetic program idea underlying MS theory has remained unaltered. This is also true with regard to the mechanisms of transgenerational inheritance. The proposition of uniquely genetic inheritance has been falsified multiple times [3], but the gene-centric position remains constitutive of the MS. The contemporary version of this position, gene regulatory network evolution, really represents only an extension of the 'gene-determines-phenotype' view.

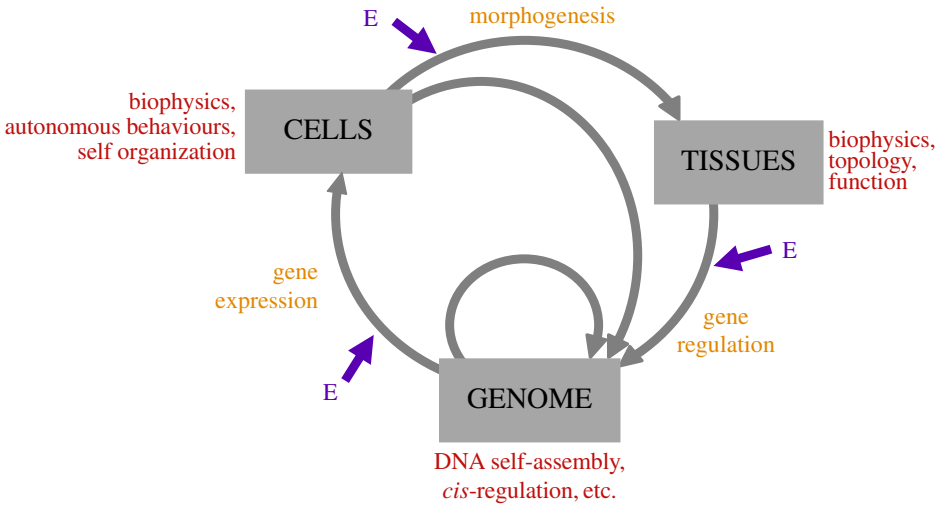

Figure 1. Feedback interactions among different levels of organization in developmental systems. Examples of autonomous properties of each level are marked in red (E, environmental influences).

The limitations of the MS theory are not only highlighted by the criticisms directed against several of its traditional tenets but also by the failure to address some of the most important phenomena of organismal evolution. The question, for instance, of how complex phenotypic organizations arise in evolution is sidestepped by the population theoretical account, as is the reciprocal influence of these features of higher levels of organization on the evolutionary process. Indeed, the MS theory lacks a theory of organization that can account for the characteristic features of phenotypic evolution, such as novelty, modularity, homology, homoplasy or the origin of lineage-defining body plans. As will be shown below, evo-devo, niche construction, systems biology and other areas harbour the capacity to address at least certain aspects of these topics where the classical theory fails.

Even though only the most prominent issues were mentioned here, this brief overview indicates that the problem agenda associated with the MS theory is extensive. The fact, often mentioned by defenders of the orthodoxy, that these issues have been raised before, does not alleviate the problems. Rather, the current evolutionary paradigm is still dominated by the very same basic assumptions that marked the origin of the synthesis approach. Despite the fact that substantial challenges to these positions have arisen in the past decades from a host of different areas of biology, they have rarely resulted in alternative proposals. Gould's 2002 comprehensive treatment of the history of evolutionary debate [42], for instance, takes up most of the criticisms and suggests alternate concepts, but it does not actually offer an alternative overall *structure* of evolutionary theory as its title suggests. All the extensive discussions, led over decades, seem not to have altered the preponderant stance to hold on to the classical prerequisites of gradualism, adaptationism, selectionism and genecentrism. The predictions that follow from the MS framework continue to be based on these prerequisites and ignore all predictions derived from alternative models. Hence, the claim of continuous incorporation of new conceptual components by the MS theory is misleading.

3. Conceptual innovation

Today, evolutionary biology exhibits a very different landscape. An abundance of new theoretical concepts has arisen since the time of the formulation of the population theoretical synthesis, some of which offer challenges to the received theory or have not been included into a common theoretical framework. Only a brief overview of the most relevant conceptual innovations is possible in the present context. For more elaborate treatments see Pigliucci & Müller [49] or Laland *et al*. [15].

3.1. Evolutionary developmental biology

A suite of new concepts emerges from evo-devo, a field of research that arose in the early 1980s from a discontent with the exclusion of developmental biology from evolutionary theory [50–53]. The subsequent rise of new molecular methodologies for a comparative analysis of gene regulation resulted in a huge increase of our understanding of how the processes of development evolve. In its theoretical domain, the evo-devo approach starts from the premise that the genotype–phenotype relation is not merely a statistical correlation, but that the rules of developmental processes govern phenotypic outcomes while relying on additional inputs not coming from the genome. It is abundantly clear that development is not a linear reading out of a code or program but a systemic process of feedback interactions between genetic and non-genetic templates, cells and tissues that mobilizes physical and autonomous properties at different scales and depends on local as well as global environments [54] (figure 1). Hence, development is a systems relation in which no component is informationally privileged. A number of evolutionary concepts result from the evo-devo study of these relations, three of which shall be mentioned here.

First, the kind of selectable phenotypic variation that can be produced by a developmental system of a given type is neither infinite nor random. Rather, selectable variation is both constrained [55] and facilitated [56] by development. Before natural selection can act, the developmental system harbours tendencies towards certain solutions, a property that has been called developmental bias [57,58]. Second, as is the case with most multilevel systems, developmental processes exhibit emergent properties. A wide array of such behaviours is known in cell and tissue organization [59]. Reaction–diffusion processes in embryos, for instance, organize cell arrangements in limb morphogenesis [60]. Third, developmental systems are characterized by bistabilities and threshold behaviours [61],

such as in the well-known case of somite formation, in which there exists a mutually inhibiting relationship between FGF and RA receptors in which an unstable state separates two stable states [62], or in the case of threshold behaviours in vertebrate digit formation [63]. When natural selection affects such kinds of systems, the resulting phenotype variation does not need to be gradual and continuous. In fact, simulations of the dynamical behaviours of gene regulatory networks in evolution demonstrate that bistable changes are more likely to occur than gradual transitions [64].

In addition, the research approach of evo-devo permits addressing the processes responsible for the evolution of phenotypic organization, a topic thoroughly avoided by the synthesis theory. The issue cannot be reduced to the evolution of gene regulation, because, on the one hand, highly conserved developmental control genes, e.g. homeotic genes, can exhibit non-homologous expression domains in embryos of closely related phylogenetic lineages, and on the other hand, homologous structures can be specified by non-homologous genes, a characteristic of the genotype–phenotype relation described by developmental systems drift [65]. Evo-devo-based concepts of structural organization emphasize the integrative stability provided by shared developmental pathways [66] and the modularity of developmental processes [67]. Morphological templates that result from the mobilization of physical forces are seen to represent basic organizing themes in animals [68] and plants [69] that become integrated through a hierarchization of regulatory networks and fixated as patterns of phenotypic construction [70]. Increasingly elaborate gene regulatory systems serve to reproduce morphological templates, and the close mapping between genotype and morphological phenotype may not represent the cause but a consequence of evolution [71]. Hence, evo-devo mechanisms of phenotypic organization could not only be responsible for higher-level complexity but could also affect further organismal evolution [4], a claim that is supported by experiment [72] and modelling [73].

Overall, the evo-devo results indicate that phenotypic variation is neither necessarily gradual nor random. Irrespective of whether they are perturbed by selectional, mutational or experimental intervention, developmental systems exhibit emergent behaviours and generate nonlinear effects, i.e. the phenotypic outcome is only indirectly related to genetic variation and yet still follows predictable pathways. In other words, the variational range of a population is not defined merely by genetic variation but by the developmental system as a whole, providing sources of phenotypic bias and novelty [24,74]. It is now possible to determine the relative importance of natural selection and of genetic and developmental determinants of organic diversity [55].

3.2. Phenotypic plasticity

The population context of development is mostly provided by the study of developmental plasticity, a component of phenotypic plasticity. Developmental plasticity is the capacity of organisms to develop altered phenotypes in reaction to different environmental conditions. Among its evolutionary effects, the influence on a population's variational response to selection and the acceleration of the colonization of novel environments are well documented [21,75,76], as are the fitness consequences of parental effects that depend on the modifications of developmental processes [77]. Plasticity can also have a critical role in determining which genetic variants will generate selectable phenotypic differences under given environmental conditions, or as a result of stress [78], through either widening or narrowing the range of the phenotypic response capacity of a population, often termed the reaction norm [79].

According to the developmental plasticity concept, fixation of environmentally induced variants may happen through phenotypic and genetic accommodation [74,80]. Phenotypic accommodation refers to the adjustment of modified parts of an organism through developmental processes that typically do not require genetic mutation [81]. Phenotypic accommodation may be followed by genetic accommodation and thus result in more rapid adaptation to novel environments [79]. The effect of a novel environment on phenotypic plasticity may be coupled with simultaneous exposure of 'hidden' developmental variation and strong selection on this variation [82] and could provide a starting point for the evolutionary persistence of phenotypic innovations [24]. Plasticity has also been linked to the ubiquitous phenomenon of homoplasy [83] and to rapid divergence of phylogenetic lineages [21]. In this perspective, developmental plasticity acts as a source of adaptive innovation, and one of its critical mechanisms is environmental induction [21,82,84], the direct action of environmental parameters on developmental processes.

3.3. Genomics

The science most central to the MS, genetics, likewise has substantially changed since the time of the synthesis and especially over the past two decades. Now that whole genomes can be studied, we have learned that in the course of evolution significant portions of the genome have been duplicated, deleted or co-opted into new functions [40]. In addition, novel genomic segments and biochemical functions can be acquired from other cells and organisms, rather than exclusively by inheritance from their progenitors. Comparative genomics has greatly changed the concepts of both the evolution of primitive life forms and eukaryotes. Among prokaryotes, viruses, plasmids, etc., horizontal gene transfer is ubiquitous and even among eukaryotes much more frequent than hitherto assumed [85,86], with compelling documentations of horizontal transfer in protists, fungi and plants, as well as in animals, including mammals and other tetrapods [7]. Mobile elements, in particular, make genomic evolution exquisitely dynamic and non-gradual [40,87]. Furthermore, functional genome reorganization can occur in response to environmental stress [14,88–90]. Thus, the properties of genetic change are found to be quite different from the assumptions made by the founders of the MS, when continued random substitution of individual alleles was the reigning understanding.

3.4. Multilevel selection

Conceptual change is also underway with regard to the understanding of natural selection. Whereas the classical view posited the individual as the unit of selection, it is now held more often that natural selection can also act at levels above and below the individual. Hierarchical selection theory [42] and multilevel selection theory [69,91] span selective processes from genetic, cellular and tissue levels up to

kin selection, group selection and possibly even species selection, making it necessary to distinguish individual fitness from group fitness. Even though the debate is still in flux, increasing attention is paid to the fact that natural selection may act at different levels simultaneously, possibly even in opposing directions, and that selection at one level can have effects that percolate up or down to other levels. Interest in multilevel selection theory has resurged in connection to work on the major transitions in evolution and definitions of biological causality [91].

3.5. Inclusive inheritance

The concepts of inheritance equally have undergone revision in recent decades. In addition to genetic inheritance, the only means of transgenerational transmission of information acknowledged by the MS, several forms of non-genetic inheritance are recognized today. These include epigenetic, behavioural, ecological and cultural forms of inheritance [3,9].

In the domain of epigenetic inheritance it is not merely the well-known patterns of post-translational modifications of histone proteins or methylation of cytosines that can be transmitted across generations [92]. Especially the transgenerational epigenetics of small RNAs is increasingly identified as a major factor of gene regulation in developing tissues, with a host of new molecules and mechanisms uncovered in recent times [93], including ways in which parental experience can alter gene expression in later generations [94] such as the human microbiome [95]. In addition, ecological and cultural forms of inheritance are now understood to affect the behaviours and phenotypic variation of subsequent generations [96] and require inclusion into the evolutionary inheritance repertoire. Initial approaches to unify genetic and non-genetic heritability, as well as their relative contributions and mutual interactions, have successfully established quantitative models of inclusive inheritance [9]. Although non-genetic inheritance is sometimes dismissed as representing exclusively proximate mechanisms whose ultimate (evolutionary) functions do not run counter to the MS [97], the shortcomings of such arguments and of the widespread proximate–ultimate distinction in general have been convincingly demonstrated [98].

3.6. Niche construction

Advances at the interface of ecology, behaviour and culture have shown that populations of organisms are not merely passively exposed to natural selection but are actively involved in the formation of those environments that constitute the selective conditions for later populations. This mode of evolution, in which organisms co-direct their own evolution and that of other species, has been characterized by niche construction theory, which includes concepts of migration, dispersal and habitat selection, but also of gene–culture co-evolution. Niche construction processes can lead to the fixation of alleles that may otherwise be deleterious, it can facilitate the endurance of organisms in adverse environments and it can be beneficial despite being costly due to advantages that accrue for later generations [99].

Niche construction captures important links between biological and cultural evolution, such as the modification of selection on a plethora of human genes in response to culturally transmitted activities, the effects of which can be shown in mathematical models [20,96]. Equally encompassing effects of niche construction have been demonstrated in plants [21,69,100]. Independently of the proximate mechanism of niche construction, cultural processes can lead to the evolution and maintenance of altruistic behaviours, the emergence of high levels of cooperation, a reduction of genetic diversity or to speciation [96]. In hominin evolution, evidence has accumulated to the effect that cultural activities, such as tool-making [101] or the domestication of plants and animals [102], can be major influences on biological evolution. Clearly, the interconnections between biological and cultural evolution cannot be sidelined [103], and niche construction's most important theoretical contribution lies in highlighting the complex evolutionary reciprocities between organismal activity and environmental change.

3.7. Systems biology

From a different domain, systems biology, arise theoretical conceptions that have the capacity to integrate several of the previously mentioned evolutionary components. The kind of systems biology capable of doing this is not the ubiquitous '-omics' blossoming today, but the theoretical framework that deals with the study of systems properties of organisms and their interactions across levels of organization, from molecules to populations of organisms, including physiological, behavioural and cultural factors. Although today's organismal systems biology is mostly rooted in biophysics and biological function [25], with pioneers including, among others, Ludwig von Bertalanffy, Paul Weiss, Alan Turing, D'Arcy Thompson and Claude Bernard, its endeavours are profoundly integrative, aiming at multiscale and multilevel explanations of organismal properties and their evolution. Rather than merely evoking the powers of computation for analysing multiple interactions of biological components, the capacity of systems biology is better interpreted as a scientific attitude that combines 'reductionist' approaches (study of constituent parts) with 'integrationist' approaches (study of internal and external interactions) [104]. Having gone historically through ups and downs [105], systems theoretical conceptions, whether explicitly or implicitly, now form part of the theoretical foundations of many different fields and are beginning to take centre stage in evolutionary biology also. Rupert Riedl was an early proponent of this position [106].

These examples of conceptual change in various domains of evolutionary biology represent only a condensed segment of the advances made since the inception of the MS theory some 80 years ago. Relatively minor attention has been paid to the fact that many of these concepts, which are in full use today, sometimes contradict or expand central tenets of the MS theory. Given proper attention, these conceptual expansions force us to consider what they mean for our present understanding of evolution. Obviously, several of the cornerstones of the traditional evolutionary framework need to be revised and new components incorporated into a common theoretical structure. Below, I will sketch out an expanded framework to which several of the authors in this issue have contributed.

4. An extended evolutionary synthesis

The EES was proposed as a theoretical framework that takes account of the plurality of factors and causal relations in

evolutionary processes [15,49]. It continues to see variation, differential reproduction, heredity, natural selection, drift, etc., as necessary components of evolution, but it differs in how these factors are conceptualized. In addition, in the EES, development assumes a constructive role, natural selection is not the only way that variation in populations can be modified, causation does not run solely in one direction from the external environment to populations and, instead of a single inheritance mechanism, several modes of transmission exist between generations. A rough arrangement of the EES's components is depicted in figure 2 in order to visualize the structural differences between the traditional framework (figure 2*a*) and the extended framework (figure 2*b*). Several significant distinctions are noticeable. Foremost among them is the abandonment of the notion that the range of phenotypic variation in a population is sufficiently explained by the statistical correlation with concomitant variation in a population's 'gene pool'. Instead, as the results from evo-devo and systems biology suggest, the capacity for variation in populations is determined by the developmental systems properties of a population that, in addition to genetic variation, include a host of dynamically interacting components, many of which are not genetically specified as discussed above. This may be called the 'developmental systems pool' of a population (figure 2*b*). Its dynamics plays out before the background of developmental plasticity and evolving gene regulation, but it also includes the self-organizing, physics-dependent and environmentally mediated properties of development. In this perspective, developmental bias and plasticity assume central roles as generators of novel and coordinated phenotypic variation by conferring directionality on the selective processes.

Inheritance is another component of the standard framework that is strongly modified in the extended picture: multiple systems of inheritance are recognized. In addition to the transmission of DNA sequences from one generation to the next, the EES includes epigenetic inheritance, in a sense that is not limited to epigenetic markings but also includes small RNAs and other maternal or paternal components as well as components of the cell that are inherited independently of the DNA. In addition, the EES accepts behavioural, ecological and cultural transmission as well as the interactions between the different modes of transgenerational inheritance. Even though the precise evolutionary contribution of each of these modes requires further study, their existence is indisputable, and distinguishing their various contributions to inclusive inheritance is essential for understanding evolutionary dynamics [9].

Natural selection remains a key factor of the EES, but its roles are reinterpreted. In the MS, at least in its bare bones interpretations, organismal shape and structure were regarded entirely as products of external selection, and the directionality of evolutionary change was supposed to result from natural selection alone. In the EES, besides the expanded range of selection to multiple levels of organization, the generative properties of developmental systems are viewed as responsible for producing phenotypic specificity, whereas natural selection serves to release that developmental potential. Particular forms of phenotypic change are taken as the result of internal generative conditions rather than external pruning. Thus, a significant amount of explanatory weight is shifted from external conditions to the internal properties of evolving populations. In addition, natural selection may be 'bypassed' by environmental

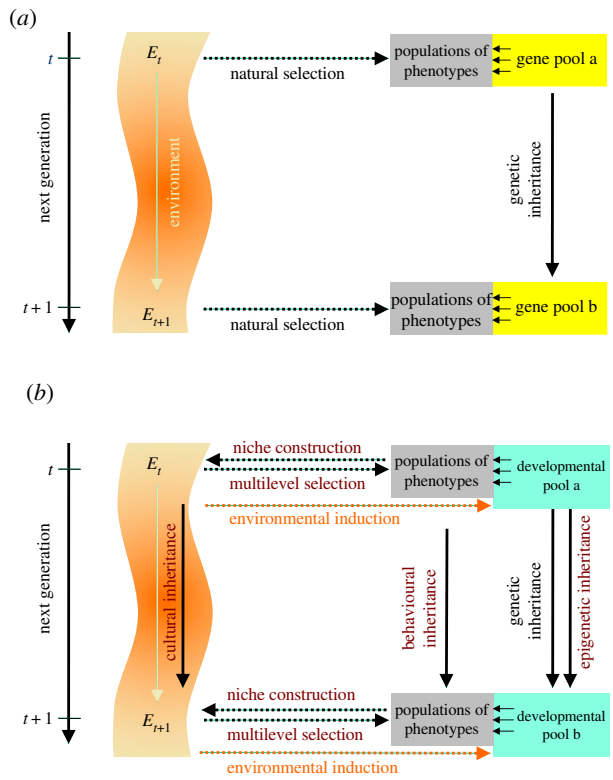

Figure 2. Schematic depiction of defining theory components and relations in (*a*) the MS (after Odling-Smee *et al*. [97]) and (*b*) the extended synthesis (after Müller [107]). Major differences are indicated by different colours. (Online version in colour.)

induction, causing potentially adaptive developmental variation in many individuals of a population at once and long before natural selection may become effective.

As a consequence, unlike the MS, the EES includes a constructive component. Instead of chance variation in DNA composition, evolving developmental interactions account for the specificities of phenotypic construction. This interpretation is also based on a fundamentally different account of the role of genes in development and evolution. In the EES, genes are not causally privileged as programs or blueprints that control and dictate phenotypic outcomes, but are rather parts of the systemic dynamics of interactions that mobilize self-organizing processes in the evolution of development and entire life cycles. This represents a shift from a *programmed* to a *constructive* role of developmental processes in evolution. Furthermore, the constructive aspect also concerns the interactions between all other levels of organization such as the behavioural, social and cultural. Together, they constitute the kernel of an organizational theory component that sets the EES apart from the MS.

Another distinctive feature of the EES is causal reciprocity. This is true for two domains. One is the construction of phenotypic complexity, in which causation not only flows from the lower levels of biological organization, such as DNA, 'upwards' to cells, tissues and organisms, but also from the higher level 'downwards', such as through environmental- or tissue-induced gene regulation. The second aspect of causal reciprocity lies in the fact that populations of organisms are not relegated to being passive recipients of external selection pressures but, through various forms of niche construction, actively modify the environments that become the selective conditions for later generations. Thus, a major feature of the EES is that causation not only runs one way but

assumes dialectical relations between its participating components, both in the relationship of populations with the environment and in the generation of heritable phenotypic architectures.

The novelty of the EES and the differences with the MS theory become most apparent in the predictions that derive from the EES framework, both with regard to short-term and long-term effects of organismal evolution. The most important predictions concern the following: (i) the generation of heritable phenotypic variation (variation will be systematically biased and facilitated by the generative features of development); (ii) the origin of phenotypic novelty (novelties are due to emergent and self-organizing properties of developmental systems); (iii) the sequence of genetic and phenotypic change (emergent phenotypic structures can be captured and stabilized by evolving gene regulatory circuitry and assume fitness subsequently); (iv) inheritance (in addition to genetic inheritance, adaptive variants are propagated by non-genetic inheritance, learning and cultural transmission, as well as by repeated environmental induction); (v) tempo of evolution (periods of rapid phenotypic evolution can alternate with periods of slow and continuous change); (vi) environmental induction (phenotypic variation can be environmentally induced in multiple individuals simultaneously); (vii) organismal activity (niche construction effectuates environmental changes that enhance the fitness of the constructors and their descendants; (viii) natural selection (the primary evolutionary effect of natural selection is not to eliminate the unfit but to release generative potential).

Overall, the EES proposes that variation is more predictable and selection effects are less directional than hitherto argued. The EES addresses organizing principles instead of statistical correlations or evolving instruction programs. It represents a pluralistic, process-based framework of dynamical interactions between a multitude of evolutionarily effective factors and generates its own set of evolutionary predictions that make it clearly distinct from the MS account. These genuine predictions of the EES give rise to new research programmes, which have already generated validating empirical results. It is beyond the scope of this article to discuss the range of predictions and their consequences in greater detail, but more extensive treatments can be found in Laland *et al*. [15].

5. Consequences

The EES is not a simple, unfounded call for a new theory but has become an ongoing project for integrating the theoretically relevant concepts that have arisen from multiple fields of evolutionary biology. Although the EES recognizes the fundaments of the classical MS theory, it differs in its interpretation of the role of some of its elements and integrates new components, such as constructive processes of development, multiple inheritance mechanisms, niche reciprocity, as well as behavioural and cultural elements (on which this overview did not dwell much, but see other contributions to this issue). It is unavoidable to notice that an integration of these concepts means not a simple add-on of a few peripheral notions to the MS model without any effects on its core logic. Rather, the EES establishes a new structure of the theoretical evolutionary framework that goes beyond the reductionist and gene-centred perspective of the past. It represents a different way of thinking about evolution, historically rooted in the organicist tradition [108]. Its predictions permit the derivation of new hypotheses and thus inspire novel and progressive research in evolutionary biology and adjacent fields.

Proposals of an EES generally elicit rather positive reactions from the representatives of different fields of science, many of whom are convinced that an expanded theoretical framework has become necessary for evolutionary biology. Opposition comes in three different versions. One is the 'absorption argument', i.e. the standard framework is said to no longer be the MS but to have continually absorbed various conceptual advances [33]. The defenders of the EES beg to differ: as long as the major predictions that can be derived from an evolutionary framework remain exactly those of the classical MS, no change to its core assumptions has happened. Adding a chapter or two on new domains of evolutionary research, as evolution textbooks increasingly do, does not mean that these concepts have been integrated into the theoretical edifice of evolutionary biology. Rather, it has become customary to treat individual research questions independently, but to accept only the population genetic approach as explanatorily essential.

The second response (also made by a participant after nearly every lecture in the Royal Society meeting on which this special issue is based) runs: 'this has been said before', implying either that the arguments are outdated or deemed irrelevant. It remains unclear why empirical findings or conceptual proposals that have been stated previously are thereby rendered irrelevant. When this objection fails, the argument usually becomes that the processes central to the EES are merely add-ons to the basic processes required by the MS, such as natural selection, mutation, recombination, drift and gene flow, but are 'not essential' for evolution [33]. Given the different explananda of evolutionary biology described above, such suggestions are beside the point. Moreover, critics infallibly call for further empirical evidence, giving the impression that the EES is an unfounded theoretical exercise that still awaits confirmation. While more empirical evidence is always desirable, all constituent parts of the EES are already abundantly supported by research results in the different domains from which they have arisen, as amply shown by the works cited in the present overview. Ideas perhaps rightly rejected in the past due to a lack of supporting evidence must now be re-evaluated in the light of contemporary knowledge.

A subtler version of the this-has-been-said-before argument used to deflect any challenges to the received view is to pull the issue into the never ending micro-versus-macroevolution debate. Whereas 'microevolution' is regarded as the continuous change of allele frequencies within a species or population [109], the ill-defined macroevolution concept [36], amalgamates the issue of speciation and the origin of 'higher taxa' with so-called 'major phenotypic change' or new constructional types. Usually, a cursory acknowledgement of the problem of the origin of phenotypic characters quickly becomes a discussion of population genetic arguments about speciation, often linked to the maligned punctuated equilibria concept [9], in order to finally dismiss any necessity for theory change. The problem of phenotypic complexity thus becomes (in)elegantly bypassed. Inevitably, the conclusion is reached that microevolutionary mechanisms are consistent with macroevolutionary phenomena [36], even

though this has very little to do with the structure and predictions of the EES. The real issue is that genetic evolution alone has been found insufficient for an adequate causal explanation of all forms of phenotypic complexity, not only of something vaguely termed 'macroevolution'. Hence, the micro–macro distinction only serves to obscure the important issues that emerge from the current challenges to the standard theory. It should not be used in discussion of the EES, which rarely makes any allusions to macroevolution, although it is sometimes forced to do so.

Interestingly, a third class of responses to the EES is this: the proposed modifications are not radical enough, a much more fundamental change is required [107]. Also, here we beg to differ. Quite evidently, the MS theory has become too narrow in several regards, but this does not mean that all its elements have been invalidated. Nevertheless, the differences in structure and consequences are substantial enough to require a new designation, because to continue using 'MS' evokes a wholly different set of assumptions and predictions. The classical theory cannot keep its label and at the same time make different predictions. The term 'EES' used here and elsewhere [4,5,9,14,15,27,28,49] is not meant as a simple extension *of* the MS, as sometimes wrongly implied, but to indicate a comprehensive new synthesis. Whether eventually that new framework will be called EES or a different name is not important. What is important is that a different theory structure is necessary to accommodate the new concepts that are in everyday use and have become part of the current toolkit of evolutionary biology. Therefore, a theory change is not a future goal, but we are in the midst of it, with the EES attempting to provide a structure for the present state of evolutionary thought.

This is an exciting period in evolutionary biology. The principal Darwinian research tradition is upheld, but the specifics of evolutionary theory structure are undergoing ferment, including the revision of some of its traditional elements and the incorporation of new elements. Instead of privileging selected mechanisms such as random variation, genetic control and natural selection, the multitude of factors that dynamically interact in the evolutionary process will be better expounded by a pluralistic theory framework. Current evolutionary research already reflects this pluralism, and as many of its underlying concepts have drifted from the standard theoretical paradigm, an adjusted evolutionary framework that adequately synthesizes the multitude of new theoretical elements has become a necessity. The EES represents one possibility for such integration.

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