The Proper Role of Population Genetics in Modern Evolutionary Theory

Massimo Pigliucci
Department of Philosophy
City University of New York
Lehman College
Bronx, NY, USA
massimo@platofootnote.org

Abstract
Evolutionary biology is a field currently animated by much discussion concerning its conceptual foundations. On the one hand, we have supporters of a classical view of evolutionary theory, whose backbone is provided by population genetics and the so-called Modern Synthesis (MS). On the other hand, a number of researchers are calling for an Extended Synthesis (ES) that takes seriously both the limitations of the MS (such as its inability to incorporate developmental biology) and recent empirical and theoretical research on issues such as evolvability, modularity, and self-organization. In this article, I engage in an in-depth commentary of an influential paper by population geneticist Michael Lynch, which I take to be the best defense of the MS-population genetics position published so far. I show why I think that Lynch's arguments are wanting and propose a modification of evolutionary theory that retains but greatly expands on population genetics.

Keywords
evolutionary theory, Extended Synthesis, Modern Synthesis, population genetics

December 9, 2008; accepted February 3, 2009
Biological Theory 3(4) 2008, 316–324.

Theodozius Dobzhansky (1973), one of the fathers of the Modern Synthesis (MS) in evolutionary biology, famously wrote that "nothing in biology makes sense except in the light of evolution." That remark, the title of a paper in *American Biology Teacher*, referred to the (still ongoing) controversy over the teaching of evolution in American public schools. The phrase has become a bit of a mantra among evolutionary biologists, and it has been adapted to a variety of not always appropriate contexts. Perhaps the latest such misappropriation is in a paper by the influential population geneticist Michael Lynch (2007a) entitled "The frailty of adaptive hypotheses for the origin of organismal complexity." Indeed, the first section of Lynch's paper is entitled "Nothing in evolution makes sense except in light of population genetics." Lynch's goal—also pursued in *The Origins of Genomic Architecture* (Lynch 2007b), particularly in the last chapter—is to put forth the view that genomic and phenotypic complexity both largely derive from nonadaptive mechanisms, and that population genetic theory is the ultimate arbiter in matters of genomic and phenotypic evolution. This is a bold agenda, one that bears further scrutiny in light of ongoing discussions on the structure of evolutionary theory (Pigliucci and Müller in press).

In this article, I examine Lynch's perspective and find it wanting. I make the case that Lynch's emphasis on nonadaptive processes surely has a place, particularly at the genomic level of biological organization. However, I also argue that it simply does not follow that similar considerations provide a sufficient account of phenotypic complexity. Moreover, I think that while population genetics is an important part of evolutionary theory, it is an error and a gross simplification to see evolution as fundamentally a matter of changes in gene frequencies over time. Finally, I show why it is likely that Lynch is mistaken in his dismissal of much work on complexity theory as applied to biological organisms, as well as of concepts such as evolvability, modularity, and robustness. My reason to focus on Lynch's paper in particular is that to my knowledge it represents the best effort so far by a prominent biologist to mount an attack on what is increasingly being recognized as an Extended Synthesis (ES: Müller 2007; Pigliucci 2007). In this sense, Lynch's paper helps to draw the conceptual boundaries of the currently reigning paradigm, boundaries that I believe are being expanded by a concerted effort of many theoretical and empirical biologists involved in the development of the ES.

Lynch's "Nine Myths About Evolution"

Interestingly, the term "Modern Synthesis" (MS) occurs only once in Lynch's paper, as part of a quotation by EvoDevo biologist Sean Carroll with which Lynch strongly disagrees. Yet, population genetics theory is inarguably the theoretical backbone of the MS, which in turn has been shaped by the reconciliation among Darwin-style natural history, Mendelian genetics, and population-statistical (i.e., quantitative) genetics (Provine 1971). Lynch's stated goal is to dispel what he considers "myths" about organismal complexity. His specific targets and general arguments are as follows (p. 8598):

1. "Evolution is natural selection." Instead, for Lynch there are four forces in evolution: natural selection, mutation, recombination, and drift.
2. "Characterization of interspecific differences at the molecular and/or cellular levels is tantamount to identifying the mechanisms of evolution." For the author, differences between species do tell us something about the end products of evolution, but not about what he considers the all-important population genetic mechanisms that actually cause them.
3. "Microevolutionary theory based on gene-frequency change is incapable of explaining the evolution of complex phenotypes." To which Lynch responds that no discovery in molecular or evolutionary biology has so far overturned any principle of population genetics, and that no new mechanisms of evolution have emerged outside of the four mentioned above.
4. "Natural selection promotes the evolution of organismal complexity." According to Lynch, there is no evidence that this is the case at any level of biological complexity.
5. "Natural selection is the only force capable of promoting directional evolution." Instead, Lynch maintains that mutation and gene conversion can bias the direction of evolutionary change, especially in small populations.
6. "Genetic drift is a random process that leads to noise in the evolutionary process, but otherwise leaves expected evolutionary trajectories unaltered." On the contrary, for the author drift has a biasing effect on evolution because it increases the likelihood of fixation of deleterious alleles.
7. "Mutation merely creates variation, whereas natural selection promotes specific mutant alleles on the basis of their phenotypic effects." According to Lynch, mutation is instead a weak directional force because it eliminates those alleles that magnify the size of mutational targets.
8. "Phenotypic and genetic modularity are direct products of natural selection." There is no evidence for this, according to Lynch, and instead we know that duplication, mutation, and drift can yield modularity.
9. "Natural selection promotes the ability to evolve." Again, for Lynch there is no evidence for this claim and so-called evolvability is a byproduct of the expansion of genome size and generation length after the transition from uni- to multicellular organisms.

I do not know of a single biologist involved in the development of the ES who holds to any of these views, especially in the strong sense implied by Lynch in his paper (interestingly, the table in which these items are listed has no references). Here, however, I take the most reasonable interpretations of Lynch's criticisms and address them to show where his defense

of the MS and the role of population genetic theory comes close to being on target, and where instead it goes astray. In the process, I therefore elaborate on some of the main differences between the MS and the ES.

Refuting Lynch's "Nine Myths About Evolution"

1. Evolution Is More Than Natural Selection

No biologist who has taken an introductory class in evolution could reasonably claim that evolution is natural selection, and not even the most adaptationist authors, as Gould and Lewontin (1979) famously labeled the corresponding intellectual position, would do so. In fact, standard population genetic theory recognizes five (not four) processes that can push a population of organisms away from the so-called Hardy–Weinberg equilibrium: selection, mutation, recombination, assortative mating, and migration. However, a claim to exclusivity is often made with regard to natural selection—that it is the only mechanism capable of accounting for adaptation. There are two important points to make here. First, even though adaptation is an evolutionary phenomenon, it is obviously not the same as evolution. Second, those who make something akin to that claim are usually defenders of the MS, not proponents of its expansion. All the discussion about complexity theory, emergence, and related concepts (Huberman and Hogg 1986; Atchley and Hall 1991; Kauffman 1993; Perry 1995; Surrey et al. 2001; Hoelzer et al. 2006) aims at exploring the possibility that natural selection is one, but not the only, mechanism capable of producing complex biological structures.

2. The Mechanisms of Evolution

Lynch maintains that the only things that count as mechanisms in evolution are the four "forces" he identifies within population genetic theory, and that differences among species at the molecular and cellular levels (as well as, I assume, a fortiori at the developmental level) are the end products, not causes, of evolution. That one cannot simply assume that observed differences among species were responsible for species divergence is a truism we must concede. Nevertheless, it seems odd to suggest the idea that, say, differences in cellular properties or developmental processes are not an integral part of the causal story that leads to diversification. For instance, it is well known that closely related species of cichlid fish are differentiated by the morphology of their jaws, some of which are adapted to grazing and others to biting. However, we also know that one species of cichlid fish (*Cichlasoma managuense*) is capable of developing both morphologies as a result of phenotypic plasticity in response to diet during early development (Meyer 1987).

There is mounting evidence consistent with the idea that in some instances an ancestral plastic response may later evolve into a canalized (genetically fixed) morph, a process known as genetic accommodation (West-Eberhard 2003). Notice that in such instances an environmentally induced developmental switch gets things started, and a change in gene frequencies follows the initial steps in the evolutionary process. In these cases, then, the population geneticist is staring at the results—not the causes—of evolution. And although nobody knows how often genetic accommodation occurs, it is an evolutionary pathway that clearly invalidates Lynch's assumption that population genetic mechanisms always constitute the real McCoy.

3. Changes in Gene Frequency Are Explanatory of Complex Phenotypic Change

Perhaps one of the most crucial points of controversy between supporters of the MS and the ES is embodied by the increasingly debatable textbook definition of evolution as change in gene frequencies (e.g., Futuyma 2006). Here it is instructive to examine closely the language used by Lynch on p. 8598: "No principle of population genetics has been overturned by an observation in molecular, cellular, or developmental biology, nor has any novel mechanism of evolution been revealed by such fields." The first part of this sentence is certainly true, but also irrelevant to the central claim. To my knowledge no one is arguing that the principles of population genetics should be overturned (after all, the idea underlying the ES is that it is an extension, not an overhaul, of the MS). The second part of the claim hinges on what one counts as a "mechanism." In this passage, Lynch sticks to a very reductionist conception of mechanism, according to which there is one and only one level of organization (i.e., the one addressed by population genetics) that is truly explanatory with respect to the phenomena at hand.

A large literature in the philosophy of biology and in theoretical biology, however, has decisively shown this not to be the case (Robert 2004; Lloyd 2005). For instance, selection can and does happen at different levels (Stevens et al. 1995; Okasha 2006), and the properties of cells and tissues that depend on chemistry and physics are just as much part of the "mechanisms" of evolution as anything else (Newman et al. 2006). Furthermore, there is no logical reason why genetic and developmental constraints, phenotypic plasticity, canalization, and so forth should not count as "mechanisms" of evolution in any meaningful sense of the term. It is true that, in the long run, any evolutionary change also implies a change in gene frequencies, but this is a matter of "bookkeeping" (Wimsatt 1980) as the genes are not always the major actors on the evolutionary stage. If so, then it follows that population genetics—while important—does not have any claim to an exclusive role in evolutionary theory.

4. Natural Selection as Promoter of Organismal Complexity

Again, I am not aware of any serious researcher who maintains that natural selection is, as Lynch puts it, the only promoter of

organismal complexity. Especially in light of the classic 1979 Gould and Lewontin take on the so-called "spandrels" (see also Pigliucci and Kaplan 2000) and the now massive literature on genetic and developmental constraints (Gould 1980; Maynard-Smith et al. 1985; Arnold 1992; Barton and Partridge 2000; Schwenk and Wagner 2004; McGhee 2007), few if any biologists would make that claim. The actual position defended by most is that natural selection is the only process capable of generating adaptive complexity. While there is reasonable doubt about even this more restricted claim, the alternative mechanisms proposed by Lynch within the classic population genetic framework can certainly generate complexity, but not adaptation. It is, again, instructive to pay attention to Lynch's exact phrasing of the "myth." When he raises the problem (left-hand column of his table) he talks about the evolution of "organismal complexity," thereby using a broad term that includes both genomic and phenomic levels. However, in the right-hand column of the table, where he explains his position, he writes about how nonselective processes drive "the evolution of *genomic* complexity" (my emphasis). Surely, Lynch knows that genomic is not synonymous with organismal, and that his argument is much stronger at the genomic level (as he magisterially shows in his 2007b book) than at the organismal (meaning phenotypic) one.

5. Selection as a Directional Force

A variant of the "myth" discussed immediately above, the charge here is that some biologists apparently think natural selection is the only mechanism that can impart directionality to evolutionary pathways. Lynch correctly points out that drift can do the same, and so can other molecular phenomena, such as meiotic drive and the well-known fact that mutations are not isotropic with respect to their phenotypic effects. But again, any biologist who has taken introductory population genetics should know this; indeed, there is an entire literature dedicated to the preferential directionality imposed on evolution by genetic and developmental constraints (Koufopanou and Bell 1991; Schluter 1996; Renaud et al. 2006; Eroukhmanoff and Svensson 2007). It is hard to avoid smelling a straw man here.

6. Genetic Drift Only Produces Noise

Lynch then provides what is essentially a mirror image of the argument just examined above. He is, again, correct in saying that drift can increase what he calls "directionality" in evolution by increasing the likelihood of fixation of deleterious mutations, clearly an effect counter to the action of natural selection. But, once more, this is an elementary consequence of population genetic theory and as such is surely well understood by professional evolutionary biologists. More subtly, notice Lynch's use of the term "directional" here, which is not at all the same as the meaning implied in most discussions in organismal biology. By directional Lynch means a nonisotropic effect, which certainly occurs. But most discussions of directionality in evolution deal with phenotypic, not genetic, changes, and with long (paleontological, not population genetic) time scales (Raup and Gould 1974; McShea 1994). This is akin to a bait and switch tactic, and it does not help to move the discussion forward.

7. The Role of Mutation

This is perhaps one of the most controversial of Lynch's claims. He suggests that the common view of mutation as simply providing raw variation for the evolutionary process is mistaken, because "mutation operates as a weak selective force by differentially eliminating alleles with structural features that magnify mutational target sizes." This is a distinct argument from the one about the anisotropy of mutational effects mentioned above, and the two should not be confused. Lynch's point here is that eukaryotes have "mutational target sizes" (i.e., nucleotide positions that can be subjected to mutation) that are two to three times larger than those of prokaryotes. A consequence of the presence of introns and of numerous regulatory sequences, this increases what he calls the "mutational hazards" for eukaryotes. Such an increase, he maintains, must have either been favored by natural selection because of a strong immediate advantage (which is hard to fathom) or was the result of drift in sufficiently small populations. Lynch prefers the second solution, and I think he is right. But all this has little to do with the concern of organismal biologists interested in phenotypic evolution, unless the genotype > phenotype mapping function (Alberch 1991; Hansen 2006; Salazar-Ciudad 2007) is very simple and linear—which we by now know for sure it is not. Certainly the genomic features of organisms have some kind of effect on their phenotypic evolution, but one cannot effortlessly shift between the two levels of organization, translating processes at one level into effects at the second level without further (and detailed) justification. Lynch offers no such justification, either in his paper or in the aforementioned book.

8. Selection and Modularity

Lynch's next "myth" is the assertion that natural selection is responsible for genetic and phenotypic modularity, to which he replies that there is no evidence that the structure of gene regulatory networks is a direct result of selection, and that nonselective mechanisms are sufficient to account for it. There are several problems with this argument. First, notice again a case of bait and switch between the two columns of Lynch's table: on the left side we see a reference to both genetic and phenotypic modularity; on the right side the latter has disappeared. Second, while I do not doubt that a good portion of the details of genetic networks is the result of nonselective processes, this is essentially a rehashing of the debate about the neutral theory

of molecular evolution (Kimura 1983), shifted from the level of individual sequences to that of networks. Just as in that historical case, the compromise reached by most biologists is to settle for a level of "quasi-neutrality" (Hey 1999), because to claim complete neutrality is to maintain that selection had nothing to do with gene-level evolution, an assertion that is both contradicted by the empirical evidence (Akashi 1995; Shepard and Purugganan 2003) and that would prompt an even bigger problem than it would solve: how, then, do we explain the clearly adaptive nature of much phenotypic evolution, when the phenotypes are affected by the details of the genetic network? The question, as always, concerns the relative roles of selective and nonselective mechanisms in specific instances, and simply cannot be settled by sweeping generalizations. Third, much of Lynch's argument here and in other places hinges on considering nonselective mechanisms as a null hypothesis, against which positive evidence for selection must be accumulated. Lynch is quite explicit on this (p. 8600): "If a successful adaptive counterargument is to be mounted, simpler nonadaptive models must be shown to be inadequate." But it is not at all clear in what sense nonadaptive models would be "simpler" (measured how?), and some authors (Dennett 1995) have gone so far as to argue that adaptation, not neutral processes, should be the null hypothesis in evolution, at least at the phenotypic level (because of the otherwise hard to explain "fit" between organismal form and function). In fact, an increasingly influential school of thought favors the idea that no hypothesis should be considered a "null" because this biases our conclusions and a priori shifts the burden of proof (Cohen 1994; Pigliucci and Kaplan 2006; Stephens et al. 2006). Instead, the available multiple hypotheses should simply be left to compete over how well they explain the data, using likelihood, Bayesian, or model comparison approaches (Sober 2008).

9. Selection and Evolvability

The last "myth" that Lynch sets out to debunk is the idea that natural selection favors evolvability. Following a now familiar pattern, he claims that there is no direct evidence of this being the case, and that differences in evolvability among lineages are better seen as the by-product of nonadaptive processes. Again, there are several issues to carefully consider. First, the literature to which Lynch refers is far from claiming that evolvability evolves by selection; rather, several authors treat this as an open question (Partridge and Barton 2000; Brookfield 2001; Bell 2005; Lenski et al. 2006). Further, there are both theoretical arguments (Earl and Deem 2004) and empirical evidence (Colegrave and Collins 2008) that evolvability *can* be selected for, and that in some instances it is (most obviously in the case of mutator genes in bacteria [Sniegowski et al. 1997], but nonequilibrium population genetic models show that this is also possible in eukaryotes; Wagner and Burger 1985). In other words, the issue of evolvability is much more fluid and complex than Lynch acknowledges (Pigliucci 2008), and it cannot simply be brushed aside with a priori statements. Second, and most important, even if evolvability turns out largely to be the result of nonselective forces, there is little doubt that it does alter the evolutionary path of lineages, thereby introducing an additional high-level mechanism into the evolutionary arena. The fact that evolvability is the indirect result of lower-level molecular processes does not invalidate the point, just as the much more obvious fact that genes are ultimately made of subatomic particles does not reduce population genetics to quantum mechanics. Third, Lynch's additional argument here—that "there are no abrupt transitions in aspects of genomic architecture or gene structure between unicellular and multicellular species, nor between viruses, prokaryotes, and eukaryotes"—seems to invalidate his own shifting back and forth between genomic and phenomic levels of organization. Since there clearly *are* major and abrupt phenomic differences between those classes of organisms, then a search for explanations that focuses exclusively on the population genomic level must be missing something important—which is one of the tenets of both research in EvoDevo and of the efforts to produce an ES (Love 2003; Müller 2007; Pigliucci 2007; Carroll 2008).

Major Themes in the Struggle for a Modern Evolutionary Theory

As I mentioned at the outset, the reason to discuss Lynch's paper in detail is that it is an outstanding example of a certain view of evolutionary theory, written by a leader in the field and published in a major journal. As such, his effort helps us identify some of the major issues of contention defining the current debate about evolutionary theory. To begin with, Lynch sees population genetics as the theoretical backbone of the general theory of evolution, the MS that emerged during the 1930s and 1940s. Indeed, the MS essentially amounted to a reframing of Darwin's original insights into a population genetic framework.

Without denying both the historical and current importance of population genetics (despite the existence of well-thought-out, in-depth critiques of it; Dupré 1993), population genetics is, in fact, a very limited theory. First, it can deal analytically only with relatively simple situations, involving few loci/alleles, and has to resort to the statistical treatment more typical of quantitative genetics (itself not without issues; Pigliucci 2006) as soon as the problems to be examined approach an interesting degree of biological complexity. A reasonably balanced way of looking at both population and quantitative genetics is that they provide biologists with conceptual tools to help them understand how, in principle, population-level dynamics affect changes in the genetic structure of evolving populations. Neither theoretical framework,

however, allows quantitative predictions of the long-term behavior of real systems; the sheer complexity of the latter, the number of interactions among disparate causal factors, and the role of contingent events in evolution make such a feat all but impossible. Fisher's dream of providing biology with the equivalent of the second principle of thermodynamics needs, I think, to be permanently set aside. This is not a failure of the theory, and much less of the theorists; it is a result of taking seriously the complexity and historicity of evolutionary biology (Cleland 2002).

More importantly, though, the fundamental limitation of population genetics was understood to some extent even by some of the founders of the MS, as in Ernst Mayr's (1963) famous quip about "bean bag genetics," of which Haldane (1964) felt compelled to write a defense. Of course population genetics, especially in its modern application to the evolution of genomes (Lynch 2007b), is much more sophisticated than Mayr gave it credit for. However, it is at its core a theory of changes in gene frequencies and cannot be a theory of change in form. This dichotomy between genes and forms helped bring about the exclusion of developmental biology from the MS, and has provided the impetus for modern-day EvoDevo research (Wilkins 2002; Robert 2004). Karl Popper famously pointed out that the MS "never gives a full explanation of anything's coming into being in the course of evolution [because it is a theory that assumes variation]" and that "[it] is strictly a theory of genes, yet the phenomenon to be explained in evolution is that of the transmutation of form" (quoted in Platnick and Rosen 1987). In fact, both problems need to be explained, and population-quantitative genetics does a reasonable job at the first task. It has little or nothing to say, however, about the second.

Lynch goes so far as to say that population genetics is a "litmus test" (p. 8598) for any evolutionary hypothesis, which must be "consistent with" population genetic principles. But consistency with a partial theoretical structure is not nearly enough. It is simply not true, as Lynch maintains, that "nothing in evolution makes sense except in light of population genetics," and it is high time that we expand our textbook definitions of evolution to include far more than simply changes in gene frequencies (Futuyma 2006).

The second major theme emerging from Lynch's analysis is the perennial debate about "internal" versus "external" forces in evolution (Resnik 1994). Here Lynch takes a position that distances him from the classic version of the Modern Synthesis. MS proponents like Fisher, Dobzhansky, and Mayr (but unlike Wright) thought that external factors (i.e., natural selection) were by far the most important drivers of evolutionary change. Lynch, on the other hand, emphasizes internal factors like mutation pressure. He rightly argues that the latter is not isotropic, and is therefore capable of imparting directionality on evolutionary change. And yet even in his insistence on internal mechanisms Lynch does not seem to consider the large literature on developmental constraints (Gould 1980; Maynard-Smith et al. 1985; Schwenk and Wagner 2004; etc.), which makes the same point about a balanced view between external and internal causality in evolution, but at the level of the generative processes of the phenotype. Again, population genetics is not, and cannot be, a theory of form.

The third theme worth considering is what Lynch terms the passive emergence of complexity by nonadaptive processes. He criticizes what he rather jarringly refers to as the "religious adherence to the adaptationist program" (p. 8599), despite the fact that such excesses have long been criticized in the literature (Gould and Lewontin 1979; Pigliucci and Kaplan 2000). Nonetheless, Lynch does present a solid argument for the idea that nonadaptive processes may have been responsible at least in part for the evolution of genomic complexity. This is, as I mentioned earlier, a genomic-level reincarnation of Kimura's (1983) neutral theory of molecular evolution. It suffers from the aforementioned issue of treating nonadaptive processes as null hypotheses, which unfairly shifts the burden of proof; instead, multiple (not mutually exclusive) mechanisms should be treated as competing hypotheses in any specific case, letting the data inform us on the relative likelihood of different causal scenarios.

The fourth theme to be addressed is Lynch's extension of his nonadaptive approach to include an organismal (i.e., phenotypic) perspective. On p. 8600, Lynch takes to task none other than François Jacob (1977: 1163) for stating that "it is natural selection that gives direction to changes, orients chance, and slowly, progressively produces more complex structures, new organs, and new species," in response to which Lynch asks adaptationists to show the supportive evidence for such statements. I am sympathetic to reactions against the excesses of adaptationism, but—once again—Lynch's nonadaptive mechanisms cannot win by default if they do not even bother to enter the playing field. Where is Lynch's evidence that organismal complexity is largely a result of nonselective processes? More generally, it is hard to imagine that high-level phenotypes, especially those traits displaying an uncanny "fit" with the environment, as Darwin would have put it, are not at least in part the result of natural selection. Indeed, Lynch himself acknowledges this later in the same section of the paper, saying that "there is no need to abandon the idea that many of the external morphological and/or behavioral manifestations of multicellularity in today's organisms are adaptive." Ironically, however, he may then be conceding too much to the MS view because he does not even consider the possibility of other nonadaptive, nongenetic mechanisms that may have helped organismal evolution. It is now well known, for instance, that the physical-chemical properties of cells and tissues yield organization "for free," as it were (Newman et al. 2006), and that this complexity need not be an outcome of selection. This is not,

however, a simple consequence of population genetic theory, because the latter is silent about the evolution of form. For a paper focused on nonadaptive processes, there is a peculiar refusal to consider sources of self-organization (Kauffman 1993; Kirschner and Gerhart 2005) other than those that can be contemplated within the narrow horizon of population genetics.

Fifth on our list of themes is the origin of modularity, a major pillar of the ES. The scenario is by now familiar: Lynch argues that nonadaptive processes can explain modularization at the subgenomic level and then seamlessly expands his range to developmental pathways and, by implication, high-end phenotypes. It is certainly possible, as Lynch maintains, that modular gene-regulatory structures (i.e., genes accompanied by transcription factors that affect their spatial and temporal expression) began to emerge at the transition between pro- and eukaryotes. However, it is again hard to imagine that such explanation will suffice, considering that gene regulation has sometimes dramatic effects on development and fitness, which pretty much guarantees some role for natural selection. Moreover, the term "modularity" in contemporary evolutionary theoretical literature often applies to genetic networks and to developmental modules, i.e., to levels of organismal complexity that are more likely to be affected by selection and where nonadaptive processes, though likely to play a role, are not the chief causal factors.

The last major theme approached by Lynch is that of evolvability. Having already discussed this above, I will not repeat my arguments here. A couple of additional comments are necessary, however, to better understand Lynch's position and to highlight in what sense evolvability is in fact a cornerstone of the ES. Perhaps the most clear example of the MS-type thinking that emerges from Lynch's paper is his statement that "evolution is a population-level feature" (p. 8603). Well, no. Multilevel selection theory (Okasha 2006) is now a mainstay of current discussions on evolutionary mechanisms, and we have ample empirical evidence that evolution occurs at multiple levels, from intragenomically to at least the species level. But of course if one begins with the axiomatic definition of evolution as a change in allelic frequencies dictated by the population genetic perspective, the rest simply does not enter the picture.

In general, Lynch seems to wish to deny the possibility that evolvability may evolve by natural selection. But this is of course only part of the reason why evolvability is so interesting. The fact remains that evolvability, complexity, modularity, and robustness are not just "buzzwords" invoked by biologists who "abhor all things mathematical" (p. 8603). Besides the undeniable fact that theory in science, and particularly in biology, is broader than a narrow mathematical conception of it (just think of the works of Darwin or of most of the authors of the MS), it is simply not the case that scientists writing about the four "buzzwords" are not mathematically savvy, as even a cursory glance at their works will surely establish. Evolvability is interesting because it is a concept that simply did not exist within the framework of the MS, and which cannot be subsumed in the simple population genetic terms upon which the MS was established.

The Evolution of Evolutionary Theory

Discussions on the evolving structure of evolutionary theory have been tense since at least Eldredge and Gould's (1972) theory of punctuated equilibria and the more than two-decades-long diatribe that followed it. Even major outlets such as *Nature* (Whitfield 2008) and *Science* (Pennisi 2008a, b) have recently dedicated full-length features to the sometimes acrimonious tone of ongoing discussions between what increasingly look like defenders of an MS-informed "orthodoxy" and proponents of a more pluralistic view of evolutionary processes. Lynch himself is conscious of this aspect of the debate, writing "this tone of dissent is not meant to be disrespectful" (p. 8603); and yet, preceding that very sentence we read: "this stance is no different from the intelligent-design philosophy of invoking unknown mechanisms to explain biodiversity" (p. 8603). One would think that accusing fellow biologists of reasoning like creationists is hardly going to move the discussion onto more polite and productive territory.

Nonetheless, and despite the emotionally charged atmosphere, there is a general sense shared by both sides that evolutionary biology is in fact approaching an important junction. Far from providing solace to creationists and their allies, who keep shouting that new developments in the field are hailing "the end of Darwinism," the debate over whether and how to produce an ES is a serious one, and it is bound to positively affect the field regardless of the outcome.

I have argued elsewhere (Pigliucci 2007) that we are not about to witness a "paradigm shift" in evolutionary biology, contrary to the sometimes hyped rhetoric of some proponents of an ES. Rather, following Gould's (2002) treatment of the structure of evolutionary theory, if the current efforts succeed, we will expand the scope and explanatory tools available to evolutionary biologists. "Darwinism," in the broad sense of a historical-mechanistic view of the diversity of life on earth that includes common descent and natural selection, is here to stay. This is also why an increasing number of authors refer to the new ideas as a "synthesis," in direct analogy with the MS of the early part of the 20th century. The MS most certainly did not reject the core of Darwin's ideas (though it did prune that intellectual tree here and there), and was a synthesis because it organically brought together new and old disciplines, showing how new empirical discoveries and ideas fit with the basic Darwinian edifice.

What is being proposed by supporters of an Extended Synthesis is a novel iteration of the same process, to evolve

evolutionary theory beyond its second major incarnation by once again retaining much of the previous core while adding major intellectual pillars built on the discoveries and concepts arising from new areas of inquiry within biology. As in the case of the MS, the ES will probably require decades of research and scholarship. Whatever shape evolutionary theory takes in the near future, however, I am quite sure that we will need a lot more than just population genetic theory to make sense of evolution.

Acknowledgments

I wish to thank Gerd Müller for insightful discussions on the structure of an Extended Synthesis, and Günter Wagner for bringing population genetic-based work on evolvability to my attention. Mark Jonas contributed comments to an earlier version of this manuscript.

References

Akashi H (1995) Inferring weak selection from patterns of polymorphism and divergence at "silent" sites in Drosophila DNA. Genetics 139: 1067–1076.

Alberch P (1991) From genes to phenotype: Dynamical systems and evolvability. Genetica 84: 5–11.

Arnold SJ (1992) Constraints on phenotypic evolution. American Naturalist 140: S85–S107.

Atchley WR, Hall BK (1991) A model for development and evolution of complex morphological structures. Biological Reviews 66: 101–157.

Barton N, Partridge L (2000) Limits to natural selection. BioEssays 22: 1075–1084.

Bell G (2005) The evolution of evolution. Heredity 94: 1–2.

Brookfield JFY (2001) The evolvability enigma. Current Biology 11: R106–R108.

Carroll SB (2008) Evo-devo and an expanding evolutionary synthesis: A genetic theory of morphological evolution. Cell 134: 25–36.

Cleland CE (2002) Methodological and epistemic differences between historical science and experimental science. Philosophy of Science 69: 474–496.

Cohen J (1994) The earth is round ($p < 0.05$). American Psychologist 49: 997–1003.

Colegrave N, Collins S (2008) Experimental evolution: Experimental evolution and evolvability. Heredity 100: 464–470.

Dennett DC (1995) Darwin's Dangerous Idea: Evolution and the Meanings of Life. New York: Simon and Schuster.

Dobzhansky T (1973) Nothing in biology makes sense except in the light of evolution. American Biology Teacher 35: 125–129.

Dupré J (1993) The Disorder of Things: Metaphysical Foundations of the Disunity of Science. Cambridge, MA: Harvard University Press.

Earl DJ, Deem MW (2004) Evolvability is a selectable trait. Proceedings of the National Academy of Sciences USA 101: 11531–11536.

Eldredge N, Gould SJ (1972) Punctuated equilibria: An alternative to phyletic gradualism. In: Models in Paleobiology (Schopf TJM, ed), 82–115. San Francisco: Freeman, Cooper.

Eroukhmanoff F, Svensson EI (2007) Phenotypic integration and conserved covariance structure in calopterygid damselflies. Journal of Evolutionary Biology 21: 514–526.

Futuyma D (2006) Evolutionary Biology. Sunderland, MA: Sinauer.

Gould SJ (1980) The evolutionary biology of constraint. Daedalus 109: 39–52.

Gould SJ (2002) The Structure of Evolutionary Theory. Cambridge, MA: Harvard University Press.

Gould SJ, Lewontin RC (1979) The spandrels of San Marco and the Panglossian paradigm: A critique of the adaptationist programme. Proceedings of the Royal Society of London B 205: 581–598.

Haldane JBS (1964) A defense of beanbag genetics. Perspectives in Biology and Medicine 7: 343–359.

Hansen TF (2006) The evolution of genetic architecture. Annual Review of Ecology and Systematics 37: 123–157.

Hey J (1999) The neutralist, the fly and the selectionist. Trends in Ecology and Evolution 14: 35–37.

Hoelzer GA, Smith E, Pepper JW (2006) On the logical relationship between natural selection and self-organization. Journal of Evolutionary Biology 19: 1785–1794.

Huberman BA, Hogg T (1986) Complexity and adaptation. Physica 22D: 376–384.

Jacob F (1977) Evolution and tinkering. Science 196: 1161–1166.

Kauffman SA (1993) The Origins of Order. New York: Oxford University Press.

Kimura M (1983) The Neutral Theory of Molecular Evolution. Cambridge: Cambridge University Press.

Kirschner MW, Gerhart JC (2005) The Plausibility of Life: Resolving Darwin's Dilemma. New Haven, CT: Yale University Press.

Koufopanou V, Bell G (1991) Developmental mutants of Volvox: Does mutation recreate the patterns of phylogenetic diversity? Evolution 45: 1806–1822.

Lenski RE, Barrick JE, Ofria C (2006) Balancing robustness and evolvability. PLoS Biology 4: 2190–2192.

Lloyd EA (2005) Why the gene will not return. Philosophy of Science 72: 287–310.

Love AC (2003) Evolutionary morphology, innovation, and the synthesis of evolutionary and developmental biology. Biology and Philosophy 18: 309–345.

Lynch M (2007a) The frailty of adaptive hypotheses for the origins of organismal complexity. Proceedings of the National Academy of Sciences USA 104: 8597–8604.

Lynch M (2007b) The Origins of Genome Architecture. Sunderland, MA: Sinauer.

Maynard-Smith J, Burian R, Kauffman S, Alberch P, Campbell J, Goodwin B, Lande R, Raup D, Wolpert L (1985) Developmental constraints and evolution. Quarterly Review of Biology 60: 265–287.

Mayr E (1963) Animal Species and Evolution. Cambridge, MA: Harvard University Press.

McGhee G (2007) The Geometry of Evolution: Adaptive Landscapes and Theoretical Morphospaces. Cambridge: Cambridge University Press.

McShea DW (1994) Mechanisms of large-scale evolutionary trends. Evolution 48: 1747–1763.

Meyer A (1987) Phenotypic plasticity and heterochrony in *Cichlasoma managuense* (Pisces, Cichlidae) and their implications for speciation in cichlid fishes. Evolution 41: 1357–1369.

Müller GB (2007) Evo-devo: Extending the evolutionary synthesis. Nature Reviews Genetics 8: 943–949.

Newman SA, Forgacs G, Müller GB (2006) Before programs: The physical origination of multicellular forms. International Journal of Developmental Biology 50: 289–299.

Okasha S (2006) Evolution and the Levels of Selection. Oxford: Oxford University Press.

Partridge L, Barton NH (2000) Evolving evolvability. Nature 407: 457–458.

Pennisi E (2008a) Deciphering the genetics of evolution. Science 321: 760–763.

Pennisi E (2008b) Modernizing the modern synthesis. Science 321: 196–197.

Perry DA (1995) Self-organizing systems across scales. Trends in Ecology and Evolution 10: 241–244.

Pigliucci M (2006) Genetic variance-covariance matrices: A critique of the evolutionary quantitative genetics research program. Biology and Philosophy 21: 1–23.

Pigliucci M (2007) Do we need an extended evolutionary synthesis? Evolution 61: 2743–2749.

Pigliucci M (2008) Is evolvability evolvable? Nature Reviews Genetics 9: 75–82.

Pigliucci M, Kaplan J (2000) The fall and rise of Dr. Pangloss: Adaptationism and the Spandrels paper 20 years later. Trends in Ecology and Evolution 15: 66–70.

Pigliucci M, Kaplan J (2006) Making Sense of Evolution: The Conceptual Foundations of Evolutionary Biology. Chicago: University of Chicago Press.

Pigliucci M, Müller GB, eds (in press) Evolution: The Extended Synthesis. Cambridge, MA: MIT Press.

Platnick NI, Rosen DE (1987) Popper and evolutionary novelties. History and Philosophy of Life Sciences 9: 5–16.

Provine WB (1971) The Origins of Theoretical Population Genetics. Chicago: Chicago University Press.

Raup DM, Gould SJ (1974) Stochastic simulation and evolution of morphology: Towards a nomothetic paleontology. Systematic Zoology 23: 305–322.

Renaud S, Auffray J-C, Michaux J (2006) Conserved phenotypic variation patterns, evolution along lines of least resistance, and departure due to selection in fossil rodents. Evolution 60: 1701–1717.

Resnik D (1994) The rebirth of rational morphology: Process structuralism's philosophy of biology. Acta Biotheoretica 42: 1–14.

Robert JS (2004) Embryology, Epigenesis, and Evolution: Taking Development Seriously. Cambridge: Cambridge University Press.

Salazar-Ciudad I (2007) On the origins of morphological variation, canalization, robustness, and evolvability. Integrative and Comparative Biology 47: 390–400.

Schluter D (1996) Adaptive radiation along genetic lines of least resistance. Evolution 50: 1766–1774.

Schwenk K, Wagner GP (2004) The relativism of constraints on phenotypic evolution. In: The Evolutionary Biology of Complex Phenotypes (Pigliucci M, Preston K, eds), 309–408. New York: Oxford University Press.

Shepard KA, Purugganan MD (2003) Molecular population genetics of the Arabidopsis CLAVATA2 region: The genomic scale of variation and selection in a selfing species. Genetics 163: 1083–1095.

Sniegowski PD, Gerrish PJ, Lenski RE (1997) Evolution of high mutation rates in experimental populations of *E. coli.* Nature 387: 703–705.

Sober E (2008) Evidence and Evolution: The Logic Behind the Science. Cambridge: Cambridge University Press.

Stephens PA, Buskirk SW, del Rio CM (2006) Inference in ecology and evolution. Trends in Ecology and Evolution 22: 192–197.

Stevens L, Goodnight CJ, Kalisz S (1995) Multilevel selection in natural populations of *Impatiens capensis*. American Naturalist 145: 513–526.

Surrey T, Nedelec F, Leibler S, Karsenti E (2001) Physical properties determining self-organization of motors and microtubules. Science 292: 1167–1171.

Wagner GP, Bürger R (1985) On the evolution of dominance modifiers II: A non-equilibrium approach to the evolution of genetic systems. Journal of Theoretical Biology 113: 475–500.

West-Eberhard MJ (2003) Developmental Plasticity and Evolution. Oxford: Oxford University Press.

Whitfield J (2008) Postmodern evolution? Nature 455: 281–284.

Wilkins AS (2002) The Evolution of Developmental Pathways. Sunderland, MA: Sinauer.

Wimsatt W (1980) Reductionistic research strategies and their biases in the units of selection controversy. In: Scientific Discovery: Case Studies (Nickles T, ed), 213–259. Dordrecht: Reidel.