DO WE NEED AN EXTENDED EVOLUTIONARY SYNTHESIS?

Massimo Pigliucci

Department of Ecology & Evolution, Stony Brook University, 650 Life Science Bldg., Stony Brook New York 11794

E-mail: pigliucci@genotypebyenvironment.org

The Modern Synthesis (MS) is the current paradigm in evolutionary biology. It was actually built by expanding on the conceptual foundations laid out by its predecessors, Darwinism and neo-Darwinism. For sometime now there has been talk of a new Extended Evolutionary Synthesis (EES), and this article begins to outline why we may need such an extension, and how it may come about. As philosopher Karl Popper has noticed, the current evolutionary theory is a theory of genes, and we still lack a theory of forms. The field began, in fact, as a theory of forms in Darwin's days, and the major goal that an EES will aim for is a unification of our theories of genes and of forms. This may be achieved through an organic grafting of novel concepts onto the foundational structure of the MS, particularly evolvability, phenotypic plasticity, epigenetic inheritance, complexity theory, and the theory of evolution in highly dimensional adaptive landscapes.

The Modern Synthesis (MS) is the current paradigm in evolutionary biology (Mayr 1993). A paradigm is essentially a conceptual framework, a set of ideas, methods and explanatory principles, that allows scientists to conduct what Thomas Kuhn (1970) called "puzzle solving" within "normal science." According to Kuhn's model of the history of science, paradigms work well for long periods of conceptual stability, but from time to time enter into a crisis generated by the discovery of new phenomena that are not easily explainable within the current paradigm. These crises are resolved by eventually adopting a new framework that explains both the facts already explained by the previous paradigm, as well as the anomalies that led to the crisis in the first place. Classical examples of paradigm shifts are the move from Ptolemaic to Copernican astronomy, and the one from Newtonian to relativistic physics.

One can reasonably argue, however, that evolutionary biology has never actually gone through a paradigm shift, at least not since Darwin (1859). Rather, evolutionary biologists have responded to various crises by augmenting the preexisting framework, building on what was already there, without overthrowing any of the previous foundations (Gould 2002). Yet, many (e.g., Rollo 1995; Schlichting and Pigliucci 1998; Muller and Newman 2003; West-Eberhard 2003; Jablonka and Lamb 2005; Pigliucci and Kaplan 2006) insist that—paradigm shift or not—the MS, whose conceptual framework goes back to the 1940s (not only pre-genomics, but also pre-molecular revolution), is in need of some significant extension.

In this essay I will provide a brief conceptual recapitulation of the history of evolutionary theory, with the aim of tracing the broad questions posed by evolutionary biologists at different points in time during the past 150 years, as well as the sort of approaches that have been used to answer such questions. I will then argue that evolutionary theory has shifted from a theory of form to a theory of genes, and that it is now in need again of a comprehensive and updated theory of form. I will conclude with a brief discussion of what I think are some promising conceptual pillars for a new Extended Evolutionary Synthesis (EES), which may come to fruition over the next decade or so. Obviously, this is meant to be a stimulus to much needed discussion, not a full-fledged outline of a new research program. That will emerge over the next few

years, if my understanding of where we are now is not entirely mistaken.

A Brief Conceptual History of Evolutionary Biology

When Darwin was writing the works that would become the foundations of evolutionary biology, there were two major questions open to the increasing number of scientists and natural philosophers who were slowly distancing themselves from religiously inspired ideas such as the fixity of species and intelligent design: first, how do we explain the history and diversity of life on earth? Second, how do we account for the obvious match between form and function in biological organisms? As is well known, Darwin provided answers inspired by Lyell's (1830) principle of uniformitarianism and Maltus' (1798) observations on the relationship between population growth and available resources. Those answers represent the first two conceptual pillars of modern evolutionary theory: descent with modification is the pattern that accounts for life's history and diversity, whereas natural selection is the mechanism that explains the form–function dilemma, the clear sense that complex structures like the vertebrate eye are "for" something, even though they were not intelligently designed.

The relevant point for our discussion is that the first modern version of evolutionary theory (I am not including here its La marck ian predecessor, nor other prescientific ideas such as those of Erasmus Darwin or of Robert Chambers, the author of *Vestiges of the Natural History of Creation*), began as a theory of form. Of course it could have hardly been otherwise, since genetics had not been established as a field of inquiry yet, although Mendel published his paper in 1866 (Darwin did not read it, although he had a book that referenced it). The problem of heredity, however, which bothered Darwin and brought him to alternately endorse elements of Lamarckism and to propose his own inviable theory of blended inheritance, soon came to the forefront of evolutionary biology, and it has remained there ever since.

Indeed, the first serious challenge faced by Darwinism centered precisely on whether to retain some sort of Lamarckian element in its theory of heredity, as Darwin, Huxley, and Romanes had proposed at different times, or to completely block the Lamarckian move, as suggested by Wallace and Weismann. It was the latter that conclusively carried the day with his well-known doctrine of the separation of somatic and germ lines, which precluded any pathway allowing the inheritance of acquired characteristics and that foreshadowed what much later became known as the "central dogma" of molecular biology (as odd as the use of the word "dogma" is in a scientific context). The shift away from Lamarckism did not go smoothly, and in fact Romanes coined the term "neo-Darwinism" to ridicule the new doctrine (as Ernst Mayr often reminded people, the term neo-Darwinism should *not*

be used to refer to the MS, because they were conceptually distinct and took place decades apart from each other).

Although Weismann had dispatched with Lamarckism (albeit on the basis of a concept that actually applies to a minority of living organisms), the problem of heredity remained, and surfaced dramatically at the turn of the 20th century, with the rediscovery of Mendel's work. The issue now was how to reconcile a theory of gradual evolution with the saltationism that many authors saw emerging from research in the new discipline of genetics. Camps again formed, with Bateson arguing for saltationism, whereas people like Pearson and Weldon supported the so-called "biometrician" school that sought a statistical answer to the conceptualization of the genetic basis of quantitative characters. The answer came from arguably one of the most important papers ever written in evolutionary biology, Fisher's (1918) "The correlation between relatives on the supposition of Mendelian inheritance," in which he convincingly showed how Mendelism could be reconciled with gradualism, thereby ushering in the era of what we now call quantitative genetics.

The 1930s and 1940s then saw the development of Fisher's, Haldane's, and Wright's ideas on population genetics that eventually crystallized in the MS. Although several authors and books are usually cited in connection with the MS, it seems to me that the three major contributions outside of theoretical population genetics were by Dobzhansky, Mayr, and Simpson. Dobzhansky's (1937) book, and of course his famous "genetics of natural populations" series of papers (Provine 1981), translated the new ideas of population genetics into empirical practice with, among its major achievements, the demonstration of the existence of ample genetic variation in nature. Mayr's (1942) book brought systematics in line with the new ideas, particularly elaborating on the shift from an essentialist to a population-type thinking regarding species, and of course with the so-called "biological" species concept (a term that still stands as a pinnacle of scientific rhetoric, with its unstated implication that any other species concept is not biological). Finally, Simpson (1944) argued that the tempo and mode of evolution as understood in population genetics were compatible with those that paleontologists are concerned with at the geological scale, thereby eliminating any controversial distinction between "micro" and "macro" evolution with its saltationary overtones (Goldschmidt 1940).

Many in the field seem to feel that from the MS on it has been and will largely be business as usual, that is, the MS provides *the* framework for current and future evolutionary biology, with no need to revisit the fundamentals. One of the cofounders of the MS said it explicitly (Stebbins and Ayala 1981), in response to one of the early challenges, the theory of punctuated equilibria (Eldredge and Gould 1972). More recently, Charlesworth (1996), speaking about evolutionary genetics (which, conceptually, by and large *is* the MS), wrote: "most evolutionary geneticists would agree that

the major problems of the field have been solved. . . . We will never again come up with concepts as fundamental as those formulated by the "founding fathers" of population genetics . . . or do experiments as path-breaking as Dobzhansky's demonstration of natural selection acting on polymorphic chromosome inversions." Well, perhaps, but some of us are not ready for retirement just yet.

Is There Something Missing from the Modern Synthesis?

Philosopher Karl Popper once said that "the [MS] is strictly a theory of *genes*, yet the phenomenon that has to be explained is that of the transmutation of *form*" (Platnick and Rosen 1987). He may have exaggerated slightly, after all, we actually need *both* a theory of genes (and other hereditary factors) and a theory of form. Nonetheless, in light of this distinction between theories of genes and theories of form, I want to suggest that there are at least four major elements missing from the MS, which I will discuss briefly. The first is the one that most people have been talking about for sometime now, including some of the very architects of the MS (Mayr 1993): development (although Mayr rather peculiarly argued that it was developmental biologists who "simply did not want to join"). It is an incontestable historical fact that embryology and developmental biology—highly sophisticated disciplines with a long history of their own by the time of the MS—have simply been left in the cold. No major developmental biologist contributed to the MS, despite early forceful endorsements of Darwinism by leading figures such as Haeckel, although, of course, his "ontogeny recapitulates phylogeny" maxim turned out to only occasionally be correct, not to mention that he fudged his results to better fit his expectations. We had to wait until Gould's (1977) *Ontogeny and Phylogeny* for a first serious attempt at bringing developmental biology within the fold of evolutionary theory. Then, of course, the 1990s saw the onset of the evo-devo (evolution of development) research program (Love 2003), which is still in full swing and has already delivered some stunning discoveries—beginning with the phylogenetic conservation of *Hox*-type genes involved in pattern formation.

What, then, is the problem? Without trivializing the great successes of evo-devo, it is hard to escape the feeling that we are making significant progress in understanding relatively circumscribed problems in the origin of form (one of the best examples is the elegant work on the evolution of eyespots in butterflies: e.g., Beldade and Brakefield 2002), and that advances are being made more at the interface between population genetics and developmental biology than in the broader field of evo-devo. For instance, baffling evolutionary novelties like the turtle carapace remain almost unscathed mysteries, with some speculation concerning their origin, but little in the way of detailed scenarios and solid empirical evidence (Rieppel 2001; Cebra-Thomas et al.

2005). In some sense, this is precisely the same sort of problem that bothered Goldschmidt so much during the shaping of the MS, and although his proposed solutions (genomic mutations and hopeful monsters) are not tenable, the uneasy feeling that we are not yet tackling directly the big questions remains. Optimists may suggest that evo-devo is just at the beginning, and that given sufficient time and resources it will succeed in the most ambitious aspects of its intellectual program. Perhaps, but the problem is that so far we are mostly seeing clever and successful applications of old conceptual tools (from population and evolutionary genetics) and new experimental ones (from the fallout of the molecular revolution). The two still do not add up to new conceptual advances toward a convincing theory of form (Muller and Newman 2005).

The second missing piece seems hardly to be noticed, although some authors have recently began to pointing it out by introducing the rather awkward term "eco-evo-devo," namely, ecology. Obviously, ecology was *implied* in the MS, but still today there is a cross-discipline distrust between ecologists and evolutionary biologists, and sometimes dichotomies are created that are rather counterproductive, such as the frequent talk of "ecological" versus evolutionary time scales. Considering that natural selection (which is the result of ecological factors) affects populations from one generation to the very next, it is hard to fathom what people might possibly mean by making the distinction between ecological and evolutionary time scales. Perhaps more importantly, ecological theory hardly features in evolutionary studies, except as a background condition. Consider the example of natural selection (Bell 1997): given that it has been a central pillar of evolutionary theory since Darwin, one would think that by now we should have a much better understanding of it than we do. Instead, many studies of selection tend to focus on a rather preliminary statistical assessment of trait-fitness covariances (Pigliucci and Kaplan 2006), and even that is often woefully inadequate by its own internal standards of replication and statistical power (Kingsolver et al. 2001). Studies of natural selection integrating ecology are hard to find, and we have almost no understanding of how ecology played in the evolution of phenotypic novelties or during major transitions in evolution (Maynard-Smith and Szathmary 1995).

The third lacuna of the MS is that it has nothing to tell us about the implications of the "-omics" revolution. True, one would not expect the original synthesis to be able to address directly the wealth of information emerging from genomics, proteomics, and the other new "−omics" sciences. Nonetheless, it is simply not convincing to look at the emerging emphasis on the properties of gene networks (as opposed to individual genes: Quayle and Bullock 2006), the amount of evidence suggesting that neutral mechanisms have played a major role in the evolution of genomes (Lynch 2007), or the increasingly compelling indications of heritable epigenetic effects (Rapp and Wendel 2005; Richards 2006) and simply state—with little further elaboration—that this is all

"compatible" with the MS. Few researchers would doubt compatibility, but does all of this truly amount only to minor details to tack on the existing conceptual framework? For instance, *pace* Dawkins, it is becoming increasingly untenable to hold a "gene-centric" view of the evolutionary process (especially considering that new discoveries in molecular biology keep questioning the very meaning of the term "gene"), and the classic textbook definition of evolution as a change in gene frequencies (Futuyma 1998)—which is a direct result of the MS' vision—simply does not begin to account for what evolution actually *is*.

Finally, there are several important biological phenomena that have either been ignored, dramatically downplayed, or were simply unknown at the time of the formulation of the MS. Three examples will suffice to make the point: phenotypic plasticity, the possibility of evolutionary capacitance, and epigenetic inheritance. Plasticity used to be dismissed as a nuisance, something that complicated evolutionary studies (Falconer 1952). Within the past two decades or so it has become a major player in the evolutionary arena, with several books, dozens of review articles, and countless empirical and theoretical papers devoted to the understanding of its impact on the evolutionary process (Pigliucci 2001; West-Eberhard 2003). The interplay between plasticity and selection, for instance, is complex, as plasticity is itself an evolvable property of the genetic-developmental system of living organisms (i.e., it can be selected for and become adaptive), whereas at other times it may buffer the action of selection, leading to the build-up of genetic redundancy (Lenski et al. 2006). Plasticity and its related opposite, developmental canalization (Waddington 1942; Flatt 2005), yield the possibility of evolutionary capacitance (Rutherford and Lindquist 1998; Masel 2005), the accumulation of hidden genetic variation that may be unleashed under conditions of stress, perhaps presenting an alternative path for the origin of new phenotypes. Finally, the evidence is now becoming clear for the existence of a whole additional layer of inheritance at the epigenetic level (Jablonka and Lamb 2005), which despite the quasi-Lamarckian memories it brings to mind, is not a contradiction but a potentially exceedingly complex augmentation of the classic view of genetic inheritance, particularly as genotype and epigenotype interact to produce a bewildering array of short- and long-term heritable combinations.

The Forthcoming Extended Evolutionary Synthesis

Assuming that the MS is, in fact, in need of some nontrivial expansion, as I have argued so far, what sort of shape might such an effort take? Here opinions vary significantly among different authors, with perhaps the most massive effort so far (literally, given the size of the volume) being the one put forth by Gould (2002) at the end of his career, although several others have contributed

bits and pieces (e.g., Rollo 1995; Schlichting and Pigliucci 1998; Muller and Newman 2003; West-Eberhard 2003; Jablonka and Lam 2005; Pigliucci and Kaplan 2006). Despite this variety of opinions, which the history of science teaches us often accompanies shifts of frameworks (Kuhn 1970), there are some recurring themes that will almost certainly constitute at least part of the augmented conceptual edifice of evolutionary theory. I will briefly discuss five such recurring ideas, a couple of which have already been mentioned.

Let me start with the concept of evolvability (Wagner and Altenberg 1996; Carroll 2002; Earl and Deem 2004; Hansen 2006; Landry et al. 2007). This is an idea that did not appear in the MS at all, particularly in the form of how the propensity of living beings to evolve may itself turn out to be a result of evolution by natural selection or other means. There is at this point little question that evolvability does evolve, although the field is plagued by a variety of hurdles, not the least of which that there seems to be a variety of (related but not identical) meanings floating around for the word "evolvability." Although the simplest conceptualization of the term has been operationalized using classic quantitative genetics theory (Jones et al. 2007), the latter is restricted to statistical, as opposed to causal, analyses, and cannot therefore but scratch the surface of a variety of biologically interesting questions (Pigliucci and Kaplan 2006). In this context, one of the most hotly contested claims is that evolvability may be the result of natural selection itself, leading for instance to the evolution of the above-mentioned "capacitance" systems that accumulate genetic variation and release it under stressful environmental conditions (Rutherford and Lindquist 1998; Masel 2005). Regardless, evolvability depends on biological phenomena that the MS simply did not consider, such as the degree of modularity of developmental systems (Wagner and Altenberg 1996; Callebaut and Rasskin-Gutman 2005), as well as their "robustness" to perturbation (A. Wagner 2005; Lenski et al. 2006). Robustness, capacitance, modularity, and evolvability are sophisticated new concepts that are solidly grounded in empirical data, and that surely represent at least one pathway to reintroducing development into evolutionary biology. These are rich areas of theoretical and experimental research, and there is not going to be an Extended Synthesis that will not place them at the forefront of its framework.

The second major area of innovation comes from the field of phenotypic plasticity, as discussed earlier (Pigliucci 2001; West-Eberhard 2003). Today we simply can no longer talk about basic concepts like, for instance heritability, without acknowledging its dependence on the sort of genotype–environment interactions that are best summarized by adopting a reaction norm perspective. Genetic variation for plasticity exists in virtually every species in which it has been looked for, and our understanding of the phenomenon is such that we now appreciate the fact that it can both be the result of natural selection as well as influence the effectiveness

of selection. The most controversial implications of phenotypic plasticity have been brought forth by West-Eberhard (2003) with her concept of phenotypic and genetic accommodation, a modern elaboration of ideas going back to Baldwin (1896), Schmalhausen (1949) and Waddington (1961)-–all authors deftly ignored during the MS. If West-Eberhard is correct, the inherent plasticity of most developmental systems may in some circumstances lead the way toward evolutionary change, preceding genetic changes in a population. The latter changes would then in some sense fix and perhaps fine tune what was initially a (pre)adaptive phenotypic response to a change in the environment. Let us be clear once again that there is no Lamarckism implied here, as Baldwin, Schmalhausen, and Waddington had already made painfully clear in their writings over the span of almost a century. But the role of phenotypic plasticity, when taken seriously, shifts the action away from a gene-centered view of evolution, and toward a more complex integration of genetics, developmental biology and, of all things, ecology.

Third, we have the very recent explosion of interest in epigenetics mentioned earlier (Newman and Muller 2001; Jablonka and Lamb 2005; Rapp and Wendel 2005; Richards 2006). Although molecular biologists have been aware of and interested in epigenetic effects for quite sometime, the phenomenon has surfaced on the radar screen of evolutionary biologists only recently, because we now have convincing evidence that at least some epigenetic effects are heritable. It is not at all clear, at the moment, how widespread heritable epigenetic effects actually are, how long they may last (although indications vary from a few generations to thousands of years in some cases of hybrid speciation: Rapp and Wendel 2005), and how they interact with "classic" genetic variation. These are, again, serious empirical and theoretical issues, that need to be addressed. The potential of epigenetics varies from simply adding an unusual mechanism of inheritance to the staggering possibility that we may need to reexamine, for instance, all our QTL-mapping studies because the genomic regions identified in such surveys may turn out to be associated with epigenes, not with standard genes. Because we know that epigenetic effects alter gene regulation, and in turn genes affect the pattern of epigenetic markers (e.g., methylation), we may face a bewildering increase in complexity of the entire inheritance system, something that may provide us with interesting new answers to old questions related to the amount and type of heritable variation in natural populations. Again, a psychological stumbling block may be that all of this smells terribly of Lamarckism, but even a cursory survey of the epigenetics literature should lay such concerns to rest, and evolutionary biologists should not fall into the trap of rejecting a priori the possibility of a broad expansion of our understanding of what counts as "genetic."

A fourth component of the Extended Synthesis seems likely to focus on a family of research projects often referred to as "complexity theory" and its more recent elaboration into so-called systems biology (Kauffman 1993; Perry 1995; Sneppen et al. 1995; Hoelzer et al. 2006). Here the challenge is leveled at one of the central tenets of evolutionary theory that has remained unchanged since the original version of Darwin's ideas: natural selection may not be the only organizing principle available to explain the complexity of biological systems. Many biologists find complexity theory too general, lacking in the sort of sufficiently specific hypotheses that can easily generate empirical research programs, and this has in fact been a (possibly inevitable) characteristic of that line of inquiry. Because the theory aims at capturing how *any* complex system made of a certain number of interacting parts behaves, it should not be surprising that the emphasis has been on high-level analogies rather than on reductionist predictions. Nonetheless, there is little doubt that certain kinds of complex physical systems—of which biological ones are an obvious example—do show a tendency for self-organization and spontaneously complex behavior, and surely there is no mysticism implied by notions such as criticality and the edge of chaos. Should these ideas in fact be organically incorporated in an EES, biologists would have not only additional sources of heritable variation, but also a new organizing principle to aid in the quest to explain the evolution of biological form. Natural selection, of course, would not thereby be denied, or even relegated to a secondary role, but would interact with self-organization to yield a more powerful theoretical architecture to finally merge the two major tendencies in the history of evolutionary biology: the pursuit of a theory of genes (or, more broadly, inheritance), and that of a theory of form.

The fifth (and not necessarily last) tassel in the emerging puzzle I have been trying to sketch out will have to be a reconsideration of the whole business of evolution on adaptive landscapes (Wright 1932; Gavrilets 1997; Pigliucci and Kaplan 2006). Originally, Wright introduced the metaphor as a visual aid to his mathematical treatment of evolutionary population biology (after the advice of his mentor, who thought that most biologists simply would not be able to follow the math). Metaphors, however, are often fraught with hidden problems, which may take time—in this case several decades—to sort out. Perhaps the most pernicious assumption pervading the literature on adaptive landscapes has been that high-dimensional landscapes will behave pretty much like the low-dimensional variety that is common in papers and textbooks (on the only ground that it can be visualized by our limited brains). Everybody knew that realistic landscapes are high dimensional, but few took seriously the possibility that this may imply radically different dynamics at work. Recent research carried out largely by Sergey Gavrilets (1997, 1999) has convincingly shown that high-dimensional adaptive landscapes behave in wholly different and hitherto unsuspected manners, including the presence of large neutral "areas" and of "extra-dimensional bypasses" that potentially dissolve the famous problem of "peak shift" that has plagued

evolutionary biologists for decades. When Gavrilets' work is coupled with Kauffman's treatment of evolution on ragged landscapes (Kauffman and Levin 1987), as well as with recent empirical studies on the evolvability of real biological functions (Bloom et al, 2006; Landry et al. 2007), we glimpse the outline of a formidable tool to conjoin the "bases of heritability" and the "theory of form" programs that have been decoupled ever since Darwin.

No Paradigm Shift

Let me again be clear on a fundamental point underlying this whole discussion: one can reasonably argue that none of this *contradicts* any tenet of the MS, although it seems to me at least reasonable to concede that the new concepts and empirical findings I have briefly outlined above may eventually force a shift of emphasis away from the population genetic-centered view of evolution that characterizes the MS. On the other hand, to attempt to go further and state that there is not much new here and that all of this is already part of the MS, implicitly or not, would be intellectually disingenuous and historically inaccurate.

What I think will happen over the next several years is a process analogous to the MS itself: not a paradigm shift a la Kuhn (1970), but another series of complex developments that build on its three major predecessors: Darwinism, neo-Darwinism, and the MS itself. This is not the place for a philosophical analysis of whether paradigm shifts ever happen, even in astronomy and physics—Kuhn's original sources for his examples. Nevertheless, I argue that biology has, in fact, never undergone a true paradigm shift, and very likely never will. If one really wishes to identify anything in biology equivalent to the move from the Ptolemaic to the Copernican system, then one has to go back in time before Darwin: we have to reach as far back as the early 19th century transformation from a natural theological to a natural philosophical understanding of the history and diversity of life, to which Darwin greatly contributed but that he did not initiate, and consider the earlier evolutionary works of Lamarck, Chambers, and Erasmus Darwin. Perhaps truly incommensurable paradigm shifts only happen when a proto-science turns into a mature science, as astronomy did during the 16th and early 17th centuries (Copernicus and Galileo), physics during the 17th and 18th centuries (Galileo and Newton), and both biology and geology during the 19th century (Darwin and Lyell). Once a science is established, conceptual frameworks tend to expand, more than being replaced, and even when replacement can be argued for (as in the transition from Newtonian to relativistic mechanics at the onset of the 20th century), the new model is not incommensurable with the older, as the latter can be interpreted as a limit case or approximation of the new and broader one.

Be that as it may, the proof for the EES is in the pudding: it is up to those who advocate a significant expansion of theoretical biology (in the broader sense of conceptual understanding of the discipline's foundations) to show tangible progress. It would be a shame, however, to curtail or dismiss the discussion in its infancy. Evolutionary biologists, whether they advocate the MS or the EES, have a lot of work to do to make sense of a rapidly growing amount of findings in molecular, developmental, and organismal biology. Instead of looking forward to retirement, we should appreciate what a truly exciting time is awaiting us all.

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