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The *Origin* at 150: is a new evolutionary synthesis in sight?

Eugene V. Koonin
National Center for Biotechnology Information, National Library of Medicine, National Institutes of Health, Bethesda MD, USA

Abstract

The 200th anniversary of Darwin and the 150th jubilee of the *Origin of Species* prompt a new look at evolutionary biology. The 1959 *Origin* centennial was marked by the consolidation of the Modern Synthesis. The edifice of the Modern Synthesis has crumbled, apparently, beyond repair. The hallmark of the Darwinian discourse of 2009 is the plurality of evolutionary processes and patterns. Nevertheless, glimpses of a new synthesis might be discernible in emerging universals of evolution.

In 2009, evolutionary biologists and all scientists that are in one way or another involved in evolution research are extremely busy celebrating great anniversaries: Darwin's 200th birthday, 150 years since the publication of *On the Origin of Species* 1, and 200 years of Jean-Baptiste Lamarck's early evolutionary synthesis *Philosophie Zoologique* 2.

Numerous scientific meetings dedicated to Darwin, Darwinism and evolutionary biology were convened in 2009, one of the most prominent obviously being the 74th Cold spring Harbor Symposium on Quantitative Biology, aptly titled 'Evolution: the Molecular Landscape' and another one certainly worth a mention, the Society for Molecular Biology and Evolution annual meeting in Iowa City named 'Darwin to the Next Generation'. And, of course, these and other meetings dedicated to Darwin are complemented by plenty of special 'Darwinian' journal issues and stand-alone articles.

One could perhaps debate the merits and excesses of such celebratory activities but Darwin jubilees have been special in the past. Most importantly, the 100th anniversary of the *Origin* was marked by the final consolidation of the Modern Synthesis of evolutionary biology, so this year the Modern Synthesis (neo-Darwinism) is also celebrating its 50th anniversary [3, 4].

Therefore, this year is perfect to ask some crucial questions: how has evolutionary biology changed in the 50 years since the 'hardening' of the Modern Synthesis? Is it still a viable conceptual framework for evolutionary thinking and research? And, if not, is a new ('post-modern') synthesis in sight?

The *Origin* centennial celebration came at the dramatic time when biology was undergoing its molecular transformation. Since then, the landscape of evolutionary biology (borrowing the phrase from the title of the 2009 Cold Spring Harbor Symposium) has changed completely owing to three distinct and non-contemporaneous but interlocked revolutions: molecular, microbiological and genomic. The molecular revolution came first and culminated, on the one hand, in the neutral theory which asserts that the majority of the mutations that are fixed during

koonin@ncbi.nlm.nih.gov.

evolution are neutral and, accordingly, the purifying selection is more common than positive selection [5], and on the other hand, in the grand molecular tree derived from rRNA comparison [6]. The microbiological revolution expanded the domain of evolutionary biology into the world of prokaryotes [7]: all the concepts of both Darwin and the architects of the Modern Synthesis applied only to multicellular eukaryotes, primarily, animals (although Darwin did perform some research on microbes, mostly, unbeknownst to microbiologists[8]). In a way, the addition of prokaryotes to the mold of evolutionary biology came as a triumph because the rRNA tree encompassed the entire scope of cellular life forms and, having revealed the three-domain assortment of organisms (bacteria–archaea–eukaryota), appeared to be the true Tree of Life [9]. However, there are also major problems with prokaryotes, which fundamentally differ from eukaryotes, in that they do not engage in regular sex but do exchange genes promiscuously, so species cannot be meaningfully defined[10], – and the concept of species was at the center of both the first, Darwinian, and the second, modern, syntheses of evolutionary biology. The third, most recent and, arguably, most momentous, genomic revolution, brought the results of the first two revolutions into a new context and made evolutionary biology 'a matter of facts' as it became possible to investigate evolutionary relationships between hundreds of complete genomes from all walks of life[11].

The biological universe seen through the lens of genomics is a far cry from the orderly, rather simple picture envisioned by Darwin and the creators of the Modern Synthesis. The biosphere is dominated, in terms of both physical abundance and genetic diversity, by 'primitive' life forms, prokaryotes and viruses. These ubiquitous organisms evolve in ways unimaginable and unforeseen in classical evolutionary biology. Above all, it is an extremely dynamic world where horizontal gene transfer (HGT) is not a rarity but the regular way of existence, and mobile genetic elements that are vehicles of HGT (viruses, plasmids, transposons and more) are ubiquitous[7, 12]. We now think of the entire world of prokaryotes as a single, huge network of interconnected gene pools, and the notion of the prokaryotic pangenome is definitely here to stay[13, 14]. Although HGT is partially curtailed in eukaryotes, especially, the multicellular plants and animals, multiple endosymbioses accompanied by massive gene transfer were key to the evolution and indeed the very origin of eukaryotes. Moreover, most eukaryotic genomes teem with mobile elements which make them no less dynamic than the prokaryotic pangenome. The discovery of the all-encompassing genomic mobility puts to rest the traditional concept of the Tree of Life that has to be replaced by a network of vertical and horizontal gene fluxes. It is important to note, however, that evolution of individual genes still can be represented with trees, and search for trends in the 'Forest of Life' comprised of these gene trees could still reveal order in the historic flow of genetic information[15].

The discovery of pervasive HGT and the overall dynamics of the genetic universe destroys not only the Tree of Life as we knew it but also another central tenet of the Modern Synthesis inherited from Darwin, gradualism. In a world dominated by HGT, gene duplication, gene loss, and such momentous events as endosymbiosis, the idea of evolution being driven primarily by infinitesimal heritable changes in the Darwinian tradition has become untenable.

Equally outdated is the (neo)Darwinian notion of the adaptive nature of evolution: clearly, genomes show very little if any signs of optimal design, and random drift constrained by purifying in all likelihood contributes (much) more to genome evolution than Darwinian selection [16, 17]. And, with pan-adaptationism, gone forever is the notion of evolutionary progress that undoubtedly is central to the traditional evolutionary thinking, even if this is not always made explicit.

The summary of the state of affairs on the 150th anniversary of the *Origin* is somewhat shocking: in the post-genomic era, all major tenets of the Modern Synthesis are, if not outright overturned, replaced by a new and incomparably more complex vision of the key aspects of evolution (Box 1). So, not to mince words, the Modern Synthesis is gone. What's next? The answer that seems to be suggested by the Darwinian discourse of 2009: a postmodern state not so far a postmodern synthesis. Above all, such a state is characterized by the pluralism of processes and patterns in evolution that defies any straightforward generalization [18] 19.

Are there any glimpses of a new synthesis on the horizon? At the distinct risk of overestimating the promise of the current advances, I will mention two candidates. The first one is the population-genetic theory of the evolution of genomic architecture according to which evolving complexity is a side product of non-adaptive evolutionary processes occurring in small populations where the constraints of purifying selection are weak [16]. The second area with a potential for major unification could be the study of universal patterns of evolution such as the distribution of evolutionary rates of orthologous genes which is nearly the same in organisms from bacteria to mammals [20] or the equally universal anticorrelation between the rate of evolution and the expression level of a gene [21]. The existence of these universals suggests that simple theory of the kind used in statistical physics might explain some crucial aspects of evolution.

Whether or not the directions mentioned above and others can be combined in a new evolutionary synthesis in the foreseeable future, is too early to tell. I will venture one confident prediction, though: those celebrating the 200th anniversary of the Origin will see a vastly different landscape of evolutionary biology.

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Table 1

The fate of the central tenets of (neo)Darwinism in the post-genomic era[a]

(neo)Darwinian principles	Post-genomic view
Random (undirected), heritable variation is the principal material for natural selection	**YES** but the relevant random changes are extremely diverse: - nucleotide substitution, insertion and deletion - duplication of genes, genome regions, and whole genomes - loss of genes and, generally, genetic material - HGT including massive gene flux after endosymbiosis - invasion and transposition of mobile selfish elements and recruitment of sequences from these elements Moreover, the wide spread of stress-induced mutagenesis and related phenomena suggests the possibility of quasi-Lamarckian variation (a part of Darwin's concept purged by the Modern Synthesis) [22]
Fixation of beneficial changes by natural selection is the main driving force of evolution that tends to generate increasingly complex adaptations; hence progress as a general trend in evolution	**NO**. Darwinian (positive) selection is important but is only one of several fundamental forces of evolution, and not necessarily the dominant one. Neutral processes constrained by purifying selection dominate evolution. Genomic complexity is not intrinsically adaptive and probably evolves as a 'genomic syndrome' in populations with small effective size and accordingly weak purifying selection. There is no consistent trend towards increasing complexity and no progress in evolution
Natural selection operates on 'infinitesimally small' variations, so evolution never makes leaps - the principle of gradualism	**NO**. Even duplication and HGT of single genes are not 'infinitesimally small' genomic changes let alone deletion or acquisition of larger regions, genome rearrangements, whole-genome duplication, and of course, endosymbiosis. Evolutionary (or even revolutionary) leaps are possible, especially, during population bottlenecks, and are crucial for major evolutionary transitions
Evolutionary processes were, largely, the same throughout the evolution of life – the principle of uniformitarianism borrowed by Darwin from geology	**YES and NO**. The principal factors of evolution, diverse as they are, probably, all were in operation through most of life's history. However, the earliest stages of evolution antedating the emergence of the three domains of cellular life should have involved processes distinct from 'normal' evolution. Furthermore, major transition in evolution, such as eukaryogenesis, occurred through unique events (e.g. endosymbiosis)
Species is a central unit of evolution, and speciation a key evolutionary process	**NO**. Species can be meaningfully defined only for organisms that engage in regular sex but not promiscuous HGT, ensuring reproductive isolation. In general, the species concept does not apply to prokaryotes and is of dubious validity for unicellular eukaryotes as well[10]
The entire evolution of life can be depicted as a single "big tree" that reflects the evolutionary relationships between organisms and species (species tree)	**NO…and YES**. The discovery of the key roles of HGT and mobile genetic elements in genome evolution deal a death knell to the traditional Tree of Life concept. Still, trees remain natural templates to represent evolution of individual genes and many intervals of evolution in groups of relatively close organisms[15]
All existing life forms descend from a single ancestral form, the Last Universal Common Ancestor (LUCA)	**YES**…but… Comparative genomics leaves no doubt of the common ancestry of all cellular life. However, there are strong indications that LUCA could have been quite different from modern cells[23]

[a]The table is based on the discussion in Ref. [11], with modifications and additions.