

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

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The 200th anniversary of Charles Darwin and the 150th jubilee of the *On the Origin of Species* could 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.

This year evolutionary biologists and all scientists involved in evolution research have been 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 have been convened in 2009, with one of the most prominent the 74th Cold Spring Harbor Symposium on Quantitative Biology, aptly titled 'Evolution: the Molecular Landscape'. Another meeting worthy of mentioning was 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 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, meaning this year the modern synthesis (or neo-Darwinism) is celebrating its 50th anniversary [3,4].

Therefore, this year is the perfect time 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 a 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 fixed during 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, unbeknown 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]. The concept of species was at the center of both the first (Darwinian) and 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' because 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 that make them no less dynamic than the prokaryotic

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; and -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 the 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, were all probably in operation throughout 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, a 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, ensuring reproductive isolation, but not promiscuous HGT. 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 the 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 would have been quite different from modern cells [23].

^aThe table is based on the discussion in [11], with modifications and additions.

pangenome. The discovery of the all-encompassing genomic mobility puts to rest the traditional concept of the tree of life; this has to be replaced by a network of vertical and horizontal gene fluxes. It is important to note, however, that the evolution of individual genes still can be represented with trees, and the search for trends in the 'forest of life' consisting 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, namely 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]. Moreover, with pan-adaptationism gone forever, so is the notion of evolutionary progress that is undoubtedly

central to 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 have been, if not outright overturned, replaced by a new and incomparably more complex vision of the key aspects of evolution (Table 1). So, not to mince words, the modern synthesis is gone. What comes next? The answer suggested by the Darwinian discourse of 2009 is 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 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.

It is too early to tell whether or not these directions and others can be combined into a new evolutionary synthesis in the foreseeable future. I will venture one confident prediction, though. Those celebrating the 200th anniversary of the *Origin* will see a vastly different landscape of evolutionary biology.

Acknowledgments

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Research Focus

Reading between the LINEs to see into the past

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Transposable elements (TEs) are an important source of genome diversity and play a crucial role in genome evolution. A recent study by Zhao *et al.* describes novel patterns of TE diversification in the genome of the extinct mammoth *Mammuthus primigenius*. Analysis of *Mammuthus* has provided a unique genome landscape, a pivotal species for understanding TEs and genome evolution and hints at the diversity we verge on discovering by expanding our taxonomic sampling among genomes. Strategies based on this work might also revolutionize investigations of the interface between TE dynamics and genome diversity.

Discovering TEs in the mammoth genome

TEs (Box 1) have had a substantial impact on eukaryotic genomes throughout history, and are responsible either

directly or indirectly for much of the genomic diversity we see today. Unsurprisingly, studies of TE impacting on human and non-human primate genomes are numerous and well developed. We know, for example, how the movement of TEs has influenced human disease [1], genome size [2–8] and the transcriptome [9–11]. But how well does our little corner of the genomic world reflect TE diversity and impact in a more general sense? The broader mammalian perspective is only now being investigated, and although we are starting to answer this question [12], many gaps in our knowledge remain.

Recently, Zhao *et al.* [13] applied next-generation sequencing (454) to address the question in a unique way – by investigating the TE amplification dynamics in the woolly mammoth (*Mammuthus primigenius*), a species that has been extinct for ~10 000 years. Using the massive amount of data available from the mammoth genome project, they determined likely TE content using an iterative

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