Article

New Ideas in Evolutionary Biology: From NDMS to EES

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The neo-Darwinian modern synthesis (NDMS) has been the bedrock of evolutionary theory for many decades. But the NDMS has proven limited and out of date with respect to several areas of biological research. A new extended evolutionary synthesis (EES), which takes into account more complex interactions between genomes, the cell and the environment, allows for a reexamination of many of the assumptions of the NDMS. To the standard paradigm of slow accumulation of random point mutations as the major mechanism of biological variation must now be added new data and concepts of symbiosis, gene duplication, horizontal gene transfer, retrotransposition, epigenetic control networks, niche construction, stress-directed mutations, and large-scale reengineering of the genome in response to environmental stimuli. There may be implications for Christian faith in this opening of evolutionary theory to a broader and more exciting view of Darwin's great theory.

Theoretical evolutionary biology has been undergoing a crescendo of transformations in recent years. After a long period of general acceptance of the traditional paradigm for how evolution works, new data and concepts from many fields of biological science have begun to challenge the status quo of evolutionary theory. There is no question that evolution occurred, but some of the new ideas are potentially exciting for Christians searching for reconciliation of their belief in a Creator with acceptance of the science of evolution.

Darwin's profound concept of evolution by natural selection remains the best explanation for the diversity of life. Darwin's theory was about natural selection of biological variants. He knew from careful observation that all species contained variants and that selective breeding could magnify variation in animals or plants. He knew nothing about the source of such variation, nor about the basis of the heritability of specific variant traits. Mendel's finding of variant alleles leading to different phenotypes was central to the understanding of the source of variation that could drive evolution.

The Neo-Darwinian Synthesis

In the middle of the twentieth century, even before the chemical nature of the gene was known, biologists were examining mutations in experimental systems of bacteria in order to answer questions about purpose and chance in mutation production. Do bacteria tend to specifically mutate those genes that would help them survive an environmental stress such as starvation or exposure to toxic drugs, or do they simply generate random mutations and then undergo selection according to their fitness? Salvador Luria and Max Delbrück addressed this question in the 1940s with an elegant system called "fluctuation analysis."[1]

The results of these experiments were clear: mutations were random, and the resulting alleles were then selected for

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their relative fitness. This finding contributed to the emerging neo-Darwinian "modern synthesis" (NDMS), in which molecular genetics plays the key role in the production of phenotypic variation, and purpose is replaced by chance in the production of variation, which is the first stage of evolution. The next five decades of research into the fundamental mechanisms of cellular and molecular biology confirmed and vastly extended our knowledge of genetic structure and function, including the details of DNA mutations.

In any field of science, if a theory is any good, it will allow for a logical consolidation of isolated fragments of data or disparate knowledge from several fields into a functional and meaningful picture. The NDMS did just that by combining observations from paleontology and evolutionary biology with genetics and molecular biology. However, the advantage of the NDMS, its simplicity as a unifying theory combining evolution and genetics, has also become its weakness, since it fails to accommodate some of the latest information on the enormous complexity of biological function at the deepest level.

The problem with the NDMS is that it has allowed the finding of random mutations in DNA to remain the single signpost of phenotypic variation among individuals. For decades, the causal chain of slow accumulation of mutations, phenotypic variation, and natural selection proved too powerful to be shaken as the foundation of evolutionary theory.

But all scientific theories are dynamic and ever changing, and this is also true for evolutionary biology. We have seen changes enter evolutionary theory for several decades. The eventual acceptance of the neutral drift theory led to a modification of the idea that positive adaptationist mutations are the only drivers of evolutionary change, especially as related to population genetics.[2]

The ideas of Gould on punctuated equilibrium, first roundly rejected by neo-Darwinians, have been debated for decades. The fossil record seems to show long periods (on the scale of hundreds of millions of years) of very little change, punctuated by remarkable brief "moments" (in geological time) of explosions of new forms. The Cambrian explosion is the best known of these, but there are many other examples. The paleontological data is consistent with brief periods of dramatic changes, and new molecular mechanisms are being put forward to explain how this can happen.

It has been suggested that the NDMS is actually serving as a block to progress in evolutionary theory.[3] The selfish gene concept,[4] which underlies a great deal of modern neo-Darwinism, has been challenged by the recognition that the complexity of life extends down to the level of the cell and the genome. As Denis Alexander wrote in a Biologos blog post:

> The "selfish gene" had its day in the sun, but has now been replaced by the image of a finely tuned genomic system in which each type of gene product cooperates via an intricate networking complex to generate the music of life. The vast array of epigenetic signals whereby genes are switched on or off ensures a steady flow of two-way communication between the genome and its wider environments.[5]

There have been a number of publications challenging the NDMS from various points of view.[6] However, while many evolutionary biologists are embracing alternative mechanisms for the source of variation, there remains a strongly opinionated and publicly active hard core of neo-Darwinians who reject any deviation from the accepted dogma, often more for philosophical than for scientific reasons.

The Extended Synthesis

So, evolutionary biology is currently in a state of splendid confusion. The mass of data from many fields, including evo devo and epigenetic control of genome function, has left the neo-Darwinian paradigm open to reinterpretation. There are parallels of the current situation in biology with the twentieth-century revolution in physics. Relativity and quantum theory did not replace Newtonian physics, but supplemented it with a new depth of understanding. Darwin remains the Newton of biology, and evolution by natural selection will not be displaced as the fundamental unifying theme of all biological information. On the other hand, the first stage of the evolutionary process, the mechanisms driving inheritable variation (which Darwin did not address) is undergoing a transformation. The concept that evolution results from a slow steady process of accumulation of minute genetic and phenotypic changes is being replaced by findings of rapid and dramatic alterations of phenotype resulting from a variety of mechanisms.

The debate between those who believe that a new extended evolutionary synthesis (EES)[7] is necessary and those who think that the NDMS covers all the new biology (and that new theoretical concepts are not necessary) has recently been featured in *Nature* with a joint commentary by the two sides.[8] This follows a meeting held six years ago of sixteen evolutionary scientists who began to formulate ideas for the EES.[9] Many of the ideas presented by this group are related to the interaction between genomes and the environment, with a focus on niche construction and epigenetic inheritance of variability. Other areas such as evolutionary development are also being incorporated. While no unifying theoretical framework has yet been proposed, it is clear that many scientists are interested in producing a coherent EES that takes into account findings from many fields.

Some of the leading figures in the efforts to build a new evolutionary synthesis (including James Shapiro, Gerd Müller, Denis Noble, Eugene Koonin, and Eva Jablonka) have established a website called The Third Way to promote their views.[10] The following is from their mission statement.

> The vast majority of people believe that there are only two alternative ways to explain the origins of biological diversity. One way is Creationism that depends upon intervention by a divine Creator. That is clearly unscientific because it brings an arbitrary supernatural force into the evolution process. The commonly accepted alternative is Neo-Darwinism, which is clearly naturalistic science but ignores much contemporary molecular evidence and invokes a set of unsupported assumptions about the accidental nature of hereditary variation. Neo-Darwinism ignores important rapid evolutionary processes such as symbiogenesis, horizontal DNA transfer, action of mobile DNA and epigenetic modifications. Moreover, some Neo-Darwinists have elevated Natural Selection into a unique creative force that solves all the difficult evolutionary problems without a real empirical basis. Many scientists today see the need for a deeper and more complete exploration of all aspects of the evolutionary process.

The above quote makes clear that many scientists are ready for a new theoretical treatment of evolutionary biology in all of its complexity. The statement also clarifies that the purpose of this movement is not at all theistic, but to advance the science of evolutionary biology.

New Sources of Inherited Variation

Ecological and physiological interactions with an active genome are being proposed as important drivers of evolution. Symbiosis and parasitism, whole genome duplication,[11] major genomic losses, horizontal gene transfer,[12] retrotransposition,[13] epigenetic changes,[14] large-scale reengineering of the genome in response to environmental stimuli,[15] and stress-directed mutations[16] are joining the standard model of point mutations in the expansive and liberating postmodern synthesis. The new theoretical contributions to evolutionary biology are based more on the complexity of systems biology than on the simplistic notion of genetic determinism and gene-centric cellular functions.

Among the various DNA sequence alterations that are now known to play dramatic roles in mutation are various degrees of gene duplication, ranging from single genes to the entire genome. There is strong evidence that a whole genome duplication event occurred at about the time of the origin of the vertebrates.[17] At some point between the origin of chordates and that of jawed vertebrates, an entire genome was duplicated at two different times. Whole genome duplication (WGD) is an extremely useful (and rare) event in evolutionary terms, because it allows for a great deal of genomic trial and error in organisms without interference from purifying or balancing selection. By providing an extra, nonessential copy of every gene, WGD allows for very rapid and dramatic evolutionary leaps, such as the development of new structures and functions like cartilage and bony skeletons. There is evidence that WGD events have occurred in flowering plants,[18] at the origin of teleost fishes,[19] and probably at many other critical evolutionary transition points.

Gene duplication is often mediated by a mechanism called retrotransposition, whereby a gene is duplicated at a new location thanks to the action of genetic elements called retrotransposons.[20] The number and locations of these genetic elements are known in the genomes of many species. There is recent evidence that the rapid evolution of karyotype in gibbons was caused by a retrotransposon insertion.[21] Such events were found to occur during primate evolution when the common ancestor of gorillas, chimps, and humans split from the orangutan line.[22] Gene amplification leads to the production of many copies of a single gene, which can then stimulate evolution at that locus. Exon shuffling and repetitive elements play an important role in gene duplication and new gene creation in flies.[23]

Another mechanism for rapid large-scale genomic change is horizontal gene transfer, whereby one organism transfers a large chunk of genetic material to another organism. This is a well-known phenomenon in bacteria. It now appears that such genetic transfers have taken place between prokaryotes such as bacteria and eukaryotes such as parasites and sponges.[24] Horizontal gene transfer could also explain the origin of animal-like alpha amylase in bacteria as coming from animals and plants. Horizontal gene transfer from bacteria to eukaryotes has been linked to the origin of mineralization in sponges, which led to the eventual development of skeletons in modern animals.

Natural Genetic Engineering

Over the past decades, microbiologist James Shapiro has applied many findings on how cells can accomplish major genomic alterations to develop a model he calls natural genetic engineering (NGE).[25] His view is that the cell can control the genome as much as the genome controls the cell. When applied to evolution, these sources of genetic variation do not fit the neo-Darwinian model of slow progressive changes, but are rapid, dramatic, and involve grand molecular events such as whole genome duplication, transposition of large DNA sections leading to massive reengineering of proteins, and horizontal transfer of coding regions from plastids, viruses, and other organisms.[26]

One such revolutionary event was the huge evolutionary step taken when a cell engulfed a bacterium that remained alive and functional within its host, giving rise to eukaryotic cells with mitochondria. Nobody thinks that event was a slow stepwise process. Richard Dawkins has described it as a one-time incredibly lucky accident, more or less equivalent to the origin of life. (In fact, it happened at least twice, since chloroplasts also started out as bacteria swallowed by an ancient plant cell.)

Stress-Directed Mutations

In 1988, a paper by John Cairns and his colleagues showed that bacteria could produce beneficial mutations targeted specifically to relieve severe stress.[27] Cairns's paper took a major step away from the "purely random" concept for mutation. These beneficial mutations (now called stress-directed mutations or SDM) are produced at rates up to five times higher than other mutations with neutral effects. Numerous researchers have confirmed this phenomenon and have found a number of molecular mechanisms to account for it.[28]

Stress leads to derepression of specific genes whose functions are related to the stress. The resulting higher level of transcription of these genes allows for unpaired and exposed bases in loop structures that are more susceptible to mutation. Several investigators have found evidence that mutants arising from SDM in starving bacteria arise from different molecular mechanisms than ordinary mutational events. Most mutations due to SDM occur in newly derepressed genes. Derepression of genes can lead to supercoiling and much higher mutation rates. Supercoiling of DNA during selective gene transcription is one of the leading molecular precursors of SDM in bacteria. Such changes in supercoiling can result from a variety of environmental stressors, such as changes in osmolarity, temperature, or anaerobiosis.

The following quote from Susan Rosenberg puts the phenomenon of SDM clearly within the context of post neo-Darwinian mechanisms.

> The long-standing assumption of random, constant, and gradual mutagenesis is refuted by observations that mutations occur more frequently when cells are maladapted to their environments …[29]

Evo Devo, Gene Regulation

Evolutionary development is a field of biological enquiry that has made profound and important discoveries in the past decade.[30] The biology of organism development has always been more mysterious than the normal functioning of cells. Questions about how cells differentiate before birth to specialized organs, and how this proceeds in different species, were difficult to address. Recent efforts in *Drosophila* and mice have yielded great insights into the field. The idea that evolutionary mechanisms might be tied to events occurring during development (evo devo) was a tremendous advance whose theoretical implications are still being formulated.[31]

At this point it is clear that animal development involves very specific genes and that many of these genes function by regulating networks of other genes.[32] The details of the complexity of this aspect of biology are still being explored, but several general principles are becoming clear. First, many of the genes involved in development are highly conserved and can function in species that are very distant in phylogenetic terms. Some of these genes, the Hox genes, have enormously complex webs of interaction, wherein the gene product of one gene might amplify or inhibit the transcription of large numbers of other genes, some of which also regulate expression of other genes in a cascade effect similar to the actions of enzyme cascades seen with hormonal actions in cells.[33] The results of the ENCODE project,[34] showing that there is far more noncoding transcription than was expected, have confirmed the extreme importance of regulation of gene expression for many areas of biology, including development and evolution.

It appears that small alterations—either by mutations or by changes in environmental conditions—in the activity of a few key genes might have major effects on the body plan of an organism. If such genetic and/or epigenetic changes are inherited, dramatic alterations in the shape and structure of organisms are possible within a brief time span.

Gene Regulatory Networks

We know that during development, there are networks of genes that are regulated by other genes, which themselves are regulated by environmental and internal signals. Research into the gene regulatory networks (GRN) that function during development has been intensive and productive, and for some organisms such as the sea urchin (an echinoderm), a vastly complex regulatory network has been described in detail.[35] Similar efforts are underway for vertebrates (chicken, fish) and even mammals (mouse).[36]

As has been postulated by evo devo scientists, mutations in certain genes can have dramatic effects on the development of body plans, allowing for rapid changes in limb morphology, segmentation patterns, and so forth. The phenomena of pleiotropy and epistasis could explain how small genetic alterations could have broad and dramatic effects on phenotypic evolution.

On the other hand, a consequence of the fact that gene regulatory networks are well conserved over deep evolutionary time is that there are strong constraints to evolutionary direction. This is consistent with the phenomenon of genetic buffering, which lends stability to patterns of gene expression and could be connected to observations of evolutionary convergence. This kind of genetic control redundancy allows for storage of genetic diversity and for rapid changes when needed due to environmental factors.

Convergence

Stephen J. Gould famously stated that if one were to rewind the tape of biological evolution and play it over, the results would be different. He was referring to the huge role of accident and random chance that he saw in the evolutionary process, especially with respect to mutation. This statement is probably incorrect. Evolutionary convergence has become clearly established as a biological phenomenon, and it tells a very different story of evolutionary direction.[37] Convergence suggests, in contrast to the ideas of some neo-Darwinists, that there may be directions in evolution. Certain common biological features that arise in unrelated lines of organisms suggest that such features are inevitable, and in fact, tend to develop in surprisingly similar ways on a molecular level.[38] On the one hand, convergence demonstrates the immense power of natural selection. On the other hand, it also tells us something about the sources and limits of variation.

Not all morphological changes are purely genetic in origin. The spines on the shells of mollusks, for example, turn out to be fairly predictable based on biomechanical principles. While they might give a selective advantage to the creatures, recent work has shown that spines arise not from a special mutation but from the biodynamics of the accretion of the mineral material that makes up the shell.[39]

Wings, eyes, fins, intelligence, echolocation, and shells are just some of the biological features that appear to be inevitable in any rewinding of the evolutionary clock. Each of these evolved independently many times. The fact that the wings of birds, bats, and insects share many common properties implies that those properties may be optimal for flight and that alternative plans were simply selected against. This is partially true, but we cannot ignore the "tool kit" paradigm of evolution.[40] Evolution does not allow for anything and everything: if it isn't in the tool kit, it doesn't happen.

One outcome of the complexity of how mutations affect phenotype may be a high level of constraint on evolutionary pathways with the resulting observed evolutionary convergence. The homology of the Hox genes across hundreds of millions of years of evolution, and between highly divergent phylogenies,[41] suggests an astounding degree of sequence stability and preserved function. An effect of this conservation of function and genetic structure is a severe limitation on the degrees of freedom that organisms have in body plan and developmental programs. These constraints have profound implications for the idea of evolutionary direction, and even of teleology.

Niche Construction

One of the most interesting areas that are part of the EES is the study of the two-way interactions between organisms and their environment. Beavers make dams, corals make islands, and there are scores of other examples of what has come to be called "niche construction." According to F. John Odling-Smee et al.,[42] niche construction (NC) is "the process whereby organisms, through their metabolism, their activities, and their choices, modify their own and/or each other's niches." The guano of seabirds produces grasslands,[43] and snails affect the quality of soil.[44] According to the theorists of NC, the coevolution of organisms and environments should be taken into account in any comprehensive theory of evolution. This process is nonrandom and directed, and is quite distinct from the effects of random environmental variation on natural selection.

Modeling the dynamics of NC-related population genetics gives results that are not consonant with the standard view of random processes of gene-environmental interaction, in which cause and effect are reversed.[45] An example in human evolution is the spread of lactose tolerance in adults. The cultural change in the human environment that involved dairy farming produced a selective advantage for lactose-tolerant alleles.[46] Current models of modern human evolution depend heavily on niche construction theories.[47] By stressing nonrandom, purposeful alterations caused by organisms on their environment (which then have selective effects on these and other organisms), NC is one of the more radical departures from neo-Darwinism within the EES.

Philosophies of Evolution

One byproduct of the NDMS and its strong emphasis on the effects of genes in controlling all of life is the philosophical view of genetic determinism. This is sometimes referred to as a gene-centric (or even "selfish gene") approach to biology. This sort of determinism has been problematic for philosophers, social scientists, and theologians for quite some time.

Physics has moved beyond pure materialist determinism since the 1920s, but biology has been slow to catch up. It seems clear that the EES, a biological framework that incorporates an enormously complex suite of interactions and reciprocal control features, also falls more in line with an open, nondeterministic mechanism for biological evolution than does the gene-centric mutational model of the NDMS. This could allow the EES to represent the first opening in evolutionary thought to a more flexible framework for the mechanisms of change and innovation in living creatures.

I have not seen many references to the EES by philosophers or theologians as yet. I would predict that once the implications of such an open and broadly based theory become better known, it is likely that there will be some interest in the EES on the part of Christian theologians, especially within the theistic evolution/evolutionary creationism community.

Of particular concern to many Christians is the idea that Darwinian evolution by natural selection is based, at least partially, on a random process of mutation. While a strong argument could be made that the natural selection aspect of evolution is entirely nonrandom, not all Christians find this argument convincing enough to view evolution as a nonrandom process. The EES model, with its focus on dramatic environmental events and complex interactions of organisms with their environments and genomes, is easier to reconcile with the concept that life on earth was not entirely shaped by accidental processes than is the neo-Darwinian model of random mutations leading to slow accumulation of tiny changes.

In his book *On the Origin of Species*, Darwin repeatedly points out the difference between artificial selection, wherein human beings exercise their conscious purpose in producing particular kinds of improvements in crops or domestic animals, and the analogous situation in nature, in which no such conscious agency is needed.[48] From this emphasis arose the concept that evolution is undirected and serves no particular purpose.

However, the idea that the source of variation in individuals of a species is random and not directed in any way did not come from Darwin. In *On the Origin of Species*, he states:

> I have hitherto sometimes spoken as if the variations … were due to chance. This, of course, is a wholly incorrect expression, but it serves to acknowledge plainly our ignorance of the cause of each particular variation.[49]

As the quote demonstrates, Darwin simply had no idea; and more importantly, the distinction between chance and purpose really had no direct consequence on the general theory.

The results to date are sufficient to put to rest the concept that all genomic changes are always produced by purely random processes, independent of extraneous conditions. The role of chance and accident can never be eliminated from any biological theory, nor should they be. But the new extended theory of evolution, unlike the neo-Darwinian synthesis, does not see chance as the only driving force for evolutionary variation.

The issue of randomness or chance is closely tied in with one of the most essential questions in biology: is there a purpose or direction to evolution? With the rise of the NDMS, the idea that evolution is devoid of purpose became engrained in biological theory. Evolution became a theory that neither required nor admitted to any degree of purpose or design.

The theologian/scientist Alister McGrath notes that "some have argued that rejection of any form of teleology is integral to the evolutionary synthesis …"[50] McGrath cites Ernst Mayr, who argued against the use of teleological arguments in biology because of the danger of the forced acceptance of theological or metaphysical doctrines into objective science. While modern science does not generally allow for teleological arguments, the question of whether there is any evidence of teleology of any kind in evolution is still open. McGrath asks, "Yet what if some kind of teleology is discerned within, not imposed upon the biological process? What if an evolutionary teleology is an a posteriori, rather than an a priori, concept?"[51]

With the emergence of the EES and other alternatives to the NDMS model, there is an increasing amount of evidence that the existence of such internal teleology (teleonomy) in evolution cannot be ruled out. The work of Simon Conway Morris on convergence, and his demonstration that evolution, in fact, follows fairly narrow pathways restricted by biological constraints, supports the idea of reexamining this question.[52] Others, such as Francisco Ayala, have found evidence for teleology in the very nature of adaptive change.[53]

McGrath and Mayr, along with Ayala, see purpose as part of natural selection and biology in general. McGrath states,

> Teleological mechanisms in living organisms are thus biological adaptations, which have arisen as a result of the process of natural selection. Such teleological explanations can be considered to be both appropriate and inevitable in biology…[54]

There is clearly a sense of purpose in the way living creatures behave, and we now can see some reflection of this sense in some of the new mechanisms of biological variation. Purpose is still purpose, whether it springs from the genome of *E. coli*, the chromosomes of a chordate, the mind of humans, or the hand of God. The new EES alternatives to neo-Darwinism are not theistic, but the opening up of evolutionary theory to embrace the fundamental complexity of biological systems may very likely contain pointers to the majesty of God's creation, including the diversity of life on Earth.[55]

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