Interciencia
ISSN: 0378-1844
interciencia@ivic.ve
Asociación Interciencia
Venezuela

Pérez, Julio E.; Alfonsi, Carmen; Muñoz, Carlos
TOWARDS A NEW EVOLUTIONARY THEORY
Interciencia, vol. 35, núm. 11, noviembre, 2010, pp. 862-868
Asociación Interciencia
Caracas, Venezuela

TOWARDS A NEW EVOLUTIONARY THEORY

Julio E. Pérez, Carmen Alfonsi and Carlos Muñoz

SUMMARY

The need to elaborate a new evolutionary theory is discussed. Several arguments are given to justify a new theory, mainly based on present interpretation of different phenomena such as endosymbiosis, reticulate evolution, the modern synthesis of embryonic development and evolution (evo-devo), phenotypic plasticity, epigenesis, evolvability, and the several evolutionary mechanisms: natural selection, gene flow, genetic drift, fusion of genomes and gene fragments, epigenetic mechanisms such as methylation of DNA, tool kits, regulatory cis-elements, hybridization and polyploidy. As well as mutations, other sources of genetic variation must also be included.

HACIA UNA NUEVA TEORÍA DE LA EVOLUCIÓN

Julio E. Pérez, Carmen Alfonsi y Carlos Muñoz

RESUMEN

Se analiza la necesidad de elaborar una nueva teoría de la evolución. Se señalan varios argumentos para justificar una nueva teoría, basados principalmente en la actual interpretación de diferentes fenómenos tales como endosimbiosis, evolución reticulada, síntesis moderna del desarrollo y la evolución (evo-devo), plasticidad fenotípica, epigénesis, y evolucionabilidad, y de varios mecanismos evolutivos: selección natural, flujo génico, deriva génica, fusión de genomas y fragmentos génicos, metilación de ADN, "cajas de herramientas", elementos reguladores cis, hibridación y poliploidía. Además, se hace necesario incluir diversas fuentes de variación, no solamente mutaciones.

RUMO A UMA NOVA TEORIA DA EVOLUÇÃO

Julio E. Pérez, Carmen Alfonsi e Carlos Muñoz

RESUMO

Analisa-se a necessidad de elaborar uma nova teoria da evolução. São apontados vários argumentos para justificar uma nova teoria, baseados principalmente na atual interpretação de diferentes fenômenos tais como endossimbiose, evolução reticulada, síntese moderna do desenvolvimento e a evolução (evo-devo), plasticidade fenotípica, epigênese, e evolucionabilidade, e de vários mecanismos evolutivos: seleção natural, fluxo gênico, deriva gênica, fusão de genomas e fragmentos gênicos, metilação de ADN, "caixas de ferramentas", elementos reguladores cis, hibridação e poliploidia. Além disso, é necessário incluir diversas fontes de variação, não somente mutações

Introduction

How can the synthetic theory be defined? In the words of one of its main proponents (Mayr, 1963) the synthetic theory maintains that all evolution is due to the accumulation of small genetic changes guided by natural selection, and that transpecific evolution (macroevolution) is nothing more than an extrapolation and magnification of the events that take place within populations and species (microevolution).

According to Stebbins (1950), another proponent of the modern synthesis, the theory also includes polyploidy, translocations, and other chromosomal mutations that allow reproductive isolation through the accumulation of these chromosome changes. These are largely independent of changes in the genes affecting external morphology; thus, morphologically undifferentiated species may exhibit substantial chromosomal differences.

But, how can polyploidy –a case of rapid speciation requiring only one or two generations through chromosomal change– be described as a small genetic change?

The synthetic theory has shown great capacity to incorporate new ideas. For example, the paper by King and Jukes (1969) on neutralism and genetic drift as a new evolutionary mechanisms was titled 'Non-Darwinian evolution', although it seems

KEYWORDS / Endosymbiosis / Epigenetic Changes / Evo-Devo / Phenotypic Plasticity / Reticulate Evolution /

Received: 11/06/2009. Modified: 09/29/2010. Accepted: 10/08/2010.

Julio E. Pérez. M.A. in Zoology, University of Kansas, USA. Ph.D. in Biology, University of Southampton, UK. Professor, Instituto Oceanográfico de Venezuela (IOV), Universidad de Oriente (UDO), Venezuela. Address: Instituto Oceanográfico de Venezuela, Universidad de Oriente, Núcleo Sucre, Cumaná, Venezuela. e-mail: jeperezr@yahoo.com

Carmen Alfonsi. M.Sc. in Marine Sciences, IOV-UDO, Venezuela. Dr. in Zoology, Universidad Central de Venezuela. Professor, IOV-UDO, Venezuela. e-mail: calfonsi@sucre.udo.edu.ve

Carlos Muñoz. M.Sc. in Marine Sciences, IOV-UDO, Venezuela. Professor, Universidad Arturo Prat, Iquique, Chile. e-mail: c.munoz@unap.cl

to have remained firmly within the fold of the synthetic theory. On the other hand, Mayr denied that random genetic drift is an evolutionary mechanism. In his book *What Evolution Is*, Mayr (2001) wrote: "Molecular genetics has found that mutations frequently occur in which the new allele produces no change in the fitness of the phenotype. Kimura (1983) has called the occurrence of such mutations 'neutral evolution', and other authors have referred to it as non-Darwinian evolution. Both terms are misleading. Evolution involves the fitness of individuals and populations, not of genes. When a genotype, favored by selection, carries along as hitchhikers a few newly arisen and strictly neutral alleles, it has no influence on evolution. This may be called 'evolutionary noise', but it is not evolution".

However, in the opinion of Stebbins and Ayala (1981), the "selectionist" and the "neutralist" views of molecular evolution are competing hypotheses within the framework of the synthetic theory of evolution.

Another example of the incorporation of new ideas into the synthetic theory is that of punctuated equilibrium, a theory developed by Eldredge and Gould (1972), according to which evolutionary change occurs relatively rapidly, as compared to longer periods of relative evolutionary stability. Most populations experience very little change for most of their geological history (stasis) followed by rapid evolutionary events. Eldredge and Gould (1972) indicated that the degree of gradualism proposed by Darwin was virtually nonexistent in the fossil record, and that stasis dominates the history of most fossil species. However, for Dawkins (1996) punctuated equilibrium merely proposes that the rate of evolution varies, and no biologist has ever claimed (not Darwin) that the speed of evolution ever varied. For him, essentially, it is a theory of differential rates of evolution; a modification of Darwin's gradualist model, not a saltationist theory.

Is another evolutionary theory needed?

Modern synthesis currently reigns as the official scientific explanation for evolution (teaching evolution in high schools and colleges means teaching the synthetic theory), having great influence on both our interpretation of biodiversity and our understanding of the world. Nevertheless, present interpretation of different phenomena such as endosymbiosis, reticulate evolution, the modern synthesis of embryonic development and evolution (evo-devo), phenotypic plasticity, evolvability and the several evolutionary mechanisms: natural selection, gene flow, genetic drift, fusion of genomes and gene fragments, methylation of DNA, tool kits, regulatory *cis*-elements, hybridization and polyploidy, indicates the necessity to develop a new evolutionary theory, a coherent alternative to modern synthesis. As well as mutations, other sources of genetic variation must also be included. (Pérez *et al*., 2008).

Gould (1980) pointed out the necessity for a new evolutionary theory that would include a variety of themes either ignored or explicitly rejected by modern synthesis theorists. In his words: "The modern synthesis, as an exclusive proposition, has broken down on both of its fundamental claims: extrapolationism (gradual allelic substitution as a model for all evolutionary changes) and nearly exclusive reliance on selection leading to adaptation." Later, Gould (1982) added that modern synthesis has sometimes been so broadly constructed, usually by defenders who wish to see it as fully adequate to confront and overcome current critiques that it loses all meaning by including everything. However, Gould (2002) wrote: "Nothing about microevolutionary genetic population, or any other aspect of microevolutionary theory, is wrong or inadequate at its level. The modern synthesis is incomplete, not incorrect."

Then Ayala (2005) asked: "Is Gould claiming an expansion with some modification of the Modern Synthesis or is he claiming something more ambitious, namely the advance of a new theory, even if within the Darwinian tradition? Gould's statements, in the structure and elsewhere, are inconsistent, if not contradictory."

Gould (2002) indicated that the study of microevolution provides little, if any, information about macroevolutionary patterns. Macroevolution is autonomous relative to microevolution. Although Ayala (2005) supported this idea, he indicated that the study of microevolutionary phenomena is important to macroevolution, because any correct theory of macroevolution must be compatible with well-established microevolutionary principles and theories. In these two senses – identity at the level of events and compatibility of theories– macroevolution cannot be decoupled from microevolution.

On the other hand, Ayala (2005) agreed with the thesis that macroevolutionary principles are not reducible to microevolutionary approaches. This does not imply that macroevolutionary studies cannot be incorporated into the synthetic theory of evolution. We need to remember that the modern theory of evolution is called "synthetic" because it incorporates knowledge from diverse autonomous disciplines, such as genetics, ecology, systematics, and paleontology.

However, Mayr (2004) saw no justification for a new evolutionary theory, even in light of new advances in molecular biology. In his own words: "It would seem justified to assert that, so far, no revision of the Darwinian paradigm has been necessary as a consequence of the spectacular discoveries of molecular biology."

Pigliucci (2007) indicated that there are some major elements missing from the modern synthesis: embryology or development biology; the role of ecology in the evolution of phenotypic novelties or during major transitions in evolution; knowledge related to genomics, proteomics, and the other new "-omics" sciences; and several important biological phenomena, such as phenotypic plasticity, the possibility of evolutionary capacitance, and epigenetic inheritance. According to Pigliucci (2007), non-random epigenetic changes must be the most important factor in a new theory of evolution. Epigenetic variation, unlike genetic variation, can be altered directly by the environment and may be inherited by future generations. Epigenetic changes offer an additional pathway for evolution.

Elements to be incorporated in a new evolutionary theory

a) Evolvability

This is the ability of biological systems to evolve, the ability of a population to respond to a selective challenge. According to Grant (2010) the synthetic theory addresses evolvability in a population genetic sense; some populations have more genetic variation than others and would therefore be expected to generate phenotypic variation at a faster rate. But evolvability should not be treated as a distinct trait of those populations, independent of the underlying genetic variation.

Evolvability is no longer seen as a matter of standing genetic variance but as a re-

sult of the propensity to vary that is afforded by the entire genetic architecture (Pigliucci, 2008).

It is not known whether the evolution of evolvability is the result of natural selection or a by-product of other evolutionary mechanisms. This dilemma has profound implications for the understanding of evolution in general (Pigliucci, 2008). Earl and Deem (2004) have claimed that evolvability itself will evolve predictably in response to environmental perturbation.

Introduced species offer unique opportunities to study evolutionary changes. Such changes might be seen in population dynamics as: a) a time lag in the wake of invasions, where initial growth is slow; b) the subsequent decline and even extinction of some invaders after an apparently successful invasion; c) the surprising success of some exotic species despite the genetic bottleneck induced by a small population size; and d) the morphological changes that species frequently undergo when introduced into new regions (Pérez *et al.,* 2006).

Why do some introduced species invade and become established, whereas many fail to invade, or persist as small, isolated populations? According to Gilchrist and Lee (2007) one possibility is a limit on evolvability.

b) Epigenesis

Epigenetic inheritance is the term for heritable changes in phenotype not explained by DNA changes. Kardong (2003) adopted the term *epigenomics* to refer to events that occur above (hence epi-) the level of the DNA (hence genomic). Epigenomics is the analysis of the normal non-genetic processes that influence the characteristics of the phenotype during the lifetime of the organism.

Epigenetic changes are based on biochemical modifications that can activate, reduce, or disable the activity of some genes by: a) the addition of a methyl group to a cytosine residue, followed by a guanine sequence in a CpG dinucleotide (methylation is often associated with reduced gene activity); b) changes in the chromatine structure through chemical modifications, especially acetylation or methylation of histone proteins, which recruit other proteins such as transcription factors and repressors that together determine the activity state of specific genes or sets of genes; and c) changes in the genetic messages transcribed. RNA editing –such as changing adenosine to inosine, which is read as guanosine– systematically alters base sequences, resulting in an entirely new message (Ho, 2009).

The epigenetic changes may be heritable through either meiosis or mitosis (Bossdorf *et al*., 2008). If the term epigenetic inheritance is used comprehensively to include mitotic inheritance, then some of the mechanisms underlying phenotypic plasticity may be based on epigenesis. But if the term refers exclusively to meiotic epigenetic inheritance, then epigenetics does not overlap phenotypic plasticity, as plasticity is a genotype-specific, environmentally-induced, and non-heritable change of the phenotype (Oliver Bossdorf, personal communication). In this paper the term is restricted to the inheritance of epigenetic variation across generations.

The best known examples of epigenetics are paramutation and parental imprinting. Paramutation is a non-Mendelian heritable epigenetic modification in the genome that can be passed to the next generation. It is an interaction between two alleles of a single locus that results in a heritable change of one allele. In paramutation, one allele affects the other in one generation and in future generations, even if the allele that causes the change is not transmitted. The phenomenon has been described in several plant species, most notably in corn. Paramutation produces a progressive increase of methylation of cytosine in the paramutable allele, the sensitive allele to be silenced (Walker and Panavas, 2001).

Parental imprinting is another example of epigenetic inheritance in which certain autosomal genes have seemingly unusual inheritance patterns. The consequence of parental imprinting is that imprinted genes are expressed as if they were hemizygous, even though there are two copies of each of these autosomal genes in each cell. Furthermore, when these genes are examined the only changes that are seen are extra methyl groups present in certain bases of the imprinted genes' DNA (Ekstrom, 1994).

A recent study (Crews *et al*., 2007) demonstrated that heritable epigenetic variation can even affect animal behavior. When rats are treated only once with a toxin (the fungicide vincozolin) that alters DNA methylation, females three generations removed from the exposure discriminate and prefer males who do not have a history of exposure, whereas similarly epigenetically imprinted males do not exhibit such preference. The toxin induces the appearance of new imprinted-like genes that transgenerationally transmit this altered epigenome to promote new phenotypes.

As behavior is regarded to be the most responsive aspect of animal phenotypes, such epigenetic effects on behavior may have particularly profound evolutionary consequences.

c) Phenotypic plasticity

In many organisms the same genotype can give rise to many different phenotypic variants whose appearance or behavior depends on its environmental setting. This phenotypic variation or "plasticity," dictates the range of habitats that a particular genotype can occupy (Kutschera and Niklas, 2004).

Nussey *et al*. (2005) indicated that phenotypic plasticity can evolve under natural selection. A Dutch population of great tits (*Parus major*) presents evidence for variation in individual plasticity in the timing of reproduction, and shows that this variation is heritable. Some great tits have shifted the timing of egg-laying, this shift giving them an edge over other great tits in dealing with global warming. These birds feed their young with caterpillars. If spring arrives earlier, caterpillars mature earlier, before tit chicks hatch, leading to a decline in the birds' reproductive success. However, there is genetic variation among tits that allows for adjustment of the egg-laying date. The birds most able to modify the timing of egg-laying in response to earlier spring are more successful at reproducing, as chicks hatch at a time when their food is most plentiful. Although there are not yet enough long-term data to state for sure that great tits are evolving greater phenotypic plasticity –says Nussey– this advantage suggests that, over time, the more flexible birds may win out, and eventually the population will be better able to respond to climate changes.

d) Evolutionary development (evo-devo)

Developmental biology was discussed in detail by Darwin in *The Origin of Species*; there is a complete chapter dedicated to this topic. Darwin (1859) saw that embryonic resemblances would be a very strong argument in favor of the connectedness of different animal groups.

In modern synthesis, however, this important element was missing: how do forms change; how do new structures arise? The key to un-

derstanding how complex structures arise and evolve is development. "Evo-devo" is the field that unites developmental and evolutionary biology, and their supporters (Carroll, 2000, 2005; Stern, 2000; Wray, 2007) claim to have revolutionized the study of both macro- and microevolution.

Evolutionary developmental biology is a discipline concerned with the discovery and understanding of the changes in developmental mechanisms and their role in the evolutionary origin of aspects of the phenotype. Ho (2009) indicated that there is no separation between development and evolution, and the organism actively participates in shaping its own development as well as the evolutionary future of the entire ecological community of which it is a part.

Extensive studies of embryology reveal that despite great differences in appearance, almost all animals share a common "tool kit" of body building genes. The best example of tool kit genes is called *Hox* genes, which control segmental patterning during development. The various *Hox* genes are situated very close to one another in the chromosome, in groups or clusters. It has also been observed in a phylogenetically widespread range of taxa that the relative spatial and/or temporal expression of *Hox* genes is correlated with their relative position within *Hox* clusters. This correspondence between gene expression and cluster organization has been termed colinearity.

The existence of colinearity implies that linkage impacts gene regulation. However, *Hox* colinearity is not universal, and no single mechanism has been identified that can explain *Hox* colinearity or the persistence of Hox clusters in diverse metazoan lineages. Rather, it seems that several different regulatory mechanisms may contribute to the stability of *Hox* clusters. For example, both higher order chromatin structure and local *cis*-regulatory elements may result in coordinated regulation of neighboring *Hox* loci. Furthermore, in some taxa, most notably *Drosophila*, *Hox* linkage does not appear to be required for appropriate *Hox* expression (Ryan *et al*., 2007).

The *Hox* genes shape the number and appearance of repeated structures along the main body axes of animals. Shifts in the expression of tool-kit genes during development not only account for large-scale differences in animal forms; they can also explain differences among closely related species, or even populations of the same species.

But, is evo-devo just a matter of genes? Are the large evolutionary changes in body pattern the result of changes in gene regulation due to natural selection? How do we explain the lack of correlation between genetic and morphological differences between species? Evo-devo is still based on the old idea that development is dominated by genes in a "genetic programme" of gene regulation (Ho, 2009). Coyne (2009) indicated that in the past three decades, virtually all the major advances in evolutionary developmental biology, or "evo-devo," have been firmly grounded in genetics.

There must be recognition of the important role of epigenetic signals from the internal and external environment that activate DNA to produce a large alteration in form and function.

The integration of evo-devo with the synthetic theory seems to be difficult. As indicated by Müller (2007), the inclusion of information from developmental systems will be difficult to achieve, as current evo-devo does not generate data that can be easily entered into population-dynamic algorithms, and will not for some time.

Furthermore, evo-devo aims at explaining how development itself evolves and how the control of developmental processes is brought about by the interplay between genetic, epigenetic, and environmental factors.

Some examples in evo-devo involve *cis*-regulatory elements (short, noncoding DNA sequences that control expressions of a nearby gene). An active debate is currently developing in relation to these claims. According to Wray (2007) there is evidence to support the claim that *cis*-regulatory mutations are more important than structural mutations in phenotypic evolution. Numerous studies have identified *cis*-regulatory mutations with functionally significant consequences for morphology, physiology, and behavior. The focus has now shifted to considering whether *cis*-regulatory and coding mutations make qualitatively different contributions to phenotype evolution. In particular, cases in which parallel mutations have produced parallel trait modifications suggest that some phenotypic changes are more likely to result from *cis*-regulatory mutations than from coding mutations.

The idea that macroevolution has mainly been the result of changes at *cis*-regulatory sites was first developed by Carroll (2000, 2005) and Stern (2000). On the other hand, Hoekstra and Coyne (2008) indicated that genomic studies show no strong evidence to support important *cis*-regulatory changes in evolution. Adaptations of both form and physiology are likely to involve a mixture of structural and *cis*-regulatory changes, and structural changes are unlikely to be negligible. Although the claim related to *cis*-regulatory changes may be true, it is at best premature (Hoekstra and Coyne, 2008).

e) Reticulate evolution

In *The Origin of Species*, Darwin wrote a chapter entitled Hybridism, in which he analyzed the causes of sterility in hybrids, not hybridization as a possible process of speciation. Neither Darwin nor the proponents of the synthetic theory developed the idea of reticulate evolution as a mechanism of speciation. Currently, there is general agreement on the great importance of hybridization as an evolutionary phenomenon (Chapman and Burke, 2007; Mallet, 2007).

Reticulate speciation can occur through polyploidy (allo- and auto-polyploidy) and diploid homoploidy. Although both modes of hybrid speciation have occurred in nature, polyploidy, especially through allopolyploidy, appears to be more common than homoploid hybrid speciation, and more is known about its overall evolutionary significance. Allopolyploidy speciation can result from somatic chromosome doubling into a diploid hybrid, followed by selfing to produce a tetraploid, as in *Primula kewensis*, an allopolyploid that arose spontaneously in 1909 among cultivated diploid hybrids of *P. verticillata* and *P. floribunda* (Ramsey and Schemske, 2002). Allopolyploidization results in instantaneous speciation because any backcrossing to the diploid parents produces sterile triploid offspring.

Certainly, allopolyploids are a sizable fraction of well-studied crop cases, such as wheat, cotton, maize, sugar cane, coffee, and tobacco.

Homoploid hybrid speciation is a normal sexual event where each gamete has a haploid complement of the chromosomes from its parents, but the gametes that

form the zygote come from different species. In this case, both parents have the same number of chromosomes, and successful backcrossing to the parents is possible, so it is thought that the hybrids have to be isolated from the parents by undergoing selection for life in the novel environment.

Diploid hybrid speciation is much rarer than allopolyploidization. Hybrid speciation is very common in some groups of organisms such as plants, fish, amphibians and some invertebrates, but is virtually absent in others like mammals and most arthropods (Linder *et al*., 2003).

In relation to homoploidy, Mallet (2007) indicated that, in plants, about 20 well-established homoploid hybrid species are known, the best documented examples being three species of desert sunflowers. Reiseberg (1997) reproduced in the greenhouse the formation of a naturally occurring species of sunflower, *Helianthus anomalus,* a diploid outcrossing species that arose from recombinational speciation. The putative ancestors are *H. annus* and *H. petiolaris*, which occur widely in the western USA and often form hybrid swarms. These offspring are largely sterile because the species differ in fixed chromosome arrangements, which causes meiotic difficulties in the heterozygous hybrids. Over several generations, however, these arrangements can sort themselves out into a new genome that is perfectly compatible with others of its type but incompatible with the genomes of its ancestors. In *H. anomalus*, this chromosomal sorting was supplemented by the fixation of new rearrangements as well, as more conventional genetic changes, some of which must involve adaptation to its peculiar habitat.

Epigenetics has played an important role in hybridization events. Hybrids frequently produce complex or unpredictable outcomes that are not easily explained, because they are derived from the interactions of different proteins encoded by divergent nucleotide sequences from two previously isolated parental genomes. According to Grant-Downton and Dickinson (2005), an indication that this explanation is inadequate comes from rare hybrids, where their phenotype is always disproportionately skewed towards one of the parents; hybridization events in plants can unlock variations not seen in either parental species.

Grant-Downton and Dickinson (2006) indicated that research of the epigenetics of allopolyploid hybrids between *Arabidopsis thaliana* and *A. arenosa* to form a stable fertile hybrid allotetraploid, *A. suecica*, reveals that the F1 hybrids showed a range of phenotypes not necessarily intermediate between the parents. Some of these phenotypes, such as pigmentation, were unstable in hybrids, indicating that dynamic epigenetic changes affecting gene expression had taken place.

f) Endosymbiosis and symbiogenesis

Endosymbiosis is a relationship in which one organism belonging to one species lives within another from a different species in a mutually beneficial manner. Endosymbiosis is viewed as a phenomenon for saltatory evolution and is seen at its most powerful in the blending of whole genomes (Ryan, 2006). Symbiogenesis is the resulting evolutionary change that occurs by permanent integration of symbionts.

Margulis (1981) stated that all life on earth is bacterial or derives, by symbiogenesis, from communities of bacteria; and Ran *et al.* (2010) indicated that an ancient cyanobacterial incorporation into a eukaryotic organism led to the evolution of plastids (chloroplasts) and subsequently to the origin of the plant kingdom.

Hotopp *et al.* (2007) have found what seems to be the entire genome of a parasitic bacterium, *Wolbachia pipientis*, inserted into the genome of the *Drosophila ananassae*. The discovery suggests that the bacterial genome must have provided some sort of evolutionary advantage to its host.

Lake (2009) showed evidence that the double-membrane, Gram-negative prokaryotes were formed as a result of a symbiosis between an ancient *Actinobacterium* and an ancient *Clostridium*. The endosymbiotic theory envisions the evolution of the first eukaryotic cells to have resulted from the permanent incorporation of once autonomous, physiologically different prokaryotic cells incorporated into a host prokaryotic cell-type (Kutschera and Niklas, 2004). According to this concept, mitochondria evolved from some form of ancient aerobic bacteria, whereas chloroplasts evolved from some form of cyanobacteria-like prokaryotes. Upon gaining permanent residency in their host cell, mitochondria and chloroplasts continued to function and replicate in such a manner that derivative confederations were produced when the host cell underwent binary fission (Margulis, 1970).

Zimmer (2009) adds additional evidence to the endosymbiotic hypothesis: genes in mitochondria closely resemble genes in alpha protobacteria, not those in eukaryotes; and some of the proteins that carry out reactions in mitochondria are encoded in nuclear DNA. The closest relatives of these genes are among bacterial genes, not eukaryote genes. It seems that after the ancestors of mitochondria entered the ancestors of today's eukaryotes, some of their genes got moved into the eukaryote genome.

Ran *et al.* (2010) sequenced the genome of a *cyanobacterium* residing extracellulary in symbiosis with the plant *Azolla filiculoides* suggesting that this cyanobacterial symbiont of *Azolla* can be considered at the initial phase of a transition from free-living organisms to a nitrogen-fixing plant entity, a transition process which may mimic what drove the evolution of chloroplasts from a cyanobacterial ancestor. The evolution by symbiotic association (symbiogenesis) is the most likely model for many evolutionary events that have resulted in rapid changes or the formation of new species of plants (Roossinck, 2005).

Virus-host partnerships, including genomic fusions, are more common than many biologists realize, and play an important and underestimated role in evolution. Some symbiologists have not considered viruses as potential symbionts. In general, this is the result of a refusal to see viruses as living organisms. An important example is the viral-eukaryotic symbiosis that occurs in the parasitoid wasp-polydnavirus interactions, in which the virus carries the essential genes required to suppress the immune system of the lepidopteran host of the wasp (Wren *et al*., 2006). In many such examples, the viral genome has been integrated into the wasp genome. Once viruses enter a genome, their capacity for evolutionary innovation remains persistently active and can interact with newly arrived exogenous viruses or with other genetic components and regulatory mechanisms, thus increasing evolutionary plasticity (Lower *et al*., 1996, cited by Ryan, 2006).

Approximately 8% of the human genome consists of human endogenous retroviruses (HERVs), and, if HERV fragments and derivatives are included, the retroviral legacy amounts to roughly half our DNA. A long term consequence of the symbiotic viral component of the human genome is an increase in genetic plasticity, which has important implications in medicine and evolutionary biology. Virus-host integrations probably played a key role in the origins of both non-adaptive and adaptive immunity. Retroviruses have also been detected

in the placenta of many different species of mammals, including non-human primates, cats, mice, and guinea pigs (Ryan, 2007, 2009).

Margulis (1970) proposed that symbiosis, not random mutation, was the driving force behind evolution, and that cooperation between organisms and the environment, rather than competition among individuals, was the chief agent of natural selection. She stated that "Darwin's great vision was not wrong, only incomplete." The same can apply to the synthetic theory. As indicated by Ryan (2006), endosymbiosis does not contradict Darwinism, although it differs from the mutation plus-selection paradigm of the synthetic theory in several respects. Natural selection does not create the symbiosis *de novo*, but instead edits the partnership once it has become established. Selection operates at the level of the partnership, rather than at the individual level.

g) Horizontal gene transfer

Horizontal (or lateral) gene transfer (HGT) overlaps with the endosymbiotic theory of organelles. Endosymbiosis basically involves the fusion of the entire genomes of two organisms. Syvaven (1994) considered this to be one part of the larger phenomenon of cross species gene transfer, which involves, in addition to endosymbiotic fusion, the insertion of smaller genetic regions, including single genes or even parts of genes. The mechanisms of transfer will likely involve viruses, direct transformation, conjugation, or other as yet unexplored means.

HGT (and endosymbiosis) is an important evolutionary phenomenon in the ancestry of many microbes. Doolittle (1999) indicated that an evolutionary model in which novel genes transferred between populations play a major role in adaptation, is radically different from one in which adaptation is achieved by selective allele replacement within populations. Its implications for phylogeny are also radically different. Nevertheless, both modes of adaptation drive the evolution of prokaryotes. At the same time, new genes from far away must impart new tempo and new modes in prokaryotic evolution. Horizontally transferred genes, because they can confer radically new and complex phenotypes, might often result in adaptive radiations and the formation of new subpopulations, perhaps in fact more often than can mutation and selection operating on already resident genes. Unlike eukaryotic speciation, bacterial speciation might be driven by a high rate of horizontal transfer, which introduces novel genes, confers beneficial phenotypic capabilities, and permits the rapid exploitation of competitive environments (Doolittle, 1999).

Although their role in plant and animal evolutionary history remains largely unexplored, suspected HGT events have recently been identified by Richards *et al*. (2009) by comparing the genome of six plant species with those of 159 prokaryotic and eukaryotic species. Through phylogenetic analyses, these researchers found five fungi-to-plant, and four plant-to-fungi transfers. Two of the fungi-to-plant transfers have added phenotypes important for life in a soil environment. These important results support the ideas of Doolittle (1999).

Conclusions

Though widely accepted as the official scientific explanation for evolution, exerting great influence on both our interpretation of biodiversity and our understanding of the world, modern synthesis lacks some major elements, to wit: endosymbiosis, reticulate evolution, the modern synthesis of embryonic development and evolution (evo-devo), epigenesis, phenotypic plasticity, evolvability; which involve several evolutionary mechanisms such as: fusion of genomes and gene fragments, methylation of DNA, tool kits, regulatiory *cis*-elements, hybridization and polyploidy. It is also necessary to include different sources of genetic variation, not only mutations. All this knowledge underscores the necessity to develop a new evolutionary theory, a coherent alternative to modern synthesis.

Evolution can occur incrementally through small changes (genetic drift and natural selection) or abruptly through hybridization, endosymbiosis, and changes in gene regulation. The environment plays an important role in the evolution of organisms, through epigenesis. Current knowledge allows for the rejection of the central dogma of biology. Although it seems that the study of macroevolution is not an extrapolation and magnification of the events that occur within populations and species, these events cannot be decoupled, since the population in which macroevolution occurs is the same population that evolves at the microevolutionary level.

Evolutionary innovations do not seem to arise at random; on the contrary, they seem to have originated from non-random processes based on the epigenetic system. As a consequence of these developments, especially that of epigenetic inheritance, a new and wider definition of evolution seems necessary, one that would be the result of several mechanisms that change both the genetic and epigenetic compositions of populations.

The integration of evo-devo with the synthetic theory seems difficult or impossible. The synthetic theory is based mainly on population dynamics, on the correlation of phenotypic variation with statistical gene frequencies in populations, whereas evo-devo explains phenotypic change through alterations in developmental mechanisms, whether they are adaptive or not.

As a final conclusion, we think that a new evolutionary theory is needed.

REFERENCES

Ayala FJ (2005) The structure of evolutionary theory: on Stephen Jay Gould's monumental masterpiece. *Theol. Sci. 3*: 97-117.

Bossdorf O, Richards CL, Pigliucci M (2008) Epigenetics for ecologists. *Ecol. Lett.* 11: 106-115.

Carroll SB (2000) Endless forms: the evolution of gene regulations and morphological diversity. *Cell* 101: 577-580.

Carroll SB (2005) Evolution at two levels: on genes and form. *PLoS Biol.* 3: 1159-1166.

Chapman MA, Burke JM (2007) Genetic divergence and hybrid speciation. *Evolution 61*: 1773-1780.

Coyne JA (2009) Evolution's challenge to genetics. *Nature 457*: 382-383.

Crews D, Gore AC, Hsu TS, Dangleben NL, Spinetta M, Schallert T, Anway MD, Skinner MK (2007) Transgenerational epigenetic imprints on mate preference. *Proc. Nat. Acad. Sc. USA 104*: 5942-5946.

Darwin C (1859) *The Origen of Species*. Peckhman M (Ed., 2006) Pennsylvania University Press. Philadelphia, PA, USA. 816 pp.

Dawkins R (1996) *The Blind Watchmaker*. Norton. New York, NY, USA. 358 pp.

Doolittle WF (1999) Lateral genomics. *Trends Genet. 15*: M5-M8.

Earl DJ, Deem W (2004) Evolvability is a selectable trait. *Proc. Nat. Acad. Sc. USA 101*: 11531-11536.

Eldredge N, Gould SJ (1972) Punctuated equilibria: an alternative to phyletic gradualism. In Schopf TJM (Ed.) *Models in Paleobiology*. Freeman, Cooper & Co. San Francisco, CA, USA. pp 82-115.

Ekstrom TJ (1994) Parental imprinting and the IGF2 gene. *Horm. Res. 42*: 176-181.

Gilchrist GW, Lee CM (2007) All stressed out and nowhere to go: does evolvability limit adaptation in invasive species? *Genetica 129*: 127-132.

Gould SJ (1980) Is a new and general theory of evolution emerging? *Paleobiology 6*: 119-130.

Gould SJ (1982) Darwinism and the expansion of evolutionary theory. *Science* 216: 380-387.

Gould SJ (2002) *The Structure of Evolutionary Theory*. Belknap Press. Cambrige, MA, USA. 1433 pp.

Grant R (2010) Should evolutionary theory evolve? *Scientist 24*: 24-25.

Grant-Downton RT, Dickinson HG (2005) Epigenetics and its implications for plant biology. 1. The epigenetic network in plants. *Ann. Bot. 96*: 1143-1164.

Grant-Downton RT, Dickinson HG (2006) Epigenetics and its implications for plant biology. 2. The "epigenetic epiphany", Epigenetics, evolution and beyond. *Ann. Bot. 97*: 11-27.

Ho MW (2009) How development directs evolution. Lecture in the Conference Evolution and the Future. Belgrade, Serbia, 14-18 October 2009. Available at www.i-sis.org.uk.

Hoekstra HE, Coyne JA (2008) The locus of evolution: Evo Devo and the genetics of adaptation. *Evolution 61*: 995-1016.

Hotopp JCD, Clark ME, Oliveira DCSG, Foster JM, Fisher P, Muñoz Torres MC, Giebel JD, Kumar K, Ishmael N, Wang S, Ingram J, Nene RV, Shepard J, Tomkins J, Richards S, Spiro DJ, Ghedin E, Slatko BE, Tettelin H, Werren JH (2007) Widespread lateral gene transfer from intracellular bacteria to multicellular eukaryoyes. *Science 317*: 1753-1756.

Kardong KV (2003) Epigenomics: The new science of functional and evolutionary morphology. *Anim. Biol. 53*: 225-243.

Kimura, M (1983) *The Neutral Theory of Molecular Evolution*. Cambridge University Press, Cambridge, MA. USA. 367 pp.

King JL, Jukes TH (1969) Non-Darwinian evolution. *Science 164*: 788-798.

Kutschera U, Niklas KJ (2004) The modern theory of biological evolution: an expanded synthesis. *Naturwissenschften 91*: 255-276.

Lake JA (2009) Evidence for an early prokaryotic endosymbiosis. *Nature 460*: 967-971.

Linder CR, Moret BME, Nakhleh LN, Warnow T (2003) *Network reticulate evolution. Biology, models and algorithms*. www.cs.utexas.edu/phylo/resorucer.pdf/papers

Mallet J (2007) Hybrid speciation. *Nature 446*: 279-283.

Margulis L (1970) *Origin of Eukaryotic Cells*. Yale University Press. New Haven, CT, USA. 371 pp.

Margulis L (1981) *Symbiosis in Cell Evolution*. Freeman. San Francisco, CA, USA. 419 pp.

Mayr E (1963) *Animal Species and Evolution*. Belknap Press. Cambridge, MA, USA. 797 pp.

Mayr E (2001) *What Evolution Is*. Basic Books. New York, NY, USA. 336 pp.

Mayr E (2004) 80 years of watching the evolutionary scenery. *Science 305*: 46-47.

Müller GB (2007) Evo-devo: extending the evolutionary synthesis. *Nat. Rev. Genet. 8*: 943-949.

Nussey DH, Postma E, Glenapp P, Visser ME (2005) Selection on heritable phenotypic plasticity in a wild bird population. *Science 310*: 304-306.

Pérez JE, Nirchio M, Alfonsi C, Muñoz C (2006) Biological invasions. The genetic adaptation paradox. *Biol. Inv. 8*:1115-1121.

Pérez JE, Alfonsi C, Nirchio M, Salazar S (2008) Bioinvaders: The acquisition of new genetic variation. *Interciencia 33*: 935-940.

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

Pigliucci M (2008) Is evolvability evolvable? *Nat. Rev. Genet. 9*: 75-82.

Ramsey J, Schemske DW (2002) Neopolyploidy in flowering plants. *Annu. Rev. Ecol. Syst. 33*: 589-639.

Ran L, Larsson J, Vigil-Stenman T, Nylander JAA, Ininbergs K, Zheng W-W, Lapidus A, Lowry S, Hasselkorn R, Bergman B (2010) Genome erosion in a nitrogen-fixing vertically transmitted endosymbiotic multicellular Cyanobacterium. *PLoS ONE 5*: e11486.

Reiseberg LH (1997) Hybrid origens of plant species. *Annu. Rev. Ecol. Syst. 28*: 359-389.

Richards TA, Soanes DM, Foster PG, Leonard G, Thomton CR, Talbot NJ (2009) Phylogenomic analysis demonstrates a pattern of rare and ancient horizontal gene transfer between plants and fungi. *Plant Cell. 21*: 1897-1911.

Roossinck ML (2005) Symbiosis versus competition in plant virus evolution. *Nat. Rev. Microbiol. 3*: 917-924.

Ryan FP (2006) Genomic creativity and natural selection: a modern synthesis. *Biol. J. Linn. Soc. 88*: 655-672.

Ryan FP (2007) Virus as symbionts. *Symbiosis 44*: 11-21.

Ryan FP (2009) An alternative approach to medical genetics based on modern evolutionary biology. Part 2: Retroviral symbiosis. *J. Roy. Soc. Med. 102*: 324-331.

Ryan JF, Mazza ME, Pang K, Matus DQ, Baxevanis AD, Martindale MQ, Finnerty JR (2007) Pre-Bilaterian Origins of the Hox Cluster and the Hox Code: Evidence from the Sea Anemone, *Nematostella vectensis*. *PLoS ONE 2*: e153.

Stebbins GL (1950) *Variation and Evolution in Plants*. Columbia University Press. New York, NY, USA. 561 pp.

Stebbins GL, Ayala F (1981) Is a new evolutionary synthesis necessary? *Science 213*: 967-971.

Stern DL (2000) Perspective: Evolutionary developmental biology and the problem of variation. *Evolution 54*: 1079-1091

Syvaven M (1994) Horizontal gene transfer: Evidence and possible consequences. *Annu. Rev. Genet. 28*: 237-261.

Walker EL, Panavas T (2001) Structural features and methylation patterns associated with paramutation and the *r1* locus of *Zea mays*. *Genetics 159*: 1201-1215.

Wray GA (2007) The evolutionary significance of *cis*-regulatory mutations. *Nat. Rev. Genet. 8*: 206-216.

Wren JD, Roossinck MJ, Nelson RS, Scheets K, Palmer MW, Melcher U (2006) Plant virus biodiversity and ecology. *Plos Biol. 4*: e80.

Zimmer C (2009) On the origen of eukaryotes. *Science 325*: 666-668.