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All Branches of the Same Tree of Knowledge

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## The Organic Whole: A Conception Worthy of Biological Life

Bhakti Madhava Puri, Ph.D.

### Molecular Biology Subsumed by Systems Biology

All the central assumptions of the Modern Synthesis (Neo-Darwinism) have been disproven. [1, 2] An article with the title, "Rocking the foundations of molecular genetics," appearing in the prestigious *Proceedings of the National Academy of Sciences* at the end of 2012 [3] would have not been possible a decade ago. Groundbreaking experimental evidence of epigenetic maternal inheritance over several generations was published in the same journal, throwing the whole foundation of 21st century molecular genetics into question. Neo-Darwinism attributed genetic change to random events, in which physiology was assumed to play little role. "The germ line was thought to be isolated from any influence by the rest of the organism and its response to the environment. [3]

Darwin in 1859 wrote in his *Origin of Species*, "I am convinced that natural selection has been the main, but not the exclusive means of modification." [4] This can no longer be maintained in light of the experimental evidence available to us today. The Neo-Darwinian concept of random genetic mutation that was synthesized with the original Darwinian concept of natural selection has also been shown to be unsupported by the evidence. In fact, the four basic assumptions of the Modern Synthesis (Neo-Darwinism) have been refuted by modern experimental evidence.

These assumptions can be listed as follows:

1. Genetic change is random. The term "random" is generally interpreted in reference to DNA copying errors or other

random events. It also assumes that influences from the phenotype, such as physiological functions or their changes in relation to environmental stresses, are not involved in such single-step errors. In general, it excludes any guidance to such changes beyond the genetic level.

2. Genetic change is gradual. Since random changes are microscopically stochastic, long periods of accumulation of such mutations would be necessary to produce any major alteration in the genome or phenome. This means that gene sequences or the protein sequences they produce would not be expected to rely on the mobility of large domains to move around or between genomes.

3. Natural selection acts on genetically mutated variants (alleles). This produces increased frequency of certain alleles in a population depending on their fitness. Thus mechanisms like genetic drift and geographical isolation can produce new species.

4. Inheritance of acquired characteristics is impossible. This assumption distinguishes Darwin (1859) from Lamarck (1809), and from any life-force that could be directing increasing complexity through evolution or adaptation. Crick's Central Dogma of Biology assumes that genetic material can be isolated from the rest of the organism and environment.

Experimental work within the field of modern molecular biology has refuted all these assumptions, more or less deconstructing its own foundations. [5]



**Genetic change is random. Disproven.**

“It is difficult (if not impossible) to find a genome change operator that is truly random in its action within the DNA of the cell where it works. All careful studies of mutagenesis find statistically significant non-random patterns of change, and genome sequence studies confirm distinct biases in location of different mobile genetic elements.” [5] Function influences both the speed and location of genomic changes. Many examples are found within the immune system. Targeted genomic changes or “natural genetic engineering” is observed in many instances outside the immune system as well. So-called “junk DNA,” the regions of the genome that do not code for proteins, has now been found to have essential functional significance in regulating genomic activity. [6]

**Genetic change is gradual. Disproven.**

Nobel Prize-winner Barbara McClintock introduced the idea of “jumping genes,” [7] chromosome transpositions (now called mobile genetic elements) that produce rapid changes in the genomic structure. Modern genome mapping has made it possible to see whole domains, up to hundreds of amino acids, can be shifted around to different locations in the genome.

DNA sequences that are first copied as RNA sequences, can again be inserted back into a different part of the genome using reverse transcriptase. These are called retrotransposons. The DNA molecule is now known to be so flexible that numerous manipulations of the fixed genetic sequences are possible, actually modifying the information in the DNA. Other mobile elements found in plasmids, viruses and bacteria can also transform DNA by introducing new genetic material. Darwin's original idea about a tree of life thus becomes difficult to retain in light of the extensive influences that can come from the environment in the form of mobile DNA elements.

**Natural selection acts on genetically mutated variants (alleles). Disproven.**

The neutral theory of evolution [8] makes natural selection superfluous. Selection for "fitness" makes natural selection ambiguous [9] as to what constitutes fitness in a given situation – what is being selected for? Reproductive success cannot be the only feature selected for, since that can also work against survival in an environment of limited resources. Drift simply refers to deviation from probabilistic expectation, but is based on sampling process, not selection. Geographical isolation is also not a selection process, but strongly influences species morphology.

**Inheritance of acquired characteristics is impossible. Disproven.**

A transgenerational effect on the transcriptome and epigenome through differential DNA methylation, as well as transgenerational disease or abnormalities have all been experimentally verified, [10, 11] Food availability to grandparents has been shown to influence grandchildren's

longevity. [12] And care of young by the parents influences offspring's behavior later on as adults. [13]

The conclusion is obvious: the organism should have never been conceived as a mere order supplier for its selfish genes.

The validity of other popularly held conceptions of molecular biology that are now subject to question [14] are:

1. An individual's genome, his or her entire DNA sequence, is fixed at the moment of conception and, with the exception of the occasional point mutation or mutations associated with, for example, cancer, does not change throughout life. Today it is known that DNA is dynamic rather than static, being subject to a wide array of rearrangements, insertions, and deletions, as mentioned above.
2. Persons have identical DNA in all the cells and tissues of their bodies (with the exception of germ cells, red blood cells, and certain cells in the immune system). It is appearing more and more likely that the normal human condition is one of somatic and chromosomal mosaicism, that is, different genomes in different cells and tissues of the same individual.
3. Specific genes are coded for the production of specific proteins. This is now known to depend upon an assumption concerning the manner in which the protein for which the gene is encoded affects behavior.

Considering all these problems with the current gene/genome-centric view of molecular biology, a metabolically or physiologically based conception of biology has become a possible alternative. [15] In addition, the field of Cognitive Biology has become recognized as an important viewpoint from which to study living organisms. [16] Developmental Systems Theory (DST) [17] is now accepted as a powerful new way to deal with the massive complexity that researchers have discovered within even the simplest living cell.

**Systems Biology – the next paradigm for biology?**

<b>Molecular Biology</b>	<b>Systems Biology</b>
<b>Reductionism</b>	<b>Holism</b>
<b>Mechanism</b>	<b>Emergentism</b>
<b>Homeostasis</b>	<b>Robustness</b>

The fundamental concepts that constitute the foundations of contemporary systems biology include holism, emergentism, and robustness, compared to the concepts of reductionism, mechanism, and homeostasis, that form the foundations of molecular biology. [18] Holism is to be contrasted with reductionism which considers a system as merely composed of a sum of parts. Emergentism, the appearance of hierarchical levels of organization, is contrasted with mechanism of

independent linear events. Robustness refers to the preservation of the functionality of a system to a certain degree despite external or internal changes, while homeostasis refers to maintaining the stability of the state of a system.

Balliol College, University of Oxford announced,

"Biology is at a crossroads. We have realized that it is not genes but networks that create change and generate function – networks so rich and complex that understanding them requires mathematical and computer science methods, not only molecular biology and bioinformatics. The early promise of the genomic era has not been realized. Even the central dogma has come into question. Systems Biology is now an integral part of biology proper – modeling and simulation are standard practice. But its fundamental concepts and methods are far from settled. Even the basic aims are not precisely formulated." [19]

Among the different approaches to Systems Biology, what is known as an agent-oriented conceptual framework has proven to provide the best models that are consistent with empirical data. These can be divided into two categories:

"Heterogeneous computational/behavioral models have led to different forms of agent classification: examples are intelligent agents — when the agent behaviour is defined in terms of high level cognitive/mentalistic structures and processes, with an explicit symbolic representation of knowledge, interaction and related reasoning processes — and reactive agents — typically characterized by sub-symbolic (such as neural networks) or imperative computational models." [20].

The Vedantic view also proposes viewing life from the Organic Whole perspective, in which consciousness forms the supporting basis. The conscious agent is an important part of that view, but the absolute conception of a unifying center is not to be omitted if a proper conception is to be achieved.

### References

1. Nelson, V.R., et al. (2012) Transgenerational epigenetic effects of Apobec1 cytidine deaminase deficiency on testicular germ cell tumor susceptibility and embryonic viability. *Proc Natl Acad Sci USA* 109:E2766–E2773.
2. Noble, D., Physiology is rocking the foundations of evolutionary biology, (2013) *Experimental Physiology*, doi:10.1113/expphysiol.2012.071134. Noble, D. (2006). *The Music of Life* Oxford, OUP.
3. Mattick, J. S. (2012) Rocking the foundations of molecular genetics, *PNAS*, vol. 109, no. 41.
4. Darwin, C. (1859) *On the Origin of Species by Means of Natural Selection, or the Preservation of Favoured Races in the Struggle for Life*, London, John Murray.
5. Shapiro, J. A. (2011) *Evolution: a view from the 21st century*. Upper Saddle River, NJ, Pearson Education Inc.; Shapiro, J. A. (2009). "Revisiting the Central Dogma in the 21st

Century." *Annals of the New York Academy of Sciences* 1178: pp. 6-28.

6. Encyclopedia of DNA Elements  
<http://genome.ucsc.edu/ENCODE/> Accessed 30 April 2013.
7. McClintock, B. (1984) "The significance of responses of the genome to challenge" *Science* Vol. 226, pp. 792-801.
8. Kimura, M. (1985) The role of compensatory neutral mutations in molecular evolution. *Journal of Genetics* Vol. 64(1), pp. 7–19.
9. Lewontin, R. C. (2001) Gene, organism and environment: A new introduction. In: *Cycles of contingency: Developmental systems and evolution*, ed. Oyama, S., Griffiths, P. E. & Gray, R. D. MIT Press; Lewontin, R. C. (1974) The analysis of variance and the analysis of causes. *American Journal of Human Genetics* Vol. 26, pp. 400–411; Lewontin, R. C. (1991) *Biology as ideology: The doctrine of DNA*. Harper Perennial.
10. Nilsson, E., et al. (2012) "Environmentally induced epigenetic transgenerational inheritance of ovarian disease" *PLoS One* 7: e36129
11. Anway, M. D., et al. (2006) "Transgenerational effect of the endocrine disruptor vinclozolin on male spermatogenesis" *Journal of Andrology* Vol. 27, pp. 868-879.
12. Pembrey, M. E., et al. (2006) "Sex-specific, male-line transgenerational responses in humans." *European Journal of Human Genetics* Vol. 14, pp. 159-166.
13. Weaver, I. C. G., et al. (2004) "Epigenetic programming by maternal behavior" *Nature Neuroscience* Vol. 7, pp. 847-854.
14. Charney, E., (2012) Behavior genetics and postgenomics, *Behavioral and Brain Sciences* Vol. 35, pp. 331–410 doi:10.1017/S0140525X11002226
15. Noble, D. (2013) op cit.
16. Puri, B.M., (November 2012) The Science of Spiritual Biology, *The Harmonizer*.
17. Oyama, S., Griffiths, P.E., and Gray, R.D. (2001). *Cycles of Contingency: Developmental Systems and Evolution*. Cambridge, Mass.: MIT Press.
18. Marcum, J. A., (2009). *Conceptual foundations of systems biology: An introduction*, Nova Science Publishers, Inc.
19. Conceptual foundations of systems biology  
<http://www.balliol.ox.ac.uk/BII/projects/biology>  
Accessed 30 April 2013
20. Cannata, N., et al. (2005) An Agent-Oriented Conceptual Framework for Systems Biology, Priami C., et al. (Eds.): *Trans. on Comput.Syst.Biol.* III LNBI 3737, pp. 105–122.