

# Re: Article: Mountains of new data are challenging old views

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- *From:* "John W Edser" <edser@xxxxxxxxxxxxxxxx>
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"Robert Karl Stonjek" <rstonjek@xxxxxxxxxxxxxxxx> wrote:–

Genome 2.0  
Mountains of new data are challenging old views  
Patrick Barry  
snip<  
..Crick expounded what he called the "central dogma" of molecular biology: DNA's genetic information flows strictly one way, from a gene through a series of steps that ends in the creation of a protein.

JE:–

This is all the information that is required to refute today's Neo Darwinian notion that selection can act empirically at the gene level of selection. Because the arrow remains strictly one way prohibiting Lamarkian inheritance, selection can only operate on the phenotype level and never at the genotype level. I have been repeating this point here for about 10 years. Yet almost all Neo Darwinian models continue to assume that selection can validly operate at the gene level. The basic, simple, biological fact remains that not one single phenotype can validly be claimed to remain separate in fitness to any another within the one, same Darwinian fertile form, i.e.all the phenotypes within one fertile form have just the one, same Darwinian fitness and have to be selected together i.e they remain 100% fitness epistatic. Just because the genes for these phenotypes can independently segregate at meiosis does not mean that a phenotype coded by one of these alleles can validly be regarded within as fitness independent which is required to allow the popular heuristic proposition that selection operates at the gene level. Independent gene segregation does NOT allow the inductive leap that genes remain independently fit. What this means to all Neo Darwinian gene centric models is that alleles at minimally TWO loci and not just the one assumed by gene centric Neo Darwinism remains MINIMALLY VALID. IOW all gene centric models that deploy just the one locus remain critically uncorrected because they were oversimplified. Such an uncorrected oversimplification can allow a reversal of cause and effect within the model. My example is Hamilton's Rule. If you correct the rule  $rb > c$  to allow just this minimal level of gene fitness epistasis (e) it becomes  $(r^e) b >$

Re: Article: Mountains of new data are challenging old views

c where  $e=2$  minimally (not just 1 so it can remain deleted and forgotten). The effect this has is to prove that MINIMALLY Hamilton's rule is out by 100%. It is not enough to sacrifice yourself to two brothers related 0.5 because  $2*0.5 = 1$  but to four of them because  $4*(0.5^2) = 1$  as a valid MINIMAL gene fitness epistatic model.

That principle developed into a modern orthodoxy, according to which a genome is a collection of discrete genes located at specific spots along a strand of DNA. This old view got the basics right: that genes encode proteins and that proteins do the myriad work necessary to keep an organism alive.

JE:–

All population genetics models assume that a pattern of independent segregation as described by the HW distribution allows the false inductive inference that each of these genes remains empirically independently selectable. A correct minimal model must tie any proposed empirical fitness (no matter how fitness is defined) to TWO loci and not just the one no matter if they independently segregate or not.

Researchers slowly realized, however, that genes occupy only about 1.5 percent of the genome. The other 98.5 percent, dubbed "junk DNA," was regarded as useless scraps left over from billions of years of random genetic mutations. As geneticists' knowledge progressed, this basic picture remained largely unquestioned. "At one time, people said, 'Why even bother to sequence the whole genome? Why not just sequence the [protein-coding part]?"' says Anindya Dutta, a geneticist at the University of Virginia in Charlottesville.

JE:–

It remained unquestioned for so long because population geneticists did not wish to correct a critical oversimplification of Darwinian evolution by natural selection because if they did so things like Hamilton's Rule, which remains the darling of population genetics, becomes untenable even as a simplified model. Researcher's like Moran et al, continue to claim (like the discredited mutationist claimed), that just a random process all-on-its-own, which in this case is random genetic drift and not the random mutation of the mutationist, can validly constitute evolution and not just temporal variation reducing evolutionary theory to the ignominious status of non falsifiable. The simple fact is the people doing these things to evolutionary theory are mathematicians and NOT scientists. Mathematics is not a science.

Re: Article: Mountains of new data are challenging old views

Closer examination of the full human genome is now causing scientists to return to some questions they thought they had settled. For one, they're revisiting the very notion of what a gene is. Rather than being distinct segments of code amid otherwise empty stretches of DNA—like houses along a barren country road—single genes are proving to be fragmented, intertwined with other genes, and scattered across the whole genome.

JE:—

As the deleted—from—all—population—genetics—models: gene fitness epistasis, predicts.

Even more surprisingly, the junk DNA may not be junk after all. Most of this supposedly useless DNA now appears to produce transcriptions of its genetic code, boosting the raw information output of the genome to about 62 times what genes alone would produce. If these active nongene regions don't carry code for making proteins, just what does their activity accomplish?

JE:—

Non coding DNA of the genome remains epistatic in FITNESS to the coding DNA.

"What we thought was important before was really just the tip of the iceberg," says Hui Ge of the Whitehead Institute for Biomedical Research in Cambridge, Mass.

With the genome sequence in hand, exploration has moved at a brisk pace during the past 6 years. A milestone was reached in June, when a project called the Encyclopedia of DNA Elements (ENCODE) thoroughly mapped the functional regions in 1 percent of the human genome. The effort involved was staggering: Thirty-five teams of scientists from around the world worked for 4 years and compiled more than 600 million data points, the consortium reported in the June 14 Nature.

From the accumulating mountains of data, scientists are building a new

picture of how the genome works as a whole. They have found mutations in nongene regions of DNA that are linked to common diseases such as diabetes and forms of cancer. And some researchers propose that DNA once labeled junk

could have spawned the complex bodies of higher organisms—even the complexities of the human brain.

SECOND FIDDLE TO A SUPERSTAR

In the emerging picture of the genome's functioning, many of the key

Re: Article: Mountains of new data are challenging old views

elements identified so far are molecules of RNA, a chemical cousin of DNA. In the old central dogma, RNA had a strictly subservient role in the all-important task of making proteins.

JE:–

The REVISED central dogma allows a 100% reversible relationship between DNA <-> RNA (representing on its own, just an empty tautology). However it also described a critical non reversible relationship between DNA <-> RNA --> polypeptide allowing an empirically falsifiable proposition for all of genetics to emerge from the original tautology.

An RNA molecule is made from units of genetic code strung together, much like DNA. But while DNA has two strands twisted together into a double helix, RNA usually has only a single strand.

Protein synthesis begins when the two strands of a section of DNA unzip. Units of RNA then pair up with their counterparts on one of the DNA strands, forming a complementary messenger RNA (mRNA) molecule. The mRNA detaches and floats off to other parts of the cell, where it hooks up with machinery that transcribes its coded message into a protein.

If RNA's only job were making proteins, then nearly all the RNAs produced in cells should be transcripts of protein-coding genes. (A small fraction of RNAs serve in the protein-transcription machinery.) But in 2005, Jill Cheng and her colleagues at Affymetrix, a genomics company in Santa Clara, Calif., showed that less than half of the RNA produced by 10 of the chromosomes in human cells represented transcripts of traditional genes. In the team's experiments, 57 percent of the RNA was transcribed from noncoding, "junk" regions.

The results from ENCODE were even more striking. In the slice of DNA studied in that project, between 74 percent and 93 percent of the genome produced RNA transcripts. What becomes of this tremendous output is uncertain. John M. Greally of the Albert Einstein College of Medicine in New York says it's likely that some portion of it is made accidentally and simply discarded. But the discovery that so much of the genome is being transcribed into RNA underscores how out-of-date the central dogma has become.

JE:–

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The revised central dogma is NOT "out-of date" just the continued misuse of it within synthetic genetics based on uncorrected, simplified/oversimplified models of Darwinian evolution by natural selection.

Indeed, the closer researchers look, the more functions they find that RNA transcripts perform. An alphabet soup of new acronyms describes the newfound roles of RNAs. First there were short nuclear RNAs (snRNAs) and short nucleolar RNAs (snoRNAs), both of which reside inside the nucleus and help control production of other RNAs. These were joined by microRNAs (miRNAs) and short interfering RNAs (siRNAs), which can modulate the activity of protein-coding genes. In mice, about 34,000 of the RNA transcripts produced by the genome are nonprotein-coding, outnumbering the roughly 32,000 transcripts that code for proteins, according to a 2005 study by an international group of scientists called the Functional Annotation of Mouse Consortium.

JE:–

The scientific method has a tried and tested way of dealing with this (if mathematical allow it to do so). If some non coding DNA (this DNA remains the overwhelming majority of the genome) transcribe RNA's it would be remains prudent to assume these RNA's must be doing something and \_entirely imprudent\_ to assume that they do nothing. It is the mathematically based population genetics applet which remains the big problem; nobody wants to upset it.

These new families of RNAs add a layer of regulation that fine-tunes the production of proteins. While scientists already knew that some proteins influence the activity of other genes, "there are many more RNAs than proteins that play a regulatory role," Ge says. Gene regulation may not sound sexy, but it's a powerful way for a cell to evolve complex behaviors using the tools–proteins–that it already has. Consider the difference between a one–bedroom bungalow and an ornate, three–story McMansion.

JE:–

Yet again I call any interested reader's attention to the model proposed by C.H. Waddington over 50 years ago which modified Haldane's basic model (which continues to form the basis of all population genetics models) which I posted twice to sbe. Waddington \_minimally included\_, i.e. did not entirely exclude gene fitness epistasis within the HW distribution as the new variables: developed in environment X and selected in environment X. This seems to have been missed by everybody.

Re: Article: Mountains of new data are challenging old views

Both are made from roughly the same materials—lumber, drywall, wiring, plumbing—and are put together with the same tools—hammers, saws, nails, and screws. What makes the mansion more complex is the way that its construction is orchestrated by rules that specify when and where each tool and material must be used.

JE:—

All of these rules require an epistatic gene fitness. Delete this and you delete the rules.

snip for brevity<

"The same sequences are being used for multiple functions," says Thomas R. Gingeras of Affymetrix. That introduces complications into the evolution of the genome, which had until recently been assumed to act through single DNA mutations affecting single genes. Now, "a mutation in one of those sequences has to be interpreted not only in terms of [one gene], but [of] all the other transcripts going through the region," Gingeras explains.

JE:—

In synthetic genetics, which attempts to join Mendelian analytical genetics with Darwinian evolutionary theory, this is termed gene fitness epistasis. It remains deleted from every population genetics model as a critical oversimplification (no matter how you define fitness).

The implications of this single mutation—multiple consequence model are still a matter of debate. In some cases, the RNA transcripts from DNA that overlaps a protein—coding gene regulate that same gene, so a mutation could affect both the structure and the regulation of a protein. But often, those transcripts regulate genes that are far away, or even on different chromosomes. This complex interweaving of genes, transcripts, and regulation makes the net effect of a single mutation on an organism much more difficult to predict, Gingeras says. More fundamentally, it muddies scientists' conception of just what

Re: Article: Mountains of new data are challenging old views

constitutes a gene. In the established definition, a gene is a discrete region of DNA that produces a single, identifiable protein in a cell. But the functioning of a protein often depends on a host of RNAs that control its activity. If a stretch of DNA known to be a protein-coding gene also produces regulatory RNAs essential for several other genes, is it somehow a part of all those other genes as well?

JE:–

Welcome to the difficult empirical world of gene fitness epistasis (which includes pleiotrophic effects of the same gene). The neat and tidy population genetics models wrongly equated the independent segregation of genes with independent gene fitness by allowing an independent gene centric level of selection, which in turn, allowed Hamilton's Rule and Dawkins' popular "selfish gene" interpretation (making Dawkins millions). However all of this represented just a misused heuristic oversimplification of empirical reality. The net result: the misuse of these models misrepresented evolutionary theory to the general public. Within these uncorrected models empirically falsifiable cause and effect was allowed to become reversed allowing organism fitness altruism to evolve even when this remained 100% prohibited within Darwinism as a falsification of that theory. It was Darwinism which provided the required empirically falsifiable theory from which all of these non refutable models remain critically oversimplified. The absurdity of the situation: an oversimplified model of a theory was allowed to contest and win against the very theory it was oversimplified from. Mathematics is most certainly not a science.

snip for brevity<

Thanks Robert,

Regards,

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