Does gene duplication provide the engine for evolution?

Jerry Bergman

Proponents of the gene-duplication hypothesis of evolution argue that a mutation can cause the duplication of a gene that allows one copy of the gene to mutate and evolve to perform a novel function, while allowing the other copy of the gene to continue to perform the original gene's function. Gene duplication is now widely believed by Darwinists to be the main source of all new genes. A review of the evidence shows that there are numerous problems and contradictions in this theory and the empirical evidence indicates that gene duplication has a role in variation within kinds but not in evolution. Darwinists therefore have nothing more to go on than to depend heavily upon extrapolations from gene similarities—a circular argument founded upon the assumption of evolution, and yet another example of evolutionary story telling.

'One of biology's greatest mysteries is how an organism as simple as a one-celled bacterium could give rise to something as complicated as a human.'[1] How life evolved from a few primordial genes to the tens of thousands of genes in higher organisms is still a major issue in Darwinism. The current primary hypothesis is that it occurred via gene duplication.[2–6] Shanks concluded that 'duplication is the way in which organisms acquire new genes. They do not appear by magic; they appear as the result of duplication.'[7] Ernst Mayr, one of the most respected Darwinists of the 20th century, agrees saying,

> 'Such a new gene is called a *paralogous* gene. At first, it will have the same function as its sister gene. However, it will usually evolve by having its own mutations and in due time it may acquire functions that differ from those of its sister gene. The original gene, however, will also evolve, and such direct descendants of the original gene are called *orthologous* genes.'[8]

Ohno goes further, concluding that 'gene duplication is the *only* means by which a new gene can arise' (emphasis mine), a view that Li concludes is 'largely valid'.[9] Furthermore, Ohno argues that not just genes but whole genomes have been duplicated in the past, causing 'great leaps in evolution—such as the transition from invertebrates to vertebrates—[which] could occur only if whole genomes were duplicated'. Kellis *et al*., agree that 'whole-genome duplication followed by massive gene loss and specialization has long been postulated as a powerful mechanism of evolutionary innovation'.[10,11]

Evolution by gene duplication is a form of exaptation.[12–14] Exaptation is the putative evolutionary process by which a structure that evolved for some other purpose is reassigned to its current role.

Evidence for gene duplication

Gene duplication does occur. For example, chromosomal recombination can result in the loss of a gene on one chromosome and the gain of an extra copy on the sister chromosome. Gene duplication can involve not only whole genes, but also parts of genes, several genes, parts of a chromosome, or even entire chromosomes.

All of these conditions are well known because they are important causes of disease (including cancer) and can even cause death. Eakin and Behringer conclude:

> 'Spontaneous duplication of the mammalian genome occurs in approximately 1% of fertilizations. Although one or more whole genome duplications are believed to have influenced vertebrate evolution, polyploidy of contemporary mammals is generally incompatible with normal development and function of all but a few tissues. Most often, divergence of ploidy from the diploid (2n) norm results in a disease state.'[15]

Li has noted that polyploidy (having more chromosomes than the usual diploid number) is 'likely to cause a severe imbalance in gene product, and their chance of being incorporated into the population is small'.[16] He concludes that for both vertebrates and invertebrates only when single genes, or a few genes, are duplicated is the possibility to evolve new genes created.

The gene-duplication idea has been researched for more than 30 years. Although first discussed by Haldane in 1932 and Miller in 1935, it was not discussed in detail until 1970 in Susumu Ohno's book, *Evolution by Gene Duplication*.[17] When Ohno proposed the idea many of his colleagues then considered his proposal 'outrageous'.[10] Gene duplication could not be evaluated experimentally, though, until the development of molecular biology techniques. Even now the primary evidence for gene duplication having a role in evolution must be inferred from gene similarity (i.e. an argument from homology). In the words of Hurles:

> 'The primary evidence that duplication has played a vital role in the evolution of new gene functions is the widespread existence of gene families. Members of a gene family that share a common ancestor as a result of a duplication event are denoted as being paralogous, distinguishing them from orthologous genes in different genomes, which

share a common ancestor as a result of a speciation event. Paralogous genes can often be found clustered within a genome, although dispersed paralogues, often with more diverse functions, are also common.'[18]

Because two genes are similar, though, does not prove that one was produced as a result of duplication.

The ideal method to prove the origin of functionally useful genes as a result of gene duplication would be to use the same techniques that have been used to prove the *adverse* effects of gene duplication. A child with an abnormality such as Down's syndrome (trisomy 21) is studied for genetic differences compared to the population as a whole and, especially, compared to his or her parents. If neither parent has a trisomy 21, and the cause, an extra chromosome 21, is determined to be a result of non-disjunction, it can be concluded that gene duplication has caused the abnormality. In the opposite case, if a child that has an exceptional ability is determined to have a gene not found in his parents and genetic studies of the family genetic history lend evidence of gene duplication and mutations in the child's genetic inheritance, this is powerful evidence for gene duplication having produced the advantageous trait. This method can be used to trace the process for several generations so as to determine cases that involve more than one mutation. So far, however, no one seems to have done this research, or if they have, the results have not supported the gene duplication theory and were not published

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The adverse effects of gene duplication, such as Down's syndrome, are well known. Although the methodology is available, evidence of functionally useful genes as a result of duplication is yet to be documented.

Chromosome doubling in plants

Chromosome abnormalities, such as triploidy, are usually harmful in most animals, especially higher animals. Conversely, polyploidy in plants is very common and can, in many circumstances, benefit the plant, although few researchers argue that it plays a significant role in large scale evolution.[19] Some evidence exists that polyploidy is a mechanism that produces variety within created kinds, similar to the effects of crossing over that occurs during meiosis. The specific effects of polyploidy depend on the environment and the plant. Polyploidy increases cell size, causing a reduction of the surface-to-volume ratio that can reduce the rate of some cell functions, including metabolism and growth. Conversely, some polyploids are more tolerant to drought and nutrient-deficient soils. In addition, some polyploids have greater resistance to pests and pathogens.[20] However, in all of these cases, a fitness cost exists, meaning that in many environments polyploidy is a disadvantage.

Much more research is needed for a proper understanding of plant polyploidy in order to determine under what specific conditions it is harmful and, conversely, under what specific conditions it is beneficial. As its biological function seems to be primarily to produce variety, it is not normally lethal (or even regularly lethal), as are most examples of animal polyploidy.

Some invertebrates can tolerate polyploidy. Male bees, for example, have a haploid number of chromosomes and females a diploid number. This does not cause the females to evolve faster, however, as the gene duplication theory might predict. In the rare cases of polyploidy in vertebrates, most examples involve unusual species that 'demonstrate a parthenogenetic mode of reproduction, lack heteromorphic sex chromosomes or have an environmentally induced sex-determining system'.[21]

Artificial gene duplication for experimental purposes has been developed in mice, but it has not provided any evidence for evolution because it is lethal:

> 'The production of tetraploid (4n) embryos has become a common experimental manipulation in the mouse. Although development of tetraploid mice has generally not been observed beyond mid-gestation [i.e. it is fatal], tetraploid:diploid (4n:2n) chimeras are widely used as a method for rescuing extra-embryonic defects [i.e. a genetic defect that is normally fatal can be artificially made to survive in the chimera].'[22]

Problems with the gene-duplication theory

The statistical challenge

Statistical evaluation of the predictions of the gene duplication theory does not appear to be favourable to it. For example, the theory predicts a positive correlation between organismal complexity and gene number, genome size and/or chromosome number. All of these predictions are contradicted by the evidence.

In regard to gene number, humans have about 25,000 genes,[23] while rice has 50,000.[24] In terms of genome size, the largest known genome does not occur in man, but rather in a bacterium! *Epulopiscium fishelsoni* carries 25 times as much DNA as a human cell, and one of its genes has been duplicated 85,000 times yet it is still a bacterium.[25]

In terms of chromosome number, the descending rank order of diploid numbers for a selection of animals is as follows: *Cambarus clarkii* (a crayfish) 200, dog 78, chicken 78, human 46, *Xenopus laevis* (South African clawed frog) 36, *Drosophila melanogaster* (fruit fly) 8, *Myrmecia pilosula* (an ant) 2. These results do not fit the predictions of the gene duplication theory—perhaps they imply that flying on your own wings or in airplanes (fruit fly and human, respectively) needs less chromosomal input than lying around in swamps (frog and crayfish, respectively).

Another statistical challenge has been noted by evolutionist genetics professor Steve Jones who concluded that an *inverse* relationship exists between the amount of DNA on one hand, and, on the other, both lethargic lifestyles and the speed at which organisms can evolve: the more DNA, the slower it is able to evolve. It takes a great deal of energy and resources to duplicate DNA, and the less of it an organism has, the faster it can reproduce (and the more efficient it is). Jones notes that 'all weeds have small genomes, while more established plants are packed with DNA and can take a month to make a single egg cell'.[26] Another example Jones cites is lungfish, which 'are stuffed with DNA (most of it with no apparent function) and their evolution has stalled altogether … bacteria are speedy and have no excess genetic material, while salamanders, torpid as they are, are filled with DNA'.[26] In his view, natural selection selects against gene duplication.

The evo-devo challenge

An important alternative to the Darwinists exclusive focus on genes is emerging in 'evo-devo' (evolutionary development theory). They claim (with a great deal of experimental evidence behind them) that the content of the genome is not the primary determinant of identity; it is the epigenetic control system that decides how the genes are used. 'A surprisingly small number of genes—"tool kit genes"—are the primary components for building *all* animals, and these genes emerged before … the Cambrian explosion [emphasis added].'[27] That means the essential genes have *not* changed significantly over time, contradicting the central claim of neo-Darwinism. The function of these genes can be compared to keys on a piano keyboard. The kind of music that is played (i.e. whether an embryo turns into a man or a mouse) is determined, not so much by the keys themselves, but by the player who strikes the keys and by the musical score that the player follows. If this is true, then arguments about gene duplication are irrelevant because 'evolution' occurs somewhere else (i.e. in the 'playing' and in 'musical score').

The functional challenge

Because whole genome duplication in animals is usually lethal, Ohno originally concluded that only two whole genome duplications had occurred throughout history; later he argued that a total of three had occurred.[28]

But Darwinists have admitted that even the process of single gene duplication is poorly understood. Lynch and Conery note that, although 'gene duplication has generally been viewed as a necessary source of material for the origin of evolutionary novelties, the rates of origin, loss, and preservation of gene duplicates are not well understood'.[29]

Photo by Robert Engelhardt. Wikipedia.org

Male bees have a haploid number of chromosomes whereas female bees are diploid. This however, does not cause females to evolve faster, as predicted by gene duplication theory.

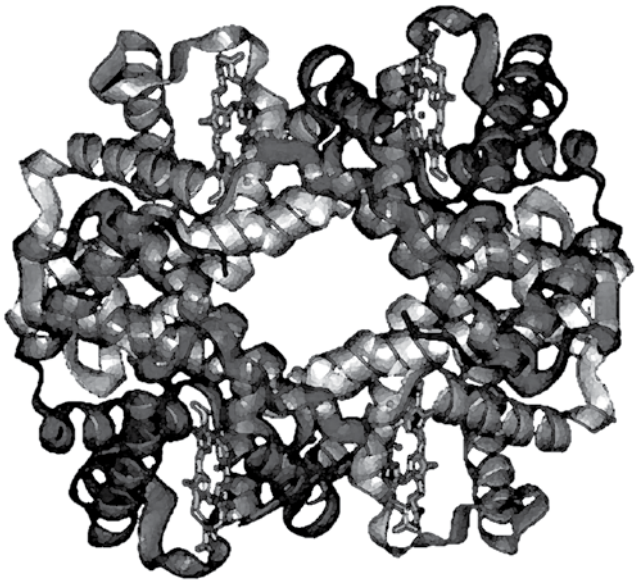
Behe and Snoke have pointed out that evolutionists must assume that multiple mutation events are required to produce a new functional gene, and each of the mutations must not be deleted until the gene has evolved to the degree that positive selection occurs.[30] Meanwhile however, a duplicated gene may produce either defective proteins that can be toxic or fatal, or, at the least, will tax the cell's resources and waste amino acids and energy. Because of this, natural selection acts on

> 'gene duplications, most often by deleting them from the gene pool or by degrading them into non-functional pseudogenes. This is because fully functional duplicated genes, in combination with the corresponding parent gene, produce abnormally abundant quantities of transcripts. This over-expression often alters the fragile molecular balance of gene products on a cellular level, ultimately resulting in deleterious phenotypic consequences.'[31]

Zhang, in a study of gene duplication, concluded that many duplicated genes become degenerate, nonfunctional pseudogenes and, in only 'rare cases', a 'new function may evolve', as is believed to have occurred in the douc langur monkey.[32] These langurs have two copies of an RNA-degrading enzyme gene, while other monkeys have only one copy. The extra copy aids the langur in digesting its specialized diet of leaves. Pseudogenes are considered by some to be damaged genes, and by others a source of new genes,[33] and recent work suggests that they may be functional.[10]

Yet another functional problem, noted by geneticist Manfred Schartl, is that

> 'it would be very difficult for the first tetraploid



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Although the globin gene family is the most commonly cited example of 'evolution by gene duplication', there is no evidence to support this. Moreover, it is known that the various globin variants of hemoglobin are designed to meet the differing demands for oxygen metabolism during the various stages of embryological, fetal and neonatal (and later) development.

> fish—those with four rather than the usual two copies of each chromosome—to engage in sexual reproduction.'[28]

Another putative mechanism is *partial duplication,* which results in a gene mosaic. This condition, called a *patchwork gene,* often consists of several different regions that are similar to other genes. Likewise, because of this similarity it is assumed that the gene segments haphazardly combined until a rare combination occurred that was beneficial, so that this gene was selected. The most common hypothetical example is the LDL (Low-Density Lipoprotein) receptor. This relationship is hypothesized because part of the LDL receptor is similar to the epidermal growth factor hormone.

Some theorize that this part of the gene evolved from a partial duplication of the epidermal growth factor gene. But how was the function of the LDL receptor maintained until this gene evolved? Without functional LDL receptors, a cell cannot effectively take in lipids, causing not only a supply deficiency in the cell, but also excess LDL in the blood, resulting in vascular problems from stroke, to embolisms, to heart disease. An example is hypercholesterolemia, a disease caused by defective lipid receptors. The victims often have strokes and heart attacks before their teens, even if on a low-fat diet.

Gene Families?

A group of genes that is closely related and theorized to have evolved by successive duplication is called a *gene family,* and an even larger group of genes that has structural similarities is titled a *gene superfamily*. No evidence of ancient genes exists to empirically document the theorized evolution of any gene family or superfamily. Instead, a gene 'family' is determined merely by making comparisons among existing genes, noting those that are similar.

But any arbitrary collection of items—words, ideas, or physical objects—can be grouped together to form 'families' and 'super families', and no exception exists for genes. An automobile and a lawnmower, for example, both belong to the 'four-wheeled machine family' but this does not necessarily imply common ancestry. We are therefore not compelled to believe that because some genes have similar components that they evolved from a common ancestor.

The first genes speculated to have evolved as a result of gene duplication were therefore the alpha and beta hemoglobin chains used to carry oxygen in erythrocytes.[9] The globin gene family is now the most commonly cited example of evolution by gene duplication. Myoglobin, a monomeric protein found mainly in muscle tissue where it serves as an intracellular storage site for oxygen, is hypothesized to have evolved into the tetrameric hemoglobin. Hemoglobin consists of two dimers, each one containing an alpha globin and a non-alpha globin. The ancestral non-alpha globin, called beta globin, supposedly gave rise to modern gamma, delta, and epsilon globin genes, and duplication of the alpha globin produced the epsilon and zeta globin genes. These globin variants are all used during different stages of embryological, fetal and neonatal (and later) development. The alpha, zeta and epsilon globin chains are produced in the early embryo and, during about the third month, the latter chains are replaced by the gamma chain and then later by the adult beta or delta chains at birth.

But all of this supposed evolution is based on nothing more than speculation. In real life, the multiple uses of globin molecules in oxygen metabolism is no more an indicator of blind replication than is the multiple use of cogwheels in a clockwork mechanism. Just as each cogwheel is specifically structured and located to do a particular job, is functionally integrated with its fellows to optimally do that job, and is precisely regulated to do it at the right time, so are the globin molecules designed to meet the differing demands for oxygen metabolism during the development of the organism. The site of hemoglobin synthesis also changes from yolk sac to liver to bone marrow during development, so differing environments and transport systems are also involved. Disruption to hemoglobin synthesis leads to a wide range of diseases, and neo-Darwinists have been unable to explain how development could have proceeded successfully before the complex system was all in place.

Another example of duplication is believed to be the evolution of the Human Major Histocompatibility Complex (MHC). But further study has likewise disputed some of these claims:

> 'Regions that are paralogous to the MHC on chromosomes 1, 9, and 19 have been proposed to result from ancient chromosomal duplications, al-

though this has been disputed based on phylogenetic analysis.'[34]

The gene duplication rate problem

Is gene duplication common enough to provide an adequate source for evolution? The rate can be as high as 17% in some bacteria to 65% in the plant *Arabidopsis* but these are extreme examples.[32] One empirical study by Lynch and Conery used steady-state demographic techniques to accurately determine the number of duplicate genes. This study evaluated seven completely sequenced genomes. From their research, they estimated that 'the average rate of duplication of a eukaryotic gene to be on the order of 0.01/gene/million years, which is of the same order of magnitude as the mutation rate per nucleotide site'. The researchers concluded from their study that '*the origin of a new function appears to be a very rare fate for a duplicate gene*' (emphasis mine).[35]

Another study by Behe and Snoke[30] evaluated gene duplication by using mathematical modeling and published gene-duplication data. Their model assumes the simplest route to produce a new gene function: a duplicated gene that is free from purifying selection and subject to point mutation, and the minimum number of biologically relevant modifications required to create a novel function. Because the minimum number of changes necessary for most new gene functions is greater than one altered amino acid, and the number of changes needed in DNA for each altered amino acid varies between one and three, definitive estimates are difficult to obtain. Nonetheless, a reasonable estimate can be obtained in attempting to evaluate the validity of the duplication-mutation model. Behe and Snoke concluded that, even given *liberal* estimates, fixation of features requiring changes in multiple residues requires both population sizes and numbers of generations so large that they 'seem prohibitive'. They concluded that gene duplication, coupled with point mutations, does *not* appear to be a promising mechanism for producing new proteins that require more than a single point mutation.

Standish concludes that the Behe-Snoke paper does not exclude the possibility that

> 'more complex mechanisms involving larger mutations and/or selection of intermediate states acting on duplicated genes may serve as engines of new gene production. The problem is that these other mechanisms appear to be even *more* complex and thus *less* probable than the conceptually simple duplication-point mutation model Behe and Snoke examined. While their paper suggests that other potential mechanisms should be rigorously examined before discarding gene duplication and modification as a potential mechanism of evolution, it clearly demonstrates that *even the most superficially reasonable sounding Darwinian mechanisms should be carefully evaluated before they are accepted as truly reasonable*' [emphases added].[36]

This study (and others) indicate(s) that gene duplication does *not* appear to provide Darwinists with a significant source of new genes. Although many, if not most, genes are assumed to have arisen by gene duplication, a clear lack of evidence exists for gene duplication as the source of specific genes.[12] Another major problem is 'distinguishing adaptations from exaptations'. In others words, how do we know a gene resulted from duplication, and not by some other means such as independent evolution?[37]

The indefinite regress problem

Gene duplication is a supposed method of exaptation—the takeover of an existing function to serve another purpose. Gould believed exaptation was so important that 'the defining notion of quirky functional shift [i.e. exaptation] might almost be equated with evolutionary change itself … in textbook parlance, "the origin of evolutionary novelites"'.[38] But this kind of argument is fundamentally flawed. If all evolutionary novelties arise from something else that was itself exapted from something else, then an indefinite regress results. The problem with an indefinite regress is that explanation 'A' depends on an earlier explanation 'B' that you have not given, and explanation 'B' itself depends upon an earlier explanation 'C' that you likewise have not given. While you may *appear* to be explaining something, there is no actual explanatory content—it is no explanation at all.

The conservation problem

Multiple information conservation mechanisms are at work in all living organisms, ranging from natural selection eliminating the unfit, through various reproductive and chromosomal controls, to error correction routines and DNA repair mechanisms, including (it appears) restoration from non-DNA sources. As a result, many, if not most, genes are 'evolutionarily conserved', meaning that they are very similar in many unrelated organisms, both 'simple' and complex, modern and ancient. Many genes in the assumed earliest forms of life are very similar to those in the most advanced forms. These facts argue strongly against gene duplication as a mechanism of evolution, because they indicate that most genes were optimally functional from the beginning.

Conclusions

The proposition that large scale evolution has occurred via gene duplication is contradicted by numerous lines of evidence. Little evidence currently exists to support the belief that gene duplication is a significant source of new genes, supporting one University of South Carolina molecular evolutionist's conclusion that scientists can not 'prove that [genome duplication] didn't happen, but [if it did], it didn't have a major impact. … For me, it's a dead issue'.[10]

It also is clear that the evidence for gene duplication at present is totally inferential, and not empirical or experimental. Chromosome duplication can produce useable variety—but only within what are most likely created kinds—in plants and invertebrates, and single gene duplication appears to do likewise in rare cases in vertebrates, but otherwise gene duplication generally causes disease and deformity. The existing experimental evidence does not support gene

duplication as a source of new genes for at least populations of fewer than one billion.[30] According to Hughes, 'Everything we've looked at [fails to] support the hypothesis.'[39] Darwinists promote gene duplication as an important means of evolution, not because of the evidence, but because they see no other viable mechanism to produce the required large number of new functional genes to turn a microbe into a microbiologist. In other words, evolution by gene-duplication is yet another example of just-so story-telling.

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