The Mutation Repair Systems: A Major Problem for Macroevolution

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Abstract

The ultimate source of all variation from which natural selection can operate is genetic mutations. Numerous cellular genetic repair systems exist to ensure that mutational expression is extremely rare. These repair systems pose major problems for evolution because virtually all genetic innovations caused by base pair changes will be corrected (and thus not expressed), or the cell itself will be destroyed. If genetic repair systems were perfect, then all macroevolution clearly would be impossible. These genetic repair systems argue against macroevolution, at least as caused by the accumulation of mutations.

Introduction

Evolutionary naturalism teaches that the creator of all forms of life is ultimately mistakes in DNA replication known as genetic mutations. As Eldredge (1982) argues:

> the *only truly significant force* underlying genetic, hence evolutionary, change is natural selection...genetic change is largely a function of natural selection working on a field of variation presented to it each generation. *New* features from time to time appear, *ultimately brought about by mutation*. Most mutations are harmful; some are neutral, or even beneficial. The neutral or beneficial ones hang on, and one day might prove to be a real advantage as the environment provides new challenges to the organisms.... Given enough time–and remember that geologists tell us that the earth is fully 4.5 billion years old–*all manner of change will accrue* (p. 69, emphasis added).

The problem of evolution via mutations has been summarized as follows:

> The evolution of mutation rates is governed by two opposing forces: the costs imposed by deleterious mutations, and the ability to adapt to a changing environment. In contrast to asexual populations, selection acting within a sexual population will always favor a mutation rate of zero (McVean and Hurst, 1997, p. 388).

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Accepted for publication: August 31, 2004

Deleterious mutations can cause not only major health problems, but also can result in the extinction of the species if unrepaired: "If these mistakes are not fixed, harmful mutations can accumulate, so the error-correcting-mismatch-repair-proteins are crucial" (Kolodner, 2000, p. 678). The number of mutations is reduced enormously by both the high fidelity of DNA replication and by the numerous highly effective repair systems. Depending on the specific organism, its environment, and other factors, unrepaired mutation rates are estimated to be only around 10^{-5} per gene per cell division (Puck et al., 1996; 1998; Mader, 1998), although such estimates will vary depending on the method used.

Mader (1998) concluded the proofreading process consists of a mechanism that achieves such high level of accuracy that "in the end, there is only one mistake for every one billion nucleotide pairs replicated" (p. 247). Other estimates differ, but all agree that the rate is extremely low. The proofreading accuracy of this system reduces the reproduction error rate estimated from approximately one mistake per 100,000 base pairs to about one per 10-billion base pairs–an astoundingly high level of accuracy (Radman and Wagner, 1988).

This low rate is reduced even further by several repair mechanisms built into the genetic system of all prokaryotes and eukaryotes to ensure that mistakes are very rare. Even organisms such as viruses that lack repair enzyme systems are protected to some degree because they use the cellular enzymes of their host for mutation repair. The arsenal of repair mechanisms are so accurate that they correct an esti-

mated 99.9 percent of initial errors (Friedberg, 2003; Jorde et al., 1997; Yang et al., 1996; Radman and Wagner, 1988). And those mutations that are not repaired often are fixed by cell maintenance mechanisms (Ridley, 2001; Harwood and Meuth, 1995).

As a result of these repair systems, the fidelity of replication is so high that fewer than an estimated three errors occur during the replication of an entire human being (three billion base pairs on the average). This "phenomenal accuracy" level "is ensured by several DNA repair enzymes, including some forms of DNA polymerase, that 'proofread' each daughter strand during and after its synthesis" (Audesirk and Audesirk, 2000, p. 130). The directionality of DNA allows the proofreading and repair enzymes to recognize the parental strand and then identify mismatches and, ultimately, correct the daughter strand, which runs in the opposite direction. This repair system is required because "in order for an organism to keep functioning, protecting the integrity of its genetic material is of utmost importance. The reason is simple: Accumulation of damage to the DNA can lead to harm, including cancer" (Marx, 1994b, p. 1321).

The accuracy of DNA repair is indicated in a study of 76,000 offspring of the survivors of the Hiroshima and Nagasaki atomic bomb blasts, who were exposed to a massive amount of radiation. The study found "no detectable effect could be seen for germ cells [and] DNA repair is at least in part responsible" (Jorde et al., 1997, p. 37). This was true even though substantial evidence of radiation effects was found in the survivors' somatic cells.

This fact is critical in the origins controversy because neo-Darwinism requires mutational change in germ-line cells, and the studies indicate that gametes are especially resistant to base-pair alteration mutations.

Preventing Mutations: The Buffered Code

The genetic code is said to be buffered, which means that the third letter of most amino acid codes can change with no effect on the results of the code. An example is GGU, GGC, GGA and GGG, all of which code for glycine. Consequently, if a mutation changes the third base in all cases, glycine will still be coded—negating or minimizing the effect of many point mutations (Ritter, 1996). For this reason, a mutation in the third base of the codon often does not change what amino acid is placed into the polypeptide being synthesized. Furthermore, if a mutation in the third position does occur, the result often codes for an amino that has a similar function, thus enabling the resulting new protein to have the same (or very close to the same) conformation as before. As a result, "a change in the third base in a codon . . . usually leads to a new codon for the same amino acid or a similar amino acid" (Ritter, 1996, p. 660). Of course, a mutation occasionally can result in an amino acid from a different family, or even a stop codon. In this case disease or death can result.

Also called the wobble effect, this mechanism enables anticodons on the tRNA to hydrogen-bond to more than one codon. In situations where a tRNA can pair with multiple codons, *all* of the codons specify the *same* amino acid. In humans, the wobble effect reduces to 32 the number of nuclear tRNAs required to read the 61 transcribed codons, saving the energy that would have been required to assemble the full set of 61 tRNAs. This system also reduces the size of the genome required because different genes usually are required to encode each unique tRNA. It also lowers the time needed to match a codon with an appropriate anticodon during translation. The mitochondrial translation mechanism allows the genetic code in mitochondria mRNAs to be decoded by only 24 tRNAs.

Furthermore, even a change in the first base in a code (the five prime base) often—but clearly not always—generates "a new codon that encodes an amino acid whose side chain is similar in polarity to the side chain of the amino acid specified by the original codon. Consequently, the polypeptide produced from the information in a gene with a point mutation is either commonly identical to the normal peptide or is similar in conformation and biological activity" (Ritter, 1996 p. 660). As a result, Ritter (1996) concludes "the polypeptide produced from the information in a gene with a point mutation is commonly identical to the normal peptide or is similar in conformation and biological activity. Since most organisms accumulate mutations over time, the buffering of the genetic code is of *major significance* from the standpoint of survival" (p. 660, emphasis added).

The code-buffering mechanism also is a major problem for macroevolution because it ensures that most of the comparatively rare, unrepaired mutations do not produce amino acid or conformational changes in the protein. Macroevolution by mutations *requires* changes in the protein's shape. Once an initiation codon is read, each consecutive nucleotide sequence usually represents another intact codon–and it is uncommon for the reading frame to shift once translation has begun, guaranteeing an extremely high fidelity of translation (Ritter, 1996).

Also, in placental mammals many gamete mutations do not result in hereditary changes because they prevent the fetus from developing to term. Partly for this reason, about one-third of all human embryos miscarry, ensuring that most unrepaired expressed germline mutations are not passed on. Non-neutral expressed mutations generally cause somatic cell disease and death. Likewise, mutations

in other life forms often cause the organism to die early in development, preventing it from passing the mutation onto offspring.

The DNA Proofreading and Repair System

The three major mechanisms to reduce errors are error avoidance (primarily due to the effectiveness of nucleotide selection), error correction during DNA replication (or proofreading), and advanced error correction to repair errors missed by the first two systems (Radman and Wagner, 1988).

Replicases play a primary role in error avoidance by accurately directing nucleotide pairing. They are also involved in the proofreading mechanism that removes mispaired nucleotides. Use of RNA primers and their automatic removal and replacement is another error-avoidance mechanism. Error frequency is slightly "greater during the joining of the first few amino acid residues in a new polypeptide strand" (Ritter, 1996, p. 725) than during its elongation. As a result, most unreported errors are removed during the last steps of protein processing, which usually clips off or modifies the first few nucleotides.

The high fidelity of DNA replication is also, in part, due to the various complex enzymatic repair processes completed by the DNA polymerase complex itself. The first level of polymerase repair is built into the structure of the DNA base pairs themselves. The DNA code consists of four chemical bases: thymine, adenine, cytosine, and guanine (RNA uses uracil instead of thymine). Adenine normally bonds stably only to thymine or uracil, while cytosine bonds only to guanine. If a nucleotide triphosphate selected by DNA polymerase from the cellular pool of nucleotides is complementary to the template nucleotide (A is complementary to T and C to G), it is converted to a nucleotide monophosphate. The energy released from this conversion is used to hydrogen-bond the two nucleotides according to the template provided by the nucleotide pattern. If the *wrong* nucleotide is bonded, the fit is unstable and the nucleotide generally is restored to its triphosphate form and released. Mader (1993) estimates that a mismatched nucleotide "slips through this selection process only once per 100,000 base pairs" (p. 243).

Another reason for the astounding replication accuracy is the existence of several different proofreading and repair systems that involve several dozen different complex enzymes (Sutherland and Woodland, 1990). As Ritter (1996) notes: "The survival of individual organisms and species of organisms depends upon the accurate replication of the genetic information" (p. 725). Multiple DNA repair pathways exist, each specializing in a specific type of damage (Culotta and Koshland, 1994). In addition most organisms manufacture numerous enzymes that can repair certain kinds of DNA damage. In humans, about 50 enzymes are known to be involved in DNA repair.

The internal errors that occasionally occur during DNA replication usually are corrected because the DNA polymerase complex also functions as a proofreader. Mismatch repair involves a multiprotein complex that recognizes mismatched bases and utilizes multiple enzymes to replace the mismatched nucleotide residue with the correct residue. One factor that can trigger the repair is the fact that a mismatch produces a base pair complex of the *wrong diameter*, and as a result the mismatched nucleotide causes a pause in replication. This triggers a process that usually results in the mismatched nucleotide being excised from the daughter strand.

The correct pair is one pyrimidine (a single-ring molecule) and one purine (a double-ringed molecule); an incorrect pair would consist of two purines (producing a pair larger than normal) or two pyrimidines (producing a pair thinner than normal). After this level of proofreading has occurred, "the error rate is only one mistake per 10 million base pairs" (Mader, 1993, p. 243). Normally, only if a purine pairs with the wrong pyrimidine (A-C, G-T) can the mistake slip by, but, even in this case, the mistake is often repaired by other repair mechanisms.

Mutations usually can cause permanent base-pair changes only in the unlikely event that both bases are changed simultaneously, such as in a double strand break. The DNA polymerase repair system uses the original DNA strand to determine the correct base (the copying machinery can determine which is the original and which is the compliment), and also which repair bases are required (Ridley, 2001). In addition, the repair system can distinguish the daughter (the copy) and parent (the original) strands by mechanisms such as their extent of methylation–the newly synthesized DNA strand is not tagged with methyl groups until after it is checked (Radman and Wagner, 1988). Parent-daughter strand discrimination is critical because the replacement of the parent-strand nucleotides would cause error propagation instead of error correction. Consequently, if *both* strands of the DNA molecule are damaged in the same region, correct repair is less likely–and if the cell divides and reproduces, the mutation will be passed on. Thus, in order for a mutation to slip by this repair mechanism, damage must occur on both DNA strands—an extremely unlikely situation.

Even the most deadly type of damage, the double strand breaks—where both phosphate backbones are severed—can be repaired by yet another repair mechanism (Bartek and

Lukas, 2003; Bakkenist and Kasten, 2003). This system induces intermolecular auto phosphorylation of several target proteins that are linked to signaling networks. These networks slow the cell's progression through cell-division and also stimulate the repair of the double strand break (Bartek and Lukas, 2003). Yet another mechanism is able to repair the Y chromosome. Since it does not have a corresponding chromosome (i.e., part of a chromosome pair), as does every other chromosome, it has back-up copies of critical genes (Rozen et al., 2003; Skaletsky et al., 2003; Willard, 2003). The chromosome then forms a loop so that the defective gene can use the copy as a template to make repairs.

If the spell-checker gene is damaged and the corrector protein is not properly able to scan for genetic errors (or detect and repair them) mistakes will accumulate rapidly in the genes that the checker system was designed to check. If the genes that prevent cells from dividing uncontrollably are affected adversely, cancer often will result. Colon cancer owes its prevalence to the fact that intestinal-lining cells divide at such a rapid rate that the entire intestinal track lining is replaced in about three days. This vividly illustrates the crucial role served by the spell-checker system.

Damage to Repair Systems Causes Disease

Many other diseases appear to result from defects in the repair system, which allow mutations to go uncorrected. The repair mechanism is critical for life because the harm caused by mutations can be enormous, and includes numerous diseases such as cancer (Bakkenist and Kasten, 2003; Aldhous, 1995). For example, a defective "mismatch repair" protein causes non-polyposis colon-cancer (Modrich, 1994). The hereditary defect involving one of two genes called hMLH1 and hMSH2 found on chromosomes 3 and 2 respectively may cause as many as 22,000 cases of colon cancer annually (Culotta and Koshland, 1993). These two genes are part of a DNA repair pathway "that may provide one of the fundamental routes to cancer when it is disrupted," and the two gene products "spot mismatches and orchestrate the enzymes that effect repairs" (Service, 1994, p. 1559). Many diseases such as *Fanconi's anemia*, *ataxia-telangiectasia*, and *Cockayne's syndrome* occur as a result of a defective repair mechanism.

Tumor Suppressor Control Systems

Some systems can block the reproduction of cells with DNA damage and direct its repair or, if the damage cannot be repaired, destroy the cell by apoptosis (discussed below). These systems can correct the damage that can cause tumors or cancer, and for this reason are called tumor suppressor systems. A protein known as pRB operates by controlling the cell cycle, specifically by functioning as a signal transducer to connect the "cell-cycle clock" with the transcriptional machinery (Weinberg, 1995, p. 323). If pRB function is impaired, full cell-cycle control is lost and, consequently, this important mechanism for controlling cell proliferation also is impaired. For this reason, pRB serves as a tumor suppressor, specifically in retinoblastoma and certain other tumors.

The p53 Repair Mechanism

Among the numerous mechanisms involved in repairing or preventing the damage from altering the phenotype or being inherited, the most well-known example is the p53 tumor suppressor gene. P53 plays a critical role in cell-cycle regulation during times of genomic stress (Wang et al., 1995; Culotta, 1993). The cell cycle involves four major stages. The first, called Gap 1 (G-1), involves the synthesis of RNA and proteins in preparation for the next stages. DNA synthesis occurs during the second stage, called Synthesis (S). During the next stage, Gap 2 (G-2), the cell readies itself for cell division and completes any repairs needed. The last stage is either mitosis or meiosis and cell division (cytokinesis).

If a cell's DNA is damaged, p53 normally causes the cell to stop growing at the G-1 stage and triggers the repair process. The p53 gene is called the "guardian angel" of the genome because it protects the body from mutations by repairing them or, if they cannot be repaired, by destroying the affected cell, thereby preventing the mutation from being passed on to its offspring (Marx, 1994b). The p53 protein does this by monitoring the G-1 cell cycle check point and halting the cell cycle by expressing proteins that directly or indirectly trigger the DNA repair machinery and by interacting directly with repair proteins.

For example, DNA damage caused by ionizing radiation and certain chemical mutagens or ultraviolet radiation (which cause DNA strand breaks) can trigger p53 accumulation that may induce G-1 cell growth cycle arrest. This allows the cell to repair the DNA damage before replication; or, if it cannot be repaired or if repair fails, p53 triggers a self-destructive mechanism designed to destroy the defective cell by apoptosis (Marx, 1994b; Sancar, 1994).

p53 controls the cell cycle partly by encoding a transcription factor that activates the p21 gene to produce p21 protein. The p21 protein blocks the cell cycle by inhibiting all cyclin-Cdk complexes until the cell is repaired. The p21 protein also prevents the synthesis of long stretches of DNA, but will not block the manufacture of the shorter segments that are required for repair (Marx, 1994b). p21 also is involved in suppressing the transcription of various promoters that lack p53 binding sites, and even inhibits

helicase activity (DNA unwinding proteins), thus blocking DNA replication.

More is known about p53 than about any other cellular control protein, partially because its clear importance has produced an enormous amount of research on this gene in the past decade (Friedberg et al., 1995). The p53 gene, and likely many others that control the cell cycle, are pleiotropic; consequently, damage to the p53 gene affects several biochemical pathways. The protein produced by this gene also functions in the maintenance of genomic plasticity and cell integrity. It binds to several transcription-repair factors, including XPD (Rad3) and XPB, and is involved in strand-specific DNA repair via its C-terminal domain (Wang et al., 1995).

Apoptosis

If a cell cannot be repaired, p53 sends the cell into a complex programmed destruction cycle called apoptosis (Culotta and Koshland, 1993). Part of the means the cell uses to produce apoptotic cell destruction is to direct lysosomes to function as "suicide bags" by causing their membrane to break. As a result, their contents spill into the cytosol, causing the digestion of the cell from the inside out. If DNA mutations occur, the p53 molecule normally will repair or destroy the cell before the mutation causes problems. If a mutation occurs that causes p53 to malfunction, the damaged cells will not be destroyed, and consequently will be able to reproduce themselves and pass the mutation on to the cell's progeny. Even in this case, beneficial results hardly ever occur, and if the mutation is expressed, the result is usually disease (such as cancer).

Breeding a line of genetically altered mice that did not produce p53 protein has helped researchers to understand how this mechanism functions. In one study, mice were all born appearing perfectly normal, but after several weeks all mice lacking the p53 protein contained tumors–and by six months, all were dead or dying of tumors. Other studies have found that, of the 6.5-million people diagnosed with cancer last year, at least fully half had p53 mutations (Modrich, 1994).

A p53 mutation in a gamete is passed on to future generations by germ cells, while those originating in somatic cells can cause cancer or another disease. Persons who inherit this condition (called *Li-Fraumeni Syndrome*) usually have healthy childhoods, but by age 30 over half develop one or more cancers, including brain tumors, osteosarcoma, leukemia, and breast cancer. The inheritance of a defective p53 gene invariably causes cancer while the victim is quite young (often before they reproduce), and over 90 percent die of cancer before age 70 (Malkin, et al., 1990). Regardless of the cause of a cancer, p53 appears to function as a safeguard. Consequently, cancer often does not develop unless the p53 safeguard mechanism is damaged. Certain chemicals in tobacco, for example, disrupt the p53 gene and/or the protein repair process, which is why the use of all types of tobacco is a major cause of a wide variety of cancers (Service, 1994).

The body's mutation defense system often can help prevent mutated genes from causing damage even if one of the cell's tumor-suppressor systems is damaged. For example, a large set of repair systems is the heat shock protein family, such as hsp 90 (Ridley, 2001). These proteins help give the cell protection against damage that can be caused by heat or other stress. All of these protection mechanisms ensure that the mutations usually cannot cause problems in cells that have been exposed to mutagens. Like a triple set of brakes, if the first set fails, the second or third can take over. The Creator knew how the cell mechanisms could go wrong, and thus built in these complex mechanisms to repair or destroy mutated cells to prevent macroevolutionary changes and disease.

Pyrimidine Dimer Repair

Even a DNA pyrimidine dimer mutation (where two adjacent thymine or cytosine bases inappropriately bind together) can be repaired. Such dimer mutations typically are caused by ultraviolet light and are fairly common in skin cells. One repair method is termed light repair or photoreactivation repair because the process is initiated by visible light. Visible light activates an enzyme that breaks the pyrimidine dimer bonds, thus repairing the mutation (Black, 1999). When bacterial cultures are irradiated with ultraviolet light in order to induce mutations, they must be stored in a dark location in order to prevent the light-dependent cellular-repair mechanisms from reversing most of the new mutations.

Another type of repair called dark repair requires several enzyme-controlled reactions to trigger the necessary repair process (Black, 1999). Specifically, a restriction endonuclease cuts the damaged pyrimidine dimers at a precise location, and an exonuclease removes the dimers and nearby nucleotides (Jorde et al., 1997). Then a polymerase repairs the area, using the correctly positioned complementary DNA strand as a master template. After DNA polymerase synthesizes new DNA to replace the defective segment, a third enzyme rejoins the old and new sections. Once these are joined, DNA ligase repairs the nucleotide side framework structure. At least seven different genes code for the repair enzymes used in this repair system. First identified in *E. coli*, research has found that similar repair mechanisms are employed in many animals and humans (Rosenfeld, 1983).

Mutations in any one of these dimer repair genes can produce a defective repair mechanism, causing diseases such as xeroderma pigmentosum or skin cancer. In xeroderma pigmentosum patients, extensive freckling begins before age 10, followed by skin tumors, mostly on the Sun-exposed parts of the body. Severe cutaneous malignancies then develop, causing death as early as age 20. Avoiding all sources of ultraviolet light can reduce the incidence of tumors, but cannot permanently prevent the development of cancer.

Chromosome Breakage Repair

Chromosome breakage that occurs during either meiosis or mitosis is repaired by a mechanism that usually fixes the break "perfectly with no damage" (Jorde, 1997) to the daughter cells. These breaks can be caused by a variety of clastogens (chemicals or energy that break chromosomes), including ionizing radiation or even viral infections. Faulty chromosome repair causes, or is part of the cause of, many diseases, including *ataxia-telangiectasia*, *Bloom's syndrome*, *Fanconi's anemia* and others (Bakkenist and Kastan, 2003).

Ataxia telangiectasia is a rare-but-fatal childhood disease that adversely affects both neurological and immunological function (Savitsky, 1995). The gene, a somatic gene that directs repair of double-strand DNA breaks, requires mutations in both copies in order to produce the disease (Bakkenist and Kastan, 2003). An estimated 2 million Americans carry a damaged ataxia telangiectasia gene.

Many Other Repair Systems Exist

Yet another recently discovered repair mechanism, the nonsense-mediated mRNA decay repair pathway, repairs mRNA before it can be used to synthesize protein (Chin, 2001). Any mutation that causes exon skipping results in the mRNA being shifted into the nonsense-mediated mRNA decay repair pathway for repair (Liu et al., 2001). Or, if a defect in mRNA results in a damaged stop codon, the ribosomes cannot be released and all the ribosomes behind it will be stalled. This problem is detected by a specific RNA structure called a tmRNA, which binds near the defective mRNA. This step adds a specific mRNA section to the defective mRNA that allows the process of protein synthesis to continue until the ribosome reaches the new stop codon added by the tmRNA. The release factor then dissembles the ribosome, allowing the ribosomes that were piled-up to finish translating the mRNA strand. The protein made by this modified mRNA has an extra set of amino acids that must be cut off, a step completed by an enzyme referred to as a tail specific protease (Silber et al., 1992; Beebe, 2000; Pallen and Wren, 1997).

Still other repair systems exist that we do not yet fully understand. During the development of an animal, the organism somehow "knows" how many and what body parts are part of the design and where each one is to be located. This system can actually override an error in the DNA instructions to ensure proper development (Ridley, 2001). Cells even have "internal-care mechanisms that fix a further fraction of the errors that have made it through the proofreading and repair enzymes filters" (Ridley, 2001, p. 96).

This system also repairs damage due to background radiation, free radicals, and other sources. The current estimate is that each cell in the body takes about 10,000 hits daily from free radicals alone (which means each DNA strand is exposed to approximately 5,000 hits daily) (Autry, 2003). This equals about 630 quadrillion free-radical hits for each person every day. It is clear that without this repair system, life above the bacterial level could not survive. Although not discussed in this paper, all of these repair systems are "irreducibly complex" (Behe, 1996)—meaning that each component of a system cannot function independent of the remaining components of that system. Behe (1996) argues that neo-Darwinian evolution cannot account for the origin of such inter-dependent biological systems. In addition, several of these repair systems are enormously complex, and despite intense study, are still not fully understood.

The Repair Process Opposes Evolution

The repair process ensures an extremely low mutation rate that works against macroevolution because mutations are "essential for evolution" and ultimately "all genetic variation" originated from random changes in DNA base sequences, which represents the raw material for the evolutionary process (Audesirk and Audesirk, 1999, p.167). This conclusion implies that an increase in the mutation level will be beneficial because more germ-cell-line mutations produce more variations, all which provide the raw material that enables evolution to occur. Although Darwinists claim that, ultimately, mutations are the original source of all genetic variation, all informed societies have taken elaborate pains to do whatever is feasible to reduce the mutation level in their society to as low as possible. An extensive body of research since the turn of the century has concluded that the harm of mutations far outweighs any hypothetical benefits that they may confer to the organism (Bergman, 1995). In fact, a clearly beneficial mutation that results in a gain of "genetic information" has never been documented (Rust, 1992).

It is not yet known how effective the mutation repair system is for all life and may be less effective in lower life

forms (Selby, 1998). In these lower level organisms, such as bacteria, mutations are not always repaired as effectively as in most organisms, and even contribute to the genetic variability of the population (Anderson, 2003). Some mutations in bacteria evidently can even induce proteins that allow replication past double strand breaks, which introduces *more* mutations in certain genes and lower replication fidelity (a similar process in higher organisms may be occurring with the hsp90 protein). This increased maintenance of mutants in a bacterial population is believed to be a survival mechanism that allows at least some variants to survive in a hostile environment (Anderson, 2003).

Darwinists argue that enough mutations occur that are not repaired to allow evolution to occur. Some non-deleterious variance found in life no doubt is due to mutations. Given the significance of mutations for naturalism, though, it would seem that evolution would select for any mechanisms that increased the level of non-lethal mutations. According to neoDarwinism, the more of these mutations that occur, the greater the chance of producing structures that facilitate improving both survival and the animal's reproduction rate, and, consequently, evolution. A mechanism that reduces the mutation rate would impede the production of variations, which is the only ultimate source of macroevolution. Of course, mutations also would increase the likelihood of unfavorable changes, but most of these would be selected against quite rapidly. Thus, in the long run, these mutations would not be a concern.

The critical factor in driving macroevolution is the occurrence of genetic mutations that are advantageous, but these changes usually are possible only if many mutations occur–and Darwinists teach that, in the long run, the more mutations that occur, the greater the chances of producing a positive mutation. Consequently, they conclude, the negative mutations are a necessary but small price to pay for improvement.

Conversely, a creation model postulates that the genome was originally perfect, as were the many mechanisms designed to produce controlled genetic variety, such as genetic crossing over during meiosis, and sexual reproduction. Random genetic changes would virtually always disrupt the original design of the genome, and thus those that are expressed almost always would be harmful (Marx, 1994a, 1994b). The existence of the complex "elaborate machinery" to ensure high fidelity of DNA replication is fully consistent with a creation model. The repair system has been studied most thoroughly in bacteria, but the mechanism used is similar in most other organisms including mammals (Aboussekhra et al., 1995).

Evolution also would seem to select *against* highly effective repair mechanisms because they oppose the process that allows macroevolution to occur. Without sufficient genetic raw material, selection cannot take place to improve a species. Evolutionists counter by claiming that too many mistakes at one time are counter-productive. McVean and Hurst (1997) argue that the mutation rate is not zero due to a trade-off between "the benefits of reducing the deleterious mutation rate, and the costs imposed by increasing fidelity (such as the time and energy spent proofreading). Alternatively, there might be a physiological limit to the degree of accuracy in DNA replication" (p. 388).

Yet, minor genomic changes are useless, and only major genetic changes in several genes can produce sufficient innovation to generate complex new structures that will function as a complete, integrated unit. A literature search of over 15 million entries located neither a single article that attempted to explain the evolution of any of the mutation-repair mechanisms, nor an article that attempted to present evidence for a theory of how the repair mechanisms could have evolved. This finding confirms the conclusion of Behe (1996) that a complete lack of evidence exists for the biochemical evolution of nearly all cell structures, systems, and proteins.

Summary

Evolutionary naturalism teaches that the ultimate source of all genetically produced traits are mutations that occur in the germ-cell line. Thus, according to this theory, the human genome is comprised mainly of mutations that were selected because they provided a survival advantage in a given environment. A major problem with this postulate is that nearly all changes in the coding genes, the exons, and evidently also many other base pairs, will be corrected by the gene-repair system or will be prevented from being expressed. Furthermore, when this repair system is not functioning properly, the eventual result is mutations that cause biological problems, not progress (Hanawalt, 1994; Modrich, 1994). Thus, gene mutations in exons or other genetic malfunctions are, as a whole, clearly regressive and not beneficial or progressive.

Unless mutations can be repaired effectively, serious or lethal health problems usually result. We now know that faulty repair systems are the cause of many diseases, such as cancer. Even bacteria, which generate more "beneficial" mutations than higher organisms, still contain complex DNA repair systems. Without such repair systems, mutations would soon have extinguished all life that might have evolved. Without the mutation repair systems, UV light alone would have rapidly destroyed all animal life. All of these repair mechanisms are major impediments in allowing the expression of the genetic mistakes that allegedly

provide the raw material for macroevolution. Without these complex repair mechanisms, the organism would undergo a rapid mutational meltdown. Thus, the recent discovery of the many DNA mutation-repair systems is yet another scientific stumbling block to Darwinian macroevolution.

Acknowledgements

I wish to thank Susan Loeffel, M.D., David A. Demick, M.D., Wayne Frair, Ph.D., and Clifford Lillo, M.A., and Bert Thompson, Ph.D. for their helpful comments on an earlier draft of this paper.

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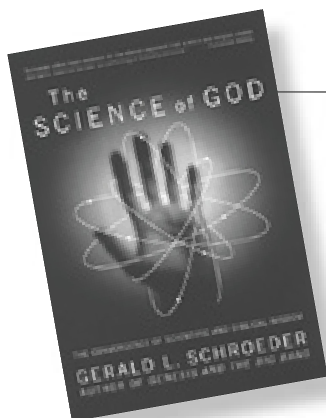

Book Review

The Science of God by Gerald Schroeder

Broadway Books, New York, 1998, $14.95

Don B. DeYoung (1998) gave an excellent review of the hardback edition of this book. Another excellent review of an earlier, similar book by Schroeder entitled *Genesis and the Big Bang* was given by Eugene F. Chaffin (1996). I will add further comments.

This book has become a classic in the field exploring the relationship between Scripture and science. For that reason it is must reading. Schroeder's attempt at reconciliation between the two is a "mixed bag" to Young Earth Creationists. As a positive point, he does a superb job in pointing out many inconsistencies in the commonly held Darwinism/gradualism concepts held so long in evolutionary circles.

Schroeder notes the significance of the tens of thousands of fossils found in the Burgess shale by Walcott in 1909 that were reburied in the Smithsonian museum for 80 years. These well-preserved fossils illustrate an "explosion" of every phyla of life at the very time life should have been gradually evolving. Schroeder shows how Darwin's concept of an evolutionary tree is totally missing from the fossil record. Transitional forms simply do not exist even after much exploration by earth scientists since Darwin's day. Rather, sudden appearance of new life forms is the trademark of paleontology.