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The Deterioration of the Human Genome Through Mutation Accumulation

Katja Spasic[1] and Hawa Camara[#]

[1]Clarksburg High School, Clarksburg, MD, USA
[#]Advisor

ABSTRACT

Mutations are held inside the human genome, which serves as an instruction manual for our body. The genome contains our total genetic parts, including our nucleotides, chromosomes, genes, DNA, and RNA. With the human mutation rate displaying a directly proportional relationship to each generation, concern has arisen amongst biologists. When looking at the continued accumulation of mutations, one could expect progressive decay within every function of humanity. However, the Primary Axiom would not be able to arise from this perspective. The Primary Axiom is an idea shaped by Neo-Darwinism, which states that humans were born from one initial genome after a series of mutations and natural selection. In this paper we will review the deleterious nature of mutations and the continued deterioration of the human genome since its inception. I will start by explaining the effects of the continued accumulation of various mutations and go on to address the process of natural selection.

Introduction

The human genome is a complex, non-linear and multi-dimensional part of our body that stores all our biological information. The genome is so complex that it cannot be replicated by any form of human technology thus far. Even if technology was one day able to replicate it, it wouldn't be able to communicate the sheer complexity of the genome. It is within our genome that random mutations occur. Random mutations are the cause of birth defects in infants that almost always follow into their adulthood. As the title suggests, these mutations are random, however they are genetically passed down. If the infant with the mutation goes on to bear children in adulthood, the mutation gene will more often than not be passed down to the child. This is precisely the problem. The accumulation of mutations from within our cells are increasing, and as a result diseases like cancer will continue to expand. Cancer in itself is the result of the continued accumulation of deleterious mutations from within our cells, which causes uncontrolled cell division.

The Primary Axiom argues that mutations are beneficial because they allow for variety within the genome, and therefore selection. According to the theory, mutations in the genome could be viewed as graphically bell-shaped. However, mutations are most often neutral and not beneficial. In fact, beneficial mutations are so rare that they are typically not shown on graphs. As a result, the graph will start to look very different. When looking at the graph on a -1 (negative), 0 (neutral), and 1 (positive) scale, the graph will produce half of a bell-shaped curve, with the positive mutations barely shown. This fact is widely accepted in the scientific community; however, it exposes a huge gap in the Primary Axiom theory. The idea of variation is also a huge crack in the theory. Suppose you were to take a math test and write English letters as opposed to numbers. Your answers will have a lot of variety; however, the variation will not be considered by the teacher when grading. Poor variation is not beneficial, no matter how you look at it.

The Rapid Growth of Mutations

The human mutation rate is now at an all-time high with around 75-175 misspellings per person. Typically, mutation rates approaching 1.0 or higher per person is considered reason to believe in genetic deterioration. Given that we are far above that number, we have to consider the number of genetic threats we are exposing future generations towards. Currently, there are around 8 billion human beings living on earth. Suppose we meet between 75 and 175 misspellings per person and consider a number of around 100 misspellings per person, per generation. This means that there will be roughly 800 billion new mutation variations coming from just this generation. Considering the fact that the human genome only contains roughly 3 billion nucleotides (molecules that link up to make nucleic acids which form DNA and RNA), it is clear that there is an overflow of mutation variance.

In addition, because of the directly proportional relationship between mutations and the human generation, each generation can be estimated to see an increase in misspellings per person. This will translate into even more mutation variation. The consequences of such high mutation rates will result in no amount of selection being able to reverse the damage that has been done, even if some of the mutation variations could be stopped in the future. This amount of genome damage is highly problematic. Because of the sheer amount of variation in munitions, genetically manifested diseases will become more and more frequent. New combinations of mutation variants can cause detrimental effects on the coming generations. For example, new and more powerful forms of cancer and cystic fibrosis can emerge from these combinations. Not only can modern day diseases continue to worsen, but there is a high possibility that new diseases will materialize because of new gene combinations. Now, we uncover that the problem isn't only the high mutation rate, but the remarkably high variation in mutations.

The human genome's functionality has always been a question within the scientific community. Looking at it from a logical perspective, given that the genome is made up of DNA, RNA, and proteins we can calculate the functionality of each of these and add them up. However, the equation for calculating the functionality of the human genome has instead been believed to be, a^0sel=% of functionality. In addition, nucleotides are not only functional but are poly functional. This can mean that the human genome's functionality could exceed 100%. Given how vastly complex the human genome is, it is likely that almost all of the genome is transcribed in both directions, meaning that the possibility of a functional genome is probable. This means that the equation would look slightly different, a^0sel>=100. Given such high functionality inside the genome, no mutations can be perfectly neutral. Instead, almost all mutations must be considered either deleterious or beneficial. In addition, beneficial mutations are extremely rare, with only 3/2000 genetic mutations resulting in positive mutations. This equates to 0.0015%, which we can multiply by 800 billion-the total mutation accumulation this generation. This gives us a total of 1 billion and 200 million beneficial mutations created this generation. This number is miniscule in comparison to the overall number of mutations at 800 billion. Assuming that the genome is truly functional, and most neutral mutations are harmful, it is clear to see that there has been irreparable damage done to the human genome.

Table 1. Many types of mutations- resulting in a remarkably high human mutation rate.

Mutation Type	Mutaions per Person	Nucleotides changed per person
1. Mitochondrial Mutations	less than 1	less than 1
2. Nucleotide Substitutions	75-175	75-175
3. Satellite Mutations	75-175	75-175
4. Deletions	2-6+	1-3000+
5. Duplications	2-6+	1-3000+
6. Inversions	numerous	thousands?
7. Conversions	thousands?	thousands?
total people per generation	**100+**	**thousands**

Power of Natural Selection?

Natural selection, according to the Primary Axiom, is why the accumulation of mutations can serve as a positive. If a deleterious mutation is negatively affecting the human population, natural selection will be there to make sure that the mutation is selected against. However, there is one fatal flaw with this thought process. Selection is not a magic wand that picks and chooses which mutations to get rid of and which to keep. If there is not only a surplus, but a superfluous of mutation variants, selection will not be able to generate enough power to get rid of all the harmful mutations. The key idea here is that selection cannot maintain better genomes. Selection is absolutely capable of working with genes, however, we fail to acknowledge that it simply cannot perform the same way at the genomic level.

Princess and the Nucleotide Paradox

There are many other theories in the Primary Axiom that were proven false in the coming generations. Take, for example, the idea that selection can select for or against many different traits at the same time. This is an assumption that is heavily relied upon in the Primary Axiom Theory. However, we now know that the idea of selection for multiple traits at the same time is completely inaccurate and very false. This raises questions as to the legitimacy of many assumptions made in the beginning of the theory.

The idea of the Princess and Nucleotide Paradox is that because selection occurs on the basis of a whole organism, molecular level mutations cannot be addressed. This introduces a phenotypic form of selection rather than genotypic. Natural selection is only capable of selecting on the basis of a phenotype, which is the basis of a whole organism (in this case humans). If natural selection was able to select based on a genotype it would be simply too easy. Selection would obviously get rid of as many deleterious mutations and keep all of the beneficial ones. Because selection does not select for or against humans on a molecular level, the idea of a pool of genes would be a long shot. Rather than jumbled in pools, all nucleotides should be seen as connected to each other- to each surrounding nucleotide. This runs contrary to the idea that nucleotides are individual units, exposing a huge crack in the Primary Axiom that was hardly addressed when making the theory.

However, there are certainly times where genetic disorders arising from poor gene combinations result in a less fit organism overall. If a child is born with extreme genetic disabilities, it could lead to untimely death, and in nature the child would most definitely be selected against. However, carriers of deleterious mutations can be born normally and live a normal life. Meeting in the middle once again, let's say that each person carries around 100 mutations. If 3/2000 people carry deleterious mutations, around 1 in 667 people will carry the same mutation. Given this proportion, 1 in every 7 (rounded up) humans will carry a mutation of harmful nature. This means that as people continue to reproduce, different combinations of genes will be produced, leading to more genetic disabilities. Because selection cannot look into the genome of each person, selection will not be able to get rid of future genetic sickness, and as a result mutations could potentially be lethal to the human race. The seemingly unbreakable power of natural selection is simply not as powerful as the Primary Axiom claims it to be.

Selection Cost

The natural selection process has a biological cost. This seems obvious- all selection must select against a certain part of the human population. As we now know, the human mutation rate is extremely high and seems to have no intention of slowing down. When looking at the current population and the rate at which people are having children, it becomes evident that mutations will continue to rise. Right now every two adults are averaging just over two children. This is beneficial in the sense that the human population rate will continue to increase, and we won't have a shortage on the reproductive scale. However, looking at the growth rate in terms of mutation rate, it's likely that new variations will continue to grow. The problem is that we cannot simply stop having children. If we were to decrease or limit the

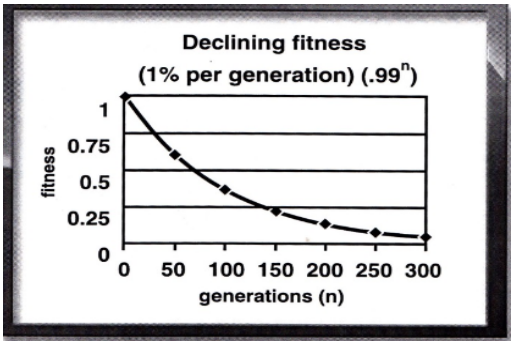
number of children per every two people on a global scale, humanity would shrink at a rapid and deadly rate. That is clearly not the answer to decreasing the mutation rate.

Aside from pure natural selection, not all children will go on to reproduce. Outside factors such as personal choice, disease, or accidental death are all part of the selection cost that must be ´paid´ for even before natural selection begins. This is why it is important to always maintain a firm surplus of any given population. If a population is only just meeting its reproductive abilities, all of these outside factors can come into effect and will lead to the death of the population. Because of both outside factors in natural selection and general population requirements for stability, it is believed that only around 10% of the human population could be used for natural selection per generation. This means that elimination of all mutant individuals is not only impossible in one generation, but would be lethal to attempt. Based on this crucial conclusion, it is plausible to suggest that natural selection is unable to select against different mutations at the same time.

To build on the idea of outside factors and randomness in natural selection, many genetic factors that allow for reproductive health are not heritable. For example, some people carry genes and mutations that work well in unison with one another, but would otherwise be harmful. The child will not directly get the same gene combinations, because genes are broken up when being transferred. As a result of this, some of the mutations that were beneficial for the carrier (parent) become deleterious and potentially deadly for the receiver (child). This is why we see parents with mutations considered neutral go on to have children with genetic disabilities. The combination of these genes is what truly determines the nature of the mutation. All of these forms of false selection must be accounted for before we even start the true natural selection process.

Only now do we get to the true natural selection process. Fitness measured on a biological scale is the trait in which natural selection acts precisely upon. Biological fitness is made measurable through tests of physicality, with components of fitness often being characteristics that you would need to survive in nature. Strength, intelligence, and reproductive potential all scale pretty high up in terms of measuring biological fitness. However, it has been proven that this trait is very rarely inherited. Biological fitness can have an inheritance rate as low as 0.004%.

The reason that fitness is so poorly inherited is because it isn't often measured by the strength of your genome (genotypic). Rather, fitness is the environmental and physical measure of strength, which is not purely genetically gifted. Of course, genetic disabilities will have an effect on biological fitness, however, many people with deleterious mutations in their genome can have extreme fitness. The measure of fitness is also adaptable to change amongst a string of generations. For example, if environmental conditions worsen and humans continue to be exposed to radiation. The radiation will start to affect the human genome. This will lead to certain mutations emerging and being passed down through each generation, changing what will be viewed as biological fitness. However, this form of fitness was made possible because the genome was affected. Natural selection based on the biological and physical fitness of an organism has little impact on future generations and can be viewed as borderline unproductive.



Graph 1. This image graphically showcases the declining rate of biological fitness per generation. As we can see, there is an inverse relationship between fitness and generations. According to Dr. Crow (1997), fitness is slowly deteriorating at a rate of 1-2% per generation. Adapted from: https://www.geneticentropy.org

Reproductive Elimination

In most cases mutant individuals are derived from randomness and invisible mutations that cannot be seen unless specifically tested for. Of course, if there is a very obvious genetic problem with one or both parents, it is likely that the child will inherit similar mutations and genes. However, to effectively reverse genomic deterioration, we have to address means in which we can stop mutant individuals from reproducing. History and social experiments done in attempts to lower the general population would tell us that it is impossible to truly stop reproduction and mutation growth on a global scale. Take, for example, the rapid increase in abortion rate and planned parenthood. Despite the fact that abortion was able to reduce the average family size, the mutation number continues to rise, showing a directly proportional relationship between abortion and mutation rate. One would think that abortion and mutation rate would be inversely related because of the declining family size, however this is not the case. There are simply too many variations of mutations to account for. This is causing mutation rates to grow just by having a positive population growth rate. Abortion is an artificial form of selection that showcases no indication of effective production against general mutation growth.

Because of selection cost, we are not in the position to artificially select against mutations. It would simply be population suicide. On a global scale this would be extremely difficult and dangerous to attempt. Artificial forms of selection are simply too probabilistic to rely on, and cannot be attempted without major biological cost. Natural selection holds the same issues as artificial selection, and sometimes to an even higher degree. Artificial selection is much more efficient and selective with its goals. With artificial selection, you can pinpoint which specific mutation within the genome you want to select against. Natural selection isn't as specific and it's unable to craft an effective method of completely eliminating unfit individuals from society. Despite artificial selection's reliance on probability, natural selection is purely based on probability because it is only able to reduce the probability that extreme mutant or unfit individuals will survive. Natural selection simply has a limited range of abilities.

The natural selection process is unable to make the same impact that it once could during the days of pre-industrialization. When humans were selected upon in nature (much like animals now), natural selection was able to get rid of many more genetically undesirable or biologically unfit individuals. In today's structure of society, many individuals are protected, and unfit or undesirable humans are allowed to continuously reproduce. This is good in spirit and allows for a more diverse society, however it is the reason as to why the accumulation of mutations will never be able to decline. When looking at a graph, the number of generations will be inversely proportional to biological fitness, and if fitness continues to decline at this rate we can expect an even faster pace of genomic degradation. The Primary Axiom never addressed these key flaws, or researched mutation levels' effect on the human genome. Neither artificial nor natural selection is able to effectively maintain, and especially create, a higher level of the human genome with such high levels of deterioration. In other words, creation on the genomic level cannot be possible by just selection, going against a claim that is central to the theory.

Conclusion

The direct and downward curve between the human generation and genomic health is highly problematic for the future of the human race. As a species, it points towards eventual death. Despite the Primary Axioms claim of genomic improvement over a series of mutations and natural selection, selection is a very limited weapon. Most deleterious mutations cannot be eliminated selectively, and as a result they begin accumulating exponentially. The human genome is now suffering because of these accumulations, and has been deteriorating due to mutations of deleterious nature. In addition, beneficial mutations are extremely infrequent. The idea that the human genome was developed based on mutations is highly unlikely because according to the Primary Axiom, scarcely any beneficial mutations existed in the initial genome. These few positive mutations could not have possibly been enough to create the complex nature of our human genome. Rather, it would have to have been something more direct causing an overall/near perfect genome to

occur. A theory of a pre-existing variation that arose by design is much more plausible than relying solely on the probabilistic nature of natural selection and the deleterious nature of mutations.

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