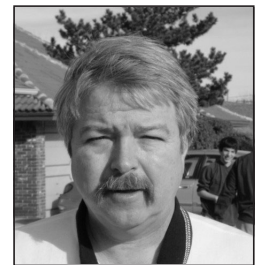


Random Worms: Evidence of Random and Nonrandom Processes in the Chromosomal Structure of Archaea, Bacteria and Eukaryotes

Glenn R. Morton and Gordon Simons

One of the central debates in Christian apologetics concerns the role of chance and randomness within living systems and the presumed incompatibility of chance with complex organisms containing high informational content. In order to address this issue, the chromosomal organization of genes for ten different species of varying levels of complexity was examined for evidence of randomness in the gene structure. The results show an interplay of random and nonrandom processes with the more complex eukaryotes evidencing more randomness in their genetic structure than is found in the simpler prokaryotic organisms: bacteria and archaea. While almost all anti-evolutionary views reject any role for chance or randomness in biology, we find that the Bible supports a much more compatible perspective.



Glenn Morton

Biology and chance

One of the philosophical issues about which Christians have debated over the past century concerns the role of chance in the biological realm. Many Christians have rejected any role for chance. The conservative creationist Henry Morris states: "Chance and design are antithetical concepts."¹

It is not only Christians opposed to evolution who reject chance in the biological realm. Rejection of chance in the biological realm is a common trait across religious and theological boundaries. The Jewish anti-evolutionist, Lee Spetner writes: "The information required for large-scale evolution cannot come from random variations."² (While noting that this second quote uses the word *random* rather than *chance*, we will not attempt to infer whether the author meant to convey a distinction. A discussion of terminology appears later.)

A member of the Reunification Church, Jonathan Wells wrote: "Furthermore, the integrated complexity of developmental programs cannot plausibly be attributed to chance."³

And even Islamic anti-evolutionists take the same position:

Laboratory experiments and probabilistic calculations have definitely made

it clear that the amino acids from which life arises cannot have been formed by chance. The cell, which supposedly emerged by chance under primitive and uncontrolled terrestrial conditions according to evolutionists, still cannot be synthesized even in the most sophisticated, high-tech laboratories of the 20th century.⁴

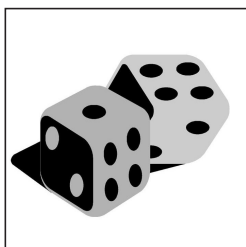
A major objective of the Intelligent Design movement has been to show that chance cannot work. Dembski states: "Now a little reflection makes clear that a pattern need not be given prior to an event to eliminate chance and implicate design."⁵



Gordon Simons

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There are many other Christians of varying theological persuasions who reject the role of chance in biology.⁶ Indeed, if this position is not the majority position in conservative Protestant theology, then it is very close to it.

Finally, we observe that Christians appear much more troubled by assertions of chance in biology than by chance in the nonlife sciences, for instance, in physics with the decay of nuclei.

The Bible and Chance

One of the difficulties raised by the rejection of chance in nature lies in the fact that God ordered or allowed the use of such systems at critical places in the biblical history. If God is incompatible with chance in his dealings with this world, it seems odd that he allowed and commanded the use of such systems. The *Urim and Thrummim* which the priest carried is widely believed to have been a tool for casting lots before the Lord.⁷ The Hebrews believed what Prov. 16:33 says: "The lot is cast into the lap, but every decision is from the Lord." Proverbs 18:18 would indicate that the Jews thought God was the true decision maker when chance was involved. That verse says: "Casting the lot settles disputes and keeps strong opponents apart." In 1 Chron. 24:1–5, 1 Chron. 24:31, and 1 Chron 25:8, David cast lots to determine the order of the service for the sanctuary officials. God used the chance lots of the sailors to identify Jonah as the source of their troubles (Jon. 1:7). In Lev. 16:8, God told the Israelites to cast lots for the sacrificial goat. God told Joshua to cast lots in order to identify Achan, the guilty keeper of the Canaanite booty. In Josh. 18:8, we see Joshua casting lots for the assignment of land to the various tribes. In Acts 1:24–26, the disciples used chance, the casting of lots, to determine who should take over the apostolic ministry of Judas. Because of the biblically widespread use of chance to determine God's will, it is truly amazing that many modern Christians reject chance in biology as being totally incompatible with God's control.

If God cannot control chance, how can he control the lots above? God predetermined the result yet used a tool of chance. If God cannot use chance, then one must logically conclude that God did not foreknow how the land would be divided among the tribes,

that God did not foreknow that Jonah would be picked, that God did not foreknow that Achan was the one who would be chosen or that Matthias would step into the apostolic line. This is a position which basically says that God is not omnipotent or omniscient. If God can use chance in his dealings with Israel and the early church, then why do we say he has no ability to use chance in biology? God can, has, and does control the stochastic process even if we do not understand how it happens.

One thing Christians must keep in mind is that our perspective on chance is not God's. Humans are not always able to distinguish between appearance of chance and the actuality of chance. But we cannot say that God is equally so limited. The molecules in a gas move according to deterministic laws, but the Maxwellian distribution of their velocities gives the appearance of chance. On the other hand, quantum phenomena appear to be the actuality of chance. But that might not be the view from God's perspective given the biblical references above. In biology, we see the fertilization of an egg as the result of a random or nearly random event. A single sperm may have only a one in fifty billion chance of being the "lucky" winner of the race to the egg. Yet God proclaims through Jeremiah: "Before I formed you in the womb I knew you, before you were born I set you apart" (1:5, NIV). If God were unable to control chance, why would he make such a statement?

Biological Evidence for Chance?

In the past, it has been difficult to actually test the chance hypothesis in biological systems. The discussion has revolved too often around debatable probability arguments. The standard argument says that there are too many possible combinations in proteins, or too many possible combinations in DNA/RNA for working sequences to be found by random mutation. These arguments are based on the assumption that very few sequences out of the entire ensemble of possibilities would be capable of performing the sought for task. Examples are legion but Gange provides a good one. He says:

Hemoglobin contains two trains totaling 574 cars—each selected from among twenty kinds of amino acids. The num-

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ber of ways we can assemble these hemoglobin trains is so vast that it is a trillion trillion (repeat twenty times more) times the entire number of stars in the universe, despite this, only one combination known to man carries oxygen most efficiently in your blood.⁸

The weakness of this argument is that Gange cannot prove the last phrase. How can he *know* that only one combination carries oxygen most efficiently? How can he *know* that hemoglobin is it? Since he has no way of comparing the efficiency of hemoglobin against all other possible molecules of that length, much less comparing it to molecules of shorter and longer length, his argument rests upon an untested assumption. On the evolutionary side, this argument is difficult to counter because, like Gange, one too cannot search and find a more efficient molecule so the argument boils down to an opinion about what is unobserved and what is unknown about biological molecules. One can have an opinion about such matters, but neither side can say much worth listening to scientifically.

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Is there a way to break out of this opinion-dominated trap? We believe there is, and the genome-sequencing projects provide a way to look at the genetic organization of various organisms. The genomes of hundreds of organisms have been sequenced in various mapping projects. These data provide an excellent platform from which to examine the role of randomness. If random processes have been active in the genome, then the structure of the chromosome should be consistent with what is expected from a random process. If there is no evidence for random processes and the genome is organized via nonrandom processes, then predictions from nonrandom models of the genome should be possible. In this article, we will test the role of randomness and nonrandomness by looking at the organization of the genes along the chromosomes.

We have examined the genetic organization for six bacteria from five species, two species of the archaea, and a plasmid found in *E. coli*. These organisms in general have one circular chromosome, the only exception being *Vibrio cholerae* which has two chromosomes, the second of which originally may have been a plasmid. At a more complex level, we also have examined the sixteen chromosomes of yeast; the eight chromosomes of the fruitfly, *Drosophila*

melanogaster; and the six chromosomes of the nematode, *Caenorabditus elegans*. We also examined but rejected as too incomplete at this time, the human genome. The results of our study show some interesting features of genetic organization relating to the central philosophical question of this article—What is the role of chance in biology?

Definitions

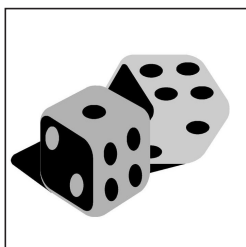
Here we will discuss *chance* and *randomness* in their varying usages.

It seems plausible to us that the widespread rejection of chance (and randomness) within the biological realm among various religious peoples is due to a widespread perception that the word chance rules out God as the causative agent—that it leaves no room for any understanding of intelligent design. In contrast, we have observed that the Bible conveys no such concern: chance mechanisms are fully under the sovereign control of God. Or, at the very least, they are never at odds with his permissive intents.

Russian mathematician A. N. Kolmogorov, in 1933, is credited with providing the first axiomatic definition of probability—a definition precise enough to gain the widespread acceptance of mathematicians, yet comprehensive enough to be applicable to a wide range of phenomena.⁹ His definition of probability places on a firm foundation the notions of *chance*, *randomness*, *random variables*, *random processes*, and a variety of related concepts, making possible a rigorous development of the subject of probability.

Mathematical treatments of probability date back to the seventeenth century when French mathematicians Blaise Pascal and Pierre de Fermat analyzed various questions of gaming and gambling. Over the intervening centuries, the subject has engaged the serious attention of many well-known scientists and mathematicians, among them Huygens, Jacob Bernoulli, Abraham de Moivre, Pierre de Laplace, Chebyshev, Markov and von Mises. Also, the subject of statistics uses probability theory at its foundation. Early uses of statistics to model biological phenomena trace back to Gregor Mendel¹⁰ and, more recently, to R. A. Fisher, who published widely on such subjects as eugenics, Mendelian inheritance, “Darwinian Evolution by Mutation,” “The Evolution of Dominance,” and much more. Moreover, he contributed widely, in fundamental ways, to the development of statistical tools and concepts.

So presently there is in place a widely applicable set of mathematical and statistical tools and concepts for modeling and analyzing biological structures and phenomena from a probabilistic perspective. However, a serious lack of understanding of these tools and concepts among non-scientists exists. In particular, most Christians lack a clear conceptual understanding of chance. Still, we believe it safe to assert that most Christians do have a fairly



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well-developed perception of what can be summarized by the phrase “chance mechanism” (such as dice, the roulette wheel, and coin tossing). Below, we will appeal to this intuitive understanding.

For the purposes of this article, we will opt for an intuitive definition of randomness. In particular, we will take *random* to mean a process relating to or being defined by events with a particular probability distribution. In this definition, there is no theological implication at all. We think this is an important point to realize about probability in the theological context. Saying that something has a definite probability of occurrence is not saying that something is totally unpredictable. Probabilities allow the prediction of the system behavior for a large number of iterations. If I have a coin, I can predict with a great deal of certainty that after two million flips of the coin, there will be very close to a 50-50 split between heads and tails. Probability and prediction are not totally incompatible.

We must place another caveat on what is meant by randomness. Randomness can only be measured against a model of randomness, i.e., a stochastic process or system. Such a process or system is inherently a mathematical “recipe” for manipulating the random occurrences and producing an output. The output may be determined from the input random events only after a complex calculation. To start simply, a coin is a simple 2-state stochastic (probabilistic) system. The die used on board games is a 6-state stochastic system. In these two examples, the probability of occurrence for each of the different states is identical, $\frac{1}{2}$ and $\frac{1}{6}$ respectively. But that does not have to be the case. One can manipulate the probabilities on a die and have an unequal probability among the six choices. These are termed “loaded dice.” Loaded dice will output a sequence of numbers that appears nonrandom if compared to the normal unloaded dice.

Other stochastic systems can be even more complex. The chance of a particular outcome might depend upon the state of affairs at the time the die is rolled. These are called Markov chains. The probability of an outcome depends upon the system state that exists *at the time*. While not subject to random chance, we do see an illustration of

this type of behavior in languages. If, in a sequence of English letters, the letter q is the current state of affairs, one can be nearly 100% certain that the next letter is a u. If one counts the symbols, one will generally find that e is a more common (higher probability) letter than z. Cryptologists use such frequency analysis to decipher coded texts. They arrive at a probabilistic model of what letters are intended by the coder. Probability models are also used in computer networks to avoid bottlenecks. Therefore, probabilistic models are not incompatible with engineering design.

How does one decide if a given sequence is random or influenced by a stochastic system? First, randomness is something that cannot be proven. After comparing a sequence of numbers with a given stochastic process, all one can ever really say is that the sequence is consistent with it being randomly generated by a particular stochastic process or that it is inconsistent with such a process. Secondly, if one is trying to decide if the numerical sequence 2,2,1,2,1,1,2 ... is random one needs to be sure that this sequence is the output of a 2-state stochastic system. If such a sequence was the outcome of a 6-sided die, the outcome is entirely *non-random when compared to an equal probability six-state system*. But if one has a Markov chain with heavy probability weighting for 1's and 2's, if the current state is a 1 or 2, then this output is entirely consistent with such a stochastic process. Thus, when examining the patterns seen in the gene strings, we need to examine several different probability models.

Chromosomal Organization

A chromosome consists of four nucleotides laid out in a double helix. This is the lowest level of organization for the chromosome. There are higher levels. Sequences of nucleotides are functionally connected forming a gene. Genes are systems of nucleotides which perform the function of providing information for the construction of proteins. This is not the end of the organization seen in the genome. At a still higher level of organization, the genes are strung out along the chromosome in groups of genes which all have the same transcription direction. The transcription direction is the direction in which the cellular machinery must read the

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gene in order to recover the proper protein information. There are two complementary strands of DNA in organisms, and genes can be found on either strand. Genes found on one strand are transcribed in one direction along the chromosome, and genes found on the opposite strand are transcribed in the other direction. Groups of genes with the same transcription direction are called *gene clusters* or *strings*. We will use the latter term, and to our knowledge this term is new.

A string is merely the consecutive genes transcribed in the same direction. It is the strings which will form the basis for our analysis. Intuitively, to a nonbiologist, it would seem that it really should not matter which direction a gene is transcribed. As we will see, this is not what is observed in the strings. Direction does matter and the amount it matters depends upon the organism.

As noted above, a gene lies along a chromosome and the biochemical machinery reads the nucleotide sequence of the gene and eventually translates that information into a protein. The gene can be read only in one direction by the machinery. But that direction is not constant for all genes on a given chromosome. Approximately half of the genes are transcribed in one direction and the other half in the opposite direction. For instance, *M. genitalium* has 297 genes which must be transcribed in the positive direction and 225 which must be transcribed oppositely in the negative direction. These genes are organized into 86 different strings—contiguous genes which must be transcribed in the same direction at the same time. String length is merely the number of genes in a string. Figure 1 below shows the string lengths for *M. genitalium*, the organism that, until recently, was the shortest known genome.

When one lists the sequence of numbers which represent the number of genes in a string, a question presents itself of immense philosophical importance to the issue of chance and randomness in biology. Is this sequence of numbers random or not? If it is random, then it would be clear evidence of random or chance processes occurring in biology and would directly speak to the issues raised in this article. If they are not random, but are ordered, then they would support the claims of the apologists that chance and random processes are not involved in biological organisms.

Why do gene strings exist? In the process of converting the information contained in DNA into proteins, a gene is first copied into mRNA which then in turn is read by the ribosome which produces the protein. If many mRNA copies of a gene are made, the ribosome will produce many copies of the protein. Two genes that are next to each other on the same DNA strand are transcribed into mRNA together. In these cases, the ribosome receives an mRNA molecule encoding for several proteins. The ribosome will recognize each mRNA separately and produce the correct protein. This is a useful procedure as it allows genes which are linked to the same biochemical processes to be transcribed together and allows the cell to operate efficiently. If several enzymes are required for a given reaction, this procedure ensures that all the proteins are created together. As we will see, this procedure only applies to the bacteria and archaea and not to the “higher” eukaryotes.

The Probability Models Compared with Gene Strings

We downloaded the huge flat files for the organisms listed in Table 1 from the National Center for Biotechnical Information and extracted the relevant gene string data arranged in chromosomes.¹¹ In the case of *D. melanogaster*, the full genome is not sequenced. The gene containing regions have been sequenced but regions of repeats have not. Thus, they are listed in Table 1 in scaffolds, which are regions of the contiguously sequenced data. It appears that groups sequencing *D. melanogaster* will maintain this format for the final version.

Using standard statistical techniques,¹² three different stochastic models were compared with the gene data. The reader is referred to Hutchison, et al. for the technical details of each model.¹³ We will describe each of the models in nontechnical terms hoping to give the reader a basic understanding of the issues. As mentioned above, randomness can only be ascertained by comparing the sequence of numbers with a stochastic model. If a given model does not produce a sequence that matches the observed string size distribution, then the model is wrong and another model must be found.

Model 1 is the simplest. In this model, we compared the chromosomal organization with a statistical model which assumes a probability distribution similar to that of a coin-

Strings 1–20	10	5	15	3	2	1	3	2	8	1	5	8	1	2	14	1	29	1	19	1
Strings 21–40	5	2	1	1	66	1	3	1	2	1	2	3	20	1	20	1	6	9	9	1
Strings 41–60	5	13	1	9	6	1	3	19	1	11	2	9	1	14	3	8	3	2	3	1
Strings 61–80	2	1	1	3	2	1	3	1	3	2	3	1	1	26	1	14	4	4	5	13
Strings 81–86	2	1	1	4	1	11														

Figure 1. String length in *M. Genitalium*, the numbers represent the numbers of genes in a row with the same orientation.