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FOREWORD

This paper was prepared for and presented at the meeting of the American Astronautical Society in Anaheim, California, May 23, 1966. Dr. Horowitz is a professor at the California Institute of Technology and divides his activities between Caltech and the Bioscience Section at the Jet Propulsion Laboratory.

THE BIOLOGICAL SIGNIFICANCE OF THE SEARCH FOR EXTRATERRESTRIAL LIFE

It is generally agreed that the search for extraterrestrial life is one of the most important scientific objectives of the national space program. This is recognized by the National Aeronautics and Space Administration and its advisory councils, who have declared that the search for life on Mars should be a major goal of the post-*Apollo* period of space exploration. Since this policy implies a special interest of biology in planetary exploration, it is important to have some understanding of the nature of this interest. This is necessary not only to justify the high priority given biological observations on Mars, but also—and equally important—to serve as a guide for the biological program itself.

Stated in its simplest terms, biologists would like to know whether life has originated elsewhere in the universe. This question implies much else: first, that we know how to recognize a living thing when we see it; second, that we know how to tell whether an extraterrestrial form of life originated independently of life on the Earth. If life is found on Mars, say, we cannot *assume* that its origin was a separate event from that which gave rise to life on the Earth. It is conceivable that life arose only once in the solar system and that it was subsequently distributed among the planets. There is only one way we know of at the present time by which the answer to this question might be obtained, and that is by comparing the chemical structure of the extraterrestrial life with that of life on Earth. This suggests that the life we know carries a trademark of some kind, one that is revealed by biochemical analysis and that says in effect "made on Earth."

In this paper I am going to show that there is a chemical mark or a whole series of marks that is stamped on all terrestrial life forms that we know, and I will show how this is related to our basic comprehension of the living state. I will argue that the discovery of any significant change in this chemical identification mark would constitute sufficient evidence for the separate origin of an extraterrestrial life form.

The most concise, unambiguous, and general definition of life that can be given at the present time is based on the *genetic* properties of living things. According to this view, the unique attribute of living matter from which all of its other remarkable features derive is its capacity for self-duplication with mutation. That is to say, living organisms are systems that reproduce, mutate, and then reproduce their mutations. Reproduction by itself is not sufficient. Many nonliving systems are self-propagating: crystals, for example, or even better, flames, which not only reproduce (by means of sparks) but also show metabolism and growth. Systems such as these increase by the same exponential law that describes the growth of living populations. Under certain circumstances—as for example, if we were interpreting the signals from an automatic life-detection instrument landed on Mars—we might well be uncertain as to whether or not such systems are alive. But nonliving systems, being immutable, are incapable of evolution. Living things, on the other hand, are endowed with the seemingly infinite capacity to adapt themselves to the needs of their existence. The endless variety and complexity of living organisms are simply the consequences of their mutability. *Any* system endowed with the capacity to mutate blindly and to reproduce its mutations must, by logical necessity, evolve.

One of the greatest achievements of modern science has been the elucidation of the chemical structures and mechanisms underlying the genetic properties of living matter. Before elaborating on this theme, however, I should like to digress to consider the following question: How useful is the genetic criterion of life in real situations? Is it applicable to Martian exploration, for instance, or even to elephants here on Earth? It has been pointed out that it takes considerable enterprise to observe the reproduction of elephants, and infinite patience to demonstrate their mutations—yet we have absolutely no doubt when we see an elephant waving his trunk in the zoo that he is in fact alive. This is all very true and it is one of the reasons for directing the search for life on Mars toward microorganisms whose capacity for reproduction and mutation are easily demonstrated. Even with the elephant we could, if necessary, show by tissue-culture methods that the cells of which he is composed are capable of self-duplication and mutation. This would suffice to prove that the whole beast was alive and would relieve us of the necessity of finding him a suitable mate and so on. We do not have to apply such measures to the elephant because we can easily recognize in him the kind of complexity and adaptiveness that are the products of biological evolution. Whether or not such easy recognition will be possible on other worlds, however, we cannot say.

The genetic definition of life is like the physicist's definition of a chemical element. We define the element carbon unambiguously by its atomic number, yet it is not usually necessary to determine atomic numbers in order to find out whether a given sample of matter contains carbon. We use other more easily observable properties of carbon, which depend ultimately on its atomic number.

Getting back to my main theme, one of the major conclusions of modern biology is that life is a manifestation of certain molecular combinations—specifically, nucleic acids and proteins. Of these two classes of compounds, the nucleic acids are the genes, or the bearers of the genetic properties of cells. The nucleic acids are the ultimate self-replicating and mutable substances. It is they that carry the genetic heritage in all species. This heritage consists of information, all of which is apparently concerned, directly or indirectly, with the construction of protein molecules. The latter form the enzymes of cells—the versatile and highly efficient catalysts that direct the enormously complex chemistry of organisms, including the production of the precursors needed for the synthesis of more nucleic acids and proteins.

The nucleic acids and proteins thus form an interlocking and interdependent system. Whatever is unique about living matter—whatever distinguishes it from the inorganic world—is inherent in this system. The genetic information encoded in the nucleic acids contains the distilled essence, so to speak, of all that the species has learned throughout its long evolutionary history. The flow of this information in the system is one way, from the nucleic acids to the proteins. We know that this is so from genetic experiments which show that specific structural changes in the genes—that is, mutations—result in the appearance of specific structural alterations in the corresponding enzymes, but the reverse is not true.

Let us briefly consider the chemistry of genes and proteins. Both are high-molecular-weight, linear polymers. The building blocks of the genes are called nucleotides, of which there are four kinds. Genetic information is encoded in linear sequences of nucleotides. The entire genetic endowment of a human being is contained in approximately 5×10^9 nucleotides or 10^{10} information bits. It is a remarkable fact that the same nucleotides are found in all known species. The only thing that distinguishes the genes of a man from those of a horse is the linear arrangement of nucleotides.

Proteins are polymers of subunits called amino acids. There are twenty different kinds of amino acids in proteins, and again the same twenty amino acids are found in all species, from viruses to man. The specific chemical properties of protein molecules are determined by the linear sequence of their constituent amino acids. That is to say, the entire difference between one protein and another is inherent in the arrangement of the same twenty amino acids.

The logic of the gene–enzyme relationship that I have just described is clear. Success in the struggle for existence depends on the ability of organisms to synthesize a large variety of specific proteins. The proteins are highly ordered, complex structures. They do not form spontaneously, but must be built up from a set of instructions. If every generation had to discover for itself how to assemble amino acids in the correct order to produce useful proteins, biological survival would be impossible. Consequently, amino-acid-sequencing information must be transmitted from parent to offspring. A mechanism for storing and copying this information is a prerequisite for successful living. Amino acid sequences cannot be copied directly from a pre-existing protein—at least no species that we know of has ever discovered a way to do this—but nucleotide sequences can be copied from a polynucleotide. Hence, instructions for assembling protein molecules are encoded in nucleic acids.

One final element must be added to make the system work. This is a means for translating nucleotide sequences into sequences of amino acids. To accomplish this feat, living cells contain an ingenious and complex translating mechanism involving several enzymes and three special kinds of nucleic acid. All of the details of this mechanism are not yet understood, but what it accomplishes is the translation of a message written in an alphabet of four symbols to one written in an alphabet of twenty symbols. An imperfect analogy would be a machine that translates messages from Morse code into English. (The analogy is imperfect because the biological mechanism not only translates, but also assembles the proteins from their constituent amino acids.) Like the translating machine, however, the biological mechanism incorporates a "dictionary sense" that enables it to relate the two different sets of symbols. This dictionary is called the "genetic code." Since four nucleotides must be translated into twenty different amino acids, it is obvious that a minimum of three nucleotides must be used to code for one amino acid. Three is, in fact, the number used. Since four nucleotides taken three at a time give the possibility of 64 different triplets, it is clear that there must be considerable synonymy, or, in the word of the communications engineer, degeneracy, in the amino acid code. That is to say, there are two or more code words for each amino acid.

A major accomplishment of molecular biology of the last few years has been the almost complete working out of the genetic code, including two triplets that represent no amino acid at all. These are the so-called nonsense triplets, one of which may serve as an end-of-message signal. Again, we find remarkable similarity among all living things; it appears that the genetic code is identical in all species. This has been most convincingly shown by recent experiments in which DNA (the genetic material) from viruses that normally grow in animal cells (vaccinia and polyoma) was used to infect bacteria. The viral DNA multiplied in the bacterial cells and produced proteins characteristic of the whole animal virus. Since only the viral DNA entered the bacteria, the viral proteins must have been produced by bacterial translating mechanisms reading the viral genetic message. These proteins were indistinguishable from those produced when the viruses infect animal cells. These experiments provide compelling evidence for the universality of the genetic code.

The universality of the genetic code and the related fact that the nucleic acids and proteins of all species are built out of the same nucleotides and amino acids lead to the conclusion that there is really only one form of life on the Earth. Despite appearances, all living species are fundamentally the same. It is impossible to avoid the conclusion that all species have descended from a common ancestor, which, in the remote past, discovered this remarkably effective and stable genetic mechanism. By the same token, it follows that if a species were to be found, on this or any other planet, which constructed its genes out of a different kind of material or its enzymes out of a different set of amino acids, or which recognized a different genetic code, then we could be certain that it originated in a different time or place from the life that we know. A single example of such an exotic life form would revolutionize our knowledge of the origin of life. It is assumed by some biologists and, in my experience, by most astronomers who consider the matter, that the probability of the origin of life, given favorable conditions,—i.e., conditions resembling those of the primitive Earth—is practically unity. I think that this optimistic estimate may be far from the mark. The minimum chemical system that exhibits the essential attributes of life is the complex nucleic acid–protein system that I have described. We have no evidence that a simpler system ever existed, nor do we have as yet a satisfactory theory that explains how the existing mechanism might have evolved from the primordial soup. In my opinion, an objective estimate, based on known chemistry and known biology, would lead to a probability for the origin of life of close to zero. The discovery of a new form of life would immediately alter the context of this argument and would remove it from the realm of speculation.

Two further points follow from this discussion. The first is that the discovery of life on Mars or any other planet will not be an end, but only the beginning of a long series of biochemical investigations. We will have many questions about the chemical organization of any extraterrestrial life form that we may discover. To obtain the answers to these questions will require the sending of a great deal of sophisticated instrumentation to the planets—or, even better, the return of samples to the Earth for study in our own laboratories.

In connection with the chemistry of extraterrestrial life forms, let me interpolate a word about the possibility of silicon-based life. This is basically a comic-book idea. The suitability of silicon as a basis of life has been discussed extensively by chemists in the past. The conclusion has been reached that silicon is not suited for the construction of the large, complex kinds of molecules that we associate with the living state. Most silicon compounds are inherently unstable, unlike compounds of carbon, which, owing to the peculiar properties of carbon, are relatively inert even when they are thermodynamically unstable. It appears that carbon is uniquely qualified among the chemical elements for the building of complex yet stable chemical structures.

My last point is that it is obvious from this discussion that the discovery of *any* kind of life on Mars would be a finding of the greatest scientific interest. To contend that only the discovery of highly evolved forms would justify the space effort, as at least one well-known biologist has argued, is to me totally incomprehensible. From the viewpoint of fundamental biology, bacteria are just as valuable as higher species. This is fortunate, because we cannot expect to find any but the simplest kinds of life on Mars. As I have shown, if a Martian expedition came to Earth, it could learn the basic facts about terrestrial life by studying the simplest microorganisms. Mars is a hostile desert—cold, dry, and airless. To put oneself in a realistic frame of mind about Mars one should think of the highest, driest deserts on Earth, where no higher form of life can be seen, and where only lichens, algae, and bacteria can survive.

People often ask me what I think are the chances of finding life on Mars. I think they are low. It is not optimism about the outcome that sustains the search for extraterrestrial life, but rather it is the immense importance that such a discovery would have. The search for life on Mars is like buying a ticket on the sweepstakes, in which the chance of winning is low but the prize to be won is very high. To find the true value of the Martian enterprise, one must multiply the one factor by the other. When one performs this mental arithmetic, it is my opinion that the answer is a reasonable number.