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Lecture #48 - Biochemical Origin of Terrestrial Life

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Experimental work in biochemical genetics has customarily involved the examination of the minutest organisms and deals with processes of microscopic, even molecular, dimensions. Likewise, the events with which it is concerned are measured on a scale of seconds, or fractions of a second. The events with which I propose to deal now are of a somewhat different magnitude. They concern eons of time, and the whole mass of the universe. And I'm referring to the events related to the ultimate origin of life on this planet, and its possible distribution elsewhere in the universe.

To obtain some perspective on the problem posed by the initial origin or origins of life, it is necessary to have a conception of the time scale of cosmic processes. We will adopt, somewhat arbitrarily, the figure of about 10 billion years for the estimated age of the universe, of about half that interval for the calculated age of the earth, and of about 1 billion years as the interval over which there is a perceptible fossil record. However, there is very little in the fossil record that can tell us of the early stages of the origin and development of life. Only those organisms with relatively hard exteriors and of relatively appreciable dimensions have any hope of being preserved. We therefore must turn from an analytical attempt to discern the primary features of living origins to a synthetic one -- to attempt to recreate from plausible arguments, ranging from cosmology to geophysics, what the status of the planet was at the time of the earth's origin and to attempt to put together the most likely features out of which living forms developed.

Perhaps the strongest evidence on which we may rely for the primary features of life's origin comes not from paleontology but from comparative biology, in particular comparative biochemistry. Plants have been separated from animals in the phylogenetic scheme for a large part, if not more than, this interval of a billion years over which there is a fossil record. Yet a biochemical analysis of the fundamental constituents of higher plants and of animals, and indeed of bacteria and of many viruses, shows an almost uniform ground plan. We find the same amino acids represented universally among the proteins of all organisms. Indeed, a hydrolysate containing the amino acids present in the tobacco mosaic virus could not readily be distinguished by the biochemist from the hydrolysate of the amino acids present in our own tissues and organs. Likewise, we have already commented on the ubiquity of deoxyribonucleic acid as the carrier of genetic information. And we have here the same fundamental structure in all organisms. In addition, we have the fact, that can be observed at a higher level of integration, of a remarkably uniform process of mitotic division of well-organized chromosomes as a basis of the uniform transmission of information to the daughters, be it of plant or of animal cells.

We must conclude from these observations, with at least reasonable certainty, that life has had a common plan since the separation of the major kingdoms of organisms, namely over an interval of nearly a billion years, which means that the nucleic acids and the proteins and their complex metabolic relationships, despite their highly dynamic features, are perhaps the most durable geochemical features on this planet.

What would be the minimum requirements for the first development of an organism from which we can then plausibly argue the rest of organic evolution? We know from the point of view of the development of life that Darwin has given us, and we are of course celebrating the centenary of his great synthesis, that it would be sufficient to start with a self-reproducing system capable of mutation, subject to some improvement by virtue of spontaneous mutation, and selected by natural forces for the continued elaboration of fitter and fitter forms. At the present time the bacteria are perhaps the simplest of the free-living organisms, and we could not in the present environment of the earth imagine any organism of simpler structure capable of survival and subject to Darwin's condition. On the other hand, we can hardly conceive of any spontaneous process by which an object as complex as a bacterium could conceivably have arisen. And we must therefore pose, on any view of the origin of living material on earth, a period, a very substantial period, of evolution of complexity of which the simple bacterium is already a final result.

To go back perhaps one stage further, we have, in the in vitro replication of DNA in an enzymatic system, one of the simplest systems which would be subject in principle to some sort of evolution. However, in such systems we must admit the role of a biochemist, to furnish extracts containing the nucleoside triphosphates and the enzyme which are accessories for the replication of the DNA. We may wonder, then, whether the primary living material was itself, in fact, already a well-organized and presently-recognizable DNA with the same structure; whether there are mechanisms of its replication simpler than those requiring the intervention of an enzyme; or whether DNA itself has evolved from simpler materials.

However, it may be a mistake to view these intermediate stages in the evolution of a living system purely from the perspective of the present terrestrial habitat. To a very large extent the shape of the earth is molded by the metabolic activities of the living forms which have evolved on its surface. These are very largely responsible for the deposition of carbon, for example, in sediments, in the coal sediments, and for the release of oxygen into the atmosphere in consequence of photosynthesis. We may therefore wonder what the early stages of the earth were like prior to the development of life, life which in certain respects is destructive. Any large accumulation of organic materials which were to form, or were to be placed, on the earth's surface would at the present time be very rapidly destroyed, by higher organisms or by simpler microorganisms which are universal in their distribution. However, if we are concerning ourselves with the primeval conditions of the earth's surface, of course there would not yet have been such organized systems to destroy organic compounds. We may therefore inquire whether the general aspect of the earth's surface may not have been far more complex in terms of the distribution of organic compounds than it is at the present time. And to do this we should pay some attention to processes which may conceivably have been responsible for the synthesis and accumulation of large amounts of organic material.

This story perhaps begins over a hundred years ago with the demonstration by Wöhler that, what were then called, organic compounds, that is to say compounds containing carbon, that had been isolated from living organisms, are really not unique to them. And it was Wöhler who had demonstrated in the test tube the easy possibility of synthesis of what was called an organic compound, urea, which is isolated of course from urine, by the heating of an inorganic salt of ammonium, namely ammonium cyanate. We have really not evolved very far in our terminology since we still adhere to the confusing statement of an area of chemistry that we call organic chemistry, and we sometimes have to correct ourselves when we refer to a compound as being organic with regard to the ambiguity of its vital biological origin or whether we simply mean that it is a compound of carbon. Since Wöhler's time we know that compounds of carbon are not unique to organic life.

I've indicated on the board a series of reactions that the Russian biochemist, Oparin, about 1928, had proposed as some of the fundamental steps for the natural production of organic compounds prior to the development of life on the earth. He had proposed principally the formation of carbides by reductive reactions involving carbon or methane with the metals, and then the hydrolysis of these carbides by analogy with the very well known hydrolysis of calcium carbide to yield acetylene. As we know, from the important use of acetylene in organic synthesis in industry, this can be used as a precursor for the formation of large numbers of other more complex, interesting, compounds, for example, its direct hydrolysis to yield acetaldehyde. Likewise, nitrogen is capable of reacting either directly with hydrogen, or through the intermediate formation of nitrides, followed by hydrolysis, to give ammonia, and the further reaction of ammonia with aldehydes is known to be capable of yielding polymers of high molecular weight which might be of great interest as precursors for biological development.

A more direct approach to the probelm of the origin of organic constituents was furnished by the experiments more recently of Miller and Urey, who subjected a mixture of gas es, of a composition which has been predicated on other grounds to be characteristic of the primitive earth's atmosphere, to ultraviolet light and, in parcitular, to spark discharges. The one point I would like to make about their work is that they have empirically demonstrated, in a very satisfying way, the production of a large amount and large variety of amino acids from these reactions. I've indicated here the synthesis of glycine, but this is only one of a large number of components that could be produced this way. The detailed chemical steps in these empirical reactions are not very well known. However we can readily suppose that the activation of methane and of ammonia and of water will give rise to free radicals which are highly reactive intermediates for the production of more complex organic compounds.

In fact, however, we can approach this problem from an even broader perspective, if we take account of the present consideration of the general composition of the whole universe. We know from our own existence on earth that it is not an unlikely place for the development of organic material, that is, for the origin of living forms and their further development. And yet, if we look at a comparative view of the atomic composition of the earth compared with the universe at large, we come to what may be a rather startling result. This table has been constructed so as to put hydrogen and helium, which are by far the most abundant components of the universe, in a separate category. These are gaseous components, and hydrogen, of course, constitutes by far the largest part of the total mass of the universe, not only in the interstellar gas but also in the stars -- for example, the sun.

However, if we sum all remaining atoms, the condensable atoms, which are capable of forming compounds that might be of some interest, and give that sum a value 1, we see that the universal composition places great weight on the abundance of oxygen, nitrogen and carbon, so that these compounds together make up almost four-fifths of the total condensable mass of the universe. These are, of course, the elements which are of the unique importance in the organic compounds that we are seeking to find some source of, for the original start of living processes. By comparison, the earth is a very poor place, indeed, for the starting point of organic chemistry that might be of biological interest, since in the earth's crust oxygen is very well represented in the oxides and carbonates and silicates, hydrogen is very much less abundant proportionately, much of the hydrogen of the earth having escaped from the atmosphere, and we find only traces, relatively speaking, of carbon, while silicon and other elements are proportionately more abundant. We should not view the universe from the perspective of the rocky earth. We should rather view these figures as indicative of the very high prevalence indeed of precisely those lighter elements which are important in biologically interesting compounds.

We must further view the primitive act of condensation of the free atoms in the interstellar or the prestellar gas as corresponding in some measure to the formation of molecules which will ultimately be of some biological interest -- whether there is a direct transition from the aggregation of atoms to form such objects as the comets, which can be viewed spectroscopically, and which we know, from such evidence, to contain groups like the CH and CN and CC and CO radicals which would be part of organic compounds. But we do not know whether they can be part of the direct historical transition from the pre-aggregation stage through to the final development of the planet. But we certainly have here, in addition, another model for the formation of complex organic molecules without the intervention of any specific biological processes. The question, of whether the original aggregation of the interstellar elements to form the earth is of any importance in its later development, is primarily related to the question of the maximum temperature through which the earth may have gone in the course of its history. If this was never too high then of course its original composition will have persisted to some extent, and on that basis some of the organic material from which life started may have had its origin in the original formation of the very stars themselves.

We can view then that in the early stages of the earth's history there were many processes which could lead to the formation of quite complex organic materials, and there were no specific processes for their degradation. Of course, the subjection of these organic compounds to ultraviolet light and to other chemical reactions might tend to reverse the synthetic reactions we have just discussed. But there surely would have been many places on the earth's surface for the possibility of the accumulation of large amounts of these materials.

Horowitz has pointed out that one can visualize the development of more nutritionally competent organisms in the following way. Let us suppose that the aboriginal earth contained large amounts of materials required as building blocks for the production of a primitive protoplasm. As each of these compounds was utilized by the existing primitive forms of life its concentration would be depleted, and there would then be a selective advantage for the development of any mutants, among that life, which would be capable of resynthesizing these compounds from simpler components. And in this way one could visualize the gradual accretion of synthetic capabilities as individual metabolites, as individual building blocks, for the development of living structure, and which were ultimately of inorganic origin as these became depleted owing to their metabolism by existent forms.

However, this problem does not entirely bridge the gap, which must be bridged, between the spontaneous development of perhaps of some relatively complex polymers and the final emergence of a specific polymer which has coded information of the kind that we see in DNA. At the present time one of the most urgent problems in recreating the early steps of the evolution of life is in bridging this gap, and this is perhaps in the direction of finding polymeric systems which have some degree, however inefficient, of self-replication.

Now, we have I think enough of an insight into the fundamental mechanisms of biological replication to anticipate with some confidence that the primeval living molecule will be a linear polymer. And it will be a polymer which will have a reasonably monotonous basic structure, but with the possibility of systematic alteration of its units, in much the same fashion as we visualize for DNA. And we, therefore, in constructing such polymers, must visualize a mechanism for the habitual attraction of monomeric units to the corresponding sites in the existing polymer and then finally some mechanism for putting the right units together. This, in effect, is a generalized version of DNA synthesis.

Now on paper it is possible to write a number of reactions which might possibly go this way, but none of them so far has succeeded in the laboratory, perhaps for lack of very urgent effort in those directions. Now that the polymer industry has exhausted some of the simpler possibilities of the construction of interesting compounds for industrial purposes, there is little question that more and more emphasis will be given to the artificial production of ordered structures, and I think it is a reasonable anticipation that a by-product of this work will be the design of linear polymers which will have at least some of the elementary attributes that we would have visualized as part of the original living molecule.

Now we have, if we look just a very few years into the future, one other possibility for active research in this area, aside from attempts to reconstruct the conditions as they may have originated and developed on our own planet. I'm referring here to the investigation of possible living forms on other bodies within the solar system. This possibility becomes a reality by virtue of the very rapid strides in rocket technology which have been made in this country and in the Soviet Union over the last very few years.

The objects in which we are most interested are the planets Mars and Venus, since these are the two closest to the earth, and the ones whose habitats, insofar as we now know them, are the most nearly compatible with forms of life which we can anticipate. In fact, an exciting and substantial beginning planetobiological investigation has been made by Dr. William Sinton, as reported very recently in "Science". Dr. Sinton's report which concerns further evidence of vegetation in Mars is an account of his studies on the infra-red spectra of this planet obtained with the help of the 200 inch telescope at Palomar. When his telescope was focussed on some of the darker regions of this planet, he was able to pick up distinct bands of absorption at 3.43, 3.56, and 3.67 μ, as are displayed on the accompanying projection. These bands are at least characteristic of a variety of organic molecules, particularly those in which there is some assymmetry, so that an atom like oxygen is bonded to a CH residue. This grouping is characteristic of a number of organic compounds of biological interest, including carbohydrates and lipids. It is too soon to state that this is definite evidence of biological activity on a planet some tens or nearly hundreds of millions of miles away. The least that we can say is that it constitutes at least plausible evidence for the occurrence of appreciable quantities of organic materials on the surface of this planet. One reasonable source of these materials would be biological synthesis, and this is especially appealing in view of the variations in the apparent color and texture of the planetary surface that astronomers have reported for many years. However, this cannot be considered to be absolutely conclusive evidence of biological activity since the very processes of inorganic synthesis, so to speak, of organic compounds, to which we have alluded before, and which must precede the development of life on a planet, could in principle also give us images of this kind. There seems to be very little doubt that for a final elucidation of this problem, it will be necessary to conduct missions directly to, or at least to the vicinity of, these planets. Planetary research has many motivations. Of these, it is difficult for me to assess one with higher scientific value than the search for definitive evidence of life on another celestial body.

We have so few precedents for the design of experiments on this scale and in this field that it is somewhat difficult to lay down the criteria for a desirable program of investigation. However, there can be very little doubt that high on a list of priorities for biological research would be a definite search for the important compounds which are so prevalent to terrestrial life and so common to all of them. In particular, the question of whether DNA is the unique replicating material, which is the basis of genetic transmission, is among the first that should be answered. In order to do this it may be necessary to develop new forms of instrumentation which will be able to conduct analyses in situ and to transmit necessary information by radio communication back to the earth. Even regardless of the existence of active forms of life, whether or not they resemble terrestrial forms, on Mars and on Venus, other biological questions which may be of great genetic import have presented themselves already.

The very fact that we now have infra-red spectroscopic evidence of the accumulation of large amounts of organic material on the Martian surface, poses the question of what would happen if there were to be deposited on the planetary surface even a single microorganism. In a discussion of clones we considered the rapidity with which bacteria would be able to multiply given an environment favorable to their continued growth. And, in fact, one can calculate by a simple exponential term that it would require not much more than 48 hours of continued multiplication of a bacterium like Escherichia coli to occupy a volume of medium which had the size of the earth. It's therefore quite possible that the genetic event of replication of terrestrial material, should a minute portion of this be transplanted to another planet, would have explosive consequences from a geochemical point of view.

And it is also easy to see how disastrous the premature transplantation of terrestrial genotypes would be for any hope of ultimate investigation of the aboriginal, indigenous, forms of life that may exist there, and even if there should not exist any active forms of life, the destruction of the accumulated organic material which may be the stuff from which life elsewhere has evolved, and for which there is the evidence from Sinton's paper, to which I have already alluded.

Now, Venus is possibly a less attractive object for this type of investigation than Mars, but this again is more a tribute to our ignorance of the conditions on its surface than it is to any direct knowledge of the habitat. Estimates of the temperature of Venus vary widely. Some of them are quite compatible with the existence of life, others are set very much too high. However, since we know nothing of the exact nature of the surface of this planet which lies beneath the opaque and highly reflecting cloud layer, it would be premature to design any approaches to this planet on the assumption that biological activity would be impossible at that site.

There is one other object which already has been reached by terrestrial investigation, and which is subject to further study. And that is the Moon, the satellite of the earth. It is quite unlikely that the Moon is a site of active living forms, since the total absence of an atmosphere and the, therefore inferred, absence of any liquid water would make terrestrial forms quite out of the question. However, it has been suggested that the moon might act as a gravitational trap for fossil spores, so to speak, which by some hypotheses might have drifted between the planets, some of them to light on the moon. Although this is quite improbable, the possibility of an interplanetary gene flow would have such weighty consequences for our general cosmic biology that it should not be totally disregarded in our plans for the exploitation and exploration of space.

We see then that the compass of genetics of microorganisms can proceed to a cosmic scale, and that we must take account of the enormous powers of replication of DNA on experiments at every level of human activity.