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Ernest O. Lawrence

*Radiation
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THE ORIGIN OF LIFE ON EARTH
AND ELSEWHERE. II.

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THE ORIGIN OF LIFE ON EARTH AND ELSEWHERE . II.

Melvin Calvin

October 19, 1960

THE ORIGIN OF LIFE ON EARTH AND ELSEWHERE . II. *

Melvin Calvin **

Department of Chemistry and Lawrence Radiation Laboratory, ***
University of California, Berkeley, CaliforniaABSTRACT

October 19, 1960

The synthesis of relatively complex organic molecules by ionizing and radical mechanisms (induced by high energy radiations, ultraviolet and electric discharge) from methane, ammonia, water, and hydrogen is described, both theoretically and experimentally. It is shown that the molecules which tend to be formed under such random conditions are the very ones which today are the common building blocks in the biological reconstruction of organic material. Such molecules are the amino acids, the simple carboxylic and hydroxy acids, purines, pyrimidines, etc.

The appearance of order among such random molecules is induced by two forces, namely, autocatalysis and crystallization. The latter is particularly important in the appearance of highly efficient macromolecular structures and arrangements which are so characteristic of present-day living organisms.

Points of contact of these theories with experiment are indicated, and where confirmation has been obtained it is described, and the areas of ignorance, requiring further experimentation, are defined. A first step in a possible test of these prebiotic organic syntheses on other astral bodies has been made by examining the organic material found in meteorites. The nature of the structures appearing therein is indicated.

* Transcription of address presented before California Section, American Chemical Society, Berkeley, California, September 19, 1960.
** Research Professor in Chemistry, Miller Institute for Basic Research, 1960-61.
*** The preparation of this report was sponsored by the U.S. Atomic Energy Commission.

THE ORIGIN OF LIFE ON EARTH AND ELSEWHERE

Melvin Calvin

Department of Chemistry and Lawrence Radiation Laboratory,
University of California, Berkeley, California

The particular sequence of thoughts indicated by the title has its origin in my interest in the process of photosynthesis. It began when I asked the question: Which came first, the plants or the animals? This question had been answered in a variety of ways, but one can't help but wonder, as one learns more and more about the detailed mechanism by which living organisms store energy and use it, how they got started in the first place. Actually, these thoughts began long before we heard of Sputnik and all of its successors. However, the fact is that it is now becoming possible for us to know, within five years, whether there are organic chemicals on the Moon and what the genetic nature of the living material on Mars might be. (I am assuming, now, that there is some.) Within the lifetime of most of us we will know these things. It therefore becomes a much more pressing matter for us to surmise how life got here (on earth) so as to have some clue as to what to look for in outer space. This is another source of the driving force for inquiry in this direction, and a very pressing driving force it is.

Therefore, in order to surmise as to what we should look for, we ought to extract some basic idea of the essential features of living material as we know it on the surface of the earth, so we can devise the proper

instrument to go ahead and look for it elsewhere. You can see that there are all sorts of pressures to examine this subject in a very concrete and practical way, other than the much broader pressure of pure human curiosity, which is the pressure that has existed since men began to think about the nature of life.

WHAT IS LIFE?

It seems best to begin the subject with a discussion of what the nature of living matter is and what kind of properties it has which we might expect to find, and which had to be generated on the surface of the earth, and which may, or may not, be going on elsewhere. Actually, what I am about to describe to you is nothing more than an extrapolation of the Darwinian idea. (It is rather impressive to find so many scientific people interested in a serious discussion of the origin of life. This would not have been the case thirty or forty years ago. It was a disreputable subject then, and, in fact, it was a disreputable subject for almost fifty years -- between 1870 and 1920. It is rather interesting to think of why this heightened interest in the thinking about this subject has arisen.) Thoughts about the nature of life itself -- really the first serious ones in the modern day -- stem from Darwin himself. You will recall that the basic contention of Darwin was expressed in the title of the Darwin-Wallace paper of 1858 which was 'on the Tendency of the Species to form Varieties; and on the Perpetuation of Varieties and Species by Natural Means of Selection.'¹ Darwin had already recognized the significance of this basic notion of a variety to depart indefinitely from original type and become

new species, and also recognized the significance of a backward extrapolation of this notion.

Thus if you start out with two species, and accept Darwin's notion that these two species were originally two varieties of one species which, in turn, was once one of a pair of varieties turned species, you can keep going back, and eventually you must come -- and Darwin recognized this as implicit in his basic notion -- to a point where there was only one type, or species, of living thing. Eventually one must come to a point at which what we would have called a living thing, if we were able to view it from a distance, was a variety of aggregates of matter, some of which we would call 'alive' and some of which we would not. Further back extrapolation leads to varieties of things even more primitive, none of which we would call alive.

This is the idea of a living organism developing in an evolutionary sequence of events in time. At some point, when material with a sufficient number of the desired properties had gathered around in a single region of space (a single system) we would call it alive. This is the notion that Darwin recognized even in his very earliest works. Shortly after the publication of Darwin's thesis there was another publication, this time by a chemist, Louis Pasteur, around 1863. He did an experiment in which he showed definitively that no life could originate on the surface of the earth under the conditions that then existed, except that it came from pre-existing life. The Darwinian notion was completely overshadowed by the Pasteur dictum that one could not obtain living material except from living material. Therefore, no one dared think seriously that living material had some other origin except from living material. It came to an end at that point.

I wondered about that point -- about why Darwin never did express himself explicitly on this matter -- but it turns out that he did, and I found here his opinion on the origin of life, written in a letter by Charles Darwin to George Wallich in 1882:

'You expressed quite correctly my views where you say that I had intentionally left the question of the Origin of Life uncanvassed as being altogether ultra vires in the present state of our knowledge, and that I dealt only with the manner of succession. I have met with no evidence that seems in the least trustworthy, in favour of so-called Spontaneous generation. I believe that I have somewhere said (but cannot find the passage) that the principle of continuity renders it probable that the principle of life will hereafter be shown to be a part, or a consequence of some general law;.....'

That passage to which Darwin refers in this letter is as follows; and it shows the fact that Darwin really did understand the significance of his basic evolutionary contention. This was written in a letter of 1871:

Darwin's Views of the Origin of Life

'It is often said that all the conditions for the first production of a living organism are now present, which could ever have been present. But if (and oh! what a big if!) we could conceive in some warm little pond, with all sorts of ammonia and phosphoric salts, light, heat, electricity, etc. present, that a proteine compound was chemically formed ready to undergo still more complex changes, at the present day such matter would be instantly devoured or absorbed, which would not have been the case before living creatures were formed.' (Darwin, L and L, 3, 18).²

This statement of Darwin, which was written in 1871, contains all of the basic concepts which have been the backbone of most 'origin of life' conjecture, experiment, and argument, that have been going on during the last

fifteen or twenty years. The idea was rediscovered, so to speak, by Haldane in the middle twenties³ and Oparin in the middle thirties.⁴

Now that we have this idea of continuity, which is so clearly expressed by the backward extrapolation of Darwin's evolutionary notions, we can see that to try to pinpoint some moment in time, at which (or before which) there were no living things and after which there were, is a mistake. The accretion of the variety of properties which today we attribute to living matter was a gradual evolutionary process itself, and only when a sufficient number of these properties found themselves in a single system in space did we call it alive. And this is a rather arbitrary point at which we will call a thing alive. Some people believe that a thing must be self-reproducing in order to be alive; others say it must convert energy into negative entropy; others say it must have the property of irritability; and there are a variety of other such descriptions which have been used to define living matter. Actually, it is the aggregation of a sufficient number of these properties on one system in space that gives rise to what we would today call a living organism. I shall not try to define how many of these properties are necessary, because it may differ, depending upon your point of view -- if you are a chemist you have one point of view and if you are a geneticist, you have another.

There is no ambiguity, of course, in distinguishing the living from the nonliving at higher levels. It is only at the primitive level that we have this difficulty, and that very fact is the result of the nature of living material, being, as it is, an aggregation of^a more or less arbitrarily sufficient number of properties on one system.

I think we must leave the idea of the nature of living materials,

now, and go on to describe how such a chemical system (physical-chemical system) could have arisen on the earth and then examine other astral bodies to see if there is any possibility (or hope) that such similar properties might have occurred elsewhere.

THE PRIMITIVE ATMOSPHERE

We know a great deal more today, I might say, about the nature of the fundamental living organism -- the actual physical-chemical processes, the construction and interaction of these molecular particles in a living organism -- than we did even ten years ago. While one can make changes each time this discussion occurs as to what we must look for, there are certain rather primitive requirements which always appear. We must, somehow, devise ways and means^{of} producing rather complex forms from relatively simple ones.

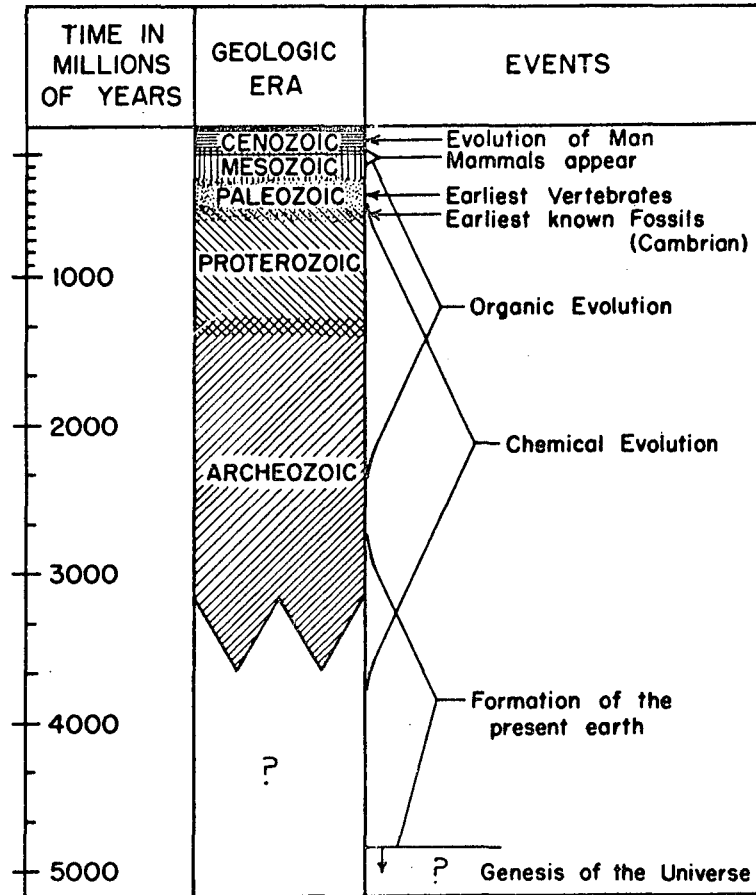
We have every reason to suppose that the primitive earth had on its surface only simple organic molecules. If it was a reducing atmosphere (and it seems to be generally agreed now that this is true), most of the carbon was very largely in the form of methane or carbon monoxide (some of it could have been carbon dioxide but the contention now is that most of the carbon was reduced), the nitrogen was mostly in the form of ammonia, there was lots of hydrogen, and the oxygen was all (or very nearly all) in the form of water. These, then, presumably, were the primitive molecules of the primeval earth, and from these we must now devise a way of constructing the more complex materials.

It was at this point that we first began to seek experimental ways of doing this in the laboratory. This was the first point of contact with

experiment that I, at least, was able to make roughly ten years ago. (At that time I wasn't so convinced nor was it so generally accepted, for that matter, that the primitive atmosphere was reduced.) We started with carbon dioxide and water to determine whether or not it was possible to make reduced carbon compounds without the presence of the photosynthetic system which we now have. We did it by using high energy ionizing radiation or by using ultraviolet and it was easy to show that by irradiating solutions of CO_2 , water, and hydrogen, we could get reduced carbon.⁵ I think that today it is a lot easier to do this type of experiment because we now believe the atmosphere to be a reduced one. For a reduced atmosphere and the same kind of ionizing radiations, instead of using carbon dioxide we use methane, and with ammonia, water and hydrogen we can get a whole variety of chemicals. The first experiment with the reduced atmosphere and ammonia was done by Stanley Miller in 1953;⁶ our experiment with CO_2 and water was done in the cyclotron in 1950 and we got formic acid, acetic acid, and things of this kind which are reduced carbon compounds. When Miller put ammonia into the gas mixture, he got glycine, alanine, beta-alanine and several other amino acids.

The Time Element

I have overlooked a rather important point in the course of getting into the chemistry of evolution and that is the geologic time element which was involved. Figure 1 gives us some idea of the time scale that we have to deal with. You can see that we have ample time to do all the things which I am going to describe to you. This not only gives some idea of the time scale, but the basic idea of the place of Chemical Evolution is shown here quite clearly.



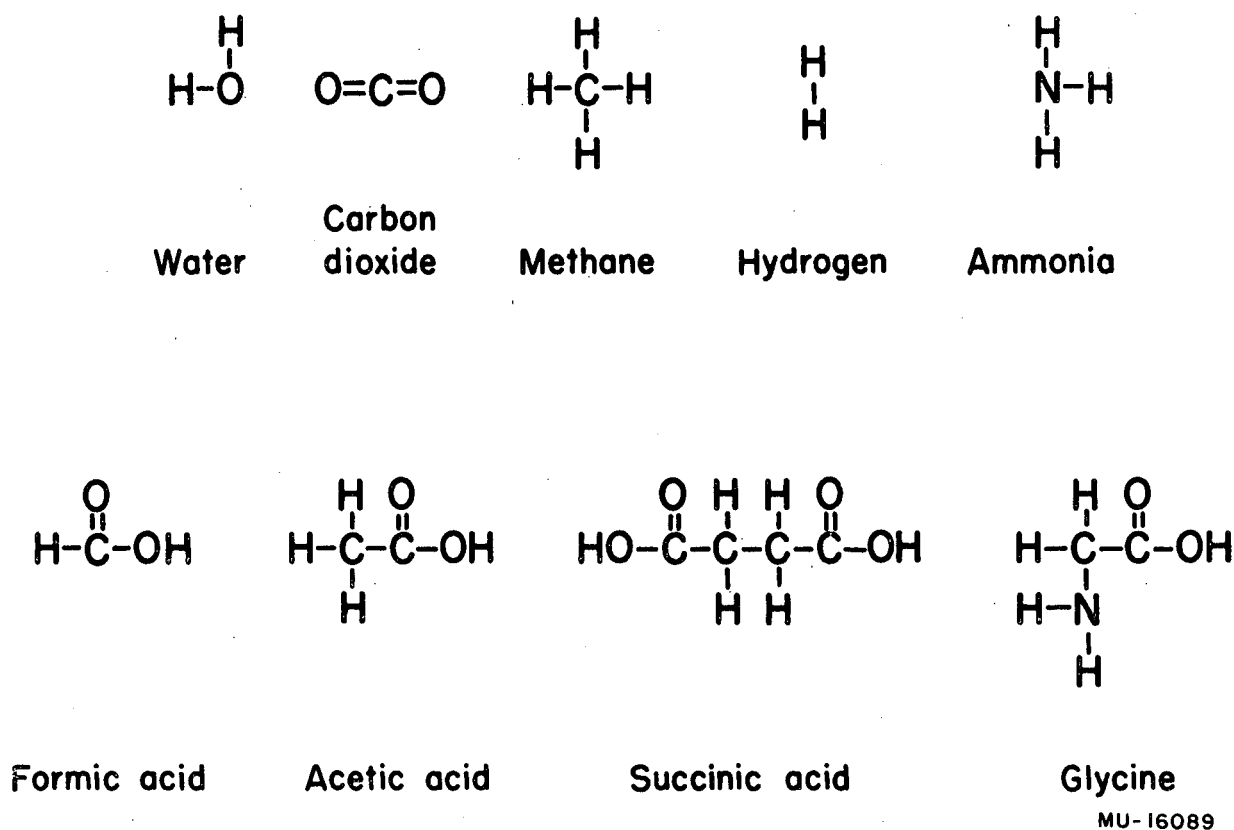
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Fig. 1. Time Scale for Total Evolution

Roughly five to six billion years ago the earth was formed and hardened into its present shell. Right after the formation of the crust of the earth, the processes of increasing the complexity of organic chemical formation began, and this long span of time (including the Archeozoic and Proterozoic geologic areas) I have called Chemical Evolution, that is, the period of time during which chemicals were transformed from relatively simple, primitive molecules into the very complex ones which eventually, somewhere in the middle of this period, evolved into some complex system which had enough of the properties which we usually attribute the living organism so that we are willing to call it alive. At this point, Organic Evolution began (Darwinian evolution). Our discussion will be concerned principally with the part of the time scale which I have labeled Chemical Evolution for which we have no fossil record on the surface of the earth. We have, roughly, from two to four billion years to accomplish these things.

Primitive Chemicals, The Primeval Atmosphere and Random Organic Synthesis

Figure 2 shows the primitive chemicals with which we had to deal and which had to be converted into the more complex ones which today represent metabolites and structural elements of a living organism. I told you a moment ago that with carbon dioxide, water and hydrogen we could make formic acid, and with methane, ammonia, hydrogen and water we could make many more complex materials, such as glycine, succinic acid, etc. You will notice that all these materials are today important simple metabolites through which carbon skeletons are very often rearranged by the present-day



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Fig. 2. Primeval and Primitive Organic Molecules

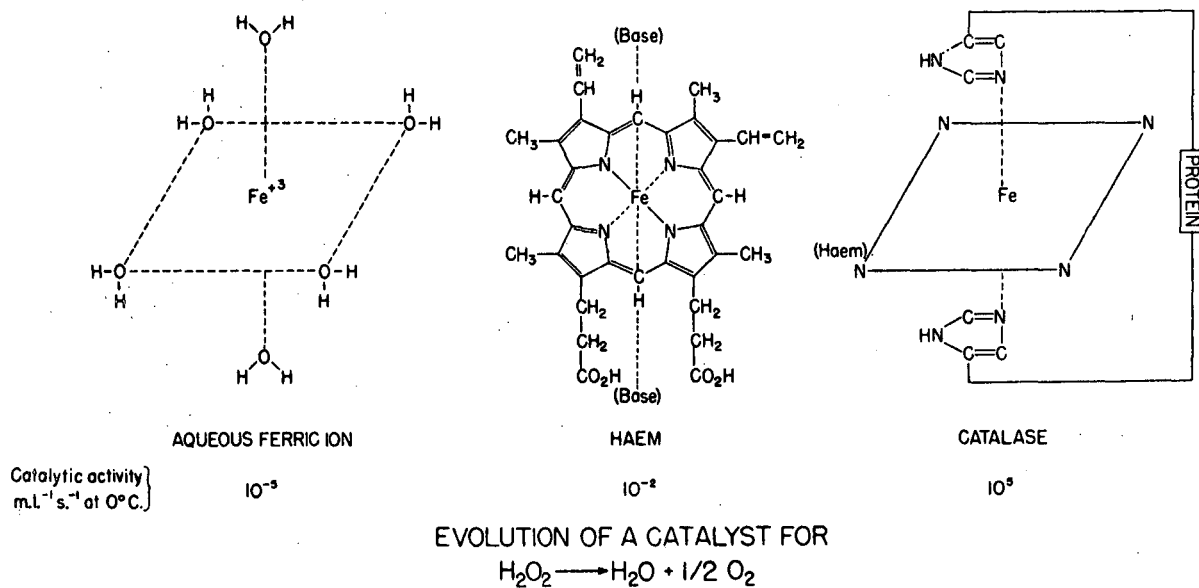
living organisms. These materials are also the very first molecules that show up in a random synthesis, that is, a synthesis which depends primarily upon the ripping apart of existing simple molecules and the resulting fragments falling together into metastable structures, that is metastable under these very highly ionizing conditions such as I have described. A few of these compounds are caught in this metastable condition and can be used for further construction.

This random synthesis, you can see, could go on for quite a while, but eventually enough of the carbon would be in these forms so that the very same processes which took these precursor molecules apart would start ripping the products apart. A few of the molecules would become still more complex, but some of them would start going back down again to more primitive forms. So, we have to introduce some kind of a selection process at this point which will permit the selection of those molecules which have some self-perpetuating survival value. This process is very familiar to the chemists, i.e., chemists have recognized its existence, and we have called it autocatalysis. Any product which has a catalytic function in its own formation will, naturally, help to transform the raw materials to itself. There is nothing profound about this idea to a chemist -- it seems rather primitive -- but it is a rather important concept. In fact, it is the very concept of self-reproduction used by the biologists, if you want to extrapolate it that far.

EVOLUTION OF CATALYSTS

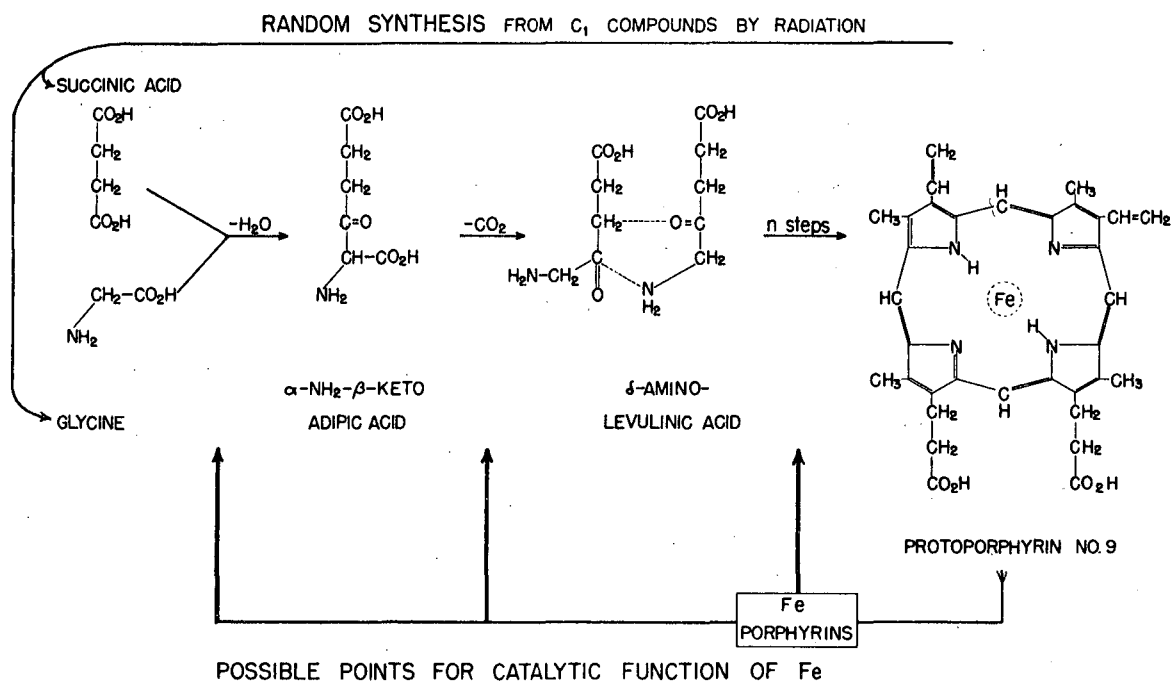
The catalytic properties of the primitive materials may themselves have been rather simple. For example, in Figure 3 we show how we can change those catalytic properties. Here we are discussing the ability of a simple, hydrated ferric ion to decompose hydrogen peroxide and give water and oxygen, or act as a peroxidase (oxidation catalyst). Simple aqueous ferric ion has a catalytic activity expressed by the number 10^{-5} . If, however, we surround that iron atom (iron ion) with a suitable organic grouping -- in this case, heme, a tetrapyrrole -- it turns out that the catalytic ability of that iron in this very same process has been enhanced by a factor of one thousand, reaching 10^{-2} . If we build the heme into a still more complex structure with a protein around it, we can increase the catalytic ability by several more powers of ten. The purpose of this figure is simply to show that the catalytic power residing in the iron for a simple reaction can be enhanced by the environment in which the iron is placed.⁷

The question is how can this come about in a natural, evolutionary way without having someone who knows all this decide that it should be so. The answer is in autocatalysis and self-selection and Figure 4 shows how one of these things might conceivably occur. Here you have a sequence of reactions, leading from the compounds which we saw were randomly synthesized by radiation (succinic acid and glycine) to the porphyrins. The sequence of reactions involves simple condensation, followed by decarboxylation and another condensation (a double condensation, really) followed by a series of oxidation steps, leading finally to the tetrapyrrole. If any of these steps is catalyzed by iron and if the iron porphyrin struc-



MJ-8400

Fig. 3. Evolution of a Catalyst



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Fig. 4. Biosynthesis of Porphyrin and the Evolution of the Catalytic Functions of Iron

tures turn out to be better catalysts for any of these steps than the bare iron itself, you can see that once this process begins (as it would have begun here by random synthesis and condensation), and an auto-selection of this sequence would enhance the transformation of the succinic acid and glycine into delta-aminolevulinic acid and finally into the porphyrin. There is already evidence that in the presence of iron and oxygen (or in iron and water, for that matter) and ionizing radiation or even ultraviolet light, one can actually synthesize small amounts of porphyrin non-enzymatically, that is by the primitive catalytic abilities of the iron and the iron porphyrins themselves.⁸

MECHANISMS OF ENERGY TRANSFER

One other aspect of the living organism which is very often alluded to, the ability of the living organism to transfer energy, is frequently called upon as one of its primary properties. It is often described in terms of the ability of the organism to transform chemical energy from one form into another, usually from the form of sugar into the form of pyrophosphate linkage. This is what most organisms are able to do today. The question arises: How does that come about? Here, again, I want to call upon the primitive catalytic abilities and show how this development of energy coupling systems might develop toward a system that might actually obtain today. Figure 5 shows how the energy involved in the oxidation of iron (the removal of an electron from ferrous iron to make ferric iron), or some part of it, may be used to condense two phosphate linkages

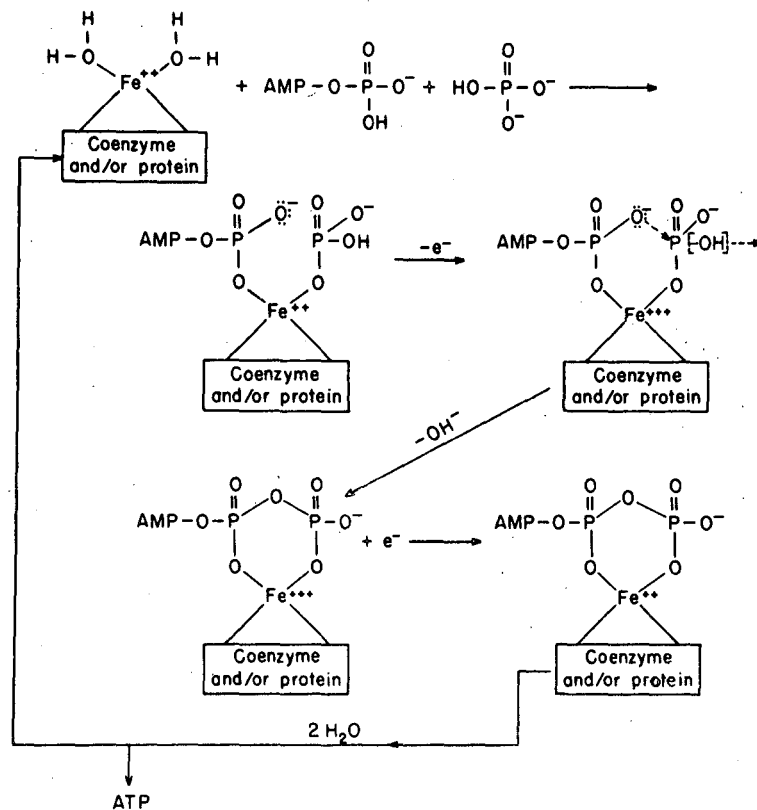


Fig. 5. Pyrophosphate Energy Storage

to form a phosphoric anhydride linkage -- a pyrophosphate bond. This suggestion of iron being able to do this for a variety of reasons was made six or eight years ago, and we actually tried using a bare, or hydrated, iron ions to synthesize pyrophosphate by oxidizing iron in the presence of orthophosphate to see if we couldn't make any pyrophosphate.⁹ We were not able to demonstrate the formation of any pyrophosphate by simply oxidizing ferrous iron with air in the presence of orthophosphate.

I just learned a few days ago, however, that one of my former colleagues and present associates, Dr. John A. Barltrop at Oxford, has indeed, at least tentatively, succeeded in doing this. The way he did it was by putting a proper organic construction around the iron. Instead of using the bare iron, as we did, he used an iron porphyrin and he was able to show the appearance of pyrophosphate when that ferrous protoporphyrin was oxidized to ferric protoporphyrin in the presence of phosphate.¹⁰ I trust that this will turn out to be a confirmed and successful experiment, because it does give us a clue as to how the iron porphyrin evolved and how the energy of oxidation of iron can be stored in the formation of pyrophosphate.

We have now discussed several aspects of the generation of living material. The first was the conversion of simple compounds into more complex ones in a random fashion; second was the auto-selection in which only certain compounds were formed, from the precursors, which have some autocatalytic function; and the third was some way in which the energy conversion and storage process might have had its beginning.

FROM CHAOS TO ORDER: MOLECULAR CRYSTALLIZATION

All of the above aspects of generation of living material have been discussed in terms of molecules in random solution, that is molecules presumably in water not oriented with respect to each other, merely dissolved, and randomly moving around in solution. We know that another aspect of a living organism is the fact that it is not random -- it isn't just a big bag full of molecules behaving randomly. Whenever you look at a living organism from its outside -- the whole man, in other words -- or into the innermost part (whether it be a man or a microbe), you find that it is an organized structure -- it is not simply a sack of catalysts and their substrates. A living organism is a highly organized structure in which all of the elements are related ^{one} to another in a rather specific way. This, to me, calls to mind the idea of crystallization which may give rise to order and we then wonder how the order arose in the first place, in living organisms.

The order of a crystal resides in the nature and symmetry of the molecular interaction which, in turn, is a property of the structure of the molecule itself -- what its shape is, what its force fields are, etc. So, the nature of the order that one gets is really built into the molecule itself. We must, therefore, look into the construction of the molecules themselves to see if there is anything in them which might give rise to the kind of order we see in living things.

Protein Structure

This is not difficult to do and there are three kinds of macromolecules upon which the structure of living organisms is based. The first, and possibly the most important of these, is the protein. The proteins, of course, are made up of amino acids in polypeptide linkage, the secondary structure being the helical structure and the tertiary structure being the various ways in which the helix itself is folded. We already know that the helical structure is at least partly dependent upon the particular geometry of the peptide structure itself and this gives rise to the helix. This, in turn, when it is properly packed will give rise to actual visible, macroscopic structure.

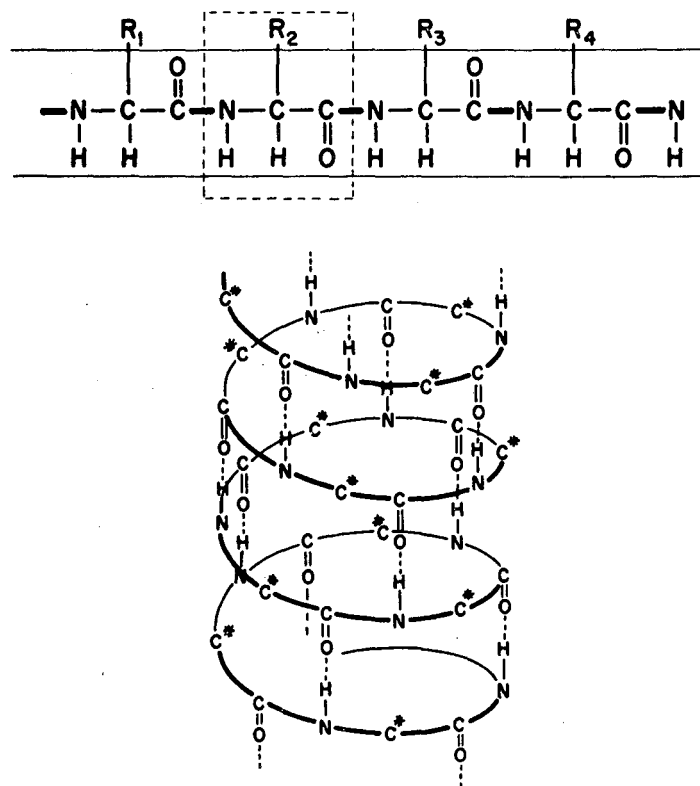
In fact, in recent years (just the last year or so) another biochemist, S. W. Fox, has been doing experiments on the conversion of the simple amino acids into proteinaceous, or proteinoid, material under non-biological conditions, that is under what he calls prebiological conditions. What he did was to take a mixture of eighteen to twenty amino acids and heat them up in molten glutamic acid, and he was able to get the amino acids to hook-up together, one to another, and make polypeptides of rather large structure (3,000 to 10,000 molecular weight). He was able to reduce the temperatures at which he had to perform this experiment by putting in some polyphosphate. When he puts polyphosphate into the reaction mixture, he finds he can get proteinoids out of mixtures of amino acids at temperatures of around 70-80° and these proteinoids are relatively high molecular weight materials. Furthermore, if he lets the proteinoids cool out of a clear aqueous solution, they begin to take up various shapes and

forms which, to Fox at least, have the appearance of cocci and they behave in some physical respects as if they were spherical organisms, or bacteria which have a spherical shape.^{11,12,13} Already, just in the proteinoid material itself, one can begin to see structural features built into the molecular structure itself.

The other aspect of the protein contribution is what it does to the catalytic properties of the elements with which it may be associated. Both aspects depend upon the protein construction, and Figure 6 shows the protein structure. The dotted square surrounds these amino acids, of the type which we can make by random synthesis, and when the amino acids are hooked together by dehydration (the removal of a water molecule between the acid and the amino group), we get these peptide linkages. When there is a long chain, because of the tendency of the hydrogen on the amide nitrogen to form a bond with the amide carbonyl of a suitably placed peptide group (more or less three residues are removed from the hydrogen), we get the well known alpha-helix formed which is a built-in element of order -- built into the polypeptides because of the very nature of the structure of the peptide linkage

Nucleic Acid Structure

Another major macromolecule of living organisms, and one which we have heard a great deal about in the last decade, is the genetic material itself, that is the nucleic acid which, presumably, carries the information which the living organism uses to reconstruct itself. The structure of nucleic acid is also one which has built into it certain elements of order.



MU-16147

Fig. 6. Protein Structure

Figure 7 shows you that nucleic acid is made up of a group of four bases (adenine and thymine, and guanine and cytosine) which are held together, in pairs, by hydrogen bonds. These bases are, in turn, attached to the ribose, or desoxyribose, sugar. The desoxyribose sugars are each held to their neighbors by phosphate linkages. You can imagine the nucleic acid as made up of a series of flat discs, along the edges of which are these ribose phosphate ribbons. If you take the two ribose phosphate ribbons and twist them into a double spiral you get the kind of structure which is seen in Figure 8 which is pretty certainly a basic structure of the desoxyribonucleic acid (DNA) molecule.¹⁴ The ribose phosphate ribbon is on the outside, the hydrogen bonds are in the middle holding these disc-shape pairs of molecules together, ^{with} one pair on top of the other, flat side on. This is an intrinsically stable kind of molecular arrangement -- a sort of molecular crystal -- which corresponds to the stable type of packing for unsaturated aromatic type molecules, or pi-molecules, here represented by these pairs of bases. The nucleic acid also represents a type of order, which is built into the molecule, and results from the structure of its component parts.

The question has arisen, and is now in the very forefront of biochemical study, namely, what is the relationship of the order of bases in the DNA helix, which presumably contains the information for the reproduction of an organism, and the construction of the protein which was shown in Figure 6. This is a very active field of investigation, at the moment. How does the nucleic acid determine the structure of the protein, or how does the protein build the nucleic acid. Which came first -- that is the kind of question we are dealing with. In evolutionary terms, the question is: How could nucleic acid evolve without the protein? How could the relationship between nucleic acid and protein have arisen?

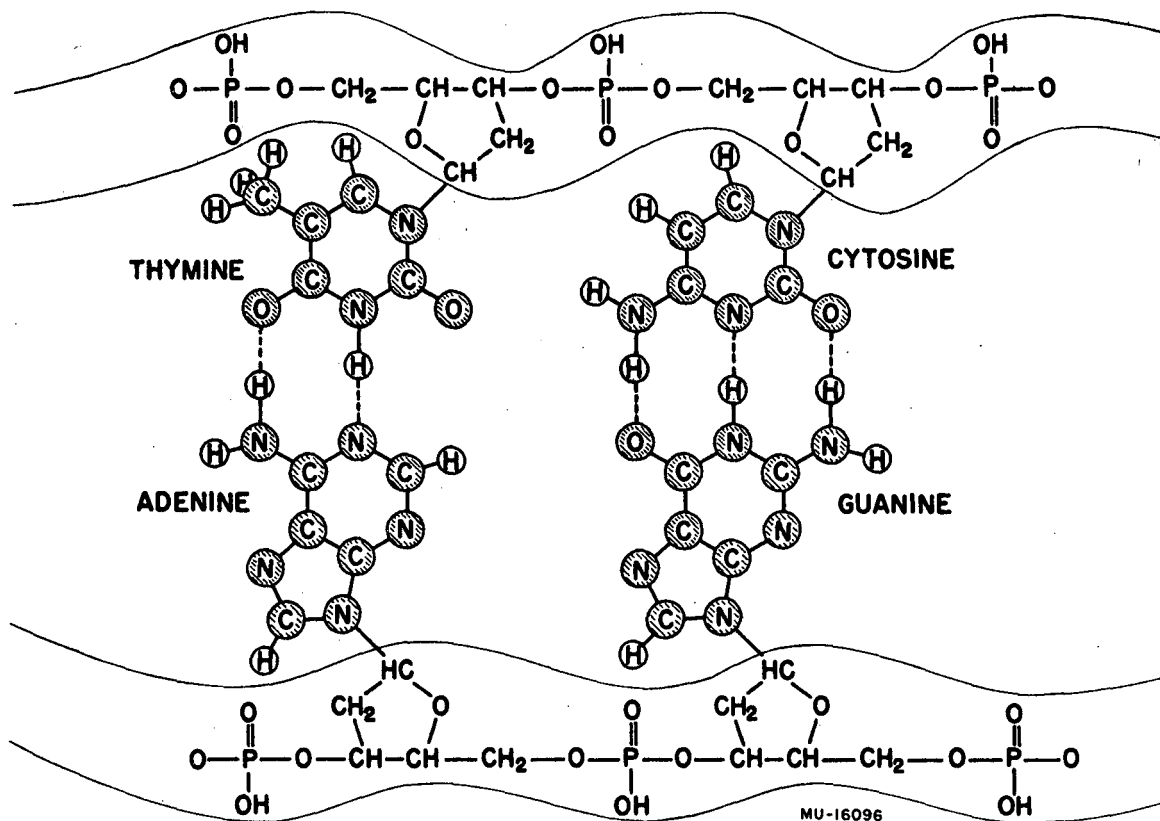
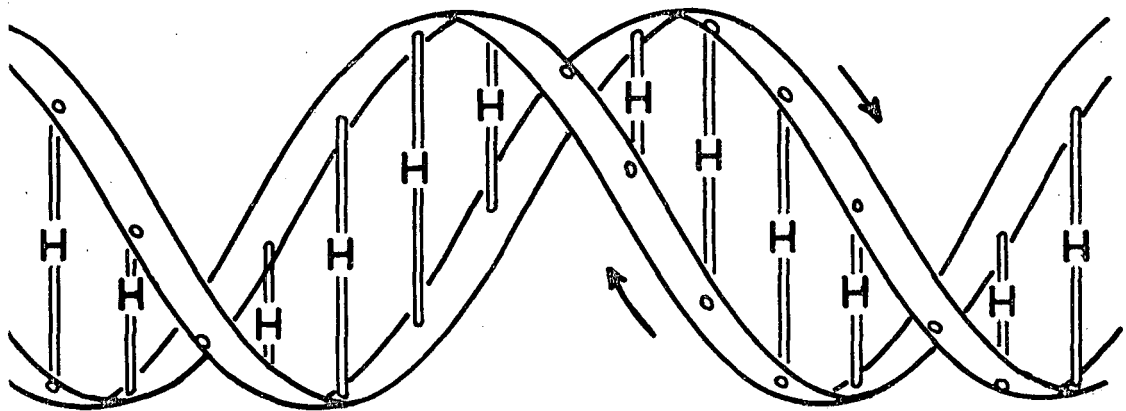


Fig. 7. Molecular Drawing of Components of Desoxyribonucleic Acid



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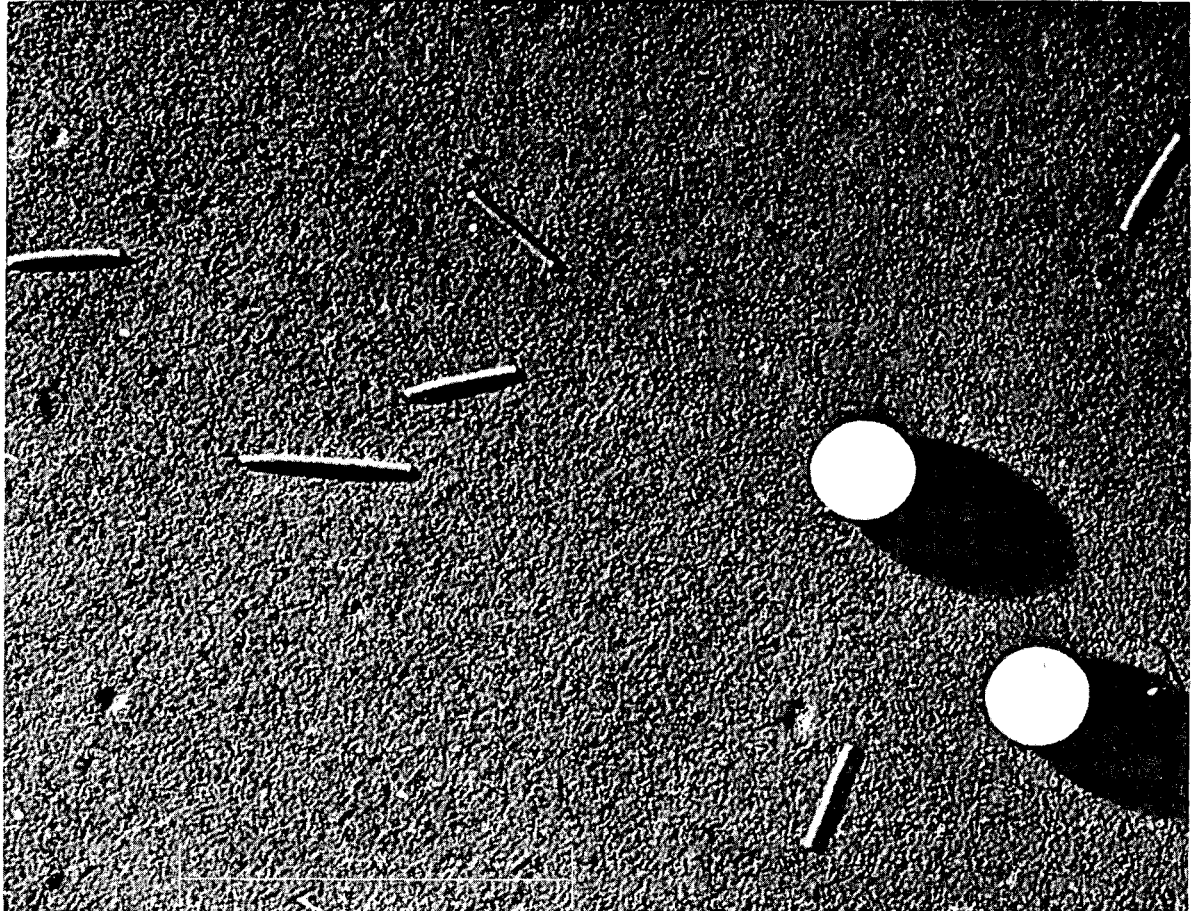
Fig. 8. Double Helix Model for DNA

There is one school of thought which emphasizes that the protein must have been developed first.¹³ There is another group, namely the geneticists, who say the essence of the living organism is the self-reproducing nucleic acid (DNA molecule).¹⁵ The question of how they got to know each other is not very clear and is, as I say, the subject of the immediate investigation.

It seems to me very likely that the two things arose in the evolutionary scheme side by side. The random synthesis which was shown in Figure 2 shows none of the nucleic acid particles; it shows only the amino acids, which are on the way to proteins. Until now, there hasn't been any real evidence that the nucleic acid components, the bases -- adenine or guanine, for example -- can be made by a random synthesis. No one had yet demonstrated this. (We will return to this later.)

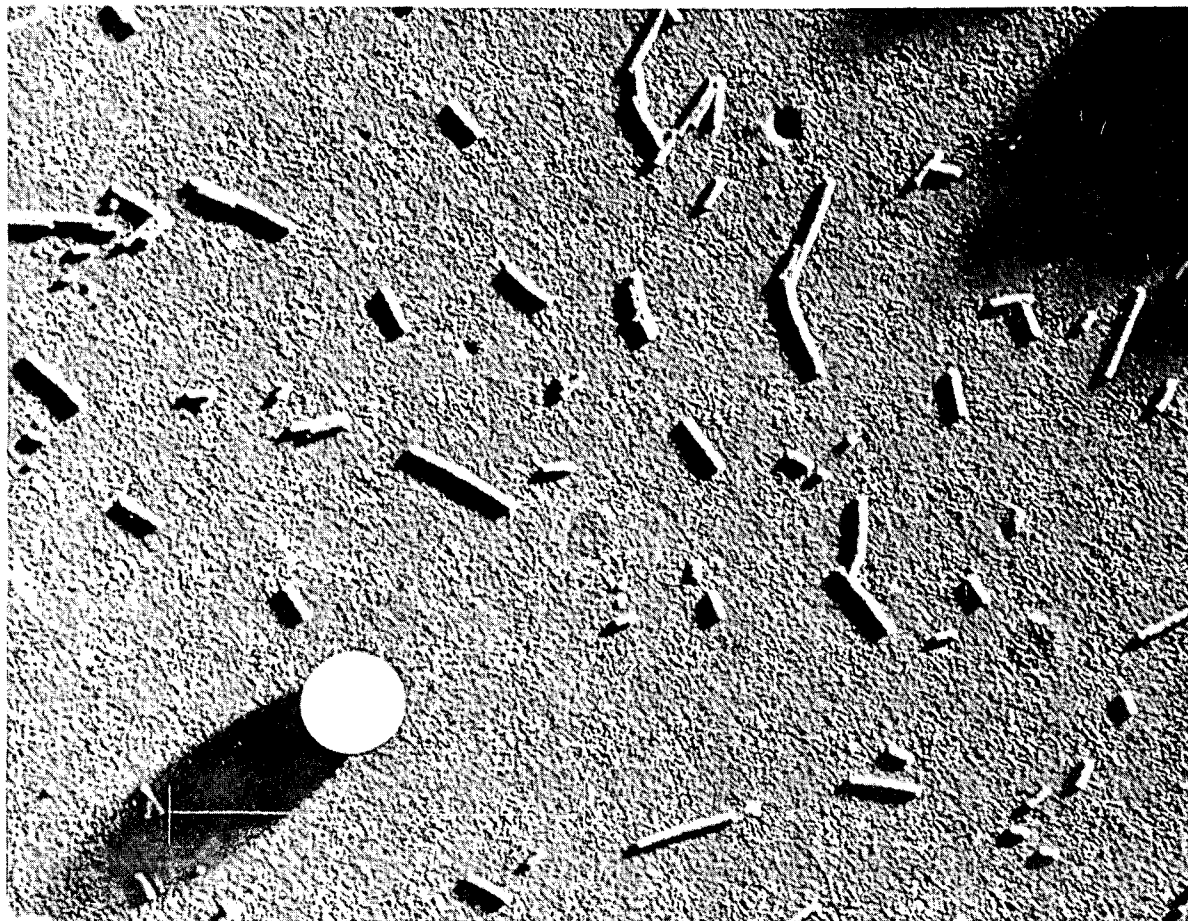
Relationship between Visible and Invisible Structures

In this stage of the story we must now put these various structural elements together to form the ordered array which one finds in the living cell, and I think that one can call upon the structural features of the molecules themselves, in general, to give rise to the macroscopic order that one sees. Figure 9 shows an electron microscope photograph of tobacco mosaic virus (TMV) and this shows the clear, clean visible structure of the TMV virus which is made up of both nucleic acids and proteins. Figure 10 shows what happens if you take the nucleic acid and protein of the TMV virus apart and then dump the proteins back into the solution under conditions such that the proteins will re-aggregate. You will



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Fig. 9. Native Tobacco Mosaic Virus (TMV)



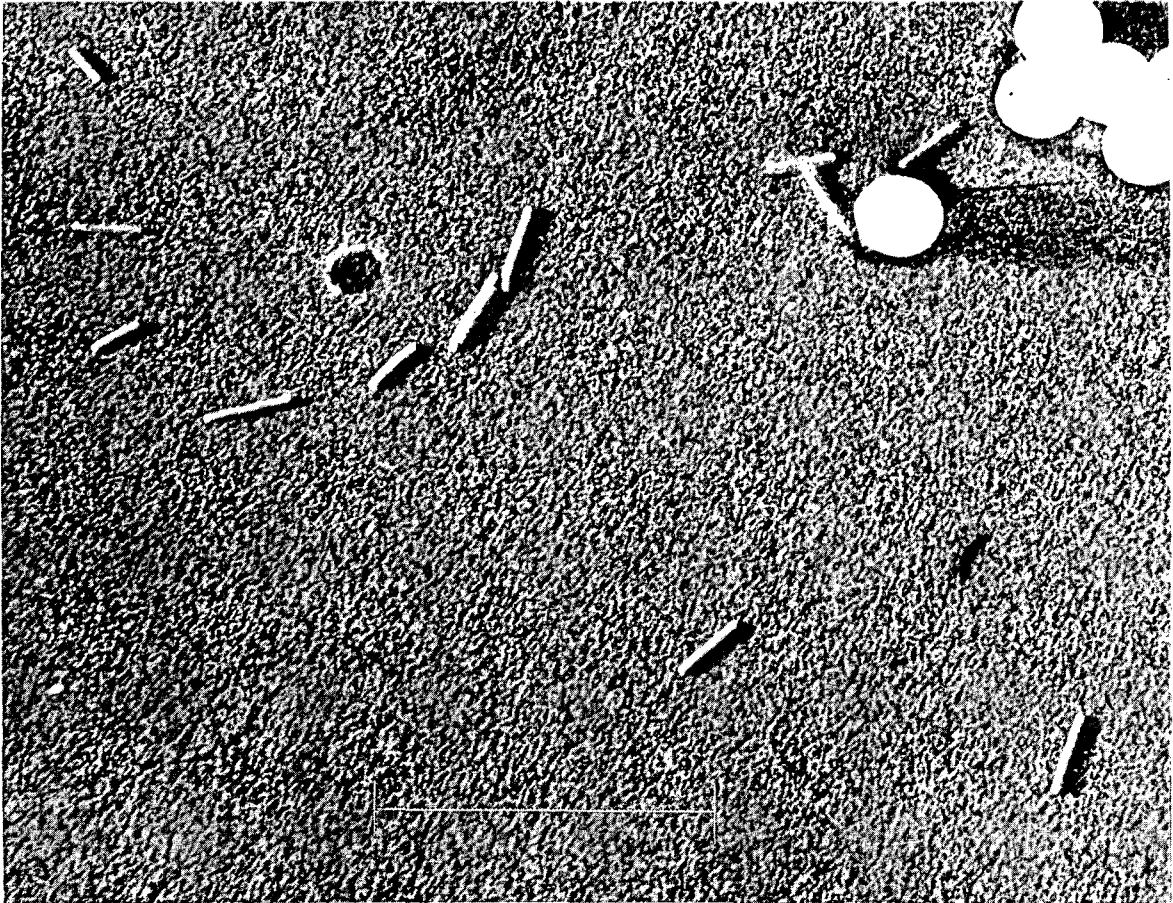
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Fig. 10. Repolymerized TMV Protein

notice that the proteins re-aggregate in long, rod-shape particles, just as the TMV itself was, but the length of the particles is varied. The nucleic acid is missing, but the protein has enough of this structural element built into it so that it re-aggregates in a crystallization phenomenon, giving something which looks very much like the structure of the intact virus. If, however, we put the protein and nucleic acid back together again, we find (Figure 11) that the TMV virus particles come out about the right length.

It is quite clear, therefore, that both of these structures (the protein and the nucleic acid) are required in order to give the right total structure for the TMV particle. There is an interaction between these two elements to bring about the final construction. This is nothing that has to be done by some unknown 'force.' These are, if you like, molecular crystallization phenomena.

There is, of course, an area of unknown, noncrystalline (colloidal) and surface chemistry for the construction of structural features, in which we are not as fully educated as we ought to be. This is one of the areas in which we should do more work. However, I don't think you will find it too difficult to make the next step from the structural features which we have outlined as intrinsic in the molecular structure itself to the construction of the cell.



ZN-2287

Fig. 11. Reconstructed TMV Protein and Ribonucleic Acid

LIFE ON OTHER PLANETS?

With this information as a background, we can proceed to the next step. We have gone through Chemical Evolution right up to the point where we have formed a primitive organism of some sort, and from here on the Darwinian selection mechanism can take over and I am not going to go any further with this aspect of the discussion.

The next idea I want to take up is the application of this type of discussion to the question of whether we are likely to find that similar events have occurred elsewhere than on the earth.¹⁶ What do we require? We require, in order for this sequence of events to occur, a certain temperature range, composition of the atmosphere, and a variety of other things, all of which are now definable. The sequence of events occurred because of the nature of the carbon atoms nitrogen atoms, hydrogen atoms, etc., giving rise, as they do, from methane to acetic acid, to formic acid, to malic acid to glycine, etc., and these, in turn, give rise to proteinoids and to the nucleic acid types of molecules, thus building up in structure the order of living organisms and the interaction of molecules of the type that are required. All this hinges, in fact, upon the nature of the elements with which we are dealing, namely, carbon, hydrogen, nitrogen, oxygen, iron, phosphorus, etc.

If we have a set of earth-like conditions (physical and chemical), we can expect this sequence of events to occur. The question we have to answer is: Are there any other places in which this set of conditions might obtain? Here we must turn to the astronomers, and they tell us that in our solar system the only places that we are likely to find a set of conditions which would correspond to the ones which we have just described are on the two neighboring planets -- Venus on the inside and Mars on the outside -- and that there is some chance that this

sort of condition might be closely enough approached on each of these two planets that a similar sequence of events, somewhere contiguous with the ones we have just described, could have occurred and might even be occurring today.¹⁷ In fact, there is some evidence that on the surface of Mars there are organic compounds, varying with the geography of the surface and with the seasons.¹⁸ However, we are so limited in our ability to observe that we can just barely make out, say, a CH frequency in the reflection spectrum of Mars and we would like to be able to do better; and I think we will, within the matter of a few years. (There are other uses of high flying vehicles and satellites besides looking down -- you can look up!)

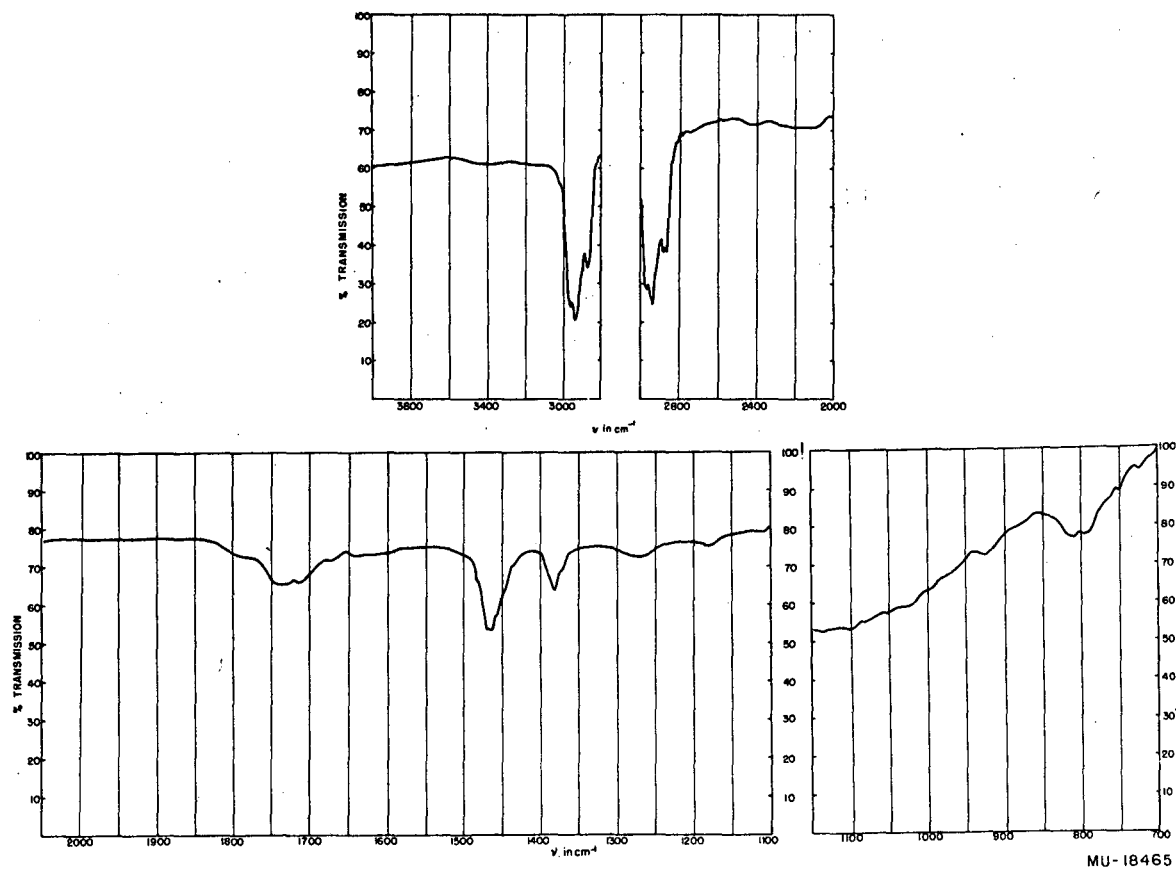
Meteorite Experiments

The other type of experiment which we can do would be to go out into space and collect bits of these various planets and other places, and bring them back to earth to see if there any organisms in them, or, if not organisms, to see if there is anything that might have constituted this prebiological environment that we are talking about. Unfortunately, we can't quite do that yet -- it will probably be more than five years before we can do that. But there is available to us a material from those regions of the solar system which should give us some kind of information about what is out there. These are, of course, the meteorites. We can't place an order for the meteorites. We have to take them when and where they come, and that isn't very frequent, and what is more, they get into museums and you can't get them out of the museums. (I don't blame the museum keepers. Actually, if they gave out the meteorites to everyone that asked for them, there would be none left. So,

they do not show an unreasonable reluctance. It is just too bad they don't have more meteorites!)

In any case, we were able to get samples of meteorites, one from the Smithsonian Institution (Murray) which fell in 1951 and one from Paris (Orgueil) which fell in 1864. These meteorites contain carbon which is the main reason for looking at these particular ones. Unfortunately, the meteorites do not contain much carbon; about 2% of the total weight of the meteorite is carbon. What is worse is that of that 2%, a large fraction of the carbon is non-extractable. The carbon is not in the form of carbide, but perhaps some other form which is non-extractable under the mild conditions we must use.

From these two meteorites one can extract, with water, an appreciable fraction of the carbon. One of them (Orgueil) contains salt which is mostly magnesium sulfate and from the other one (Murray) the water extract contains a salt which is mostly calcium sulfate. The carbon content of these water extracts is also not the same for the two meteorites. However, both meteorites show ultraviolet and infrared absorbing material, which might lead one to believe that there is a wide variety of compounds present in these water extracts, including hydrocarbons and heterocyclic bases. Figure 12 shows, respectively, the infrared absorption in a carbon tetrachloride extract (of Murray) and you can see a clear carbon-hydrogen absorption ($\sim 2900 \text{ cm}^{-1}$) and there is a carbonyl absorption as well ($\sim 1725 \text{ cm}^{-1}$). This is a rather complex material (a mixture of many things). Figure 13 shows the ultraviolet absorption of the water extract as a function of pH. You can see that there is a pH-sensitive absorption band right where cytosine absorbs and it behaves very much like a cytosine-type of absorption.¹⁹ I don't think this is cytosine; it's not pure, for one thing -- it is a mixture.



MU-18465

Fig. 12. Infrared Absorption Spectra of Meteorite Murray Extract

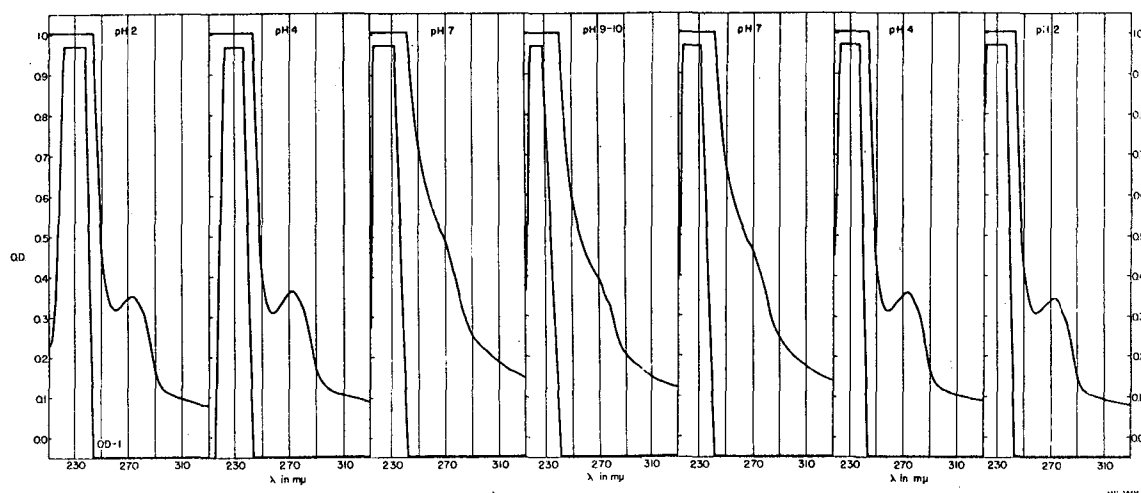


Fig. 13. Ultraviolet Absorption Spectra of Meteorite Murray Extract

The meteorite analysis is proceeding. Unfortunately, we don't have enough of either one of these meteorites, so I can't give you a definitive statement of the construction of this cytosine-like material in the meteorite. I can only tell you the general character of the compounds that are found in the meteorites.

I might say that we have found no amino acids in the aqueous extracts of the meteorites. This is harking back, now, to the question of which came first, the protein or nucleic acid. I point out that neither of the meteorites had amino acids which could be detected in the extracts, although they both showed this type of ultraviolet absorption as well as hydrocarbon-like material in the infrared.

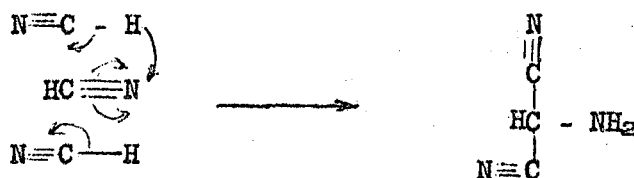
Amino Acid Synthesis under Primitive Earth Conditions

The other thing I want to call your attention to is the fact that there is much in the way of organic material in the solar system and interstellar space as we can recognize it in the form of light emission from, for example, the comets. There is much CH emission and lots of cyanide in the comet tails. This is a rather important observation, and the reason for this is that in the experiments of Miller⁶ in which he irradiated methane, ammonia and water and got glycine and alanine (and a few other amino acids), it turns out, when you look at it carefully (and we have done the same experiments here) that these amino acids represent an extremely small fraction of the amount of methane that has been converted to organic material -- less than 1%. Most of it is something else, as yet undetermined.

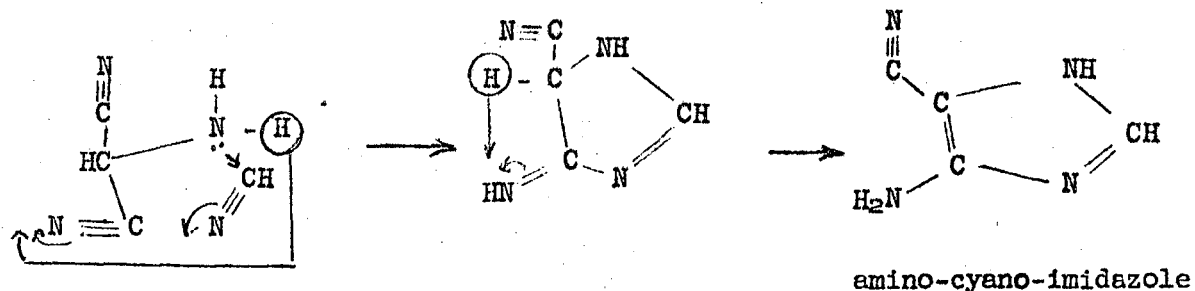
The mechanism of the formation of these amino acids, however, seems easy to understand, although here, again, it is subject to uncertainty.

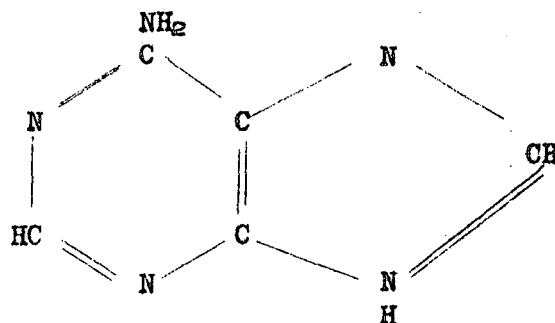
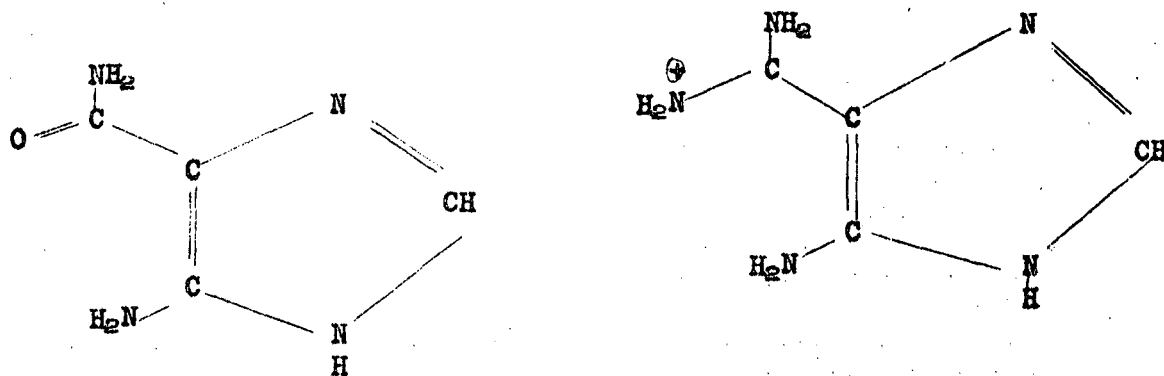
Presumably it is an HCN addition onto an aldehyde in the presence of ammonia to form an amino acid -- a Strecker type of synthesis. This means that when you put ionizing radiation through methane and ammonia you get HCN. It turns out that HCN and ammonia is a very sensitive mixture. This sensitivity has been demonstrated by a number of people, but most recently by Oro.²⁰⁻²³ Oro was able to show that mild heating ($> 100^{\circ}\text{C}$) of a mixture of ammonia and HCN (approximately 1 N equivalent ammonium cyanide) produces, in addition to a large amount of black polymer,²⁴ identifiable compounds in small amounts. By extraction and chromatography, Oro was able to identify the two imidazoles and adenine shown in Figure 14. It is interesting to note that adenine is isomeric with a pentamer of HCN, that is, it has the empirical formula $(\text{HCN})_5$. The two imidazoles can be formulated in terms of a sequence of self-additions of HCN and they might very well be intermediates on the way to the formation of adenine.

In fact, two HCN additions across a third to produce the known but unstable trimer, aminomalonitrile,²⁵ could be followed by an addition (of the



inverted type) of the resulting amino group across a fourth HCN to produce the amino-cyano-imidazole which would be the parent of the two that have been found:

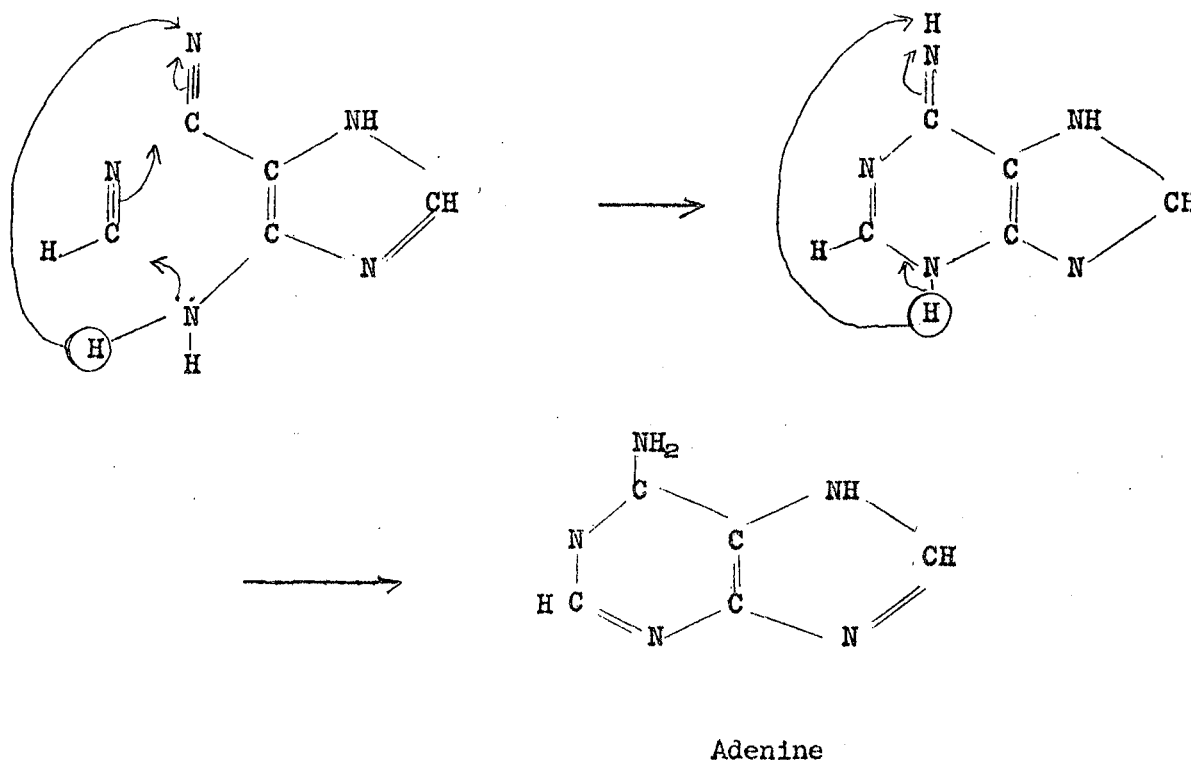




Adenine

Figure 14

A final addition of the amino group thus formed across another HCN with ring closure leads to adenine. Thus,



We, ourselves, have done a bombardment experiment, starting with a mixture of methane, ammonia, hydrogen and water, and found a small amount of amino acids of the general distribution that Miller has reported. In addition, however, we found a large number and variety of other compounds on the paper chromatogram which we have located, by using radioactive methane, but which as yet are unidentified. It is not at all unlikely that some of these will turn out to be aromatic types of heterocycles, and we are thus brought to the view that both the heterocyclic compounds as well as the amino acids may have been formed in the very earliest stages of Chemical Evolution.

CONCLUSION

It thus appears that there are two separate functions (the catalytic development of the proteins and the code development of the polynucleotides) arising and growing simultaneously. This could account for the present-day close relationship between these two substances. It remains for us to develop both kinds of observations, that is to explore, as the biochemists are doing, the present-day mode by which the code contained in the polynucleotides is translated into the chemically versatile protein, and, secondly, approaching from the other direction, to examine the modes of chemical reactions which might lead to structural interrelationships between the purine and pyrimidine bases, their polymerization into polynucleotides, and the generation of amino acids and polypeptides.

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