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ORIGIN OF LIFE

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ORIGIN OF LIFE

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You have had an opportunity in the last five lectures of this series to hear a good deal about the way in which the universe became what it is today -- not only what it is today but how it got that way. You have heard about galactic evolution, stellar evolution, and something of the evolution of the solar system and how the earth evolved. Tonight we are going to make the transition between the first five lectures (which were completely concerned with the evolution of the physical universe) and the next five lectures which will be completely concerned with biological problems. I am "squeezed" in the middle between these two heavyweights, to try and make a bridge between the physical evolution of galaxies, stars and solar systems (such as our own and the earth) and the growth of living organisms on the surface of the earth.

This kind of a question, i.e., how life originated, is, of course, a major one with which the human race has been concerned ever since it began to think about itself. Since I began writing about it, I have been keeping an eye out for ways in which this question has been answered. I have chosen a couple of examples of the answers which have been provided in the past.

FIGURE 1 shows a set of Israeli stamps representing the six days of creation as they were described in Genesis. Reading from right to left:

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The first day is that of light, the second is the day of the firmament and the heavens, the third day that of the earth and plants, the fourth day the day of creation of the sun and the moon, the fifth day being that for the animals, and the sixth day for man. This is a concept which was well described several thousand years ago, and was not very far from what the present-day concept is. What I hope to do tonight is to outline for you what some of the present-day points of view are -- what the present-day answer might be -- in the context of modern science and within the framework of natural laws as we know them.

A more recent evidence of how this might develop can be found in the writings of Charles Darwin himself. One of the very first expressions of the way in which evolution works was contained, I think, in the title of a paper by Darwin and Wallace, which was never published, at least not under that title. The title to which I refer is "On the Tendency of Varieties to Depart Indefinitely from Original Types", and it really expresses the nature of <u>biological</u> evolution, as Darwin saw it and as we know it to be. Of course, there are no two individuals of a species which are identical, and sometimes if they are separated after they come into existence and are not allowed to interbreed, these two individuals can gradually become separate varieties of a given species; if they are kept far enough apart so that they can never cross, they can eventually, with later modifications, change into different species which no longer can cross. This is basically Darwin's idea of the "Origin of Species". If we now take Darwin's idea and trace it backwards, i.e., start with a pair of related but different species and trace them back in time, we

find them getting closer together as we go further back in history. Eventually those two species will be found to have arisen from two varieties of the same species. If you go back still further, there will be a single variety of a species which, in turn, will have been one of several varieties of still another species. By continuity, as Darwin said (and I will read you his letter in a moment), you must arrive at a single starting point. That starting point is what we tend to mean by the "origin" of living matter.

Our problem is to get to that point from the terrestrial and interstellar atmospheres which have been discussed in the last three or four lectures. Darwin wrote a letter about this idea, in response to a query in 1882. FIGURE 2 shows a picture of that letter in his handwriting, found in Cambridge University (England) about four years ago. This letter states:

"You expressed quite correctly my views where you said 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 matter 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 consequence, of some general law.

(The statement to which Darwin refers, and which he had forgotten, was written earlier, in 1871.)

It is often said that all the conditions for the first production of a living organisms are now present, which could ever have been present. But if (and oh what a big if) (this is Darwin's parenthetical remark) we could conceive in some warm little pond with all sorts of ammonia and phosphoric salts -- light, heat, electricity, etc. -- present, that a protein 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 was a very perspicacious man. He not only could see what was possible, but he also recognized his own limitations, and the limitations of the knowledge of his time. He was not yet ready (nor was science ready) to go through the exercise which we will go through tonight, one hundred years later. Now, of course, we have much more information about the rules by which molecules, of which living matter is constructed, interact, change and transform. We will make use of thatknowledge of what the molecules are, and what the rules of their transformations are, which have been evolved over the last one hundred years, since Darwin, and we will try to perform in the laboratory as much of the kind of event which might have occurred in the early history of the earth, more or less according to the plan which Darwin himself had already laid down.

CHEMICAL EVOLUTION

In order to trace the events from the beginning of the earth, about 4.7 billion years ago,until the first organized element which might be called "alive" appeared, we have to know what the starting points might be. (That is, of course, what the first five lectures were all about.) I am not going to repeat what has already been said, and will merely summarize it insofar as it is relevant to the subject at hand.

Let's have a look at the structure of our solar system (FIGURE 3) which gives us the place of the sun and the earth in that system. Here there are two types of diagrams, one giving the distances between the bodies of the solar system (the sun and the various planets in their orbits, as they extend outwards), the other being a dimensional relationship which shows approximately the correct dimension of the sun with respect to the earth, the third planet. The earth is quite small with respect to the size of the sun as well as the giant planets, Jupiter and Saturn. You have heard

a great deal about the evolution of this solar system and how the atmospheres of the planets might have been generated.

A view of the earth, which was taken by satellite, about 300,000 miles out, is given in FIGURE 4. It's easy to recognize South America under the clouds, and the Florida peninsula. The main idea to gain from this figure is to recognize the nature of the "ball" upon which we live. It has its present-day skin of a very thin atmosphere, compared to the size of the entire globe, but that atmosphere is not necessarily the same in composition as the original atmosphere. You heard last week an extensive discussion of the nature of the earth's atmosphere originally, and how it almost surely was lost, and that a secondary atmosphere was generated from gases evolved from within the earth itself. A little bit later the nature of those gases will be discussed and how they could, in fact, be the sources of the biologically important materials which would be necessary for living things to appear.

Before that, however, let me review briefly what we know about the history of this earth in geological terms. The outline of the earth's geological history is given in FIGURE 5. The column on the left shows the years back from the present. The right-hand column shows that the fossil record is fairly complete only for the first 600 million years back; from there on, the fossil record is only now being discovered and recognized. The algal and bacterial microfossils, which are labeled as appearing about 3.5 billion years ago, are only now being recognized as entities in the ancient rocks. "Biological evolution" is this enormous period of time, from somewhat less than 4 billion years ago to the present time.

Tonight we wish to discuss the period labeled "chemical evolution", and at the present time we don't really know when it started, because one of the requirements for its beginning was an atmosphere, and the formation of the earth itself, a little less than 5 billion years ago. The period labeled chemical evolution in Figure 5 is what we will be discussing for the rest of this evening.

Primitive (Prebiotic) Chemistry

The description of the period of chemical evolution has been expanded, as shown in FIGURE 6, and as we progress I will be able to indicate to you some of the things which we will try to describe as events which could be simulated in the laboratory to test the various notions of how these various operations might have occurred. You should realize, of course, that we are speculating about what could have happened 4.5 billion years ago. What we actually do is to attempt the same kind of "creation" in the laboratory, under conditions which we think might have obtained at that time, and see what the results are, i.e., see if useful materials appear.

You have already heard that most of the material in the universe consists of hydrogen and a few other elements -- carbon, nitrogen, oxygen, sulfur, phosphorus (roughly in the order of their abundance) -- which are the important materials of which living things are constructed. The first two stages of cosmic evolution have already been discussed; The way in which the heavenly bodies are formed from hydrogen and how the other elements, elements heavier than carbon, are formed from hydrogen as well. We now come to a situation in which the whole scale of things has changed. We are no longer dealing with transmutations of the nuclei from one element to another; we are now talking about a "cold" situation, in which the atoms can combine with each other and hold together.

FIGURE 7 shows some chemical symbols of the molecules which we believe to have been present not only in the first atmosphere of the earth, but also in its second (ammonia, methane, hydrogen, water). You remember that the primary atmosphere of the earth, which must have been composed of hydrogen, methane and ammonia, must have been lost because of the lack of atmospheric helium. So, all the primary molecules vanished, and the earth's atmosphere with which we must deal is supposed to have been generated by gases liberated from the inside of the earth, a process which still continues. Most of these gases are carbon dioxide,carbon monoxide, hydrogen sulfide and nitrogen. There is the problem of how we can get from oxidized carbon (carbon combined with oxygen) and molecular nitrogen to reduced carbon and nitrogen (carbon combined with hydrogen and nitrogen combined with hydrogen). The materials CO_2, CO, etc. apparently had to be reduced by the hydrogen, which would not stay in the atmosphere because it was too light and was escaping from the gravitational pull of the earth. You may remember that one of the arguments that has been used is that it is necessary to have hydrogen in order to get the molecules necessary to create life. It is a "circular argument" of a sort.

From the small organogenic molecules (Figure 6) the biomonomers can be formed, and this is the first stage of chemical evolution. Biomonomers are the small molecules which are required to be hooked together in long chains (biopolymers) to make up the substance of living matter. Originally, the biomonomers must have been created in an abiogenic manner (without life).

These three phases -- from the original simple molecules, to the biomonomers; from the biomonomers to the biopolymers; and, finally, from

the biopolymers to the membranes and the first living systems (which occurred roughly abut 4 billion years ago) -- are necessary for the creation of life as we know it on the present-day earth.

The question of how the first biomonomers might have appeared is before us. (Please keep this general chart in mind, because we will return to these three stages as we progress.) What are the molecules which we start with, for the creation of the biomonomers? We will start with the first group (Figure 6) which are supposed to have been the primary atmosphere of the earth (and also its secondary atmosphere) and which is today the atmosphere of the heavier planets (methane, ammonia, hydrogen and water vapor). FIGURE 7 shows models of the primary molecules of the primitive earth. These are molecular representations of hydrogen, water, ammonia and methane (a carbon hooked to four hydrogen atoms). These first four are presumed to be the primary molecules of the earth's atmosphere. From these evolved the amino acids, sugars, the fragments which eventually form the nucleic acids (of which genetic material is composed) and the polysaccharides and fats (of which cell walls are constructed). It is from the primitive molecules that the small biomonomers are constructed.

Several ways for this construction have been devised in the laboratory. The principal route which was first suggested in the middle twenties was tried experimentally and successfully first in 1950 in Berkeley. Using the primary primitive molecules (CO, CO_2, H_2O, NH_3, H_2, CH_4) as the starting material and irradiating them by various kinds of intense energy sources (such as solar ultraviolet, ionizing radiation from radioactive material from the earth's crust, or cosmic rays, or from another form of the sun's energy which is created when the sun heats the atmosphere, making the gases on the earth flow with respect to each other, creating

static charges, and resulting in lightning) the molecules are broken up and the free atoms which are formed as a result of breaking the bonds then recombine. The laws of recombination are intrinsic to the atoms, and they are not random. This can be seen by noting that the carbon atom combines with four hydrogen atoms, the nitrogen combines with three hydrogen atoms, etc. The rules of combination (the valence rules) for chemical combination continue to operate for recombination after the molecules are broken up. Thus, different kinds of combinations of atoms are created which are stable for a long period of time.

This is exactly what occurred when such an experiment was performed, in Berkeley in 1950, using the cyclotron as a radiation source and using hydrogen, carbon dioxide and a trace of iron and water as the target. We created some reduced compounds, one of which is represented in the second row of FIGURE 8 (formaldehyde), as well as a whole variety of other products (acetic acid, glycolic acid). What was left out of the experiment which we did in Berkeley was a source of nitrogen. Miller, at the University of Chicago, in 1953 put ammonia into the reaction mixture, and created a variety of products, including HCN (hydrocyanic acid). This particular molecule contains atoms still high up on the energy scale; that is, there is energy stored in the molecules enabling them to perform other chemical events in the proper environment. It is possible to make many other important molecules from HCN, and this has been done extensively under simulated conditions in the laboratory.

The apparatus that Miller used for this series of experiments is shown in FIGURE 9. He used electric discharge as a source of energy, put methane, ammonia,water and hydrogen into the apparatus, and collected

the products in the water as the gases were pumped through the discharge for several days. The water was taken out and analyzed. Many different chemical compounds had formed. Because there was nitrogen in the original reaction mixture, there were more products than in the first experiment which lacked ammonia.

You remember that most of the carbon which comes out of the earth today is in the form of carbon dioxide, and most of the methane which is seen today is biologically produced. The question is: Where did the methane come from on the original primitive earth? When primitive molecules are broken up, you get more of the "useful" molecules in the bottom row of Figure 8 when methane is present in the atmosphere than when only carbon dioxide is present, which is the basis for the "circular argument" suggestion that it is necessary to have methane in the atmosphere in order to create a situation where life could arise. The molecules in the bottom row of Figure 8 are those which are used by today's living organisms as material for food.

Today's living organisms construct themselves out of the materials in the bottom row of Figure 8. They are amino acids -- note the amino group (NH_2) attached to a carbon which, in turn, is attached to the -COOH (the essential component of an organic acid). All living matter is constructed from them. When these materials are hooked together in a certain way, it is possible to get proteins. Acetic acid, in the second row of Figure 8, is the first of the fats which give rise to the membranes of living cells. The carbohydrates (the sugars and cellulose of plants) generally are composed of formaldehyde polymerized in various ways.

We have now found ways of transforming the primitive atmosphere,

which is represented by the top row of Figure 8, into biomonomeric molecules, represented by the bottom row. The materials in the middle row are intermediates, molecules which are temporarily there and can give rise to the molecules of the bottom row. This is, of course, a generalized picture of the kind of material which the introduction of energy into the earth's primitive atmosphere will produce. This part is no longer a question of speculation. A more significant speculation is: What was the earth's primitive atmosphere? We really still do not know what the primary, primitive atmosphere was.

Interstellar Molecules

Having created the primitive biomonomers and having realized that there was some problem about having the molecules of the top row of Figure 8 present in large enough amounts to produce this type of result, recent indications of another possible source of these molecules has been especially attractive. This turned out to be interstellar space itself, a rather unlikely place to find such large molecules. Until three or four years ago, the only molecules which were known in intersteller space were simple fragments, such as a hydrogen atom attached to an oxygen atom, or a carbon atom attached to a nitrogen atom (a cyanide radical). These fragments were incomplete molecules, but they had been observed in various parts of the sky. The astronomers are able to see molecules of this type by virtue of the light they absorb when the vibrations begin, or the light they emit when the vibrations cease. The cyanide and the hydroxyl radical have long been recognized as constituents in interstellar space. However, in

the last three of four years, the development of radioastronomy by means of which one can observe not only the vibrational modes of the molecule (or its fragments) but also the way it rotates, has accumulated. The molecule absorbs or emits energy depending upon the speed of rotation. The energy of rotation is, of course, a much lower energy quantum than a vibrational one, and does not lie in a region which can be seen by optical telescopes. It is necessary to have powerful radiotelescopes to find these types of molecules, or fragments, in interstellar space by searching in the radiofrequency region. When the radiotelescopes were set on certain wavelengths, various important biomonomeric molecules were actually discovered in interstellar space itself.

The regions in space in which these molecules were discovered were all over the sky. One particular place was in the Orion nebula shown in FIGURE 10. If you examine it carefully, you can see that this is a cloud of visible-light-emitting molecules, behind which there are stars. The starlight shows through the gas cloud in the Orion nebula, and this starlight can be used as a light source to watch for the kinds of light which can be picked up by the gas cloud. One region of the Orion nebula when examined with radiofrequencies contains a great deal of formaldehyde (four atoms: one oxygen, one carbon and two hydrogens), and the region near the upper edge of the nebula is richer in carbon monoxide (CO).

Many molecules have been found in interstellar space, in three or four years of intensive effort, and the status today is shown in FIGURE 11. The longest known molecules (or fragments), are CH, CN and OH. There was a great outburst of discovery, beginning roughly in 1968, using radiotelescopes with longer wavelengths, and a great array of mole-

cules have been found: ammonia, water, carbon monoxide, formaldehyde, etc., each one being more and more complex.

One of the more interesting molecules in interstellar space is cyanogen, C_2N_2, and HCN itself. In 1970 with the discovery of cyanoacetylene in interstellar space (H-C≡C-C≡N) it became possible to conceive the formation of almost any material which a living organism might require. Cyanoacetylene is a very reactive molecule, having two triple bonds in it, one between carbon and nitrogen and one between carbon and carbon.

After these discoveries, I felt that it was not so important to design experiments simulating biomonomeric formation. With the discovery of cyanoacetylene in interstellar space, I became persuaded that most if not all the materials required for biomonomer formation could, indeed, have come from outer space when the earth was formed. When the earth was formed, these molecules may have been trapped inside it to come out later with the water and other materials. In other words, the primary materials were there in the very beginning, formed by interstellar energy.

Since 1970 the list of interstellar molecules has been extended from cyanoacetylene to include acetonitrile (methyl cyanide), which has a triple bond, as does methyl acetylene. Acetaldehyde, a molecule with seven atoms, was discovered in 1971. This is a large molecule indeed to find in interstellar space and, surprisingly enough, the molecule has a relatively long life, even under those conditions.

I personally do not feel that the problem of converting a primitive atmosphere (of hydrogen-methane-ammonia-water-carbon dioxide-carbon monoxide) into amino acids, nucleotides, and sugars, which are necessary to build up living organisms, is such a problem any more.

SYNTHESIS OF BIOPOLYMERS

The next problem, however, is more difficult. How are the biomonomers hooked together to make biopolymers, for example, proteins (a string of amino acids hooked together in a long line)? FIGURE 12 shows the structural requirements for the formation of some biopolymers. The first row shows the process for the formation of proteins. You can see in the monomeric amino acids, the amino group (NH_2), the carboxyl group (COOH), and between them there is a collection of other carbon, hydrogen, oxygen and nitrogen atoms which vary to form the different amino acids; these are designated by the symbol R. Roughly twenty of the amino acids are needed for living organisms. The essential structure, though, is the row of four atoms, across the top line of the figure. Note the dotted lines around the atoms of which water is made. When the OH group is taken from one of the molecules and an H from another, with the resulting water escaping, two of these molecules are hooked together creating a dipeptide. (This process is known as dehydration condensation.) The same functions still exist at the ends of the dipeptide; the H_2N at one end and the OH at the other end. Therefore, it is possible to continue this combination process at each end, to create large molecules called polymers. The polymers formed from amino acids are known today as proteins; they can be strings of peptides hundreds in length. In fact, insulin is made up of two chains, one of thirty units and the other twenty-one units, hooked together. Another common example is ribonuclease, an enzyme which breaks up nucleic acids and consists of 128 units. Growth hormone contains approximately 150 units. An almost infinite variety of proteins is possible because of the twenty, or so, R groups which can be hooked together, hundreds long.

The same processes are involved in every one of the biopolymer constructions. In the case of the polysaccharides, sugar molecules are involved. Again, you can see how the water is removed with the dotted line. If the H is taken from one molecule, the OH from another, and the two remaining fragments hooked together, a dimer (disaccharide) results; hooking several of these together creates another polymeric molecule. an identical condensation process is involved for the lipids (fats). These three different substances (proteins, polysaccharides, lipids) are very important constituents of living organisms.

The structure of nucleic acid is shown in FIGURE 13. There are three such dehydration steps in the formation of this molecule. The process goes on and on, making materials millions of units long. The nucleic acid is the molecule which contains the genetic information. It is a long sequence made up of four different kinds of nitrogen (N) containing units combined in many different ways.

How is it possible to create the nucleic acid-type material abiogenically, i.e., without a living organism to do the job? Notice that the two types of reactions I have been discussing for the creation of the polymeric materials involve the removal of the water from two molecules (OH from one molecule and H from another molecule) leaving two free "fingers" looking for other molecules with which to combine. The entire process can be repeated indeinitely. This type of reaction must be achieved in an aqueous environment. In other words, the water molecule must be removed in a water environment. This is a very difficult step to perform chemically, but you know it can be done, because you are here; and you are composed largely of water. This kind of process is going on continually in all living organisms. However, energy must be fed into

the system to take the water out, because under ordinary circumstances, without any interference, protein or carbohydrate dissolved in water will break up, that is, the reaction would go in the opposite direction. Here is where the marvelous features of molecular construction, the way in which energy can be stored in molecular bonds, come into play. Some molecules have two bonds between a pair of atoms and others may have three. There is energy stored in those multiple bonds, and it is that energy which can be used to remove the water from between other molecules. That energy which is stored in cyanoacetylene, for example, a molecule which is found in interstellar space, came from the light from the stars. The energy is stored, and remains there, until the molecule (in this case, cyanoacetylene) comes in contact with some other type of material with which it can react, such as amino acids. From these intermediates, polypeptides could be formed, and the result is the formation of the biopolymers.

I shall not discuss the mechanical details of how this occurs, except to say that this type of experiment has been done in the laboratory. We have been able to take monomeric materials in an aqueous environment, add some compounds which contain multiple bonds, and remove water from beteween the two amino acids, for example, to create dipeptides, tripeptides, etc.

Therefore, the very materials which are found in interstellar space (water, cyanoacetylene, ammonia) just by being brought together in liquid water, at the correct temperature, will bring about the reactions necessary to create the polymeric materials in a nonbiological fashion. The requirements for this occurrence are built into and are a result of the electronic structure of the atoms of which the molecules are composed.

We have now taken the second step, that is, the step from biomonomers to biopolymers. We have gone from biogenic molecules -- the primitive molecules -- to biomonomers, and we have also gone from the biomonomers to the biopolymers. Both of these steps have been demonstrated in the laboratory. We are still a long way from a "living" thing, but we at least have the materials of which living things can be constructed.

THREE-DIMENSIONAL STRUCTURE AND SELF-ASSEMBLY

Once we have achieved the long polypeptides (200-300 amino acids long, for example), it becomes possible to see how order is built into the molecule itself. The structure which that long chain of amino acids will assume is not random. There is a secondary structure built into the primary structure. The primary structure is the particular sequence of amino acids; the secondary structure is shown in FIGURE 14. At the top, is represented the primary structure, with various R groups representing the different amino acids. This primary chain is not a loose string. When such material is placed in water and kept at the proper temperature (16°C) it usually takes up a helical structure partly because of the way in which the carbon-oxygen bond is related to the nitrogen-hydrogen bond, three or four groups from it. This characteristic is shown in the spiral representation at the bottom of Figure 14. The string of polypeptides does not fall into a random coil but takes a helical shape, because of the special arrangements of the atoms in the string itself.

Similar structural requirements appear in the nucleic acids, the much more complex material in which the genetic information is stored. You remember that the nucleic acid is composed of three pieces (the heterocyclic base, the sugar and the phoshporic acid). FIGURE 15 is a photograph of a

model of the nucleic acid showing the heterocyclic bases stacked on top of each other, like a deck of cards, with the sugar-phosphate chain forming a helical structure. This is the DNA double helix model, and its construction (the linear array of bases, sugars, phosphates) is such that when you let loose of it, it will spring into the double helical arrangement as a more stable configuration. If the DNA material is heated above 60-70°C, the helix will collapse; if it is cooled down again, it will reaggregate. This property of the structure is built into it by the arrangement of the atoms themselves.

Each step which I have discussed -- thy formation of the biomonomers from the biogenic molecules, the formation of polymers from biomonomers, and the formation of secondary structure in the biopolymers -- are the results of the electronic structure of the atoms of which they are composed. The DNA, of course, is still not a living thing, so it is necessary to proceed to the next stage of chemical evolutionary development.

Molecular Symmetry, or "Handedness"

The next idea which needs to be introduced is that having made these biopolymers, by some random process, it is necessary that certain of the materials be selected. Two new ideas have to be introduced at this point. One is that living things today have in them a "handedness". One way this can be demonstrated is in FIGURE 16 which shows a shell and its reflection in a mirror. The shell is standing on its point, and immediately above it is a mirror, so that the upper part of the figure is the reflection of the top of the shell in a mirror and, therefore, is a mirror image of the bottom part of the photograph. If, in your ima-

gination, the bottom part could be twisted into the position of the upper one, you will see that the two are not identical, they are mirror images. It is not possible to superimpose one on top of the other. (Incidentally, when I was thinking about this idea, I tried to figure out how to make the concept familiar. I found a book on shells and was amazed to discover that all of the shells that were coiled, which I could find in the book, were all right-handed. That is, if you think of a shell as a screw, they are all right-handed.

The concept that mirror images may not be superimposiable is amplified by FIGURES 17 and 18. Figure 17 shows a pair of hands; the black part of the picture is a mirror and the mirror image of the left hand; the right hand is on the part of the photograph with the white background. You can see that the mirror image of the left hand is identical with the right hand. The right hand is not superimposable on the left hand. Putting the palms together is <u>not</u> superimposition; they are facing each other. Figure 18 exhibits the same idea in a slightly different fashion. The coils are models of the protein structure, which was given in primary and secondary form in Figure 14. The mirror represented by the line (M) has the right-handed coil on the right side of Figure 18 and the left-handed coil on the left. The R coil and the middle L coil are mirror images of each other; the one on the left is not a mirror image of the L in the center. They are identical, and the two L's can be superimposed on each other. It is not possible to superimpose R on top of L. The idea is that mirror images are not superimposable, and those figures which are superimposable are not mirror images.

All living things contain molecules which have "handedness" in them, and they are all made, generally, of one of the "handedness" kinds of molecules. The amino acids, for example, are all left-handed; the sugars are all of one kind. I repeat: The molecules of which living material is composed are usually all of one "handedness" type.

AUTOCATALYSIS

Another characteristic of living things is that they are all autocatalysts, that is, they make each other. This second idea, autocatalysis, is necessary in order to completely understand biological selection. The idea of an autocatalyst is shown in FIGURE 19. Here, we see the possibility of A being transformed along three possible routes: A to B, A to C, or A to D. If D happens to be a material which will make the transition from A to D easier, then, quite clearly, A will not go to C or B, it will go to D, because as soon as any D is formed, D will then catalyze, or induce, the transformation of A into D. It's autocatalytic, and all of the material will go to D. One of the reasons that biological material is all of one-handedness is that it is composed of autocatalytic materials. There is a geometrical fitting which is very specific, and living things use that characteristic in their construction.

When we have the possibility of stereospecific (geometrical specificity) autocatalysis, we are able to see the whole process of selection taking place, reducing random events. As soon as the autocatalytic phenomenon developed the selection processes were no longer random.

Autocatalysis therefore is the next stage in the chemical evolution process, involving either a single reaction or sequence of reactions in which the product(s) of a further reaction catalyze the initiation of the

entire sequence, leading to itself; this latter we call reflexive catalysis. The phenomena resulting from the appearance of such systems is the same regardless of whether it is one reaction or several. Clearly the materials which participate in such autocatalytic systems will soon select for themselves over those which do not so participate.

A simple example, not particularly biological, but easy to see, is the autocatalytic system consisting of cupric acetate dissolved in pyridine or quinoline in the presence of molecular hydrogen. This system is unstable thermodynamically, but will remain that way for indefinite and random periods of time. If by some random event a small amount of the Cu^{+2} is transformed into the Cu^{+1}, the system takes off, because the Cu^{+1} is a catalyst for the hydrogenation of Cu^{+2} to Cu^{+1}. Once this process begins, the entire system is transformed form Cu^{+2} and hydrogen to Cu^{+1} and eventually to metallic copper itself.

Here is a case of autocatalysis selecting for a particular system, and it is this kind of event occurring on a much more subtle and widespread foundation which will lead to the selection of autocatalytic systems capable of reproducing themselves. This would include not only the catalytic proteins but the information-bearing polynucleotides as well. The primitive catalysis systems already exist in the form of trace metal ions such as iron and manganese, and the bifunctional small molecules. When these are combined properly, they give rise to improved catalytic systems for their own formation.

HIGHER ORDERS OF MOLECULAR STRUCTURE

The next stage in our development of the characteristics of living material is the appearance of tertiary protein structure. The secondary structure actually gives rise to the tertiary structure (FIGURE 20) because of the characteristics inherent in the secondary structure itself. Figure 20, which is the structure of myoglobin, shows the helical structure, on the left-hand side, and it is possible to observe the folding, as well as the helical parts. The right-hand side of the picture shows space fillingprojection of the same structure, so you can see the molecule as a solid object rather than as a collection of atoms. To a chemist, the image on the left-hand side is the important one, but to an artist it wouldbe the image on the right-hand side. Again, this tertiary structure (complex folding) is built into secondary structure, both the helical and nonhelical parts. The place where the bends occur are there because of certain sequences. It is now possible to go conceptually from the tertiary to the quaternary structure, the actual packing of the molecules together.

Self-Assembly Phenomena

The relatively simple tobacco mosaic virus (TMV) is shown in FIGURE 21. This virus is composed of a large helix of nucleic acid with smaller protein molecules (about 2000 of them) packed around it to make the small rod. The virus particle can be taken apart chemically, into the component protein and nucleic acid molecules. When the protein molecules alone are taken, and the salt and acid concentrations in the solution adjusted correctly, they will reassemble into rods (FIGURE 22).

You will notice that the rods are not all the same length, as there is no genetic material (nucleic acid) in the rods to give them a definite size. The protein has all the necessary information about stacking, but there is no information about the problem of when the stacking should cease; this results in random-sized protein rods. If the aggregate of protein molecules is then taken apart, the nucleic acid returned to the solution, and the whole thing put back together again, the result is shown in FIGURE 23, where you can see uniform TMV particles. Thus, the virions can be reassembled again. This assembly process is built into the structure of the nucleic acids and proteins themselves. It is an excellent example of the process of self-assembly.

This is still not the living cell as we know it. The virus particles are not really "living". They have all the necessary requisites for replication, and one might talk about viruses as being alive. However, they are not alive in the sense of a eukaryotic cell, a cell with a nucleus, membrane, a boundary between it and the outer world. Another step in the evolutionary process is the formation of the membrane, a major role of the lipids (shown in some of the earlier chemical evolutionary schemes). Here, again, experiments in the laboratory have shown that the fats, because of their structure and because they have both hydrophobic(water-repelling) and hydrophyllic (water-loving) parts will form films on the surface of water. When such a water solution containing dissolved protein is shaken, it will form vesicles (little sacks), similar to a membrane. This phenomenon is shown in FIGURE 24, which exhibits a whole set of heterogeneous vesicles, each

a different size, constructed by shaking up some phospholipids (soap-type molecules) with protein, when closed sacks are formed. Each one may be considered as a model of a cell membrane.

We have now reached from the primitive hydrogen of the earth's atmosphere to some cell-like structure with replicative capability.

CONCLUSION

Thus, starting with astronomical knowledge, and in the context of modern chemistry and modern biology, a sequence of events has been traced which could have taken place and one which could be a conceptual framework upon which to build further. To finish tonight's discussion, I want to show a modern picture, an artist's concept, of the origin of life (FIGURE 25) which some of you may recognize. This is "Verbum" by the Dutch artist, Maurits Escher. Our first illustration this evening was "The Word" (Figure 1) and the last is a concept of the origin of life. In this figure is shown "The Word" in the center, and from it grew all of the life on the earth. Mr. Escher describes it himself, as follows:

> Out of the nebulous grey of the Verbum center (in the beginning was the Word) triangular figures emerge. The further they are removed from the center, the sharper becomes the contrast between light and dark, while their original straight outlines become serrated and curved. Alternatively the white becomes background for the black objects, and the black for the white objects. Near the edges the figures have evolved into birds, fish and frogs, each species in its proper element: sky, water and earth. At the same time there are gradual transitions from bird into fish, from fish into frog, and from frog again into bird.

0 0 0 0 3 9 0 0 2 8 9

REFERENCES

There have been many books and articles written on the general subject of chemical evolution. A few of the ones which are particularly pertinent to the lecture are listed below.

1. M. Calvin. "Chemical Evolution: Molecular Evolution Towards the Origin of Living Systems on the Earth and Elsewhere", Oxford University Press, New York (1969).

2. F.H.C. Crick, "Of Molecules and Men', University of Washington Press, Seattle (1966).

3. S. W. Fox (ed). "The Origins of Prebiological Systems and of Their Molecular Matrices", Academic Press, New York (1965)4.

4. D. H. Kenyon and G. Steinman, "Biochemical Predestination", McGraw-Hill, New York (1969).

5. A. I. Oparin, "The Origin of Life" (3rd Eng. ed., trans. by Ann Synge), Oliver and Boyd, London (1957).

6. D. L. Rohlfing (ed). "Molecular Evolution: Prebiological and Biological", Plenum Press, New York (1972).

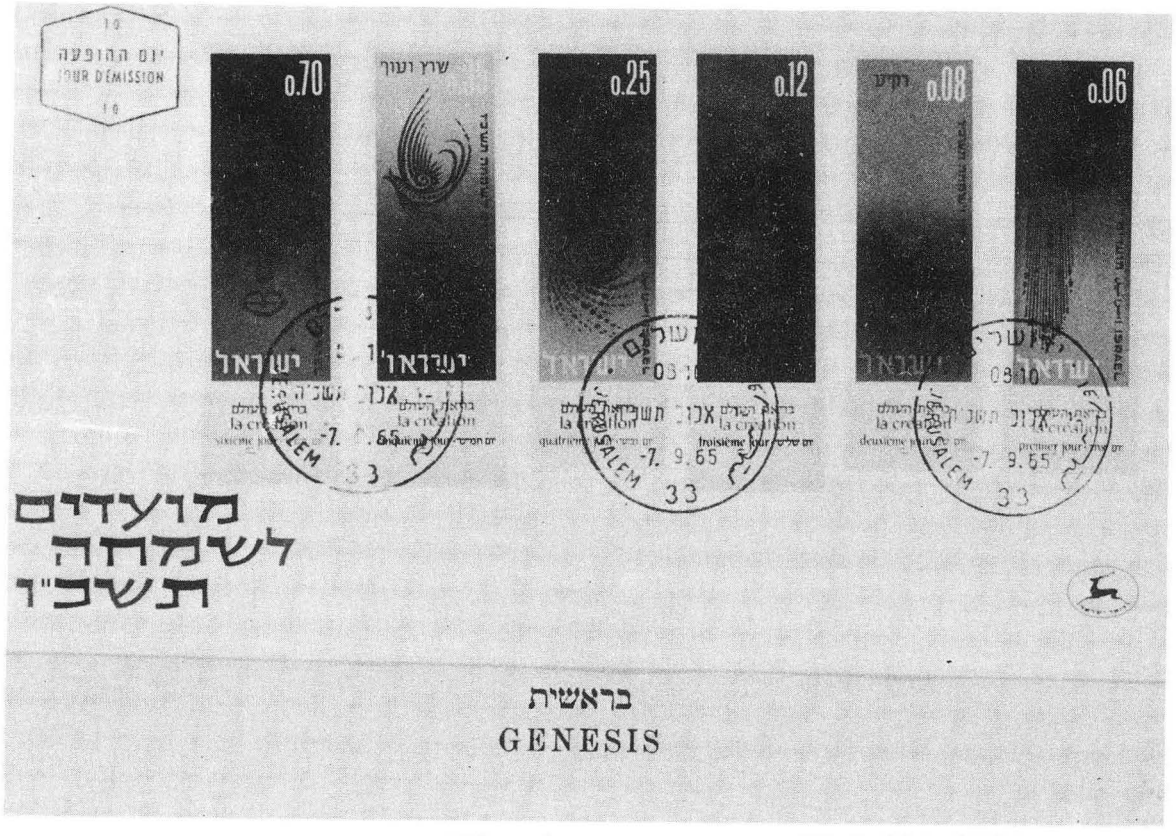


Fig. 1 XBC 683-2581

Feb. 1/71

Bentham Down Bromley Kent. S.E.

My dear Hooker

I return the pamphlets, which I have been very glad to read. — It will be a curious discovery if Mr Lowne's observation that boiling does not kill certain moulds is proved true; but then how on earth is the absence of all living things in Pasteur's experiment to be accounted for? — I am always delighted to see a word in favour of Pangenesis,

Little pond with all sorts of ammonia & phosphoric salts, — light, heat, electricity &c present, that a protein 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! —

Henrietta makes handy my progress, & God knows when she will be well. —

Until some day, I believe, will have a resurrection

Mr Dyer's paper strikes me as a very able Spencerian production. — It is often said that all the conditions for the first production of a living organism are now present, which could even have been present. — But if (& oh what a big if) we could conceive in some warm

I enjoyed much the visit of you from Gentlemen, i.e. after the Saturday night, when I thought I was quite done for. —

Yours affec'

C. Darwin

XBL 682-4053

Calvin, Figure 2

Darwin Letter

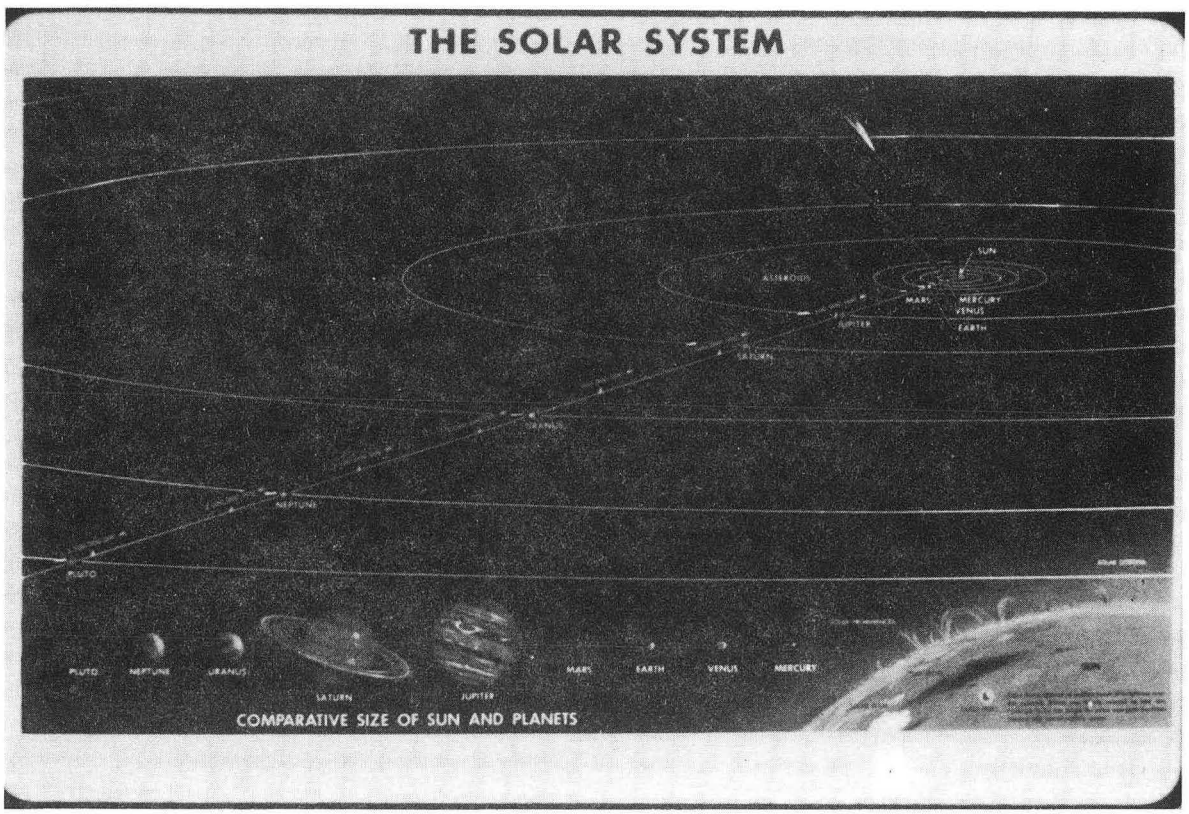


Fig. 3 XBC 727-3836

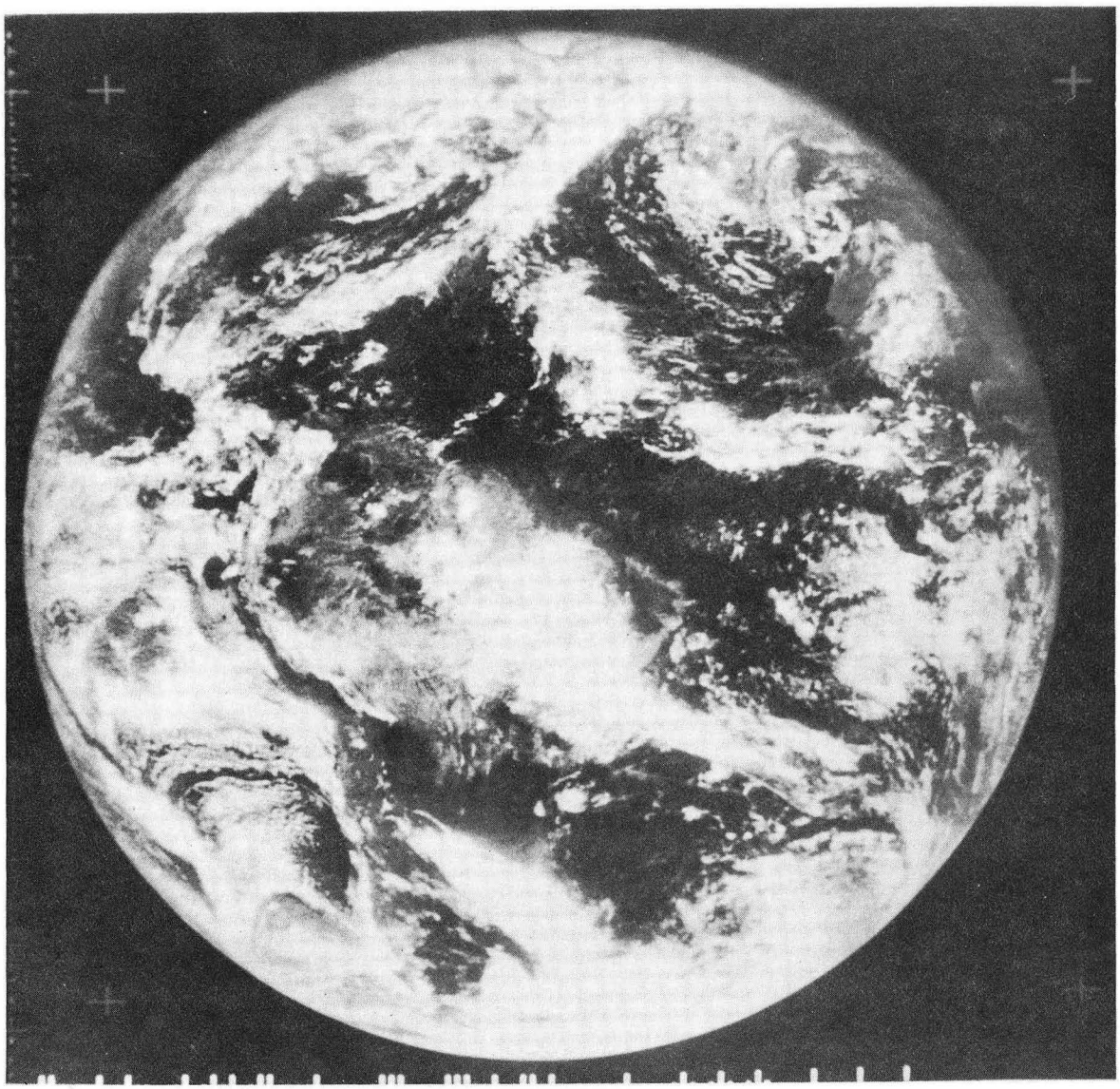
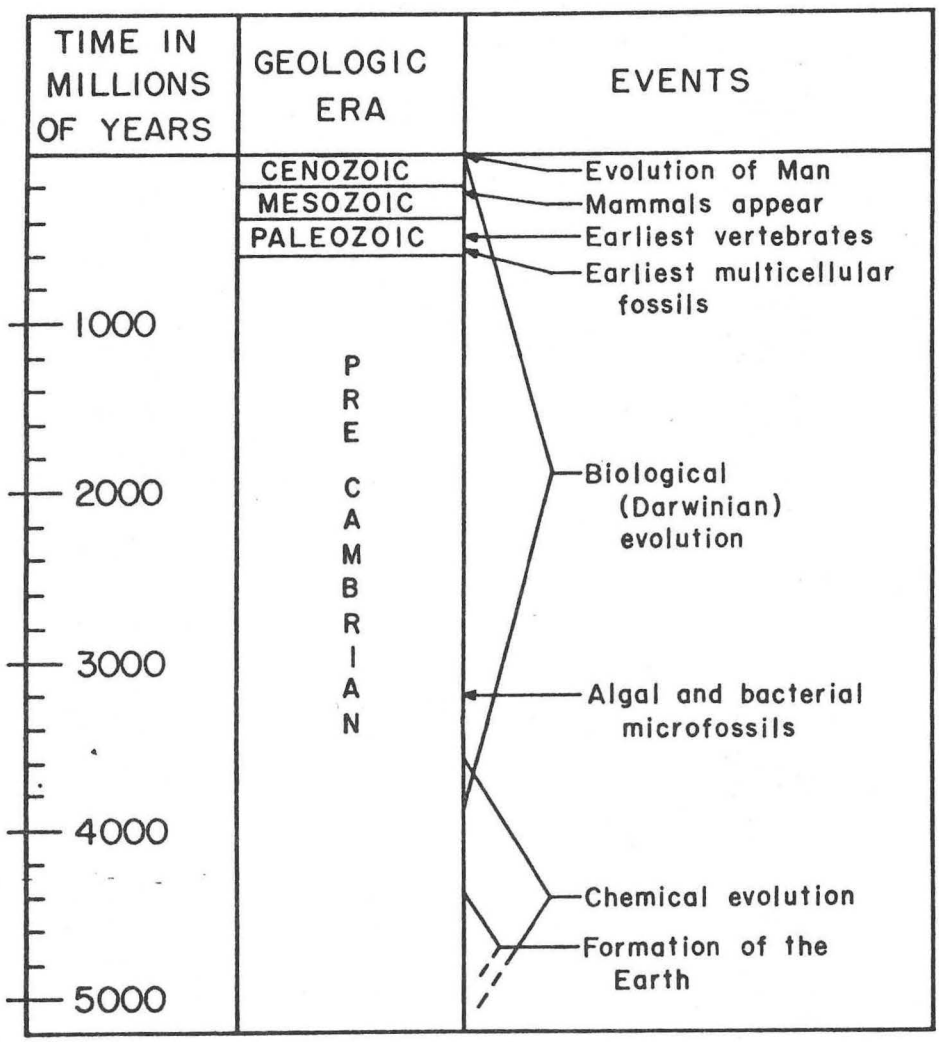


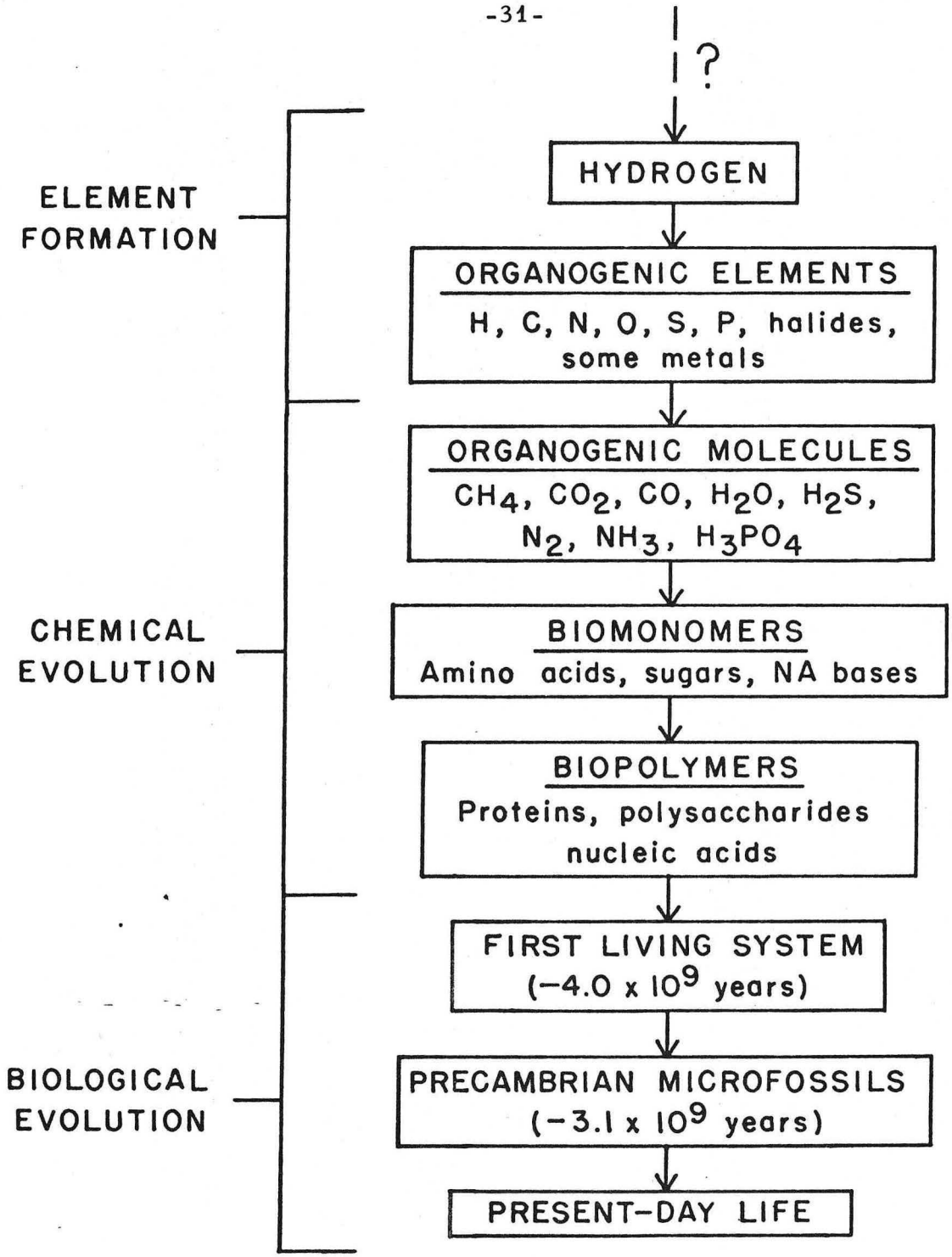
Fig. 4 XBC 681-27



XBL715-5177

Calvin, Figure 5

Time Scale for Evolution



XBL714-5137

Calvin, Figure 6

Evolution Scheme, from Elements to Present Day

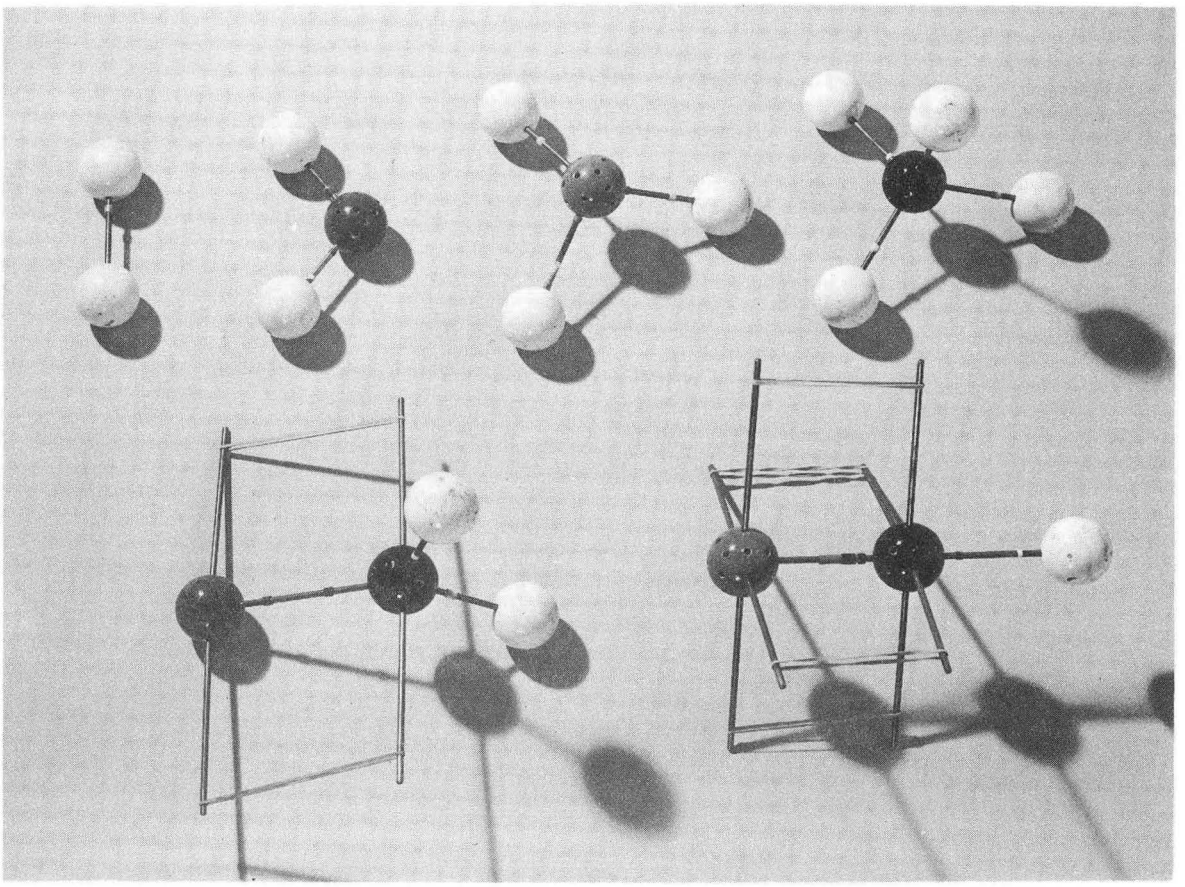


Fig. 7 CBB 728-3862

0 0 0 0 3 9 0 0 2 9 3

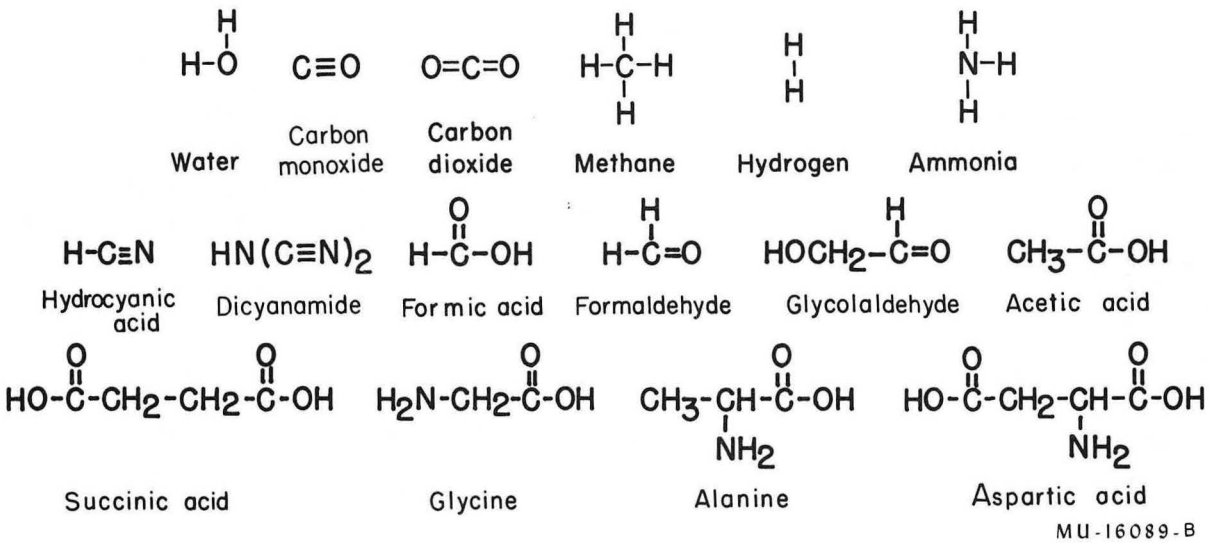
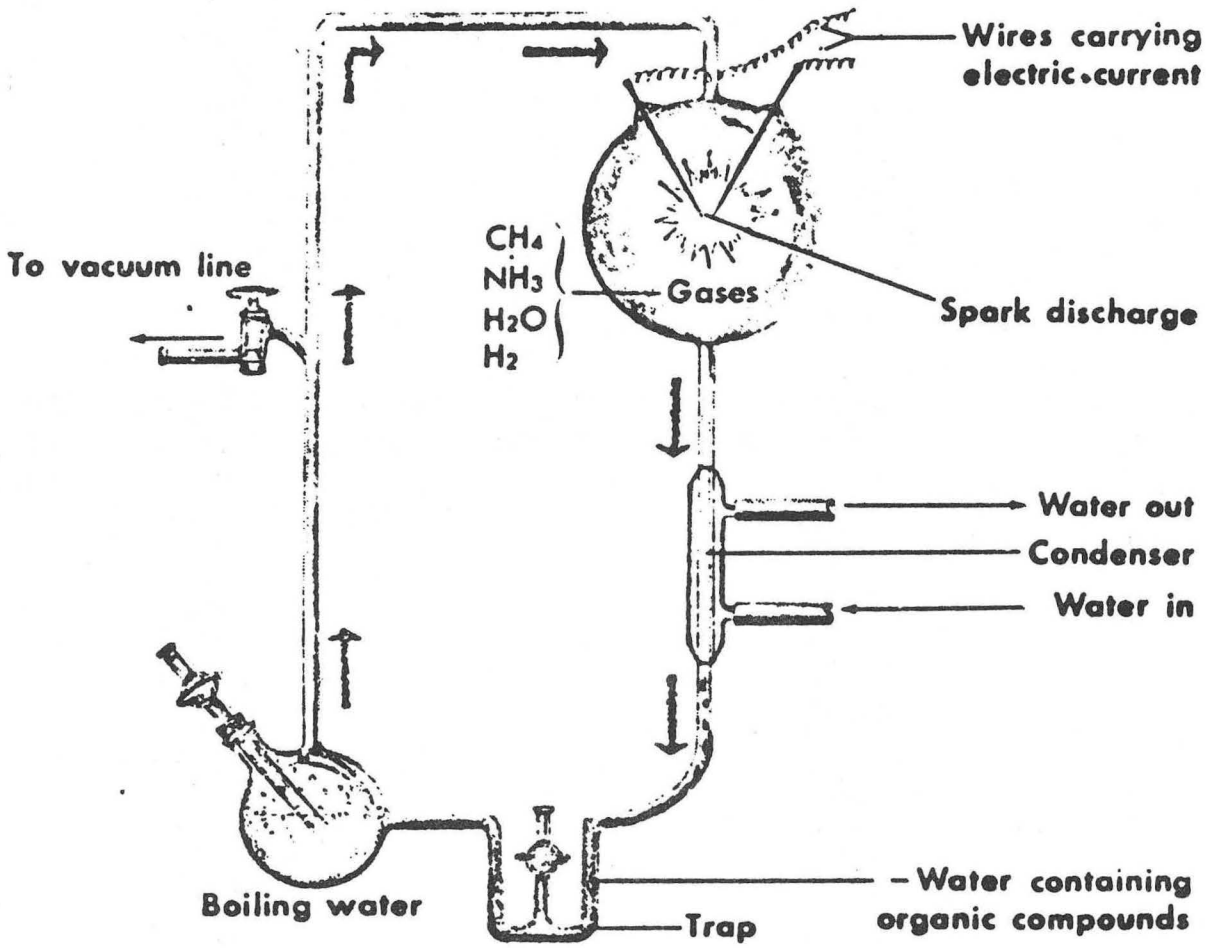


Fig. 8



Diagrammatic representation of apparatus used by Stanley Miller for the synthesis of amino acids by electric discharge.

XBL 728-1510

Calvin, Figure 9

Miller Spark Discharge Apparatus for Synthesis of Amino Acids

Fig. 10 XBC 727-3835

Molecules Found in the Interstellar Medium

Year	Molecule	Symbol	Wavelength
1937		CH	4300 Å
1940	Cyanogen	CN	3875 Å
1941		CH^+	3745–4233 Å
1963	Hydroxyl	OH	18, 6.3, 5.0 and 2.2 cm
1968	Ammonia	NH_3	1.3 cm
1968	Water	H_2O	1.4 cm
1969	Formaldehyde	H_2CO	6.2, 2.1 and 1 cm; 2.1 and 2.0 mm
1970	Carbon monoxide	CO	2.6 mm
1970	Cyanogen	CN	2.6 mm
1970	Hydrogen	H_2	1100 Å
1970	Hydrogen cyanide	HCN	3.4 mm
1970	X-ogen	?	3.4 mm
1970	Cyano-acetylene	HC_3N	3.3 cm
1970	Methyl alcohol	CH_3OH	36 and 1 cm; 3 mm
1970	Formic acid	CHOOH	18 cm
1971	Carbon mono-sulphide	CS	2.0 mm
1971	Formamide	NH_2CHO	6.5 cm
1971	Silicon oxide	SiO	2.3 mm
1971	Carbonyl sulphide	OCS	2.7 mm
1971	Acetonitrile	CH_3CN	2.7 mm
1971	Isocyanic acid	HNCO	3.4 mm; 1.4 cm
1971	Hydrogen iso-cyanide	HNC	3.3 mm
1971	Methyl-acetylene	CH_3C_2H	3.5 mm
1971	Acetaldehyde	CH_3CHO	28 cm
1971	Thioformaldehyde	H_2CS	9.5 cm

XBL 728-1511

Calvin, Figure 11

Chart of Interstellar Molecules Discovered through April 1971

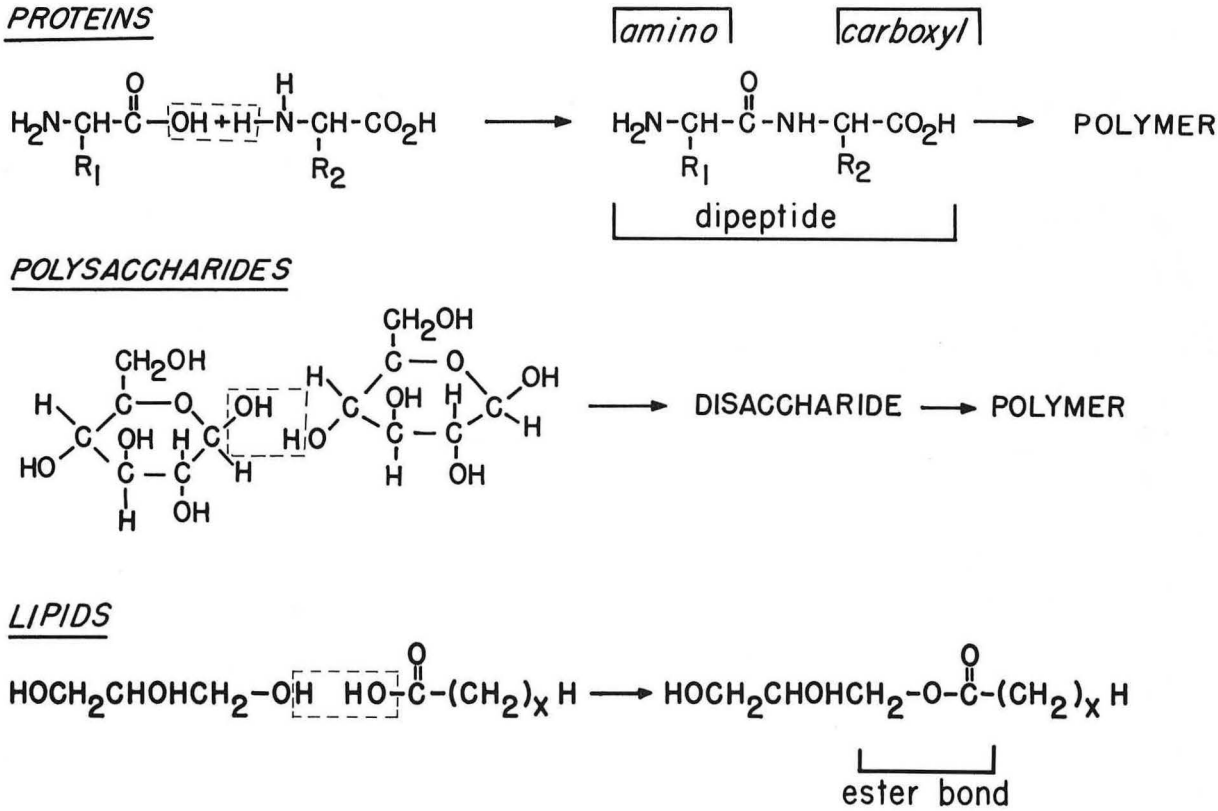


Fig. 12

MUB-5261

NUCLEIC ACIDS (3 STAGES) RNA SHOWN - DNA LACKS OH ON 2' POSITION

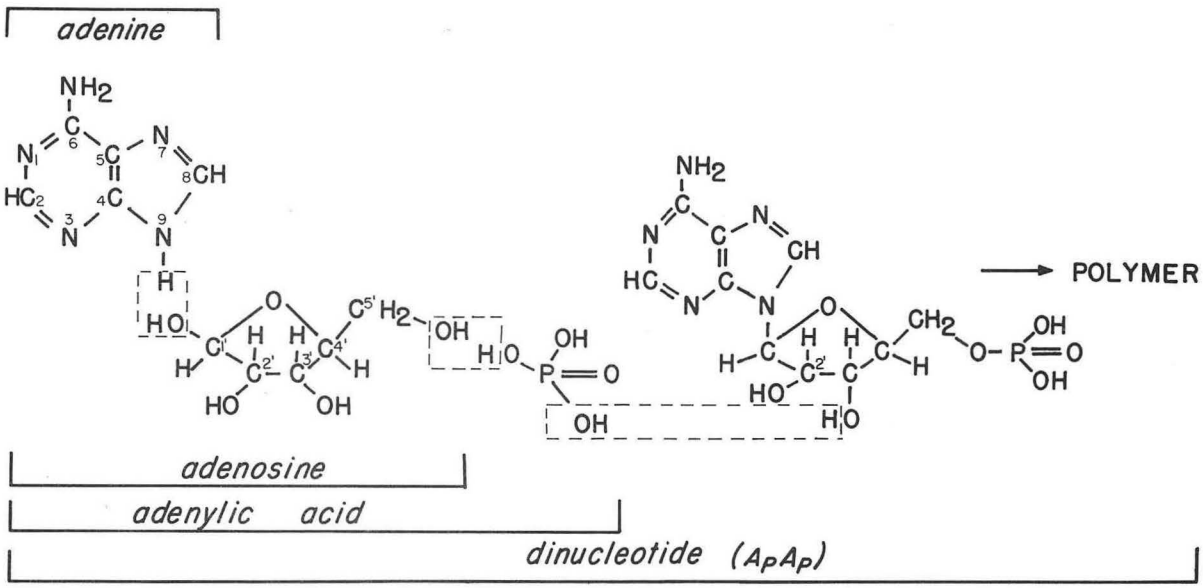
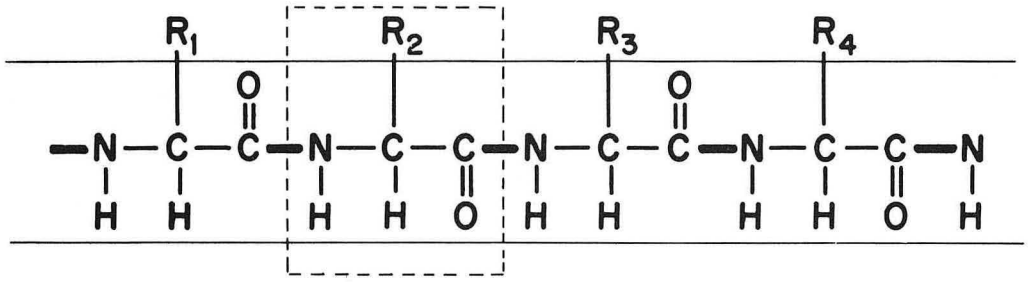
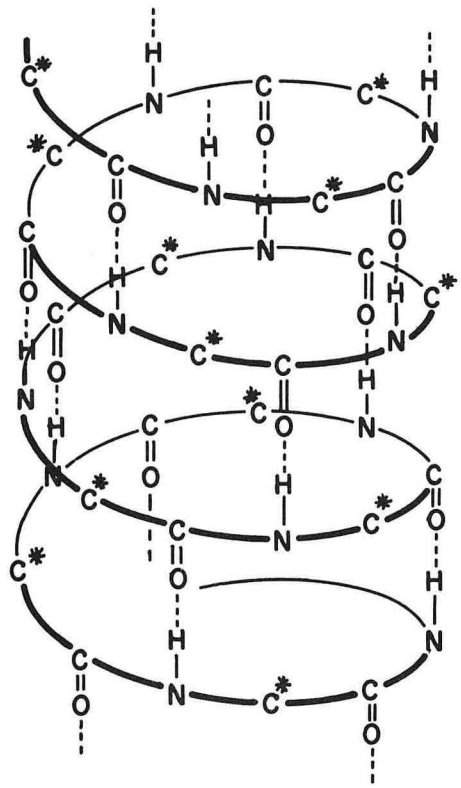


Fig. 13

MUB-5262

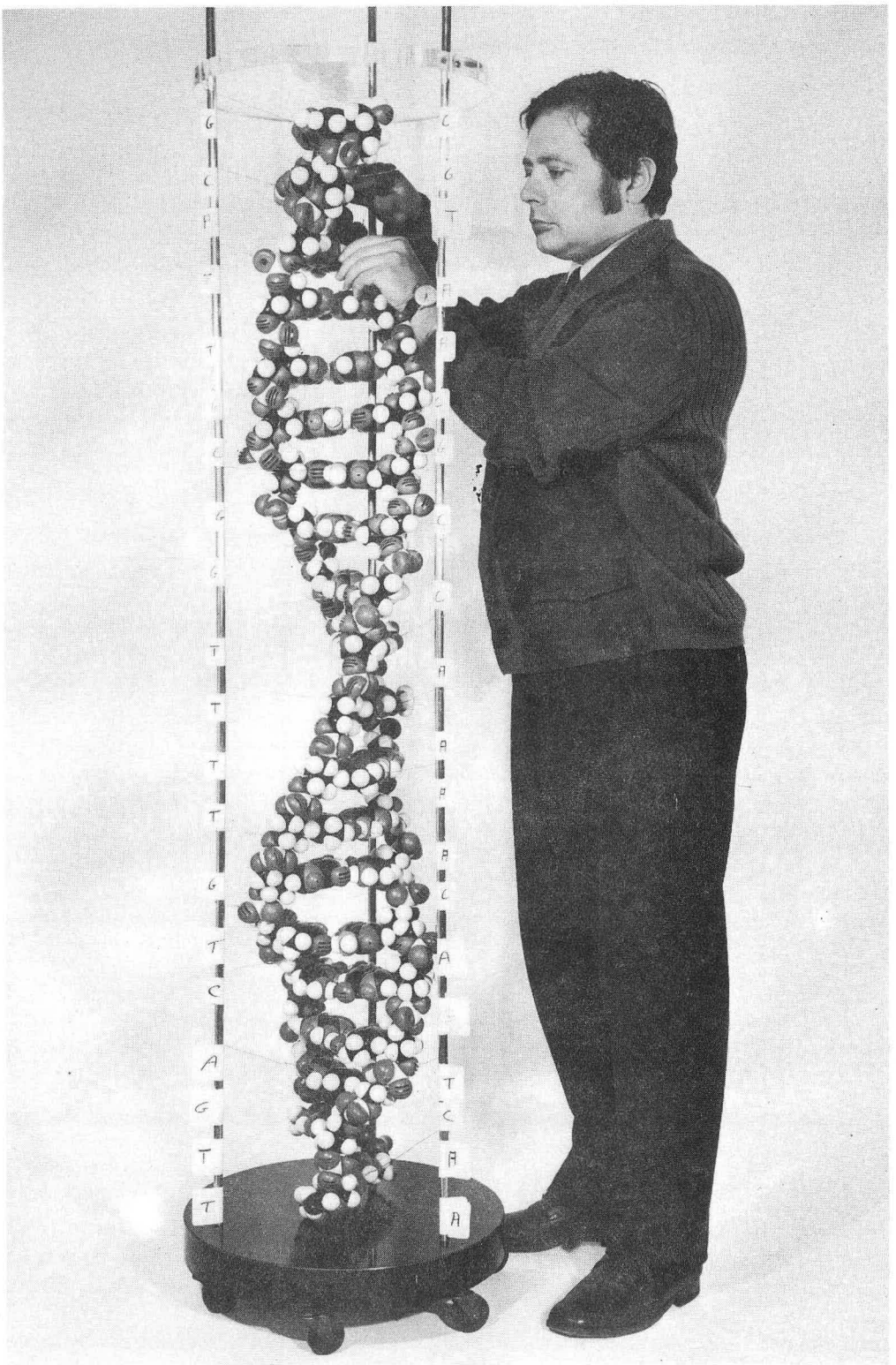
0 0 0 0 3 9 0 0 2 9 3





MU-16147

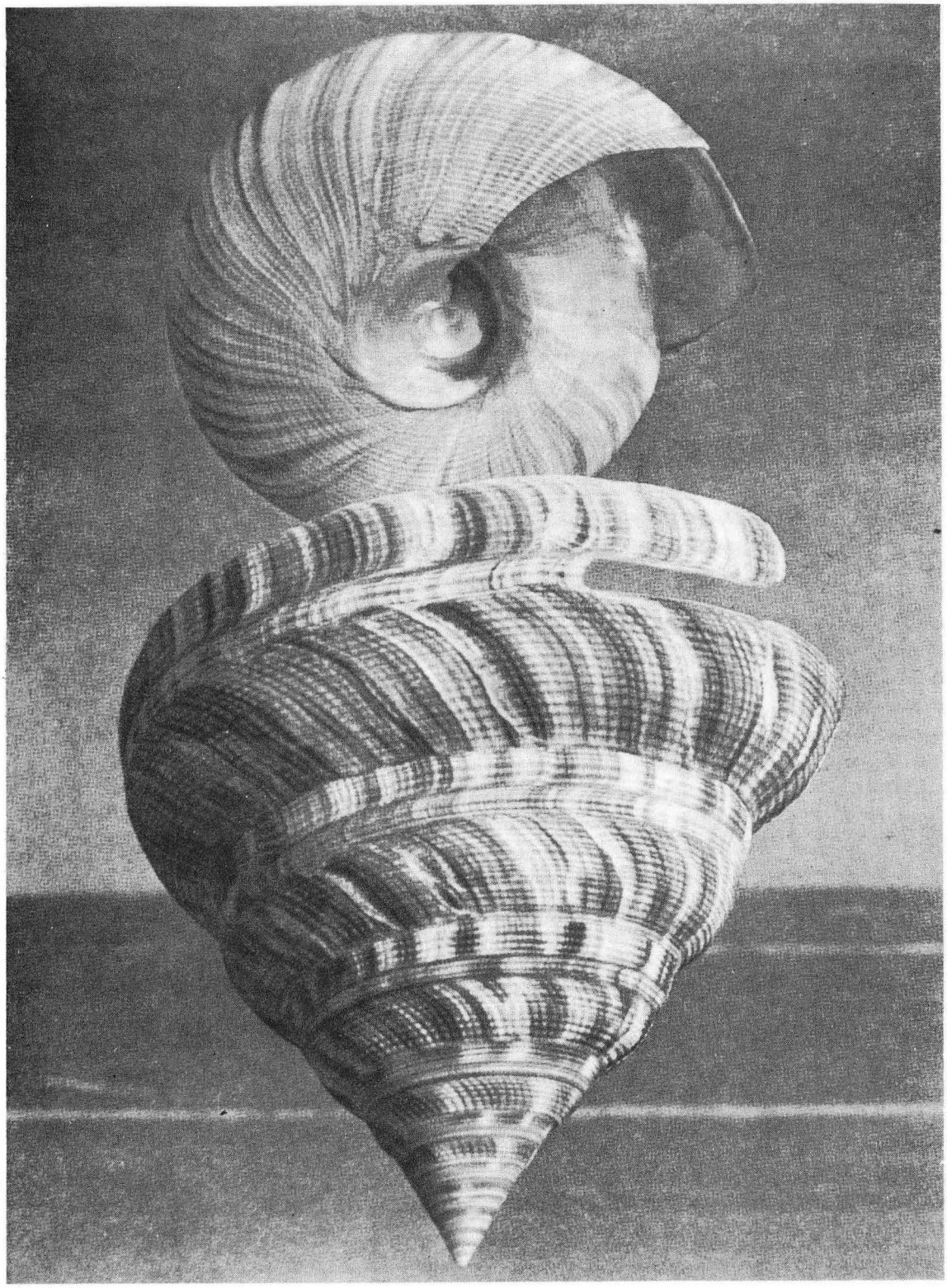
Fig. 14



CBB 706-2607

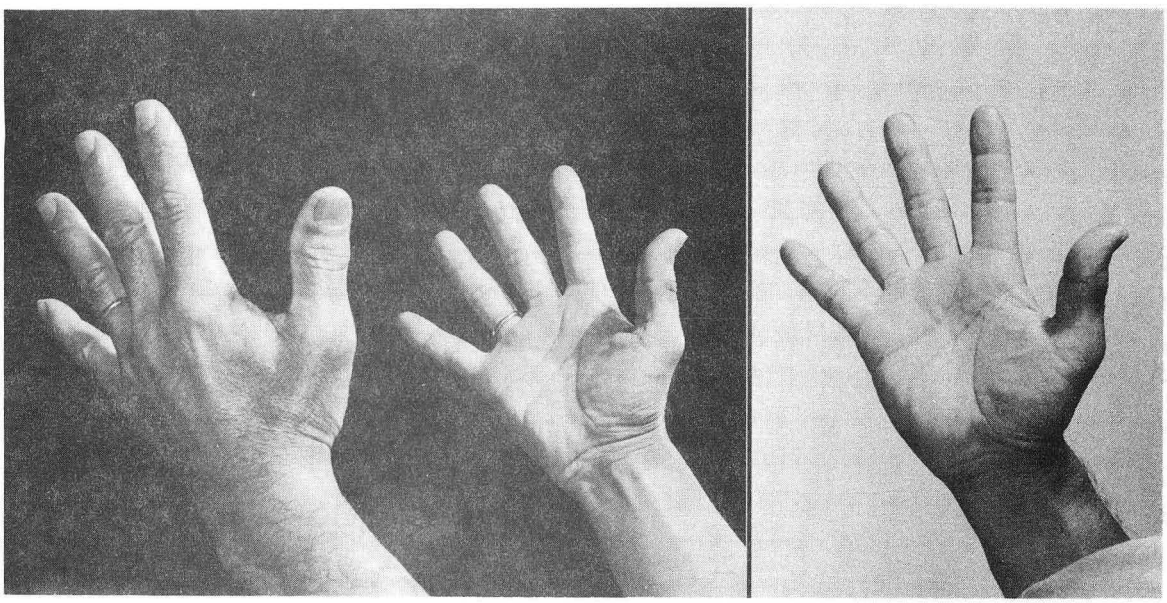
Fig. 15

0 0 0 0 3 9 0 0 2 9 6



CBB 728-4140

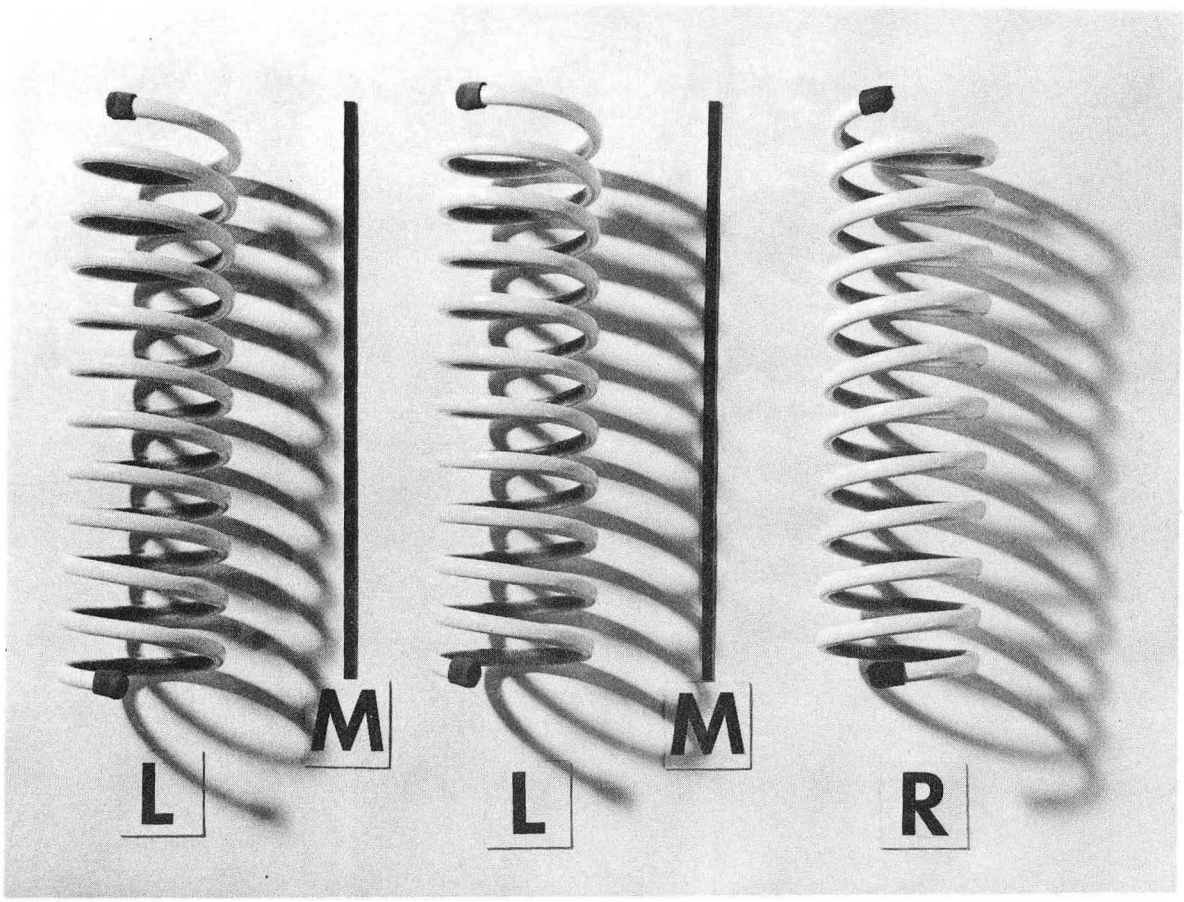
Fig. 16



XBB 728-3865

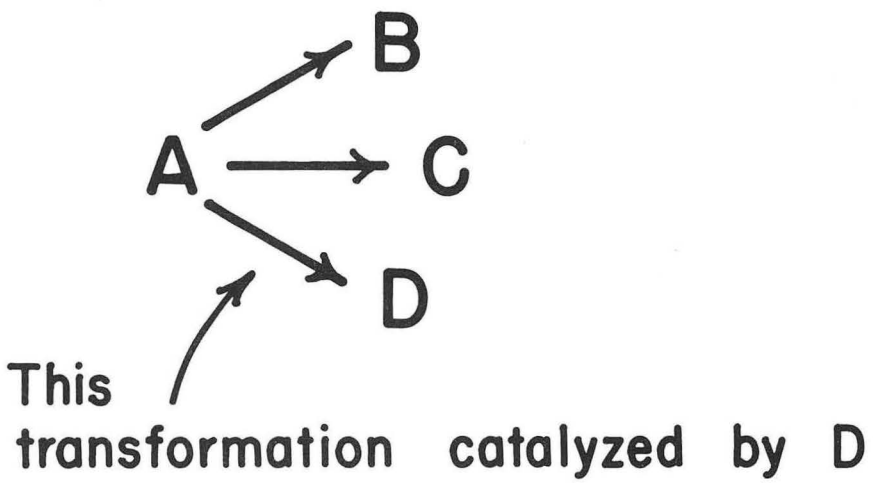
Fig. 17

0 0 0 0 3 9 0 0 2 9 7



XBB 728-3864

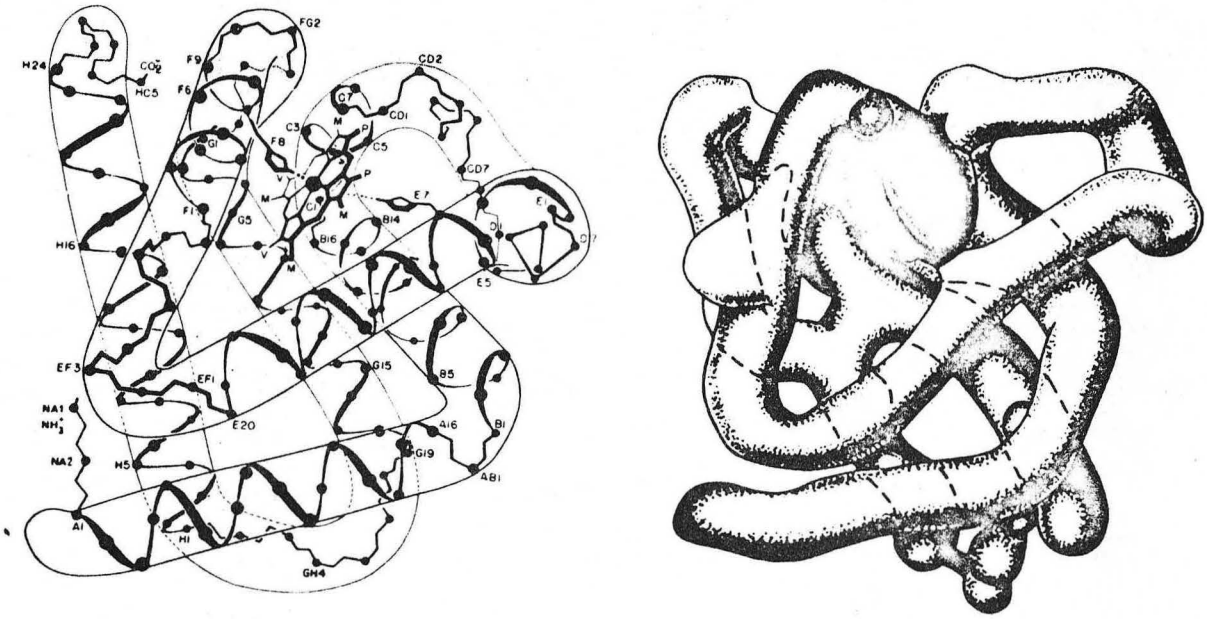
Fig. 18



AUTOCATALYSIS

MU-16090

Fig. 19



XBL 727-4704

Calvin, Figure 20

Structure of Myoglobin

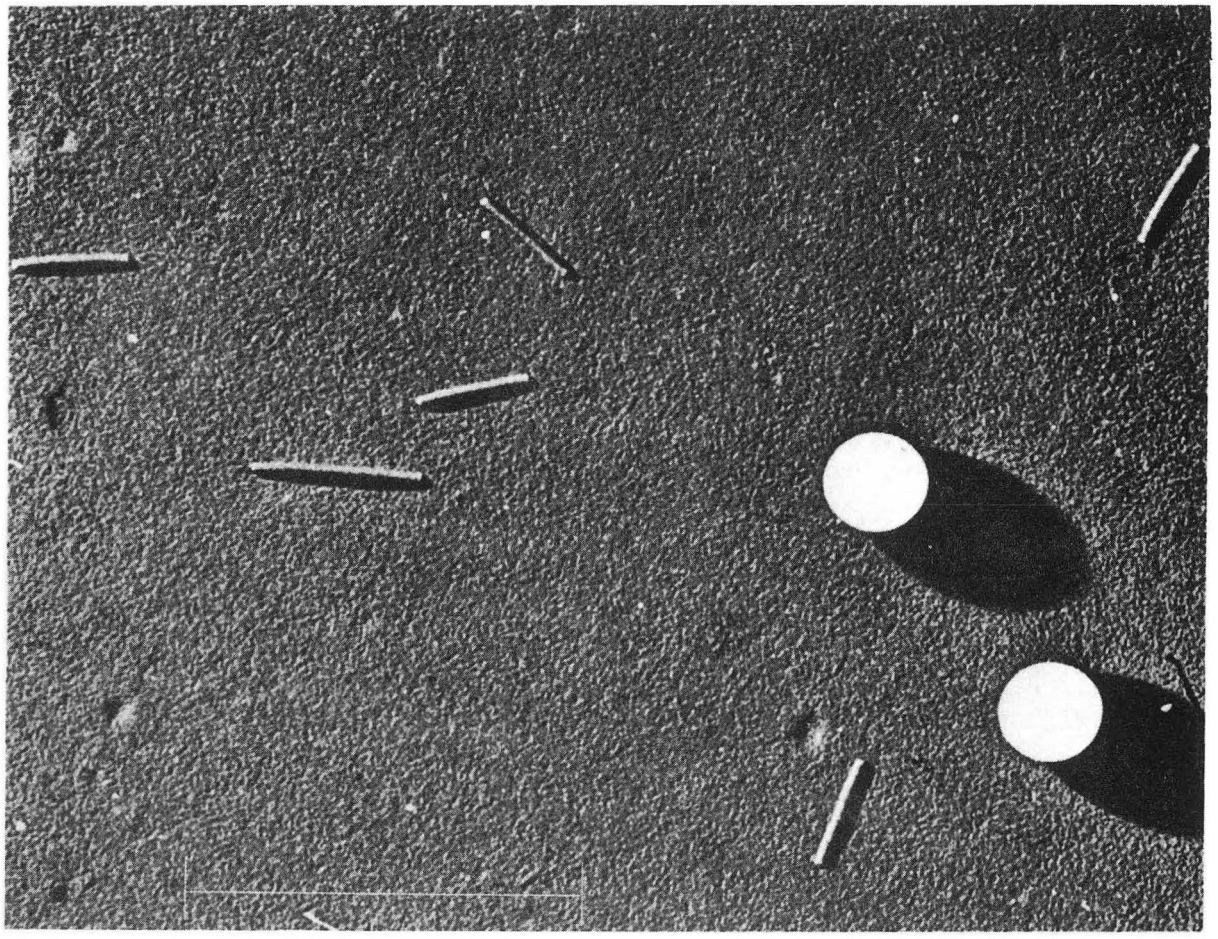


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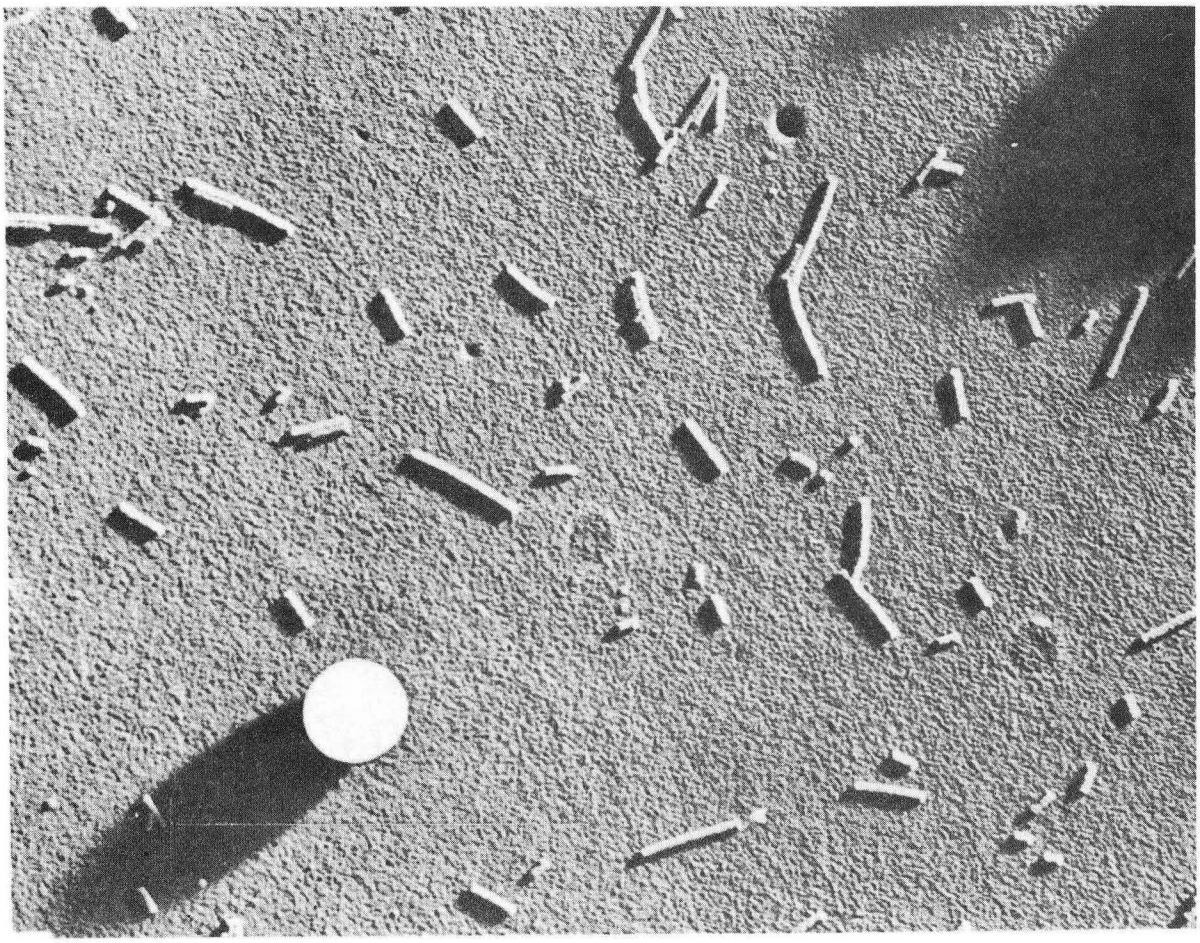
Fig. 21



BC-541

Fig. 22

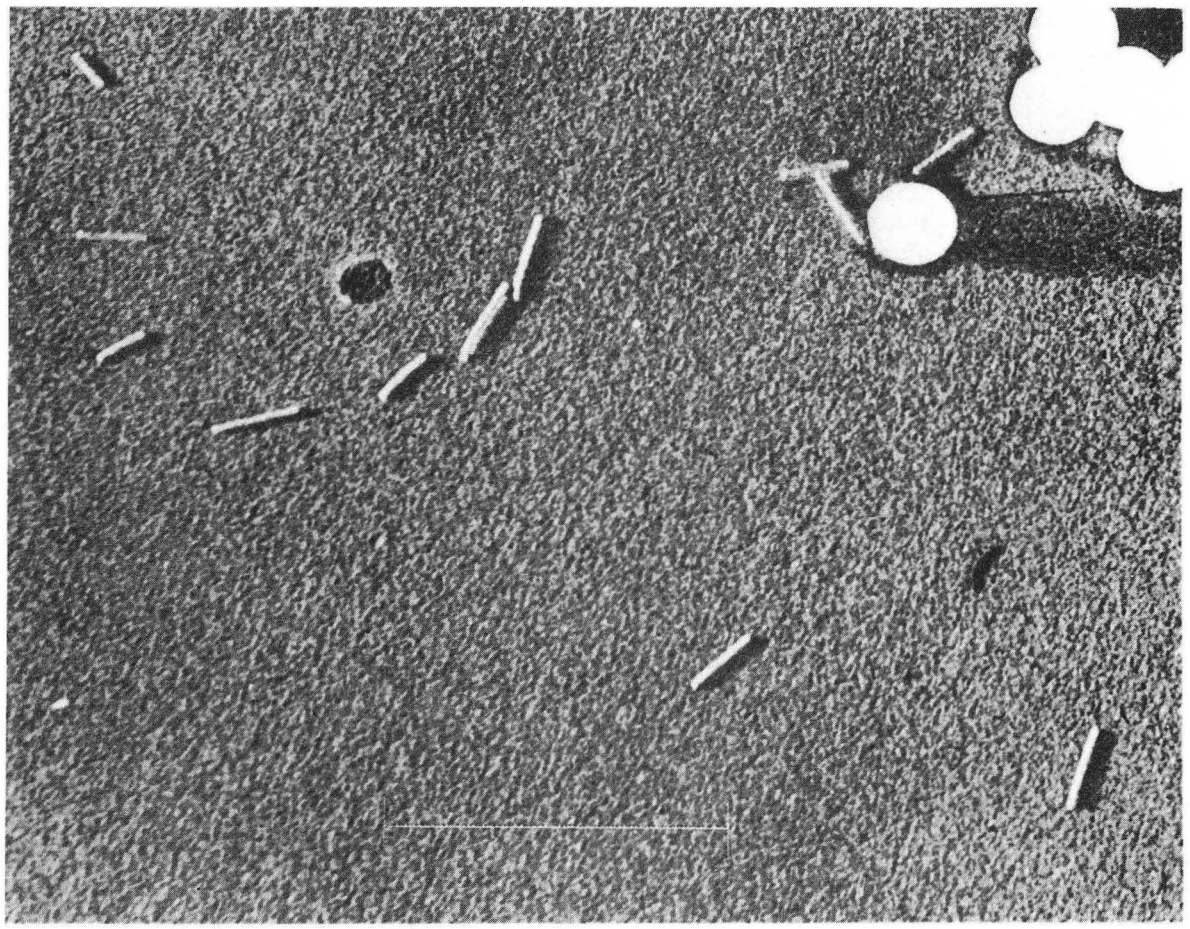


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Fig. 23

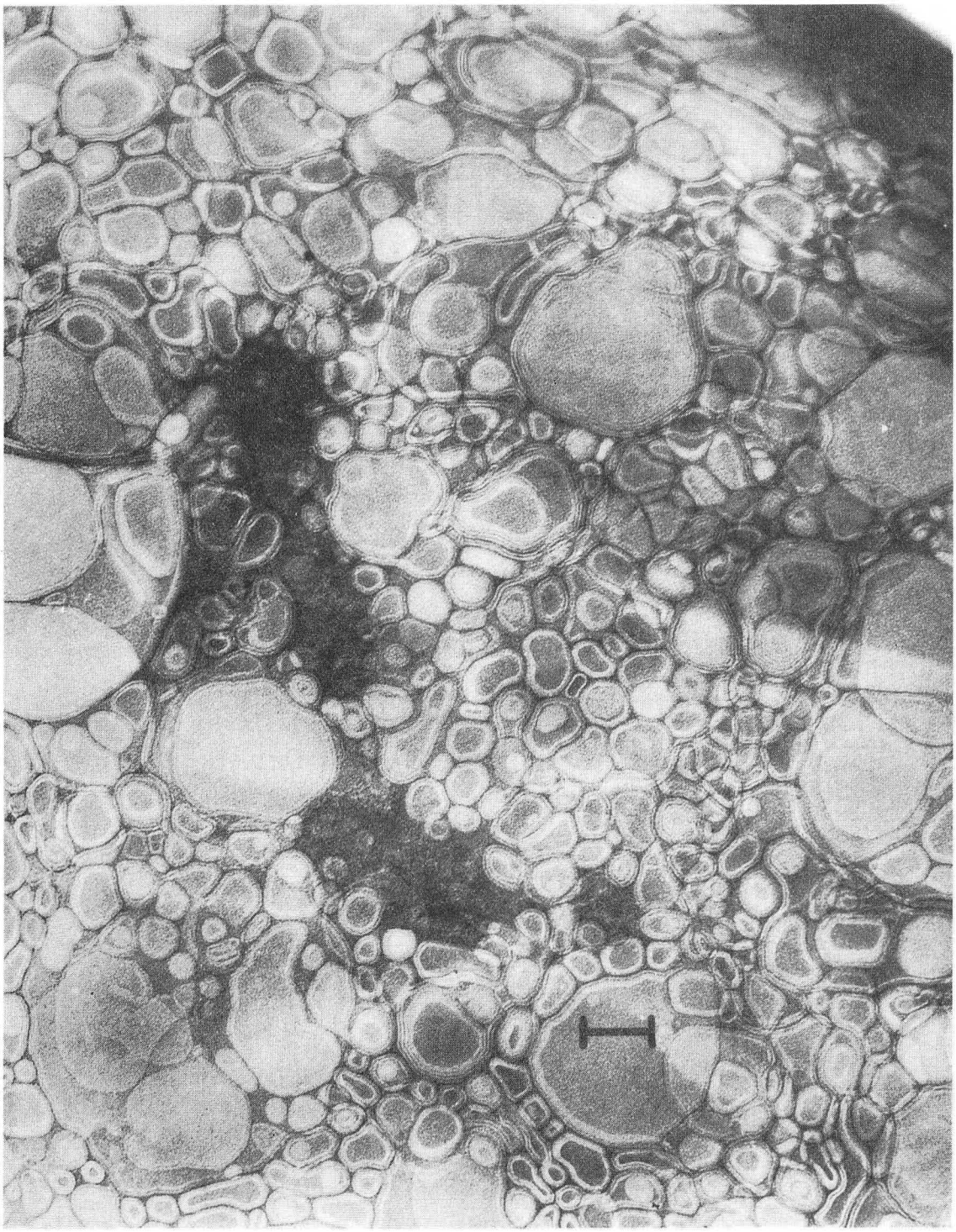
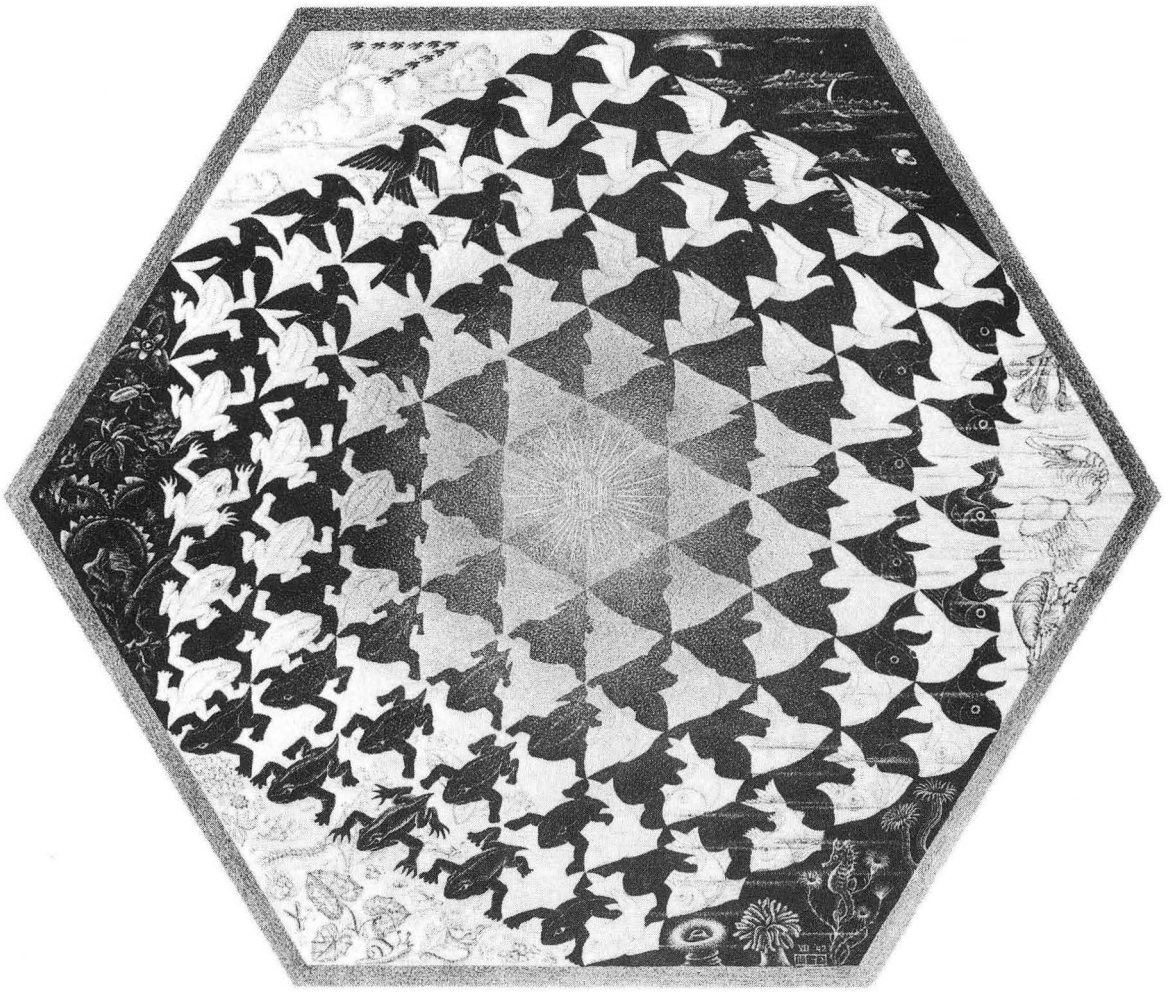


Fig. 24 XBB 728-4179



MU-23353

Fig. 25

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