

Lawrence Berkeley National Laboratory

Lawrence Berkeley National Laboratory

Title

Chemical Evolution and the Origin of Life

Permalink

<https://escholarship.org/uc/item/6c258066>

Author

Calvin, Melvin

Publication Date

1955-08-11

UCRL-2124 Rev
Unclassified Health and Biology

UNIVERSITY OF CALIFORNIA

Radiation Laboratory
Berkeley, California

Contract No. W-7405-eng-48

CHEMICAL EVOLUTION AND THE ORIGIN OF LIFE

Melvin Calvin

August 11, 1955

Printed for the U. S. Atomic Energy Commission

CHEMICAL EVOLUTION AND THE ORIGIN OF LIFE*

Melvin Calvin

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

August 11, 1955

ABSTRACT

A discussion is presented of the elements, or at least most of the elements, that are usually thought of as required and characteristic of living materials. A continuous evolutionary process is conceived, beginning with a bare earth and leading to the random formation of more or less complex molecules from simple ones, and gradually, by the processes of random variation, autocatalysis, and selection, to more complex systems and the ordered array of desoxynucleic acid molecules which are the units that carry the continuity and order of present-day living systems.

*Transcription of address delivered at Amherst College, Amherst, Massachusetts, November 19, 1954. The preparation of this paper was sponsored by the U. S. Atomic Energy Commission.

CHEMICAL EVOLUTION AND THE ORIGIN OF LIFE*

Melvin Calvin

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

August 11, 1955

The question that I am going to discuss is one that men have asked since they first recognized a distinction between living and nonliving substances. And they have answered it in many ways. Here, I would like to speak and answer within the scope of science. This is not to say that I believe or am convinced that an answer can be found within the scope of science--a complete answer--it may not be. I would like to explore with you how much of an answer can be found within this scope without questioning it any further.

Precisely where life began is perhaps the wrong way to ask the question. You will notice that the title does not use the term "the beginning of life"--it has the term "origin of life" in it. And therein lies an essential point. The whole burden of this discussion will be to try to show you that it is possible to devise schemes within the scope of modern science that will lead to the development of defined systems--by a system I mean a confined region in space--which can have the attributes that we now recognize as belonging to living materials, without having to postulate a cataclysmic, improbable event at any one time. This, in substance, is the essence of what I would like to say. And now the chain of argument that leads to it.

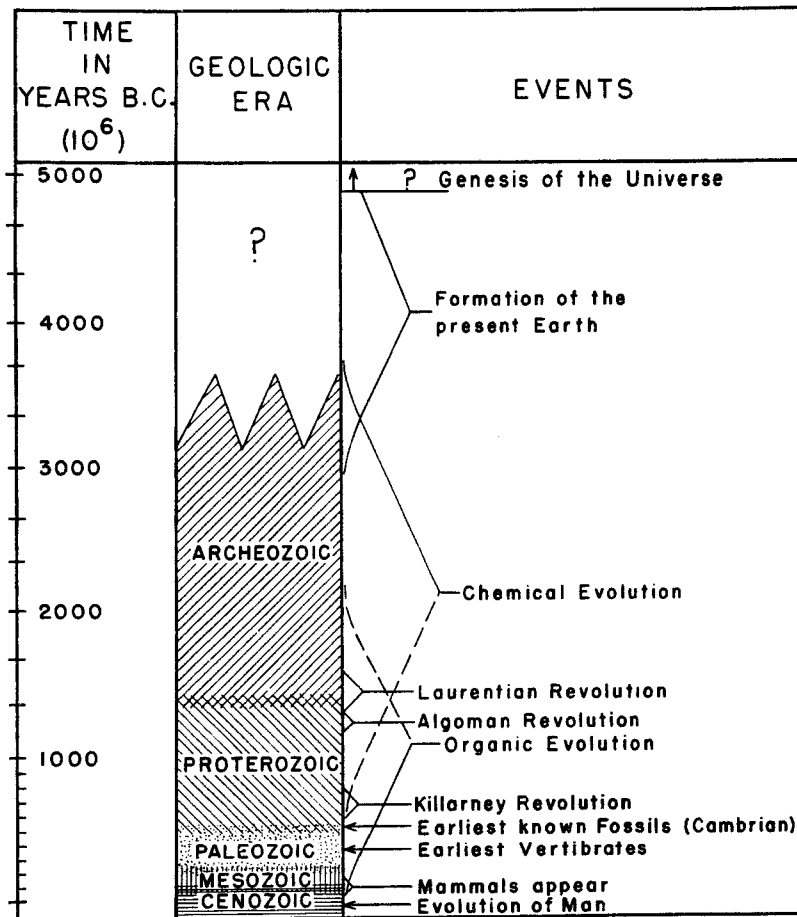
The term "evolution" has been most commonly used and developed by the biologists, and has a fairly clear-cut definition in their language. It has been used to describe the changes and development of various forms of life as they have been read in the paleontological record and interpreted in the light of modern genetics and biochemistry. It calls for the possibility of random variation amongst systems together with a mechanism for selecting amongst those random variations. This, in essence, is what the term "evolution", as I understand it, means in biological language. What I would like to do is to extend the very same terms into nonbiological systems and show that they apply, and

*Transcription of address delivered at Amherst College, Amherst, Massachusetts, November 19, 1954. The preparation of this paper was sponsored by the U. S. Atomic Energy Commission.

that their application to a nonliving system will give rise, in the normal course of events, to confined systems in space which we could call living cells.

The time element that is involved is a very long one. By extrapolating the idea of evolution to include nonliving systems as well as living ones, we can go clear back to a time when the universe and the stars were evolved and eventually an earth was formed. This time period starts roughly about 10 billion years ago, as far as the astrophysicists can tell us. Roughly 10 billion years ago the universe was formed by an explosion of matter in some way and the elements were formed in an evolutionary pattern, a discussion of which would be beyond our present scope, and which may more properly be called "nuclear evolution." The next period that we can characterize after the earth's formation is the time for the formation of chemicals of various degrees of complexity upon the surface of the earth, but before the appearance of systems that we could call living--"chemical evolution". Finally, as the systems evolve in complexity, then at some period of time they may acquire all of the collection of qualities that are usually attributed to living things, and we can say the thing is alive, or that there is a living system present. Then we come to the period of biological evolution, which we know most about, and which took place over a period of a billion years, or thereabouts. In the last 50,000 years or so we have the period in which man has evolved and the new kinds of evolution which we might call "psychosocial evolution" has begun. We thus have four periods--or four types or kinds--of evolution into which we can divide time (Figure 1), and the one with which we are concerned here is the second one, the period that I have called "chemical evolution," the period after the formation of the earth and before biological evolution can be said to have begun. This period, as nearly as we can define it in time, lies between 2-1/2 and 1 billion years ago. (We have roughly 2 billion years to do chemical evolution; this is a great deal of time and we can do many improbable things in that time. This, of course, is one of the saving graces of the problem.)

In order to begin chemical evolution, if you like, we have to decide on what sort of an earth we had to work on--what sort of a chemical system did we have about 2-1/2 billion years ago, when the earth first began to take its present form? I might point out that these various periods that I have tried to delineate are, of course, simply regions in time, and there is no sharp dividing line between them; they grade one into the other. One can say simply that the earth gradually took shape, by some process--perhaps just by aggregation, which is one of the modern cosmological theories. Regardless of what



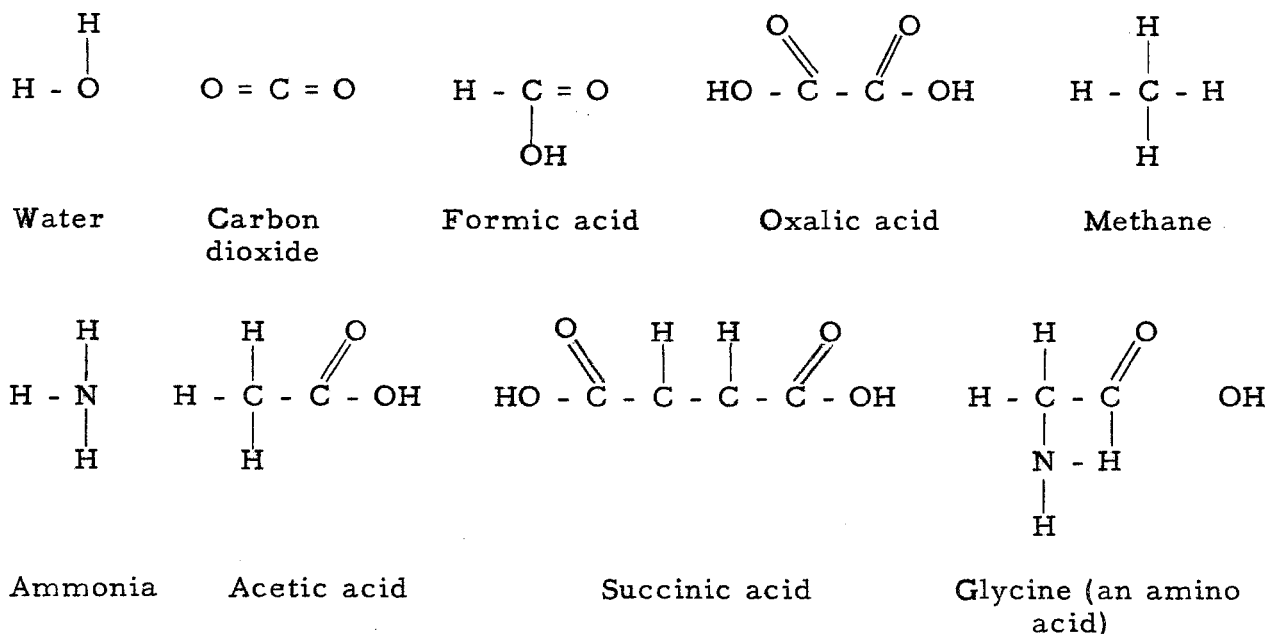
MU-9665

Fig. 1

path its formation followed, we can say that at some period of time the earth had acquired very nearly its present form, and we might say that chemical evolution was well under way--it had already begun. We should try to decide, at least, what sort of an earth--what sort of chemicals--we had to deal with, and what the earth was like at that time. Unfortunately, the geochemists can't agree on whether the atmosphere of the earth was an oxidized one or a reduced one, and by this I mean whether the carbon atoms (and other atoms too) that were present on the surface of the earth combined mostly with oxygen or combined mostly with hydrogen; the reduced form would be the one in which the atoms were combined with hydrogen, the oxidized atmosphere would be the one where the carbon atoms were combined mostly with oxygen. And, of course, we could have one or the other, or some intermediate stages between.

For the present purpose it isn't necessary to know exactly what form the atmosphere of the earth had during that period. The reason is that there exist at least four different ways in which more or less complicated chemical compounds could have been formed in either condition--oxidized or reduced--although the reduced starting point seems the easier one to develop. These ways have been described as follows, and in this order. The first method by which larger molecules containing more than one carbon atom could have been formed from simple ones was suggested by J. B. S. Haldane about 1926 (1), and has been experimentally checked. (We, among others, have checked it.) Under the influence of ultraviolet light from the sun, it is possible to make more or less complex substances, like the amino acids and heterocyclic compounds that are now found in biological materials, by simply illuminating aqueous solutions containing simple carbon compounds such as formic acid or formaldehyde (one-carbon compounds) and a nitrogen-containing material such as ammonia, nitric acid, or nitrates; and one can get fairly complex organic materials. Another possible method is the one that was suggested by the Russian biochemist Oparin (2). He had the idea that the earth cooled down from a hot miasma and that carbon was mostly in the form of metallic carbide which, upon being put in contact with water, formed acetylene; the acetylene (a two-carbon compound containing an excess of electrons looking for mates) under suitable catalytic influences such as rocks and minerals could polymerize and form large chains which could give rise to molecules of the type we now see in biological materials. The third way in which simple organic substances could have been formed in a world without life is by means of the action of very high-energy radiation, such as is produced by radioactive materials or comes to

us from the stars in the form of cosmic rays. This we have also checked in an experimental way (3). We have taken solutions of carbon dioxide and water and irradiated them in the cyclotron and have gotten formic acid, and irradiation of formic acid produced oxalic acid (a two-carbon compound). My colleagues have irradiated a variety of other substances since then. They have irradiated two-carbon substances and gotten four-carbon compounds such as succinic acid, which are even now important metabolites in modern living organisms. The structural relationships of some of these compounds can be seen from their formulas:



These three methods have permitted the building up of complex chains of atoms from simple ones, and this is essentially what we are trying to do: to devise ways and means of getting more complex substances--chains of atoms hooked together--from simple ones, without the intervention of living organisms, which today is the only way it occurs in nature, outside the laboratory.

The last method that has been suggested, and tested experimentally (4), is the one involving an electric discharge in the upper atmosphere, like a lightning discharge, when there are present methane and ammonia and water (methane is a carbon with four hydrogens around it, ammonia is nitrogen with three hydrogens--therefore, a reduced atmosphere). If you pass an electric discharge through such a mixture you can get a variety of compounds in which there are carbon atoms tied to each other, and compounds of the type of amino

acids, which are the essential building blocks of proteins. We have thus devised at least four ways in which relatively complex organic substances can arise; we have tested them all in a nonliving system.

Why are we doing all this? You see, today organic matter cannot accumulate on the surface of the earth, and the reason for this is that there are too many living things to eat it up. At the time we are talking about there weren't any such living things, and if organic substances--that is, materials containing carbon-carbon bonds and carbon-hydrogen bonds--were created by any one of these methods, they would remain. They would change only under the agencies such as the ones I have described; there would not be any microorganisms to reconvert them back again into carbon dioxide and other gases of the atmosphere. And so they would accumulate. We have arrived, therefore, at a point where we can visualize the accumulation in a random fashion of relatively complex organic substances under the influence of physical agencies--all of which we have tested experimentally and all of which there is every reason to suppose were operating 2 billion years ago.

I have omitted, so far, to do a thing that most the the "speculators" in this area do--and there are many, I might say, who do this (it's especially popular today to speculate about this subject because new concepts have opened up new avenues of thought as yet experimentally untried)--and that is to define the nature of life itself, the thing that we are trying to describe the origin of. And, of course, this is the pitfall, really, in which most of the people who have speculated in this area have been trapped. They have tried to define it in too simple and precise a way--life must have this particular set of properties to deserve the name. Therein, I think, is the difficulty: they set themselves up an impossible task when they do that. Actually life has many attributes, almost any one of which we can reproduce in a nonliving system. It is only when they all appear to a greater or lesser degree in the same system simultaneously, that we call it living. What are these attributes--some of them; anyway? (I can't name them all.) The ones that are usually used are growth and reproduction; irritability (the ability to respond to a stimulus); the phenomenon of autocatalysis in evolution, that is, the capacity for variation and change. All these things are characteristic of living systems. All of them can be reproduced individually in nonliving systems. There are volumes--pages and pages can be found--in physical-chemical and biological literature, in which model systems are described as having the property of a living system. (For example: a suspension of carbon tetrachloride in certain concentrated

sugar solutions will, because of the surface-tension relationships, behave as though it had the processes of an amoeba--it has just the kind of appearance under a microscope. This system, though, has only one of the attributes that we give to living systems.) It is only when all these properties occur together to a certain degree that we call it living.

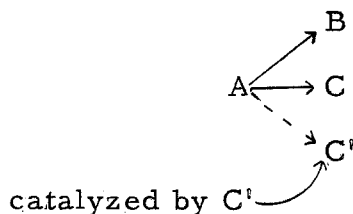
The essence of what I want to say is this, then. As these properties accumulated some time in the past, they would have reached a degree of development of which, if we had been there viewing it from outside, we would have said "that, now, is living." It wouldn't have been a sudden thing. Moreover, it would have been a pretty arbitrary decision whether it was or it wasn't alive. For example, the viruses of today may be such things. The argument goes on and on--they have some of the attributes of living things but they don't have them all. This is the type of thing I am referring to. All we have to do, then, is to devise ways and means of accumulating these properties--each of them--in chemical systems, and once those ways and means of accumulating each of these properties in chemical systems have been devised, then eventually as they are developed and combined and confined, the systems will become sufficiently highly organized so that we can, as I say, call them living. With that kind of definition it is much easier to proceed.

We have already outlined possible methods to obtain a solution containing a random mixture of relatively complex organic substances. Thus, we have made complex organic material from inorganic material and very simple (one-carbon atom) organic ones; incidentally, this ability to make organic material out of mineral material is but one of the attributes of life. Life as we know it today, however, doesn't do it in a random fashion. It does it in a very ordered way. It selects certain chemical reactions and neglects others. We should, therefore, devise some way of getting chemical evolution to do the same thing.

Here, again, I must return to the concept of variation and selection as it has been developed in biological evolution, and apply it directly to this chemical system which has been developed in a random fashion so far. This chemical system has many random variations in it; there is no difficulty about that. The chemicals are formed by any one of these four different ways into more or less complex materials, but there is no selection; it is a random process, so far. This situation need not be permanent when you recall that some of the chemicals that are formed may themselves be catalysts for their

own formation. As soon as you recognize this, then you have available the essence of the process of selection within the chemical system itself. Think of it in these terms. If we have a random selection of chemicals that can transform themselves from one into another, and if at some given instant in a random way one chemical happens to form that will catalytically cause the transformation of some of the others into itself, you can see that those others will all go to this one that has randomly formed as a catalyst instead of going in other directions. And thus we have the process of selection.

Consider, for example, the group of chemicals A, B, and C, related as in the diagram, i. e., A may be transformed into either B or C. Suppose



that through some random occurrence a product C' is formed, slightly different from C, and such that C' is a catalyst for the conversion of A into C'. Then, instead of A's going into B, most of A will go into C', because there is no catalyst for speeding up of the former, whereas there is a selective speeding up of the latter. There are many beautiful examples of this kind of autocatalysis in chemistry. For example, the simple system cupric ion (that is, oxidized copper) and molecular hydrogen is an unstable system, but it will remain in this form indefinitely until, by some random occurrence, one of the cupric ions is reduced to cuprous ion. This cuprous ion happens to be a catalyst for the reaction of hydrogen plus copper to give cuprous ion plus hydrogen ion. (This is no accident; it is one of the fundamental properties of this species of the copper atom.) As soon as this happens once, then all of the copper is converted from the cupric form into the cuprous form. This is the essence of the selection process operating on the random formation of chemicals.

The next step in the evolutionary process is the development (elaboration and improvement) of these catalysts. They were developed by a process exactly analogous to the way in which they were originally formed. They were selected originally because of their rudimentary catalytic property, and all we have to do now is to improve the process.

Figure 2 indicates the development of a catalyst. It illustrates the essential point of the present discussion. We know, for example, that iron ion in water solution is a catalyst for the decomposition of hydrogen peroxide to give water and molecular oxygen. Now the catalyst activity is measured by a number that is pretty small--it is 10^{-5} . If, however, the iron is incorporated or gets surrounded by a special structure such as a tetrapyrrole ring, called a porphyrin--a structure very common in present-day organisms--then the catalytic activity for this reaction is increased by a factor of a thousand. Thus, we may speak of the improvement or evolution of a catalyst. Now, why does this occur? This porphyrin happens to be an organic molecule that is very stable and is very likely to form. In fact, we can show how this molecule can be formed from succinic acid and glycine, and we have already shown how we can form glycine and succinic acid from carbon dioxide and ammonia. And so we have the elementary units for the formation of this molecule in a nonliving system.

The most interesting thing is that this molecule, in a very dilute solution of hydrogen peroxide--which is formed by the action of high-energy radiation on water--will facilitate one or more of the reactions in the sequence leading to porphyrin. Here is another case, then, where a substance once formed will catalyze its own formation. A molecule of this type is responsible for the red color of blood, and it is a most important type of catalyst in all living systems that require oxygen or form oxygen--this means both animals and plants. It is not surprising that it should be, particularly now that we can visualize a sequence of reactions that might have given rise to its formation in prebiological time. When the haem (iron porphyrin compound) is combined with a specific protein, then the catalytic activity goes up by a factor of another million or ten million. In all probability, this evolution from simple iron ion to iron in porphyrin took place during the period that we have called chemical evolution. The change from porphyrin to hemoprotein probably took place, for the most part, during the period that we call biological evolution. There are other examples of this sort of transformation or development of chemicals. It is an evolution of chemicals, and you will notice that the evolution is toward (at least it looks from here as though it is "toward") the kind of chemicals we now have in biological systems. But this is looking at it from the back side. The essential stability of the compound and the fact that it is a good catalyst for its own formation are the crucial points.

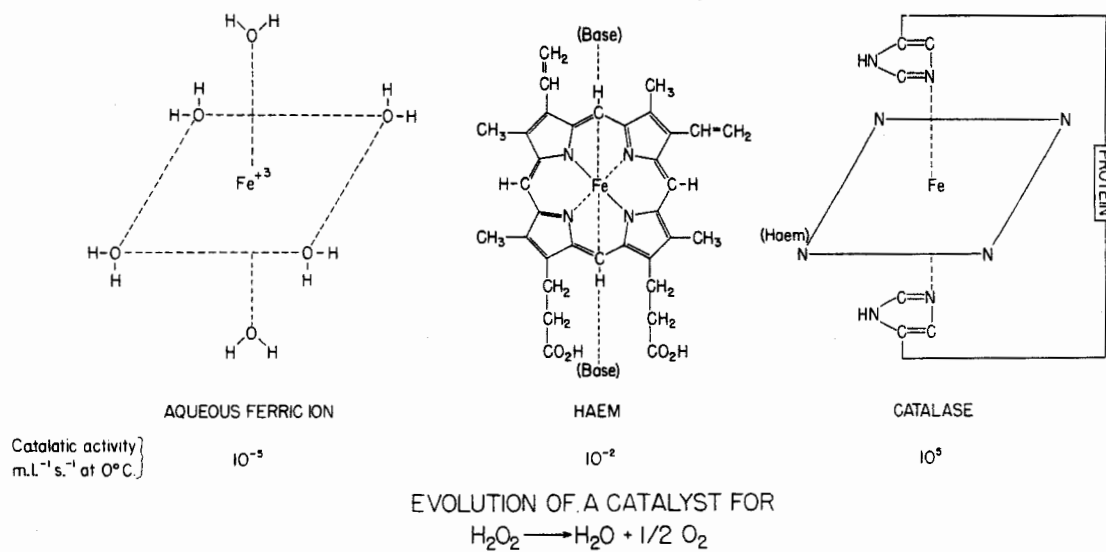
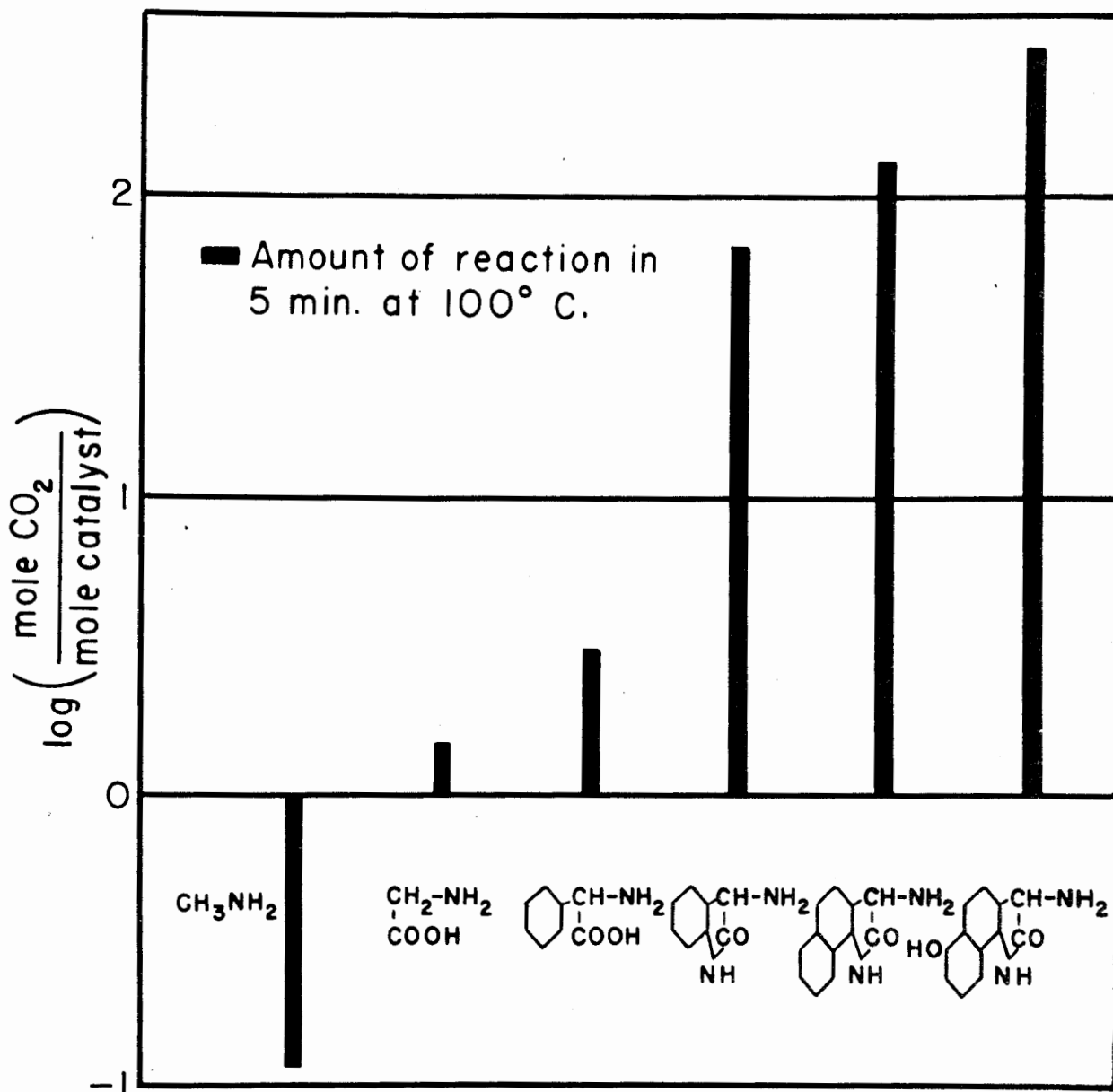


Fig. 2

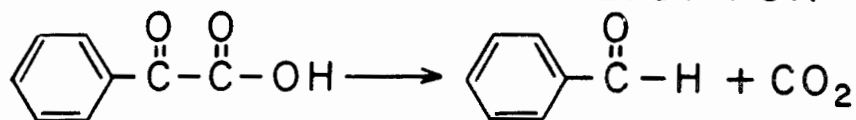
There are other examples of this autocatalysis phenomenon in which chemicals are evolved that don't necessarily involve metal atoms as the center; Figure 3 shows the evolution of another type of catalyst. This is a catalyst of a decarboxylation reaction, derived by gradually increasing the complexity of a molecule of methylamine first to glycine, then to phenylglycine, etc. The catalytic activity becomes greater and greater. Here, again, you can see that it is possible, by gradually changing the chemical a little at a time, to improve its catalytic ability. If this catalytic ability happens to be one that is helpful for its own formation, it will facilitate the conversion of all the suitable raw material into itself. Gradually, then, the very simple molecules that are initially available are converted into the more efficient catalysts. These very simple molecules, which are formed by the processes that I described a moment ago, would thus be evolved into still more complex ones.

We have now developed the essence of nearly all the processes that we need for chemical evolution: a source of energy leading to the formation of intermediates; random variations amongst their transformations, both as new energy is stored from prime sources and as the stored chemical potential is degraded; and a mechanism for selection among those random variations. These are precisely the qualities of any process that the biologists know actually is required for an evolutionary system. We are still a long way, however, from the kind of molecules which we now know carry the essential organization of living things. These are the genes and the chromosomes.

So far, all the catalytic activity and changes that I have talked about are occurring in a homogeneous system, that is, there is no order; the molecules are all in a solution and arranged in a random fashion. We must now devise ways and means of creating some sort of molecular order out of this disorder. This is one of the essential qualities of living things--the ability to use energy to create order. There are some very technical definitions for life and living systems; for example, they are called "open systems" in which some substance with high potential energy comes in at one end and degraded energy goes out at the other, and in the energy-degradation process order is created. A living system does this--creates this order--in a variety of ways, and one of them is the ability it has developed to couple a reaction that is spontaneous (that is, gives off energy) with one that is not, i. e., to use that energy to make a reaction which requires energy to go. Actually, all the reactions that create order are, in general, reactions that require energy. The burning



EVOLUTION OF A CATALYST FOR

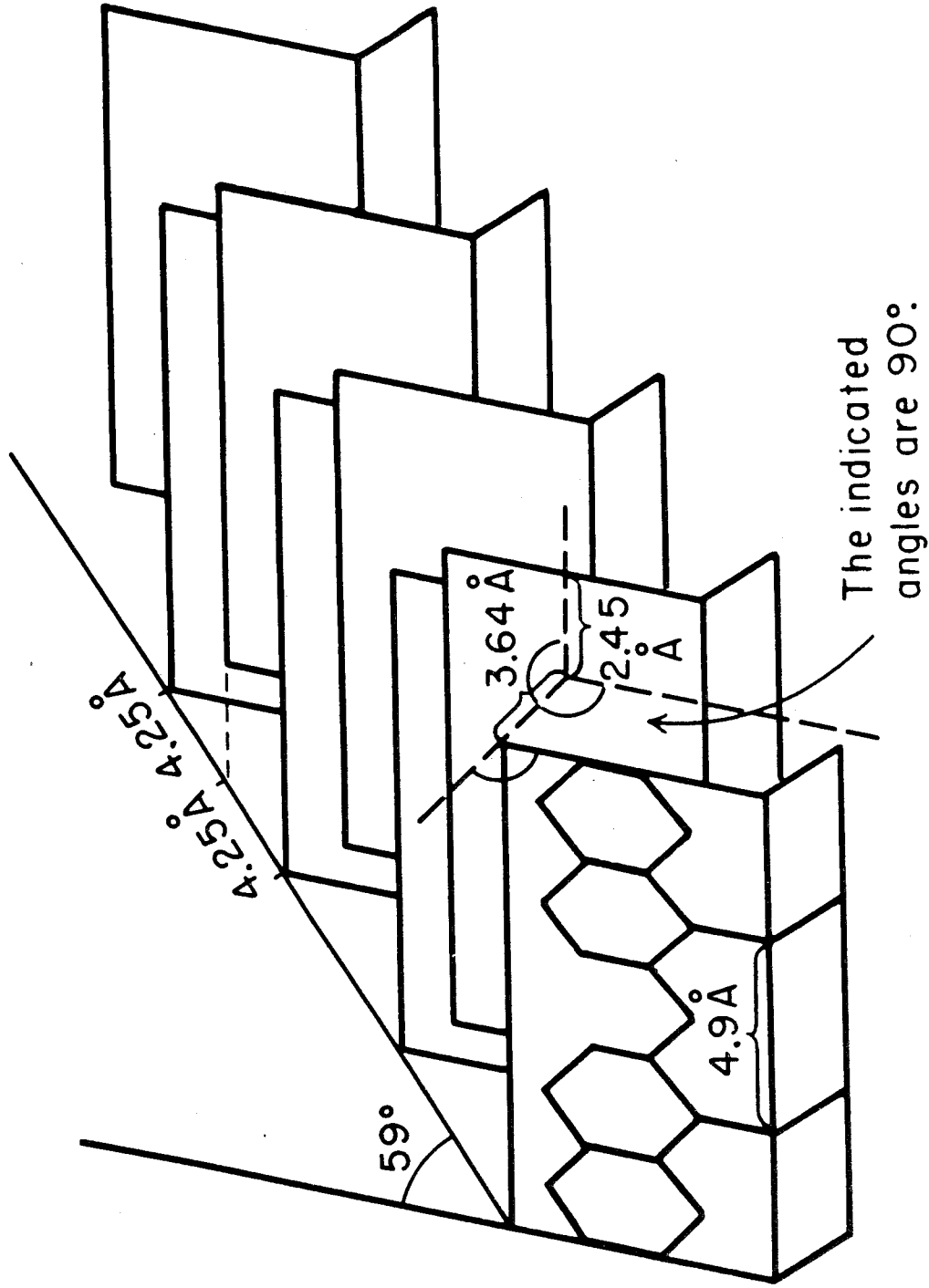


[W. Langenbeck, R. Hutschenreuter, Zeit. anorg. allg. Chem. 188, 10 (1930); W. Langenbeck, R. Hutschenreuter, R. Jüttemann, Ann. 485, 60, (1931).]

of sugar is one reaction that generates energy by combining oxygen atoms with the atoms of the carbon and hydrogen that constitute the sugar. And you want to be able to use this available energy to create the order that is required to construct, for example, the nucleic acid molecules in the chromosomes.

How, then, can this have come about? We now have to seek primitive ways of spontaneously generating a kind of order that we find particularly in the desoxynucleic acid molecules, which are the carriers of genetic continuity and biological order. The interesting thing is that there is a beautiful way in which this kind of order can arise--I should say there is a beautiful model for it. Whether it has arisen this way or not is a moot question; but there is a very nice model for it. It so happens that when the molecules of certain kinds of organic substances, particularly substances that have aromatic character, that is, molecules that are flat (tend to have all their constituent atoms in one plane) come together, they tend to come together in a specific way--in a rather obvious way, in fact--and this seems to be a general rule of organic chemistry. They come together by piling up face to face or plane to plane; the big, flat molecules, one on top of the other, in a pile, like a deck of cards. When organic substances of this type crystallize, they crystallize in this way. Crystallization is the obvious way of creating order, and this is what I am going to call upon--an incipient crystallization while still in solution.

There are certain types of organic molecules that are great flat planes. When their concentration in solution is raised to what we call 10^{-4} M, which is quite a dilute solution, the molecules tend to come together face to face and pile up, and this is without any additional help. The arrangement of the atoms and electrons in these molecules is such that they pull one another together plane to plane. This happens to be precisely the structure which we now know--and have known the elements of for some years, in fact--to be an essential characteristic of the structure of desoxynucleic acid (DNA), the material that carries the genetic character--in other words, the continuity and order--of present-day life. Figure 4 shows an example of a specific organic molecule and how it tends to orient itself in solution. The shape of the molecule is that of a large, flat plane. These molecules have piled one on top of the other, and the distance between the sheets is 3.6 \AA along the direction vertical to the plane. In this case, they also happen to be tilted a bit instead of flat-on, but they also can be formed with flat-on faces--face to face as well as tilted.

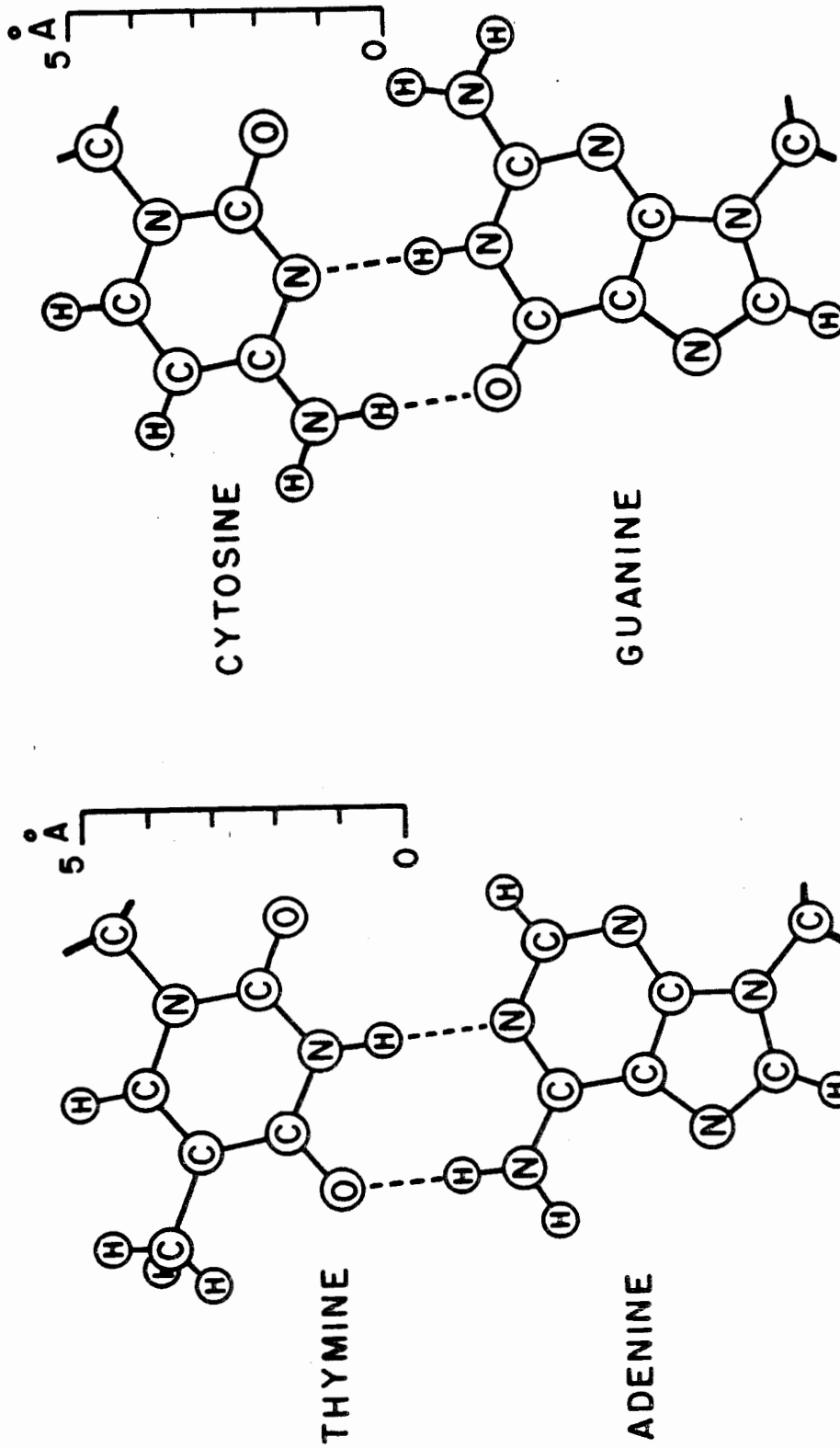


Arrangement of the plate-like molecules of Pseudo-iso-cyanin when they associate. [G. Scheibe, Zeit. f. Elekt. 52, 283 (1948).]

ZN-1362

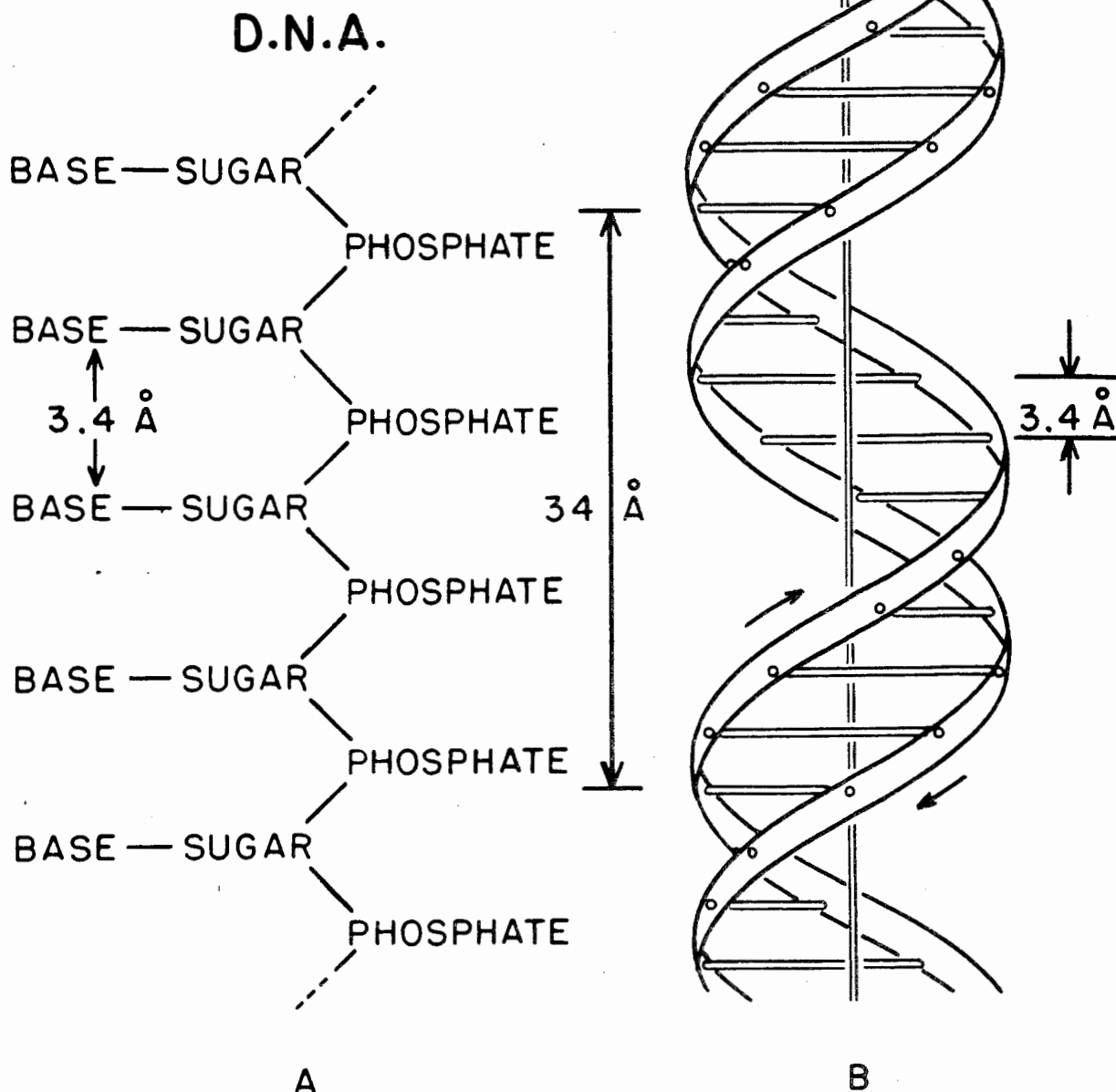
Figure 5 shows certain of the elements of nucleic acids (the bases). These are the units of nucleic acid which have aromatic character--the heterocyclic rings which pile up if a solution of them is made sufficiently concentrated. Figure 6 shows how they do pile up. The bases are planar molecules here viewed edge on, and you will notice that the distance between them (between the planes piles up one on top of the other) is 3.4 \AA (an Angstrom, \AA , is 10^{-8} cm, a pretty small distance). The bases are hooked together by a sugar and a phosphate in a long chain, so it is not at all surprising that if they form this kind of combination and pile up together, they form a still more ordered array, which constitutes what we now know to be the structure of the genetic material of present-day living organisms. We thus come to the conclusion that we actually can't avoid the formation of such ordered structures as now constitute some of the essential structural features of living things. The types of molecules that now carry the continuity of order are the very ones which, if they were present in random solutions, would spontaneously order themselves in this way. Furthermore, once they were formed, they would have "handles" sticking out after they had piled up, in the form of a variety of functional groups arranged along the vertical axis. Such a handle might be expected to influence the order in which a neighboring pile would grow. And this is exactly the way in which the present-day pairing process, as described by the biologists, is supposed to take place.

We thus have developed the mechanism not only for creating intermediates, for selecting amongst random variations in those intermediates, and making them more and more complex, but also for spontaneously ordering them. This word "spontaneous" is a term which means that the process uses up energy to create that order. The energy used resides in the structural features of the molecules that come together--when they come together the energy level goes down a little bit, and that is where the energy is used for creating order. We have, then, all of the elements that we need, except one which I haven't discussed explicitly, and that is the mechanism of the coupling of one reaction which gives off energy to another one which absorbs it. Here, again, in order to develop the idea, we have to find a rudimentary case that might be found in a strictly nonliving system. And once we have seen such a rudimentary case of energy coupling, and have defined the conditions that could improve it--which we have already done--we have all that is required.



The flat planar units (of bases) in the construction of desoxynucleic acid. [J. D. Watson and F. H. C. Crick, *Nature*, 171, 964 (1953)]

ZN-1361



- (A) Chemical formula of a single chain of deoxyribonucleic acid.
- (B) The figure is purely diagrammatic. The two ribbons symbolize the two phosphate-sugar chains, and the horizontal rods the pairs of bases holding the chains together. The vertical line marks the fibre axis.

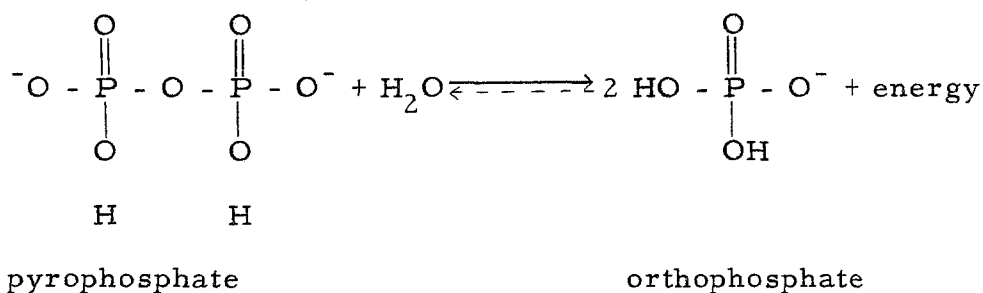
[J. D. Watson and F. H. C. Crick, *Nature*, 171, 964 (1953)]

ZN-1364

Fig. 6

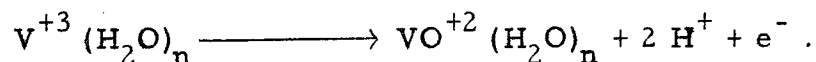
In order to look for such energy coupling we do the simplest thing, namely, have a look at the kind of coupling that living systems use today. We examine closely the nature of such coupled reactions as they have been described for present-day living organisms, and we find that there is at least one outstanding reaction of this kind. This is the reaction of oxidative phosphorylation. The energy of oxidation of sugar molecules, that is, the energy that one would get if one could burn sugar in a controlled fashion as an organism does, can be converted into another special form of chemical energy instead of letting that energy escape as heat, if the burning is done irreversibly. This special form can then be used to do mechanical work as in muscle, or electrochemical work as in vision, or thinking, or whatever type of biological activity may be required of it. There is one type of chemical which apparently has such a universal application--or at least has a very broad application--and that is a molecule known as adenosine triphosphate (ATP) and in it there is a structure in which three phosphorus atoms are linked through two oxygen atoms. The linkage of two phosphorus atoms to each other through an oxygen atom is called a pyrophosphate linkage, and this kind of linkage has been widely used in biological systems to do all sorts of biological work. All I am trying to do now is to devise a system for creating this kind of linkage.

In ordinary water solutions, the pyrophosphate linkage is thermodynamically unstable, that is, if it were to react with water to form two orthophosphate groups, energy would be released:

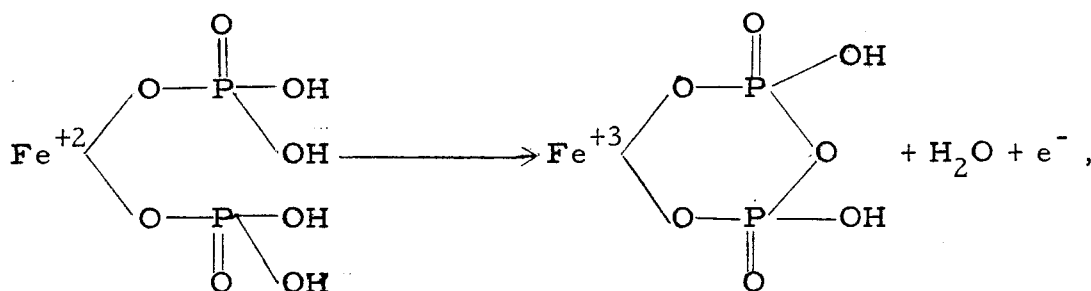


Fortunately this reaction goes extremely slowly without catalysts, so that present-day living organisms have been able to develop specific catalytic systems which carry out this reaction in such a manner as to usefully absorb the liberated energy. In order to make the reaction go from right to left, energy must be supplied. The problem, as it is thus simplified, is to bring two orthophosphate groups together and squeeze a molecule of water out from between them. Now the participation of oxidizable metal ion couples ($\text{Fe}^{+2} \rightarrow \text{Fe}^{+3}$;

$V^{+3} \rightarrow V^{+4}$) in the present-day process of oxidative phosphorylation seems pretty certain. One of the general properties of such ions is their tendency to squeeze a water molecule out of their coordination spheres when they pass from the lower to the higher oxidation number; thus,



A similar process might be written in which orthophosphate would replace a pair of water molecules, thus,



the electron eventually, if not directly, being passed on to oxygen. This would constitute a coupling of the energy-yielding oxidation of ferrous iron with the energy-requiring dehydration of orthophosphate to form pyrophosphate. This is but a rudimentary coupling reaction, possibly present in a totally nonliving system--in a system which certainly was present at the time we are speaking of. All that is required now is to improve the efficiency of this system. If the iron, for example, combines with one or another of the organic molecules that make the efficiency of this reaction greater, then, of course, the organo-iron survives. The organisms dependent upon iron that is not in such combination do not survive.

We have now all the elements--or at least most of the elements--that we usually think of as required for and characteristic of living organisms. We have provided experimental rationale for these. Thus, we now can conceive of a continuous process, beginning with a bare earth (I can't go beyond that, although actually the evolutionary process should be thought of as beginning with the initial explosion), leading to the random formation of more or less complex molecules, then gradually, by this process of random variation, autocatalysis, and selection to more complex systems, and eventually to the ordered arrays that I described a while back, which even today are the units that carry the continuity and order of present-day living systems. The thing

that differentiates what we have said here from what has heretofore been suggested within this scope of thought is that we don't require a single cataclysmic instant of change. We can't define a single instant of time such that before that instant there was no life and after that instant there was life. The systems that we define as "living" are defined in terms of all of the entire concatenation of properties, and when one has been developed by the processes I have described to a sufficiently high degree, then the system is spoken of as being alive. We have plenty of time to do this--we have 2-1/2 billion years. Although every one of the processes that I have described is probable--there is no great improbable event that I have required--the selection amongst the random probable events of a particular sequence is a highly improbable thing and has required the billion years or so that it took to do it. And that is why I doubt very much that we will ever be able to put all the chemicals in a pot and place it in a radiation field and go away and leave it for a while and come back and find nucleic acids.

REFERENCES

1. Collection of essays on "The Origin of Life", New Biology No. 16, Penguin Books, Ltd., London, England (1954).
2. A. I. Oparin, "The Origin of Life", translated by S. Margulis, MacMillan and Company, New York, N. Y. (1938).
3. W. M. Garrison, D. C. Morrison, J. G. Hamilton, A. A. Benson, and M. Calvin, *Science* 114, 416 (1951).
4. H. C. Urey, "The Planets", Yale University Press, New Haven Connecticut (1952); S. L. Miller, *J. Am. Chem. Soc.* 77, 2351 (1955).
5. From Figure 3: W. Langenbeck, et al., *Z. anorg. u. allgem. Chem.* 188, 10 (1930); *Ann.* 485, 60 (1931).
6. From Figure 4: G. Scheibe, *Z. Elektrochem.* 52, 283 (1948).
7. From Figures 5 and 6: J. D. Watson and F. H. C. Crick, *Nature* 171, 964 (1953).

General references on the subject of "Evolution"

1. "Evolution". Symposium VIII of the Society for Experimental Biology (Great Britain), Cambridge University Press (1953); particularly the article entitled "The Origin of Life" by J. W. S. Pringle.
2. "Evolution in Action", Julian Huxley, Harpers, New York, N. Y. (1953).