est in remote portions of the world and the corresponding need for specialist training in the local languages. The present status of linguistics as a science is on the whole an encouraging one. Aided, no doubt, by a subject matter of transparently systematic type, it has been able to develop sophisticated and effective methods of descriptive analysis and historical reconstruction which give it a unique place among the sciences concerned with human behavior (*12*).

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Evolution of Enzymes and the Photosynthetic Apparatus

Primitive photochemistry and porphyrin catalysis after separate genesis join in modern photosynthesis.

Melvin Calvin

The basic idea of evolution can be applied to prebiological times as well as to the transformations that occurred after living organisms appeared on the earth. In order for biological types of processes to have functioned, it is clearly necessary that an independent mechanism be developed for the production of organic material on the surface of the earth by methods which do not depend on living things as we now know them.

A number of such methods are chemically conceivable and, in fact, some of them have actually been tried out experimentally (*1, 2*). Ultraviolet radiation, for example, was one of the earliest (*3*). Thermal energy was also among the early sources considered as a possible means of generating organic material (*3*). The first application of thermal sources involved the generation of heavy metal carbides and their hydrolysis to produce unsaturated hydrocarbons such as ethylene and acetylene (*3*). These latter substances could then undergo a variety of reactions, including polymerization, to produce large organic molecules.

More recently (*4*), a thermal step has been introduced at a later stage in the development of organic material, after the primary development of such molecules as the simple amino acids and keto acids, through the agency of ionizing radiation. This ionizing radiation might have been of several types —electrical discharge, cosmic radiation entering from outer space, or radioactivity on the earth itself. All three of these types of ionizing radiation have since been experimentally demonstrated to be capable of producing the kinds of molecules that were needed to begin the process of chemical evolution.

If one adds to this the recognition that the fundamental character of the important catalysts (enzymes) of present-day living organisms is the result of the evolutionary development of rudimentary catalytic powers present in the simple ions or molecules of the inorganic, or prebiological, environment, all the elements necessary for the ultimate appearance of living organisms are available to us.

Development of Rudimentary Catalysts

Even the most cursory examination of what is now known about the nature of present-day enzymatic mechanisms cannot fail to impress one with the apparent identity in kind between the enzymatic reactions and the reactions as they are known to the organic chemist in the laboratory. For example, glyoxalase, by which methyl glyoxal is converted to lactic acid, is nothing more or less than an internal Cannizarro reaction that is catalyzed by bases. Almost all of the hydrolytic reactions—those of esterase, proteases, phosphatases — have their nonenzymatic counterparts in the form of generalized acid or base catalysis, or more specialized catalysis by metal salts. For example, again in the case of the phosphatases, the freshly precipitated trivalent metal hydroxides are extremely effective, or manganese ion is effective as a rudimentary phosphotransferase (*5*).

One particular group of catalysts which is widely dispersed in present-day biological systems is that centered around the element iron—particularly catalase, peroxidase, and cytochrome. Here, a rather quantitative comparison can be made between the ability of the bare iron atom to perform some catalytic function and the ability of the iron atom to perform the same catalytic function as it has been developed in biological systems. Thus, in Fig. 1 one sees a comparison of the hydrated iron ion, the iron ion surrounded by a por-

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phyrin as it is in heme, and the iron ion porphyrin, or heme, as it is incorporated into a protein, surrounded by two or more coordinating groups of the protein to form catalase. The progressive increase in catalytic ability is from 10^{-5} for the aqueous ferric ion to 10^{-2} for the heme, to 10^{5} for the complete enzyme.

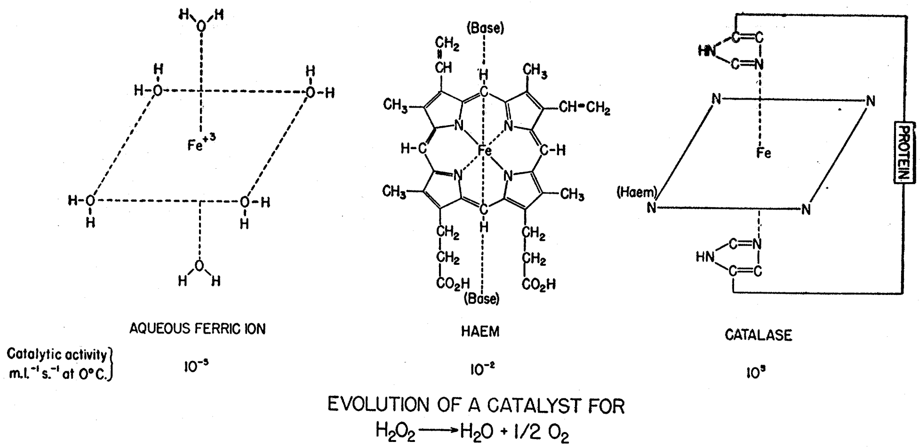

Fig. 1. Evolution of a catalyst for hydrogen peroxide.

These are definitions of the catalytic function of the iron for the reaction involving the decomposition of hydrogen peroxide. However, we know that the iron has many other functions as well, most of which involve oxidation or reduction. For example, even catalase itself can function as a peroxidase, using hydrogen peroxide to oxidize organic substrates, provided the hydrogen peroxide is sufficiently dilute. Undoubtedly the iron is also involved in what we now recognize as oxidative phosphorylation—that is, the conversion of the energy liberated upon the passage of an electron from a highly reducing potential to an oxidizing agent, such as oxygen or other material, with the concomitant storage of some of that energy in the form of unstable (pyrophosphate) linkages which may be later used for other purposes.

In order to convert the rudimentary catalytic functions which must exist in all the elements and their simple compounds into the highly efficient ones that we now recognize as enzymes, we must introduce two additional ideas, one from the realm of chemistry and the other from the realm of genetics, both of which, however, could be considered manifestations of exactly the same phenomena. The first of these, from the realm of chemistry, is the idea of autocatalysis—that is, the basic notion that the product of a reaction may itself be a catalyst for the conversion of precursors into itself *(6)*. This is a very common phenomenon in chemistry and perhaps is best illustrated in one of the simplest cases—namely, the reaction of molecular hydrogen with cupric ion. This reaction leads, thermodynamically, to the formation of cuprous ion and oxidized hydrogen, either as acid or water, depending upon the anion with which the cupric ion is associated. It so happens that the reaction of molecular hydrogen with cupric ion, although thermodynamically possible, is extremely slow without catalysis. However, the product of this reaction—that is, cuprous ion—is an extremely good catalyst for the reaction between hydrogen and cupric ion. Therefore, one can imagine (and indeed we realized this experimentally long ago) *(7)* a system consisting of molecular hydrogen and cupric ion which would remain in this form for a long period of time. However, should either a very slow noncatalytic reduction lead to cuprous ion, or some random electron transfer lead to the formation of an appreciable number of cuprous ions in the mixture, then immediately the entire reaction mixture would go over to the more stable system. Thus, we can provide a basis for chemical selection for the development of prebiotic evolution, leading to progressively more complex and specific organic structures.

Synthetic Sequences

The other notion that I would like to introduce is the one developed by the geneticist Horowitz *(8)* as a basis for biochemical selection after the appearance of mutable organisms. He suggested that the very complex sequences that we are now finding to be responsible for the synthesis of most of our existing biological material could have developed in a backward manner, beginning with the completely heterotrophic organisms. He postulated that the first organisms, the first living things, were complete heterotrophs and had available to them all possible precursors for their own duplication, and that their only function was to bring these together to produce themselves. One can then visualize a process in which at first one essential constituent of the mixture is depleted. Then, the particular organizational unit that has found a way to manufacture the depleted item from remaining molecules will, of course, survive, whereas those units which are unable to do so will disappear, since they can no longer reproduce themselves. Such a process of gradual depletion of available substrates, with the evolution of continually longer and longer chains of synthesis, would then constitute the origin of the synthetic sequences that we are now finding in present-day living organisms.

Enzymes

With these two ideas we can see how an enzyme, or, I should say, a highly efficient catalyst, could be built. It is perhaps worth while to trace such a development in a specific instance with which we might be familiar: for example, the iron porphyrin. Fortunately, the essential steps in the present-day biosynthetic route to porphyrin have been unraveled for us *(9)*. One could begin with succinic acid and glycine, two compounds which we already know can be made by the various random methods mentioned above, such as gaseous discharge or ionizing radiation or ultraviolet light *(2, 4)*. From these (succinic acid and glycine) an alpha-amino-beta-keto acid is formed, followed by decarboxylation to delta-aminolevulinic acid; two of these molecules then condense to form a pyrrole nucleus, porphobilinogen. This molecule then passes through a series of steps, involving a number of oxidations, leading finally to protoporphyrin *(9)*. The skeleton of this is shown in Fig. 2.

With the introduction of iron into the protoporphyrin—or perhaps a bet-

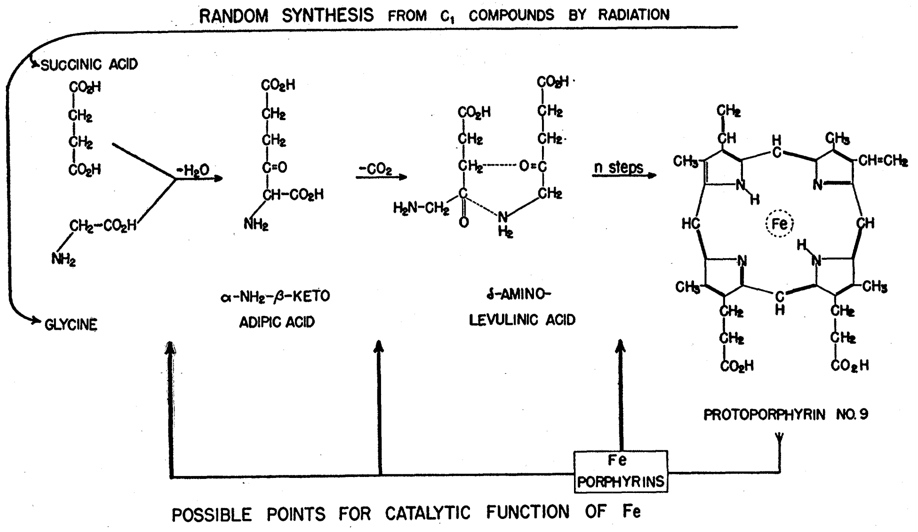

Fig. 2. Possible catalytic function of iron in a modern biosynthetic sequence (from succinic acid and glycine).

ter way to view it would be, with the surrounding of the iron by the protoporphyrin grouping—the iron becomes a better oxidation catalyst, and, as is shown in Fig. 2, there are several oxidation steps along the biosynthetic route as we now know it. Thus, one has only to suppose that one or more of the sequences of steps leading to protoporphyrin is dependent upon an iron-catalyzed oxidation (and this is almost certainly so) to arrive at the conclusion that once such an iron protoporphyrin is manufactured it will itself accelerate its own synthesis from such precursors as succinic acid and glycine, and thus will tend to build up the supply of the material and improve the iron catalyst that will be available for a variety of other functions as well. As yet, a nonenzymatic (modern biological catalyst) synthesis of this general type has not been described, but it appears that very few attempts have been made.

Development of the Photosynthetic Apparatus: Carbon Reduction

I shall review briefly what our present state of knowledge appears to be with respect to the existing mechanism by which the photosynthetic apparatus in the green plant and in the lower organisms can convert electromagnetic energy into chemical potential as reduced carbon and molecular oxygen. One need hardly do more than point out the essential features of the process to recognize its present-day separation into several distinct parts (*10*). The reduction of carbon dioxide, we now have every reason to suppose, occurs in a series of reactions which can take place entirely in the dark. In fact, all the enzyme systems that we now know participate in the conversion of CO_2 to carbohydrates have been found in a wide variety of organisms, many of which are not photosynthetic. For example, the *Thiobacillus* (*11*) contains very nearly all the necessary enzymes, and *Escherichia coli* (*12*) grown in xylose contains not only carboxydismutase but also a number of other enzymes involved in the carbon-reduction cycle. The final step was indeed taken when Racker (*13*) was able to make a mixture of all the requisite enzymes and the energy-storing compounds (reduced triphosphopyridine nucleotide and adenosine triphosphate) which produced hexose phosphate from carbon dioxide, all in the dark.

We can therefore follow van Niel (*14*) and reaffirm the suggestion that the photochemical apparatus in the green plants is primarily concerned with the splitting of the water molecule and the generation of reducing agent and intermediate oxidant. The latter (intermediate oxidant) will eventually find its way into molecular oxygen. The former (reducing agent) will be used to reduce the compounds formed by combination of carbon dioxide with suitable intermediates in the cell. From our knowledge of the nature of the carbon cycle (*10*) it is already clear that adenosine triphosphate is also required for this latter process, and this adenosine triphosphate may be generated either by oxidative phosphorylation or by a recombination of the intermediate oxidant with some intermediate reductant that has been formed by direct photolysis. Thus, we can suppose that the reaction sequence that is now used by green plants for the reduction of carbon dioxide was developed independently of the photosynthetic apparatus, and was presumably later coupled to the energy-capturing and -transforming mechanism which the photosynthetic apparatus represents.

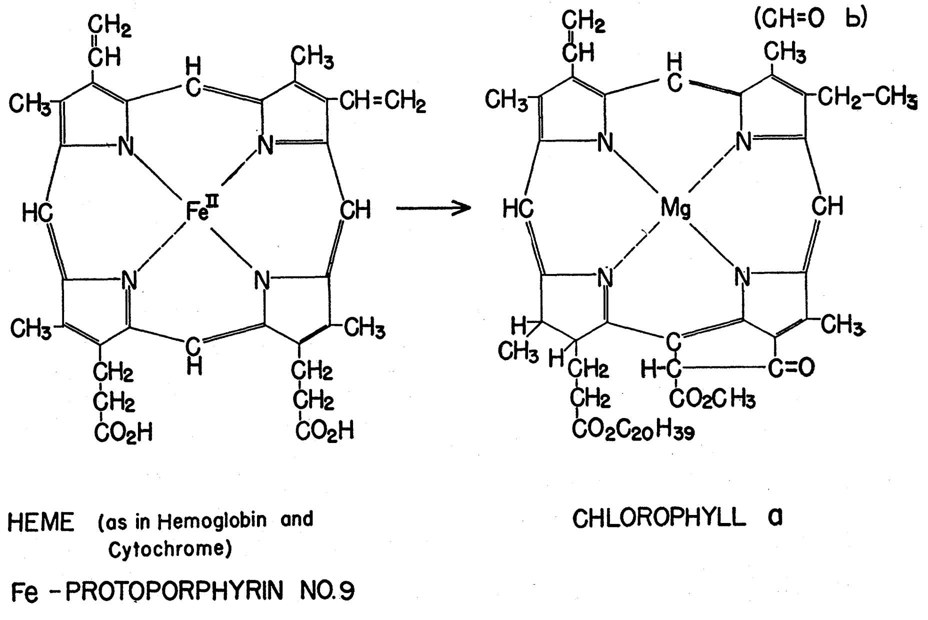

Fig. 3. Structural relationships between heme and chlorophyll-a.

Photon Conversion

We must now examine the nature of the photochemical apparatus to see if we can discover something of its origin. The primary energy-trapping molecule is, of course, a porphyrin, chlorophyll. In recent years, the work of Granick (*15*) has clearly indicated, if not conclusively demonstrated, that present-day synthesis of chlorophyll is a branch in the synthetic sequence leading also to the hemes. This branch seems to occur just before the insertion of the iron into the phorphyrin ring (Fig. 3).

We can thus see that the most likely course for the evolution of the photosynthetic apparatus involved the prior existence of the porphyrin type of catalytic structure. This catalytic structure was evolved not in response to the existence of sunlight but, rather, in response to the other evolutionary driving force which we have already seen operative in the development of the porphyrin nucleus—namely, the oxidative catalysis at which iron compounds of the porphyrins are so efficient. This leads to the suggestion that either the development of the porphyrin was not directly dependent upon the existence of oxygen in the primordial atmosphere and occurred in response to its function in other oxidative dismutations not involving molecular oxygen or that there was molecular oxygen in the earth's atmosphere prior to the advent of the photosynthetic apparatus producing it now.

The development of such highly organized structures as are now found in the organelles of the cells, such as the chloroplasts and mitochondria (*16*), seems to me to be incompatible with the degree of penetration of the ultraviolet radiation from the sun in the wavelength around 2500 angstroms, which would have occurred had there been no oxygen in the atmosphere. Today, of course, the oxygen in the upper atmosphere is photodissociated by this very ultraviolet light and is thus converted into quantities of ozone, which, in turn, strongly absorbs in the region between 2200 and 3000 angstroms. While it is possible to conceive of the development of heterotrophic organisms in the shelter of deep water, and thus not exposed to the destructive ultraviolet, it is difficult to conceive of the evolution of a photosynthetic apparatus, even a primitive one, also in the same environment, since there would be little visible light available, either, for the selective mechanism.

Thus, we are constrained to believe that not only was the evolution of higher organisms delayed until appreciable amounts of oxygen appeared in the atmosphere but that the evolution of the porphyrin catalysis itself, and of some of the more complex structural elements of living cells, also had to await this protection. Presumably, it came about by virtue of the photodissociation of water into hydrogen and oxygen, followed by the escape of the hydrogen from the gravitational field of the earth and the leaving behind of an appreciable quantity of oxygen, even though it is now entirely photosynthetic in origin. We can thus envisage the development of the highly organized structural units which we see today, in the form of mitochondria prior to the development of the chloroplasts and the photochemical apparatus. The similarity in the structure of these two organelles is very striking, and it is not unreasonable to suppose that the latter had its origin in the former (Fig. 4).

Coupling

Thus, the porphyrin molecule and the structural unit into which it is built had an independent evolution. Only at a much later time did the coupling of the optical properties of the porphyrin molecule to the energy demands of the carbon-reduction cycle take place. This presumably occurred at a time when there may already have been a rudimentary photosynthetic energy-yielding apparatus in the near ultraviolet, perhaps using sulfur compounds as direct absorbers. The more efficient light-energy-capturing molecule, such as porphyrin, could not be used in energy conversion until it was divested of the iron atom which was its principal reason for being. A reason for this is the requirement for a long-lived excitation after the capture of the quantum. The iron porphyrin, although absorbing a good deal of visible light, cannot have a very long-lived excitation because of the presence of the magnetic iron atom in the molecule. The inhomogeneous magnetic field surrounding the iron atom breaks down the selection prohibitions and does not allow long-lived excitation of porphyrin. However, if the iron is replaced by magnesium, or some other diamagnetic divalent cation such as zinc, then these molecules can have long-lived excitations which are essential for energy migration and conversion with any high degree of efficiency.

The rudimentary beginnings of a chlorophyll type of photosynthesis may have occurred in the precellular period, in a period that had already seen the appearance of lipid-type coacervates (*3*) and in which the disc-like molecules of chlorophyll could assume a pseudocrystalline arrangement facilitating energy transport and conversion (*17*). In all probability, it was at this point (or very near this point) that the cellular habitat of life took shape. Finally, the generation of the oxygen-evolving mechanism, perhaps requiring the participation of the carotenoids and other such materials, occurred, leading to development of the higher plants (*18*).

As is the case with the precursor forms in biotic chains of evolution, it is not likely that we will discover on earth any of the rudimentary prebiotic systems of which we have spoken (*19*). However, the time is fast approaching when it will be possible to explore at least three nonterrestrial environments—those of the Moon, Venus, and Mars. The possibility of finding materials in an evolutionary stage which might correspond to the early stages of terrestrial evolution is real and finite (*20*). It is,

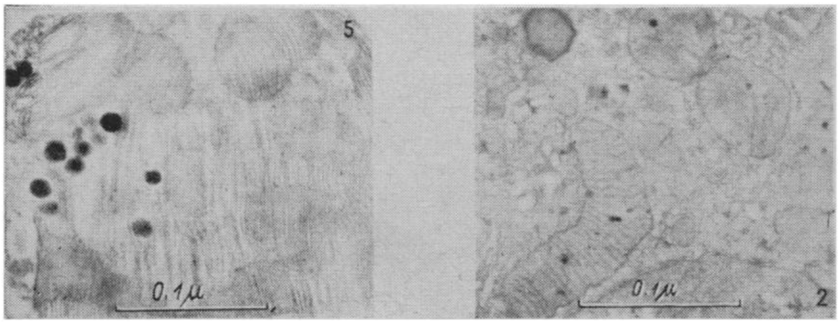

Fig. 4. Comparison of structure of mitochondria and chloroplasts. [After Sjöstrand]

therefore, of the utmost importance to avoid any action which will, by terrestrial contamination, forever jeopardize, or even destroy, the possibility of distinguishing organisms or prebiotic chemical forms which might be discovered, particularly on Mars.

Suitable methods of close-in spectroscopic investigation and upper atmosphere sampling should be developed and used so as to make knowledge available prior to any direct contact, and it is to be hoped that any vehicles which are at all likely to make contact with these surfaces will be biologically sterile and as chemically and biochemically clean as it is possible to make them (*21*).

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Science in the News

Building for Unique Science High School Dedicated in the Bronx

A new building for New York's Bronx High School of Science was dedicated on 27 October. The dedication focuses deserved attention on this unique institution, which provided secondary education for more than 1 in 200 of all persons who received their doctorates in the United States during 1957. Most of the doctoral degrees that have been earned by Bronx High alumni were in the pure sciences and in engineering, according to a study that is being conducted by Samuel Strauss of McKinley High School, Washington, D.C., for the Office of Scientific Personnel, National Academy of Sciences—National Research Council.

An earlier study, made in 1952, determined that approximately 80 percent of the school's graduates are associated with science, mathematics, or science-related professions, and that many alumni are now occupying important posts in universities, scientific and engineering institutions, and private and government laboratories. This record has been achieved in a relatively short span of time, for the school is only 21 years old.

History

The Bronx High School of Science is a school for the gifted. It was established in 1938 by the Board of Education of the City of New York as a public academic high school for boys with a particular interest and ability in science and mathematics. In 1946 the school was opened to girls, who have since that time been admitted in the ratio of one girl to every two boys. The current population of the school is approximately 1800 boys and 900 girls.

For its first 20 years, the school was headed by Morris Meister, whose portrait hangs in the entrance of the building that was dedicated on Tuesday. Last year Meister resigned to assume the presidency of the newly founded Bronx Community College. He was succeeded as principal by Alexander Taffel, former head of Haaren High School in New York City and a physicist who studied under Isidor I. Rabi and the late Enrico Fermi.

Curriculum and Academic Performance

The students at the Bronx school are selected from applicants from every part of the city of New York on the basis of an entrance examination, as well as on previous scholastic record and achievement. The effect of the selection process is to produce an entering class with a median IQ of 140, achievement in reading and arithmetic about 2 years beyond chronological age, and an aptitude for science and mathematics. The school is harder to get into than many colleges; in 1957, 3900 of New York's superior students applied, and only 750 were accepted.

The curriculum consists of a basic core of required courses, supplemented by a number of elective courses in the areas of the pupil's special interest. Required courses for 4 years at Bronx High are as follows: 3 years of mathematics (most students take more); 5 years of the sciences; 4 years of English; 4 years of social studies; 1 year of mechanical drawing; ½ year of science laboratory techniques; at least 3 years of Latin, Spanish, French, German, or Hebrew; and music, art, and health education. For outstanding students, there are special courses in English, mathematics, physics, biology, and chemistry that lead to college admission with advanced standing.

The achievements of the students in scholarship competitions have been consistently outstanding. At the present time the school holds top place in the nation in the winning of awards in