(Geological Society of America, 1962), "Serpentines, Orogeny, and Epeirogeny" in *Crust of the Earth* (Geological Society of America, 1955), and (with R. L. Fisher) "Trenches" in *The Sea* (Interscience, 1963).

THE ORIGINS OF LIFE

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We have had a century in which to assimilate the concept of organic evolution, but only recently have we begun to understand that this is only part, perhaps the culminating part, of cosmic evolution. We live in a historical universe, one in which stars and galaxies as well as living creatures are born, mature, grow old, and die. That may indeed be true of the universe as a whole; if so, it appears by some recent estimates to be about 20 billion (twenty thousand million) years old. But whatever doubt is held of the transitory nature of the universe, such a galaxy as ours surely had a beginning, and pursues its course toward an eventual end; and this, the Milky Way—perhaps 15 billion years old,[1] about 100,000 light years across, and containing about 100 billion stars—provides a quite adequate stage on which to explore the enterprise of life.

Many of our ideas concerning the beginnings of life on this planet have become familiar, since the modern argument was introduced about 30 years ago by J. B. S. Haldane[2] and in much greater detail by A. I. Oparin.[3] I shall review that argument very briefly here, in order to discuss certain aspects of it further, and to examine some of its universal implications.[4]

The Earth is about 4.5 billion years old. The first condensations of interstellar gases and dust that formed the Earth and other planets are considerably older, probably nearly as old as the Sun, perhaps 5–6 billion years; but it is about 4.5 billion years since the Earth's core separated from its mantle.[5]

It is a curious fact, not yet well understood, that the oldest rocks on the Earth, wherever found, are about 3 billion years old. It may be only so long ago that the Earth's crust became reasonably stable. Not long afterward, on a time scale of this magnitude, life must have appeared, for cherts in the Gunflint iron formation in southern Ontario, Canada, which are at least 1.6 billion years old, contain evidences of microscopic organisms, including what seem to be both fungi and algae.[6] If algae, and hence photosynthesis, existed at least 1.6 billion years ago, life in its more primitive forms must go back much further.

How had it begun? We assume that during the early history of the planet, in an atmosphere almost wholly lacking free oxygen, such simple gases as methane, water vapor, ammonia, and hydrogen, later probably also carbon monoxide and dioxide and nitrogen, reacted slowly but continuously with one another to form the smaller organic molecules. Most of this chemistry probably took place in the upper reaches of the atmosphere, activated mainly by ultraviolet radiation from the Sun and by electric discharges. Leeched out of the atmosphere over long ages into the waters of the Earth, organic molecules accumulated in the seas and there interacted with one another so that the seas gradually acquired an increasing concentration and variety of such molecules.

Model experiments have shown how such processes can yield amino acids,[7-9] nucleotide bases,[10] and other molecules that enter into the composition of living organisms. One of the most difficult problems is to attempt to understand how such unit structures combined with one another and polymerized against thermodynamic gradients that tended rather toward hydrolysis—how amino acids could have combined to form polypeptides and proteins, and nucleotides to form nucleic acids, apart from the precise activating mechanisms that guide and provide the energy for such syntheses in cells. Several interesting models for amino acid polymerization have been described, yet involving circumstances that seem to differ significantly from those that could have worked on an adequate scale in nature.[11]

It is thought that over long ages such molecules, large and small, collected in the oceans and there came together eventually to form aggregates which in turn grew more numerous and complex. These competed with one another, so that some aggregates, by virtue of particularly favorable constitution or organization, proved more efficient than others at sweeping organic molecules out of their surroundings, and so grew at the expense of the others—a primitive beginning of natural selection.[3] It is supposed that sometime, somewhere, or perhaps several times in several places, such an aggregate reached a state that an experienced biologist, had one been present, would have been willing to call alive.

A great question concerns the composition of the primitive atmosphere and hence the gases which were available for the synthesis of the unit organic molecules. Urey[12, 13] has defended strongly the thesis that this was a reducing atmosphere, containing large amounts of methane, hydrogen, ammonia, and water vapor. This is the mixture of gases with which Miller first demonstrated the synthesis of amino acids and other organic molecules.[7] Later, Abelson[8] observed amino acid formation in similar experiments with gas mixtures that included carbon monoxide and dioxide, and nitrogen, always in combinations that involved at least one reducing gas. Heyns *et al.*[9] found that adding hydrogen sulfide to similar mixtures led to the synthesis of a variety of organic sulfur compounds.

A central point is that the primitive atmosphere was anaerobic, and all such model experiments are performed in the absence of oxygen. Under those circumstances they lead to the synthesis of organic molecules; were oxygen present, they would end simply in combustions.

The maintenance of a reducing atmosphere depends upon the presence of reasonably high pressures of hydrogen. The lightest of gases, this escapes from the Earth's atmosphere so rapidly that it would have maintained a sufficiently high concentration only throughout the planet's early history. Urey has calculated that a hydrogen pressure of 1.5×10^{-3} atm should suffice to maintain a reducing atmosphere, and that this may have declined to the present level of about 10^{-6} atm at the Earth's surface some two billion years ago.[13] Ammonia and methane, which are unstable in the absence of hydrogen, may shortly afterward have left the atmosphere, to be replaced mainly by nitrogen and carbon dioxide. By that time the organic syntheses we have discussed were presumably already well completed.

It should be noted, however, that this type of discussion rests entirely upon thermodynamic considerations, and takes no account of the kinetics of the reactions concerned. It assumes that the great expanses of geological time are sufficient to complete all spontaneous chemical reactions and to bring all chemical systems into equilibrium. In fact that is by no means true. Abelson,[14] for example, has shown that the spontaneous decarboxylation of alanine requires more than 10 billion years at 20°C to be half completed; and the same is likely to be true of any first-order reaction with an Arrhenius energy of activation of more than 40,000 cal per mole. Second-order reactions, the rates of which depend of course upon concentration as well as activation energy, must in given instances take equally long. Not all possible reactions therefore need to be completed even within geological times; and obviously this must be an important consideration in dealing with the evolution of the atmosphere. It may well be that simple inertia of reaction permitted much more varied mixtures of gases to persist over long periods than could have occurred under equilibrium conditions.

The existence of molecular oxygen in the atmosphere is a separate issue, and so crucial for our argument that however plausible the geochemical reasons for believing that oxygen was absent initially, some further reassurance would not be amiss (cf. ref. 15).

I think that the present organization of cellular metabolism, together with what we can surmise to have been the course of its evolution, provides internal evidence that organisms went through much of their early development on this planet in the absence of oxygen. It would otherwise be difficult to understand the ingenuity they have displayed in developing anaerobic pathways of metabolism. The whole basic structure of cellular metabolism is anaerobic. Reactions with molecular oxygen appear as a late epiphenomenon, added to an already complete and, within its bounds, adequate substructure. The nub of the argument is outlined in Tables 1 and 2.

If, as we suppose, life first appeared in an organic medium in the absence of oxygen, it must first have been supported by fermentations[3]—Pasteur's "life

TABLE 1

EVOLUTION OF ENERGY METABOLISM

Anaerobic Phase

(1) *Fermentation:* a chemical source of energy; by-product CO_2
e.g., $C_6H_{12}O_6 \rightarrow 2C_2H_5OH + 2CO_2 + 2 \sim P$

(2) *Hexosemonophosphate cycle:* metabolic hydrogen for reductions
$6C_6H_{12}O_6 + 6H_2O + 12 \sim P \rightarrow 12H_2 + 5C_6H_{12}O_6 + 6CO_2$

(3) *Photophosphorylation:* light into high-energy phosphates
$\xrightarrow[\text{chlorophylls, cytochromes}]{\text{light}} \sim P$

(4) *Photosynthesis:* light into new organic molecules; by-product O_2
Bacteria: $6CO_2 + 12H_2A \xrightarrow[\text{chlorophyll}]{\text{light}} C_6H_{12}O_6 + 6H_2A + 12A$
Algae, higher plants: $6CO_2 + 12H_2O \xrightarrow[\text{chlorophyll}]{\text{light}} C_6H_{12}O_6 + 6H_2O + 6O_2$

Aerobic Phase

(5) *Respiration:* metabolic energy from combustions
$C_6H_{12}O_6 + 6H_2O + 6O_2 \rightarrow 6CO_2 + 12H_2O + 30\text{–}40 \sim P$

without air." Insofar we beg the question. But fermentation remains in a sense the basic way of life. Fermentative processes underlie all other forms of metabolism; and virtually all types of cell can survive for periods on fermentation if deprived of oxygen. Fermentation degrades organic molecules anaerobically, making the free energy so released available to the cell in the form of high-energy phosphates (e.g., adenosine triphosphate, ATP, represented here by the symbol $\sim$P). Certain familiar forms of fermentation, e.g., the alcohol fermentation shown in Table 1, produce as by-product carbon dioxide. This gas, like oxygen, was probably in very low concentration in the primitive atmosphere, and its production by fermentation probably played a great role in the further evolution of metabolism.

There is good reason to believe that the next type of metabolism to develop was the hexosemonophosphate (HMP) cycle. Since this has been worked out relatively recently, it still tends to be thought of as rather esoteric; in fact it is basic. It is often characterized as an alternative ("shunt") pathway of respiration; but it is that only when frustrated. In fact it is essentially an anaerobic process, more closely related therefore to fermentation. This process develops hydrogen for organic reductions and reductive syntheses anaerobically, from sugar with the aid of energy derived from ATP. Incidentally it yields carbon dioxide as by-product.[16] It presents us also with a first example of a reaction of fundamental importance, the metabolic splitting of water, for half the hydrogen produced by the HMP cycle is derived ultimately from water.

If the primitive atmosphere contained much hydrogen, it may be asked why cells could not have used this directly, rather than having to produce hydrogen metabolically. The answer is probably, as already indicated, that by the time living cells had developed to this point, all but the last remnants of hydrogen had already escaped from the atmosphere.

The next process to develop was probably photophosphorylation—the direct utilization of sunlight to produce ATP.[17] This involves also the first appearance in metabolism of the metalloporphyrins: the pigment, chlorophyll, a magnesium porphyrin to absorb the light; and cytochromes, iron porphyrin proteins, to aid in the transduction of the absorbed energy to ATP.

With that, the way was open to a fourth development, photosynthesis, largely an integration of developments already achieved in steps (2) and (3). In photosynthesis the energy of sunlight, transduced through chlorophylls and then in part through ATP, is used to synthesize glucose on the basis of a modified HMP cycle, running in reverse.[16, 17] The over-all process involves the splitting of hydrogen from a donor molecule, and its use to reduce carbon dioxide to carbohydrate. A variety of organic and inorganic molecules serve as hydrogen donors in photosynthetic bacteria; but in algae and higher green plants water itself donates the hydrogen, and molecular oxygen is released as by-product.

This is the means by which molecular oxygen entered our atmosphere. When it had reached a sufficient concentration—about 10^{-3} to 10^{-2} atmospheres at sea level—that at last made possible the first aerobic form of metabolism, cellular respiration. In its over-all effects, and even to a large extent in its mechanisms, respiration is the reverse of algal and higher plant photosynthesis. Chemical energy obtained by the combustion of glucose and other organic molecules is made available in the form of ATP, with carbon dioxide and water as principal end products.

Since its advent, respiration and the reverse process of photosynthesis have been pitted against each other. Presumably they came into balance ages ago. Yet there must have been a great interval in which organisms were slowly turning an anaerobic into an aerobic world; and the increase of oxygen in our atmosphere from negligible beginnings to its present content of 21 per cent testifies to the long period in which photosynthesis overbalanced respiration.

It is usual to think of the physical environment as given, as the absolute setting to which organisms must at all times adapt if they are to survive. It is becoming plain, however, that some of the salient features of our physical environment are themselves the work of living organisms. They not only put molecular oxygen into the atmosphere. By now also organisms have spread upon the Earth on such a scale that the atmosphere and hydrosphere have become components in their metabolism. It is estimated that at present all the oxygen in the atmosphere passes through organisms—in by respiration and out by photosynthesis—every 2000 years; that all the carbon dioxide in both the atmosphere and hydrosphere cycles through organisms in the reverse direction every 300 years; and that all the waters of the Earth are decomposed and recomposed by photosynthesis and respiration every 2,000,000 years.[18]

The combustion of organic molecules is an over-all effect of respiration, but not its mechanism. The actual mechanism is peculiarly significant for our problem. Biological oxidations, with rare exceptions, are performed, not by adding oxygen, but by removing hydrogen. Even when the oxygen content of some molecule in the organism is increased, this is almost always done by adding water and removing hydrogen. Organisms are remarkably adept at performing their oxidations anaerobically. Their only direct combustion is the burning of hydrogen; and the incorporation of part of the energy of this process into ATP is the principal contribution of cellular respiration. But this is still, with relatively few exceptions, the only use that organisms make of molecular oxygen.

The point can perhaps be made clearer with a simple industrial analogy (Table 2). Coal can be burned in either of two ways: directly with oxygen to carbon dioxide, as in a furnace; or it can be used to draw an atom of oxygen out of water, yielding as products the inflammable mixture of carbon monoxide and hydrogen called water gas. Water gas in turn might simply be burned with oxygen to carbon

TABLE 2

ALTERNATIVE WAYS OF BURNING CARBON

Aerobic:
$C + O_2 \rightarrow CO_2$ (combustion of coal)

Anaerobic—Aerobic:
$C + H_2O \rightarrow CO + H_2$ (water gas)
$CO + H_2O \rightarrow CO_2 + H_2$ (industrial production of hydrogen)
$2H_2 + O_2 \rightarrow 2H_2O$ (combustion of hydrogen)

Metabolism of Living Organisms:
$(CH_2O)_n$ = carbohydrate (n equivalents of water gas)
$(CH_2O) + H_2O \rightarrow CO_2 + H_2$ (glycolysis)
$2H_2 + O_2 \rightarrow 2H_2O$ (respiration)

dioxide and water; but instead the carbon monoxide can be used to draw another atom of oxygen out of water, yielding another hydrogen molecule, as in the process for the industrial production of hydrogen. Finally, the hydrogen can be burned with oxygen to water.[19]

Glucose, the principal metabolite for energy production in living organisms, is a form of carbohydrate, the unit structure of which is CH_2O (taken 6 times over in glucose and other hexoses, $C_6H_{12}O_6$). This has the same composition as water gas. Like water gas, a unit of carbohydrate could be burned with one molecule of oxygen to CO_2 and H_2O; but that is not the organism's way. Instead, the carbohydrate is used to split water according to the fundamental equation, $CH_2O + H_2O \rightarrow CO_2 + 2H_2$, a somewhat disguised equation of preparatory glycolysis, exactly analogous to the industrial production of hydrogen. This is then followed by the combustion of hydrogen, $2H_2 + O_2 \rightarrow 2\,H_2O$, the fundamental equation of cellular respiration.

Horowitz[20] has proposed a plausible mechanism by which biosynthetic pathways may have evolved during the period when organic metabolites were still plentiful in the environment. He suggests that biosynthetic sequences developed in reverse, starting at the end of the chain, and working backward by adding one enzyme at a time. An organism dependent upon some available metabolite, as that became depleted, might develop an enzyme for performing the last step in its synthesis, so that the organism's needs were now transferred to the immediate precursor. As that in turn became depleted, the organism might evolve an enzyme for the previous step in synthesis. So it would work its way step by step backward through the sequence until the entire synthesis could be performed from simple and readily obtainable precursors.

This seems then to have been the history of life upon this planet: the slow combination of the gases of the primitive atmosphere to form simple unit organic molecules which accumulated in the sea; the polymerization of some of those molecules to form the first macromolecules comparable with our present proteins and nucleic acids; the aggregation of such large and small molecules in the sea to form micelles of various sizes and grades of complexity, with the final achievement of the living state. Then the gradual mastery of the fundamental problems of deriving energy and preparing new organic molecules with which life could eventually spread upon a cosmic scale, in the process transforming radically the atmosphere of the planet.

I think that some such account as this would now be widely accepted as describing the origin of life on the Earth. What is perhaps more interesting is the dawning realization that this problem involves universal elements, that life in fact is probably a universal phenomenon, bound to occur wherever in the universe conditions permit and sufficient time has elapsed.

Those conditions almost surely involve a planet somewhat resembling the Earth, of about this size and temperature, and receiving about this quality and amount of radiation from its sun. To mention a few points of the argument: a much smaller planet could not hold an adequate atmosphere, a much larger one might hold too dense an atmosphere to permit radiation to penetrate to its surface. Too cold a planet would slow down too greatly the chemical reactions by which life arises; too warm a planet would be incompatible with the orderly existence of macromolecules. The limits of temperature are probably close to those at which water remains liquid, itself almost surely a necessary condition for life. Life can arise without continuously absorbing radiation, though, as we have noted, radiation prepares the way by activating organic syntheses in the atmosphere; but it is difficult to see how life can go far, or even persist indefinitely without an external source of energy. By now all life upon the Earth runs on sunlight, with the exception of a few chemosynthetic bacteria. Not all radiations are adequate; a range of wavelengths, *ca.* 300–1100 mμ, is needed. Shorter wavelengths than 300 mμ destroy macromolecules; on the Earth they denature proteins and depolymerize nucleic acids. Longer wavelengths than about 1100 mμ involve quanta too small to excite molecules electronically, and hence to activate photochemical reactions.

How many such planets exist? By present estimates about 1–5 per cent of the stars in our galaxy might possess planets capable of supporting life.[22] That would mean at least one billion such planets in our galaxy alone; and since there are about 100 million galaxies now within range of the most powerful telescopes, the number of planets suitable for life in the already observed universe may be of the order of 10^{17}. This number is so vast—even if it were reduced a million times—as to make it difficult to avoid the conclusion that life is widespread in the universe.

On this planet, living organisms are composed almost entirely of 16–21 elements—16 found in almost all organisms, 5 more restricted to particular groups (Table 3). A first striking regularity is that these tend to be light elements. All the bioelements except molybdenum and iodine occur within the lighest 30 of the 92 natural elements. That in itself does not seem strange, for the lightest elements tend also to be the most abundant, on the Earth as elsewhere in the cosmos.

The bioelements fall into three natural groups, according to the uses organisms make of them: those that form water and the bulk of the organic molecules; the monatomic ions; and the trace elements.

The group of monatomic ions may have been chosen mainly on the basis of their relative abundance, though I do not think that is the whole story even with them. They are the ions most prevalent in the sea; and that may account largely not only for their appearance in cells, but for the fact that animal blood tends to resemble sea water so closely. Most marine invertebrates circulate a solution of ions in their bloods that is essentially sea water. The ionic composition of vertebrate blood so closely resembles sea water diluted 3–4 times as to have prompted the suggestion that it represents sea water of the remote period in which the ancestors of the vertebrates closed off their circulations.[23]

An argument from abundance, however, cannot be consistently maintained for the other two groups of bioelements. Some of them are abundant; others of equal

TABLE 3

AN ALPHABET OF ORGANISMS

Elementary particles	Bioelements	Unit molecules
Protons	*Water:* H, O	Glucose, ribose
Electrons	*Organic:* H, C, N, O; P, S	Fat, phosphatide
Neutrons	*Ions:* Na$^+$, K$^+$, Mg^{++}, Ca^{++}, Cl$^-$	20 amino acids
Photons	*Trace elements:* Mn, Fe, Co, Cu, Zn (B, Al, V, Mo, I)*	5 nucleotide bases
4	16–21	29

* The elements within parentheses are restricted to special groups of organisms; the others are very generally distributed.

importance are relatively rare, and organisms concentrate them many times over out of very dilute environments. These elements were selected on the basis of their essential properties rather than their availability; and that is true to a degree even of the monatomic ions. One has a strong indication of this in the fact that the three groups into which the bioelements are divided functionally are reflected in their positions in the Periodic System, where, except for the halogens Cl and I, they form three clusters: the organic elements at the right in the first three periods, the monatomic cations at the left of the third and fourth periods, the major trace elements toward the middle of the fourth (the first long) period, all of them but zinc being so-called transition elements. Being transition elements, these last readily form complexes, as does also zinc; and—being atoms of variable valence—they readily exchange electrons, properties that fit them admirably for the roles we find them principally playing in organisms, as the nuclei of metallo-organic complexes and oxido-reduction enzymes.

The most important such argument, however, involves the four elements hydrogen, oxygen, nitrogen, and carbon, which together make up about 99 per cent of the living parts of living organisms. I think that a responsible examination of the possibilities leads inevitably to the conclusion that life everywhere in the universe must be constructed primarily of these four elements.

Hydrogen, of course, is the most abundant element in the universe, and hydrogen and oxygen constitute large fractions (15.40 and 55.19%) of the atoms in those portions of the Earth accessible to living organisms (the whole hydrosphere and atmosphere, and the crust to a depth of 10 miles).[24] On the other hand, carbon must be extracted from the last 0.44 per cent of the accessible atoms, and nitrogen from the last 0.16 per cent (one may add that phosphorus must be found in the last 0.23% and sulfur in the last 0.12% of the accessible atoms). These are therefore not consistently the most plentiful elements. They owe their status rather to their essential "fitness": they alone among the natural elements possess the critical properties upon which the existence of life everywhere in the universe must depend.

(I have been asked sometimes how one can be sure that elsewhere in the universe there may not be further elements, other than those in the Periodic System. I have tried to answer by saying that it is like asking how one knows that elsewhere in the universe there may not be another whole number between 4 and 5. Unfortunately, some persons think that is a good question, too.)

We are, understandably, so greatly impressed with the regularities in the Periodic System that we sometimes exaggerate them. The lightest elements, specifically those in the first two periods, in fact exhibit quite distinctive properties, not repeated in the lower periods. It hardly needs urging that silicon has quite different properties from carbon, phosphorus from nitrogen, and sulfur from oxygen. Hydrogen, of course, has wholly unique properties.

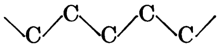
The special distinction of hydrogen, oxygen, nitrogen, and carbon is that they are the four smallest elements in the Periodic System that achieve stable electronic configurations by gaining, respectively, 1, 2, 3, and 4 electrons. Gaining electrons, in the form of sharing them with other atoms, is the means of making chemical bonds, and so of making molecules. The special point of smallness is that these smallest elements make the tightest bonds and so the most stable molecules; and that carbon, nitrogen, and oxygen are the only elements that regularly form double and triple bonds. Both properties are critically important.

It is frequently suggested that elsewhere in the universe silicon may substitute for carbon in living organisms. The reasons for considering silicon are that it falls just below carbon in the Periodic System; like carbon it can combine with itself to form long chains, and hence very complex molecules; and here on Earth there is about 135 times as much silicon as carbon in the areas accessible to life.

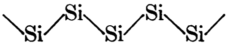
Silicon, however, cannot replace carbon in living organisms.[25] For one thing, it forms looser, less stable compounds, but that, though a disadvantage, might be tolerated (Table 4). Silicon chains, however, are susceptible to attack by molecules possessing lone pairs of electrons, in part because of their open structure, but still more because silicon, a third-period element, possesses 3*d* orbitals available for further combination. For this reason silicon chains cannot exist for long in the presence of oxygen, ammonia, or water. I think that in itself must eliminate silicon as a possible basis for life.

TABLE 4

CARBON AND SILICON CHAINS



C–C distance, 1.54 A (bond energy, 83.1 kcal per mole)



Si–Si distance, 2.34 A (bond energy, 42.5 kcal per mole)

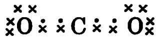
Such silicon chains are unstable to O_2, NH_3, H_2O, lone electron pairs of which attack by occupying 3*d* orbitals of Si.

Silicon, however, has another fatal disability, its failure to form multiple bonds. The importance of this factor can be understood if one compares carbon dioxide with silicon dioxide (Table 5). In carbon dioxide, double bonds between the carbon and oxygen atoms completely saturate their combining capacities. The molecule goes off freely as a gas, and dissolves in and combines with water, the forms in which organisms obtain it. In silicon dioxide, however, silicon remains singly bonded to oxygen, leaving four unpaired electrons on the molecule. These promptly form bonds with adjacent silicon dioxide molecules, and they in turn with others. The result is a huge polymer, a supermolecule such as quartz, so hard because it can be broken only by breaking covalent bonds. That is why silicon is fit for making quartz, but living organisms must be made of carbon.

TABLE 5

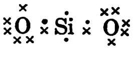
CARBON DIOXIDE AND SILICON DIOXIDE

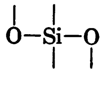
Carbon dioxide: CO_2

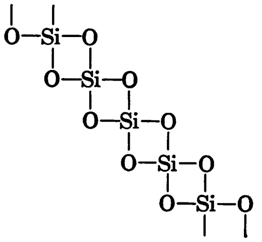


O=C=O

Silicon dioxide: $(SiO_2)_n$







The diagram of the silicon dioxide polymer is intended only to represent the mutual saturation of valences, not at all the spatial relationships in the crystal.

TABLE 6

HIGH-ENERGY BONDS OF P AND S

$$\mathrm{C}\overset{1.431}{\text{——}}\mathrm{O}\overset{1.76}{\text{——}}\mathrm{P}$$

$$\mathrm{P}\overset{1.76}{\text{——}}\mathrm{O}\overset{1.76}{\text{——}}\mathrm{P}$$

$$\mathrm{N}\overset{1.80}{\text{——}}\mathrm{P}$$

$$\mathrm{C}\overset{1.81}{\text{——}}\mathrm{S}$$

The valence electrons of P and S are in the third shell, which, beyond holding 8 electrons in its *s* and *p* orbitals, can accept further electrons in its *d* orbitals. This, in addition to the large bond radii of P and S, opens the compounds of these elements to attack by molecules possessing lone pairs of electrons, such as H_2O.

Somewhat less compelling arguments of special fitness involve phosphorus and sulfur,[25] which among the other functions they perform in organisms have the special role of forming high-energy compounds (e.g., ATP, acyl coenzyme A) which transfer energy and organic groups within the cell. The very factors that constitute a disability in silicon become an advantage in phosphorus and sulfur (Table 6). The openness of their bonds and their possession of 3*d* orbitals capable of receiving further electrons make their compounds susceptible to attack by molecules that can offer lone pairs of electrons; and this provides a mechanism for the participation of phosphorus and sulfur compounds in the energy- and group-transfer reactions that constitute their principal contribution to cellular metabolism.

The major bioelements therefore present unique properties indispensable for the formation and function of living organisms. They—particularly carbon, hydrogen, nitrogen, and oxygen—form also a number of unique molecules, indispensable or of quite singular importance for organisms. Of these the chief is water, which I believe to be altogether indispensable. Carbon dioxide must be hardly less important, a gas highly soluble in water, which therefore permeates the atmosphere and hydrosphere, and so is uniquely suitable for circulating carbon among organisms. Carbon dioxide possesses many other fortunate properties—great stability, high density, the capacity rapidly to achieve complex equilibria involving the gas, carbonic acid, and solid carbonates and bicarbonates—all potentially of the highest importance for the formation and maintenance of life.[26]

As already noted, organisms seem to have arisen on Earth, and might conceivably have persisted indefinitely in the absence of molecular oxygen. Yet oxygen, in permitting the development of cellular respiration, provides by far the most efficient chemical source of energy available to organisms, based upon the most energetic of combustions, that of hydrogen. On this planet, organisms, when not living directly upon the energy of sunlight, live for the most part on respiration. Living organisms everywhere should have to solve sooner or later the problem of obtaining energy economically by chemical means, in order to survive periods of darkness, even if only cycles of day and night. It is doubtful that such needs can be met more effectively than by combustions.

Oxygen makes another kind of contribution to the evolution of life. As it accumulates, a layer of ozone, formed from it by high-energy radiation in the upper atmosphere, screens out the far ultraviolet that would otherwise destroy all exposed organisms. Not much ozone is needed for this. The amount in the Earth's atmosphere, isolated and brought to 0° C and 1 atm pressure, would form a layer only 3 mm thick. Water also screens out the hard ultraviolet; and until such a layer of ozone had developed in our atmosphere, life presumably remained aquatic. The entry of oxygen into the atmosphere not only permitted the development of respiration, but allowed life to emerge from the water onto land. For both reasons, oxygen, though not indispensable for life, must be reckoned among the special molecules needed for its fullest development.[27]

It has often been suggested that elsewhere in the universe liquid ammonia may take the place of water as a substrate for life. In most important regards, however, liquid ammonia is inferior to water in the properties upon which organisms most depend.[26] An obvious disadvantage is that ammonia remains liquid over a much narrower temperature range than water (Table 7); keeping ammonia liquid therefore demands a greater stability of temperature over long periods than many planets afford. But to keep it liquid demands also temperatures that would never rise above perhaps −40°C, that is, at least 60° below prevailing temperatures upon the Earth. (Raising the atmospheric pressure considerably would, of course, permit ammonia to stay liquid at higher temperatures, but would introduce other equally serious difficulties.) If we assume the modest temperature coefficient ($Q_{10°}$) of 2, chemical processes in general would take about 2^6 as long to complete at −40°C as upon the Earth. The processes that led to the origin of life within perhaps a billion years upon this planet might then take some 64 billion years in an environment of liquid ammonia. That is far greater than any present estimates of the age of our galaxy, and much longer than a star like the Sun could remain on the main sequence, i.e., remain adequately supplied with hydrogen to maintain conditions that would make life possible on one of its planets.

TABLE 7

PROPERTIES OF AMMONIA

Boiling point: −33.35°C (at 1 atm pressure)
Freezing point: −77.7° (at 1 atm pressure)
Density at −79°C:
  Liquid: 0.7354 gm per cm^3[*]
  Solid: 0.817 gm per cm^3[†]

[*] Cragoe, C. S., and D. R. Harper, 3d, *Sci. Papers, U. S. Bur. Stand.*, 17, 287 (1921).

[†] McKelvy, E. C., and C. S. Taylor, *Sci. Papers, U. S. Bur. Stand.*, 18, 655 (1922–23).

L. J. Henderson,[26] in his classic exposition of the many extraordinary properties which make water critically important for living organisms, made much of one of its most peculiar properties—that ice floats. If ice did not float, the waters of the Earth would long ago have frozen solid. Even relatively long periods of warm weather could not have thawed them; and life arising or persisting under such conditions would be well-nigh impossible.

Water owes this strange property to the fact that though on cooling it contracts, as do other well-behaved substances, below 4°C it expands, so that at its freezing point (0°) it has a lower density than liquid water. The reason for this is that below 4°C water molecules become increasingly hydrogen-bonded to one another. By the freezing point every hydrogen atom is engaged in both covalent and hydrogen bonding to adjacent oxygen atoms, holding all the water molecules rigidly in an open structure in which they are less densely packed than in liquid water.

Some years ago I began to wonder whether ammonia ice floats. Unable to find this information in the literature, I was glad to have the question answered for me experimentally.[28] Later, wanting to be doubly sure, I repeated the experiment myself; and just afterward found that the information had been published 20 years before (Table 7). Ammonia ice sinks in liquid ammonia, rapidly and unequivocally, hitting the bottom of the vessel with a distinct thud. That can be added to the disabilities of ammonia as a medium for life.

The splitting of water in higher plant photosynthesis yields as by-product molecular oxygen, permitting eventually the development of cellular respiration. A comparable process performed with ammonia might instead yield nitrogen, a depressingly inert gas. An English astronomer was reported recently to have said that there may be places in the universe where life is based on ammonia rather than water, and where living creatures respire nitrogen instead of oxygen. One can of course *breathe* nitrogen, as we do all the time; but respiration is in essence a combustion, and nitrogen cannot support combustions here or anywhere. For that oxygen is needed, the most electron-avid element after fluorine, so facile at removing electrons from other atoms that that process (oxidation) has been named for it.

For these and similar reasons I have become convinced that life everywhere must be based primarily upon carbon, hydrogen, nitrogen, and oxygen, upon an organic chemistry therefore much as on the Earth; and that it can arise only in an environment rich in water. Though the preparatory geochemical syntheses of organic molecules seem to demand an anaerobic environment, and are probably fostered by a generally reducing atmosphere, the later history of these developments must be greatly furthered by the more or less automatic appearance of carbon dioxide as the atmosphere loses hydrogen; and living organisms having arisen would in time almost surely find their way to the production and utilization of molecular oxygen.

How formidable a condition is the geochemical accumulation of unit organic molecules—the building blocks of which macromolecules and eventually the first primitive organisms are to be composed? How many such units are needed, at a minimum? I think perhaps fewer than is generally supposed.

I have had the experience lately of introducing young students, many of whom had not studied chemistry before, to some of the basic essentials of biochemistry. I build the subject up from the elementary particles, then the atoms we have been discussing, to end with what I call an alphabet of biochemistry (Table 3). It turns out that about 29 organic molecules are enough to introduce the bare essentials. They include glucose, the major product of photosynthesis and major source of metabolic energy and hydrogen; fats as a principal storage form of metabolic energy; phosphatides as a means of circulating lipids in aqueous media and for their remarkable structure-forming proclivities; then the 20 amino acids from which all proteins, including all enzymes, are derived. Five nitrogenous bases (adenine, guanine, cytosine, uracil, thymine), together with ribose or its simple derivative deoxyribose and phosphoric acid, form all the nucleic acids, both RNA and DNA. These 29 molecules give students a first entry into the structures of proteins and nucleic acids, the coding of genetic information, the structures of enzymes, the composition and general properties of cell structures, and bring them to a point from which they can begin to explore the complexities of energy metabolism. That this is not the whole of biochemistry goes without saying; the extraordinary thing is that it makes so good a start. Yet this alphabet of biochemistry is hardly longer than our verbal alphabet. That seems to me to imply that the provision of unit molecules preparatory to the rise of living organisms is a reasonably limited enterprise. I cannot help but feel that this situation, that makes it relatively easy to give young students a first taste of biochemistry, must have made it easier also for the first primitive cells to obtain the molecules they needed.

Many of these molecules display in solution the property of optical activity, the capacity to rotate the plane of polarized light to the right or left. This property is almost uniquely associated with the components and products of living organisms; it is as characteristic of life as any property we know. It has its source in so-called asymmetric carbon atoms, carbon atoms bonded to four different groups. All molecules possessing such asymmetric atoms can exist in right- and left-handed forms (dextro- and levo-, D- and L-). When synthesized artificially, such molecules always emerge as equal mixtures of the D- and L-forms, hence optically inactive. Living organisms, however, invariably incorporate one form or the other. Thus, virtually all natural amino acids are L-, all natural sugars D-, α-phosphatides L-, and so on.[29]

The point is not that L-amino acids are intrinsically better suited for living organisms than D-, or D-sugars than L-, but that organisms derive important advantages individually and collectively from working consistently with one configuration or the other.[30] Large portions of native proteins exist in the form of the α-helix. They assume that configuration spontaneously, but could do so only with great difficulty, if at all, were they made of mixtures of both D- and L-amino acids. This is an important consideration, since most of the specific properties of proteins depend in part upon this feature of their geometry. Similarly, the two-stranded helical structure characteristic of DNA and long sections of RNA demands specific choices in the configurations of three asymmetric carbon atoms in deoxyribose or ribose—carbon atoms 1, 3, and 4. Enzymes, being proteins, are themselves optically active, and in many cases react only with L- or D-substrates, not with both. For these and other reasons organisms consistently choose one configuration or the other, though in each category of molecule either choice would do equally well. Since also the molecules of organisms are in constant flux and interchange, and are passed about widely from one organism to another in complex food chains, there is enormous advantage in staying with consistent series of configurations throughout the whole metabolism, and indeed throughout the population of the planet. For this reason I would suppose that biota that may incorporate amino acids on other planets divide about equally between the L- and D-configurations, keeping their other choices consistent with this one.

To go a step further, I think that when confronted with the necessity to develop a molecule to perform some basic cellular function, organisms are highly limited in their choices, though not as limited in their first choices as in their last. Such molecules as the chlorophylls for photosynthesis, the heme pigments for cellular respiration, the carotenoids and vitamins A for photoreception, all represent the outcome on this planet of long and rigorous selective processes that tended constantly toward achieving optimal solutions. All these molecules possess properties that fit them particularly to perform their functions in organisms; and I have no doubt that the better we come in each case to understand the nature of the problem, the clearer it will be why those molecules and not others were selected. Sometimes these molecules present strange mixtures of fortunate and disadvantageous properties; the chlorophylls, for example, all have the strange property of absorbing light most poorly at those wavelengths at which sunlight at the surface of the Earth or under water is most intense. Obviously the chlorophylls must possess other advantages for photosynthesis that far outweigh this disability; and those advantages, since they have given the chlorophylls a unique status in photosynthesis on the Earth, might be equally effective in promoting their selection elsewhere.[21]

Again, three animal phyla on the Earth, having developed three very different kinds of eye in complete independence from one another, have all arrived at the same molecule, 11-*cis* retinene (11-*cis* vitamin A aldehyde), as the chromophore of their visual pigments. Yet the 11-*cis* isomer is an improbable, intrinsically unstable variant of retinene. Why then choose it repeatedly for this function? It has turned out that the only action of light in vision is to change the *shape* of a molecule; and 11-*cis* retinene fills that role in an exemplary way, light isomerizing it from the bent and twisted 11-*cis* configuration to the relatively straight all-*trans* with high efficiency. The same forces that guided the selection of this improbable molecule three times independently on this planet might well arrive at the same or similar solutions elsewhere.[21, 31]

To sum up, faced with well-nigh universal problems, organisms everywhere may tend to gravitate toward common solutions, types of molecule that within the bounds of organic structure may represent optimal or near-optimal solutions. I say types rather than individual molecules, since in each of the cases mentioned we find here upon the Earth not one molecule but a category of them at work: at least five different chlorophylls, a variety of hemes, several active carotenoids, two vitamins A.

Such choices must be governed everywhere by natural selection, the process described a century ago by Darwin and Wallace. This is at once the formative and conservative principle in the evolution of living things. It involves three components: a mechanism of inheritance, without which life could not continue to exist anywhere; a continuous intrusion of "noise" into the genetic message, appearing in the offspring as random inherited variations (mutations); and the struggle for existence, the competition for the necessities of life, any temporary alleviation of which is met with a leap in population that brings it back into force. These are universal elements, hardly to be avoided in any population of living things. Their outcome is the survival of the fittest—the continuous trend toward optimization, the effects of which on molecular design were invoked above.

It has sometimes been argued that natural selection is "not enough"—not enough to account for the evolution of an eye, or a wing, or the near-perfection of embryonic development, or the mating behavior of gulls. But one cannot dismiss natural selection just because it works better than one thinks it should. A hypothesis should be damned for its failures, not its successes—cases in which evolution has appeared to work to the net disadvantage of organisms. That is, of course, just the problem raised by some instances of the extinction of species in the course of evolution; and some cases of extinction do represent a failure of natural selection, owing, we believe, to the inertia of the selective process, which on occasion operates too slowly to cope with abrupt changes in the conditions of existence.

Wigner[32] has recently remarked upon "what appears to be a miracle from the point of view of the physicist: that there are (living) structures which produce further identical structures." Fortunately, no such miracle occurs. If it did, heredity might seem to work better, but natural selection would not work at all. Wigner offers a calculation to show the quantum-mechanical impossibility of keeping the information coded in the genes from growing increasingly disordered as it is transmitted. The point is that the genetic message is continuously disordered by mutation; but that the selective process as continuously prunes it back to orderly, and indeed toward optimal, sequences. Wigner's calculation can be turned to positive account; it provides some assurance that any molecular genetic code must continually produce such random variations as natural selection demands. Order in living organisms is introduced not beforehand, by preconceived design, but after the fact—the fact of random mutation—by a process akin to editing. We are the products of editing rather than of authorship.

I have thought sometimes that it would be interesting to set up an experimental model for some features of this process. Suppose that random words of the English language were fed out on a tape, and that half a dozen persons independently selected words out of the same random sequence so as to compose first a meaningful sentence, from this beginning a paragraph, and eventually a connected narration. Probably each operator would select a different first sentence; and that sentence, even the first phrases in it, would begin to influence the next choices. Beginnings of meaning would rapidly develop a momentum of their own, exercising stronger and stronger suggestion upon later selections. Compared with natural selection, this model of course has the serious flaw of employing a willful selector, whose history and purposes would necessarily influence the final product. It must be equally plain, however, that the outcome might, and I think usually would, depart widely from any design the selector first had in mind. Most of it would probably emerge as the result of a dialectical interplay between the selector's preconceptions and the suggestions evoked in him by the emerging words. I think such an experiment well worth a try, if not as science, then as experimental literature. It might mark the birth of the organic novel.

I have tried in this paper to consider all too briefly some of the conditions that have molded life here, and some of the reasons for believing that they would mold life anywhere. The nub of such an argument is to bring life within the order of nature, to see its development as an orderly process, everywhere affording full play to chance, but not in any important degree accidental.

We living things are a late outgrowth of the metabolism of our galaxy. The carbon that enters so importantly into our composition was cooked in the remote past in a dying star. From it at lower temperatures nitrogen and oxygen were formed. These, our indispensable elements, were spewed out into space in the exhalations of red giants and such stellar catastrophes as supernovae, there to be mixed with hydrogen, to form eventually the substance of the sun and planets, and ourselves. The waters of ancient seas set the pattern of ions in our blood. The ancient atmospheres molded our metabolism.

We have been told so often and on such tremendous authority as to seem to put it beyond question, that the essence of things must remain forever hidden from us; that we must stand forever outside nature, like children with their noses pressed against the glass, able to look in, but unable to enter. This concept of our origins encourages another view of the matter. We are not looking into the universe from outside. We are looking at it from inside. Its history is our history; its stuff, our stuff. From that realization we can take some assurance that what we see is real.

Judging from our experience upon this planet, such a history, that begins with elementary particles, leads perhaps inevitably toward a strange and moving end: a creature that knows, a science-making animal, that turns back upon the process that generated him and attempts to understand it. Without his like, the universe could be, but not be known, and that is a poor thing.

Surely this is a great part of our dignity as men, that we can know, and that through us matter can know itself; that beginning with protons and electrons, out of the womb of time and the vastnesses of space, we can begin to understand; that organized as in us, the hydrogen, the carbon, the nitrogen, the oxygen, those 16 to 21 elements, the water, the sunlight—all, having become us, can begin to understand what they are, and how they came to be.

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[28] This experiment was first done for me by R. C. Bray and H. W. Dougherty, then graduate students in the Biochemistry Department at the Columbia University College of Physicians and Surgeons.

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