In the second place, we intended to say that we do not believe that high-temperature processes in the neighborhood of 150°C were important in the origin of life. We also conclude this because of the data given in Table 1. The total heat from volcanoes is very small indeed; it is most ineffectively used for chemical processes, is very sporadic, and is localized on the surface of the earth.

What is needed in the prephotosynthetic time on the earth is a steady source of free energy that permits a primitive type of metabolic process during which organized life could evolve before photosynthesis occurred. We disagree with Fox's statement that only a small amount of material is sufficient. We maintain that a steady source of production of compounds is required, which then go through spontaneous chemical reactions to produce more stable compounds again. A small amount of high temperature produced at one spot on the earth, with many years going by before any additional source of energy is available at that location, can make little contribution to an evolutionary process. Only continuous processes enable metabolic experimentation to go on. Of course, a very small amount of "organic stuff of the proper sort and organization" would suffice, provided it were a living cell, but it is the origin of this which is being discussed, and it should not be assumed.

Aside from these general remarks, we wish to criticize certain points in the arguments of Fox.

Fox has not answered our objections to the thermal theory of the origin of life. The question of the source of the malic acid and urea in his experiments has still not been answered, and much of the theory stands or falls on this point. The stability of proteins with respect to coagulation when dry or in the presence of acidic polymers is not an answer to our criticism. We were discussing the stability of the amino acids contained in the protein, and there is no reason to assume that they would be more stable as dry peptides than as amino acids in solution. In fact, serine and threonine would be less stable. Evidence for instability of amino acids in proteins is given by Abelson's experiments with ancient fossils. Only six out of the 18 amino acids present in the original proteins of the sea shell remained, the others having decomposed.

We are surprised that Fox does not accept the fact that most organic compounds are decomposed by long heating. His doubts on this point can, of course, be settled by his conducting experiments on the thermal decomposition of amino acids and other compounds under various "protective" conditions. We do not understand how regions of high temperature (~150°C) can be maintained for appropriate periods of time to produce his polymerization, with the material being expelled after reaction into appropriate lower temperatures. Where does this occur on the earth now? Why should such circumstances have occurred in the past?

We think that the use of such terms as *proteinoid* and *protein-like* is unfortunate. The polypeptides synthesized by Fox are essentially random, except for the end groups. Fox has not shown that these polypeptides have *any* biological activity and has certainly not shown that they have enzymatic activity, which is the activity that is pertinent to the origin of life. The use of the terms *cell-like* and *cell-like membrane* [S. W. Fox *et al.*, *Science* **129**, 1221 (1959)] is also unfortunate. The formation of round particles in the micron range by heating and then cooling a solution of polypeptide and sodium chloride does not justify calling them "cell-like." Naturally there is a boundary between the particle and the solution, but is this a membrane? It is well known that biological membranes are lipid in character. Fox added no lipids to his polypeptide solution, so the particles can hardly have a "cell-like membrane." Also, biological membranes are not inert casings, but they actively transport ions and organic compounds and allow the entry of only a limited number of specific organic compounds.

If, as Fox states, the case for thermal pathways can "rest alone on relationships to biochemical and evolutionary principles," we think that this case will collapse. A scientific theory rests on experiment, and not on crude analogies to accepted theories dealing with other types of processes.

When we spoke of similarity between prebiological and biological chemistry, we meant the similarity of the gross aspects and not of the detailed processes. Were the first organisms made up of proteins, nucleic acids, sugars, and lipids, or were other types of compounds used in place of these? It would be convenient for the investigator if the primitive pathways followed the present ones, but surely this is not necessary. If there are different pathways for the synthesis of a certain compound in different organisms, how do we pick the more primitive pathway? If we choose the pathway of the more primitive organism, then why should not even more primitive organisms have used pathways different from these? And certainly one would expect that the chemical reactions which occurred before enzymes were present might have been different. In any case, Fox's pathways do not follow present biochemical pathways particularly closely, in spite of his claims.

Finally, we do not agree that Fox has synthesized polymers "markedly like those of natural proteins." His "relatively comprehensive outline suggestive of the origin of biochemical and cellular systems" is a "theory" that is not testable in its present form. It says little more than the statement that life arose from a rare event by chance.

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Discomfort Index

The letter by Kenneth H. Jehn [*Science* **130**, 826 (1959)] presents two arguments against the use of a "discomfort index." The first argument is that the index does not include all the factors that affect comfort. The second is that there are individual differences in personal reaction to the environment.

These two difficulties are true of many indexes now in use. You can't declare an index useless merely by stating the existence of these problems. The usefulness of an index is determined by how much information it yields in spite of these difficulties, the value of this information, and the convenience with which the index can be computed.

As a most elementary example, the spoken word is a useful index to our thoughts and emotions in spite of the fact that words cannot express all the factors involved and the meaning of words varies from person to person. The existence of difficulties does not render speech useless. In a more formal manner, the science of statistics has developed quite a body of techniques, some of them quite elementary, for reducing the number of factors in representing a complex process and for expressing information about processes that are so complex as to appear to be random.

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