THE ORIGIN OF LIFE[1],[3]

H. BURR STEINBACH[2]

(Received May 1, 1966)

"It is wrong to hold that Man is born of Heaven and Earth Purposely. Certain fluids are combined and man is born accidentally. All things are formed of fluid and each species reproduces itself." (Wang Ch'ung, 100 A.D.) This is the text that we can use today for a discussion of the origin of life. I would change the translation only slightly, to speak of life rather than of man. I suspect that the original Chinese meant life rather man since man is the most livable thing we know anyway, a fact certainly appreciated by our ancestors.

How life arose has been debated since debate was possible and from many different points of view, philosophical, theological and scientific. Only a few centuries ago a turning point was reached when the question of the origin of organisms as we know them today was settled. Positive evidence was brought forth that flies did not really originate from hot dung heaps nor mice from dirty shirts. Spontaneous generation of whole animals was shown to be a wrong idea. Modern plants and animals arose from existing plants and animals and slight changes from generation to genertion lead to the evolutionary variety we know now.

This lecture is not concerned with the origin of plants and animals as they exist. It is an inquiry into possible ways in which the substance of life could have arisen. How was the stuff formed which could then give rise to more stuff and lead to the evolutionary processes to culminate in the evolution of Man? These are questions that have been debated more and more for the past half century, not what is the origin of man or of fish or of rice but the origin of the stuff that gave rise to them.

It is a peculiar form of science that tries to reconstruct the story of the origin of life. For one thing, the very existence of life on this planet

(1) Lecture delivered to the general public at the College of Medicine, National Taiwan University, April 27, 1966.

(2) Head, Dept. of Zoology, the University of Chicago, concurrently Director of Marine Research Institute of Woodshole, Mass., U.S.A. also the adviser and the special chair of the Biological Center of Academia Sinica, The Republic of China.

(3) Professor Steinbach consented to have this paper published in our bulletin.

so changed the air and the oceans and the rocks that the process. can never again be repeated on a scale that could lead to the evolution of complex organisms. All we can really hope to do, and are doing, is to try and re-create, in the test-tube, the conditions that might have existed in the most primitive times and determine what could have happened then. Not necessarily, let us emphasize, what did happen but what could have happened. Which, of a number of possible events looks the most probable.

Why should we bother about such things? Why worry about trying to make some slimy stuff that might bear some resemblance to that from which the first living cells developed? Mostly we bother about these things because man, as a thinking machine, must always try to describe and explain that which constitutes his universe. To call a thing unknown or unknowable is a challenge that mankind has never declined, be it climbing a mountain or telling a story in music or doing a scientific experiment. Man must seek "exhaustively to investigate the reason in all things, And things include not only the grass and the shrubs but the height of the heaven and the thickness of the earth "to quote another Chinese philosopher group, the Ch'eng brothers (1000)

But of recent years there has been a greatly increased interest in this problem of the origin of life. A practical reason is a sense. The poet Browning says the "Man's reach should always exceed his grasp". And Man's grasp is extending at supersonic speeds. We now see what was unseeable ten years ago, we measure distances that were unmeasurable and we make substances that were unmakeable. In a very real sense, man's grasp is expanding. We now send out planetary probes to look at Mars and at Venus and Man's own little hands will soon grasp the stuff that is on these faroff places. This being so, an important question is "Is there life on these planets?" And most importantly, if there is life, how will we recognize it? All we really know is the life that we see on one planet, the planet earth. Must all life be the same? Must all men have two legs. Must all cells have mitochondria and must all living stuff have proteins and nucleic acids?

Since these questions are now real and will need answers perhaps even in our lifetime scientists find themselves in the odd position of, for the first time, really trying to say what are the fundamentals of life. Is there a real distinction between life and non-life? And one way to tackle this question is the historical one of deciphering the processes that might have lead to what we now call life and living. Truly our modern ventures into space have raised the most fundamental questions that could be raised in science.

We cannot yet give a good clear and simple definition of life. When asked what is life? most of us emulate Albert Szent Gyorgi, the famous scientist who won a Nobel Prize for the isolation of Vitamin C. When he was asked, "What is a vitamin? he shrugged his shoulders in a creative Hungarian way and said "Oh you all know what I mean anyway". So it is with most of us when asked the question, "What is Life"? We all know what we mean. We just can't talk about it. However, we do need to talk about something so we will make a statement if not a definition. We will assume that three properties are shared by all living stuff at some time during its existence.

1. Living things have a characteristic structure.
2. Living things have continuous chemical change, they exhibit metabolism.
3. Living things can store and use information. Self-duplication is essential to life and this needs information.

Stated in other ways, living things always exist as distinct from that in which they live, living things while staying distinct are always changing and living things can form more living things according to their own patterns.

Now which these statements, definitions if you will, as a starting point, how goes the investigations of the origings of life?

First we must know what there was to start with. What sort of earth was there at a time when life might have arisen and what were the chemical substances that could be used. Certianly we had a solid sphere of rocks and minerals and they bore some resemblance to the deeper layers of the earth today. And we know the chemistry of these. Certainly there was a gas around the solid earth. There was an atmosphere around the lithosphere. It also seems quite certain that there was water, both as a gas and as a fluid. So we can add a hydrosphere and all that is lacking now is that which we seek, the biosphere.

The primitive atmosphere was certainly far different from that we know/ today. Many lighter elements had not escaped into space at that time, especialy hydrogen. It was a strongly reducing atmosphere, a fact of importance it means that organic stuffs formed would not burn up as they would today in our oxidising atmosphere. Moreover there were without much doubt high concentrations of small molecules that would be very poisonous today. Ammonia, methane and hydrocyanic acid were probably in the atmosphere along with other simple molecular odds and ends.

Modern science has gone a long way towards identifying and studying the essental parts of modern cells. Even more, it is now possible to take some of the parts and fragments and, under proper conditions get some of the original structures back again. These have been wonderful achievements and certainly point to the directions in which to look for the early origins of living things. But the putting together of these parts still can be done only with the aid of enzymes which themselves are the products of living things. What we need to know, is how could these delicate processes be started before there was anything living to tell how to do it.

We can, on the basis of what we know of modern cells, make some good guesses as to the basic things we could need.

1. We would need water. No one has been able to visualize a living system that was not water based. There are almost-equivalents but none that will do the job.
2. We need building blocks of carbon chains. These seem to be mainly amino acids and nitrogenous bases.
3. We need metastable compounds for immediate chemical energy. ATP is the one apparent in the modern cell.
4. We need a linear library system so that things can duplicate themselves in an orderly fashion.

Now as a first step in reconstruction let us imagine a possible situation. Energy from the sun was penetrating with short wave ultraviolet much stronger than today. With the odd mixture of gases and with the water boiling off from the rocks there must have been terrible storms and downfalls of rain. But this was a potent rain. For one thing it was acid and as it fell it dissolved rocks to provide the salts that give us our present-day oceans. Moreover the rain would contain the other substances of the atmosphere and still more importantly, the rain would have formed in the presence of large bursts of energy, electrical energy from the lightening, radiant energe from the sun and heat energy from the sun and by emission from the earth. The first question asked in recent years was, could this combination of circumstances have given rise to the formation of what we think are essential building blocks, the amino acids and the nitrogenous bases needed for nucleic acids. About a dozen years ago an adventurous graduate student at the University of Chicago tried to get and answer and he did, touching off an ever expanding chain reaction of investigations. Mr. Miller took a long glass tubes, rigged it for electrical discharges and filled it with a reducing gas, hydrogen with water vapor, ammonia and methane. He then passed sparks through the system for a week or so and analysed the resulting contents of the tube. He proved beyond all doubt that amino acids were formed and thus a first answer was obtained. Miller demonstrated a very important fact if we start with the probable circumstances on primitive earth, then building blocks for presentday living substance could have been formed.

Since the Miller experiment, a whole mess of substances have been shown to be formed under comparable conditions and say "Mess of substances" advisedly—some strange and complicated things are reported. But we certainly can be sure that under the assumed conditions some basic necessities for life were indeed present.

So we go a step further. Not only did the rains bring down acids to dissolve the rocks to start providing the soils of the oceans but they also brought down mixtures of organic substances which could have accumulated in rather large amounts since there was no oxidation to destroy them. The oceans became then, huge warm nutrient baths or, as described in the scientific literature, they became bowls of hot soup. At this is the outline of the hot soup theory for the origin of the first organic building blocks.

Now to go a step further. Living stuff, to have structure and order cannot do with small molecules, it must have large molecules. Polymers must be formed. So the next question, could polymers arise in the hot soup had to be answered. Again the answer has been yes as shown by a number of methods. For one thing, merely the presence of the tiny particles of soil could have served as focal points for condensation and polymerization. Also most intriguing suggestion, with experimental verification of the process, is that of Dr. Fox. He pointed out that if some hot soup splashed up on land and evaporated, a very concentrated mixture of building blocks, even a dry mixture, could result. He has shown that, especially if this happened near volcanoes where there was excess heat, polymerization was sure to occur. Dr. Fox, being an imaginative person actually took some of the mixture formed by a Miller type experiment, placed it in a depression of a chunk of lava from a volcano of Hawaii, held it at a reasonable surface temperature for a short time and demonstrated that long chains of amino acids were indeed formed and that these long chains had many of the properties of proteins.

So our second step is possible. Large molecules could have been formed in primitive times before there was really life.

Given the large molecules another step is necessary. In living stuff processes occur in an ordered fashion. Things happen at the right time and the right place. It is necessary to have not only a solution of large molecules but to have association of these molecules with each other. This is a fairly simple question to answer in the abstracts. Polymers do associate and do so in a variety of fashions. Furthermore, they can do so in very specific fashions. The best illustration here is one obtained by working backwards, that is, taking complex association, breaking it into parts, and then showing that the re-association gives the same structure back again. For example, collagen, the protein of tendon and ligaments, has a definite and recognizable structure in the electron microscope. Collagen is composed of long fibers with beautiful cross striations. If collagen is dissolved to give a solution of single protein molecules, all traces of structure are lost. Now if the collagen is precipitated, the fibers reform and the cross striations are as they were before. Polymerization certainly could have taken place in the hot soup on its products.

The next question relates to the ability of a mixture of different polymers to form complex ordered structures and here we enter into a very old area of study, the formation of cell models. Since the early days of microscopy, biologists and chemists have been astounded to find that, if one mixes solutions of fats, oils, proteins and salts, one ends up with specific kinds of bodies that look a lot like living cells with memoranes and inclusion and even the ability to move and metabolize. More pertinent perhaps are the microspheres that Dr. Fox has shown to be formed from his hot soup-generated polymers. Periodically over the last half century or so, scientists have become so enamoured of these structures that they have announced the formation of artificial cells. Better to call them cell models and admit that all they really show is that the answer to the question is yes. Given a mixture of polymers, regular, recognizable structure will be formed of a nature that shows that the structure of the first living cells is possible to think about. One can doubt that this particular question will be answered more fully for a long time to come.

So now have a sequence: building blocks, polymers, aggregates, structures and complex forms, each stage of which can be shown to take place under conditions assumed to have been present on primitive earth.

We need to have more components. One, a source of energy and two, the directions for orderly duplication. Energy and information-are essential nature for any enterprise.

The source of immediate chemical energy possess no special problems although there is no definite answer. In modern cells, ATP (comparable to detergents used for washing clothes) is the ubiquitous source of chemical energy. There are many phosphates in the rocks and with Miller-type methods it can be shown that ATP like phosphates can be formed.

The written molecular directions would have been a real difficult thing ten years ago. But now we can study the genetic code as a chemical structure. We know the basis for the written instructions that causes like to give rise to like. We do not, of course, have any idea how the message system might have started. Which molecule first found could tell another molecule what to do and how much to do will remain a mystery for a long time. Probably the first message was indeed the simplest of all, yes and no. Modern messages after all are really just a complicated series of yeses and noes.

I think that the vast majority of scientists, when they think about the origins of life on this plant, do so in terms of some variation of the Hot Soup

Theory, However, we must not think all are of the same opinion. That would never do among scientists and especially among Chinese. There are some strong supporters for a theory that we do not have to worry about how life arose here. It arose someplace else and earth life was started because spores and other kinds of minute dried fragments drifted across the vast spaces and seeded the earth.

This theory of pangenesis is an old one and it has recently been revived for fairly good reasons. Some of the meteorites that fall on the earth from outer space are the so-called carbonaceous meteorites. As their name implies, they contain carbon compounds, itself a fact to make one think of life on the heavenly bodies of origin. However, hydrocarbons can be formed other ways. But to go further, people who have examined these microscopically, claim there are bodies of such form and regularity that they must have been living cells. Others claim this not so and the argument rages with great spirit.

To the scientist the progress has been exciting and very satifactory. We know steps can be taken in a possible and may be probable fashion. And on the basis of this we can hope not only to recognize more manifestations of life but perhaps control them.

Let me repeat an important thing, however, these studies have not been directed to a study of the origin of modern plants or animal or bacteria. They have been directed to the origin of a primitive living substance. While it may be that living stuff can be created in a sense, the possibility that viable living objects can be created is very remote and, in a way, of minor importance, the philosophic and indeed the aesthetic satisfactions for all these efforts comes from the deeper understanding of what life is, not the potential power of creating life. For with the deeper understanding comes the ability to make a better and more livable material world and that, after all, is a major objective of all science.