Has Man Created Life?

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At an elaborate press conference staged on the Stanford University campus December 15, 1967, Dr. Arthur Kornberg, Nobel laureate of Stanford, Dr. Mehran Goulian, now at the University of Chicago, and Dr. Robert L. Sinsheimer, of the California Institute of Technology, announced the synthesis of infectious phage $\phi\chi$ 174 DNA. A speech delivered by President Lyndon B. Johnson the day before had alerted the nation's press concerning the significance attached to the announcement that would be made the next day by Kornberg and associates. In this speech, President Johnson hailed these scientists for "unlocking a fundamental secret of life," and stated that the story to be released would be "one of the most important stories you ever read."

Our nation's press rose to the occasion. The United Press International release that followed the next day, headlined "Two Scientists Create Living Virus," went on to say that "two scientists announced yesterday they have manufactured a 'simple or primitive form of life' in a test tube." The same day the Associated Press article, headlined "Scientists Synthesize Infectious Virus," stated that Doctor Kornberg had said that the genetic material he had helped to synthesize in a test tube could be considered "with reservations," a primitive form of life.

Two years previous to the announcement by Kornberg, Dr. Sol Spiegelman had announced the same accomplishment,[1] except that the viral nucleic acid he had duplicated was RNA (ribonucleic acid) rather than DNA (deoxyribonucleic acid). The difference attached to the significance of these two results was probably due, first, to the elaborate press conference staged by Kornberg before the publication of his paper, and, second, to the fact that

DNA and not RNA is the type of hereditary material found in the cell. One interesting newspaper account that followed Spiegelman's announcement, however, was a syndicated column by Ralph McGill.[2] In this article, McGill stated: "About two years ago knowledgeable persons were saying, out of personal awareness of laboratory experiments, that within 'three to five years' at least one research laboratory would report the creation of life. This prediction now has become fact." After describing what Spiegelman had done, and drawing a few implications from this work, McGill went on to say: "Theology, too, will need to cope with this test-tube creation of a living, reproducing 'thing.' The fundamentalists will be the most strained by this awe-producing secular success. Stuck, or bound, as he is by literalness, the fundamentalist will be troubled."

The implication of McGill's article is clear. Now that man has created life, according to McGill, the fundamentalist must revise his interpretation of Genesis. Did life really require God for its creation? Perhaps if mere man can create life, it simply arose spontaneously by natural processes.

In both Kornberg's and Spiegelman's cases, the scientists were very careful in stating exactly what had been accomplished. The details of Kornberg's work were in press at the time of the news conference.[3] A scientist who is careful in announcing his results cannot be held responsible for the way these results may be interpreted by others, nor for the implications that may be conveyed to the public by the popular press. Nevertheless, a distorted view of the results of Kornberg's work was given to the public.

My purpose in this paper is to interpret the results of Kornberg and associates and to relate these results to the creation of life.

An examination of their report of their work reveals that no virus was synthesized, nor was life, primitive or otherwise, created. In fact, nothing at all was created, for only biologically active material was duplicated. Let us see exactly what was accomplished.

The bacteriophage $\phi\chi$ 174 is a small, simple, circular virus that infects *Escherichia coli,* a common beneficial intestinal bacterium that, among biochemists, has become a favorite object for research. A particular strain of *E. coli* was infected with the virus in the presence of tritiated thymidine, a radioactive substance that labels DNA as it is produced, forming tritium-labeled phage DNA. The phage was obtained from these infected cells, and the circular DNA strands were separated from the protein of the virus. These single, circular strands are called the (+) strands. This isolated viral DNA was placed in a flask along with two enzymes isolated from *E. coli, E. coli* DNA polymerase, and *E. coli* polynucleotide joining enzyme. The DNA poly-

merase is the enzyme that joins the nucleotide building blocks together to form the DNA chain, and the joining enzyme forms the bond that unites the two ends of the DNA chain to close the circle. Another absolute requirement for an active mixture is the presence of the four deoxyribonucleoside triphosphates which are the building blocks for the synthesis of DNA, and the phosphate bonds of which provide the energy necessary for this synthesis. For good activity, a boiled extract of *E. coli* was also required. Synthesis in the absence of this extract amounted to only about five percent of that obtained in its presence. The reason for the effect of this extract on the synthesis is not known. The complete system included the following components:

0.18 mM tritium-labeled $\phi\chi$ 174 phage DNA
0.45 mM each of the deoxyribonucleoside triphosphates
E. coli DNA polymerase
E. coli joining enzyme
8 μM DPN
E. coli boiled extract
5 mM magnesium chloride
20 mM potassium phosphate buffer, pH 7.0
1 mM β-mercaptoethanol
albumin

In this mixture, the DNA polymerase, using the (+) strands as a template, joins the deoxynucleotides together in a chain that is complementary to the (+) strand. (FIGURE 1)

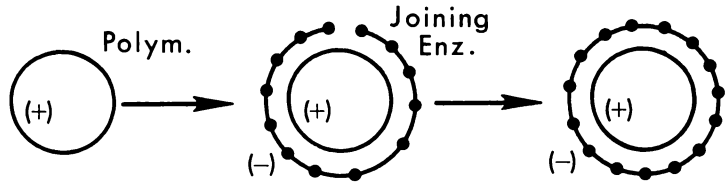

FIGURE 1

This complementary strand is called the (–) strand. In this strand, adenine in the (–) strand pairs with thymine in the (+) strand, cytosine pairs with guanine, thymine pairs with adenine, and guanine pairs with cytosine. When the new chain is complete, the joining enzyme forms the bond between the two ends of the chain to close the circle. The result is a double stranded, circular viral DNA, known as the replicative form.

In order to permit the separation of the synthetic (–) strand from the natural (+) strand of this double stranded replicative form, the synthesis was carried out in the presence of 5-bromodeoxyuridine triphosphate in the place of deoxythymidine triphosphate. Bromouracil has a spatial configuration almost the same as that of thymine, and it can replace thymine for synthesis of DNA. The chain containing bromouracil is heavier than the chain containing thymine, and the two can be separated by centrifugation. DNA synthesis in the presence of bromouracil resulted in a double stranded replicative form, the (+) or natural strand of which contained thymine and the (–) or synthetic strand of which contained bromouracil.

The two strands were separated from one another by brief treatment with pancreatic deoxyribonuclease. This treatment resulted in some cases with opening of the (+) circles, leaving the (–) circles intact, and in other cases with opening of the (–) circles, leaving the (+) circles intact. The natural (+) circles were then separated from the heavier synthetic (–) circles and open chain forms by density-gradient sedimentation. (FIGURE 2)

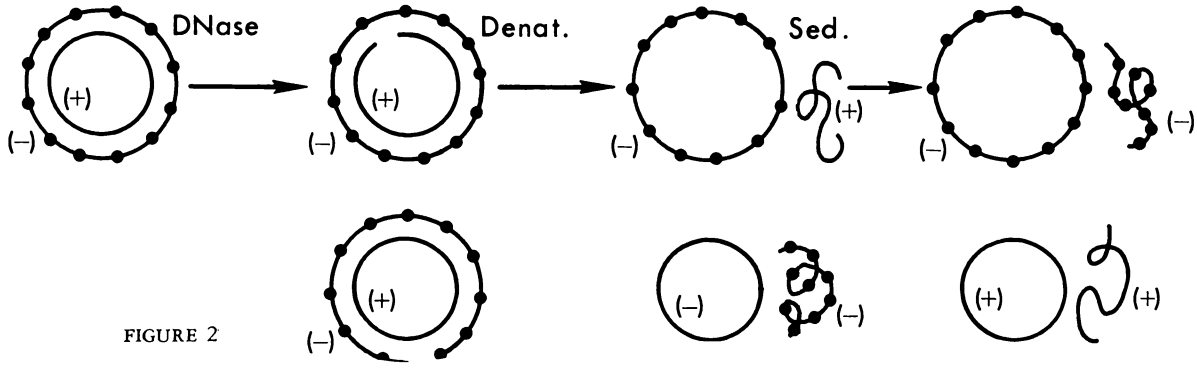

FIGURE 2

The synthesis was then repeated, with the use of the synthetic (–) circular strands as the template. This resulted in a fully synthetic double stranded circular replicative form. (FIGURE 3)

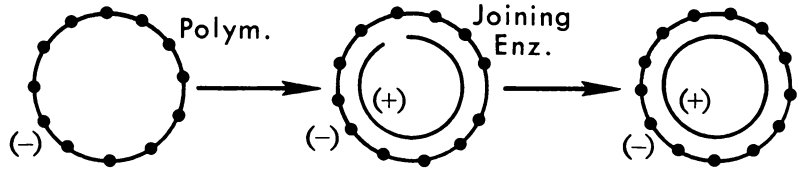

FIGURE 3

The synthetic single strands and the synthetic double stranded replicative form were found to be infective in *E. coli,* although their relative infectivity was lower than the corresponding natural forms isolated from infected *E. coli.* With the naturally occurring forms, the (–) or complementary circles have about twenty percent of the relative infectivity of the (+) circles (the viral DNA is isolated from infected cells). The replicative form has about five percent of the relative infectivity of the (+) circles, unless denatured, in which case the relative infectivity is increased to that of the (+) circles.

This work by Kornberg and his associates was significant in that it showed, as Spiegelman had shown in the case of viral RNA, that DNA polymerase can produce accurate copies of viral DNA outside of the cell when the nucleotide building blocks, energy, and certain other requirements are provided. The twentyfold increase in synthesis brought about by addition of the boiled extract of *E. coli* suggests that there is some other, as yet unrecognized, requirement for synthesis. The low level of synthesis in the absence of the extract may have been due to contamination by an unknown component or components in the viral DNA or bacterial enzymes. Nevertheless, it was shown that intact cells are not required for the synthesis of biologically active DNA.

It must be noted, however, that nothing was created in the true sense of the word, since the product produced, viral DNA, was an absolute requirement in the starting mixture. Without addition of viral DNA, isolated from infected cells, no synthetic DNA could have been produced. What was present in this mixture to begin with could not be said to have been created, but rather that it was replicated or multiplied. Neither can it be said that the viral DNA replicated itself, for without the presence of the two enzymes no viral DNA would have been formed. The function of DNA in this process is entirely passive. Lederberg has stated: "According to the simplest nucleic doctrine, DNA plays no active role in its own replication other than furnishing a useful pattern."[4] It should be said that the two enzymes, with the use of the viral DNA as a pattern, replicated the viral DNA. There is no self-replicating molecule known anywhere in nature, and it is certain that there never has been.

Contrary to statements in the news releases, no virus was synthesized. A virus includes not only nucleic acid, but also a vitally important protein coat. The information required for synthesis of both the viral nucleic acid and the protein apparently is contained in the nucleic acid. Thus, the function of the nucleic acid is to bear information. One known function of the protein is to serve as a protective coat. Naked viral DNA would be readily inactivated in

nature. The protein coat is therefore a vital part of the virus. It may serve additional functions, as viral research is already beginning to indicate.[5] The complete virus was not produced until the viral DNA was used to infect *E. coli.*

The bacteria produced the complete virus. It has been said that almost every part of the cell is involved in protein synthesis. When we have assembled in a test tube the apparatus necessary to synthesize a complete virus, including both DNA and protein, what we will have will be essentially the cell itself.

Another claim that was made for the accomplishment of Kornberg and co-workers was that they had, "with reservations," created a primitive form of life. This is utter nonsense. Neither viral DNA nor the complete virus possesses any metabolic activity whatsoever. It possesses no enzymes nor energy source. It can form or break no chemical bonds. It cannot replicate itself. Alone, it is totally inert. It possesses no more "life" than any other biologically active molecule.

What would constitute the most primitive organization that could be called "life"? Lederberg has listed the following requirements as the least requirements of a primeval organism:[6]

1. DNA.
2. The four deoxyribotide pyrophosphates in abundance.
3. One molecule of the protein DNA polymerase.
4. Ribotide phosphates as precursors for RNA.
5. One molecule of the protein RNA polymerase.
6. A supply of the 20 aminoacyl nucleotidates or, failing these, each of the 20 enzymes which catalyze the condensation of an amino acid and corresponding RNA fragments together with sources of these components.
7. One molecule of the protein aminoacyl-RNA polymerase.

Although this list describes a complex apparatus indeed, probably it is an incomplete list. There must surely be a membrane for maintaining the integrity of this organization and for regulating exchange with the environment. A membrane capable of functioning in such a way would in itself be complex. Furthermore, even a most primitive organism must possess regulatory mechanisms. Genes must be turned on and off at the right time. This mechanism might require, among other things, the presence of certain proteins, similar to the histones. Some mechanism must be present to tell the organism when to divide. The DNA required would be very complex indeed, for it must code for all the macromolecules present as well as provide for all the control mechanisms.

Omitted also in Lederberg's formulation is a provision for a constant supply of energy. The deoxyriboside triphosphates would supply energy. But from where would these high energy compounds come? A truly independent, self-replicating form of life must be capable of providing for its own energy needs. In the cell as we know it, a complex system of enzymes contained in structures known as mitochondria make up the apparatus, or part of it, that is necessary for the production of the energy required by the cell. These mitochondria are complex in themselves and are now known to contain DNA peculiar to mitochondria and found nowhere else in the cell. This metabolic machinery is capable of converting an exogenous source of energy into a form of energy utilizable by the cell, and delivering it to the right place, at the right time, and in the right amount.

Our expanding knowledge of the cell should serve to induce an awareness of the incredible complexity of the cell.[7]

A living organism must have certain minimal requirements: 1. It must be capable of self-replicating. 2. It must have a definite structure that allows the maintenance of its internal organization and that permits a dynamic interchange with its environment. 3. It must have a metabolic system that permits synthesis of vital macromolecules and other essential constituents, provides for a continuous and regulated source of energy, and allows growth and repair to take place. 4. It must include control mechanisms that initiate replication and allow for the orderly regulation of its metabolism. Although there are other simpler definitions for the term "life,"[8] all such definitions seem to me to fall far short of being realistic.

Even if we can assume that Lederberg's formulation is sufficient to constitute a living thing, we can see that it is a formidable organization for man to duplicate. In fact, one can say that man's ability to duplicate a living thing is infinitesimally small. One might go even further and say that man will never create life until he knows everything about life — and that means never.

If we assume that man could duplicate a living thing, or "create life" as it is often called (I use the term duplicate rather than create, because man would be merely duplicating something God had already created), what would be the implication? The atheist, the materialist, would claim that this achievement had dealt the final blow to the concept of Deity, certainly to the belief that God is required for creation of life. If man can "create life," then God is no longer needed. At the least, as McGill said, the fundamentalist would be strained and troubled by this event.

Would the fact that highly intelligent creatures — using the results of

knowledge accumulated over many decades by thousands and thousands of highly trained investigators, endowed with multimillion-dollar laboratories outfitted with sophisticated and complex apparatus — were able to *duplicate* a living thing prove that life could have evolved from a dead, inorganic world? Would it not only reaffirm the simple statement of Scripture, "In the beginning God created"?

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