FROM THE EDITOR'S DESK

# science and the salesmen's art

Between "life in the test tube" and "the first successful synthesis of viable DNA" there may be only a semantic difference. They are both phrases employed by the National Institutes of Health, justifiably proud of having supported a significant piece of research—the synthesis of replicating DNA by Dr. Arthur Kornberg and others at Stanford University.

Dr. Kornberg himself said, in answer to a question about what he had done, "You can call it a simple form of life if you want to."

He obviously didn't want to; most journalists did and the public Dec. 14 and 15 was greeted by headlines reading, "Life Created in Lab Test Tube," and "Scientists Create 'Molecule of Life'."

Dr. Kornberg's work is indeed significant. He refined an enzyme that could create from off-the-shelf chemicals a functioning, viable replica of natural DNA. It was a natural, if not inevitable step, in the chain of related steps that have always characterized science.

But there are few single developments, in the logical progress of basic research, that are hailed as "awesome" by the President of the United States, and a "landmark achievement" by Dr. James A. Shannon, the director of NIH.

What is awesome, in fact, is the acclaim with which Dr. Kornberg's work was greeted. Its publication in the PROCEEDINGS OF THE NATIONAL ACADEMY OF SCIENCES was accompanied by press releases by Stanford University and the Academy itself, and statements issued by the White House and Dr. Shannon's office.

This acclaim may not be unjustified; in fact, it has been said, it is only when a society builds massive public monuments to its scientists and scholars, rather than its soldiers and statesmen, that it can be said to have become truly civilized.

But we suspect that it does not diminish the significance of Dr. Kornberg's contribution to understanding of the life sciences to suggest that the massive outpouring of publicity that accompanied this particular development might not have been wholly ingenuous.

Are the accolades in fact a reward for the meticulous effort that went into this one achievement?

Or do they represent a more cynical juncture of science and public policy? They come at a time when Dr. Shannon has just emerged from a scathing session of Congressional controversy over his fiscal 1968 budget, and is trying to save what he can from Federal planners drawing up next year's budget and more concerned with the costs of Vietnam than with scientific research.

Science itself is a complicated process. So is the public administration and support of science. When the two mix, as they apparently have in the present case, public awareness of science may be enhanced by the salesmen's art, but balanced public understanding of either process, in perspective, is bound to suffer.

*Science News' editor and Dr. Kornberg are unrelated.*

SCIENCE NEWS
OF THE WEEK

# Viable Synthetic DNA

## Eleven years' effort brings success and wild acclaim

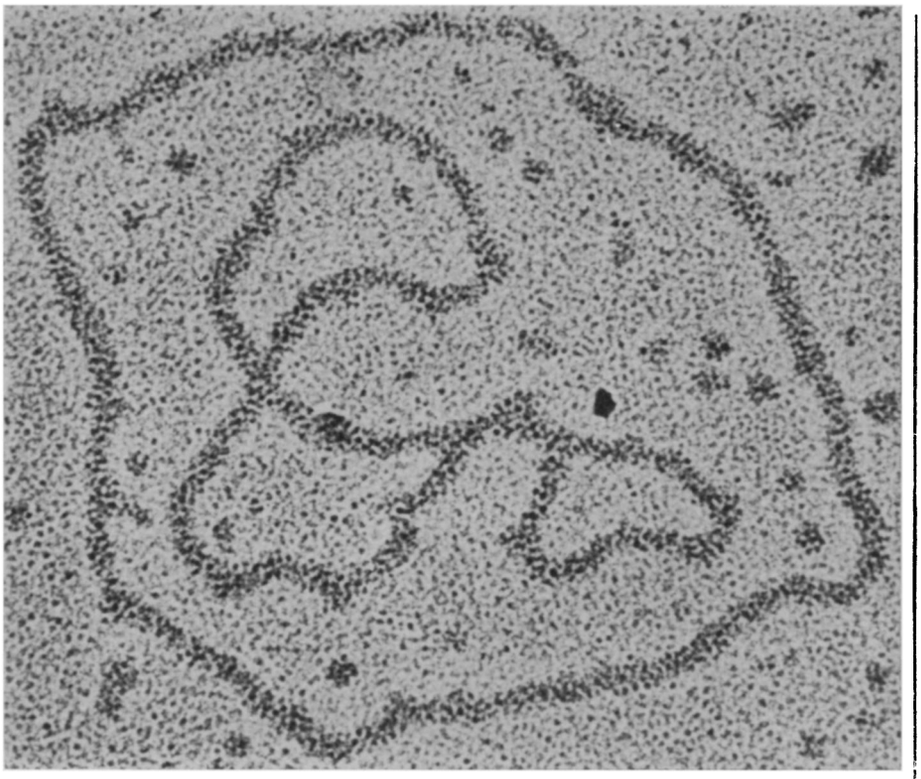
Enthusiastic news reports that three California scientists created a man-made molecule of life's basic genetic material raised at once the spectre and the promise of man's eventual control of his own heredity.

Headlines proclaimed life in a test tube. There were predictions that future generations will see mankind make exact duplicates of its geniuses, that the secret of cancer is near disclosure and that a remedy for inherited diseases will be the next research step.

**Though there may be** an element of probability in these forecasts, there is no element of immediacy, and the scientists involved said so. Nevertheless, disregarding all the exaggeration, the first synthesis of a biologically active molecule of DNA (deoxyribonucleic acid) is a major event. After 11 years of research on DNA synthesis, Dr. Arthur Kornberg of Stanford University produced in a test tube a totally artificial copy of a type of DNA virus; the copy is every bit as infectious as its natural counterpart.

The DNA core of a virus is the portion of the molecule that attacks and destroys living cells while using their genetic machinery to make copies of itself. The synthetic viral DNA Dr. Kornberg created comprises, in effect, man-made genes. He was assisted by Dr. Mehran Goulian of the University of Chicago, formerly of Stanford, and by Dr. Robert L. Sinsheimer of the California Institute of Technology. They report their success in the December PROCEEDINGS OF THE NATIONAL ACADEMY OF SCIENCES.

The particular type of viral DNA (called Phi X174) the researchers made is an extremely simple molecule of only five or six genes. Their achievement, however, lays the foundation for eventual synthesis of more complex DNAs —such as those in human cells—by



Stanford University

*Rings of viral DNA synthesized in a California laboratory.*

proving that active DNA can be produced in the laboratory and by showing scientists how to do it. The key lies in purification and skillful use of the proper enzyme or catalytic system.

It was for the purification of the necessary enzyme that Dr. Kornberg received his Nobel Prize in 1959. The work he reported now was made possible by a refinement of that process.

**"If we know** how to use an enzyme to copy this particular virus then we can copy other viruses," Dr. Kornberg says. "And we can copy them in ways in which we can modify their genetic structure to make them noninfectious." Such noninfectious viruses could be used as tools to study the replicating mechanisms of disease-causing viruses once they infect a cell; they might also be used as the active ingredient in antivirus vaccines.

DNA has coded within it the information needed to program the development of all hereditary characteristics. Its code contains four words: the names of the chemicals adenine, guanine, cytocine and thymine. They transmit information by the sequence of triplets in which they appear. The possibilities of variation are infinite because DNA molecules can contain hundreds of thousands of words, each in different triplet sequence. Even the simple viral DNA Dr. Kornberg synthesized is 6,000 words long.

An enzyme, DNA polymerase, is the instructor that orders the four-word genetic language into its proper sequence.

To make the synthetic molecule Phi X174 DNA virus, Dr. Kornberg combined in a test tube a natural DNA virus to serve as a blueprint for the artificial copy, molecules of adenine, guanine, cytocine and thymine and some E. coli DNA polymerase to guide the copying procedure.

Dr. Kornberg's first success at creating DNA in a test tube had come in 1959 when he similarly produced a molecule with all of the physical and chemical properties of natural DNA but without its biological activity. In other words, his first man-made virus was like its natural counterpart in almost every respect, but it could not infect a bacterial cell and replicate.

**One reason** it was inactive, Dr. Kornberg concluded, was that the polymerase enzyme, extracted from the common intestinal bacteria Escherichia coli, was contaminated. Therefore it dictated certain minor but critical mistakes in the copying process it directed.

To create a fully active synthetic copy of the natural DNA, the four chemical bases must be directed to line up against the blueprint model in precisely the correct order. Extraneous material in the enzyme confused the procedure just enough to put a few words in the wrong sequence; hence, no activity.

This time a refined enzyme directed the four bases to fall in line in virtually perfect complement to the natural blueprint; and as a result, the code words in the synthetic spelled viral DNA.

But the natural, infectious DNA virus on which the synthetic was modeled is not a straight molecule. It has a closed, circular form. So Dr. Kornberg added a polynucleotide enzyme called ligase to his test tube; it joined the two ends of the synthetic DNA.

When the synthetic DNA was then separated in a centrifuge from the natural genetic material, Dr. Kornberg added it to a culture of E. coli cells. Within minutes, the man-made DNA virus infected the cells, usurped their genetic machinery and produced more DNA viruses. These viruses then went on to infect other cells and replicate again, producing a second generation of synthetic viruses identical to the original natural virus.

**The issue** of whether Dr. Kornberg's man-made DNA virus constitutes the creation of life by man seems to be of more concern to laymen than to scientists. Scientists disagree as to whether viruses are alive in the first place.

Cells are able to replicate by themselves. Viruses are not. Viral particles replicate only inside living cells because they do not contain all the machinery necessary to do the job on their own.

However, when scientists take the next step—the synthesis of DNA from a bacterial or animal cell rather than from a virus, there will be neither question nor controversy.

The ultimate synthesis of cellular DNA seems assured; when depends on the intensity of the effort.

Dr. Sol Spiegleman of the University of Illinois believes the speed "really depends on society's interest in spending the money, because it will require massive research efforts."

Using an enzyme called replicase and following procedures similar to those of Dr. Kornberg, Dr. Spiegelman synthesized viral RNA (ribonucleic acid) in 1965. RNA is second-string genetic material. It reads the hereditary message coded in DNA and carries it to the cells' ribosomes, small organelles where proteins are made.

**Dr. Kornberg's** research was supported largely by funds from the National Institutes of Health and the National Science Foundation. NIH director Dr. James A. Shannon cited Dr. Kornberg's work as a "landmark achievement." His success, he said, "in effect adds up to a handsome reward for the American people as a result of their investment in basic health research through Federal agencies. It seems well to make this point at this time because the end products of basic research, although highly essential to progress in clinical medicine, are seldom so clearly visible in terms of potential health applications as that of Dr. Kornberg and his associates."

President Johnson also lauded Dr. Kornberg for "a spectacular breakthrough in human knowledge. . . ."