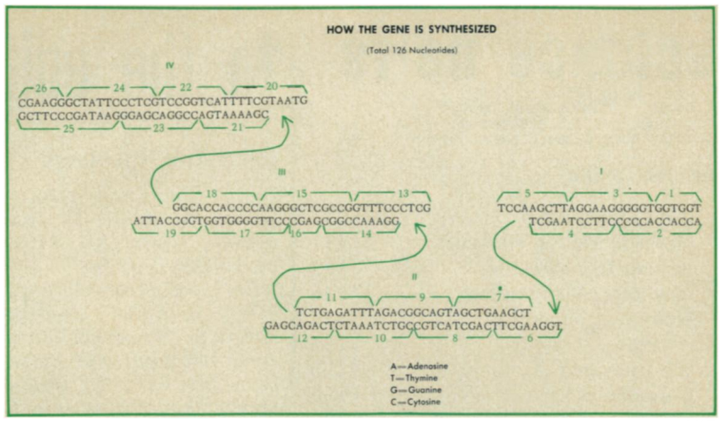
A 126-unit artificial gene

MIT scientists have synthesized the first gene with the potential to function detectably within the living cell

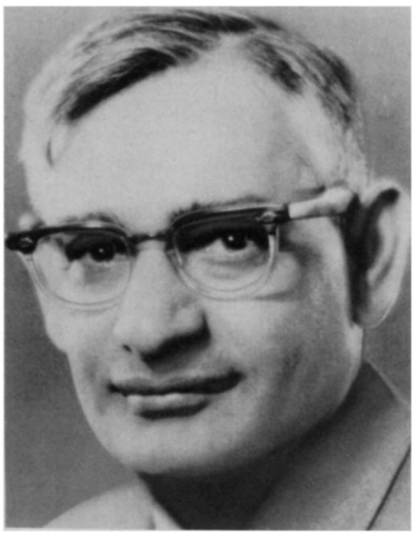


MIT

One of the biggest challenges in molecular biology is determining the chemistry of genes and how this chemistry orders genetic information. A major step toward this end was announced in 1970 by Nobel laureate chemist Har Gobind Khorana and his team. They were the first scientists to synthesize a copy of a real gene. The gene, found in yeast cells, orders transfer RNA to line up the amino acid alanine into protein (SN: 6/6/70, p. 547).

The artifical gene had two drawbacks though. Because the start and stop signals for the alanine tRNA gene were not known, the scientists could not attach these signals to the artificial gene. And without the start and stop signals, the artificial gene could not be made to function in a yeast cell. And even if the artificial gene could have functioned in a yeast cell, alanine tRNA activity ordered by it could not have been detected. This is because the yeast cell's natural genes activate alanine tRNA as well.

Khorana and his team have now synthesized another gene. This one is the first synthesized gene that has potential for both functioning in a living cell and for having its product detected in a living cell. The achievement was reported this week by Kanhiya Lal Agarwal, one of Khorana's colleagues at the Massachusetts Institute of Technology, at a meeting of the American Chemical Society in Chicago.


Khorana: Heads gene-synthesis team.

The gene is a copy of one present in the bacterium *E. coli* that orders tRNA to line up the amino acid tyrosine into protein. Hence the name of the artificial gene is "tyrosine transfer RNA gene." The MIT researchers have not yet completely figured out the start and stop signals on the natural gene, nor completely grafted the signals onto the artificial gene, but they have made ample progress toward this end. Once they get the start and stop signals on the artificial gene, the gene can be introduced into a bacterium via an infectious virus. Once the gene is inside a bacterium, the scientists will be able to see whether it is functional.

Khorana and his colleagues originally began synthesizing a tyrosine tRNA gene with 85 nucleotides. Nucleotides are the chemical building blocks of genes. Then Sidney Altman and John Smith of the University of Cambridge, England, found that there are 41 more nucleotides on the gene. The 126-nucleotide gene was longer than the functional tRNA gene. For some unknown reason, after the long tRNA gene is synthesized, the extra 41 nucleotides break off, creating the functional tRNA gene. So the MIT investigators set out to synthesize the longer gene.

They began building their gene by synthesizing small segments of 10 to 14 nucleotides. Each segment consisted of a complementary portion of two opposing segments of the two-stranded molecule. Thus, each segment acted as a splint to attract and hold together two opposing segments, which could then be tied together by an enzyme called DNA ligase. The scientists designed the synthesis so that these joined segments still had a left-over, single-stranded segment extending beyond the double-stranded segment. This left-over segment was used as a splint to join more segments of the gene. The scientists joined overlapping segments this way until they produced four large portions of the gene. These were joined to produce the entire gene.

As for the stop signal on the gene, Khorana and his colleagues have synthesized 24 nucleotides. They believe these nucleotides comprise a major portion of the stop signal. They are now sequencing the start signal of the gene using the natural gene as a guide.

However important the MIT team's achievements, they are but a beginning in understanding the chemistry of genes. The yeast gene that Khorana and his colleagues synthesized was 77 nucleotides long, the bacterium gene 126 nucleotides. Human genes, in awesome contrast, contain millions of nucleotides each. □

Controlling epilepsy by biofeedback

One of the most popular gadgets to come out of psychological technology is the alpha machine. Basically, it is an electroencephalograph recorder with sound or light that signals or feeds back to the user whenever a specific brainwave pattern is being produced. Using this biofeedback technique, people are attempting to learn to emit more than the normal amount of alpha waves. These waves are associated with relaxation, but not all psychologists agree there is any benefit to be derived from producing extra amounts of them (SN: 11/6/71, p. 314). What psychologists do agree on is the value and eventual importance of the biofeedback technique for brainwave control. And some researchers are now using it in