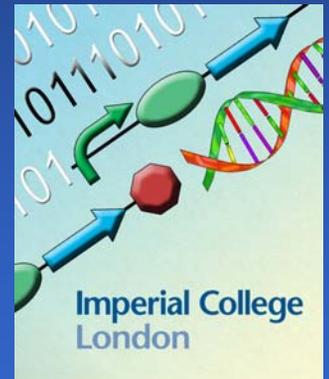


# Building Living Machines with Biobricks

## The Promise of Synthetic Biology

**Professor Richard Kitney, Professor Paul Freemont**

*Support by Matthieu Bultelle, Dr Robert Dickinson,  
Dr Suhail Islam, Kirsten Jensen, Paul Kitney, Dr Duo  
Lu, Dr Chueh Loo Poh, Vincent Rouilly, Baojun Wang.*



# The Fathers of Biological Engineering

**Imperial College London**

Department of Bioengineering

Division of Molecular Biosciences

Imperial College  
London

100 years of living science

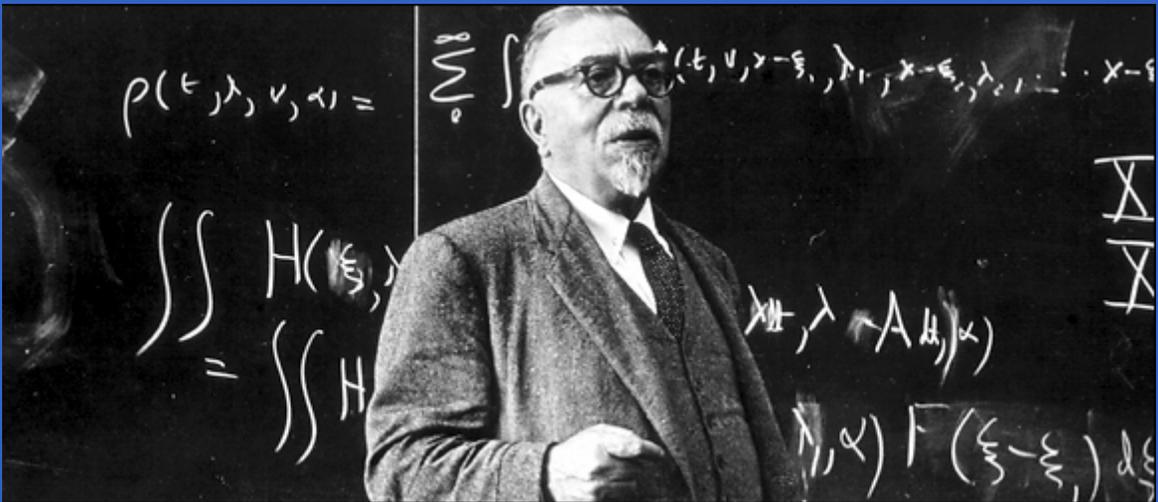
100

# Norbert Wiener

## *American Mathematician (1894-1964)*

Throughout his life Wiener had many extra-mathematical interests, especially in biology and philosophy. At Harvard his studies in philosophy led him to an interest in mathematical logic and this was the subject of his doctoral thesis, which he completed at the age of 18.

In 1920 he joined the faculty of the Massachusetts Institute of Technology, where he became professor of mathematics (1932). He made significant contributions to a number of areas of mathematics including harmonic analysis and Fourier transforms.



Norbert Wiener is best known for his theory of cybernetics, the comparative study of control and communication in humans and machines. He also made significant contributions to the development of computers and calculators.

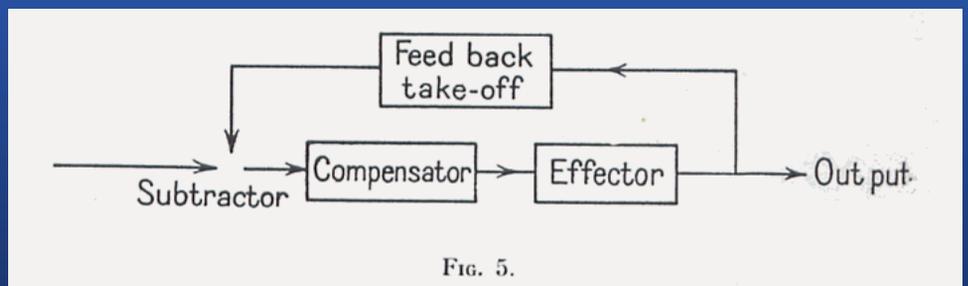
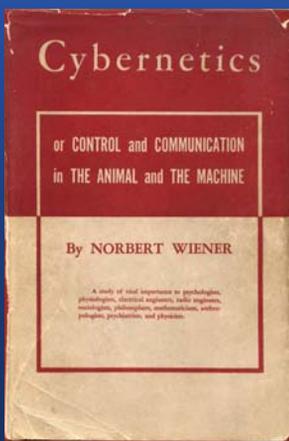


FIG. 5.

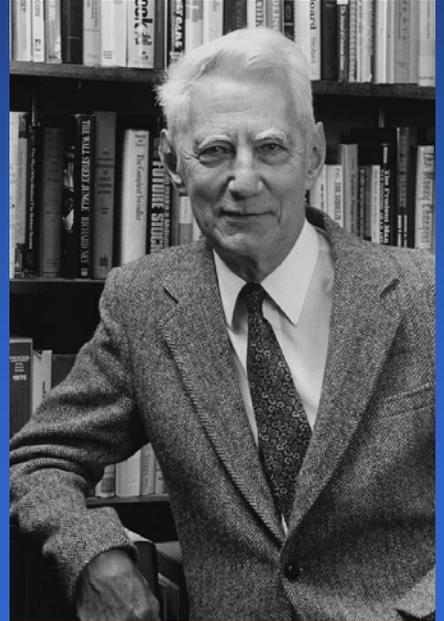
*The Feedback Loop: A crucial concept of Cybernetics*

# Claude Elwood Shannon

## *American Mathematician (1916-2001)*

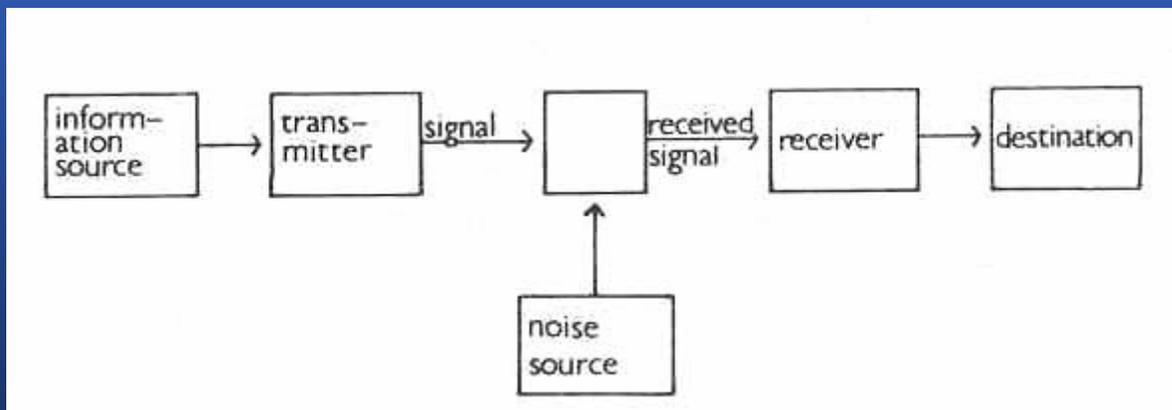
Shannon graduated from the University of Michigan in 1936. He later worked both at the Massachusetts Institute of Technology and the Bell Telephone Laboratories. In 1958 he returned to MIT as Donner Professor of Science, held until his retirement in 1978.

Shannon's greatest contribution was in laying the mathematical foundations of communication theory. The resulting theory found applications in such wide-ranging fields as circuit design, communication technology in general, and even in biology, psychology, semantics, and linguistics.



The central problem of communication theory is to determine the most efficient ways of transmitting messages. Shannon showed a way to solve the problem thanks to the introduction of information entropy as a measure for the uncertainty in a message. He first published his ideas in 1948 in collaboration with Warren Weaver in *A Mathematical Theory of Communication*.

Shannon also made important contributions to computer science. In his paper *A Symbolic Analysis of Relay and Switching Circuits* (1938) he drew the analogy between truth values in logic and the binary states of circuits.



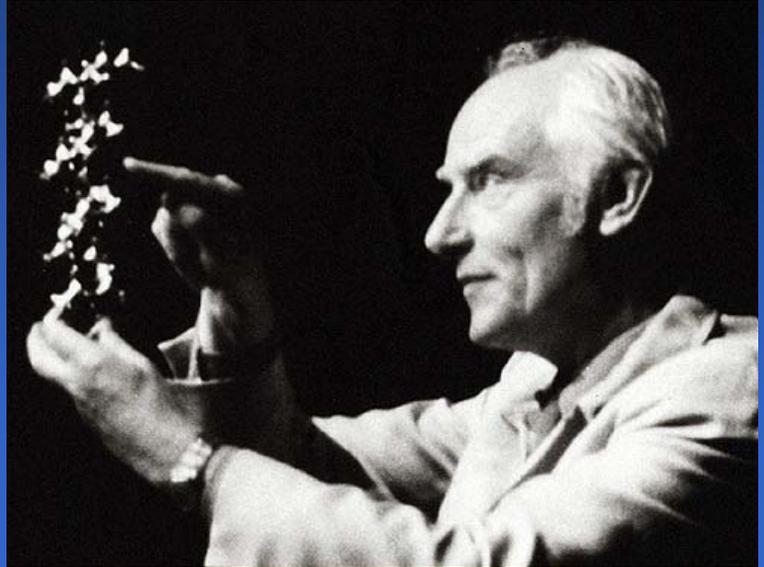
*Claude Shannon's Communication Theory: (from The Mathematical Theory of Communication, with W. Weaver, 1949)*

# Francis Crick

## *British Biophysicist 1916-2004*

Francis Crick graduated in Physics and Mathematics from University College, London in 1937. During the war, he worked on weapons for the British Admiralty. By the time the war ended, he had decided to pursue a career in biology, not physics.

In 1949 he joined the Medical Research Council Unit for Molecular Biology at Cavendish Laboratory for a PhD.



There he met James D. Watson, who shared his interest in the gene and the genetic material, deoxyribonucleic acid (DNA). In 1953 Crick and Watson jointly proposed their double helical model of the DNA molecule, which brought them the **Nobel Prize in 1962**, an honour they shared with English biophysicist Maurice Wilkins. The discovery of the structure of DNA is considered to be one of the greatest events in 20th-century biology.

After the publication of DNA's structure and the completion of his PhD in 1954, Crick turned his attention to understanding the coding function of DNA. He and Watson proposed that the order of bases in a gene encoded the order of amino acids in a protein. Crick also used the term "central dogma" to summarize an idea that implies that genetic information flow between macromolecules would essentially be one-way.

Over the next decade, the details of this insight were worked out by a large group of scientists, including Crick, Watson, Sydney Brenner, George Gamow, Seymour Benzer, Marshall Nirenberg, and Har Gobind Khorana. As part of this work, Crick hypothesized the existence of an "adaptor" that links DNA and proteins. This led to the discovery of messenger RNA and transfer RNA, which serve this function.

# Sidney Brenner

## *South African-British molecular Biologist (1927-)*

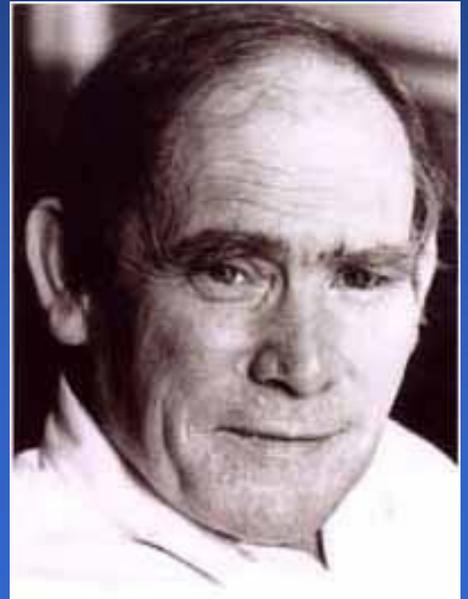
Sidney Brenner was educated at the universities of Witwatersrand and Oxford, where he obtained his DPhil in 1954. In 1957 he joined the staff of the Medical Research Council's molecular biology laboratory in Cambridge.

In 1957 he demonstrated that the triplets of nucleotide bases that form the genetic code do not overlap along the genetic material (DNA). The basic idea was that the amino-acid sequence of a protein is determined by the sequence of the four nucleotides – A, T, C, and G –with a specific amino acid being specified by a sequence of three nucleotides (codon).

In 1961 Brenner, in collaboration with Francis Crick and others, reported the results of careful experiments with the bacteriophage T4, which clearly showed that the code did consist of base triplets that neither overlapped nor appeared to be separated by 'punctuation marks'.

The same year also saw Brenner, this time in collaboration with François Jacob and Matthew Meselson, discovering a new form of RNA, messenger RNA (mRNA). With this came one of the central insights of molecular biology – an explanation of the mechanism of information transfer whereby the protein-synthesizing centres (ribosomes) play the role of non-specific constituents that can synthesize different proteins, according to specific instructions, which they receive from the genes through mRNA.

Sidney Brenner shared the **2002 Nobel Prize in Physiology or Medicine** with H. Robert Horvitz and John Sulston. He founded the Molecular Sciences Institute (Berkeley, California) and is currently associated with the Institute of Molecular and Cell Biology (Singapore).



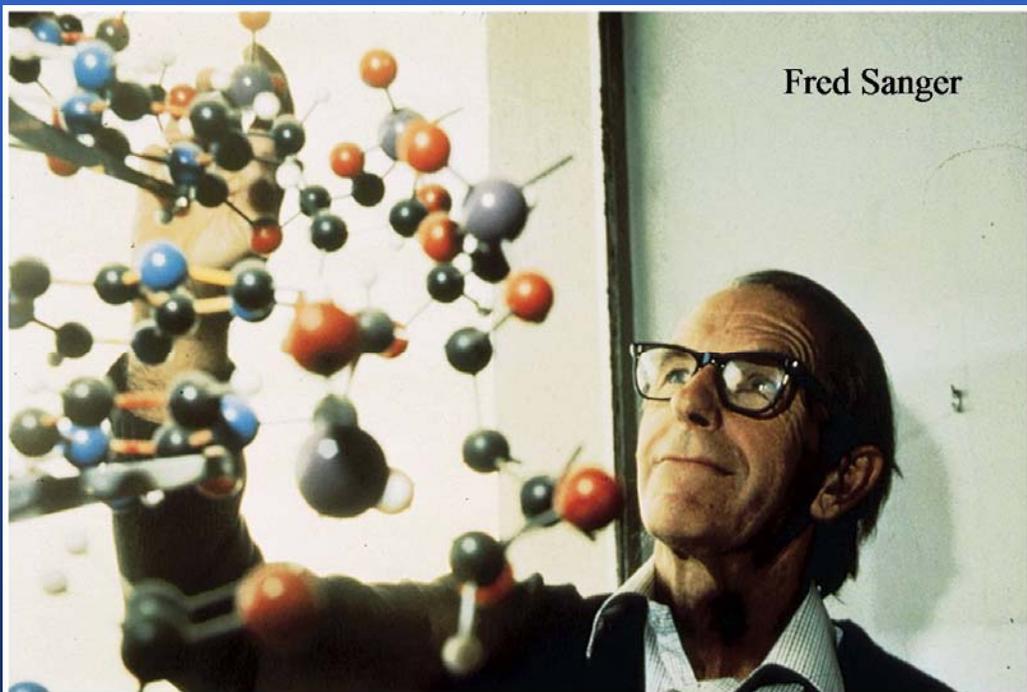
# Fred Sanger

## *British Molecular Biologist 1918-*

Fred Sanger has been breaking new ground in chemistry for decades. In fact, he is the only person to have won a Nobel Prize in chemistry twice, and is only one of four people ever to have won a Nobel Prize more than once.

While at Cambridge University in England he developed a new method for sequencing amino acids in proteins, which he used to identify the complete sequence of insulin. For this he was awarded his first **Nobel Prize in chemistry in 1958**.

In 1961 Sanger moved to the MRC Laboratory of Molecular Biology, where he became head of the division of protein chemistry. His colleagues' interest in nucleic acids inspired him to turn his interest in sequencing to the research of nucleic acids. In 1977 Sanger developed a sequencing method, called the "dideoxy" method, with which he determined the entire sequence of a bacterial virus called phi-X174. This was the first time a complete sequence of a DNA molecule had been established. For this achievement he was awarded the **1980 Nobel Prize in chemistry**. Sanger's original sequence contained only 5,375 nucleotides, but his technology is now being used to determine sequences that are millions of nucleotides longer, including, importantly, the human genome.

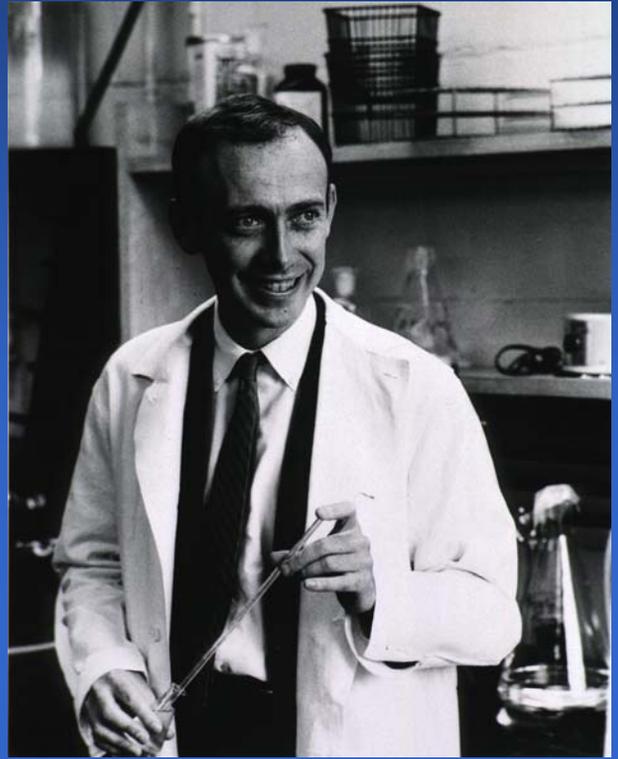


# James Dewey Watson

## *American Biologist 1928-*

A precocious student, James Watson entered the University of Chicago at the age of 15 and graduated in 1947. He then went to Indiana, for a Ph.D. in genetics, setting out on the "search for the gene."

In 1950, Watson joined the Cavendish laboratories at a time when Francis Crick, Maurice Wilkins, Rosalind Franklin, and Linus Pauling were racing to determine the structure of DNA. The X-ray crystallography experiments of Franklin and Wilkins provided much information about DNA - in particular that DNA was a molecule in which two "strands" formed a tightly linked pair.



Crick and Watson made the intuitive leap: in 1953, they proposed that the structure of DNA was a winding helix in which pairs of bases (adenine paired with thymine and guanine paired with cytosine) held the two strands together. The Watson-Crick model of the DNA double helix provided enormous impetus for research in the emerging fields of molecular genetics and biochemistry, and Crick, Watson, and Wilkins were awarded the **Nobel Prize in 1962**.

In subsequent decades, Watson taught at Harvard and CalTech, and he became director of the Cold Spring Harbor Laboratory in New York. In 1988, his scientific achievement and his success as an administrator led to his appointment as the head of the **Human Genome Project** at the NIH. Designed to sequence the human genome in its entirety, the Human Genome Project is by far the most ambitious and generously funded endeavour in biology.

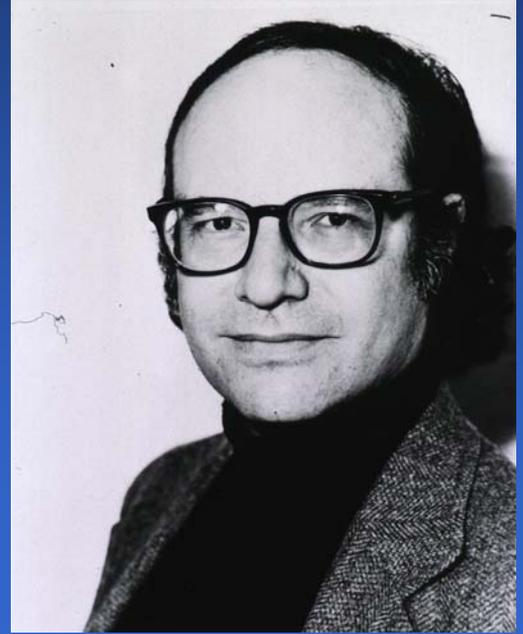
# Walter Gilbert

## *American Molecular Biologist (1932-)*

Walter Gilbert was educated at the universities of Harvard and Cambridge, later joining the faculty at Harvard.

With Allan Maxam he developed a new DNA sequencing method. His approach to the first synthesis of insulin lost out to Genentech's approach, which used genes built up from the nucleotides rather than from natural sources.

Gilbert was awarded the **1980 Nobel Prize in Chemistry** with Frederick Sanger for devising methods for determining the sequence of nucleotides in a nucleic acid.

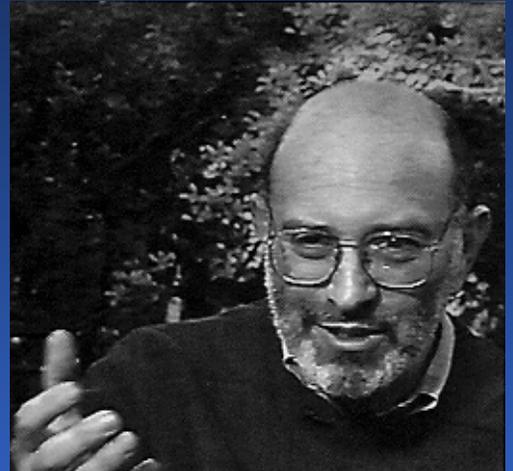


Walter Gilbert first proposed 'the RNA World' hypothesis for the origin of life. He is a co-founder of the biotech start-up company Biogen and was the first chairman on the board of directors. He is currently the chairman of the Harvard Society of Fellows.

# Stanley Norman Cohen

## *American Geneticist (1935-)*

Stanley Cohen is a graduate of Rutgers University and received his doctoral degree from the University of Pennsylvania School of Medicine in 1960. He joined the faculty of Stanford University in 1968. There he explored the field of bacterial plasmids. He wanted to understand how the genes of plasmids could make bacteria resistant to antibiotics.



In 1972, Cohen's investigations, combined with those of Herbert Boyer, led to the development of methods to combine and transplant genes. This discovery signalled the birth of genetic engineering.

Today, Cohen is a professor of genetics and medicine at Stanford, where he works on a variety of scientific problems including cell growth and development

# Herbert Wayne Boyer

## *American Biochemist (1936-)*

Herbert Boyer was educated at St. Vincent College, Latrobe, and the University of Pittsburgh where he obtained his PhD in 1963. He joined the faculty of the University of California, San Francisco, shortly afterward in 1966.

In 1972, Boyer met Stanley Cohen, and together they pioneered the field of recombinant DNA. Their work led to the founding of biotechnology firms such as Genentech, which Boyer co-founded in 1976 with Robert Swanson.



Boyer is now a professor emeritus of biochemistry and biophysics at UCSF.