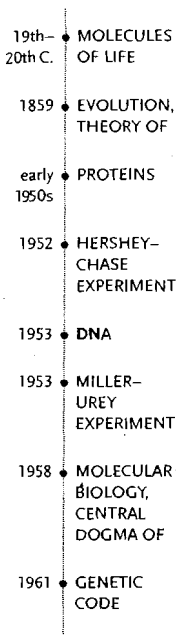


DNA

The DNA molecule has the shape of a double helix, and replicates by a process in which each side of the double helix acts as a template for the assembly of new molecules



Today, we know that the molecule we call DNA carries the code that runs the chemistry of living things (see MOLECULAR BIOLOGY), and DNA's double-helix structure has become a familiar scientific icon. Like nearly all great discoveries, this was not the work of a lone genius, but followed from a long chain of experimental results. The HERSHEY-CHASE EXPERIMENT, for example, had established* that it was DNA, and not PROTEINS, that carry genetic information in cells. In the 1920s, the Russian-American biochemist Phoebus Levene (1869-1940) had established that the basic building blocks of DNA are the five-carbon sugar known as deoxyribose (this molecule is the "D" in DNA); a phosphate group; and the four bases named thymine, guanine, cytosine, and adenine, usually denoted by the letters T, G, C, and A. In the late 1940s, the Austrian-American biochemist Erwin Chargaff (1905-) established that in all DNA the amounts of T and A are the same, and, similarly, the amounts of G and C are the same. The relative proportions of T/A and G/C in the DNA molecule, however, varies from one species to the next.

In the early 1950s, two further pieces of evidence about the nature of DNA became available: The American chemist Linus Pauling (1901-94) showed that long molecules such as proteins can form links that twist them into a helical shape, and the laboratory of Maurice Wilkins and Rosalind Franklin in London produced X-ray data (based on advanced use of BRAGG'S LAW) that suggested that DNA might have a helical structure.

It was at this time that a young American biochemist, James Watson, went to spend a year at Cambridge University, hooking up with a young English theoretical physicist, Francis Crick. ("I was almost totally unknown at the time," Crick would reminisce later, "and Watson was regarded ... as too bright to be really sound.") Working with metal models, they tried to find how the various molecular components would fit into a three-dimensional DNA molecule.

The easiest way to visualize their results is to imagine a tall ladder. The uprights of the ladder are made of molecules of sugar, oxygen, and phosphorus. The important working information in the molecule is carried on the rungs of the ladder. The rungs are made of two molecules, one attached to each upright. These molecules are the four bases. The bases are basically single or double rings containing carbon, nitrogen, and oxygen atoms, so constructed that they have either two or three positions where they can form hydrogen bonds (see CHEMICAL BONDS) with other bases. Because of the shape of these molecules, only certain kinds of links—certain completed rungs—are allowed. These are the links between A and T, and between G and C. No other links are allowed. Each rung, then, consists of either A-T or G-C. Once this ladder is assembled, imagine grabbing the two ends and twisting, producing the familiar double helix of DNA.

The Meselson–Stahl Experiment

Once Crick and Watson had suggested the double-helix structure of DNA, it had to be verified experimentally, as does any scientific hypothesis. Two molecular biologists at the California Institute of Technology, Matthew Meselson (1930–) and Franklin Stahl (1910–), carried out the relevant series of experiments in 1957. Their technique depended on being able to distinguish between the masses of very similar molecules. They began by growing bacteria in a medium in which the only nitrogen available was the isotope ^{15}N (normal nitrogen, ^{14}N , is slightly lighter). After several generations, all of the bacterial DNA was constructed from the heavier nitrogen. The bacteria were then transferred to an environment in which all of the nitrogen was in the form of ^{14}N . (Nitrogen appears in the base pairs of DNA, and will therefore be taken up by any organism creating new strands of the molecule.) After one cell division cycle, the DNA of the bacteria had a weight midway between that associated with ^{15}N and ^{14}N . After two cell divisions, one DNA strand in four contained heavy DNA, and so on. By this ingenious experiment, then, Meselson and Stahl verified that with each cell division, the complementary strands of DNA contained half of the old (heavy) DNA and half of the new (light) DNA, just as the Watson–Crick hypothesis predicted.

A section of DNA replicates by unzipping itself and assembling new strands.

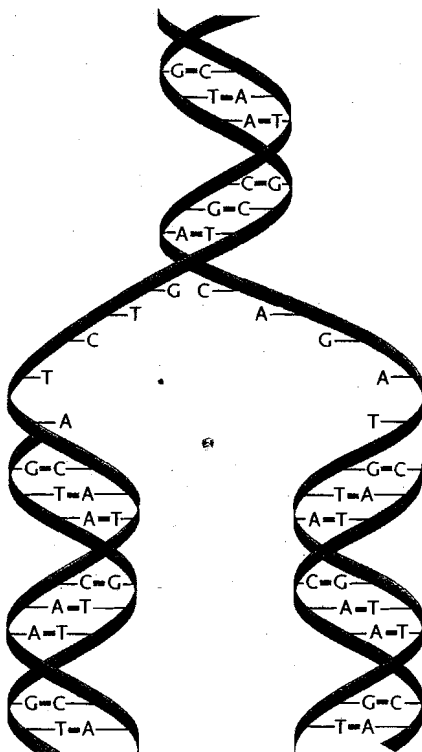
If you read down the rungs on one side of the DNA molecule, you will find a sequence of bases. Think of this as a message written in an alphabet that has only four letters. It is this message which determines how the cell runs its chemistry, and which therefore determines the characteristics of the living thing of which that cell is part. There is no new information contained in the other side of the helix, because if you know what base is on one side, you know what the other half of the rung has to be. In a sense, the two strands of the double helix bear the same relationship to each other as a photograph does to its negative.

When Watson and Crick discovered the double-helix structure of DNA, they also realized that there was a straightforward way in which a molecule of DNA could replicate itself—as it must when a cell divides. In their words, “It has not escaped our notice that the specific pairing we have postulated suggests a possible copying mechanism for genetic material.”

This “possible copying mechanism” depends on the structure of DNA. When a cell starts to divide, so that extra DNA is needed to supply daughter cells, enzymes (*see* CATALYSTS AND ENZYMES) start to “unzip” the DNA ladder, leaving the individual bases exposed. Other enzymes cause

appropriate bases in the surrounding fluid to attach to the appropriate exposed bases—A to T, C to G, and so on. As a result, each of the two split strands of DNA assembles a match for itself from the surrounding medium, creating two double helices from the original molecule.

Just as every great discovery rests on the work that preceded it, so too does it give rise to fruitful research as scientists use the new information to move on. The discovery of the double helix can be said to have generated a half century of progress in molecular biology, culminating in the success of the HUMAN GENOME PROJECT.



FRANCIS HARRY COMPTON CRICK (1916–) English molecular biologist (right). He was born in Northampton, where his father was a shoe manufacturer. He graduated in physics from University College, London, in 1938, and spent the war designing acoustic and magnetic mines. He then decided to study “the mystery of life.” In 1951 he was examining the structure of proteins at a new unit set up by the Medical Research Council at Cambridge’s Cavendish Laboratory, when a visiting student, James Watson, suggested that if the function of the DNA molecule was to be understood, its structure needed to be found. Their success in this quest earned them a share of the 1962 Nobel Prize for Physiology or Medicine. Crick’s later work included the formulation of the central dogma of molecular biology. In 1977 he moved to the Salk Institute at San Diego to continue his pursuit of “the mystery of life,” this time investigating consciousness.

JAMES DEWEY WATSON (1928–) American biochemist. He was born in Chicago, Illinois, and entered the University of Chicago

at the age of 15, graduating four years later. He received his Ph.D. in 1950 from the University of Indiana for studies of viruses. His visit to the Cavendish Laboratory the next year led to the collaboration with Francis Crick that led to the discovery of the structure of DNA. Their 1962 Nobel Prize for Physiology or Medicine was shared with Maurice Wilkins (1916–), whose X-ray diffraction results had been instrumental in elucidating the double-helix structure. Such recognition eluded Rosalind Franklin (1920–58), whose contribution was felt by many to be also significant.

