...where molecules become real™

The Discovery of DNA

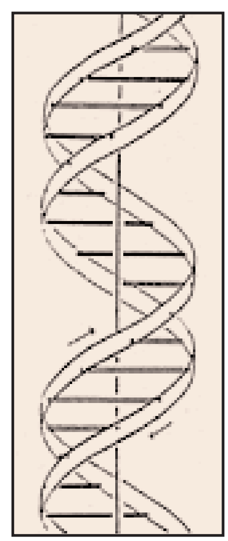
On April 25, 1953, a one-page paper entitled, *A Structure for Deoxyribonucleic Acid,* appeared in the British journal, *Nature*. The authors of this paper were James Watson, a young American post-doctoral candidate who had recently received a Ph.D. from the University of Illinois, and Francis Crick, a physicist who was completing his doctoral dissertation at Cambridge University, England. The paper began; *"We wish to suggest a structure for the salt of deoxyribose nucleic acid (D. N. A.). This structure has novel features which are of considerable biological interest."*

This initial description of the structure of DNA marked a major milestone in the development of molecular biology. In addition to reporting the correct structure of DNA, the paper also contained their classic understatement in scientific literature: *"It has not escaped our notice that the specific pairing we have postulated immediately suggests a possible copying mechanism for the genetic material."* Their paper serves as an excellent example of what has become a recurring theme in the molecular biosciences — ***Forms Follows Function***. That is, the structure of a macromolecule often explains the macromolecule's function (how the macromolecule) works.

Watson and Crick's achievement is notable in several ways, including the fact that they determined the structure of DNA without performing a single experiment. They used the information from numerous other scientists who were investigating various properties of DNA. Modeling was the major approach Watson and Crick used. Using paper cut-outs of the shapes of the four nitrogenous bases (A,T, G and C), they were able to combine all of the different facts that had accumulated to that date into a plausible model for the structure of DNA.

...The structure has two helical chains coiled around the same axis (see diagram). We have made the usual chemical assumptions, namely, that each chain consists of phosphate diester groups joining B-D-deoxyribofuranose residues with 3',5' linkages. The two chains (but not their bases) are related by a dyad perpendicular to the fibre axis. Both chains follow right-handed helices, but owing to the dyad the sequences of the atoms in the two chains run in opposite direction.

— Watson, J.D. and Crick, F.H.C., *Nature*, 171, 737-738 (1953)



Student Handout

The DNA Student Challenge

Your challenge today is to see if you can discover the correct structure of double-stranded DNA, just as Watson and Crick did over 50 years ago.

Your model should satisfy all of the pieces of experimental information that was known in 1953, as noted in the blue box below. Rather than using paper cut-outs to represent the DNA bases, you will use plastic models of the four deoxyribonucleotides whose 3D structures are based on known atomic coordinates of the B-form DNA. In these nucleotide models, magnets are used to represent both:

- the phosphodiester bonds that link the nucleotide units together into a long, linear polymer
- the hydrogen bonds that bond one base to another.

Information Available to Watson and Crick in 1953

DNA is a Polymer: Previous studies identified DNA as the genetic material of cells, and that DNA was a polymer consisting of three components:

- A nitrogenous base
- A pentose (5-carbon) sugar called deoxyribose
- A phosphate group.

Moreover, experiments suggested that the DNA molecule was unbelievably large, with molecular weights ranging from 25×10^6 to 3×10^9 daltons. (Since each nucleotide has a mass of 330 daltons, DNA molecules were believed to be composed of between 76,000 and 9,000,000 nucleotides.)

DNA is more dense than protein. At a density of 1.6 gm/cm^3, DNA was known to be more dense than protein (1.3gm/cm^3). This suggested that DNA was a densely packed structure.

Chargaff's Rules: In 1947, Erwin Chargaff demonstrated that while the four nucleotides were not present in equal amounts in the DNA from different organisms, the amount of adenine was the same as thymine, and the amount of guanine was the same as cytosine. This became known as *Chargaff's Rules:*

- The proportion of A always equals that of T, and the proportion of G always equals that of C. Thus, A = T and G = C.

X-ray Crystallography Data: In the laboratory of Maurice Wilkins, Rosalind Franklin used X-ray diffraction to analyze fibers of DNA. The pattern of spots on the X-ray diffraction pattern suggested that:

- Phosphate was on the outside, nitrogenous bases were on the inside.
- DNA was a double helix, made up of two strands.
- The two strands of DNA run in opposite directions (anti-parallel).
- There are 10 base pairs per turn of the double helix.
- The base pairs were the same width, since the double helix was uniformly wide.

Background information

You should have physical models of the four nucleotides, separated into their component parts. These include:

- Phosphate group – which is negatively charged
- Deoxyribose group — which is a cyclic ring structure
- Four nitrogenous bases (A, G, C and T)

Each component of the nucleotides is color coded according to atom type, following the standard CPK coloring scheme:

Oxygen is RED **Nitrogen is BLUE** **Phosphorus is YELLOW**
Carbon is GRAY **Hydrogen is WHITE**