Lesson one

**Discovery of the structure of DNA**

The structure of DNA double helix and how it was discovered: Chargaff, Watson and Crick, Wilkins and Franklin.

**Introduction**

Today, the DNA double helix is probably the most iconic of all biological molecules. It's inspired staircases, decorations, pedestrian bridges (like the one in Singapore), and more.

I have to agree with the architects and designers: the double helix is a beautiful structure, one whose form fits its function in a remarkable way. But the double helix was not always part of our cultural lexicon. In fact, until the 1950s, the structure of DNA remained a mystery.

In this article, we'll briefly explore how the double-helical structure of DNA was discovered through the work of James Watson, Francis Crick, Rosalind Franklin, Maurice Wilkins, and other researchers. Then, we'll take a look at the properties of the double helix itself.

**The components of DNA**

From the work of biochemist Phoebus Levene and others scientists in Watson and Crick's time knew that DNA was composed of subunits called **nucleotides.**

**The nucleotides**

 A nucleotide is made up of a sugar (deoxyribose), a phosphate group, and one of four nitrogenous bases: adenine (A), thymine (T), guanine (G) or cytosine (C).

C and T bases, which have just one ring, are called **pyrimidines**, while A and G bases, which have two rings, are called **purines**.

DNA nucleotides assemble in chains linked by covalent bonds, which form between the deoxyribose sugar of one nucleotide and the phosphate group of the next. This arrangement makes an alternating chain of deoxyribose sugar and phosphate groups in the DNA polymer, a structure known as the **sugar-phosphate backbone.**

**Chargaff's rules**

One other key piece of information related to the structure of DNA came from Austrian biochemist Erwin Chargaff. Chargaff analyzed the DNA of different species, determining its composition of A, T, C, and G bases. He made several key observations:

 A, T, C, and G were not found in equal quantities (as some models at the time would have predicted)

 The amounts of the bases varied among species, but not between individuals of the same species

 The amount of A always equalled the amount of T, and the amount of C always equalled the amount of G (A = T and G = C)

These findings, called **Chargaff's rules**, turned out to be crucial to Watson and Crick's model of the DNA double helix.

**Watson, Crick, and Rosalind Franklin**

In the early 1950s, American biologist James Watson and British physicist Francis Crick working at came up with their famous model of the DNA double helix. They were the first to cross the finish line in this scientific "race," with others such as Linus Pauling (who discovered protein secondary structure) also trying to find the correct model.

Rather than carrying out new experiments in the lab, Watson and Crick mostly collected and analyzed existing pieces of data, putting them together in new and insightful ways.

Some of their most crucial clues to DNA's structure came from Rosalind Franklin, a chemist working at the King’s College with the physicist Maurice Wilkins. Maurice Wilkins was who showed some Franklin’s data to Watson and Crick.

Franklin was an expert in a powerful technique for determining the structure of molecules, known as **X-ray crystallography**. When the crystallized form of a molecule such as DNA is exposed to X-rays, some of the rays are deflected by the atoms in the crystal, forming a **diffraction pattern** that gives clues about the molecule's structure.



X-ray diffraction image of DNA. The diffraction pattern has an X shape representative of the two-stranded, helical structure of DNA.

Franklin’s crystallography gave Watson and Crick important clues to the structure of DNA. Some of these came from the famous “image 51,” a remarkably clear and striking X-ray diffraction image of DNA produced by Franklin and her graduate student. (A modern example of the diffraction pattern produced by DNA is shown above.) To Watson, the X-shaped diffraction pattern of Franklin's image immediately suggested a helical, two-stranded structure for DNA.

**Did Watson and Crick steal Franklin’s data?**

Watson and Crick got additional information from an unpublished report by Franklin, which discussed the dimensions of the helix and the orientations of the two strands, details that proved crucial to their model.

 Franklin's report also included her conclusion that the nitrogenous bases were hidden on the inside of the DNA molecule.

Franklin's X-ray diffraction image and unpublished report were shown to Watson and Crick without Franklin's permission or knowledge. Interestingly, Franklin had shared most of the data contained in the report at an earlier, public presentation, one which Watson himself attended. Because Watson wasn't very familiar with chemistry and didn't take notes, however, he didn't remember the data correctly.

Watson and Crick did not steal Franklin's data per se, in that neither the diffraction image nor the report was confidential.

Nonetheless, they obtained and used her results in ways that showed a lack of transparency, professionalism, and respect. Watson and Crick did not ask Franklin for permission to interpret and use her data, nor did they acknowledge the extent of her contributions to their model (either when they published their work, or, nine years later, when they received the Nobel Prize).

 Indeed, during her lifetime, Franklin probably never knew how extensively Watson and Crick had relied on her data in building their mode.

**The Nobel Prize**

Watson and Crick brought together data from a number of researchers (including Franklin, Wilkins, Chargaff, and others) to assemble their celebrated model of the 3D structure of DNA. In 1962, James Watson, Francis Crick, and Maurice Wilkins were awarded the Nobel Prize in Medicine. Unfortunately, by then Franklin had died, and Nobel prizes are not awarded posthumously.

Lesson two

**Watson and Crick's model of DNA**

The structure of DNA, as represented in Watson and Crick's model, is a double-stranded, antiparallel, right-handed helix. The sugar-phosphate backbones of the DNA strands make up the outside of the helix, while the nitrogenous bases are found on the inside and form hydrogen-bonded pairs that hold the DNA strands together.

In the model above, the orange and red atoms mark the phosphates of the sugar-phosphate backbones, while the blue atoms on the interior of the helix belong to the nitrogenous bases.

**Antiparallel orientation**

Double-stranded DNA is an **antiparallel** molecule, meaning that it's composed of two strands that run alongside each other but point in opposite directions. In a double-stranded DNA molecule, the 5' end (phosphate-bearing end) of one strand aligns with the 3' end (hydroxyl-bearing end) of its partner, and vice versa.

**Right-handed helix**

In Watson and Crick's model, the two strands of DNA twist around each other to form a **right-handed helix**. All helices have a handedness, which is a property that describes how their grooves are oriented in space.

The twisting of the DNA double helix and the geometry of the bases creates a wider gap (called the **major groove**) and a narrower gap (called the **minor groove**) that run along the length of the molecule, as shown in the figure above. These grooves are important binding sites for proteins that maintain DNA and regulate gene activity.

**Base pairing**

In Watson and Crick's model, the two strands of the DNA double helix are held together by hydrogen bonds between nitrogenous bases on opposite strands. Each pair of bases lies flat, forming a "rung" on the ladder of the DNA molecule.

Base pairs aren't made up of just any combination of bases. Instead, if there is an A found on one strand, it must be paired with a T on the other (and vice versa). Similarly, an G found on one strand must always have a C for a partner on the opposite strand. These A-T and G-C associations are known as **complementary base pairs**.

**The impact of the double helix**

The structure of DNA unlocked the door to understanding many aspects of DNA's function, such as how it was copied and how the information it carried was used by the cell to make proteins.

As we'll see in upcoming articles and videos, Watson and Crick's model ushered in a new era of discovery in molecular biology. The model and the discoveries that it enabled form the foundations for much of today's cutting-edge research in biology and biomedicine.

