

The Race to Discover DNA's Structure



Francis
Crick



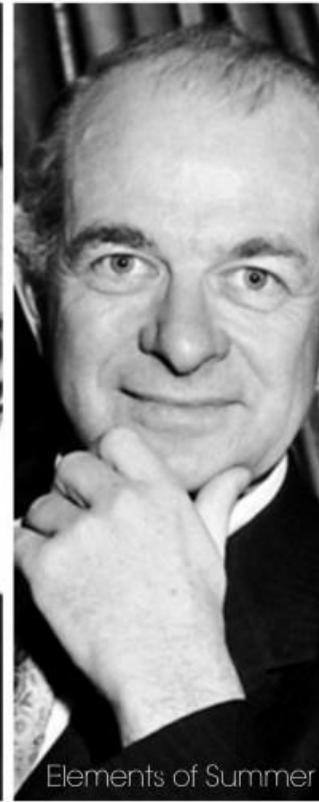
James
Watson



Rosalind
Franklin



Maurice
Wilkins



Linus
Pauling



Questions to Consider

- What developments resulted in the formation of molecular biology by the 1930s?
- What factors contributed to the discovery of the structure of the DNA molecule and its function of transmitting genetic code?
- What was the cultural, political, and social context of international science in the 1950s?
- How did this conflict shape the race to discover the structure of DNA and who ultimately got credit for it?

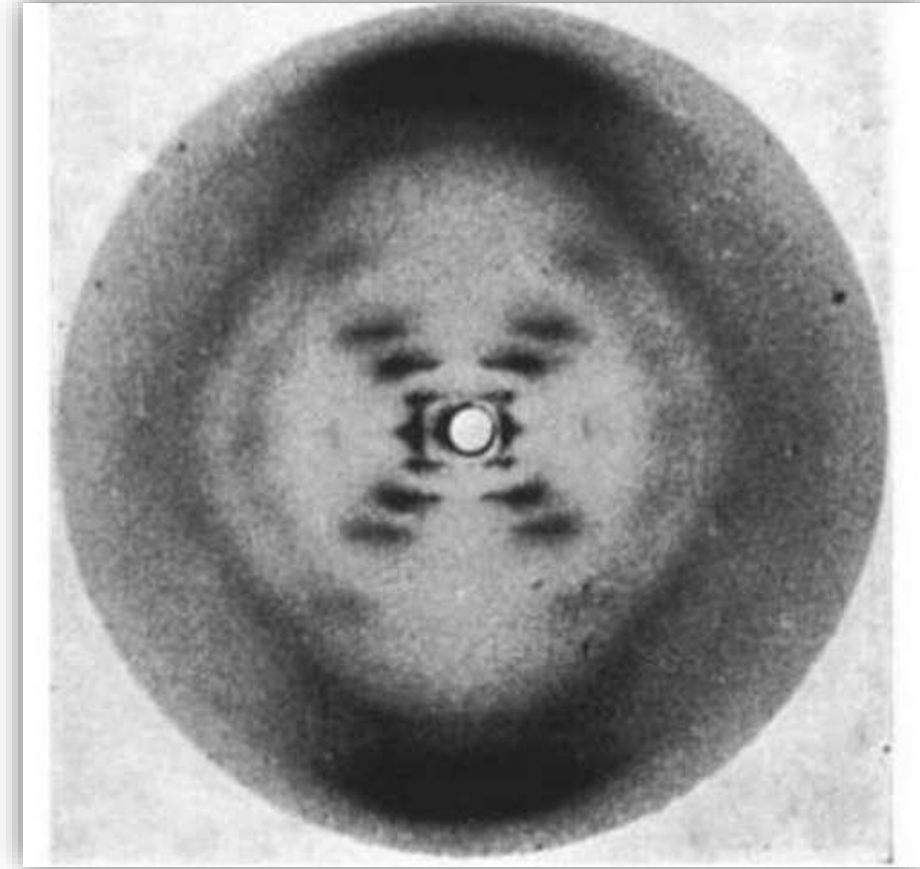
I. Scientific Context: Toward Molecular Biology

Molecular Biology: New science at the intersection of genetics, biochemistry, and biophysics that emerged in the 1930s

1869: nucleic acid (later: DNA & RNA) identified

1910-1915: “Classical Genetics” (T.H. Morgan)

1920s: New tool to study cell molecules from chemistry and physics: **x-ray crystallography**



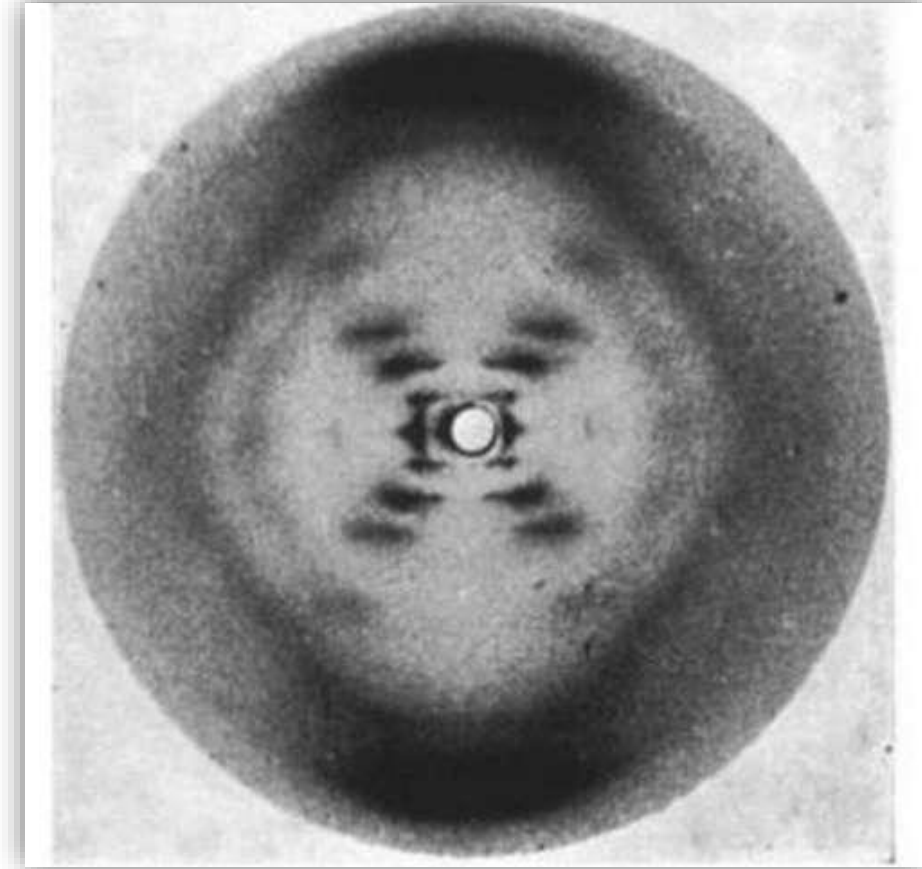
Photograph 51:
Raymond Gosling and Rosalind Franklin
Kings College London (1952)

I. Scientific Context: Toward Molecular Biology

1930-1950: Debate: do **proteins** or **nucleic acid** transmit genetic information?

Core Question: What is the structure and mechanism of DNA?

Scientific race to discover this in the early 1950s.



Photograph 51:
Raymond Gosling and Rosalind Franklin
Kings College London (1952)

II. Historical Context: 1950s Britain and America

Red Scare: deep anxieties about communism

Postwar return to gender conservatism

- white, middle-class ideal
- competitive male professional in the workplace
- domestic, nurturing female housewife and mother

Expanding opportunities for international travel



American Airlines Ad (1950s)

III. Social Context: International Science

Science had long been an international endeavor

- journals, meetings, private correspondence

20th Century International Science

- quicker travel and communications opportunities
- international organizations
- international conferences
- international journals
- international prizes

Nobel Prizes (Since 1901)

- Alfred Nobel (1833-1896) – chemist / dynamite inventor
- Chemistry, Physics, Medicine, Literature, and Peace
- became the TOP prize for a scientist

Cooperation and Competition



Linus and Ava Pauling Dancing at
His Nobel Prize Banquet (1954)

Nature (Journal)

- published in Britain since 1869
- became leading international journal during mid-20th century

Science (Journal)

- published in U.S. since 1882
- became leading international journal during mid-20th century

Publishing a first-author paper in *Nature* or *Science* can make a scientific career

Watson's & Crick's
First Description of
DNA's Double Helix in *Nature*
April 25, 1953

King's College, London. One of us (J. D. W.) has been aided by a fellowship from the National Foundation for Infantile Paralysis.

J. D. WATSON
F. H. C. CRICK

Medical Research Council Unit for the
Study of the Molecular Structure of
Biological Systems,
Cavendish Laboratory, Cambridge.
April 2.

James Watson
Francis Crick

¹ Pauling, L., and Corey, R. B., *Nature*, 171, 346 (1953); *Proc. U.S. Nat. Acad. Sci.*, 39, 84 (1953).

² Furberg, S., *Acta Chem. Scand.*, 6, 634 (1952).

³ Chargaff, E., for references see Zamenhof, S., Brawerman, G., and Chargaff, E., *Biochim. et Biophys. Acta*, 9, 402 (1952).

⁴ Wyatt, G. R., *J. Gen. Physiol.*, 36, 201 (1952).

⁵ Astbury, W. T., *Symp. Soc. Exp. Biol.*, 1, Nucleic Acid, 66 (Camb. Univ. Press, 1947).

⁶ Wilkins, M. H. F., and Randall, J. T., *Biochim. et Biophys. Acta*, 10, 192 (1953).

Molecular Structure of Deoxypentose Nucleic Acids

WHILE the biological properties of deoxypentose nucleic acid suggest a molecular structure containing great complexity, X-ray diffraction studies described here (cf. Astbury¹) show the basic molecular configuration has great simplicity. The purpose of this communication is to describe, in a preliminary way, some of the experimental evidence for the polynucleotide chain configuration being helical, and existing in this form when in the natural state. A fuller account of the work will be published shortly.

The structure of deoxypentose nucleic acid is the same in all species (although the nitrogen base ratios alter considerably) in nucleoprotein, extracted or in cells, and in purified nucleate. The same linear group of polynucleotide chains may pack together parallel in different ways to give crystalline¹⁻³, semi-crystalline or paracrystalline material. In all cases the X-ray diffraction photograph consists of two regions, one determined largely by the regular spacing of nucleotides along the chain, and the other by the longer spacings of the chain configuration. The sequence of different nitrogen bases along the chain is not made visible.

Oriented paracrystalline deoxypentose nucleic acid ('structure B' in the following communication by Franklin and Gosling) gives a fibre diagram as shown in Fig. 1 (cf. ref. 4). Astbury suggested that the strong 3.4-A. reflexion corresponded to the internucleotide repeat along the fibre axis. The ~34 Å. layer lines, however, are not due to a repeat of a polynucleotide composition, but to the chain configuration repeat, which causes strong diffraction as the nucleotide chains have higher density than the interstitial water. The absence of reflexions on or near the meridian immediately suggests a helical structure with axis parallel to fibre length.

Diffraction by Helices

It may be shown⁵ (also Stokes, unpublished) that the intensity distribution in the diffraction pattern of a series of points equally spaced along a helix is given by the squares of Bessel functions. A uniform continuous helix gives a series of layer lines of spacing corresponding to the helix pitch, the intensity distribution along the n th layer line being proportional to the square of J_n , the n th order Bessel function. A straight line may be drawn approximately through

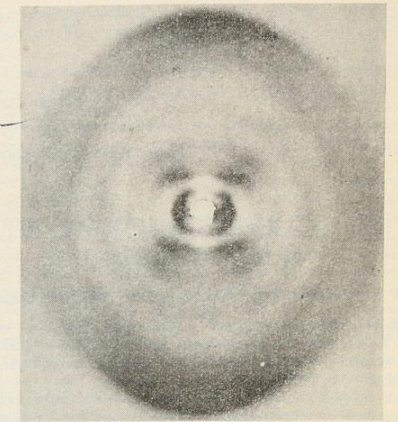


Fig. 1. Fibre diagram of deoxypentose nucleic acid from *B. coli*. Fibre axis vertical

the innermost maxima of each Bessel function and the origin. The angle this line makes with the equator is roughly equal to the angle between an element of the helix and the helix axis. If a unit repeats n times along the helix there will be a meridional reflexion (J_0^2) on the n th layer line. The helical configuration produces side-bands on this fundamental frequency, the effect⁶ being to reproduce the intensity distribution about the origin around the new origin, on the n th layer line, corresponding to C in Fig. 2.

We will now briefly analyse in physical terms some of the effects of the shape and size of the repeat unit or nucleotide on the diffraction pattern. First, if the nucleotide consists of a unit having circular symmetry about an axis parallel to the helix axis, the whole diffraction pattern is modified by the form factor of the nucleotide. Second, if the nucleotide consists of a series of points on a radius at right-angles to the helix axis, the phases of radiation scattered by the helices of different diameter passing through each point are the same. Summation of the corresponding Bessel functions gives reinforcement for the inner-

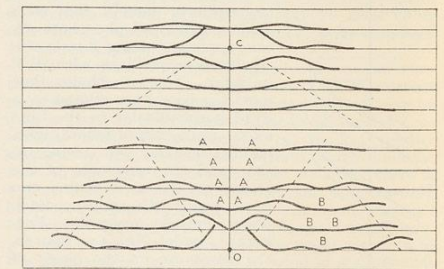


Fig. 2. Diffraction pattern of system of helices corresponding to structure of deoxypentose nucleic acid. The squares of Bessel functions are plotted about 0 on the equator and on the first, second, third and fifth layer lines for half of the nucleotide mass at 20 Å. diameter and remainder distributed along a radius, the mass at a given radius being proportional to the radius. About C on the tenth layer line similar functions are plotted for an outer diameter of 12 Å.

IV. Race to Discover DNA's Structure



Francis Crick
British
Ph.D. (1954)
Cavendish
Laboratory
University of
Cambridge



James Watson
American
Ph.D. (1950)
Cavendish
Laboratory
University of
Cambridge



Rosalind
Franklin
British
Ph.D. (1945)
King's College
London



Maurice
Wilkins
New Zealander
Ph.D. (1940)
King's College
London



Linus Pauling
American
Ph.D. (1925)
California
Institute of
Technology

A. Linus Pauling: California Institute of Technology

California Institute of Technology

Linus Pauling (1901-1994)

- leading American chemist of the 20th century
- famous anti-war and anti-nuclear weapons activist

The Nature of the Chemical Bond (1939)

Focused on protein as transmitter of genetic code until 1952



Linus Pauling at Caltech 1935

B. Watson and Crick: University of Cambridge

Cavendish Laboratory

- Cambridge University
- W.L. Bragg: leading X-Ray crystallographer

James Watson

- geneticist
- postdoc researcher

Francis Crick

- biophysicist
- Ph.D. student

Focus on DNA as transmitter of genetic code since 1951



James Watson and Francis Crick

C. Rosalind Franklin and Maurice Wilkens: Kings College

Kings College London

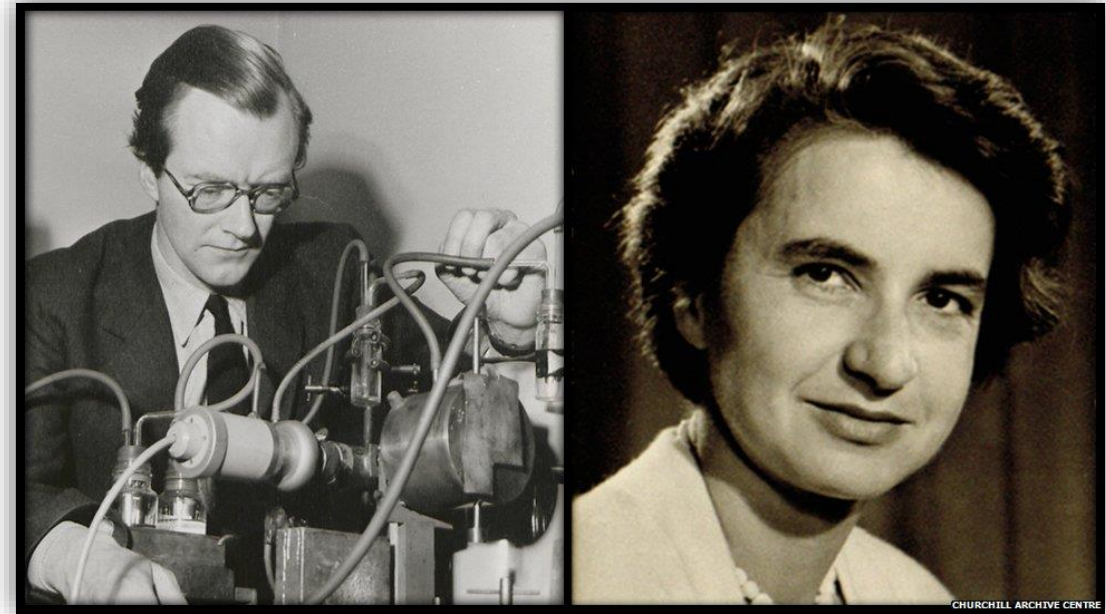
Rosalind Franklin

- chemist and X-Ray crystallographer
- research scientist

Maurice Wilkens

- physicist
- research scientist

Focus on perfecting X-Ray crystallography
photographs of DNA molecule



Maurice Wilkins and Rosalind Franklin

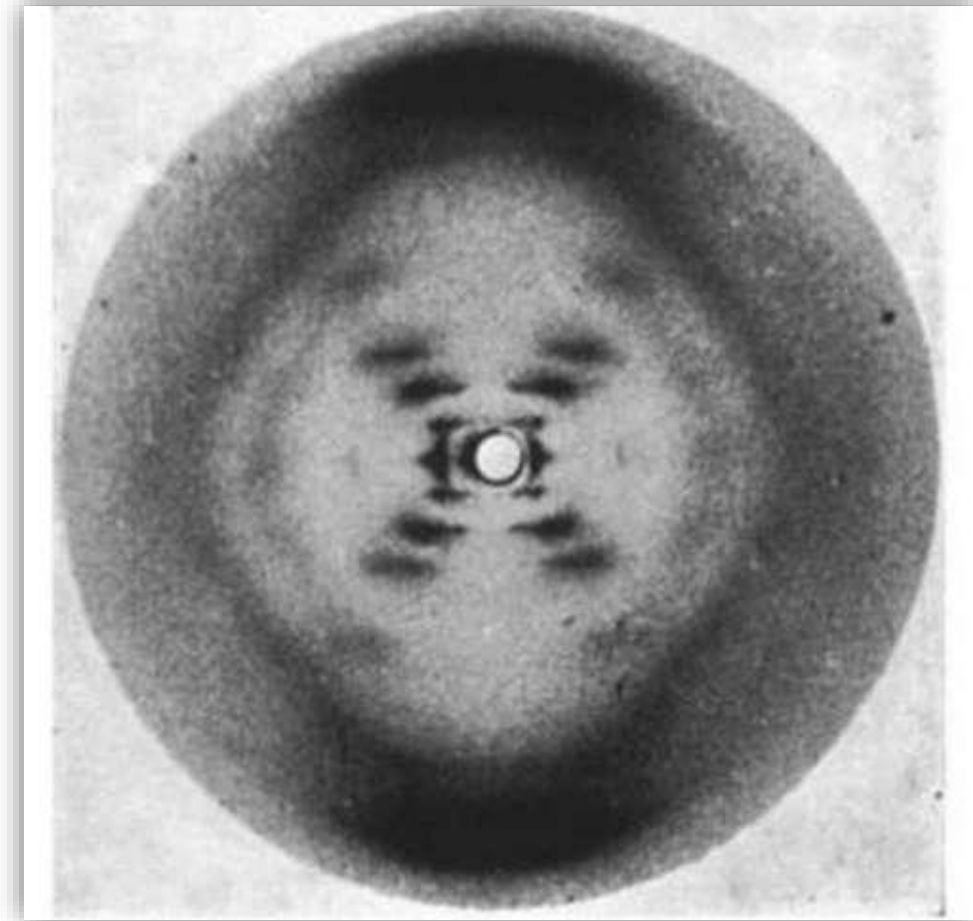
D. Rosalind Franklin Provides the Evidence

May 1952

Franklin and her student, Raymond Gosling, take a series of clear X-Ray photographs of DNA structure

Photographs 51 and 52: shows clearly the double helix structure of DNA

Sent article manuscripts out for publication in March 1953



Photograph 51:
Raymond Gosling and Rosalind Franklin
Kings College London (1952)

E. Pauling's Triple Helix

Summer 1952: Pauling invited to conference in UK

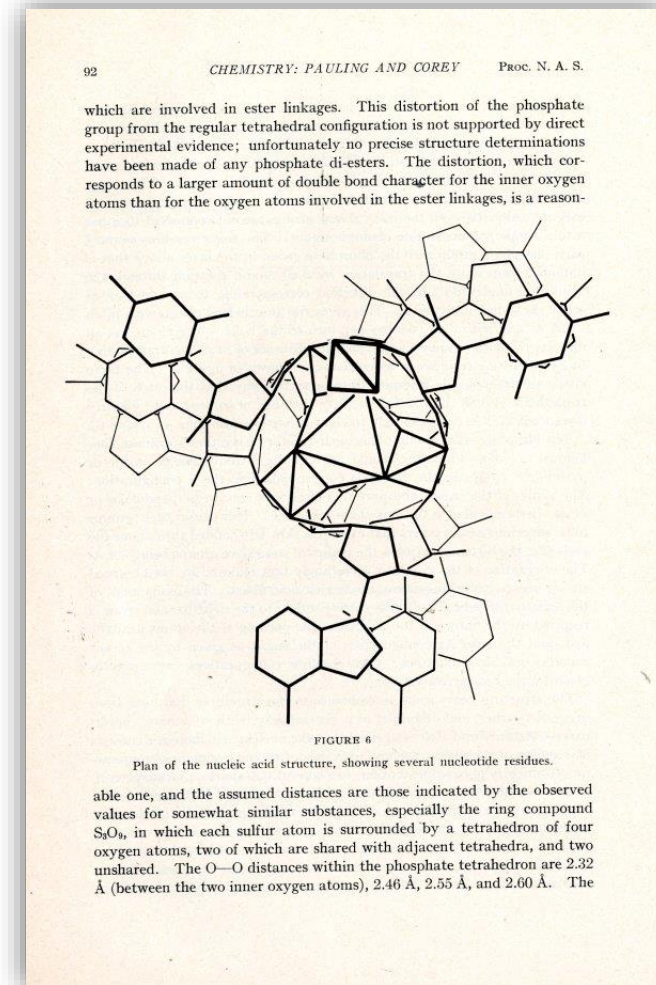
Pauling denied a passport by U.S. government

- falsely accused of being a communist
- finally got a passport but did not visit Kings College

Son working at Cavendish Laboratory and told him that Watson's & Crick's were close to completing their model of DNA

Rushed to publish his Triple Helix model of DNA

- Dec 1952 - submitted manuscript
- Feb 1953 – published in *Nature*



Linus Pauling's Triple Helix Model
February 1953

E. Watson and Crick's Double Helix Model

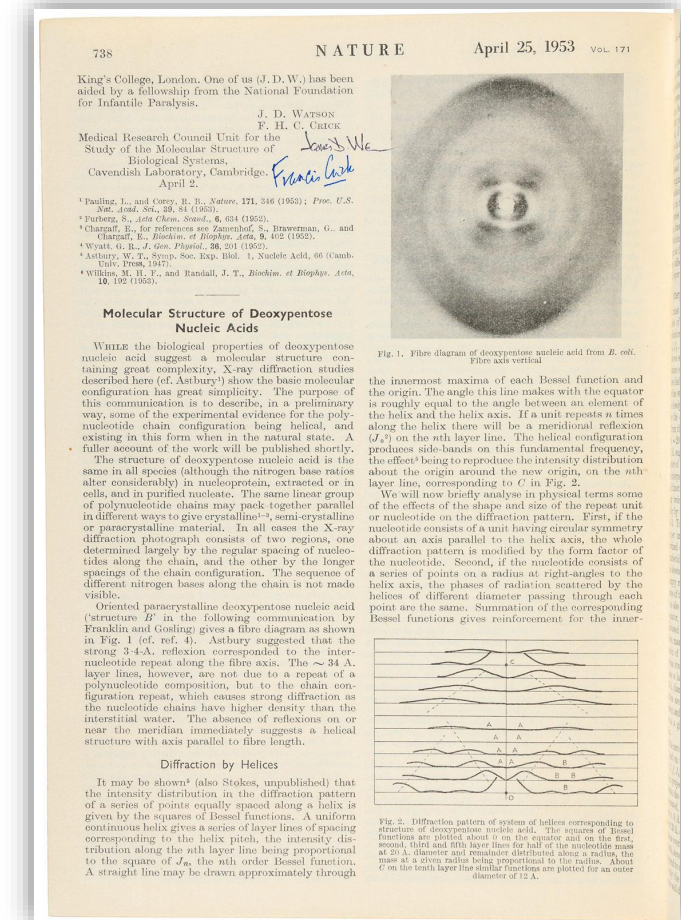
Learned about Pauling's article and were initially disappointed

Maurice Wilkins showed Franklin's Photographs 51 & 52 to Watson and Crick without her permission

Evidence they needed to confirm their double helix model of DNA – Pauling was wrong

Rushed to publish the Double Helix model of DNA

- Feb 1953 - submitted manuscript
- Apr 1953 – published in *Nature*



Watson's & Crick's
First Description of
DNA's Double Helix in *Nature*
April 25, 1953

V. Nobel Prize for Discovery of DNA Structure

1962 Nobel Prize in Physiology or Medicine

- Watson
- Crick
- Wilkens

Rosalind Franklin had died in 1958

- her work was not recognized by Nobel Prize committee

Linus Pauling won a Nobel Prize in Chemistry in 1954 for his work on protein structure



Watson, Crick, Wilkins, and Other Nobel Prize Winners in 1962