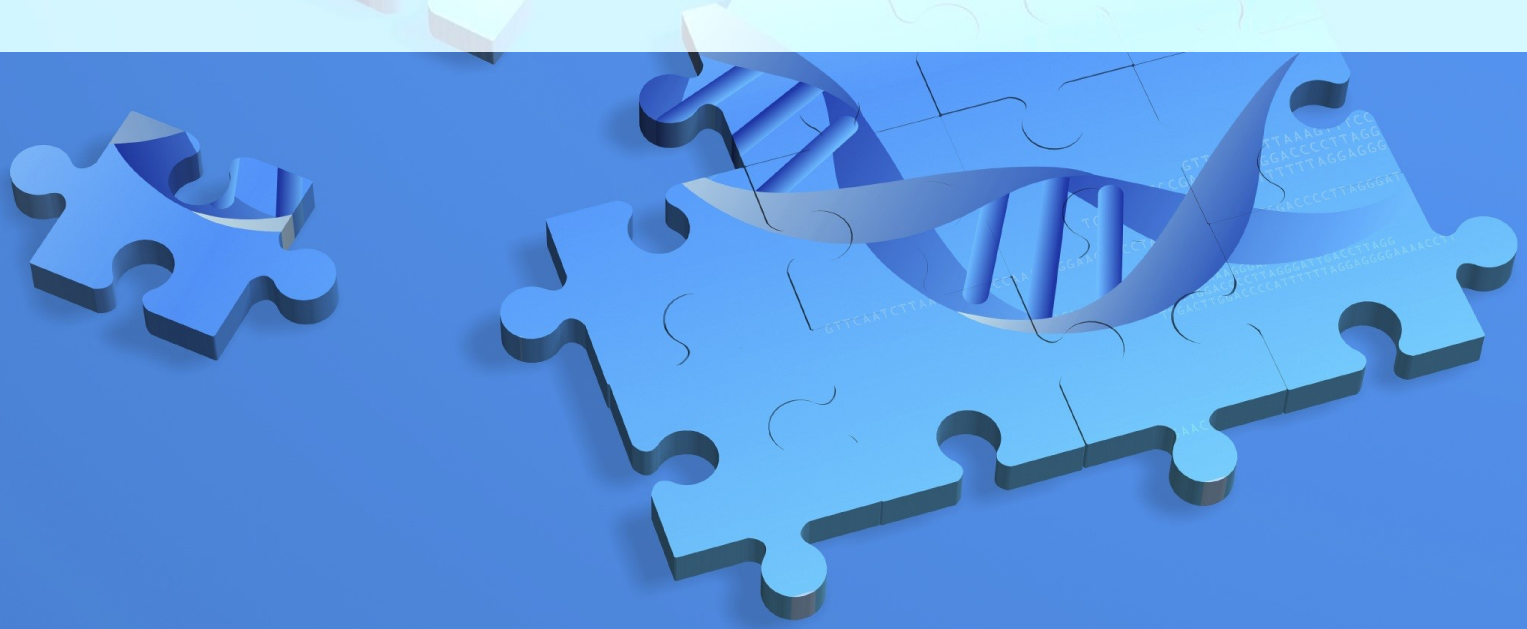
The Puzzle:
Determining the Structure of DNA



Watson, Crick, Franklin and Wilkins

World Happenings of 1953

Politics

Dwight D. Eisenhower Elected

Joseph Stalin Dies

Queen Elizabeth II Coronation

War

Korean War armistice signed


THE DEMOCRAT

RUSSIA HAS ATOMIC BOMB!

U. S. Learns of Recent Explosion, President Discloses

Pentagon Shows Excitement, But Officials Mum

Bargaining In Steel Resumed

Russ Possession of Bomb Peace Threat, Congressmen Believe

U. S. Still Ahead of Russians

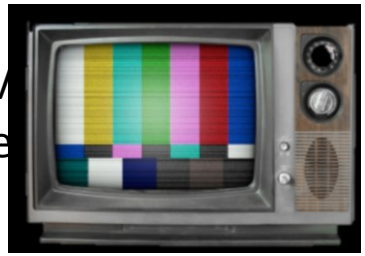
Details on Blast in USSR Not Revealed; Vishinsky Urges Pact

ALCOA Fights Bettendorf's Adoption Plan

Soviet Union announces H-bomb

Social Aspects

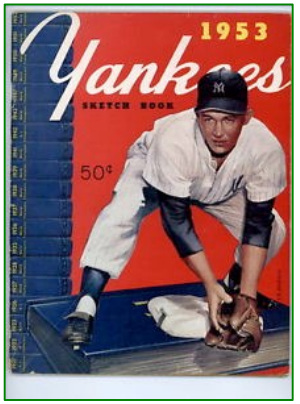
First Corvette manufactured by Chevorlet



First Color TV for sale

Hugh Hefner releases first Playboy

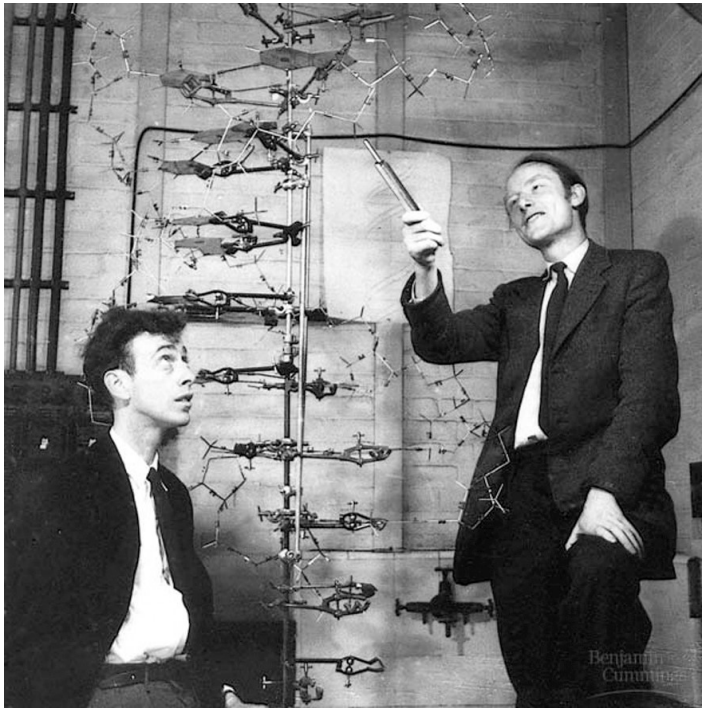
Mickey Mantle hit longest homerun in history



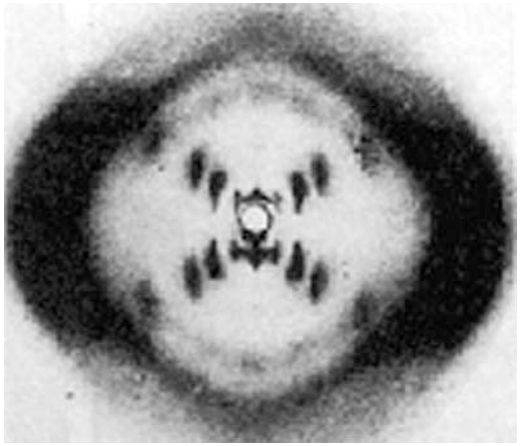
Science Happenings of 1953

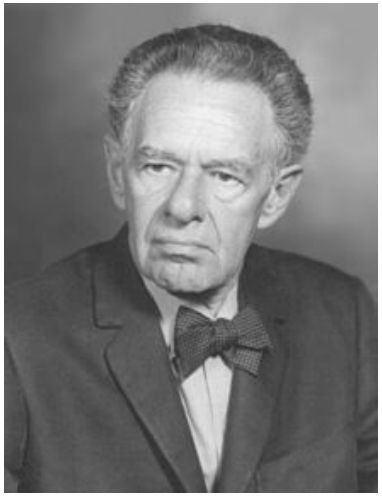
Polio Vaccine developed by Jonas Salk

Francis Crick and James Watson publish "Molecular Structure of Nucleic Acids: A Structure for DNA" in *Nature*



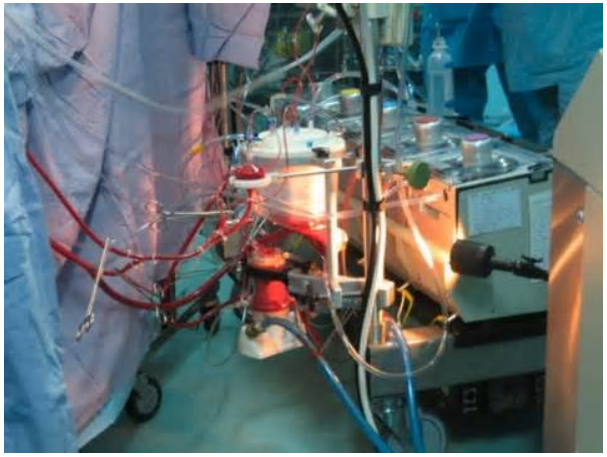
Maurice Wilkins publishes X-ray crystallography results for DNA in *Nature*



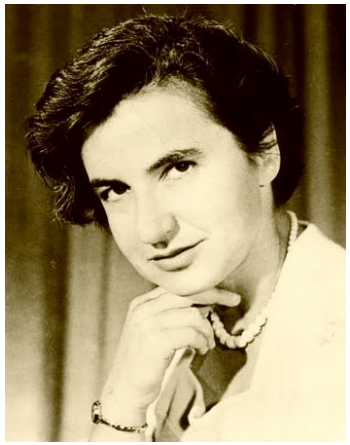


Nobel prize in Physiology or Medicine awarded to Fritz Albert Lipmann for the discovery of coenzyme A

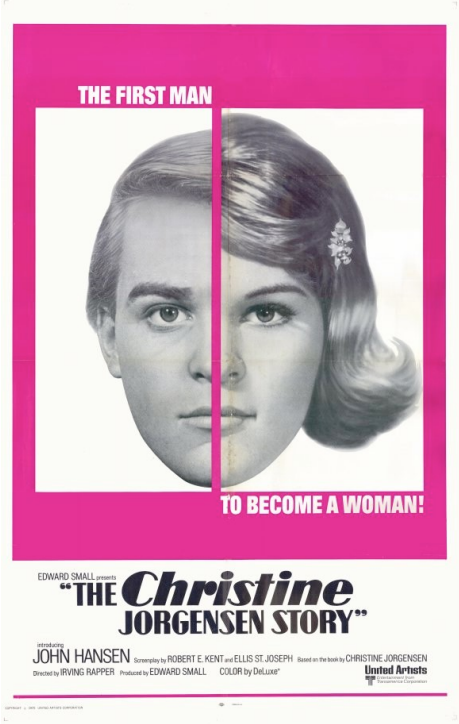
Science Happenings of 1953



The first successful open heart surgery on a human utilizing a cardiopulmonary bypass pump is performed by John Gibbon

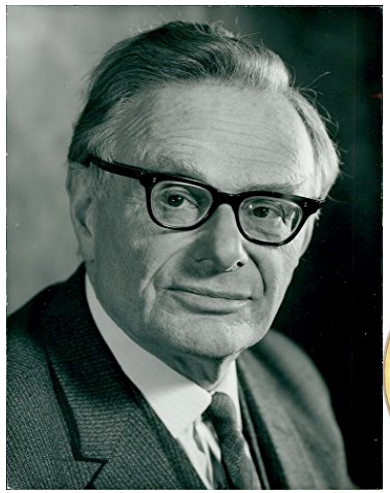


Rosalind Franklin and Raymond Gosling publish on “Molecular Configuration in Sodium Thymonucleate” in *Nature*



Christine Jorgenson, the first widely known American transsexual, returns to New York after successful sexual reassignment surgery in Denmark.

Nobel prize in Physiology or Medicine awarded to Sir Hans Adolf Kreb for the work on cellular respiration (Kreb Cycle)



Day1

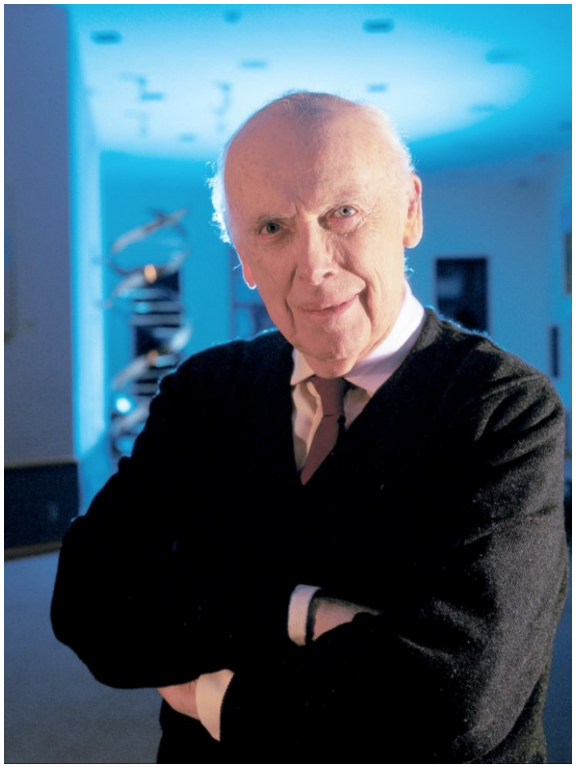
James Dewey Watson

- American molecular biologist, geneticist and zoologist
- Born April 6, 1928 In Chicago, IL

- Luria and Delbruck's work inspired him to pursue Molecular Biology
- Enrolled at University of Chicago at the age of 15 (B.S., 1947 in Zoology)
- Indiana University (Ph.D., 1950) under Salvad Luria in the "Phage Group"
- Postdoctoral research under Herman Kalckar in Copenhagen in England
  - enzymatic synthesis of nucleic acids
  - Kalcker did not want him to pursue his DNA structure interest

James Dewey Watson

- Worked at the University of Cambridge's Cavendish Laboratory in England
- From 1956 to 1976, Harvard Faculty in the Biology Department
- 1962 Received the Nobel Prize in Physiology or Medicine
- 1968 he served as director of Cold Spring Harbor Laboratory on Long Island, New York where he focused on Cancer research



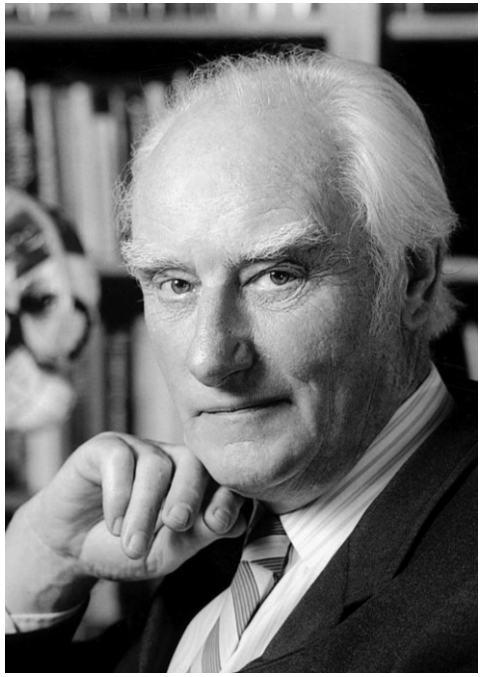
- Helped to establish the Human Genome Project
- Between 1988 and 1992, Watson was associated with the NIH

Francis Harry Compton Crick

- British molecular biologist, biophysicist, and neuroscientist
- June 8,1916– July 28, 2004
- Grandfather was a naturalist that corresponded with Darwin
- Age 8 – Northampton Grammar school
- Age 14- Mill Hill School in London for mathematics, physics, and chemistry

- Age 21 – B.S. in physics from University College London
- PhD from Gonville and Caius College, Cambridge
  - Started in Physics measuring the viscosity of water at high temperatures

Francis Harry Compton Crick



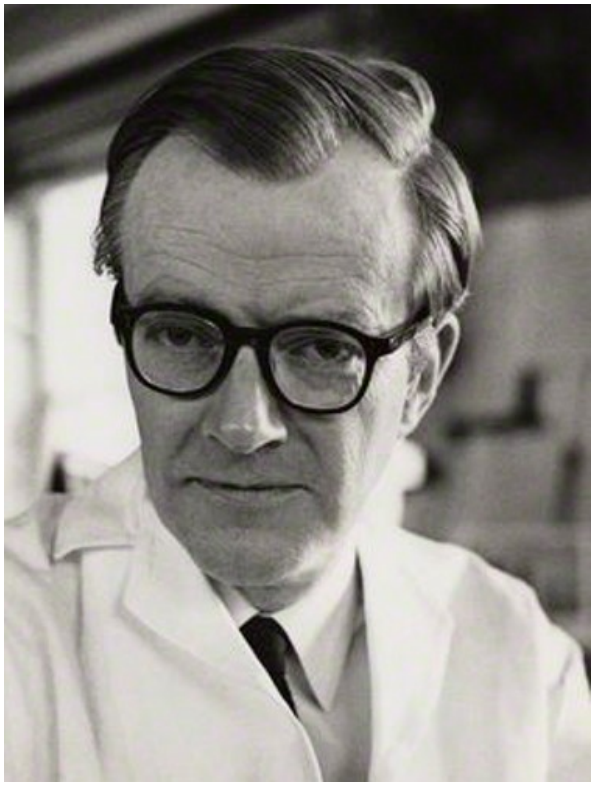
- During WWII he worked on magnetic and acoustic mines
- 1947 began work on the physical properties of cytoplasm at Cambridge under Bragg
- Known for the use of the term “Central Dogma”
- Awarded Nobel Prize for Physiology or Medicine in 1962
- Later research focused on theoretical neurobiology and attempts to advance the scientific study of human consciousness
- “He was editing a manuscript on his death bed, a scientist until the bitter end” – Christof Koch

Maurice Hugh Frederick Wilkins

- New Zealand born English physicist and molecular biologist
- December 15, 1916 – October 5, 2004
- Phosphorescence, isotope separation, optical microscopy, X-ray diffraction, and radar development
- Wylde Green College & King Edward's school (1929-1935)
- B.A. in Physics and Natural science from St. John's College, Cambridge in 1935

Maurice Hugh Frederick Wilkins

- Ph.D . from Randall at Birmingham University (1945)
  - Phosphorescence and electron traps



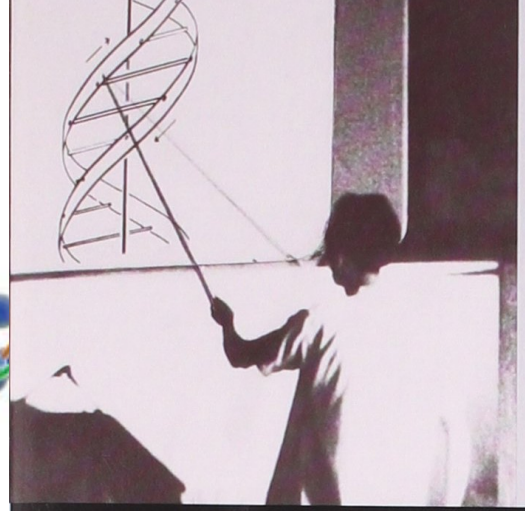
- WWII he worked to improve radar screens and was part of the Manhattan project at UC-Berkley (1944-1945)
- King's College
  - X-ray diffraction on ram sperm and DNA from calf thymus
- Accepted Rosalind Franklin into his lab to aid in the DNA x-ray diffraction study
- Awarded Nobel Prize for Physiology or Medicine in 1962

Rosalind Elise Franklin

- July 25, 1920 – April 16, 1958
- English chemist and x-ray crystallographer
- Contributed to DNA, RNA, viral, and graphite structure determination
- 1941 graduated from Natural Sciences at Newnham College, Cambridge
- 1941 University of Cambridge under Ronald Norrish
- 1942 Switched to British Coal Utilization Research Association

Rosalind Elise Franklin

- 1945 Ph.D. under Jacques Mering
  - X-ray crystallography
- 1951 Kings College as a research associate
  - Randall's lab with Wilkins
- Faced major adversity
- Published in sequence with Watson and Crick as well as Wilkins
- Watson, Crick, and Wilkins, but not Franklin, were awarded the 1962 Nobel
  - Watson believed Franklin should have been awarded the Nobel in Chemistry



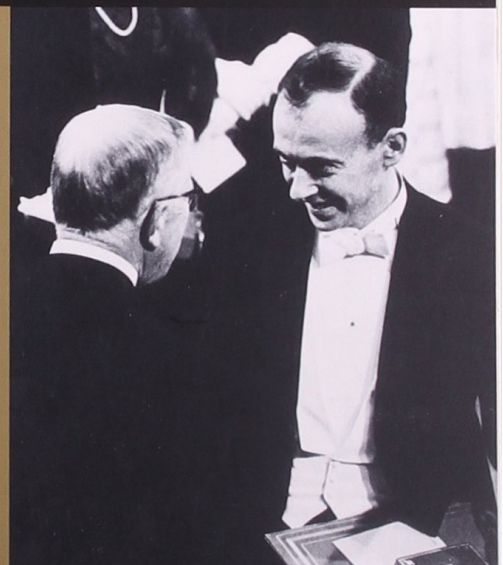
"A fascinating case history . . . Describes the events that led up to one of the great biological discoveries of our time."
—Robert K. Merton, *The New York Times Book Review*

THE DOUBLE HELIX

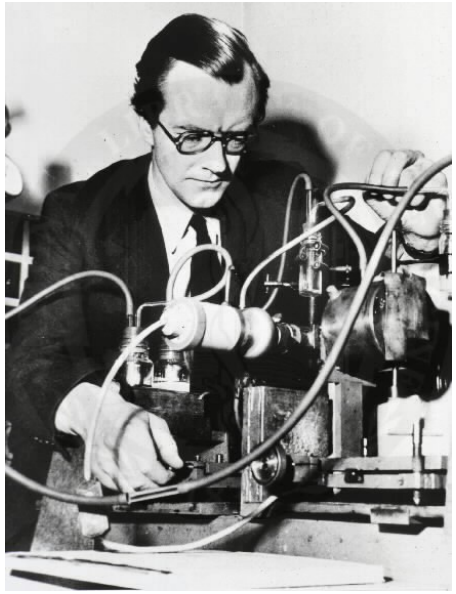
A Personal Account of the Discovery of THE STRUCTURE OF DNA

JAMES D. WATSON

Introduction by
SYLVIA NASAR
Author of *A Beautiful Mind*



Determining the Structure of DNA: Putting the Pieces Together



Wilkins

From 1948–50, Wilkins worked on his initial attempts to produce the first clear X-ray images of DNA - which he did successfully

November 1951 - evidence that DNA in cells as well as purified DNA had a helical structure

From 1951–52 he produced clear "B form" "X" shaped images from squid sperm

Began working with Watson after 1951 presentation in Naples.

- Watson was convinced of the Helical structure of DNA
- Crick thought he should put his efforts toward proteins

After Watson and Crick solved the structure of DNA
he verified and made significant corrections to the model

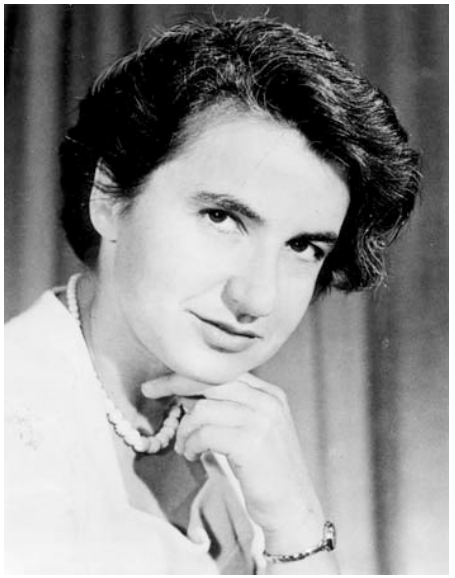
Determining the Structure of DNA: Putting the Pieces Together

Franklin

Was very "secretive" about her work in that she would not share her X-ray diffraction images with Wilkins

She presented her findings along with her image of DNA - She was more or less ignored

Watson and Crick took an interest in her images (water content)



Lead to three chain helical model (Watson/Crick first attempt)

She did not believe the structure was helical

Her "B" model was then determined and shown to Watson without here permission

Really lead to **double** helix model

Determining the Structure of DNA: Putting the Pieces Together

Watson and Crick

Watson and Crick Met at Cambridge in England

Also met Wilkins and Franklin through visits to King's College in London

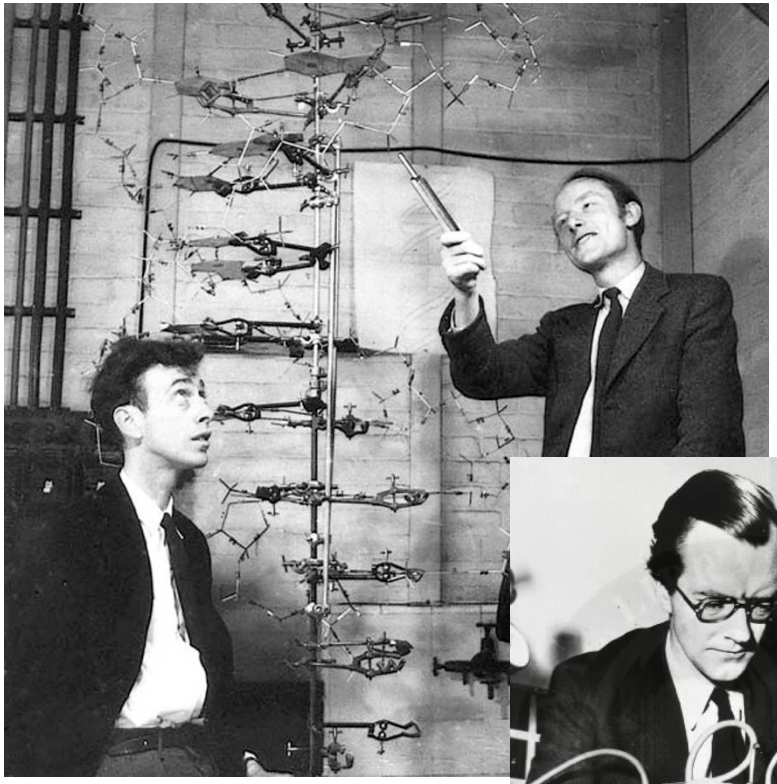
Watson finally was able to pursue his interest in determining the structure of DNA

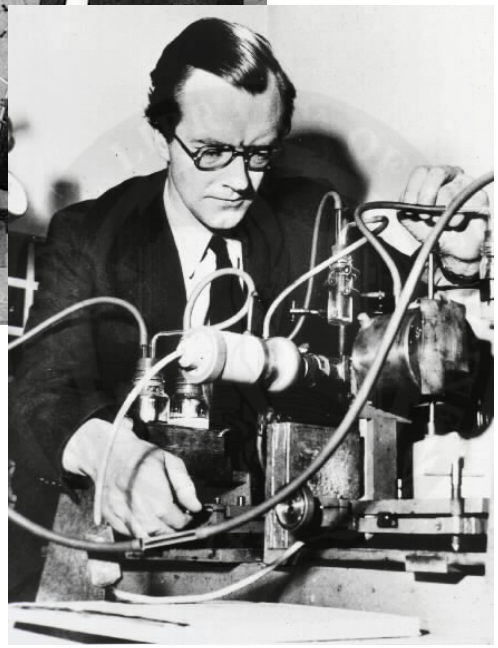
First model was a triple helix – lead to Bragg banning them from working on DNA structure

Using experimental data collected by Rosalind Frankli and Maurice Wilkins, as well as thoughts from other scientist such as Chargaff and Pauling, Watson and Cr deduced the double helix structure of DNA

The Nobel Prize 1962

Watson, Crick, and Wilkins were awarded the 1962 Nobel Prize in Physiology or Medicine **"for their discoveries concerning the molecular structure of nucleic acids and its significance for information transfer in living material"**





Maurice H. F. Wilkins

MOLECULAR STRUCTURE OF DEOXYPENTOSE NUCLEIC ACIDS

Rosalind Elise Franklin

R. G. Gosling

MOLECULAR CONFIGURATION IN SODIUM THYMONUCLEATE

Nature

April 25, 1953

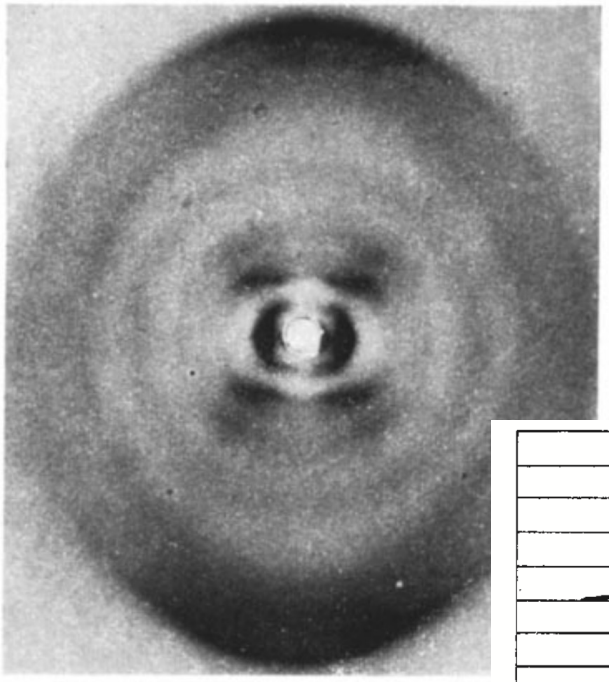


Fig. 1. Fibre diagram of deoxypentose nucleic aci
Fibre axis vertical

Wilkins

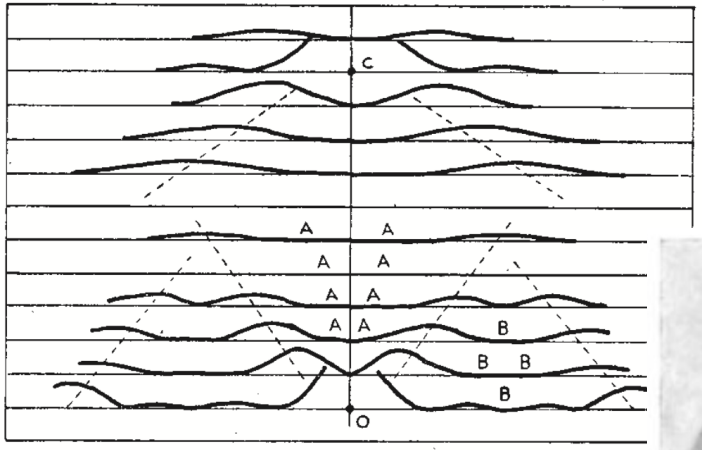
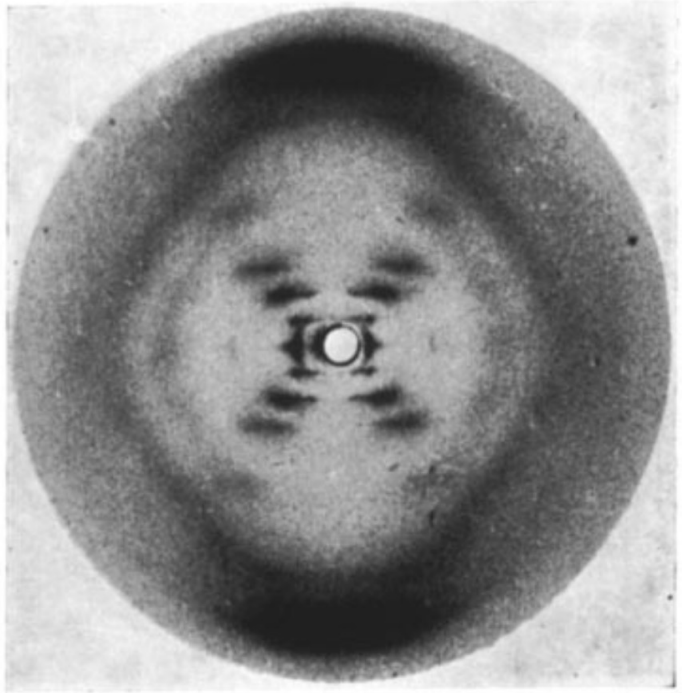


Fig. 2. Diffraction pattern of system of helices corresponding
structure of deoxypentose nucleic acid. The squares of Be
functions are plotted about 0 on the equator and on the fi
second, third and fifth layer lines for half of the nucleotide n
at 20 A. diameter and remainder distributed along a radius,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

Wilkins

Franklin



Sodium deoxyribose nucleate from calf thymus. Structure *B*

***Nature* April 25, 1953**

Wilkins' X-ray Diffraction Paper

- Biological properties of DNA suggest a complex molecular structure the x-ray diffraction patterns seen in this study show great simplicity
    - This was a major surprise
        - How could something that encodes everything be "simple"

- Purpose of the paper
    - Show that the conformation of DNA was helical and that this form was conserved across species

Wilkins' X-ray Diffraction Paper

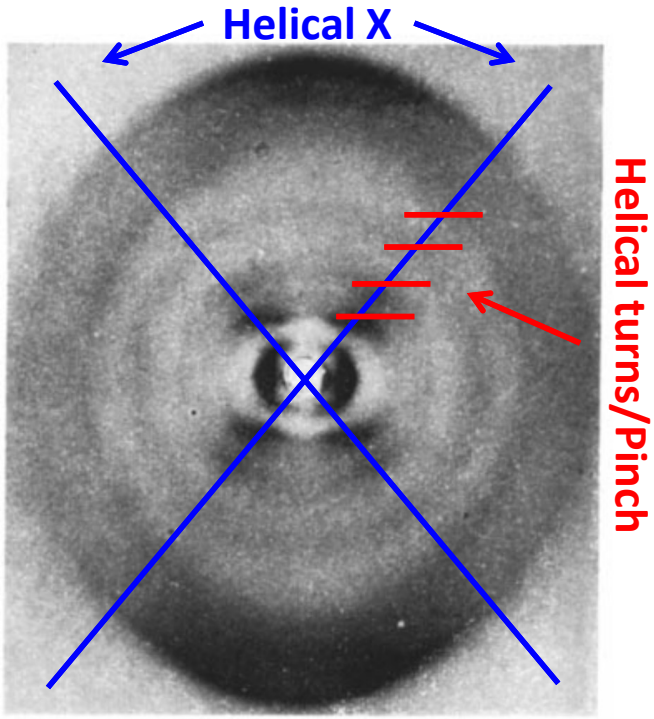


Fig. 1. Fibre diagram of deoxypentose nucleic acid from *B. coli*. Fibre axis vertical

- Lots of math involved
- General idea of Xray diffraction norms of a helix
    1) formation of an "x"
    2) Series of points equally spaced from the core to the outside
- This information can then be used to determine:
    - Distance between turns
    - How far apart nucleotides are spaced
    - The angles of the axis

Wilkins' X-ray Diffraction Paper

Interpretation of Results

- Could be one or multiple helices
  - Just have to adjust the helical pinch to fit within parameters
- To have enough nucleotides seems likely that two or three helices are required

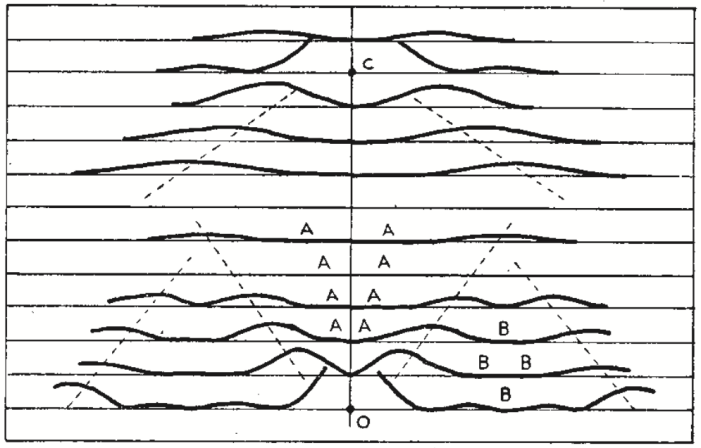
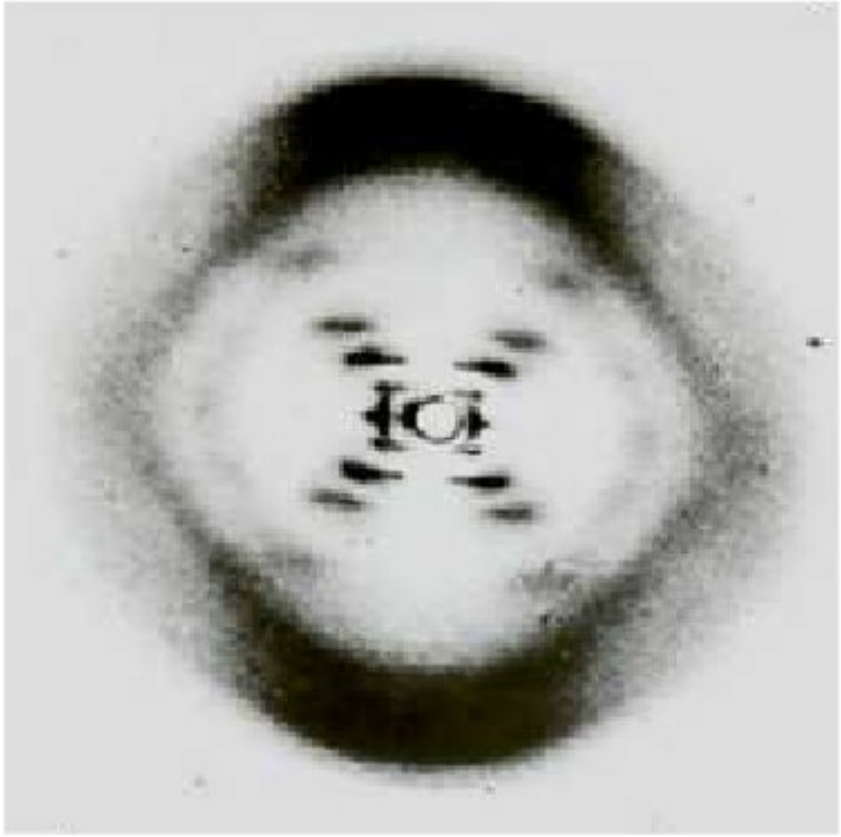


Fig. 2. Diffraction pattern of system of helices corresponding to structure of deoxypentose nucleic acid. The squares of Bessel functions are plotted about 0 on the equator and on the first, second, third and fifth layer lines for half of the nucleotide mass at 20 A. diameter and remainder distributed 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 A.

- Sharps "spots" from X-ray (helical turn/pinch points) indicate a degree of order
  - Multiple helices must be ordered relative to one another
- Helices have a max diameter of 20 angstroms
- Based on data, Watson and Crick's model seems plausible

Rosalind's B-Form Crystallography Paper

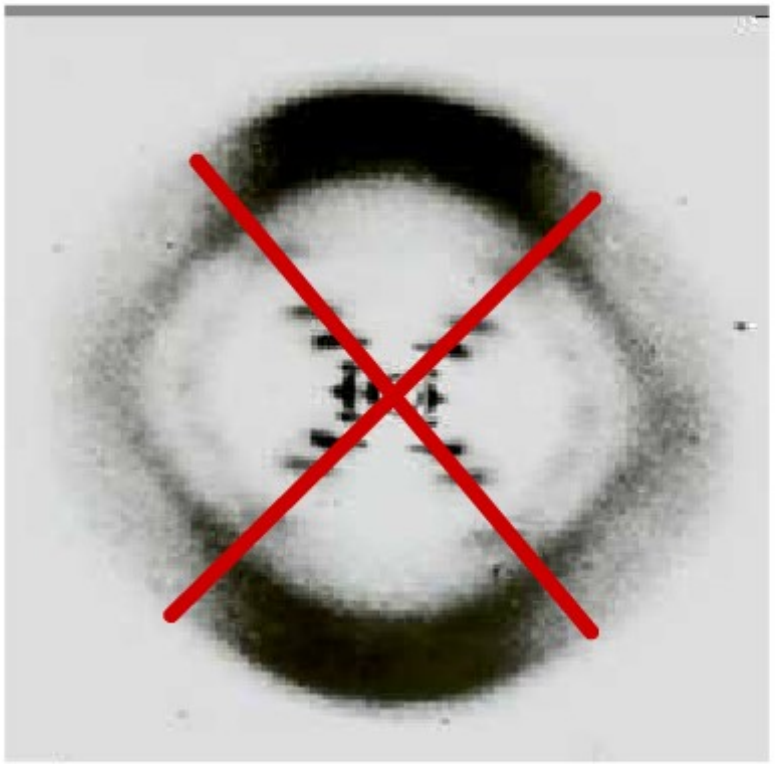
Rosalind and Gosling X-ray crystallography image of the B form of DNA. This image was of better quality due to **the presence of water in the sample**



***Nature* April 25, 1953**

Rosalind's B-Form Crystallography Paper

The "X" pattern formed here is a telltale pattern of a helix.

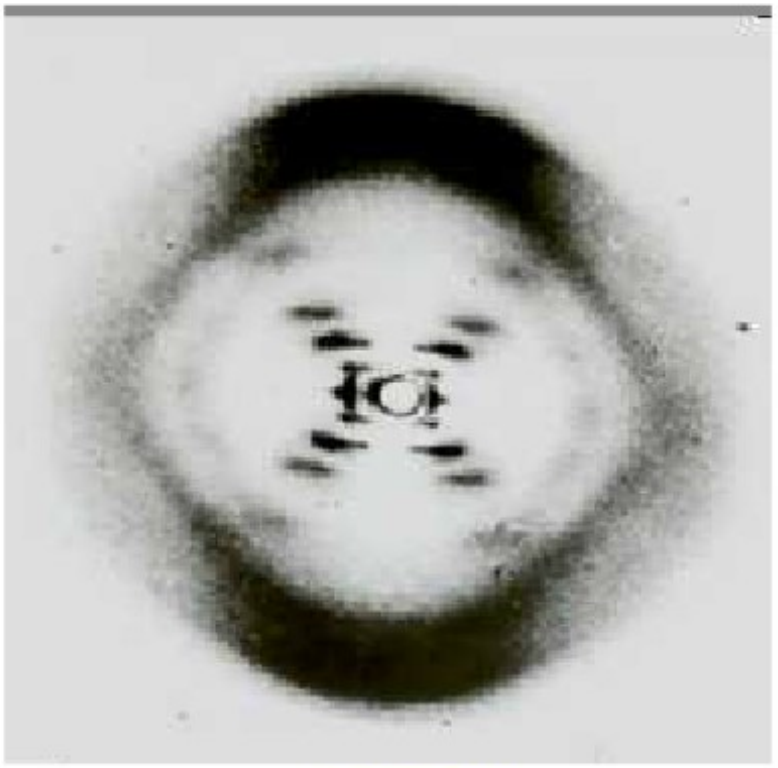


B-FORM

FRANKLIN

Rosalind's B-Form Crystallography Paper

This pattern in the x-ray image is so clear that the helix must be constant, as in the diameter stays the same throughout

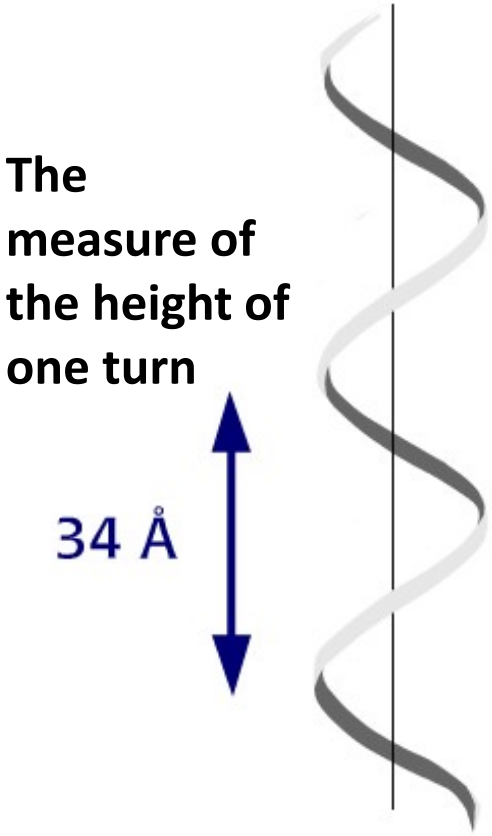


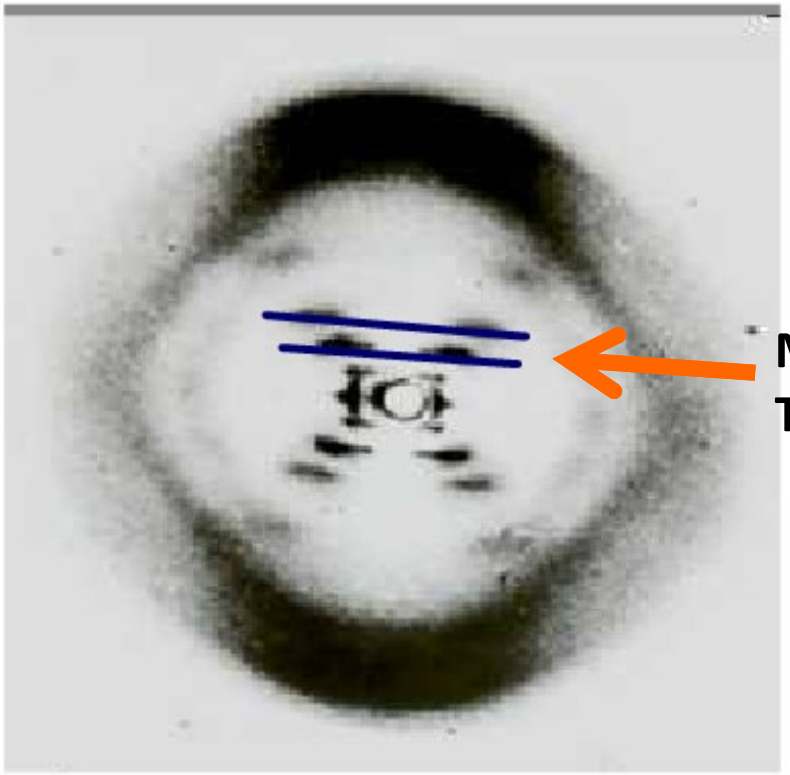
B-FORM

FRANKLIN

Rosalind's B-Form Crystallography Paper

Spots of along the "X" patter indicate distance.
The closer spots the larger the distance.

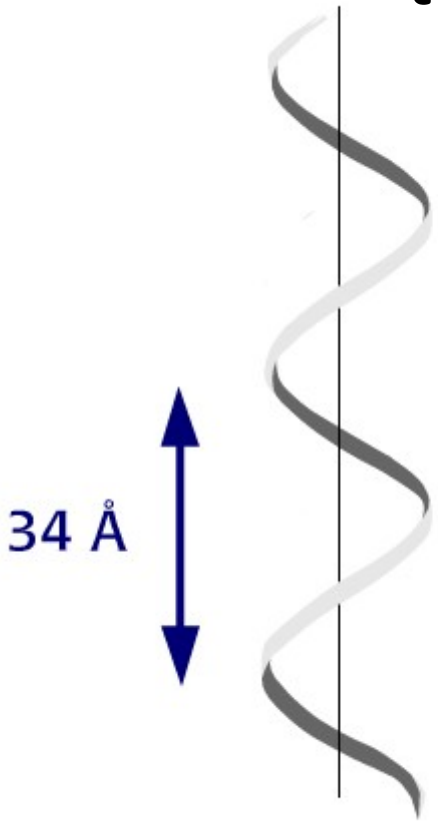


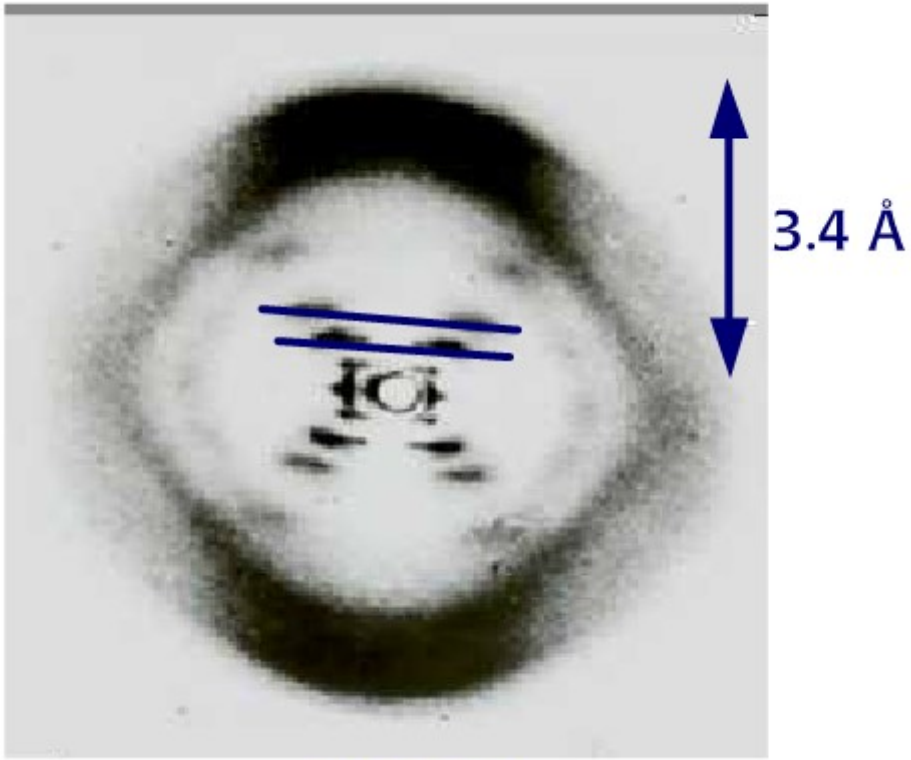


FRANKLIN

Rosalind's B-Form Crystallography Paper

The distance between the middle of the X-ray pattern to the top indicates distance between two stacked base pairs



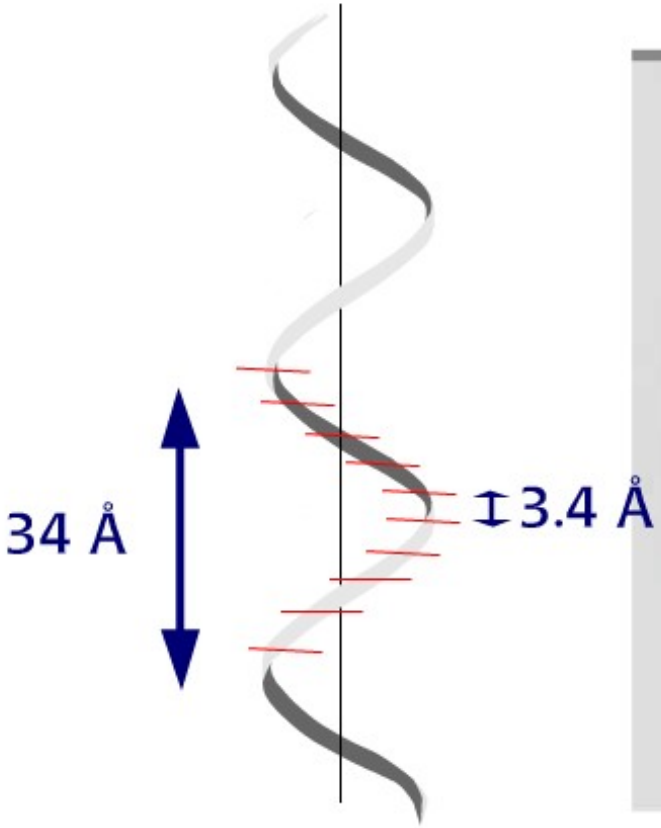


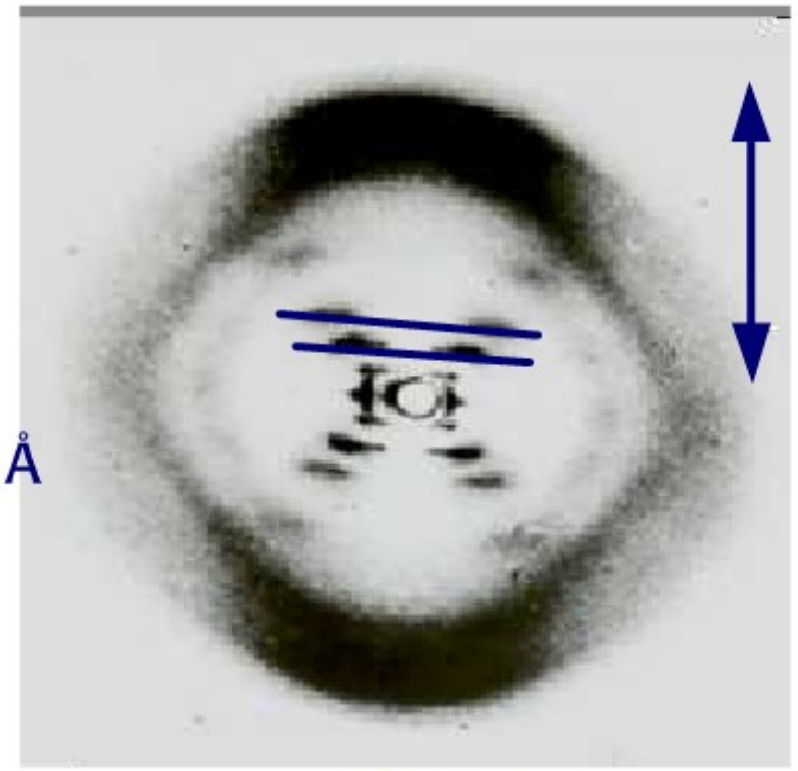
B-FORM

FRANKLIN

Rosalind's B-Form Crystallography Paper

Height of one helical repeat = 34 angstroms
Distance between stacked base pairs = 3.4 angstroms
10 nucleotides per helical repeat



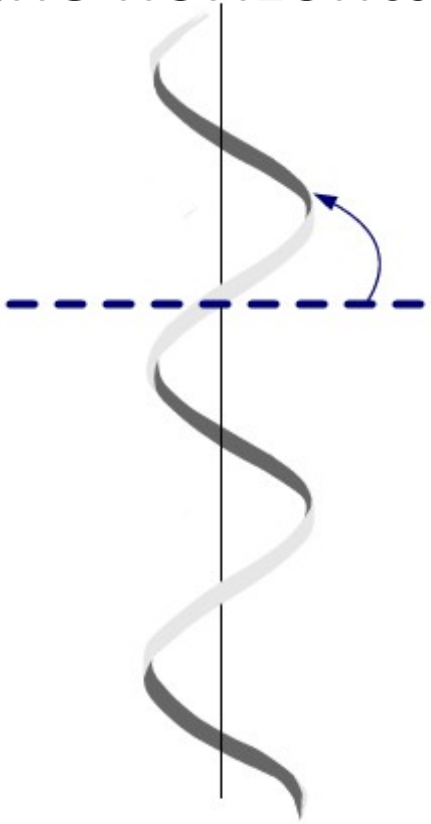


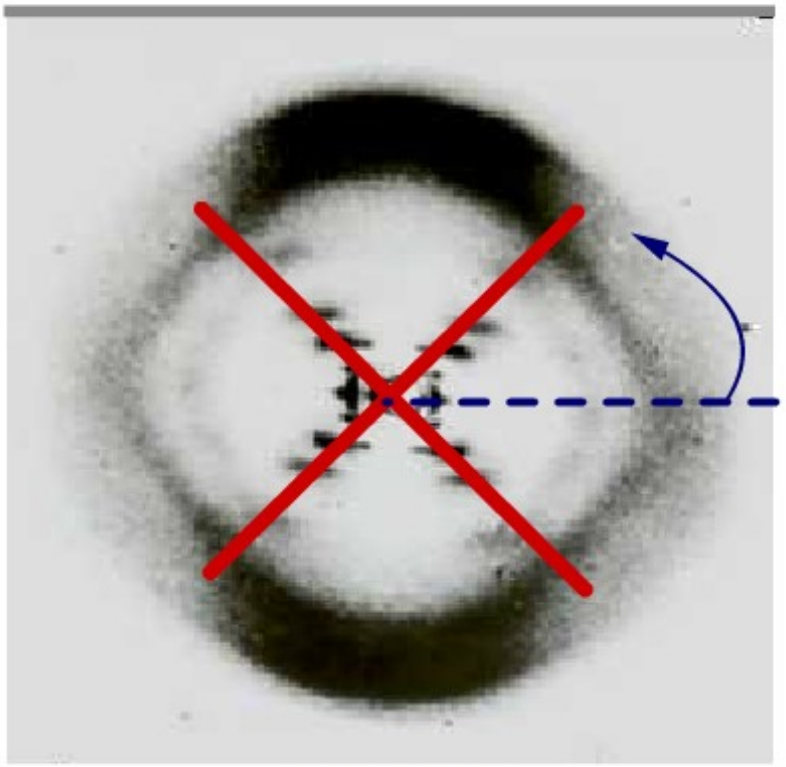
B-FORM

FRANKLIN

Rosalind's B-Form Crystallography Paper

The degree of rise of the helix could be determine by determining the angle between the horizontal axis and the "x" of the helix





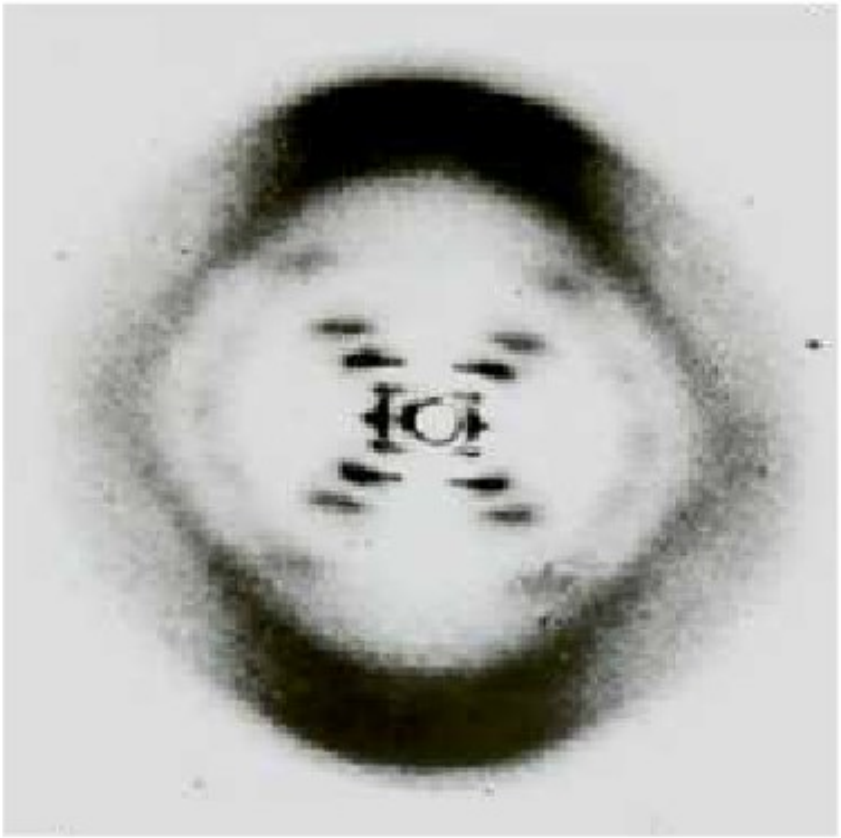
B-FORM

FRANKLIN

Rosalind's B-Form Crystallography Paper

Interpretation of Results

- Cannot for certain say that DNA is helical but this image is evidence for that
- Pauling and Linus were incorrect in placing the phosphates internally
  - No dense core observed
- Deduced that phosphate groups were on the outside (due to diameter)
- This places sugars/bases internally
- Basic dimensions determined
  - 20 angstrom diameter
  - 34 angstrom height
  - Bases 3.4 angstrom appart
- No matter the number of helices, they are not equally spaced
  - Major/minor grooves



James D. Watson
Francis H. C. Crick

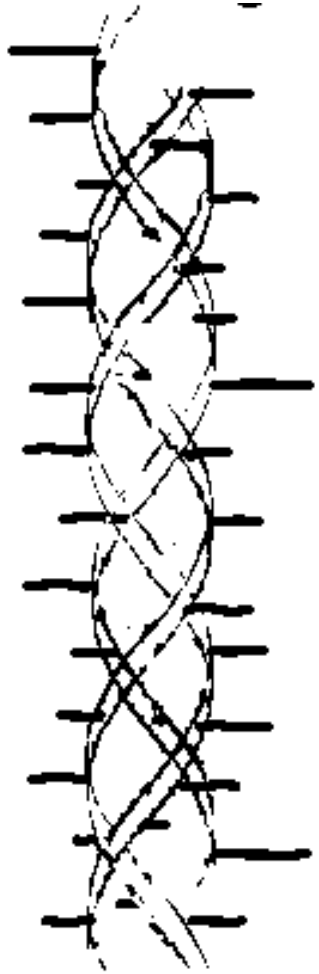
MOLECULAR STRUCTURE OF NUCLEIC ACIDS

A STRUCTURE FOR DEOXYRIBOSE NUCLEIC ACID

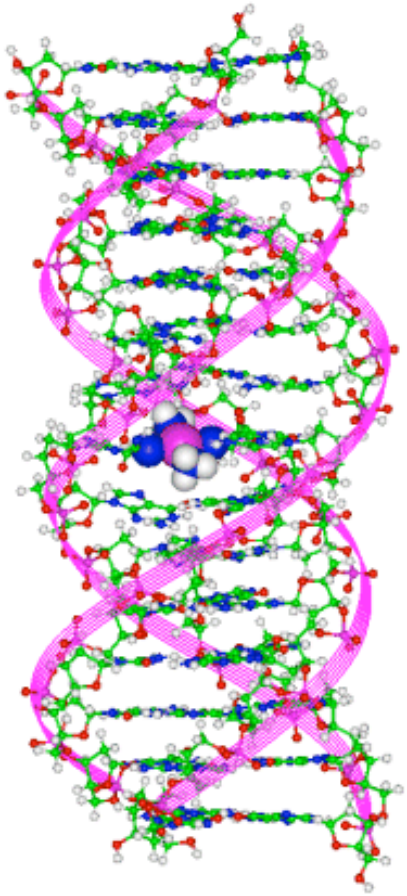
Nature
April 25, 1953

The Models for DNA

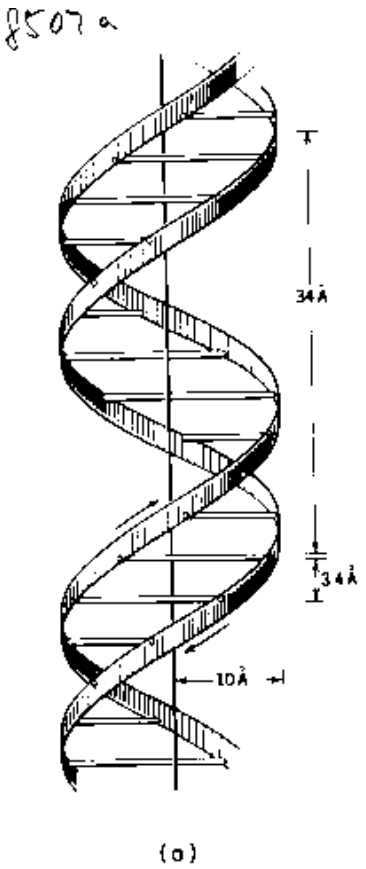
Pauling and Corey



Fraser Model



Watson and Crick

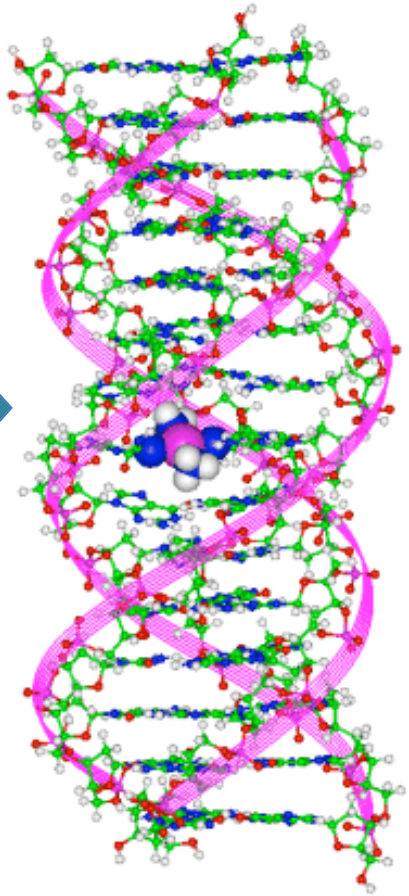


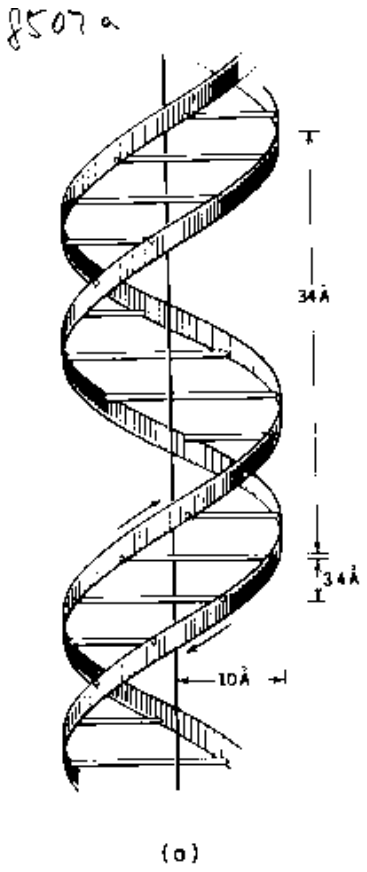
The Models for DNA

Pauling and Corey:

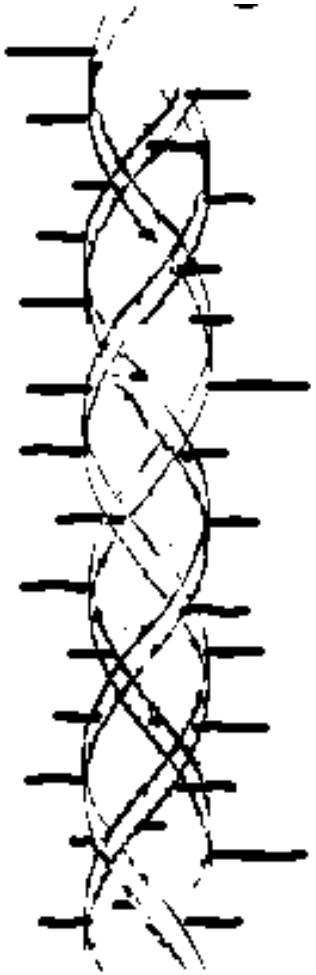
- Triple Helix
- Three phosphate chains with PO4 facing the center
- Based on X-ray diagram if what was being seen was free acid
- Individual bases point out from the central axis

Published 1951





The Models for DNA

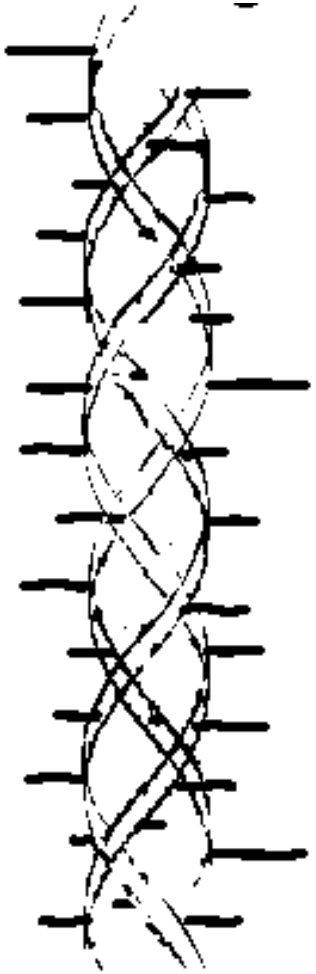


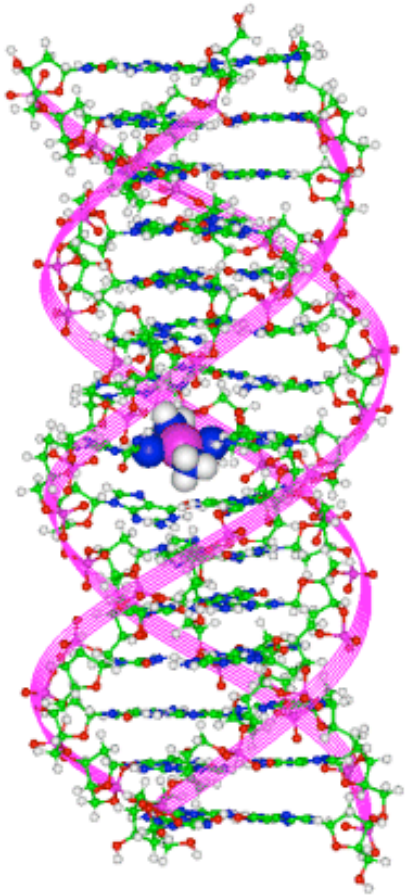
Fraser's Changes:

- Electrostatic attractions between negatively charged phosphate groups and the the sodium ions
- Van der Walls attraction between the planar purine and pyrimidine residues
- Hydrogen bonds formed between the C=O, NH, NH and OH groups of the purine and pyrimidine residues

Transcript March 17, 1953

The Models for DNA



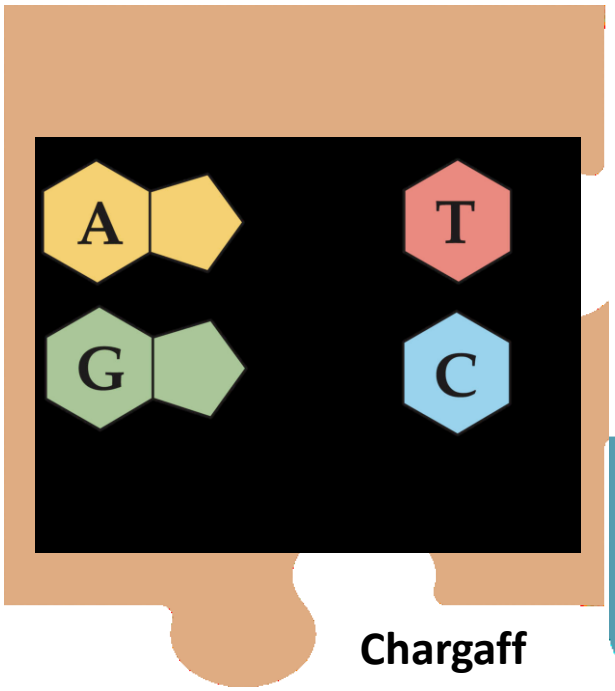


Watson and Crick:

- Fraser model
  - ill-defined
- Pauling and Corey's model
  - X-ray diffraction is salt
  - Not clear what forces hold the structure together
  - Negative phosphates would repel each other
  - Van der Waals forces distances were too far apart

Publishes 1953

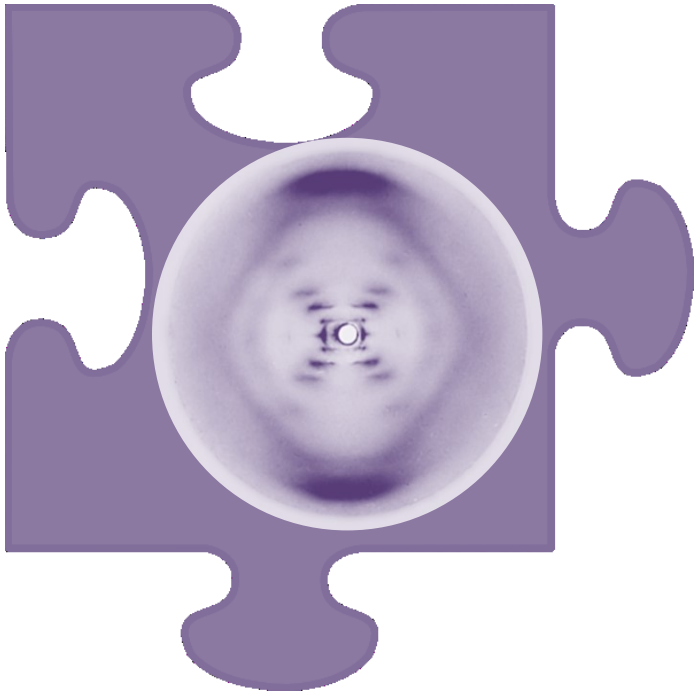
The Pieces of the Puzzle



Chargaff

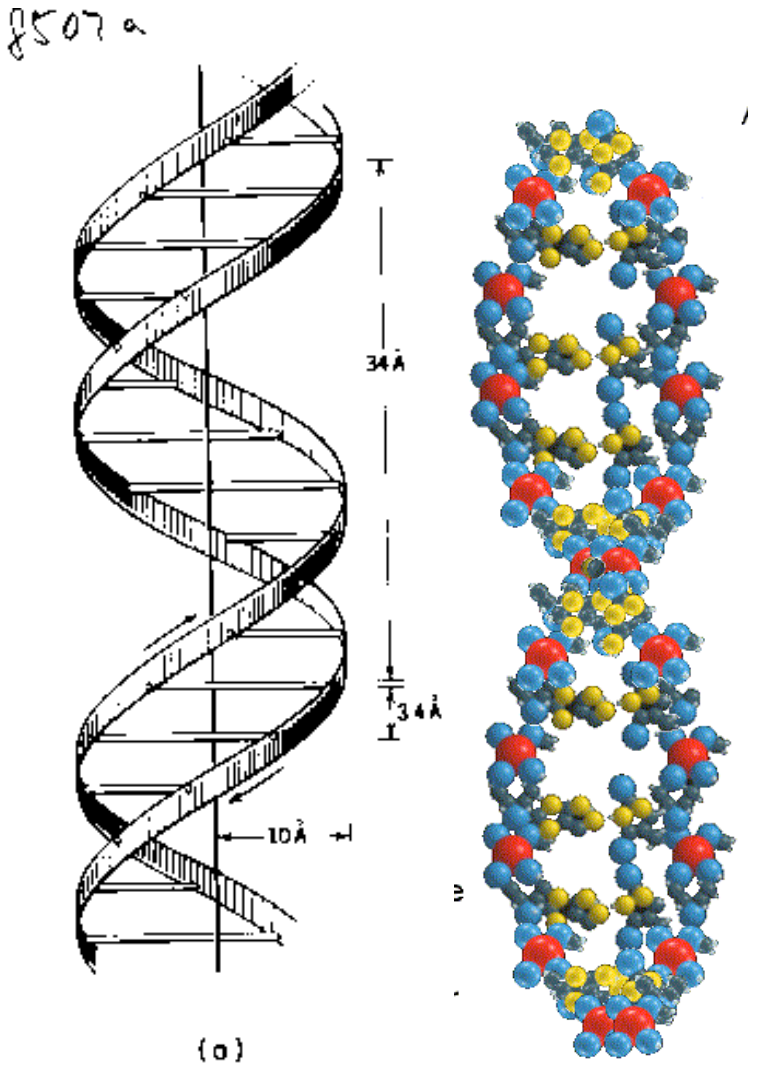
Pauling, Corey, and Fraser

Wilkins and Franklin



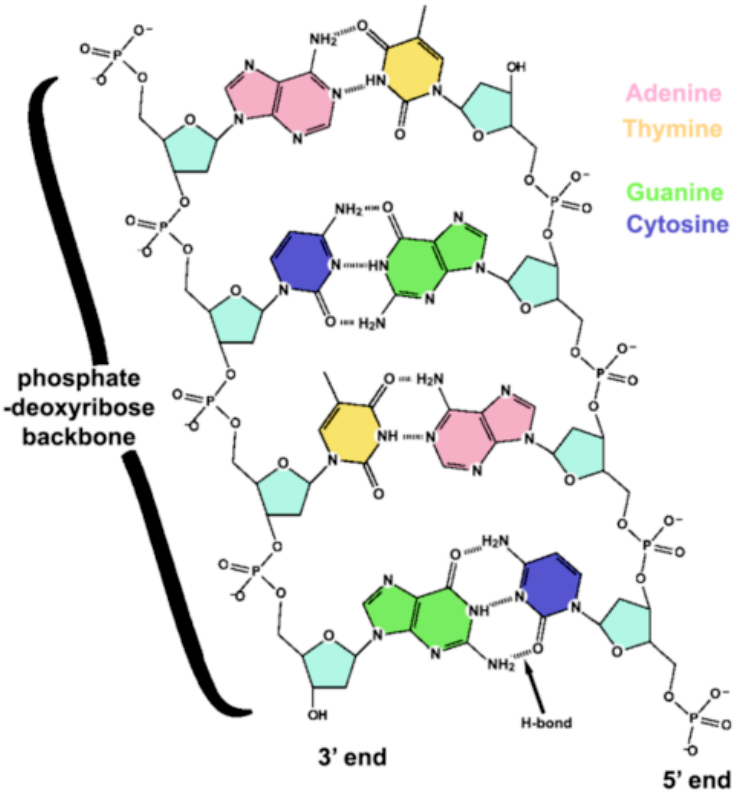
The Watson-Crick Model

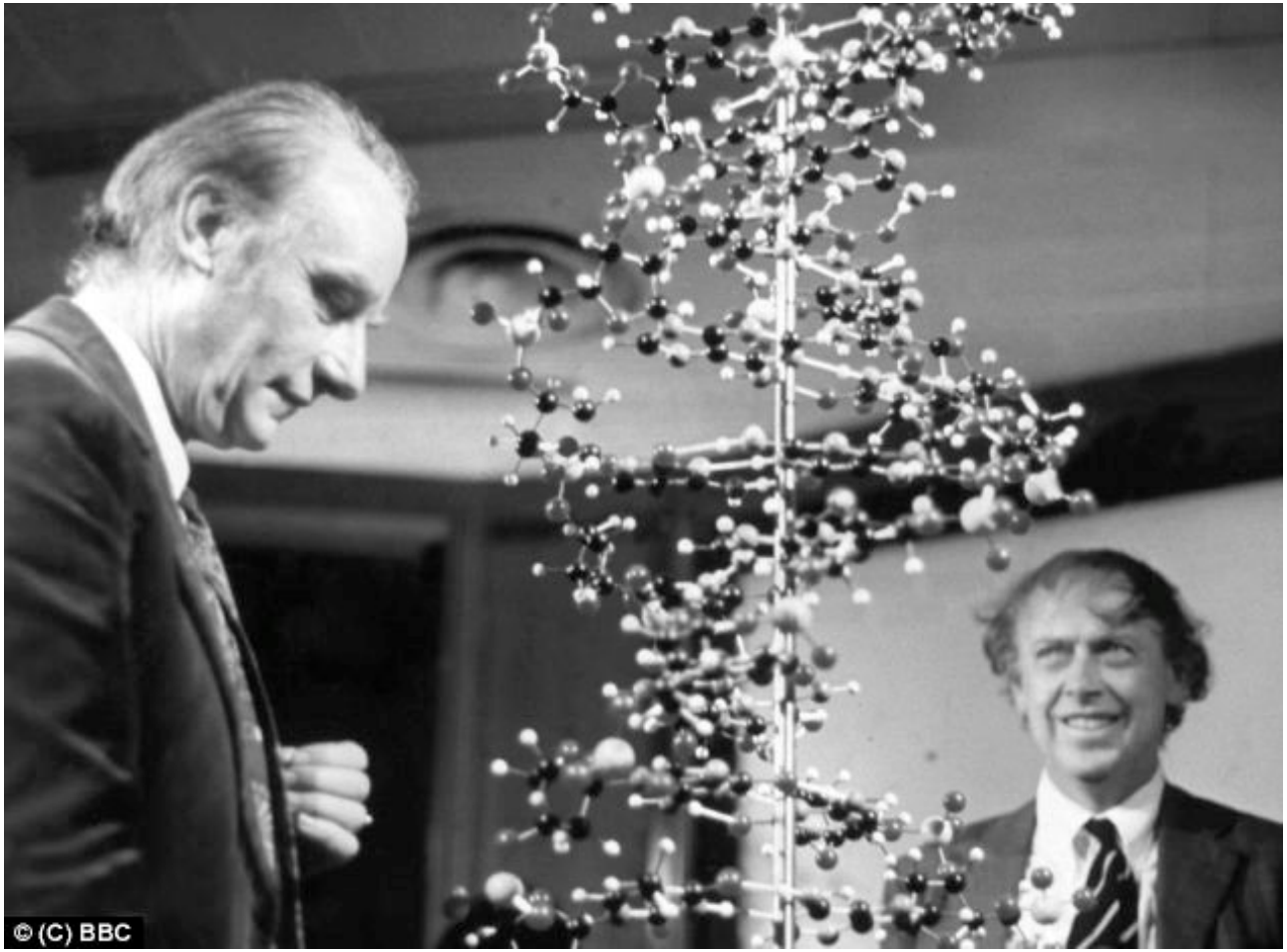
- Two helical chains coiled around a central axis
- Each hain consists of phosphodiester groups on the outside with 3’-5’ linkages
- Both chains are right handed helices
- The travel in opposite directions
- Bases are on the inside
- Sugars are perpendicular to each base



The Watson-Crick Model

- 36 degrees between adjacent residues
- Residues repeat every 10 angstom
- Structure is open to water contact
- Chains held together by hydrogen bonding between purine and pyrimidine bases
- One pair must be purine the other Pyrimidine
- A-T and C-G if in the keto form





“It has not escaped our notice that the specific pairing we have postulated immediately suggest a possible copying mechanism for the genetic material”