

**Watson & Crick (1953)**  
**Wilkins, Stokes & Wilson (1953)**  
**Franklin & Gosling (1953)**

## **Structure of Deoxyribose Nucleic Acid (DNA)**

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# Historical Context

- ❖ < 1950s: DNA structure unknown
  - ❖ Deoxyribose sugar,  $\text{PO}_4$ , & nucleosides
  - ❖ Levene (1928) suggested 1:1:1:1 stacks of A C G T nucleotides
  - ❖ Astbury (1947) identified 3.4 Å nucleotide spacing
- ❖ Pauling (1953) proposed (incorrect) **three-chain DNA** model
- ❖ Competition [?] drove rapid progress in 1951 ~ 1953
- ❖ Several laboratories racing [?] toward **3D structure**

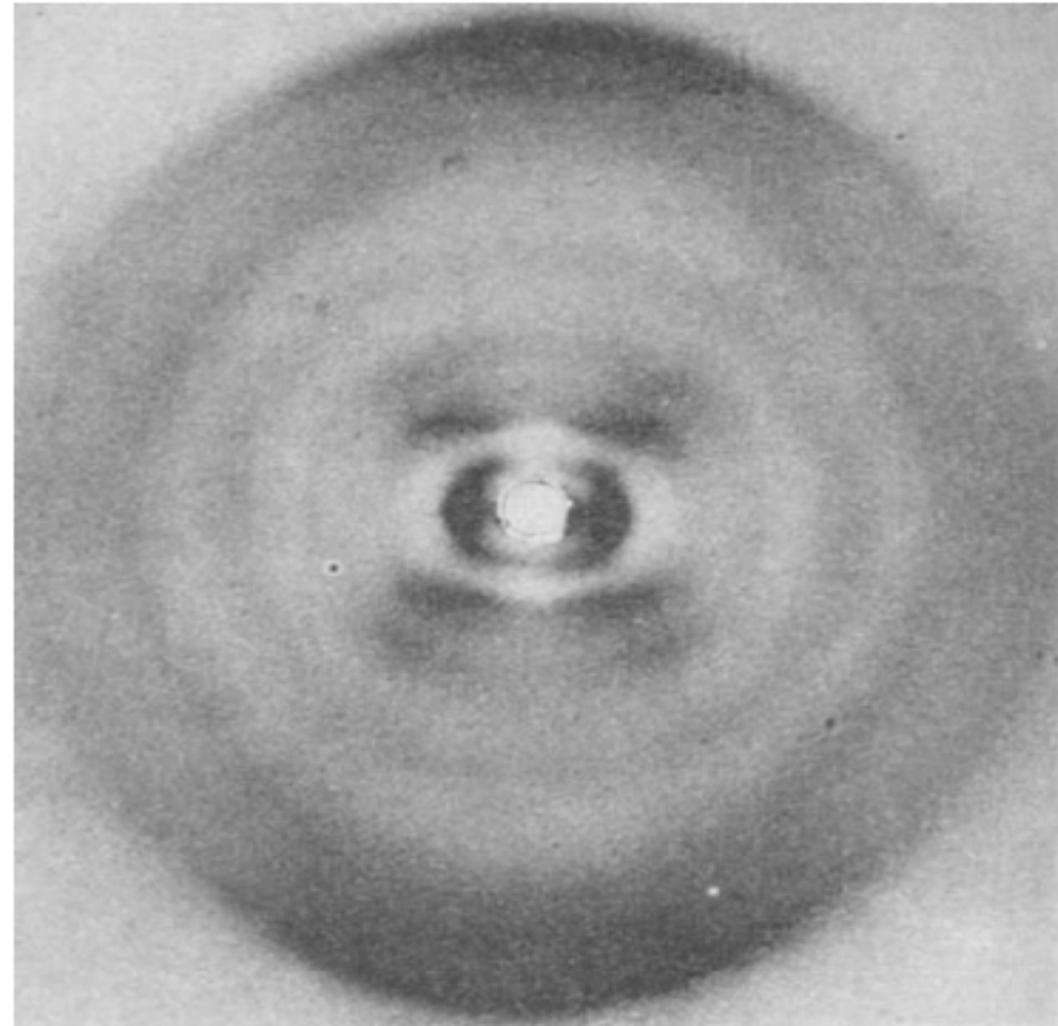
# DNA Fiber Preparation

- ❖ **Sodium thymonucleate** extracted from calf thymus
- ❖ **X-ray diffraction analysis** of parallel fibres
- ❖ **Structure B** obtained at ~75% humidity
- ❖ Water content: 40 ~ 50% of dry weight
- ❖ **Paracrystalline** material showing partial order maintained

# X-Ray Diffraction Experiment

- ❖ X-ray beam perpendicular to fibers
- ❖ Film captures diffraction pattern positions
- ❖ Fiber axis vertical during exposure
- ❖ Long exposure times required for pattern
- ❖ Multiple samples analyzed for consistency

Figure 1 - X-ray diffraction photograph of **B-form DNA**  
(Wilkins et al. 1953)



# Key Features of Diffraction Pattern

## Can you explain Figure 2 ?

- ❖ Strong 3.4 Å meridional reflection
- ❖ Layer lines at  $\sim 34$  Å intervals
  - ❖ 4<sup>th</sup> layer line absent
- ❖ Cross-wise "X" pattern
- ❖ No reflections near meridian
- ❖ Strong equatorial reflection at  $\sim 20$  Å

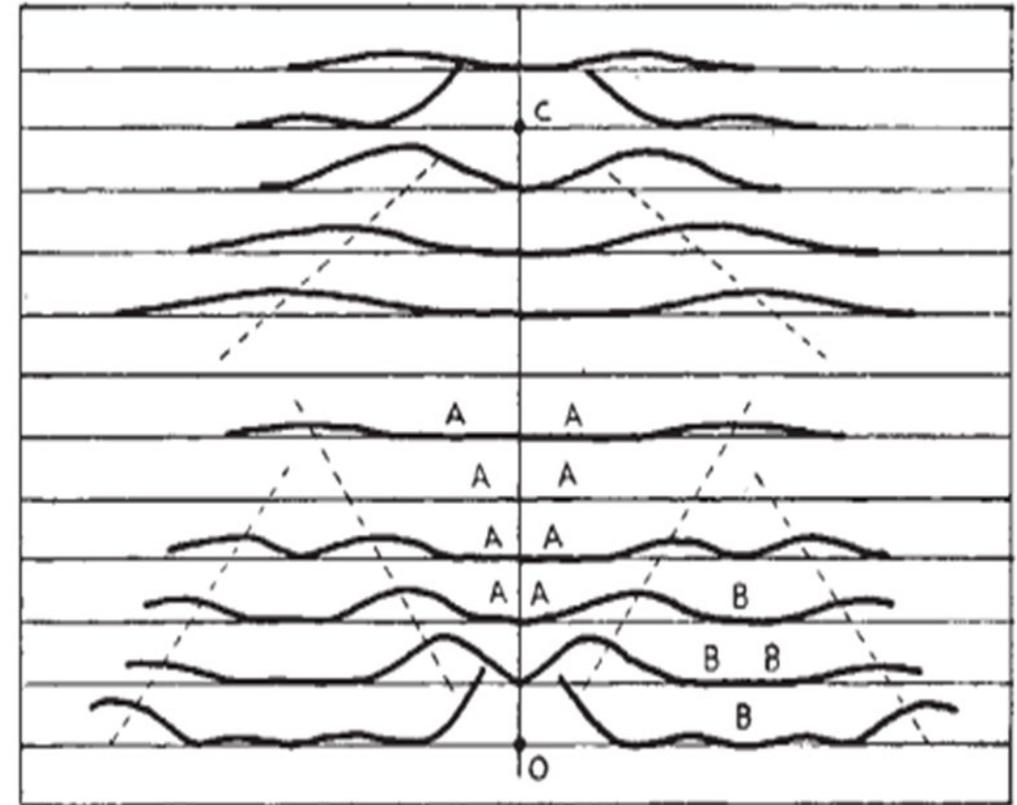


Figure 2 - Bessel function diagram

# Mathematical Theory of Helical Diffraction

- ❖ **Bessel functions** describe helical diffraction intensities ("*spots*")
- ❖  **$n$ th layer** proportional to  $J_n^2$
- ❖ **Pitch** is vertical distance per turn
- ❖ **Helix radius** from intensity maxima
- ❖ **Ten residues** per helical turn

TABLE 1: Structural Parameters from Different DNA Sources

DNA Source	Helical Pitch (Å)	Helix Diameter (Å)	Residues per Turn	Pattern Quality
Calf thymus	34	~20	10	Excellent
Pig thymus	34	~20	10	Excellent
Herring sperm	34	~20	10	Very good
Human tissue	34	~20	10	Good

# Evidence for Helical Structure

- ❖ **Layer line intensity** matches **Bessel function** predictions
- ❖ **Straight lines** through maxima ("**X arms**") radiate from origin
- ❖ Absence of **meridional reflections** diagnostic
- ❖ **Pitch 34 Å**
- ❖ **Diameter 20 Å**
- ❖ **Pattern consistent** across sources

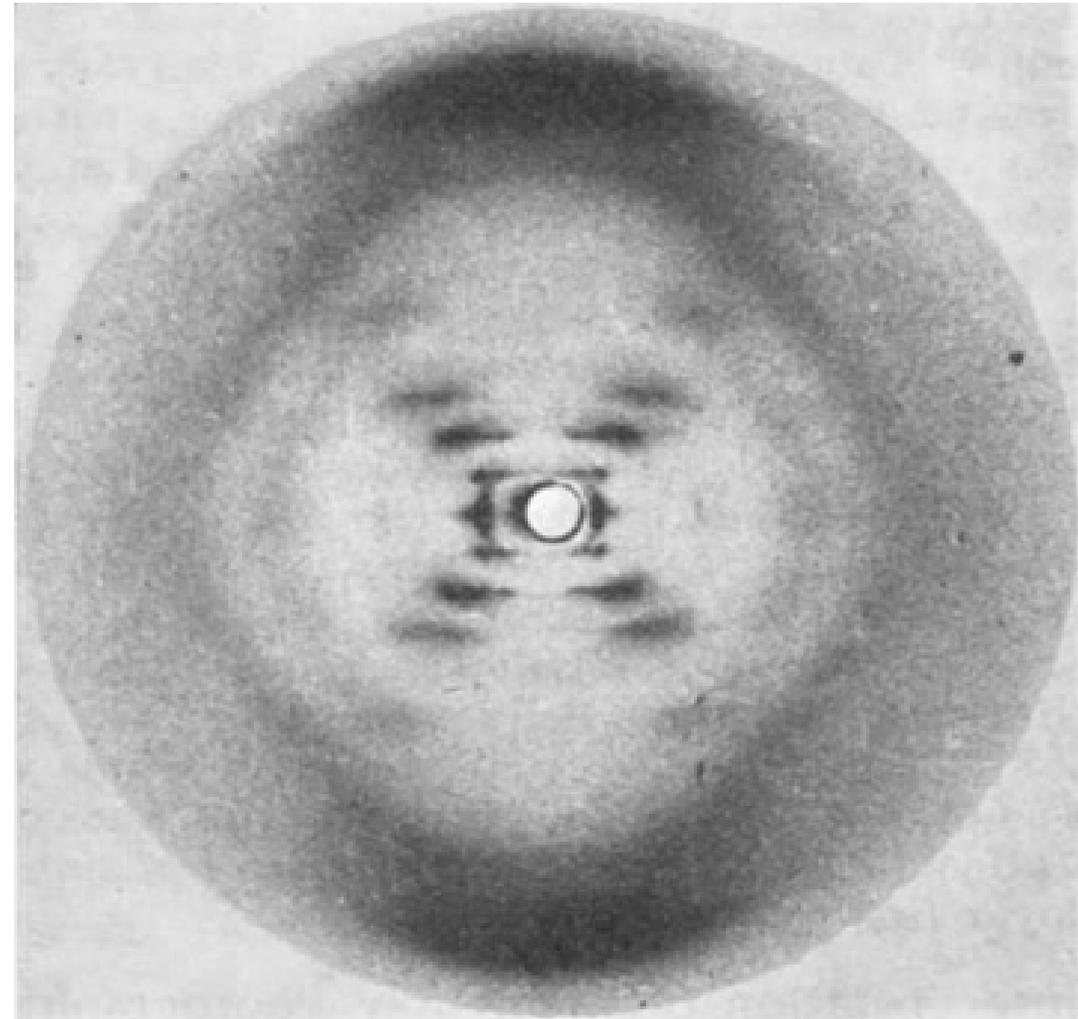
# How many DNA Chains?

- ❖ Density calculations require **30 nucleotides / turn**
- ❖ **Patterson function** indicates **two chains**
- ❖ **Three-chain model** gives different layer patterns
- ❖ **Two coaxial helices** best fit data
- ❖ *Dry* "A"  $\leftrightarrow$  *wet* "B" reversibility supports **two chains**

# Radial Mass Distribution Analysis

- ❖  $\text{PO}_4$  groups at outer surface of helix
- ❖  $\sim 20 \text{ \AA}$  diameter for outer phosphate helix
- ❖ **Bases & Pentose** oriented toward center
- ❖ Radial distribution => empty equator
- ❖ "*Pile of pennies*" stacking of bases

Figure 3: Cross-Section of **DNA** Helix Shows Radial Mass Distribution:  
Franklin & Gosling (1953)



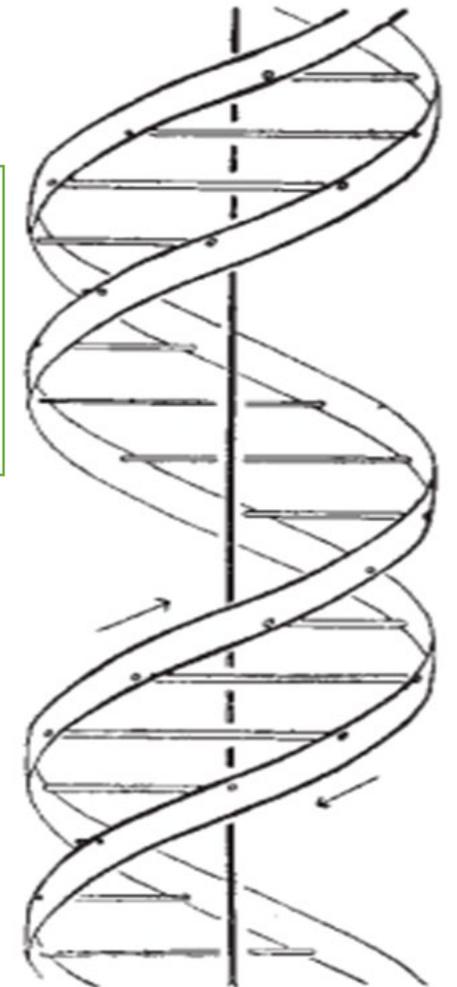
# Arguments for Phosphate Backbone

- ❖ **Ten  $\text{PO}_4$**  groups per helical turn
- ❖ Fully extended  **$\text{PO}_4$  - ester** backbone
- ❖  **$\text{PO}_4$**  separated **7.1 Å**
- ❖ "*Accessibility to titration*" supports exterior location
- ❖ **Negative charges** stabilized by **Na** counterions

## *X-Ray data support Watson-Crick model*

- ❖ Both agree with **double helix**
- ❖ Both place **P<sub>O</sub>4** on **outside**
- ❖ Both support **~20 Å** diameter
- ❖ Both indicate **ten base pairs / turn**
- ❖ Both require strands **antiparallel**
- ❖ *Experiment validates theory ! ? !*

Figure 4:  
Structural Model of  
**DNA Double Helix**  
(Watson & Crick 1953)



# Critical Evaluation, 1953 *versus* 2026

- ❖ **Limited resolution** compared to modern **XRD** techniques
- ❖ **Ambiguities in equatorial reflection** interpretation remain
  - ❖ E.g., "*helicopter*" (*helico-pter* en Francais) twist: base pairs not co-planar
- ❖ **Method *does not*** (cannot) visualize **A+T** , **G+C** base pairing
- ❖ **Paracrystalline** nature limits detailed atomic positions
- ❖ Required integration of **physical** & **modelling** approaches
- ❖ **Good Science, or Not ?**

# Scientific Impact & Significance

- ❖ "*It has not escaped our attention*": implied method for **gene replication**
- ❖ **Nobel Prize** recognition in 1962
- ❖ "*Molecular Biology of Gene*" proceeds in tandem with *Genetics*
- ❖ **Physio-chemical** basis of **heredity mechanism**
- ❖ **X-Ray diffraction** as a tool for **biological macromolecules**

# Conclusions & Legacy

- ❖ ~~Double-Helical DNA structure~~ definitively established experimentally
- ❖ ~~Phosphates exterior, bases interior~~ confirmed
- ❖ ~~Universal structure across species~~ demonstrated clearly
- ❖ ~~Foundation laid for molecular biology~~ revolution
- ❖ ~~Integration of theory and experiment~~ exemplified

# References

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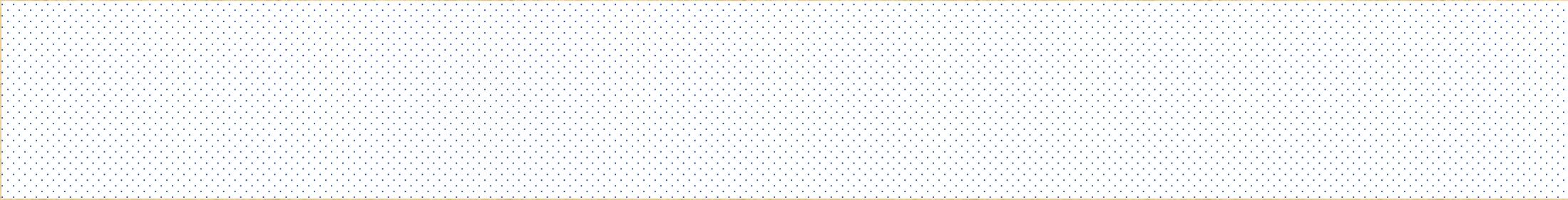
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# Evidence from Biological Systems

- ❖ Sperm head X-ray spectra match fiber patterns
- ❖ Structure exists in intact biological systems
- ❖ Helical configuration present in living cells
- ❖ Universal structure across all life forms
- ❖ Structure-function relationship implications emerge clearly

# Introduction

- ❖ Molecular structure of deoxyribose nucleic acids
- ❖ *Nature*, 1953, pp. 738-740
- ❖ Wilkins, Stokes, & Wilson
- ❖ X-ray diffraction reveals DNA's helical structure
- ❖ Foundational work in molecular biology history