When do Scientists Change their Minds?

Week 3 – The structure of DNA

EGMT-1520 Mon., Jan 31, 2022
Bill Pearson wrp@virginia.edu

Overview of this session:

- Goals of "Gravity" presentation
- What are genes made of: Avery (1944) to Watson-Crick (1953)
  - Hershey and Chase (1952) (phage transfer DNA)
- The Nature papers (25-April-1953)
  - Watson,Crick Nature (1953) "Molecular Structure of Nucleic Acids: A Structure for Deoxyribose Nucleic Acid" **171:**737–738
  - Wilkins et al. Nature (1953) "Molecular Structure of Nucleic Acids: Molecular Structure of Deoxypentose Nucleic Acids" **171:**738–740
  - Franklin, Gosling Nature (1953) "Molecular Configuration in Sodium Thymonucleate" **171:**740–741
- The Nature paper (30-May-1953)
  - Watson & Crick (1953) "Genetical implications of the structure of deoxyribonucleic acid." *Nature* **171:**964–967
- The next steps
  - Semi-conservative Replication of DNA (Meselson and Stahl, 1958)
  - Crick et al (Dec., 1961) Nature "General Nature of the Genetic Code for Proteins" **192:**1227–1232
  - "cracking" the Genetic Code – Nirenberg, Oct. 1961 PNAS " The Dependence of Cell-Free Protein Synthesis in E. Coli upon Naturally Occurring or Synthetic Polyribonucleotides" 47:1588–1602.

1

For Wednesday:

- Gravity presentations – 5 min per group (30 min)
  - Please make sure that I can download the presentation 15 min before class. Google Slides share with "william.pearson@gmail.com"
- There will be a brief (15 min max) quiz based on the Deichmann paper, and the general question of why Avery et al. had modest recognition, while Watson and Crick was immediately accepted
- In groups – possible final project topic discussion. Identify one topic that is non-intuitive to a "naïve" listener (or to you)
  - it should be easy to explain (probably not quantum mechanics)
  - the incorrect explanation should be logical
  - the correct explanation may require a major shift in perspective
- On Wednesday, I will meet with each group to discuss project topics

2

Project ideas

(Counter) Intuitive

- Why does ice float
- The "Monty Hall Problem"
- ?Surface tension
- Entropy and energy
- Newton's 3rd law – equal/opposite reaction
- symbiosis

Not Intuitive

- Placebo effect
- Quantum mechanics
- ?Special relativity
- Menstrual synchrony
- ?Enzyme catalysis
- ?Fluorescence

3

Why Gravity *DOESN'T* make sense

- Intuitive experience:
  - heavy objects are "heavier", they seem to want to go down more
  - wanting to go down more implies going down faster
  - therefore: heavy objects should fall faster
- *Non-intuitive* critical insight:
  - objects at rest, remain at rest (heavy objects "want" to stay in place) (example: horizontal motion) – why isn't this intuitive?
- Non-intuitive correct conclusion:
  - since heavy objects "want" to stay in place, it takes more force to move them (cause them to fall, pull them down)
  - the extra force required to move them ($F=m_1a$) exactly balances the additional force they gain by being heavier ($F=(m_1*m_2)/r^2$), so 'a' (acceleration) remains the same

4

The structure of DNA – Nature (1953)

- The Nature papers (25-April-1953)
  - Watson,Crick (1953) "Molecular Structure of Nucleic Acids: A Structure for Deoxyribose Nucleic Acid" *Nature* **171:**737–738
  - Wilkins et al. (1953) "Molecular Structure of Nucleic Acids: Molecular Structure of Deoxypentose Nucleic Acids" *Nature* **171:**738–740
  - Franklin, Gosling (1953) "Molecular Configuration in Sodium Thymonucleate" *Nature* **171:**740–741
- The Nature paper (30-May-1953)
  - Watson & Crick (1953) "Genetical implications of the structure of deoxyribonucleic acid." *Nature* **171:**964–967

5

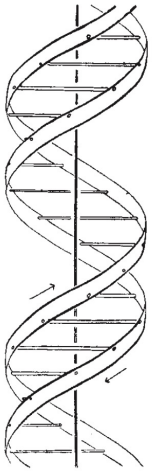
Watson,Crick (1953) (25-April)

MOLECULAR STRUCTURE OF NUCLEIC ACIDS

A Structure for Deoxyribose Nucleic Acid

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.

A structure for nucleic acid has already been proposed by Pauling and Corey[1]. They kindly made their manuscript available to us in advance of publication. Their model consists of three intertwined chains, with the phosphates near the fibre axis, and the bases on the outside. In our opinion, this structure is unsatisfactory for two reasons: (1) We believe that the material which gives the X-ray diagrams is the salt, not the free acid. Without the acidic hydrogen atoms it is not clear what forces would hold the structure together, especially as the negatively charged phosphates near the axis will repel each other. (2) Some of the van der Waals distances appear to be too small.



This figure is purely diagrammatic. The two ribbons symbolize the two phosphate—sugar chains, and the horizontal rods the pairs of bases holding the chains together. The vertical line marks the fibre axis

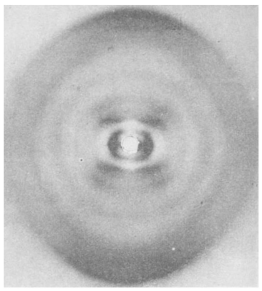
6

Watson,Crick (1953) "Molecular Structure of Nucleic Acids: A Structure for Deoxyribose Nucleic Acid"

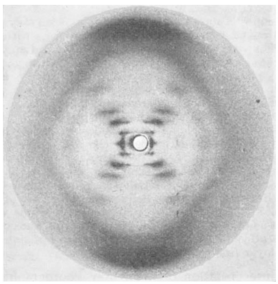
The novel feature of the structure is the manner in which the two chains are held together by the purine and pyrimidine bases. The planes of the bases are perpendicular to the fibre axis. They are joined together in pairs, a single base from one chain being hydrogen-bonded to a single base from the other chain, so that the two lie side by side with identical z-co-ordinates. One of the pair must be a purine and the other a pyrimidine for bonding to occur. The hydrogen bonds are made as follows : purine position 1 to pyrimidine position 1 ; purine position 6 to pyrimidine position 6.

The (other) Nature papers

- Wilkins et al. (1953) "Molecular Structure of Nucleic Acids: Molecular Structure of Deoxypentose Nucleic Acids" *Nature* **171:**738–740
  - helix
  - bases stacked at 3.4 A
  - repeated turn at 34 A
  - diameter 20 A
  - present in vivo



- Franklin, Gosling (1953) "Molecular Configuration in Sodium Thymonucleate" *Nature* **171:**740–741
  - two forms (A, B)
  - bases stacked at 3.4 A
  - repeated turn at 34 A
  - diameter 20 A



Watson & Crick, one month later

GENETICAL IMPLICATIONS OF THE STRUCTURE OF DEOXYRIBONUCLEIC ACID

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

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

THE importance of deoxyribonucleic acid (DNA) within living cells is undisputed. It is found in all dividing cells, largely if not entirely in the nucleus, where it is an essential constituent of the chromosomes. Many lines of evidence indicate that it is the carrier of a part of (if not all) the genetic specificity of the chromosomes and thus of the gene itself. Until now, however, no evidence has been presented to show how it might carry out the essential operation required of a genetic material, that of exact self-duplication.

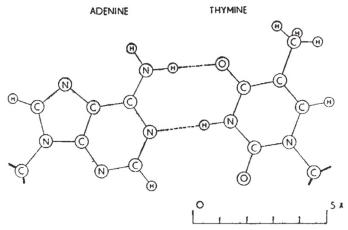


Fig. 4. Pairing of adenine and thymine. Hydrogen bonds are shown dotted. One carbon atom of each sugar is shown

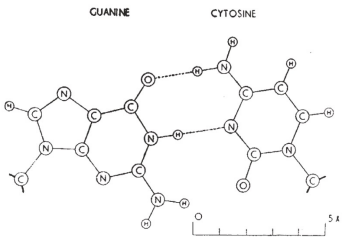
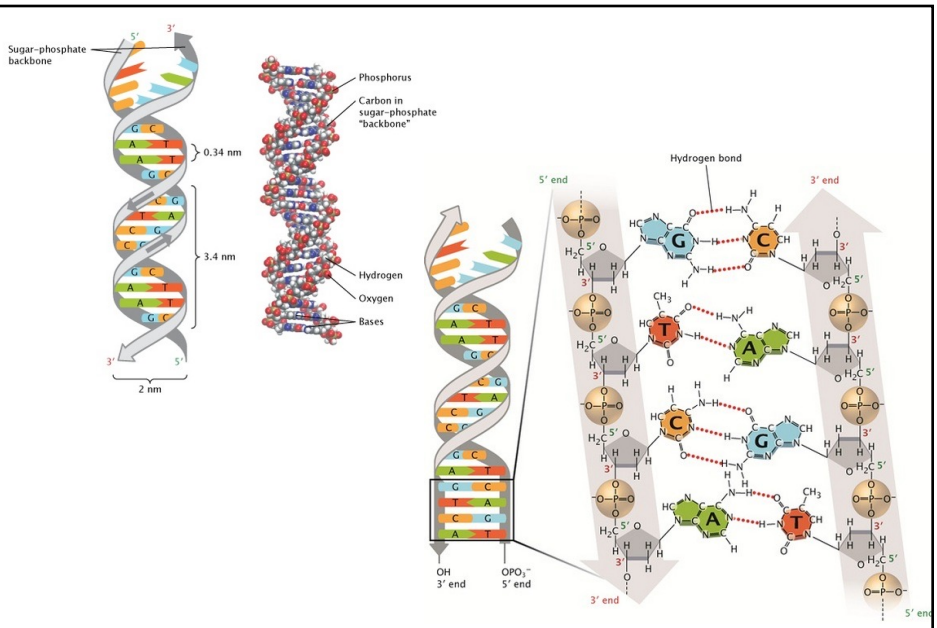


Fig. 5. Pairing of guanine and cytosine. Hydrogen bonds are shown dotted. One carbon atom of each sugar is shown

Why did the DNA structure matter so much?

- Avery et al (1944) showed that DNA was the transforming principal
- Hershey and Chase (1952) showed that when bacteriophage infect bacteria, the protein is left on the outside and only the DNA gets inside the bacteria

Until now, however, no evidence has been presented to show how it might carry out the essential operation required of a genetic material, that of exact self-duplication.



https://www.nature.com/scitable/topicpage/discovery-of-dna-structure-and-function-watson-397/

11

Why did the DNA structure matter so much?

- 10,000 BCE – 1860 – heredity happens
- 1865 – Mendel – heredity has rules
- 1900's – genes are on chromosomes
- 1944 – Avery et al – genes are made of DNA

How does DNA work??

- 1953 – Watson & Crick
  - double stranded helix
  - complementary base rules (A:T, G:C)

It works by each of the two helical strands being copied, following the complementary base rules

12

Why did the DNA structure matter so much?

How does DNA work??

- 1953 – Watson & Crick
  - double stranded helix
  - complementary base rules (A:T, G:C)

It works by each of the two helical strands being copied, following the complementary base rules

We go from a clear phenomenon – heredity
To a set of rules that describe the phenomenon (Mendel)
To an uncharacterized substance that produces the phenomenon
To a structure that explains the central problem – making a copy

13

How does DNA work – the genetic code

- Crick et al (Dec., 1961) Nature "General Nature of the Genetic Code for Proteins" **192:**1227–1232
  - 3 nucleotide codons, non overlapping
- "cracking" the Genetic Code – Nirenberg, Oct. 1961 PNAS " The Dependence of Cell-Free Protein Synthesis in E. Coli upon Naturally Occurring or Synthetic Polyribonucleotides" 47:1588–1602.

14

Why did the DNA structure matter so much?

- We go from a clear phenomenon – heredity
- To a set of rules that describe the phenomenon (Mendel)
- To an uncharacterized substance that produces the phenomenon (Avery)
- To a structure that explains the central problem – making a copy (Watson+Crick)
- To experiments to show how the copy is made (Messelsohn and Stahl)
- To experiments that explain how only 4 nucleotides can make proteins (and be genes) (Crick, Nirenberg)

15

For Wednesday:

- Gravity presentation: 30 min for 6 groups
- Read the Deichmann (2004) paper (collab, week4) as well as the two Watson and Crick papers
- There will be a brief (15 min max) quiz based on the Deichmann paper, and the general question of why Avery et al. had modest recognition, while Watson and Crick was immediately accepted
- In groups – revisit possible final project topics. Identify one topic that is non-intuitive to a "naïve" listener (or to you)
  - it should be easy to explain (probably not quantum mechanics)
  - the incorrect explanation should be logical
  - the correct explanation may require a major shift in perspective
- On Wednesday, I will meet with each group to discuss project topics

16