https://www.youtube.com/watch?v=HgOha2D5kt8

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One ring to rule them all,
One ring to find them,
One ring to bring them all,
And in the darkness, bind them

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Lord Dwar
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Watch on YouTube

One ring to rule them all,
One ring to find them,
One ring to bring them all,
And in the darkness, bind them

Like the one ring of power in Tolkien's "Lord of the Rings," deoxyribonucleic acid (DNA) is the master molecule of every cell

https://en.wikipedia.org/wiki/One_Ring

https://science.howstuffworks.com/life/cellular-microscopic/dna.htm

How did we get from

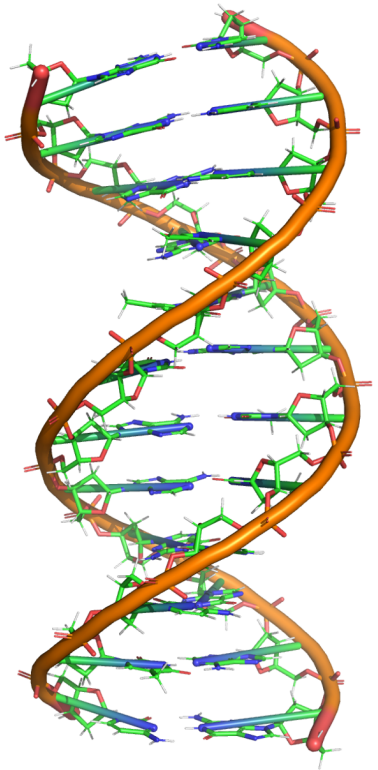
Mendel's traits and alleles to

DNA?

Molecular basis of inheritance

Slide from Lecture 3

Reverse engineering a "living machine"
One of the approaches



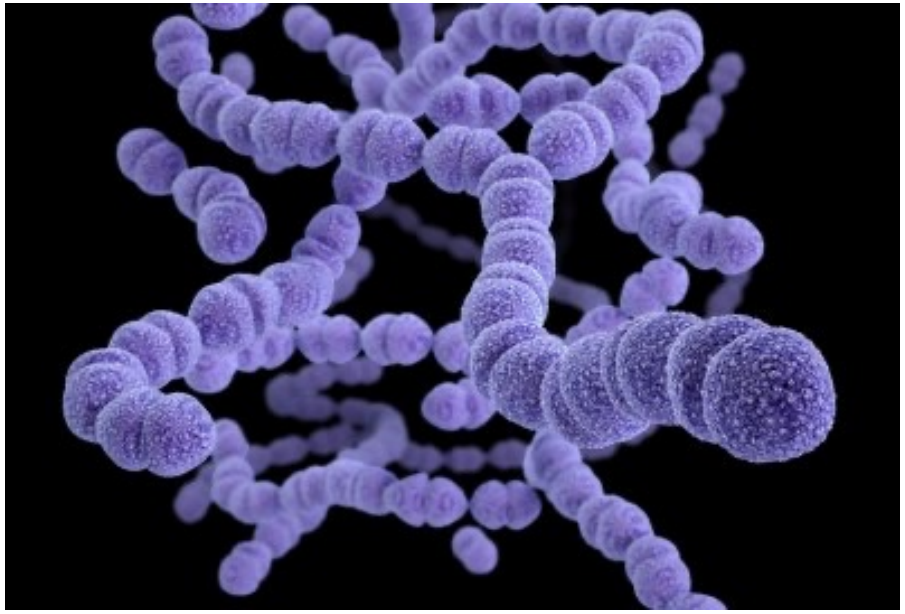
Protein databank id: 2EZE.pdb

- Discovering the existence of an instruction manual
- Proving that DNA is the instruction manual
  - Frederick Griffith
  - Oswald Avery, Colin MacLeod, Maclyn McCarty
  - Alfred Hershey and Martha Chase
  - James Watson and Francis Crick
  - Matthew Meselson and Franklin Stahl
- Decoding the instruction manual

Today's topics

- Frederick Griffith
  - Developing vaccine for pneumonia
- Oswald Avery, Colin MacLeod, Maclyn McCarty
  - Identified DNA as the transforming principle
- Alfred Hershey and Martha Chase
  - James Watson and Francis Crick
  - Matthew Meselson and Franklin Stahl
- DNA packaging
- Applications in day-to-day life

While developing a vaccine for pneumonia...



Frederick Griffith
(1879-1941)
British medical
officer and
bacteriologist

- *Streptococcus pneumoniae* is a bacterium
- It causes pneumonia in mammals
- Griffith was trying to develop a vaccine
- DNA, RNA, and proteins were known at this time
- Most likely genetic material is... protein!

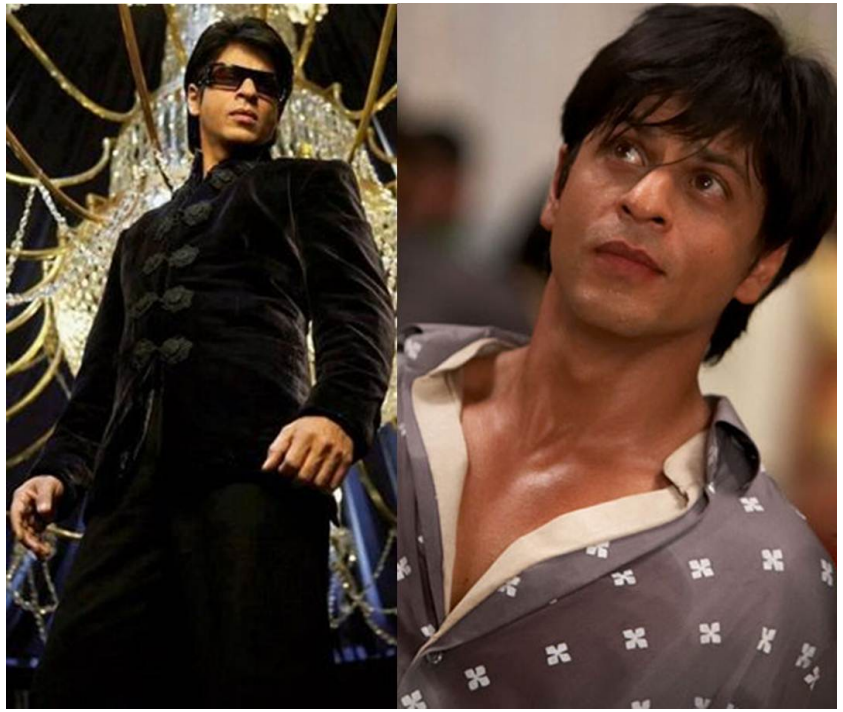
Shown above is a digitally colorized image of Streptococci.
It is taken from https://www.nfid.org/infectious-diseases/pneumococcal/

Pathogenic and non-pathogenic strains

Streptococcus pneumoniae

Strain S – appears smooth
Has an outer capsule
protects from the defense system of mice
Pathogenic strain
Causes pneumonia in mice

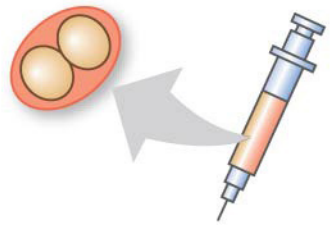
Strain R – appears rough
Lacks the outer capsule
Non-pathogenic strain
Does NOT cause pneumonia in mice



http://www.planetsrk.com/community/threads/5-movies-before-fan-in-which-shah-rukh-khan-played-double-roles.32656/

Transforming a good strain into a bad strain

Living S cells (pathogenic control)



Results

Mouse dies

Figure 16.2 in Campbell Biology. 10th edition

Transforming a good strain into a bad strain

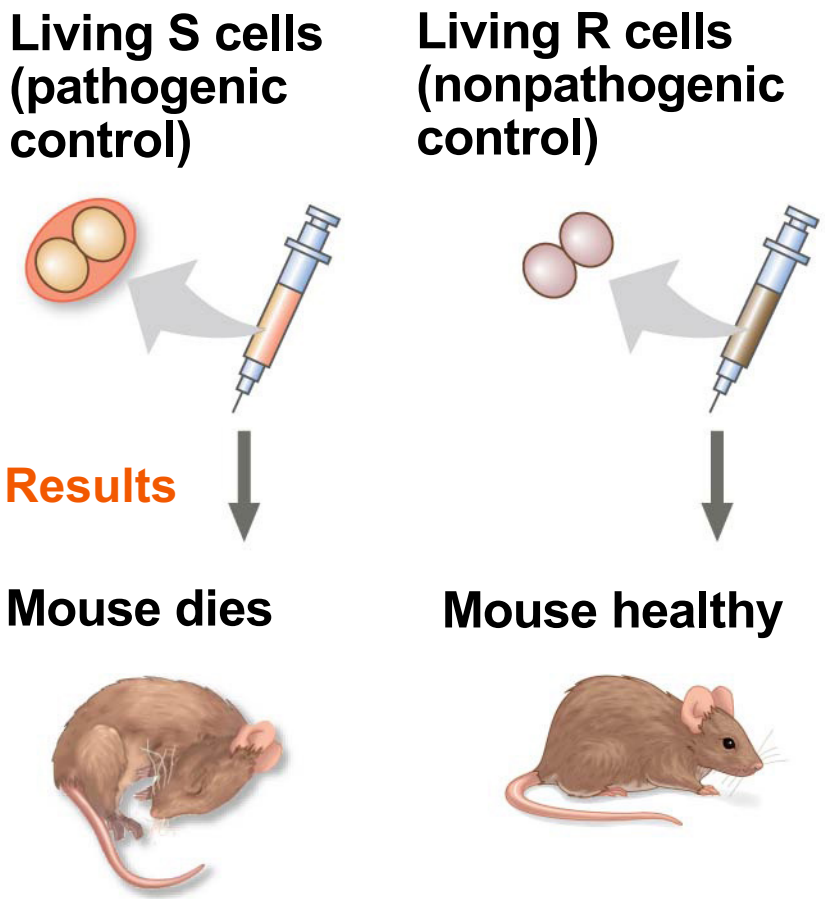


Figure 16.2 in Campbell Biology. 10th edition

Transforming a good strain into a bad strain

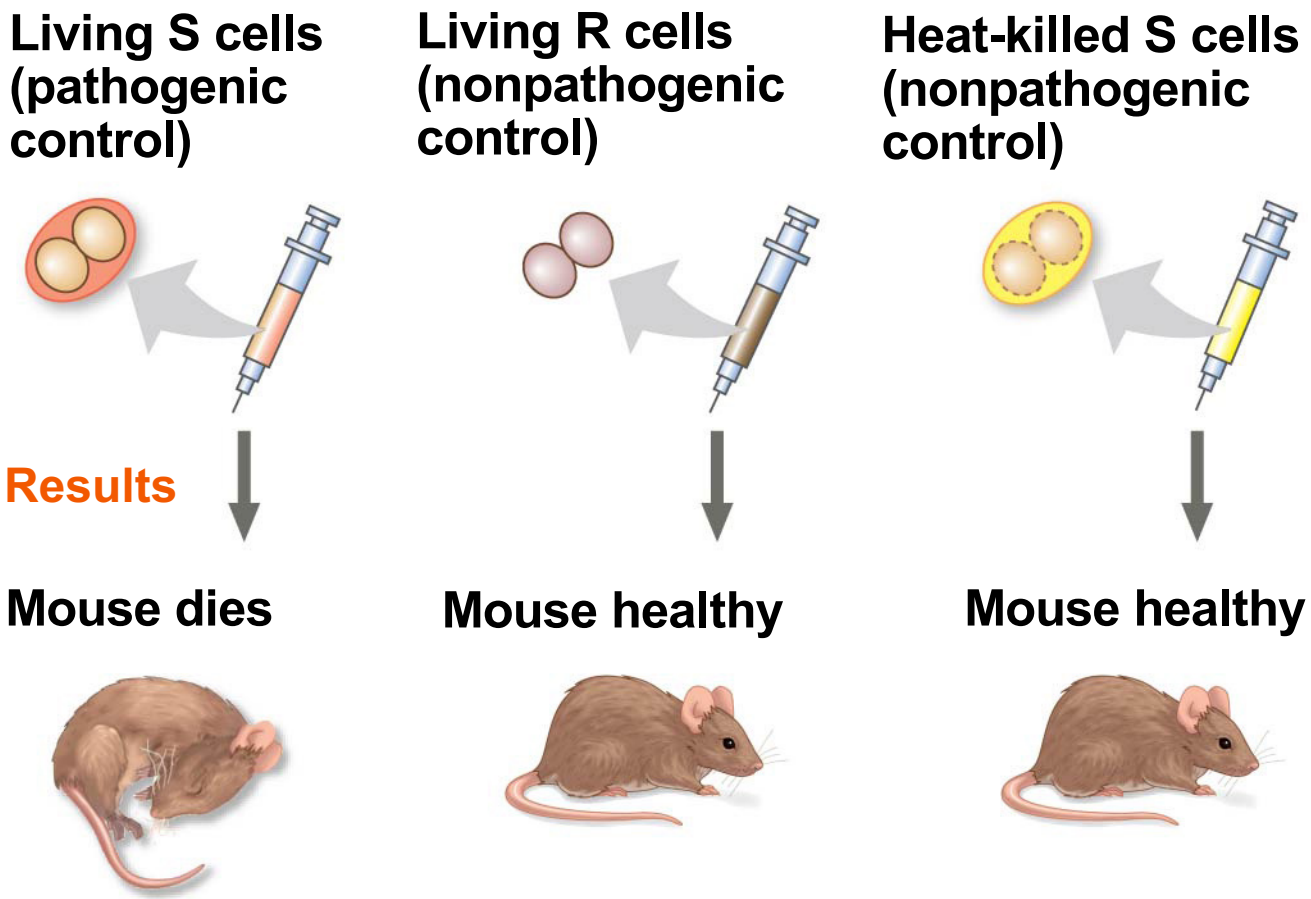
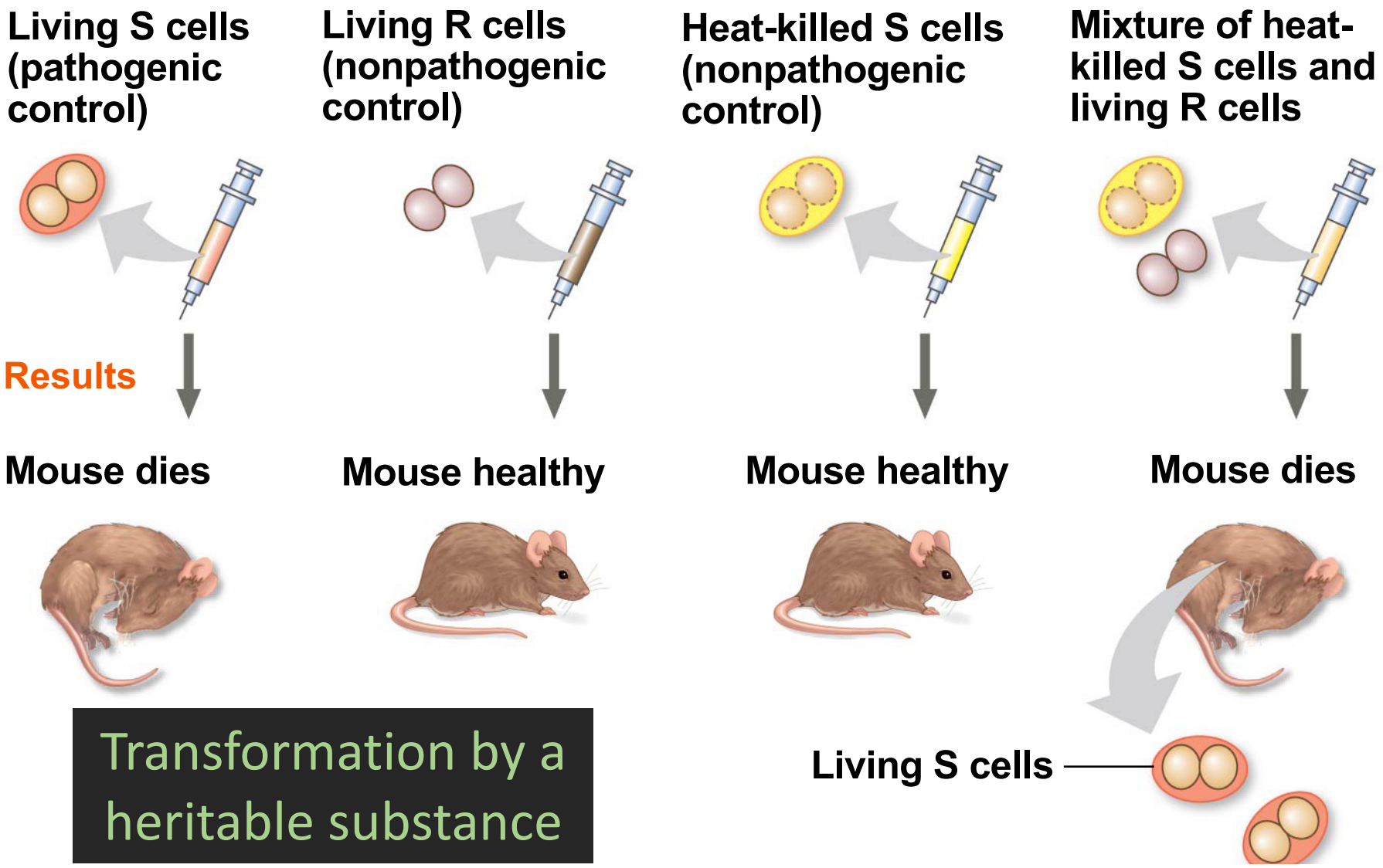


Figure 16.2 in Campbell Biology. 10th edition

Transforming a good strain into a bad strain



Transformation by a heritable substance

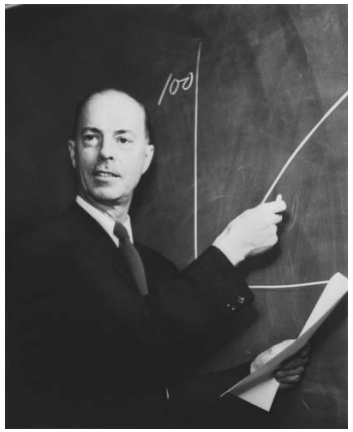
Figure 16.2 in Campbell Biology. 10th edition

Gregor Mendel vs Frederick Griffith

- Gregor Mendel: showed inheritance between generations
- Frederick Griffith: showed transfer of a trait between bacteria
  - The newly acquired trait of pathogenicity was inherited by all the descendants of the transformed bacteria

Nature of the transforming factor?

Oswald Avery



Colin MacLeod

Heat-killed pathogenic bacteria

DNA — inactivate

Protein — inactivate

RNA — inactivate

Test for the ability to transform

✗ ✓ ✓

Maclyn McCarty

Images: wikipaedia

Today's topics

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  - Developing vaccine for pneumonia
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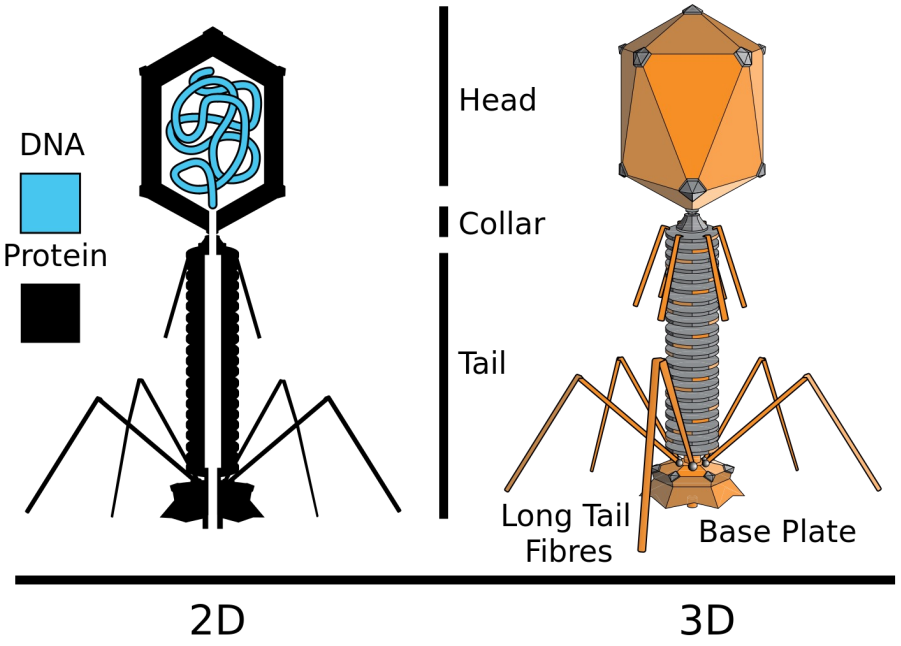
- Applications in day-to-day life

Phages are viruses that infect bacteria

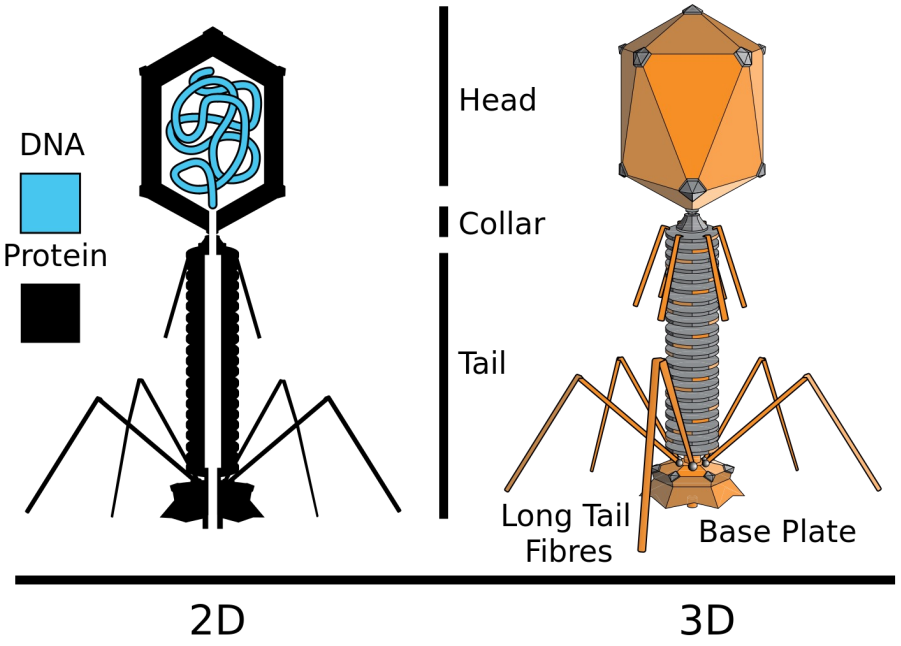


Schematic copied from Wikipedia

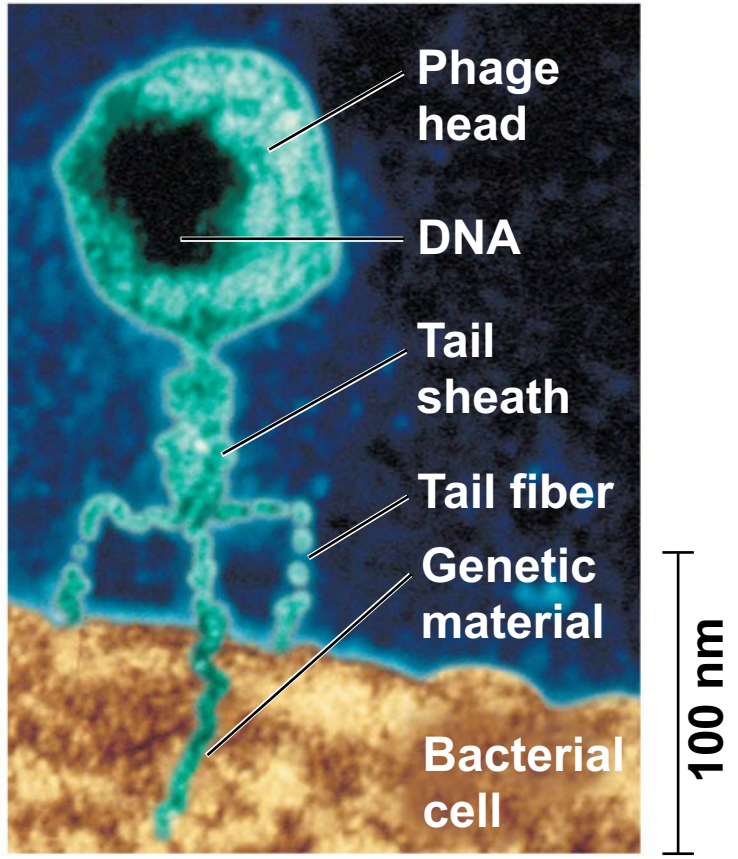
Phage T2

- Is attached to its host cell
- Injects the genetic material into the host cell
- Head and tail parts remain outside the host

Phages are viruses that infect bacteria



Schematic copied from Wikipedia



Colorized transmission electron micrograph

Figure 16.2 in Campbell Biology. 10th edition

What is the genetic material of phage T2

1952

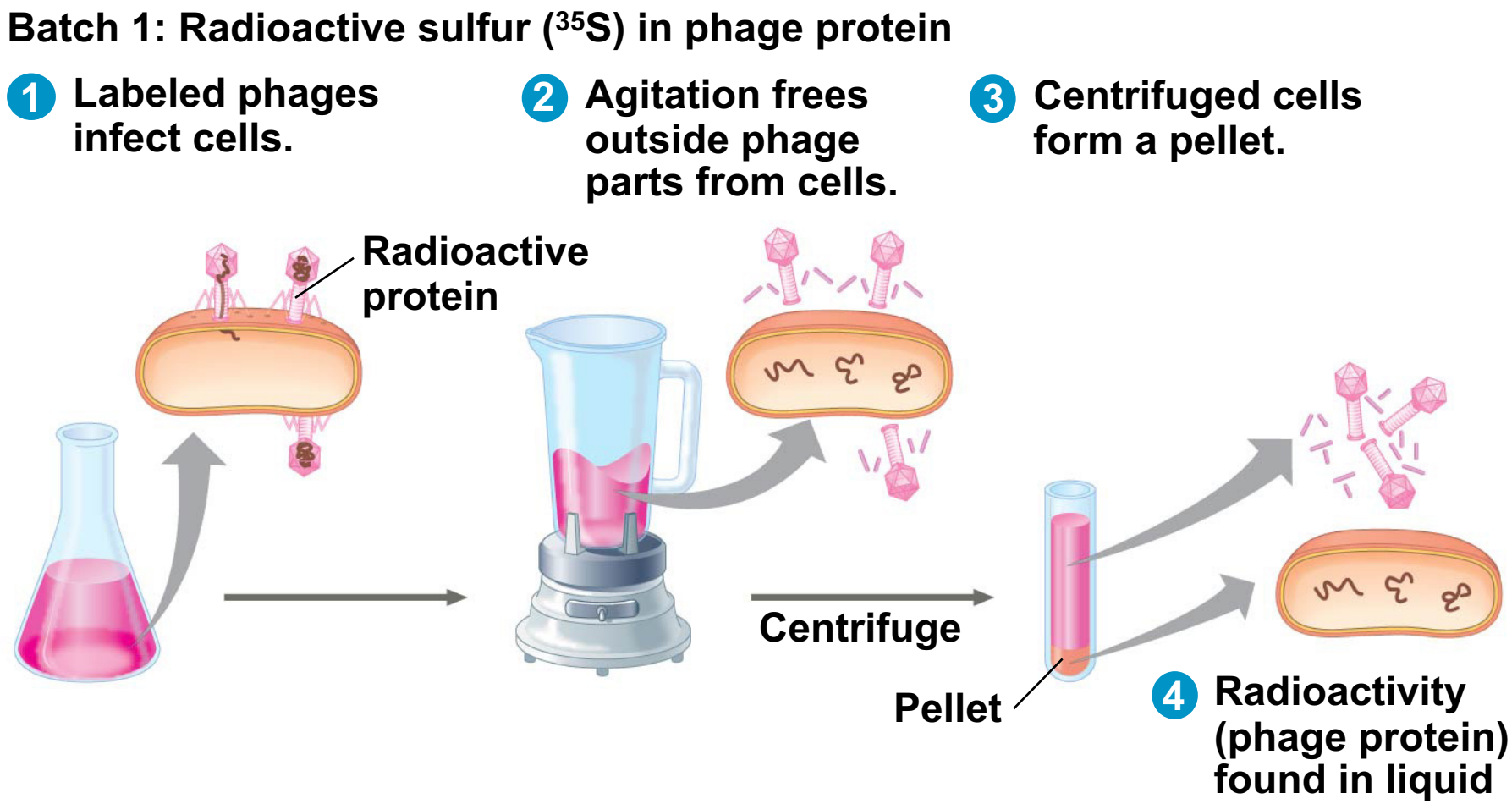
Martha Chase

Alfred Hershey

https://paulingblog.wordpress.com/2009/08/18/the-hershey-chase-blender-experiments/

Exclusive presence of S (in proteins) and P (in DNA)

S: sulfur; P: phosphorous



Hershey-Chase experiment

Figure 16.4 in Campbell Biology. 10th edition

DNA has to be the genetic material

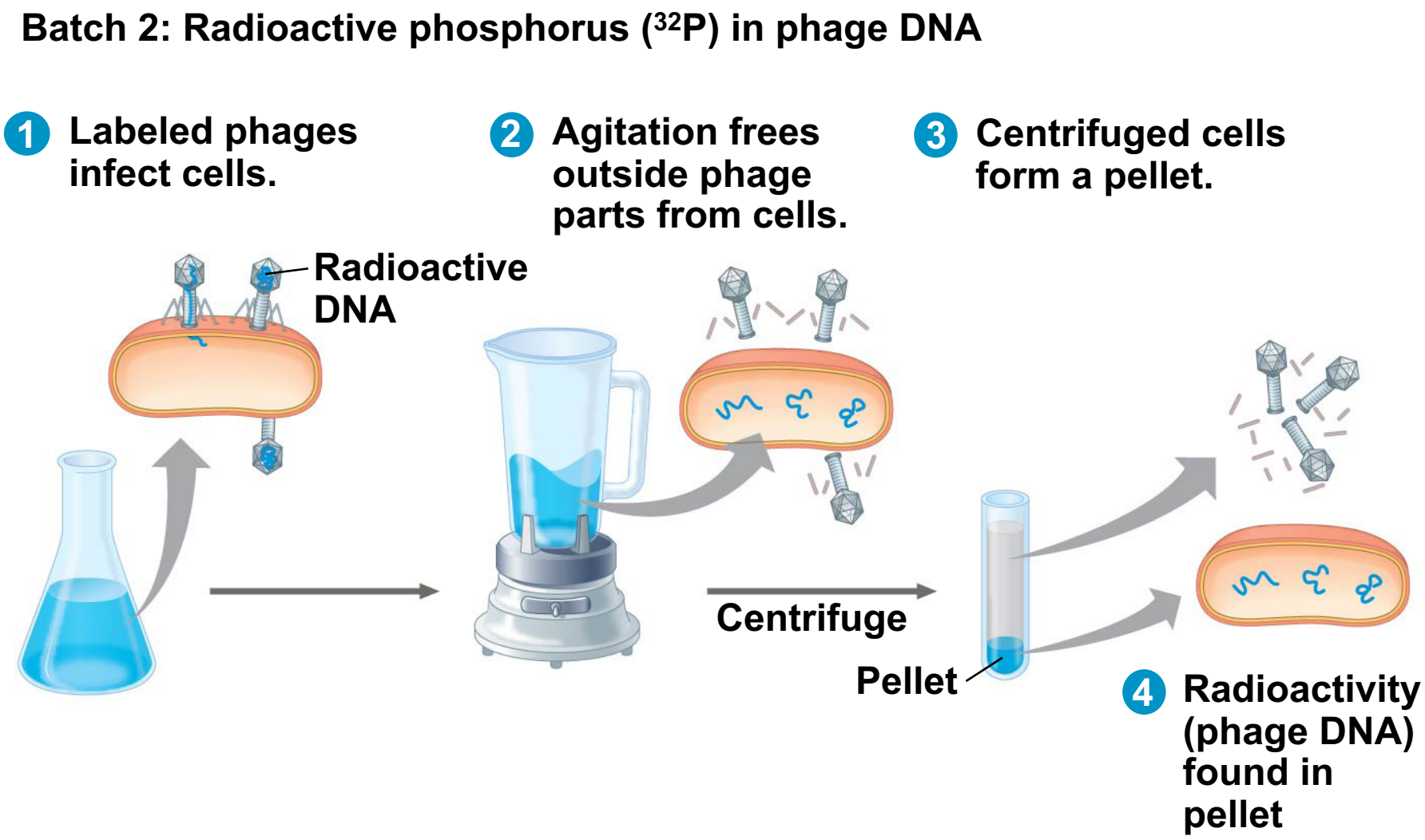


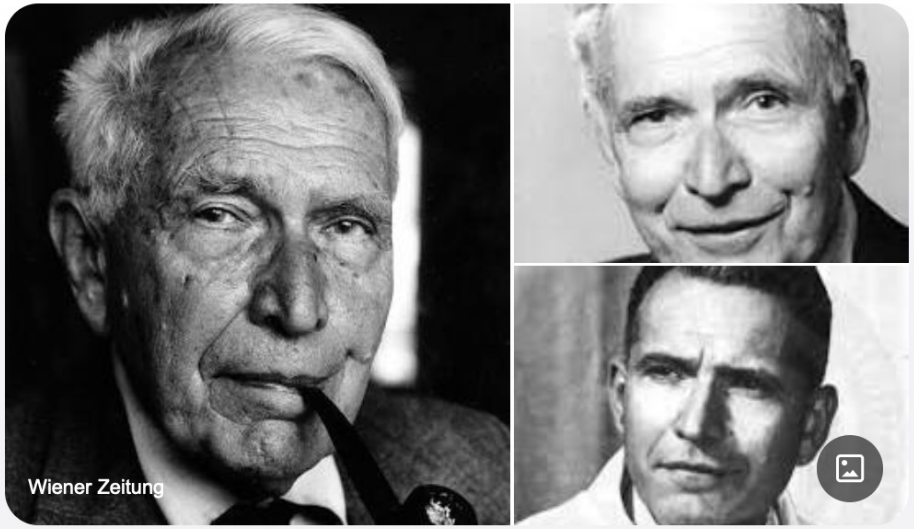
Figure 16.4 in Campbell Biology. 10th edition

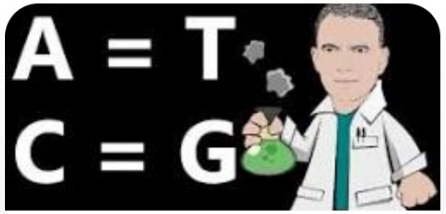
Chargaff's observations

Erwin Chargaff

American biochemist

Overview | Awards





Famous Scientists

Erwin Chargaff - Biography, Facts and Pictures

Lived 1905 – 2002. Erwin Chargaff's research paved the way for the discoveries of DNA's structure and its method of replication. His observation ...

09-Aug-2016

National Scienc...

Erwin Chargaff

Children

Thomas Chargaff

Died

20 June 2002, Manhattan, New York, United States

Wikipedia
https://en.wikipedia.org › wiki › Erwin_Chargaff

Erwin Chargaff

Erwin Chargaff (11 August 1905 – 20 June 2002) was an Austro-Hungarian-born American biochemist, writer, Bucovinian Jew who emigrated to the United States ...

Known for: Chargaff's rules
Awards: Pasteur Medal (1949), Nation…
Education: Maximiliansgymnasium
Born: 11 August 1905; Czernowitz, Du…

Columbia University · Chargaff's rules · Later life · Books authored

About

Erwin Chargaff was an Austro-Hungarian-born American biochemist, writer, Bucovinian Jew who emigrated to the United States during the Nazi era, and professor of biochemistry at Columbia University medical school. He wrote a well-reviewed autobiography, Heraclitean Fire: Sketches from a Life Before Nature. Wikipedia

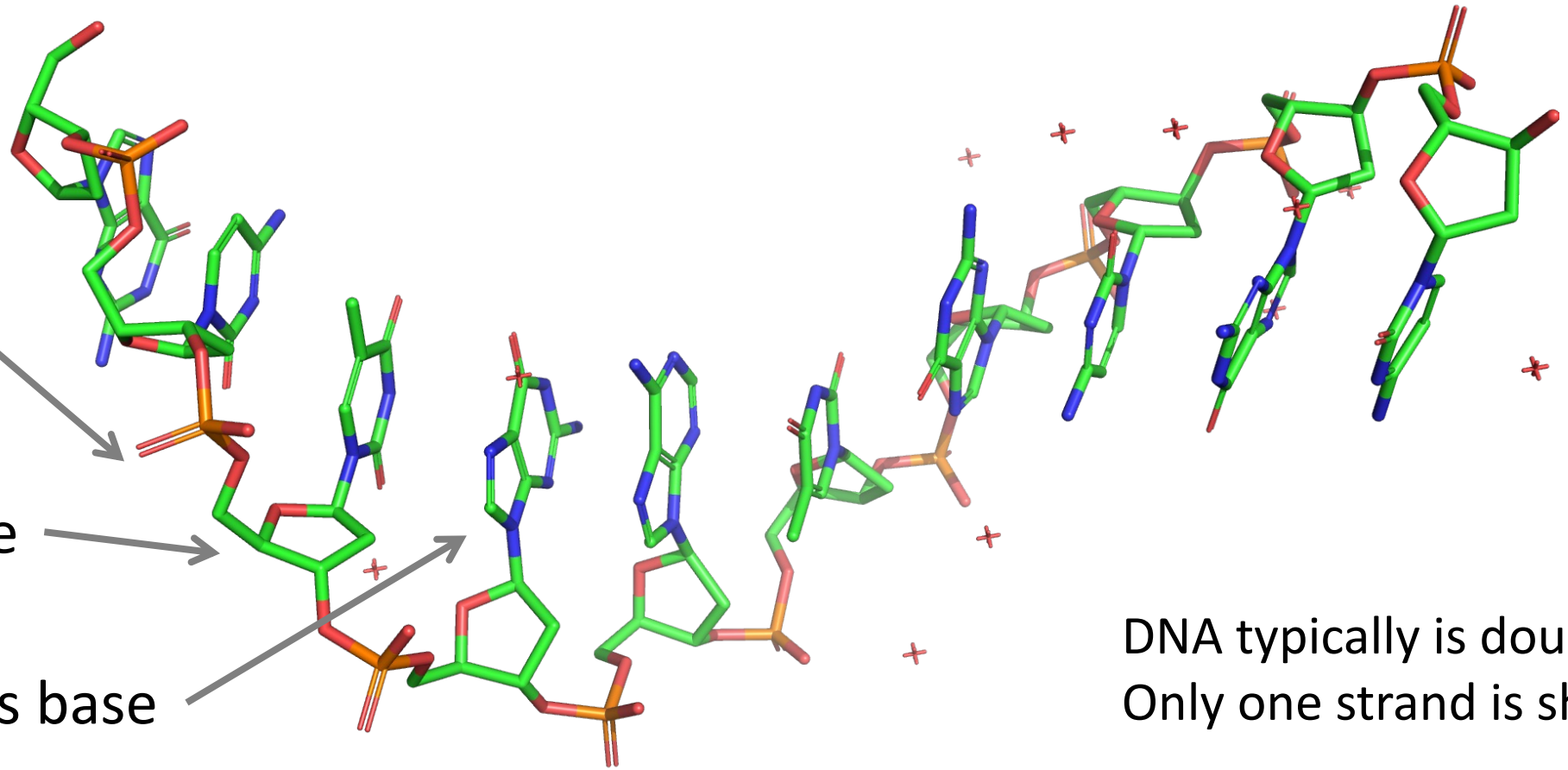
Born: 11 August 1905, Chernivtsi, Ukraine

Died: 20 June 2002, Manhattan, New York, United States

People also ask

3D structure of a strand of a DNA

A linear polymer



DNA typically is double stranded
Only one strand is shown here

monomer: base + deoxyribose + phosphate

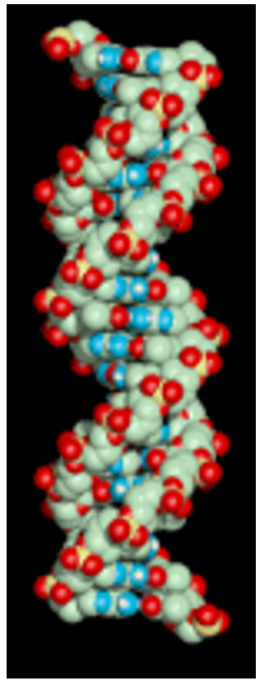
Base: A (adenine), C (cytosine), G (guanine), T (Thymine)

Protein databank id: 1BPX.pdb

Slide from Lecture 1

DNA is like Coca Cola but… it carries information

Coke	DNA	Solubility
Water	Water	Not applicable
Sugar (sucrose)	Sugar (deoxyribose)	Very high
Phosphate	Phosphate	Moderate
Caffeine (a nitrogenous base)	A, C, G, and T (nitrogenous bases)	Extremely low



DNA is THE manual

https://commons.wikimedia.org/wiki/File:CocaColaGlassBottle.jpg
DNA image – from Prof. Swati Patankar

Base composition of DNA

Source of DNA	Base percentage			
	Adenine	Guanine	Cytosine	Thymine
Sea urchin	32.8	17.7	17.3	32.1
Salmon	29.7	20.8	20.4	29.1
Wheat	28.1	21.8	22.7	27.4
E. coli	24.7	26.0	25.7	23.6
Human	30.4	19.6	19.9	30.1
Ox	29.0	21.2	21.2	28.7

From Concept 16.1 of Campbell Biology, 10th ed.
Chapter 16 review. Q #2 in Test your understanding

Erwin Chargaff's observations

What was already known: DNA is a polymer consisting of A, C, G and T (referred to as nucleotide bases)

- **Observation #1**: Base composition of one organism differs from that of another
  Example: Adenine base constitutes 30.4% of human DNA but only 24.7% of *E. coli* (*Escherichia coli*)

  Implication: DNA captures the molecular diversity among species

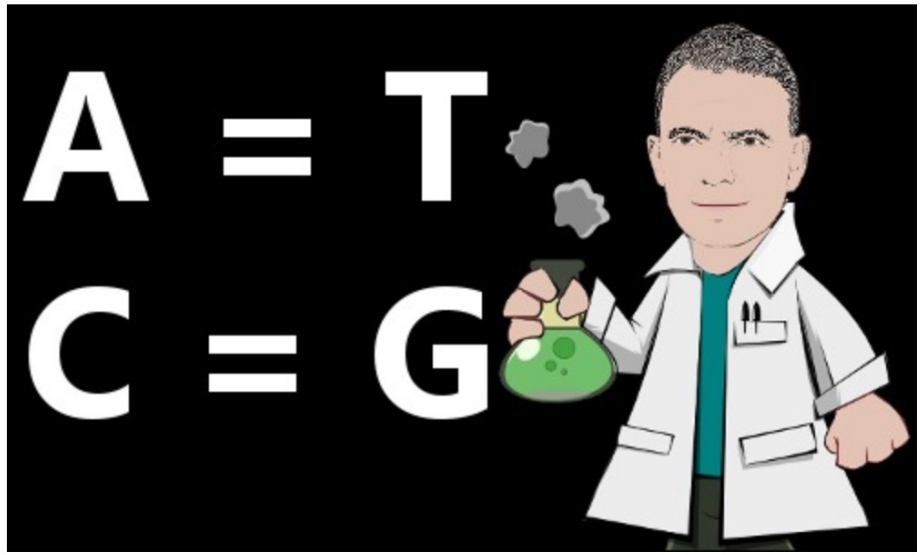
- **Observation #2**: No. of A ≃ No. of T; No. of G ≃ No. of C
  Example: human DNA: A = 30.4%, C = 19.9%, G = 19.6%, T = 30.1%

Erwin Chargaff (1905-2002)

Famous Scientists
The Art of Genius

Home | Top 100 Scientists | List of Scientists | Blog

Erwin Chargaff



Lived 1905 – 2002.

Erwin Chargaff's research paved the way for the discoveries of DNA's structure and its method of replication.

His observation that DNA varies from species to species made it highly credible that DNA was genetic material.

His identification of 1:1 ratios in DNA's bases allowed James Watson and Francis Crick to see how these bases slotted into the double helix and how DNA could act as a template for copies of itself.

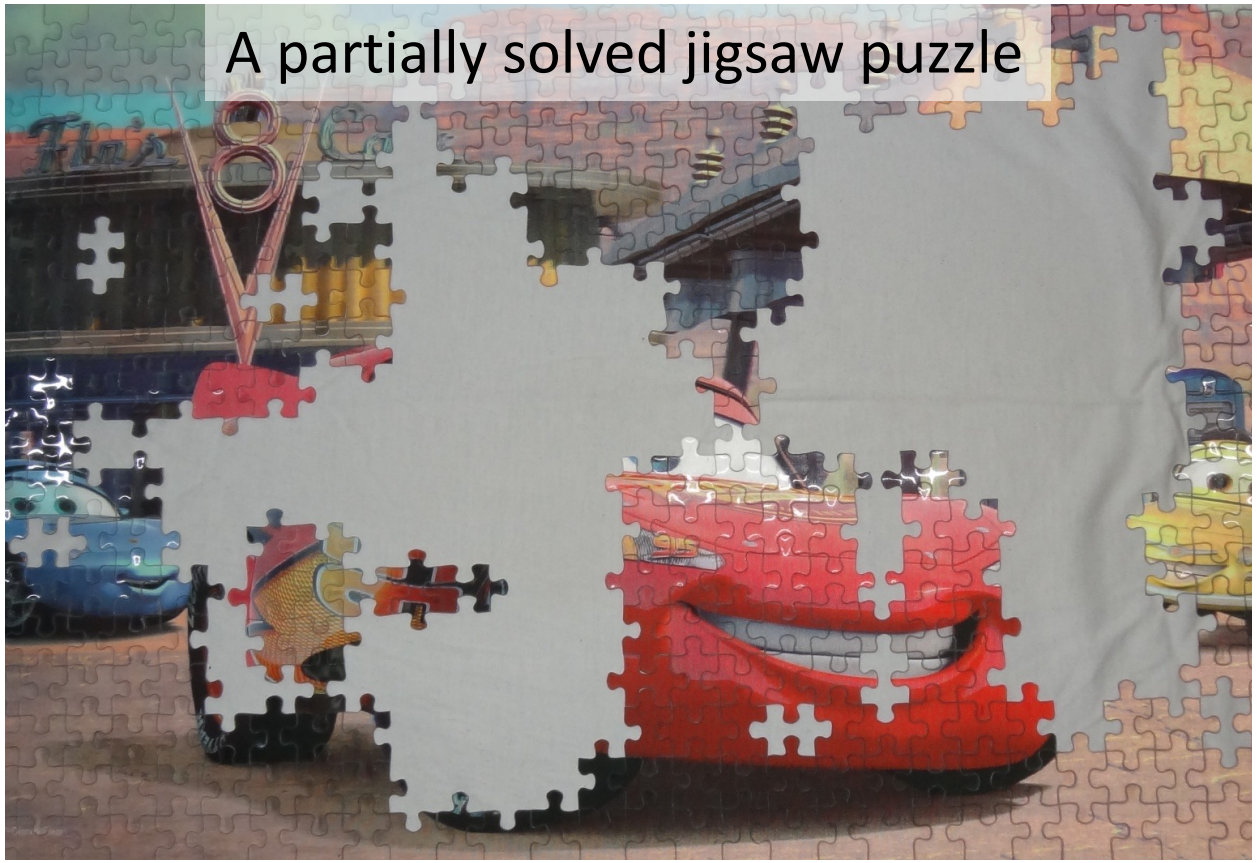
https://www.famousscientists.org/erwin-chargaff/

Is DNA the genetic material?

Several experimental observations indicated that DNA is indeed the genetic material

But was the evidence conclusive?

Have we solved the problem "sufficiently enough" to arrive at the final answer?



Is there a definite end point to solving the problem?

What is the structure of DNA?

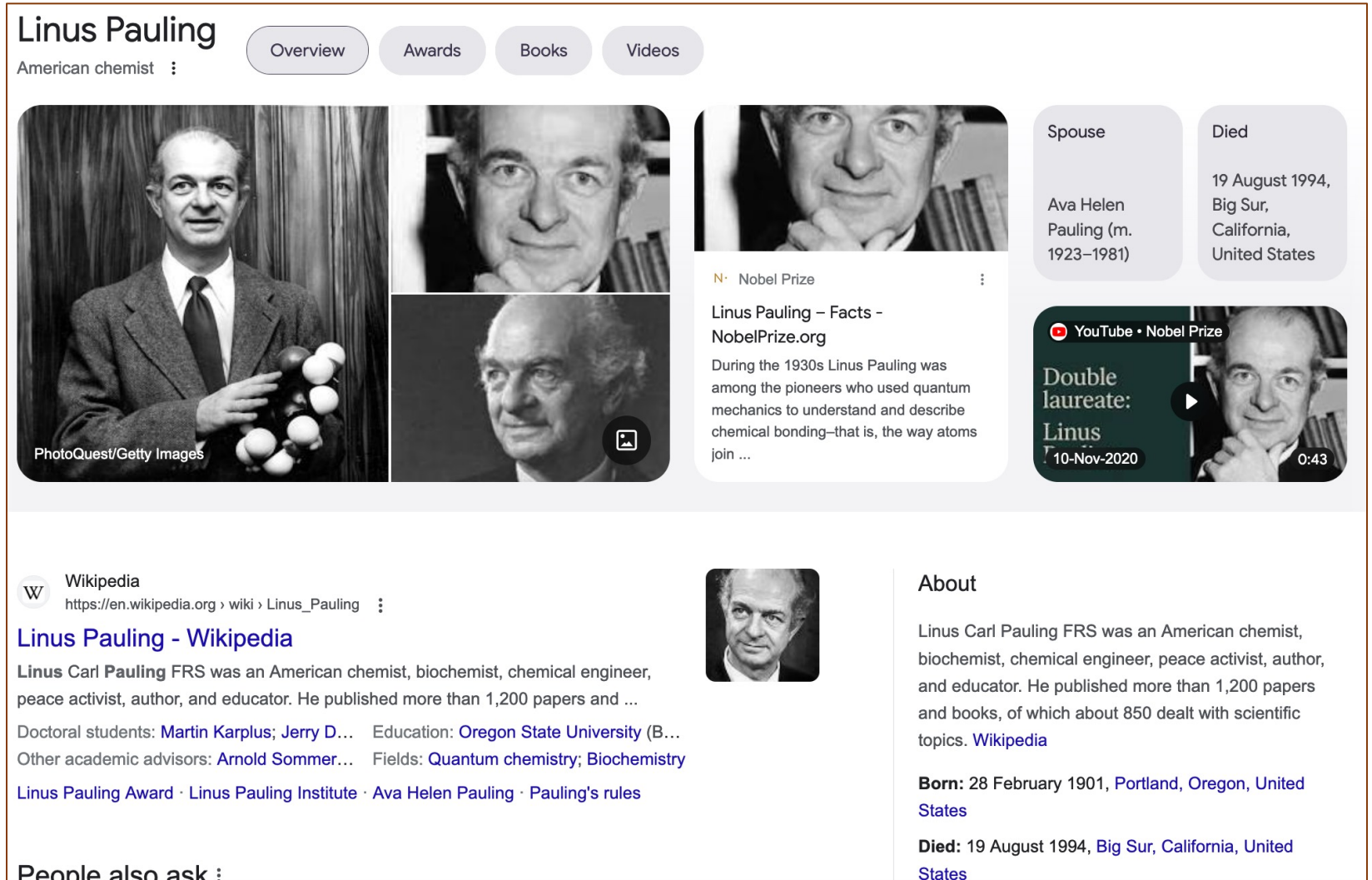
Key question

If DNA is indeed the genetic material…

What is its structure?
How does the structure account for it being the genetic material?

Hunt for the structure of DNA...

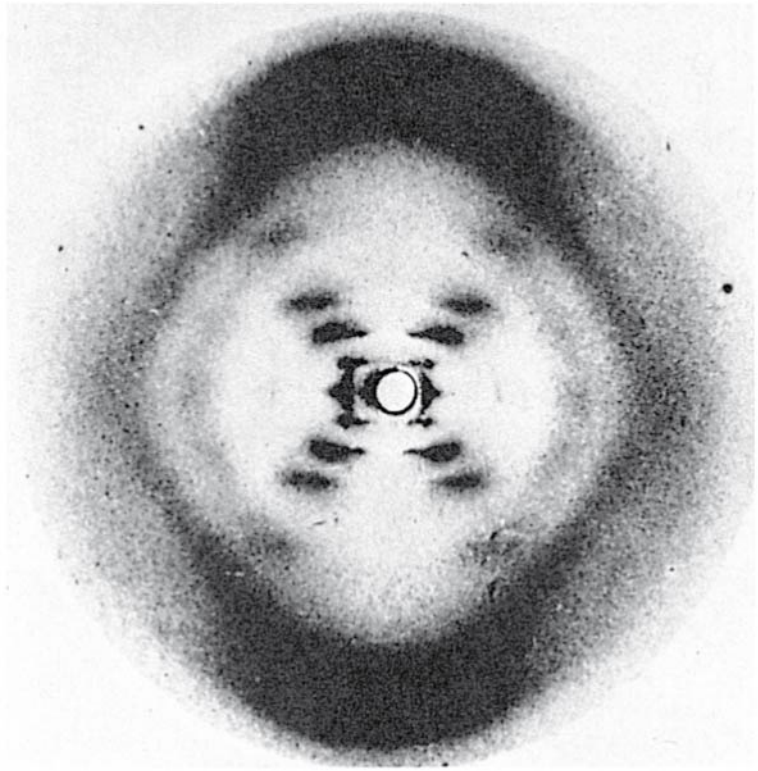
Rope-like strand consisting of three intertwined polymeric chains



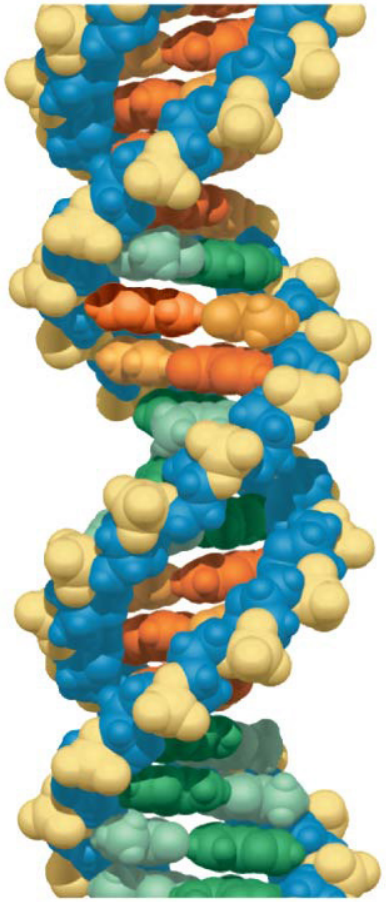
X-ray diffraction pattern of DNA fibers

Top quality diffraction pattern that no one else could produce!

(a) Rosalind Franklin



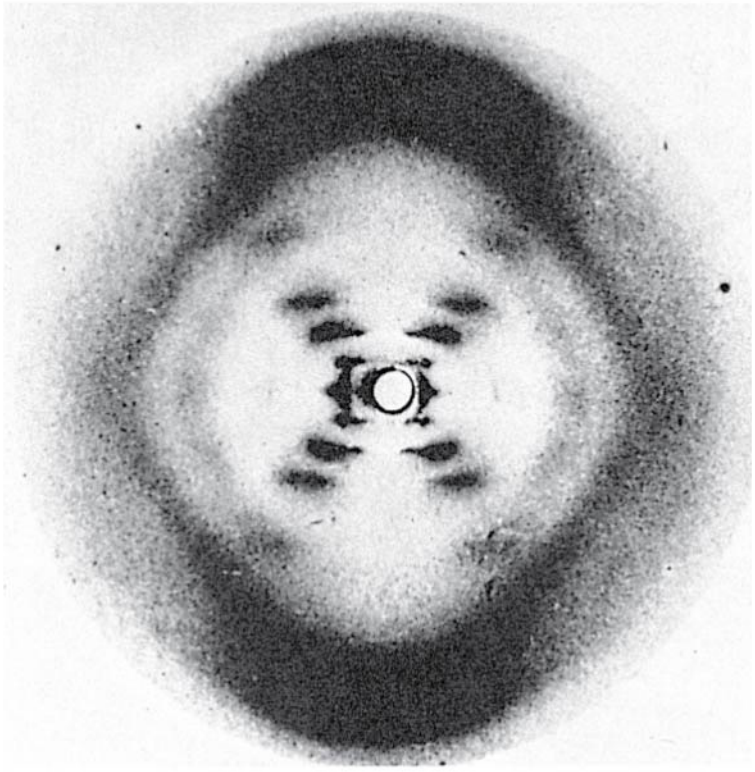
(b) Franklin's X-ray diffraction photograph of DNA



She could infer that sugar-phosphate are outside,
but could not propose a model based on this data!

Figures 16.6 and 16.7 of Campbell Biology, 10th ed.

Diffraction data to model



(b) Franklin's X-ray diffraction photograph of DNA

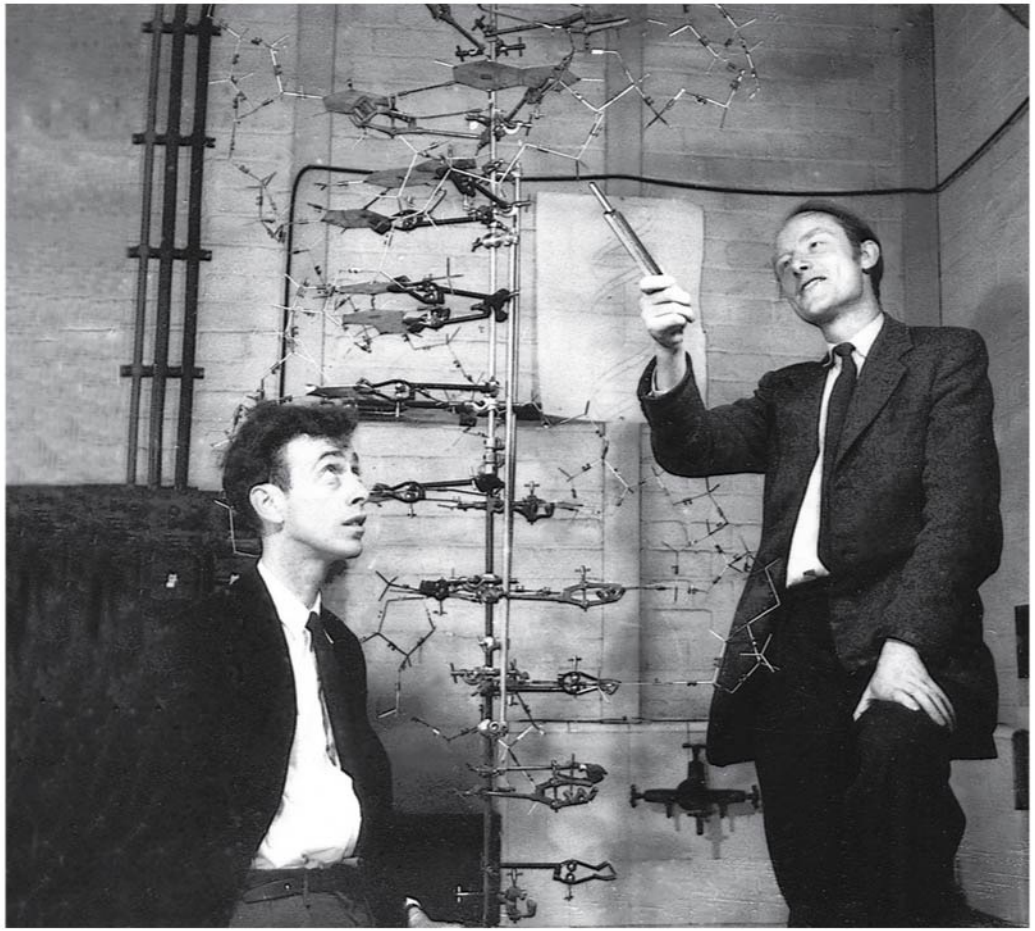
Watson and Crick's inferences from this data

- DNA is helical
- Width of the helix is 2 nm
- Spacing between two bases is 0.34 nm
- There are 10 bases per turn of the helix
- DNA has two strands

From Concept 16.6 of Campbell Biology, 10th ed.

Discovery that revolutionized Biology

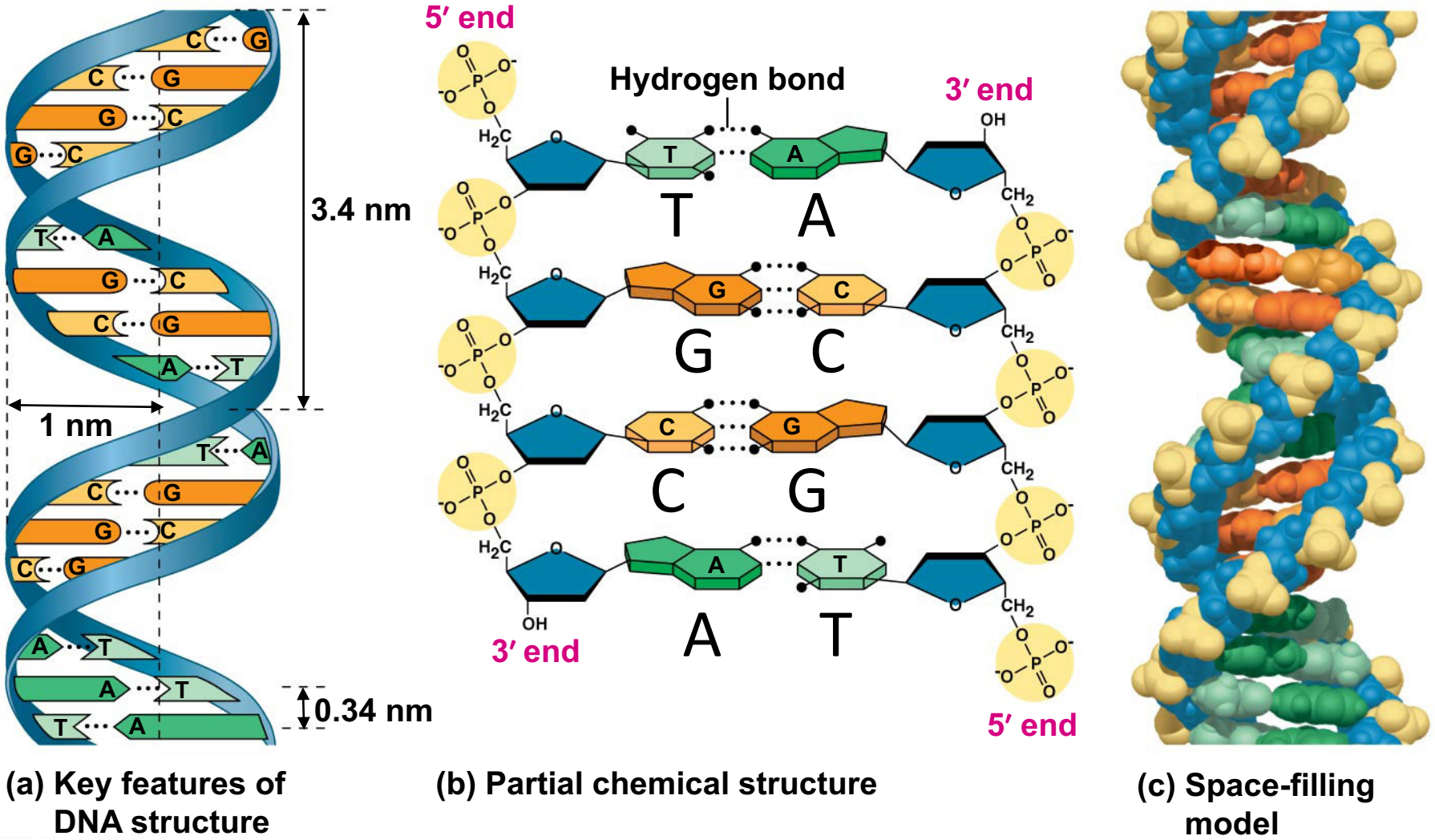
James Watson



Francis Crick

Figure 16.1 of Campbell Biology, 10th ed.

Double helix model of DNA

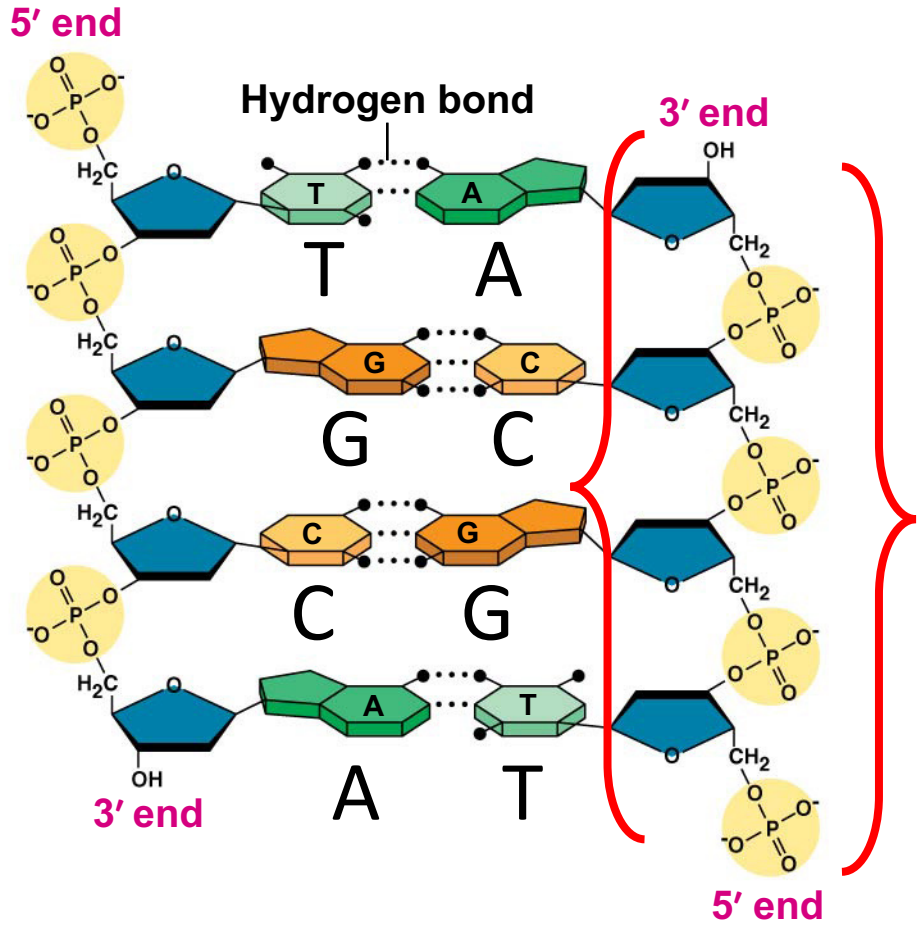


Accounts for Chargaff's observation also

Figure 16.7 of Campbell Biology, 10th ed.

Features of DNA double helix

The two strands of a DNA are aligned in opposite directions (anti-parallel orientation)



Sugar phosphate backbone

Has specific end points viz., 5’-end (starting) and 3’-end (ending)

Figure 16.7 of Campbell Biology, 10th ed.

Today's topics

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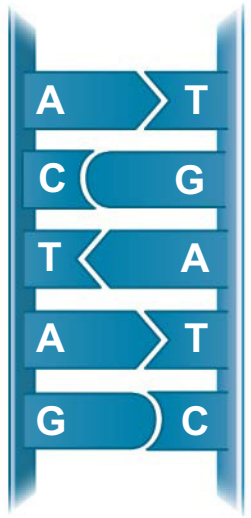
Can structure be related to function?



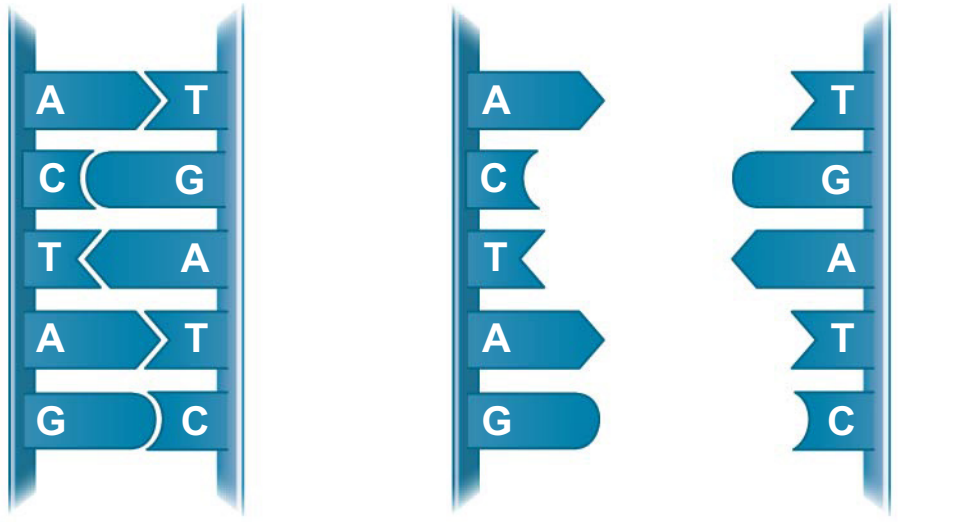
(a) Parental molecule

Structure (form) and function (purpose)

If DNA is indeed the genetic material,
does the proposed structure offer
a “simple” mode of copying (replication)?

Figure 16.9 of Campbell Biology, 10th ed.

Structure gives clues to how DNA is copied



(a) Parental molecule

(b) Separation of parental strands into templates

Replication model envisaged by Watson and Crick

Figure 16.9 of Campbell Biology, 10th ed.

Parental strands become the templates

Dark blue: parental strand

Light blue: daughter (new) strand

(a) Parental molecule

(b) Separation of parental strands into templates

(c) Formation of new strands complementary to template strands

Replication model envisaged by Watson and Crick

Semi-conservative replication model

Other proposals: conservative model, dispersive model

Figure 16.9 of Campbell Biology, 10th ed.

Experimental proof for replication model

Matt Meselson and Frank Stahl

Designed one of the most innovative experiments

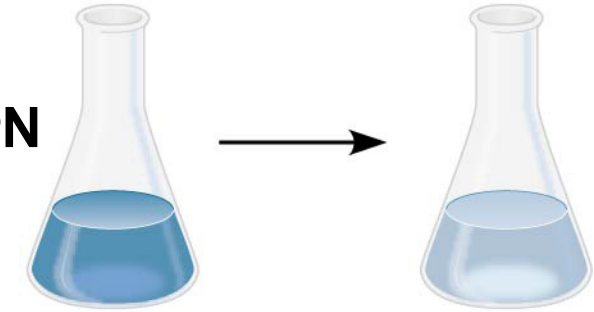
Aim: does DNA replication follow semi-conservative mechanism?

Novelty: exploiting the availability of a heavy isotope of nitrogen

Meselson-Stahl experiment: design

Experiment

1 Bacteria cultured in medium with ^{15}N (heavy isotope)



2 Bacteria transferred to medium with ^{14}N (lighter isotope)

Results

3 DNA sample centrifuged after first replication

4 DNA sample centrifuged after second replication

Less dense

More dense

Figure 16.11 of Campbell Biology, 10th ed.

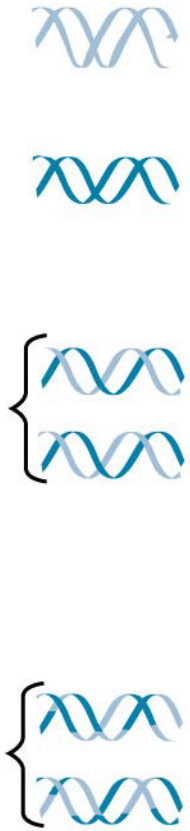
Meselson-Stahl experiment: expectation

Predictions: **First replication**

Conservative model

Semiconservative model

Dispersive model



^{14}N-DNA

^{15}N-DNA

Figure 16.11 of Campbell Biology, 10th ed.

Possible models of replication

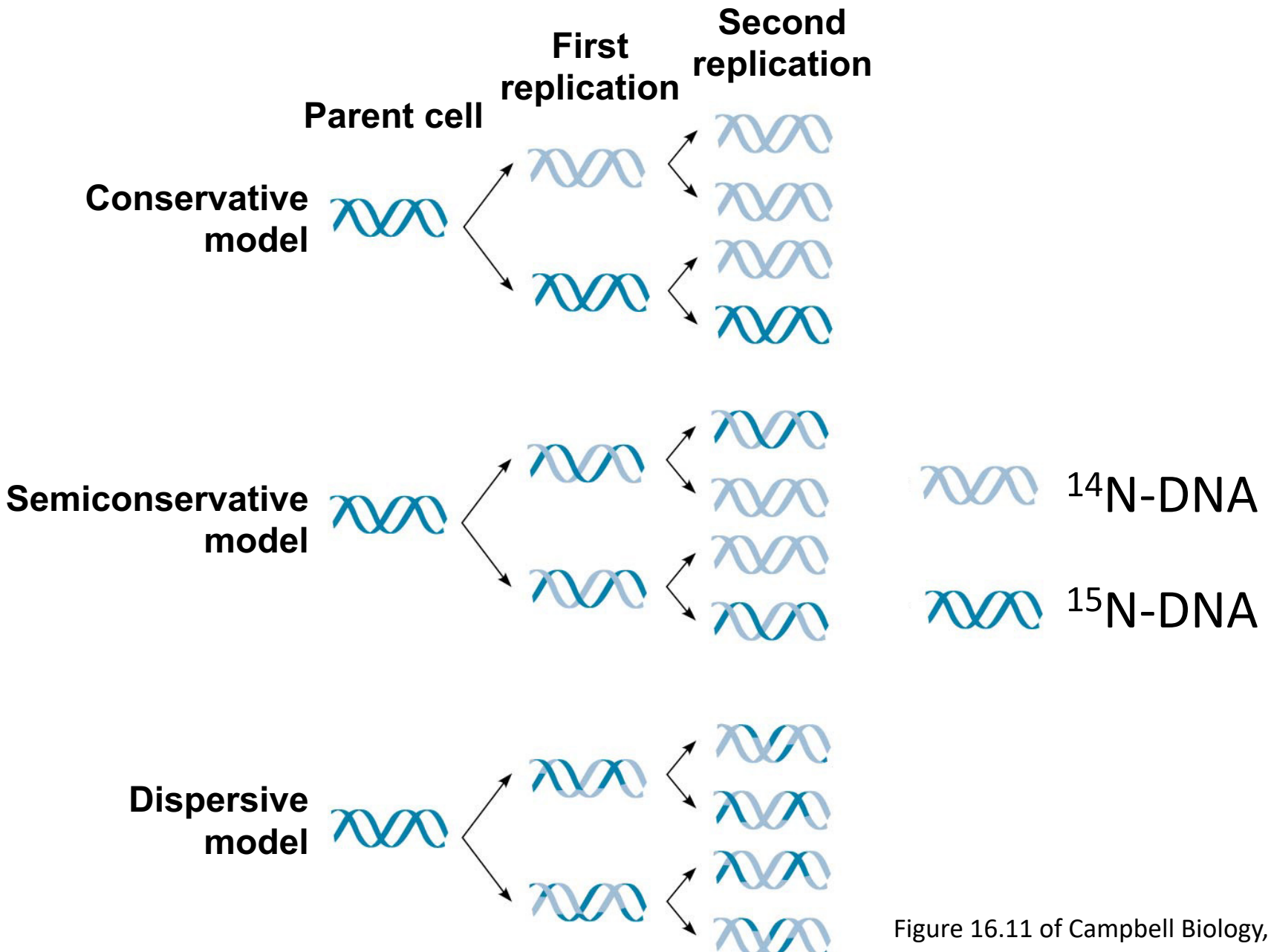


Figure 16.11 of Campbell Biology, 10th ed.

Meselson-Stahl experiment: expectation

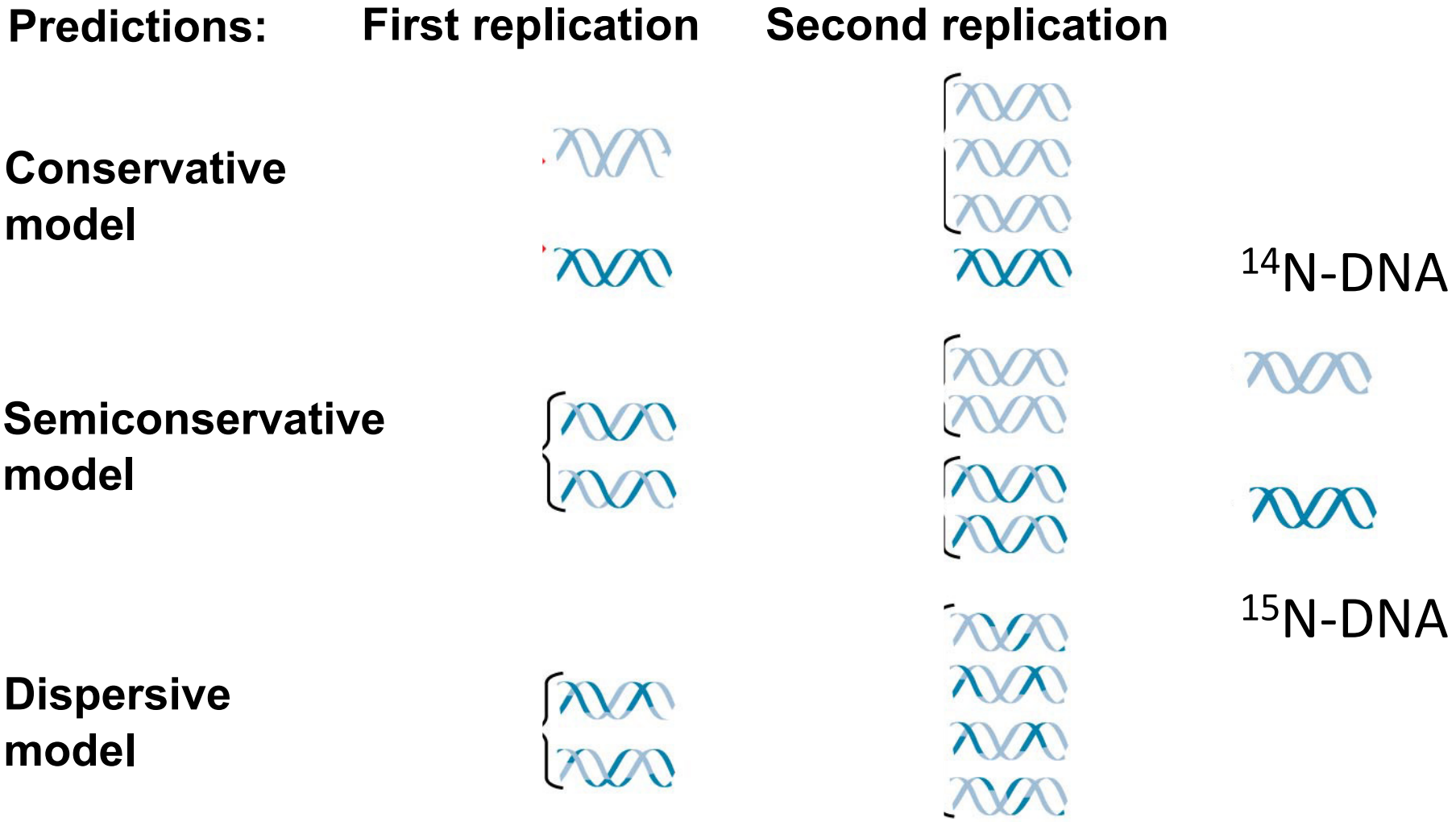


Figure 16.11 of Campbell Biology, 10th ed.

Meselson-Stahl experiment: results

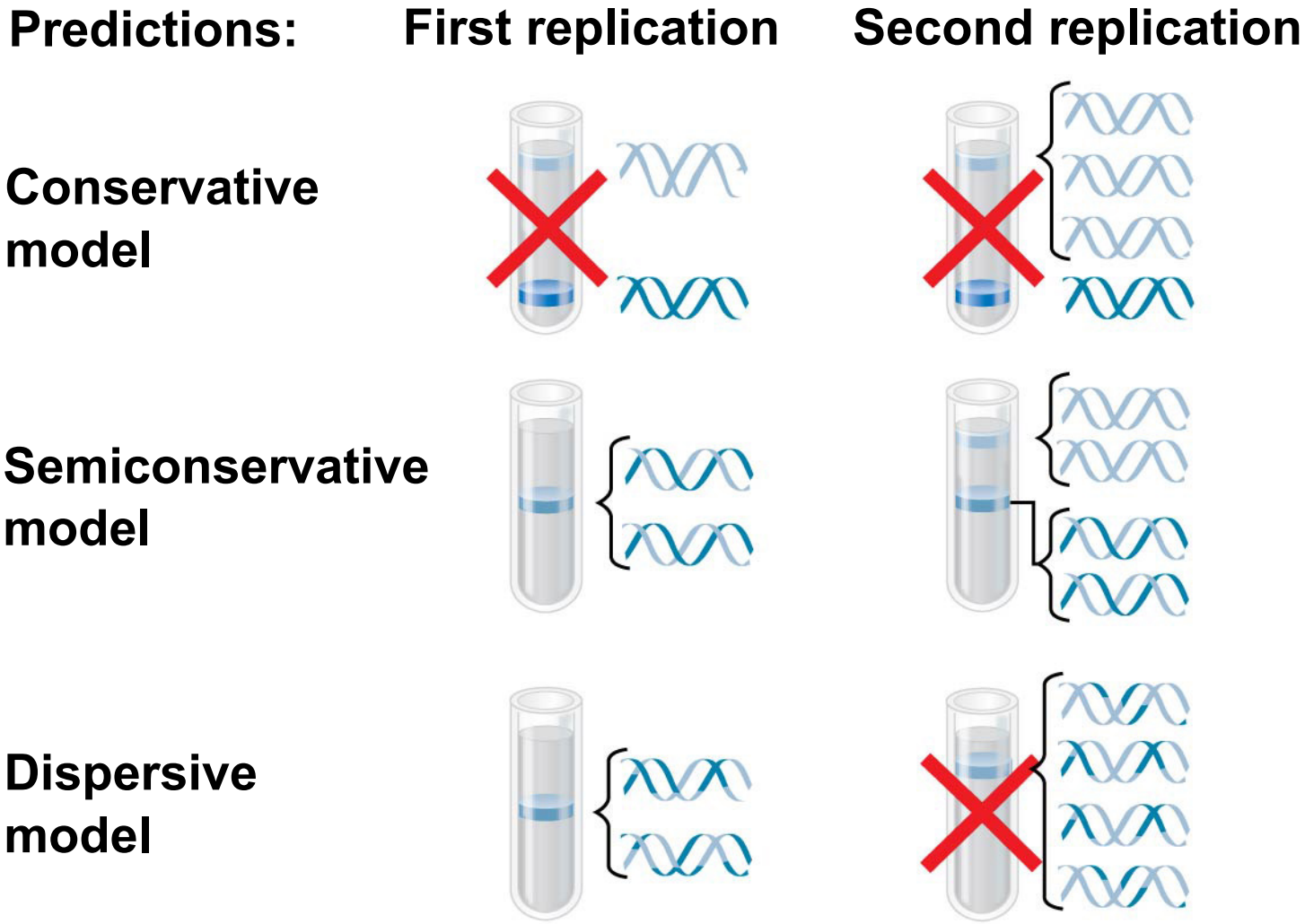


Figure 16.11 of Campbell Biology, 10th ed.

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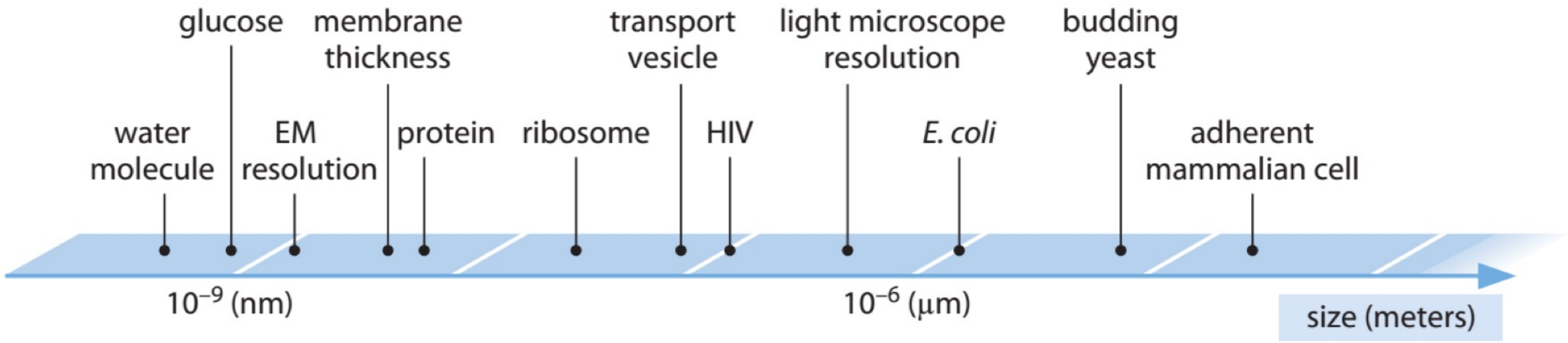
Length comparison: DNA and cell



Watson-Crick model: 10 base pairs: 3.4 nm

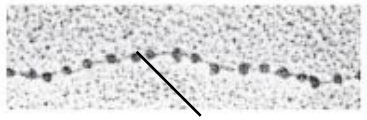
Number of bases in human chromosome #1 is $\sim 250 \times 10^6$ bp

Length: $250 \times 10^6 \times 0.34$ nm = 85 mm

Figure 1.1
Cell Biology by the numbers

Packaging of DNA

Nucleosome (bead)
+ linker DNA (string)

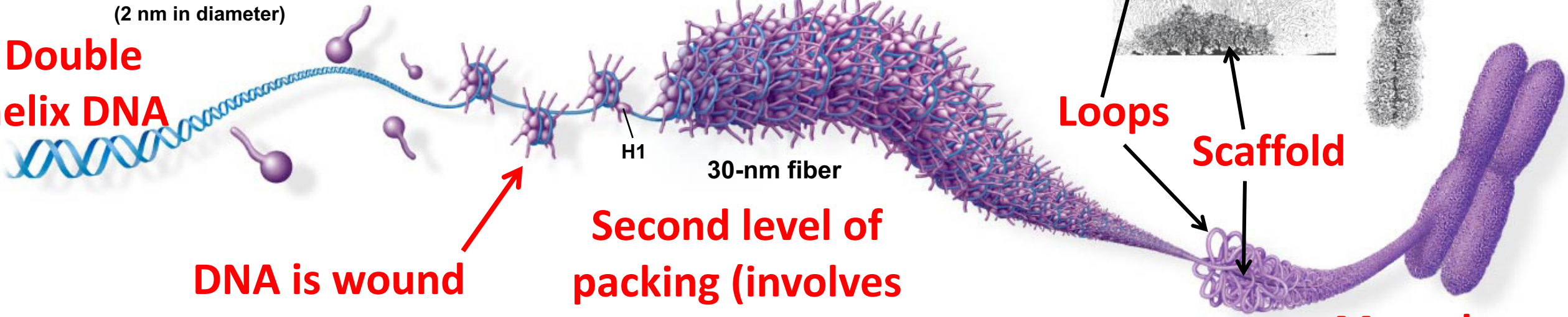


Nucleosome
(10 nm in diameter)

DNA double helix
(2 nm in diameter)

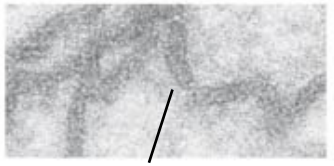
Histones

Double
helix DNA

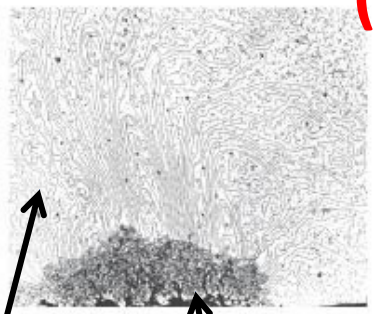


H1

30-nm fiber



30-nm fiber



Two chromatids
(700 nm)

Loops

Scaffold

DNA is wound
around histones

Second level of
packing (involves
histone tails)

Looped domains
(300 nm fibers)

Metaphase
(replicated)
chromosome
(1400 nm)

Accessing books in a library

Books arranged in shelves

Shelves spaced out to facilitate access

Photo courtesy:
Dr. Manju Naika
Chief Library Officer
IIT Bombay

Requires a lot of space
Not all shelves are accessed simultaneously
Sub-optimal space utilization

Storage compactors

Arrange the book shelves on a railing
Each book shelf will have a steering wheel
Pack shelves next to each other
Easy to move shelves along the rails
Make space if and when required

Saves a lot of space

Especially useful when usage is infrequent

Today's topics

- Frederick Griffith
  - Developing vaccine for pneumonia
- Oswald Avery, Colin MacLeod, Maclyn McCarty
  - Identified DNA as the transforming principle
- Alfred Hershey and Martha Chase
  - James Watson and Francis Crick
  - Matthew Meselson and Franklin Stahl
- DNA packaging
- Applications in day-to-day life

Genome of an organism

Genome: entire genetic content of an organism

It is a collection of chromosomes (In humans, one copy each of 22 chromosomes AND either X or Y chromosome)

Each chromosome is a double stranded DNA molecule

Each chromosome consists of several genes

Human chromosomes

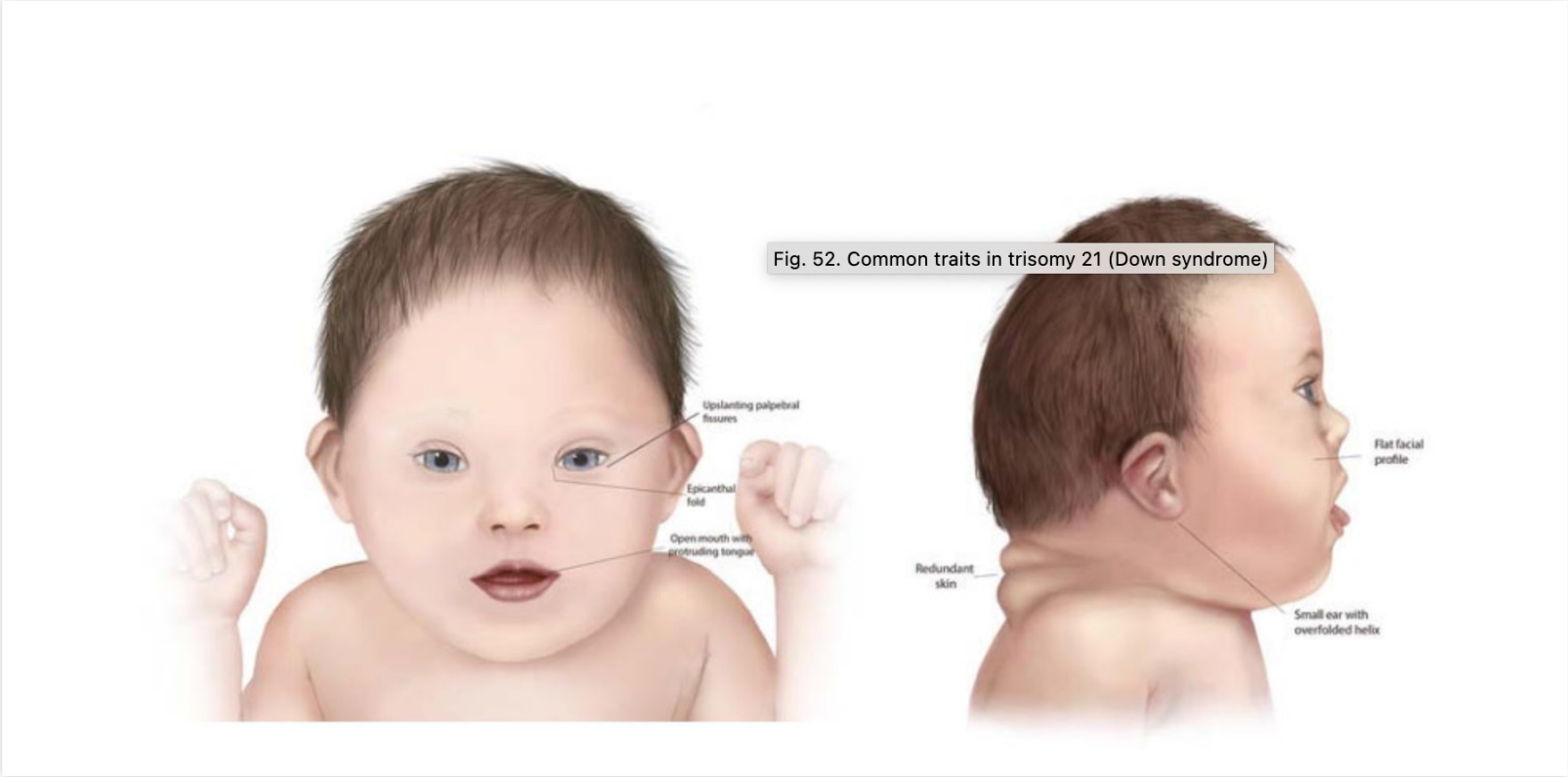
Figure 13.3. Biology. A global approach

Chromosomal Abnormalities: Trisomy 21 (Down Syndrome)

Print

Trisomy 21, also known as Down syndrome, is a condition characterized by a distinctive pattern of minor and major anomalies associated with excess chromosome 21 material.

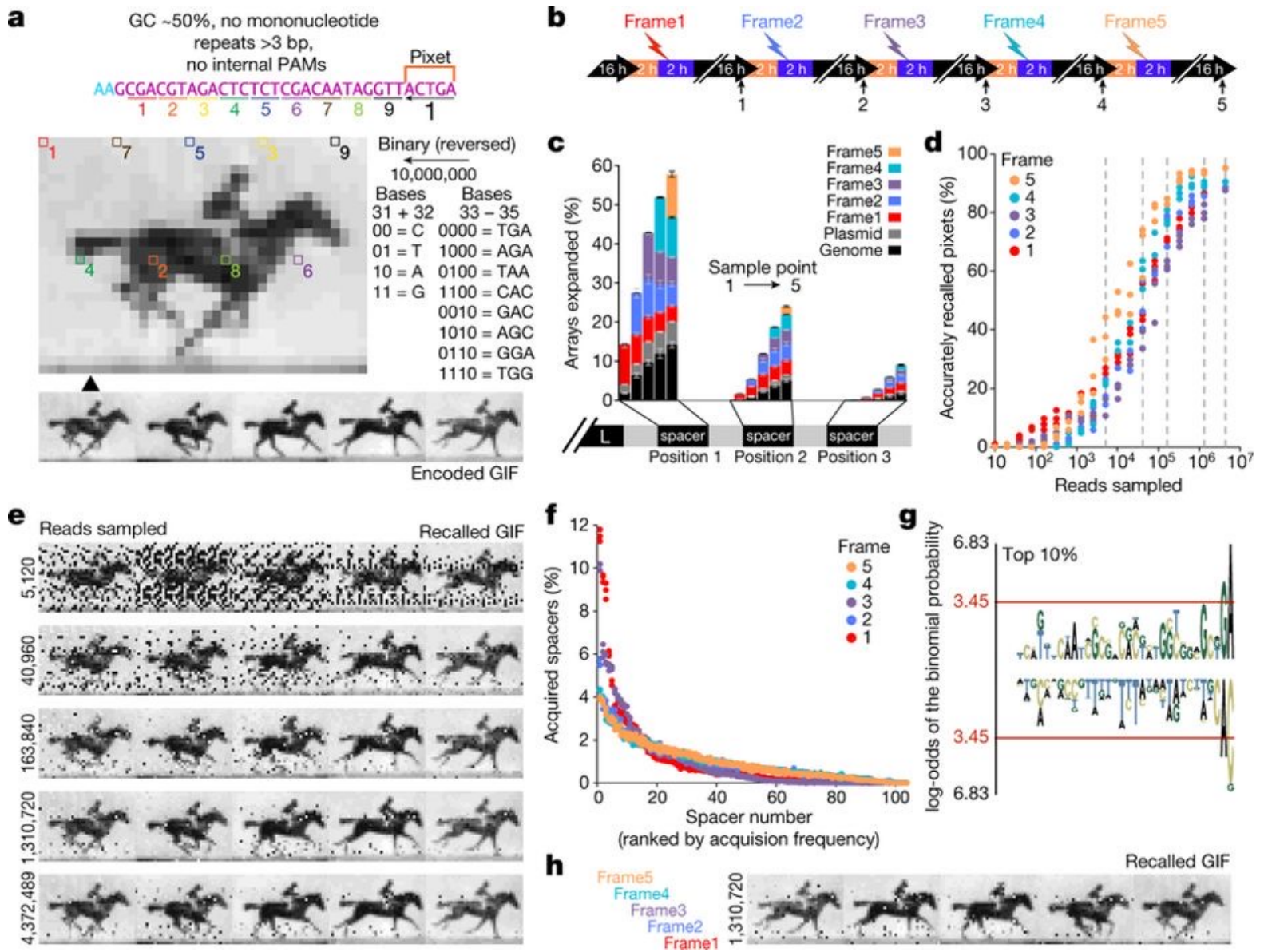
Fig. 52. Common traits in trisomy 21 (Down syndrome)



https://www.cdc.gov/ncbddd/birthdefects/surveillancemanual/quick-reference-handbook/trisomy-21-down-syndrome.html

Encoding an image in bacteria

Steganography: hiding
a file in another file,
a text in another text,
an image in another image,
a video in another video



CRISPR–Cas encoding of a digital movie into the genomes of a population of living bacteria

Seth L. Shipman, Jeff Nivala, Jeffrey D. Macklis & George M. Church

Nature **547**, 345–349 (20 July 2017) | Download Citation