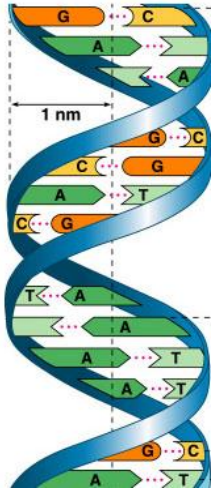
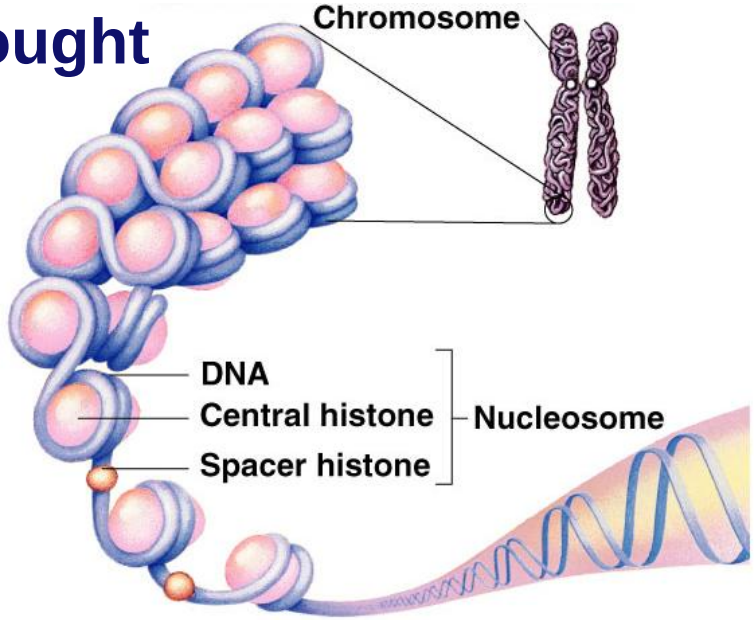


DNA
The Genetic Material

1908 | 1933

Genes are on chromosomes

- Morgan's conclusions
  - genes are on chromosomes
  - but is it the protein or the DNA of the chromosomes that are the genes?
    - initially proteins were thought to be genetic material… Why?

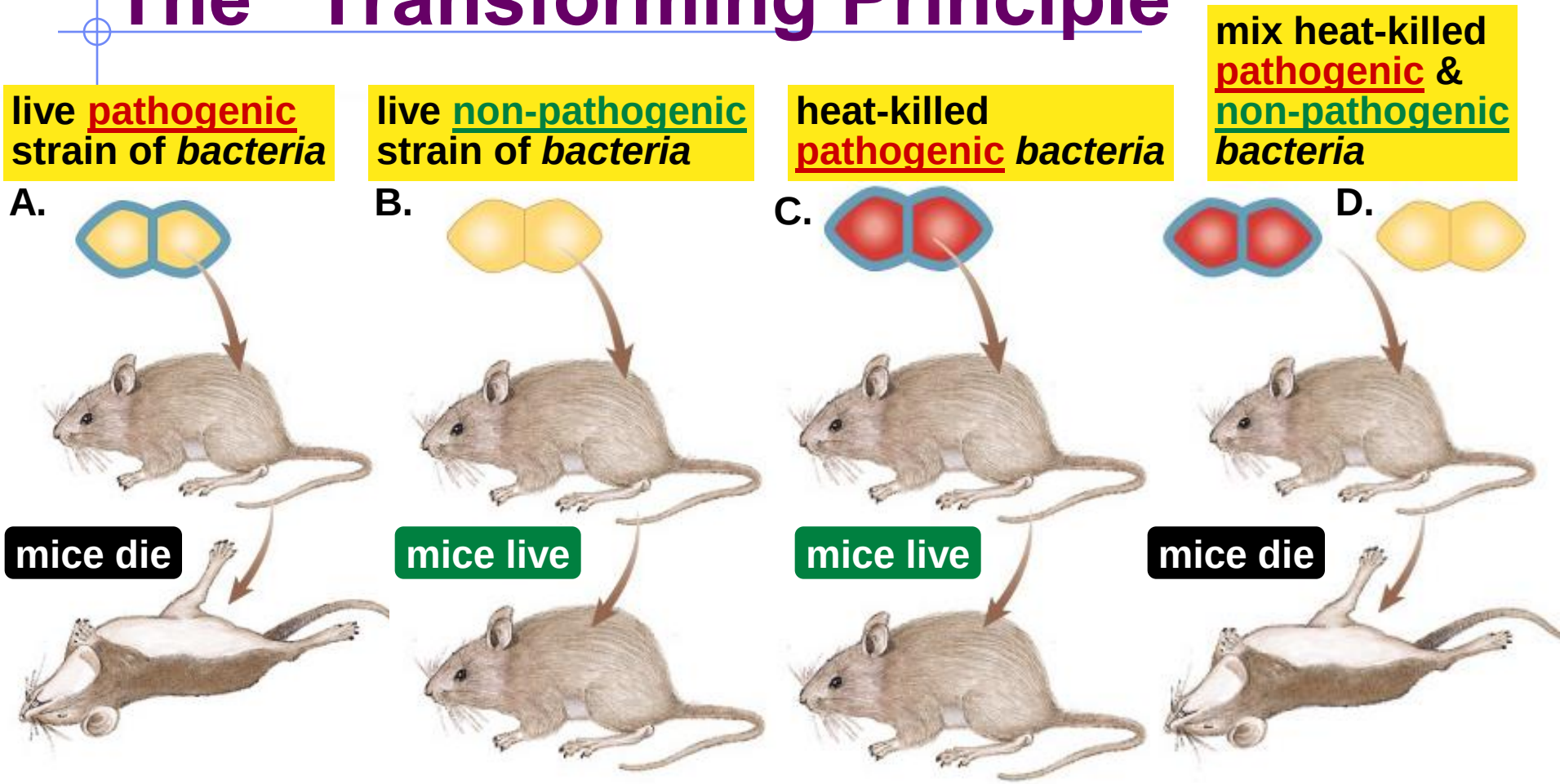


The "Transforming Principle"

1928

- **Frederick Griffith**
  - ***Streptococcus*** **pneumonia bacteria**
    - **was working to find cure for pneumonia**
  - **harmless live bacteria ("rough") mixed with heat-killed pathogenic bacteria ("smooth") causes fatal disease in mice**
  - **a substance passed from dead bacteria to live bacteria to change their phenotype**
    - **"Transforming Principle"**

The "Transforming Principle"

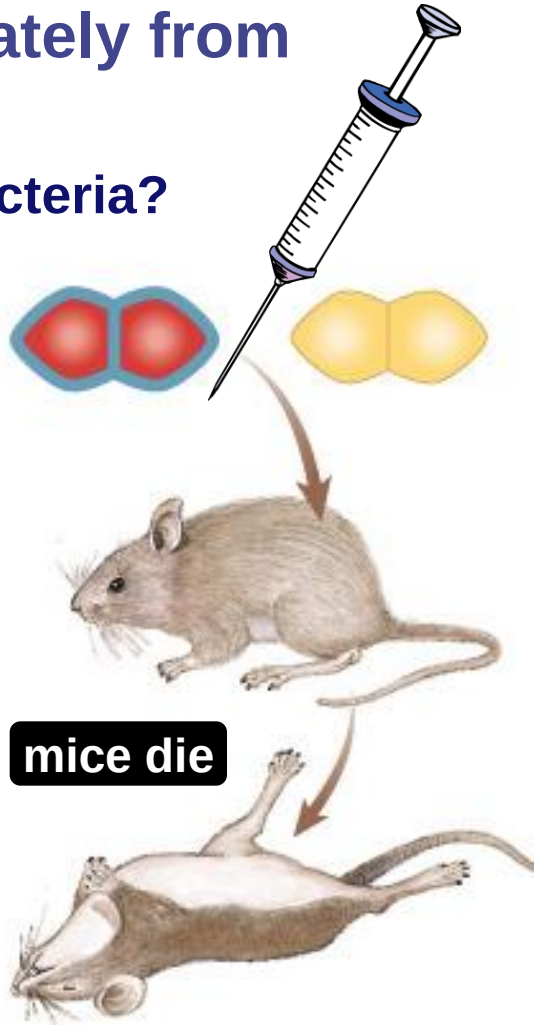


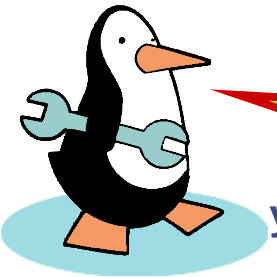
Transformation = change in phenotype

something in heat-killed bacteria could still transmit disease-causing properties

DNA is the "Transforming Principle" 1944

- **Avery, McCarty & MacLeod**
  - purified both DNA & proteins separately from *Streptococcus* pneumonia bacteria
    - which will transform non-pathogenic bacteria?
  - injected protein into bacteria
    - no effect
  - injected DNA into bacteria
    - transformed harmless bacteria into virulent bacteria



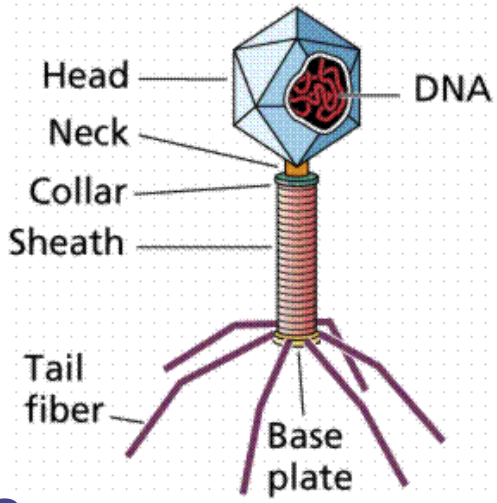


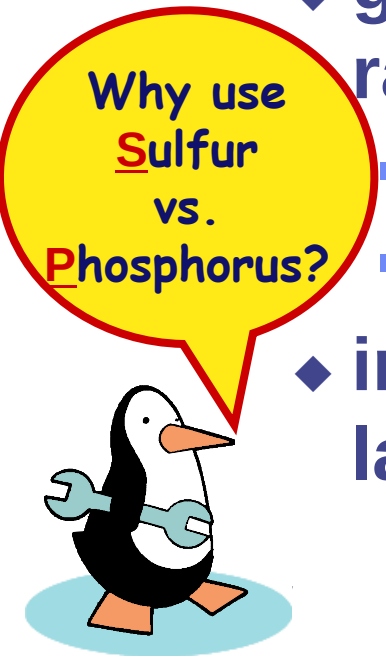
What's the conclusion?

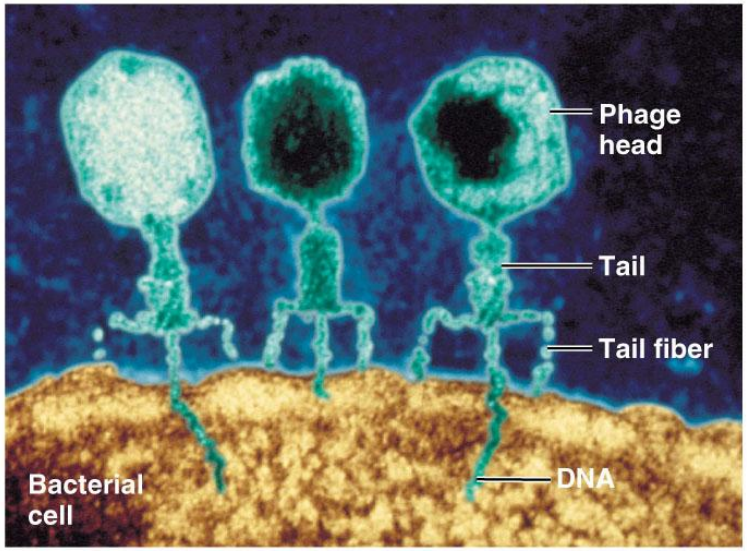
1952 | 1969
Hershey

Confirmation of DNA

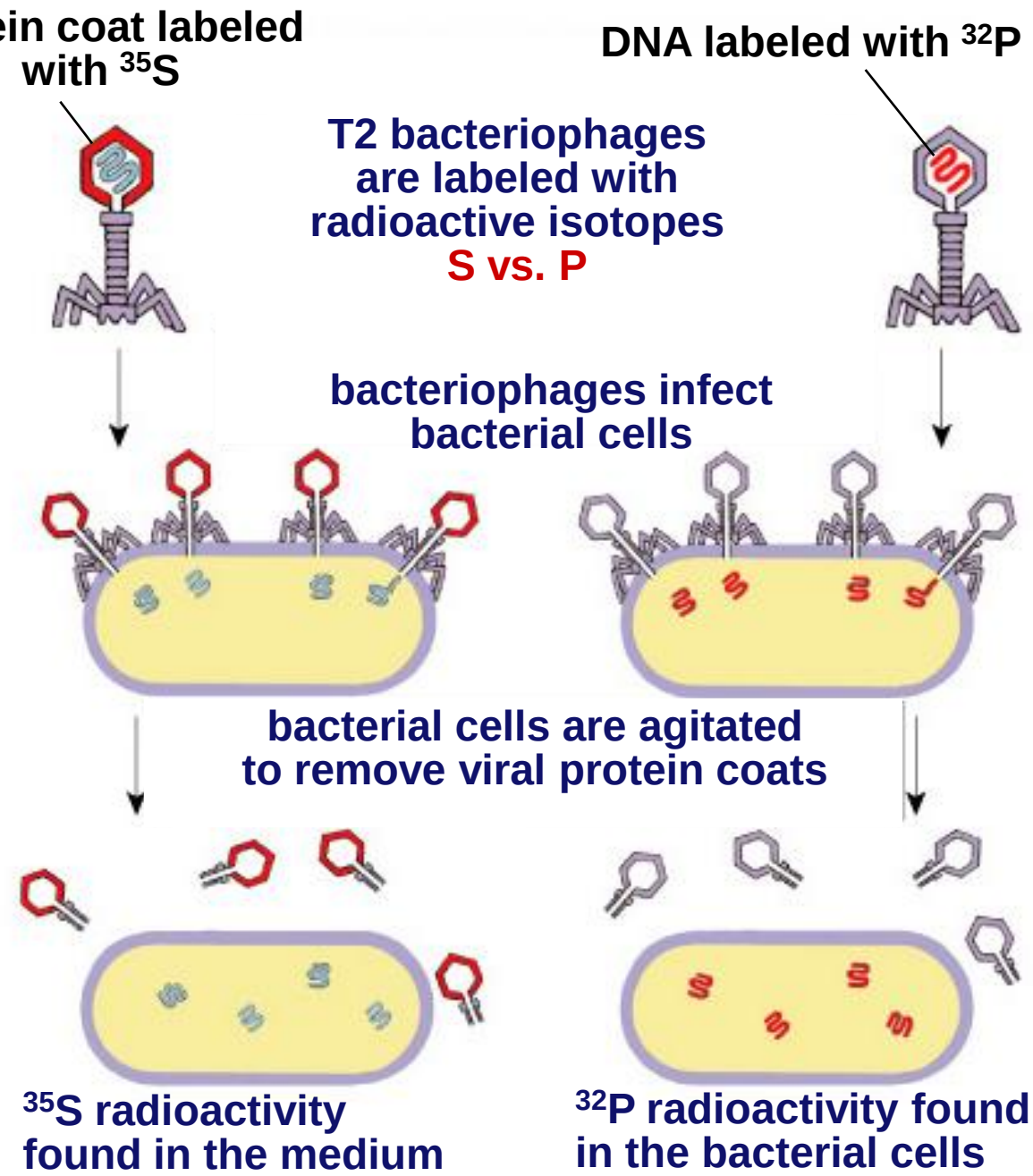
- Hershey & Chase
  - classic "blender" experiment
  - worked with bacteriophage
    - viruses that infect bacteria
  - grew phage viruses in 2 media, radioactively labeled with either
    - ^{35}S in their proteins
    - ^{32}P in their DNA
  - infected bacteria with labeled phages





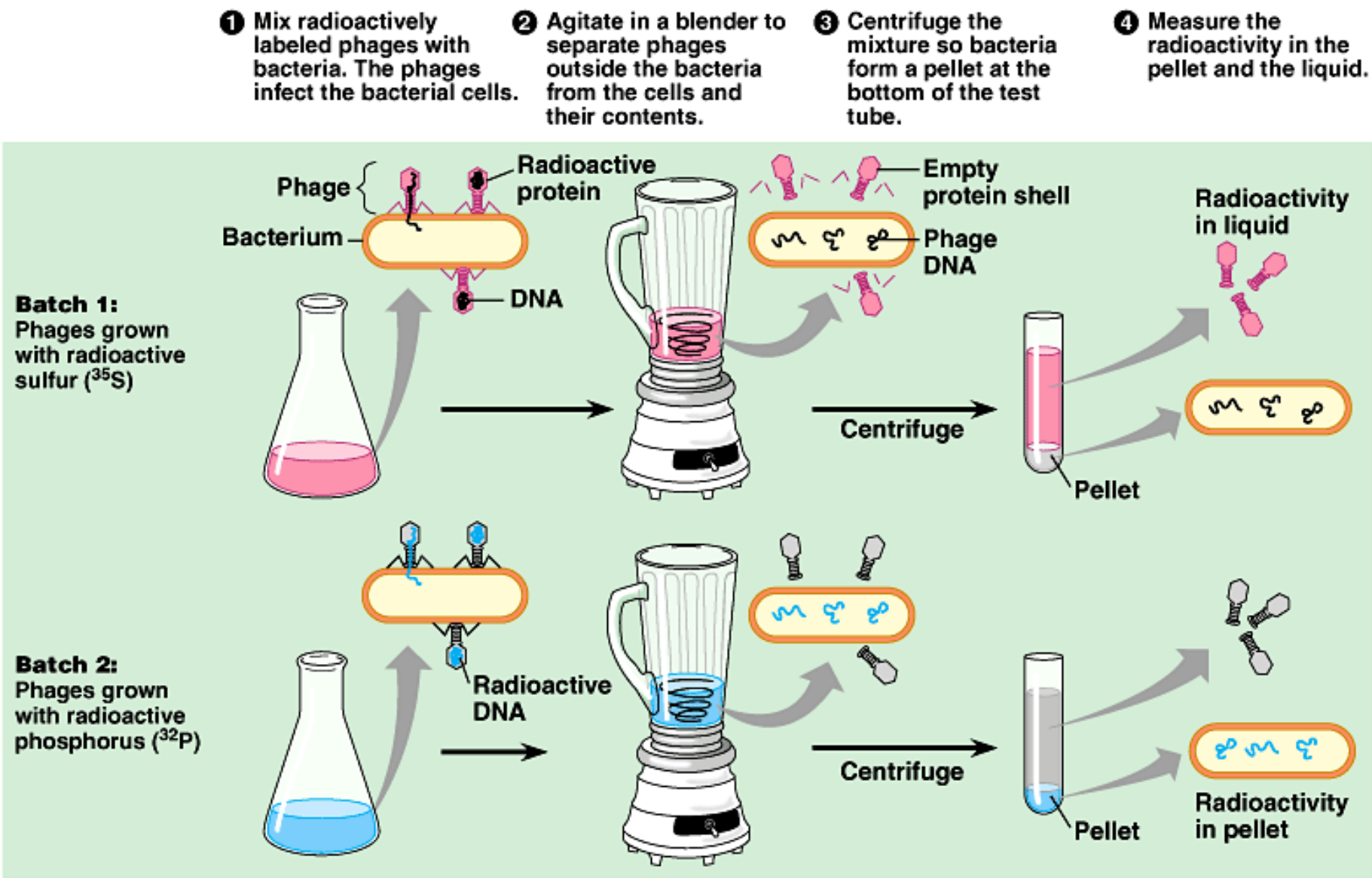


Hershey & Chase



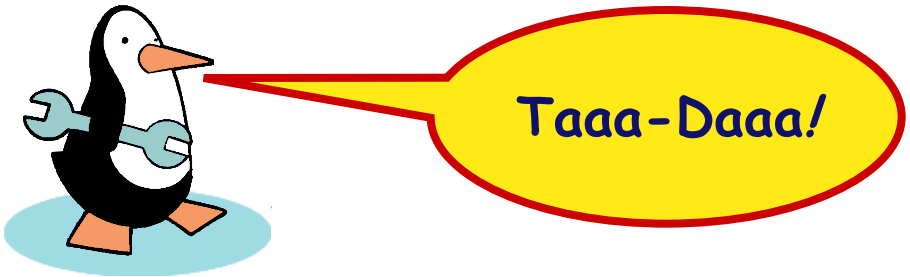
Which radioactive marker is found inside the cell?

Which molecule carries viral genetic info?


1 Mix radioactively labeled phages with bacteria. The phages infect the bacterial cells.
2 Agitate in a blender to separate phages outside the bacteria from the cells and their contents.
3 Centrifuge the mixture so bacteria form a pellet at the bottom of the test tube.
4 Measure the radioactivity in the pellet and the liquid.
Phage
Radioactive protein
Bacterium
DNA
Empty protein shell
Phage DNA
Radioactivity in liquid
Batch 1: Phages grown with radioactive sulfur (35S)
Centrifuge
Pellet
Radioactive DNA
Batch 2: Phages grown with radioactive phosphorus (32P)
Centrifuge
Pellet
Radioactivity in pellet

Blender experiment

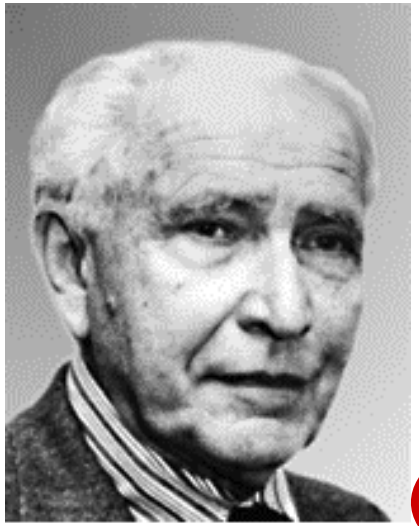
- Radioactive phage & bacteria in blender
  - ^{35}S phage
    - radioactive proteins stayed in supernatant
    - therefore viral protein <u>did NOT</u> enter bacteria
  - ^{32}P phage
    - radioactive DNA stayed in pellet
    - therefore viral DNA <u>did</u> enter bacteria
  - <u>Confirmed DNA is "transforming factor"</u>



1947

Chargaff

- **DNA composition: "Chargaff's rules"**
  - varies from species to species
  - all 4 bases not in equal quantity
  - bases present in characteristic ratio
    - humans:



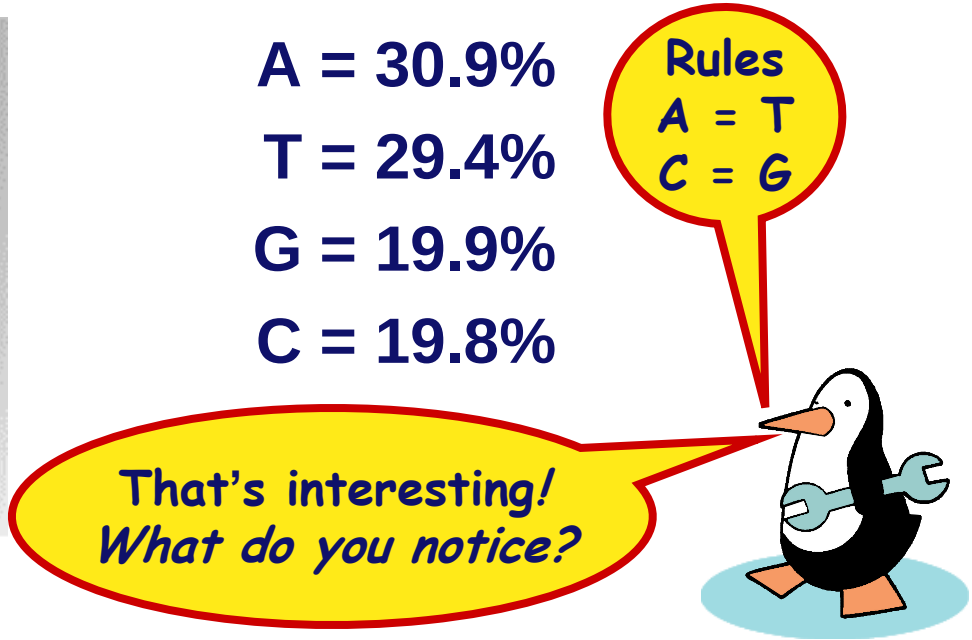
Erwin Chargaff

A = 30.9%

T = 29.4%

G = 19.9%

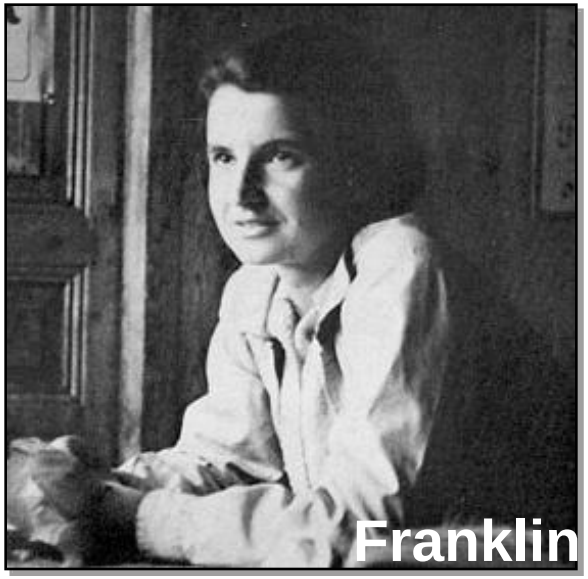
C = 19.8%

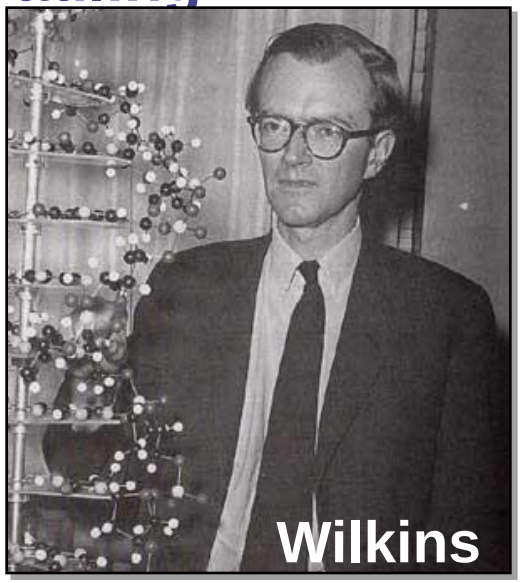


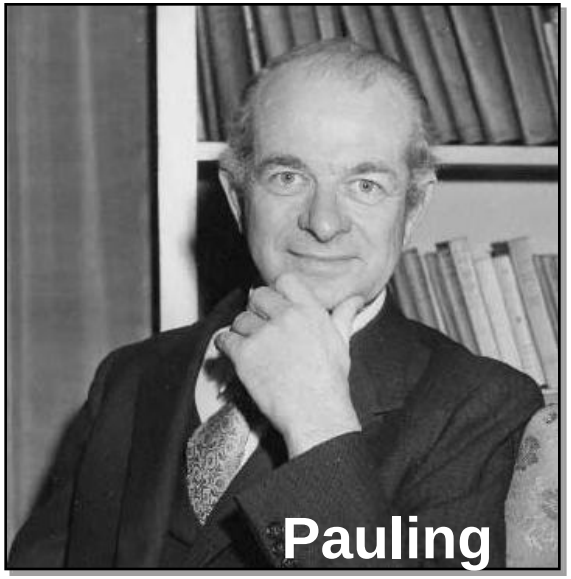
1953 | 1962

Structure of DNA

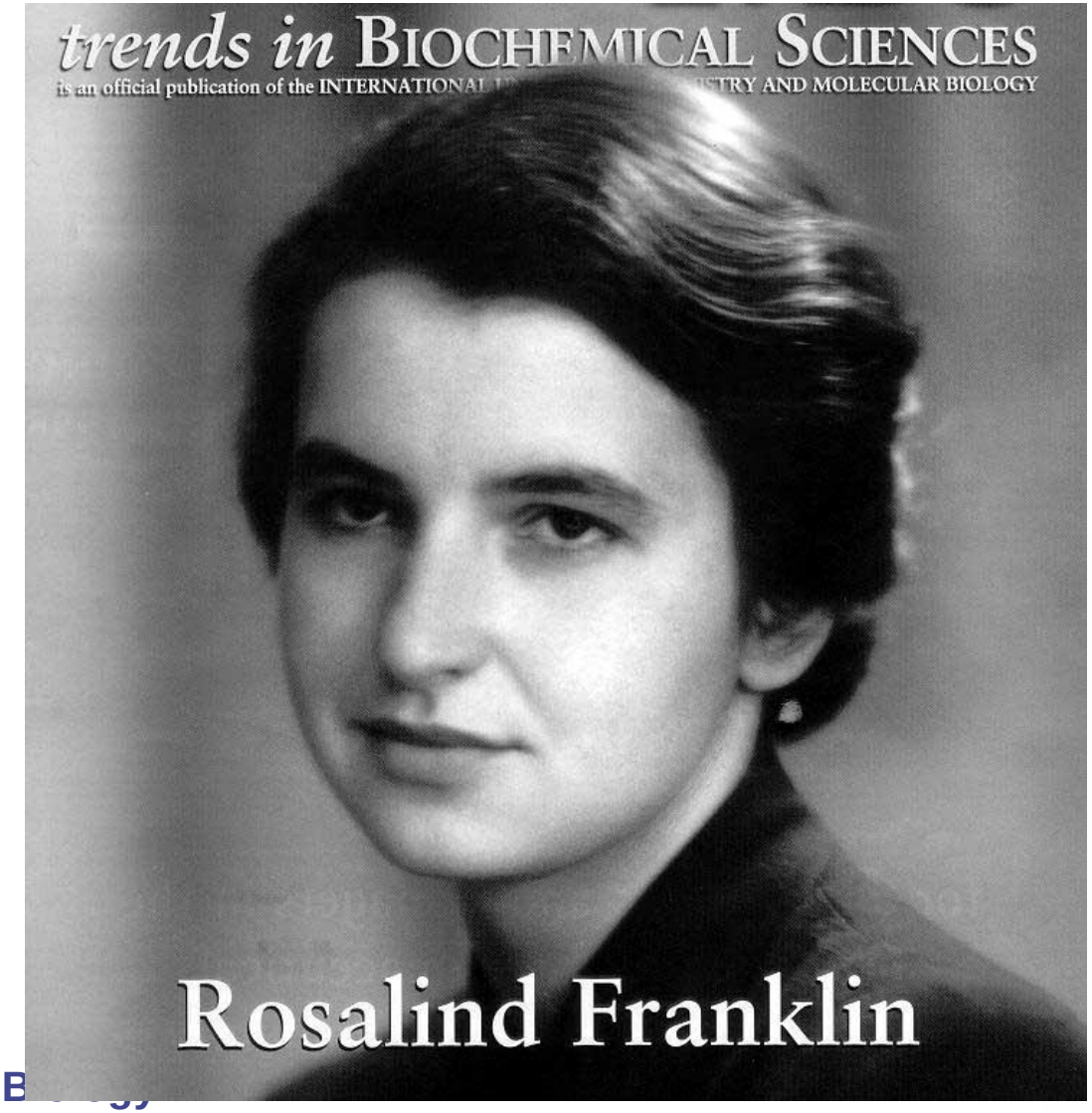
- Watson & Crick
  - developed double helix model of DNA
    - other leading scientists working on question:
      - Rosalind Franklin
      - Maurice Wilkins
      - Linus Pauling

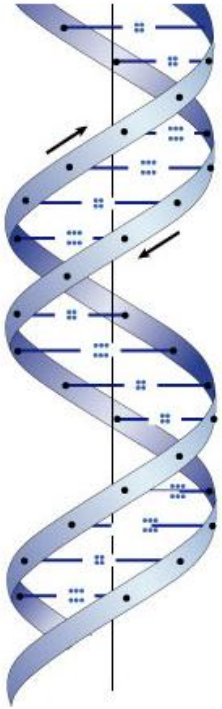


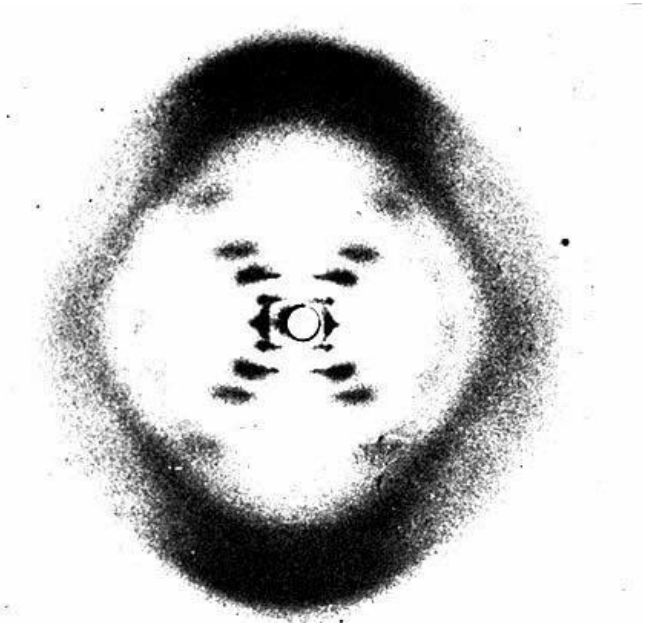




Rosalind Franklin (1920-1958)

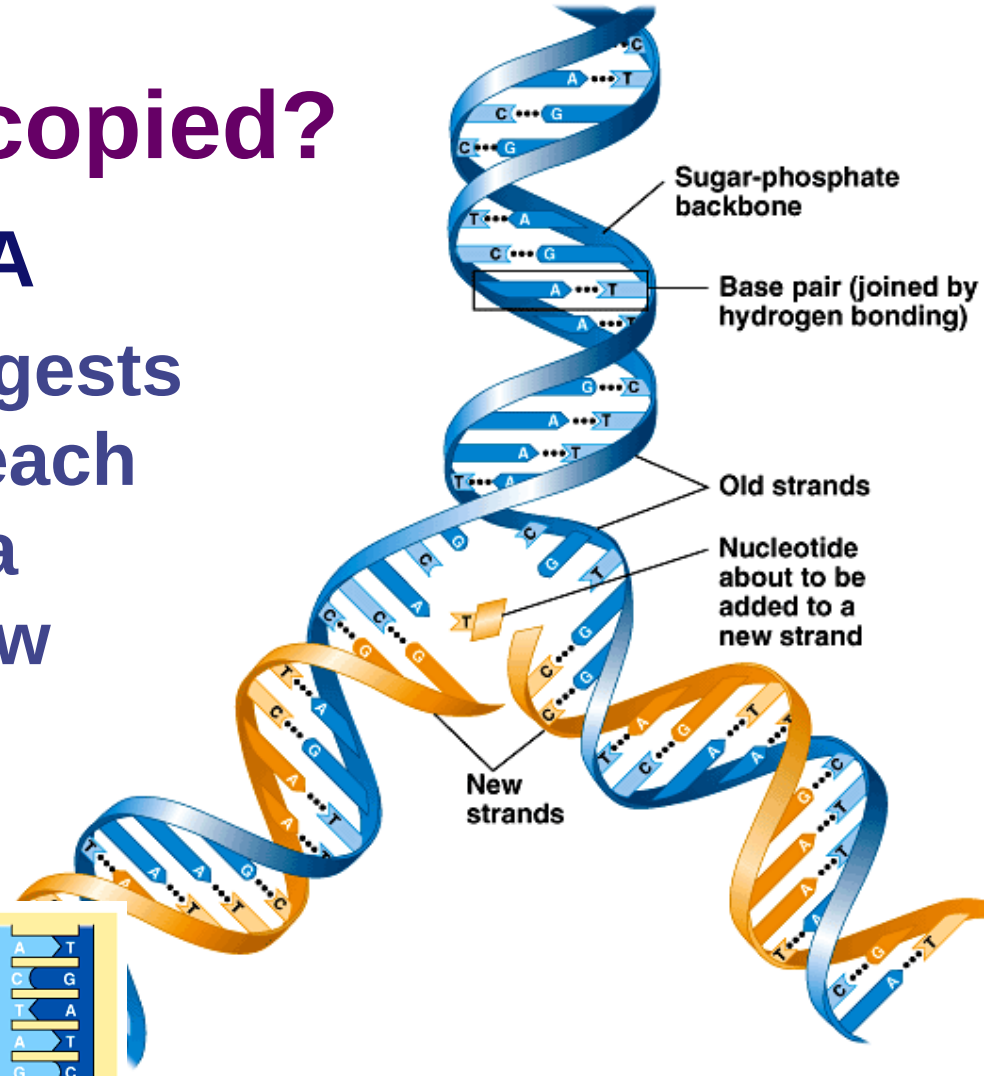


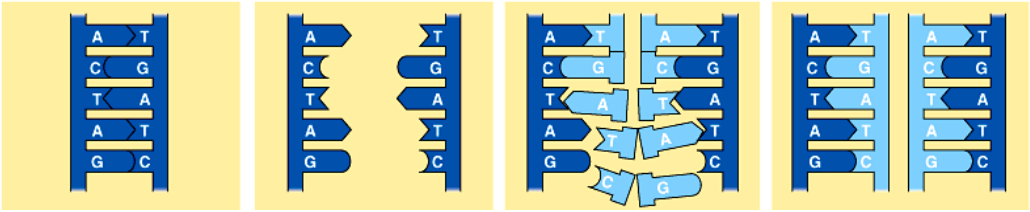




But how is DNA copied?

- **Replication of DNA**
  - base pairing suggests that it will allow each side to serve as a <u>template</u> for a new strand



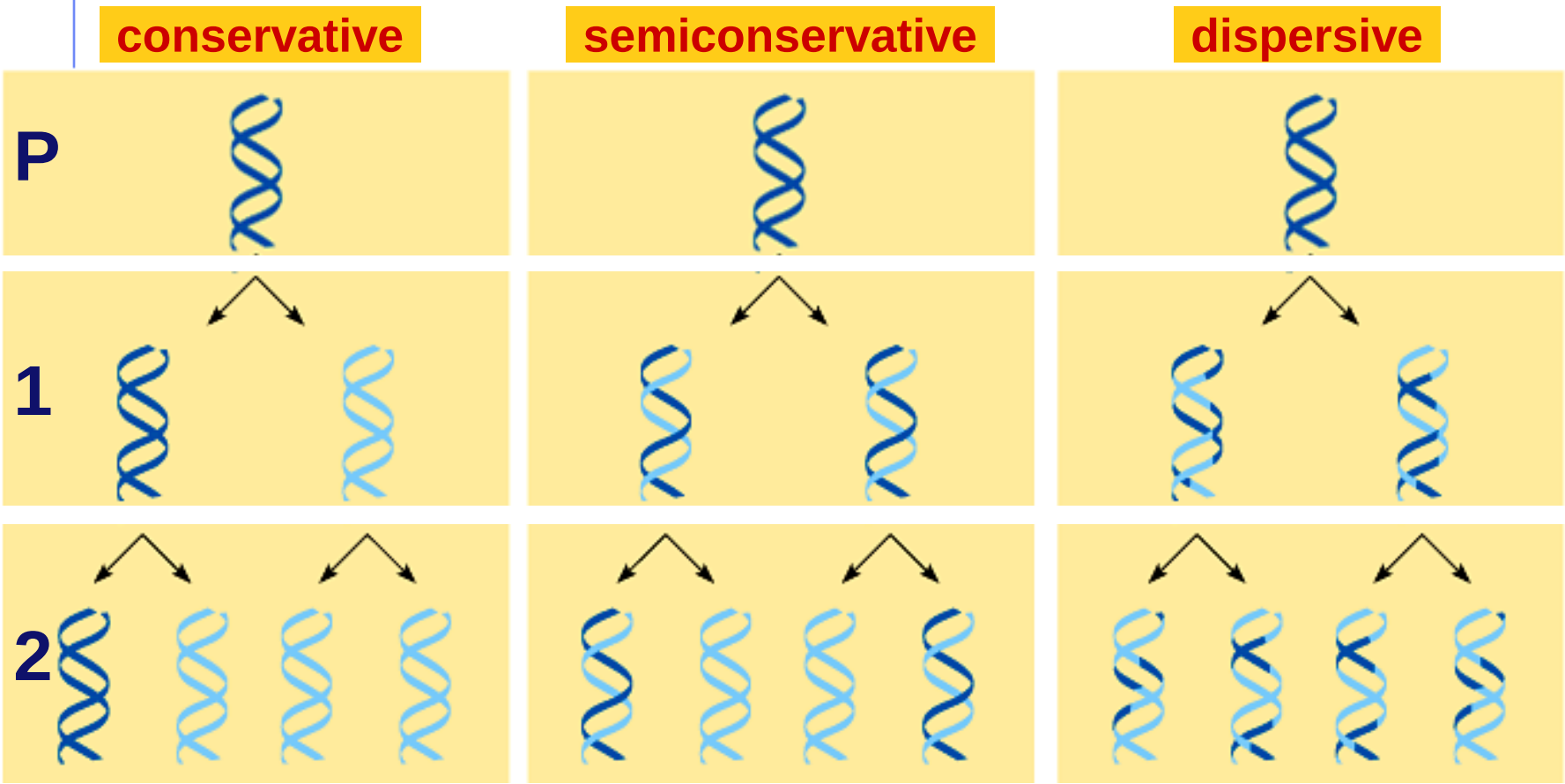


"It has not escaped our notice that the specific pairing we have postulated immediately suggests a possible copying mechanism for the genetic material."

— Watson & Crick

Models of DNA Replication

- **Alternative models**
  - **become experimental predictions**



Scientific History

- March to understanding that DNA is the genetic material
  - T.H. Morgan (1908)
    - genes are on chromosomes
  - Frederick Griffith (1928)
    - a transforming factor can change phenotype
  - Avery, McCarty & MacLeod (1944)
    - transforming factor is DNA
  - Erwin Chargaff (1947)
    - Chargaff rules: A = T, C = G
  - Hershey & Chase (1952)
    - confirmation that DNA is genetic material
  - Watson & Crick (1953)
    - determined double helix structure of DNA
  - Meselson & Stahl (1958)
    - semi-conservative replication

The “Central Dogma”

- Flow of genetic information in a cell