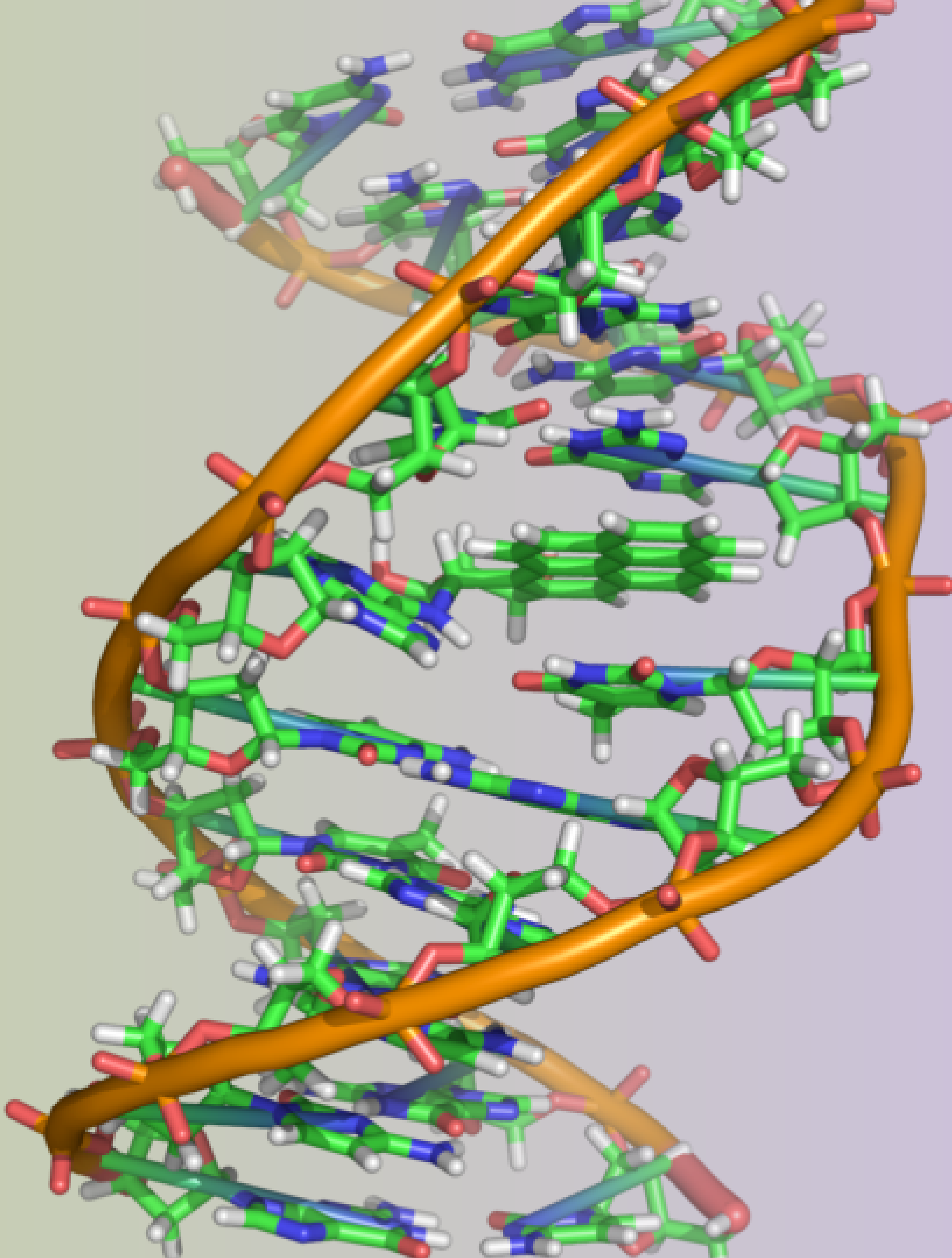
DNA
(Ch. 12)



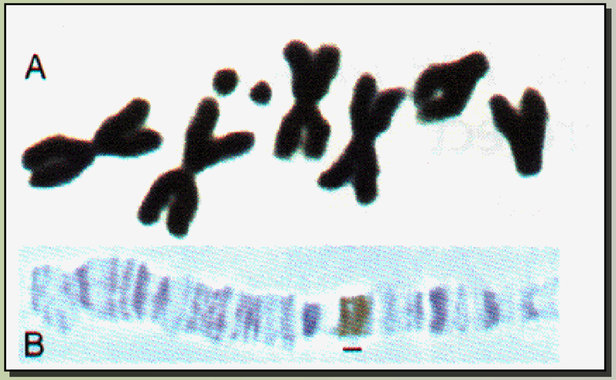
Brief History

- Many people contributed to our understanding of DNA
  - T.H. Morgan (1908)
  - Frederick Griffith (1928)
  - Avery, McCarty & MacLeod (1944)
  - Erwin Chargaff (1947)
  - Hershey & Chase (1952)
  - Watson & Crick (1953)
  - Meselson & Stahl (1958)

1908 | **1933**

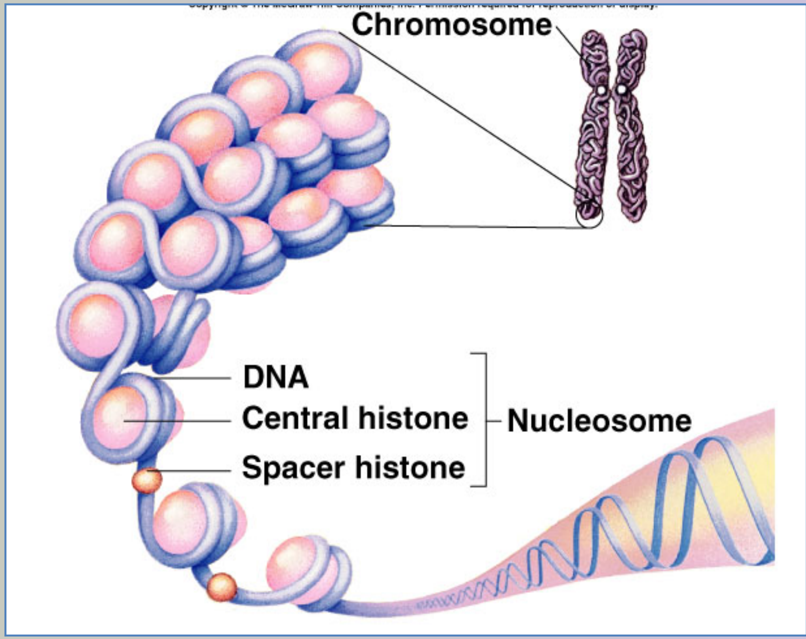
Chromosomes related to phenotype

- T.H. Morgan
  - working with *Drosophila*
  - associated phenotype with specific chromosome
    - white-eyed male had specific X chromosome



Genes are on chromosomes **1908 | 1933**

- 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?

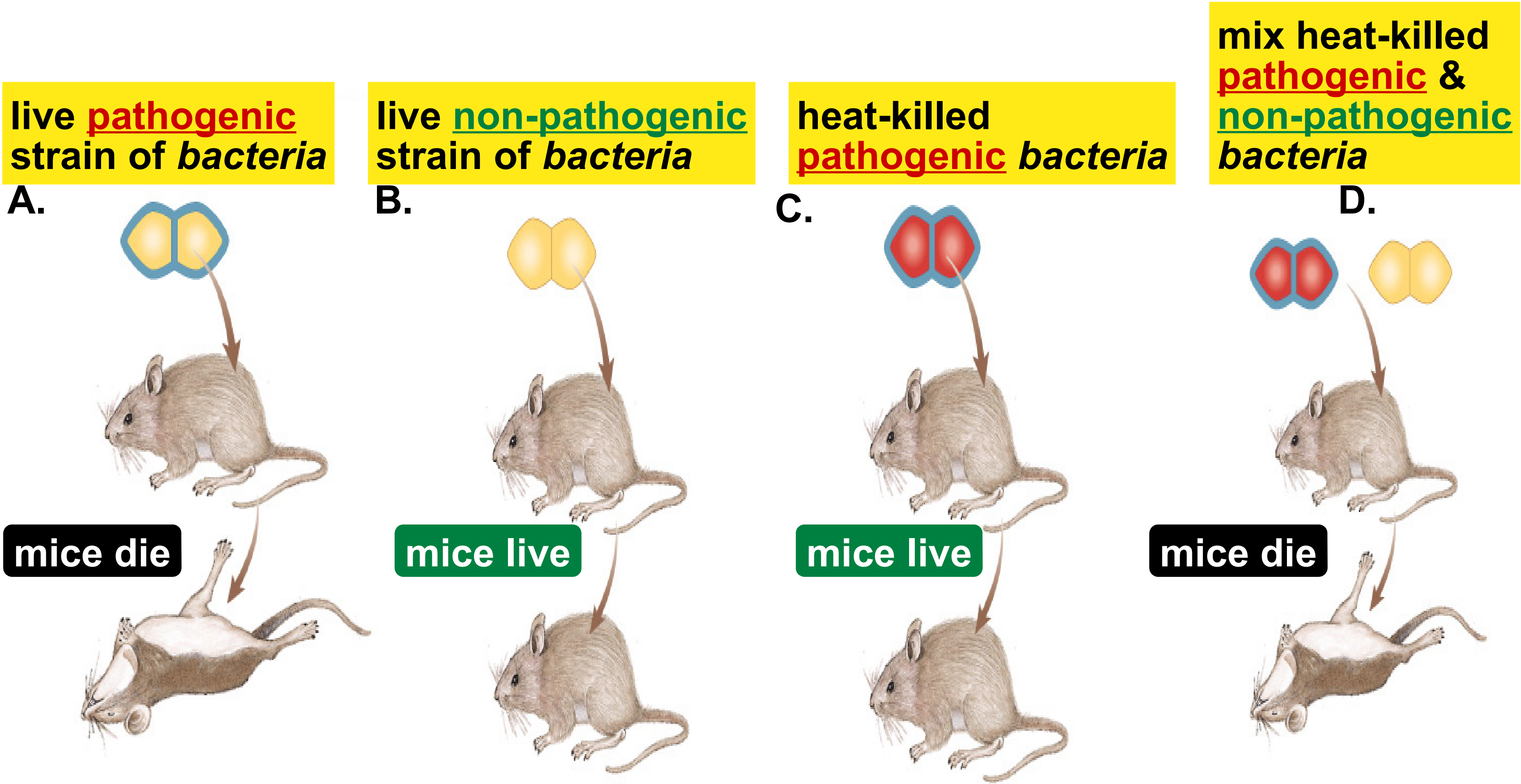


The "Transforming Principle"

1928

- Frederick Griffith
  - *Streptococcus* pneumonia bacteria
  - 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
    - "Transforming Principle"

The "Transforming Principle"

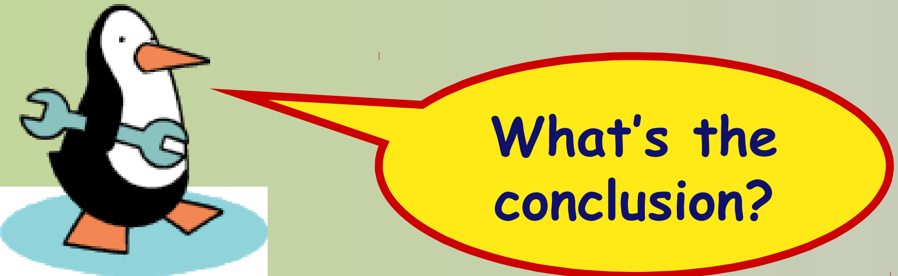


Transformation = change in phenotype

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

DNA is the "Transforming Principle" **1944**

- Avery, McCarty & MacLeod
  - Purified DNA & proteins from *Streptococcus* pneumonia bacteria
  - injected protein into bacteria
    - no effect
  - injected DNA into bacteria
    - transformed harmless bacteria into virulent bacteria

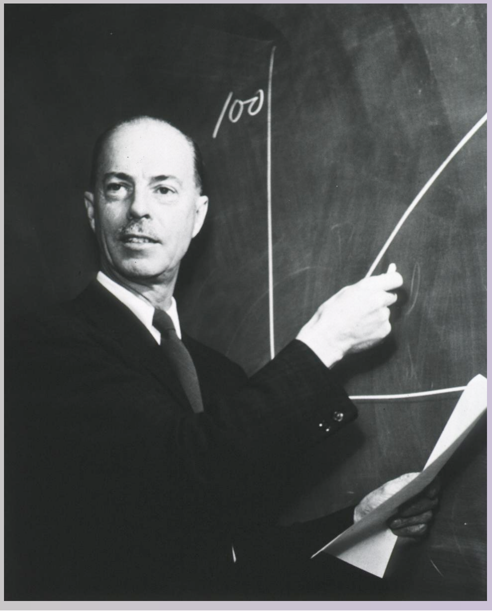


Avery, McCarty & MacLeod **1944** | **??!!**

- Conclusion
  - first experimental evidence that DNA was the genetic material

Oswald Avery

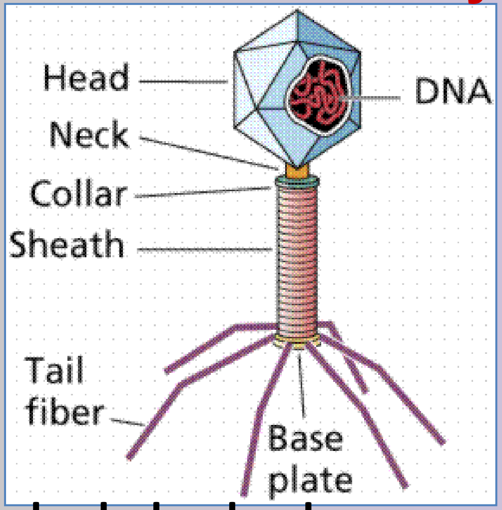
Maclyn McCarty



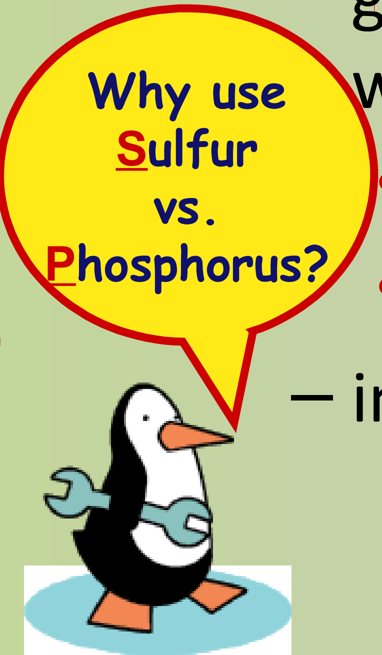
Colin MacLeod

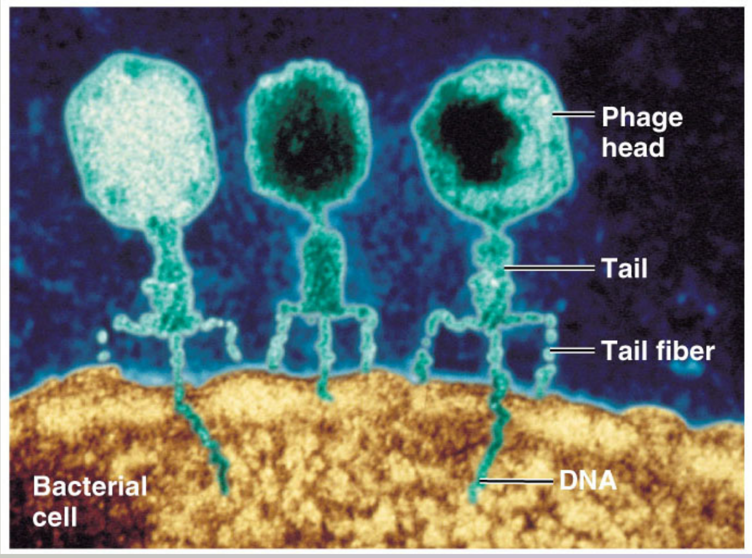
Confirmation of DNA

1952 | 1969
Hershey

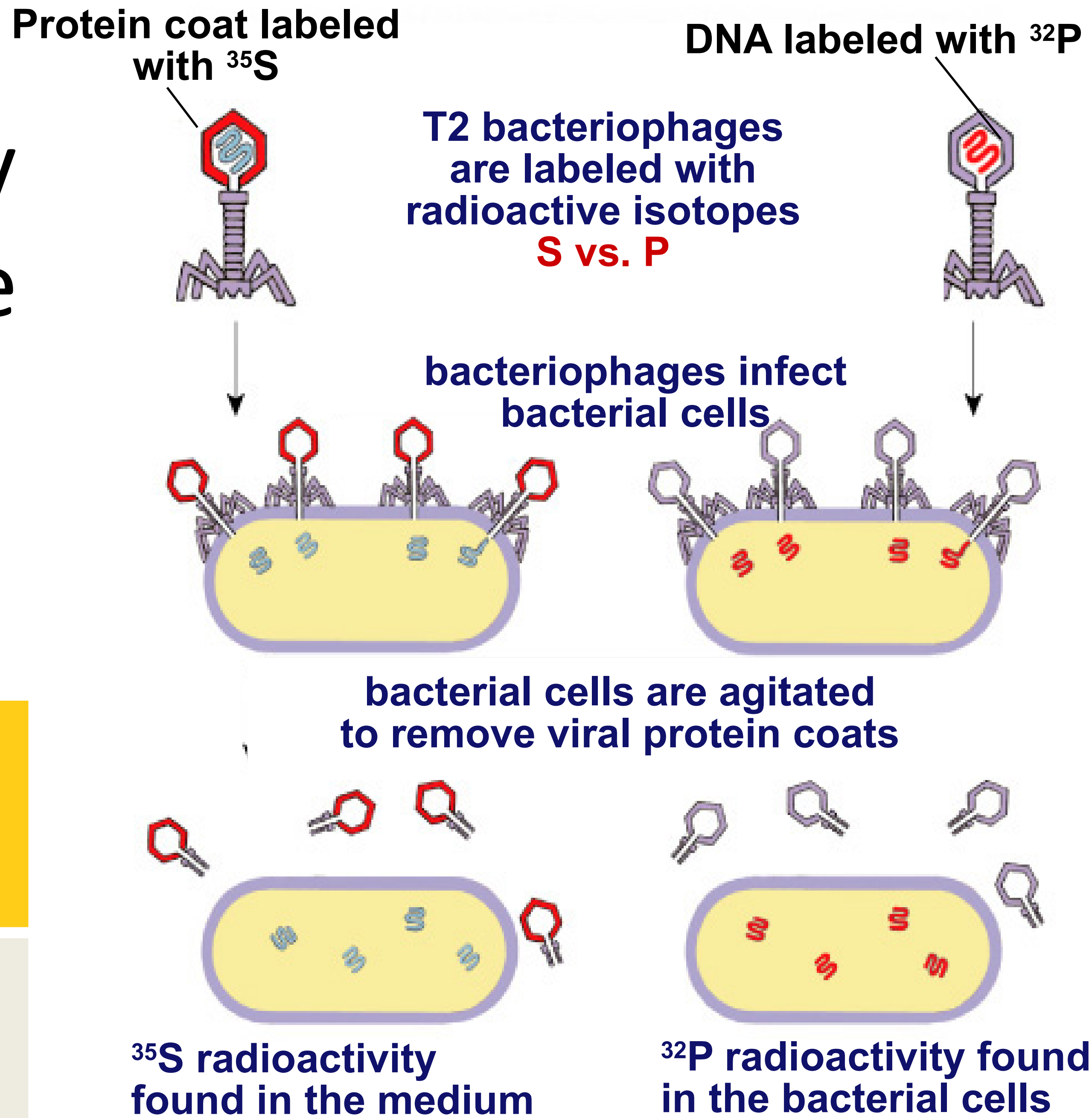


- Hershey & Chase
  - classic "blender" experiment
  - worked with bacteriophage
    - viruses that infect bacteria
  - grew phages in 2 media, radioactively labeled with either
    - ^{35}S in their proteins
    - ^{32}P in their DNA
  - infected bacteria phages





Hershey & Chase

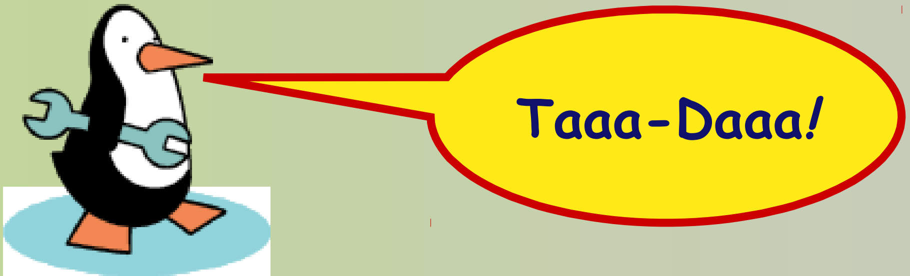


Which radioactive marker is found inside the cell?

Which molecule carries viral genetic info?

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>



Hershey & Chase

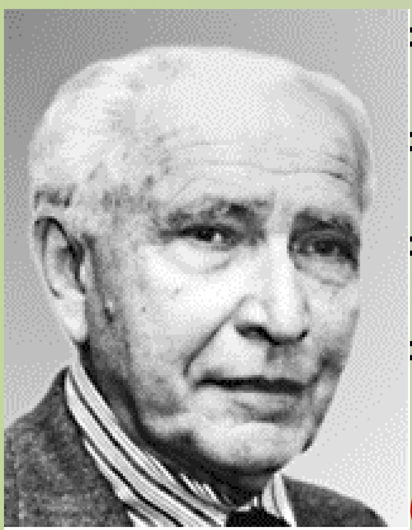
1952 | **1969**
Hershey

Martha Chase **Alfred Hershey**

Erwin Chargaff

1947

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



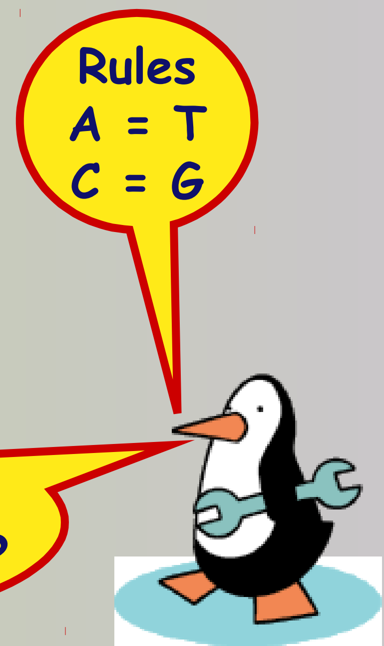
Erwin Chargaff

= 30.9%

= 29.4%

= 19.9%

= 19.8%



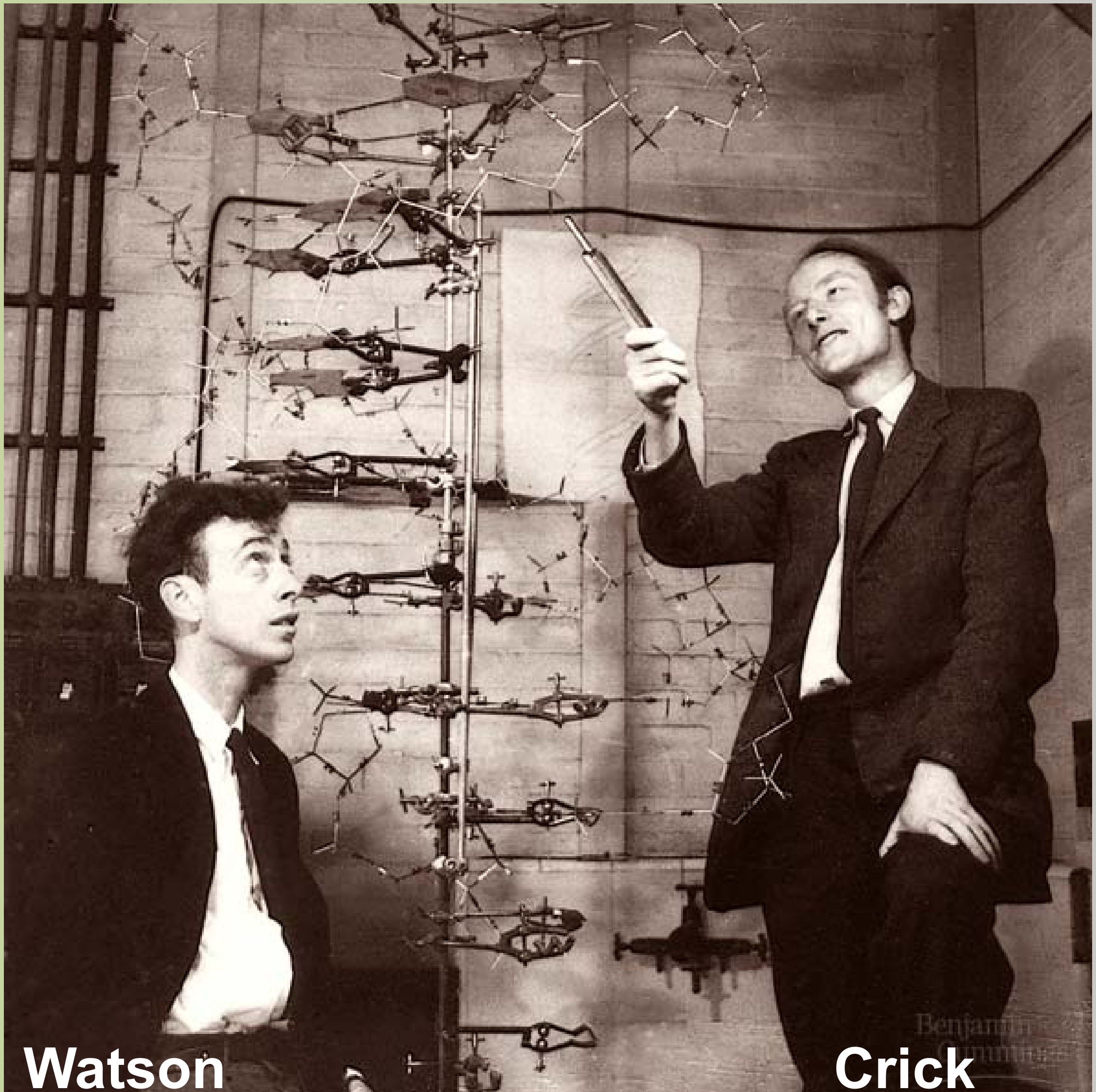
Structure of DNA

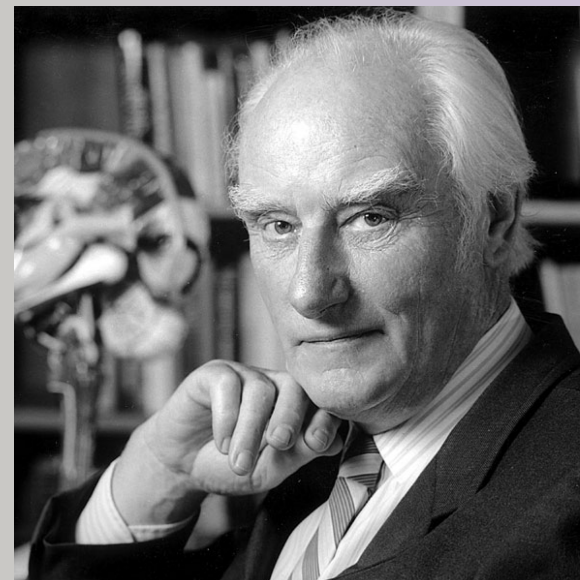
1953 | 1962

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

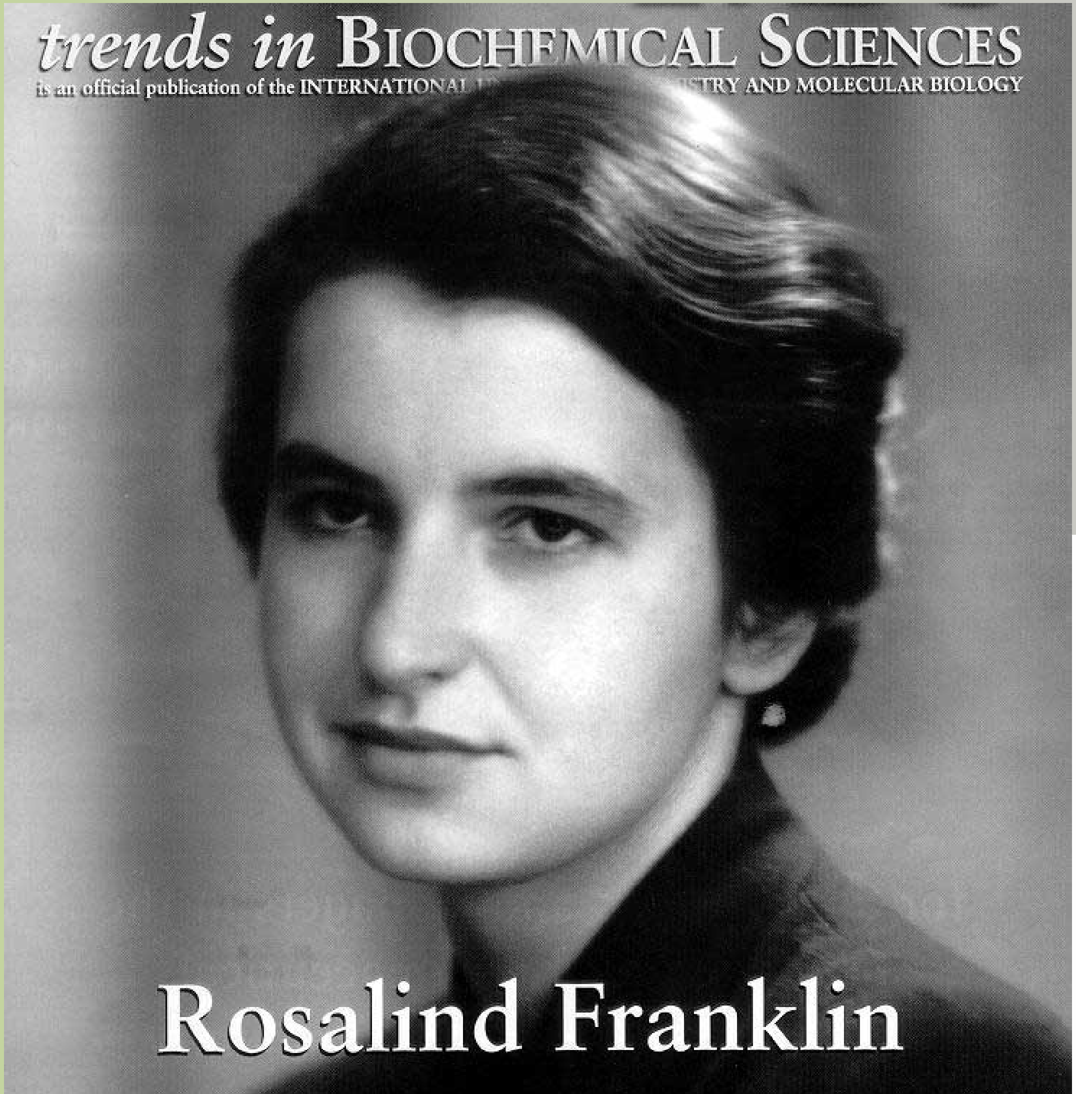
Watson and Crick

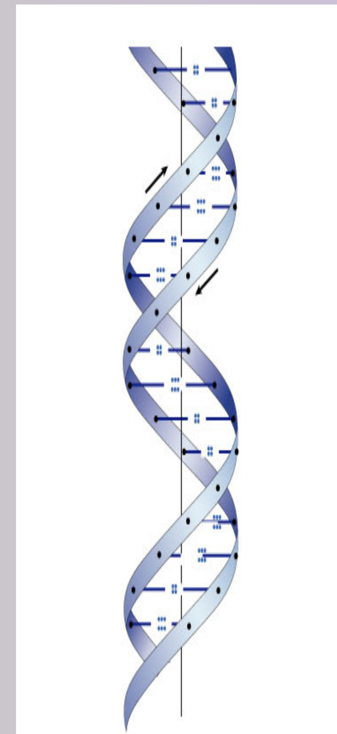
[1953 article in Nature]

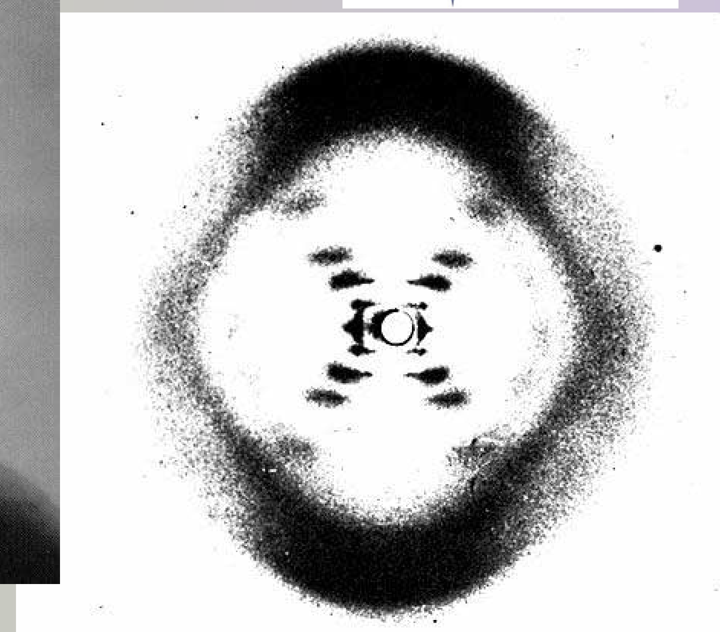




Rosalind Franklin (1920-1958)

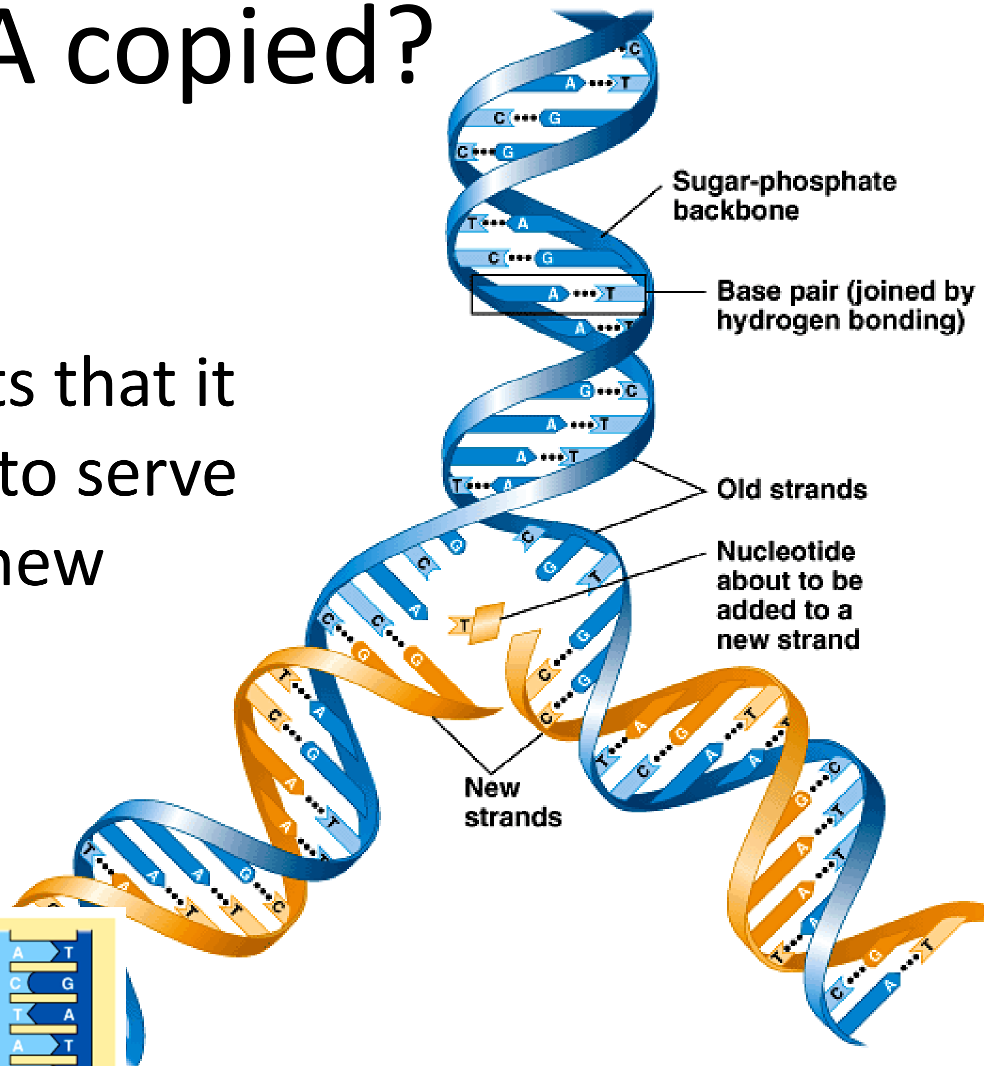


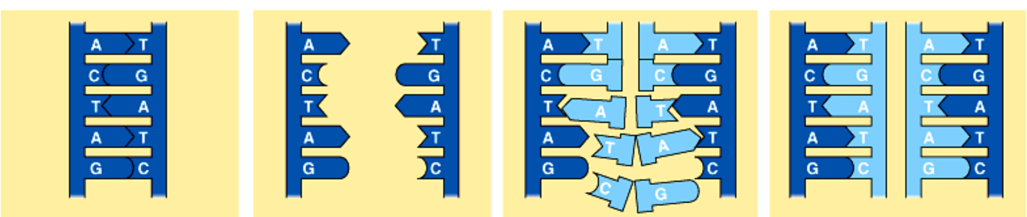




But how is DNA copied?

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



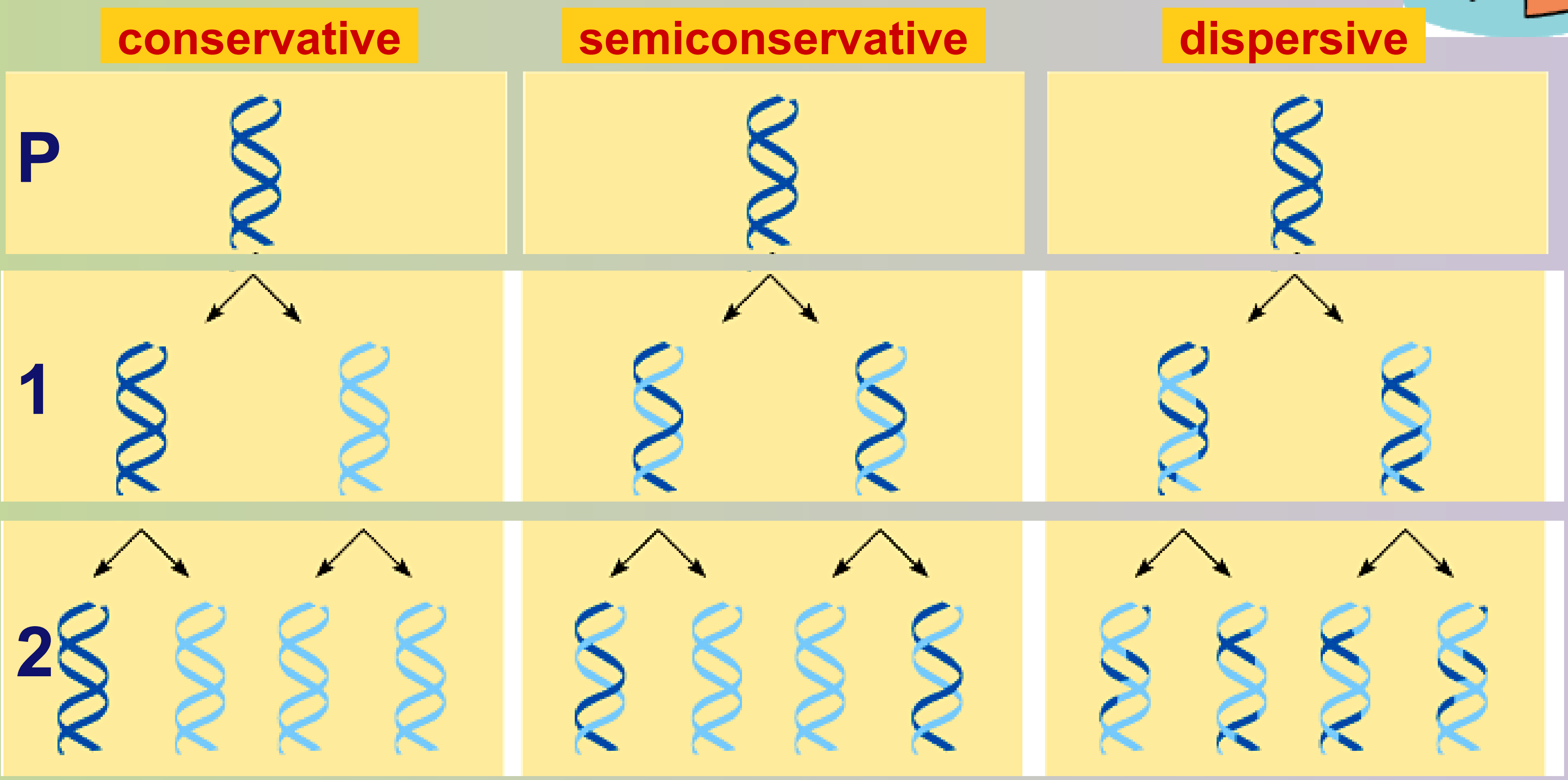


"It has not escaped our notice that the specific pairing we have postulated immediately suggests a possible copying mechanism for the genetic material."

— Watson & Crick

Models of DNA Replicatio

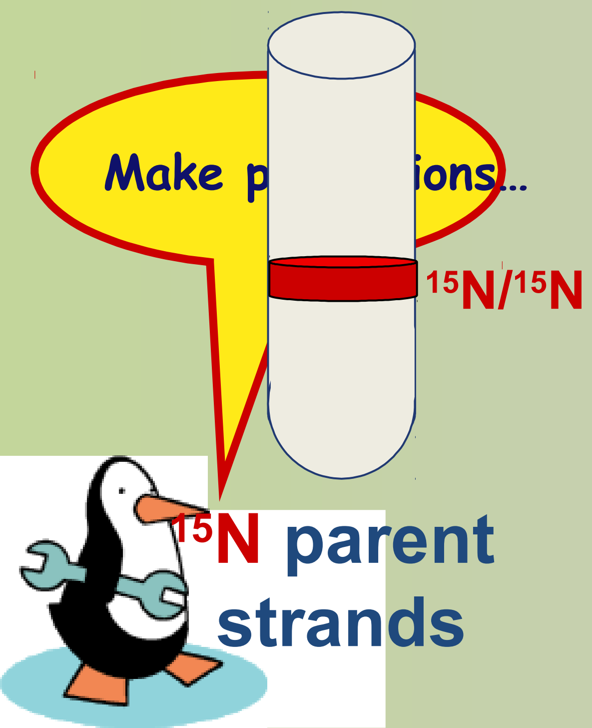
- Alternative models
  - become experimental predictions

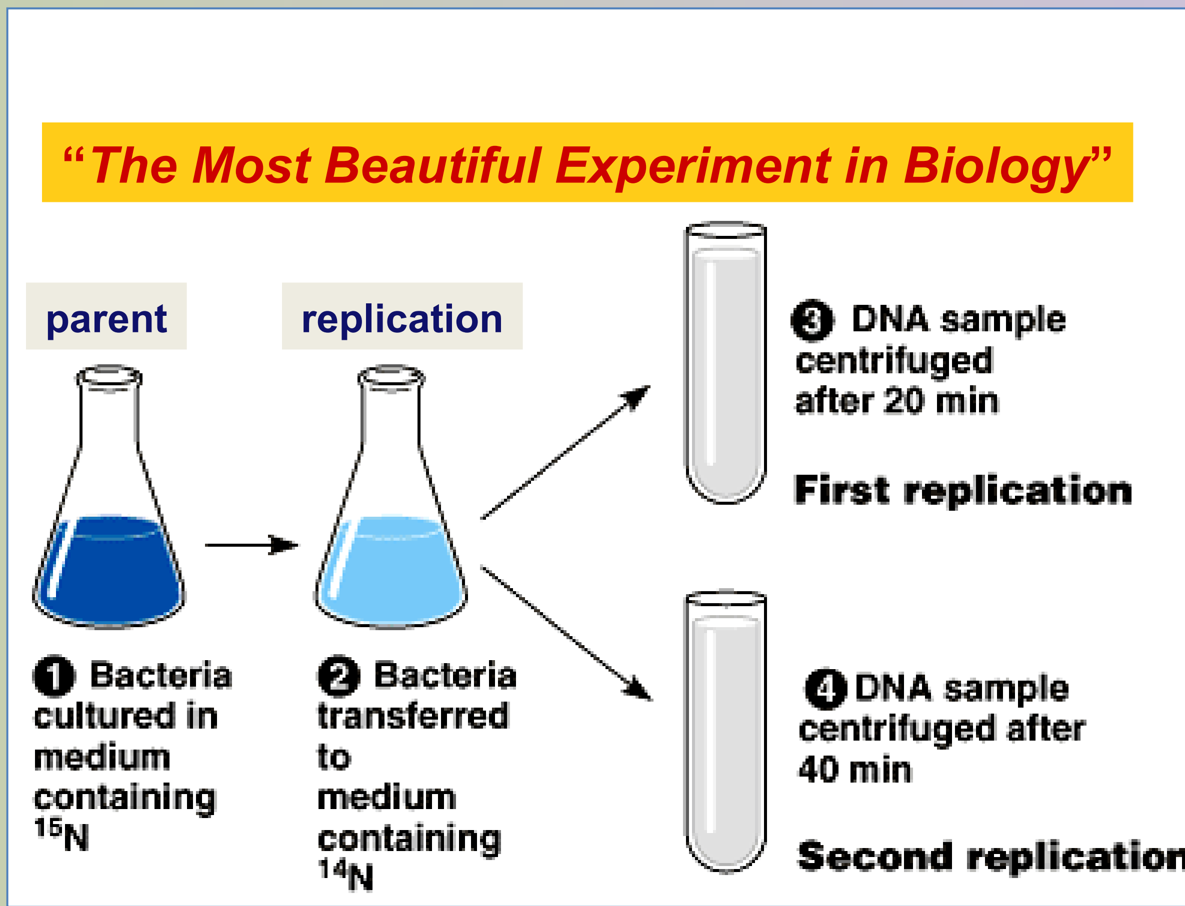


Semiconservative replication

1958

- Meselson & Stahl
  - label "parent" nucleotides in DNA strands with heavy nitrogen = ^{15}N
  - label new nucleotides with lighter isotope = ^{14}N

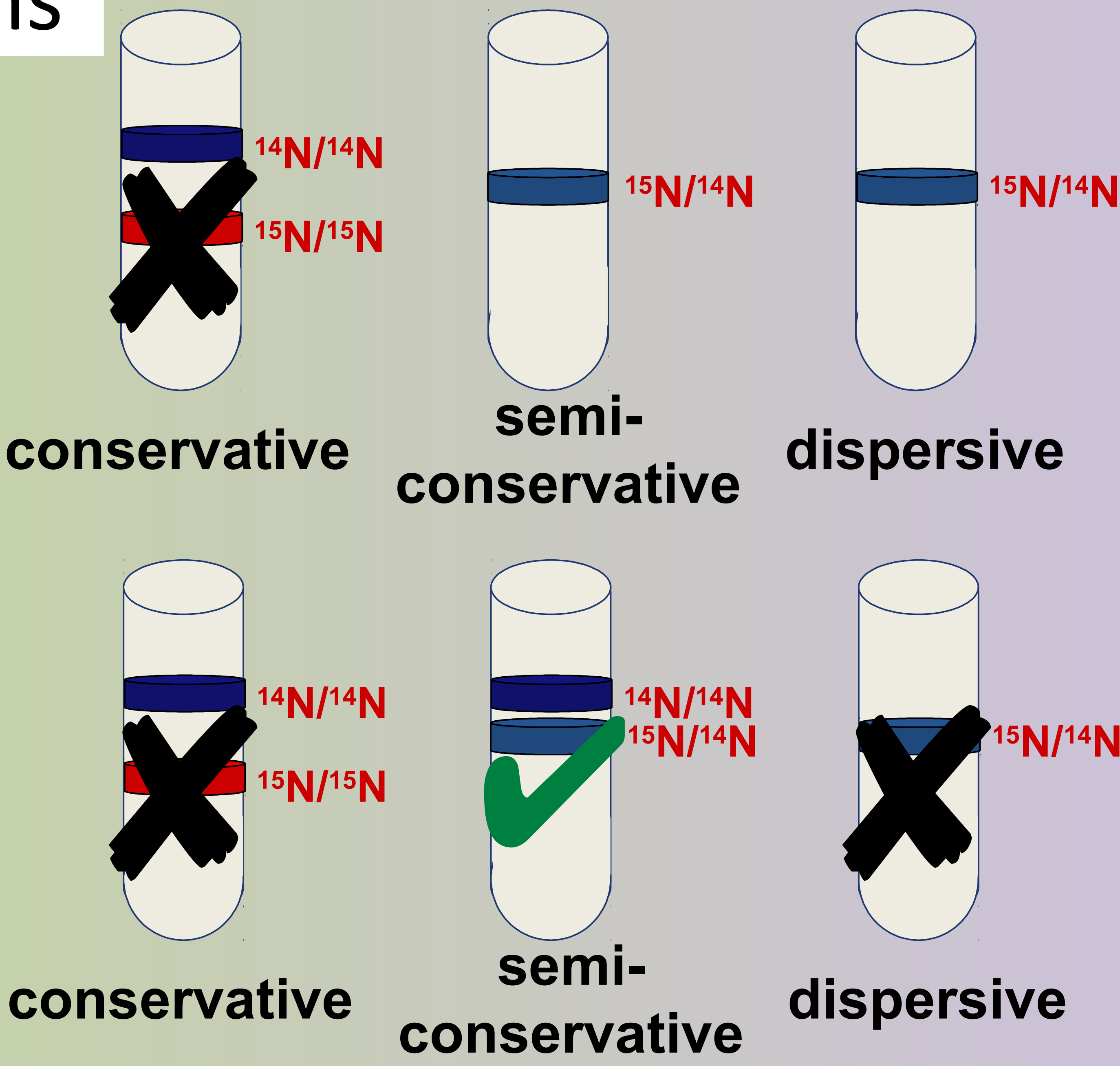


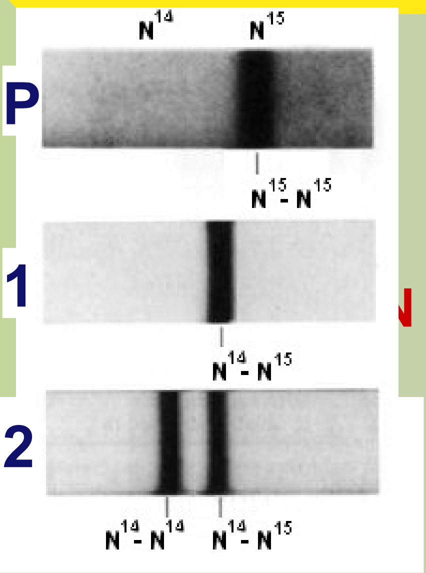


Predictions

1st round of replication

2nd round of replication





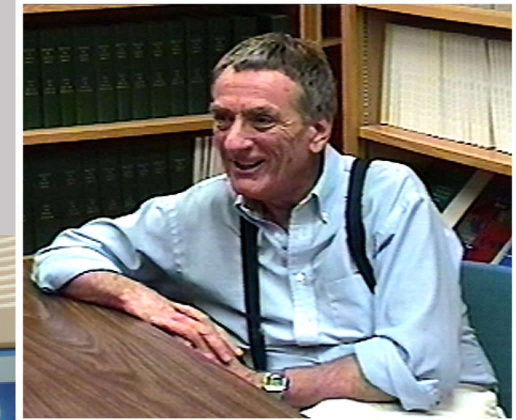
Meselson & Stahl

Matthew Meselson

Franklin Stahl

FIGURE 9-3. (Left) Matthew Meselso
[Courtesy of M. Meselson.]

Matthew Meselson



Franklin Stahl

Courtesy of Dr. M. Meselson, Harvard University.

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

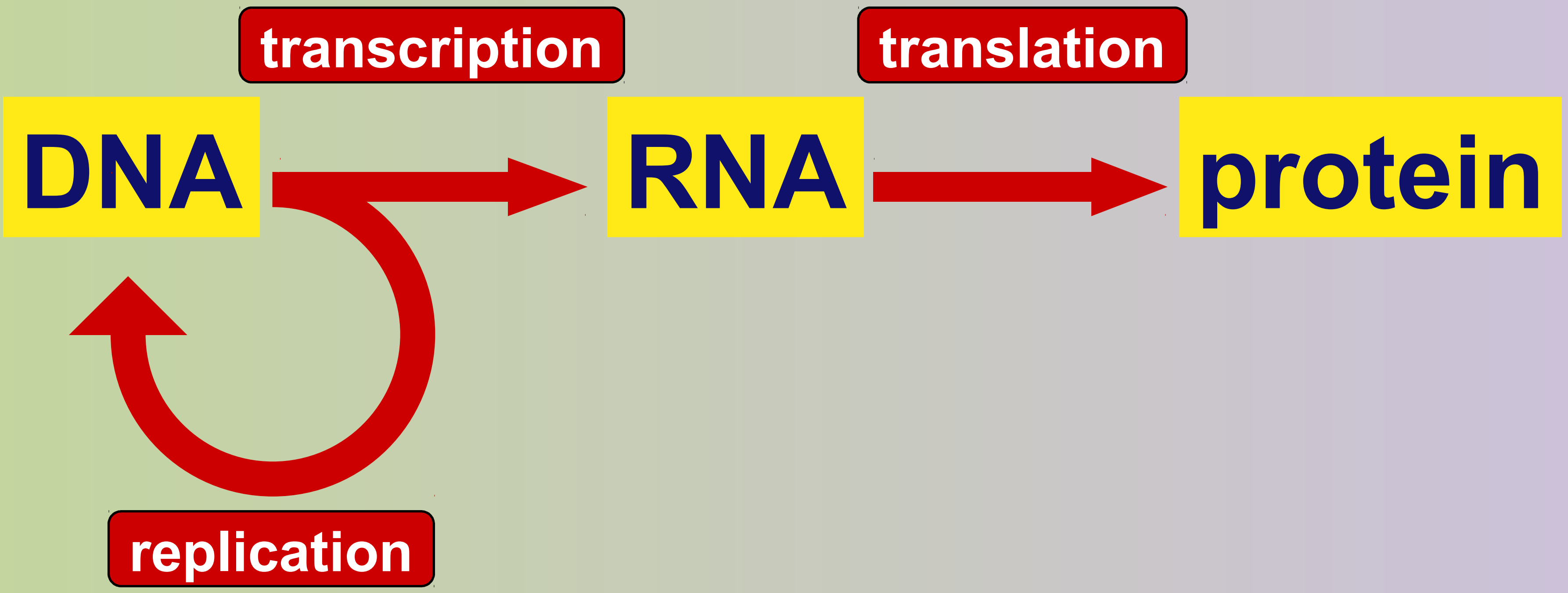
Hershey & Chase (1952): confirmation that DNA is genetic material

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



Science …. Fun

Party Time*!*

Any Questions??

Courtesy of Dr. M. Meselson, Harvard University.

Review Questions

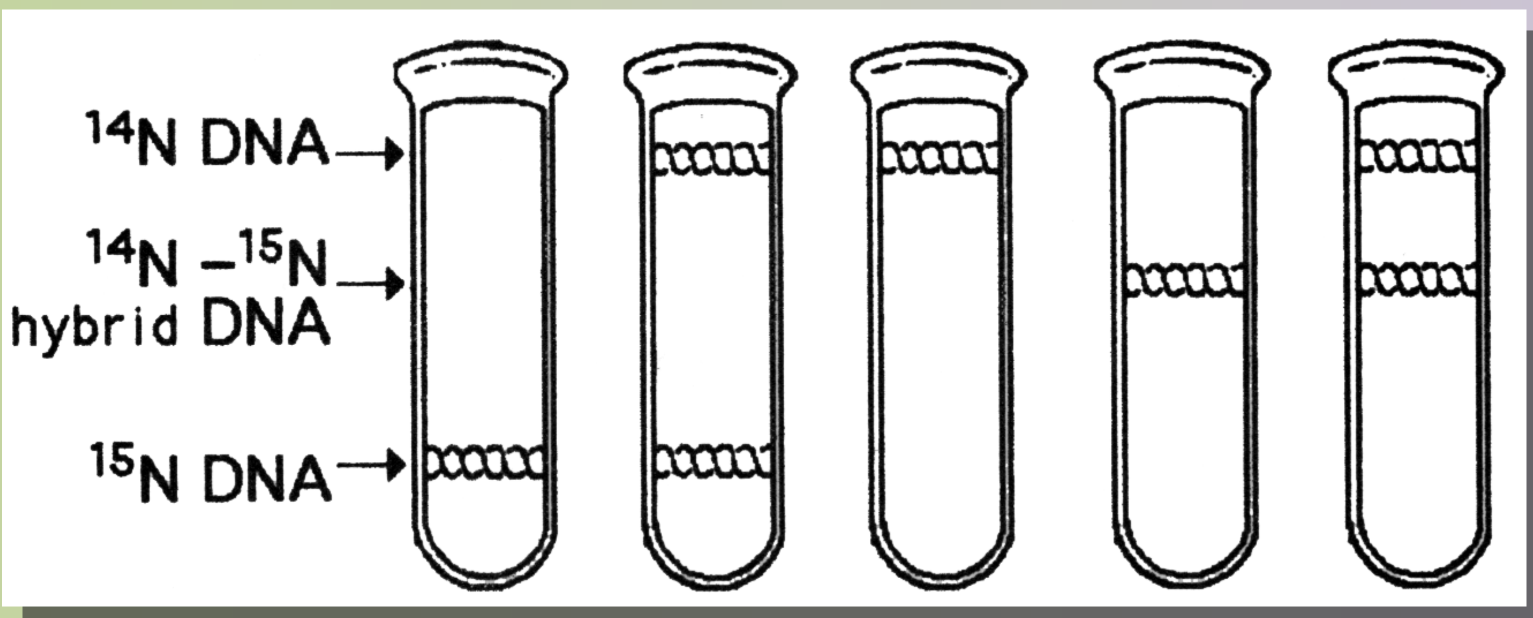
1. Tobacco mosaic virus has RNA rather than DNA as its genetic material. In a hypothetical situation where RNA from a tobacco mosaic virus is mixed with proteins from a related DNA virus, the result could be a hybrid virus. If that virus were to infect a cell and reproduce, what would the resulting "offspring" viruses be like?
    A. tobacco mosaic virus
    B. the related DNA virus
    C. a hybrid: tobacco mosaic virus RNA and protein from the DNA virus
    D. a hybrid: tobacco mosaic virus protein and nucleic acid from the DNA virus
    E. a virus with a double helix made up of one strand of DNA complementary to a strand of RNA surrounded by viral protein

2. Cytosine makes up 38% of the nucleotides in a sample of DNA from an organism. What percent of the nucleotides in this sample will be thymine?
   A. 12
   B. 24
   C. 31
   D. 38
   E. It cannot be determined from the information provided.

3. In an analysis of the nucleotide composition of DNA, which of the following is *true*?

   A. A = C
   B. A = G and C = T
   C. A + C = G + T
   D. A + T = G + C
   E. Both B and C are true

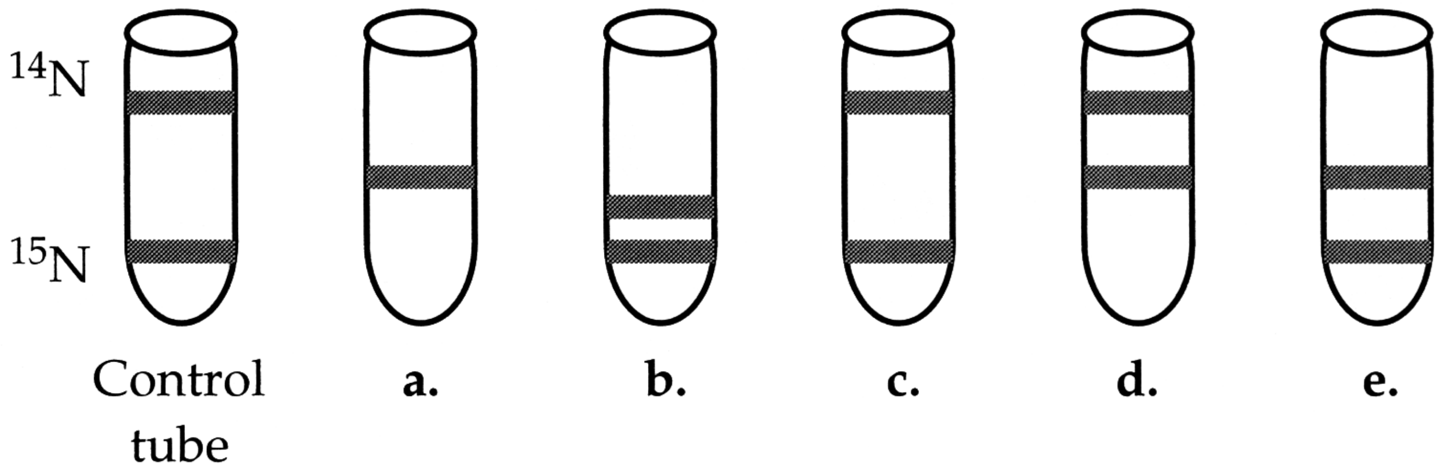
4. A space probe returns with a culture of a microorganism found on a distant planet. Analysis shows that it is a carbon-based life form that has DNA. You grow the cells in ^{15}N medium for several generations and then transfer it to ^{14}N medium. Which pattern in this figure would you expect if the DNA were replicated in a conservative manner?



a. b. c. d. e.

5. In analyzing the number of different bases in a DNA sample, which result would be consistent with the base-pairing rules?
   A. A = G
   B. A + G = C + T
   C. A + T = G + T
   D. A = C
   E. G = T

6. Imagine the following experiment is done: Bacteria are first grown for several generations in a medium containing the *lighter* isotope of nitrogen, ^{14}N, then switched into a medium containing ^{15}N. The rest of the experiment is identical to the Meselson and Stahl experiment. Which of the following represents the band positions you would expect after two generations? *



Bands after one replication on ^{14}N