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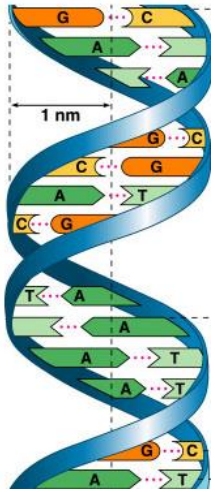
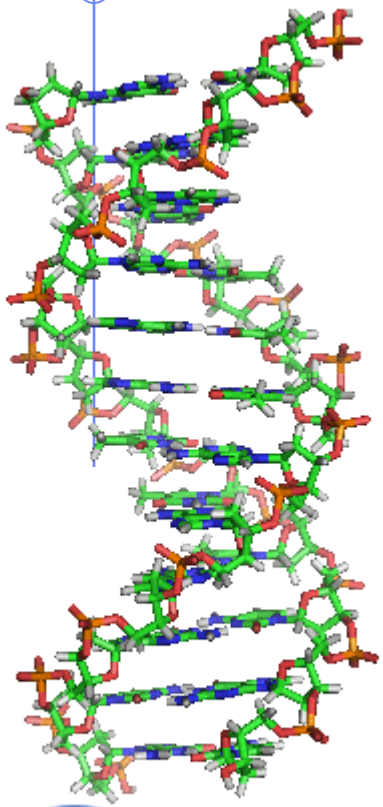
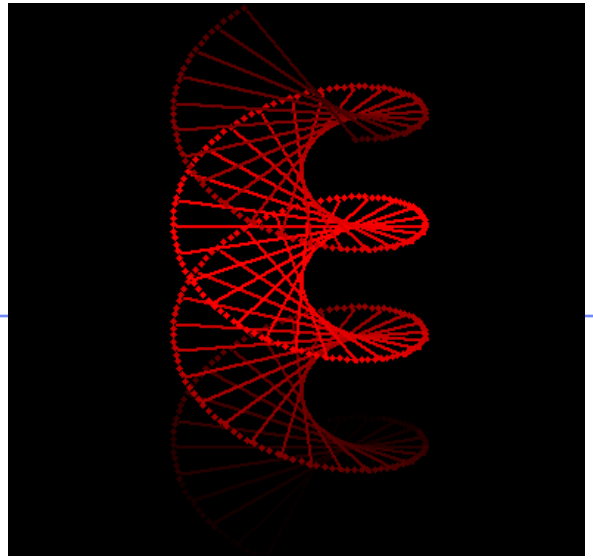
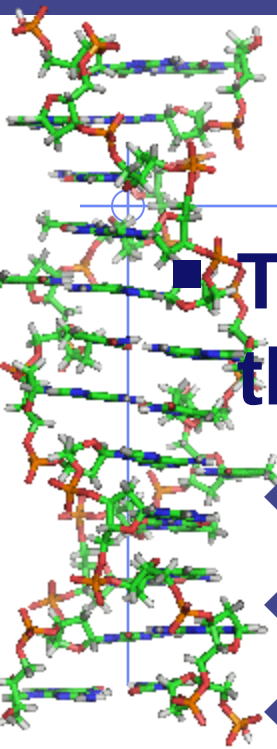
http://www.youtube.com/watch?v=_Q2Ba2cFAew



DNA
The Genetic Material

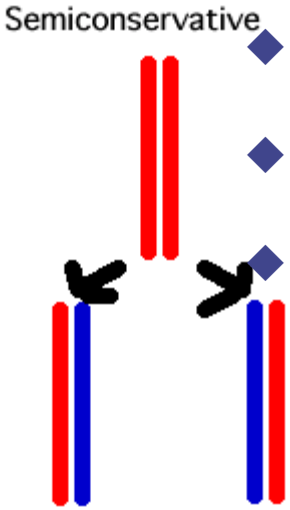


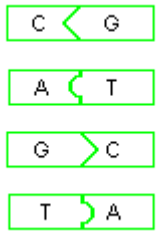




Scientific History

- The march to understanding that DNA is the genetic material
  - T.H. Morgan (1908)
  - Frederick Griffith (1928)
  - Avery, McCarty & MacLeod (1944)
  - Erwin Chargaff (1947)
  - Hershey & Chase (1952)
  - Watson & Crick (1953)
  - Meselson & Stahl (1958)



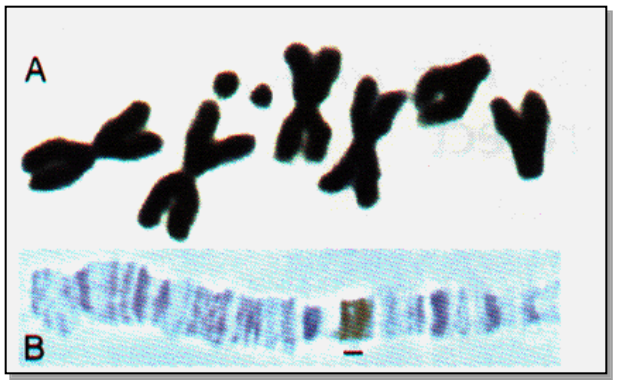


Scientific History

- 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

1908 | 1933
Chromosomes related to phenotype

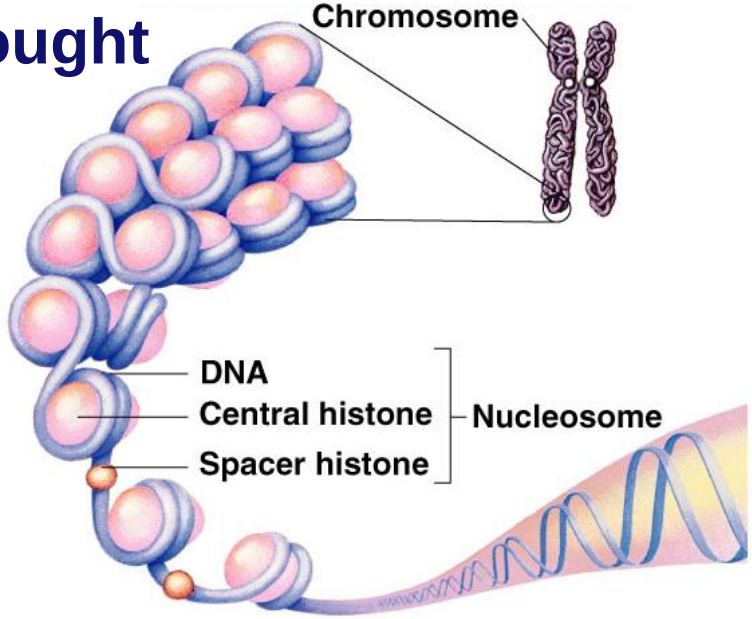
- **T.H. Morgan**
  - working with *Drosophila*
    - fruit flies
  - associated phenotype with specific chromosome
    - white-eyed male had specific X chromosome



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
    - 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"

A. live pathogenic strain of *bacteria*

B. live non-pathogenic strain of *bacteria*

C. heat-killed pathogenic *bacteria*

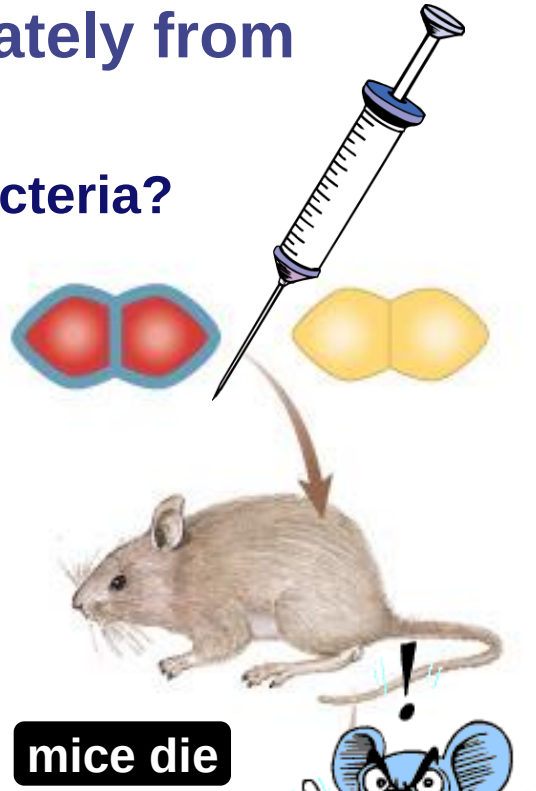
D. mix heat-killed pathogenic & non-pathogenic *bacteria*

Transformation = change in phenotype

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

DNA is the "Transforming Principle" 1944

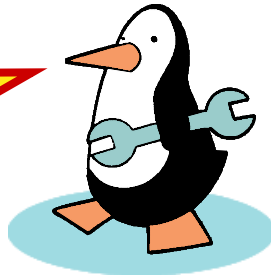
- Avery, McCarty & MacLeod
  - purified both DNA & proteins separately from *Streptococcus* pneumonia bacteria
    - which will transform non-pathogenic bacteria?
  - injected protein into bacteria
    - no effect
  - injected DNA into bacteria
    - transformed harmless bacteria into virulent bacteria

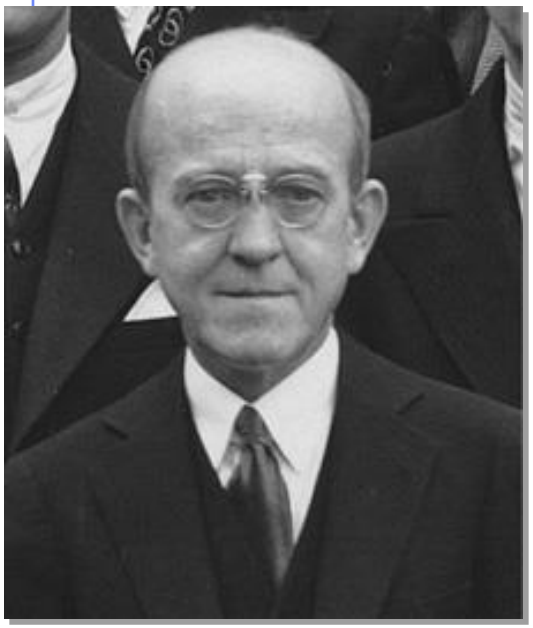


Avery, McCarty & MacLeod

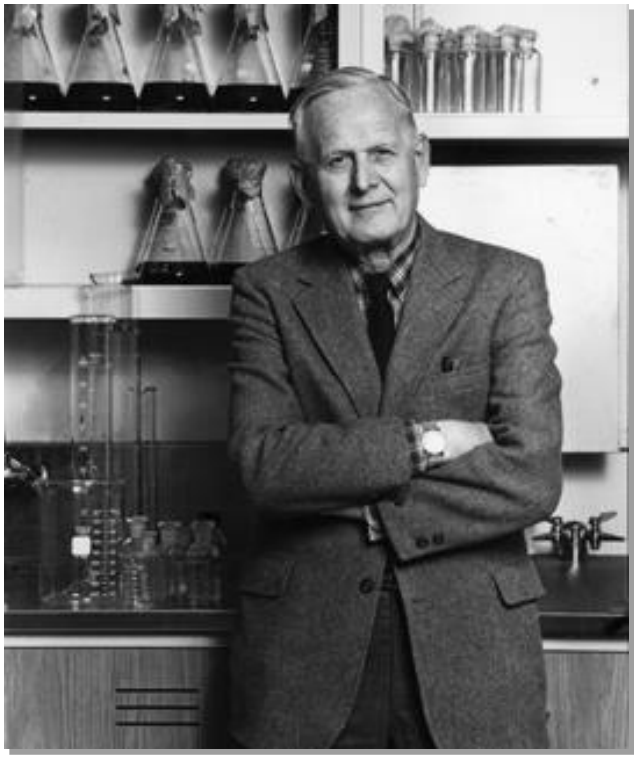
- Conclusion
  - DNA is the genetic material

1st experimental evidence!

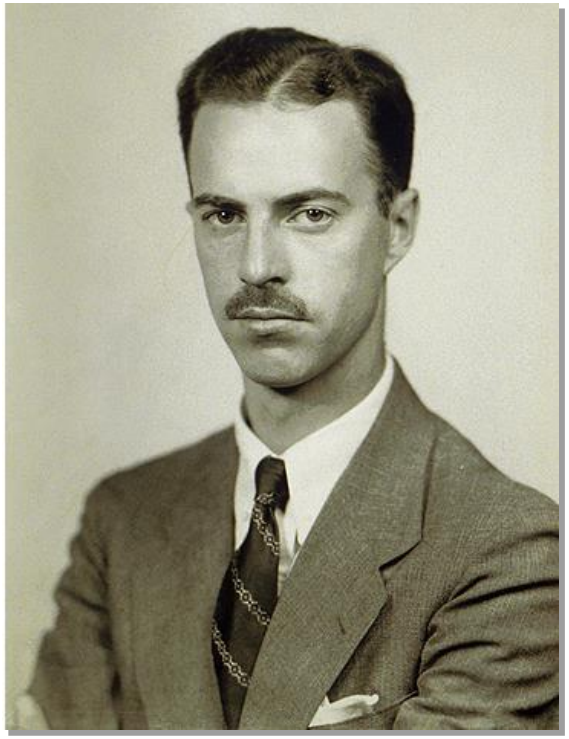




Oswald Avery



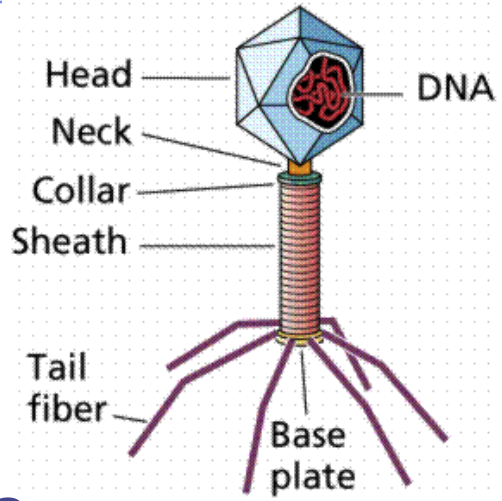
Maclyn McCarty



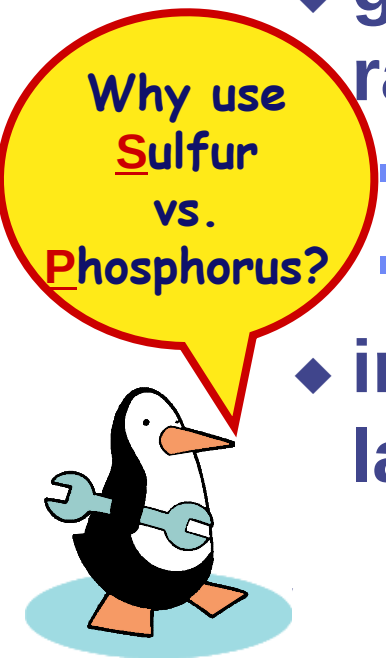
Colin MacLeod

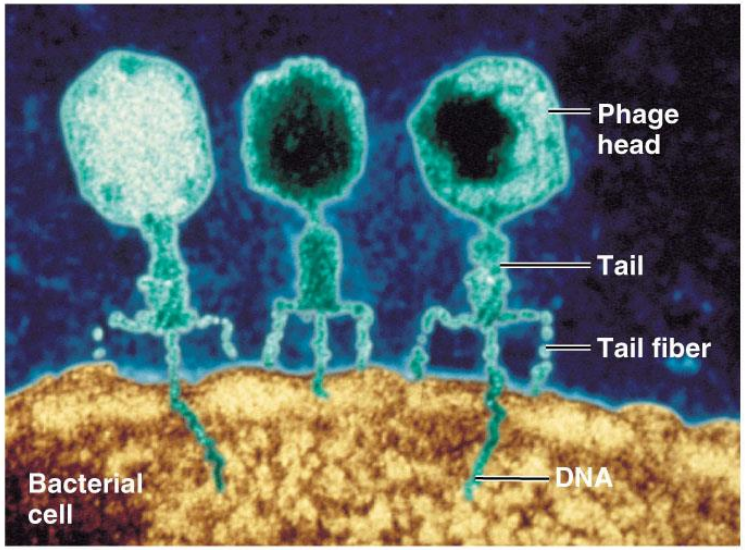
Confirmation of DNA

1952 | 1969
Hershey



- **Hershey & Chase**
  - classic "blender" experiment
  - worked with **bacteriophage**
    - viruses that infect bacteria
  - grew 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

Protein coat labeled with ^{35}S

DNA labeled with ^{32}P

T2 bacteriophages are labeled with radioactive isotopes
S vs. P

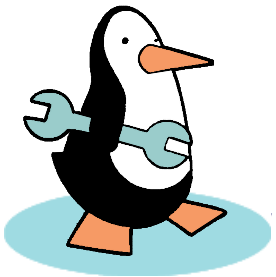
bacteriophages infect bacterial cells

bacterial cells are agitated to remove viral protein coats

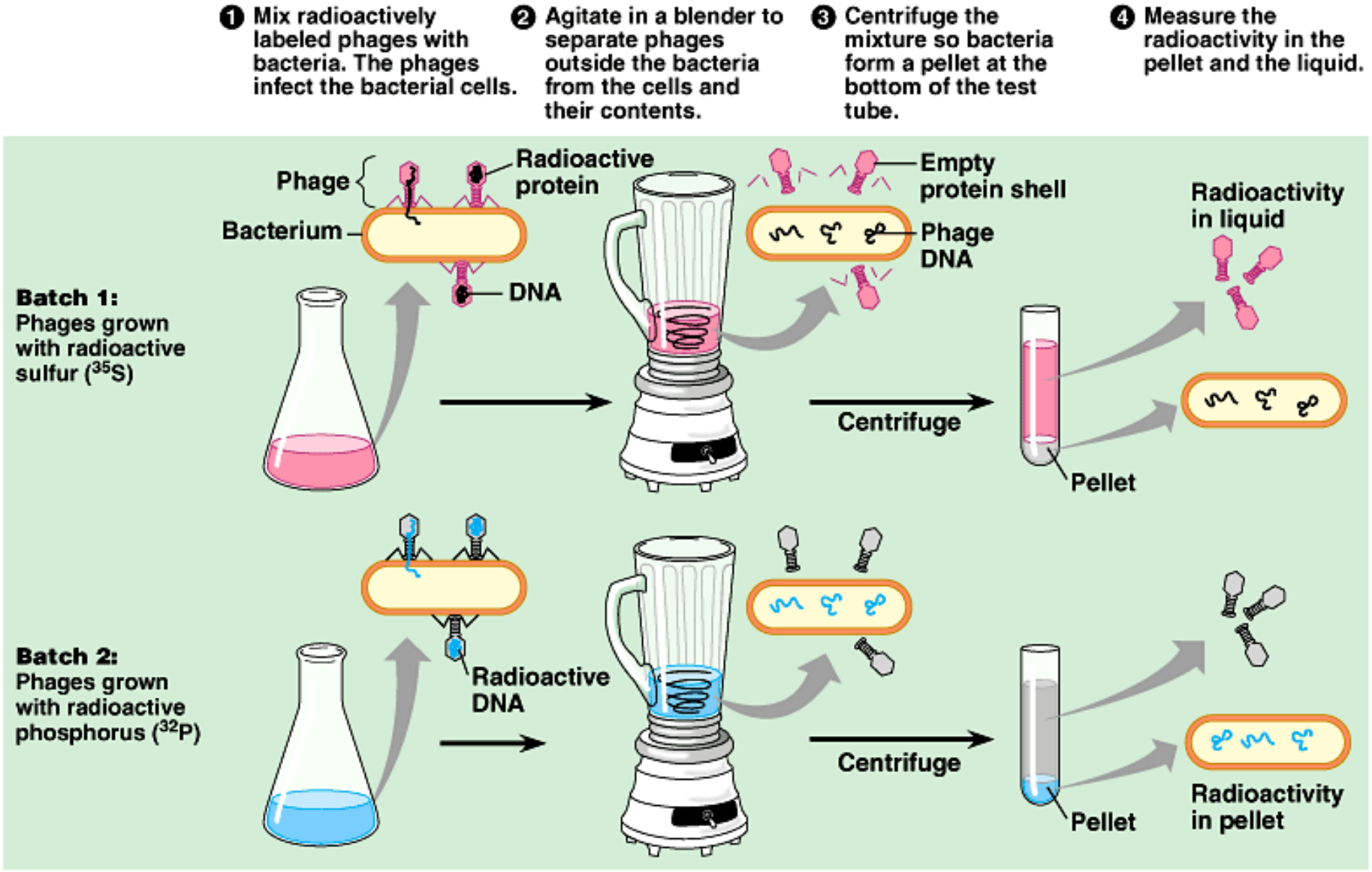
^{35}S radioactivity found in the medium

^{32}P radioactivity found in the bacterial cells

Which molecule carries viral genetic info?

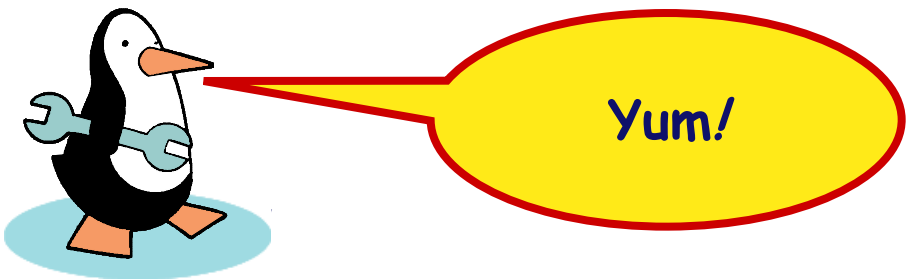


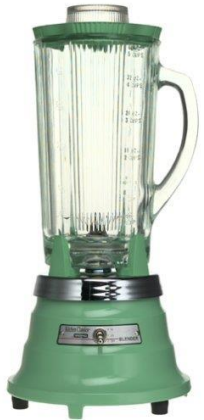
http://highered.mcgraw-hill.com/olcweb/cgi/pluginpop.cgi?it=swf::535::535::/sites/dl/free/0072437316/120076/bio21.swf::Hershey and Chase Experiment



Blender experiment

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





Hershey & Chase

CSHL

1952 | 1969

Hershey

lab assistant

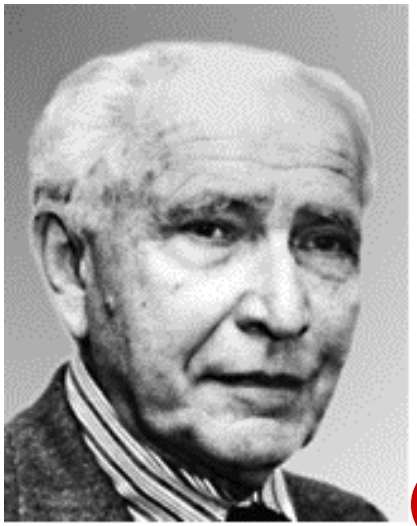
http://highered.mcgraw-hill.com/olcweb/cgi/pluginpop.cgi?it=swf::535::535::/sites/dl/free/0072437316/120076/bio21.swf::Hershey and Chase Experiment

Martha Chase Alfred Hershey

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:



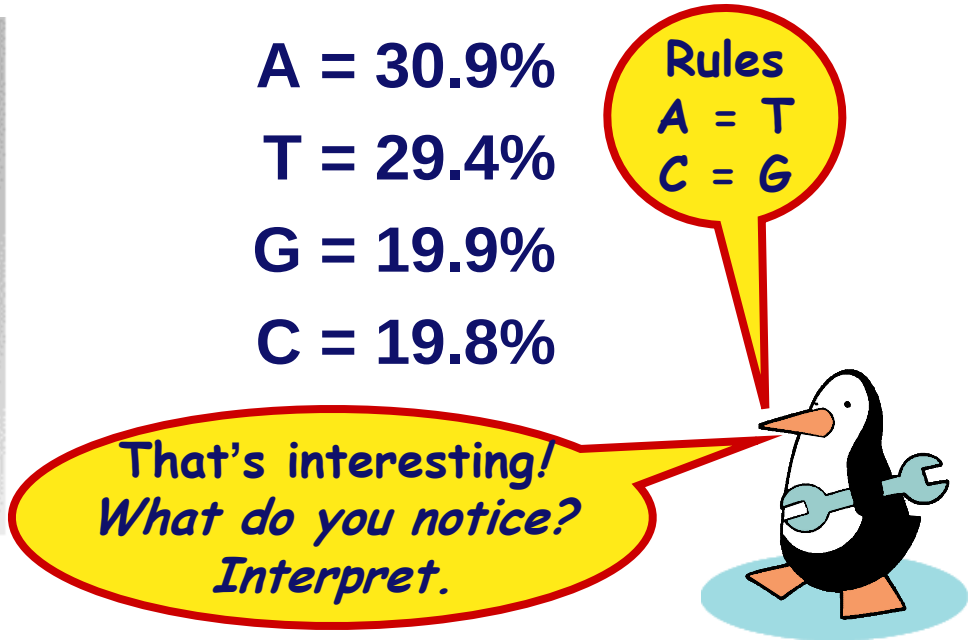
Erwin Chargaff

A = 30.9%

T = 29.4%

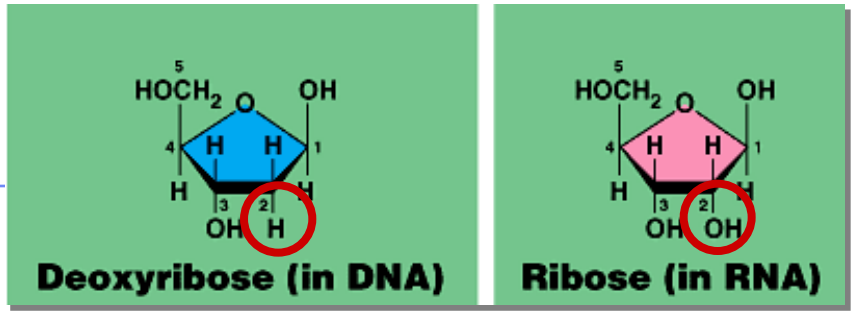
G = 19.9%

C = 19.8%



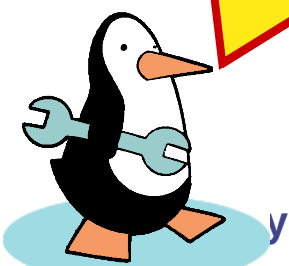
Nucleotides

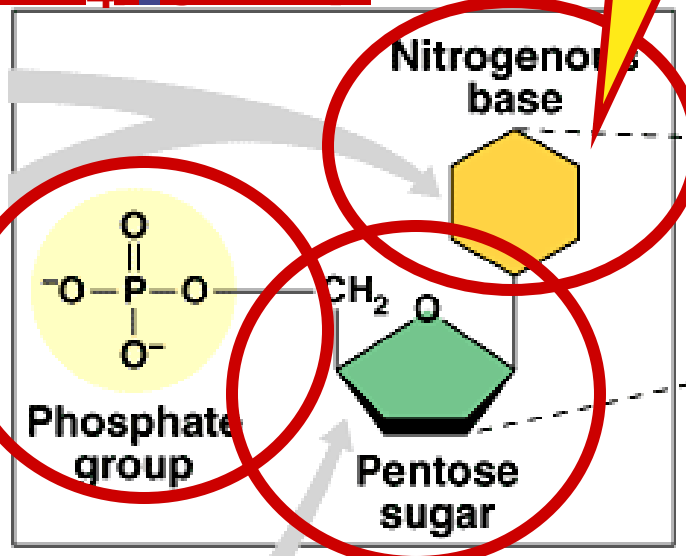
- 3 parts
  - nitrogen base (C-N ring)
  - pentose sugar (5C)
    - ribose in RNA
    - deoxyribose in DNA
  - phosphate (PO_4) group

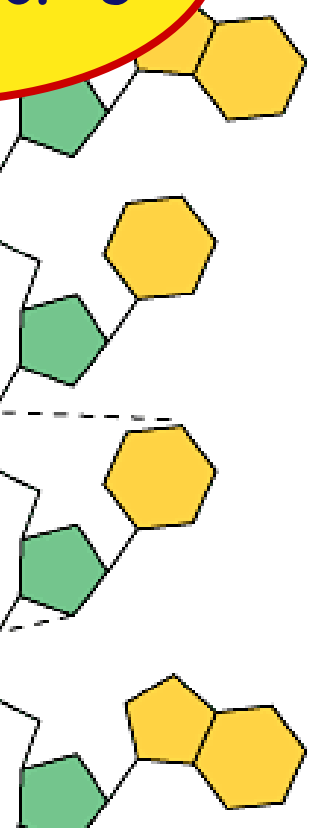


Nitrogen base
I'm the A,T,C,G or U part!

Will nucleic acids freely cross the membrane?

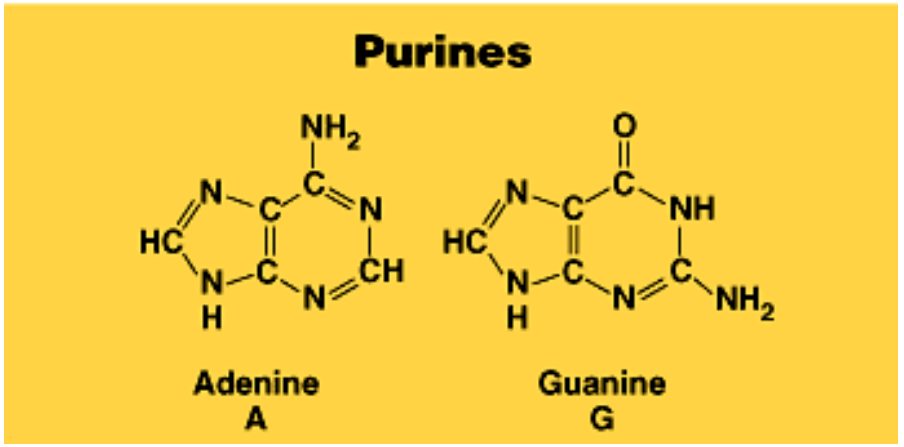


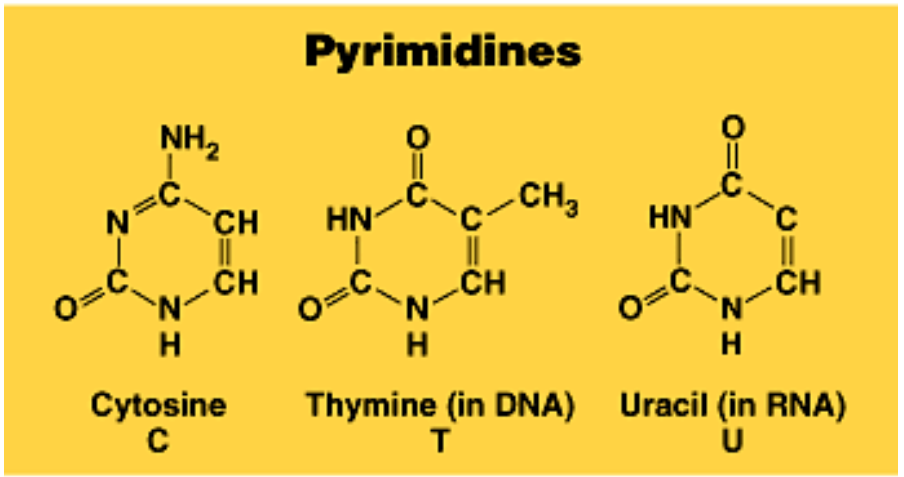




Types of nucleotides

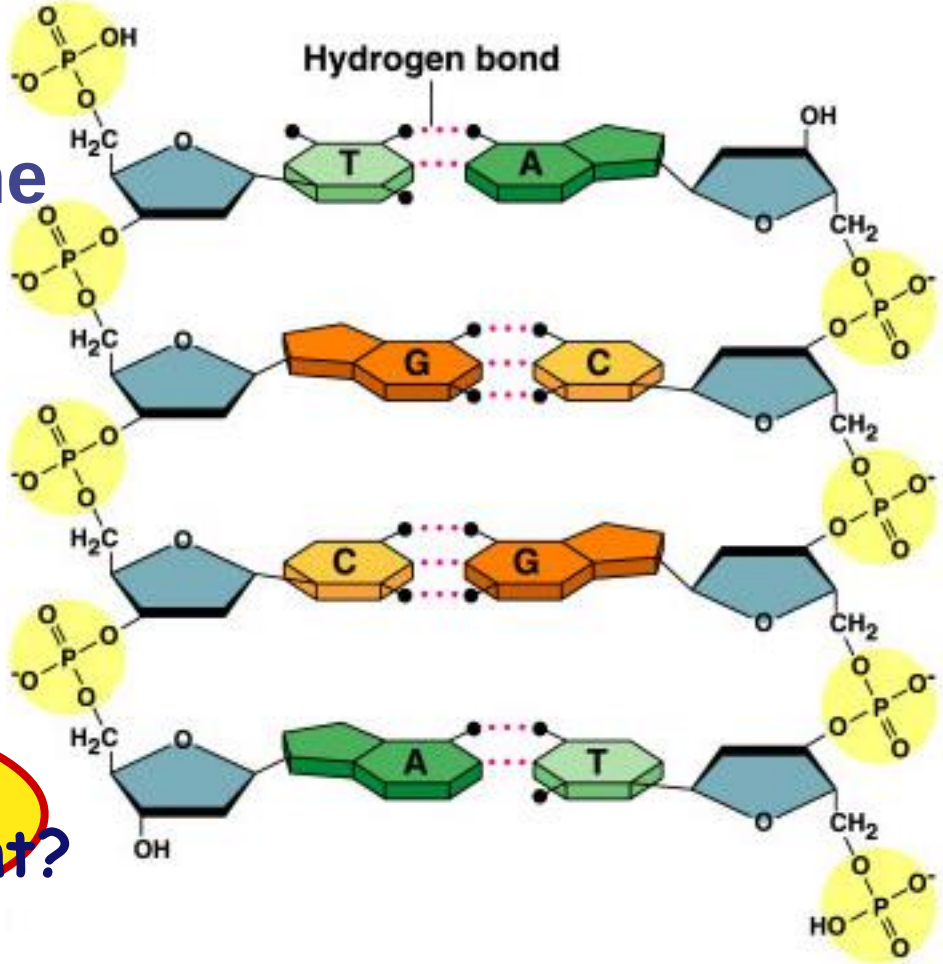
- 2 types of nucleotides
  - different nitrogen bases
  - purines
    - double ring N base
    - adenine (A)
    - guanine (G)
  - pyrimidines
    - single ring N base
    - cytosine (C)
    - thymine (T)
    - uracil (U)

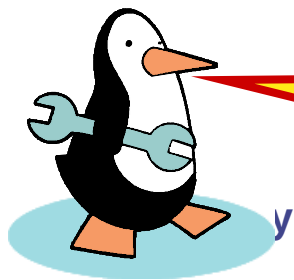




Pairing of nucleotides

- Nucleotides bond between DNA strands
  - H bonds
  - purine :: pyrimidine
  - A :: T
    - 2 H bonds
  - G ⁝⁝ C
    - 3 H bonds



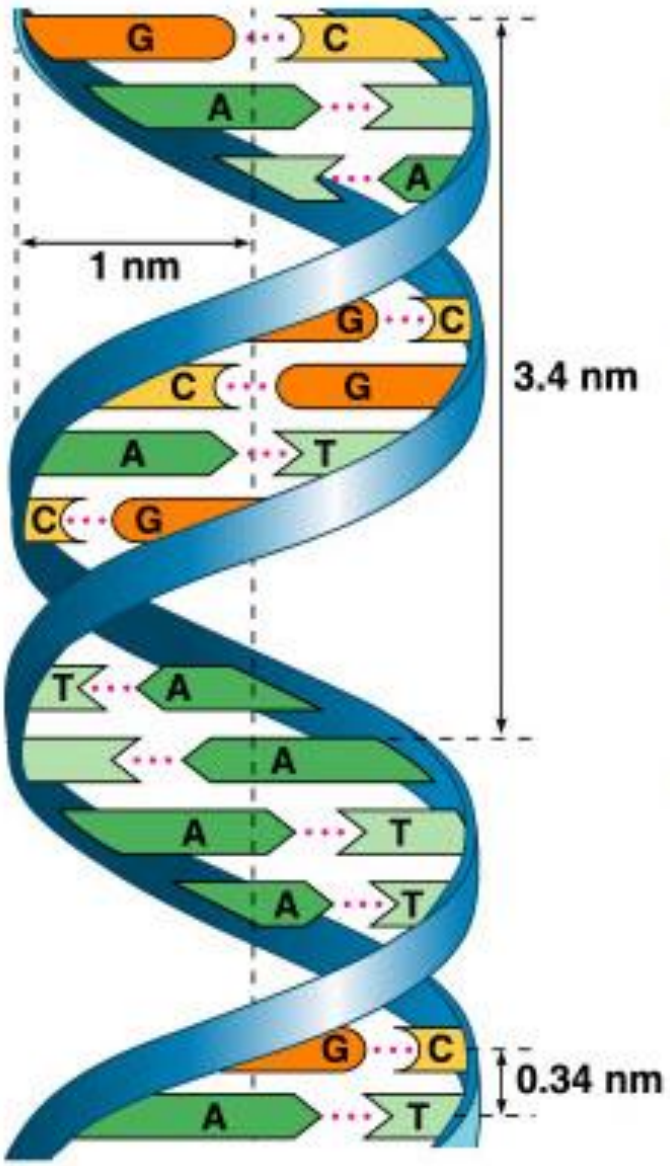


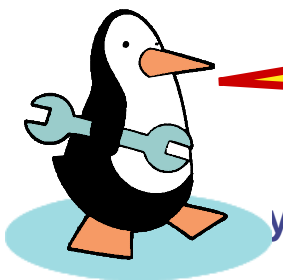
Matching bases?
Why is this important?

http://www.youtube.com/watch?v=ZK6YP1Smbxk

DNA molecule

- Double helix
  - H bonds between bases join the 2 strands
    - A :: T
    - C :: G



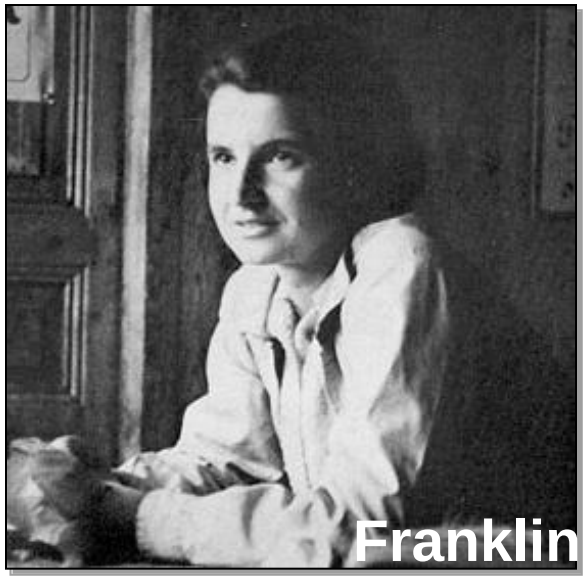


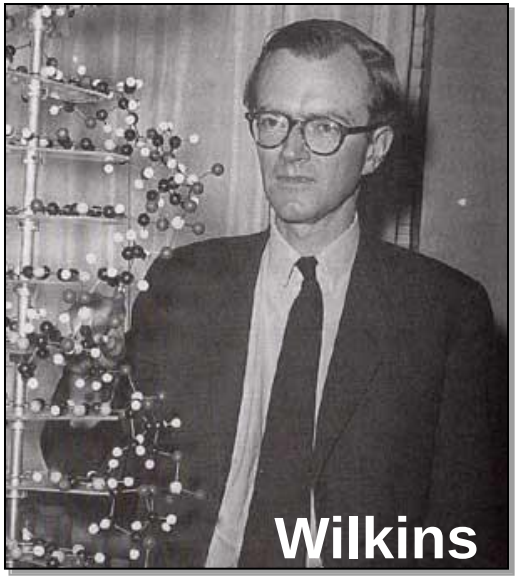
H bonds?
Why is this important?

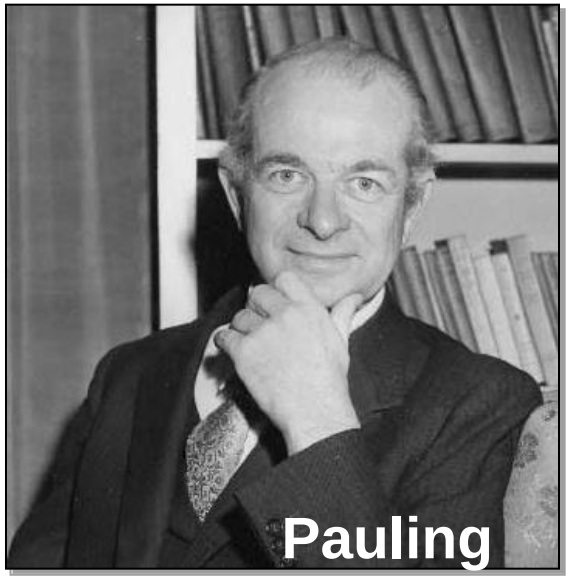
Structure of DNA

1953 | 1962

- Watson & Crick
  - developed double helix model of DNA
    - other leading scientists working on question:
      - Rosalind Franklin
      - Maurice Wilkins – X-ray crystallography
      - Linus Pauling – α helical structure of a protein

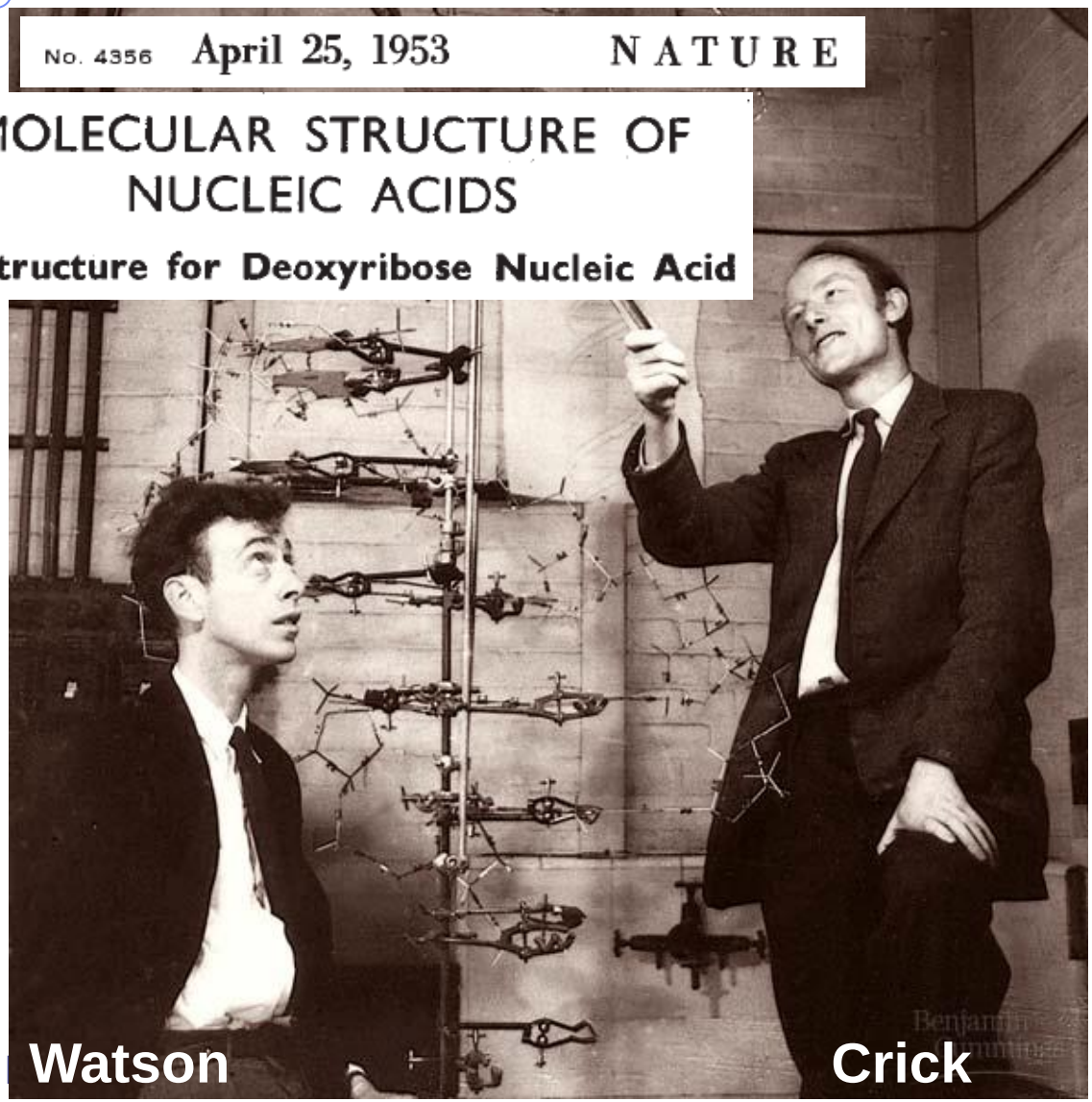




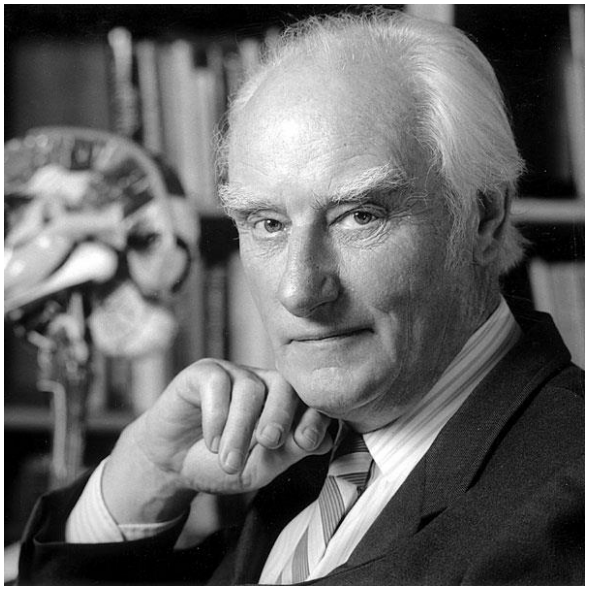


Watson and Crick

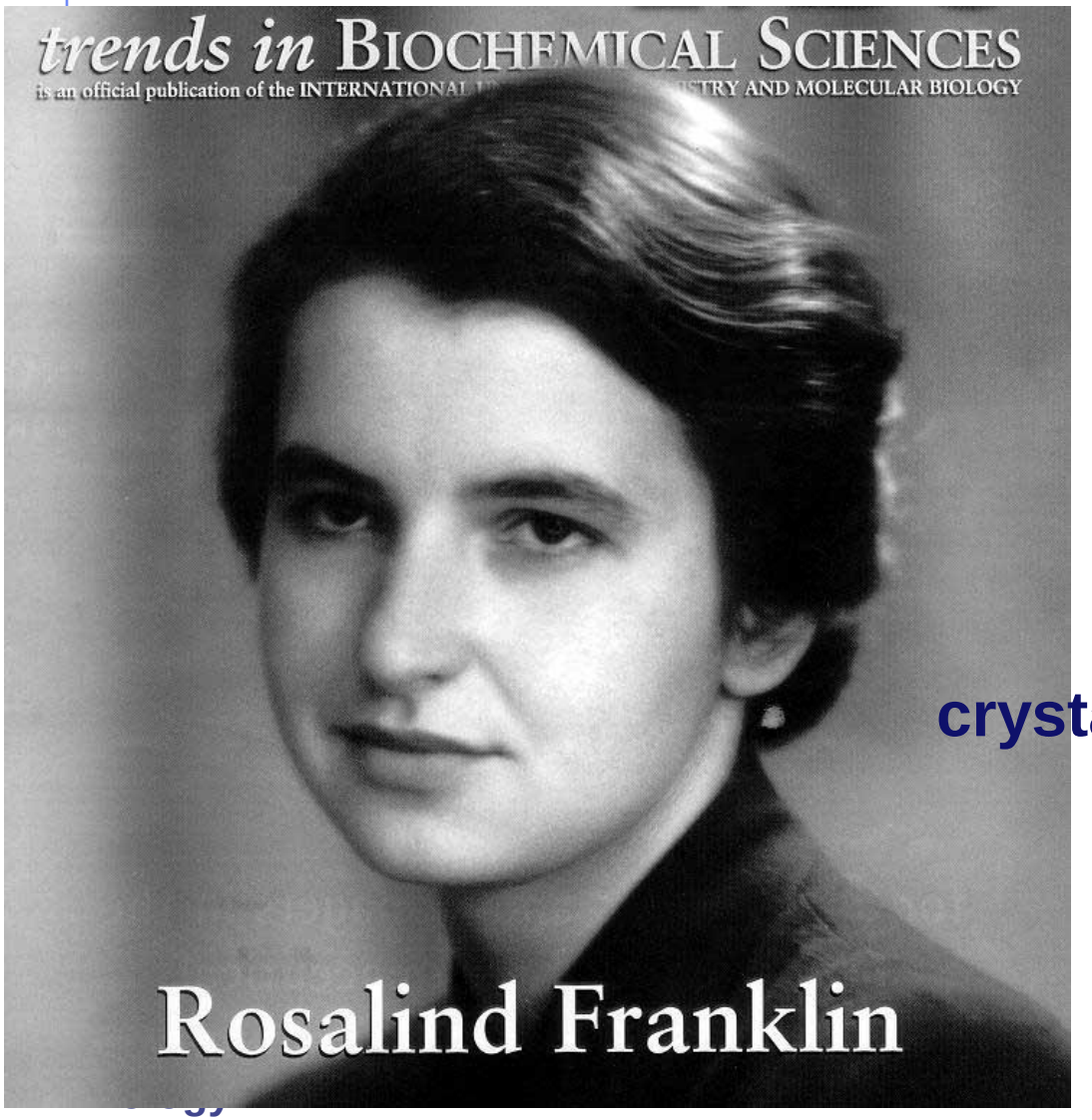
1953 article in Nature



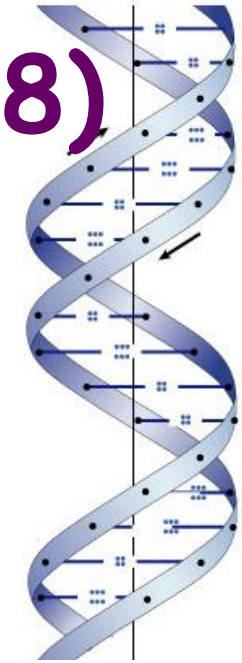
AP | Watson Crick



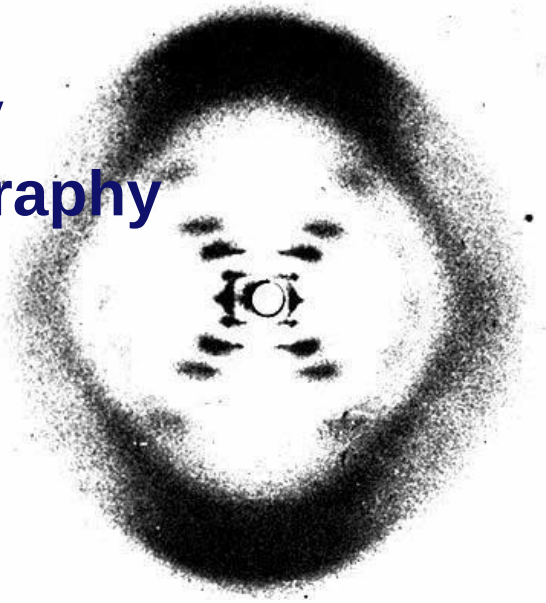
Rosalind Franklin (1920-1958)



Sugar-phosphate backbone lies on the outside

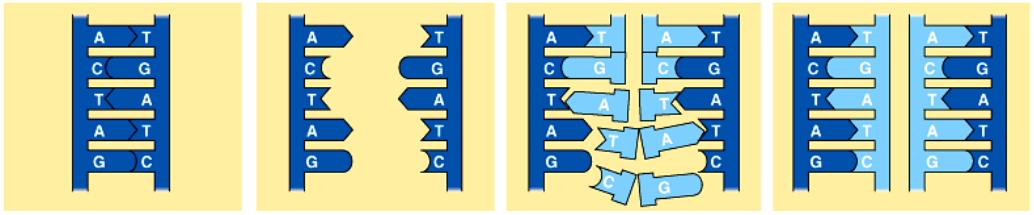


X-ray crystallography



But how is DNA copied?

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

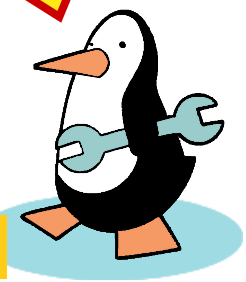


"It has not escaped our notice that the specific pairing we have postulated immediately suggests a possible copying mechanism for the genetic material."

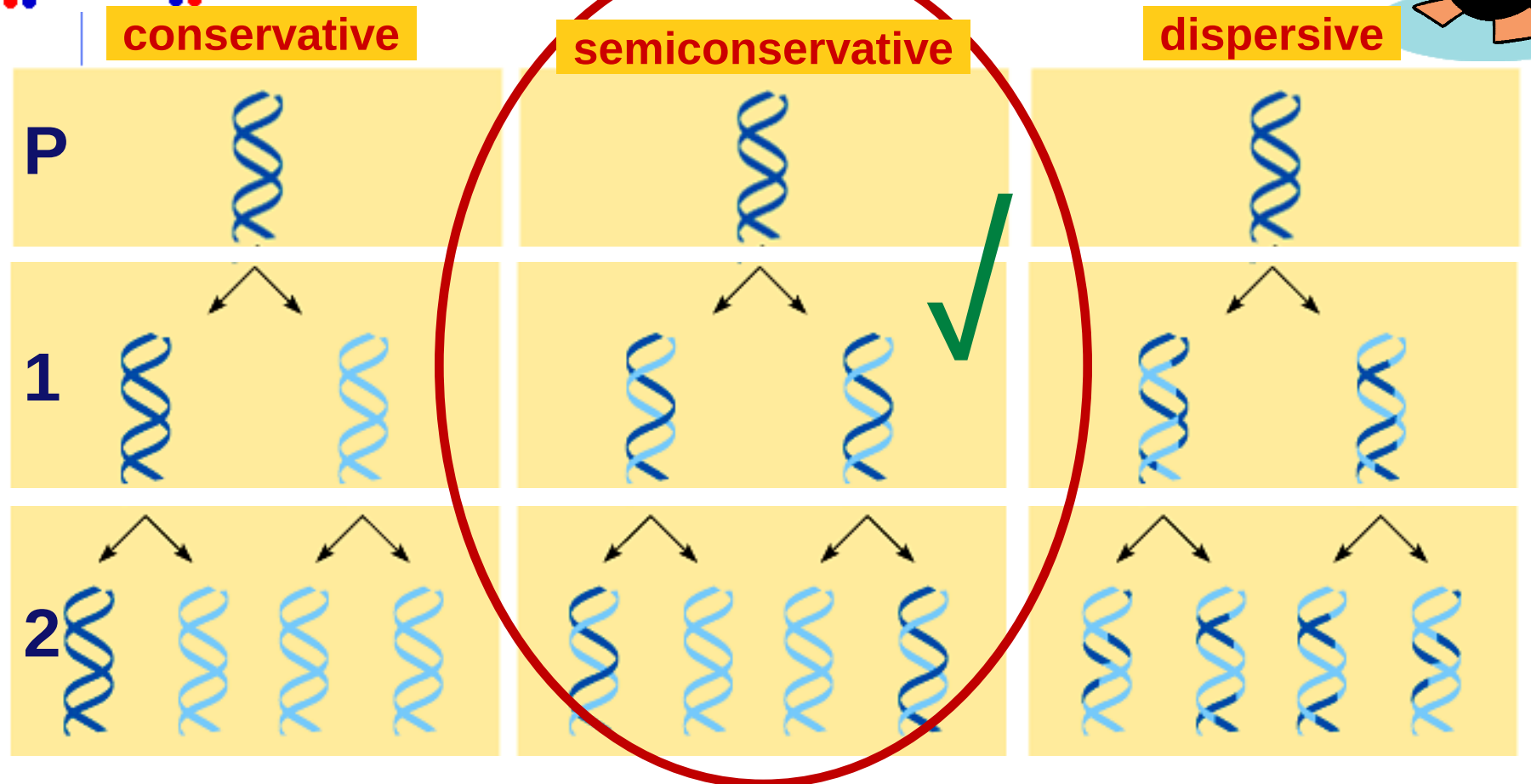
— Watson & Crick

Models of DNA Replication

Design a nifty experiment to determine which is correct.

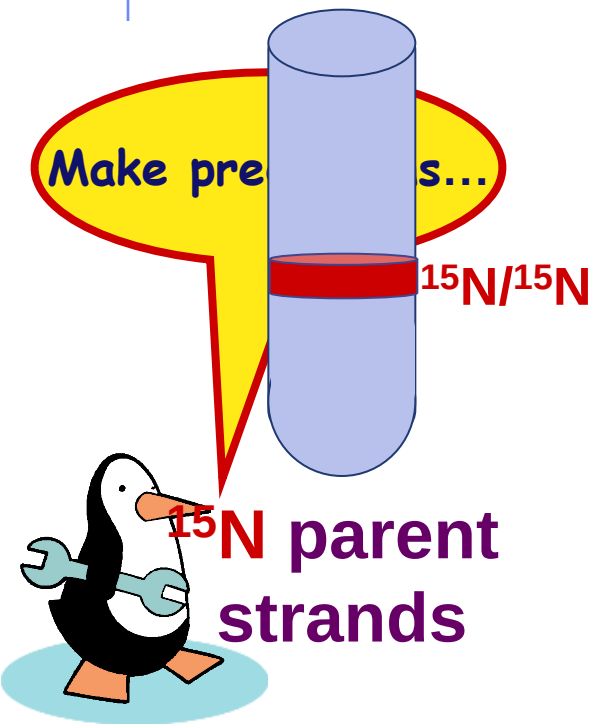


- Alternative models
  - become experimental predictions

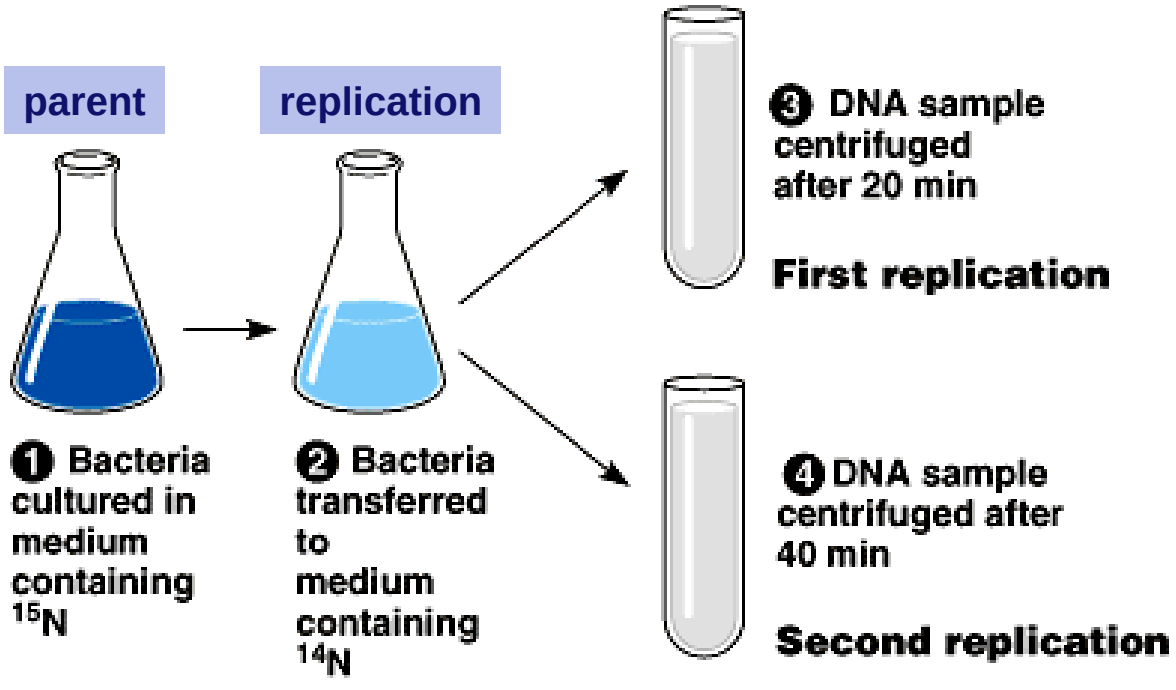


Semiconservative replication 1958

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



"The Most Beautiful Experiment in Biology"

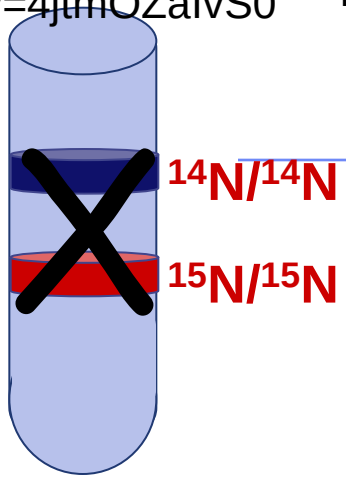


http://www.youtube.com/watch?v=4jtmOZaIvS0

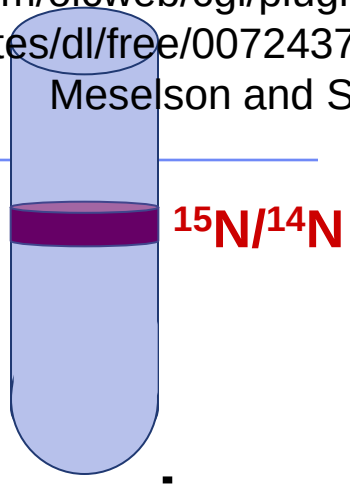
http://highered.mcgraw-hill.com/olcweb/cgi/pluginpop.cgi?it=swf::535::535::/sites/dl/free/0072437316/120076/bio22.swf::Meselson and Stahl Experiment

Predictions

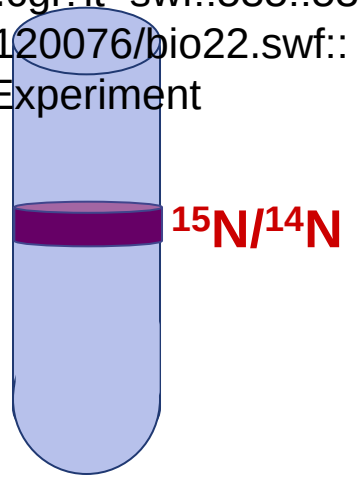
1st round of replication



conservative

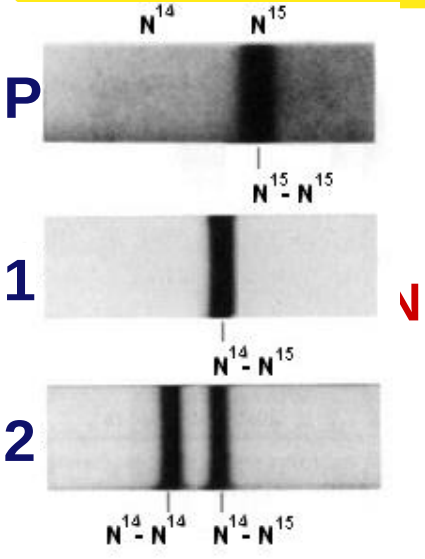


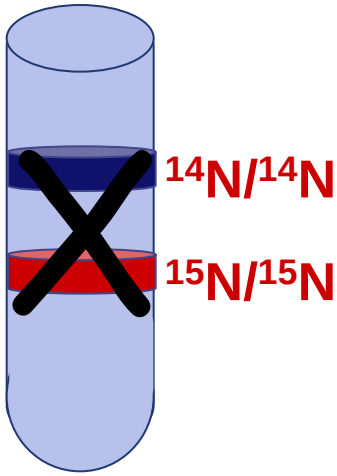
semi-conservative



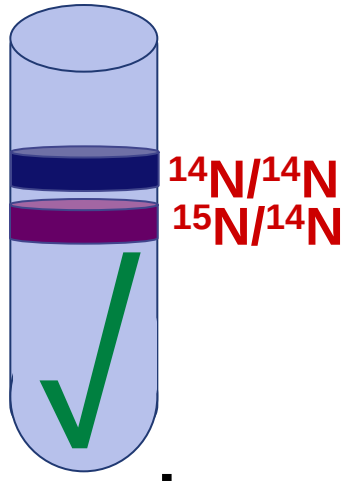
dispersive

2nd round of replication

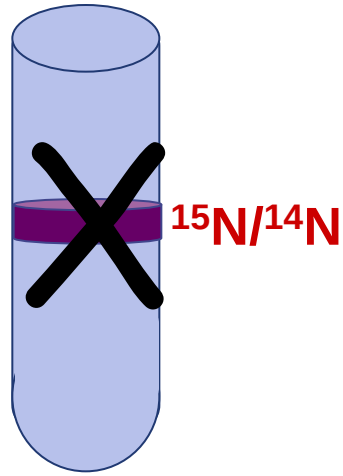




conservative

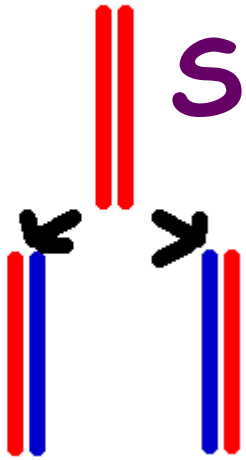


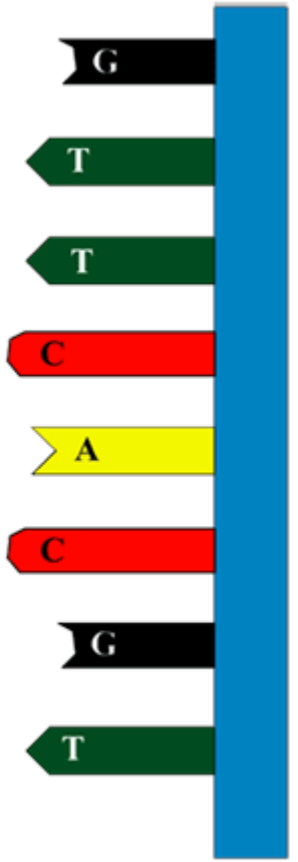
semi-conservative



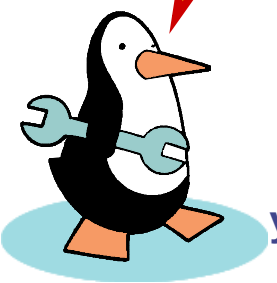
dispersive

Semi-conservative Replication





Template strands are shown… draw in the newly synthesized strands



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DNA Replication

DNA replication animation with description:
http://www.youtube.com/watch?v=teV62zrm2P0

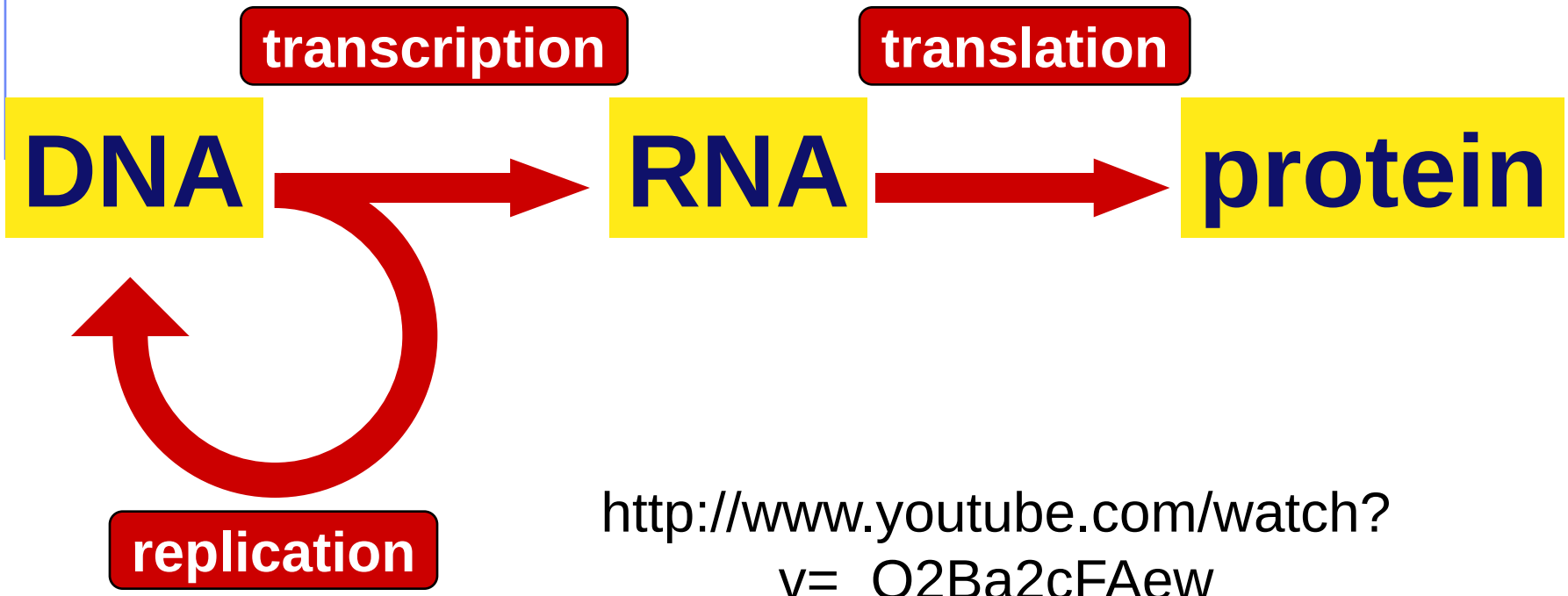
DNA replication
http://glencoe.mcgraw-hill.com/sites/9834092339/student_view0/chapter14/dna_replication.html

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



http://www.youtube.com/watch?v=_Q2Ba2cFAew

http://www.youtube.com/watch?v=ZK6YP1Smbxk