DNA

The Chemical Nature of the Gene

Topics

- The Elegantly Stable Double Helix: Ice Man's DNA
- Characteristics of Genetic Material
- The Molecular Basis of Heredity
- Early Studies of DNA
- DNA As the Source of Genetic Information
- Watson and Crick's Discovery of the Three-Dimensional Structure of DNA
- RNA as Genetic Material
- The Structure of DNA
- The Primary Structure of DNA
- Secondary Structures of DNA
- Special Structures in DNA and RNA
- DNA Methylation Bends in DNA

The Elegantly Stable Double Helix: Ice Man's DNA

- This analysis revealed that Ice Man's **mitochondrial DNA sequences** resemble those found in present-day Europeans living north of the Alps and are quite different from those of sub-Saharan Africans, Siberians, and Native Americans.
- Together, radiocarbon dating, the artifacts, and the DNA analysis all indicate that Ice Man was a Neolithic hunter who died while attempting to cross the Alps 5000 years ago.
- That some of Ice Man's DNA persists and faithfully carries his genetic instructions even after the passage of 5000 years is testimony to the remarkable stability of the double helix.
- Even more ancient DNA has been isolated from the fossilized bones of Neanderthals that are at least 30,000 years old.

Characteristics of Genetic Material

• Genetic material must contain complex information.

First and foremost, the genetic material must be capable of storing large amounts of information instructions for all the traits and functions of an organism. This information must have the capacity to vary, because different species and even individual members of a species differ in their genetic makeup. At the same time, the genetic material must be stable, because most alterations to the genetic instructions (mutations) are likely to be detrimental.

• Genetic material must replicate faithfully.

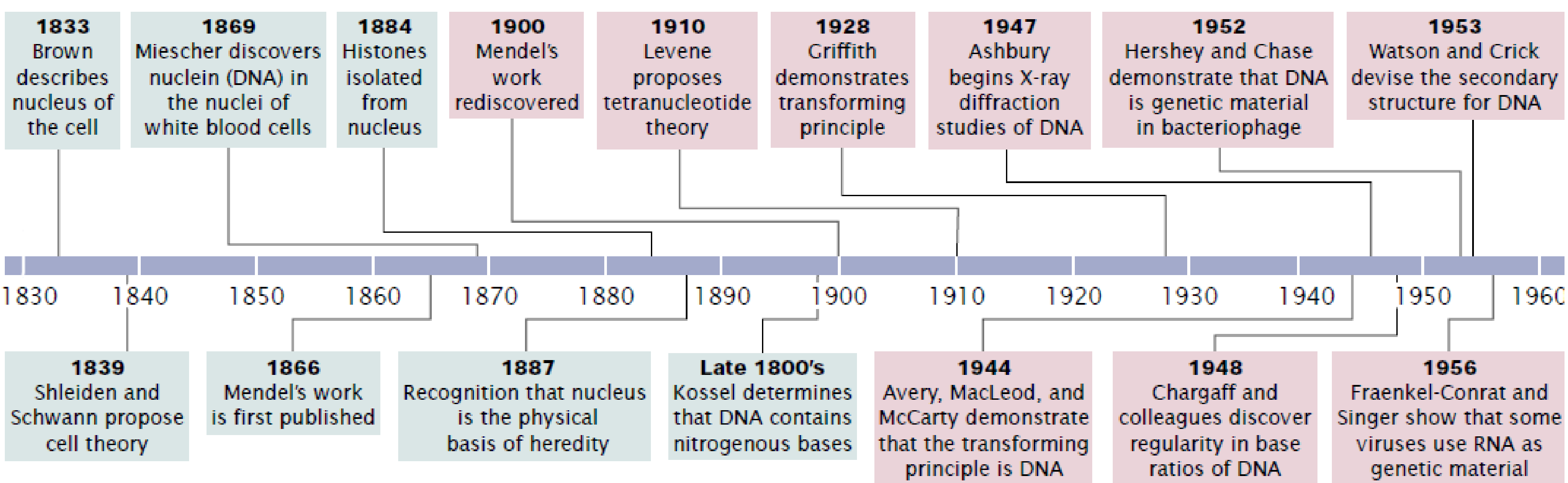
A second necessary feature is that genetic material must have the capacity to be copied accurately. Every organism begins life as a single cell, which must undergo billions of cell divisions to produce a complex, multicellular creature like yourself. At each cell division, the genetic instructions must be transmitted to descendent cells with great accuracy. When organisms reproduce and pass genes to their progeny, the coding instructions must be copied with fidelity.

• Genetic material must encode phenotype.

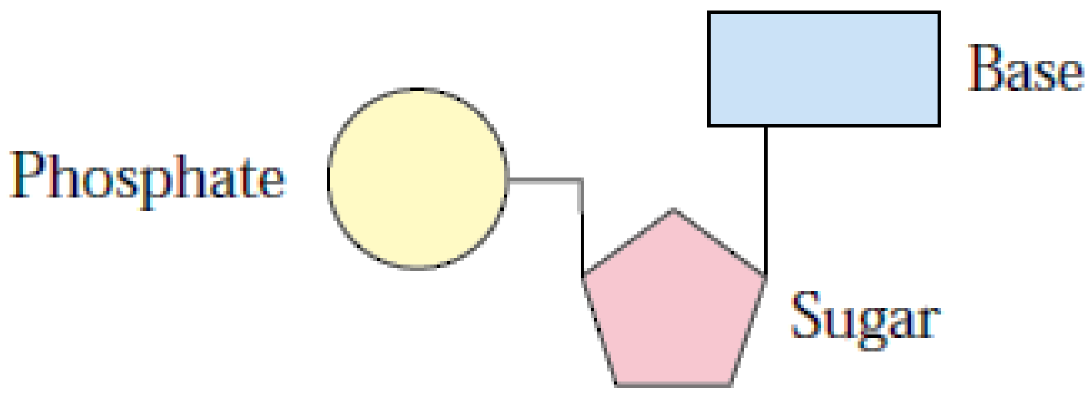
The genetic material (the genotype) must have the capacity to “code for” (determine) traits (the phenotype). The product of a gene is often a protein; so there must be a mechanism for genetic instructions to be translated into the amino acid sequence of a protein.

The Molecular Basis of Heredity

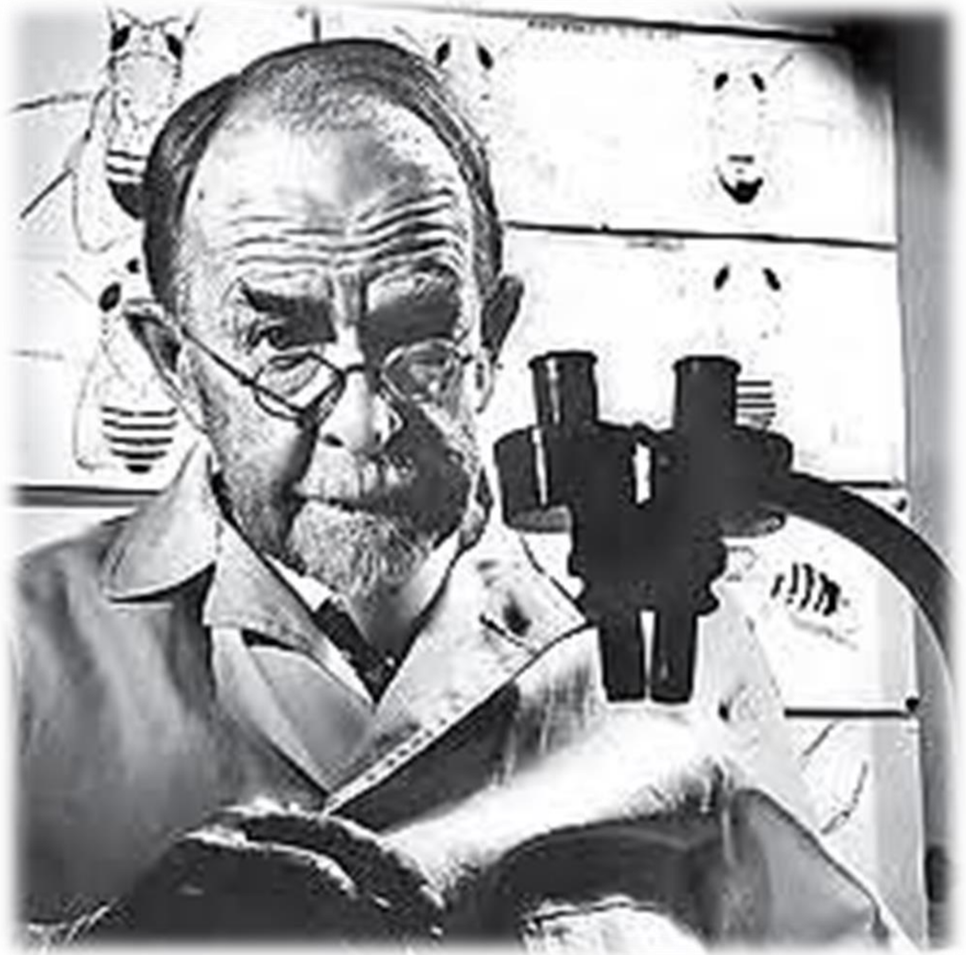
Early Studies of DNA In 1868, Johann Friedrich Miescher graduated from medical school in Switzerland. Influenced by an uncle who believed that the key to understanding disease lay in the chemistry of tissues, Miescher traveled to Tubingen, Germany, to study under Ernst Felix Hoppe- Seyler, an early leader in the emerging field of biochemistry. Under Hoppe-Seyler's direction, Miescher turned his attention to the chemistry of pus, a substance of clear medical importance. Pus contains white blood cells with large nuclei; Miescher developed a method of isolating.

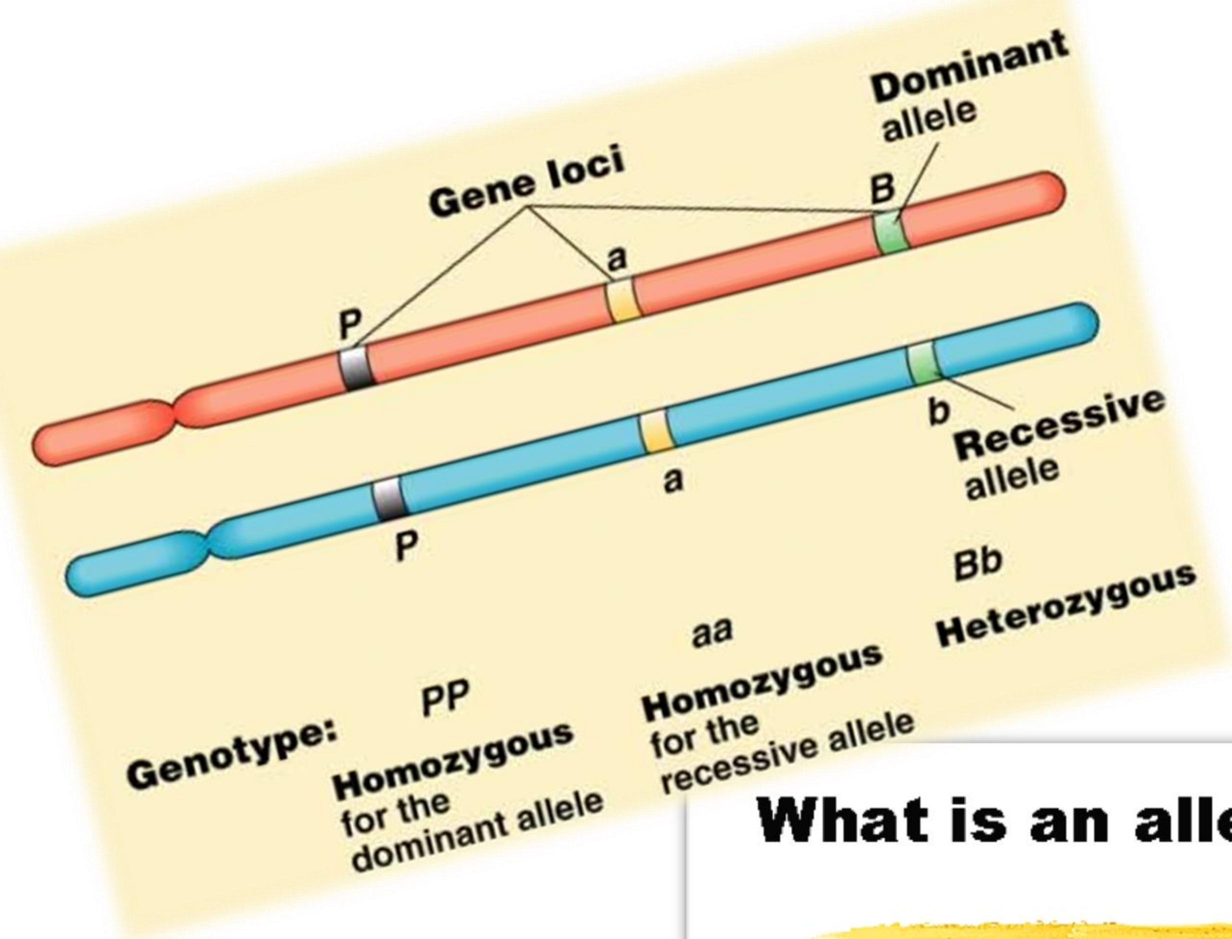


In the early twentieth century, the Rockefeller Institute in New York City became a center for nucleic acid research. Phoebus Aaron Levene joined the Institute in 1905 and spent the next 40 years studying the chemistry of DNA. He discovered that DNA consists of a large number of linked, repeating units, each containing a sugar, a phosphate, and a base (together forming a **nucleotide**).



Nucleotide





What is an allele?

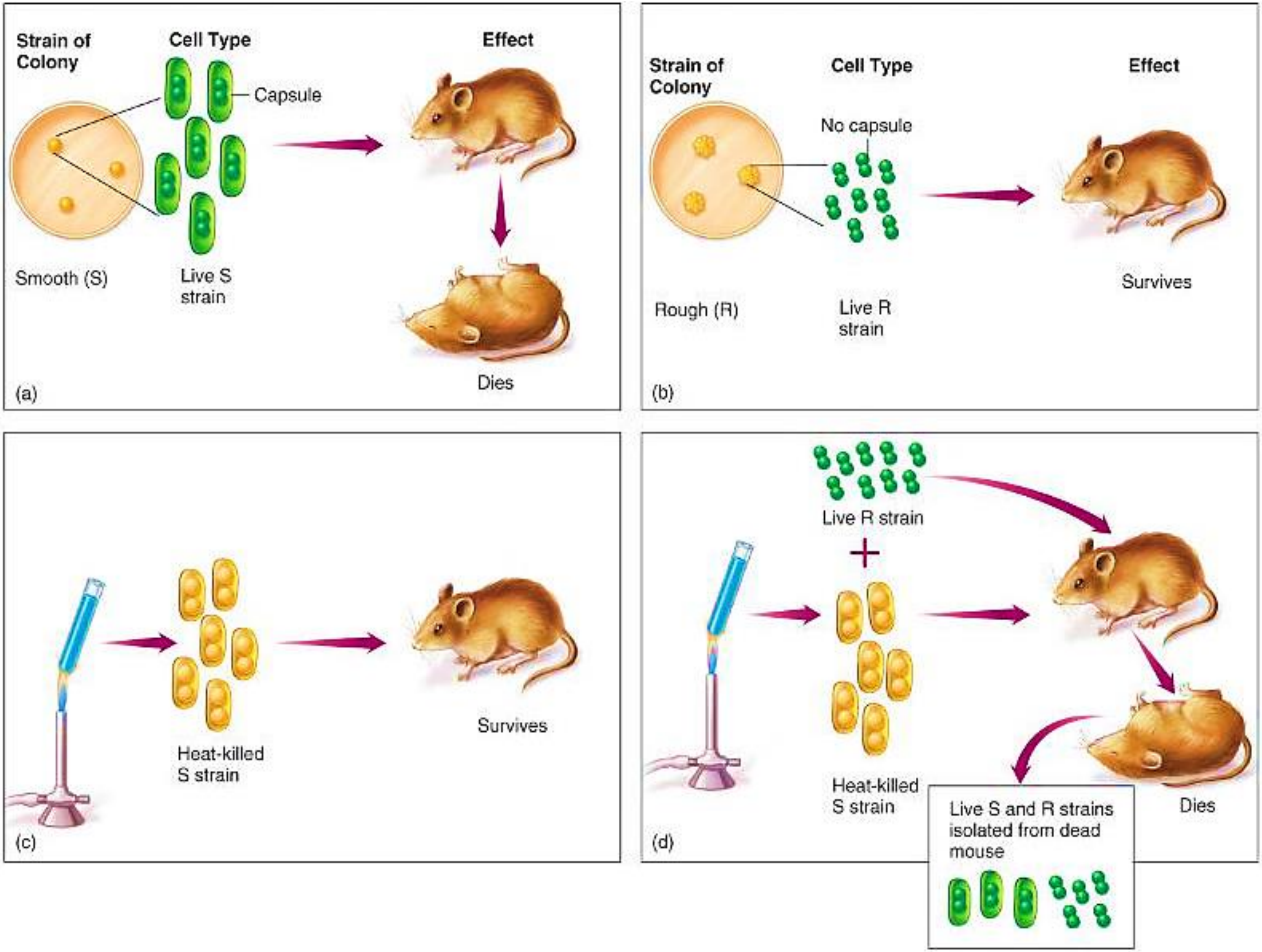
- An allele is ONE variant of a gene. Many genes have two, several, or many different variants of the same basic genetic information.
- Some alleles are minor differences that to not significantly affect the organism, others cause profound changes.

DNA As the Source of Genetic Information

While chemists were working out the structure of DNA, biologists were attempting to identify the source of genetic information. Two sets of experiments, one conducted on bacteria and the other on viruses, provided pivotal evidence that DNA, rather than protein, was the genetic material.

The discovery of the transforming principle

The first clue that DNA was the carrier of hereditary information came with the demonstration that DNA was responsible for a phenomenon called *transformation*. The phenomenon was first observed in 1928 by **Fred Griffith**, an English physician whose special interest was the bacterium that causes pneumonia, *Streptococcus pneumonia.* Griffith had succeeded in isolating several different strains of *S. pneumonia* (type I, II, III, and so forth).



Strain of Colony
Cell Type
Effect
Capsule
Smooth (S)
Live S strain
Dies
(a)
Strain of Colony
Cell Type
Effect
No capsule
Rough (R)
Live R strain
Survives
(b)
Heat-killed S strain
Survives
(c)
Live R strain
+
Heat-killed S strain
Dies
Live S and R strains isolated from dead mouse
(d)

Avery, McCarty & MacLeod

Oswald Avery

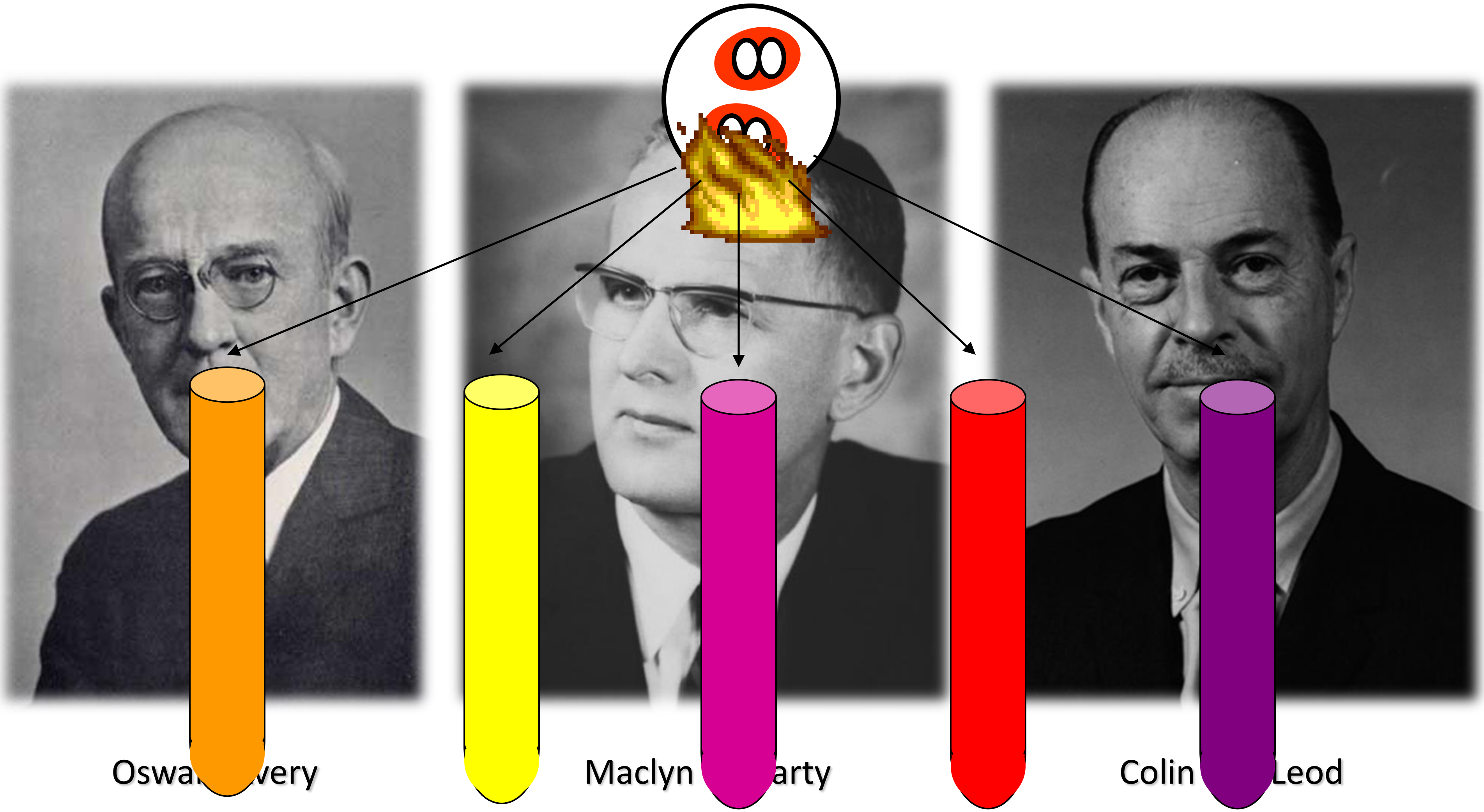
Maclyn McCarty

Colin MacLeod

1944

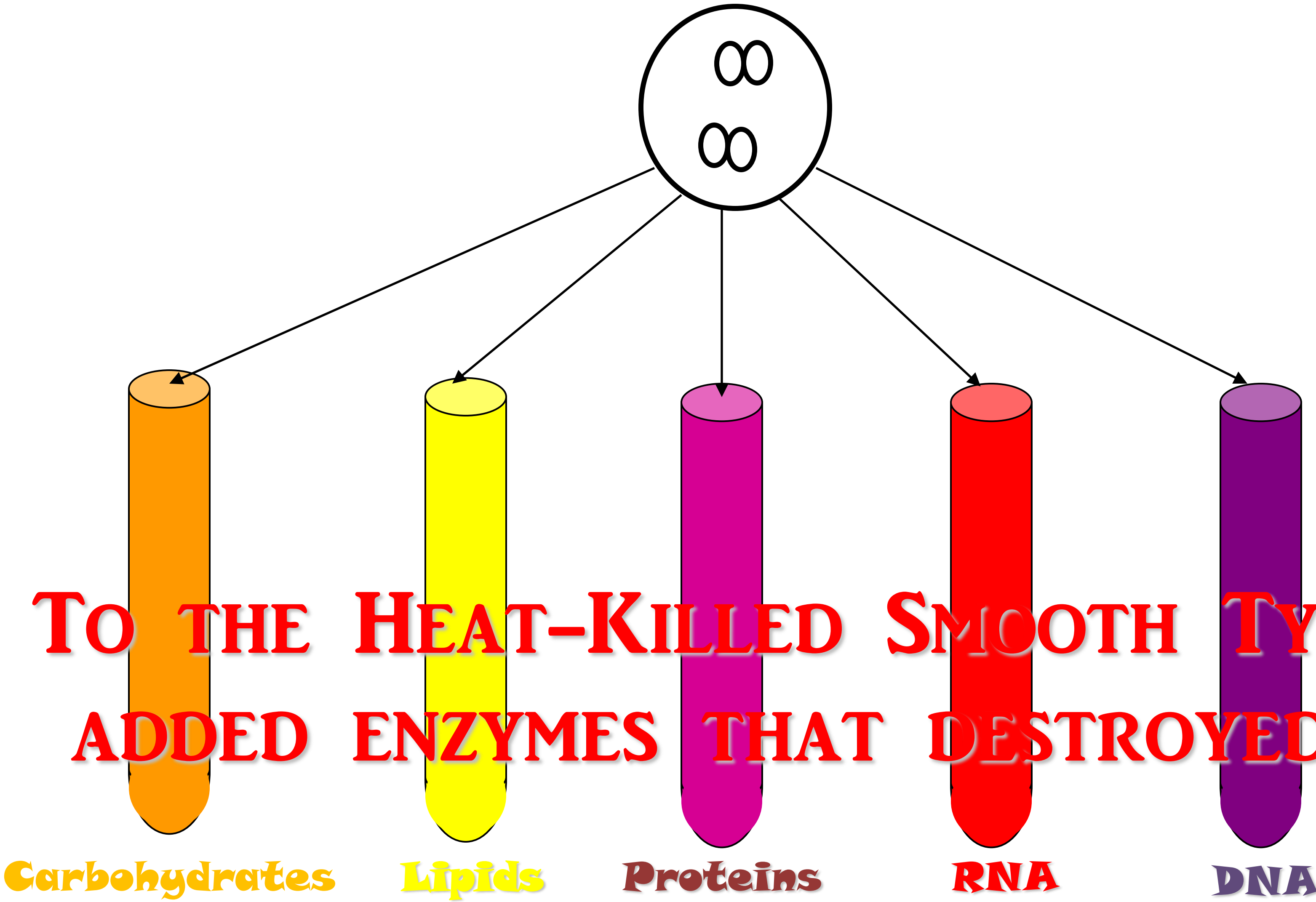
Avery, McCarty & MacLeod

Repeated Griffith's Experiment



Avery, McCarty & MacLeod

Added the non deadly Rough Type of Bacteria to the Heat Killed Smooth Type



To the Heat-Killed Smooth Type, added enzymes that destroyed...

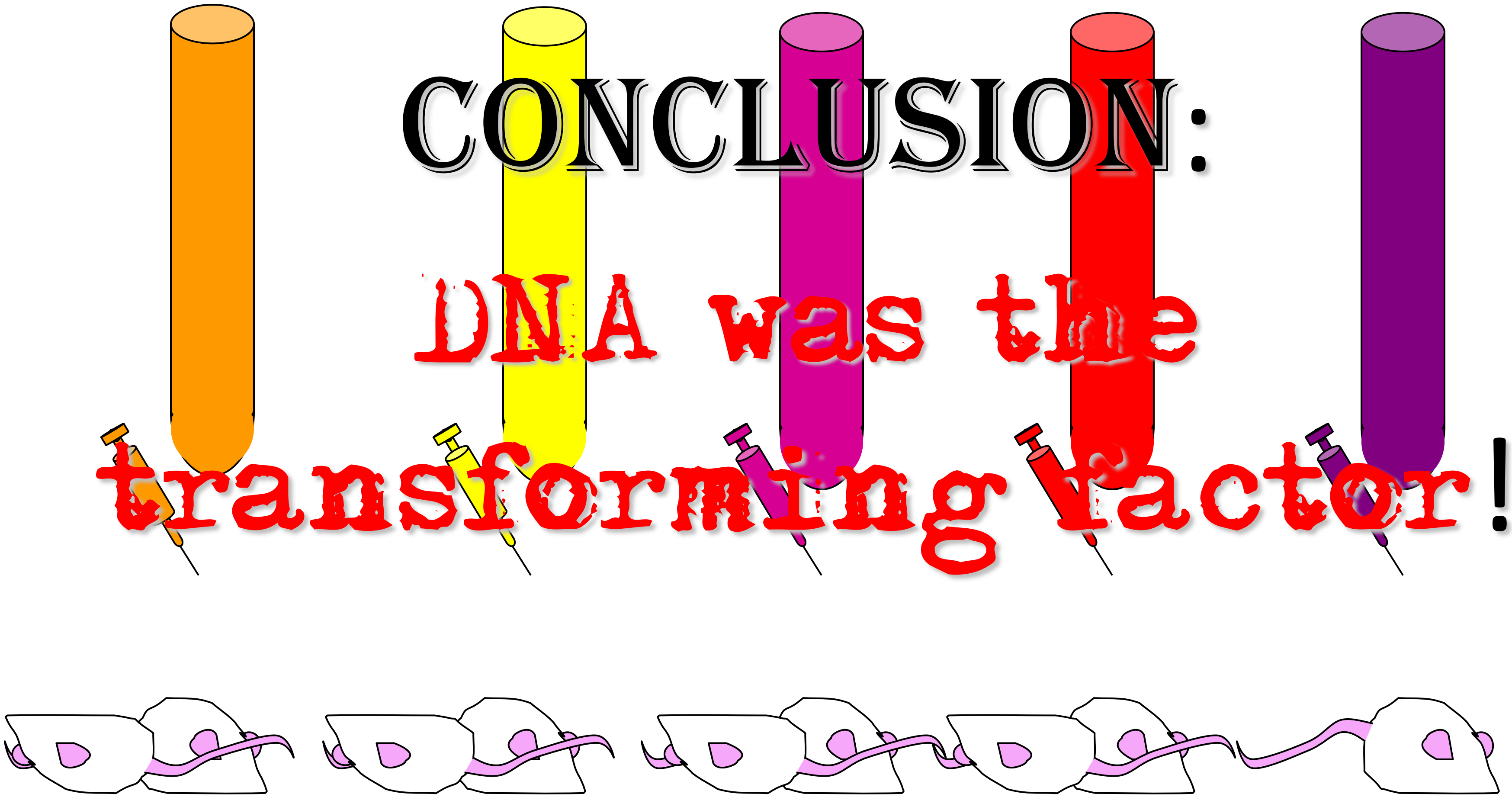
S-Type Carbohydrates Destroyed

S-Type Lipids Destroyed

S-Type Proteins Destroyed

S-Type RNA Destroyed

S-Type DNA Destroyed

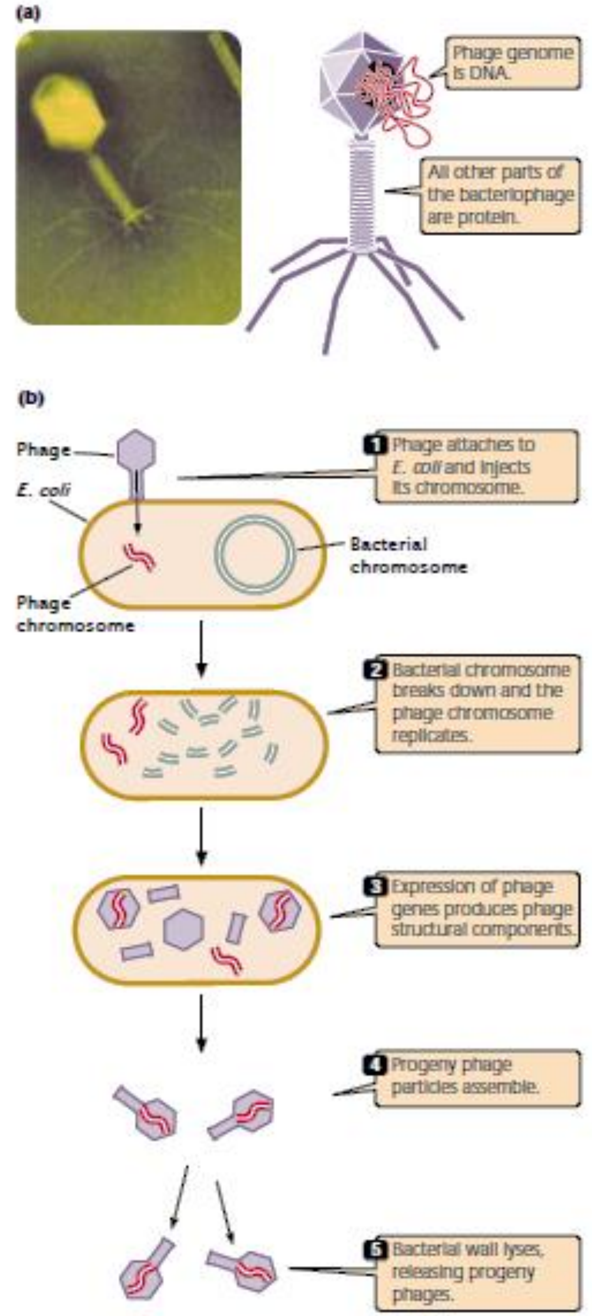


CONCLUSION:

DNA was the transforming factor!

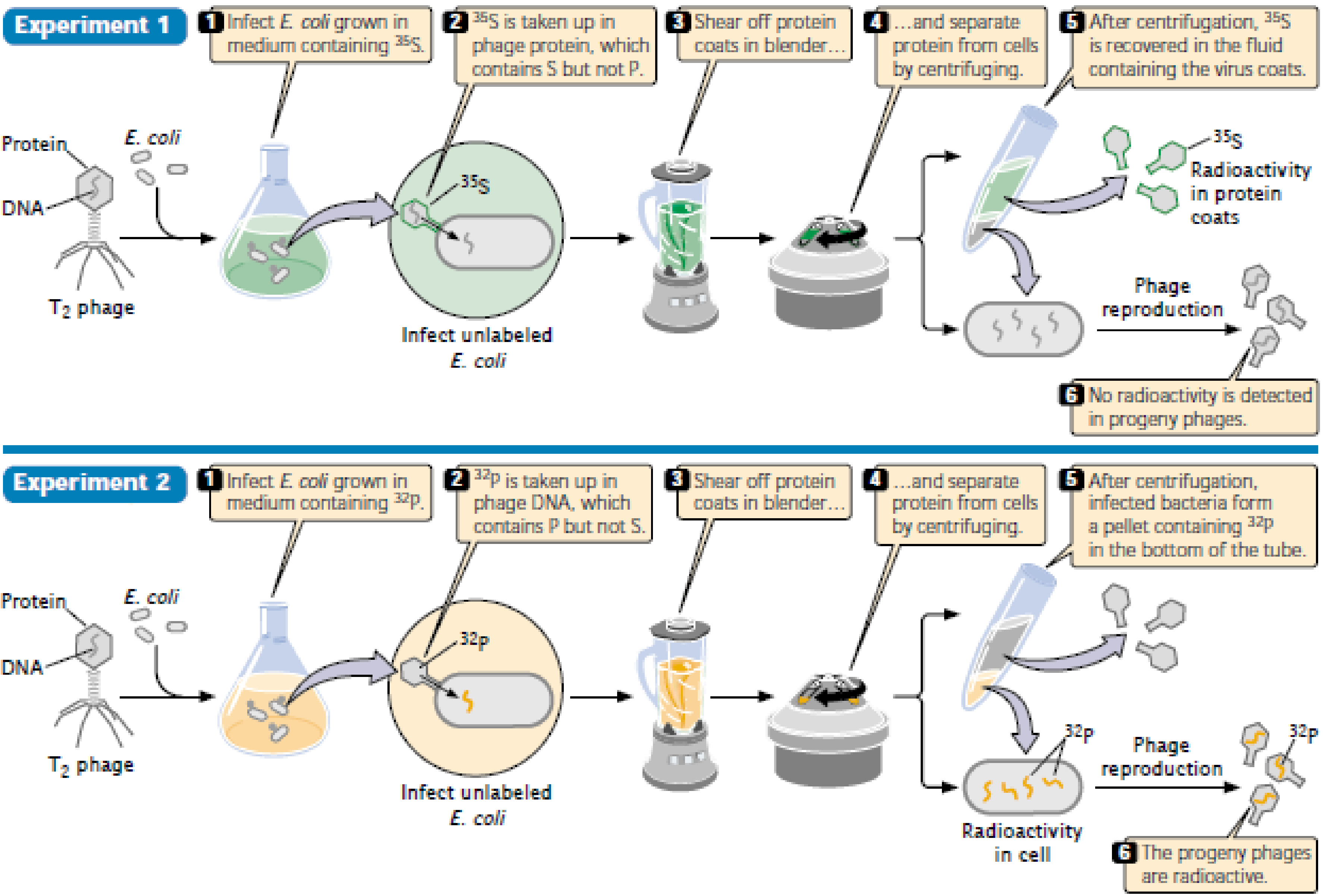
The Hershey-Chase experiment

A second piece of evidence implicating DNA as the genetic material resulted from a study of the T2 virus conducted by Alfred Hershey and Martha Chase. T2 is a *bacteriophage* (phage) that infects the bacterium *Escherichia coli*. A phage reproduces by attaching to the outer wall of a bacterial cell and injecting its DNA into the cell, where it replicates and directs the cell to synthesize phage protein. The phage DNA becomes encapsulated within the proteins, producing progeny phages that lyse (break open) the cell and escape.



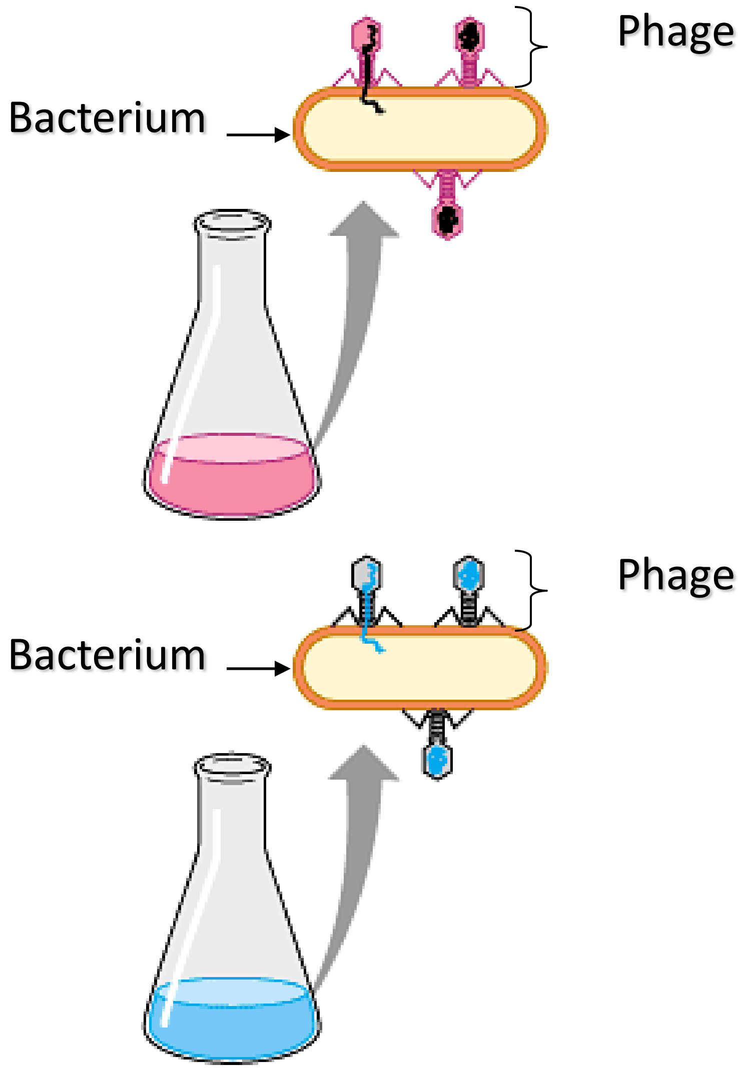
Experiment

Question: Which part of the phage—its DNA or its protein—serves as the genetic material and is transmitted to phage progeny?



Conclusion: DNA—not protein—is the genetic material in bacteriophages.

Protein coats of bacteriophages labeled with Sulfur-35

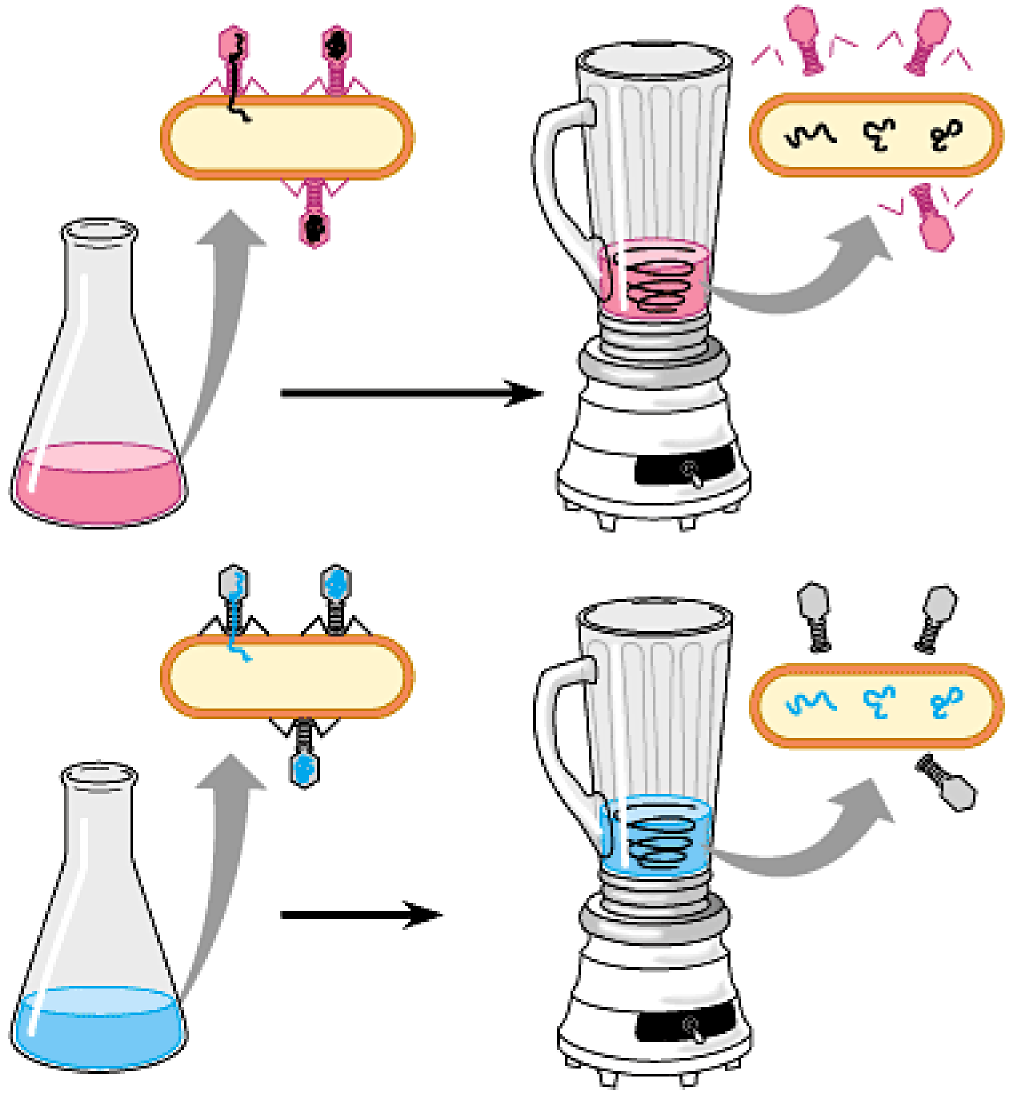


DNA of bacteriophages labeled with Phosphorus-32

1. Hershey and Chase mixed the radioactively-labeled viruses with the bacteria

The viruses infect the bacterial cells.

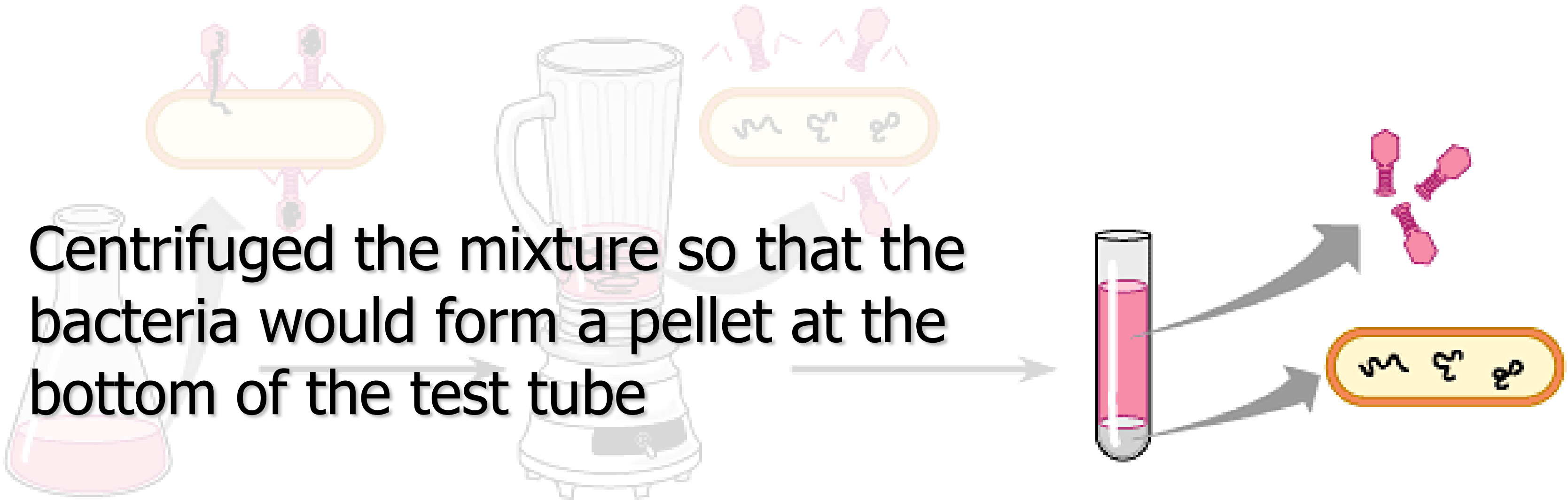
Protein coats of bacteriophages labeled with Sulfur-35



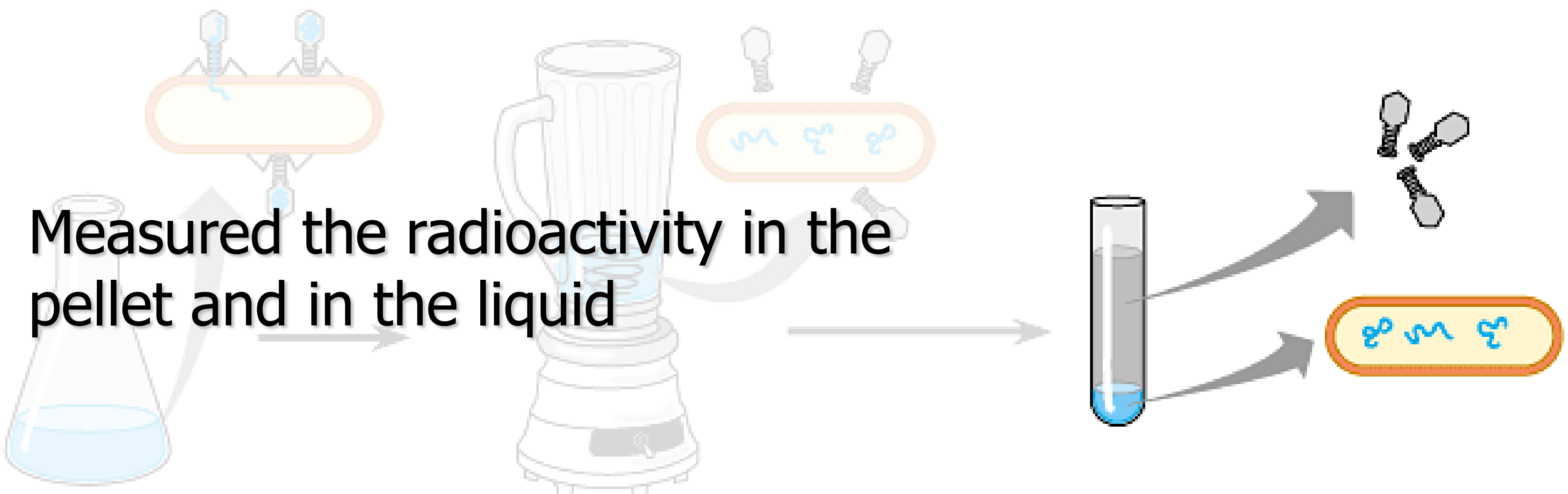
2. Separated the viruses from the bacteria by agitating the virus-bacteria mixture in a blender

DNA of bacteriophages labeled with Phosphorus-32

Protein coats of bacteriophages labeled with Sulfur-35



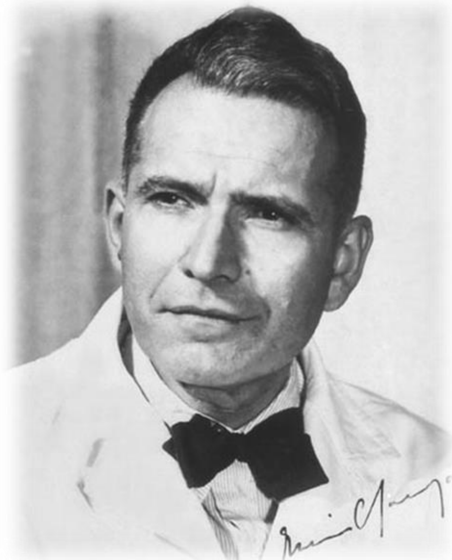
3. Centrifuged the mixture so that the bacteria would form a pellet at the bottom of the test tube



4. Measured the radioactivity in the pellet and in the liquid

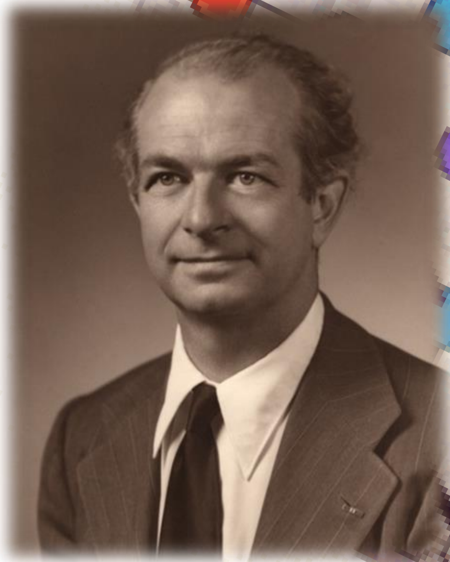
DNA of bacteriophages labeled with Phosphorus-32

The Race to Discover DNA's Structure



The Race to Discover DNA's Structure

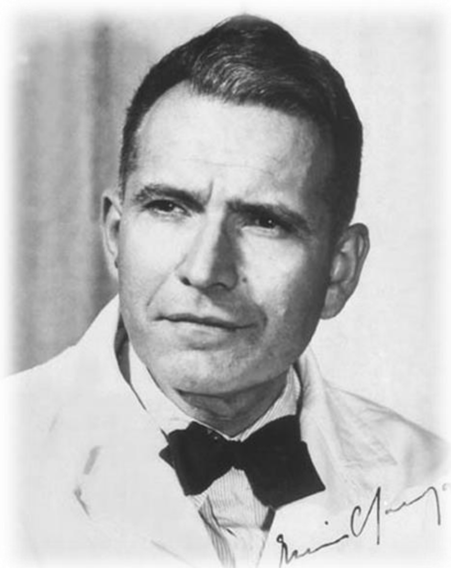


Linus Pauling

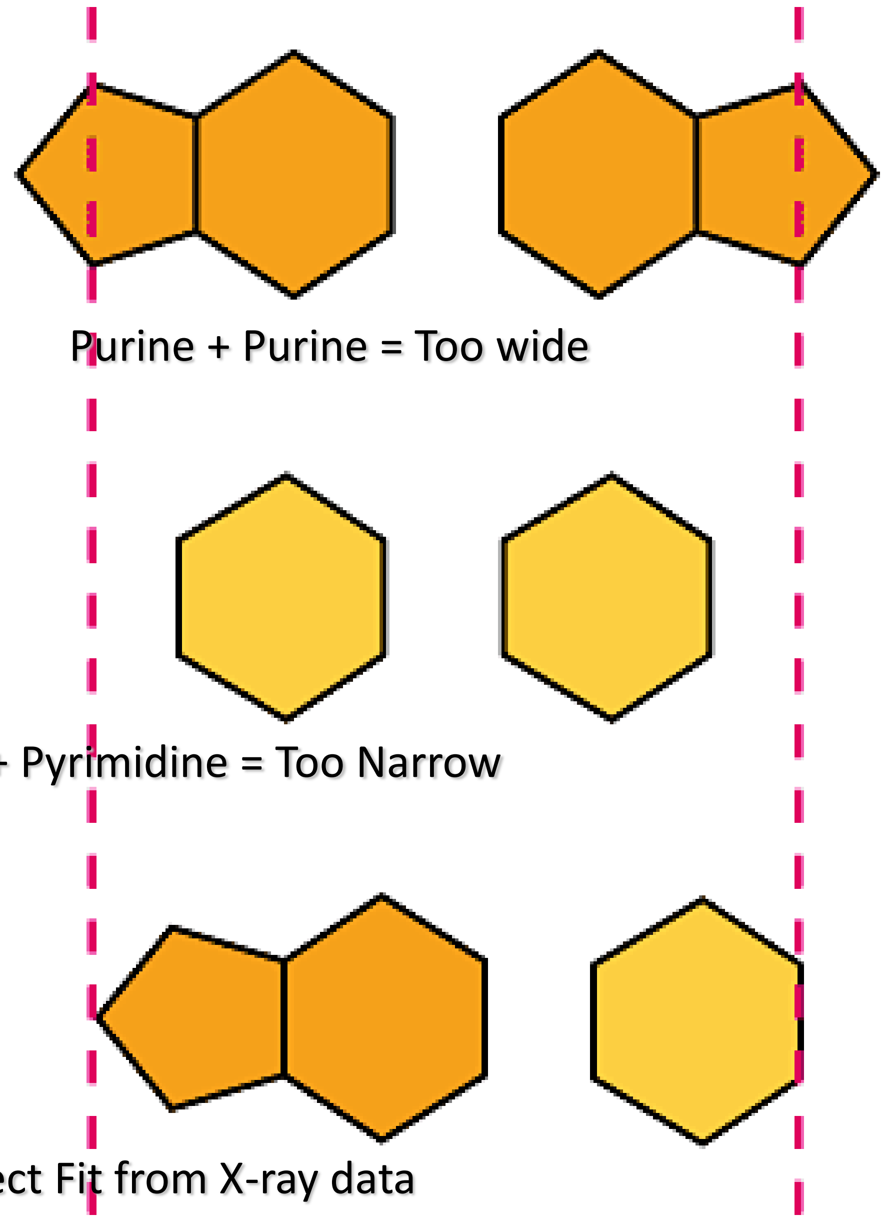
1940s

Discovered the alpha-helical structure of proteins.

The Race to Discover DNA's Structure



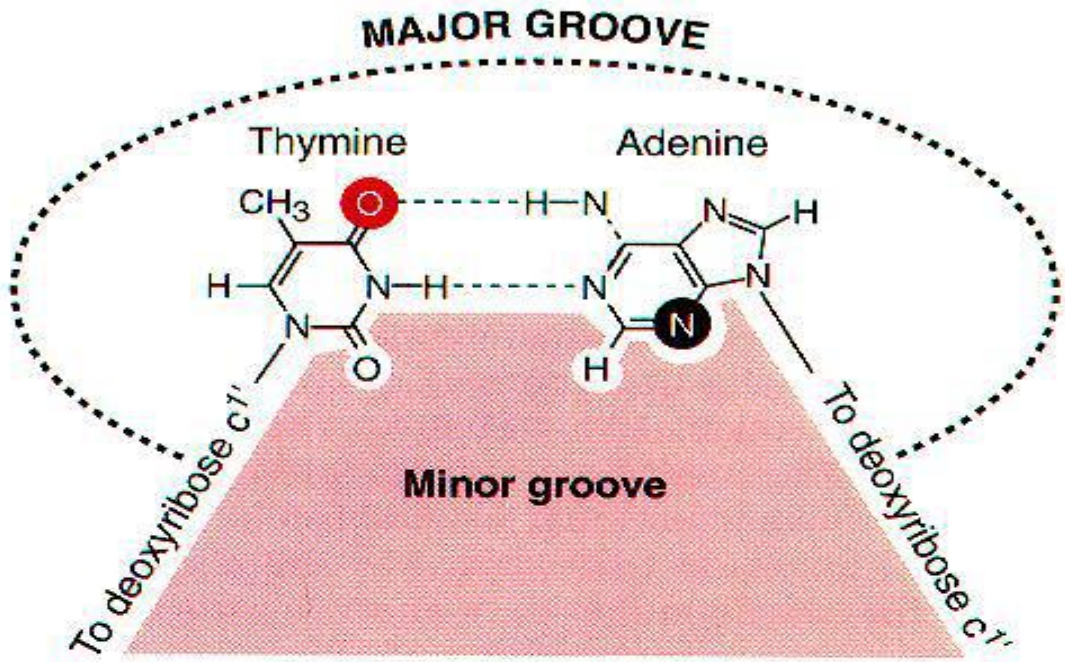
Erwin Chargaff

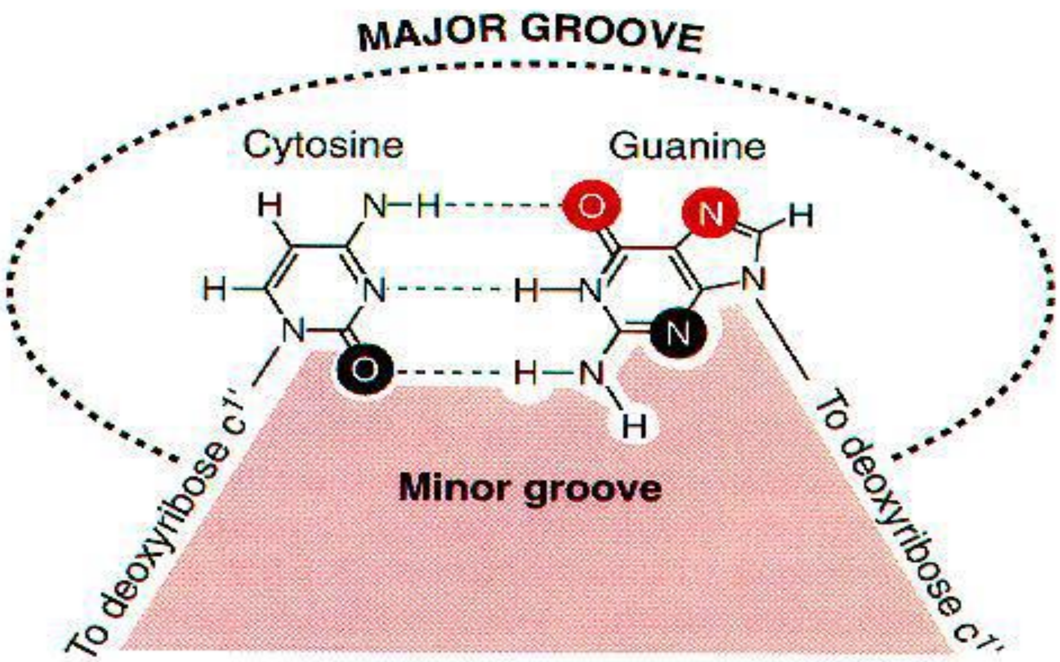


Purine + Purine = Too wide

Pyrimidine + Pyrimidine = Too Narrow

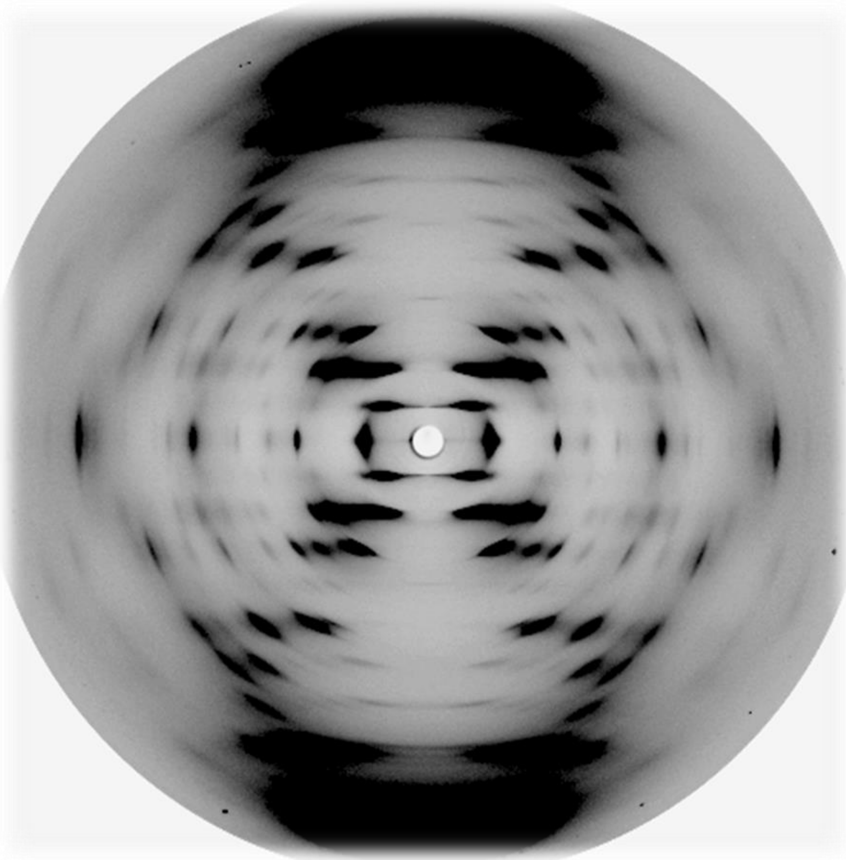
Purine + Pyrimidine = Perfect Fit from X-ray data


MAJOR GROOVE
Thymine
Adenine
Minor groove
To deoxyribose c1'
To deoxyribose c1'


MAJOR GROOVE
Cytosine
Guanine
Minor groove
To deoxyribose c1'
To deoxyribose c1'

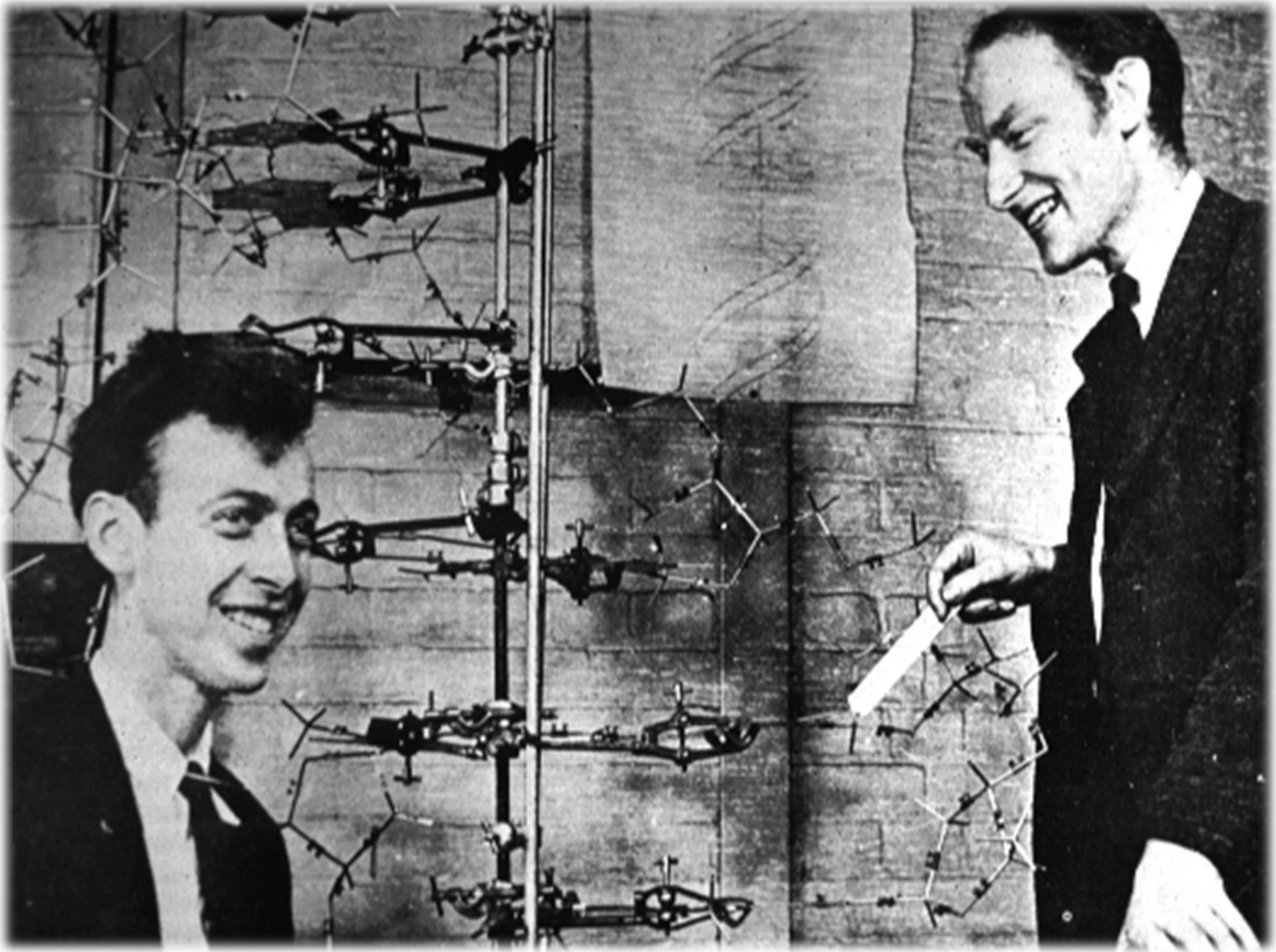
The Race to Discover DNA's Structure

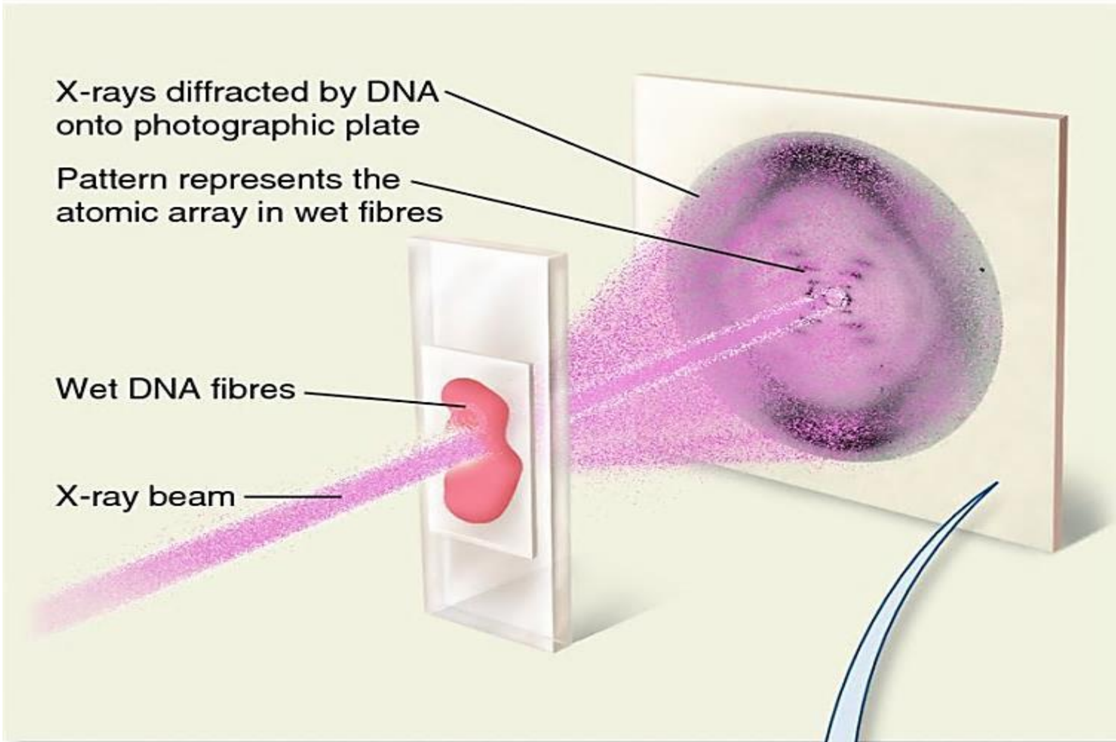
Maurice Wilkins



X-Ray diffraction image of DNA taken by Franklin in 1951

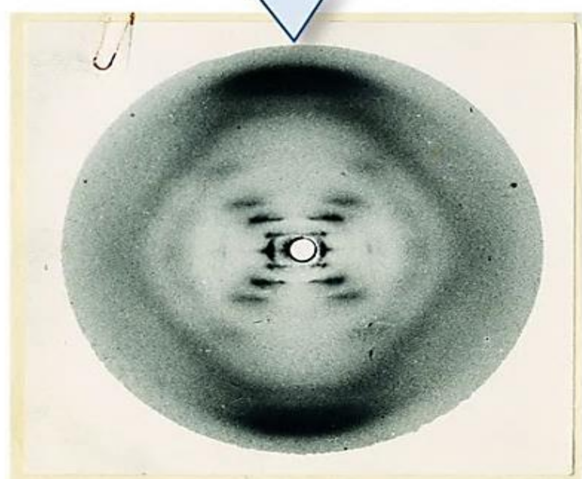
Rosalind Franklin





(a) The method of X-ray diffraction

(b) Rosalind Franklin



(c) Franklin's X-ray diffraction pattern of wet DNA fibres

The Structure of DNA

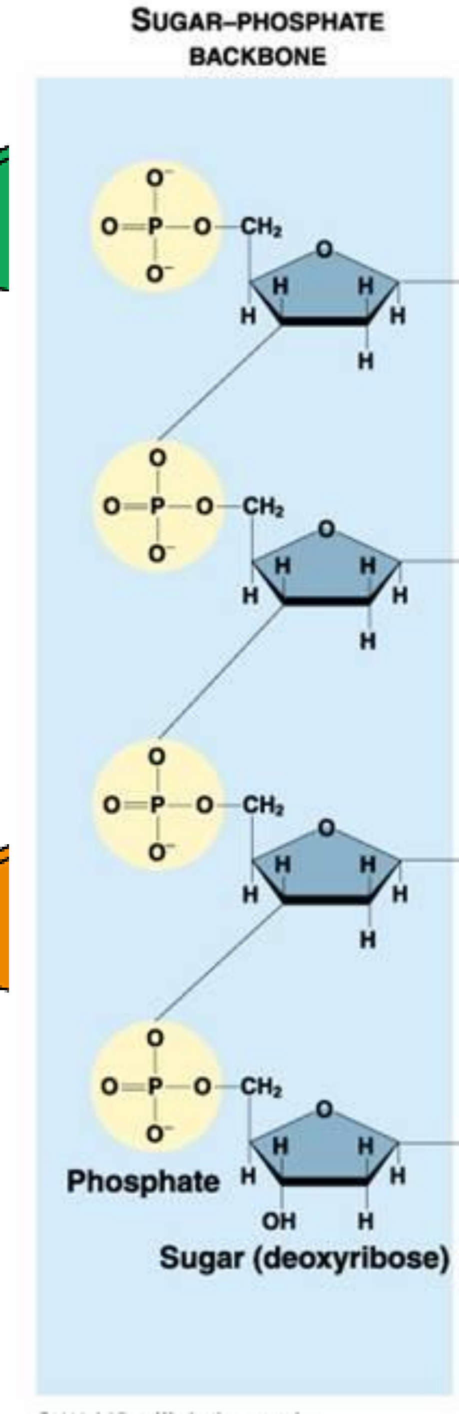
DNA, though relatively simple in structure, has an elegance and beauty unsurpassed by other large molecules. It is useful to consider the structure of DNA at three levels of increasing complexity, known as the primary, secondary, and tertiary structures of DNA. The primary structure of DNA refers to its nucleotide structure and how the nucleotides are joined together. The secondary structure refers to DNA's stable three-dimensional configuration, the helical structure worked out by Watson and Crick.

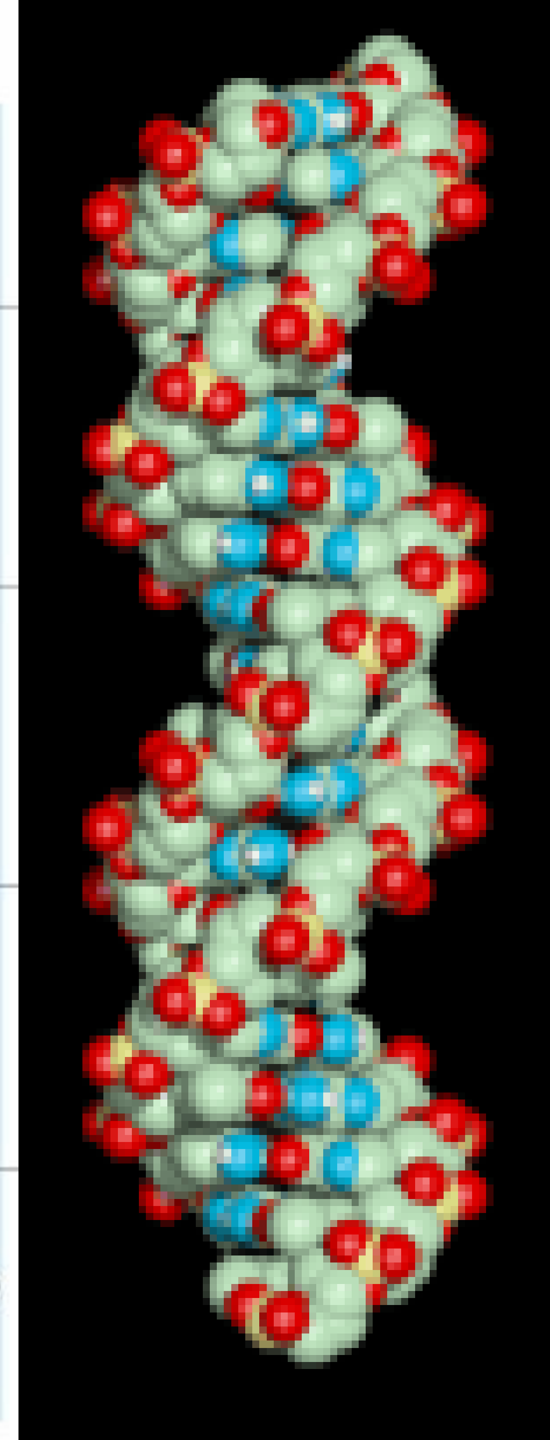
The Primary Structure of DNA

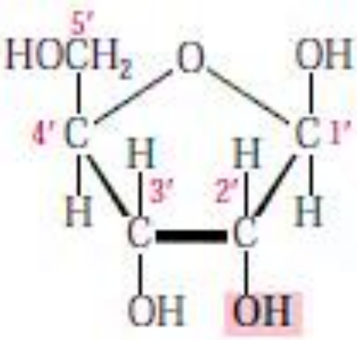
The primary structure of DNA consists of a string of nucleotides joined together by phosphodiester linkages. Nucleotides DNA is typically a very long molecule and is therefore termed a macromolecule. For example, within each human chromosome is a single DNA molecule that, if stretched out straight, would be several centimeters in length. In spite of its large size, DNA has a relatively simple structure: it is a polymer, a chain made up of many repeating units linked together. As already mentioned, the repeating units of DNA are nucleotides, each comprising three parts: (1) a sugar, (2) a phosphate, and (3) a nitrogen-containing base.

The Race to

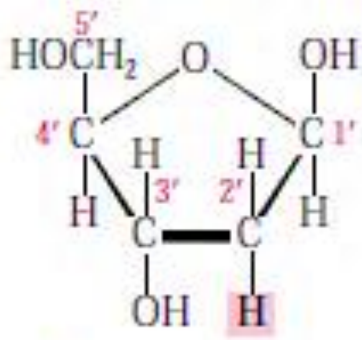
- DNA is made
  - Four nucleoti
    and Cytosine
  - These follow
    - Adenine bor
    - Guanine bor
  - A sugar-phos
- DNA is arranc



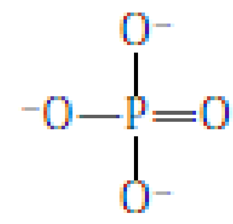




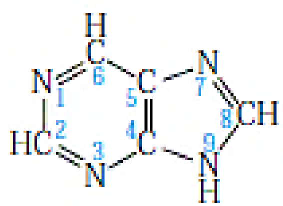
Ribose



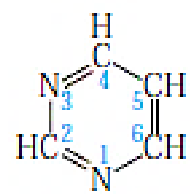
Deoxyribose



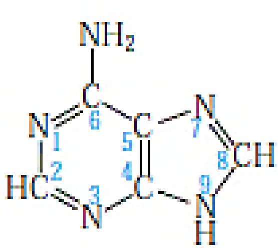
Phosphate



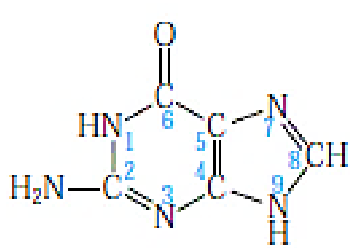
Purine
(basic structure)



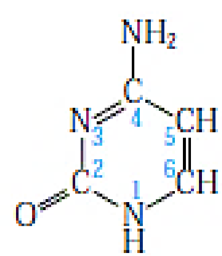
Pyrimidine
(basic structure)



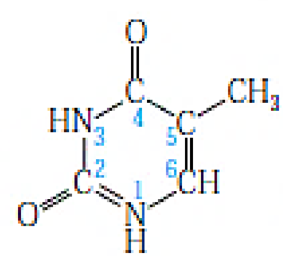
Adenine (A)



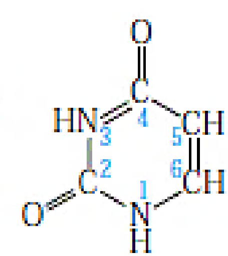
Guanine (G)



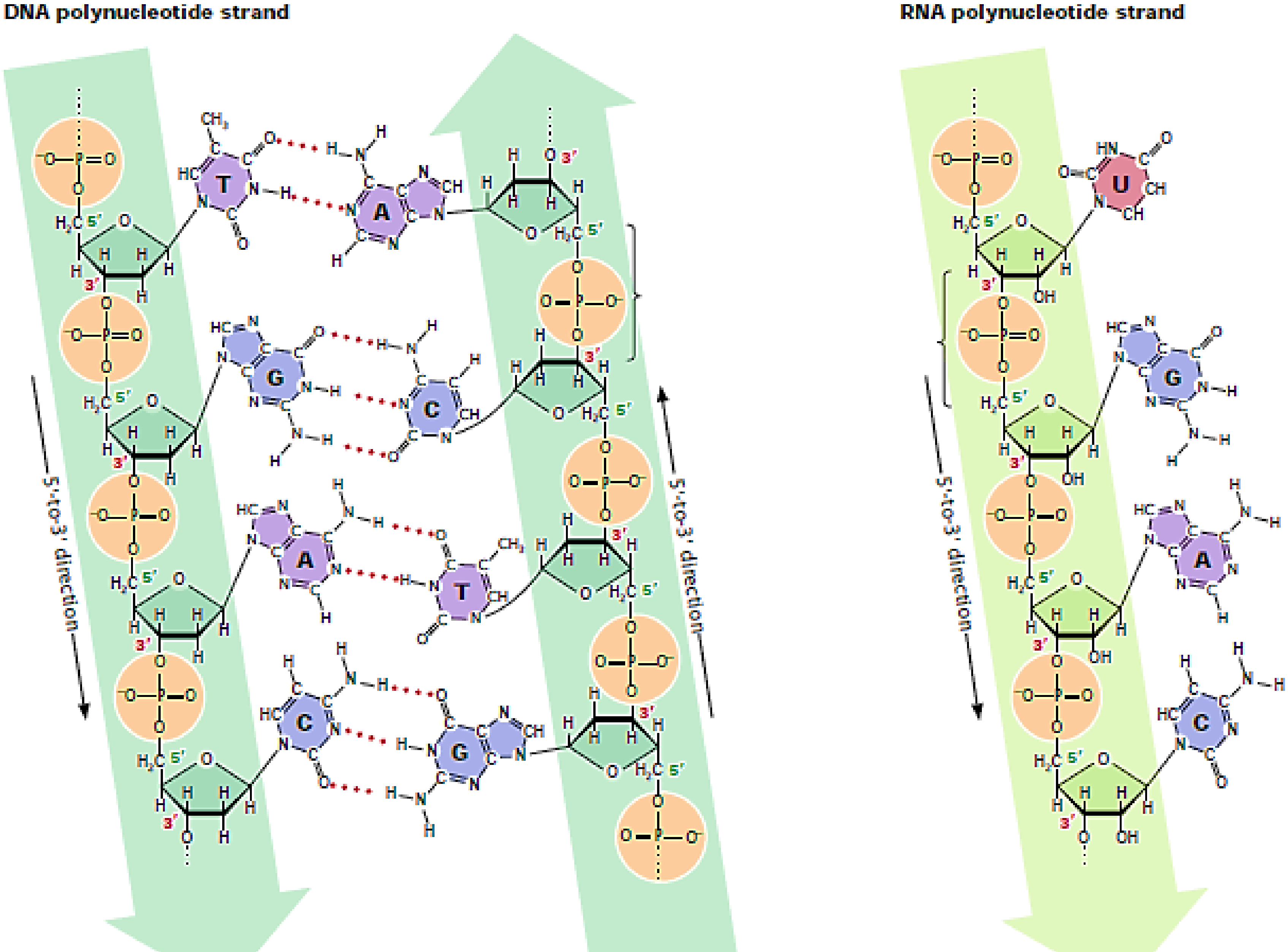
Cytosine (C)



Thymine (T)
(present in DNA)



Uracil (U)
(present in RNA)


DNA polynucleotide strand
RNA polynucleotide strand
5'-to-3' direction
5'-to-3' direction
5'-to-3' direction

Any Question??