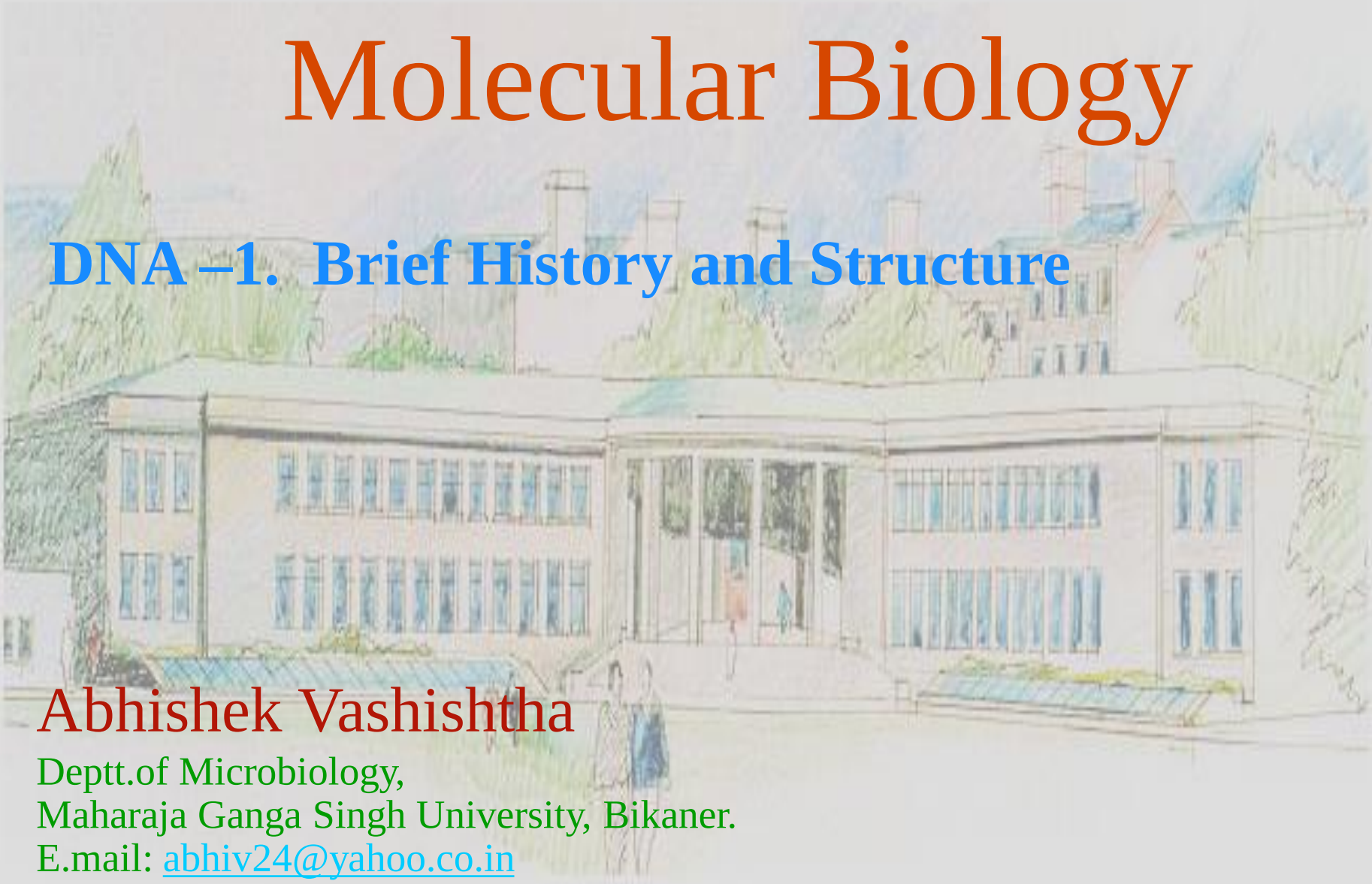
Molecular Biology

DNA –1. Brief History and Structure



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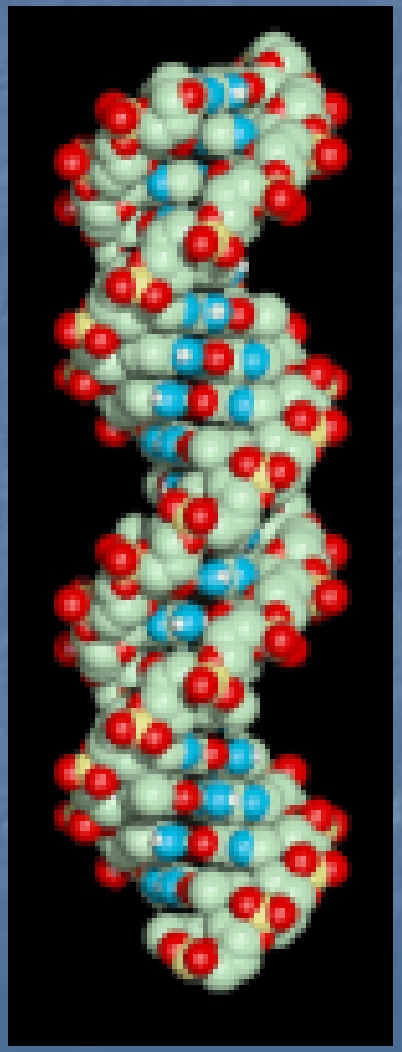
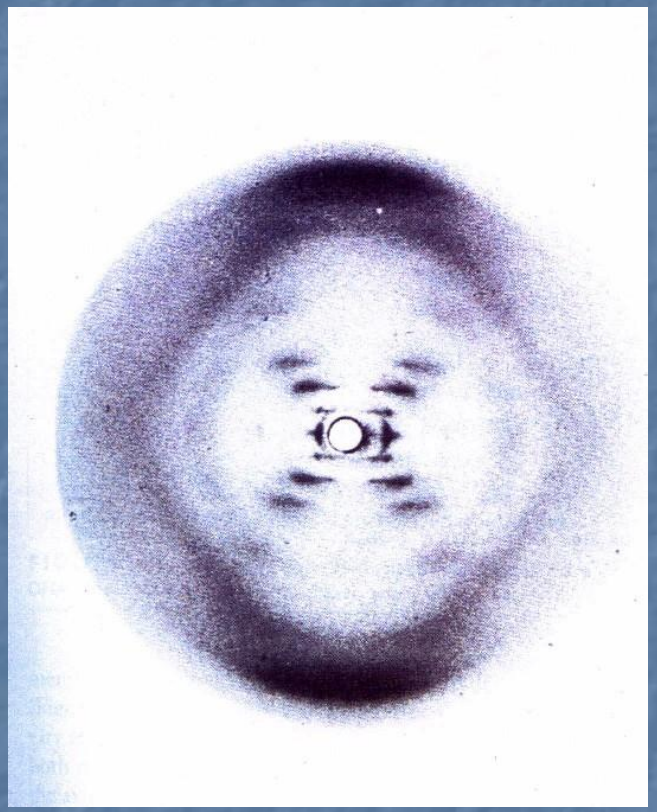
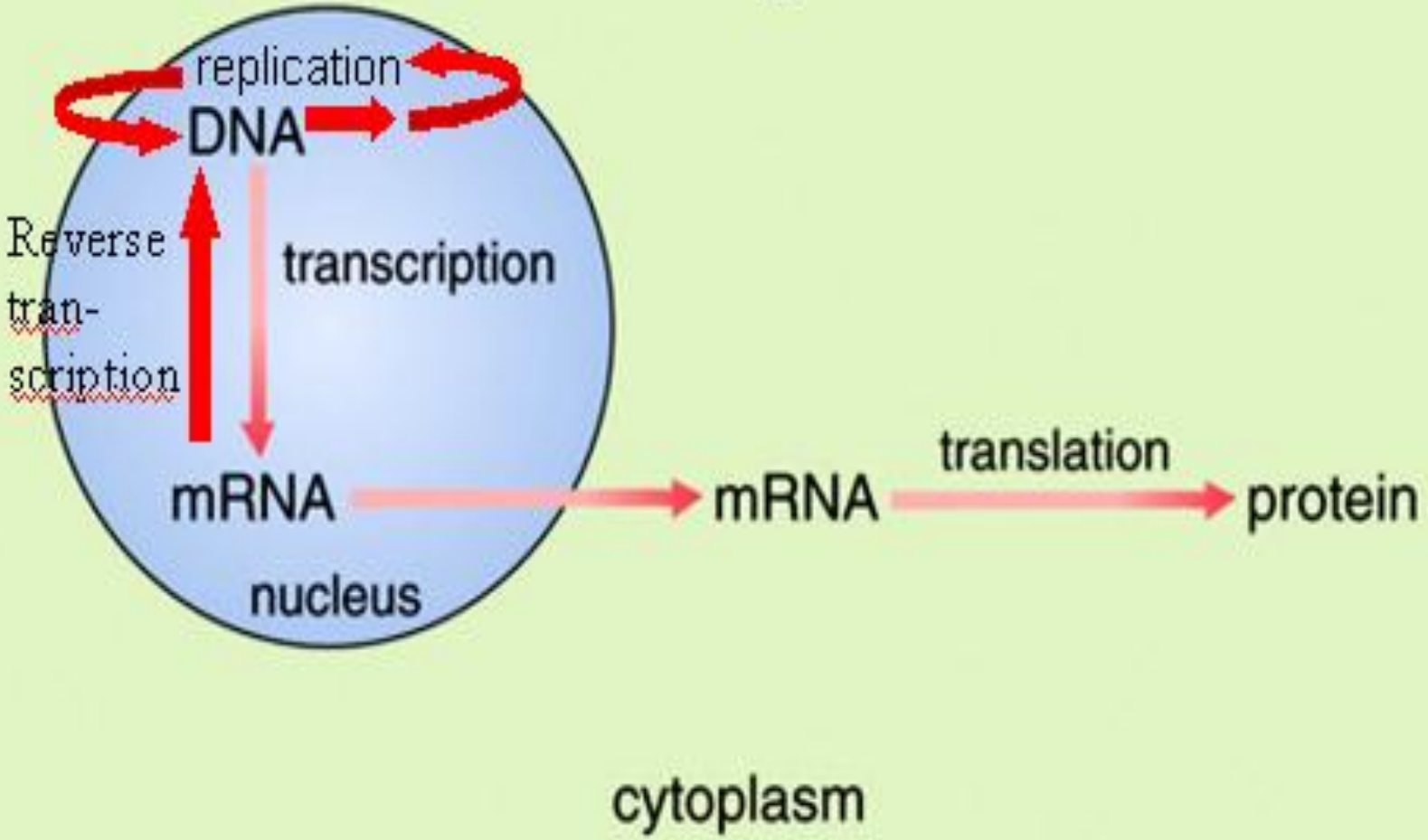
60 Years of DNA





http://web.math.fsu.edu

The Central Dogma of Life.



Chromosome

- threadlike structures in the nucleus that carry genetic information

Gene

- fundamental unit of heredity
- inherited determinant of a phenotype

Locus

- position occupied by a gene on a chromosome

Gene

- sequence of DNA that instructs a cell to produce a particular protein

DNA

- deoxyribonucleic acid,
- the genetic material
- the biochemical that forms genes

Role of the genetic material

"A genetic material must carry out two jobs: duplicate itself and control the development of the rest of the cell in a specific way."

-Francis Crick

A short history of DNA

Friedrich Miescher, 1871

- isolated nuclei from pus
- identified nuclein, later called nucleic acid.

Archibald Garrod, 1902

- linked inheritance of "inborn errors of metabolism" with the lack of particular enzyme proteins

Discovery of a "transforming principle"

Frederick Griffith, 1928

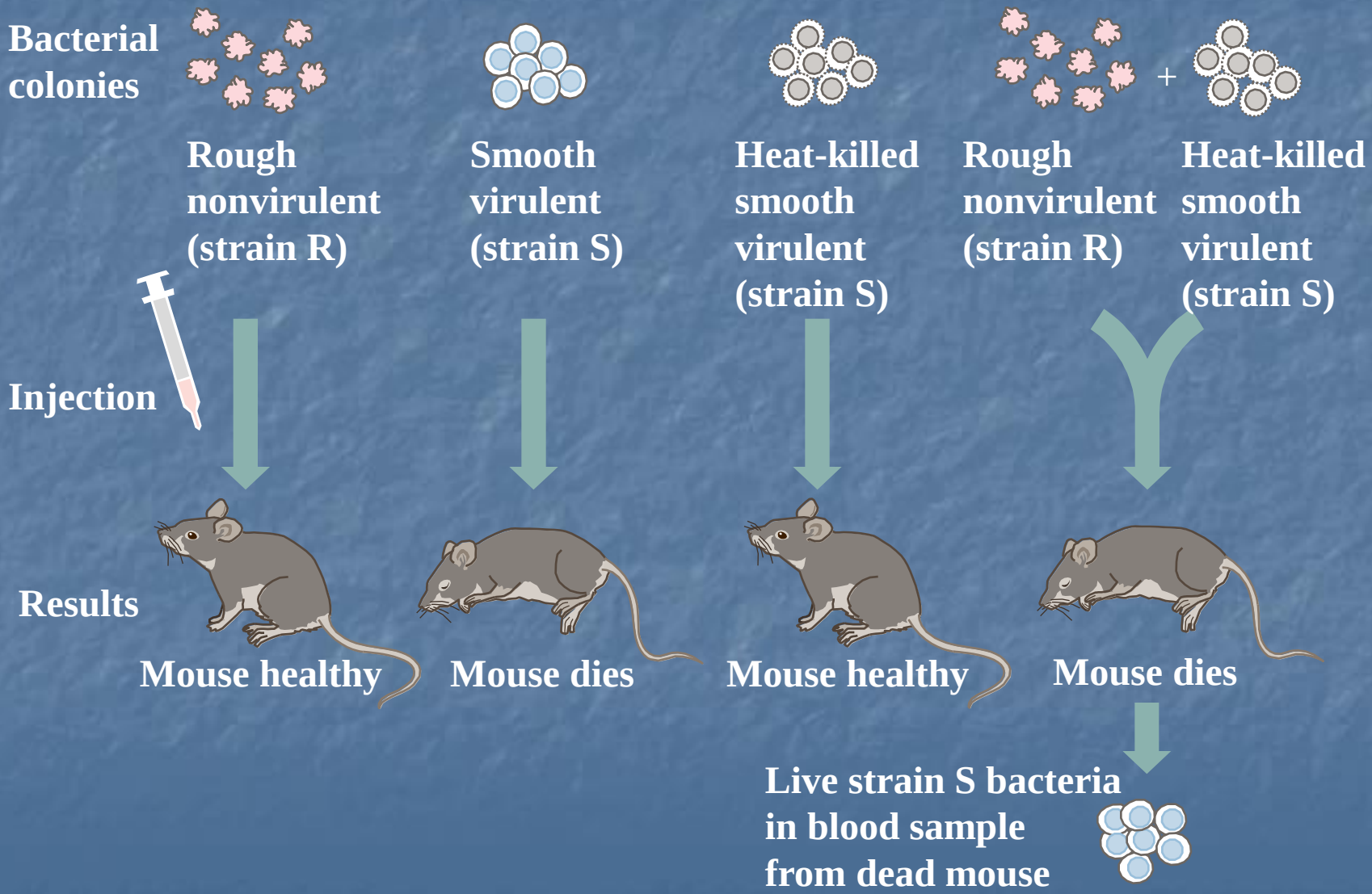
- Pneumonia (*Diplococcus pneumoniae*) infects mice.
- Mice develop pneumonia and die.

Two types of bacteria:

- R bacteria rough coat - no pneumonia
- S bacteria smooth coat- pneumonia

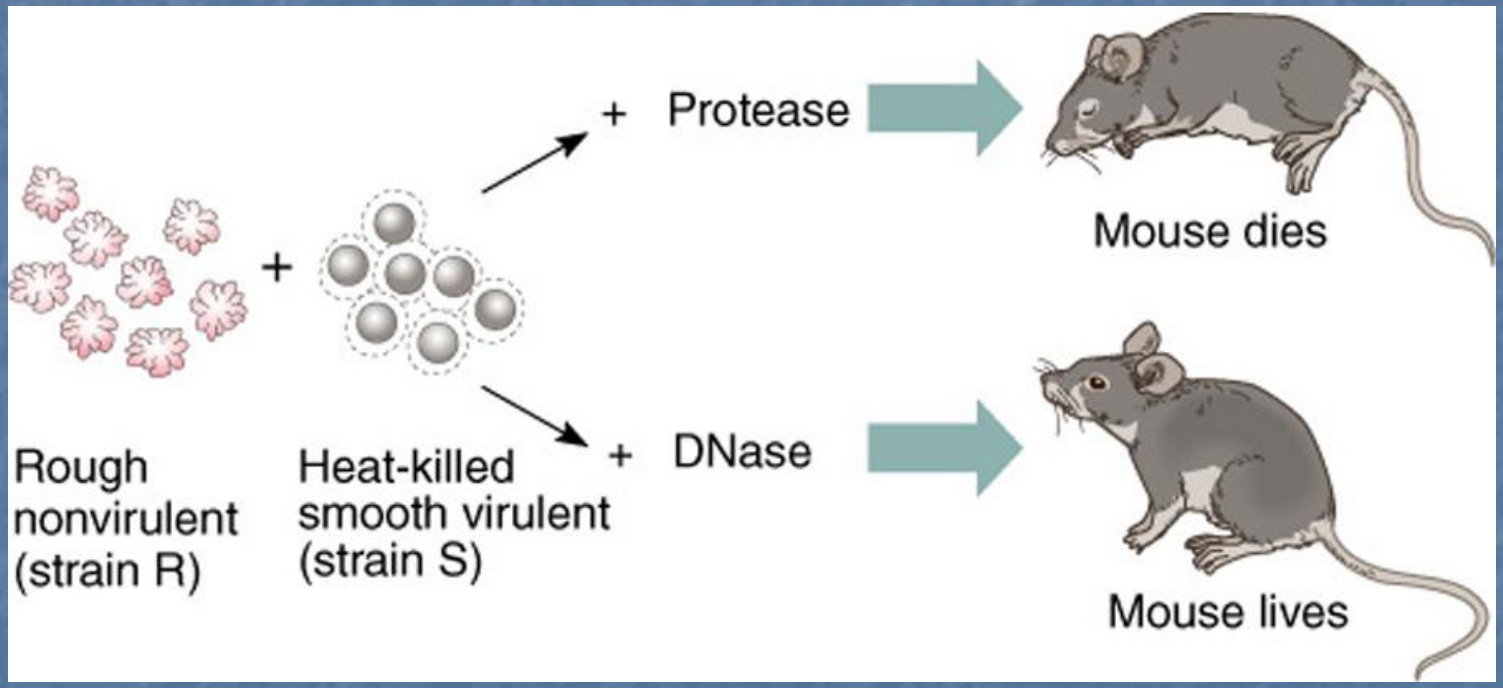
Coat type is associated with virulence.

Griffith's experiment identifying the "transforming principle"



What is the “transforming principle”?

Oswald Avery, Colin MacLeod and Maclyn McCarty, 1944
- Heat-killed S bacteria “transformed” the R bacteria to a form that causes pneumonia



- Conclusion: DNA is the transforming principle allowing R bacteria to make a smooth coat and allow infection.

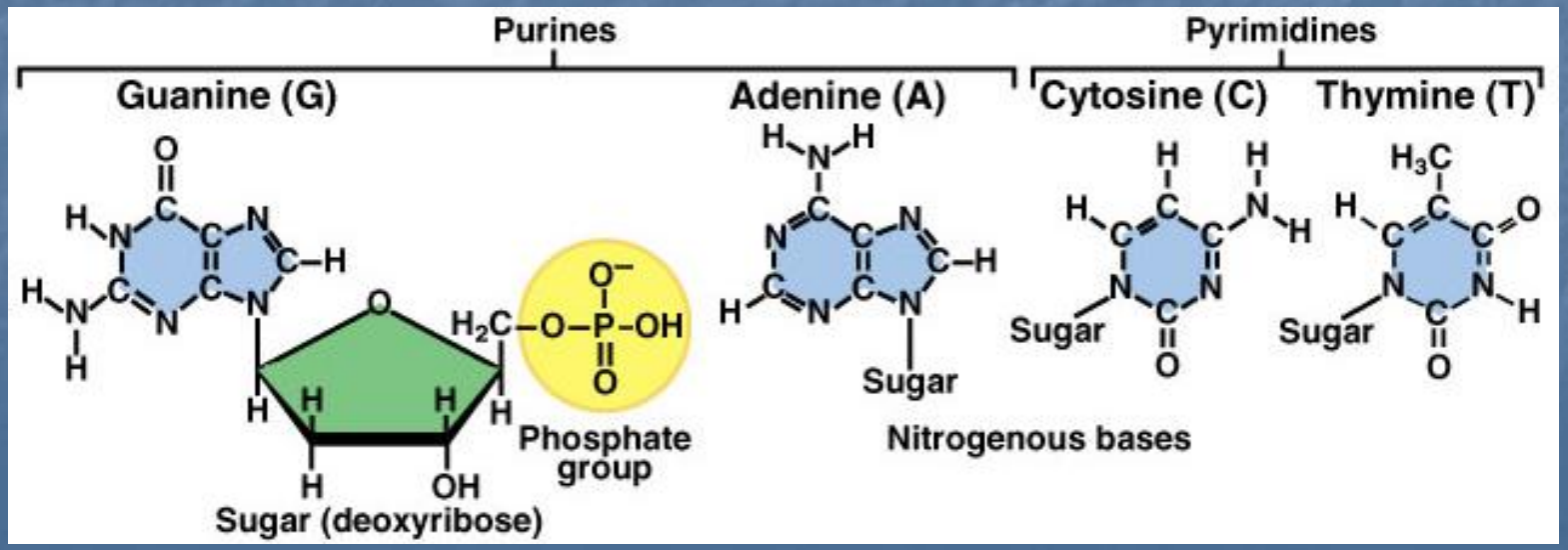
DNA (deoxyribonucleic acid) is a chain of nucleotides

Nucleotides are composed of:

Sugar - deoxyribose

Phosphate

Base - one of four types: adenine (A), thymine (T)
guanine (G), cytosine (C)



DNA bases pair via hydrogen bonds

Erwin Chargaff observed:

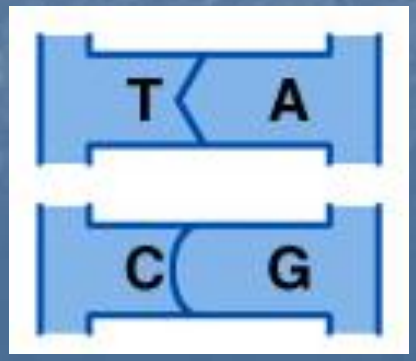
# of adenine = # of thymine

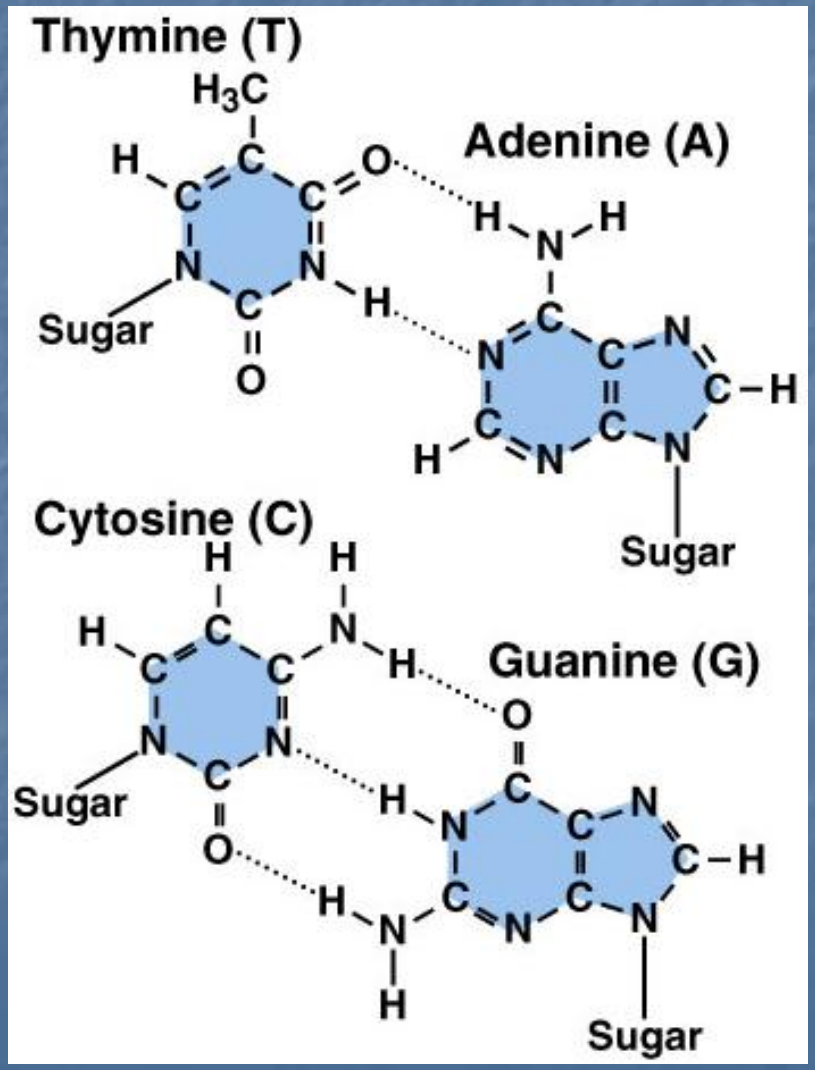
# of guanine = # of cytosine

Complementary bases pair:

A and T pair

C and G pair

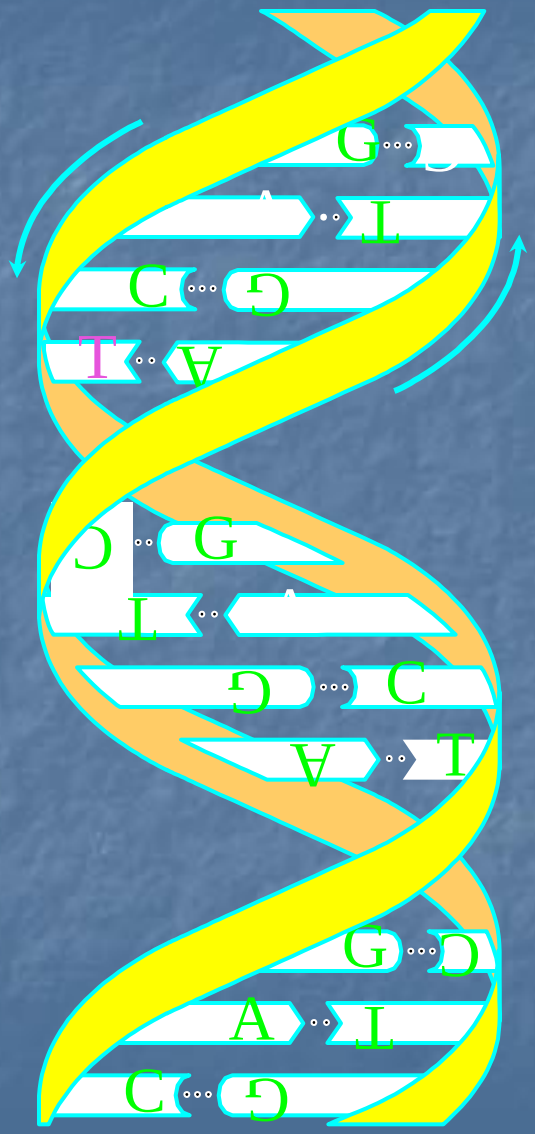




DNA exists as a double helix

- X-ray diffraction indicated DNA has a repeating structure.
  - Maurice Wilkins and Rosalind Franklin

- DNA is double-stranded molecules wound in a double helix.
- -James Watson and Francis Crick



DNA is a double helix

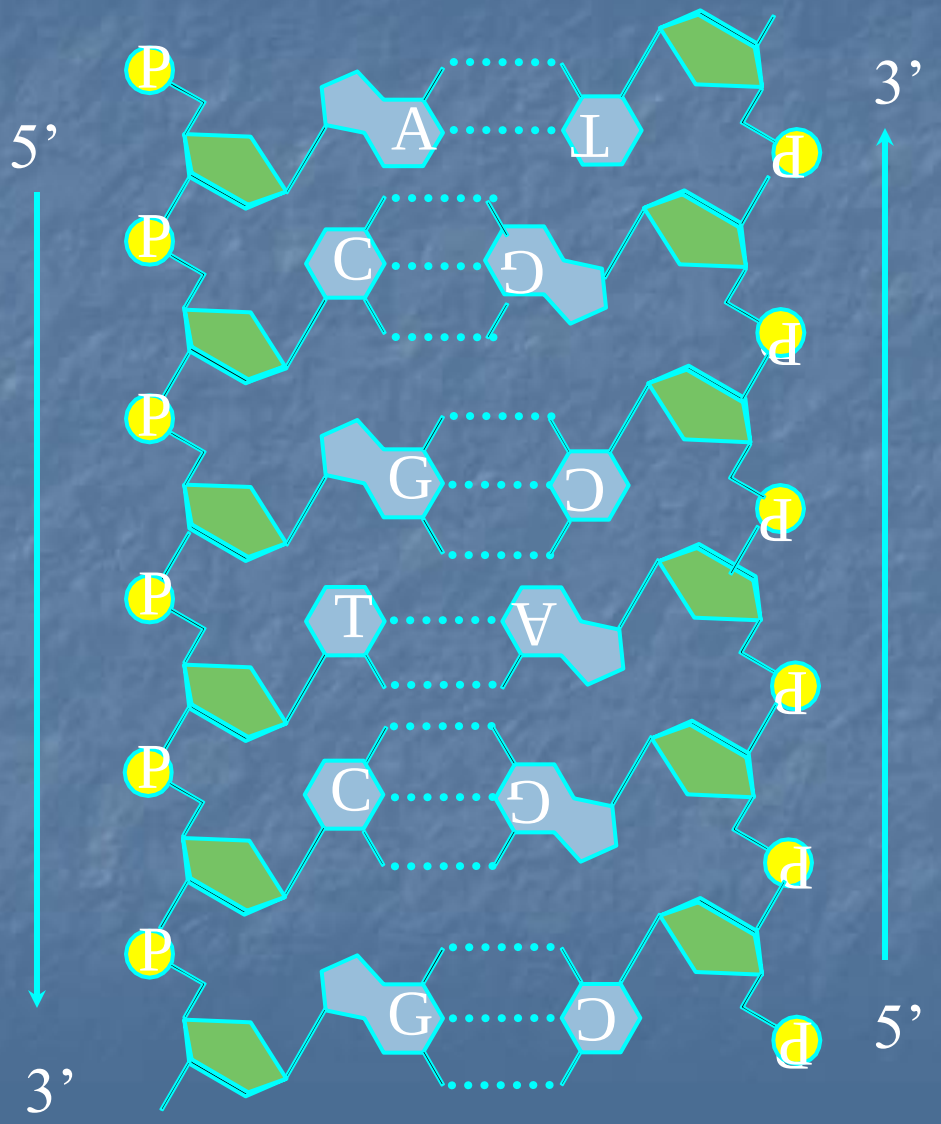
A sugar and phosphate "backbone" connects nucleotides in a chain.

DNA has directionality.

Two nucleotide chains together wind into a helix.

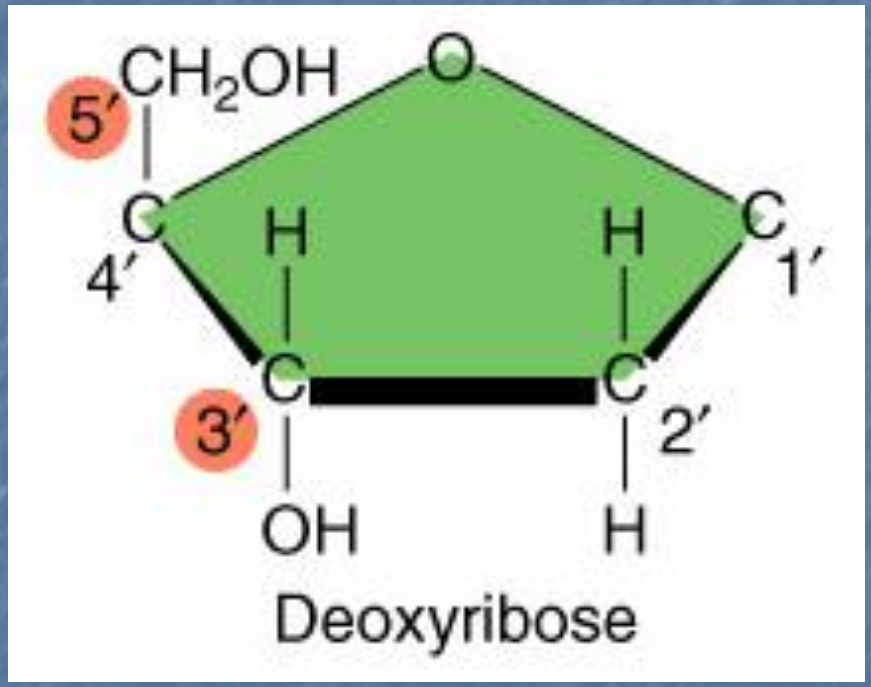
Hydrogen bonds between paired bases hold the two DNA strands together.

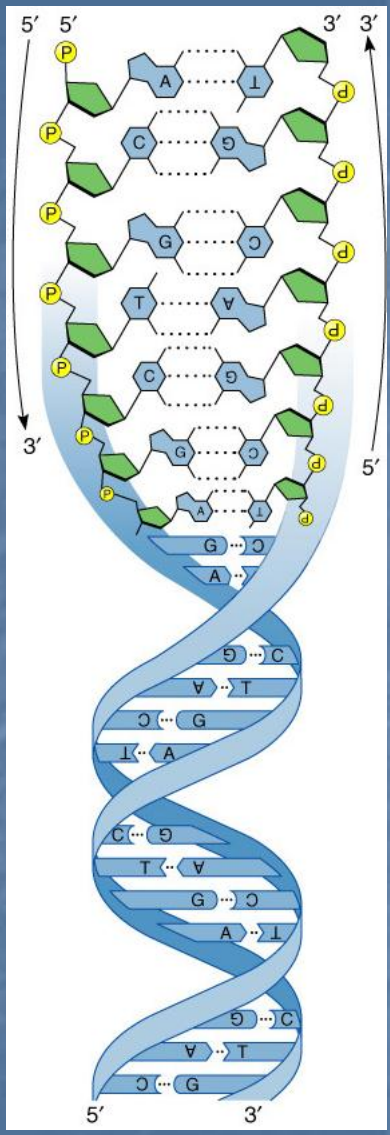
DNA strands are antiparallel.



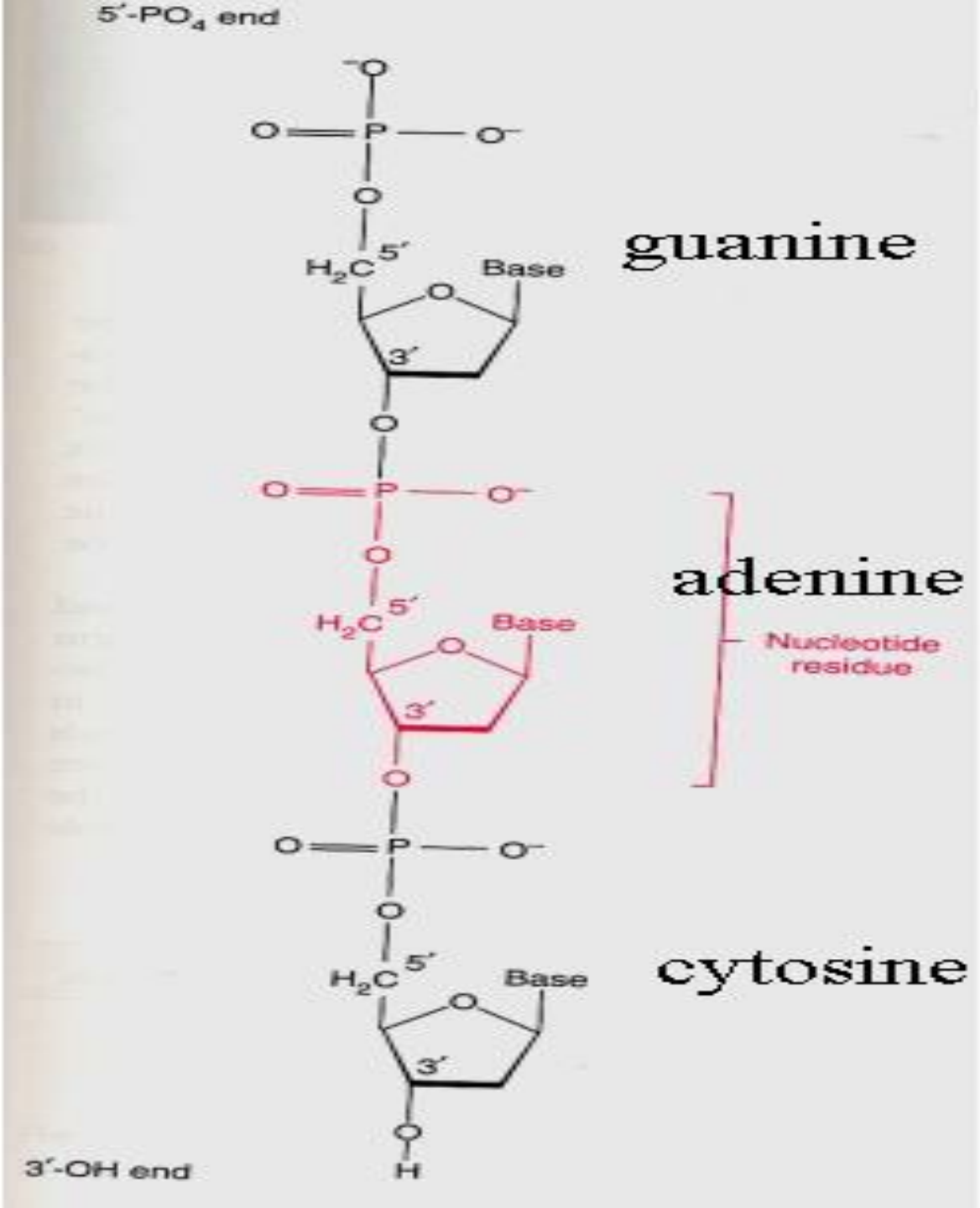
Orientation of DNA

The carbon atoms on the sugar ring are numbered for reference. The 5’ and 3’ hydroxyl groups (highlighted on the left) are used to attach phosphate groups.



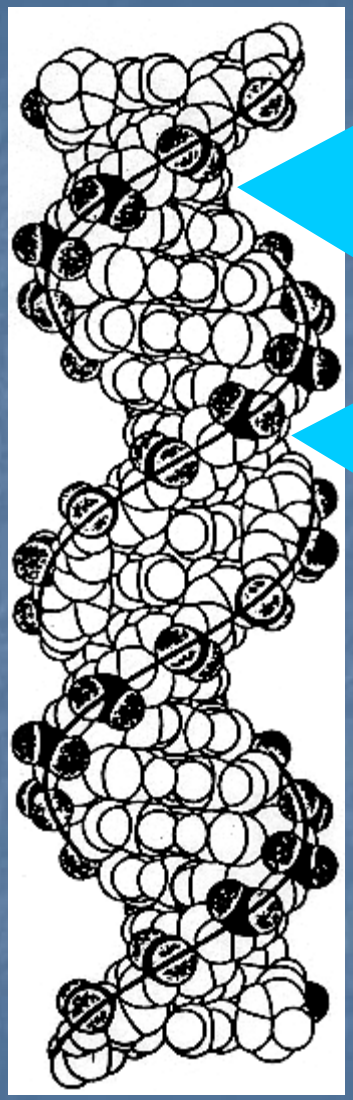


- The directionality of a DNA strand is due to the orientation of the phosphate-sugar backbone.


5′-PO4 end
guanine
Base
5′
3′
adenine
Nucleotide residue
cytosine
3′-OH end

5’- GAC- 3’

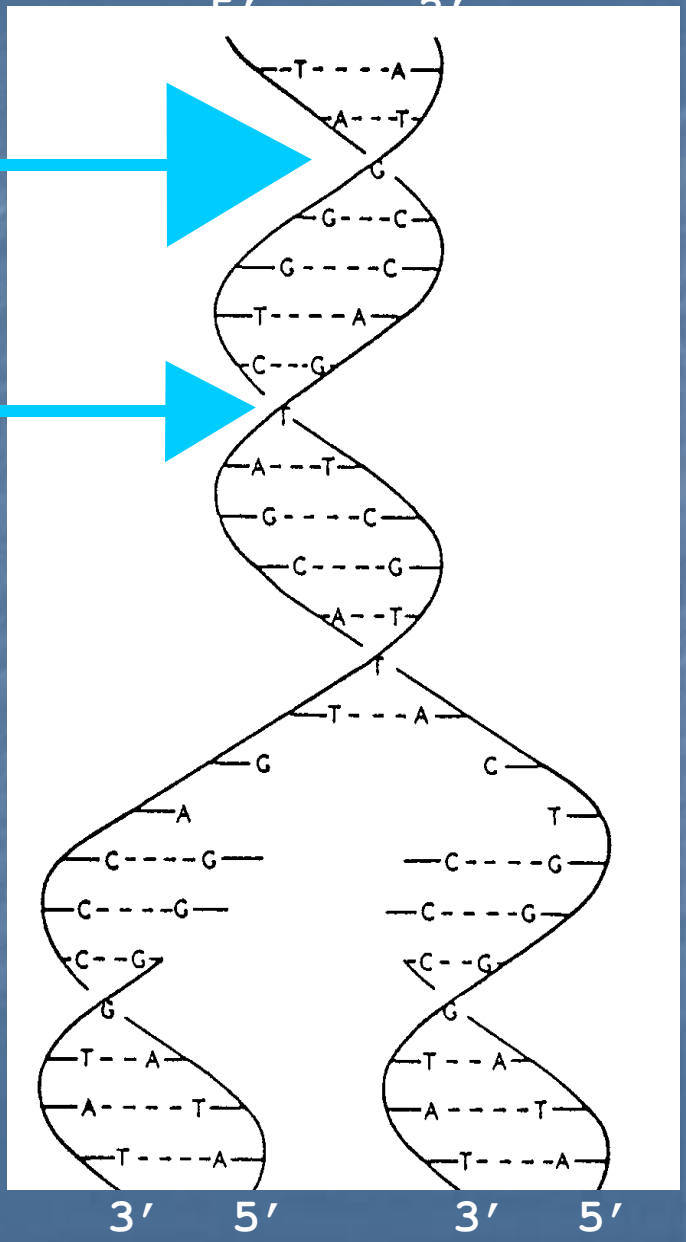
Double-stranded DNA



"B" DNA

Major groove

Minor groove



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Chemistry of DNA

Forces affecting the stability of the DNA double helix

- hydrophobic interactions - stabilize
  - hydrophobic inside and hydrophilic outside
- stacking interactions - stabilize
  - relatively weak but additive van der Waals forces
- hydrogen bonding - stabilize
  - relatively weak but additive and facilitates stacking
- electrostatic interactions - destabilize
  - contributed primarily by the (negative) phosphates
  - affect intrastrand and interstrand interactions
  - repulsion can be neutralized with positive charges
    (e.g., positively charged Na^+ ions or proteins)