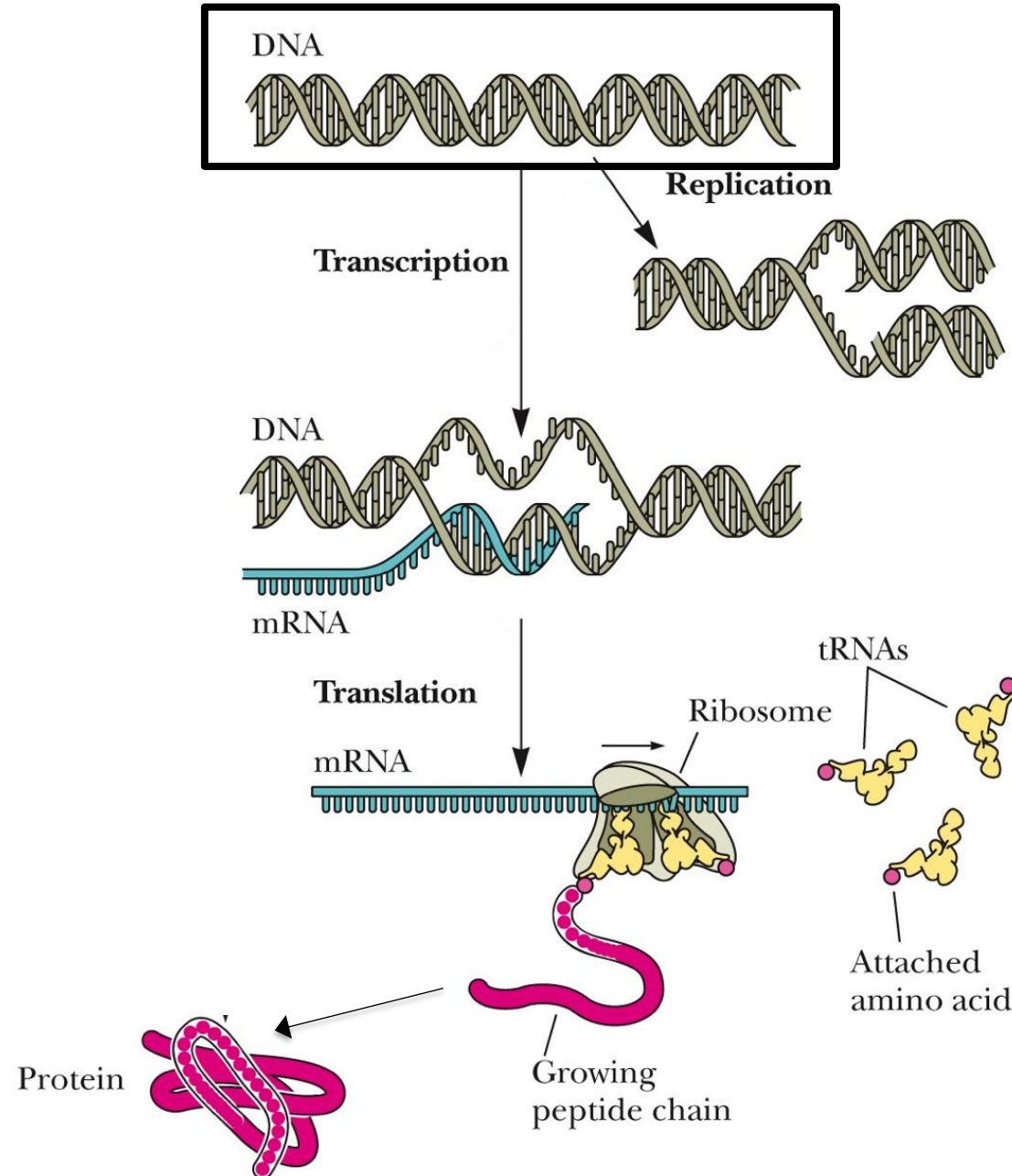


DNA and RNA Structure

The central dogma of molecular biology



Learning Objectives

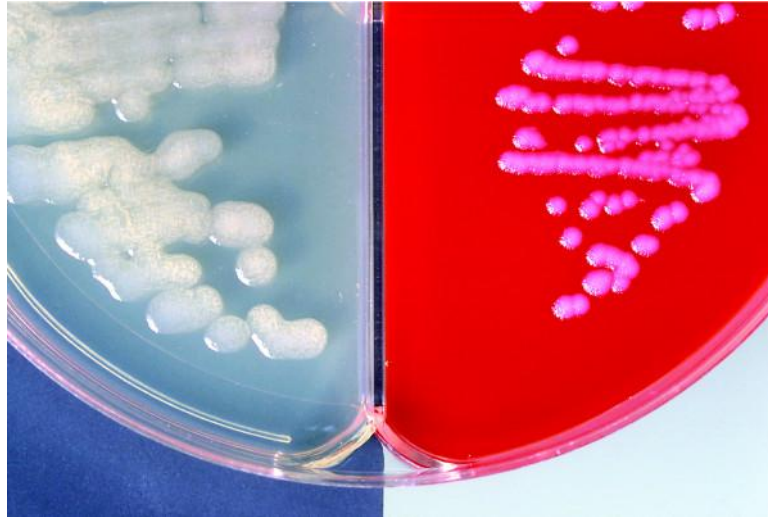
1. Understand the methodology and conclusions made from landmark experiments that helped us to understand the function and structure of DNA.
2. Be familiar with Chargaff's rules and be able to compare and contrast the three models of DNA structure.
3. Be able to draw base pair interactions and a nucleic acid structure from a given sequence.
4. Know the stabilizing forces of the DNA double helix.
5. Understand the effects of temperature, GC content, ionic strength, and hydrogen bonds on the stability of DNA and its melting temperature.
6. Know the structural differences between RNA and DNA and how these differences affect their stability.

Nucleic acids have a wide variety of functions

| Nucleic Acid | Abbreviation | Function |
|-----------------------|--------------|--|
| Deoxyribonucleic Acid | DNA | Stores heritable information to make all functional material in the cell |
| Ribonucleic Acid | RNA | Many! (See below) |
| Messenger RNA | mRNA | Carries “message” encoded by gene to site of protein synthesis |
| Transfer RNA | tRNA | Adapter molecules that carry amino acids and match to codon in mRNA |
| Ribosomal RNA | rRNA | Composes over half of the ribosome where proteins are made |
| Small nuclear RNA | snRNA | Processing of eukaryotic transcripts into mature mRNA |
| Small interfering RNA | siRNA | Regulation of gene expression |
| Long noncoding RNA | linRNA | Regulation of gene expression |

Classic Experiment 1: Frederick Griffith (1928)

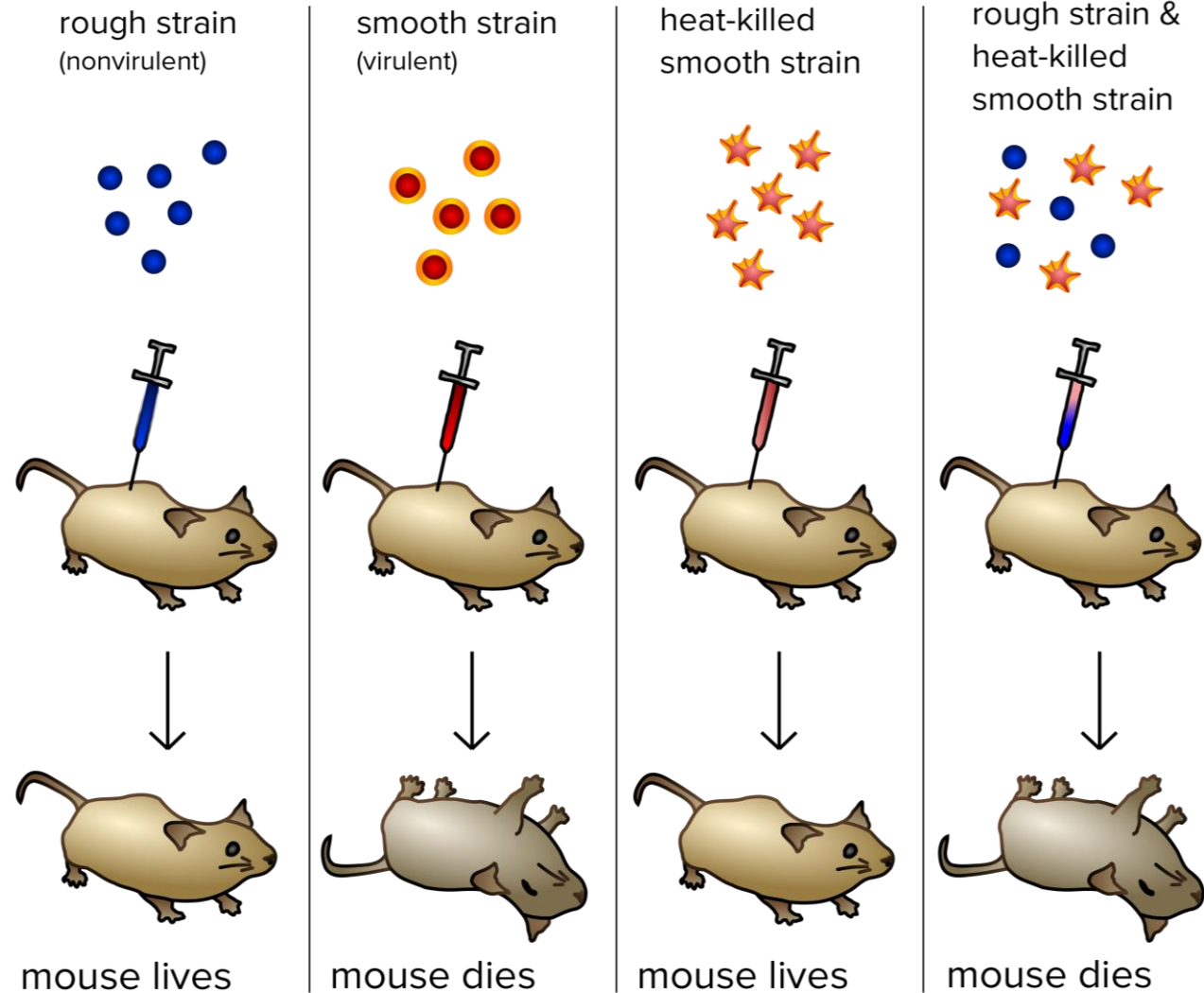
PMID: 17081278



Rough

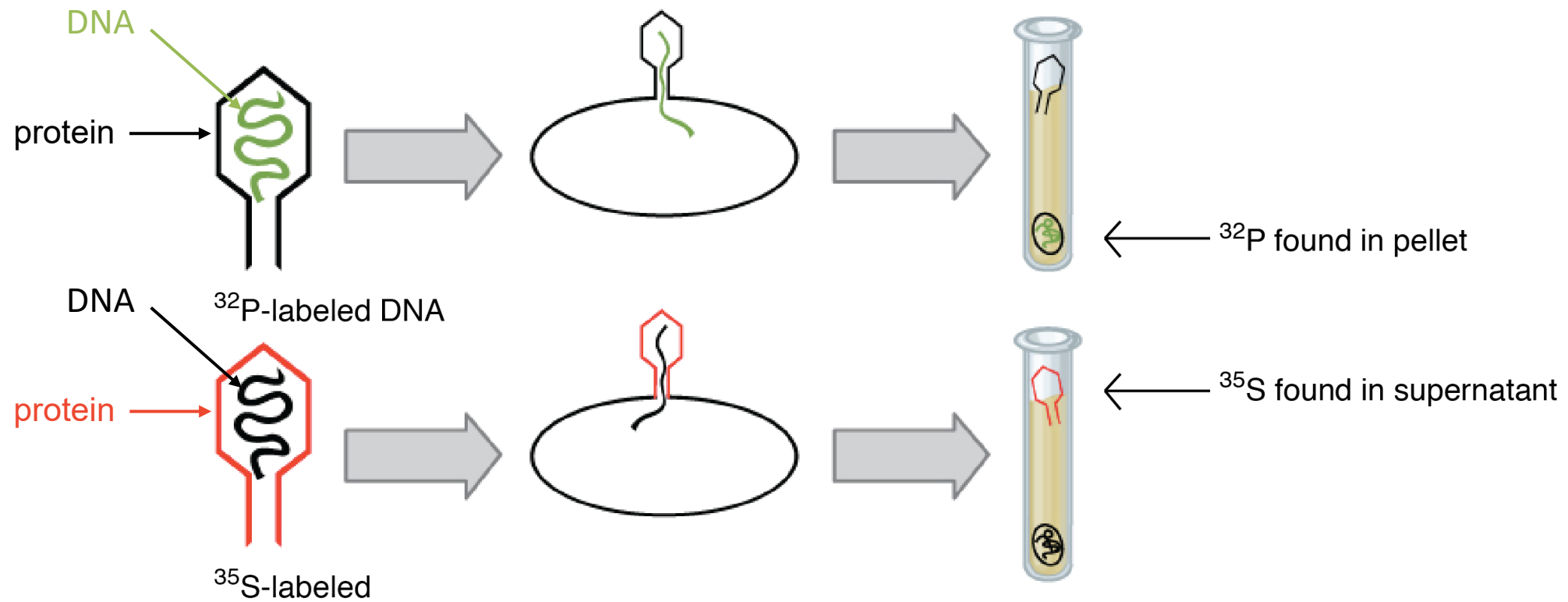
Smooth

Streptococcus pneumoniae



Griffith concluded that the R strain took up a “transforming principle” from the S-strain which allowed it to become virulent.

Classic Experiment 2: Alfred Hershey and Martha Chase (1952)



The Hershey-Chase experiments definitively proved DNA as the genetic material.

DNA Structure 1: Erwin Chargaff (1950)

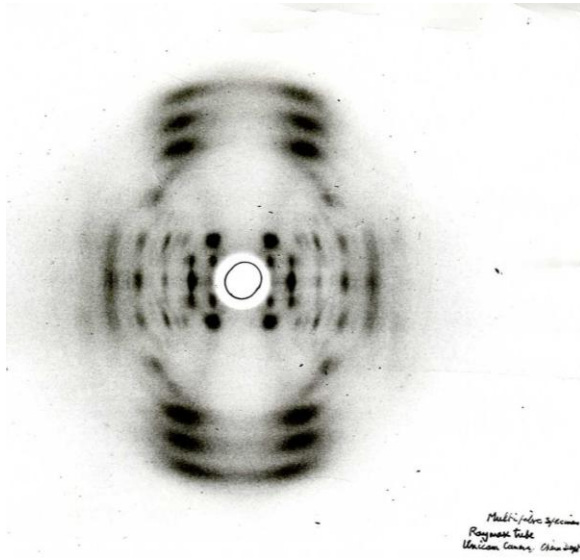
| Nitrogen Base Make-Up of Different Organisms' DNA (in Percentages) | | | | |
|--|-------|-------|-------|-------|
| Organism | A | T | G | C |
| <i>Mycobacterium tuberculosis</i> | 15.1% | 14.6% | 34.9% | 35.4% |
| Yeast% | 31.3% | 32.9% | 18.7% | 17.1% |
| Wheat% | 27.3% | 27.1% | 22.7% | 22.8% |
| Sea urchin% | 32.8% | 32.1% | 17.7% | 17.3% |
| Marine crab% | 47.3% | 47.3% | 2.7% | 2.7% |
| Turtle% | 29.7% | 27.9% | 22.0% | 21.3% |
| Rat kidney% | 28.6% | 28.4% | 21.4% | 21.5% |
| Rat liver% | 28.7% | 28.3% | 21.6% | 21.3% |
| Human kidney% | 30.9% | 29.4% | 19.9% | 19.8% |
| Human liver% | 30.8% | 29.5% | 20.0% | 19.7% |

?

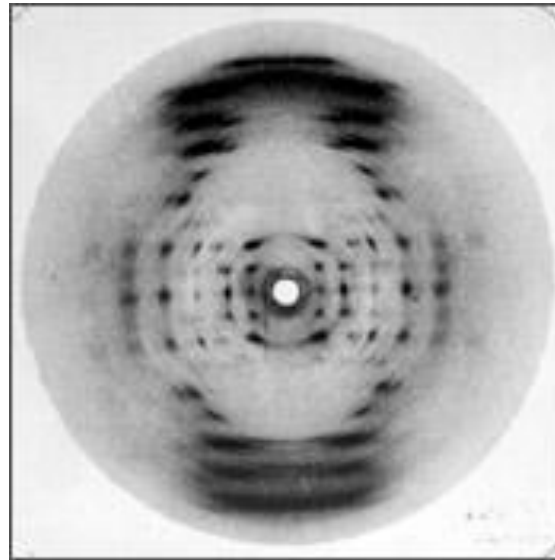
Chargaff's Rules:

1. Base composition between of DNA generally varies from one species to another.
2. DNA specimens from different tissues in the same organism have same base composition.
3. $[A]=[T]$; $[G]=[C]$; [purines]=[pyrimidines] or $[A+G]=[T+C]$

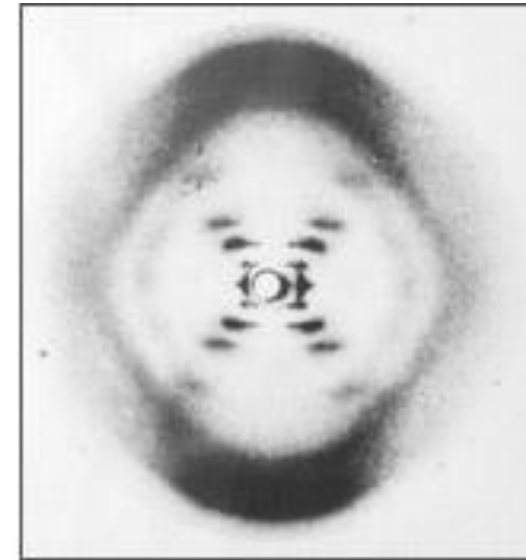
DNA Structure 2: Rosalind Franklin, Maurice Wilkins, Raymond Gosling (1951)



Wilkins and Gosling



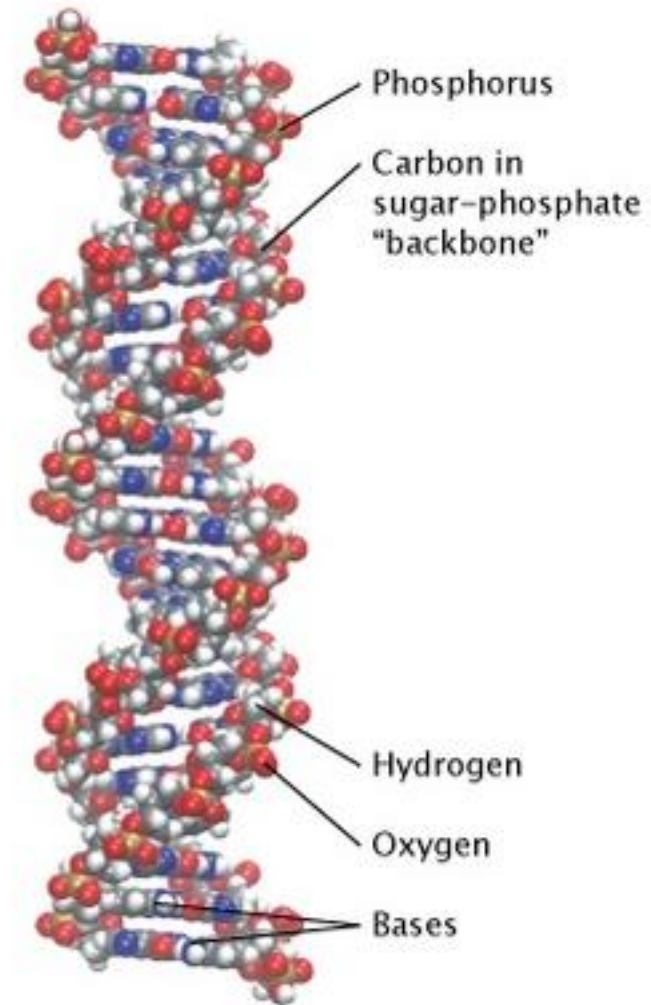
Franklin



Franklin

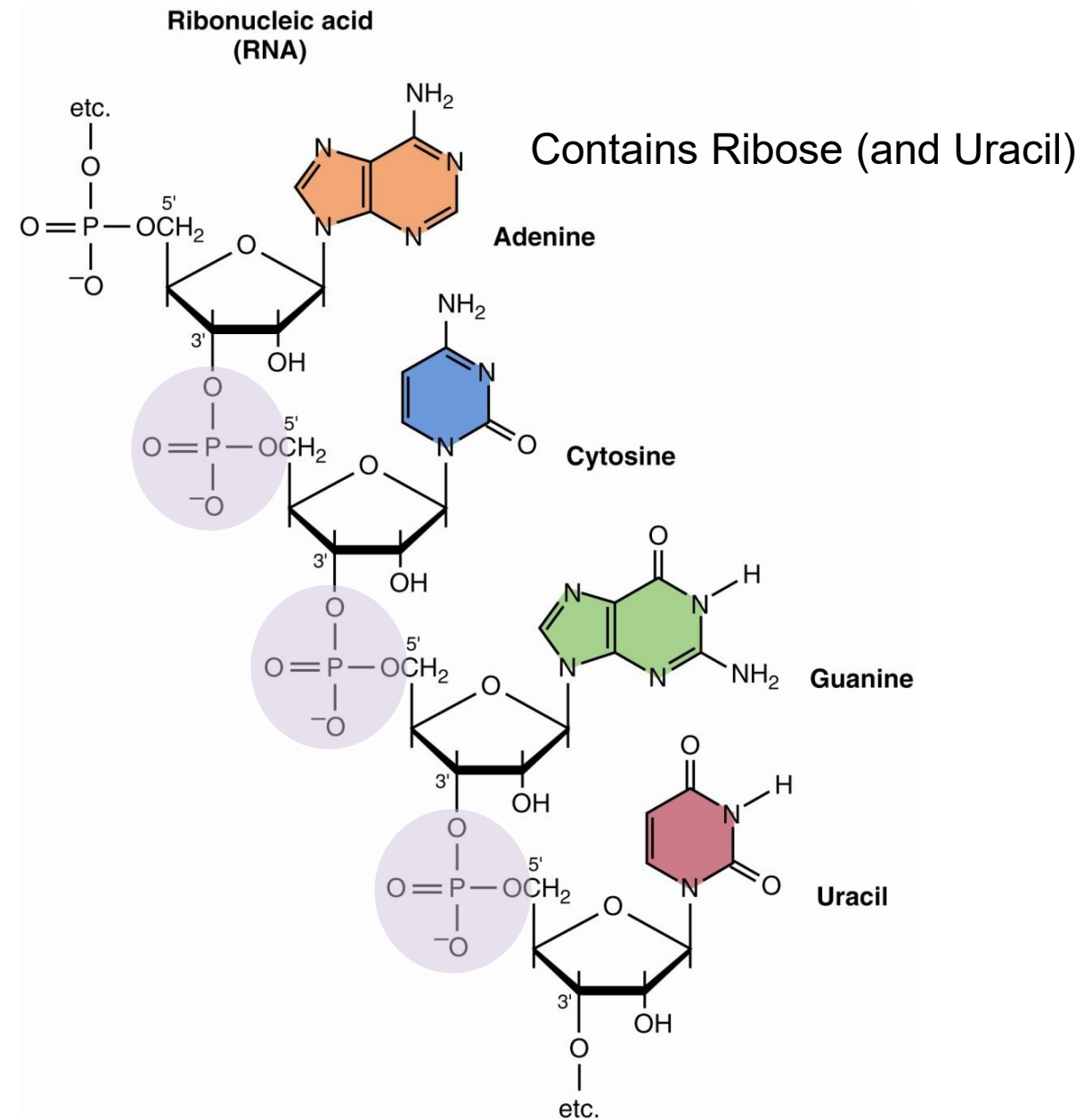
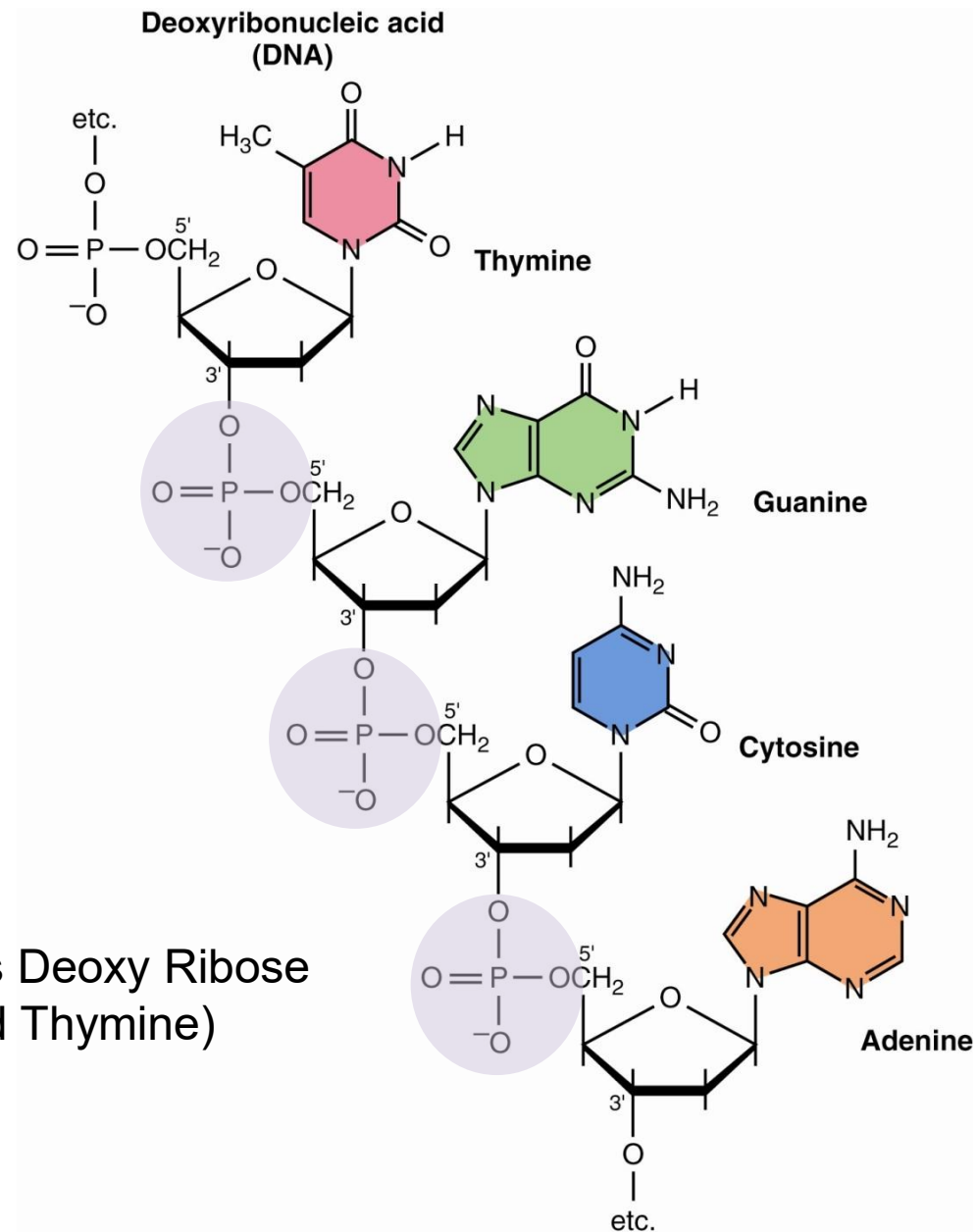
Franklin, Gosling, and Wilkins discovered two forms of DNA, and obtained high quality X-ray images of each. Franklin cautiously proposed a **helical structure, with bases inside, phosphates outside, and antiparallel strands.**

DNA Structure 3: James Watson and Francis Crick (1953)



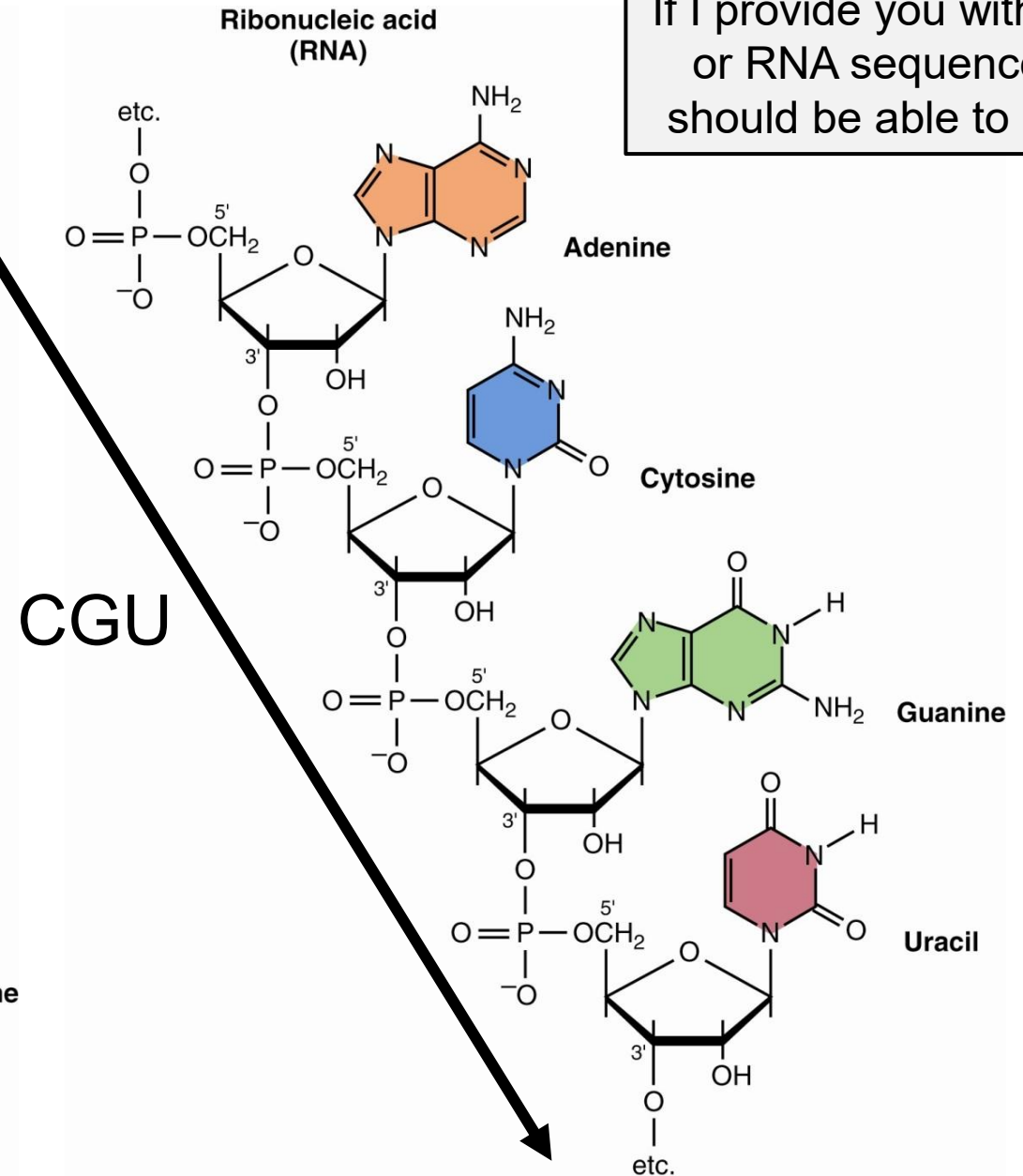
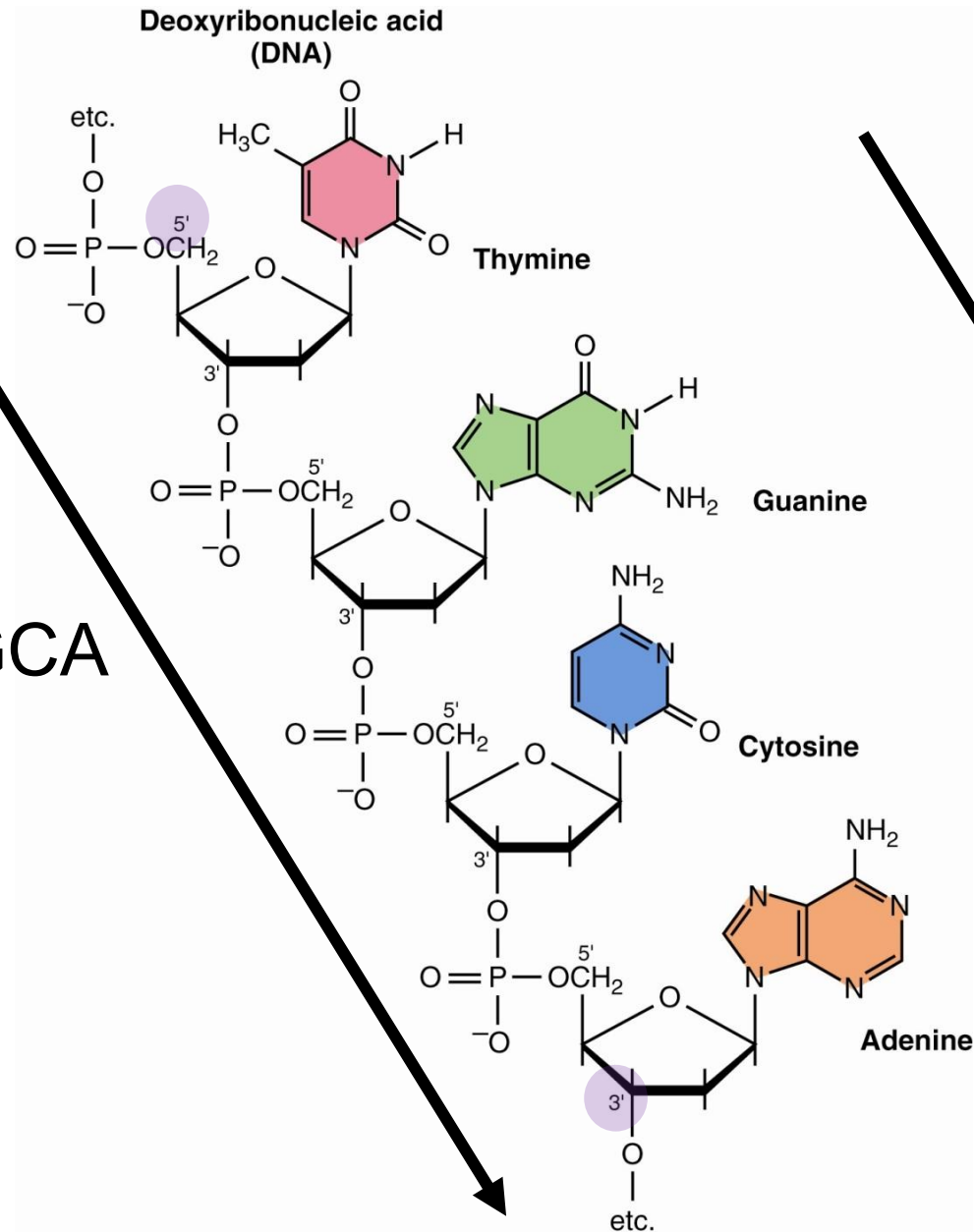
While Watson and Crick identified the correct model of DNA, the discovery would not have been possible without the work of many other scientists and decades of work.

Nucleic Acids: polymers of nucleotides linked by phosphodiester bonds

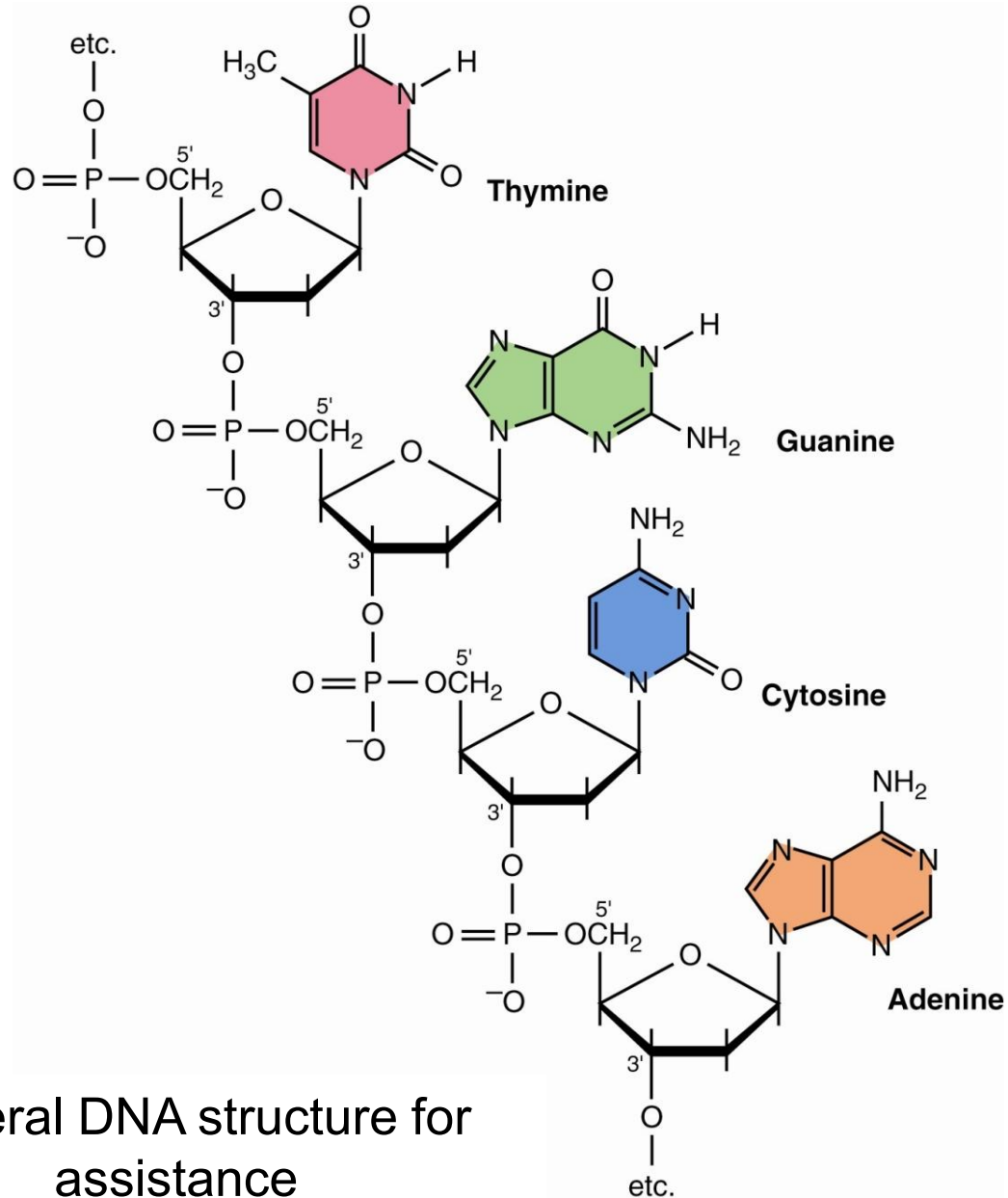


Nucleic acid sequences are always written from 5' → 3'

If I provide you with a DNA or RNA sequence, you should be able to draw it!

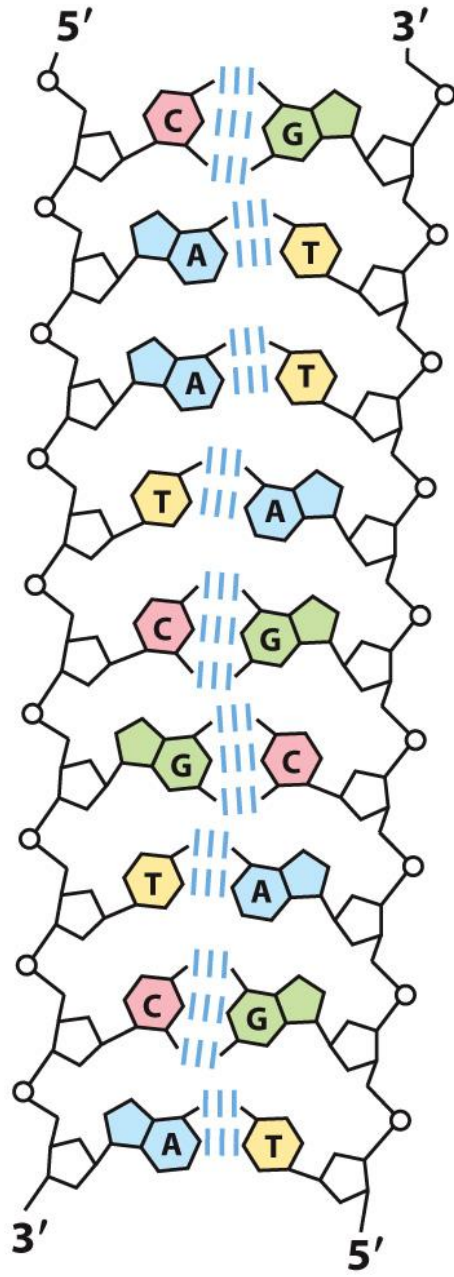


Check-in #1: Draw d-pATCcpp

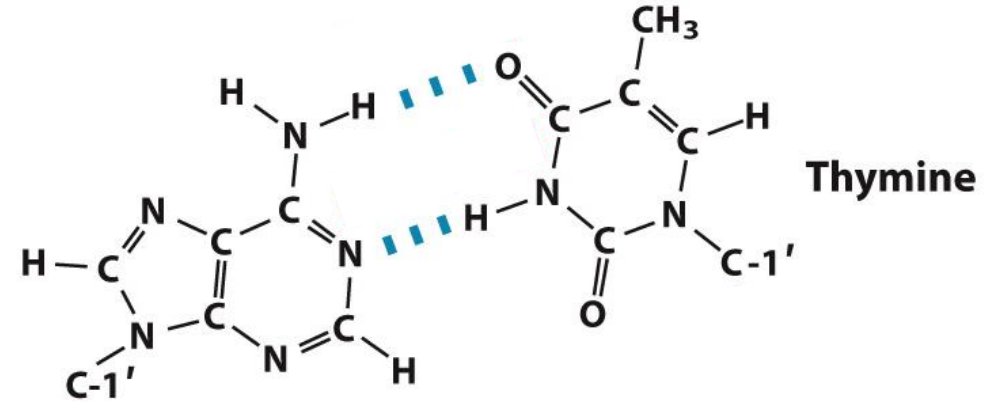


General DNA structure for
assistance

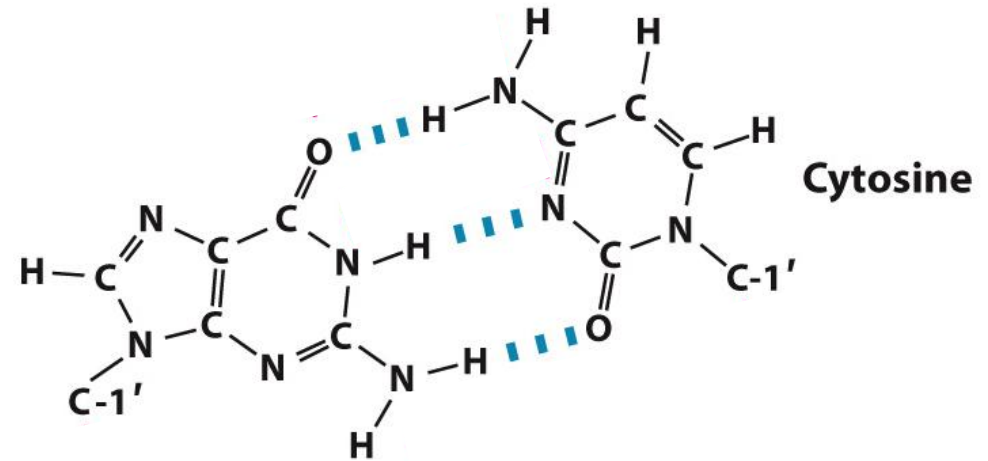
DNA strands are antiparallel and complementary



Adenine

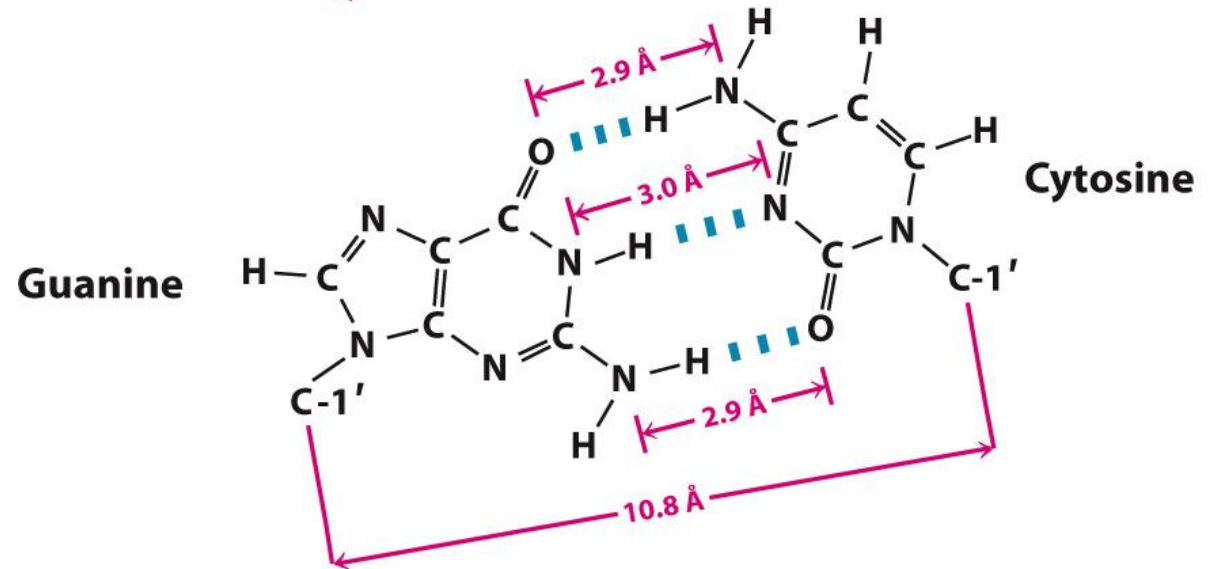
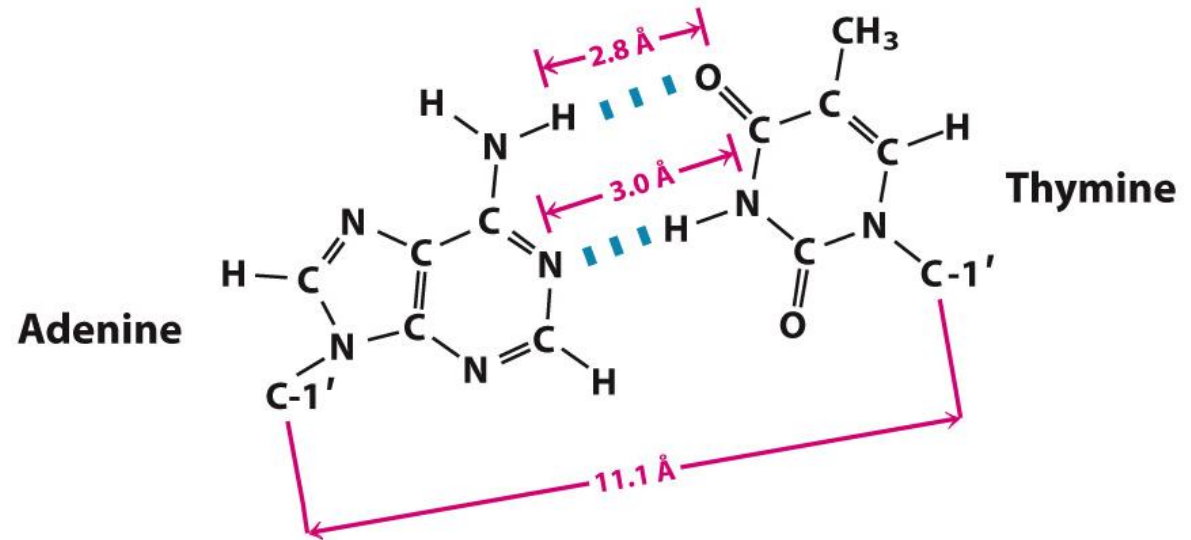
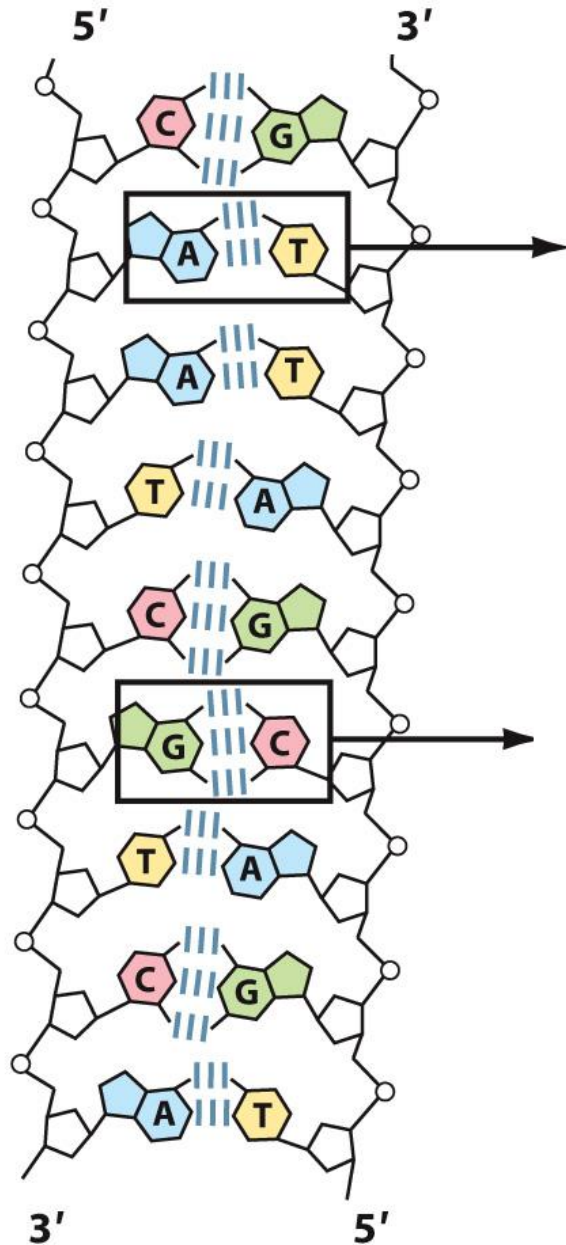


Guanine

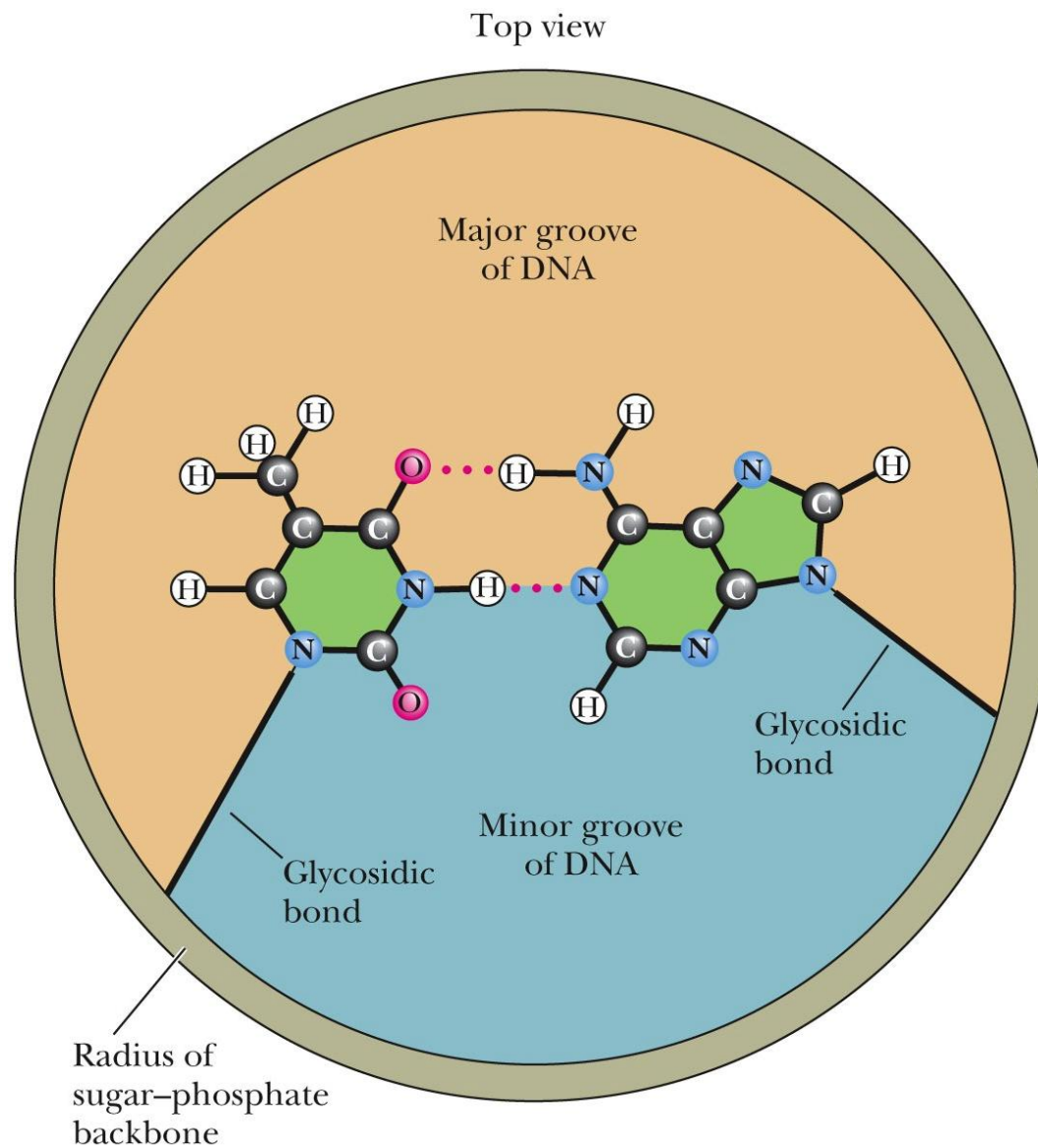


Base Pairing

Watson Crick base pairs have nearly identical dimensions

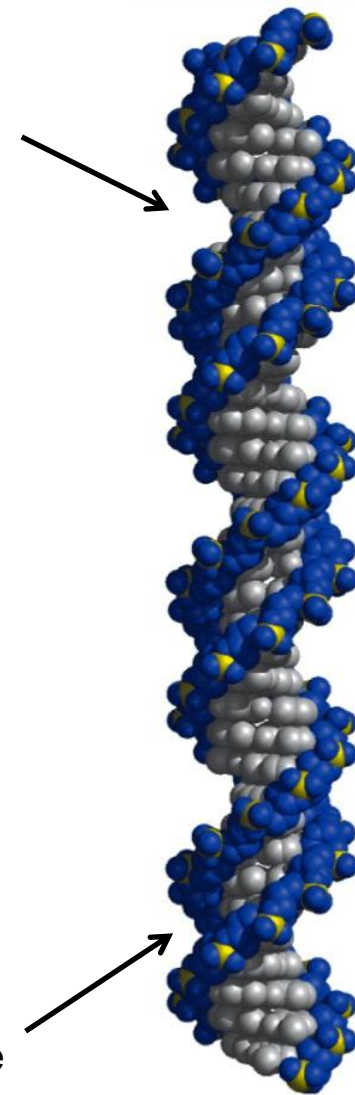


Dimensions of base pairs create major and minor grooves

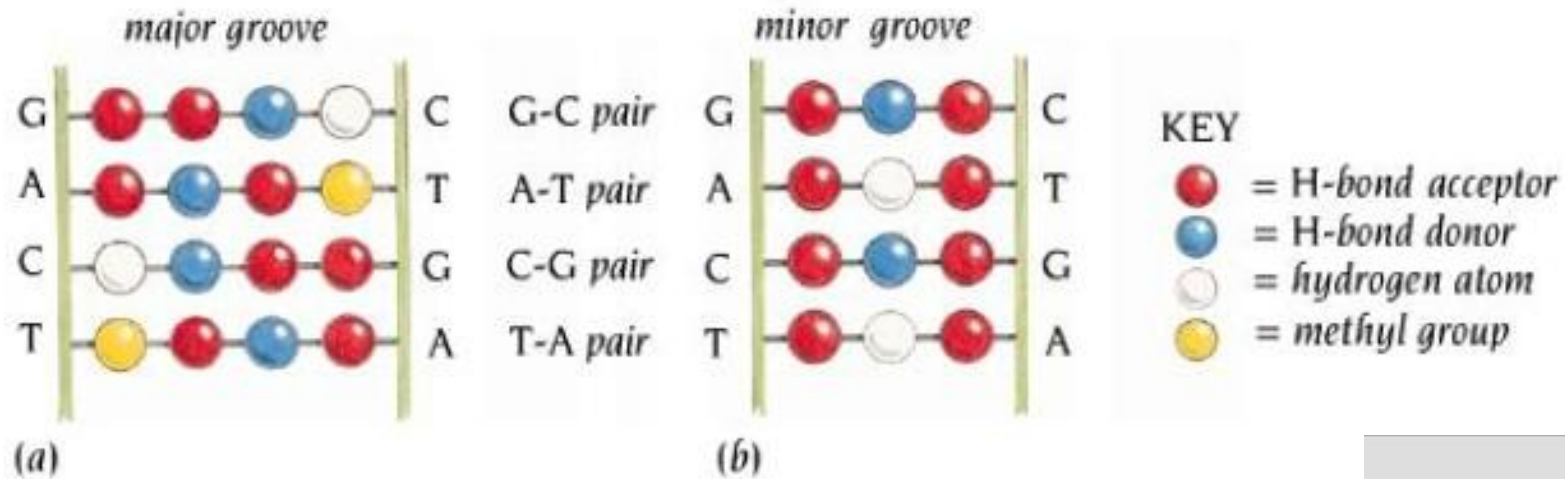


Major groove

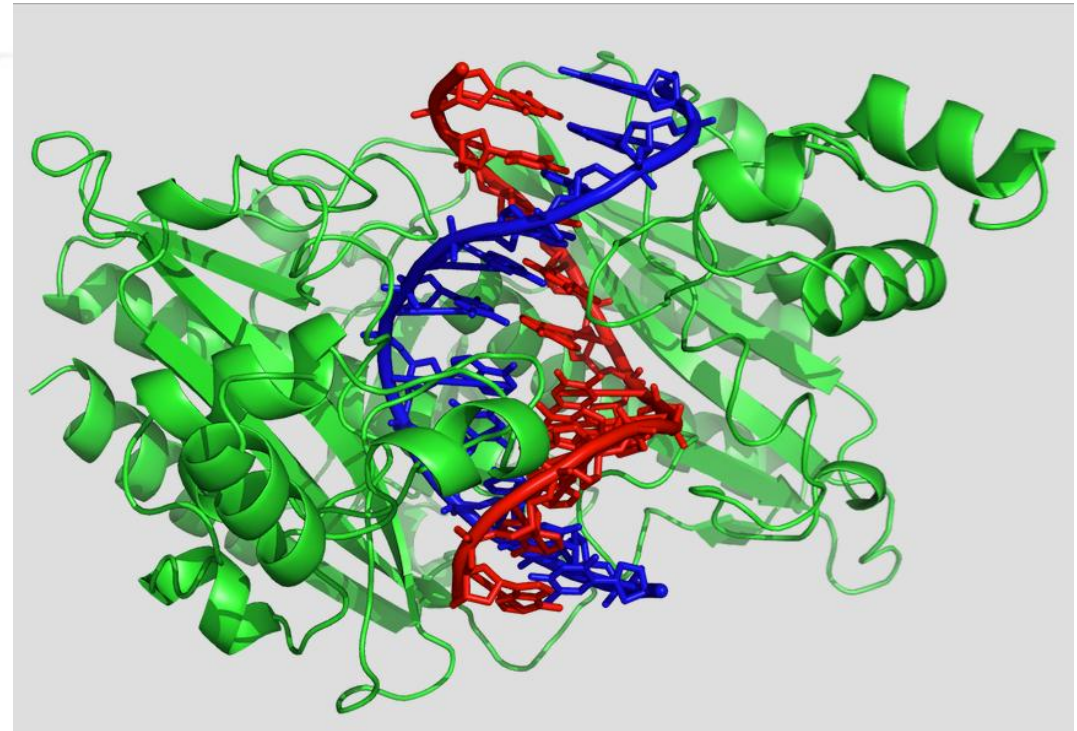
Minor groove



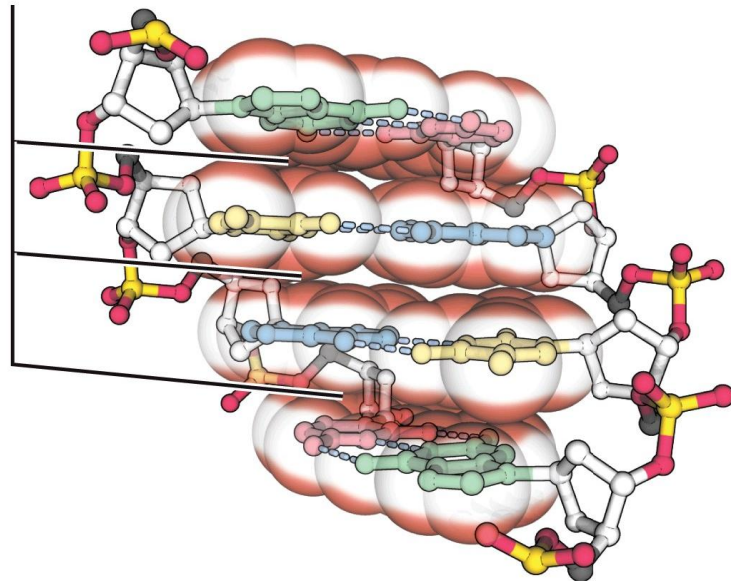
Base pairs are distinguishable in the major groove



EcoRI, a restriction enzyme, recognizes the sequence GAATTC in the major groove



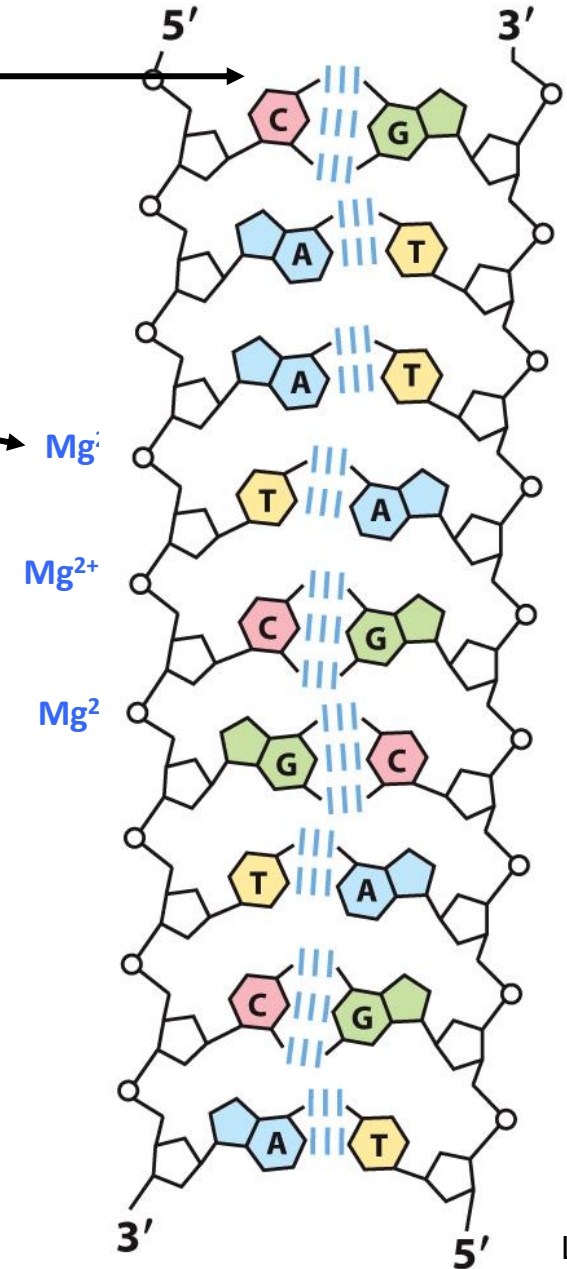
The double helix is stabilized by several intermolecular forces



Base-Stacking:
Pi-pi interactions
(Van der Waals)

Base-Pairing:
Hydrogen bonding

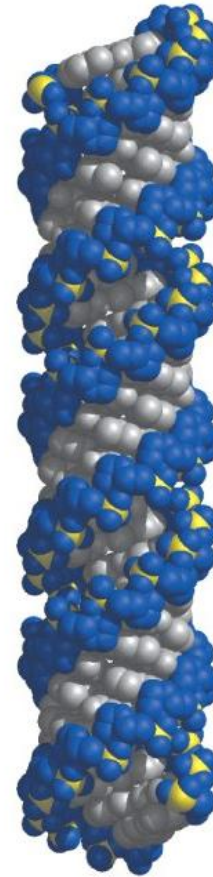
Backbone:
Ionic interactions



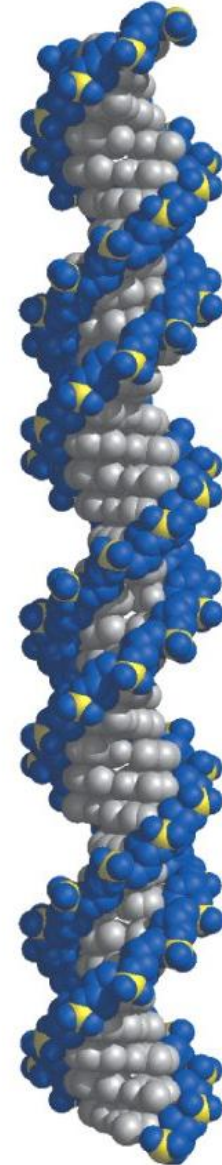
DNA can be found in three different f

The structures are a result of:

- Conformations of pentose sugar
- Free rotation of the backbone
- Rotation about glycosidic bond



A form

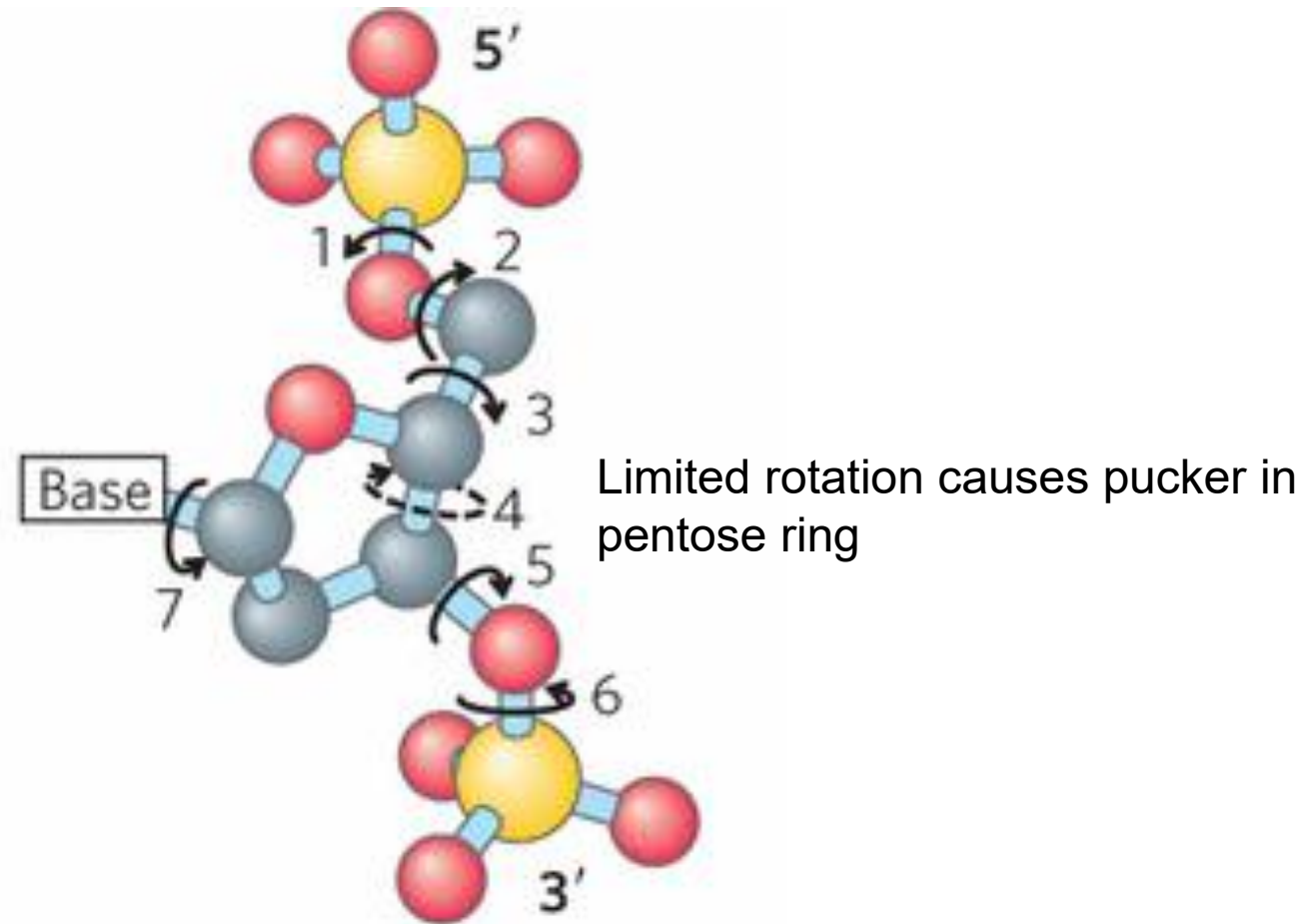


B form

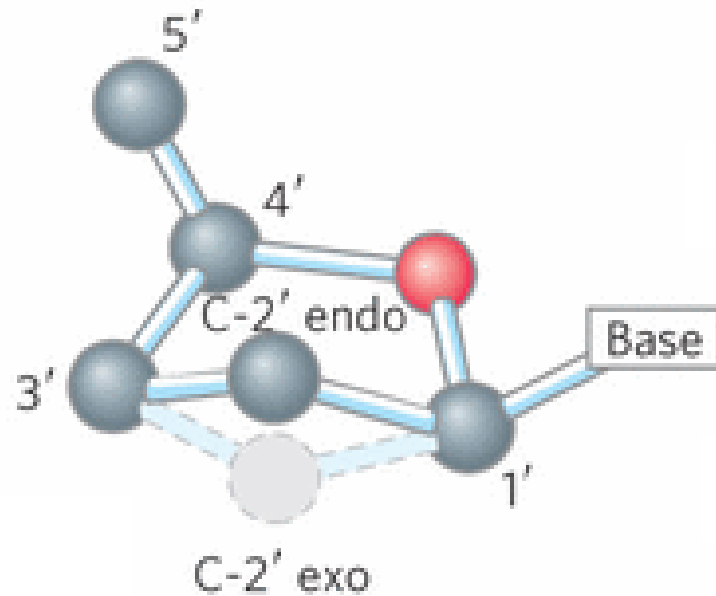


Z form

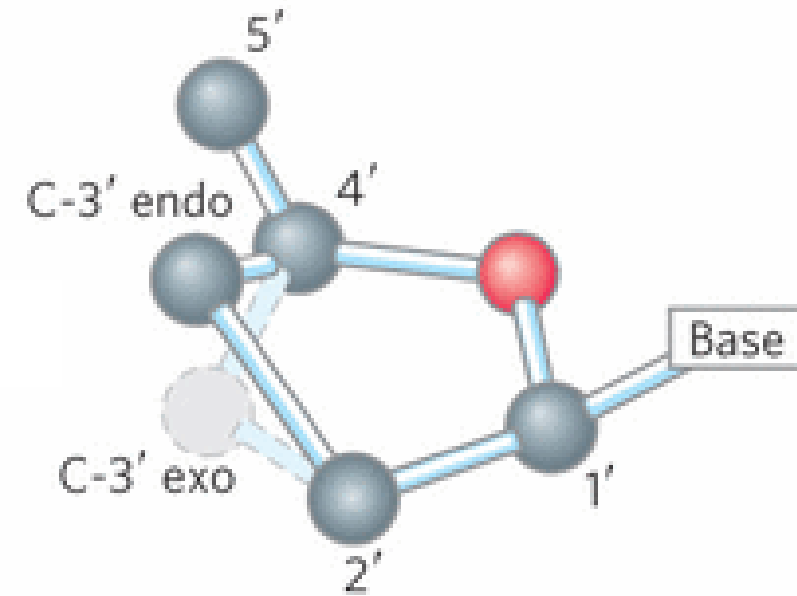
Free rotation around bonds in phosphodiester backbone



Four puckered conformations of pentose sugar

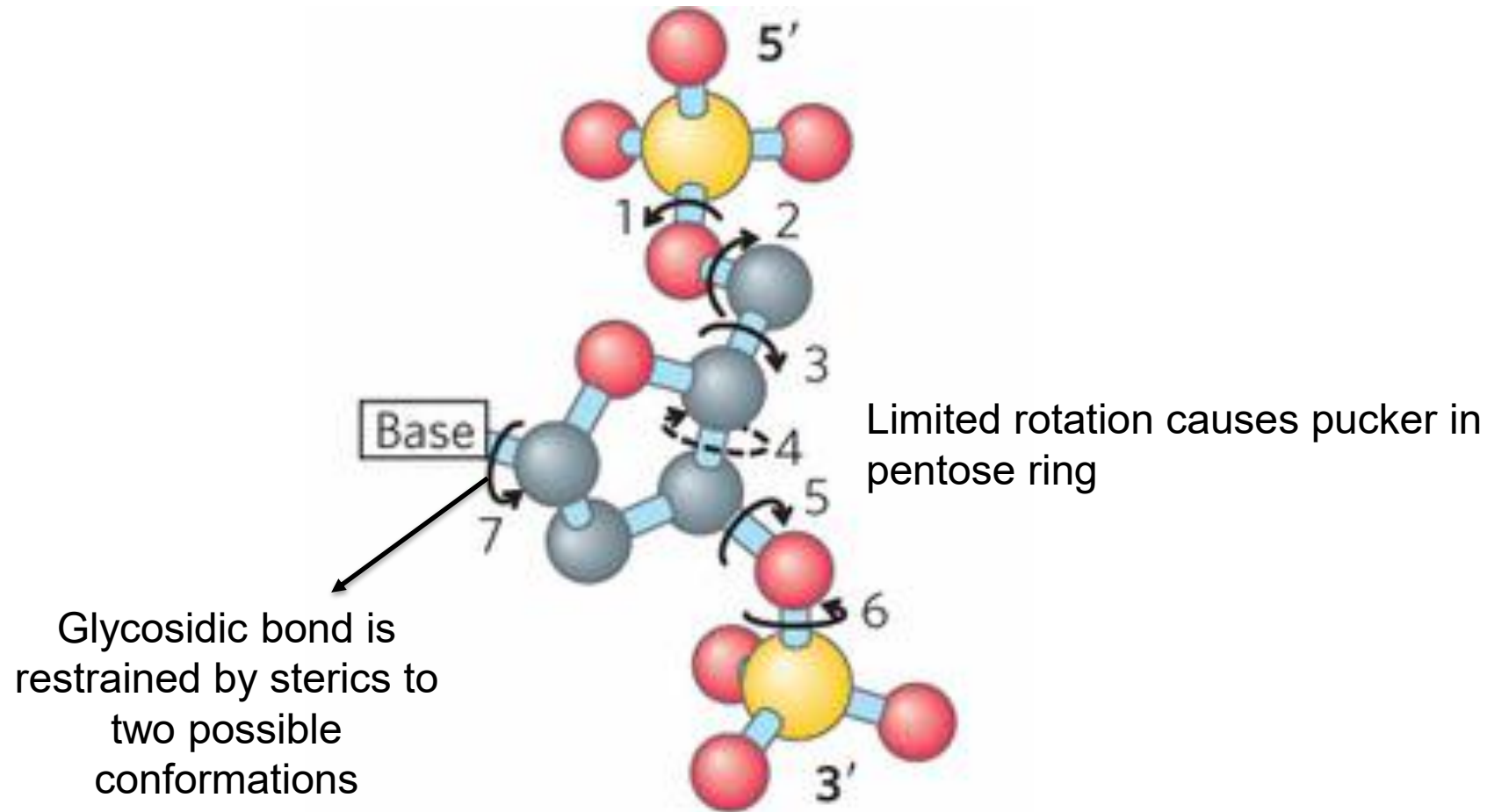


C-2' endo: C2' on same side of ring as C5'
C-2' exo: C2' on opposite side of ring as C5'

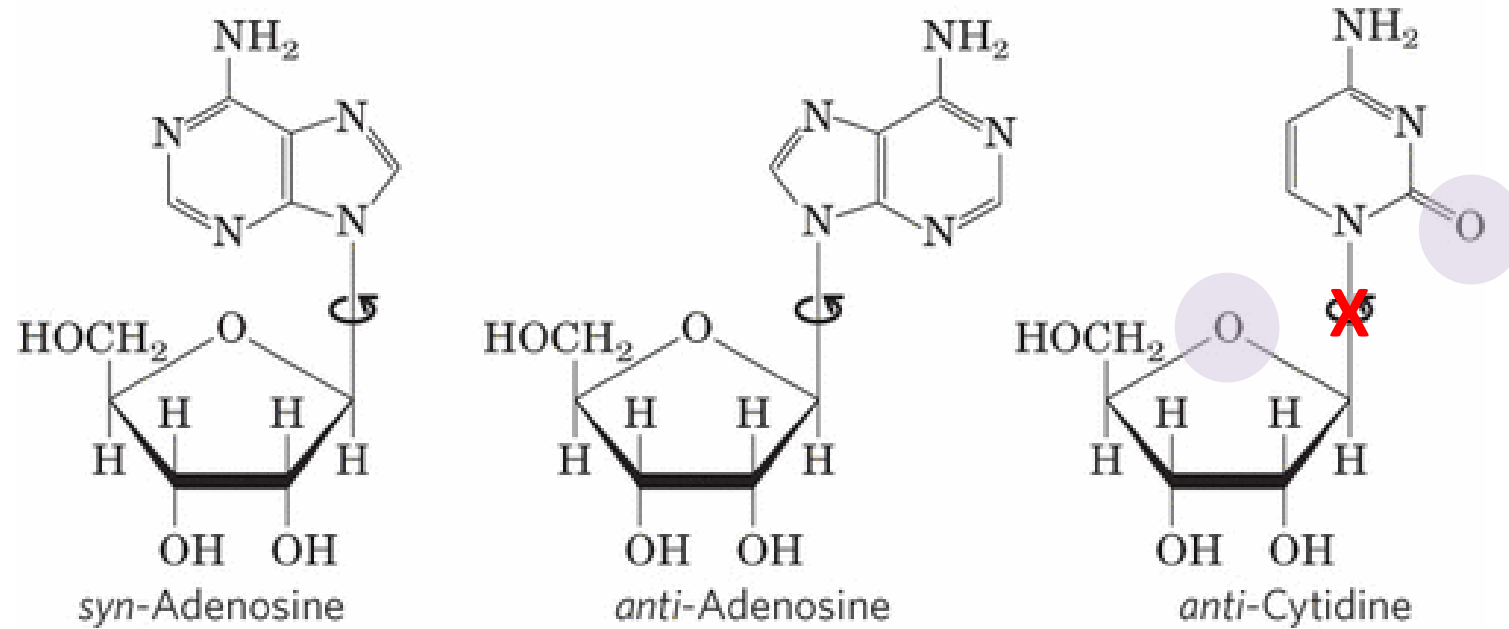


C-3' endo: C3' on same side of ring as C5'
C-3' exo: C3' on opposite side of ring as C5'

Free rotation around bonds in the phosphodiester backbone



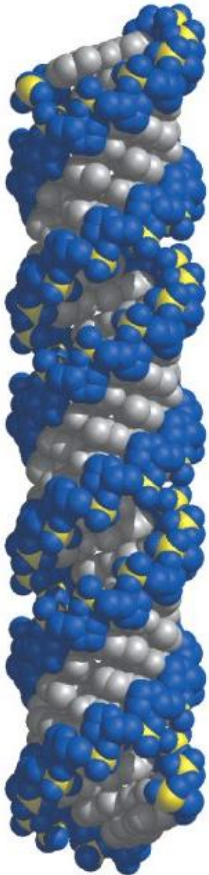
Rotation about the glycosidic bond



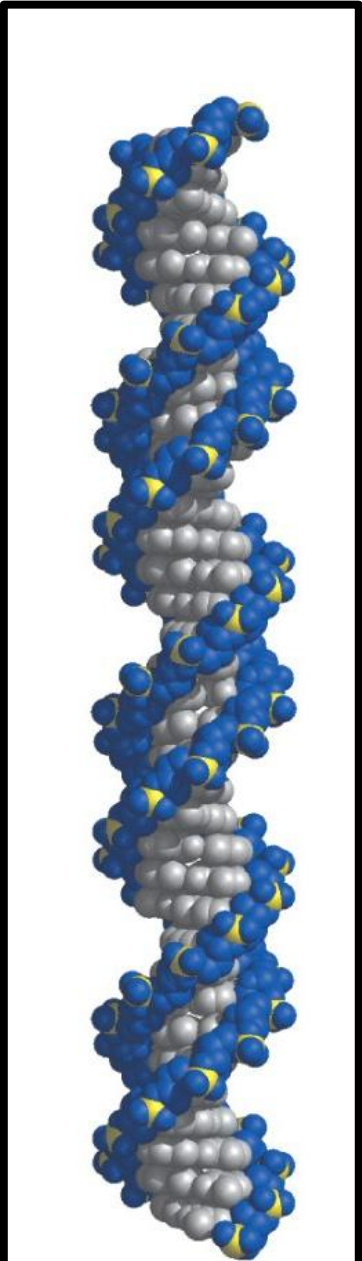
Purines: *syn* or *anti*
Pyrimidines: *anti* only

DNA can be found in three different f

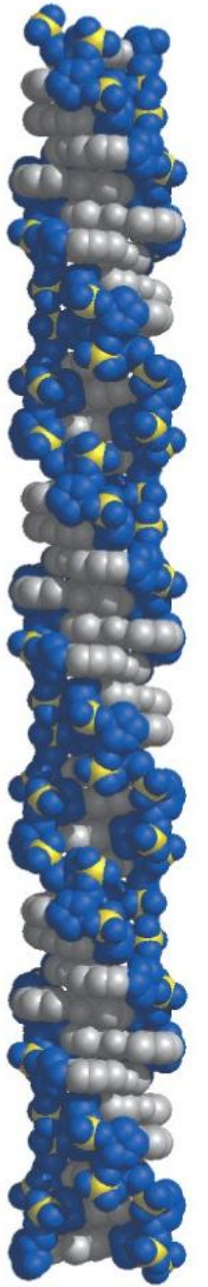
| | A Form | B Form “Watson-Crick” | Z Form |
|----------------------------|-------------------------|--------------------------|---|
| Helix | Right-handed | Right-handed | Left-handed |
| Shape | Short and broad | Longer and thinner | Longest and thinnest |
| Bp/Helical Turn | 11 | 10.5 | 12 |
| Sugar Conformation | C-3’ endo | C-2’ endo | C-2’ endo for pyrimidines; C-3’ endo for purines |
| Glycosyl Bond Conformation | Anti | Anti | Anti for pyrimidines; Syn for purines |
| Found In | Low moisture conditions | Most living forms | High salt conditions, requires alternating CG sequences |



A form

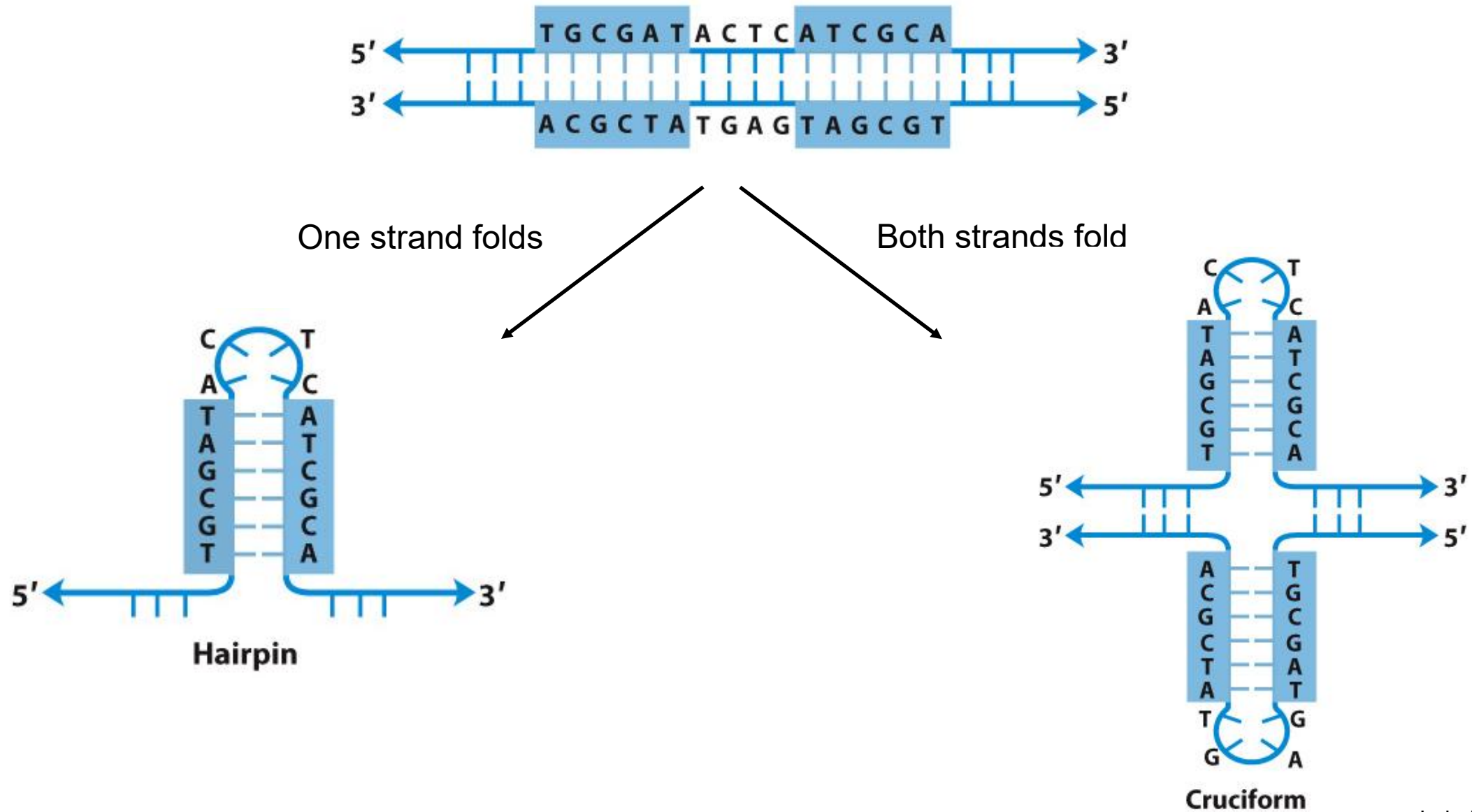


B form

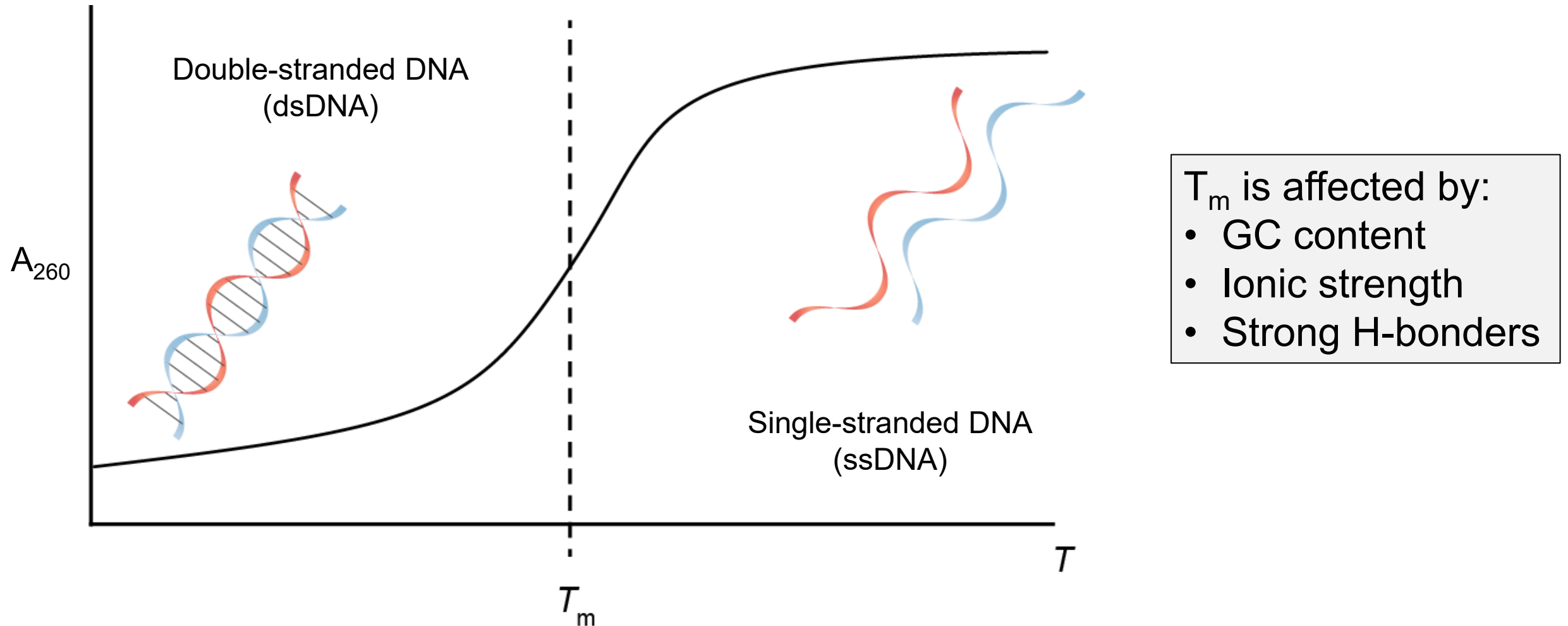


Z form

Palindromic DNA sequences can adopt other structures

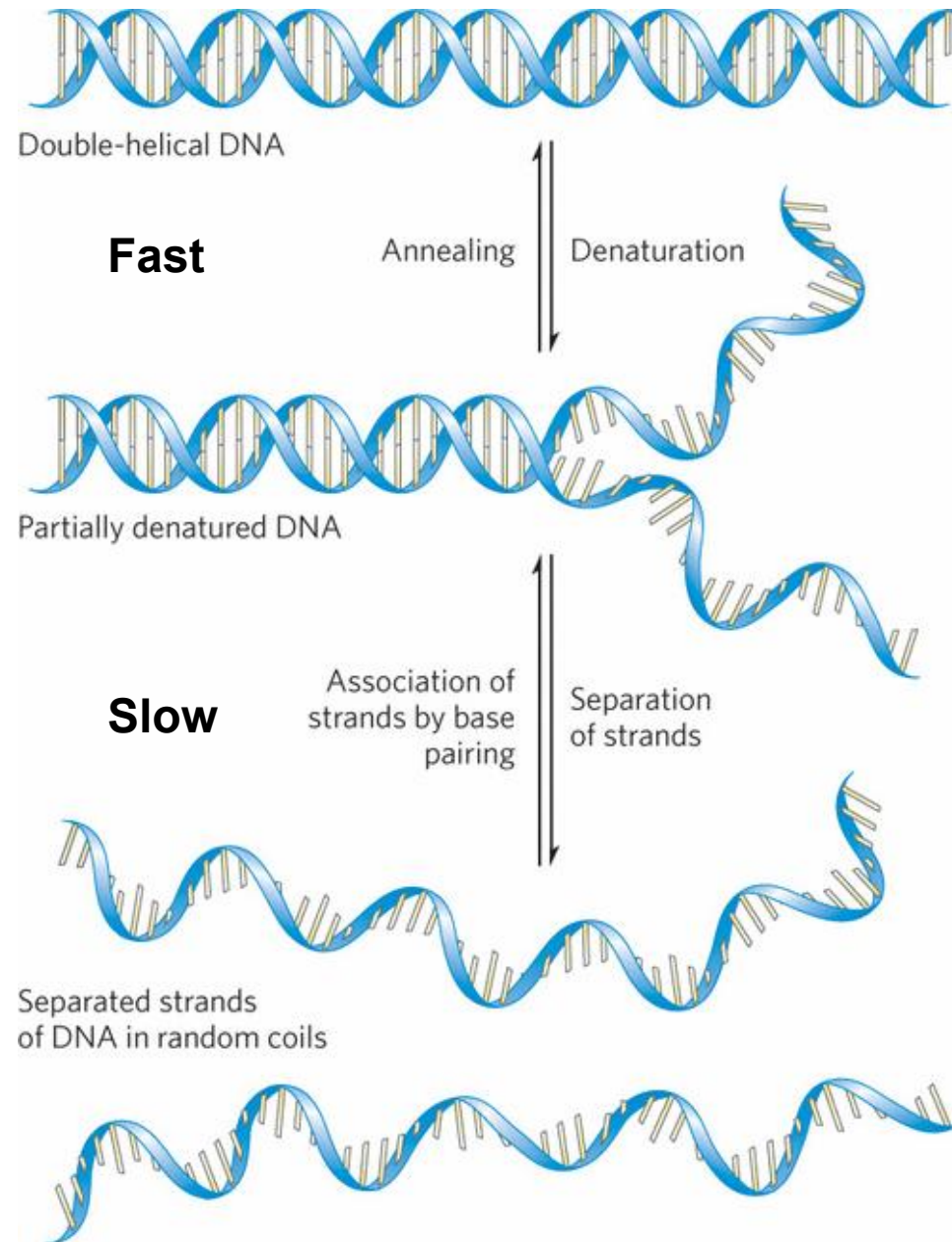


The DNA double helix is sensitive to changes in temperature



DNA “melting curve” can be followed with absorbance – hyperchromic shift

DNA can be de-natured and re-natured





0 response submitted

What is the complementary DNA sequence to the DNA oligonucleotide GCATTACT?

Scan the QR or use
link to join



<https://forms.office.com/r/QfgpLk8t8a>

Copy link

CGTAATC

AGTAATGC

AACGTTGG

Treemap

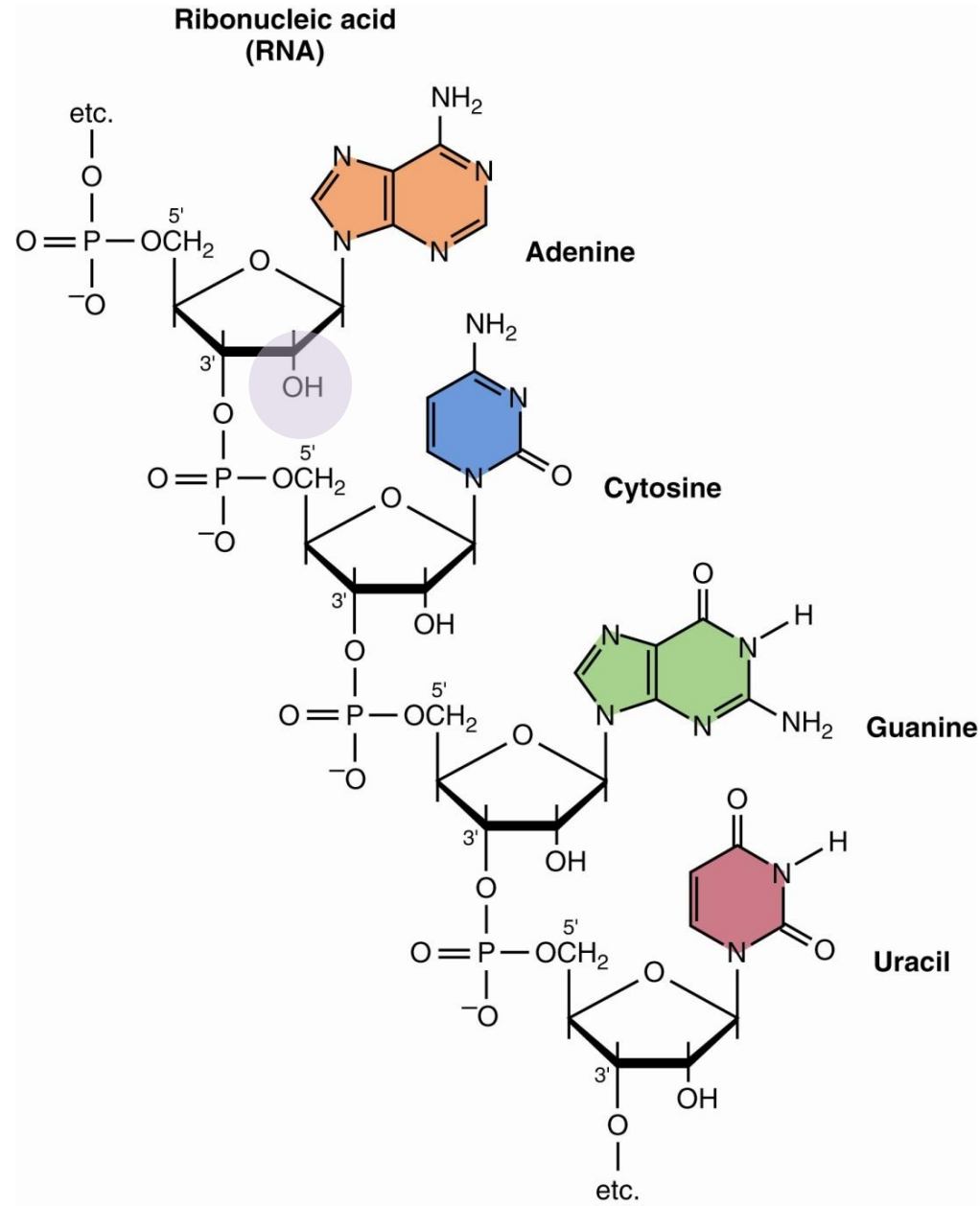
Bar



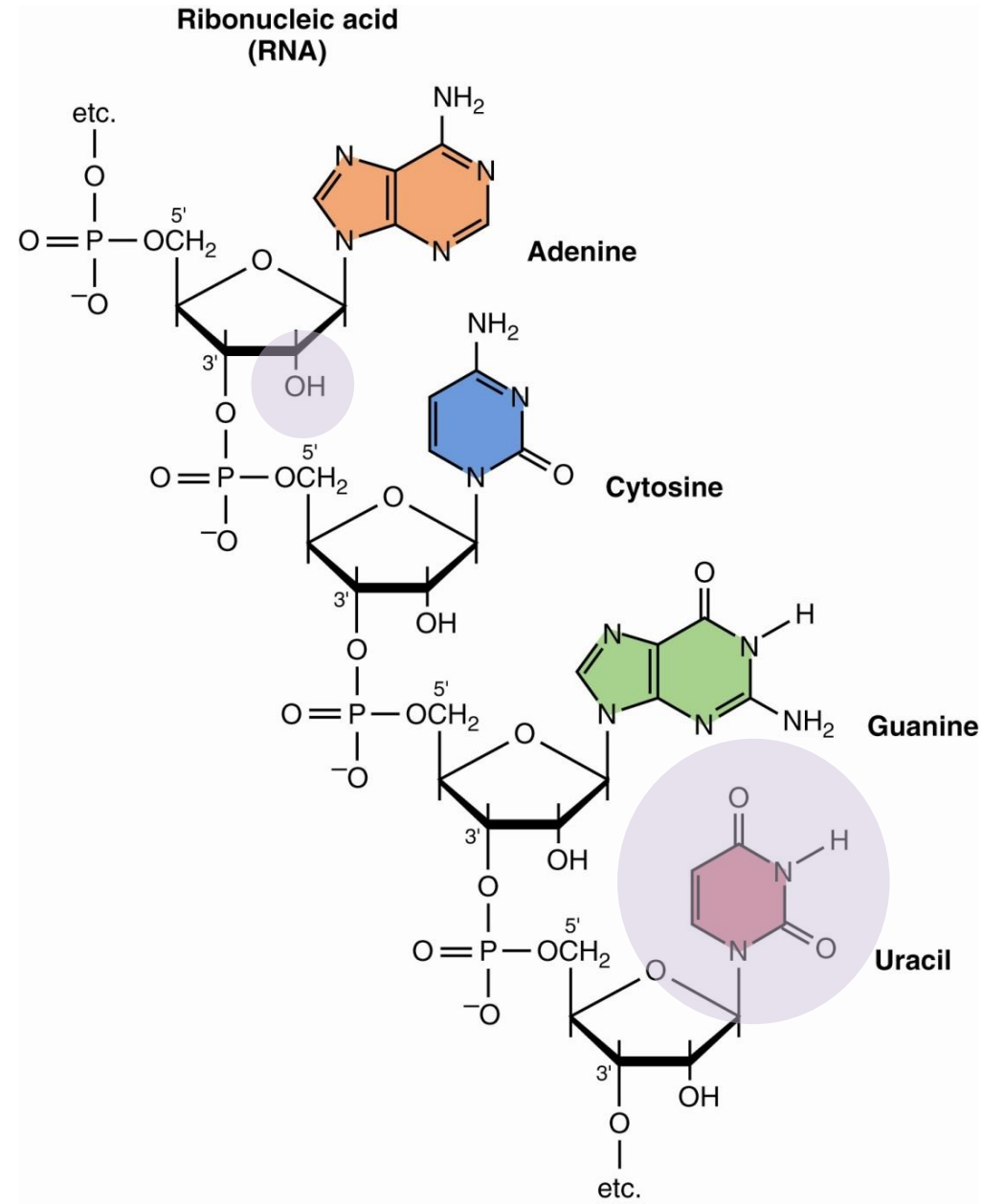
1 of 3



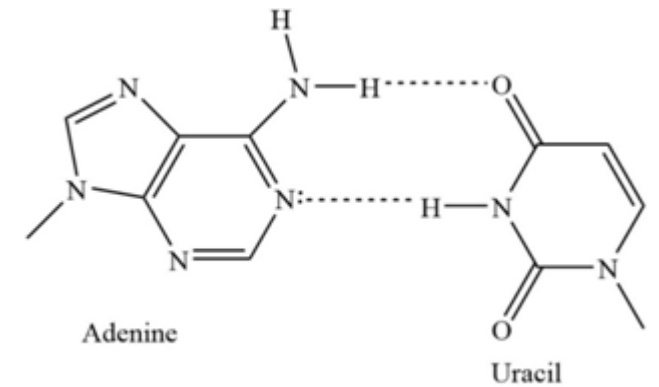
Quick Review: Differences between RNA and DNA



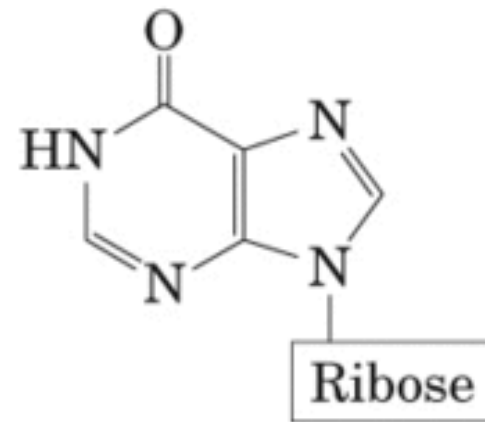
Quick Review: Differences between RNA and DNA



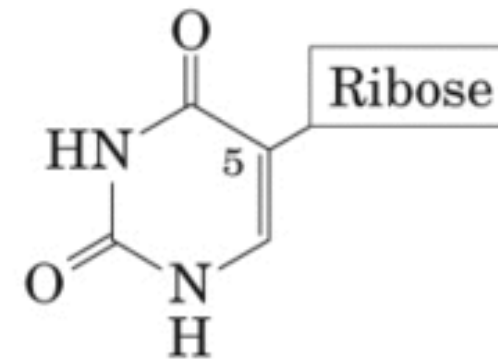
In RNA, uracil H-bonds with adenine



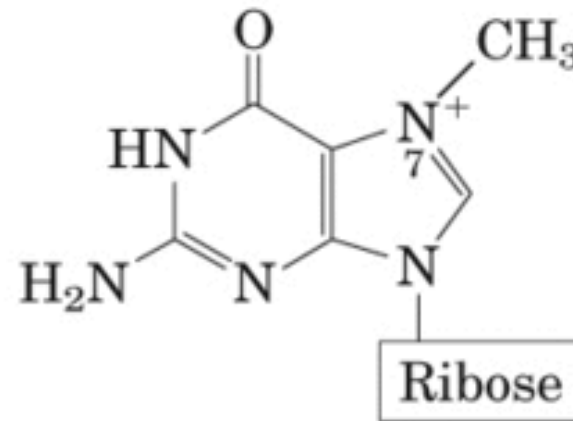
Unusual bases can be found in RNA



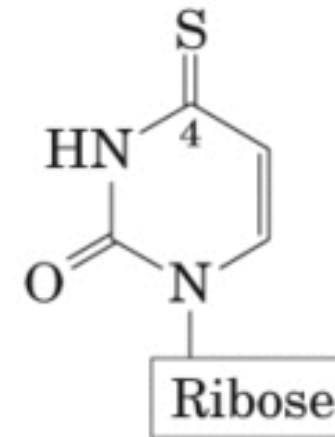
Inosine



Pseudouridine

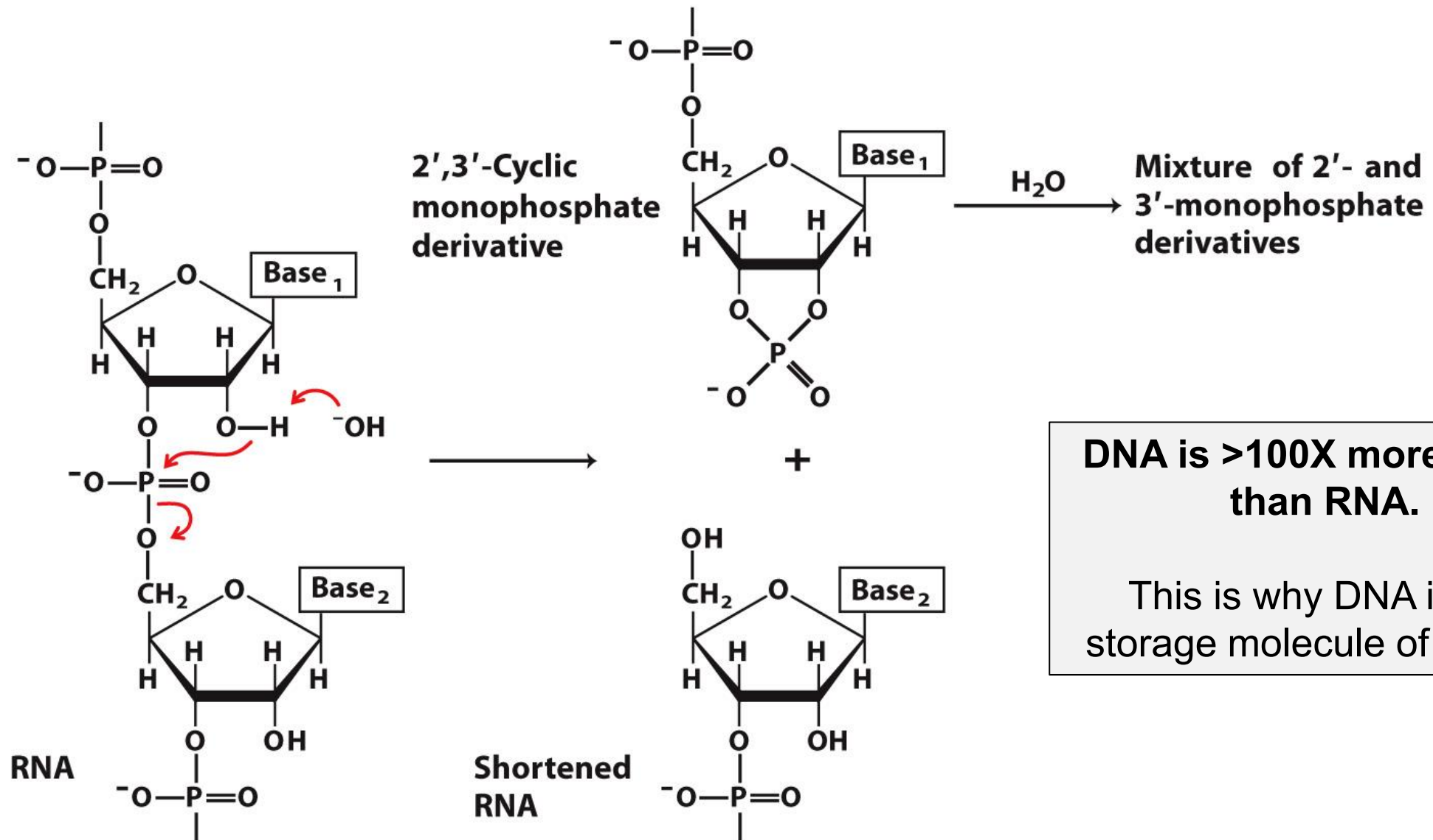


7-Methylguanosine



4-Thiouridine

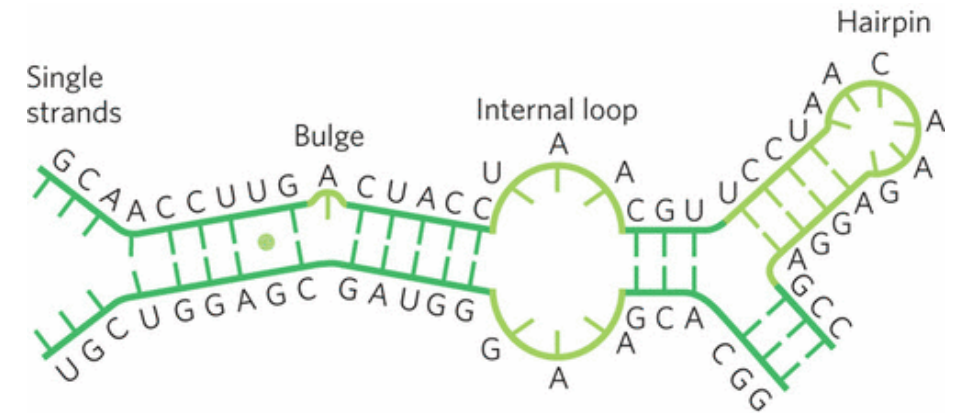
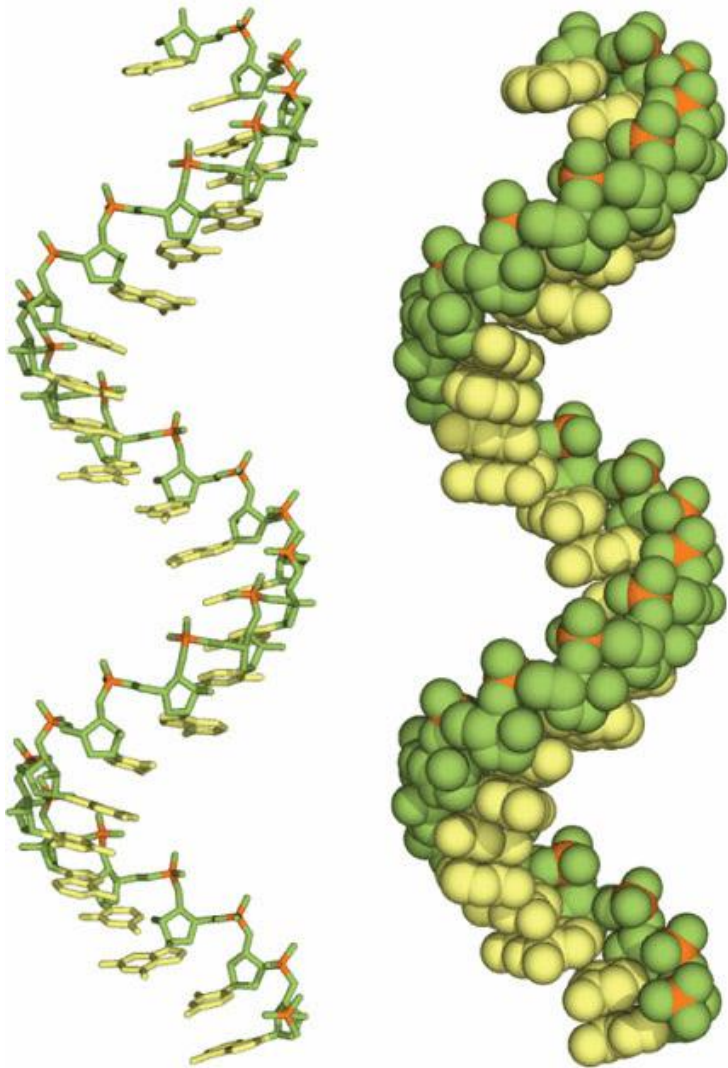
The ribose 2' OH makes RNA susceptible to hydrolysis



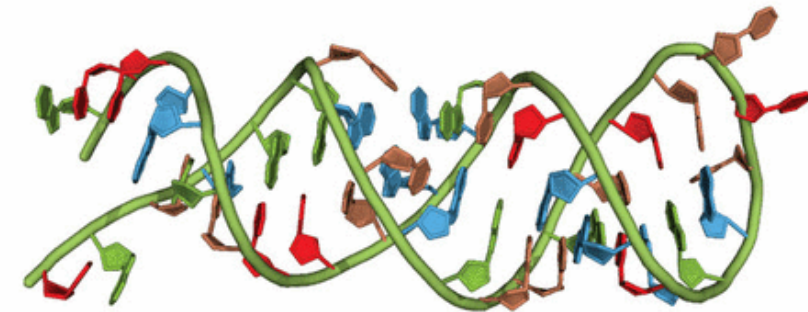
DNA is >100X more stable than RNA.

This is why DNA is our storage molecule of choice!

RNA can adopt multiple secondary structures



(a)



Hairpin double helix

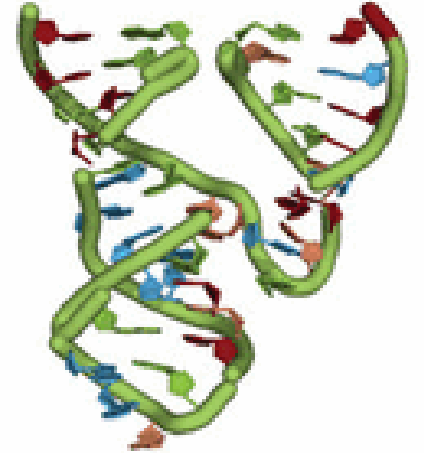
(b)

Tertiary structures of RNA are as diverse as their functions

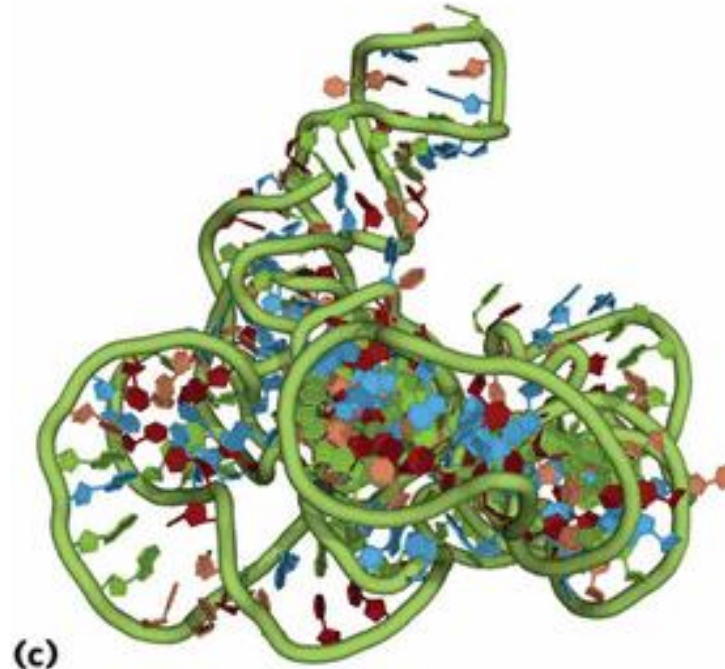


Transfer RNA (tRNA)

Messenger RNA (mRNA)



Ribozyme (RNA enzyme)



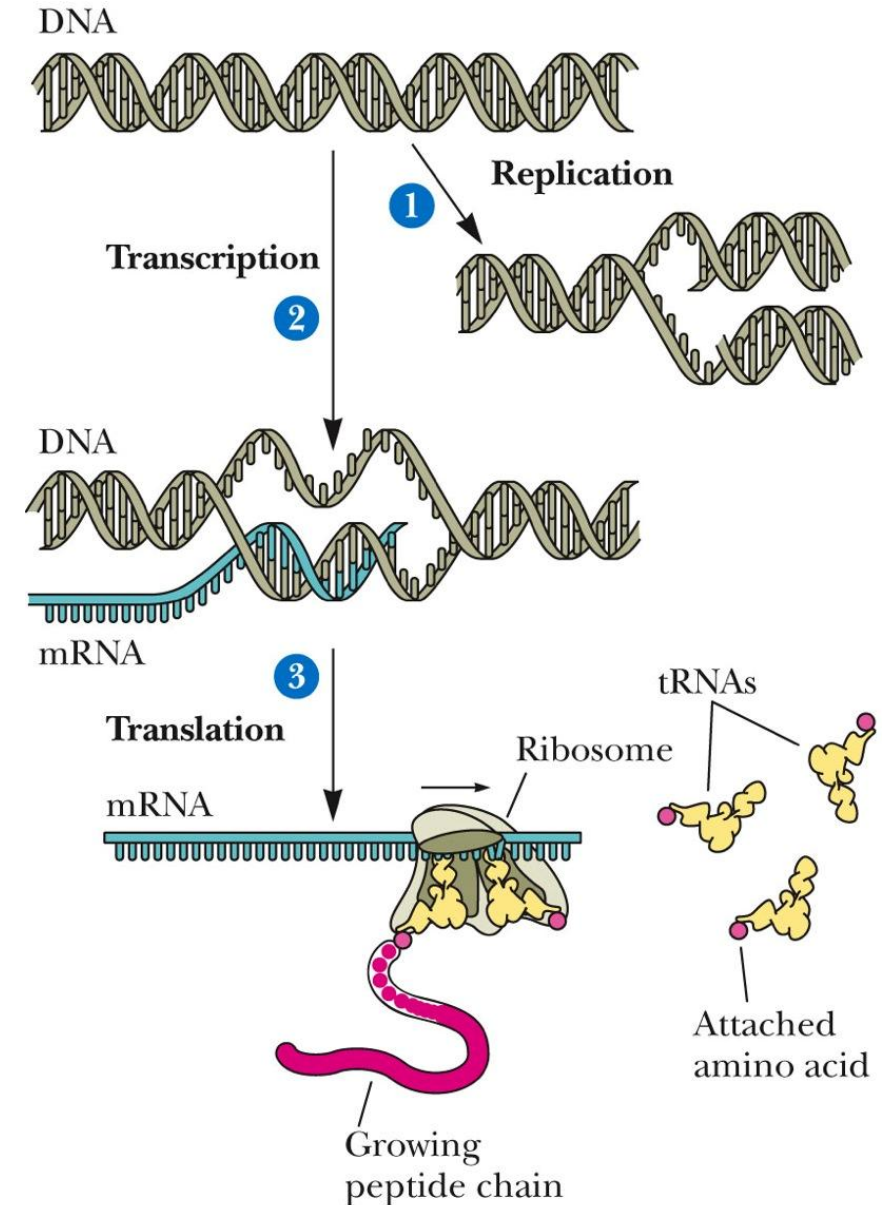
Which came first, DNA or RNA? RNA!

The RNA World Hypothesis:

Long ago, RNA was *both* the genetic and catalytic material

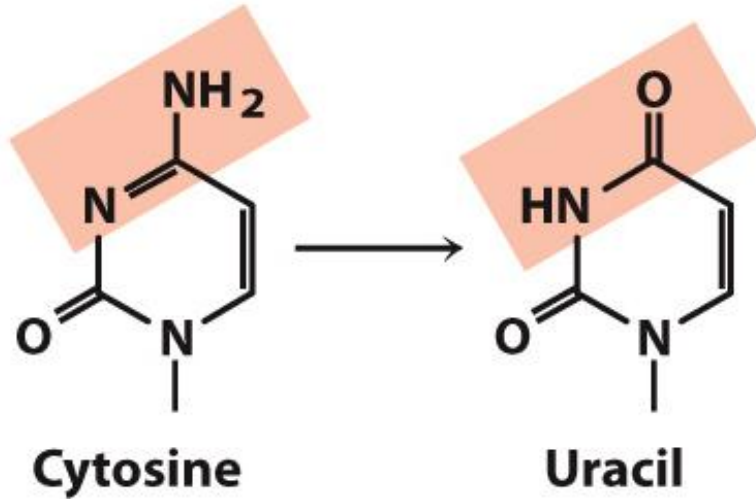
RNA is central to life's basic processes:

- Ribosome
- Ribozymes
- dNTPs
- Cofactors

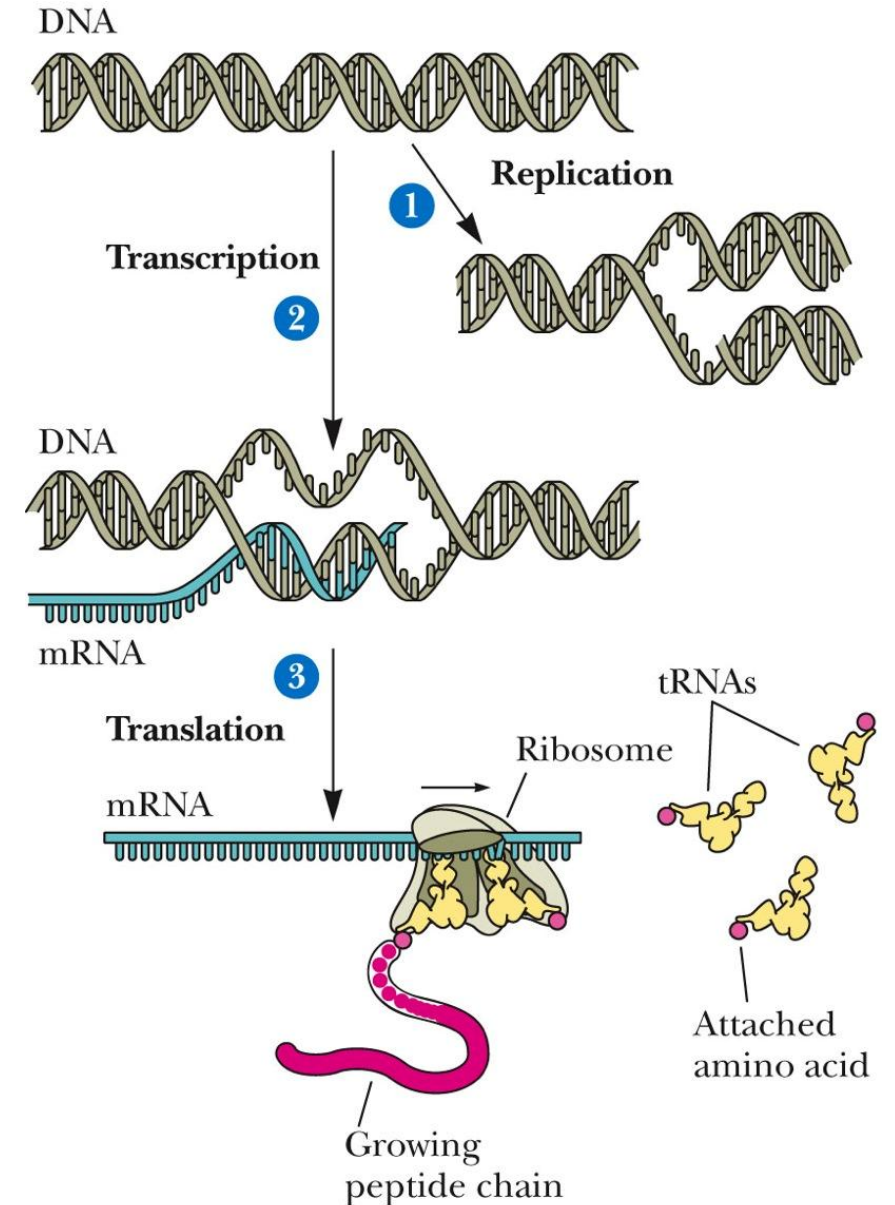


Why is DNA a great molecule for information storage?

1. DNA is ~100x more stable than RNA
2. DNA is double stranded
3. U vs. T



10^7 cytidine residues every 24 hrs!



Check-in #3: A comparison of DNA and RNA

| Feature | DNA | RNA |
|---------------------------|-----|-----|
| Function | | |
| Bases | | |
| Type of Pentose Sugar | | |
| Single or Double Stranded | | |
| Stability | | |