

Lecture 7

Nucleic Acid

Structure

and DNA

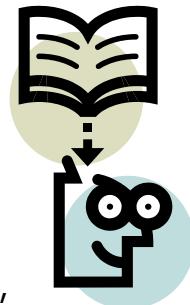
Replication

Nucleic Acid Structure and DNA Replication

Lecture Outline:

- Nucleic Acid Structure
- A Double-Helical Structure
- DNA Double Helices Can Adopt Multiple Forms
- Eukaryotic DNA
- RNA Can Adopt Elaborate Structures
- DNA Is Replicated by Polymerases
- DNA Replication Is Highly Coordinated

Readings:

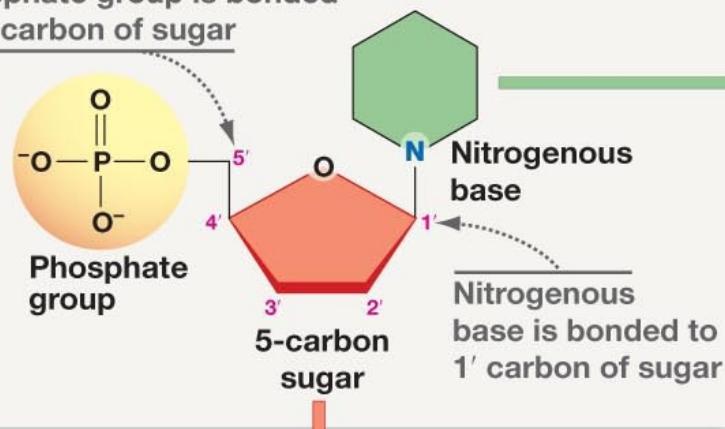


Tymoczko, Berg, Stryer,
Biochemistry, 2nd Edition,
Ch. 33 - 34, pp. 575 - 612
3rd Edition, Ch. 33-34, pp. 575 - 622
4th Edition, Ch. 33-34, pp. 673 - 707

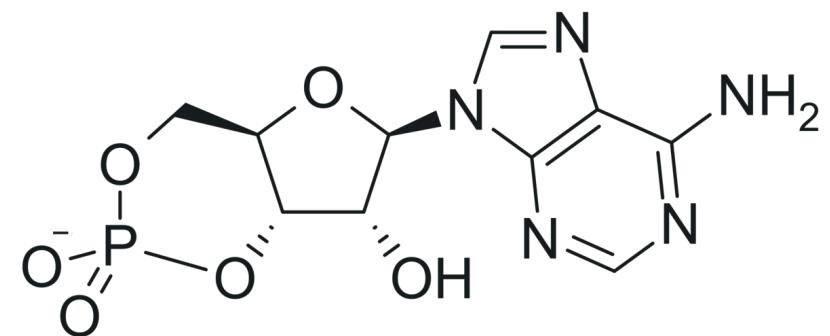
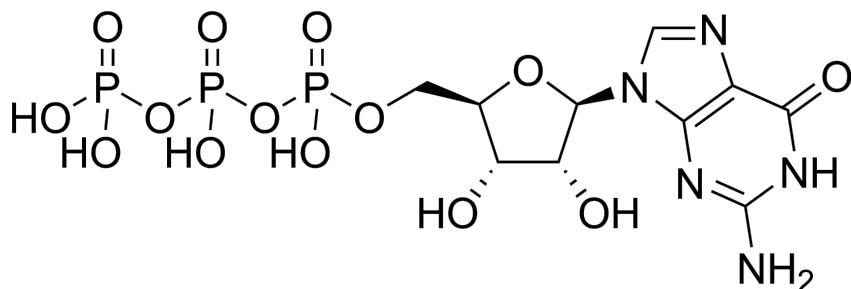
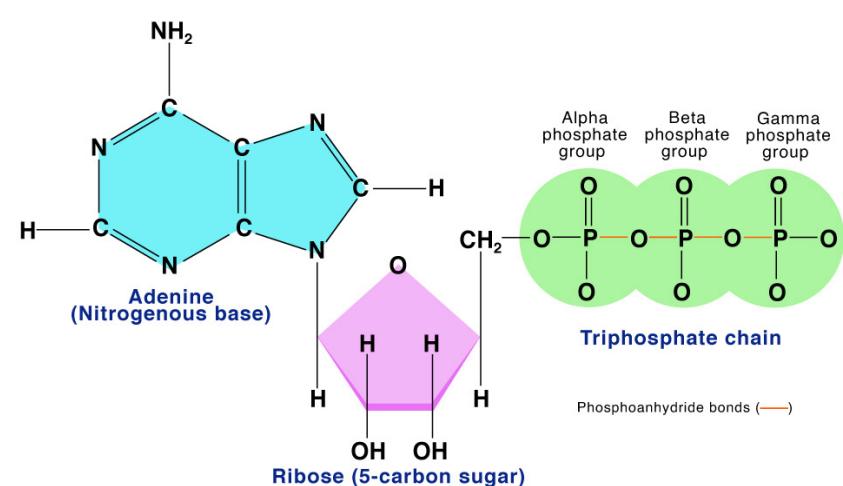
Nucleotides And Nucleosides

(a) Nucleotide

Phosphate group is bonded to 5' carbon of sugar



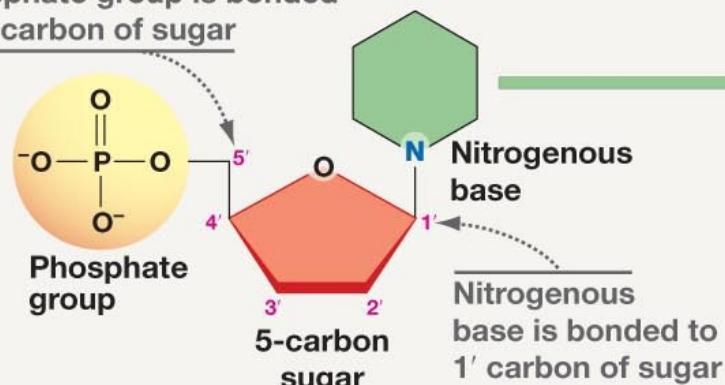
Nitrogenous base is bonded to 1' carbon of sugar



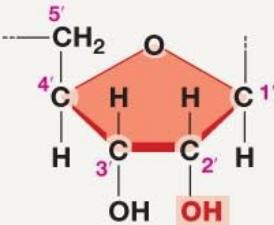
Nucleotides And Nucleosides

(a) Nucleotide

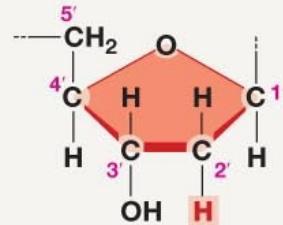
Phosphate group is bonded to 5' carbon of sugar



(b) Sugars

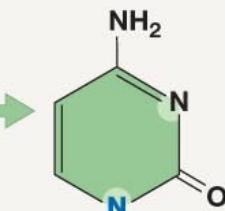


Ribose in RNA

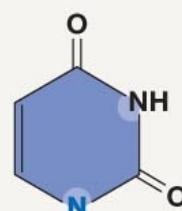


Deoxyribose in DNA

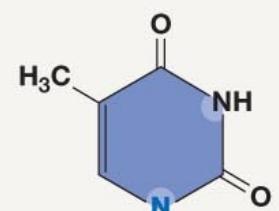
(c) Nitrogenous bases



Cytosine (C)

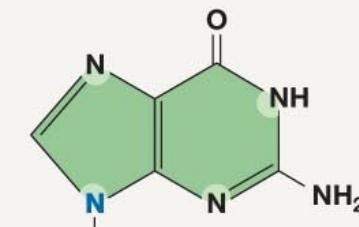


Uracil (U) in RNA

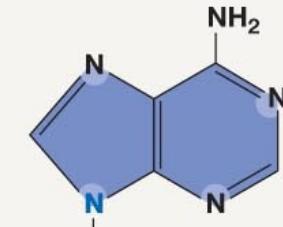


Thymine (T) in DNA

Pyrimidines



Guanine (G)



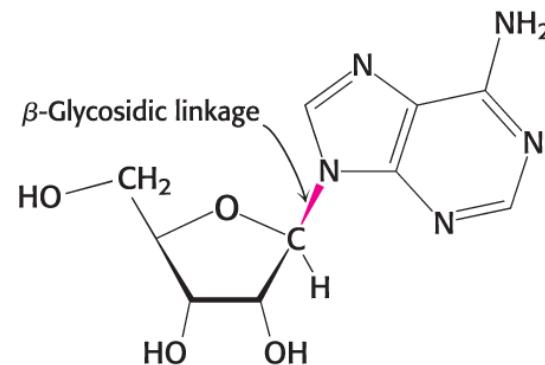
Adenine (A)

Purines are larger than pyrimidines

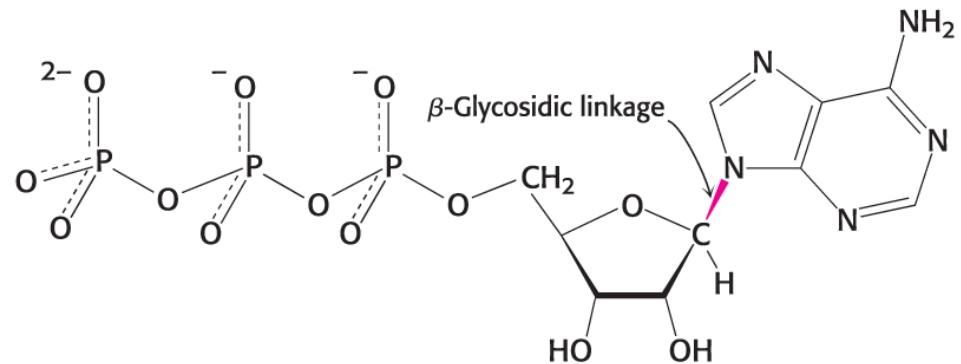
Purines

Nucleotides And Nucleosides

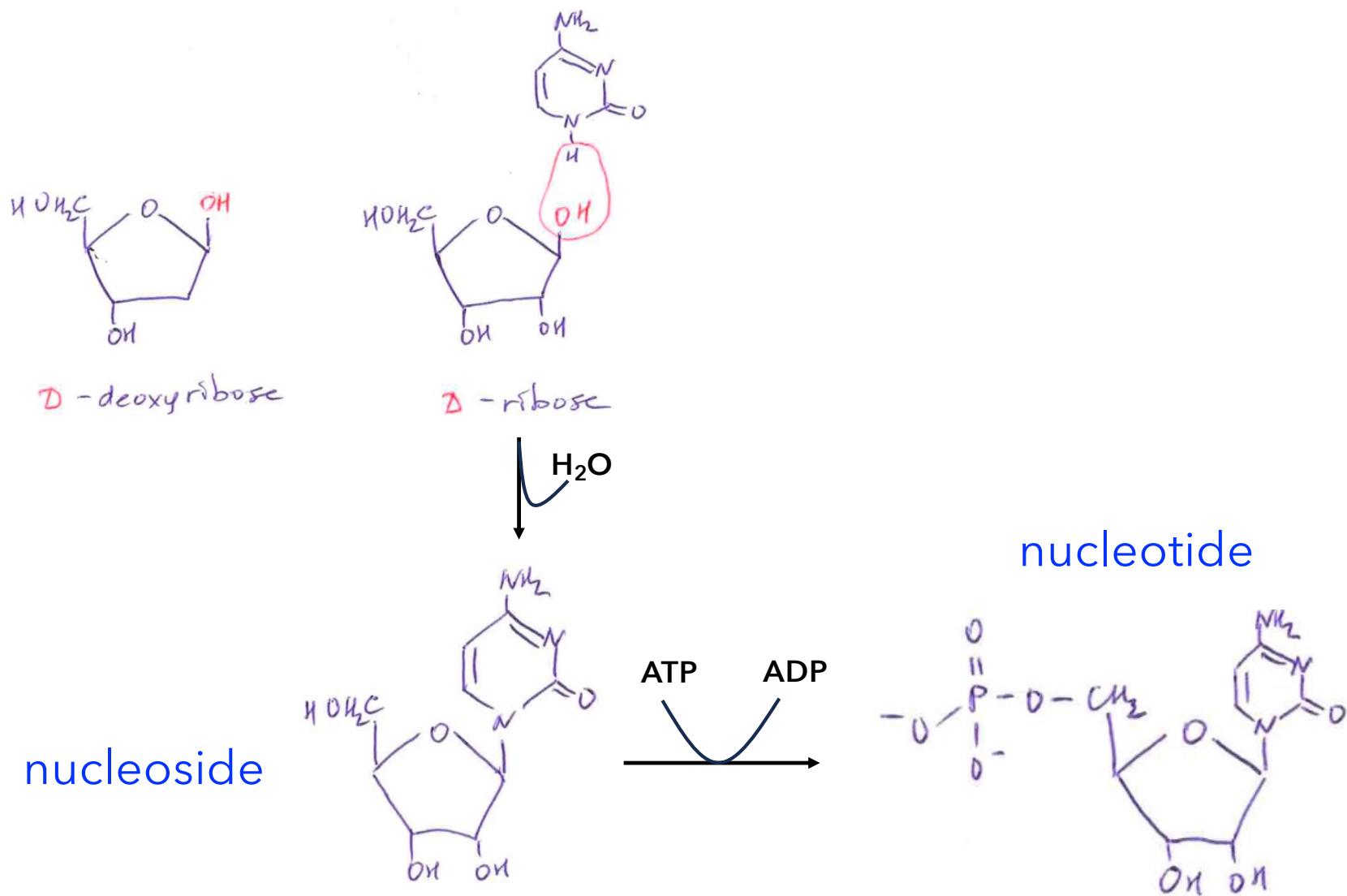
- A base bound to a sugar is called a **nucleoside**. The nucleosides of DNA are deoxyadenosine, deoxyguanosine, deoxycytidine, and deoxythymidine. By convention, deoxythymidine, which rarely occurs in RNA, is simply called thymidine.
- The nucleosides of RNA are adenosine, guanosine, cytidine, and uridine.
- In all cases, the C-1' of the sugar is attached to the N-9 of the purine or the N-1 of the pyrimidine.
- A **nucleotide** is a nucleoside with one or more phosphoryl groups attached.
- Nucleoside triphosphates are the building blocks of DNA and RNA.



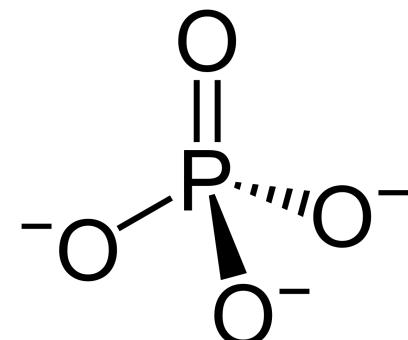
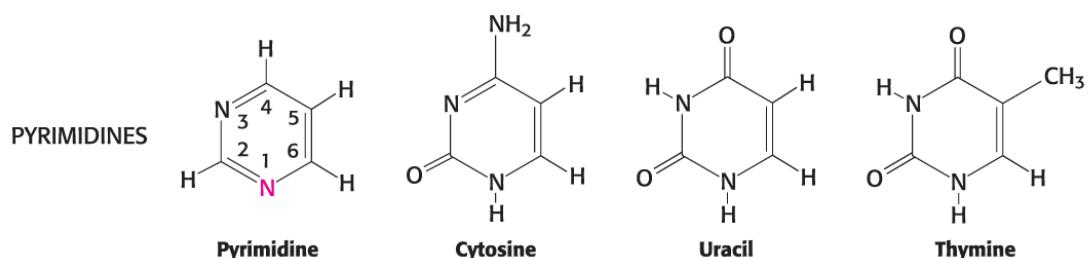
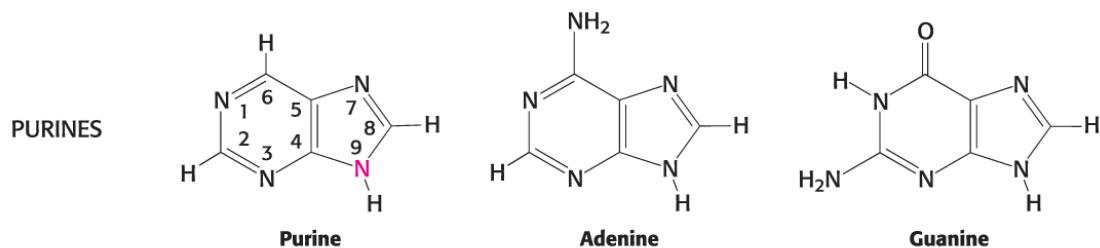
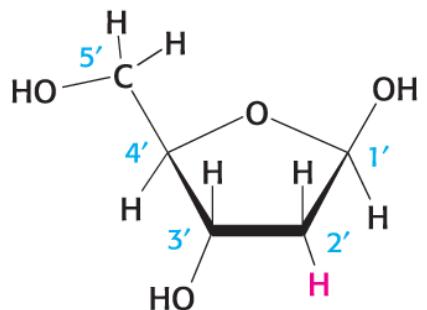
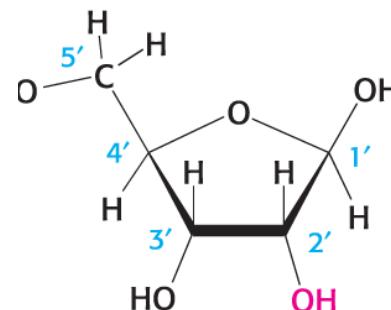
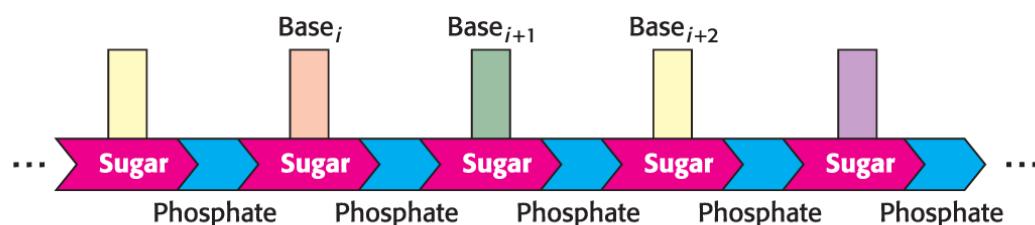
A nucleoside
(Adenosine)



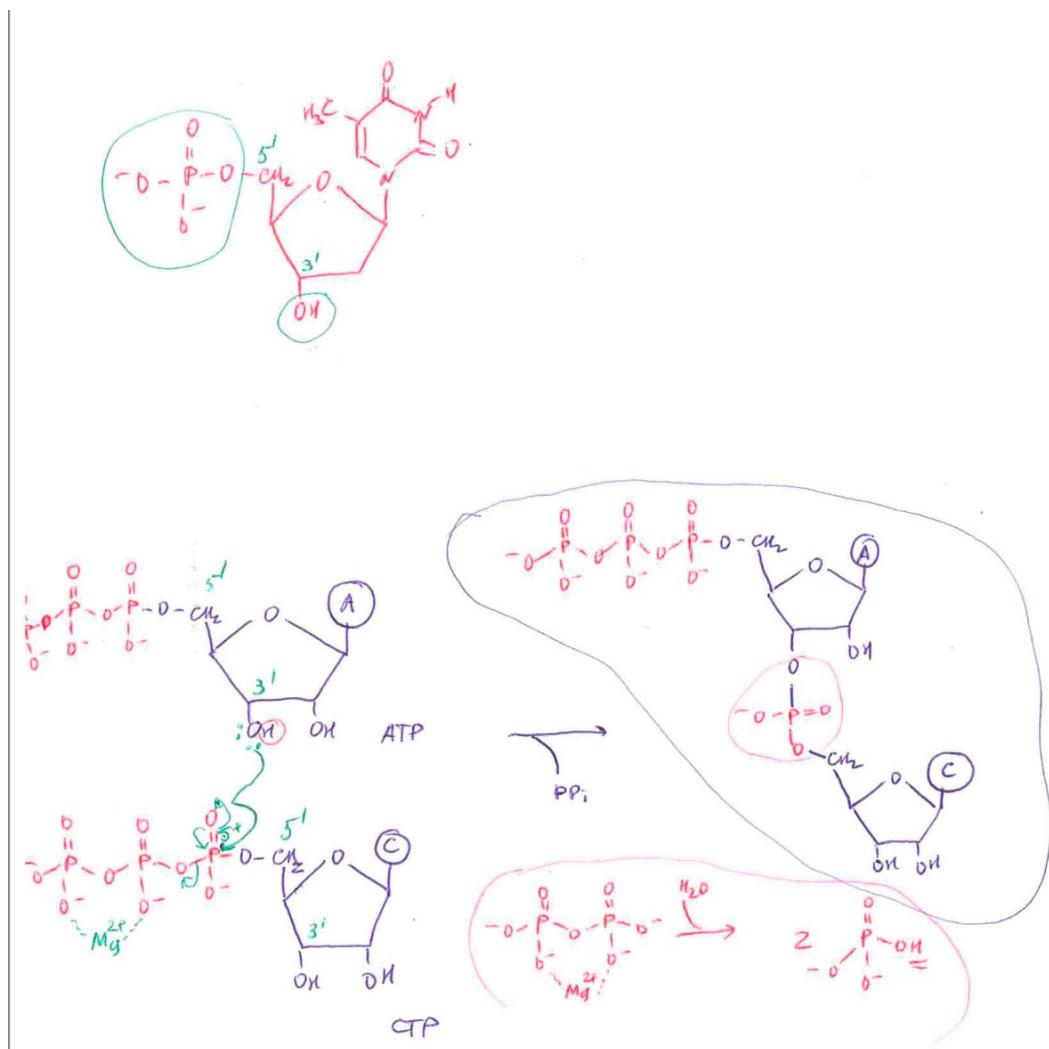
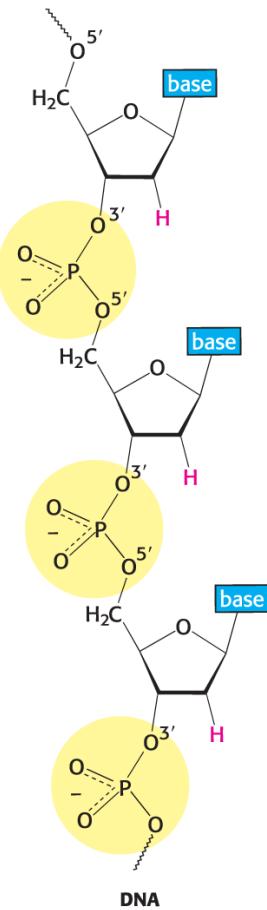
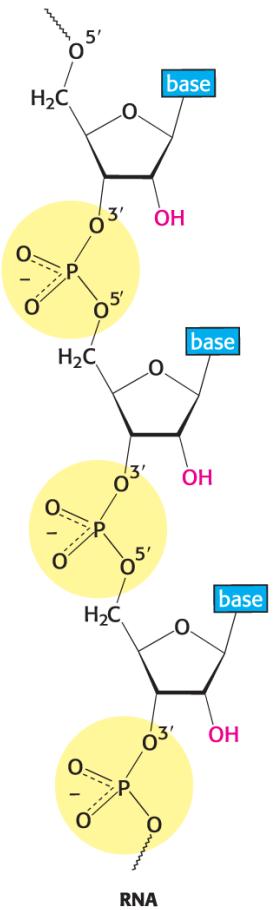
A nucleotide
(Adenosine 5'-triphosphate [5'-ATP])



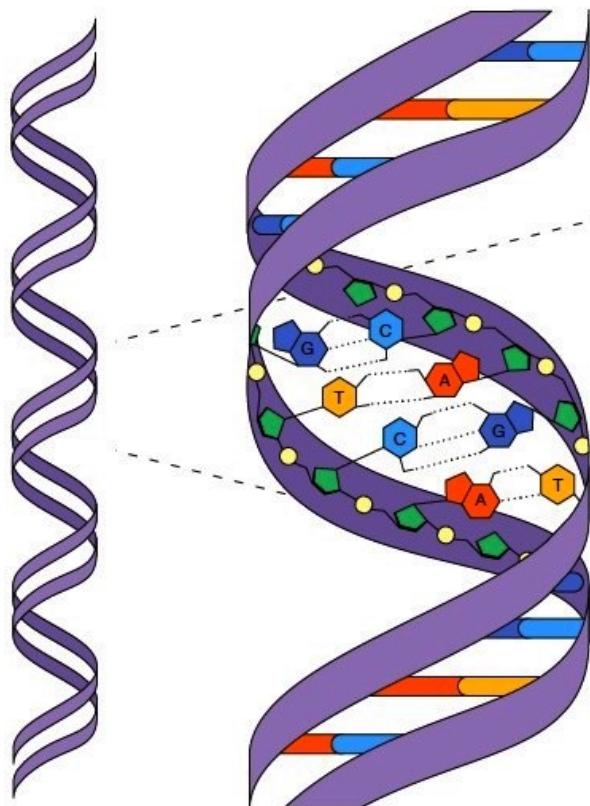
Nucleic Acid Structure: bases linked to a sugar-phosphate backbone



Nucleic Acid Structure: bases linked to a sugar-phosphate backbone

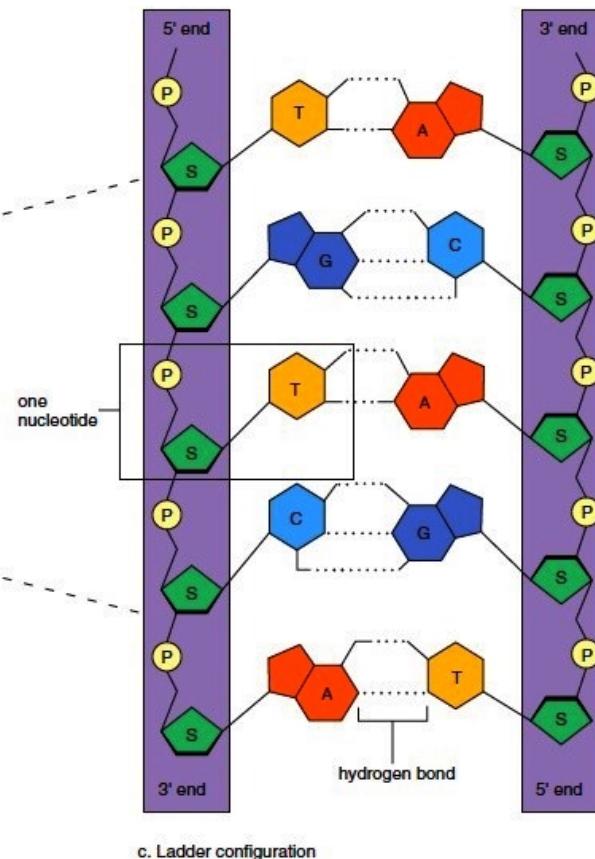


DNA forms a double helix



a. DNA double helix

b. Complementary base pairing



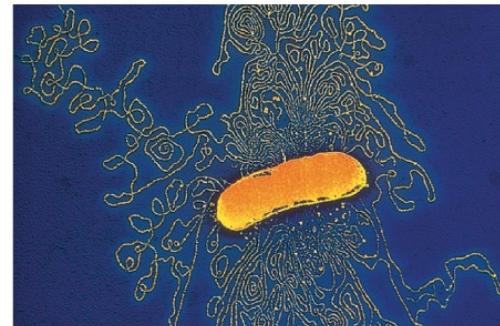
c. Ladder configuration

- DNA, the genetic information that is passed from one generation to the next, is composed of four nucleotides with the bases **A, G, C, and T**.
- DNA forms a double helix of two separate strands with complementary sequences.
- During replication, the two strands unwind, each serving as a template for a new daughter double helix. ⁹

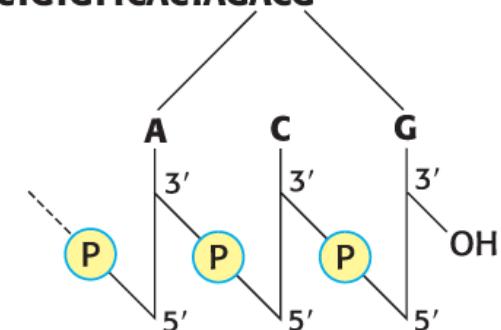
DNA Molecules

- Nucleic acid chains are presented by abbreviations such as pApGpCpT, pAGCT or more simply AGCT.
- Nucleic acid chains have directionality in that the two ends are different. One end has a phosphoryl group attached to the 5' carbon atom of the sugar and one end has a free hydroxyl attached to the 3' carbon of the sugar.
- Nucleic acid chains are written in the 5' to 3' direction.
- DNA molecules can be extremely long, some consisting of more than 1 billion nucleotides in length.

... ACATTTGCTTCTCGACAGACAACTGTGTTCACTAGACG



Dr. Gopal Murti/Science Source.



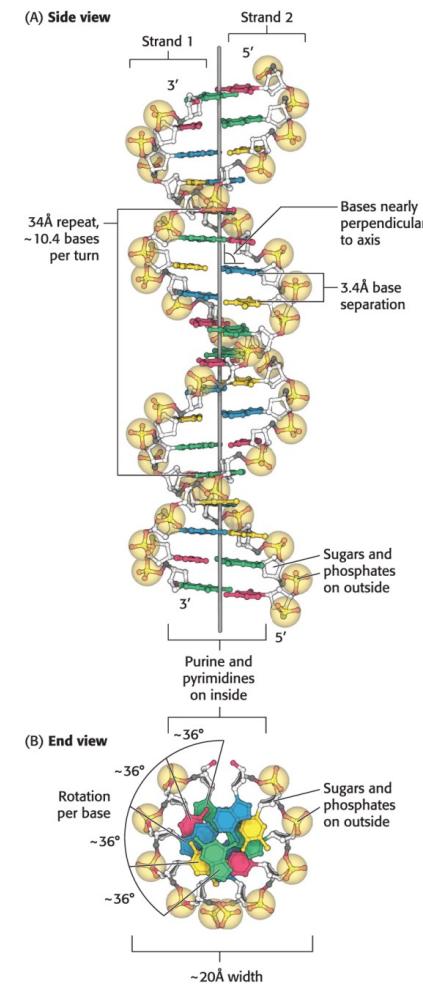
Most human cells have 6 billion base pairs of information. All 6 billion base pairs would be 3.6 meters in length if all of the molecules were laid end to end. Human beings are composed of approximately 10 trillion cells. If all of this DNA were strung end to end, it would reach to the sun and back about 65 times.

DNA Strands Can Form a Double-Helical Structure

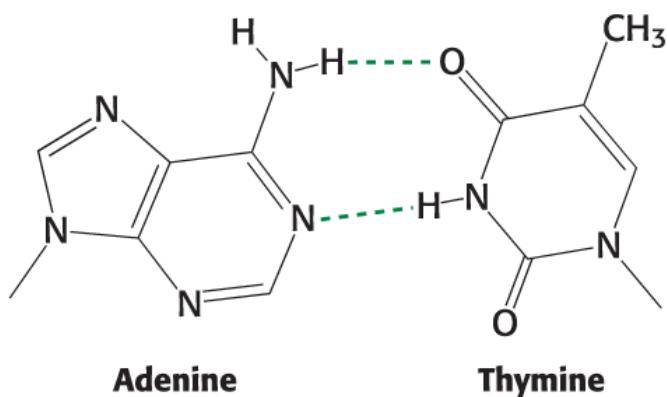
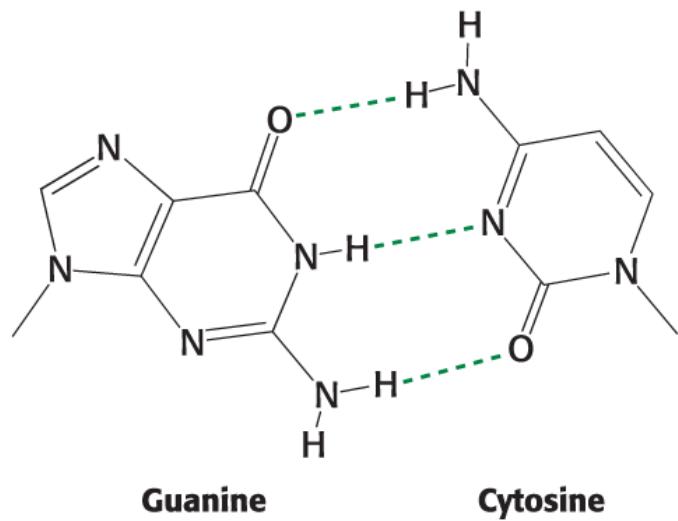
- The double helix is stabilized by **hydrogen bonds** and the **hydrophobic effect**.

General features of DNA are:

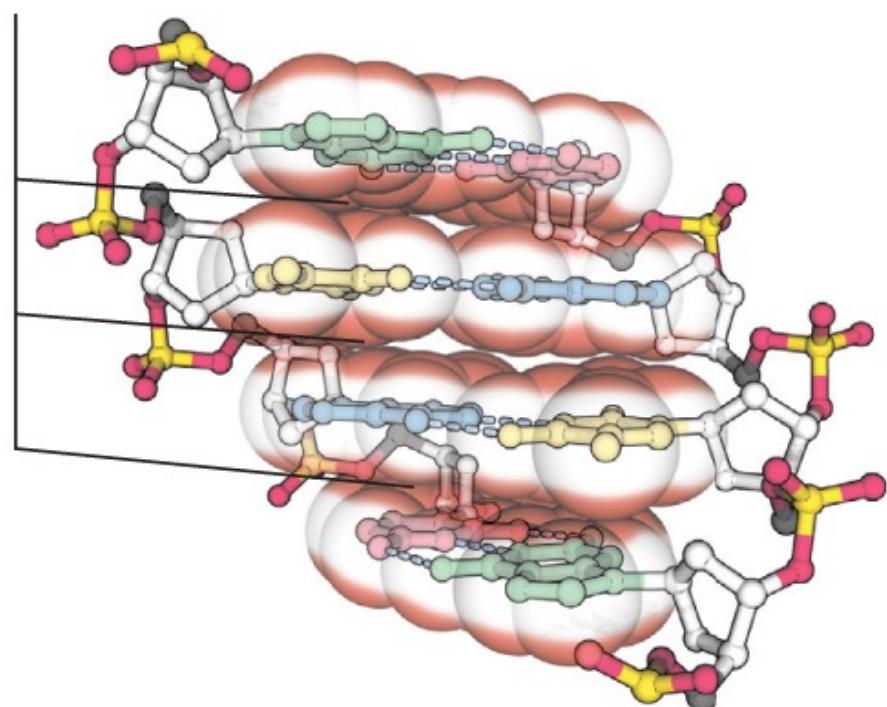
1. DNA molecules consist of two chains of opposite directionality—one strand runs in the 5' to 3' direction and the other in the 3' to 5' direction—intertwined to form a right-hand double helix.
2. The sugar-phosphate backbones are on the outside of the helix, whereas the bases are inside the helix.
3. The bases are perpendicular to the axis of the helix with adjacent bases separated by 3.4 Å.
4. The helix is approximately 20 Å wide.



Forces that stabilize the double helix



Base stacking
(van der Waal interactions)



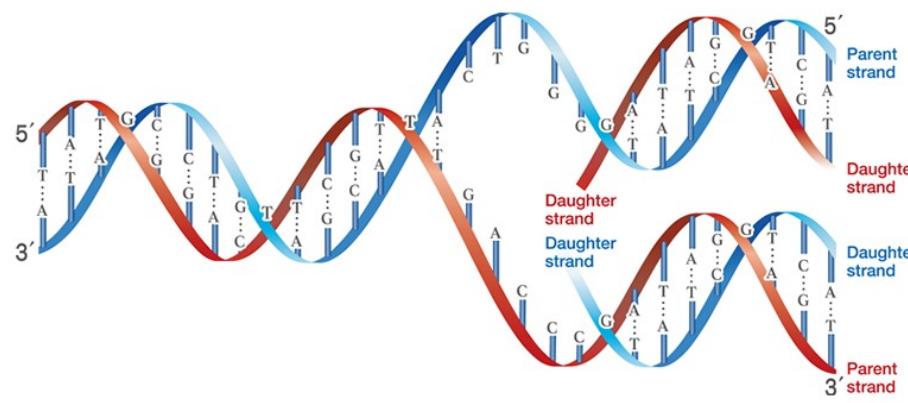
Quick Quiz 1

Which of the following is found in DNA but not in RNA?

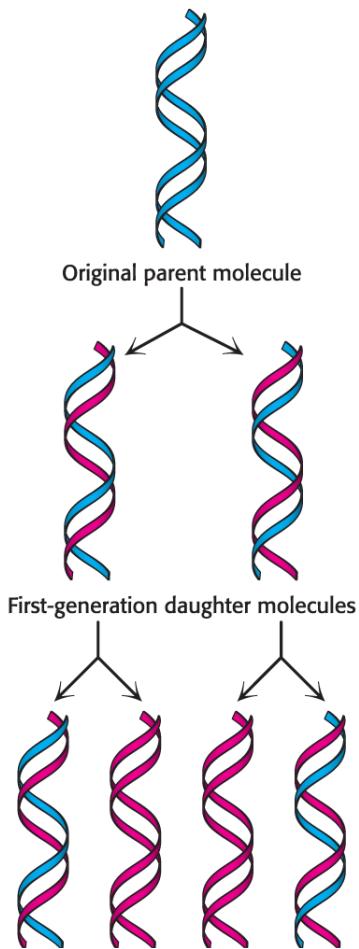
- A. ribose
- B. guanosine triphosphate
- C. purine
- D. uracil
- E. thymine

The Double Helix Facilitates the Accurate Transmission of Heredity Information

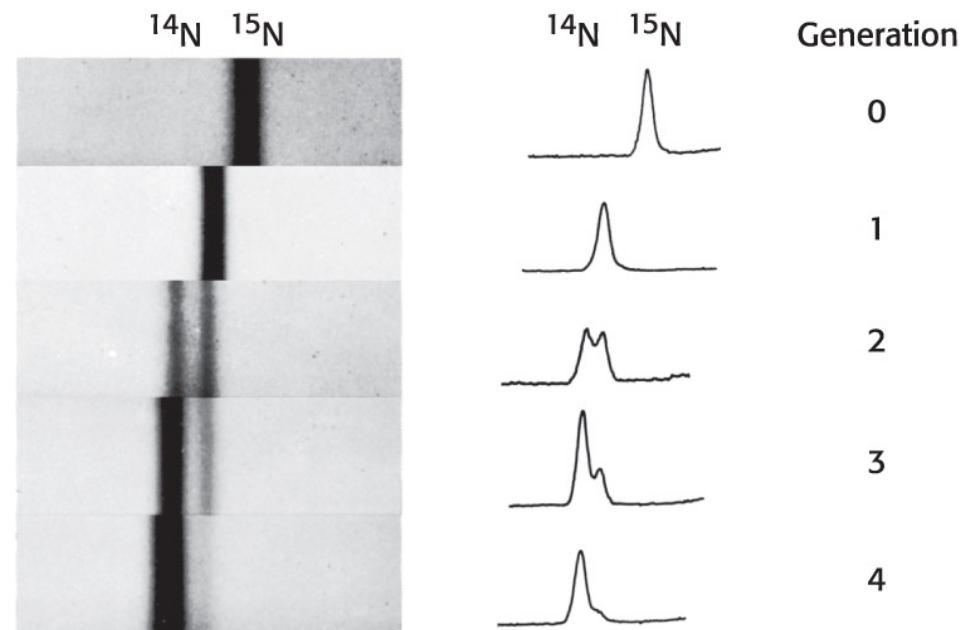
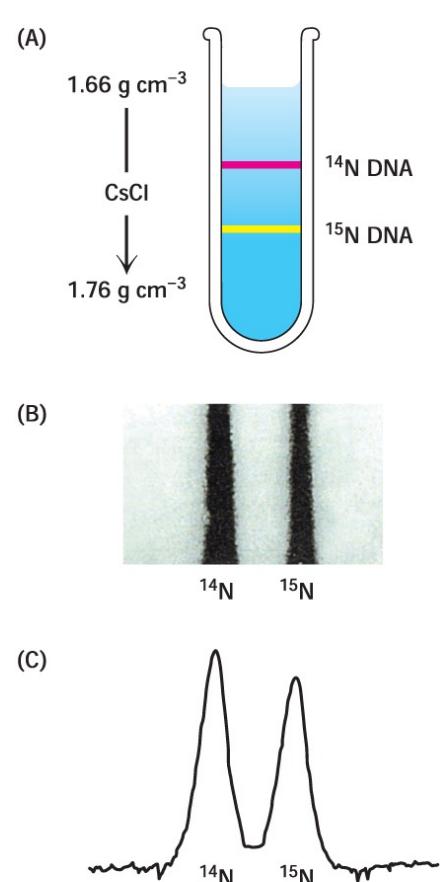
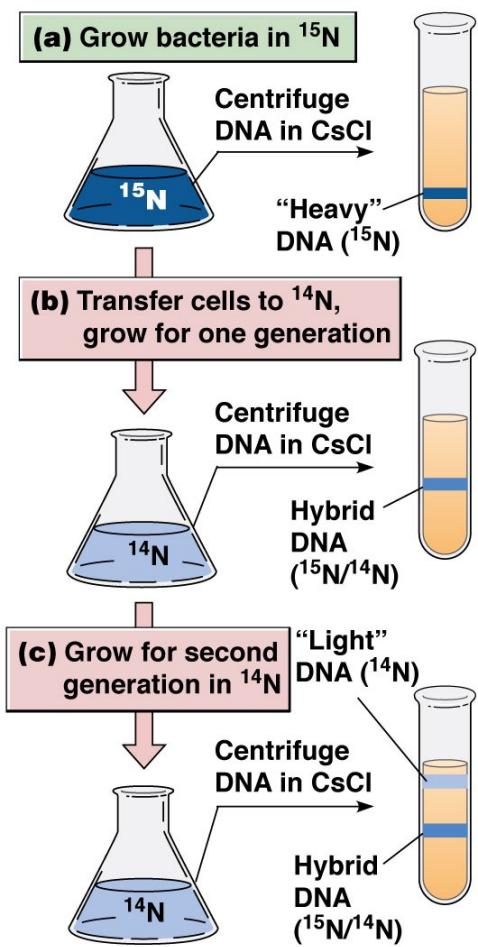
- Because of the base pairing rules, the sequence of one strand determines the sequence of the partner strand.
- The two strands can be separated and complementary sequences synthesized to generate two identical daughter strands.
- Because the two daughter helices have one parent strand and one newly synthesized strand, the replication process is called semiconservative replication.



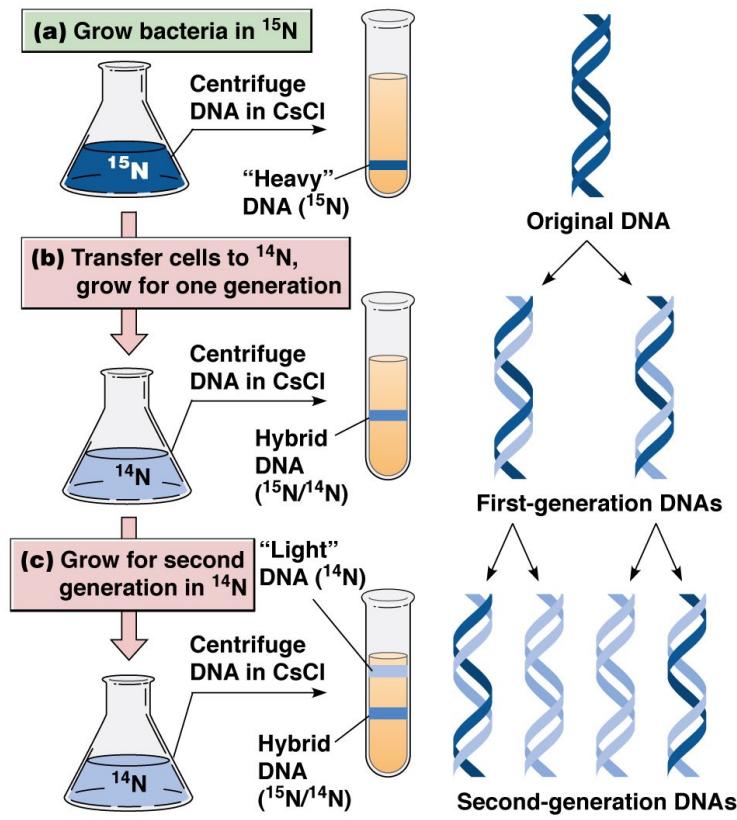
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The Double Helix Facilitates the Accurate Transmission of Heredity Information



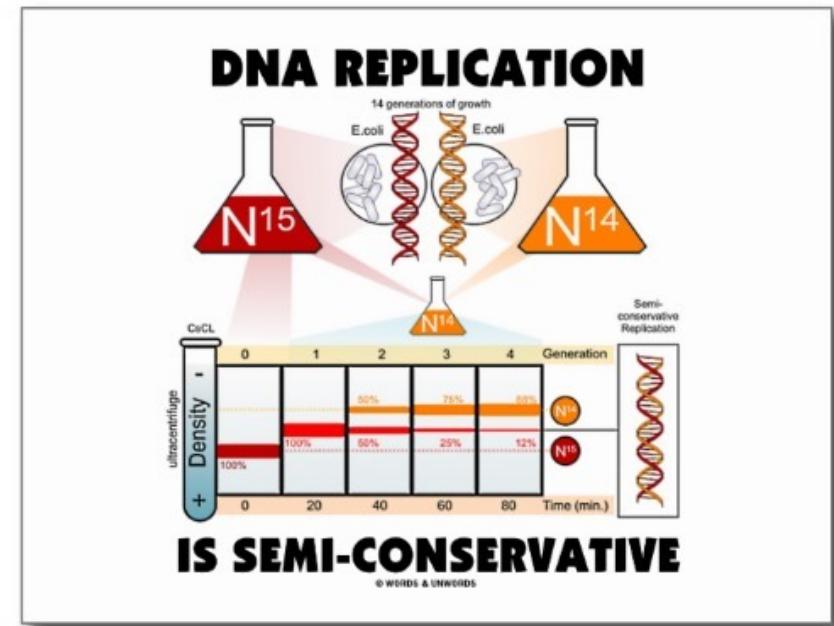
The Double Helix Facilitates the Accurate Transmission of Heredity Information



- Meselson and Stahl elegantly demonstrated that replication is semiconservative by growing bacteria in growth media supplemented with ^{15}N . The bacteria were then shifted to growth media with ^{14}N as the nitrogen source.
- Density gradient centrifugation established that upon the shift to ^{14}N medium, newly synthesized DNA consisted of DNA with equal parts ^{15}N -DNA and ^{14}N -DNA, a result consistent with semiconservative replication.

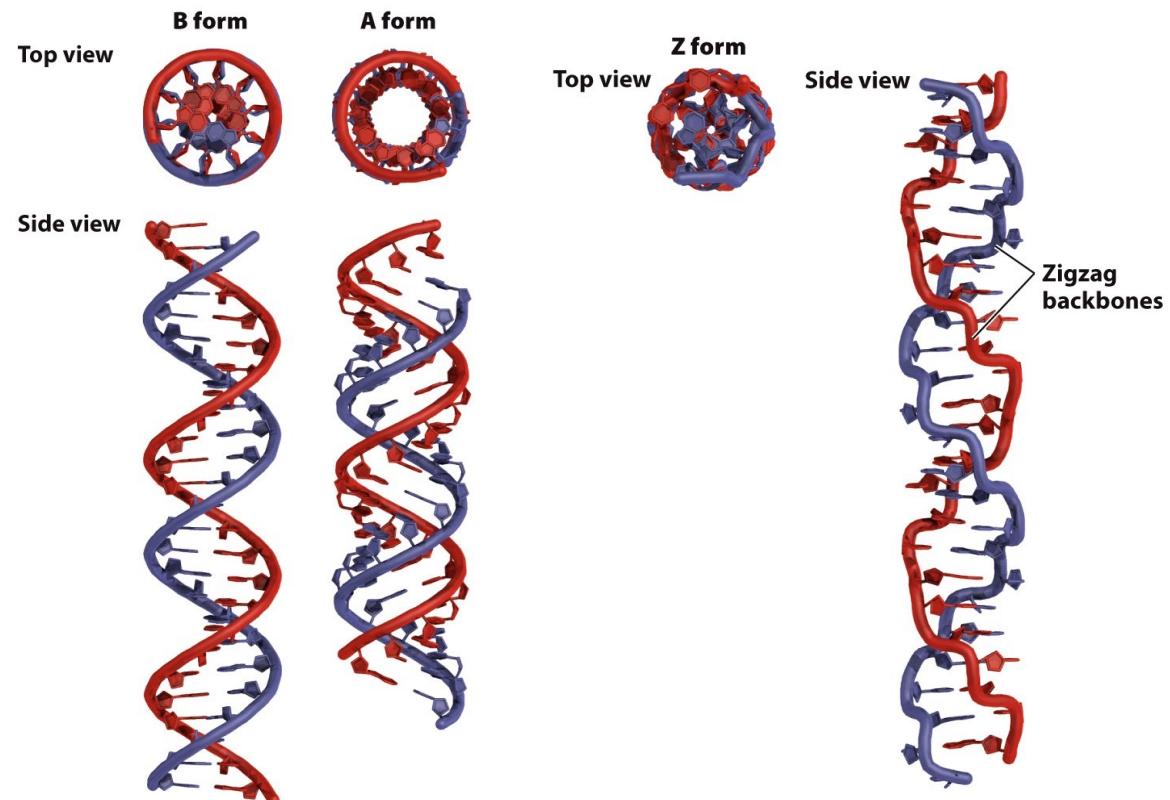
The Strands in the Double Helix can be Reversibly Separated

- During replication or transcription, the two strands of the DNA double helix must be separated.
- In the laboratory, DNA strands can be separated by heating a solution of DNA, a process called denaturation or melting. The temperature at which half of the DNA molecules are denatured is called the **melting temperature (T_m)**.
- Upon cooling, the two strands can bind to one another to reform the double helix, a process called **reannealing**.



DNA Double Helices Can Adopt Multiple Forms

- In the cell, the most commonly seen form of DNA double helix is called the **B** form or the Watson-Crick helix.
- The double helix can also exist in an **A** form, which is shorter and wider than the B form with the bases at an angle rather than perpendicular to the helix axis.
- The **A** form is seen in RNA double helices and in RNA-DNA hybrid helices, structures observed in transcription and RNA processing.
- The double helix can also form **Z** DNA. **Z DNA** is left-handed and the backbone is zigzagged, accounting for the name "**Z DNA**."



Quick Quiz 2

When RNA adopts a tertiary structure, which of the following can occur?

- A. non-standard base-pairing
- B. Watson-Crick base-pairing
- C. metal coordination
- D. All of the above.
- E. unpaired bases

The Major and Minor Grooves

- DNA in the **B** form has a **major groove** and a **minor groove**.
- The presence of the grooves allows access to the hydrogen-bonding capabilities of the exposed bases.
- The hydrogen bonding capability provides a means of sequence-specific interactions between DNA and the molecules it must interact with in the processes of replication and transcription.

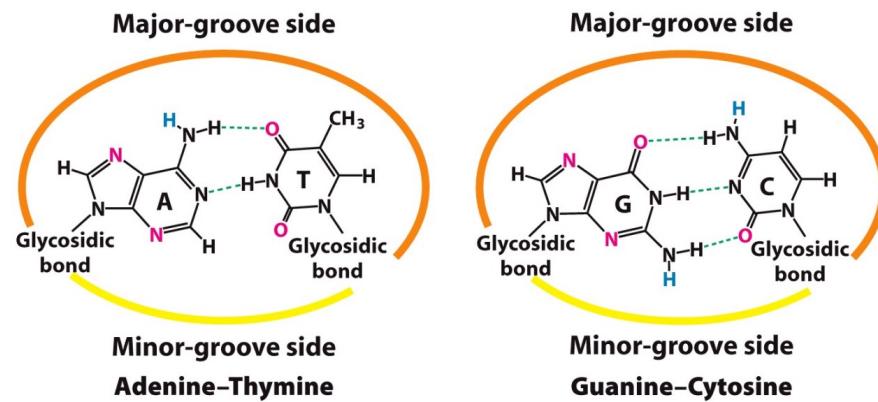


Figure 33.19
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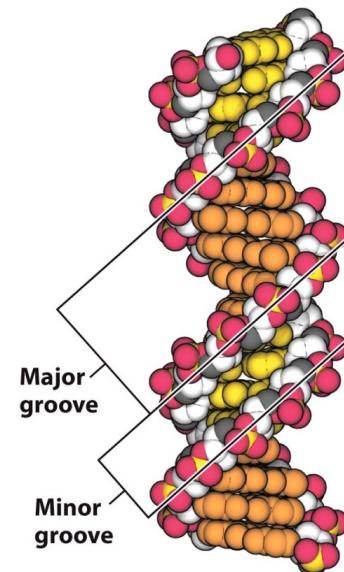
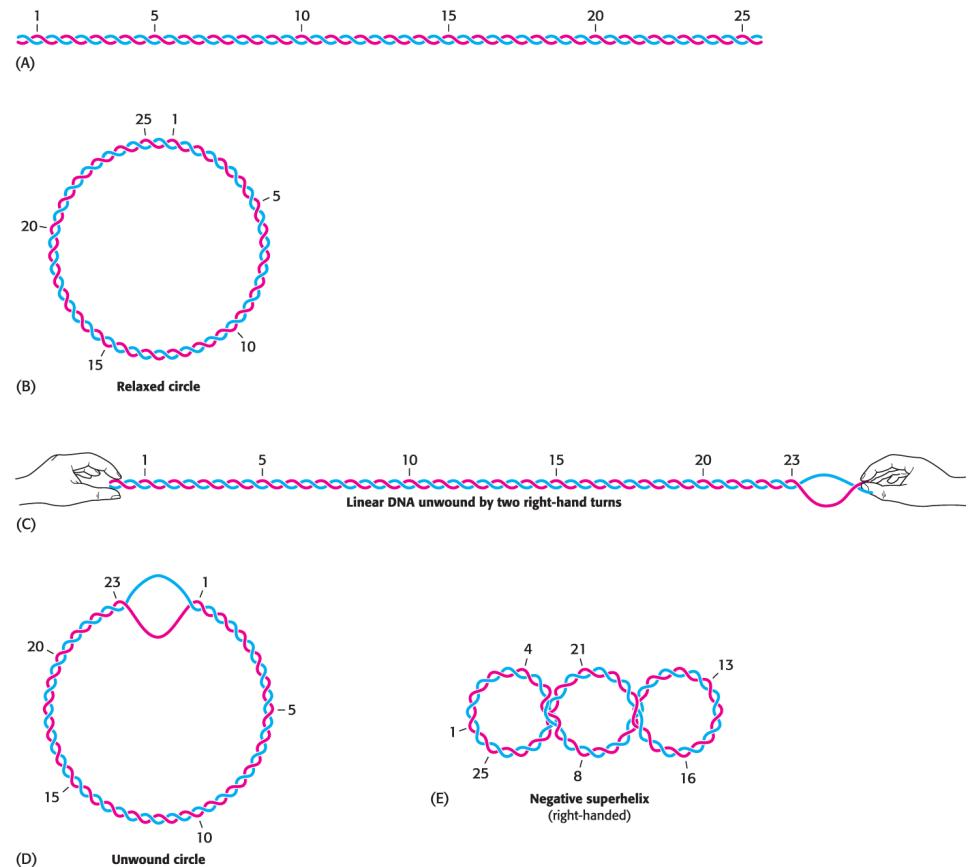


Figure 33.20
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Double-Stranded DNA can wrap around itself to form supercoiled structures

- The DNA molecules in human chromosomes are linear.
- The term *circular* refers to the continuity of the DNA chains, not to their geometric forms.



Eukaryotic DNA Is Associated with Specific Proteins

- There are 3.6 meters of DNA in a human cell, packaged into 46 chromosomes.
- Supercoiling accounts for some of the compaction of the DNA, but further compaction occurs by binding certain proteins to the DNA.
- **Chromatin** is the entire complement of a cell's DNA and its associated proteins.
- **Histones** are highly basic proteins that are components of chromatin.
- Two copies each of histones H2A, H2B, H3, H4 and 200 bp of DNA comprise a **nucleosome**.
- Nucleosomes are joined by **linker DNA**, to which histone H1 binds, so that the histone-DNA complex has the appearance of beads on a string.
- Digestion of the linker DNA yields the **nucleosome core particle**.

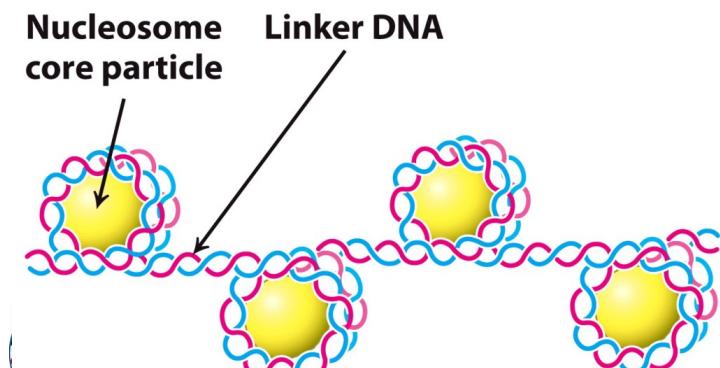


Figure 33.25
Don W. Fawcett/Science Source.

Eukaryotic DNA Is Wrapped Around Histones to Form Nucleosomes

- The eight histones of the core particle are arranged as an octamer composed of $(H3)2(H4)2$ tetramer and a pair of $(H2A-H2B)$ dimers.
- DNA wraps around the outside of the octamer.
- Nucleosomes themselves are arranged in a helical array that further compacts the DNA. Further folding generates the **chromosome**.

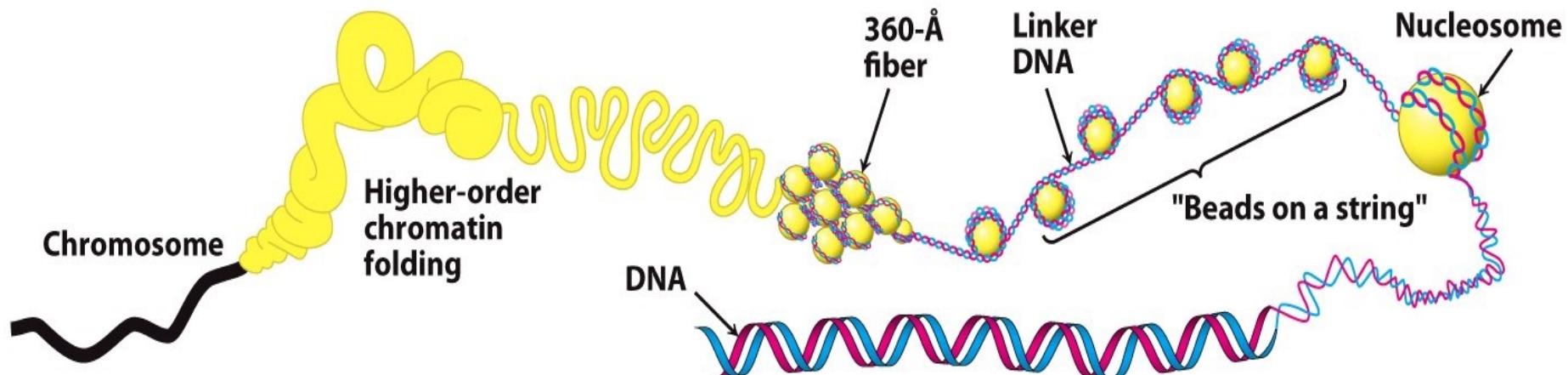


Figure 33.28

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Quick Quiz 3

Eukaryotic DNA is tightly bound to a group of small basic proteins called .

- A. chromatin
- B. histones
- C. nucleosomes
- D. transcription factors
- E. ubiquitin