Slide 1

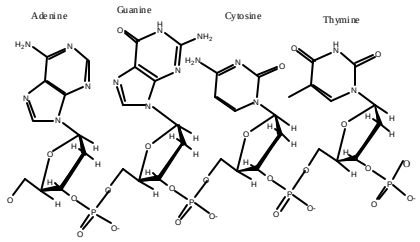
Nucleic Acid Structure

- Linear polymer of nucleotides
- Phosphodiester linkage between 3' and 5' positions
- See Figure 11.17

Slide 2

Nucleic Acid Sequence Abbreviations

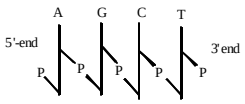
- Sequence normally written in 5'-3' direction, for example:



Slide 3

Sequence Abbreviations, con't.

Let Letter stand for **base:**



Let Letter stand for **nucleoside**

5'-end pApGpCpTp 3'-end

Let Letter stand for **nucleotide**

5'-end AGCT 3'-end

Slide 4

Biological Roles of Nucleic Acids

- DNA carries genetic information
  - 1 copy (haploid) or 2 copies (diploid) per cell
  - See "History of Search for Genetic Material"
- RNA at least four types and functions
  - messenger RNA—structural gene information
  - transfer RNA—translation "dictionary"
  - ribosomal RNA—translation "factory"
  - small nuclear RNA—RNA processing

Slide 5

DNA Structure

- Watson-Crick Double Helix
  - Clues from Chargaff's Rules
    - A=T, C=G, purines=pyrimidines
  - Helical dimensions from Franklin and Wilkins X-ray diffraction studies
  - Recognition of complementary base pairing possibility given correct tautomeric structure (See Fig's. 11.6, 11.7, 11.20)

Slide 6

Nature of DNA Helix

- Antiparallel strands
- Ribose phosphate chain on outside
- Bases stacked in middle like stairs in a spiral staircase
  - Figure 11.19—schematic representation
- Complementary strands provide possible mechanism for replication
  - Figure 11.21 representation of replication process

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Size of DNA Molecules

- 2 nm diameter, about 0.35 nm per base pair in length
- Very long, millions of base pairs

Organism	Base Pairs	MW	Length
• SV 40 virus	5.1 Kb	3.4×10^6	1.7 µm
• λ phage	48 Kb	32×10^6	17 µm
• E. coli	4,600 Kb	2.7×10^9	1.6 mm
• Yeast	13,500 Kb	9×10^9	4.6 mm
• Human	2.9×10^6 Kb	1.9×10^{12}	0.99 m

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Packaging of DNA

- Very compact and folded
  - E. coli DNA is 1.6 mm long, but the E. coli cell is only 0.002 mm long
    - See Figure 11.22
  - Eukaryotic cells have DNA packaged in chromosomes, with DNA wrapped around an octameric complex of **histone** proteins
    - See Figure 11.23

Histones are rich in the basic amino acids lysine and arginine, which have positive charges. These positively charged residues provide binding for the negatively charged ribose-phosphate chain of DNA.

Slide 9

Messenger RNA

- "Transcription" product of DNA
- Carries sequence information for proteins
  - Prokaryote mRNA may code for multiple proteins
  - Eukaryote mRNA codes for single protein, but code ("exon") might be separated by non-coding sequence ("introns")
    - See Figure 11.24

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Ribosomal RNA

- "Scaffold" for proteins involved in protein synthesis
- RNA has catalytic activity as the "peptidyl transferase" which forms the peptide bond
- Prokaryotes and Eukaryotes have slightly different ribosomal structures (See Figure 11.25)
- Ribosomal RNA contains some modified nucleosides (See Figure 11.26)

Remember that the sedimentation rate is related to molecular weight, but is not directly proportional to it because it depends both on molecular weight (which influences the sedimentation force) and the shape of the molecule (which influences the frictional force).

Slide 11

Transfer RNA

- Small molecules—73-94 residues
- Carries an amino acid for protein synthesis
- One or more t-RNA's for each amino acid
- "Anti-codon" in t-RNA recognizes the nucleotide "code word" in m-RNA
- 3'-Terminal sequence always CCA
- Amino acid attached to 2' or 3' of 3'-terminal A
- Many modified bases (Also Figure 11.26)

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Small Nuclear RNA's

- Found in Eukaryotic cells, principally in the nucleus
- Similar in size to t-RNA
- Complexed with proteins in **small nuclear ribonucleoprotein particles** or **snRNPs**
- Involved in processing Eukaryotic transcripts into m-RNA

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Chemical Differences Between DNA and RNA

- Base Hydrolysis
  - DNA stable to base hydrolysis
  - RNA hydrolyzed by base because of the 2'-OH group. Mixture of 2' and 3' nucleotides produced
    - See Figure 11.29
  - DNA more susceptible to mild (1 N) acid
    - Hydrolyzes purine glycosidic bond, forming **apurinic acid**

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DNA Secondary Structure, details

- Notice the dimensions of the double helical "twisted ladder" structure for DNA (See Figure 12.9)
  - Sugar-phosphate backbone on outside
  - Bases inside with AT and GC specific pairings
  - Twisted structure gives base-pair spacing of 0.34 nm

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Features of the Helix

- Note the dimensions of the AT and GC base pairs are almost identical. (Figure 12.10).
- Major and Minor Grooves (See Figure 12.11)
- See Chime tutorial on DNA structure.
  - (Note—doesn't work with Internet Explorer, and sometimes gives problems with javascript errors)

Major groove is large enough to accommodate an alpha-helix of a protein. The edges of the bases in the major and minor grooves show a different hydrogen bonding possibility for each base pair, hence proteins can recognize which base pair is which. Many regulatory proteins (as well as the restriction enzymes we discussed earlier) are therefore capable of recognizing specific base sequences.
The propeller twist of the bases increases the hydrophobic overlap of bases in the same strand.

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Other DNA Helical Structures

- B-DNA—first one determined
  - Right-handed; 2.37 nm diameter
  - 0.33 nm rise; ~10 bp per turn
- A-DNA—dehydrated fibers (and RNA)
  - Right-handed; 2.55 nm diameter
  - 0.23 nm rise; ~11 bp per turn
- Z-DNA—GC pair sequences
  - Left-handed; 1.84 nm diameter
  - 0.38 nm rise; 12 bp per turn
  - (See Table 12.1)

A-DNA is "short and broad"; B-DNA is a little "longer and thinner"; Z-DNA is "longest, thinnest"

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A, B, and Z DNA, con't.

- See Figure 12.13 for side-by-side comparisons of the three helices.
- See also a Chime presentation of A, B, and Z DNA side by side written by David Marcey, California Lutheran University.

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A, B, and Z DNA, con't.

- The G in Z-DNA has the *syn* conformation.
  - (See Figure 12.14)
- Base pair rotated to form left-handed structure (G flips *anti* to *syn*, while the C-ribose flips as a unit).
  - (See Figure 12.15)
- See Chime presentation of syn and anti conformations.
- Methylation of C also favors B to Z switch

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Supercoiling

- The two strands of DNA wrap around each other. The number of turns is called the **linking number** (L). It can be manifest in two ways:
  - The number of turns of the strands make around the helix axis is is called the **twist** (**T**).
  - The number of times the helix axis wraps around itself is called the **writhe**. This is called **supercoiling**.
  - You experience supercoiling with your telephone cord, or by coiling a rope.

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Supercoiling, con't.

- Linking number is defined only if ends are unable to rotate:
  - Circular DNA with closed ends.
  - Stretch of DNA in a much larger molecule.
- There is a natural twist in DNA
  - B-DNA is 10.5 bases per turn.
  - Z-DNA has a left-handed (negative) twist.
- If **L** is different than **T**, the difference shows up in **W.**

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Supercoiling of Circular DNA

- L = T + W
- Phenomenon studied in circular DNA plasmids.
- In closed circle, L is fixed.
- T can be influenced by conversion to Z-DNA, or by intercalating agents.
  - (Both would lower T)

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Supercoiling of Circular DNA, con't.

- Plasmids can be negatively supercoiled (L<T) or positively supercoiled (L>T).
- Plasmids with different W are called **topoisomers**. They can be separated by electrophoresis.
  - The greater the supercoiling, the more compact the structure. See Fig. 12.23.

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Supercoiling of Circular DNA, con't.

- Two classes of enzymes that can change the linking number by breaking and forming phosphodiester linkage.
  - Topoisomerase 1 makes single strand cut. DNA "relaxes", **w** changes toward zero.
  - Topoisomerase 2 makes double strand cut, passing strand through space. Decreases linking number by 2—introducing negative supercoiling. ATP is required.

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Supercoiling

- Most natural DNA is negatively supercoiled (**W** is negative).
- Supercoiling needed to compact the DNA, and in eukaryotes to wrap around histones.
- Negative supercoiling makes it easier to pull strands apart for both replication and transcription.