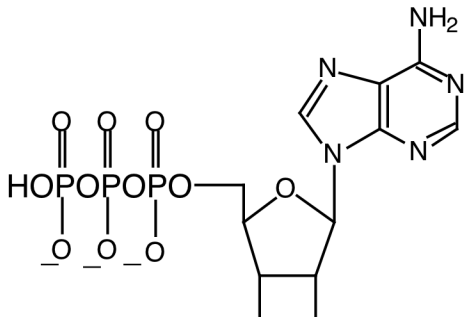
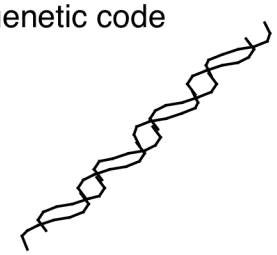
recombinant DNA



17

genetic code

viruses



AIDS

Nucleic Acids

CHAPTER SUMMARY

17.1 The Chemical Structure of Nucleic Acids

Nucleic acids are the biopolymers which constitute our genes. The monomer unit is called a **nucleotide**. A nucleotide is composed of a **heterocyclic base**, either a **purine** or **pyrimidine**, a **ribose** or **deoxyribose** sugar unit, and a **phosphat**e group.

The two types of nucleic acids are **DNA (deoxyribonucleic acid)** and **RNA (ribonucleic acid)**. These differ in their chemical makeup in the sugar group: deoxyribose in DNA and ribose in RNA; and in the heterocyclic bases: **DNA has adenine(A), guanine(G), thymine(T), and cytosine(C) while RNA has uracil(U) in place of thymine.** The primary structures of DNA and RNA polymers have phosphodiester bridges between (deoxy)ribose units to form a sugar-phosphate backbone. The bases are covalently bound from the hemiacetal group of the sugar to a ring nitrogen. Nucleic acid polymers are usually written from the 5' end (of the sugar unit) to the 3' end, left to right. Often the backbone is represented simply as a horizontal line with the bases protruding. The acidity of the polyprotic phosphate imparts a negative charge and hydrophilicity to the sugar-phosphate backbone at physiological pH. The polymerization of just a few nucleotides produces an **oligonucleotide** while many comprise a **polynucleotide** and a very large number, a nucleic acid.

The secondary structure of nucleic acids involves **hydrogen bonding** between the heterocyclic bases. A and T can form two hydrogen bonds (A ⋯ T) as can A and U (A = U) while G and C form three (G ≡ C).

17.2 Other Structures Involving Nucleotides

A. Energy Intermediates

Mononucleotides and dinucleotides are important in metabolism. Adenosine tri-, di- and mono-phosphates, **ATP, ADP and AMP**, are energy intermediates.

B. Chemical Messengers

Cyclic adenosine monophosphate (**cAMP**) acts as an intermediary in transferring a chemical signal from outside a cell to the metabolic processes inside a cell.

C. Redox Factors - Nucleotide Vitamins

Nicotinamide(niacinamide) adenine dinucleotide, **NAD^+**, and the flavin mono- and di- nucleotides (**FMN, FAD**) exist in oxidized and reduced forms. This makes them invaluable cofactors in enzymatically catalyzed oxidation-reduction reactions.

17.3 The Hierarchy of Nucleic Acid Structure

A. DNA Structure: The Double Helix

In DNA two polynucleotide strands hydrogen bond to each other through their bases in an **antiparallel** fashion. Bond angles in the sugar-phosphate backbone cause the double strand to twist into a helix. This is the classical **double helix structure of DNA** as postulated by Watson, Crick and Wilkinson. DNA is complexed with basic proteins called **histones** forming supercoiled coils. RNA can appear as a double helix but is usually found as a single strand (ss) taking on a variety of secondary structures depending upon its function.

B. RNA Structure

RNA has a polymeric structure similar to that of DNA with the substitution of a uracil for thymine. The overall structure of RNA can be single or double-stranded and RNA performs a variety of functions having to do with the transcription and translation of the DNA genetic code into functional proteins.

17.4 The Genetic Code

The main function of DNA is to **store genetic information in its nucleotide sequence**. The genetic code consists of base triplets (**codons**) most of which correspond to one of the 20 fundamental amino acids in proteins.

A. DNA Replication

Replication or duplication of DNA is a **semiconservative** process which depends upon **base pairing**, that is, hydrogen bonding. The double helical DNA partially unwinds and cellular nucleotide triphosphates pair with the exposed bases. Enzymes effect the polymerization process with the result being two DNA helices, each with a parent strand and a daughter strand.

CONNECTIONS 17.1 The Human Genome Project

B. Transcription and Translation

The **transcription**(copying in mRNA reciprocal code) **and translation**(using the mRNA to place amino acids in the proper sequence) of the DNA code to protein products proceeds through a complicated series of steps first involving the formation of a **messenger RNA (mRNA)** having a base sequence complementary to that of the parent DNA strand. The mRNA then associates with **ribosomal RNA (rRNA)** - protein complexes. **Transfer RNA (tRNA)** molecules bearing specific amino acids are then base-paired with the mRNA. Many enzyme-catalyzed reactions later, a protein product is formed.

A higher order (eukaryotic) gene contains both coding (**exon**) sequences and intervening (**intron**) or noncoding sequences. Therefore the transcription and translation process is also one of cutting and splicing the exon sequences for the production of a functional protein.

17.5 Characteristics of Transcription and Translation

Among the key characteristics of DNA code interpretation are that the code is nearly universal, is degenerate, has no coding overlaps, is fairly reliable, and consumes energy.

17.6 Mutation of DNA

Although the replication and transcription/translation processes occur with high fidelity, occasionally **mutations** can occur. These can lead to death,

predisposition to disease, congenital malformations or syndromes, or evolutionary progress.

CONNECTIONS 17.2 Acquired Immune Deficiency Syndrome: AIDS

17.7 Viruses

Viruses are species consisting of nucleic acids, usually ssRNA, encased in a **protein coat** and require a host organism for their replication. Once a virus invades a host cell, it uses its own **reverse transcriptase** enzyme to encode its genome into the host DNA thereby ensuring its survival. **AIDS, acquired immune deficiency syndrome**, is produced by a **retrovirus** that attacks the immune system.

17.8 Oncogenes

Oncogenes are those genes which are believed responsible for uncontrolled, cancerous cell growth. Cancer can be due to the production of growth factors or the inhibition of growth suppressors.

17.9 Recombinant DNA and Biotechnology

Manipulation of the genetic code through **recombinant DNA** allows molecular biologists to modify and transfer genes both for the study of disease and the production of new cellular characteristics.

CONNECTIONS 17.3 DNA Fingerprinting

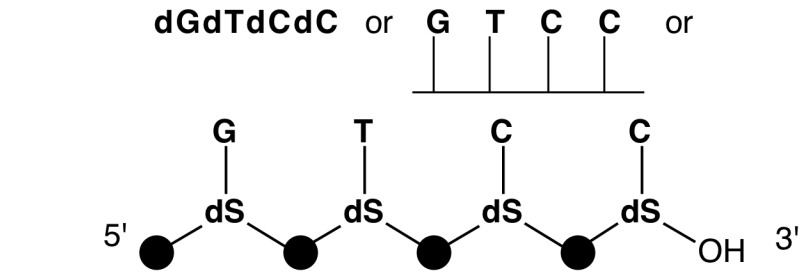
SOLUTIONS TO PROBLEMS

17.1 Structure: Section 17.1, Chapters 15, 16, 17

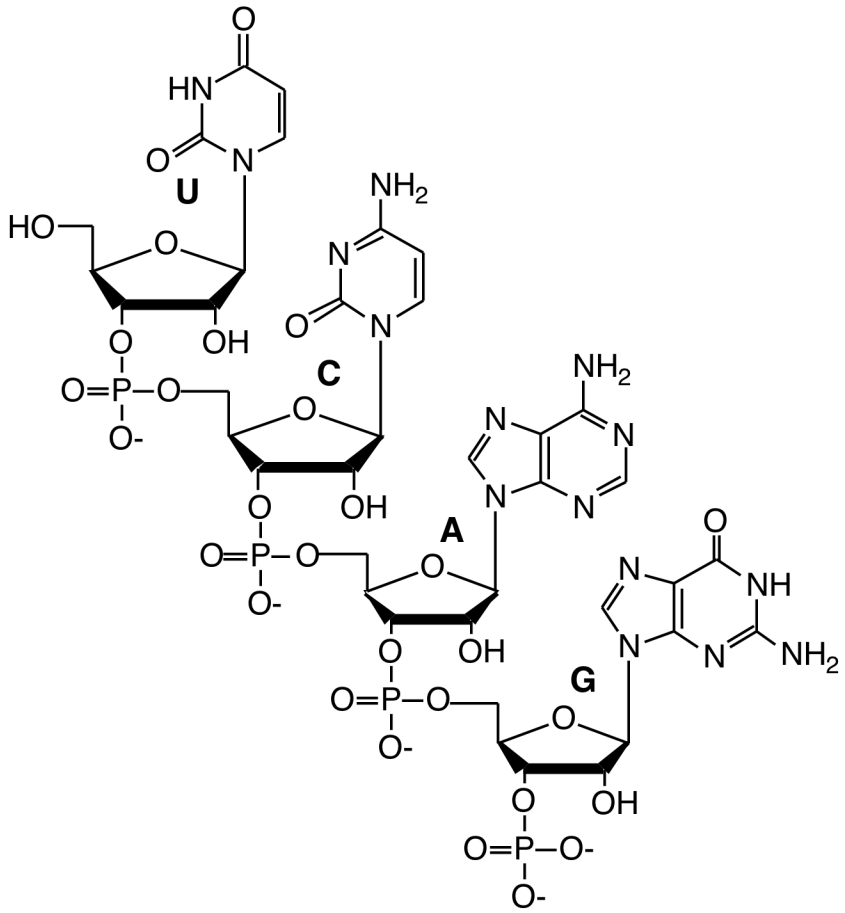
	Carbohydrates	Lipids	Proteins	Nucleic Acids
Functional Groups	●aldehydes ●ketones ●alcohols	●alkyl groups and rings ●carboxylic and phosphoric acids and esters	●amines ●carboxylic acids ●amides	●carbohydrate ●heterocyclic bases ●phosphate esters
Macro Structure	●polymers of saccharides	●no polymers ●aggregates	●polymers of amino acids	●polymers of nucleotides (base, sugar, phosphate)

17.3 Polynucleotide Structure: Section 17.1

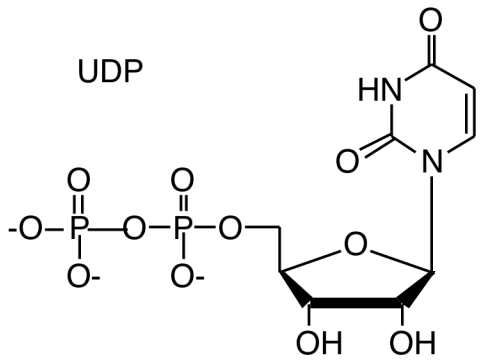
Following the example in Section 17.1 in the text
GTCC could also be represented schematically as

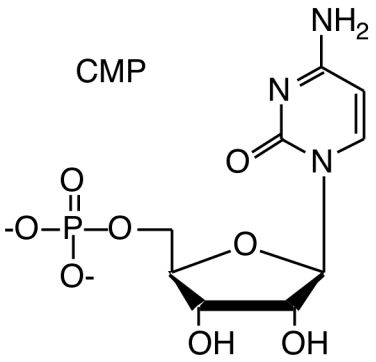


17.3 Structure: Section 17.2

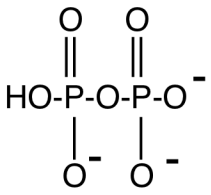


17.4 Structure: Section 17.2





17.5 Structure: Section 17.2



17.6 Structure: Section 17.3

Histones should contain basic amino acids such as lysine and arginine. These amino acids have a (+) charge at physiological pH and would interact with the negatively (-) charged phosphates as well as with the electronegative oxygens in the sugar alcohol groups.

17.7 The Genetic Code: Section 17.4

The sequence of DNA, 5' to 3', should start at band 1 and be

G T T C G G A T

17.8 The Genetic Code: Section 17.4

coding (sense) strand	5'	GGT ACT CCC TGA	3'
antisense strand	3'	CCA TGA GGG ACT	5'
codon	5'	- GGU ACU CCC UGA -	3'
anticodon	3'	CCA UGA GGG ACU	5'
peptide		Gly Thr Pro Stop	

17.9 The Genetic Code: Section 17.4

a)

modified codon	5' - GGU A**A**CU CCC UGA - 3'	
	GGU AAC UCC CUG A	
anticodon	3' CCA UUG AGG GAC U	5'
peptide	Gly Asn Ser Leu	

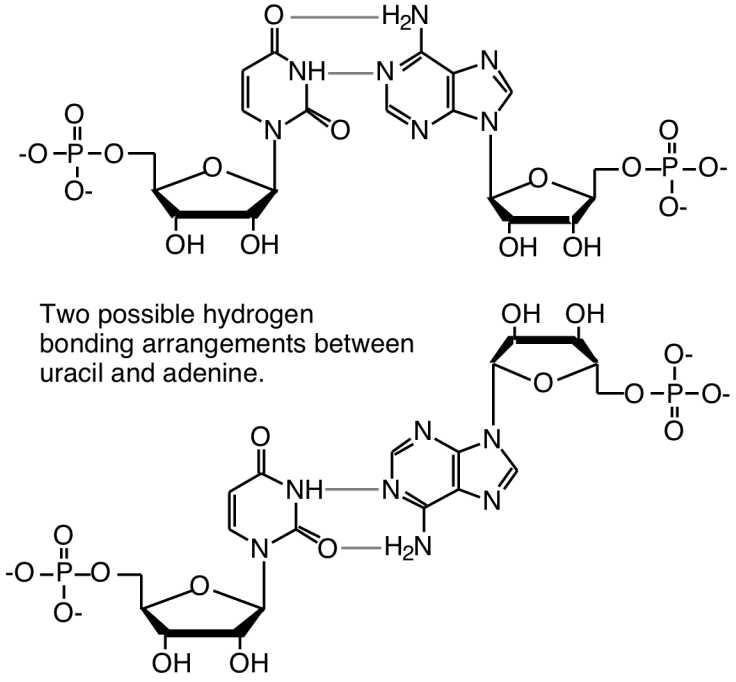
b)

modified codon	5' - GGU ACU CCC GUG UGA - 3'	
anticodon	3' CCA UGA GGG CAC ACU	5'
peptide	Gly Thr Pro Val Stop	

17.10 Structure: Section 17.1

DNA uses adenine, thymine, cytosine, and guanine as bases; RNA uses uracil rather than thymine. DNA has deoxyribose; RNA has ribose. DNA usually can be found as a double helix; RNA is commonly found single stranded and nonhelical.

17.11 Structure: Section 17.1



17.12 Genetic Code: Section 17.4

sense DNA	5'	G T A A C G T C G C T T 3'
antisense DNA	3'	C A T T G C A G C G A A 5'
mRNA	5'	G U A A C G U C G C U U 3'

mRNA as triplet code(codon)	GUA ACG UCG CUU
tRNA (anticodon)	CAU UGC AGC GAA
peptide	Val Thr Ser Leu

17.13 Structure: Section 17.1

One mole of the polynucleotide sequence in problem 17.12 would produce the following upon hydrolysis:

3	moles	G
4	moles	T
2	moles	A
3	moles	C
12	moles	deoxyribose
12	moles	phosphate

17.14 Structure: Section 17.1

$$10^6 \text{ nucleotides}\left(\frac{\text{helix turn}}{10 \text{ nucleotides}}\right)\left(\frac{34 \text{ Å}}{\text{helix turn}}\right)\left(\frac{10^{-10} \text{ meters}}{\text{Å}}\right) = 3.4 \times 10^{-4} \text{ meters}$$

17.15 Energy-Related Nucleotides: Section 17.2

Species		Number of moles		
	Bases	Ribose		Phosphate
ATP	adenine	1	1	3
FAD	flavin	1	2	2
	adenine	1		
NADH	nicotinamide	1	2	2
	adenine	1		
FMN	flavin	1	1	1

17.16 Genetic Code: Section 17.4

Glucagon would require a minimum of (37 x 3) + 6 (start/stop) nucleotides, that is, 117 nucleotides.

17.17 Genetic Code: Section 17.4

For hemoglobin E the amino acid substitutions are lysine for glutamic acid. The codons for Lys are AAA and AAG while those for Glu are GAA and GAG. The difference is A - G in the first nucleotide of the triplet. Both of these bases are purines and would fit about the same in the helix of DNA. The hydrogen bonding patterns are different, with A involved in 2 while G is involved in 3, but hydrogen bonding to a lesser extent could still occur.

For hemoglobin M_{Boston} the tyrosine would come from UAU and UAC codons while the normal hemoglobin's histidine is derived from CAU and CAC. Again we see the substitution of U for C (T for C in the parent DNA). Both are pyrimidines. U (T) usually forms 2 hydrogen bonding pairs while C forms 3.

Mutations could change the bases in the DNA complementary strand such that only 2 hydrogen bonds were available and in the correct orientation. Such a change would cause the aberrant base to be paired during replication.