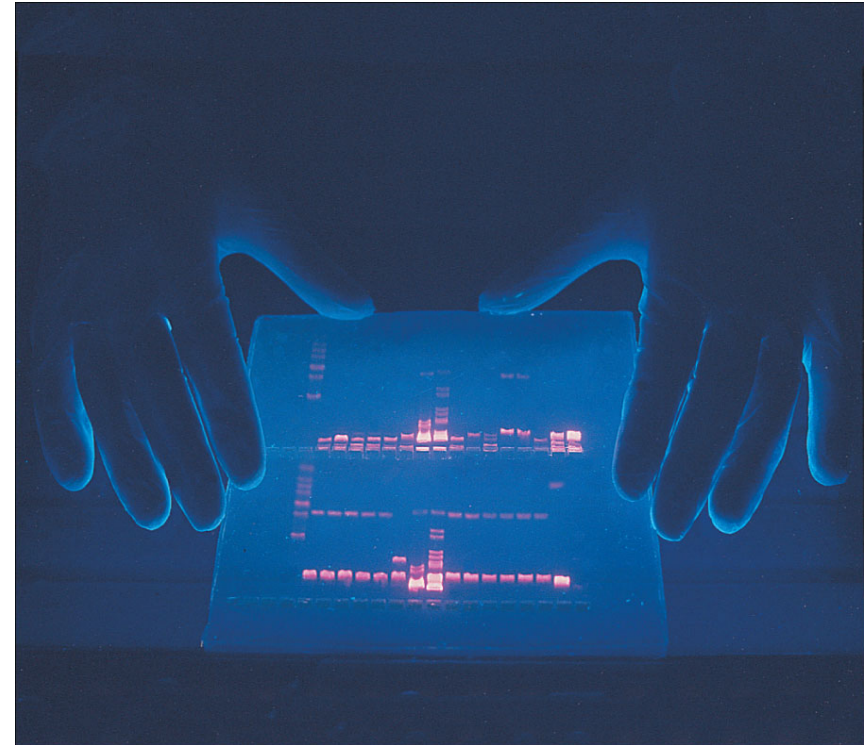


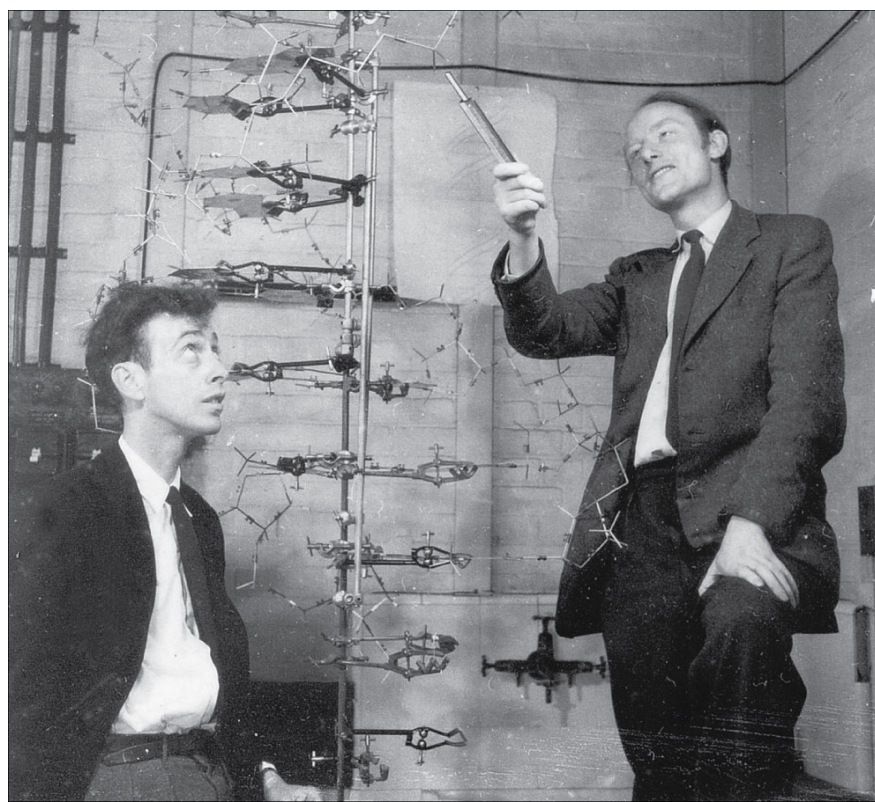
# Chapter 17

## *Overview*

- Genetic information – who we are
- DNA – blue print for cell processes
- RNAs – operating instructions
- Gene expression - proteins



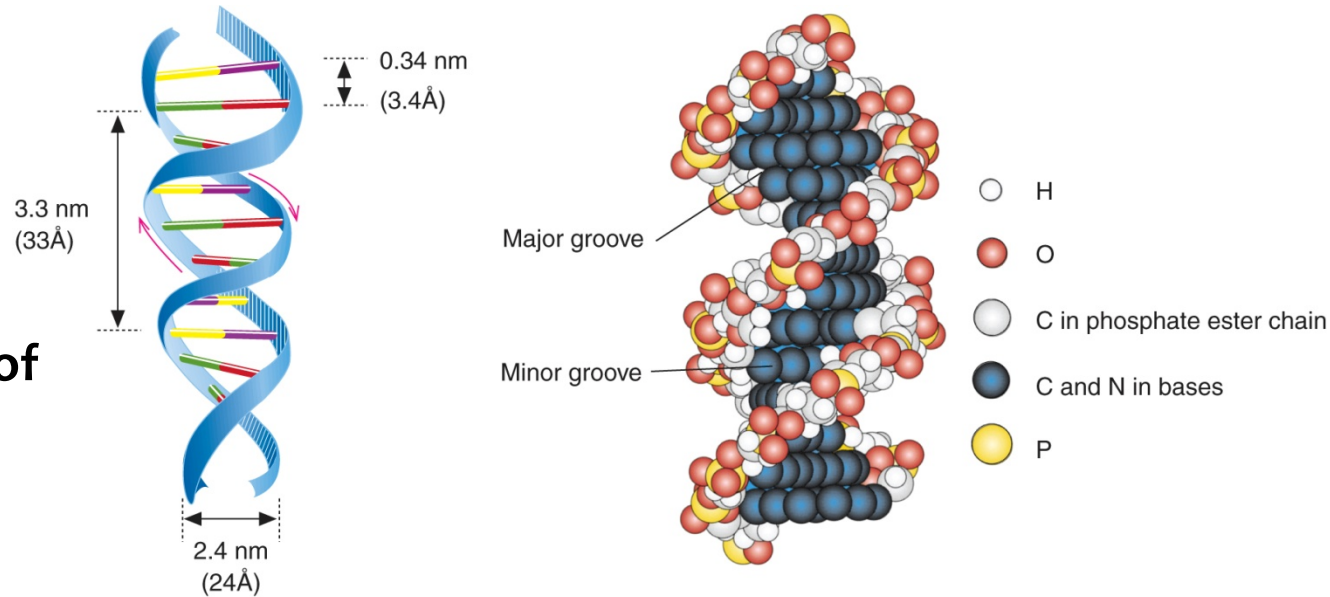
## Section 17.1: DNA



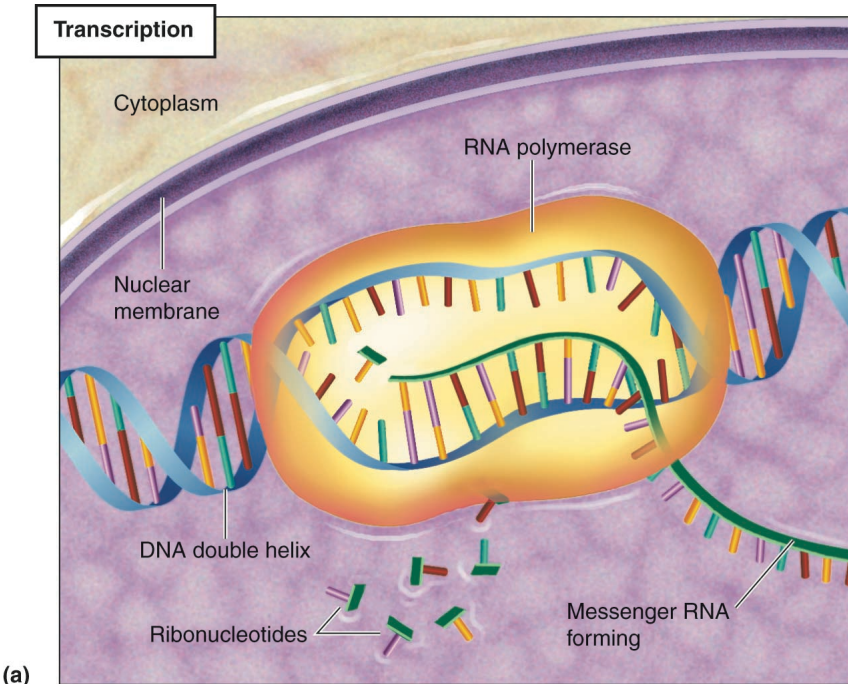
**Figure 17.1 The First Complete Structural Model of DNA**

- **Genetics** – study of heredity
  - *Artificial Selection* – selective breeding or cross-pollination to produce desirable traits
  - *Genes* – unit of heredity
  - *Chromosomes* – repository of genetic information
    - Largest, most complex structure
  - *Deoxyribonucleic acid (DNA)* - genetic information carrier
- **Molecular biology** – deals elucidating structure & functional properties of genomes

**Figure 17.2 Two Models of DNA Structure**



1. DNA directs the function of living cells and is transmitted to offspring
  - **Double helix** - two polydeoxynucleotide strands
  - **Gene** - DNA sequence containing base sequence information to code for a gene product, protein, or RNA
  - **Genome** - complete DNA base sequence of an organism
  - **Replication** - DNA synthesis involves complementary base pairing between the parental and newly synthesized strand

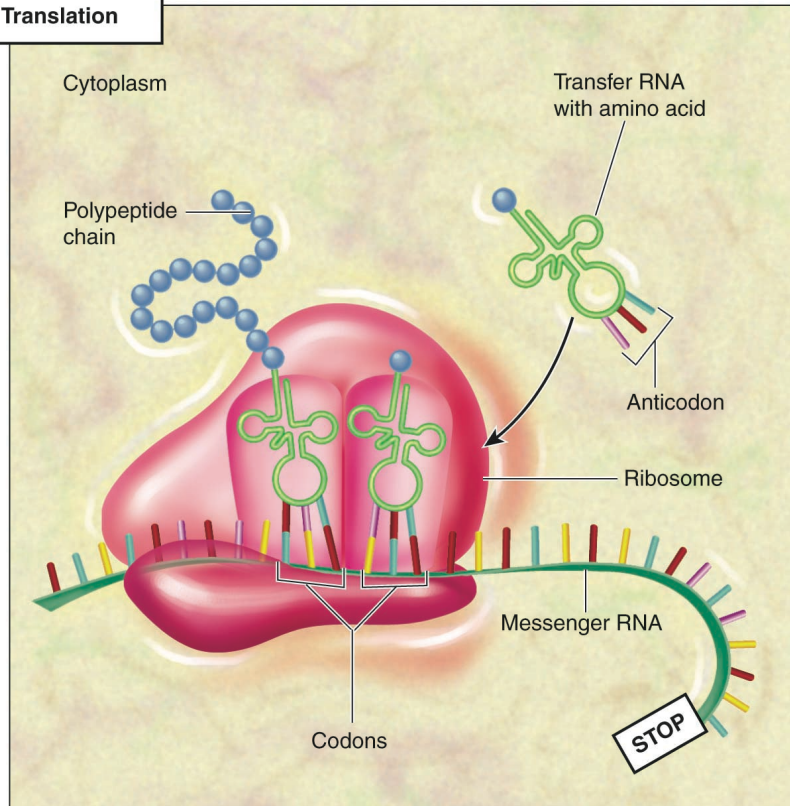


**Figure 17.3a An Overview of Genetic Information Flow**

## 2. RNA synthesis – begins decoding process of genetic information

- **Transcription** – information in a strand of DNA is copied into RNA molecules
- **Transcript** – newly synthesized RNA molecule
- **Transcriptome** - total RNA transcripts for an organism
- **mRNA, rRNA, tRNA**

## Translation

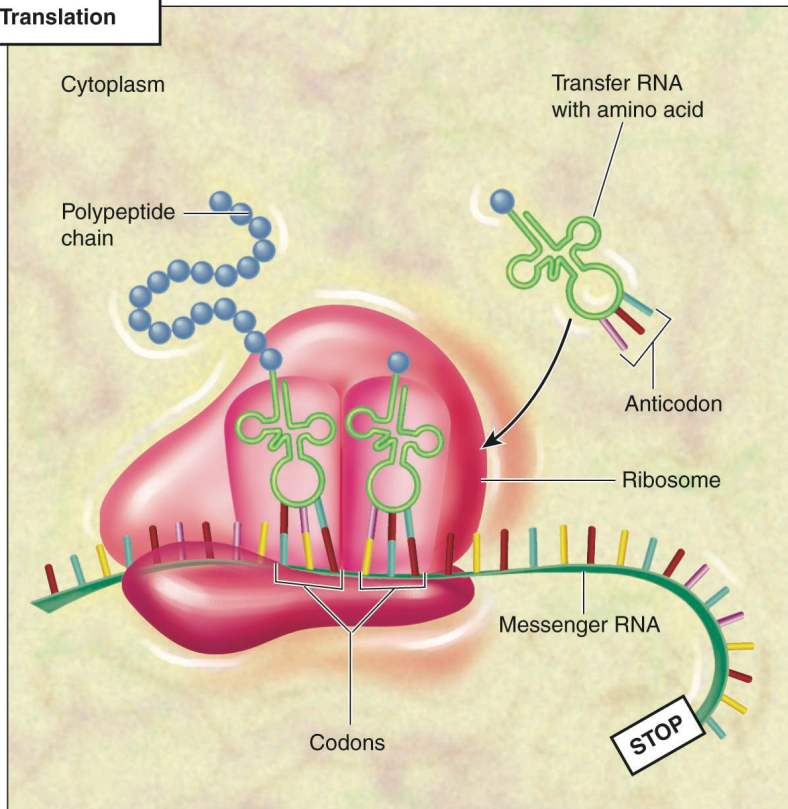


### 3. Translation – protein synthesis; decoding of mRNA by ribosome to produce polypeptide

- mRNA - specifies the primary protein sequence
- rRNA – location of protein synthesis
- tRNA - delivers the specific amino acid
- *Proteome* -entire set of proteins synthesized

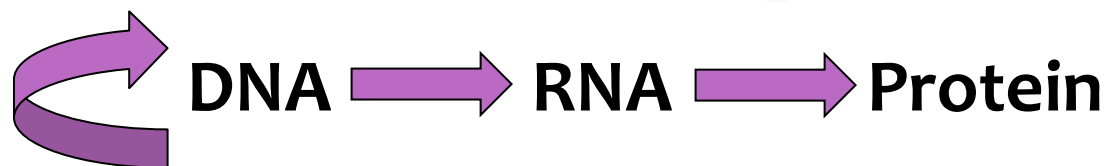
Figure 17.3b An Overview of Genetic Information Flow

## Translation

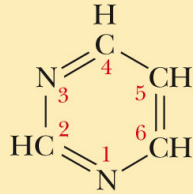


4. **Gene expression** -control of timing of gene product synthesis in response to environmental or developmental cues
- **Transcription factors** – regulate gene expression
  - **Metabolome** - sum total of low molecular weight metabolites produced by the cell

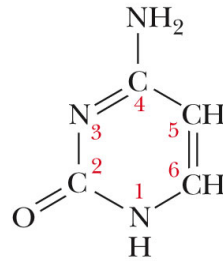
## Central dogma



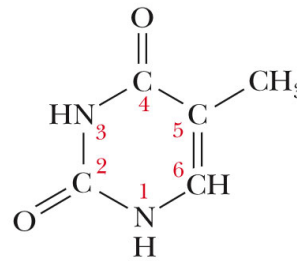
# Section 17.1: Nucleotide



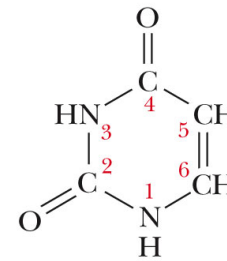
**Pyrimidine**



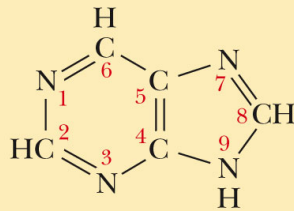
**Cytosine**  
(in DNA & RNA)



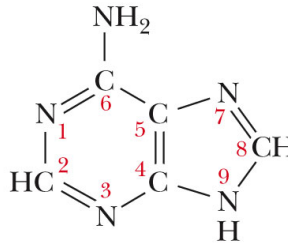
**Thymine**  
(in DNA & some RNA)



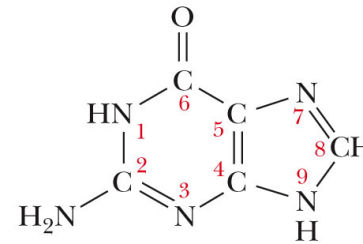
**Uracil**  
(in RNA)



**Purine**



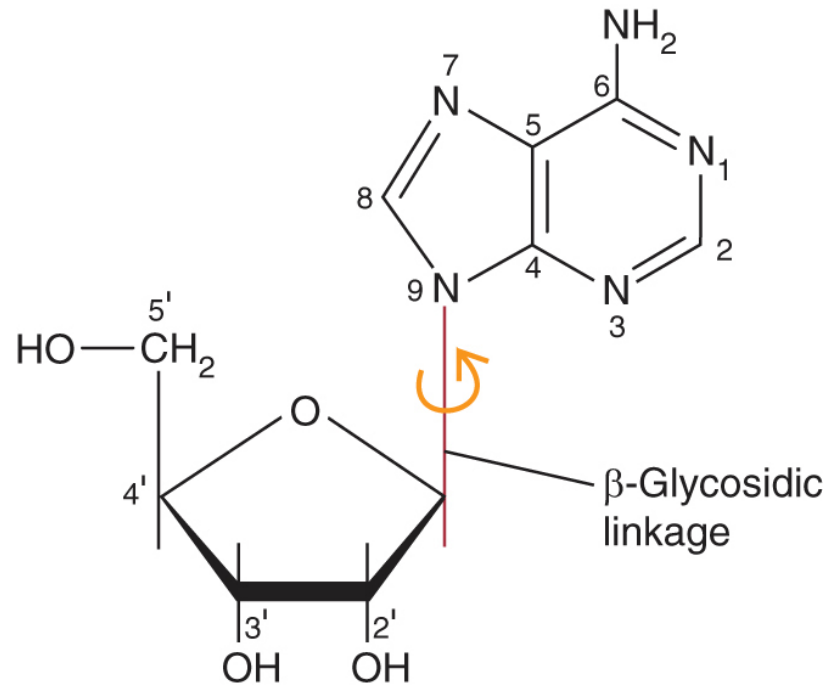
**Adenine**  
(in DNA & RNA)



**Guanine**  
(in DNA & RNA)

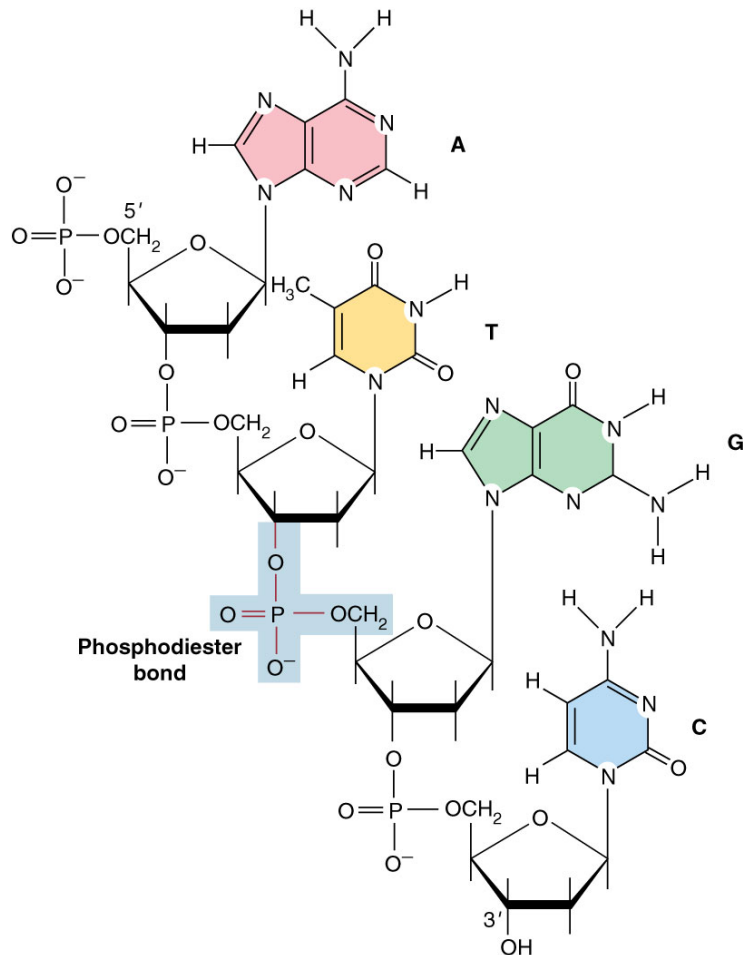
- **Nitrogenous bases** - derivatives of **purine** or **pyrimidine**, planar heterocyclic aromatic compounds
  - Common pyrimidines: thymine, cytosine, uracil
  - Common purines: adenine, guanine

Figure 14.25 Nucleoside Structure



- **Nucleoside** -nitrogenous base linked via a glycosidic linkage to a pentose sugar
  - Ribose (e.g., adenosine) for RNA
  - Deoxyribose (e.g., deoxyadenosine) for DNA

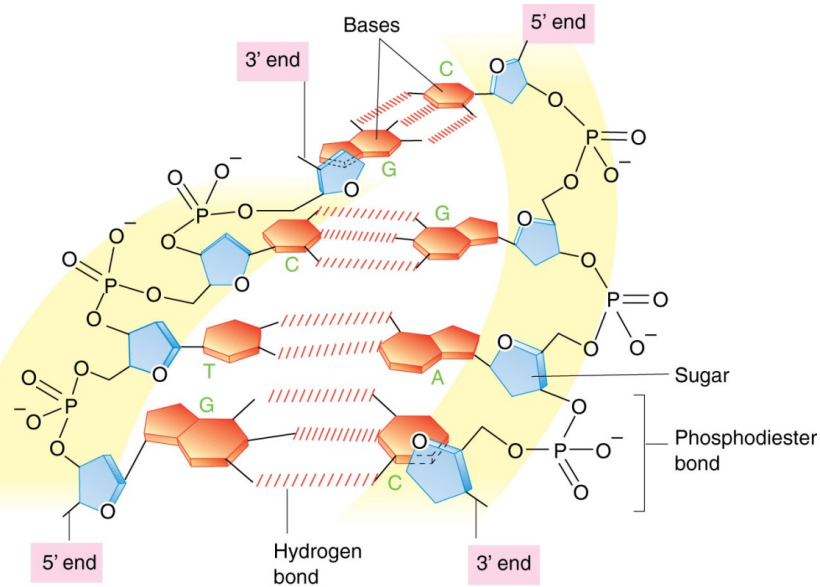




- **Nucleotides** - nucleosides with one or more phosphate groups
  - Most naturally occurring are 5'-phosphate esters
  - Designation – A (adenine); G (guanine); C (cytosine), T (thymine), U (uracil)
- **Nucleic Acids** – polymerization via 3',5'-phosphodiester bonds
  - Join the 3'-hydroxyl of one nucleotide to the 5'-phosphate of another

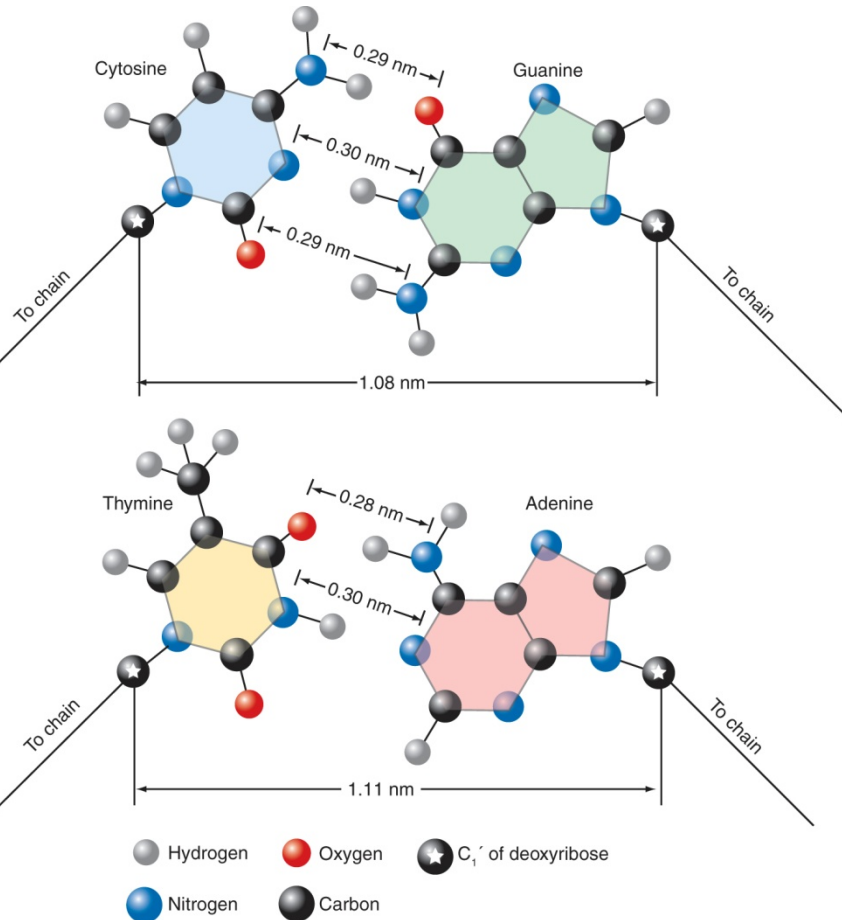
Figure 17.4 DNA Strand Structure

Figure 17.5 DNA Structure



- **Primary structure** - sequence of bases along pentose-phosphodiester backbone
  - **Base sequence** read from 5' to 3' (5'-GCCATTTCCCG-3')  
read →
  - **α-double helix** – two **antiparallel** strands wrapped around in right-hand manner
  - **Base pairing:** A-T; G – C
    - **Hydrogen bonding:** 3 G-C; 2 A-T

**Figure 17.6 DNA Structure:  
GC Base Pair Dimensions**



## ■ Dimensions of B-DNA

1. One turn spans 3.32 nm;  
consists of 10.3 base pairs
2. Diameter is 2.37 nm, only  
suitable for base pairing a  
purine with a pyrimidine
3. Distance between adjacent  
base pairs is 0.29-0.30 nm

- Stabilizing DNA
  1. **Hydrophobic interactions**—internal base clustering
  2. **Hydrogen bonds**—3 between CG base pairs; 2 between AT base pairs
  3. **Base stacking**—bases are nearly planar and stacked, weak van der Waals forces between the rings
  4. **Hydration**—water interacts with the structure of DNA
  5. **Electrostatic interactions**—destabilization by negatively charged phosphates of sugar-phosphate backbone are minimized by the shielding effect of water on  $Mg^{2+}$

### ■ DNA Structure: The Nature of Mutation

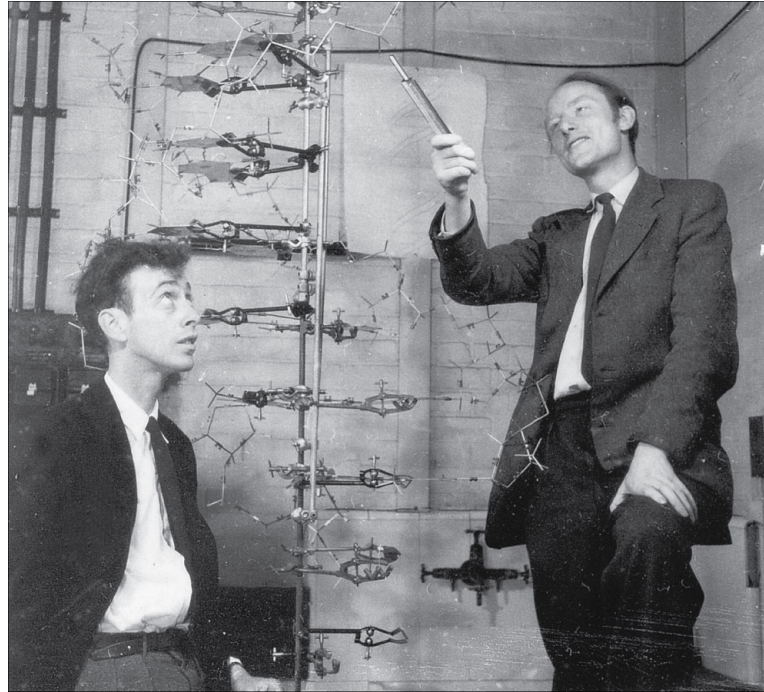
- Mutations – small alterations to large chromosomal abnormalities
  - Most negative or neutral; rare positive mutations can enhance the adaptation of the organism
  - Raw material of evolution
  - Mutation rate low
    - Accuracy of DNA replication
    - Efficiency of DNA repair
    - Reduces error rate from  $1/10^5$  base pairs to  $1/10^9$  base pairs

- **Point mutations**—small single base changes
  - **Transition mutations** - purine for purine or pyrimidine for pyrimidine substitutions
  - **Transversion mutations** - purine is substituted for a pyrimidine or vice versa
  - **Single nucleotide polymorphisms (SNPs)**- point mutations that occur in a population with some frequency
    - **Classification if in coding portion:**
      - **Silent mutations** have no discernable effect
      - **Missense mutations** have an observable effect
      - **Nonsense mutations** changes a codon for an amino acid to that of a premature stop codon

- **Indels** - one to thousands of bases are inserted or removed
  - **Frameshift mutation** - Indels in coding region not divisible by three
- **Genome rearrangements** can cause disruptions in gene structure or regulation.
  - **Inversions** - deleted DNA is reinserted into its original position in opposite orientation
  - **Translocation** - DNA fragment inserts else where in the genome
  - **Duplication** - creation of duplicate genes or parts of genes.
- **Causes of DNA Damage** - exogenous and endogenous forces
  - **Endogenous** sources - tautomeric shifts, depurination, deamination, ROS-induced oxidative damage
  - **Exogenous** factors - radiation and xenobiotic exposure can also be mutagenic

### ■ DNA Structure: The Genetic Material

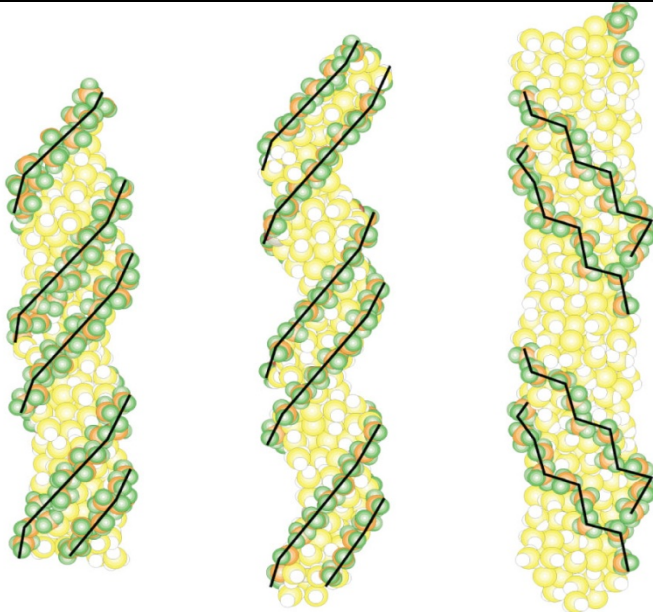
- Watson and Crick – DNA structure in 1953
  - Chemical structures/molecular dimensions of deoxyribose, nitrogenous bases, phosphate
  - Chemical analyses of base concentrations
    - $A = T, C = G$
    - **Chargaff's rules** - base pairing
      - ✓ A pairs with T; C pairs with G on opposite strands
  - X-ray diffraction patterns
    - Symmetrical & helix – Rosalind Franklin
    - Diameter & pitch – Wilkins & Stokes
  - Linus Pauling - Proteins could exist in helical conformation



**Figure 17.1 The First Complete Structural Model of DNA**



# Section 17.1: Other DNA



A form

B form

Z form

**Figure 17.10 A-DNA, B-DNA, and Z-DNA**

## ■ B-DNA

- Physiological form
- Right-handed helix, diameter 11Å
- 10 base pairs per turn (34Å) of helix

## ■ A-DNA

- Right-handed helix, thicker than B-DNA
- 11 base pairs per turn of helix
- Not found *in vivo*

## ■ Z-DNA

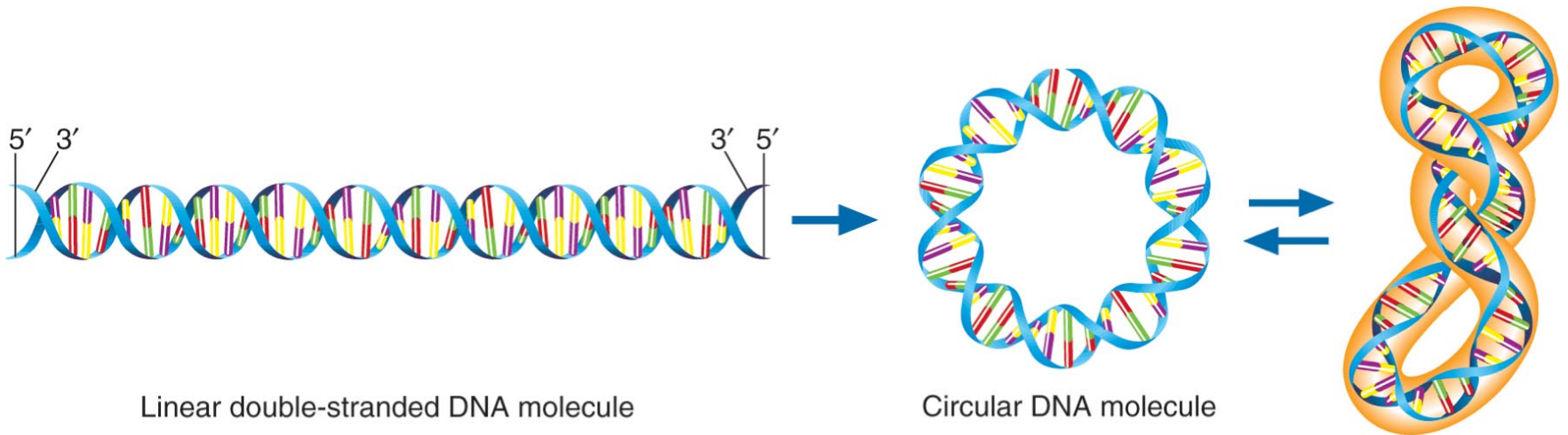
- Left-handed double helix
- May play a role in gene expression

**TABLE 17.1** Selected Structural Properties of B-, A-, and Z-DNA

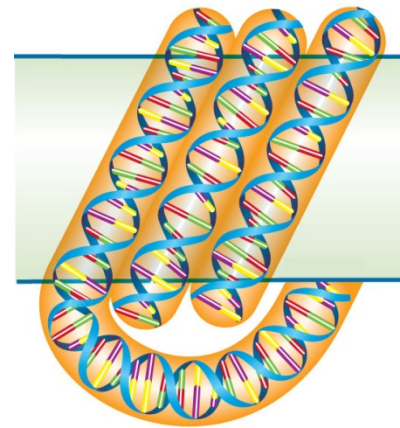
	B-DNA (Watson-Crick Structure)	A-DNA	Z-DNA
Helix diameter	2.37 nm	2.55 nm	1.84 nm
Base pairs per helical turn	10.5	11	12
Helix rise per helical turn	3.32 nm	2.46 nm	4.56 nm
Helix rise per base pair	0.34 nm	0.24 nm	0.37 nm
Helix rotation	Right-handed	Right-handed	Left-handed

# Section 17.1: DNA Supercoiling

- Linear and circular DNA can be in a relaxed or supercoiled shape



- Two forms of supercoils
  - Toroidal – spiral
  - Plectonemic – coils wrapped around each other



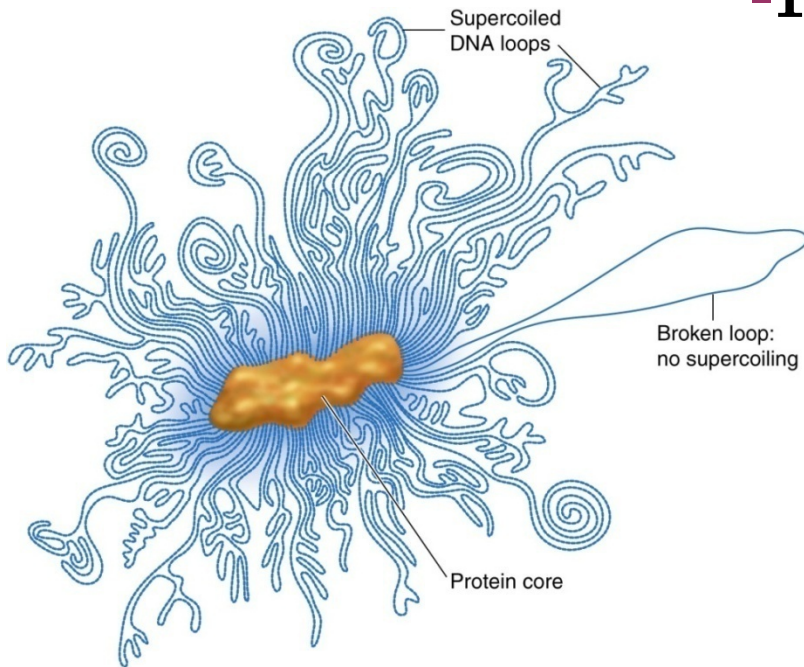
(a)



(b)

**Figure 17.11 Linear and Circular DNA and DNA Winding**

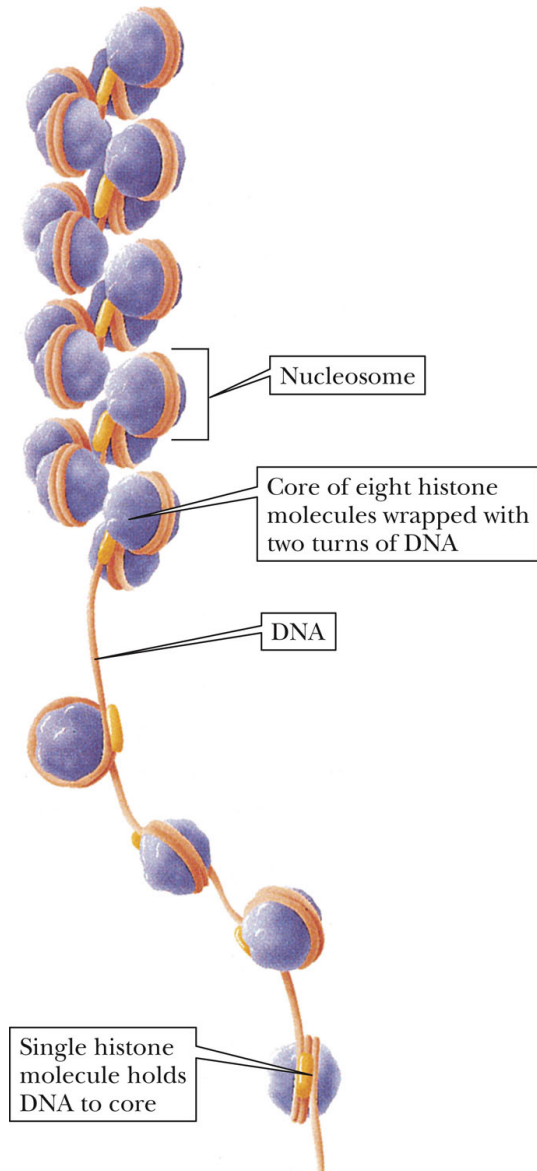
- **Negative supercoiling** – linear underwound DNA is twisted left then sealed into a circle twists to right to relieve strain
  - Stores potential energy – facilitates strand separation
- **Positively supercoiling** – linear overwound DNA is twisted right then sealed into a circle twists to left to relieve strain
- **Topoisomerases** – relaxes supercoiling formed during strand separation
  - Make reversible cuts allowing supercoiled segments to unwind



**Figure 17.15 The *E. coli* Chromosome Removed from a Cell**

## ■ Prokaryotic Chromosomes

- *E. coli* chromosome - circular DNA molecule; extensively looped and coiled
- Supercoiled DNA complexed with a protein core
- **Nucleoid** – chromosome attached in at least 40 places
- Limits the unraveling of supercoiled DNA



## ■ Eukaryotes Chromosomes

- Genomes are large
  - Chromosomes vary in length and number
- **Chromatin** - consists of a single, linear DNA molecule complexed with histone proteins
- **Nucleosomes** - binding of DNA and histone proteins
  - Beaded appearance when viewed by electron micrograph
  - Five major classes: H1, H2A, H2B, H3, H4
  - **Bead** - positively coiled DNA wrapped around a histone core

- **Genome** – organism's operating system
  - **Genes** – units of inheritance determining primary structure of gene products
  - Most prokaryotic genomes are smaller than eukaryotic genomes
  - Larger information-coding capacity of eukaryotic DNA
    - Majority of sequences do not code for gene products

### ■ Prokaryotic Genomes

1. **Genome size**—relatively small, 4.6 megabases ( $10^6$ ) coding for 4377 protein-coding genes
  2. **Coding capacity**—compact and continuous; ~15% noncoding DNA sequences
  3. **Gene expression**—functionally related genes organized into operons for regulation
- **Plasmids** - small and circular DNA with additional genes (e.g., antibiotic resistance)

## ■ Eukaryotic Genomes

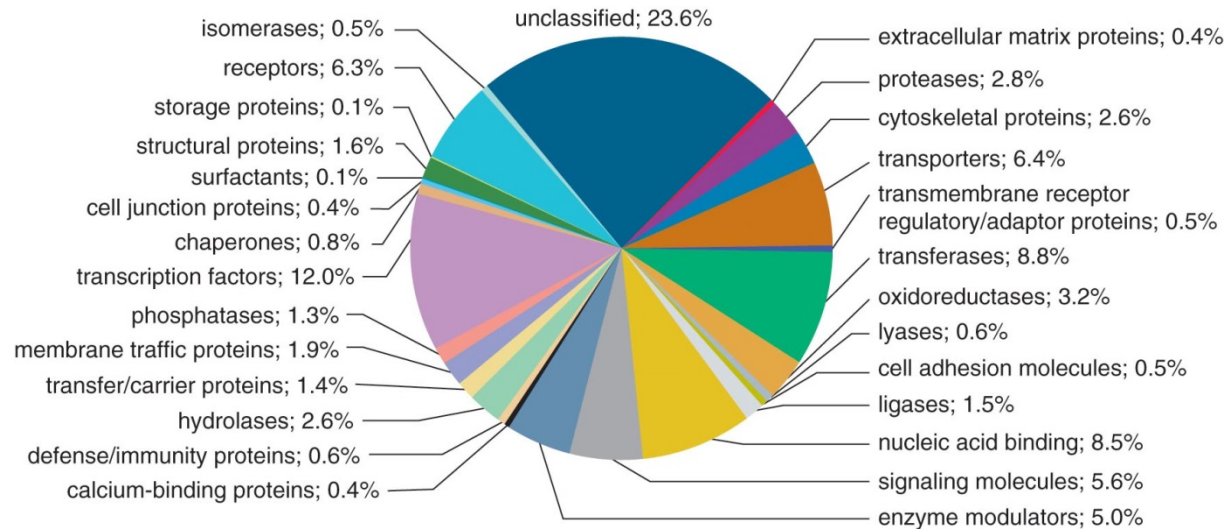
1. **Genome size**—does not necessarily indicate complexity
  - Human haploid genome – 3200 megabases
  - Peas haploid genome – 4800 megabases
  - Salamander haploid genome – 40,000 megabases
2. **Coding capacity**—only 1.5% devoted to proteins; 80% of human DNA sequences have biological functions
3. **Coding continuity**—genes are discontinuous; interrupted by noncoding sequences - **introns**
  - Introns removed by splicing mechanisms

**Exons** – coding sequences



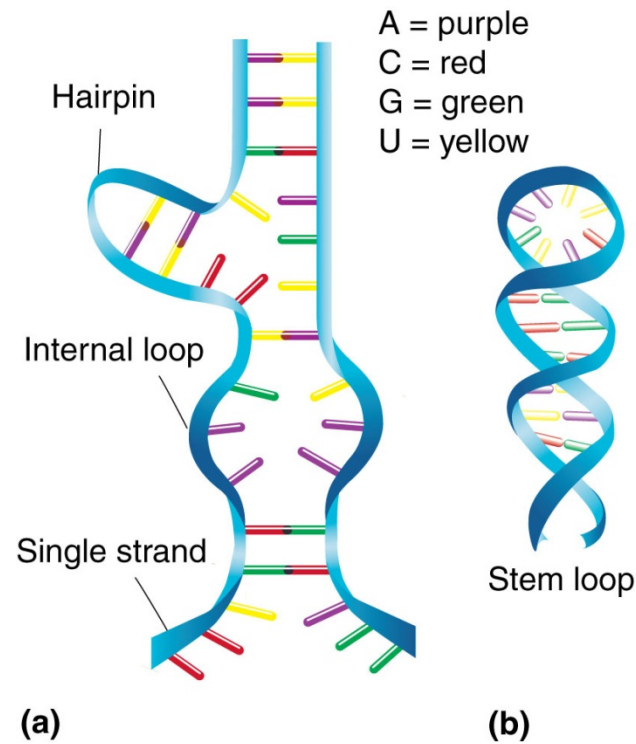
# Section 17.1: Genome Structure

- 25% - related to DNA synthesis and repair
- 21% signal transduction
- 17% general biochemical functions
- 38% other activities; transport, folding, structural, immunological
- About 80-90% of the human genome is intergenic or noncoding sequences



**Figure 17.22 Human Protein-Coding Genes**

- **Functions of noncoding sequences - regulation**
  - **Promoters** are in close proximity to a start site of a specific gene
  - **Enhancer** interacts with and stimulates the activity of an RNA polymerase complex
  - **Silencer** inhibits transcription of its gene
  - **Insulator** blocks interaction with Enhancers and Promoters
  - **Pseudogenes** are nonfunctional DNA sequences homologous to a known protein or RNA gene
  - **Repetitive DNA** - DNA patterns occurring in multiple copies
    - **Tandem repeats (satellite DNA)** - multiple copies are arranged next to each other
      - **Centromeres** – attach chromosomes to mitotic spindle
      - **Telomeres** – structures at the end of chromosome, prevents loss of coding sequences



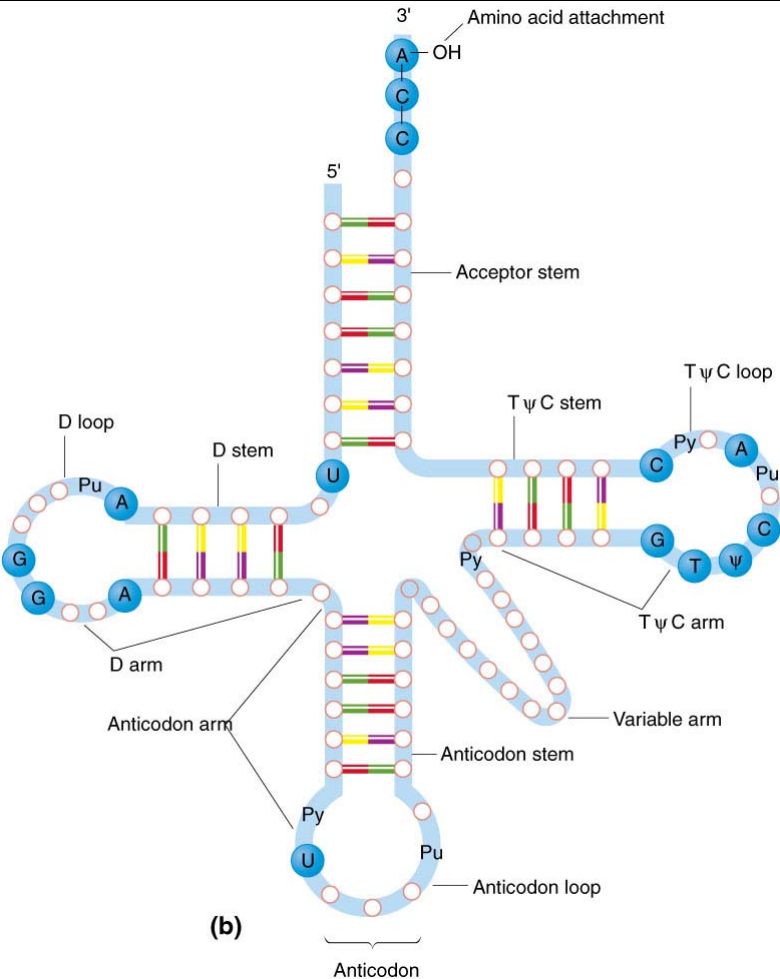
**Figure 17.23 Secondary Structure of RNA**

- Differences between DNA and RNA primary structure:
  - 1. Ribose sugar instead of deoxyribose
  - 2. Uracil nucleotide instead of thymine
  - 3. RNA exists as a single strand; forms complex three-dimensional structures
  - 4. **Ribozymes** - catalytic properties

## Section 17.2: Transcription

- **Transcription** – process of making RNA from DNA
  - Major control point in expression of genes and production of proteins
- **Template strand** (antisense strand) – DNA strand that directs synthesis
  - RNA polymerase reads 3' to 5'  
DNA 5'-GCCATTCCCG-3'  
RNA 5'-CGGGAAAUGGC-3'  
← read
- **Coding strand** (complementary strand) – DNA sequence will be same as RNA sequence
  - **Sense strand** – same sequence as RNA produced  
DNA 5'-CGGGAAATGGC-3'

# Section 17.2: Transfer RNA



- Transport amino acids to ribosomes for assembly (15% of cellular RNA)
  - Average length: 75 bases
- At least one tRNA for each amino acid
- Structurally look like a warped cloverleaf due to extensive intra-chain base pairing
- **Aminoacyl-tRNA synthetases** 3' – attaches aa to end of anticodon
  - Anticodon allows recognition of correct mRNA codon; properly aligns amino acid for protein synthesis
  - tRNA loops help facilitate interactions with the correct aminoacyl-tRNA synthetases

Figure 17.24 Transfer RNA

## Section 17.2: Ribosomal RNA

Cytoplasmic protein complexes - protein synthesis

- Components of ribosomes – small and large subunits
  - Eukaryotic are larger (80S) with a 60S and 40S subunit
    - ✓ S – sedimentation coefficient
  - Prokaryotic are smaller (70S) with 50S and 30S subunits
- rRNA plays a role in scaffolding as well as enzymatic functions
- **Peptidyl transferase** – peptide bond formation within rRNA subunits

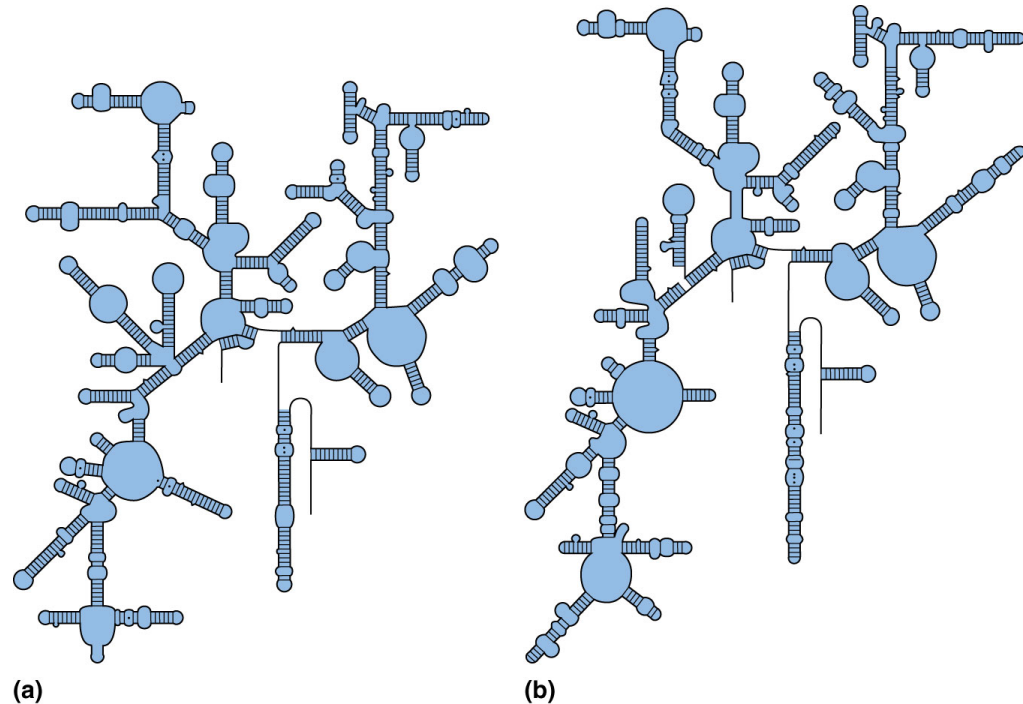


Figure 17.25 rRNA Structure

- Carrier of genetic information from DNA to protein synthesis (approximately 5% of total RNA)
- Least abundant – 5% to 10% total cellular RNA
- Formed when needed; rapid turnover
- Prokaryote – protein synthesis can occur while mRNA is being synthesized
- Eukaryote - mRNA must leave nucleus entering cytoplasm

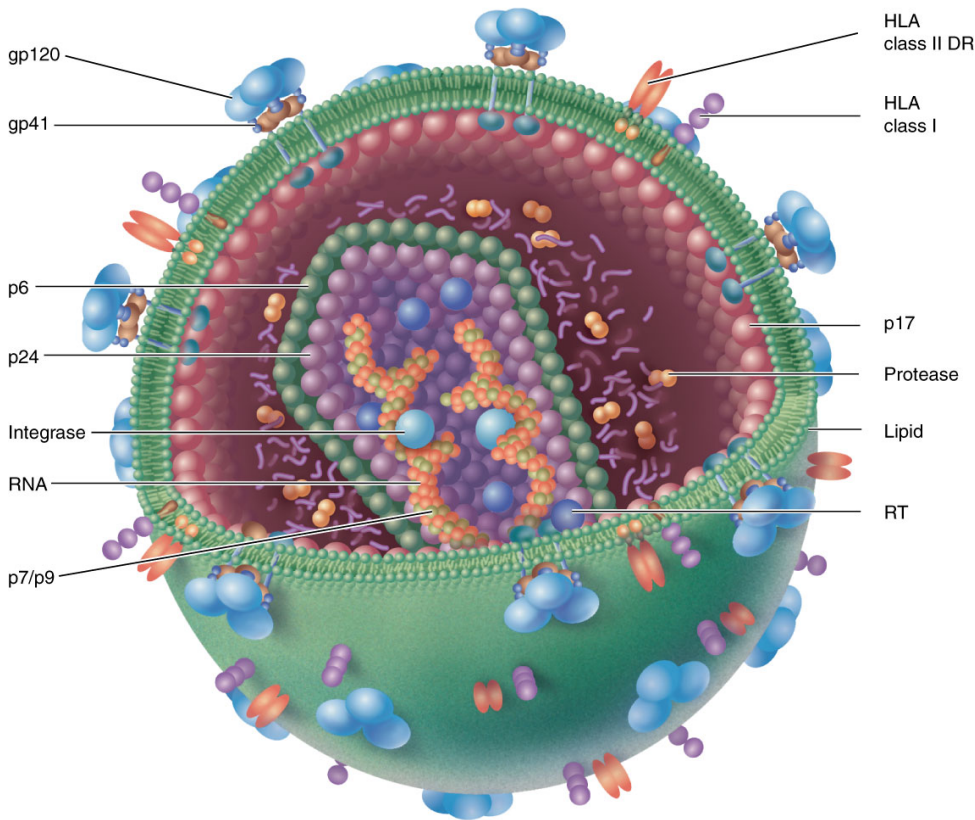
- **Noncoding RNAs (ncRNAs)** - do not directly code for polypeptides
  - **Micro RNAs and small interfering RNAs** – shortest; involved in the RNA-induced silencing complex
  - **Small Nucleolar RNAs (snoRNAs)** facilitate chemical modifications to rRNA in the nucleolus
  - **Small interfering RNAs (siRNAs)** are 21-23 nt double stranded RNAs that play a crucial role in RNA interference (RNAi)
  - **Small nuclear RNAs (snRNAs)** combine with proteins to form small nuclear ribonucleoproteins (snRNPs) and are involved in splicing



- Viruses lack the properties that distinguish life from nonlife (e.g., no metabolism)
  - Infects cell - its nucleic acid can hijack the host's nucleic acid and protein-synthesizing machinery
    - Make copies of itself until it ruptures the host cell or integrates into the host cell's chromosome

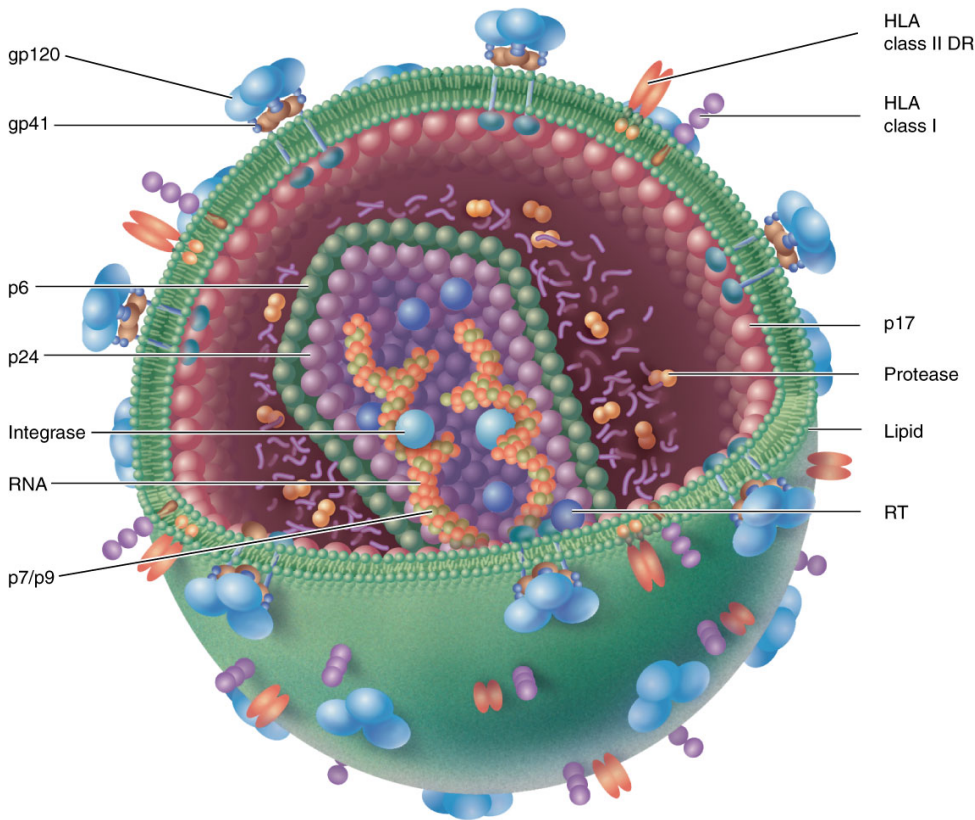
### ■ Structure of Viruses

- Simple **virions** are composed of a **capsid**, which encloses nucleic acid
  - Most capsids are helical or icosahedral
  - Nucleic acid is DNA or RNA
    - Can be single- or double-stranded, and the single-stranded RNA viruses can be + or – (e.g. (-)-ssRNA) based on whether they are positive- or negative- sense strands
    - (-)-ssRNA viruses need reverse transcriptase to synthesize mRNA
- More complex viruses may have a membrane envelope or have proteins that protrude from the surface, called **spikes**



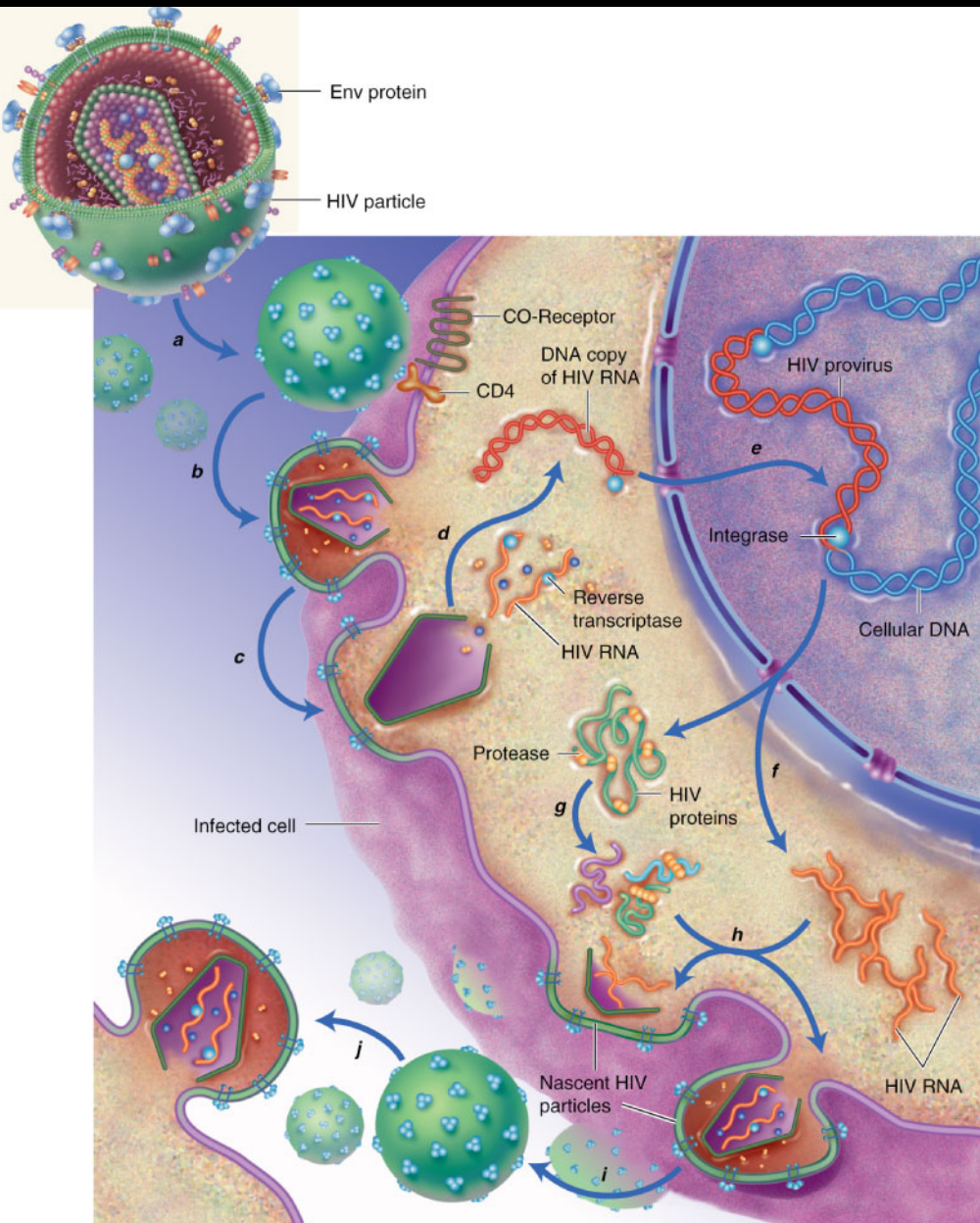
- **HIV** is the causative agent of acquired immunodeficiency syndrome (AIDS)
  - Belongs to a unique group of RNA viruses called **retroviruses**, which contain reverse transcriptase

**Figure 17J HIV Structure**



**Figure 17J HIV Structure**

- HIV is an enveloped virus with a cylindrical core within its capsid
  - The core contains two copies of the (+)-ssRNA, reverse transcriptase, ribonuclease, and integrase
- HIV binds to T-4 helper lymphocytes of the immune system

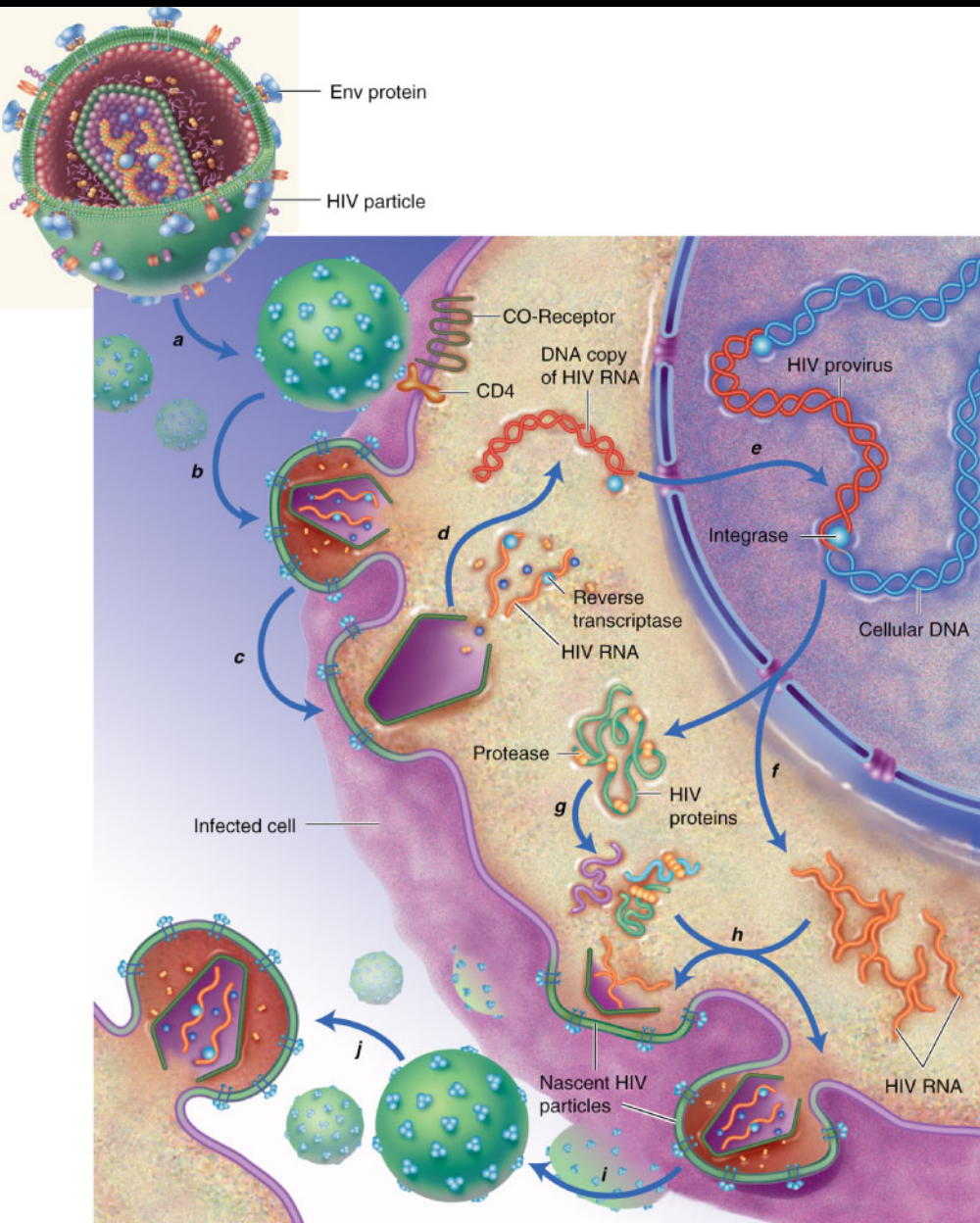


- Once bound, HIV fuses with the host cell membrane and releases ssRNA and reverse transcriptase

- Immediately makes ssDNA from the viral RNA, which is integrated into the host cell chromosome by the integrase enzyme

**Figure 17K Reproductive Cycle of HIV, a Retrovirus**

# Biochemistry in Perspective



- Proviral components are not activated until the T cell is activated by the immune response
  - Newly synthesized virus buds from the infected cell
- Within hours, an infected host cell's mRNA has been replaced with viral RNA and the virus has taken over the cell

**Figure 17K Reproductive Cycle of HIV, a Retrovirus**