27.23
Pyrimidines and Purines
In order to understand the structure and properties of DNA and RNA, we need to look at their structural components.

We begin with certain heterocyclic aromatic compounds called pyrimidines and purines.
Pyrimidine and purine are the names of the parent compounds of two types of nitrogen-containing heterocyclic aromatic compounds.
Pyrimidines that occur in DNA are cytosine and thymine. Cytosine and uracil are the pyrimidines in RNA.
Adenine and guanine are the principal purines of both DNA and RNA.
Caffeine and Theobromine

Caffeine (coffee) and theobromine (coffee and tea) are naturally occurring purines.

Caffeine

Theobromine
Nucleosides

The classical structural definition is that a nucleoside is a pyrimidine or purine N-glycoside of D-ribofuranose or 2-deoxy-D-ribofuranose.

Informal use has extended this definition to apply to purine or pyrimidine N-glycosides of almost any carbohydrate.

The purine or pyrimidine part of a nucleoside is referred to as a *purine or pyrimidine base*.
Uridine and adenosine are pyrimidine and purine nucleosides respectively of D-ribofuranose.

Uridine (a pyrimidine nucleoside)

Adenosine (a purine nucleoside)
27.25
Nucleotides
Nucleotides

Nucleotides are phosphoric acid esters of nucleosides.
Adenosine 5'-monophosphate (AMP) is also called 5'-adenylic acid.
Adenosine 5'-monophosphate (AMP) is also called 5'-adenylic acid.
Adenosine Diphosphate (ADP)
Adenosine Triphosphate (ATP)
ATP Stores Energy

ATP

Each step is endothermic.

Energy for each step comes from carbohydrate metabolism (glycolysis).

Reverse process is exothermic and is the source of biological energy.

ΔG° for hydrolysis of ATP to ADP is −35 kJ/mol
Adenosine 3'-5'-Cyclic Monophosphate (cAMP)

Cyclic AMP is an important regulator of many biological processes.
27.26
Nucleic Acids
Nucleic Acids

Nucleic acids are polymeric nucleotides (polynucleotides).

5' Oxygen of one nucleotide is linked to the 3' oxygen of another.
A section of a polynucleotide chain.
27.27
Structure and Replication of DNA:
The Double Helix
Erwin Chargaff (Columbia Univ.) studied DNAs from various sources and analyzed the distribution of purines and pyrimidines in them. The distribution of the bases adenine (A), guanine (G), thymine (T), and cytosine (C) varied among species. But the total purines (A and G) and the total pyrimidines (T and C) were always equal. Moreover: $%A = %T$, and $%G = %C$
### Composition of Human DNA

For example:

<table>
<thead>
<tr>
<th>Purine</th>
<th>Pyrimidine</th>
</tr>
</thead>
<tbody>
<tr>
<td>Adenine (A) 30.3%</td>
<td>Thymine (T) 30.3%</td>
</tr>
<tr>
<td>Guanine (G) 19.5%</td>
<td>Cytosine (C) 19.9%</td>
</tr>
<tr>
<td>Total purines: 49.8%</td>
<td>Total pyrimidines: 50.1%</td>
</tr>
</tbody>
</table>
Watson and Crick proposed that A and T were equal because of complementary hydrogen bonding.
Likewise, the amounts of G and C were equal because of complementary hydrogen bonding.
The DNA Duplex

Watson and Crick proposed a double-stranded structure for DNA in which a purine or pyrimidine base in one chain is hydrogen bonded to its complement in the other.
Two antiparallel strands of DNA are paired by hydrogen bonds between purine and pyrimidine bases.
Helical structure of DNA. The purine and pyrimidine bases are on the inside, sugars and phosphates on the outside.
As the double helix unwinds, each strand acts as a template upon which its complement is constructed.
Fig. 27.26 DNA Replication
27.28
DNA-Directed Protein Biosynthesis
According to Crick, the "central dogma" of molecular biology is:
"DNA makes RNA makes protein."

Three kinds of RNA are involved.
- messenger RNA (mRNA)
- transfer RNA (tRNA)
- ribosomal RNA (rRNA)

There are two main stages.
- transcription
- translation
Transcription

Transcription is the formation of a strand of mRNA using one of the DNA strands as a template.

The nucleotide sequence of the mRNA is complementary to the nucleotide sequence of the DNA template.

Transcription begins at the 5' end of DNA and is catalyzed by the enzyme RNA polymerase.
As double-stranded DNA unwinds, a complementary strand of mRNA forms at the 5' end.
Uracil is incorporated in RNA instead of thymine.
Translation

The nucleotide sequence of mRNA codes for the different amino acids found in proteins.

There are three nucleotides per codon.

There are 64 possible combinations of A, U, G, and C.

The genetic code is redundant. Some proteins are coded for by more than one codon.
**Table 27.4: mRNA Codons**

<table>
<thead>
<tr>
<th>Alanine</th>
<th>Arginine</th>
<th>Asparagine</th>
<th>Aspartic Acid</th>
<th>Cysteine</th>
</tr>
</thead>
<tbody>
<tr>
<td>GCU</td>
<td>GCA</td>
<td>AAU</td>
<td>GAU</td>
<td>UGU</td>
</tr>
<tr>
<td>GCC</td>
<td>GCG</td>
<td>AAC</td>
<td>GAC</td>
<td>UGC</td>
</tr>
<tr>
<td>Glutamic acid</td>
<td>Glutamine</td>
<td>Glycine</td>
<td>Histidine</td>
<td>Isoleucine</td>
</tr>
<tr>
<td>GAA</td>
<td>CAA</td>
<td>GGU GGA</td>
<td>CAU</td>
<td>AUA AUA</td>
</tr>
<tr>
<td>GAG</td>
<td>CAG</td>
<td>GGC GGG</td>
<td>CAC</td>
<td>AUC</td>
</tr>
<tr>
<td>Leucine</td>
<td>Lysine</td>
<td>Methionine</td>
<td>Phenylalanine</td>
<td>Proline</td>
</tr>
<tr>
<td>UUA</td>
<td>CUU</td>
<td>AAA</td>
<td>UUU</td>
<td>CCU CCA</td>
</tr>
<tr>
<td>CUA</td>
<td>UUG</td>
<td>AAG</td>
<td>UUC</td>
<td>CCC CG</td>
</tr>
<tr>
<td>CUC</td>
<td>CUG</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Serine</td>
<td>Threonine</td>
<td>Tryptophan</td>
<td>Tyrosine</td>
<td>Valine</td>
</tr>
<tr>
<td>UCU</td>
<td>UCA</td>
<td>ACU ACA</td>
<td>UAU</td>
<td>GUU GUA</td>
</tr>
<tr>
<td>AGU</td>
<td>UCC</td>
<td>ACC ACG</td>
<td>UAC</td>
<td>GUC GUG</td>
</tr>
<tr>
<td>UCG</td>
<td>AGC</td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>
There are 20 different tRNAs, one for each amino acid.

Each tRNA is single stranded with a CCA triplet at its 3' end.

A particular amino acid is attached to the tRNA by an ester linkage involving the carboxyl group of the amino acid and the 3' oxygen of the tRNA.
This AAA triplet is complementary to a UUU triplet of mRNA; it is an anticodon.
27.29 DNA Sequencing
Restriction enzymes cleave the polynucleotide to smaller fragments.

These smaller fragments (100-200 base pairs) are sequenced.

The two strands are separated.
DNA Sequencing

Single stranded DNA divided in four portions.

Each tube contains adenosine, thymidine, guanosine, and cytidine plus the triphosphates of their 2'-deoxy analogs.
DNA Sequencing

The first tube also contains the 2,'3'-dideoxy analog of adenosine triphosphate (ddATP); the second tube the 2,'3'-dideoxy analog of thymidine triphosphate (ddTTP), the third contains ddGTP, and the fourth ddCTP.
DNA Sequencing

Each tube also contains a "primer," a short section of the complementary DNA strand, labeled with radioactive phosphorus ($^{32}$P).

DNA synthesis takes place, producing a complementary strand of the DNA strand used as a template.

DNA synthesis stops when a dideoxynucleotide is incorporated into the growing chain.
The contents of each tube are separated by electrophoresis and analyzed by autoradiography.

There are four lanes on the electrophoresis gel.

Each DNA fragment will be one nucleotide longer than the previous one.
Figure 27.29

Sequence of fragment

ddA  ddT  ddG  ddC

T
TG
TGA
TGAC
TGACA
TGACAT
TGACATA
TGACATAC
TGACATACG
TGACATACGT
Figure 27.29

<table>
<thead>
<tr>
<th>ddA</th>
<th>ddT</th>
<th>ddG</th>
<th>ddC</th>
</tr>
</thead>
<tbody>
<tr>
<td>T</td>
<td>A</td>
<td></td>
<td></td>
</tr>
<tr>
<td>TG</td>
<td>AC</td>
<td></td>
<td></td>
</tr>
<tr>
<td>TGA</td>
<td>ACT</td>
<td></td>
<td></td>
</tr>
<tr>
<td>TGAC</td>
<td>ACTG</td>
<td></td>
<td></td>
</tr>
<tr>
<td>TGACA</td>
<td>ACTGT</td>
<td></td>
<td></td>
</tr>
<tr>
<td>TGACAT</td>
<td>ACTGTA</td>
<td></td>
<td></td>
</tr>
<tr>
<td>TGACATA</td>
<td>ACTGTAT</td>
<td></td>
<td></td>
</tr>
<tr>
<td>TGACATAC</td>
<td>ACTGTATG</td>
<td></td>
<td></td>
</tr>
<tr>
<td>TGACATACG</td>
<td>ACTGTATGC</td>
<td></td>
<td></td>
</tr>
<tr>
<td>TGACATACGT</td>
<td>ACTGTATGCA</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>