

Module 14 Nucleic Acids

Lecture 36 Nucleic Acids I

Nucleic acids are targets of many important drugs, including several anticancer agents. There are two types of nucleic acids: deoxyribonucleic acid (DNA) and ribonucleic acid (RNA). DNA encodes the hereditary details and controls the growth and division of the cells. The genetic information stored in DNA is then transcribed into RNA, and the details in RNA are then translated for the synthesis of the proteins.

14.1 Nucleosides and Nucleotides

- Nucleic acids are chains of five membered ring sugars linked by phosphate groups (Figure 1). The anomeric carbon of each sugar is bonded to a nitrogen of heterocyclic amine in a β -glycosidic linkage. In RNA, the five membered sugar is D-ribose. In DNA, the five membered sugar is 2'-deoxy-D-ribose.

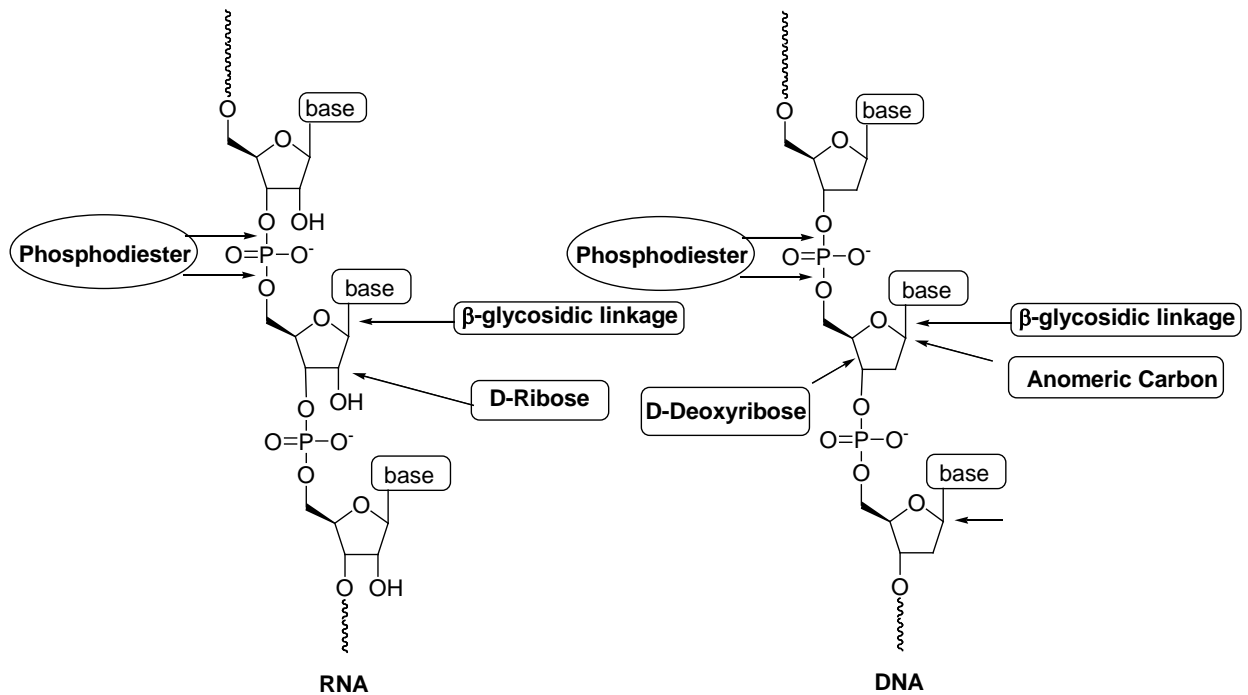
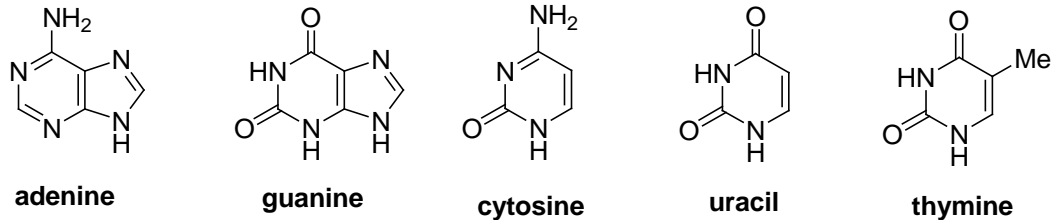


Figure 1

- The difference in heredity among the species is determined by the sequence of the bases in DNA. DNA has four bases: adenine, guanine, cytosine and thymine.
- RNA also contains four bases. Three-adenine, guanine and cytosine- are same as those in DNA. But the fourth base in RNA is uracil instead of thymine.



- A compound with a base bonded to D-ribose or 2'-deoxy-D-ribose is called **nucleoside**. Figure 2 shows an example using adenine as base. Similarly, other bases (guanine, cytosine, uracil and thymine) can also make bond to the sugar to give the corresponding nucleotides. The stereochemistry of the linkage between the base and the ribose is most commonly β .

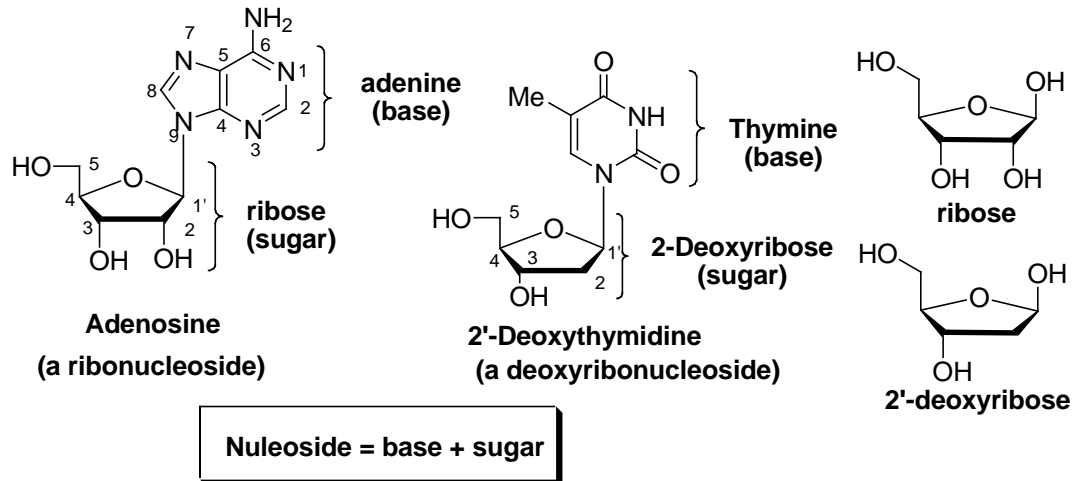


Figure 2

- **Nucleotide** is nucleoside with either the 5' or the 3'-OH group bonded in an ester linkage to phosphoric acid. The nucleotide where the sugar is D-ribose is called

ribonucleotide, whereas the nucleotide with 2'-deoxy-D-ribose is called **deoxyribonucleotide** (Figure 3).

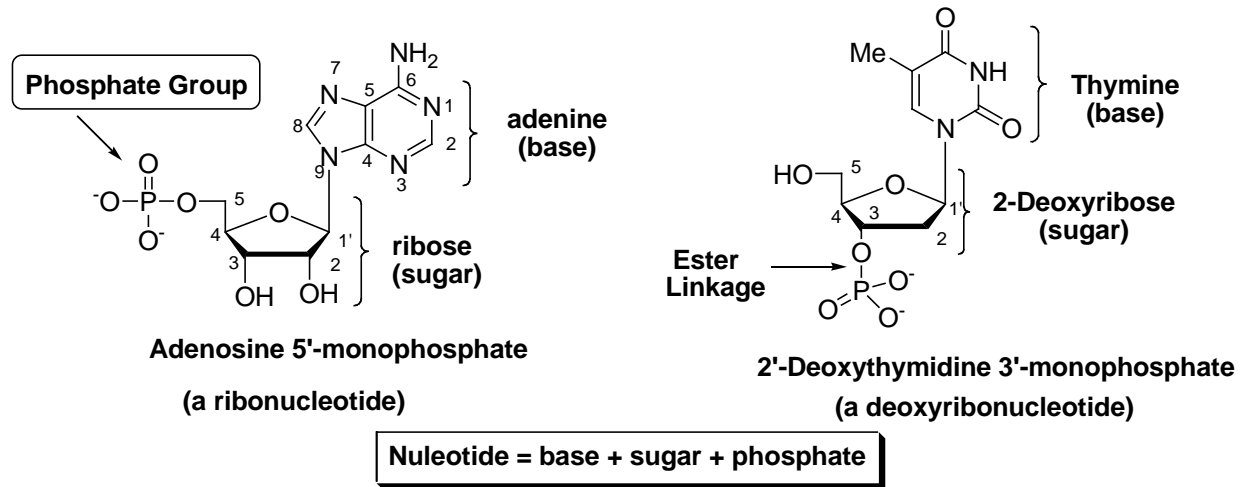


Figure 3

14.2 Nucleic Acids

- Nucleic acids are biopolymers composed of nucleotide subunits linked by phosphodiester bonds. DNA and RNA are polynucleotides. Nucleotide triphosphate serves as substrate precursor for the biosynthesis of nucleic acids. The nucleotides are linked by the nucleophilic attack of 3'-OH of one nucleotide triphosphate on the α -phosphorus of another nucleotide (Figure 4).

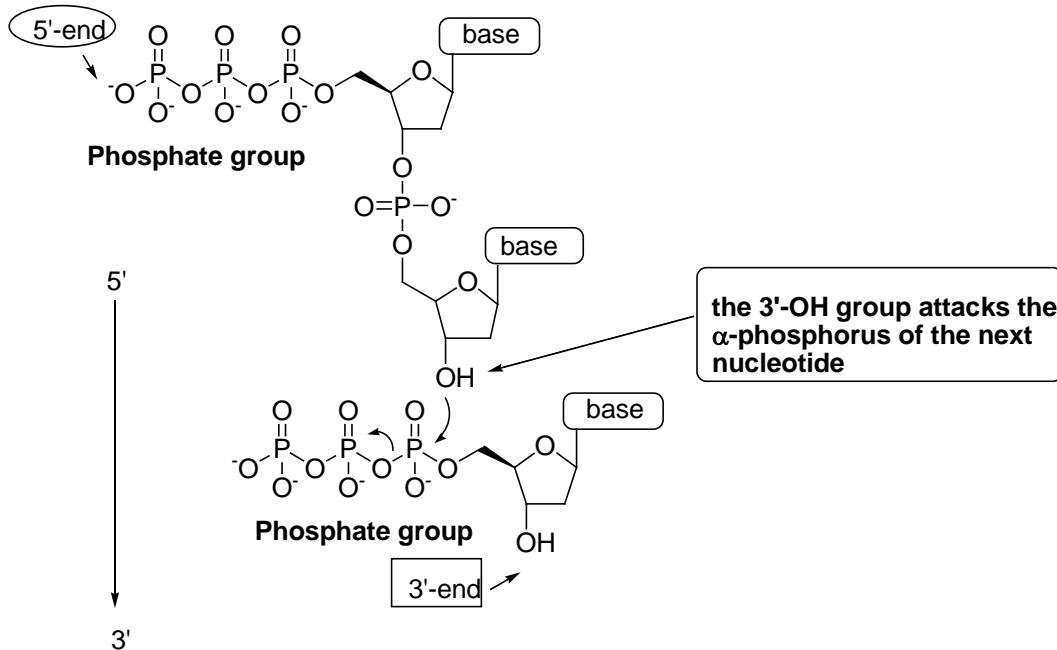
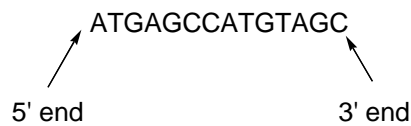


Figure 4

- **Primary Structure:** It describes the sequence of bases in the strand. By convention, the sequence of bases is written in the 5' to 3' direction.



- **Secondary Structure:** DNA consists of two strands of nucleic acids with the sugar-phosphate backbone outside and the base inside. The chains are held together by H-

bonding between the base of one strand with the base of another strand. Adenine pairs with thymine, while guanine pairs with cytosine through two and three H-bonds, respectively. This means if we know the sequences bases in one strand, we will be able to sequence the bases in the other strand (Figure 5a). If the two strands run in opposite directions, the strands are not linear. Instead they are twisted into a helix around common axis, which is known as *double helix* (Figure 5b).

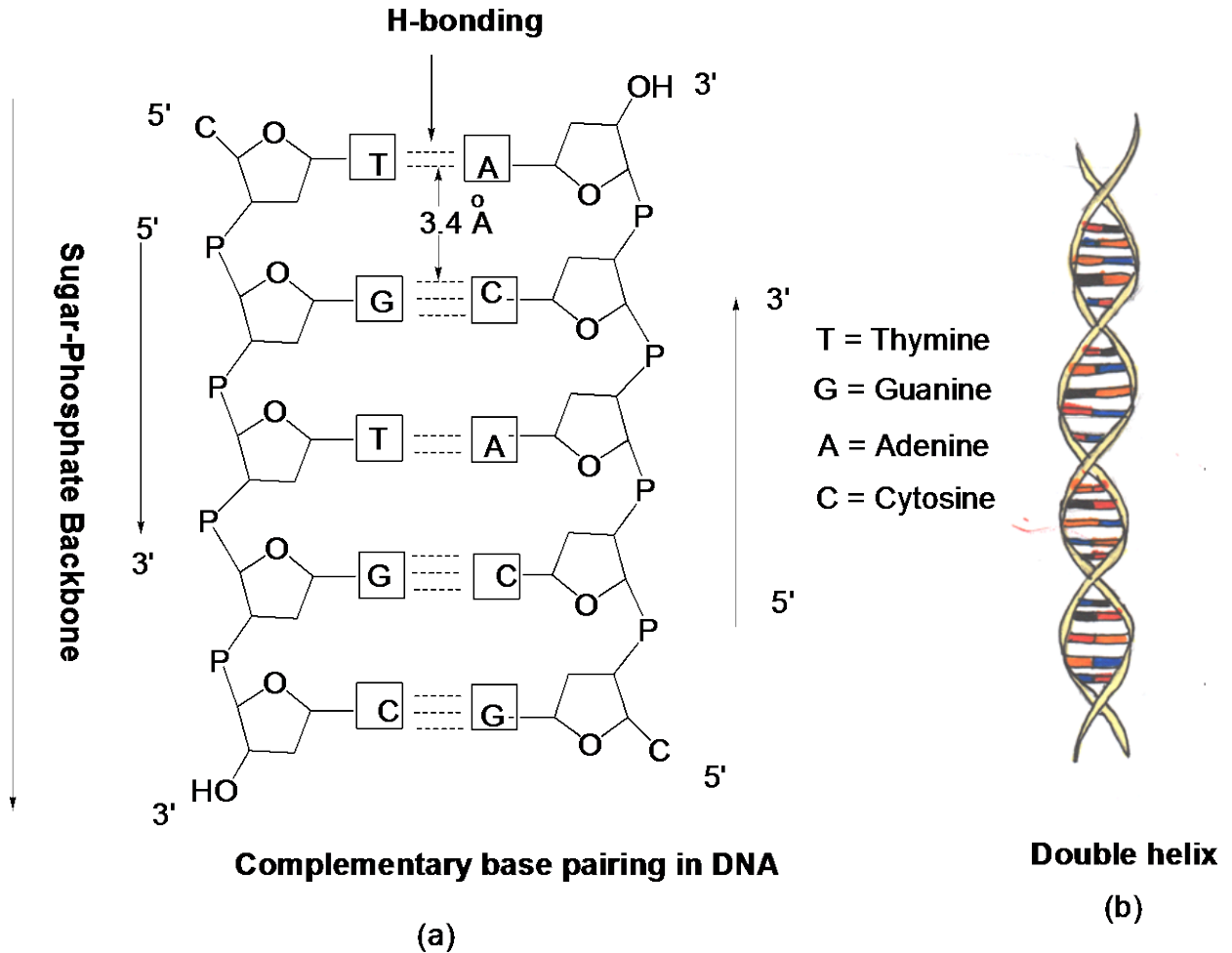


Figure 5

- Figure 6 shows the base pairing in DNA: adenine and thymine form two H-bonds; cytosine and guanine form three H-bonds

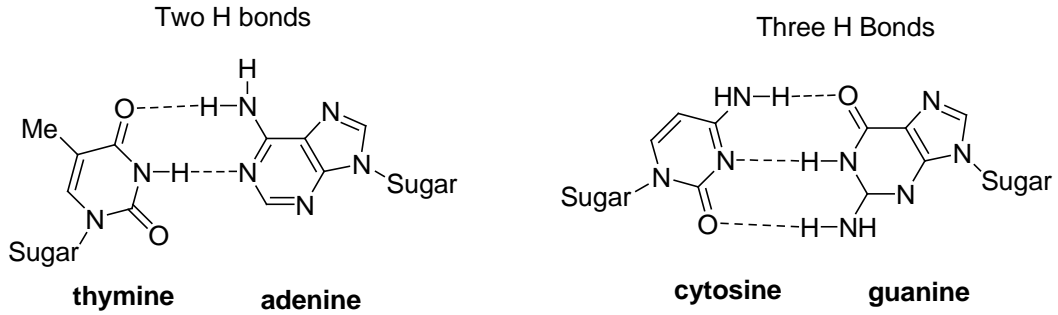


Figure 6

14.3 Stability of DNA and RNA

In RNA, the 2'-OH of ribose attacks the adjacent phosphodiester group that leads to the cleavage of the strand (Figure 7). This reaction does not take place in DNA, because it does not have the 2'-OH group. Thus, DNA remain intact throughout the life span of cells

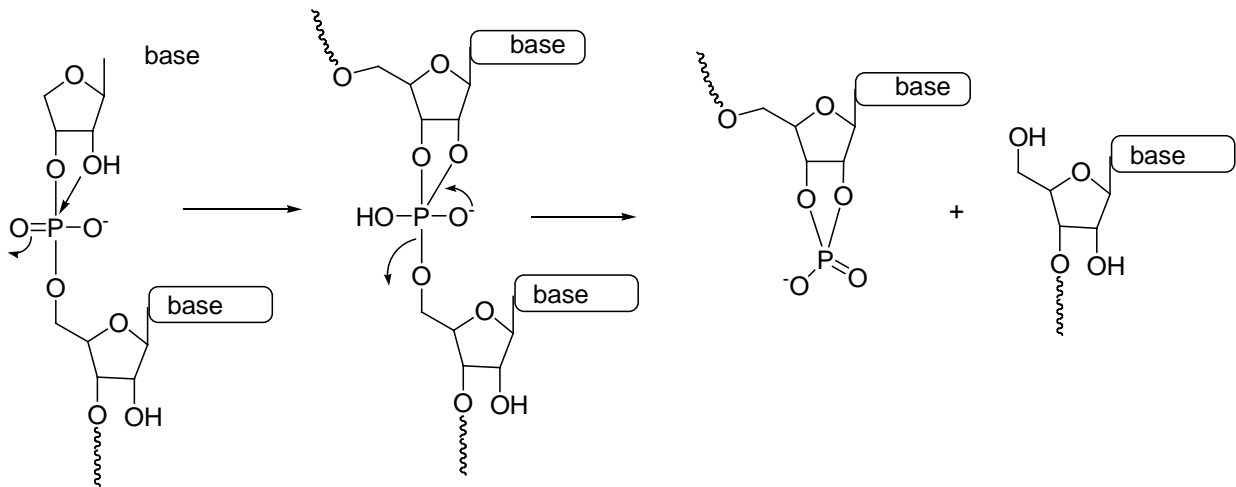


Figure 7

Module 14 Nucleic Acids

Lecture 37 Nucleic Acids II

14.4 Biosynthesis of DNA: Replication

Each strand of DNA acts as a template for the formation of complementary new strand (Figure 1). The new (daughter) DNA molecules have the same genetic information as that of the parent DNA. The synthesis of the identical copies of DNA is known as *replication* (Figure 1).

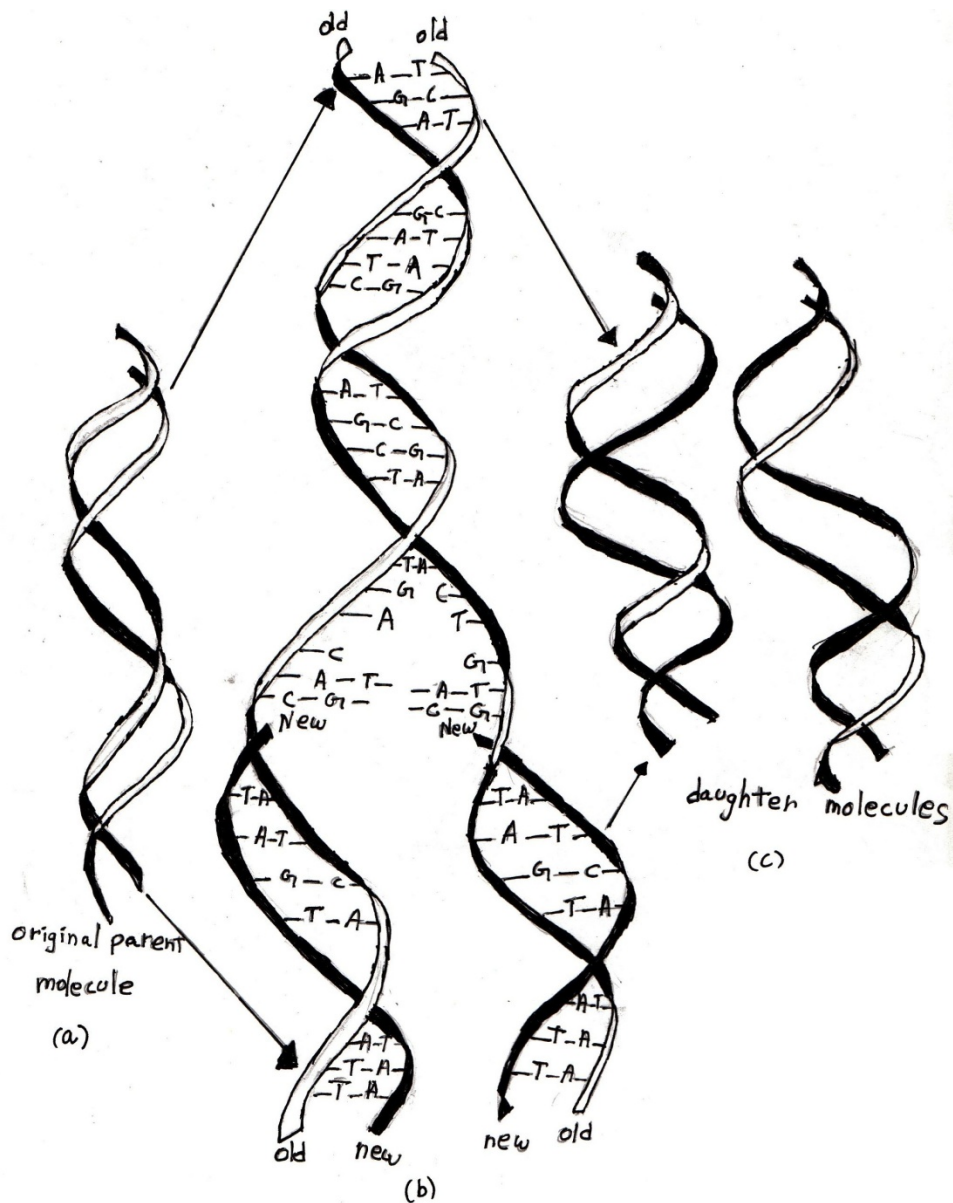


Figure 1

- The synthesis take place in a region where the strands have started to separate, because a nucleic acid can be synthesized only in the 5' to 3' direction.
- The synthesis is catalyzed by enzyme is known as DNA polymerase, and the fragments are joined together by an enzyme is called DNA ligase.
- In each of daughter DNA molecules, one strand comes from the parent DNA and another strand is synthesized. This process is called *semiconservative replication*.

14.5 Biosynthesis of RNA: Transcription

- The synthesis of RNA from DNA blueprint is known as *transcription*. It starts by DNA at a particular region to afford two single strands: (i) sense strand and (ii) template strand (Figure 2).
- The template strand read in 3' to 5' direction, and the RNA is synthesized in 5' to 3' direction.
- The base in the template strand specifies the base sequence to be incorporated in RNA.

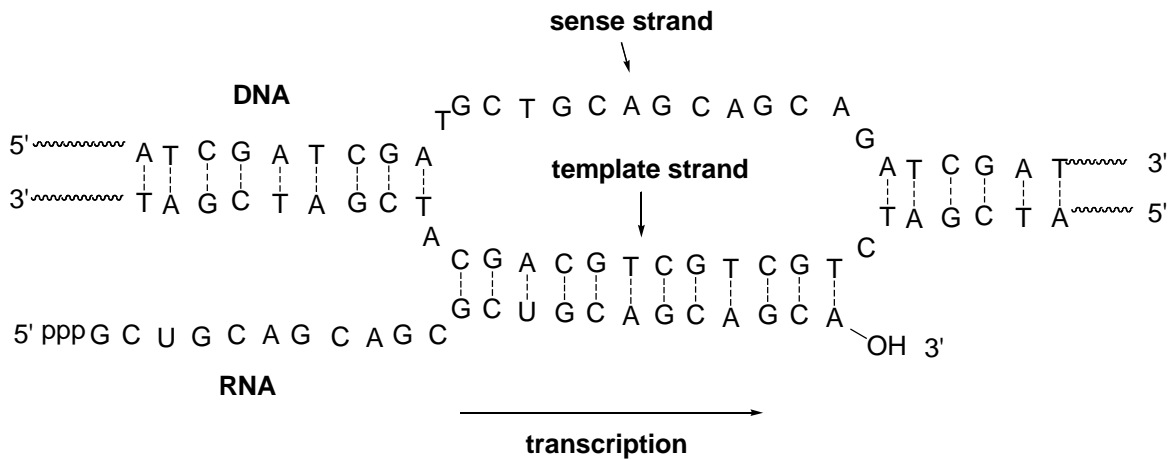


Figure 2. Biosynthesis of RNA

14.6 RNA

RNA is a single stranded polymer and does not form double helix. There are three types of RNA:

- **Messenger RNA** (mRNA), whose base sequence specifies the amino acid sequence in protein.
- **ribosomal RNA** (rRNA), that comprises the particles on which the biosynthesis of protein occurs.
- **transfer RNA** (tRNA), which carries the amino acid that will be incorporated into the protein.
 - tRNAs are shorter than mRNA and rRNA, and folded into a characteristic cloverleaf like structure (Figure 3). They have a CCA sequence at the 3' end, and the three bases at the bottom are called **anticoden**.
 - Each tRNA carries an amino acid as an ester to its terminal 3'OH. The amino acid will be inserted into a protein during the protein synthesis.

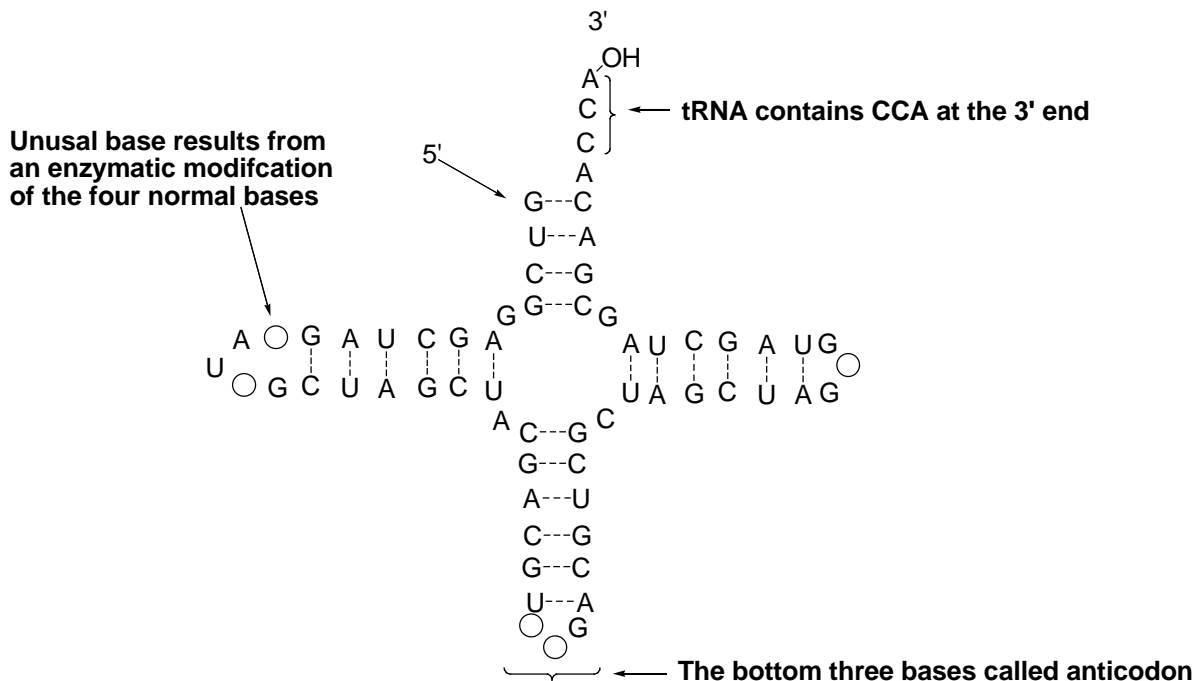


Figure 3. tRNA that carries alanine.

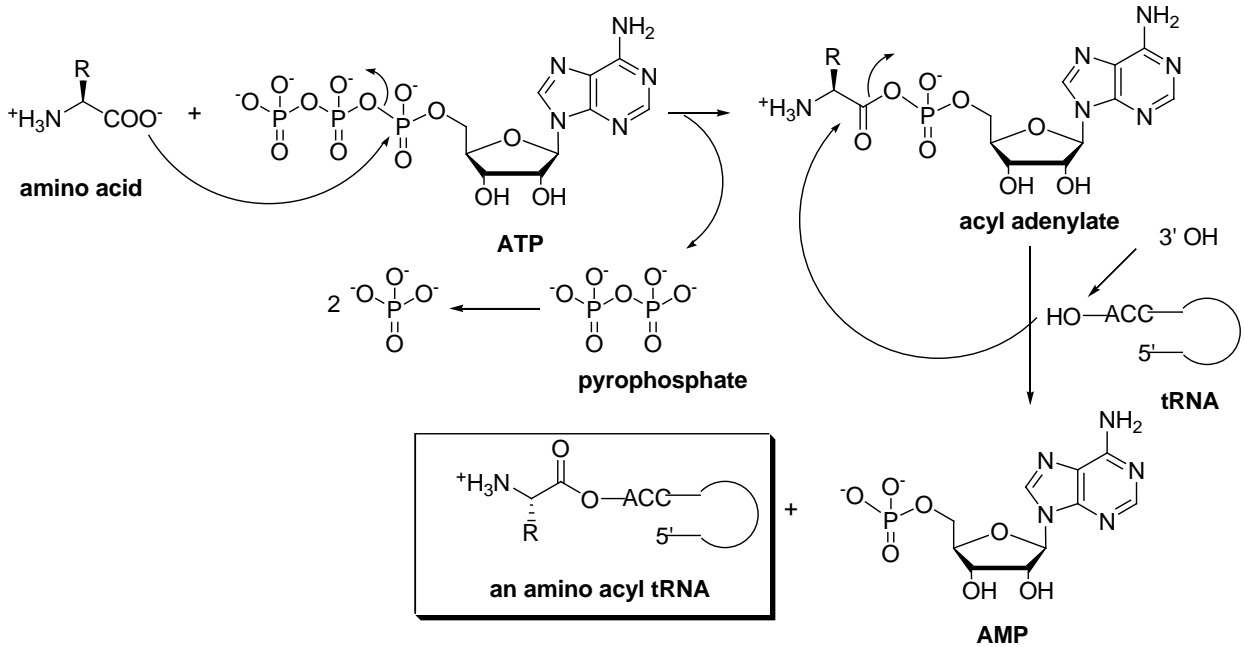


Figure 4. Mechanism for amino acyl tRNA synthetase-the enzyme that catalyzes the attachment of an amino acid to tRNA

- Figure 4 shows the mechanism for the attachment of an amino acid in tRNA.
- In the first step, the CO_2^- of amino acid attacks the α -phosphorus of ATP. The carboxylic acid of amino acid is now activated with good leaving group.
- The 3'-OH group of tRNA attacks the carbonyl carbon via nucleophilic addition to give the amino acid attached tRNA.

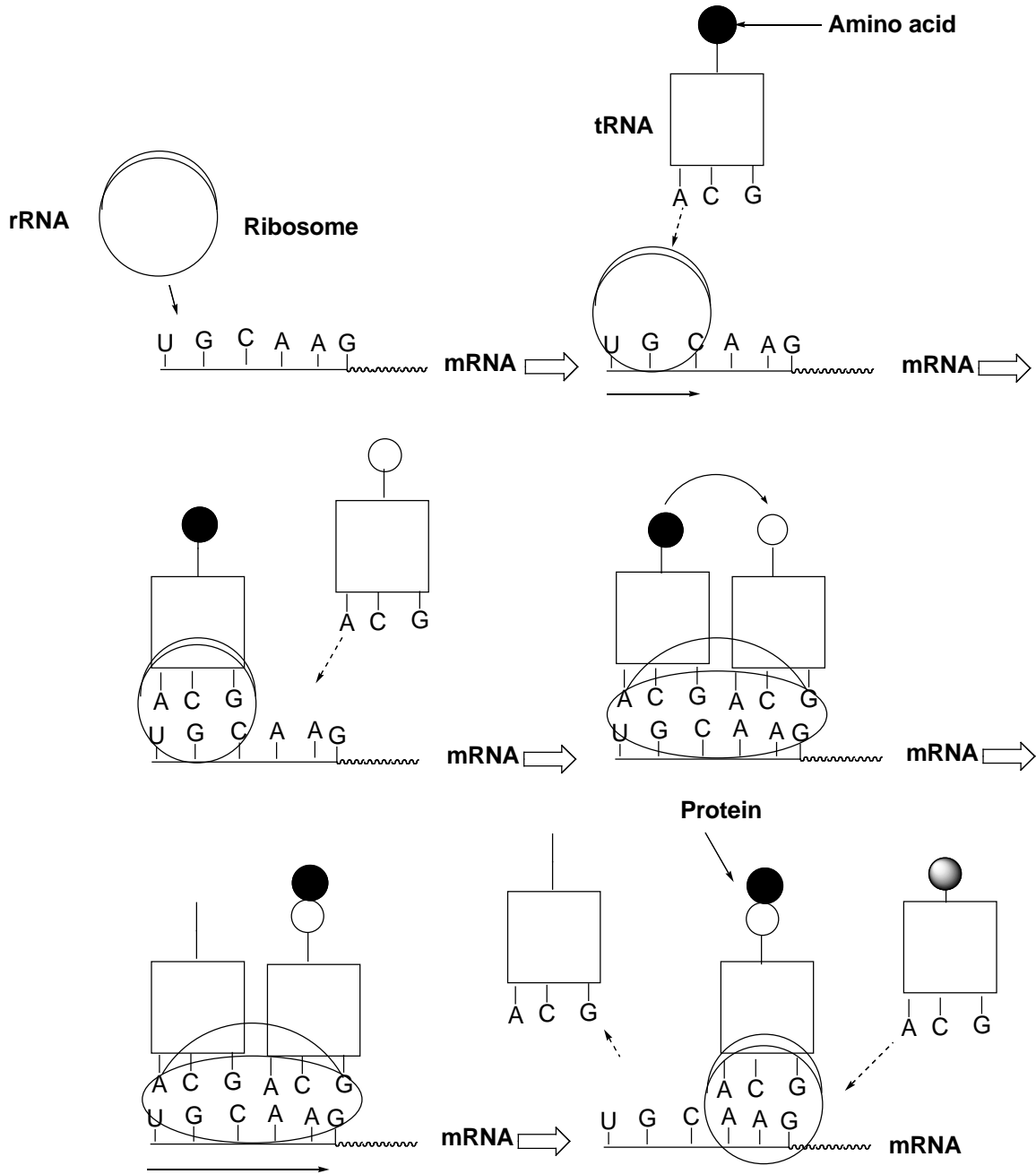


Figure 5. The sequence of bases in mRNA that determines the sequence of amino acids in protein.

14.7 Biosynthesis of Proteins: Translation

During the synthesis, rRNA attaches to one end of the mRNA strand and travels along the strand (Figure 5). As it travels, the nucleic acid bases of mRNA are read as triplets. The tRNA that recognizes that triplet is bound and brings the amino acid coded by that triplet. The protein is constructed on tRNA and transferred from one tRNA to the next until the synthesis is completed.