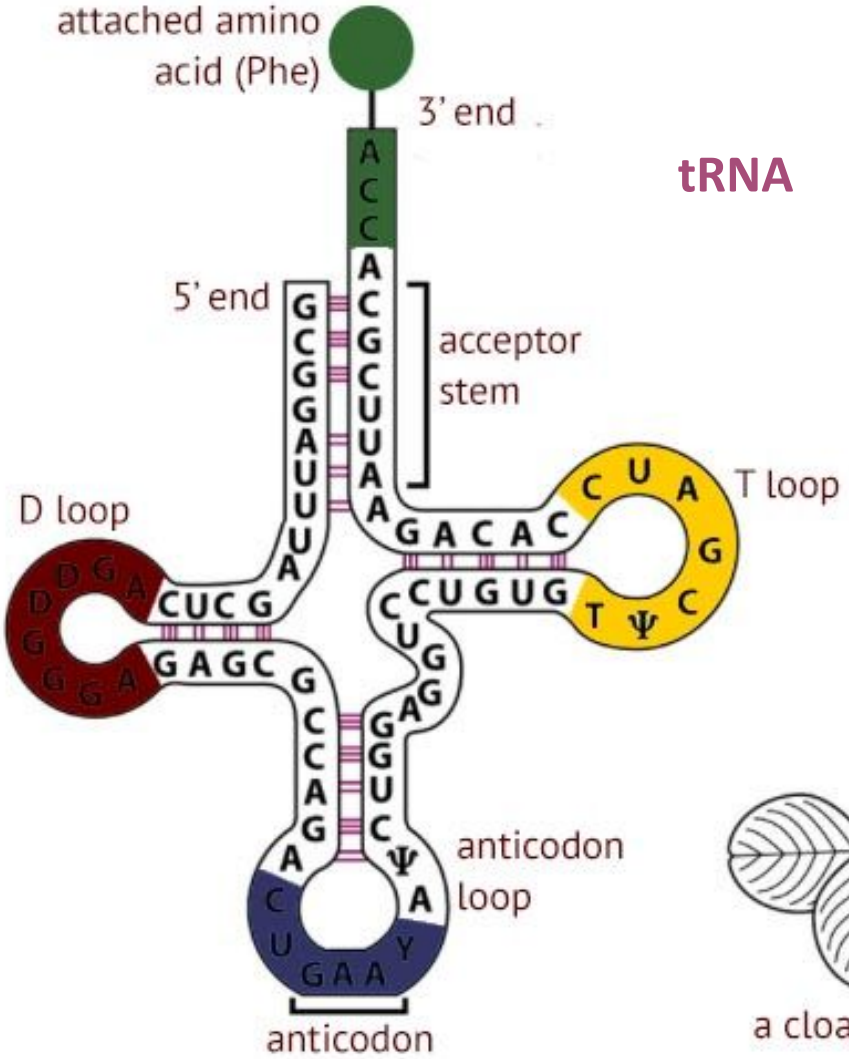
RNA Structure

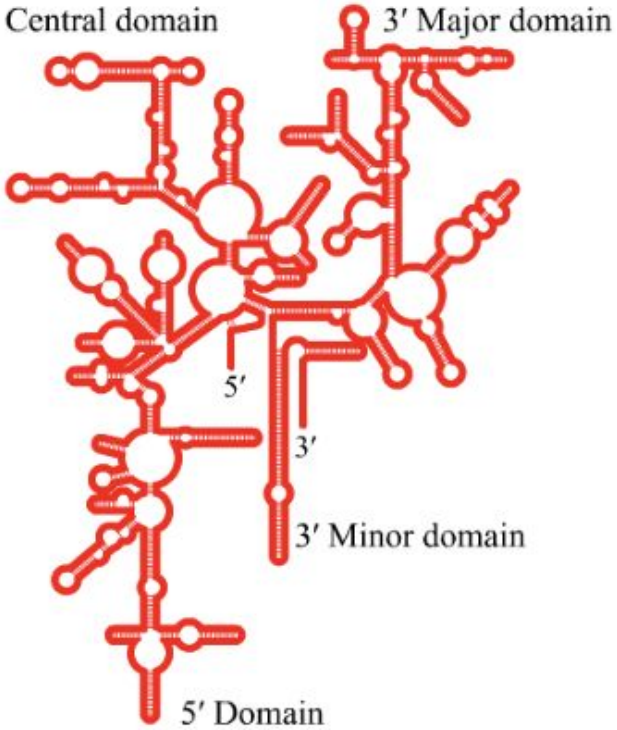
B.Sc. 3rd Semester

A typical cell contains about 10 times as much RNA as DNA. With the exception of some RNA phages and a few eukaryotic viruses, RNA usually exists as a single-stranded polynucleotide. In bacteria, there are three major types of RNA, ribosomal RNA (of which there are three types in bacteria), transfer RNA (of which there are about 50 different types), and messenger RNA (of which there are almost as many different types as there are genes). All of these molecules superficially resemble single-stranded DNA in that single-stranded regions are interspersed with intramolecular, double-stranded regions. Typically between one-half and two-thirds of the bases in RNA are paired. In single-stranded DNA, the pairing is random with short regions containing six or fewer base pairs. Because the base pairing in single-stranded DNA is between short complementary sequences that occur by chance in any stretch of DNA, if a sample of identical DNA molecules is denatured and intramolecular hydrogen bonds are allowed to form, the base-pairing pattern may differ from one molecule to the next. In contrast, in RNA, the double-stranded regions may contain up to 50 base pairs, and each molecule has a specific base-pairing pattern.



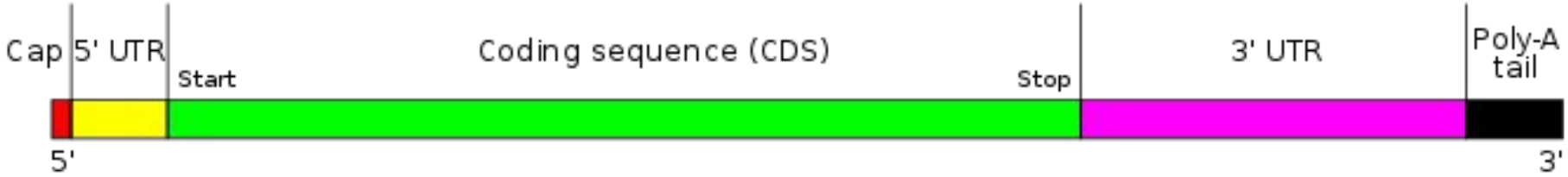
tRNA

a cloaver leaf



rRNA

The structure of a typical human protein coding mRNA including the untranslated regions (UTRs)



RNA (Ribonucleic acid)

- RNA is a polymer of ribonucleotides linked together by 3’-5’ phosphodiester linkage

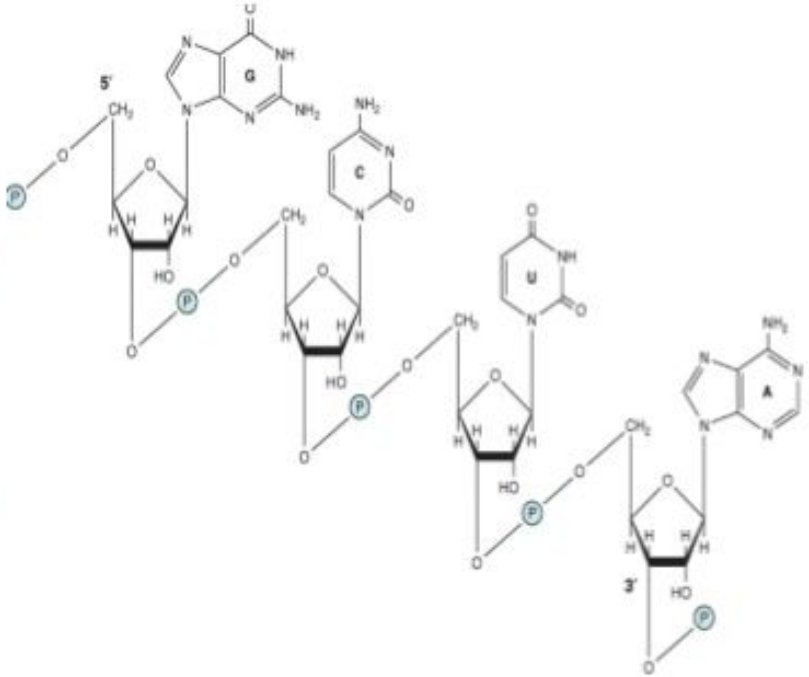
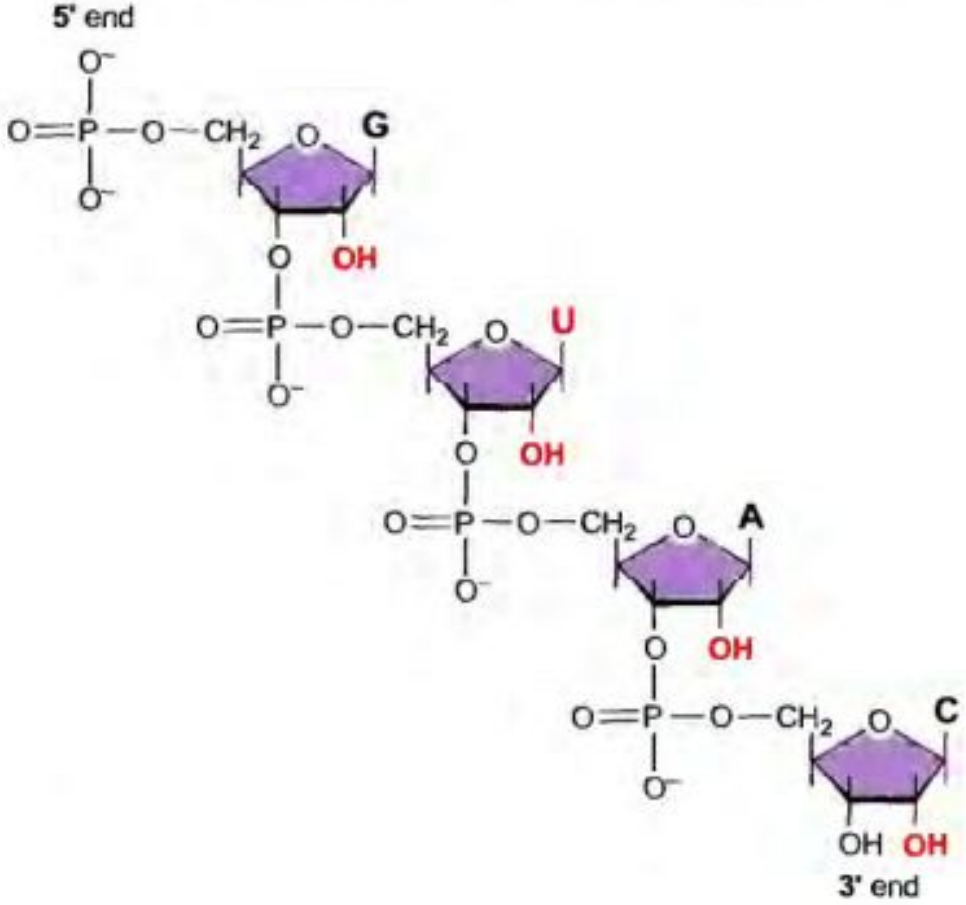


FIGURE 6-29 Structural features of RNA. The figure shows the structure of the backbone of RNA, composed of alternating phosphate and ribose moieties. The features of RNA that distinguish it from DNA are highlighted in red.



Differences between RNA and DNA

S.No.	RNA	DNA
1)	Single stranded mainly except when self complementary sequences are there it forms a double stranded structure (Hair pin structure)	Double stranded (Except for certain viral DNA s which are single stranded)
2)	Ribose is the main sugar	The sugar moiety is deoxy ribose
3)	Pyrimidine components differ. Thymine is never found(Except tRNA)	Thymine is always there but uracil is never found
4)	Being single stranded structure- It does not follow Chargaff's rule	It does follow Chargaff's rule. The total purine content in a double stranded DNA is always equal to pyrimidine content.

Differences between RNA and DNA

S.No.	RNA	DNA
5)	RNA can be easily destroyed by alkalies to cyclic diesters of mono nucleotides.	DNA resists alkali action due to the absence of OH group at 2' position
6)	RNA is a relatively a labile molecule, undergoes easy and spontaneous degradation	DNA is a stable molecule. The spontaneous degradation is very 2 slow. The genetic information can be stored for years together without any change.
7)	Mainly cytoplasmic, but also present in nucleus (primary transcript and small nuclear RNA)	Mainly found in nucleus, extra nuclear DNA is found in mitochondria, and plasmids etc
8)	The base content varies from 100- 5000. The size is variable.	Millions of base pairs are there depending upon the organism

Differences between RNA and DNA

S.No.	RNA	DNA
9)	There are various types of RNA – mRNA, r RNA, t RNA, Sn RNA, Si RNA, mi RNA and hn RNA. These RNAs perform different and specific functions.	DNA is always of one type and performs the function of storage and transfer of genetic information.
10)	No variable physiological forms of RNA are found. The different types of RNA do not change their forms	There are variable forms of DNA (A to E and Z)
11)	RNA is synthesized from DNA, it can not form DNA(except by the action of reverse transcriptase). It can not duplicate (except in certain viruses where it is a genomic material)	DNA can form DNA by replication, it can also form RNA by transcription.
12)	Many copies of RNA are present per cell	Single copy of DNA is present per cell.

Rather, RNA functions as the intermediate, the mRNA, between the gene and the protein-synthesizing machinery. Another function of RNA is as an adaptor, the tRNA, between the codons in the mRNA and amino acids. RNA can also play a structural role, as in the case of the RNA components of the ribosome. Yet another role for RNA is as a regulatory molecule, which through sequence complementarity binds to, and interferes with the translation of, certain mRNAs. Finally, some RNAs (including one of the structural RNAs of the ribosome) are enzymes that catalyze essential reactions in the cell. In all of these cases, the RNA is copied as a single strand off only one of the two strands of the DNA template, and its complementary strand does not exist. RNA is capable of forming long double helices, but these are unusual in nature.

RNA Chains Fold Back on Themselves to Form Local Regions of Double Helix Similar to A-Form DNA

Despite being single-stranded, RNA molecules often exhibit a great deal of double-helical character (Figure 6-30). This is because RNA chains frequently fold back on themselves to form base-paired segments between short stretches of complementary sequences. If the two stretches of complementary sequence are near each other, the RNA may adopt one of various **stem-loop structures** in which the intervening RNA is looped out from the end of the double-helical segment as in a hairpin, a bulge, or a simple loop.

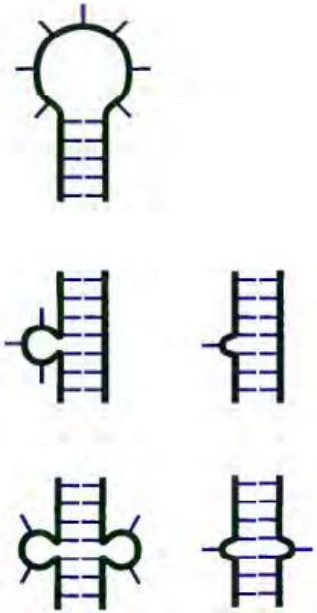


FIGURE 6-30 Double helical characteristics of RNA. In an RNA molecule having regions of complementary sequences, the intervening (noncomplementary) stretches of RNA may become "looped out" to form one of the structures illustrated in the figure. (a) hairpin (b) bulge (c) loop

The stability of such stem-loop structures is in some instances enhanced by the special properties of the loop. For example, a stem-loop with the "tetraloop" sequence UUCG is unexpectedly stable due to special base-stacking interactions in the loop (Figure 6-31). Base pairing can also take place between sequences that are not contiguous to form complex structures aptly named **pseudoknots** (Figure 6-32). The regions of base pairing in RNA can be a regular double helix or they can contain discontinuities, such as noncomplementary nucleotides that bulge out from the helix.

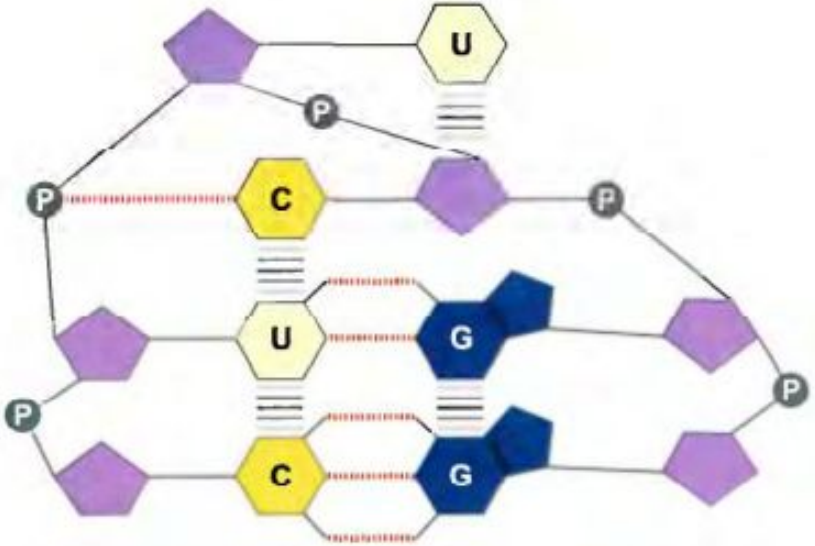
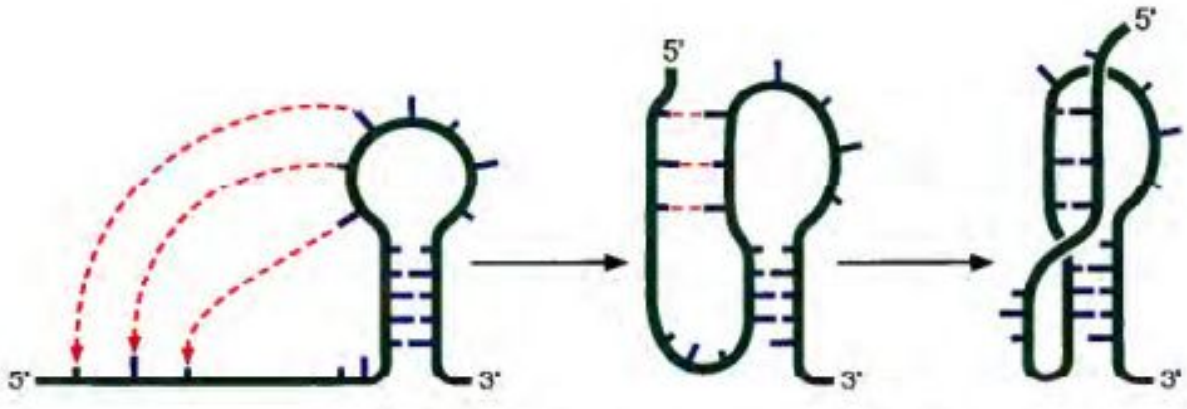


FIGURE 6-31 Tetraloop. Base stacking interactions promote and stabilize the tetraloop structure. The gray circles between the riboses shown in purple represent the phosphate moieties of the RNA backbone. Horizontal lines represent base stacking interactions.

FIGURE 6-32 Pseudoknot. The pseudoknot structure is formed by base pairing between noncontiguous complementary sequences.



A feature of RNA that adds to its propensity to form double-helical structures is an additional, non-Watson-Crick base pair. This is the G:U base pair, which has hydrogen bonds between N3 of uracil and the carbonyl on C6 of guanine and between the carbonyl on C2 of uracil and N1 of guanine (Figure 6-33). Because G:U base pairs can occur as well as the four conventional, Watson-Crick base pairs, RNA chains have an enhanced capacity for self-complementarity. Thus, RNA frequently exhibits local regions of base pairing but not the long-range, regular helicity of DNA.

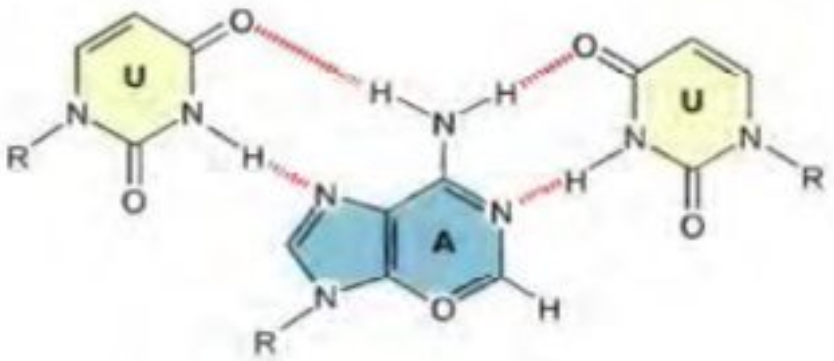
The presence of 2′-hydroxyls in the RNA backbone prevents RNA from adopting a B-form helix. Rather, double-helical RNA resembles the A-form structure of DNA. As such, the minor groove is wide and shallow, and hence accessible, but recall that the minor groove offers little sequence-specific information. Meanwhile, the major groove is so narrow and deep that it is not very accessible to amino acid side chains from interacting proteins. Thus, the RNA double helix is quite distinct from the DNA double helix in its detailed atomic structure and less well suited for sequence-specific interactions with proteins (although some proteins do bind to RNA in a sequence-specific manner).

FIGURE 6-33 G:U base pair. The structure shows hydrogen bonds that allow base pairing to occur between guanine and uracil.

RNA Can Fold Up into Complex Tertiary Structures

Freed of the constraint of forming long-range regular helices, RNA can adopt a wealth of tertiary structures. This is because RNA has enormous rotational freedom in the backbone of its non-base-paired regions. Thus, RNA can fold up into complex tertiary structures frequently involving unconventional base pairing, such as the base triples and base-backbone interactions seen in tRNAs (see, for example, the illustration of the U:A:U base triple in Figure 6-34). Proteins can assist the formation of tertiary structures by large RNA molecules, such as those found in the ribosome. Proteins shield the negative charges of backbone phosphates, whose electrostatic repulsive forces would otherwise destabilize the structure.

FIGURE 6-34 U:A:U base triple. The structure shows one example of hydrogen bonding that allows unusual triple base pairing.



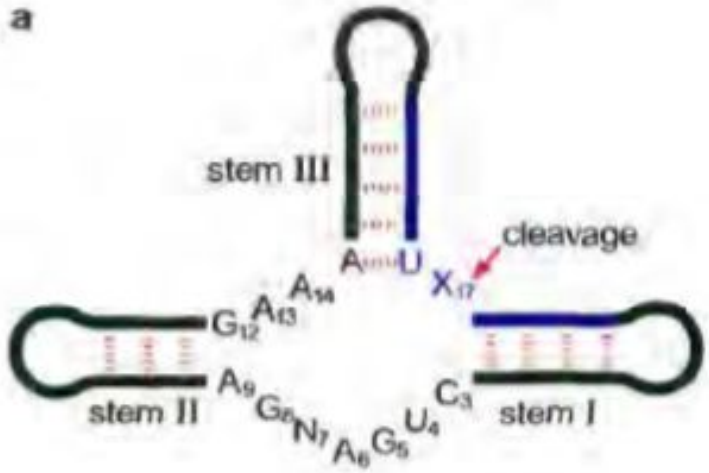
U:A:U base triple

Some RNAs Are Enzymes

It was widely believed for many years that only proteins could be enzymes. An enzyme must be able to bind a substrate, carry out a chemical reaction, release the product and repeat this sequence of events many times. Proteins are well-suited to this task because they are composed of many different kinds of amino acids (20) and they can fold into complex tertiary structures with binding pockets for the substrate and small molecule co-factors and an active site for catalysis. Now we know that RNAs, which as we have seen can similarly adopt complex tertiary structures, can also be biological catalysts. Such RNA enzymes are known as **ribozymes,** and they exhibit many of the features of a classical enzyme, such as an active site, a binding site for a substrate, and a binding site for a co-factor, such as a metal ion.

One of the first ribozymes to be discovered was **RNAse P,** a ribonuclease that is involved in generating tRNA molecules from larger, precursor RNAs. RNAse P is composed of both RNA and protein; however, the RNA moiety alone is the catalyst. The protein moiety of RNAse P facilitates the reaction by shielding the negative charges on the RNA so that it can bind effectively to its negatively-charged substrate. T[redacted]

Other ribozymes carry out trans-esterification reactions involved in the removal of intervening sequences known as **introns** from precursors to certain mRNAs, tRNAs, and ribosomal RNAs in a process known as **RNA splicing** ([redacted]



(a) The figure shows the predicted secondary structures of the hammerhead ribozyme.

FIGURE 6-35 Secondary structure of the hammerhead ribozyme.