RNA AND ITS STRUCTURE, FUNCTION AND TYPES

Ribonucleic acid (RNA) is a type of molecule that consists of a long chain of nucleotide units. Each nucleotide consists of a nitrogenous base, a ribose sugar, and a phosphate. RNA is very similar to DNA, but differs in a few important structural details: in the cell, RNA is usually single-stranded, while DNA is usually double-stranded; RNA nucleotides contain ribose while DNA contains deoxyribose (a type of ribose that lacks one oxygen atom); and RNA has the base uracil rather than thymine that is present in DNA.

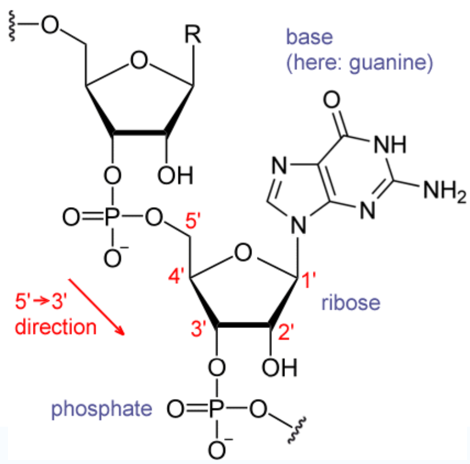
RNA is transcribed from DNA by enzymes called **RNA polymerases.** RNA is central to the synthesis of proteins., a type of RNA called messenger RNA carries information from DNA to structures called ribosomes. These ribosomes are made from proteins and ribosomal RNAs, which come together to form a molecular machine that can read messenger RNAs and translate the information they carry into proteins. The RNA form the genomes of most viruses.

Ribose Nucleic Acids

Most cellular RNA is single stranded, although some viruses have double stranded RNA. The single RNA strand is folded upon itself, either entirely or in certain regions. In the folded region a majority of the bases are complementary and are joined by hydrogen bonds. This helps in the stability of the molecule. In the unfolded region the bases have no complements. Because of this RNA does not have the purine, pyrimidine equality that is found in DNA.

RNA also differs from DNA in having ribose as the sugar instead of deoxyribose. The common nitrogenous bases of RNA are adenine, guanine, cytosine and uracil. Thus the pyrimidine uracil substitutes thymine of DNA. In regions where purine pyrimidine pairing takes place, adenine pairs with uracil and guanine with cytosine. In addition to the four bases mentioned above, RNA also has some unusual bases.

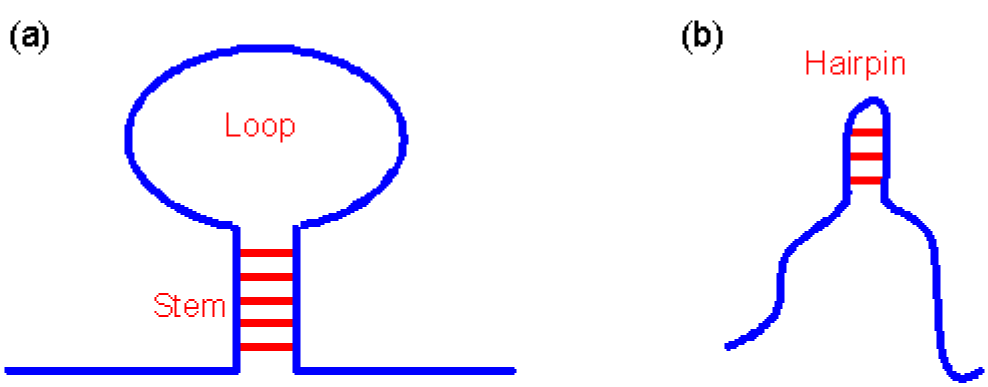
CHEMICAL STRUCTURE OF RNA



An important structural feature of RNA that distinguishes it from DNA is the presence of a hydroxyl group at the 2' position of the ribose sugar.

Most cellular RNA molecules are single stranded. They may form secondary structures such as stem-loop and hairpin.

Secondary structure of RNA. (a) stem-loop. (b) hairpin.



There are more unusual bases in RNA than in DNA. All normal RNA chains either start with adenine or guanine: Three types of cellular RNA have been distinguished:

Messenger RNA (mRNA) or template RNA

Ribosomal RNA (rRNA) and

Soluble RNA (sRNA) or transfer RNA (tRNA)

Ribosomal and transfer RNA comprise about 98% of all RNA. All three forms of RNA are made on a DNA template.

Transfer RNA and messenger RNA are synthesized on DNA templates of the chromosomes, while ribosomal RNA is derived from nucleolar DNA. The three types of RNA are synthesized during different stages in early development. Most of the RNA synthesized during cleavage is mRNA. Synthesis of tRNA occurs at the end or cleavage, and rRNA synthesis begins during gastrulation.

Comparison between DNA and RNA

	DNA	**RNA**
1.	DNA is the usual genetic material	RNA is the genetic material of some viruses.
2.	DNA is usually double-stranded, (In certain viruses DNA is single stranded, e.g. φ X 174).	Most cellular RNA is single stranded. (Some viruses e.g. retrovirus, have double stranded RNA).
3.	The pentose sugar is deoxyribose.	The pentose sugar is ribose.
4.	The common organic bases are adenine, guanine, cytosine and thymine.	The common organic bases are adenine, guanine, cytosine and uracil.
5.	Base pairing: adenine pairs with thymine and guanine with cytosine.	Adenine pairs with uracil and guanine with cytosine.
6.	Pairing of bases is throughout the length of the molecule.	Pairing of bases is only in the helical region
7.	There are fewer uncommon bases	There are more uncommon bases.
8.	DNA is only of one type	There are three types of RNA messenger, ribosomal and transfer RNA.

9.	Most of the DNA is found in the chromosomes. Some DNA is also found in the cytoplasm e.g. in mitochondria and chloroplasts.	Messenger RNA is formed on the chromosomes, and is found in the nucleolus and cytoplasm. rRNA and tRNA are also formed on the chromosomes, and are found in cytoplasm.
10.	Denaturation (melting) is partially reversible only under certain conditions of slow cooling (renaturation).	Complete and practically ireversibility of the process of melting.
12.	DNA on replication forms DNA, and on transcription forms RNA.	Usually RNA does not replicate or transcribe. (In certain viruses RNA can synthesize an RNA chain).
13.	Genetic messages are usually encoded in DNA.	The usual function of RNA is translating messages encoded in DNA into proteins.
14.	DNA consists of a large number of nucleotides, up to 4.3 million	RNA consists of fewer nucleotides, up to 12,000.

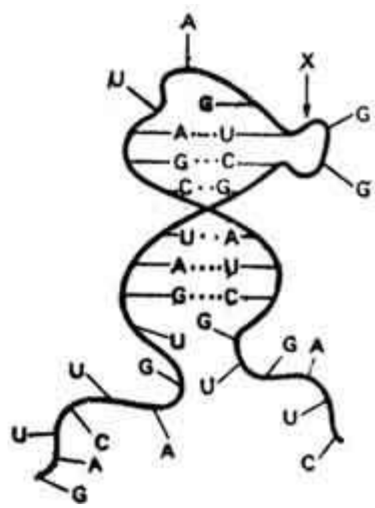
Ribosomal RNA – rRNA

Ribosomal RNA, as the name suggests, is found in the ribosomes. It comprises about 80% of the total RNA of the cell. The base sequence of rRNA is complementary to that of the region of DNA where it is synthesized.

In eukaryotes ribosomes are formed on the nucleolus. Ribosomal RNA is formed from only a small section of the DNA molecule, and hence there is no definite base relationship between rRNA and DNA as a whole.

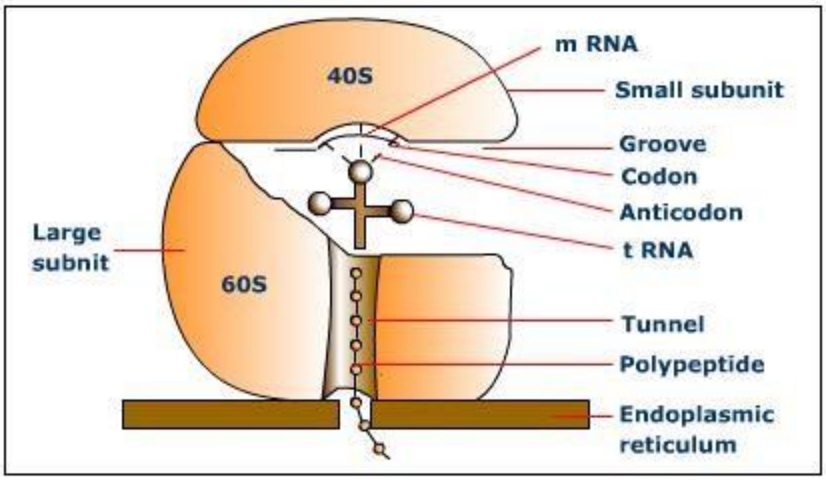
Ribosomal RNA consists of a single strand twisted upon itself in some regions. It has helical regions connected by intervening single strand regions. The helical regions may show presence or absence of positive interaction. In the helical region most of the base pairs are complementary, and are joined by hydrogen bonds. In the unfolded single strand regions the bases have no complements.

Ribosomal RNA contains the four major RNA bases with a slight degree of methylation, and shows differences in the relative proportions of the bases between species. Its molecules appear to be single polynucleotide strands which are unbranched and flexible. At low ionic strength rRNA behaves as a random coil, but with increasing ionic strength the molecule shows helical regions produced by base pairing between adenine and uracil and guanine and cytosine.



Hence rRNA does not show purine-pyrimidine equality. The rRNA strands unfold upon heating and refold upon cooling. Ribosomal RNA is stable for at least two generations. The ribosome consists of proteins and RNA. The 70S ribosome of prokaryotes consists of a 30S subunit and a 50S subunit. The 30S subunit contains 16S rRNA, while the 50S subunit contains 23S and 5S rRNA.

The 80S eukaryote ribosome consists of a 40S and a 60S subunit. In vertebrates the 40S subunit contains 18S rRNA, while the 60S subunit contains 28-29S, 5.8S and 5S rRNA.



Messenger RNA - mRNA - Jacob and Monod (1961) proposed the name messenger RNA for the RNA carrying information for protein synthesis from the DNA (genes) to the sites of protein formation (ribosomes). It consists of only 3 to 5% of the total cellular RNA.

Since most proteins contain at least a hundred amino acid residues, mRNA must have at least 100 X 3= 300 nucleotides on the basis of the triplet code.

Stability of Messenger RNA - mRNA - The cell does not contain large quantities of mRNA. This is because mRNA, unlike other RNAs is constantly undergoing breakdown. It is broken down to its constituent ribonucleotides by ribonucleases.

Structure of Messenger RNA - mRNA

Messenger RNA is always single stranded. It contains mostly the bases adenine, guanine, cytosine and uracil. There are few unusual substituted bases. Although there is a certain amount of random coiling in extracted mRNA, there is no base pairing. In fact base pairing in the mRNA strand destroys its biological activity

Since mRNA is transcribed on DNA (genes), its base sequence is complementary to that of the segment of DNA on which it is transcribed.

Usually each gene transcribes its own mRNA. Therefore, there are approximately as many types of mRNA molecules as there are genes. There may be 1,000 to 10.000 different species of mRNA in a cell. These mRNA types differ only in the sequence of their bases and in length.

When one gene (cistron) codes for a single mRNA strand the mRNA is said to be monocistronic. In many cases, however, several adjacent cistrons may transcribe an mRNA molecule, which is then said to be polycistronic or polygenic.

The mRNA molecule has the following structural features:

1. Cap. At the 5' end of the mRNA molecule in most eukaryote cells and animal virus molecules is found a 'cap'. This is blocked methylated structure, m7Gpp Nmp Np or m7Gpp Nmp Nmp Np. where: N = any of the four nucleotides and Nmp = 20 methyl ribose. The rate of protein synthesis depends upon the presence of the cap. Without the cap mRNA molecules bind very poorly to the ribosomes.

2. Noncoding region 1 (NC1). The cap is followed by a region of 10 to 100 nucleotides. This region is rich in A and U residues, and does not translate protein.

3. The initiation codon is AUG in both prokaryotes and eukaryotes

4. The coding region consists of about 1,500 nucleotides on the average and translates protein It is made up of 73-93 nucleotides.

Each bacterial cell probably contains about a hundred or more different types of tRNA. The function of tRNA is to carry amino acids to mRNA during protein synthesis. Each amino acid is carried by a specific tRNA. Since 20 amino acids are coded to form proteins, it follows that there must be at least 20 types of tRNA.

It was formerly thought that only 20 tRNA molecular types exist, one for each amino acid. It has, however, been shown that in several cases there are at least two types of tRNA for each amino acid. Thus there are many more tRNA molecules than amino acid types. These are probably coded by one gene.

Transfer RNA is synthesized in the nucleus on a DNA template. Only 0.025% of DNA codes for tRNA. Synthesis of tRNA occurs near the end of cleavage stages. Transfer RNA is an exception to other cellular RNAs in that a part of its ribonucleotide sequence (-CCA) is added after it comes off the DNA template. Like rRNA, tRNA is also formed from only a small section of the DNA molecule.

Transfer RNA - tRNA OR Soluble RNA – sRNA

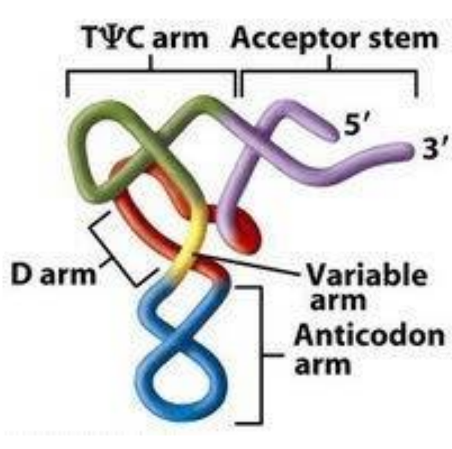
After rRNA the second most common RNA in the cell is transfer RNA. It is also called soluble RNA because it is too small to be precipitated by ultracentrifugation at 100,000 g.

It constitutes about 10-20% of the total RNA of the cell. Transfer RNA is a relatively small RNA having a molecular weight of about 25,000 to 30,000 and the sedimentation coefficient of mature eukaryote tRNA is 3.8S.

Transfer RNA (tRNA) is an essential component of the protein synthesis reaction. There are at least twenty different kinds of tRNA in the cell[1] and each one serves as the carrier of a specific amino acid to the site of translation.

tRNA's are L-shaped molecules. The amino acid is attached to one end and the other end consists of three anticodon nucleotides. The anticodon pairs with a codon in messenger RNA (mRNA) ensuring that the correct amino acid is incorporated into the growing polypeptide chain.

The L-shaped tRNA is formed from a small single-stranded RNA molecule that folds into the proper conformation. Four different regions of double-stranded RNA are formed during the folding process.

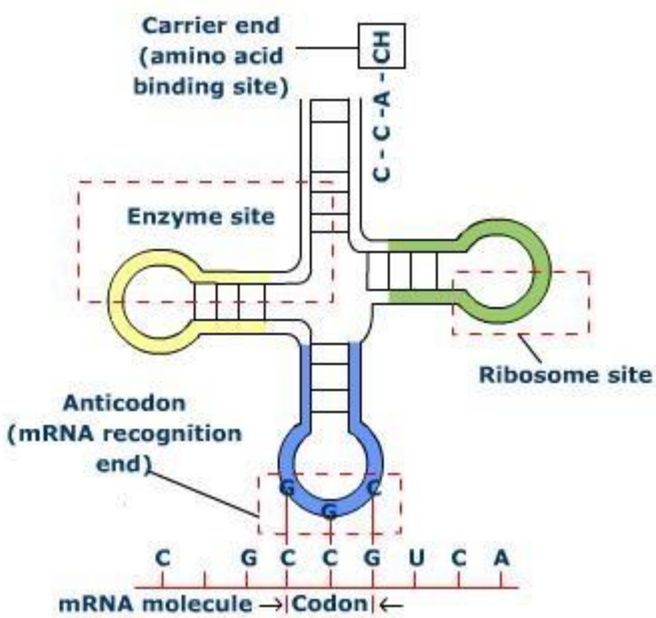


The two ends of the molecule form the *acceptor stem* region where the amino acid is attached. The anticodon is an exposed single-stranded region in a loop at the end of the *anticodon arm*.

The two other stem/loop structures are named after the modified nucleotides that are found in those parts of the molecule. The *D arm* contains dihydrouridylate residues while the *TΨC arm* contains a ribothymidylate residue (T), a pseudouridylate residue (Ψ) and a cytidylate (C) residue in that order. All tRNA's have a similar *TΨC* sequence. The *variable arm* is variable, just as you would expect. In some tRNA's it is barely noticable while in others it is the largest arm.

tRNA's are usually drawn in the "cloverleaf" form (below) to emphasize the base-pairs in the secondary structure.

Clover leaf model of tRNA



Unusual Bases in tRNA

In addition to the usual bases A, U, G and C, tRNA contain a number of unusual bases, and in this respect differs from mRNA and rRNA. The unusual bases of tRNA account for 15-20% of the total RNA of the cell. Most of the unusual bases are formed by methylation (addition of -CHa or methyl group to the usual bases), e.g. cytosine and guanine on methylation yield methylcytosine and methyl/guanine, respectively.

Precursor tRNA molecules transcribed on the DNA template contains the usual bases. These are then modified to unusual bases. The unusual bases are important because they protect the tRNA molecule against degradation by RNase. This protection is necessary because RNA is found floating freely in the cell.

Some of the unusual bases of tRNA are methyl guanine (GMe), dimethylguanine(GMe2), methylcytosine (Me), ribothymine (T), pseudouridine (ψ), dihydrouridine (DHU, H2U, UH2), inosine (I) and methylinosine (IMe, MeI). In general, organisms high in the evolutionary scale contain more modified bases than lower organisms.

Initiator Transfer RNA - tRNA

The starting amino acid in eukaryote protein synthesis is methionine, while in prokaryotes it is N-formyl methionine. The tRNA molecule3 specific for these two amino acids are methionyl tRNA (tRNAmet) and N-formyl- methionyl IRNA (tRNAfmet) respectively.

These tRNAs are called initiator tRNAs, because they initiate protein synthesis. Initiator tRNAs have certain features which distinguish them from other tRNAs, and the initiator tRNAs of prokaryotes' and eukaryotes also differ.

In most prokaryotes the 5' terminal nucleoside is C. It has opposite it (i.e. in the fifth position from the 3' end) an A nucleotide. There is no Watson-Crick base pairing between the two. In the blue green 'alga' Anacystis nidulans, however, the fifth nucleotide from the 3' end is C. In eukaryotes there is an A.U base pair at the acceptor stem.

Specificity of Tranfer RNA - tRNA

Two important steps in translation during protein synthesis are the activation of amino acids and the transfer of amino acids to tRNAs. Each amino acid has a specific activating enzyme tRNA aminoacyl synthetase. Thus there are 20 different tRNA aminoacyl synthetases for the 20 common amino acids found in proteins.

Table - Various types of RNA

RNA type	Abbreviation	Cellular process	Function
Messenger RNA	mRNA	Translation	Template for protein synthesis
Ribosomal RNA	rRNA	Translation	Assembly of mRNA, tRNA, and translation factors for peptide bond formation
Transfer RNA	tRNA	Translation	Selection, activation, and transport of amino acids to the ribosome
Small nuclear RNA	snRNA	Pre-mRNA splicing (removal of introns and joining of flanking exons)	Spliceosome components: specification of sites of exon-intron cleavage (5′ and 3′ splice sites) and branch-point A residue (nucleophile)
Small nucleolar RNA	snoRNA	Pre-rRNA maturation	Specification of sites of modified nucleoside components (2′-*O*-methylnucleosides and pseudouridine)
Small Cajal body RNA	scaRNA	Maturation of snRNAs and snoRNAs	Specification of sites of modified nucleoside components (2′-*O*-methylnucleosides and pseudouridine)
Small RNA	sRNA	Pre-RNA maturation	Counterpart in Archaea of snoRNA in eukaryotes
Guide RNA	gRNA	mRNA editing	Small antisense RNA that provides the information for editing
MicroRNA	miRNA	RNA interference	Small, naturally occurring antisense RNA involved in gene regulation
Small interfering RNA	siRNA	RNA interference	Processed counterpart of miRNA, mediating inactivation or degradation of complementary mRNA or viral RNA