

RNAs, Structure and Function

RNA structure and characteristics

Structure

- Ribonucleic acid (RNA) is a biopolymer macromolecule as DNA. It consists of small subunits called nucleotides composed of:
 - Purine nucleobases [Adenine–(A), Guanine–(G)]
 - Pyrimidine nucleobases [Cytosine–(C), Uracil–(U)]
 - D-ribose pentose sugars [$C_5H_{10}O_5$]
 - Phosphate groups [PO_4^{3-}]
- The nucleobase is attached on the D-ribose by an N-glycosidic bond
- The ribose is bonded to the phosphate group through ester bonds
- The backbone bonding between RNA nucleotides (i.e. the bonds between the phosphate group and an adjacent ribose sugar) occurs through phosphodiester bonds. A phosphate group is attached to the 3'-carbon position of one ribose and on the 5'-carbon position of the next

Characteristics

- RNA does not self replicate in order to multiply; instead it is encoded by DNA genes
- RNA is synthesized in order for the translation of DNA to be possible
- The DNA-RNA function is highly interdependable, i.e., if there is problem with DNA, there will be a problem with the RNA functions and vice versa (no RNA = no DNA translation can occur, thus DNA is useless without its RNA genes)

RNA—DNA differences

RNA and DNA are very similar in structure but they differ in 5 major points:

1. DNA nucleotides include Adenine, Guanine, Thymine or Cytosine whereas RNA nucleotides, instead of Thymine they involve Uracil
2. DNA is always in a double helix conformational arrangement with the 2 strands always running in anti parallel orientation whereas RNA usually exists as a single strand but it has the ability to form a double strand structure also
3. DNA has a 2'-deoxy-D-ribose pentose sugar whereas RNA has a D-ribose
4. DNA has equal portions of Adenine—Thymine and Guanine—Cytosine nucleobases as it exists as a double stranded molecule (i.e. since Adenines bind to Thymines and Guanines to Cytosines, it indicates that the number of Adenines and Guanines present, equal to the number of Thymines and Cytosines respectively) where as RNA does not as it usually exists in a single stranded form
5. RNA is relatively unstable in comparison to the DNA molecule as it contains a 2'-OH hydroxyl group that acts as a nucleophil, enhancing the cleavage of the phosphodiester bond between adjacent nucleotides and phosphates

RNA and DNA Characteristics

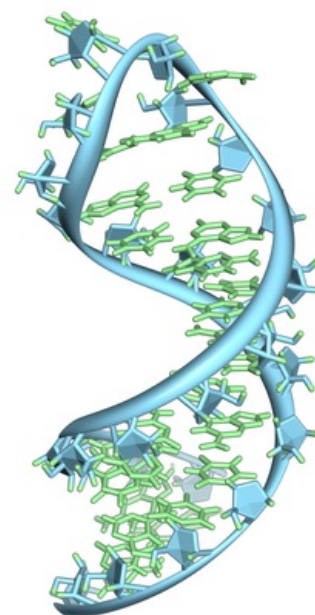
DNA	RNA
A,G,C or T nucleobase	A,G,C or U nucleobase
Double stranded conformation	Single or Double stranded conformation
2'-deoxy-D-ribose pentose sugar	D-ribose pentose sugar
Adenine=Thymine and Guanine=Cytosine	Adenine≠Uracil , Guanine≠Cytosine

Types of RNA

RNA genes of DNA encode for 3 major types of RNA:

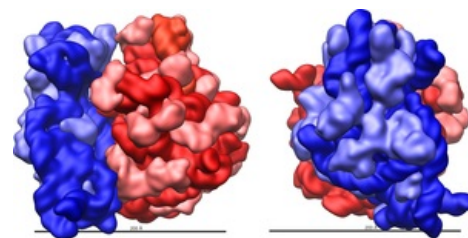
- ribosomal RNA
- messenger RNA
- transfer RNA

Ribosomal RNA [rRNA]



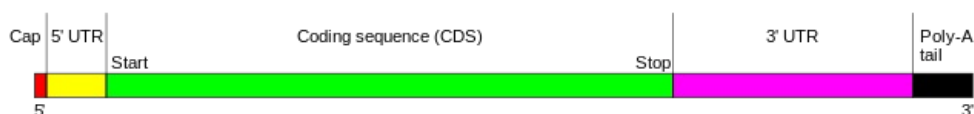
A hairpin loop from a pre-mRNA. Highlighted are the nucleobases (green) and the ribose-phosphate backbone (blue).

Ribosomes are non membranous organelles that participate in the translation of mRNA into a protein product. The ribosome structure is composed of 2 subunits. A small and a large subunit each of which primarily consists of rRNA of various size and a small quantity of proteins. rRNA constitutes about the 80% of the whole RNA present in an eukaryotic cell. The large subunit consists of rRNA of 5S, 5.8S and 28S sizes whereas the small subunit consists of rRNA of 18S size. (where S is the unit for rRNA size). These rRNAs are synthesized by transcription of the rRNA genes. However, the rRNA genes encode for all rRNAs except from the 5S rRNA, which is synthesized by the tRNA genes along with all the nuclear tRNAs. RNA polymerase type I is responsible for the transcription of rRNA genes by binding on the core element—CE, which overlaps the Transcription Start Site—TSS, along with the Transcription Factors inducing the so called Transcription Initiation Complex designated as TIC. The rate of the transcription is controlled by an Upstream Control Sequence—UCS located 100 base pairs upstream to the TSS. The transcription process begins and the genes are transcribed into pre-rRNA in the following order as situated on the gene: -18S - 5.8S - 28S-. The transcription comes to an end when the Transcription Complex reaches an area rich in Adenines found at about 600 base pairs downstream of the gene, indicating its end. The pre-rRNA formed includes all rRNAs on a single strand so that cleavage has to be performed so that different size rRNAs are separated. This task is undertaken by RNases that cleave the rRNA giving rise to the differential size rRNAs.



Ribosomal RNA (rRNA) is the RNA component of a ribosome

Messenger RNA [mRNA]



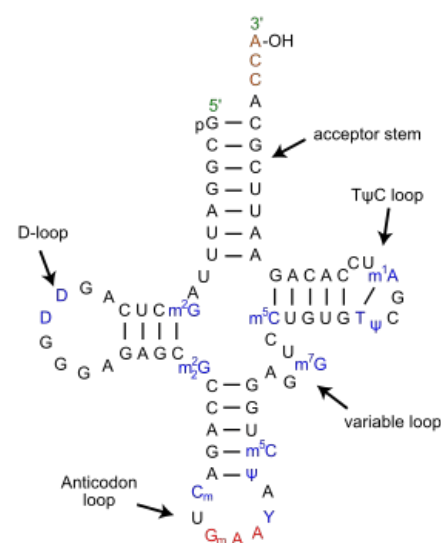
The structure of a mature eukaryotic mRNA. A fully processed mRNA includes a 5' cap, 5' UTR, coding region, 3' UTR, and poly(A) tail.

mRNA genes are the genes that encode only for proteins but this encoding has an RNA intermediate. The DNA is firstly transcribed into mRNA and subsequently translated into a protein product. So the mRNA genes are the genes that encode for mRNA in order to synthesize proteins. mRNA constitutes only the 5% of the total RNA. RNA polymerase II is the enzyme responsible for the transcription of the corresponding genes into mRNA. The polymerase binds on the TATA box which acts more or less as a promoter, located about 25 base pairs upstream the Transcription Start Site—TSS, along with the transcription factors giving rise to the Transcription Initiation Complex—TIC. In order for this complex to be functional a proper sequence of events of binding the TF and the polymerase on the promoter must occur as: TFII-D, TFII-A, TFII-B, RNA pol II, TFII-F, TFII-H TFII-E TFII-J. As soon as the TIC is formed then transcription begins giving rise to pre-mRNA which include both exons and introns. Transcription ends without recognition of an adenine rich area but rather by automatic disassembling of the Transcription Complex. The pre-mRNA is then submitted to processing that involves splicing - removal of introns and merging of the adjacent exons- and capping - addition of 7-methylguanosine on the 5' end of the mRNA so that mRNA cannot be cleaved by exonucleases. It also serves as a recognition site of the mRNA prior to translation for the small ribosomal subunit.

Transfer RNA [tRNA]

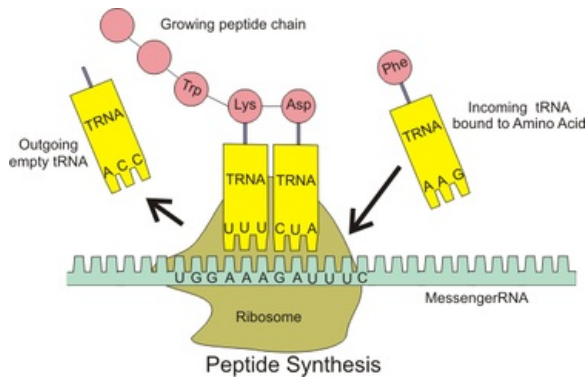
Transfer RNA is encoded by genes that also encode for the 5S size rRNA. RNA polymerase III is responsible for the transcription of these genes by binding on the promoter, situated about 100 base pairs downstream the Transcription Start Site -TSS, along with the Transcription Factors giving rise to the Transcription Initiation Complex. As soon as this complex is formed transcription process can begin and when the Transcription Complex faces an Adenine rich region transcription comes to an end as this area is an indication for the gene end. tRNA constitutes 15% of the total RNA and is directly involved in the translation of the mRNA. More specifically tRNA binds onto a specific amino acid and brings it along the translation site so that it is bound on the newly synthesized peptide.

- tRNA binds to its specific amino acid recognized by its side R chain in presence of the aminoacyl tRNA synthetase enzyme. The synthetase binds the 5'-CCA-OH-3' acceptor arm with the —COOH group of the amino acid.
- When the small ribosomal subunit faces an AUG codon on the mRNA it indicates the commencing of the peptide formation. As soon as the AUG codon is recognized then the first tRNA binds on the small ribosomal subunit and on the mRNA through its anticodon arm, giving rise to the Translation Initiation Complex designated as $tRNA_i^{met}$. Eventually the large ribosomal subunit binds on the complex indicating the initiation of the translation process. Translation always begins with the methionine amino acid on the newly synthesized peptide.
- After translocation of the Translation complex the $tRNA_i^{met}$ enter the Peptidyl site of the complex leaving the Aminoacyl site vacant for the next tRNA to enter, bringing together the two adjacent amino acids so that a



Secondary cloverleaf structure of $tRNA^{Phe}$ from yeast.

peptide bond can be formed in presence of the peptidyl transferase enzyme. As soon as the peptide bond is formed, the tRNA is released from its amino acid in presence of the tRNA deacylase.



The interaction of tRNA and mRNA in protein synthesis

Other types of RNA

- **Small interfering RNA [siRNA]:** Known as short interfering RNA, a class of double stranded RNA molecules involved in the RNA interference (RNA_i) pathway. There, it interferes with the expression of specific genes controlling the stability of the mRNA. In this way the mRNA disintegrates (when necessary), avoiding its overexpression with a consequent overproduction of proteins.
- **Small nuclear RNA [snRNA]:** They are RNA molecules transcribed by either RNA polymerase II along with mRNA or by RNA polymerase III along with all nuclear tRNAs and the 5S rRNA. They are primarily involved in mRNA processing such as splicing by removal of introns from pre-mRNA and also in maintenance of the telomeres. They are always associated with proteins giving rise to complexes are referred to as small nuclear ribonucleoproteins—snRNP directly associated with the splicing process.
- **Heterogeneous nuclear RNA [hnRNA] :** hnRNA is an immature single strand of mRNA. The terms hnRNA and pre-mRNA are almost identical and thus used interchangeably.

