

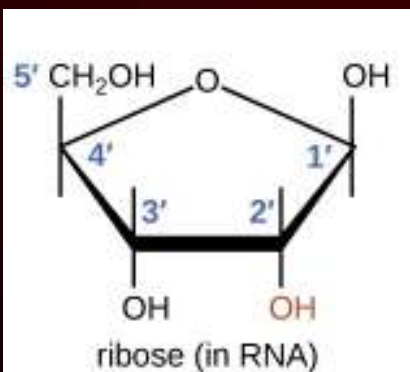
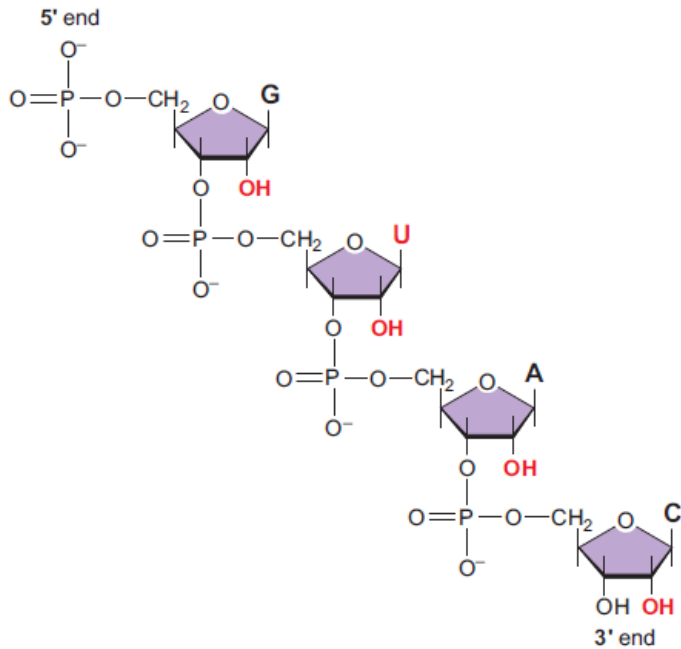
Types of RNAs

RNA Types

- 1. mRNA**
- 2. Transfer RNA (tRNA)**
- 3. Ribosomal RNA (rRNA)**
- 4. Small Nuclear RNA (snRNA)**
- 5. Regulatory RNAs (miRNA)**
- 6. Transfer-messenger RNA (tmRNA)**
- 7. Ribozymes (RNA enzymes)**
- 8. Double-stranded RNA (dsRNA)**

What is RNA?

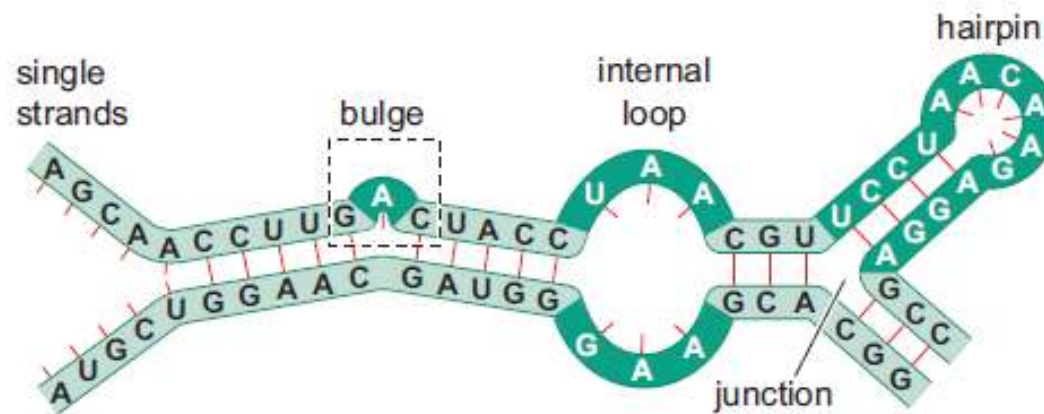
- RNA is principally found as a **single-stranded** molecule.
- It is known as **Ribonucleic Acid**. The backbone of RNA contains **ribose** rather than 2'-deoxyribose.
- Four nitrogenous bases are **Guanine, Cytosine, Adenine and Uracil**.
- RNA contains the **pyrimidine uracil** in place of thymine found in DNA.
- The strand has a **5' end (with a phosphate group)** and a **3' end (with a hydroxyl group)**.
- It is composed of ribonucleotides (ribonucleotides are adenosine, guanosine, cytidine and uridine).
- The **ribonucleotides are linked together by 3' → 5' phosphodiester bonds**.



Functions of RNA

- RNA is a nucleic acid **messenger** between DNA and ribosomes.
- It serves as the **genetic material** in some organisms (**viruses**).
- Some RNA molecules play an **active role within cells by catalyzing biological reactions, controlling gene expression, or sensing and communicating responses to cellular signals.**
- **Messenger RNA (mRNA)** copies DNA in the nucleus and **carries the info to the ribosomes (in cytoplasm).**
- **Ribosomal RNA (rRNA)** makes up a large **part of the ribosome; reads and decodes mRNA.**
- **Transfer RNA (tRNA)** carries **amino acids** to the ribosome where they are joined to form proteins.
- Certain RNAs are able **to catalyze chemical reactions such as cutting and ligating other RNA molecules,** and the catalysis of peptide bond formation in the ribosome; these are known as **ribozymes.**

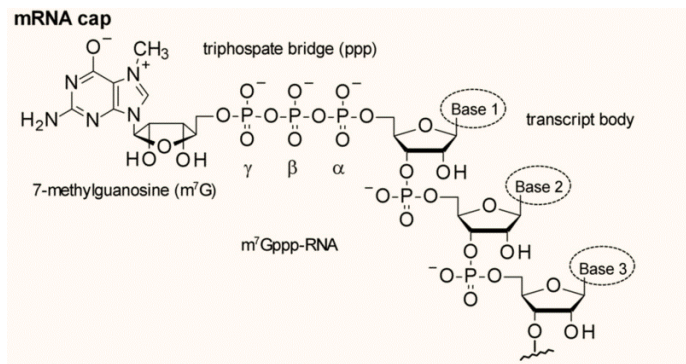
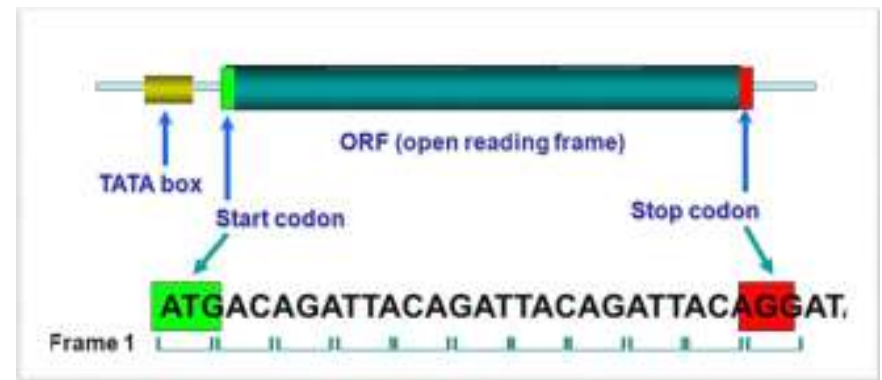
Double-helical characteristics of RNA



- Most RNA molecules are single-stranded but an RNA molecule may contain regions which can form **complementary base pairing where the RNA strand loops back on itself**. Non complementary sequences may become **looped out to form the bulge structure, an internal loop or hairpin loop**.
- If so, some part of RNA will have some double-stranded regions.
- Ribosomal RNAs (rRNAs) and transfer RNAs (tRNAs) exhibit substantial secondary structure, as do some messenger RNAs (mRNAs).

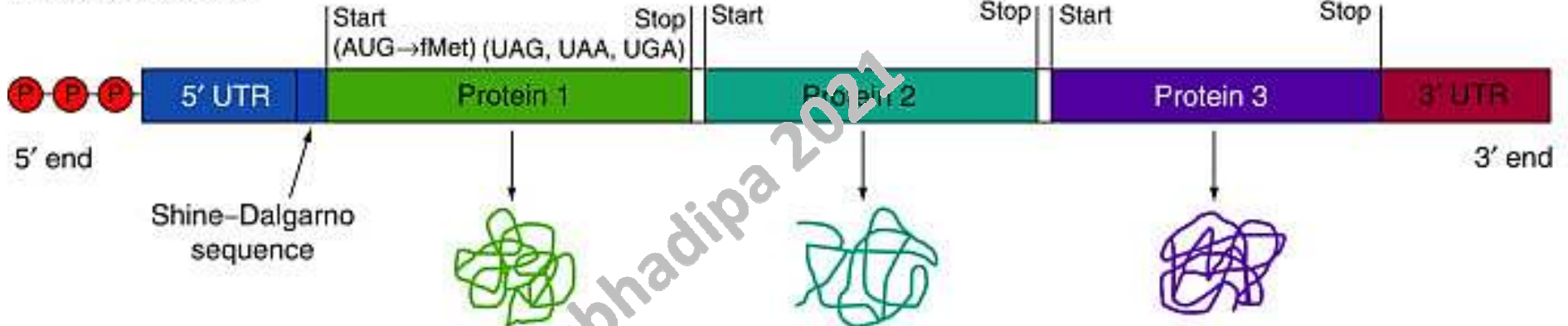
mRNA Structure (eukaryotic)

mRNA Structure (prokaryotic)

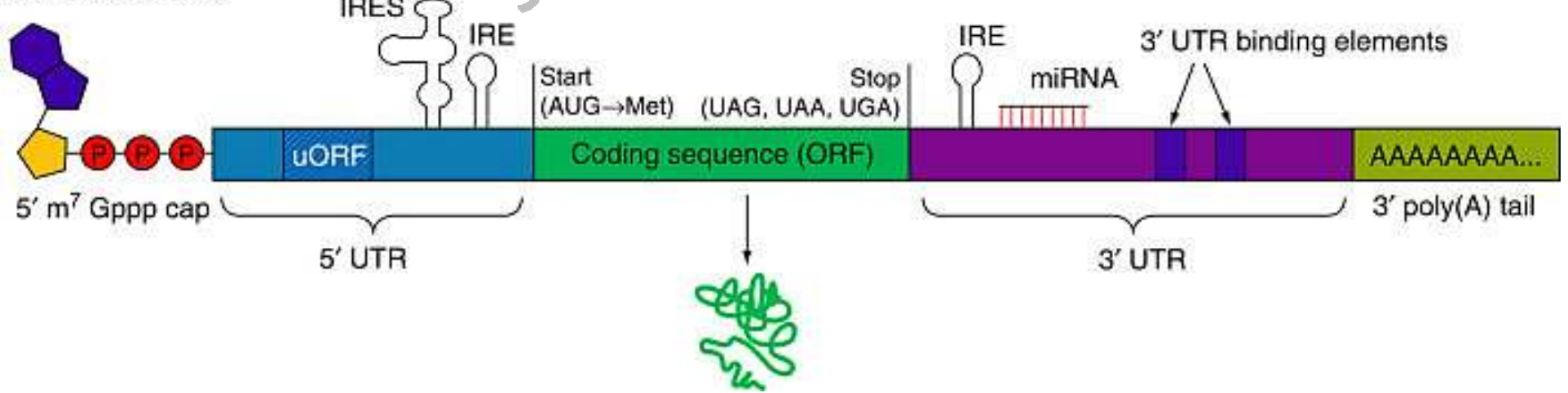


This type of RNA functions by transferring the genetic material into the ribosomes and pass the instructions about the type of proteins, required by the body cells. Based on the functions, these types of RNA is called the messenger RNA. Therefore, the mRNA plays a vital role in the process of transcription or during the protein synthesis process.

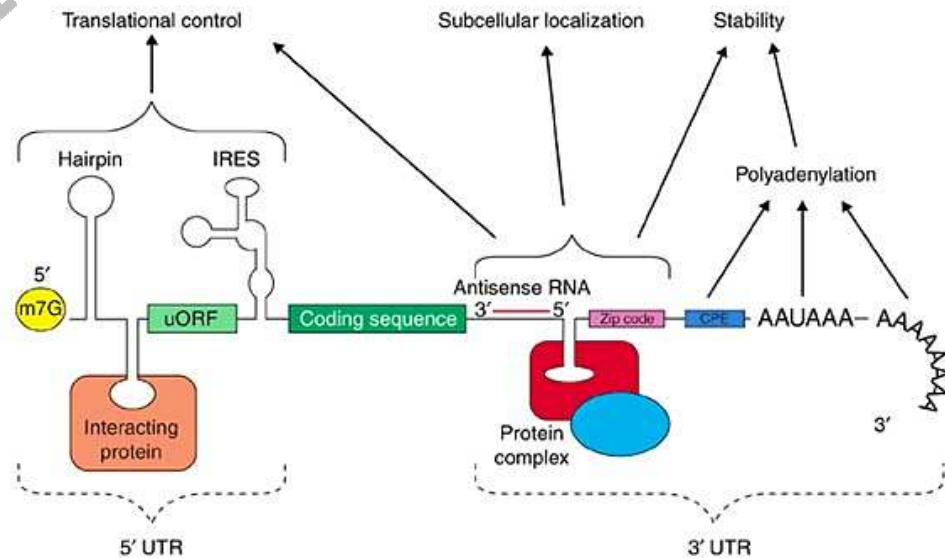
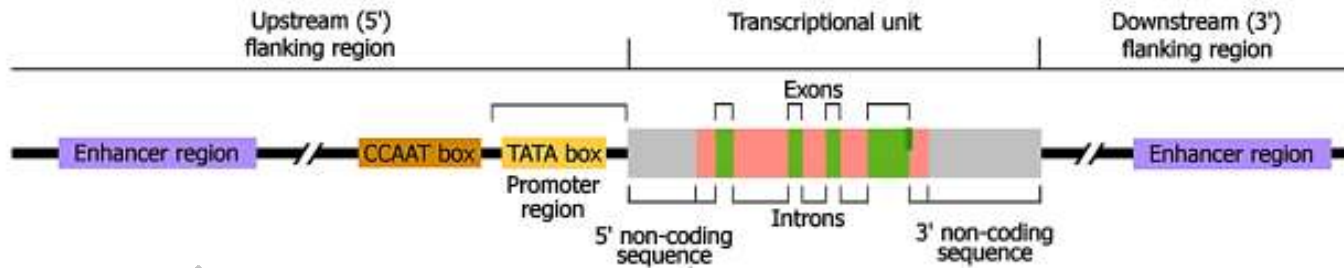
Prokaryotic mRNA:



Eukaryotic mRNA:



Structure of Eukaryotic mRNA can be complex and associated with proteins



Subhadipa 2021

Structure and Functions of eukaryotic mRNA

5' Cap

The **5' end** has a guanine nucleotide that is connected to mRNA by a 5' to 5' triphosphate linkage. The guanine nucleotide is methylated by methyltransferase on the 7th position, referring to it as a **7-methyl guanylate cap (m7G)** after capping.

5' untranslated region (5' UTR)

- This is the region of mRNA that **is directly upstream from the initiation codon.**
- It is essential for the **regulation of translation of a transcript in viruses, prokaryotes, and eukaryotes.**
- In some organisms, the 5' UTR is not translated therefore it forms the **complex secondary structure to regulate translation.**

Coding region

- This is the region on RNA that **codes for proteins.**
- The coding region in DNA flanks the **promoter sequence** which on proceeding to transcription, the RNA polymerase binds to the promoter sequence moving along the template strand to the coding region. the RNA polymerase adds RNA nucleotides that are complementary to the coding region forming the mRNA, by substituting thymine with uracil. The mechanism takes place until the occurrence of the termination sequence.

Three prime untranslated region (3' UTR)

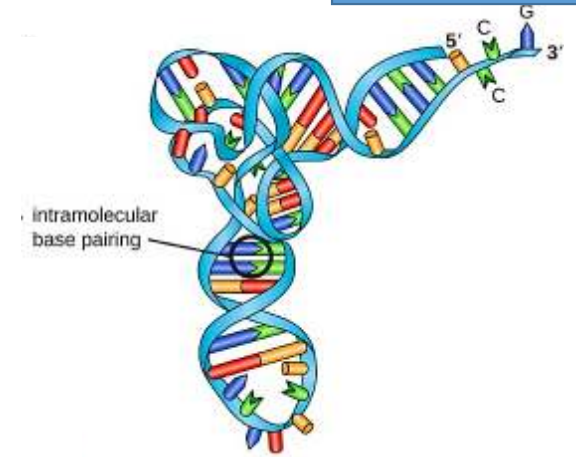
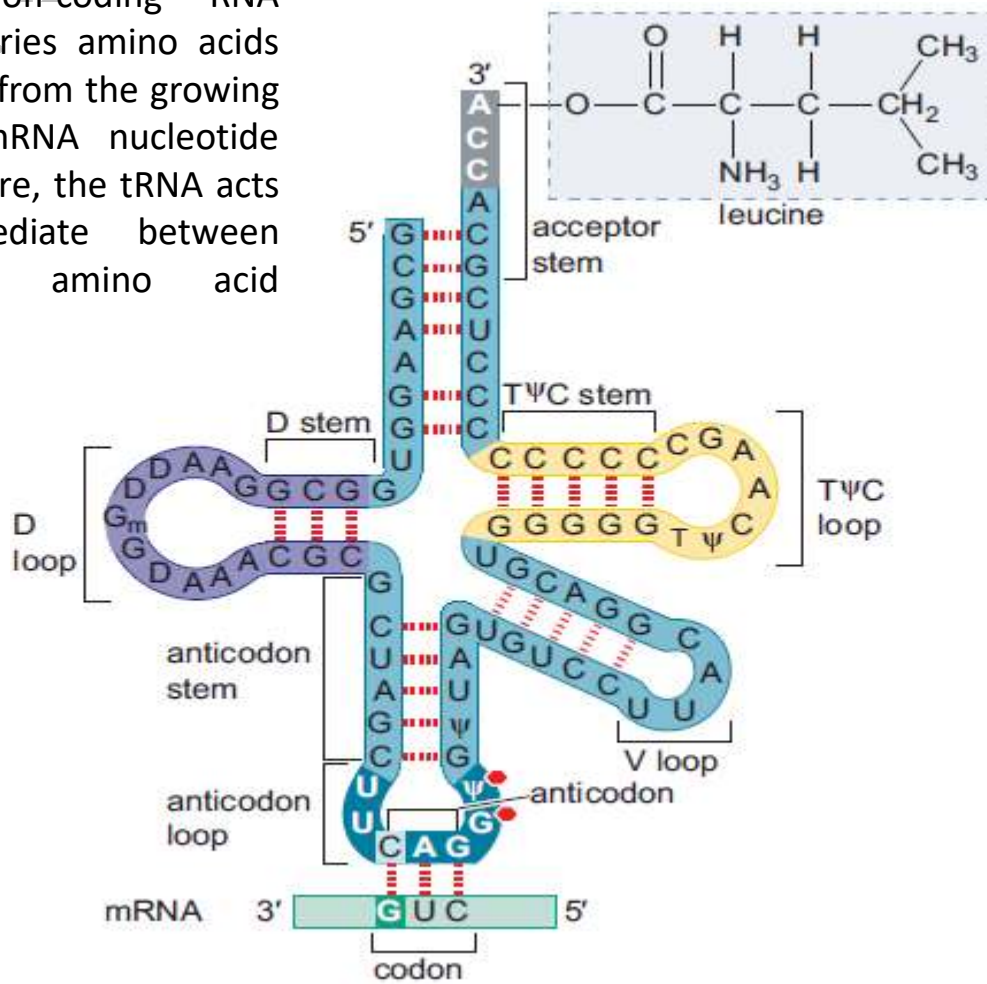
- This is the part of mRNA that follows the translation termination codon. This unit contains the **regulatory regions that post-transcriptionally influence gene expression.**
- The 3' UTR is **not translated** to proteins, same as the 5' untranslated region.
- However, regulatory regions found in the 3 UTR influences polyadenylation, the efficiency of **translation, translation localization, and the stability of mRNA.**
- It has binding sites that are used for **regulatory proteins and microRNAs (miRNAs)**, which regulate and decreases gene expression of various mRNAs by either inhibiting translation or directly causing transcript degradation.
- The 3' UTR also has a silencer region that binds to the repressor proteins, which inhibits the expression of the mRNA.
- Several 3' UTRs also contain Adenine-Uracil (AU) rich elements sequences as (AAUAAA) which **directs adding adenine residues known as poly (A) tail to the end of the mRNA transcript.**
- Generally, the **3' UTR helps to regulate genes and ensure the right genes are expressed correctly at the right time.**

Poly A tail

- The poly(A) tail is made up of **multiple adenosine monophosphates i.e it is a stretch of RNA that is made up of adenine bases.**
- It is bound with poly-A binding proteins (PABP) and they play a primary role in the **regulation of mRNA translation, stability, and export.**

tRNA Structure

This is the non-coding RNA molecule that carries amino acids to the ribosomes, from the growing peptide chain (mRNA nucleotide sequence). Therefore, the tRNA acts as the intermediate between nucleotide and amino acid sequences.



tRNA 3-D Structure



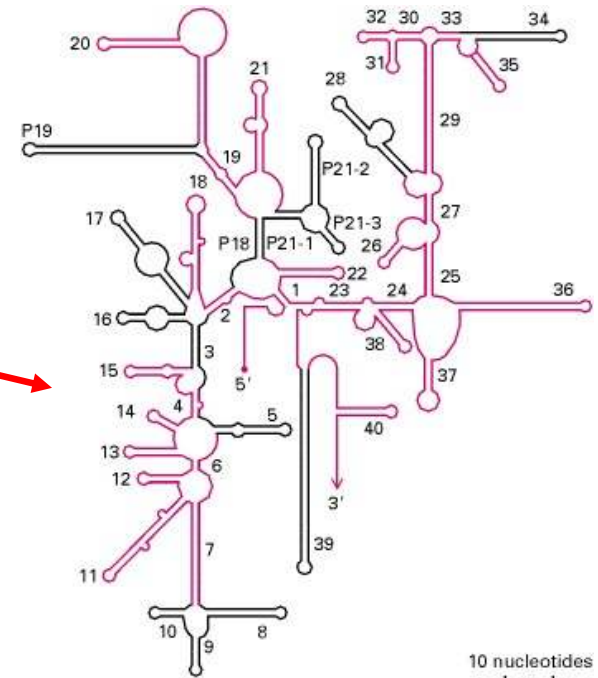
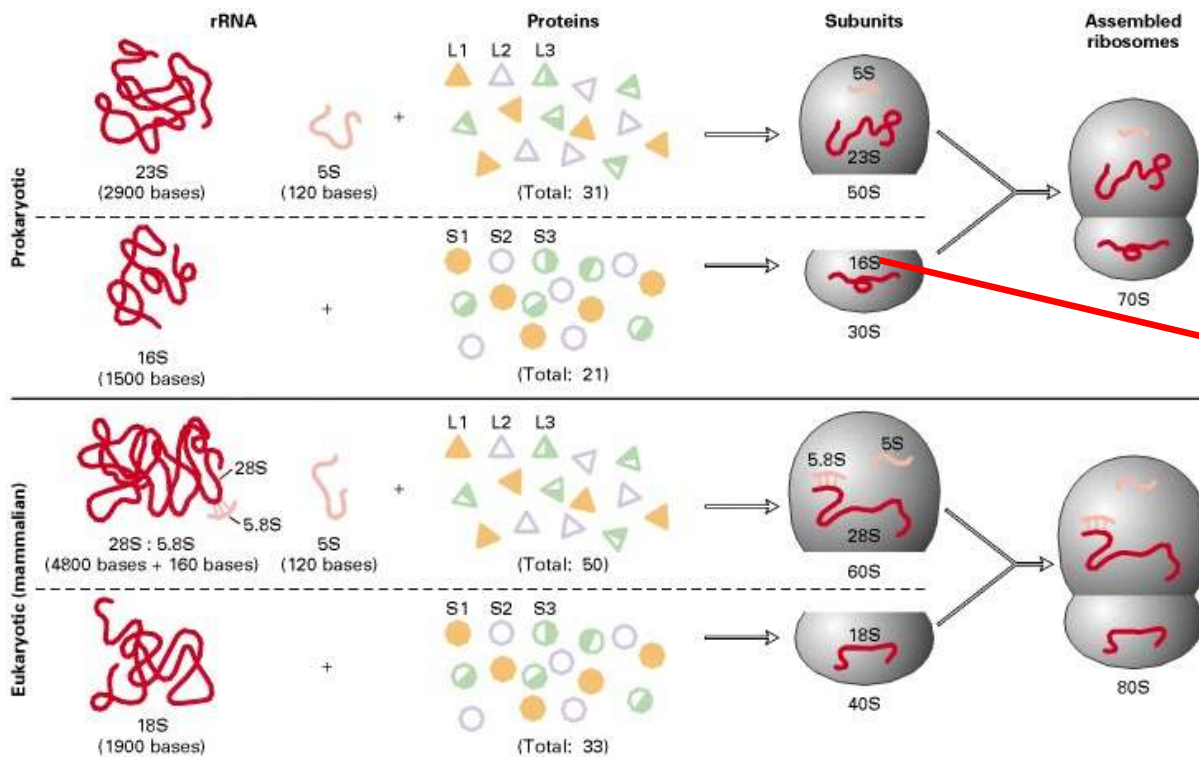
Clover-Leaf

Structure and Function

- It is a small RNA chain of about **80 nucleotides**.
- The set of the **three nucleotides on the mRNA is known as a codon**, while the **corresponding sequence on tRNA is known as an anticodon**. The base pairing of the codon and the anticodon forms a translation mechanism.
- At the end of the **tRNA 3' hydroxyl base**, there is an **anticodon amino acid sequence that is attached**, linking the ribosomes to form a peptide bond, thus elongating the polypeptide chain.
- Therefore, tRNA major parts are the anticodon and the 3' hydroxyl group terminal.
- Other parts of the tRNA structure are the **D-arm and the T-arm**, which are highly specific and are highly effective.
- tRNAs have a sugar-phosphate backbone which gives it directionality.

- One end of the tRNA has a reactive phosphate group, which is attached to the fifth carbon atom of the ribose (5') and another end which has a free hydroxyl group on the third carbon (3'), giving rise to the 5' to 3' ends of RNA.
- The **3' terminal end has three bases CCA (Cytosine, cytosine, adenine) which make part of the acceptor arm** of the molecule which is covalently attached to the hydroxyl group on the ribose sugar.
- The acceptor arm also contains parts of the 5' end of the tRNA, made up of 7-9 nucleotides on the opposite ends of the molecule base pairing with each other.
- The **anticodon loop which is recognized by the aminoacyl tRNA synthetase (AATS) is paired to mRNA and it determines the amino acid that attaches to the acceptor's arm.**
- The AATS reads and recognizes the D-arm from the 5' end of tRNA.
- The **D-arm plays a major role in stabilizing the structure of RNA**; it affects and influences the kinetics and accuracy of translation at the ribosomes.
- The **T-arm also influences the tRNA effect on the translation by interaction** with the ribosomes.
- The D-arm, T-arm, and the anticodon loop combined **resembles a cloverleaf**. When RNA folds into a tertiary structure, it becomes L-shaped with an extended structure of the acceptor stem, T-arm, anticodon loop, and D-arm.

rRNA Structure and assembly



rRNAs exhibit a generally similar pattern of stem-loops

Structure and Functions

- Ribosomal ribonucleic acid (rRNA) is the type of RNA that is **part of the ribosomes.**
- It is defined as the **molecular machine that catalyzes the synthesis of proteins.**
- It makes up to **60% of the weight of the ribosomes** since they play a major part in the functions of the ribosomes such as binding to mRNA and the recruitment of tRNA, and the catalyzation of peptide bond formation between amino acids.
- They also **determine the shape of ribosomes** using the rRNA core.
- rRNA has a **distinctive three-dimensional shape which is made up of internal loops and helices that creates specific sites, A, P, and E, within the ribosome.**
- The proteins on the ribosome surface stabilize its structure by interacting with the rRNA core.

- The rRNA is synthesized or transcribed in the cell nucleus, **specifically in the nucleoli**. The nucleoli play a major role in the biogenesis of ribosomes via the sequestration of ribosomal proteins.
- Both **prokaryotic and eukaryotic ribosomes are made of a larger and smaller subunit and these two units** come together during the translation of mRNA.
- The **small subunits** of the **prokaryotes** are made of an **RNA molecule of about 1500 nucleotides in length with a Svedberg coefficient of 16S**. The small subunit along with ribosomal proteins has a sedimentation rate of the 30S. This is paired with **the larger subunit**, having two RNA molecules – one that is nearly **3000 nucleotides (23S) in length and the other is a short sequence of 120 nucleotides (5S)**. These RNA molecules are accompanied by proteins that give rise to the larger **50S subunit**.
- The **eukaryotic** ribosomes are made up of **two subunits also i.e the large subunit 60S and the small subunit 40S**. The **small subunit** is made up of **two short rRNA molecules that are less than 200 nucleotides in length (5S and 5.8S)**, and the **large subunit** which is made up of **two large molecules that are longer, one which has over 5kb (28S) and a second one with 2kilobases (18S)**. Totally, the eukaryotic ribosome has a **Svedberg coefficient of the 80S**.
- **Eukaryotic cells also have rRNA in mitochondria and chloroplast.**

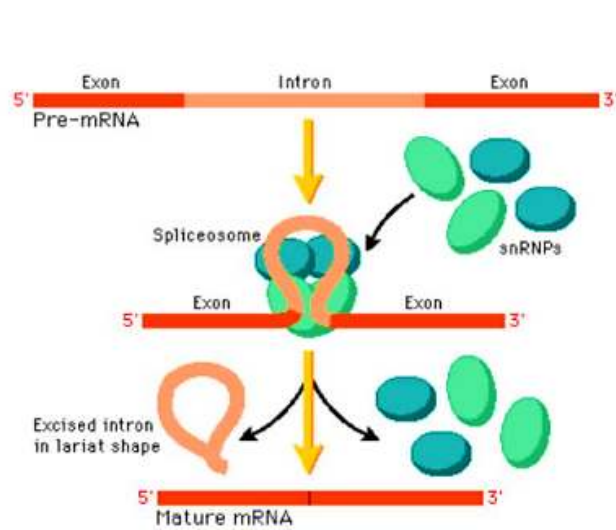
Other types of RNA



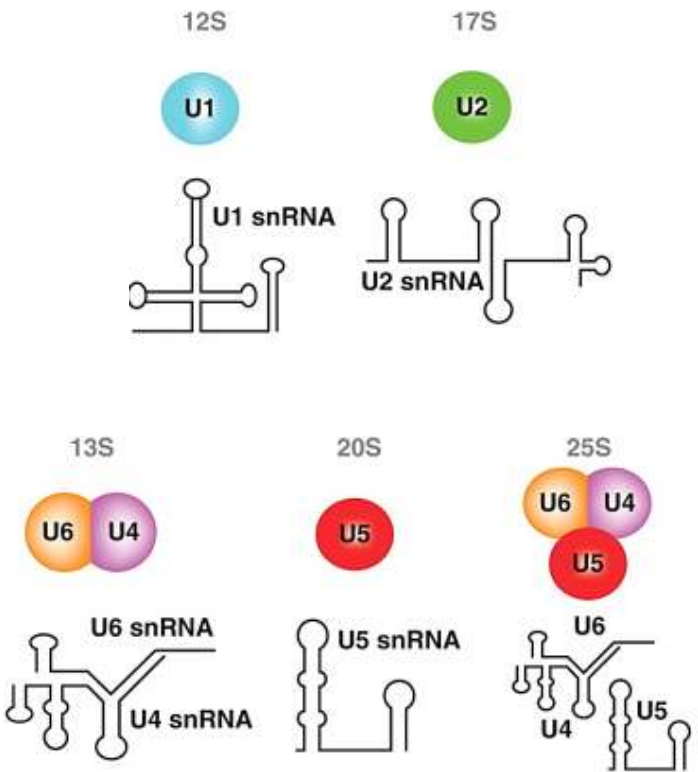
Small Nuclear RNA (snRNA)

Major human spliceosomal snRNAs and RNPs

snRNA is involved in the processing of pre-messenger RNA (pre-mRNA) into mature mRNA. They are very short, with an average length of only 150 nucleotides.

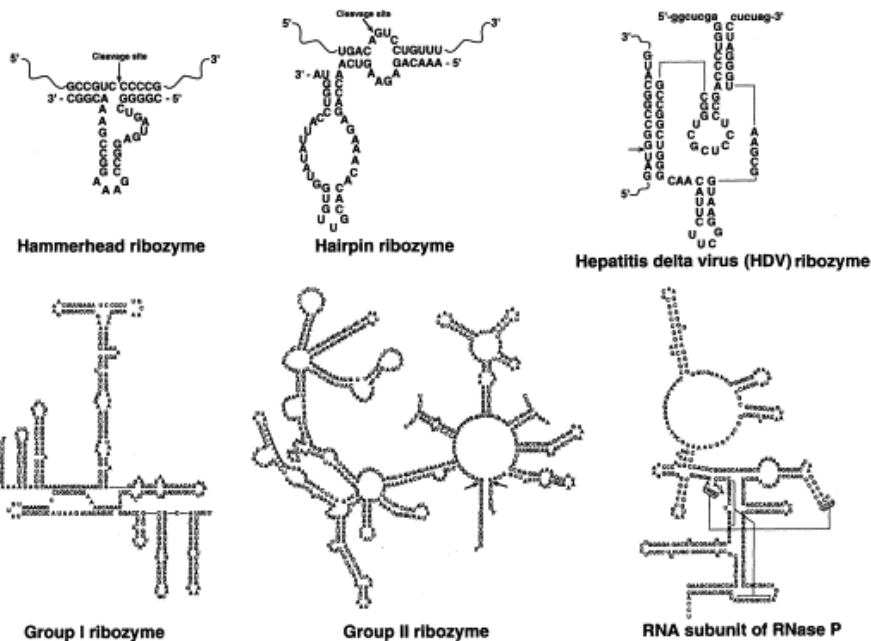


Sn RNAs are involved in the process of splicing (intron removal) of primary transcript to form mature mRNA. The Sn RNAs form complexes with proteins to form Ribonucleoprotein particles called snRNPs



Ribozyme

A ribozyme is an RNA molecule with a **well-defined tertiary structure** that enables it to act like a protein enzyme in **catalyzing biochemical and metabolic processes**. 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.



Natural ribozymes and what they do

Ribozyme	Number identified	Biological source	Reaction catalysed (product)
Group I introns	>1000	Eukaryotes (nucleus and mitochondria), prokaryotes, bacteriophages	Self-splicing transesterification (5'-OH)
Group II introns	>700	Eukaryotes (organelles), prokaryotes	Self-splicing transesterification (5'-OH)
Group-I intron like	6	<i>Diatyrisia</i> , <i>Moeglinin</i>	Hydrolysis (3'-OH)
RNase P RNA	>100	Eukaryotes (nucleus and organelles), prokaryotes	Hydrolysis (3'-OH)
Hammerhead ribozyme	11	Plant viroids and satellite RNAs, newt	Self-cleaving transesterification (2',3'-cyclic phosphate)
Hairpin ribozyme	4	Plant viroids and satellite RNAs	Self-cleaving transesterification (2',3'-cyclic phosphate)
Hepatitis delta virus ribozyme	2	Human hepatitis delta virus	Self-cleaving transesterification (2',3'-cyclic phosphate)
VS ribozyme	1	<i>Neurospora</i> mitochondria	Self-cleaving transesterification (2',3'-cyclic phosphate)
Ribosomal RNAs	>5000	Eukaryotes, prokaryotes	Peptidyl transfer (peptide bond)
Spliceosomal RNAs	>100	Eukaryotes	Trans-splicing transesterification (3'-OH)

Regulatory RNAs

- RNA molecules are more than messengers between DNA and protein and exhibit rich regulatory functions in development and disease. A number of types of RNA are involved in regulation of gene expression, including micro RNA (miRNA), small interfering RNA (siRNA) and antisense RNA (aRNA).
- **miRNA** (21-22 nt) is found in eukaryotes, and acts through RNA interference (RNAi). miRNA can break down mRNA that it is complementary to, with the aid of enzymes. This can block the mRNA from being translated, or accelerate its degradation.
- **siRNA** (20-25 nt) are often produced by breakdown of viral RNA, though there are also endogenous sources of siRNAs. They act similarly to miRNA. An mRNA may contain regulatory elements itself, such as riboswitches, in the 5' untranslated region or 3' untranslated region; these cis-regulatory elements regulate the activity of that mRNA.

Double-stranded RNA (dsRNA)

- This type of RNA has two strands bound together, as with double stranded DNA. dsRNA forms the genetic material of some viruses.

Piwi-interacting RNAs (piRNA)

- Piwi-interacting RNAs bind the PIWI subfamily proteins that are involved in maintaining genome stability in germline cells. Piwi-interacting RNAs also play a role in gametogenesis.