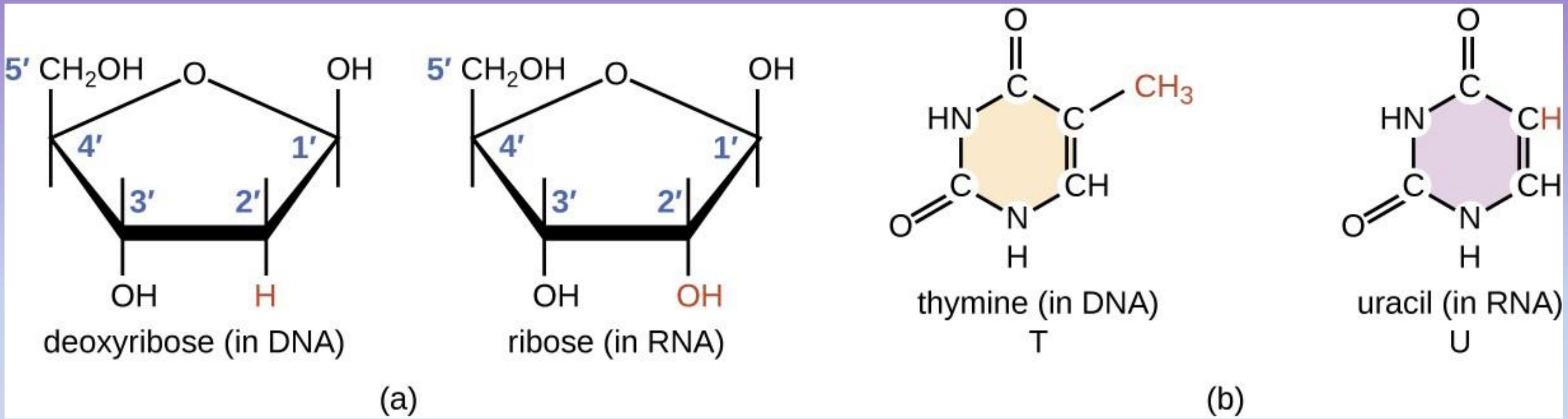
Molecular Biology , Sem III

RNA structure

objectives

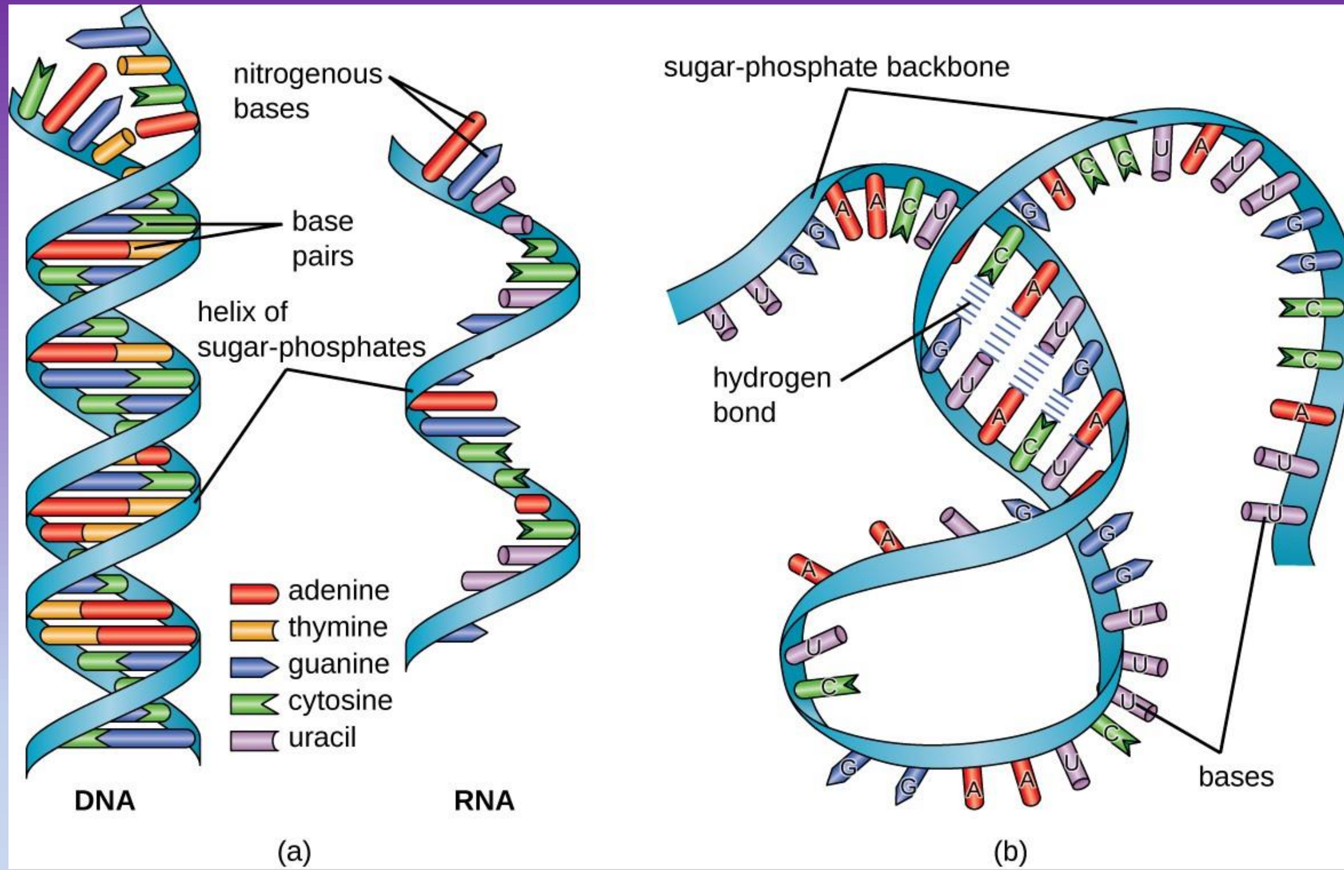
- Biochemical structure of ribonucleotides
- Similarities and differences between RNA and DNA
- Types of RNA
- Functions of RNA
- How RNA can serve as hereditary information

RNA structure



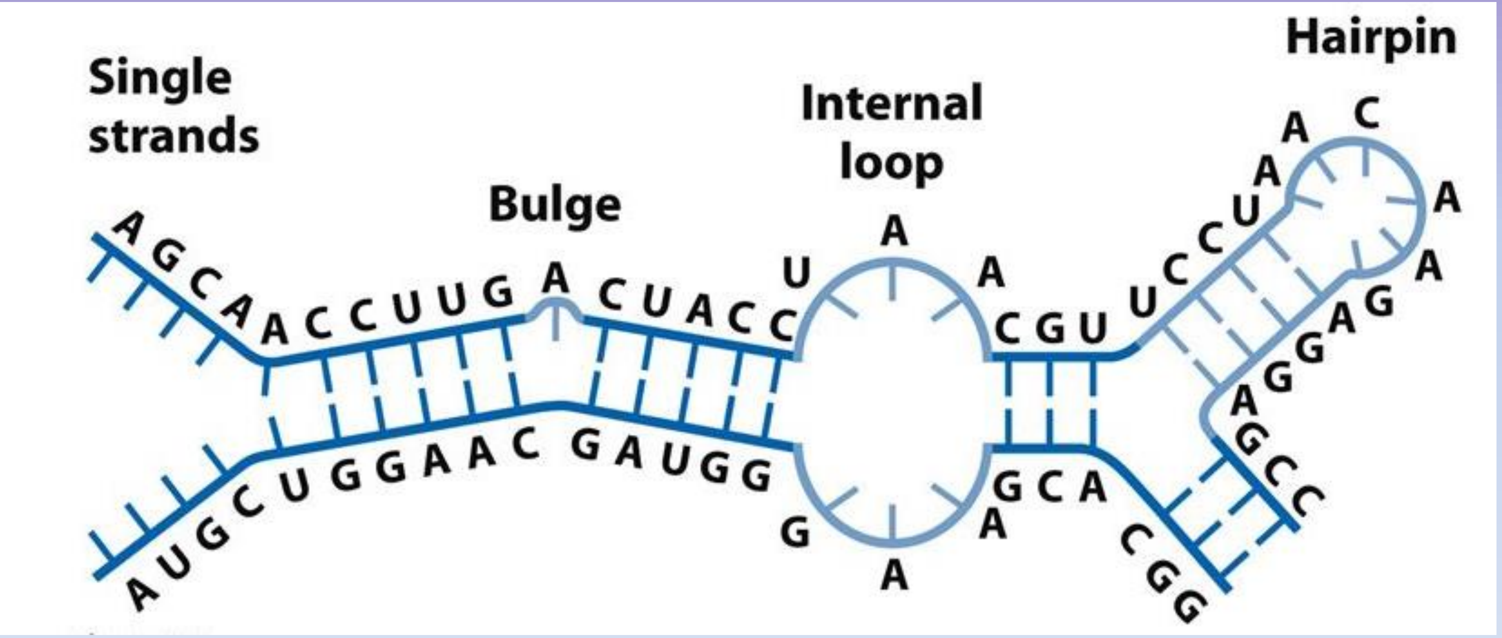
RNA structure

- RNA is typically single stranded
- Is made of **ribonucleotides** that are linked by phosphodiester bonds.
- A ribonucleotide in the RNA chain contains ribose (the pentose sugar), one of the four nitrogenous bases (A, U, G, and C), and a phosphate group.
- The subtle structural difference between the sugars gives DNA added stability, making DNA more suitable for storage of genetic information, whereas the relative instability of RNA makes it more suitable for its more short-term functions.
- The RNA-specific pyrimidine **uracil** forms a complementary base pair with adenine and is used instead of the thymine used in DNA.
- Even though RNA is single stranded, most types of RNA molecules show extensive intramolecular base pairing between complementary sequences within the RNA strand, creating a predictable three-dimensional structure essential for their function



a) DNA is typically double stranded, whereas RNA is typically single stranded. (b) Although it is single stranded, RNA can fold upon itself, with the folds stabilized by short areas of complementary base pairing within the molecule, forming a three-dimensional structure.

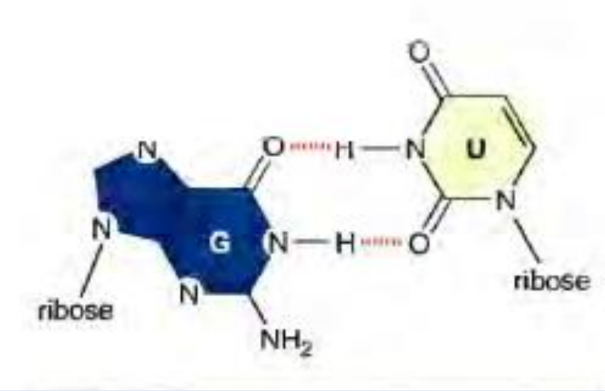
RNA secondary structures



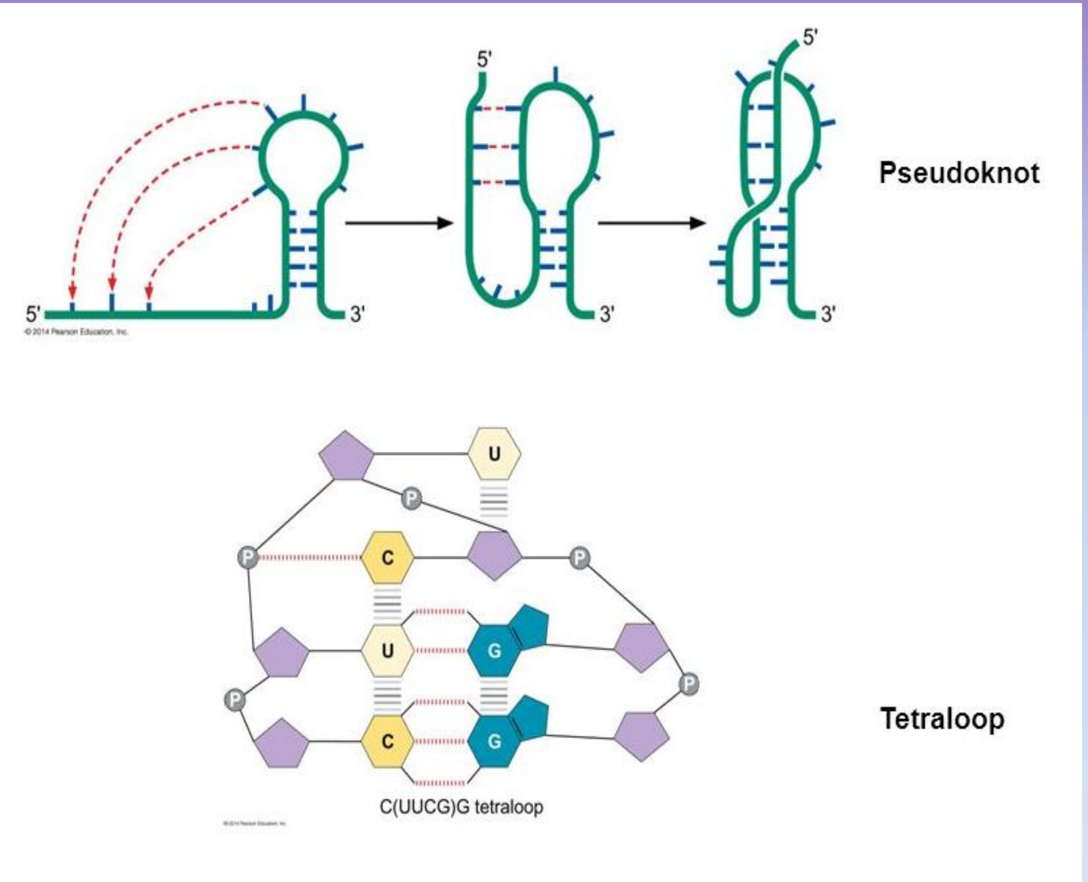
Double helical characteristics of RNA

- Stem and loop structure
- Internal loops
- Bulges
- Junctions
- Pseudoknots
- Stem loop with the tetraloop sequence UUCG is exceptionally stable due to base stacking interactions in the loop
- Shows additional non watson-Crick base pairing (eg: G:U base pairing, GA and GU base pairing commonly found in rRNA). It enhances capacity for self complementarity
- RNA secondary structure can have important biological function (eg: pfrA based activation of virulence genes in *L monocytogenes)*

RNA secondary and tertiary structures



G:U base pair



ribozymes

- RNA can be biological catalysts and can have complex tertiary structures like enzymes and can have other classical features of enzyme like active site, binding site for cofactors etc. called ribozymes. Eg:
  - RNaseP - one of the first Ribozyme to be discovered, involved in generating tRNA molecules from larger precursor RNA
  - hammerhead -sequence specific ribonuclease
- Regulatory RNA (riboswitches) bind and respond to small molecules- ligands and control transcription and translation steps.

RNA bases

The bases used for RNA are attached to ribose. However, many are significantly modified from the typical four bases normally considered to be part of RNA. This is particularly true for tRNA. The modified bases include pseudouracil and methylated versions of cytosine and adenine.

- The three main types of RNA directly involved in protein synthesis are
- **messenger RNA (mRNA)**,
- **ribosomal RNA (rRNA)**
- **transfer RNA (tRNA)**.

- In 1961, French scientists François **Jacob** and Jacques **Monod** hypothesized the existence of an intermediary between DNA and its protein products, which they called messenger RNA.

mRNA

- Messenger RNA (mRNA) mRNA molecules contain the coding sequence for proteins. The mRNA molecules can vary considerably in size, with eukaryotic transcripts including the largest known ribonucleic acids. This is most obvious before splicing of introns, because many transcripts exceed 100 kb in length.

rRNA

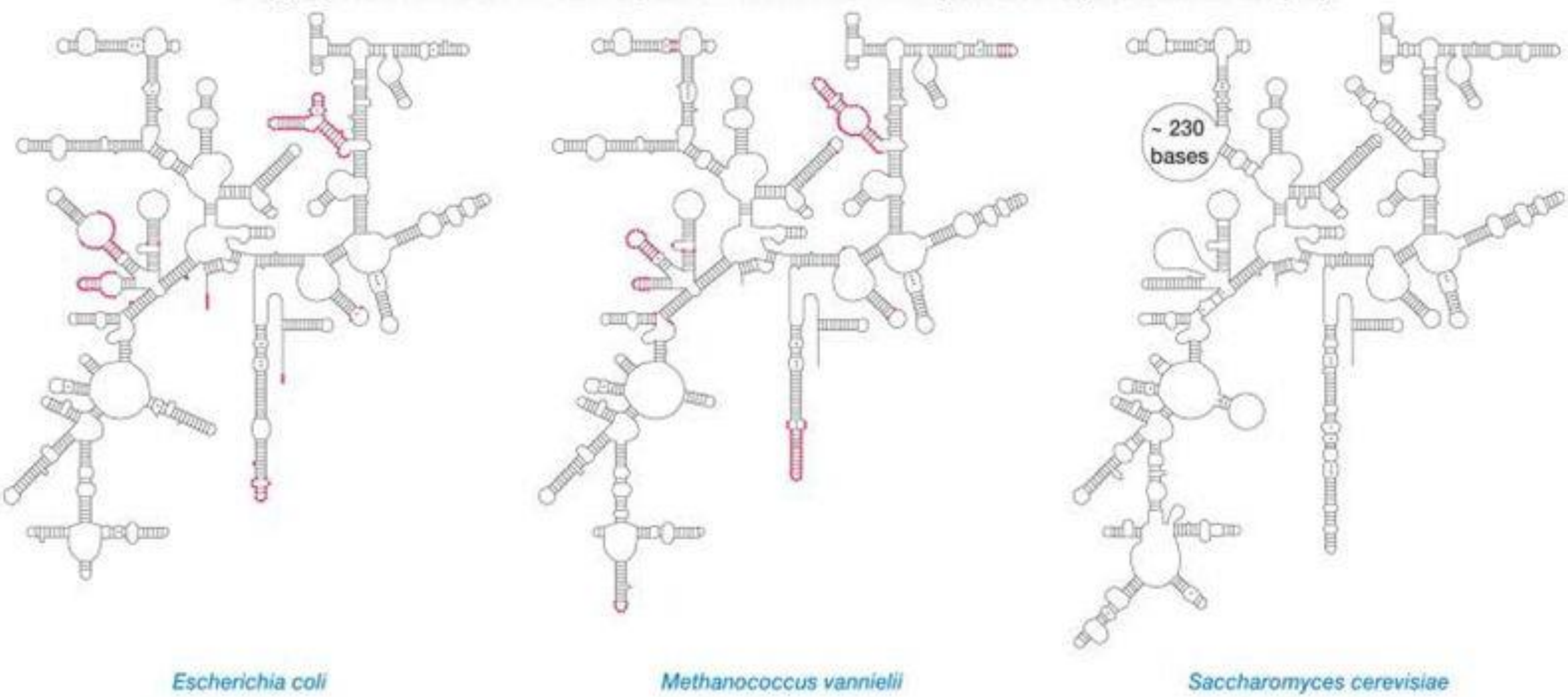
- Ribosomal RNA molecules comprise 65 to 70% of the mass of the ribosome
- Made in the nucleolus
- In the cytoplasm, rRNA and ribosomes combine to form nucleoprotein called ribosome
- The rRNA ensures the proper alignment of the mRNA, tRNA, and the ribosomes; the rRNA of the ribosome also has an enzymatic activity (**peptidyl transferase**) and catalyzes the formation of the peptide bonds between two aligned amino acids during protein synthesis.

rRNA

- Although rRNA had long been thought to serve primarily a structural role, its catalytic role within the ribosome was proven in 2000.
- Scientists in the laboratories of Thomas **Steitz** (1940–) and Peter **Moore** (1939–) at Yale University were able to crystallize the ribosome structure from *Haloarcula marismortui*, a halophilic archaeon isolated from the Dead Sea.
- Steitz shared the 2009 Nobel Prize in Chemistry with other scientists who made significant contributions to the understanding of ribosome structure.

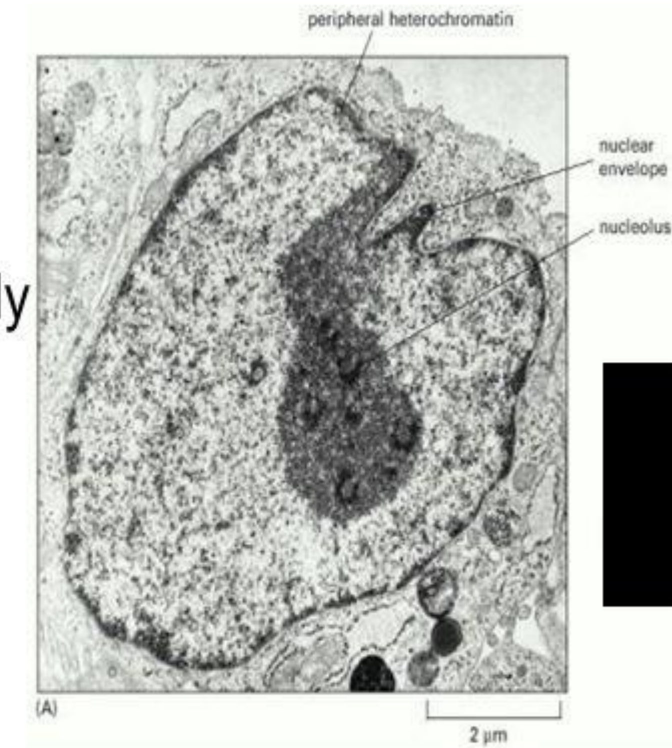
Ribosomal RNA (rRNA)

Has changed very little over time and can serve as an indicator of evolutionary relatedness



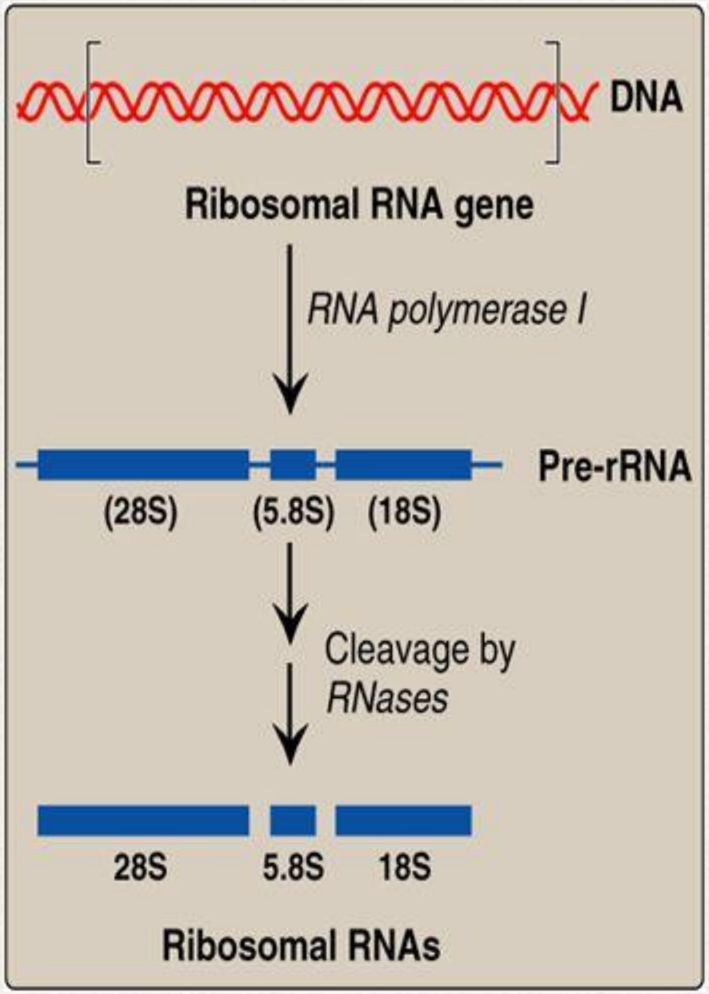
Ribosomal RNA (rRNA)

- 80% of RNA in cells (3-5% is mRNA)
- rRNA is the functional product of the rRNA gene,
- Each growing cells require 10 million copies of each type of rRNA,
- Each cell contain multiple copies of the rRNA genes
- rRNAs form the core of ribosome
- Nucleolus: Site of rRNA processing and ribosome assembly
  - Large aggregate of macromolecules mainly genes coded for rRNAs, snoRNAs and proteins required for ribosome assembly
- Types of rRNAs:
  - Eukaryotes: 28S, 18S, 5.8S & 5S
  - Prokaryotes: 23S, 16S & 5S

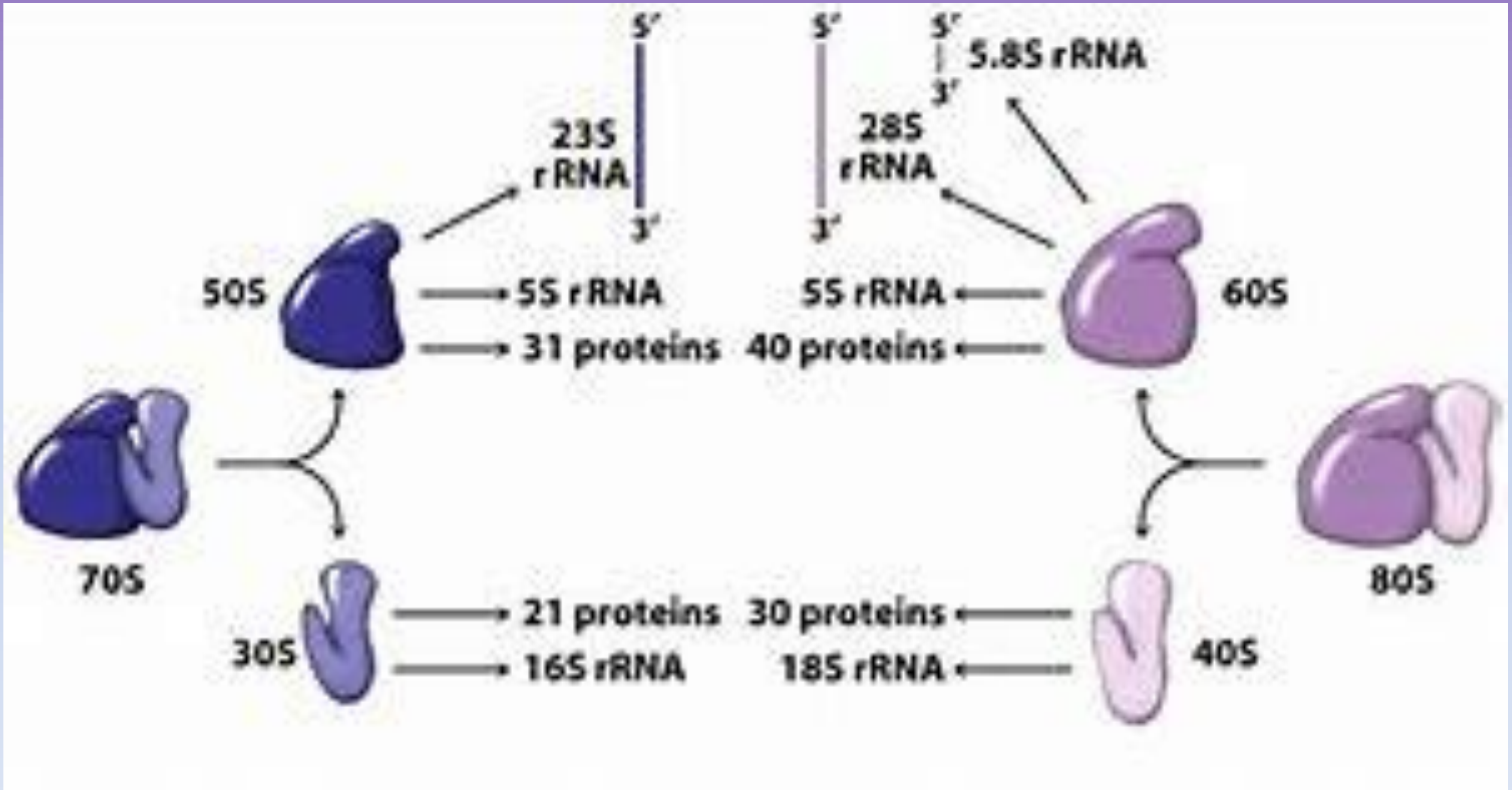


A. Ribosomal RNA

- rRNAs of both prokaryotic and eukaryotic cells are generated from long precursor molecules called pre-rRNAs.
- The 23S, 16S, and 5S rRNA of prokaryotes are produced from a single pre-rRNA molecule, as are the 28S, 18S, and 5.8S rRNA of eukaryotes.
- The pre-rRNAs are cleaved by ribonucleases to yield intermediate-sized pieces of rRNA, which are further processed (trimmed by exonucleases and modified at some bases and riboses) to produce the required RNA species.



Posttranscriptional processing of eukaryotic ribosomal RNA by *ribonucleases (RNases).*



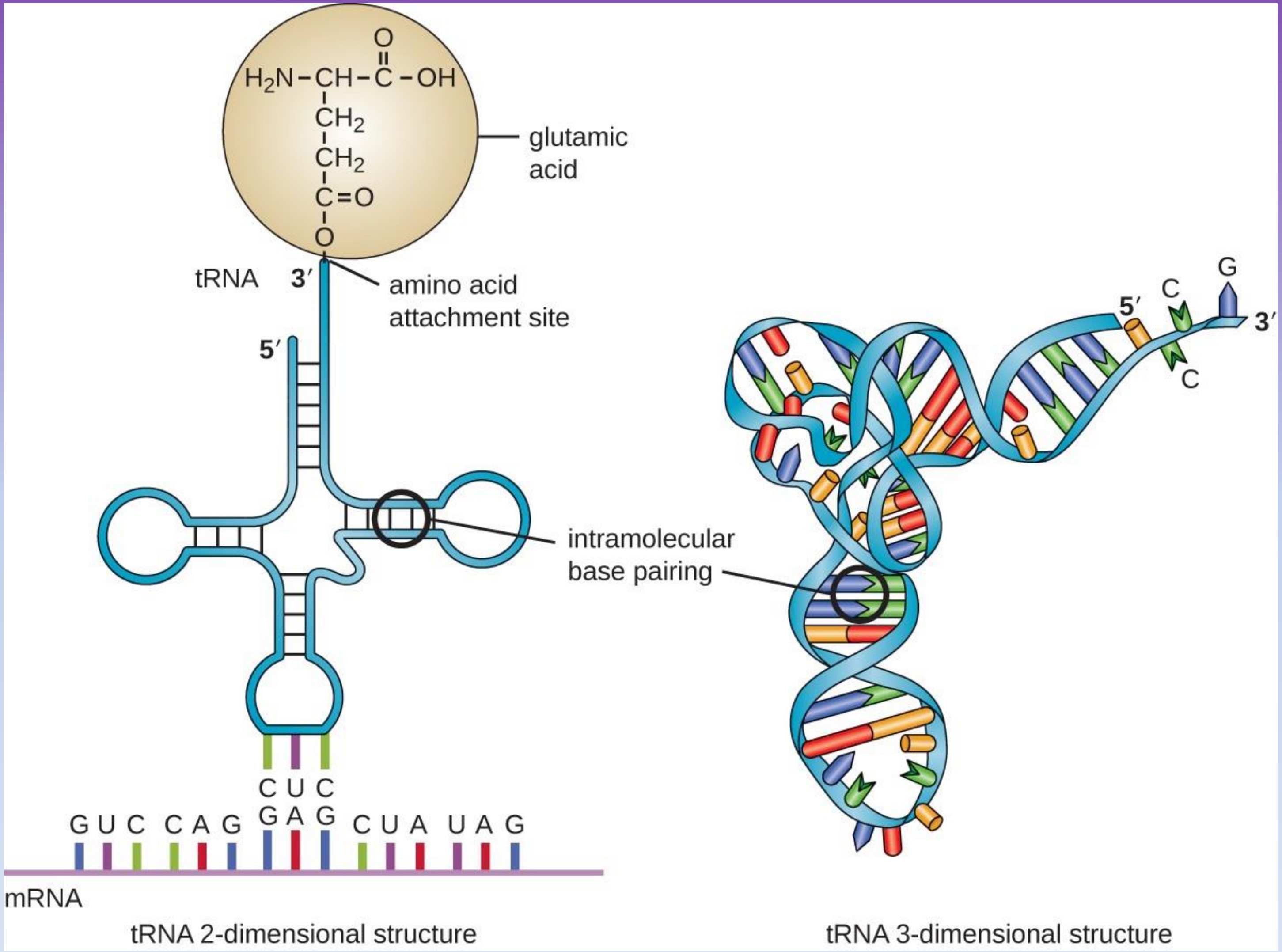
5′
23S
rRNA
3′
5′
28S
rRNA
3′
5′
5.8S rRNA
3′
50S
5S rRNA
31 proteins
5S rRNA
40 proteins
60S
70S
80S
21 proteins
16S rRNA
30S
30 proteins
18S rRNA
40S

Table. Structure and Function of RNA			
	mRNA	rRNA	tRNA
Structure	Short, unstable, single-stranded **RNA** corresponding to a gene encoded within DNA	Longer, stable RNA molecules composing 60% of ribosome's mass	Short (70-90 nucleotides), stable RNA with extensive intramolecular base pairing; contains an amino acid binding site and an mRNA binding site
Function	Serves as intermediary between **DNA** and protein; used by ribosome to direct synthesis of protein it encodes	Ensures the proper alignment of mRNA, tRNA, and ribosome during protein synthesis; catalyzes **peptide bond** formation between amino acids	Carries the correct amino acid to the site of protein synthesis in the ribosome

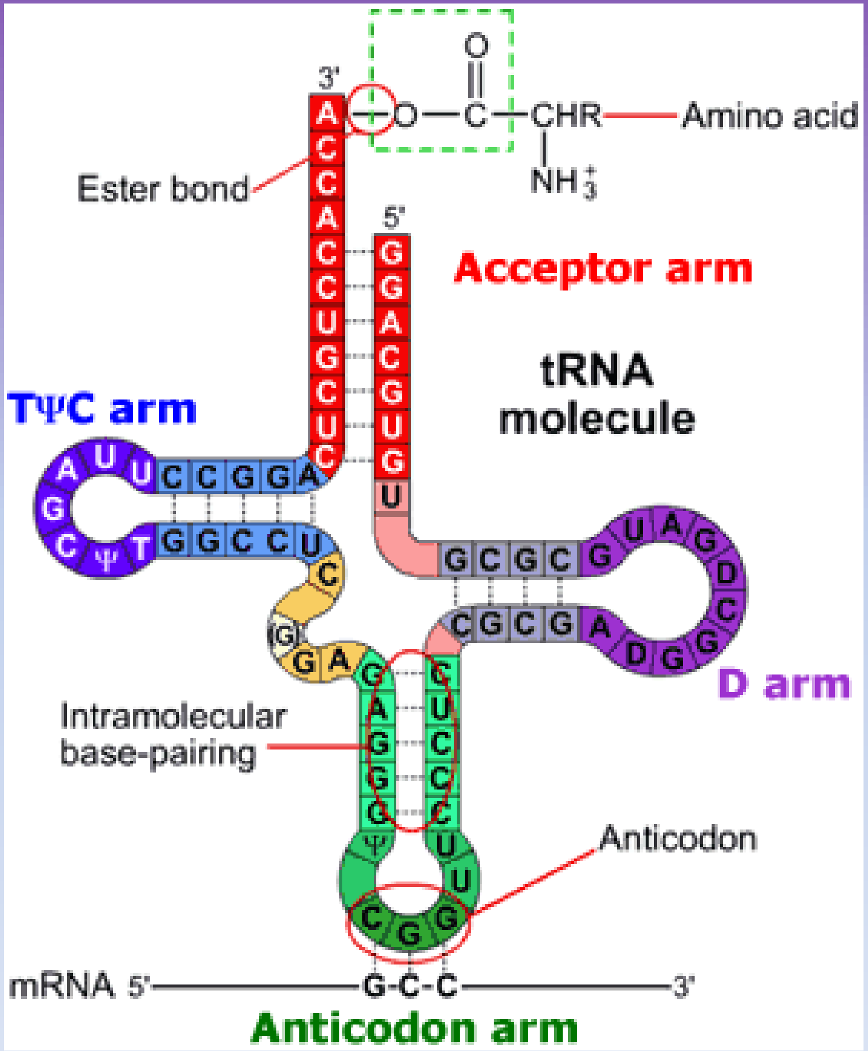
- **Different types of RNA:**

Type	Molecular Weight Range (g/mol)	Number of Nucleotides	Percentage of Cell RNA
mRNA	25,000 - 1,000,000	75 - 3,000	2
tRNA	23,000 - 30,000	73 - 94	16
rRNA	35,000 - 1,100,000	120 - 2904	82

Type of RNA	Functions in	Function
Messenger RNA (mRNA) 	Nucleus, migrates to ribosomes in cytoplasm	Carries DNA sequence information to ribosomes
Transfer RNA (tRNA) 	Cytoplasm	Provides linkage between mRNA and amino acids; transfers amino acids to ribosomes
Ribosomal RNA (rRNA) 	Cytoplasm	Structural component of ribosomes



$H_2N-CH-C(=O)-OH$
CH_2
CH_2
$C=O$
O
glutamic acid
tRNA 3′
amino acid attachment site
5′
intramolecular base pairing
C U C
G A G
G U C C A G
C U A U A G
mRNA
tRNA 2-dimensional structure
5′ C G 3′ C
tRNA 3-dimensional structure



3'
5'
O
CHR
Amino acid
NH_3^+
Ester bond
Acceptor arm
tRNA molecule
TΨC arm
D arm
Intramolecular base-pairing
Anticodon
mRNA 5'
G-C-C
3'
Anticodon arm

RNA as Hereditary Information

- Although **RNA** does not serve as the hereditary information in most cells, RNA does hold this function for many viruses that do not contain **DNA**.
- Thus, RNA clearly does have the additional capacity to serve as genetic information.
- Although RNA is typically single stranded within cells, there is significant diversity in viruses.
- Rhinoviruses, which cause the common cold; influenza viruses; and the Ebola virus are single-stranded RNA viruses.
- Rotaviruses, which cause severe gastroenteritis in children and other immuno-compromised individuals, are examples of **double-stranded RNA** viruses. Because double-stranded RNA is uncommon in eukaryotic cells, its presence serves as an indicator of viral infection.