Nucleic Acid

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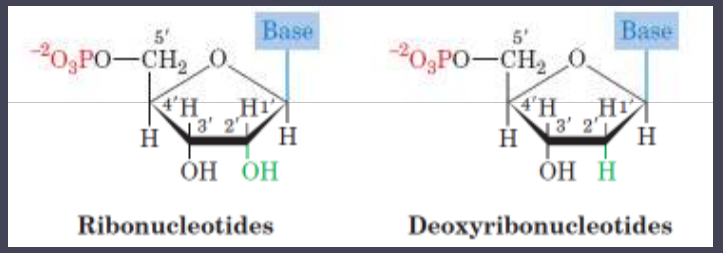
Introduction:

- The nucleic acids play a central role in the storage and expression of genetic information.
- They are divided into two major classes: deoxyribonucleic acid (DNA) functions solely in information storage, while ribonucleic acids (RNAs) are involved in most steps of gene expression and protein biosynthesis.
- All nucleic acids are made up from nucleotide components, which in turn consist of a base, a sugar, and a phosphate residue.
- DNA and RNA differ from one another in the type of the sugar and in one of the bases that they contain.

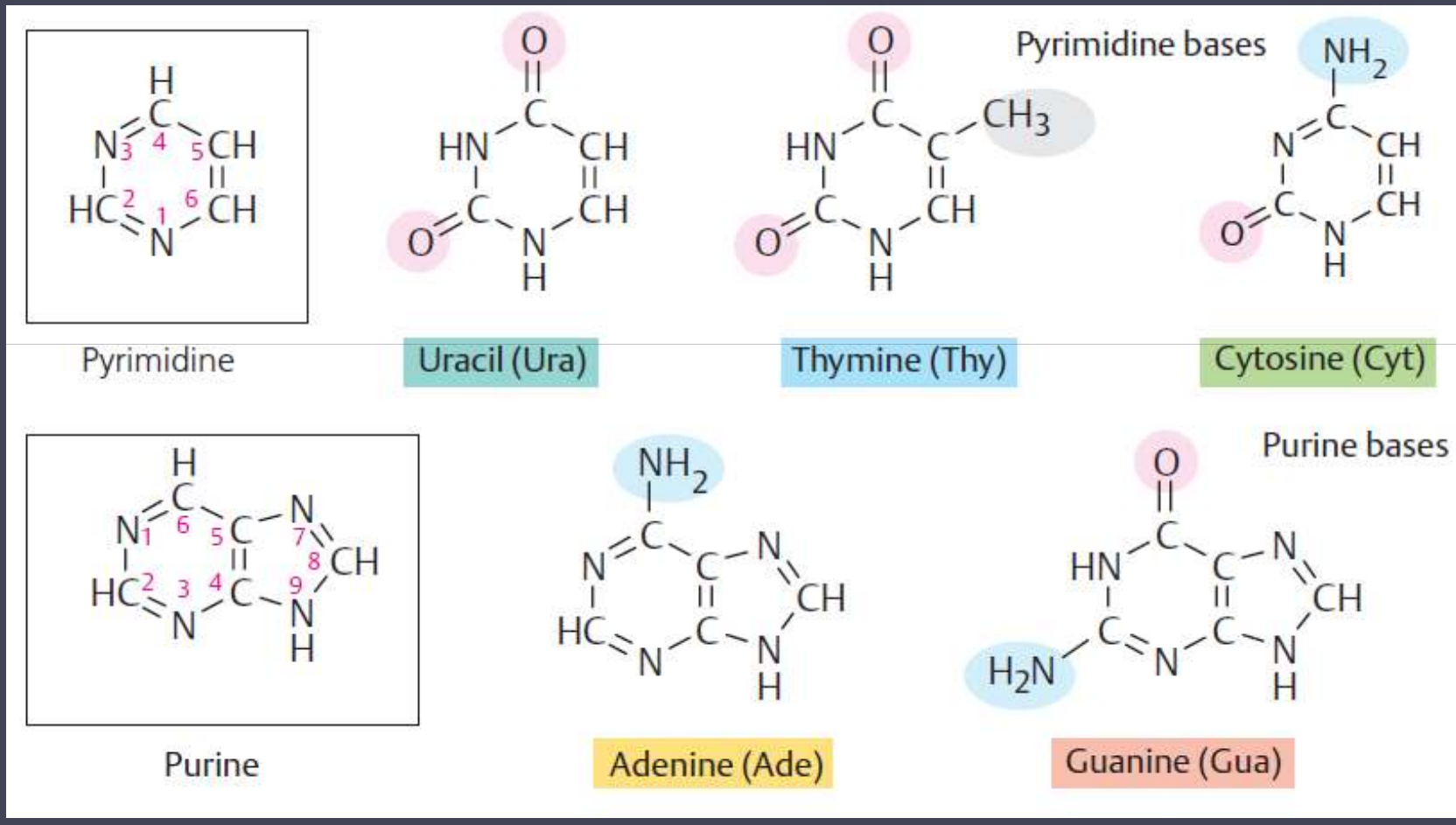
Nucleotides:

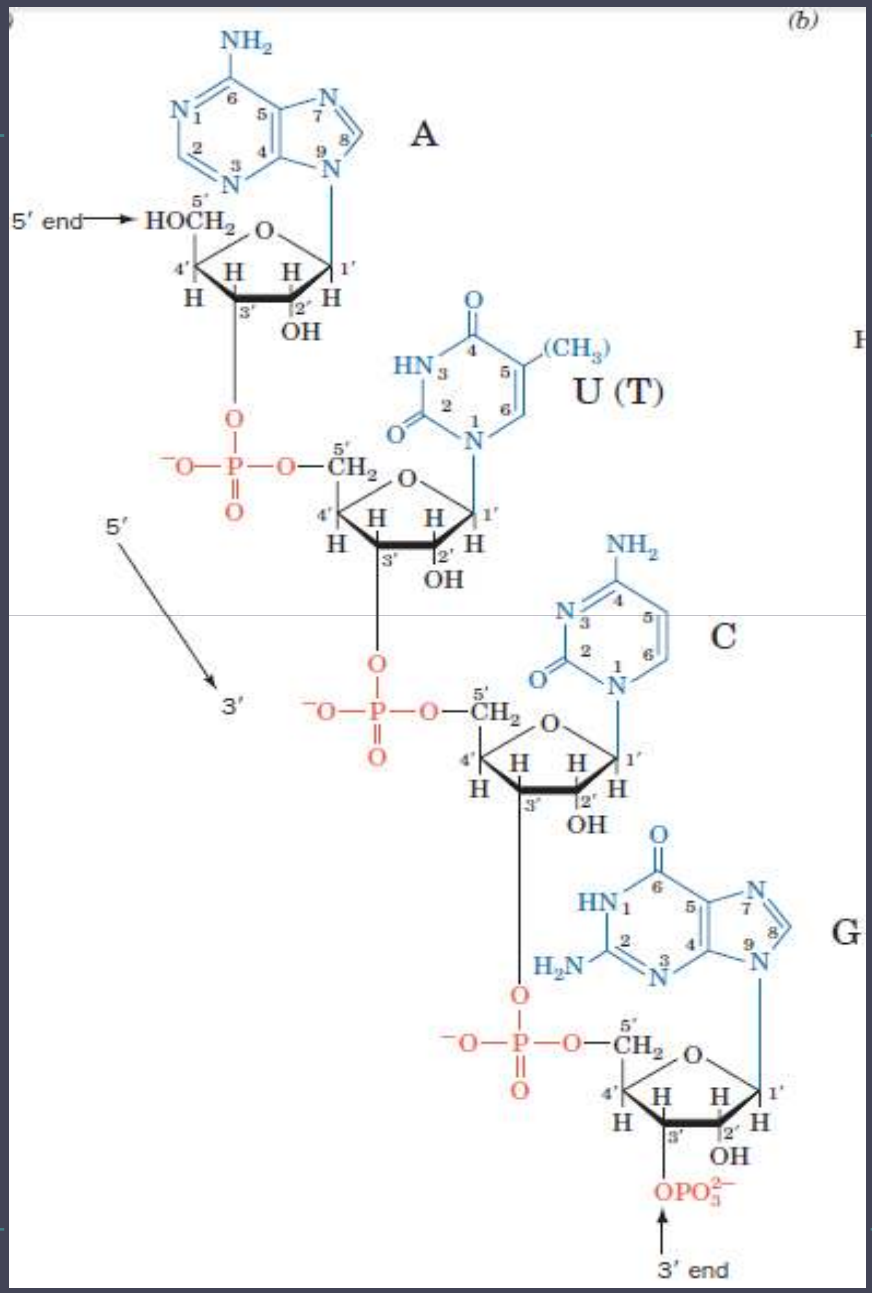
- Nucleotides are phosphate esters of a five-carbon sugar (pentose) in which a nitrogenous base is covalently linked to C1' of the sugar residue.
- In ribonucleotides, the monomeric units of RNA, the pentose is ribose, whereas in deoxyribonucleotides the monomeric units of DNA, the pentose is deoxyribose The phosphate group may be bonded to C5' of the pentose to form a 5' -nucleotide or to its C3' to form a 3'-nucleotide.
- If the phosphate group is absent, the compound is known as a nucleoside.



Nucleic acid bases:

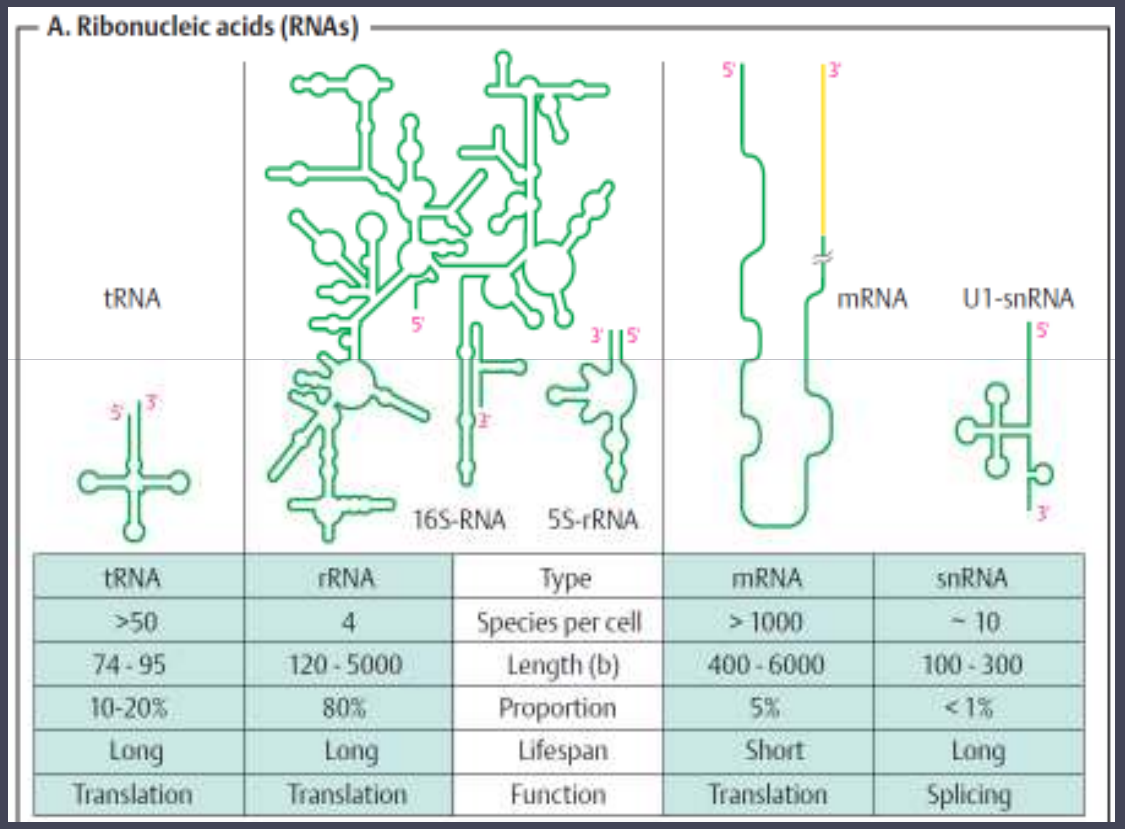
- The bases that occur in nucleic acids are aromatic heterocyclic compounds derived from either pyrimidine or purine.
- Five of these bases are the main components of nucleic acids in all living creatures.
- The purine bases adenine (abbreviation Ade, not "A") and guanine (Gua) and the pyrimidine base cytosine (Cyt) are present in both RNA and DNA. In contrast, uracil (Ura) is only found in RNA.
- In DNA, uracil is replaced by thymine (Thy).


Pyrimidine bases
Pyrimidine
Uracil (Ura)
Thymine (Thy)
Cytosine (Cyt)
Purine bases
Purine
Adenine (Ade)
Guanine (Gua)


(b)
A
5′ end
U (T)
C
G
5′
3′
3′ end

RNA

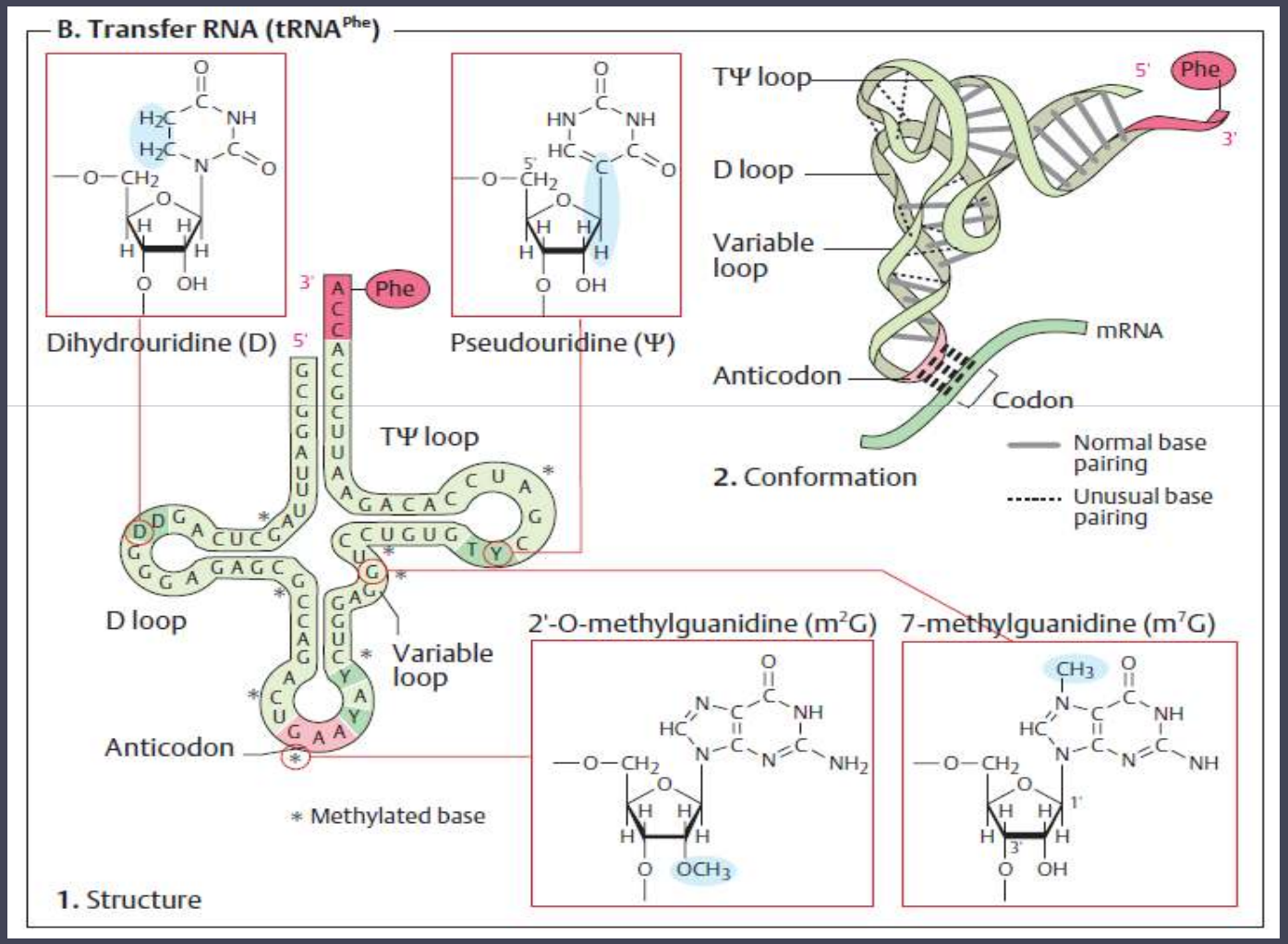
- Ribonucleic acids (RNAs) are polymers consisting of nucleoside phosphate components that are linked by phosphoric acid diester bonds.
- The bases the contain are mainly uracil, cytosine, adenine, and guanine, butmany unusual andmodified bases are also found in RNAs.



tRNA	rRNA	Type	mRNA	snRNA
>50	4	Species per cell	> 1000	~ 10
74 - 95	120 - 5000	Length (b)	400 - 6000	100 - 300
10-20%	80%	Proportion	5%	< 1%
Long	Long	Lifespan	Short	Long
Translation	Translation	Function	Translation	Splicing

t-RNA

- The transfer RNAs (tRNAs) function during translation as links between the nucleic acids and proteins. They are small RNA molecules consisting of 70–90 nucleotides, which "recognize" specific mRNA codons with their anticodons through base pairing. At the same time, at their 3 end (sequence CCA-3) they carry the amino acid that is assigned to the relevant mRNA codon according to the genetic code.
- The molecule contains a high proportion of unusual and modified components. These include pseudouridine (Ψ), dihydrouridine (D), thymidine (T), which otherwise only occurs in DNA, and many methylated nucleotides such as 7- methylguanidine (m7G) and—in the anticodon— 2-O-methylguanidine (m2G).


B. Transfer RNA (tRNA^Phe)
Dihydrouridine (D)
Pseudouridine (Ψ)
3'
Phe
5'
TΨ loop
D loop
Variable loop
Anticodon
* Methylated base
1. Structure
TΨ loop
D loop
Variable loop
mRNA
Anticodon
Codon
5'
Phe
3'
2. Conformation
Normal base pairing
Unusual base pairing
2'-O-methylguanidine (m²G)
7-methylguanidine (m⁷G)

rRNA

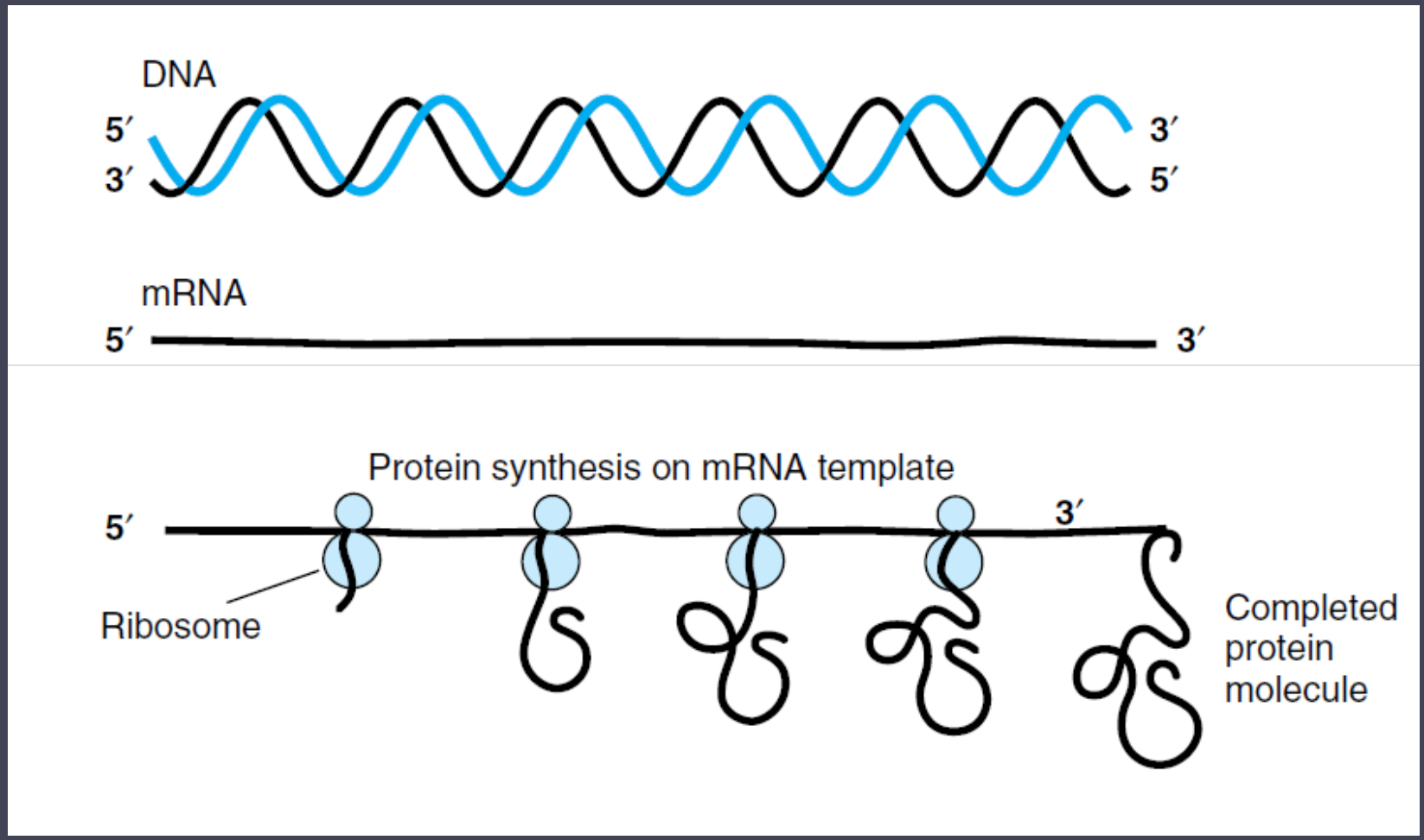
- Ribosomal RNA is produced from DNA by transcription in the nucleolus, and it is processed there and assembled with proteins to form ribosome subunits.
- A ribosome is a cytoplasmic nucleoprotein structure that acts as the machinery for the synthesis of proteins from the mRNA templates. On the ribosomes, the mRNA and tRNA molecules interact to translate into a specific protein molecule information transcribed from the gene.

Component	Mass (mw)	Protein		RNA		
		Number	Mass	Size	Mass	Bases
40S subunit	1.4×10^6	~35	7×10^5	18S	7×10^5	1900
60S subunit	2.8×10^6	~50	1×10^6	5S	35,000	120
				5.8S	45,000	160
				28S	1.6×10^6	4700

mRNA

- Messenger RNAs (mRNAs) transfer genetic information from the cell nucleus to the cytoplasm. mRNA carry genetic information from DNA.
- mRNA function as messengers conveying the information in a gene to the protein synthesizing machinery, where each serves as a template on which a specific sequence of amino acids is polymerized to form a specific protein molecule, the ultimate gene product.
- Messenger RNAs, particularly in eukaryotes, have some unique chemical characteristics. The 5′ terminal of mRNA is "capped" by a 7-methylguanosine triphosphate. The cap is involved in the recognition of mRNA by the translating machinery, and it probably helps stabilize the mRNA by preventing the attack of 5′-exonucleases.

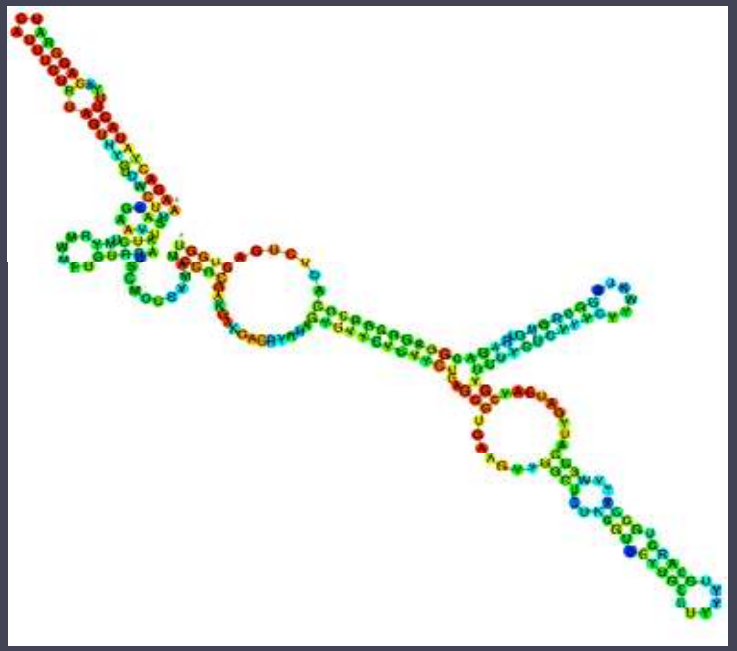
- The other end of most mRNA molecules, the 3′-hydroxyl terminal, has an attached polymer of adenylate residues 20–250 nucleotides in length. The specific function of the poly(A) "tail" at the 3′-hydroxyl terminal of mRNAs is not fully understood, but it seems that it maintains the intracellular stability of the specific mRNA by preventing the attack of 3′-exonucleases.


DNA
5′
3′
3′
5′
mRNA
5′
3′
Protein synthesis on mRNA template
5′
3′
Ribosome
Completed protein molecule

snRNA

- Small nuclear RNAs (snRNAs) are involved in the splicing of mRNA precursors. They associate with numerous proteins to form "spliceosomes."
- Small nuclear ribonucleic acid (snRNA), also commonly referred to as U-RNA, is a class of small RNA molecules that are found within the nucleus of eukaryotic cells. The length of an average snRNA is approximately 150 nucleotides.
- snRNA are always associated with a set of specific proteins, and the complexes are referred to as small nuclear ribonucleoproteins (snRNP) often pronounced "snurps".

- Each snRNP particle is composed of several Sm proteins, the snRNA component, and snRNP specific proteins.
- The most common snRNA components of these complexes are known, respectively, as: U1 snRNA, U2 snRNA, U4 snRNA, U5 snRNA, and U6 snRNA. Their nomenclature derives from their high uridine content.

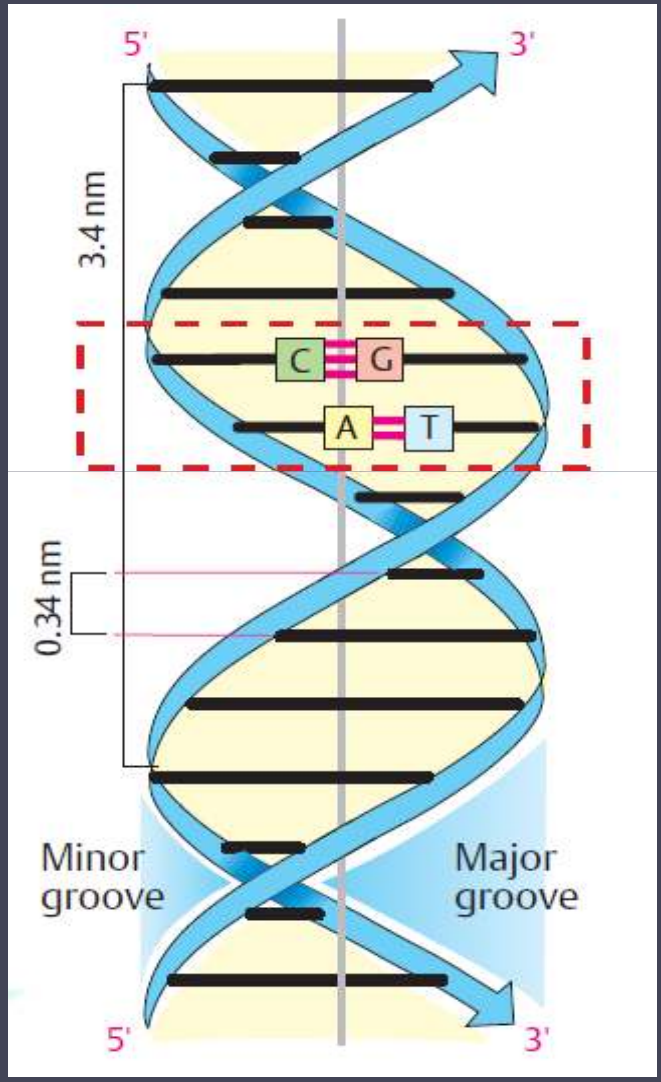


DNA

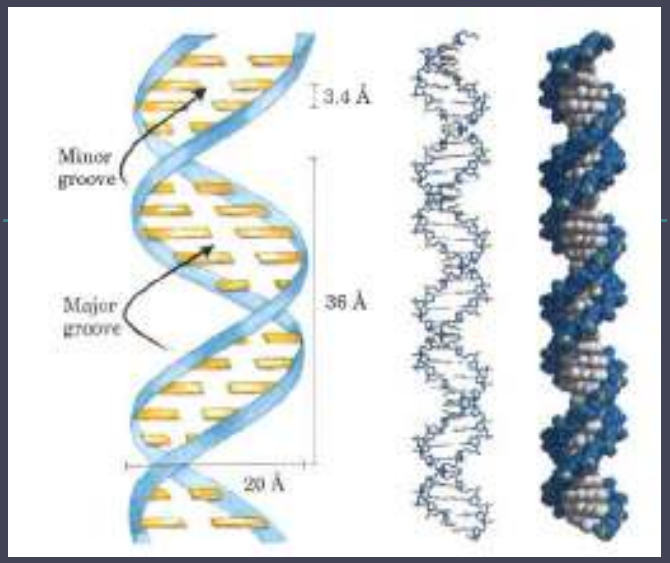
- Nucleic acids were first isolated in 1869 by Friedrich Miescher and so named because he found them in the nuclei of leukocytes (pus cells).
- in the 1930s and 1940s in what was termed the tetranucleotide hypothesis, that nucleic acids have a monotonously repeating sequence of all four bases, so that they were not suspected of having a genetic function.
- In 1928, Frederick Griffith made a startling discovery. In 1944, Oswald Avery, Colin MacLeod, and Maclyn McCarty, after a 10-year investigation, reported that transforming principle is DNA.
- DNA must therefore be the carrier of genetic information.

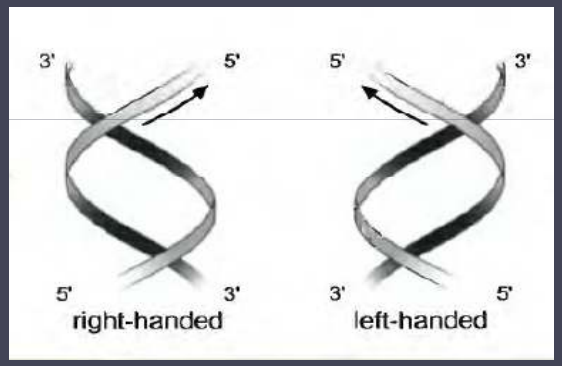
Watson–Crick structure of B-DNA

- It consists of two polynucleotide strands that wind about a common axis with a right-handed twist to form 20-Å-diameter double helix. The two strands are anti parallel (run in opposite directions) and wrap around each other such that they cannot be separated without unwinding the helix.
- Each base is hydrogen bonded to a base on the opposite strand to form a planar base pair. It is these hydrogen bonding interactions, a phenomenon known as complementary base pairing.

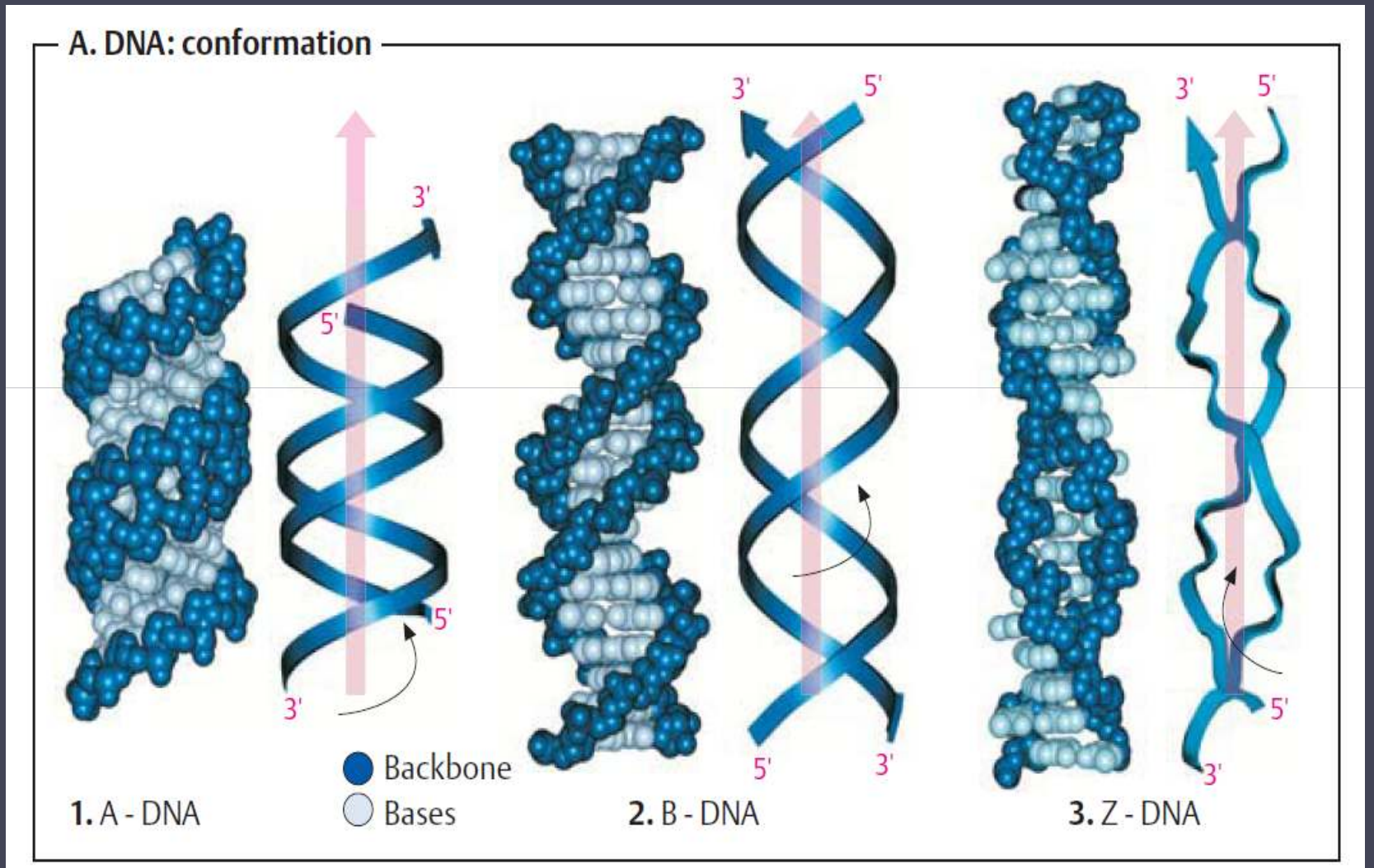


- The minor groove opening toward the bottom, whereas the major groove exposes the opposite edge of each base pair.
- DNA is either righter handed or left handed sense (twisting).
- Based on sense, nucleotide in per turn DNA are tree types B, A and Z DNA.
- The most common Watson-crick model DNA is B DNA.





	A form	B form	Z form
Helical sense	Right handed	Right handed	Left handed
Diameter	~26 Å	~20 Å	~18 Å
Base pairs per helical turn	11	10.5	12
Helix rise per base pair	2.6 Å	3.4 Å	3.7 Å


A. DNA: conformation
3'
5'
5'
3'
3'
5'
5'
3'
3'
5'
3'
5'
Backbone
Bases
1. A - DNA
2. B - DNA
3. Z - DNA


Thankyou