Macromolecule : Nucleic acid

(Part 1 of 2)

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Overview

1. Structure of Nucleic Acids
2. DNA structure
3. RNA structure
4. Nucleic acid biosynthesis (Part 2)

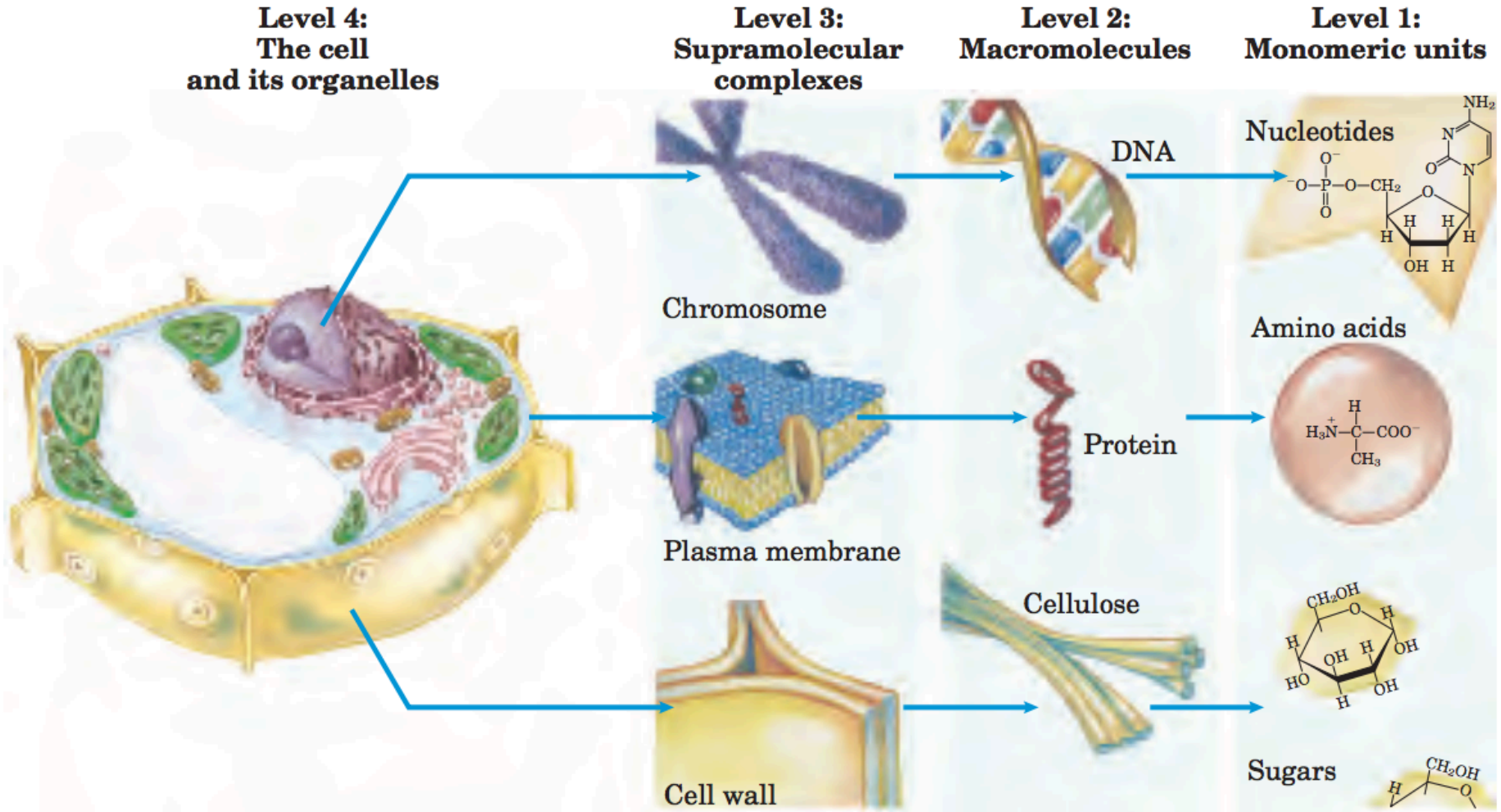
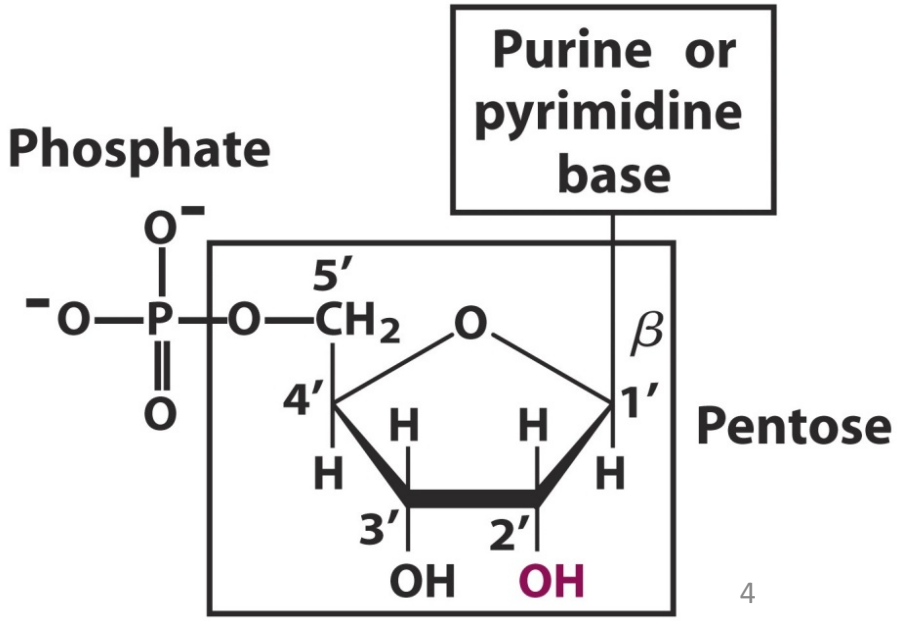


FIGURE 1–11 Structural hierarchy in the molecular organization of cells. In this plant cell, the nucleus is an organelle containing several types of supramolecular complexes, including chromosomes. Chromosomes consist of macromolecules of DNA and many different proteins. Each type of macromolecule is made up of simple subunits—DNA of nucleotides (deoxyribonucleotides), for example.

Structure of Nucleic Acids :
DNA and RNA composed of nucleotides monomers

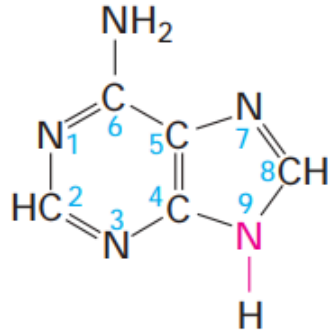
- Nucleic acids are polymers of nucleotides, joined together by phosphodiester linkages between the 5’- hydroxyl group of one pentose and the 3’- hydroxyl group of the next.
- Two types of nucleic acid : DNA (deoxyribonucleic acid) and RNA (ribonucleic acid), are the principal information-carrying molecules of the cell.
- Nucleotides consist of
  - Nitrogeneous base
    - Purine: adenine (A), guanine (G)
    - Pyrimidine: cytosine (C), uracil (U), thymine (T)
  - Sugar : Pentose
    - Ribose
    - Deoxy-ribose
  - One or more phosphate groups



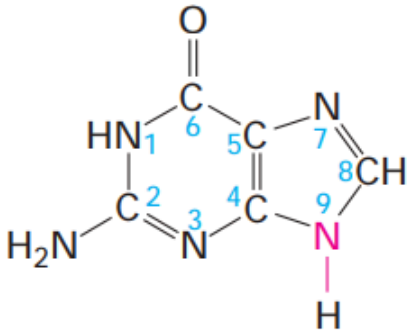
Nitrogenous Bases

- Planar, aromatic, and heterocyclic
- Derived from purine or pyrimidine
- In nucleic acids and nucleotides, nitrogen 9 of purines and nitrogen 1 of pyrimidines (red) are bonded to the 1' carbon of ribose or deoxyribose.
- U is only in RNA, and T is only in DNA.
- Both RNA and DNA contain A, G, and C.

PURINES

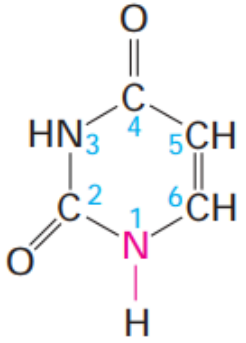


Adenine (A)

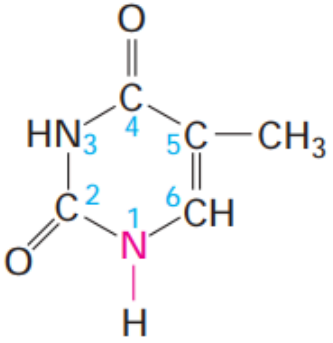


Guanine (G)

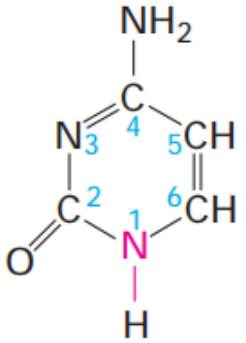
PYRIMIDINES



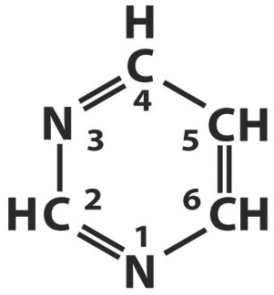
Uracil (U)



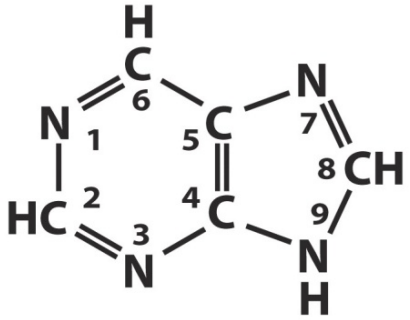
Thymine (T)



Cytosine (C)



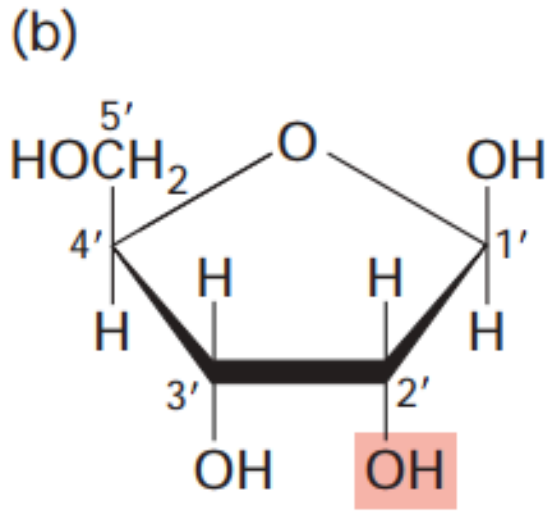
Pyrimidine



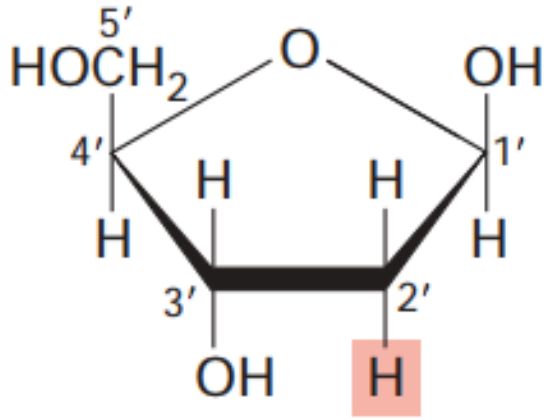
Purine

Sugars

- Pentoses (5-C sugars)
- D-Ribose and 2’-Deoxyribose
- By convention, the carbon atoms of the pentose sugar in nucleotides are numbered with primes



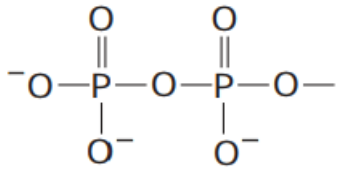
Ribose



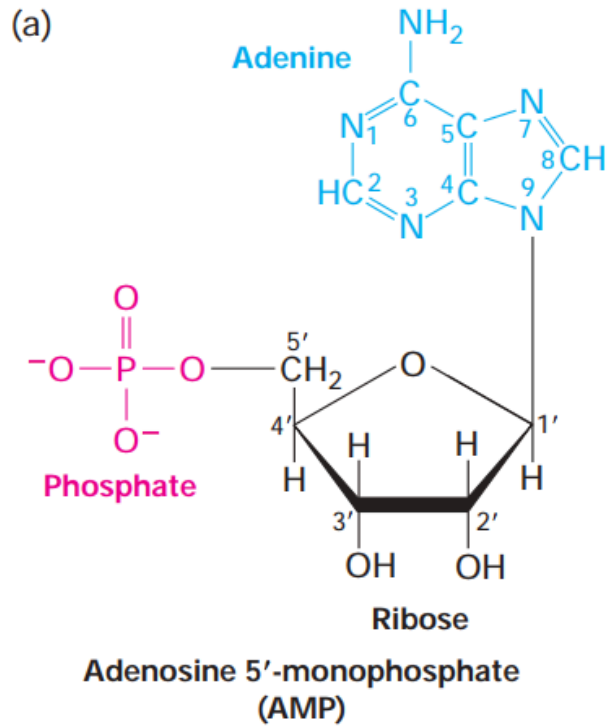
2-Deoxyribose

Nucleoside vs Nucleotide

- Cells and extracellular fluids in organisms contain small concentrations of nucleosides, combinations of a base and a sugar without a phosphate.
- Nucleotides are nucleosides that have one, two, or three phosphate groups esterified at the 5’ hydroxyl.
- Nucleoside monophosphates have a single esterified phosphate, diphosphates contain a pyrophosphate group, and triphosphates have a third phosphate.

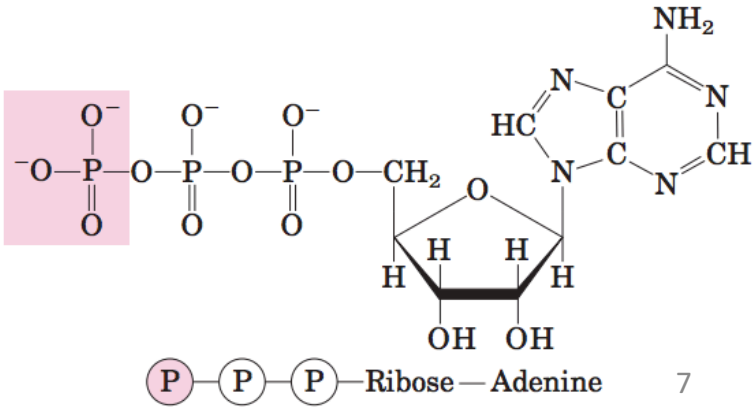


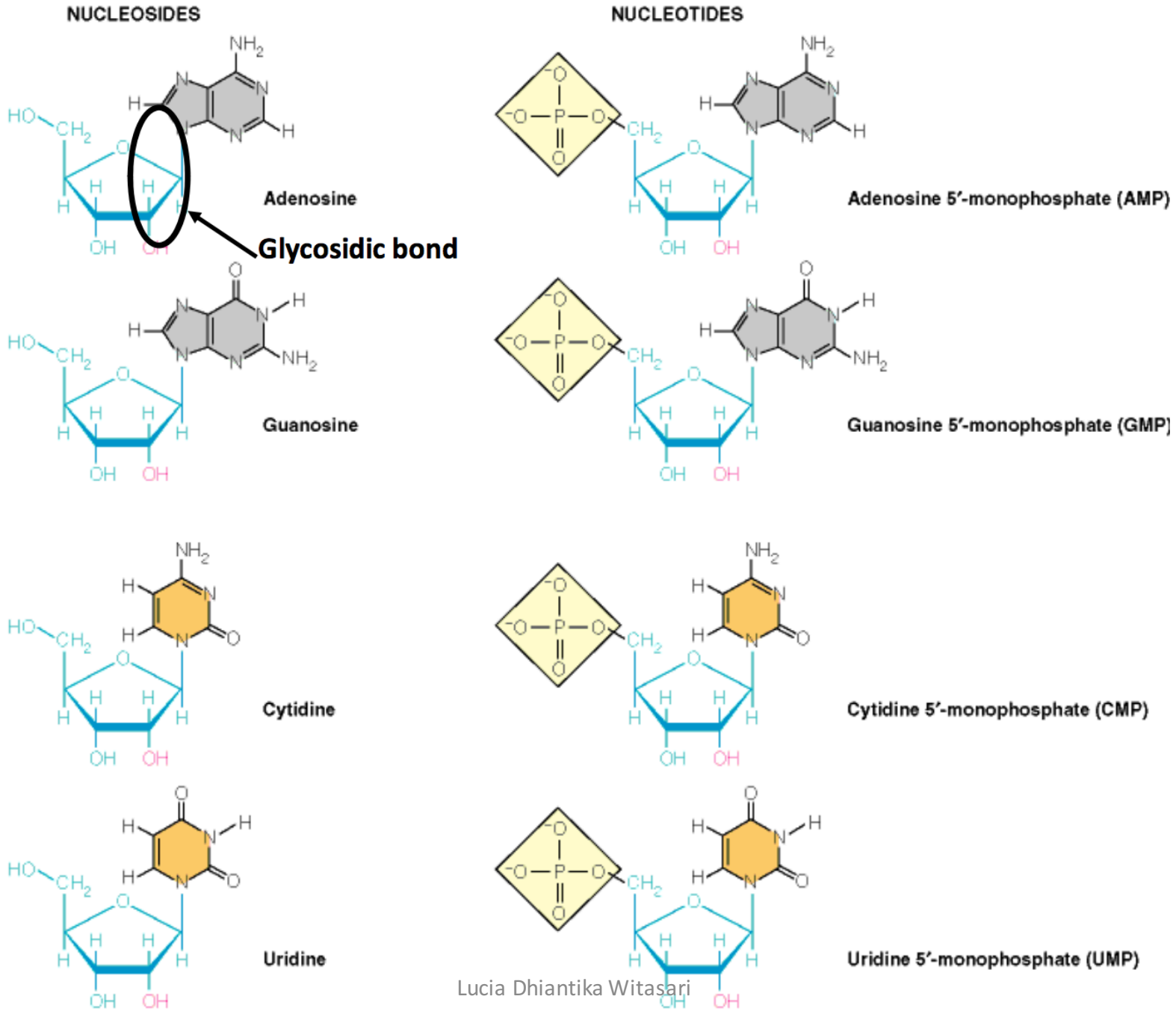
Pyrophosphate

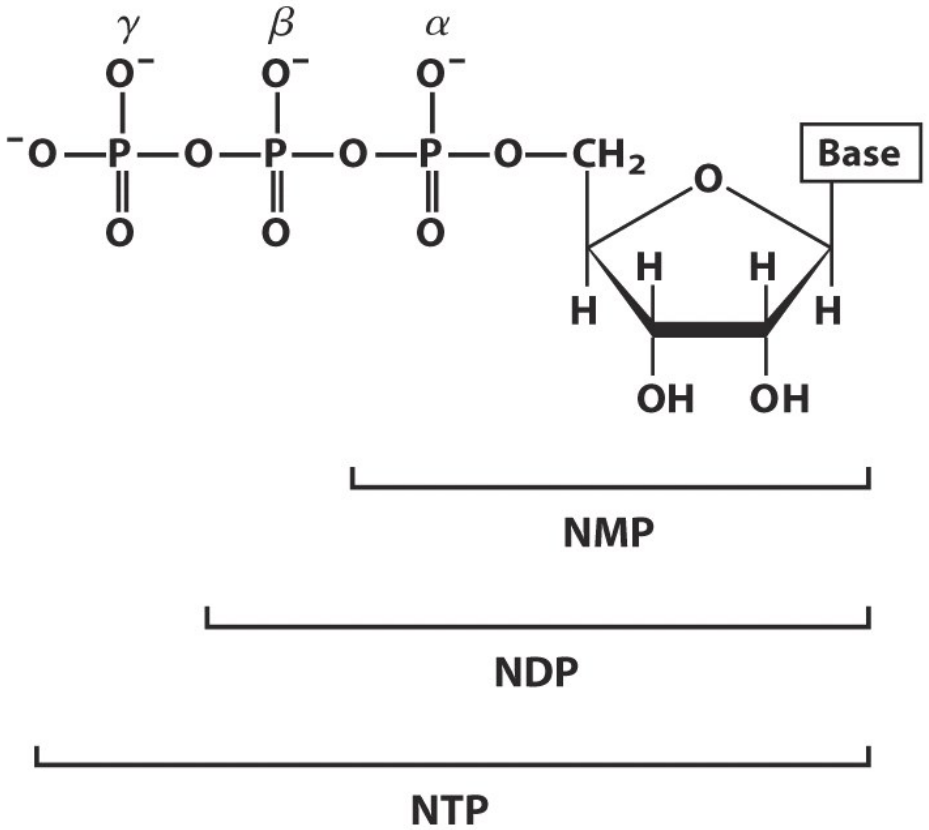


Adenosine 5′-monophosphate (AMP)

ATP




NUCLEOSIDES
NUCLEOTIDES
Adenosine
Glycosidic bond
Adenosine 5′-monophosphate (AMP)
Guanosine
Guanosine 5′-monophosphate (GMP)
Cytidine
Cytidine 5′-monophosphate (CMP)
Uridine
Uridine 5′-monophosphate (UMP)



Abbreviations of ribonucleoside 5′-phosphates			
Base	**Mono-**	**Di-**	**Tri-**
Adenine	AMP	ADP	ATP
Guanine	GMP	GDP	GTP
Cytosine	CMP	CDP	CTP
Uracil	UMP	UDP	UTP

Abbreviations of deoxyribonucleoside 5′-phosphates			
Base	**Mono-**	**Di-**	**Tri-**
Adenine	dAMP	dADP	dATP
Guanine	dGMP	dGDP	dGTP
Cytosine	dCMP	dCDP	dCTP
Thymine	dTMP	dTDP	dTTP

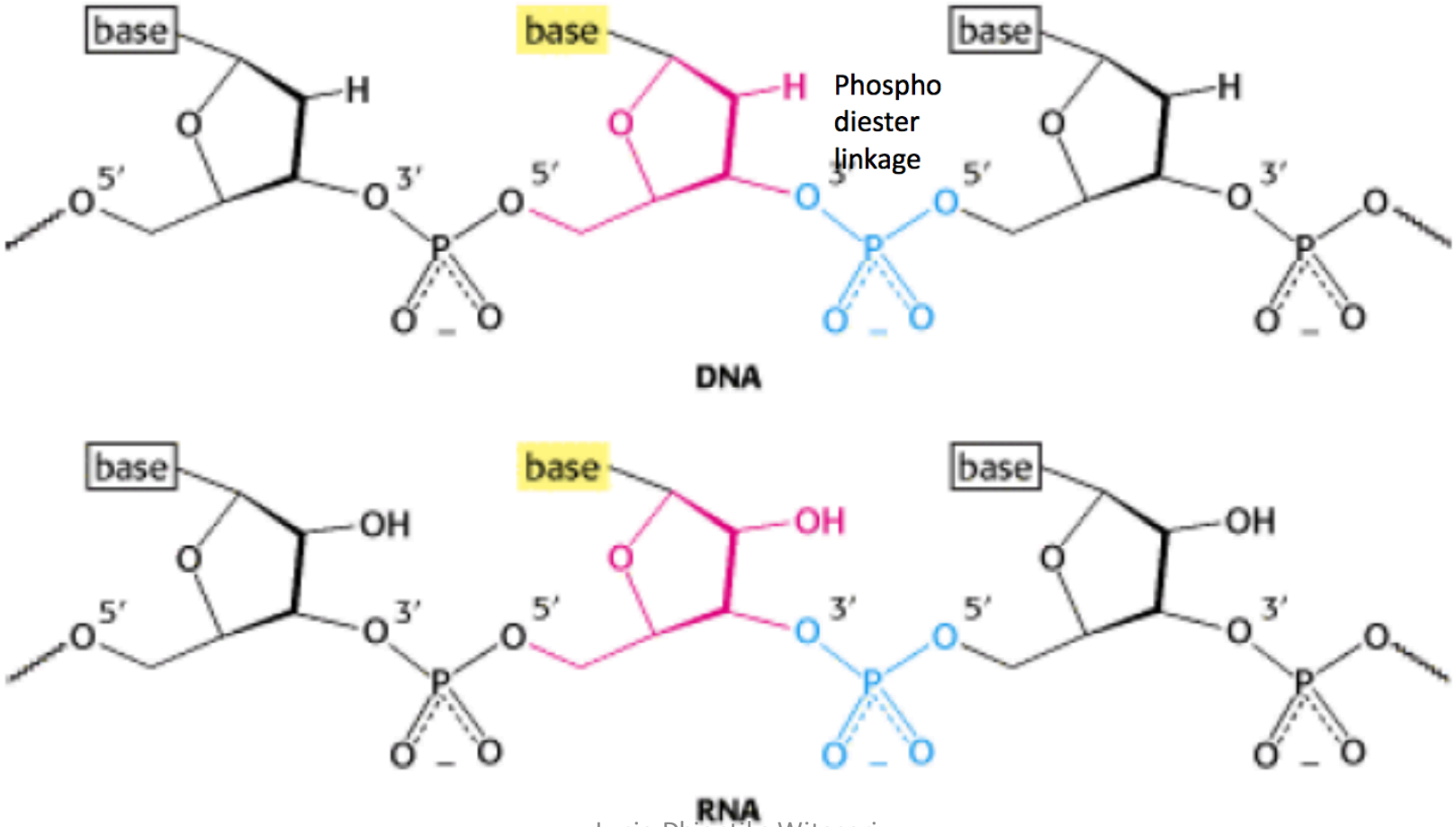
Nucleotide and nucleic acid nomenclature

Base	*Nucleoside*	*Nucleotide*	*Nucleic acid*
Purines			
Adenine	Adenosine	Adenylate	RNA
	Deoxyadenosine	Deoxyadenylate	DNA
Guanine	Guanosine	Guanylate	RNA
	Deoxyguanosine	Deoxyguanylate	DNA
Pyrimidines			
Cytosine	Cytidine	Cytidylate	RNA
	Deoxycytidine	Deoxycytidylate	DNA
Thymine	Thymidine or deoxythymidine	Thymidylate or deoxythymidylate	DNA
Uracil	Uridine	Uridylate	RNA

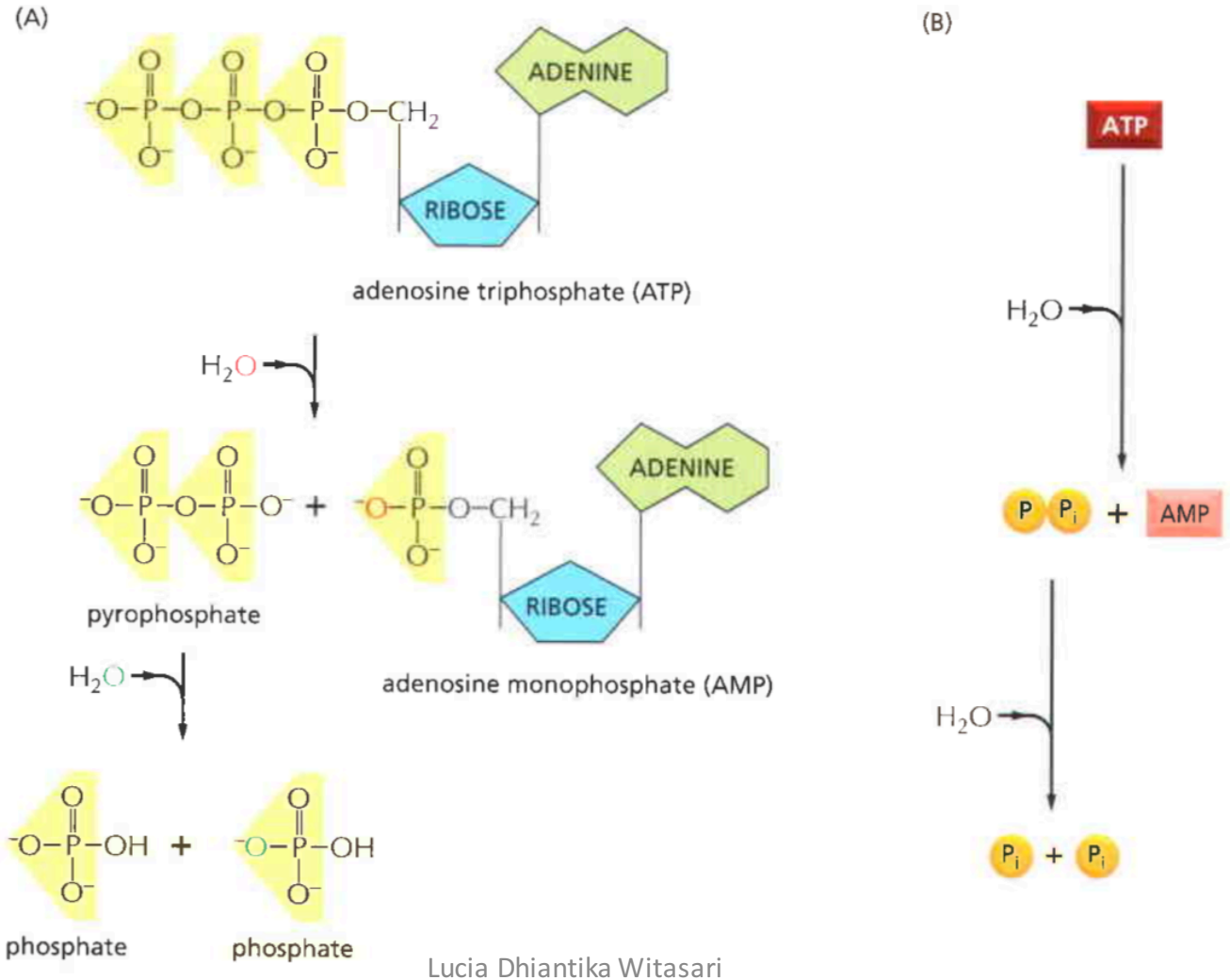
Role of Nucleotides in Biochemical Processes

- Precursors of DNA and RNA.
- Activated intermediates in many biosyntheses: e.g UDP-glucose: precursor for glycogen, CDP-diacylglycerol: precursor phosphoglycerides, S-adenosylmathionine as methyl donor, etc.
- Nucleoside triphosphates, especially ATP, as the universal currency of energy in biological systems.
- Adenine nucleotides are components of the coenzymes, $NAD(P)^+$, FAD, and CoA.
- Metabolic regulators: **(a)** c-AMP is the mediator of hormonal actions; **(b)** ATP-dependent protein phosphorylation - activates phosphorylase and inactivates glycogen synthase; **(c)** adenylation of a Tyr of bacterial glutamine synthetase - more sensitive to feedback inhibition and less active; **(d)** allosteric regulator - glycogen phosphorylase activated by ATP and inactivated by AMP.

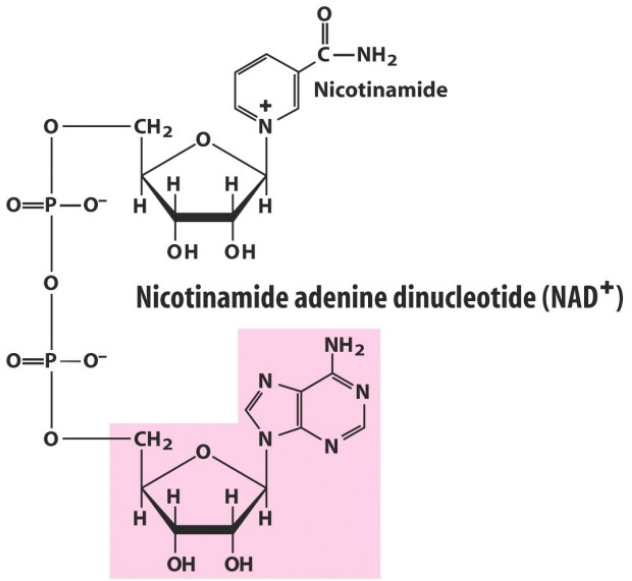
Backbones of DNA and RNA

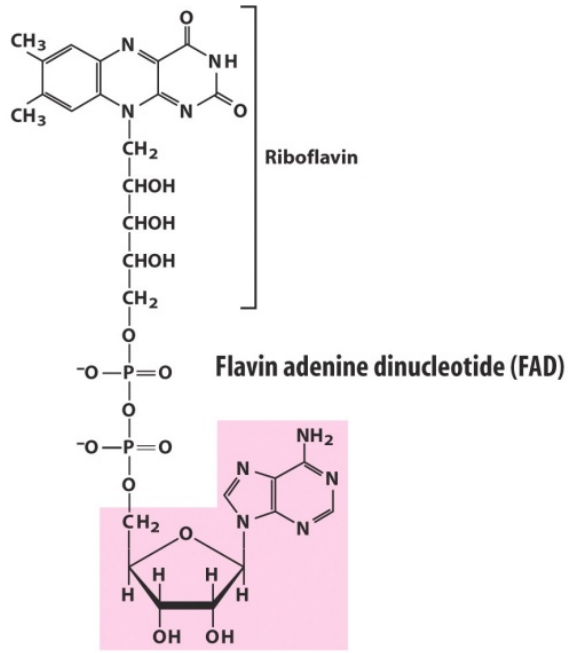


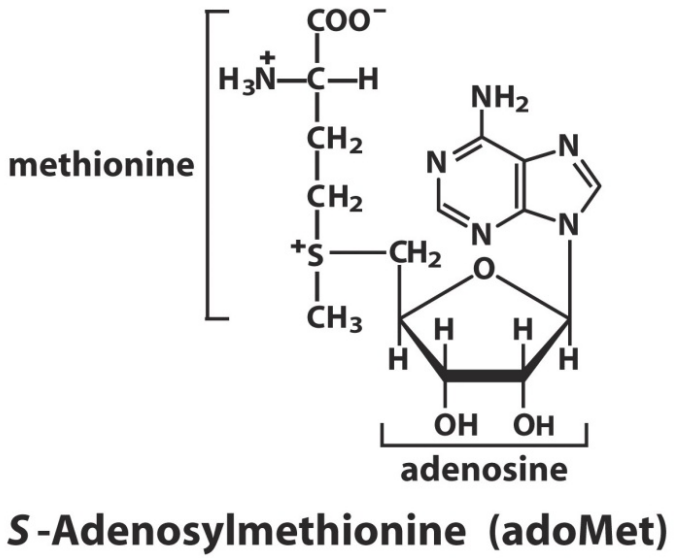
Chemical energy

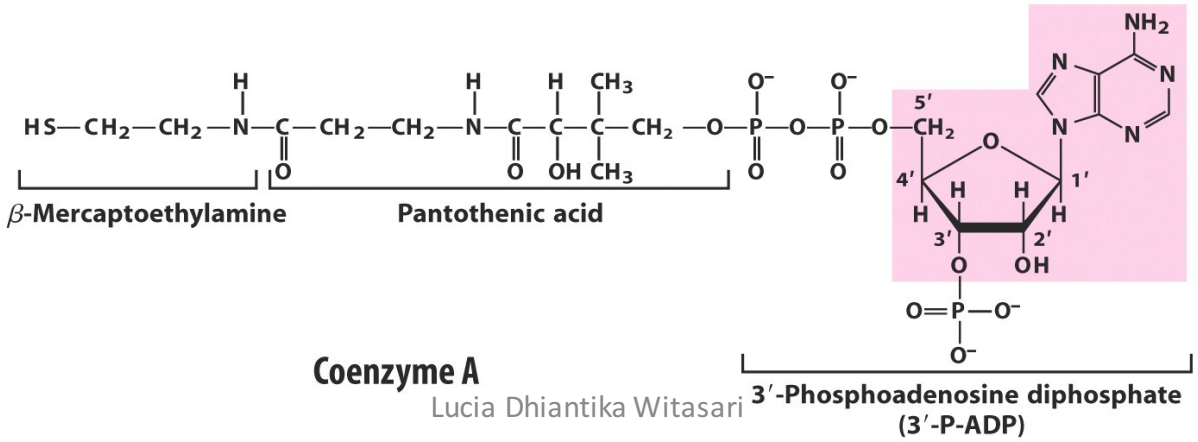


Component of cofactor

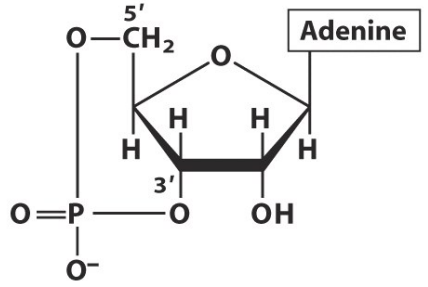




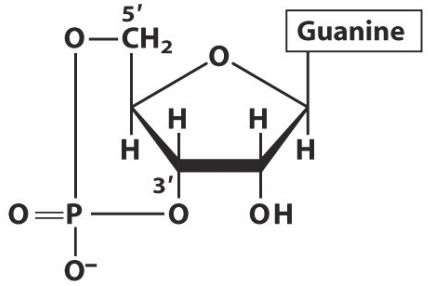




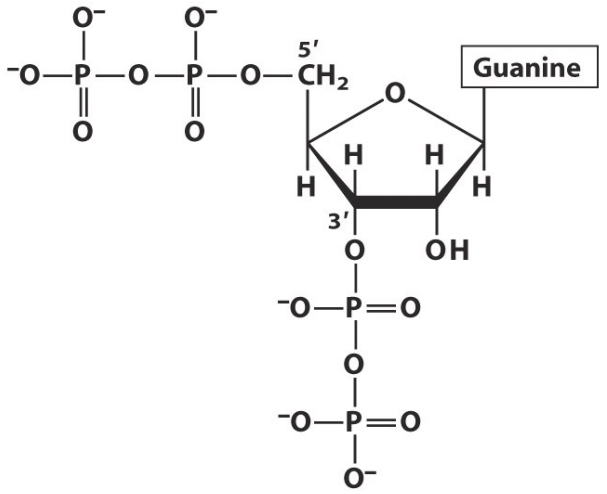
Regulatory molecules



Adenosine 3′,5′-cyclic monophosphate
(cyclic AMP; cAMP)



Guanosine 3′,5′-cyclic monophosphate
(cyclic GMP; cGMP)



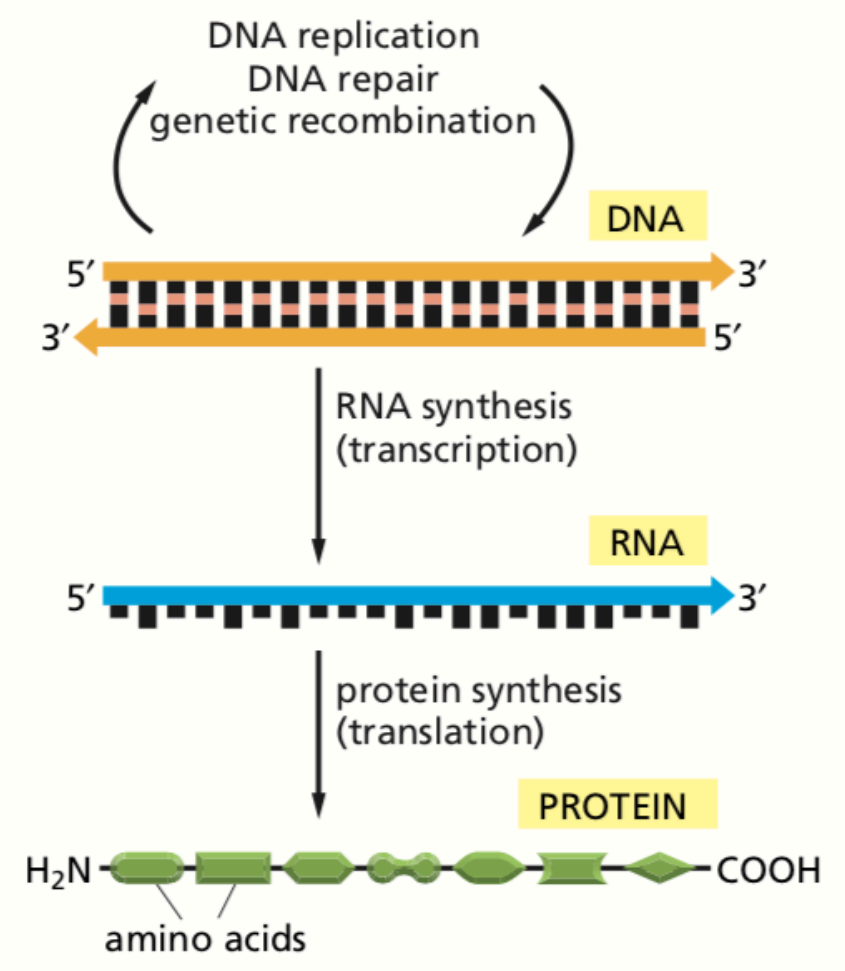
Guanosine 5′-diphosphate, 3′-diphosphate
(guanosine tetraphosphate)
(ppGpp)

Homework

Write down the chemical structures of:

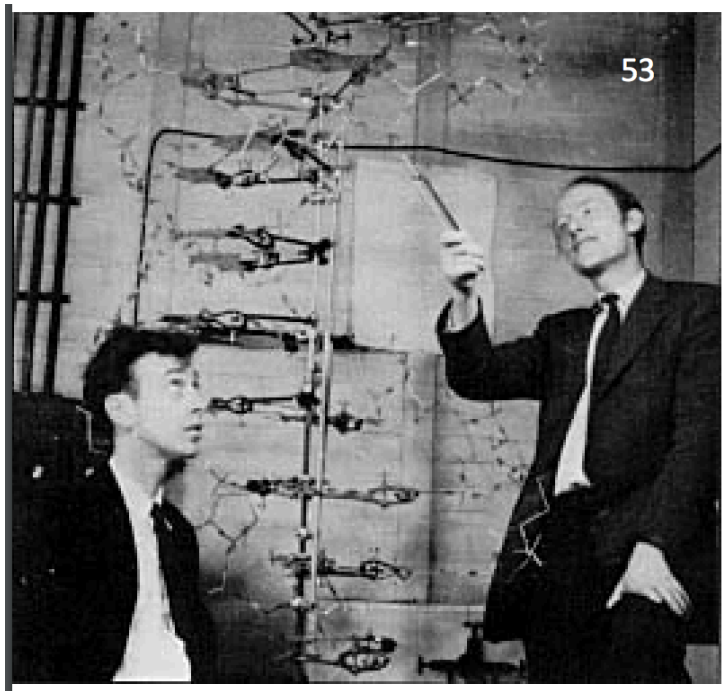
- AMP and dAMP
- GTP and dGTP
- CTP and dCTP
- dTTP
- UTP

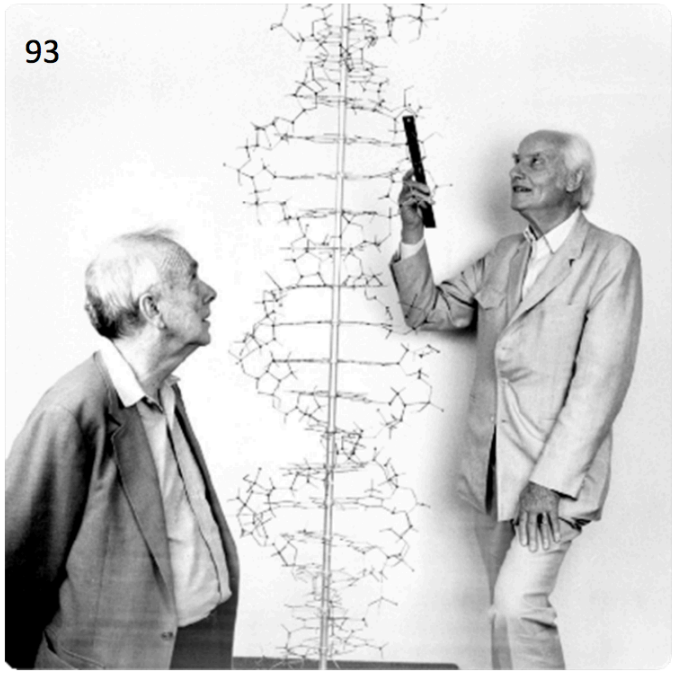
The pathway from DNA to Protein



DNA STRUCTURE

The discovery of the structure of DNA by Watson and Crick in 1953





James D. Watson (6 April 1928 – now) and Francis Crick (8 June 1916 – 28 July 2004)

2003

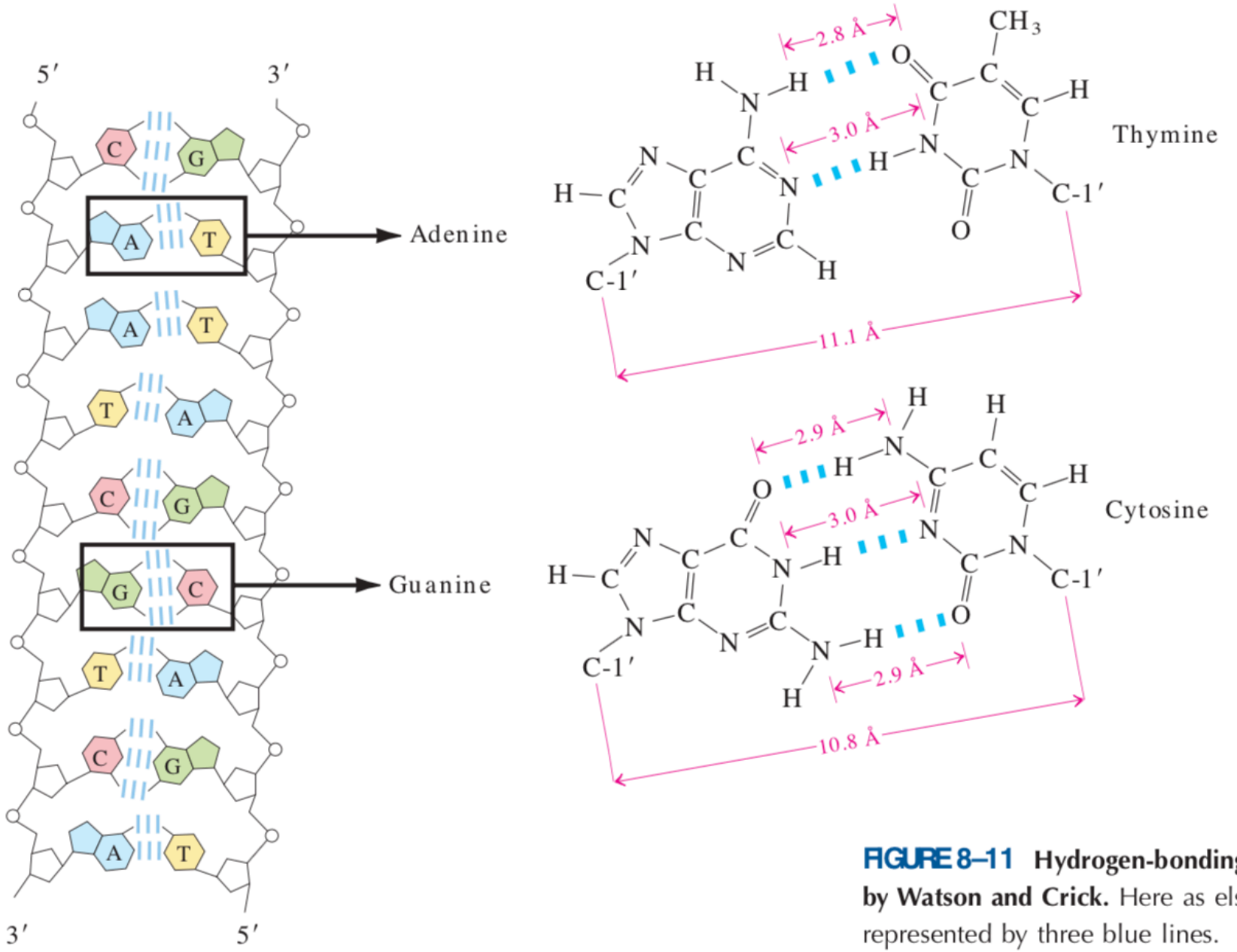


FIGURE 8–11 Hydrogen-bonding patterns in the base pairs defined by Watson and Crick. Here as elsewhere, hydrogen bonds are represented by three blue lines.

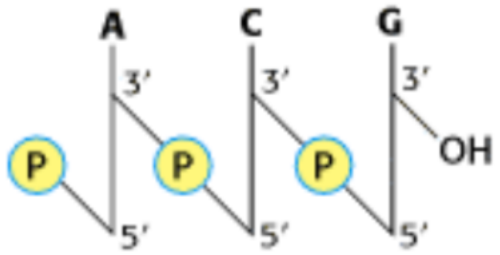
Phosphodiester linkages in the covalent backbone of DNA and RNA

The backbone of alternating pentose and phosphate groups in both types of nucleic acid is highly polar :

- The hydroxyl groups of the sugar residues form hydrogen bonds with water.
- The phosphate groups, with a p*K*a near 0, are completely ionized and negatively charged at pH 7.

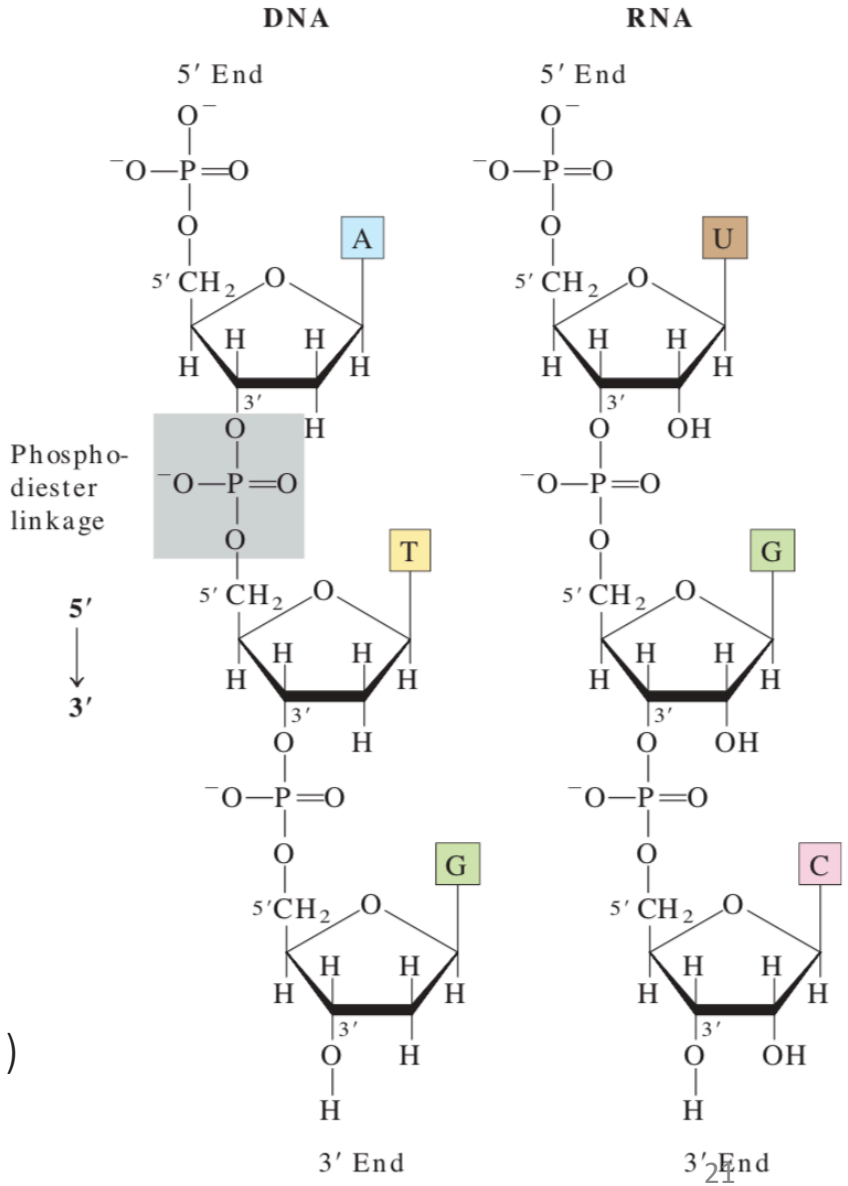
By definition, the **5' end** lacks a nucleotide at the 5' position and the **3' end** lacks a nucleotide at the 3' position.

By convention, the structure of a single strand of nucleic acid is always written with the 5' end at the left and the 3' end at the right—that is, in the 5'→ 3'direction.

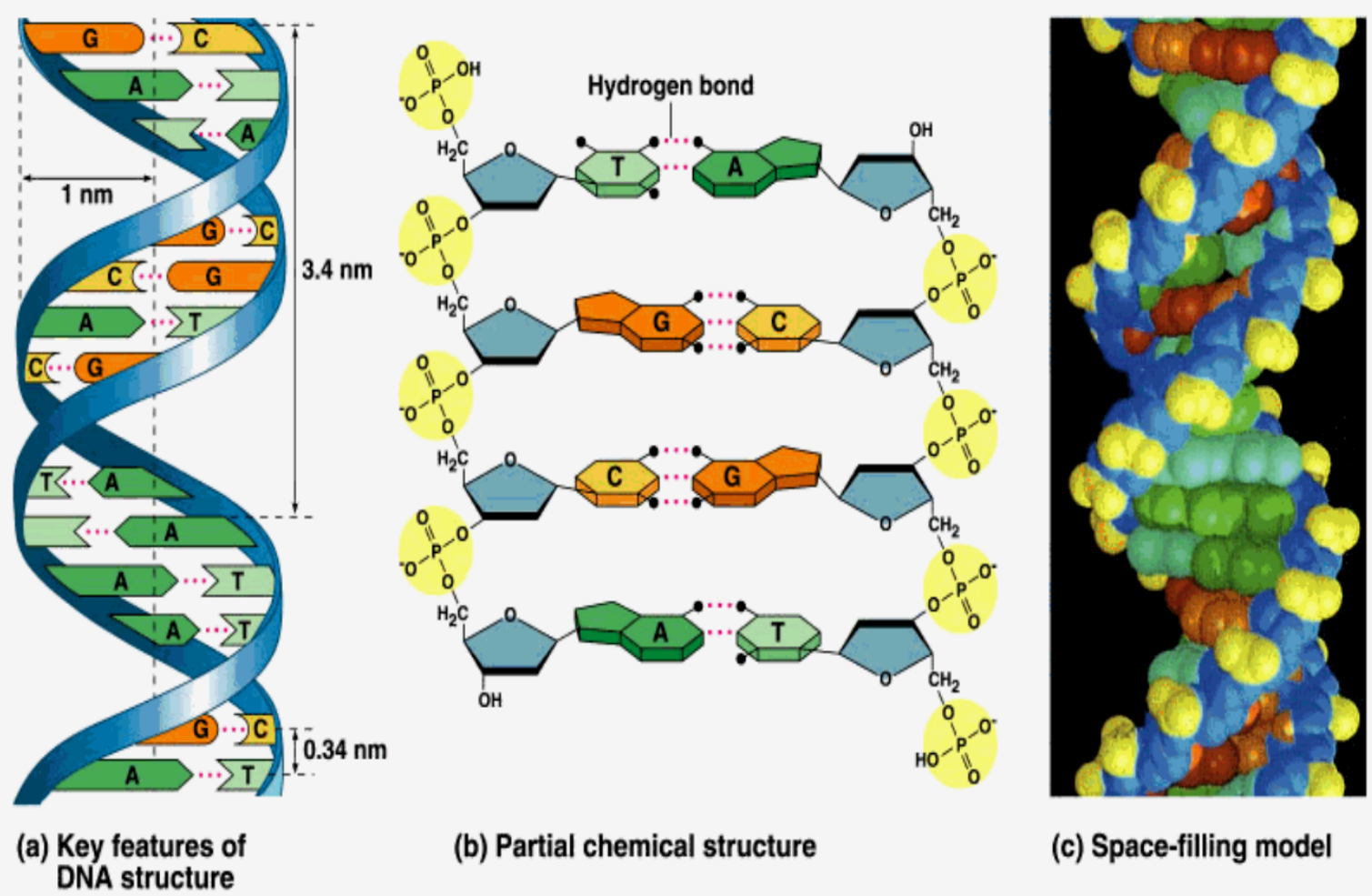


5'- A C G -3'

A short nucleic acid (< 50 nucleotides) is referred to as an **oligonucleotide.**



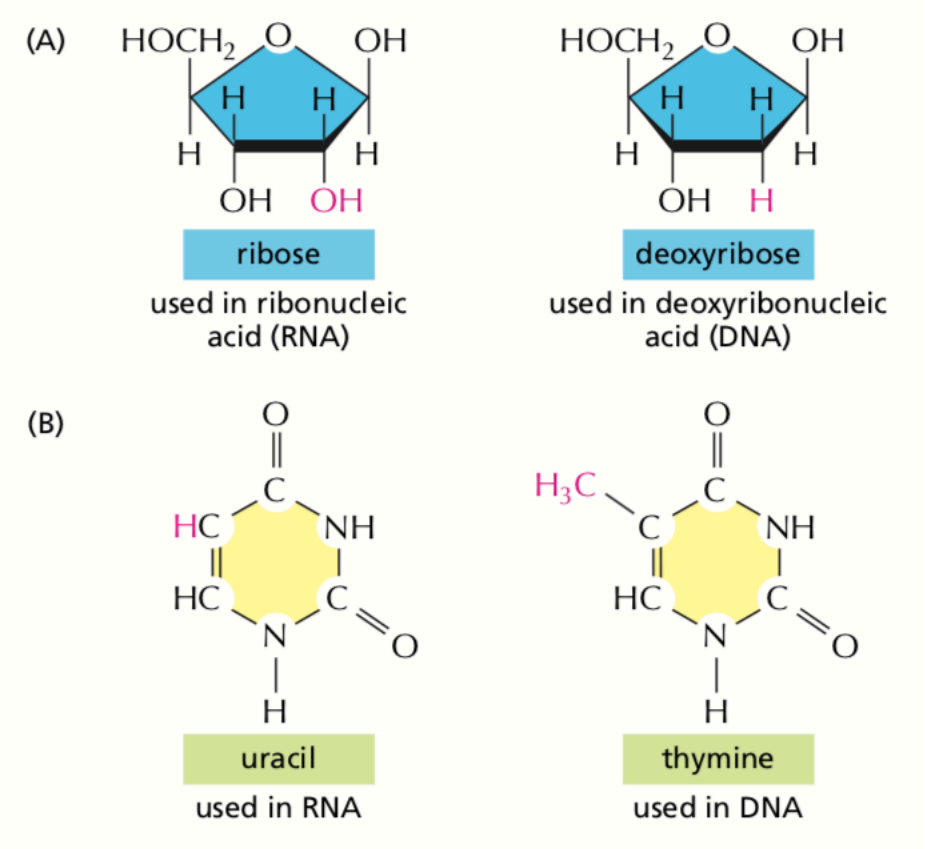
Watson and Crick Model for the Structure of DNA

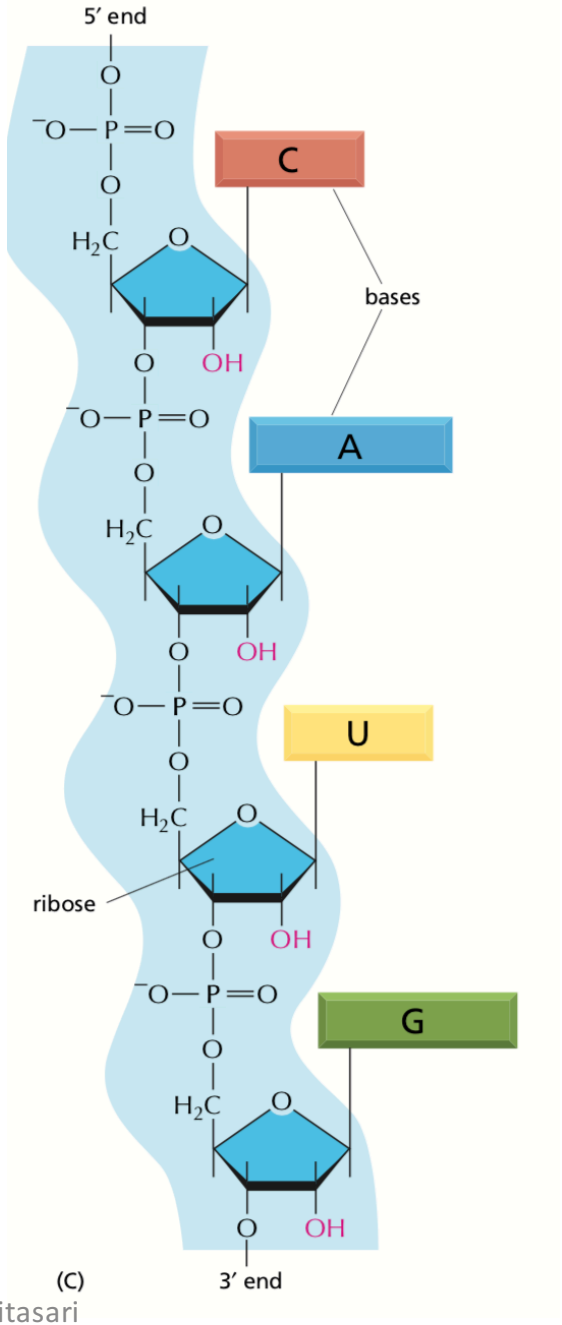


DNA always occurs in cells as a double-stranded helix

RNA STRUCTURE

RNA is single-stranded





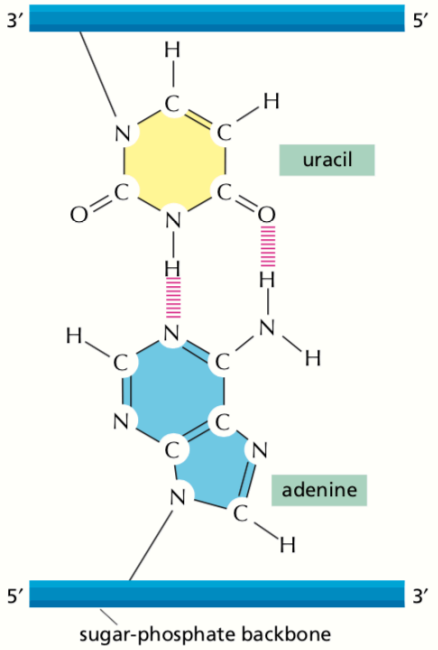


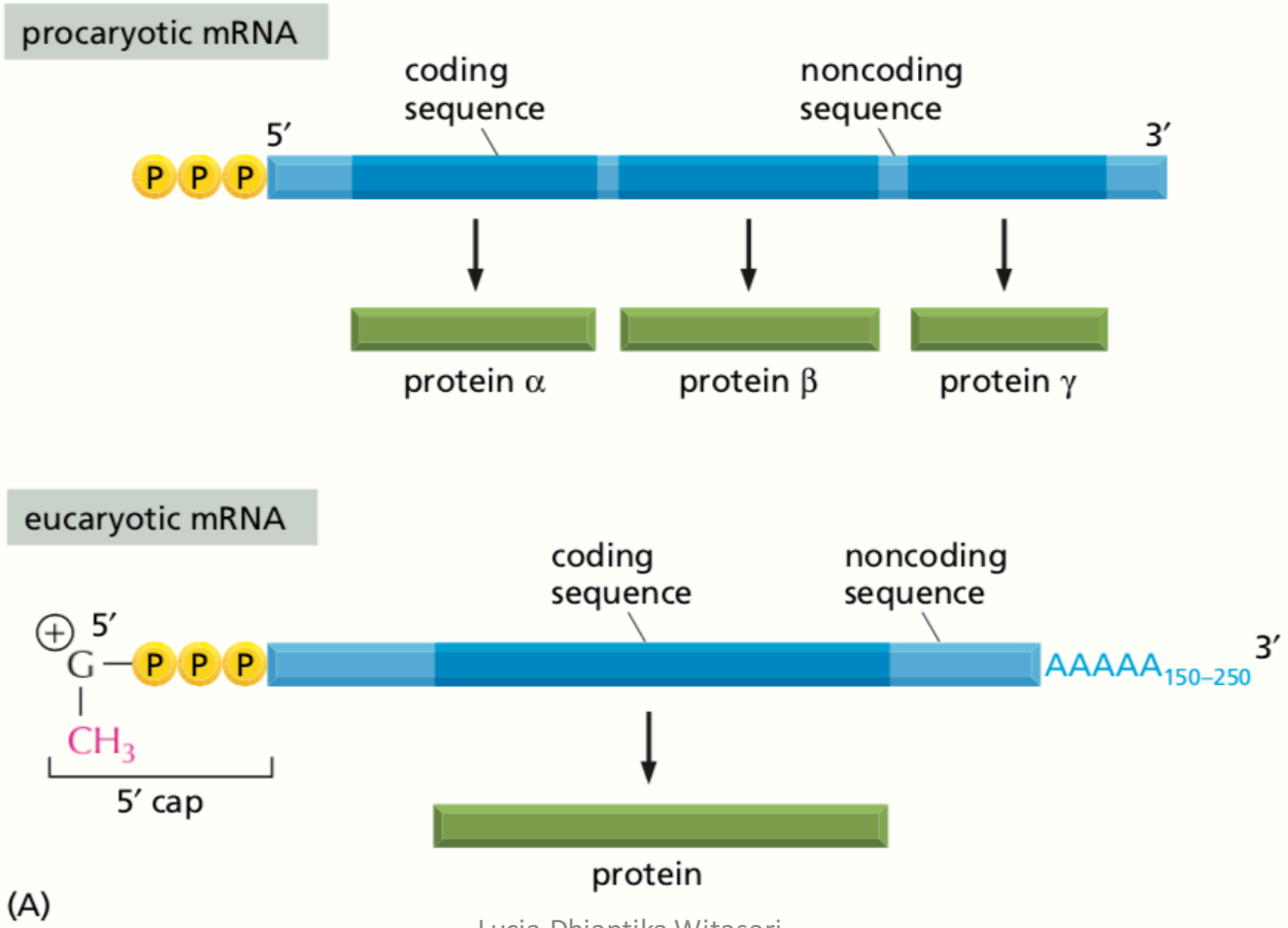
Table 6–1 Principal Types of RNAs Produced in Cells

TYPE OF RNA	FUNCTION
mRNAs	messenger RNAs, code for proteins
rRNAs	ribosomal RNAs, form the basic structure of the ribosome and catalyze protein synthesis
tRNAs	transfer RNAs, central to protein synthesis as adaptors between mRNA and amino acids
snRNAs	small nuclear RNAs, function in a variety of nuclear processes, including the splicing of pre-mRNA
snoRNAs	small nucleolar RNAs, used to process and chemically modify rRNAs
scaRNAs	small cajal RNAs, used to modify snoRNAs and snRNAs
miRNAs	microRNAs, regulate gene expression typically by blocking translation of selective mRNAs
siRNAs	small interfering RNAs, turn off gene expression by directing degradation of selective mRNAs and the establishment of compact chromatin structures
Other noncoding RNAs	function in diverse cell processes, including telomere synthesis, X-chromosome inactivation, and the transport of proteins into the ER

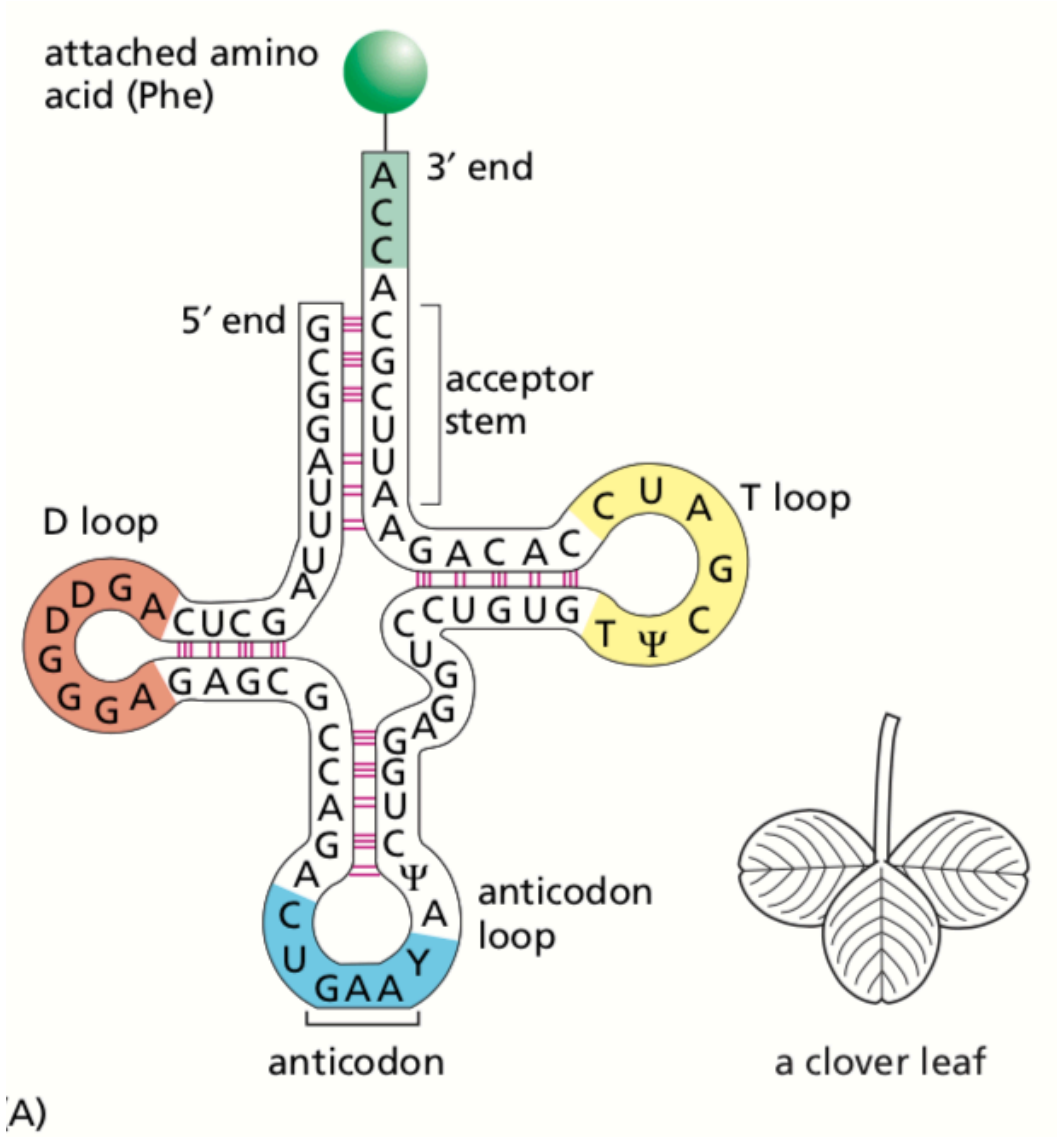
RNAs Play Key Roles in Gene Expression

- **Messenger RNAs (mRNAs)** are the template for protein synthesis or *translation*
  - mRNAs carrying genetic information from one or a few genes to a ribosome.
- **Ribosomal RNAs (rRNAs)** are components of ribosomes, the complexes that carry out the synthesis of proteins.
  - In *E. coli*, there are three kinds of rRNA, called *23S* (3700 nucleotides), *16S* (1700 nucleotides), and *5S* (120 nucleotides) *RNA* because of their sedimentation behavior.
- **Transfer RNAs (tRNAs)** are adapter molecules that faithfully translate the information in mRNA into a specific sequence of amino acids.
  - at least one kind of tRNA for each of the 20 amino acids.
  - Transfer RNA consists of about 75 nucleotides

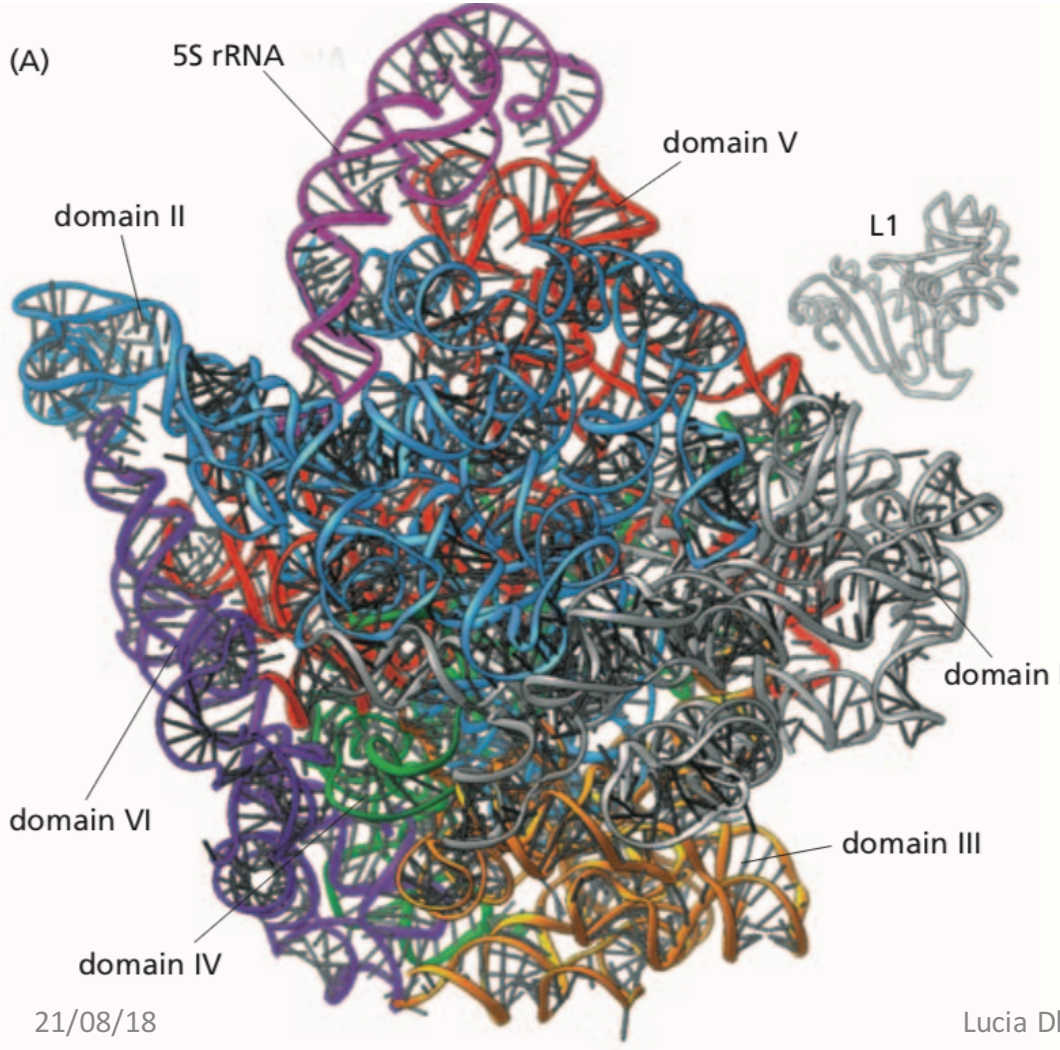
the structures of procaryotic and eucaryotic mRNA molecules

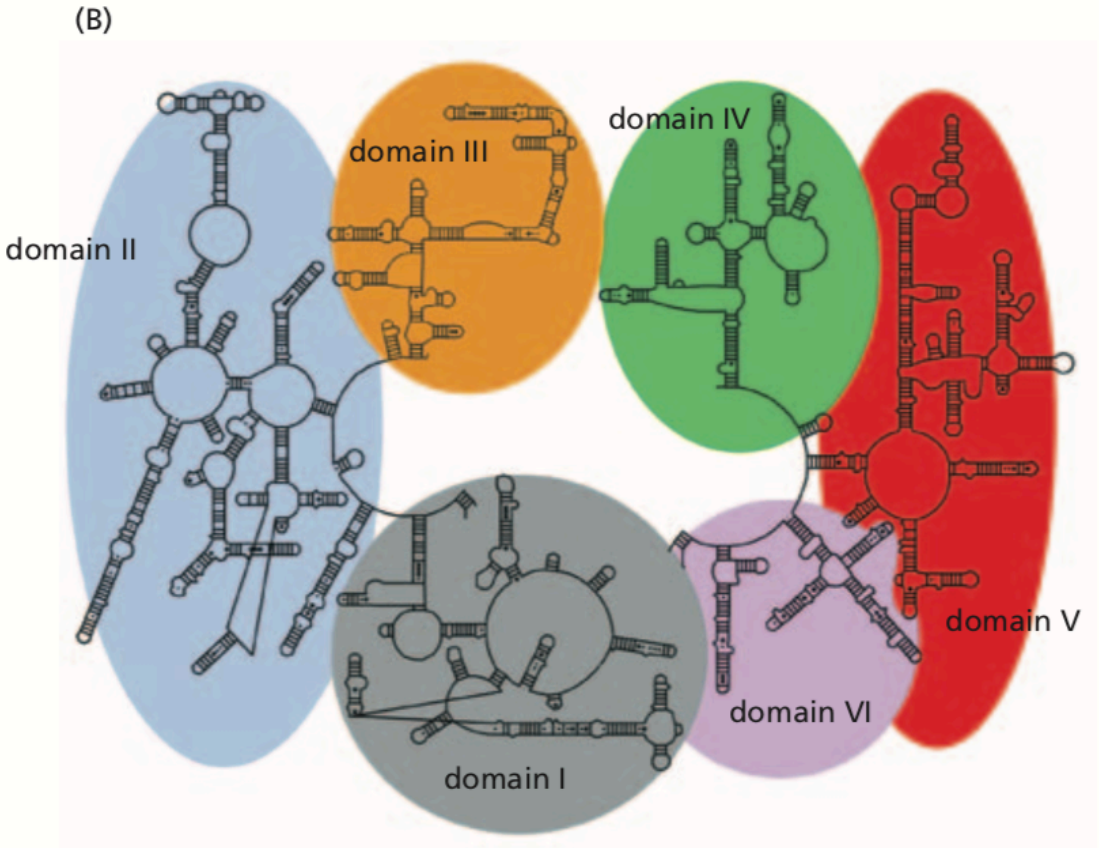


tRNA molecule



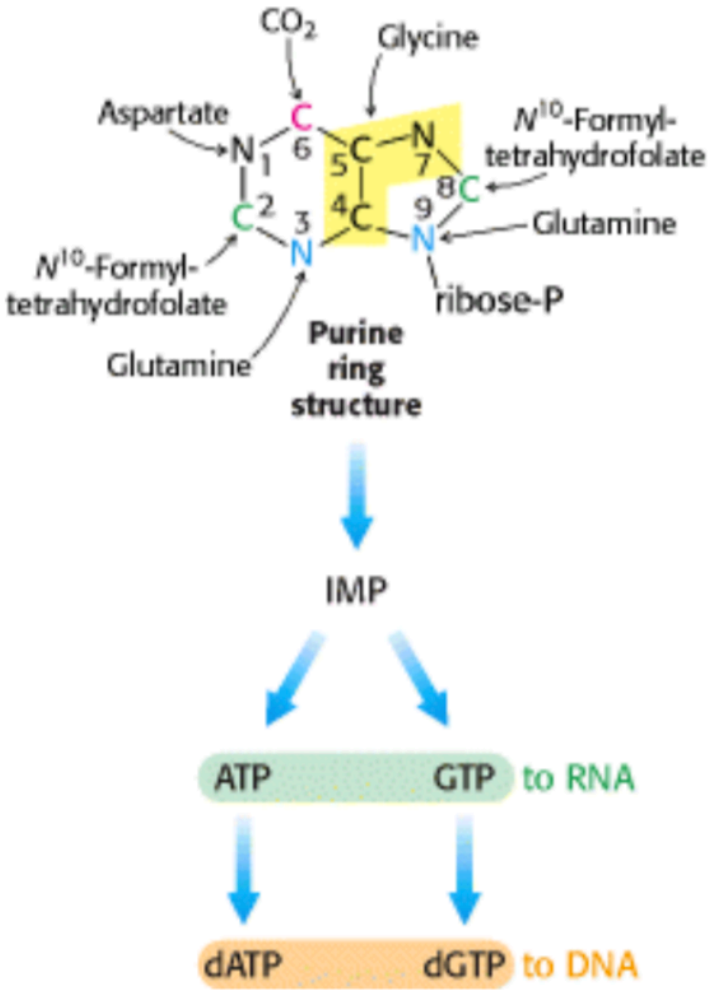
rRNAs in the large subunit of a bacterial ribosome





Nucleic acid biosynthesis

PURINE BIOSYNTHESIS



de Novo pathway

$$\text{Adenine} + \text{PRPP} \longrightarrow \text{adenylate} + PP_i$$

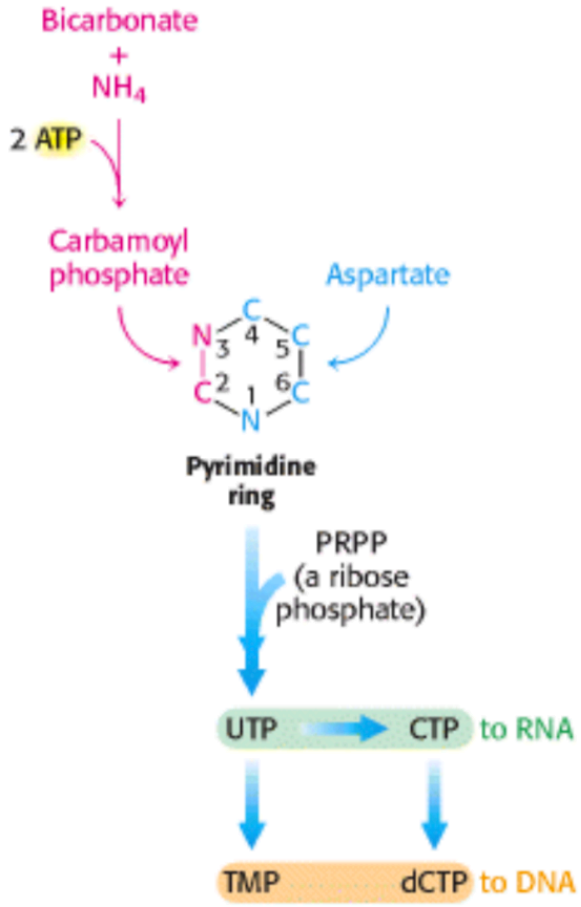
$$\text{Guanine} + \text{PRPP} \longrightarrow \text{guanylate} + PP_i$$

$$\textit{Hypoxanthine} + \text{PRPP} \longrightarrow \text{inosinate} + PP_i$$

Salvage Pathways

PYRIMIDINE BIOSYNTHESIS

de Novo pathway



Recommended video for learning

- https://www.youtube.com/watch?v=o_-6JXLYS-k
- https://www.youtube.com/watch?v=MA-ouz1LtpM

References

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