

BIOL 158: NUCLEIC ACIDS

by

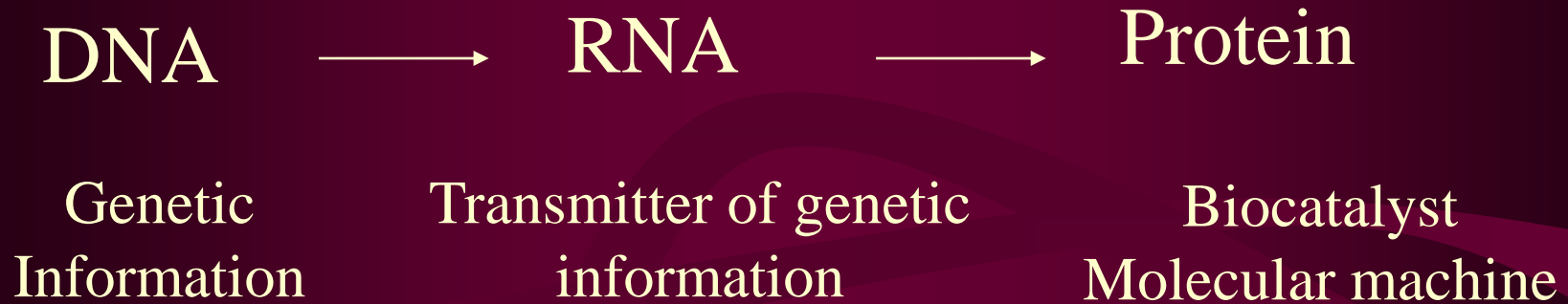
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Nucleotides and Nucleic acids

The central dogma of the biosciences



Deoxyribonucleic acid and Ribonucleic acid---Macromolecules

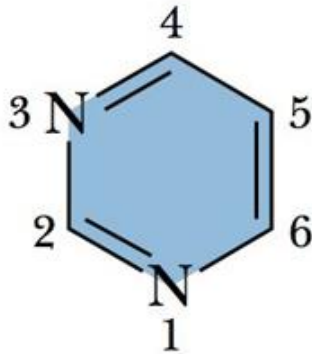
Linear polymers of nucleotides: Heterocyclic nitrogenous bases

- What are the structures of the nucleotides?
- How are nucleotides joined together to form nucleic acids?
- How is information stored in nucleic acids?
- What are the biological functions of nucleotides and nucleic acids?

What are the structures of the nucleotides?

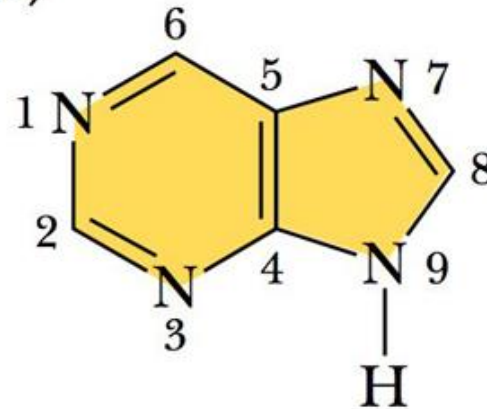
Nitrogenous bases: derivatives of pyrimidine or purine

(a)



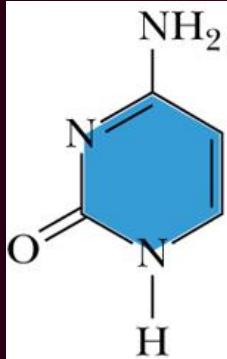
The pyrimidine ring

(b)

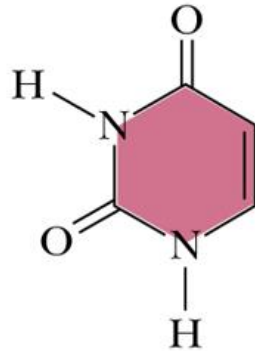


The purine ring system

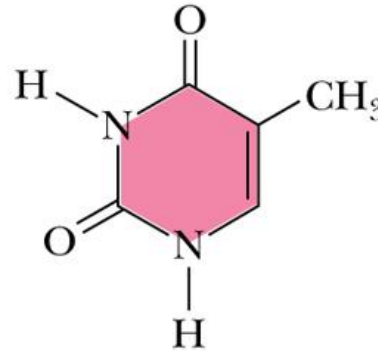
Three pyrimidines and two purines are commonly found in cells



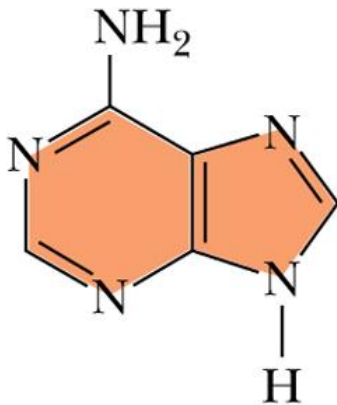
Cytosine
(2-oxy-4-amino
pyrimidine)



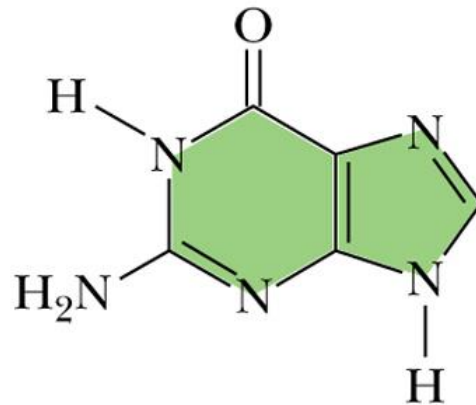
Uracil
(2-oxy-4-oxy
pyrimidine)



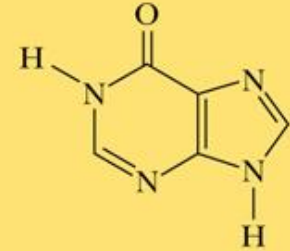
Thymine
(2-oxy-4-oxy
5-methyl pyrimidine)



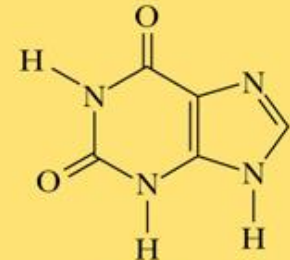
Adenine
(6-amino purine)



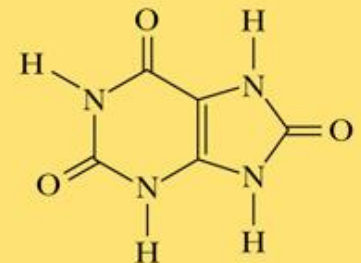
Guanine
(2-amino-6-oxy purine)



Hypoxanthine



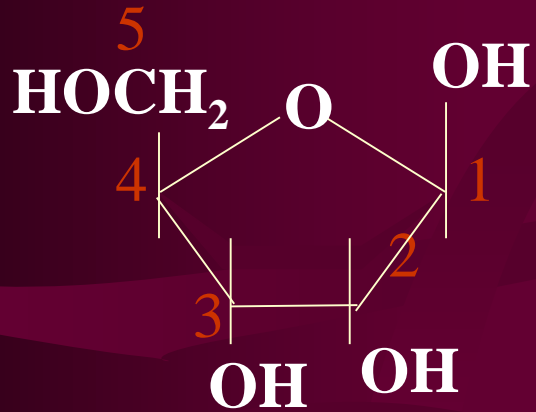
Xanthine



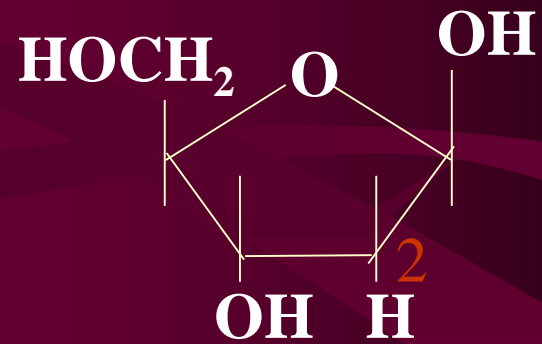
Uric acid

Purine derivatives

Ribose



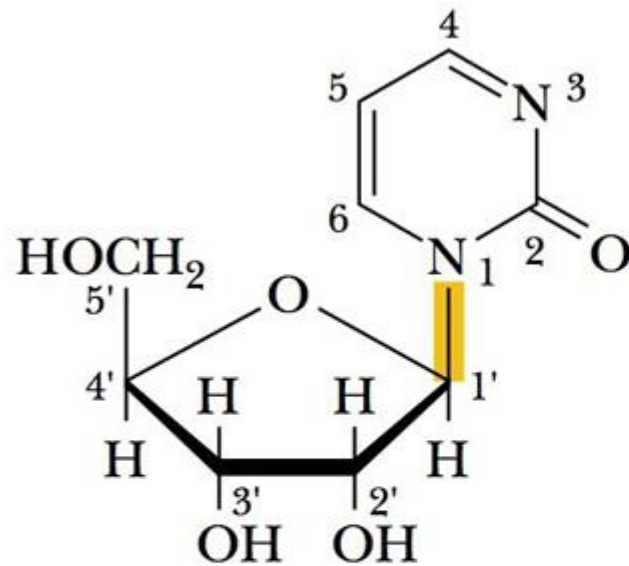
β -D-Ribofuranose



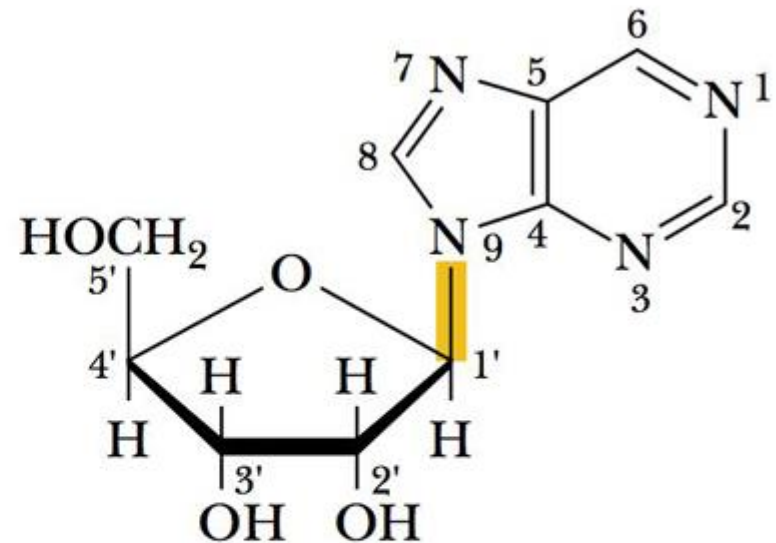
Deoxyribose
 β -D-2-Deoxyribofuranose

Nucleosides (ribose + base)

β -N-glycosidic bond

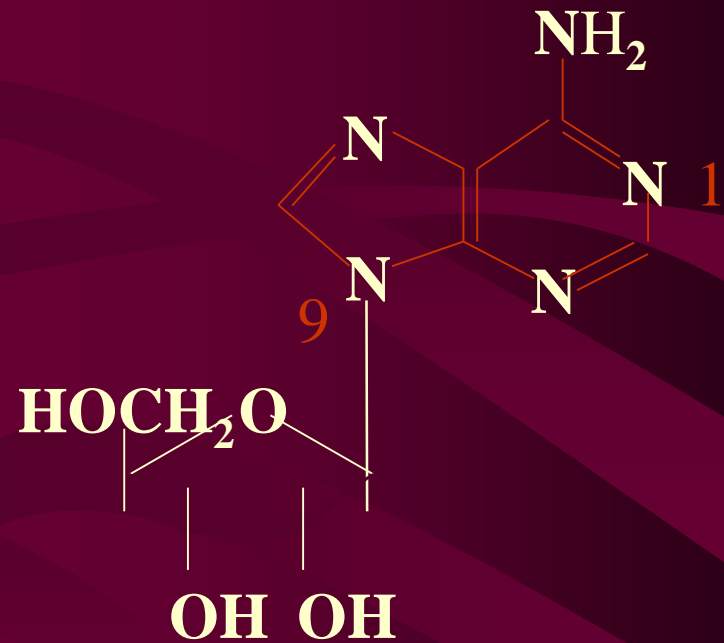
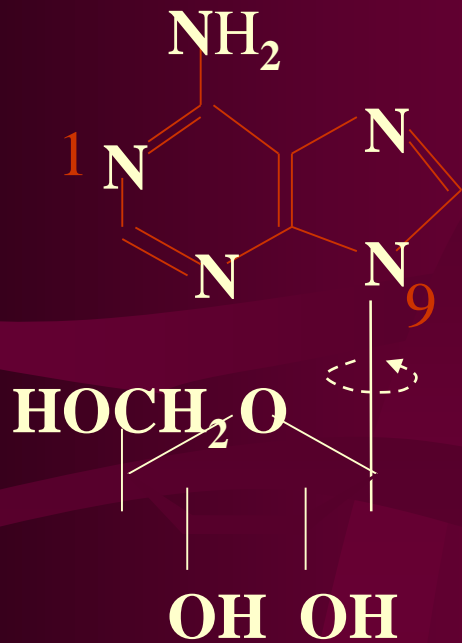


β -N₁-glycosidic
bond in pyrimidine
ribonucleosides



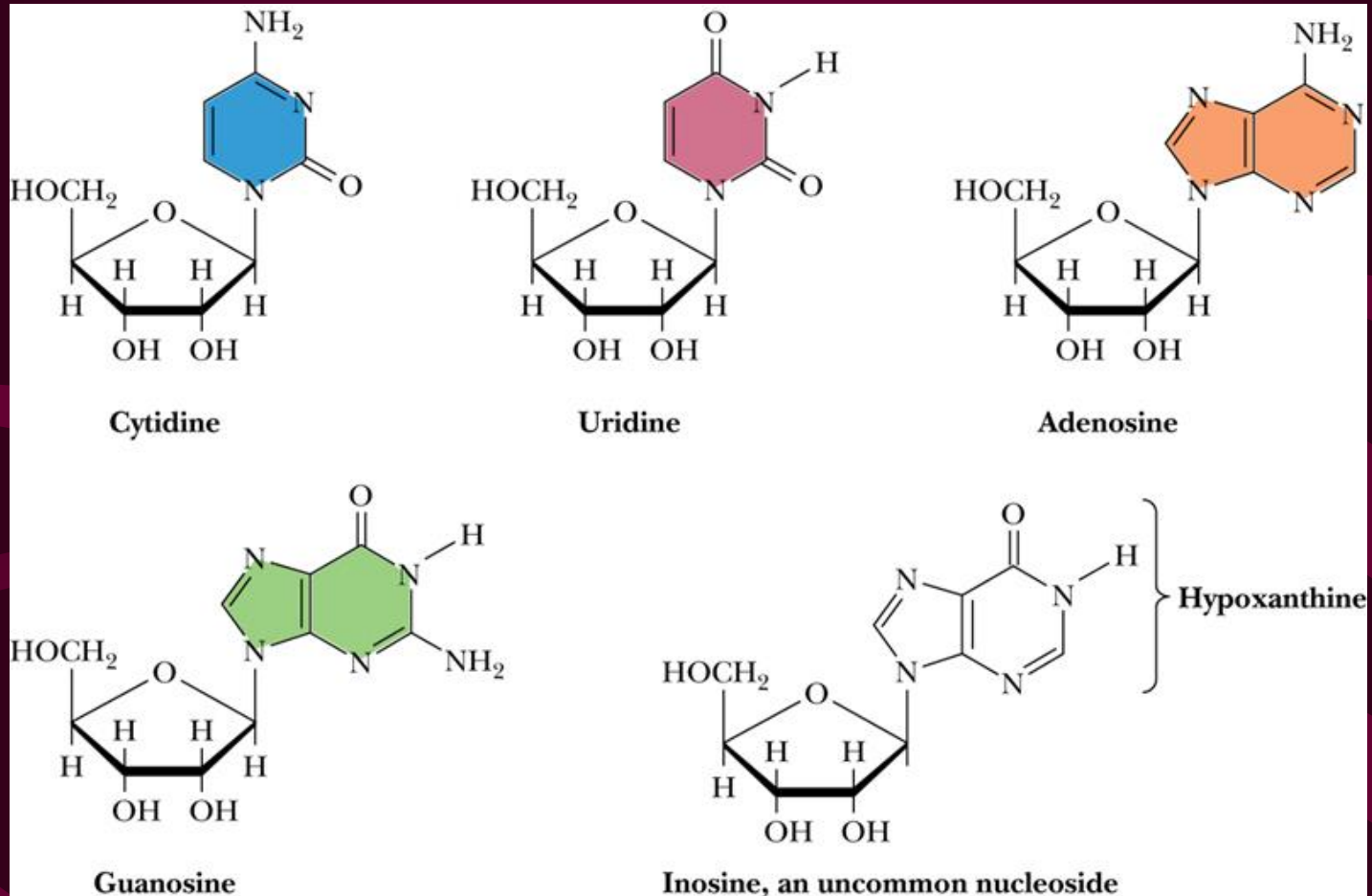
β -N₉-glycosidic
bond in purine
ribonucleosides

Syn and *anti* conformations of nucleosides



The *anti* conformations predominate in nucleic acids, the polymers of nucleotides.

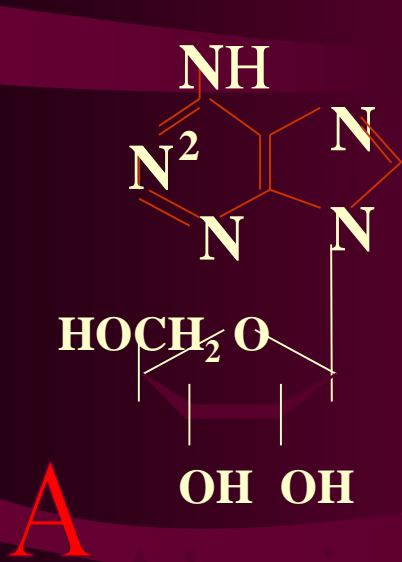
Nucleosides are more water soluble than free bases



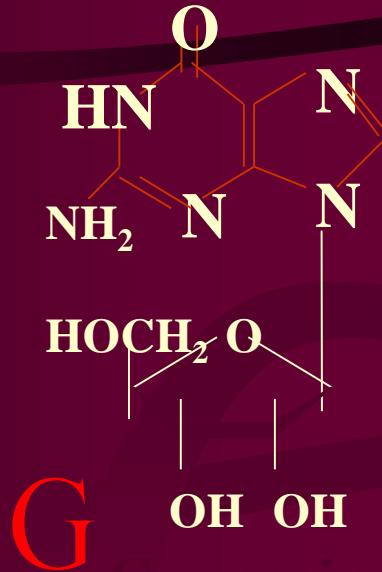
Both kinds of nucleosides are stable in alkali

Pyrimidine nucleosides are resistant to acid hydrolysis (but purine-

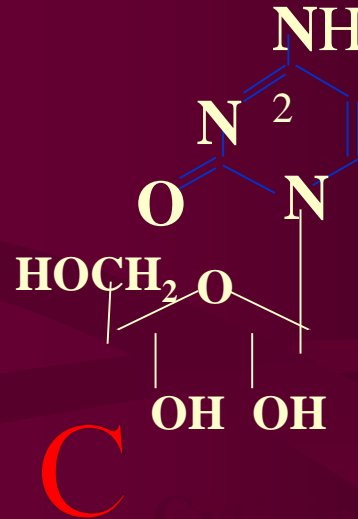
RNA



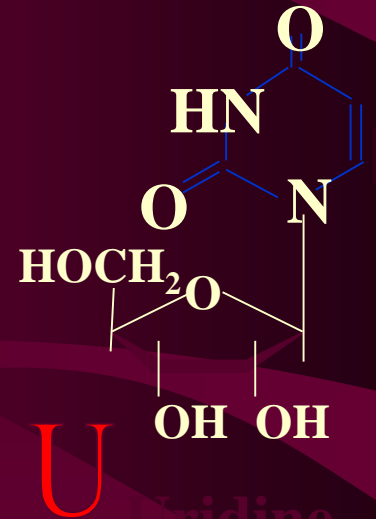
Adenosine



Guanosine

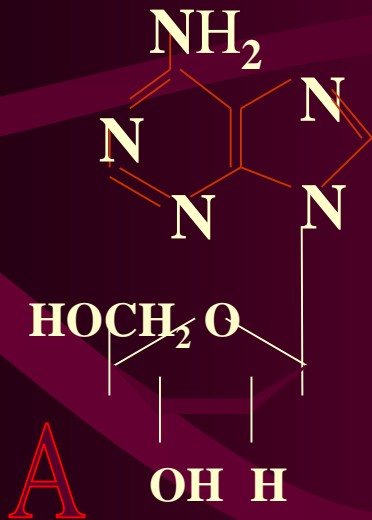


Cytosine

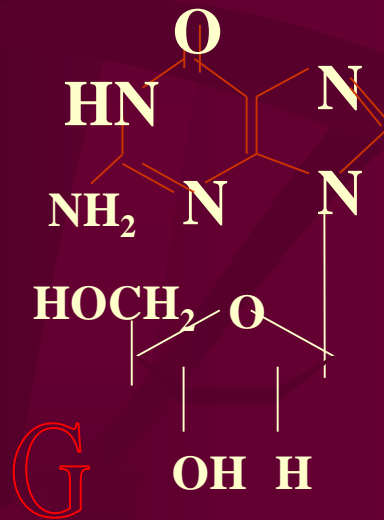


Uridine

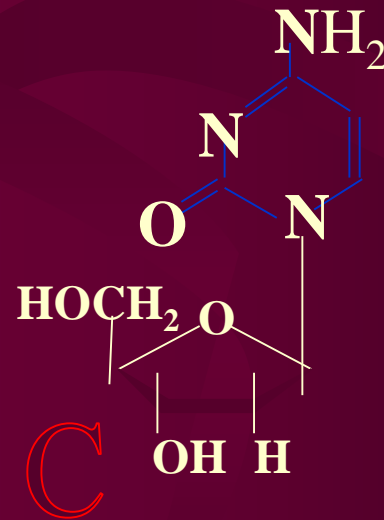
DNA



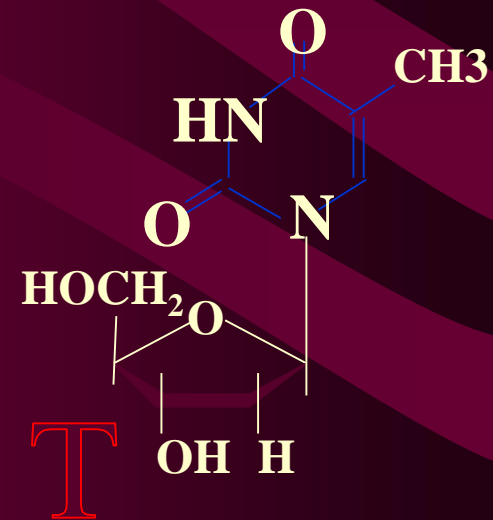
Deoxyadenosine



Deoxyguanosine



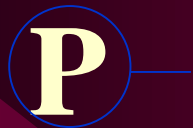
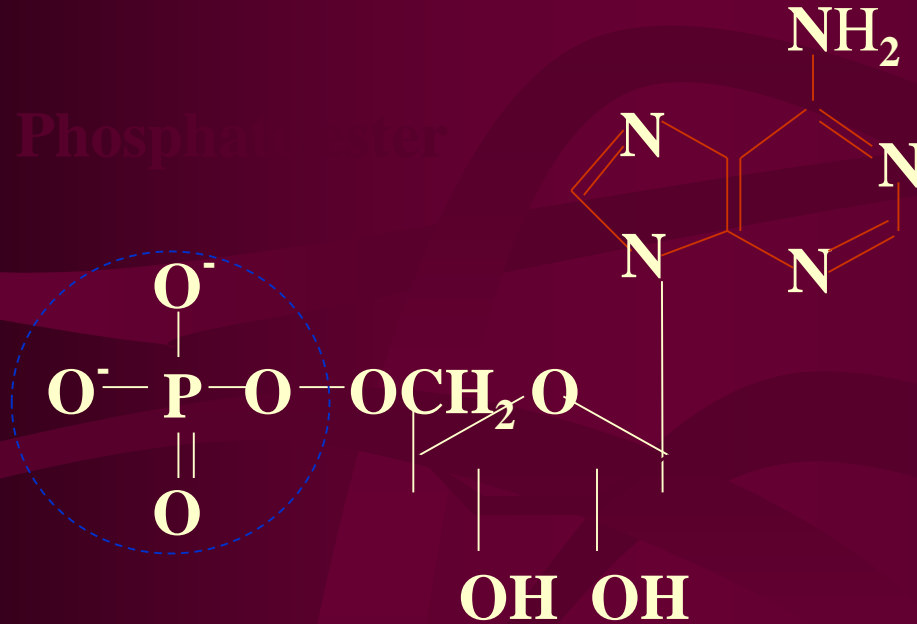
Deoxycytosine



Deoxythymine

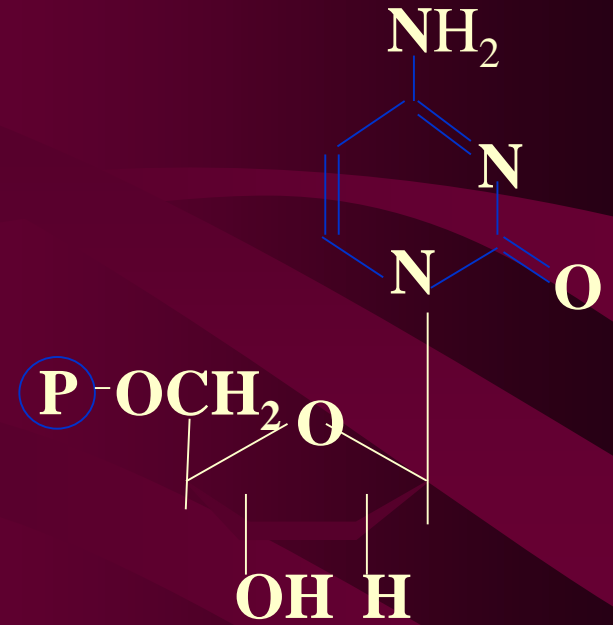
Nucleotides (phosphated nucleosides)

Phosphate ester



Adenosine monophosphate
AMP

Phosphoryl group

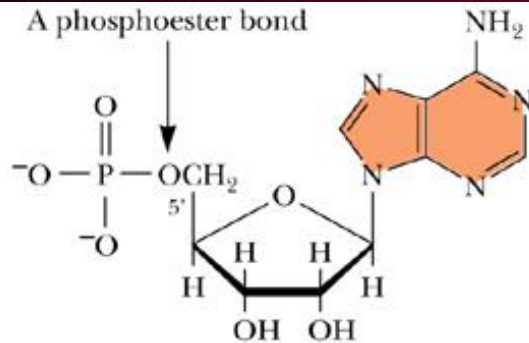


deoxycytidine
monophosphate

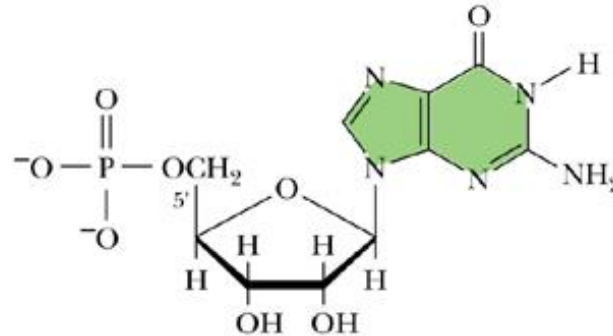
dCMP

Structures of common ribonucleotides

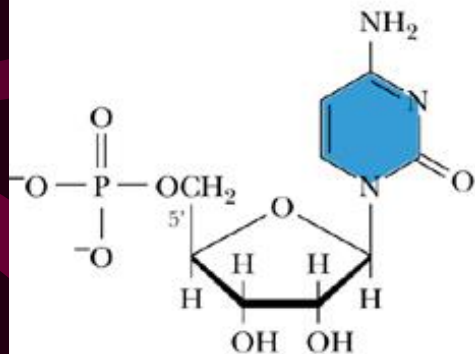
— AMP, GMP, CMP, and UMP



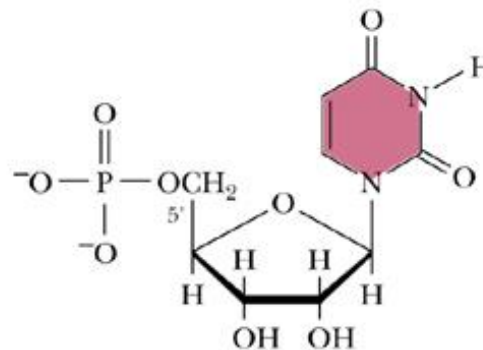
Adenosine 5'-monophosphate
(or AMP or adenylic acid)



Guanosine 5'-monophosphate
(or GMP or guanylic acid)



Cytidine 5'-monophosphate
(or CMP or cytidylic acid)

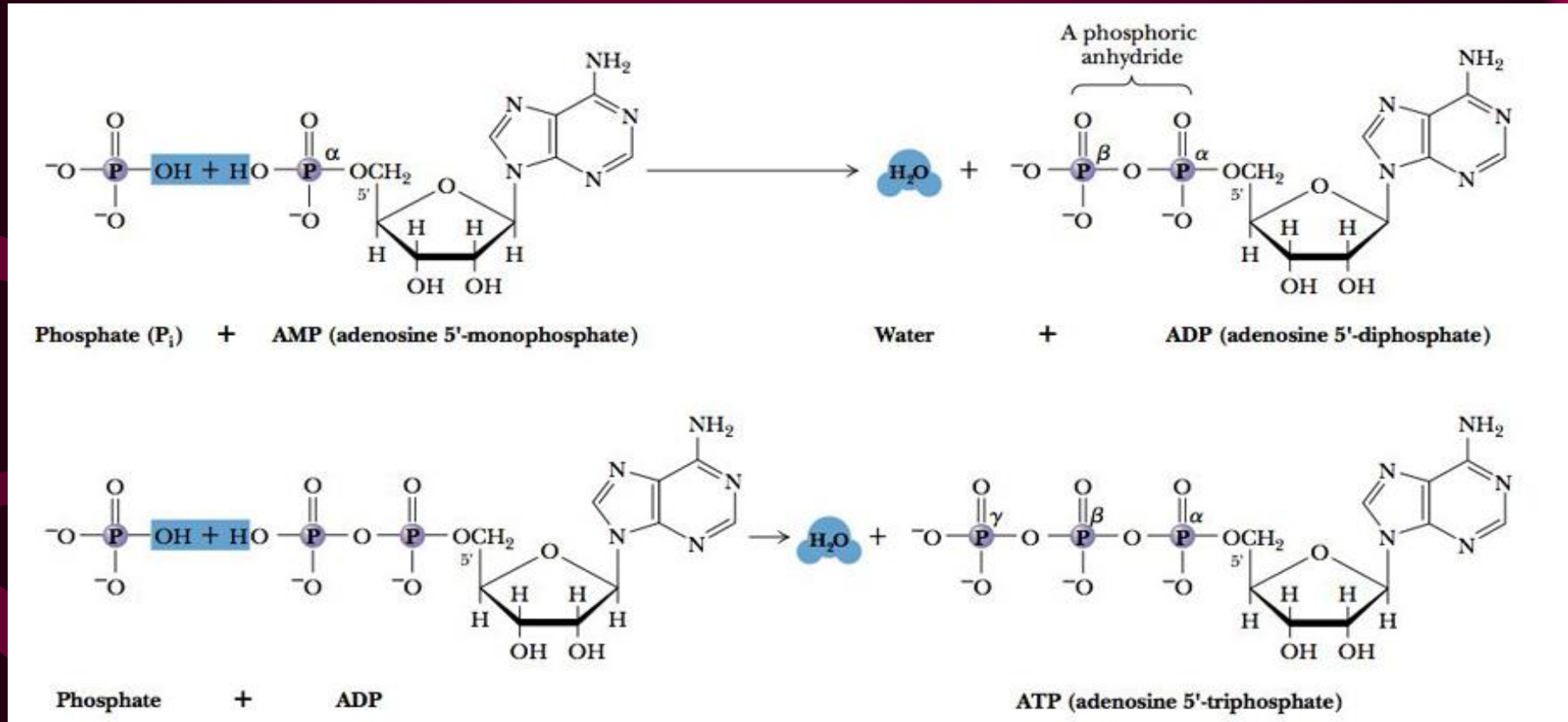


Uridine 5'-monophosphate
(or UMP or uridylic acid)



A nucleoside 3'-monophosphate
3'-AMP

Nucleoside diphosphates and triphosphates are nucleotides with two or three phosphate groups

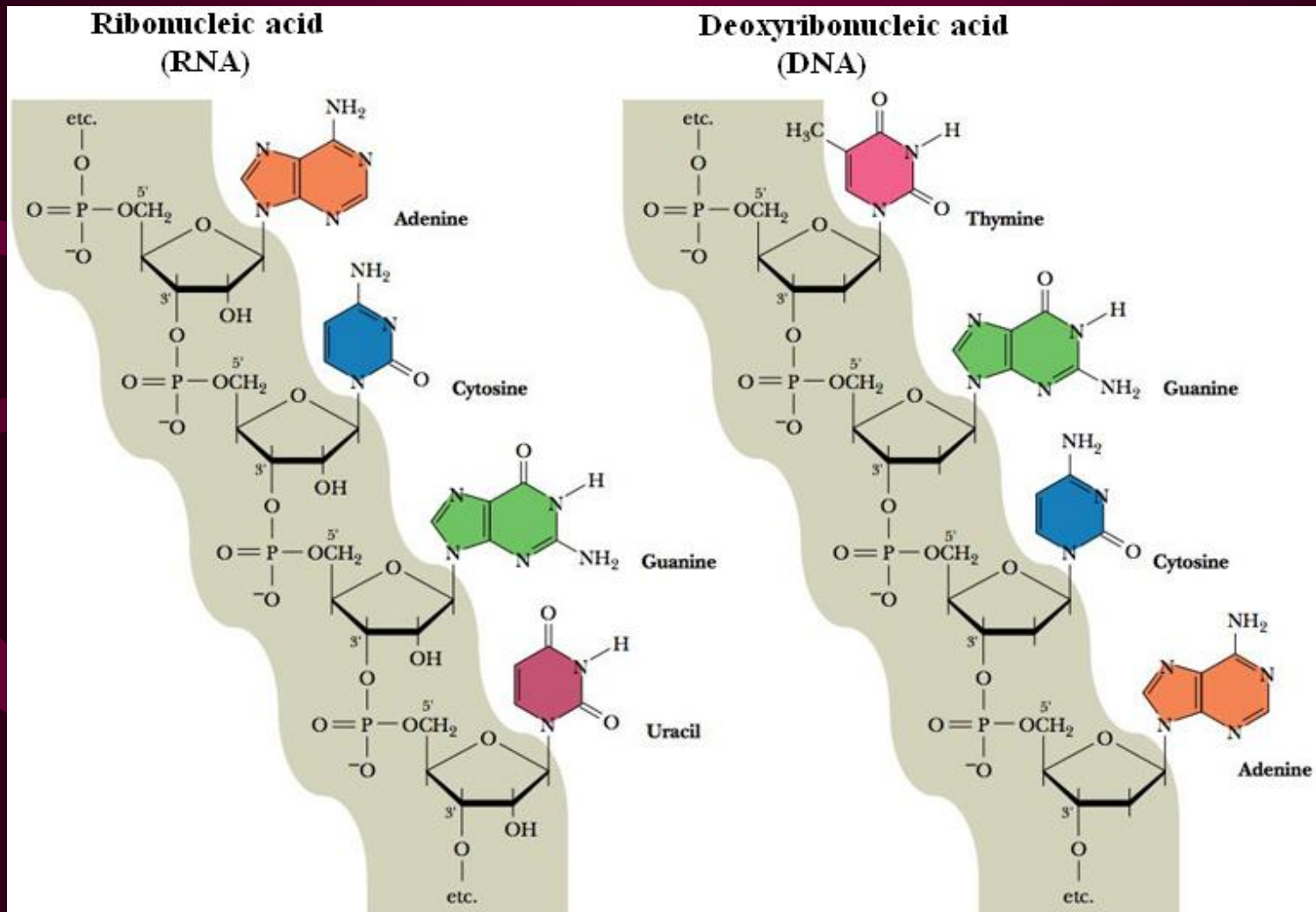


Nucleoside 5'-diphosphates/triphosphates (NDPs/NTPs):
strong polyprotic acids

Form stable complexes with divalent cations: Mg^{2+} , Ca^{2+}

What are the structures and functions of the NA?

- Nucleic acids are polynucleotides: linear polymers of nucleotides linked by 3',5'-phosphodiester bridge



The base sequence of a nucleic acid is its distinctive characteristic

Pi-

Sugar-phosphate
backbone

Two termini of
Polynucleotides:

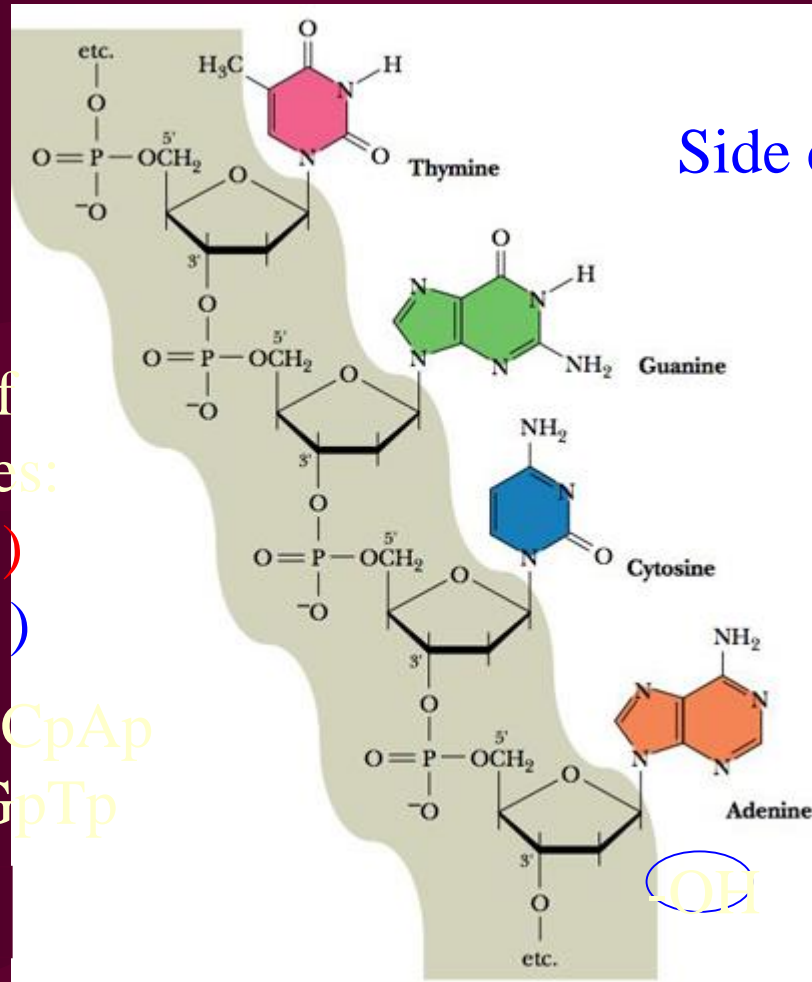
5'-Pi (5'-)

3'-OH (3'-)

5'-end: pTpGpCpAp

3'-end: ApCpGpTp

5'-TGCA.....



Side chains: bases

DNA: A, G, C, T

RNA: A, G, C, U

Direction of the
polynucleotide
chain

From 5'- to 3'-

The different classes of a nucleic acid: DNA and RNA

What is the different between structures of DNA and RNA?

DNA:

quite large

- only a single molecular (chromosome DNA) in simple life
Escherichia coli: 2.9×10^9 D (> million nucleotides)
- Many chromosomes in eukaryotic cells, in two copies principally; also occurs in mitochondria and in chloroplasts.

RNA:

small

- Occurs in multiple copies and various forms in cells
- As biological functions, they are categorized into 3 major types: messenger RNA, transfer RNA, ribosomal RNA (in all lives), and another kind, small nuclear RNA (only in eukaryotic cells).

mRNA, tRNA, rRNA and snRNA (see table 10.2--p.319)

The fundamental structure of DNA is a double helix

Chargaff's rules: in late 1940s, Amounts of the four bases: (p.320)

- Vary from species to species
- $A = T$; $G = C$ (in each
- Purine ($A+G$) = pyrimidine ($T+C$)

X-ray diffraction studies (R
Franklin and M Wilkins):
Helix with two different loops
in outside

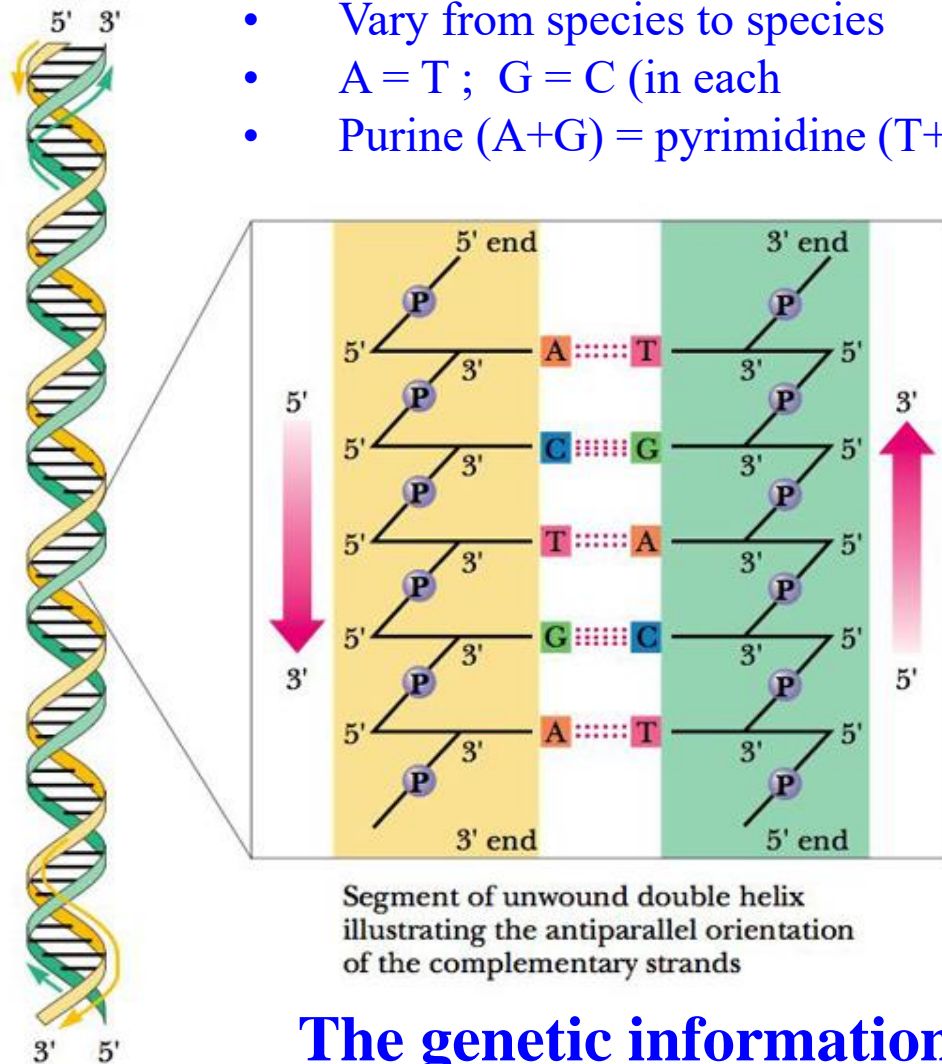
James Watson and Francis
Crick at Cambridge University in
1953:

*DNA was a complementary
double helix;*

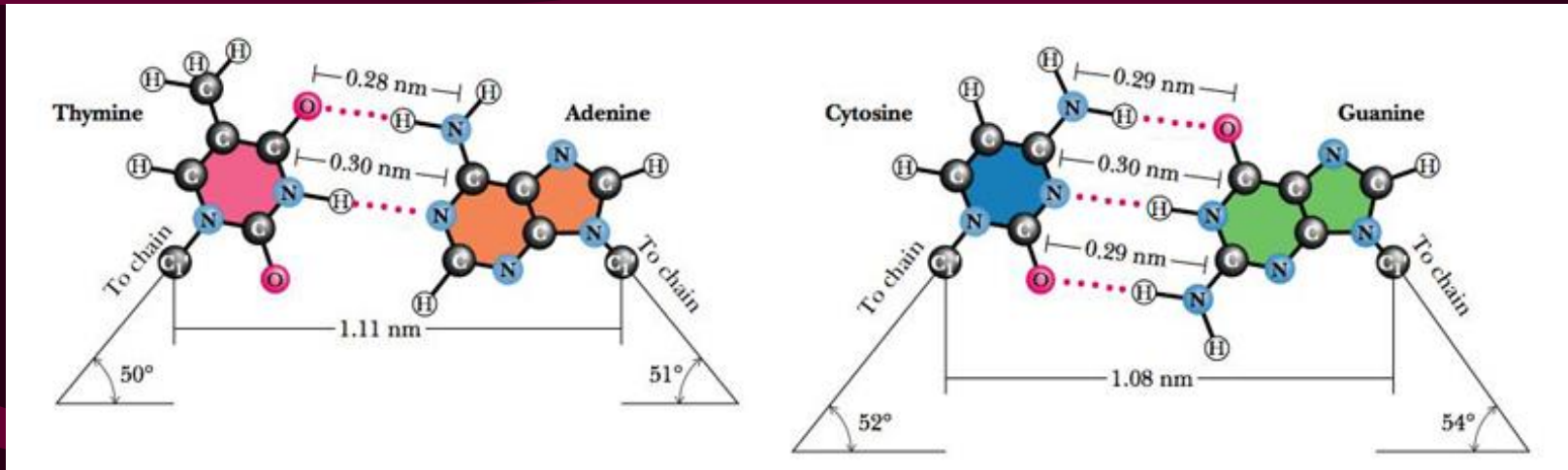
*Two strands of DNA are
held together by the*

bonding interactions
Size of DNA: ~bp; ~kb
between unique base pairs.

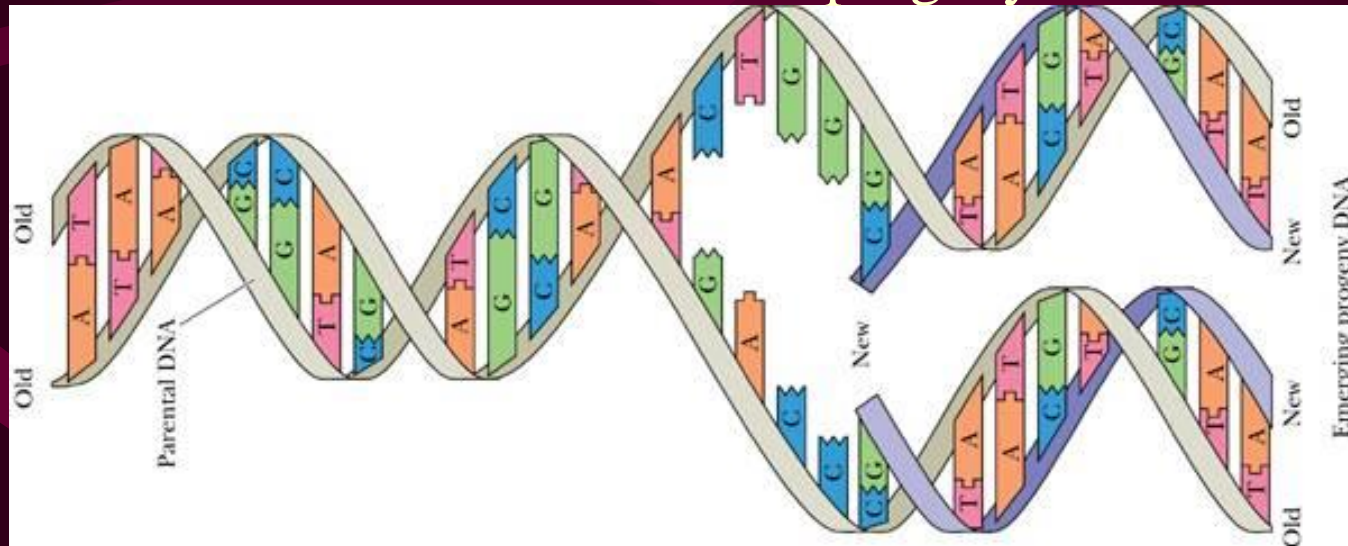
The genetic information in DNA is encoded in digital fo



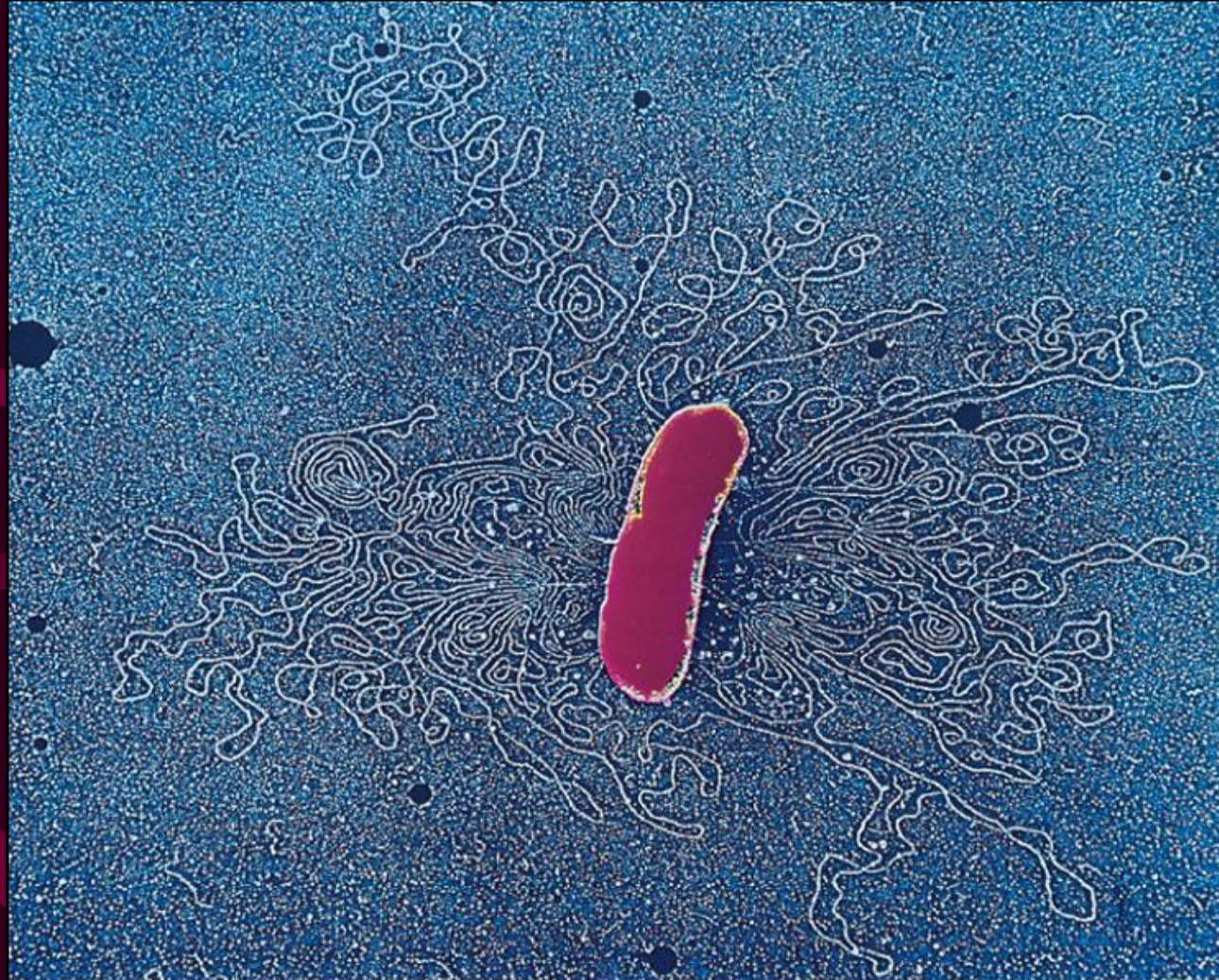
Base pairing: interaction between bases—H bonds



Replication of DNA: two identical progeny molecules by base pairing



DNA is in the form of enormously long, threadlike molecules



E. coli are
partially
digested
and diluted
with water

DNA in cells occurs in the form of chromosomes

Prokaryotic cell:

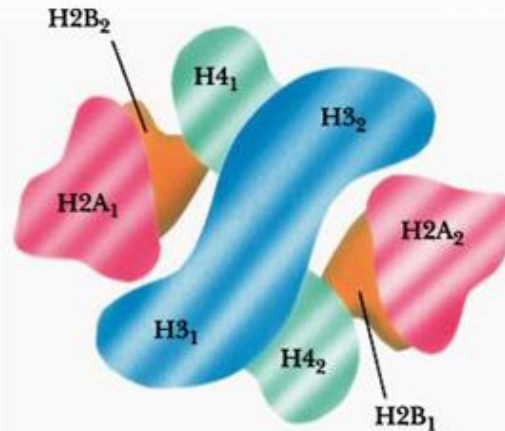
circular form, bind proteins, chromosomes are no ordered structure

Eukaryotic cell:

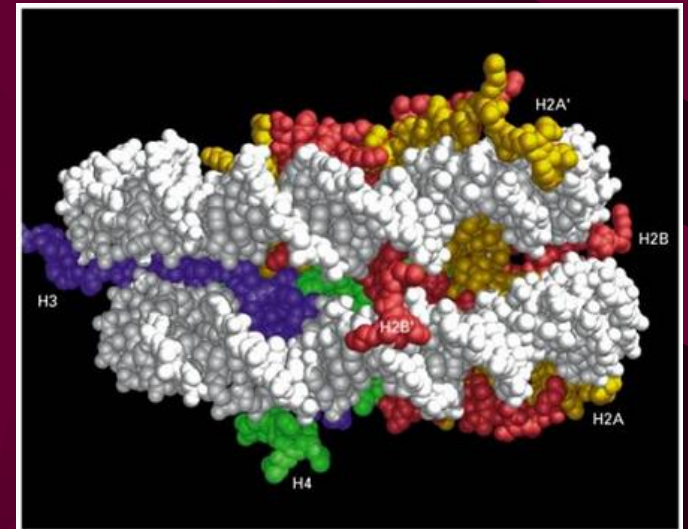
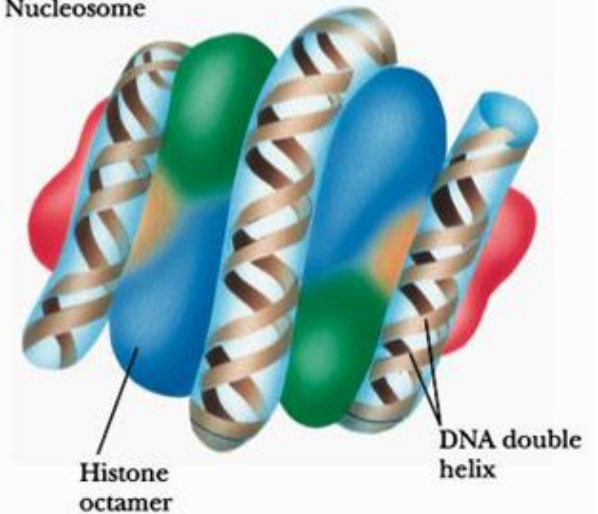
Basic unit--nucleosome

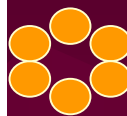
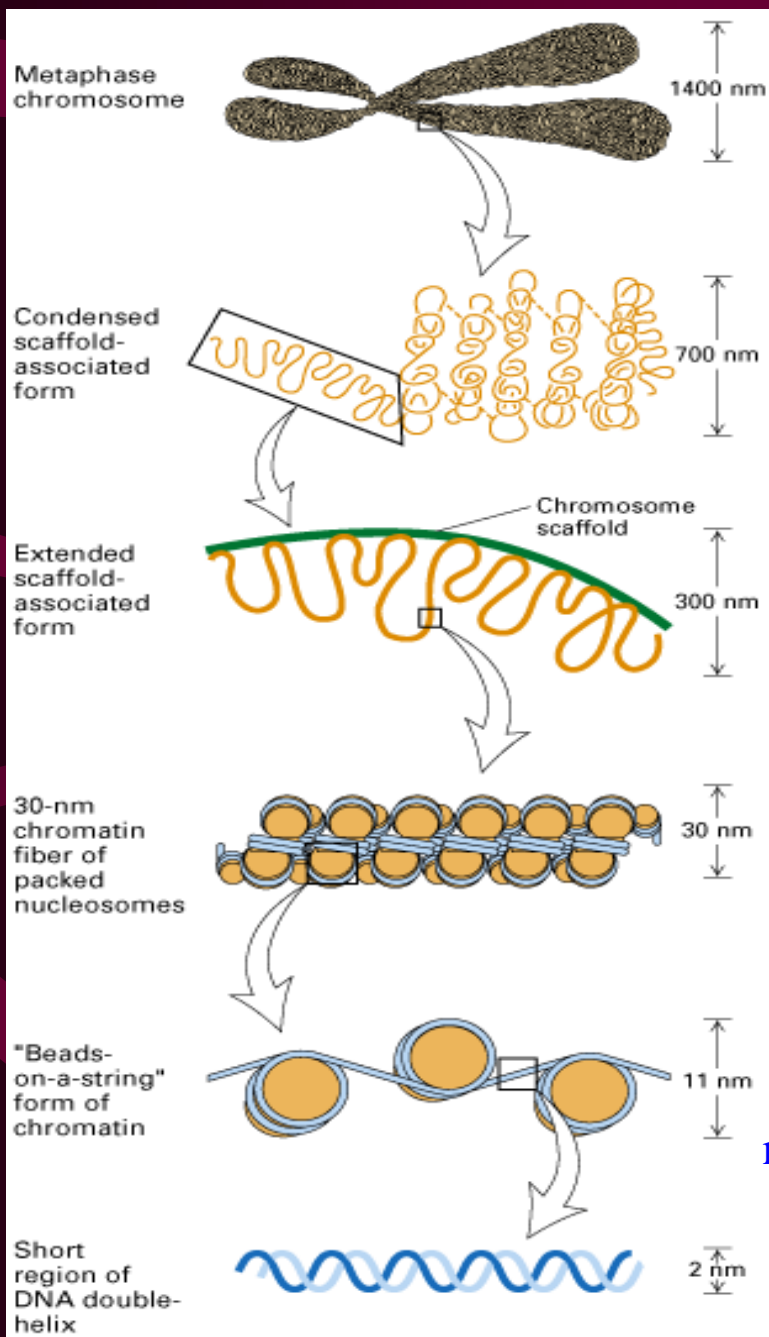
Histones,
a class of Arg- and Lys-rich basic protein,
interact ionically with the anionic phosphate groups of DNA backbone

Histone "core" octamer
(here shown in cross section)

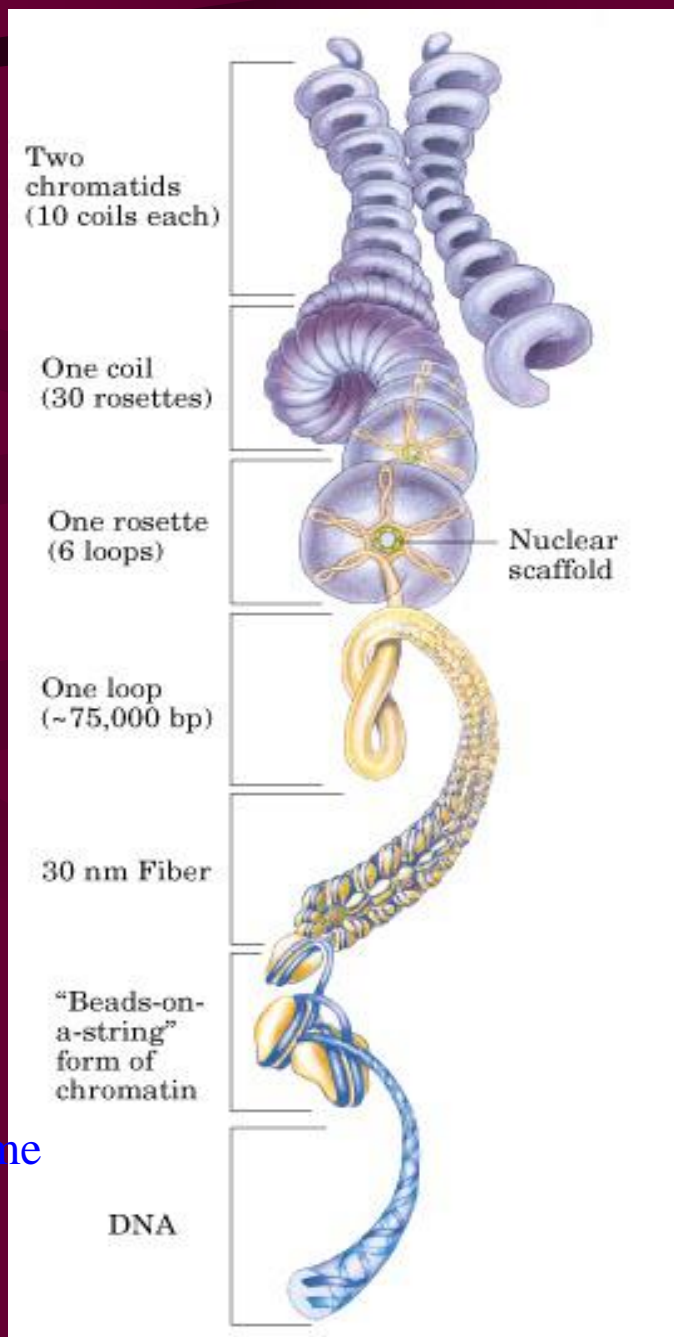


Nucleosome





nucleosome



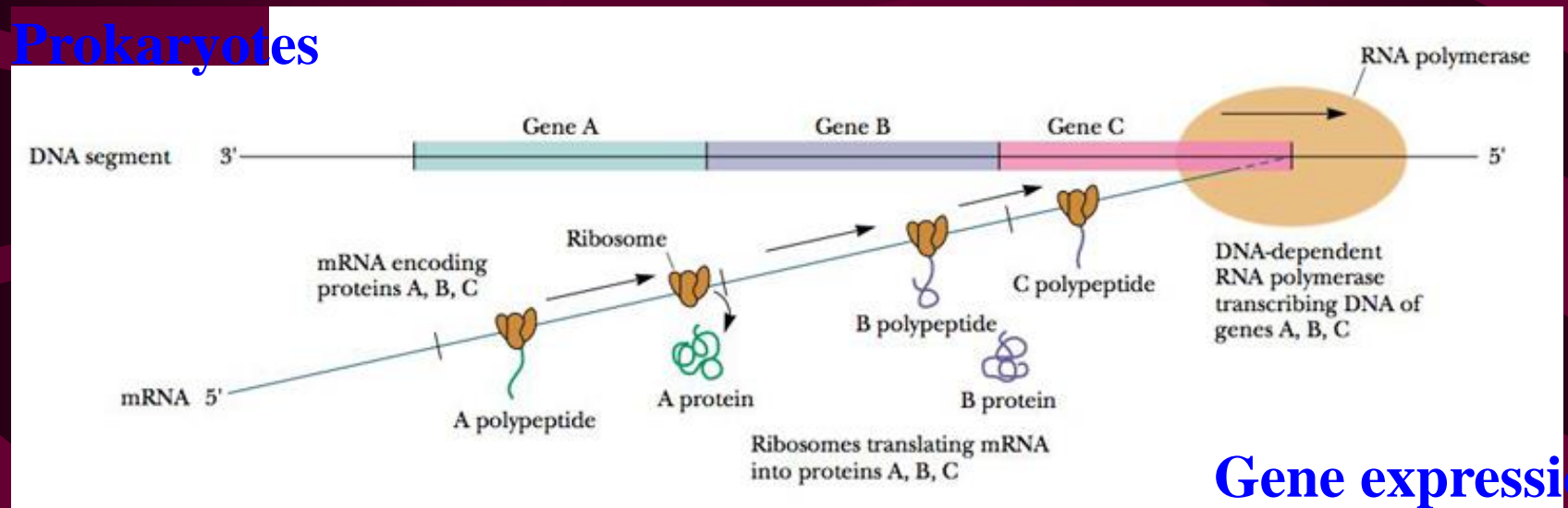
Various forms of RNA serve different roles in cells

mRNA, tRNA, rRNA, and small RNA

1. **Messenger RNA carries the sequence information for synthesis of a protein**

Transcription : synthesis RNA from DNA by RNA polymerase

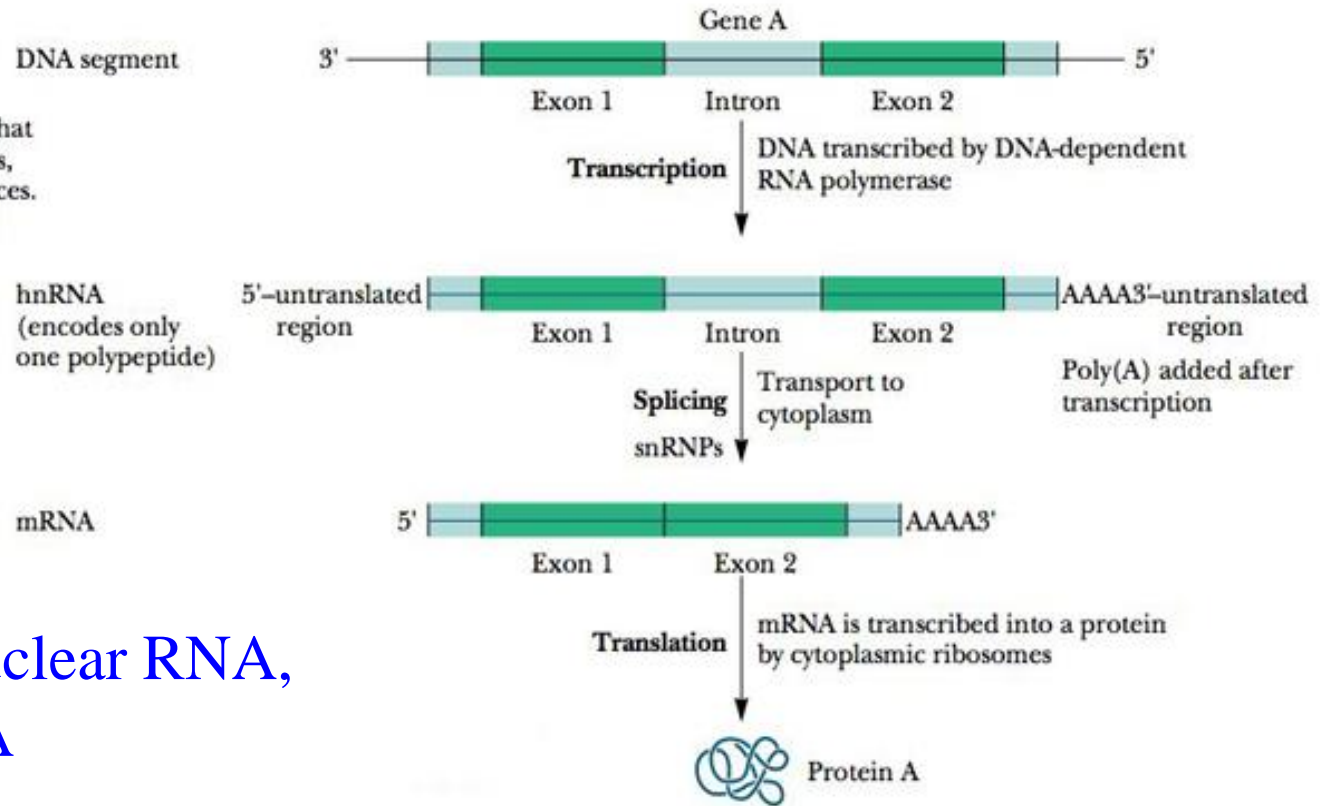
Prokaryotes



Translation : synthesis protein from RNA by ribosome

Eukaryotes

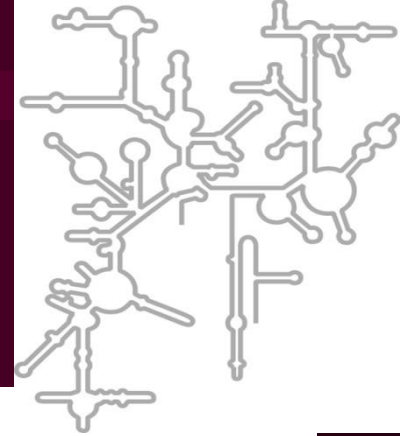
Exons are protein-coding regions that must be joined by removing introns, the noncoding intervening sequences. The process of intron removal and exon joining is called splicing.






Heterogeneous nuclear RNA,
hnRNA

Gene expression




2. Ribosomal RNA provides the structural and functional foundation for ribosomes



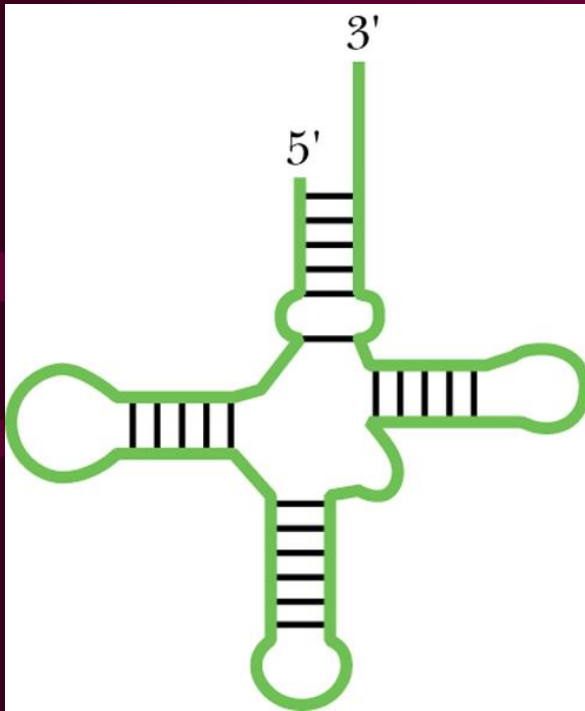
PROKARYOTIC RIBOSOMES (*E. coli*)

Ribosome (2.52×10^6 D)	
	
Subunits	
	
(0.93×10^6 D)	(1.59×10^6 D)
RNA	
16S RNA (1542 nucleotides)	23S RNA (2904 nucleotides) 5S RNA (120 nucleotides)
Protein	
21 proteins	31 proteins

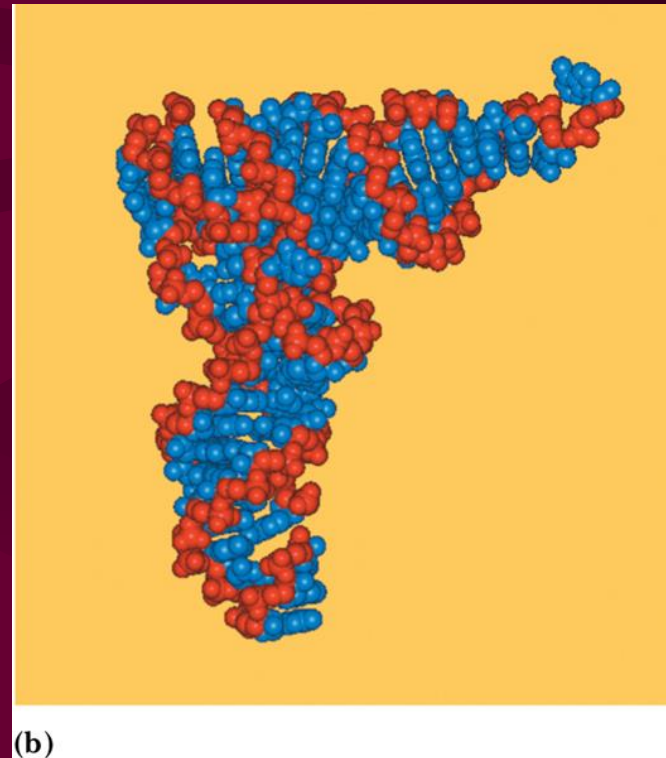
EUKARYOTIC RIBOSOMES (Rat)

Ribosome (4.22×10^6 D)	
	
Subunits	
	
(1.4×10^6 D)	(2.82×10^6 D)
RNA	
18S RNA (1874 nucleotides)	28S + 5.8S RNA (4718 + 160 nucleotides) 5S RNA (120 nucleotides)
Protein	
33 proteins	49 proteins

3. Transfer RNAs carry amino acids to ribosomes for use in protein synthesis



73~94 residues (bases)



4. Small nuclear RNAs mediate the splicing of Eukaryotic gene transcripts (hnRNA) into mRNA

Contain 100~200 nucleotides, found in stable complexes with specific proteins forming small nuclear ribonucleoprotein particles, or **snRNPs**, are important in the processing of hnRNA.

5. Small RNAs serve a number of roles, including post-transcriptional gene silencing

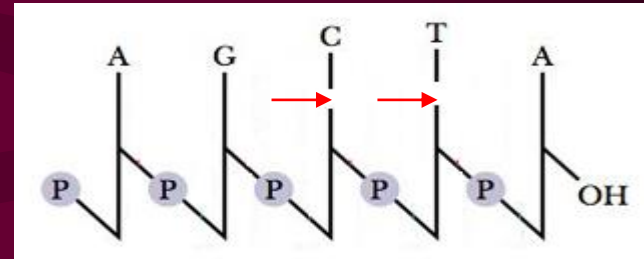
Only 21~28 nucleotides, can target DNA or RNA through complementary base pairing—direct readout.

Small interfering RNA (siRNA): disrupt gene expression by binding mRNA complementally to form double-stranded RNA, which is easily degraded and eliminating the mRNA.

Are nucleic acids susceptible to hydrolysis?

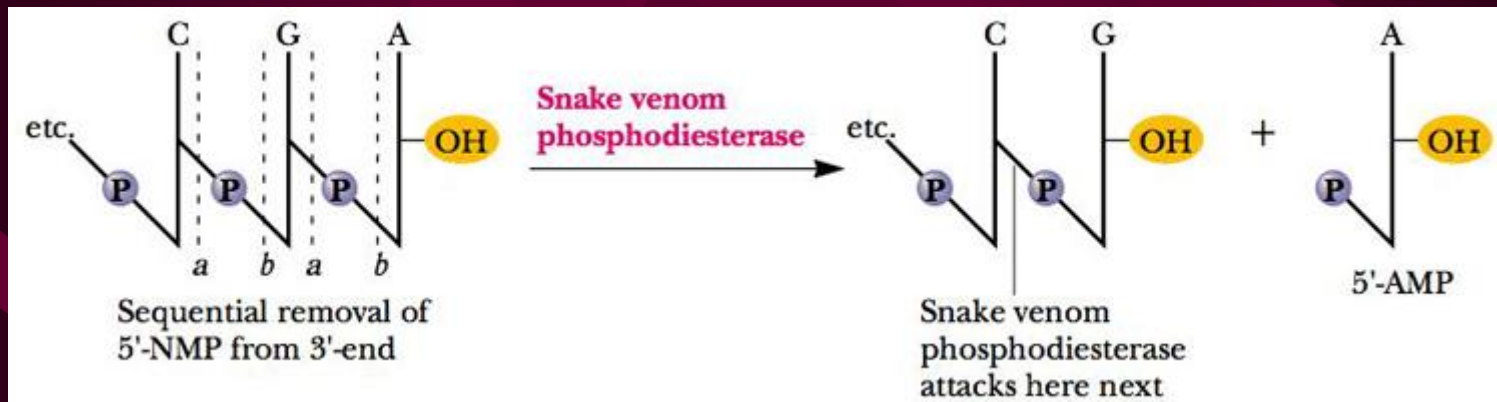
- RNA is susceptible to hydrolysis by base, but DNA is susceptible to hydrolysis by acid

DNA: HCl—hydrolyzing purine
glycosidic bond (apurinic acid)



RNA: NaOH—randomly hydrolyzing glycosidic bond

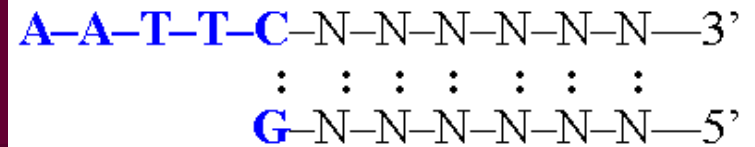
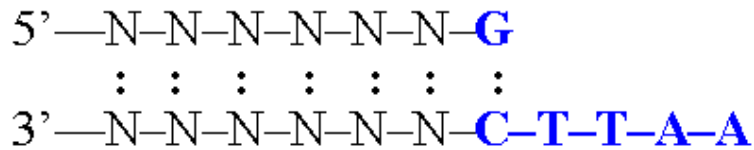
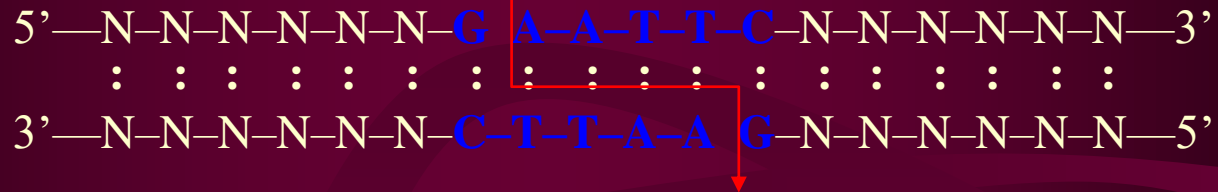
- The enzymes that hydrolyze nucleic acids are phosphodiesterases



- Nucleases differ in their specificity for different forms of nucleic acid
 - DNase, RNase only act on DNA or RNA respectively
- Restriction enzymes are nucleases that cleave double-stranded DNA molecules
 - There are types I, II and III restriction endonucleases
 - Type I and III require ATP to hydrolyze DNA, Type I cleave DNA randomly, Type III cut DNA in specific sequence.
 - **Type II restriction enzymes:** no need ATP, specific recognition sequences are typically 4 or 6 nucleotides in length and have a twofold axis of symmetry

Type II restriction endonuclease

EcoRI



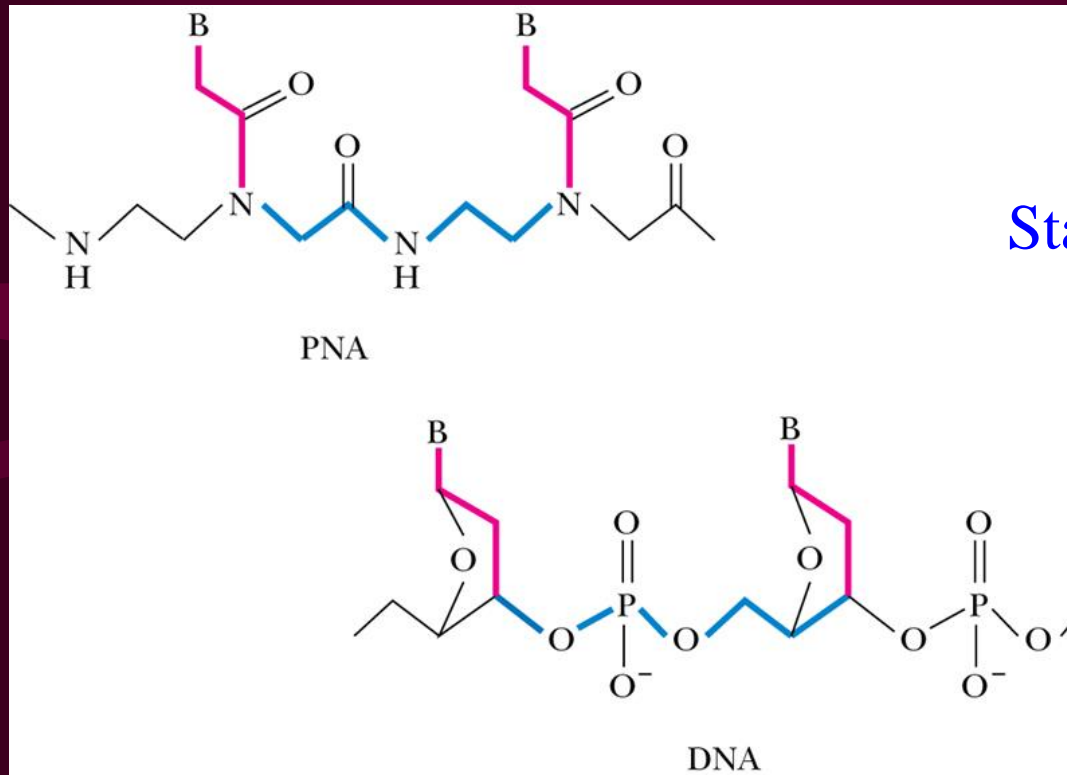
“sticky” ends—cohesive ends

Restriction endonucleases can be used to map the structure of a DNA

Specificity of restriction endonuclease see Tab 10.5 (p 333)

Peptide nucleic acids (PNAs) are synthetic mimics of DNA and RNA

The sugar phosphate backbone is replaced by a peptide backbone



Stable probe

PNAs are resistant to nucleases and also are poor substrates for protease

Key points:

- Structures of purine and pyrimidine bases, nucleosides and nucleotides.
- Structure of polynucleotide strand.
- Difference between DNA and RNA (structure and function).