Nucleic Acids

DNA & RNA

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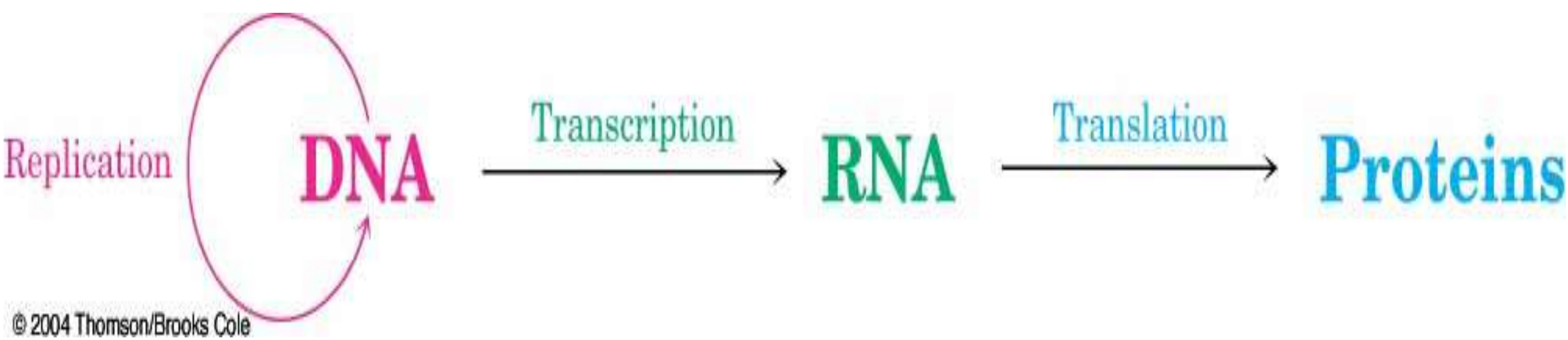
Nucleic Acids and Heredity

- Processes in the transfer of genetic information:
- Replication: identical copies of DNA are made
- Transcription: genetic messages are read and carried out of the cell nucleus to the ribosomes, where protein synthesis occurs.
- Translation: genetic messages are decoded to make proteins.



Two types of Nucleotides
(depending on the sugar they contain)

1- Ribonucleic acids (RNA)
The pentose sugar is Ribose (has a hydroxyl group in the 3rd carbon---OH)

2-
The pentose sugar is (has just an hydrogen in the same place---eoxy = "minus oxygen"

Definitions

Nucleic acids are polymers of nucleotides

- **Nucleotides are carbon ring structures containing nitrogen linked to a 5-carbon sugar (a ribose)**
- **5-carbon sugar is either a ribose or a deoxy-ribose making the nucleotide either a ribonucleotide or a deoxyribonucleotide**

In eukaryotic cells nucleic acids are either:

- **Deoxyribose nucleic acids (DNA)**
- **Ribose nucleic acids (RNA)**
  - **Messenger RNA (mRNA)**
  - **Transfer RNA (tRNA)**
  - **Ribosomal RNA (tRNA)**

Nucleic Acid Function

DNA

Genetic material - sequence of nucleotides encodes different amino acids

RNA

Involved in the transcription/translation of genetic material (DNA)

Genetic material of some viruses

Nucleotide Structure

Despite the complexity and diversity of life the structure of DNA is dependent on only 4 different nucleotides

Diversity is dependent on the nucleotide sequence

All nucleotides are 2 ring structures composed of:

5-carbon sugar :	β-D-ribose (RNA) β-D-deoxyribose (DNA)
Base	**Purine** **Pyrimidine**
Phosphate group	A nucleotide **WITHOUT** a phosphate group is a **<u>NUCLEOSIDE</u>**

NUCLEIC ACIDS (DNA and RNA) Notes

DNA – **Deoxyribonucleic Acid**

- DNA controls all living processes including production of new cells – **cell division**
- DNA carries the genetic code – **stores** and **transmits** genetic information from one **generation** to the next
  - Chromosomes are made of **DNA**
- DNA is located in the **nucleus** of the cell

What are they made of ?

- Simple units called nucleotides, connected in long chains
- Nucleotides have 3 parts:

  1- 5-Carbon sugar (pentose)

  2- Nitrogen containing base

  (made of C, H and N)

  3- A phosphate group (P)
- The P groups make the links that unite the sugars (hence a "sugar-phosphate backbone"

TABLE 8–1 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

Note: "Nucleoside" and "nucleotide" are generic terms that include both ribo- and deoxyribo- forms. Also, ribonucleosides and ribonucleotides are here designated simply as nucleosides and nucleotides (e.g., riboadenosine as adenosine), and deoxyribonucleosides and deoxyribonucleotides as deoxynucleosides and deoxynucleotides (e.g., deoxyriboadenosine as deoxyadenosine). Both forms of naming are acceptable, but the shortened names are more commonly used. Thymine is an exception; "ribothymidine" is used to describe its unusual occurrence in RNA.

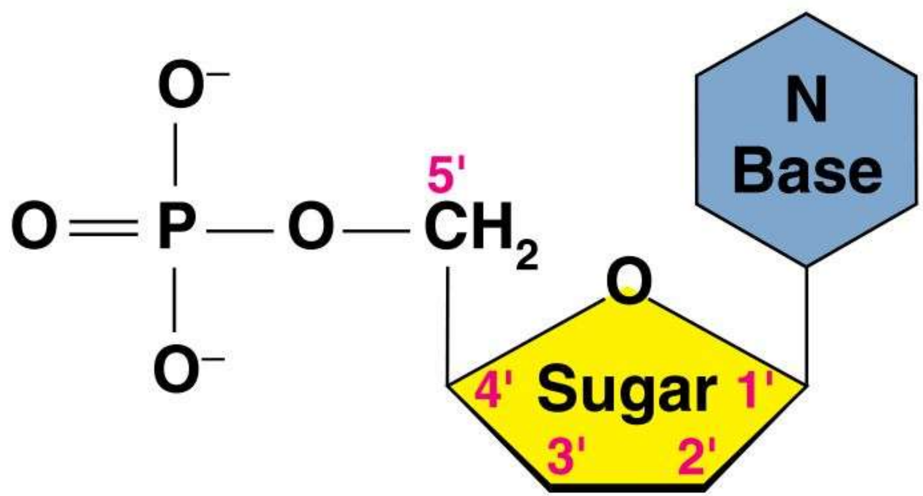
Table 8-1

Lehninger Principles of Biochemistry, Fifth Edition

Nucleic Acids

- **Nucleic acids** are molecules that store information for cellular growth and reproduction
- There are two types of nucleic acids:

  - **deoxyribonucleic acid (DNA)** and **ribonucleic acid (RNA)**
- These are polymers consisting of long chains of monomers called nucleotides
- A **nucleotide** consists of a nitrogenous base, a pentose sugar and a phosphate group:

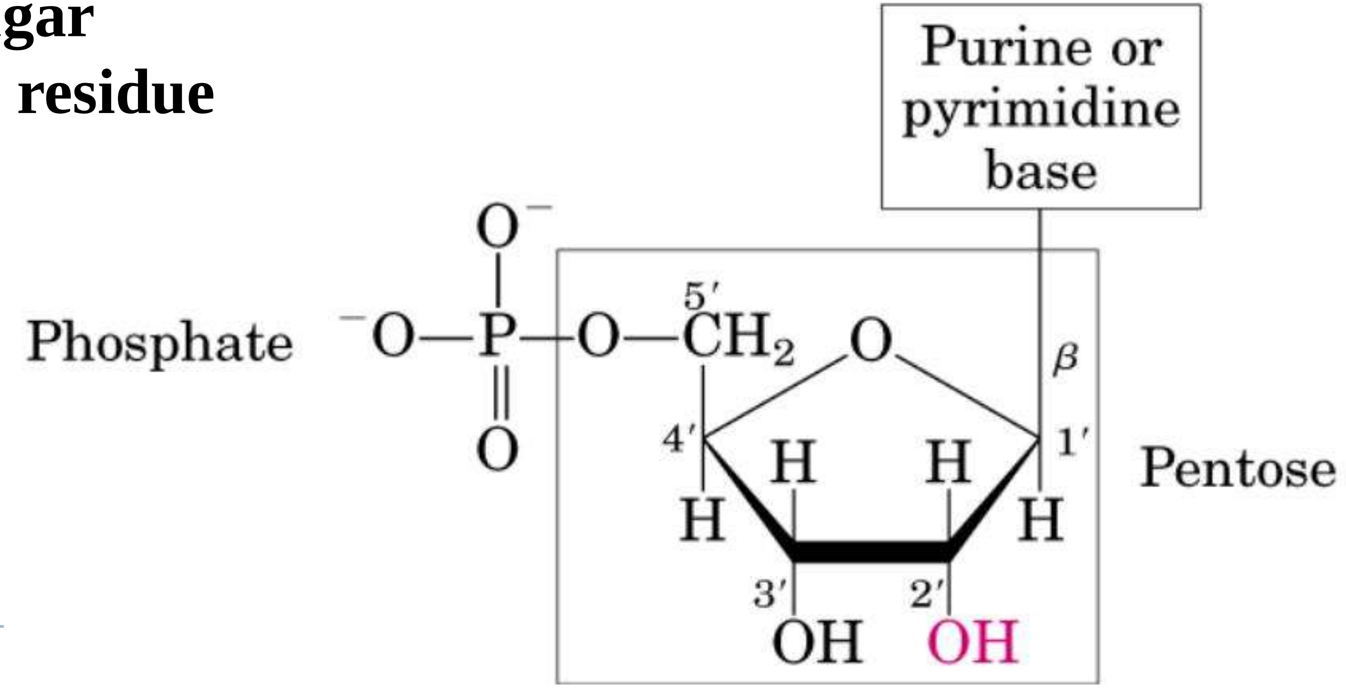


Nucleic Acids

DNA and RNA are nucleic acids, long, thread-like polymers made up of a linear array of monomers called nucleotides

All nucleotides contain three components:

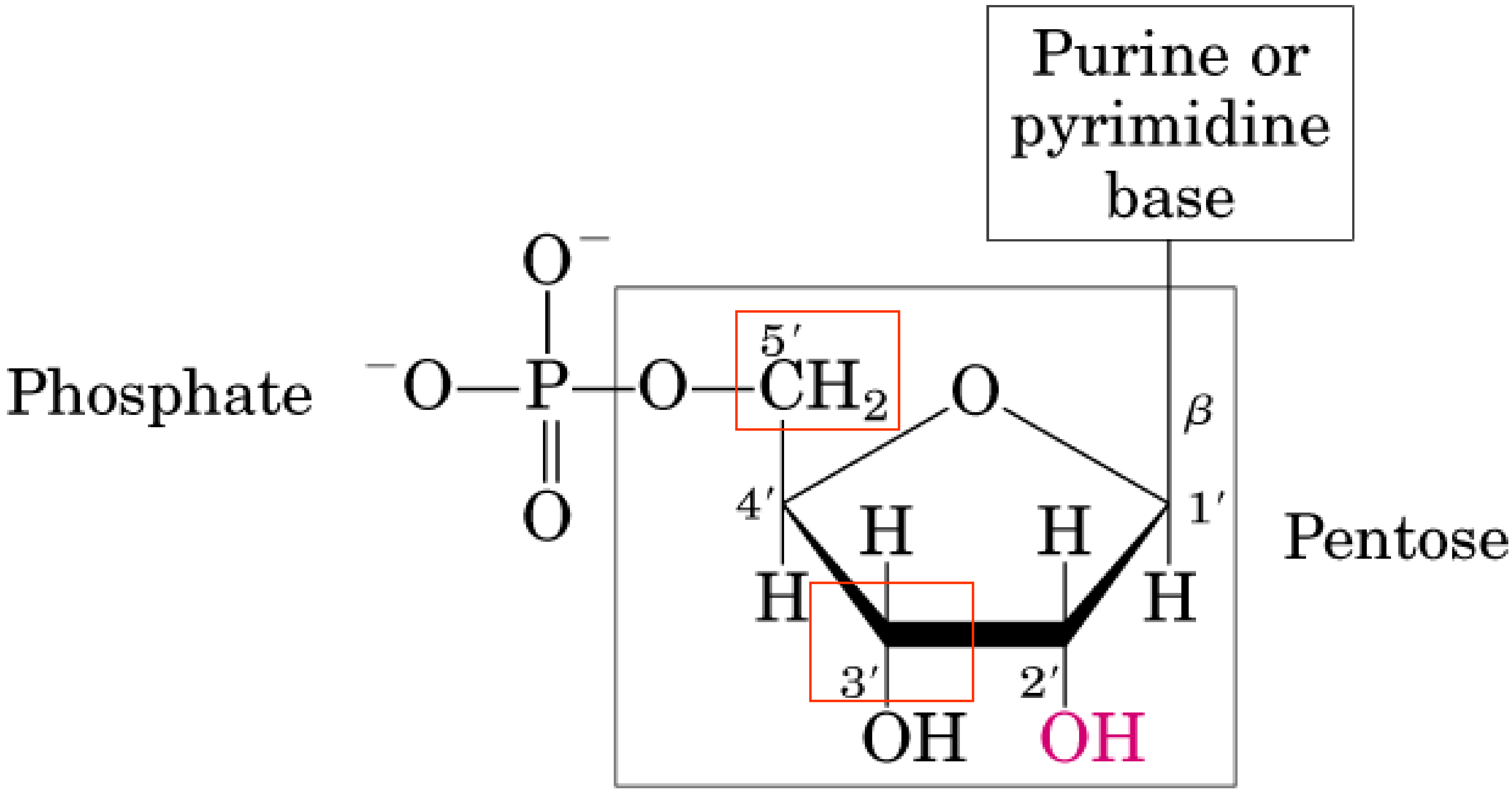
1. **A nitrogen heterocyclic base**
2. **A pentose sugar**
3. **A phosphate residue**



Chemical Structure of DNA vs RNA

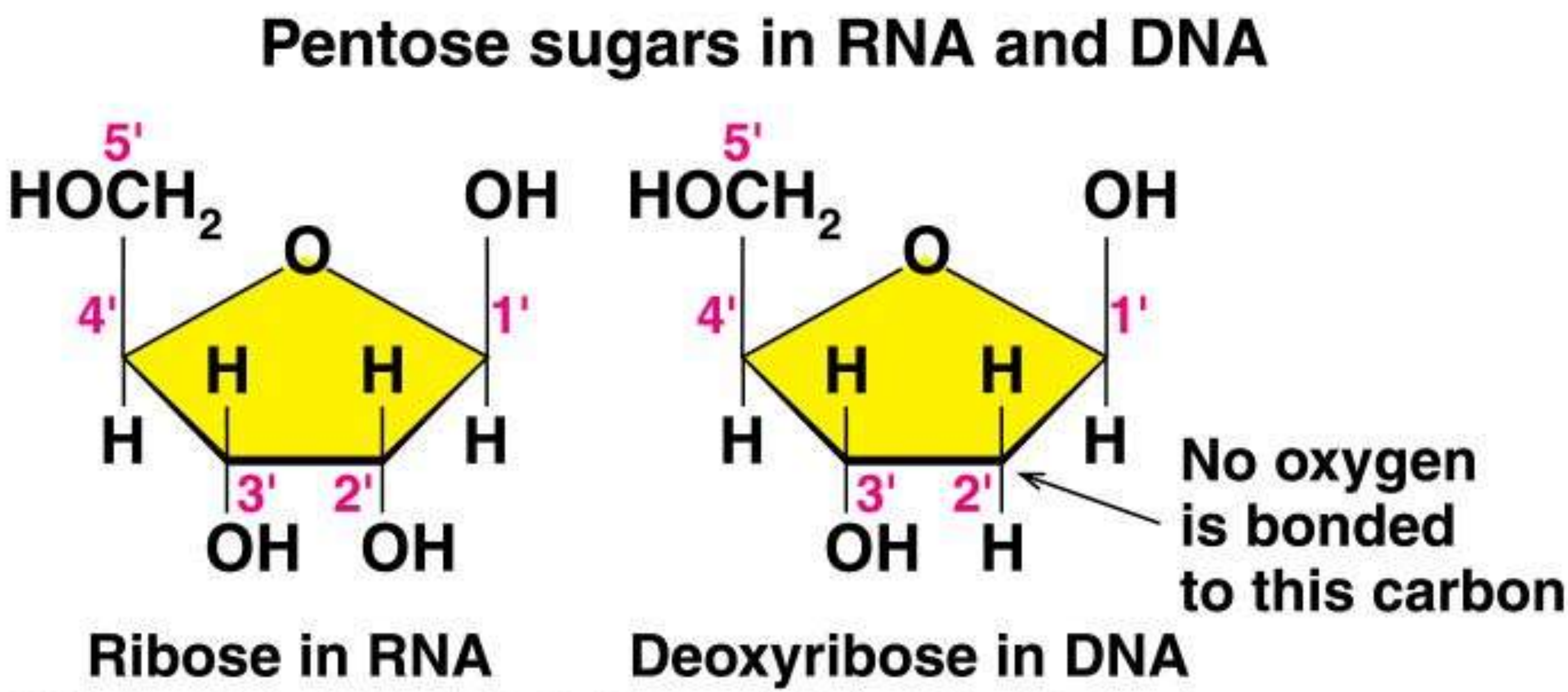
Ribonucleotides have a 2'-OH

Deoxyribonucleotides have a 2'-H



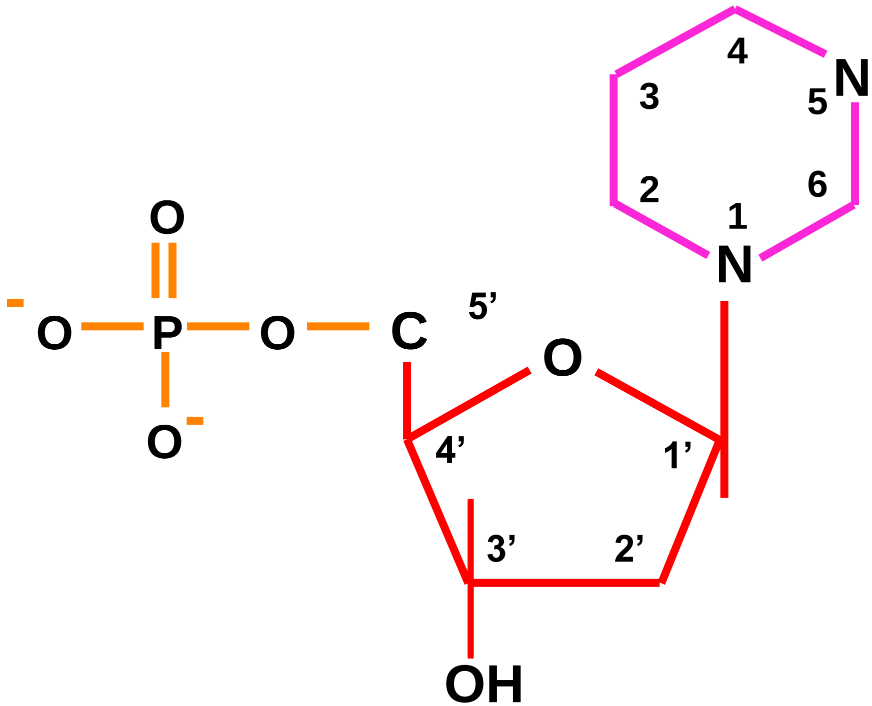
Pentose Sugars

- There are two related **pentose sugars**:
  - RNA contains **ribose**
  - DNA contains **deoxyribose**
- The sugars have their carbon atoms numbered with primes to distinguish them from the nitrogen bases



Nucleotide Structure - 4

Base-Sugar-PO_4^{2-}



Monophosphate

Nucleotide Function

Building blocks for DNA and RNA

Intracellular source of energy - Adenosine triphosphate (ATP)

Second messengers - Involved in intracellular signaling (e.g. cyclic adenosine monophosphate [cAMP])

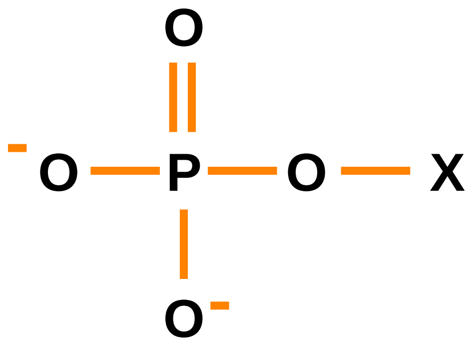
Intracellular signaling switches (e.g. G-proteins)

Nucleotide Structure - 4
Phosphate Groups

Phosphate groups are what makes a nucleoside a nucleotide

Phosphate groups are essential for nucleotide polymerization

Basic structure:

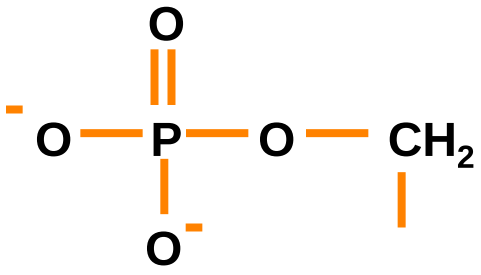


Nucleotide Structure - 4
Phosphate Groups

Number of phosphate groups determines nomenclature

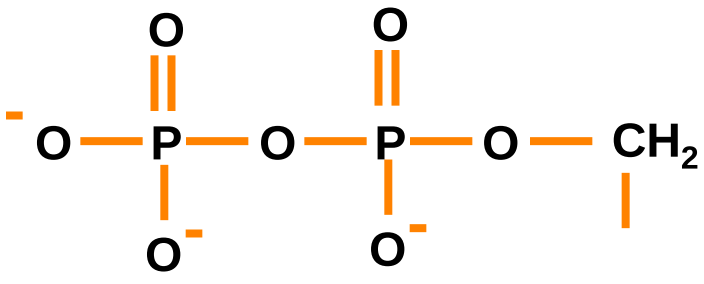
Monophosphate
e.g. AMP

Free = inorganic
phosphate (Pi)



Diphosphate
e.g. ADP

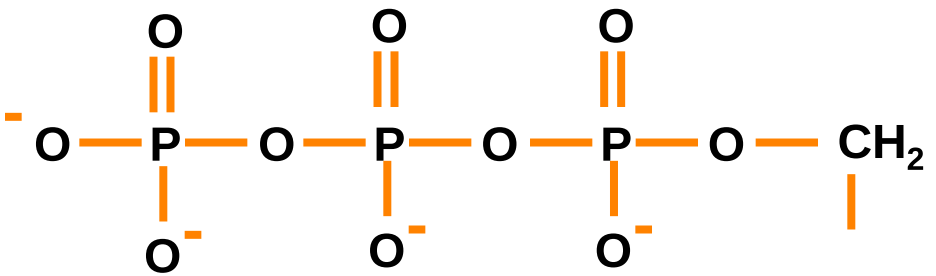
Free = Pyro-
phosphate (PPi)



Nucleotide Structure - 4
Phosphate Groups

Triphosphate
e.g. ATP

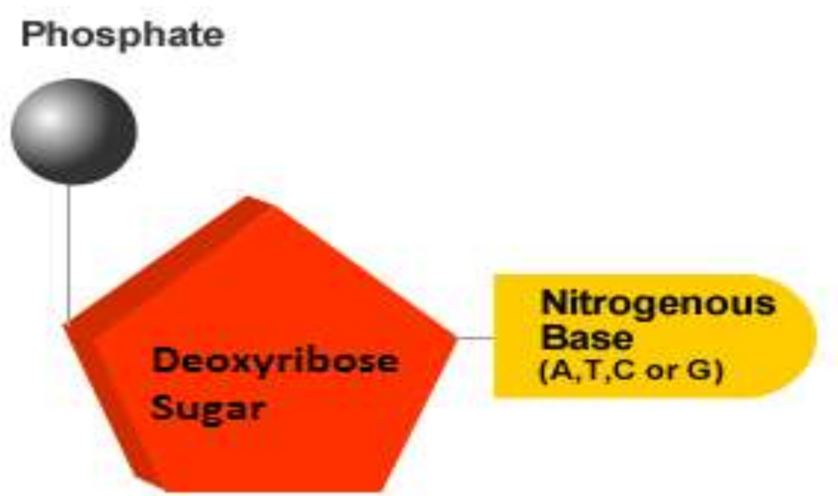
No Free form exists



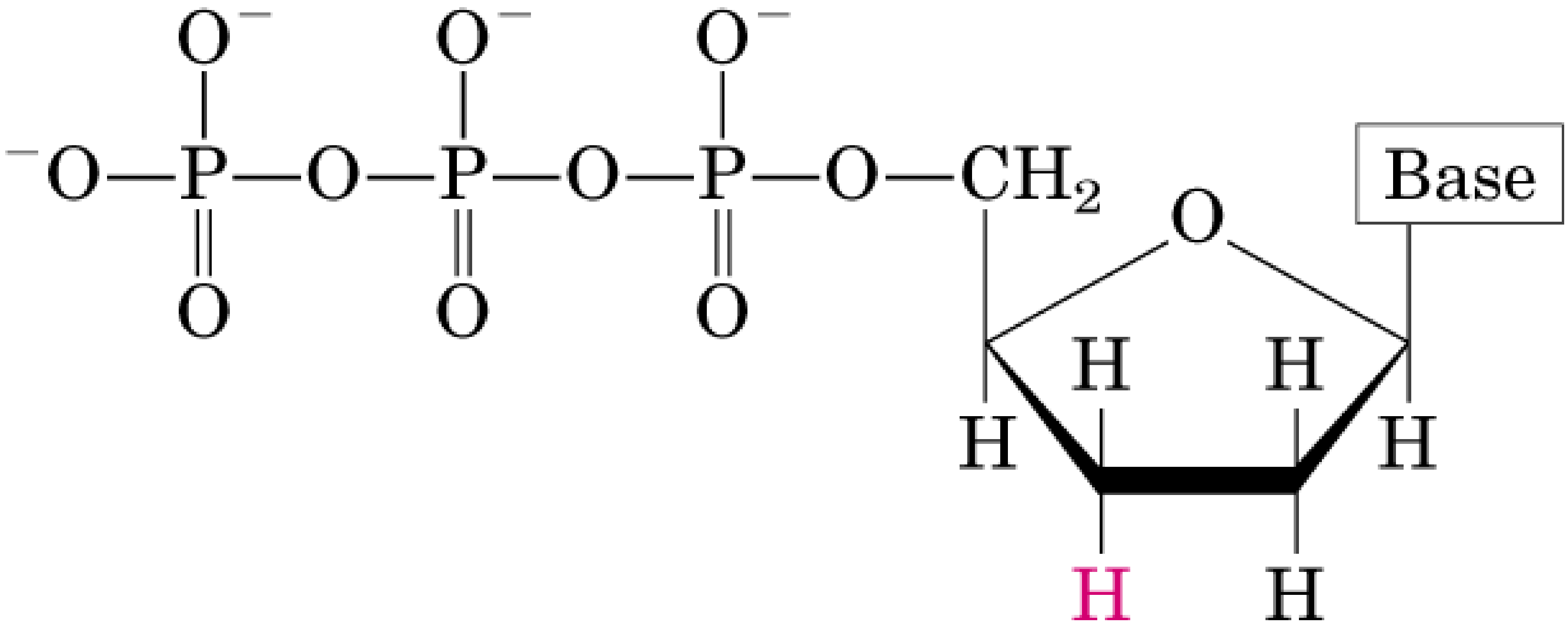
- It is the order of these **base pairs** that determines **genetic makeup**

- One **phosphate** + one **sugar** + one **base** = one **nucleotide**

- Nucleotides are the **building blocks** of DNA – thus, each strand of DNA is a string of **nucleotides**



Sanger dideoxy sequencing incorporates dideoxy nucleotides, preventing further synthesis of the DNA strand



ddNTP analog

base（purine、pyrimdine）+ribose（deoxyribos

↓ N-glycosyl linkage

nucleoside+phosphate

↓ phosphoester linkage

nucleotide

↓ phosphodiester linkage

nucleic acid

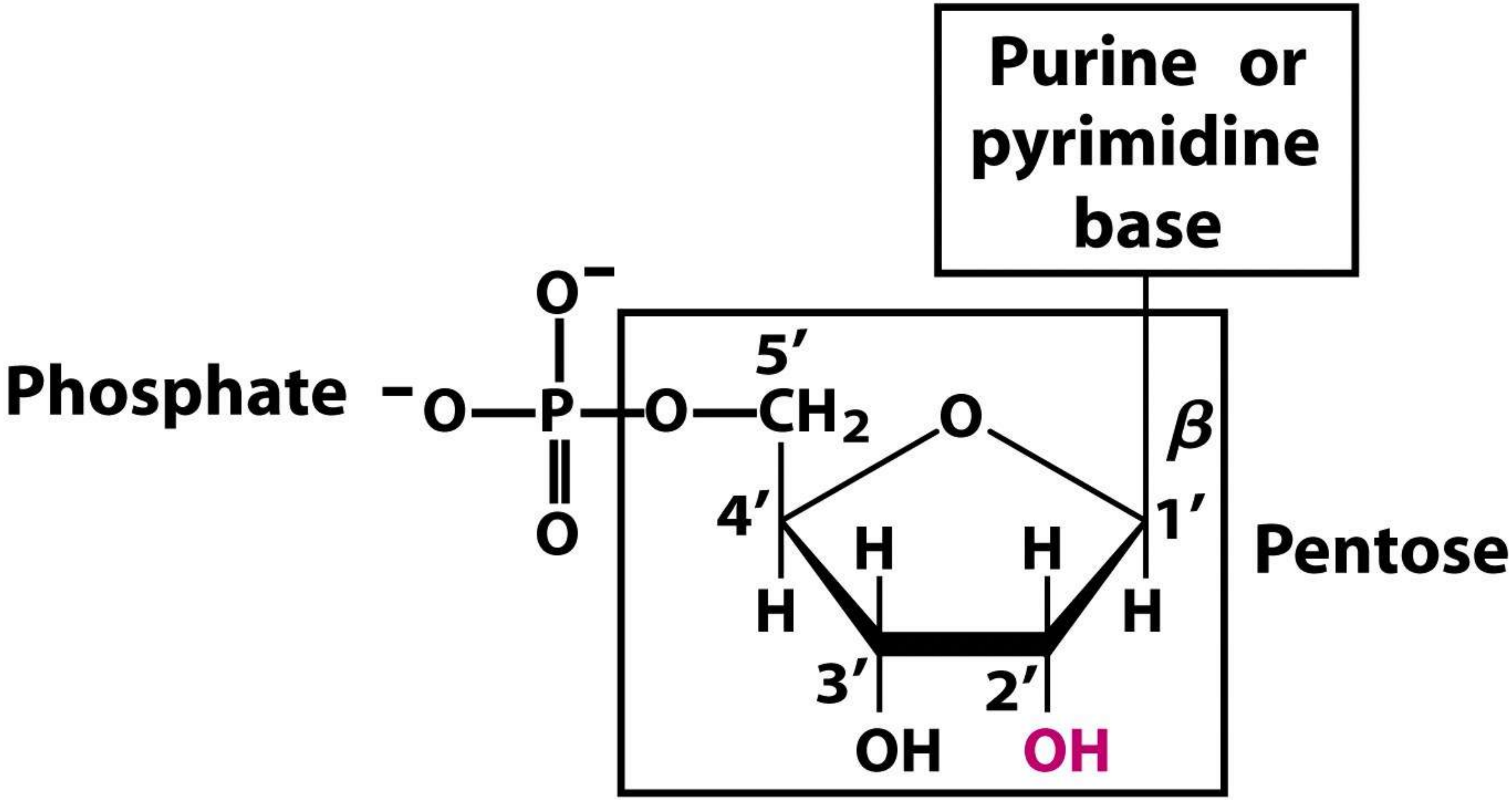
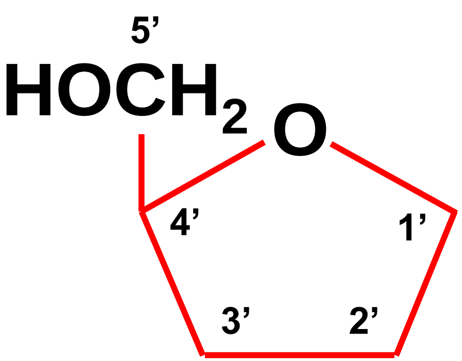
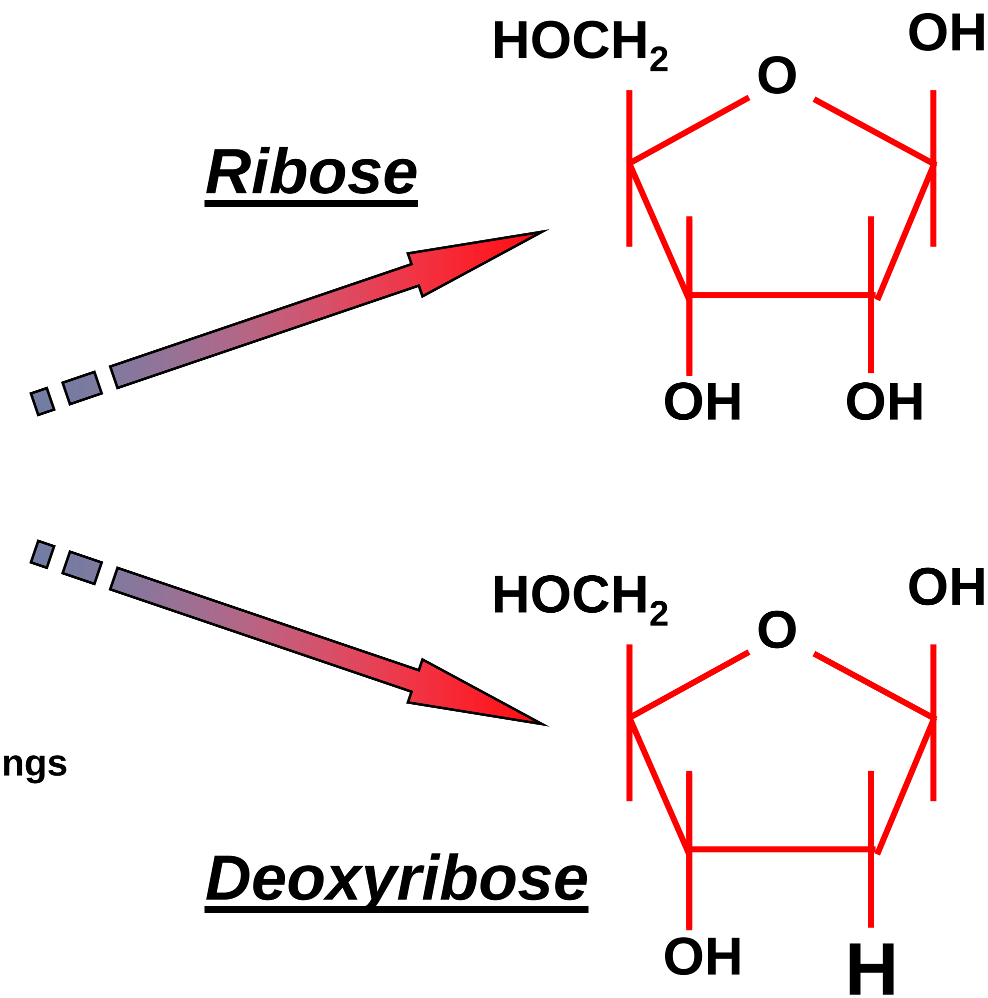


Figure 8-1a
Lehninger Principles of Biochemistry, Fifth Edition

Nucleotide Structure - 1
Sugars

Generic Ribose Structure

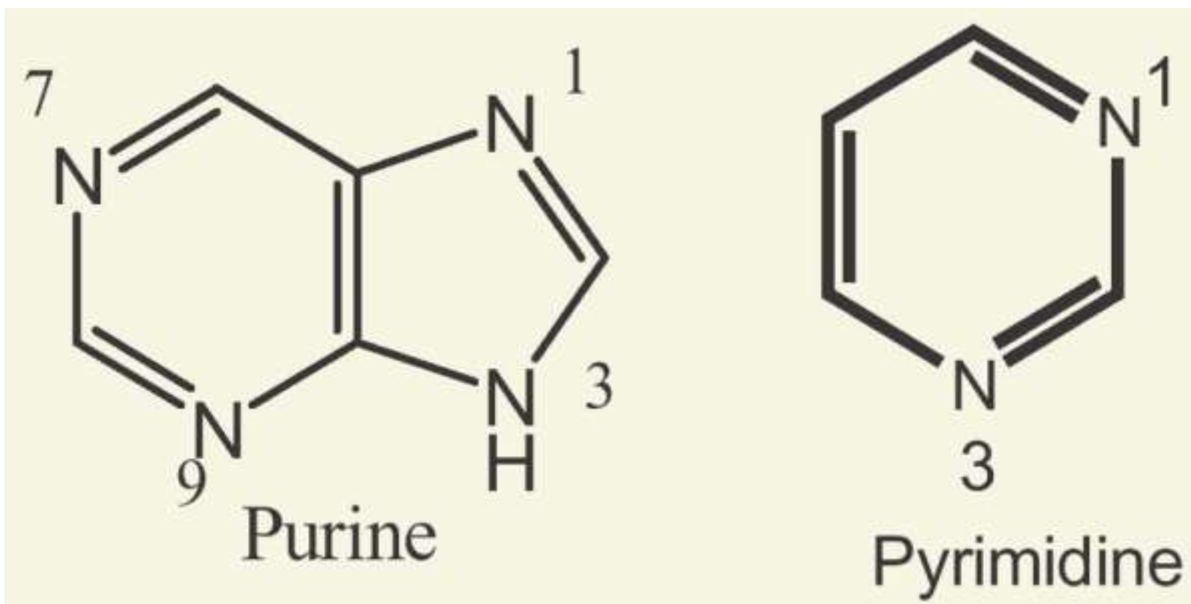




N.B. Carbons are given numberings as a prime

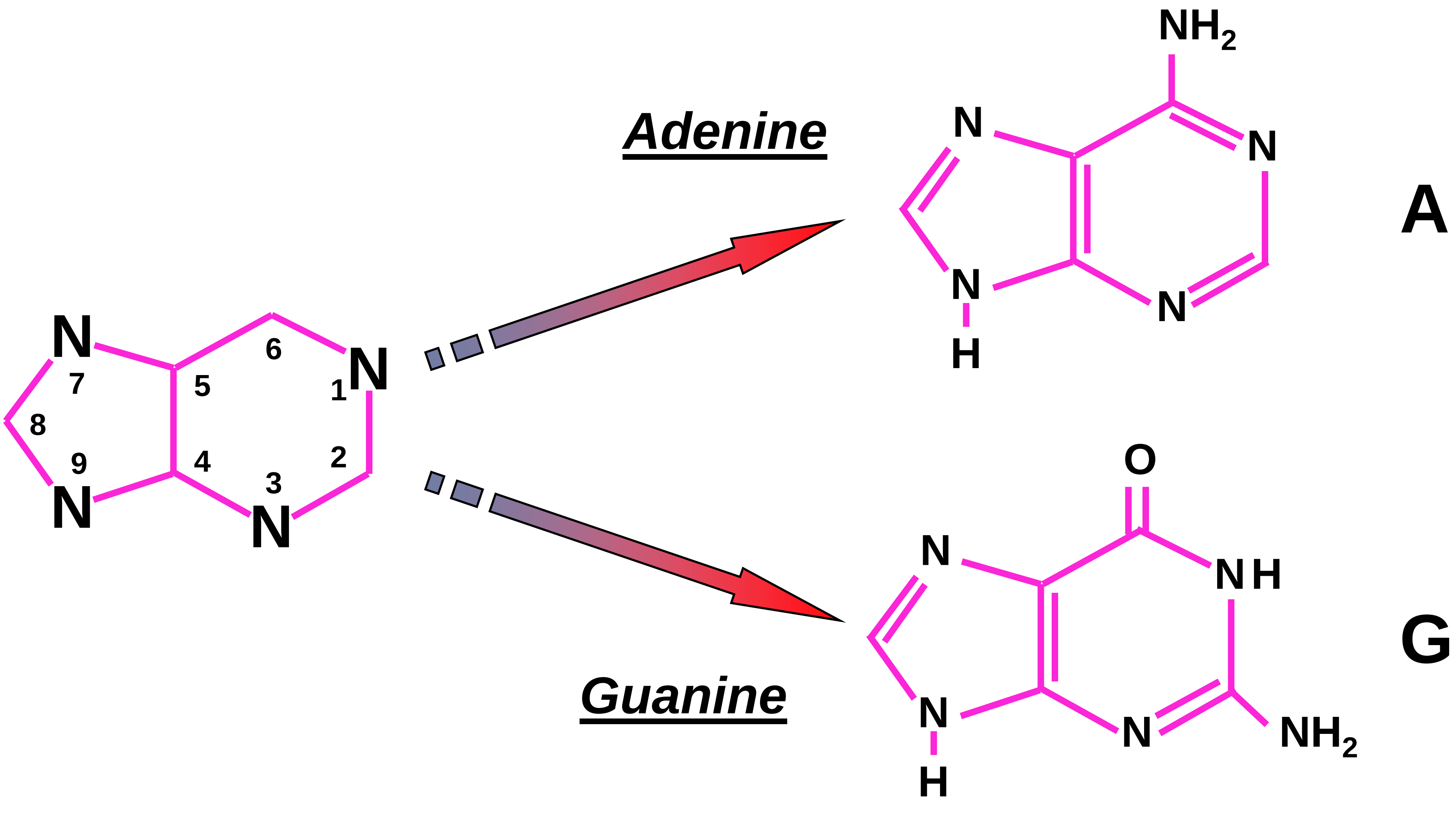
Purine and Pyrimidine

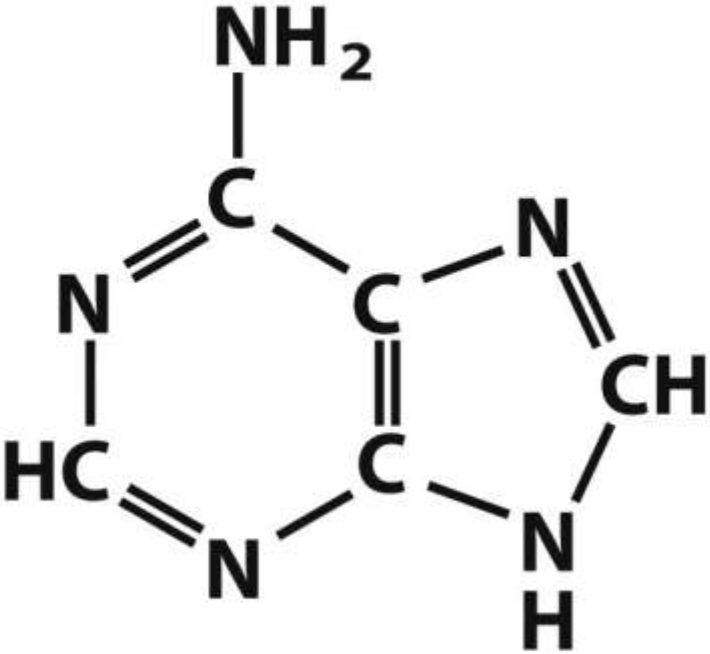
- Pyrimidine contains two pyridine-like nitrogens in a six-membered aromatic ring
- Purine has 4 N's in a fused-ring structure. Three are basic like pyridine-like and one is like that in pyrrole



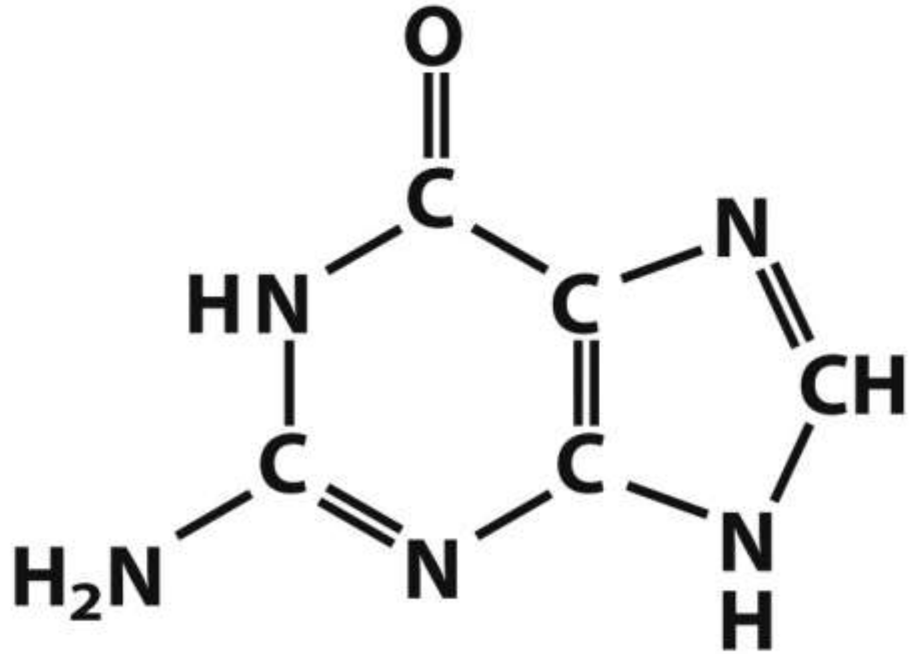
Based on McMurry, Organic Chemistry, Chapter 28, 6th edition, (c) 2003

Nucleotide Structure - 2
Bases - Purines





Adenine



Guanine

Purines

Figure 8-2 part 1
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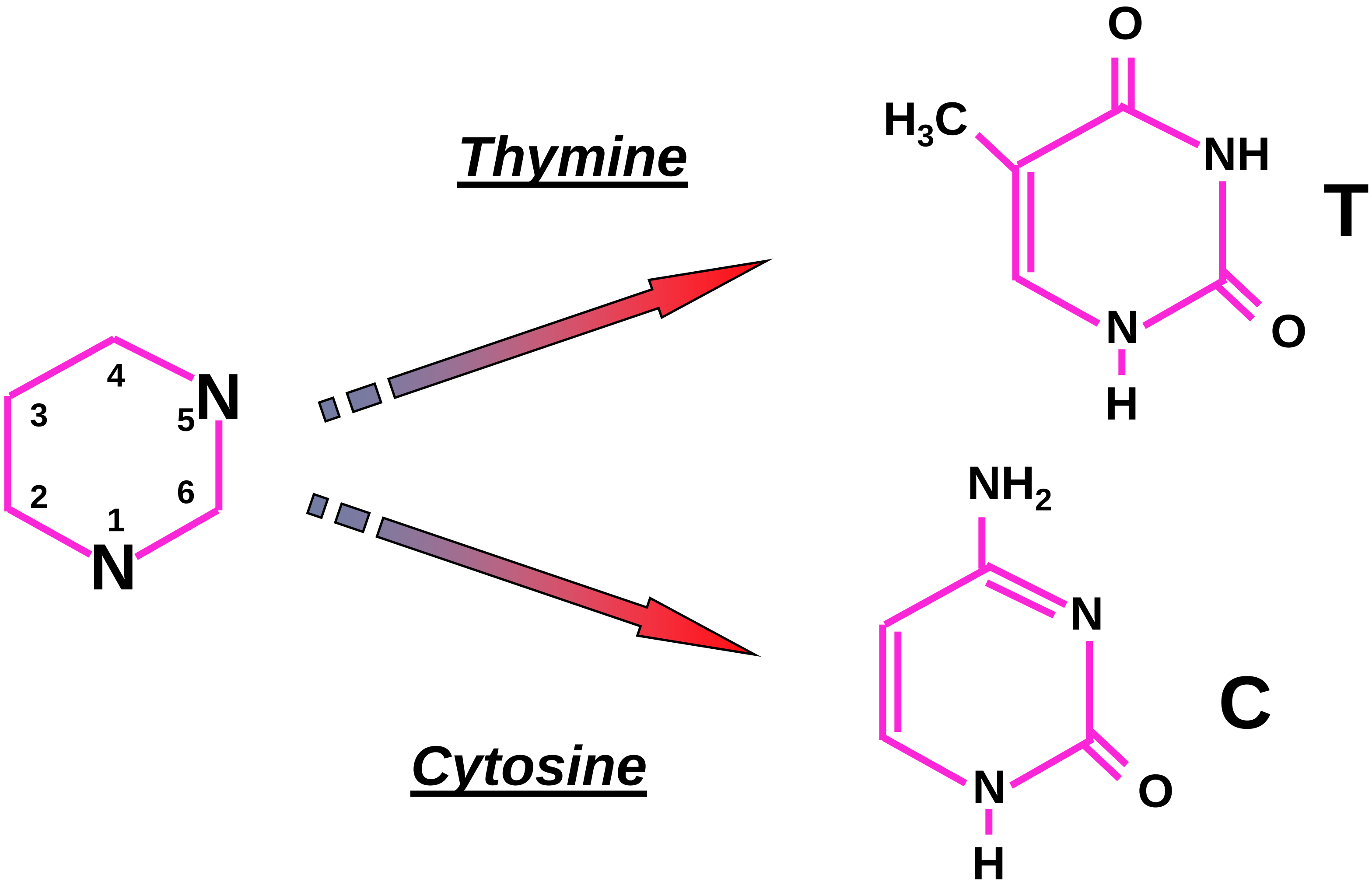
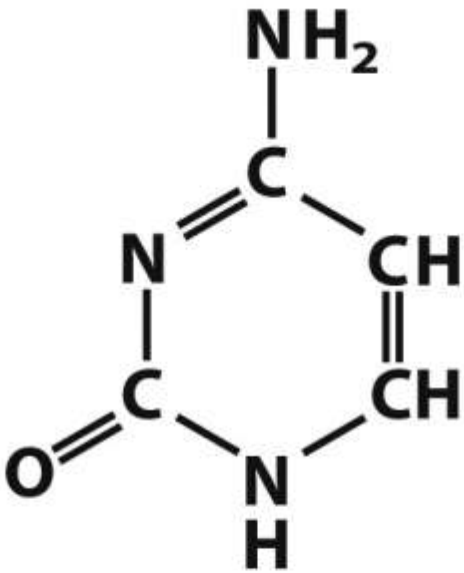
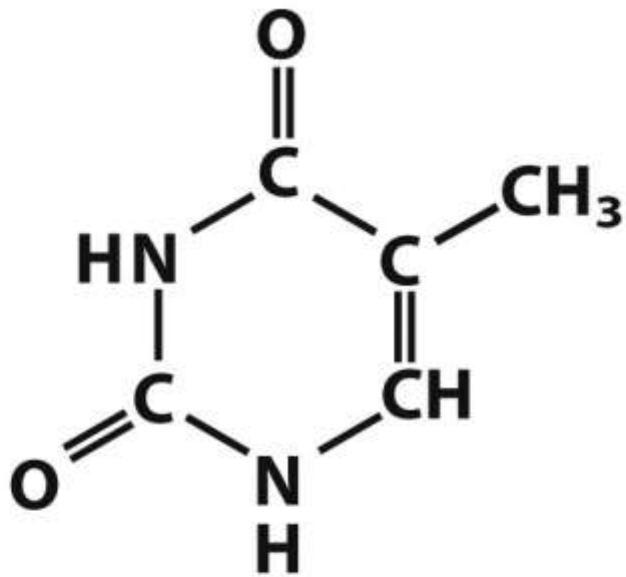
Nucleotide Structure - 3

Bases - Pyrimidines

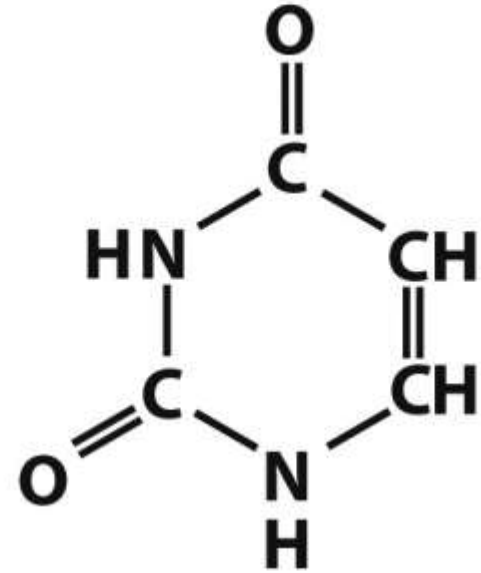




Cytosine



Thymine (DNA)



Uracil (RNA)

Pyrimidines

Figure 8-2 part 2
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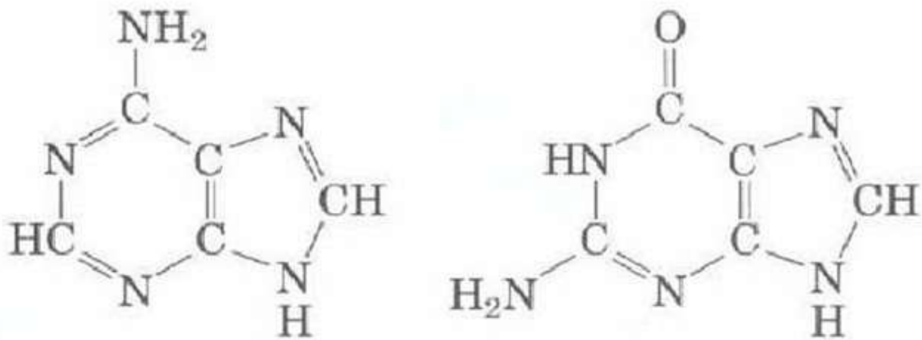
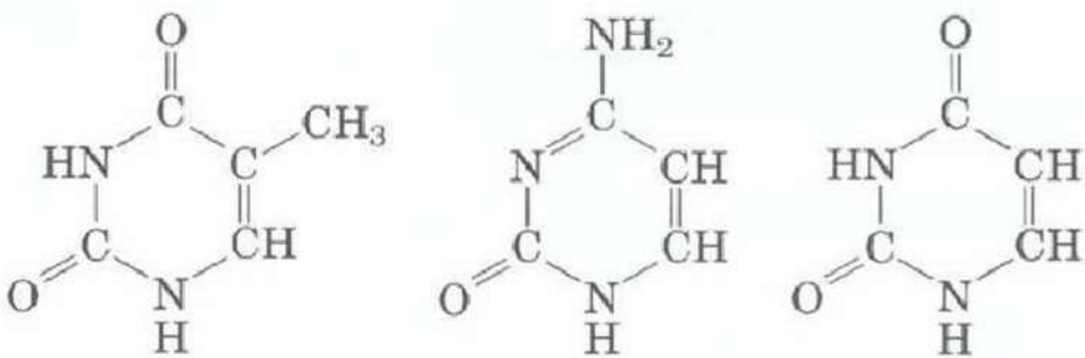


Adenine Guanine

Purines



Thymine (DNA) Cytosine Uracil (RNA)

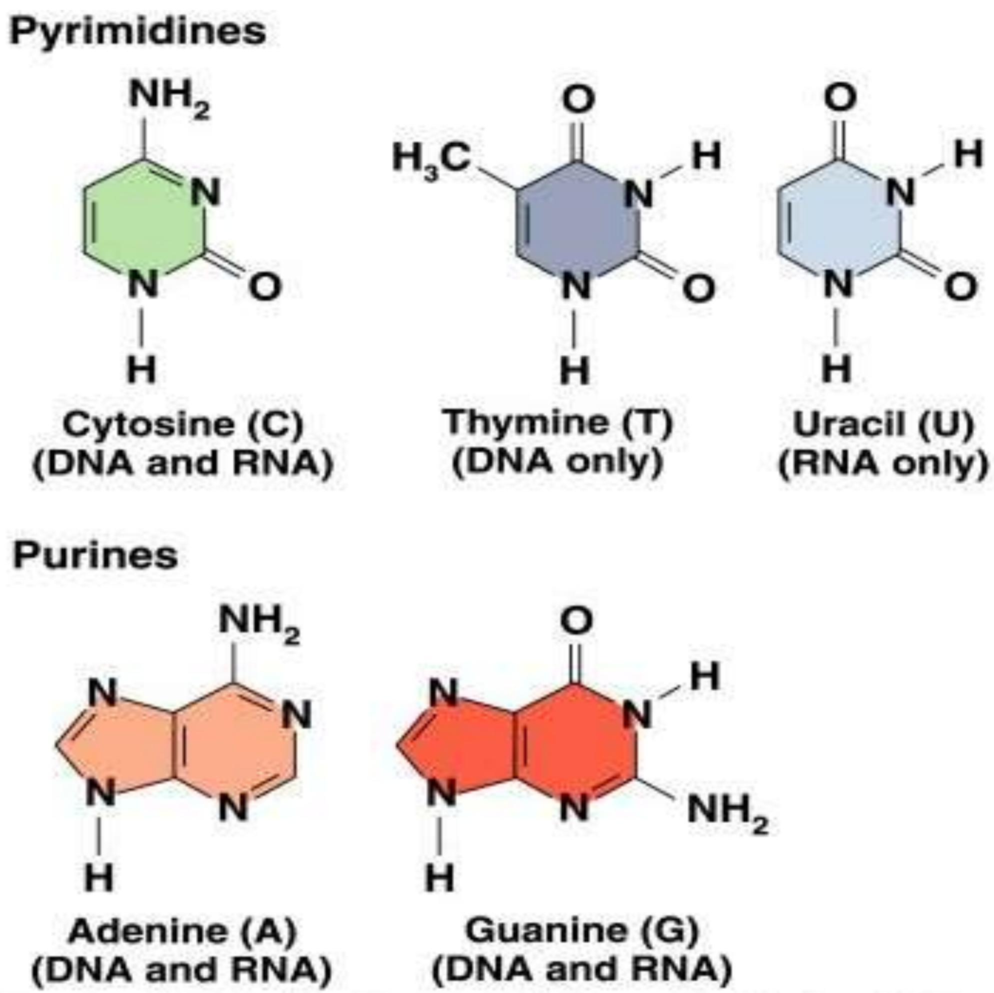
Pyrimidines

Nitrogen Bases

- The **nitrogen bases** in nucleotides consist of two general types:

- purines: adenine (A) and guanine (G)

- pyrimidines: cytosine (C), thymine (T) and Uracil (U)

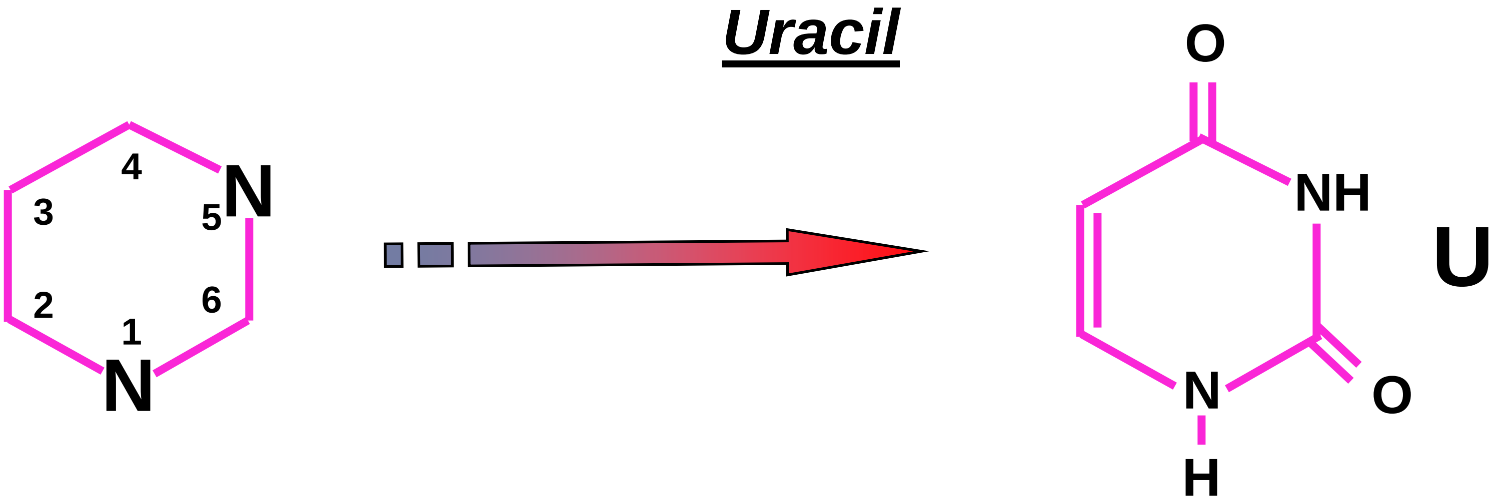


Nucleotide Structure - 4
Bases - Pyrimidines

Thymine is found ONLY in DNA.

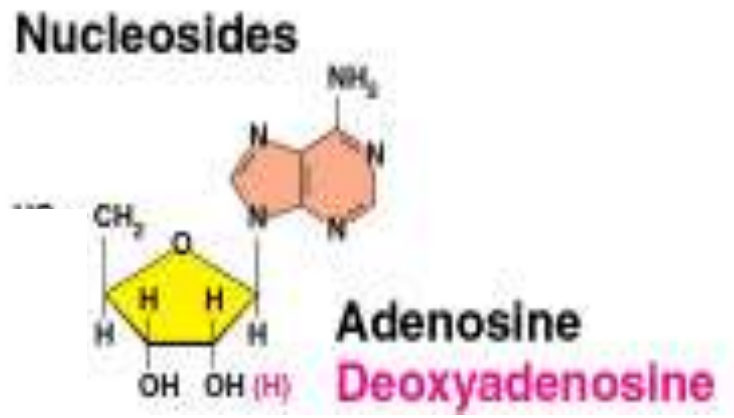
In RNA, thymine is replaced by uracil

Uracil and Thymine are structurally similar



Nucleosides and Nucleotides

- A nucleoside consists of a nitrogen base linked by a glycosidic bond to C1' of a ribose or deoxyribose
- Nucleosides are named by changing the the nitrogen base ending to *-osine* for purines and *–idine* for pyrimidines
- A nucleotide is a nucleoside that forms a phosphate ester with the C5' OH group of ribose or deoxyribose
- Nucleotides are named using the name of the nucleoside followed by *5'-monophosphate*

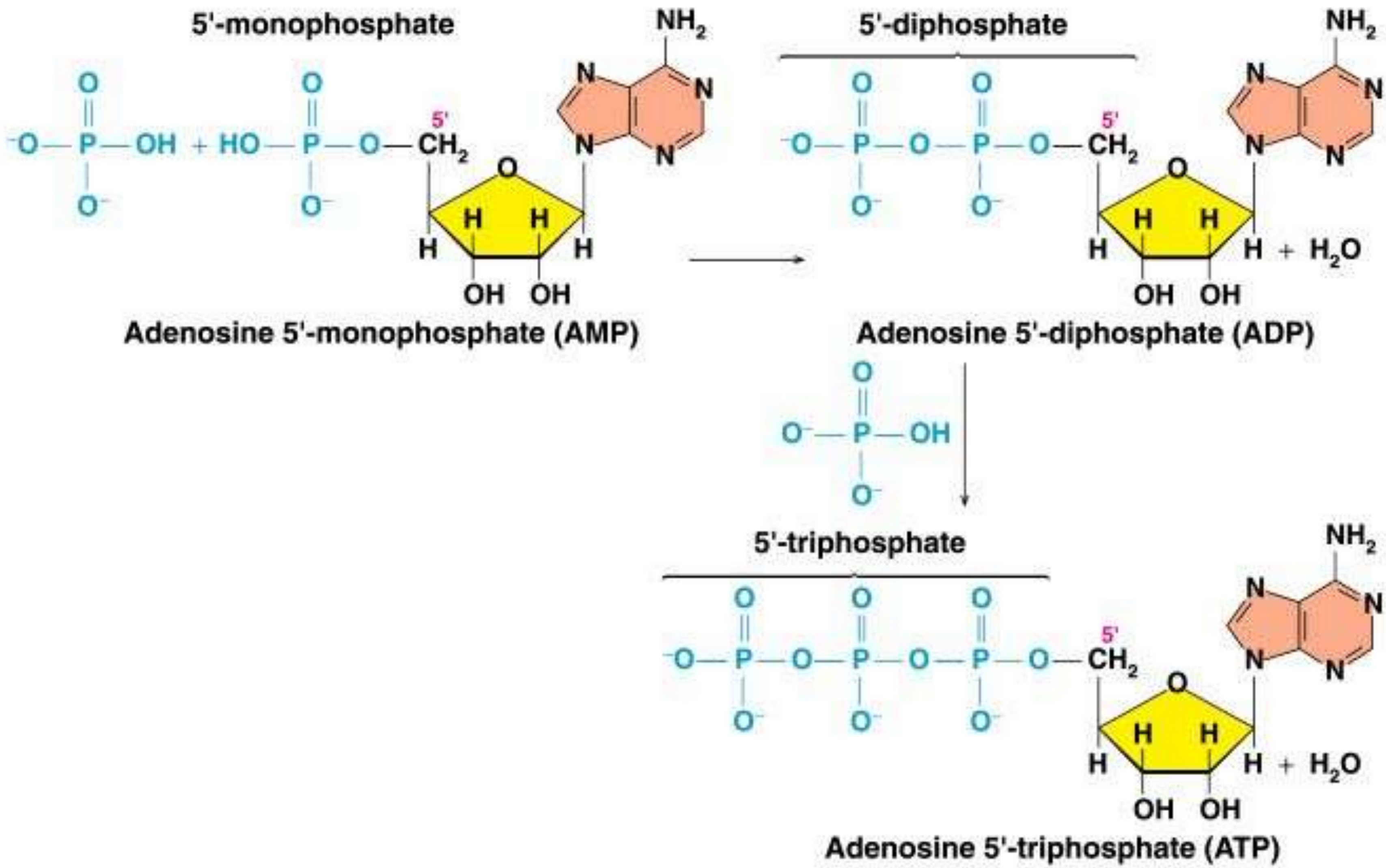


Names of Nucleosides and Nucleotides

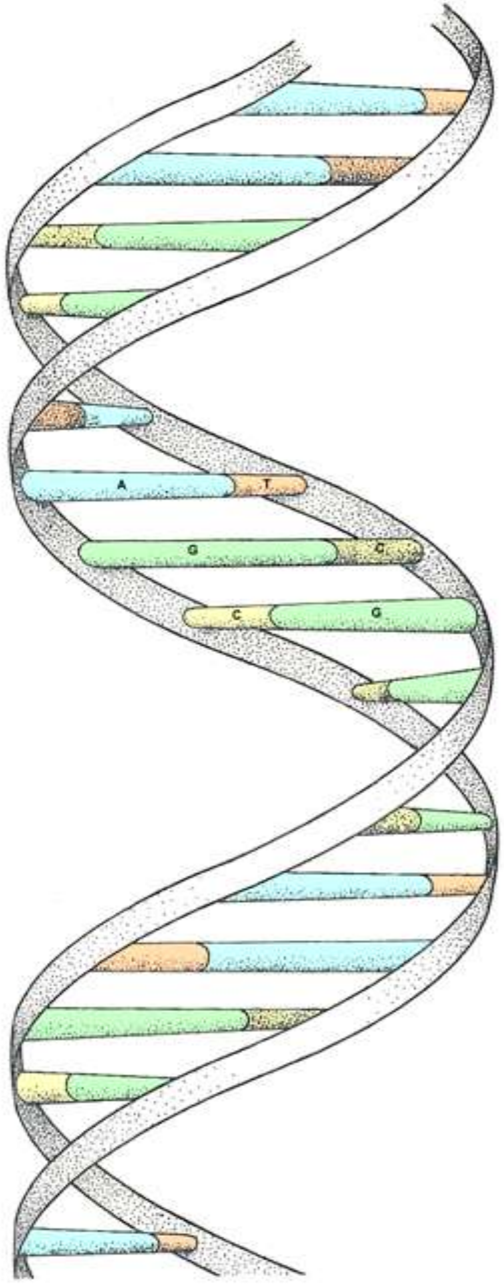
Base	Nucleosides	Nucleotides
RNA		
Adenine (A)	Adenosine (A)	Adenosine 5'-monophosphate (AMP)
Guanine (G)	Guanosine (G)	Guanosine 5'-monophosphate (GMP)
Cytosine (C)	Cytidine (C)	Cytidine 5'-monophosphate (CMP)
Uracil (U)	Uridine (U)	Uridine 5'-monophosphate (UMP)
DNA		
Adenine (A)	Deoxyadenosine (A)	Deoxyadenosine 5'-monophosphate (dAMP)
Guanine (G)	Deoxyguanosine (G)	Deoxyguanosine 5'-monophosphate (dGMP)
Cytosine (C)	Deoxycytidine (C)	Deoxycytidine 5'-monophosphate (dCMP)
Thymine (T)	Deoxythymidine (T)	Deoxythymidine 5'-monophosphate (dTMP)

AMP, ADP and ATP

- Additional phosphate groups can be added to the nucleoside 5'-monophosphates to form **diphosphates** and **triphosphates**
- **ATP** is the major energy source for cellular activity



DNA



Died in 2004

DNA

DNA stands for **deoxyribose nucleic acid**

This chemical substance is present in the nucleus of all cells in all living organisms

DNA controls all the chemical changes which take place in cells

The kind of cell which is formed, (muscle, blood, nerve etc) is controlled by DNA

DNA molecule

DNA is a very large molecule made up of a long chain of sub-units

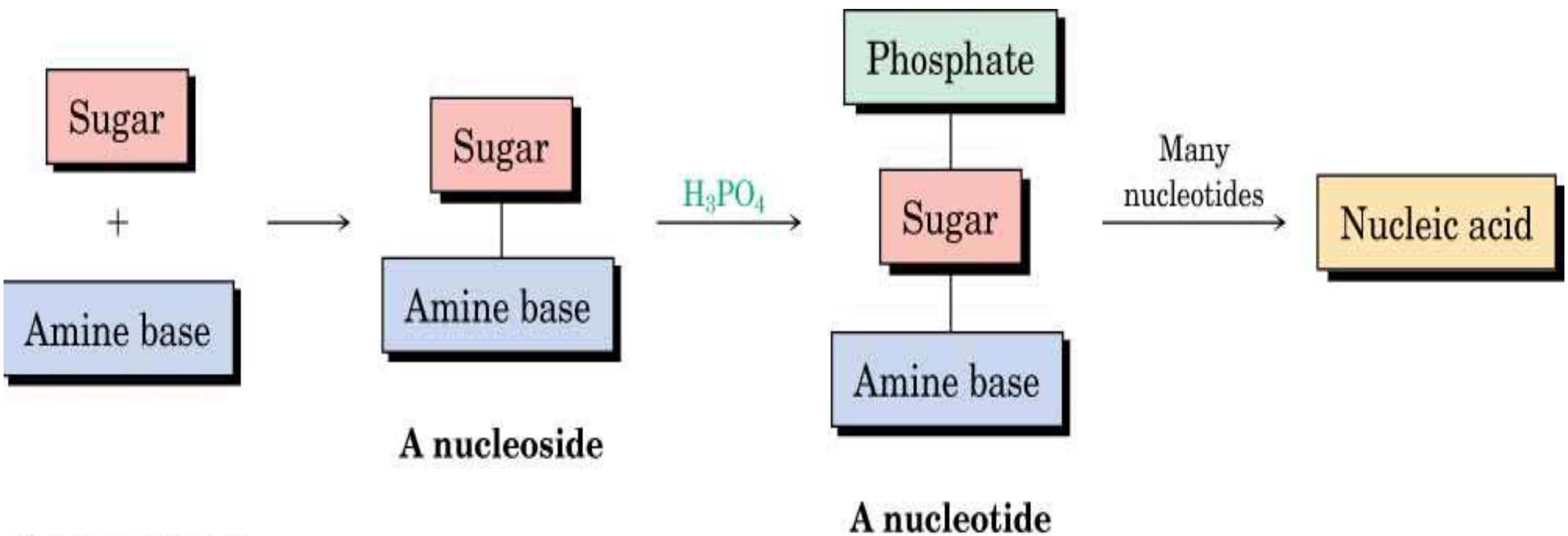
The sub-units are called **nucleotides**

Each nucleotide is made up of

- a sugar called **deoxyribose**
- a phosphate group **$-PO_4$** and
- an **organic base**

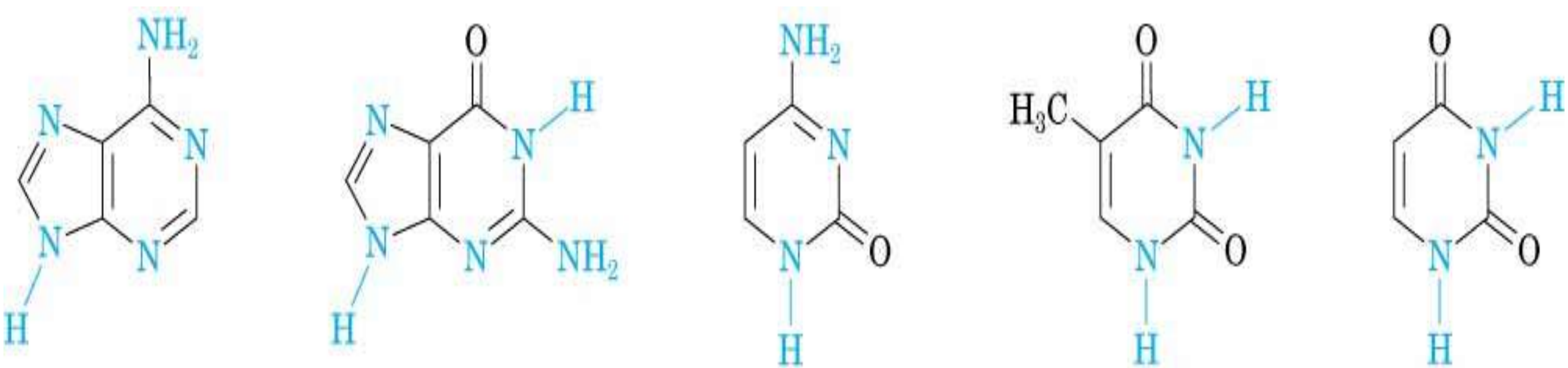
Nucleic Acids and Nucleotides

- Deoxyribonucleic acid (DNA) and ribonucleic acid (RNA), are the chemical carriers of genetic information
- Nucleic acids are biopolymers made of nucleotides, aldopentoses linked to a purine or pyrimidine and a phosphate



Heterocycles in DNA and RNA

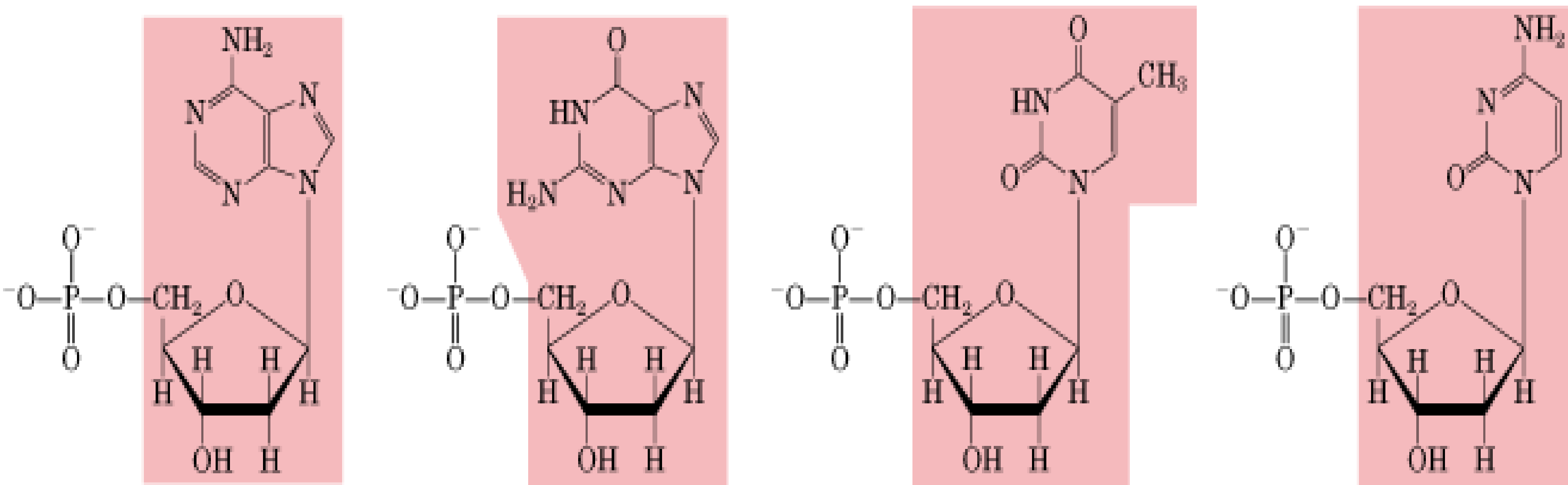
- Adenine, guanine, cytosine and thymine are in DNA
- RNA contains uracil rather than thymine



Adenine (A)	Guanine (G)	Cytosine (C)	Thymine (T)	Uracil (U)
DNA	DNA	DNA	DNA	RNA
RNA	RNA	RNA		

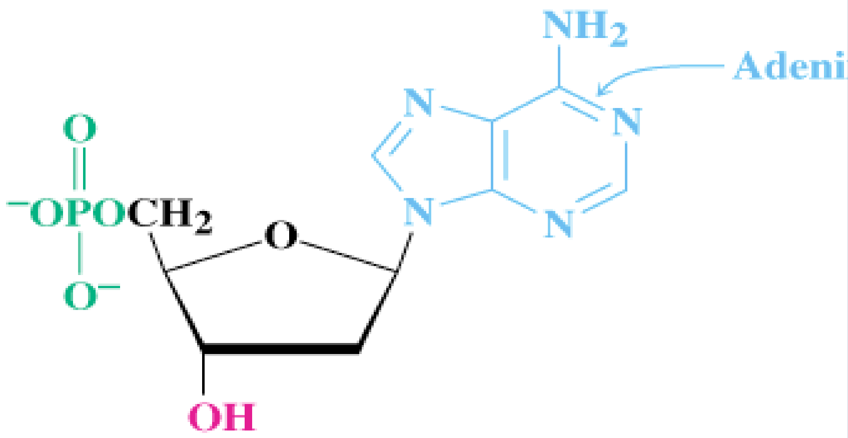
Based on McMurry, Organic Chemistry, Chapter 28, 6th edition, (c) 2003

Deoxyribonucleotides found in DNA

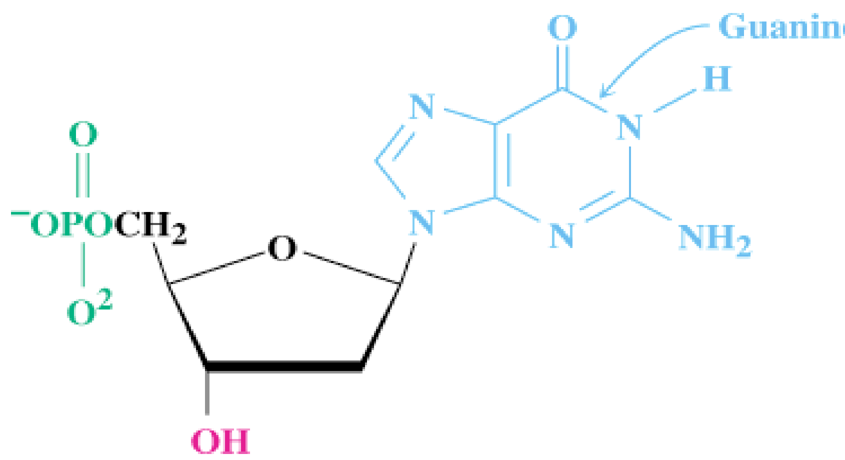


Nucleotide:	Deoxyadenylate (deoxyadenosine 5′-monophosphate)	Deoxyguanylate (deoxyguanosine 5′-monophosphate)	Deoxythymidylate (deoxythymidine 5′-monophosphate)	Deoxycytidylate (deoxycytidine 5′-monophosphate)
Symbols:	A, dA, dAMP	G, dG, dGMP	T, dT, dTMP	C, dC, dCMP
Nucleoside:	Deoxyadenosine	Deoxyguanosine	Deoxythymidine	Deoxycytidine
	dA	dG	dT	dC

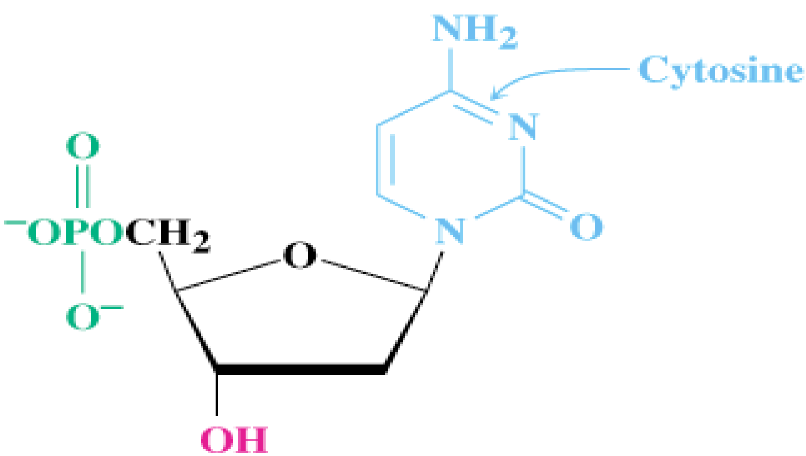
The Deoxyribonucleotides



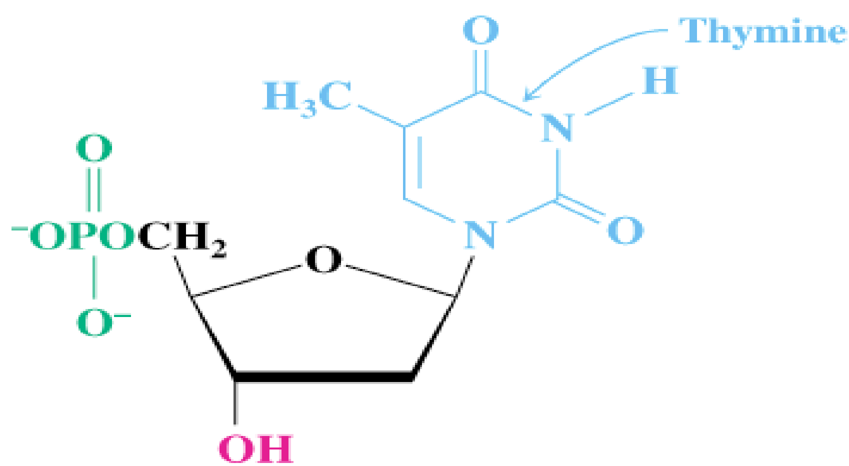
2′-Deoxyadenosine 5′-phosphate



2'-Deoxyguanosine 5'-phosphate



2'-Deoxycytidine 5'-phosphate



2'-Deoxythymidine 5'-phosphate

Hydrogen Bonding Interactions

- Two bases can hydrogen bond to form a base pair
- For monomers, large number of base pairs is possible
- In polynucleotide, only few possibilities exist
- Watson-Crick base pairs predominate in double-stranded DNA
- A pairs with T
- C pairs with G
- Purine pairs with pyrimidine

一、the building block molecule of nucleic acid--nucleotide

In RNA:

AMP、CMP、GMP、TMP

In DNA:

dAMP、dCMP、dGMP 、dUMP

Functions of Nucleotides and Nucleic Acids

- Nucleotide Functions:
  - Energy for metabolism (ATP)
  - Enzyme cofactors (NAD^+)
  - Signal transduction (cAMP)

- Nucleic Acid Functions:
  - Storage of genetic info (DNA)
  - Transmission of genetic info (mRNA)
  - Processing of genetic information (ribozymes)
  - Protein synthesis (tRNA and rRNA)

二、the linkage ----

phosphodiester bridge

3’terminal

5’terminal

Nucleotide residues

DNA Nucleotides Composition (3 parts):

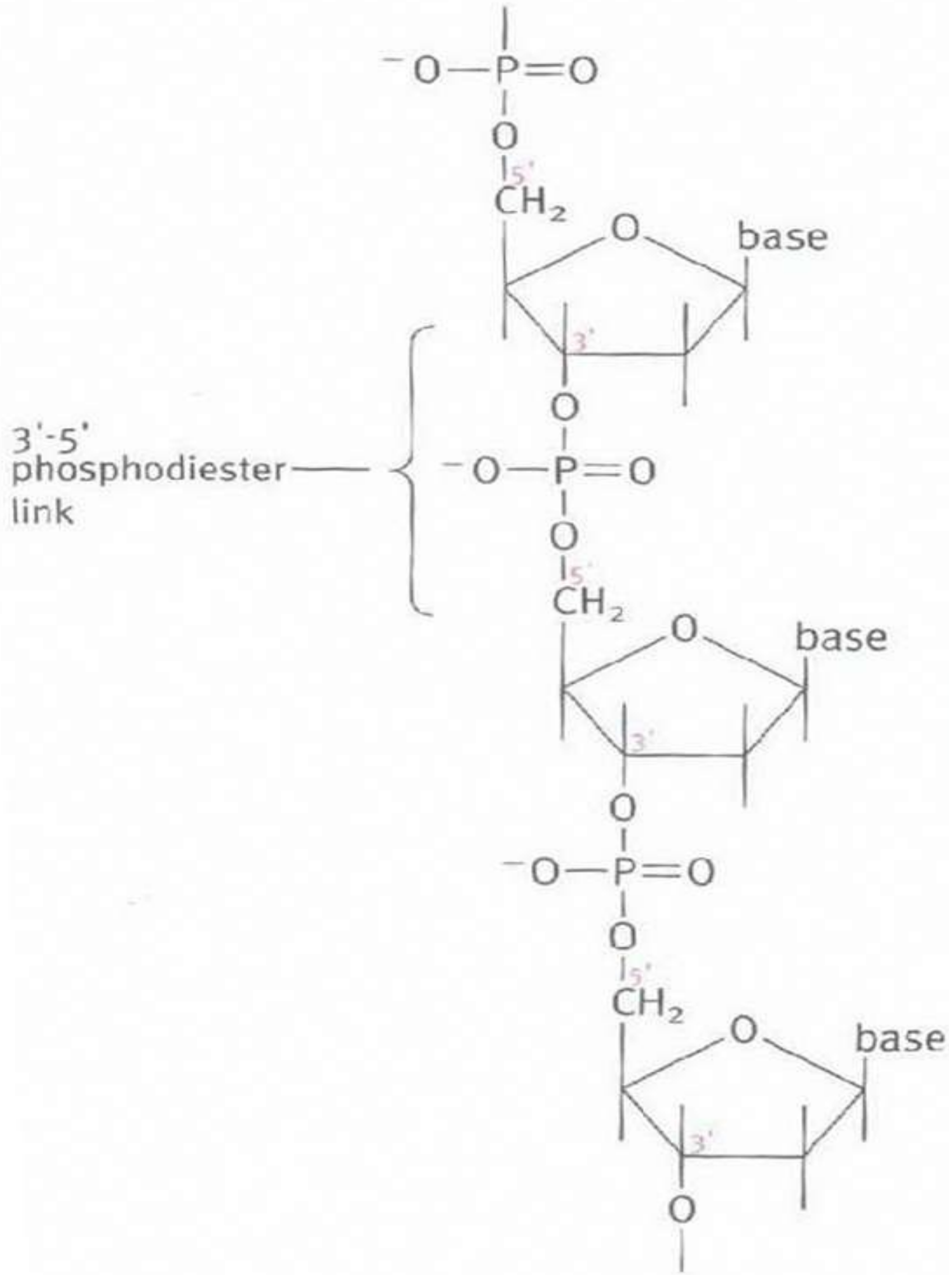
1- Deoxyribose sugar (no O in 3rd carbon)
2- Phosphate group
3- One of 4 types of bases (all containing nitrogen):
   - Adenine
   - Thymine (Only in DNA)
   - Cytosine
   - Guanine

Base Pairing in DNA: The Watson–Crick Model

- In 1953 Watson and Crick noted that DNA consists of two polynucleotide strands, running in opposite directions and coiled around each other in a double helix
- Strands are held together by hydrogen bonds between specific pairs of bases
- Adenine (A) and thymine (T) form strong hydrogen bonds to each other but not to C or G
- (G) and cytosine (C) form strong hydrogen bonds to each other but not to A or T

The Difference in the Strands

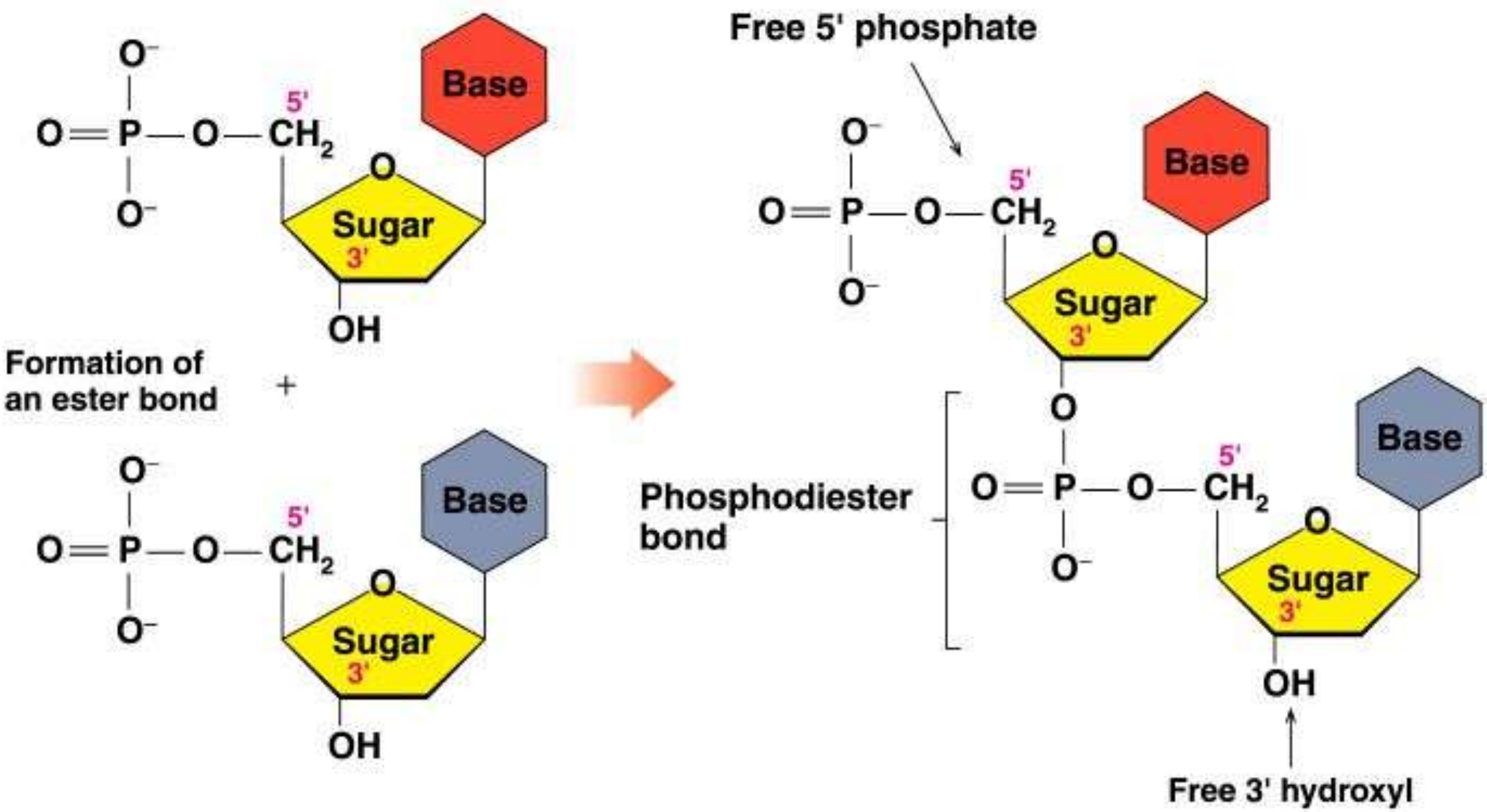
- The strands of DNA are complementary because of H-bonding
- Whenever a G occurs in one strand, a C occurs opposite it in the other strand
- When an A occurs in one strand, a T occurs in the other



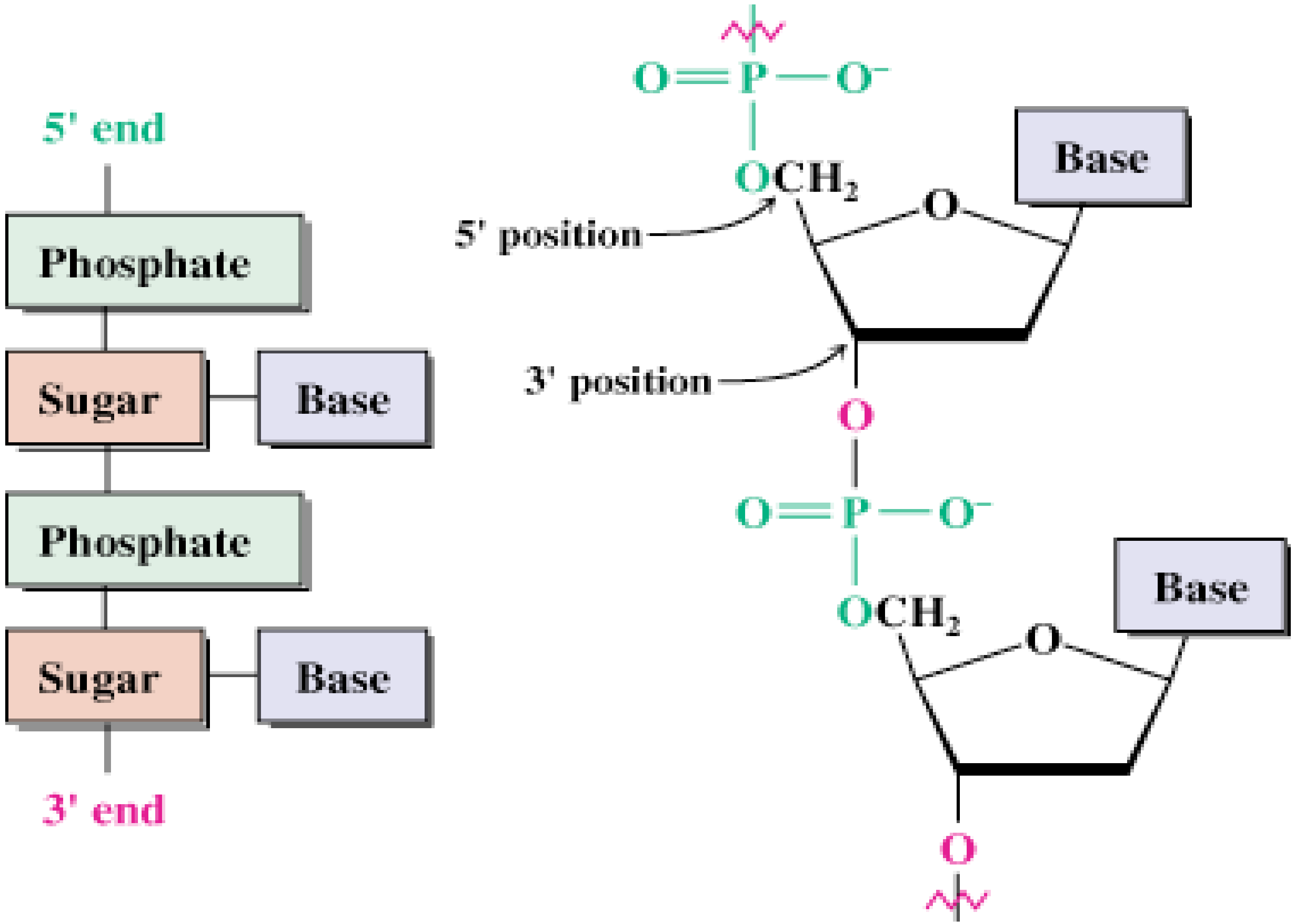
base
3'-5'
phosphodiester
link
base
base

Primary Structure of Nucleic Acids

- The **primary structure** of a nucleic acid is the nucleotide sequence
- The nucleotides in nucleic acids are joined by phosphodiester bonds
- The 3'-OH group of the sugar in one nucleotide forms an ester bond to the phosphate group on the 5'-carbon of the sugar of the next nucleotide



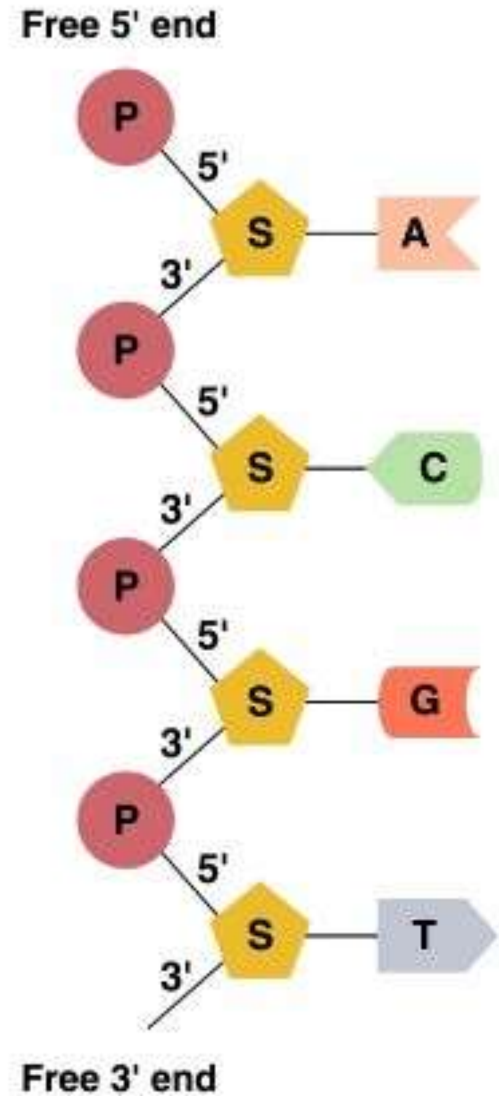
Generalized Structure of DNA



Reading Primary Structure

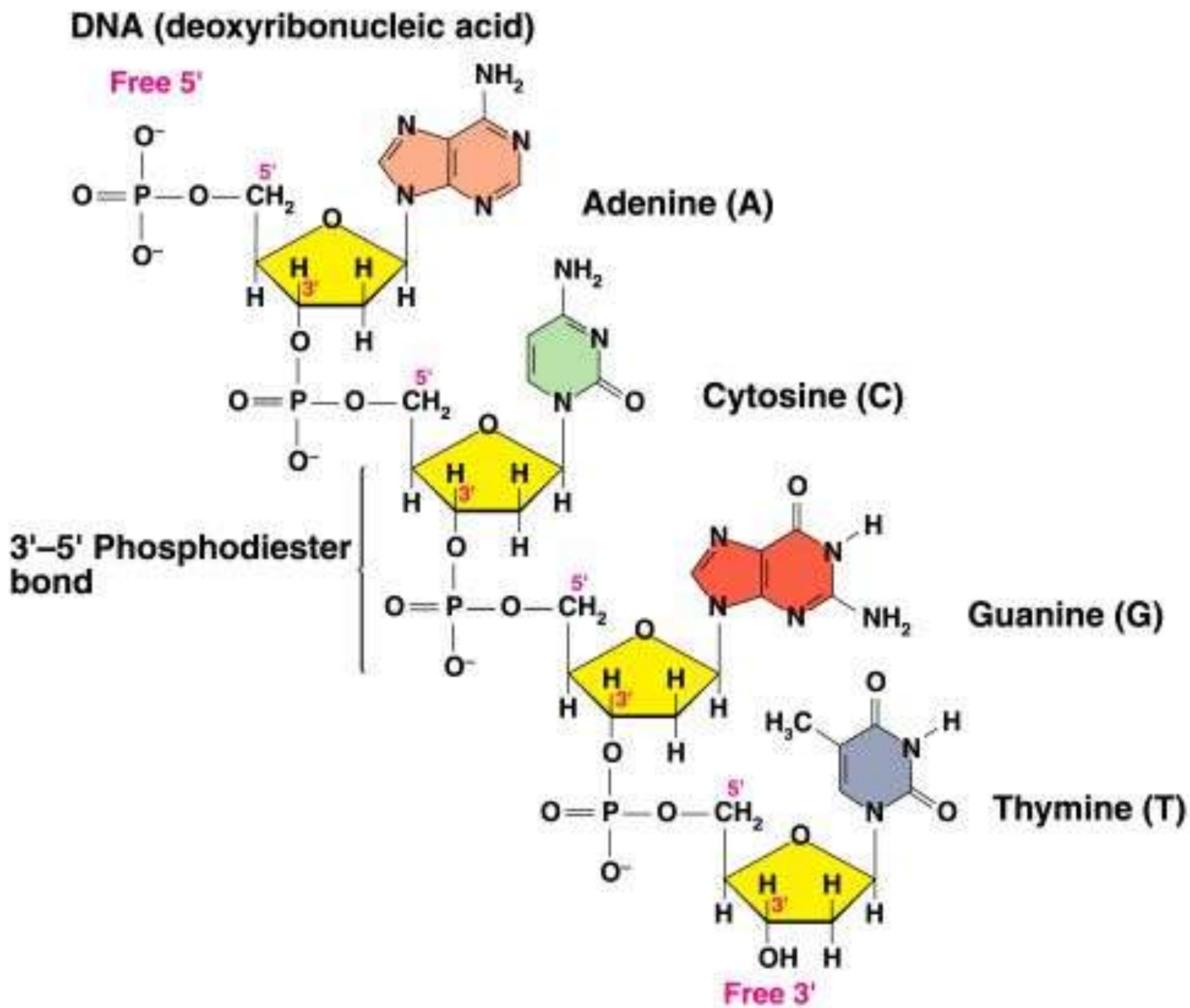
- A nucleic acid polymer has a free 5'-phosphate group at one end and a free 3'-OH group at the other end
- The sequence is read from the free 5'-end using the letters of the bases
- This example reads

  5'—A—C—G—T—3'



Example of DNA Primary Structure

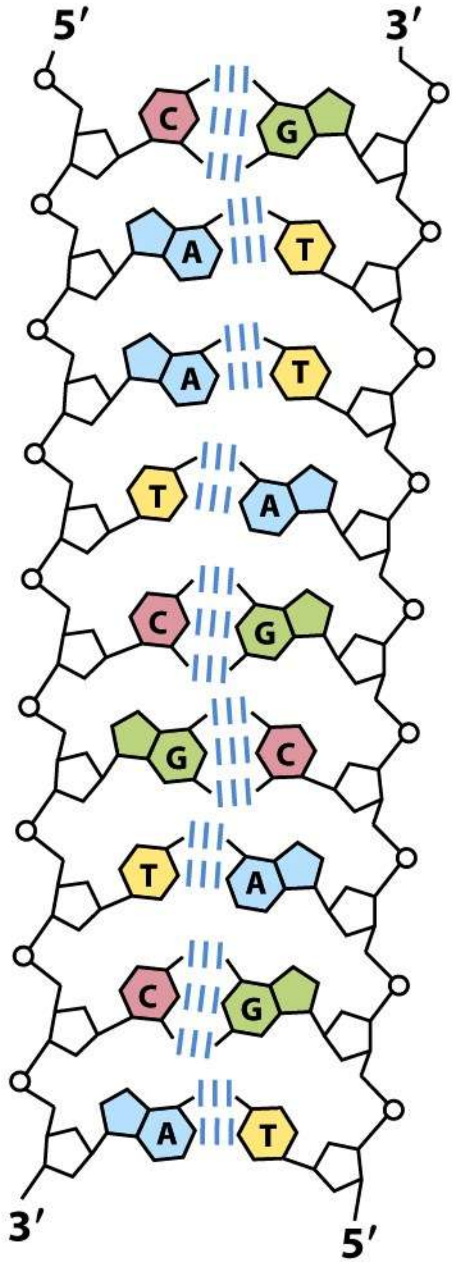
- In DNA, A, C, G, and T are linked by 3'-5' ester bonds between deoxyribose and phosphate



Describing a Sequence

- Chain is described from 5′ end, identifying the bases in order of occurrence, using the abbreviations A for adenosine, G for guanosine, C for cytidine, and T for thymine (or U for uracil in RNA)
- A typical sequence is written as TAGGCT

Properties of a DNA double helix



The strands of DNA are antiparallel

The strands are complimentary

There are Hydrogen bond forces

There are base stacking interactions

There are 10 base pairs per turn

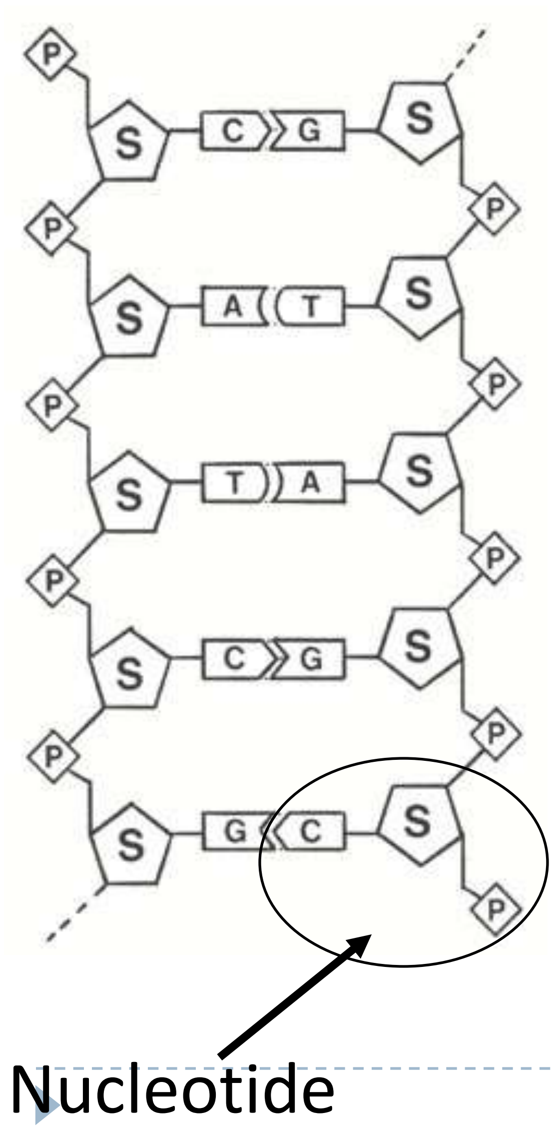
The Double Helix (DNA)
Structural model:

- Model proposed by Watson & Crick, 1953
- Two sugar-phosphate strands, next to each other, but running in opposite directions.
- Specific Hydrogen bonds occur among bases from one chain to the other:

  A---T , C---G

  Due to this specificity, a certain base on one strand indicates a certain base in the other.
- The 2 strands intertwine, forming a double-helix that winds around a central axis

Untwisted it looks like this:



- The **sides** of the ladder are:

  P = **phosphate**

  S = **sugar** molecule

- The **steps** of the ladder are C, G, T, A = **nitrogenous bases**

  (Nitrogenous means containing the element **nitrogen**.)

A = **Adenine** **(Apples are Tasty)**

T = **Thymine**

A always pairs with T in DNA

C = **Cytosine** **(Cookies are Good)**

G = **Guanine**

C always pairs with G in DNA

Secondary Structure: DNA Double Helix

- In DNA there are two strands of nucleotides that wind together in a **double helix**

  - the strands run in opposite directions

  - the bases are are arranged in step-like pairs

  - the **base pairs** are held together by hydrogen bonding
- The pairing of the bases from the two strands is very specific
- The **complimentary base pairs** are **A-T** and **G-C**

  - two hydrogen bonds form between A and T

  - three hydrogen bonds form between G and C
- Each pair consists of a purine and a pyrimidine, so they are the same width, keeping the two strands at equal distances from each other

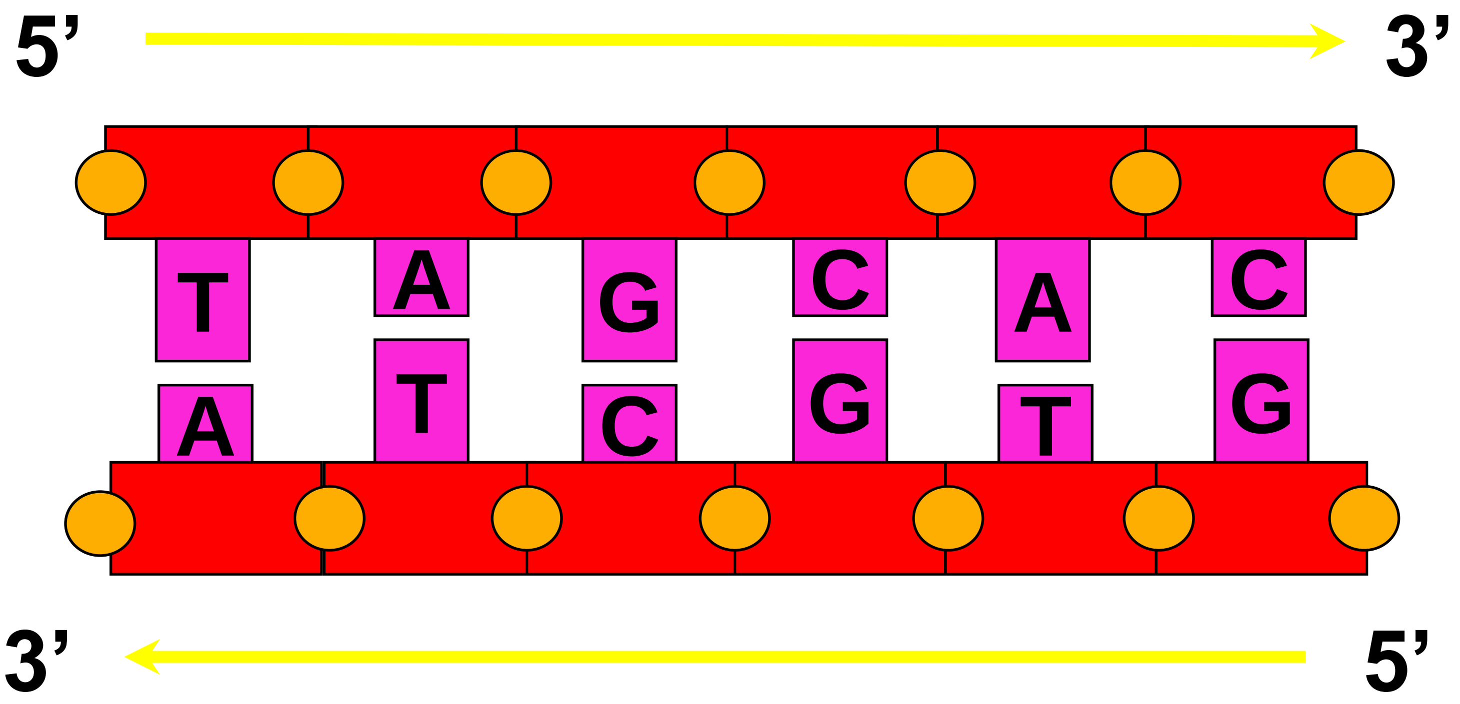
Model of **DNA**:

- The model was developed by **Watson** and **Crick** in 1953.
- They received a **nobel prize** in 1962 for their work.
- The model looks like a twisted ladder – **double helix**.

Nucleic Acid Structure
"Base Pairing"

DNA base-pairing is **antiparallel**

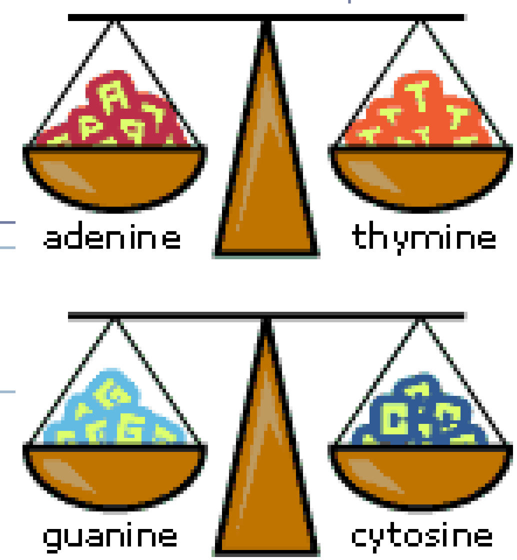
i.e. 5' - 3' (l-r) on top : 5' - 3' (r-l) on



Discovering the structure of DNA

Erwin Chargaff – (1905-2002)

- Columbia University, NY
- Investigated the composition of DNA
- His findings by 1950 strongly suggested the base-pairings of A-T & G-C
- Met with Watson and Crick in 1952 and shared his findings
- "Chargaff's rule" A = T & C = G



Nucleic Acid Structure
The double helix

First determined by Watson & Crick in 1953

Most energy favorable conformation for double stranded DNA to form

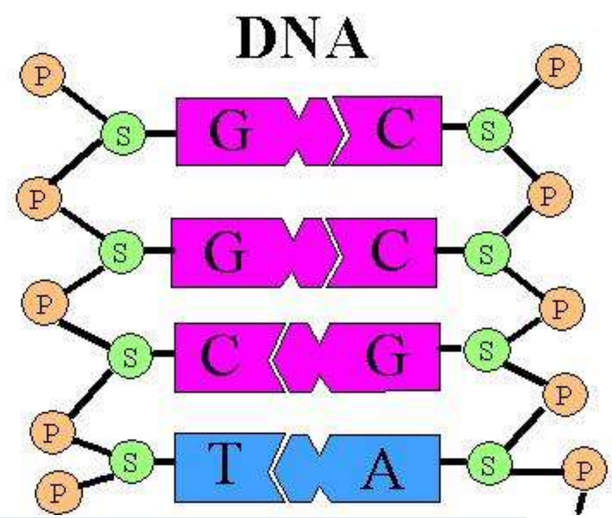
Shape and size is uniform for all life (i.e. DNA is identical)

Without anti-parallel base pairing this conformation could not exist

Structure consists of “major” grooves and “minor” grooves

Major grooves are critical for binding proteins that regulate DNA function

- **<u>DNA</u> = Deoxyribose nucleic acid**
  - **Present in all living cells**
  - **Contains all the infc**



- **<u>Nucleotides</u>:**
- **a subunit that consists of:**
  - **a sugar (deoxyribose)**
  - **a phosphate**
  - **and one nitrogen base – 4 different bases**
    - **Adenine (A) and Thymine (T)**
    - **Guanine (G) and Cytosine (C)**

The paired strands are coiled into a spiral called

A DOUBLE HELIX

Nucleic Acid Structure
“Base Pairing”

RNA [normally] exists as a single stranded polymer

DNA exists as a double stranded polymer

DNA double strand is created by hydrogen bonds between nucleotides

Nucleotides always bind to complementary nucleotides

A ⟷ T (2 H-bonds)

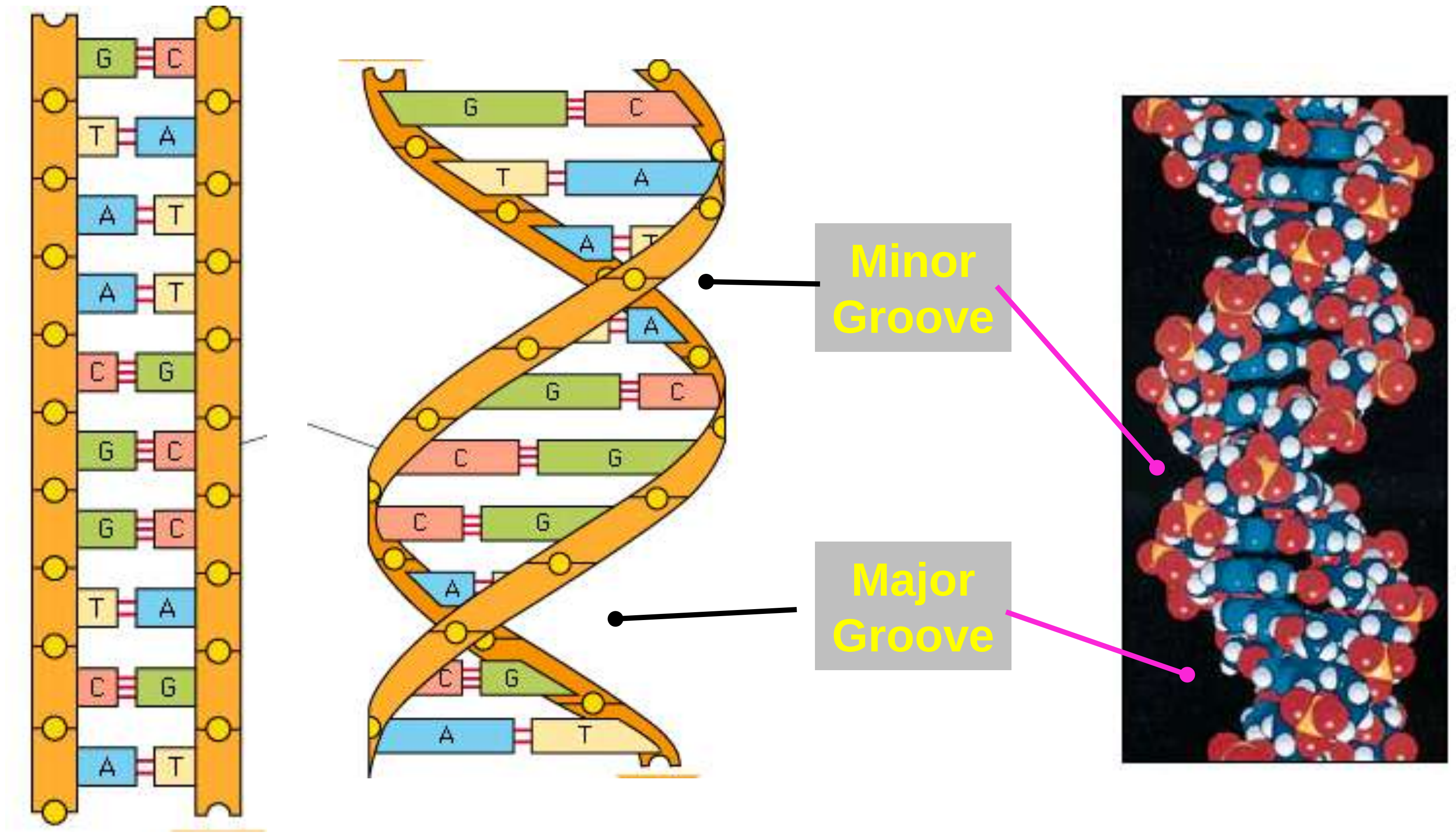
G ⟷ C (3 H-bonds)

Practice DNA Base Pairs

G A T T A C A

C T A A T G T

Nucleic Acid Structure
The double helix



replication

Before a cell divides, the DNA strands unwind and separate

Each strand makes a new partner by adding the appropriate nucleotides

The result is that there are now two double-stranded DNA molecules in the nucleus

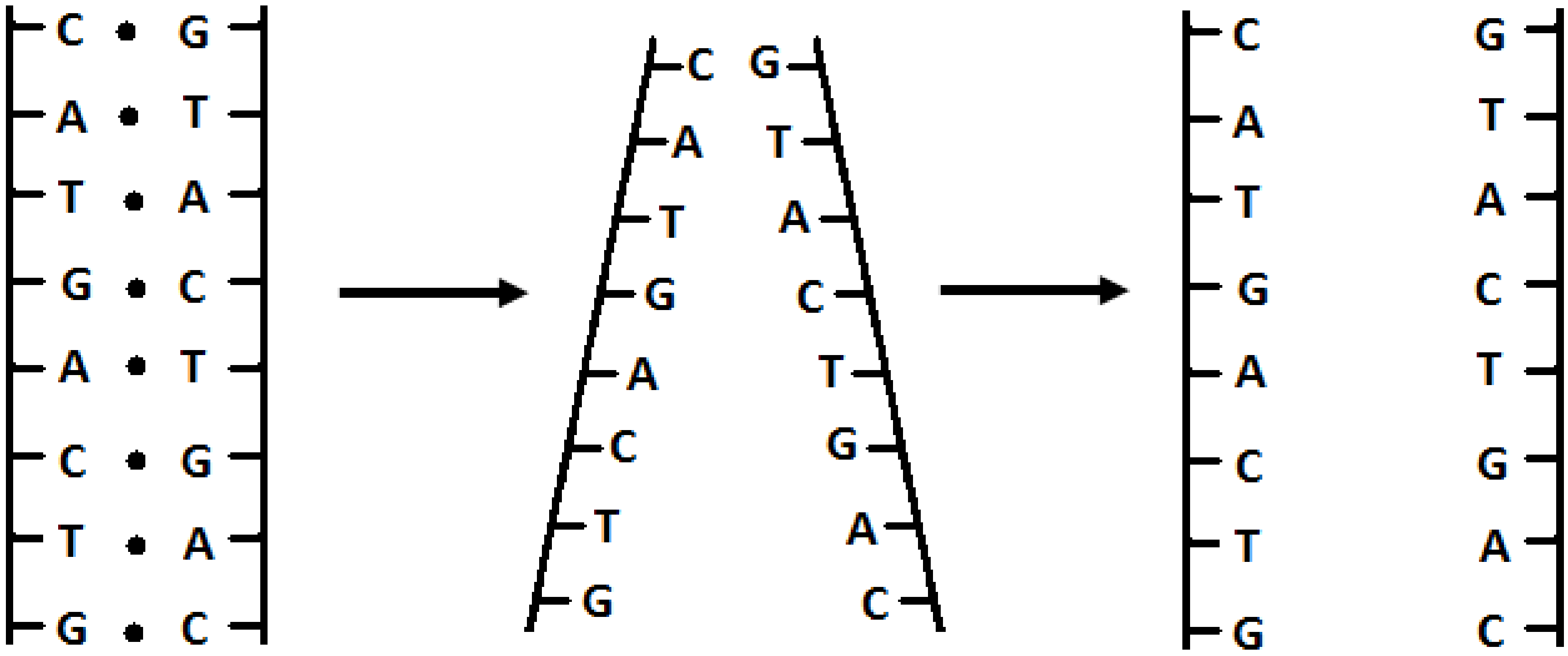
So that when the cell divides, each nucleus contains identical DNA

This process is called replication

STEP 1

Hydrogen bonds between base pairs are **broken** by the enzyme **Helicase** and DNA molecule **unzips**

DNA molecule separates into **complementary halves**

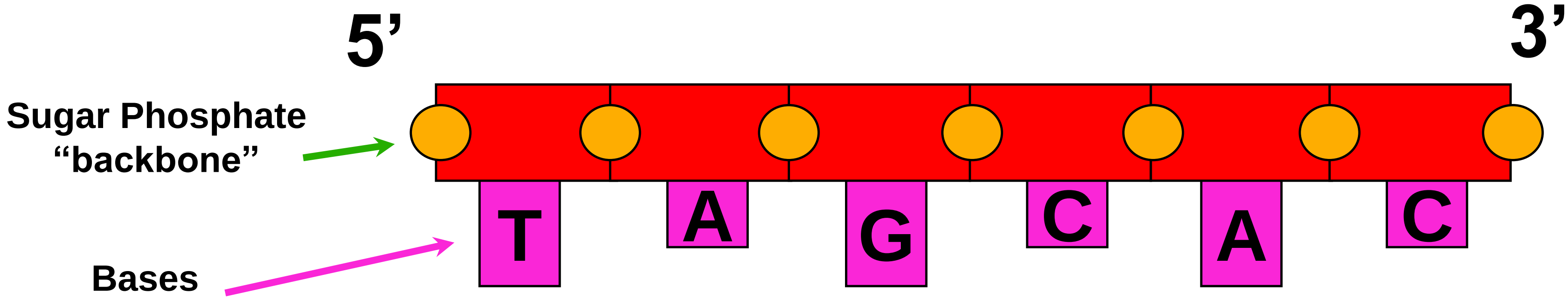


Complementarity of DNA strands

- Two chains differ in sequence

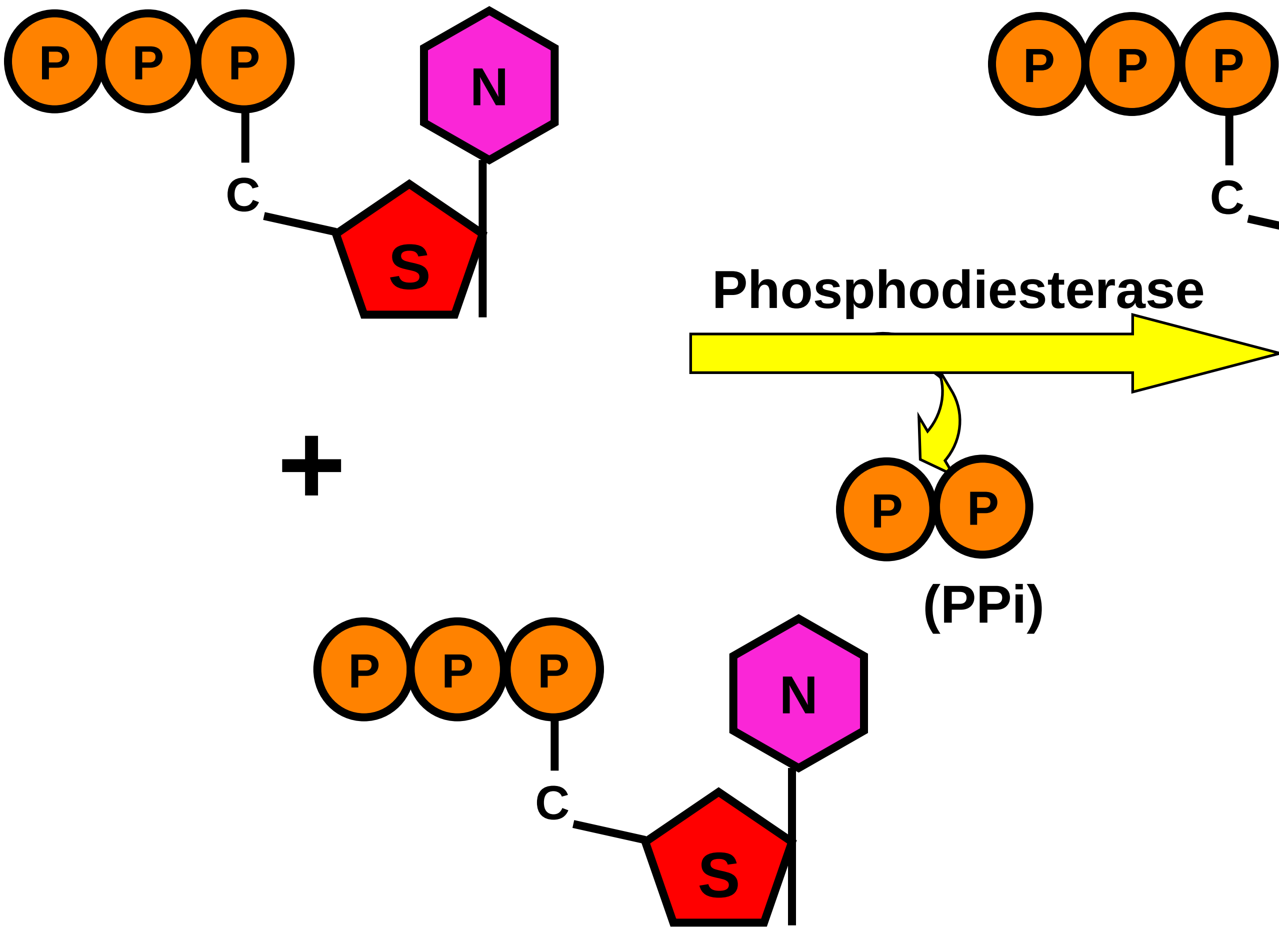
  (sequence is read from 5’ to 3’)
- Two chains are complementary
- Two chains run antiparallel

Nucleic Acid Structure
Polymerization



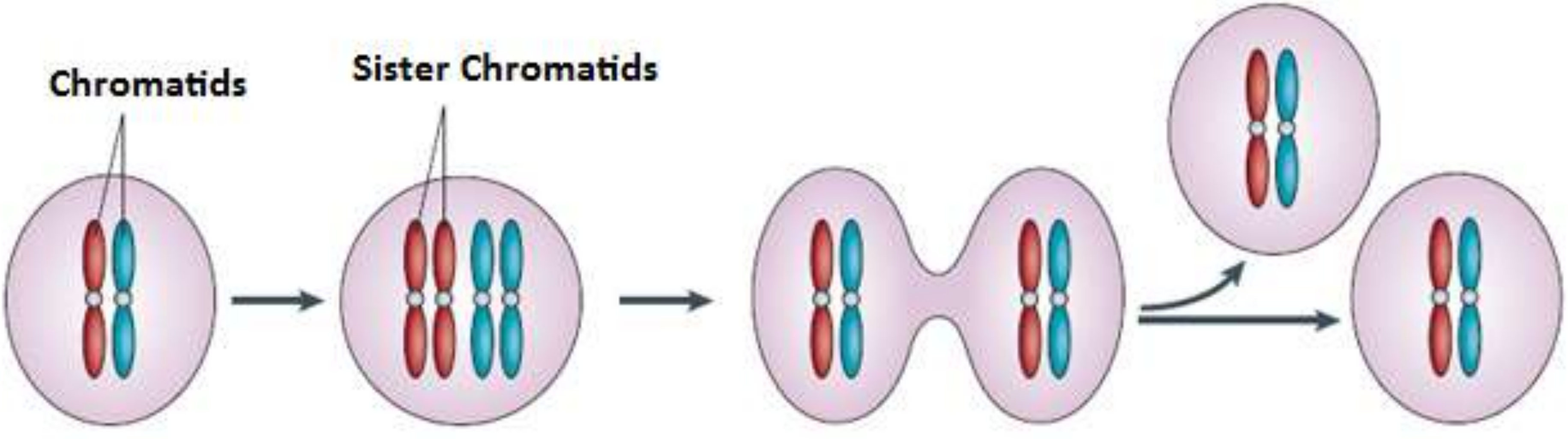
5' TAGCAC 3'

Nucleic Acid Structure
Polymerization



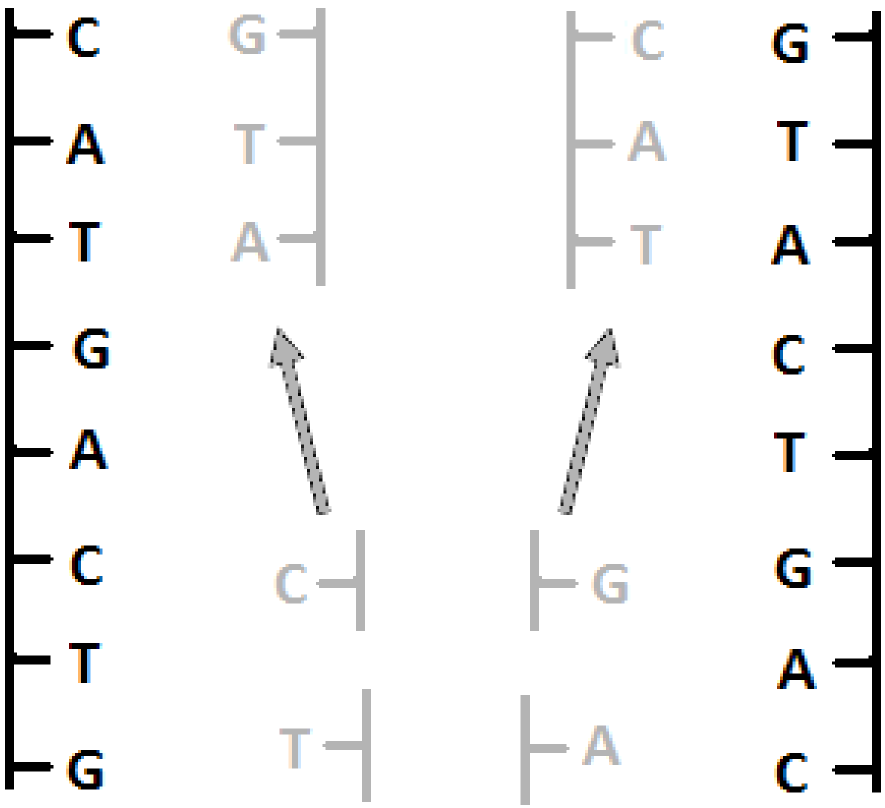
DNA Replication

- Cell division involving **mitosis** produces 2 **daughter** cells that are genetically **identical** to each other and genetically identical to the **parent** cell
- Remember that for this to happen, DNA in the parent cell must be **replicated** (copied) **before** the cell divides – this process occurs during **Interphase** in the cell cycle



STEP 2

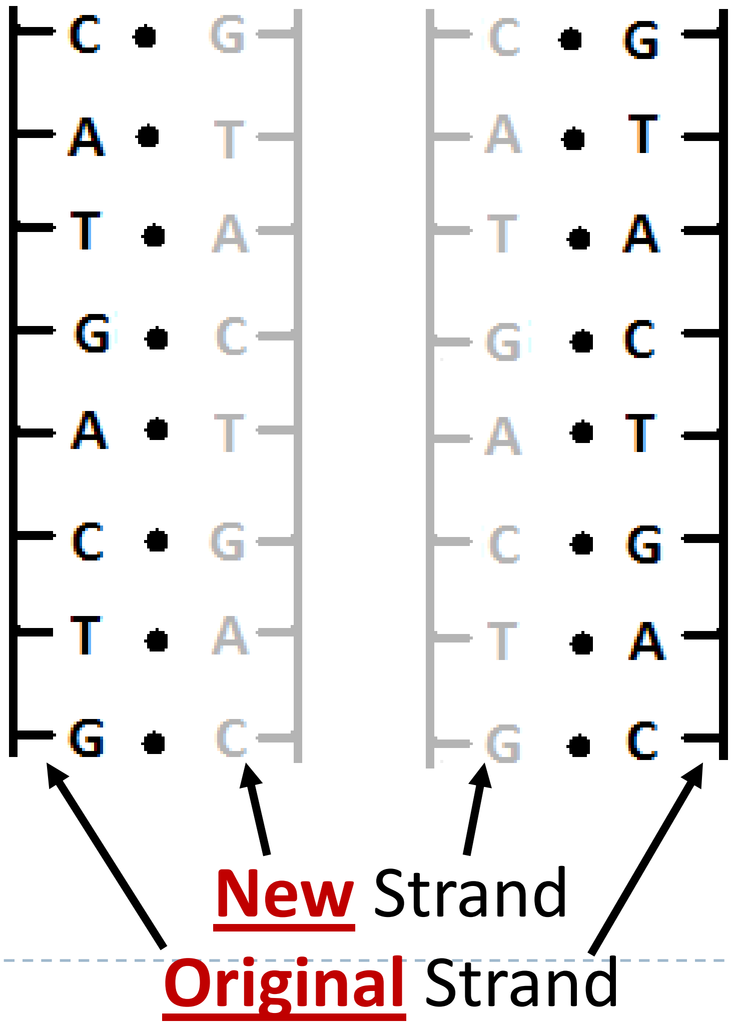
Nucleotides match up with complementary bases



Free nucleotides abundant in **nucleus**

STEP 3

Nucleotides are linked into 2 new strands of DNA by the enzyme, **polymerase**—DNA polymerase also **proofreads** for copying errors



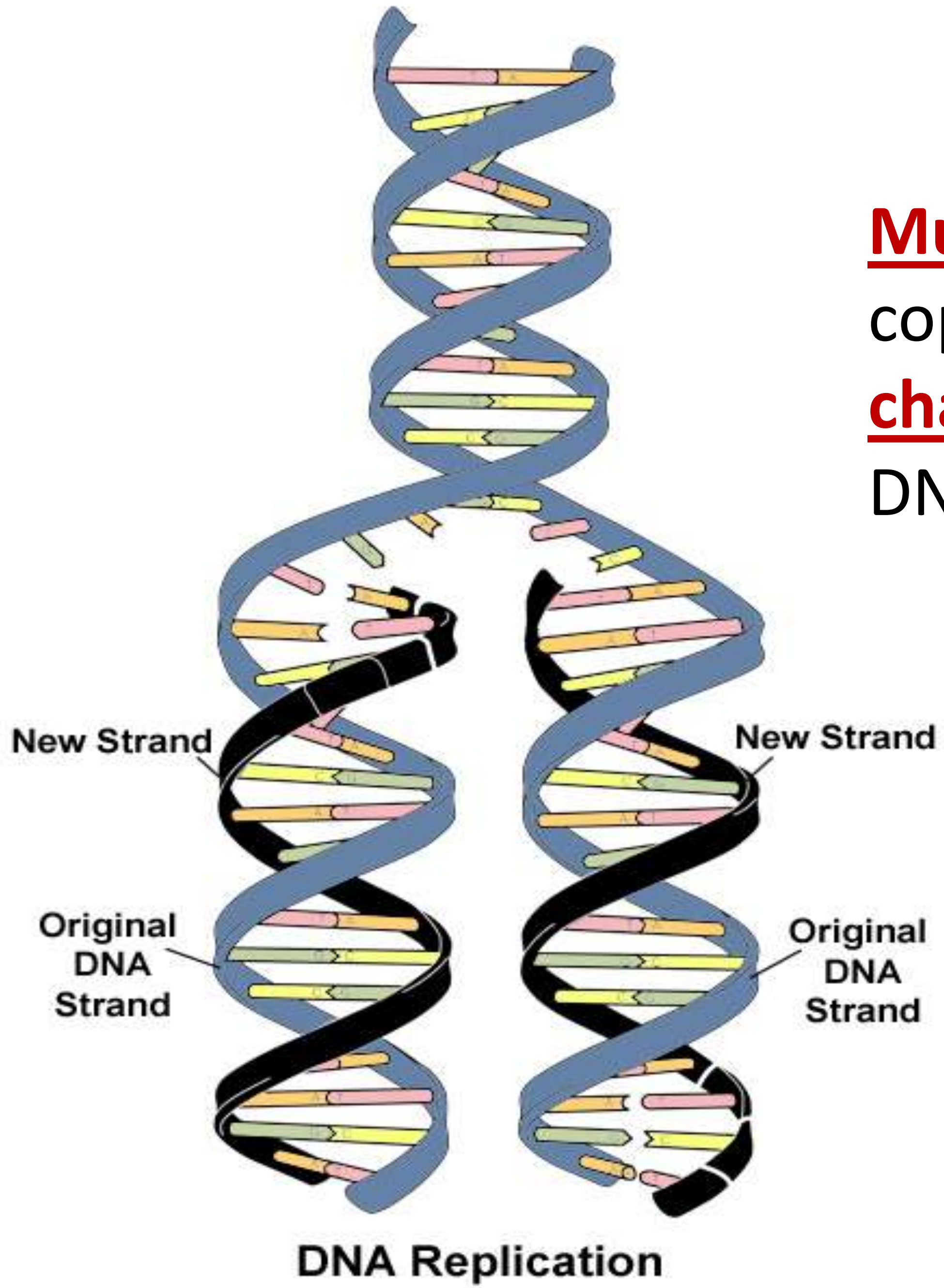
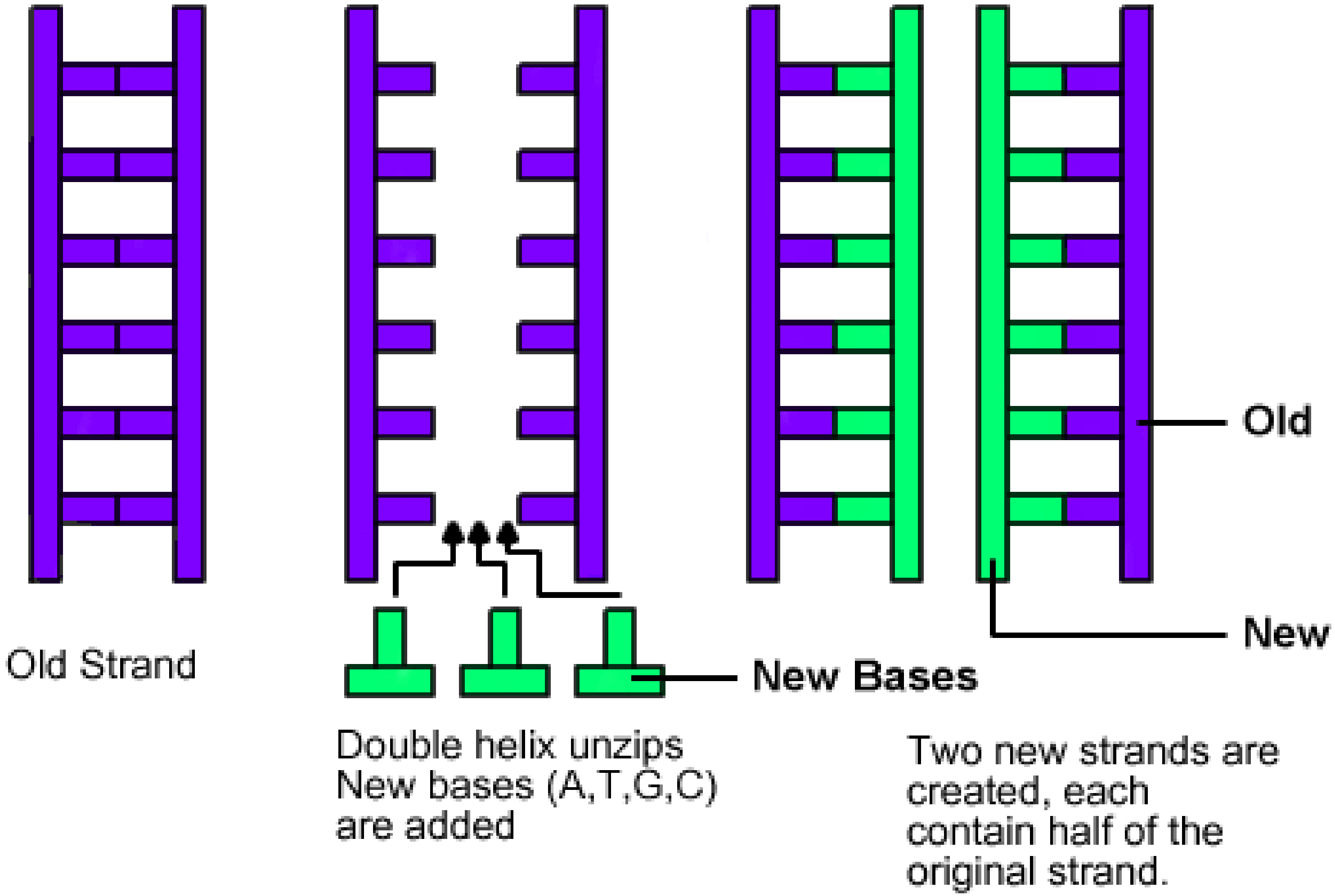


Image adapted from: National Human Genome Research Institute.

Mutations occur when copying **errors** cause a **change** in the **sequence** of DNA nucleotide bases

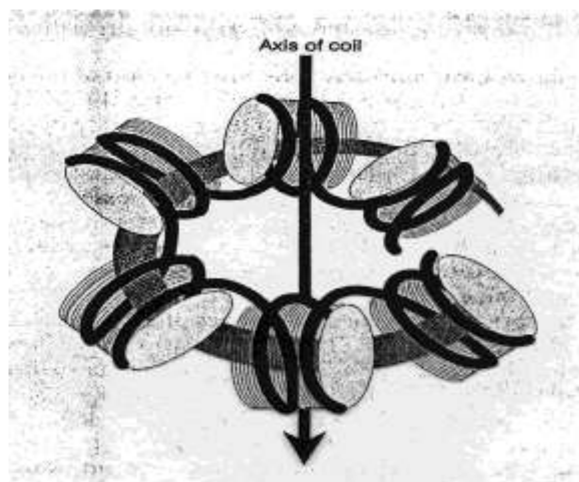
Diagram Examples of DNA Replication:

(You could see DNA replication represented different ways.)



Storage of DNA

- In **eukaryotic** cells (animals, plants, fungi) DNA is stored in the **nucleus**, which is separated from the rest of the cell by a semipermeable membrane
- The DNA is only organized into **chromosomes** during cell replication
- Between replications, the DNA is stored in a compact ball called **chromatin**, and is wrapped around proteins called **histones** to form **nucleosomes**



DNA Replication

- When a eukaryotic cell divides, the process is called **mitosis**

  - the cell splits into two identical daughter cells

  - the DNA must be replicated so that each daughter cell has a copy
- **DNA replication** involves several processes:

  - first, the DNA must be unwound, separating the two strands

  - the single strands then act as templates for synthesis of the new strands, which are complimentary in sequence

  - bases are added one at a time until two new DNA strands that exactly duplicate the original DNA are produced
- The process is called **semi-conservative replication** because one strand of each daughter DNA comes from the parent DNA and one strand is new
- The energy for the synthesis comes from hydrolysis of phosphate groups as the phosphodiester bonds form between the bases

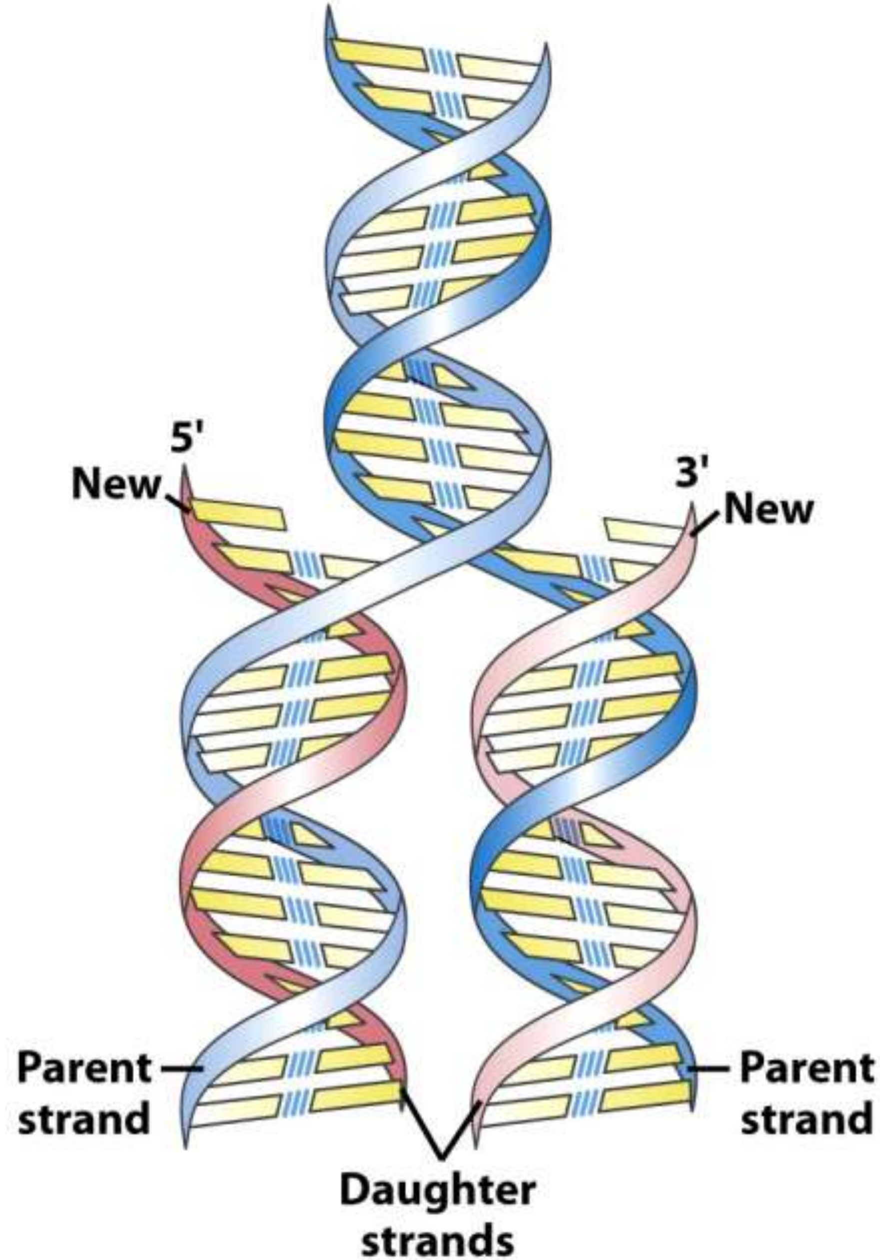
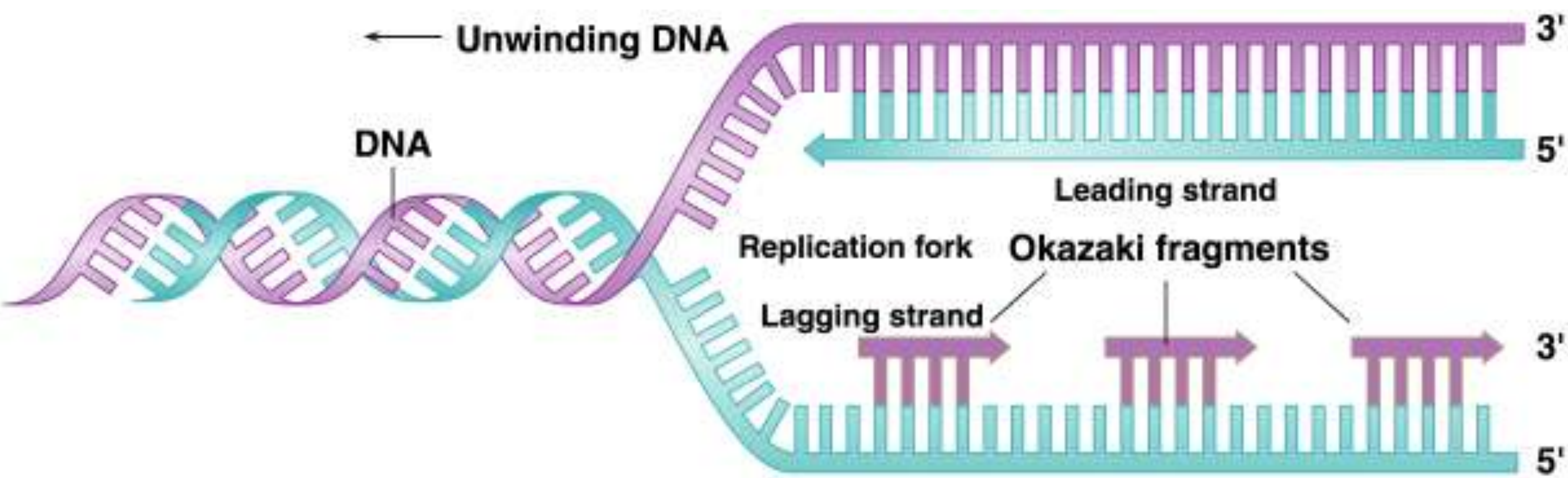
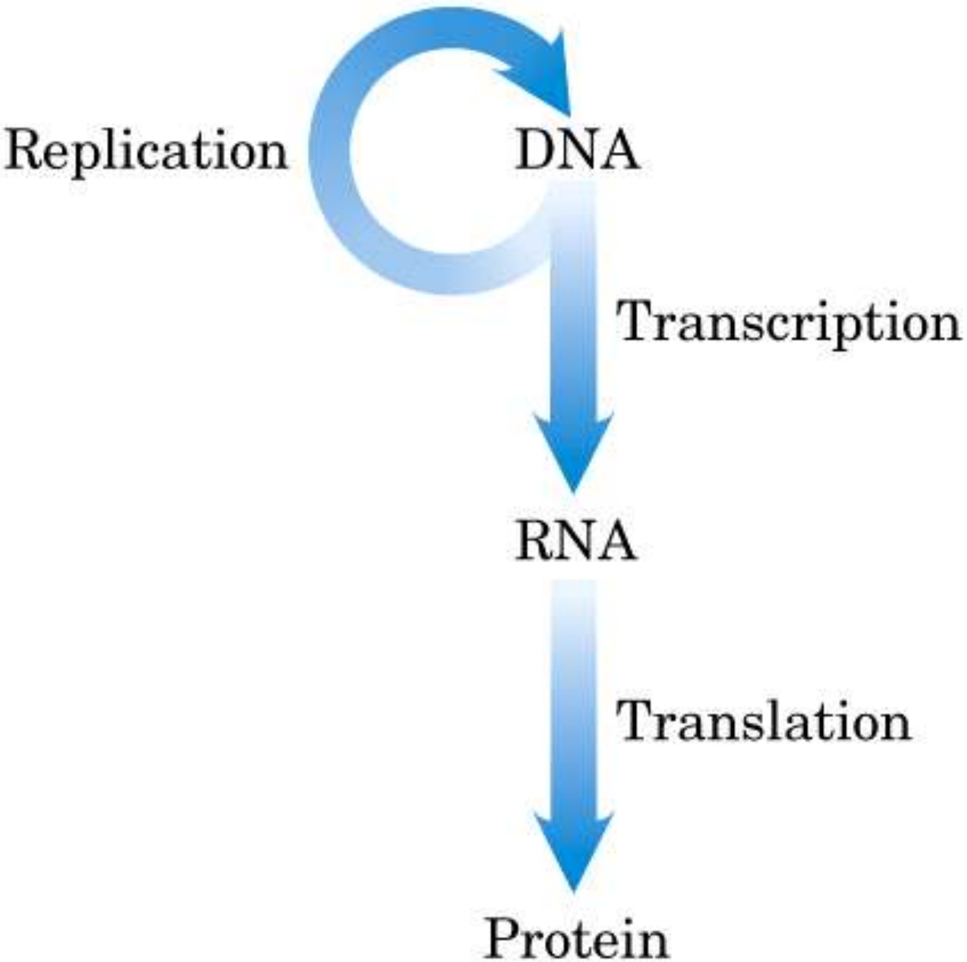


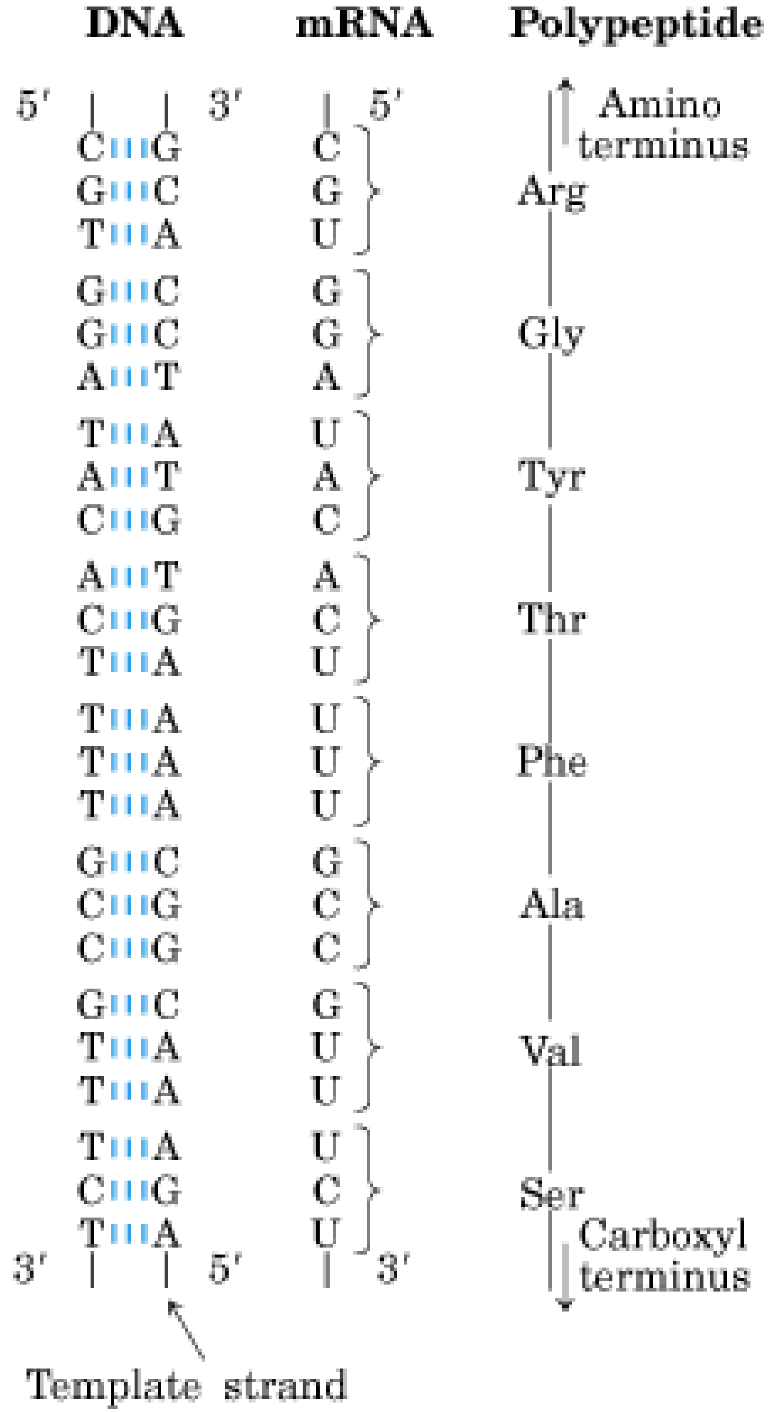
Figure 8-15
Lehninger Principles of Biochemistry, Fifth Edition

Direction of Replication

- The enzyme *helicase* unwinds several sections of parent DNA
- At each open DNA section, called a **replication fork**, DNA *polymerase* catalyzes the formation of 5'-3'ester bonds of the **leading strand**
- The **lagging strand**, which grows in the 3'-5' direction, is synthesized in short sections called **Okazaki fragments**
- The Okazaki fragments are joined by DNA *ligase* to give a single 3'-5' DNA strand




Replication
DNA
Transcription
RNA
Translation
Protein


DNA
mRNA
Polypeptide
5′
3′
5′
Amino terminus
C G C
G C G
T A U
Arg
G C G
G C G
A T A
Gly
T A U
A T A
C G C
Tyr
A T A
C G C
T A U
Thr
T A U
T A U
T A U
Phe
G C G
C G C
C G C
Ala
G C G
T A U
T A U
Val
T A U
C G C
T A U
Ser
3′
5′
3′
Carboxyl terminus
Template strand

RNA Nucleotides

Composition (3 parts):

1- Ribose sugar (with O in 3rd carbon)

2- Phosphate group

3- One of 4 types of bases (all containing nitrogen):

- Adenine
- Uracyl (only in RNA)
- Cytosine
- Guanine

Ribonucleic Acid (RNA)

- RNA is much more abundant than DNA
- There are several important differences between RNA and DNA:

  - the pentose sugar in RNA is ribose, in DNA it's deoxyribose

  - in RNA, uracil replaces the base thymine (U pairs with A)

  - RNA is single stranded while DNA is double stranded

  - RNA molecules are much smaller than DNA molecules
- There are three main types of RNA:

  - ribosomal (rRNA), messenger (mRNA) and transfer (tRNA)

Types of RNA

Table 22.3 Types of RNA Molecules

Type	Abbreviation	Percentage of Total RNA	Function in the Cell
Ribosomal RNA	rRNA	75	Major component of the ribosomes
Messenger RNA	mRNA	5–10	Carries information for protein synthesis from the DNA in the nucleus to the ribosomes
Transfer RNA	tRNA	10–15	Brings amino acids to the ribosomes for protein synthesis

Messenger RNA (mRNA)

- Its sequence is copied from genetic DNA
- It travels to ribsosomes, small granular particles in the cytoplasm of a cell where protein synthesis takes place

Ribosomal RNA (rRNA)

- Ribosomes are a complex of proteins and rRNA
- The synthesis of proteins from amino acids and ATP occurs in the ribosome
- The rRNA provides both structure and catalysis

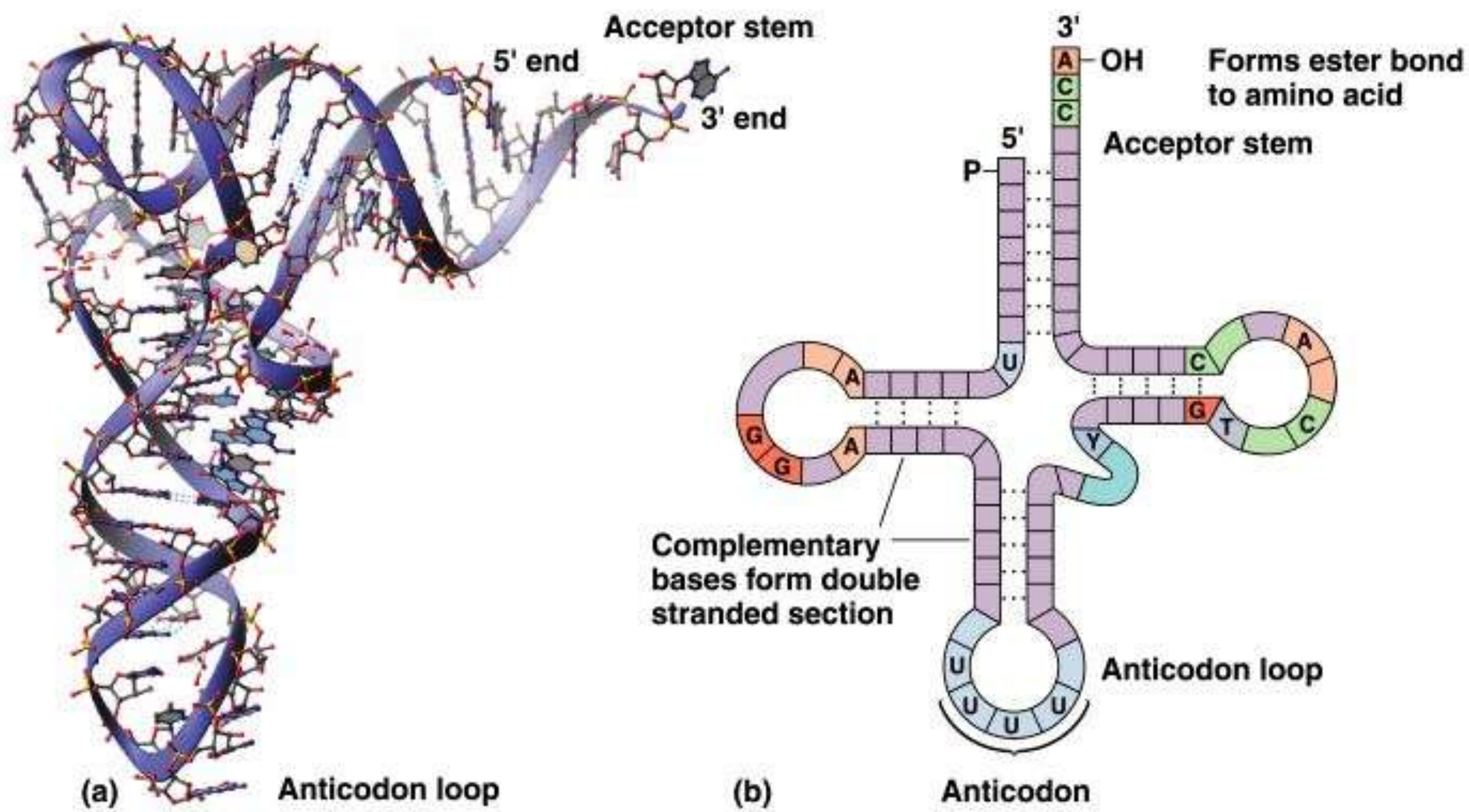
Transfer RNA (tRNA)

- Transports amino acids to the ribosomes where they are joined together to make proteins
- There is a specific tRNA for each amino acid
- Recognition of the tRNA at the anti-codon communicates which amino acid is attached

Transfer RNA

- **Transfer RNA** translates the genetic code from the messenger RNA and brings specific amino acids to the ribosome for protein synthesis
- Each amino acid is recognized by one or more specific tRNA
- tRNA has a tertiary structure that is L-shaped

  - one end attaches to the amino acid and the other binds to the mRNA by a 3-base complimentary sequence



Ribosomal RNA and Messenger RNA

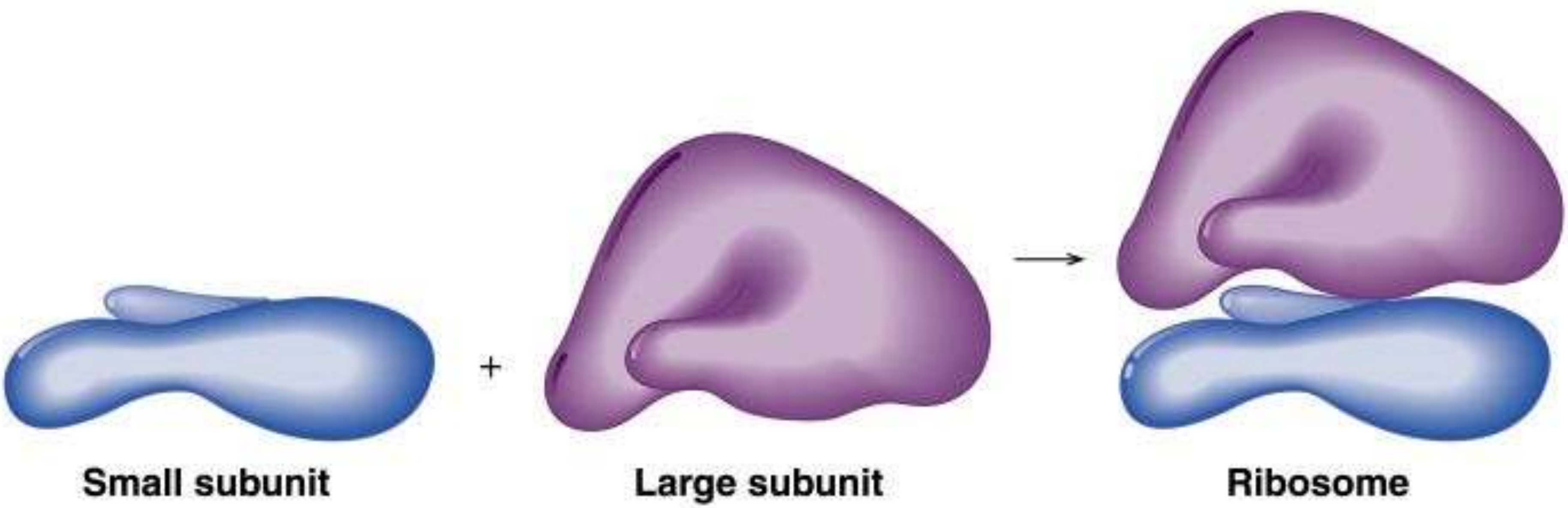
- **Ribosomes** are the sites of protein synthesis

  - they consist of **ribosomal DNA** (65%) and proteins (35%)

  - they have two subunits, a large one and a small one

- **Messenger RNA** carries the genetic code to the ribosomes

  - they are strands of RNA that are complementary to the DNA of the gene for the protein to be synthesized



How DNA Works

1- DNA stores genetic information in segments called genes

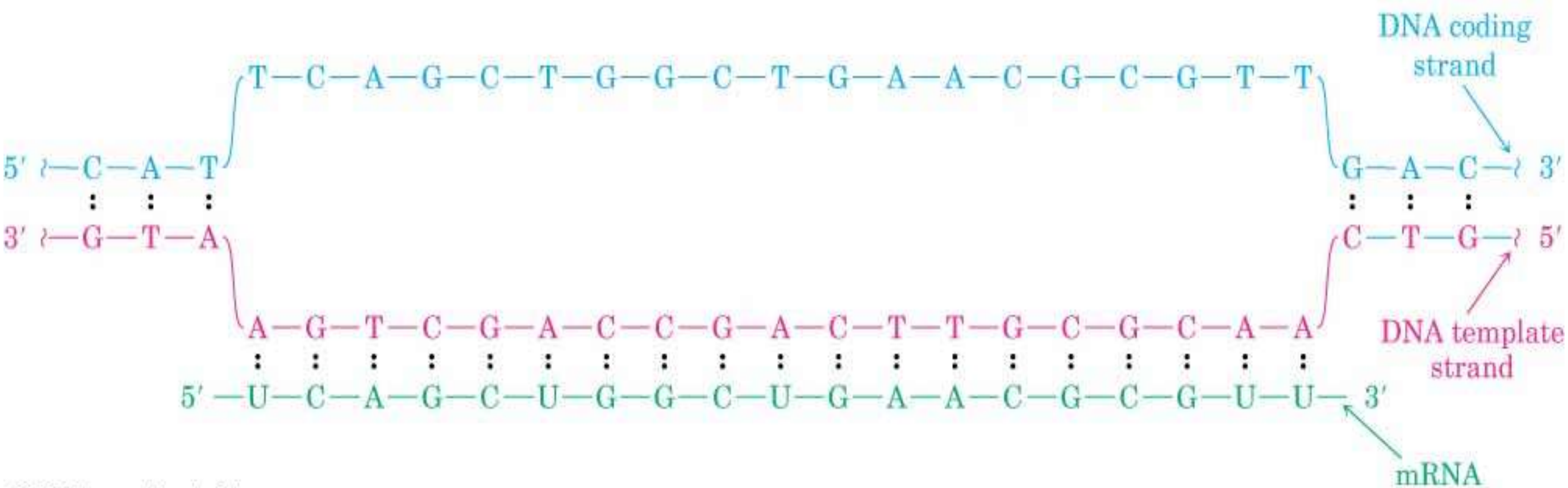
2- The DNA code is in Triplet Codons (short sequences of 3 nucleotides each)

3- Certain codons are translated by the cell into certain Amino acids.

4. Thus, the sequence of nucleotides in DNA indicate a sequence of Amino acids in a protein.

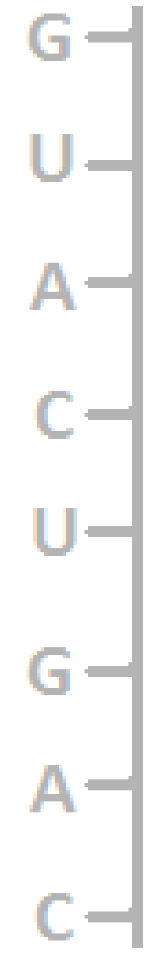
Transcription Process

- Several turns of the DNA double helix unwind, exposing the bases of the two strands
- Ribonucleotides line up in the proper order by hydrogen bonding to their complementary bases on DNA
- Bonds form in the $5' \rightarrow 3'$ direction,



RNA—**Ribonucleic Acid**

- RNA is a **messenger** that allows the **instruction of DNA** to be delivered to the **rest of the cell**
- RNA is different than DNA:
  1. The sugar in RNA is **ribose**; the sugar in DNA is **deoxyribose**
  2. RNA is a **single strand** of nucleotides; DNA is a **double strand** of nucleotides
  3. RNA has **Uracil** (U) instead of **Thymine** (T) which is in DNA
  4. RNA is found **inside and outside** of the **nucleus**; DNA is found **only inside** the nucleus

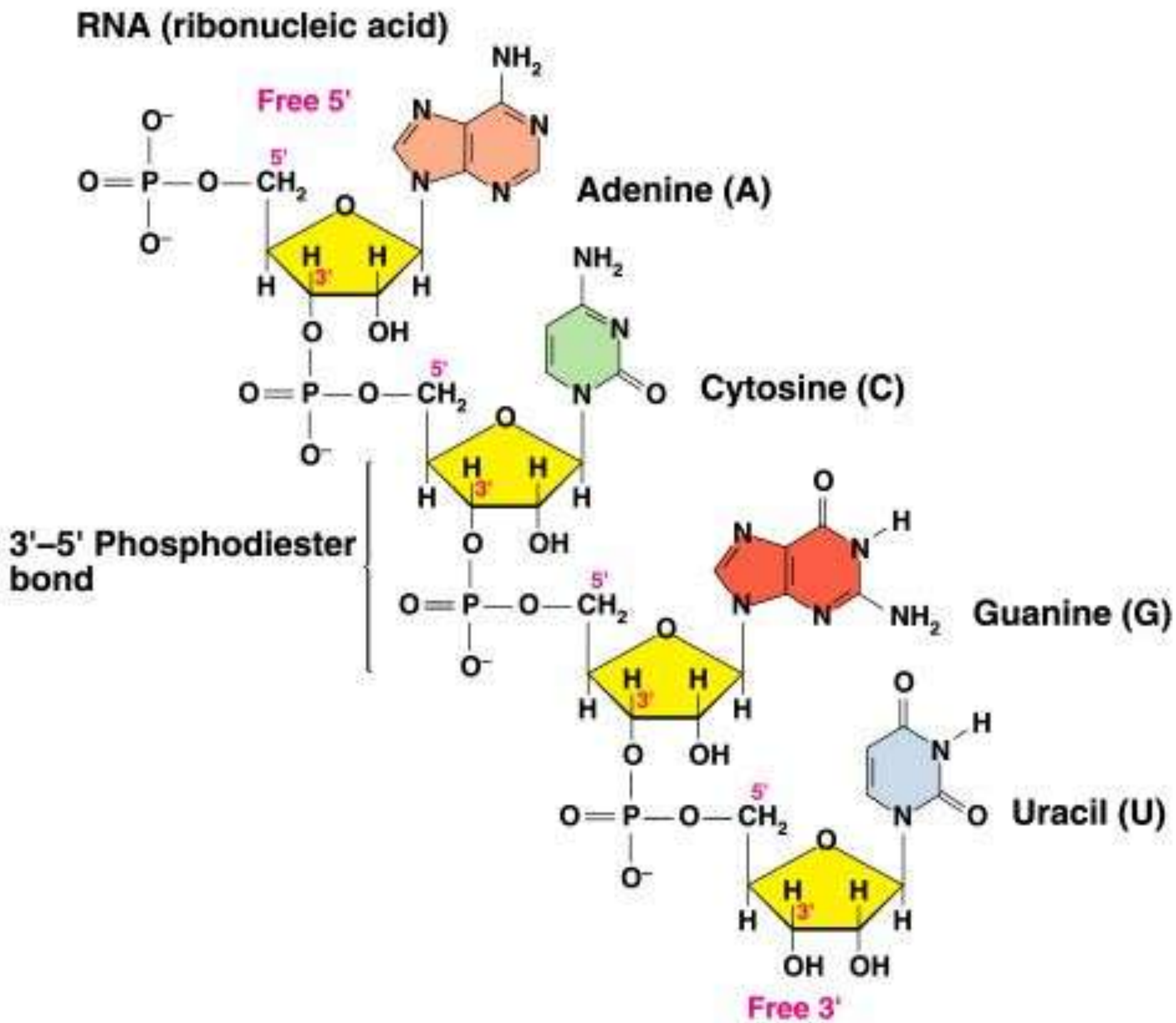


Transcription of RNA from DNA

- Only one of the two DNA strands is transcribed into mRNA
- The strand that contains the gene is the coding or sense strand
- The strand that gets transcribed is the template or antisense strand
- The RNA molecule produced during transcription is a copy of the coding strand (with U in place of T)

Example of RNA Primary Structure

- In RNA, A, C, G, and U are linked by 3'-5' ester bonds between ribose and phosphate



The Parts of Transfer RNA

- There are 61 different tRNAs, one for each of the 61 codons that specifies an amino acid
- tRNA has 70-100 ribonucleotides and is bonded to a specific amino acid by an ester linkage through the 3′ hydroxyl on ribose at the 3′ end of the tRNA
- Each tRNA has a segment called an anticodon, a sequence of three ribonucleotides complementary to the codon sequence

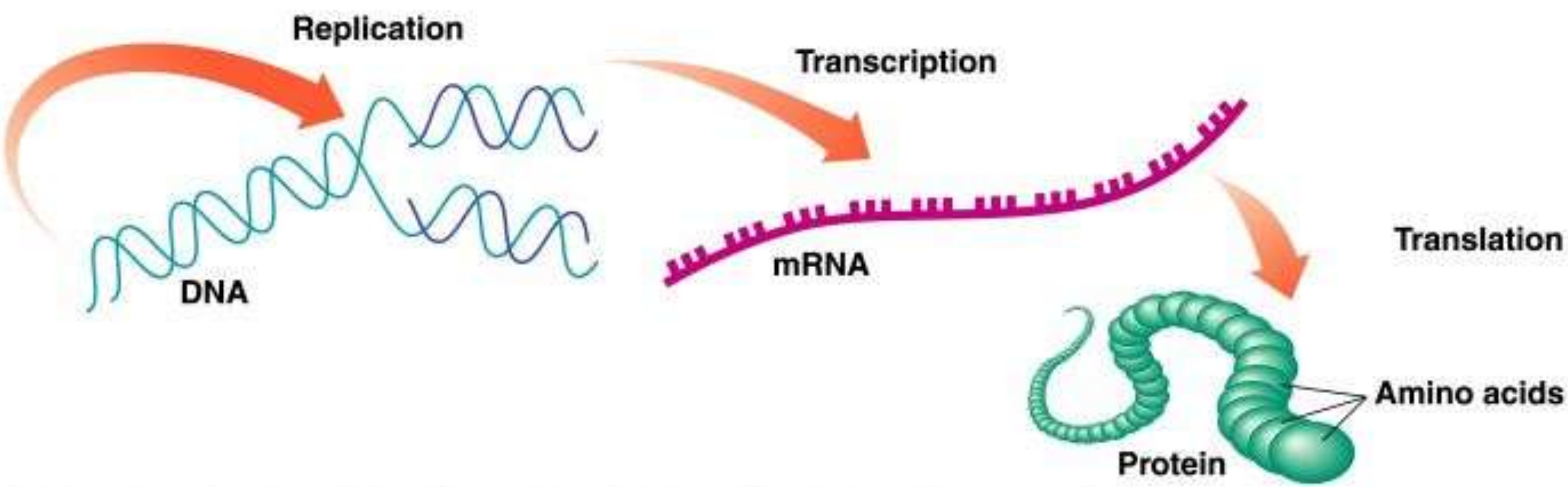
Protein Synthesis

- The two main processes involved in **protein synthesis** are

  - the formation of mRNA from DNA **(transcription)**

  - the conversion by tRNA to protein at the ribosome (**translation**)

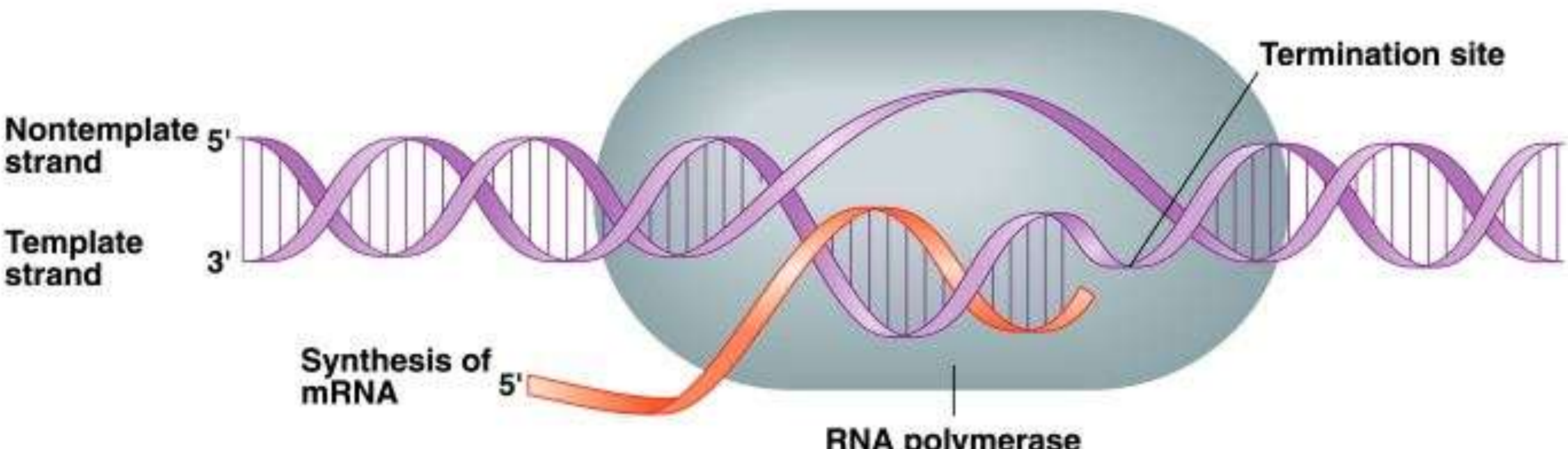
- Transcription takes place in the nucleus, while translation takes place in the cytoplasm
- Genetic information is transcribed to form mRNA much the same way it is replicated during cell division



Timberlake, *General, Organic, and Biological Chemistry.*

RNA Polymerase

- During transcription, RNA *polymerase* moves along the DNA template in the 3’-5’direction to synthesize the corresponding mRNA
- The mRNA is released at the termination point

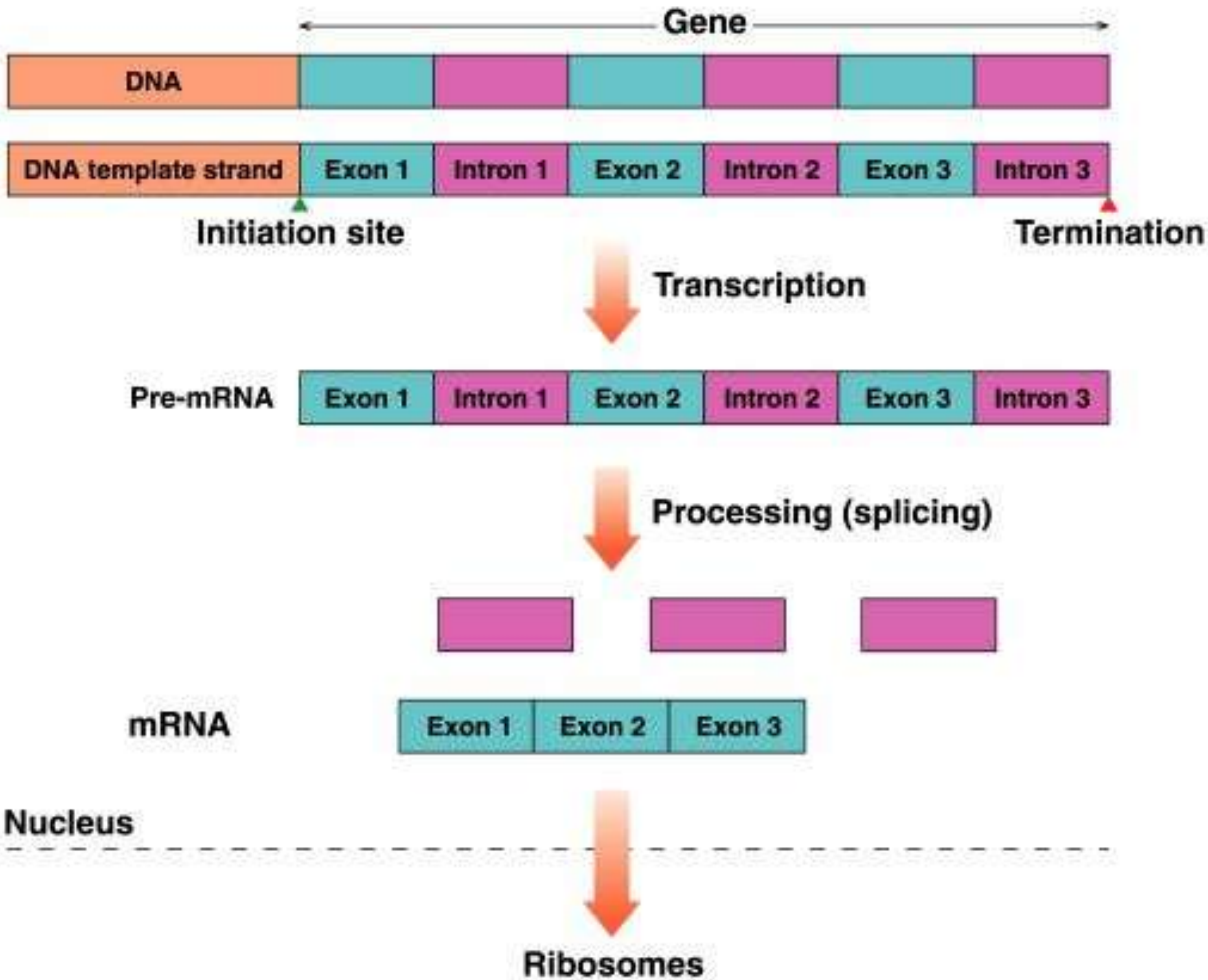


Timberlake, *General, Organic, and Biological Chemistry*.

Processing of mRNA

- **Genes** in the DNA of eukaryotes contain **exons** that code for proteins along with **introns** that do not
- Because the initial mRNA, called a **pre-RNA**, includes the noncoding introns, it must be processed before it can be read by the tRNA
- While the mRNA is still in the nucleus, the introns are removed from the pre-RNA
- The exons that remain are joined to form the mRNA that leaves the nucleus with the information for the synthesis of protein

Removing Introns from mRNA



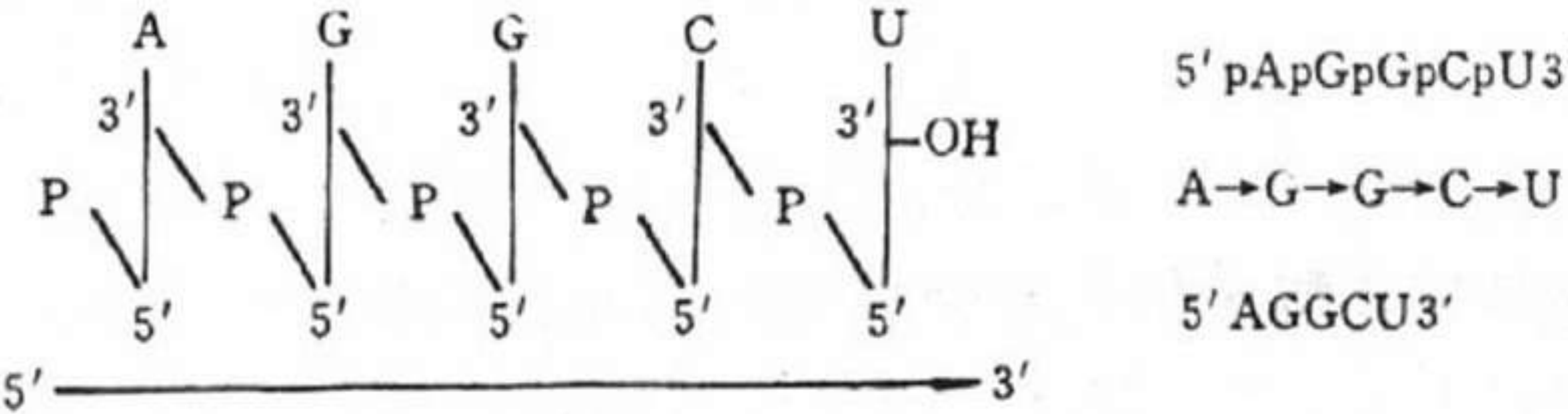


图 3-8 核酸简式

Transcription

- Several steps occur during **transcription**:

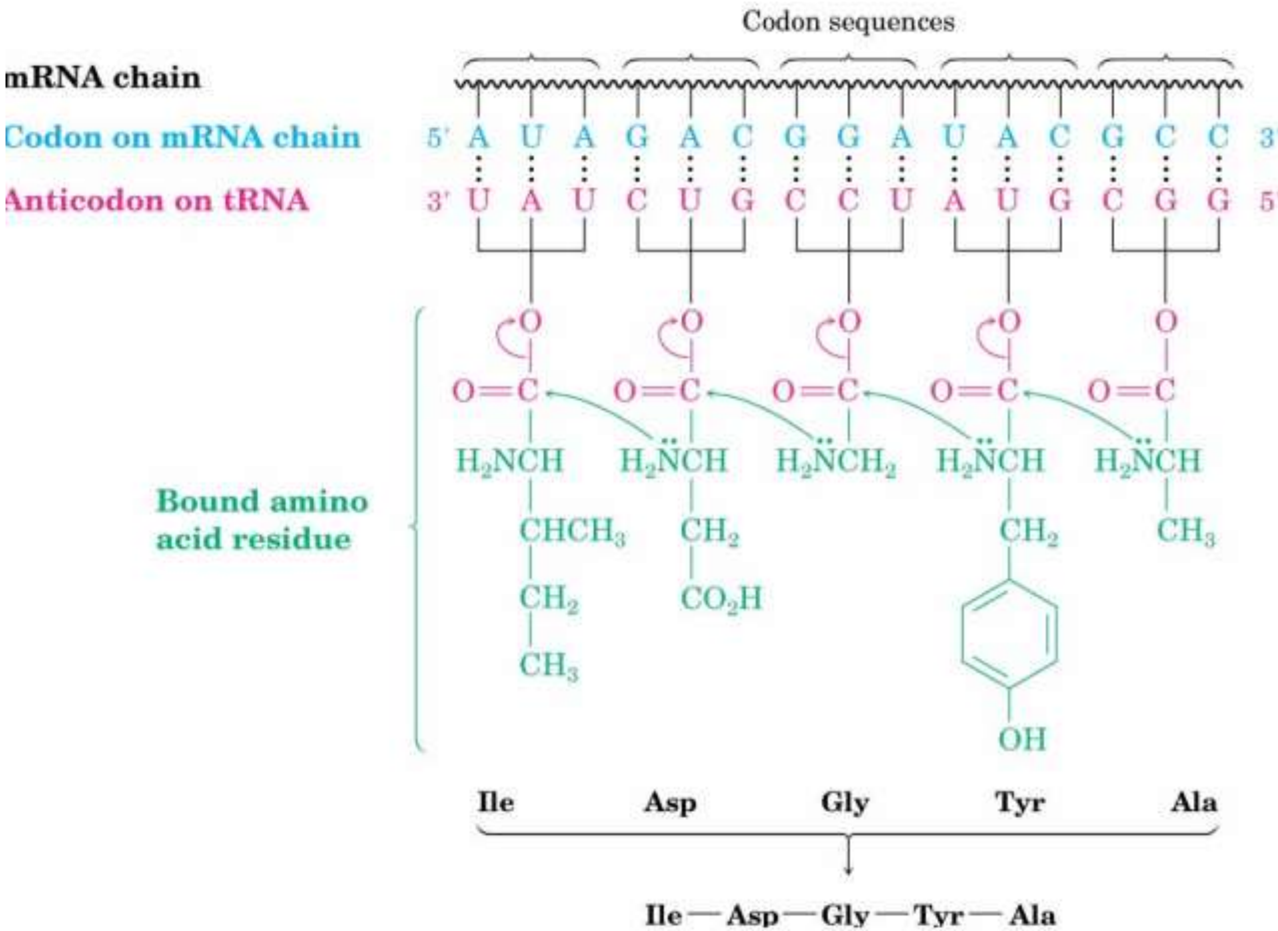
- a section of DNA containing the gene unwinds

- one strand of DNA is copied starting at the initiation point, which has the sequence TATAAA

- an mRNA is synthesized using complementary base pairing with uracil (U) replacing thymine (T)

- the newly formed mRNA moves out of the nucleus to ribosomes in the cytoplasm and the DNA re-winds

The Structure of tRNA



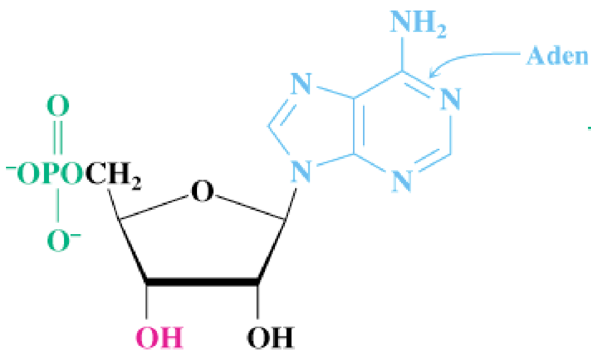
Regulation of Transcription

- A specific mRNA is synthesized when the cell requires a particular protein
- The synthesis is regulated at the transcription level:

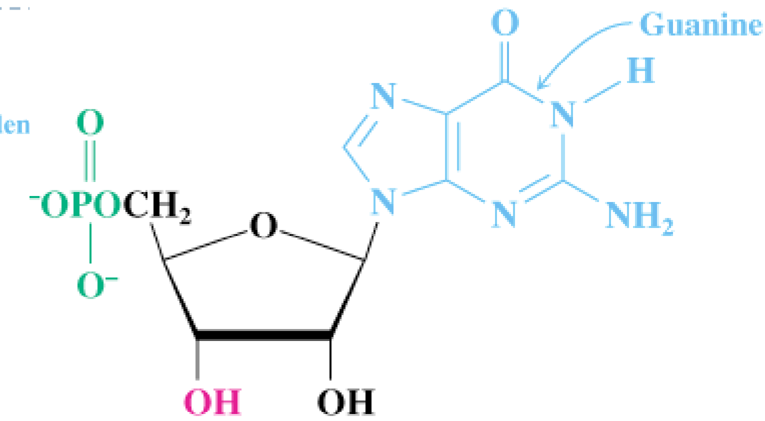
  - **feedback control**, where the end products speed up or slow the synthesis of mRNA

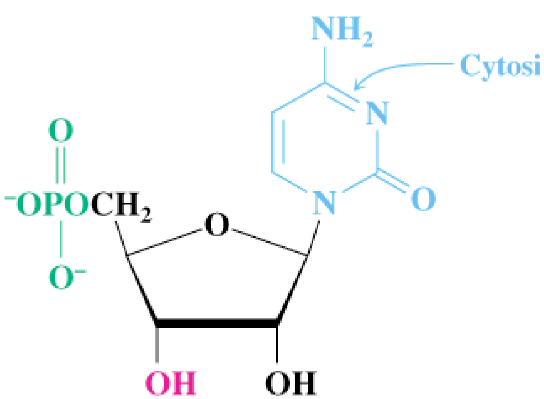
  - **enzyme induction**, where a high level of a reactant induces the transcription process to provide the necessary enzymes for that reactant
- Regulation of transcription in eukaryotes is complicated and we will not study it here

The Ribonucleotides

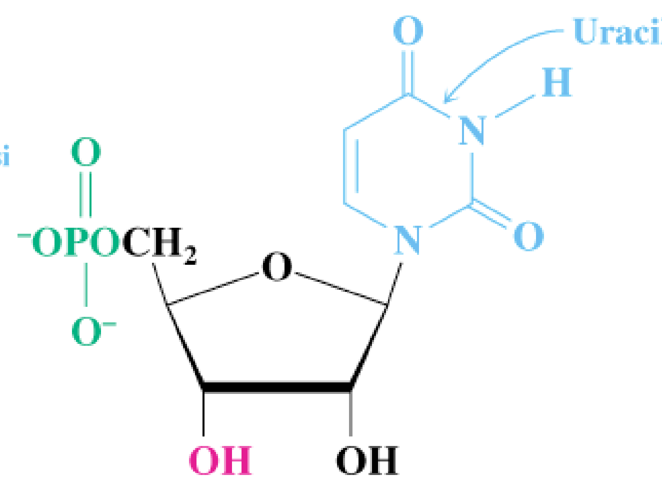


Adenosine 5'-phosphate





Cytidine 5'-phosphate



Uridine 5'-phosphate

The Genetic Code

- The **genetic code** is found in the sequence of nucleotides in mRNA that is translated from the DNA
- A **codon** is a **triplet** of bases along the mRNA that codes for a particular amino acid
- Each of the 20 amino acids needed to build a protein has at least 2 codons
- There are also codons that signal the "start" and "end" of a polypeptide chain
- The amino acid sequence of a protein can be determined by reading the triplets in the DNA sequence that are complementary to the codons of the mRNA, or directly from the mRNA sequence
- The entire DNA sequence of several organisms, including humans, have been determined, however,

  - only primary structure can be determined this way

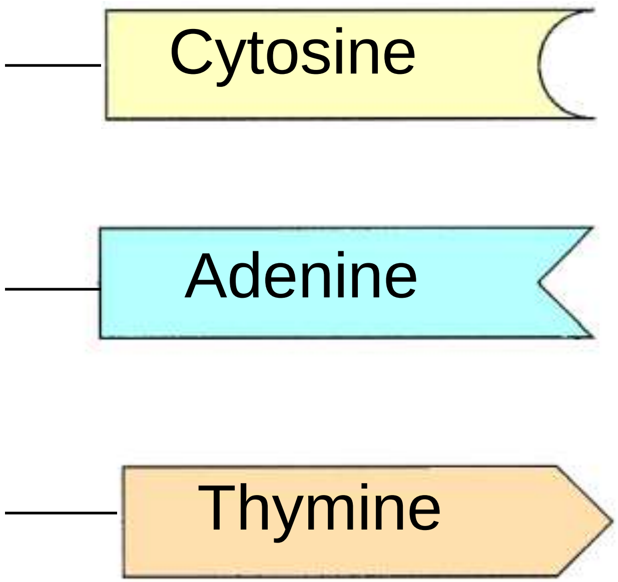
  - doesn't give tertiary structure or protein function

The sequence of bases in DNA forms the Genetic Code

**A group of three bases (a triplet) controls
the production of a particular amino acid in
the cytoplasm of the cell**

The different amino acids and the order in which they are joined up determines the sort of protein being produced

For example



Codes for **Valine**

Cytosine (C)
Guanine (G)
Adenine (A)

Codes for **Alanine**

This is known as the **triplet code**

Each triplet codes for a specific amino acid

CGA - CAA - CCA - CCA - GCT - GGG - GAG - CCA -

Ala Val Gly Gly Arg Pro Leu Gly

The amino acids are joined together in the correct sequence to make part of a protein

—Ala—Val— Gly— Gly—Arg— Pro— Leu—Gly—

mRNA Codons and Associated Amino Acids

First Letter	Second Letter: U		Second Letter: C		Second Letter: A		Second Letter: G		Third Letter
U	UUU	Phe	UCU	Ser	UAU	Tyr	UGU	Cys	U
	UUC	Phe	UCC	Ser	UAC	Tyr	UGC	Cys	C
	UUA	Leu	UCA	Ser	UAA	STOP	UGA	STOP	A
	UUG	Leu	UCG	Ser	UAG	STOP	UGG	Trp	G
C	CUU	Leu	CCU	Pro	CAU	His	CGU	Arg	U
	CUC	Leu	CCC	Pro	CAC	His	CGC	Arg	C
	CUA	Leu	CCA	Pro	CAA	Gln	CGA	Arg	A
	CUG	Leu	CCG	Pro	CAG	Gln	CGG	Arg	G
A	AUU	Ile	ACU	Thr	AAU	Asn	AGU	Ser	U
	AUC	Ile	ACC	Thr	AAC	Asn	AGC	Ser	C
	AUA	Ile	ACA	Thr	AAA	Lys	AGA	Arg	A
	[a]AUG	Met/start	ACG	Thr	AAG	Lys	AGG	Arg	G
G	GUU	Val	GCU	Ala	GAU	Asp	GGU	Gly	U
	GUC	Val	GCC	Ala	GAC	Asp	GGC	Gly	C
	GUA	Val	GCA	Ala	GAA	Glu	GGA	Gly	A
	GUG	Val	GCG	Ala	GAG	Glu	GGG	Gly	G

[a] Codon that signals the start of a peptide chain.
STOP codons signal the end of a peptide chain.

Reading the Genetic Code

- Suppose we want to determine the amino acids coded for in the following section of a mRNA

  5'—CCU —AGC—GGA—CUU—3'

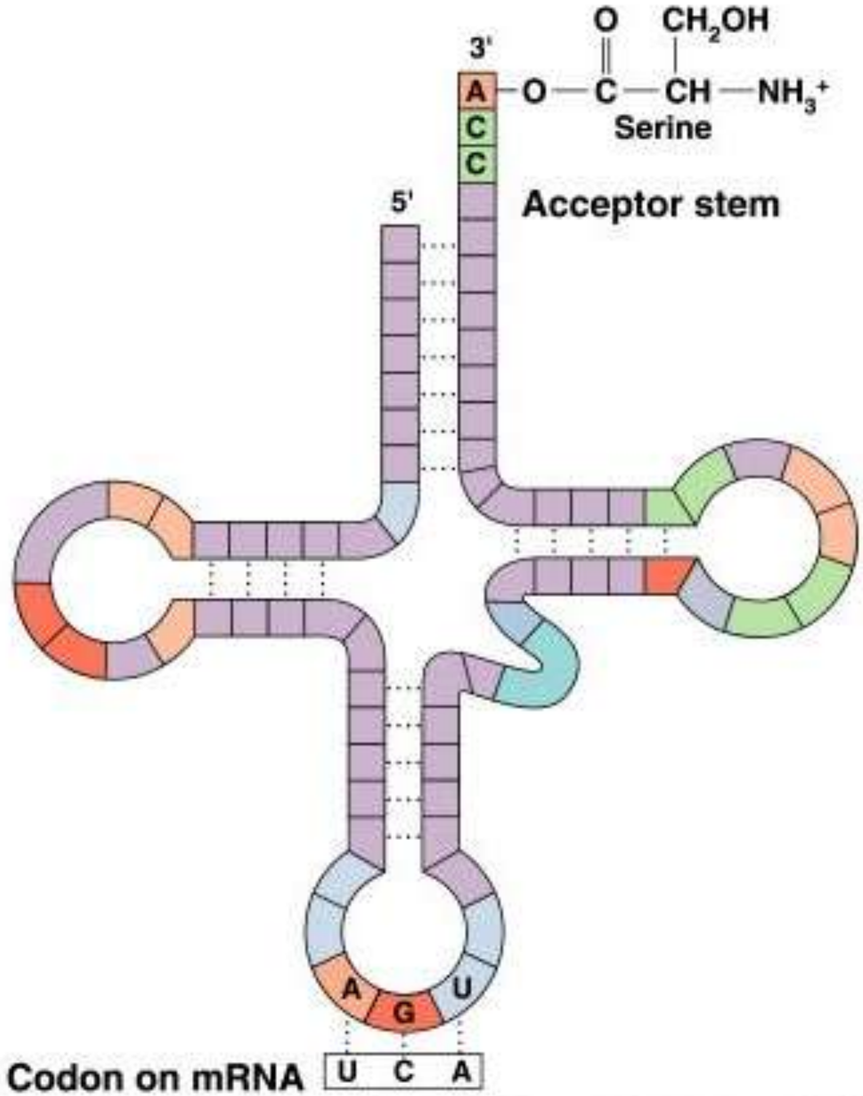
- According to the genetic code, the amino acids for these codons are:

  CCU = Proline AGC = Serine
  GGA = Glycine CUU = Leucine

- The mRNA section codes for the amino acid sequence of Pro—Ser—Gly—Leu

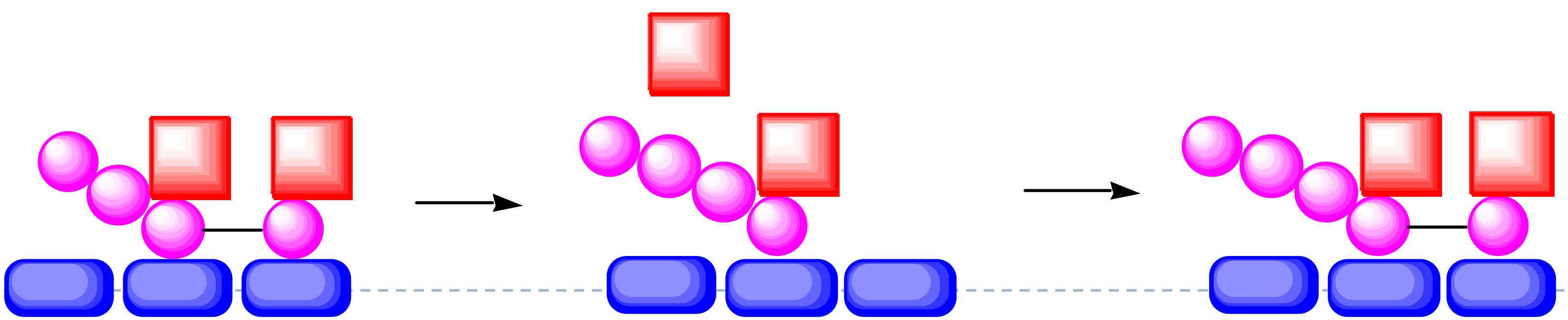
Translation and tRNA Activation

- Once the DNA has been transcribed to mRNA, the codons must be tranlated to the amino acid sequence of the protein
- The first step in **translation** is activation of the tRNA
- Each tRNA has a triplet called an **anticodon** that complements a codon on mRNA
- A *synthetase* uses ATP hydrolysis to attach an amino acid to a specific tRNA



Initiation and Translocation

- Initiation of protein synthesis occurs when a mRNA attaches to a ribosome
- On the mRNA, the **start codon (AUG)** binds to a tRNA with methionine
- The second codon attaches to a tRNA with the next amino acid
- A peptide bond forms between the adjacent amino acids at the first and second codons
- The first tRNA detaches from the ribosome and the ribosome shifts to the adjacent codon on the mRNA (this process is called **translocation**)
- A third codon can now attach where the second one was before translocation



Termination

- After a polypeptide with all the amino acids for a protein is synthesized, the ribosome reaches the the **"stop" codon**: UGA, UAA, or UAG
- There is no tRNA with an anticodon for the "stop" codons
- Therefore, protein synthesis ends (**termination**)
- The polypeptide is released from the ribosome and the protein can take on it's 3-D structure

  (some proteins begin folding while still being synthesized, while others do not fold up until after being released from the ribosome)

The proteins build the cell structures

They also make enzymes

The DNA controls which enzymes are made and the enzymes determine what reactions take place

The structures and reactions in the cell determine what sort of a cell it is and what its function is

So DNA exerts its control through the enzymes

A sequence of triplets in the DNA molecule may code for a complete protein

Such a sequence forms a **gene**

There may be a thousand or more bases in one gene

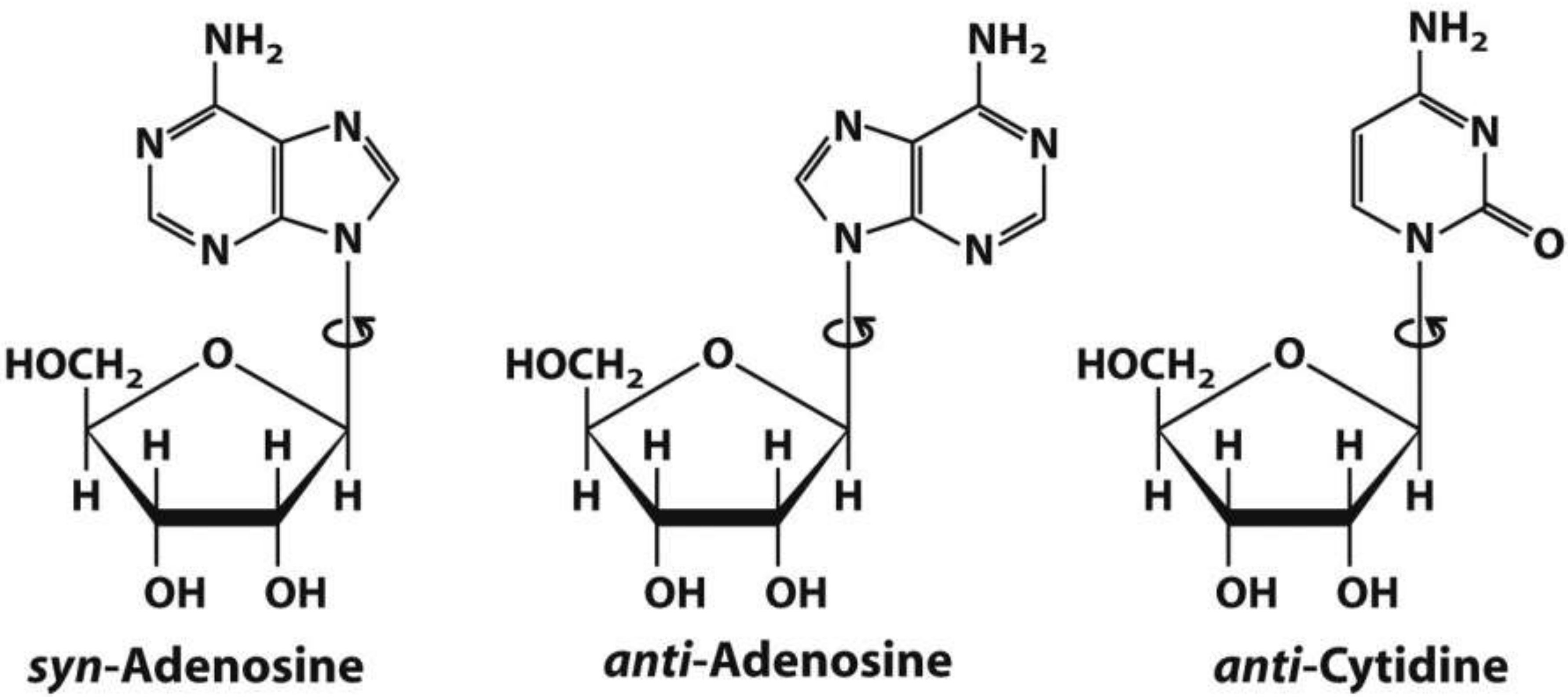
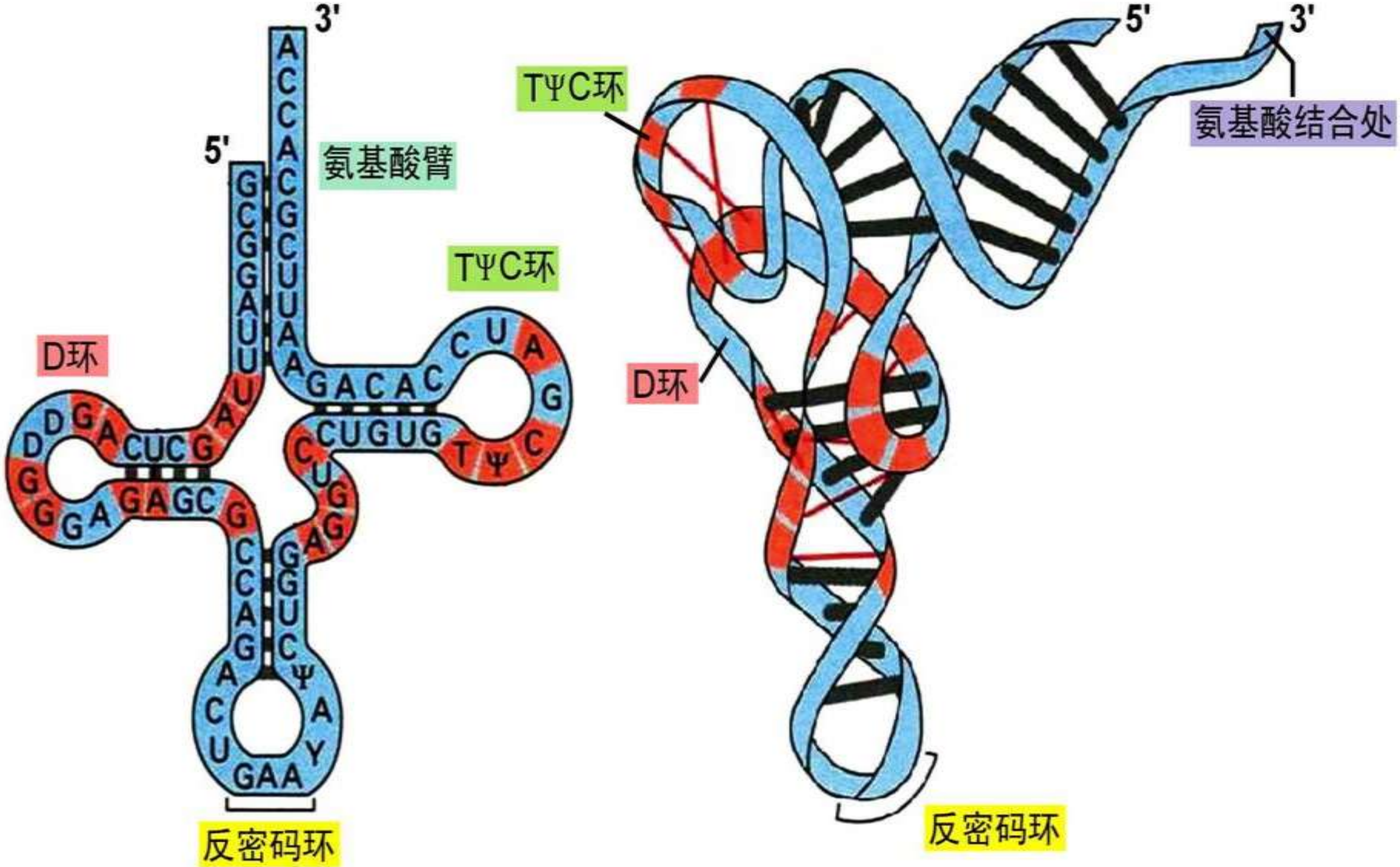


Figure 8-16b
Lehninger Principles of Biochemistry, Fifth Edition



(A)　　(B)

图3-16　tRNA的二级(A)及三级结构(B)

Conformation around *N*-Glycosidic Bond

- Relatively free rotation can occur around the N-glycosidic bond in free nucleotides
- The torsion angle about the N-glycosidic bond (N-C1') is denoted by the symbol χ
- The sequence of atoms chosen to define this angle is O4'-C1'-N9-C4 for purine,

  and O4'-C1'-N1-C2 for pyrimidine derivatives
- Angle near 0°corresponds to *syn* conformation
- Angle near 180° corresponds to *anti* conformation
- Anti conformation is found in normal B-DNA

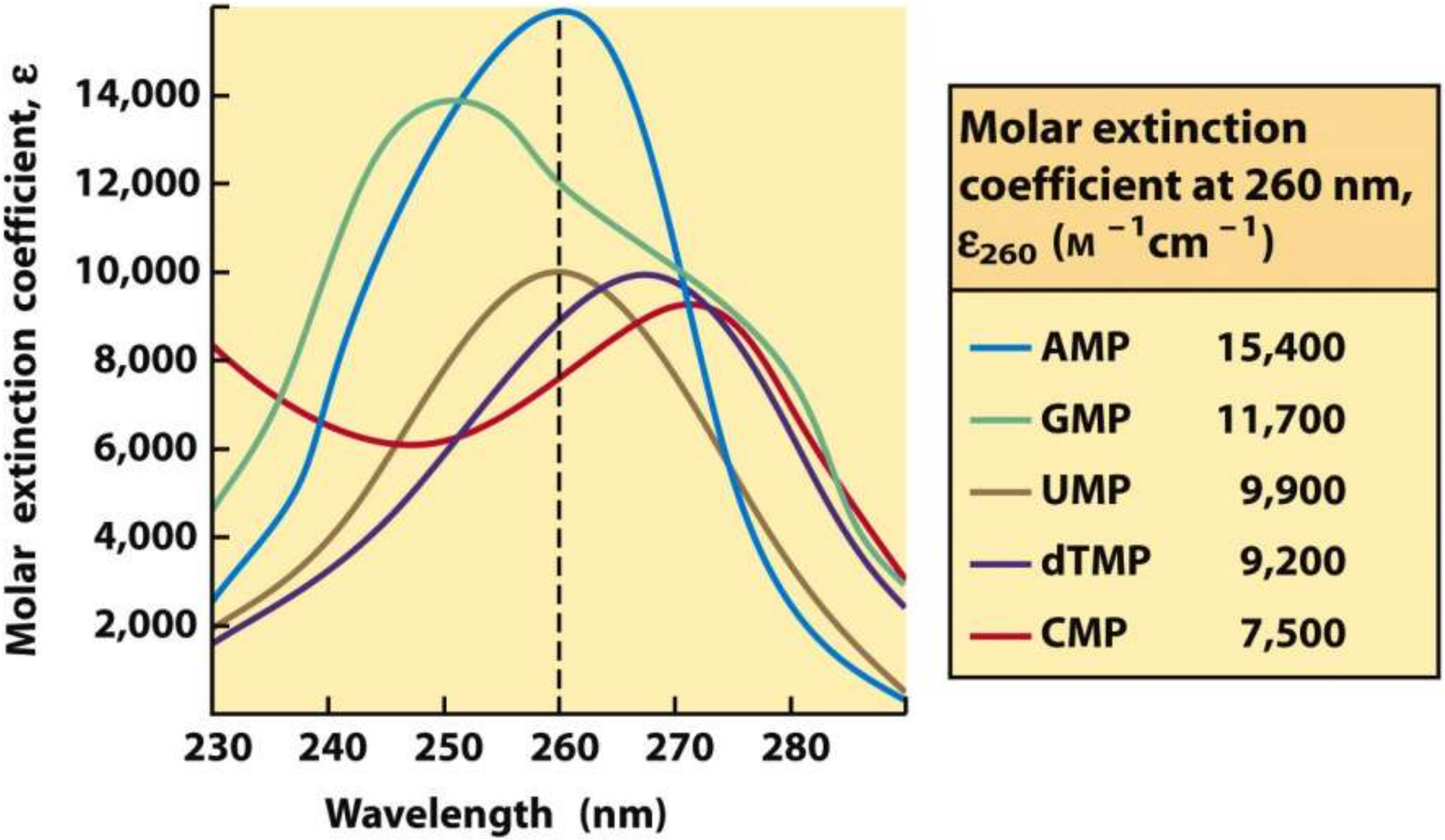


Figure 8-10
Lehninger Principles of Biochemistry, Fifth Edition

Replication of Genetic Code

- Strand separation occurs first
- Each strand serves as a template for the synthesis of a new strand
- Synthesis is catalyzed by enzymes known as DNA polymerases
- Newly made DNA molecule has one daughter strand and one parent strand.

"*It has not escaped our notice that the specific pairing we have postulated immediately suggests a possible copying mechanism for the genetic material*"

Watson and Crick, in their Nature paper,1953

Messenger RNA:
Code Carrier for the Sequence of Proteins

- Is synthesized using DNA template
- Contains ribose instead of deoxyribose
- Contains uracil instead of thymine
- One mRNA may code for more than one protein

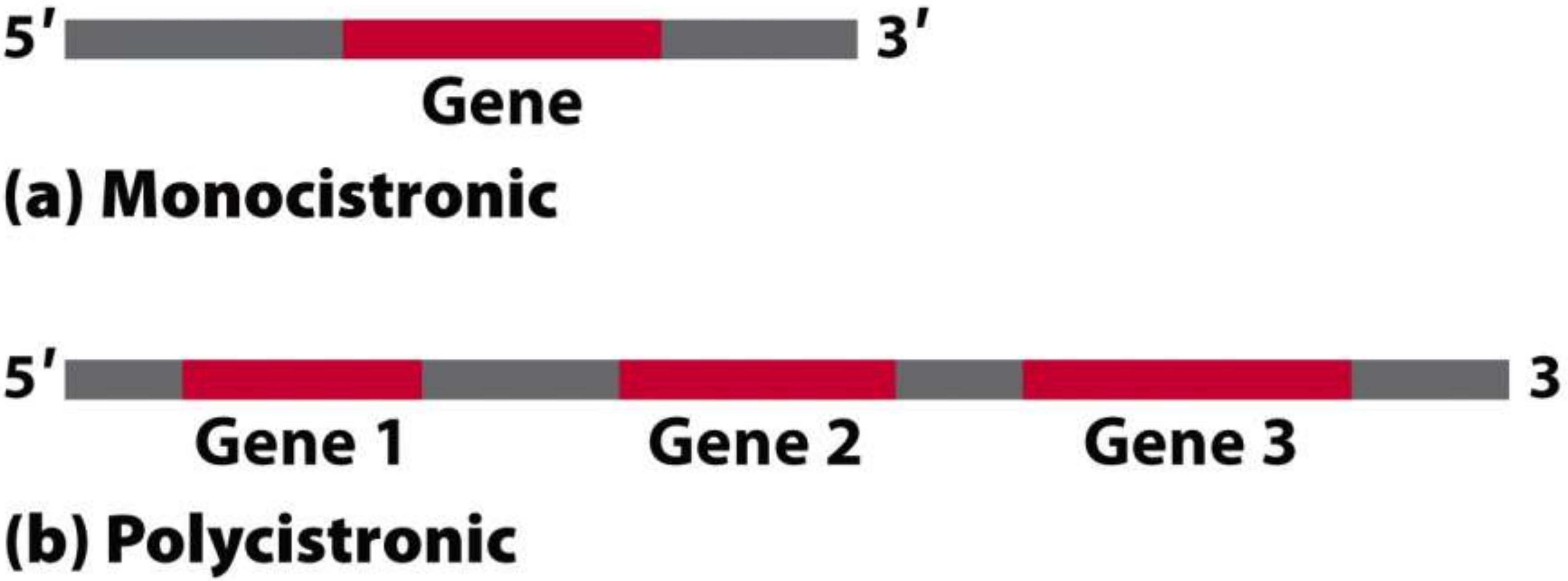


Figure 8-21
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Factors Affecting DNA Denaturation

- The midpoint of melting (T_m) depends on base composition
  - high CG increases T_m
- T_m depends on DNA length
  - Longer DNA has higher T_m
  - Important for short DNA
- T_m depends on pH and ionic strength
  - High salt increases T_m