NUCLEIC ACIDS

- **Nucleic acids store and transmit hereditary information.**
- **There are two types of nucleic acids:**

  1)- ribonucleic acid (RNA);

  2)- deoxyribonucleic acid (DNA).

The distribution of nucleic acids in the eukaryotic cell

- DNA is found in the nucleus

with small amounts in mitochondria and chloroplasts

- RNA is found throughout the cell

Role of DNA

- DNA comes with a complete set of instructions to make an entire organism.
- While you are growing you need DNA to produce more cells.
- As an adult you also need DNA for growth, repair of damaged cells and to make proteins.

NUCLEIC ACID STRUCTURE

- Nucleic acids are **polynucleotides**
- Their building blocks are **nucleotides**
- **Nucleotide consist of phosphate group ,pentose suger ,and nitrogen base**

PHOSPHATE

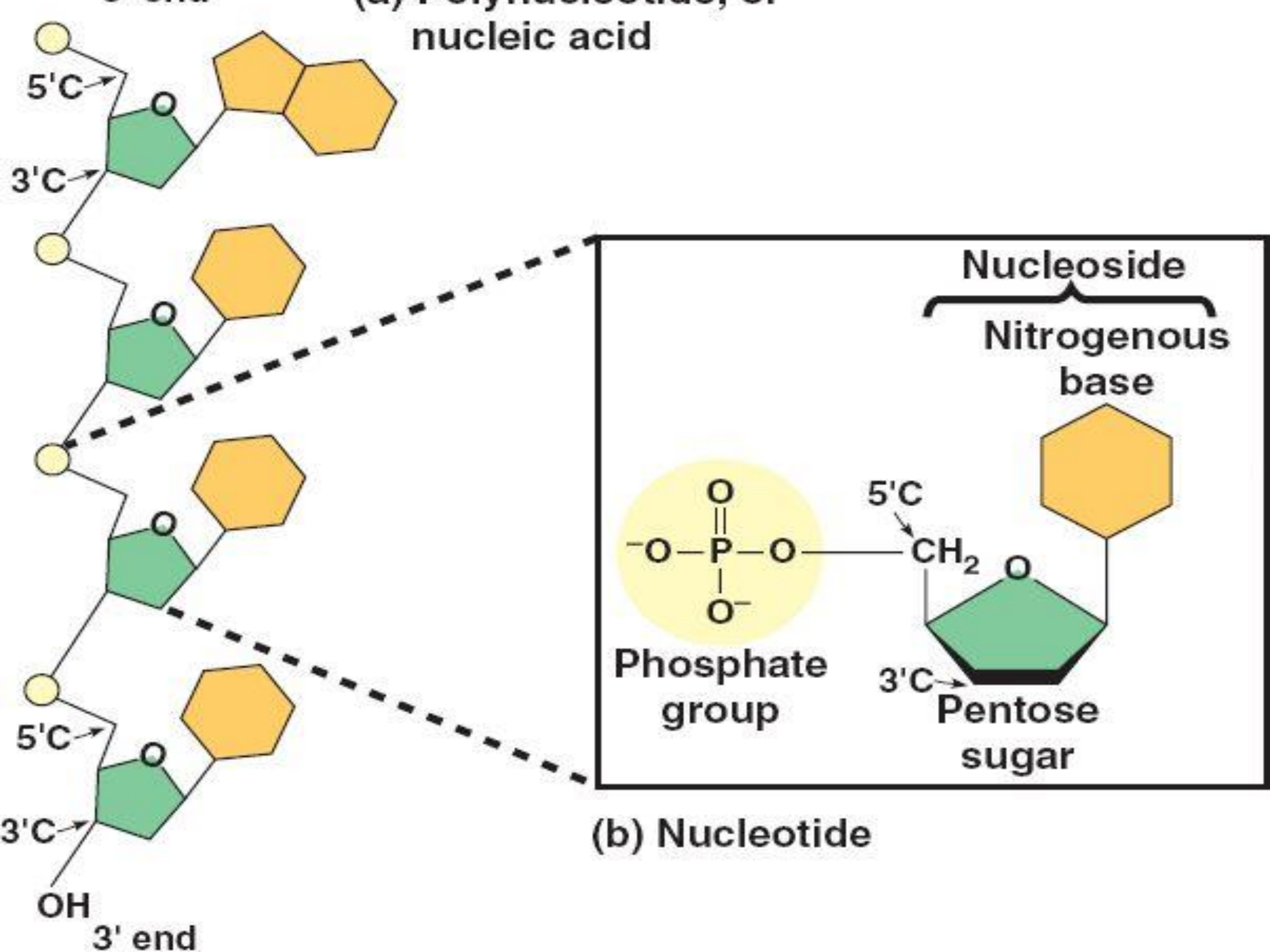
Pentose SUGAR

Ribose or Deoxyribose

Nitrogen BASE

PURINES	PYRIMIDINES
Adenine (A) Guanine(G)	Cytocine (C) Thymine (T) Uracil (U)

NUCLEOTIDE

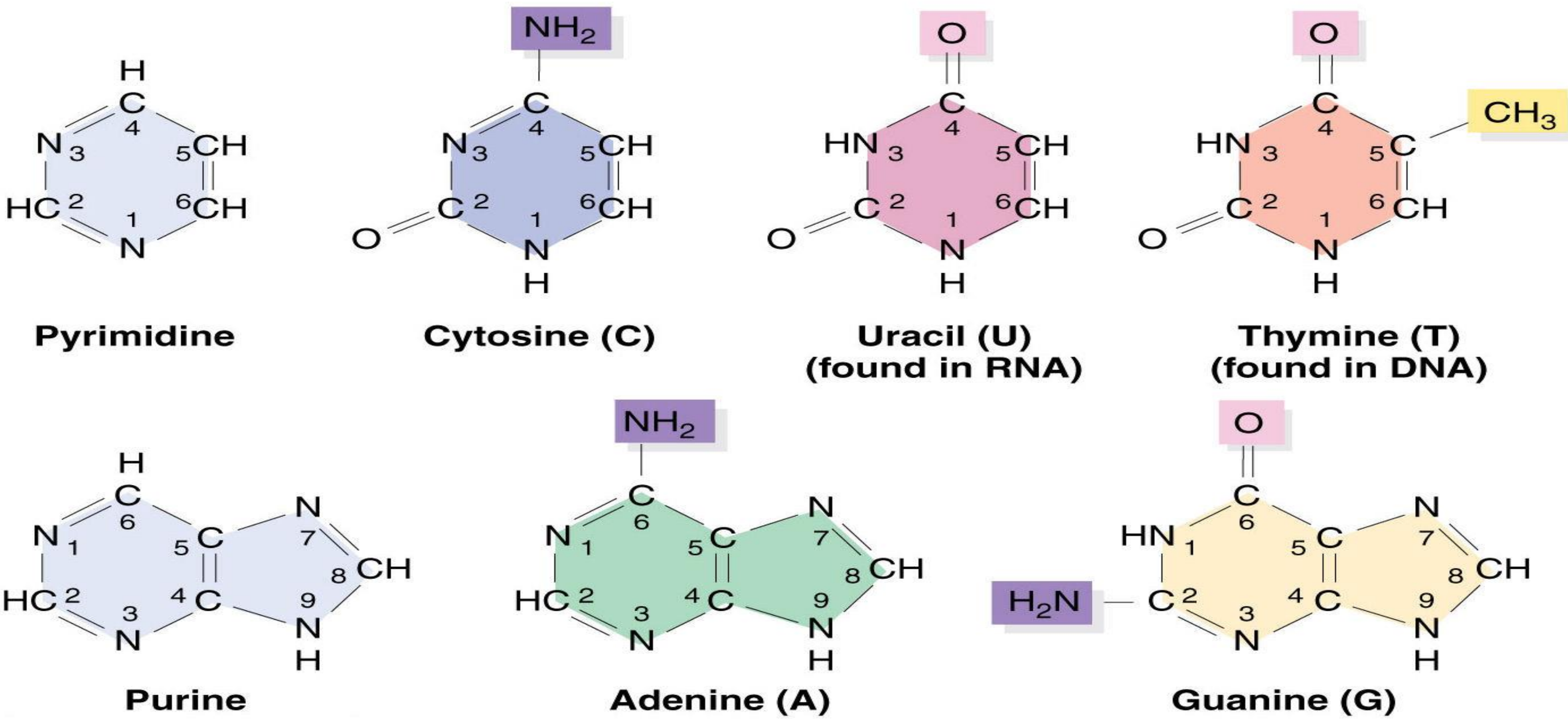


nucleic acid

(b) Nucleotide

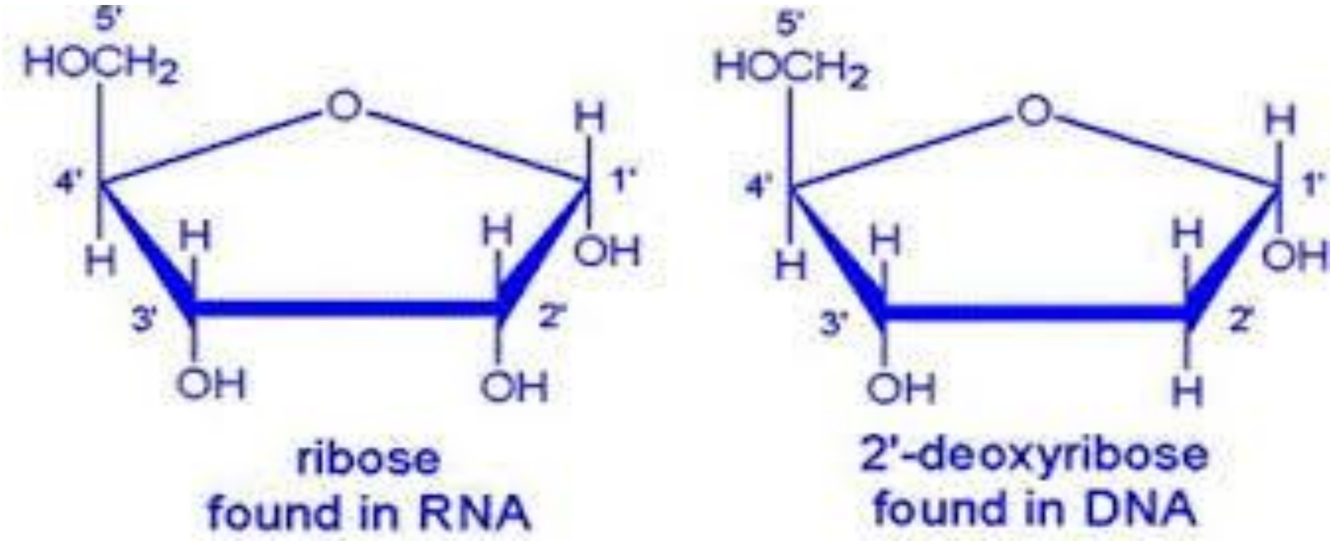
Nitrogen base

The nitrogen bases (rings of carbon and nitrogen**) come in two types: Purines and Pyrimidines.**



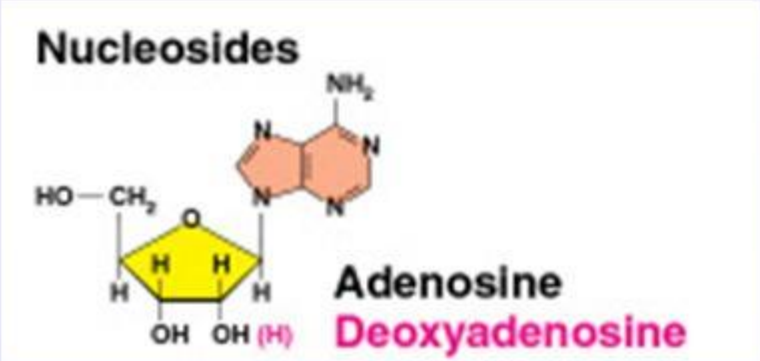
Pentose Sugar

- The pentose sugar joined to the nitrogen base is ribose in nucleotides of RNA and deoxyribose in DNA. The only difference between the sugars is the lack of an oxygen atom on carbon 2 in deoxyribose. To differentiate the atoms of the pentose suger from the nitrogen base, the position number of the carbohydrate is followed by a ´ (prime).



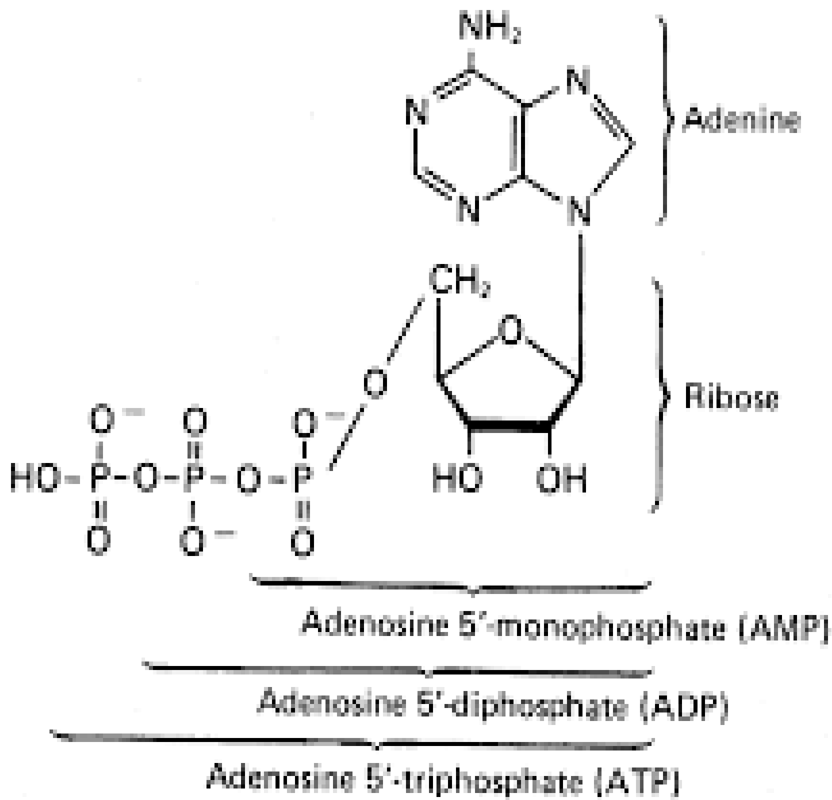
Nucleosides and Nucleotides

- 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 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*
- 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)



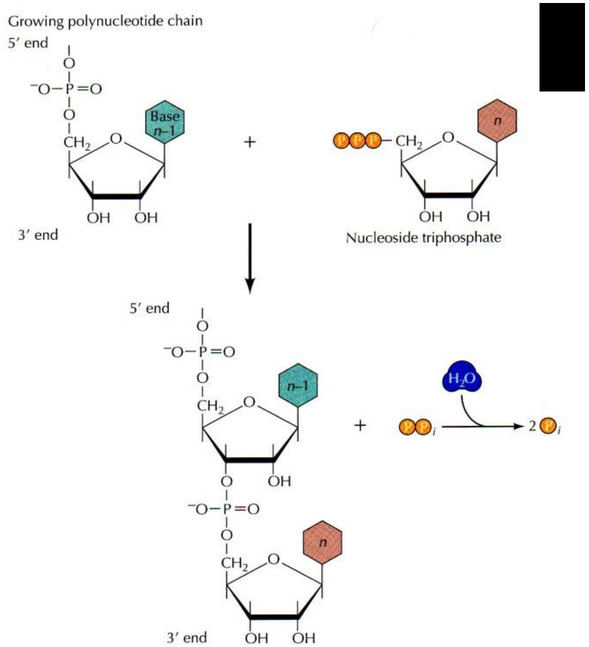
Base	Nucleosides	Nucleotides
RNA		
Adenine (A)	Adenosine (A)	Adenosine 5'-monophosphate (AMP)
Guanine (G)	Guanosine (G)	Guanosine 5'-monophosphate (GMP)
Cytosine (C)	Cytidine (C)	Cytidine 5'-monophosphate (CMP)
Uracil (U)	Uridine (U)	Uridine 5'-monophosphate (UMP)
DNA		
Adenine (A)	Deoxyadenosine (A)	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)

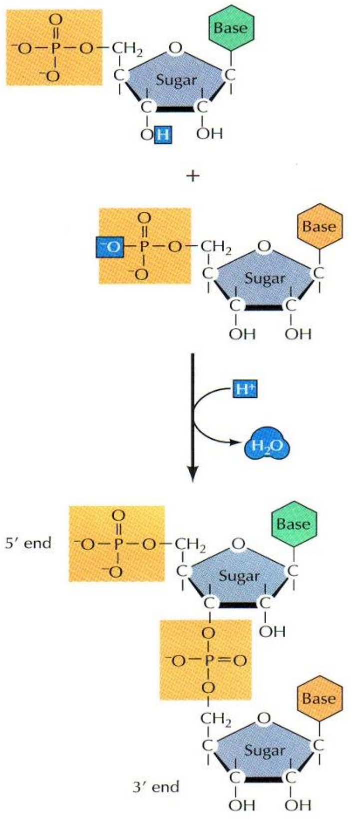
AMP, ADP and ATP



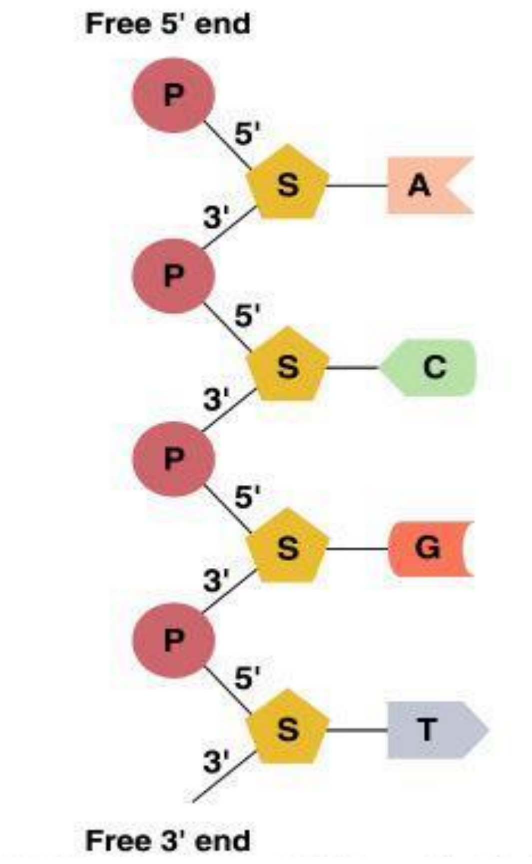
Linear Polymerization of Nucleotides

- Nucleic acids are formed of nucleotide polymers.
- Nucleotides polymerize together by ***phospho-diester bonds*** via condensation reaction.
- The phospho-diester bond is formed between: 5' phosphate group of one nucleotide and 3' hydroxyl group of another nucleotide.
- Polynucleotide chains are always synthesized in the 5' to 3' direction, with a free nucleotide being added to the 3' OH group of a growing chain.





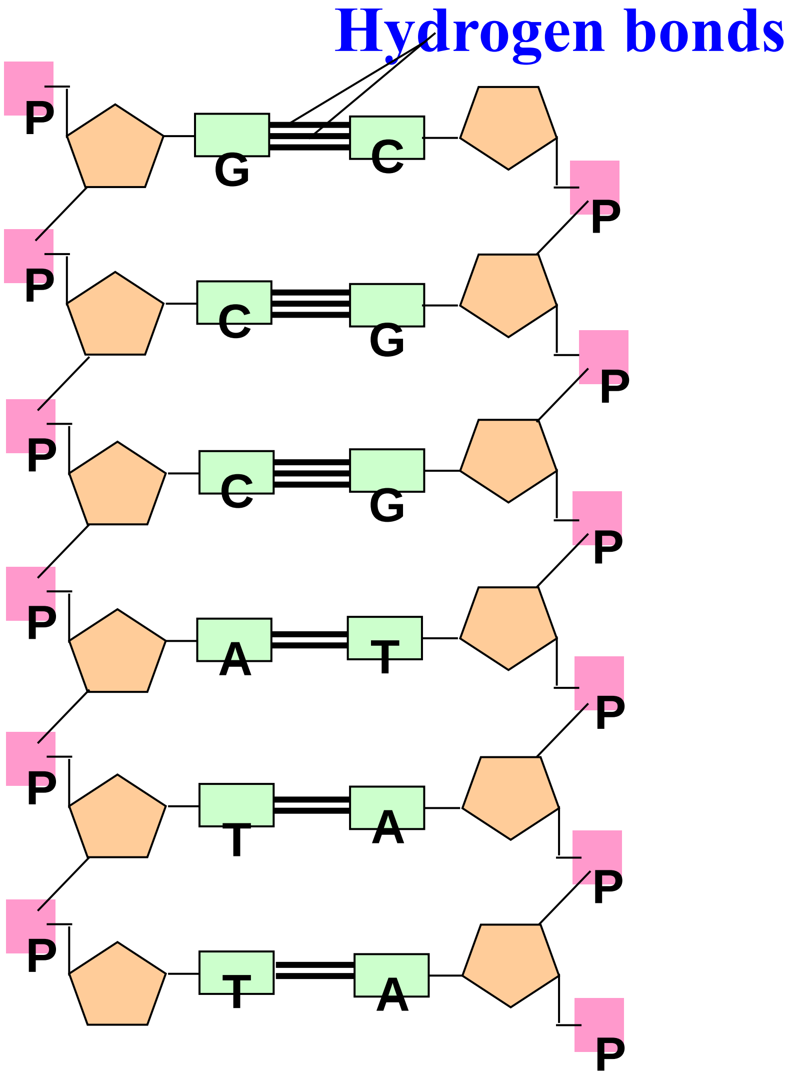
- **The following examples represent the orientation of the DNA strand from 5^{-} to 3^{-}**
- **5^{-} A-C-G-T 3^{-}**



- **DNA molecules have two polynucleotide strands (double strand) that spiral around تدور حلزونيا to form a double helix حلزون مزدوج.**

- **The sugar-phosphate backbones of the two polynucleotides are on the outside of the helix.**

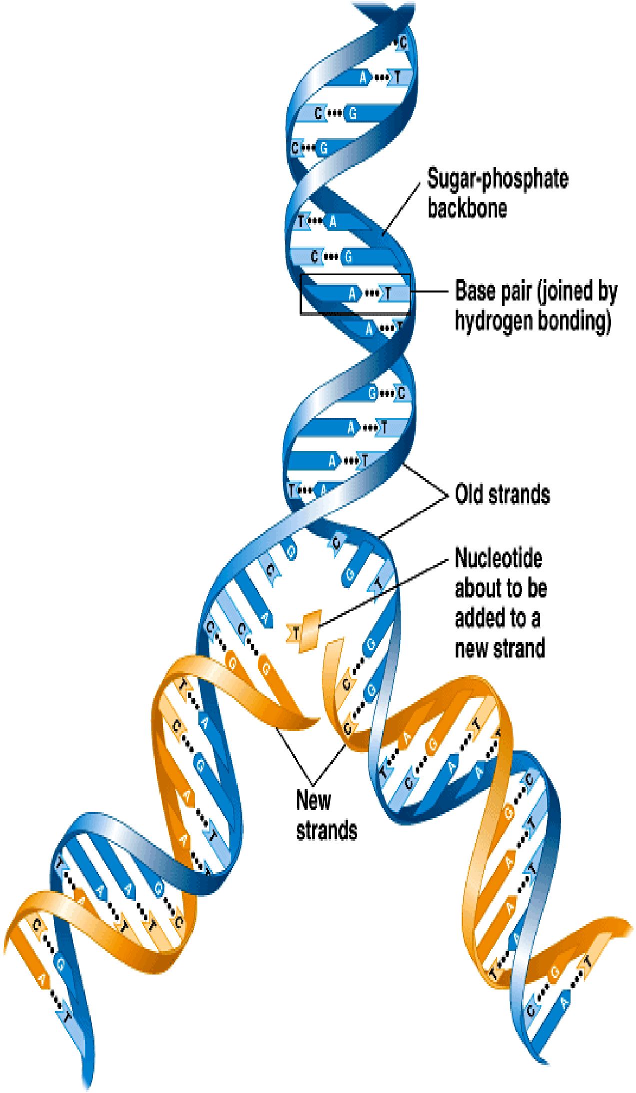
- The bases are attached to the 1st Carbon through glycosidic bond
- Their order is important
  It determines the genetic information of the molecule



- **Pairs of nitrogenous bases (one from each strand) connect the polynucleotide chains with hydrogen bonds.**

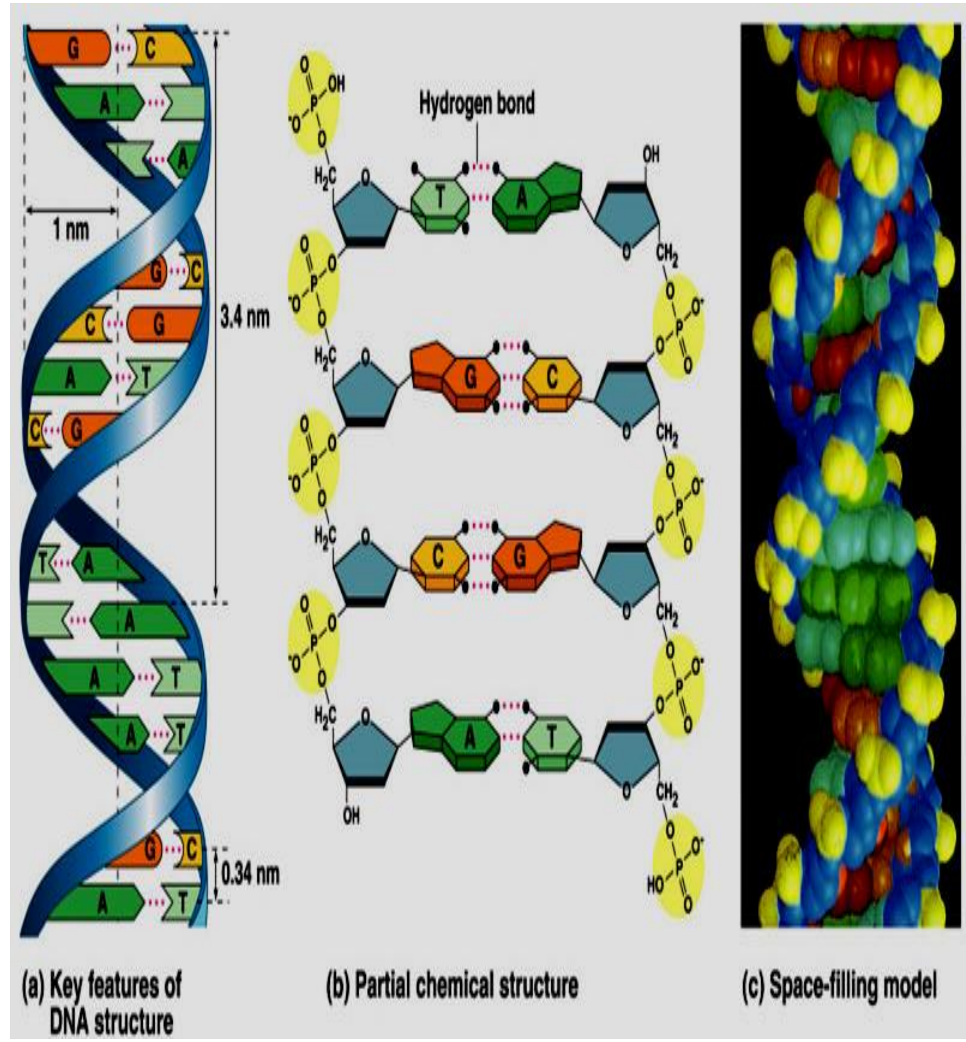
- **Most DNA molecules have thousands to millions of base pairs**

زوج من القواعد (bP).

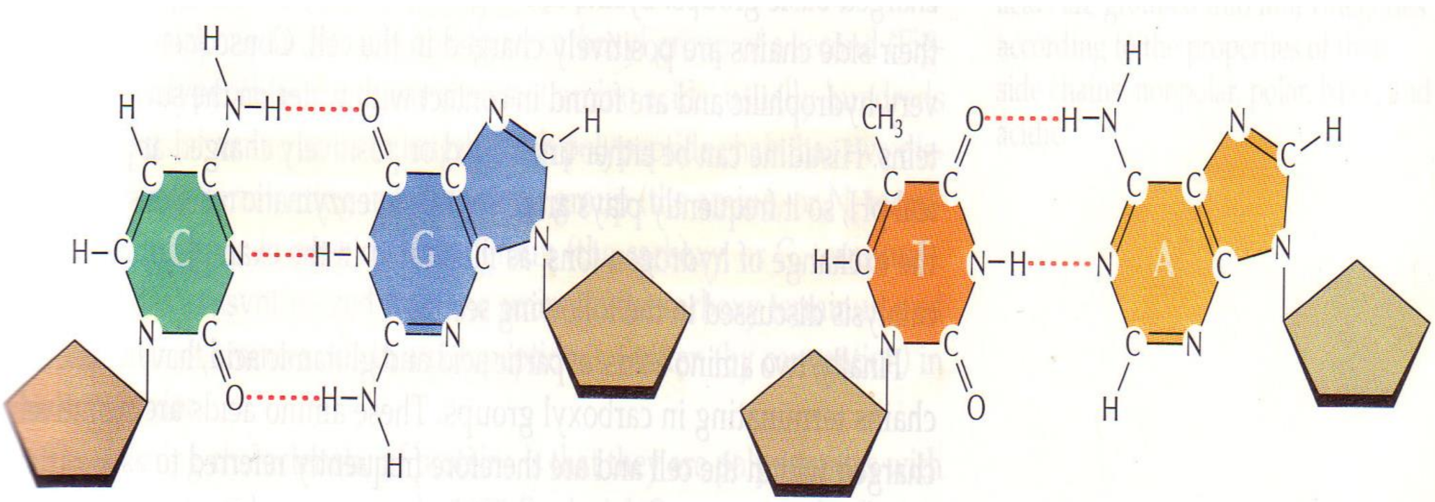


WATSON AND CRICK MODEL

- The sister strands of the DNA molecule run in opposite directions (**antiparallel**)
- They are joined by the bases
- Each base is paired with a specific partner:



•**A** is always paired with **T by double H-bond and G** is always paired with **C by triple H-bond .**
•Each base pair consist of Purine with Pyrimidine**,**Thus the sister strands are **complementary** but **<u>not</u>** identical
•The bases are joined by **hydrogen bonds**, individually weak but collectively strong.



Significance of complementary base pairing

- The importance of such complementary base pairing is that each strand of DNA can act as template to direct the synthesis of other strand similar to its complementary one.

- Thus ***nucleic acids are uniquely capable of directing their own self replication***.

- The information carried by DNA and RNA direct the synthesis of specific proteins which control most cellular activities.

Storage of DNA

- Within eukaryotic cells, DNA is organized into long structures called chromosomes.
- Before typical cell division, these chromosomes are duplicated in the process of DNA replication, providing a complete set of chromosomes for each daughter cell.
- Eukaryotic organisms (animals, plants, fungi and protists) store most of their DNA inside the cell nucleus and some in organelles, such as mitochondria or chloroplasts.[4] In contrast, prokaryotes (bacteria and archaea) store their DNA only in the cytoplasm.
- Within eukaryotic chromosomes, chromatin proteins, such as histones, compact and organize DNA. These compact structures guide the interactions between DNA and other proteins, helping control which parts of the DNA are transcribed.

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.**

Discovering structure of DNA BY Chargaff

- Chargaff discovered two rules that helped lead to the discovery of the double helix structure of DNA.
- The first rule was that in DNA the number of guanine units is equal to the number of cytosine units, and the number of adenine units is equal to the number of thymine units. This hinted at the base pair makeup of DNA.
- The second rule was that the relative amounts of guanine, cytosine, adenine and thymine bases vary from one species to another. This hinted that DNA rather than protein could be the genetic material.

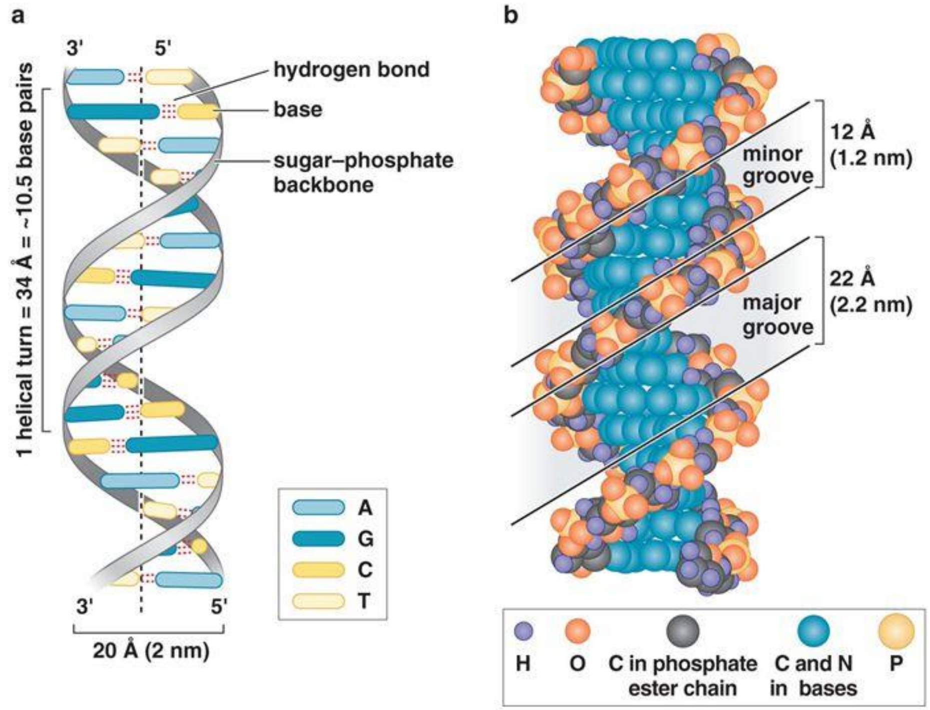
Properties of DNA

- The structure of DNA is dynamic along its length, being capable of coiling into tight loops and other shapes.[8] In all species it is composed of two helical chains, bound to each other by hydrogen bonds.
- Both chains are coiled around the same axis, and have the same pitch of 34 angstroms (3.4 nanometers). The pair of chains has a radius of 10 ångstroms (1.0 nanometer)

- Twin helical strands form the DNA backbone. Another double helix may be found tracing the spaces, or grooves, between the strands. These voids are adjacent to the base pairs and may provide a binding site. As the strands are not symmetrically located with respect to each other, the grooves are unequally sized.
- One groove, the major groove, is 22 Å wide and the other, the minor groove, is 12 Å wide.[47] The width of the major groove means that the edges of the bases are more accessible in the major groove than in the minor groove.
- As a result, proteins such as transcription factors that can bind to specific sequences in double-stranded DNA usually make contact with the sides of the bases exposed in the major groove

DNA STRUCTURE

DNA is composed of polynucleotide chains



The helical structure of DNA

DNA Denaturation

- The process of breaking double-stranded DNA into single strands is known as DNA denaturation, or DNA denaturing.
- The temperature at which the DNA strands are half denatured, meaning half double-stranded, half single-stranded, is called the melting temperature(Tm).
- The amount of strand separation, or melting, is measured by the absorbance of the DNA solution at 260nm.
- Nucleic acids absorb light at this wavelength because of the electronic structure in their bases, but when two strands of DNA come together, the close proximity of the bases in the two strands quenches some of this absorbance. When the two strands separate, this quenching disappears and the absorbance rises 30%-40%.This is called Hyperchromicity. The Hypochromic effect is the effect of stacked bases in a double helix absorbing less ultra-violet light.

C.Causes of Denaturation.

Denaturation can occur when proteins and nucleic acids are subjected to :

1-elevated **temperature**.

2-extremes of **pH**.

3-nonphysiological concentrations of salt, organic solvents, urea, or other chemical agents.

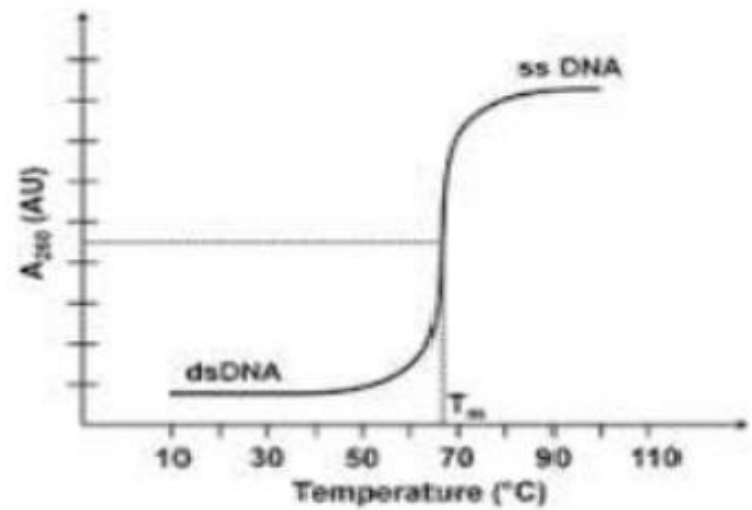
C.1-elevated temperature.

The most common type of denaturation is thermal denatuation.

Tm : temp at which DNA is half denatured.

*above Tm DNA is single strands.

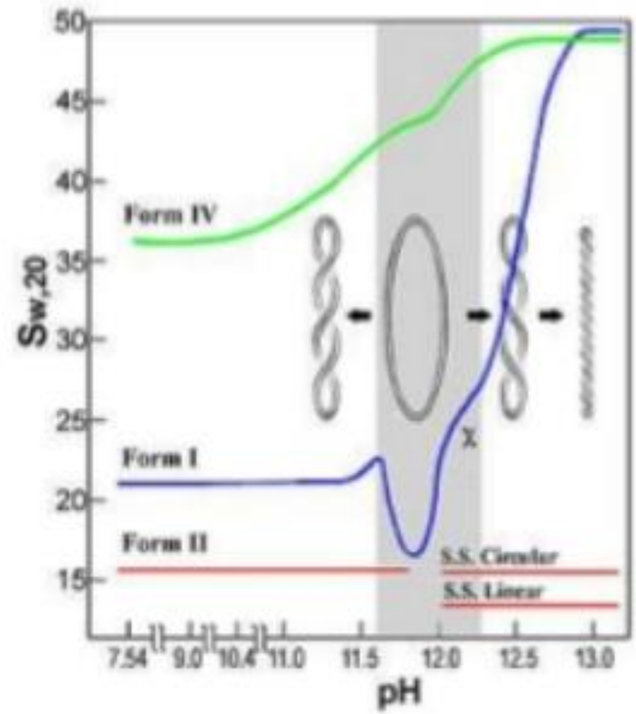
*below tm DNA is double strands.



- Tm depends on:
  - base composition
  - length
  - ionic strength
  - pH
  - denaturing agents

C.2-extremes of pH

At high PH the hydroxide ions ((negatively charged ions)) can pull hydrogen ions from base pairs – forming H bond between two strands – causing them to separate.



C.3 non physiological salts

Low salt concentration could also denature DNA double-strands by removing ions that stabilize the negative charges on the two strands from each other.

D. Characters of Denatured DNA

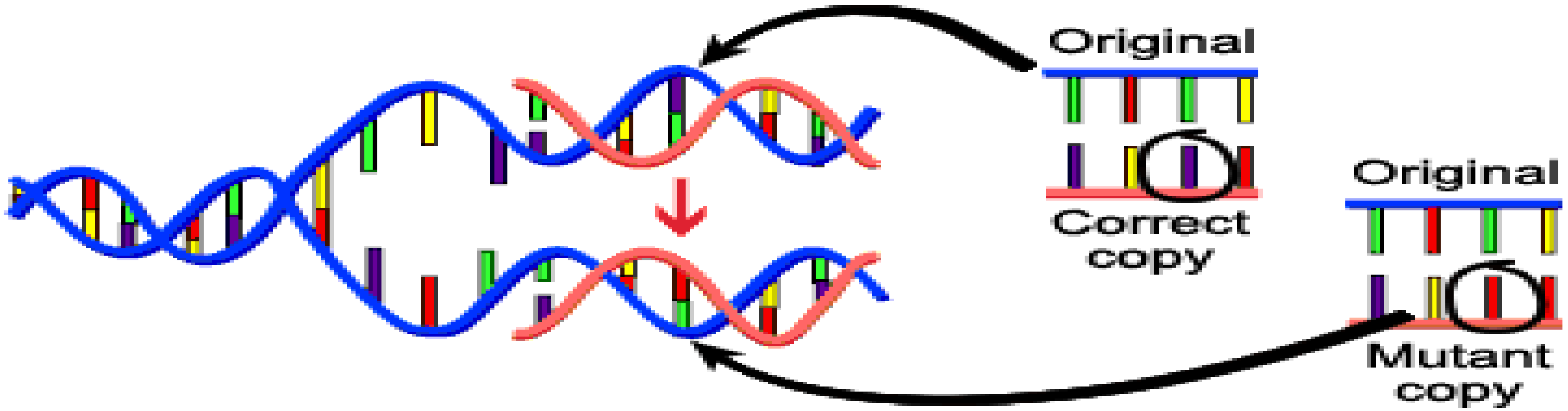
1. **Hyperchromic** : increase the absorbance (A260) upon denaturation.

2. The rate of **increase** in absorbance is directly proportional to the rate of denaturation.

3. **Viscosity** decrease upon denaturation.

What Are Mutations?

- Changes in the nucleotide sequence of DNA
- May occur in somatic cells (aren't passed to offspring)
- May occur in gametes (eggs & sperm) and be passed to offspring



Are Mutations Helpful or Harmful?

- Mutations happen **regularly**
- Almost all mutations are **neutral**
- **Chemicals & UV** radiation cause mutations
- Many mutations are **repaired** by enzymes

CLASSES OF MUTATION

- ***SPONTANEOUS MUTATION***
- ***INDUCED MUTATION***

➢ SPONTANEOUS MUTATION

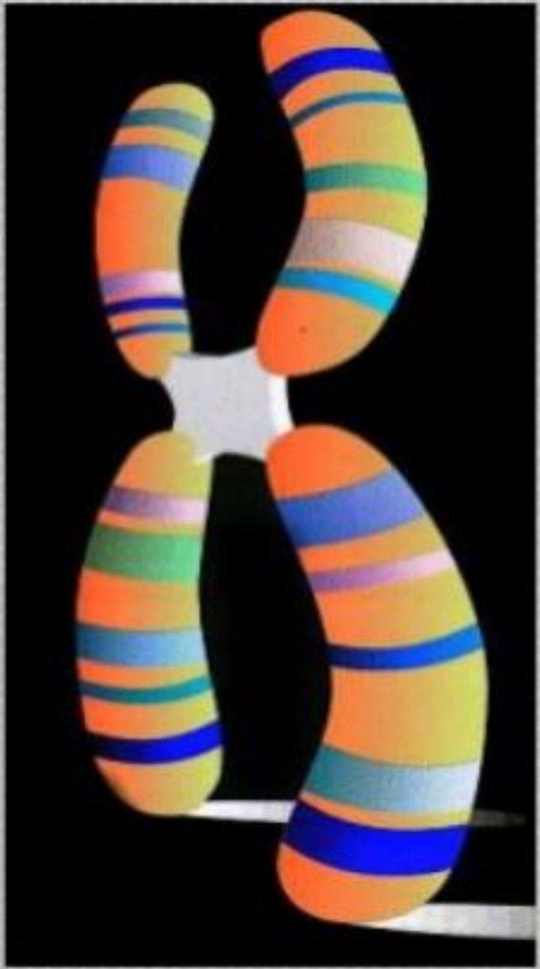
- ***they are mainly caused during dna replication or by incorporation of incorrect nucleotide in the growing dna chain .***
- ***They occur naturally by changes in DNA sequence during replication.***

➢INDUCED MUTATION

- ***Induced mutation are caused by the changes in DNA brought about by some environmental factor called mutagens.***
- ***E.g.- UV light,x-rays,gamma rays etc...,***

Chromosome Mutations

- *May Involve:*
  - ***Changing the structure*** ***of a chromosome***
  - ***The loss or gain of part of a chromosome***



Gene Mutations

- ***Change in the nucleotide sequence of a gene***
- ***May only involve a single nucleotide***
- ***May be due to copying errors, chemicals, viruses, etc.***

Types of Gene Mutations

- **Include:**
  - ***Point Mutations***
  - ***Substitutions***
  - ***Insertions***
  - ***Deletions***
  - ***Frameshift***

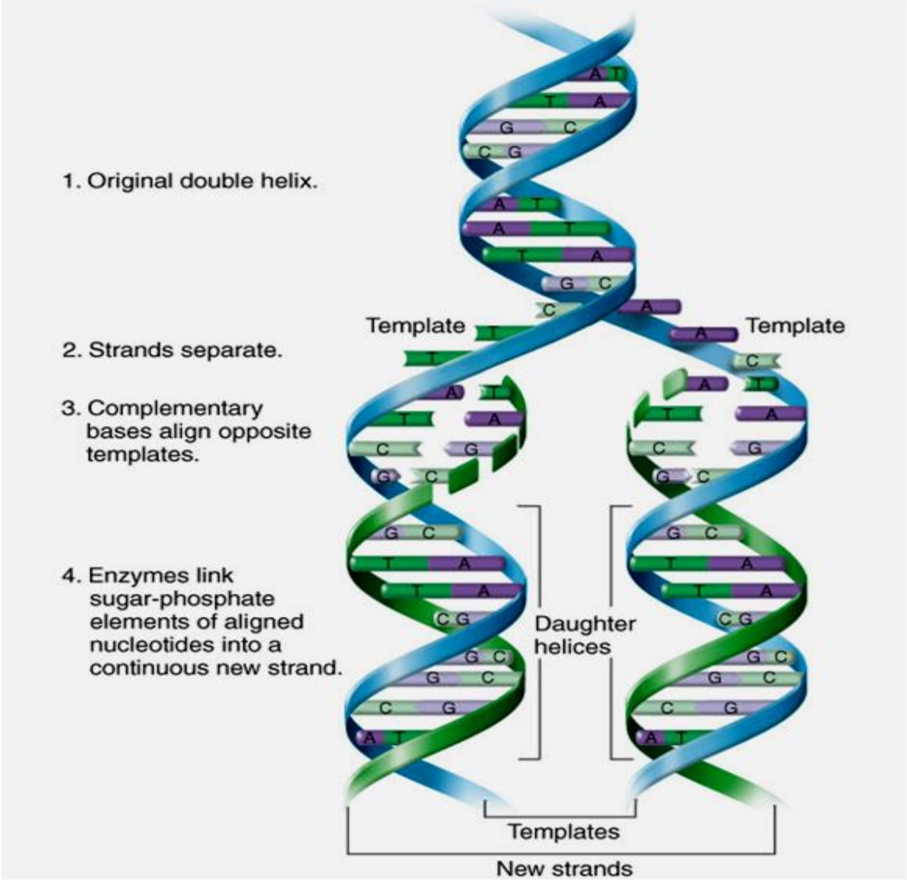
DNA Replication- Introduction

- Basis for inheritance
- Fundamental process occurring in all cells for copying DNA to transfer the genetic information to daughter cells
- Each cell must replicate its DNA before division.

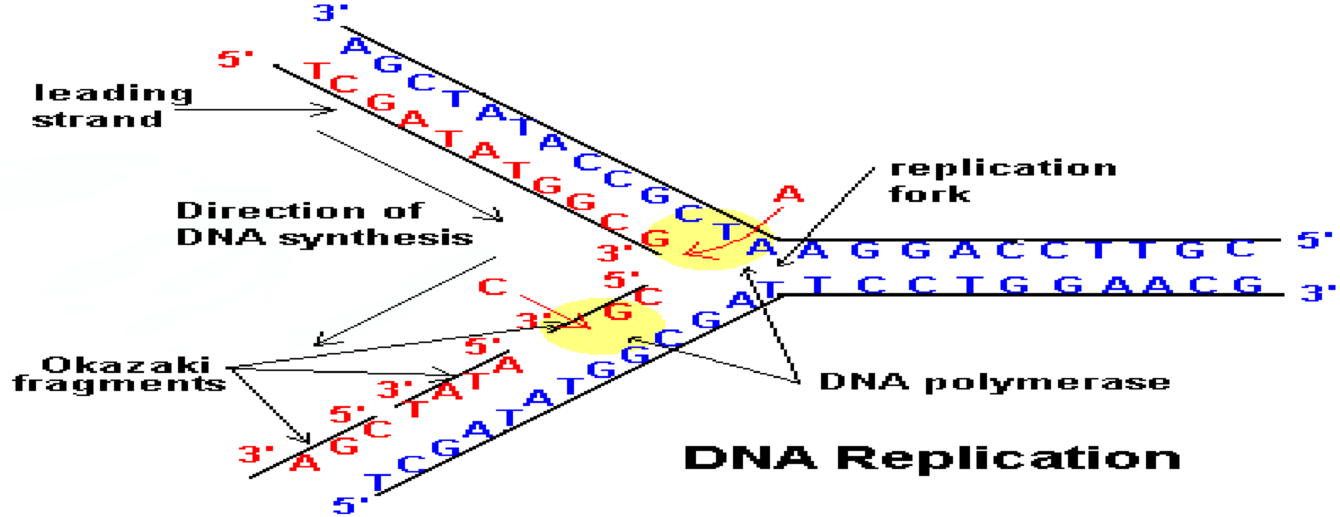
Basic rules of replication

A. Semi-conservative
B. Starts at the 'origin'
C. Synthesis always in the 5-3' direction
D. Can be uni or bidirectional
E. Semi-discontinuous
F. RNA primers required

- DNA is made up of a double helix of two complementary strands.
- During replication, these strands are separated. Each strand of the original DNA molecule then serves as a template for the production of its counterpart, a process referred to as semiconservative replication.
- As a result of semi-conservative replication, the new helix will be composed of an original DNA strand as well as a newly synthesized strand



- In a cell, DNA replication begins at specific locations, or origins of replication, in the genome.[4]
- Unwinding of DNA at the origin and synthesis of new strands, accommodated by an enzyme known as helicase, results in replication forks growing bi-directionally from the origin.
- A number of proteins are associated with the replication fork to help in the initiation and continuation of DNA synthesis.



Most prominently, DNA polymerase synthesizes the new strands by adding nucleotides that complement each (template) strand. This process accompanied by releasing energy

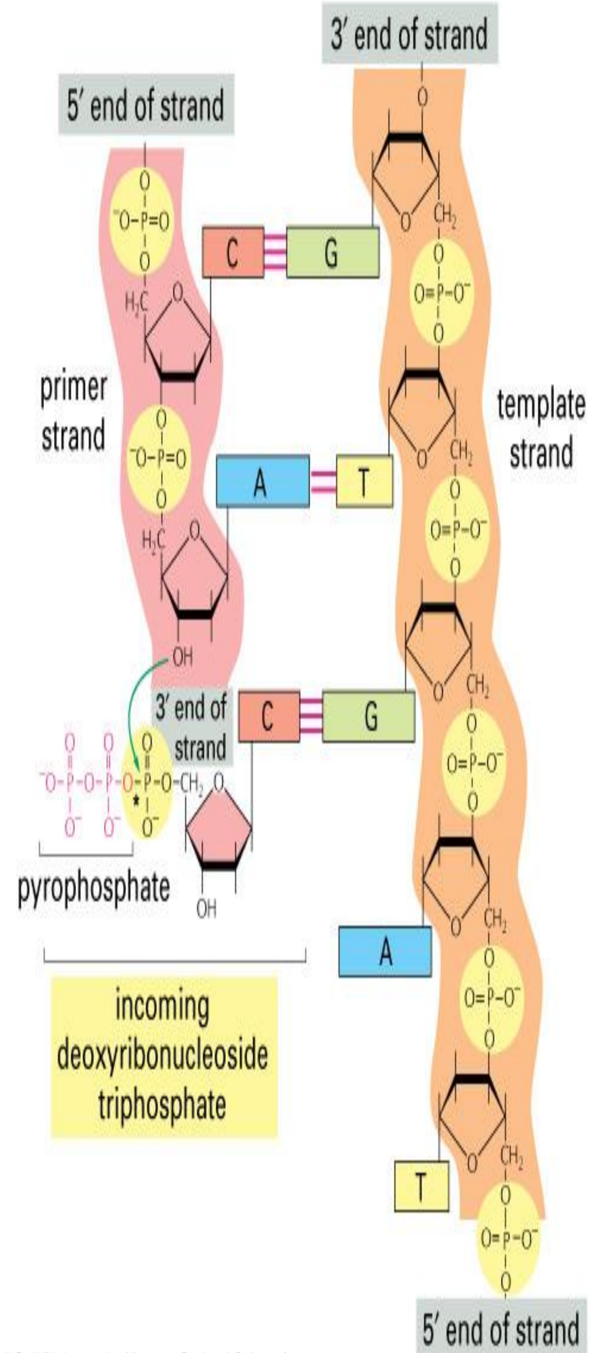
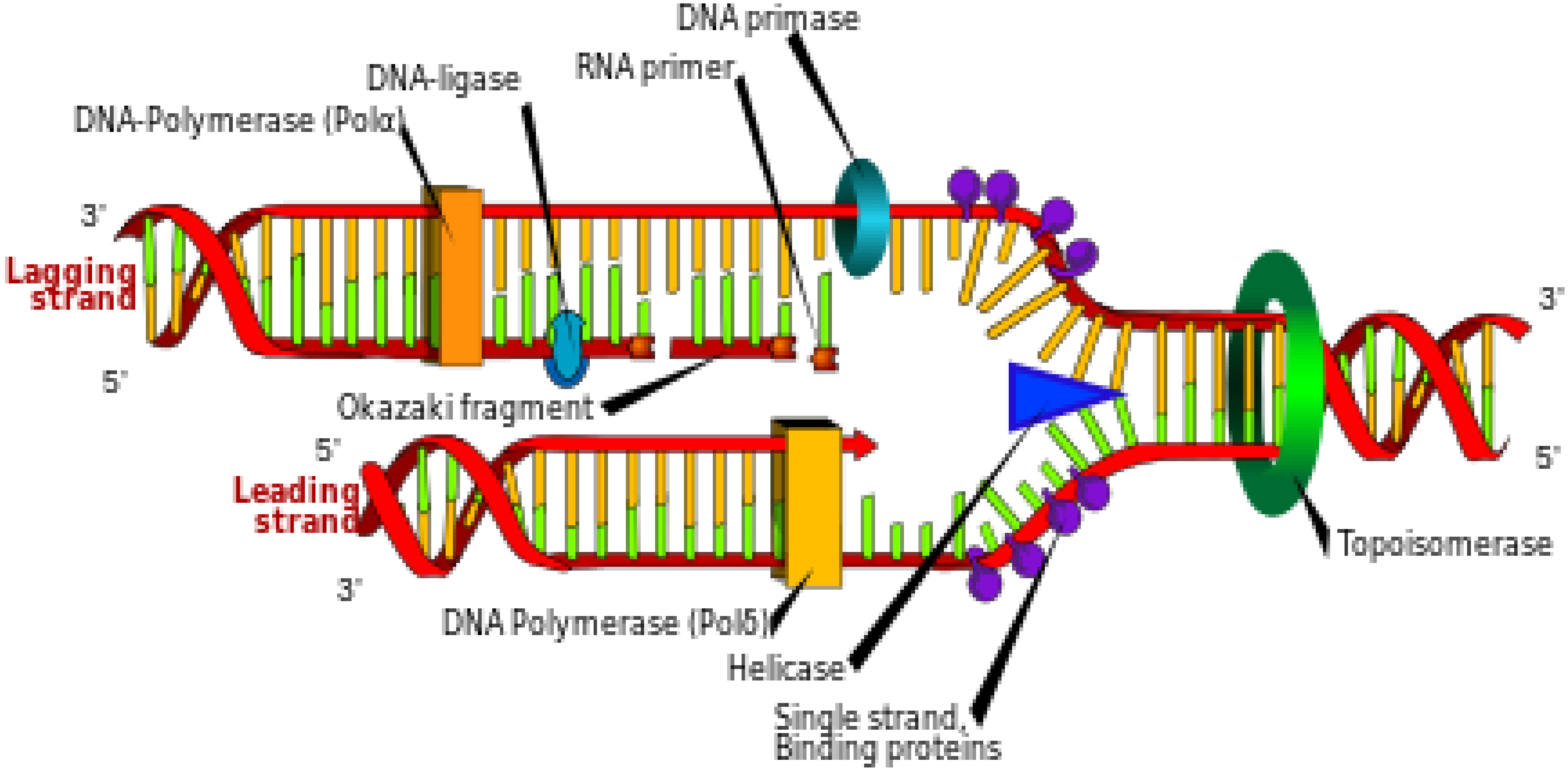


Figure 6-10 Essential Cell Biology, 2/e. (© 2004 Garland Science)

Direction of replication

- DNA polymerase has 5′–3′ activity. **DNA is always synthesized in the 5′ to 3′ direction.** Since the leading and lagging strand templates are oriented in opposite directions at the replication fork
- **Leading strand** is the strand of nascent DNA which is being synthesized in the same direction as the growing replication fork. This sort of DNA replication is continuous.

- **Lagging strand**
- The lagging strand is the strand of nascent DNA whose direction of synthesis is opposite to the direction of the growing replication fork. The lagging strand is synthesized in short, separated segments. On the lagging strand *template*, a primase "reads" the template DNA and initiates synthesis of a short complementary RNA primer. A DNA polymerase extends the primed segments, forming Okazaki fragments. The RNA primers are then removed and replaced with DNA, and the fragments of DNA are joined together by DNA ligase.



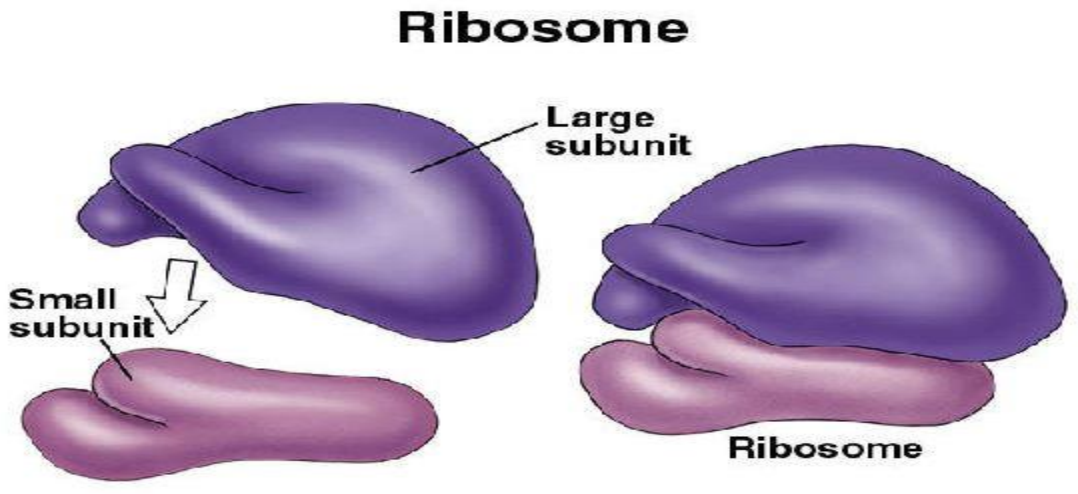
DNA primase
RNA primer
DNA-ligase
DNA-Polymerase (Polα)
3'
Lagging strand
5'
Okazaki fragment
3'
5'
5'
Leading strand
3'
DNA Polymerase (Polδ)
Helicase
Single strand Binding proteins
Topoisomerase

- **Ribonucleic acid** (**RNA**) is a biologically important type of molecule that consists of a long chain of nucleotide units. Each nucleotide consists of a nitrogenous base, a ribose sugar, and a phosphate.
  - SUGAR
    - Ribose
  - Phosphate group
  - Nitrogen containing base
    - Adenine
    - Guanine
    - Cytosine
    - Uracil

In all, there are **three differences** between RNA and DNA

RNA	**DNA**
1. Ribose sugar	**Deoxyribose sugar**
2. Uracil as a base **GCAU**	**Thymine as a base** **GCAT**
3. Single strand	**Double strand**

The **ribosome** is a complex molecular machine, found within all living cells, that serves as the site of biological protein synthesis(translation).
Ribosomes consist of two major components: the small ribosomal subunits, which read the RNA, and the large subunits, which join amino acids to form a polypeptide chain. Each subunit comprises one or more ribosomal RNA (rRNA) molecules and a variety of ribosomal proteins .



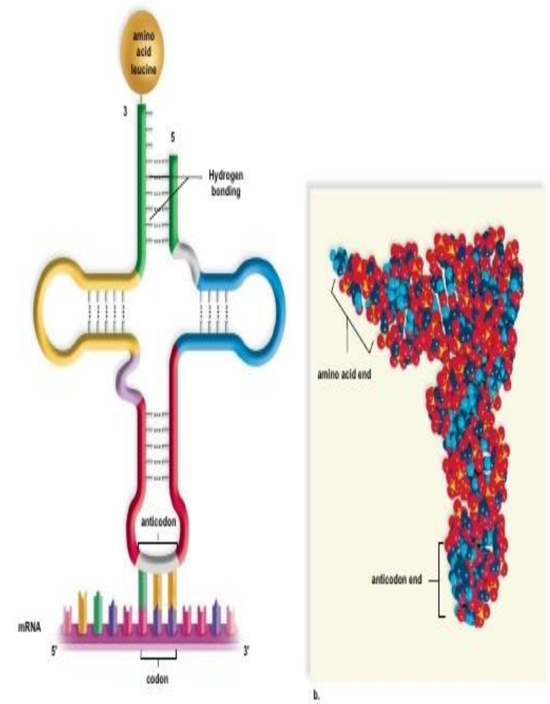
mRNA

- **Messenger RNA** (**mRNA**) is a large family of RNA molecules that transport genetic information from DNA to the ribosome, where they specify the amino acid sequence of the protein products of gene expression

Transfer RNA (tRNA)

- tRNA is a small molecule (~80 nucleotides).
- Single stranded and folded into a clover leaf shape with one end of the chain slightly longer.
- This longer section is attached to an amino acid.
- Each tRNA can carry a different amino acid.
- 3 bases at the opposite end of the tRNA are called an anticodon.
- Each amino acid has a different anticodon.
- The anticodon pairs with the complementary codon on the mRNA.

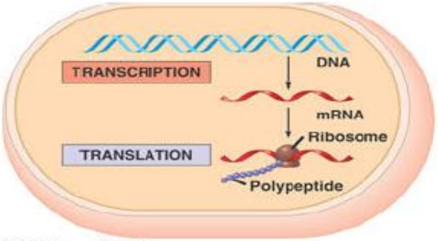
Structure of tRNA



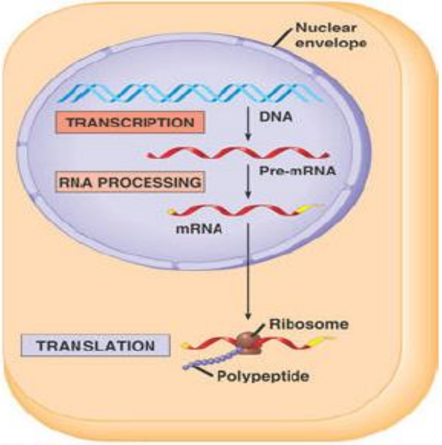
PROTIN SYNTHESIS

Protein Synthesis: What Is It?

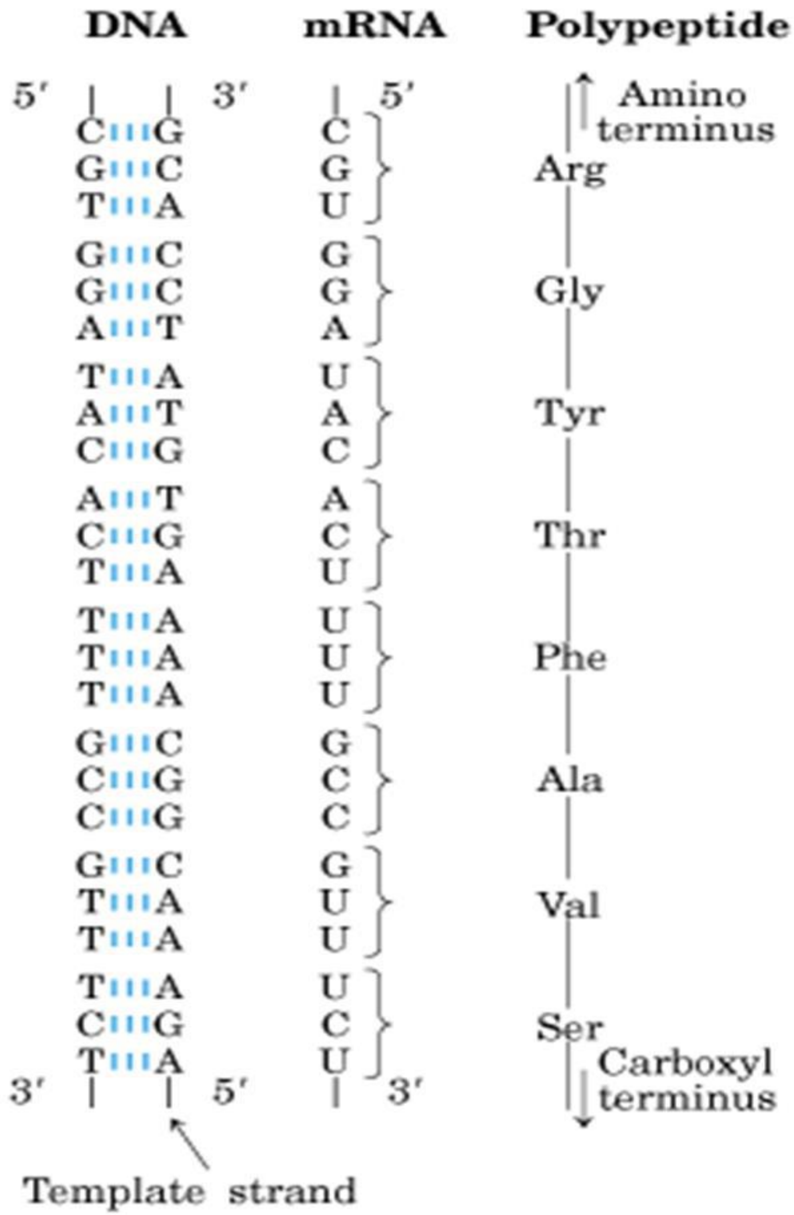
- All proteins are synthesized according to instructions contained in the DNA nucleotide sequence, which is unique to every individual
- Protein synthesis is a two step process that consists of *transcription* and *translation.*



(a) Prokaryotic cell



(b) Eukaryotic cell


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

Transcription is the first step of gene expression, in which a particular segment of DNA is copied into RNA (especially mRNA) by the enzyme RNA polymerase. Both DNA and RNA are nucleic acids, which use base pairs of nucleotides as a complementary language. During transcription, a DNA sequence is read by an RNA polymerase, which produces a complementary, antiparallel RNA strand called a primary transcript.

- Transcription proceeds in the following general steps:
- RNA polymerase, together with one or more general transcription factors, binds to promoter DNA.
- RNA polymerase creates a transcription bubble, which separates the two strands of the DNA helix. This is done by breaking the hydrogen bonds between complementary DNA nucleotides.
- RNA polymerase adds RNA nucleotides (which are complementary to the nucleotides of one DNA strand).
- RNA sugar-phosphate backbone forms with assistance from RNA polymerase to form an RNA strand.
- Hydrogen bonds of the RNA–DNA helix break, freeing the newly synthesized RNA strand.
- If the cell has a nucleus, the RNA may be further processed. This may include polyadenylation, capping, and splicing.
- The RNA may remain in the nucleus or exit to the cytoplasm through the nuclear pore complex.

- The strand of DNA which is transcribed to RNA called as template strand.
- Opposite strand is referred as coding strand.

coding strand (+sense)

- 5'—G T C A A T C C G A A C T—3'

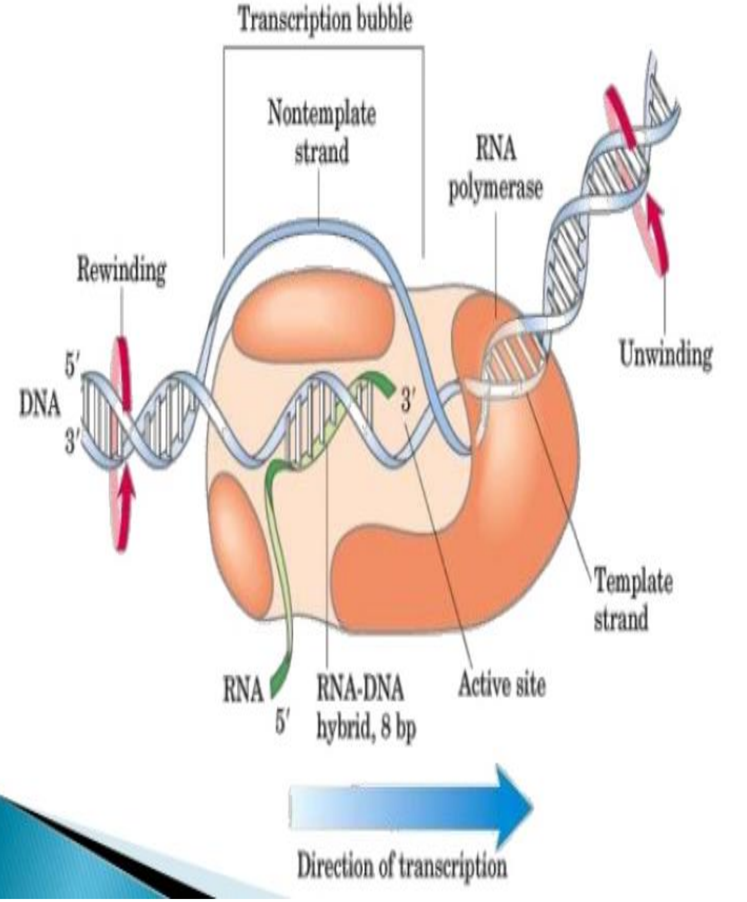
||| || ||| || || || ||| ||| ||| || || ||| ||

- 3'—C A G T T A G G C T T G A—5'

- Template (antisense)

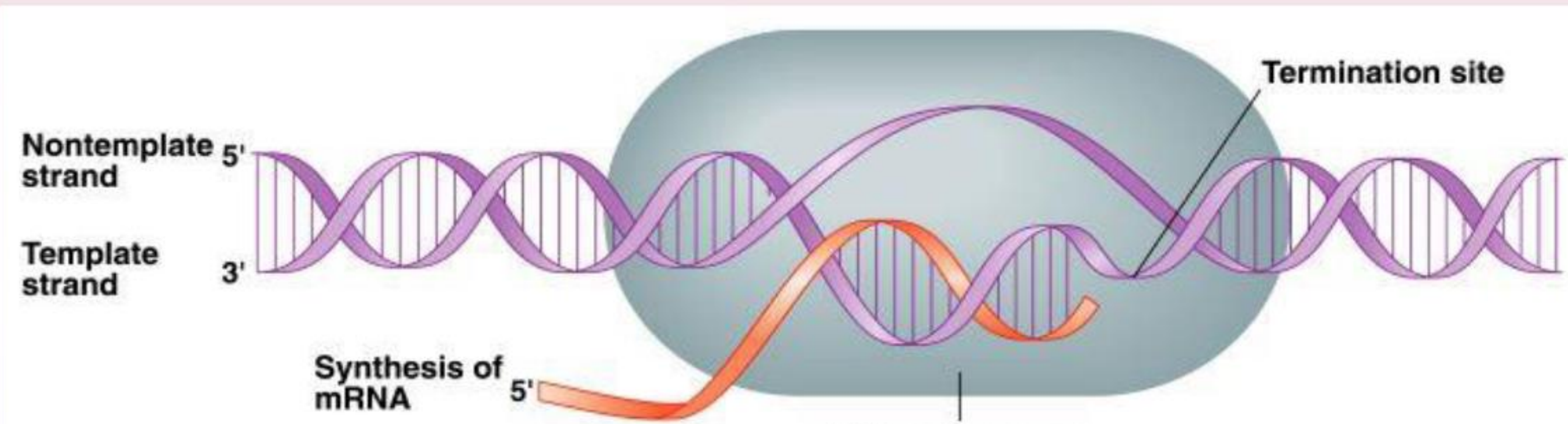
RNA 5'– G U C A A U C C G A A C U– 3'

Transcription bubble



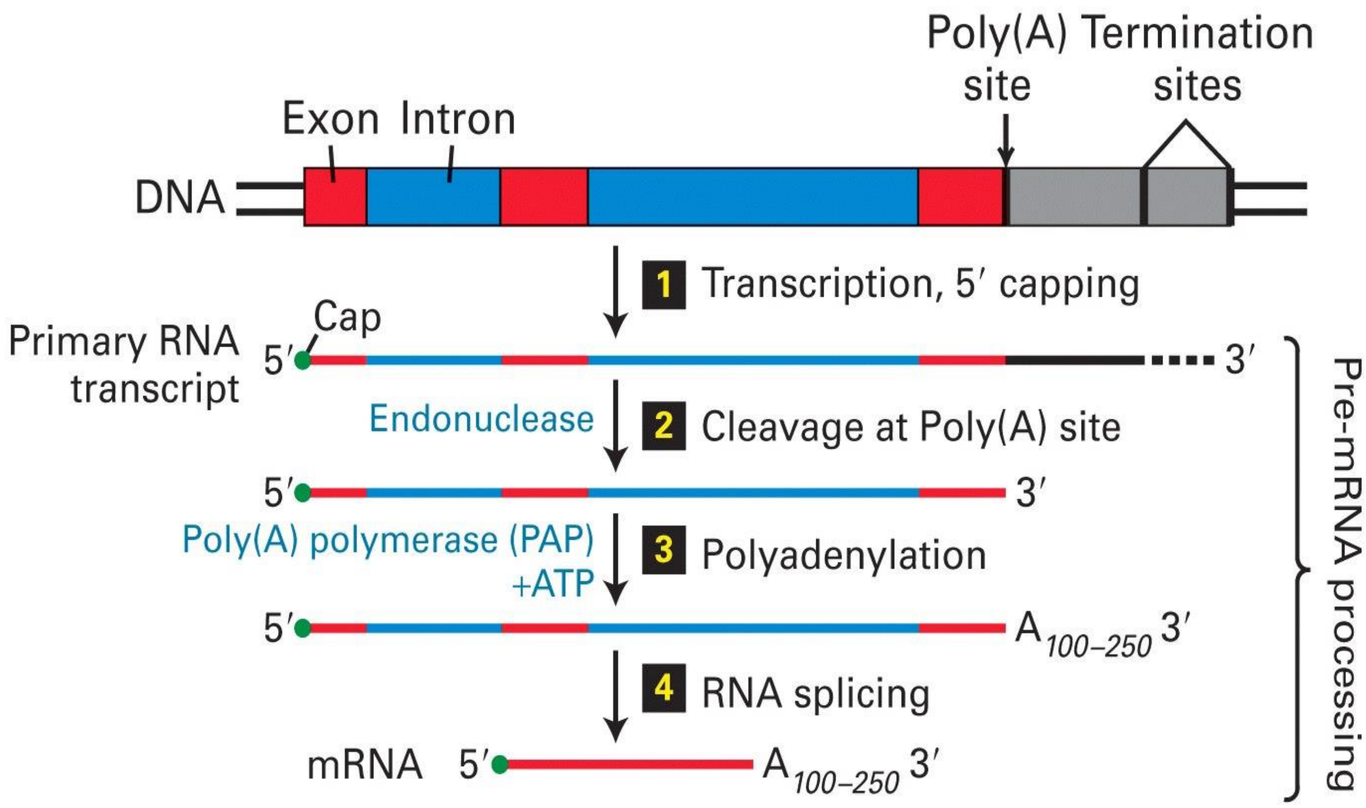
RNA Polymerase

- 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

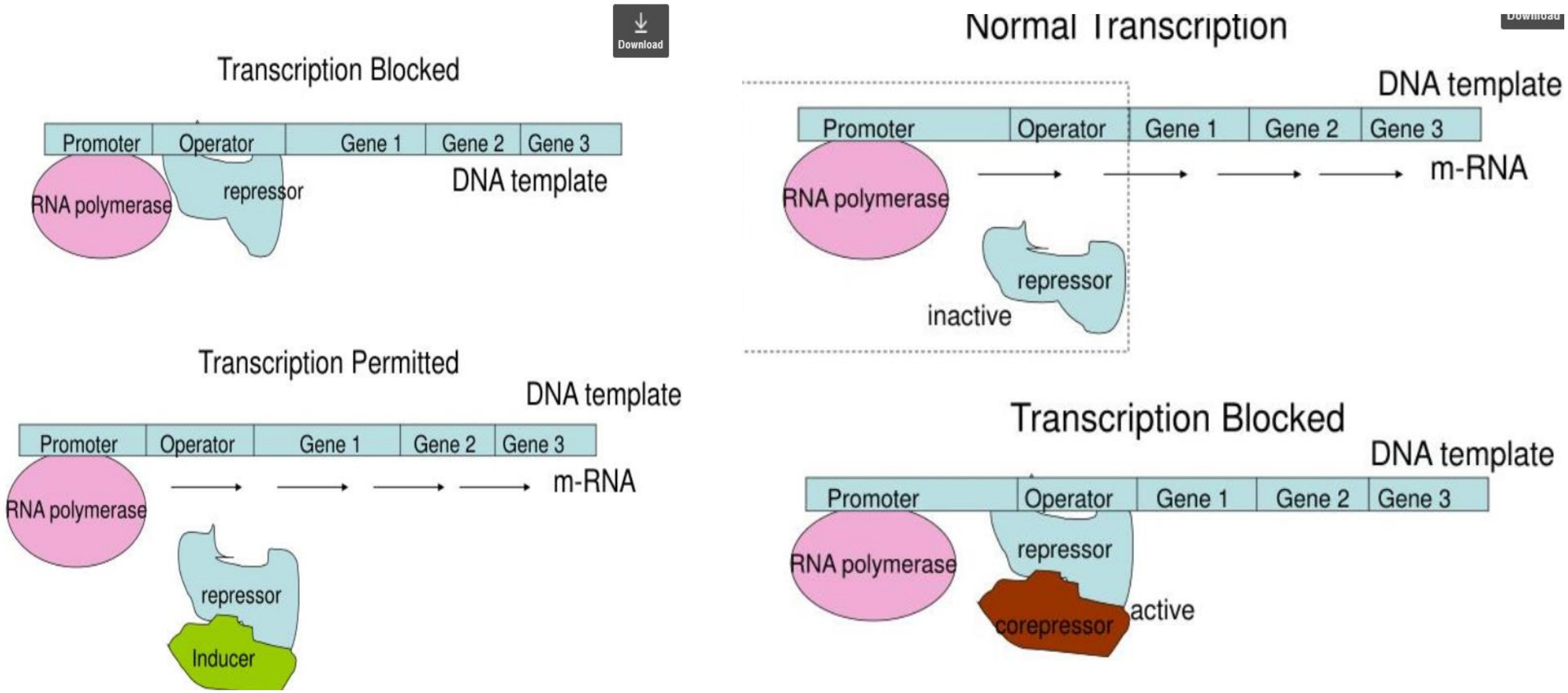


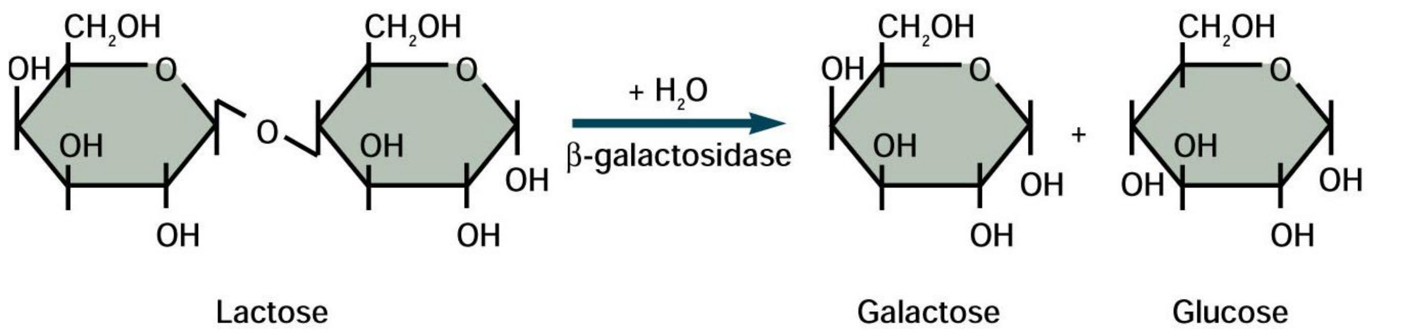
Processing of RNA

Pre-mRNA processing includes 5' capping, 3’ polyadenylation, and intron splicing (Fig. 8.2). These reactions occur in the nucleus, and begin while the primary transcript is being elongated (co-transcriptional). Mature mRNAs then are transported to the cytoplasm for translation.



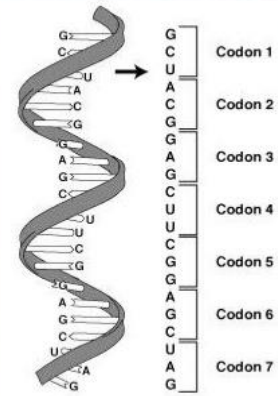
Regulation of Transcription





Genetic Code

- The genetic code is the set of rules by which information encoded in genetic material is translated into proteins by living cells.
- The information in DNA is in the form of triplet codons.
- It is first transcribed into RNA and then into proteins.
- Every triplet codon in the DNA specifies one amino acid in the protein.



RNA

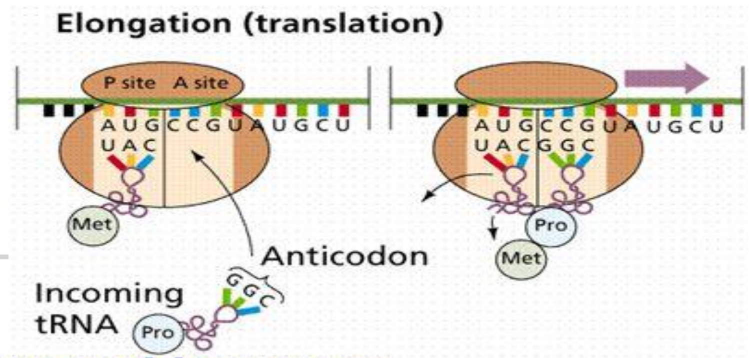
Ribonucleic acid

- 64 codons in total and three out of these are Non Sense codons.
- 61 codons for 20 amino acids

Second Letter

1st letter	U		C		A		G		3rd letter
U	UUU	Phe	UCU	Ser	UAU	Tyr	UGU	Cys	U
	UUC		UCC		UAC		UGC		C
	UUA	Leu	UCA		UAA	Stop	UGA	Stop	A
	UUG		UCG		UAG	Stop	UGG	Trp	G
C	CUU	Leu	CCU	Pro	CAU	His	CGU	Arg	U
	CUC		CCC		CAC		CGC		C
	CUA		CCA		CAA	Gln	CGA		A
	CUG		CCG		CAG		CGG		G
A	AUU	Ile	ACU	Thr	AAU	Asn	AGU	Ser	U
	AUC		ACC		AAC		AGC		C
	AUA		ACA		AAA	Lys	AGA	Arg	A
	AUG	Met	ACG		AAG		AGG		G
G	GUU	Val	GCU	Ala	GAU	Asp	GGU	Gly	U
	GUC		GCC		GAC		GGC		C
	GUA		GCA		GAA	Glu	GGA		A
	GUG		GCG		GAG		GGG		G

Three stages of translation

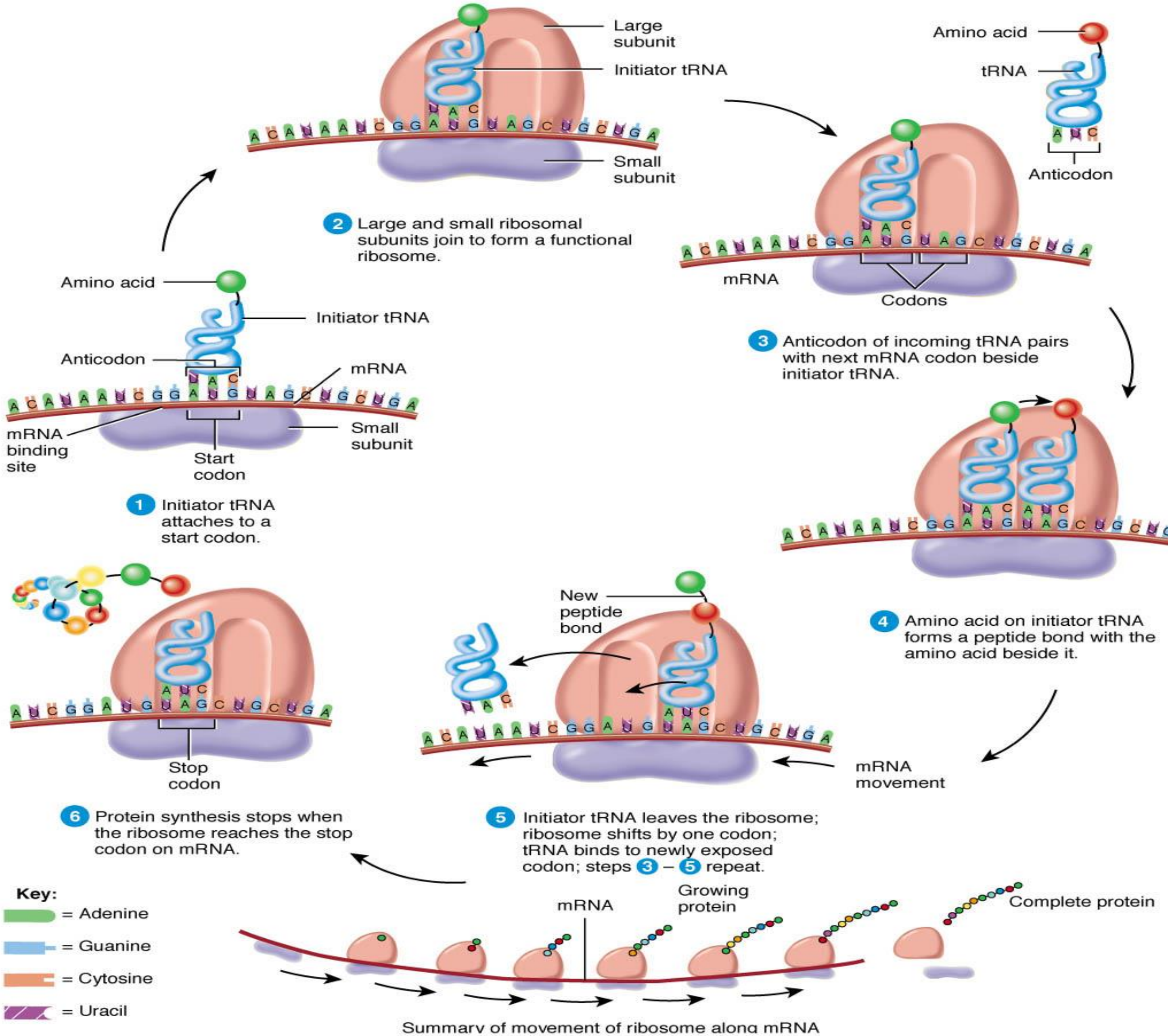


Translation (Protein Synthesis)

The steps of translation:

1. **Initiation**: mRNA enters the cytoplasm and becomes associated with ribosomes (rRNA + proteins). tRNAs, each carrying a specific amino acid, pair up with the mRNA codons inside the ribosomes. Base pairing (A-U, G-C) between mRNA codons and tRNA anticodons determines the order of amino acids in a protein.
2. **Elongation**: addition of amino acids one-by-one: As the ribosome moves along the mRNA, each tRNA transfers its amino acid to the growing protein chain, producing the protein
3. **Termination**: when the ribosomes hits a stop codon - UAA, UGA, or UAG - the ribosome falls apart

Note: The same mRNA may be used hundreds of times during translation by many ribosomes before it is degraded (broken down) by the cell


Large subunit
Initiator tRNA
Small subunit
2 Large and small ribosomal subunits join to form a functional ribosome.
Amino acid
tRNA
Anticodon
mRNA
Codons
3 Anticodon of incoming tRNA pairs with next mRNA codon beside initiator tRNA.
Amino acid
Initiator tRNA
Anticodon
mRNA
mRNA binding site
Start codon
Small subunit
1 Initiator tRNA attaches to a start codon.
4 Amino acid on initiator tRNA forms a peptide bond with the amino acid beside it.
New peptide bond
mRNA movement
5 Initiator tRNA leaves the ribosome; ribosome shifts by one codon; tRNA binds to newly exposed codon; steps 3 – 5 repeat.
Stop codon
6 Protein synthesis stops when the ribosome reaches the stop codon on mRNA.
Key:
= Adenine
= Guanine
= Cytosine
= Uracil
mRNA
Growing protein
Complete protein
Summary of movement of ribosome along mRNA