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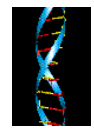
Dr. Shamim Ahmad

DNA and RNA

The Code of Life



The Human Genome Project

Gene Expression

- Genes are DNA sequences that encode proteins (the gene product)
- Gene expression refers to the process whereby the information contained in genes begins to have effects in the cell.
- DNA encodes and transmits the genetic information passed down from parents to offspring.

Genetic code

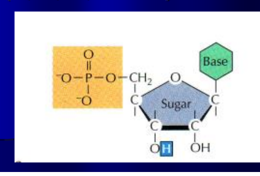
- The alphabet of the genetic code contains only four letters (A,T,G,C).
- A number of experiments confirmed that the genetic code is written in 3-letter words, each of which codes for particular amino acid.
- A nucleic acid word (3 nucleotide letters) is referred to as a ***codon.***

Nucleic acids

- Principle information molecule in the cell.
- All the genetic codes are carried out on the nucleic acids.
- Nucleic acid is a linear polymer of nucleotides

Nucleotides

- Nucleotides are the unit structure of nucleic acids.
- Nucleotides composed of 3 components:
  - Nitrogenous base (A, C, G, T or U)
  - Pentose sugar
  - Phosphate

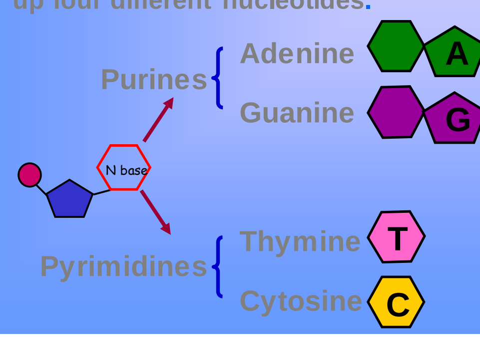


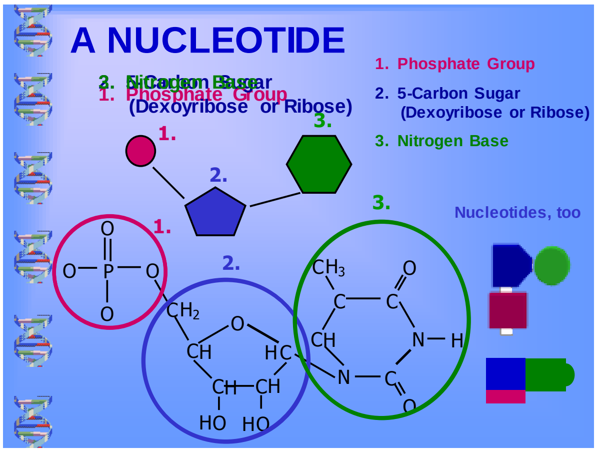
Nitrogenous bases

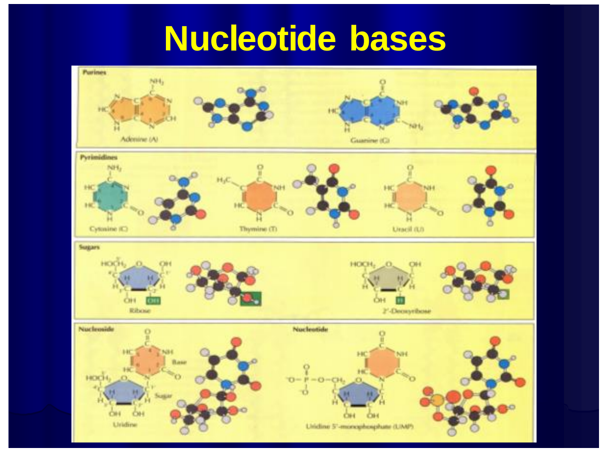
- There are 2 types:
  - Purines(py*oo*r-een):
    - Two ring structure
    - Adenine (A) and Guanine (G)
  - Pyrimidines(pahy-**rim**-i-deen,):
    - Single ring structure
    - Cytosine (C) and Thymine (T) or Uracil (U).

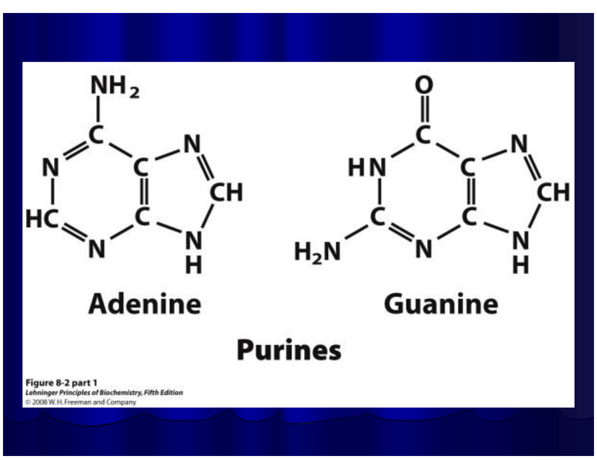
Nucleotides

- There are four nitrogen bases making up four different nucleotides.




A NUCLEOTIDE
1. Phosphate Group
2. 5-Carbon Sugar
(Dexoyribose or Ribose)
3. Nitrogen Base
Nucleotides, too


Nucleotide bases
Purines
Adenine (A)
Guanine (G)
Pyrimidines
Cytosine (C)
Thymine (T)
Uracil (U)
Sugars
Ribose
2'-Deoxyribose
Nucleoside
Nucleotide
Uridine
Uridine 5'-monophosphate (UMP)


Adenine
Guanine
Purines
Figure 8-2 part 1
Lehninger Principles of Biochemistry, Fifth Edition
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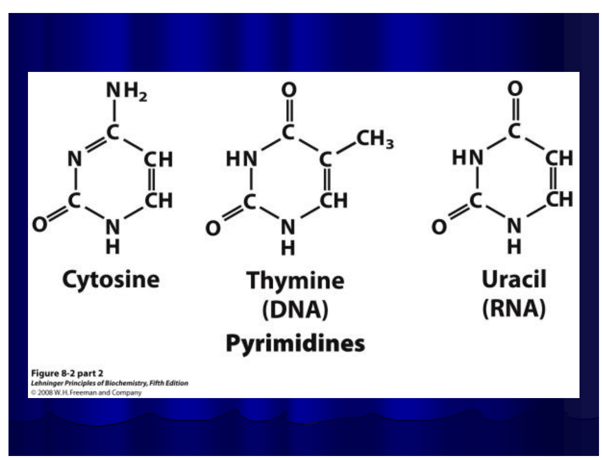
Cytosine
Thymine
(DNA)
Uracil
(RNA)
Pyrimidines
Figure 8-2 part 2
Lehninger Principles of Biochemistry, Fifth Edition
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Role of Nucleotides

- They carry packets of chemical energy—in the form of the nucleoside triphosphates
  ATP(Adenosine triphosphate)
  GTP(Guanosine triphosphate
  CTP(Cytidine triphosphate)

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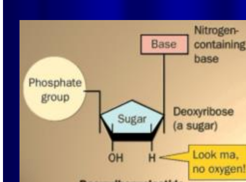
Role of Nucleotides

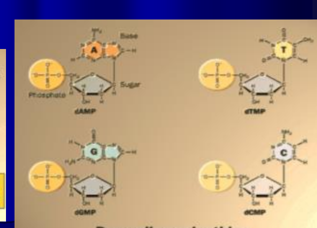
- throughout the cell to the many cellular functions that demand energy
  - synthesizing amino acids
  - synthesizing proteins
  - cell membranes and parts
- Moving the cell and moving cell parts
  - internally and intercellularly
- Dividing the cell
- Participate in cell signaling
  - (cGMP and cAMP

Types of Nucleic acids

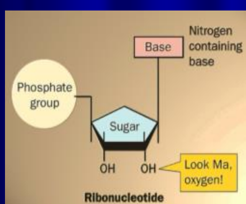
There are 2 types of nucleic acids:

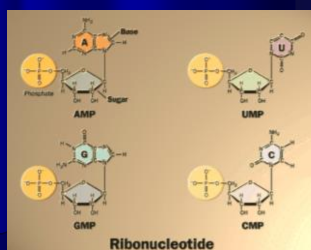
1. **Deoxy-ribonucleic acid (DNA)**
   - **Pentose Sugar is deoxyribose (no OH at 2' position)**
   - **Bases are Purines (A, G) and Pyrimidine (C, T).**





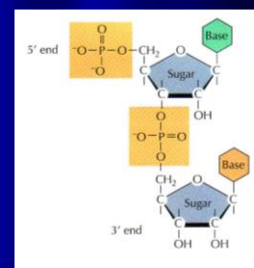
2. <u>Ribonucleic acid</u> (RNA)
   - Pentose Sugar is Ribose.
   - Bases are Purines (A, G) and Pyrimidines (C, U).





Polymerization of Nucleotides

- The formed polynucleotide chain is formed of:
  - Negative (-ve) charged Sugar-Phosphate backbone.
    - Free 5' phosphate on one end (5' end)
    - Free 3' hydroxyl on other end (3' end)
  - Nitrogenous bases are not in the backbone
    - Attached to the backbone
    - Free to pair with nitrogenous bases of other polynucleotide chain



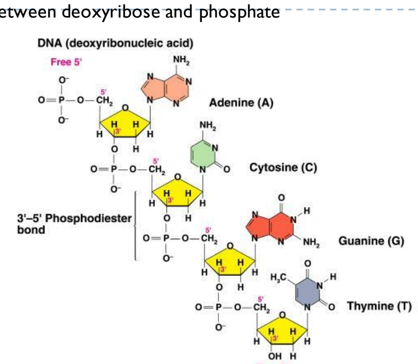
Polymerization of Nucleotides

- Nucleic acids are polymers of nucleotides.
- The nucleotides formed of purine or pyrimedine bases linked to ***phosphorylated sugars*** (nucleotide back bone).
- The bases are linked to the pentose sugar to form ***Nucleoside***.
- The nucleotides contain one phosphate group linked to the 5' carbon of the nucleoside.

Nucleotide = Nucleoside + Phosphate group

Example of DNA Primary Structure

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



N.B.

- The polymerization of nucleotides to form nucleic acids occur by condensation reaction by making phospho-diester bond 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.**

Example of DNA Primary Structure

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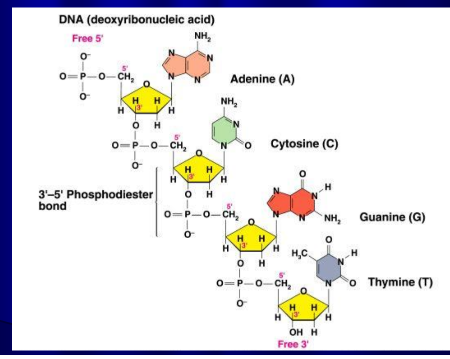
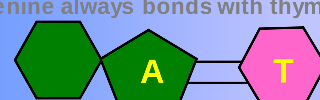


Complementary base pairing

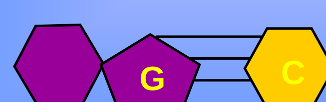
- **It is the most important structural feature of nucleic acids**
- **It connects bases of one polynucleotide chain (nucleotide polymer) with complementary bases of other chain**
- **Complementary bases are bonded together via:**
  - **Double hydrogen bond between A and T (DNA), A and U (RNA) (A=T or A=U)**
  - **Triple H-bond between G and C in both DNA or RNA (G≡C)**

Chargaff's Base Pair Rules

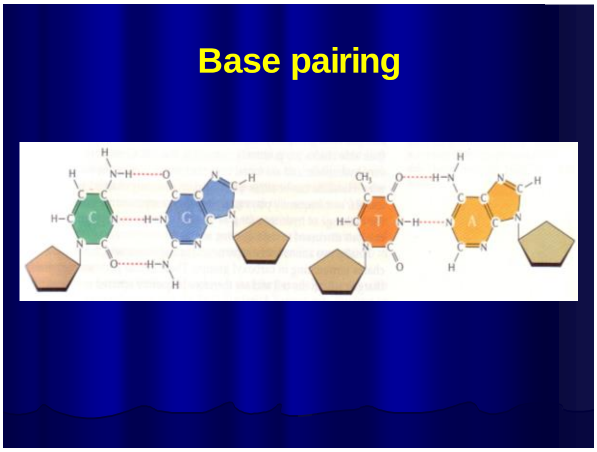
- Adenine always bonds with thymine. A = T



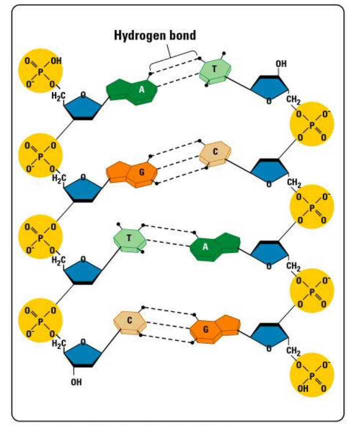
The lines between the bases represent hydrogen bonds

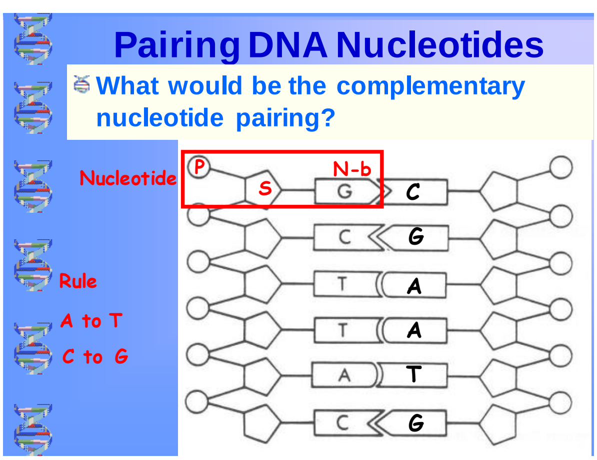


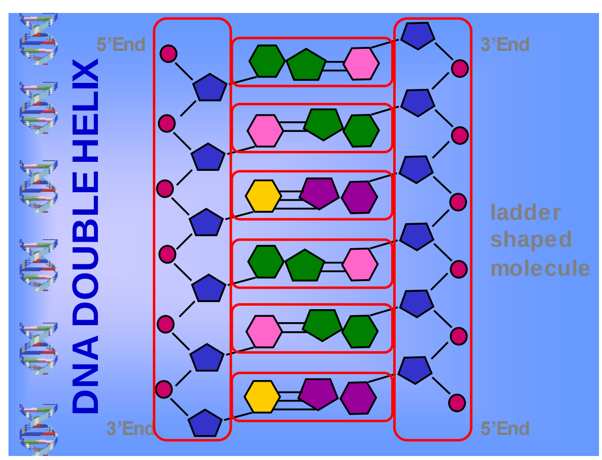
- Guanine always bonds with Cytosine. G ≡ C



Base pairing in DNA:

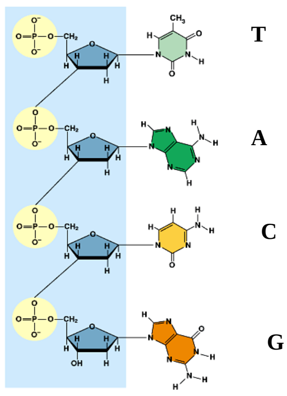






A single strand of DNA

Sugar-phosphate backbone



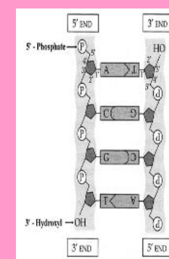
How Do Nitrogen Bases Pair Up?

- Adenine(A) pairs up w/ Thymine(T)
- Guanine(G) pairs up w/ Cytosine(C)

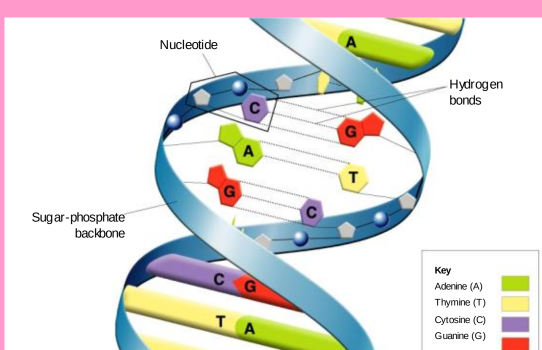
Example:

3' A G C   T A C   G C A 5'

5' T C G   A T G   C G T 3'



Structure of DNA



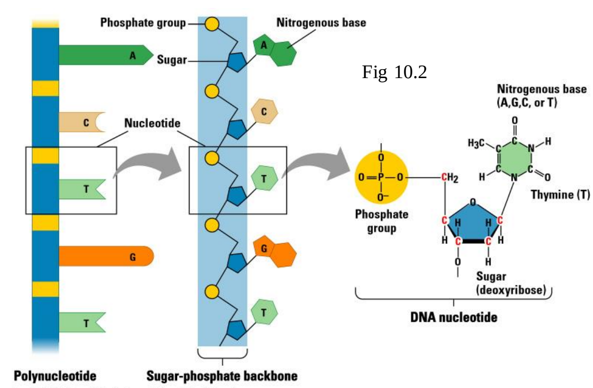
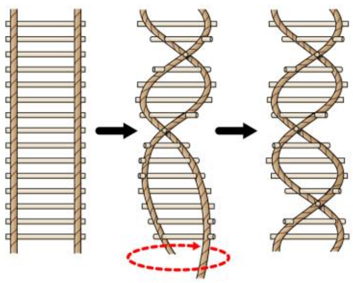


Fig 10.2

DNA is like a rope ladder twisted into a spiral



DNA Structure

- Consists of 2 strands joined together **by weak hydrogen bonds**
- Rungs of the ladder are hydrogen bonded N-bases

Fig 10.4

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.

Artificial Nucleotides

1989

- Steven Benner
  - Swiss Federal Institute of Technology
- Modified forms
  - Cytosine
  - Guanine
- DNA molecules in **vitro**

Artificial Nucleotides

2002

Ichiro Hirao's group, Japan

Unnatural base pair between 2-amino-8

2006

7-(2-thienyl)imidazo

2013

Applied the Ds-Px pair to DNA in vitro

2012

American scientists led by Floyd R

- The two new artificial nucleotides or Unnatural Base Pair (UBP)
- **d5SICS and dNaM**
- Bearing hydrophobic nucleobases
- team designed a variety of in vitro

Artificial Nucleotides

2014

- A team synthesized a stretch of circular DNA known as a plasmid containing natural T-A and C-G base pairs along with the best-performing UBP (Unnatural Base Pair).

Artificial Nucleotides

2014

- inserted it into *E. coli* (intestines)
- that successfully replicated the unnatural base pairs through multiple generations.
- This is the first known example of a living organism passing along an expanded genetic code
- **300 variants** to refine the design of nucleotides

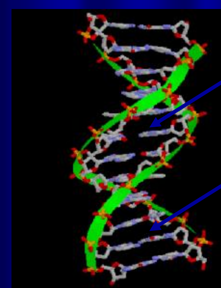
DNA structure

- DNA is a double stranded molecule consists of 2 polynucleotide chains **running in opposite directions.**
- Both strands are complementary to each other.
- The bases are on the inside of the molecules and the 2 chains are joined together by double **H-bond** between A and T and triple H-bond between C and G..

DNA structure

- The base pairing is very specific which make the 2 strands complementary to each other.
- So each strand contain all the required information for synthesis (replication) of a new copy to its complementary.

Forms of DNA



Minor groove

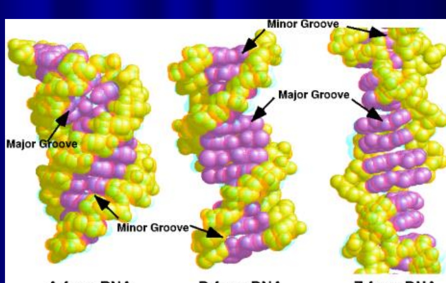
The minor groove is generated by the smaller angular distance between sugars.

Major groove

major groove:
The larger of the two grooves that spiral around the surface of the B-form of DNA.

DNA structure:
Secondary Structure: alternative conformations

Lecture 7.2
10/4/2006



Forms of DNA

1- *B-form helix*:

- It is the most common form of DNA in cells.
  - Right-handed helix
  - Turn every **3.4 nm.**
  - Each turn contain **10 base pairs** (the distance between each 2 successive bases is 0.34 nm)
  - Contain 2 grooves;
    - Major groove (wide): provide **easy access to bases**
    - Minor groove (narrow): provide poor access.

2- *A-form DNA*:

- Less common form of DNA , more common in RNA
  - Right handed helix
  - Each turn contain **11 b.p/turn**
  - Contain 2 different grooves:
    - Major groove: very **deep and narrow**
    - Minor groove: very shallow and wide (binding site for RNA)

3- *Z-form DNA*:

- Radical change of B-form
  - Left handed helix, very extended
  - It is **GC rich DNA regions.**
  - The sugar base backbone form Zig-Zag shape
  - The B to Z transition of DNA molecule may play a role in gene regulation**.**

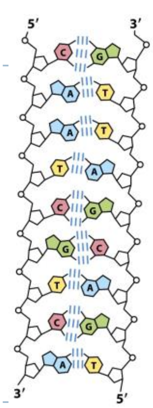
Denaturing and Annealing of DNA

- The DNA double strands can denatured if heated (95ºC) or treated with chemicals.
  - **AT regions denature first (2 H bonds)**
  - **GC regions denature last (3 H bonds)**
- DNA denaturation is a **reversible process**, as denatured strands can re-annealed again if cooled.
- This process can be monitored using the hyperchromicity (melting profile**).**

Hyperchromicity (melting profile)

- It is used to monitor the DNA denaturation and annealing.
- It is based on the fact that single stranded (SS) **DNA gives higher absorbtion reading than double stranded (DS) at wavelength 260º.**
- Using melting profile we can differentiate between single stranded and double stranded DNA**.**

Properties of a DNA double helix

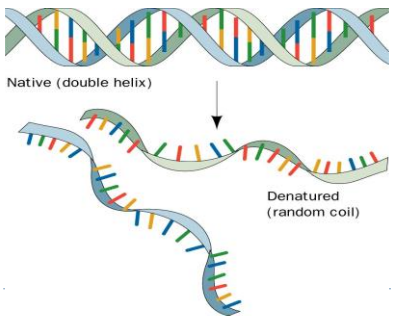


The strands of DNA are antiparallel

The strands are complimentary

There are Hydrogen bond forces

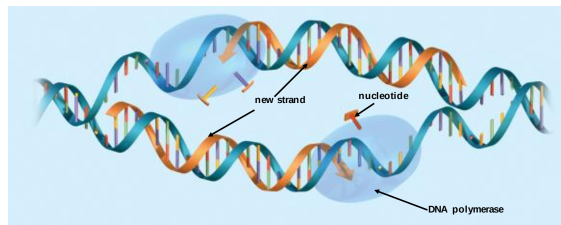
Schematic representation of the strand separation in duplex DNA resulting from its heat denaturation.



Page 90

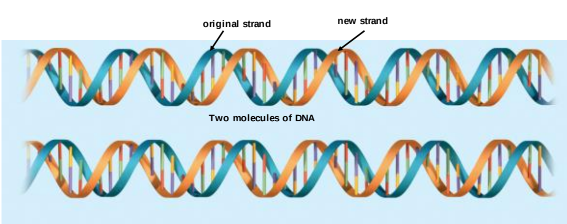
8.3 DNA Replication

- **DNA polymerase** enzymes bond the nucleotides together to form the double helix.
- Polymerase enzymes form covalent bonds between nucleotides in the new strand.



8.3 DNA Replication

- Two new molecules of DNA are formed, each with an original strand and a newly formed strand.
- DNA replication is therefore, **semiconservative.**



DNA Replication

- **Replication of the DNA molecule is semi-conservative, which means that each parent strand serves as a template for a new strand and that the two (2) new DNA molecules each have one old and one new strand.**
- **DNA replication requires:**
  - **A strand of DNA to serve as a *template***
  - ***Substrates* - deoxyribonucleoside triphosphates (dATP, dGTP, dCTP, dTTP).**
  - ***DNA polymerase* - an enzyme that brings the substrates to the DNA strand template**
  - **A source of *chemical energy* to drive this synthesis reaction.**

DNA Replication

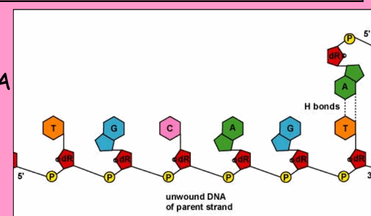
- **Nucleotides are always added to the growing strand at the 3' end (end with free -OH group).**
- The hydroxyl group reacts with the phosphate group on the 5' C of the deoxyribose so the chain grows
- Energy is released when the bound **linking 2 of the 3** phosphate groups to the deoxyribonucleoside **triphosphate breaks**
- Remaining phosphate group becomes part of the sugar-phosphate backbone

Replication of DNA

•During cell division a *copy* of DNA must be made

•When new cells are formed each new cell gets an *exact copy* of the genetic information.

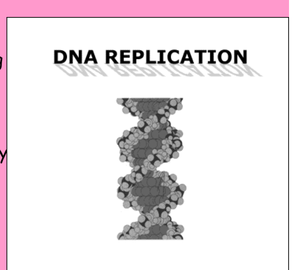
•This *copy* of DNA is made through a process known as ***Replication.***



Steps of Replication

•During replication, each strand serves as a pattern to make new DNA molecule.

1. The 2 nucleotide strands separate at base pairs.
   - They unzip like a zipper using *DNA Helicase (enzyme)*
2. Each strand then builds its opposite strand by base pairing with nucleotides that float freely in the nucleus.
3. Each new DNA molecule has 1 nucleotide strand from the *original* DNA molecule and 1 nucleotide strand made from *free* nucleotides in the nucleus.

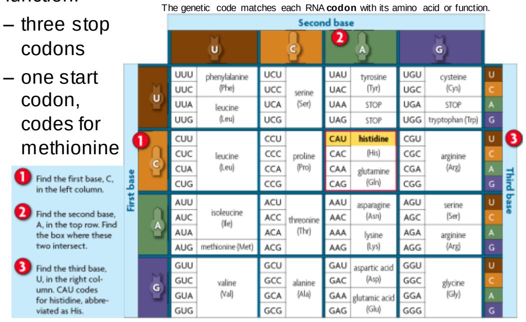


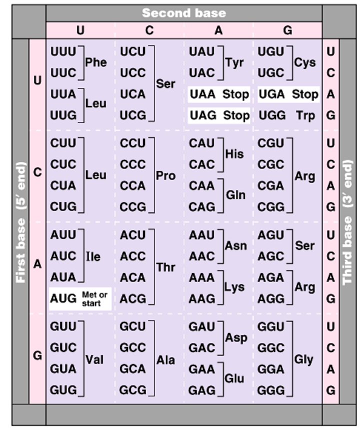
Let's see DNA Replication at Work!

8.5 Translation

- The genetic code matches each codon to its amino acid or function.
  - three stop codons
  - one start codon, codes for methionine

The genetic code matches each RNA **codon** with its amino acid or function.





<u>Codon</u> = 3 letter section of mRNA that codes for one amino acid

Amino Acid	SLC	DNA codons
Isoleucine	I	ATT, ATC, ATA
Leucine	L	CTT, CTC, CTA, CTG, TTA, TTG
Valine	V	GTT, GTC, GTA, GTG
Phenylalanine	F	TTT, TTC
Methionine	M	ATG
Cysteine	C	TGT, TGC
Alanine	A	GCT, GCC, GCA, GCG
Glycine	G	GGT, GGC, GGA, GGG
Proline	P	CCT, CCC, CCA, CCG
Threonine	T	ACT, ACC, ACA, ACG
Serine	S	TCT, TCC, TCA, TCG, AGT, AGC
Tyrosine	Y	TAT, TAC
Tryptophan	W	TGG
Glutamine	Q	CAA, CAG
Asparagine	N	AAT, AAC
Histidine	H	CAT, CAC
Glutamic acid	E	GAA, GAG
Aspartic acid	D	GAT, GAC
Lysine	K	AAA, AAG
Arginine	R	CGT, CGC, CGA, CGG, AGA, AGG
Stop codons	Stop	TAA, TAG, TGA