BIOLOGY 12 **NAME: ______________________________**

CELL BIOLOGY: DNA

IMPORTANT FACTS:

Nucleic acids are organic compounds found in all living cells and viruses.

Two classes of nucleic acids:

1. DNA = deoxyribonucleic acid; found in the nucleus only.
2. RNA = ribonucleic acid; found in the nucleus and cytoplasm

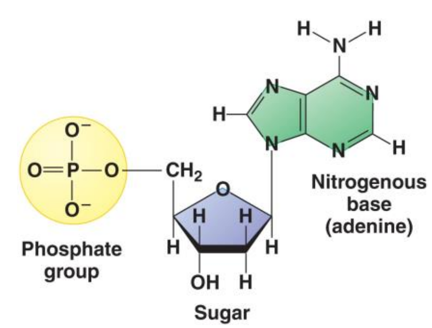
Nucleic acids are polymers made up of chains of building block monomers called nucleotides

NUCLEOTIDES:

Each nucleotide monomer is made up of three linked molecules:

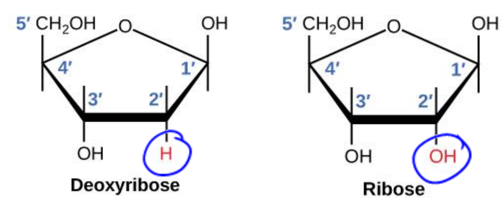
1. phosphate
2. pentose sugar
3. nitrogen-containing base
   A, G, T, C, U

Generalized nucleotide structure:



1. 5 - Carbon sugar:
   The sugar in DNA is called deoxyribose
   Its empirical formula is $C_5H_{10}O_4$

   The sugar in RNA is called ribose
   Its empirical formula is $C_5H_{10}O_5$



2. Phosphate group:
   The phosphate groups on all nucleotides are the same

3. Nitrogenous organic bases:

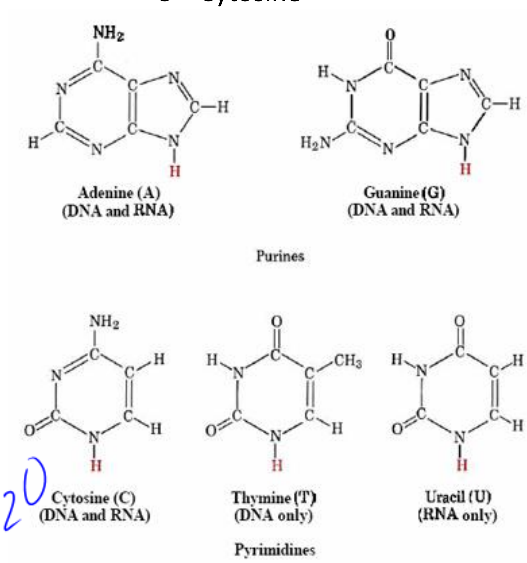
DNA contains four organic bases:		RNA contains four organic bases	
A = Adenine	G = Guanine	A = Adenine	G = Guanine
T = Thymine	C = Cytosine	U = Uracil	C = Cytosine

Adenine and Guanine are called purines bases

➢ They have a double ring of carbon and nitrogen bases

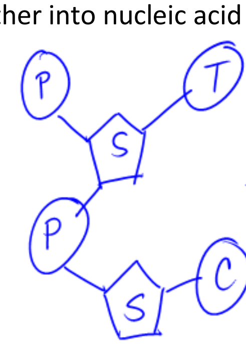
Cytosine, Thymine and Uracil are called pyrimidines bases

➢ They have a single ring of carbon and nitrogen bases



The process of joining nucleotide monomers together into nucleic acid polymers is called DEHYDRATION SYNTHESIS:

nucleotide + nucleotide →



$+ H_2O$

A strong covalent bond is formed between the sugar of one nucleotide and the phosphate of an adjacent nucleotide.

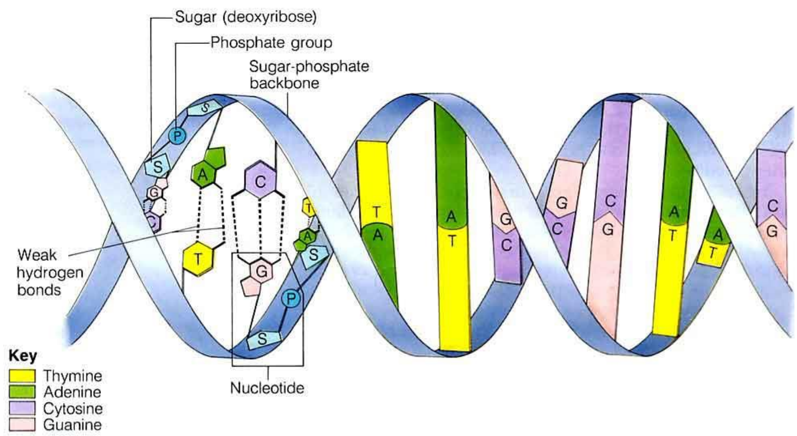
- A nucleic acid strand has a "backbone" made up of alternating phosphate and sugar molecules.

DNA STRUCTURE: THE DOUBLE HELIX

The structure of DNA was first described in 1953 by James Watson and Francis Crick and is therefore referred to as the Watson - Crick Model of DNA.

Refer to page 114 in your textbook

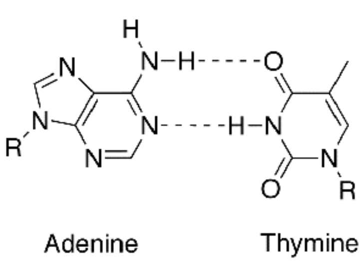
- DNA is made up to two strands of nucleotides that are joined together like a "ladder"
    - The deoxyribose sugars and phosphate groups form the sides
    - The nitrogenous bases form the rungs



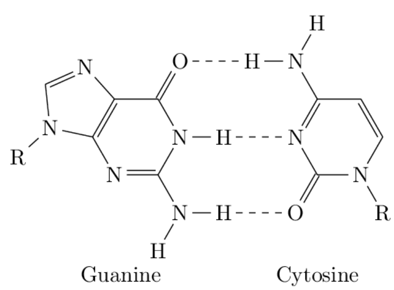
The two strands are held together by weak hydrogen bonds between the bases that twists the two strands to form a spiral structure called a DNA double helix.

__Complementary base pairing:__

- Adenine (A) always pairs with Thymine (T)
- Cytosine (C) always pairs with Guanine (G)



2 Hydrogen bonds



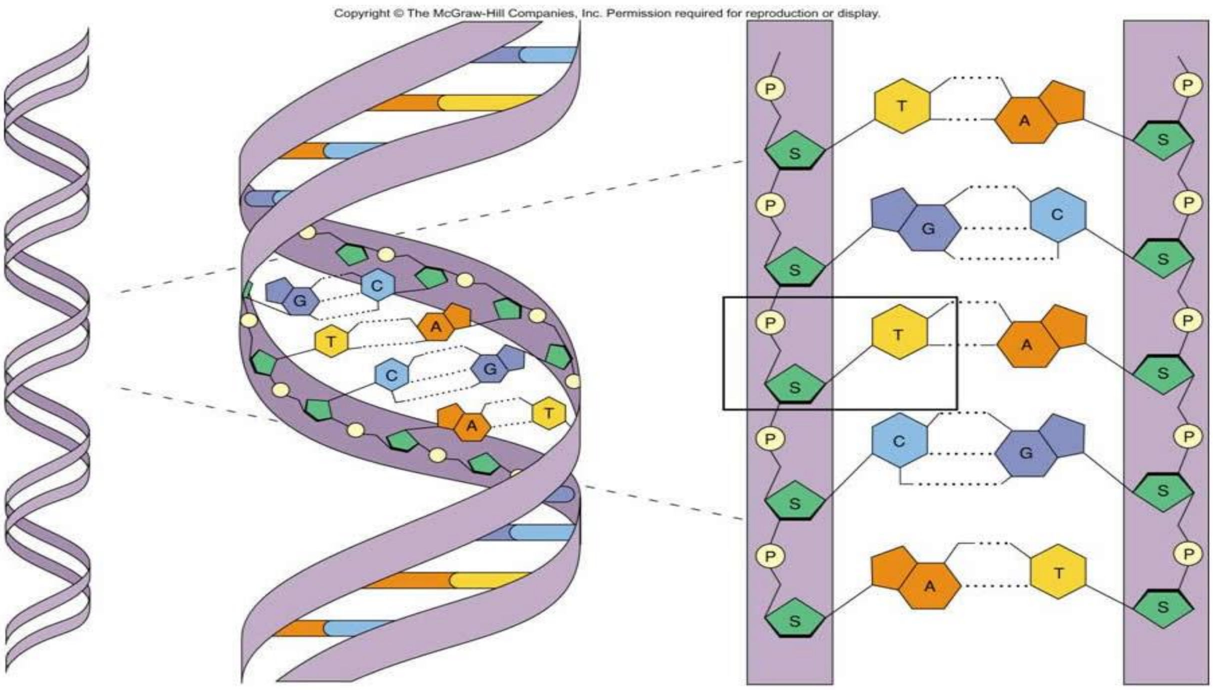
3 Hydrogen bonds

Complementary base pairing occurs because the structure of Adenine complements that of Thymine in such a way that two hydrogen bonds are formed, and Cytosine complements Guanine so that three hydrogen bonds are formed. Therefore, Adenine and Thymine fit together like two puzzle pieces and Cytosine and Guanine fit together. Because of this special fit, Thymine never pairs with anything but Adenine, and Guanine never pairs with anything but Cytosine.

A purine always pairs with a pyrimidine.

Overview of DNA Structure:

The double helix structure is a twisted ladder. Unwound DNA shows that the sides of the ladders are composed of phosphate and sugar molecules and the rungs are complementary-paired bases.



a. DNA double helix   b. Complementary base pairing   c. Ladder configuration

FUNCTIONS OF DNA:

DNA, as the hereditary material, has at least three functions:

1) DNA makes exact copies of itself DNA must pass on hereditary characteristics from one generation to the next. DNA replicates with high accuracy prior to cell division when a copy is distributed to daughter cells. It is also transmitted in the gametes from parents to offspring.

2) DNA controls cellular activities DNA must trigger the manufacture of specific proteins that control both the development and the metabolic activities of the cell and the organism. In order to make a particular protein, cells must have a code – DNA provides this code.

3) DNA undergoes mutations Although DNA replicates with high accuracy, it must have the ability to undergo rare changes called mutations (more later). Mutations provide genetic variability and are the raw materials for evolutionary change.

DNA REPLICATION:

DNA replicates before mitosis during the growth phase of the cell cycle (known as interphase), so that each new cell receives a copy of the genetic material.

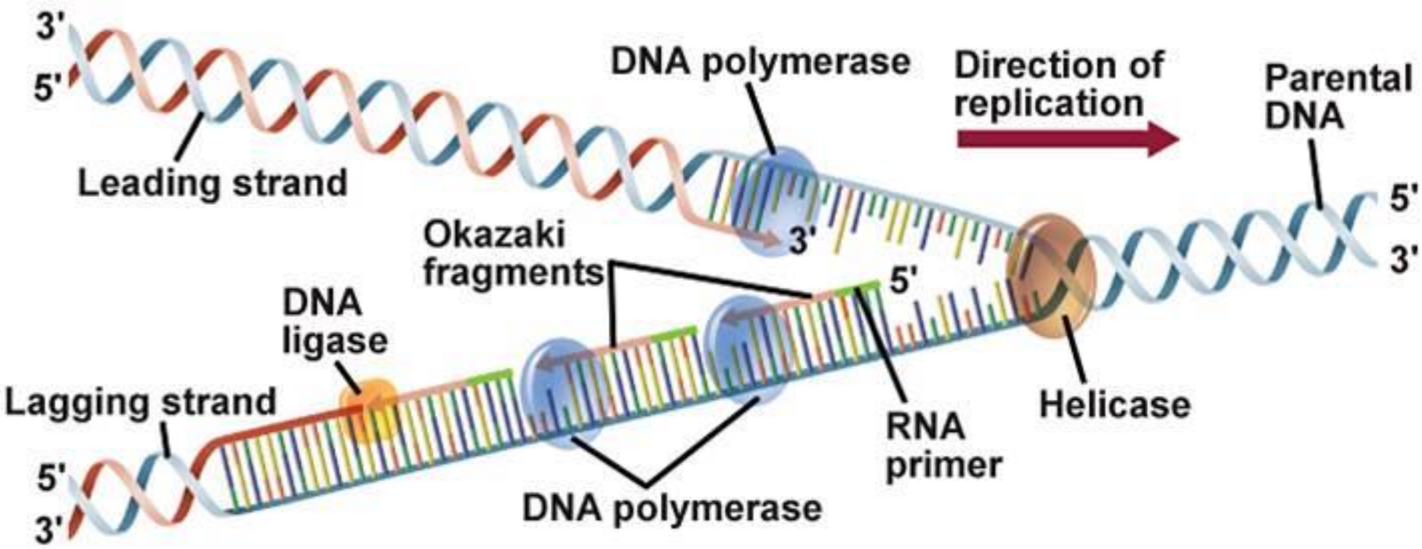
DNA REPLICATION HAS THREE STAGES:

1. "Unzipping"

DNA replication begins in the nucleus of the cell, when the DNA helix unwinds and an enzyme called DNA helicase attaches to the DNA molecule and moves along the molecule "unzipping" the two strands of DNA. DNA helicase acts by breaking the weak hydrogen bonds between the nitrogenous bases.

Primase is an enzyme that synthesizes short RNA sequences called primers. These primers serve as a starting point for DNA synthesis. Since primase produces RNA molecules, the enzyme is a type of RNA polymerase.

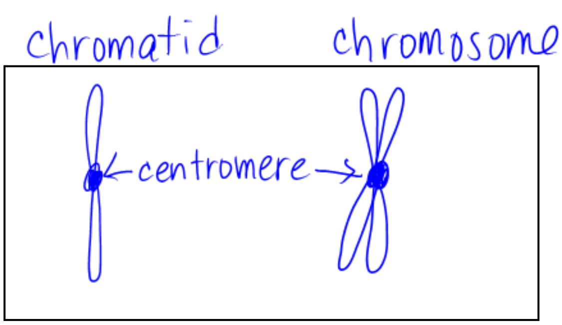
-Primase adds RNA primers onto the lagging strand, which allows synthesis of Okazaki fragments from 5' to 3'
The primase generates short strands of RNA that bind to the single-stranded DNA to initiate DNA synthesis by the DNA polymerase. DNA Polymerase can work only in the 5' to 3' direction, so it replicates the leading strand continuously. Lagging-strand (3’ to 5’) replication is discontinuous, with short Okazaki fragments being formed and later linked together.



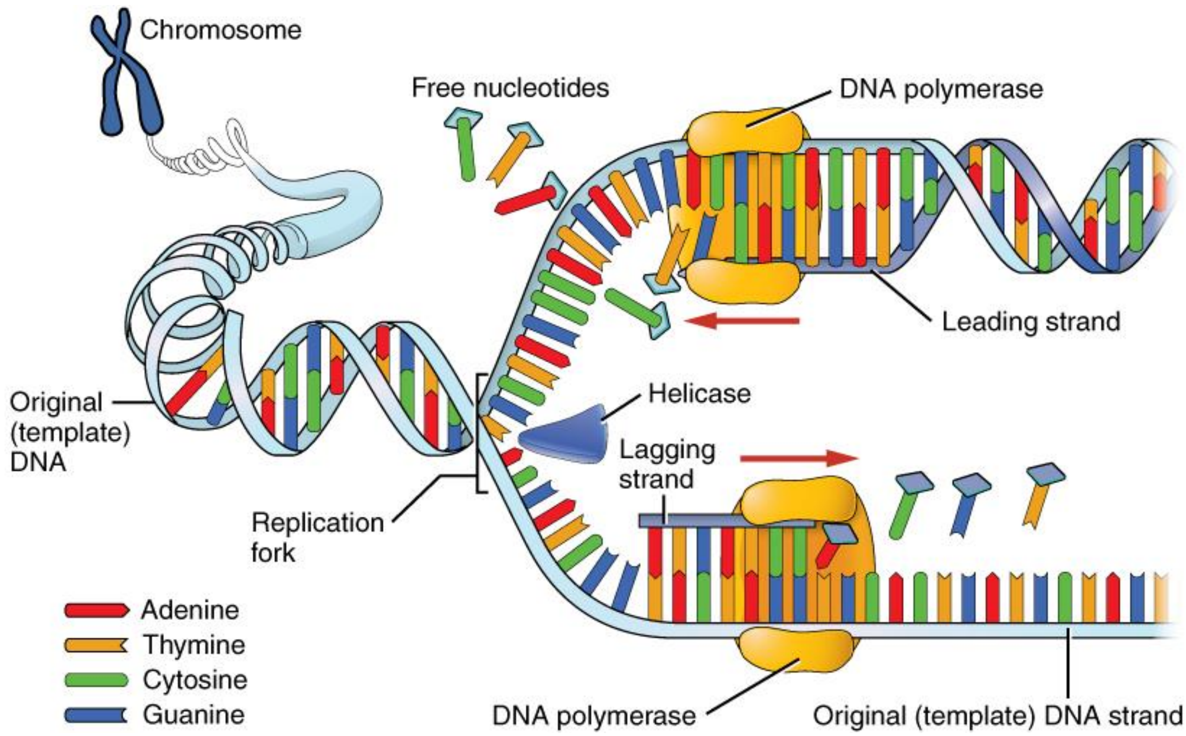
2. Complementary Base Pairing
As the DNA strands separate, free nucleotide monomers (always present floating free in the nucleus) form hydrogen bonds with the exposed nitrogenous bases by the process of complementary base pairing. I.e. A joins with T; C joins with G

3. Adjacent Nucleotides bond
As each new set of hydrogen bonds pairs with the nitrogenous bases, an enzyme called DNA ligase catalyzes the formation of the sugar-to-phosphate covalent bonds (via dehydration synthesis) that connect one nucleotide monomer to the next one (creating the nucleic acid backbone of this new DNA strand).

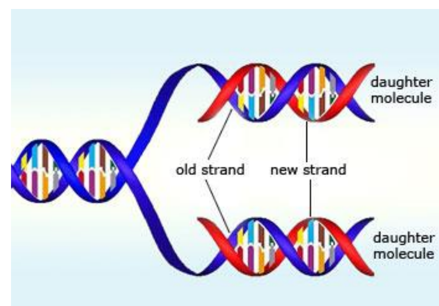
- The two DNA molecules rewind into their “corkscrew” double helix shape again.
- Each double helix is then coiled around histone proteins to form separate chromatids (which are still joined by the centromere). This new chromosome now has twice (2x) as much DNA as a regular (non-replicated/single chromatid) chromosome.
- The two chromatids will become separated in the cell division (mitosis) process to form separate chromosomes.



DNA REPLICATION DIAGRAM:



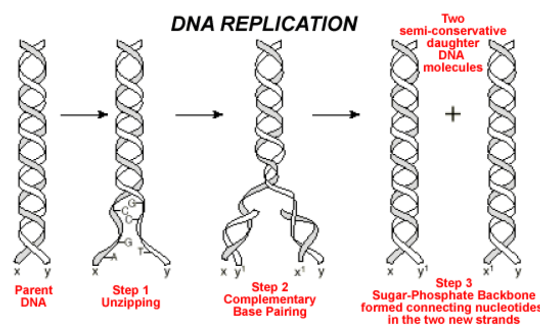
SEMICONSERVATIVE REPLICATION



DNA replication is termed SEMICONSERVATIVE because each new double helix of DNA has one "_old_" or parental strand and one "_new_" or daughter strand.

- Therefore, one of the parental strands is present, or conserved, in each new DNA molecule.

These two new DNA molecules each have the same base sequence as the original (parental) DNA molecule. Therefore, the information content of the DNA is UNCHANGED, just _replicated_.



REPLICATING ACCURATELY

The entire process of DNA replication occurs with great accuracy:

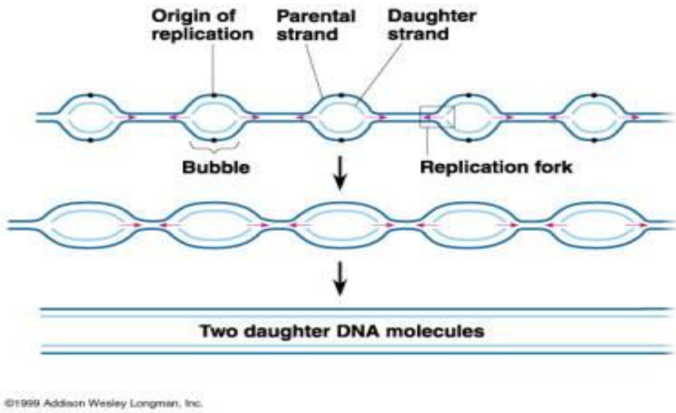
- The nitrogenous bases seldom pair incorrectly because **DNA Polymerase** has a _Proof-reading_ function (like spell check!) It checks each complementary base pairing as soon as they occur, and if it finds a mistake, with the help of other enzymes, it removes the incorrect nucleotide and replaces it with the correct one.
- If an error is NOT corrected, a MUTATION has occurred (more to come later).

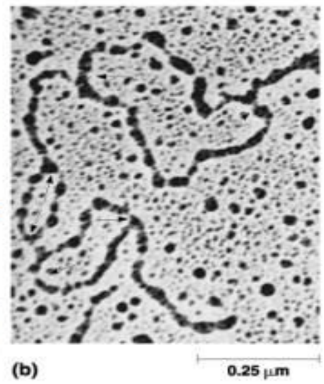
FINAL FACTS ON DNA REPLICATION

Replication of DNA doesn't begin at one end of the molecule and proceed to the other.

- Copying of DNA occurs simultaneously at many points on the molecule, called "_Replication_ _Fork_."
- **DNA Polymerase** enzymes join the individual segments of new DNA to each other as they are copied.

Because of the size of the DNA molecule, if replication DIDN'T occur in this way, ~~it would take~~ 16 days to copy just one DNA molecule of a fruit fly! Actually, the replication of this fruit fly DNA takes only about 3 minutes, because about 6,000 sites are being copied simultaneously.





In this micrograph, three replication bubbles are visible along the DNA of cultured Chinese hamster cells.

SECOND FUNTION OF DNA: **PROTEIN SYNTHESIS**

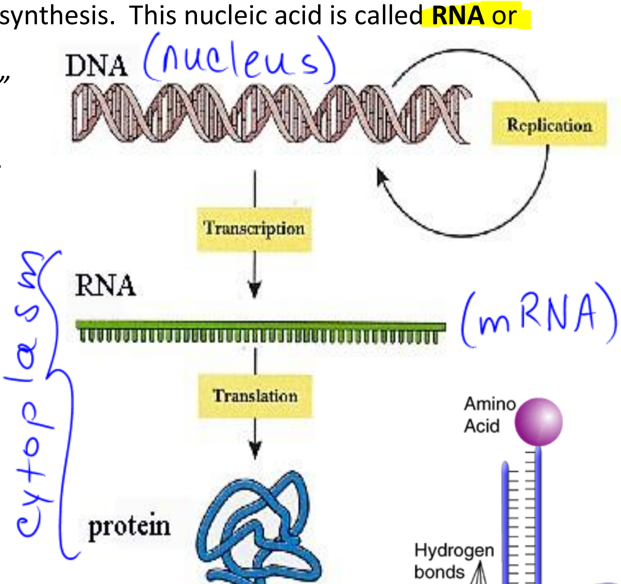
IMPORTANT BACKGROUND INFORMATION

DNA stores and transmits the information needed to make proteins, but it is not that information that is used to synthesize proteins.

DNA, with its blueprints for protein synthesis, is located in the cell __nucleus__.
Yet the manufacture of protein molecules takes place in the __cytoplasm__ of the cell, on structures called __ribosomes__ (also found on __E.R.__).

DNA molecules do not leave the nucleus to control the production of proteins. Instead, another type of nucleic acid acts as a messenger between DNA and ribosomes, and carries out protein synthesis. This nucleic acid is called **RNA or Ribonucleic acid.**

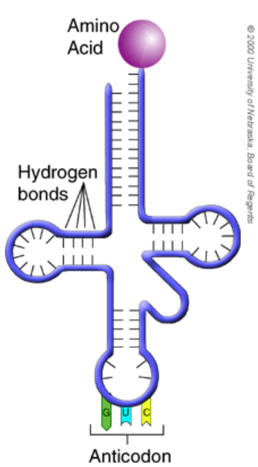
- ➢ *Refer to sheet: "DNA structure compared with RNA structure."*



Therefore, DNA not only serves as a template for its own replication (DNA replication), but it also acts in the nucleus as a template for RNA formation: __Transcription__; which in turn is used to make proteins in the cytoplasm of the cell : __Translation__.

THERE ARE THREE KINDS OF RNA:

1) __Messenger RNA__ (__mRNA__)
= single, uncoiled strand of RNA that carries the sequence of nucleotides that code for protein, from the nucleus to the cytoplasm.



2) __Transfer RNA__ (__tRNA__)
= a single strand of RNA folded back on itself in a "cloverleaf" fashion, that picks up individual amino acids in the cytoplasm and carries them to the ribosomes. There the amino acids are rejoined together in proper order to make a protein.

3) __Ribosomal RNA__ (__rRNA__)
= a globular form of RNA which is the main constituent of the ribosome. Produced in the __nucleolus__ where it joins with the proteins made in the cytoplasm. The small subunit (of a ribosome) contains one RNA molecule and many different types of proteins, and the large subunit (of a ribosome) contains three

RNA molecules (eukaryotes) and also many different types of proteins. Among these proteins is the enzyme that joins amino acids by means of peptide bonds.

THE GENETIC CODE:

- ➢ The information that DNA transfers to messenger RNA is in the form of a code.
- An organism's genetic makeup is determined by the way in which the 4 nitrogenous bases are arranged in the original DNA strand.
- DNA has only four nitrogenous bases (A, T, C, G), but proteins contain 20 different amino acids: How can 4 bases provide enough combinations to code for these 20 amino acids?

- *One base cannot code for one amino acid (four possible amino acids only)*
- *Two bases cannot code for one amino acid (4^2 = 16 different amino acids only)*
- *Three bases can & do code for one amino acid (4^3 = 64 different amino acids)*

- Therefore, a triplet code (bases in groups of three) of the 4 bases would supply 64 different triplets, far more than needed to code for 20 different amino acids.

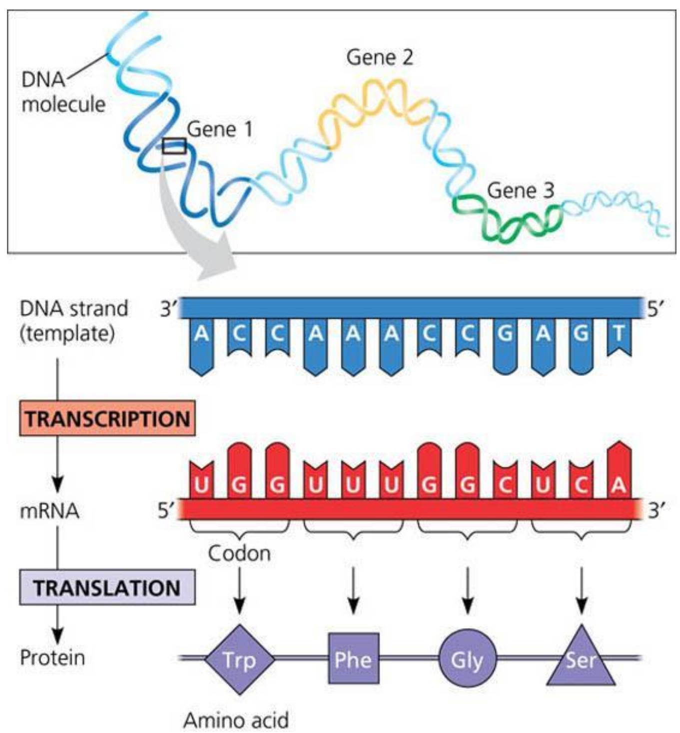
CODONS:

- During protein synthesis mRNA is transcribed using DNA as a template. The genetic code inherent in the DNA is thus reflected in the sequence of the bases of mRNA.
- A codon is a specific group of these sequential bases of mRNA that match the DNA triplet code.
- Each codon codes for a particular amino acid that is to be placed in the polypeptide chain.

Table of mRNA codons (coding for amino acids)

Codons Found in Messenger RNA

First Base	Second Base: U	Second Base: C	Second Base: A	Second Base: G	Third Base
U	Phe	Ser	Tyr	Cys	U
U	Phe	Ser	Tyr	Cys	C
U	Leu	Ser	Stop	Stop	A
U	Leu	Ser	Stop	Trp	G
C	Leu	Pro	His	Arg	U
C	Leu	Pro	His	Arg	C
C	Leu	Pro	Gln	Arg	A
C	Leu	Pro	Gln	Arg	G
A	Ile	Thr	Asn	Ser	U
A	Ile	Thr	Asn	Ser	C
A	Ile	Thr	Lys	Arg	A
A	Met	Thr	Lys	Arg	G
G	Val	Ala	Asp	Gly	U
G	Val	Ala	Asp	Gly	C
G	Val	Ala	Glu	Gly	A
G	Val	Ala	Glu	Gly	G



- ➢ Note that there is more than one codon for each amino acid i.e. the amino acid leucine has six different codons
- ➢ AUG codon can either specify the amino acid methionine or serve as a starter for the synthesis of a protein. For this reason, AUG is called an "initiator" or "**start**" codon
- ➢ Note that there are also three "**stop**" codons. They do not code for an amino acid. Instead, these codons act like the period at the end of a sentence: they signify the end of a polypeptide.

Genetic Code is Universal
Research indicates that the genetic code is essentially universal. The same codons stand for the same amino acids in most bacteria, protists, plants, and animals. This illustrates the remarkable biochemical unity of living things and suggests that all living things have a common evolutionary ancestor.

Practice with the Genetic Code:

For the following DNA sequence, write the corresponding mRNA sequence and then determine the sequence of the amino acids that would be synthesized.

a) TACTTCAAACCGCGT

mRNA: AUG AAG UUU GGC GCA

Methionine - Lysine - Phenylalanine - Glycine - Alanine

b) TTATACAAAGACAAC

mRNA: AAU AUG UUU CUG UUG

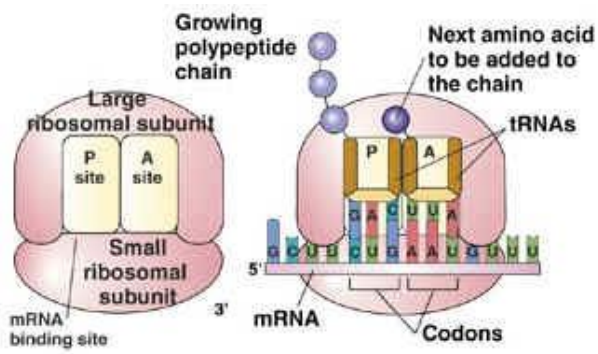
Start

Methionine - Phenylalanine - Leucine - Leucine

PROTEIN SYNTHESIS

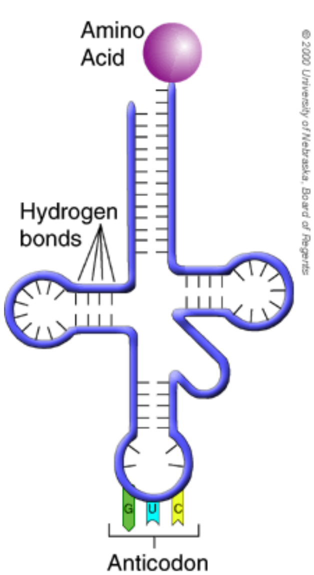
The Ribosome:

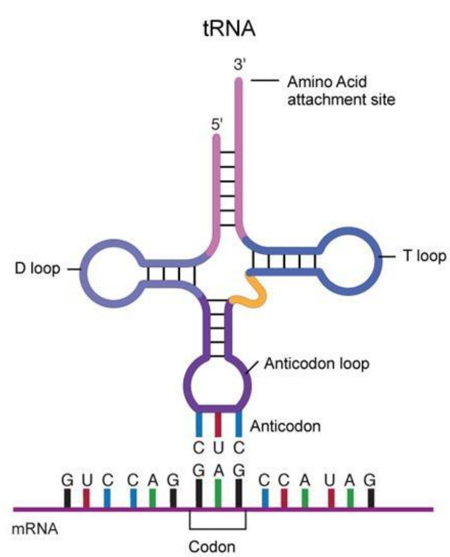
- When the ribosomes are not involved in protein synthesis, the subunits are separate. When protein synthesis begins, messenger RNA (mRNA) binds to the small subunit and the large subunit then joins to form a functioning mRNA-ribosome complex.
- (P) A ribosome has two sites where transfer RNA can bind: the "OUTGOING" SITE holds the tRNA carrying the growing polypeptide chain, while the "INCOMING" SITE (A) holds a tRNA carrying the next amino acid to be added to the chain.



The tRNA:
= small molecules of tRNA located in the cytoplasm bring amino acids to the ribosomes.

- tRNA is a single strand of RNA that loops back on itself in the shape of a "cloverleaf"
  Each tRNA molecule has two important sites of attachment: one site, called the anticodon, contains a sequence of three bases that complement a codon on the mRNA molecule; the other site attaches to a specific amino acid.



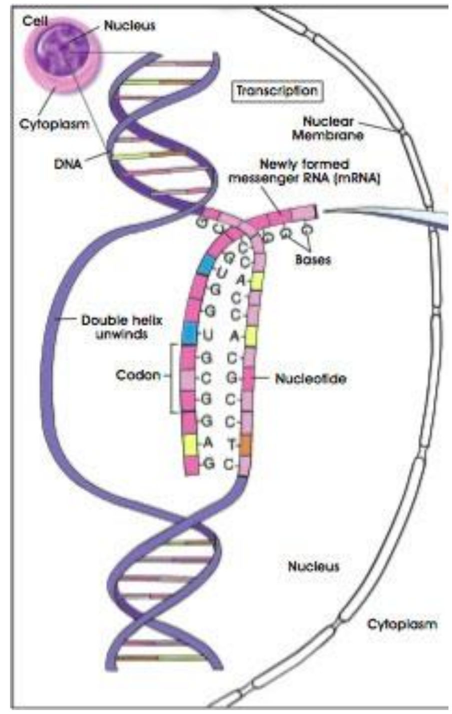


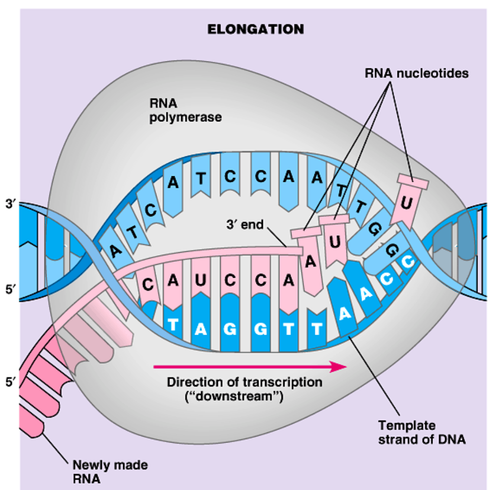
THE STEPS IN PROTEIN SYNTHESIS:

Protein synthesis occurs in two steps: **TRANSCRIPTION** and **TRANSLATION.**

1.) TRANSCRIPTION (Transfer of information from DNA to mRNA)
Transcription begins when a cell is ready to produce a protein.

- An enzyme called ___RNA Polymerase___ first binds to a DNA molecule and then causes a segment of DNA helix to unwind and separate ("unzip"), temporarily exposing the two strands.
  - One of these strands serves as a template, or pattern, to make a molecule of mRNA. The other strand of DNA does not take part in transcription.
- Next, mRNA nucleotides found floating free in the nucleus, bind to their complementary DNA nucleotides on the exposed strand of DNA. RNA polymerase then moves along the section of mRNA, joining the adjacent mRNA nucleotides, thus forming a single strand of mRNA.
  - Note that complementary base pairing determines the sequence of bases on the mRNA:
    - The base uracil (U) in RNA always pairs with adenine in DNA. All other nucleotides pair as in DNA.





- When the RNA polymerase reaches the sequence of bases on the DNA that acts as a termination signal ("stop" codons), the enzyme triggers the release of the newly made mRNA.
  - Recall that each triplet of bases on the mRNA is called a codon, and provides the code for the placement of one amino acid in a protein.

2.) **TRANSLATION** (Making a protein from information encoded in mRNA)

Translation begins when mRNA moves **out of the nucleus** by passing through nuclear pores. The mRNA then migrates to a group of ribosomes, where the actual synthesis of proteins takes place.

Translation occurs in 3 steps:

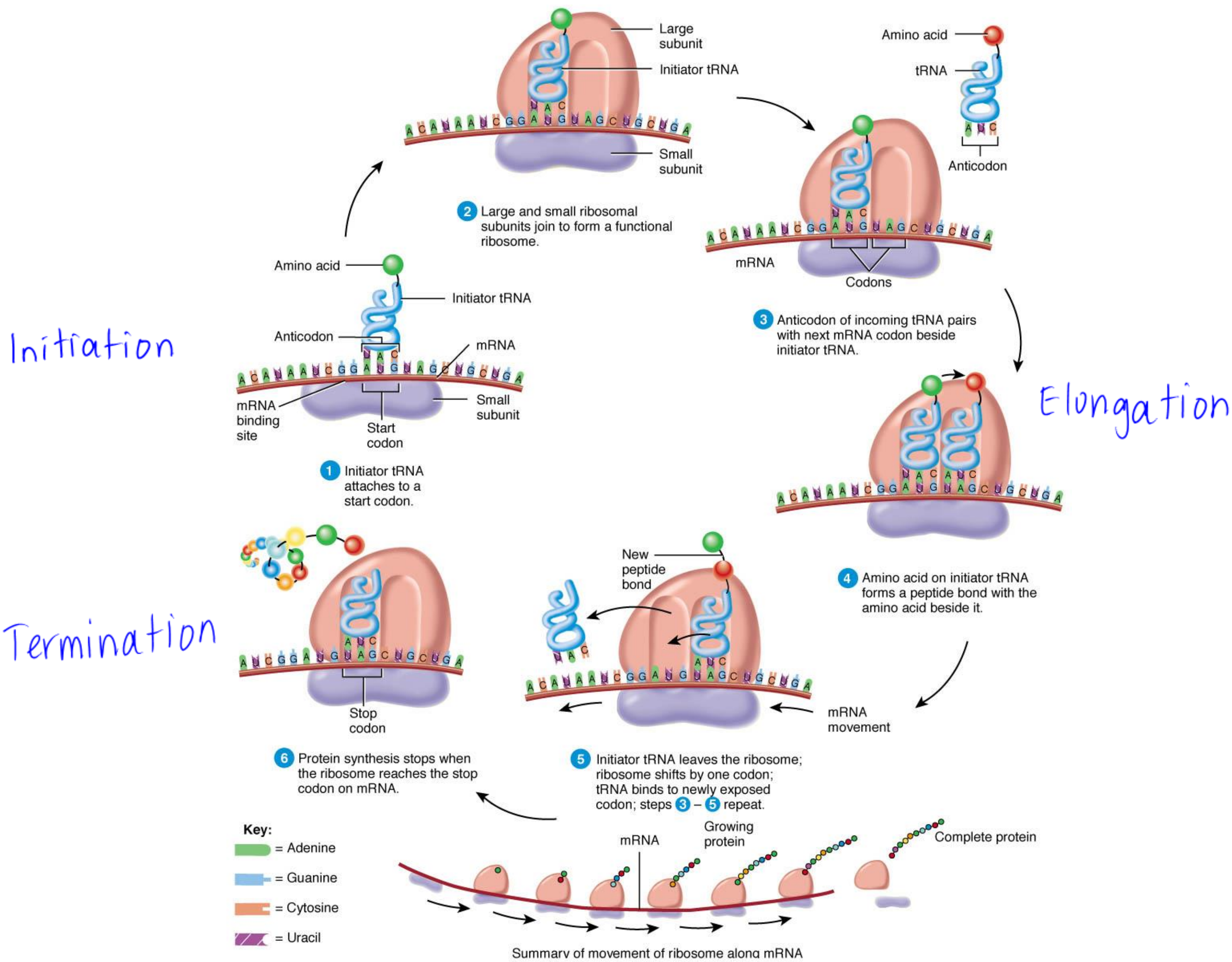
= ___Initiation___; ___Elongation___; and ___Termination___.

1. **INITIATION:**

- The assembly of a protein begins when mRNA binds to the smaller of the 2 ribosomal subunits: then the larger subunit joins the smaller one.

2. **ELONGATION:**
   - During elongation, the ribosomes move along the strand of mRNA and indicate each codon to approaching molecules of tRNA carrying their amino acids.
   - A specific tRNA anticodon then matches up with the mRNA codon, through complementary base pairing.
   - A ribosome is large enough to accommodate two tRNA molecules: the incoming tRNA and the outgoing tRNA. Therefore, two tRNA molecules can be at a ribosome at one time. Once the second tRNA has bound to the mRNA, an enzyme in the ribosome links the new amino acid to the neighbouring amino acid by means of a **peptide bond** (DEHYDRATION SYNTHESIS).
   - After the amino acids are linked, the outgoing tRNA is released and returns to the cytoplasm to collect another amino acid ("used-up tRNA" = has no amino acid attached). As each ribosome moves along the mRNA, a chain of amino acids is assembled in the proper sequence to form a certain protein.

3. **TERMINATION:**
   - The process of elongation continues until the ribosome reaches a **"stop" codon** on the mRNA strand. There is no tRNA molecule for this codon, therefore protein synthesis stops. The ribosome then dissociates into its 2 subunits and falls off the mRNA strand. The mRNA molecule then **disintegrates,** breaking apart in the cytoplasm. The resulting protein is then available for the cell to use immediately (free-floating ribosomes), or it can be secreted from the cell to be used elsewhere (attached to the rough ER).



***Note:** Several ribosomes can move along one mRNA at a time. Therefore, several proteins of the same type can be synthesized using one mRNA molecule.*

(Polyribosome)