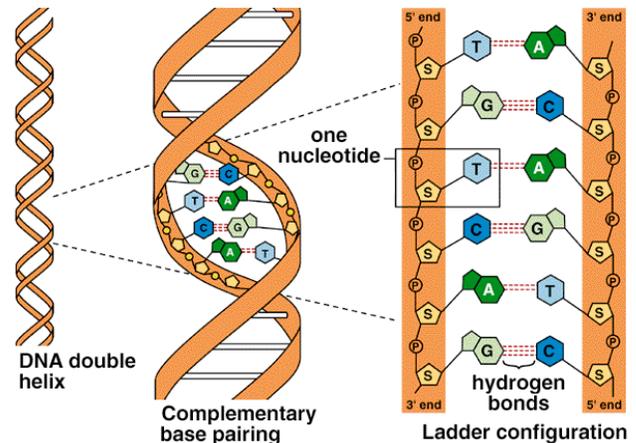


# DNA and Protein Synthesis - "Life is a Three Letter Word!" - CHAPTER NOTES

## What is DNA?

- DNA is the **control molecule** of life. DNA has three major functions:
- DNA CONTROLS CELLULAR ACTIVITIES**, including reproduction.
  - DNA **carries a CODE**. Genetic **instructions** are encoded in the **sequence of bases** strung together in DNA.
  - DNA from male and DNA from female together become the **genetic information of offspring** in sexual reproduction.
  - RNA molecules function in the processes by which those DNA instructions are used in building the **proteins** on which all forms of life are based.
- DNA MAKES EXACT COPIES OF ITSELF** to pass onto other cells.
    - DNA does this through a process called "**replication**."
- DNA UNDERGOES MUTATIONS**
    - mutations** and **recombinations** in the structure and number of DNA molecules are the source of life's **diversity**.
    - Evolution**, in essence, proceeds from the level of DNA. Different combinations of DNA sequences due to mutations and sexual reproduction explain the existence of all the different species that have lived on this Earth.



## Furthermore...

- DNA is the source of the **unity of life**
- Life most likely began as a nucleic acid.** (recall that there are **TWO** Types of Nucleic acids: **DNA & RNA**).
- The first form of life on this planet is thought by many biologists to be a **self-replicating strand of RNA**.

## A BRIEF HISTORY OF DNA RESEARCH (no, this is not on the test!)

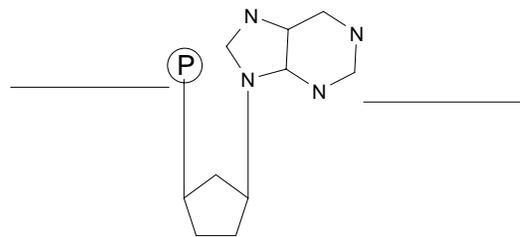
- DNA was first isolated by the Swiss biochemist Johann Friedrich **Miescher** in **1869**. Because DNA molecules are acidic and are found in the nucleus, Miescher called them nucleic acids. Over 80 years passed, however, before scientists understood that DNA contains the information for carrying out the activities of the cell. How this information is coded or passed from cell to cell was unknown. To break the code, scientists first had to determine the structure of DNA..
- During the 1950's, a fierce competition to determine the three dimensional structure of DNA took place. The race was won in 1953 by **James Watson**, an American biologist, and **Francis Crick**, a British physicist. Working together at Cambridge University in England, Watson and Crick solved the puzzle using scale models of nucleotides. Their success depended a great extent on evidence collected by other biologists, especially X-ray data from British biochemists **Rosind Franklin** and **Maurice Wilkins**.
- In 1958, the mechanism for DNA replication was determined by **Meselson** and **Stahl**. In the **GENETIC CODE** of **3 DNA nucleotides for 1 amino acid** was worked out by Crick and his coworkers.

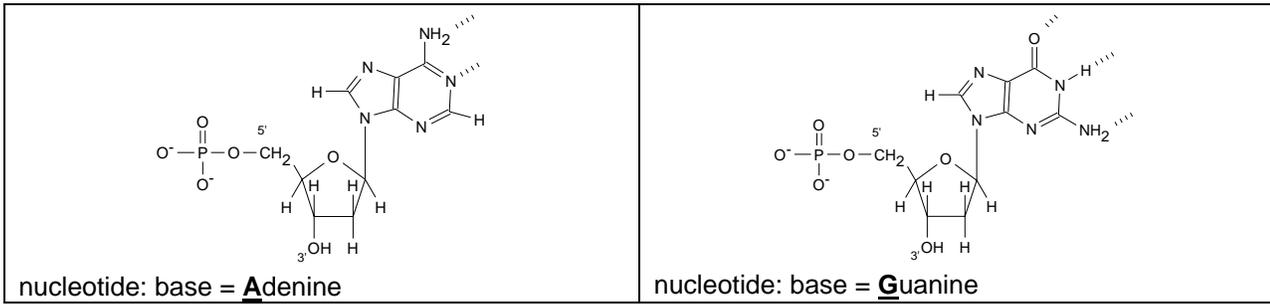
## Important Dates in early DNA research:

Date	Discovery
1869	• Nucleic Acids identified
1928	• Transfer of genetic material between bacteria observed (Frederick Griffith)
1944	• DNA carries genetic code (Oswald Avery and coworkers)
1950	• Protein chains sometimes helical; DNA structure similar (Linus Pauling)
1951	• X-ray data for DNA structure produced (Franklin, Wilkins)
1951	• Nitrogen base ratio related to genetic code (Chargaff)
1953	• DNA double helix discovered (James Watson, Francis Crick)
1958	• Mechanism for DNA replication determined (Matthew Meselson, Franklin Stahl)
1961	• 3 DNA nucleotide code for 1 amino acid (Crick and coworkers)

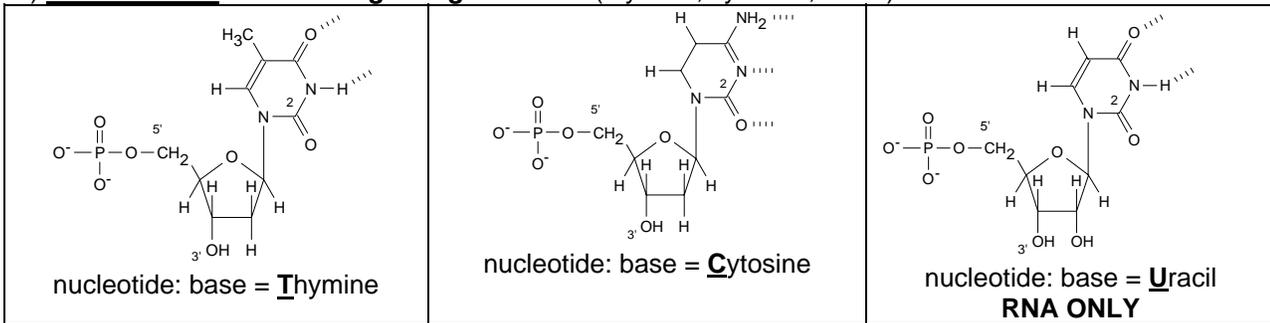
## The Structure of Nucleic Acids

- DNA & RNA are **POLYMERS** of **NUCLEOTIDES**
- Each nucleotide is composed of:
  - a **pentose** (5 carbon) **SUGAR**
  - a **PHOSPHATE group**
  - a **nitrogenous BASE**
- there are **two types** of bases:
  - PURINES** - have a **double ring structure** (adenine & guanine)

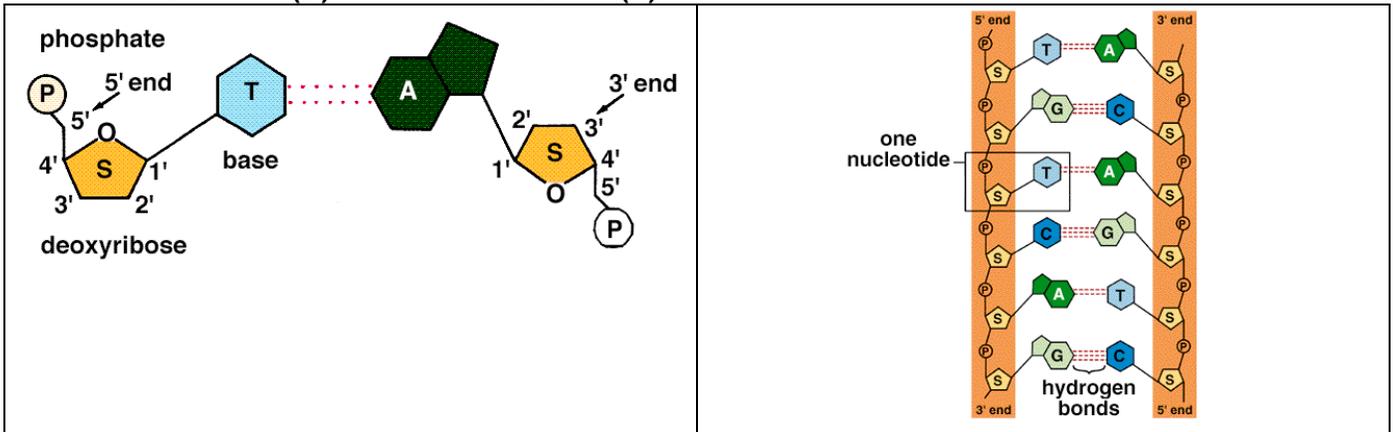




ii) **PYRIMIDINES** - have a **single ring structure** (thymine, cytosine, uracil)



- The DNA strand consists of a sequence of nucleotides linked together to form a **DOUBLE HELIX** that can be visualized as an immensely **long, twisted ladder**.
- Each strand, or one side of the ladder, is composed of **alternating molecules of deoxyribose and phosphate** with a nitrogenous base attached to each deoxyribose unit.
- Pairs of **joined bases project crosswise**, forming the **rungs** of the ladder. The bases stick out the side of the sugar molecules, and are linked to the bases of the other strand by **hydrogen bonds** in a very strict pattern. ⇒ always a **purine** with a **pyrimidine**.
- There is **COMPLEMENTARY BASE PAIRING BETWEEN STRANDS**
- ADENINE (A) bonds with THYMINE (T)**
- GUANINE (G) binds with CYTOSINE (C)**

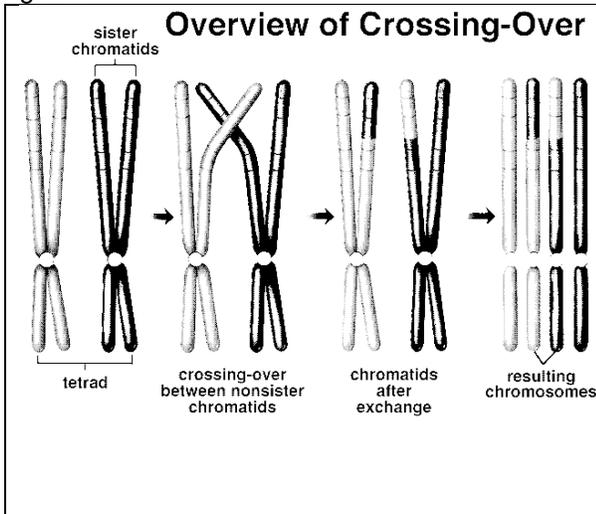
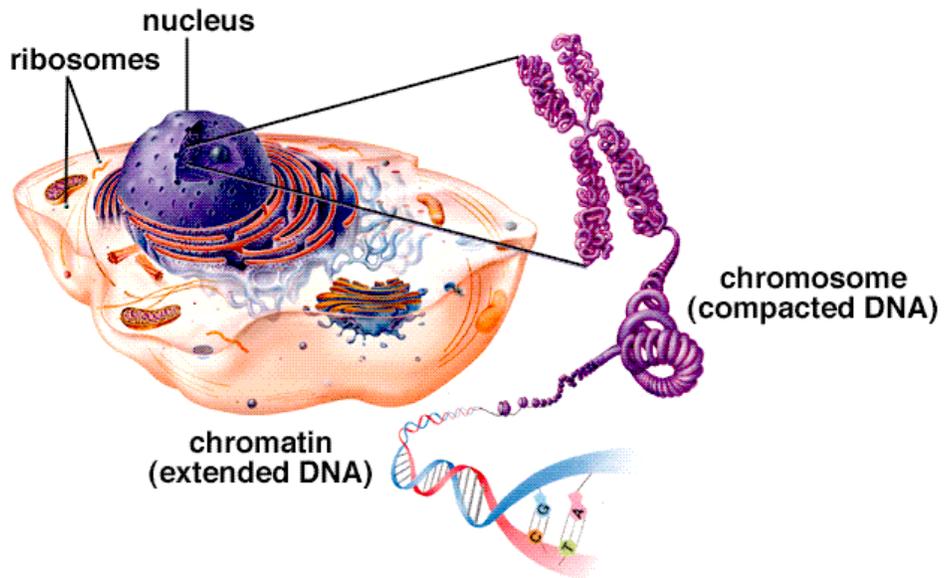


- Note that the **number of purine** bases equals the number of **pyrimidine** bases.
- the bases **can be in any order**, but **always** pair as above
- It is the **SEQUENCE OF BASES** that **codes heredity information** in the genetic code in DNA and RNA.
- Review the rules of complementary base pairing below:

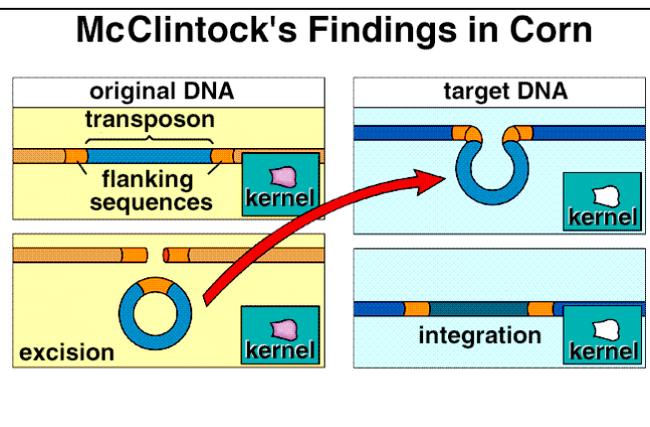
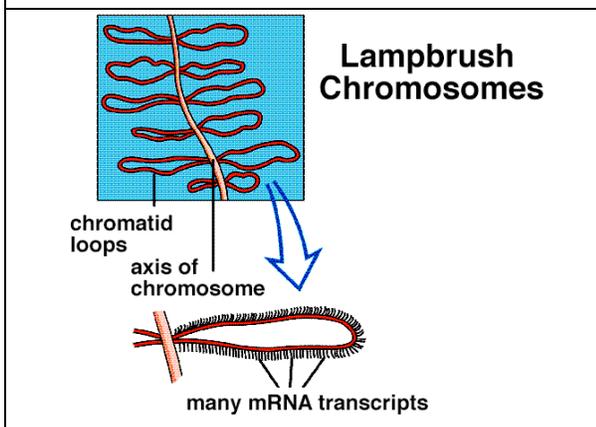
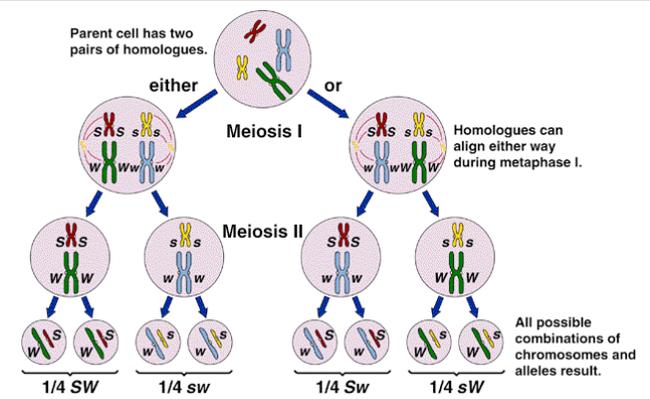
5'	3'
A	T
T	A
G	C
C	G
A	T
T	A
C	G
G	C
A	T
T	A
C	G
G	C
A	T
T	A
C	G
G	C
A	T
T	A
C	G
G	C
A	T
T	A
C	G
G	C
A	T
T	A
C	G
G	C
A	T
T	A
C	G
G	C
A	T
T	A
C	G
G	C
A	T
T	A
C	G
G	C
A	T
T	A
C	G
G	C
A	T
T	A
C	G
G	C
A	T
T	A
C	G
G	C
A	T
T	A
C	G
G	C
A	T
T	A
C	G
G	C
A	T
T	A
C	G
G	C
A	T
T	A
C	G
G	C
A	T
T	A
C	G
G	C
A	T
T	A
C	G
G	C
A	T
T	A
C	G
G	C
A	T
T	A
C	G
G	C
A	T
T	A
C	G
G	C
A	T
T	A
C	G
G	C
A	T
T	A
C	G
G	C
A	T
T	A
C	G
G	C
A	T
T	A
C	G
G	C
A	T
T	A
C	G
G	C
A	T
T	A
C	G
G	C
A	T
T	A
C	G
G	C
A	T
T	A
C	G
G	C
A	T
T	A
C	G
G	C
A	T
T	A
C	G
G	C
A	T
T	A
C	G
G	C
A	T
T	A
C	G
G	C
A	T
T	A
C	G
G	C
A	T
T	A
C	G
G	C
A	T
T	A
C	G
G	C
A	T
T	A
C	G
G	C
A	T
T	A
C	G
G	C
A	T
T	A
C	G
G	C
A	T
T	A
C	G
G	C
A	T
T	A
C	G
G	C
A	T
T	A
C	G
G	C
A	T
T	A
C	G
G	C
A	T
T	A
C	G
G	C
A	T
T	A
C	G
G	C
A	T
T	A
C	G
G	C
A	T
T	A
C	G
G	C
A	T
T	A
C	G
G	C
A	T
T	A
C	G
G	C
A	T
T	A
C	G
G	C
A	T
T	A
C	G
G	C
A	T
T	A
C	G
G	C
A	T
T	A
C	G
G	C
A	T
T	A
C	G
G	C
A	T
T	A
C	G
G	C
A	T
T	A
C	G
G	C
A	T
T	A
C	G
G	C
A	T
T	A
C	G
G	C
A	T
T	A
C	G
G	C
A	T
T	A
C	G
G	C
A	T
T	A
C	G
G	C
A	T
T	A
C	G
G	C
A	T
T	A
C	G
G	C
A	T
T	A
C	G
G	C
A	T
T	A
C	G
G	C
A	T
T	A
C	G
G	C
A	T
T	A
C	G
G	C
A	T
T	A
C	G
G	C
A	T
T	A
C	G
G	C
A	T
T	A
C	G
G	C
A	T
T	A
C	G
G	C
A	T
T	A
C	G
G	C
A	T
T	A
C	G
G	C
A	T
T	A
C	G
G	C
A	T
T	A
C	G
G	C
A	T
T	A
C	G
G	C
A	T
T	A
C	G
G	C
A	T
T	A
C	G
G	C
A	T
T	A
C	G
G	C
A	T
T	A
C	G
G	C
A	T
T	A
C	G
G	C
A	T
T	A
C	G
G	C
A	T
T	A
C	G
G	C
A	T
T	A
C	G
G	C
A	T
T	A
C	G
G	C
A	T
T	A
C	G
G	C
A</	

## GENES AND CHROMOSOMES

- **GENES** are the units of inheritance that control particular characteristics or capabilities of an organism. Genes are located on the chromosomes of the cell nucleus and **consist of segments of DNA molecules**.
- A gene consists of a sequence of about **1000 DNA base-pairs** (though there is considerable variation in this length). About **175,000** genes compose the DNA molecule of a single human chromosome. The genes act in pairs that dictate **traits**.
- Genes **control cellular chemical reactions**, by directing the formation of **enzymes**.
- Genes always occur in **pairs**. Half of each person's genes come from the mother and half from the father. Most ordinary characteristics like height and eye color are determined by **combinations** of several different genes.



Chromosomes are also capable of exchanging genetic information with one another. This process, diagramed on the left, is known as "Crossing Over." Crossing over helps to contribute to genetic diversity in sexual reproduction.



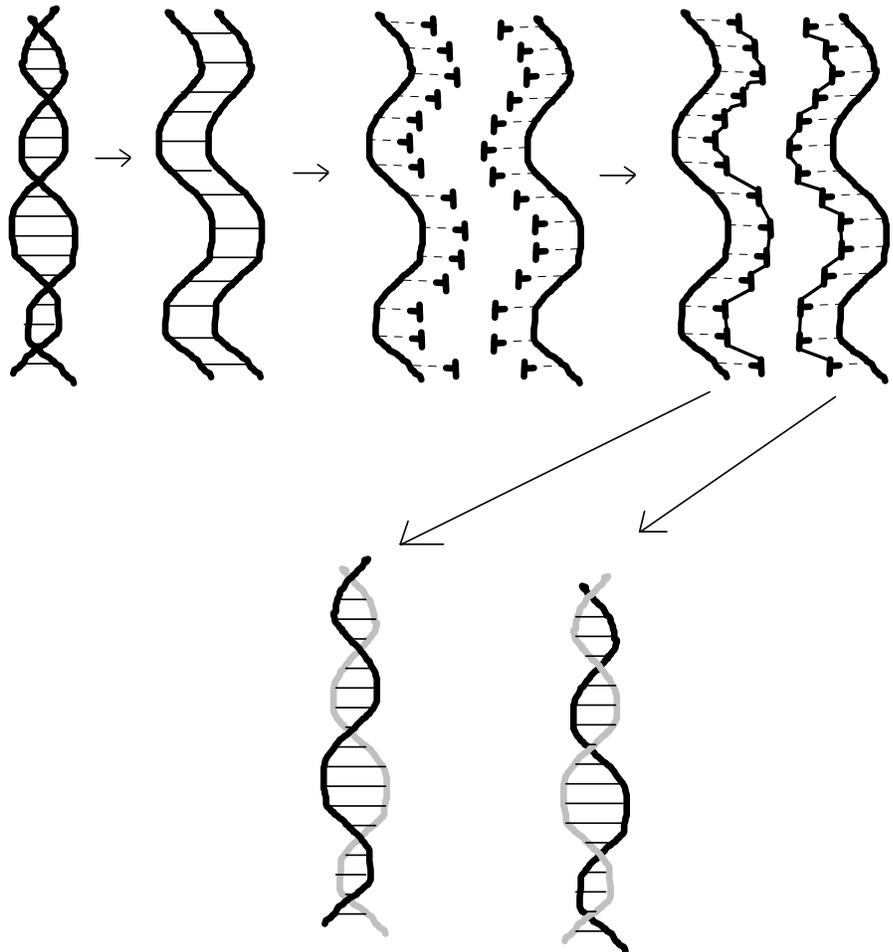
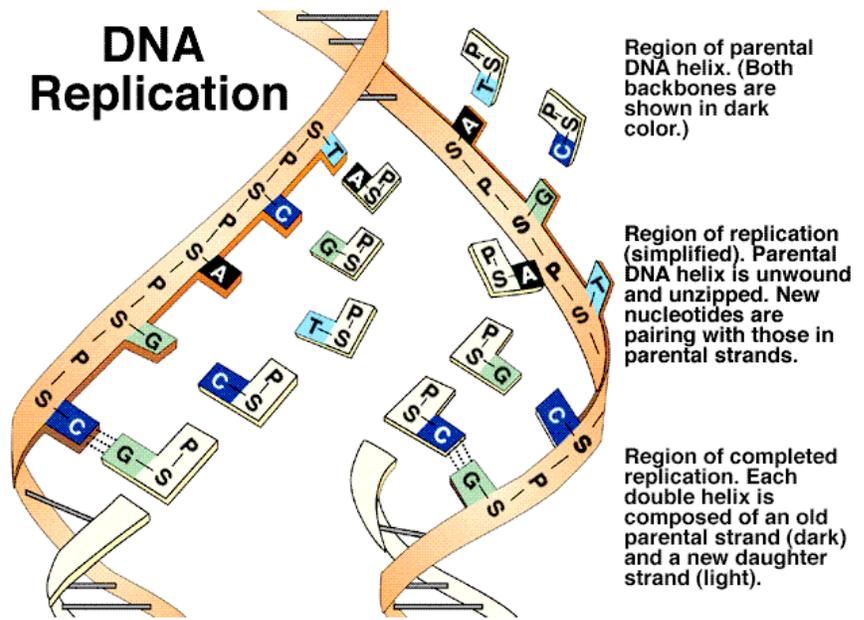
## REPLICATION - DNA making identical copies of itself

- Inherent in DNA's structure is a mechanism for reproducing itself. Before a cell can divide, all of the DNA must be  **duplicated** .
- This duplication process is called  **REPLICATION** .
- each strand**  of DNA can be viewed as a  **template** : like a potter's mold, it can produce a " **reverse image** " copy of itself (a  **complementary copy** ). Each new strand of DNA produced has a sequence of bases exactly complementary to the template strand.

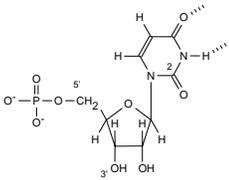
**Sequence of Events in Replication:**

- UNZIPPING** : the DNA double helix  **unwinds** , and the two strands of DNA  **separate** ;  **hydrogen bonds**  between the bases  **break**
  - COMPLEMENTARY BASE PAIRING** :  **new nucleotides move in to pair up**  with bases of each template strand of DNA. These new nucleotides are always floating around within the nucleoplasm.
  - ADJACENT NUCLEOTIDES BOND** :  **sugar-phosphate bonds form between adjacent nucleotides**  of the new strand to complete the molecule. The new molecule  **winds**  into a  **double helix** .
- each new strand of DNA produced contains one "old" strand (the template) and one new strand. This is known as " **SEMI-CONSERVATIVE** " replication. Since half of the original molecule is conserved in each of the new molecules, this ensures that there will be  **very, very accurate replication**  of the parent molecule.
  - this process proceeds by the action of several very specific  **enzymes**  (e.g. DNA Polymerases, gyrase, helicase)
  - product of replication by on DNA molecule is  **two complete double-stranded DNA molecules** , each with one new strand and one original stand that  **acted as a template**  for replication.

# DNA Replication



**RNA: RIBONUCLEIC ACID: how DNA communicates its message.**



### Uracil

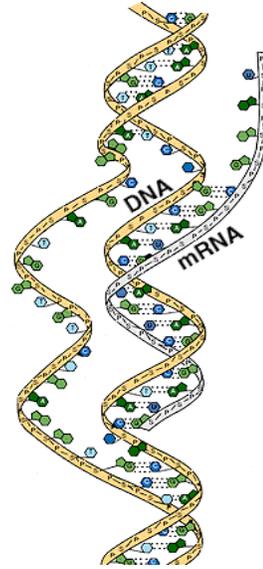
- RNA is the genetic material of some **viruses** and is necessary in all organisms for **protein synthesis** to occur. RNA could have been the “original” nucleic acid when life first arose on Earth some 3.8 billion years ago.
- Like DNA, all RNA molecules have a similar chemical organization, consisting of **nucleotides**.
- Like DNA, each RNA nucleotide is also composed of three subunits:

1. a 5-carbon sugar called **RIBOSE**.
2. a **PHOSPHATE group** that is

attached to one end of the sugar molecule

3. one of several different **nitrogenous BASES** linked to the opposite end of the ribose.
- There is **one base that is different** from DNA -- the base **URACIL** is used instead of **thymine**. (G, A, C, are otherwise the same as for DNA)
  - RNA is **SINGLE-STRANDED**, unlike DNA which is double stranded. RNA, therefore, is **not** a double helix.
  - **RNA is produced from DNA** by a process called **TRANSCRIPTION**. The steps of transcription are as follows:

1. A specific section of **DNA unwinds**, exposing a set of bases
  2. Along **one strand** of DNA (called the "**sense**" strand), **complementary RNA bases** are brought in. In RNA, **Uracil binds to the Adenine on DNA**. As in DNA, **cytosine** binds to **guanine**. The other strand of the DNA molecule (the "**missense**" strand), isn't read in eukaryotic cells.
  3. **Adjacent RNA nucleotides form sugar-phosphate bonds**.
  4. The **RNA strand is released** from DNA (RNA is a single-stranded nucleic acid).
  5. The **DNA molecule rewinds**, and returns to its normal double helix form.
  6. Once produced, the mRNA strand is often **processed** (certain sections called **introns** are cut out, a "Poly-A" tail is added to the 3' end, and a "cap" is added to the 5' end).
- RNA can then **leave the nucleus** and go into the **cytoplasm**.
  - The enzyme involved in transcription is known as **RNA polymerase**.
  - This process occurs in the **nucleus** (and, in particular, **dark coloured spots** in the nucleus called **nucleoli** (singular = **nucleolus**))

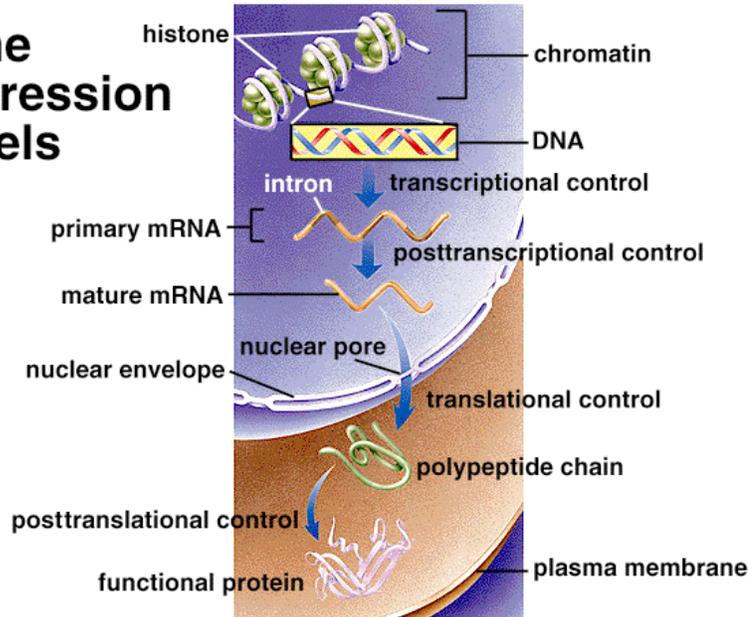


This mRNA transcript is ready to move into the cytoplasm.

Transcription is going on here—the nucleotides of mRNA are joined by the enzyme RNA polymerase in an order complementary to a strand of DNA.

One portion of DNA—a particular gene or genes—is transcribed at one time.

## Gene Expression Levels



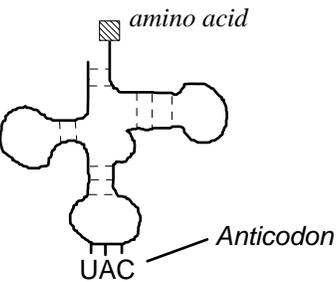
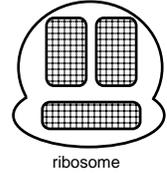
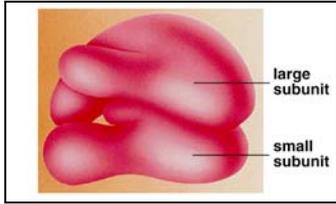
G	A	C	A	A	C	T	G	G	A	T	C	G	A	C
III	II	III	II	II	III	II	III	III	II	II	III	III	II	III

DNA  
mRNA

- There are **3 types of RNA**, each with different functions.

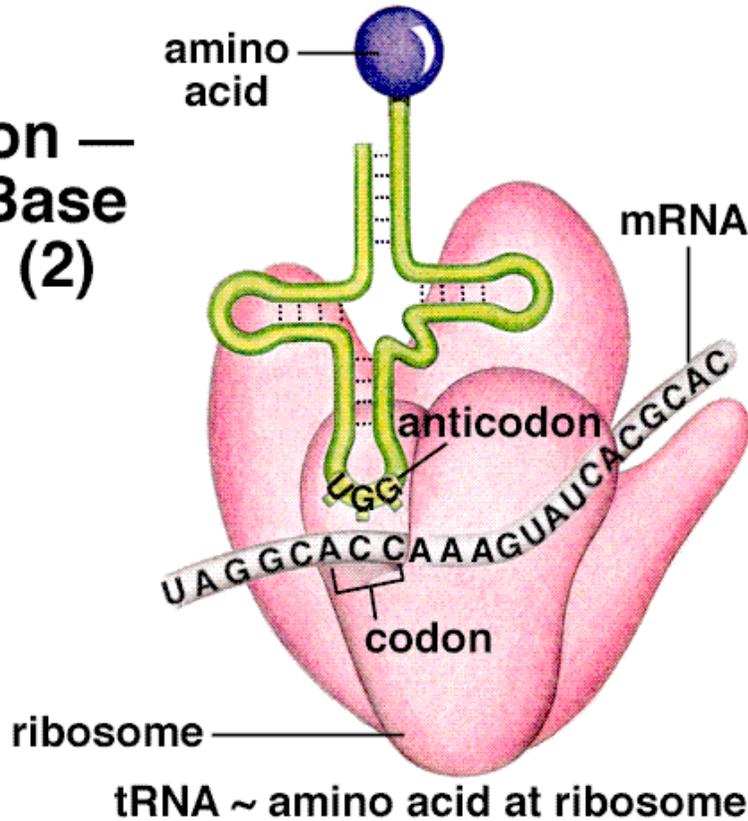
**rRNA, tRNA, and mRNA – The agents of Protein Synthesis**

- RNA that is involved in protein synthesis belongs to one of three distinct types: **ribosomal RNA (rRNA)**, **transfer RNA (tRNA)**, and **messenger RNA (mRNA)**.

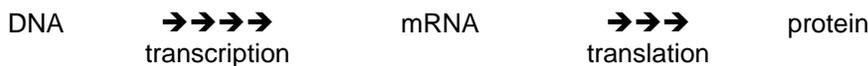


- **RIBOSOMAL RNA (rRNA)** - becomes a **structural part of ribosomes** and serves as a genetic link between mRNA and tRNA. Ribosomal RNA is associated with protein, forming bodies called **ribosomes**. Ribosomes are the **sites of protein synthesis**.
- Ribosomal RNA varies in size and is the **most plentiful** RNA. It **constitutes 85% to 90%** of total cellular RNA.
- **TRANSFER RNA (tRNA)** - is used to **deliver amino acids from the cytoplasm to the ribosome**. There is a different tRNA for each amino acid. The function of each type of tRNA is to bring its specific amino acid to a ribosome.
- The tRNA molecules consist of about **80 nucleotides** and are structured in a **cloverleaf** pattern. They constitute about **5%** of the cell's total RNA.
- **MESSENGER RNA (mRNA)** - **carries the genetic code** contained in the sequence of bases in the cell's DNA **from the nucleus to the Ribosome**.
- mRNA: acts as a "go-between" for DNA in the nucleus and the ribosomes in the cytoplasm.
- mRNA constitutes 5% to 10% of the cell's RNA.

**Anticodon — Codon Base Pairing (2)**

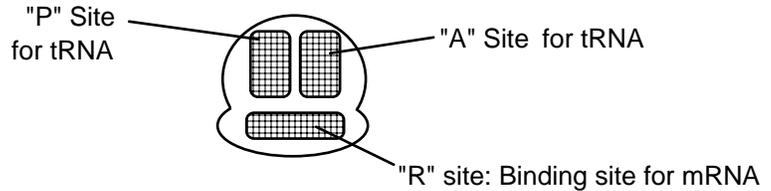


**The Central Dogma of Molecular Biology**



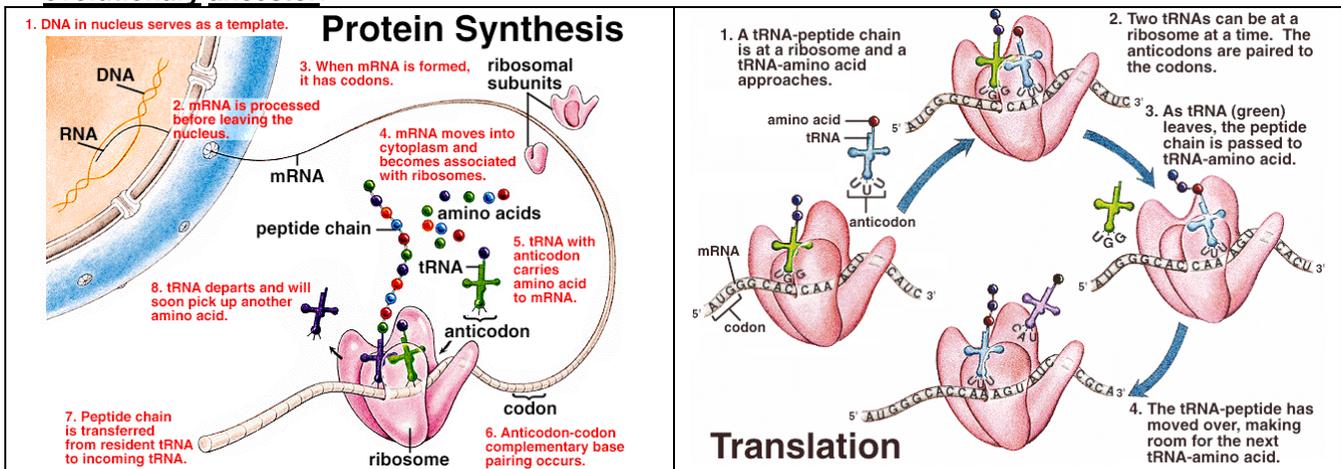
- this is sometimes summed up as "**one gene, one protein**"

- mRNA, once produced, leaves the nucleus through pores in the nuclear envelope, and enters the cytoplasm. This is where **TRANSLATION** occurs.
- Translation is the process that changes the RNA message into the actual protein.** It occurs at the surface of the **RIBOSOME**.
- The **order of the bases in DNA**, and then subsequently **mRNA**, **determines the amino acid sequence** of the protein being made.
- Each amino acids **is coded for by 3 bases** (this is known as a **TRIPLET CODE**)
- There are **20 different amino acids**, but only **4 different bases** in DNA/RNA.
- Each three-letter unit of mRNA is called a **CODON**.
- There are  $4^3$  (= 64) codons possible --> therefore there are **easily enough codons to code for all the necessary amino acids**.
- In fact, the **same amino acid** is often **specified by more than one codon**. However (and this is **very important**), the reverse is **never** true: that is, any **one codon** only specifies **ONE amino acid** -- there is **no vagueness** in the code (e.g. CCU will *always* produce proline).
- The code also contains "**punctuation**." It tells when to **start** reading the gene for a particular protein and when to **stop**.
- Each codon corresponds to an **amino acid**, or a "**start**" or "**stop**" synthesis signal. And *here it is*, the most important chart in all of Biology: the **GENETIC CODE!**



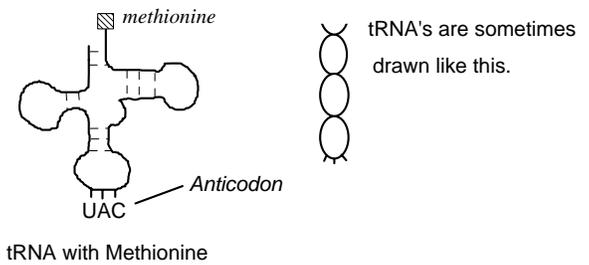
AAU AAC AAA AAG	ASPARAGINE  LYSINE	CAU CAC CAA CAG	HISTIDINE  GLUTAMINE	GAU GAC GAA GAG	ASPARTIC ACID  GLUTAMIC ACID	UAU UAC <b>UAA</b> <b>UAG</b>	TYROSINE  <b>STOP</b> <b>STOP</b>
ACU ACC ACA ACG	THREONINE	CCU CCC CCA CCG	PROLINE	GCU GCC GCA GCG	ALANINE	UCU UCC UCA UCG	SERINE
AGU AGC AGA AGG	SERINE  ARGININE	CGU CGC CGA CGG	ARGININE	GGU GGC GGA GGG	GLYCINE	UGU UGC <b>UGA</b> UGG	CYSTEINE  STOP TRYPTOPHAN
AUU AUC AUA <b>AUG</b>	ISOLEUCINE  METHIONINE <b>*START</b>	CUU CUC CUA CUG	LEUCINE	GUU GUC GUA GUG	VALINE	UUU UUC UUA UUG	PHENYLALANINE  LEUCINE

- The genetic code is **universal!**: the **same codons** stand for the **same amino acids** in all living things (well, *almost* all living things). This "**Biochemical Unity**" suggests that all living things have a **common evolutionary ancestor**.

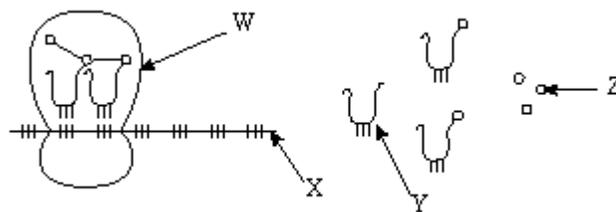


- The steps in **TRANSLATION**: can be **divided into 3 subprocesses**:
  - INITIATION**: the mRNA, with its **START CODON (AUG)** attaches to the "R" site of the ribosome.
    - The **AUG** codon **always initiates translation** and codes for the amino acid **methionine**.

- b. **tRNA** binds to the **start codon** of mRNA. The tRNA has a **binding site of 3 bases** called an **ANTICODON** that is **complementary** to the mRNA codon. Therefore, the codon of mRNA of AUG is "read" by a tRNA that has a **UAC anticodon**. The tRNA that has this anticodon carries, at it's tail, the amino acid **methionine**.
- c. This **methionyl-tRNA** is in the **P** site of the ribosome. The **A** site next to it is **available** to the tRNA bearing the next amino acid.
- There is a specific tRNA for each mRNA codon that codes for an amino acid.

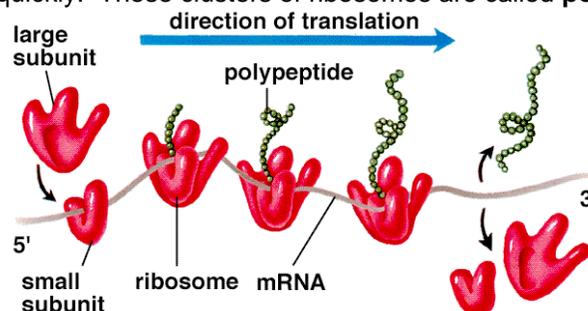


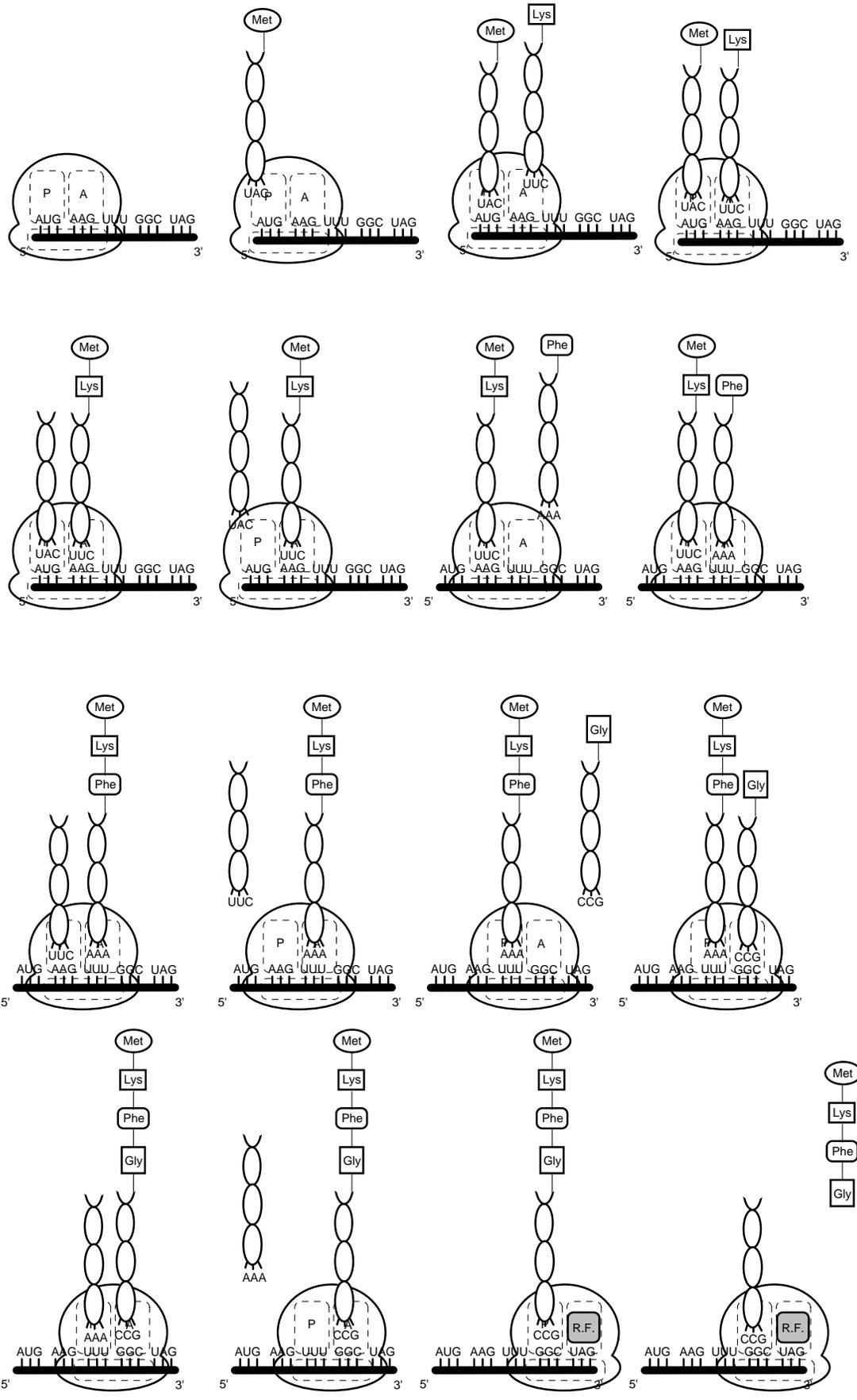
2. **ELONGATION: more amino acids are added** and connected together to form a **polypeptide**, as specified by the mRNA sequence.
  - a. an incoming amino-acyl-tRNA (lets call this AA<sub>2</sub>-tRNA<sub>2</sub>) recognizes the codon in the A site and binds there.
  - b. a peptide bond is formed between the new amino acid and the growing polypeptide chain.
  - c. the amino acid is removed from tRNA<sub>1</sub> (bond breaks between aa<sub>1</sub> and tRNA<sub>1</sub>)
  - d. the tRNA<sub>1</sub> that was in the P site is released, and the tRNA in the A site is translocated to the P site.
  - e. the **ribosome moves over one codon** along the mRNA (to the right in our diagram, or more specifically in the 5' ----> 3' direction.)
  - f. This movement shifts the tRNA<sub>2</sub> (which is attached to the growing amino acid chain) to the P site.
  - g. tRNA<sub>3</sub> with aa<sub>3</sub> can now move into A site and bind with the next codon on mRNA.
  - h. **THIS PROCESS REPEATS**, and the CHAIN **ELONGATES** as long as there are new codons to read on the mRNA.
3. **TERMINATION:** The process above repeats until a special codon, called a **STOP CODON**, is reached. There are 3 Stop codons: **UAA, UAG, UGA**.
  - a. the stop codons **do not code for amino acids** but instead act as **signals to stop translation**.
  - b. a protein called **release factor** binds directly to the stop codon in the A site. The release factor causes a **water molecule** to be added to the end of the polypeptide chain, and the **chain then separates from the last tRNA**.
  - c. **the protein is now complete**. The **mRNA is now usually broken down**, and the ribosome splits into its large and small subunits.
  - d. the new protein is sent for **final processing** into the **endoplasmic reticulum** and **golgi apparatus**.



Please Label these Parts

- Often, **many ribosomes** will **simultaneously transcribe** the **same mRNA**. In this way, **many copies** of the same protein can be made quickly. These clusters of ribosomes are called **polysomes**.





## GENETIC MUTATIONS

- During the molecular maneuvering that occurs with DNA replication, if nucleotides are **lost, rearranged, or paired in error**, the resulting change in instruction of the genetic code **could lead to a protein that does not function properly** when the DNA's code is translated.
- A **MUTATION** is a **change in an organism** resulting from a **chemical change in the structure of a gene**.
- Although mutations have occurred throughout history, it wasn't until 1927 that **Herman Muller**, an American geneticist, developed the first experiments to study how and why they occurred. Genetic mutations can be caused by both **internal** and **external** factors. Any factor that can cause a mutation is called a **MUTAGEN** (e.g. **Dioxins, benzene, UV light, asbestos, DDT, cigarette smoke, x-rays etc. etc.**)
- Change will first be reflected in the **RNA** copy, then in the enzyme or other protein that the RNA codes for, and finally in the appearance of new traits in the living organism.
- There are two main categories of mutations: **GENE MUTATIONS** (*affect only one gene*), and **CHROMOSOMAL MUTATIONS** (*affect many genes* because they affect entire chromosomes or parts of chromosomes).
- A mutation occurs because of the **alteration in one or more base pairs** of the DNA molecule, **garbling** the existing genetic code. Sometimes the pattern of normal base pairing is altered, causing the substitution of one base pair for another. Sometimes the pairing capacity of a specific base is changed, producing abnormal base pairing. Sometimes an extra base is **added**, sometimes a base is **deleted**. Mutations where bases are added or deleted are called **frameshift mutations**.
- It takes only a **single** different pair of bases to produce a different or imperfect organism.
- *Consider an analogy of a "mutation" to a sentence in English.*

### EXAMPLE OF THE EFFECT OF A MUTATION:

ORIGINAL MESSAGE: THE BIG DOG BIT TED AND RAN OFF

DELETION/FRAME SHIFT: THE BID OGB ITT EDA NDR ANO FF

- Try it for yourself: Here is a section of DNA **before** a mutation.

DNA	T	A	C		G	G	G		C	T	C		T	A	G		C	G	A		G	A	T		A	T	T
mRNA	A	U	G		C	C	C		G	A	G		A	U	C		G	C	U		C	U	A		U	A	A
a.a.	Methionine				Proline				Glut. acid				Isoleucine				Alanine				Leucine				Stop		

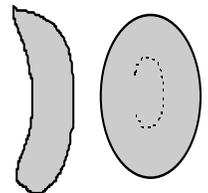
- Here the same section is after **one extra base** (a G in the third codon) has been **added** to the original sequence.

DNA	T	A	C		G	G	G		<b>G</b>	C	T		C	T	A		G	C	G		A	G	A		T	A	T
mRNA	A	U	G		C	C	C		<b>C</b>	G	A		G	A	U		C	G	C		U	C	U		A	U	A
a.a.	Methionine				Proline				Arginine				Valine				Arginine				Serine				Isoleucine		

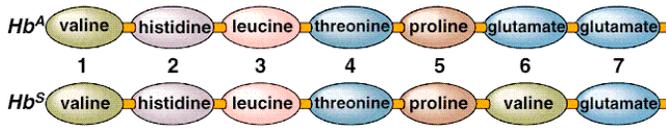
- Here the same section is after **two bases** have been **switched** from the original sequence.

DNA	T	A	C		<b>C</b>	G	G		C	T	C		T	A	G		C	G	<b>G</b>		G	A	T		A	T	T
mRNA	A	U	G		<b>G</b>	C	C		G	A	G		A	U	C		G	C	<b>C</b>		C	U	A		U	A	A
a.a.	Methionine				Alanine				Glut. Acid				Isoleucine				Alanine				Leucine				Stop		

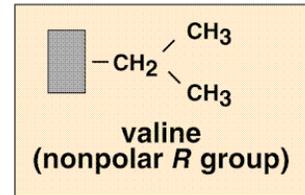
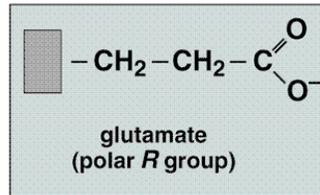
- Notice the **different effects** that different "**point**" mutations can have!
- If there is a change in the DNA that causes a change in the significant part of the mRNA codon(s), a different amino acid will be translated, and a different protein will be made. **Usually random changes are HARMFUL** (frequently mutations are **lethal**). About one time in million, the change might actually improve the protein (this is called a **BENEFICIAL MUTATION**. Beneficial mutations, while infrequent, drive the **evolution of species!**)
- Occasionally, a mutations will be "**neutral**" – that is it will have no effect on the protein produced (as in the case of the second mutation in the second example above), or it will change an amino acid on a non-vital part of the protein.
- Gene mutations **can cause GENETIC DISORDERS**. For example, with the disease of **SICKLE CELL ANEMIA**, the **normal round-shaped red blood cells** are intermingled with some having a **sickle** shape. The sickle cells **block the veins and arteries**. As fewer and fewer normal red blood cells are able to pass through the **congested blood vessels**, the tissue and cells become **starved for oxygen and other nutrients**. This disease occurs when **one amino acids** present in the **hemoglobin** (the molecule of red blood cells responsible for oxygen and carbon dioxide transport) is misplaced because of an error in the messenger RNA which was made by a piece of **DNA with one of its base pairs out of arrangement**.



## Sickle-cell Disease— Hemoglobin Chain

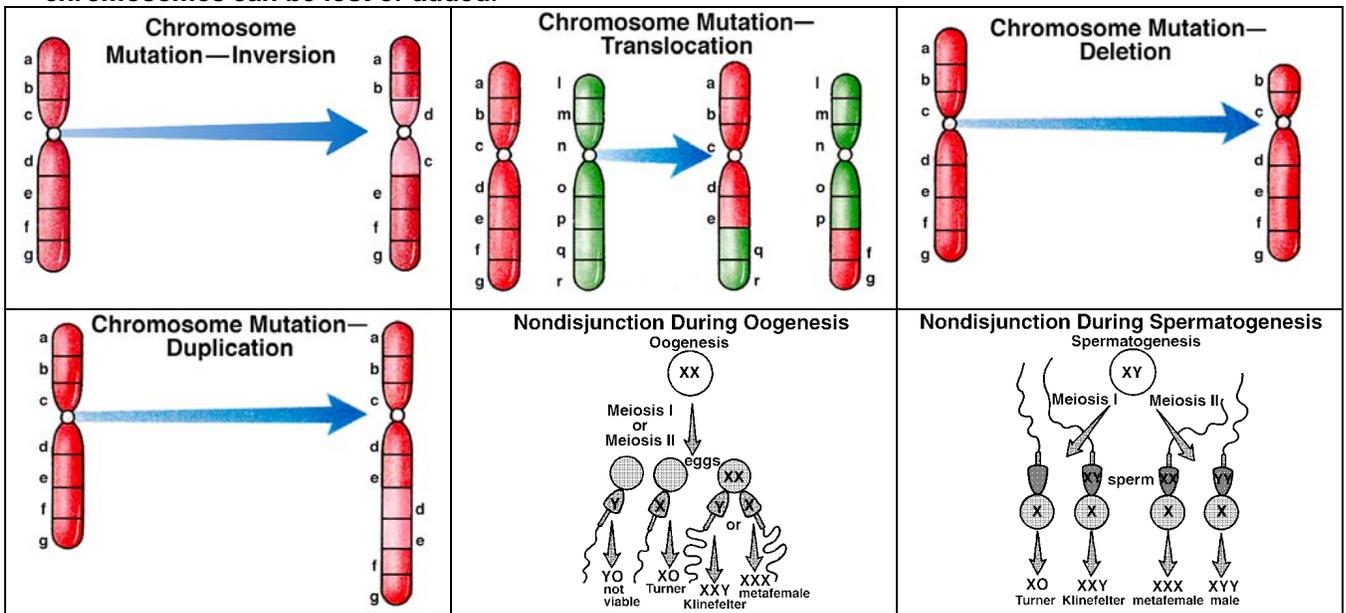


## Sickle-cell Disease— Glutamate vs. Valine



So, there are two main types of mutations:

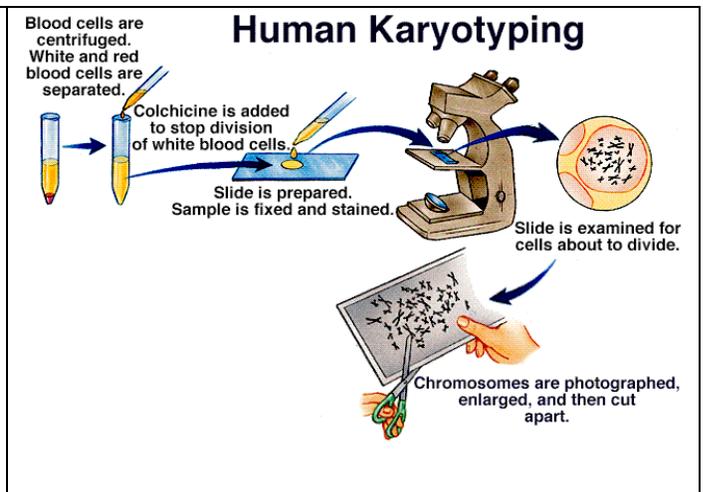
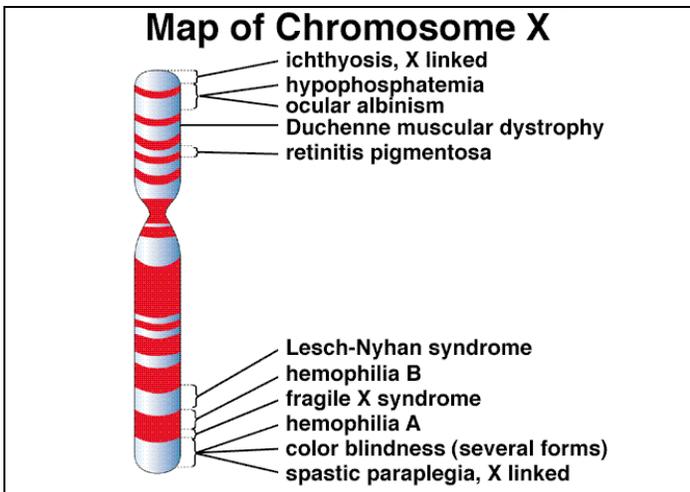
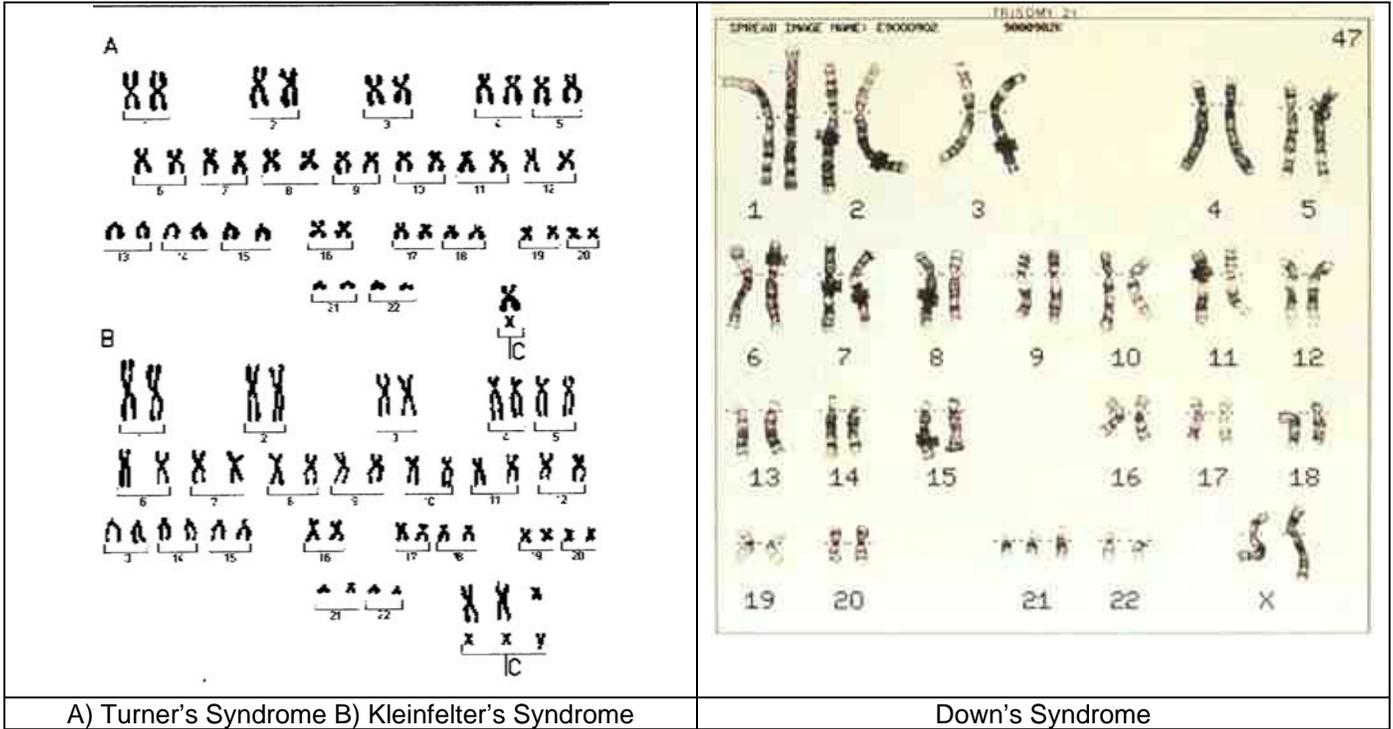
- GENE Mutations:** affect only a single gene. May be caused by a change (e.g. substitution, deletions, additions) in a single nucleotide. The effect on the individual depends on the gene's role. The sickle-cell anemia is a good example of a genetic disorder caused by a gene mutation.
- CHROMOSOMAL Mutations:** occur after chromosomes are broken (e.g. due to exposure to radiation, addictive drugs, pesticides) and reform abnormally. Pieces of chromosomes can be lost, added, or whole chromosomes can be lost or added.

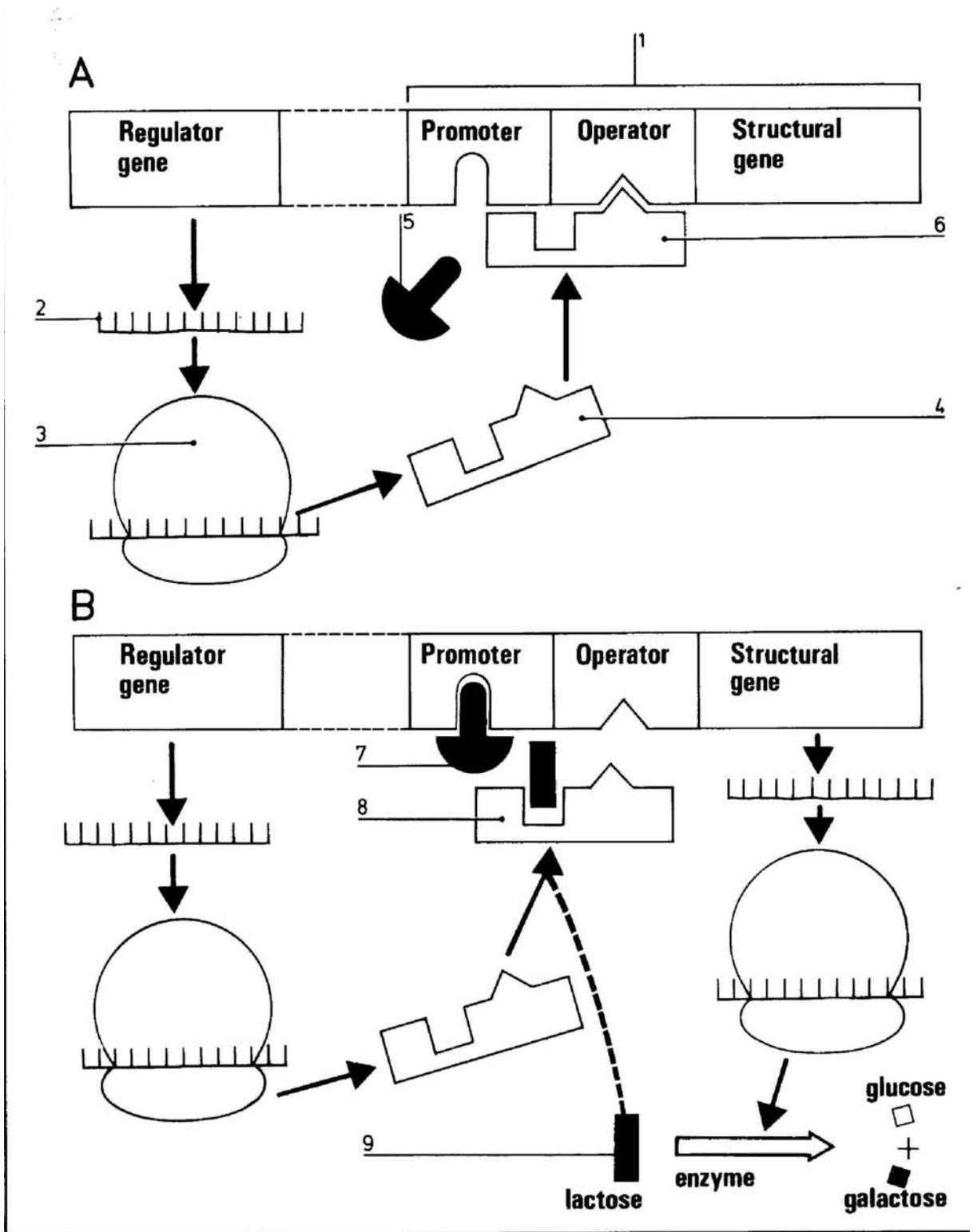


## Genetic Disorders

- since changes in DNA can directly affect protein synthesis, this in turn can **drastically affect metabolism and body structure/function**).
- For example, consider **PKU (phenylketonuria)**: Caused by defect in the **enzyme** that converts **phenylalanine** to **tyrosine** (in PKU, tyrosine gets converted phenylpyruvic acid). This acid can build up and cause severe nervous system damage/mental retardation.
- ALBINISM**: if the **enzyme** that converts **tyrosine** to **melanin** is defective, albinism occurs. These subjects will have no skin or hair pigment, and hence appear almost pure white.
- Most **birth defects** result from a **chromosomal abnormality**. The abnormality most frequently appears during **meiosis** when the egg and sperm cells are formed.
- One of the most common disorders is **DOWN'S SYNDROME**, or **trisomy 21**. It occurs in 1,000 out of every 100,000 births. (The chances of having a child with Down's syndrome, or *mongolism*, increases with the mother's age).
- There is **one chance in 60** that the children of a woman over the age of 40 will be affected. For women under 40 there is **one chance in 800**. Such children are born with an **extra chromosome #21** (47 chromosomes instead of the normal 46).
- During the formation of the egg, both number 21 chromosomes end up in the same egg cell.
- When the egg is fertilized by the sperm cell with its single number 21 chromosome, it produces a child with three number 21 chromosomes per cell.

- Other **trisomies** (having three chromosomes instead of the normal pair of chromosomes) which produce severe mental handicap are **trisomy 18** (*Edward's syndrome*) and **trisomy 13** (*Patau's syndrome*).
- **TURNER'S SYNDROME** is an example of an even rarer chromosomal abnormality. This condition is caused by the **absence of a second X or of the Y sex chromosome**. The result is a female child who is short and infertile.
- Some abnormalities are caused by the presence of an **extra sex chromosome**. The most common is **KLEINFELTER'S SYNDROME**, which occurs in about 1 out of every 700 males born. These babies have **three sex chromosomes**, two X chromosomes and one Y. They generally grow tall with long limbs and generally have IQ's that are **significantly below** those of their siblings. **Spermatogenesis** may be **reduced or absent**.





Gene induction –  $\beta$  galactosidase in *Escherichia coli*  
**A** Operon repressed (structural gene switched off)  
**B** Operon derepressed (structural gene switched on)

- 1 Operon
- 2 mRNA
- 3 Ribosome
- 4 Active repressor
- 5 RNA polymerase

- 6 Repressor bound to operator blocking RNA polymerase binding site
- 7 RNA polymerase bound to promoter
- 8 Repressor inactivated by inducer
- 9 Inducer (lactose)