

Biology Module 1: Foundational Concepts in Biology

IMBUE: Internship Program for Increased Local Bioinformatics
Utility and Expertise

Outline

1. Pre-assessment Test
2. Definition of Biology
3. The Properties of Life
4. Modern Cell Theory
5. Classification of Living Things
6. Chemical Composition of Living Things
7. The Genetic Material
8. The Central Dogma of Molecular Biology
9. Post-assessment Test

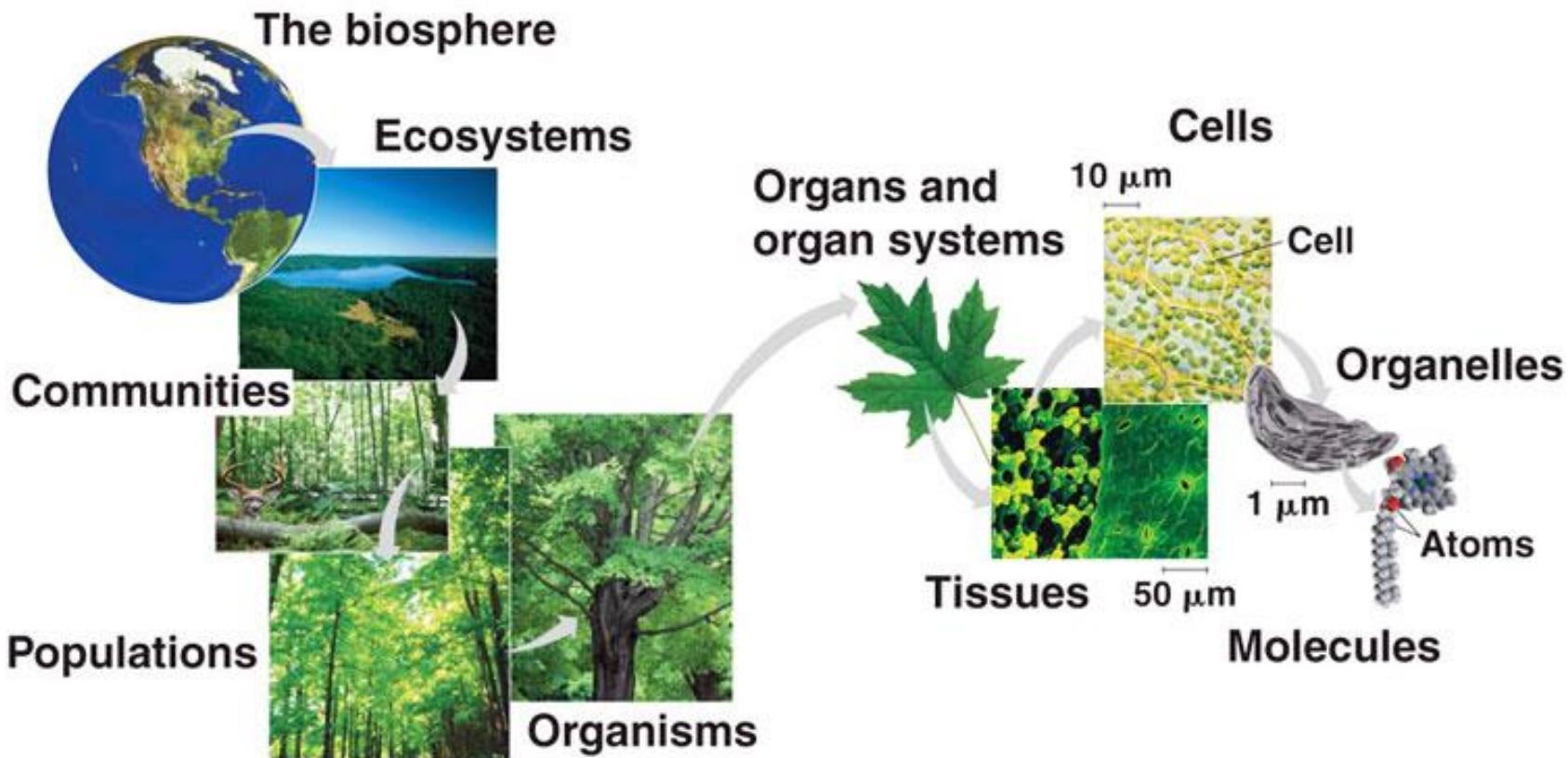
Biology

- A term of Greek origin: *bios* (“life”) + *logia* (“to speak”)
- The branch of science involved in studying living things.

Definition of Life

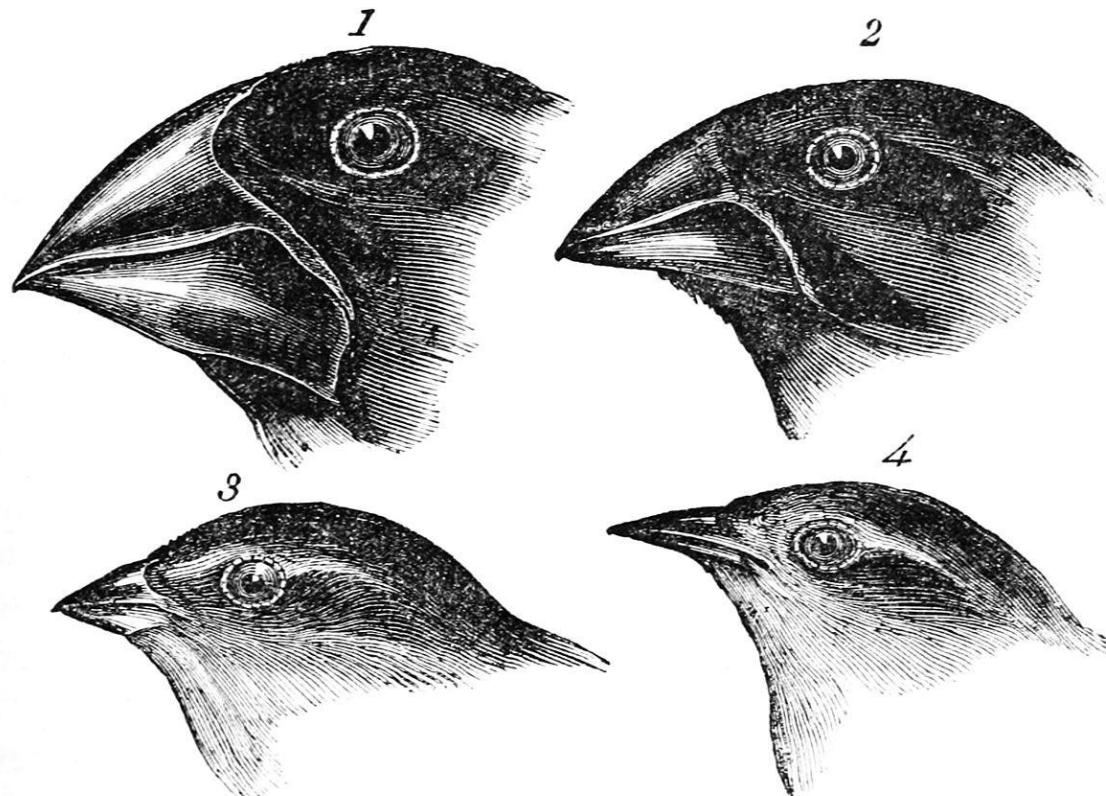
1. Organization
2. Evolutionary Adaptation
3. Response to Stimuli
4. Homeostasis
5. Metabolism
6. Growth
7. Reproduction

Biological Organization



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Properties: Adaptation



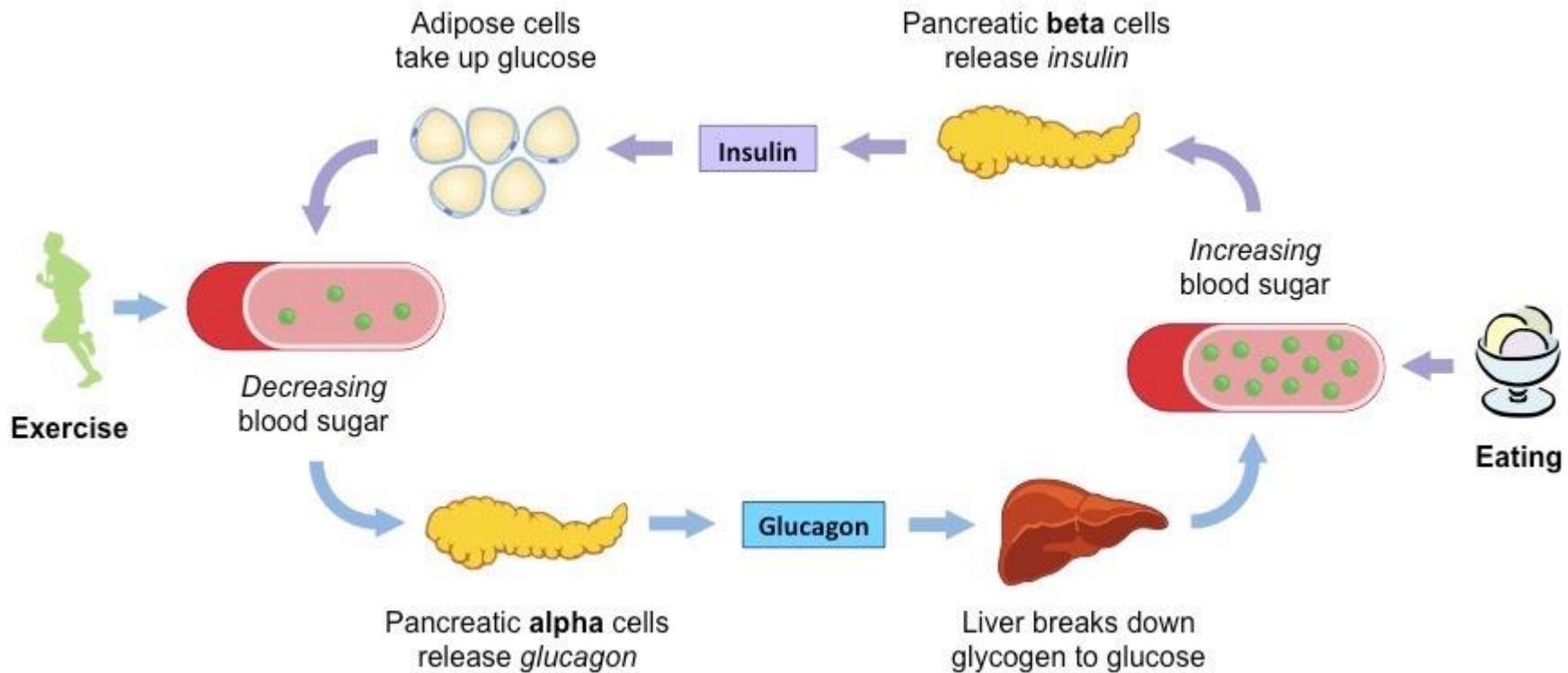
1. *Geospiza magnirostris.*
3. *Geospiza parvula.*

2. *Geospiza fortis.*
4. *Certhidea olivacea.*

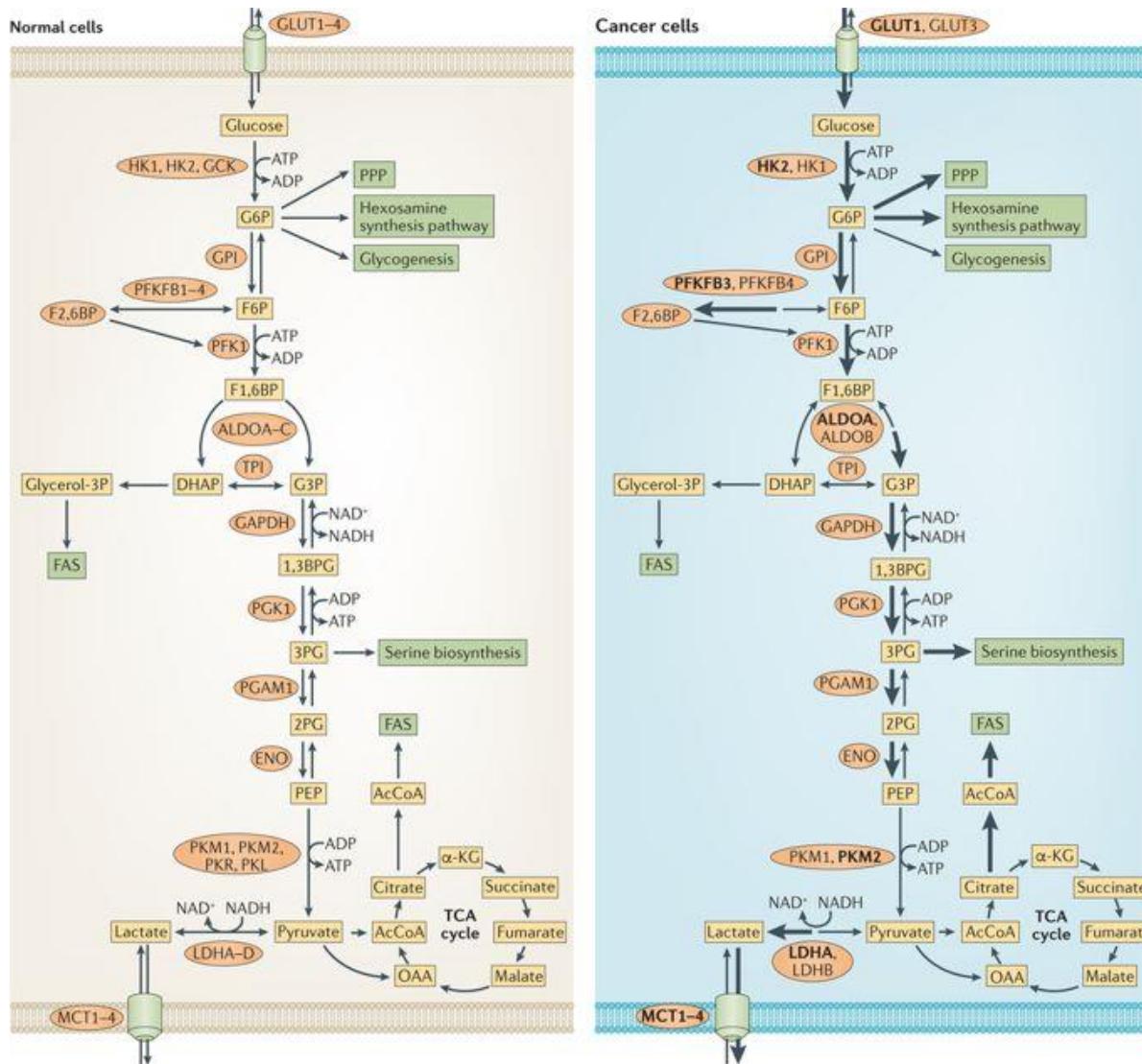
Properties: Response to Stimuli



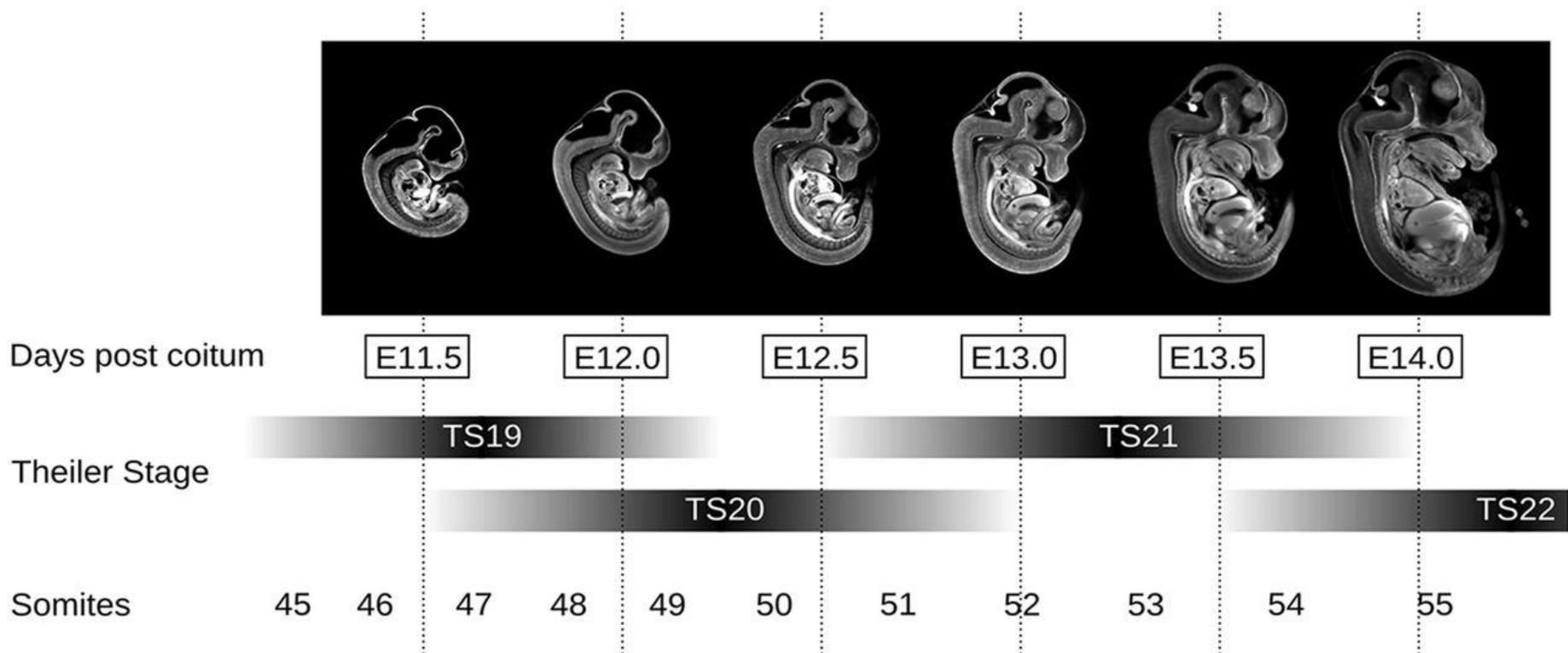
Properties: Metabolism



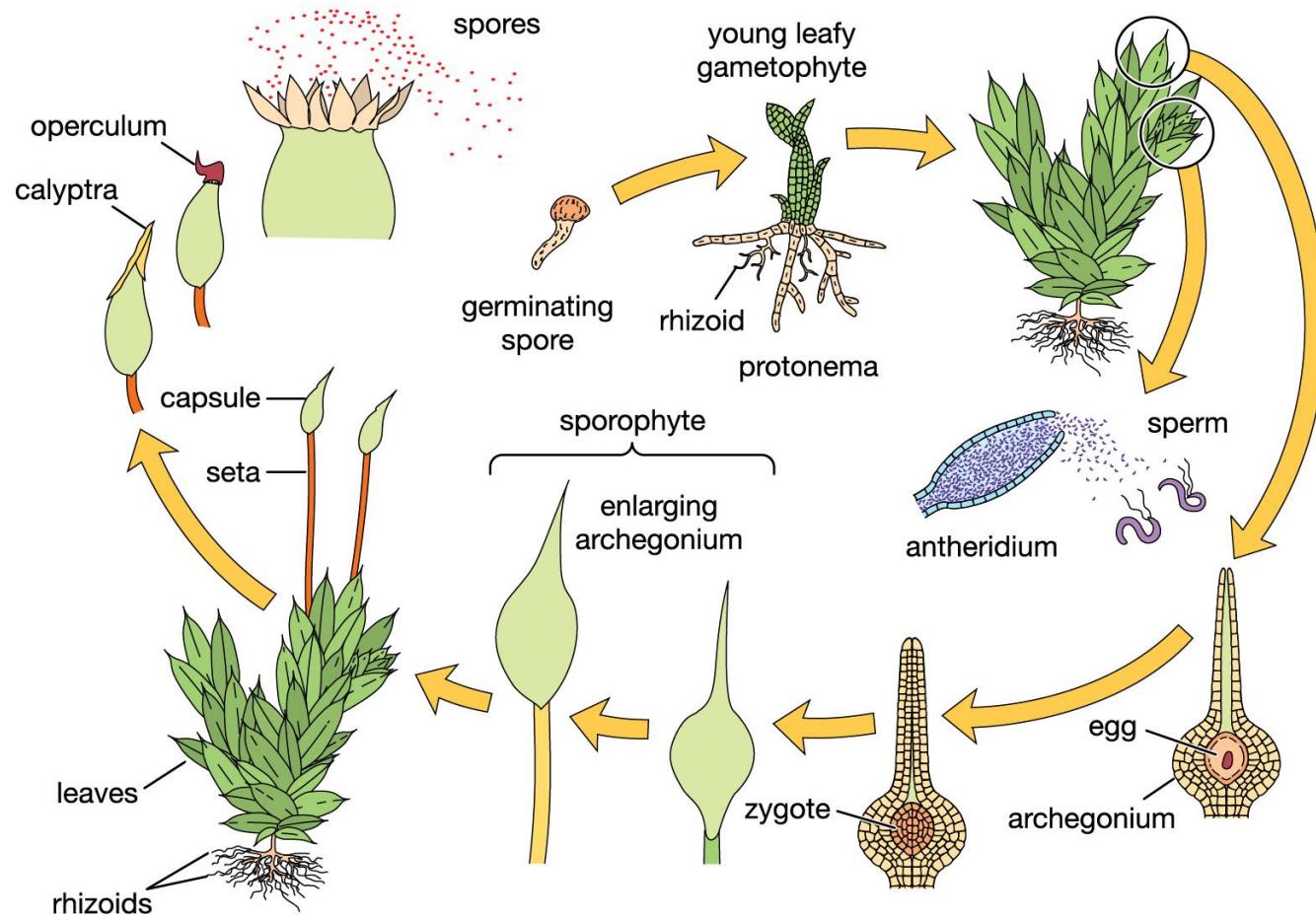
Properties: Metabolism



Properties: Growth

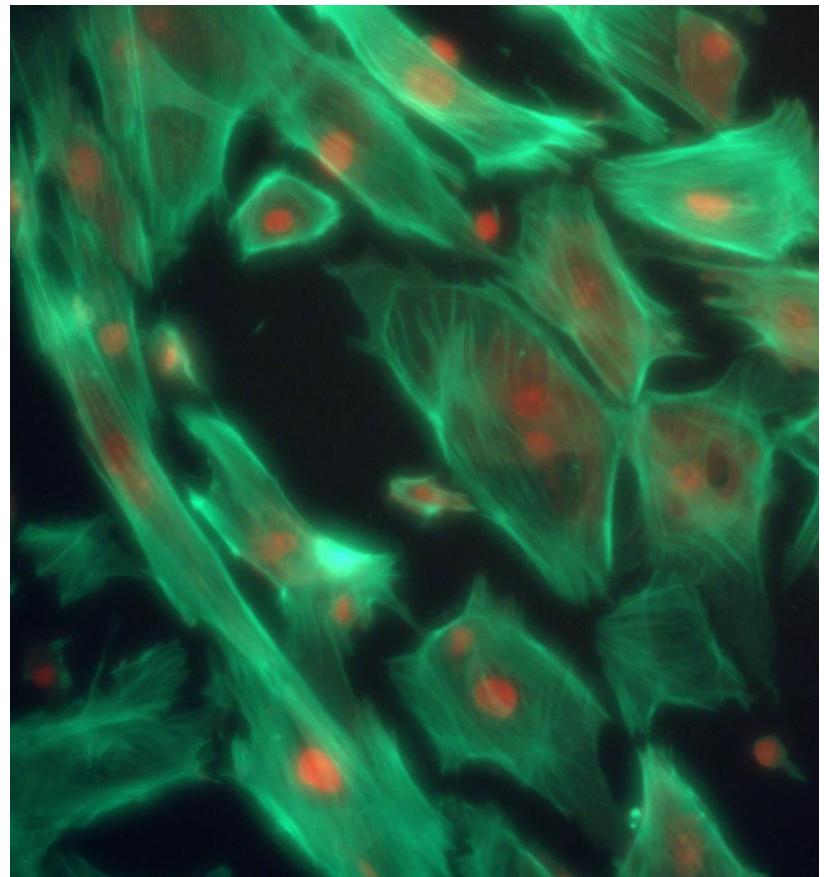


Properties: Reproduction



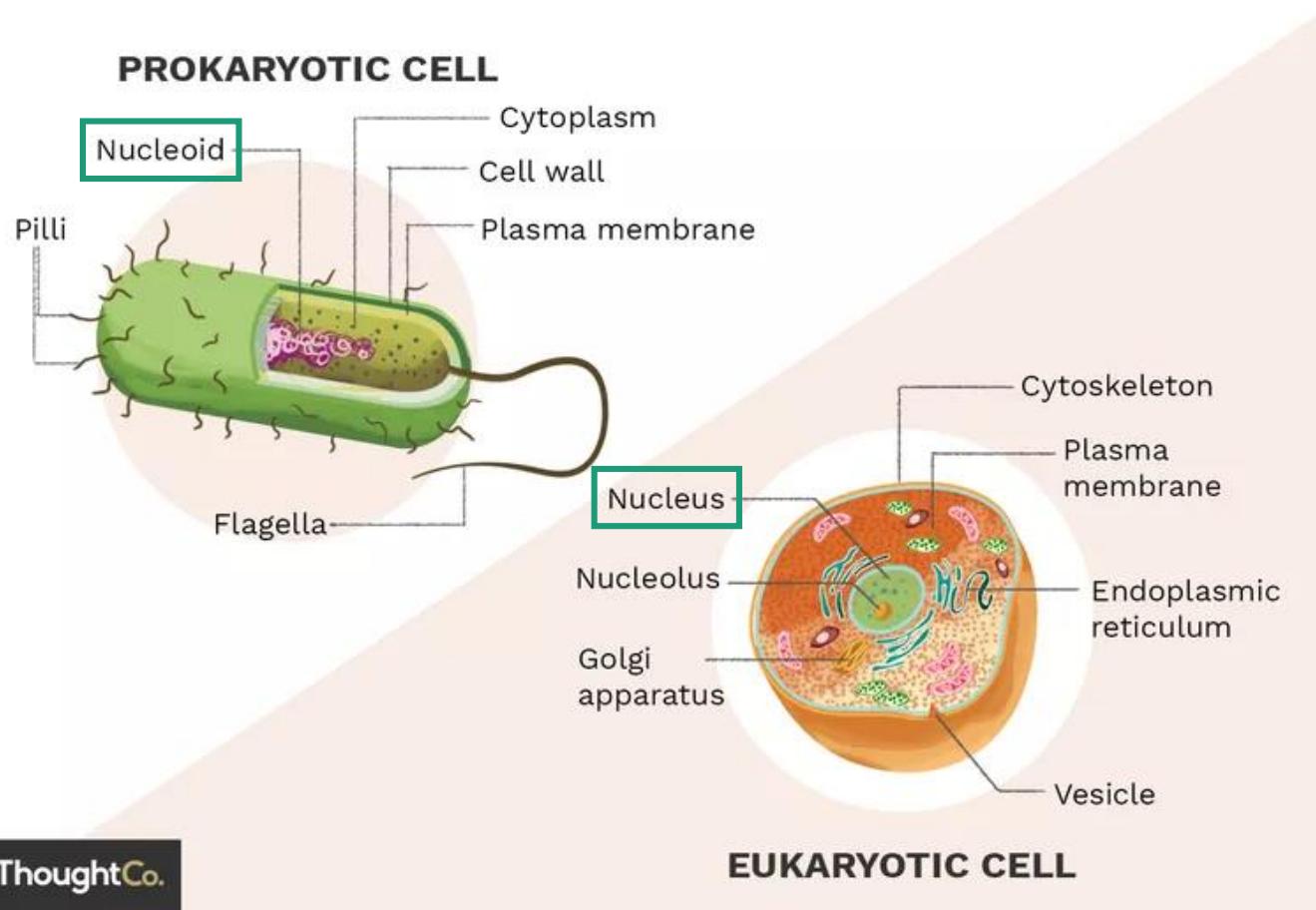
Modern Cell Theory

1. All living organisms are made of cells.
2. Cells are the basic unit of life.
3. Cells arise from pre-existing cells.
4. **Hereditary information is passed from cell to cell.**
5. **All cells have the same basic chemical composition.**
6. Energy flow occurs within cells.



1° mouse liver culture. Stained with 568 Phalloidin and DAPI.
MBB 125 (2017)

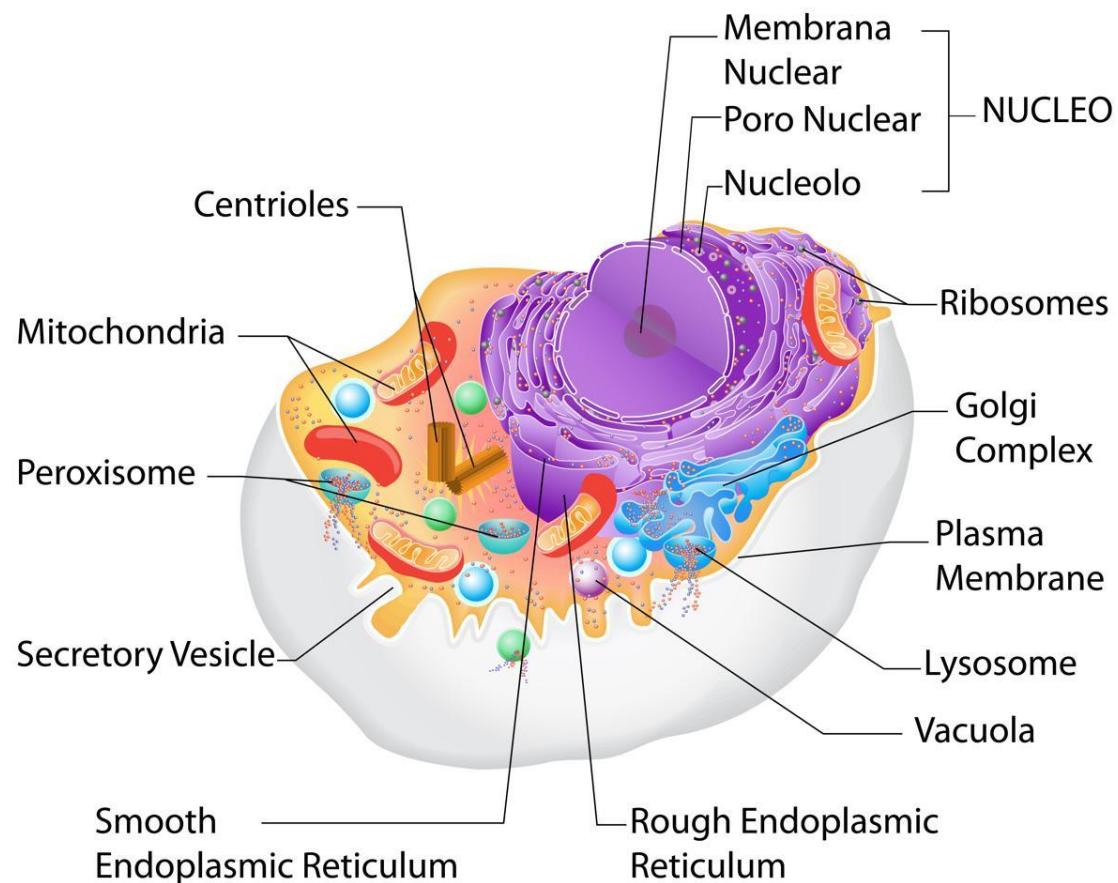
Classification of Life



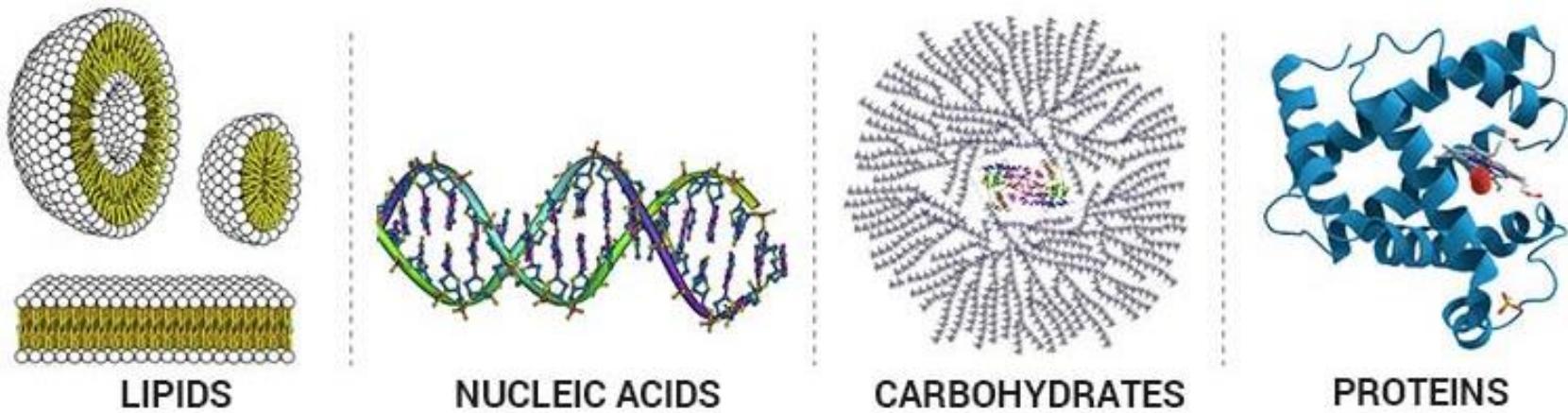
Classification of Life



Part of a Cell

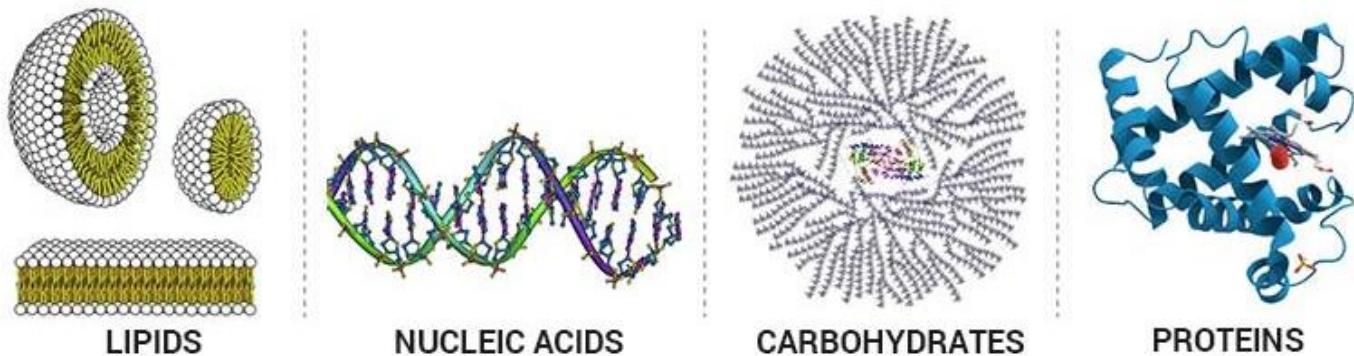


Chemical Composition of Life



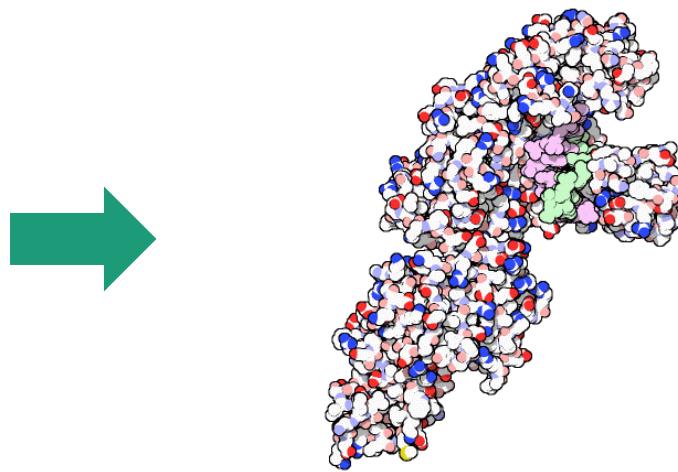
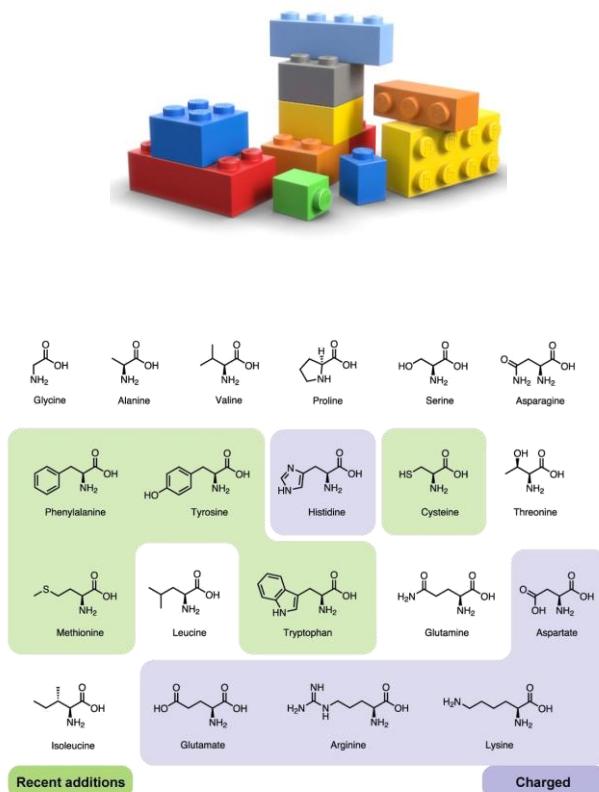
- Large polymers
- Made up of repeating subunits called monomers
 - Emerging characteristics: the ability to **store information, carry out chemical reactions, create support structures**

Chemical Composition of Life

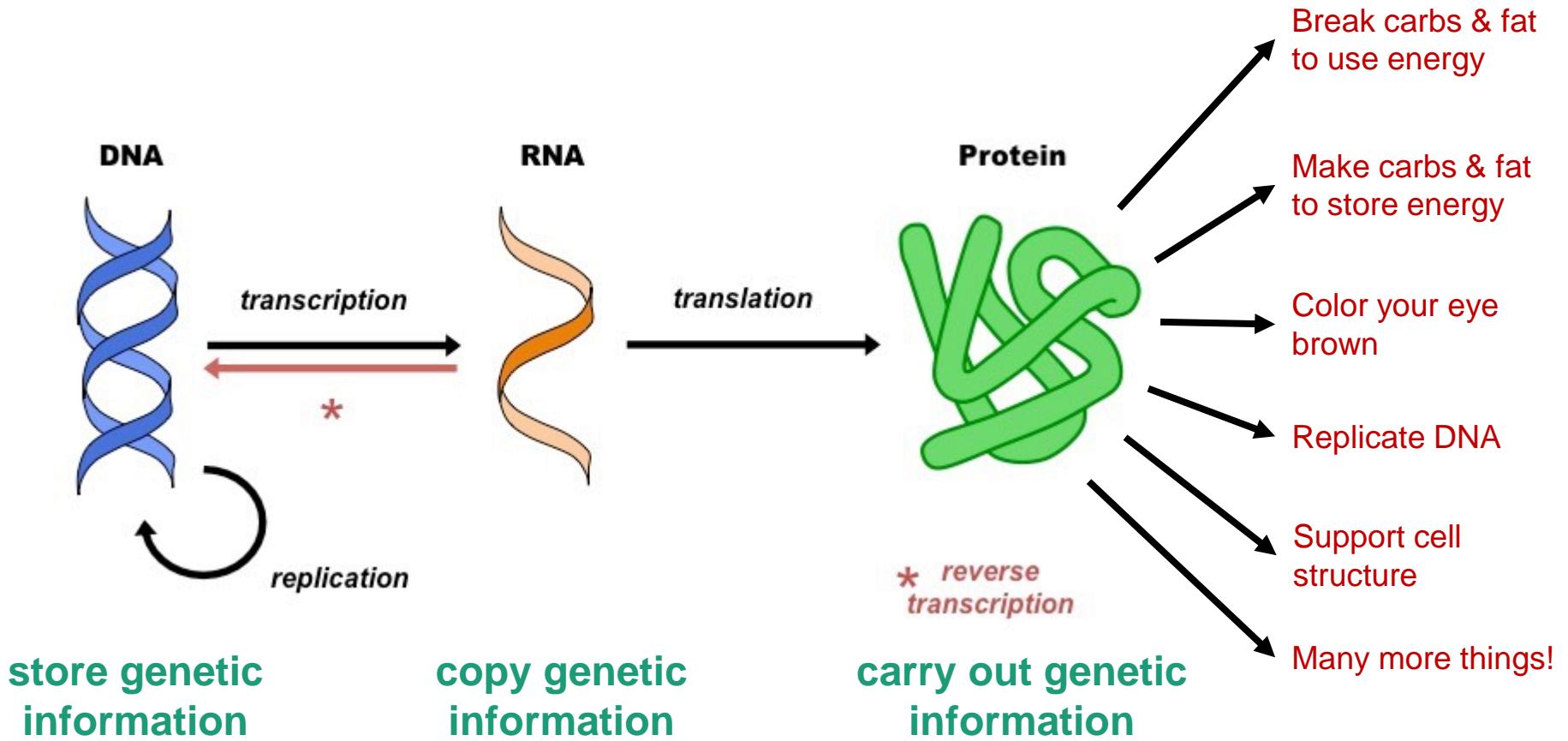


Monomer	fatty acid	nucleotide	monosaccharide	amino acid
Function	energy storage, signaling, membranes	storage of genetic information, catalysis of chemical reactions, signaling, energy transfer	energy storage, structural support	catalysis of chemical reactions, structural support, signaling
Example	lipid bilayer	DNA	starch	whey

Biomolecules are like Lego



The Central Dogma



store genetic information

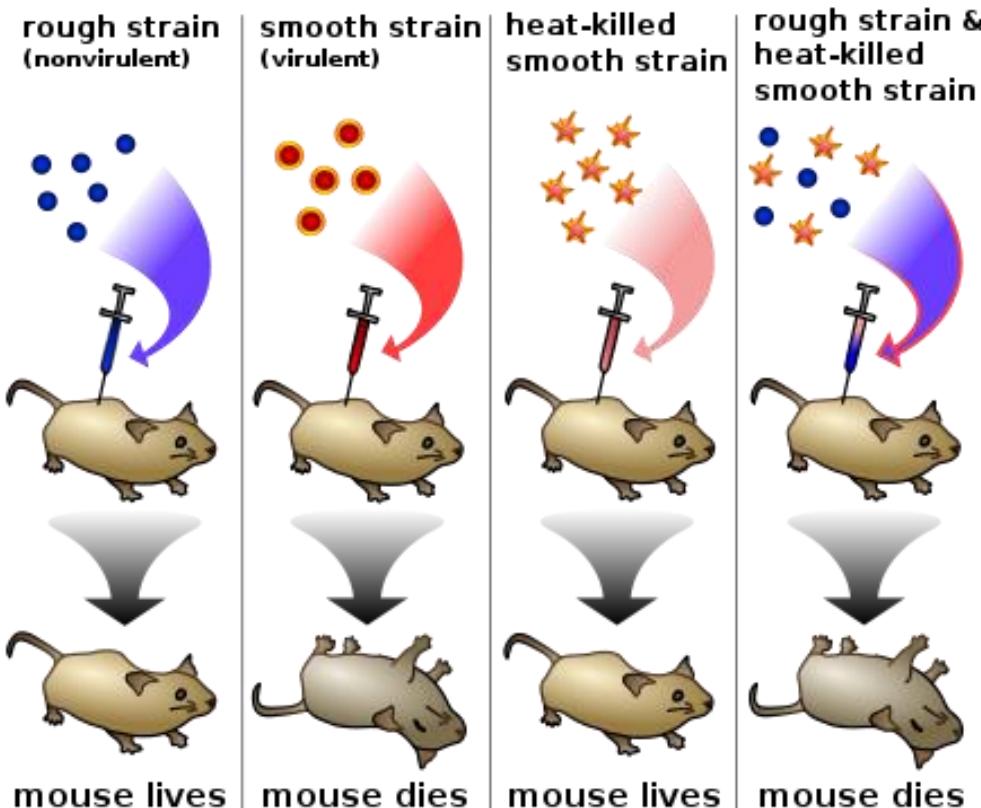
copy genetic information

carry out genetic information

DNA

Deoxyribonucleic Acid

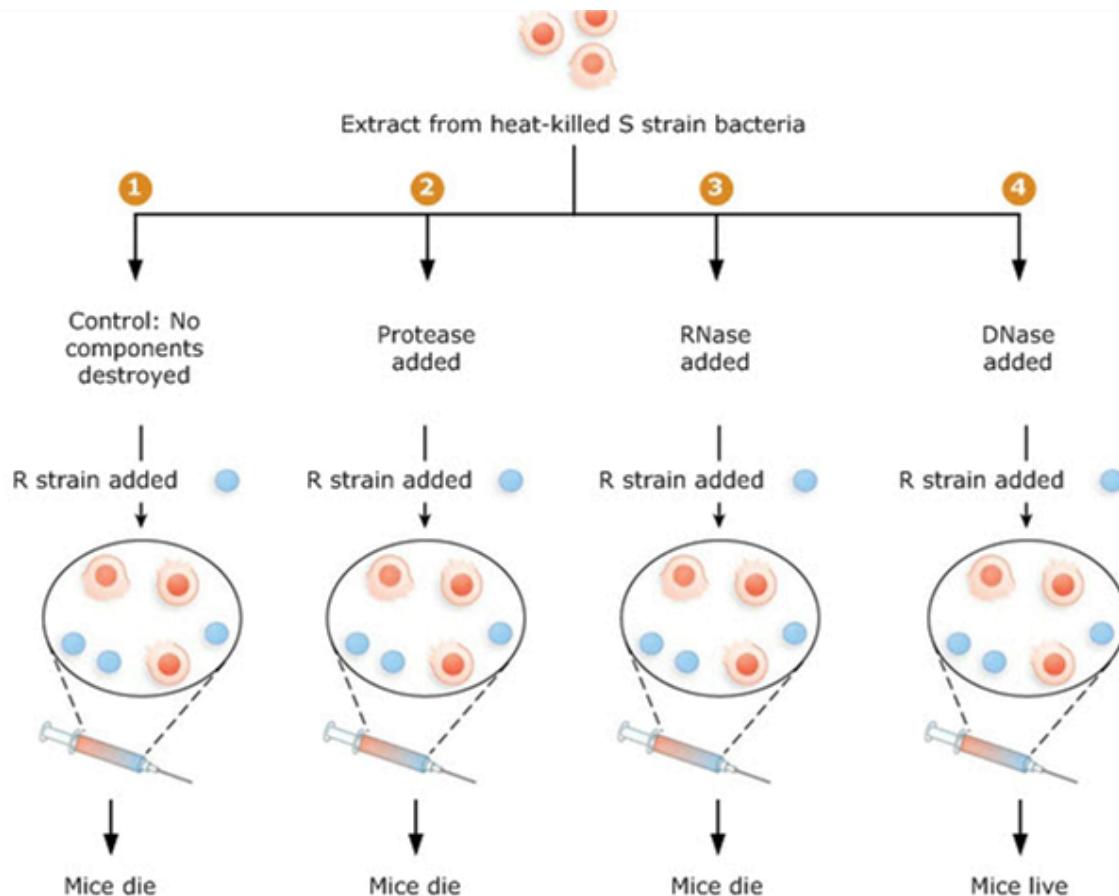
Frederick Griffith's Transformation Experiment



Using two strains of *Streptococcus pneumoniae*

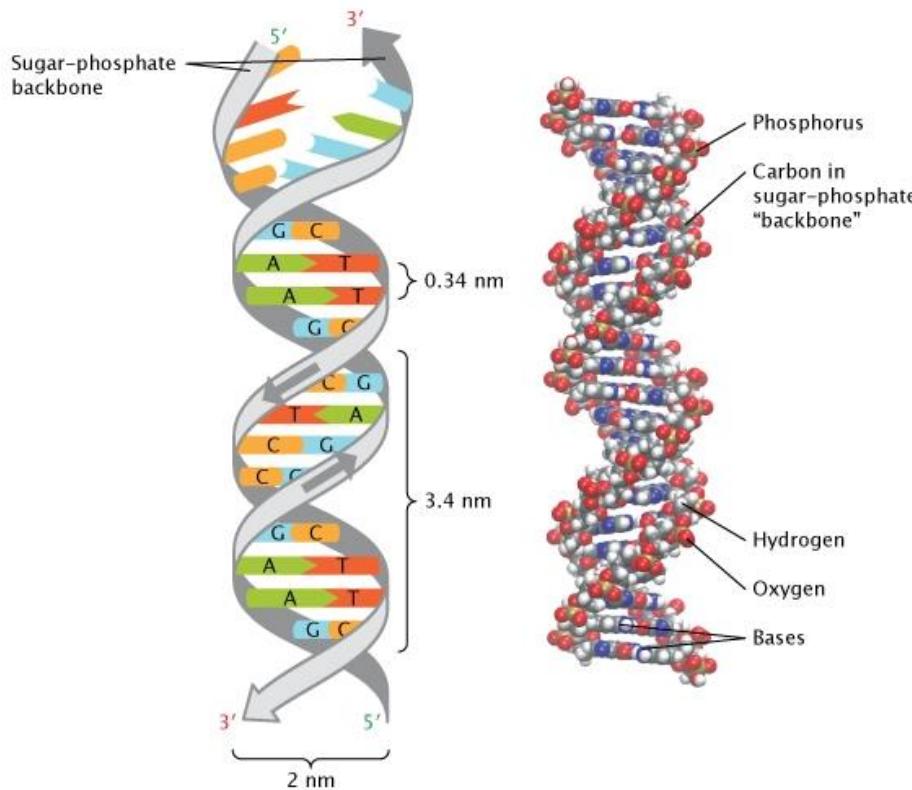
What could be causing transformation?

Avery, Macleod & McCarty: Modified Transformation (1944)



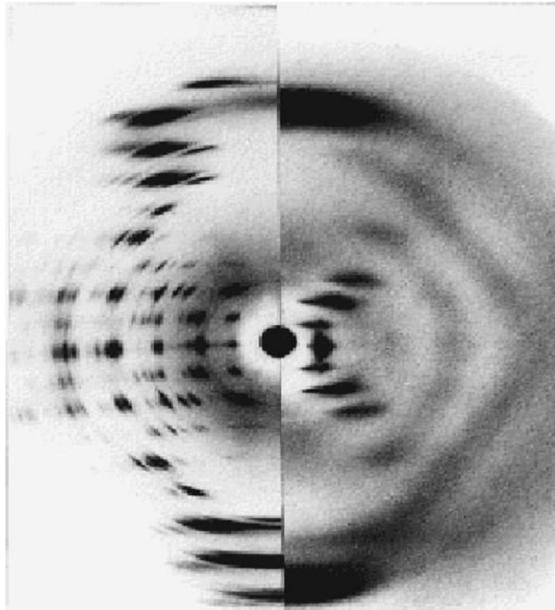
DNA is the transforming factor

DNA Structure



- Right-handed double helix
- Nitrogenous bases on the inside.
- Negatively charged phosphates on the outside

The DNA Double Helix (1953)



A-DNA

B-DNA



Rosalind
Franklin



Maurice
Wilkins



James Watson
Francis Crick

1962 Nobel Prize in Medicine or Physiology

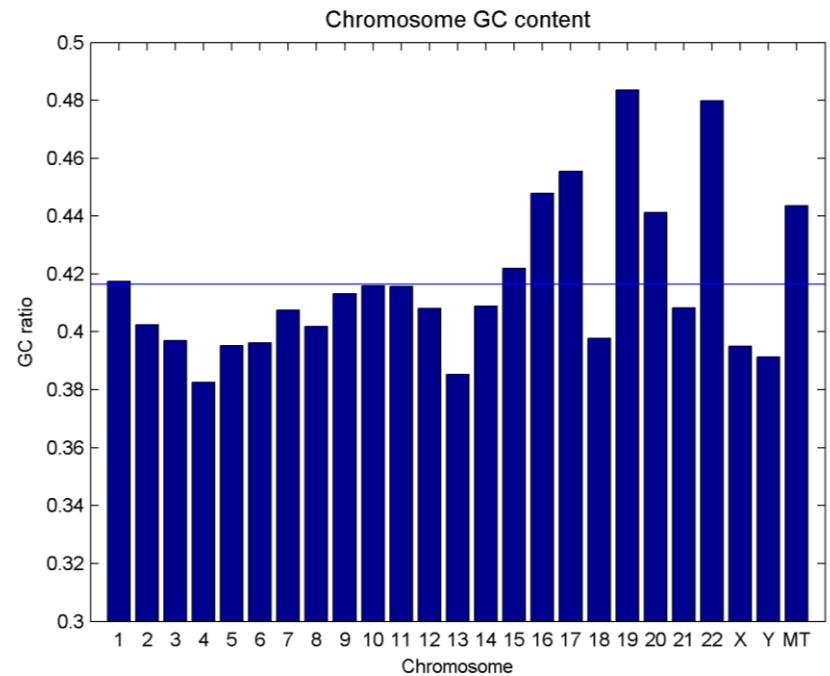
Chargaff's Rules

- Chargaff's Rules
 - Globally, the proportion of adenines equals that of thymines and the proportion of guanines equals that of cytosines.
 - The number of purines ($A + G$) equals that of the pyrimidines ($T + C$).

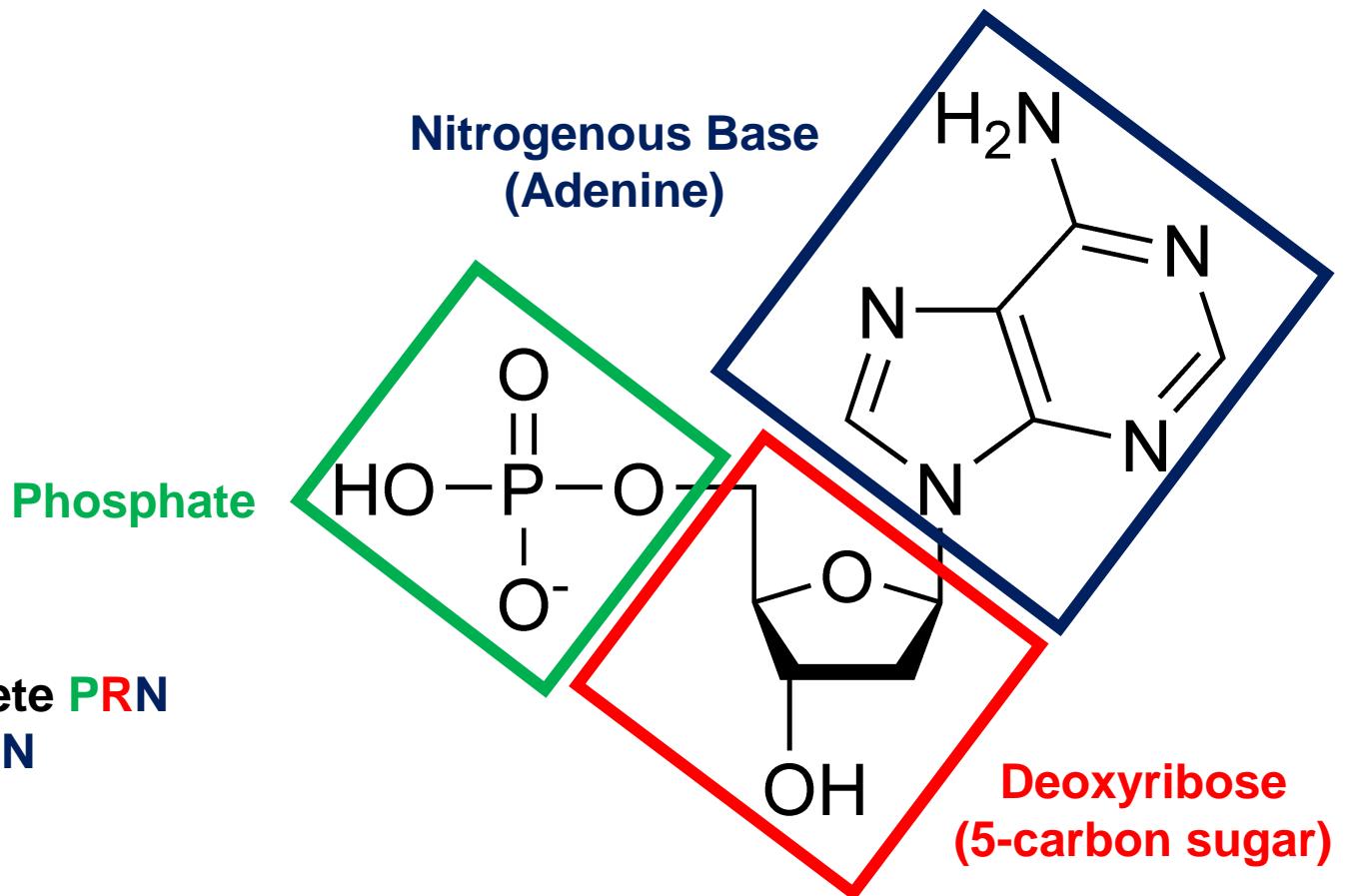
Relative Proportions (%) of Bases in DNA				
Organism	A	T	G	C
Human	30.9	29.4	19.9	19.8
Chicken	28.8	29.2	20.5	21.5
Grasshopper	29.3	29.3	20.5	20.7
Sea Urchin	32.8	32.1	17.7	17.3
Wheat	27.3	27.1	22.7	22.8
Yeast	31.3	32.9	18.7	17.1
E. coli	24.7	23.6	26.0	25.7

Chargaff's Rules

- Chargaff's Rules
 - The proportion of A+T can differ from G+C per organism.



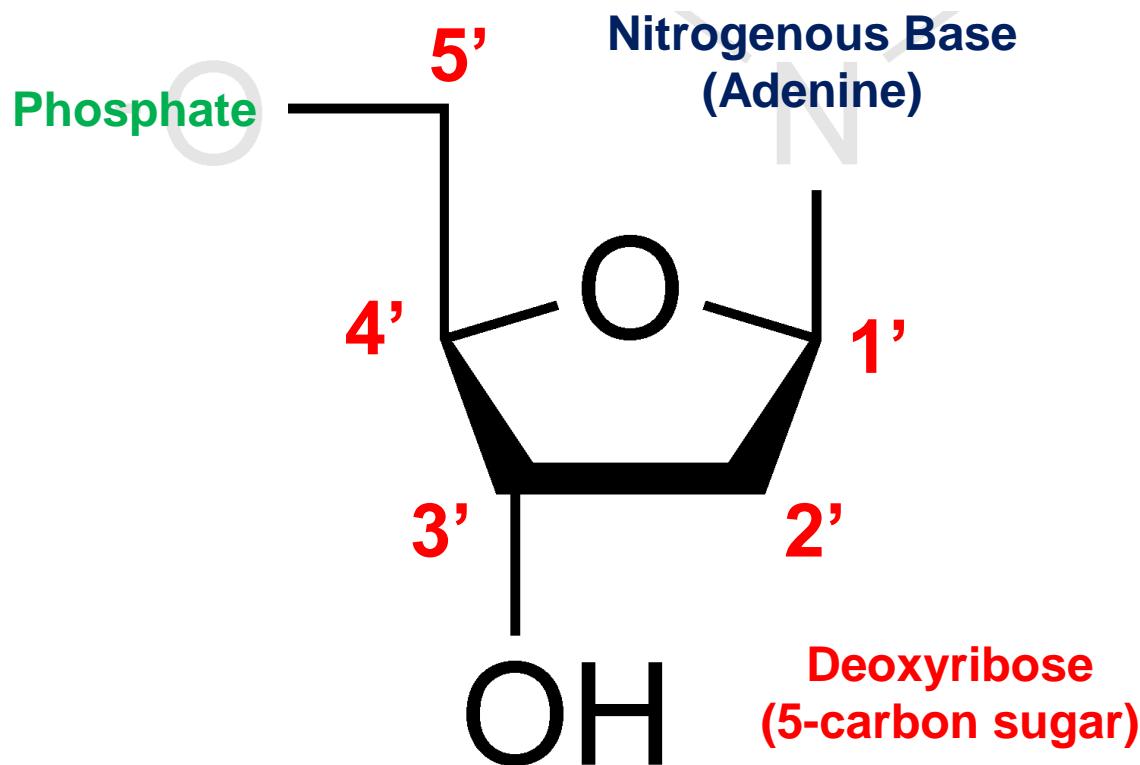
Nucleotide Structure



Nucleotide: Complete PRN

Nucleoside: Only RN

Nucleotide Structure



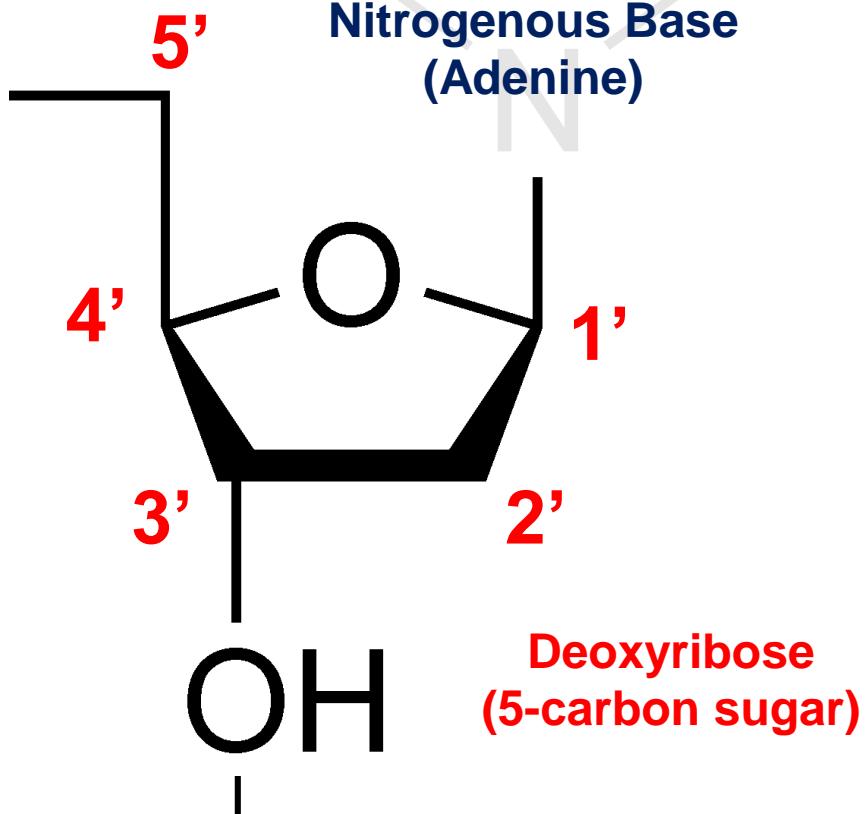
DNA Directionality

Connection to previous nucleotide

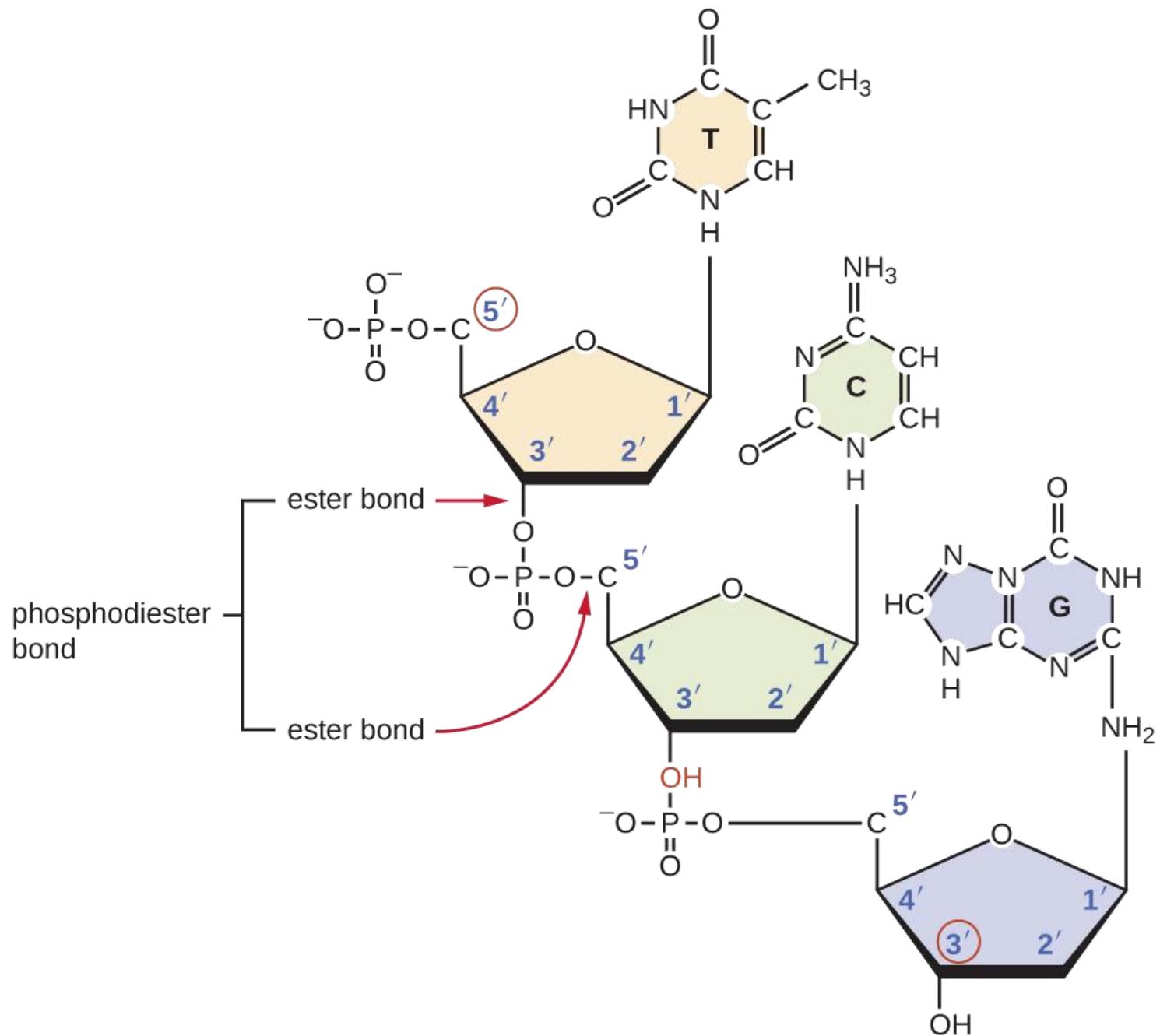
Phosphate

The information in a single strand of DNA is **directional**.

By convention, we read DNA from 5' to 3'. The reason for this will become clear later.



Connection to next nucleotide

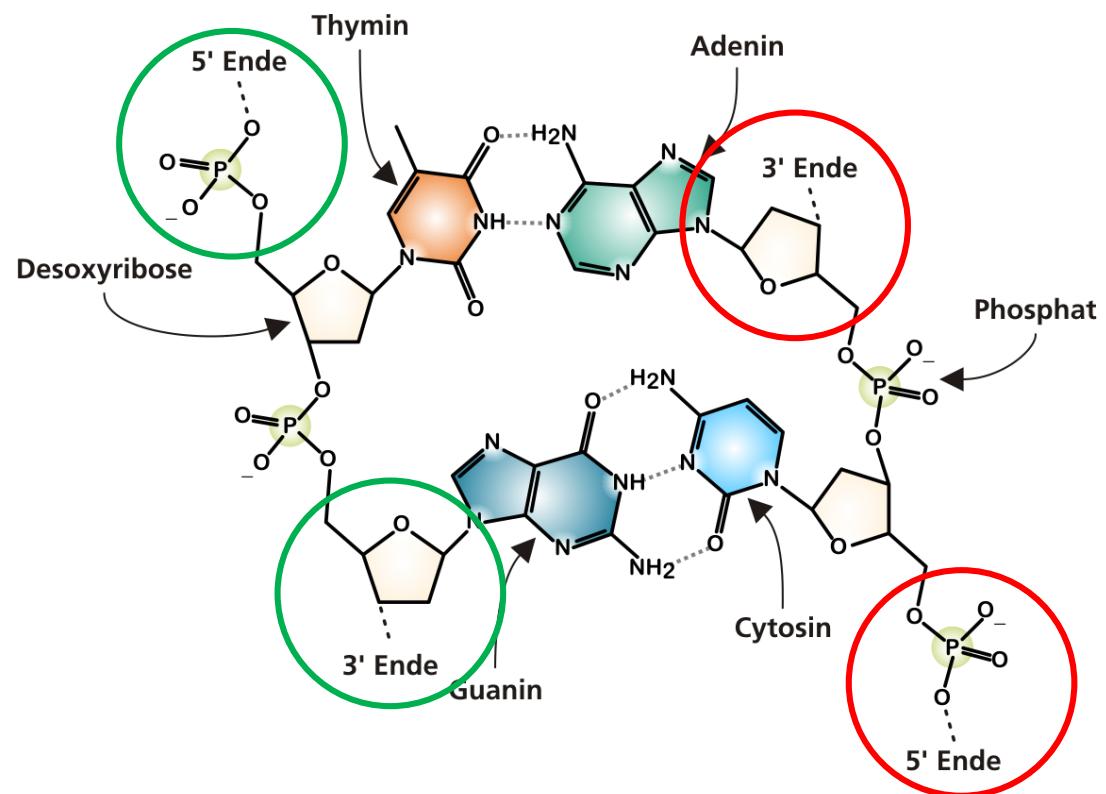


DNA Directionality

A DNA double-helix is anti-parallel. The opposing strands run in opposite directions.

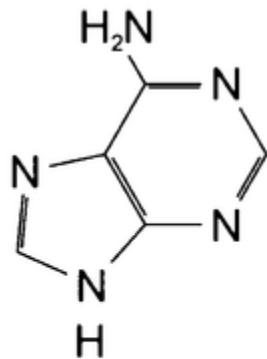
If one strand is runs 5'-3', its complementary strand should run 3'-5'.

The double helix is held together by interactions between opposing nitrogenous bases.

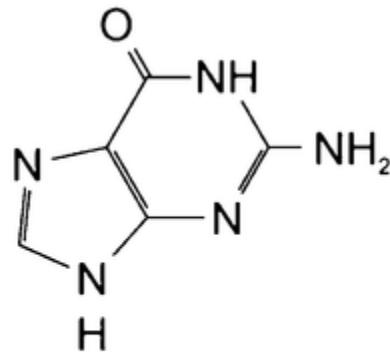


Nucleotide Structure

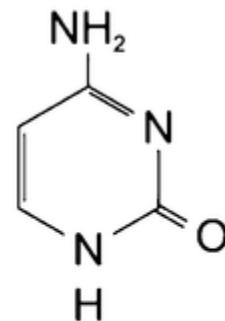
Nitrogenous bases are made of rings of carbon and nitrogen.



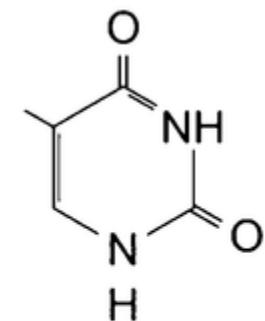
Adenine



Guanine



Cytosine



Thymine

Purines

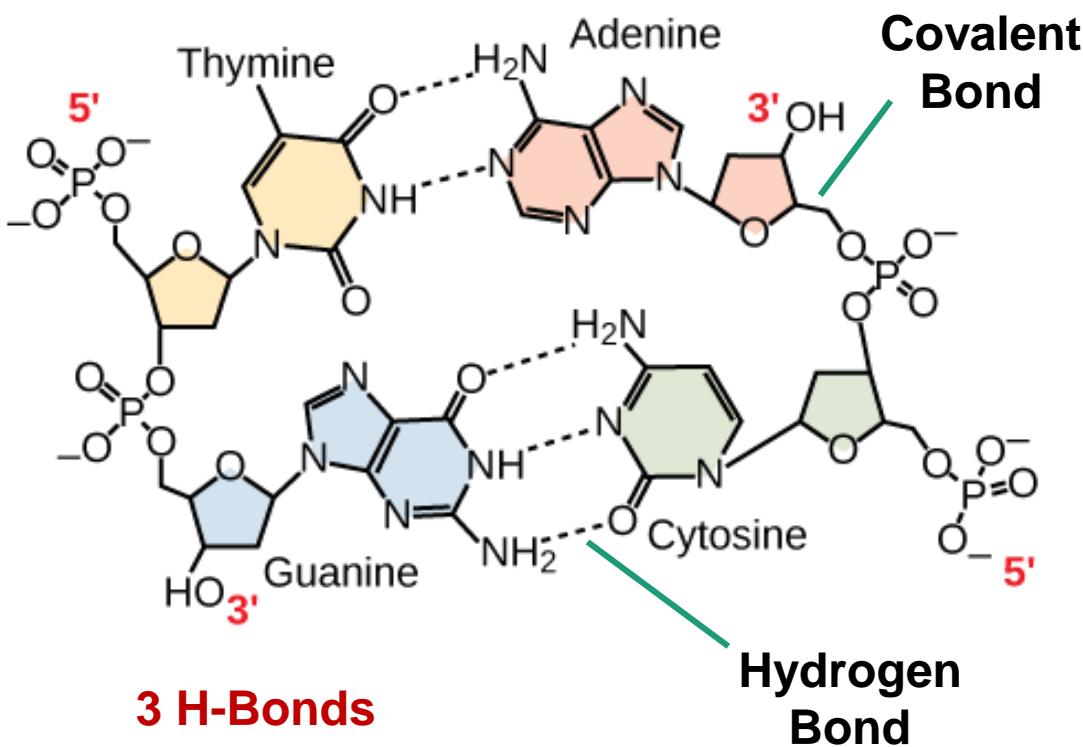
Two rings: a 6- and 5-member ring

Pyrimidines

One ring: a 6-member ring

DNA Structure

2 H-Bonds



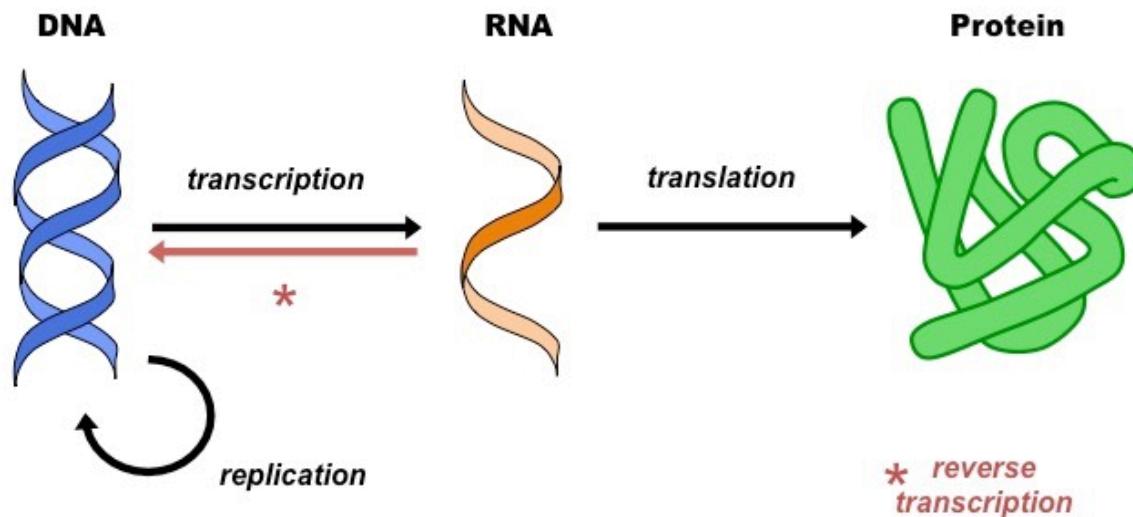
DNA is held together by **hydrogen bonds** between base pairs.

Hydrogen bonds are a type of interaction which are **weaker than molecular (covalent) bonds**, but **stronger than other types of intermolecular forces**.

DNA Function

DNA is the genetic material for all organisms (and some viruses).

The human genome is 3 billion base pairs, containing around 19,000 - 20,000 genes



DNA Function

DNA is the genetic material for all organisms (and some viruses).

The human genome is 3 billion base pairs, containing around 19,000 - 20,000 **genes**.

A gene is an information-containing region of DNA that contains a discrete, heritable characteristic.

- Information to make and code **protein**. (**~1.5-2.2%**)
- Information to make **transfer and ribosomal RNA**. (**~2%**)

DNA Function

The human genome is 3 billion base pairs, containing around 19,000 - 20,000 genes

- Information to make and code **protein**. (~1.5-2.2%)
- Information to make **transfer and ribosomal RNA**. (~2%)
- **Regulatory sequences**- information to regulate protein and RNA production.
- **Repetitive sequences (50%)**- repeating/non-informational DNA sequences (plays a role evolution)
- **Pseudogenes**
- **Introns**

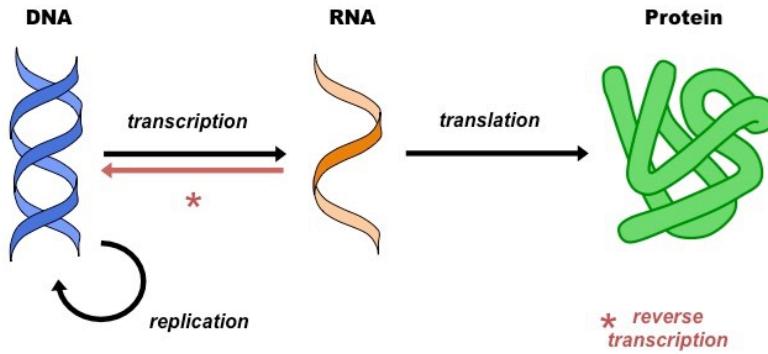
DNA in Prokaryotes and Eukaryotes

PROKARYOTE

- DNA in cytoplasm/nucleoid region.
- One to two chromosomes.
- Circular chromosome.
- Smaller (a few megabases).
- No DNA packing.
- Simple gene structure (no introns)
- Polycistronic

EUKARYOTE

- DNA contained in nucleus.
- Several chromosomes.
- Linear chromosomes.
- Larger (gigabases)
- DNA packed and organized.
- Complex gene structure (intronic)
- Monocistronic.

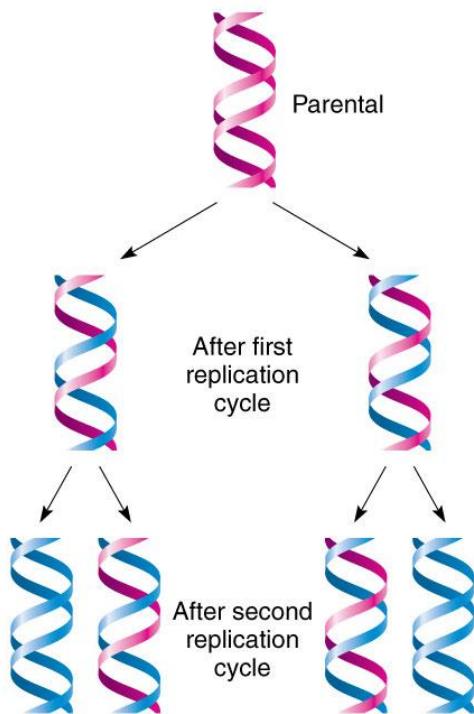


DNA Replication

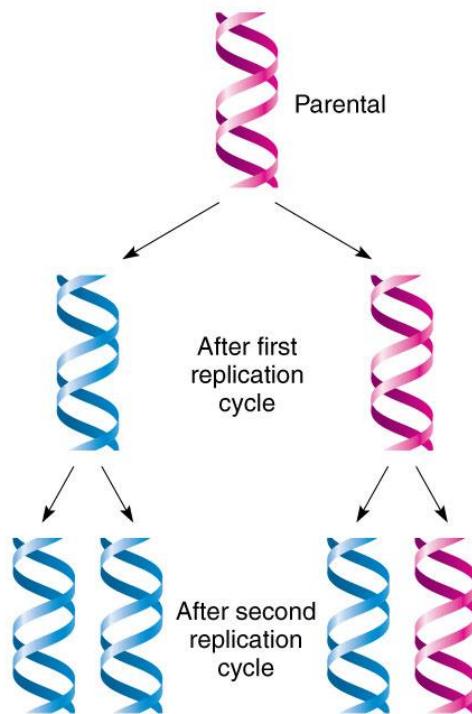
Transmission of genetic information.

DNA Replication

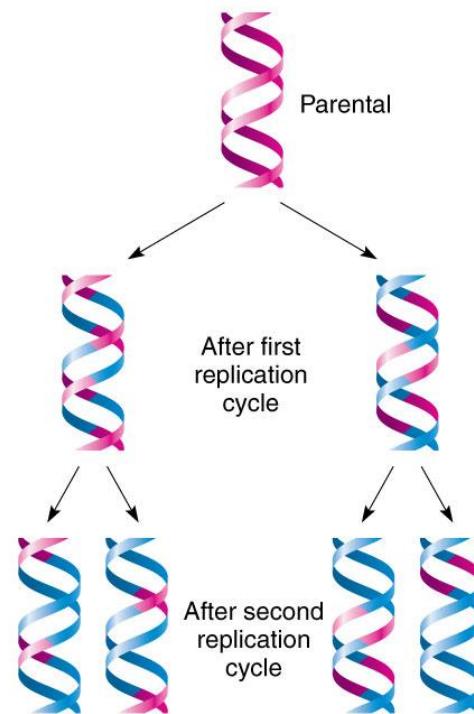
a) Semiconservative model



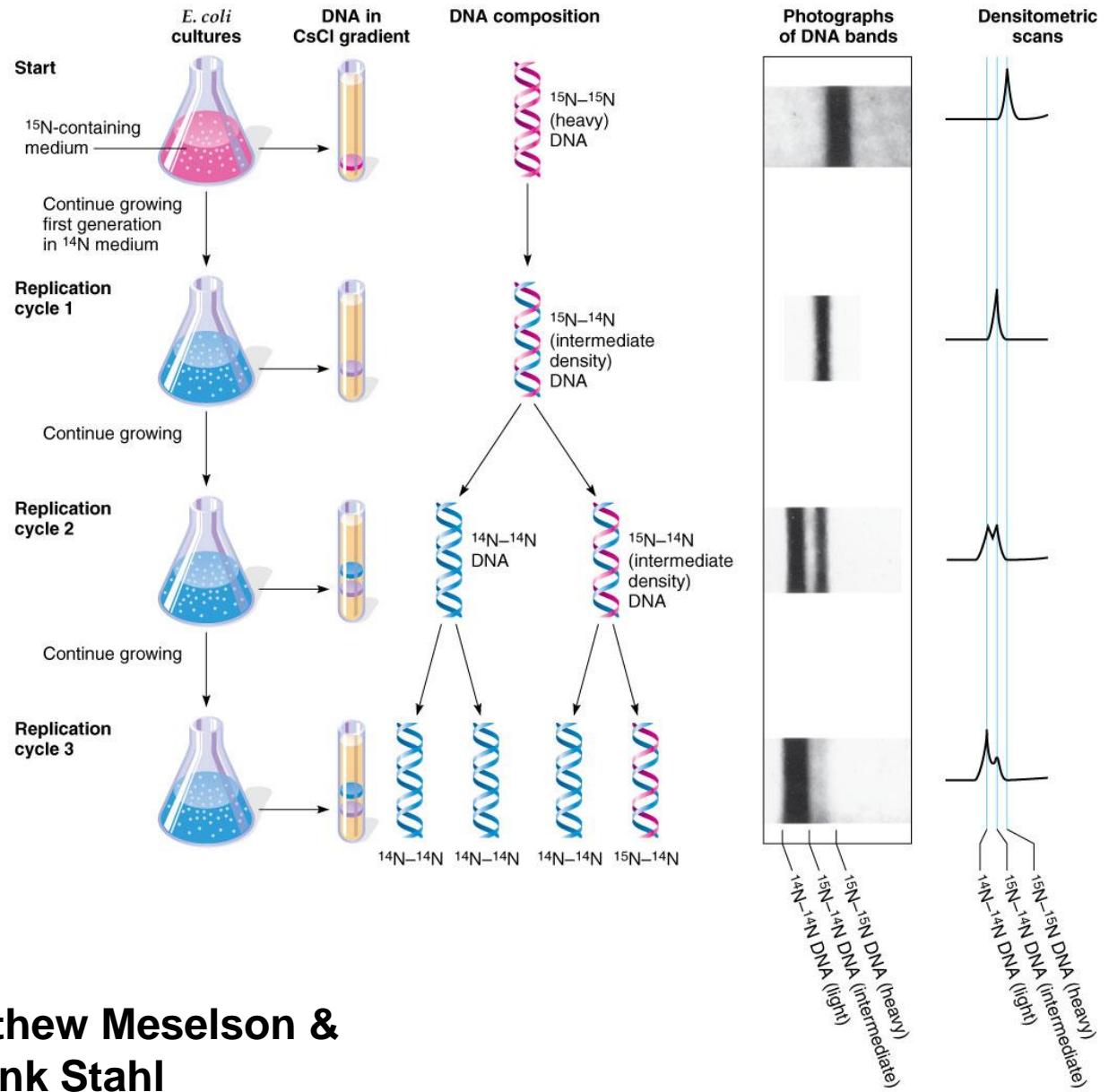
b) Conservative model



c) Dispersive model



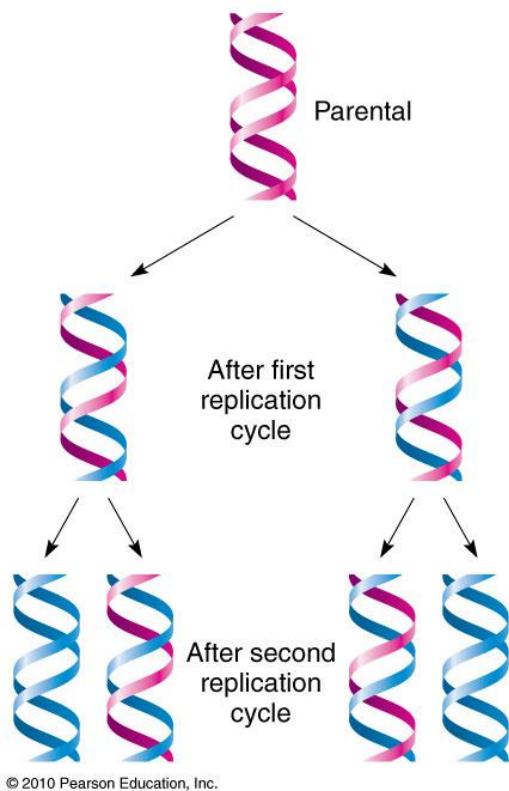
The Most Beautiful Experiment in Biology (1958)



Mathew Meselson & Frank Stahl

Semi-conservative Replication

a) Semiconservative model



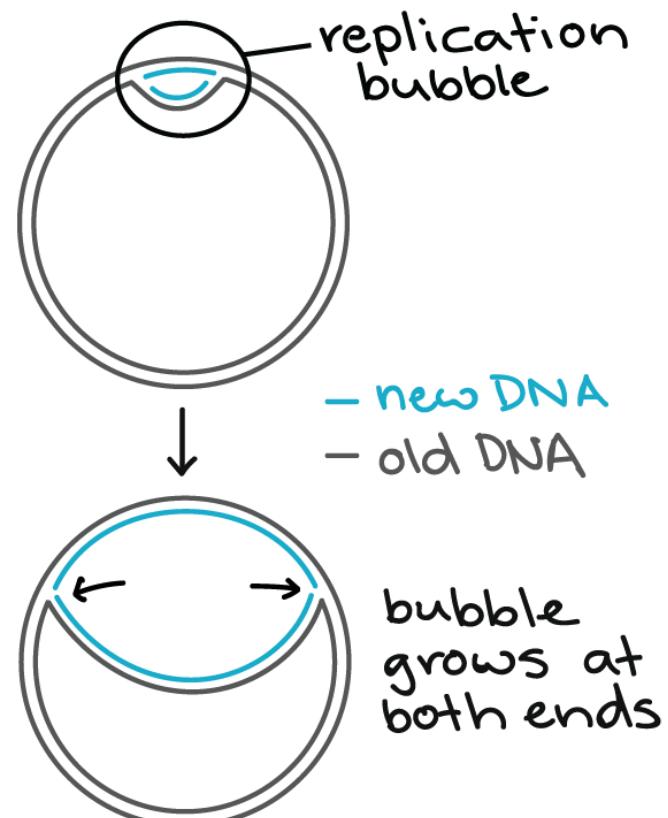
The parent DNA stand is split into two, and the complementary strand is re-constructed from the information of the parent strand.

Three Main Steps

1. **Initiation** – formation of a replication complex machinery at **origins of replication**.
2. **Elongation** – synthesis of the new DNA stand.
3. **Termination** – elongation of the new strand is terminated.

Prokaryotic Replication Initiation

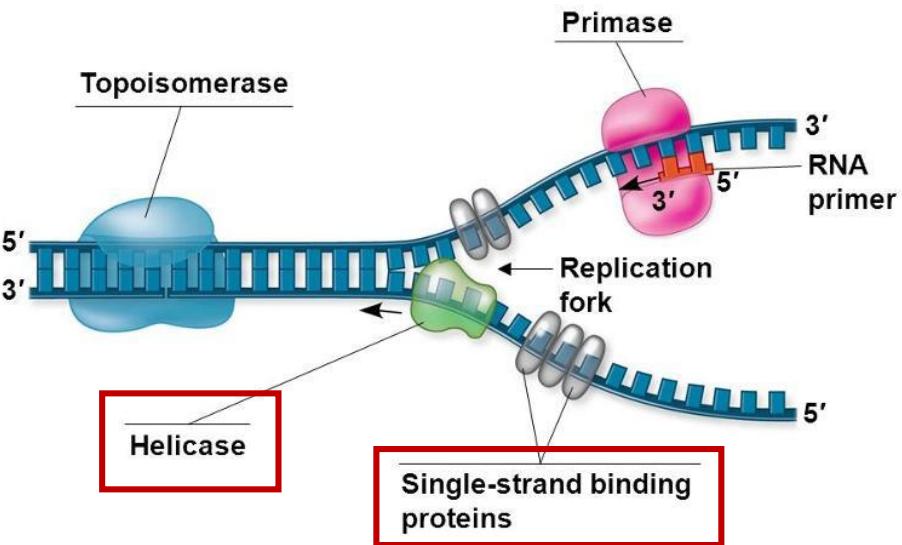
1. Binding of **initiation proteins** to the replication origin.
 - Origin is AT rich as it is easier to pull apart.
2. **Helicase** forms at the exposed single DNA strand.
3. The helicase continues to **unzip DNA 5' to 3'**, forming the replication fork and bubble.
4. Exposed single strands are stabilized by **single-strand DNA binding proteins (SSBs)**.



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Figure 16.13

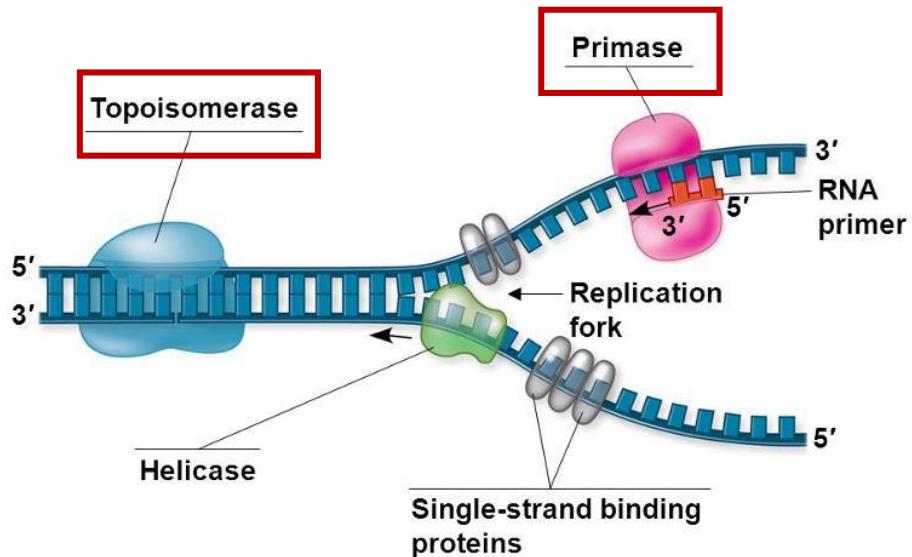


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Prokaryotic Replication Elongation

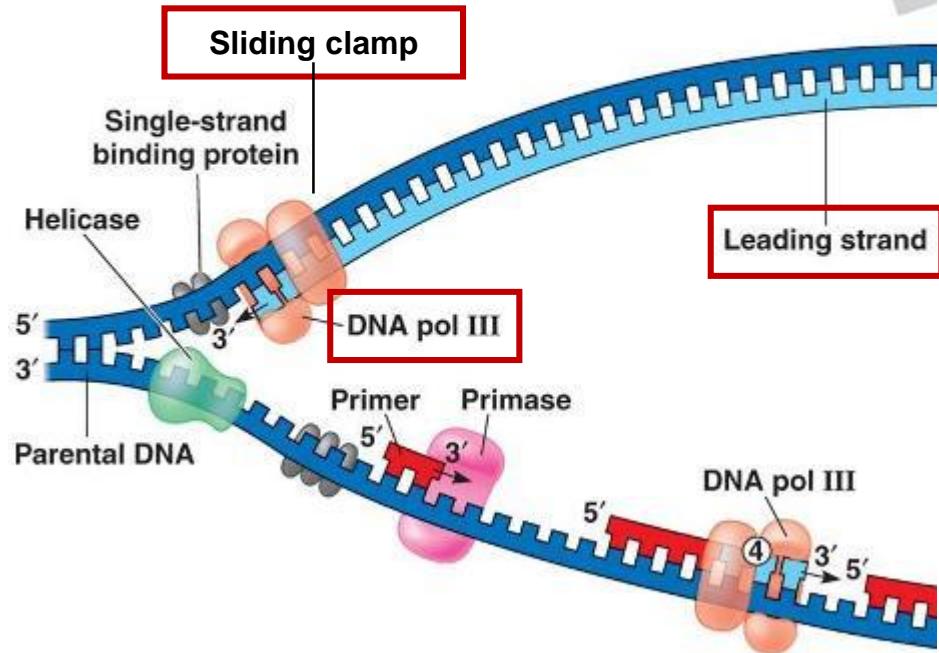
4. **RNA primase** makes a 5'-3' **RNA primer** to prime DNA elongation.
5. **DNA polymerase III** moves **3'-5' of the leading strand** and makes DNA in a 5'-3' direction, starting from the RNA primer.
 - DNA pol III is stabilized by a protein called the **sliding clamp**.
6. **Unzipping by helicases causes strain** in the DNA molecule, which is released by **topoisomerase**.

Figure 16.13



Prokaryotic Replication Elongation

4. **RNA primase** makes a 5'-3' **RNA primer** to prime DNA elongation.
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Prokaryotic Replication Elongation and Termination

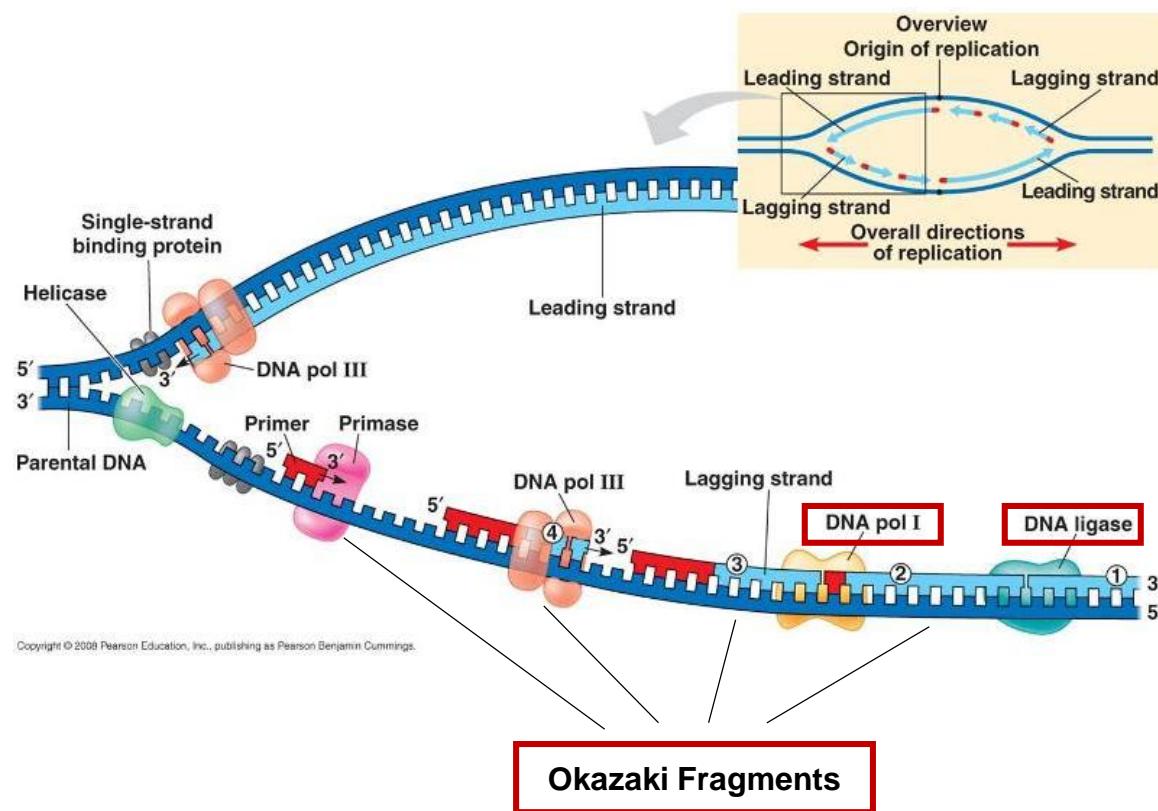
7. In the lagging strand, **new RNA primers are constantly created by RNA primase** followed by DNA elongation by DNAPolIII.

- This creates **Okazaki Fragments**.

8. Once DNAPolIII reaches the RNA primer **it stops**.

9. **DNA polymerase I** then removes the RNA primer and **replaces it with DNA**.

10. Nicks between strands are closed by **DNA ligase**.



DNA Repair

- DNAPlII is very accurate, with a mutation rate of **1 for every 10^8 bases replicated.**
- DNAPlII's accuracy **is dependent** on RNA primers. Primers are needed to prime DNA replication. DNAPlII **requires that 3' edge it attaches** to is perfectly complementary to the template stand.
 - If this is not perfect, DNAPlII has 3'-5' exonuclease activity.
- **DNA polymerase II** repairs damaged nucleotides.

Prokaryotic vs Eukaryotic Replication

Prokaryote

1. One replication bubble
2. Long Okazaki fragments (2000 bp)
3. **DNA size remains the same after replication**

Eukaryote

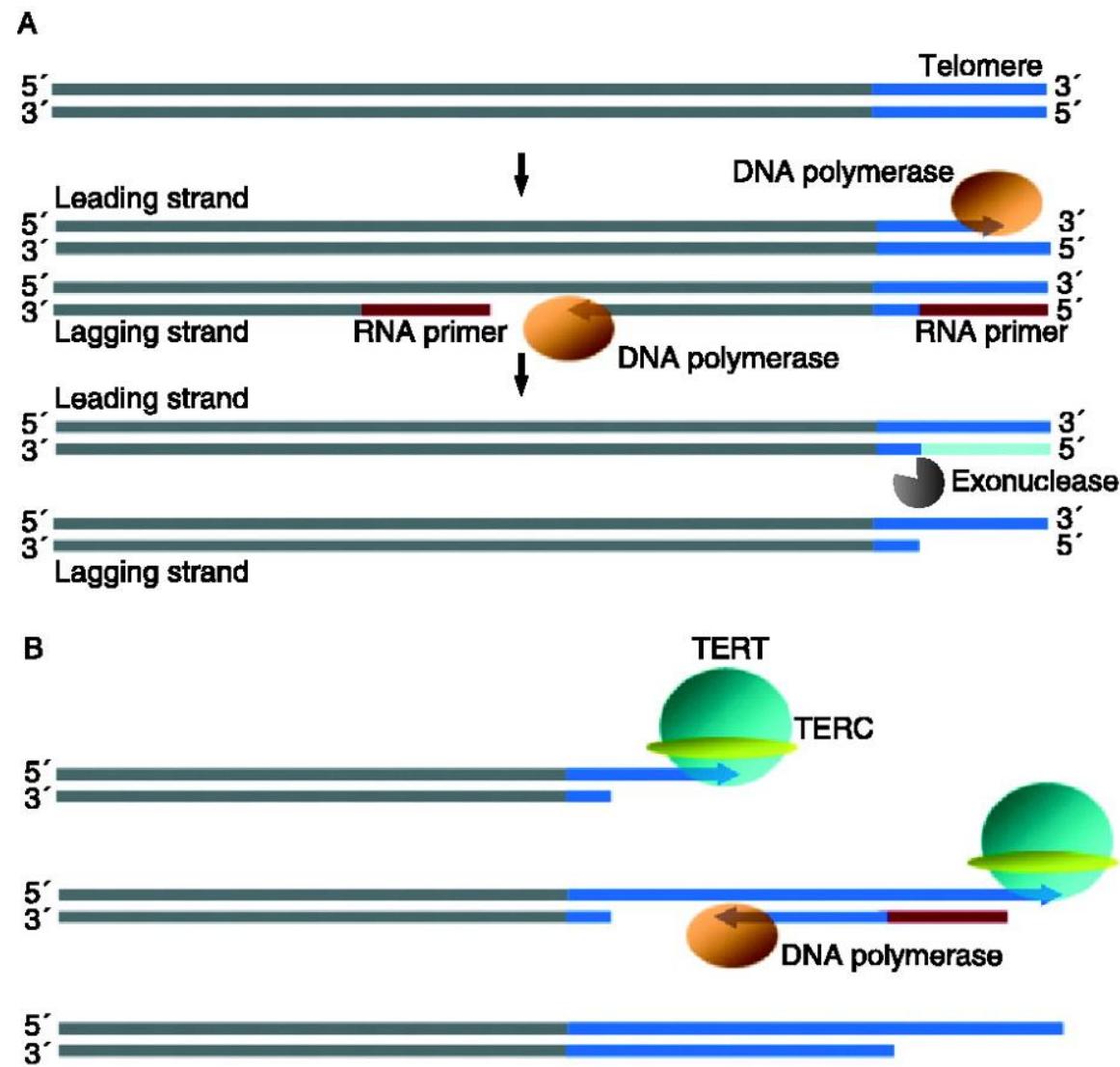
1. Multiple replication bubbles
2. Short Okazaki fragments (200-100 bp)
3. **DNA becomes shorter after replication (endpoint shortening)**

Endpoint Shortening

The RNA primer at the end of the linear DNA cannot be replaced with DNA. **The lagging strand becomes shorter than the leading stand after one replication cycle.**

Eukaryotes have **repetitive DNA elements called telomeres** which serve as buffer for endpoint shortening.

Some cells need greater replicative capacity (embryonic stem cells, gametes). This is where **telomerase reverse transcriptase (TERT)**.

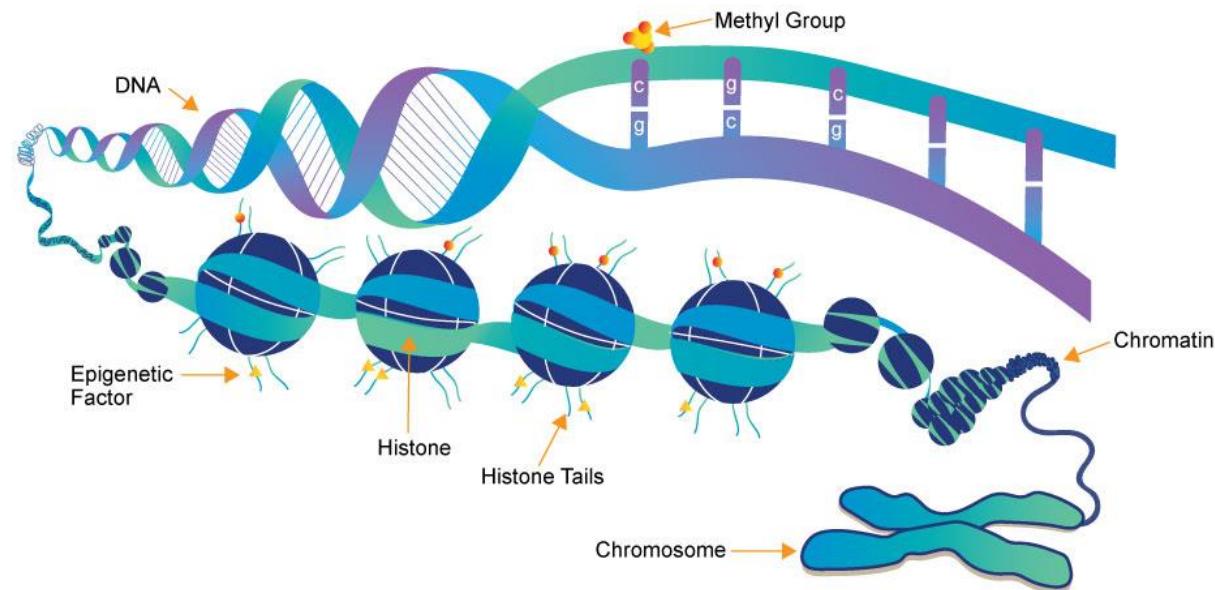


DNA Structure in Eukaryotes

Per single **100 micrometer-diameter human cell**, there is **3 meters of DNA packed inside.**

DNA is organized by proteins called **histones**, which condenses the DNA into **chromatin**.

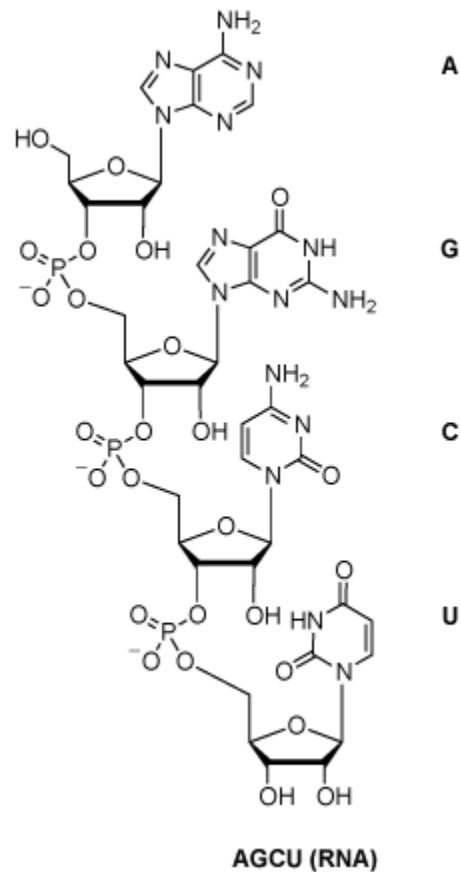
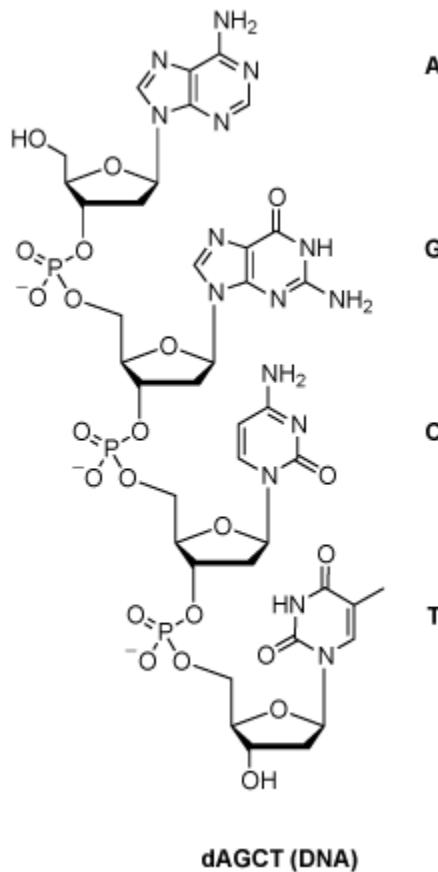
How densely packed the chromatin in a DNA region determines the accessibility of the genetic information.



RNA

Ribonucleic Acid

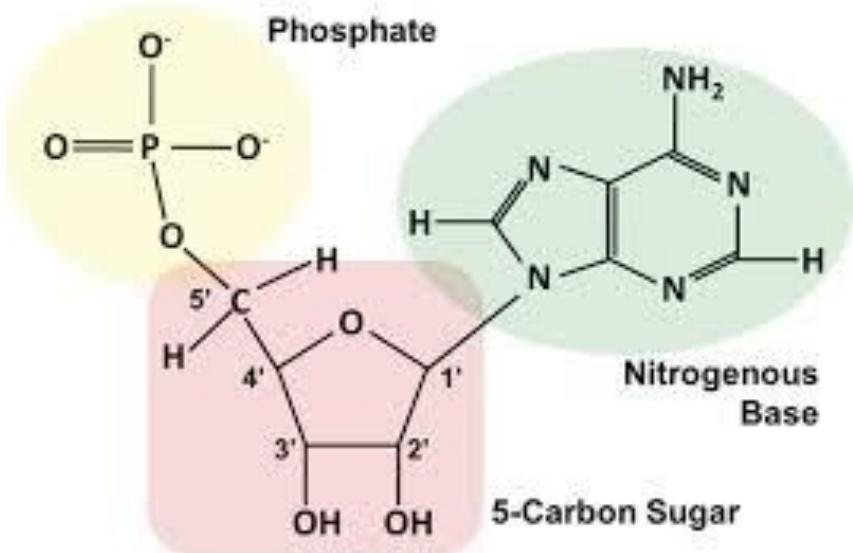
RNA Structure



RNA has a hydroxyl group at the ribose **2' carbon**

Also, thymine is replaced with uracil

RNA Structure



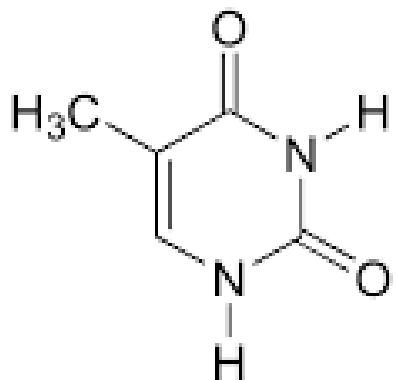
The **additional oxygen** in RNA makes it more **unstable**.

- A lot of enzymes take advantage of this to destroy RNA.

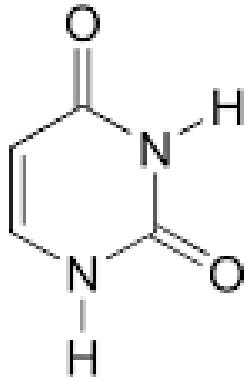
Thus RNA is more **transient** than DNA.

This also makes RNA chemically **more reactive**. Some RNAs act like proteins.

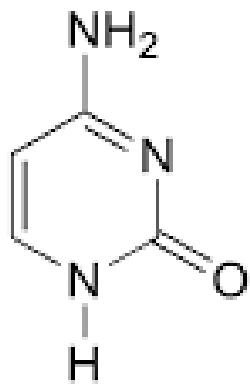
RNA Structure



thymine



uracil



cytosine

In most RNA, thymine is replaced with **uracil**.

Uracil is **easier** to make than thymine.

- For a transient copy, it would be more cost effective.

Sometimes cytosine can decompose to uracil.

- This makes it easy to repair DNA.

DNA vs RNA

DNA

- Uses **deoxyribose**
- Uses **thymine**
- **Double stranded**
- Storage and transfer of genetic material.
- Only one use – genetic material.

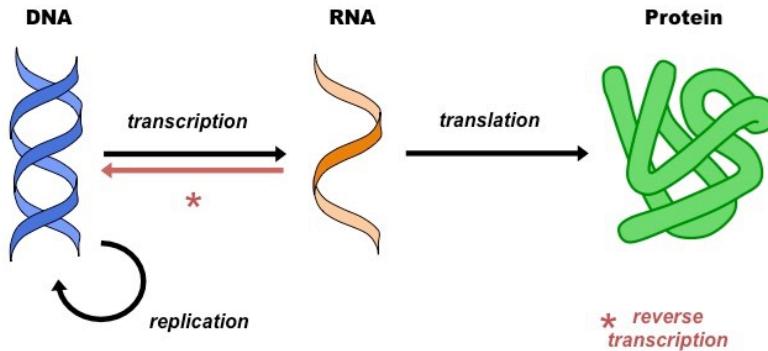
RNA

- Uses **ribose**
- Uses **uracil**
- In most use cases it is **single-stranded**
- Temporary copy of genetic material.
- Many uses!

To think about

- Do Chargaff's rules apply to RNA? Why or why not?

Relative Proportions (%) of Bases in DNA				
Organism	A	T	G	C
Human	30.9	29.4	19.9	19.8
Chicken	28.8	29.2	20.5	21.5
Grasshopper	29.3	29.3	20.5	20.7
Sea Urchin	32.8	32.1	17.7	17.3
Wheat	27.3	27.1	22.7	22.8
Yeast	31.3	32.9	18.7	17.1
E. coli	24.7	23.6	26.0	25.7



RNA Transcription

Processing of genetic information.

Why transcribe?

- Protects DNA from excessive manipulation.
- Signal amplification.
- Transient expression.
- Additional layer of control.
 - Transcriptional control
 - Translational control

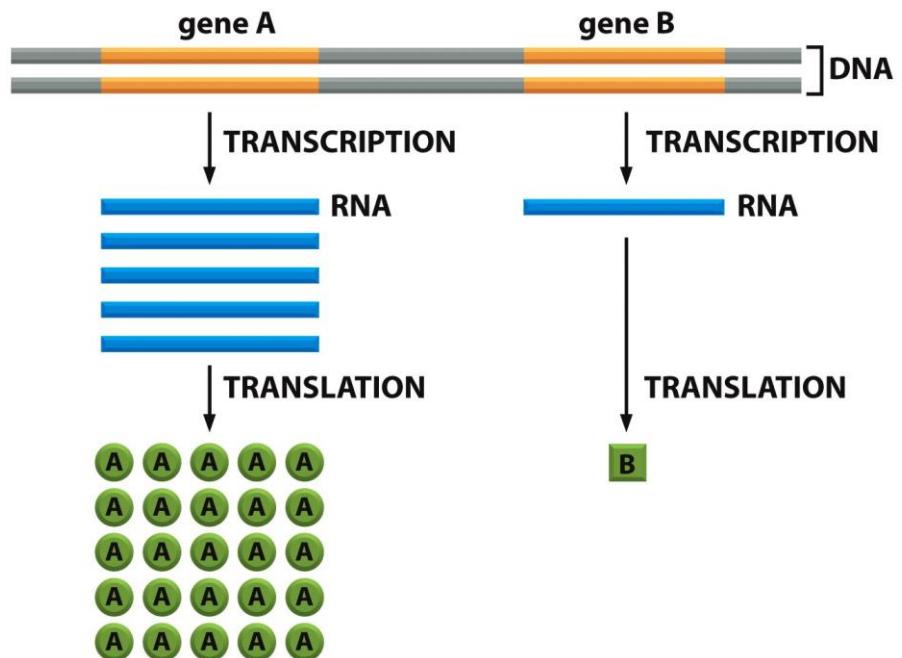


Figure 6-3 Molecular Biology of the Cell 5/e (© Garland Science 2008)

Why transcribe?

- RNA transcripts are not necessarily turned into protein.
 - RNAs have function other than being an intermediate between DNA and protein.
- By folding in on itself, RNA can form structures that mimic protein.
 - **Ribozymes**

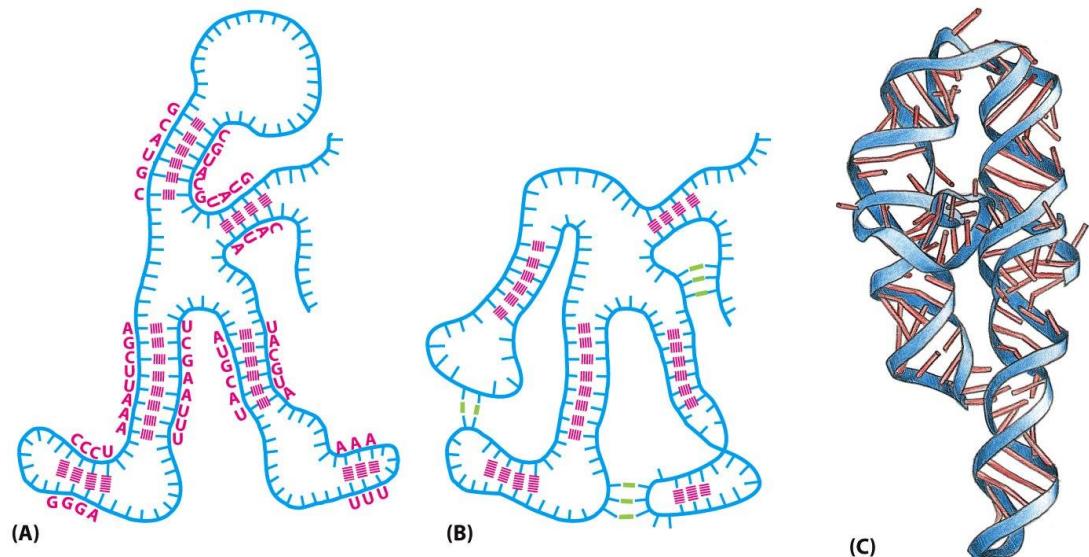


Figure 6-6 Molecular Biology of the Cell 5/e (© Garland Science 2008)

Why transcribe?

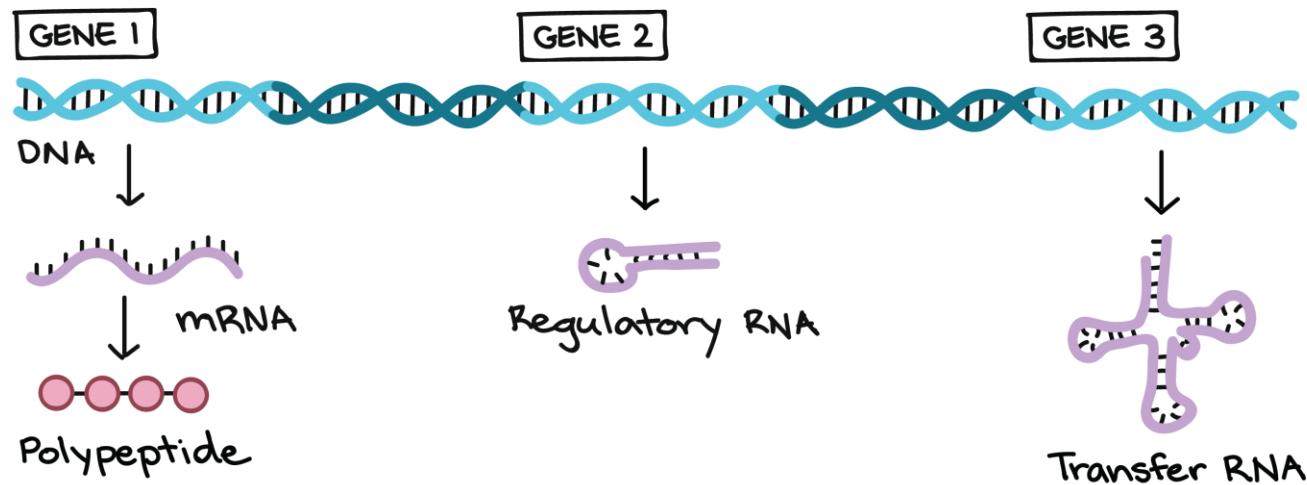
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 - **Ribozymes**

Table 6–1 Principal Types of RNAs Produced in Cells

TYPE OF RNA	FUNCTION
mRNAs	messenger RNAs, code for proteins
rRNAs	ribosomal RNAs, form the basic structure of the ribosome and catalyze protein synthesis
tRNAs	transfer RNAs, central to protein synthesis as adaptors between mRNA and amino acids
snRNAs	small nuclear RNAs, function in a variety of nuclear processes, including the splicing of pre-mRNA
snoRNAs	small nucleolar RNAs, used to process and chemically modify rRNAs
scaRNAs	small cajal RNAs, used to modify snoRNAs and snRNAs
miRNAs	microRNAs, regulate gene expression typically by blocking translation of selective mRNAs
siRNAs	small interfering RNAs, turn off gene expression by directing degradation of selective mRNAs and the establishment of compact chromatin structures
Other noncoding RNAs	function in diverse cell processes, including telomere synthesis, X-chromosome inactivation, and the transport of proteins into the ER

messenger RNA

messenger RNA (mRNA) specifically refers to RNA which **carry gene information** to be **translated** to protein.



Prokaryotic Transcription Initiation

RNA polymerase, on its own, does not know where to start transcription.

It first binds (1) with a protein called a **σ -factor** which knows where to start transcription.

- There are different kinds of σ -factors.
- The RNA polymerase coupled with the σ -factor is called the **RNA polymerase holoenzyme**.
- The σ -factor is analogous to a **transcription factor**.

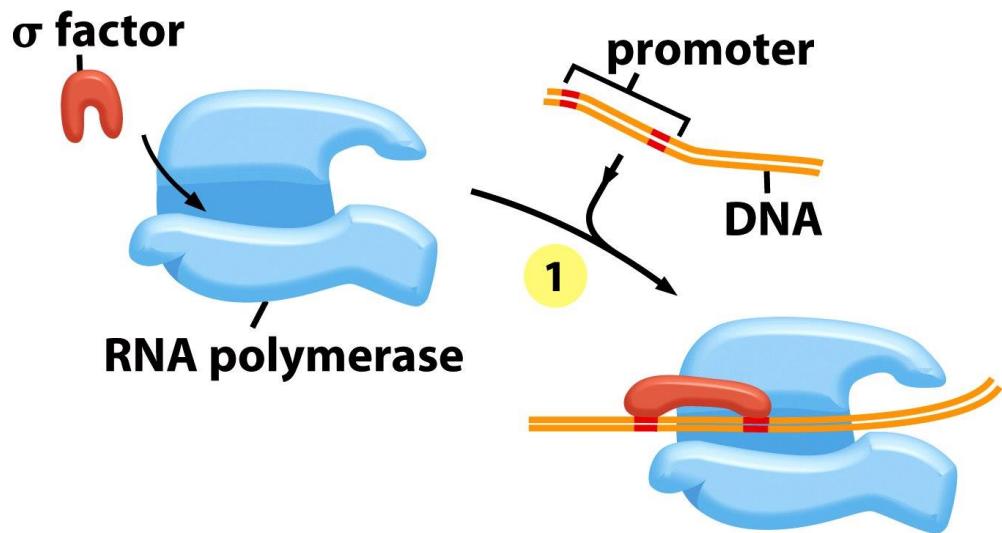


Figure 6-11 part 1 of 7 Molecular Biology of the Cell 5/e (© Garland Science 2008)

Prokaryotic Transcription Initiation

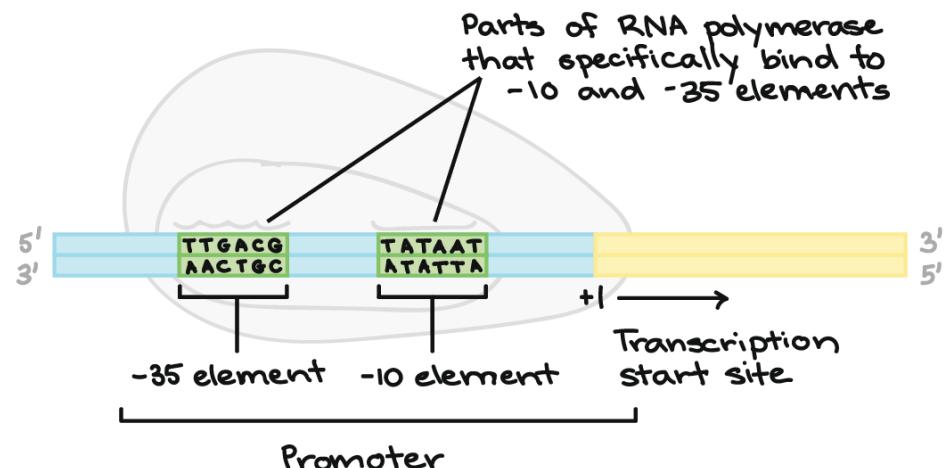
RNA polymerase

holoenzyme then searches along the DNA until it finds a **promoter**.

- The promoter contains two regions, a **-35 and a -10 element**.

The promoter is a region which is AT rich. This is the region where DNA unwinds.

- **RNA polymerase** therefore has helicase activity.
- DNA unwinds at the **-10 element**.



Eukaryotic Transcription Initiation

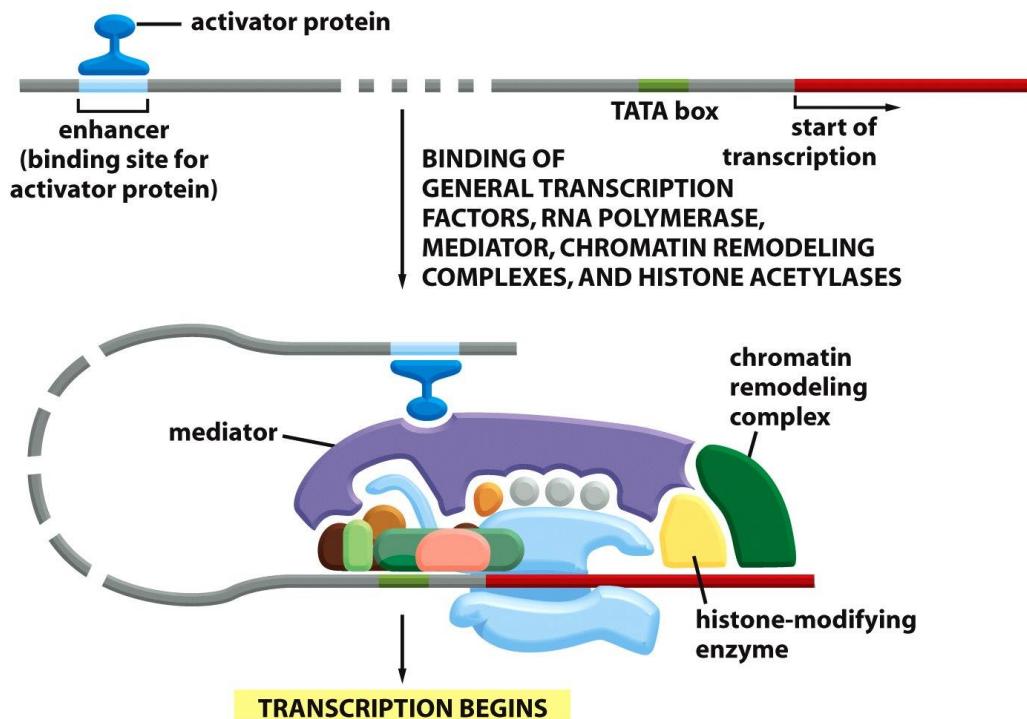


Figure 6-19 Molecular Biology of the Cell 5/e (© Garland Science 2008)

General transcription factors bind to proximal promoter sequences and provide basal transcription.

Activator proteins bind to distal enhancer sequences. Activators exert influence over the transcriptional machinery through mediators. This enhances transcription.

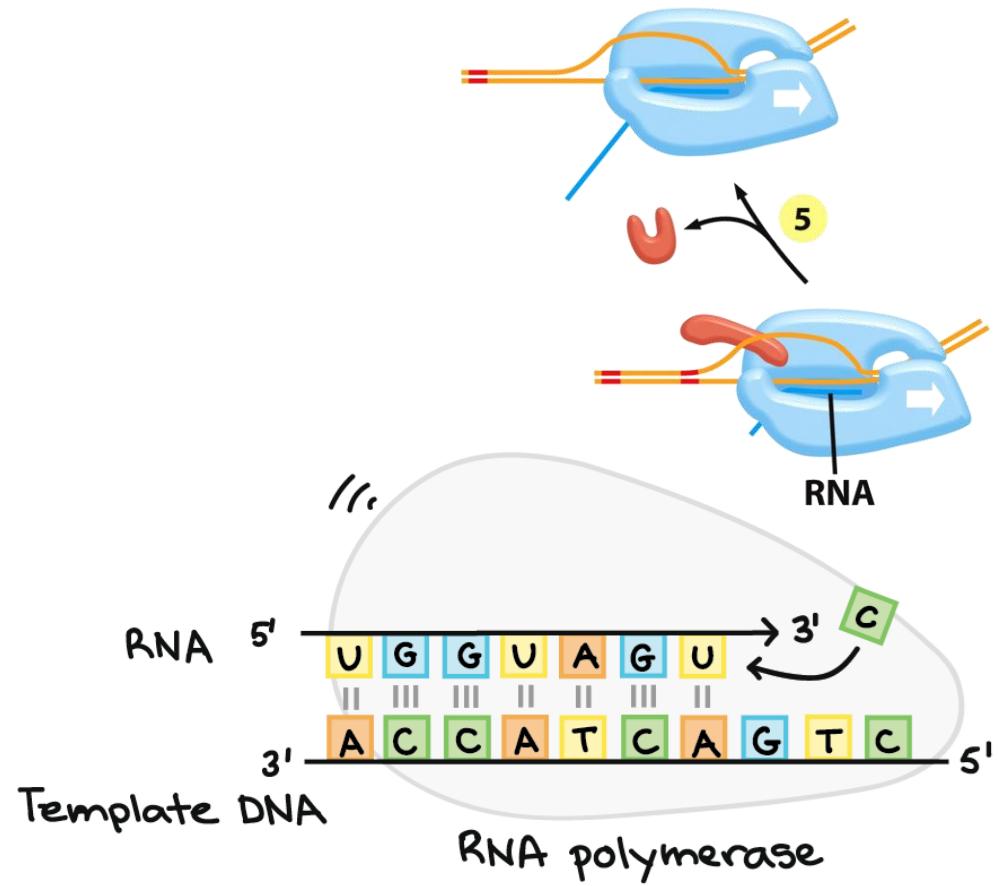
Prokaryotic Transcription Elongation

Elongation is highly processive and is efficient.

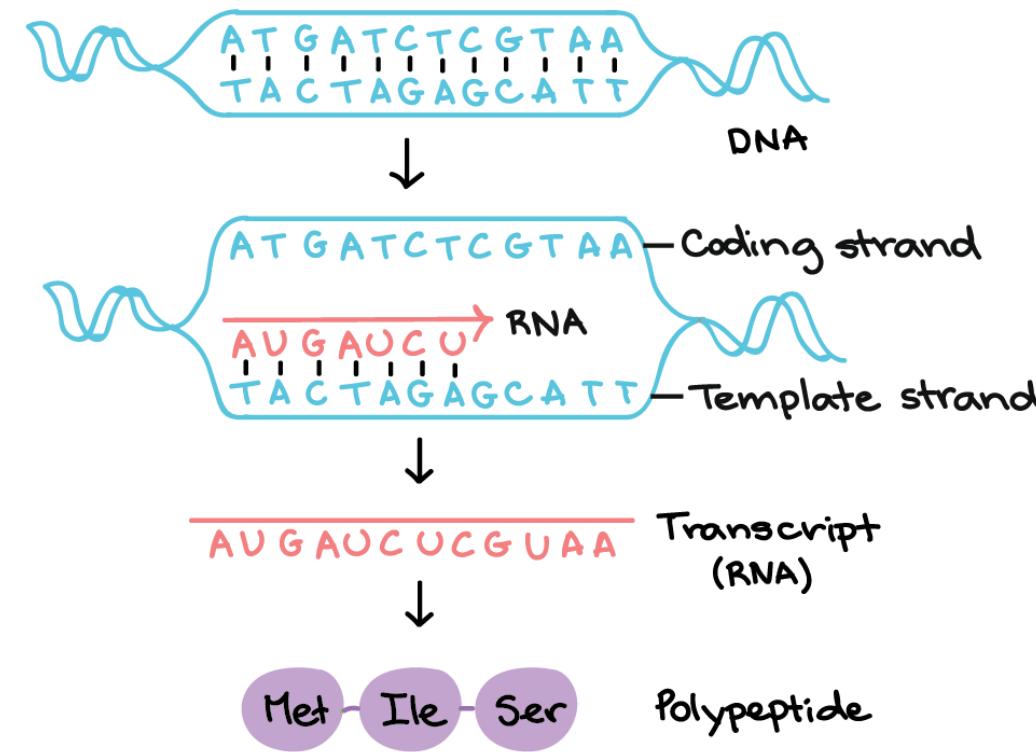
It is important to take note the **RNA polymerase**, like DNA polymerase, **adds at the 3' end**.

- Unlike DNA polymerase, RNA polymerases can make a strand *de novo*.

The DNA **reforms to a double-helix immediately** after RNA polymerase passes through.



Prokaryotic Transcription Elongation



RNA polymerase makes an **exact* copy** of the **coding strand** called the **RNA transcript**.

To do so it uses the information from the **template stand**.

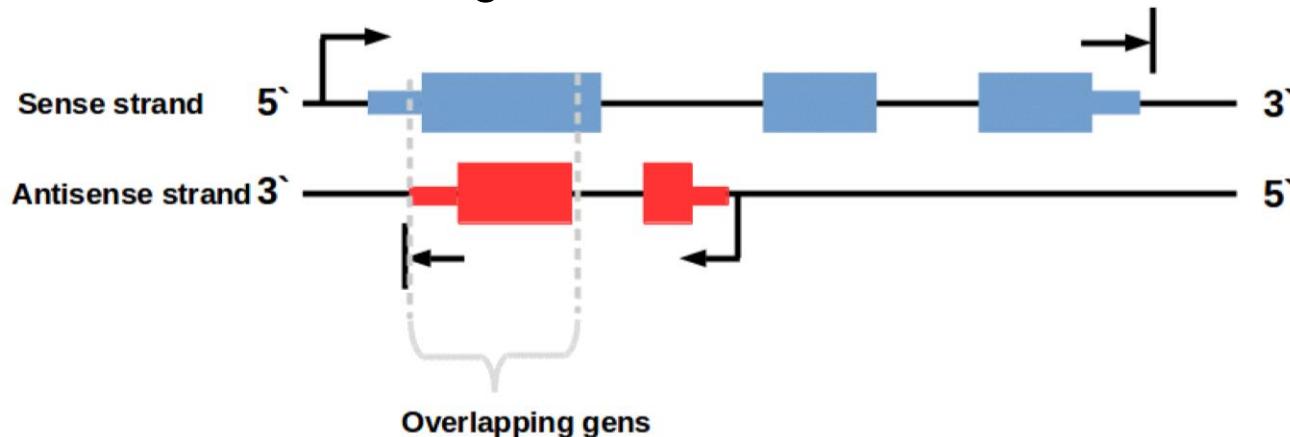
The coding strand is **read from the 5' to the 3'**. Therefore, RNA polymerase **moves 3'-5'** with respect the to the template strand.

Prokaryotic Transcription Elongation

Information in **genes** are read from **5'-3'**, much like how we write and read from left to right.

Genes can be found in either strand of DNA, therefore the **definitions for coding and template strand depend on the location/orientation of the gene**.

Another name for the coding strand is the **sense strand**. Another name

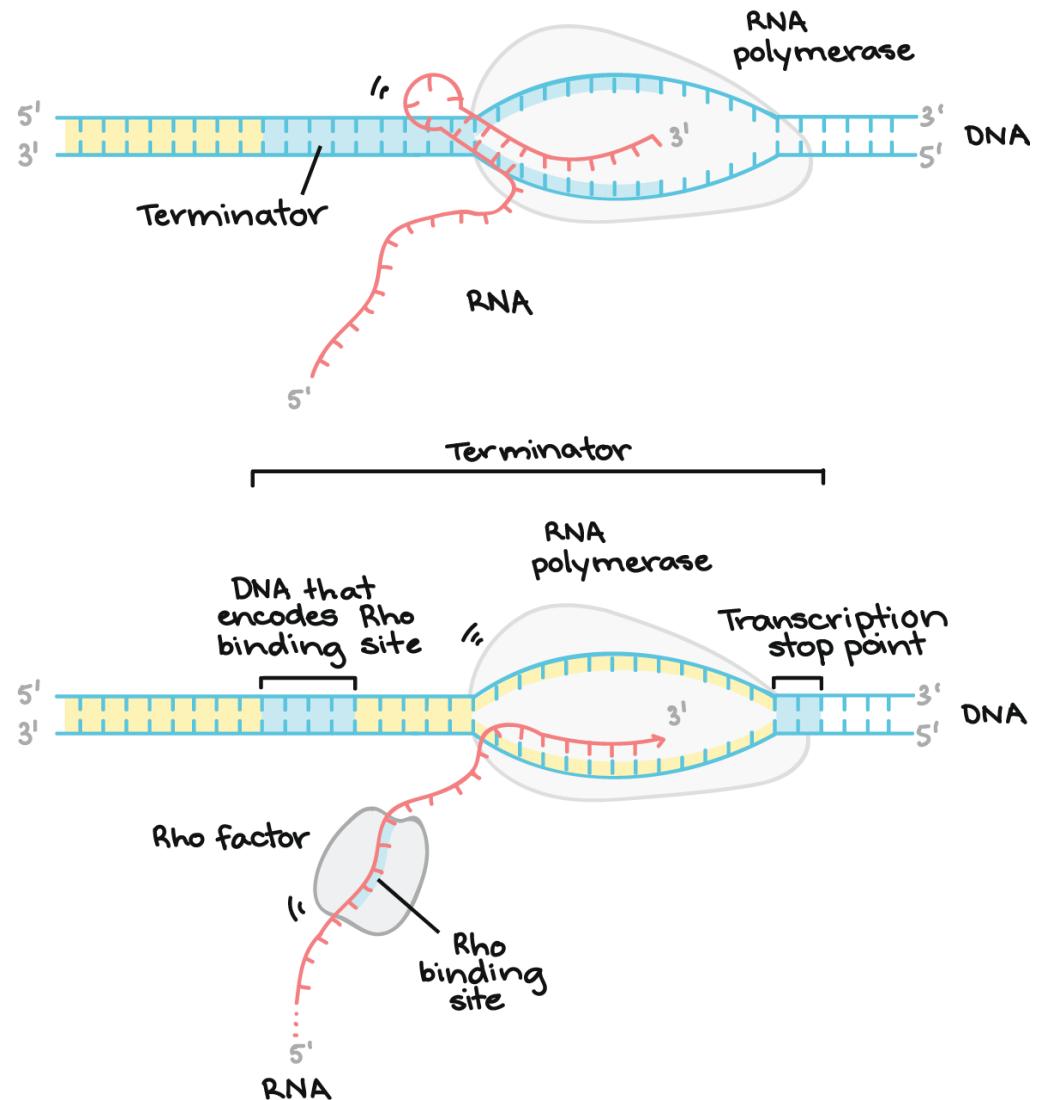


Prokaryotic Transcription Termination

Termination signals are encoded in the DNA (within the gene itself).

Two types:

1. May contain **structural information** that causes RNA to fold and **pull itself** from the RNA polymerase (usually a **hairpin structure**).
2. May contain a **sequence which is recognized** by a termination protein called the **Rho factor**.



Prokaryotic vs Eukaryotic Transcription

Prokaryotic

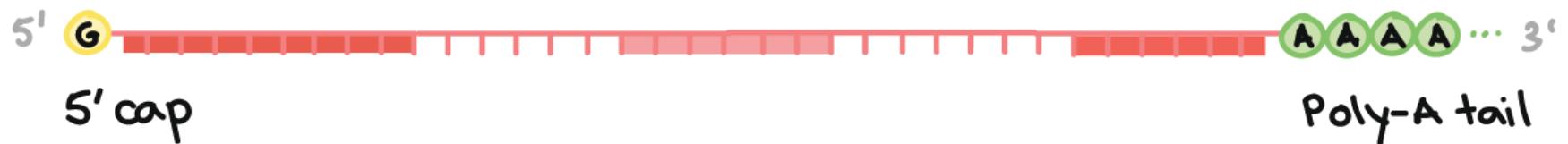
- One RNA polymerase
- Only one additional protein required for transcription. (σ -factor).
- Polycistronic – **one mRNA** transcript can contain **many genes**.
- mRNA is translated as is.

Eukaryotic

- Three RNA polymerases (Pol II)
- Many transcription factors required (the general transcription factors).
- Monocistronic – **one mRNA** only contains **one gene**.
- mRNA is processed prior to translation.

Eukaryotic mRNA Processing

1. **5'-capping** – protects the pre-mRNA transcript from degradation from the 5' end.
2. **3'-polyadenylation** – protects the 3' end from degradation.
3. **Splicing** – removes intervening sequences.

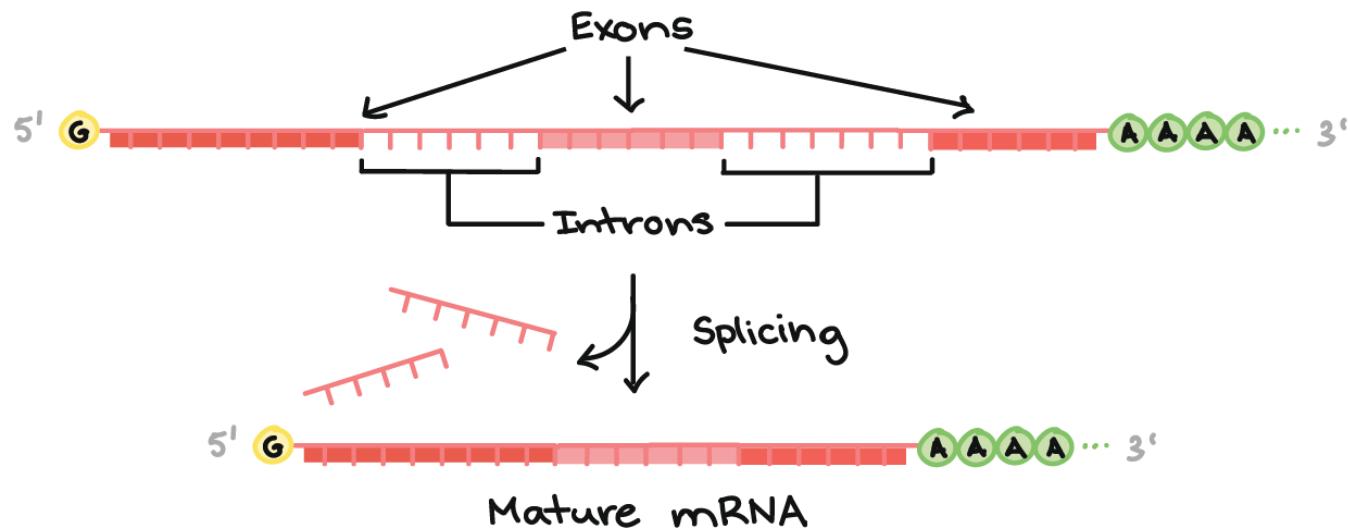


Eukaryotic mRNA Processing

3. Splicing – removes intervening sequences.

Eukaryotic genes are not straightforward. They contain sequences which are **not translated** into protein called **introns**.

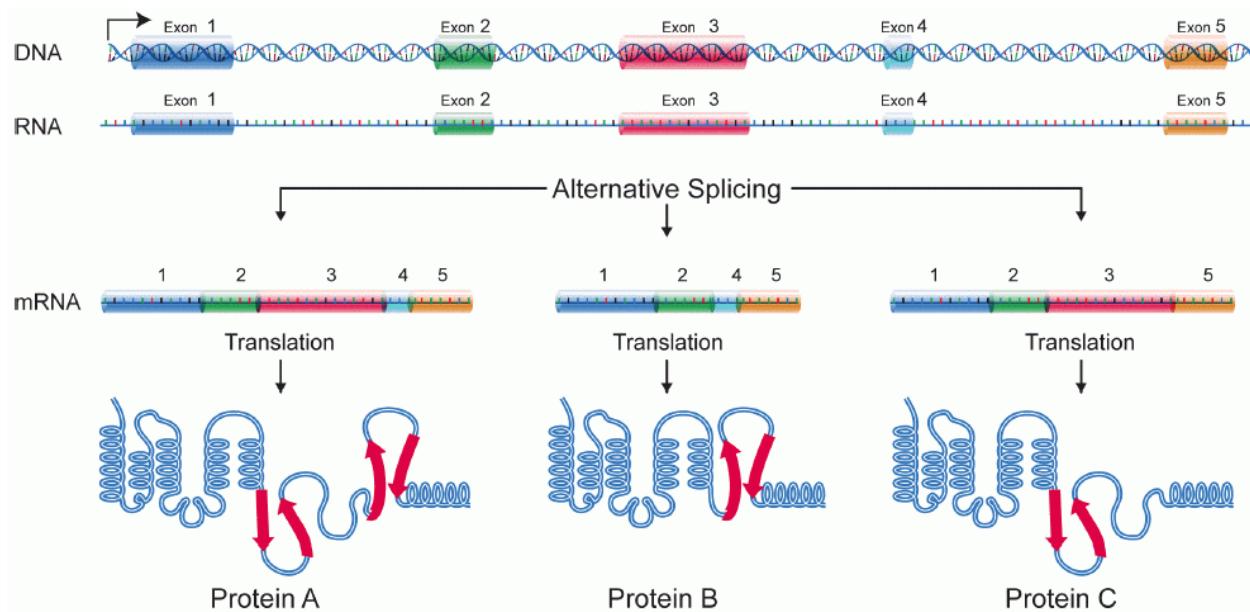
In **splicing**, these introns are removed, joining the coding strands, called **exons**.



Eukaryotic mRNA Processing

3. Splicing – removes intervening sequences.

A single eukaryotic gene can make several isoforms of a protein through the process of alternative splicing.



Eukaryotic mRNA Processing

3. Splicing – removes intervening sequences.

A single eukaryotic gene can make several isoforms of protein through the process of alternative splicing.

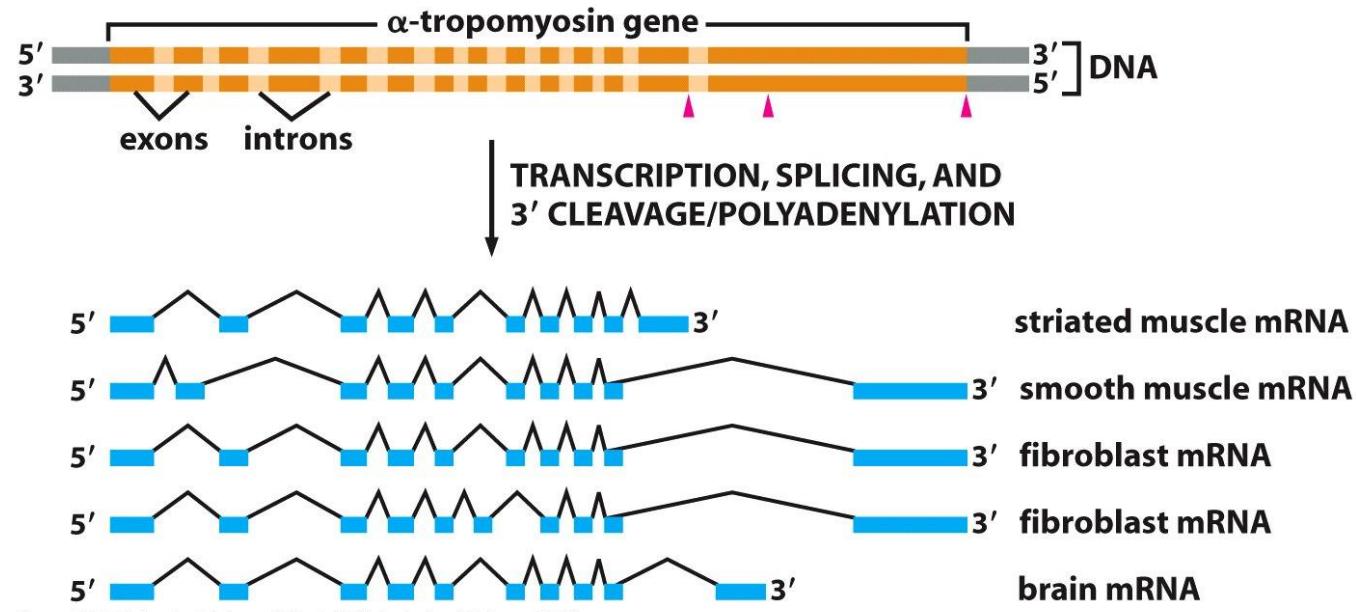
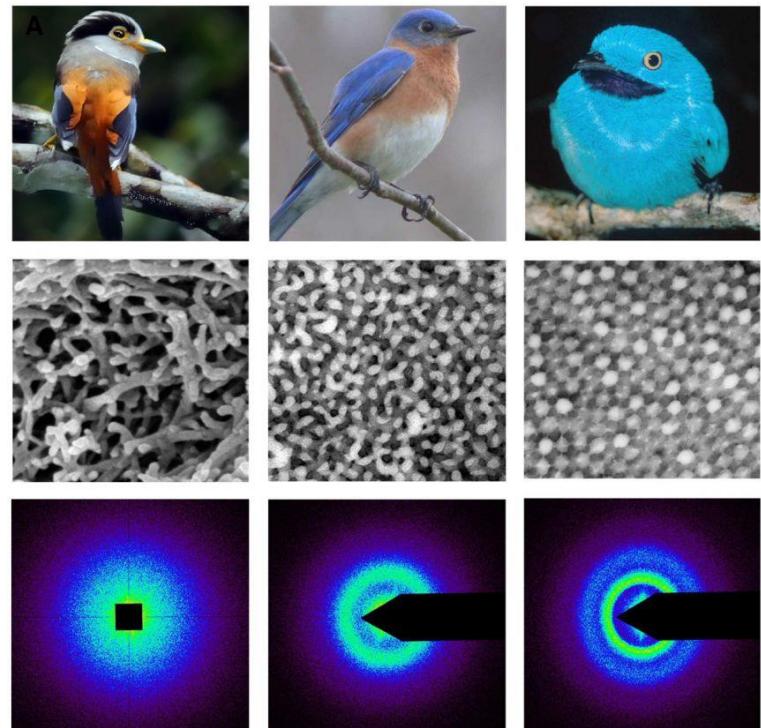


Figure 6-27 Molecular Biology of the Cell 5/e (© Garland Science 2008)

Proteins

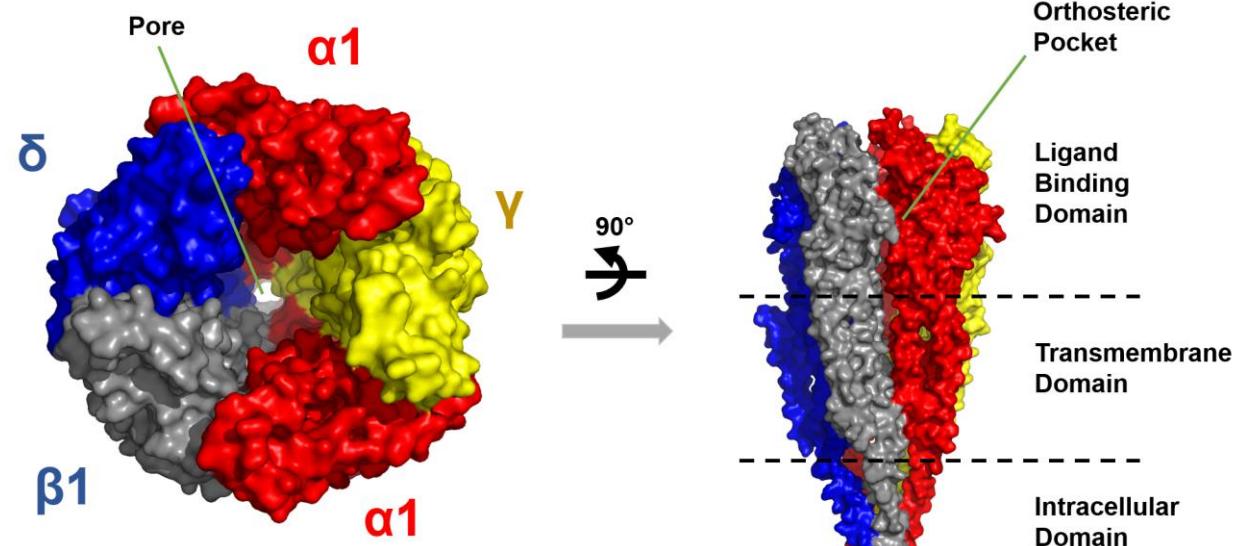
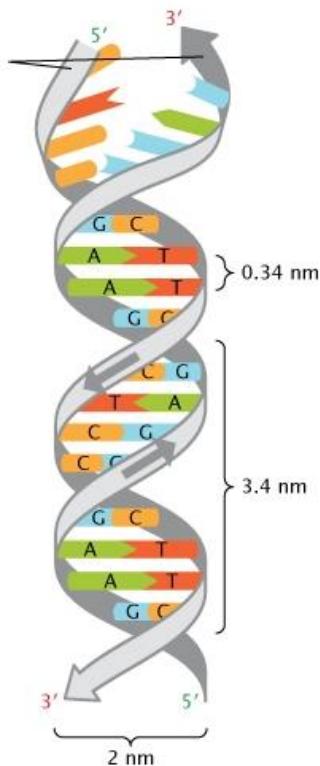
Biological Structure

One of the key ideas in biology is **structure determines function**.

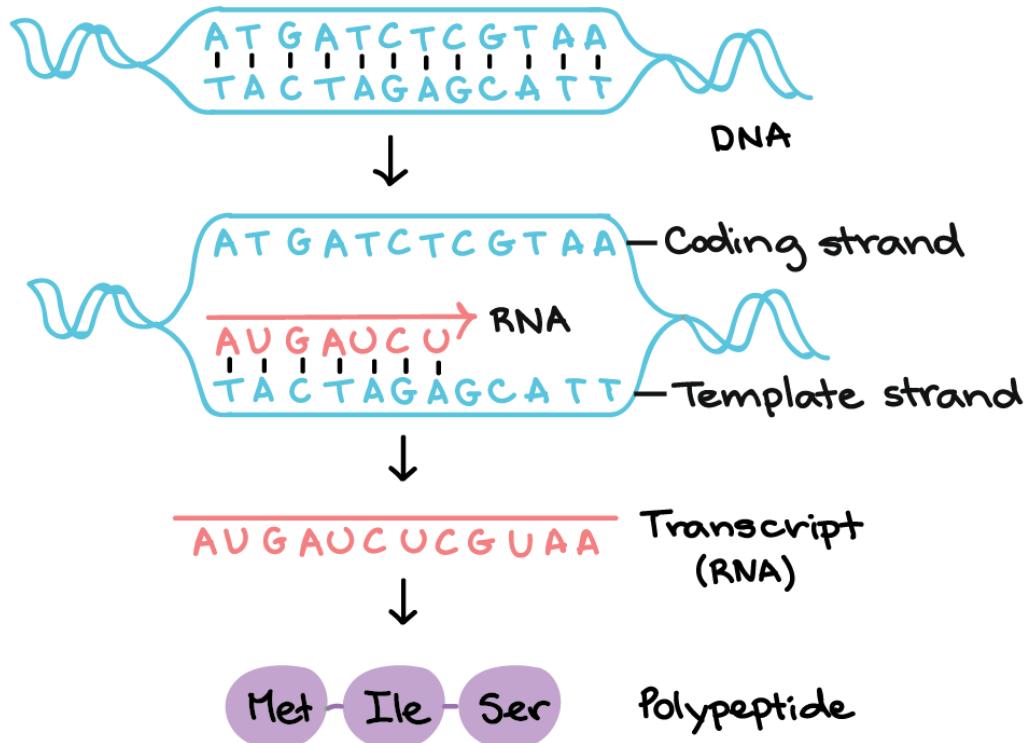


Protein Structure

One of the key ideas in biology is **structure determines function**.



Protein Structure



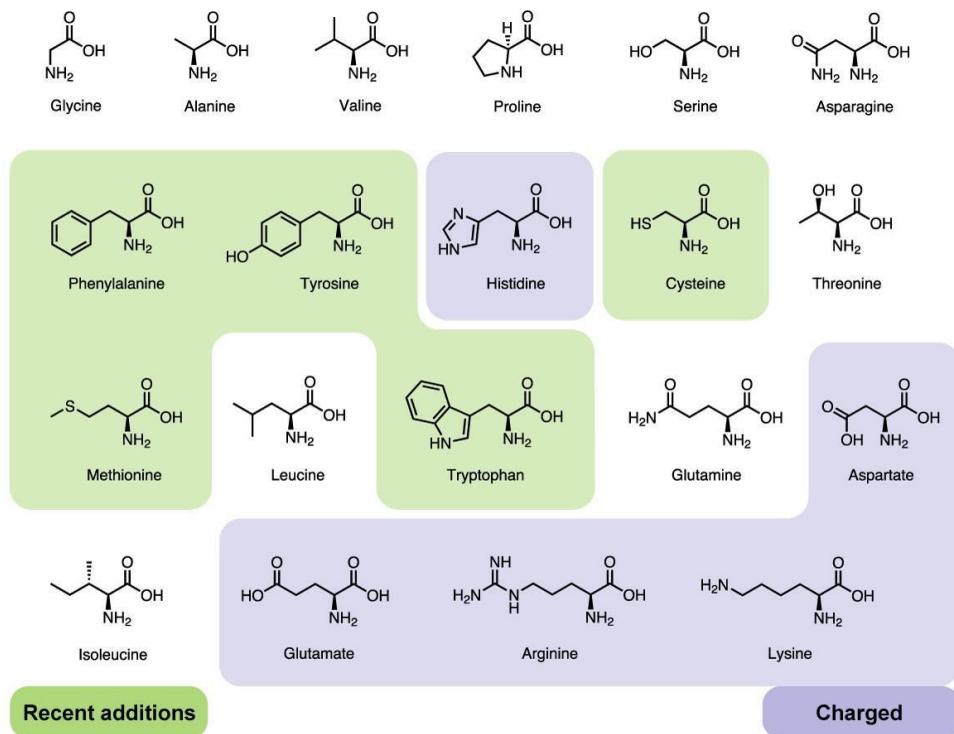
One of the key ideas in biology is **structure determines function**.

Genetic information from DNA that is transcribed into RNA is then **translated into protein**.

The genetic information contains instructions on how to arrange **amino acids** in proteins.

The **sequence** of amino acids dictate the **structure** of the protein.

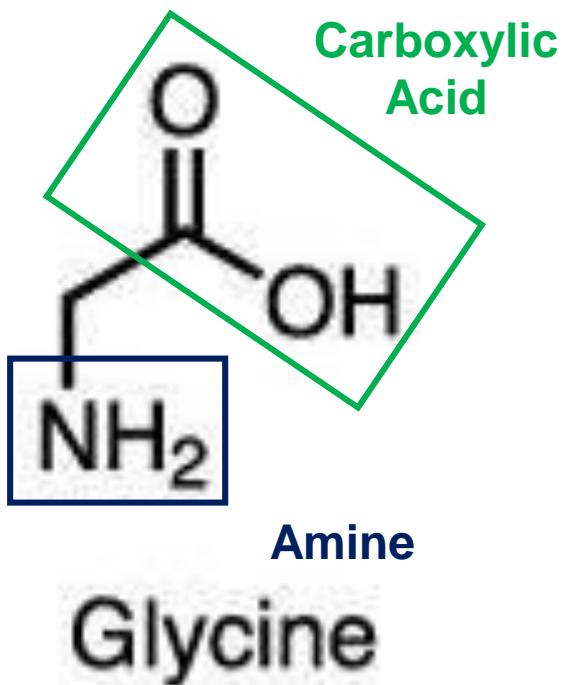
Protein Structure



The **amino acid** is the basic repeating subunit of a protein (**the monomer**). There are **20 basic** amino acids.

Each amino acid shares the **same backbone** but have **varying side chains**. The side chains have **different chemical properties**, which make them act differently from one another.

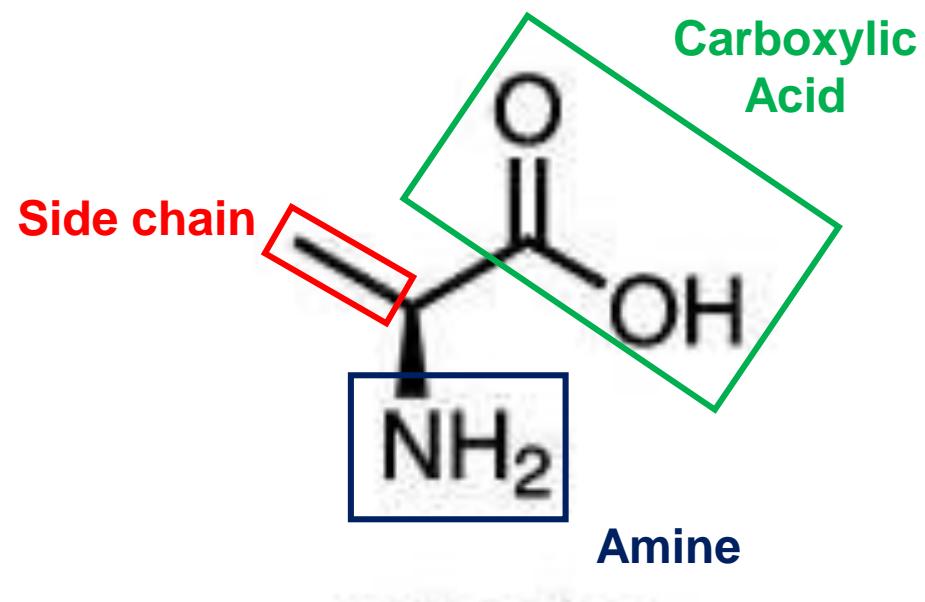
Protein Structure



An amino acid composed of an **amine group**, a **carboxylic acid**, and a **varying side chain**.

The side chains can be grouped into five types: **acidic**, **basic**, **polar** and **hydrophobic**.

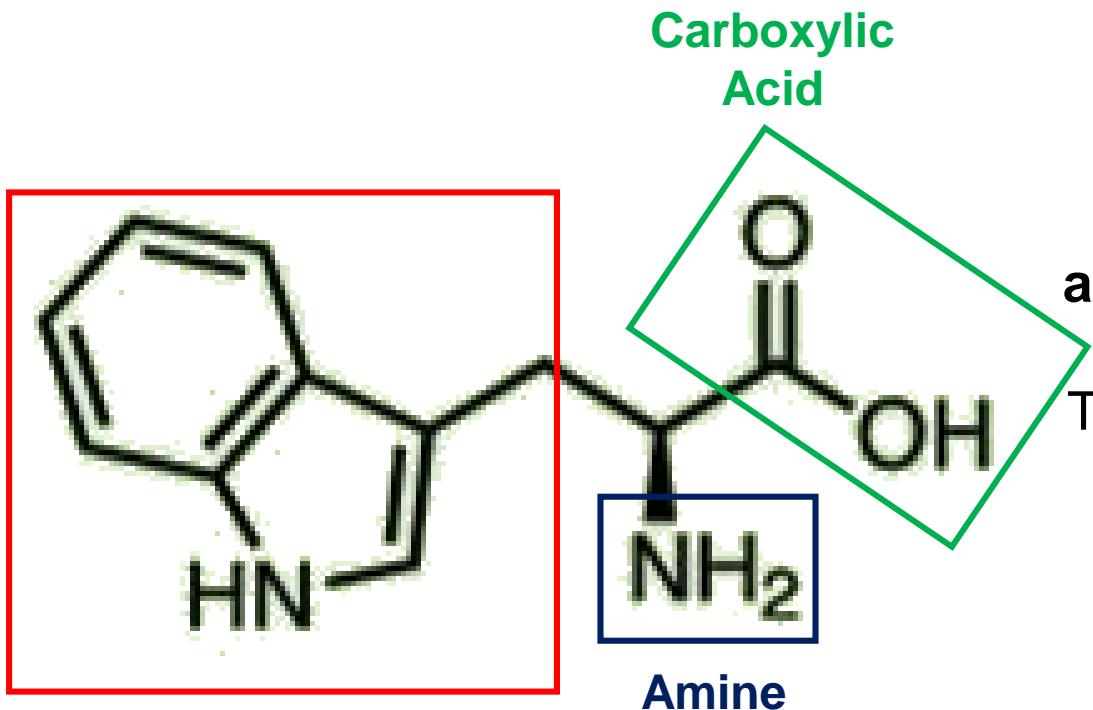
Protein Structure



An amino acid composed of an **amine group**, a **carboxylic acid**, and a **varying side chain**.

The side chains can be grouped into five types: **acidic**, **basic**, **polar** and **hydrophobic**.

Protein Structure



Side chain

Tryptophan

An amino acid composed of an **amine group**, a **carboxylic acid**, and a **varying side chain**.

The side chains can be grouped into five types: **acidic**, **basic**, **polar** and **hydrophobic**.

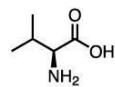
Amino Acid Groups



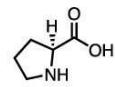
Glycine



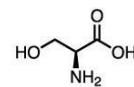
Alanine



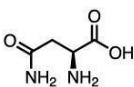
Valine



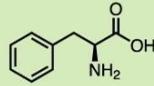
Proline



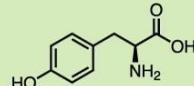
Serine



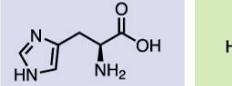
Asparagine



Phenylalanine



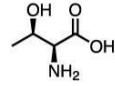
Tyrosine



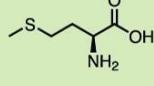
Histidine



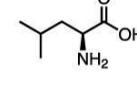
Cysteine



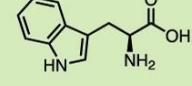
Threonine



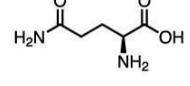
Methionine



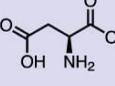
Leucine



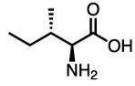
Tryptophan



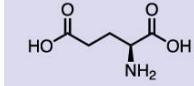
Glutamine



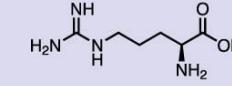
Aspartate



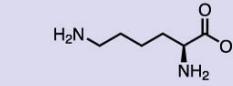
Isoleucine



Glutamate



Arginine



Lysine

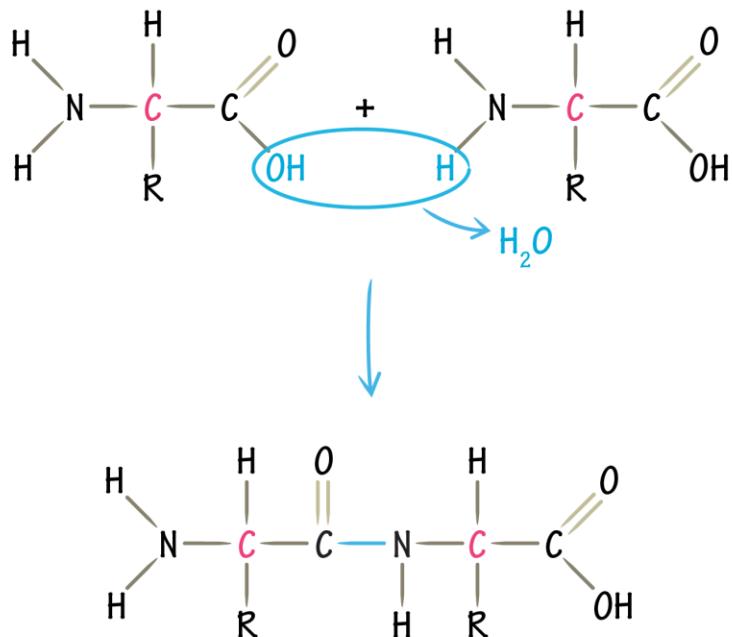
Recent additions

Charged

- Acidic
- Basic
- Polar
- Hydrophobic

Protein Structure

Peptide Bond Formation



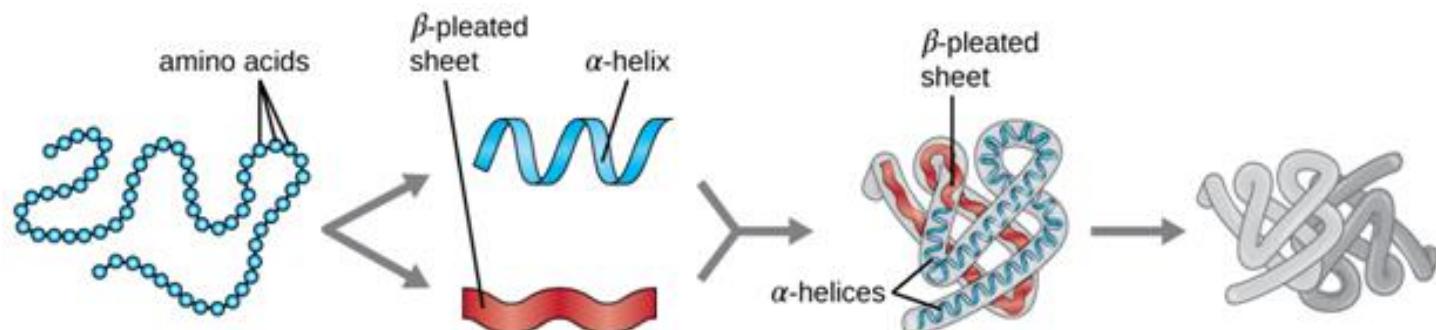
Amino acids are connected to one another through a **peptide bond**. The peptide bond connects the **carboxylic acid** of the previous amino acid to the **amine** of the next.

Like DNA and RNA, information in protein is **directional**. By convention, we read the information from the **N-terminal (amine)** to the **C-terminal (carboxylic acid)**.

Protein Structure

The sequence of amino acids dictate how a protein folds into itself. This why the **amino acid sequence is called the primary structure.**

There are other levels of protein structure. **Secondary structure** describes the local structure. **Tertiary structure** describes the shape of the protein molecule. **Quaternary structure** describes how proteins interact with one another.



Primary Protein Structure
Sequence of a chain of amino acids

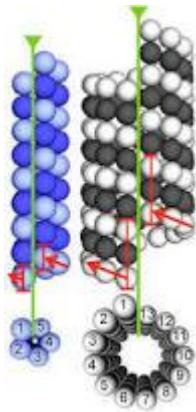
Secondary Protein Structure
Local folding of the polypeptide chain into helices or sheets

Tertiary Protein Structure
three-dimensional folding pattern of a protein due to side chain interactions

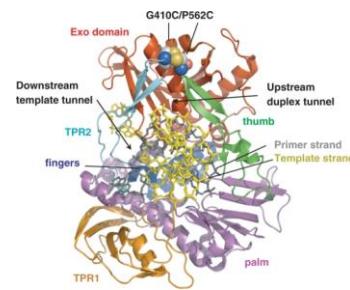
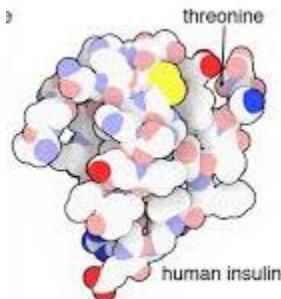
Quaternary Protein Structure
protein consisting of more than one amino acid chain

Protein Function

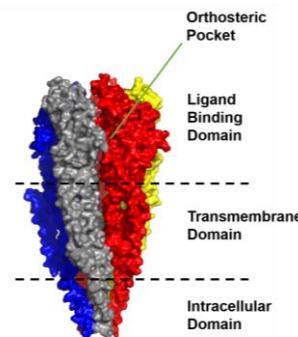
Structural integrity
tubulin



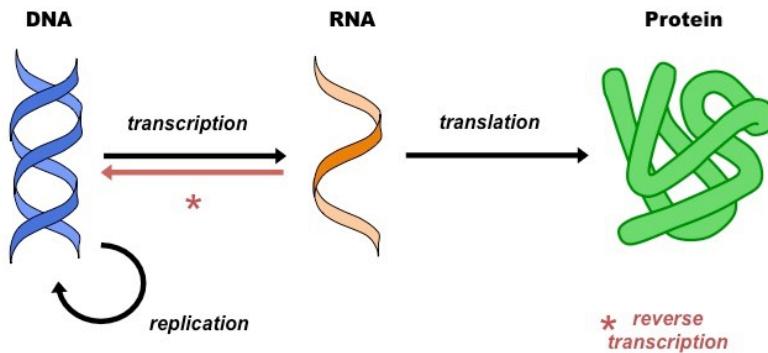
Relay signals
insulin



Catalyze chemical reactions
DNA polymerase (**enzymes**)



Regulate homeostasis
ion channels



Protein Translation

Execution of genetic information.

The Genetic Code

Math Problem:

How do four (4) nucleotides code for twenty (20) amino acids?

By forming words (codons)!

One (1) nucleotide:
4 combinations

Two (2) nucleotides:
 $4 \times 4 = 16$ combinations

Three (3) nucleotides:
 $4 \times 4 \times 4 = 64$ combinations

The Genetic Code

Nucleotides are read in **groups of three called codons**. Each codon specifies a specific signal (amino acid or stop).

Properties of the genetic code:

1. Occurs in triplets
2. Unambiguous
3. Non-overlapping
4. Commaless
5. Directional
6. Degenerate
7. Universal
8. Start and stop signals.

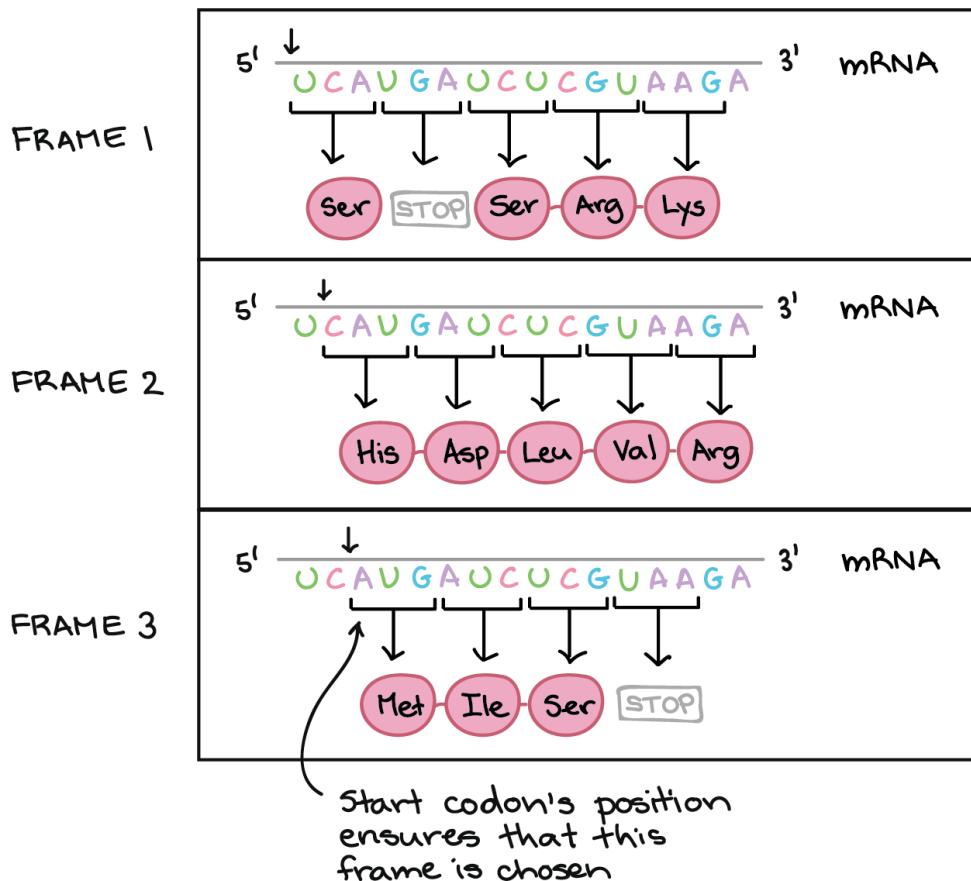
		Second letter					
		U	C	A	G		
		UUU UUC UUA UUG } Phe	UCU UCC UCA UCG } Ser	UAU UAC UAA UAG } Tyr Stop	UGU UGC UGA UGG } Cys Stop Trp	Third letter	
First letter	c	CUU CUC CUA CUG } Leu	CCU CCC CCA CCG } Pro	CAU CAC CAA CAG } His Gln	CGU CGC CGA CGG } Arg	U C A G	
	a	AUU AUC AUA AUG } Ile Met	ACU ACC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

Reading Frames

A consequence of the triplet nature of the codon and the non-overlapping nature of the genetic code, transcripts have **reading frames**.

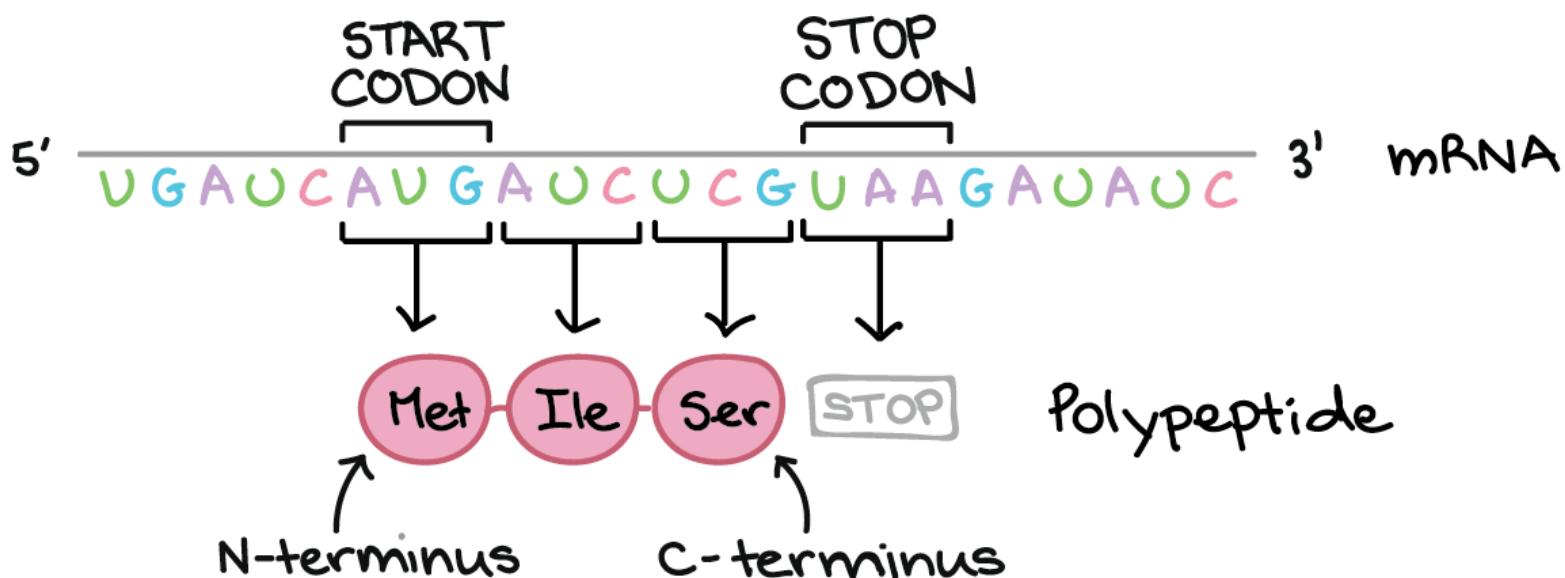
Reading frames **dictate how the information is read**. This depends on the **start position of translation**.

There are always three possible reading frames: +1, +2 and +3.

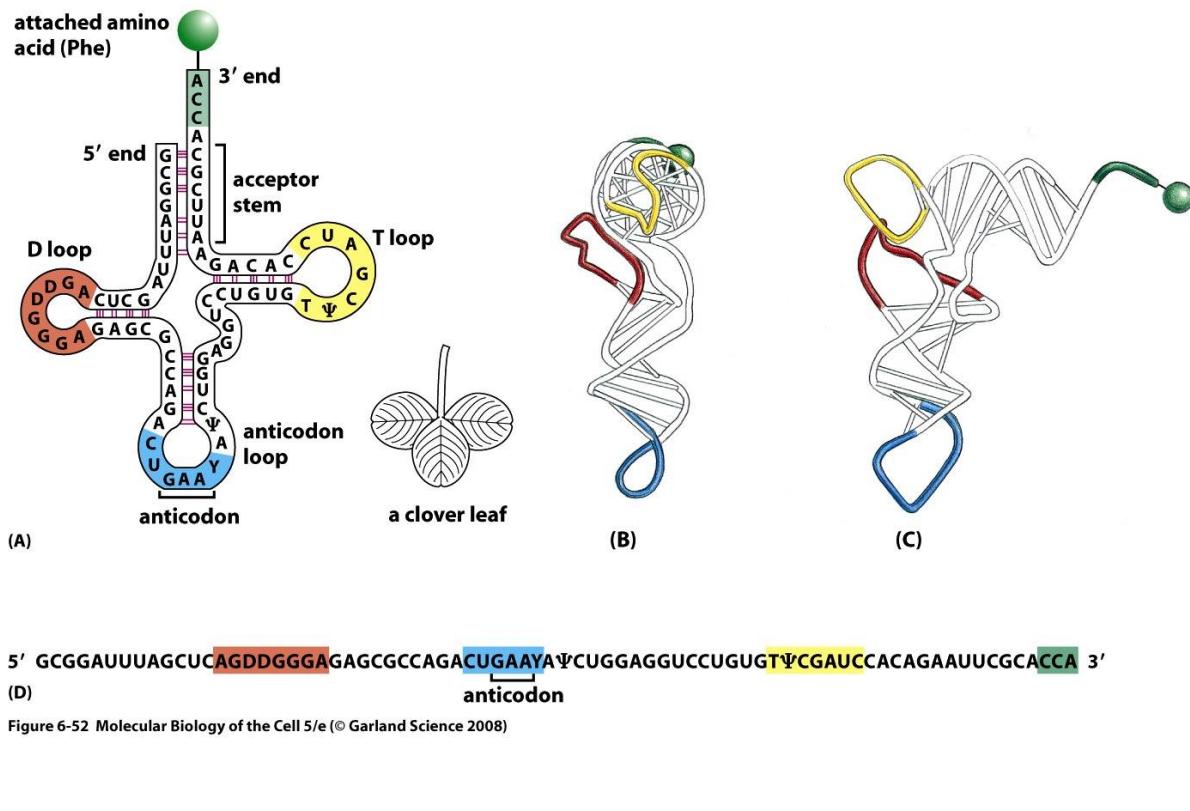


The Genetic Code

mRNA is translated from **5'** to **3'** in triplets called codons.
Translation starts from the **start codon** and ends when a **stop codon** is found.



transfer RNAs



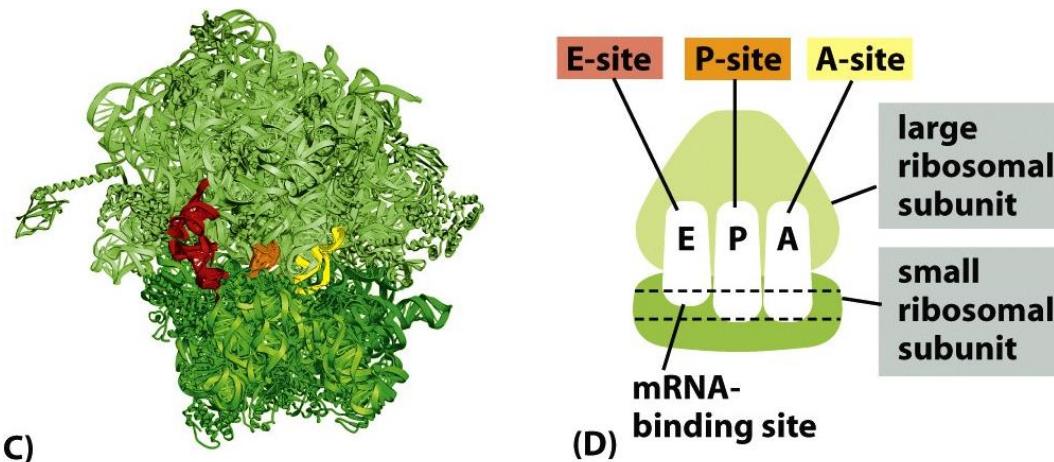
Codons are decoded by **transfer RNAs (tRNA)**. tRNAs carry sequences complementary to codons, called **anticodons**.

tRNAs correspond to a specific **amino acid**. Once connected to their respective amino acids, they are called **aminoacyl-tRNA**.

Ribosomes and ribosomal RNA

Ribosomes are the **sites of protein translation**. They are made up of a **complex of proteins and rRNA**. Two subunits, the large and small. The mRNA is sandwiched between these two subunits.

Three important regions for binding of tRNA: **Exit**, **Peptidyl-tRNA** and **Aminoacyl-tRNA**



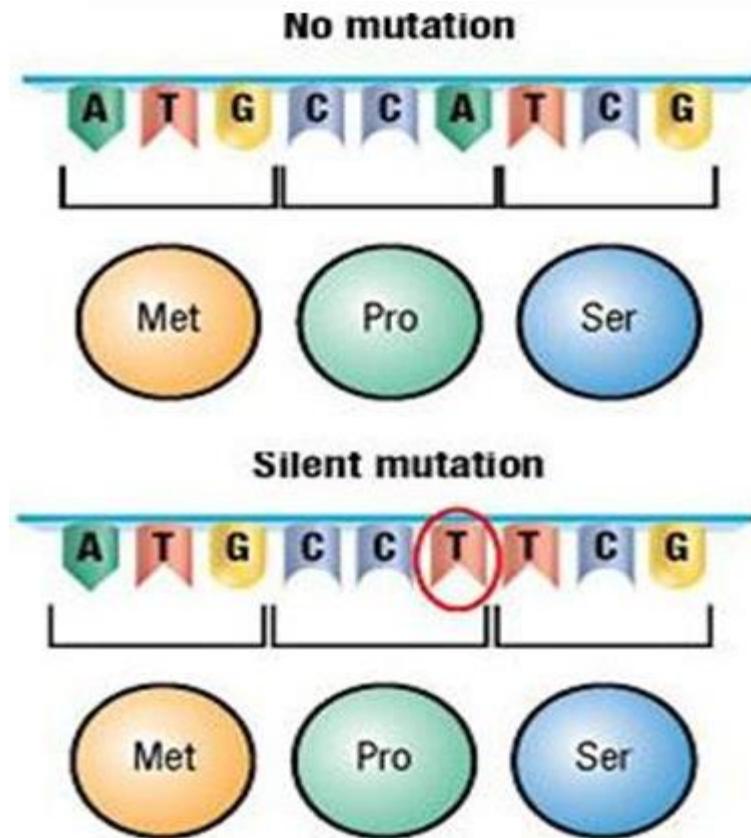
Mutations

Mutations: Silent Mutations

Due to the degeneracy of the genetic code, **single base mutations in the second or third base pairs sometimes end up coding for the same amino acid.**

These are called **silent mutations**, as there is a change in the genetic information, but no change in the protein sequence.

This is the most benign type of mutation.

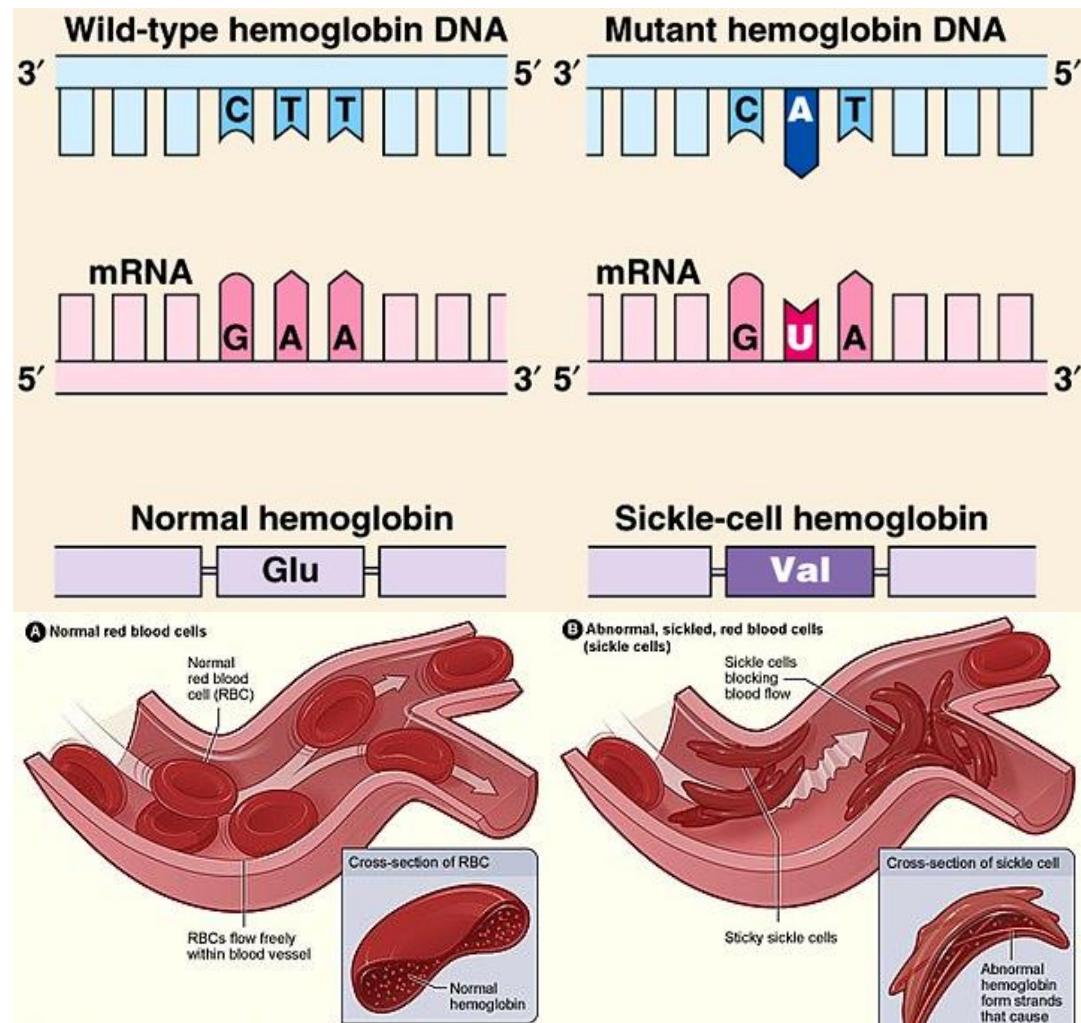


Mutations: Missense Mutations

Sometimes, a single base change mutation results in a change of amino acid during translation.

The consequences of such mutations may vary depending on the circumstances.

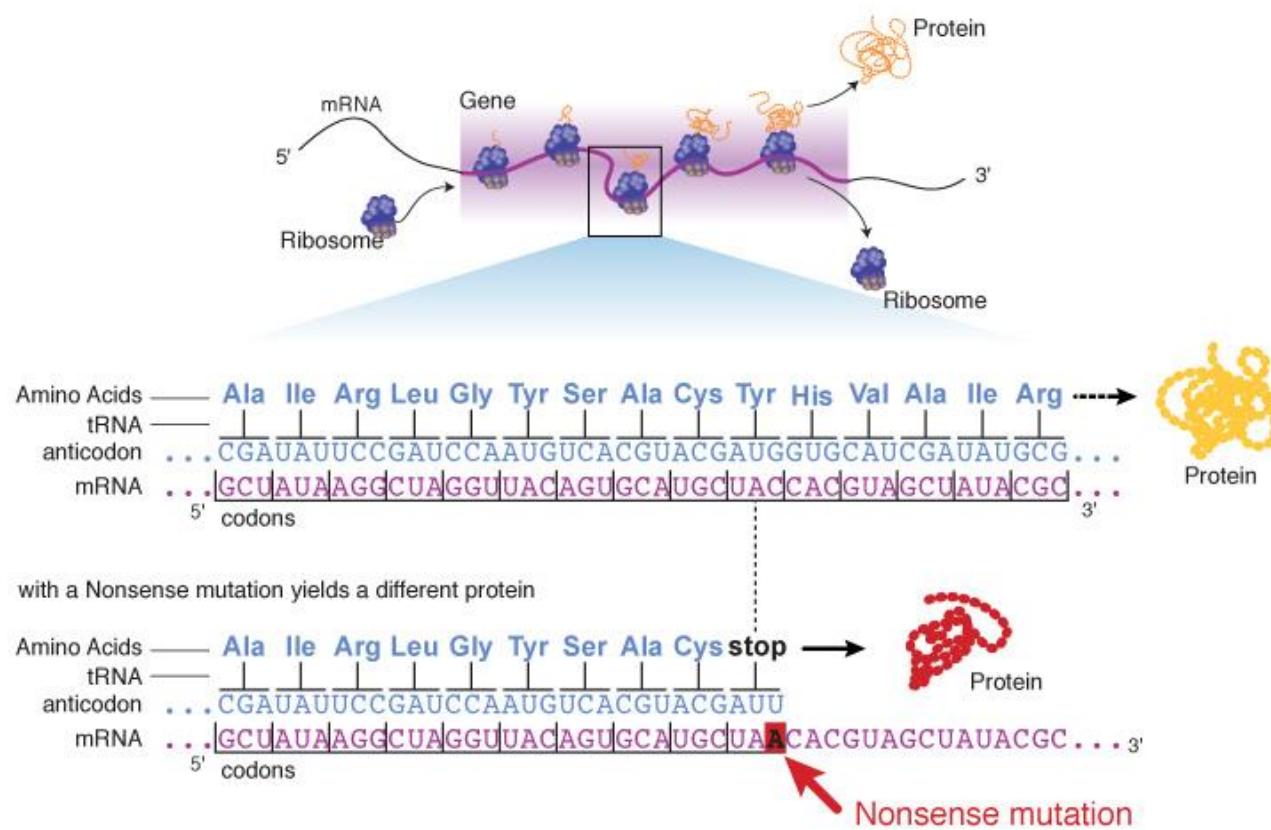
Amino acid changes of the same group may have less consequences than a group change.



Mutations: Nonsense Mutations

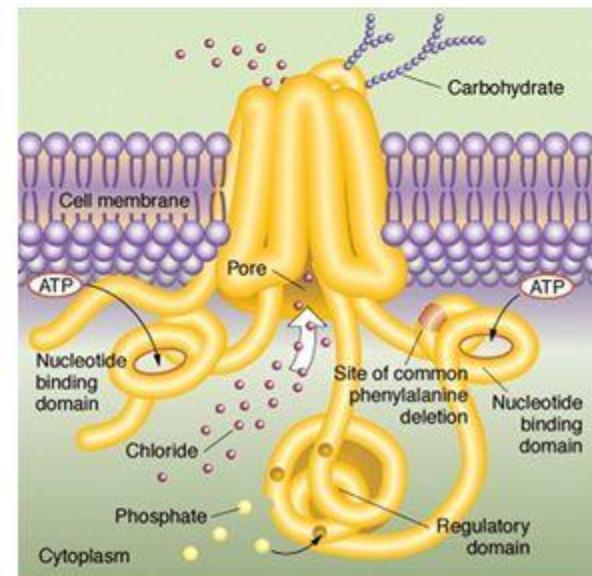
Sometimes, a single base change mutation **results in a premature stop codon** during translation. This is called a nonsense mutation.

As a result, the rest of the mRNA is not translated when it should be. The resulting protein is truncated.



An example of a Nonsense mutation: Cystic fibrosis.

- A huge gene encodes a protein of 1480 amino acids called the **cystic fibrosis transmembrane conductance regulator (CFTR)**.
- The protein is responsible for transporting chloride ions out of cells.

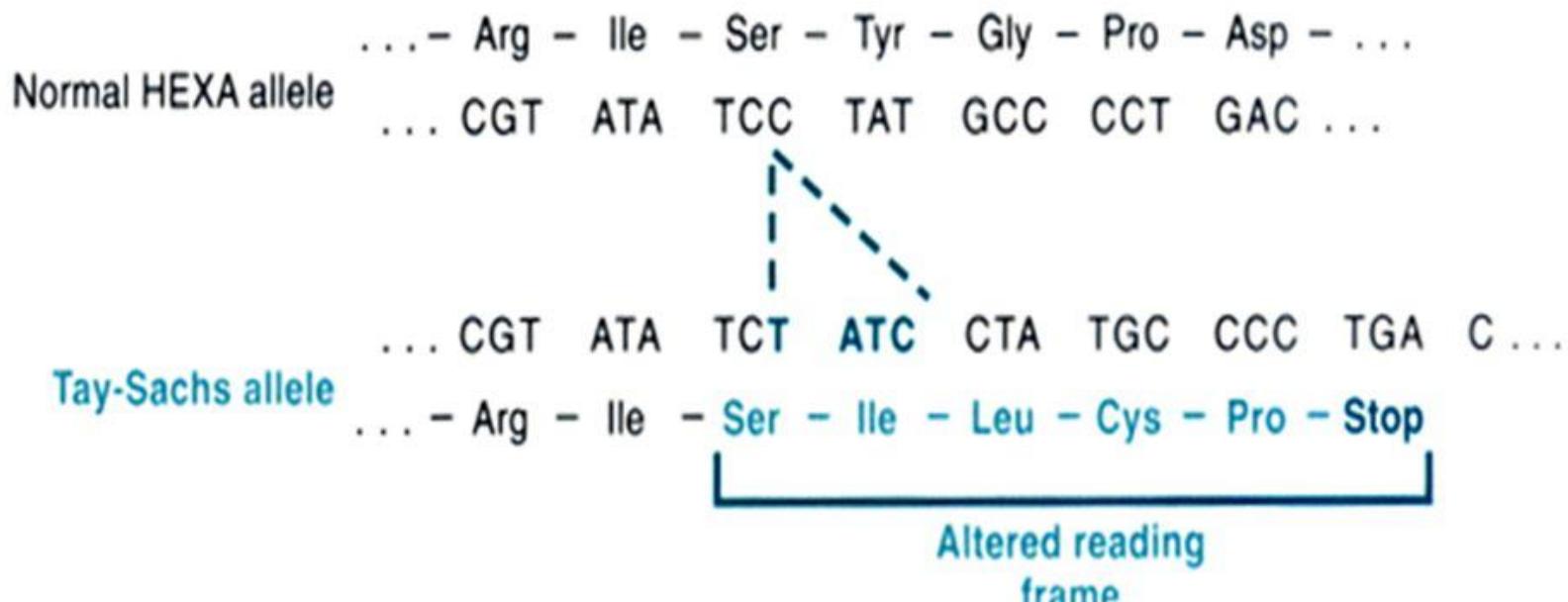


Mutations: Frameshifts

Sometimes, a mutation may involve **the addition or subtraction of bases**. If not added correctly, this results in a **frameshift**. A frameshift **totally changes the meaning of the genetic information** following the point of mutation.

Normal	
mRNA	AUG GGG GCC AAA AGU UAG UUUG ...
polypeptide	Met - Gly - Ala - Lys - Ser Stop
Insertion	
	+U ↓
mRNA	AUG GGC GCC AAA UAG UUAGUUUG ...
polypeptide	Met - Gly - Ala - Lys Stop
Deletion	
	-G ↓
mRNA	AUG GGC CCA AAA GUU AGU UUG
polypeptide	Met - Gly - Pro - Lys - Val - Ser - Leu
Random	

Tay Sachs Disease: Frameshift Mutation



Four-base insertion in the hexosaminidase A gene in Tay-Sachs disease, leading to a frameshift mutation

Even Silent Mutations have Consequences

MDR-1 is a human protein involved in the export of toxic substances from cells.

Silent mutation have been shown to change the folding kinetics of proteins, which consequently alters protein structure and function.

