Fundamentals of Molecular Biology

JONATHAN POHL, MLS (ASCP)^{CM} MB^{CM}

CLEVELAND CLINIC CENTER FOR PATHOLOGY EDUCATION

Disclaimer

This presentation was developed by Cleveland Clinic's Center for Pathology Education (CPE) for use in Cleveland Clinic's Molecular Biology Tech Categorical Exam Preparation Program (TCEPP) and Cleveland Clinic's School of Medical Laboratory Science.

This presentation is intended for educational purposes only.

Information in this presentation is not meant to substitute or replace the policies and standard operating procedures of Cleveland Clinic or RT-PLMI.

Images of and references to specific brands of instrumentation, consumables, reagents, or other purchasable items are used as examples and are not endorsements of those specific brands or items.

Objectives

- Describe the structure and function of nucleic acids (DNA, RNA)
- Categorize the central Dogma of molecular biology based on functionality
  - Replication
  - Transcription
  - Translation
- Describe the storage and replication of the human genome
- Describe genetic recombination in sexual reproduction
- Describe the storage and replication of bacterial and viral genomes
- Describe recombination in asexual reproduction

References and Additional Resources

- Buckingham, Lela. *Molecular Diagnostics: Fundamentals, Methods, and Clinical Applications.* 3rd ed., F.A. Davis, 2019.
  - Chapter 1: Nucleic Acids and Proteins
  - Chapter 2: Gene Expression and Epigenetics
  - Chapter 7: Chromosomal Structure and Chromosomal Mutations (pages 179-184)

Nucleic Acids

Nucleic acid: a macromolecule made of **nucleotides** bound together by the phosphate and hydroxyl groups on their sugars.

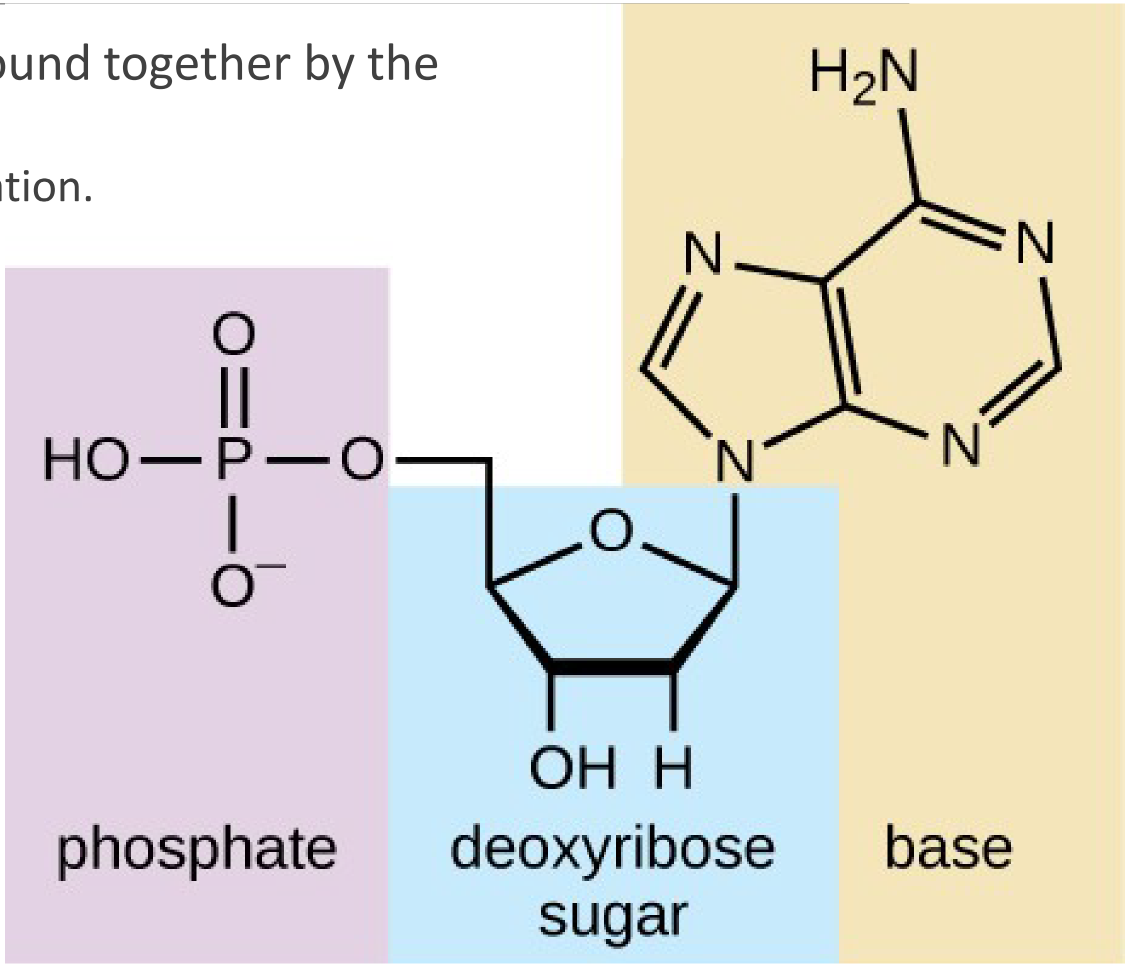
- Responsible for storage and expression of genetic information.

Types:

- Deoxyribonucleic acid (**DNA**)
- Ribonucleic acid (**RNA**)

Nucleotide components:

- **Nitrogenous base**
- **Pentose sugar**
- **Phosphate group**



Nitrogenous Bases

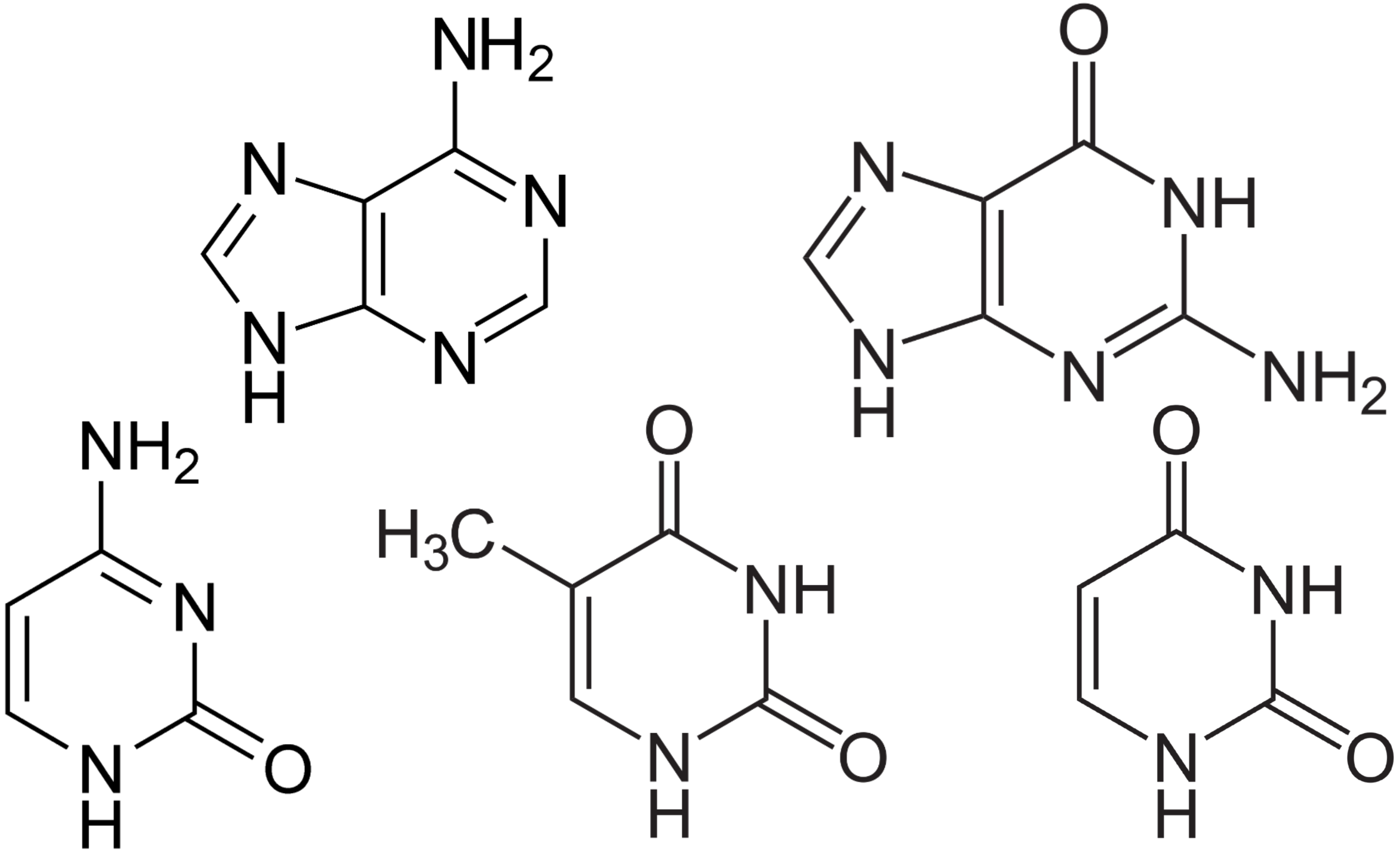
Adenine (A)

Guanine (G)

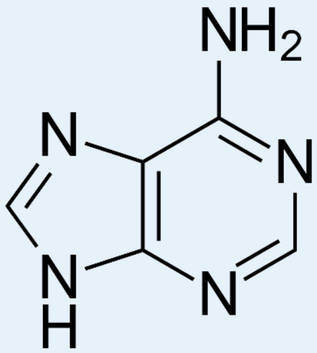
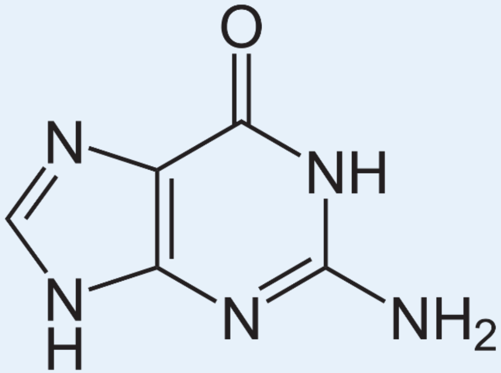
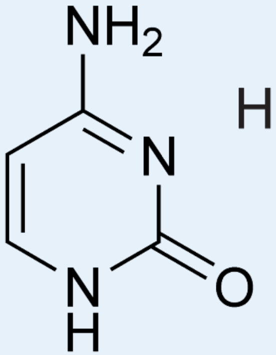
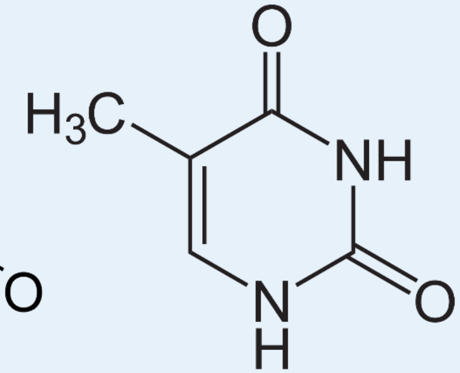
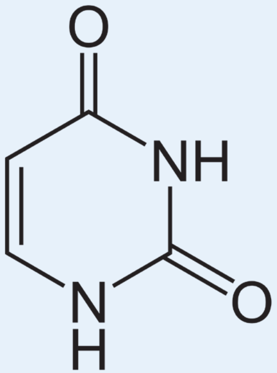
Cytosine (C)

Thymine (T)
- (DNA only)

Uracil (U)
- (RNA only)



Nitrogenous Bases (cont.)

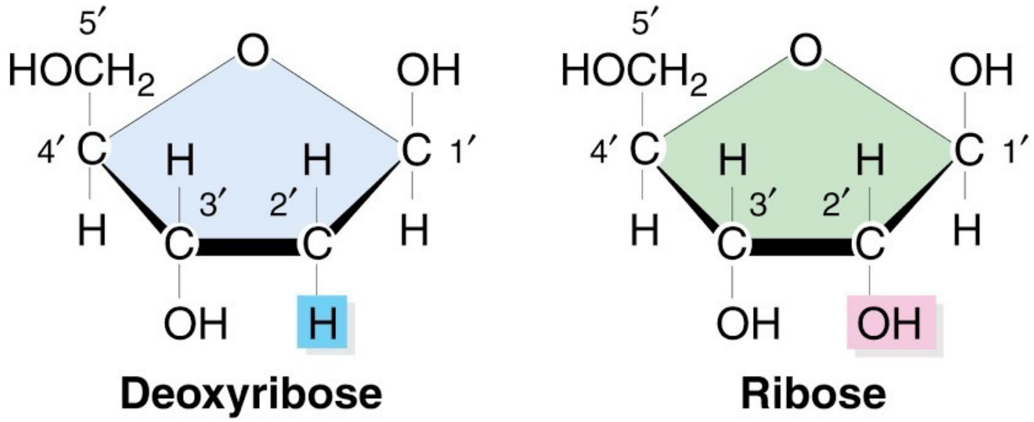
Purines		**Pyrimidines**		
Double-ring structure		Single-ring structure		
adenine	*guanine*	*cytosine*	*thymine*	*uracil*
				

Pentose Sugar

5-carbon sugar molecule

Functional group at 2' carbon differentiates sugars

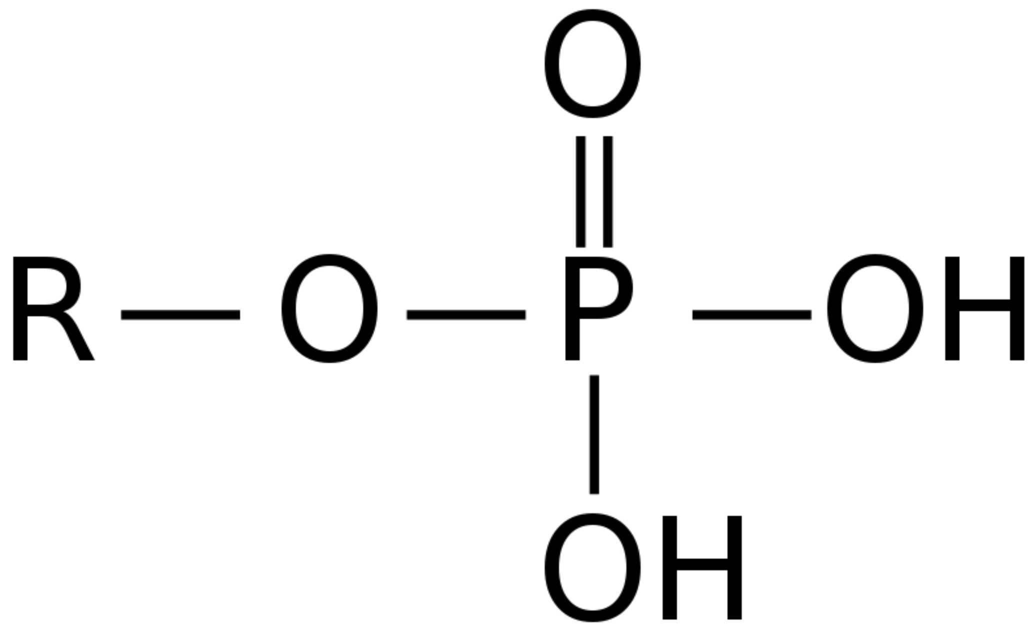
- **Ribose** = has a 2' hydroxyl group
  - Sugar found in RNA
- **Deoxyribose** = lacks a 2' hydroxyl group
  - Sugar found in DNA



Phosphate Group

Functional group characterized by a phosphorus atom bonded to four oxygen atoms

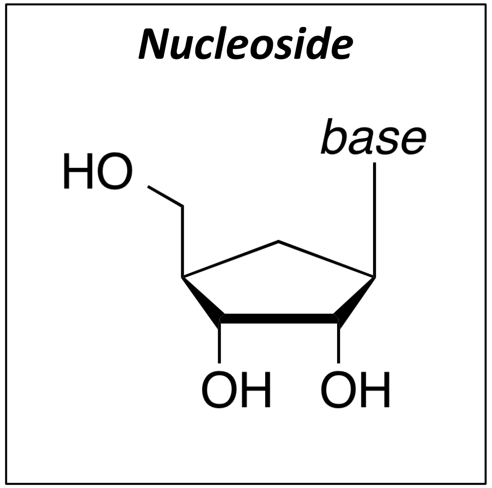
The presence/absence of a phosphate group differentiates nucleotides and nucleosides

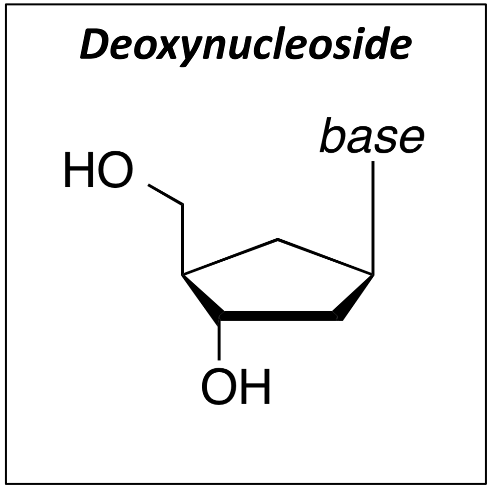


Nucleosides

Nucleoside

- an un-phosphorylated (deoxy)ribose sugar bound to a nitrogenous base
- Base is covalently linked to the 1’ carbon of the sugar



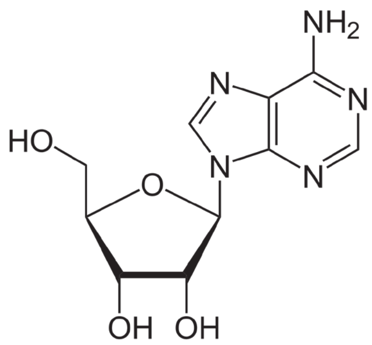


Naming

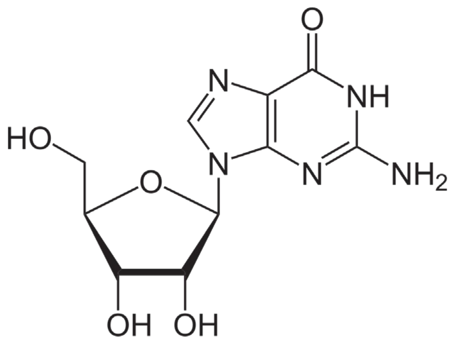
- Add the suffix ***-osine*** to the end of purines
  - adenosine
  - guanosine
- Add the suffix ***-idine*** to the end of pyrimidines
  - cytidine
  - thymidine
  - uridine
- Add the prefix ***deoxy-*** to nucleosides containing deoxyribose sugar

Nucleosides (cont.)

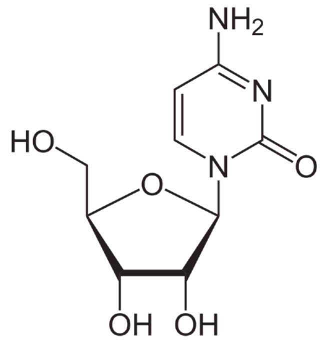
adenosine



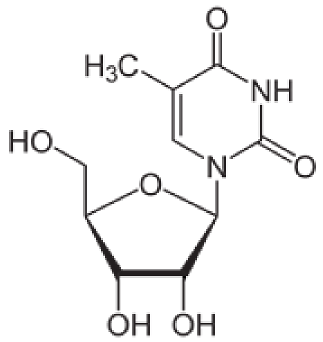
guanosine



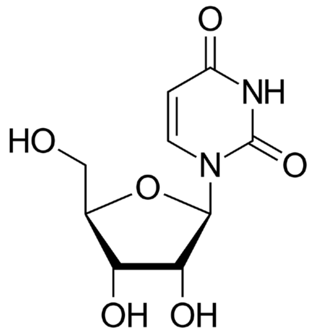
cytidine



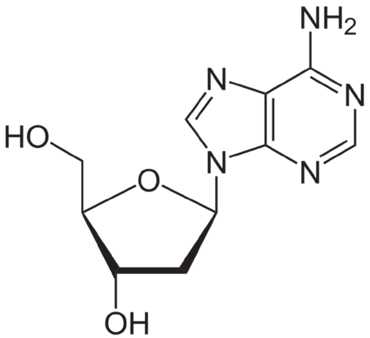
thymidine



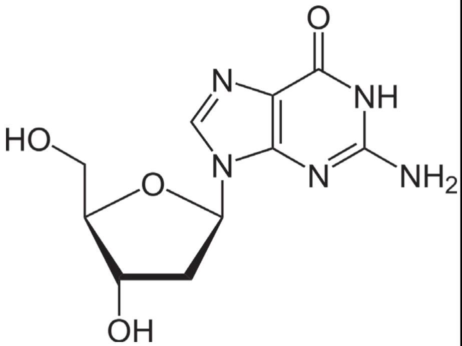
uridine



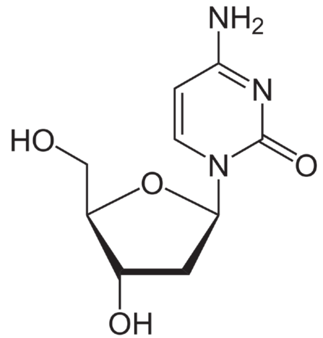
deoxyadenosine



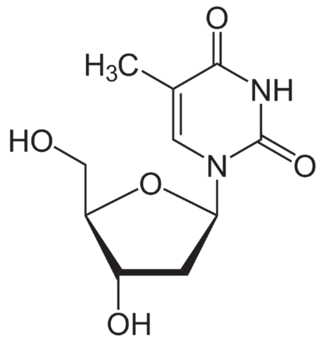
deoxyguanosine



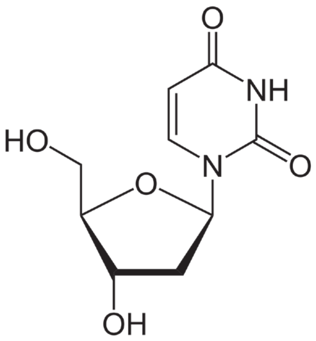
deoxycytidine



deoxythymidine



deoxyuridine



Nucleotides

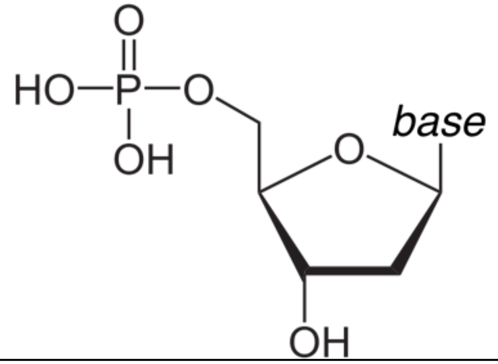
Nucleotide

- a phosphorylated (deoxy)ribose sugar bound to a nitrogenous base.
- Base covalently linked to 1’ carbon of sugar
- Phosphate covalently linked to 5’ carbon of sugar

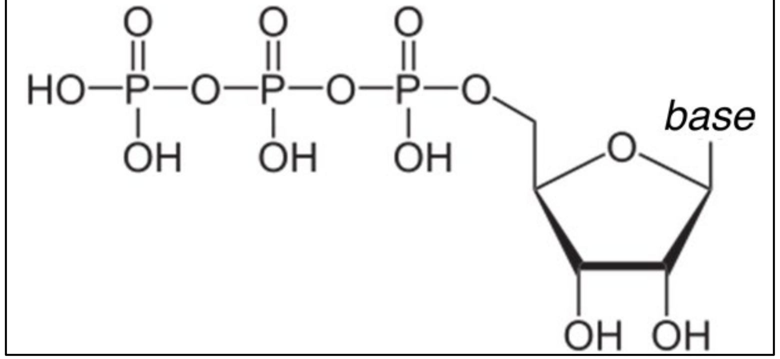
Naming

- Nucleoside name + phosphate
  - ***Mono-***, ***di-***, ***tri-*** prefixes denote number of phosphate groups

deoxynucleoside monophosphate

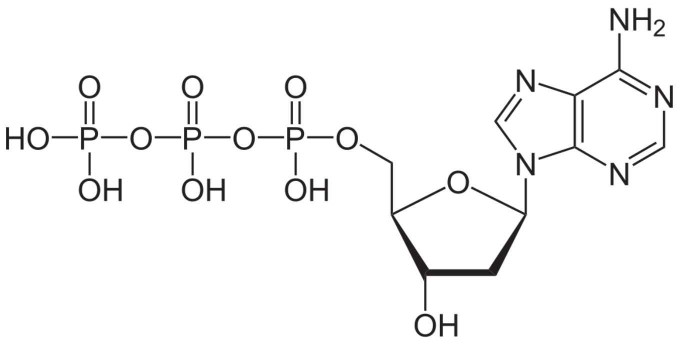


nucleoside triphosphate

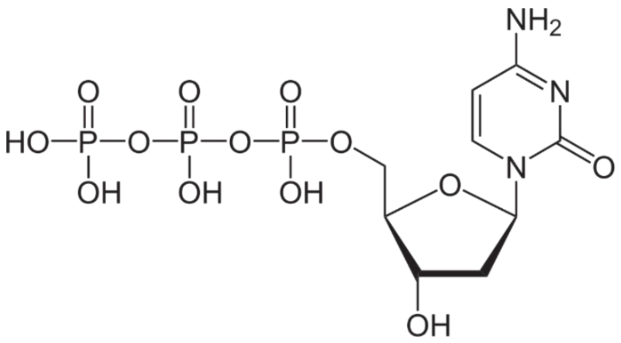


Nucleotides (cont.)

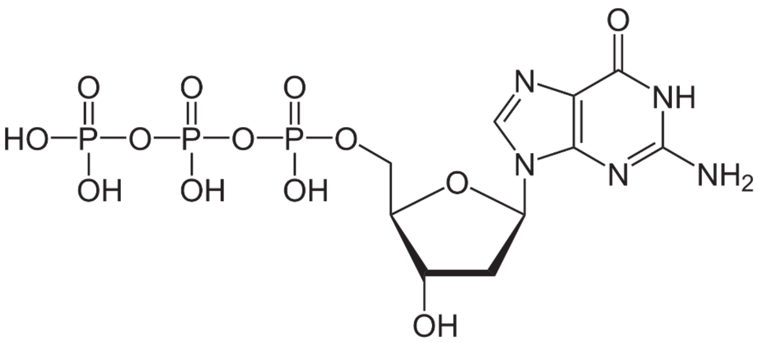
deoxyadenosine triphosphate (dATP)



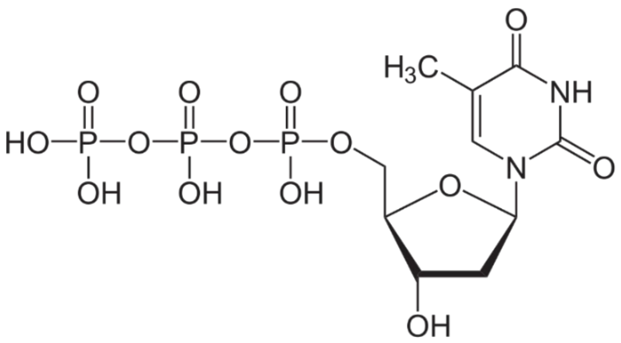
deoxycytidine triphosphate (dCTP)



deoxyguanosine triphosphate (dGTP)



deoxythymidine triphosphate (dTTP)



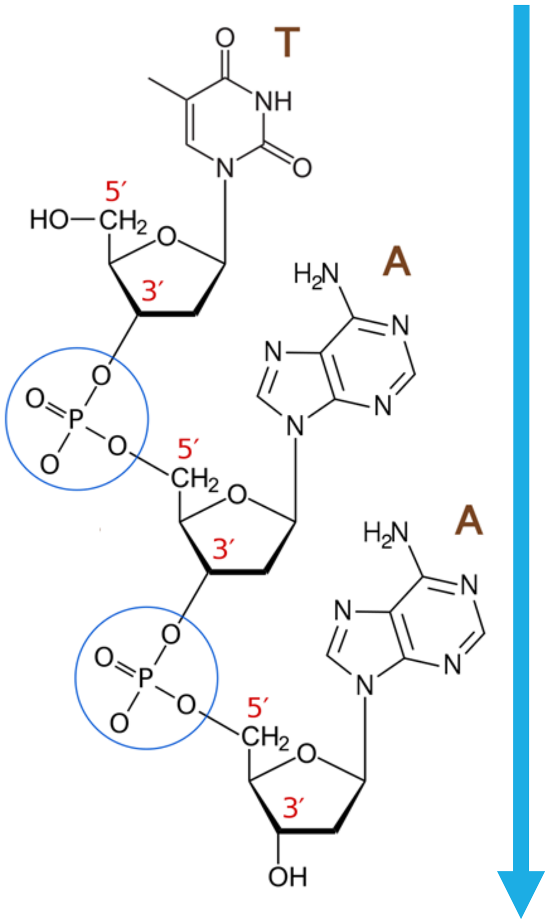
DNA Structure

DNA has a **sugar-phosphate backbone**

- The nucleotides of individual strands of DNA are connected by a series of **phosphodiester bonds**
  - Covalent attachment of the hydroxyl oxygen of one phosphorylated ribose (or deoxyribose) sugar to the phosphate phosphorous of the next

Nucleic acid chains are read according to their **5’ to 3’ polarity**

- Addition of nucleotides to a nucleic acid chain occurs by attachment of the 5’ phosphate group of an incoming nucleotide to the 3’ hydroxyl group on the last nucleotide of the chain
- The chain to the right would be red 5’-TAA-3’



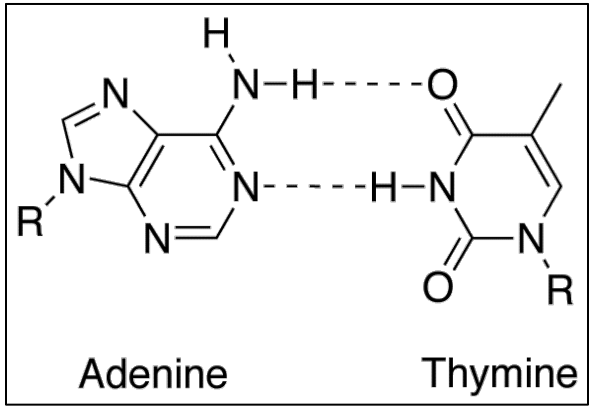
DNA Structure (cont.)

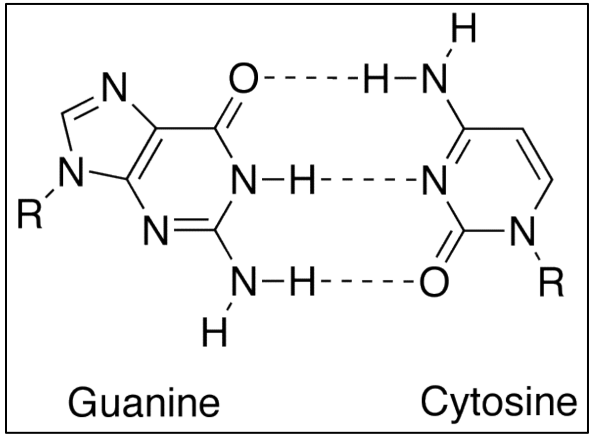
DNA strands are connected by hydrogen bonds formed between **complementary** bases

- A:T (or A:U in RNA)
- C:G

Chargaff's Rules, aka the **Complementary Base Pairing Rules**, can be explained three ways:

- In dsDNA, there is a 1:1 ratio of pyrimidine and purine bases
- T + C = A + G
- %A=%T and %C=%G



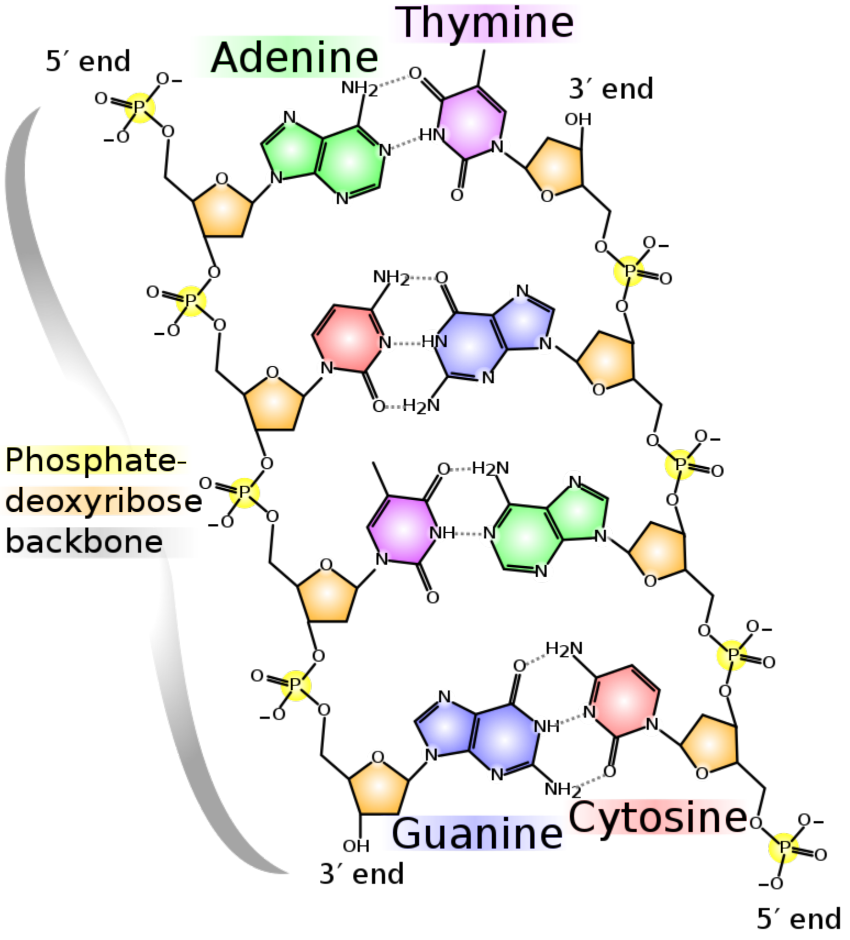


DNA Structure (cont.)

The formation of hydrogen bonds between two complementary strands is called **hybridization**

Complementary strands have **antiparallel** orientations

- 5’ end (phosphate) of one strand at the 3’ end (hydroxyl) of the other

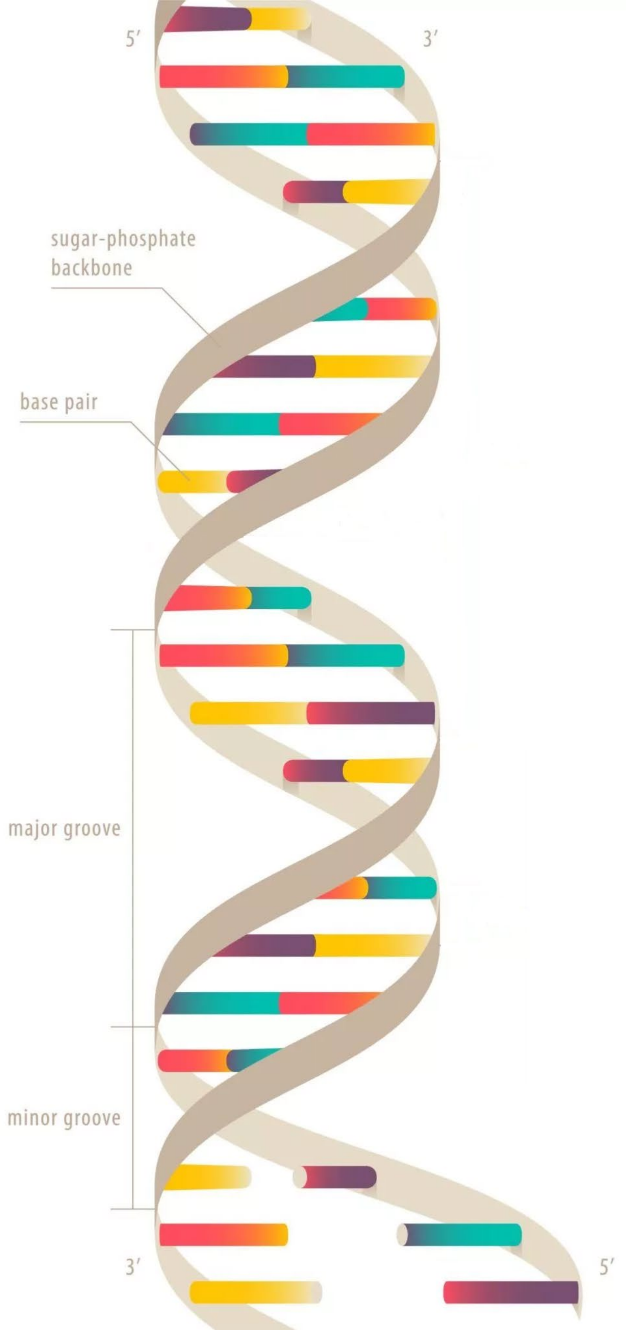


DNA Structure (cont.)

Sugar-phosphate backbones form a characteristic **double-helix** structure, with hybridized bases oriented toward the center

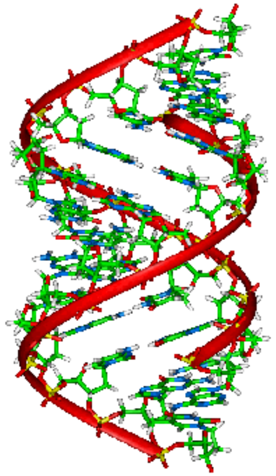
Double-helical structure creates **major** and **minor grooves**

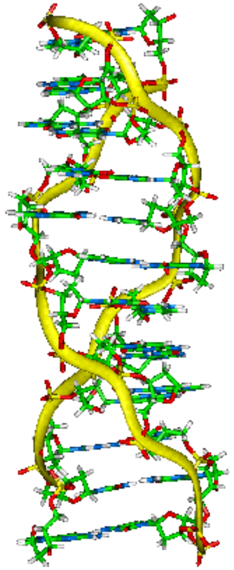
- Sites of interaction with proteins and intercalating agents (*e.g.*, fluorescent dyes used for DNA detection and quantification)



DNA Structure (cont.)

A-form DNA	B-form DNA	Z-form DNA
Form of DNA when dehydrated	Standard form of DNA when hydrated	Form of DNA when under torsional stress
Right-handed turn	Right-handed turn	Left-handed turn
11bp/turn	10.5bp/turn	12bp/turn
Turns at 2.3nm	Turns at 3.4nm	Turns at 4.6nm

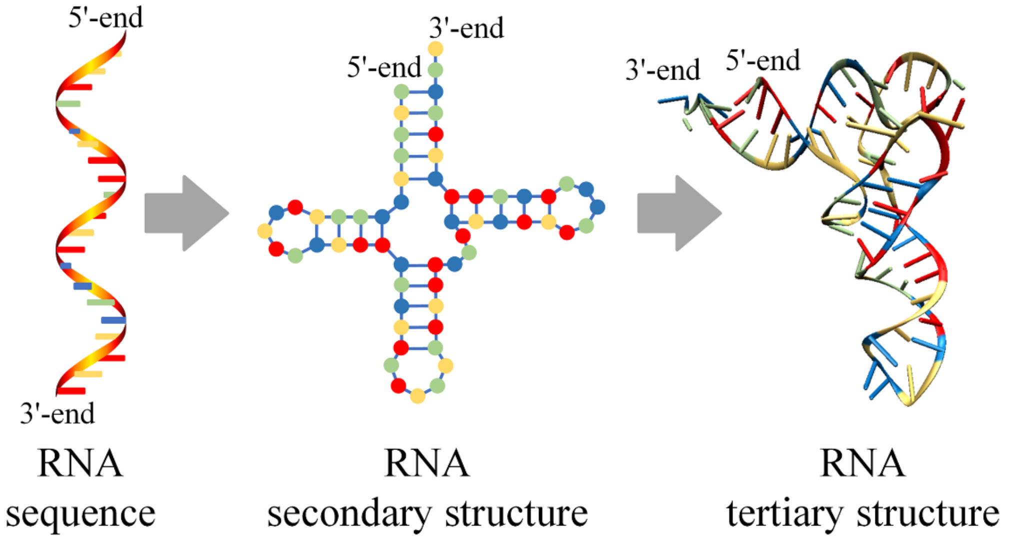




RNA Structure

Very similar structure to DNA with a few key differences:

- Formed from ribonucleotides, which contain **ribose** sugars
  - 2'-hydroxyl group can cause auto-hydrolysis
  - Less stable than DNA
- Sequences contain **uracil** instead of thymine
  - Uracil is also complementary to adenine
- Single-stranded in nature
  - Complementary sequences along ssRNA will hybridize, causing strand to fold and loop upon themselves
  - Secondary and tertiary structures give RNAs specific functionality



Comparing DNA and RNA structure

DNA

Polymer of nucleotides linked by 3’-5’ phosphodiester bonds

- A, **T**, C, and G
- **Deoxyribose** sugar without a 2’-OH

Double-stranded with complementary bases connected by hydrogen bonds

- Double-helix structure

Relatively **stable**

RNA

Polymer of nucleotides linked by 3’-5’ phosphodiester bonds

- A, **U**, C, and G
- **Ribose** sugar with a 2’-OH

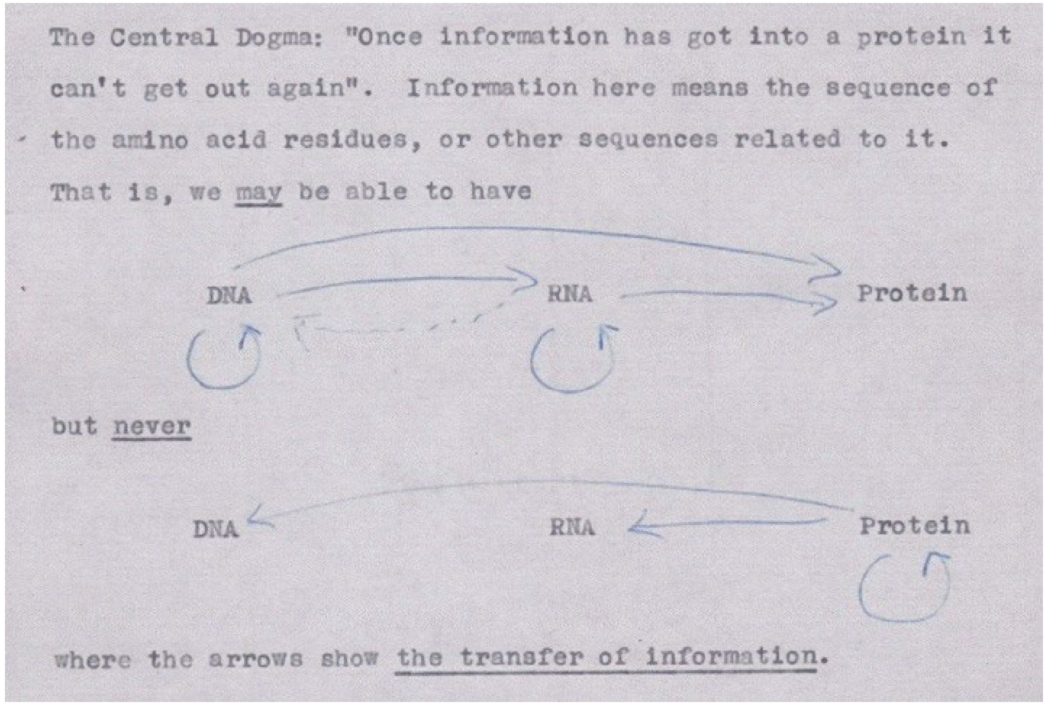
Single-stranded, with complementary sequences sometimes hybridizing to one another to form secondary/tertiary structure

Relatively **unstable**

Central Dogma of Molecular Biology

First described by Francis Crick in 1957.

“This states that once ‘information’ has passed into protein it cannot get out again. In more detail, the transfer of information from nucleic acid to nucleic acid, or from nucleic acid to protein may be possible, but transfer from protein to protein, or from protein to nucleic acid is impossible. Information means here the precise determination of sequence, either of bases in the nucleic acid or of amino acid residues in the protein.”



The Central Dogma: "Once information has got into a protein it can't get out again". Information here means the sequence of the amino acid residues, or other sequences related to it.

That is, we may be able to have

DNA RNA Protein

but never

DNA RNA Protein

where the arrows show the transfer of information.

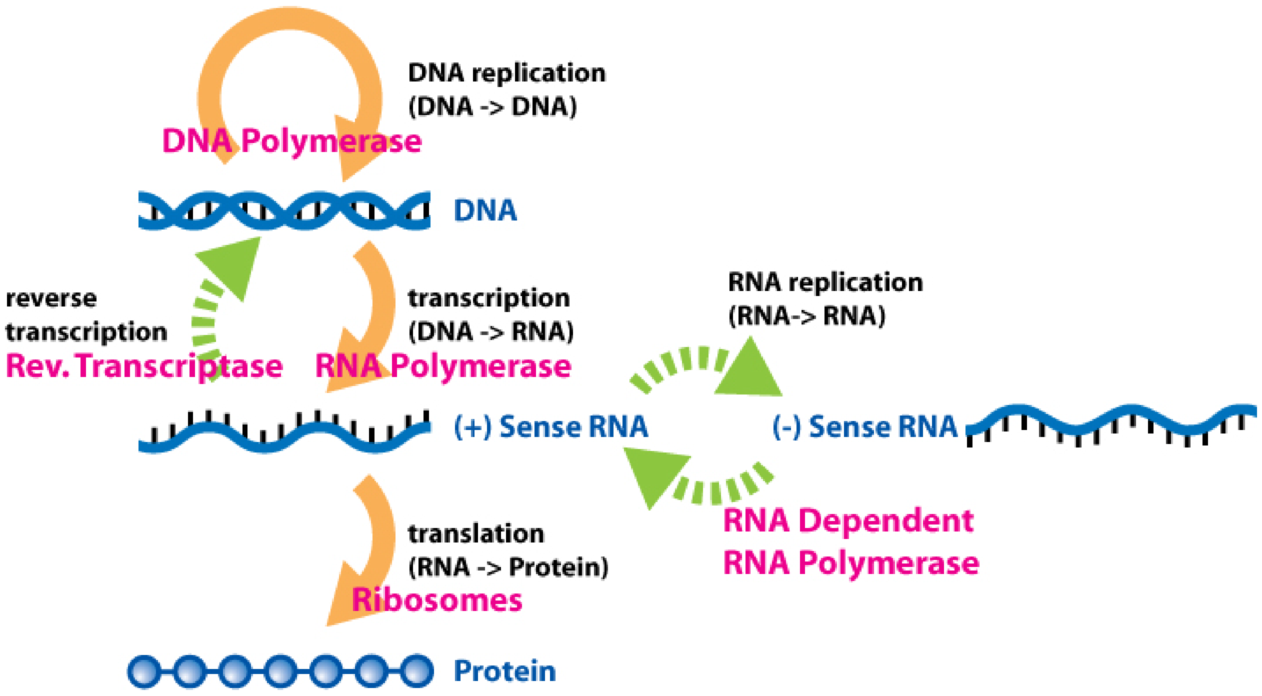
Central Dogma of Molecular Biology (cont.)

Central Dogma is often misrepresented as "DNA makes RNA makes Protein"

- Captures the usual flow of stored genetic information into protein expression
- Does not capture exceptions
  - RNA to DNA reverse transcription
  - RNA to RNA replication

Bad quotes make good lecture outlines

- Replication
- Transcription
- Translation



DNA Replication

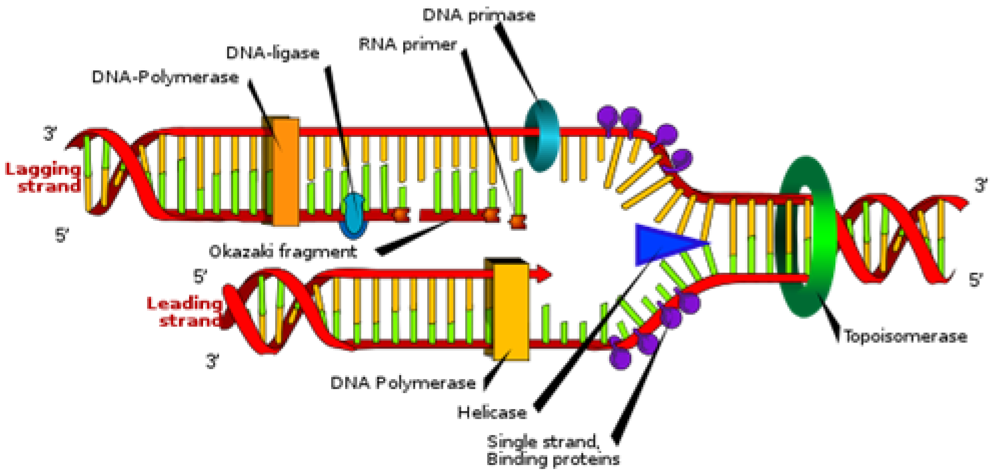
The process of DNA replication is **semi-conservative**

- Each strand of the dsDNA serves as a **template** for newly synthesized strand(s)
- Pre-existing strand, serving as template, is referred to as the **parent strand**
- Newly synthesized strand is referred to as the **daughter strand**

DNA Replication (cont.)

The **replisome** is a multiprotein molecular machine that drives DNA replication:

- Topoisomerase
- Helicase
- Single-strand binding proteins
- Primase
- DNA Polymerase
- RNAse H
- DNA Ligase



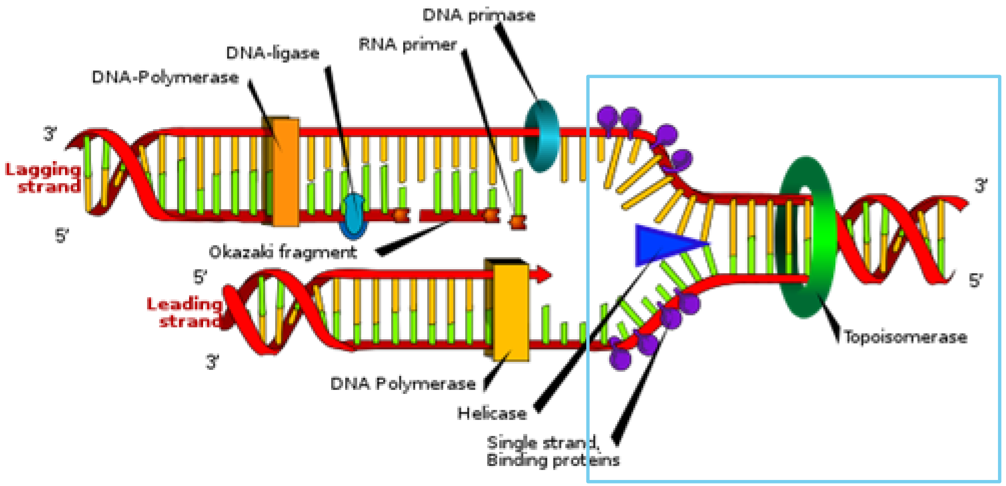
DNA Replication (cont.)

Parent strands must first be separated:

- **Topoisomerase** unwinds helical structure of dsDNA.
- **Helicase** separates the two strands of DNA. Site of separation is known as the **replication fork**.
- **Single-strand binding proteins** help stabilize separated parent strands.

Separated parent strands are used as templates for **DNA Polymerase** to read and synthesize a new daughter strand

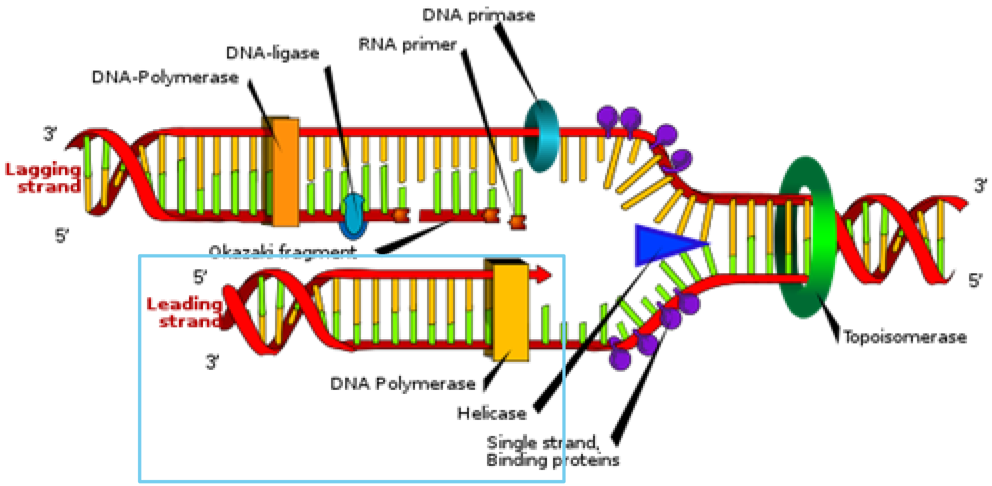
- DNA Polymerase reads the template (parent) strand in the 3’ to 5’ direction
- This means that DNA synthesis of daughter strands proceeds in the 5’ to 3’ direction
- Due to the antiparallel nature of dsDNA, this means each daughter is synthesized differently



DNA Replication (cont.)

The **leading strand** is synthesized continuously by DNA polymerase.

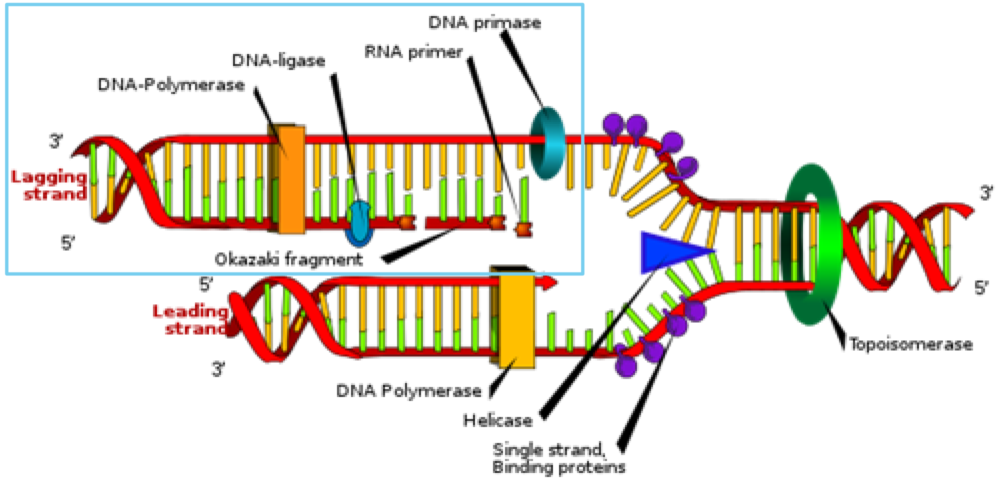
- Parent strand is already oriented in the 3’ to 5’ direction for DNA polymerase to read
- Synthesis can proceed easily in 5’ to 3’ direction
- Nucleotides, complementary to parent strand, are incorporated into growing daughter strand by DNA polymerase-driven synthesis of new phosphodiester bonds



DNA Replication (cont.)

The **lagging strand** is synthesized discontinuously by DNA polymerase due to its orientation.

- Parent strand is oriented in the 5' to 3' direction, making it impossible for polymerase to read continuously
- **Primase** continuously adds RNA primers upstream of DNA replication
- **DNA Polymerase** attaches at primed location and reads the parent strand "backwards" in the 3' to 5' direction, allowing for synthesis of short fragments of DNA in the 5' to 3' direction
  - These are known as **Okazaki fragments**
- **RNAse H** removes the primers from newly synthesized DNA fragments
- **DNA Ligase** joins the fragments to the growing strand

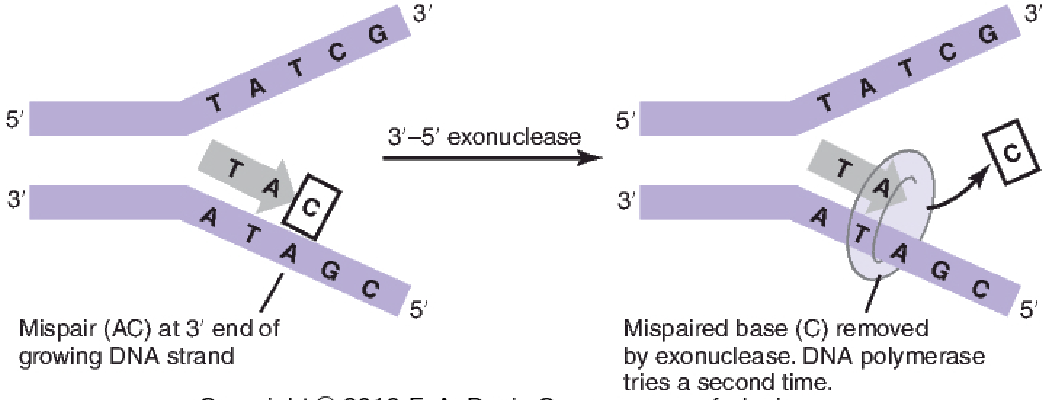


DNA Repair

DNA repair functions

- During new strand synthesis, mismatched nucleotides can be removed by DNA polymerase using its **3’ to 5’ exonuclease function** (see image to the right)

- The **base excision repair** function of specialized DNA polymerases can correct damaged DNA (*e.g.*, oxidation, alkylation, deamination)



DNA Polymerases

DNA Polymerases from prokaryotes (specifically *E. coli*)

Polymerase	Function(s)	Specific in vivo activities
DNA Pol I	Recombination, repair, replication	repair
DNA Pol II	Repair	repair
DNA Pol III	Replication	primary replication enzyme

DNA Polymerases from eukaryotes

Polymerase	Function(s)	Specific in vivo activities
Pol α (alpha)	replication, repair	primase activity
Pol β (beta)	repair	base excision repair (BER)
Pol δ (delta)	replication, repair	lagging strand synthesis
Pol ε (epsilon)	replication, repair	leading strand synthesis
Pol γ (gamma)	replication, repair	mitochondrial replication/repair

Transcription

Transcription is the copying of one strand of DNA into RNA

Similar to the process of replication
- Catalyzed by **RNA polymerase**

Several types of RNA are transcribed from DNA
- Ribosomal (rRNA)
  - Serves as a structural and functional component of ribosomes
- **Messenger (mRNA)**
  - **Responsible for carrying the genetic information to be translated into protein**
- Transfer (tRNA)
  - Adaptors that link codons in messenger RNA with amino acids – more on this later

RNA Polymerases from eukaryotes

Polymerase	Template	Product
RNA Pol I	DNA	rRNA
RNA Pol II	DNA	mRNA
RNA Pol III	DNA	tRNA

Transcription (cont.)

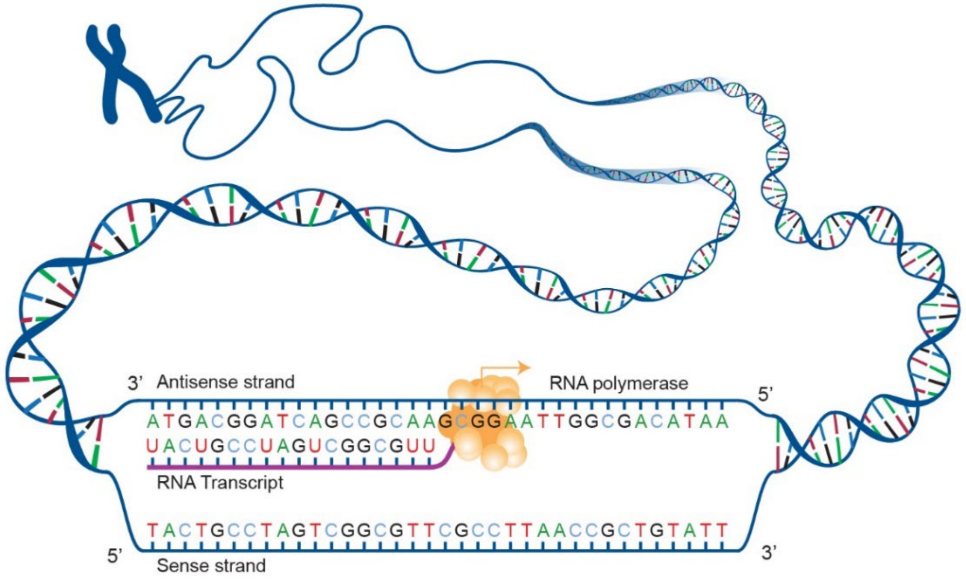
DNA strands are referred to as **sense** or **antisense** based on their ability to transcribe mRNA

Sense strand = coding strand

- DNA strand containing the sequence of nucleotides that codes for the production of proteins
- Transcriptionally inactive

Antisense strand = noncoding strand

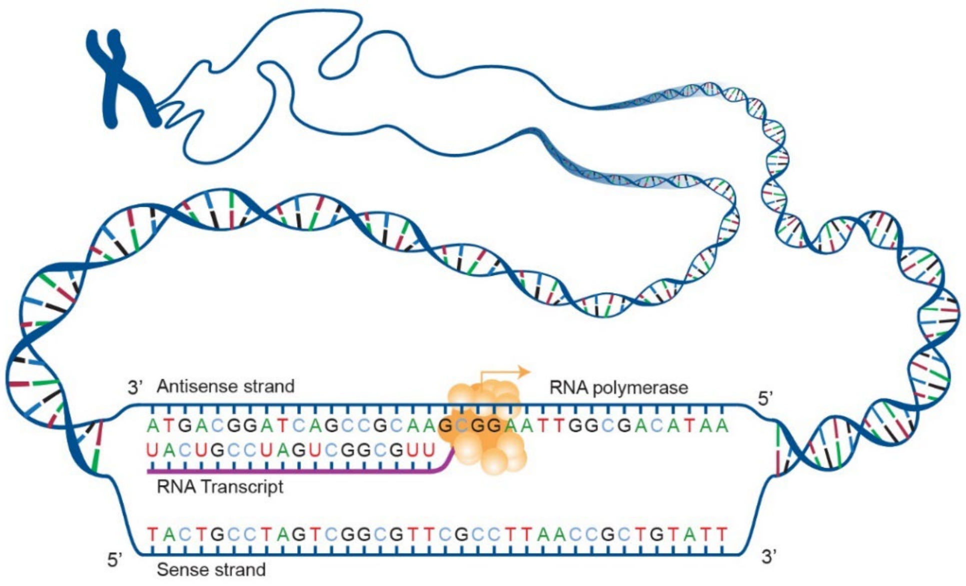
- DNA strand that is used as the template for complementary mRNA synthesis
- Transcriptionally active



Transcription (cont.)

mRNA Transcription (eukaryotic)

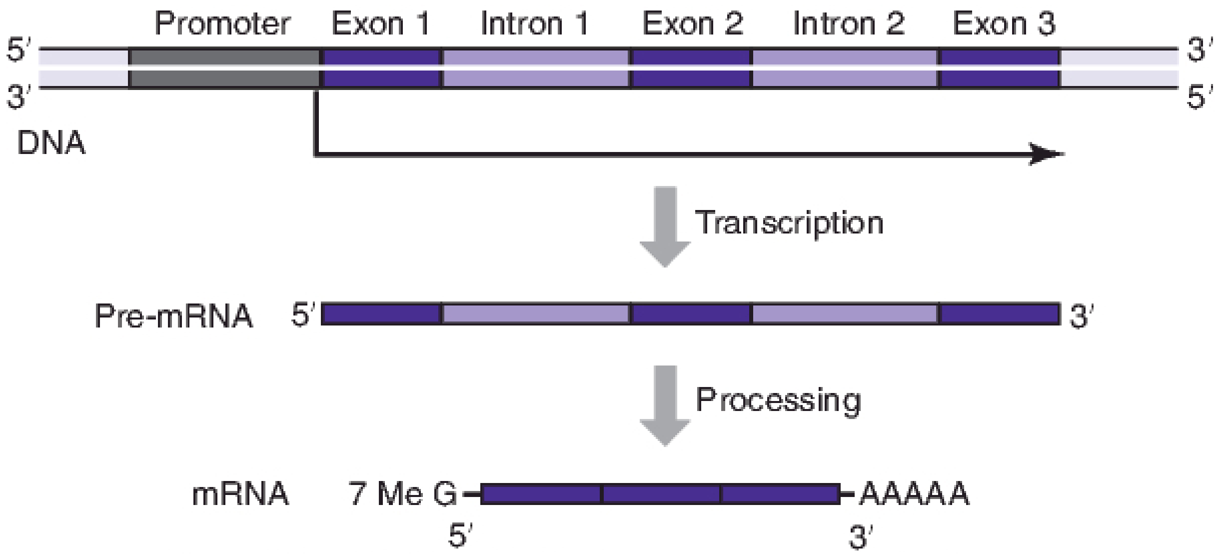
- Initiation
  - **Promoter** – DNA sequence that binds RNA polymerase and associated transcription factors
- Elongation
  - RNA polymerase reads the antisense strand in the 3’ to 5’ direction and synthesizes mRNA in the 5’ to 3’ direction without the need for priming
  - Transcribed mRNA sequence matches the sense strand, or coding strand, of DNA
- Termination
  - When RNA polymerase encounters a **polyadenylation signal** (**polyA site**), pre-mRNA is released and transcription is terminated



Post-Transcriptional mRNA Processing

Three primary post-transcriptional processing mechanisms of the pre-mRNA molecule:

- **Polyadenylation** – terminal (3’)
  - **polyA tail** = run of adenines (**5’-AAUAAA-3’**) added to the 3’ end of mRNA by template independent polyA RNA pol
  - Roles in termination, transport, and protection (maybe…) of mRNA
- **Capping** – initial (5’)
  - **Methyl Cap** = pyrophosphate linkage of 7-methyl guanosine to either a 2’ O-methyl guanine or 2’ O-methyl adenine
  - Protects mRNA molecule (definitely!) and serves as recognition site for subsequent translation
- **Splicing** – internal (between 5’ and 3’)
  - Removal of intronic and preservation of exonic sequences to form final mRNA product (more on this later)



Translation

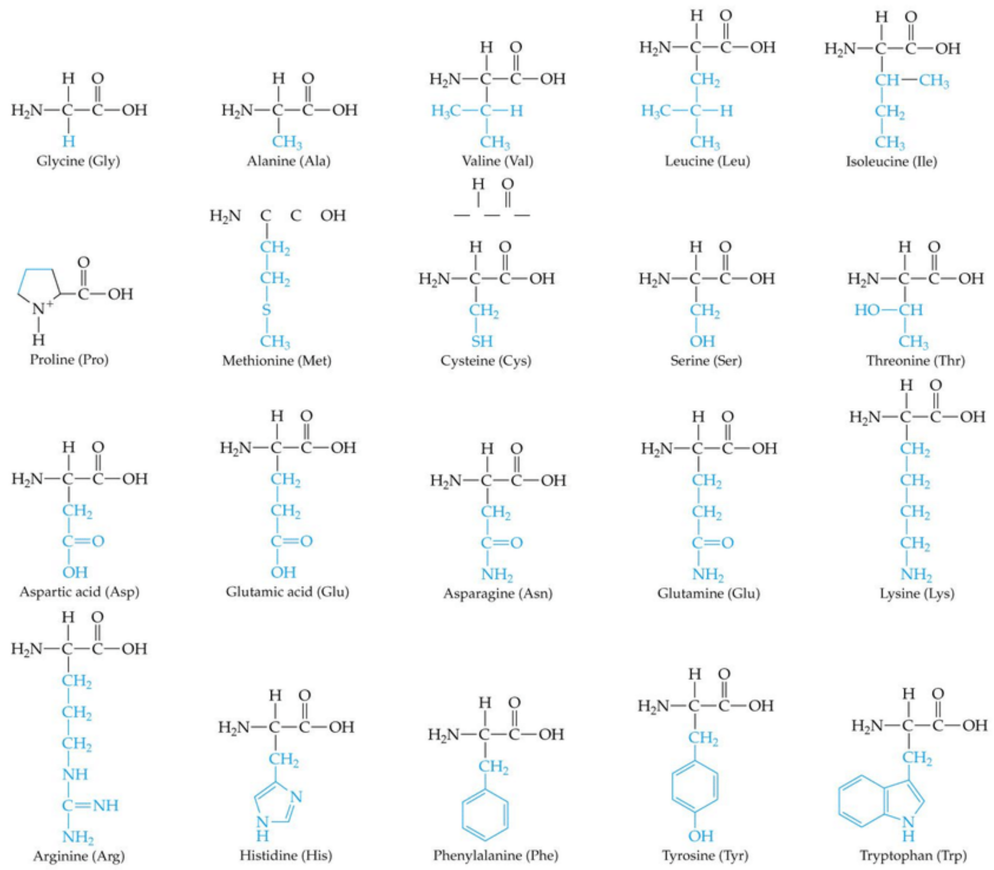
Translation is the synthesis of proteins by the reading of an mRNA transcript

Proteins are constructed of a string of amino acids, known as a **polypeptide chain**

There are 20 amino acids, each composed of:

- Common structure of a carbon atom bound to amino and carboxylic acid groups
- Unique **side chain**, with specific biochemical properties (*i.e.*, hydrophobic, hydrophilic, negatively charged, positively charged)

Interaction of the side chains between one another, the environment, and other proteins determine a protein's structure and function



Translation (cont.)

Codons are a three-nucleotide sequence in mRNA that guide the incorporation of a specific amino acid into a polypeptide chain

Wobble Rule: the third of these nucleotides is often **degenerate**, meaning it can be swapped out for other nucleotides without changing the amino acid it incorporates

- "Wobble" creates redundancy, with all but two amino acids (Met and Trp) having multiple codons

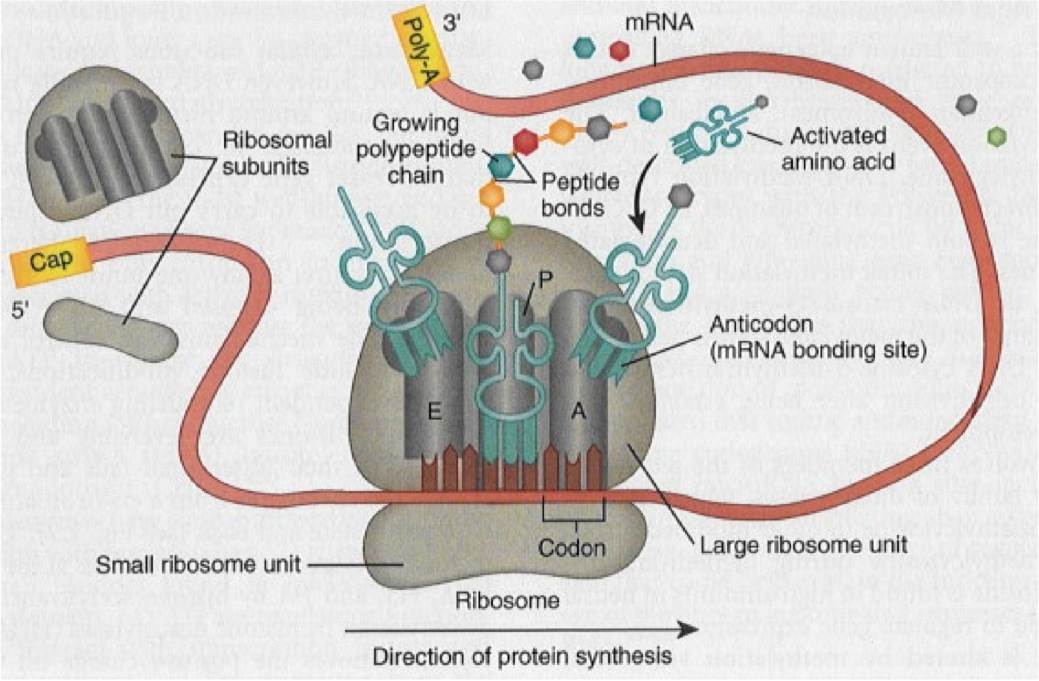
Second letter

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

Translation (cont.)

Translation occurs within **ribosomes** and consists of three phases:

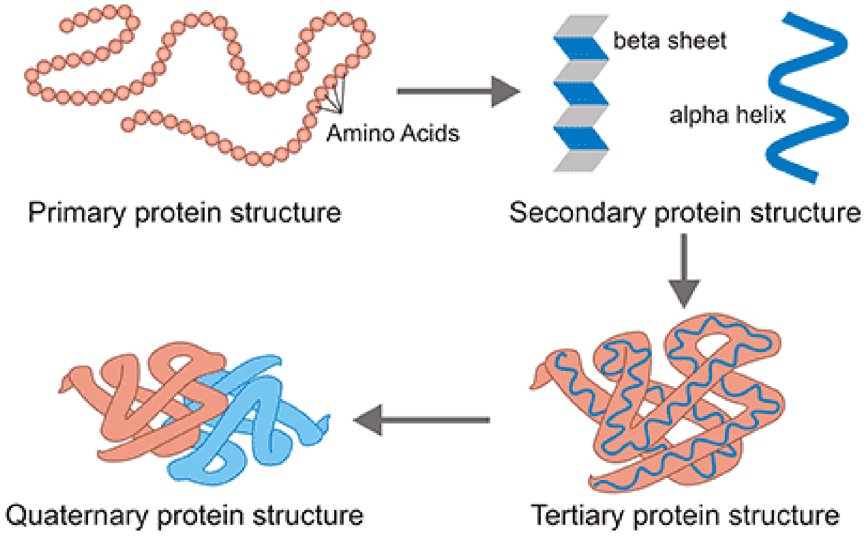
- Initiation
  - Starts with **Met (AUG) start codon**
  - Reads mRNA in 5’ to 3’ direction
- Elongation
  - Transfer RNA (tRNA) facilitates incorporation of amino acids into the growing polypeptide chain
- Termination
  - Signaled by one of three **nonsense/stop codons** (**UAA, UAG, UGA**)



Protein Structure

Four different classes:

- **Primary** Structure: sequence of amino acids
- **Secondary** Structure: folding of a linear polypeptide chain into beta sheets or alpha helices
- **Tertiary** Structure: overall 3-dimensional structure which gives a protein specific function
  - Denaturation, or loss of tertiary structure, can reduce or eliminate protein function
- **Quaternary** Structure: functional association of separate proteins



Genome Storage in Humans

The DNA from one human cell, laid out in a straight line, is about 6 feet in length. For all DNA from a single human, it's about 67 billion miles.

To conserve space, DNA is condensed into macromolecules called **chromosomes**, located in the cell nucleus.

The condensation of DNA into chromosomes is achieved by specialized proteins.

- Histones
- Non-histone proteins

G-banded metaphase chromosomes

Histone and Non-Histone Proteins

Histone proteins

- Found in ~1:1 ratio by weight to DNA
- Responsible for coiling DNA into chromatin
- Highly basic (arginine- and lysine- rich)
- Positively charged histones bind to the negatively charged phosphate backbone of DNA

Non-histone proteins

- More numerous and variable than histones, but make up a smaller proportion of chromatin mass
- Involved in chromosomal metabolism, gene expression, and higher order structure

Histones

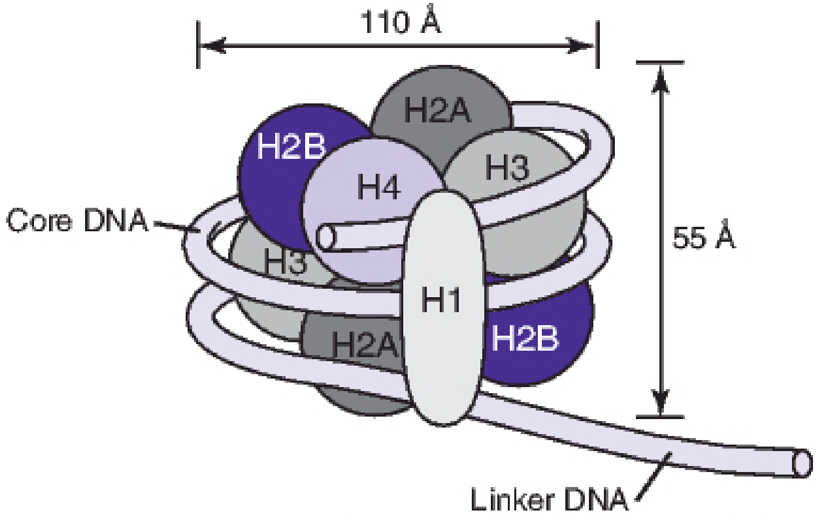
Types:

- H1
- **H2A**
- **H2B**
- **H3**
- **H4**
- H5

Core histone proteins

Eight histone proteins combine to form a histone octamer, around which DNA coils

- Two each of H2A, H2B, H3, and H4

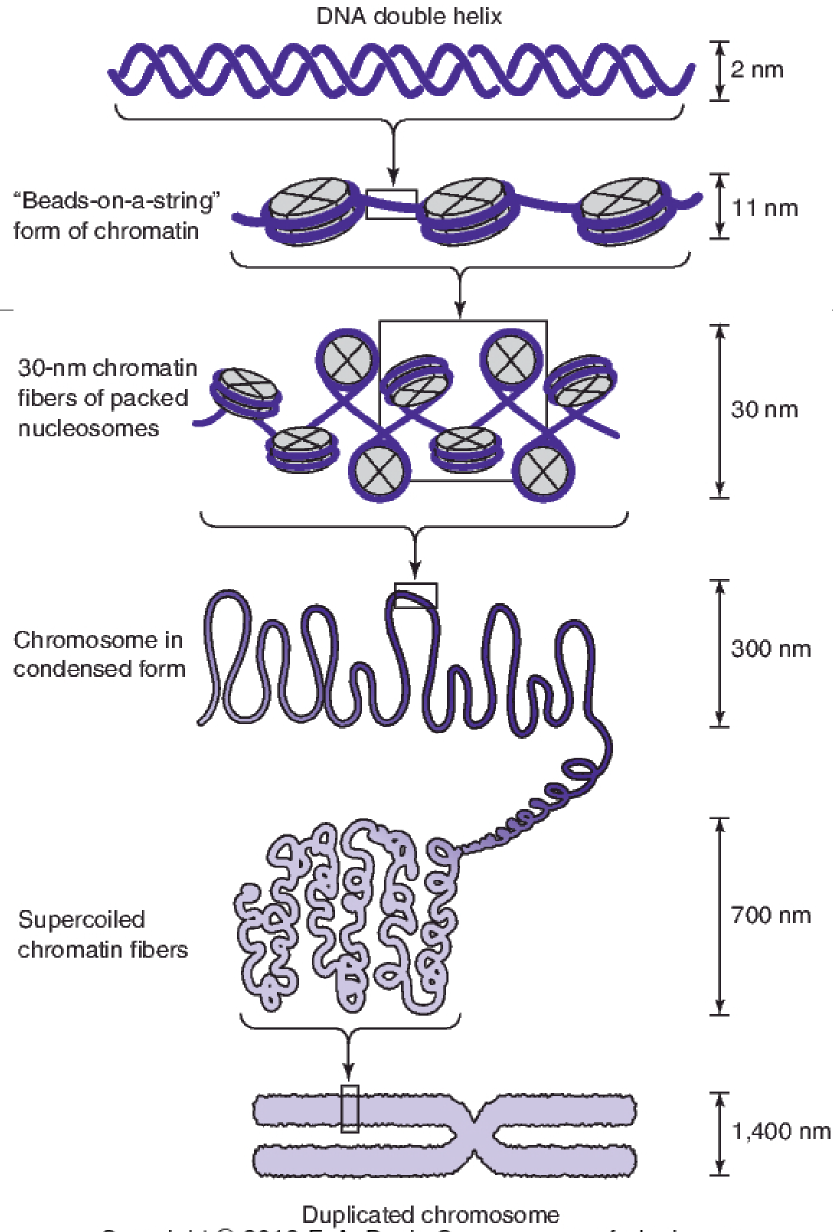


Nucleosome

Nucleosome: the fundamental structural unit of a chromosome, consisting of DNA coiled around a histone core

- Think of the histone octamer as the "spool" around which the DNA "thread" is wound

Nucleosomes are connected by linker regions of DNA, creating a "beads-on-a-string" appearance



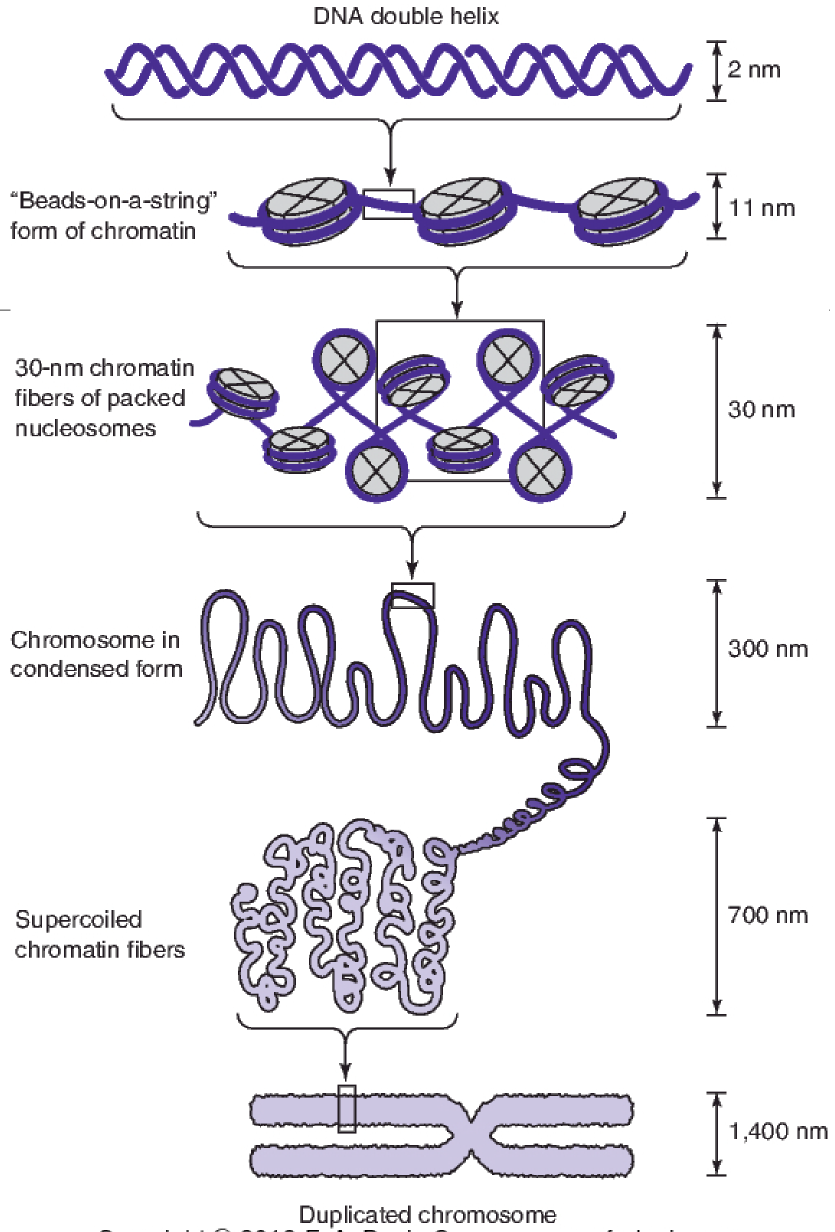
Chromatin

Additional histones (H1, H5) and non-histone proteins connect and condense nucleosomes into chromatin fibers

Chromatin fibers are further condensed into the final chromosome structure

How loosely/tightly chromatin is condensed determines its genetic activity

- Euchromatin vs. Heterochromatin



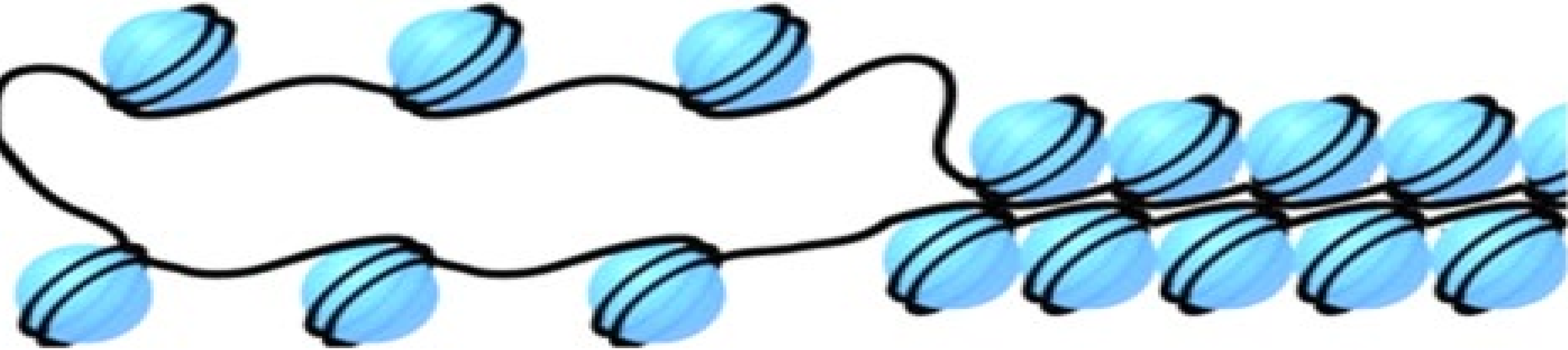
Chromatin (cont.)

Euchromatin

Loosely condensed
Genetically active
GC-rich
Stains lightly with Giemsa

Heterochromatin

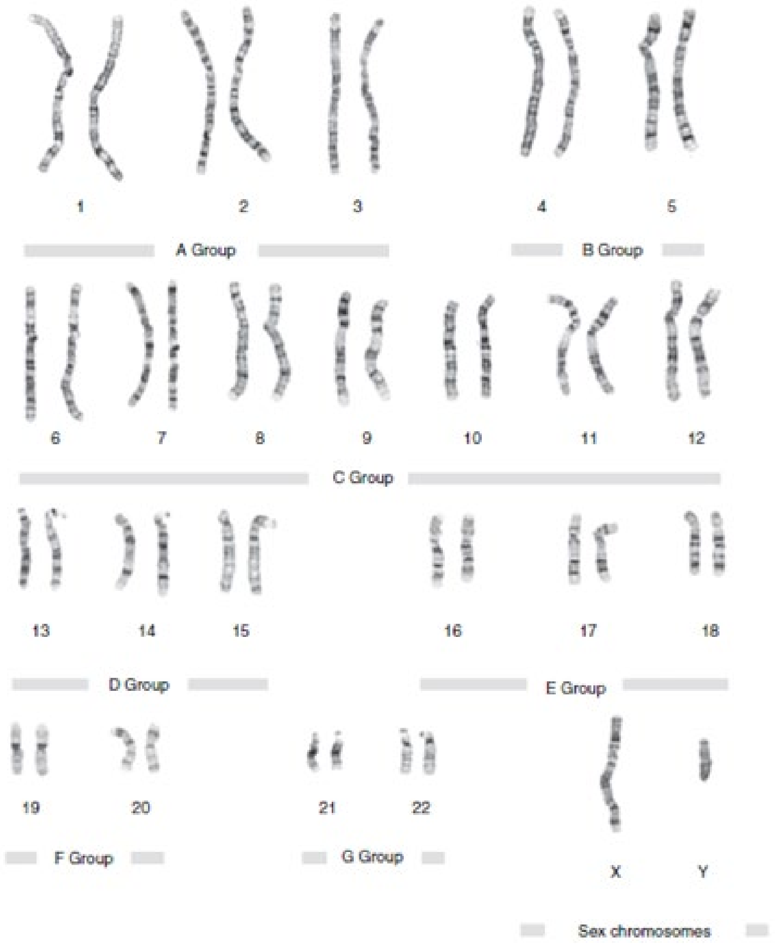
Tightly condensed
Genetically inactive
AT-rich
Stains darkly with Giemsa



Human Chromosomes

The complete complement of chromosomes in a cell is its **karyotype**.

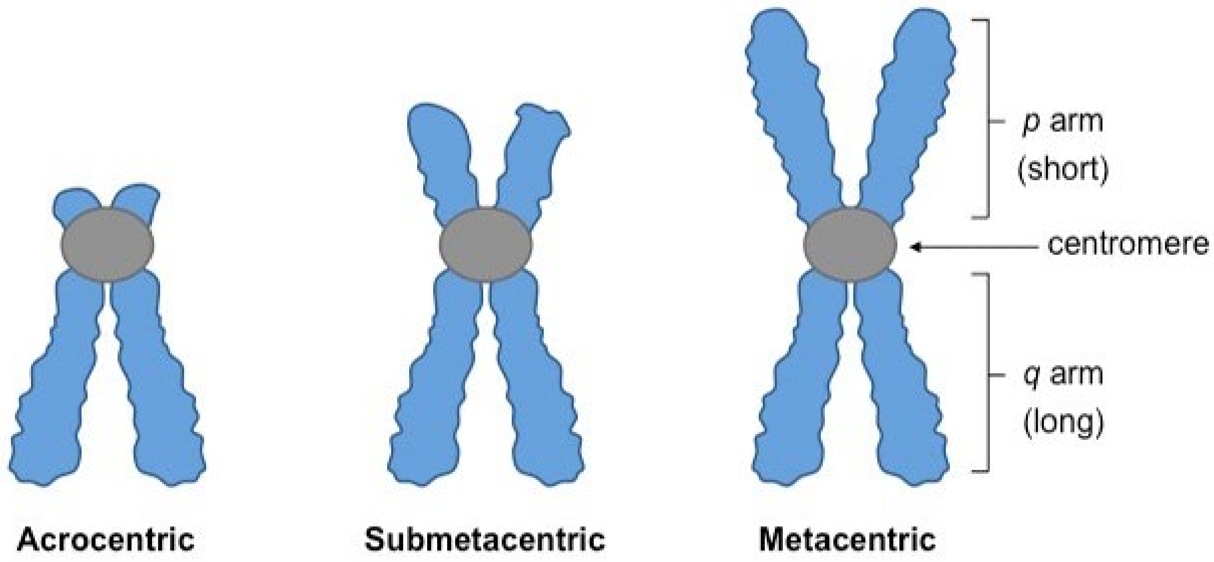
- **Somatic** cells are **diploid**, having two copies of each of the 22 **autosomes** and one pair of **sex chromosomes** for a total of 46 chromosomes per cell.
- Human **gametes** (eggs, sperm) are **haploid**, meaning they have only one copy of each of the 22 autosomes and one of the sex chromosomes.
  - The **germline** cells that produce the gametes are diploid.



Human Chromosome Structure

Human chromosomes have a **p arm** (short arm) and **q arm** (long arm) separated by a **centromere**.

- Metacentric = centromere is in the middle, p and q arms are equal in size
- Submetacentric = centromere is offset from the middle, p arm is shorter than the q arm
- Acrocentric = centromere is very close to one end, p arm is significantly shorter than the q arm



The Cell Cycle

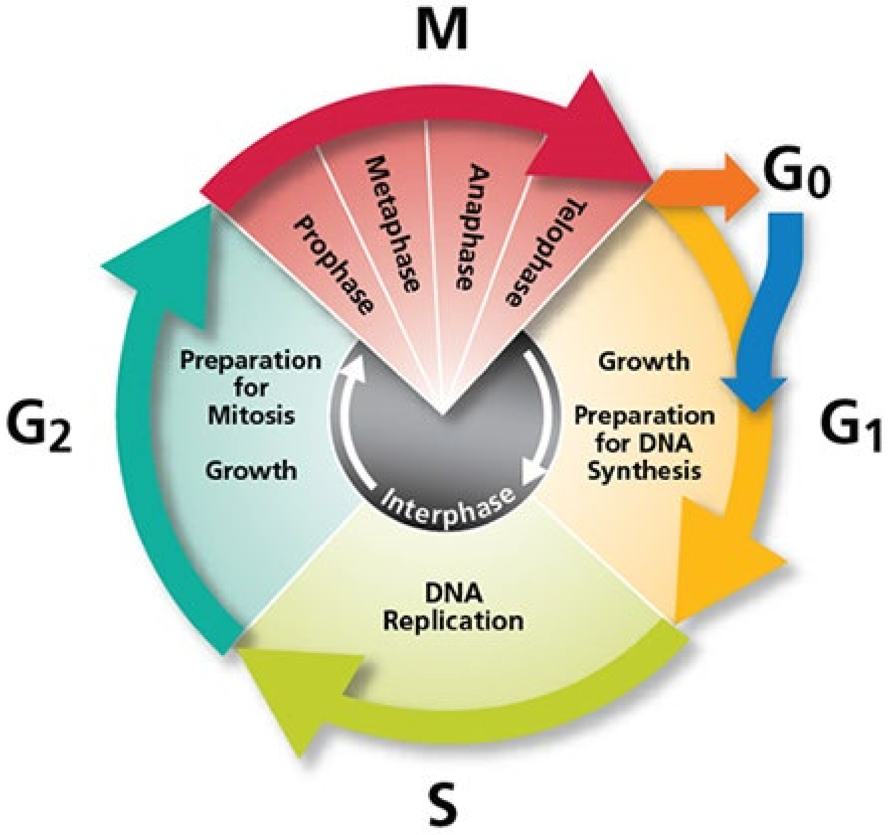
4 major stages

- Gap 1 (G_1): Growth
- Synthesis (S): Synthesis of DNA
- Gap 2 (G_2): Growth
- Mitosis (M)

Interphase = G_1, S, G_2

- Chromosomes duplicate during S

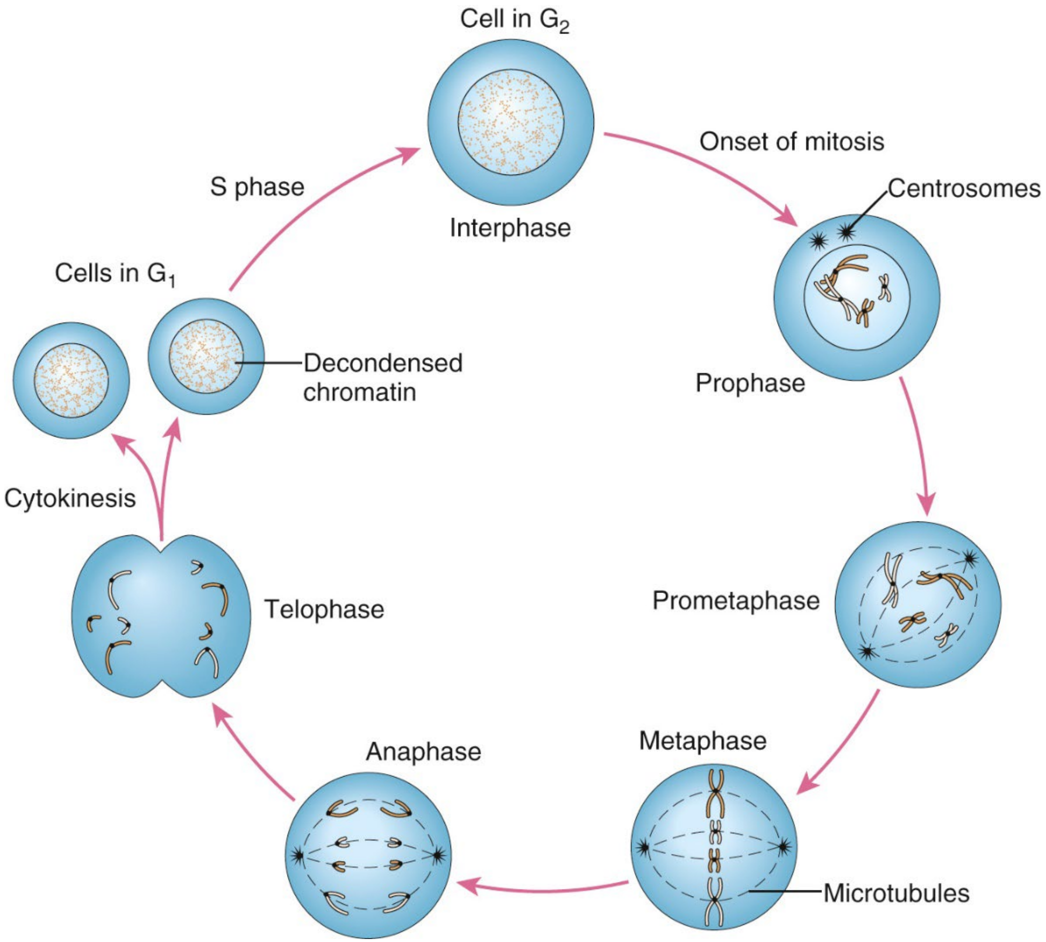
G_0: resting stage where cells are not actively preparing to divide



Mitosis

Mitosis is the process by which a single parent cell divides into two diploid daughter cells.

- Prophase
  - Duplicated chromosomes condense to form sister chromatids, joined at the centromere
  - Spindle fibers form, radiating from two centrioles at opposite poles of cell
  - Prometaphase: nuclear envelope breaks down
- Metaphase
  - Chromosomes line up at the metaphase plate
  - Period of maximum chromosome condensation
- Anaphase
  - Sister chromatids are separated into daughter chromosomes and pulled to opposite ends of the cell
- Telophase
  - Nuclear envelope reforms around each set of daughter chromosomes
  - Cytokinesis: cytoplasm is divided by the formation of new cell membranes

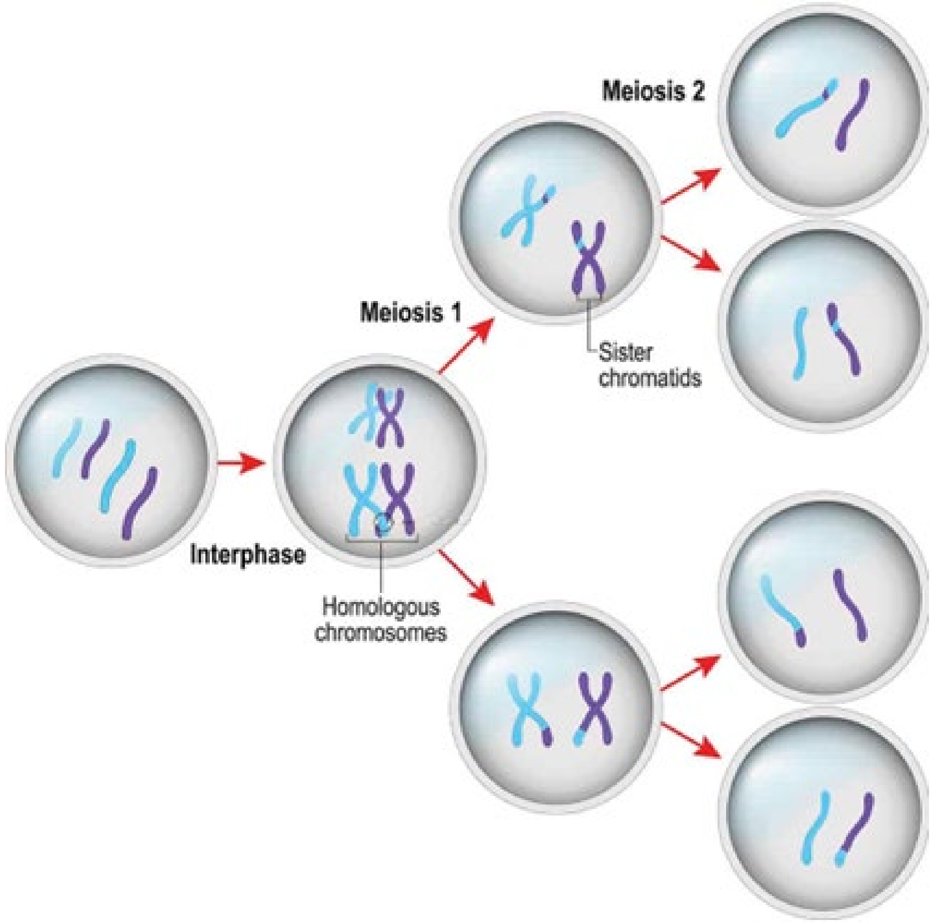


Meiosis

Meiosis is the process by which a single parent cell divides into four haploid daughter cells.

Subdivided into two processes:

- Meiosis I
  - Separates homologous chromosomes
  - **Produces two diploid daughter cells**
- Meiosis II
  - Separates sister chromatids
  - **Produces four haploid daughter cells**

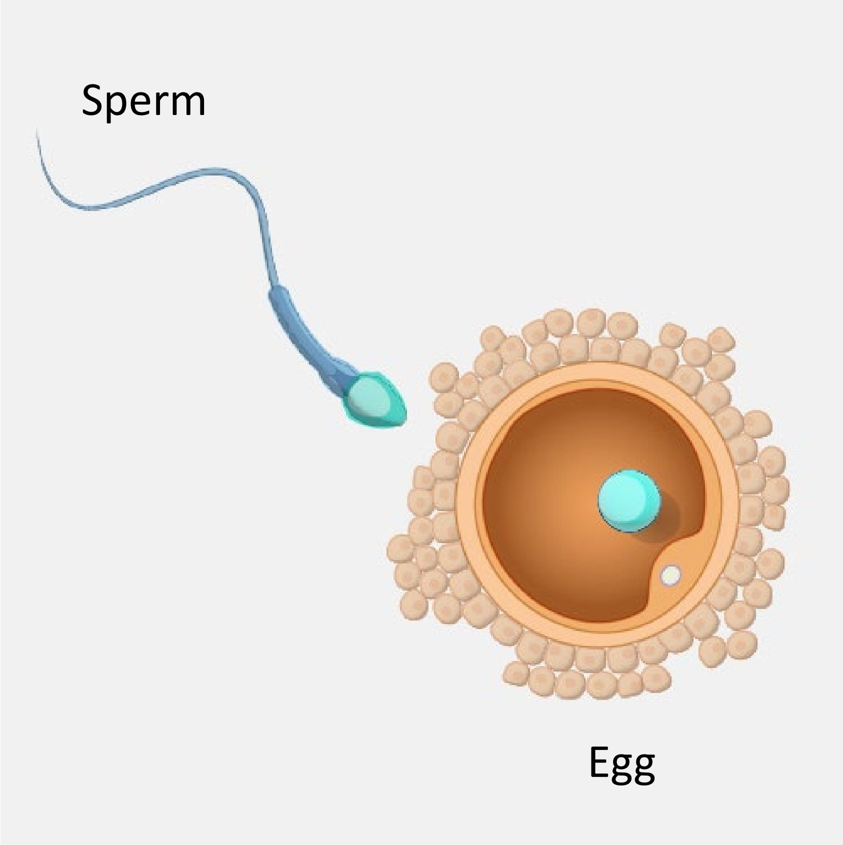


Human Gametes

Meiosis is the process by which human **gametes**, the haploid reproductive cells, are made.

Humans have two types of gamete:

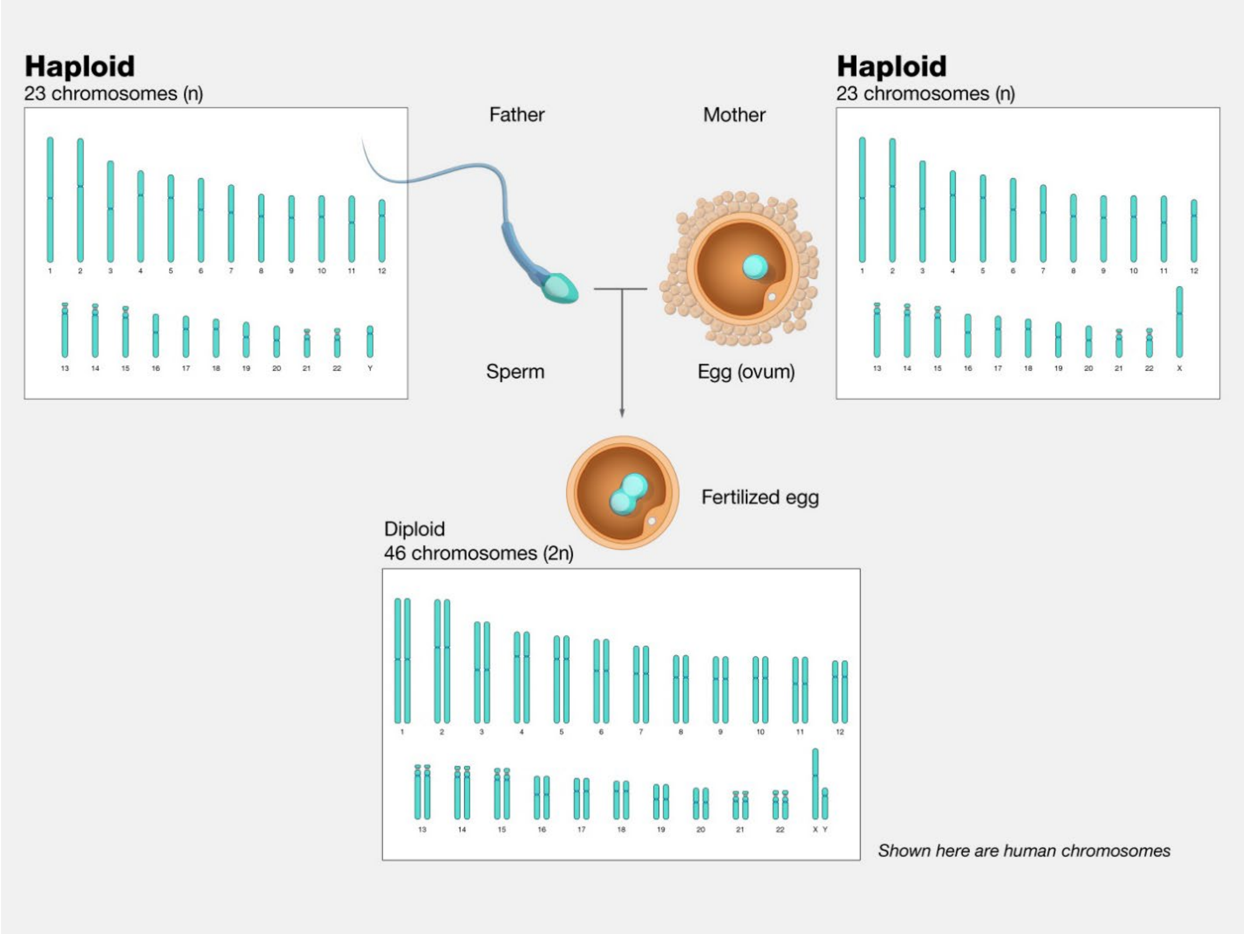
- Spermatazoa (sperm): male gamete
- Ovum (egg): female gamete



Sexual Reproduction

Fertilization occurs when haploid sperm penetrates haploid ovum, creating a diploid **zygote**.

Zygote, now with a complete complement of chromosomes, mitotically divides into diploid daughter cells and proceeds with embryological development (embryogenesis).

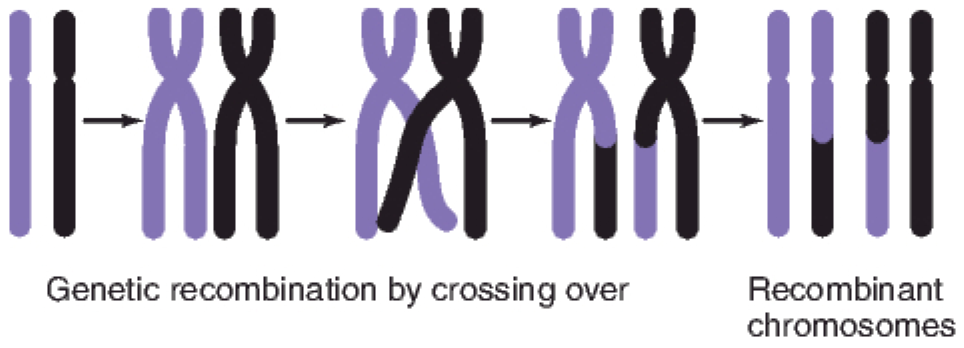


Recombination in Sexual Reproduction

Recombination is the mixture and assembly of new genetic combinations.

Recombination occurs in three ways in sexual reproduction:

- **Crossing over** at the beginning of meiosis I, when duplicated chromosomes are lined up and breakage and reunion of the DNA duplexes generates recombinant chromosomes.

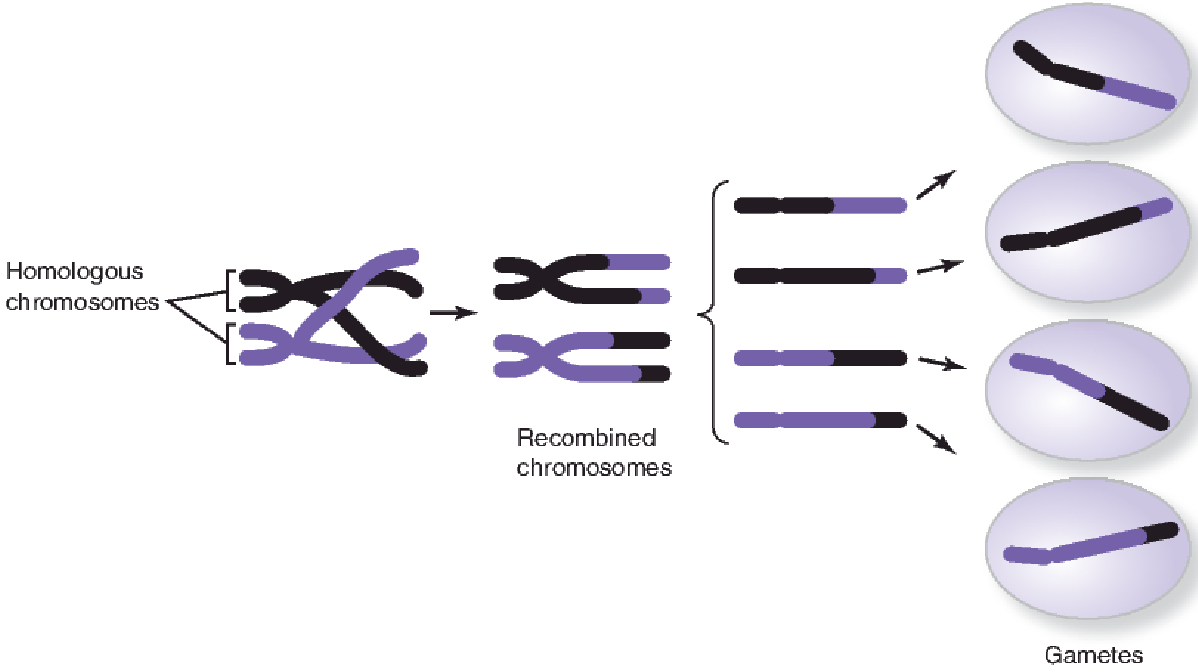


Recombination in Sexual Reproduction

Recombination is the mixture and assembly of new genetic combinations.

Occurs in three ways in sexual reproduction:

- **Crossing over** at the beginning of meiosis I, when duplicated chromosomes are lined up and breakage and reunion of the DNA duplexes generates recombinant chromosomes.
- Random assortment of recombinant chromosomes into gametes at the end of meiosis II.

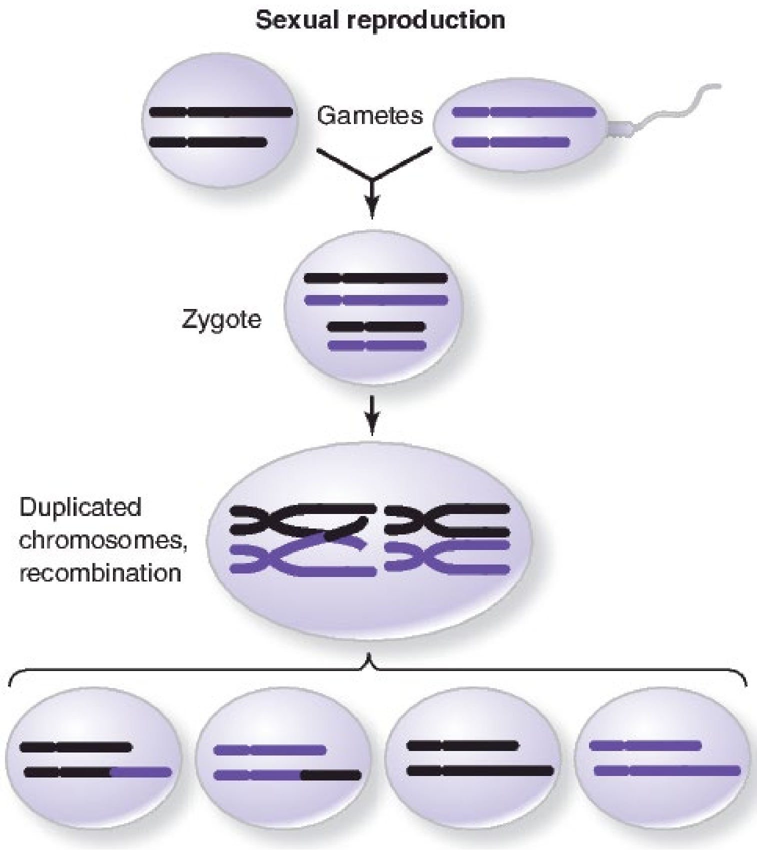


Recombination in Sexual Reproduction

Recombination is the mixture and assembly of new genetic combinations.

Occurs in three ways in sexual reproduction:

- **Crossing over** at the beginning of meiosis I, when duplicated chromosomes are lined up and breakage and reunion of the DNA duplexes generates recombinant chromosomes.
- Random assortment of recombinant chromosomes into gametes at the end of meiosis II.
- Parental gametes merge to produce offspring with a new recombination of parental chromosomes and genes.



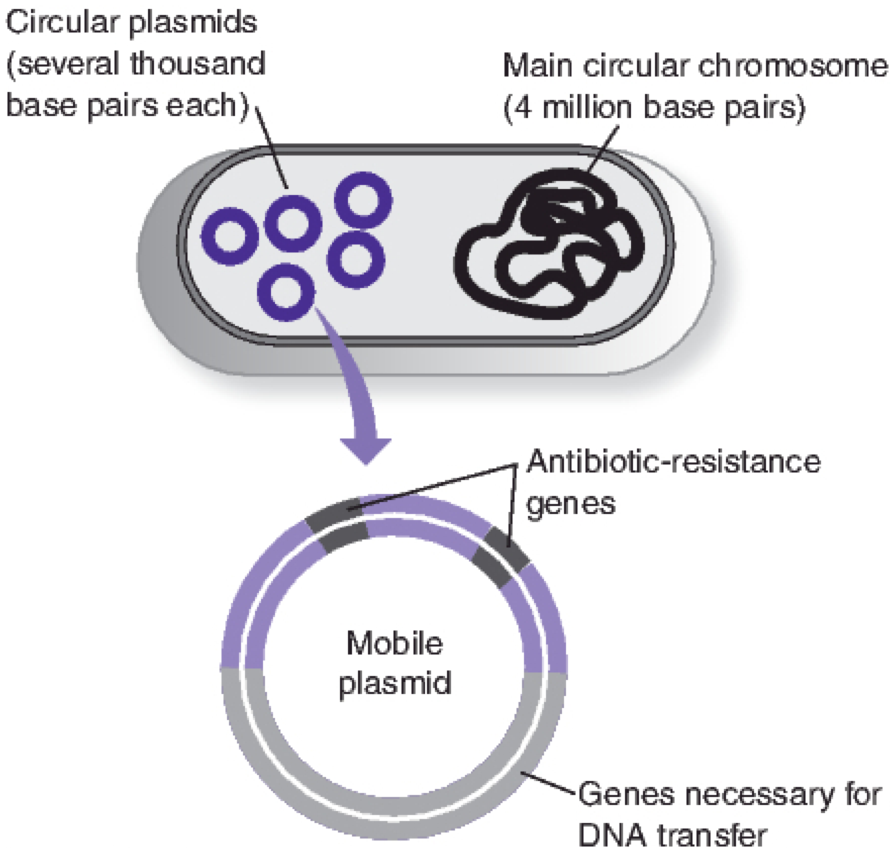
Genome Storage in Bacteria

Most of a bacteria's genome is stored in a single circular chromosome of dsDNA.

- Much smaller than eukaryotic genome

Bacterial genome can also contain **plasmids**

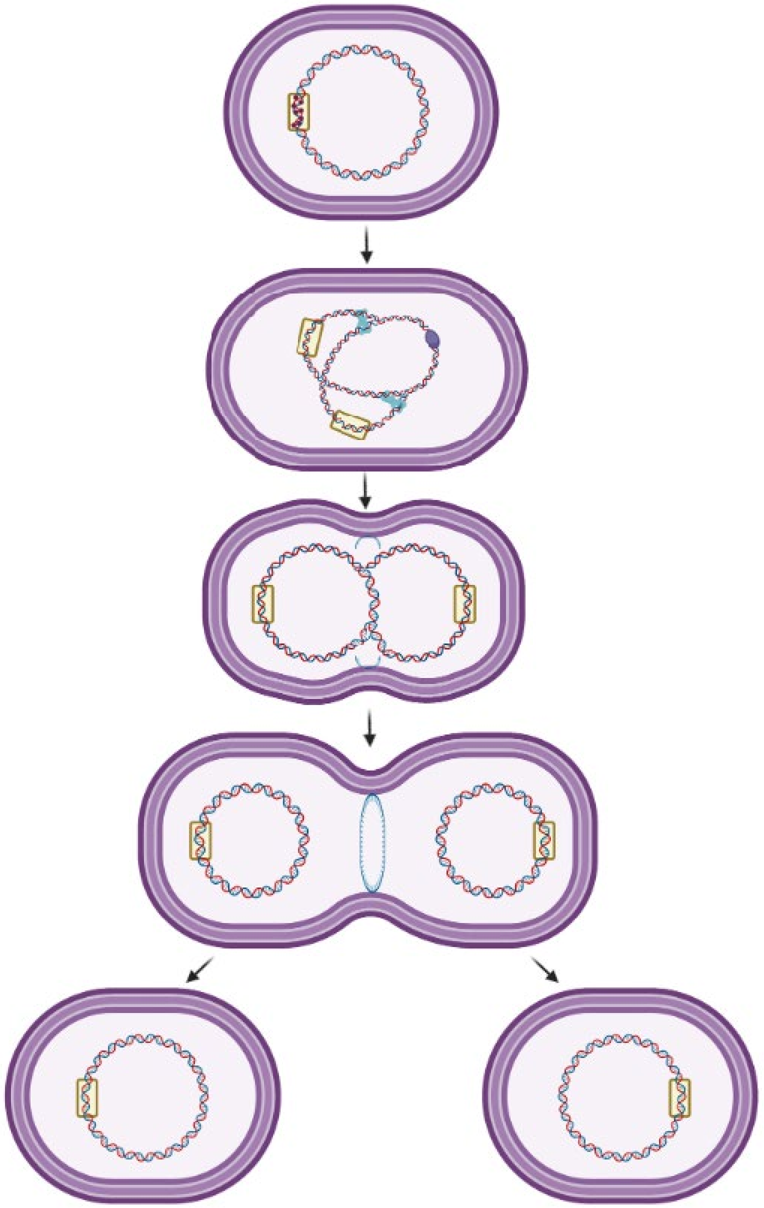
- Small, circular extrachromosomal dsDNA
- Capable of migration from one bacteria to another
- Carries genetic information (*e.g.*, antibiotic-resistance gene) that can be recombined into new host bacteria



Bacterial Replication

Bacteria multiply asexually by **binary fission**.

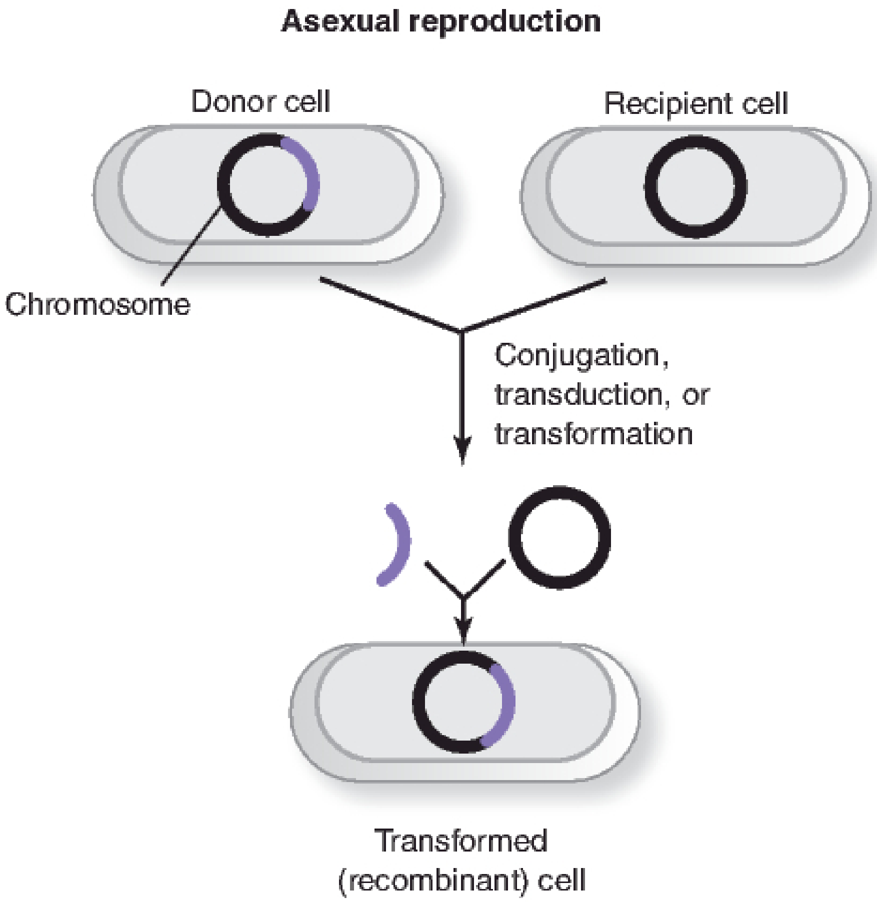
- Parent cell replicates its DNA bi-directionally
- Cell elongates and separates into two daughter cells



Recombination in Asexual Reproduction

Recombination in bacteria occurs in three ways:

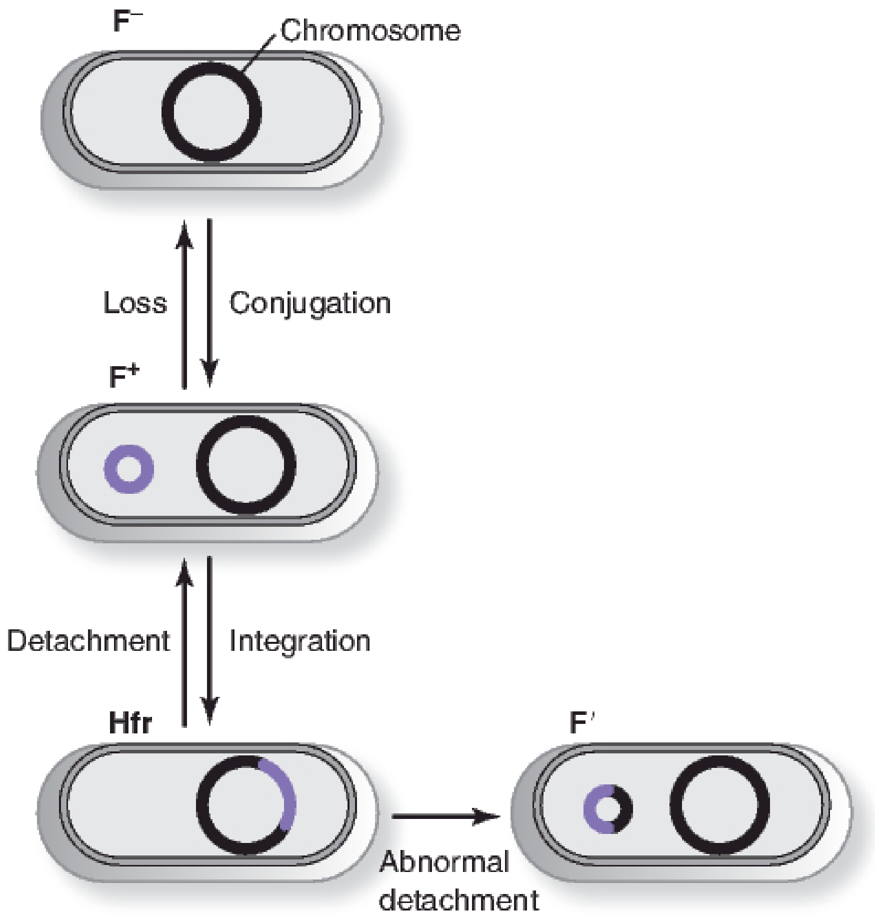
- **Conjugation**: transfer of genetic information by physical association of cells
- **Transduction**: transfer of genetic information from one cell to another through a viral intermediate
- **Transformation**: transfer of genetic information among cells without physical association, such that a new phenotype is produced in the recipient cells



Conjugation

Conjugation: transfer of genetic information by physical association of cells

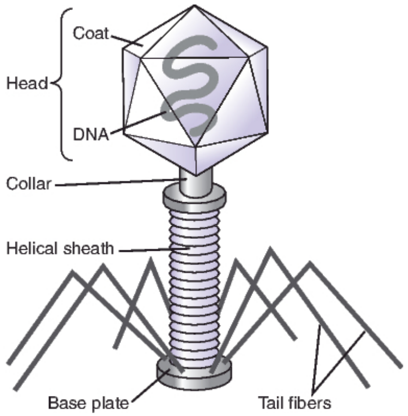
- Participatory bacteria can be defined as one of two "sexes": **F+** or **F-**
- "F" indicates the **fertility factor** (**F factor**), an extrachromosomal plasmid carrying genes necessary for construction of a filamentous bridge used for transfer of genetic material from the F+ to the F- cell
- Integration and detachment of F factor plasmid into host cell's chromosome allows for transfer of additional chromosomal material from F+ to F- cell

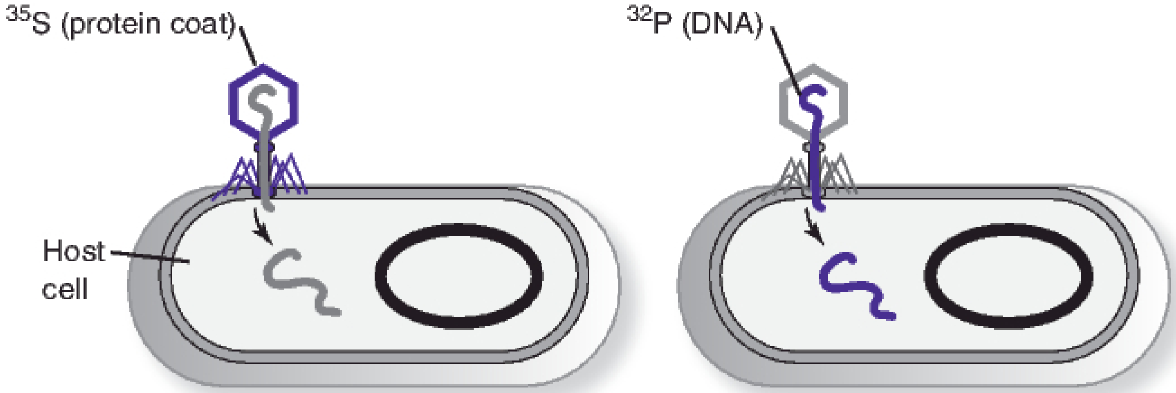


Transduction

Transduction: transfer of genetic information from one cell to another through a viral intermediate

- **Bacteriophages**, viruses that infect bacteria, inject their genome into the host cell and use host replicatory machinery for viral genome replication.
- Mediate indirect genetic exchange between bacterial genomes.
  - Viral genome integrated into host cell genome by infection
  - Host cell genes can become integrated into viral genome during viral replication
  - Original host cell genes, now integrated into viral genome, can be transferred into new bacterial host in subsequent infections

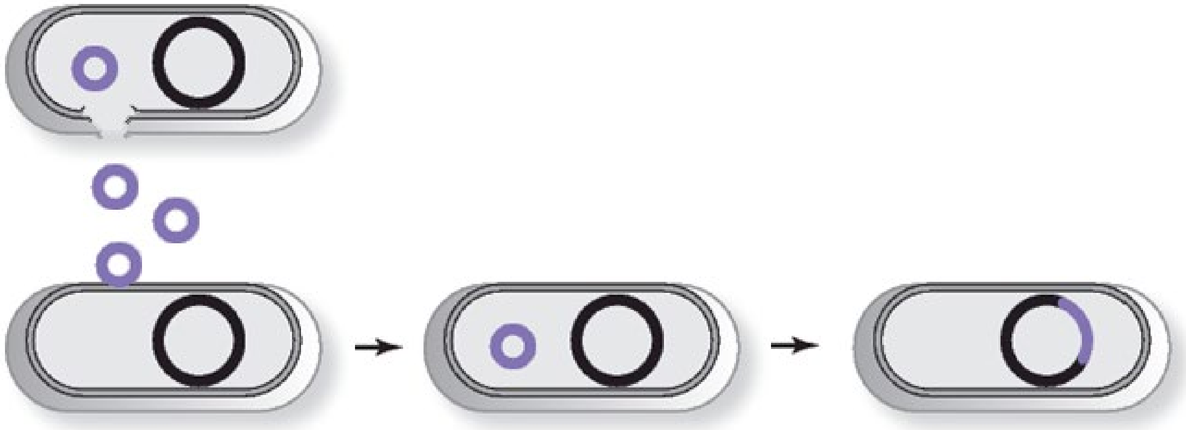




Transformation

Transformation: transfer of genetic information among cells without physical association, such that a new phenotype is produced in the recipient cells

- Lysed bacterial cell releases unprotected DNA or mobile plasmid into environment
- Unlysed, living bacterial cell can then take up genetic information and integrate it into its own genome



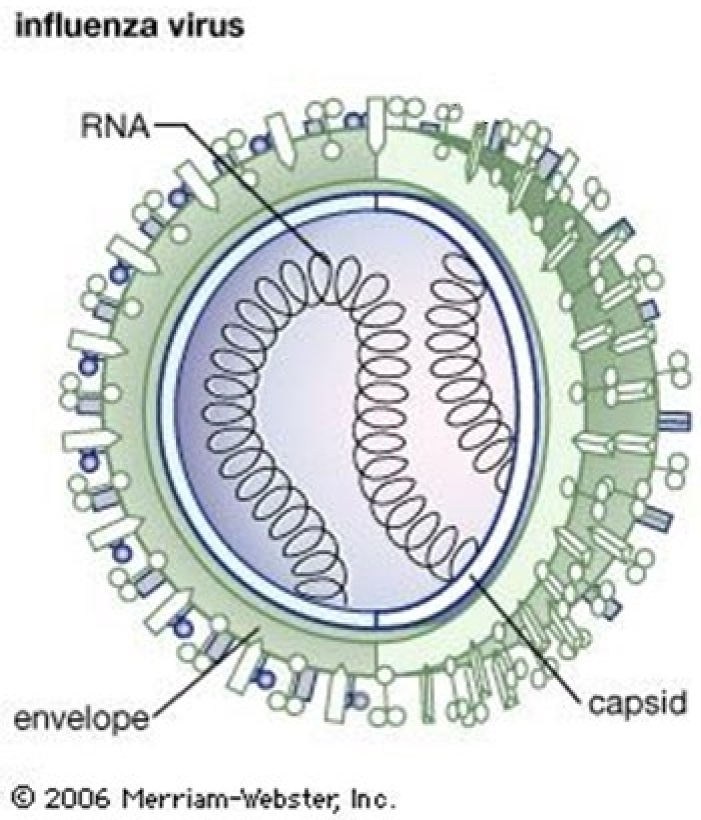
Viruses

Submicroscopic, obligate intracellular parasites

- Use host cell machinery to replicate and make energy
- Not technically "living" due to their inability to reproduce independently

Consists of:

- Nucleic acid core (RNA or DNA)
- Protein-containing **capsid** that surrounds and protects the core.
- Lipid-containing **envelope** that further (not all viruses are enveloped)



Genome Storage in Viruses

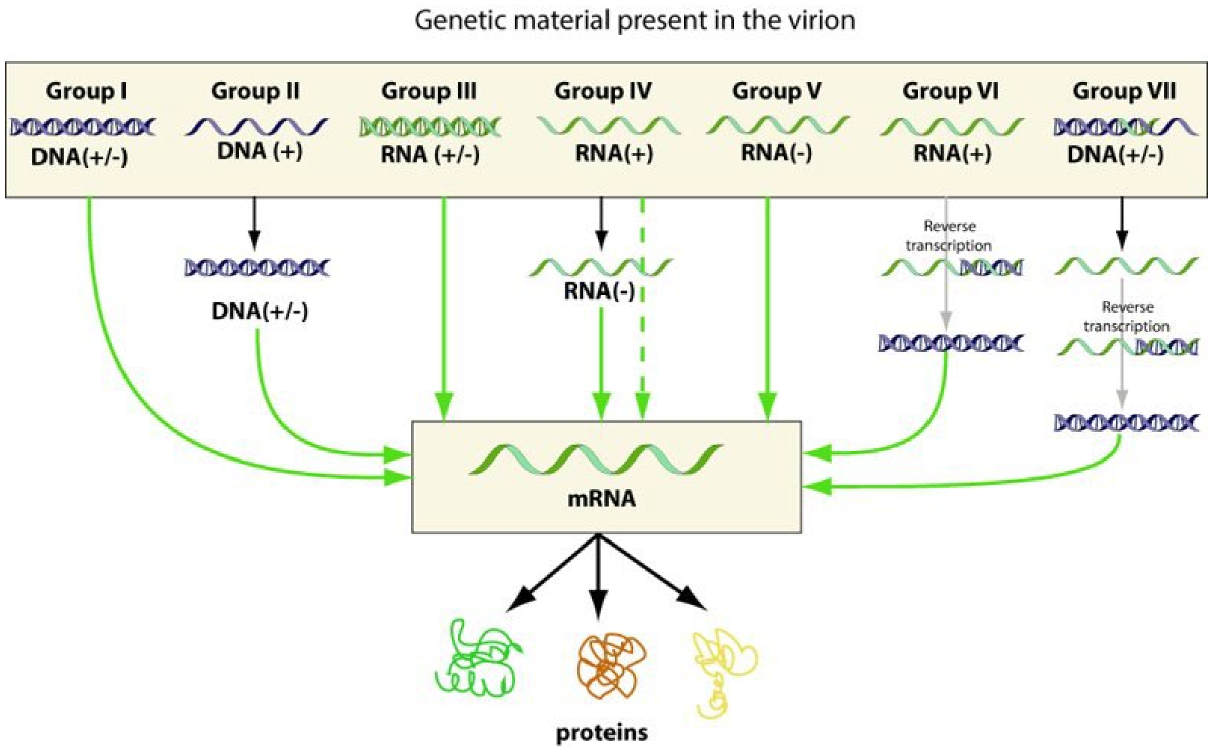
Viruses can be categorized by how they store their genetic material:

DNA vs. RNA

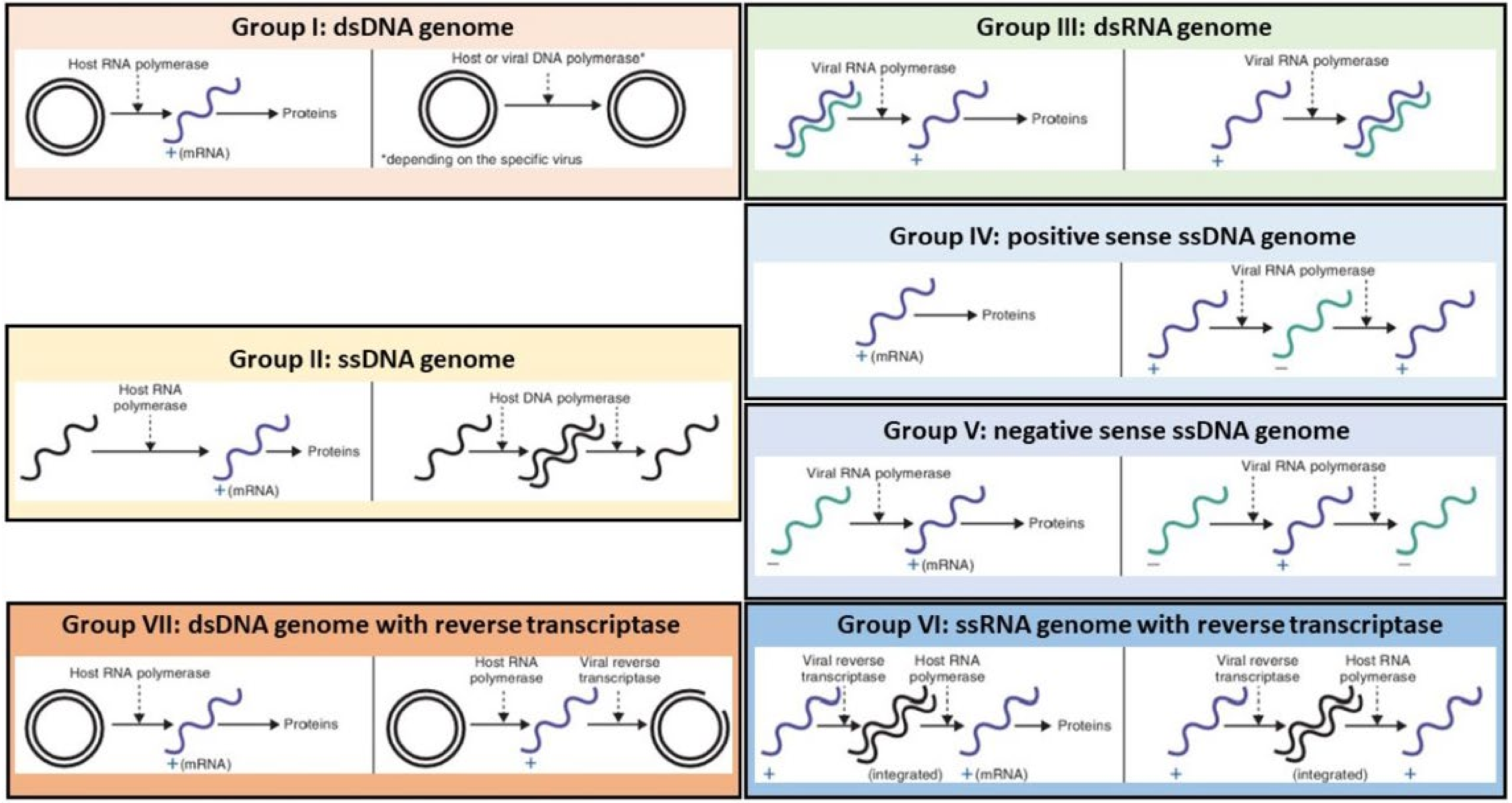
Single- vs. Double-stranded

Positive- vs. Negative- sense

- Positive-sense RNA can be immediately translated to protein by host cell
- Negative-sense RNA requires transcription into positive-sense RNA prior to translation



Viral Genome



Adapted from Schaechter's Mechanisms of Microbial Disease, 6th ed.

Questions?

EMAIL: POHLJ@CCF.ORG

WORK PHONE: 216 308-0801

This concludes the presentation.

CLEVELAND CLINIC CENTER FOR PATHOLOGY EDUCATION