BIO 201
INTRODUCTION TO GENETICS

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Lecture Guide

THE SCIENCE OF GENETICS

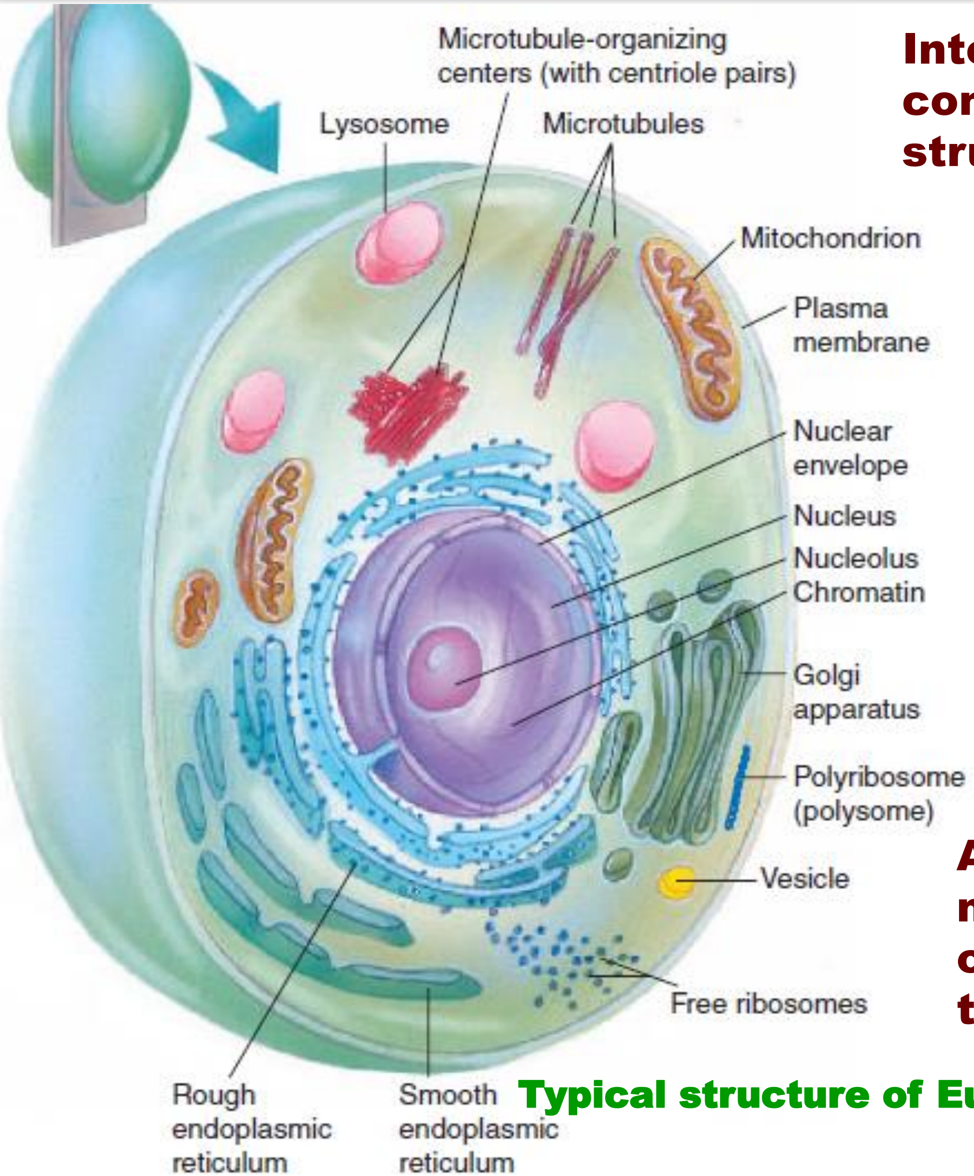
Genetics may be defined as the scientific study of heredity, or the study of how traits are inherited.

It is the field of Biology devoted to understanding how characteristics (traits) are transmitted from parents to offsprings.

Traits are controlled by factors known as genes (located on chromosomes), and are transmitted through gametes from generation to generation.

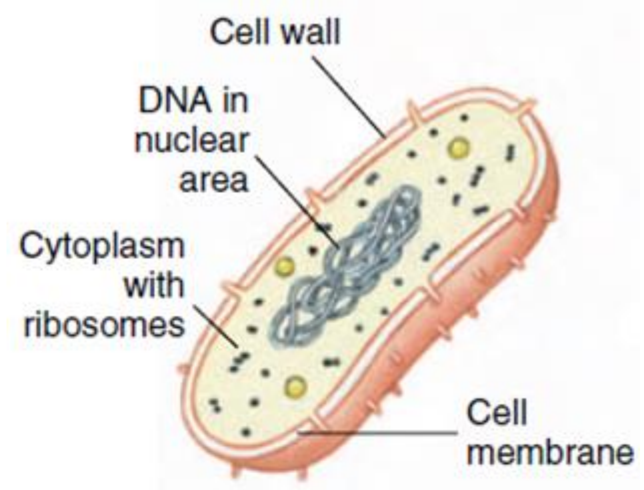
The material for heredity is also known as the Genetic material and it resides within the nucleus of Eukaryotic cells and within the nuclear zone in Prokaryotic cells.

TYPES OF CELL



Typical structure of Eukaryotic cell

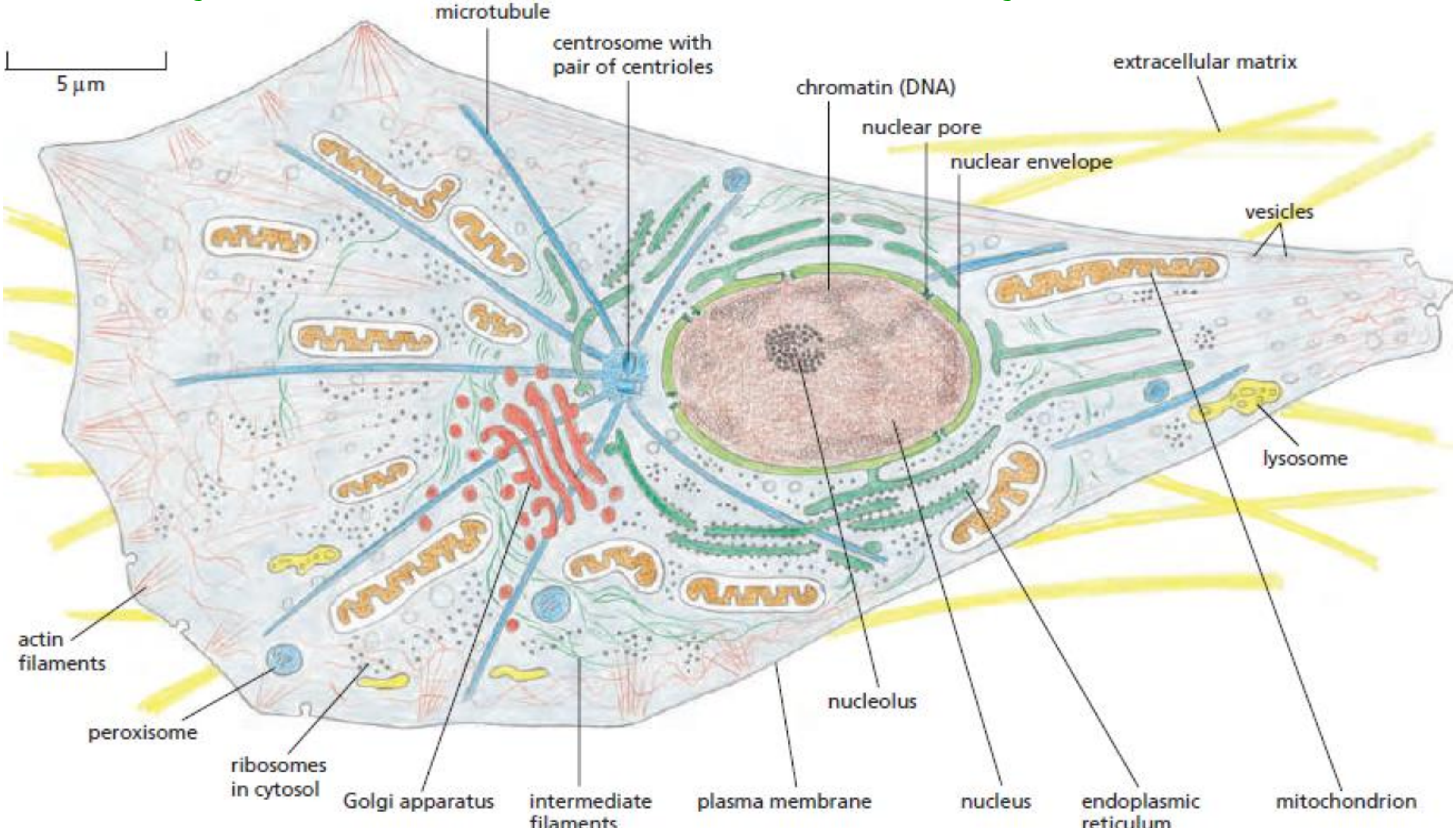
Internally, eukaryotic cells are more complex than prokaryotic cells- both structurally and functionally.



Typical structure of Prokaryotic cell

All Eukaryotic cells have membrane-bound nucleus and other membrane-bound organelles that perform specific functions.

Typical structure/features of a Eukaryotic cell



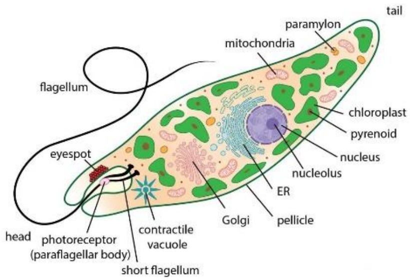
Eukaryotic cells, in general, are bigger and more elaborate than prokaryotic cells, and their genomes are bigger and more elaborate, too. The greater size is accompanied by radical differences in cell structure and function.

By definition, eukaryotic cells keep their DNA in an internal compartment called the nucleus. The nuclear envelope, a double layer of membrane, surrounds the nucleus and separates the DNA from the cytoplasm.

CELLULAR ORGANIZATION OF EUKARYOTES

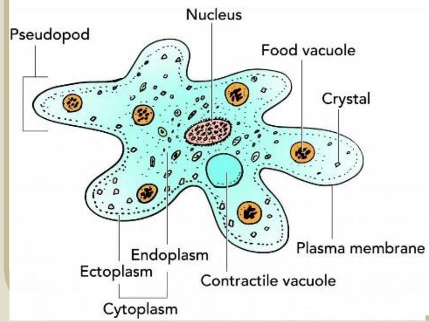
Eukaryotic organisms (Eukaryotes) may be classified as unicellular or multicellular.

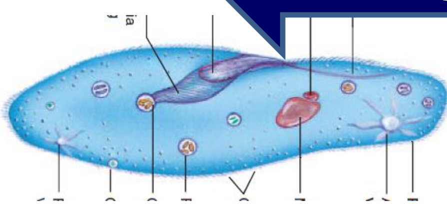
Unicellular organisms are made up of single eukaryotic cell. They are classified under the Kingdom Protista. Multicellular organisms on the other hand are made up of many cells, organised into tissues and organs, that perform specific functions. They may belong to one of the following three Kingdoms: Kingdom Plantae, Kingdom Fungi, or Kingdom Animalia.



Eukaryotes

Prokaryotes





THE GENETIC MATERIAL

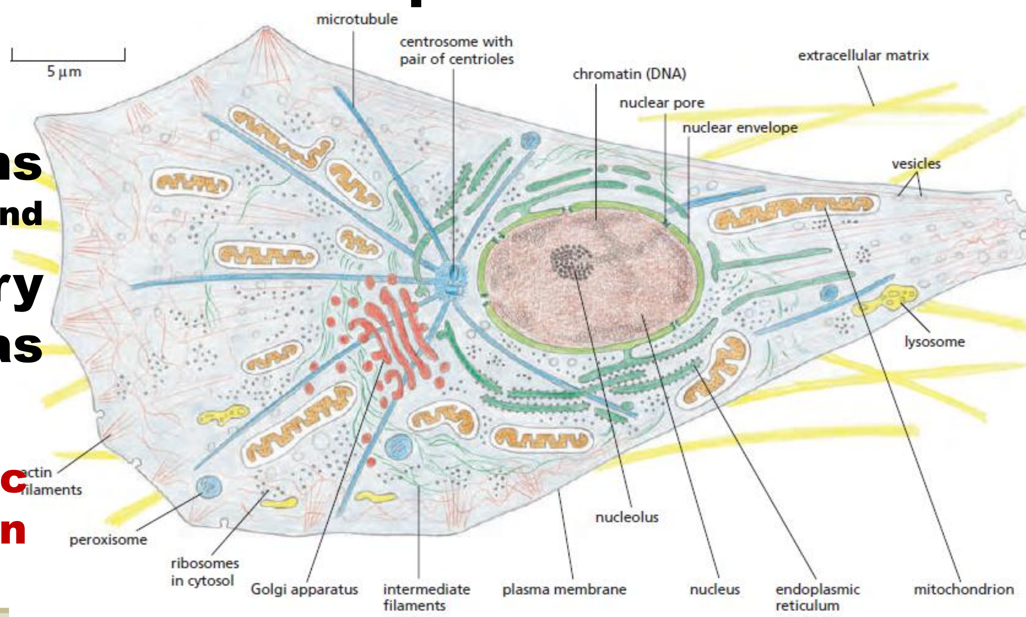
Although life is characterized by tremendous diversity, the coding instructions of all living organisms are written in the same genetic language- that of nucleic acids (DNA or RNA).

In all cellular organisms, the genetic material is DNA.

Several lines of indirect evidence suggested that DNA harbours the genetic information of living organisms. For example, most of the DNA of cells is located in the chromosomes (which resides in the nucleus), whereas RNA and proteins are abundant in the cytoplasm.

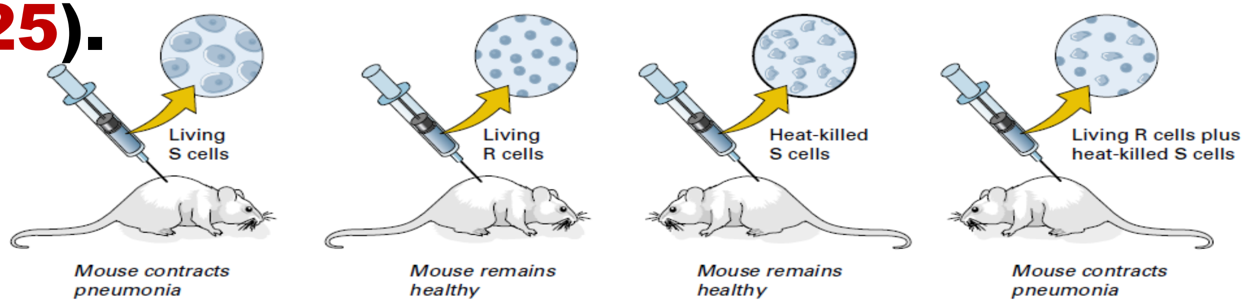
Several line of investigations were conducted in the 2nd quarter of the 20th Century which showed that DNA was truly the genetic material.

The nucleus is where the genetic material (Genomic DNA) of an organisms resides.

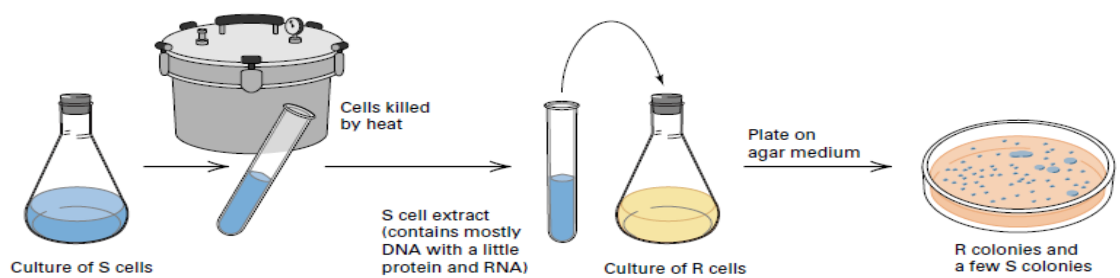


THE GENETIC MATERIAL

Sir Frederick Griffith demonstrated transformation in bacterial (1925).



Oswald Avery, Colin MacLeod, and Maclyn McCarty- demonstrated that the transformation material is DNA (1944).



Alfred Hershey and Martha Chase provided convincing evidence that DNA is the genetic material (1952).

FUNCTIONS OF THE GENETIC MATERIAL

The genetic material must be able to perform three essential functions:

The Genotypic function (Storage & Replication) The genetic material must store genetic information and accurately transmit that information from parents to offspring, from one generation to another.

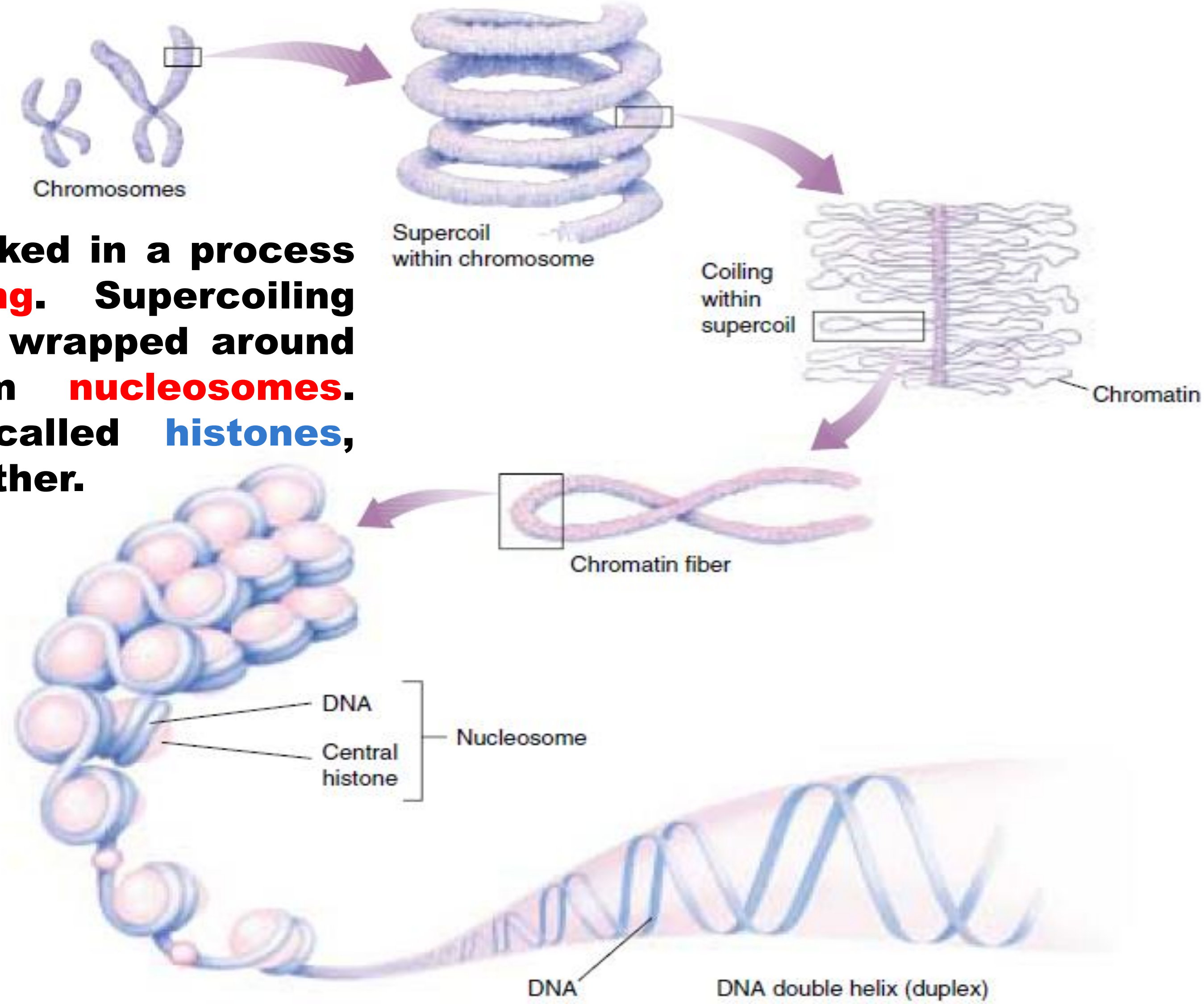
The Phenotypic function (Gene expression) The genetic material must control the development of the phenotype of the organism – it must dictate the growth of the organism from the single-celled zygote to the mature adult.

The Evolutionary function (Mutation)

The genetic material must allow for necessary changes to produce variations that allow organisms to adapt to modifications in the environment so that evolution can occur.

The Chromosome

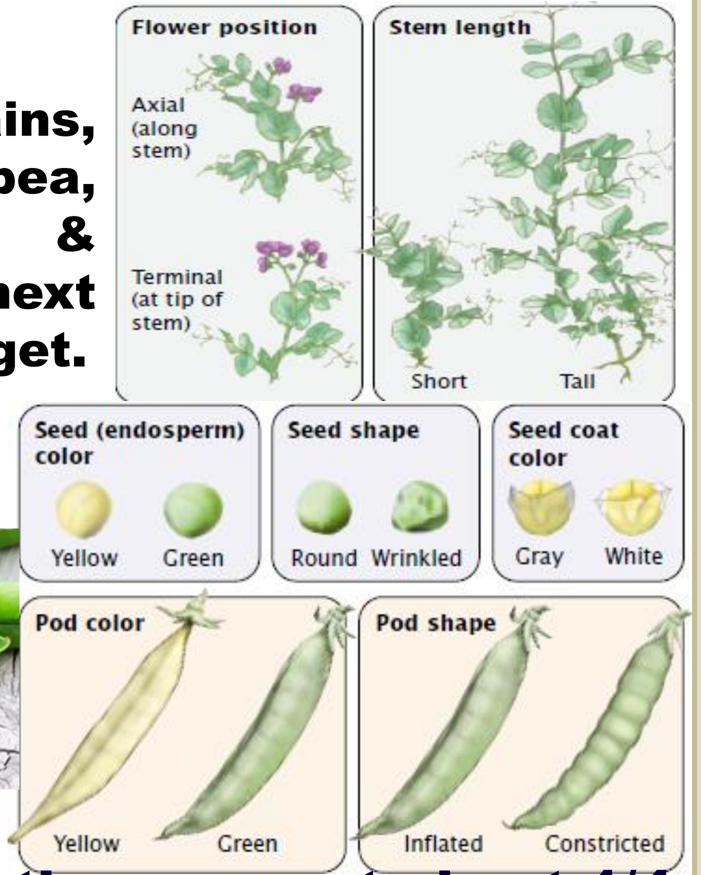
DNA is tightly packed in a process called supercoiling. Supercoiling allows DNA to be wrapped around proteins to form nucleosomes. Other proteins, called histones, hold the coils together.

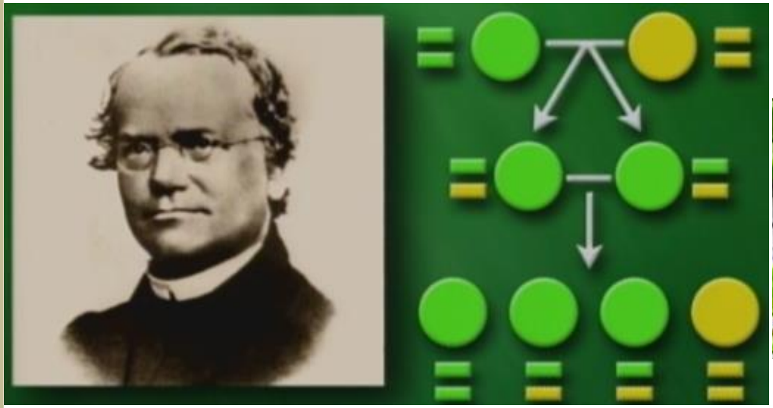


MENDELS EXPERIMENTS

The modern approach to genetics can be traced to the mid-nineteenth century with Gregor Mendel's careful analyses of inheritance in peas.

The idea of taking two pure-breeding strains, in this case, green pea and yellow pea, crossing them together & observing & counting in the next generation and the next generation, how many of each colour you get.

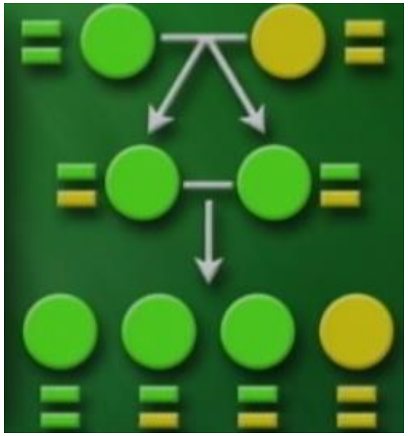




He observed that in the second generation, you get about 1/4 of yellow peas. Mendel's incredible clarity really organized the ideas of genetics for us.

LAWS OF INHERITANCE

1. The characteristics of a diploid organism are determined by alleles which occur in pairs. Of a pair of such alleles, only one can be carried in a single gamete.



2. Each of a pair of alleles for a particular gene can combine randomly with either of another pair of alleles for a different gene.

CONCEPTS & DEFINITIONS

A gene is the fundamental unit of heredity.

Genes come in multiple forms called alleles.

Genes encode phenotypes.

The genetic information that an individual organism possesses is its genotype while the trait (physical characteristics) is its phenotype.

Genes are located on chromosomes.

Chromosomes are made up of DNA and associated proteins called Histones.

The cells of each species have a characteristic number of chromosomes. for example, bacterial cells normally possess a single chromosome; human cells possess 46 chromosomes; pigeon cells possess 80 chromosomes.

Cells can be categorized into Somatic cells and gametes

Chromosomes can be categorized into Autosomes and sex chromosomes

Chromosomes separate through the processes of mitosis and meiosis.
Genetic information is transferred from DNA to RNA to protein.

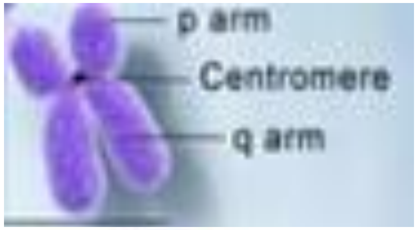
INFORMATION MACROMOLECULE

DNA resides in the nucleus of Eukaryotic organisms in structures known as Chromosomes.

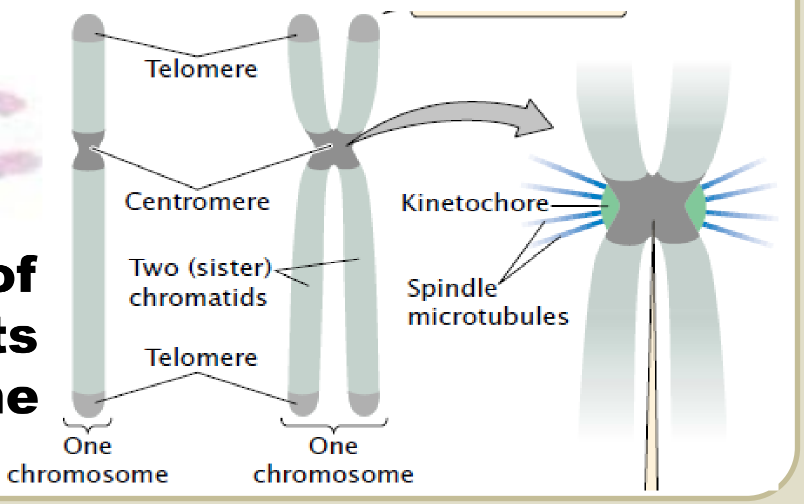
Chromosomes consists of DNA coiled many times around proteins called histones that stabilize their structure.

Chromosomes have centromeres, which are points at which they constrict and divides the chromosomes into two sections or arms.

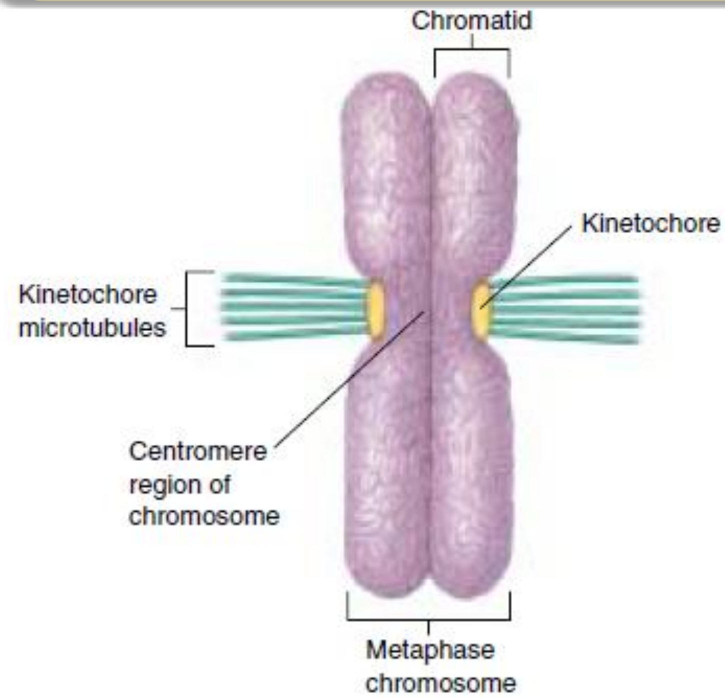
The short arm is labeled the "p arm", the long "q arm". Centromere location gives the chromosome its characteristic shape.

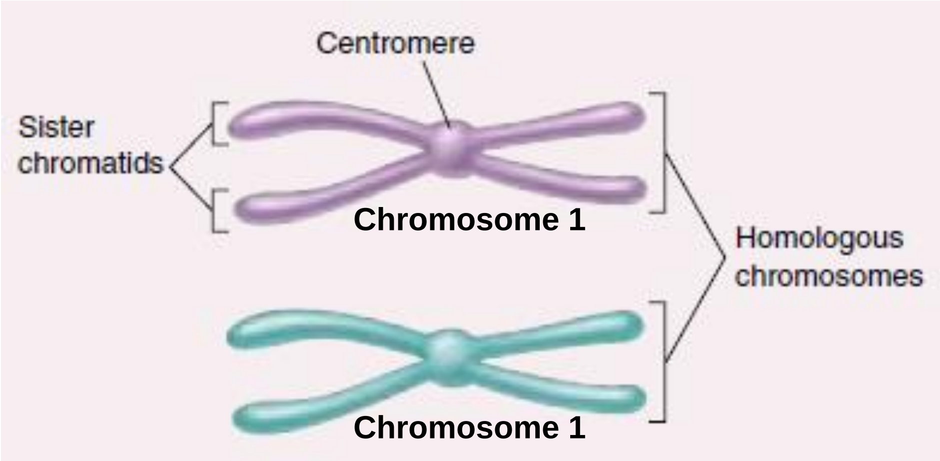


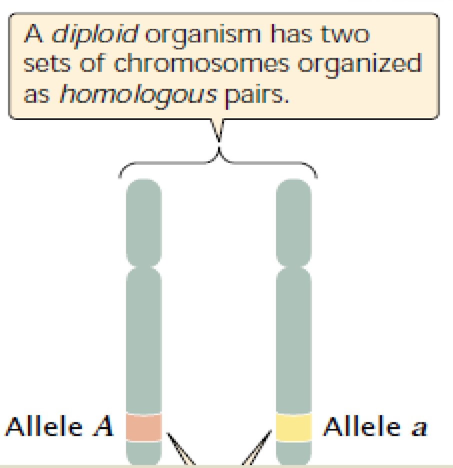
Chromatin is the general structure of any chromosome, and the basic units are nucleosome (DNA + Histone proteins)

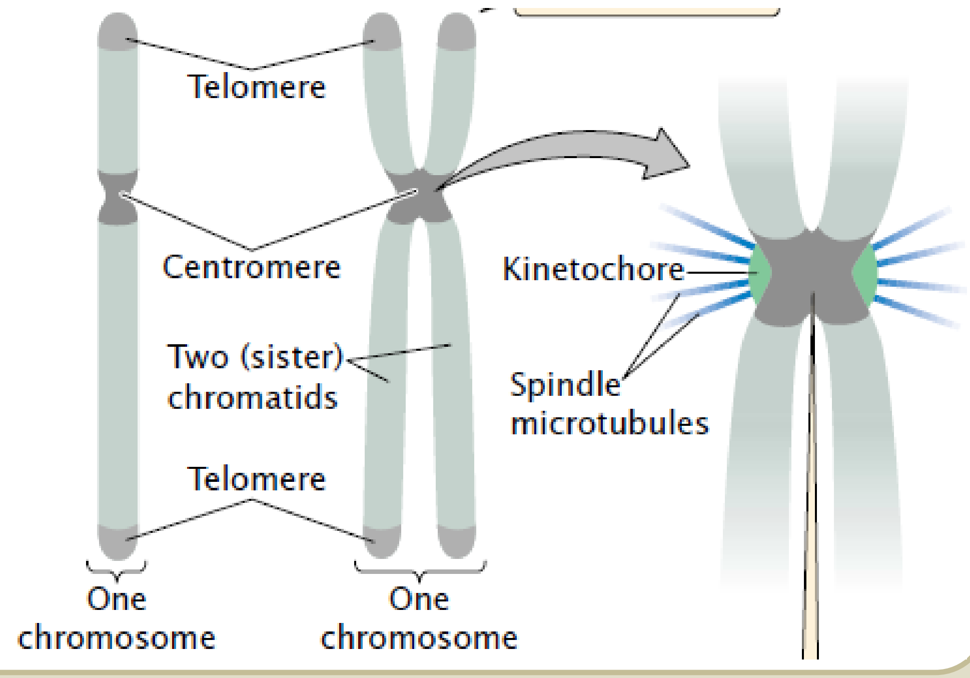


The Chromosome









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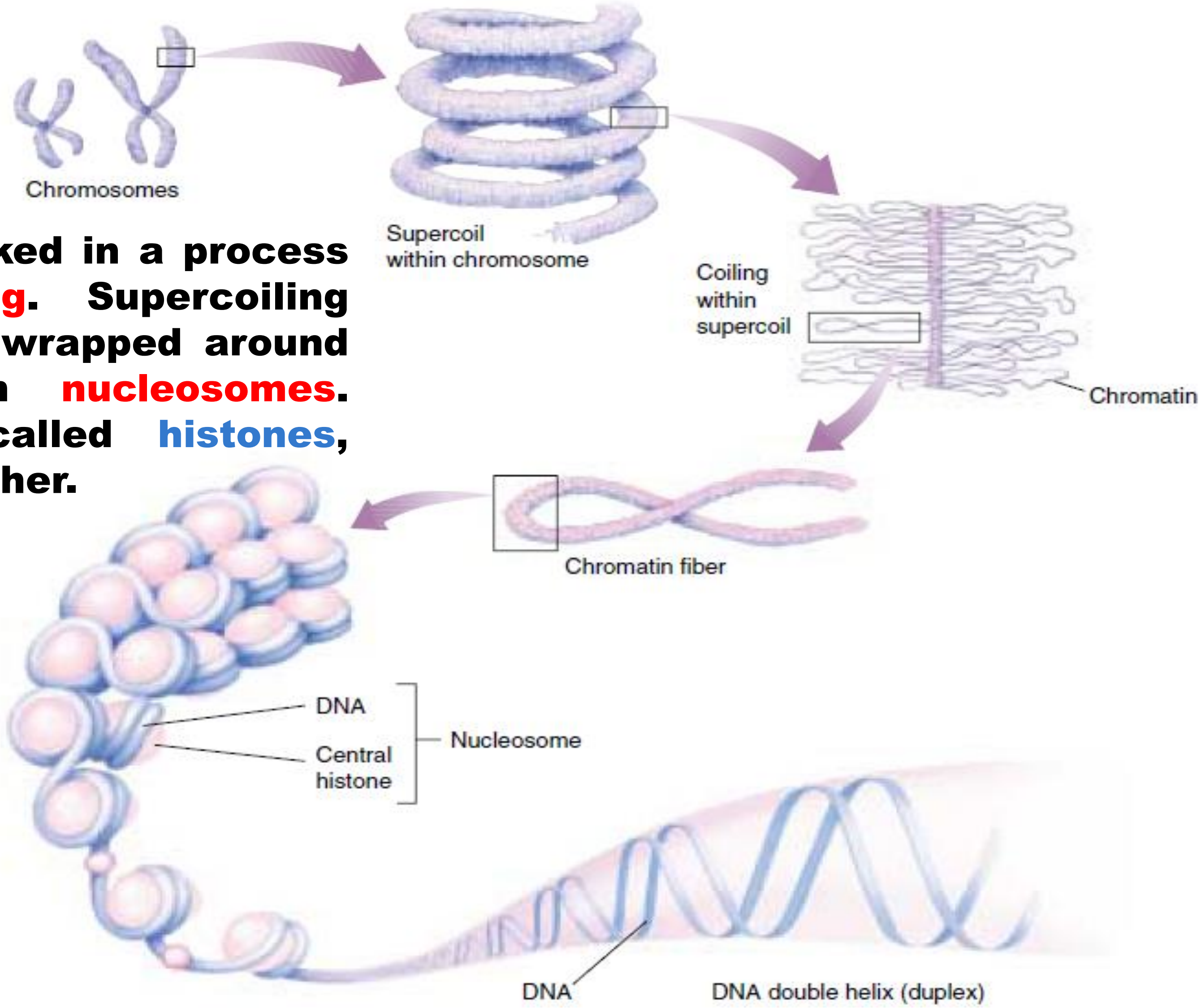
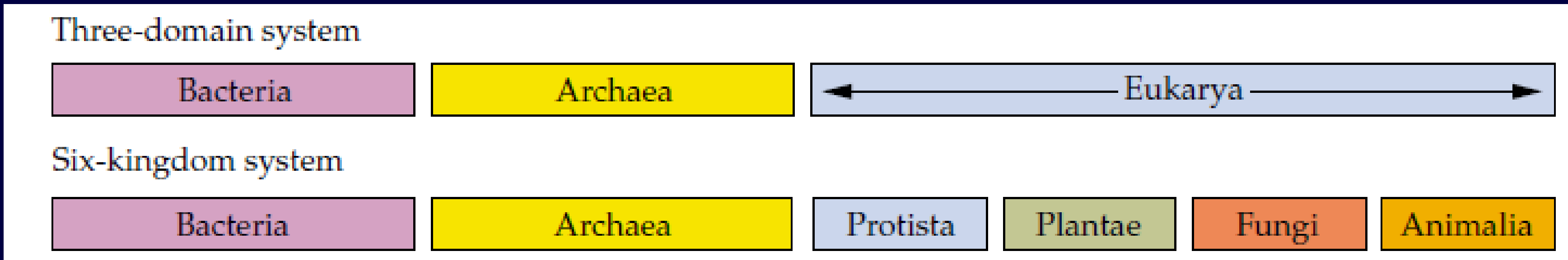
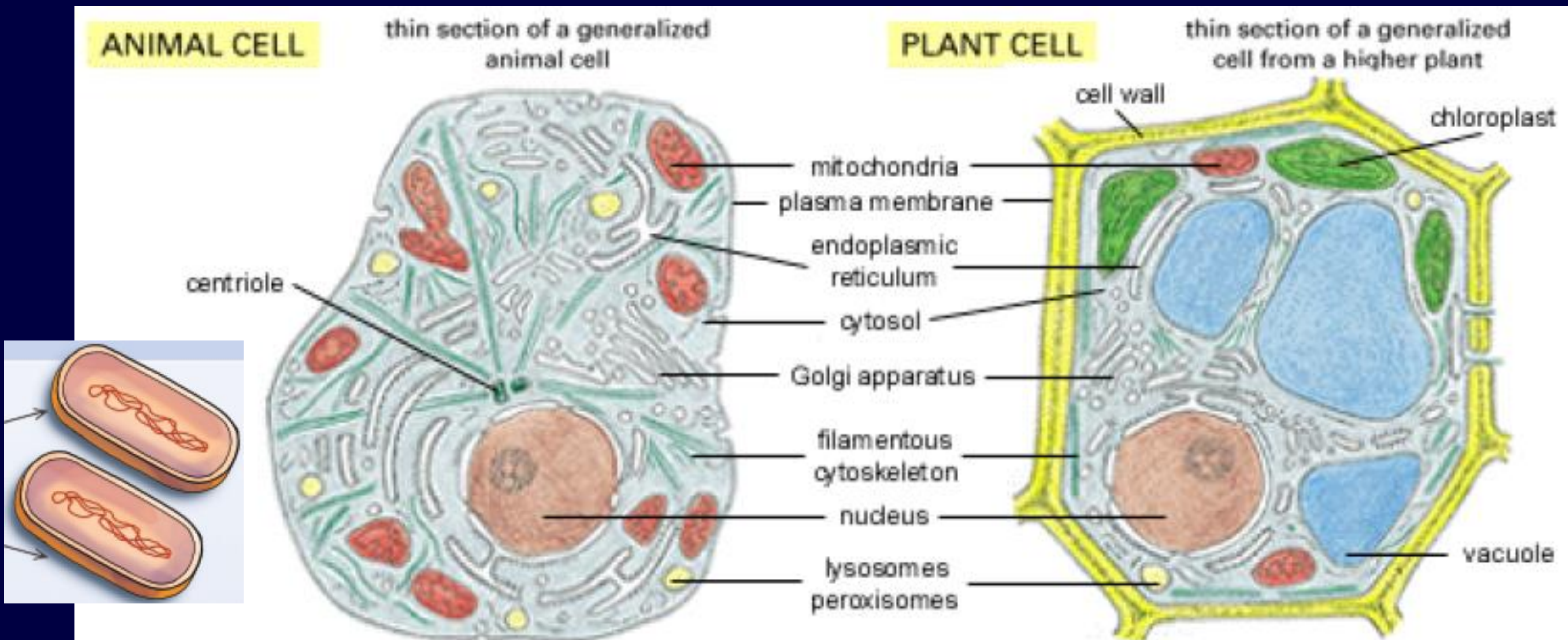


DNA IN LIVING ORGANISMS



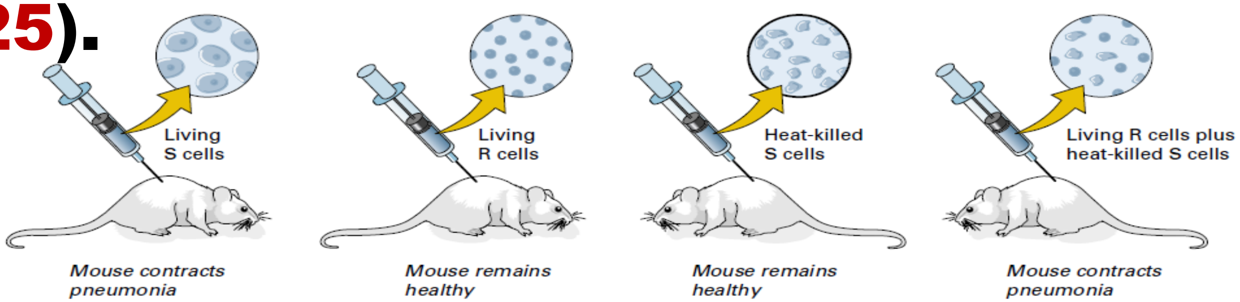


Most organisms carry their genetic information as DNA, but a few viruses carry it as RNA.

In Eukaryotes, individual DNA molecules are found in the chromosomes of the nucleus and in mitochondria, and also in the chloroplast of plant cells.

THE GENETIC MATERIAL

Sir Frederick Griffith demonstrated transformation in bacterial (1925).



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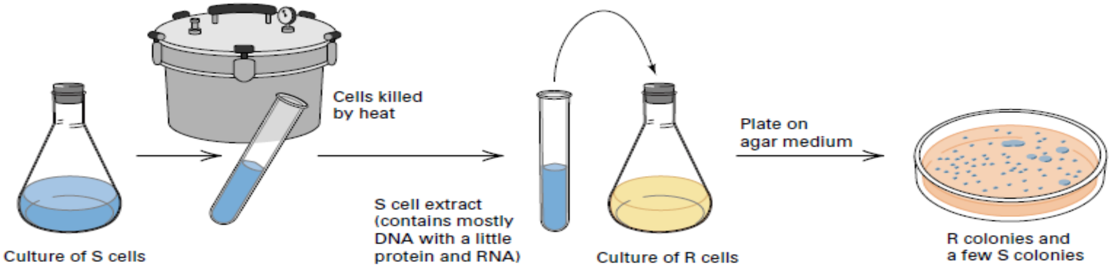


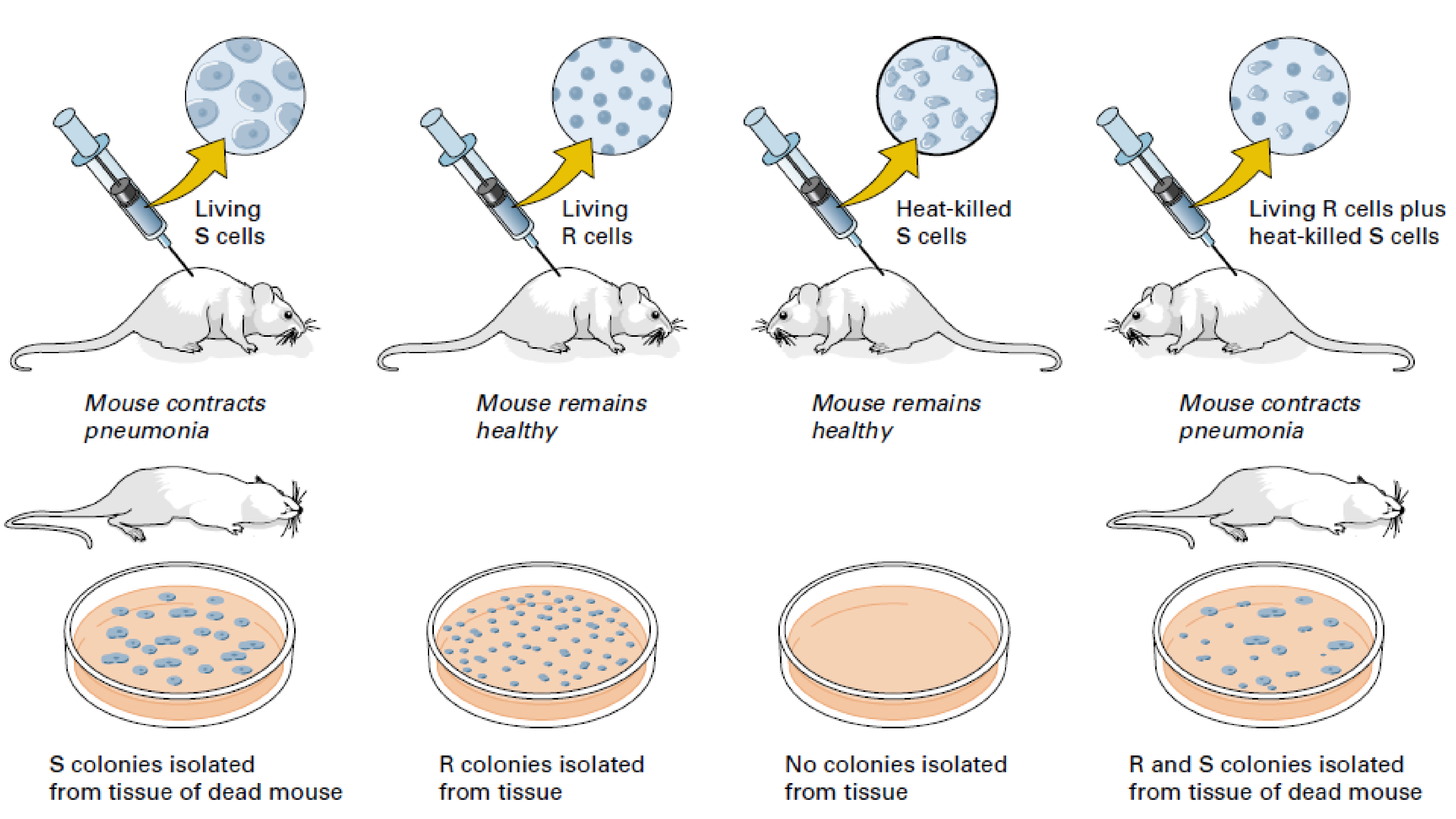
Alfred Hershey and Martha Chase provided convincing evidence that DNA is the genetic material (1952).

THE GENETIC MATERIAL

The first clue that DNA was the carrier of hereditary information came with the demonstration that DNA was responsible for a phenomenon called *transformation*. *The phenomenon* was first observed in 1928 by Sir Frederick Griffith, an English physician whose special interest was the bacterium that causes pneumonia, *Streptococcus pneumonia.*

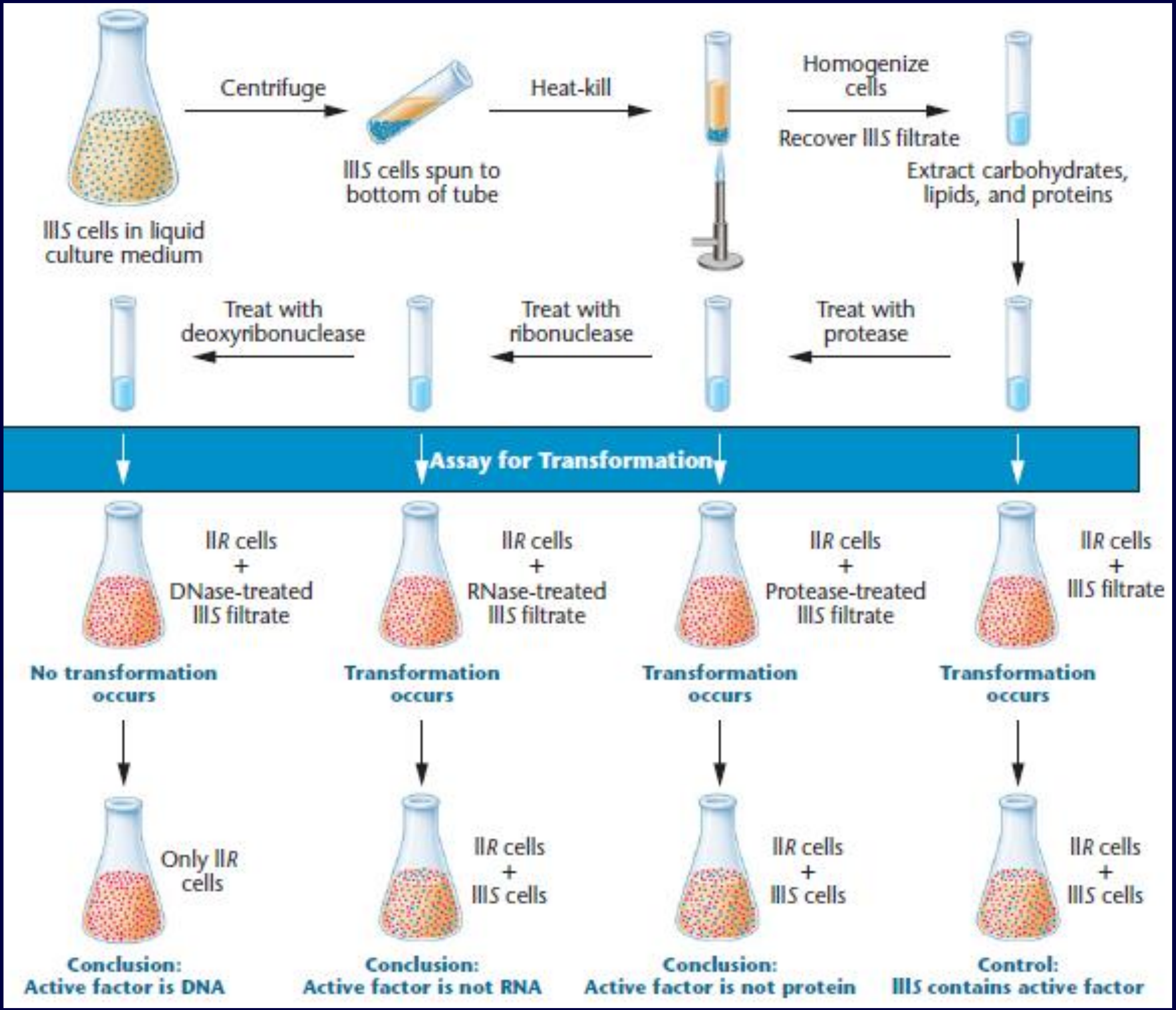
***Griffith had* succeeded in isolating several strains of *S. Pneumonia* (type I, II, III, and so forth). In the virulent (disease-causing) forms of a strain, each bacterium is surrounded by a polysaccharide coat, which makes the bacterial colony appear smooth when grown on an agar plate; these forms are referred to as S, for smooth. Griffith found that these virulent forms occasionally mutated to non-virulent forms, which lack a polysaccharide coat and produce a rough appearing colony on an agar plate; these forms are referred to as R, for rough.**

Griffith's transformation experiment



The Griffith's experiment demonstrating bacterial transformation. A mouse remains healthy if injected with either the nonvirulent R strain of *S. pneumoniae or heat-killed cell fragments* of the usually virulent S strain. R cells in the presence of heat-killed S cells are transformed into the virulent S strain, causing pneumonia in the mouse.

The Avery, MacLeod, and McCarty Experiment



A diagram of the Avery–MacLeod–McCarty experiment that demonstrated that DNA is the active material in bacterial transformation.

(A) The transforming activity is not destroyed by either protease or RNase.

(B) The transforming activity is not destroyed by either protease or RNase.

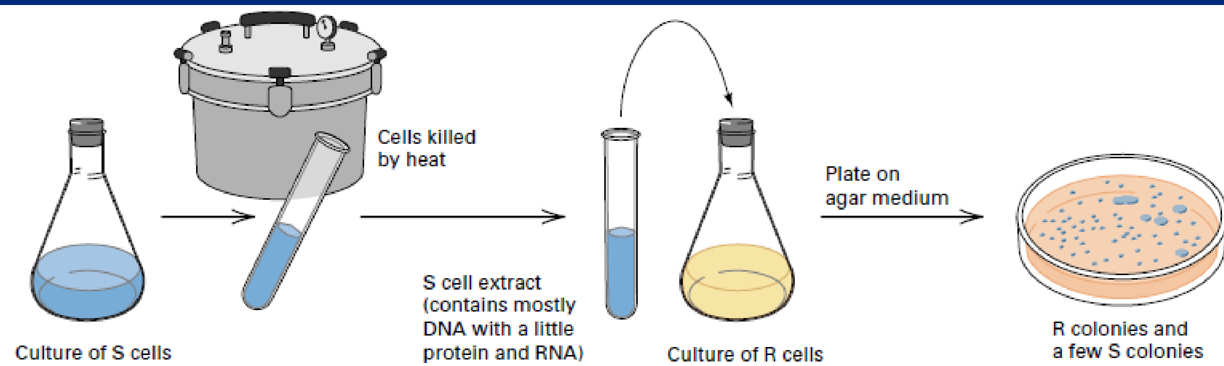
(C) The transforming activity was destroyed by DNase and so probably consists of DNA.

<u>Conclusion:</u> The evidence presented supports the belief that a nucleic acid of the deoxyribose type is the fundamental unit of the transforming principle of Pneumococcus Type IIIS

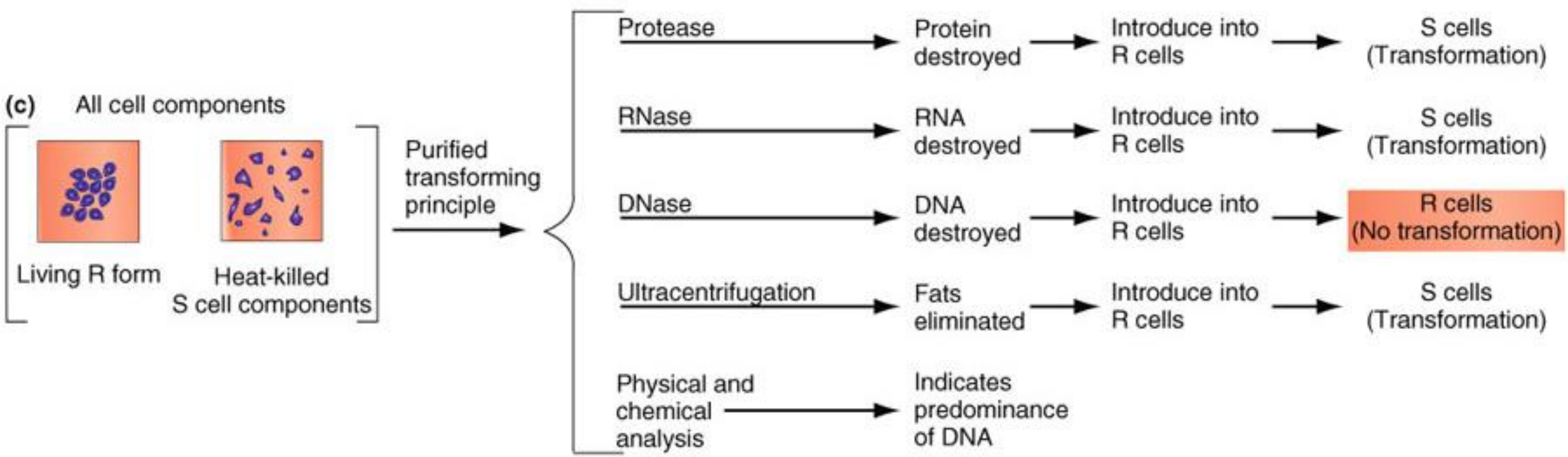
The Avery, MacLeod, and McCarty Experiment

Experiment

Question: What is the chemical nature of the transforming substance?



The transforming activity in S cells is not destroyed by heat.

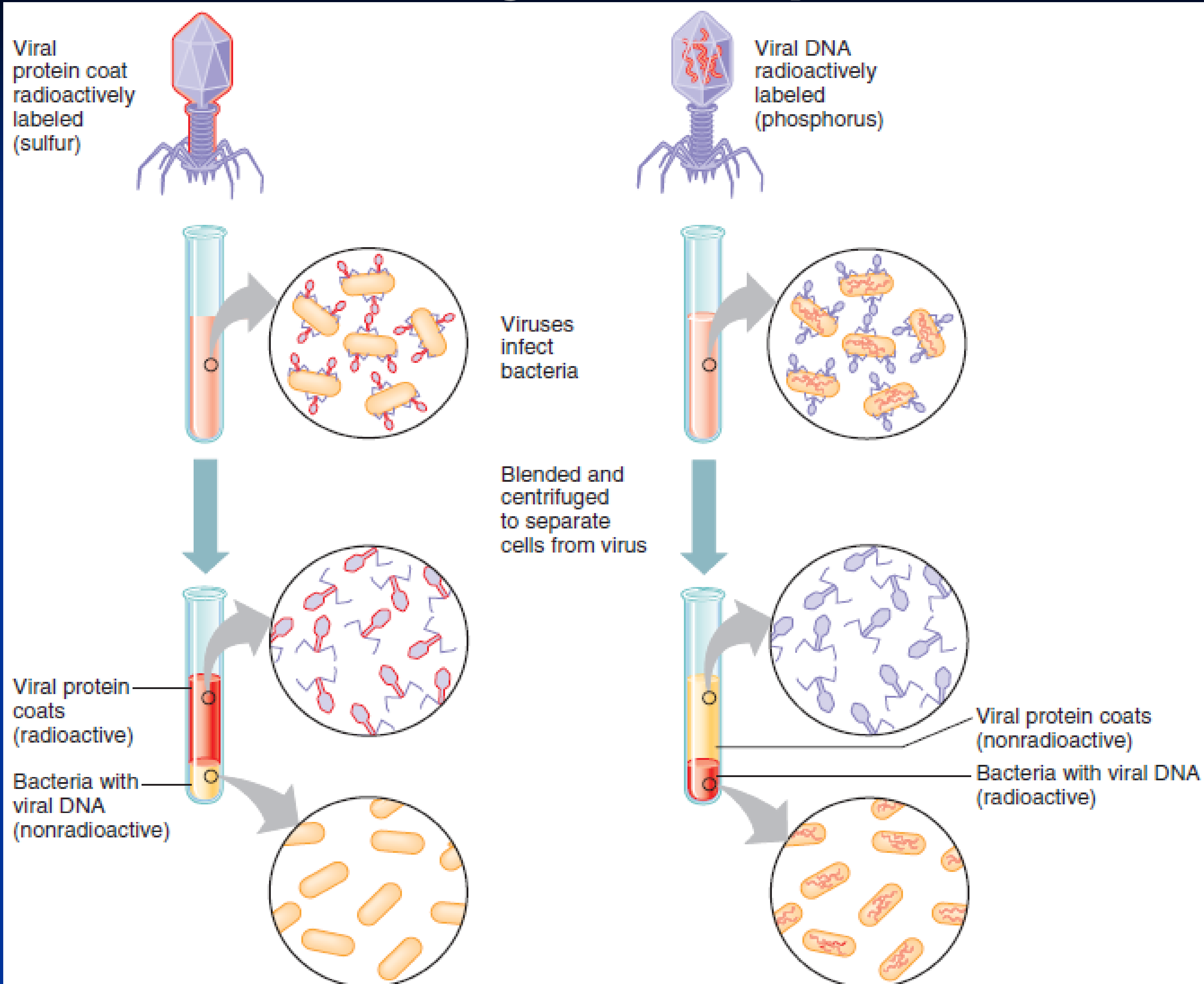


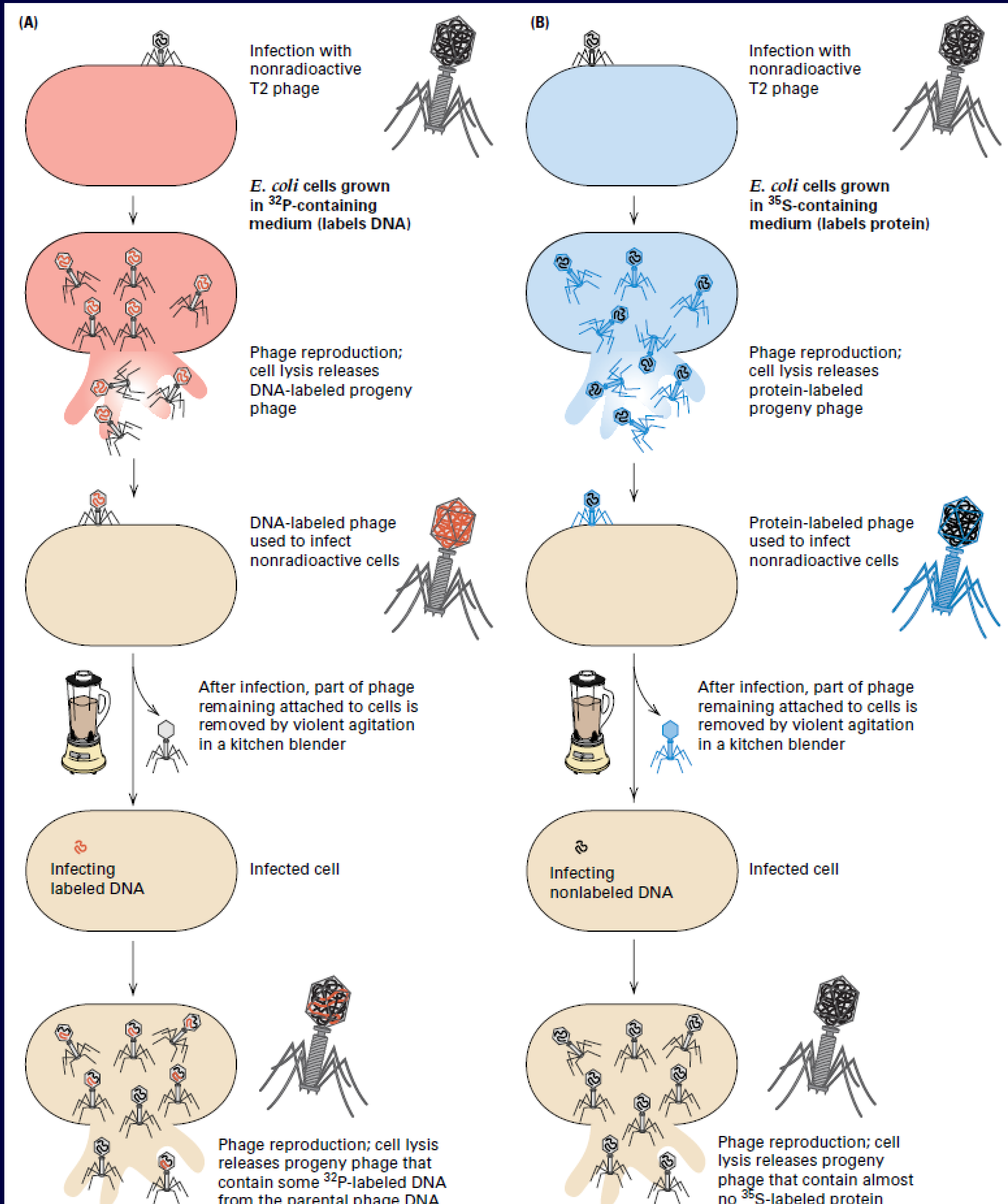
Hershey and Chase experiments

- 1952 – Alfred Hershey and Martha Chase provide convincing evidence that DNA is genetic material
- Performed experiment using T2 bacteriophage and bacteria
- Radioactive labels ^{32}P for DNA and ^{35}S for protein

Hershey and Chase designed a series of experiments to determine whether the phage protein or the phage DNA was transmitted in phage reproduction. To follow the fate of protein and DNA, they used radioactive forms (isotopes) of phosphorus and sulfur. A radioactive isotope can be used as a tracer to identify the location of a specific molecule, because any molecule containing the isotope will be radioactive and therefore easily detected. DNA contains phosphorus but not sulfur; so Hershey and Chase used ^{32}P to follow phage DNA during reproduction. Protein contains sulfur but not phosphorus; so they used ^{35}S to follow the protein.

The Hershey–Chase Experiment





The Hershey–Chase Experiment

The Hershey–Chase ("blender") experiment demonstrating that DNA, not protein, is responsible for directing the reproduction of phage T2 in infected *E. coli* cells.

(A) Radioactive DNA is transmitted to progeny phage in substantial amounts. ^{32}P

(B) Radioactive protein is transmitted to progeny phage in negligible amounts. ^{35}S

FUNCTIONS OF THE GENETIC MATERIAL

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DNA STRUCTURE & FUNCTION

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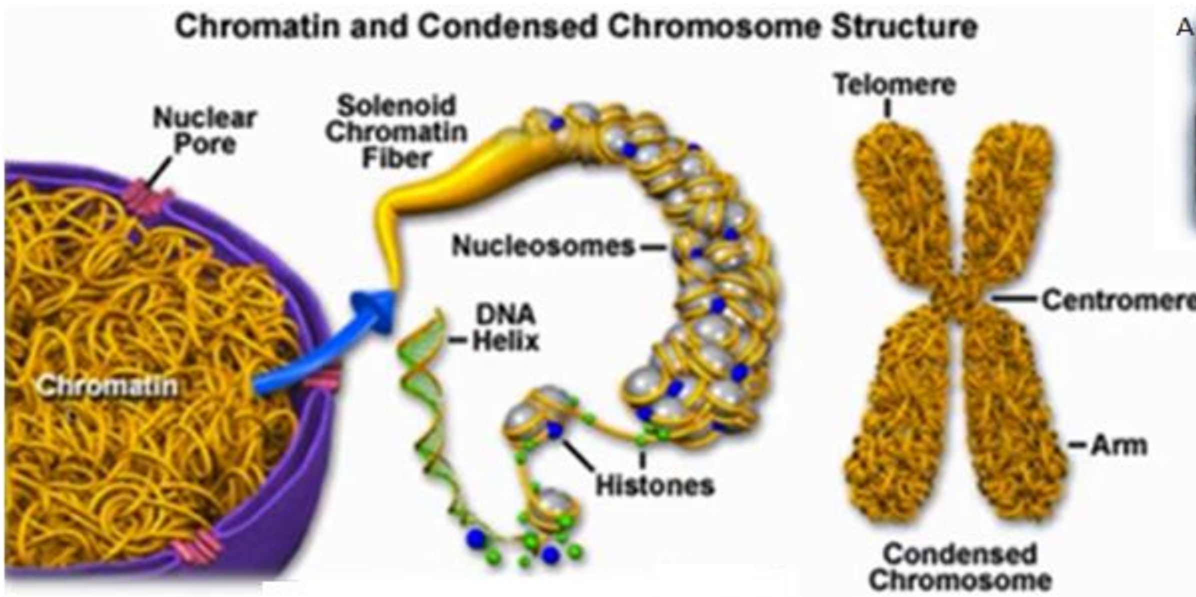
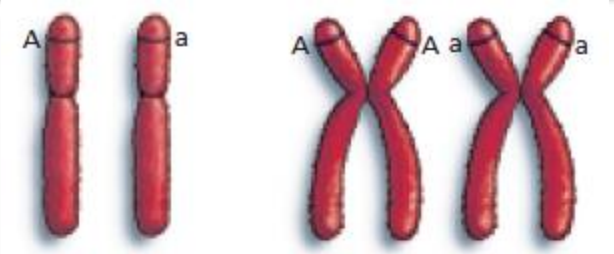
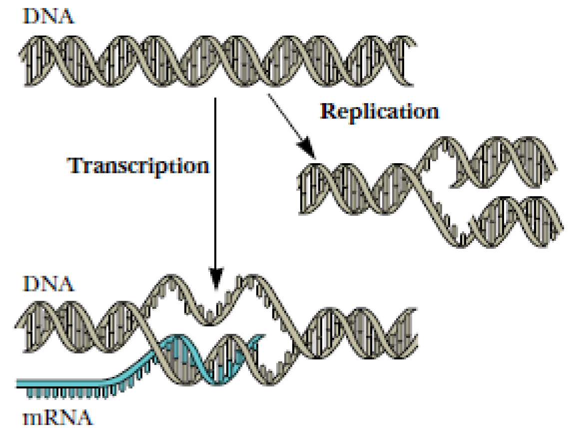
CELL: DNA FUNCTIONS







The Genotypic function

Stores and transmit (replicate) genetic information

The Phenotypic function (Gene expression)

Specifies protein synthesis (Transcription & Translation), determines characteristics/traits, controls growth

The Evolutionary function

Maintains genetic integrity, allows for adaptation

GENETIC MATERIAL & NUCLEIC ACIDS

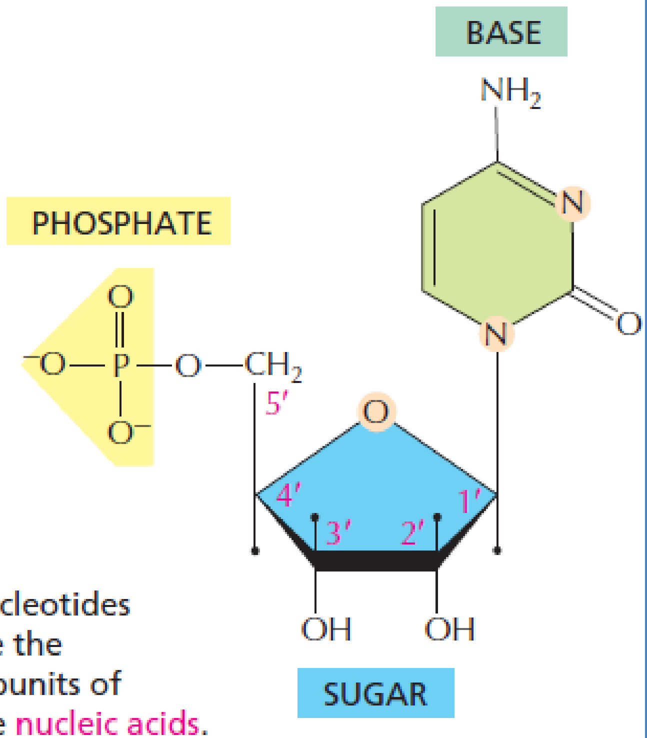
We have established from three experiments discussed in the previous class that DNA is the Genetic Material.

However, genetic information may be carried in DNA or RNA. DNA and RNA are referred to as Nucleic acids.

The basic building block of nucleic acids (DNA or RNA) is nucleotide.

NUCLEOTIDES

A nucleotide consists of a nitrogen-containing base, a five-carbon sugar, and one or more phosphate groups.



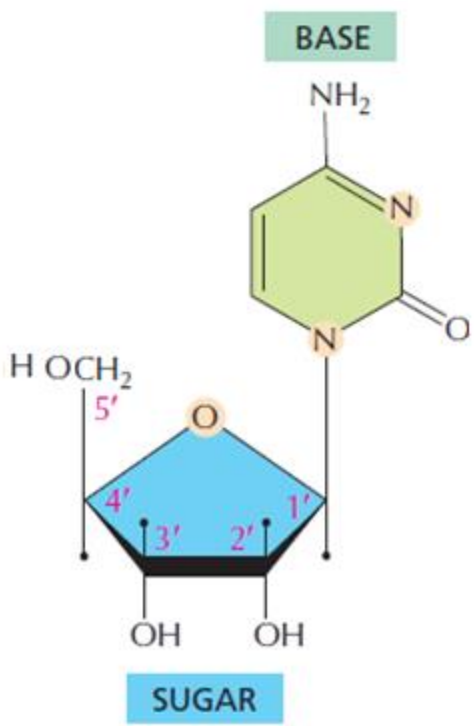
Nucleotides are the subunits of the nucleic acids.

NUCLEOSIDES VS NUCLEOTIDES

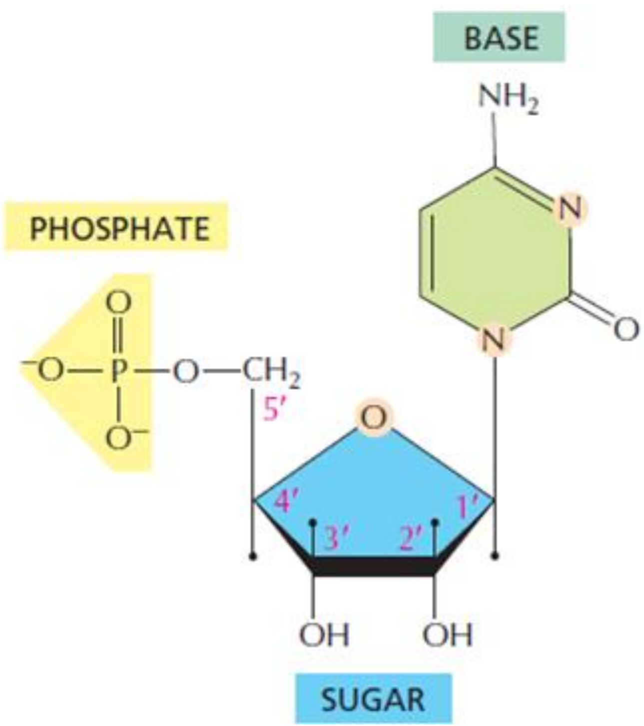
Nucleoside= **Nitrogenous base + Pentose Sugar**

Nucleotide= **Nitrogenous base + Pentose Sugar + Phosphate**

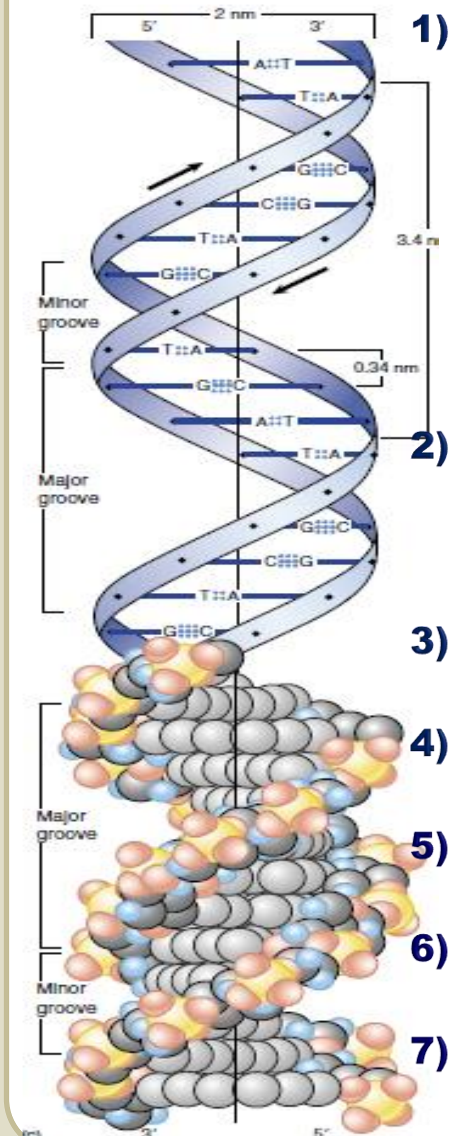
NUCLEOSIDE



NUCLEOTIDE



DNA STRUCTURE & COMPOSITION



1) **DNA has the structure of a double helix, consisting of two anti-parallel polynucleotide chains, held together by hydrogen bonds between complementary bases- adenines and thymines, and between guanines and cytosines.**

2) **Adenine always pair with thymine (A-T), while cytosine will always pair with guanine (G-C).**

3) **The proportion of adenine in DNA always equals that of thymine, and the proportion of guanine always equals that of cytosine.**

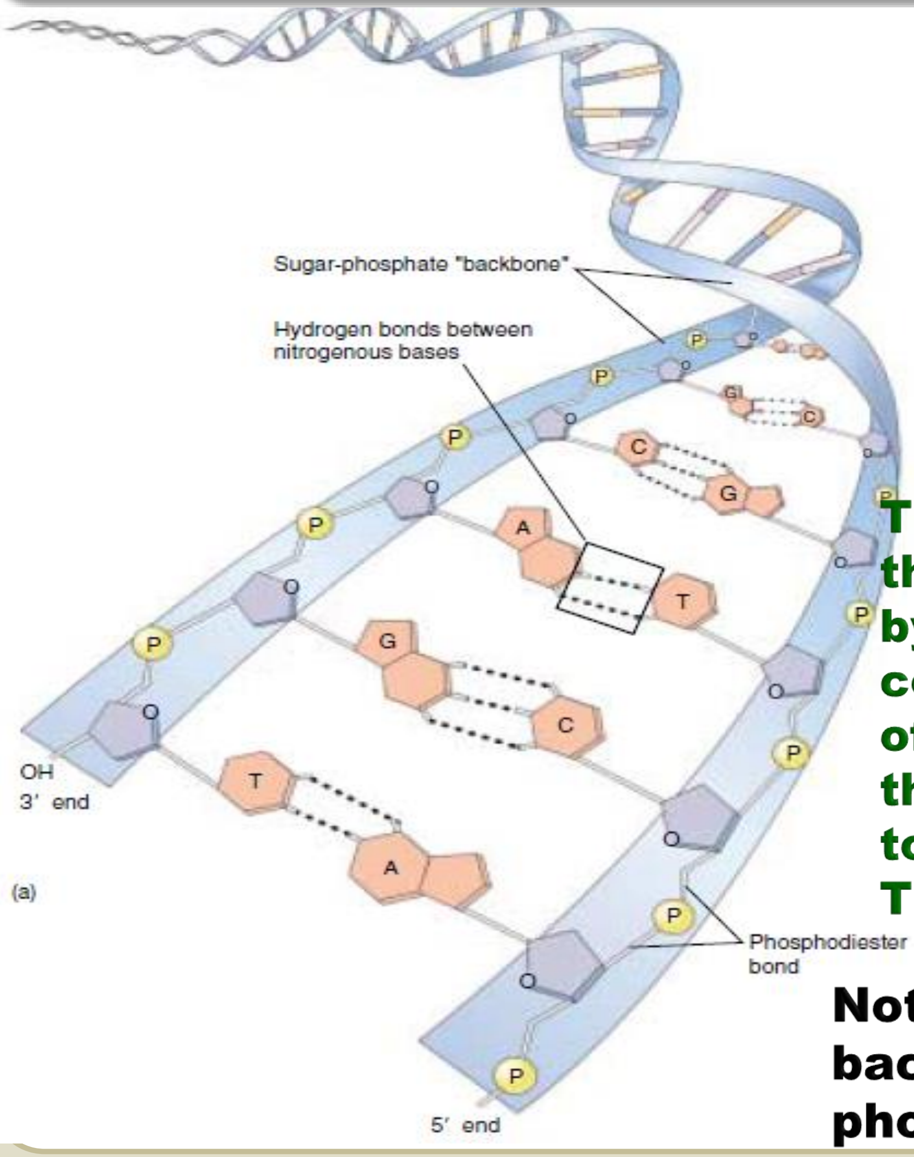
4) **Furthermore, the proportion of purines (A and G) and pyrimidines (C and T) is always equal.**

5) **The base composition of DNA generally varies from one species to another.**

6) **DNA specimens isolated from different tissues of the same species have the same base composition.**

7) **The base composition of DNA in a given species does not change with an organism's age, nutritional state, or changing environment.**

DNA STRUCTURE AND BASE PAIRING



Chargaff's rules:

1. **The proportion of A always equals that of T, and the proportion of G always equals that of C:**
A = T, and G = C.

2. **It follows that there is always an equal proportion of purines (A and G) and pyrimidines (C and T).**

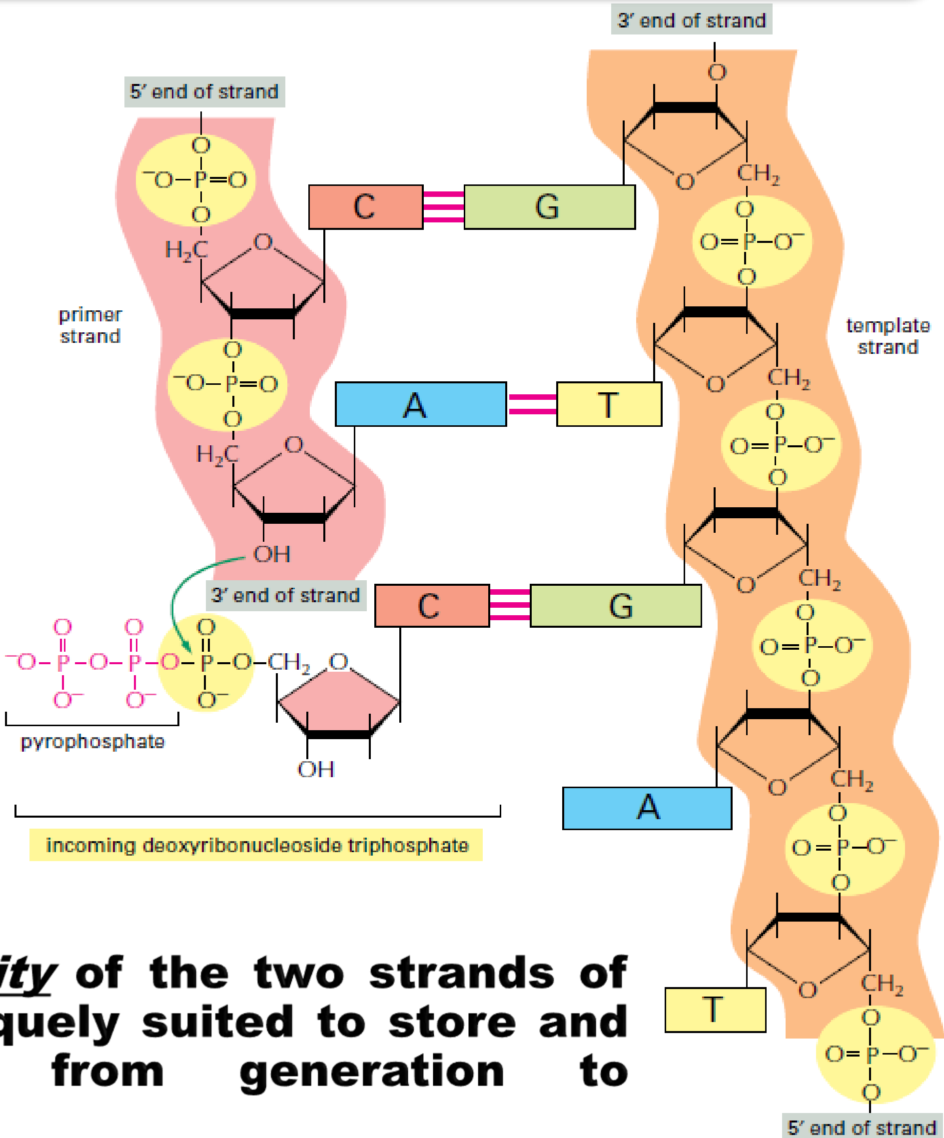
The base composition of DNA can therefore be specified unambiguously by quoting its %GC (=%G + %C) composition. For example, if a source of DNA is quoted as being 42%GC, the base composition can be inferred to be: G=21%; C=21%; A= 29%; T=29%.

Note that DNA consist of linear backbone of alternating sugar and phosphate residues.

DNA STRUCTURE

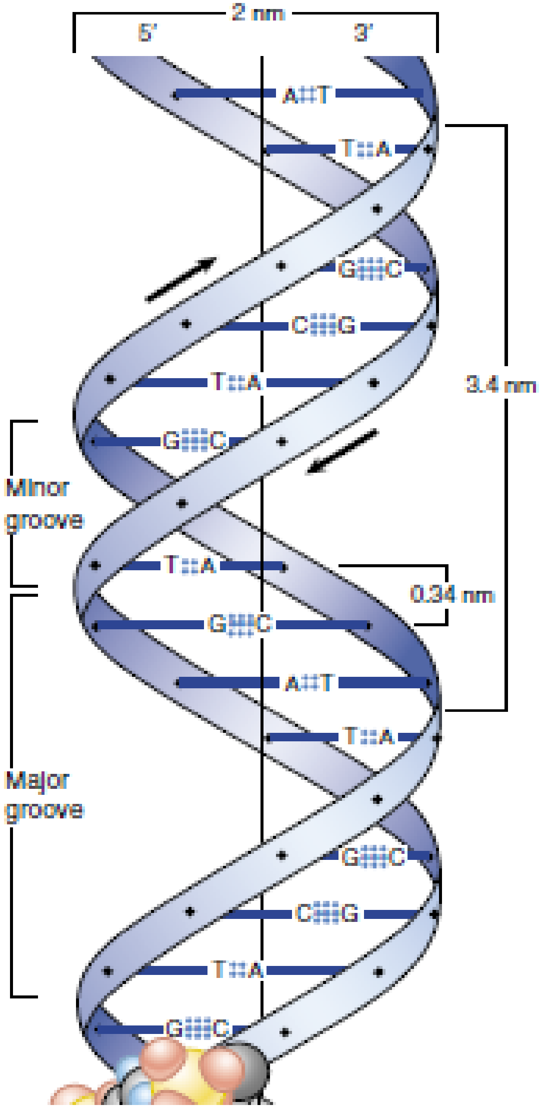
The two strands of a DNA duplex are said to be antiparallel because they always associate in such a way that the 5'-3' direction of one DNA strand is the opposite to that of its partner.

The two strands of a DNA double helix are said to be complementary or exhibit complementarity as the sequence of bases of one DNA strand can readily be inferred if the DNA sequence of its complementary strand is already known.



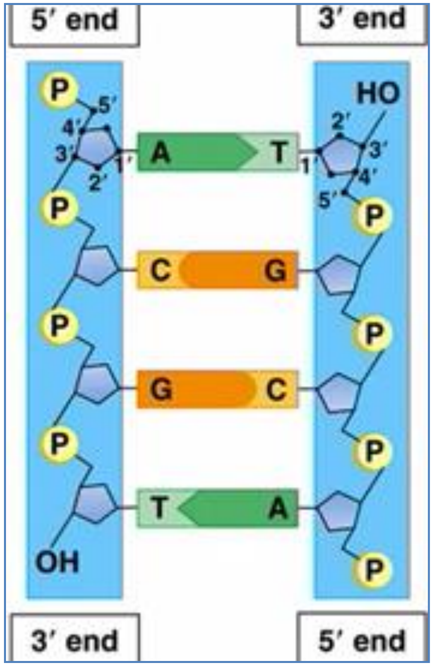
This property, the *complementarity* of the two strands of the double helix, makes DNA uniquely suited to store and transmit genetic information from generation to generation.

DNA STRUCTURE



The DNA double helix is ~ 2 nanometers in diameter. It also consists of a major groove and a minor groove. One turn (pitch) of a double helix = 10 base pairs = ~ 3.4nm (distance occupied by a single turn of the helix).

Thus, the base pairs in DNA are stacked about 0.34nm apart, with 10 base pairs per turn (360) of the double helix.



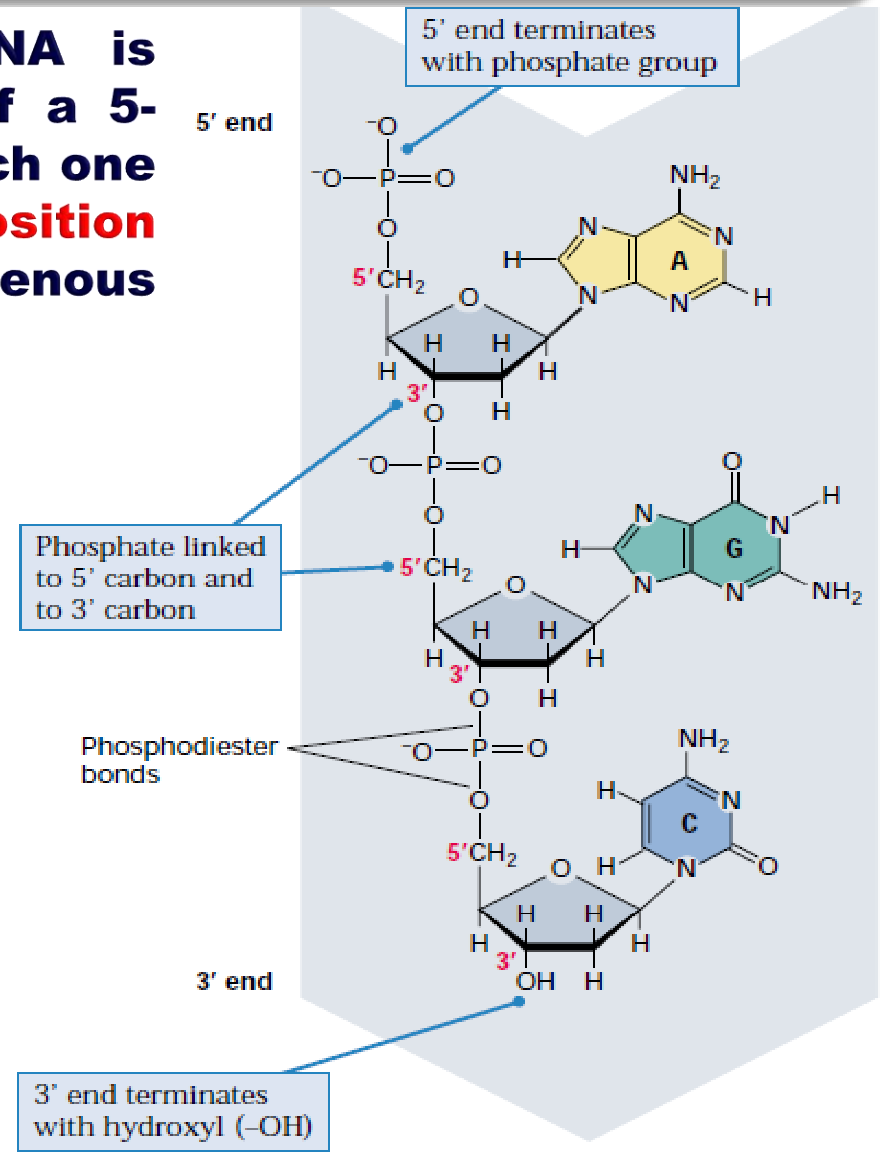
DNA is antiparallel

DNA STRUCTURE

The basic building block of DNA is **nucleotide**. Nucleotide consists of a 5-carbon sugar (deoxyribose) to which one phosphate is attached at the 5' position of the sugar ring and one nitrogenous base is attached at the 1' site.

The bond linking an individual sugar residue to the neighbouring sugar residues (OR a nucleotide to another nucleotide) is a covalent 3',5' -phosphodiester bond. Covalently attached to carbon atom 1' of each sugar residue is a nitrogenous base.

Because of the phosphate group in the DNA molecule, DNA is negatively charged hence, soluble in water.



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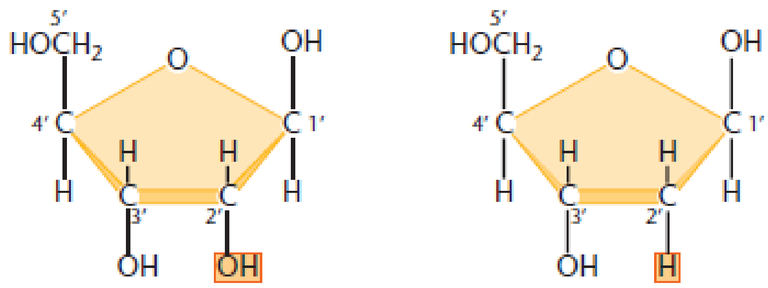
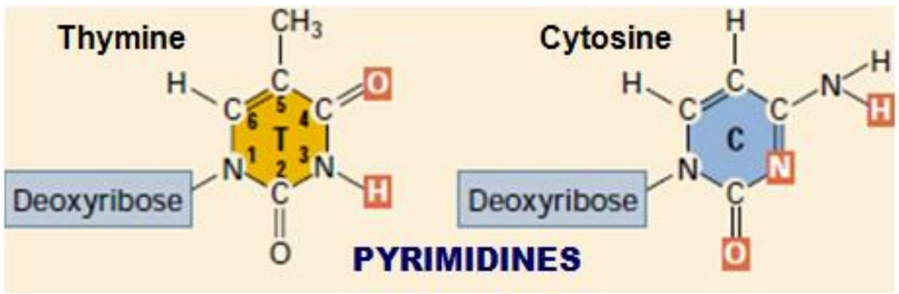
COMPOSITION OF NUCLEIC ACIDS

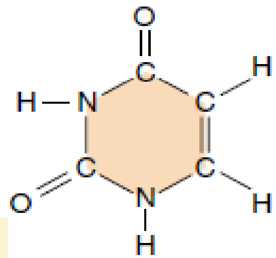
Nucleic acids (DNA or RNA) are polymers consisting of repeating units of nucleotides. Each nucleotide consists of a five-carbon sugar, a phosphate, and a heterocyclic nitrogenous base. The nitrogenous bases in DNA are A, C, G, and T while in RNA, they are are A, C, G, and U. Of these, A and G are known as Purines while C, T and U are known as Pyrimidines.



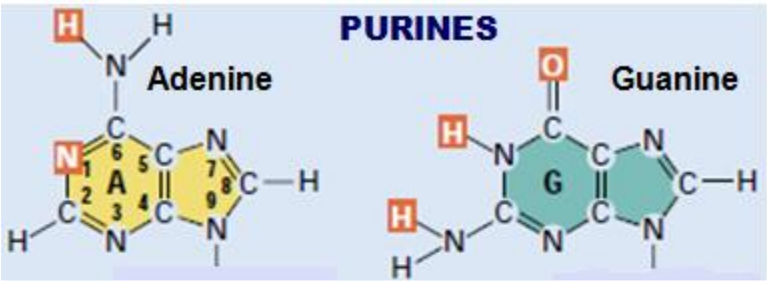
Ribose   2-Deoxyribose



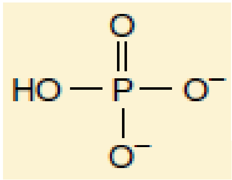
5-carbon sugar (Pentose)



Uracil (RNA only)



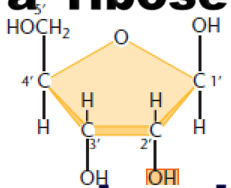
The five-carbon sugar in DNA is 2-deoxyribose; in RNA, it is ribose.

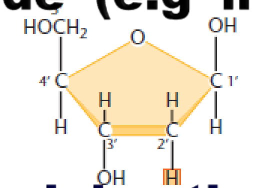


Phosphate

DNA STRUCTURE- NUCLEOSIDES & NUCLEOTIDES

A molecule which consists of one of the four nitrogenous bases linked to a pentose sugar is known as a <u>nucleoside</u>. If the sugar is deoxyribose, the nucleoside is a deoxyribonucleoside (e.g in DNA); If the sugar is a ribose, the nucleoside is ribonucleoside (e.g in RNA).



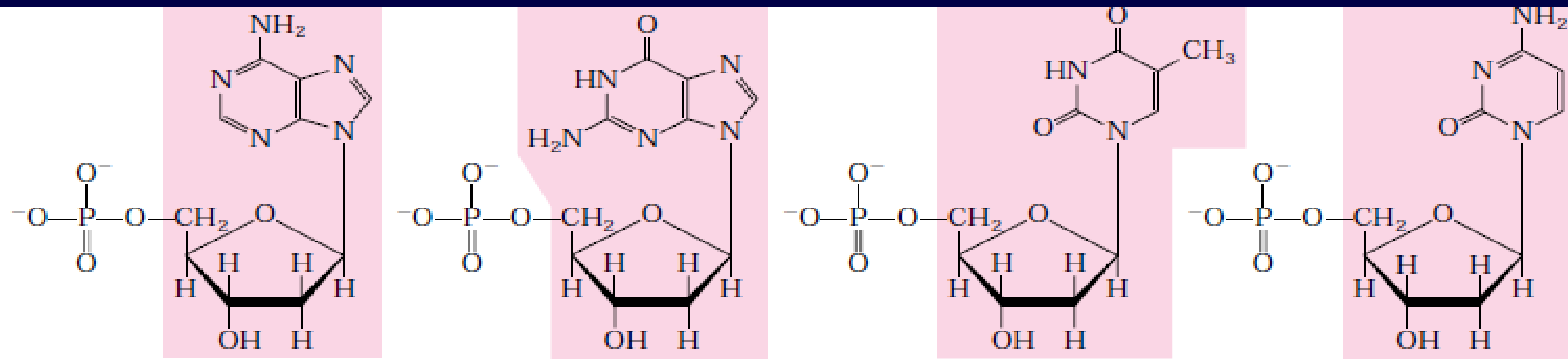


There are four major deoxyribonucleosides distinguished by the attached base: deoxyadenosine, deoxyguanosine, deoxythymidine, and deoxycytidine.

If the nucleoside has one or more attached phosphate groups (generally at the 5' position, but alternatively at the 3' position), the molecule is a <u>nucleotide</u>. Examples include: deoxyadenosine monophosphate (dAMP), deoxyguanosine diphosphate (dGDP), deoxythymidine monophosphate (dTMP) and deoxycytidine triphosphate (dCTP). The nucleotides employed in energy metabolism, such as adenosine triphosphate (ATP), are ribose-containing molecules.

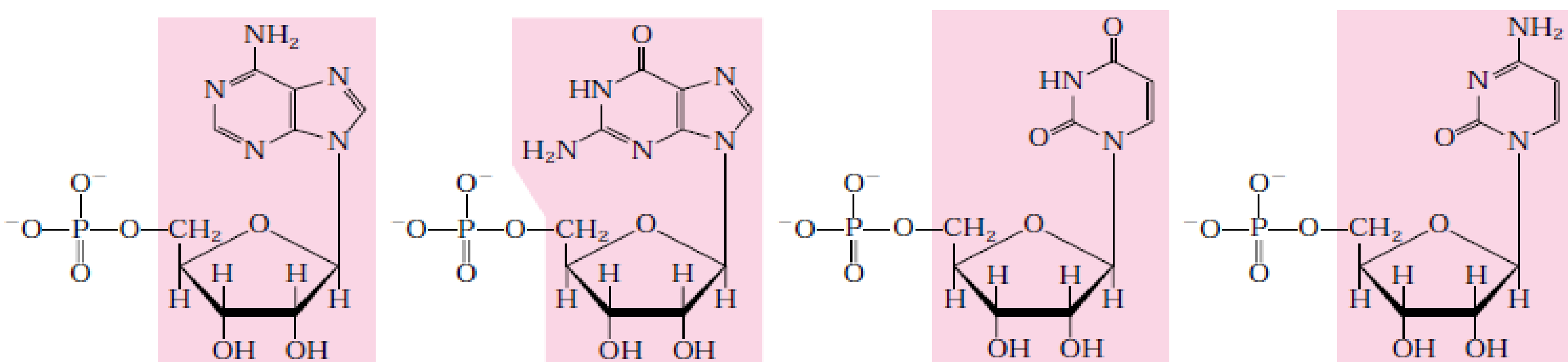
Nucleotides are covalently linked to one another to form a linear polymer, or strand with a backbone composed of alternating sugar and phosphate groups joined by 3'-5'- phosphodiester bonds.

STRUCTURE OF NUCLEIC ACIDS



Nucleotide:	Deoxyadenylate (deoxyadenosine 5′-monophosphate)	Deoxyguanylate (deoxyguanosine 5′-monophosphate)	Deoxythymidylate (deoxythymidine 5′-monophosphate)	Deoxycytidylate (deoxycytidine 5′-monophosphate)
Symbols:	A, dA, dAMP	G, dG, dGMP	T, dT, dTMP	C, dC, dCMP
Nucleoside:	Deoxyadenosine	Deoxyguanosine	Deoxythymidine	Deoxycytidine

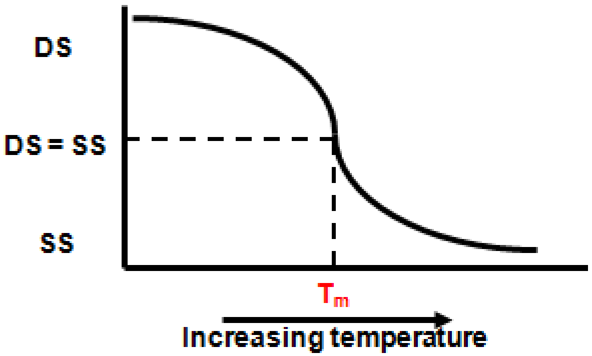
(a) Deoxyribonucleotides



Nucleotide:	Adenylate (adenosine 5′-monophosphate)	Guanylate (guanosine 5′-monophosphate)	Uridylate (uridine 5′-monophosphate)	Cytidylate (cytidine 5′-monophosphate)
Symbols:	A, AMP	G, GMP	U, UMP	C, CMP
Nucleoside:	Adenosine	Guanosine	Uridine	Cytidine

(b) Ribonucleotides

DNA CHEMISTRY/ BIOPHYSICS



The maximum absorbance of DNA is at 260 nm.

The melting temperature of DNA is the temperature at which the double stranded DNA "melts" forming two single strands, *OR* The temperature at which 50% of a nucleic acid is hybridized to its complementary strand.

The Tm is the temperature when 50% of the double strands unwound. GC pairs have three hydrogen bonds and AT have two. A high GC% leads to high Tm.

The relationship between the melting temperature (T_m) and GC content can be expressed in its much simplified form by the formula T_m= 69.3°C + 0.41(%GC)°C

GC content has a direct effect on Tm. The following examples, demonstrate the point.

Tm = 69.3°C + 0.41(45)°C = 87.75°C

Tm = 69.3°C + 0.41(40)°C = 85.7°C

Tm = 69.3°C + 0.41(60)°C = 93.9°C

DNA REPLICATION

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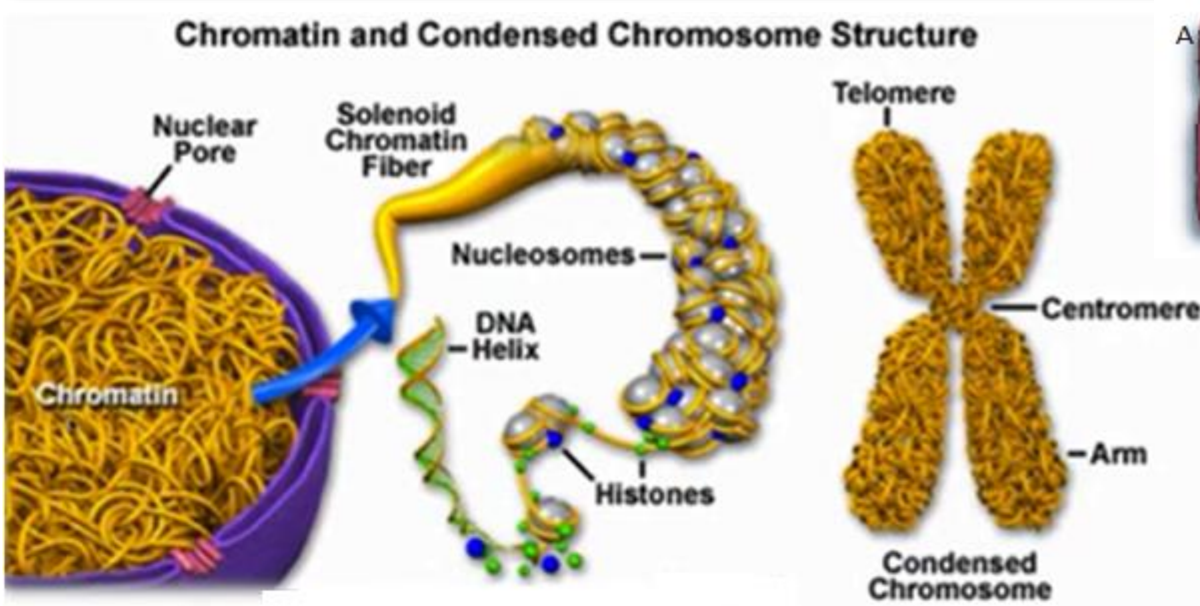
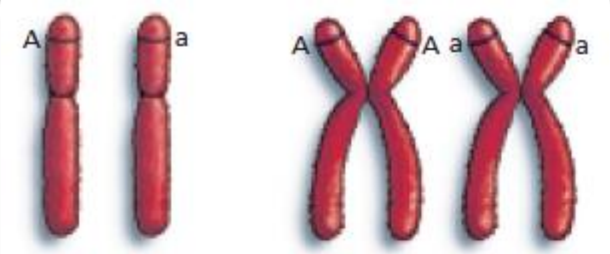
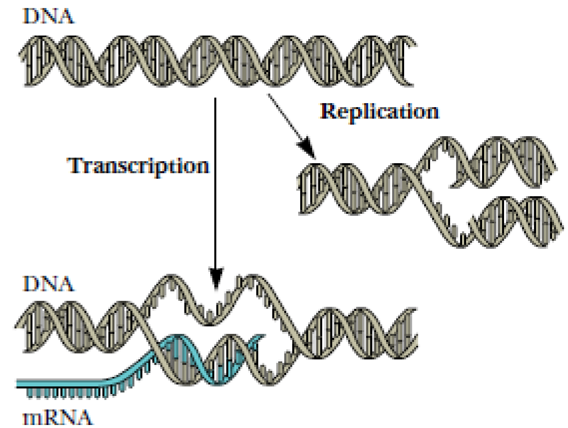
Department of Animal & Environmental Biology

Lecture Guide

CELL: DNA FUNCTIONS







The Genotypic function

Stores and transmit (replicate) genetic information

The Phenotypic function (Gene expression)

Specifies protein synthesis (Transcription & Translation), determines characteristics/traits, controls growth

The Evolutionary function

Maintains genetic integrity, allows for adaptation

DNA REPLICATION

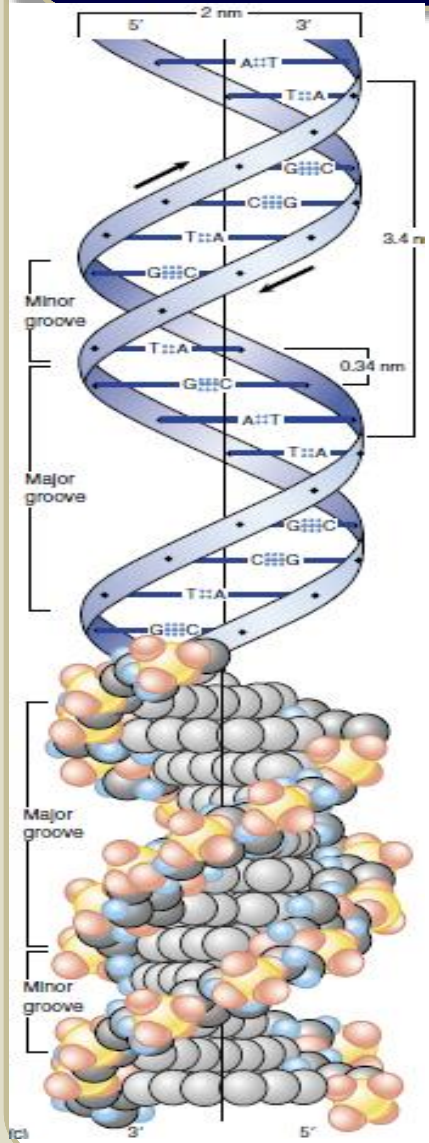
The ability of cells to maintain a high degree of order in a chaotic universe depends upon the accurate duplication of vast quantities of genetic information carried in chemical form as DNA.

This process is called *DNA replication*.

All organisms must duplicate their DNA with extraordinary accuracy before each cell division, so DNA replication must occur before a cell can produce two genetically identical daughter cells.

In humans, the synthesis of a new strand of DNA occurs at the rate of about 3000 nucleotides per minute. In bacteria, about 30,000 nucleotides are added to a nascent DNA chain per minute. This implies that the cellular machinery responsible for DNA replication must work very fast, but even more importantly, it must work with great precision.

DNA REPLICATION- Structural basis



DNA has the structure of a double helix, consisting of two polynucleotide chains, held together by hydrogen bonds between complementary bases- adenines and thymines, and between guanines and cytosines

The physical structure of DNA proposed by Watson and Crick has great explanatory power.

The fact that adenine can pair only with thymine and that cytosine can pair only with guanine suggest a simple way in which the DNA molecule could be copied, or replicated: The original strands could serve as templates on which to build the new strands.

DNA REPLICATION

The ability of each strand of a DNA molecule to act as a template for producing a complementary strand enables a cell to copy or replicate its gene before passing them on to its descendants.

PROCESS OF DNA REPLICATION

1. The hydrogen bonds connecting the two strands are broken.

2. Breaking the hydrogen bonds would cause the two strands to unwind and separate.

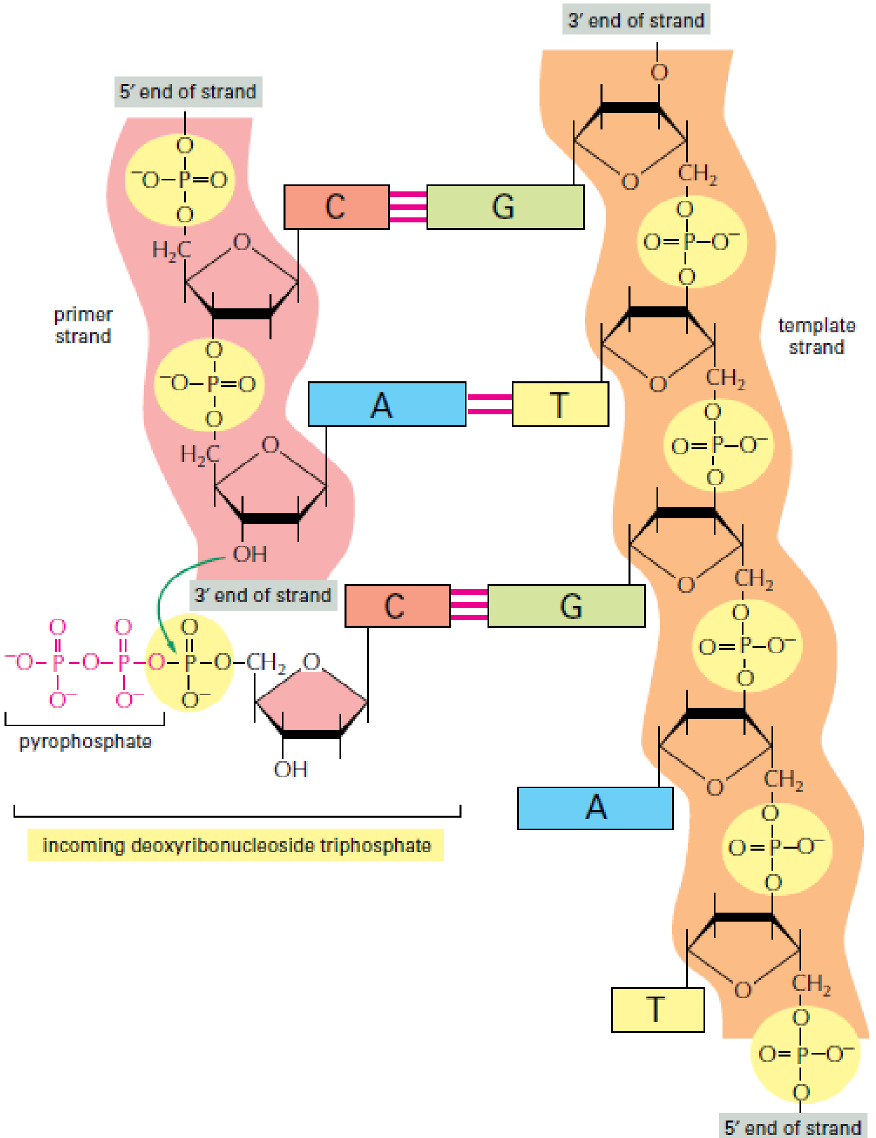
3. Each strand could then be used as a template for the construction of a new strand of DNA. We now know that the main enzyme involved in the replication of DNA is called DNA polymerase.

4. When this process is completed, there would be two copies of the DNA molecule, each composed of one "old" strand of DNA (from the parent DNA molecule), and one newly synthesized strand of DNA.

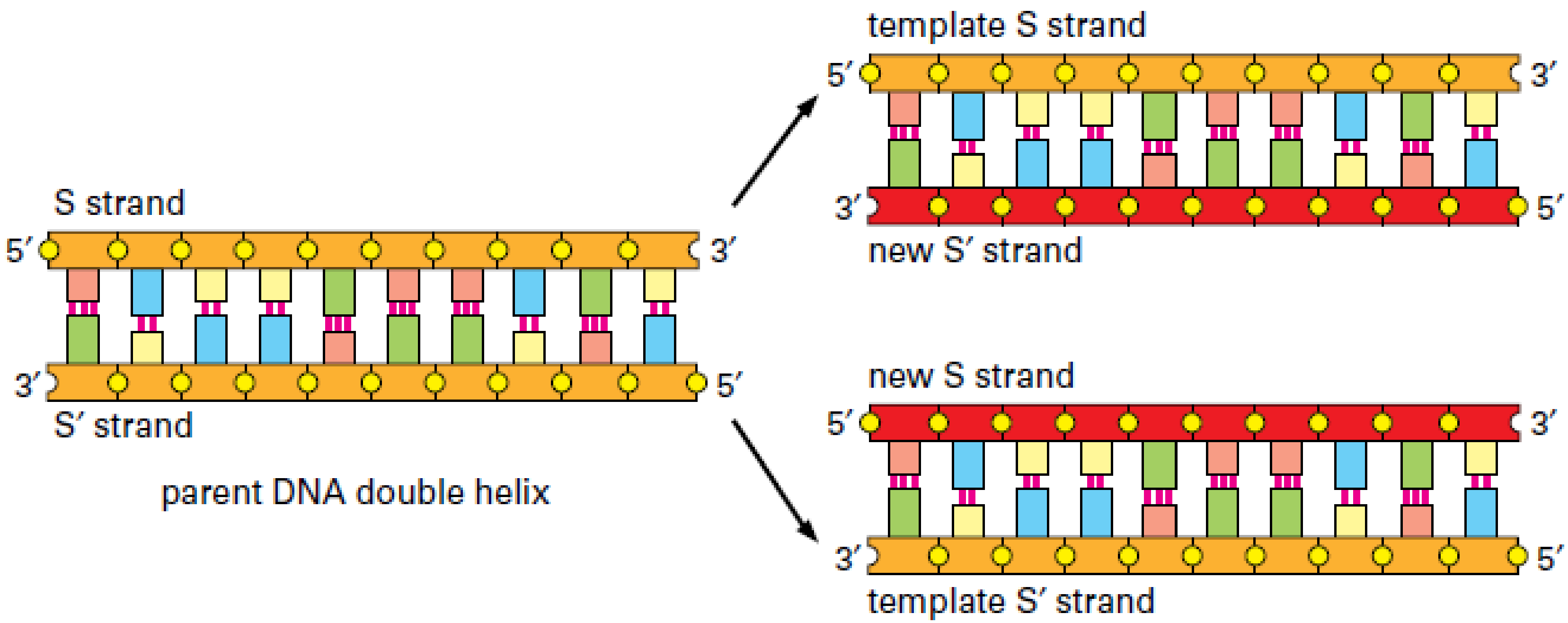
DNA STRUCTURE

If the two complementary strands of a double helix is separated, by breaking the hydrogen bonds of each base pair, each parental strand could direct the synthesis of a new complementary strand.

DNA replication is semi-conservative because each daughter DNA double helix is composed of one of the original (parent) strands plus one newly synthesized strand.



DNA REPLICATION



During DNA replication inside a cell, each of the two old DNA strands serves as a template for the formation of a new strand. Because each of the two daughters of a dividing cell inherits a new DNA double helix containing one old and one new strand, the DNA double helix is said to be replicated "semi-conservatively" by DNA polymerase.

REQUIREMENTS OF DNA REPLICATION

Although the process of replication includes many components, they can be combined into three major groups:

1. A template consisting of single-stranded DNA;

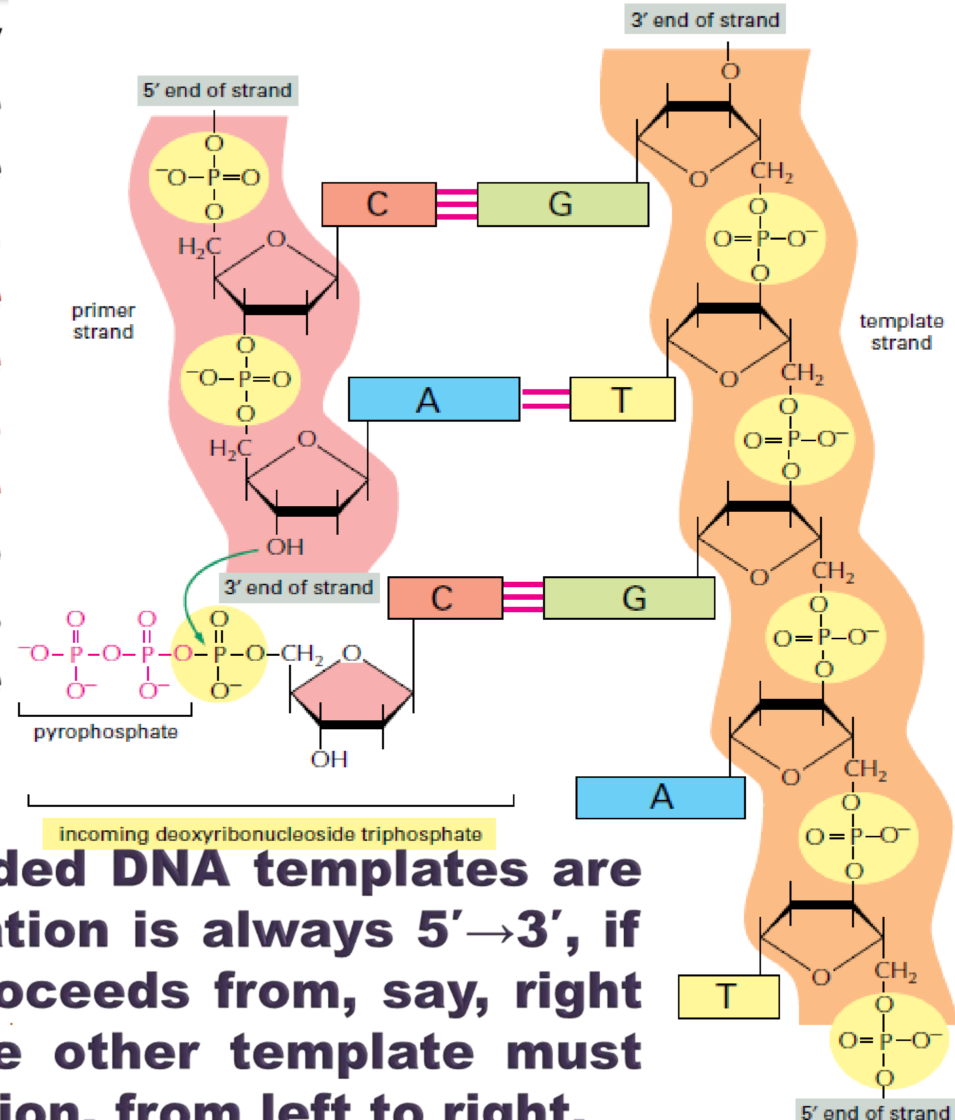
2. Raw materials (substrates) to be assembled into a new nucleotide strand (dNTPs); and

3. Enzymes and other proteins that "read" the template and assemble the substrates into a DNA molecule.

The positions at which the DNA is first opened are called **origins of replication**. They are marked by a particular sequence of nucleotides which attract initiator proteins.

DNA REPLICATION

In DNA synthesis, new nucleotides are joined one at a time to the 3′ end of the newly synthesized strand. **DNA polymerases, the enzymes that synthesize DNA, can add nucleotides only to the 3′ end of the growing strand** (not the 5 end), so new DNA strands always elongate in the same 5-to-3 direction (5′→3′).



Because the two single-stranded DNA templates are antiparallel and strand elongation is always 5′→3′, if synthesis on one template proceeds from, say, right to left, then synthesis on the other template must proceed in the opposite direction, from left to right.

DNA REPLICATION MECHANISM

Initiator proteins bind to origin of replication or site of initiation and cause a short section of DNA to unwind. This unwinding allows helicase and other single-strand-binding proteins to attach to the polynucleotide strand.

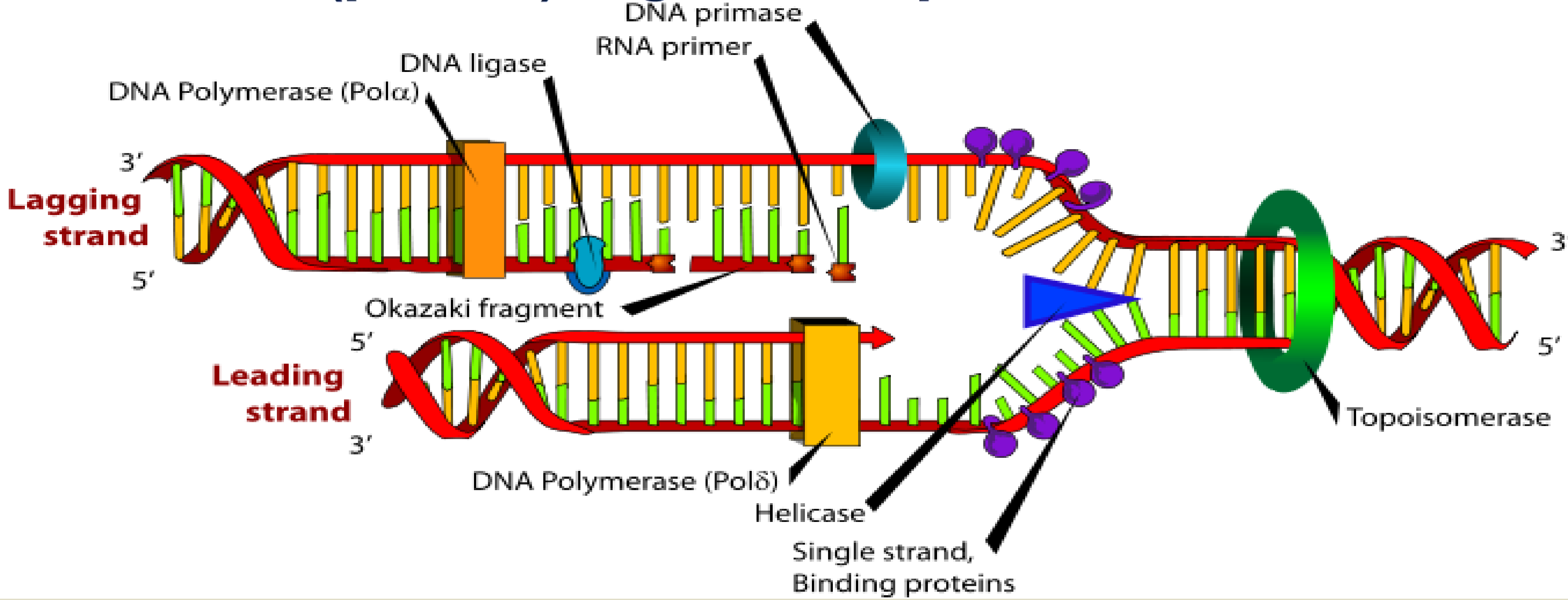
DNA helicases break the hydrogen bonds that exist between the bases of the two nucleotide strands of a DNA molecule. The initiator proteins first separate DNA strands at the origin, providing a short stretch and then helicases unwound the double-stranded DNA.

To stabilize the single-stranded DNA long enough for replication to take place, single-strand-binding (SSB) proteins attach tightly to the exposed single-stranded DNA.

DNA REPLICATION MECHANISM

Another protein essential for the unwinding process is the enzyme DNA gyrase, a topoisomerase which controls the supercoiling of DNA. In replication, DNA gyrase reduces torsional strain (torque) that builds up ahead of the replication fork as a result of unwinding

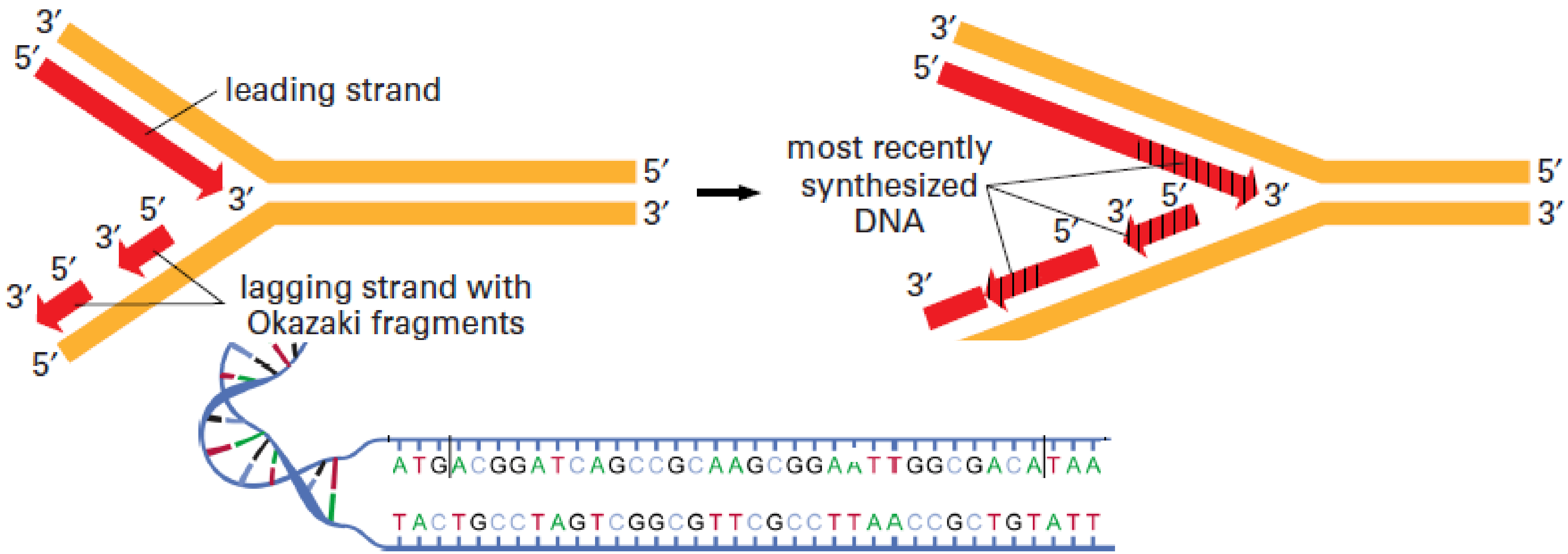
An enzyme called primase synthesizes short stretches of nucleotides (primers) to get DNA replication started.



DNA REPLICATION

As DNA unwinds during replication, the antiparallel nature of the two DNA strands means that one template is exposed in the 5′→3′ direction and the other template is exposed in the 3′→5′ direction.

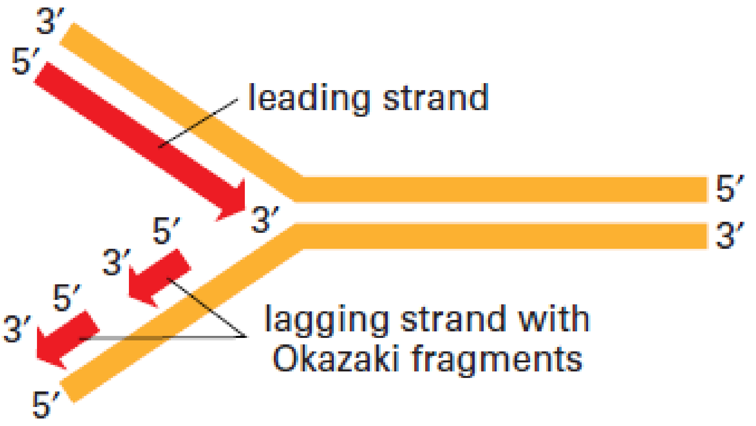
As the DNA unwinds, the template strand that is exposed in the 3′→5′ direction allows the new strand to be synthesized continuously, in the 5′→3′ direction. This new strand, which undergoes continuous replication, is called the leading strand.



DNA REPLICATION

The other template strand is exposed in the 5′→3′ direction. After a short length of the DNA has been unwound, synthesis proceed in the 5′→3′, i.e the direction *opposite that* of unwinding. Because only a short length of DNA needs to be unwound before synthesis on this strand gets started, the replication machinery soon runs out of template.

By that time, more DNA has unwound, providing new template at the 5 end of the new strand. DNA synthesis must start anew at the replication fork and proceed in the direction opposite that of the movement of the fork until it runs into the previously replicated segment of DNA.



DNA REPLICATION

This process is repeated again and again, so synthesis of this strand is in short, discontinuous bursts. The newly made strand that undergoes discontinuous replication is called the lagging strand.

The short lengths of DNA produced by discontinuous replication of the lagging strand are called Okazaki fragments, which are then linked together to create a continuous new DNA molecule.