Nucleic Acids & Chromosomes

Learning Objectives:

- ❖ Define the terms “Nucleotide”, “ Nitrogenous bases”. Describe the structure of a nucleotide and list the types of nitrogen bases.
- ❖ Compare between DNA & RNA and describe briefly their structure & functions . List the types of RNA and mention the function of each type.
- ❖ Describe briefly the Chargaff's rule.
- ❖ Describe briefly the double helix of DNA. Define the terms “ minor grooves”, “major grooves”, “B DNA”, “Z DNA”,
- ❖ Describe the term “genome”
- ❖ Describe briefly the structure and replication of chromosomes.
- ❖ Define the terms “Nucleosome”, “Solenoid”, “Centromere”, “replication bubble”, “RNA primer”.

Nucleic Acids:

- Nucleic acids form the structure of genes, which provide the basic blueprint of life. They are the largest molecules in the body. There are two different types of nucleic: ***Ribonucleic acid (RNA)*** and ***Deoxyribonucleic acid (DNA).***

- Every gene dictates protein structures. ***The sum total of all gene action, via its protein-determining role***, ***determines the development of the cell, and ultimately of the entire organism, thus determining the species and type of organism.***

- Nucleic acids consist of ***carbon, oxygen, hydrogen, nitrogen and phosphorus atoms***.

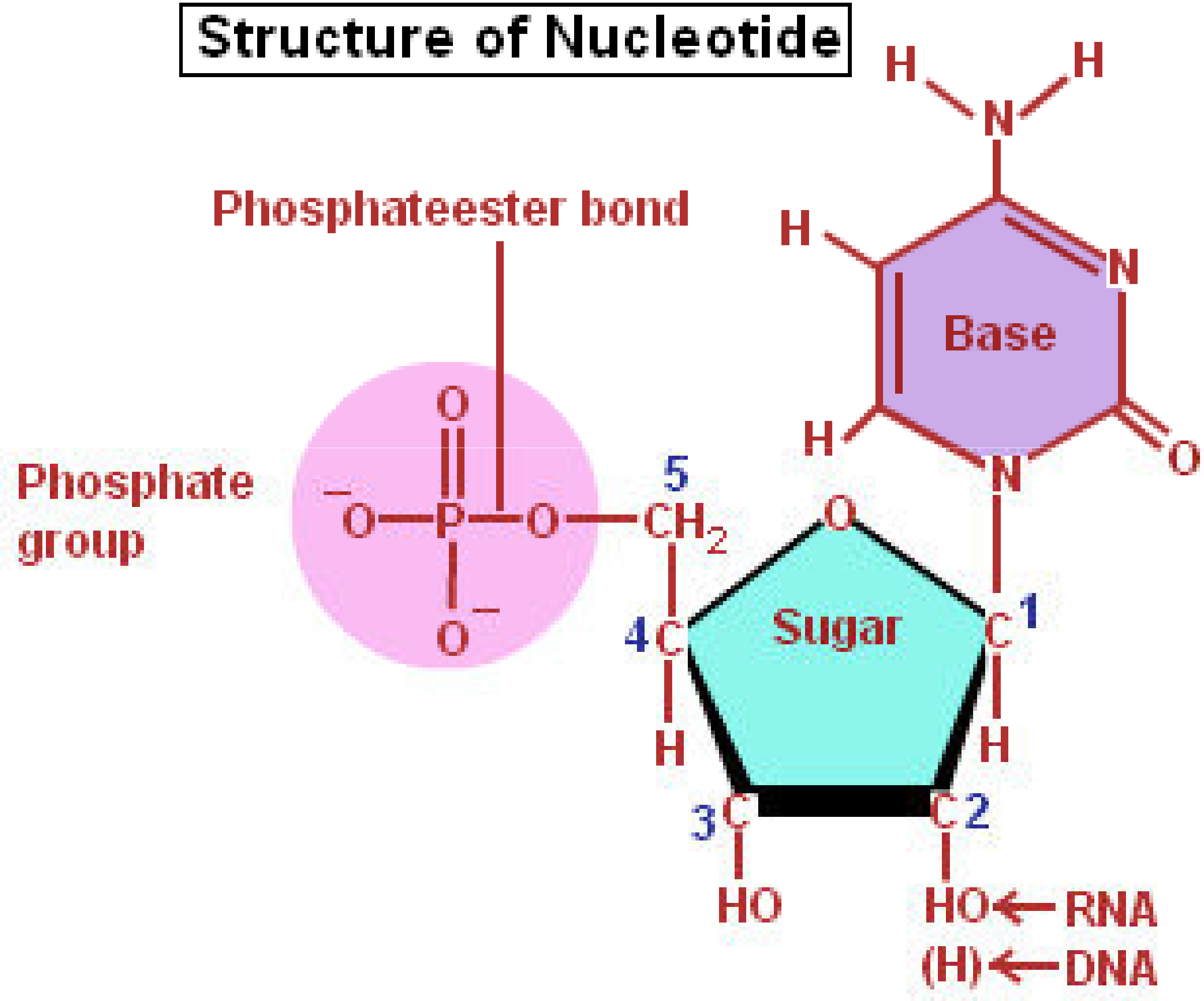
- **Nucleotides** are building blocks of nucleic acids. ***Each nucleotide has three parts***:

  - **Nitrogen-containing base** (2 major types): ***Purines*** & ***Pyrimidines***, of four different possible subtypes.

  - **Pentose sugar** (***ribose in RNA*** or ***deoxyribose in DNA***).

  - **Phosphate group**.

Nucleic Acids – *Nucleotide Structure:*



Nucleic Acids – *Nitrogenous Bases:*

- There are two main types of nitrogen-containing bases commonly found in nucleotides:

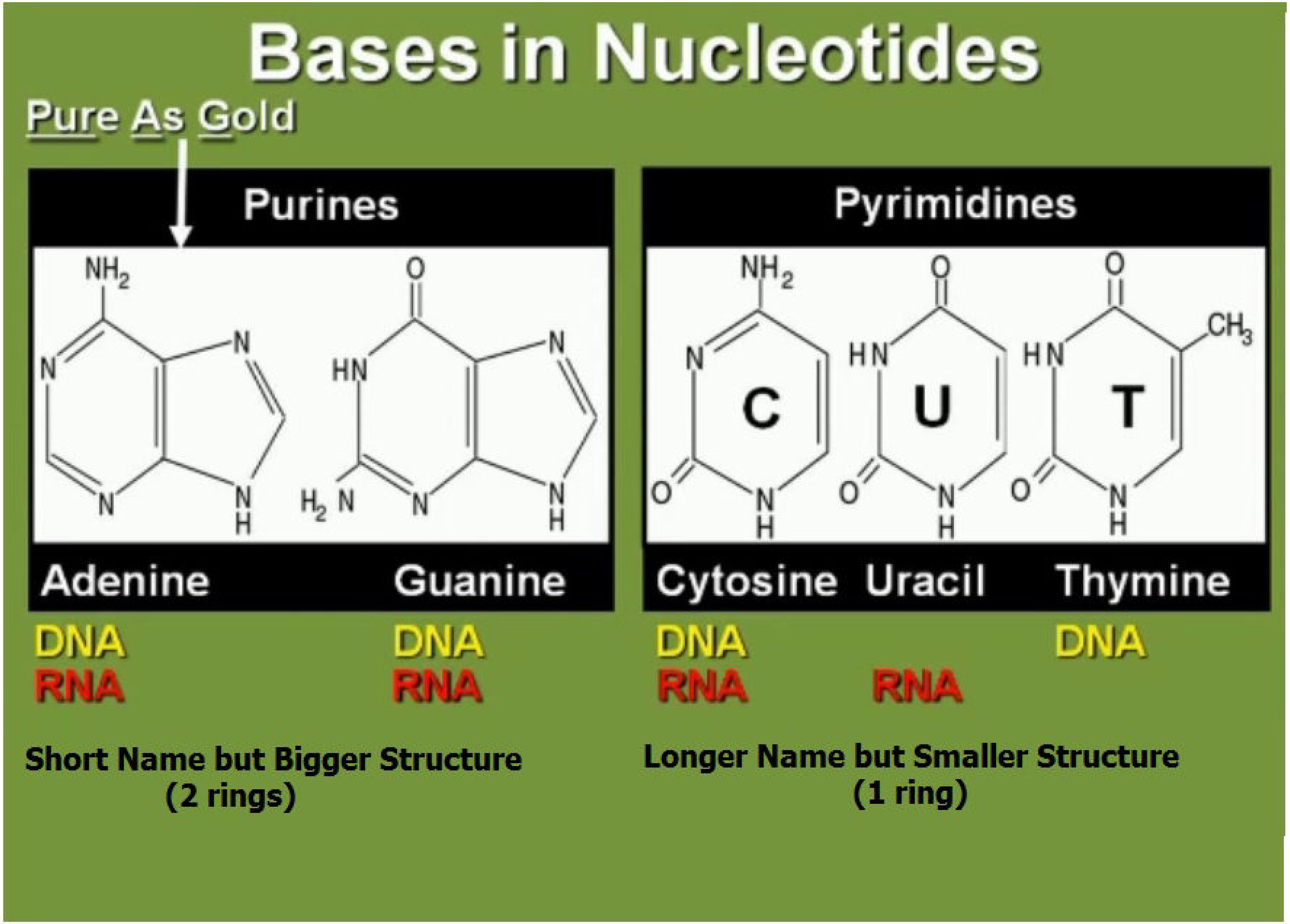
  - **Purines** ***contain two rings in their structure***. The two commonly found in nucleic acids are **Adenine (A)** & **Guanine (G)**; ***both found in DNA & RNA.***

  - **Pyrimidines** ***have only one ring***. **Cytosine (C)** ***is present in both DNA & RNA*** while **Thymine (T)** ***is usually found only in DNA***, whereas **Uracil (U)** ***is found only in RNA.***

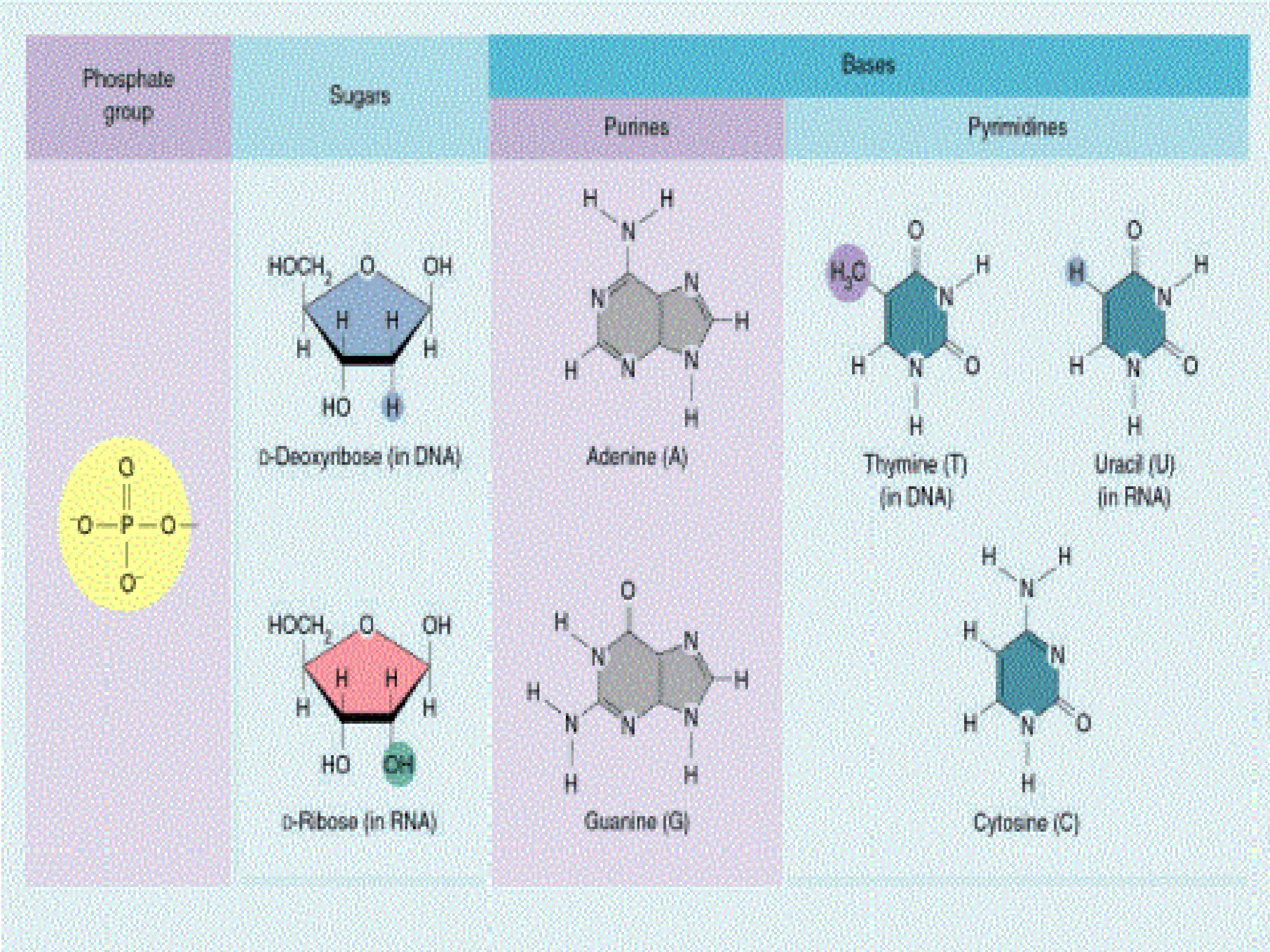
  - **Mnemonics to learn:**

    Purine= Pure As Gold, Pyrimidine= CUT

Nucleic Acids – *Nitrogenous Bases:*



Nucleic Acids – *Nucleotide Structure:*



DNA Structure & Function:

- DNA is found ***within the nucleus***, and consists of a ***double chain of nucleotides***.

- The two nucleotide chains are held together by ***hydrogen bonds between the bases***.

- ***Alternating sugar & phosphate molecules form the backbone*** of a ***"ladder-like"*** structure. ***The bases, bonded in pairs, forming the "rungs" of the ladder.***

- **Bonding of base pairs is very specific**. ***"A" always bonds with "T", and "G " with "C".***

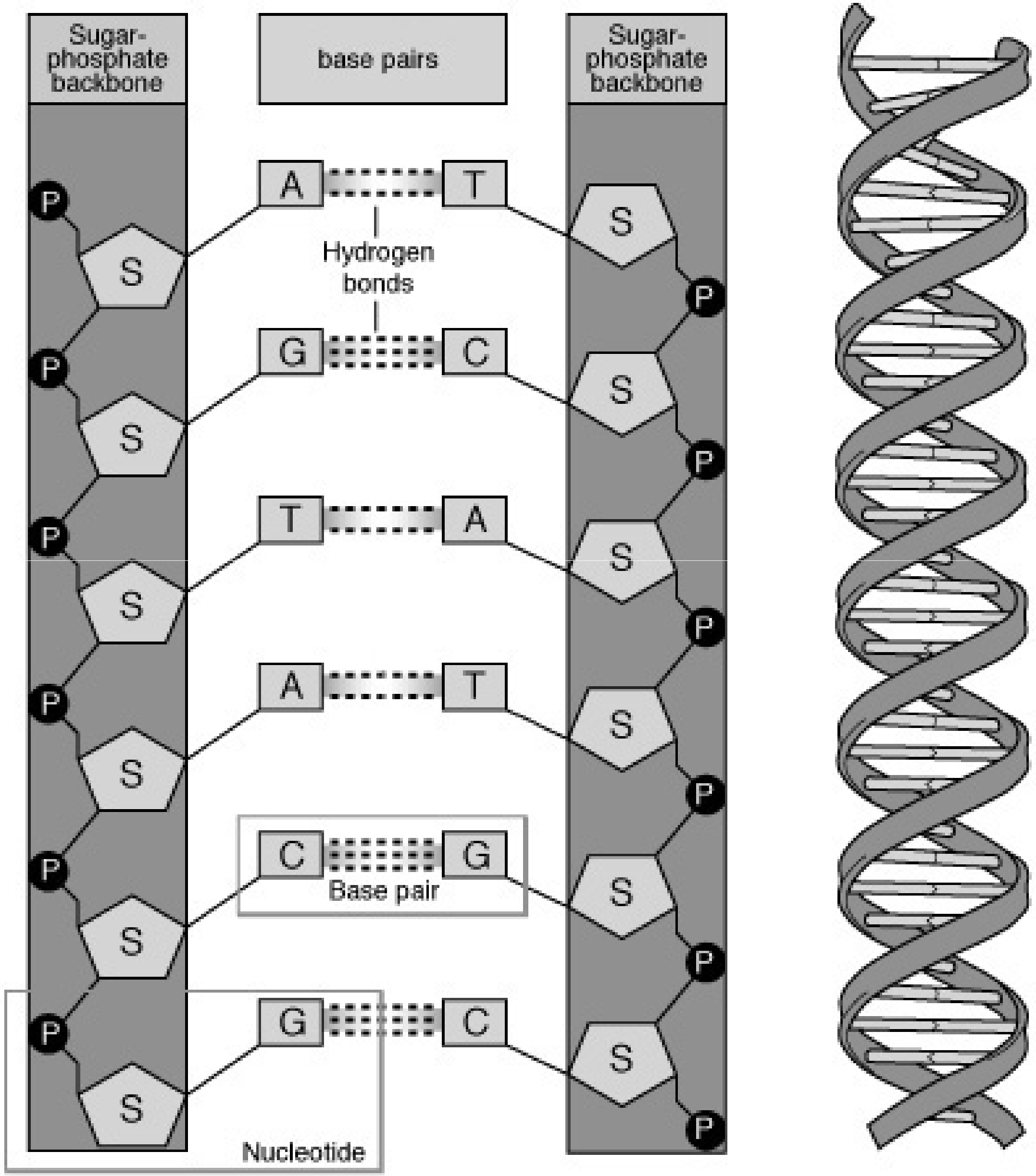
- These are ***"complementary bases". A/T pairs have 2 hydrogen bonds; G/C have 3 hydrogen bonds.***

- **The entire double-stranded molecule spirals to form a *double helix.***

- ***DNA replicates itself exactly, to ensure identical genetic information in every cell.***

- ***DNA provides instructions for building every single protein in the whole body***.

DNA STRUCTURE:
The Ladder and The Double Helix



RNA Structure & Function:

- **RNA is located outside the nucleus**, and is a ***single strand of nucleotides.***

- RNA bases are similar to DNA: ***A, G & C are the same***, ***Uracil (U) replaces Thymine (T).***

- There are three forms of RNA:

  - **Messenger RNA**: It takes the DNA info out of the nucleus, to be used for protein synthesis.

  - **Ribosomal RNA**: It allows the ribosomes to hold the mRNA in position for translation.

  - **Transfer RNA**: It brings amino acids into position on ribosomes, for the protein sequence.

Comparison of DNA and RNA		
CHARACTERISTIC	DNA	RNA
Major cellular site	Nucleus	Cytoplasm (cell area outside the nucleus)
Major functions	Is the genetic material; directs protein synthesis; replicates itself before cell division	Carries out the genetic instructions for protein synthesis
Sugar	Deoxyribose	Ribose
Bases	Adenine, guanine, cytosine, thymine	Adenine, guanine, cytosine, uracil
Structure	Double strand coiled into a double helix	Single strand, straight or folded

Comparison between DNA & RNA

History of Elucidation of DNA Structure:

- 1953, Watson & Crick used X-ray diffraction to deduce the double-stranded helix.

- **Chargaff's rule:** *Number of purines in DNA is equal to the number of pyrimidines*: **%A=%T and %G=%C. e.g. if a DNA has 10% G; what is the % of T? Answer: if G is 10%, G=C so C is also 10%. Thus A+T is 80%, and A=T so T= 40%.**

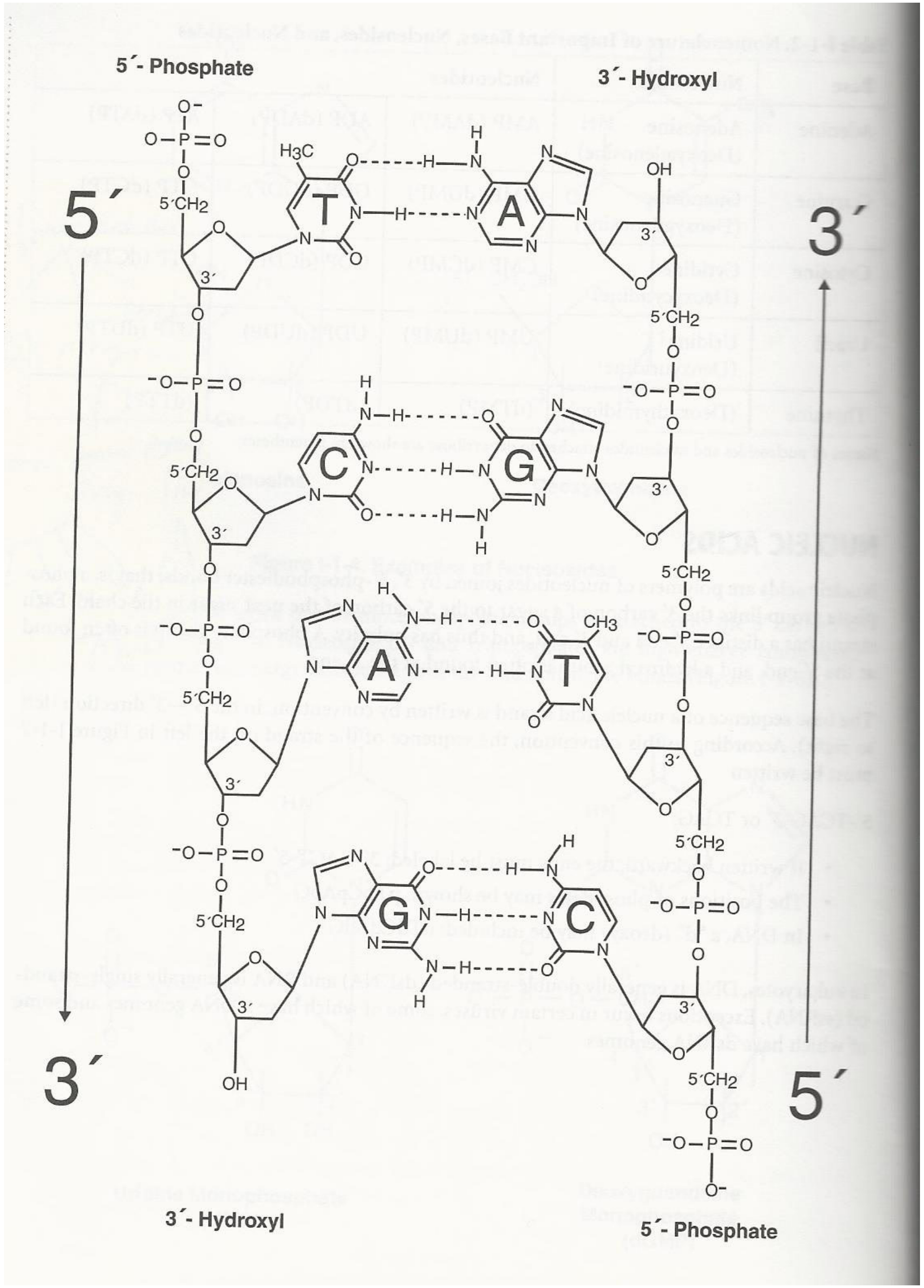
- Watson & Crick deduced that ***the hydrogen bonds must link a purine with a pyrimidine. Purines & pyrimidines face the center of the helix, forming "steps" in a "spiral staircase".***

- The way in which the two strands are twisted together, forms ***major & minor grooves***, *because the distance between the hydrogen-bonded strands is smaller than the distance between regions of the strands that are not hydrogen-bonded* (see diagram in the next slide).

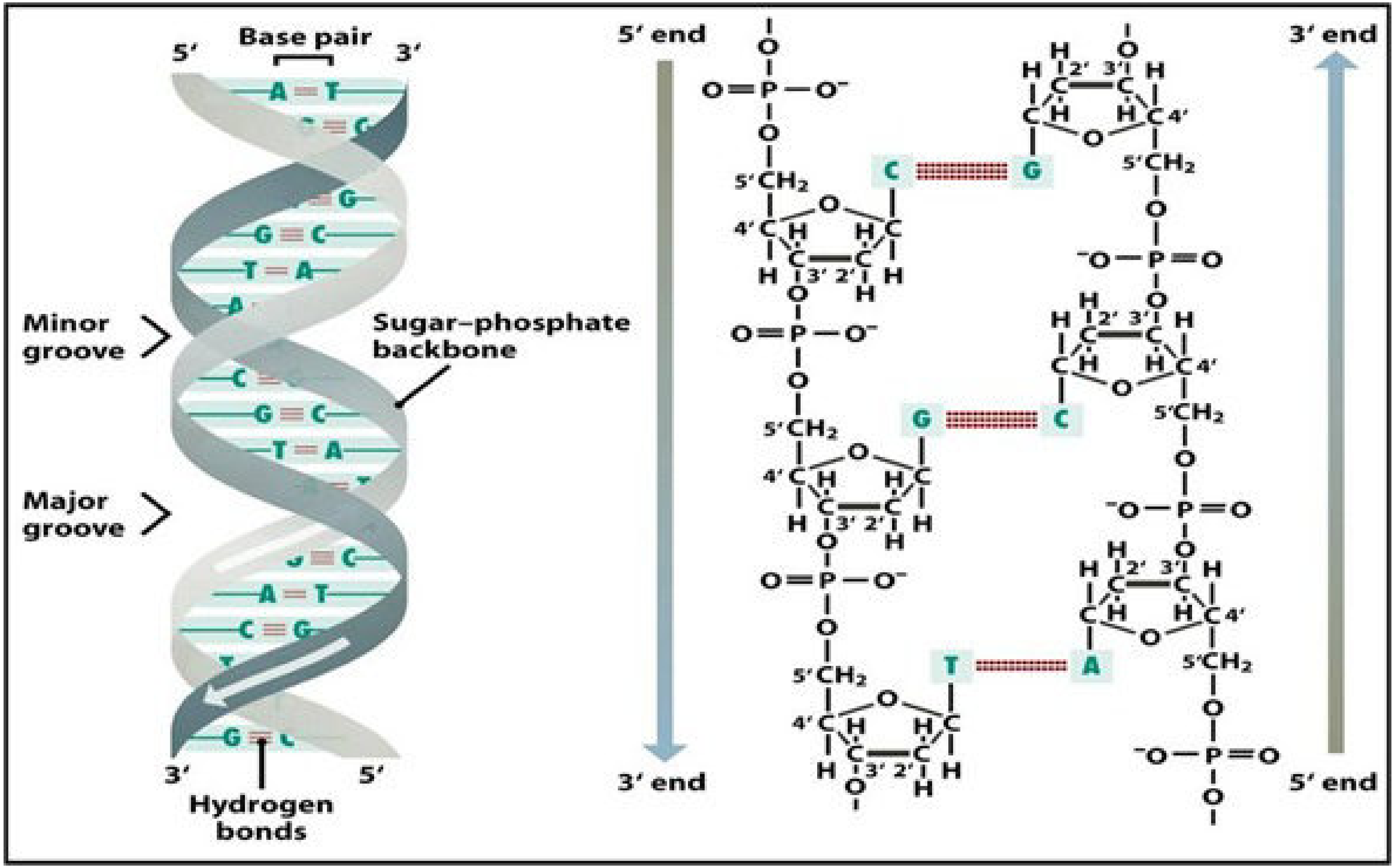
- **"ANTIPARALLEL" POLARITY**: Each phosphate joins the 3' carbon of one deoxyribose, and the 5' carbon of another. ***Thus one end of the strand is a 3' end, and the other end is a 5' end. Complementary strands are orientated so that the 5'-3' strand is opposite a 3'-5'strand.***

DNA Structure:

Hydrogen – Bonded Base Pairs in DNA



DNA Structure:



History of Elucidation of DNA Structure- *B-DNA & Z-DNA:*

- Watson & Crick originally suggested that ***all DNA follows a right-handed helix .***
- But it became clear in 1979, that ***some segments of DNA follow a left-handed coil.***
- When the helix is ***right-handed***, we see the ***normal pattern of major and grooves.***
- But when it's ***left-handed***, the sugar-phosphate backbone follows ***a zig-zag pattern.***
- ***The right-handed helix is called*** **B-DNA**, and ***the left-handed helix is called*** **Z-DNA**.
- ***Z-DNA regions undergo less RNA transcription***, ***so may be important in gene regulation.***

DNA Denaturation:

- Hydrogen bonds holding DNA strands together are separated in certain conditions.

- *Strand separation is an integral part of DNA replication and RNA transcription.*

- **Strand separation by heat, is called** ***denaturation;*** it occurs at a ***critical temperature.***

- Scientists use reversible heat-denaturation of DNA to determine base composition.

- ***G-C pairs are held by triple hydrogen bonds; A- T pairs are held by double ones. This makes the G-C bonds more resistant to breaking. Denaturation temperature is higher for DNA with a higher proportion of G-C bonds.***

- Denaturation is measured by ultraviolet absorption of a nucleic acid solution at 260 nm. This "melting" parallels an increase in absorption at 260 nm UV light. This is called the "***melting temperature" (T_m),*** and shows the base composition.

- **DNA Renaturing** takes place spontaneously when conditions return to normal. ***It depends on random collisions, so it is concentration dependent.***

Genomes:

- ***The genome of an organism* *is one complete copy of the genetic information of that organism.***
- Human cells have a ***nuclear genome as well as a mitochondrial genome***. ***Our nuclear genome is 23 chromosomes***.
- Genome size is expressed as ***numbers of nucleotide pairs per haploid genome.***
- ***In viruses and bacteria, all of the DNA is usually contained in a single molecule***.
- ***In eukaryotes it is always dispersed among several chromosomes.***
- ***Generally, genome size increases with complexity of the organism***. Viruses have enough DNA to code for just a few proteins or a few dozen. Eukaryotic cells have enough DNA to code for millions of proteins.

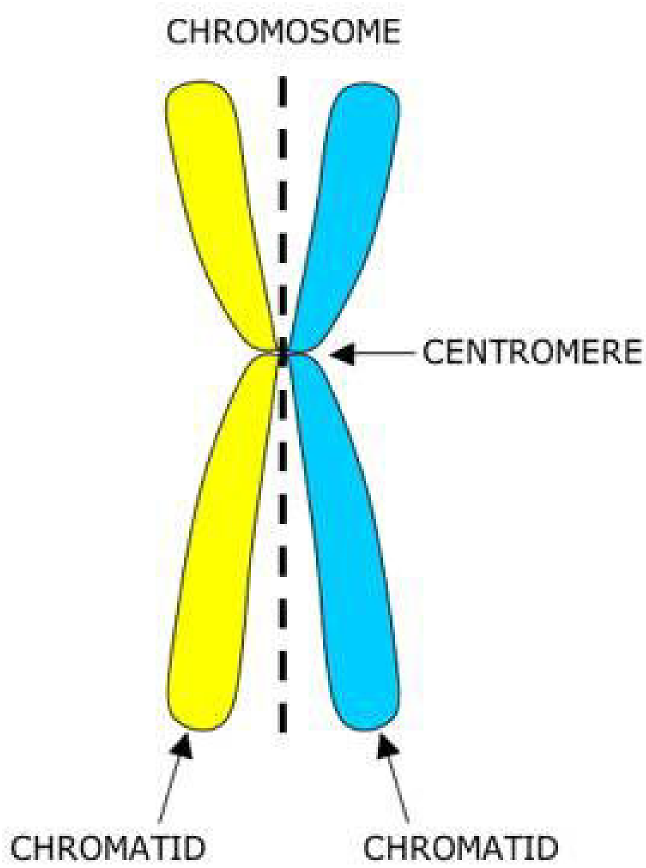
Chromosomes- *Nucleosomes:*

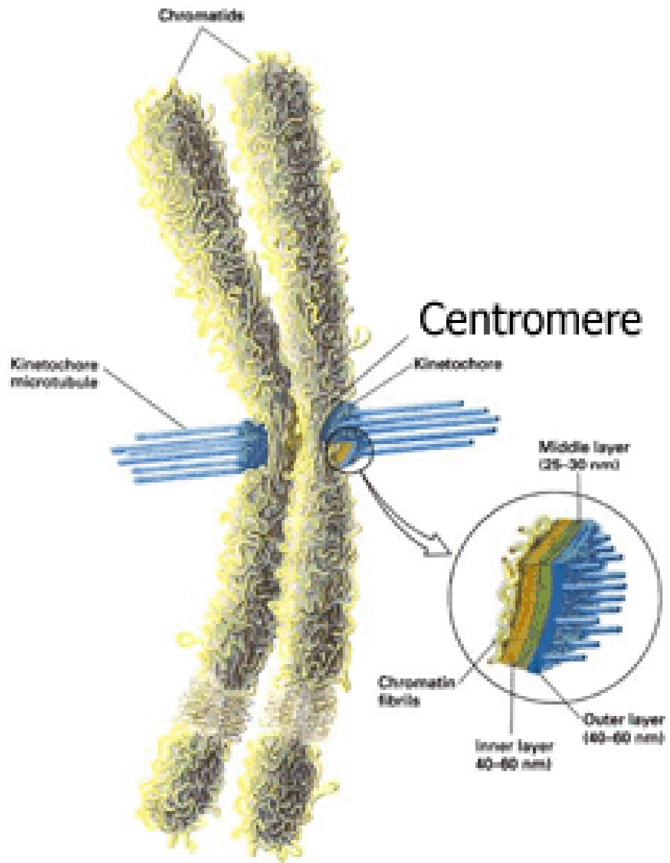
- The basic structure of the chromosome is a complex called the ***nucleosome***. Nucleosome is a-helical DNA, coiled around ***histones***, which are proteins.
- ***All eukaryotic cells contain histones, except sperm cells, which have protamines instead***.
- **Histones** are classified into **five types**, ***H1, H2A, H2B, H3 and H4***.
- **Each nucleosome is an** ***octamer (eight molecules) of histones and 146 nucleotide pairs of DNA.***
- ***Histone H1 is not in the nucleosome core, but is a spacer between nucleosomes.***
- ***Negatively charged DNA & positively charged histones hold together by ionic bonds.***

Chromosomes:

- **Chromatin Fibers:** Nucleosomes create a long chain called a chromatin fiber about 10 nm thick.
- Each chromatin fiber forms ***a helical coil called a solenoid***, 30 nm thick. ***Each coil of the solenoid has about 6 nucleosomes per coil***.
- This solenoid, in turn, coils to form ***a hollow tube*** about 200-300 nm thick in interphase.
- In mitosis, further thickening occurs to form 600-700nm thick ***chromatids.***
- ***A chromosome consists of two chromatids attached by a centromere***. ***The two chromatids of a chromosome will separate during mitosis.***

Chromosomes:





Chromosomes – *Packing Ration of DNA:*

- ***The extent of this coiling of DNA is described quantitatively as the packing ratio.***

- Packing ratio = length of linear DNA molecule divided by length of the coiled structure.

- ***The initial coiling of DNA around the histones reduces the length by a factor of seven.***

- ***Solenoid formation reduces. it further by a factor of six. Thus the packing ratio of the solenoid is 42.***

- ***The hollow tube shortens it by a factor of 18, so overall packing ratio is about 750.***

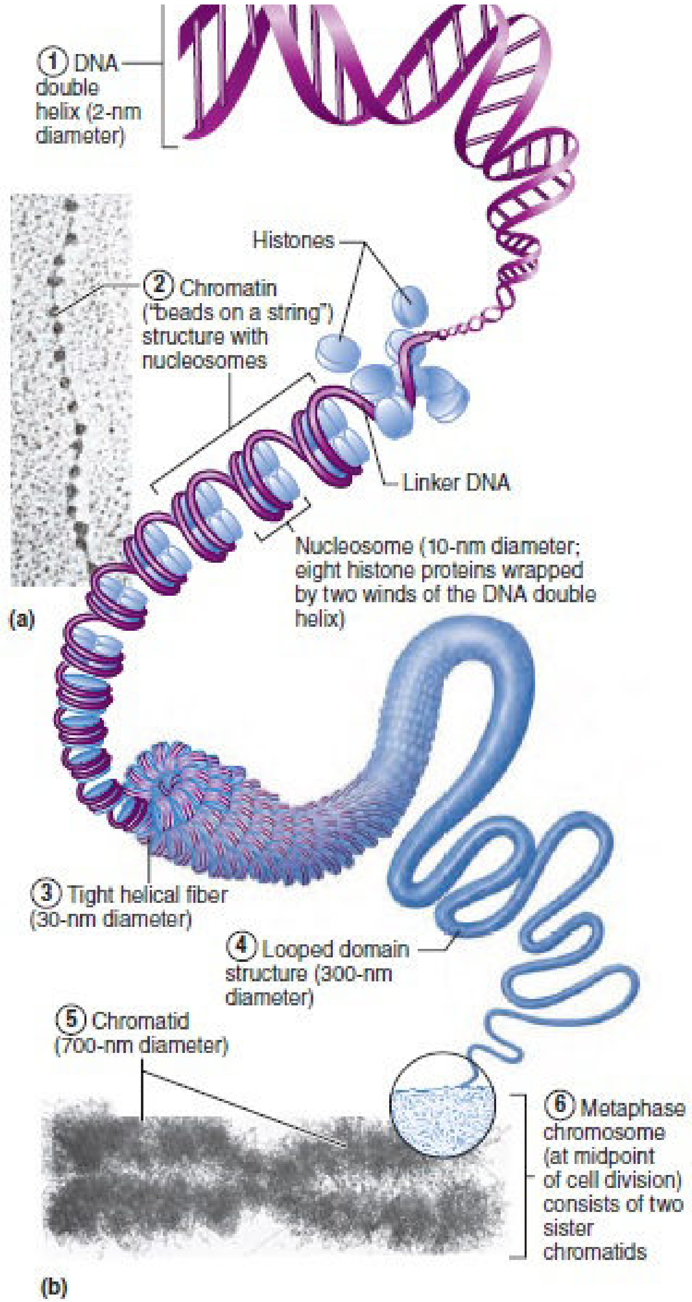
- The packing ratio for ***a chromosome in cell division*** is in the range of ***15,000 to 20,000.***

Chromosomes:

Chromatin and Chromosome Structure:

(a) Electron micrograph of chromatin fiber (Magnification: 125,000X).

(b) DNA packed in a chromosome. The levels of increasing structural complexity (coiling) from the DNA helix to the metaphase chromosome are indicated in order from the smallest ("1" DNA double helix) to the largest and most complex ("6" chromosome).



Chromosomes – *Replication:*

- **S Phase:** All the DNA in the genome is completely replicated before cell division begins. Recall that ***interphase*** is divided up into; ***G1 phase (first growth phase), S phase (synthesis of DNA), and G2 phase (2nd growth phase)***. ***All three must be absolutely complete before mitosis begins.*** ***The replication process:***

  - Segments of DNA strands separate to expose strands of unpaired bases.

  - Unpaired bases are added upon by ***DNA polymerase enzyme complex***. This enzyme complex brings appropriate bases into position to form new DNA strands. This enzyme cannot start a new DNA strand from scratch. They can only add new nucleotides to a strand that already exists. This problem is solved by formation of a short, complementary **RNA primer, about 10 bases long, by a *primase enzyme.*** Eventually DNA polymerases replace the primers with DNA nucleotides.

  - New bases are lined up so adenine is opposite thymine, guanine is opposite cytosine. ***The presence of adenine dictates that the new strand must be thymine, etc.*** Each of the separated strands now has a new paired strand ***(making 4 strands in all).***

Chromosomes – *Replication contd.:*

- **Replication Bubbles:** The entire strand doesn't replicate all at once.

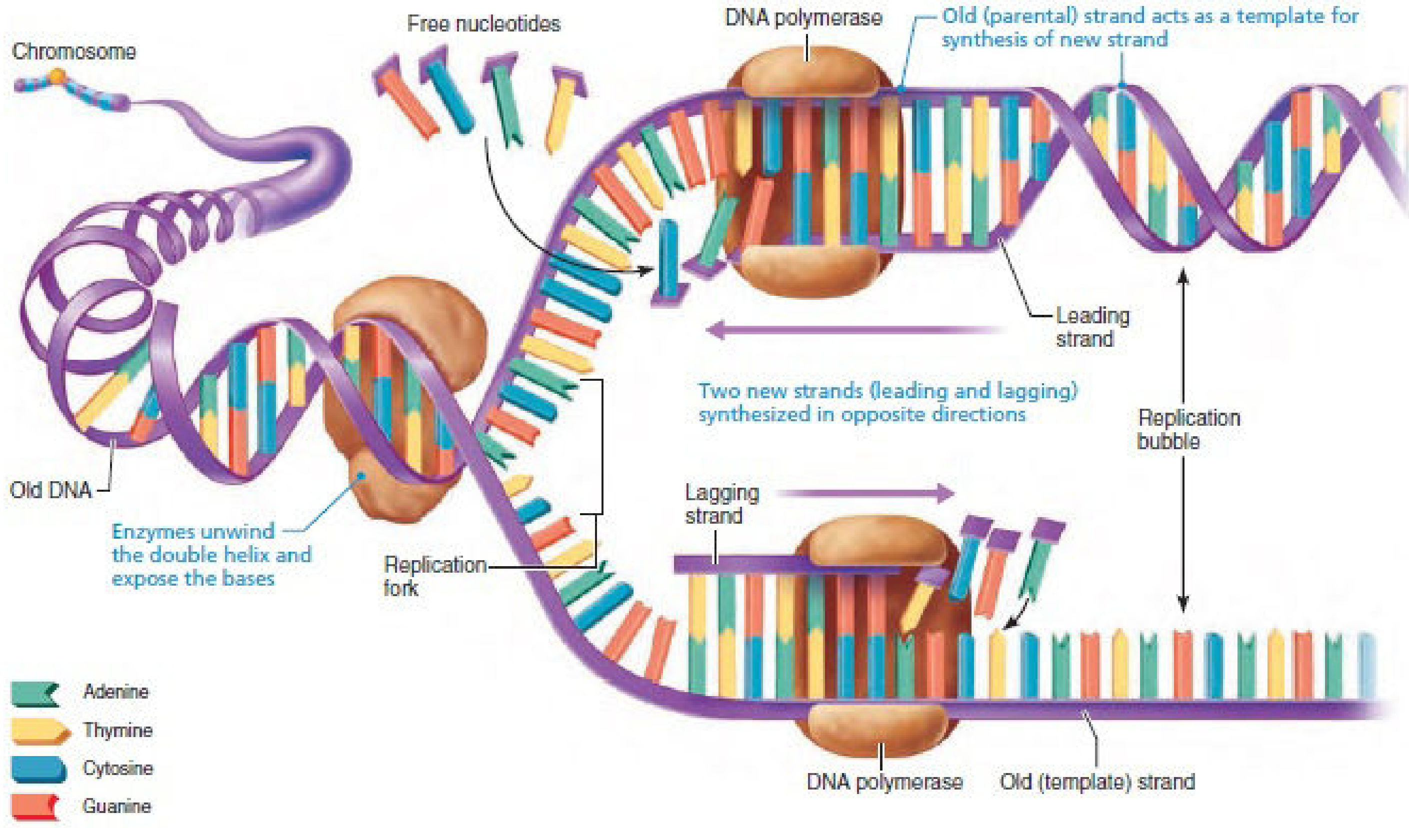
- ***Segments separate and replicate, forming regions of replication which look like bubbles.***

- Each eukaryotic chromosome has hundreds of initiation points. forming bubbles. ***Then, adjacent bubbles fuse to generate larger bubbles.***

- Later, ***Y-shaped intermediates*** are formed, with ***unreplicated DNA on the stem of the Y***, and with ***new strands present on the two prongs of the Y***.

- It is a semiconservative replication; eventually, each double-stranded chromosome forms two new double-stranded ones. ***New ones are double-stranded, but each has one original strand and one new strand.***

- ***So we have two new chromosomes, neither of which is fully new, or fully original.***



Replication of DNA Summary: Once the DNA helix is uncoiled, and the hydrogen bonds between its base pairs are broken, each nucleotide strand of the DNA acts as a template for constructing a complementary strand, as illustrated on the right-hand side of the diagram. (The step in which RNA primers are formed to start the process at replication bubbles is not shown.) DNA polymerases work in one direction only, so the two new strands (leading and lagging) are synthesized in opposite directions. (***The DNA ligase*** enzymes that join the DNA fragments on the lagging strand are not illustrated.) Each DNA molecule formed consists of one old (template) strand and one newly assembled strand and constitutes a chromatid of a chromosome.