The Cell Cycle

I. The chromosomes structure during cell cycle

The Cell Cycle

The chromosomes structure during cell cycle

- **The nucleus is a membrane bound organelle that contains the genetic information in the form of chromatin, highly folded ribbon-like complexes of deoxyribonucleic acid (DNA) and a class of proteins called histones.**

- **When a cell divides, chromatin fibers are very highly folded, and become visible in the light microscope as chromosomes. During interphase (between divisions), chromatin is more extended, a form used for expression genetic information.**

The DNA of chromatin is wrapped around a complex of histones making what can appear in the electron microscope as "beads on a string" or nucleosomes. Changes in folding between chromatin and the mitotic chromosomes is controlled by the packing of the nucleosome complexes.
•passed on to daughter cells.

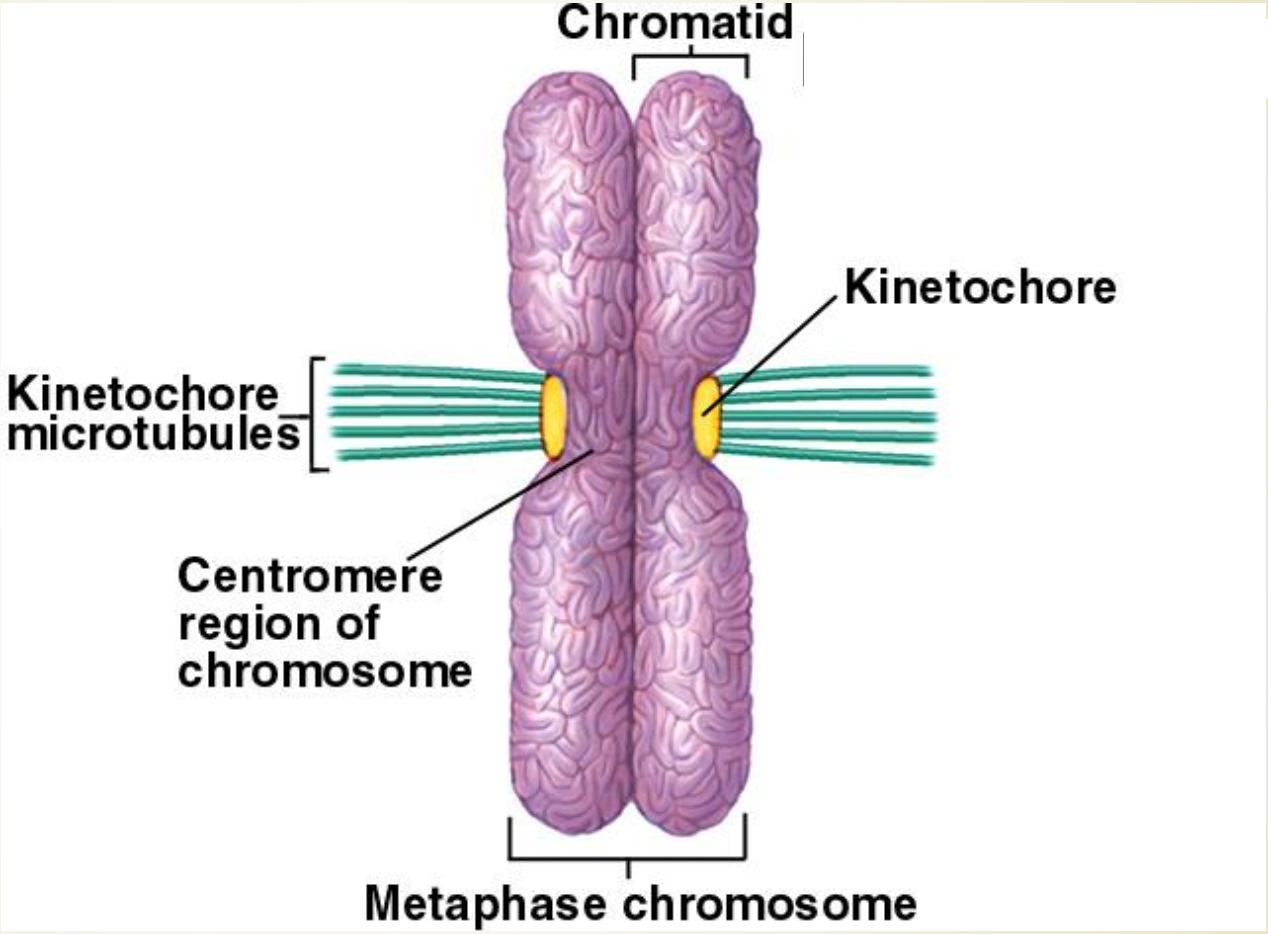
The Cell Cycle

The chromosomes structure during cell cycle

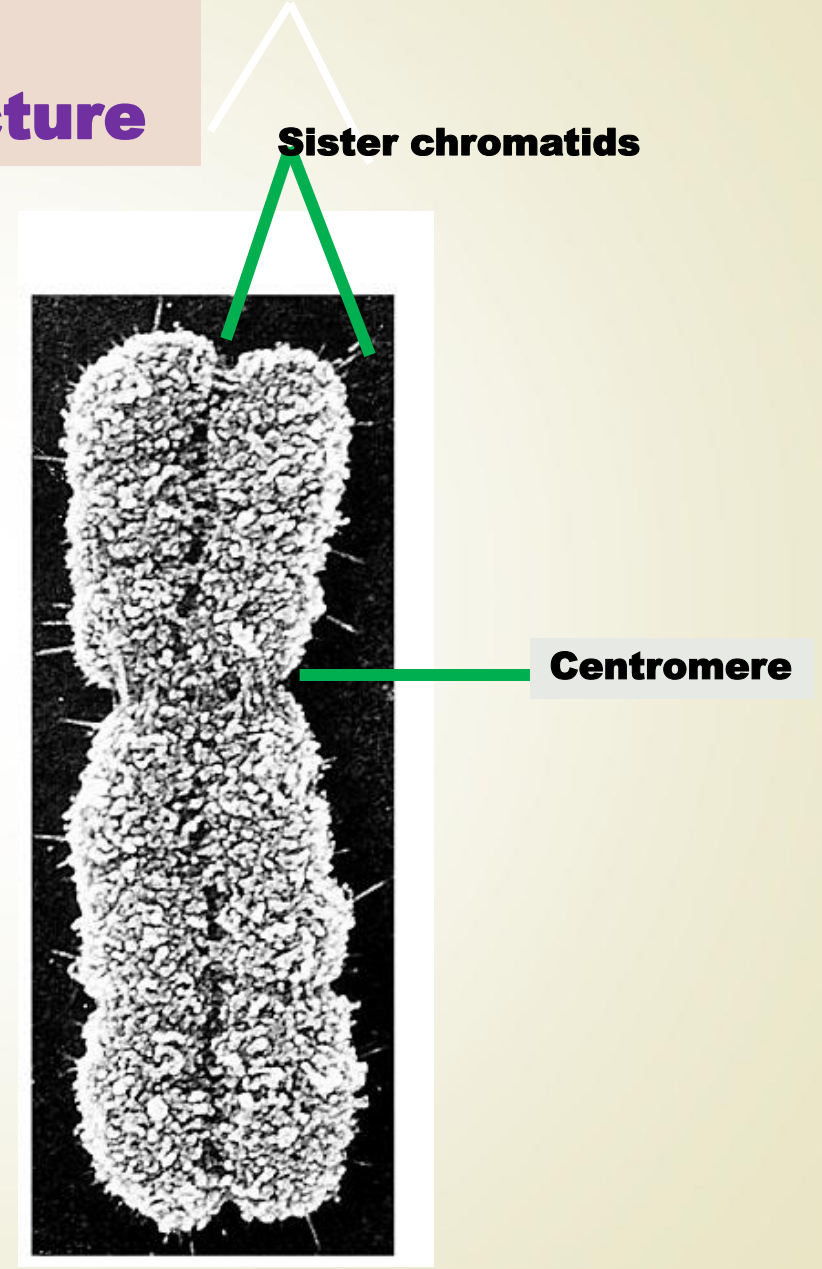
- **DNA or deoxyribonucleic acid is a large molecule structured from chains of repeating units of the sugar deoxyribose and phosphate linked to four different bases abbreviated A, T, G, and C.**

- **The process of mitosis is designed to insure that exact copies of the DNA in chromosomes are passed on to daughter cells.**

The Metaphas chromosomes structure



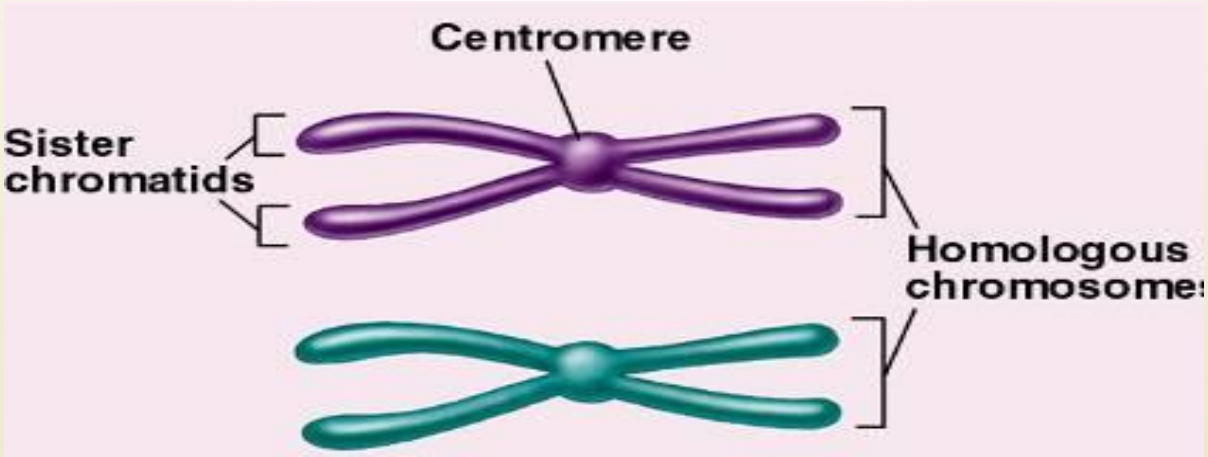
The Metaphas chromosomes structure



- **Before a cell starts dividing, the chromosomes are duplicated**
  - **This process produces sister chromatids**
  - **EM of human chromosome that has duplicated**

The Metaphas chromosomes structure

- **Homologous chromosomes are identical pairs of chromosomes.**
- **One inherited from mother and one from father**
- **made up of sister chromatids joined at the centromere.**



The Cell Cycle

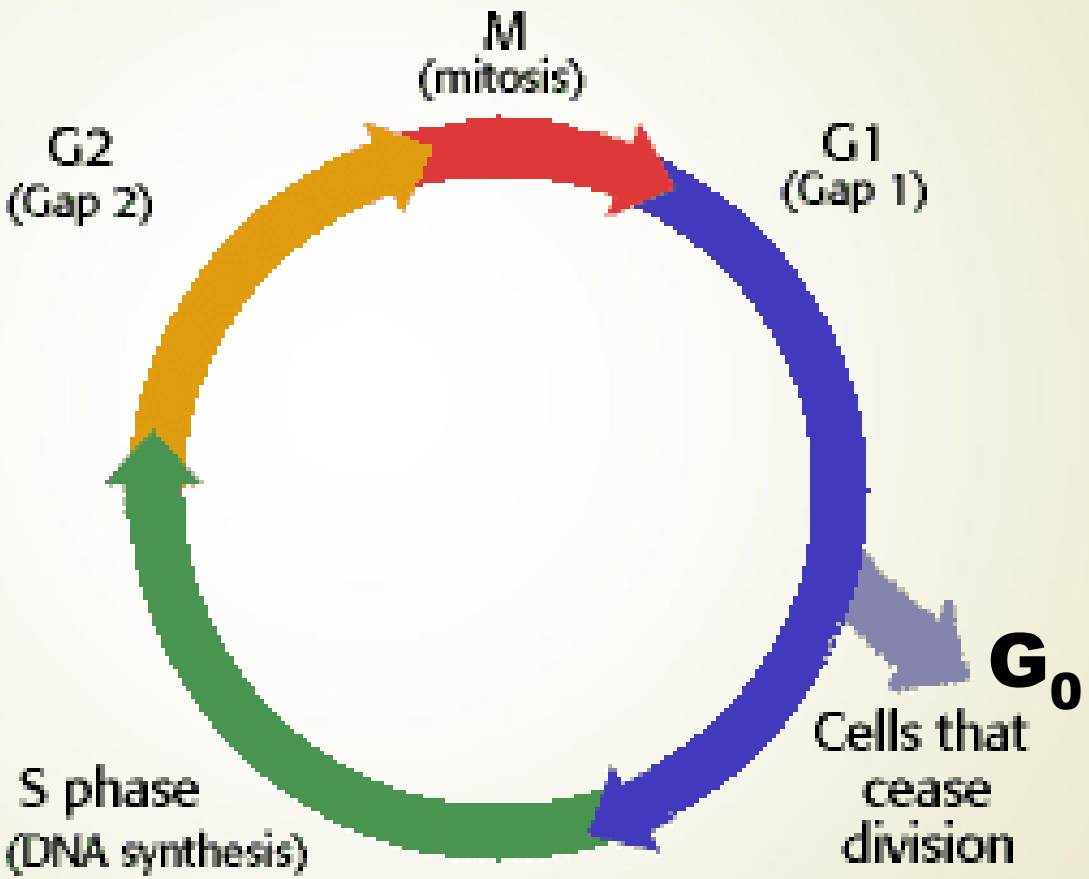
- The cell cycle is an ordered set of events, culminating in cell growth and division into two daughter cells.

- Non-dividing cells not considered to be in the cell cycle.
- The stages, pictured to the left, are G1-S-G2-M.

a. The G1 stage stands for "GAP 1".
b. The S stage stands for "Synthesis". This is the stage when DNA replication occurs.
c. The G2 stage stands for "GAP 2".
d. M stage stands for "mitosis or Meiosis", and when nuclear (chromosomes separate) and cytoplasmic (cytokinesis) division occur. Mitosis is further divided into 4 phases,

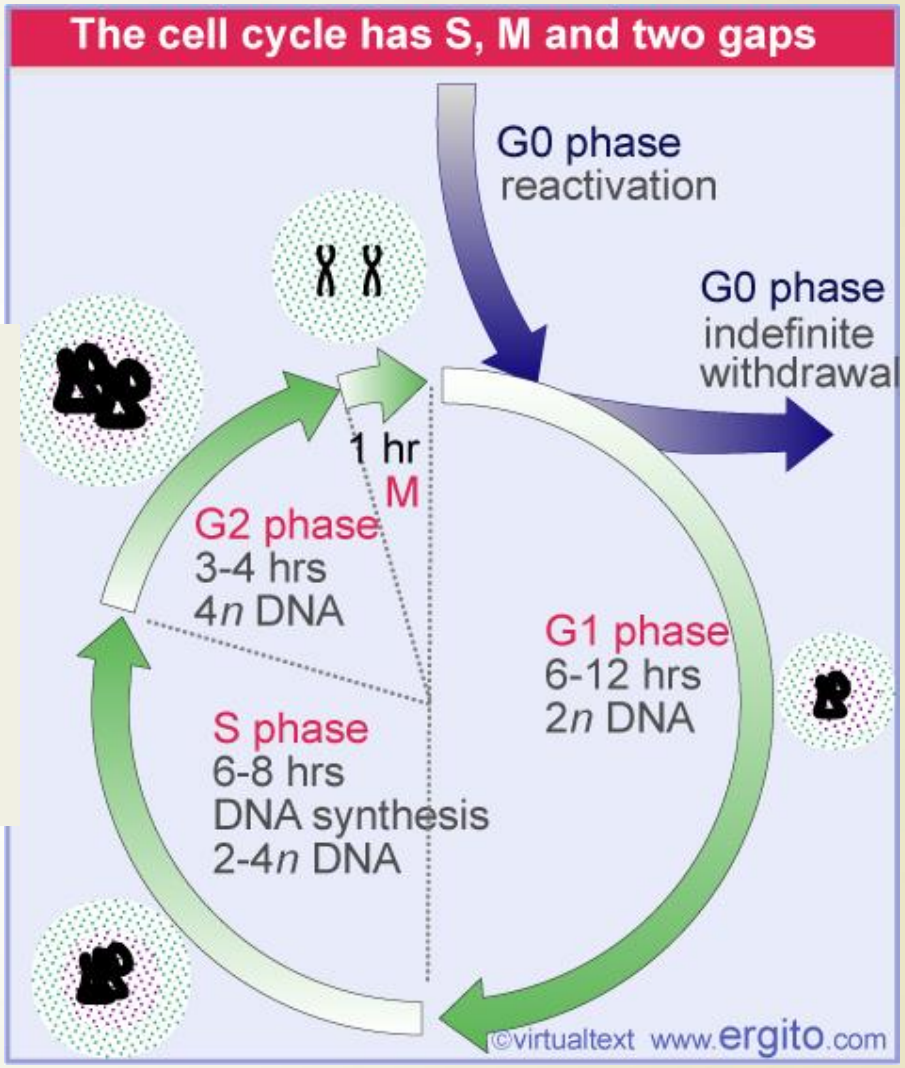
The Cell Cycle

The Cell Cycle Stages of the cell cycle



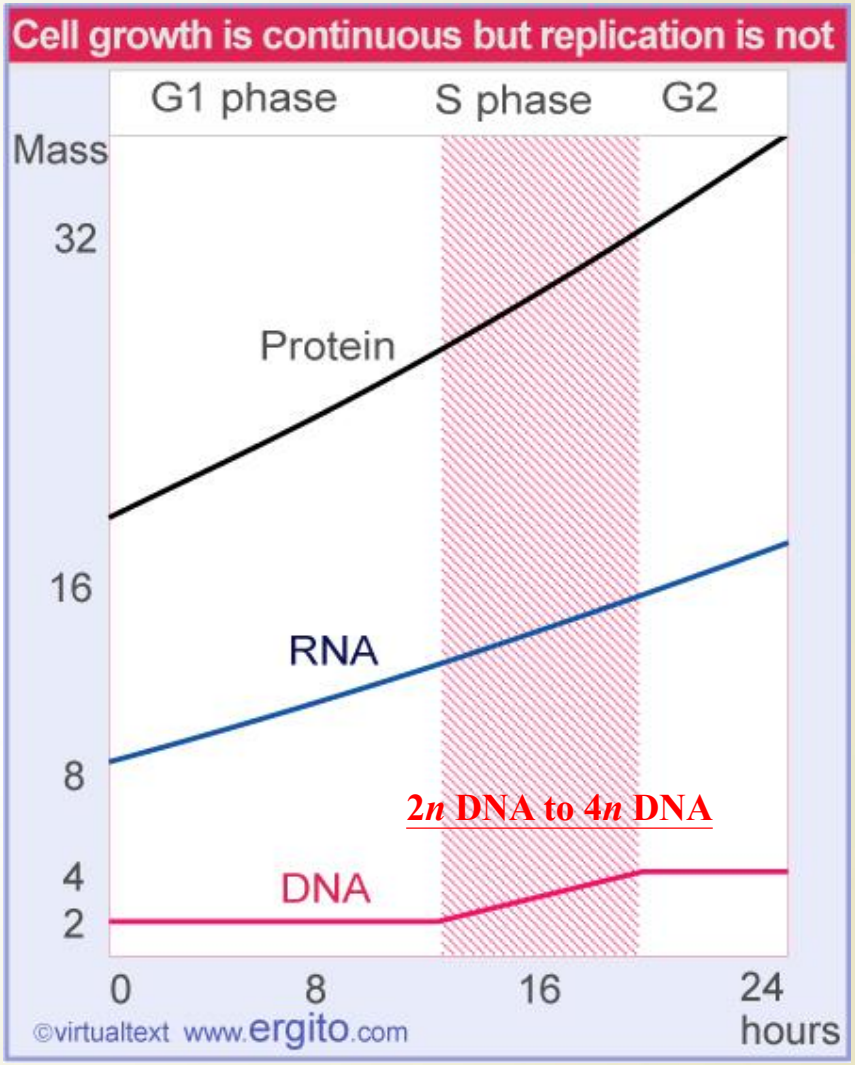
Overview of Cell Cycle

- Interphase: G1, S, and G2 phase
  (The end of cell division to The start of next cell division)
- Mitosis: M phase
  (The period of cell divided into two daughter cells)



Synthesis at S Phase

- S phase: synthetic period
  (DNA is specifically & largely replicated)
  (Genetic information is duplicated)
- Interphase:
  (Continuous increase of RNA & protein)



The Cell Cycle

Regulation of the cell cycle

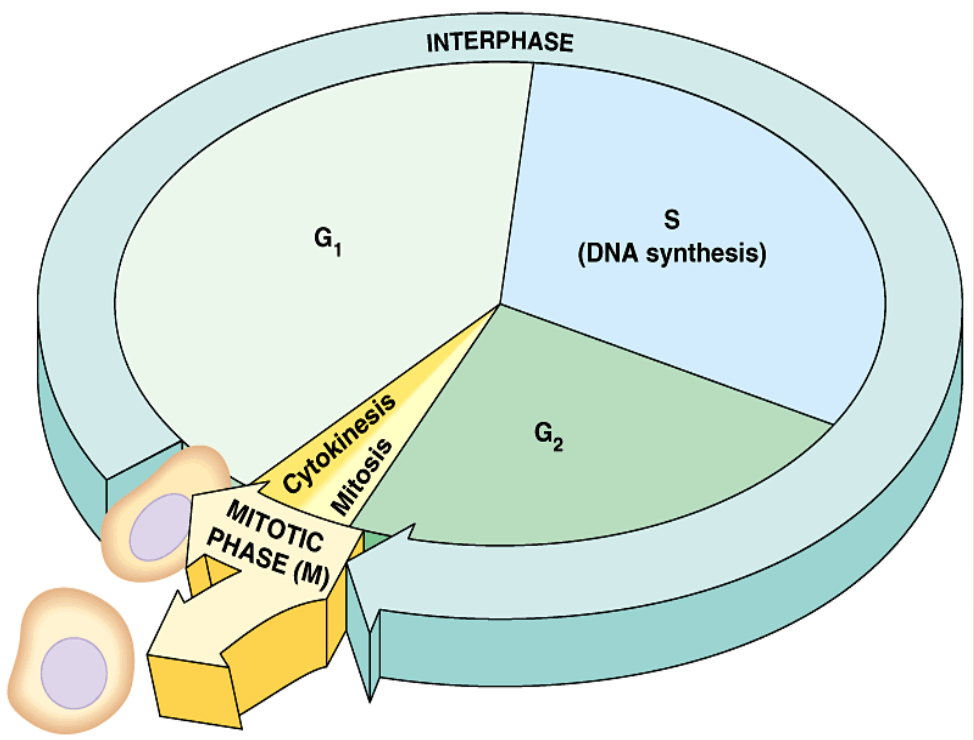
- How cell division (and thus tissue growth) is controlled is very complex. The following terms are some of the features that are important in regulation, and places where errors can lead to cancer. Cancer is a disease where regulation of the cell cycle goes awry and normal cell growth and behavior is lost.
- Cyclins (D,E ,A & B) & Cdk (cyclin dependent kinase, adds phosphate to a protein), along with cyclins, are major control switches for the cell cycle, causing the cell to move from G1 to S or G2 to M.

MPF (Maturation Promoting Factor) includes the CdK and cyclins that triggers progression through the cell cycle.

The life cycle of a cell
Cell cycle consists of 2 major phases

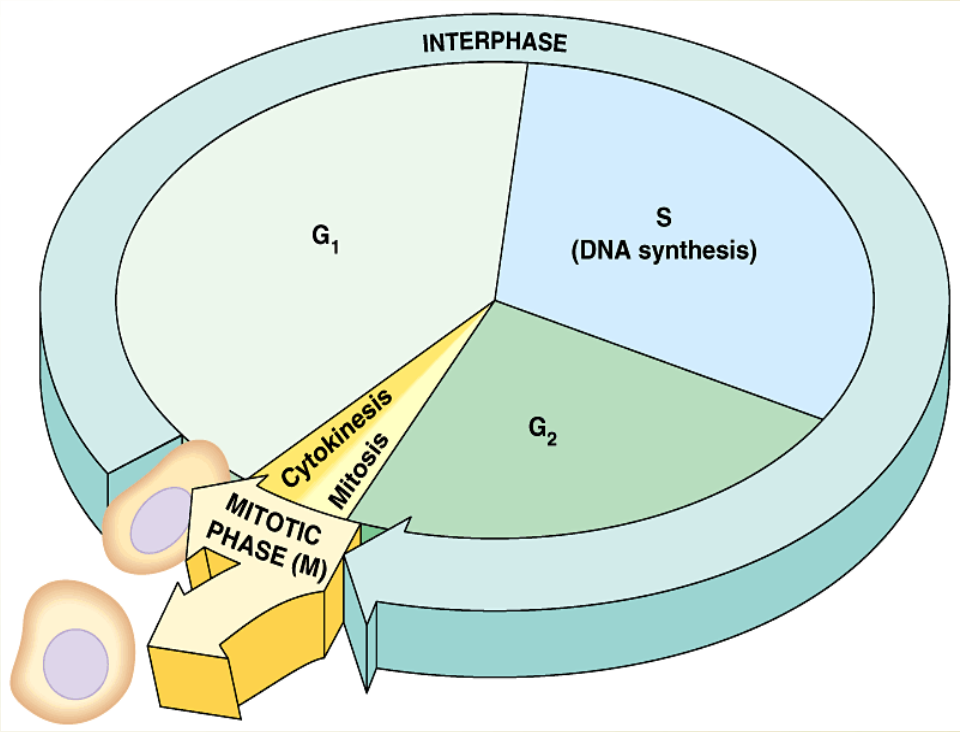
- **Interphase**
  where chromosomes duplicate and cell parts are made.

- **The mitotic phase**
  when nuclear division occurs.

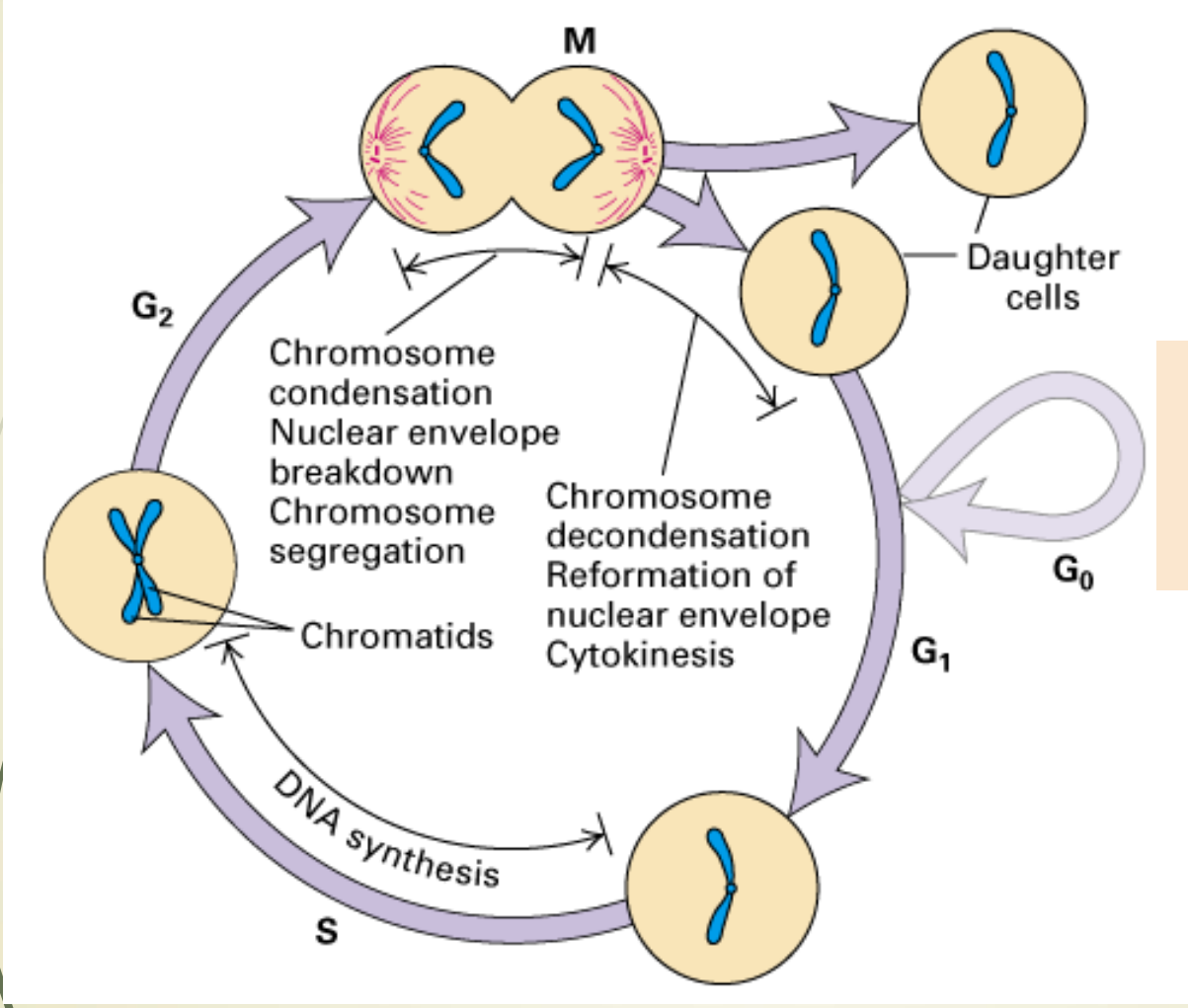


- **Most of the life of a cell is spent in Interphase.**
- **Cell does most of its' growth during interphase**

- **During interphase a cell performs all of its regular functions and gets ready to divide**
- **Metabolic activity is very high**



The Eukaryotic cell cycle



Cell arrest

CONTROL OF THE CELL CYCLE

Three checkpoints:

The **G1/S cell cycle checkpoint**

G2/M DNA damage checkpoint

Mitosis checkpoint

G1/S cell cycle checkpoint

controls the passage of eukaryotic cells from the first 'gap' phase (G1) into the DNA synthesis phase (S).

Checks:

That the size is CORRECT

That the environment is CORRECT

External agents regulate progression

Kinases – add a phosphate group (phosphorylate)

G1/S cell cycle checkpoint How do they do that?

Major proteins involved:

Cyclins (proteins) - level fluctuate in the cell cycle.

&

Cyclin dependent KINASES* (Cdks)

They add phosphate groups to proteins that control processes in the cell cycle.

They only do this when the cyclins are present.

*Kinases – add a phosphate group (phosphorylate)

G_0 phase

- Nonproliferative cells in multicellular eukaryotes generally enter the stable G_0 state from G_1 and may remain stable for long periods of time, possibly indefinitely (as is often the case for neurons).
- This is very common for cells that are fully differentiated.
- it is often a biochemical reaction; division of such a cell could, for example, become cancerous.
- Some cells enter the G_0 phase semi-permanentally e.g., some liver, kidney, stomach cells.

Interphase

- Before a cell can enter cell division, it needs to take in nutrients. All of the preparations are done during interphase.
- Interphase is a series of changes that takes place in a newly formed cell and its nucleus, before it becomes capable of division again. It is also called preparatory phase or intermitosis.
- Previously it was called resting stage because there is no apparent activity related to cell division.
- Typically interphase lasts for at least 90% of the total time required for the cell cycle.
- Interphase proceeds in three stages, G_1, S, and G_2, preceded by the previous cycle of mitosis and cytokinesis.
- The most significant event is the replication of genetic material (DNA) in S phase.

G_1 Phase

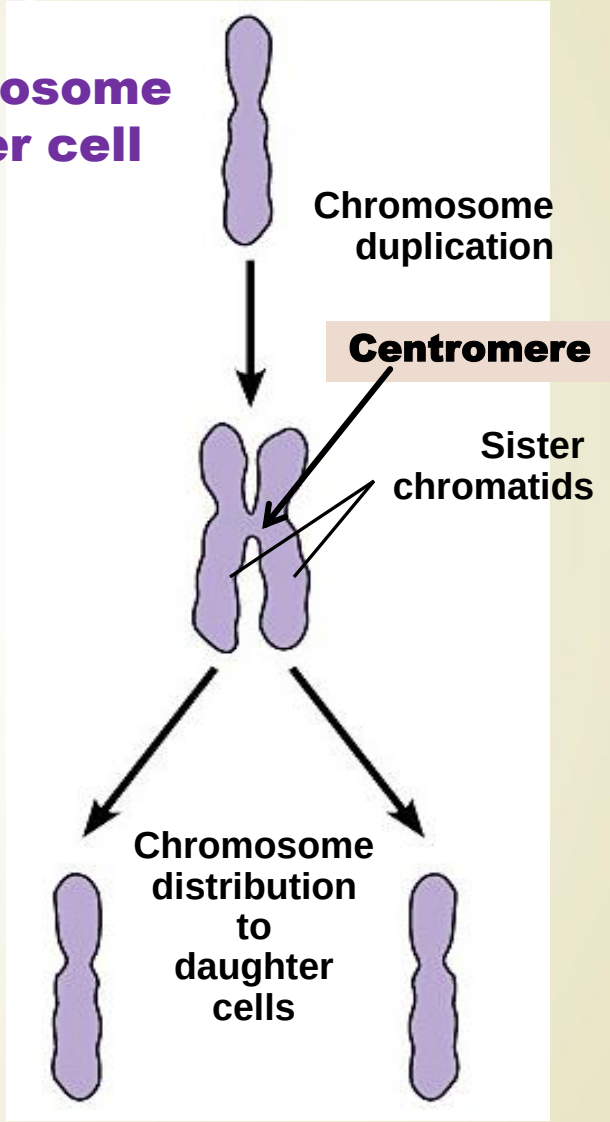
- The first phase within interphase, from the end of the previous M phase until the beginning of DNA synthesis, is called G_1 (G indicating *gap*).
- It is also called the growth phase. During this phase the biosynthetic activities of the cell, which are considerably slowed down during M phase, resume at a high rate.
- This phase is marked by the use of 20 amino acids to form millions of proteins and later on enzymes that are required in S phase, mainly those needed for DNA replication.
- It is under the control of the p53 gene. We can say that in this phase, cell increases its supply of proteins, increases the number of organelles (such as mitochondria, ribosomes), and grows in size.

S Phase

- The S phase starts when DNA replication begins; when it is complete, all of the chromosomes have been replicated, i.e., each chromosome has two (sister) chromatids.
- Thus, during this phase, the amount of DNA in the cell has effectively doubled, though the ploidy of the cell remains the same.
- During this phase, synthesis is completed as quickly as possible due to the exposed base pairs being sensitive to harmful external factors such as mutagens.

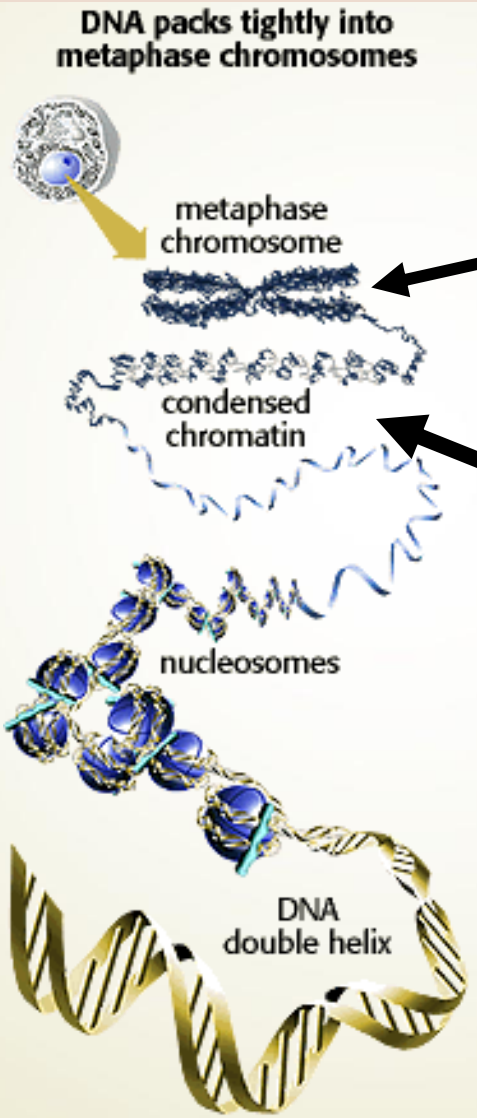
The chromosomes structure during cell cycle

- The Chromosome of the mother cell



- When the cell divides, the sister chromatids separate
- And when Two daughter cells are produced.
- Each has a complete and identical set of chromosomes

The chromosomes structure during cell cycle



Double Chromatid

(End of S stage)

Single Chromatid

Levels of DNA Packaging in Eukaryotes

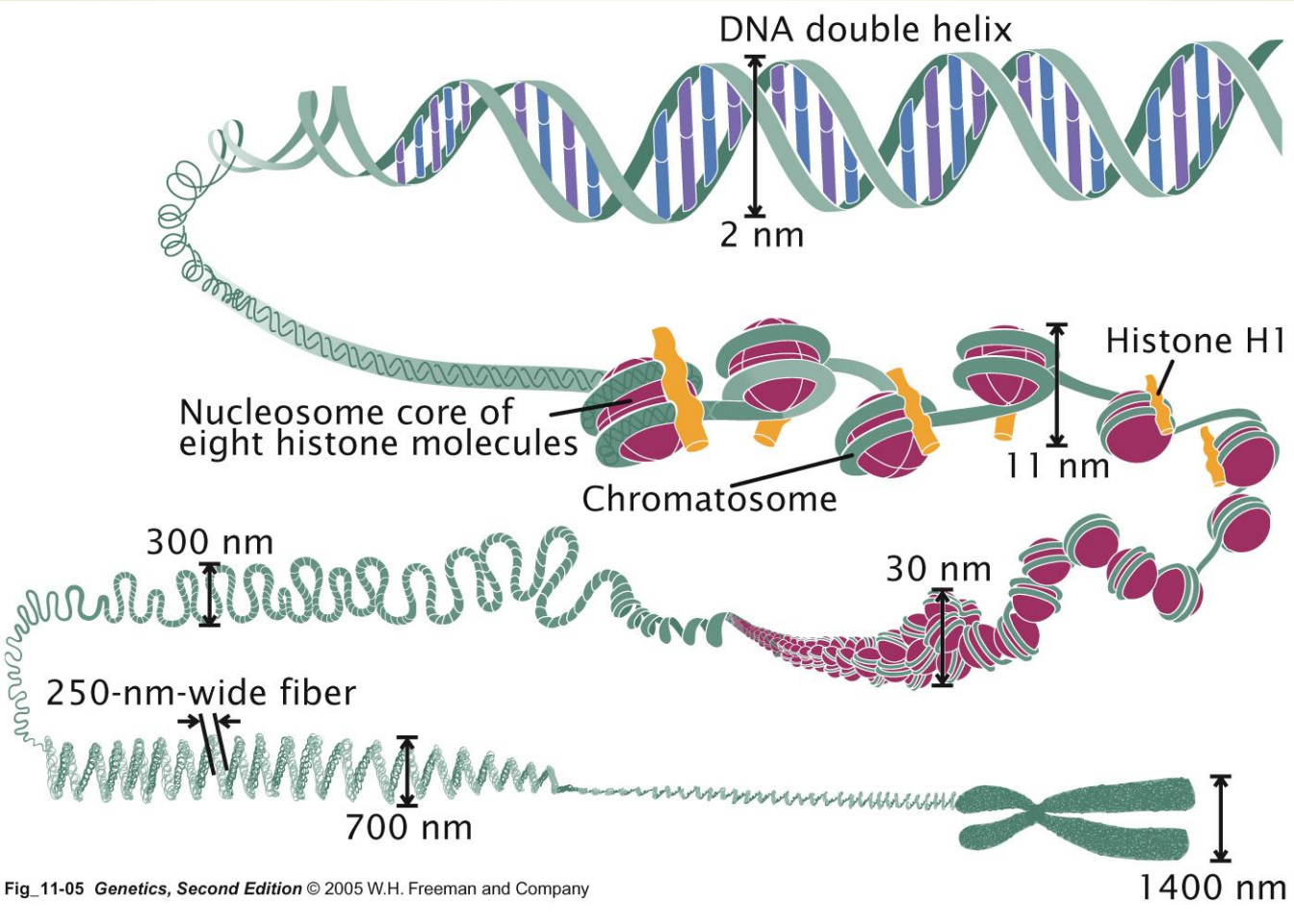
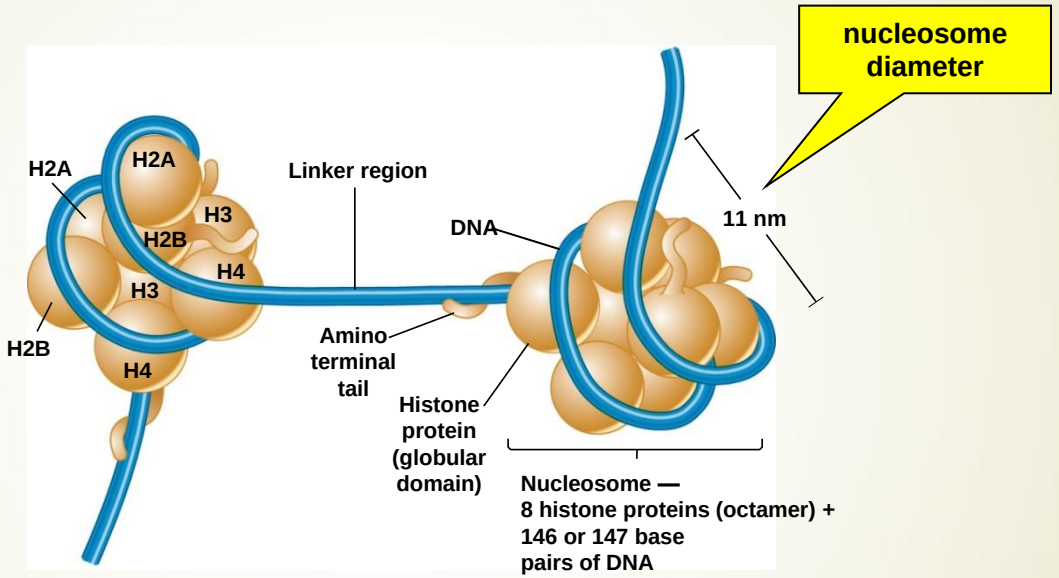


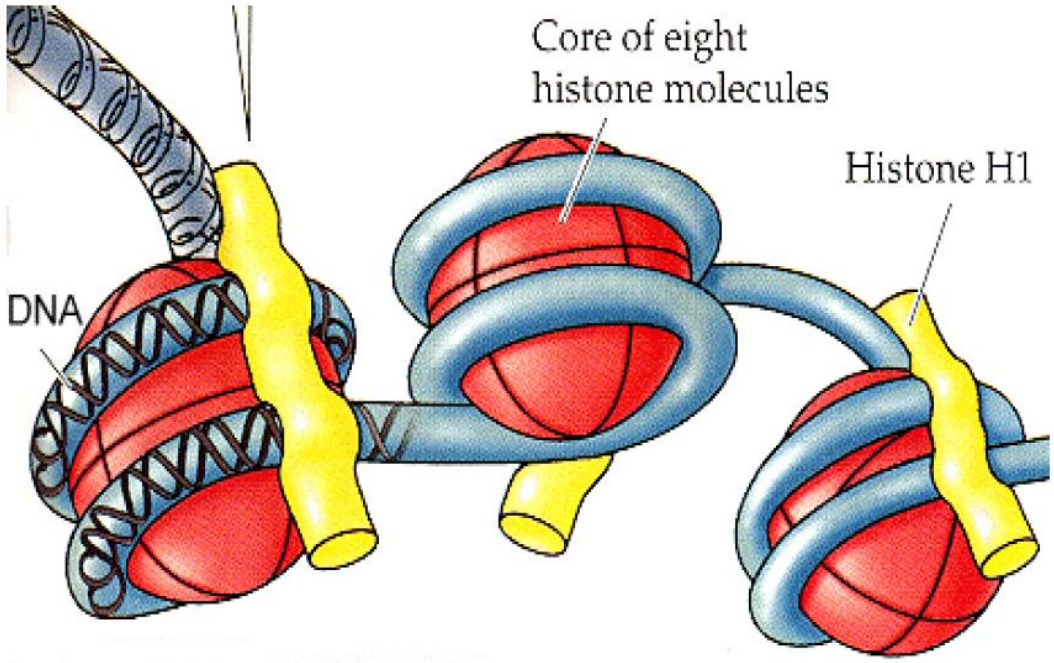
Fig_11-05 *Genetics, Second Edition* © 2005 W.H. Freeman and Company

Nucleosomes shorten DNA ~seven-fold

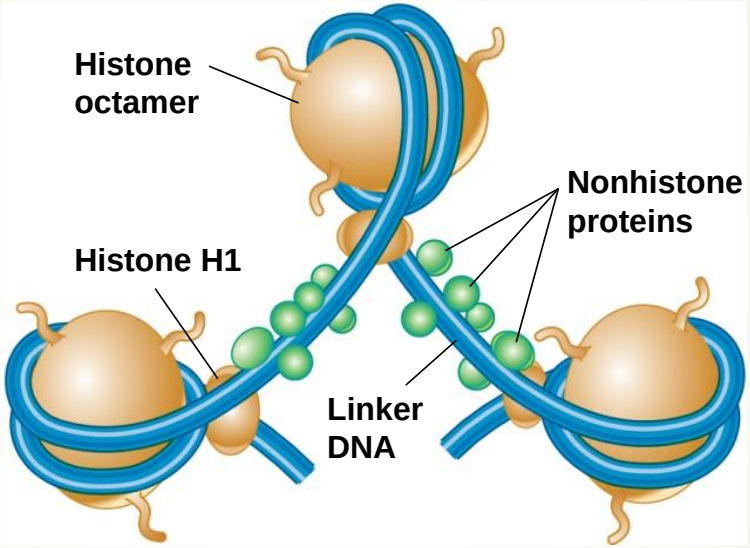


(a) Nucleosomes showing core histone proteins

Nucleosome core particle

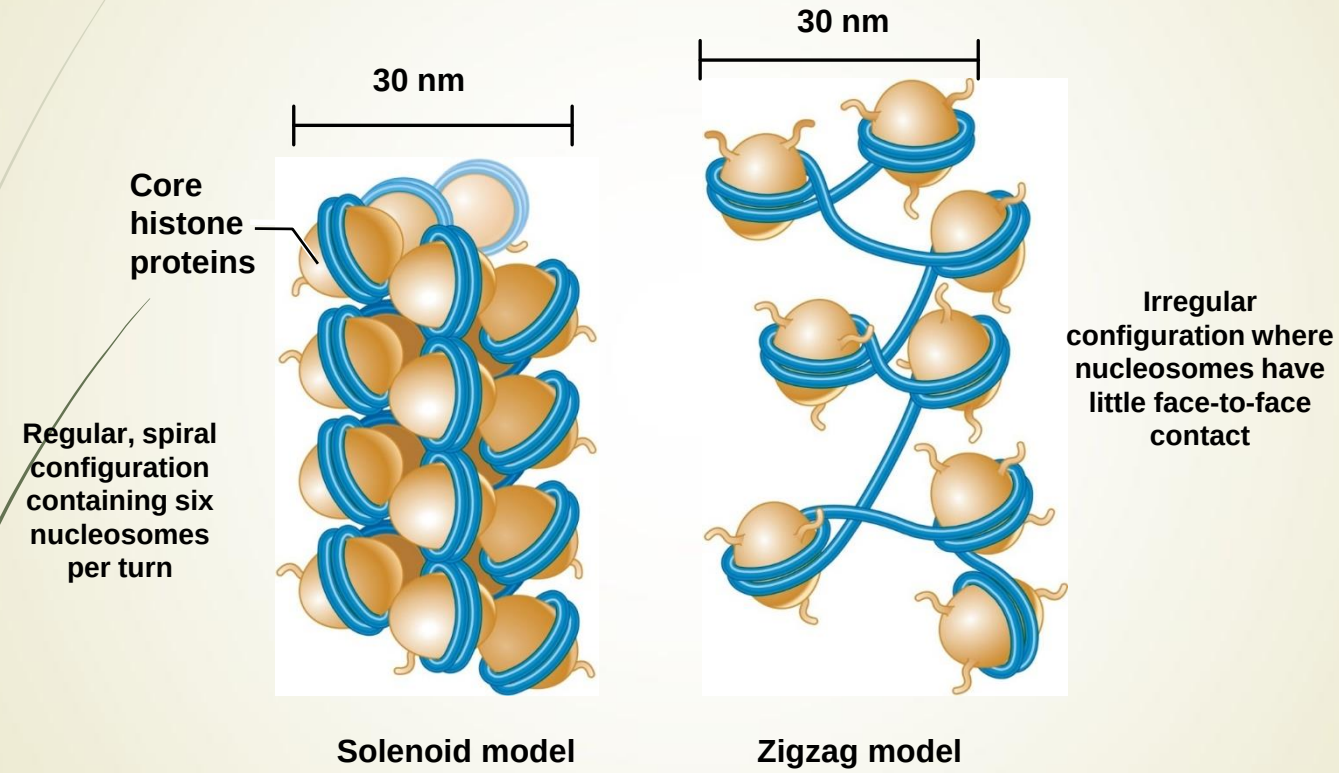


Non-histone proteins play role in chromosomes organization and compaction

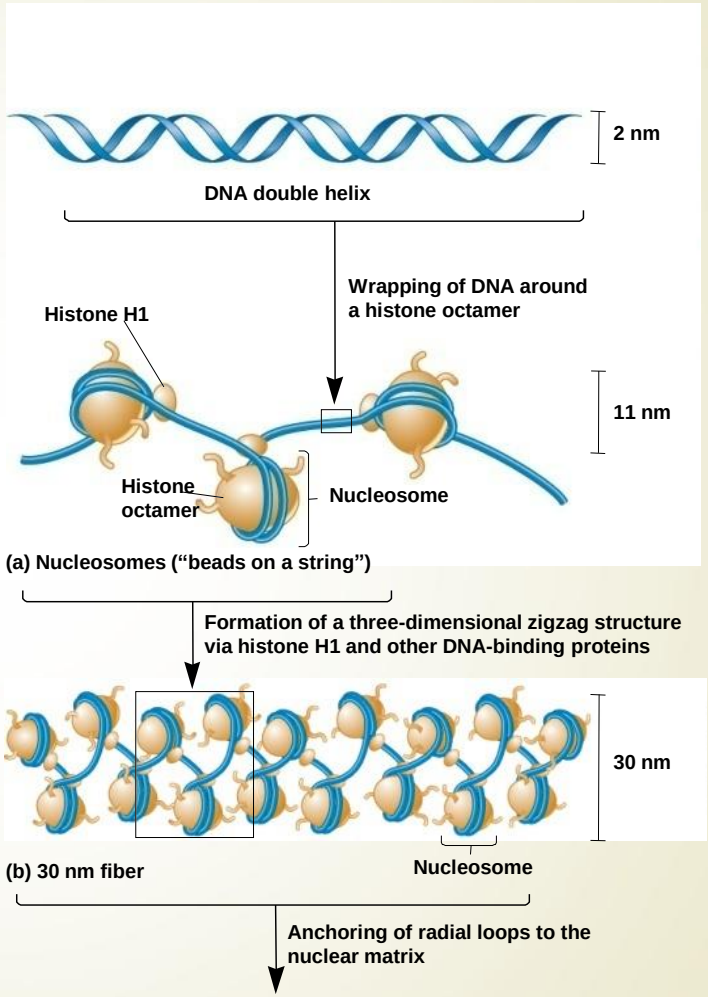


Nucleosomes showing linker histones and nonhistone proteins

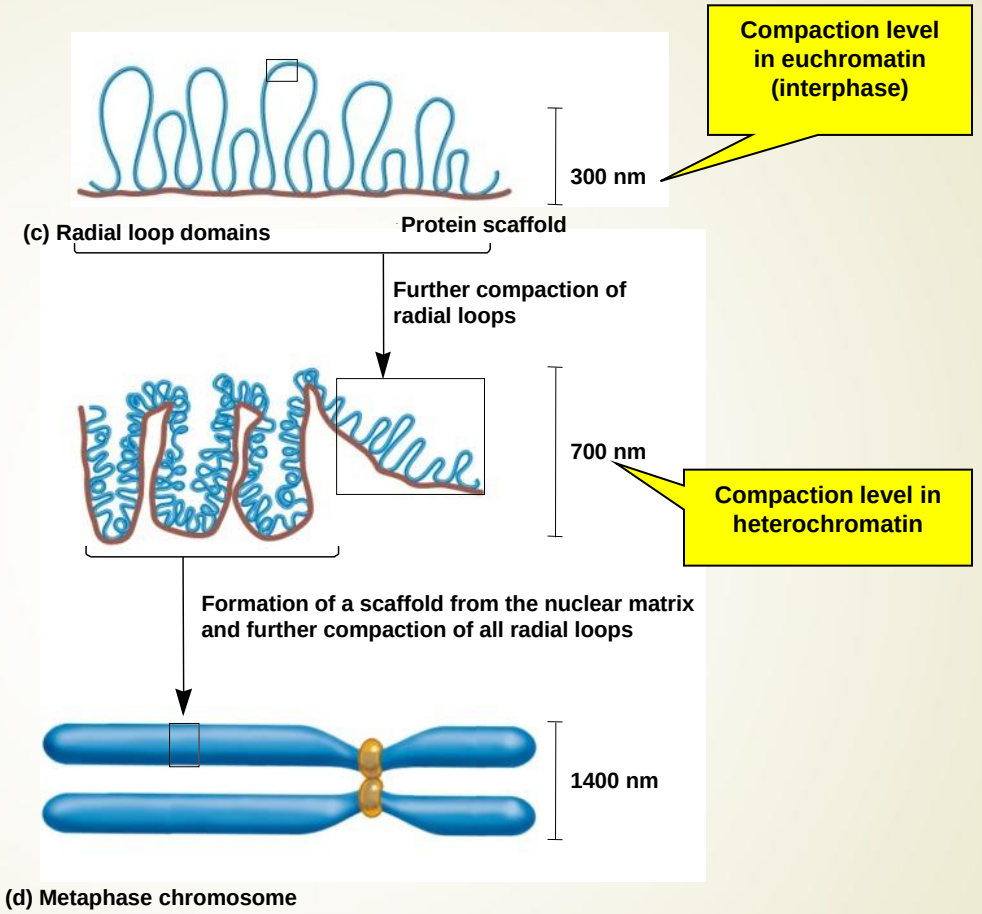
Nucleosomes closely associate to form 30 nm fiber (shortens total DNA by another 7 fold)



Levels of DNA Packaging



Levels of DNA Packaging, cont.



THE END