Paper IV -Cell and Molecular Biology

UNIT- III

Cell Cycle : Role of Microtubules in cell cycle. Cyclines and cycline dependent kinases, Regulation of CDK – cyclin activity; Check points of cell cycle. Biology of Aging: Maximum life span and life expectancy, Causes of aging, genetic instability, free radicals, oxidative damage and antioxidants, Telomerase.

Cell Death: Necrosis and Apoptosis; genes involved in apoptosis.

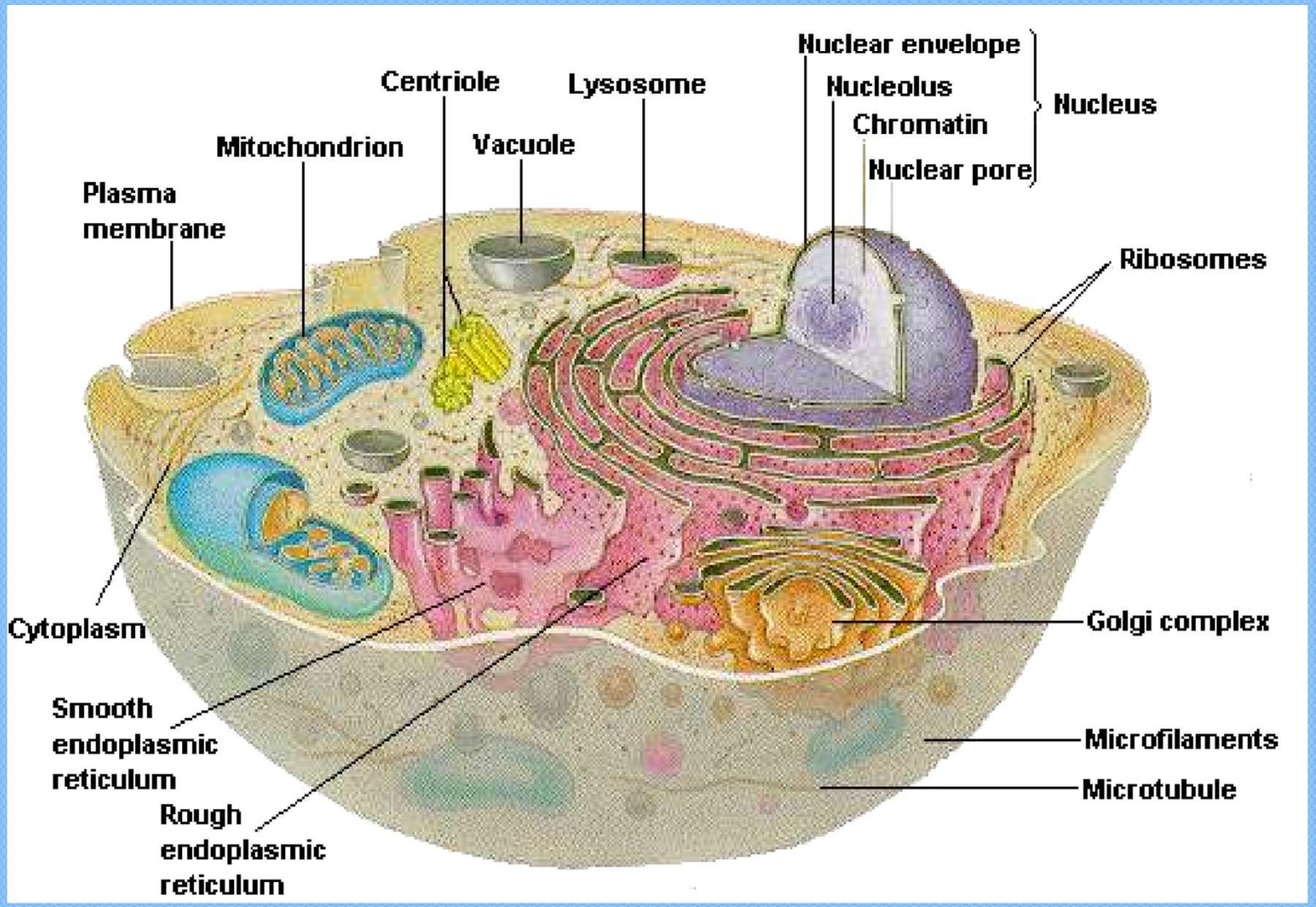
What is a cell?

What is cell biology?

What is molecular biology?

What is cell & molecular biology?

What is a cell?



What is a Cell ?

A cell is defined as the fundamental, structural and functional unit of all life *responsible for all of life's processes*

Robert Hooke discovered cells.

What is Cell Biology?

The study of cells from its basic structure to the functions of every cell organelle is called Cell Biology.

A branch of **biology** that **includes** study of **cells** regarding their physiological properties, structure, and function; the organelles they **contain**; interactions with their environment; and their life cycle, division, and death. This **is** done both on a microscopic and molecular level.

What is Molecular Biology?

Molecular Biology is the field of **biology** that studies the composition, structure and interactions of cellular **molecules** – such as nucleic acids and proteins – that carry out the **biological** processes essential for the cell's functions and maintenance.

What is Cell and Molecular Biology?

The study of cells and the macromolecules (DNA, RNA, protein, lipids, carbohydrates) that define their structure and function

UNIT I

Biomembranes: Basic structure, Transport across cell membranes, Diffusion, Osmosis (Uniports, Symports and Antiports), Ion Channels, Active Transport and Membrane Pumps, Electrical properties of biomembranes and Membrane potential.

UNIT II

Cell adhesion and Communication: Tight junctions, Gap junctions, Connexins, Desmosomes and Spot desmosomes.

Cell–Cell signalling : Second messenger system, cAMP , Cell surface receptors and intra cellular receptors. Protein mediated signalling in mammalian and bacterial system (G-proteins, Tyrosine kinase, Serine/threonine kinase,).

UNIT III

Cell Cycle : Role of Microtubules in cell cycle. Cyclines and cycline dependent kinases, Regulation of CDK – cyclin activity; Check points of cell cycle.

Biology of Aging: Maximum life span and life expectancy, Causes of aging, genetic instability, free radicals, oxidative damage and antioxidants, Telomerase.

Cell Death: Necrosis and Apoptosis; genes involved in apoptosis.

UNIT IV

Intracellular transport : Intracellular protein trafficking, Signal hypothesis. Golgi sorting Post and co-transitional modifications. Lysosomal polymorphism. Regulation of intracellula transport.

Metabolic Pathways and its Network: A broad outline of metabolic pathways and the linkage, metabolism of primary metabolites – monosaccharaides, lipids, essential amin acids and nucleotides.

UNIT V

DNA repair and recombination, RNA synthesis and processing, Protein synthesis and processing, Control of gene expression at transcription and translation level.

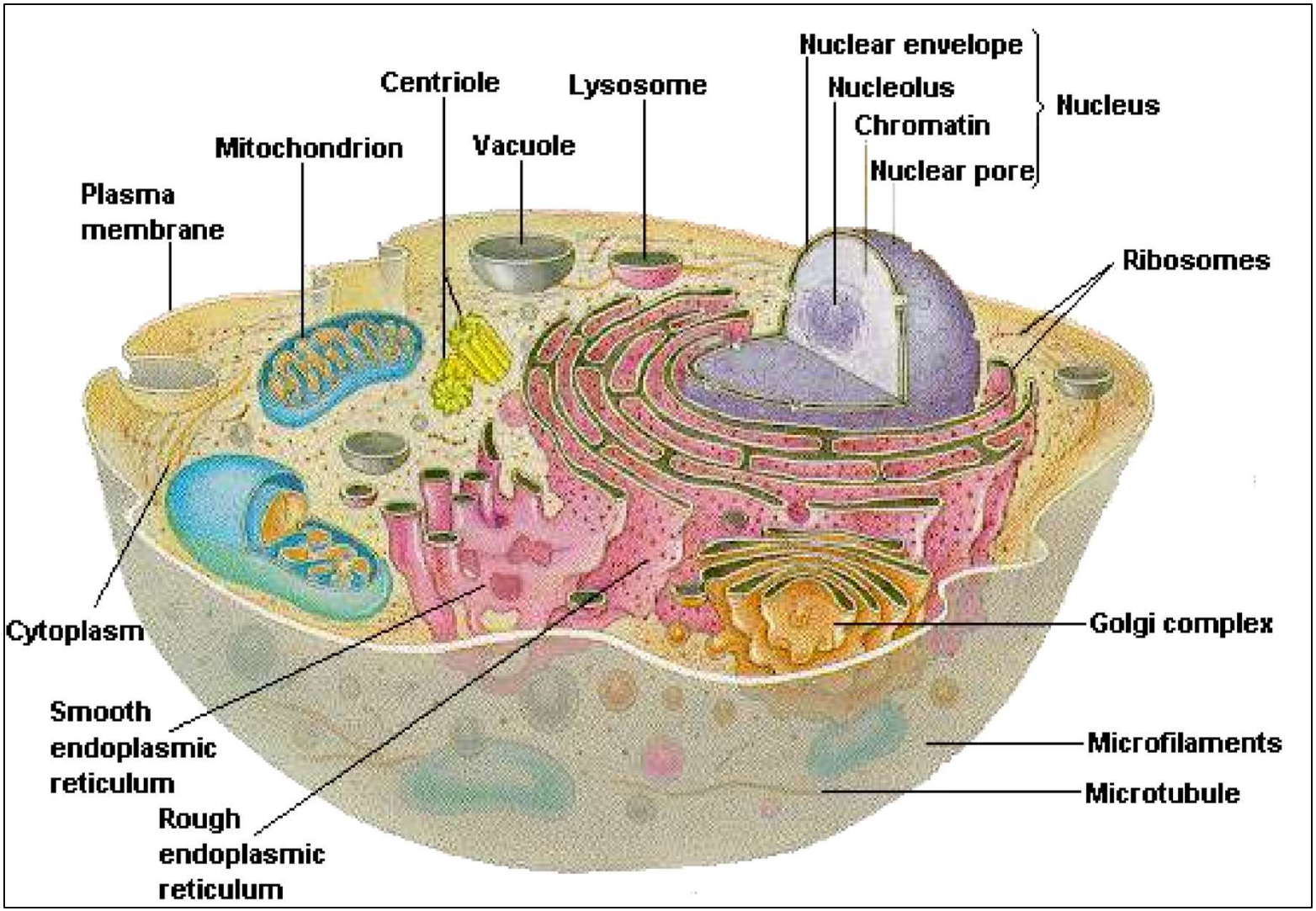
C-value Paradox, Euchromatin and Heterochromatin. Human karyotype, Chromosomal banding (Paris conference nomenclature).

Somatic Cell Genetics : Cell fusion and hybrid agents, mechanism of fusion Formation of Heterokaryon (Hybrid selection and chromosomal segregation). Applications of Hybridoma technology.

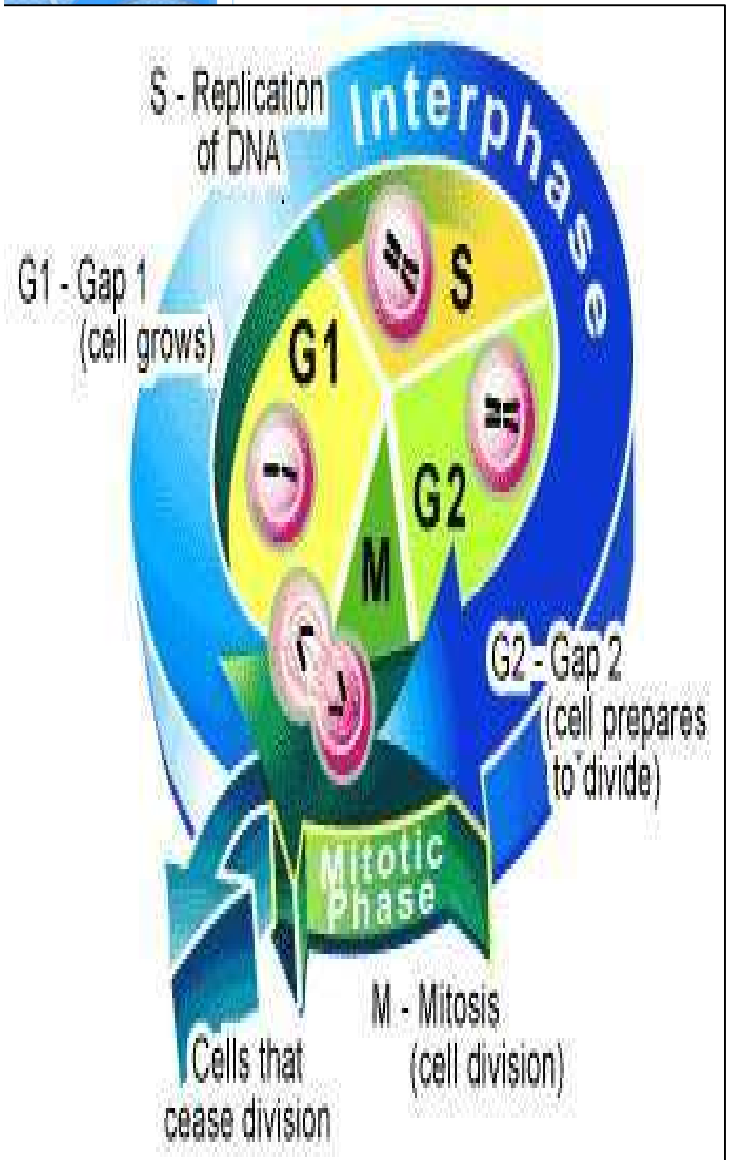
CONTENTS

- Definition
- Different phases of cell cycle
- Various checkpoints
- Growth factors that effect cell cycle
  - Positive regulators
  - Negative regulators

THE CELL


Nuclear envelope
Centriole
Lysosome
Nucleolus
Nucleus
Chromatin
Mitochondrion
Vacuole
Nuclear pore
Plasma membrane
Ribosomes
Cytoplasm
Golgi complex
Smooth endoplasmic reticulum
Microfilaments
Microtubule
Rough endoplasmic reticulum

CELL CYCLE



- A cell cycle is a series of events that a cell passes through from the time until it reproduces its replica.
- It is the growth and division of single cell into daughter cells and duplication (replication).
- In prokaryotic cells, the cell cycle occurs via a process termed binary fission. In eukaryotic cells, the cell cycle can be divided in two periods-

a) interphase

b) mitosis

PHASES OF CELL CYCLE

It consists of 2 major activities.

- **INTER PHASE**
  - **G_1 (pre-synthetic phase)**
  - **S (DNA synthesis)**
  - **G_2 (pre-mitotic phase)**

- **CELL DIVISION (MITOTIC PHASE)**

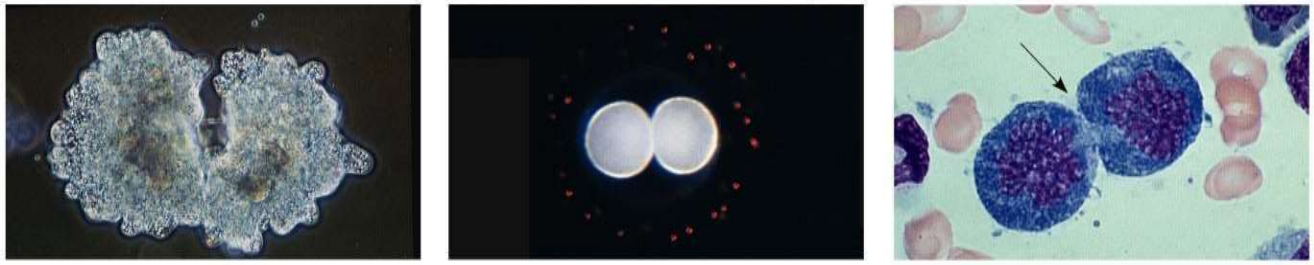
- **a) Interphase-** During this phase the cell grows, accumulating nutrients needed for mitosis and duplicating its DNA.
- **b) Mitosis (M)-phase-** During which the cell splits itself into two distinct cells.
- The duration of the cell cycle varies from hours to years. A typical human cell has duration of 90h.

OVERVIEW: THE KEY ROLES OF CELL DIVISION

The ability of organisms to reproduce best distinguishes living things from non-living matter.

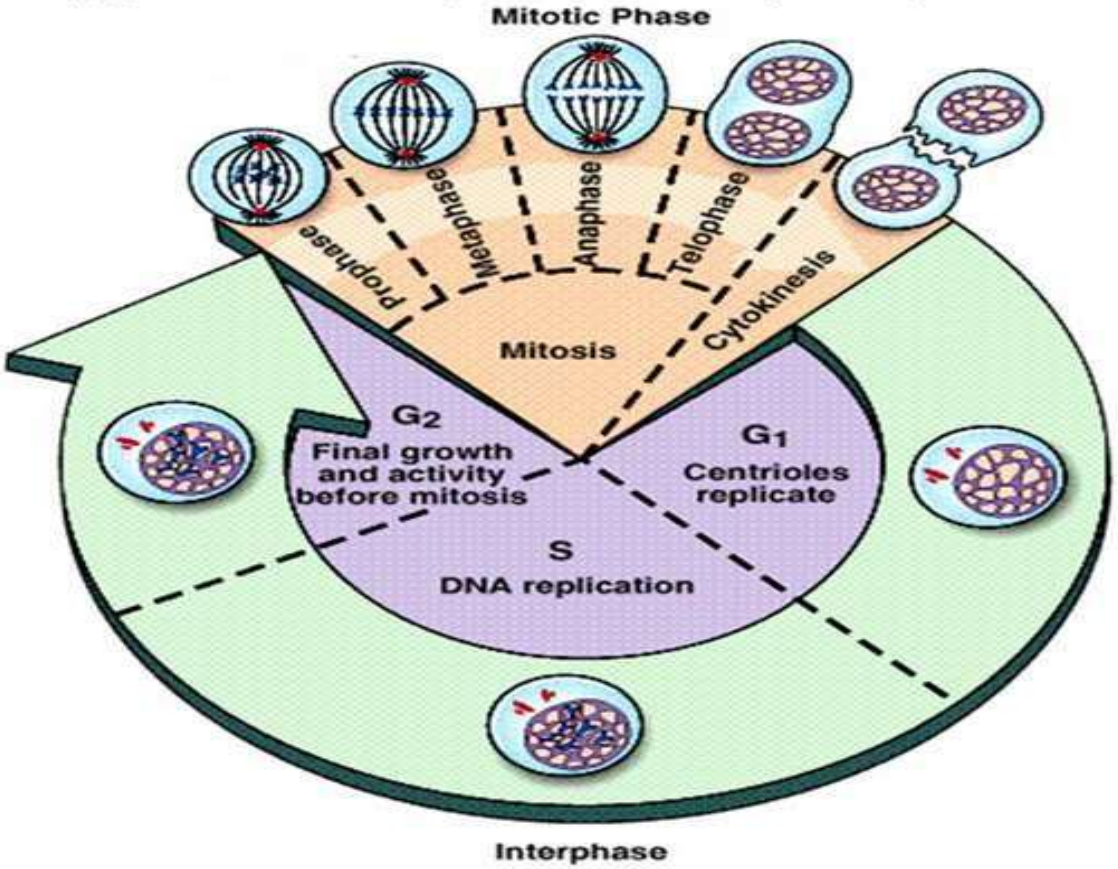
The continuity of life is based upon the reproduction of cells, or cell division.

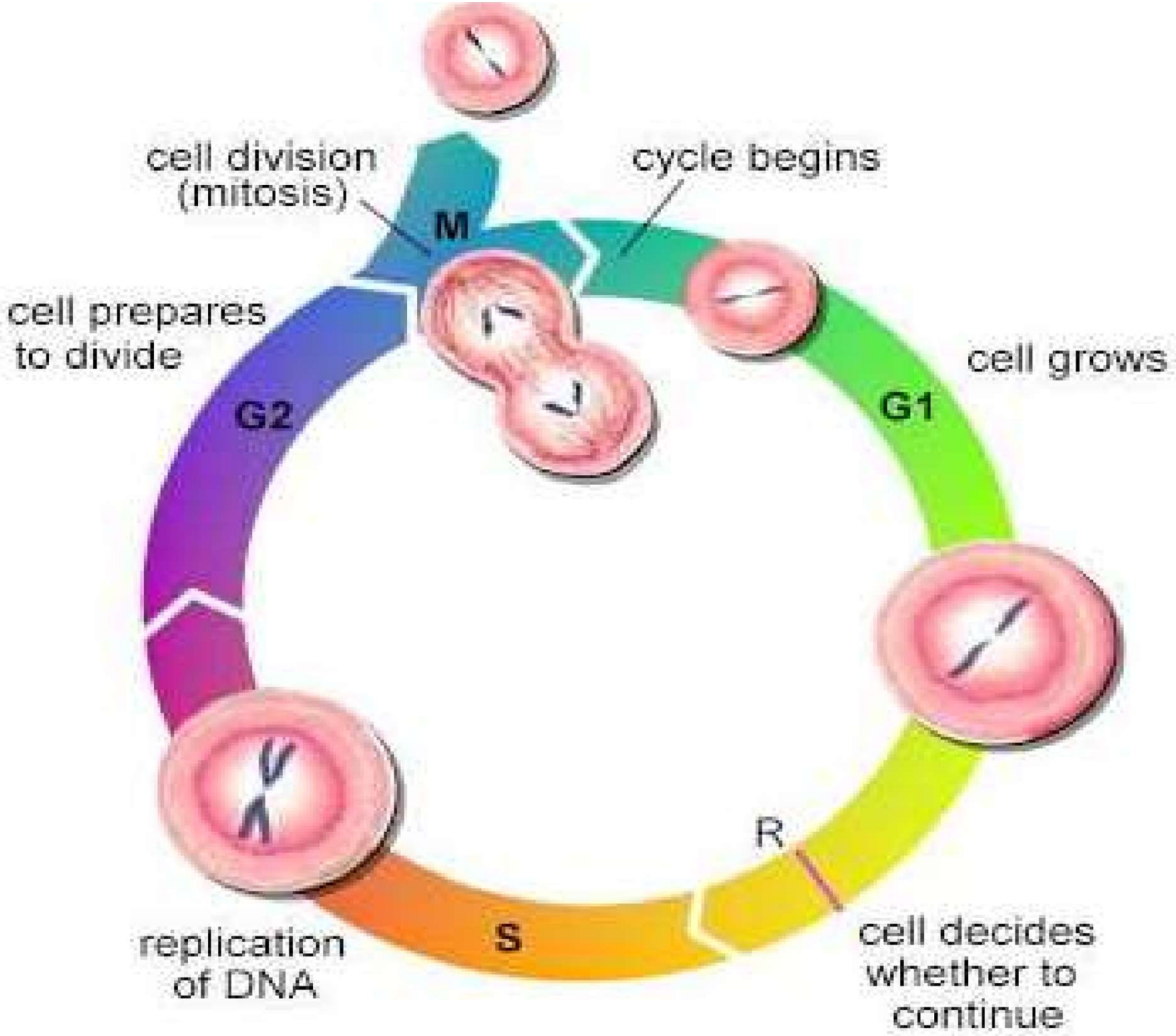
Cell division is integral part of cell cycle.



(a) (b) (c)

OVERVIEW OF THE CELL CYCLE




cell division
(mitosis)
M
cycle begins
cell prepares
to divide
G2
cell grows
G1
R
replication
of DNA
S
cell decides
whether to
continue

INTERPHASE

Interphase includes:

- G_1 Phase:
- S Phase:
- G_2 Phase:

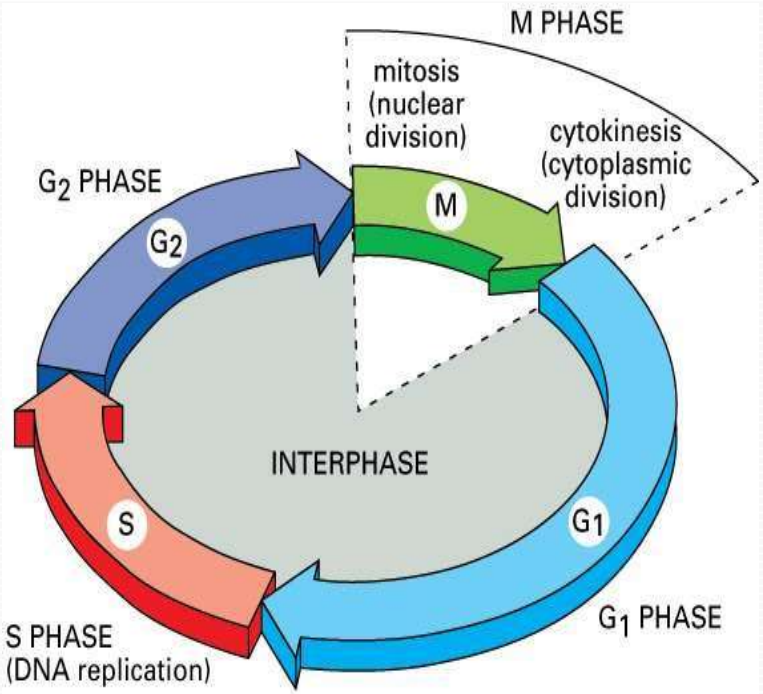


Figure 17–3. Molecular Biology of the Cell, 4th Edition.

INTERPHASE: G1 PHASE

- Recovery from previous division
- Cell doubles its organelles
- Cell grows in size
- Accumulates raw materials for DNA synthesis (DNA replication)

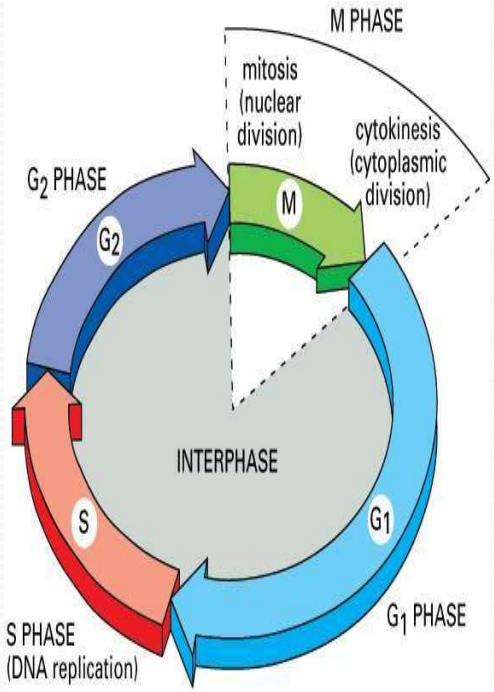
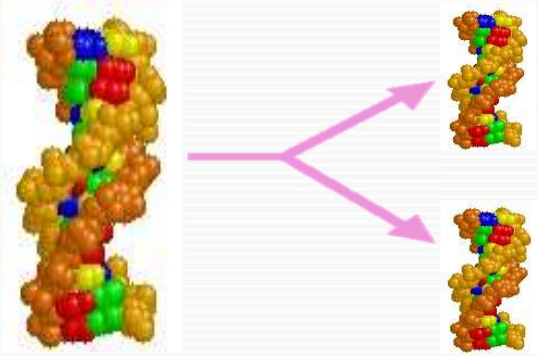


Figure 17–3. Molecular Biology of the Cell, 4th Edition.

INTERPHASE: S PHASE

- DNA replication
- Proteins associated with DNA are synthesized



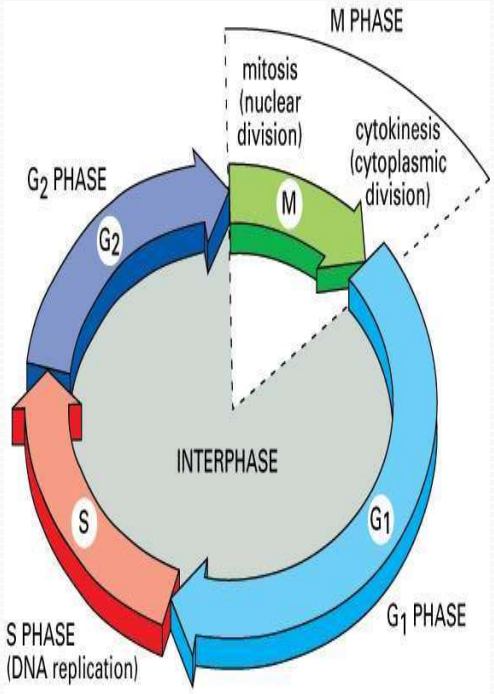


Figure 17–3. Molecular Biology of the Cell, 4th Edition.

INTERPHASE: G2 PHASE

- Between DNA replication and onset of mitosis
- Cell synthesizes proteins necessary for division

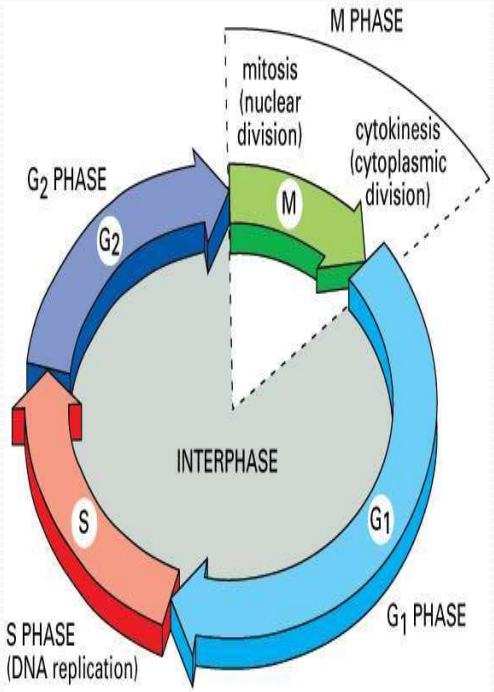


Figure 17–3. Molecular Biology of the Cell, 4th Edition.

CELL CYCLE: MITOSIS PHASE

Mitosis phase includes:

- Mitosis (karyokinesis)
  - Nuclear division
  - Daughter chromosomes distributed to two daughter nuclei
- Cytokinesis
  - Cytoplasm division
  - Results in two genetically identical daughter cells

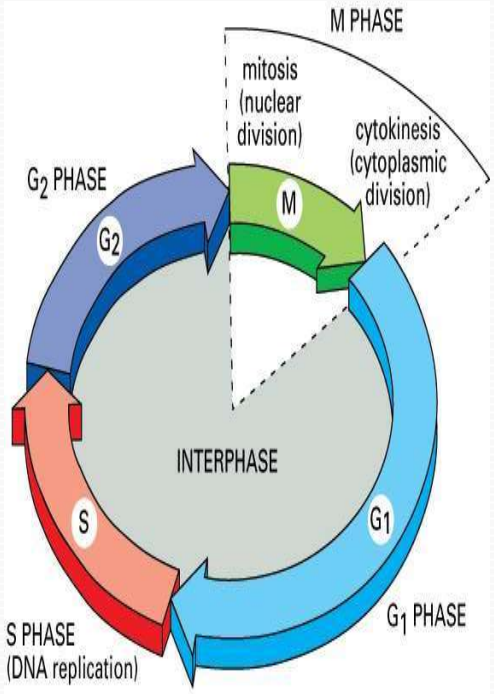


Figure 17–3. Molecular Biology of the Cell, 4th Edition.

CELL CYCLE: MITOSIS PHASE

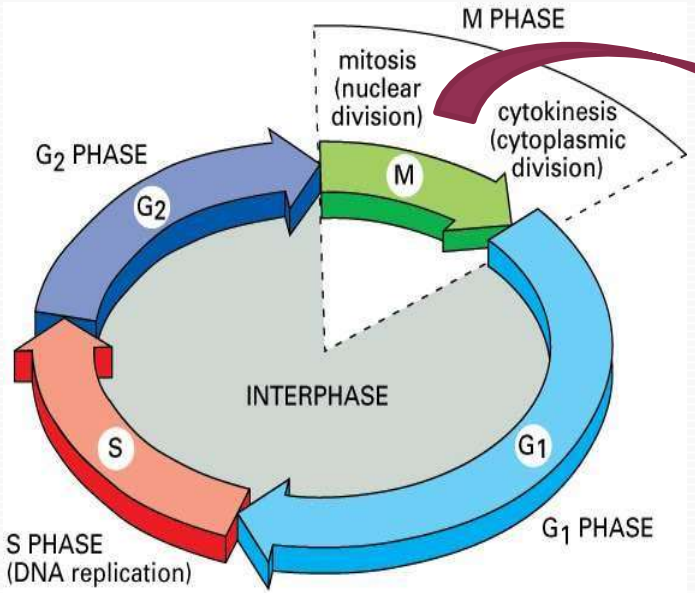
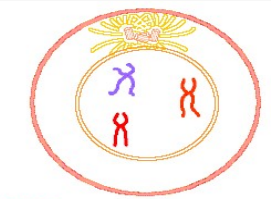


Figure 17–3. Molecular Biology of the Cell, 4th Edition.

Prophase:
- condensation of chromosomes
- disappearance of nucleoli and nuclear envelope

SIGNIFICANCE OF MITOSIS



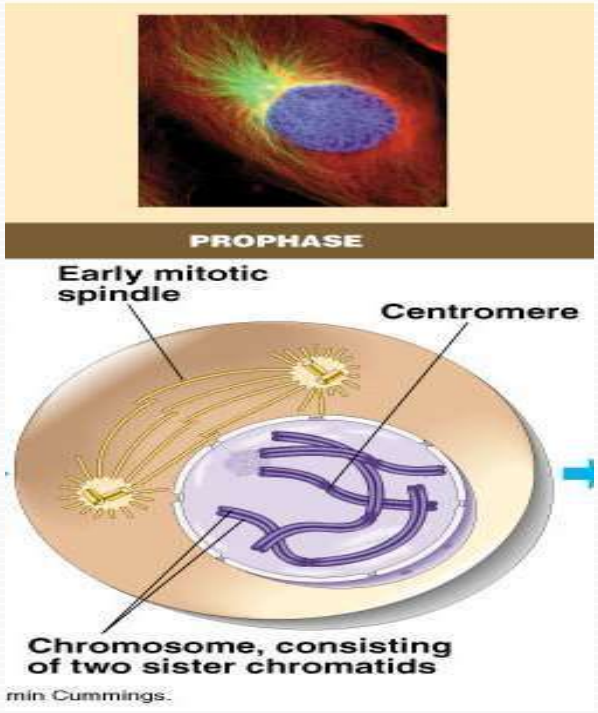
- **Permits growth and repair.**
- **In plants it retains the ability to divide throughout the life of the plant**
- **In mammals, mitosis is necessary:**
  - Fertilized egg becomes an embryo
  - Embryo becomes a fetus
  - Allows a cut to heal or a broken bone to mend

MITOSIS PHASE: PROPHASE

What's happening?

- **Chromatin condenses.**
- **Centrosomes separate, moving to opposite ends of the nucleus**
- **The centrosomes start to form a framework used to separate the two sister chromatids called the mitotic spindle, that is made of microtubules**
- **Nucleolus disappears**
- **Nuclear envelope disintegrates**

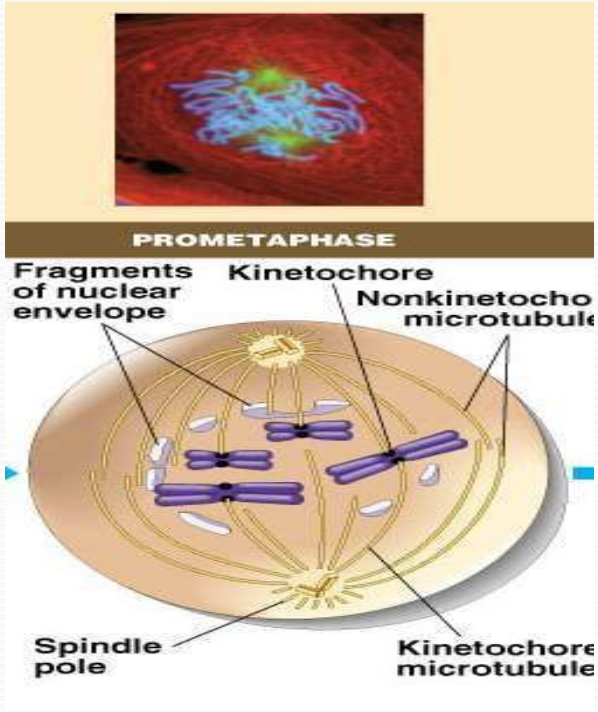
What the cell looks like?



MITOSIS PHASE: PROMETAPHASE

What's happening? **What the cell looks like?**

- **Nuclear envelope fragments**
- **Chromosomes become more condensed**
- **A kinetochore is formed at the centromere, the point where the sister chromatids are attached**
- **Microtubules attach at the kinetochores**

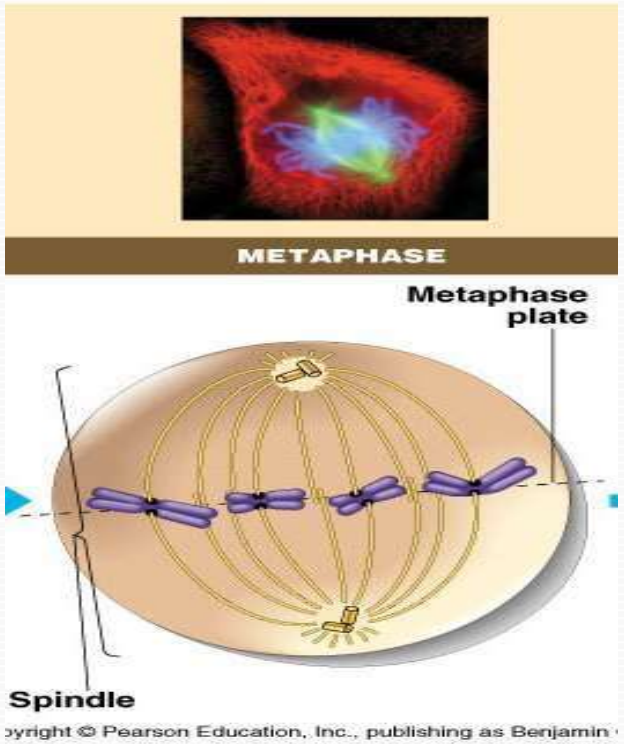


MITOSIS PHASE: METAPHASE

What's happening?

- **Chromosomes align on an axis called the <u>metaphase plate</u>**
- **Note: the spindle consists of microtubules, one attached to each chromosome**

What the cell looks like?

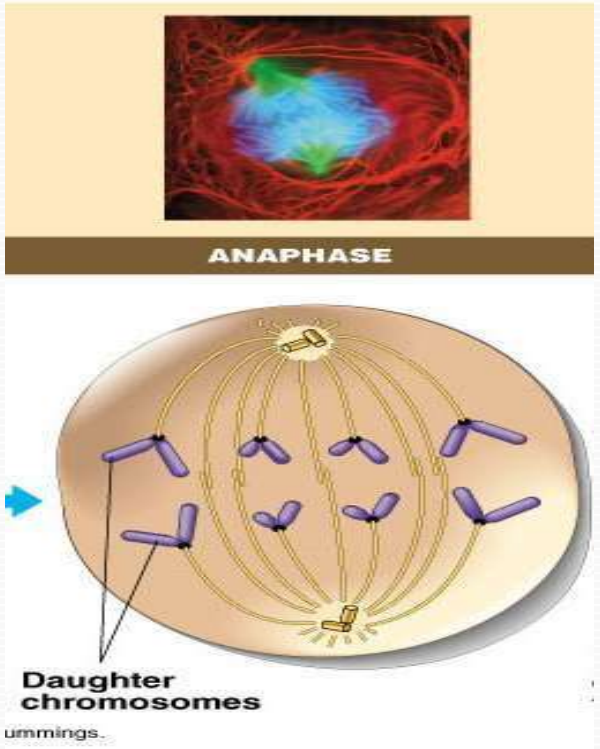


MITOSIS PHASE: ANAPHASE

What's happening?

- **Each centromere splits making two chromatids free**
- **Each chromatid moves toward a pole**
- **Cell begins to elongate, caused by microtubules not associated with the kinetochore**

What the cell looks like?

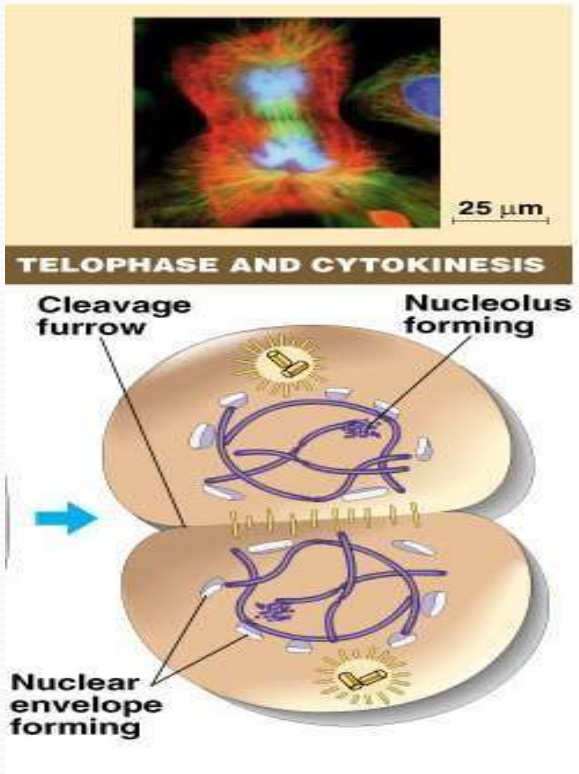


MITOSIS PHASE: TELOPHASE

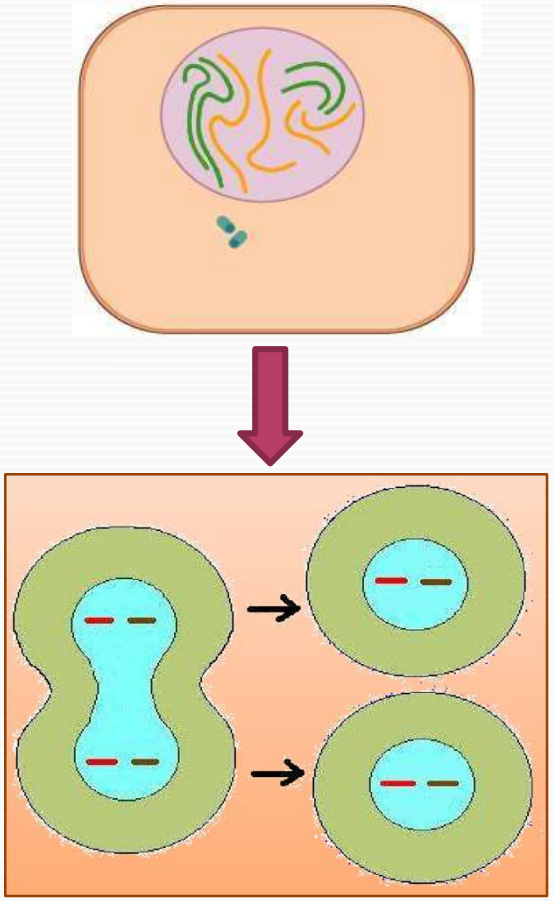
What's happening?

- **Formation of nuclear membrane and nucleolus**
- **Short and thick chromosomes begin to elongate to form long and thin chromatin**
- **Formation of the <u>cleavage furrow</u> - a shallow groove in the cell near the old metaphase plate**
- **<u>Cytokinesis</u> = division of the cytoplasm**

What the cell looks like?



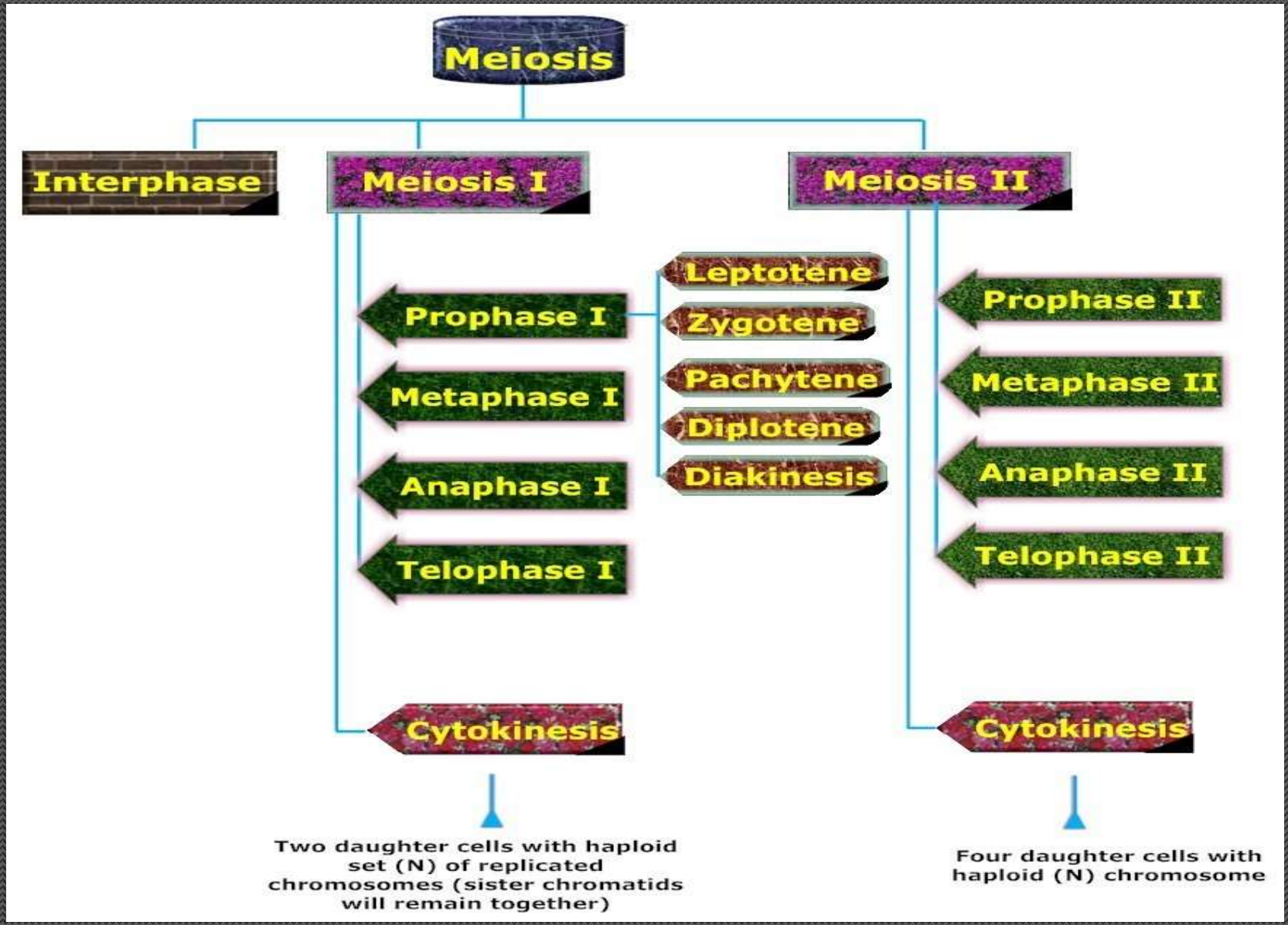
RESULTS OF MITOSIS



- Two daughter nuclei
- Each with same chromosome number as parent cell (2n)
- Genetically identical to each other and the parent cell

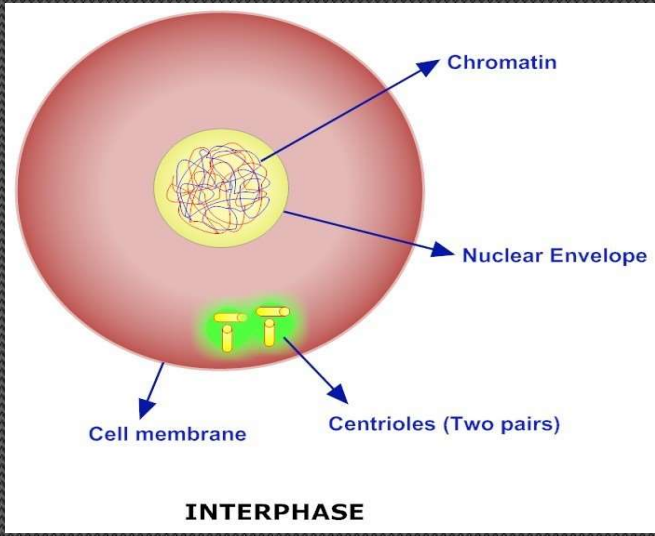
- The meiotic cell division first time described by **Van Beneden** in 1883
- Meiotic cell division occurs in germ cells of all living organism.
- During meiosis, the genetic material of a diploid germ cell undergoes two nuclear divisions and resulting in to four haploid daughter cells.
- Each daughter cells has one half of the number of chromosomes as the parent cell.
- There are two successive nuclear divisions in meiosis as compared to the one division found in mitosis.

- The two stages of meiosisare
1. ***Meiosis I***
2. ***Meiosis II***
- ***Meiosis I*** also called as Reductional Division
- ***Meiosis II*** also called as Equational Division
- Before a dividing cell enters meiosis, it undergoes a period of growth called *Interphase*.


Meiosis
Interphase
Meiosis I
Meiosis II
Prophase I
Metaphase I
Anaphase I
Telophase I
Leptotene
Zygotene
Pachytene
Diplotene
Diakinesis
Prophase II
Metaphase II
Anaphase II
Telophase II
Cytokinesis
Cytokinesis
Two daughter cells with haploid set (N) of replicated chromosomes (sister chromatids will remain together)
Four daughter cells with haploid (N) chromosome

INTERPHASE

- The interphase just prior to the entry of cell in to meiosis is known as pre meiotic interphase.
- During the S phase of pre meiotic interphase, chromosome replication takes place.



MEIOSIS I

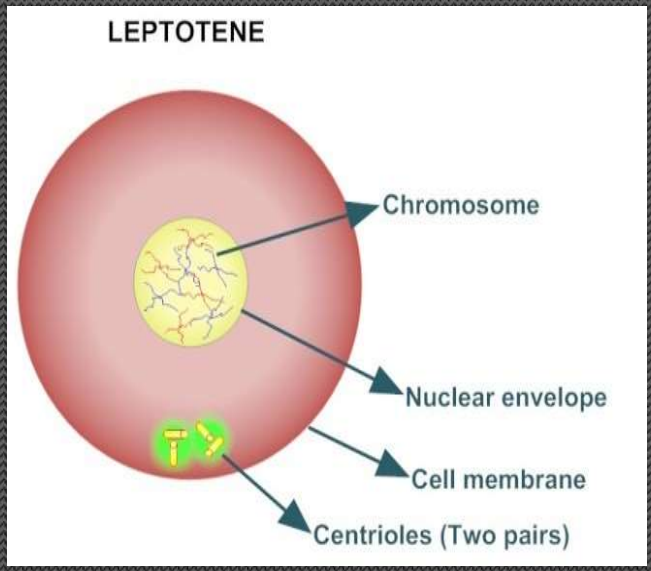
- Meiosis I separate homologous chromosomes and produce two cells with haploid chromosome number (N) for that reason it is known as **Reductional Division**.
- Meiosis I consist of four stages,
  - Prophase I
  - Metaphase I
  - Anaphase I and
  - Telophase I.

PROPHASE I

- Prophase I is the longest in duration compared to Prophase in mitosis.
- It takes about 85 - 95 percent of the total time for meiosis and also much more complex.
- The Prophase I divided into 5 stages (Le Za Pa Di Dia).
  - Leptotene
  - Zygotene
  - Pachytene
  - Diplotene and
  - Diakinesis

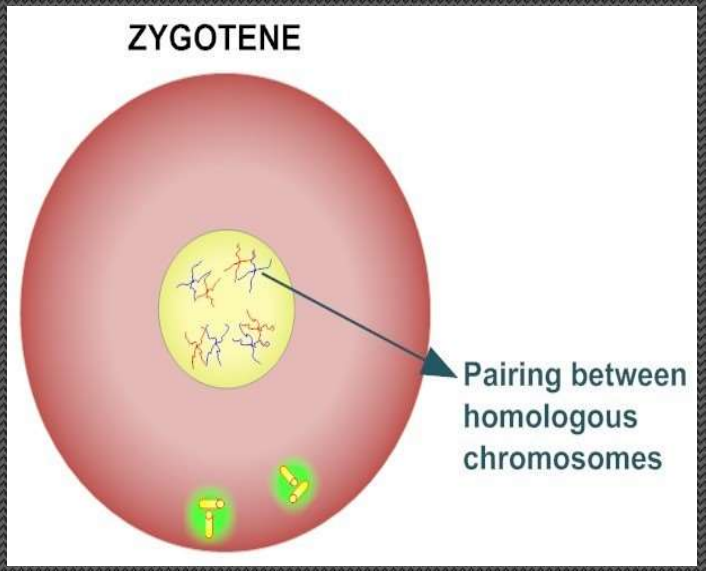
LEPTOTENE

- The first stage of Prophase I is called ***Leptotene*** or ***leptonema***.
- All the chromosomes begin to condense, so, they become visible as fine thread.
- There is marked increase in the nuclear volume.
- A process of *'**homology search**'* which is essential to the initial pairing of homologs, begins during

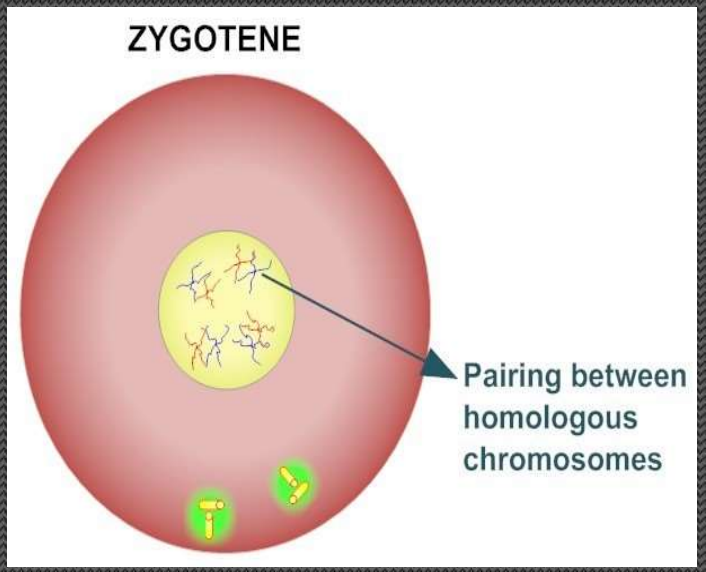


ZYGOTENE

- The ***zygotene*** stage also known as ***zygonema***.
- This stage begins with the initiation of pairing between homologus chromosomes and it ends with complete pairing.
- The process of pairing (at end to end) between homologus chromosomes is known as **Synapsis (Homologous dyads)**.

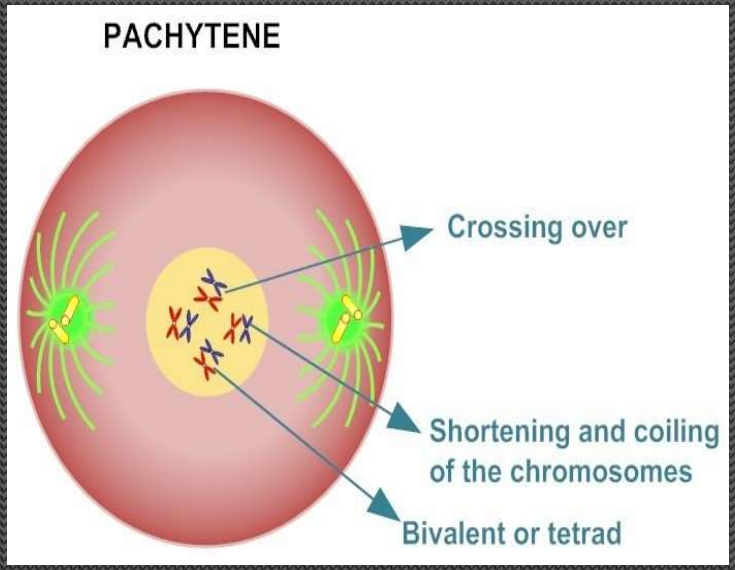


- The synaptonemal complex is form during these zygotene stage.
- At the completion of zygotene, the paired homologs take the form of bivalents.
- ***The number of bivalents in each species is equal to the haploid number.***

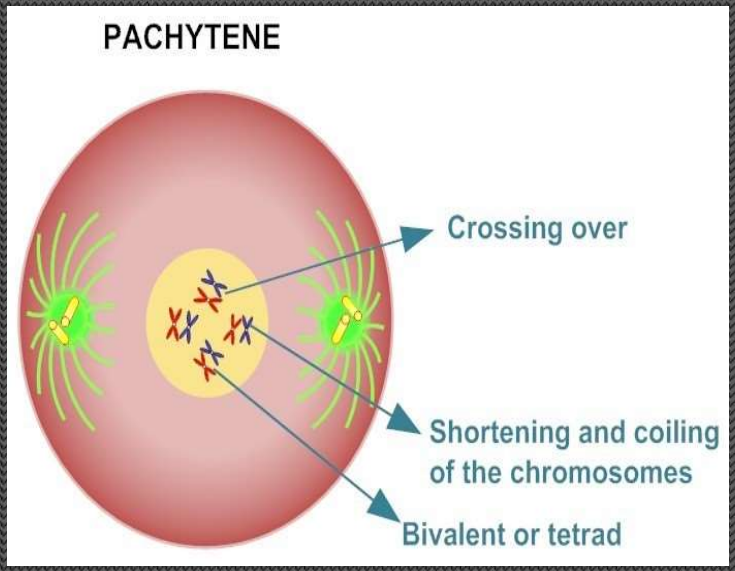


PACHYTENE

- The ***pachytene*** stage also known as ***pachynema***.
- The process of synapsis is complete.
- The two homologus of each bivalent appears to be attached with each other at one or more points, these attachments are known as **chiasmata**.

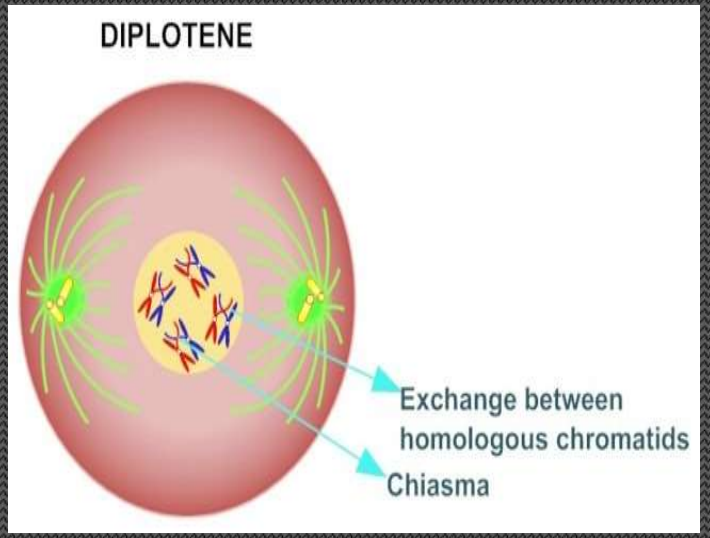


- Crossing over is a precise breakage, swapping and reunion between two non-sister chromatids.
- Crossovers make new gene combinations and which are an important source of genetic variations in populations.

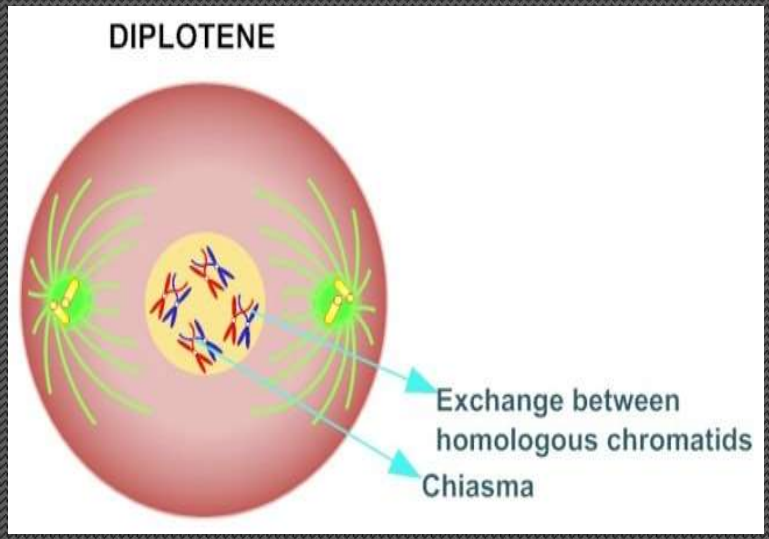


DIPLOTENE

- The diplotene stage also known as **diplonema**.
- DNA recombination is complete.
- The chromatids continue to shorten and thicken and the four sister chromatids in a group is called a **tetrad**.
- The synaptonemal complex begins to break down.

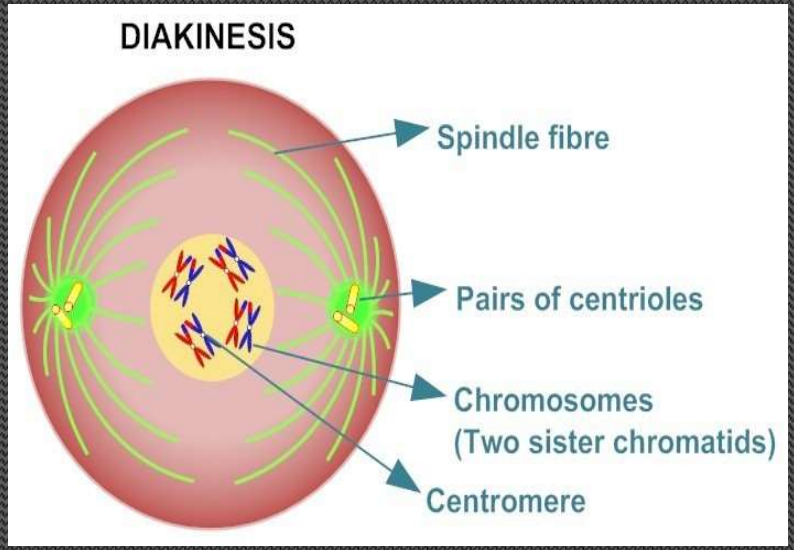


- The paired chromatids begin to pull apart, causing the strands to separate longitudinally.
- The chiasmata tend to become terminalised as the meiotic prophase continues.

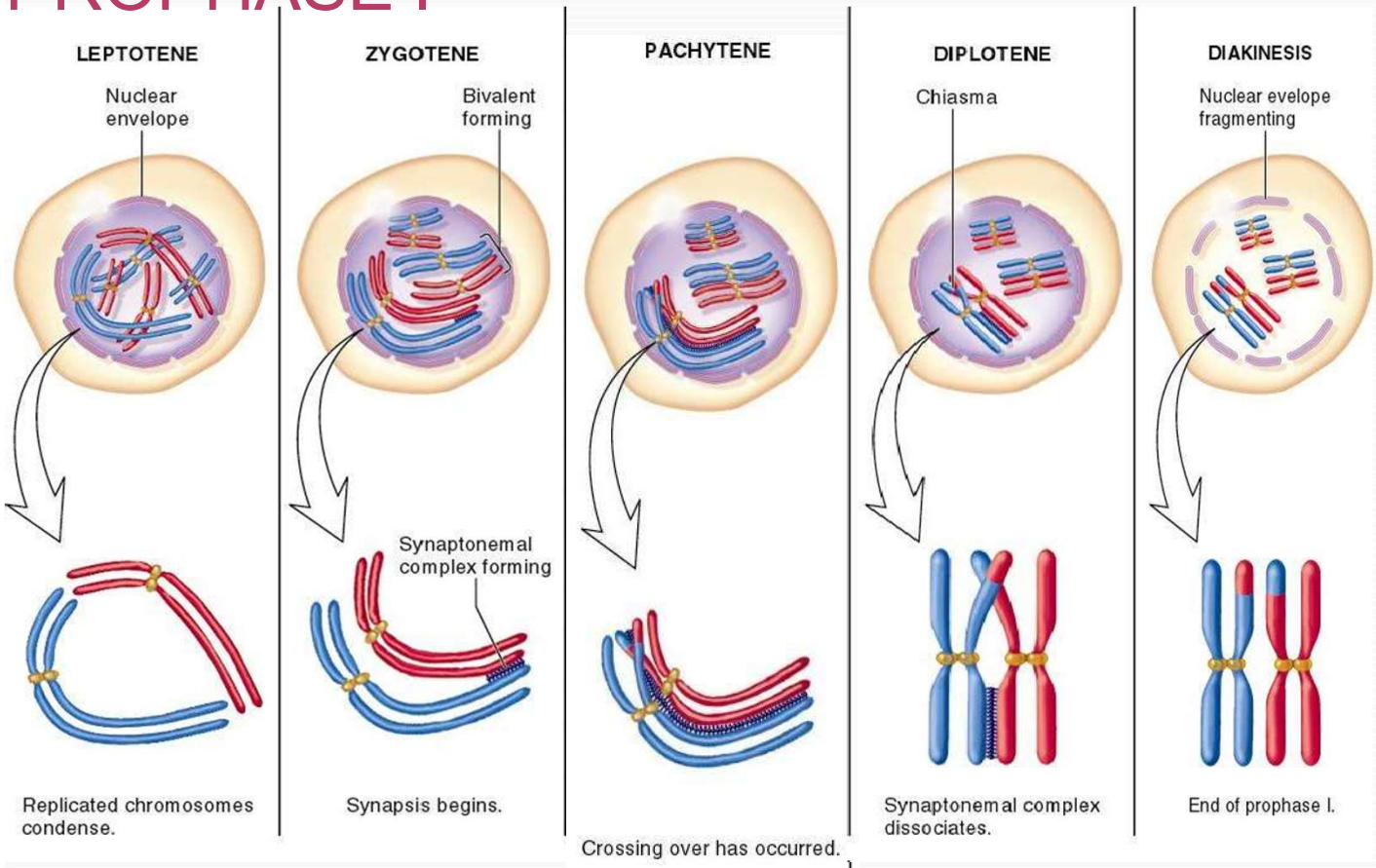


DIAKINESIS

- The chromomes become shorter and thicker due to condensation.
- Nucleolus and nuclear envelope disappear towards the end of diakinesis.
- The spindle apparatus becomes organized.
- The centrioles migrate away from one another.



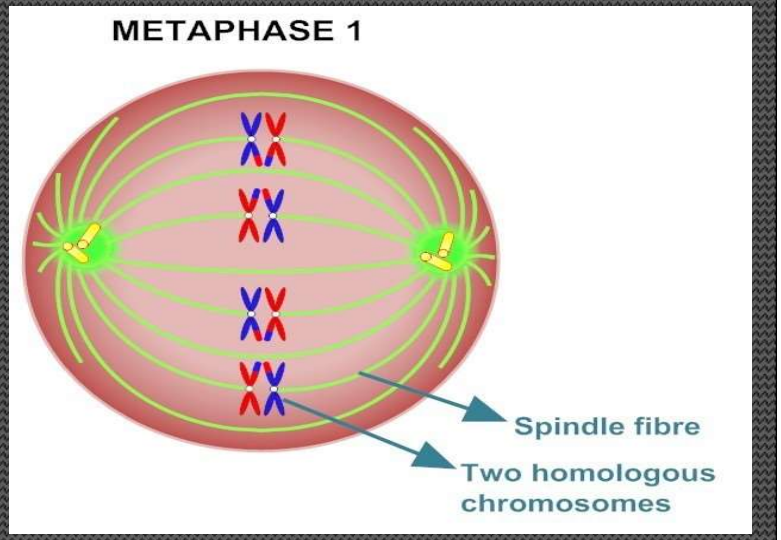
PROPHASE I



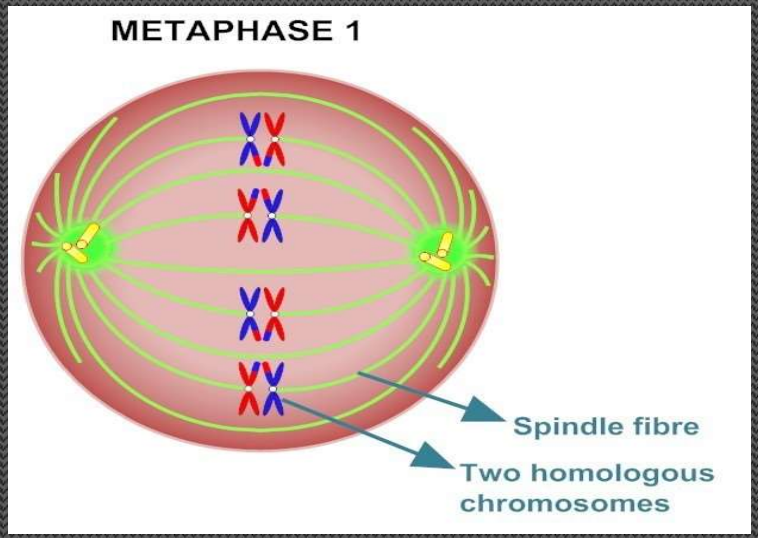
A physical exchange of chromosome pieces

METAPHASE I

- All the bivalents migrate within a cell migrate to metaphase plate.
- One homologue is pulled above the metaphase plate, the other below.
- The centromeres of homologous chromosomes of each bivalent stretch out on either side.

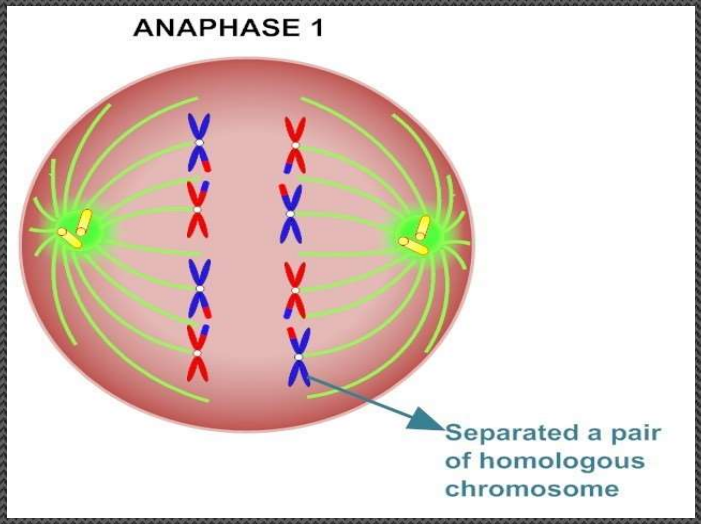


- The centrioles are at opposite poles of the cell.
- Spindle fibers from one pole of the cell attach to one chromosome and spindle fibers from the opposite pole attach to the homologous chromosome.

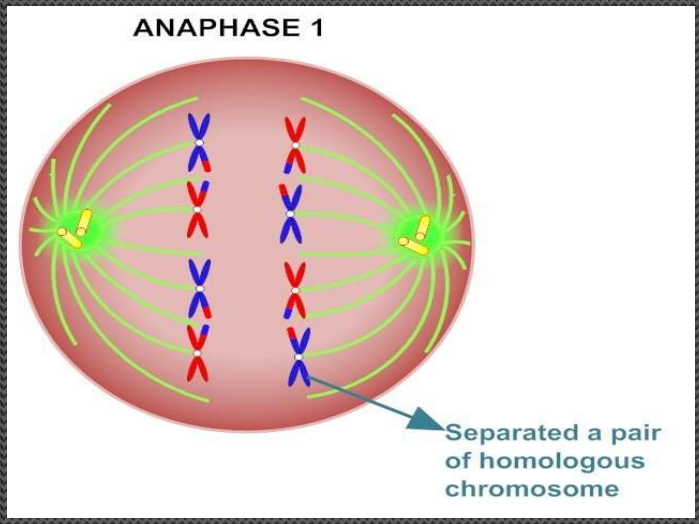


ANAPHASE I

- Chromosomes move to the opposite poles.
- The microtubules and the kinetochore fibers interact, which cause the movement.
- ***A difference between mitosis and meiosis is that sister chromatids remain joined after metaphase in meiosis I, whereas in mitosis they separate.***

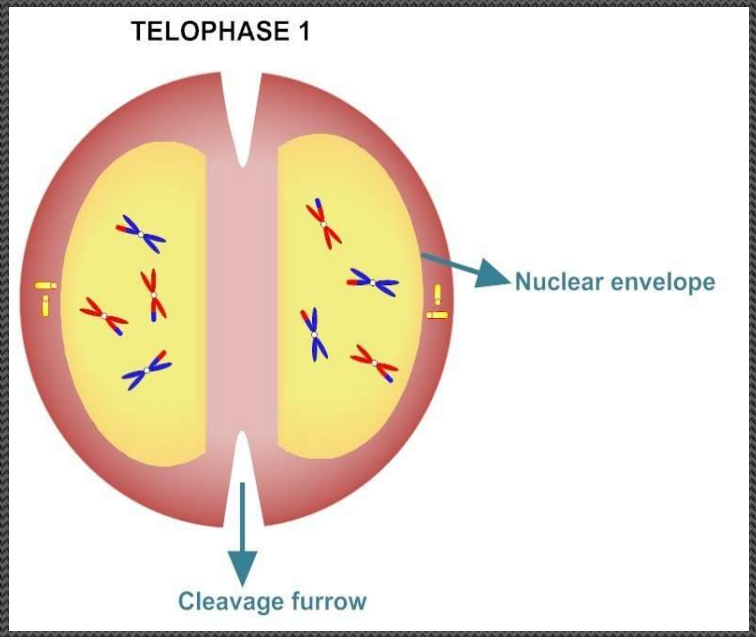


- During Anaphase I original chromosomes separate, so reduction in the number of chromosomes from 2N to N number, yet the sister chromatids remain together.



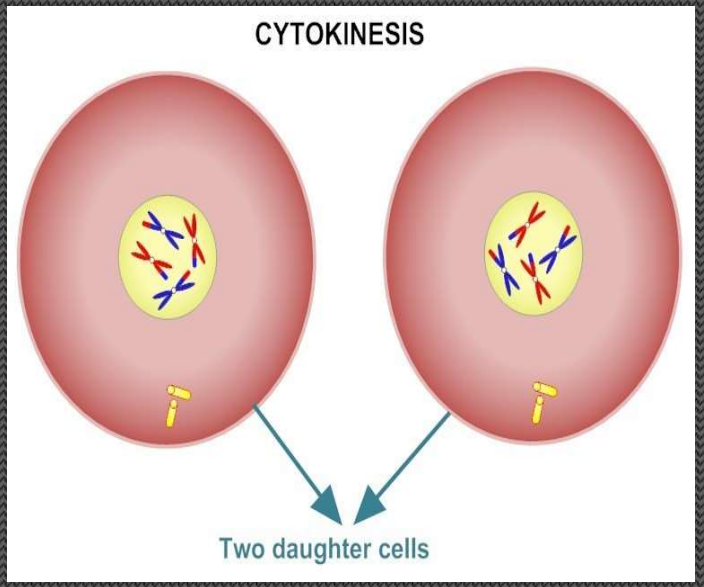
TELOPHASE I

- The homologouschromosome complete their migration to the two poles b/c shortning of spindles.
- The nuclear envelope organized around two groups of chromosomes.
- The nucleolus alsoreappears.



Cytokinesis

- Cytokinesis involves the formation of a cleavage furrow, resulting in the pocketing of the cell into two cells.
- At the end of Telophase I and Cytokinesis, two daughter cells are produced, each with one half of the number of chromosomes (haploid set of replicated chromosomes) of the original parent cell.



INTERKINESIS

- Interkinesis (Interphase II) is similar to interphase

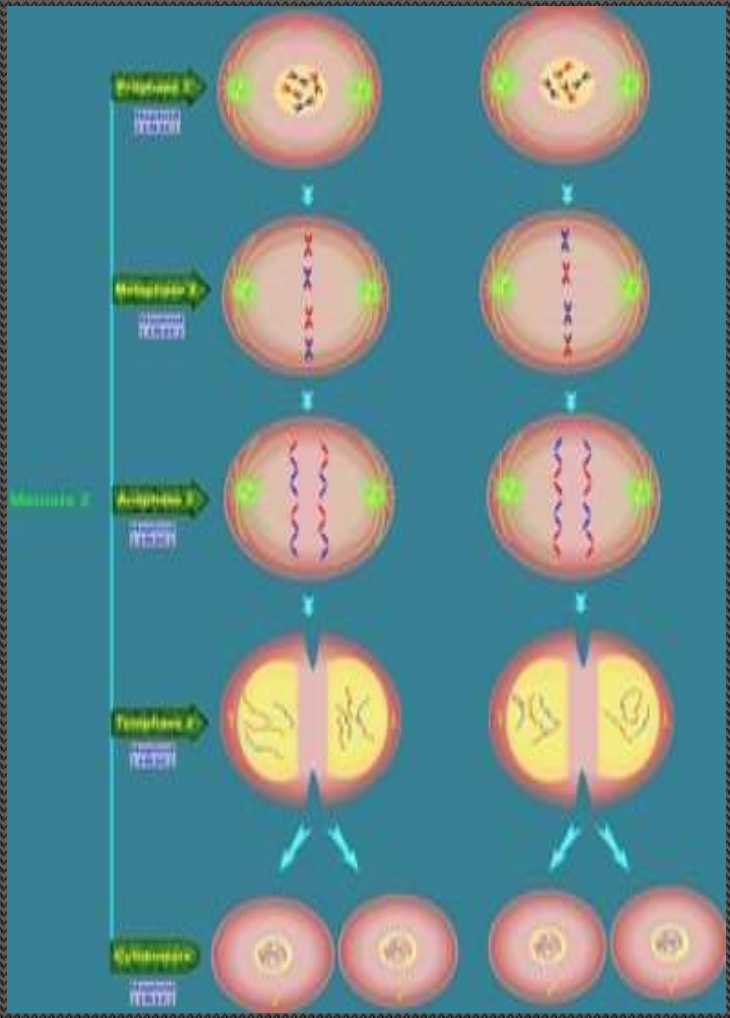
MEIOSIS II

- Meiosis II is the second part of the meiotic process.
- The Meiosis II consists
- Prophase II

  Each dyad is composed of a pair of sister chromatids attached by a common centromere.
- Metaphase II

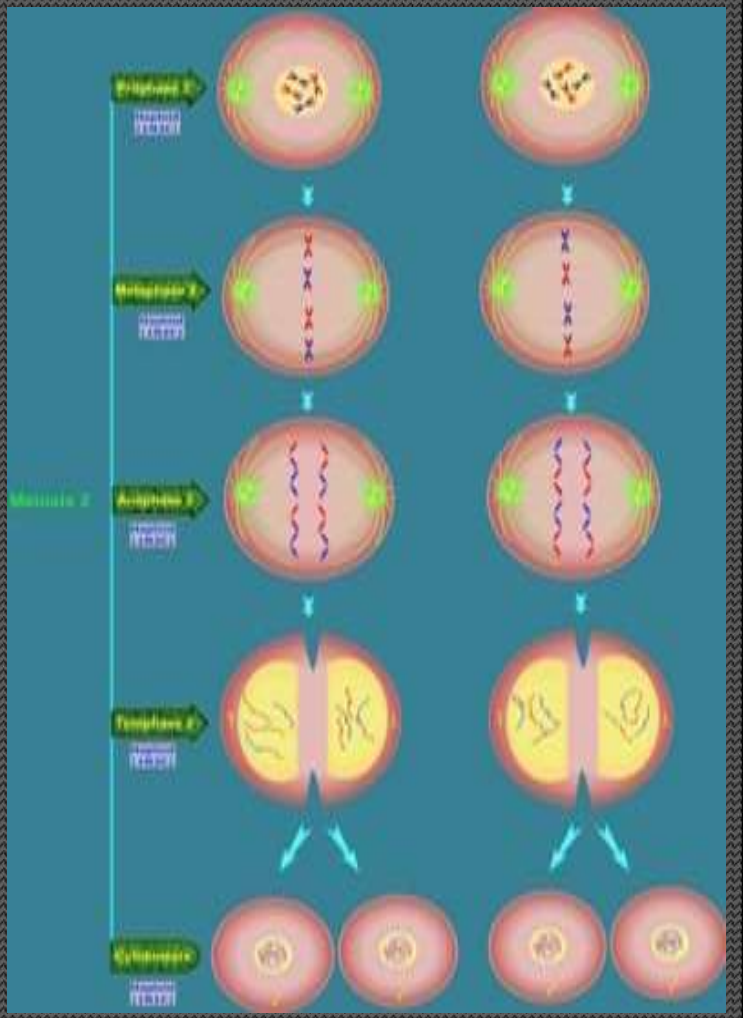
  Centromeres are positioned at the equatorial plane.
- Anaphase II

  Centromeres divide and the sister chromatids of each dyad are pulled to opposite poles



Telophase II

- One member of each pair of homologous chromosome present in each pole.
- Each chromosome is referred as monad (a combination of maternal and paternal genetic information).
- Nuclei reform around chromosomes at the poles.
- Following cytokinesis and finally four haploid gametes result from a single meiotic event.



Functions of Meiosis

1. Production of haploid (n) gametes: so, that fertilization restores the normal somatic (2n) chromosome number.
2. Production of tremendous amounts of genetic variation.
3. Segregation of the two alleles of each gene. This take place due to pairing between the two homologues of each chromosome and their separation at the first anaphase.

4. Recombination between linked genes due to crossing over during pachytene stage.
5. Meiosis facilitates segregation and independent assortment of chromosomes and genes.
6. In sexually reproducing species, meiosis is essential for the continuity of generation. Because meiosis results in the formation of male and female gametes and union of such gametes leads to the development of zygotes and thereby new individual.

	Mitosis	*Meiosis*
1.	Occurs in somatic cells	Occurs in reproductive cells
2.	One cell produces two daughter cells	One cell produces four daughter cells
3.	It is an equational division separating sister chromatids.	It is a reduction division. The first stage is a reduction division which separates homologous chromosomes at first anaphase. Sister chromatids separate in an equational division at II anaphase.
4.	Only one division per cycle i.e. one cytoplasmic division division.	Two divisions per cycle i.e. two cytoplasmic divisions, one reduction (cytokinesis) per equational division and equation division.
5.	Chromosomes fail to synapse. No chiasmata formation.	Chromosomes synapse and form chiasmata.
6.	Genetic exchange between homologous chromosomes does not occur.	Genetic exchange through chiasmata occurs between homologous chromosomes.

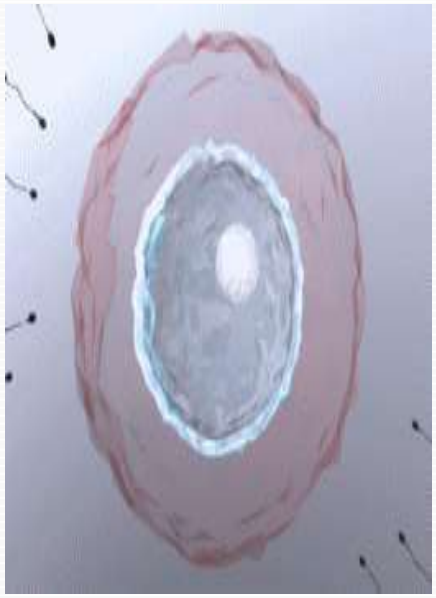
	Mitosis	*Meiosis*
7	Genetic contents of daughter cells are identical.	Genetic contents of daughter cells are different.
8	Chromosome number of daughter cells is the same as that of mother cell.	Chromosome number of daughter cells is half of that of mother cells.
9	Daughter cells are capable of undergoing additional mitotic divisions.	Daughter cells are not capable of undergoing another meiotic division although they may undergo mitotic division.
10	Start at the zygote stage and continues through the life of the organism.	Occurs only after puberty, in higher organisms, but occurs in the zygote of algae and fungi.

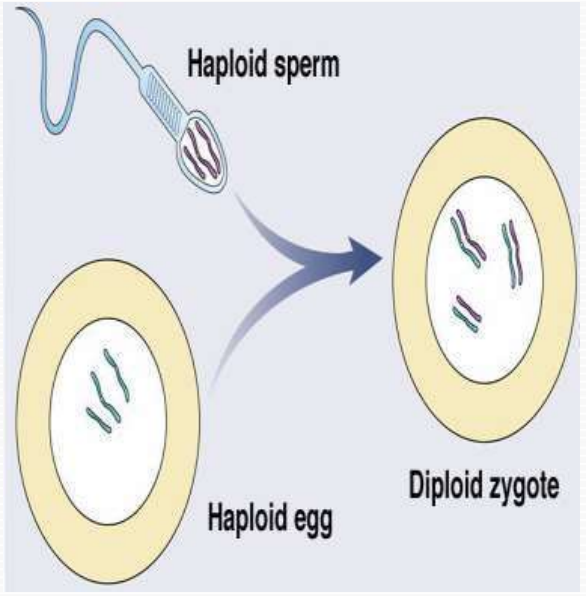
MEIOSIS

- Formation of Gametes (Eggs & Sperm)
- Called Reduction- division
- Preceded by interphase which includes chromosome replication
- Two meiotic divisions
  - Meiosis I and Meiosis II
- Original cell is diploid (2n)
- Four daughter cells produced that are haploid (n)

SIGNIFICANCE OF MEIOSIS

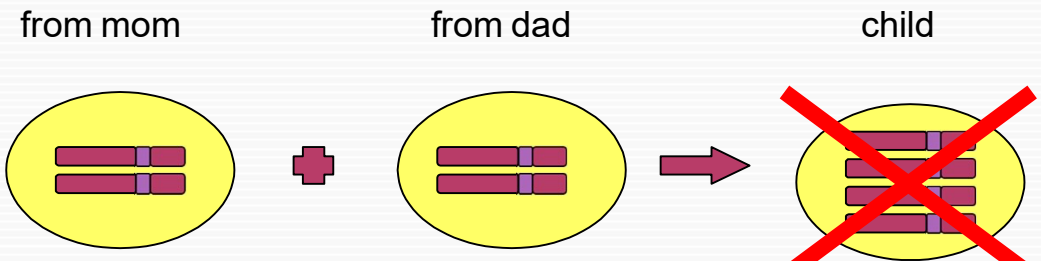
- Two haploid (1n) gametes are brought together through fertilization to form a diploid (2n) zygote





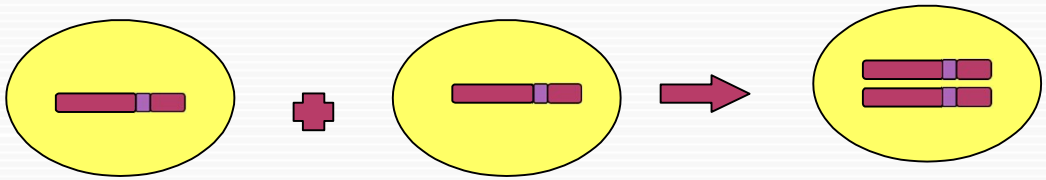
SIGNIFICANCE OF MEIOSIS

- Meiosis must reduce the chromosome number by half
- Fertilization then restores the 2n number



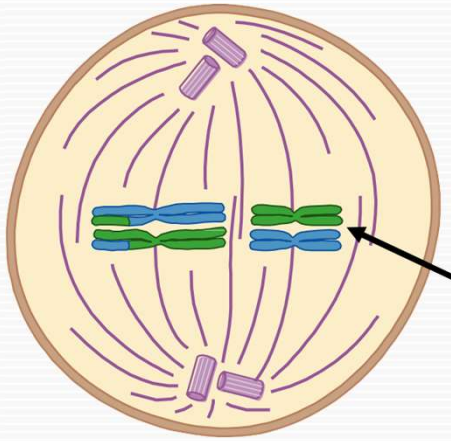
Too much!

meiosis reduces genetic content



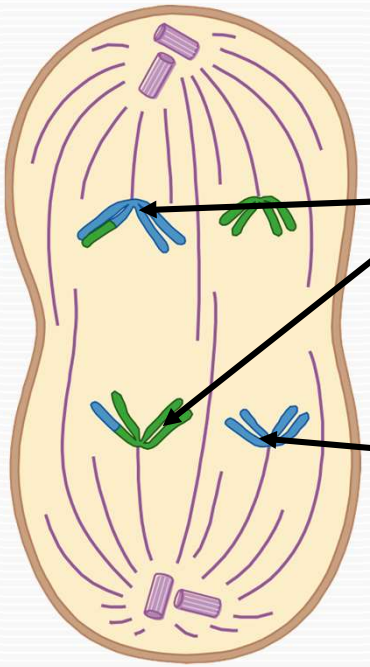
The right number!

METAPHASE I



Homologous pairs of chromosomes align along the equator of the cell

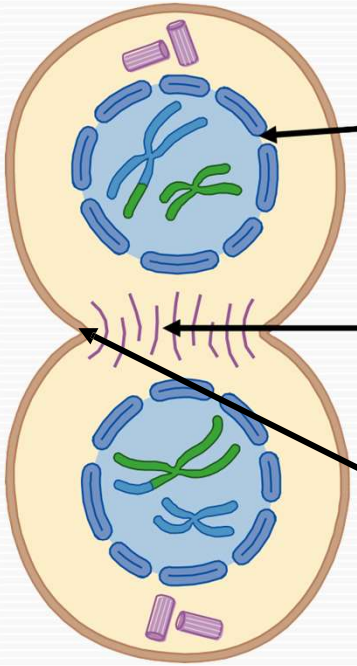
ANAPHASE I



Homologs separate and move to opposite poles.

Sister chromatids remain attached at their centromeres.

TELOPHASE I

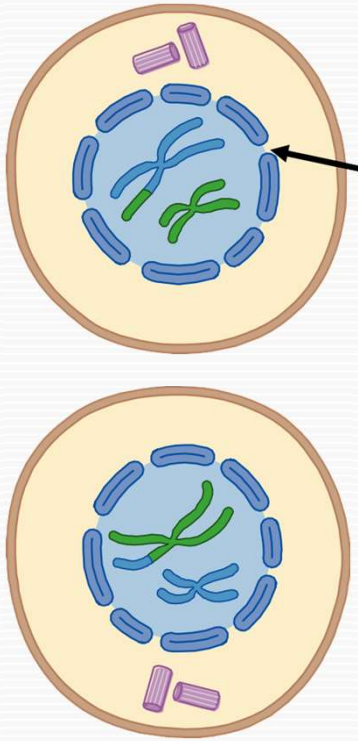


Nuclear envelopes reassemble.

Spindle disappears.

Cytokinesis divides cell into two.

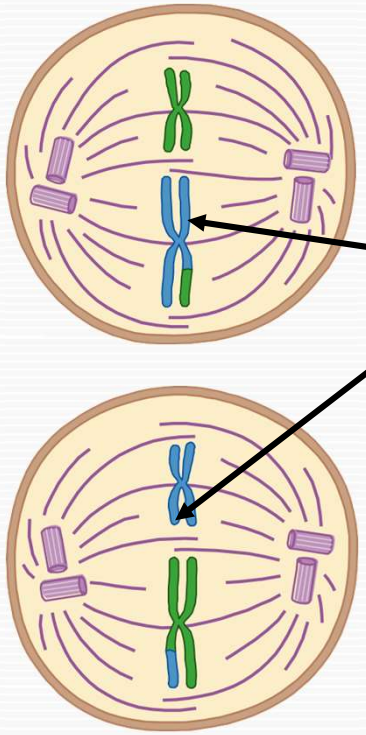
MEIOSIS II: PROPHASE II



Nuclear envelope fragments.

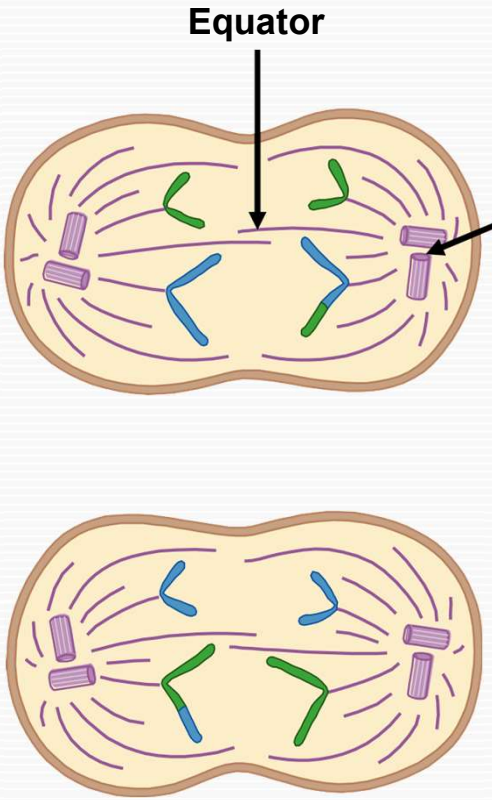
Spindle forms.

MEIOSIS II: METAPHASE II



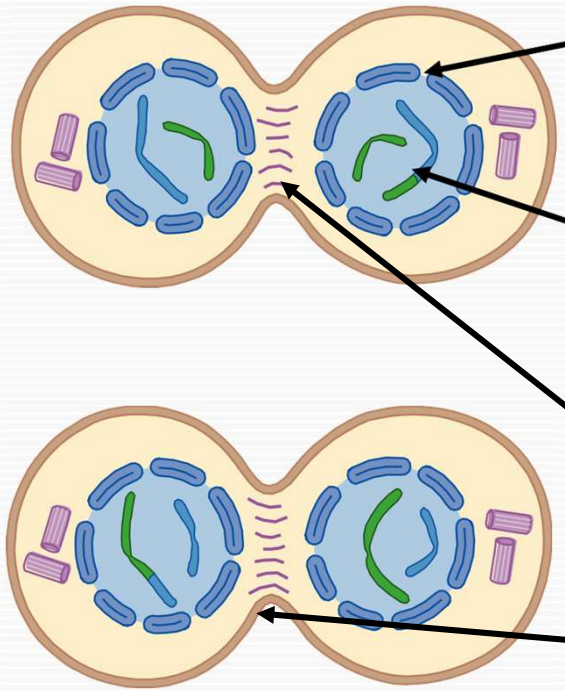
Chromosomes align along equator of cell.

MEIOSIS II: ANAPHASE II



Sister chromatids separate and move to opposite poles.

MEIOSIS II: TELOPHASE II



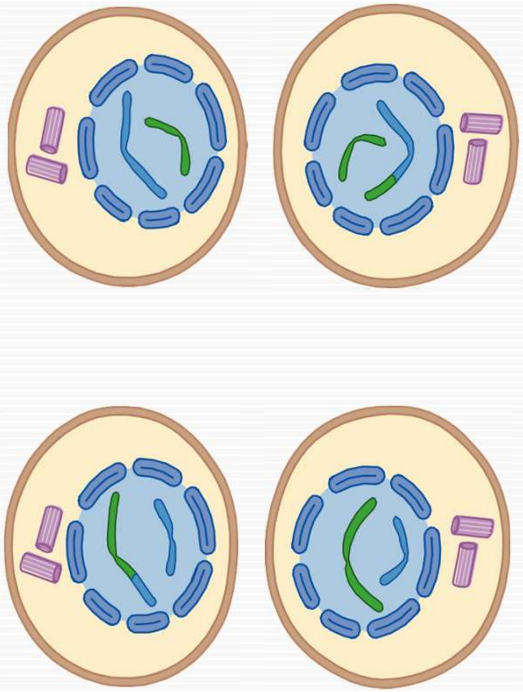
Nuclear envelope assembles.

Chromosomes decondense.

Spindle disappears.

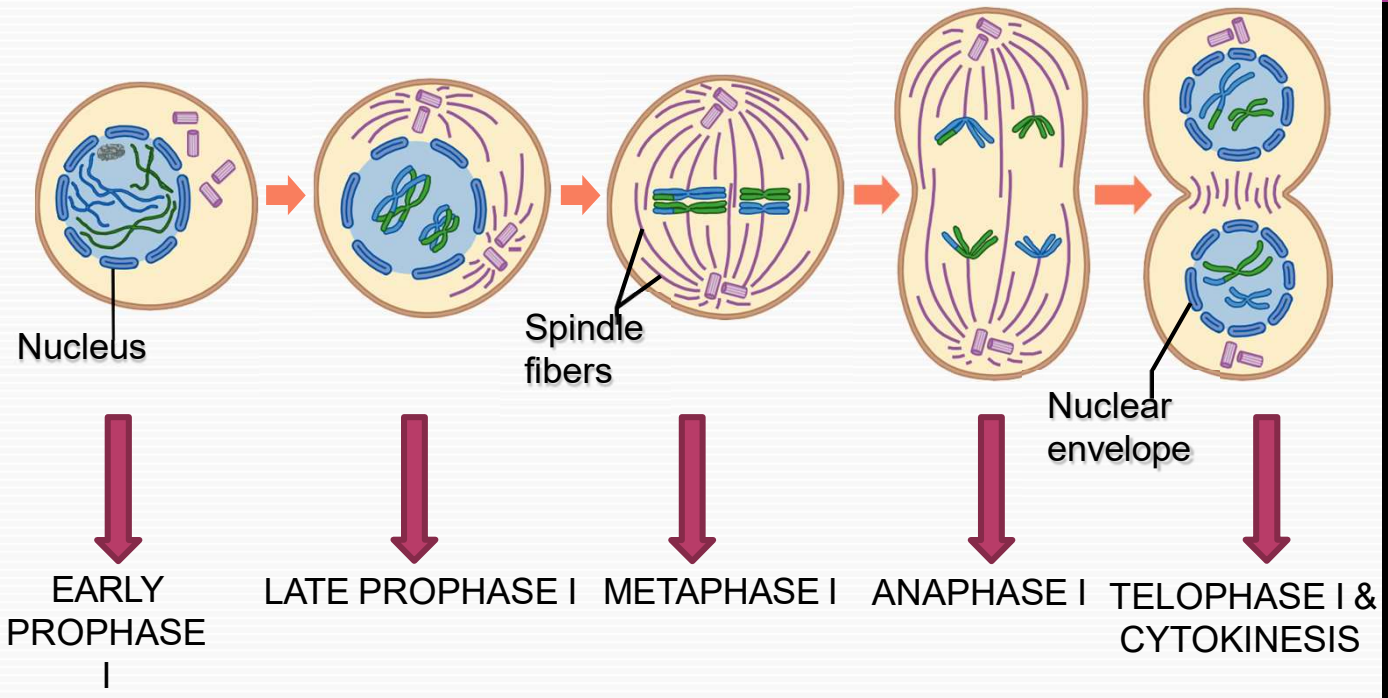
Cytokinesis divides cell into two.

RESULTS OF MEIOSIS



- Four haploid cells with one copy of each chromosome

SUMMARY OF MEIOSIS I



SUMMARY OF MEIOSIS II