CELL CYCLE

<u>CELL CYCLE</u>

- Described by Howard and Pele in 1953

- ***Cell Cycle is defined*** *as "The sequence of events involving growth and division, a cell undergoes from the time of its formation by division of <u>parent cell</u> to its own division into <u>daughter cells</u>."*

Five Phases of the Cell Cycle

- Interphase

It is divided into three phases-:

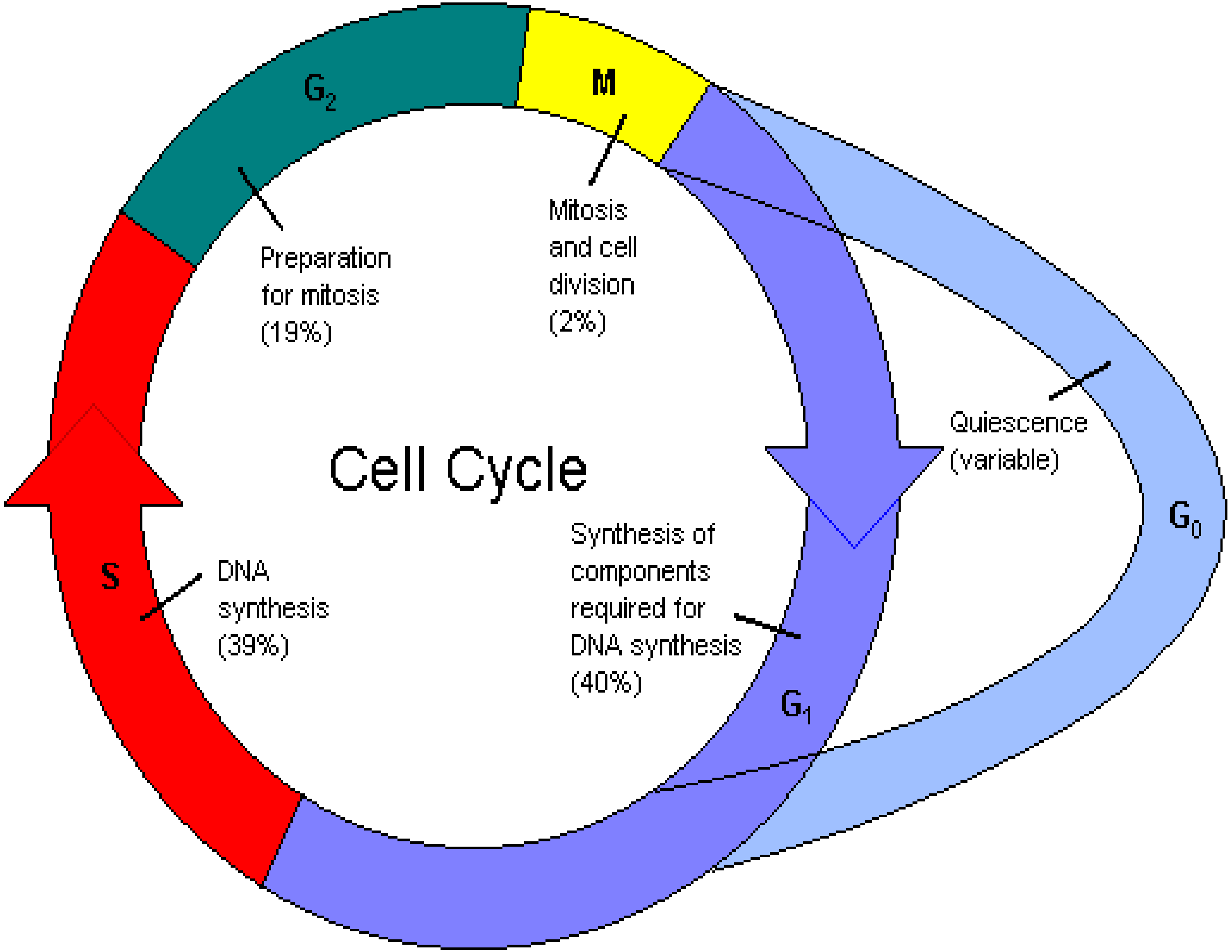
G_1 - primary growth phase

S – synthesis; DNA replicated

G_2 - secondary growth phase

collectively these 3 stages are called interphase

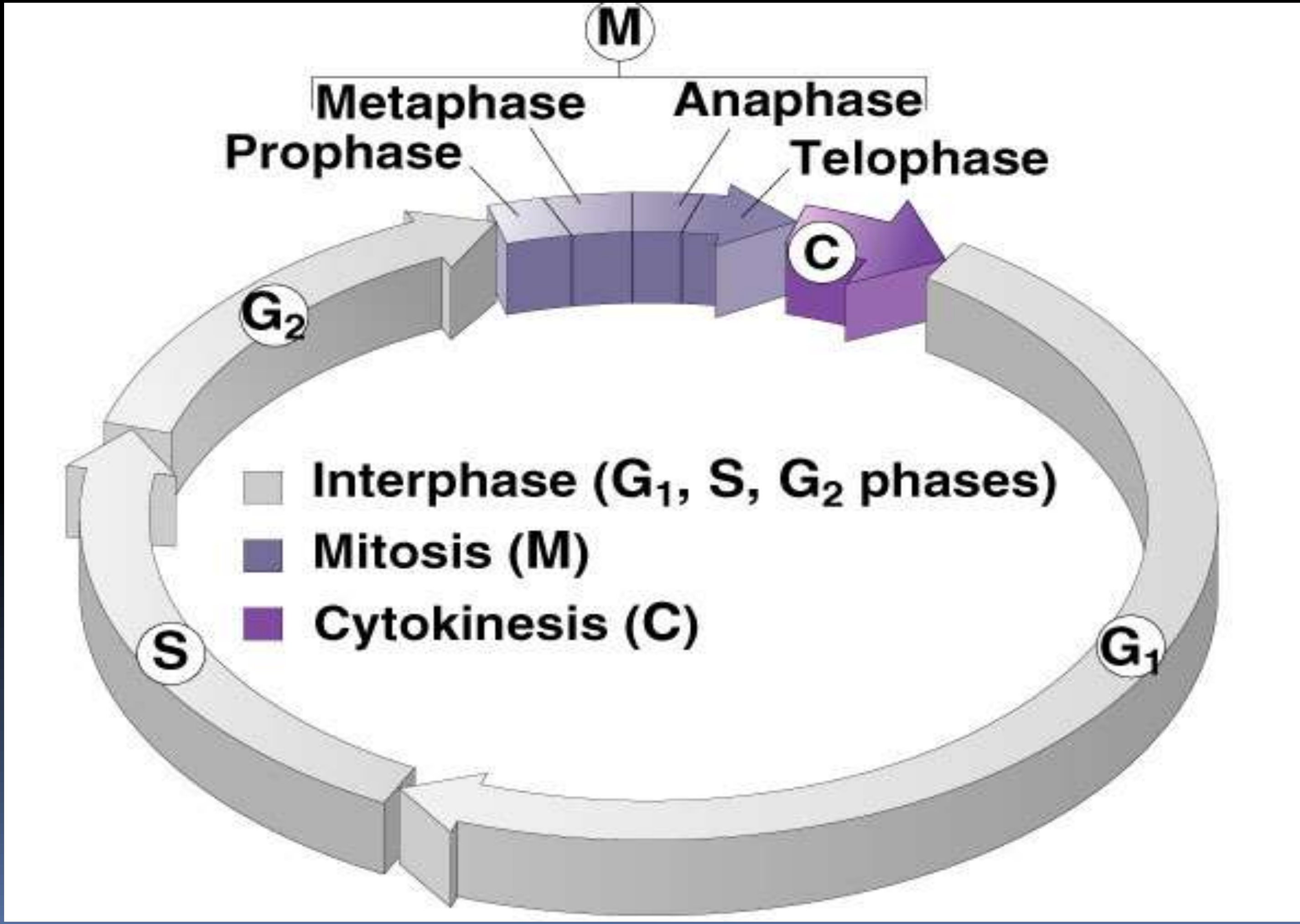
- M - Mitosis
- C – Cytokinesis


G2
M
Preparation for mitosis (19%)
Mitosis and cell division (2%)
Cell Cycle
Quiescence (variable)
G0
S
DNA synthesis (39%)
Synthesis of components required for DNA synthesis (40%)
G1

CONCEPT OF G0 PHASE-

- Nonproliferative cells in eukaryotes generally enter the quiescent G_0 state from G_1 and remain quiescent for long periods of time, possibly indefinitely , e.g. neurons
- Cellular senescence occurs in response to DNA damage or degradation that would make a cell's progeny nonviable.
- Some cells enter the G_0 phase for a short period of time e.g., liver and kidney cells.
- Many cells do not enter Go and continue to divide throughout an organism's life, e.g. epithelial cells

Cell Cycle



M
Metaphase
Anaphase
Prophase
Telophase
C
G2
S
G1
Interphase (G1, S, G2 phases)
Mitosis (M)
Cytokinesis (C)

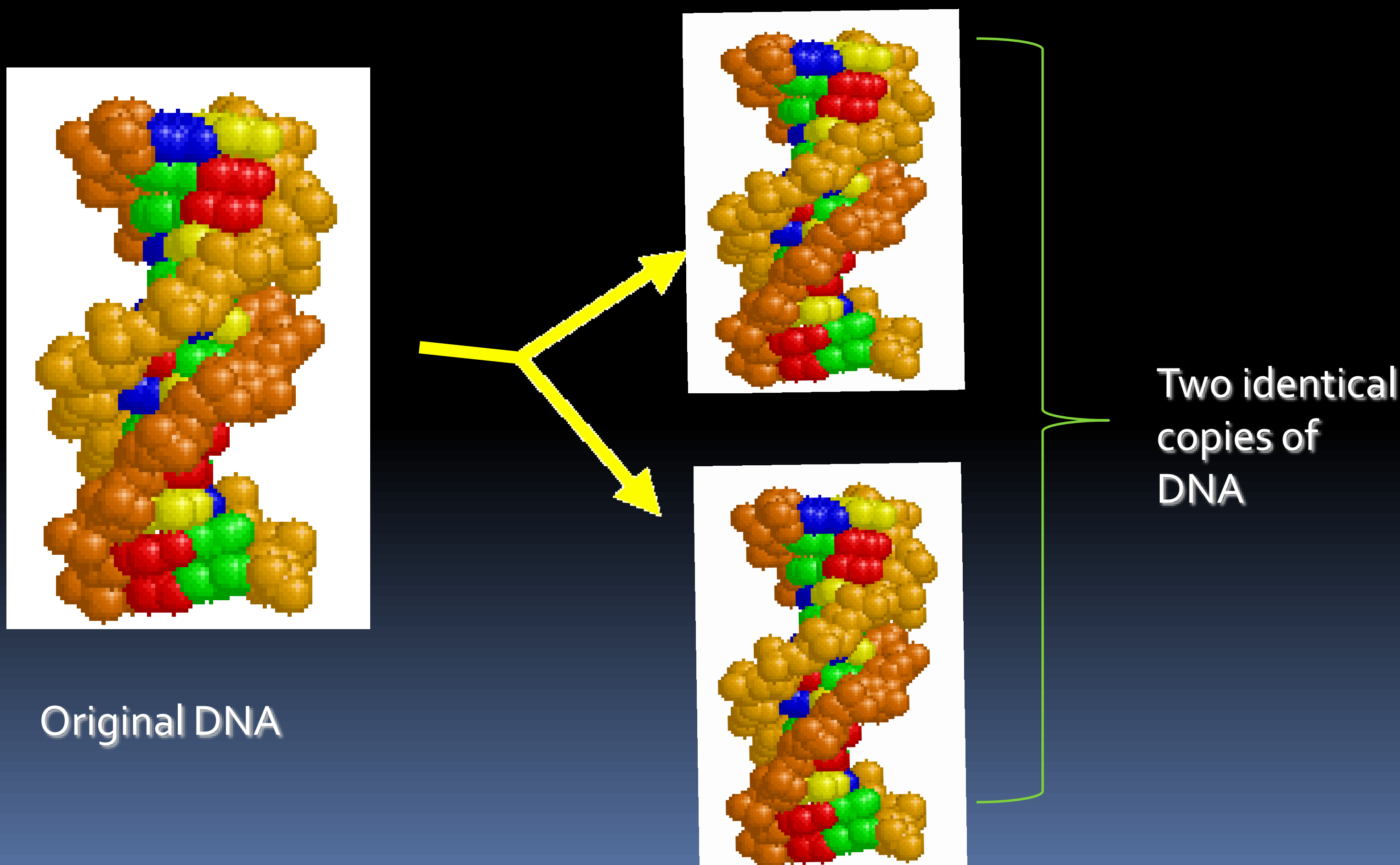
Interphase

(a) G_1 Stage

- 1st growth stage after cell division
- Cells mature by making more cytoplasm & organelles
- Cell carries on its normal metabolic activities

Interphase -> S Stage

- ✓Synthesis stage
- ✓DNA is copied or replicated



Interphase – G_2 Stage

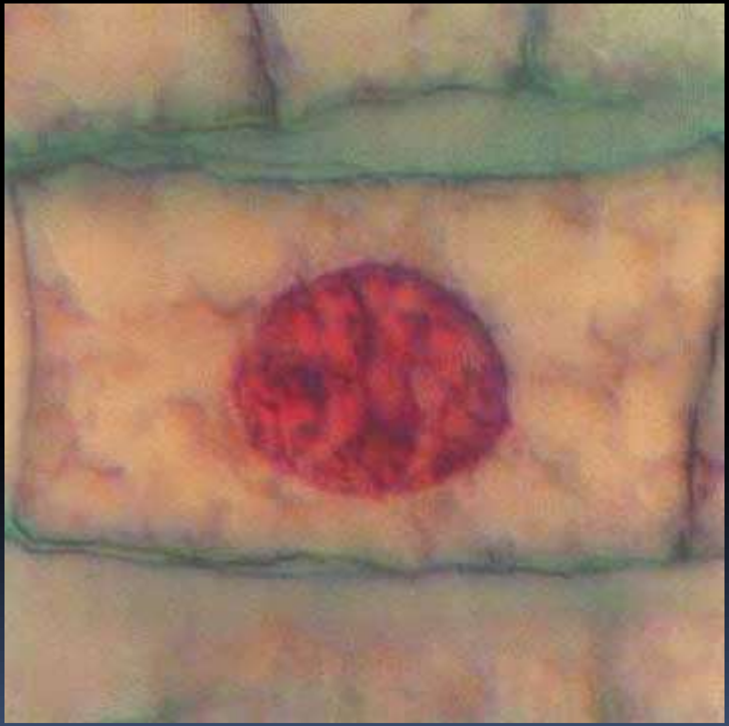
- 2nd Growth Stage

- Occurs after DNA has been copied
- All cell structures needed for division are made (e.g. centrioles)
- Both organelles & proteins are synthesized

Interphase

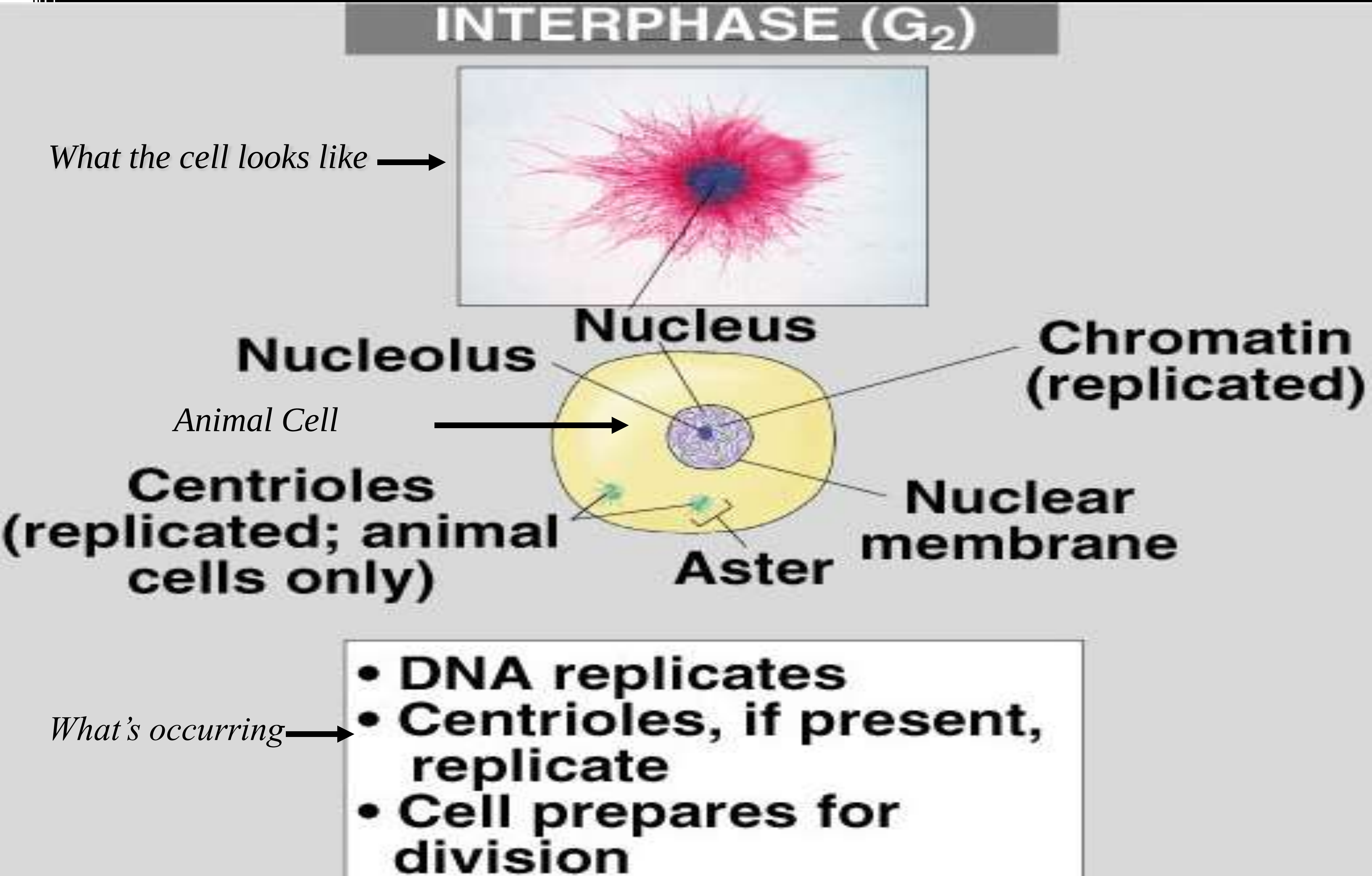
Animal Cell

Plant Cell

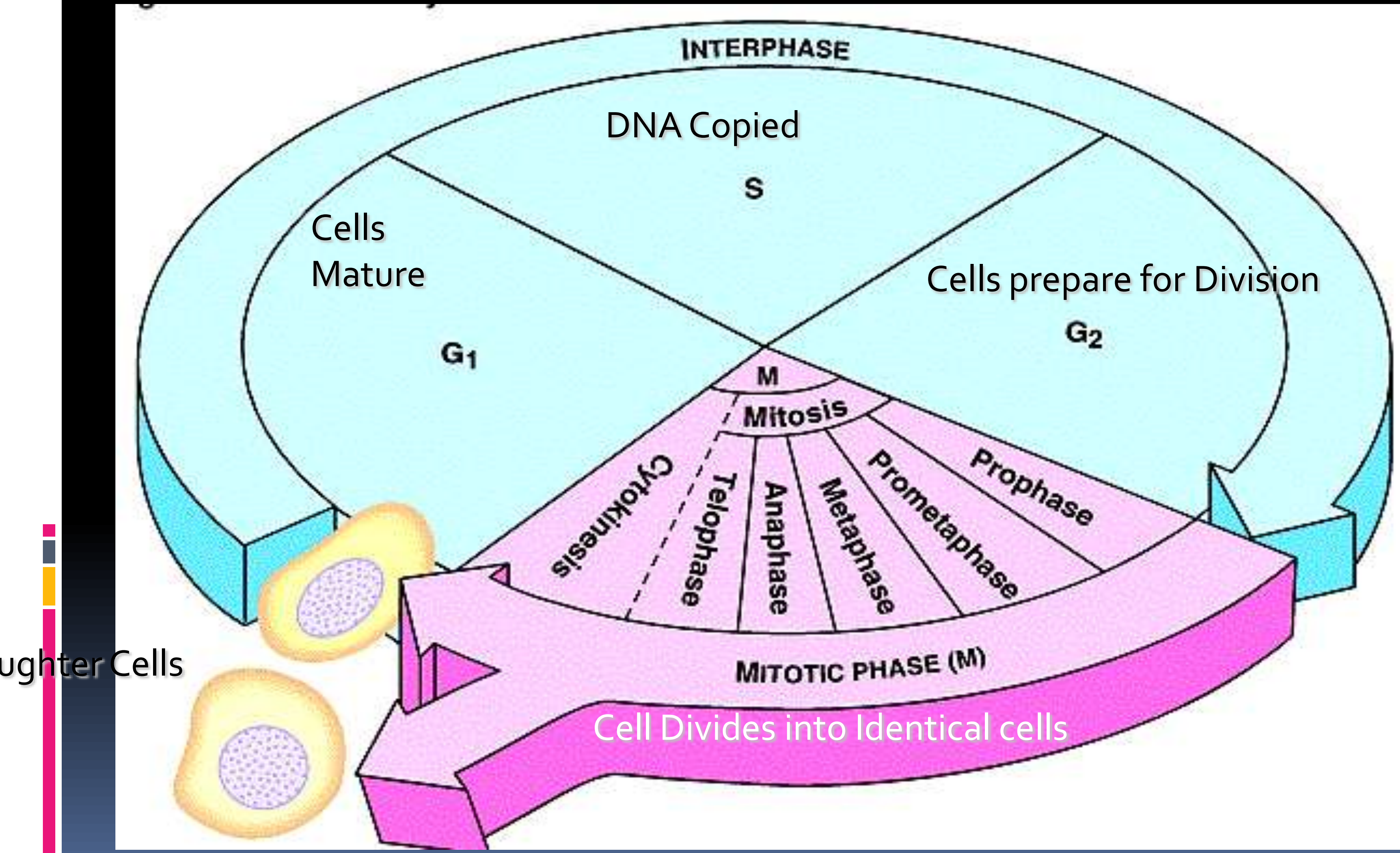


Photographs from: http://www.bioweb.uncc.edu/biol1110/Stages.htm

What Happens in Interphase G_2……..



Cell Cycle



INTERPHASE
DNA Copied
S
Cells
Mature
G1
Cells prepare for Division
G2
M
Mitosis
Prophase
Prometaphase
Metaphase
Anaphase
Telophase
Cytokinesis
MITOTIC PHASE (M)
Cell Divides into Identical cells
ughter Cells

Chromosomes

- All eukaryotic cells store genetic information in chromosomes.
  - Human cells have 46 chromosomes.
  - 23 nearly-identical pairs

Structure of Chromosomes

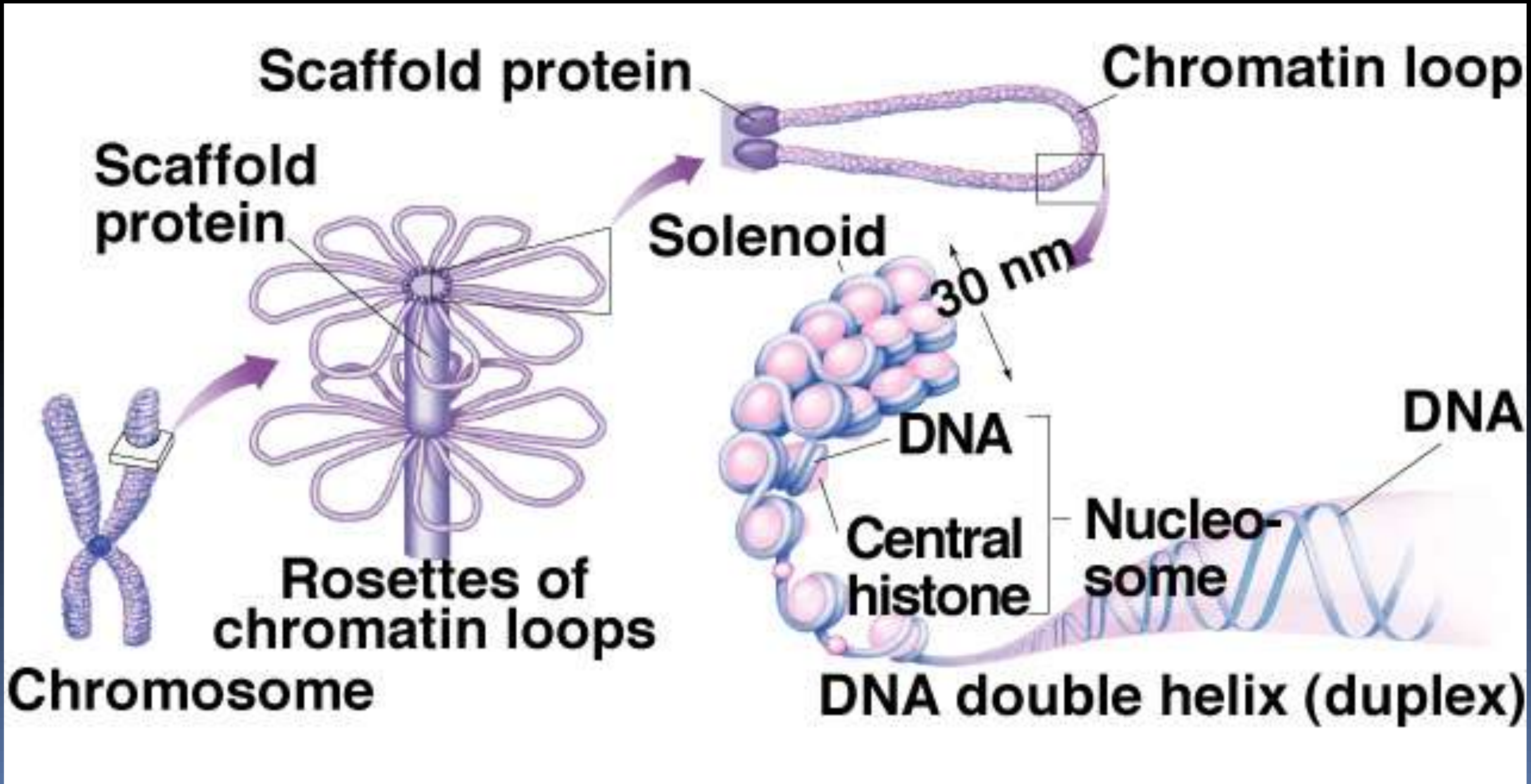
- Chromosomes are composed of a complex of DNA and protein called chromatin that condenses during cell division

- DNA exists as a single, long, double-stranded fiber extending chromosome's entire length.

- Each unduplicated chromosome contains one DNA molecule, which may be several inches long

Structure of Chromosomes

- After every 200 nucleotide pairs, the DNA wraps twice around a group of 8 histone proteins to form a nucleosome.
- Higher order coiling and supercoiling also helps in condensing and packaging the chromatin inside the nucleus.

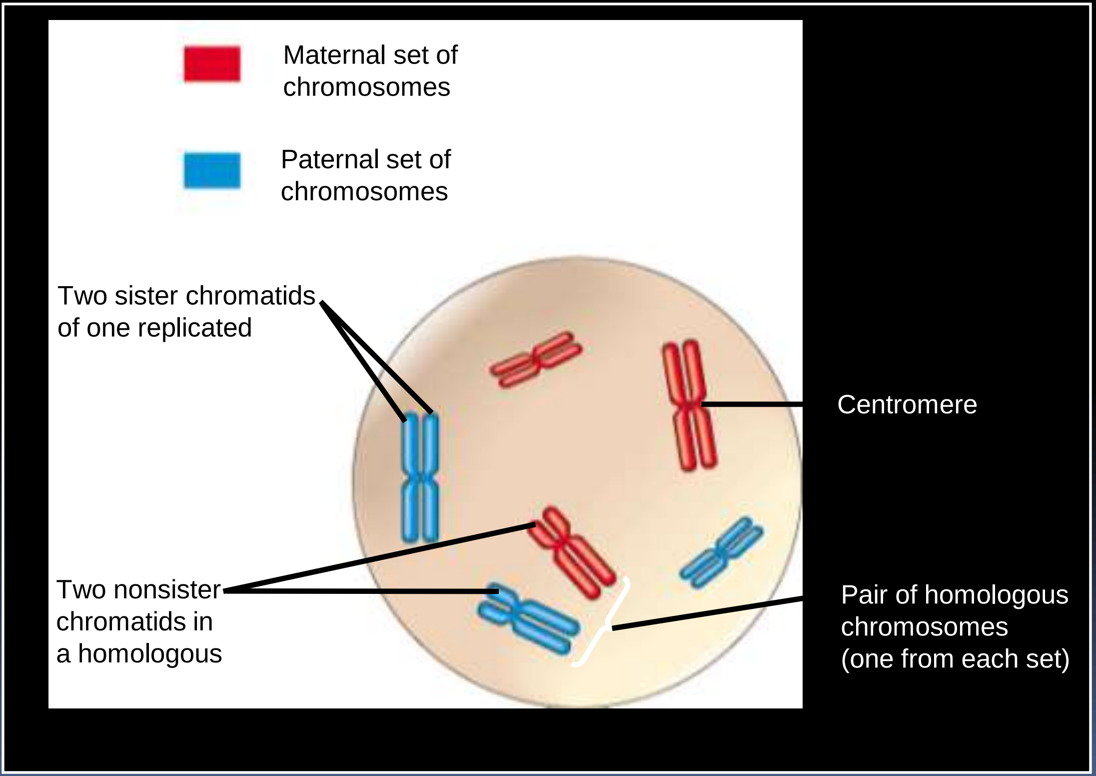


Chromosomes

- Non-homologous chromosomes
  - Look different
  - Control different traits
- Sex chromosomes
  - Are distinct from each other in their characteristics
  - Are represented as X and Y
  - Determine the sex of the individual, XX being female, XY being male
- In a diploid cell, the chromosomes occur in pairs. The 2 members of each pair are called homologous chromosomes or homologues.

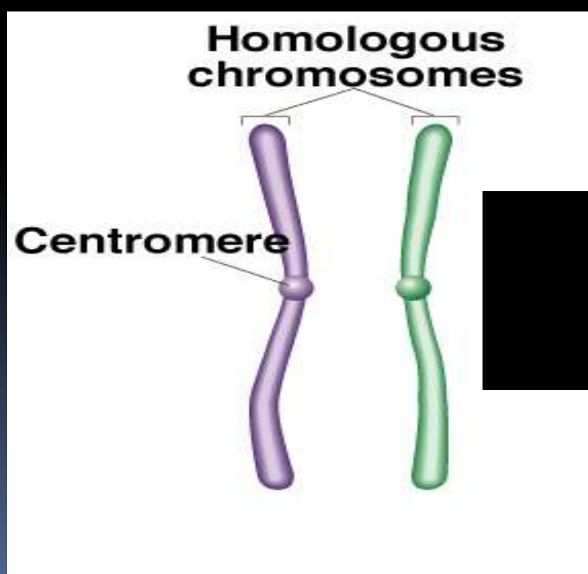
Chromosomes

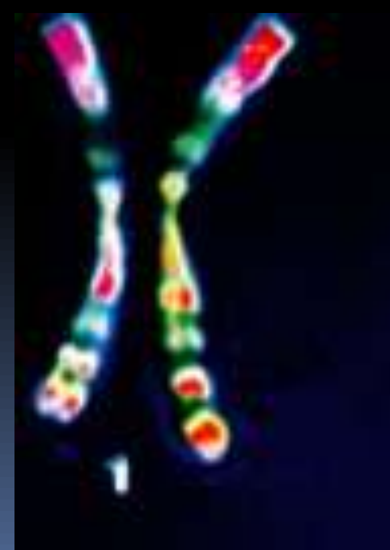
- A diploid cell has two sets of each of its chromosomes
- In human being 46 chromosomes are present(2n = 46)
- In a cell in which DNA synthesis has occurred all the chromosomes are duplicated and thus each chromosome consists of two identical sister chromatids



Homologues Chromosomes

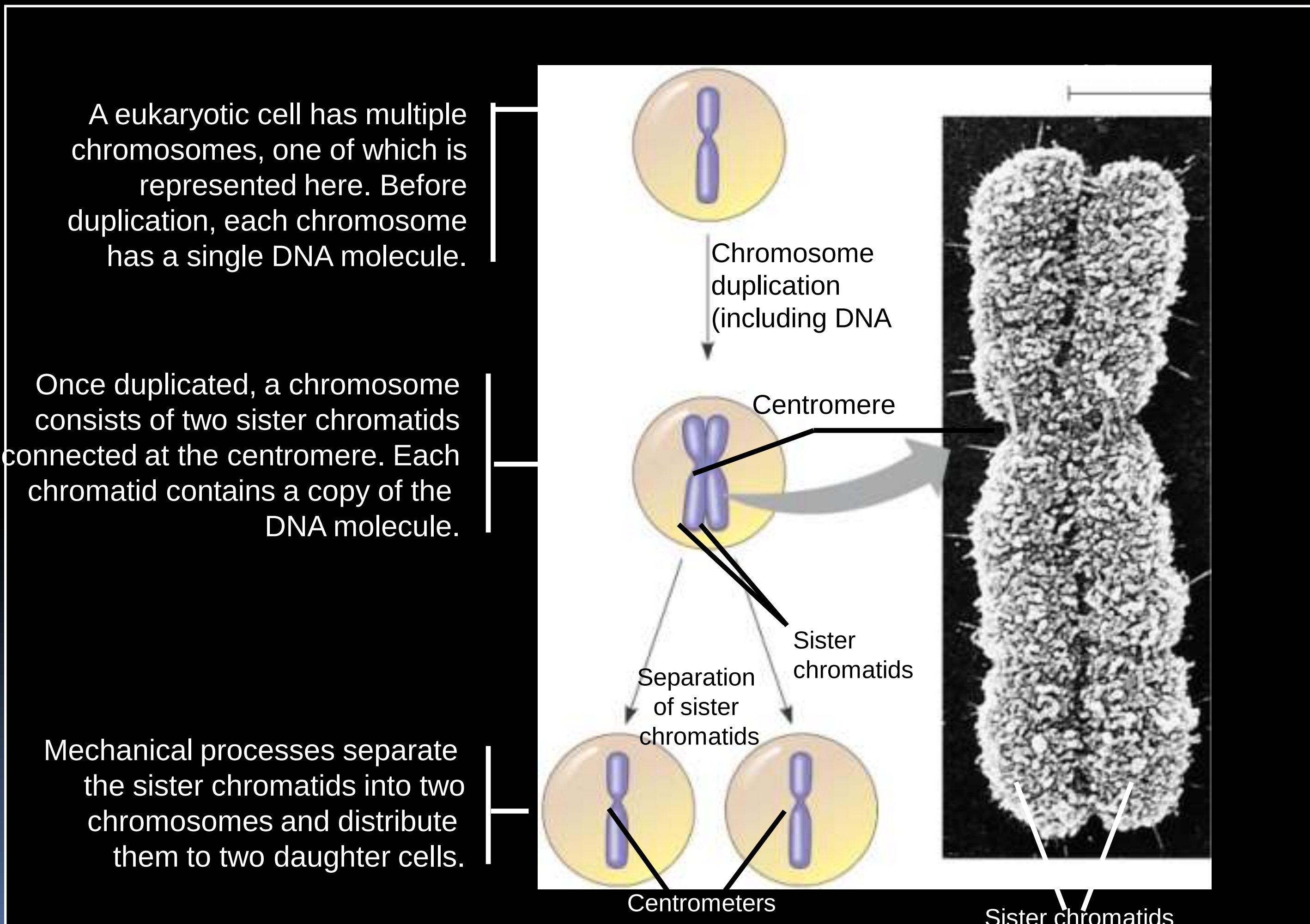
- Homologous chromosomes:
  - Look the same
  - Control the same traits
  - May code for different forms of each trait
  - Independent origin - each one was inherited from a different parent





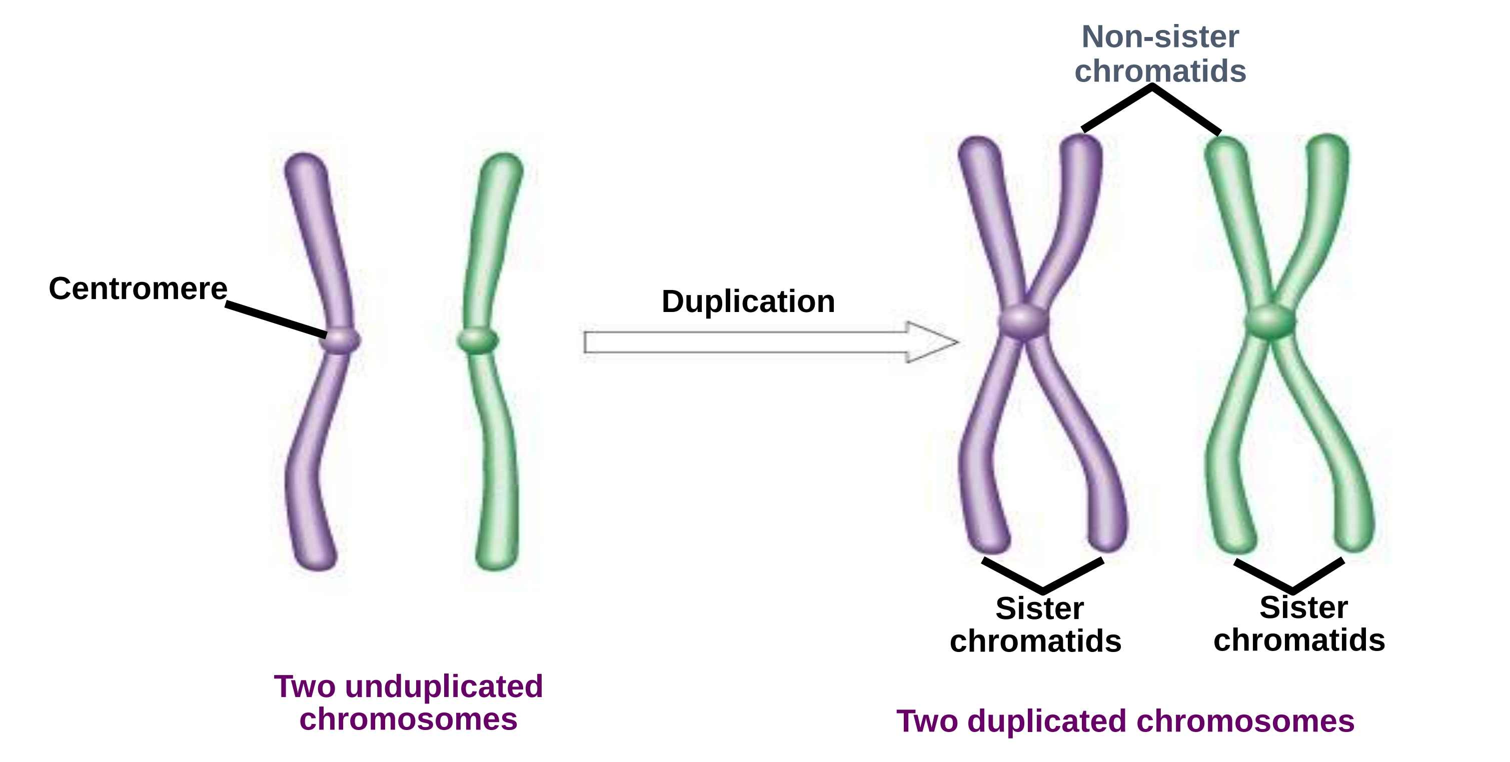
Chromosome Duplication

- In preparation for cell division, DNA is replicated and the chromosomes condense



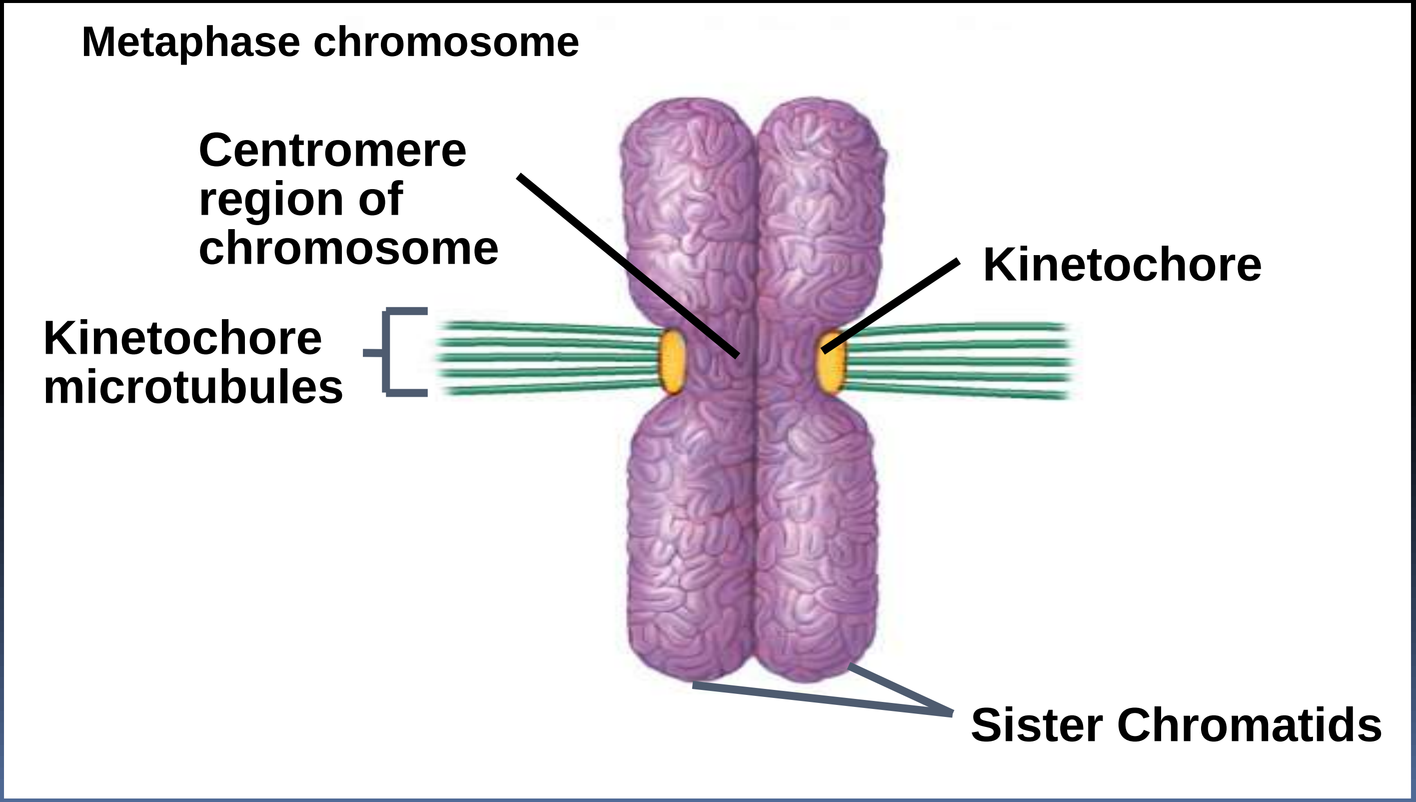
Chromosome Duplication

- Because of duplication, each condensed chromosome consists of 2 identical chromatids joined by a centromere.
- Each duplicated chromosome contains 2 identical DNA molecules (unless a mutation occurred), one in each chromatid:



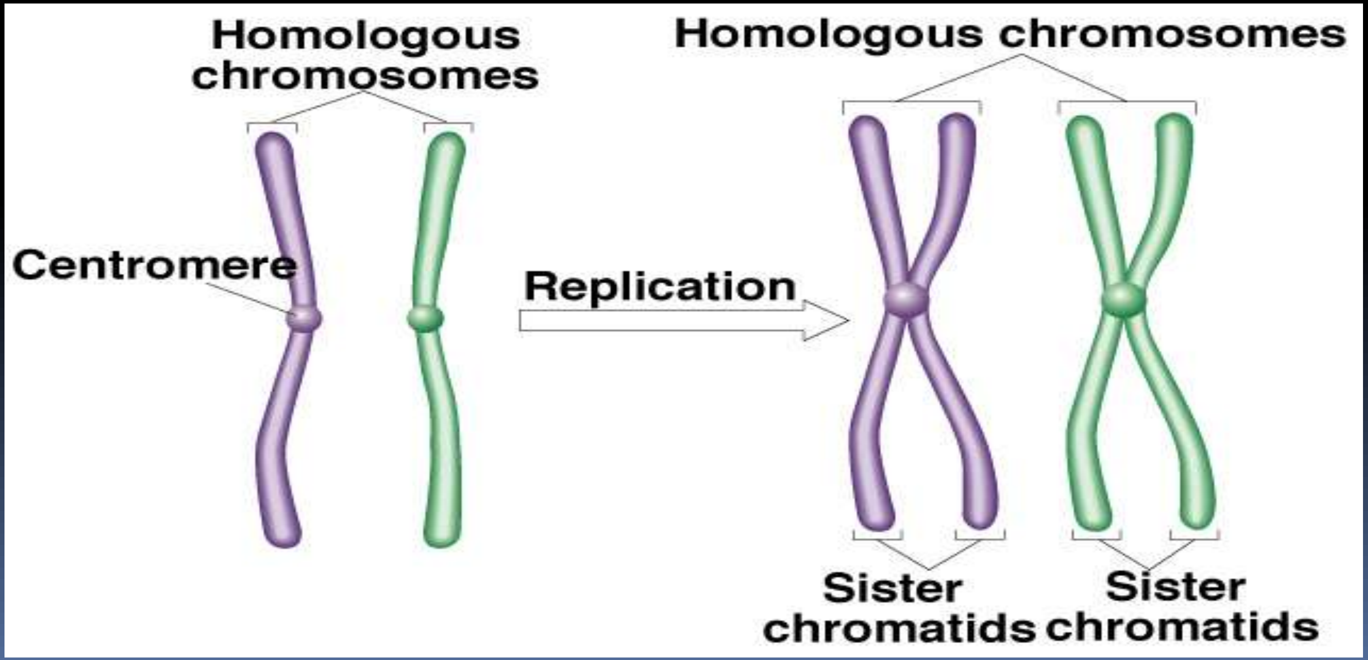
Structure of Chromosomes

- The centromere is a constricted region of the chromosome containing a specific DNA sequence, to which is bound 2 discs of protein called kinetochores.
- Kinetochores serve as points of attachment for microtubules that move the chromosomes during cell division:

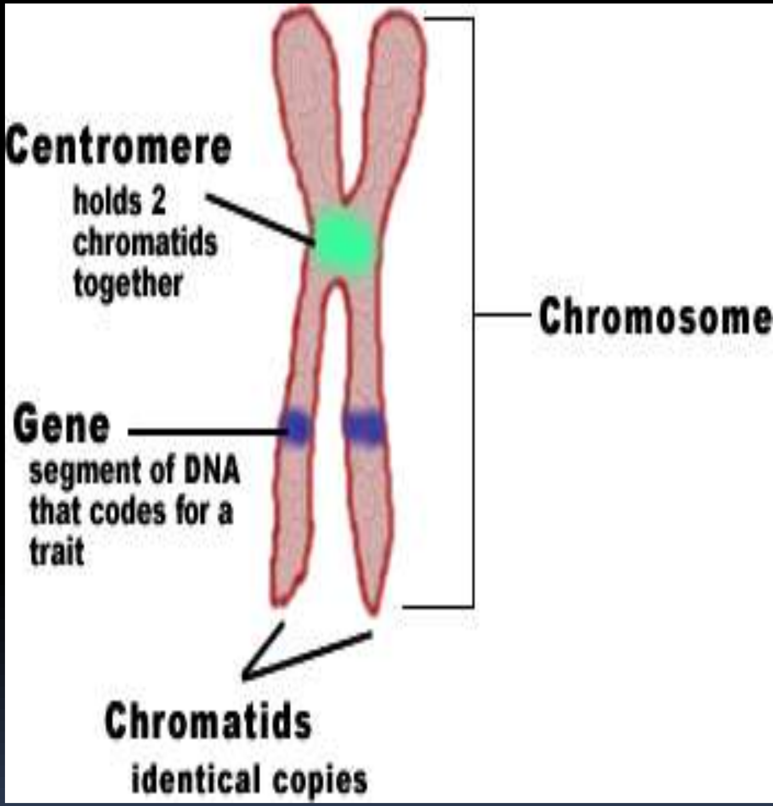


Structure of Chromosomes

- Diploid - A cell possessing two copies of each chromosome (human body cells).
  - Homologous chromosomes are made up of sister chromatids joined at the centromere.
- Haploid - A cell possessing a single copy of each chromosome (human sex cells).



- *KARYOTYPE it is a chromosome complement of a cell or organism depicting the number , size and form of the chromosome as seen in metaphase of mitosis.*
- *Chromosomes are assembled as homologous pairs in decreasing order of length.*



CELL DIVISION

- Cell division involves a single cell (called a *mother cell*) dividing into two daughter cells. This leads to growth in multicellular organisms (the growth of tissue) and to procreation (vegetative reproduction) in unicellular organisms.

- Prokaryotic cells divide by binary fission.

- Eukaryotic cells usually undergo a process of nuclear division, called mitosis, followed by division of the cell, called cytokinesis.

- A diploid cell may also undergo meiosis to produce haploid cells, usually four. Haploid cells serve as gametes in multicellular organisms, fusing

- DNA replication, or the process of duplicating a cell's genome, is required every time a cell divides. Replication, like all cellular activities, requires specialized proteins for carrying out the job.

Protein synthesis

- Cells are capable of synthesizing new proteins, which are essential for the modulation and maintenance of cellular activities.
- This process involves the formation of new protein molecules from amino acid building blocks based on information encoded in DNA/RNA.
- Protein synthesis generally consists of two major steps: transcription and translation.

Transcription

- Process by which genetic information encoded in DNA is copied onto messenger RNA
- Occurs in the nucleus
- DNA → mRNA

Translation

- Process by which information encoded in mRNA is used to assemble a protein at a ribosome
- Occurs on a Ribosome
- mRNA → protein

CELL DIVISION OCCURS IN 3 WAYS-

- *AMITOSIS*
- *MITOSIS*
- *MEIOSIS*

AMITOSIS

- Amitosis is very simple, it occurs without the formation of spindle and appearance of chromosome
- Nuclear envelope remains intact.
- E.g – Macromolecules of ciliates such as paramecium.
- In each case division of nucleus called KARYOGENESIS, occurs before the division of cytoplasm termed CYTOKINESIS

MITOSIS

- MITOSIS was 1ST described by GERMAN BIOLOGIST EDUARD STRASBURGER in plant cell in1875

  and later by another GERMAN BIOLOGIST WALTHER FLEMMING in animal cell 1879.

- TERMED MITOSIS by WALTHER FLEMMING in 1882.

DEFINITION

- It is defined as" the division of a parent cell into 2 identical daughter cells each with a nucleus having the same amount of DNA, the same number and kind of chromosomes and same hereditary instructions as parent cell."
- Hence also known as EQUATIONAL DIVISION.

INTERPHASE

- Period between two successive division.
- Greater part of interphase is called G_1 stage.
- S Stage: - Synthesis of DNA takes place.
- G2: - Protein synthesis takes placed required for cell division.

MECHANISM OF MITOSIS

- *It involve a series of changes in nucleus as well as cytoplasm*

Therefore often called as indirect division

Two main events in mitosis -:

- *Karyokinesis*
- *Cytokinesis*

<u>Karyokinesis may be divided into four stages →</u>

- *PROPHASE*
- *METAPHASE*
- *ANAPHASE*
- *TELOPHASE*

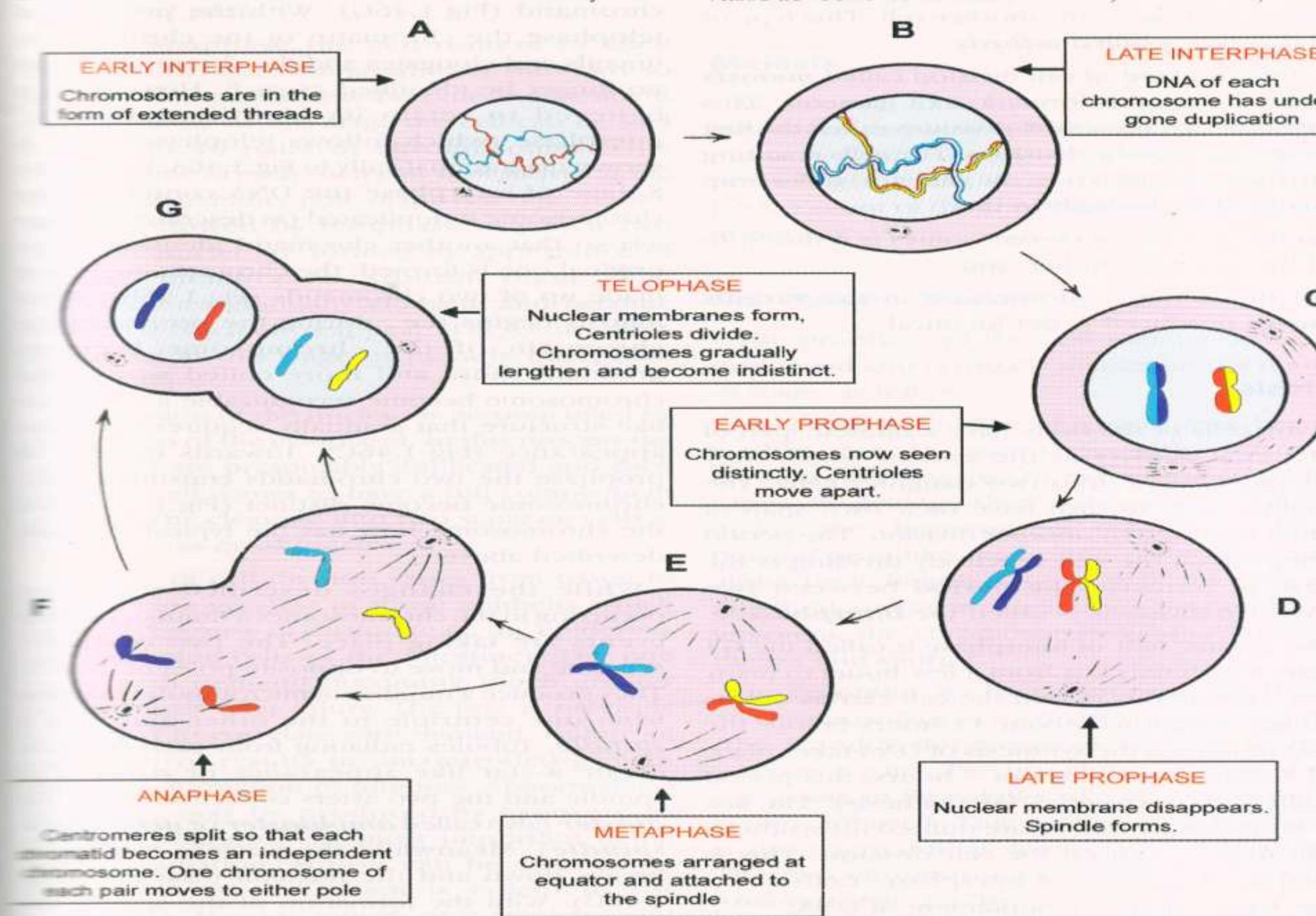
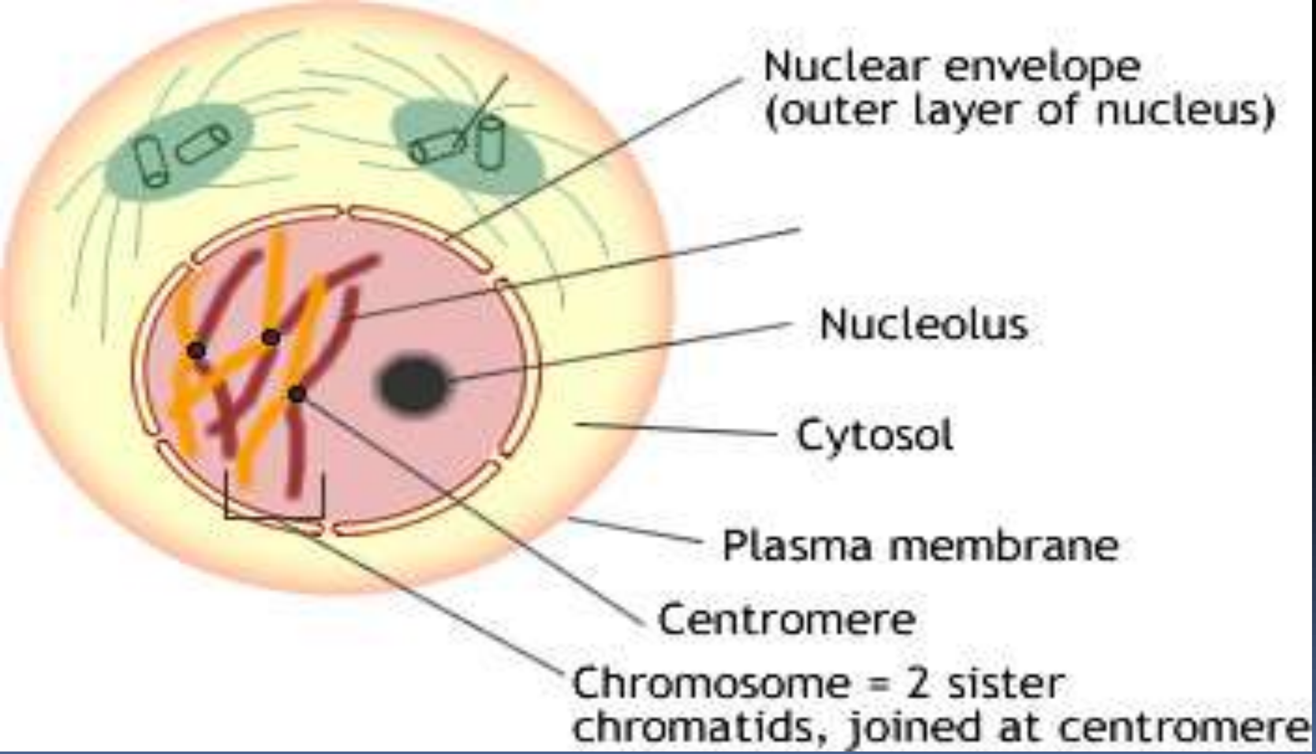


Fig. 1.46. Scheme to show the main steps in mitosis.

STAGES OF MITOSIS

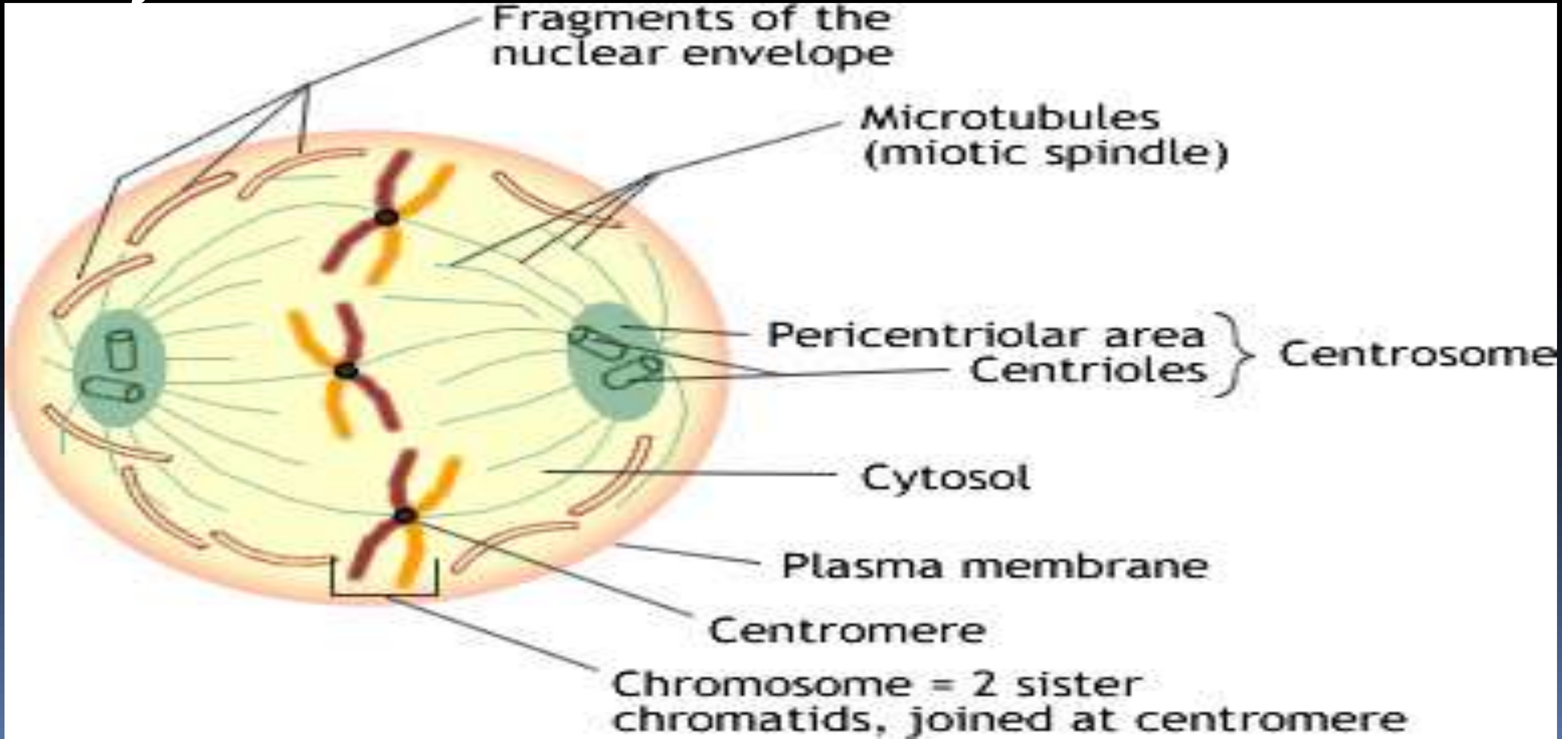
EARLY PROPHASE

- *Early in the prophase stage the chromatin fibers shorten into chromosomes*
- *Each prophase chromosome consists of a pair of identical double-stranded chromatids.*

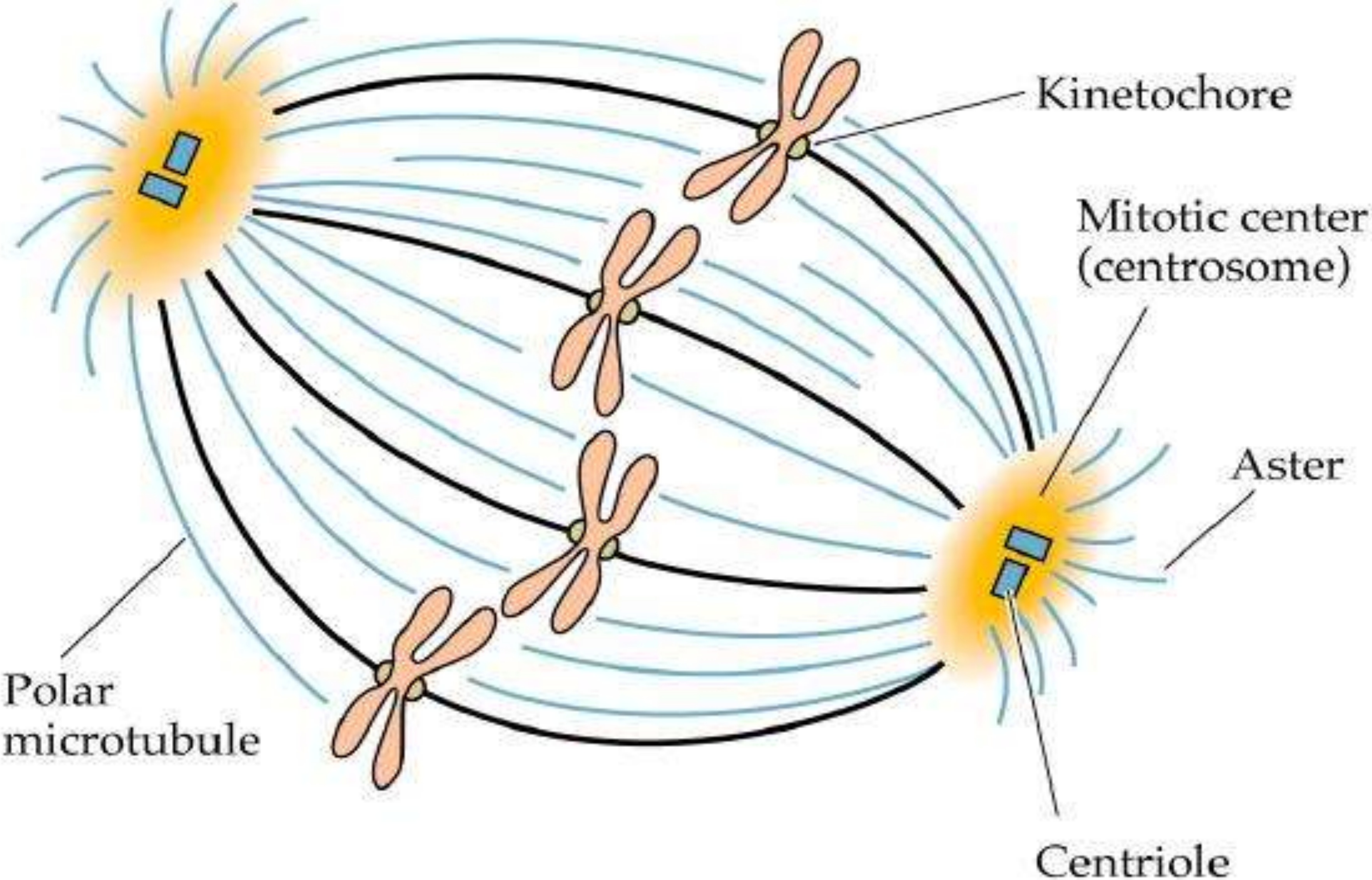


LATE PROPHASE

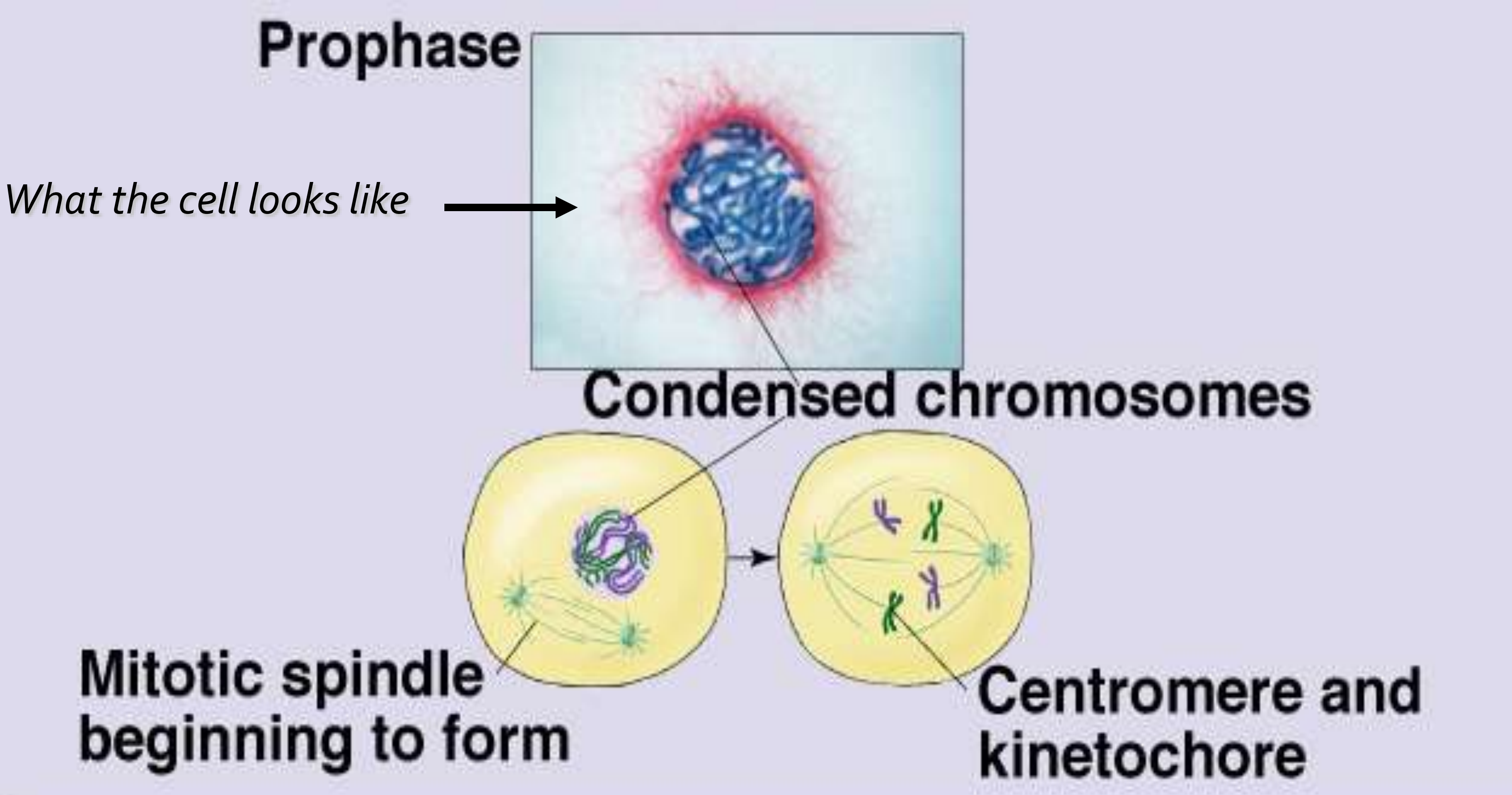
- *Nucleolus disappears, the nuclear envelope breaks down, and the two centrosomes begin to form the **mitotic spindle** (which is an assembly of microtubules).*
- *As the microtubules extend in length between the centrosomes, the centrosomes are pushed to opposite "poles" (extremes) of the cell.*
- *Eventually, the spindle extends between two opposite poles of the cell.*



The Spindle


Kinetochore
Mitotic center
(centrosome)
Aster
Polar
microtubule
Centriole

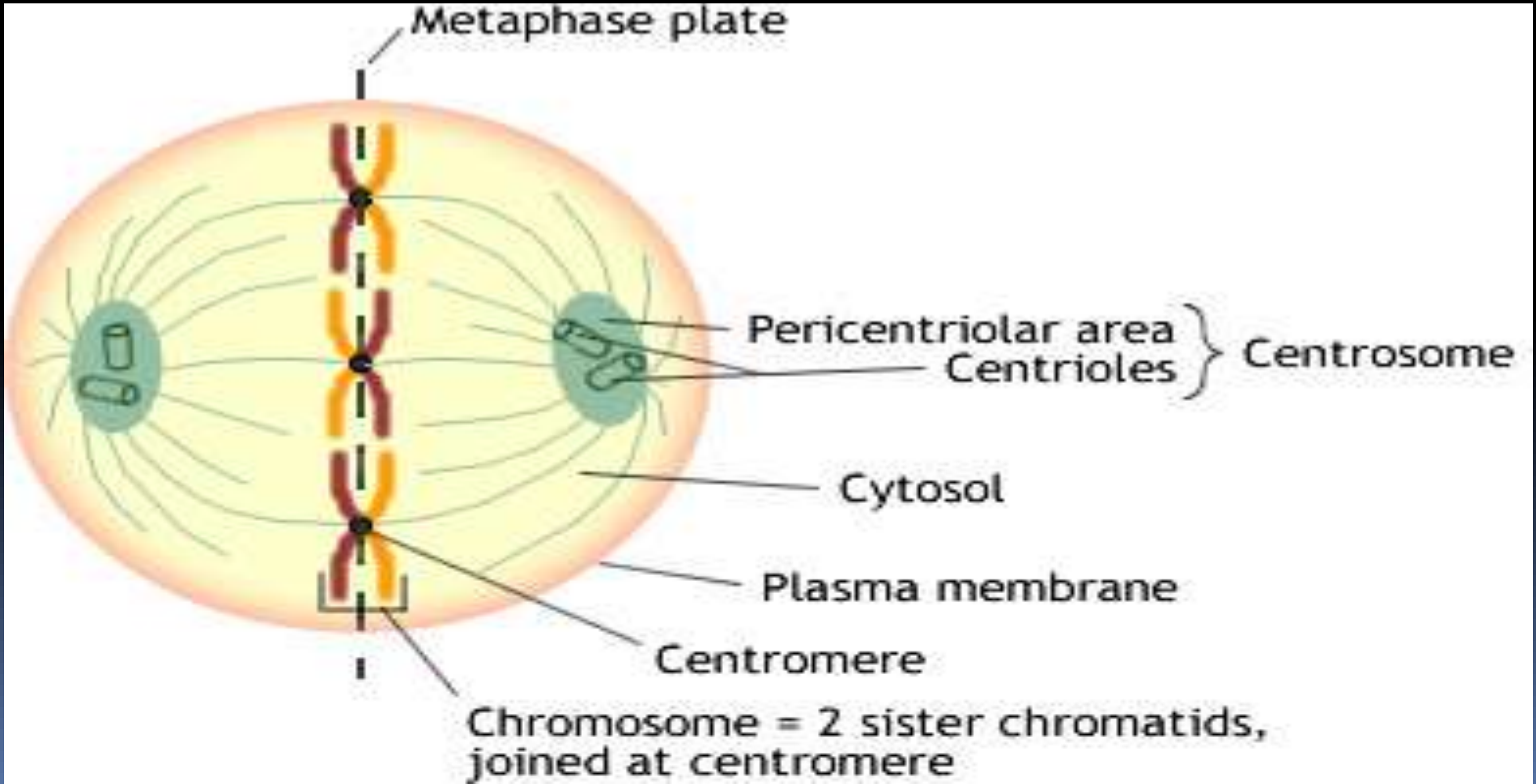
Review of Prophase



- Nuclear membrane disintegrates, and nucleolus disappears
- Chromosomes condense
- Mitotic spindle begins to form and is complete at the end of prophase
- Kinetochores begin to mature and attach to spindle

METAPHASE

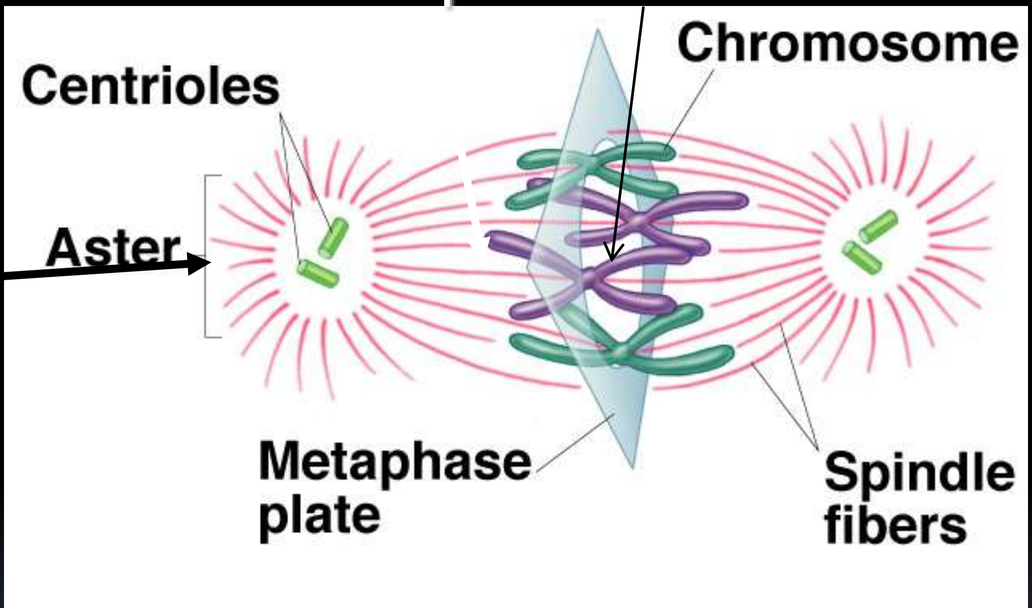
- CHROMOSOME CONDENSATION CONTINUES INTO METAPHASE.
- MOST STRIKING FEATURE-CHROMOSOMES BECOME ALIGNED WITH THERE CENTOMERES IN A SINGLE TRANSVERSE PLANE.
- THIS PLANE LIES PERPENDICULAR TO THE LONG AXIS OF SPINDLE AND IS KNOWN AS EQUTORIAL PLATE.
- OFTEN KNOWN AS METAPHASE PLATE.



Metaphase

Equator of Cell

Poles



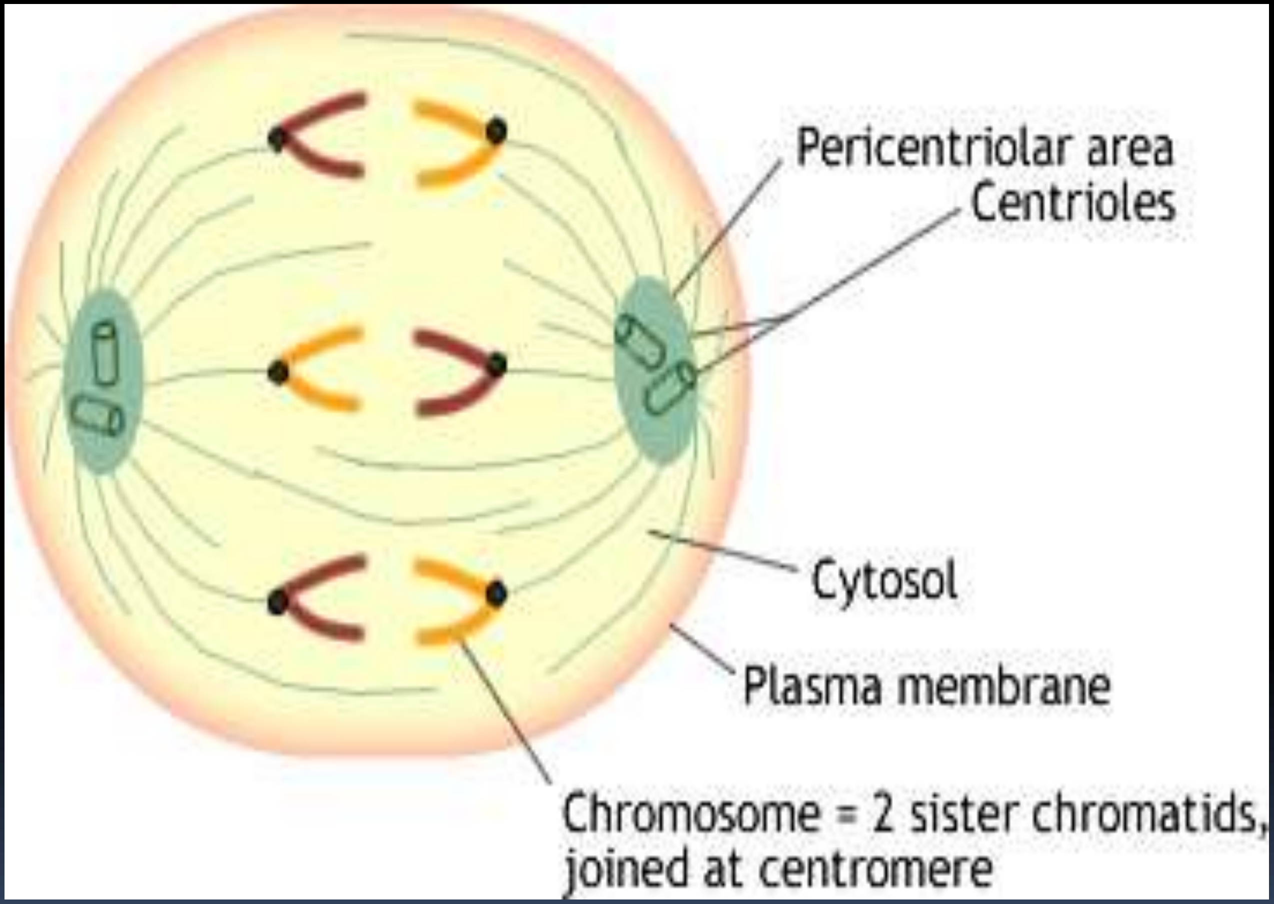
ANAPHASE

- *The centromeres split separating the two members of each chromatid pair - which then move to the opposite poles of the cell.*

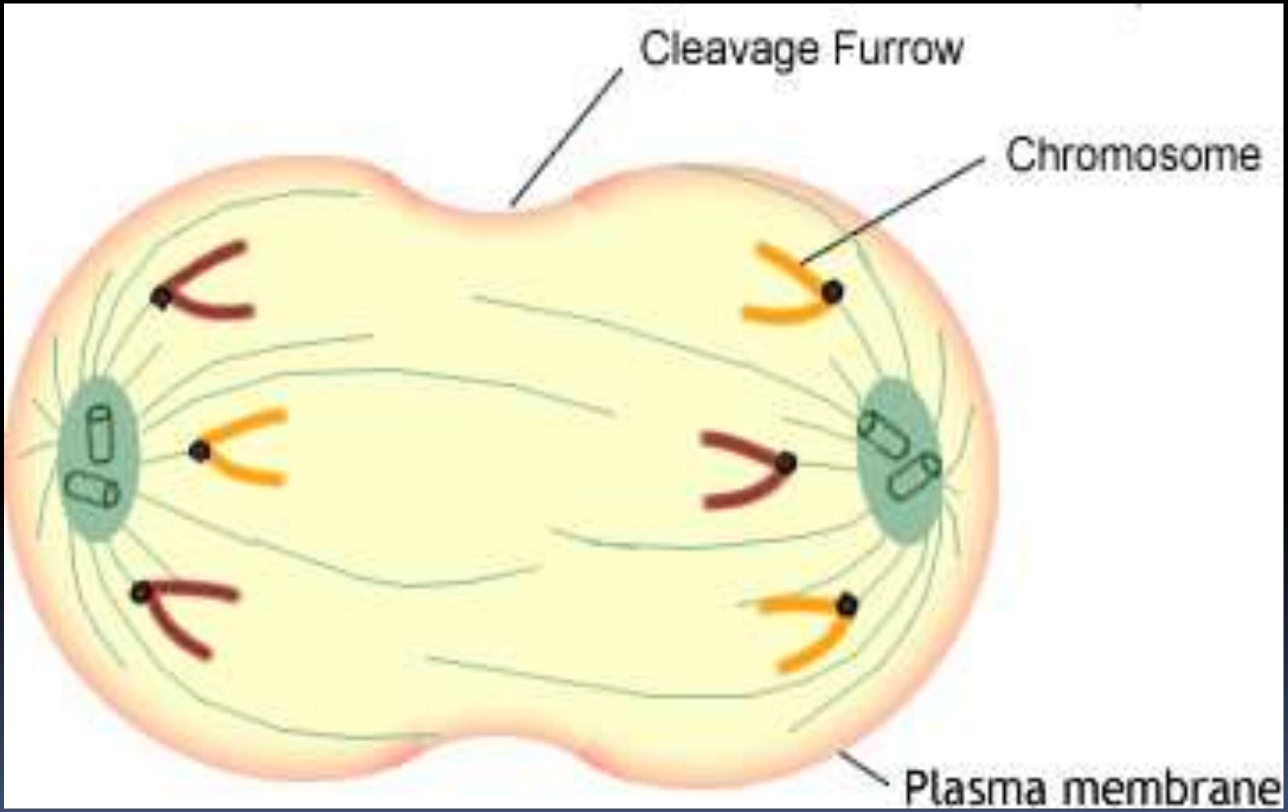
- ***When they are separated , the chromatids are now called as chromosomes****.*

- *As the chromosomes are pulled by the microtubules during anaphase, they appear to be "V"-shaped because the centromeres lead the way, dragging the trailing arms of the chromosomes towards the poles*

- *EARLY ANAPHASE*



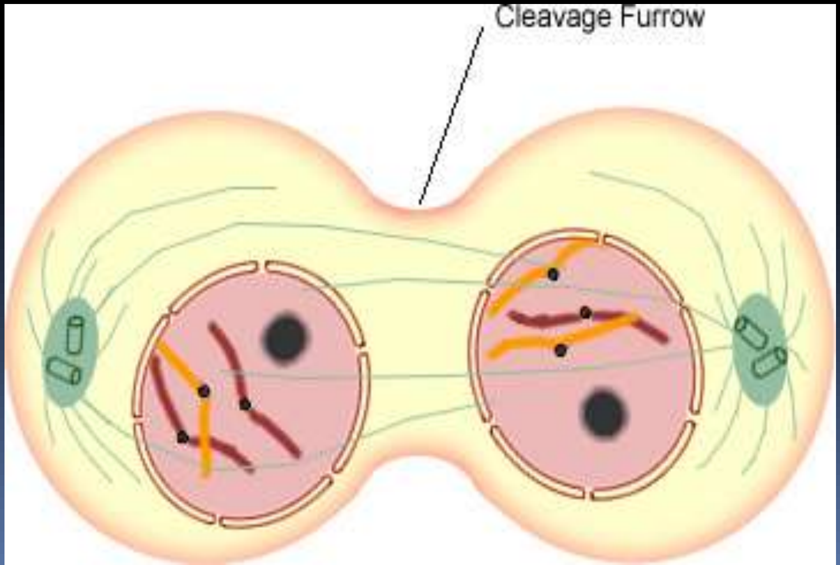
LATE ANAPHASE



TELOPHASE

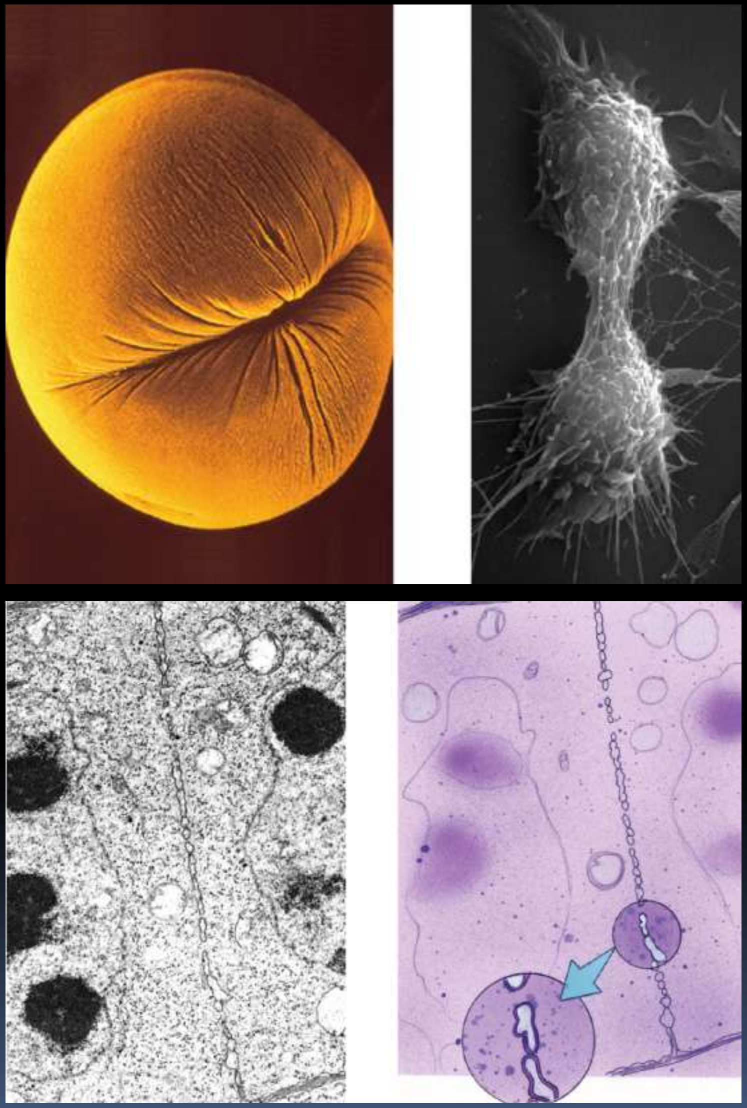
Telophase begins after the chromosomal movement stops.

- *The identical sets of chromosomes - which are by this stage at opposite poles of the cell, uncoil and revert to the long, thin, thread-like chromatin form.*
- *A new nuclear envelope forms around each chromatin mass.*
- *Nucleoli appear.*
- *Eventually the miotic spindle breaks-up.*

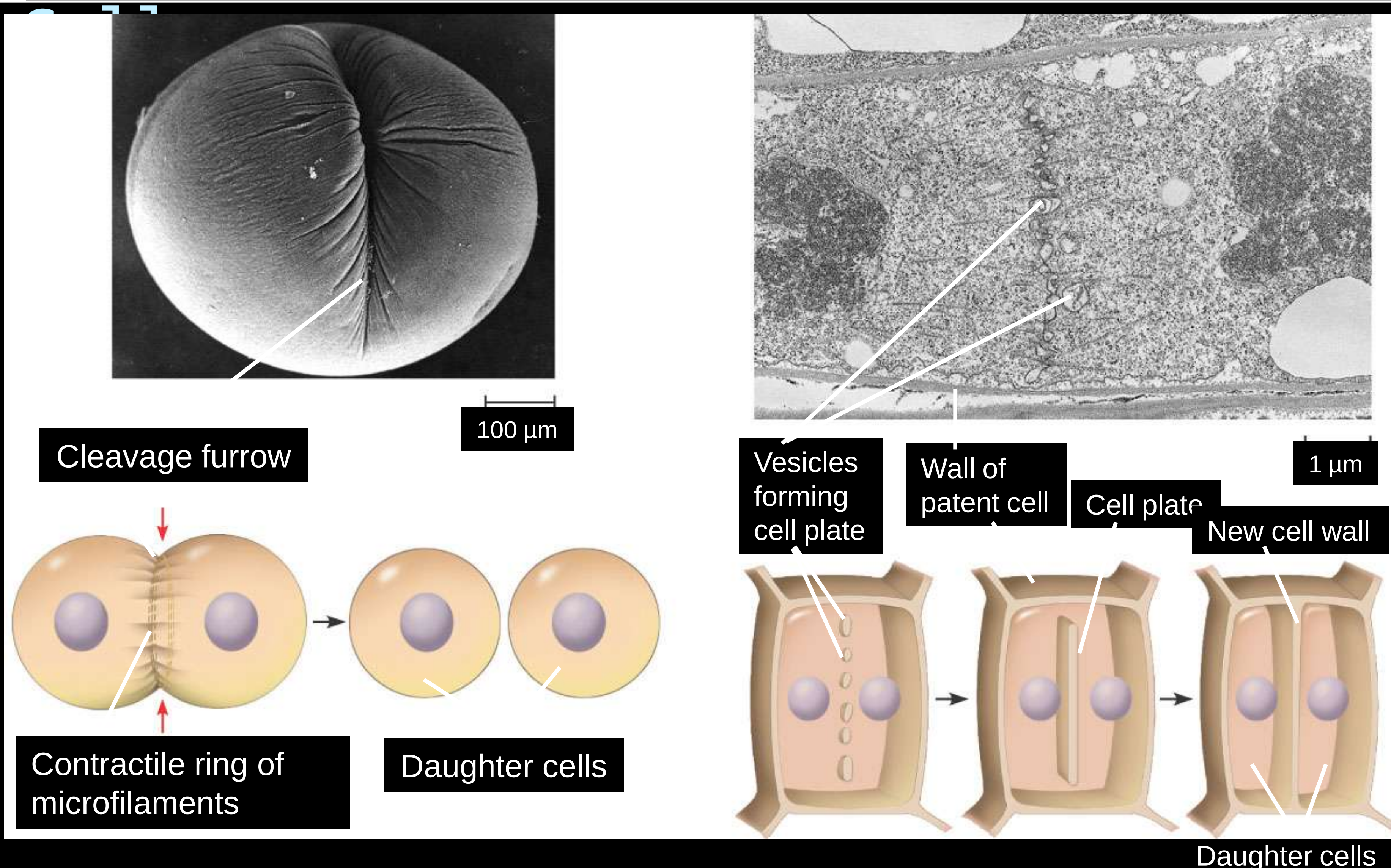


Cytokinesis

- Cleavage of cell into two halves
  - Animal cells
    - Constriction belt of actin filaments
  - Plant cells
    - Cell plate
  - Fungi and protozoa
    - Mitosis occurs within the nucleus



Cytokinesis In Animal And Plant



(a) Cleavage of an animal cell (SEM)

(b) Cell plate formation in a plant cell (SEM)

Meiosis

Specialized type of cell division that produces germ cells.ova and spermatozoa.

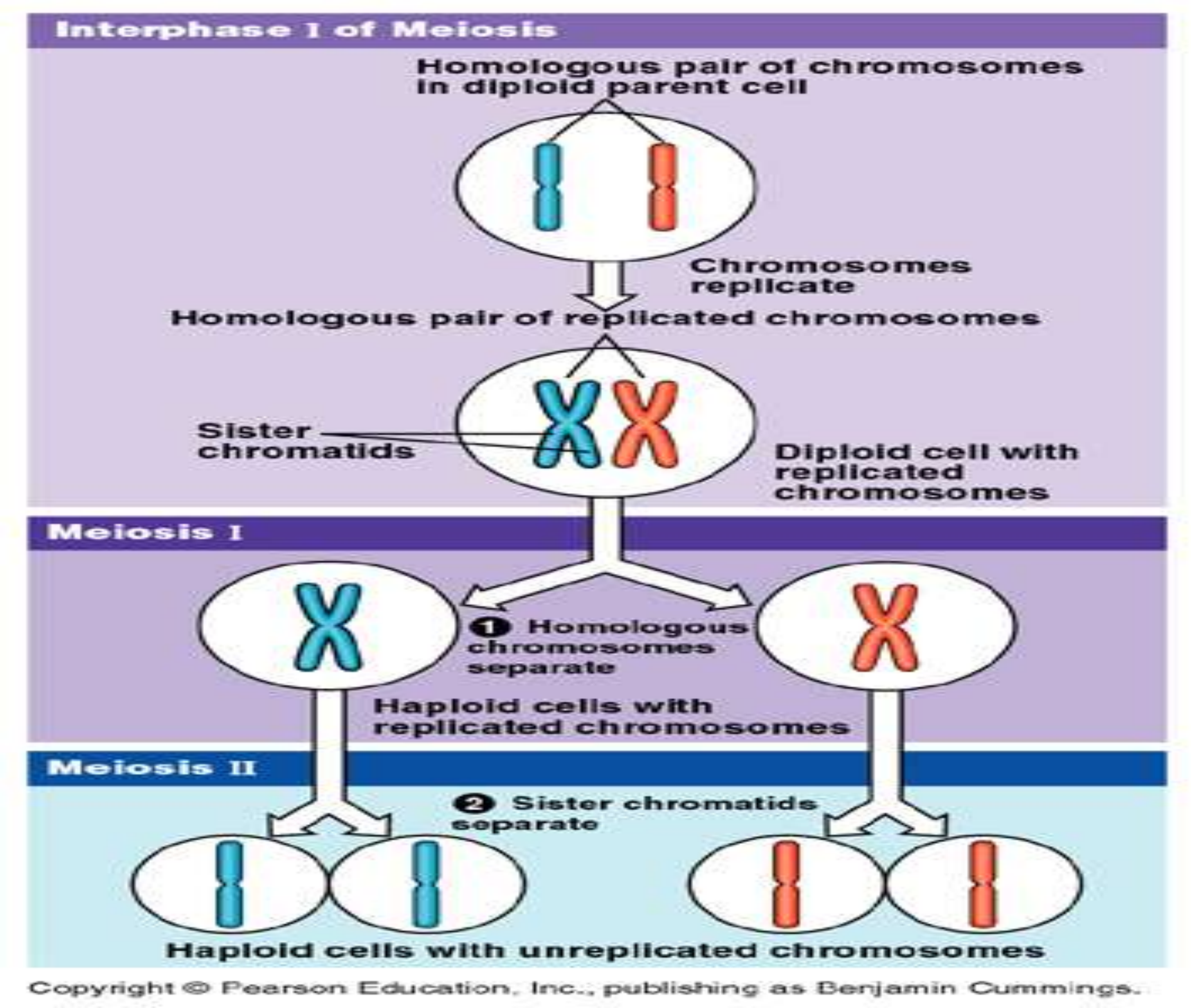
This process has 2 crucial results:-

- *Reduction in number of chromosomes from diploid (2n) to haploid (1n).*
- *Recombination of genes.*

It is divided in 2 separate divisions-

- *Meiosis 1/reductional division.*
- *Meiosis 2/equatorial division.*

MEIOSIS- An Overview



MEIOSIS I

- ***Amount of DNA is doubled to 4n and the chromosome number is also doubled to 4n during S phase.***

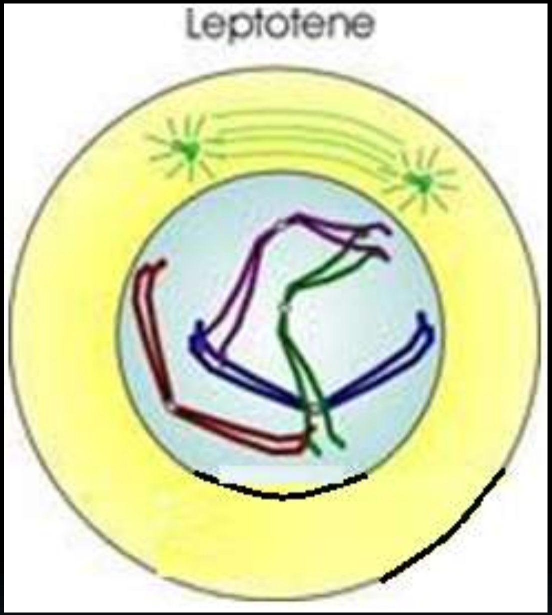
Prophase 1 -:

PROPHASE 1 is subdivided into following 5 phases -:

1. *Leptotene*
2. *Zygotene*
3. *Pachytene*
4. *Diplotene*
5. *Diakinesis*

1. LEPTOTENE

Chromosomes condense forming long strands.



- Chromosome become visible each chromosomes consists of two chromatids.
- At first the chromosomes are seen as threads bearing bead thickening (chromosome) along their length.

2. ZYGOTENE -:

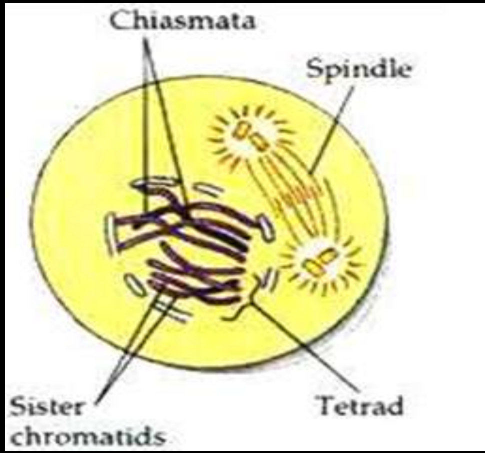
- Pairing of chromosome also referred as synapsis, takes place.

- ***Synaptonemal complex is formed*** by a pair of synapsed homologous chromosomes i called a bivalent or a tetrad.

3. *PACHYTENE*

Chiasmata (crossing over sites) start forming

- 2 chromatid of each chromosomes become distinct. The bivalent now has formed chromatids in it called a Tetrad which is clearly visible at this stage.
- Two central chromatids becomes coiled over each other so that they cross at number of points called crossing over.



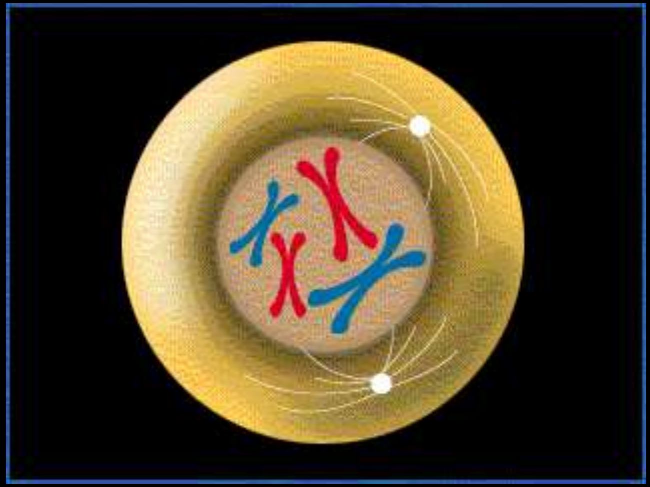
4. DIPLOTENE

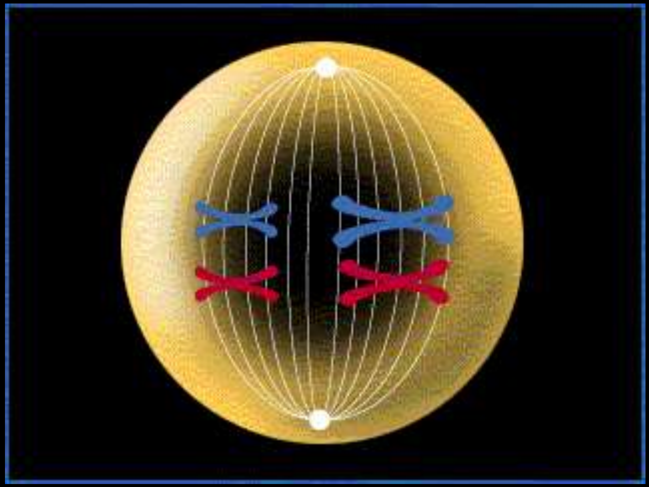
- Dissolution of the synaptonemal complex
- Chromosome continue to condense and then begin to separate, revealing X shaped structures, called chiasmata.
- 2 chromosomes of bivalent now try to move apart as they do so chromatid break at the point of crossing.

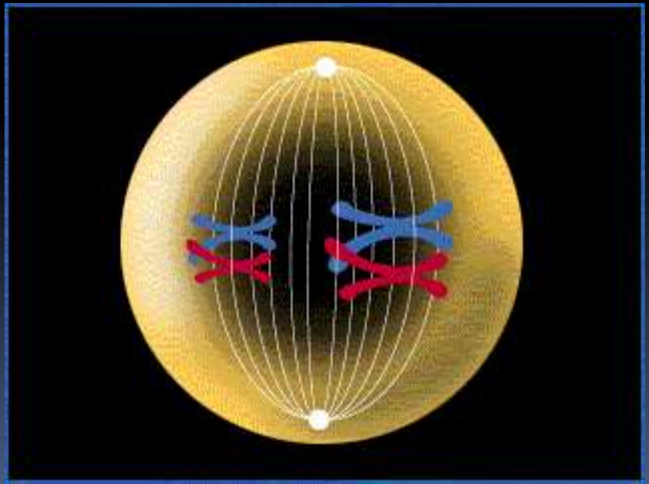
DIAKINESIS

- The final stage of meiotic prophase I.
- Marked by terminalisation of chiasmata
- Nucleolus and nuclear envelop disappear, freeing the chromosomes into the cytoplasm.
- Diakinesis represents transition to metaphase- 1

Prophase I

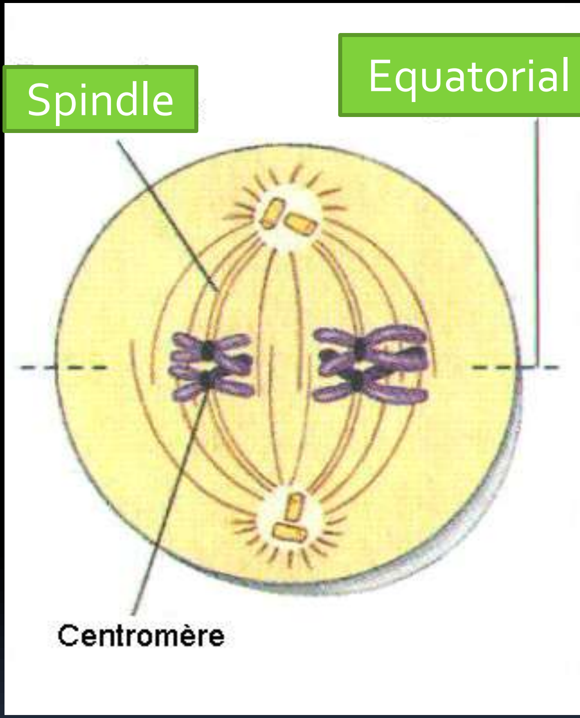






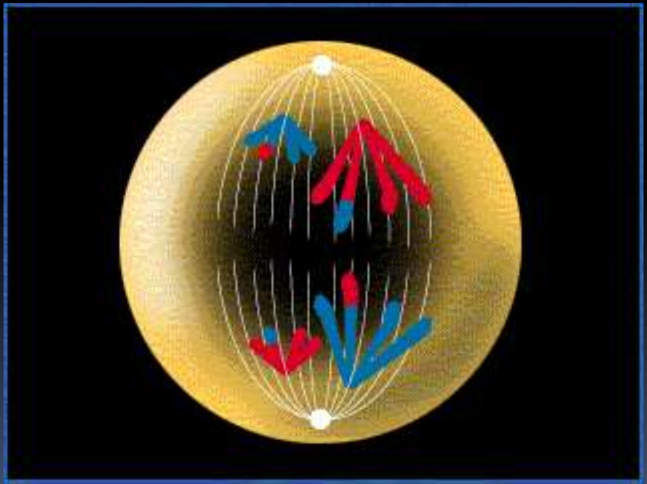
- ***METAPHASE 1-***

  Homologus chromosomes align as pairs on the equatorial plate of spindle apparatus.



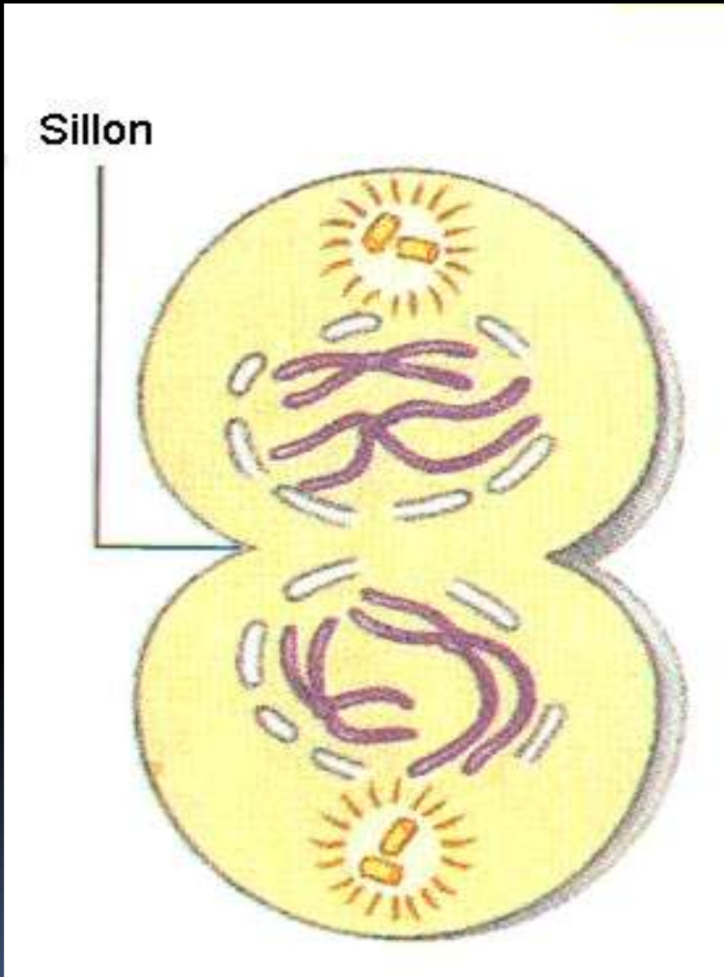
ANAPHASE 1-

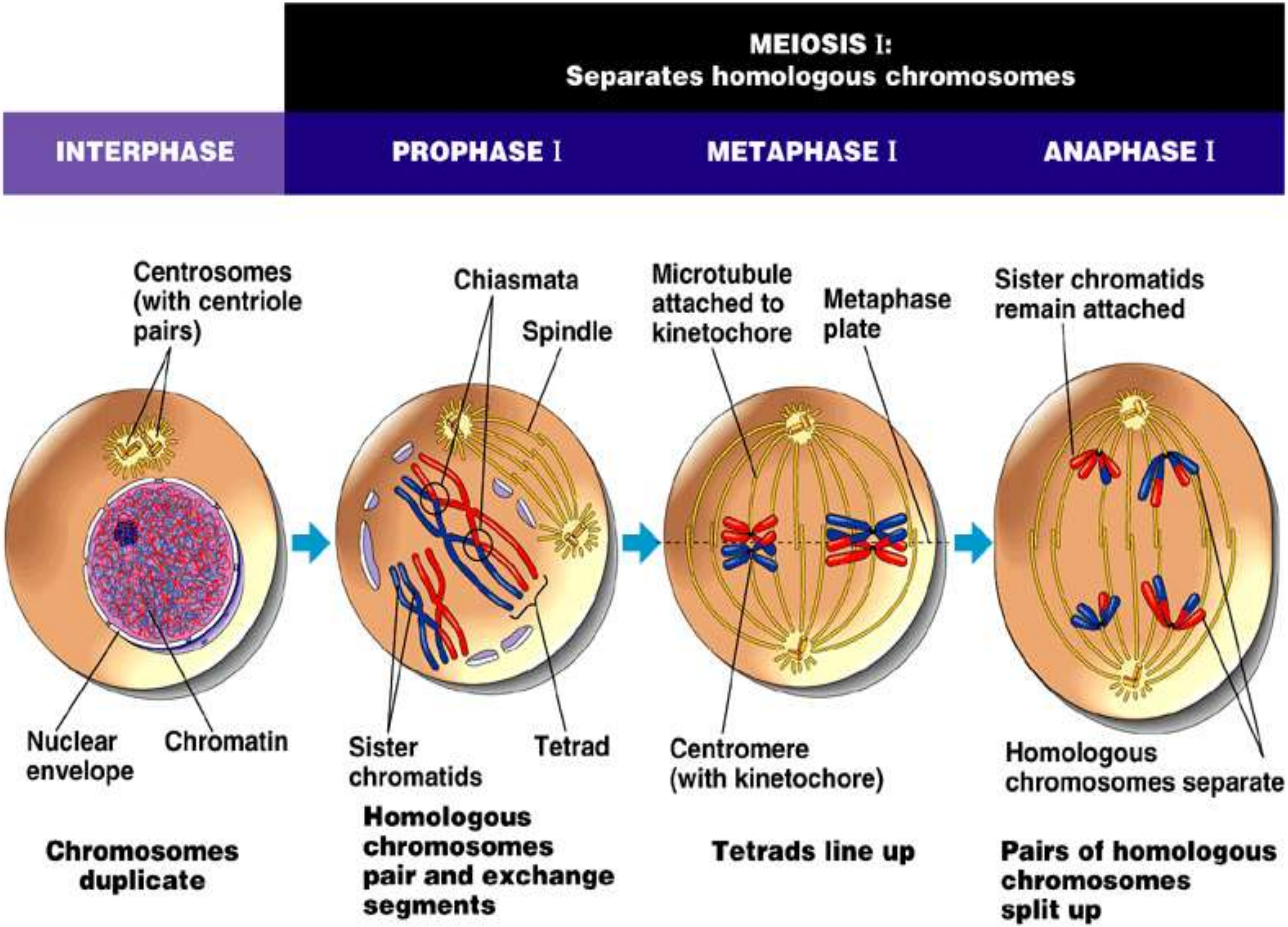
- *Homologous chromosomes migrate away from each other going to opposite poles.*
- Sister chromatids still remain associated at their centromeres



TELOPHASE 1-

- Nuclear membrane and nucleolus reappear .
- Nuclei are formed
- Cytokinesis occur giving rise to 2 daughter cells.

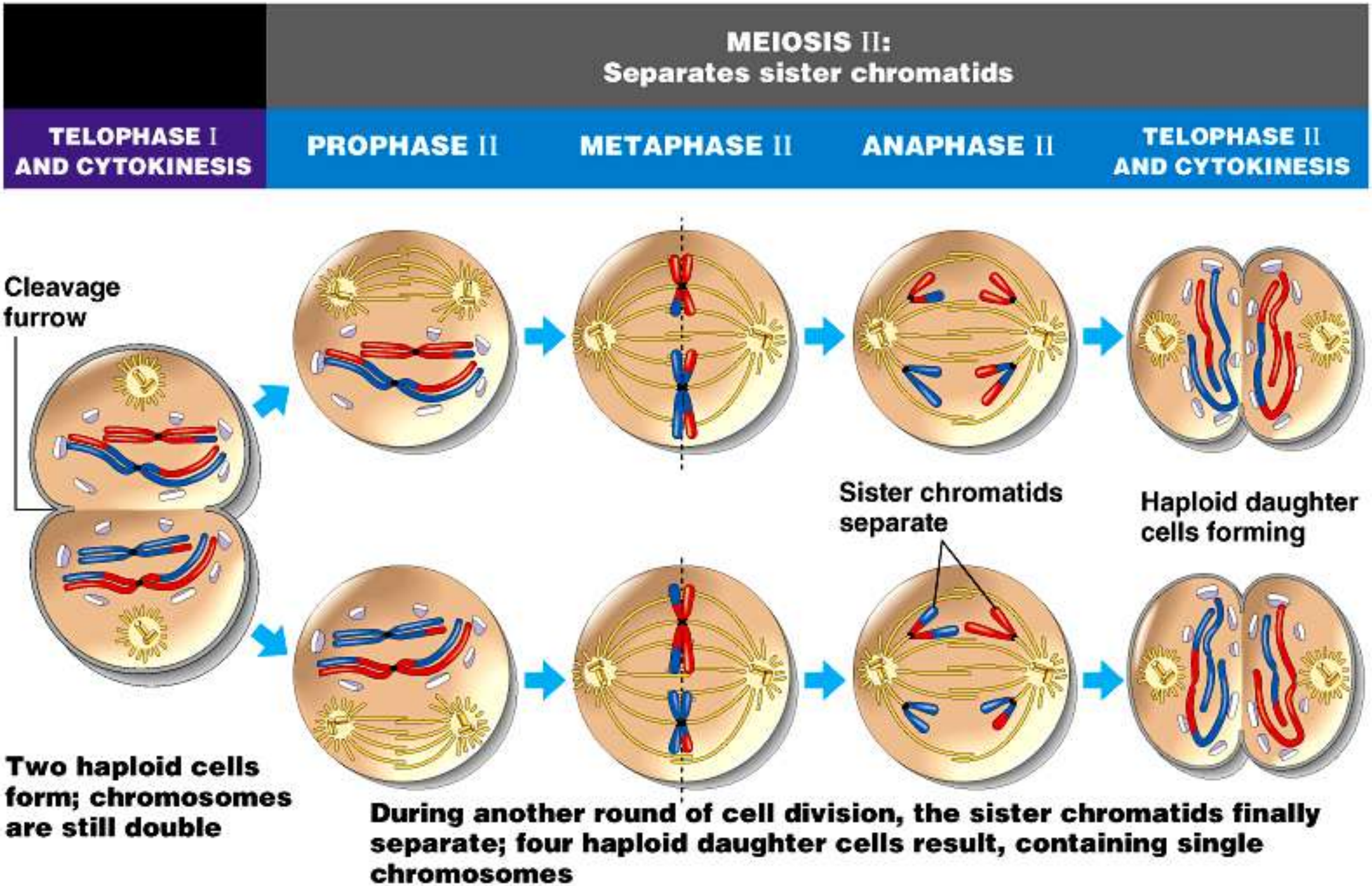



MEIOSIS I:
Separates homologous chromosomes
INTERPHASE
PROPHASE I
METAPHASE I
ANAPHASE I
Centrosomes (with centriole pairs)
Nuclear envelope
Chromatin
Chromosomes duplicate
Chiasmata
Spindle
Sister chromatids
Tetrad
Homologous chromosomes pair and exchange segments
Microtubule attached to kinetochore
Metaphase plate
Centromere (with kinetochore)
Tetrads line up
Sister chromatids remain attached
Homologous chromosomes separate
Pairs of homologous chromosomes split up

- The stage between the two meiotic divisions is called interkinesis and is generally short lived.

- Interkinesis is followed by prophase II, a much simpler prophase than prophase I.

gure 13.7 The stages of meiotic cell division: Meiosis II

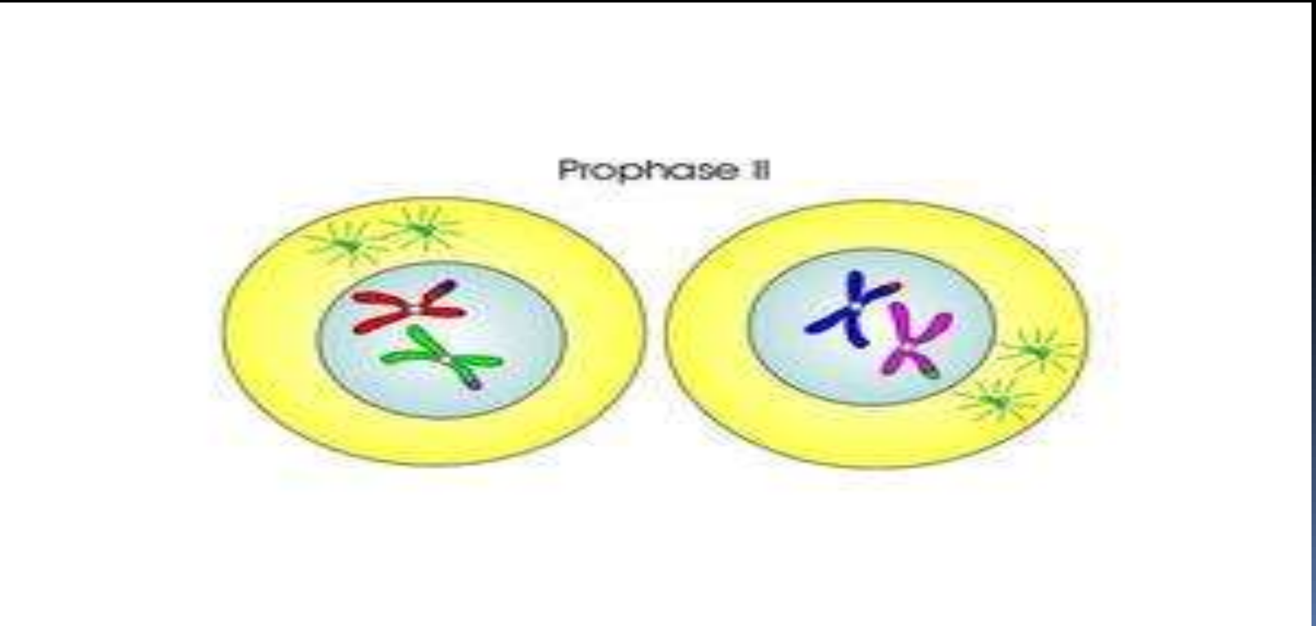


Meiosis II : Separates sister chromatids

- Proceeds similar to mitosis
- ***THERE IS NO INTERPHASE II !***

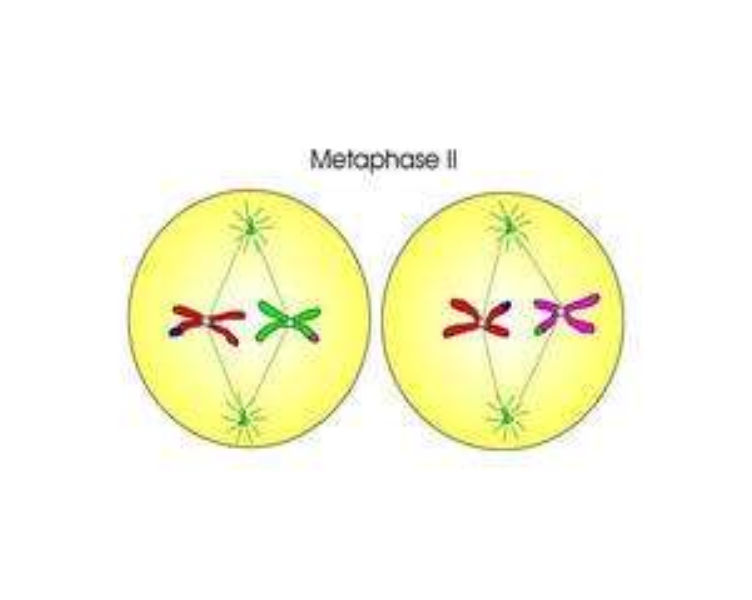
Prophase II

- A spindle apparatus starts forming
- The nuclear membrane disappears by the end of prophase II .
- The chromosomes again become compact.



Metaphase II

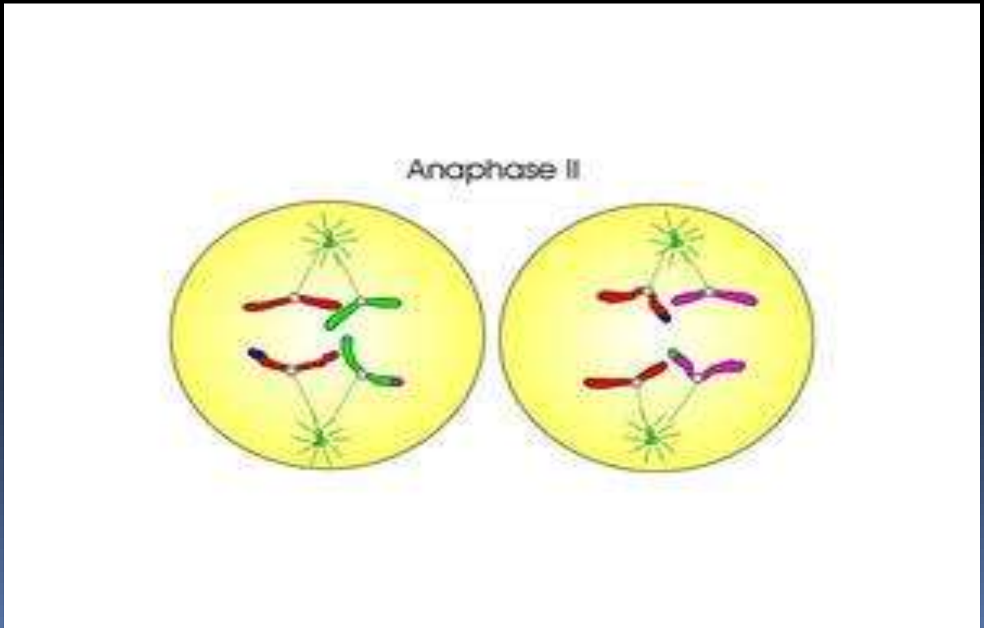
- The chromosomes are positioned on the metaphase plate in a mitosis-like fashion
- Kinetochores of sister chromatids of each chromosome pointing toward opposite poles



Anaphase II

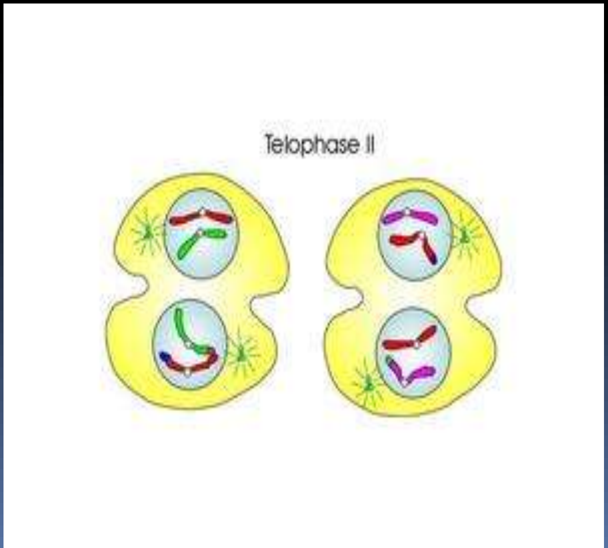
- The centromeres of sister chromatids finally separate
- The sister chromatids of each pair move toward opposite poles

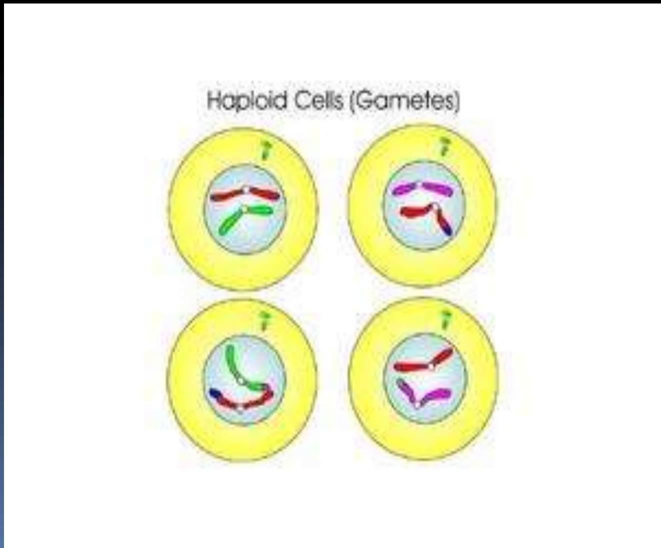
(Now individual chromosomes)



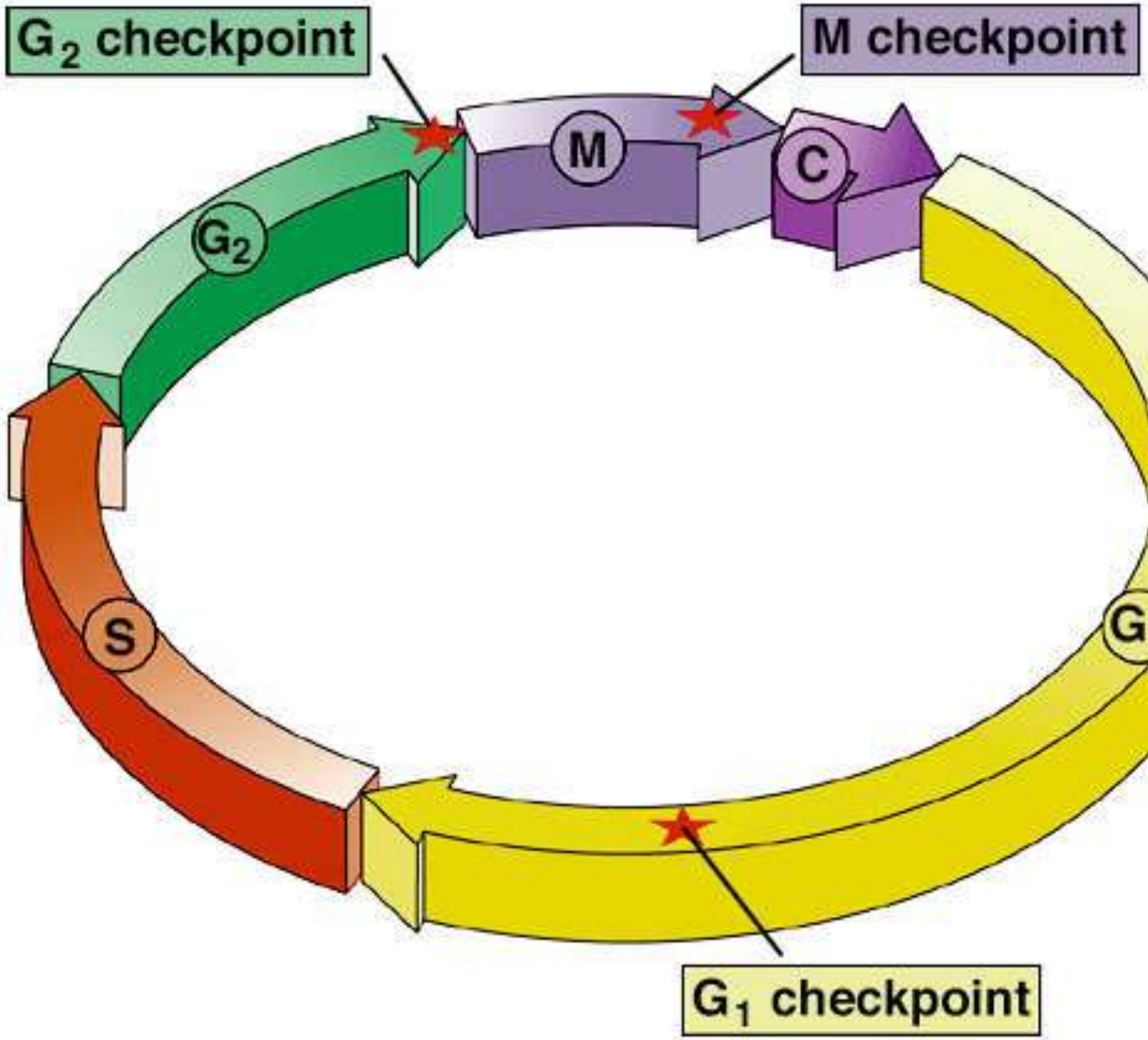
Telophase II and Cytokinesis

- Nuclear envelop forms around two groups of chromosomes once again .
- Cytokinesis follows resulting into four haploid daughter cells.





Cell Cycle Control



Cell cycle checkpoints

- They are used by the cell to monitor and regulate the progress of the cell cycle.

- Checkpoints prevent cell cycle progression at specific points, allowing verification of necessary phase processes and repair of DNA damage.

- The cell cannot proceed to the next phase until checkpoint requirements have been met.

Several checkpoints are designed to ensure that damaged or incomplete DNA is not passed on to daughter cells.

- Three main checkpoints exist:

1. G_1/S checkpoint . G_1/S transition is a rate-limiting step in the cell cycle and is also known as restriction point.

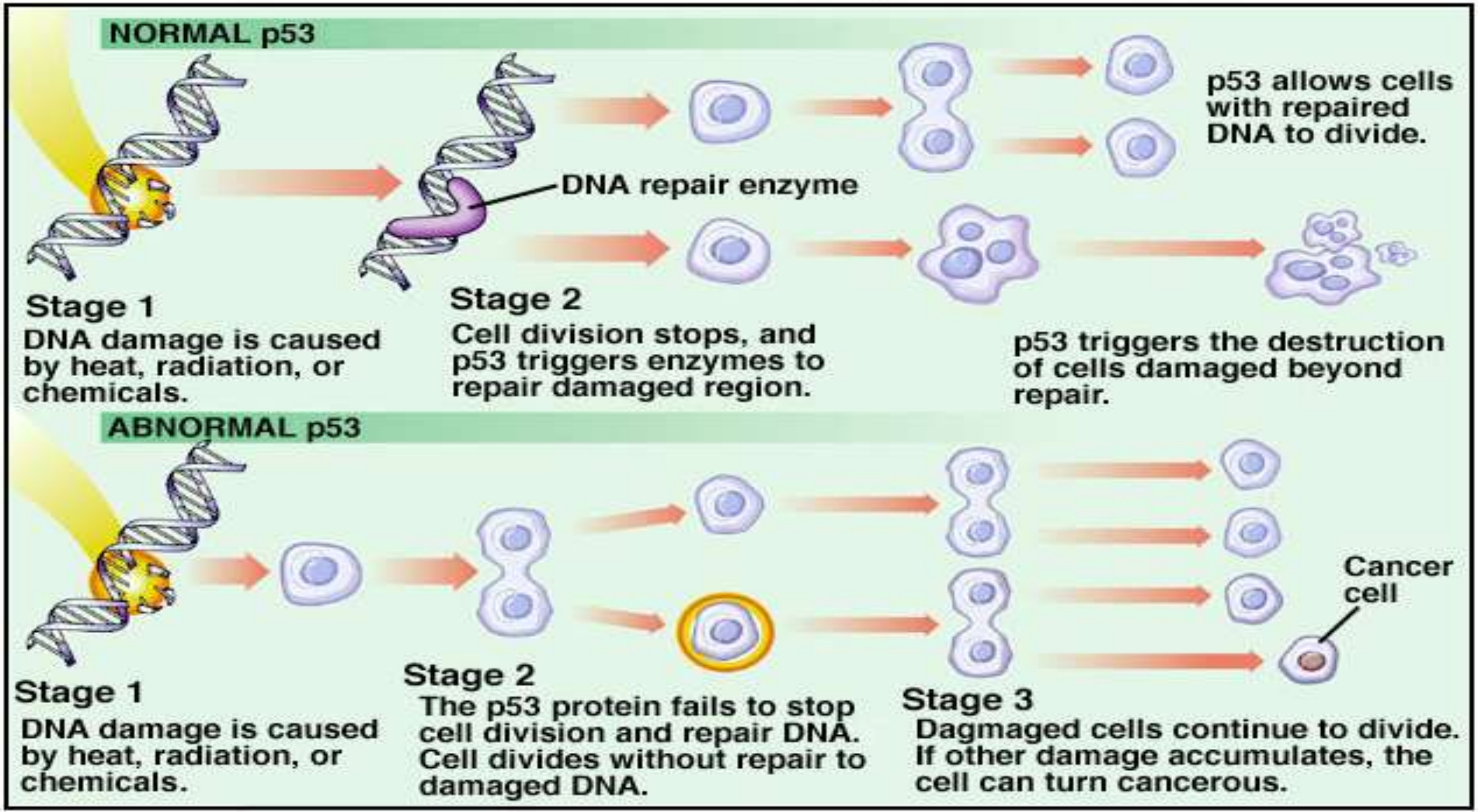
2. G_2/M checkpoint.

p53 plays an important role in triggering the control mechanisms at both G_1/S and G_2/M checkpoints.

3. Spindle assembly checkpoint, between metaphase and anaphase

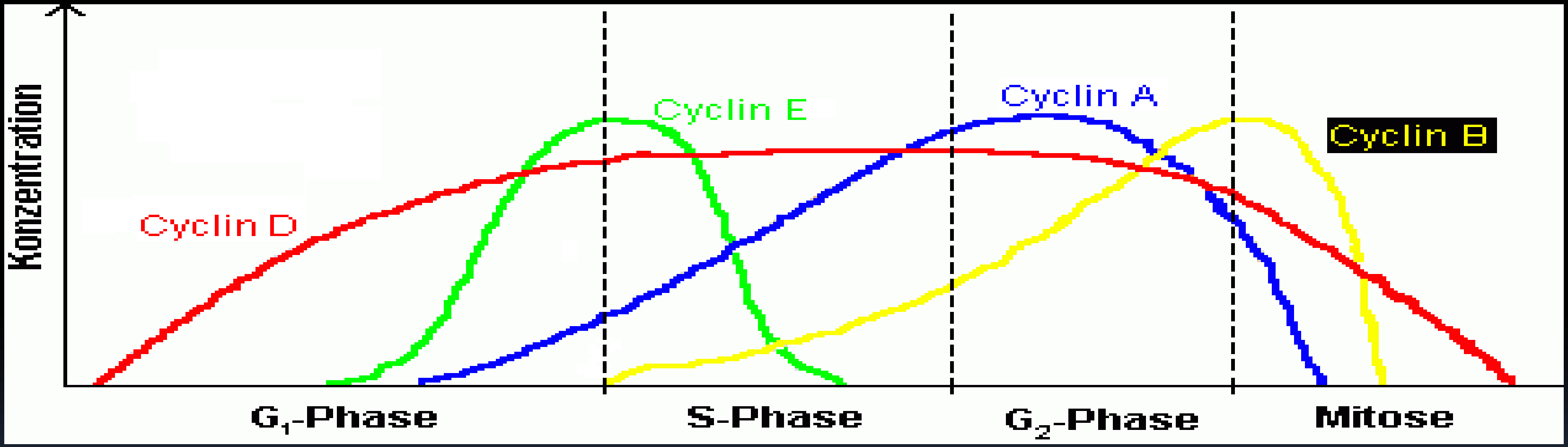
Cell cycle can be arrested if spindle fibers are not attached properly to chromatids

Cell Division and p53 Protein



Regulation of the Cell Cycle

- **Cyclin**: major control switch for the cell cycle
- **Cdk** (Cyclin-dependent kinase (*phospohorylation*)): major control switch; activated by cyclin; causes G1 → S or G2 → M.
- Cyclins form the regulatory subunit and Cdks the catalytic subunit



- Checkpoints
  - DNA damage checkpoints, including tumor suppressor genes
    - p53: protein that blocks the cell cycle if DNA is damaged and can cause apoptosis. A p53 mutation is the most frequent mutation leading to cancer.
  - Spindle checkpoints

Two families of proteins are involved in involved in the regulation process—
i) Cyclin-dependent protein kinases (Cdks)
ii) Cyclins.

a)Cyclin-Dependent Protein Kinase (Cdks)

❖A Cdks is an enzyme that adds negatively charged phosphate groups to other molecules in a process called phosphorylation.
❖Through phosphorylation, Cdks signal the cell that it is ready to pass into the next stage of the cell cycle.
❖Cyclin-Dependent Protein Kinases are dependent on cyclins & Cyclins bind to Cdks, activating the Cdks to phosphorylate other molecules.

b)Cyclins

➢Cyclins are named such because they undergo a constant cycle of synthesis and degradation during cell division.
➢When cyclins are synthesized, they act as an activating protein and bind to Cdks forming a cyclin-Cdk complex.
➢This complex then acts as a signal to the cell to pass to the next cell cycle phase.
➢Eventually, the cyclin degrades, deactivating the Cdk, thus signaling exit from a particular phase.

THANK YOU