Cell communication and Cell Cycle

Lecture – 8

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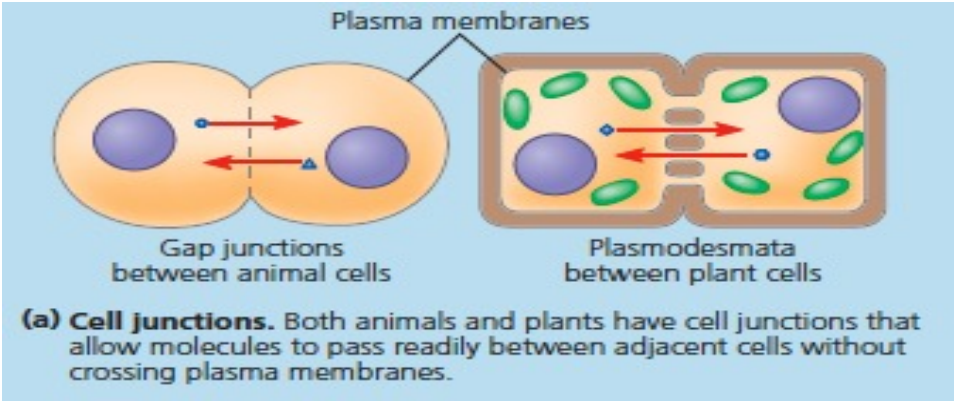
Outline

- Cell communication and signaling pathways
- Cell cycle – Mitosis and Meiosis
- Difference in normal vs. cancer cells

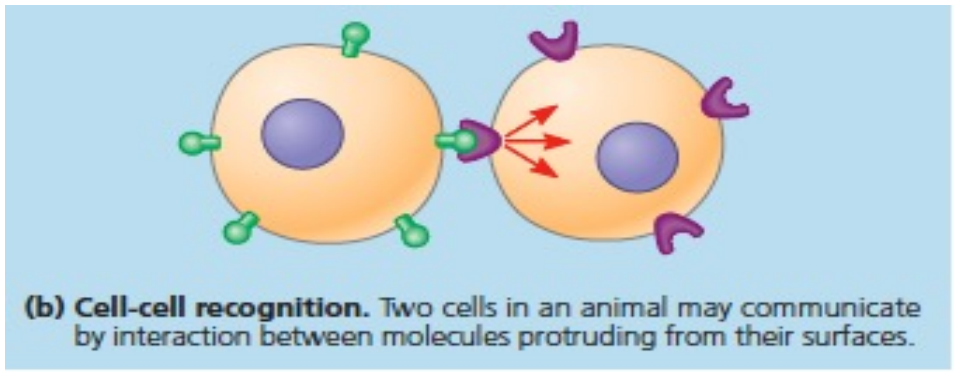
Why do Cells need to Communicate?

Multicellular organisms need communication to occur within & between the cells for different cellular processes

- Growth
- Cell division
- Differentiation
- Movement
- Metabolism
- Secretion
- Cell death (apoptosis)



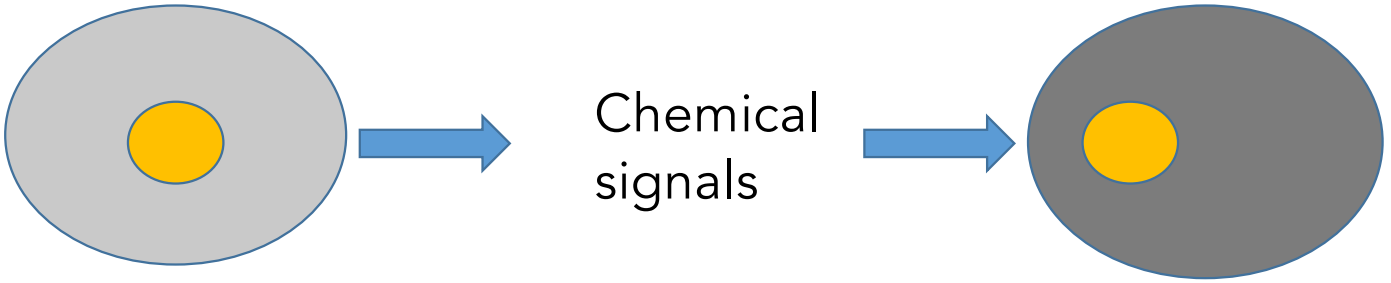
(a) Cell junctions. Both animals and plants have cell junctions that allow molecules to pass readily between adjacent cells without crossing plasma membranes.



(b) Cell-cell recognition. Two cells in an animal may communicate by interaction between molecules protruding from their surfaces.

How do Cells Communicate?

Cells use chemical signals for communication

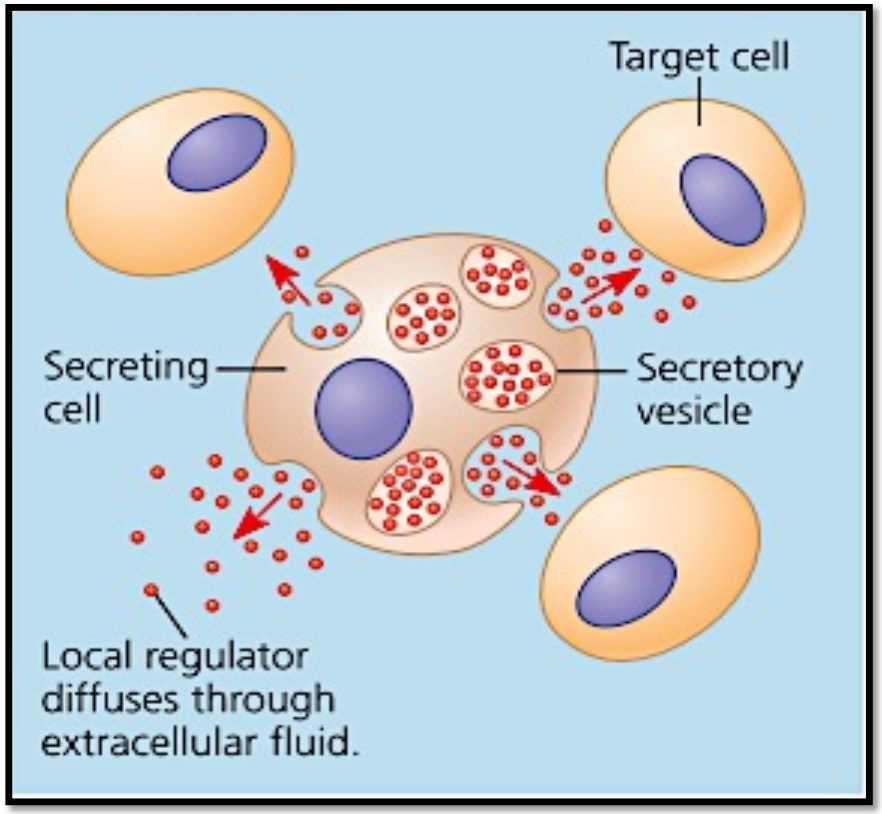


Talking cell or
Transmitting cell

Listening cell or
Target cell

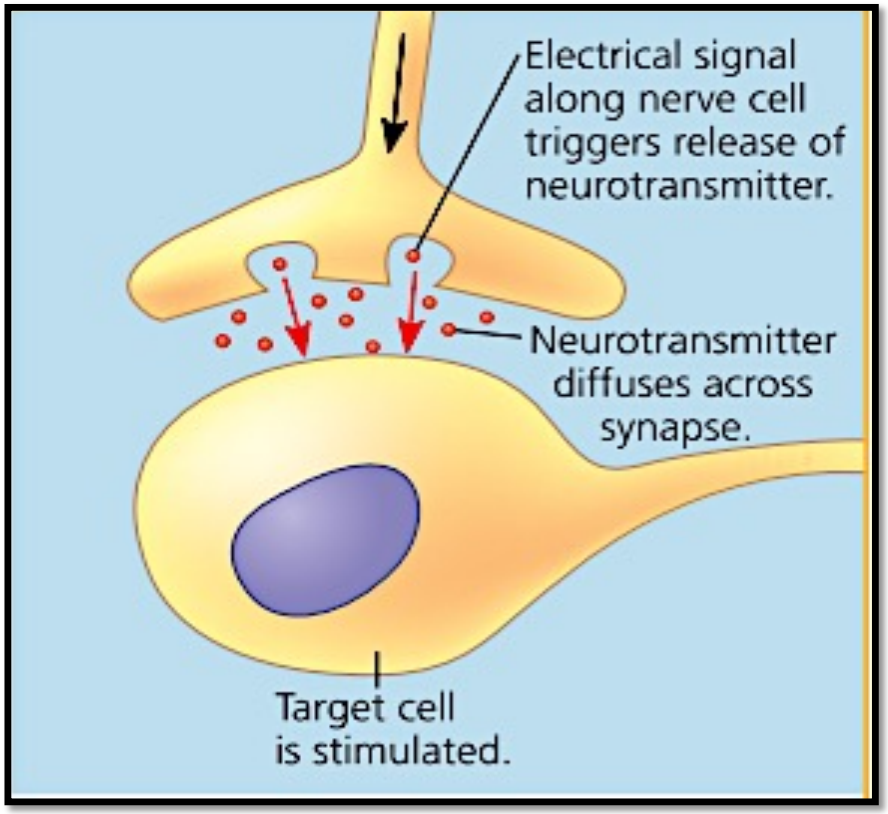
Signaling transduction pathway

Signaling Pathways: Local Signaling



Paracrine Signaling

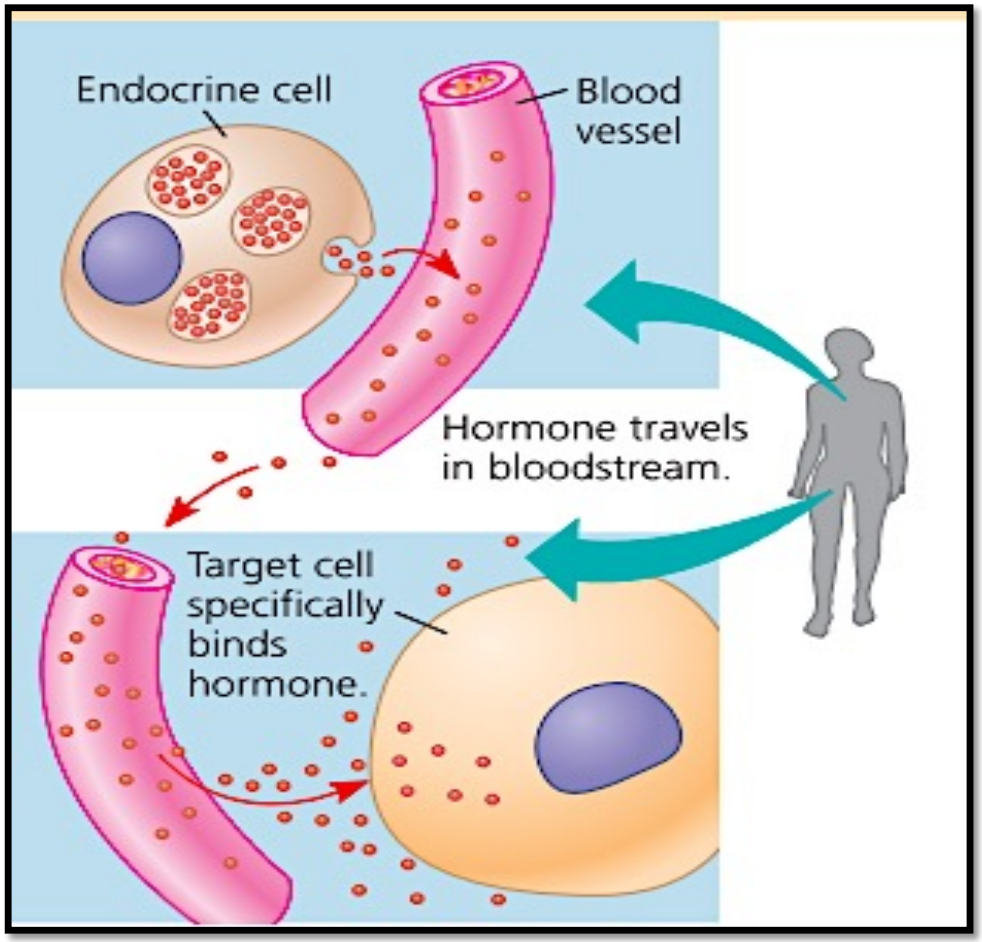
Growth factor



Synaptic Signaling

Neurotransmitter

Signaling Pathways: Long Distance Signaling



Endocrine/ Hormonal Signaling

Signal transduction

transduce: to convert energy or message into another form

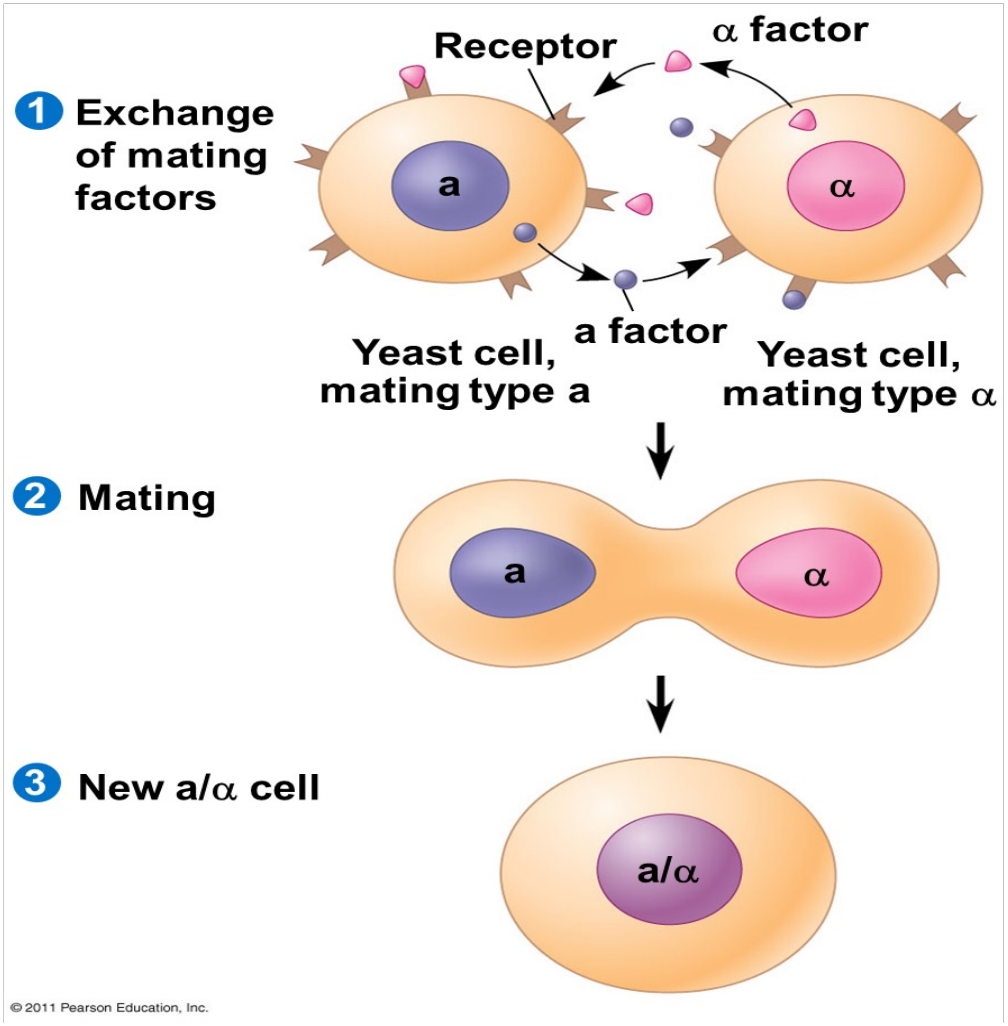
A chemical outside a cell…
triggers a response inside the cell

- Quorum sensing…
  illustrates the concept of cell-cell communication and intra-cellular signal transduction

- Communication among microbes…
  insight into cell communication in multicellular organisms

Eukaryotic cells also communicate

- Two different types of yeast cells can signal to each other when they decide to mate



Signal transduction: three stages

- The cell is compartmentalized
- External signals need to reach the nucleus

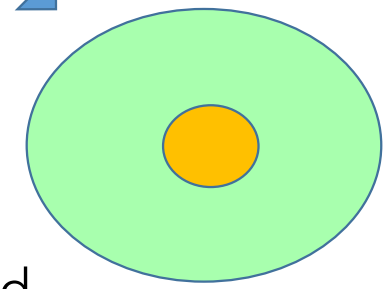
Reception

A knock on the door

Transduction

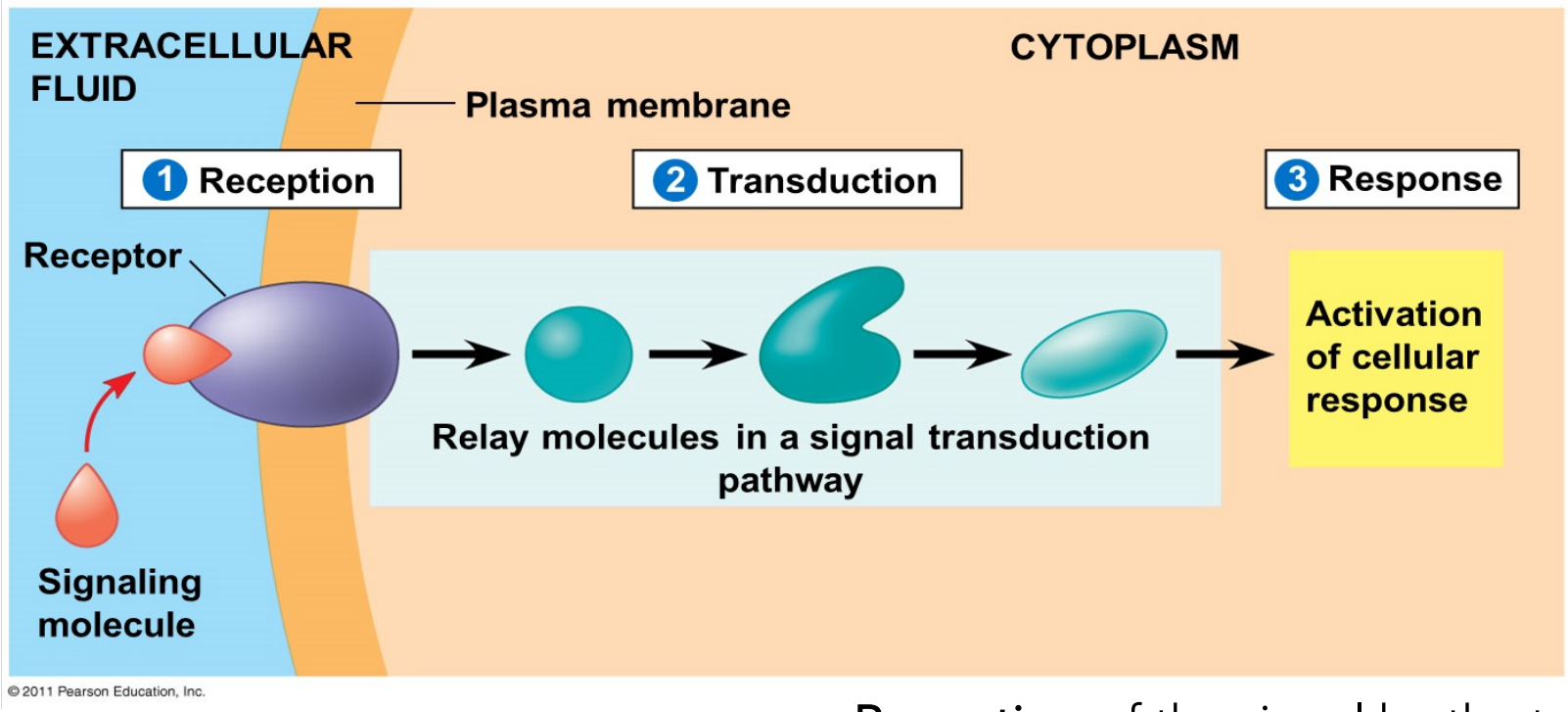
message received at the door

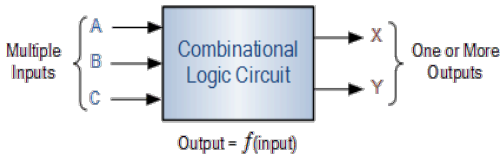
Response

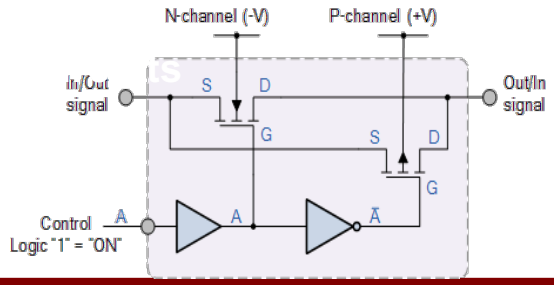


message conveyed to the inside… and an action is triggered

Three Stages of Cell Signaling







- **Reception** of the signal by the target cell
- **Transduction** of the signal within the cell
- **Response** generation by the cell

Signal transduction: 1. Reception

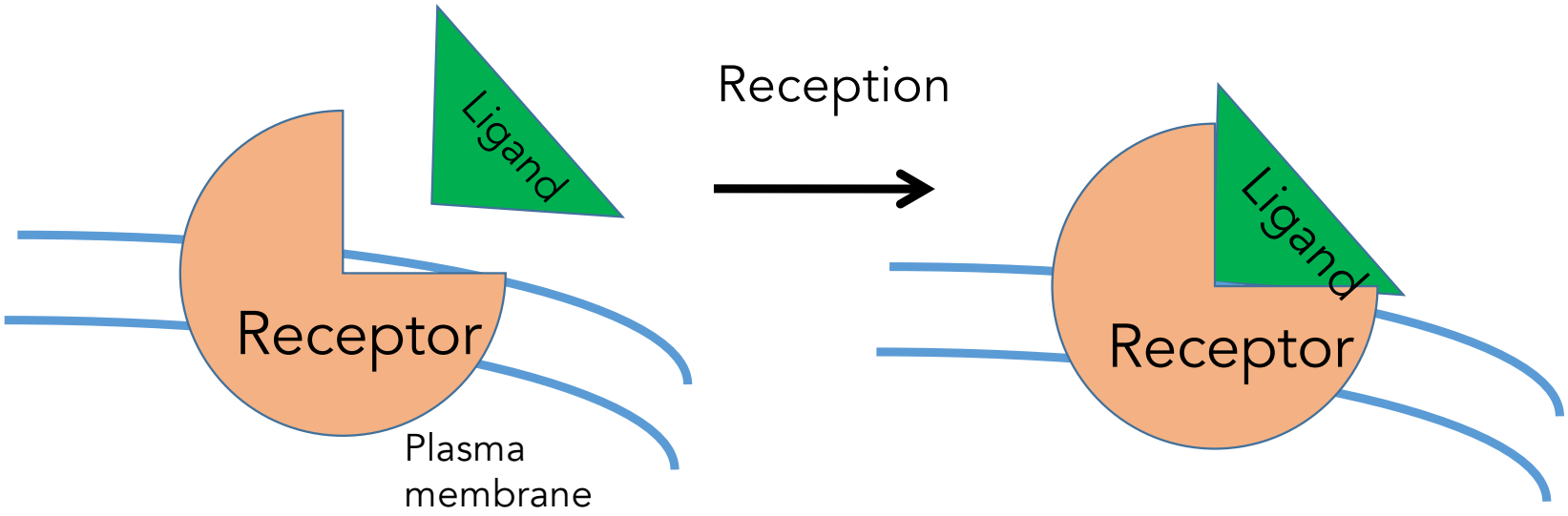
- A signaling molecule binds to a cell surface receptor
- Receptor is on the target cell

Figure 11.6

Cell Signaling – Reception

Reception | Transduction | Response

Reception occurs when the chemical signaling molecule binds to the receptor present in a plasma membrane



Receptors involved in Cell Signaling

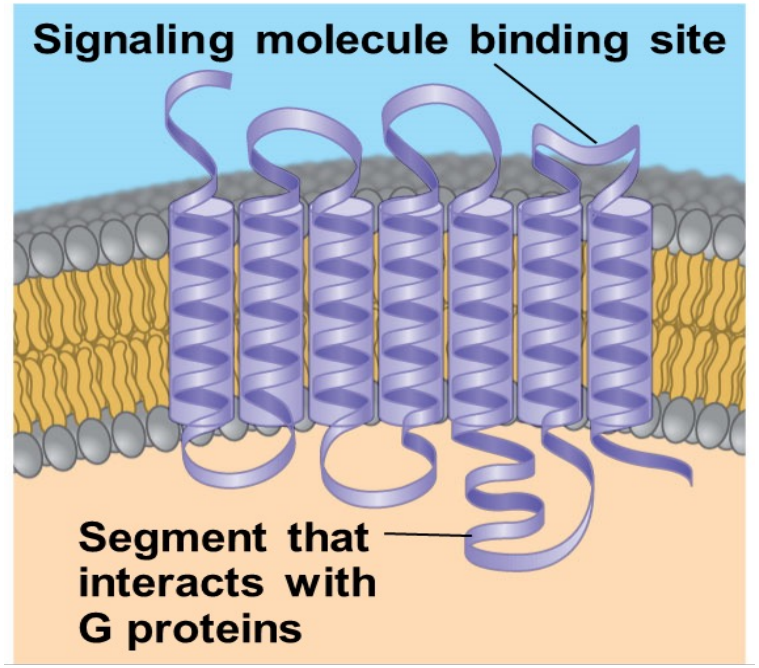
- Membrane associated receptors involved in cell signaling

  1. G protein-Coupled Receptors
  2. Tyrosine Kinases Receptors
  3. Intracellular Receptors
  4. Ion Channel Receptors

Cell Signaling – Reception

Reception | Transduction | Response

(1) G-Protein-Coupled Receptor (GPCRs)

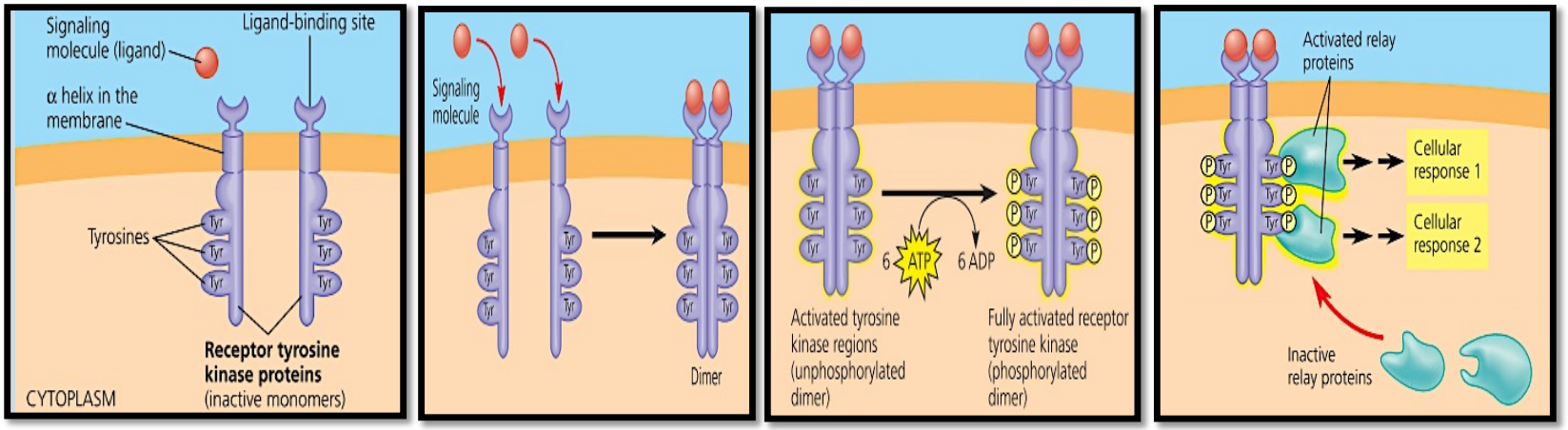


- Largest family of cell-surface receptors
- GPCR is a plasma membrane receptor that works with help of a **G protein**
- G protein (a protein that binds energy-rich molecule GTP) acts as an on/off switch: If GDP is bound to the G protein, the G protein is inactive
- G protein systems are involved in many human diseases

Cell Signaling – Reception

Reception | Transduction | Response

(2) Tyrosine Kinase Receptors



- Receptors are transmembrane protein, exist as monomers before ligand binding
- Each receptor monomer has a binding site for ligand & tyrosine kinase region

- Dimerization of receptors occurs after ligand binding

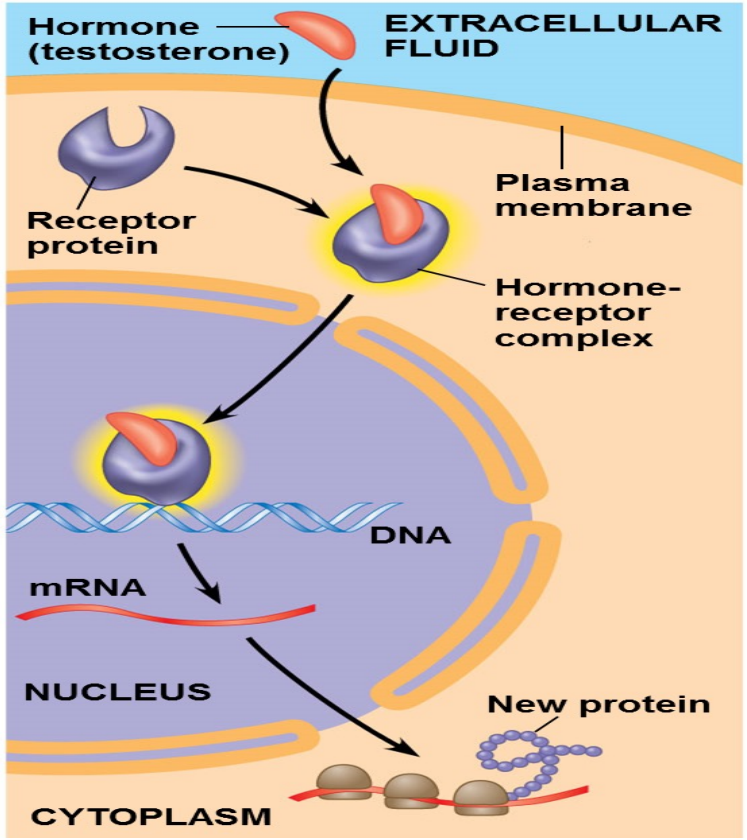
- Activation of tyrosine kinase region after dimerization leads to phosphorylation of tyrosines of the other monomer

- Fully activated receptors are recognized by relay proteins that transduce the signal resulting in respective cell response

Cell Signaling – Reception

Reception | Transduction | Response

(3) Intracellular receptors

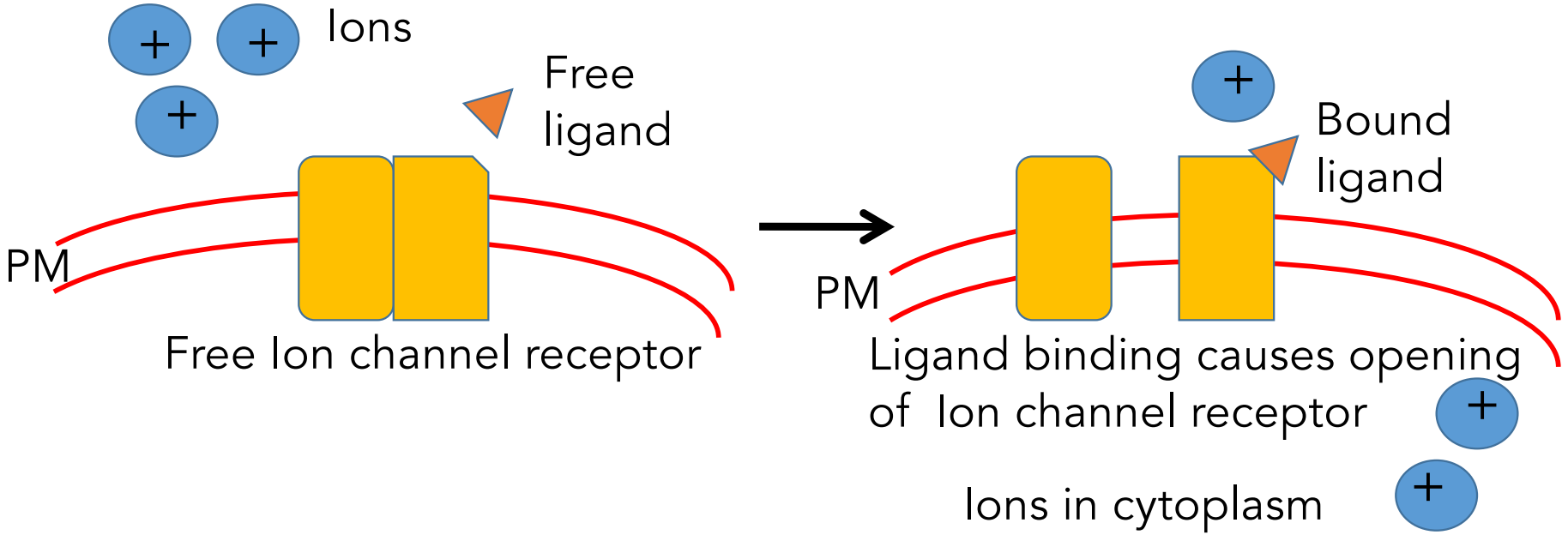


- *Ligand* in extracellular fluid; *receptors* present in cytoplasm
- Plasma membrane permeable ligands like steroids bind to these receptors
- Ligand receptor complex enters the nucleus and binds to specific gene
- Receptor ligand complex acts as transcription factor and causes expression of that gene

Cell Signaling – Reception

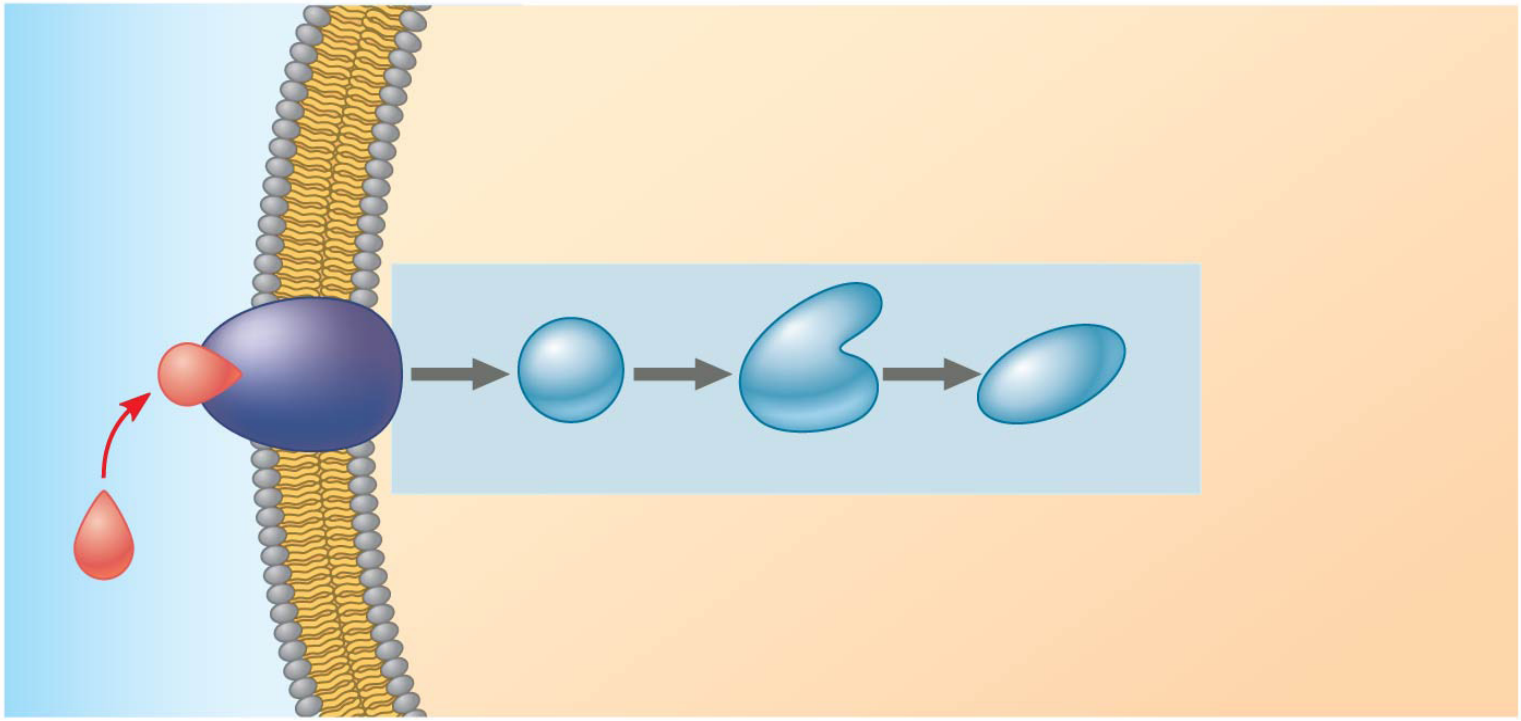
Reception | Transduction | Response

(4) Ion Channel Receptors



These receptors act as *channels for specific ions*, which open on ligand binding and close in absence of ligand

Signal transduction: 2. Transduction



- Binding leads to a change in the shape of the receptor
- Shape change leads to a cellular response
- Can be in one step; often, in multiple steps and involves relay molecules

Cell Signaling – Transduction

Reception | Transduction | Response

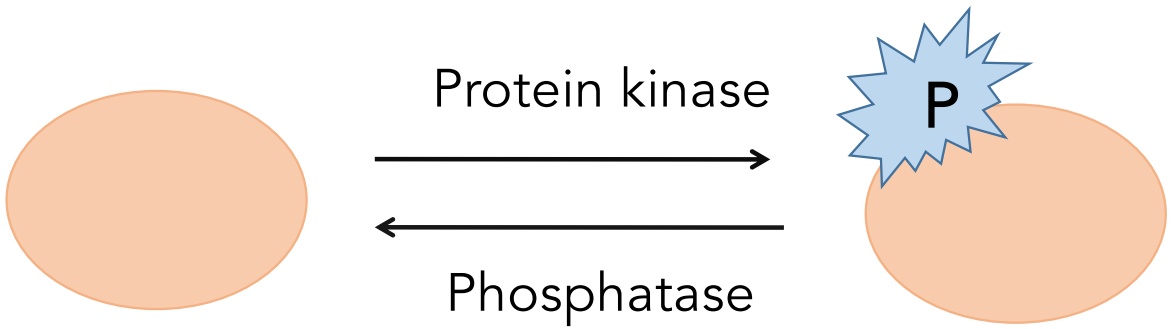
- Relay of signal from receptor molecule through a cascade of molecular interactions to the target molecules in cell, involves multiple steps:
  - Signal amplification
  - Coordination and regulation of cellular response
- Relay of information is carried by interactions between different proteins which constitute a signaling pathway

Protein Kinases and Phosphatases:
Major relay Molecules

Reception | Transduction | Response

Protein Kinases: transfer phosphate group from ATP to substrate protein

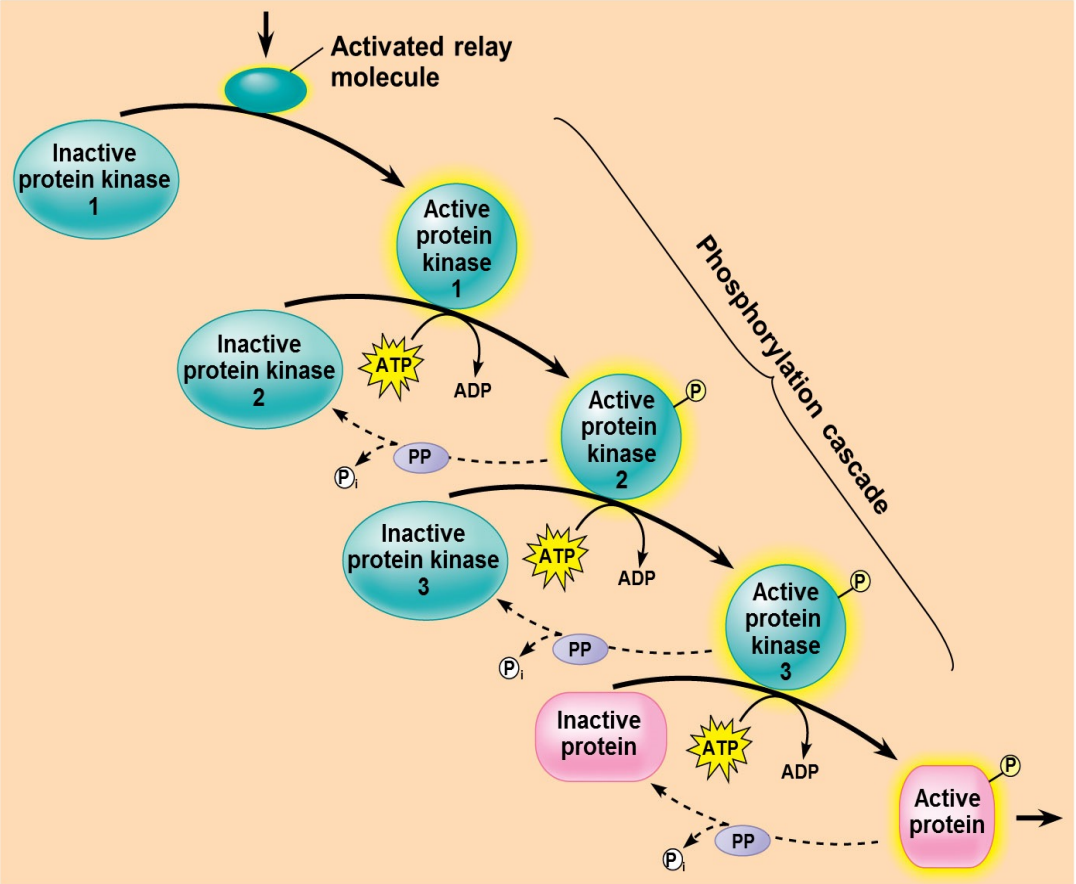
Phosphatases: remove phosphate from phosphorylated proteins



Phosphorylation Acting as a Signal

Reception | Transduction | Response

- Series of different molecules in a pathway are *phosphorylated*, in turn, each molecule adds a phosphate group to next one in line
- *Dephosphorylation* returns it to its inactive form
- Activation is usually associated with a *change in molecular shape*



Second Messengers

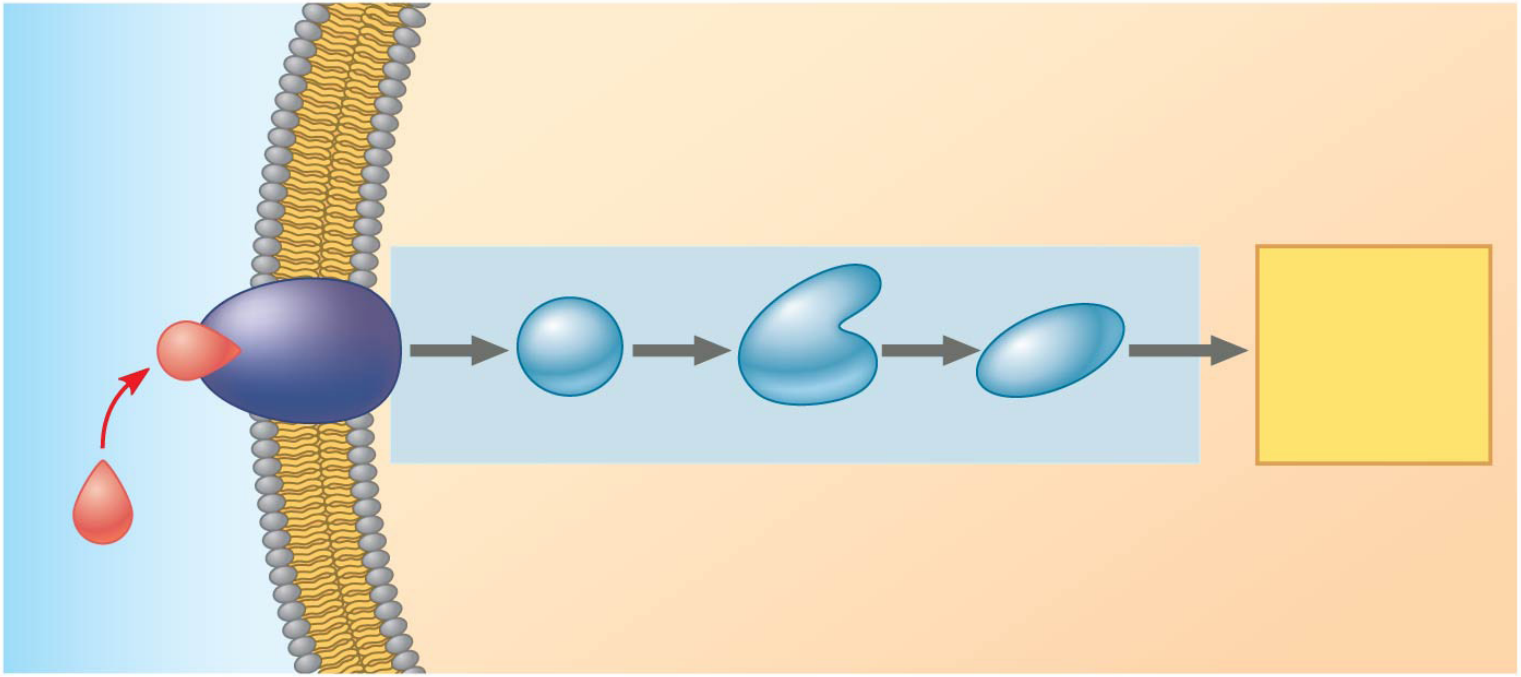
Reception | Transduction | Response

- Non-protein, water soluble small molecules or ions as members of signaling pathways (e.g. Cyclic AMP, Calcium ions and Inositol Triphosphate)

- Concentration of these molecules change after the activation of the membrane receptors by the first messenger (Ligand)

- Change in their concentration allows further relay of the signal in the cytoplasm and finally to the target molecule

Signal transduction: 3. Response



Response can be of different types:

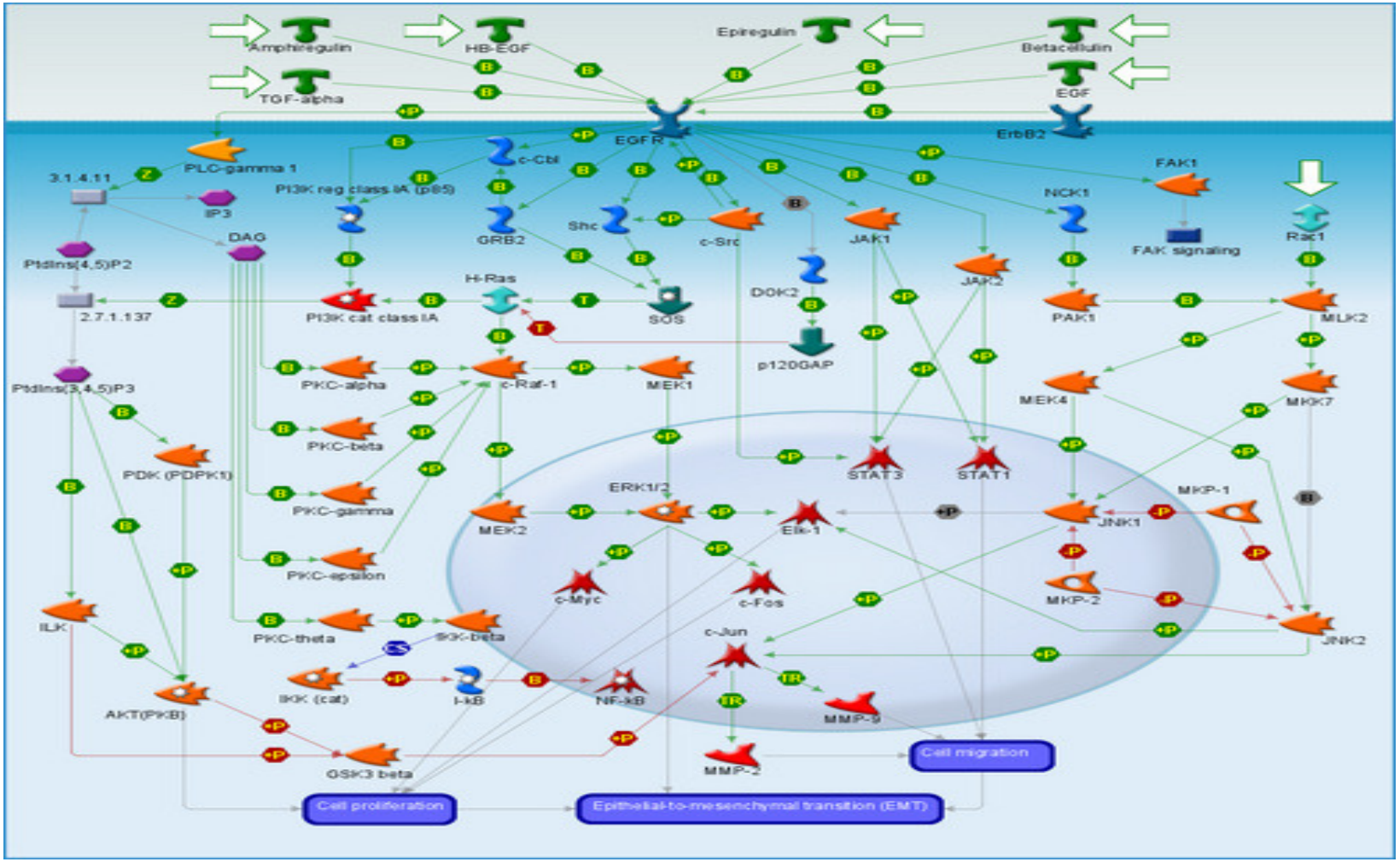
1. Catalysis of a reaction by an enzyme
2. Rearrangement of the cytoskeleton
3. Activation of specific genes (gene expression)
4. Many others….

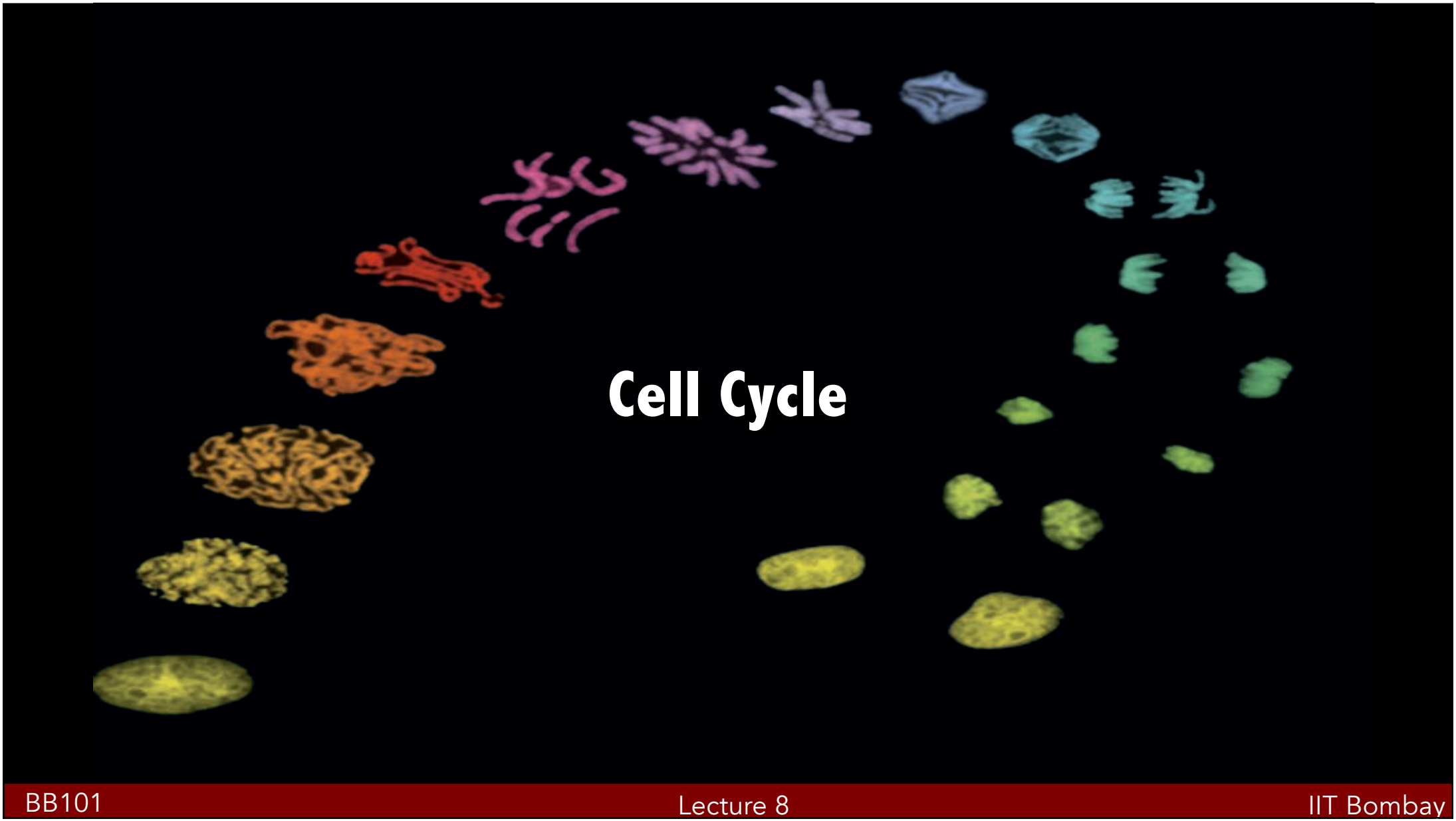
Second Messengers

Reception | Transduction | Response

- Once the signal reaches the target molecule the cell responds accordingly by different mechanisms:
  - Increase or decrease in expression of genes
  - Transportation of proteins to required location
  - Degradation of proteins

Epidermal growth factor receptor (EGFR) Signaling Pathway




Cell Cycle

Role of Cell Division

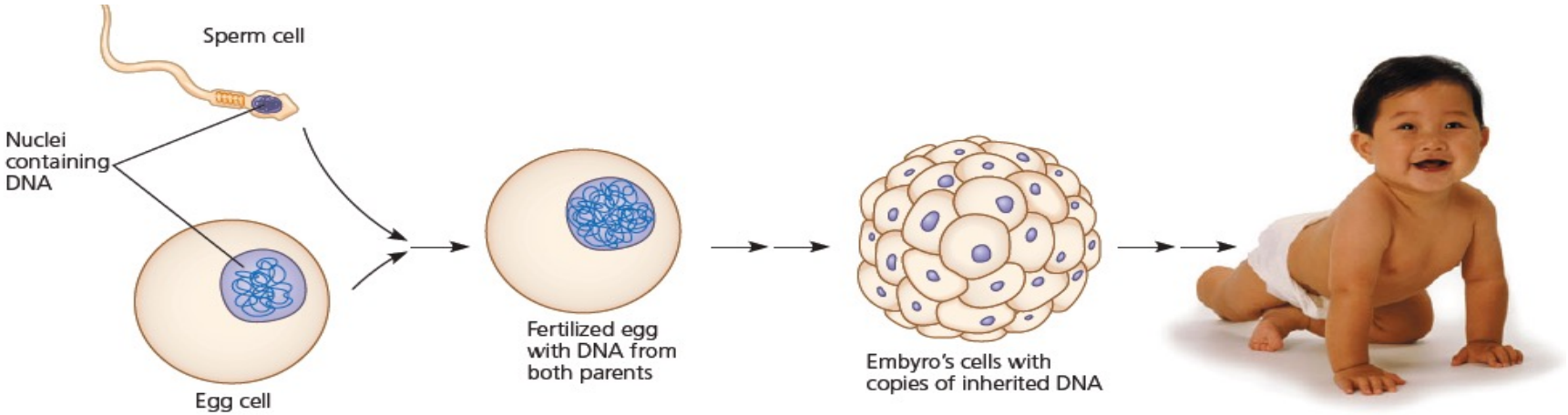


Figure 1.6

Life begins from a Single Cell: Continues with Regulated Cell Division

- Cell division distributes DNA (chromosomes) of a mother cell equally between two daughter cells thereby allowing a cell to proliferate
- Cell proliferation is essential for growth, repair & reproduction

The Cell Cycle

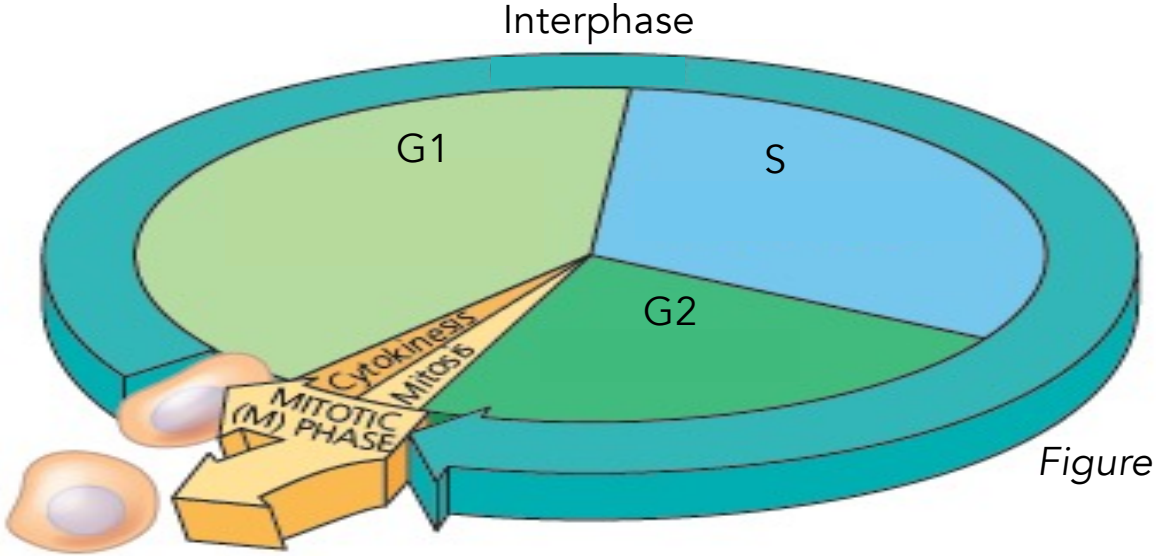
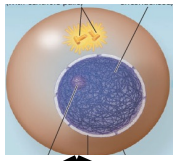


Figure 12.6

- Mitotic (M) phase alternates with interphase (growth period)
- **G1 phase** – first part of interphase
- **S phase** - chromosomes duplicate
- **G2 phase** - last part of interphase
- **M phase** - mitosis distributes chromosomes to daughter nuclei
- **Cytokinesis** - divides cytoplasm and produces two daughter cells

The Cell Cycle



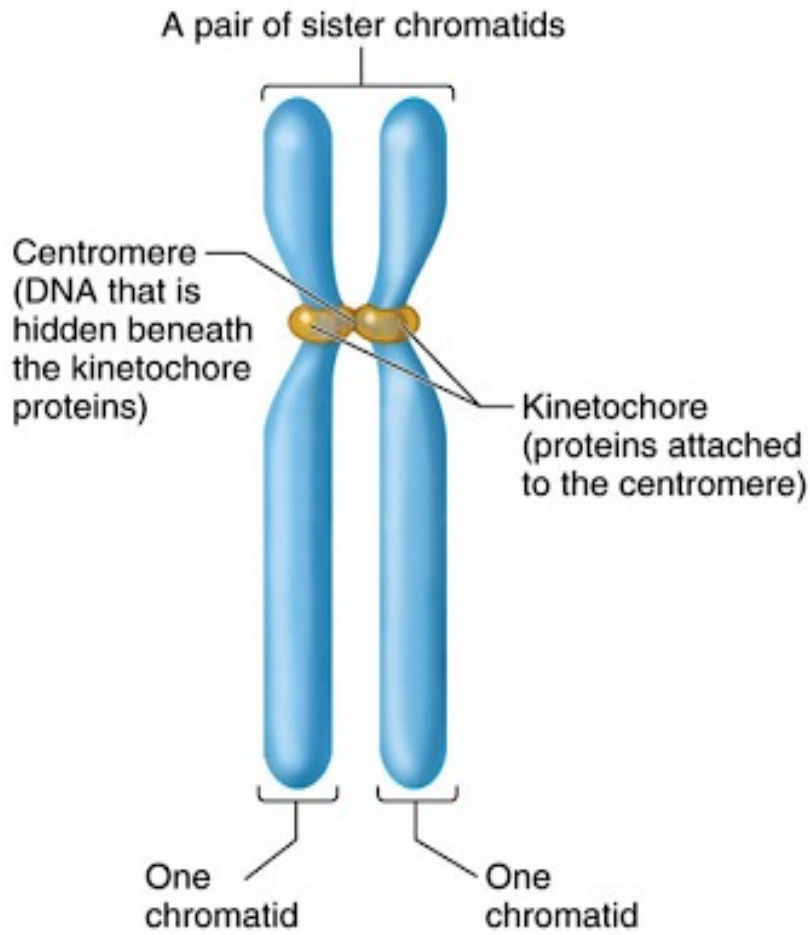
Mitosis

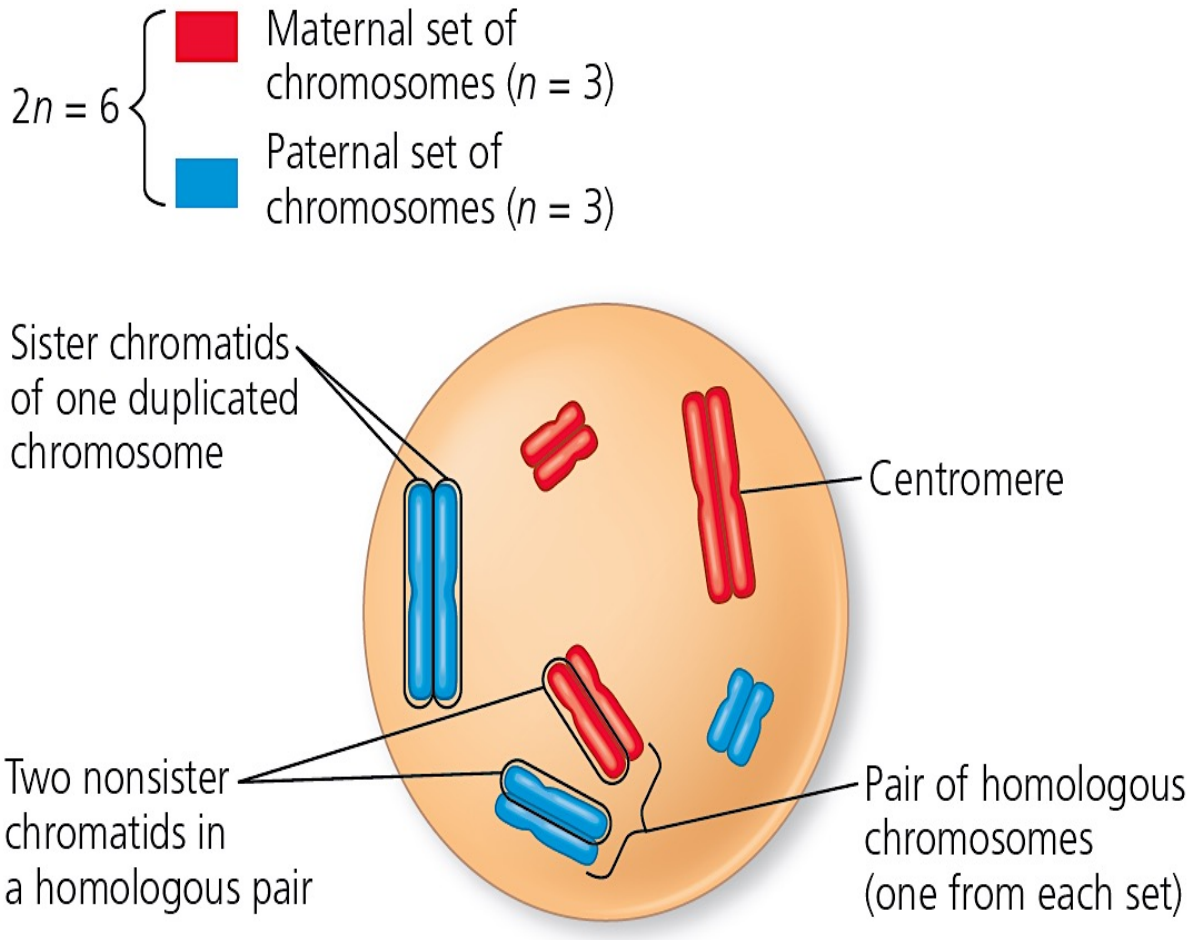
Meiosis

- Division of somatic cells
- Two daughter cells are produced with *same amount of DNA* as mother cell

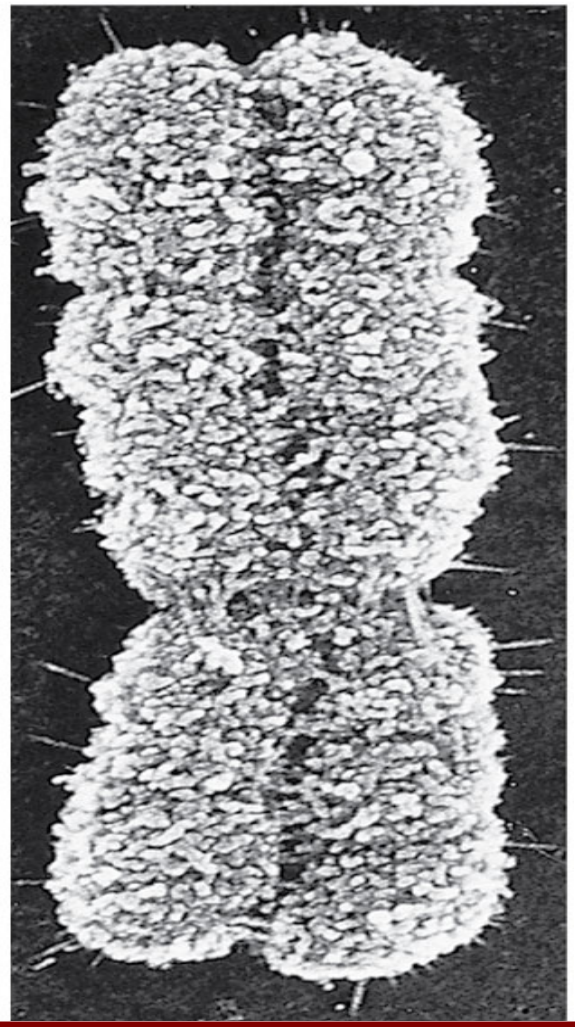
- Division of gamete cells (Sperm and ovum)
- Four daughter cells are produced with *half the amount of DNA* as mother cell

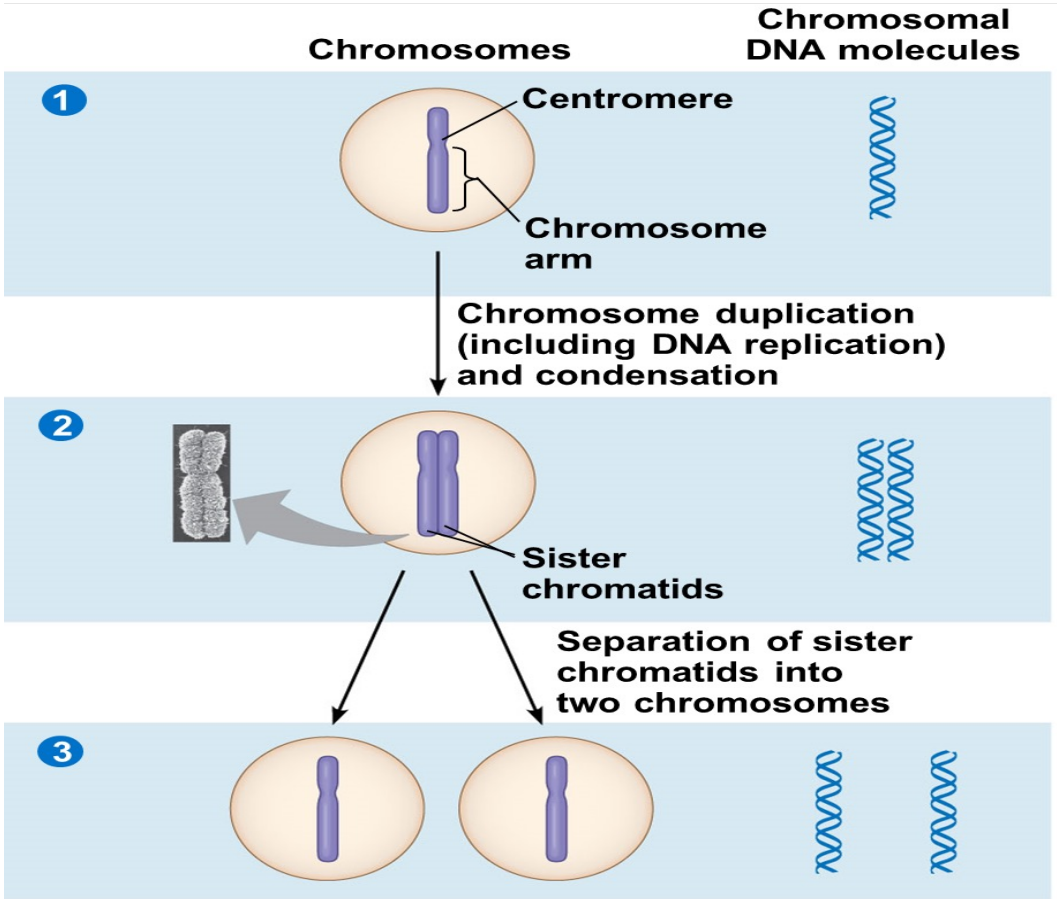
Basics & terminologies





Distribution of Chromosomes in Eukaryotic Cell Division

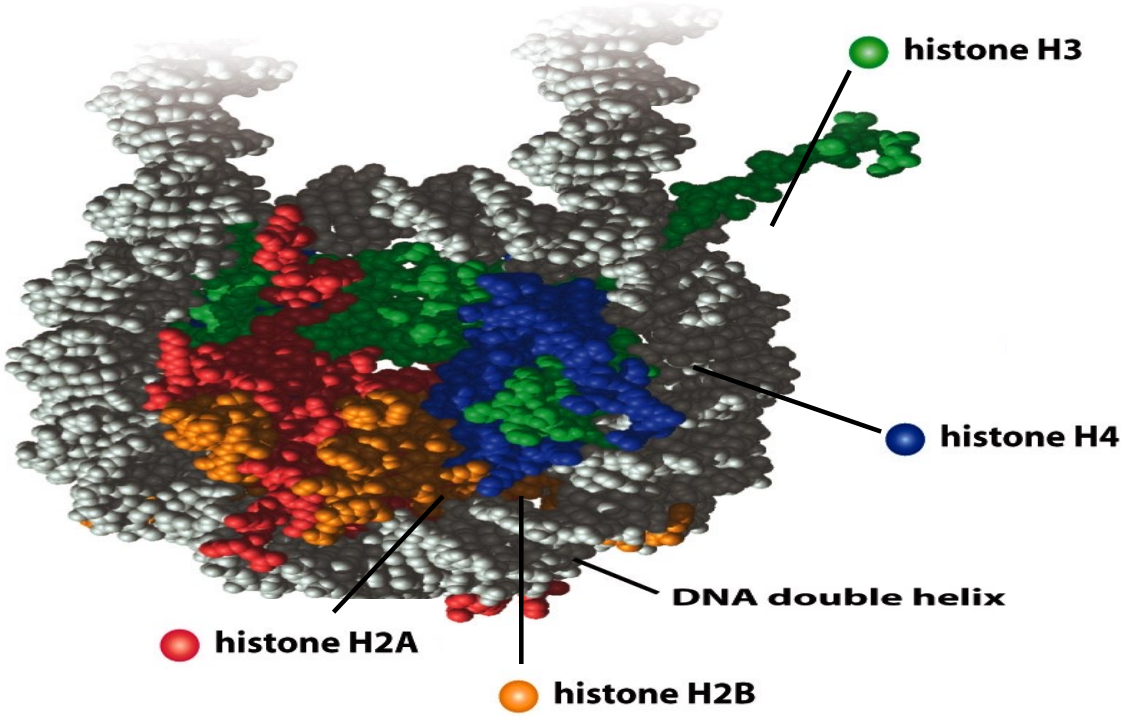


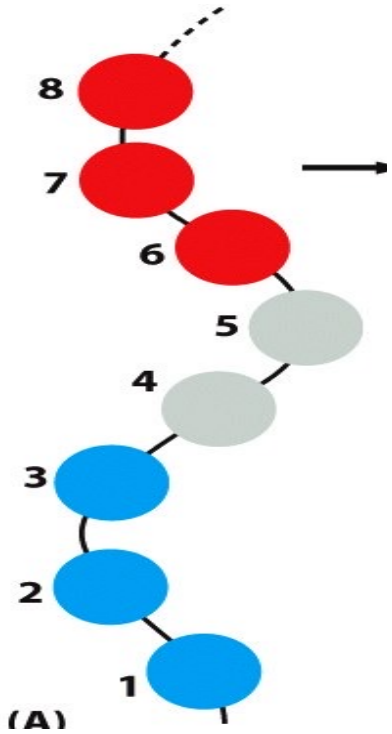


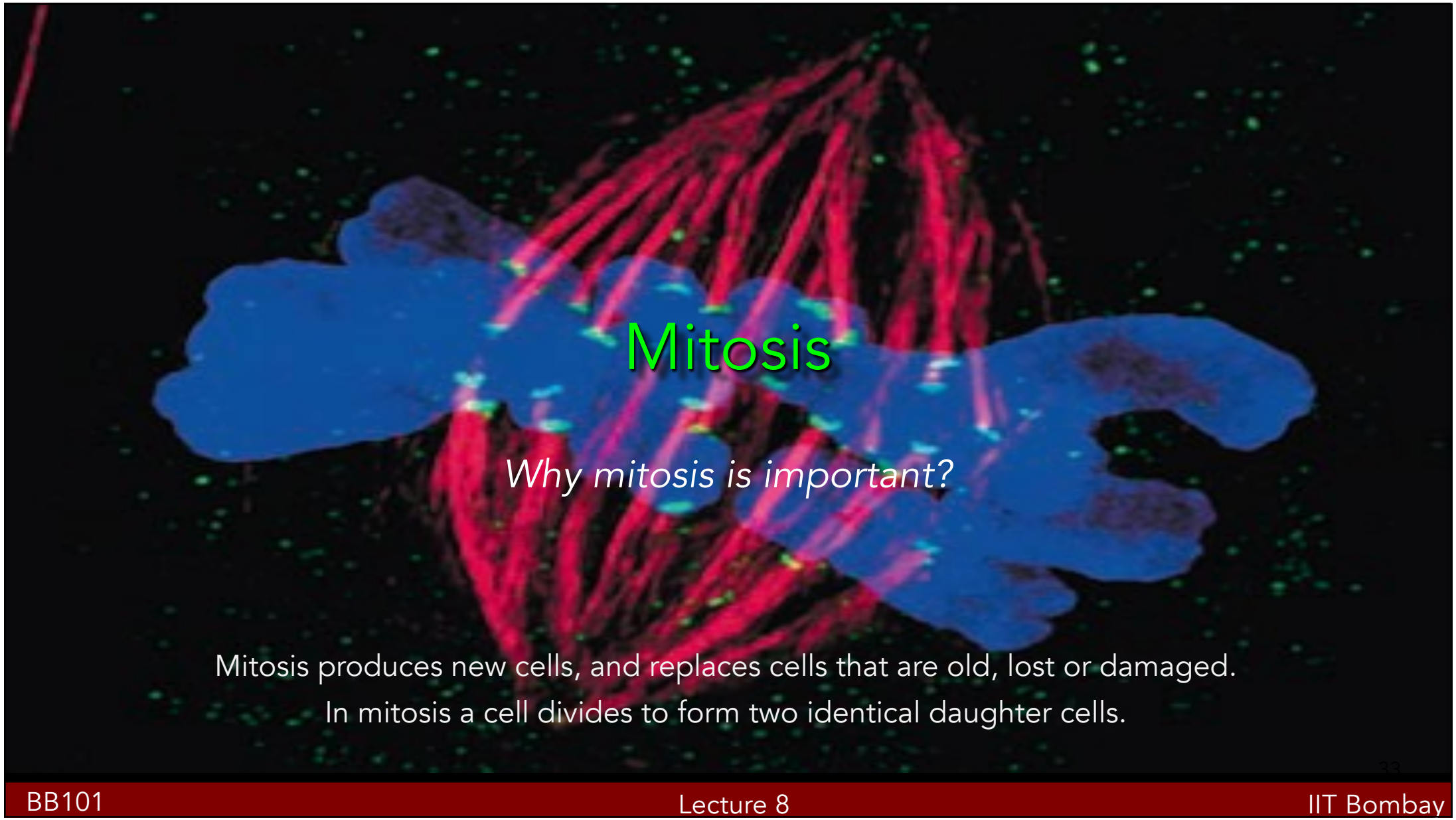
Duplication of chromosome and separation of sister chromatids

DNA is tightly packed in nucleus of every cell

- 8 separate histone proteins attach to the DNA molecule and form nucleosome
- Fiber of packed nucleosome is known as chromatin







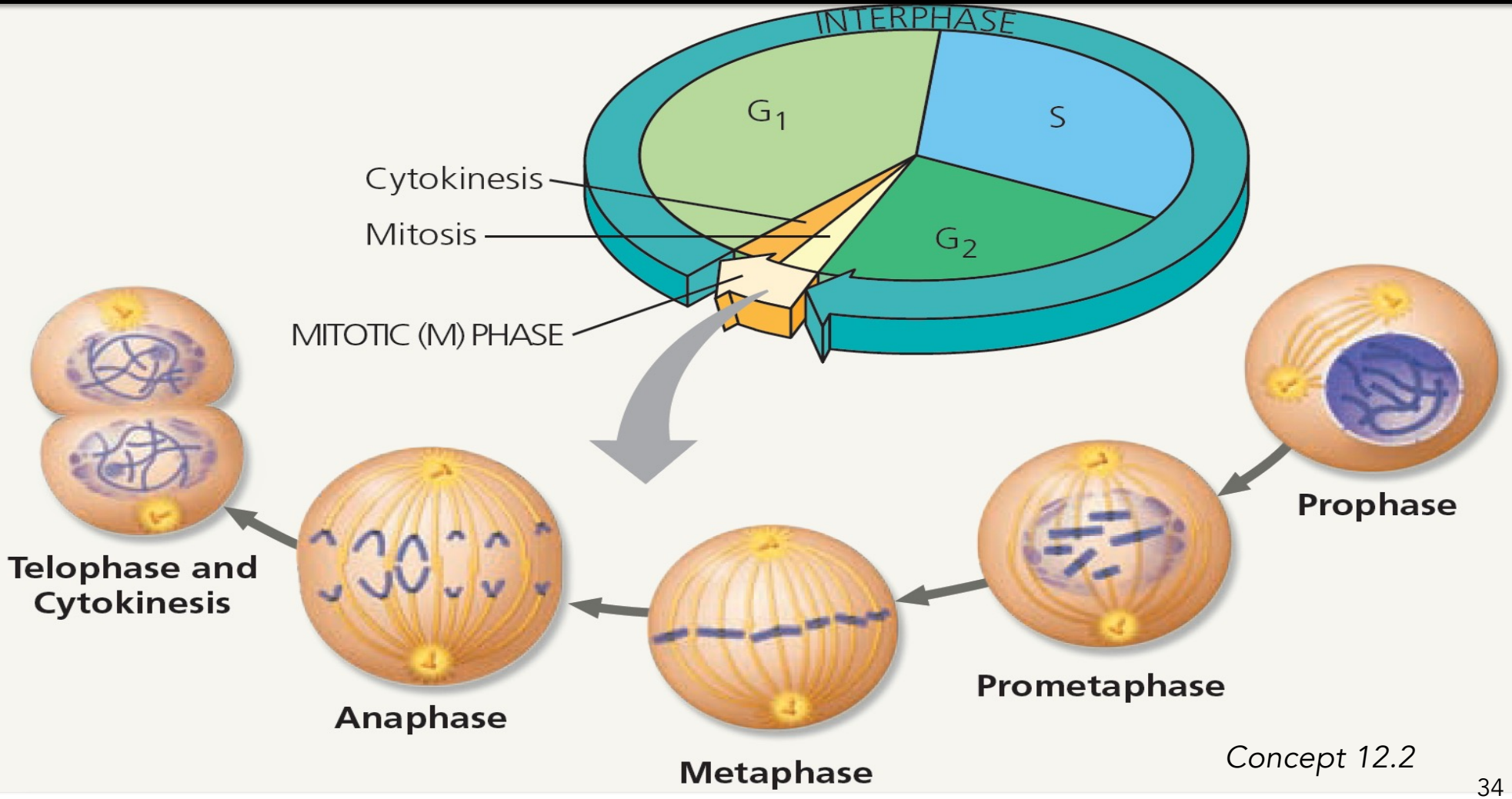
Mitosis

Why mitosis is important?

Mitosis produces new cells, and replaces cells that are old, lost or damaged.

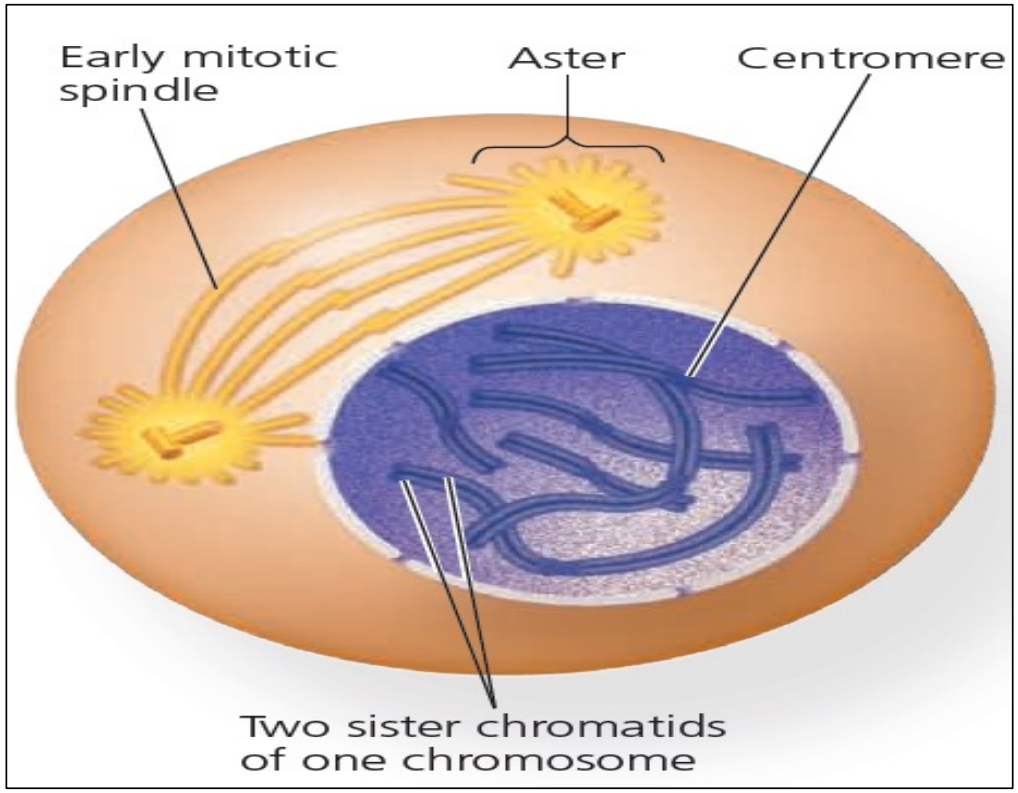
In mitosis a cell divides to form two identical daughter cells.

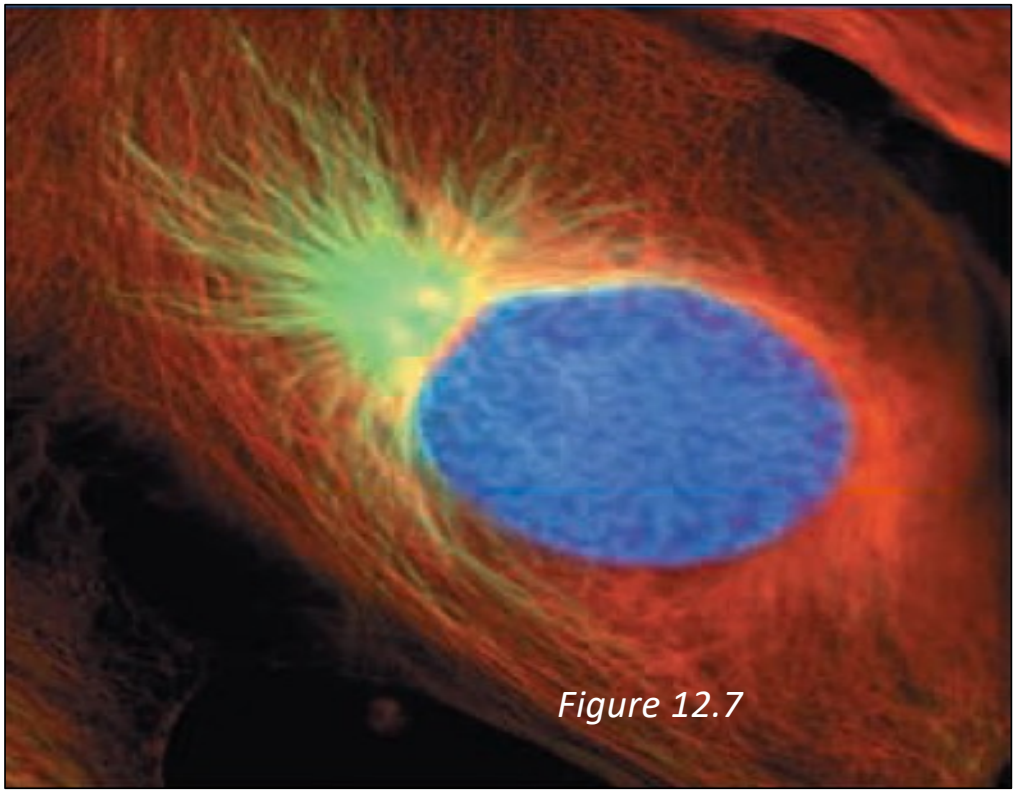
The Cell Cycle: Mitosis



Concept 12.2

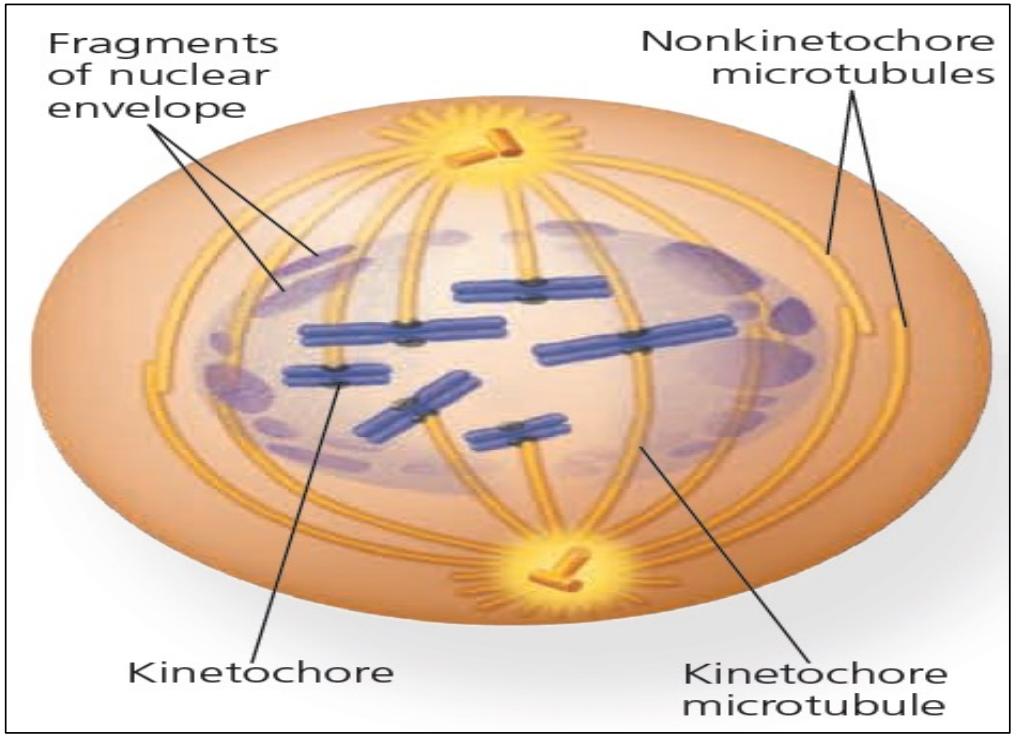
Mitosis: Prophase

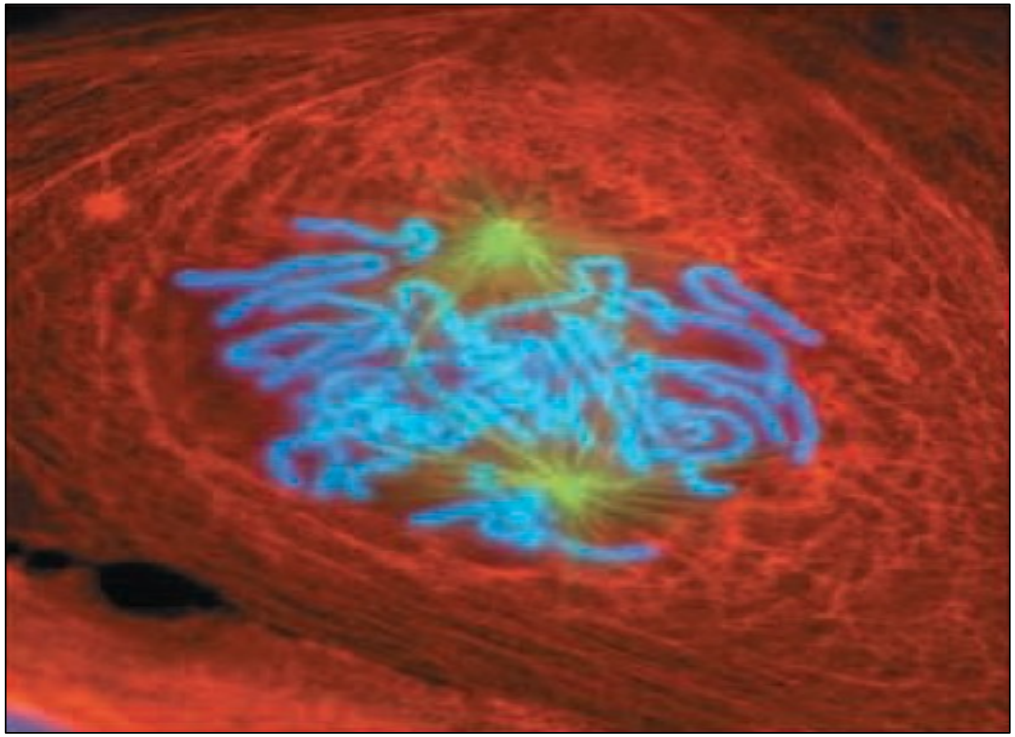




- Chromatins condense into discrete chromosomes and nucleoli disappear
- Each chromosome appears as two sister chromatids, joined at centromere
- Centrosomes move apart and mitotic spindle begins to form

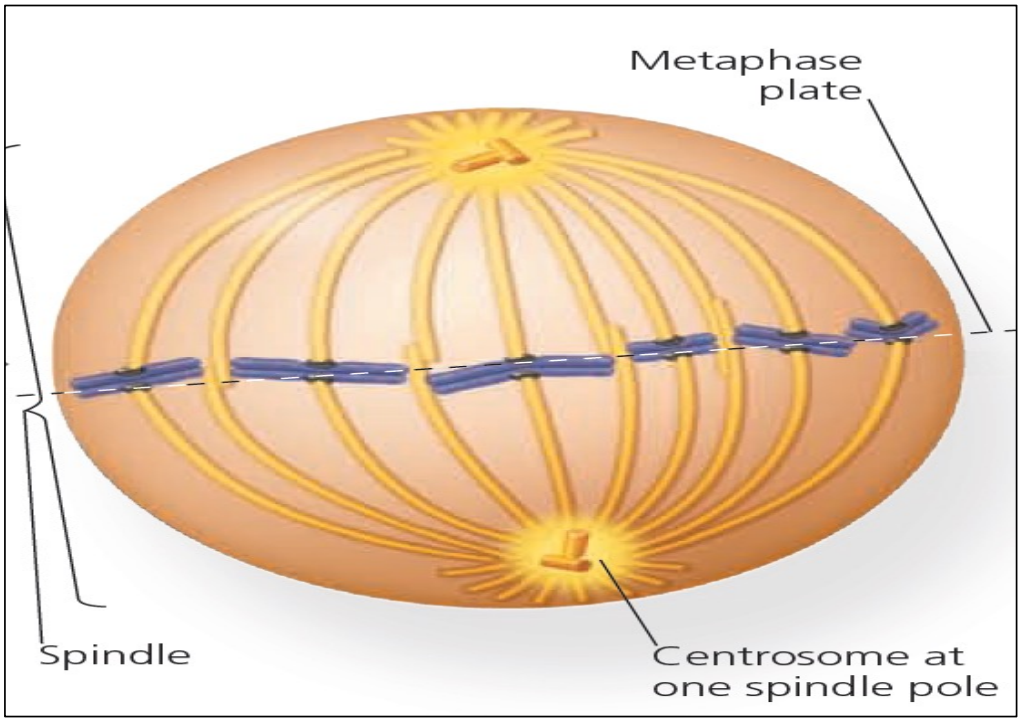
Mitosis: Prometaphase

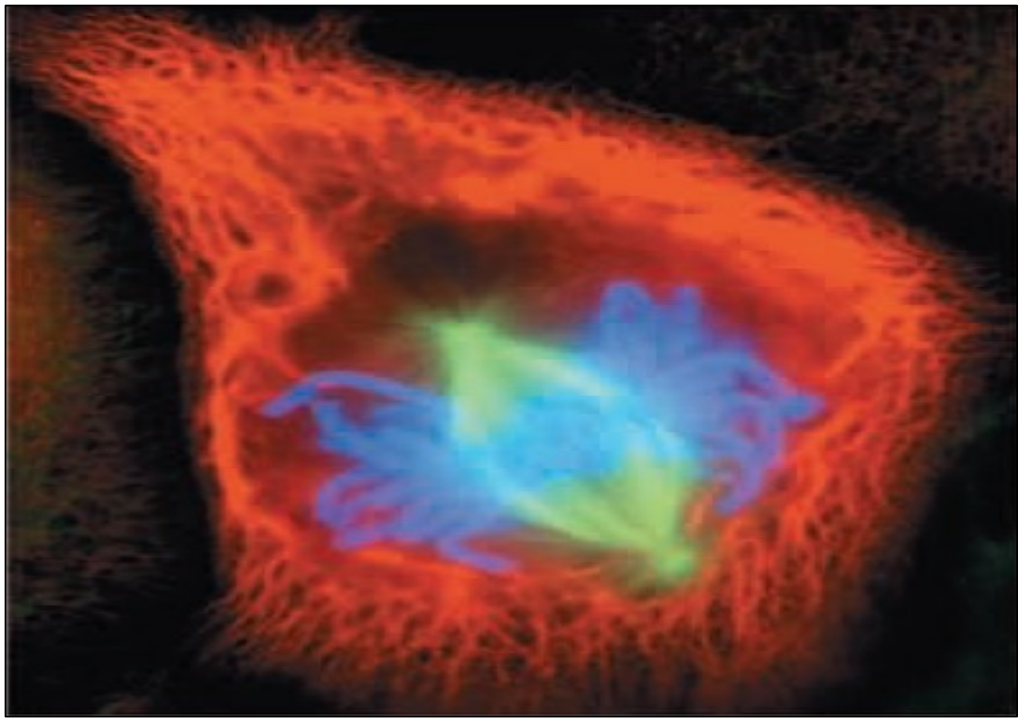




- Nuclear membrane fragments, microtubules grow
- Each of the two chromatids have kinetochore proteins at the centromere
- Microtubules attached to kinetochores “kinetochore microtubules”

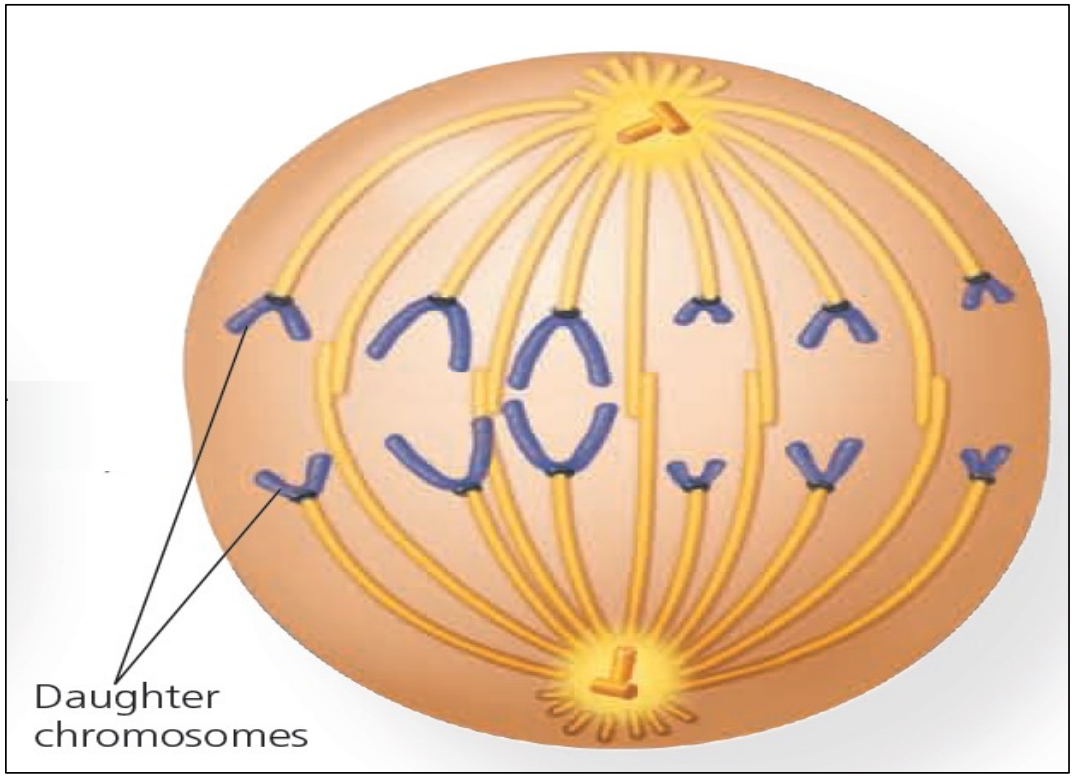
Mitosis: Metaphase

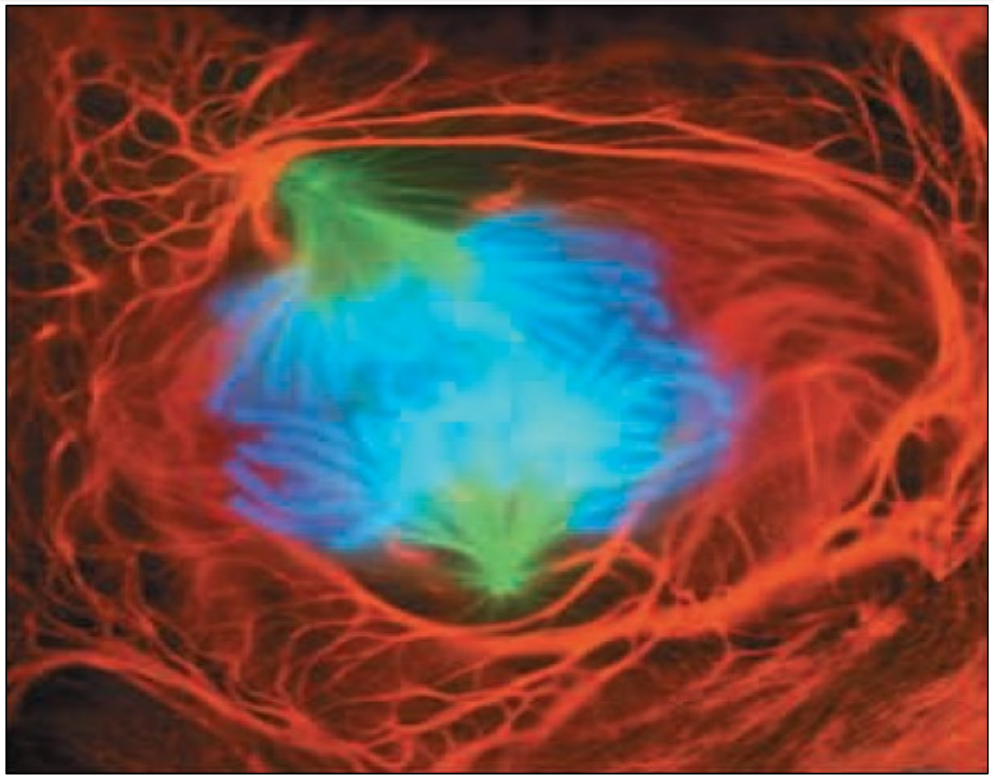




- Chromosomes assemble at *metaphase plate "equidistant between spindle's 2 poles"*
- Each chromosome sister chromatids are attached to microtubules arising from opposite poles

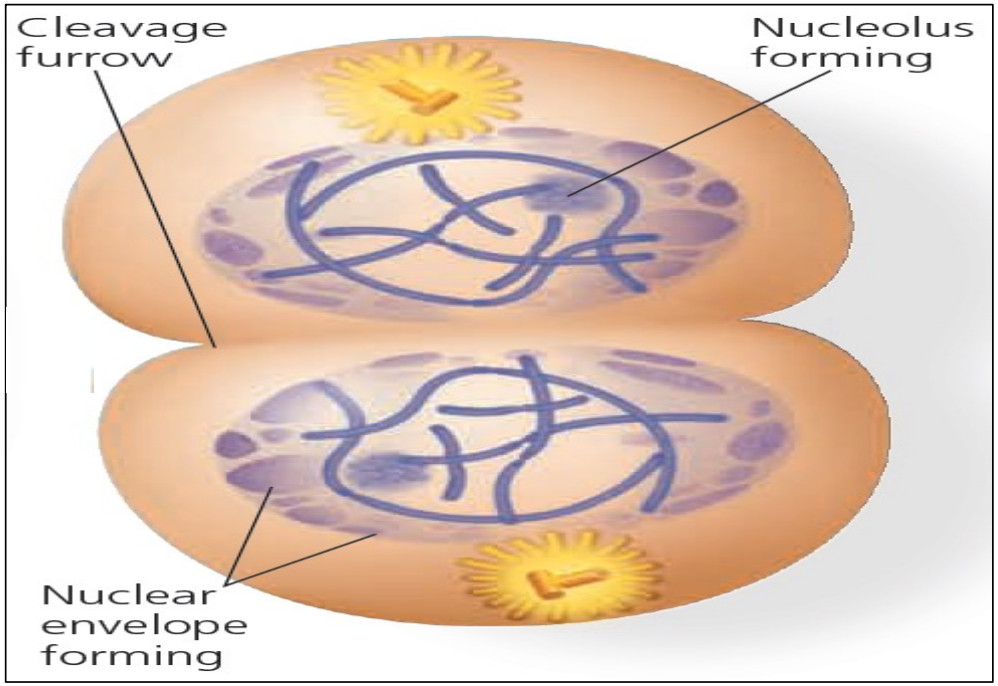
Mitosis: Anaphase

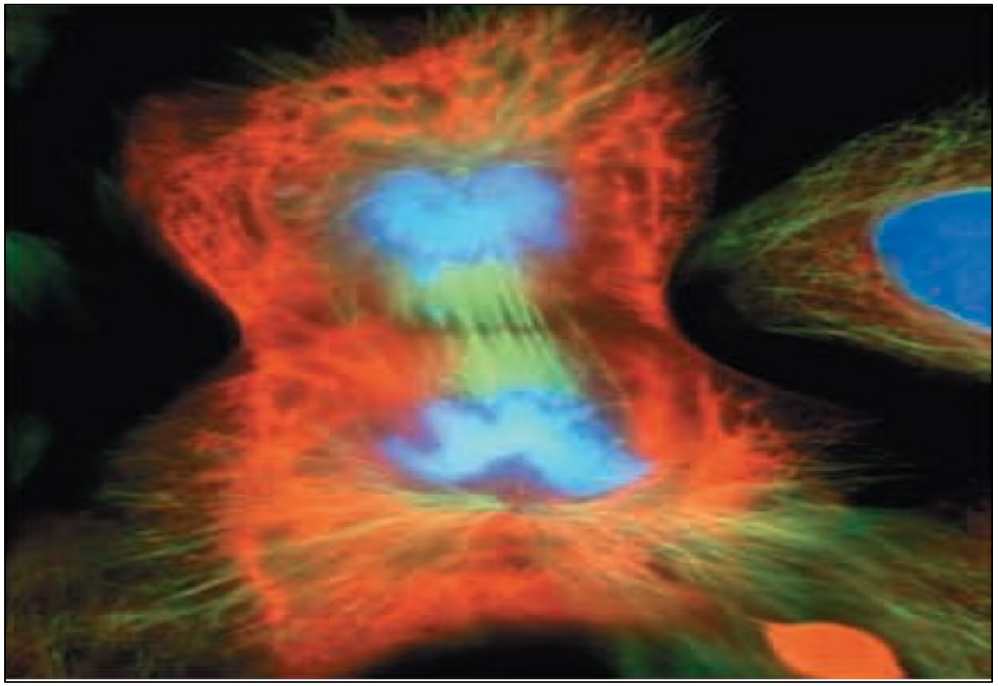




- Sister chromatids separate & each chromatid behaves as a chromosome
- Daughter chromosomes move towards opposite poles

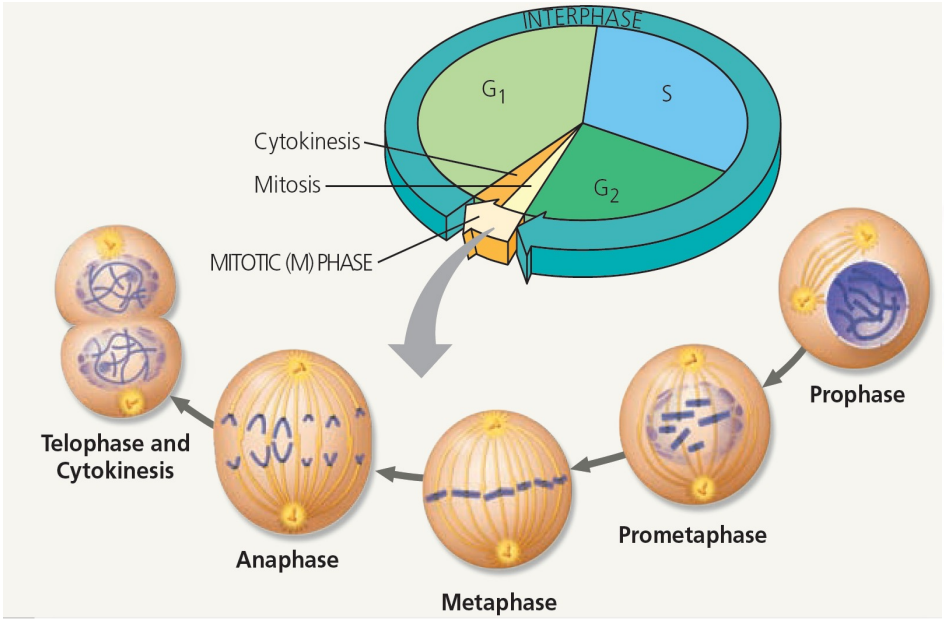
Mitosis: Telophase & Cytokinesis

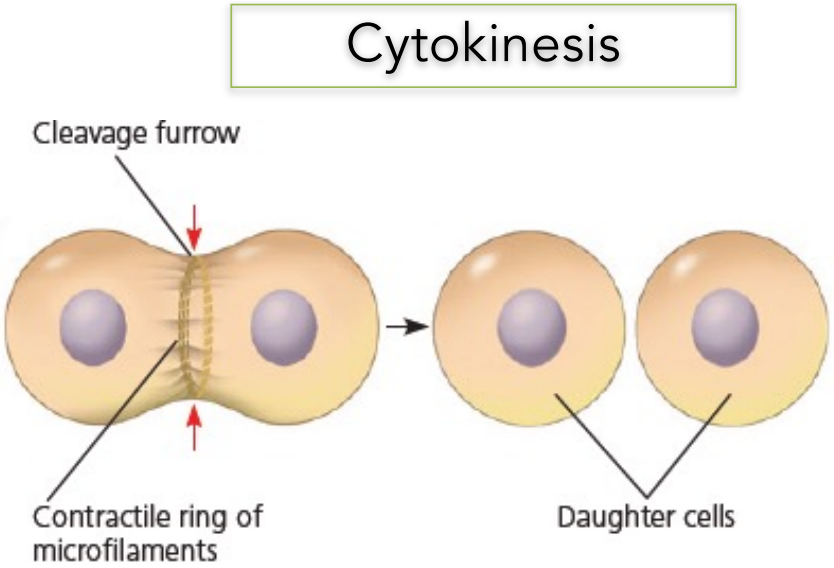




- Two daughter nuclei form in the cell, nuclear envelope reappears
- Spindle microtubules depolymerize, chromosomes become less condensed; karyokinesis (division of nucleus) completes

Mitosis: Cytokinesis

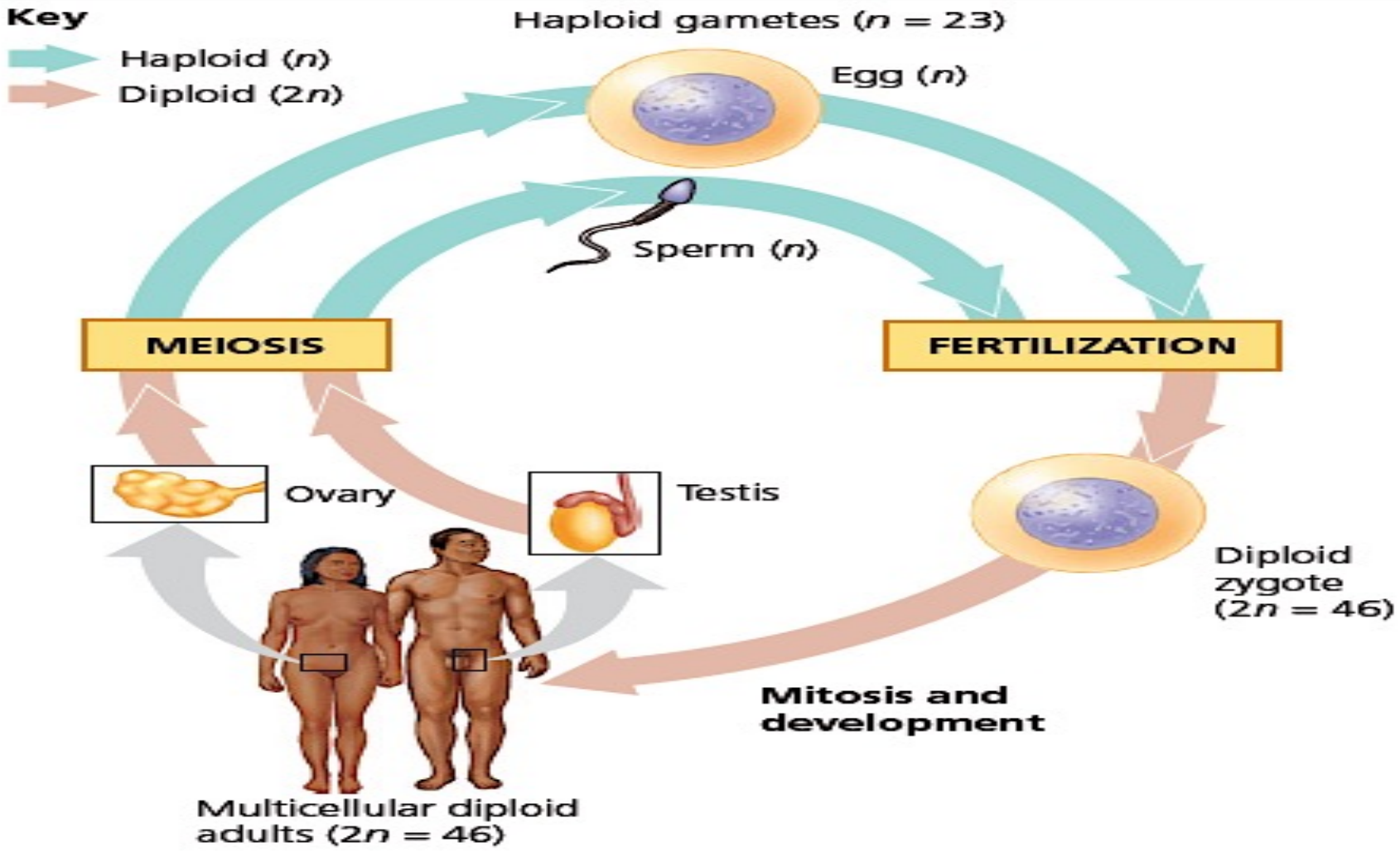




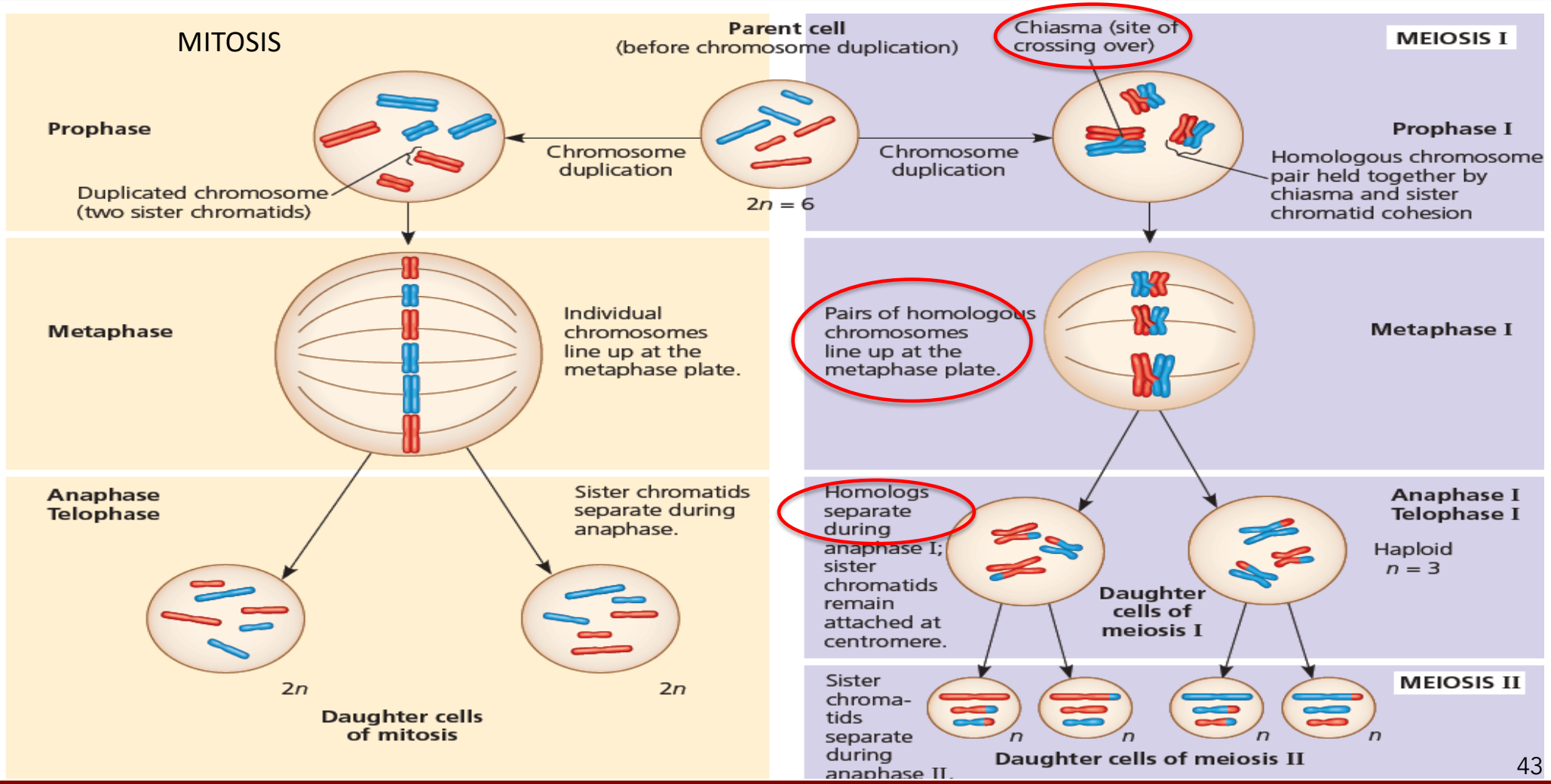
- Formation of cell furrow
- Division of cytoplasm to give rise to two daughter cells

Able to generate genetic variation in offspring because the process of meiosis randomly shuffles genes across chromosomes

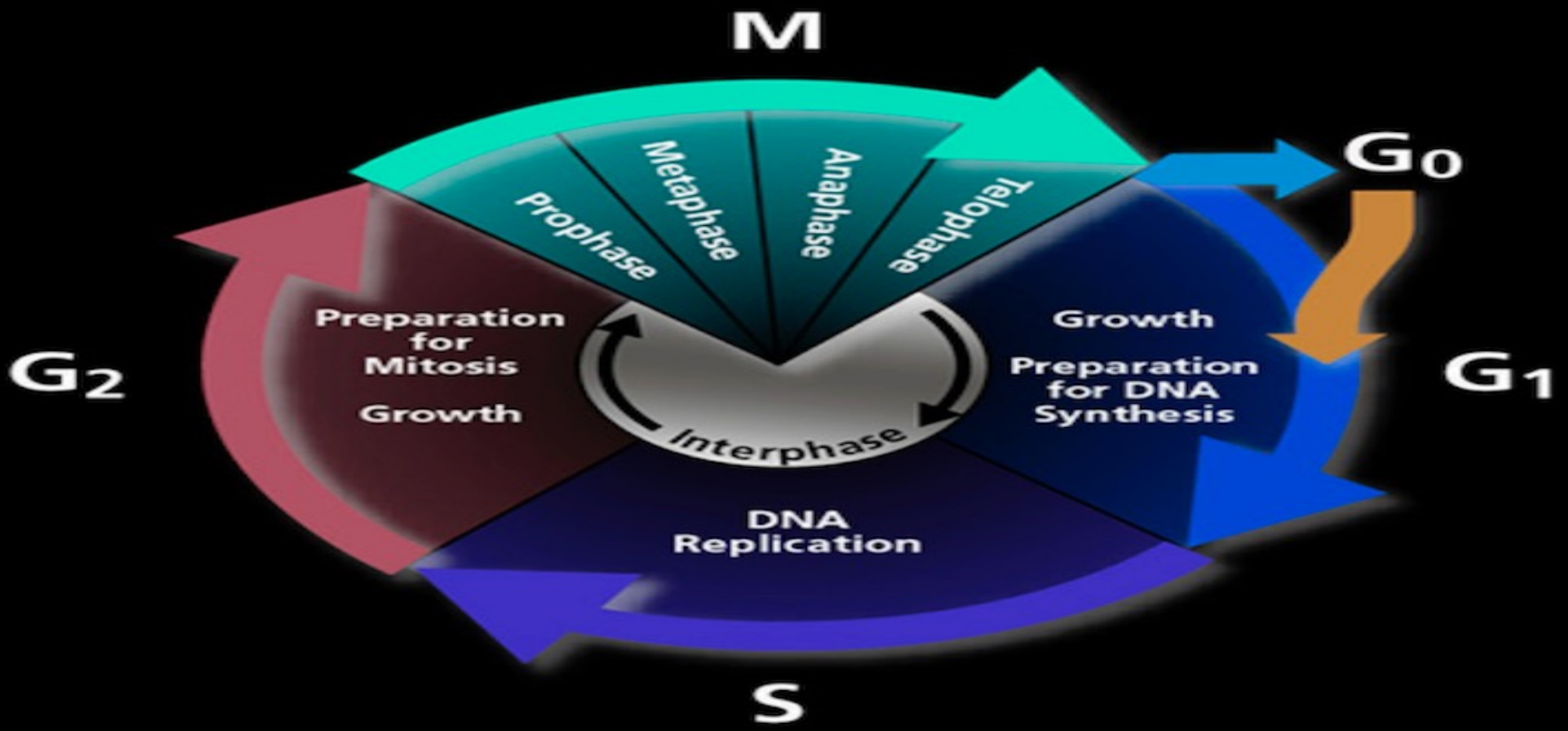
Meiosis: Central to Reproduction



Cell Division: Mitosis vs. Meiosis



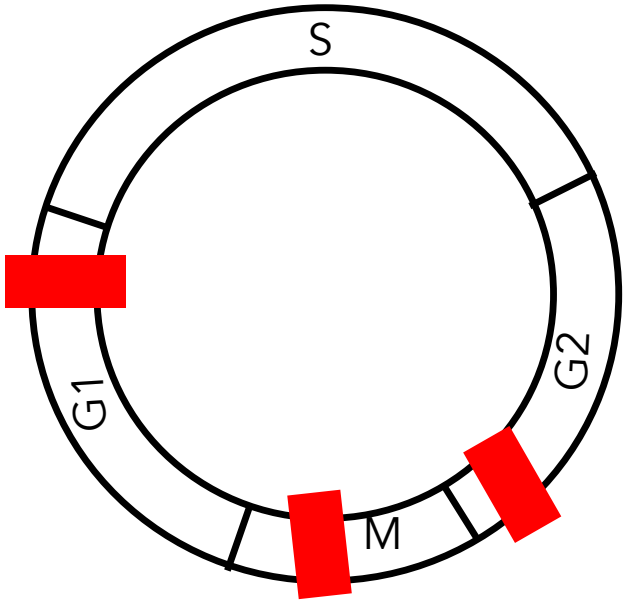
Cell cycle dysregulation & Cancer



Cancer cells disrupt normal cell cycle regulation and divide out of control, forming tumors

Cell Cycle Checkpoints

Parent DNA strands are intact before DNA replication begins



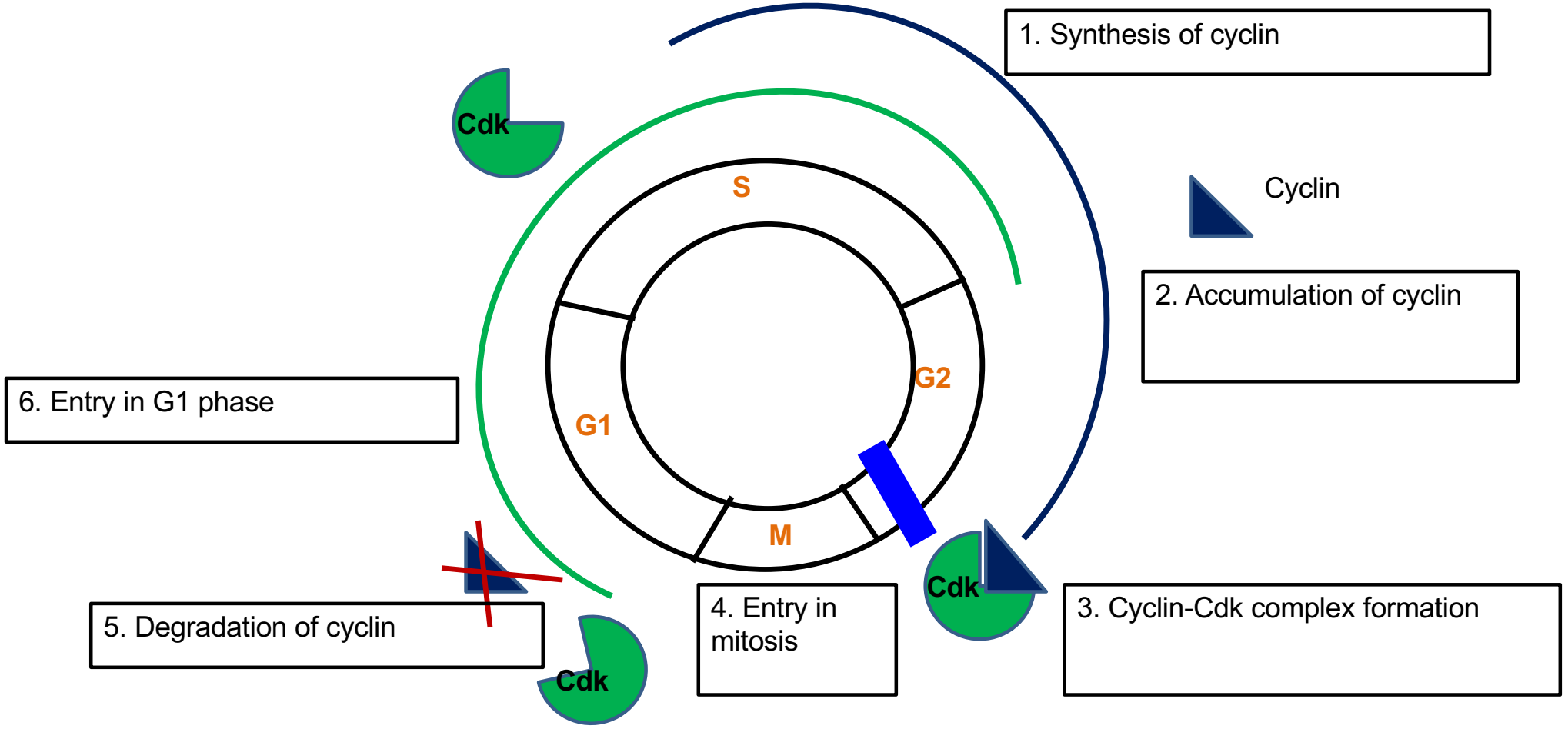
Newly synthesized DNA strands are complete and intact before mitosis

Chromosomes are aligned properly at the metaphase plate before Anaphase

Checkpoints are essential for the correct distribution of complete chromosome sets between daughter cells

Figure 12.15

Regulation of Cell Cycle by Cyclins and Cyclin Dependent Kinases



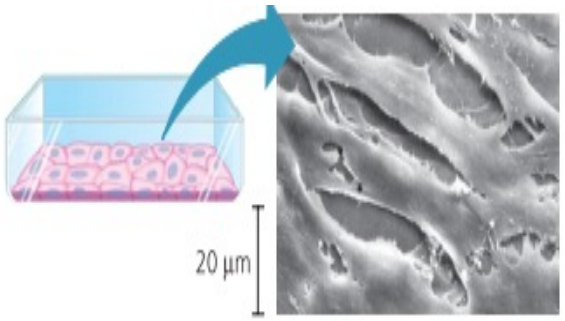
Regulation of Cell Cycle by External Signals

In addition to the internal signals following external signals are also required for the progression of cell cycle

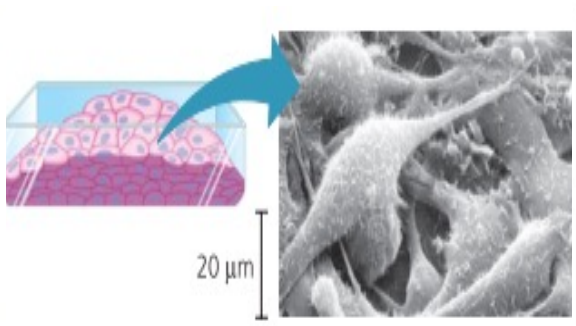
- Nutrients
- Growth factors
- Space (Crowded cells stop dividing) also known as density dependent inhibition
- Substratum for anchorage (anchorage dependence)

Cancer cells lose Dependence on Internal and External signals for Proliferation

- Cancer cells do not stop at cell cycle checkpoints
- Do not exhibit density dependent inhibition (form multiple layers of cells)
- Do not require anchorage with the substratum



Normal mammalian cells



Cancer cells

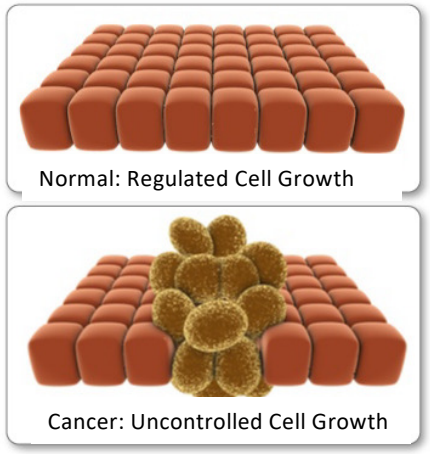


Figure 12.19

Food for thought:
How do Healthy Cells become Cancerous?

Why is cell growth a problem in cancer?

A cell is continuously receiving messages, both from its own genes and from other cells. Some tell it to grow and multiply, others tell it to stop growing and rest, or even to die. If there are enough 'grow' messages, the next stage of the cell's life starts. In a cancer cell, the messages to grow may be altered, or the messages to stop growing or to die may be missing. The cell then begins to grow uncontrollably and divide too often.

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How long do cancer cells live for?

Every time a normal cell divides, the ends of its chromosomes become shorter. Once they have worn down, the cell dies and is replaced. Cancer cells cheat this system - they retain their long chromosomes by continually adding bits back on. This process allows cancer cells to live forever. Cells from Henrietta Lacks, an American woman who was diagnosed with cervical cancer in 1951, are still growing. They are used in research laboratories all over the world, many years following her death.

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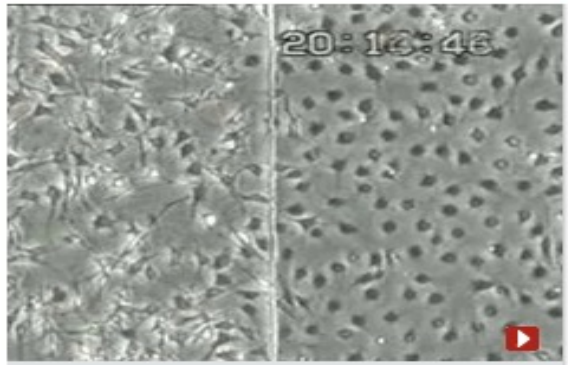
Why are cancer cells so powerful?

All the cells in your body usually work together as a community. But if a cell acquires a gene mutation that makes it multiply when it should not, or helps it survive when other cells die, it has an advantage over the others. Eventually, the abnormal cells acquire mutations in more genes, causing uncontrolled growth. These abnormal cells have a competitive advantage over normal cells. This is like natural selection in evolution, where a species that produces more offspring has a better chance of survival.



The growth of cancer cells (left) compared to normal cells (right).

Figure 12.15

Summary

- Cell division results in genetically identical daughter cells
- In cell cycle mitotic phase alternates with interphase
- Meiosis reduces the number of chromosome sets from diploid to haploid
- Eukaryotic cell cycle is regulated by a molecular control involving cyclins & Cdks
- Cancer cells disrupt normal cell cycle regulation and divide out of control, forming tumors

References

• Campbell Biology - Reece, Urry, Cain, Wasserman, Minorsky, Jackson 10th Edition, Pearson