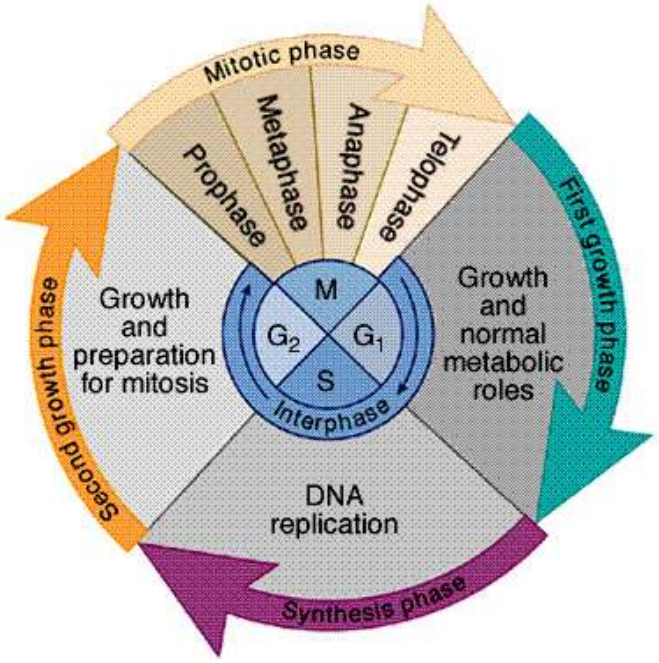
Chapter 12

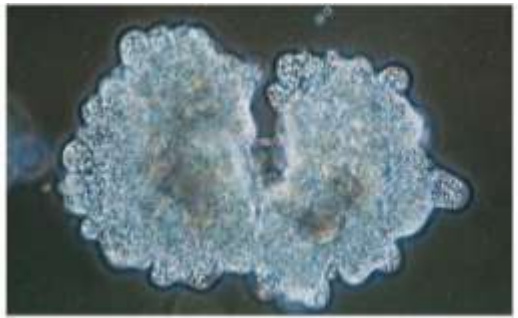
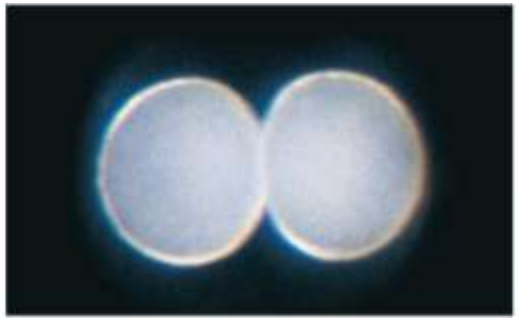
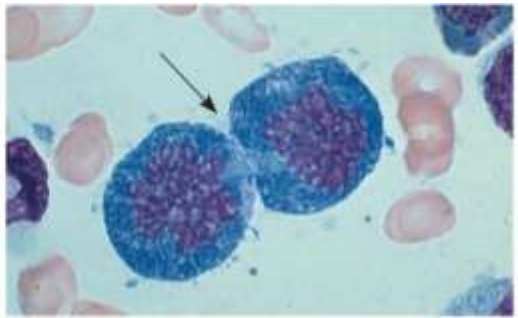
The Cell Cycle



AP Biology

Overview: The Key Roles of Cell Division

- The continuity of life is based on the reproduction of cells, or **cell division**
  - Cell division plays many important roles in the life of an organism:
  - Reproduction, growth, and development
    - The division of a single cell reproduces an entire unicellular organism (Ex: Amoeba)
    - Some multicellular organisms can reproduce asexually through many cell divisions (Ex: Plants growing from cuttings, budding hydra)
    - Sexually reproducing organisms develop from a single fertilized egg (zygote) through cell division
  - Renewal and Repair
    - After an organism is fully grown, cell division continues to function in renewal and repair by replacing cells that die from normal wear/tear or accidents (Ex: Dividing cells in bone marrow continuously make new blood cells)

Overview: The Cell Cycle

- Cell division is an integral part of the cell cycle
  - **Cell cycle**: life of cell, from its formation until its own division into two cells
  - In this chapter, you will learn about:
    - How cell division distributes identical genetic material to daughter cells
    - The cellular mechanics of cell division in eukaryotes and bacteria
    - The molecular control system that regulates progress through the eukaryotic cell cycle and what happens when this control system malfunctions

Concept 12.1:
Cell division results in genetically identical daughter cells

Cell Division

- Most cell division involves the distribution of identical genetic material (DNA) to 2 daughter cells
    - A special type of division called meiosis produces nonidentical daughter cells called gametes (sperm and egg cells)
- Cell division involves 3 main steps:
    - 1) A dividing cell duplicates it DNA
    - 2) This duplicated DNA is then allocated to opposite ends of the dividing cell
    - 3) The dividing cell splits into two genetically identical daughter cells

Prokaryotic vs. Eukaryotic Genomes

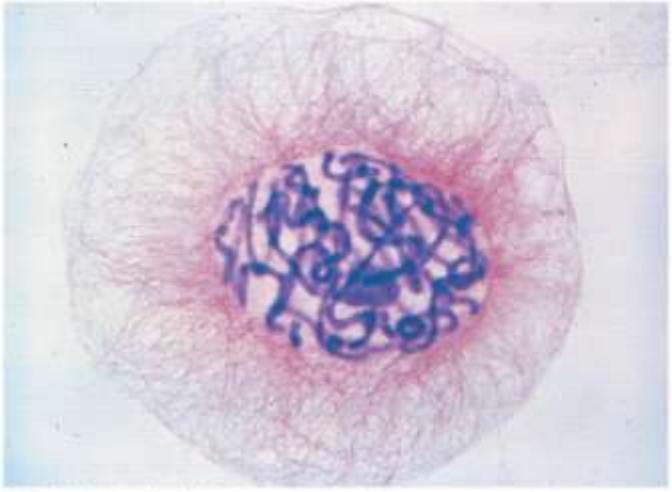
- A cell's complete collection of DNA is called its **genome**
  - A prokaryotic genome is usually only one long DNA molecule
  - A eukaryotic genome usually consists of many DNA molecules
    - As a result, the overall length of DNA in a eukaryotic cell is enormous
      - Ex) Typical human cell has ~ 2 meters of DNA

Somatic Cells vs. Gametes

- Replication and distribution of such large amounts of DNA during cell division is manageable because the DNA molecules are packaged into **chromosomes**
    - Each eukaryotic species has a characteristic number of chromosomes in each cell nucleus
    - The nuclei of human **somatic** (body) cells have 46 chromosomes made from 2 sets of 23, one set inherited from each parent
        - The number of chromosomes in somatic cells varies widely among species
            - Chromosome number, however, does not necessarily correlate with complexity
                - Ex) Elephants have 56 chromosomes, while one species of alga has 148
        - Reproductive cells (egg and sperm cells), called **gametes**, have half as many chromosomes as somatic cells
            - Ex) Human gametes have one set of 23 chromosomes

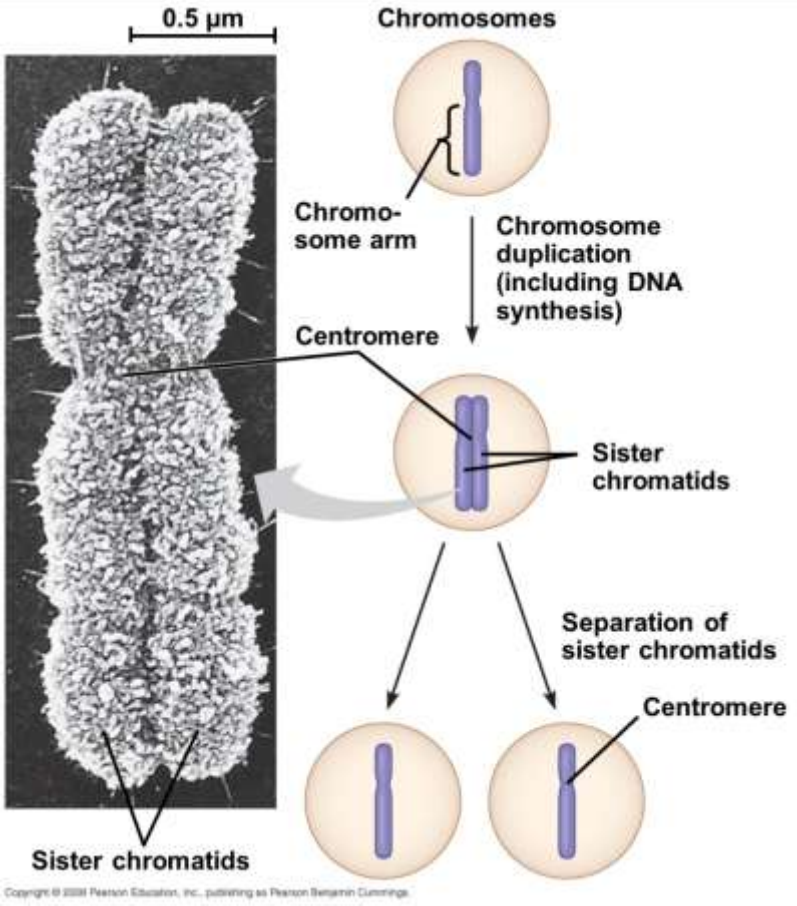
Cellular Organization of the Genetic Material

- Eukaryotic chromosomes are made of complexes of DNA molecules and associated proteins, collectively known as **chromatin**
  - Each chromosome contains one long linear DNA molecule carrying 100s-1000s of genes
    - Genes are the units that specify an organism's inherited traits
    - The associated proteins of chromatin maintain the structure of chromosomes and help control gene activity
  - Each chromosome remains in the form of a long, thin chromatin fibers when a cell is not actively dividing, and even as the cell duplicates its DNA in preparation for cell division
    - After DNA duplication, however, the chromosomes condense as each chromatin fiber becomes densely folded and coiled
      - At this point, the chromosomes are much shorter and thicker, and can thus be seen individually with a light microscope



Sister Chromatids

- After DNA duplication, each condensed chromosome consists of 2 sister chromatids and is known as a duplicated chromosome
  - These **sister chromatids**, which separate during cell division, each contain identical DNA
    - They are initially attached along their lengths by protein complexes called *cohesins*
      - This attachment is known as *sister chromatid cohesion*

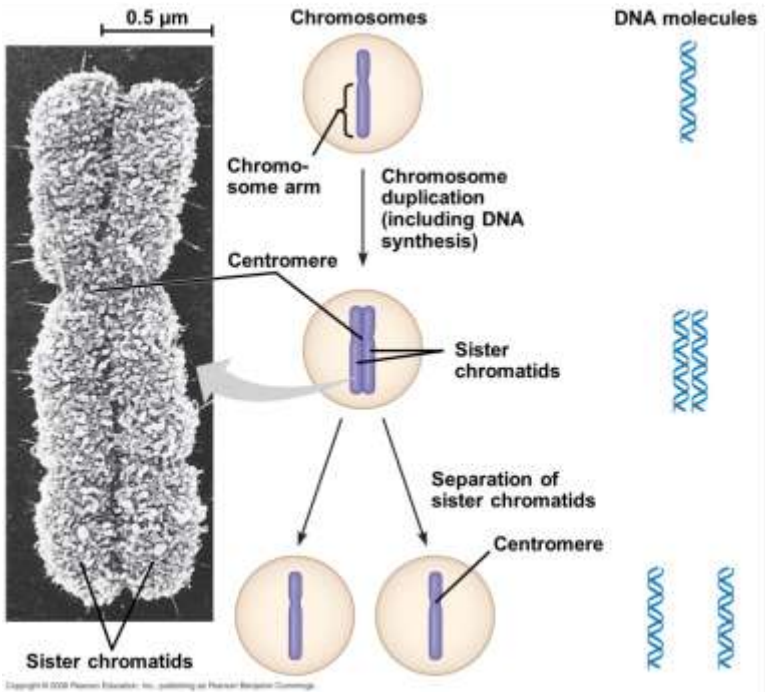


Distribution of Chromosomes

- In condensed form, the region where these 2 sister chromatids are most closely attached is called the **centromere**
    - The part of a chromatid on either side of the centromere is referred to as an *arm* of the chromatid

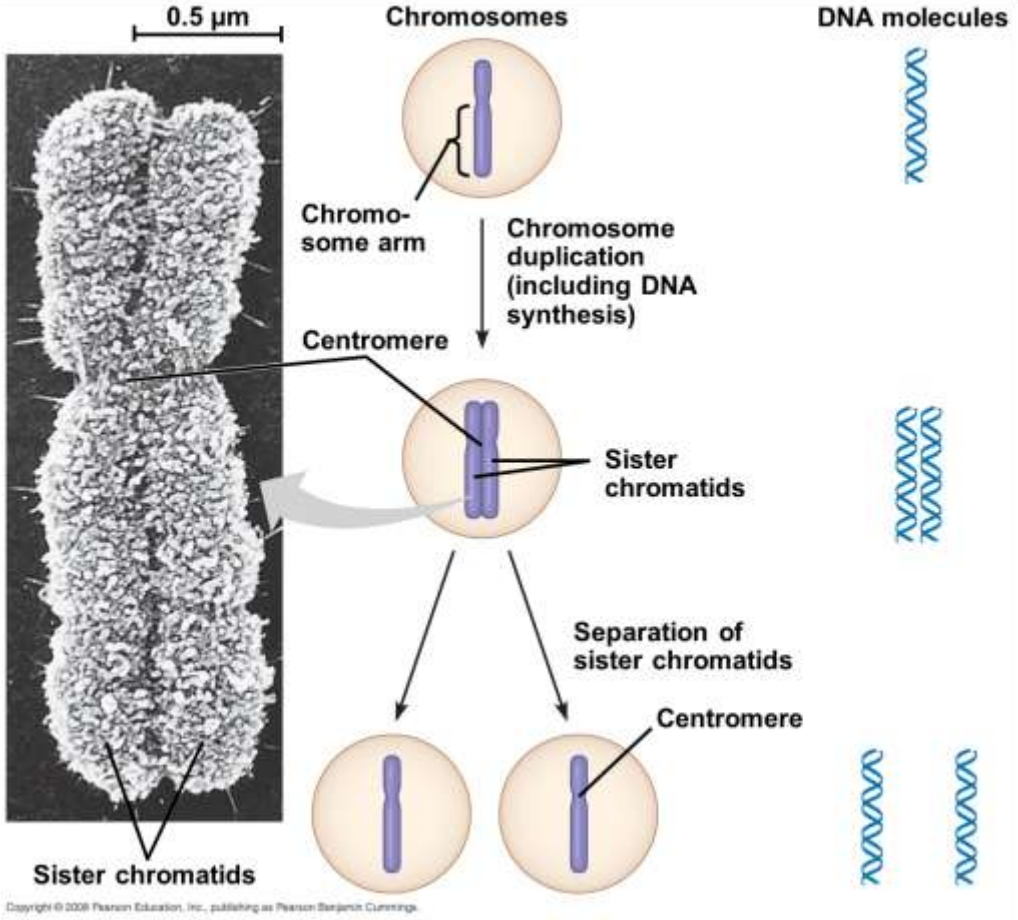
– Once the sister chromatids separate later in cell division, moving into 2 new nuclei, they are considered to be individual chromosomes

- Thus, each new nucleus receives a collection of chromosomes identical to that of the parent cell



Mitosis and Cytokinesis

- Eukaryotic cell division consists of 2 separate yet overlapping events:
  - **Mitosis** - the division of the nucleus
    - The 2 sister chromatids of each duplicated chromosome separate and move into 2 new nuclei forming at opposite ends of the cell
  - **Cytokinesis** - the division of the cytoplasm



Meiosis

- Gametes are produced by a variation of cell division called **meiosis**
  - Meiosis yields nonidentical daughter cells that have only one set of chromosomes (half as many as the parent cell)
    - Meiosis occurs only in the gonads (ovaries and testes)
    - Ex) In each generation of humans, meiosis reduces the chromosome number from 46 (2 sets of chromosomes) to 23 (one set of chromosomes
  - Fertilization fuses 2 gametes together, restoring the original number of chromosomes in the resulting zygote
    - Ex) Fertilization of a human egg cell by human sperm returns the chromosome number to 46, and mitosis conserves this number in every somatic cell nucleus of the new individual

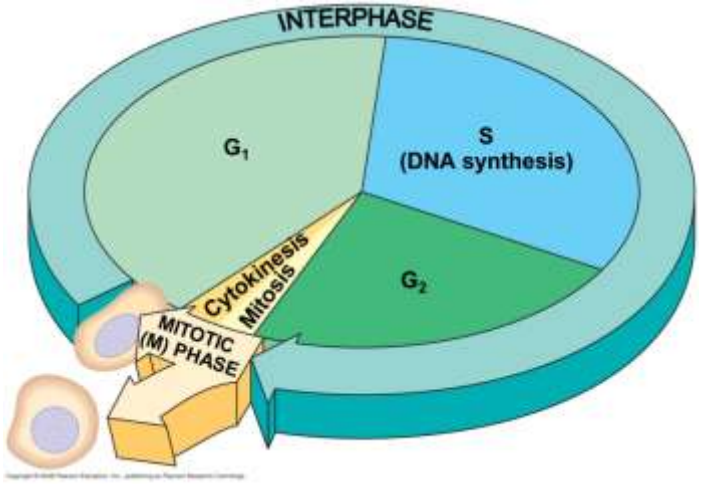
Concept Check 12.1

- 1) Starting with a fertilized egg (zygote), a series of 5 cell divisions would produce an early embryo with how many cells?
- 2) How many chromatids are in a duplicated chromosome?
- 3) A chicken has 78 chromosomes in its somatic cells. How many chromosomes did the chicken inherit from each parent? How many chromosomes are in each of the chicken's gametes? How many chromosomes will be in each somatic cell of the chicken's offspring?

Concept 12.2:
The mitotic phase alternates with interphase in the cell cycle

Phases of the Cell Cycle

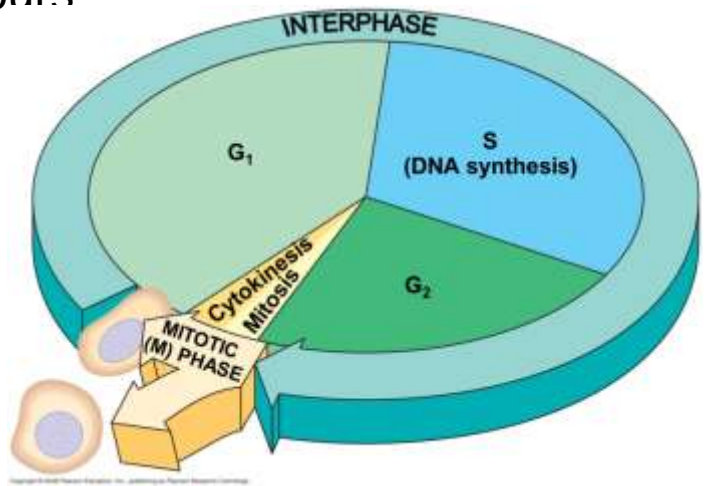
- The cell cycle (life of a cell) consists of 2 phases:
  - 1) The **Mitotic (M) phase** – includes both mitosis and cytokinesis
    - This is usually the shortest part of the cell cycle
  - 2) **Interphase** – includes cell growth and copying of chromosomes in preparation for cell division
    - This is a much longer stage than the M phase, often accounting for ~90% of the cell cycle
    - Interphase can be divided into 3 subphases:
      - **G_1 phase** (“first gap”)
      - **S phase** (“synthesis”)
      - **G_2 phase** (“second gap”)



    - The cell grows by means of producing proteins and organelles during all three phases, but chromosomes are duplicated only during the S phase

Time Spent in Each Phase of the Cell Cycle

- A typical human cell might undergo one division in 24 hours
  - Of this time:
    - The M phase would occupy < 1 hour
    - The S phase would last 10-12 hours (~ ½ the cell cycle)
    - The rest of the time (11-13 hours) would be apportioned between the G_1 and G_2 phases
      - The G_2 phase typically takes 4-6 hours
      - The G_1 phase usually occupies 5-6 hours
        - This phase is, however, the most variable in length in different types of cells

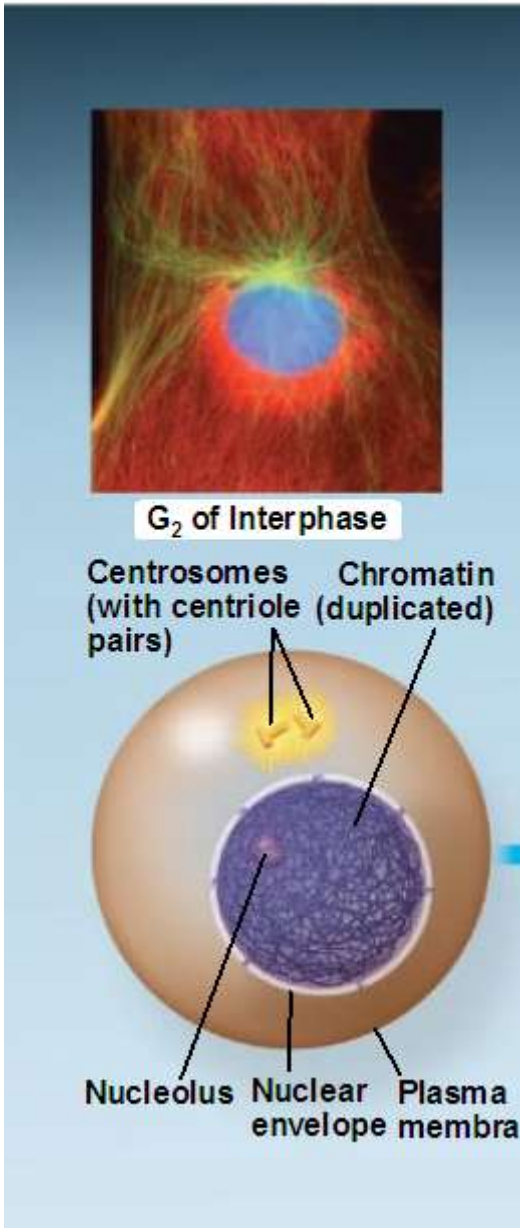


Phases of the Cell Cycle: Mitosis

- Mitosis is conventionally divided into five phases:
  - **Prophase**
  - **Prometaphase**
  - **Metaphase**
  - **Anaphase**
  - **Telophase**
- Cytokinesis overlaps with the latter stages of mitosis
  - It is well underway by late telophase

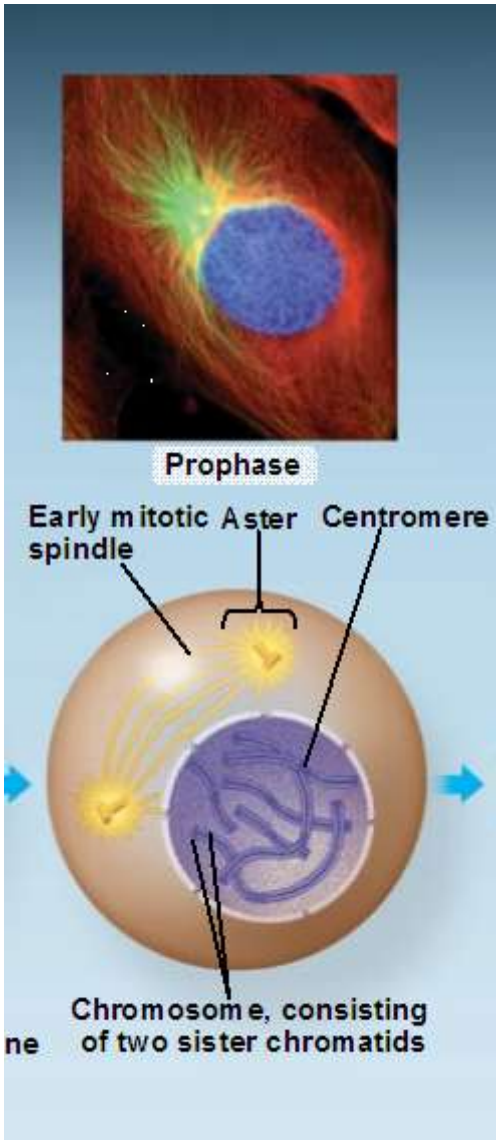
G_2 of Interphase

- **G_2 of Interphase**
  - A nuclear envelope bounds the nucleus
    - The nucleus contains 1+ nucleoli
  - 2 centrosomes have formed by replication of a single centrosome
    - Each centrosome has 2 centrioles in animal cells
  - The duplicated chromosomes have not yet condensed and thus cannot be seen individually



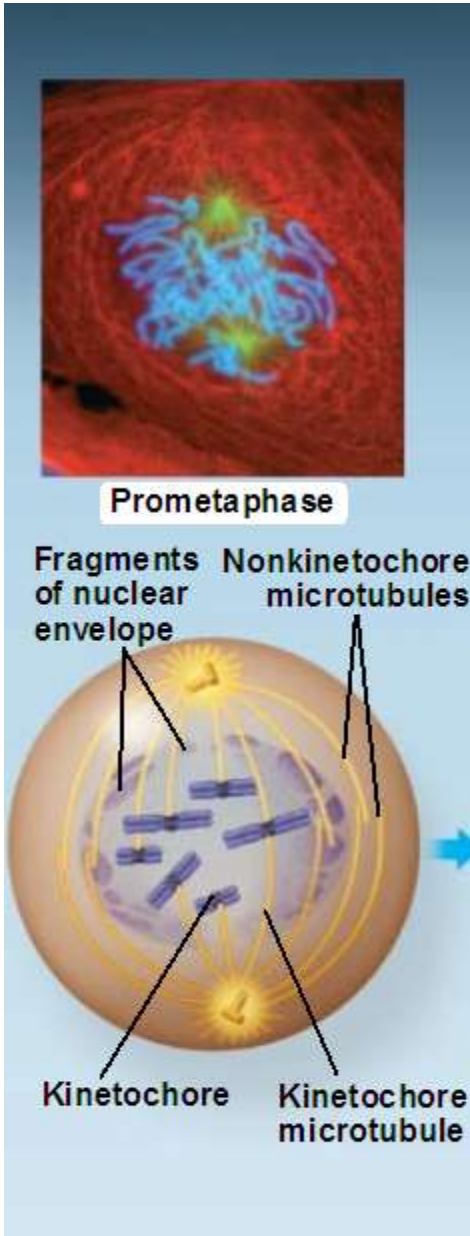
Prophase

- **Prophase**
  - Chromatin fibers condense into discrete chromosomes
    - Become observable with light microscope
  - Nucleoli disappear
  - Each duplicated chromosome appears as 2 identical sister chromatids joined at their centromeres and all along their arms by cohesins (sister chromatid cohesion)
  - The mitotic spindle begins to form
    - It is composed of centrosomes and the microtubules that extend from them
      - The radial arrays of shorter microtubules that extend from the centrosomes are called asters
  - The centrosomes move away from each other
    - They are propelled by lengthening microtubules between them



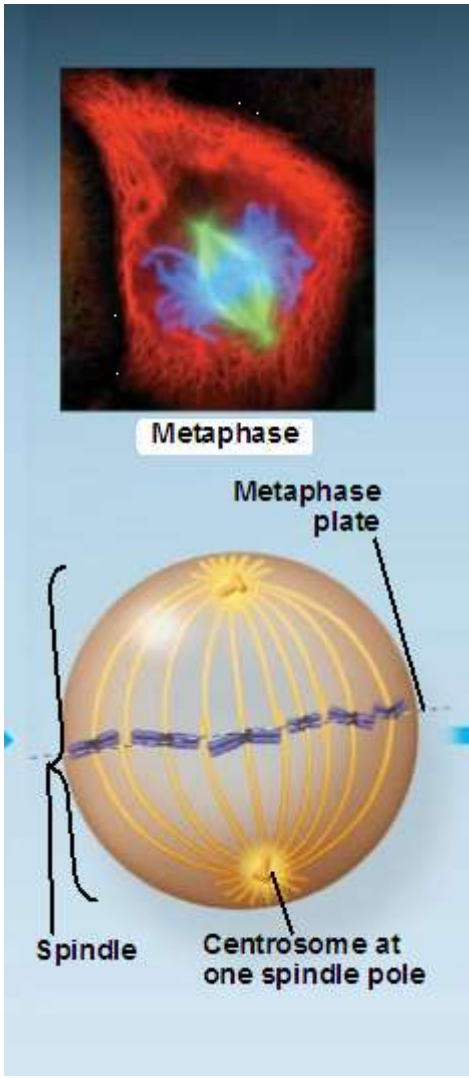
Prometaphase

- **Prometaphase**
  - The nuclear envelop fragments
    - The microtubules extending from each centrosome can now invade the nuclear area
  - The chromosomes further condense
  - Each chromatid now has a specialized protein structure located at the centromere called a kinetochore
    - Some microtubules attach to kinetochores (known as kinetochore mictrotubules)
      - These microtubules jerk chromosomes back and forth
  - Nonkinetochore microtubules interact with those from opposite poles of spindle



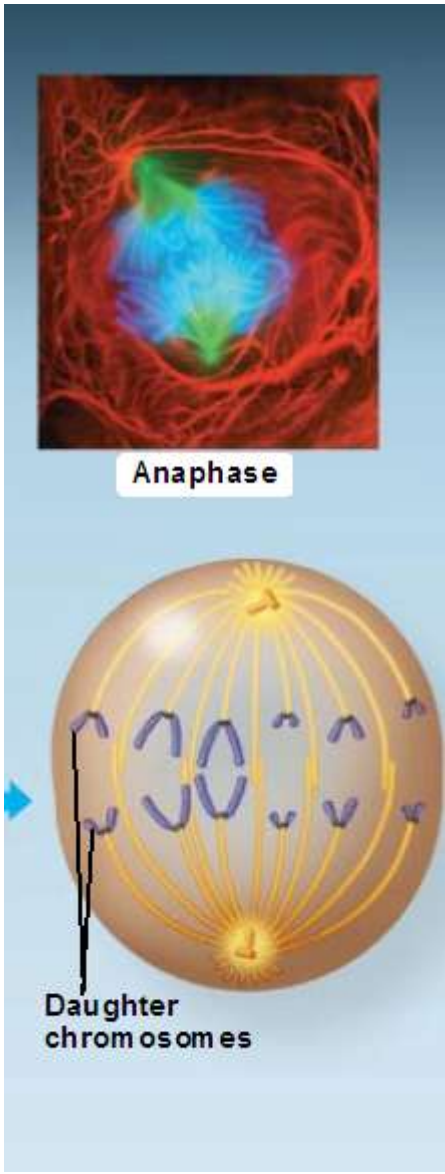
Metaphase

- **Metaphase**
  - This is the longest phase of mitosis
    - It often lasts ~20 minutes
  - The centrosomes are now at opposite poles of cells
  - The chromosomes convene on the metaphase plate
    - This is an imaginary plane that is equidistant between the spindle's two poles
    - The chromosomes' centromeres lie on the metaphase plate
  - For each chromosome, the kinetochores of the sister chromatids are attached to kinetochore microtubules coming from opposite poles



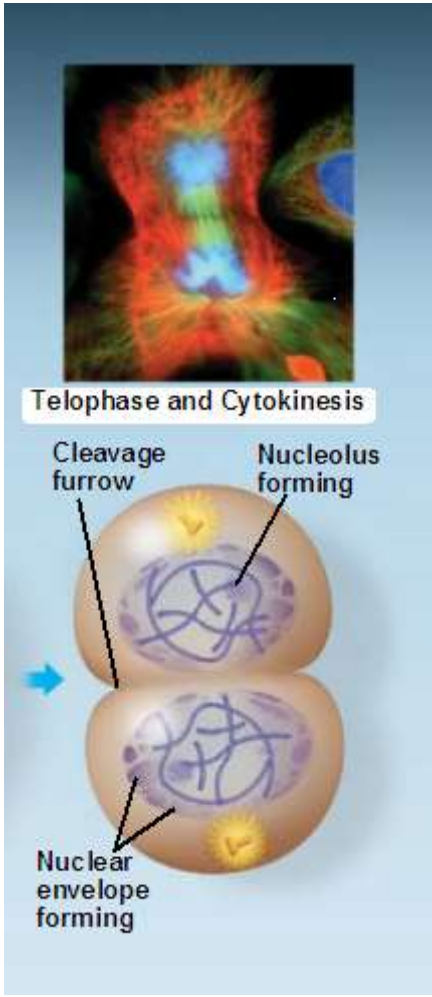
Anaphase

- **Anaphase**
  - This is the shortest stage of mitosis
    - It often only lasts a few minutes
  - It begins when cohesin proteins are cleaved
    - This allows sister chromatids of each pair to part
    - Each chromatid thus becomes a full-fledged chromosome
      - These 2 liberated daughter chromosomes begin move toward opposite ends of the cell as their kinetochore microtubules shorten
      - The chromosomes move centromere first (at 1 µm/min) because these microtubules are attached at the centromere region
    - The cell elongates as nonkinetochore microtubules lengthen
    - By the end of anaphase, each end of the cell has equivalent and complete collections of chromosomes



Telophase and Cytokinesis

- **Telophase**
  - 2 daughter nuclei form in the cell
    - Nuclear envelopes arise from fragments of the parent cell's nuclear envelope and other portions of the endomembrane system
    - Nucleoli reappear
  - The chromosomes become less condensed
  - Mitosis is now complete
    - One nucleus has been divided into 2 genetically identical nuclei
- **Cytokinesis**
  - Division of cytoplasm is well underway by late telophase
  - In animal cells, cytokinesis involves formation of a cleavage furrow
    - This protein belt pinches the cell in two

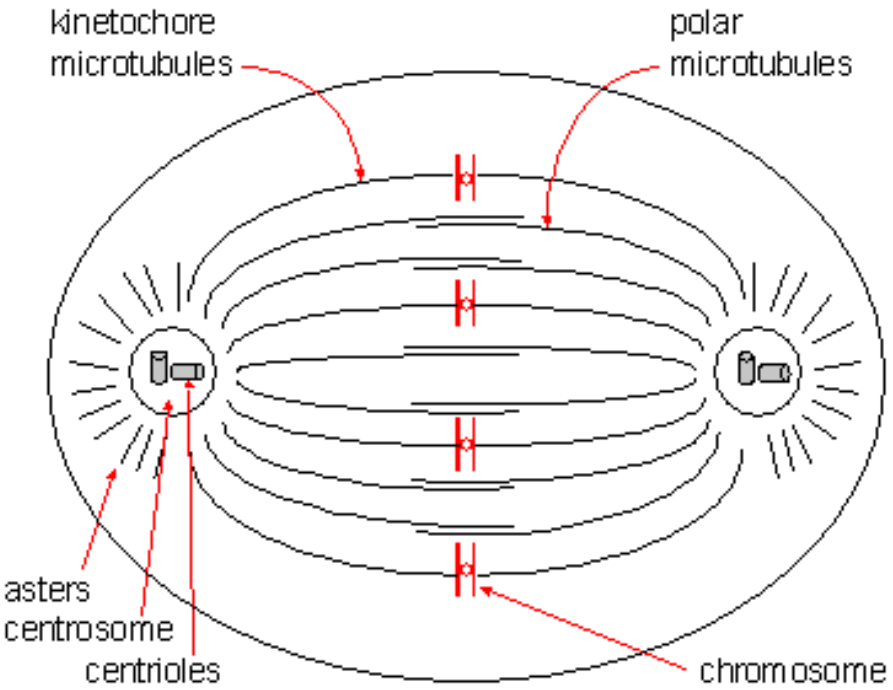


The Mitotic Spindle: *A Closer Look*

- Many of the events of mitosis depend on the mitotic spindle
    - The **mitotic spindle** is an apparatus of microtubules and associated proteins that controls chromosome movement during mitosis
  - It begins to form in the cytoplasm during prophase
    - While the mitotic spindle assembles, other cytoskeletal microtubules partially disassemble, probably to provide materials to construct it
  - Spindle microtubules elongate (polymerize) by incorporating more subunits of the protein tubulin
    - Alternatively, the microtubules shorten (depolymerize) by losing subunits

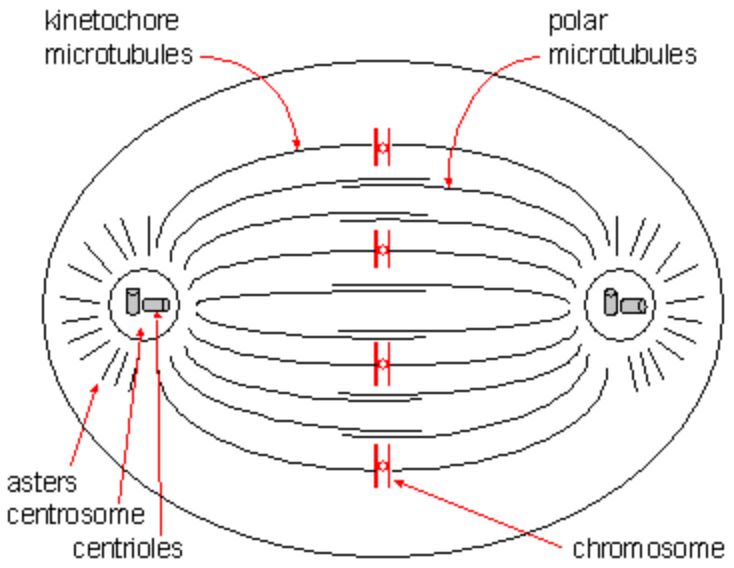
The Mitotic Spindle: Centrosomes

- In animal cells, the assembly of spindle microtubules begins at the **centrosome**
  - The centrosome is a subcellular region containing material that functions throughout the cell cycle to organize the cell's microtubules
    - For this reason, it is also called the microtubule-organizing center
  - A pair of centrioles is located at the center of the centrosome
    - These centrioles are not essential for cell division
      - The mitotic spindle still forms during mitosis when these structures are destroyed experimentally
      - Centrioles are also not even present in plant cells, which also form mitotic spindles



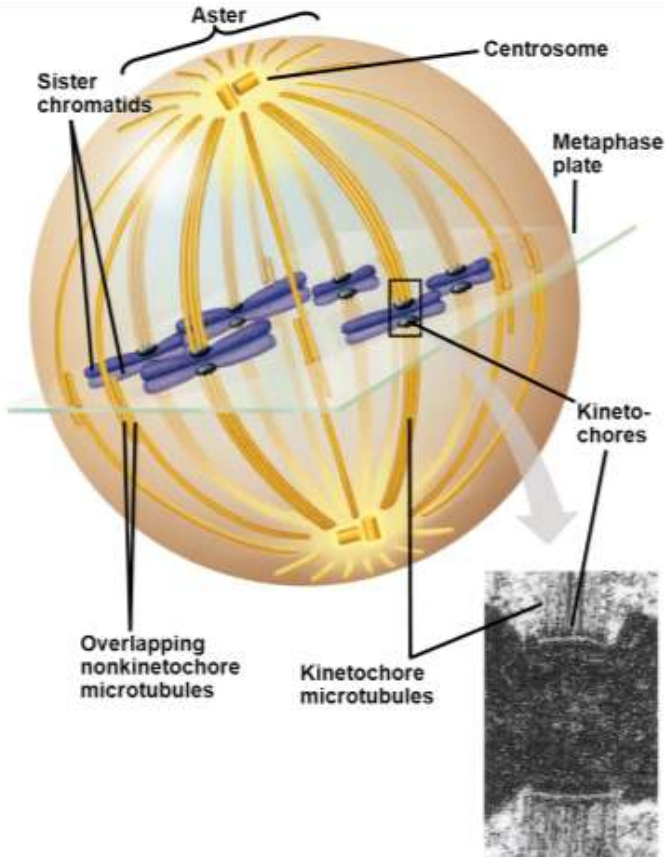
Movement of Centrosomes During Mitosis

- A single centrosome replicates to form two centrosomes during interphase in animal cells
  - These two centrosomes remain together near the nucleus throughout the remainder of interphase
  - They then begin to move apart during prophase and prometaphase of mitosis as spindle microtubules grow out of them
    - By the end of prometaphase, the 2 centrosomes have migrated to opposite ends of the cell so that one centrosome is located at each pole of the spindle
      - At this point, an **aster** (a radial array of short microtubules) extends from each centrosome
- The spindle includes the centrosomes, the spindle microtubules, and the asters



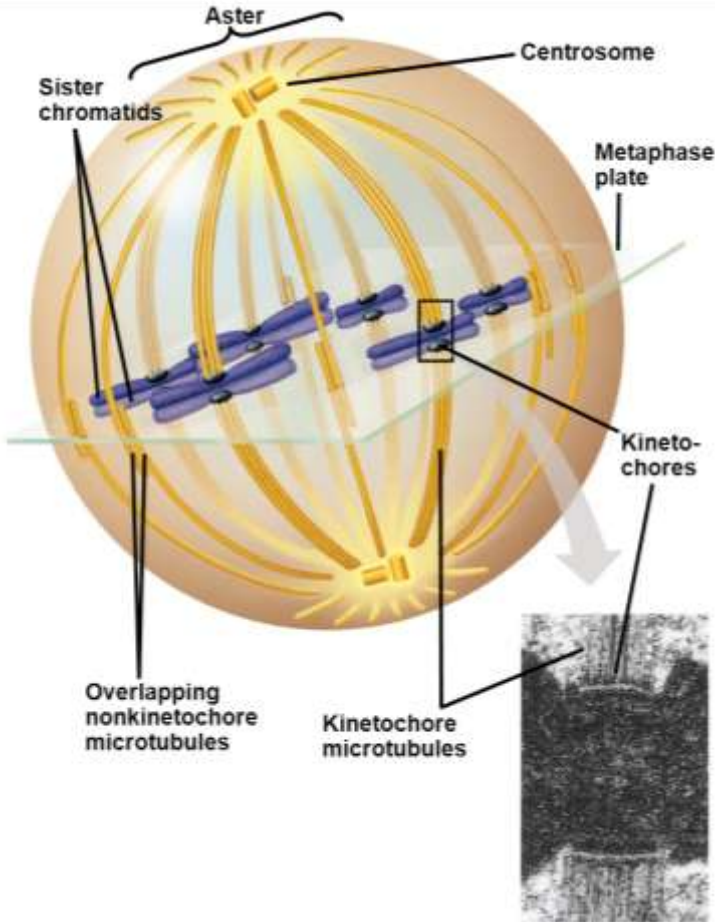
Movement of Chromosomes During Mitosis

- During prometaphase, some of the spindle microtubules (called kinetochore microtubules) attach to the **kinetochores** of chromosomes
    - A kinetochore is a structure of proteins associated with specific sections of chromosomal DNA at the centromere
  - These kinetochore microtubules begin to move the chromosomes toward the pole from which the microtubules extend
    - This chromosome movement, however, is “checked” when microtubules from the opposite pole attach to the other kinetochore
        - The result is a tug-of-war in which the chromosome moves first in one direction, then the other, finally settling midway between the 2 ends of the cell



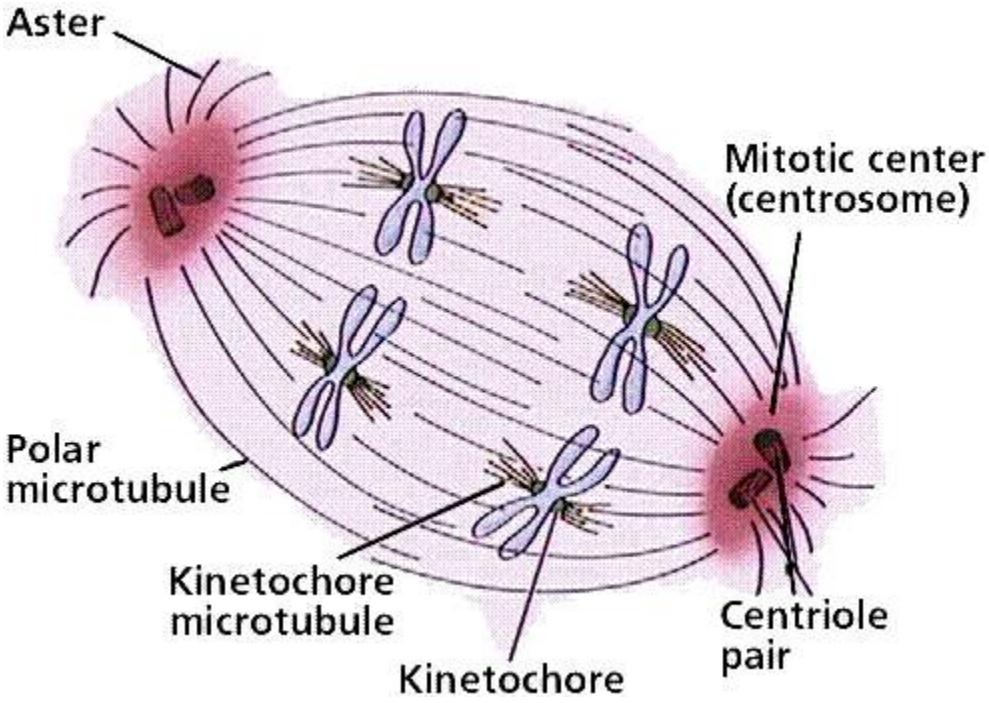
The Mitotic Spindle at Metaphase

- At metaphase, the chromosomes are all lined up at the **metaphase plate**, the midway point between the spindle's two poles
  - Meanwhile, microtubules that do not attach to kinetochores have been elongating during the early stages of mitosis
    - By metaphase, these microtubules overlap and interact with other nonkinetochore microtubules from the opposite pole of the spindle
    - At the same time, the microtubules of the asters have also grown and are in contact with the plasma membrane
  - At this point, the spindle is complete



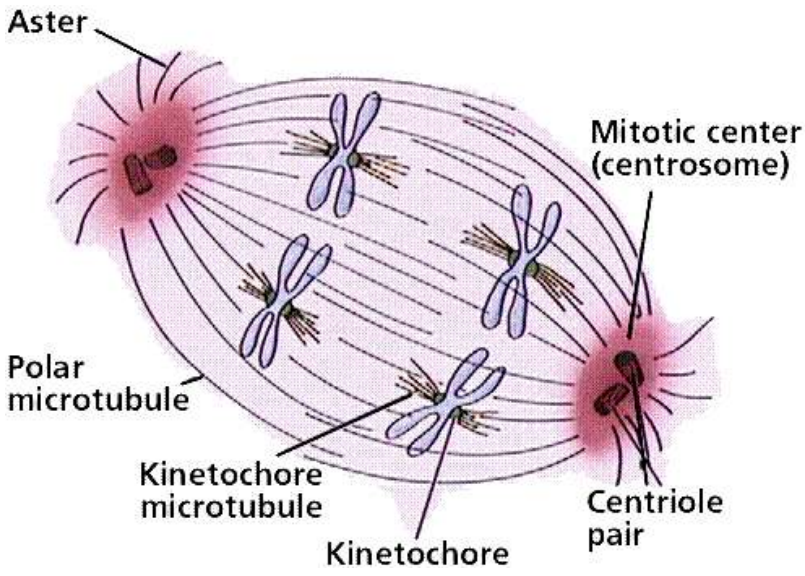
The Function of the Mitotic Spindle During Anaphase

- Anaphase begins when cohesins that hold sister chromatids of each chromosome together are cleaved by enzymes
  - As a result, the sister chromatids separate, becoming full-fledged chromosomes, and are moved along the kinetochore microtubules by motor proteins toward opposite ends of the cell
    - The microtubules shorten by depolymerizing at their kinetochore ends after the motor proteins have passed



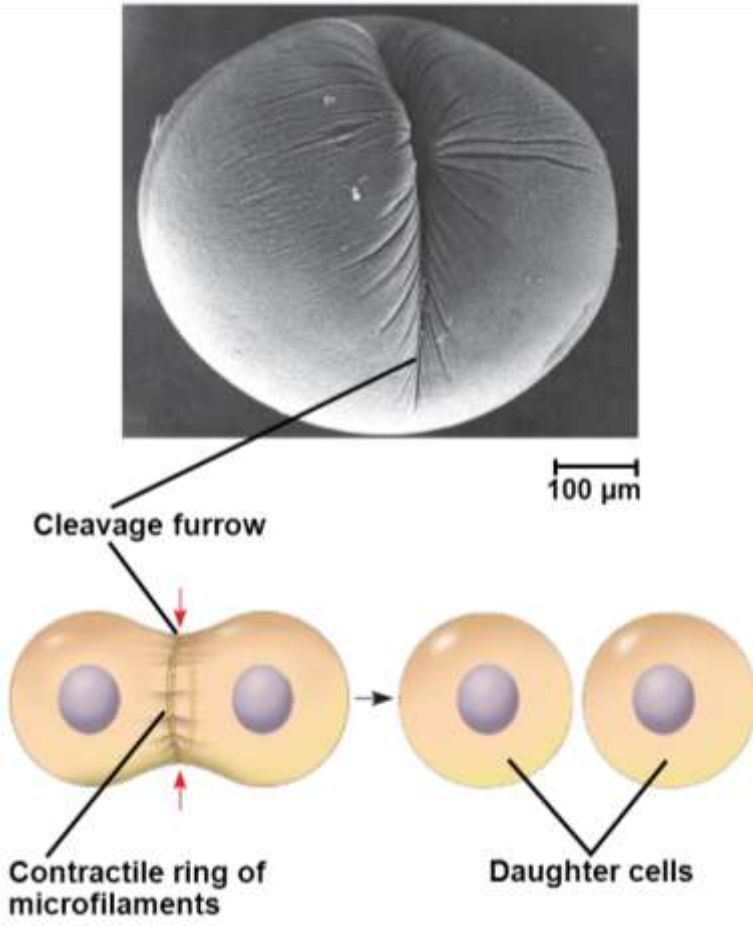
Function of Nonkinetochore Microtubules During Anaphase

- Nonkinetochore microtubules are responsible for elongating the cell during anaphase
  - Nonkinetochore microtubules from opposite poles of the cell overlap each other extensively during metaphase
    - During anaphase, this region of overlap is reduced as motor proteins attached to the microtubules “walk” them away from each other, using energy from ATP
    - As these microtubules push apart from each other, their spindle poles are also pushed apart, resulting in elongation of the cell
  - At the end of anaphase, duplicate groups of chromosomes have arrived at opposite ends of the elongated parent cell
  - In telophase, genetically identical daughter nuclei reform at opposite ends of the cell
  - Cytokinesis generally begins during anaphase or telophase



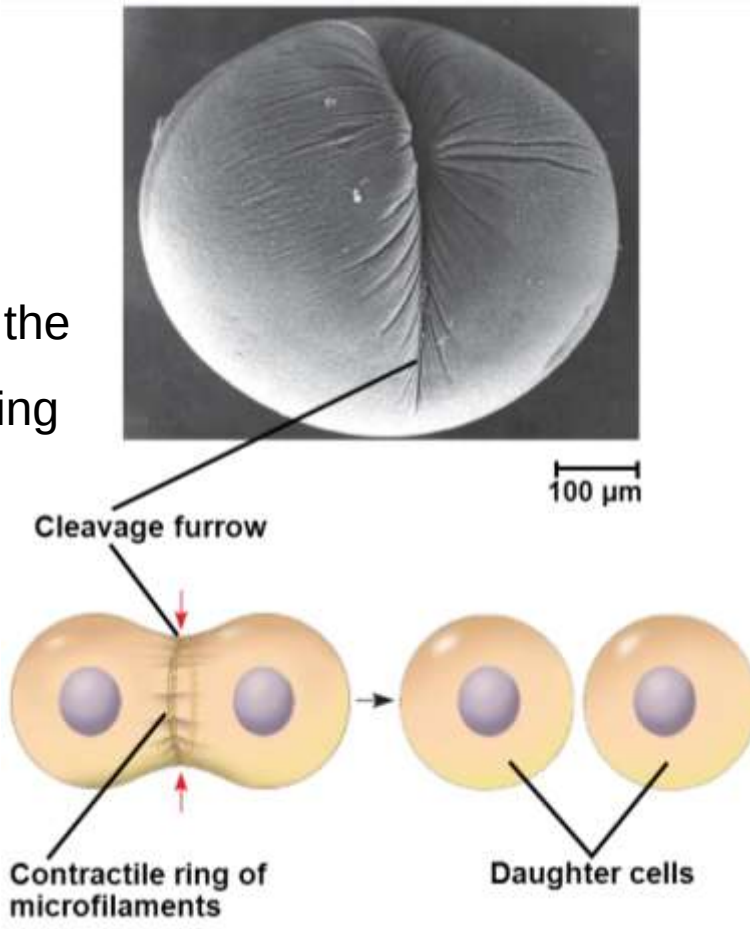
Cytokinesis in Animal Cells

- In animal cells, cytokinesis occurs by a process known as **cleavage**
  - The 1st sign of cleavage is the appearance of a shallow groove in the cell surface near the old metaphase plate
    - This groove is known as a **cleavage furrow**



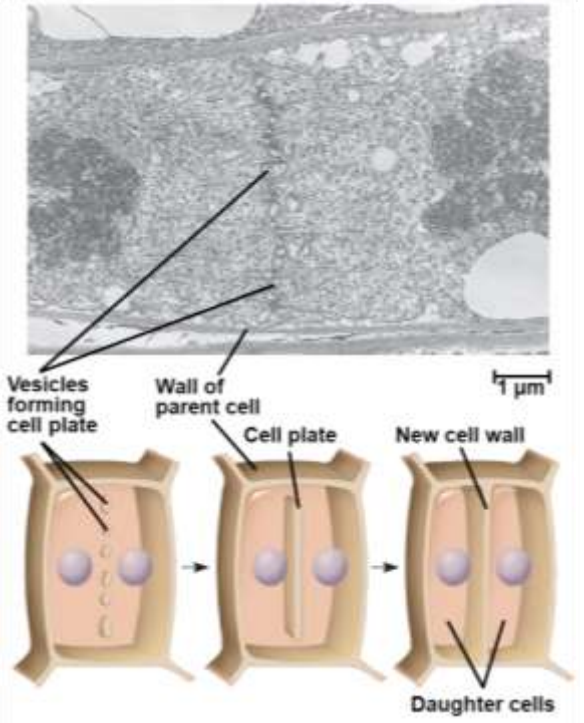
Cytokinesis in Animal Cells

- A contractile ring of actin filaments associated with molecules of the protein myosin forms on the cytoplasmic side of the furrow
  - The actin microfilaments interact with myosin molecules, causing the ring to contract
    - This contraction is like the pulling of drawstrings
      - It deepens the cleavage furrow until the parent cell is pinched in two, producing 2 completely separated cells
        - Each cell has its own nucleus, cytosol, organelles, and other subcellular structures

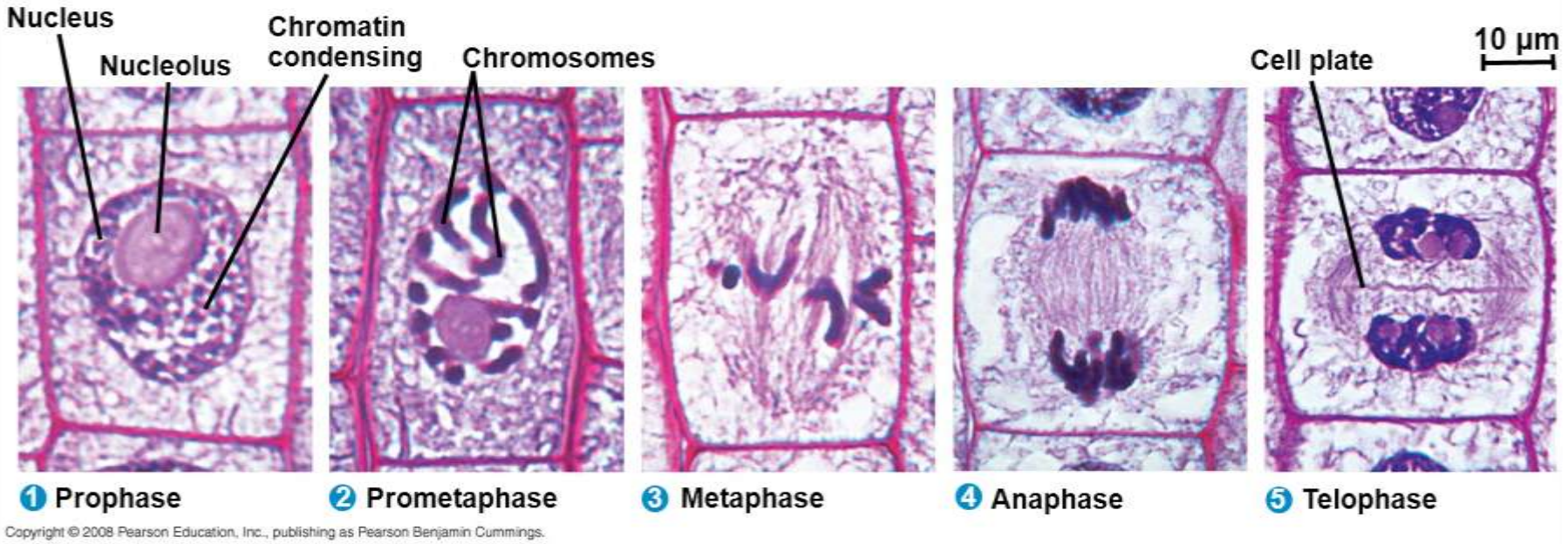


Cytokinesis in Plant Cells

- Cytokinesis in plant cells is markedly different because they have cell walls
  - In plant cells, a **cell plate** forms during cytokinesis (rather than a cleavage furrow)
  - During telophase, vesicles derived from the Golgi apparatus move along microtubules to the middle of the cell
    - Here, these vesicles coalesce to form the cell plate
    - Cell wall materials carried in the vesicles collect in the cell plate as it grows
    - The plate enlarges until its surrounding membrane fuses with the plasma membrane along the perimeter of the cell
  - Two daughter cells result, each with its own plasma membrane
    - Meanwhile, a new cell wall arising from contents of the cell plate has formed between the daughter cells

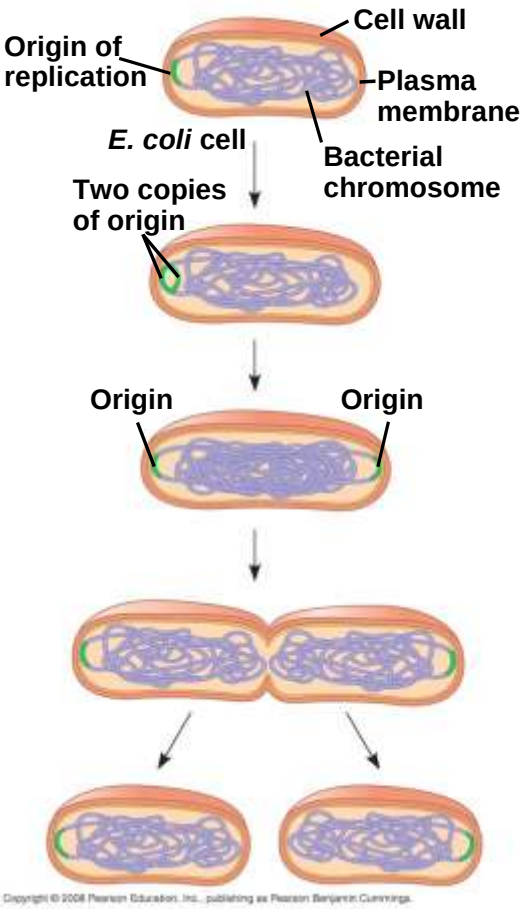


Mitosis In a Plant Cell



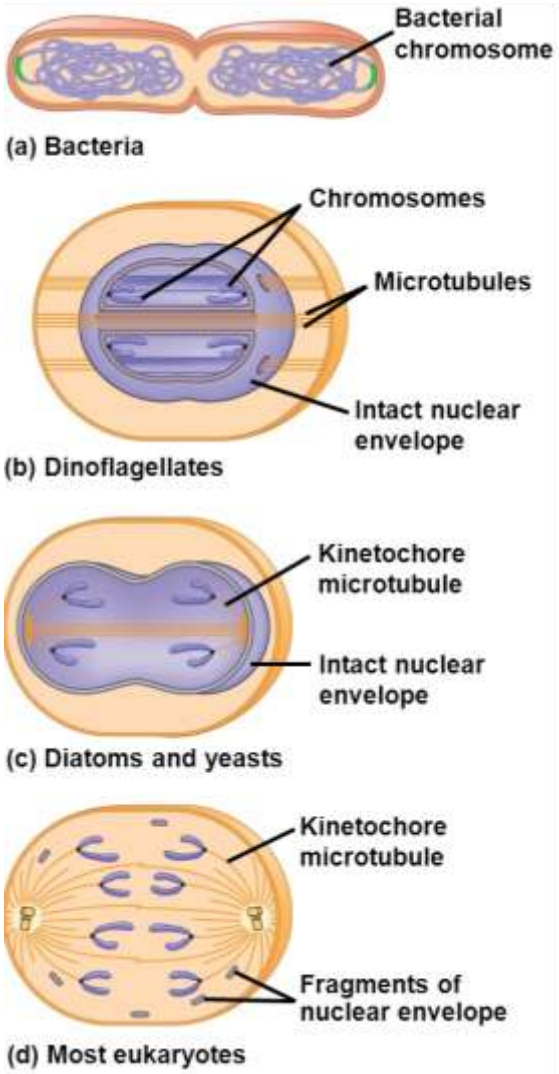
Binary Fission

- Prokaryotes (bacteria and archaea) reproduce asexually by a type of cell division called **binary fission**
  - This process begins when the single circular chromosome of a bacterium begins to replicate
    - This occurs in a specific place on the chromosome called the **origin of replication,** producing 2 origins
    - As the chromosome continues to replicate, one origin moves toward the opposite end of the cell
      - This results in one copy of the origin at each end of the cell
      - In the meantime, the cell also elongates
    - When replication finishes, the plasma membrane grows inward, and a new cell wall is deposited
      - This divides the parent cell into 2 genetically identical daughter cells, each with a complete genome



The Evolution of Mitosis

- Since prokaryotes evolved before eukaryotes, mitosis probably evolved from binary fission
    - This hypothesis is supported by the fact that some proteins involved in bacterial binary fission are related to eukaryotic proteins in mitosis
    - Possible intermediate stages are represented by two unusual types of nuclear division found today in certain unicellular eukaryotes
        - In both types, the nuclear envelope remains intact
            - In dinoflagellates, replicated chromosomes are attached to the nuclear envelope and separate as the nucleus elongates prior to dividing
            - In diatoms and yeasts, a spindle within the nucleus separates the chromosomes
        - In most eukaryotic cells, in contrast, the nuclear envelope breaks down and a spindle separates the chromosomes



Concept Check 12.2

- 1) How many chromosomes are shown in the diagram in Figure 12.7 (pp.234)? How many chromatids are shown?
- 2) Compare cytokinesis in plant and animal cells.
- 3) What is a function of nonkinetochore microtubules?
- 4) Identify 3 similarities between bacterial chromosomes and eukaryotic chromosomes, considering both structure and behavior during cell division.
- 5) Compare the roles of tubulin and actin during eukaryotic cell division with the roles of tubulin-like and actin-like proteins during bacterial binary fission.
- 6) During which stages of the cell cycle does a chromosome consist of 2 identical chromatids?

Concept 12.3:
The eukaryotic cell cycle is regulated by a molecular control system

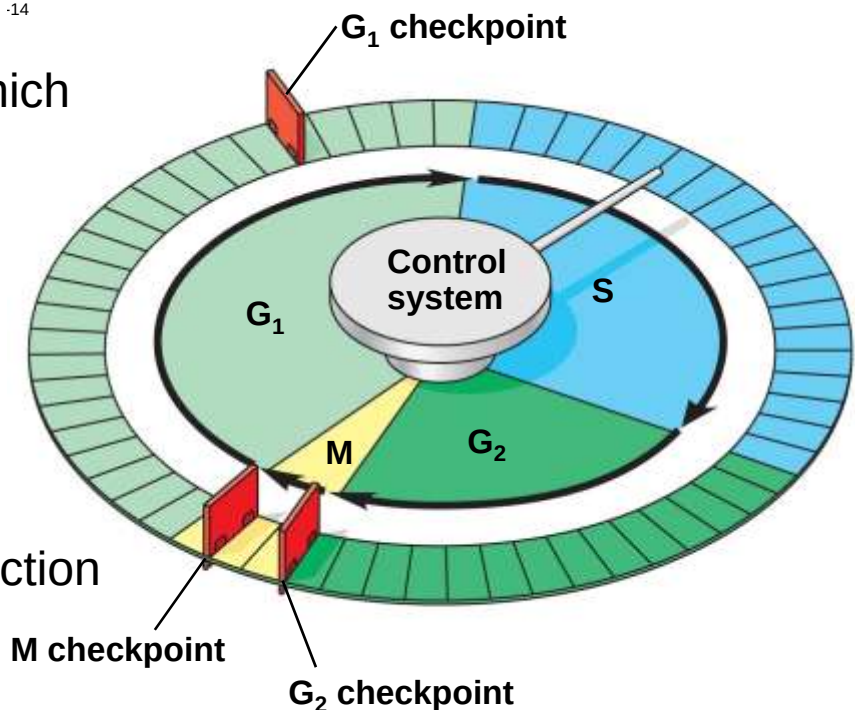
Timing and Rate of Cell Division

- The timing and rate of cell division in an organism are crucial to normal growth, development and maintenance
  - The frequency of cell division varies with the type of cell:
    - Ex) human skin cells divide frequently
    - Ex) Liver cells divide only when repair is needed
    - Ex) Some of the most specialized cells, including mature nerve and muscle cells, do not divide at all
  - These cell cycle differences result from regulation at the molecular level

The Cell Cycle Control System

- The cell cycle appears to be driven by specific chemical signals present in the cytoplasm

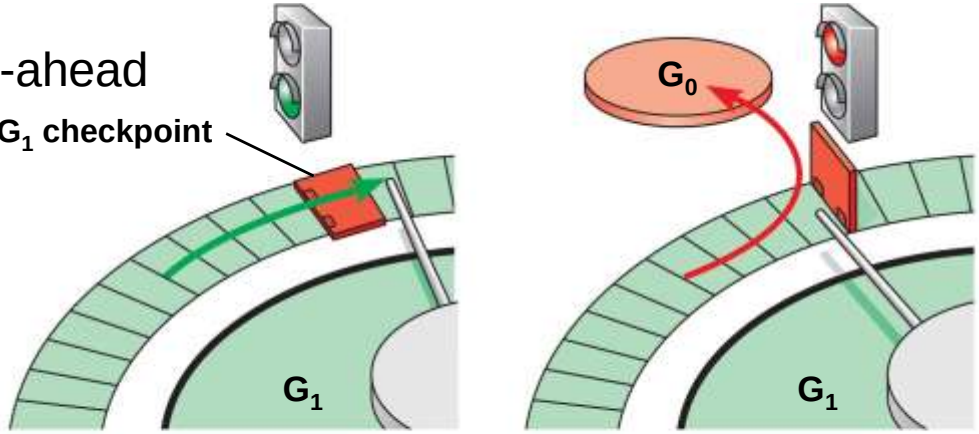
  - A distinct **cell cycle control system**, which consists of a cyclically operating set of molecules in the cell, both triggers and coordinates key events in cell cycle
    - This control system uses both internal and external controls to regulate the cell cycle
    - It has specific **checkpoints** that function as control points where the cell cycle stops until a go-ahead signal is received



      - Many signals come from surveillance mechanisms inside cell that report whether essential cellular processes have occurred and been completed correctly
        - These signals determine whether or not the cell cycle should proceed

The G_1 Checkpoint and the G_0 Phase

- For many cells, the G_1 checkpoint (called the "restriction point" in mammalian cells) seems to be the most important one
  - If a cell receives a go-ahead signal at the G_1 checkpoint, it will usually complete the G_1, S, G_2, and M phases and divide
  - If the cell does not receive the go-ahead signal, it will exit the cycle
    - The cell then switches into a nondividing state called the **G_0 phase**
      - Most cells in a mature organism are actually in the G_0 phase



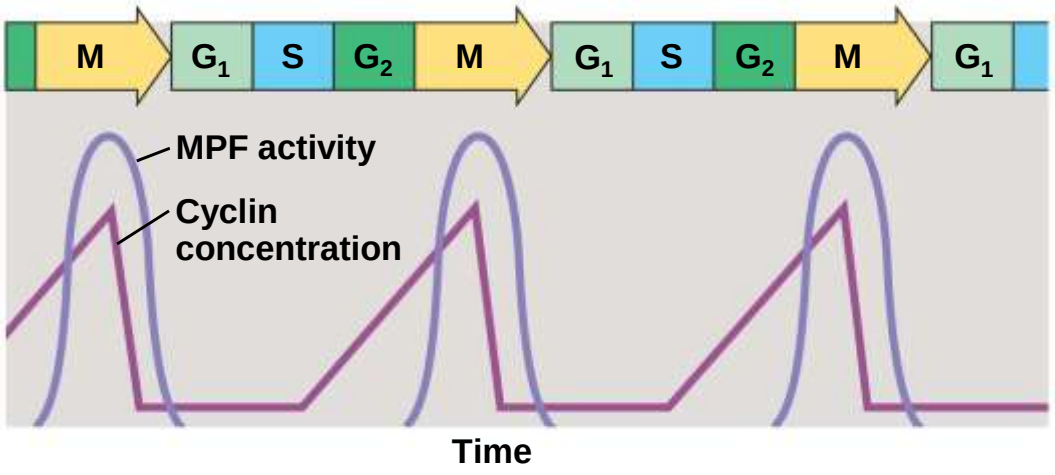
  - These cells can be "called back" from the G_0 phase to the cell cycle by external cues
    - Ex) Growth factors released in response to injury may stimulate liver cells to begin division

The Cell Cycle Clock: Cyclins and Cyclin-Dependent Kinases

- There are 2 main types of regulatory proteins involved in cell cycle control:
  - **Cyclins:** regulatory protein whose cellular concentration fluctuates
  - **Protein kinases:** enzymes that activate or inactivate other proteins by phosphorylating them
    - Many kinases are present at a constant concentration but remain inactivated until they become attached to a cyclin
      - These kinases are therefore called **cyclin-dependent kinases (Cdks)**
    - The activity of Cdks thus fluctuates with changes in cyclin concentrations

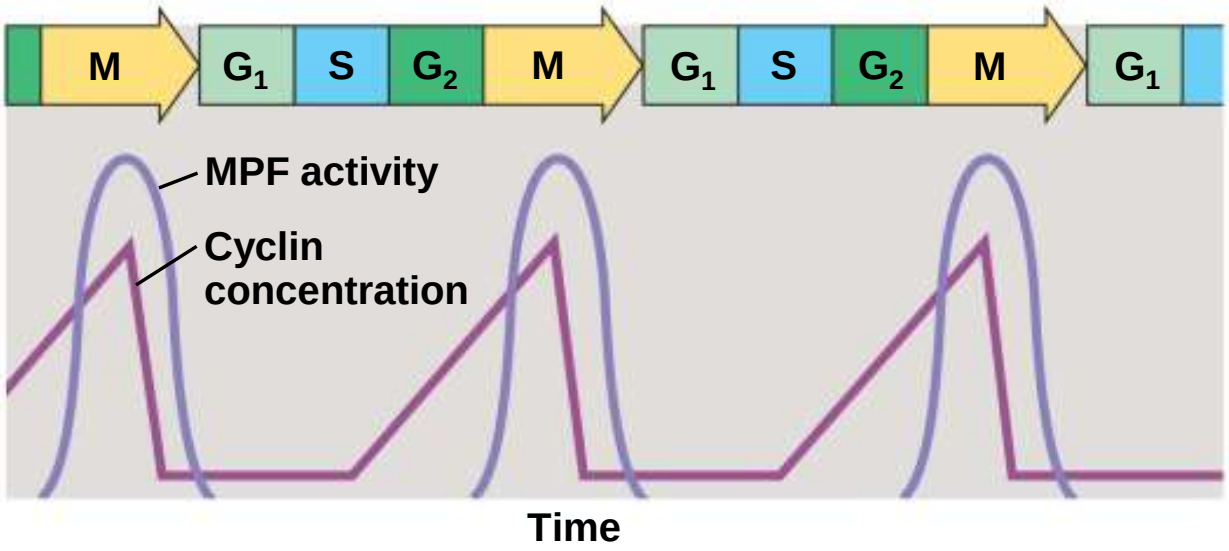
MPF

- **MPF** (maturation-promoting factor) is one cyclin-Cdk complex that triggers a cell's passage past the G_2 checkpoint into the M phase
    - For this reason, it can also be thought of as "M-phase-promoting factor"
- As cyclins accumulate during G_2 associate with Cdk molecules , the MPF complex is created
    - This complex then phosphorylates a variety of proteins that initiate mitosis
- MPF acts both directly as a kinase and indirectly by activating other kinases
    - MPF causes phosphorylation of proteins that promote fragmentation of the nuclear envelope
    - It also contributes to molecular events required for chromosome condensation and spindle formation during prophase



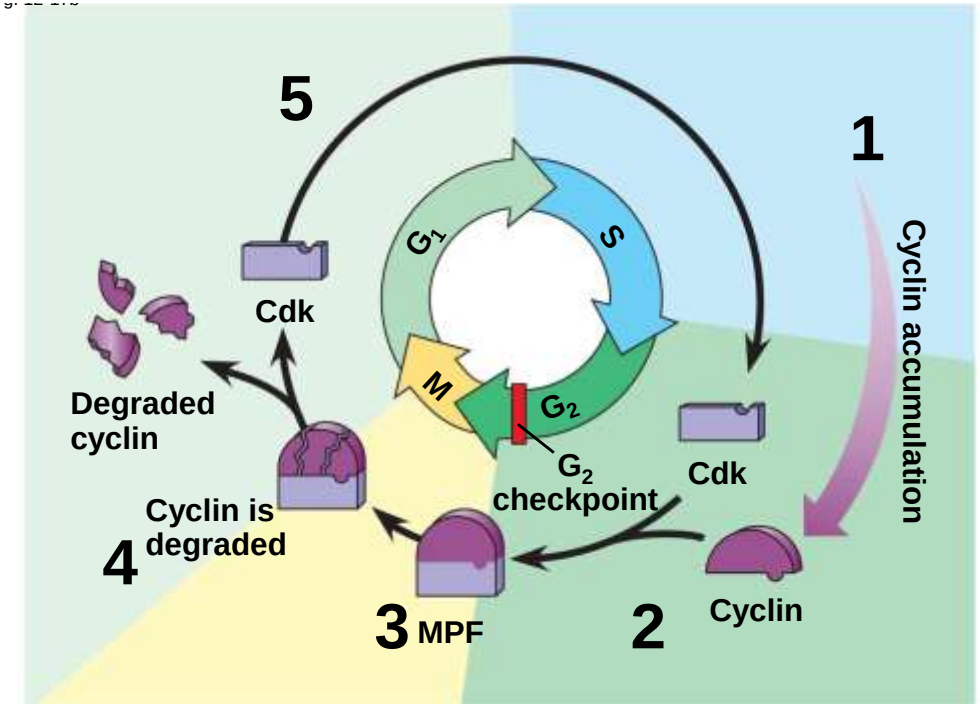
MPF Degradation

- MPF helps switch itself off by initiating a process that leads to the destruction of its own cyclin
  - The noncyclin part of MPF (Cdk) remains in the cell in inactive form until it associates with new cyclin molecules
    - These cyclin molecules are not synthesized until the S and G2 phases of the next round of the cell cycle



MPF and the Cell Cycle

- 1) Synthesis of cyclin begins late in the S phase and continues through G_2
  - Cyclin accumulates since it is protected from degradation at this stage
- 2) Accumulated cyclin combines with recycled Cdk, producing enough MPF to pass G_2 checkpoint and begin mitosis
- 3) MPF promotes mitosis by phosphorylating various proteins
  - MPF activity peaks during metaphase
- 4) During anaphase, the cyclin component of MPF is degraded
  - This terminates the M phase
  - The cell enters the G_1 phase
- 5) During G_1, cellular conditions favor degradation of cyclin
  - The Cdk component of MPF is recycled

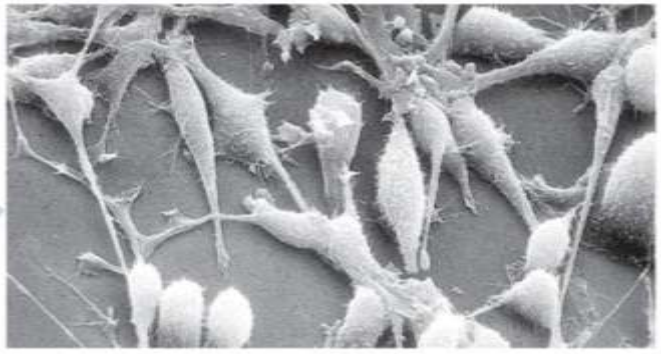


Stop and Go Signs: Internal Signals at the Checkpoints

- Both internal and external signals produce responses by Cdks and other proteins
    - One internal signal occurs at the M phase checkpoint
    - Anaphase (separation of sister chromatids) will not begin until all chromosomes are properly attached to the spindle at the metaphase plate
        - This occurs because kinetochores that are not attached to spindle microtubules send a molecular signal that delays anaphase
            - Only when the kinetochores of ALL chromosomes are attached to the spindle does the appropriate regulatory protein become activated
        - Once activated, this protein sets off a chain of molecular events that ultimately results in the enzymatic cleavage of cohesins and separation of sister chromatids
            - This mechanism ensures that daughter cells do not end up with missing or extra chromosomes

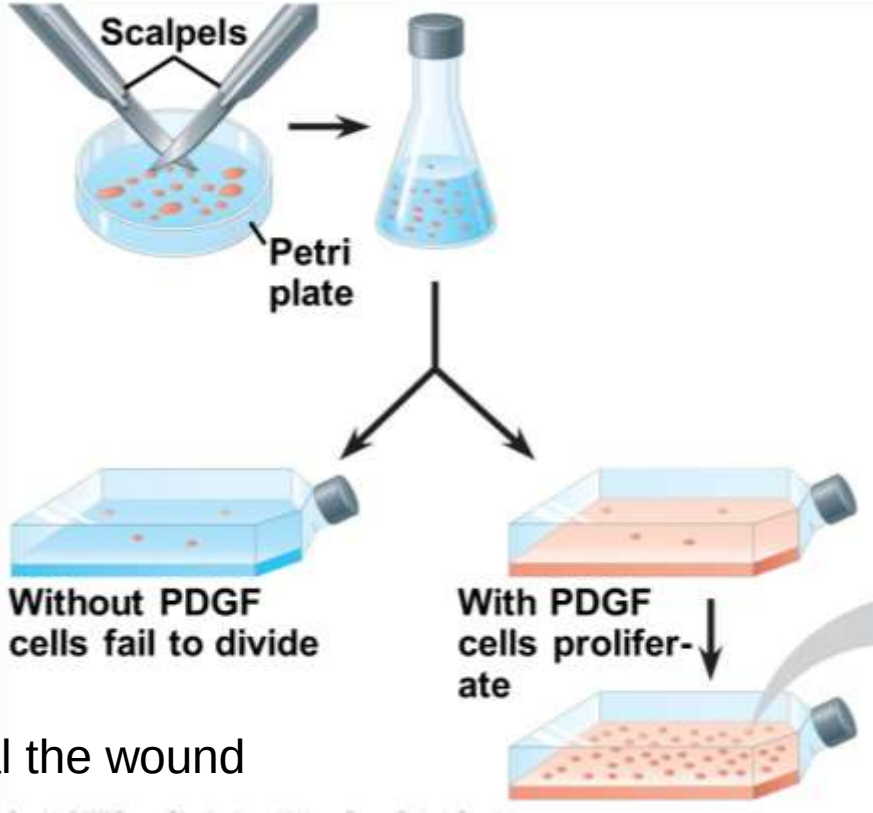
Stop and Go Signs: External Chemical Signals at the Checkpoints

- In addition, many external factors, both chemical and physical, can influence cell division
  - Cells will fail to divide if an essential nutrient is lacking in their culture medium
    - Furthermore, most mammalian cells divide in culture only if the growth medium includes specific growth factors
      - Recall: **Growth factors** are proteins released by certain cells that stimulate other cells to divide
    - Ex) *Platelet-derived growth factor* (PDGF), made by blood cell fragments called platelets, is required for the division of fibroblasts in culture



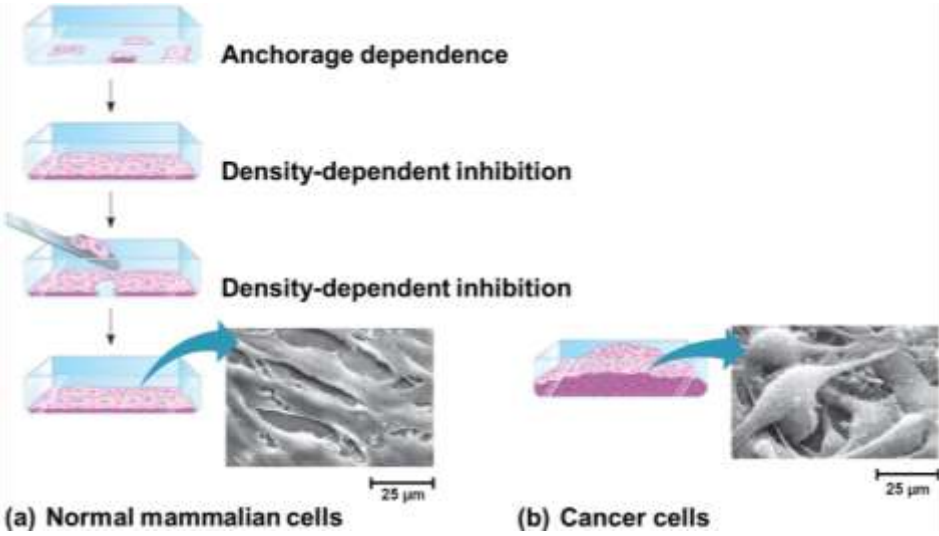
External Chemical Signals at the Checkpoints: PDGF

- Fibroblasts are a type of connective tissue cell that have PDGF receptors on their plasma membranes
  - Binding of PDGF molecules to these receptors (which are receptor tyrosine kinases) triggers a signal transduction pathway that allows cells to pass the G_1 checkpoint and divide
    - PDGF stimulates fibroblast division both in the artificial conditions of cell culture (see illustration) and in an animal's body
  - When an injury occurs, platelets release PDGF in the vicinity, resulting in proliferation of fibroblasts to help heal the wound



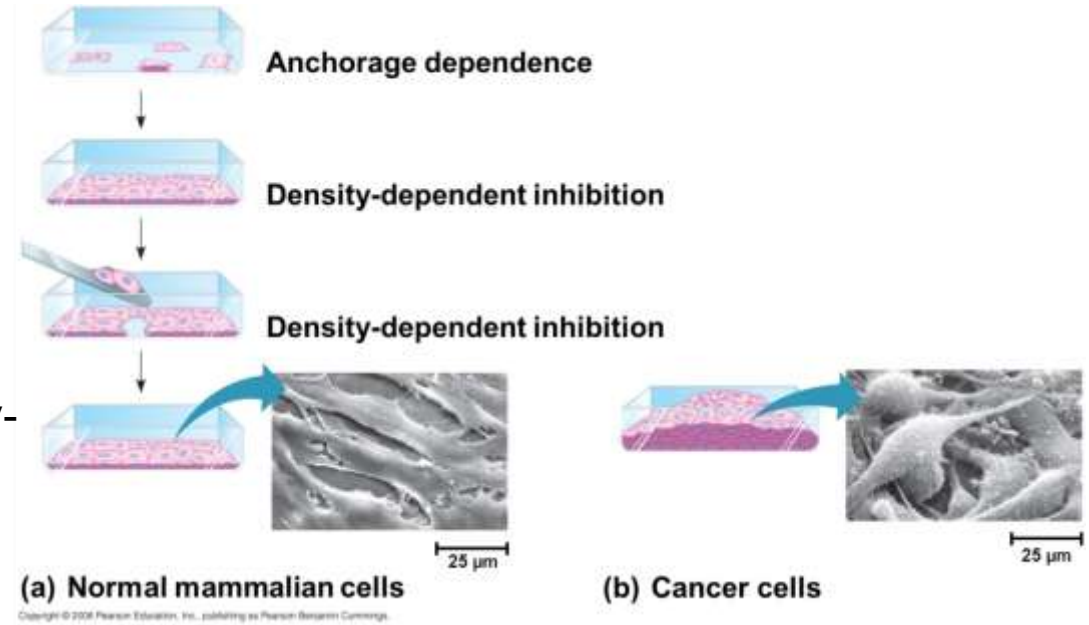
External Physical Signals: Density-Dependent Inhibition

- External signals that are physical can also regulate cell division
  - One common example is **density-dependent inhibition**, which causes crowded cells to stop dividing
  - It has been observed that cultured cells normally divide until they form a single layer of cells on the inner surface of the culture container
    - At this point, the cells in the culture stop dividing
    - Furthermore, if some cells are removed, those cells bordering the open space begin dividing again and continue until the vacancy is filled
  - Studies have shown that binding of a cell-surface protein to its counterpart on an adjoining cell sends a growth-inhibiting signal to both cells
    - This signal prevents the cells from moving forward in the cell cycle, even in presence of growth factors



External Physical Signals: Anchorage Dependence

- External signals that are physical can also regulate cell division
  - Another example of external physical signals that regulate cell division is anchorage dependence
    - This phenomenon is exhibited by most animal cells
  - In this type of dependence, cells must be attached to some sort of substratum (ex: inside of culture jar, extracellular matrix of tissue) in order to divide
    - Experiments suggest that anchorage is signaled to the cell cycle control system via pathways involving plasma membrane proteins and elements of the cytoskeleton that are linked to these proteins
- Cancer cells exhibit neither density-dependent inhibition nor anchorage dependence



Loss of Cell Cycle Controls in Cancer Cells

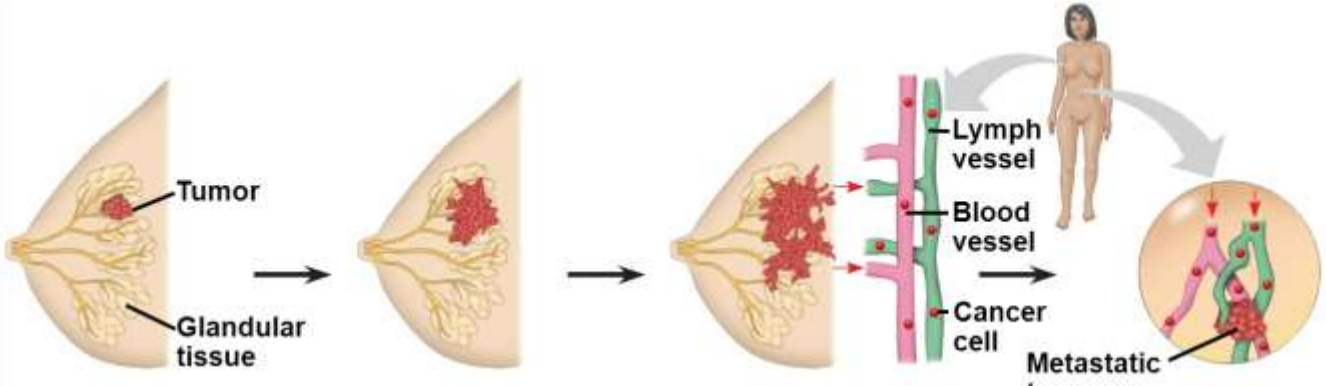
- Cancer cells do not respond normally to the body's control mechanisms
  - They divide excessively and invade other tissues
  - As mentioned, cancer cells lack density-dependent inhibition and anchorage dependence
    - They also do not stop dividing when growth factors are depleted
      - It is hypothesized that cancer cells may not need growth factors to grow and divide:
        - They may make their own growth factor
        - They may convey a growth factor's signal by themselves, without the presence of the growth factor
        - They may have an abnormal cell cycle control system
  - Cancer cells are also different from normal cells because they are "immortal"
    - Cancer cells can go on dividing indefinitely in culture if they are given a continual supply of nutrients
      - In contrast, nearly all normal mammalian cells divide only 20-50X before they die

Conversion of Normal Cells to Cancer Cells

- A normal cell is converted to a cancerous cell by a process called **transformation**
  - The immune system normally recognizes transformed cells and destroy them
  - If these transformed cells do evade destruction, however, they may proliferate and form tumors
    - Tumors are masses of abnormal cells within otherwise normal tissue
  - If the abnormal cells remain at the original site, the lump is called a **benign tumor**
      - Most benign tumors do not cause serious problems and can be surgically removed
  - **Malignant tumors** invade surrounding tissues and can **metastasize**
    - Metastasis means that cancer cells have been exported to other parts of the body, where they may form secondary tumors

Malignant Tumors

- Cells of malignant tumors are abnormal in many ways
  - They may have unusual numbers of chromosomes
  - Their metabolism may be disabled, causing them to stop functioning properly
  - Abnormal changes on their cell surfaces may cause them to lose attachments to neighboring cells and the extracellular matrix
    - This thereby allows them to spread to nearby tissues
      - This metastasis occurs when cancer cells secrete signal molecules that cause blood vessels to grow toward the tumor
      - Tumor cells may then separate from the original tumor and enter the blood and lymph vessels and travel to other parts of body
      - There, they may proliferate and form a new tumor



Treatment of Malignant Tumors

- Localized malignant tumors may be treated with high-energy radiation
  - This radiation damages DNA in cancer cells much more than DNA of normal cells
    - This occurs because most cancer cells have lost their ability to repair such damage
- Furthermore, drugs that are toxic to actively dividing cells can also be administered to the circulatory system in a treatment called chemotherapy
  - These drugs interfere with specific steps in cell cycle
    - Ex) The chemotherapy drug Taxol freezes the mitotic spindle by preventing microtubule depolymerization, which stops actively dividing cells from proceeding past metaphase
  - The undesirable side effects of chemotherapy are due to the effect of these drugs on normal cells that divide often
    - Nausea results from effects on intestinal cells
    - Hair loss results from effects on hair follicle cells
    - Susceptibility to infection results from effects on immune system cells

Concept Check 12.3

- 1) What is the go-ahead signal for a cell to pass the G2 phase checkpoint and enter mitosis (see Figure 12.17, pp. 240)?
- 2) What phase are most of your body cells in?
- 3) Compare and contrast a benign tumor and a malignant tumor.
- 4) What would happen if you performed the experiment in Figure 12.18 (pp.241) with cancer cells?

You should now be able to:

1. Describe the structural organization of the prokaryotic genome and the eukaryotic genome
2. List the phases of the cell cycle; describe the sequence of events during each phase
3. List the phases of mitosis and describe the events characteristic of each phase
4. Draw or describe the mitotic spindle, including centrosomes, kinetochore microtubules, nonkinetochore microtubules, and asters

5. Compare cytokinesis in animals and plants

6. Describe the process of binary fission in bacteria and explain how eukaryotic mitosis may have evolved from binary fission

7. Explain how the abnormal cell division of cancerous cells escapes normal cell cycle controls

8. Distinguish between benign, malignant, and metastatic tumors