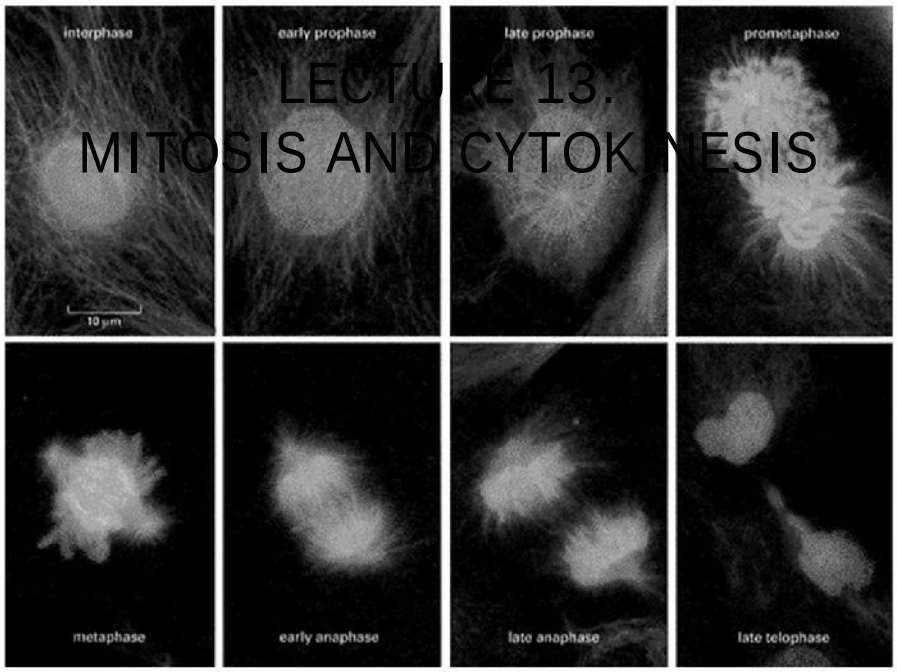


LECTURE 13: MITOSIS AND CYTOKINESIS

LEARNING OUTCOME

Students, after mastering materials of the present lecture, should be able

1. to explain signal transduction
2. to explain cell division
3. to explain cytokinesis in the life of plants
4. to explain the position of mitosis in cell cycle
5. to explain the process of mitosis

LECTURE LAYOUT

I. INTRODUCTION

1. **Changes**
2. **Signal**
3. **Signal Transduction**

II. CELL DIVISION

1. Eukaryotic Cell Division

2. Definition

2. Genetic Material

3. Spindle apparatus

III. MITOSIS AND CYTIKINESIS

1. Cell Cycle

2. Interphase

3. Mitosis

4. Cytokinesis

QUESTIONS

- Who orders the cells to start to divide?

  or

- What triggers mitosis/cell division to start?
  - There is no one event or set of conditions that will stimulate all cells to begin mitosis.
  - A small number of eukaryotic cells are genetically programmed to pass through the cell cycle and undergo mitosis as soon as they can.
  - Yeast cells are good examples of this; so long as there is ample food, they will grow and reproduce as quickly as possible.

https://www.adapaonline.org/bbk/tiki-index.php?page=Leaf%3A+What+triggers+mitosis%2Fcell+division+to+start%3F

I. INTRODUCTION

1. Changes

"You cannot step twice into the same river"

- Heraclitus of Ephesus (c.535 BCE-475 BCE), a Greek philosopher before Socrates, is known for his doctrine of change being central to the universe with an epigram;

  Everything changes and nothing remains still ... and ... you cannot step twice into the same stream for other waters are ever flowing on to *you*

- Good character is not formed in a week or a month. It is created little by little, day by day. Protracted and patient effort is needed to develop good character.

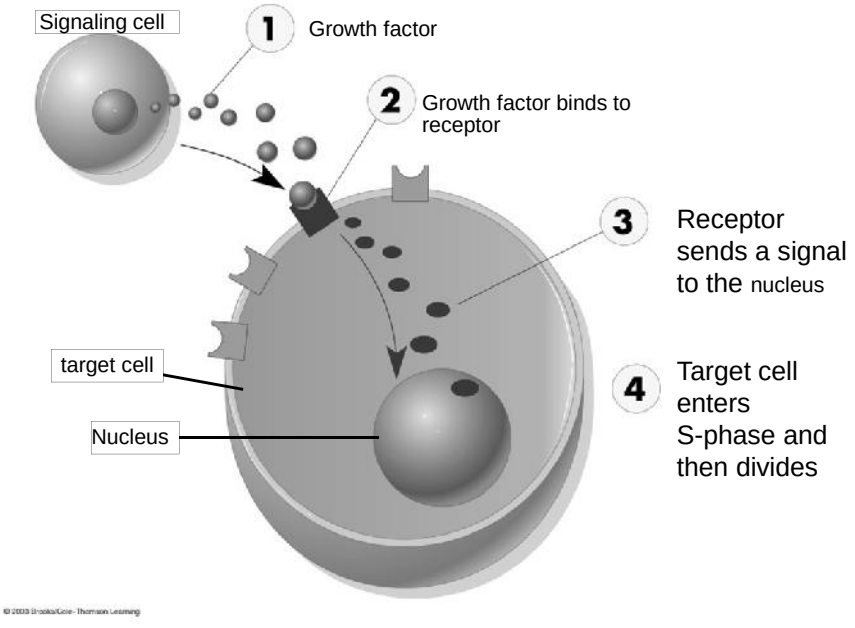
- You literally are not the same person you were in the past
  - Your bone marrow is producing 2 million red blood cells PER SECOND!
  - Skin cells divide once every 20-30 minutes
- Changes are due partly to cell division that is required for Growth & Development and Repair
  - Human zygote = **1 cell** →Mature adult = **1 X 10^{14} cells**
  - Cell division is used to *replace damaged cells* and *repair worn out tissues.*

2. Signals

- In multicellular organisms, nearly all cells wait for specific conditions (**signals**) before they progress through mitosis.

- For example, normal hepatocytes (liver cells) divide about once a year. Yet if the liver is injured or damaged, within a few hours they begin dividing to replace the damaged cells

- Some cells get a **signal** to divide so frequently and seem to be dividing continuously (like yeasts).
  - The cells lining our stomach are good examples, and replaced every 2 days, and take about 1.5 days to divide, and so appear never to stop.
- Other cells rarely, if ever, get the **signal** to divide.
  - Until a few years ago, biologists thought neurons never divided once a mammal reached maturity.
  - On average, each neuron in a person's nervous system will divide once or twice in their lifetime.

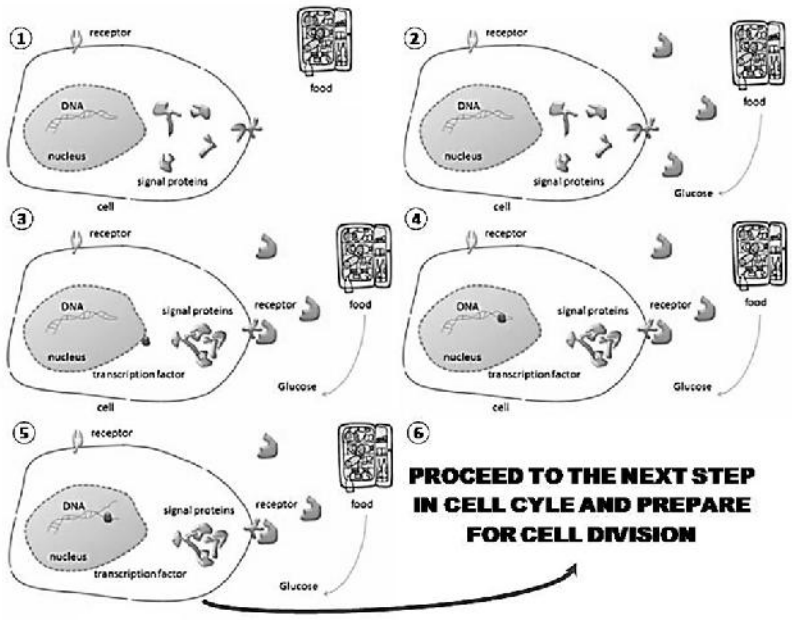


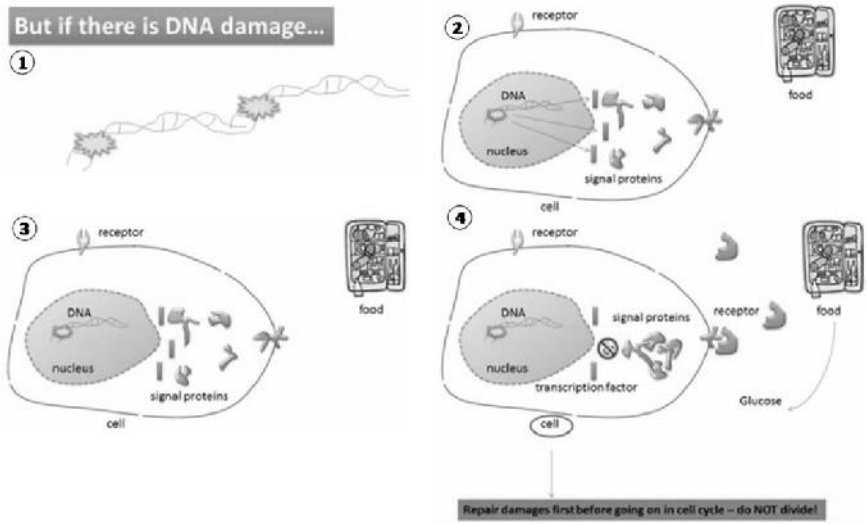
3. Signal Transduction

- How do cells sense the conditions that trigger the start of mitosis?
  - Signal transduction is a general term for **paths and mechanisms cells use** to sense and respond to external or internal factors. Signal transduction pathways (STP) let cells:
    - Detect conditions and chemical signals in their surroundings, and Monitor intracellular conditions
  - STP, depending on what signal the cells detect in the environment, can:
    - Amplify and transmit messages
    - Turn specific genes on or off
    - Change cell shape or behavior
    - Secrete substances
    - Start down the pathway to mitosis.

An example of signal transduction: how yeast cells begin mitosis

- Yeast cells "decide" to undergo mitosis based on
  - food availability to support a new generation (an external signal).
- But yeast cells with damaged DNA (internal signal) should not divide.
  - to prevent to transmit the mutation to the next generation.
- The external factor (nutrient availability) and internal factor (state of the DNA) are starting signals that activate receptor proteins that turn on protein cascades.
  - Ample food activates transcription of the proteins a yeast cell needs to pass through the G1 checkpoint.
  - DNA damage blocks transcription of these proteins


1
receptor
food
DNA
nucleus
signal proteins
cell
2
receptor
food
DNA
nucleus
signal proteins
Glucose
cell
3
receptor
DNA
signal proteins
receptor
food
nucleus
transcription factor
Glucose
cell
4
receptor
DNA
signal proteins
receptor
food
nucleus
transcription factor
Glucose
cell
5
receptor
DNA
signal proteins
receptor
food
nucleus
transcription factor
Glucose
6
PROCEED TO THE NEXT STEP
IN CELL CYLE AND PREPARE
FOR CELL DIVISION


But if there is DNA damage…
1
2
receptor
food
DNA
nucleus
signal proteins
cell
3
receptor
food
DNA
nucleus
signal proteins
cell
4
receptor
DNA
signal proteins
receptor
food
nucleus
transcription factor
Glucose
cell
Repair damages first before going on in cell cycle – do NOT divide!

II. CELL DIVISION

1. The signaling pathways

- **Cell division** (*segregation of the chromosomes duplicated in S phase*)**,** is **triggered at the end of G2 phase,** and followed by **cytokinesis** (*division of the cytoplasm or cell per se*).
- The daughter cells require a complete set of genetic instructions in order to

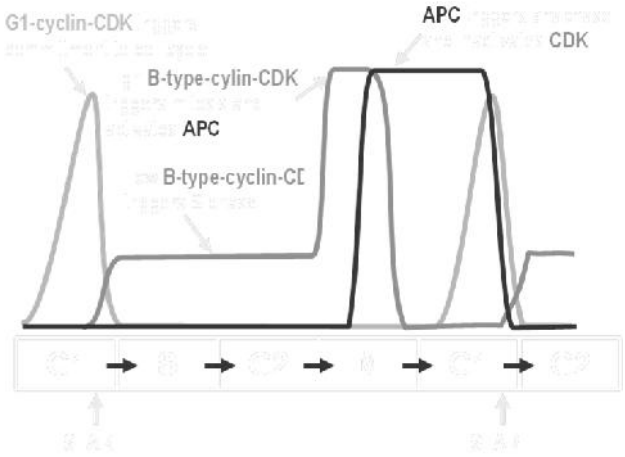
  (i) produce required molecules, and

  (ii) direct life processes.
- An orderly process is required to duplicate and distribute chromosomes through successive cell divisions.

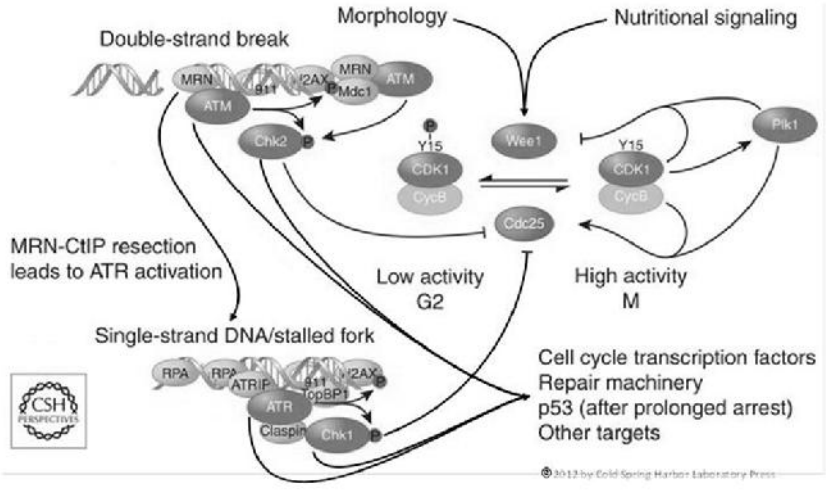
2. CDK1 and APC

- Two major transitions are required for cell division to occur:
  - the **G2/M transition** and
  - the M**etaphase/Anaphase transition**.
- These are regulated by the protein kinase **cyclin-dependent kinase 1** (**CDK1**) and the **anaphase-promoting complex** (**APC**, an **E3 ubiquitin ligase**) respectively.
- **CDK1** is maintained at a low level of activity during G2 phase.
- Full CDK activation triggers mitosis and activates APC, which triggers anaphase and feeds back to inactivate CDK activity.

- The onset of mitosis is brought about by the activation of CDK1.



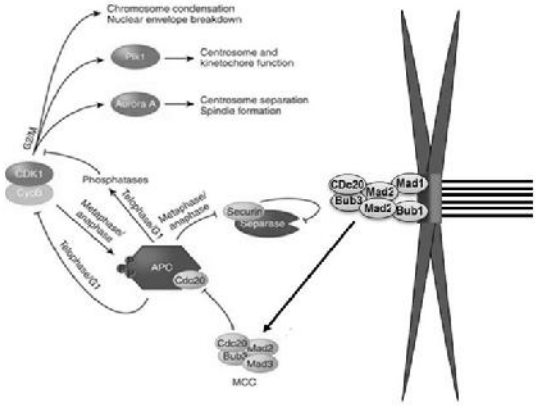
The major events of the cell cycle



Signaling at the G2/M transition. The rate-limiting step for the transition from G2 to mitosis is the dephosphorylation of CDK1 on Y15, and in some organisms T14.

Signaling at the M/A transition

To establish metaphase, CDK1 directly, and indirectly through a network of kinases including Plk1 and Aurora A, phosphorylates substrates that trigger nuclear envelope breakdown, chromosome condensation, centrosome separation, and spindle assembly.

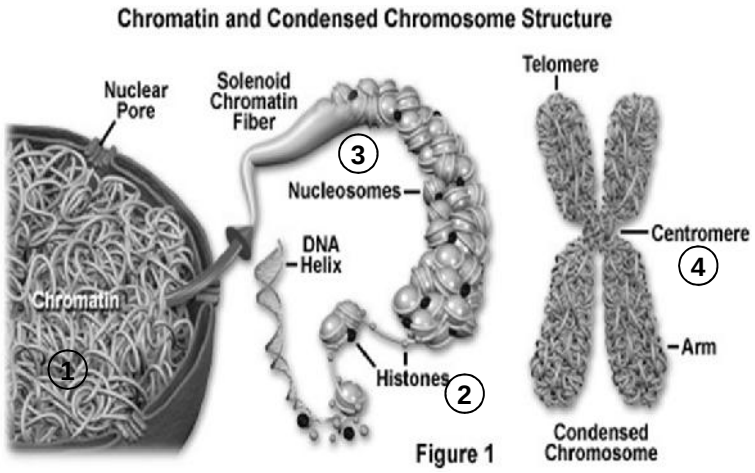


In addition, in animal cells CDK1 activates the Greatwall kinase, which indirectly inactivates the CDK-antagonizing PP2A-B55 phosphatase via phosphorylation of the small phosphatase inhibitors Arpp19 and endosulfine.

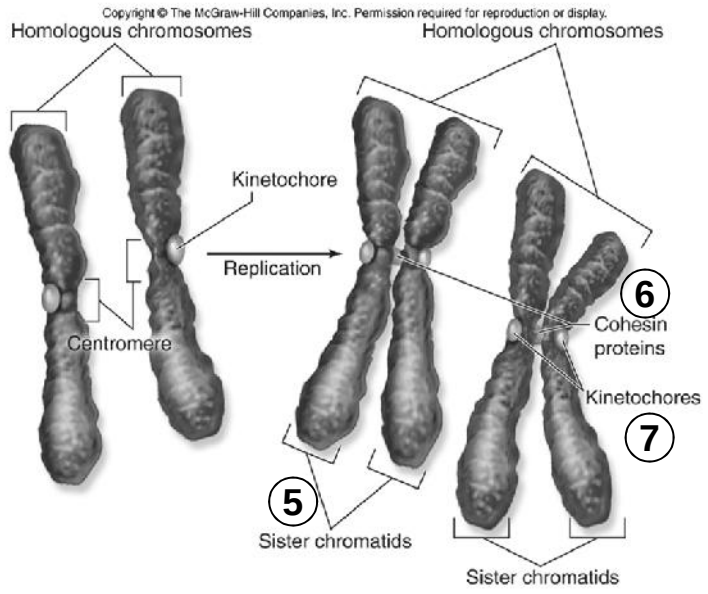
3. Genetic Material

1. During cell division, the genetic material **DNA** needs to be **copied** and divided between the two new cells
2. DNA in cells is divided into long chains called **chromosomes** (“volumes” of DNA).
3. Normally chromosomes are spread out, not identifiable, in a form called **chromatin**
4. During mitosis, chromosomes condense and then fold up
5. Chromosome DNA is wrapped around proteins called **histones** to organize it
6. **Nucleosome:** unit of DNA wrapped around histones.
7. The replicated chromosomes stay together and are called **sister chromatids.**
8. Sister chromatids are attached at the **centromere** by proteins called **cohesins.**

9. The other side of the centromeres contain other proteins called **kinetochore**



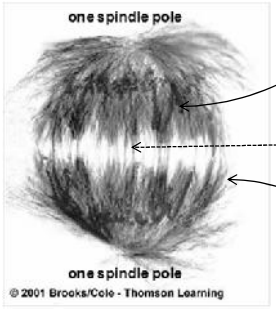
1. Chromatin **2. Histones** **3. Nucleosome** **4. Centromere**



5. Sister chromatids **6. Cohesins** **7. Kinetochore**

4. Spindle apparatus

- Spindle apparatus consists of two distinct sets of microtubules
  - Each set extends from one of the cell poles
  - Two sets overlap at spindle equator
- This helps to move chromosomes during mitosis
- In both plant and animal cells, spindle fibers originate from centrosomes; in animal cells, centrosomes are centrioles



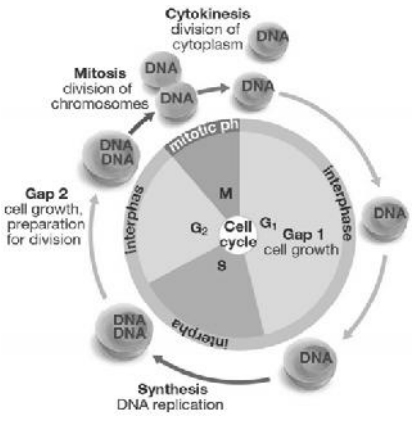
III. MITOSIS AND CYTOKINESIS

1. Cell Cycle

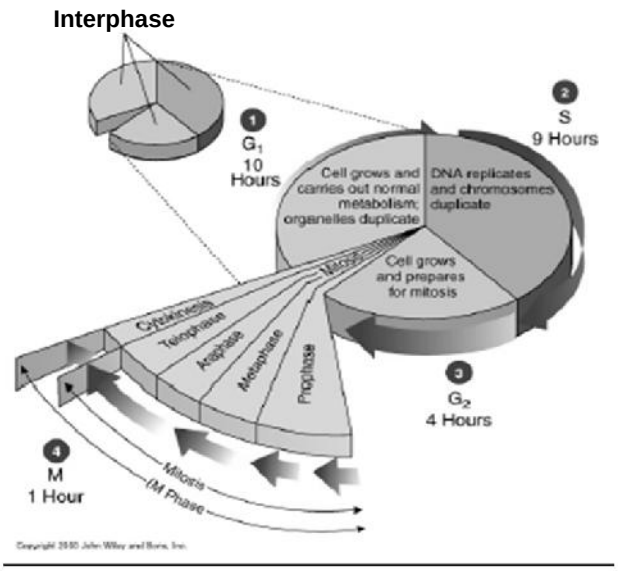
1. Interphase
- G phase
- S phase

2. Mitosis (M Phase)
- Nuclear Division

3. Cytokinesis (C phase)
- Cytoplasmic Division



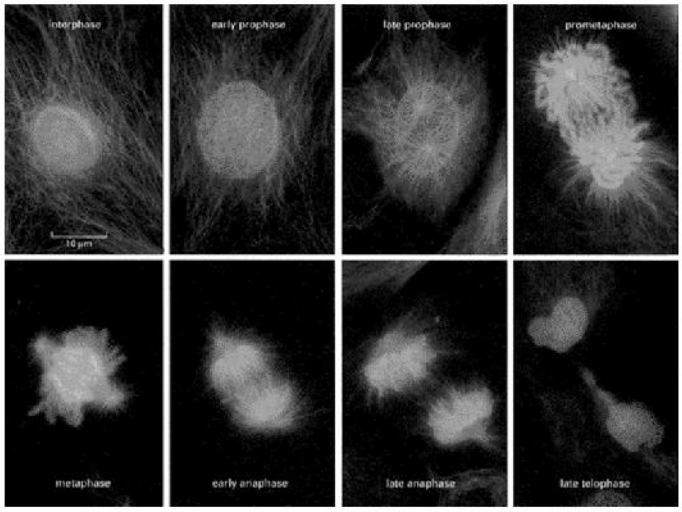
In multicellular organisms like us, progress through the cell cycle is carefully regulated.



For fast-dividing mammalian cells, the length of the cycle is approximately 24 hours

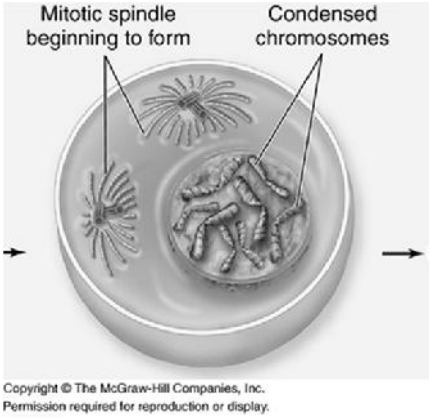
- Mitosis can be subdivided into six distinct phases:
  - (1) prophase, in which the spindle begins to assemble in the cytoplasm and chromosomes begin to condense in the nucleus;
  - (2) prometaphase, in which the nuclear envelope breaks down and chromosomes attach to the spindle;
  - (3) metaphase, in which chromosomes align at the spindle midzone;
  - (4) anaphase A, in which chromosomes move to the centrosomes, which form the spindle poles;
  - (5) anaphase B, in which the spindle elongates; and
  - (6) telophase, in which the nuclear envelope reforms around the new daughter nuclei.

Mitosis in Action



Blue shows DNA, green shows spindle fibers.

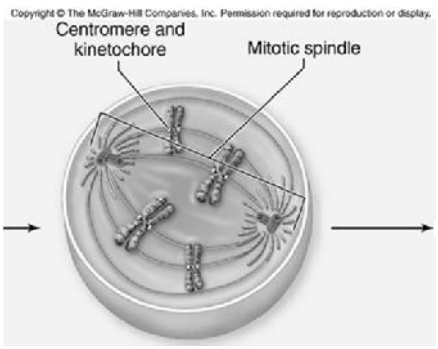
1. Prophase:
   1. Chromosomes continue to condense and become visible
   2. Chromosomes appear as two sister chromatids held together at centromere
   3. Centrioles move to each pole of the cell



   4. Cytoskeleton is disassembled, and spindle apparatus is assembled
   5. Nuclear envelope dissolves, golgi and ER are dispersed

2. Prometaphase:

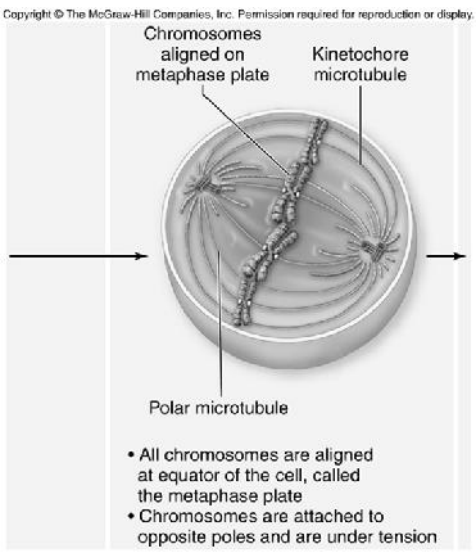
1. Chromosomes become attached to the microtubules or spindle apparatus at the kinetochores
2. Each chromosome is oriented such that the kinetochores of sister chromatids are attached to microtubules from opposite poles

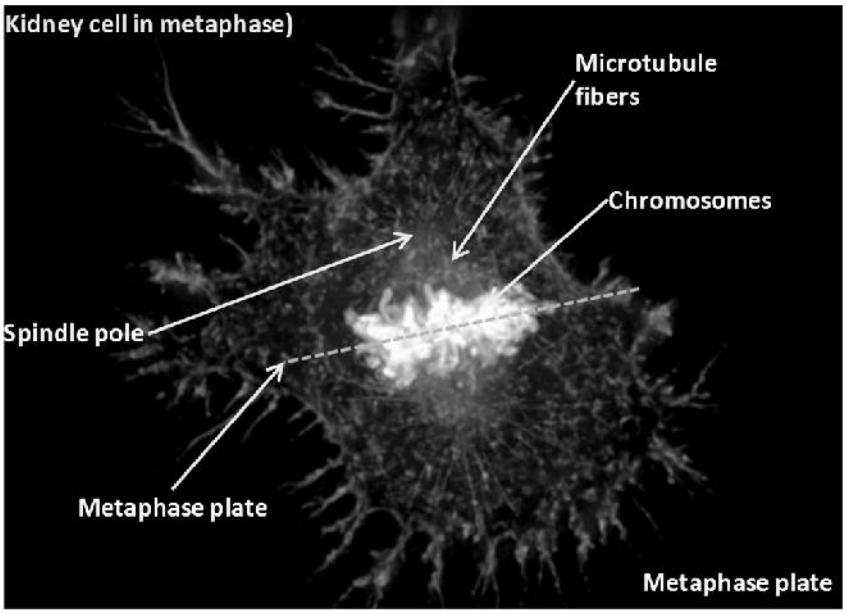


3. Microtubules begin to pull each chromosome toward the center (the equator) of the cell

3. Metaphase:

1. Microtubules pull the chromosomes to align them at the center of the cell
2. **Metaphase plate**: imaginary plane through the center of the cell where the chromosomes align



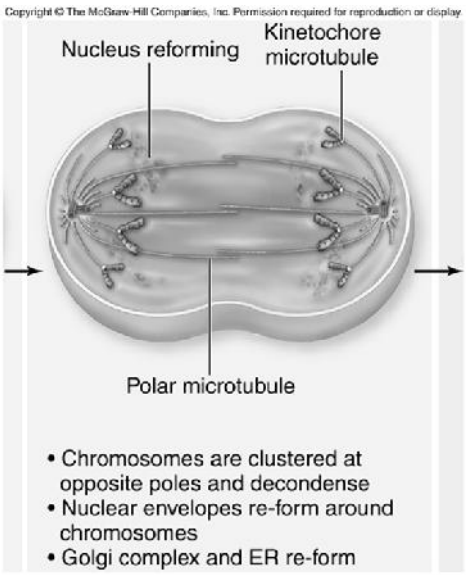


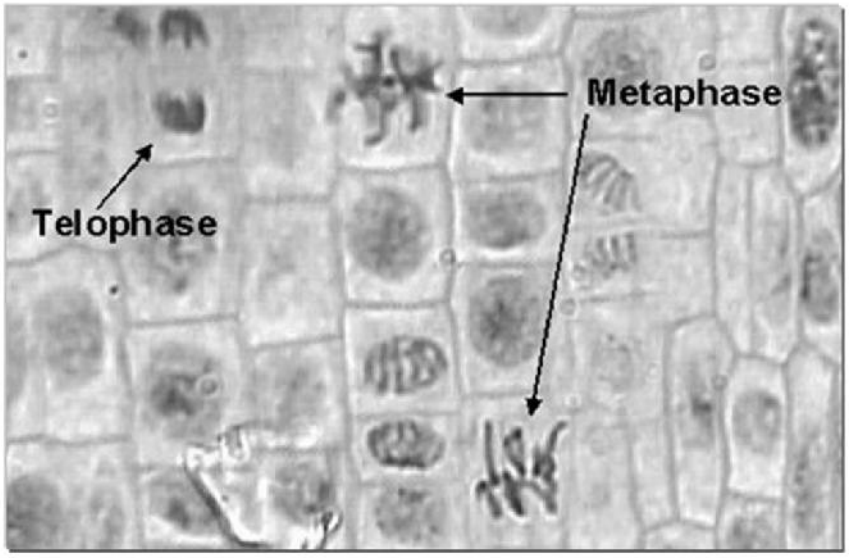
Kidney cell in mitosis (metaphase) showing actin by Dr. Paul Andrews at 100x objective

http://fyeahmedlab.tumblr.com/post/27469407377/fyeahuniverse-kidney-cell-in-mitosis

5. Telophase:

1. Spindle apparatus disassembles
2. Nuclear envelope forms around each set of sister chromatids
3. Chromosomes begin to uncoil
4. Nucleolus reappears in each new nucleus

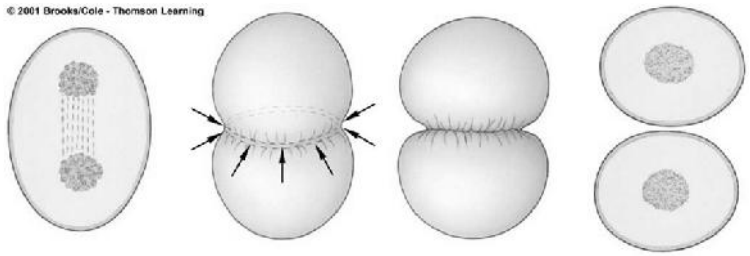




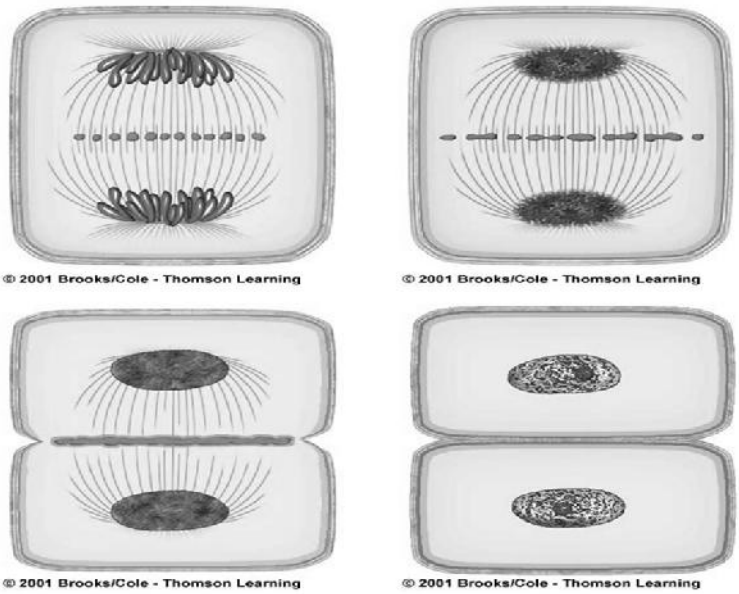
Onion root tip cells undergoing mitosis (http://tinyurl.com/c42amb3)

4. Cytokinesis

- **Cytokinesis is division of the cytoplasm** to produce two daughter cells, usually begun during telophase or occurs between late anaphase and end of telophase.
- Two mechanisms: (i) Cleavage (animals), and (ii) Cell plate formation (plants).



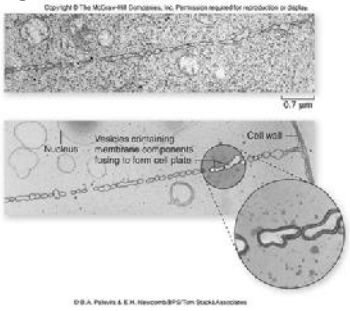
- Plants: Cell Plate Formation



Cytokinesis-division of the cytoplasm

- In animal cells, the membrane pinches closed at a point called cleavage furrow.
- In plant cells, vacuoles join together and form a cell plate.
- Result-2 identical daughter cells with identical copies of genetic material-DNA

- **Mitosis/Cytokinesis outcome**
  - 1 parent cell → 2 identical daughter cells
  - Chromosome number remains the same from one generation to the next



Mitosis: plant vs. animal cells

	Plant cell	Animal Cell
Centrioles	Absent	Present
Cytokinesis	Cell plate formation	Cleavage furrow