"...Breaking Up is Hard to Do" (At Least in Eukaryotes) Mitosis

Prokaryotes Have a Simpler Cell Cycle

- Cell division in prokaryotes takes place in two stages, which together make up a simple cell cycle
 - 1. Copy the DNA
 - this process is called replication
 - 2. Split the cell in two to form daughter cells
 - this process is called **binary fission**
- The hereditary information in a prokaryote is stored in DNA
 - the prokaryotic chromosome is a single circle of DNA
 - DNA replication begins with the unzipping of the double-stranded DNA at a point called the **origin of replication**
 - a new double helix is formed by adding complementary nucleotides to the exposed DNA strands that have been unzipped
 - the end result of replication is that the cell possess two complete copies of the hereditary information
- After replication, the cell grows in order to partition the replicated DNA molecules
 - when the cell reaches an appropriate size, the cell splits into two equal halves
 - new plasma membrane and cell wall are added at a point between the partitioned DNA
 - eventually the cell constricts in two to form two daughter cells
 - each daughter cell is a complete, living cell with its own DNA

Cell division in prokaryotes

Chromosomes Revisited

- Chromosomes were first observed by the German embryologist Walther Fleming in 1882.
- The number of chromosomes varies enormously from species to species.
 - The Australian ant Myrmecia spp. has only 1 pair.
 - Some ferns have more than 500 pairs.
- Again, chromosome number varies among organisms
 - most eukaryotes have between 10 and 50 chromosomes in their somatic cells
- Chromosomes are paired in somatic cells
 - these pairs are called homologous chromosomes, or homologues
 - homologues contain information about the same traits but the information may vary
 - cells that have two of each type of chromosome are called diploid cells
 - one chromosome of each pair is inherited from the mother and the other is inherited from the father

- Prior to cell division, each of the homologous chromosomes replicates, forming two identical copies called **sister chromatids**
 - the sister chromatids are joined together by a structure called a **centromere**
 - humans have 23 pairs of homologous chromosomes
 - The difference between homologous chromosomes and sister chromatids
- A karyotype is an arrangement of chromosomes
- Chromosomes can be compared based on size, shape, and centromere location
- The karyotype at right shows the 23 pairs of human chromosomes
- Chromosomes are comprised of chromatin, a complex of DNA (~ 40%) and protein (~ 60%).
- A typical human chromosome contains about 140 million nucleotides in its DNA.
 - This is equivalent to
 - About 5 cm in stretched length
 - 2,000 printed books of 1,000 pages each!
 - there is also some RNA associated with chromosomes
 - the DNA in a chromosome is one very long double-stranded fiber that extends unbroken for the length of the chromosome
 - the DNA is coiled in order to allow it to fit into a small space despite being very long
- DNA is coiled around proteins called histones
 - the histones have positive charges to counteract the negative charges associated with the phosphate groups of the DNA
- The DNA coils around a core of eight histone proteins to form a complex called a **nucleosome**
 - the nucleosomes in turn can be coiled together further to form ultimately a compact chromosome

Levels of eukaryotic chromosomal organization

Eukaryotes Have a More Complex Cell Cycle

- Eukaryotic cells contain more DNA than prokaryotic cells and the DNA is also packaged differently
 - cell division in eukaryotic cells is more complex
 - DNA in eukaryotic cells is linear and packaged into a compact chromosome
 - there is more than one chromosome in a eukaryotic cell
- Eukaryotic cells undergo two different mechanisms to divide up the DNA
 - mitosis is a cell division mechanism that occurs in non-reproductive cells
 - these cells are called **somatic cells**
 - **meiosis** is a cell division mechanism that occurs in cells that participate in sexual reproduction
 - these cells are called **germ cells**

The Cell Cycle

- The cell cycle is an ordered set of events, culminating in cell growth and division into two daughter cells.
- Non-dividing cells are not considered to be in the cell cycle.
- The phases in the cell cycle are G₁-S-G₂-M.
- G_1 -S- G_2 together make up what is known commonly as Interphase.
- These are the traditional subdivisions used, however, sometimes there is a G₀ phase.

The G Phases of the Cell Cycle

- The G₁ phase stands for "GAP 1".
- It is the interval between the completion of mitosis and the beginning of DNA synthesis.
- Most cells spend the majority of their lifespan in this phase
- The G₂ phase stands for "GAP 2".
- It is the interval between the end of DNA synthesis and the beginning of mitosis.
- Further preparation for cell division, including replication of mitochondria and synthesis of microtubules
- During G₁, the cell looks over its environment and its current size.
- If everything looks right, the step is taken to commit the cell to DNA replication and completion of the cell cycle.
- The G₂ phase provides a safety gap for the cell to ensure that DNA replication is complete before the cell is thrown into cell division.
- G₀ is a place where, the cell can rest or pause, if the cell has not committed itself to DNA replication.

The S Phase

- The S phase stands for "Synthesis". This is the stage when DNA replication occurs.
- In this phase, the cell's genome (DNA) is doubled.
- The DNA in this phase is, at this point, prepared to undergo division in the M phase.
- The M phase stands for "mitosis", and is when nuclear (chromosomes separate) and cytoplasmic (cytokinesis) division occur.

How the cell cycle works

Cell Division

- Interphase sets the stage for cell division
 - chromosomes are first duplicated
 - although not visible, chromosomes begin to wind up tightly in a process called **condensation**
 - sister chromatids are held together by a protein complex called **cohesin**
- The cell division that follows interphase is a division of the nuclear contents, known as **mitosis**
 - mitosis is a continuous process but it is divided, for ease of study, into four distinct stages

- 1. Prophase
- 2. Metaphase
- 3. Anaphase
- 4. Telophase

Prophase

- The beginning of mitosis and the point where the condensed chromosomes first become visible
- The nuclear envelope begins to disintegrate and the nucleolus disappears
- Centrioles separate in the center of the cell and migrate to opposite ends ("poles") of the cell
 - the centrioles start to form a network of protein cables called the spindle
 - each cable in the spindle is made of microtubules
 - some of the microtubules extend toward the centromere of the chromosomes

 these microtubules will grow from each pole until attached to a centromere at a disc of protein called a kinetochore

Metaphase

- Spindle fibers align the chromosomes along the middle of the cell nucleus.
- The centromeres are aligned along an imaginary plane that divides the cell in half, known as the **equatorial plane**
- This organization helps to ensure that in the next phase, when the chromosomes are separated (into individual chromatids), each new nucleus will receive one copy of each chromosome.

Anaphase

- The centromeres replicate and the paired chromosomes separate at the kinetochores and move to opposite sides of the cell.
- Enzymes break the cohesin and the kinetochores
- Motion results from a combination of kinetochore movement along the spindle microtubules and through the physical interaction of polar microtubules.
- Simply, the microtubules are reeled in towards the centrioles.
- This gives each pole a set of chromosomes.

Telophase

- Chromosomes arrive at opposite poles of cell, and new membranes form around the daughter nuclei.
- The chromosomes disperse and are no longer visible under the light microscope.
- The spindle fibers disperse, and cytokinesis or the partitioning of the cell may also begin during this stage.

Cytokinesis

- Occurs at the end of mitosis and is a division of the cytoplasm into roughly equal halves
 - in animals, cytokinesis occurs by actin filaments contracting and pinching the cell in two
 - this action is evident as a **cleavage furrow** that appears between the daughter cells (which can be seen at the end of Telophase)
 - in plants, a new cell wall is laid down to divide the two daughter cells

• the cell wall grows at right angles to the mitotic spindle and is called the **cell plate**

How cell division works

How cell division works

Cytokinesis

Controlling the Cell Cycle

- The cell cycle is controlled by checkpoints to ensure that a previous phase is fully completed before advancing to the next phase
 - feedback from the cell determines whether the cycle switches to the next stage
 - three principal checkpoints control the cycle in eukaryotes
 - G₁, G₂, and M checkpoints
- G₁ checkpoint
 - this checkpoint makes the decision about whether the cell should divide and enter S $_{-}$ some cells never pass this point and are said to be in G₀
- G₂ checkpoint
 - this checkpoint leads to mitosis
- M checkpoint
 - this checkpoint occurs during metaphase and triggers the exit process of the M phase and entry to the G₁ phase

Control of the cell cycle

Nothing lasts forever...

- Cells can die by injury due to exposure to toxic chemicals, hard mechanical damage, or programmed cell death.
- Programmed cell death (apoptosis) is a process in which the cell ends its own life.
- Apoptosis results in cell shrinking, the mitochondria releasing toxic substances, the nuclear material degrading, etc.

How does it know?

- Well, signals alert the cell as to when it should die.
- If positive signals are withdrawn (growth factors are gone), then the cell sees no reason to carry on.
- If negative signals are given (toxicity or oxidative damage) then the cell will die to prevent harm to the organism that it resides in.
- Unprogrammed cell death (necrosis) occurs when the cell dies by the other means mentioned.
- Injury, mechanical stress, and lack of blood flow can all be classified as necrosis.

What Is Cancer?

- **Cancer** is a growth disorder of cells
 - begins when apparently normal cells grow uncontrollably and spread to other parts of the body
 - the result is a growing cluster of cells called a tumor
 - benign tumors are surrounded by a healthy layer of cells (also known as encapsulated) and do not spread to other areas
 - malignant tumors are not encapsulated and are invasive
 - cells from malignant tumors leave and spread to different areas of the body to form new tumors
 - » these cells are called **metastases**

Lung Cancer

- Cancer is caused by a genetic disorder in somatic tissue in which damaged genes fail to properly control the cell cycle
 - mutations cause damage to genes
 - may result from chemical or environmental exposure, such as UV rays
 - viral exposure may also alter DNA
- There are two general classes of genes that are usually involved in cancer
 - proto-oncogenes
 - these genes encode proteins that stimulate cell division
 - mutations to these genes can cause cell to divide excessively
 - when mutated, these genes become oncogenes
 - tumor-suppressor genes
 - these genes normally turn off cell division in healthy cells
 - when mutated, these genes allow uncontrolled cell division Cancer and Control of the Cell Cycle
- Cancer results from damaged genes failing to control cell division
 - one such gene, p53, affects the G₁ checkpoint
 - its normal action is to detect abnormal DNA
 - it prevents cell division of a cell with damaged DNA until the DNA is repaired or directs the cell to be destroyed if the damage cannot be fixed
 - if this gene itself becomes damaged, it will allow damaged cells to divide unchecked

Cell division and p53 protein