BIOL 300 – Foundations of Biology
Summer 2017 – Telleen
Lecture Outline

The Cell Cycle, Mitosis, and Cytokinesis

I. The Cell Cycle
   A. The Cell Cycle has three main phases:
      1. Interphase
      2. Mitosis (nuclear division, chromosome division)
      3. Cytokinesis (cell division)
   B. The time between cell divisions is the **interphase**. This is where cells spend most of their time
   C. **Mitosis** and **cytokinesis** usually happen together
   D. Interphase is divided into three (sometimes four) parts:
      1. **G1 (gap 1) –** Begins immediately after mitosis. RNA, protein, and other molecules are synthesized. This is basically the cell doing everything that is not associated with cell division
      2. **S (synthesis) –** DNA is replicated. Chromosomes become duplicated.
      3. **G2 (gap 2) –** Mitochondria (and chloroplasts) divide. Precursors of the spindle fibers are synthesized.
      4. **G0 –** This stage can only be reached from G1. It is basically a pause in the cell cycle. Cells in G0 do not divide or undergo mitosis. Cells in G0 can return to G1 to continue the cell cycle.
   E. The net results of the complete cell cycle is two daughter cells that start again in G1
   F. In humans, each daughter cell receives a set of 46 chromosomes derived from a single parent cell with 46 replicated chromosomes
   G. Cancer and the cell cycle
      1. **Cancer** is a disease of the cell cycle
      2. Cell division is a highly regulated process
      3. Checkpoints during the cell cycle ensure that cells divide (or don't divide) appropriately
      4. Cancer is caused by mutations that alter the regulation of the cell cycle
      5. Cancer cells grow and divide faster than normal cells

II. Chromosome structure revisited
   A. We've already talked about how DNA is wound up into chromosomes, but condensed chromosomes have some feature that we need to discuss before we get into mitosis
   B. The **Centromeres –** Regions of the chromosomes where spindle fibers attach during mitosis. Their location gives a chromosome its characteristic shape.
   C. The **Telomeres –** The ends of the chromosomes/chromatids. They have a characteristic foldback structure that we won't talk about
   D. Chromosome **arms –** The parts of the chromosome on either side of the centromere. Often there is a long arm and a short arm.

E. Replicated chromosomes and chromatids
    1. Each **Chromatid** is half of a **replicated chromosome**. When two are joined at the centrome they are known as **sister chromatids**

H. Counting chromosomes
    1. The number of chromosomes present is sometimes confusing when discussing mitosis and meiosis, but there is a trick to remember
    2. The number of chromosomes equals the number of centromeres
    3. Whenever there is confusion, count the centromeres. Note that even though a chromosome is replicated (and consists of two sister chromatids) so it has twice the amount of DNA as it did in G1 it is still a single chromosome until the centromere divides.

I. We refer to the how many sets of chromosomes are in a cell as the **ploidy level**.
    1. We refer to one set (i.e. one of each type of chromosome) as **haploid** and the number of chromosomes in a haploid set is denoted by **n** (each species has a characteristic value of n).
    2. Typically, cells contain pairs of chromosomes of each type. Thus, most cells contain **2n** chromosomes and are said to be **diploid**.
    3. For example, human cells normally are diploid and contain 46 chromosomes (2n=46). Therefore n=23; there are 23 types of chromosomes that each exist as pairs.
    4. Although we won't talk much about it, it is possible to have other ploidy levels (particularly in plants) such as triploid (banana), tetraploid (cotton), and even hexaploid (wheat)!
    5. Understanding the ploidy level of cells will be critical to following what occurs in mitosis and meiosis

III. Mitosis

A. **Mitosis** is often divided into four stages
    6. The process is continuous, but the stages represent significant events that make discussing it easier
    7. Each phase follows the behavior and organization of the chromosomes

B. The four stages are:
    1. Prophase
    2. Metaphase
    3. Anaphase
    4. Telophase

C. Prophase
    1. **Prophase** marks the beginning of mitosis
    2. The cell has already replicated its DNA/Chromosomes during interphase
    3. At the beginning of prophase, the chromatin condenses and the individual chromosomes become visible
    4. At first, the chromosomes long thin threads, but they become shorter and thicker as prophase continues

5. By the end of prophase, each chromosome consists of two strands called chromatids
6. Near the end of prophase, the nuclear membrane breaks down and a network of **spindle fibers** forms in the cytoplasm that stretches across the cell. The spindle fibers are made of microtubules

D. Metaphase

1. **Metaphase** begins once the condensed chromosomes are free in the cytoplasm
2. The chromosomes move to the equator of the cell where the spindle fibers attach to the centromeres
3. In humans, there are 46 centromeres each attached to two sister chromatids. Each organism has a characteristic number of chromosomes
4. The key characteristic of metaphase is the lining up of the chromosomes on the **metaphase plate** (at the equator of the cell)
5. The spindle fibers connect the centromeres to structures on opposite sides of the cell

E. Anaphase

1. The centromeres divide. This converts each chromatid into a chromosome (since now it has its own centromere)
2. As **anaphase** continues, the chromosomes are pulled toward opposite ends of the cell by the spindle fibers
3. One copy of each chromosome is ends up at each end of the cell to ensure that each daughter cell gets a complete set of chromosomes
4. This is the shortest phase of mitosis
5. Roberts syndrome is a genetic disorder that causes lack of limb development and sometimes mental retardation caused by centromeres that separate too early and interfere with normal mitosis

F. Telophase

1. At the beginning of **telophase**, each set of chromosomes has reached opposite ends of the cell.
2. The chromosomes begin to uncoil and the spindle fibers break down
3. A new nuclear membrane begins to form from the ER
4. Once these steps are done, mitosis is completed leaving two separate nuclei with a complete set of genetic material

G. Cytokinesis

1. This is the division of the cytoplasm and a separate event from mitosis, which can occur without **cytokinesis**.
2. The cell becomes constricted in the plane of the metaphase plate

3. The constriction gradually tightens by contractions of cytoskeletal filaments attached to the membrane
4. Eventually, the cell is basically pinched in two
5. The result is two daughter cells, each with a single nucleus and half the cytoplasm and organelles from the parent cell

H. The role of mitosis in multicellular organisms

1. Single celled organisms reproduce by mitosis/cytokinesis, but **multicellular organisms use mitosis/cytokinesis to produce cells that differentiate into cells with different functions**
2. Different cell types divide at different rates:
    1. Bone marrow cells and skin cells are continually dividing
    2. Many other cell types (like muscle cells) enter G0 and do not divide once they are differentiated
3. In humans, the maximum number of cell divisions a cell can go through is under genetic control. In the lab, embryo cells can only divide about 50 times. Adult cells usually will only divide 10-30 times.
4. Human cell cultures used in research are cancer cell lines that are mutated to be unaffected by this genetic limit so they continually divide
5. In humans, once cells are differentiated they cannot divide and make cells of other types. This is why we hear so much about stem cells research in the news.
6. Plants do not have a limit to the number of cell divisions they can go through (though their cell cycle is still highly regulated). Plant cells are called **totipotent** because a single differentiated cell can be made to regenerate an entire plant under the right conditions.

Meiosis and Sexual Reproduction

I. The Purpose of Sexual Reproduction

A. In addition to cell division for the purposes of growth, repair, and differentiation or asexual reproduction (ie. Mitosis), most eukaryotic cells also undergo a specialized cell division process called **Meiosis**.
B. Superficially, this process is very similar to mitosis, but the result of the process is quite different, as is its purpose.
C. The **purpose of meiosis is to create genetic variation by producing offspring with different combinations of alleles**
D. Initially, mutations introduce genetic variation into a population by producing new forms of genes (alleles) at the level of the DNA
E. Once mutation has created new alleles, the process of natural selection acts upon that variation, increasing the fitness of the population for the prevailing environmental conditions
F. Because different combinations of alleles from different genes might be particularly advantageous in a given setting, eukaryotic organisms developed **sexual reproduction**
G. Sexual reproduction **creates new combinations of alleles in two ways:**
    1. Combinations of alleles located on the two homologs of each chromosome are scrambled during meiosis in a process called crossing over or recombination. This creates novel combinations of alleles not present on single chromosomes from the parents
    2. Fertilization further increases the level of genetic variation by bringing together sets of chromosomes with different profiles of alleles into the same organism. Once together new combinations of alleles an interact in novel ways, either increasing or decreasing the organism's fitness
C. An example: *Neurospora crassa* (the bread mold fungus)
    1. Consider a strain of *Neurospora* that has orange hyphae and black spores that germinate rapidly. A spore from this strain lands on the immature fruiting body of another strain that has white hyphae and pale spores that germinate slowly
    2. Neither strain is surviving well in a glacial moraine in southern Alaska. The first strain is being eaten by an insect that can see the hyphae and dark spores easily against the pale moraine background. The pale strain is safe from the insect, but grows to slowly to establish itself in a single day before being subjected to the freezing conditions at night
    3. Fertilization occurs when the nuclei of the two strains merge in the immature fruiting body of the recipient strain. As a result, a cell exists in the fruiting body that contains the alleles of both strains for the three genes

under study. The cell now has homologous pairs of each type of chromosome in the cell so that meiosis is now possible

Possible Phenotypes of daughter *Neurospora* strains:

Hyphae	Germination Mode	Spore Color
Orange	Rapid	Black
White	Slow	Pale
Orange	Rapid	Pale
Orange	Slow	Black
Orange	Slow	Pale
White	Rapid	Black
White	Slow	Black
White	Rapid	Pale

Which of these strains is likely to thrive when it germinates in the moraine environment? Can you see what meiosis has accomplished in this example? Do you understand what is meant by the scrambling of alleles?

II. Meiosis

A. Some genes are located on the same chromosome and some are located on different chromosomes. To maintain diversity, meiosis must be able to scramble alleles that are located on the same chromosome as well as those different ones

B. **Meiosis** involves two cell divisions that usually happen in quick succession. The first division is **Meiosis I (MI)**. The second division is **Meiosis II (MII)**

C. The Stages of Meiosis are similar to those of mitosis (ie. Prophase, Metaphase, Anaphase, and Telophase)

D. Meiosis I: Prophase I

1. **Prophase I is the stage where alleles located on the same chromosome are scrambled**
2. As in prophase of mitosis, the chromosomes condense and become visible
3. Special proteins mediate the association of each homologous pair of chromosomes
4. Homologous chromosomes exchange sequences in a process call **crossing over, or recombination**
5. This is the exact point at which allelic combinations between genes located on the same chromosome are scrambled to create genetic diversity

E. Crossing Over

1. You can think of **crossing over** as a cutting and pasting process. Both **homologs** are cut at precisely the same spot and then exchange arms. If the cut is close to the centromere, almost the entire arm of a chromosome is exchanged. However, if the cut occurs close to the tip, then only the tip of the arms switch places. The choice of where the cut is on each arm in each individual Prophase I appears to be entirely random. This process is also called recombination.

F. Meiosis I: Metaphase I

1. Chromosome pairs line up at the metaphase plate during Metaphase I
2. As a consequence of crossing over, the homologs are still connected and paired together as they are pulled to the metaphase plate by the spindle fibers
3. **Each pair of homologs approaches the plate independently from all other homolog pairs**
4. This is important point because the independent orientation of homolog pairs with respect to the metaphase plate at this time results in the scrambling of allelic combinations of genes located on different chromosomes

G. Scrambling Allelic Combinations in Meiosis
1. Nature has devised two completely different methods of scrambling allelic combinations among genes during meiosis
2. In Prophase I, crossing over scrambles allelic combinations among genes located on the same chromosome
3. In Metaphase I, the random orientation of different homolog pairs with respect to the metaphase plate scrambles allelic combinations among genes located on different chromosomes

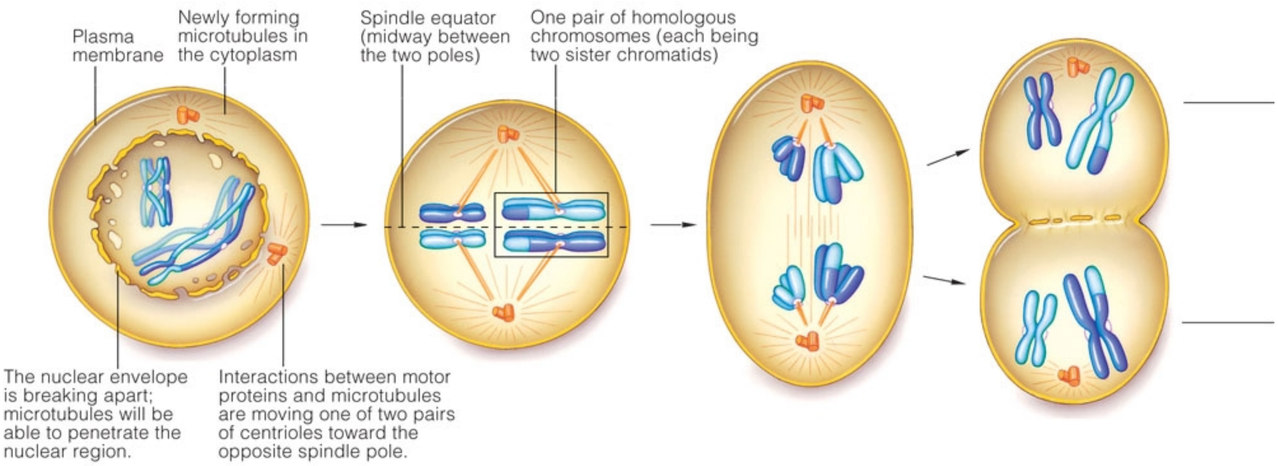
H. Meiosis I: Anaphase I
1. During Anaphase I, homologs separate from one another. Sister chromatids do not separate at this time the way they do in mitosis
2. Meiosis I is a reductional division. The separation of homologs halves the number of chromosome sets in the cell. Each daughter cell of Meiosis I has only one copy of each chromosome. Such cells are called haploid (n), whereas cells with two chromosomes of each type are called diploid (2n). Thus, all human sperm and egg cells are haploid, and each contributes exactly half of all the genetic information needed by the embryo following fertilization
3. Note, however, that each of these daughter cells contains its set of chromosomes in the duplicated state since sister chromatids have not yet separated from one another

D. Meiosis I: Telophase I
1. At Telophase I, the separated homologs gather at the poles and the cell prepares to divide. Telophase I is immediately followed by cytokinesis and cytokinesis is immediately followed by Meiosis II

E. Meiosis II
1. Meiosis II is basically a mitotic division of each of the two haploid daughter cells produced by Meiosis I. The end result of meiosis II is 4 haploid cells, also called gametes (eggs or sperm).
2. Notice in particular the behavior of the homologous chromosomes during metaphase of MII, which is the same as in Metaphase of Mitosis, except that the number of chromosomes has been halved. It is different in Metaphase I of Meiosis I.

Here are diagrams of Meiosis I and II from a textbook:

Meiosis I



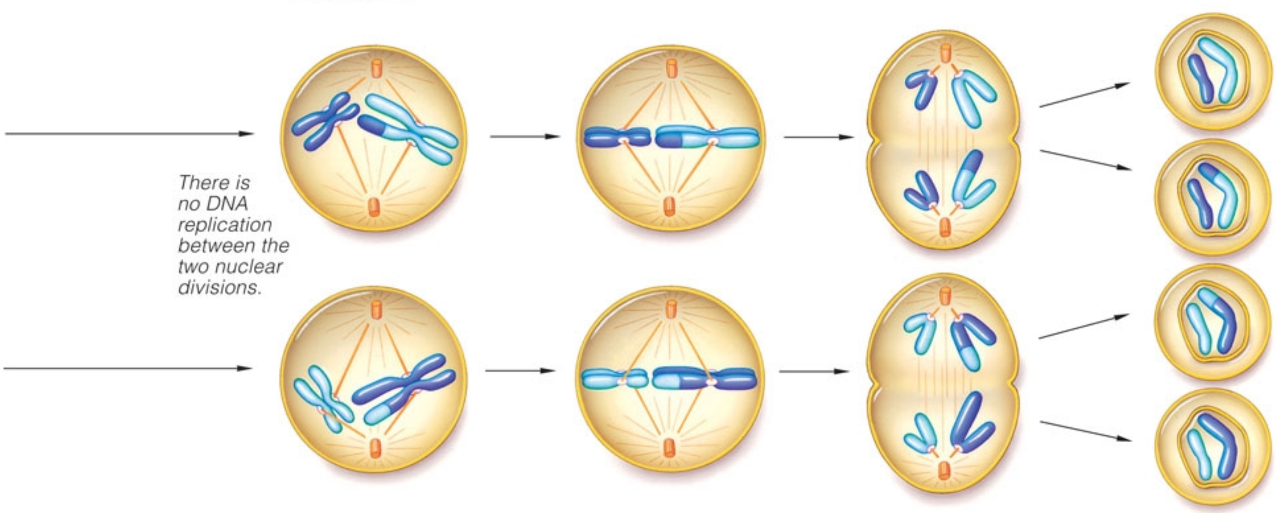
(a) Prophase I
At the end of interphase, chromosomes are duplicated and in threadlike form. Now they start to condense. Each pairs with its homologue, and the two usually swap segments. The swapping, called crossing over, is indicated by the break in color on the pair of larger chromosomes. Newly forming spindle microtubules become attached to each chromosome.

(b) Metaphase I
Motor proteins projecting from the microtubules move the chromosomes and spindle poles apart. Chromosomes are tugged into position midway between the spindle poles. The spindle becomes fully formed by the dynamic interactions among motor proteins, microtubules, and chromosomes.

(c) Anaphase I
Some microtubules extend from the spindle poles and overlap at its equator. These *lengthen* and push the poles apart. Other microtubules extending from the poles *shorten* and pull each chromosome away from its homologous partner. These motions move the homologous partners to opposite poles.

(d) Telophase I
The cytoplasm of the cell divides at some point. There are now two haploid (n) cells with one of each type of chromosome that was present in the parent ($2n$) cell. *All chromosomes are still in the duplicated state.*

Meiosis II



(e) Prophase II
Microtubules have moved one member of the centriole pair to the opposite spindle pole in each of two daughter cells. During prophase II, microtubules attach to the chromosomes, which motor proteins slide toward the spindle's equator.

(f) Metaphase II
The microtubules, motor proteins, and duplicated chromosomes interact, which positions all of the duplicated chromosomes midway between the two spindle poles.

(g) Anaphase II
The attachment between the sister chromatids of each chromosome breaks, and the two are moved to opposite spindle poles. Each former "sister" is now a chromosome on its own.

(h) Telophase II
By the time telophase II is finished, there are four daughter nuclei. When cytoplasmic division is over, each daughter cell is haploid (n). All chromosomes are in the unduplicated state.

F. Gametogenesis in Humans

1. The production of eggs and sperm is called **gametogenesis** and it occurs by Meiosis
2. The process is slightly different in male and female animals because the female needs to produce as large an egg as possible to provide the cytoplasm and organelles fro the embryo. The sperm mostly just provides DNA.
3. In males, the diploid primary spermatocytes undergoes meiosis to produce four equally-sized and equally-viable haploid mobile sperm
4. In females, the diploid primary oocyte undergoes Meiosis I to produce two cells of unequal size: a secondary oocyte and a primary polar body. Each then undergoes Meiosis II. The secondary oocyte produces the oocyte or egg (which is usually the only viable gamete) and one secondary polar body. The primary polar body produces two secondary polar bodies. All the polar bodies are then degraded, leaving the egg as the only female gamete that is fertilized