# Cell Division

All life is made of cells, and all cells divide. The purpose of cell division is for (1) reproduction and/or (2) growth. If cells didn't divide didn't, growth would be impossible (beyond a certain extent) and extinction would be inevitable. In this section we will review the steps of the different types of cell division (namely binary fission, mitosis, and meiosis).

## 1 Characteristics of cells

Most cells are tiny (approximately 10-20 micrometers). Why is this? If one of the primary objectives of cell division is growth, why don't the cells just grow without dividing? Four reasons for division as a mechanism of growth (over just growing without dividing) are:

1. **Structural limit**: As a cell increases in size, the surface area to volume ratio decreases. As a cell increases in size, eventually the amount within the cell (volume) will become to great for the membrane/cell wall (surface area) to contain. To understand this in more detail, think about the surface area to volume ratio of a cube. The surface area of a cube is calculated by 6 x (length x width). The area of a cube is calculated by length x width x height (where length = width = height). For a cube with side lengths of 4, the surface area is 6 x (4 x 4) = 96, whereas the area = 2 x 2 x 2 = 64. If we increase the size of the cube so the sides are of length 6, the surface area is now = 6 x (6 x 6) = 216, and the volume of the cube is 6 x 6 x 6 = 216 (the surface area and volume are now equal). If we increase the size of the cube yet again so the sides are of length 8, the surface area is now = 6 x (8 x 8) = 384, whereas the volume of the cube is 8 * 8 * 8 = 512. If we continue this progression, we will see an exponential increase in volume size compared to surface area. Eventually the pressure within the increasing volume will overwhelm the membrane/wall of the cell, and it will burst.

2. **Physiological limit**: The demands of the cytosol can't be met by a small surface area. The cell membrane/wall is the medium through which nutrients and waste must pass in order to get within the cell. As a cell increases in size, the need to uptake nutrients and dispose of waste also increases. At a certain point during growth, the surface area will not be able to facilitate transport of these molecules at a rate necessary for the demands of the cytosol. This is due to the same concept as that described in the "Structural limit" section above, but the constraining factor is physiological rather than structural.

3. **Transcription and translation limit**: The nutrients brought into the cell need to be metabolized using products encoded by the DNA of a single nucleus (remember, all of the proteins/RNA in a cell are created from the DNA). However, in an overgrown cell it becomes challenging for a single nucleus to provide the products necessary to respond to this need in a timely manner.

4. **Dangerous resource investment**: This is the same concept as the common phrase "don't put all your eggs in one basket". If an organism invests all of its resources into a single cell (i.e., just focuses on that single cell's maintenance and growth), when something goes wrong with that cell the organism has no other options. By dividing and creating many cells (i.e., diversifying), a mishap with a single cell is no longer as detrimental.

While these exceptions are major factors behind the ubiquitous nature of cell division, there are exceptions (as is almost always the case in biology). For example, neurons reach from your spinal column all the way to the tips of your toes (neurons within the laryngeal nerve of extinct sauropods were as long as a basketball court), bubble algae (a.k.a. sailor's eyeball) is a

single-celled organism that can grow the size of a tennis ball, and muscle cells of the sartorius in humans stretch from the hip to the knee. Each of these exceptions avoid the limits described above by maximizing surface area to volume ratio with special shapes (the incredible length of neurons is contrasted by their diameter of 0.1 millimeters [thinner than a strand of hair]), cytosol or wall/membrane adjustments (bubble algae possess a large vacuole that reduces the pressure of the cytosol on the cell wall along with extra reinforcement invested in their cell walls for greater strength), and/or increased number of nuclei (and therefore, the number of transcription hubs) in a single cell (bubble algae and skeletal muscle cells are multi-nucleated). The modifications that help these exceptional cells overcome the limits of cell growth show the strength of the four limiting constraints described above. Because of these limits, the vast majority of cells are small and growth is achieved via cell division.

# 2 The Cell Cycle

A cell grows, divides, and repeats. Because of this repetitive lifestyle, we refer to this as the **cell cycle**. The cell cycle can be broken up into different phases. The first phase is **G1**, which is the primary growth phase. During this phase nutrients are being consumed, proteins are being created, and waste is being disposed in order to ensure the cell grows enough for it to replicate. However, before the cell can divide it needs to copy its genetic material (otherwise the next cell won't contain the blueprint necessary to build stuff and live). So the second phase is called **S** phase, which stands for "**synthesis**". Synthesis is just a fancy word for creation- and in this phase a new copy of the DNA is created (through **semiconservative replication**). Therefore, after S phase the cell contains double the number of DNA molecules it contained before.

For example, in a human somatic cell there are 23 molecules of DNA in G1 phase (i.e., each chromosome is made up of a single molecule of DNA). After S phase, the cell contains 46 molecules of DNA (i.e., each chromosome is made up of two molecules of DNA [because the original strand was replicated]). The third phase is **G2**, which is the secondary growth phase. During this phase the cell continues to grow, however this phase is shorter and growth is significantly less in comparison to G1. G1, S, and G2 phases are together called **interphase**. The fourth and final phase of the cell cycle is **M** phase, which stands for **mitosis** for normal cell division and **meiosis** for cell division that leads to **gamete** (sex cell) creation. M phase is broken up into individual "sub"-phases: **prophase**, **metaphase**, **anaphase**, and **telophase**. The nature of these sub-phases depend on whether they are in Mitosis, Meiosis I, or Meiosis II (all three of which are different types of cell division), and we will break these down in detail below. The final step of the cell cycle is called **cytokinesis**, and it is when the cells finally split apart.

Importantly, in order for a cell to progress from one phase to another (i.e., G1→S, S→G2, G2→M, M→cytokinesis), certain check-points must be passed. At these check-points, the cell is examined by check-point proteins to ensure sufficient growth, undamaged DNA, replication success, and correct spindle attachment. Failure to pass these checkpoints will result in the cell being "arrested" (it ceases to progress to cell division) or even killed (through programmed cell death, a.k.a. **apoptosis**).

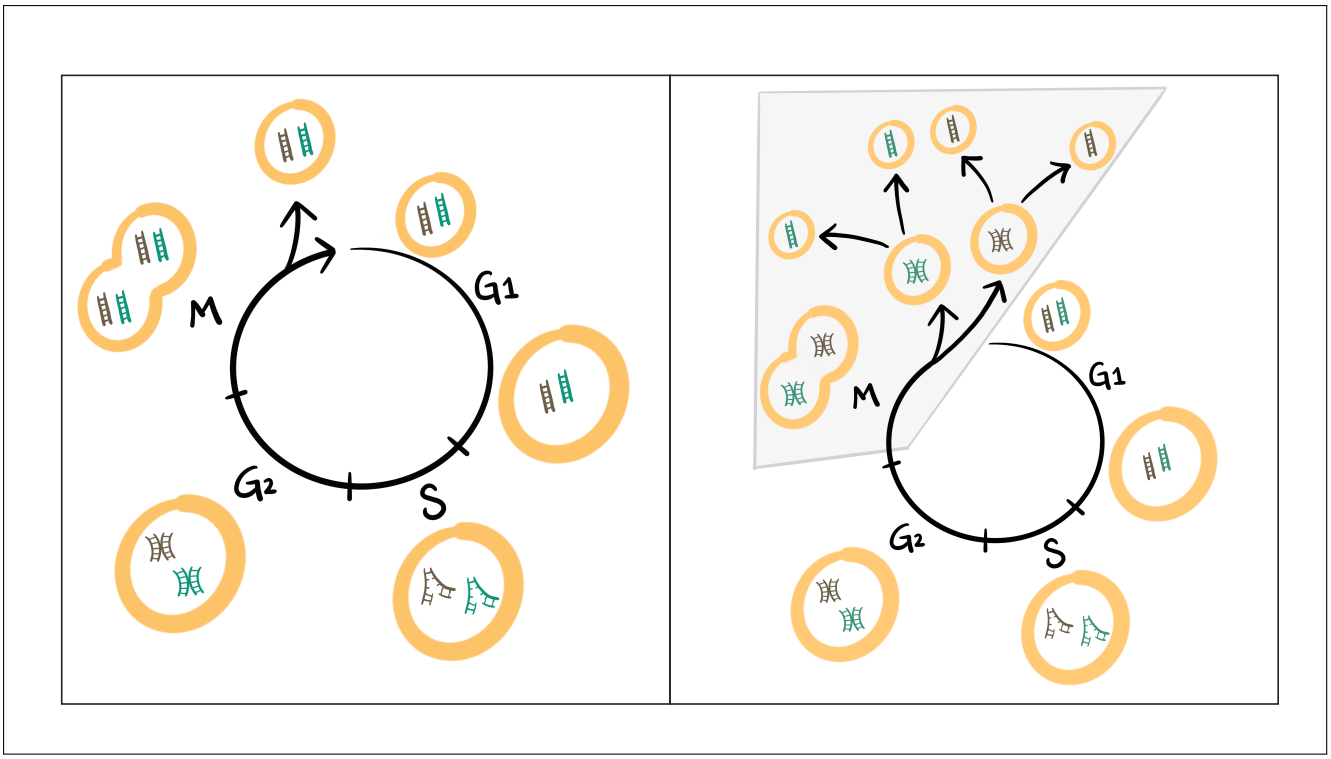


Figure 1: Cell cycle for a cell with a single chromosome. Left: Showing 'Mitosis' as M phase. Right: Showing 'Meiosis' as M phase, with Meiosis I and Meiosis II shown.

# 3 Chromosome and genome terminology

Before jumping into the details of the sub-phases within M phase, it will be helpful to go over genome/chromosome terminology. A chromosome is a DNA structure that contains genes. Most eukaryotes contain linear chromosomes in the nucleus and a circular chromosomes in the mitochondrion (which is usually referred to as the mitochondrial genome). It is important to note that in this section the chromosomes referenced in the cell cycle are nuclear chromosomes. Before S phase a chromosome is one molecule of DNA. After S phase a chromosome is two molecules of DNA. Sometimes you see chromosomes drawn like an "X" – this is a chromosome after S phase (it has already been replicated). These "X"-looking chromosomes are made up of two DNA molecules joined at a location known as the **centromere** (the center of the "X"). Be careful to not confuse the word "centromere" with "centrosome"/"centriole" (which we will talk about later).

Each DNA molecule in a chromosome after S phase (i.e., each side of the "X") is known as a **sister chromatid**. Humans have 23 chromosomes with a unique set of genes, however we have two copies of each chromosome (one copy from each biological parent). Having two sets of each chromosome means we are **diploid**. A chromosome and its partner are known as a **homologous pair**. **Homologous chromosomes** contain the same genes, but those genes may have differences based on unique ancestry (e.g., for the gene that encodes earlobes, the paternally-inherited chromosome may have a version of the gene that encodes attached earlobes whereas the maternally-inherited chromosome may have a version of the gene that encodes detached earlobes). Different versions of the same gene are called **alleles**. In other words, we have 46 total chromosomes in our somatic cells. Before S phase, a somatic cell contains 46 chromosomes (46 molecules of DNA, because each chromosome is a single molecule of DNA). After S phase, a somatic cell contains still contains 46 chromosomes (92 molecules of DNA, because each chromosome is made up of two molecules of DNA). Chromosomes have their own anatomy.

The ends are known as **telomeres**. The "center" is known as the **centromere**. We will discuss other components of chromosomal anatomy in later sections of the book.

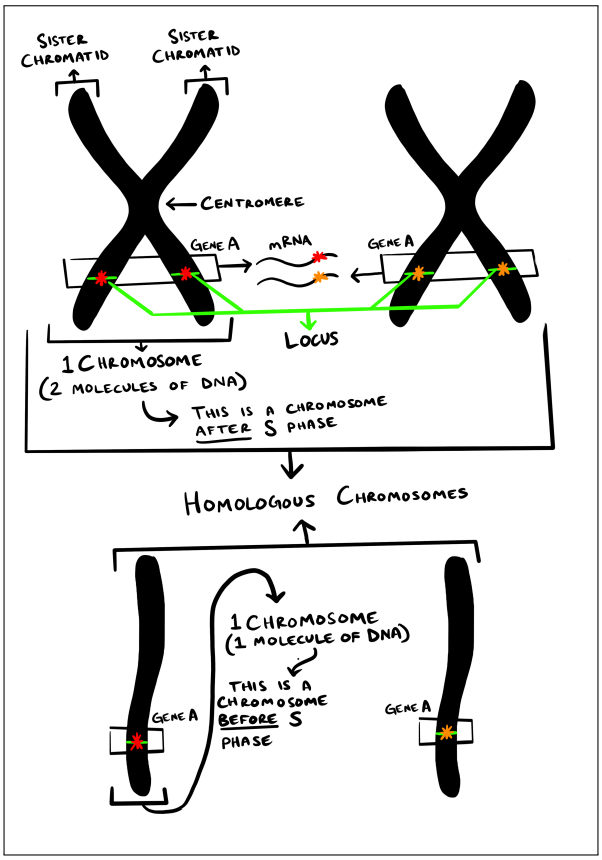


Figure 2: Chromosome terminology. Two alleles for a gene (Gene A) are shown with red and orange asterisks. The green band shows the locus (i.e., site) of variance for these alleles. It is important to note that while here the locus referenced is inside of the gene, a locus can also be a larger region that contains a gene (or even many genes).

The number of chromosome sets in a cell is referred to as "**ploidy**". A cell that has two chromosome sets is called **diploid**. Diploid cells have two sets of every gene that may/may not be identical (they all have their own ancestry). For example, human somatic cells are diploid: there is a genome that was inherited from the maternal parent (i.e., "mom") and a genome that was inherited from the paternal parent (i.e., "dad"). Each genome is a complete set of chromosomes. Diploid can be abbreviated as "2n". A cell that is 1/2 the ploidy of the normal somatic cells is called **haploid** (e.g., sperm or egg cells); for diploid organisms, the haploid cells are **monoploid** (contain only one set of chromosomes). Monoploid (which is the ploidy for haploid cells for humans and other diploid organisms) is abbreviated as "1n".

**Common pitfall**: Many people get confused by how the cell cycle affects ploidy. *Ploidy is not altered by whether chromosomes are duplicated or not.* In other words, a diploid organism is diploid before and after S phase. Mitosis also doesn't change ploidy; a diploid organism is diploid before and after Mitosis. However, Meiosis does change ploidy. You will read about this in the section on Meiosis below.

**Practice problem**: How many molecules of DNA are in a human somatic cell nucleus in G2? Try to solve this by yourself before looking at the solution!

**Solution**: A single human genome is made up of 23 chromosomes. Before S phase, each chromosome is a single molecule of DNA. After S phase, each chromosome is made up of two molecules of DNA (that are exact copies of each other). Therefore, a single human genome in G2 (which is after S phase) contains 46 molecules of DNA. Lastly, we have to remember that somatic cells contain a homologous pair of each chromosome (i.e., there are two sets of chromosomes: one set that was inherited from the maternal parent and the other set inherited from the paternal parent]). This means that we need to multiply our number by two: 46 x 2 = 92. There are 96 molecules of DNA in a human somatic cell nucleus in G2.

**Practice problem**: How many nucleotides are in all of the linear chromosomes of a human somatic cell in G2? Try to solve this before looking at the solution!

**Solution**: A human genome is made up of 3 billion base pairs. Because human somatic cells are diploid, that means there are 2 genomes in the cell (one inherited from each parent). 2 x 3 = 6. However, we also have to account for the cell being in G2 (the DNA has been replicated). This means that there are two molecules of DNA for each chromosome. 6 x 2 = 12. Lastly, we need to remember that DNA is double stranded, and each strand contains its own set of nucleotides (i.e., while a genome contains 3 billion base pairs, 1 base pair is made up of 2 nucleotides). 12 x 2 = 24. That means that there are 24 billion nucleotides in the linear chromosomes of a somatic cell in G2.

# 4 Mitosis

**Mitosis is the process of cell division for somatic cells, and it is a critical process for proper organismal growth and development** beginning immediately after **fertilization** (when sperm and egg join to create a **zygote**, which is the first cell of a multicellular organism). Coordinated mitosis across tissues and organs is required for correct body plan formation. Mitosis that occurs too slow or too fast can result in abnormalities, and unchecked mitosis can result in cancer. Importantly, mitosis is a form of asexual reproduction where the two resulting daughter cells are identical to the parent cell (Figure 3).

## 4.1 Sub-phases of M phase for Mitosis

1. **Prophase**: The chromosomes begin to condense. The nucleoli (sections within the nucleus where ribosomes are synthesized) are broken down. Centrosomes (organelles made up of two centrioles, proteins, and microtubules) move to opposite sides of the cell. The nuclear envelope (membrane of the nucleus) breaks down. The microtubules of the centrosomes reach out and attach to each chromosome at the **kinetochore** (special proteins located at the centromere of each chromosome).

2. **Metaphase**: Chromosomes become completely condensed, and are arranged in single-file on the "**metaphase plate**" (an imaginary line between the centrosomes) by the microtubules of the centrosomes. The meta phase plate runs through the middle of the chromosomes, so that the sister chromatids of a single chromosome are on opposite sides of the plate.

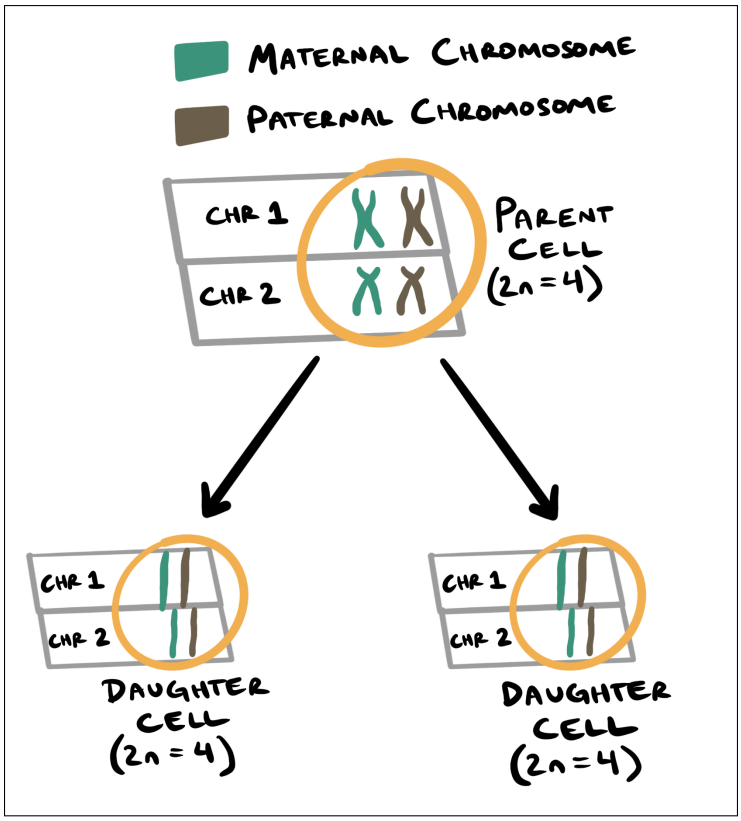


Figure 3: The daughter cells that are produced from Mitosis.

3. **Anaphase**: The sister chromatids separate from one another and move toward the centrosomes on opposite sides of the cell.

4. **Telophase**: The nuclear envelopes (now there are two of them) start to reform and chromosomes (notice we now call them "chromosomes" and not "sister chromatids" because they are separate from each other and in their own nuclear envelope) begin to de-condense.

You should have a thorough understanding of Mitosis and should be able to draw it out and explain it. Watch this online video on the subphases of Mitosis:

https://www.youtube.com/watch?v=RNwJbMovnVQ

# 5 Meiosis

**Meiosis is the process of cell division for germ (sex) cells, and it is a critical process for reproduction in organisms that reproduce sexually** (where genetic contribution from more than one individual is used to create offspring). Proper meiosis is critical to ensure that the right quantity of genetic information is passed on to the offspring; too much or too little information can result in harmful effects to the health of future offspring. Meiosis is different than mitosis because there are two M phases which occur one after the other: **Meiosis I** and **Meiosis II**. This results in four daughter cells (Meiosis I creates two daughter cells, and then these each go through Meiosis II to create their own two daughter cells). **Remember: In Mitosis one cell becomes two cells; in Meiosis one cell becomes four cells. The resulting cells of Meiosis are called gametes, and they are used for sexual reproduction (egg and sperm cells are gametes).**

## 5.1 Meiosis I

Meiosis I occurs in-place of mitosis after interphase (G1, S, and G2), so it is important to recognize that, just as in Mitosis, the DNA has already been replicated. Also similar to Mitosis, Meiosis I has "sub"-phases (although we put a "I" after these to indicate they are for Meiosis I ["Prophase I", "Metaphase I", "Anaphase I", and "Telophase I"]). Although the "sub"-phases of Meiosis I are named the same and are very similar to those of Mitosis, there are important differences.

### 5.1.1 Key differences between Meiosis I and Mitosis / Meiosis II:

- In Prophase I, the homologous chromosomes pair in a process known as **synapsis**. At this time (during Prophase I), **crossing over** happens (DNA from the maternal chromosome links with the DNA of the paternal chromosome and *vice-versa*), resulting in **genetic recombination** (rearrangement or shuffling of DNA- the maternal chromosome now has a chunk of paternal DNA and the paternal chromosome now has a chunk of maternal DNA). *recombination only occurs in Prophase I*, not in Prophase of Mitosis or Prophase II.
- During Metaphase I, the chromosomes align next to their homologous pairs (rather than in single file, as is the case in Metaphase of Mitosis and Metaphase II). The metaphase plate goes between the homologous chromosomes rather than through the centromeres of each chromosome.
- In Anaphase I, the homologous pairs are separated from each other (instead of sister chromatids being separated) and one chromosome of each pair will end up in the resultant daughter cells.
- In Meiosis I, *ploidy is not conserved*. For example, a human germ cell starts as a diploid, and by after Meiosis I the daughter cells are each haploid. In both Mitosis and Meiosis II, the ploidy of the resulting daughter cells is the conserved (e.g., diploid→diploid in Mitosis, haploid→haploid in Meiosis II). For this reason Meiosis I is known as "**reduction division**.

You should have a thorough understanding of Mitosis and should be able to draw it out and explain it. Watch this online video on the subphases of Mitosis:

https://www.youtube.com/watch?v=5pvwIsDE6eg

### 5.1.2 Critical concept: Independent Assortment

The way chromosomes arrange on either side of the metaphase plate in Metaphase I affects the combinations of chromosomes that will be in the resulting gametes. Homologous pairs assort independently of each other, in a process called **independent assortment**. This principle allows for genetically diverse gametes to be created (Figure 4).

### 5.1.3 Critical concept: Segregation of Alleles

For diploid organisms, each gamete will contain only one copy of each gene. No gamete will contain multiple copies of a given gene. Referring to the earlobe gene referenced in section 3, each gamete of that individual (who both alleles) will only contain one of the alleles.

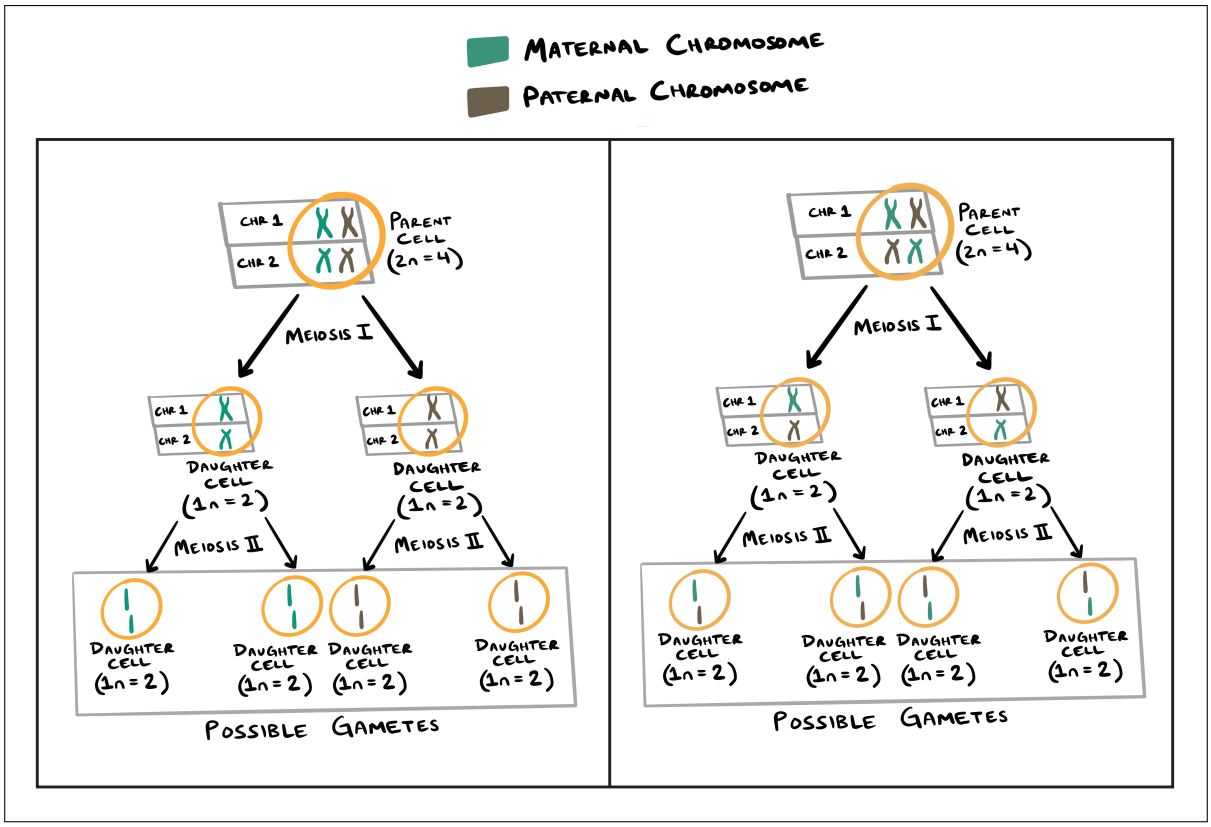


Figure 4: The gametes that are possible from a diploid organism with two chromosomes. There are 4 possible gametes (although there are 8 possible gametes shown, you'll notice that half of them have an identical version). Importantly, this is ignoring recombination (which would increase the number of diverse gametes dramatically).

**Practice problem**: How many chromosomes are in a human germ cell preparing to undergo Meiosis I? How many chromosomes are in each daughter cell after Meiosis I? How many molecules of DNA are in each daughter cell after Meiosis I?

**Solution**: A human germ cell preparing for Meiosis I has a pair of homologous chromosomes for each of the 23 chromosomes, making 46 chromosomes in total. The two cells after Meiosis I only have one chromosome for each of the 23 chromosomes, making 23 chromosomes in total within each of the daughter cells. These chromosomes are still composed of two sister chromatids (in their "X"-looking form), meaning that there are 46 molecules of DNA within each of the daughter cells after Meiosis I.

## 5.2 Meiosis II

Rather than going through another round of interphase, after Meiosis I is completed the resulting daughter cells go straight into Meiosis II. The chromosomes are still made up of two sister chromatids. Also similar to Mitosis and Meiosis I, Meiosis II has "sub"-phases (we put a "II" after these to indicate they are for Meiosis II ["Prophase II", "Metaphase II", "Anaphase II", and "Telophase II"]). Although the "sub"-phases of Meiosis II are named the same and are very similar to those of Mitosis and Meiosis I, there are important differences.

### 5.2.1 Key differences between Meiosis II and Mitosis / Meiosis I:

- During Metaphase II, the chromosomes align in single-file along the metaphase plate; through the centromeres of each chromosome. This is the same as Metaphase of Mitosis, but remember that only half of the chromosomes are present in Meiosis II.
- In Anaphase II, the sister chromatids are separated and move to opposite sides of the cell. This is the same as Anaphase of Mitosis, but remember that only half of the chromosomes are present in Meiosis II.
- You should notice that Meiosis II is very similar to Mitosis– the only difference being that half of the chromosomes are missing in Meiosis II (Meiosis II occurs with haploid cells).

**Practice problem**: How many chromosomes are in each human daughter cell after Meiosis II?

**Solution**: A human germ cell preparing for Meiosis I has a pair of homologous chromosomes for each of the 23 chromosomes, making 46 chromosomes in total. The two cells after Meiosis I only have one chromosome for each of the 23 chromosomes, making 23 chromosomes in total within each of the cells. These chromosomes are no longer made up of two sister chromatids (because they were separated in Anaphase II), meaning that there are 23 molecules of DNA in the daughter cells after Meiosis II.

**Practice problem**: For a human cell containing 6 pg of DNA before S phase, how much DNA is in the cell after S phase? If it is a somatic cell, how much after Mitosis? If it is a sex cell, how much after Meiosis I? How much after Meiosis II?

**Solution**: The DNA is doubled with S phase, so after there would be 12 pg. Mitosis then splits the sister chromatids apart, so the daughter cells would be back to 6 pg. In a sex cell, after Meiosis I the daughter cells would be back to 6 pg- but not because the sister chromatids were split apart, rather because the homologous pairs were separated. After Meiosis II the daughter cells would be at 3 pg due to the sister chromatids being split apart. (see Figure 5)

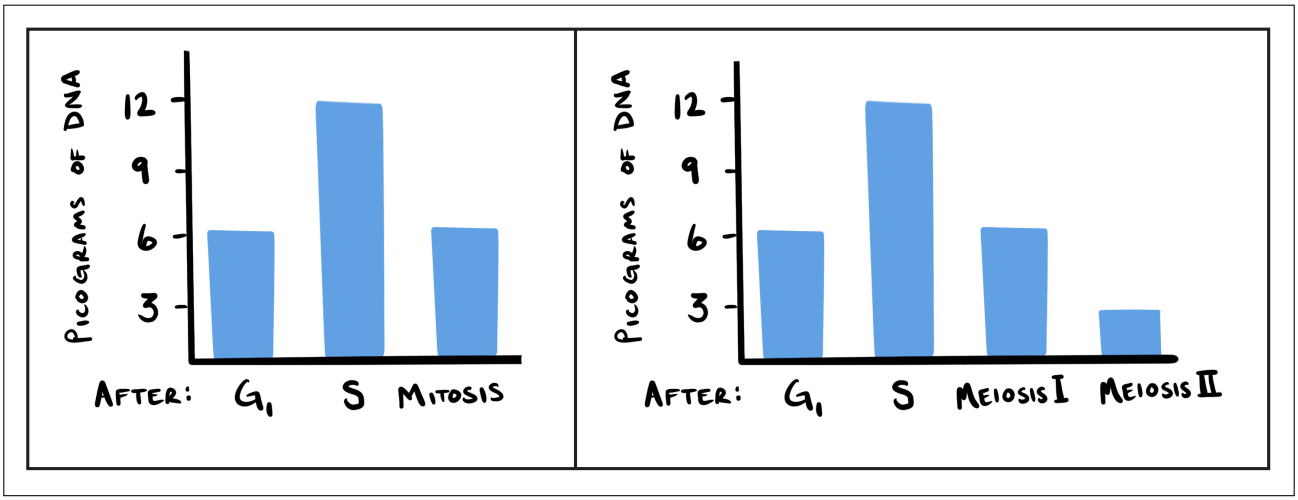


Figure 5: Quantity of DNA in a cell following stages of cell cycle.

## 5.3 Fertilization

The haploid gametes that are produced by meiosis are then used for sexual reproduction. Just as ploidy is reduced via Meiosis (diploid→haploid), it is restored via **fertilization** (the union of sperm and egg gametes) in sexual reproduction (haploid + haploid = diploid). The egg is the larger gamete that contains many of the components that will be inherited by the offspring (e.g., mitochondria, endoplasmic reticulum, golgi apparatus), and by biological definition the egg-creating sex is called **female**. The sperm is the smaller gamete that primarily serves to deliver DNA to the egg, and by biological definition the sperm-creating sex is called **male**. While these definitions are useful models that help scientists understand patterns in nature, they are not perfect models and therefore their application to all scenarios (such as those outside of biological science) may not be appropriate (e.g., there are individuals that cannot produce gametes, this does not mean they should not be considered either male or female in societal policies).

The cell formed after fertilization is called a **zygote**. This cell will develop into the organism through Mitosis, with the tissues, organs, and organ systems all differentiating from this single cell. One cell diversifies into the vast array of cells that make up an organism, including the germ cells that will eventually undergo Meiosis to create gametes.

The proportion of gametes that will become a zygote is remarkably small. Of all sperm produced by a male individual during his lifetime (which can be more than 1 quadrillion sperm cells for a human), If that person has 4 children only 1 / 250,000,000,000 of his gametes went on to become offspring. Once a male human becomes reproductively mature, sperm cells are generated through Meiosis in the testes just as it is described above (one germ cell becomes four gametes).

However, egg creation is different. Meiosis begins in before a female human is even born, in fact you may have heard that female humans are born with all of their eggs they will have (approximately six million). This is true, but these eggs are not yet gametes- they are cells called **primary oocytes** that get stalled in Prophase I. When a female human becomes reproductively mature, Meiosis I becomes re-activated one cell at a time on a monthly cycle. Ovulation is when Meiosis I is complete, and a **secondary oocyte** (daughter cell from Meiosis I) is released by the ovary. Notably, only one daughter cell from Meiosis I is **viable** (capable of surviving), the other daughter cell is called a polar body and does not contain the materials required to become an egg (which is terminated and its materials are recycled). A secondary oocyte will become an **ovum** (egg gamete) only if a sperm cell penetrates the egg membrane, which will stimulate the completion of Meiosis II in the egg. The other daughter cell is another polar body. So, to recap, while the process of Meiosis creates four cells, in human egg production it really only produces one cell.

# 6 Other Forms of Reproduction

While reproduction through the union of two sex cells (a.k.a., sexual reproduction) is ubiquitous among vertebrate organisms (i.e., 99.99% of vertebrates reproduce via sexual reproduction), many other organisms reproduce using other mechanisms. Here are a few examples:

- **Binary fission**: The mechanism of asexual reproduction used by bacteria where the bacterial chromosome is inherited by the descendant cells through cell division.
- **"Budding"**: Offspring are created through mitosis; an outgrowth of the organism is eventually broken off and becomes its own organism that is genetically identical to the parent.

- **Sporophytes**: Many plant, algae, and fungi use an alternating generation strategy for reproduction. Spores are haploid cells created by these organisms that are not used for fertilization- instead they are sent off and divide via mitosis to create a multicellular "sporophyte" stage and later will create gametes that will be used for sexual reproduction.
- **Parthenogenesis**: Some organisms, including vertebrates, reproduce through sexual reproduction. Although the exact mechanism for this kind of reproduction can vary, most of them utilize a modified version of meiosis to create clones of themselves