THE CELL BIOLOGY (PART TWO)

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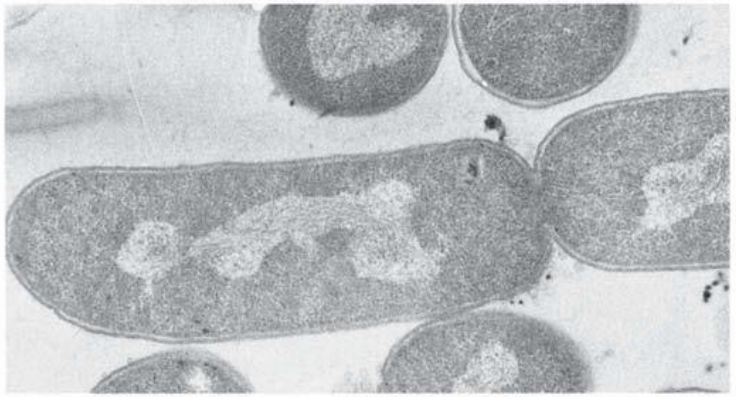
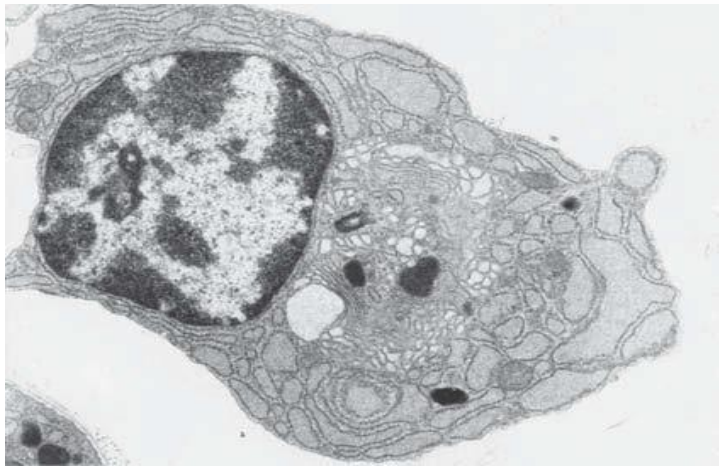
PROKARYOTIC VS. EUKARYOTIC

- The biological universe:
  - Prokaryotic cells:
    - single closed compartment
    - Surrounded by a plasma membrane
    - lack a defined nucleus
    - simple internal organization
  - Eukaryotic cells:
    - defined membrane-bounded nucleus
    - extensive internal membranes
    - organelles

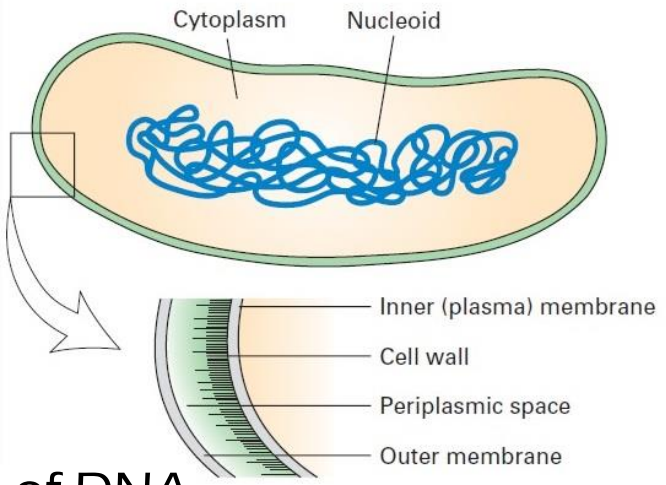




PROKARYOTIC CELLS

Two Kingdoms: *Archaea* and Eubacteria

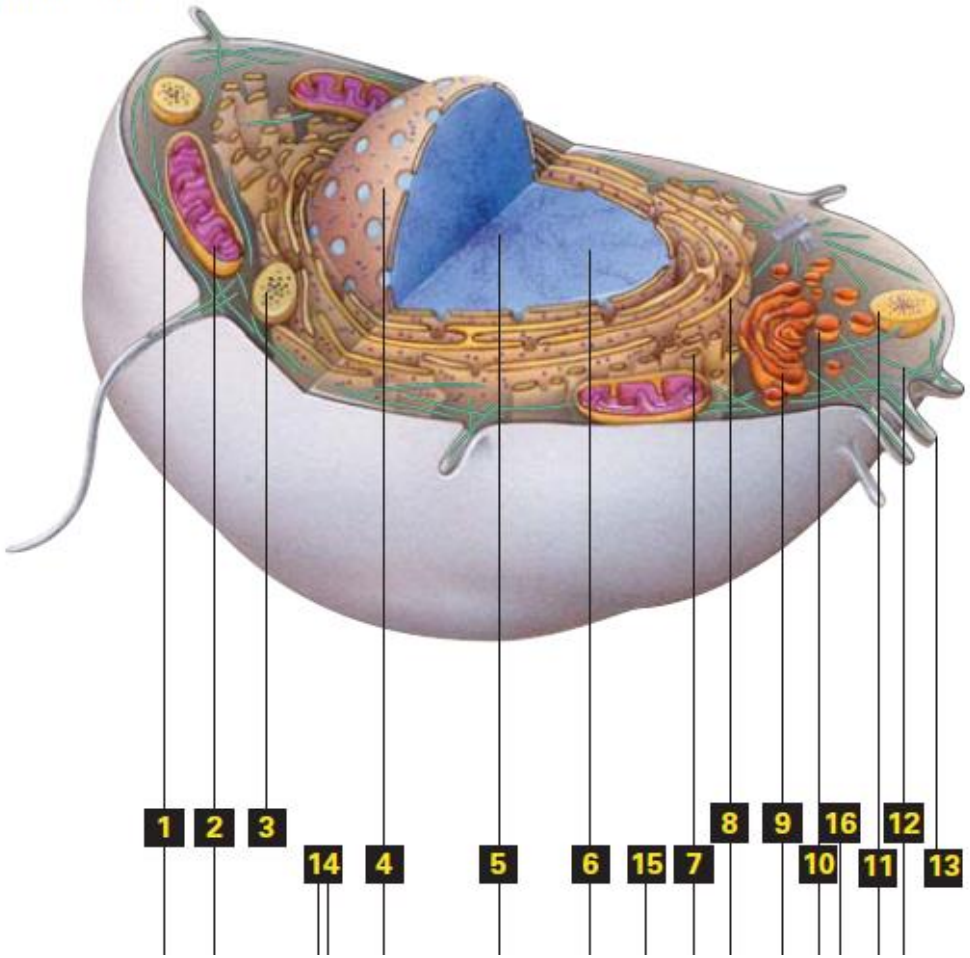
- Eubacteria
  - single-celled organisms, 1-2 μm in size
  - **Cytoplasm**, bounded by the **plasma membrane**
  - **genome** is composed of a single circular DNA molecule
  - Additional small circular DNA called ***plasmids***
  - DNA is extensively folded and condensed called the **nucleoid**
  - **mesosome**, invagination of the cell membrane, places for: synthesis of DNA and secretion of proteins
  - **cell wall**, adjacent to the external side of the plasma membrane
    - peptidoglycan, protect the cell and maintain its shape
    - **Gram-negatives:** thin inner cell wall, outer membrane, separated by the periplasmic space. *(e.g. E.coli)*
    - **Gram-positives:** thicker cell wall, no outer membrane (e.g., *Bacillus polymyxa*)



PROKARYOTIC CELLS

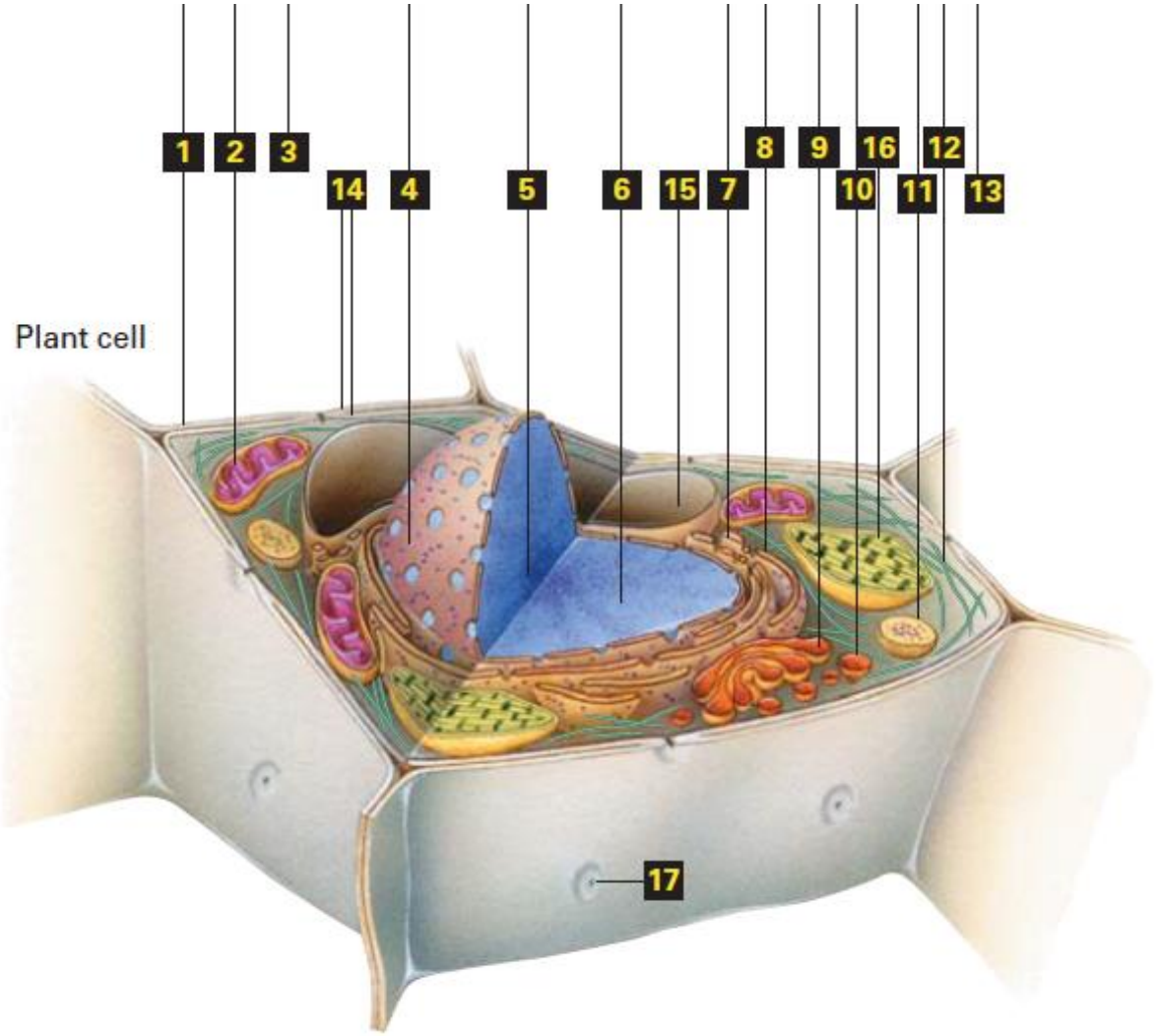
- Archaea
  - **DNA sequence** distinctions from eubacterias
  - **cell membranes** that differ dramatically in composition
  - grow in **extreme environments**
    - halophiles ("salt lovers")
    - thermoacidophiles ("heat and acid lovers")
    - other archaeans live in oxygen-free milieus and generate methane (CH4) by combining water with carbon dioxide.

Animal cell



1. Plasma membrane controls movement of molecules in and out of the cell and functions in cell-cell signaling and cell adhesion.
2. Mitochondria, which are surrounded by a double membrane, generate ATP by oxidation of glucose and fatty acids.
3. Lysosomes, which have an acidic lumen, degrade material internalized by the cell and worn-out cellular membranes and organelles.
4. Nuclear envelope, a double membrane, encloses the contents of the nucleus; the outer nuclear membrane is continuous with the rough ER.
5. Nucleolus is a nuclear subcompartment where most of the cell's rRNA is synthesized.
6. Nucleus is filled with chromatin composed of DNA and proteins; site of mRNA and tRNA synthesis.
7. Smooth endoplasmic reticulum (ER) contains enzymes that synthesize lipids and detoxify certain hydrophobic molecules.
8. Rough endoplasmic reticulum (ER) functions in the synthesis, processing, and sorting of secreted proteins, lysosomal proteins, and certain membrane proteins.
9. Golgi complex processes and sorts secreted proteins, lysosomal proteins, and membrane proteins synthesized on the rough ER.
10. Secretory vesicles store secreted proteins and fuse with the plasma membrane to release their contents.
11. Peroxisomes contain enzymes that break down fatty acids into smaller molecules used for biosynthesis and also detoxify certain molecules.

EUKARYOTIC CELL



12 Cytoskeletal fibers form networks and bundles that support cellular membranes, help organize organelles, and participate in cell movement.

13 Microvilli increase surface area for absorption of nutrients from surrounding medium.

14 Cell wall, composed largely of cellulose, helps maintain the cell's shape and provides protection against mechanical stress.

15 Vacuole stores water, ions, and nutrients, degrades macromolecules, and functions in cell elongation during growth.

16 Chloroplasts, which carry out photosynthesis, are surrounded by a double membrane and contain a network of internal membrane-bounded sacs.

17 Plasmodesmata are tubelike cell junctions that span the cell wall and connect the cytoplasms of adjacent plant cells.

CHARACTERISTICS OF EUKARYOTIC CELLS

Characteristics of eukaryotic cells

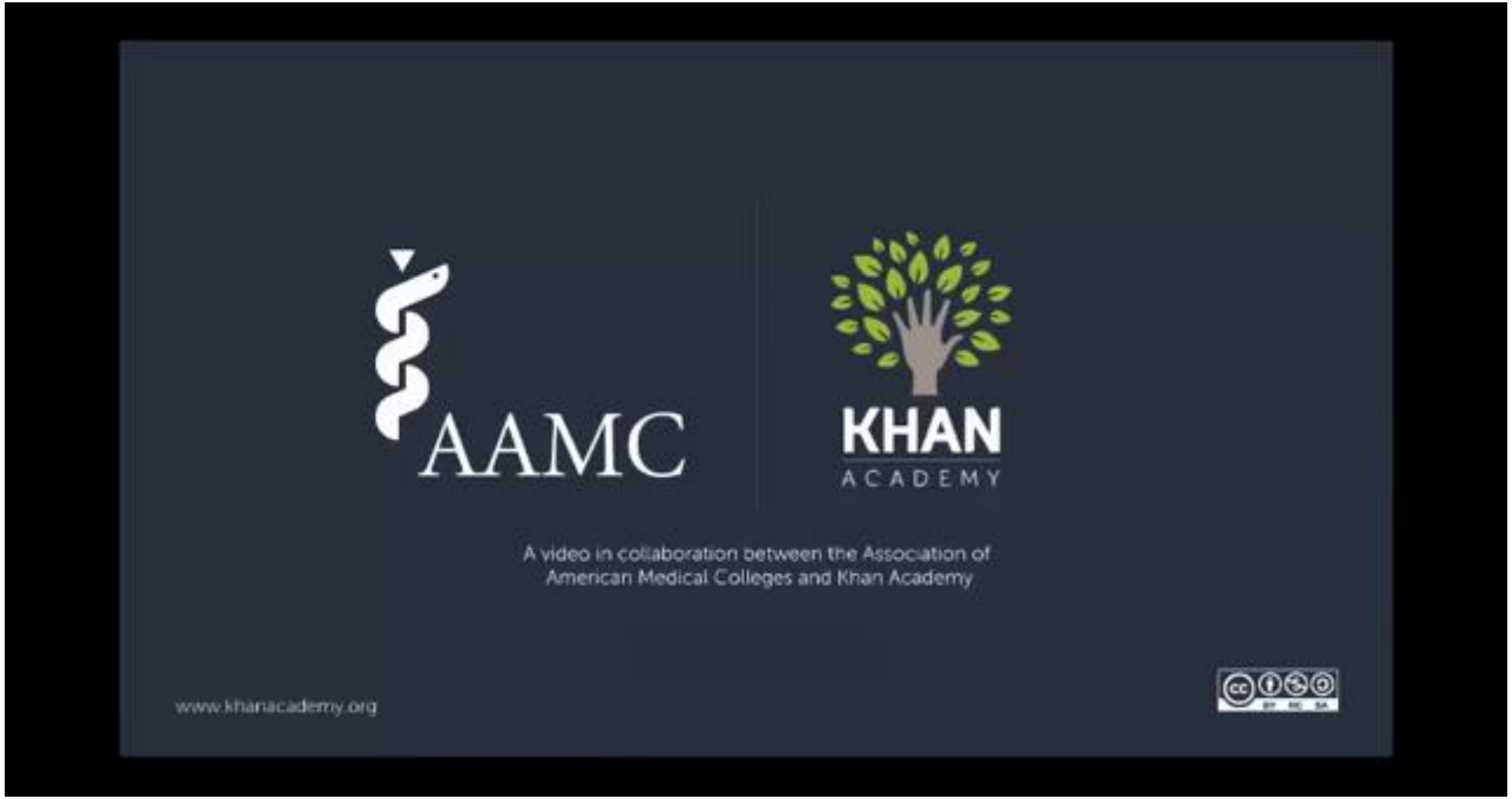
THE NUCLEUS

The nucleus

LYSOSOMES AND PEROXISOMES

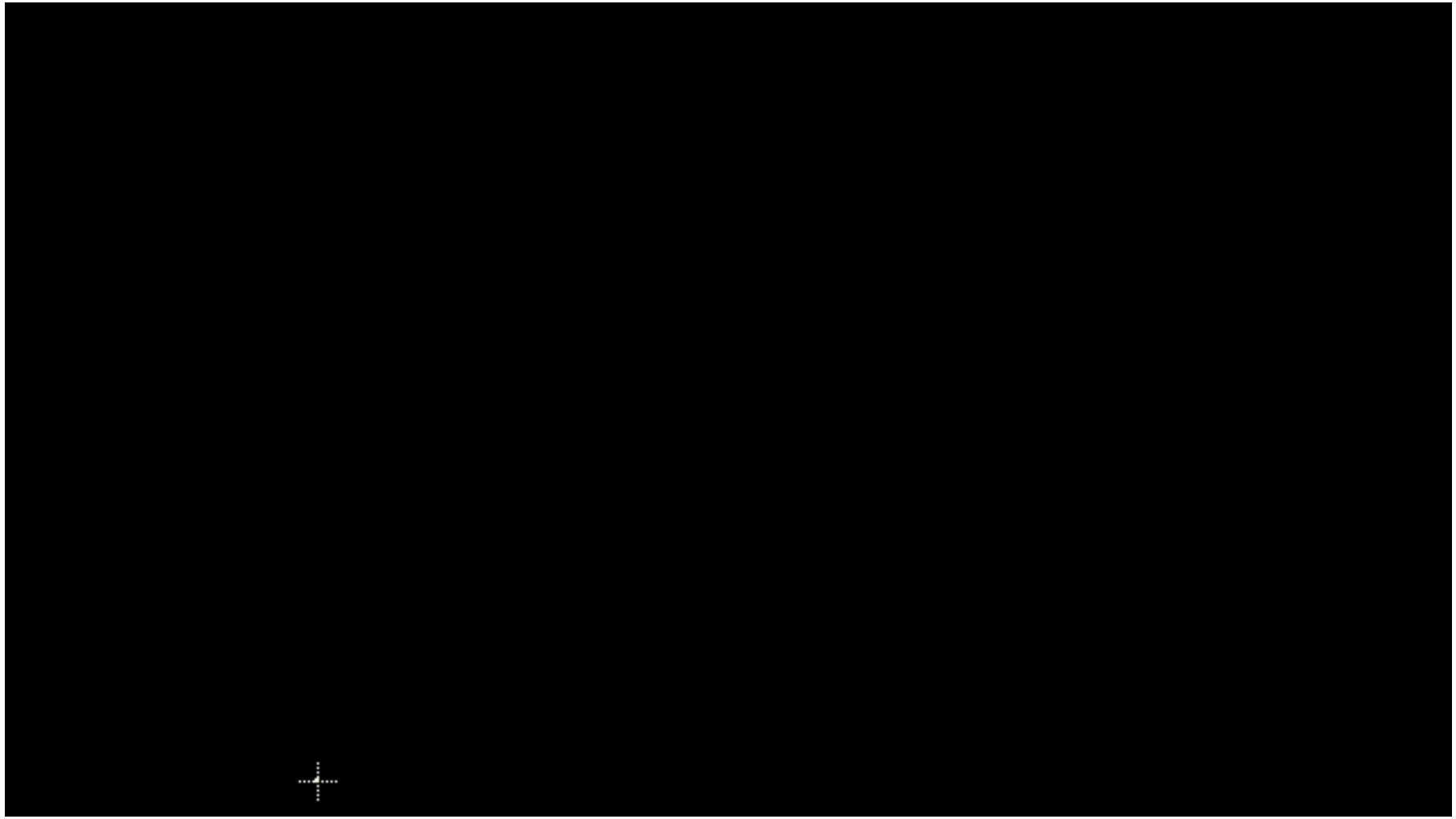
Lysosomes and peroxisomes

INTRODUCTION TO CYTOSKELETON



Introduction to cytoskeleton

CHROMOSOMES, CHROMATIDS, CHROMATIN, ETC.



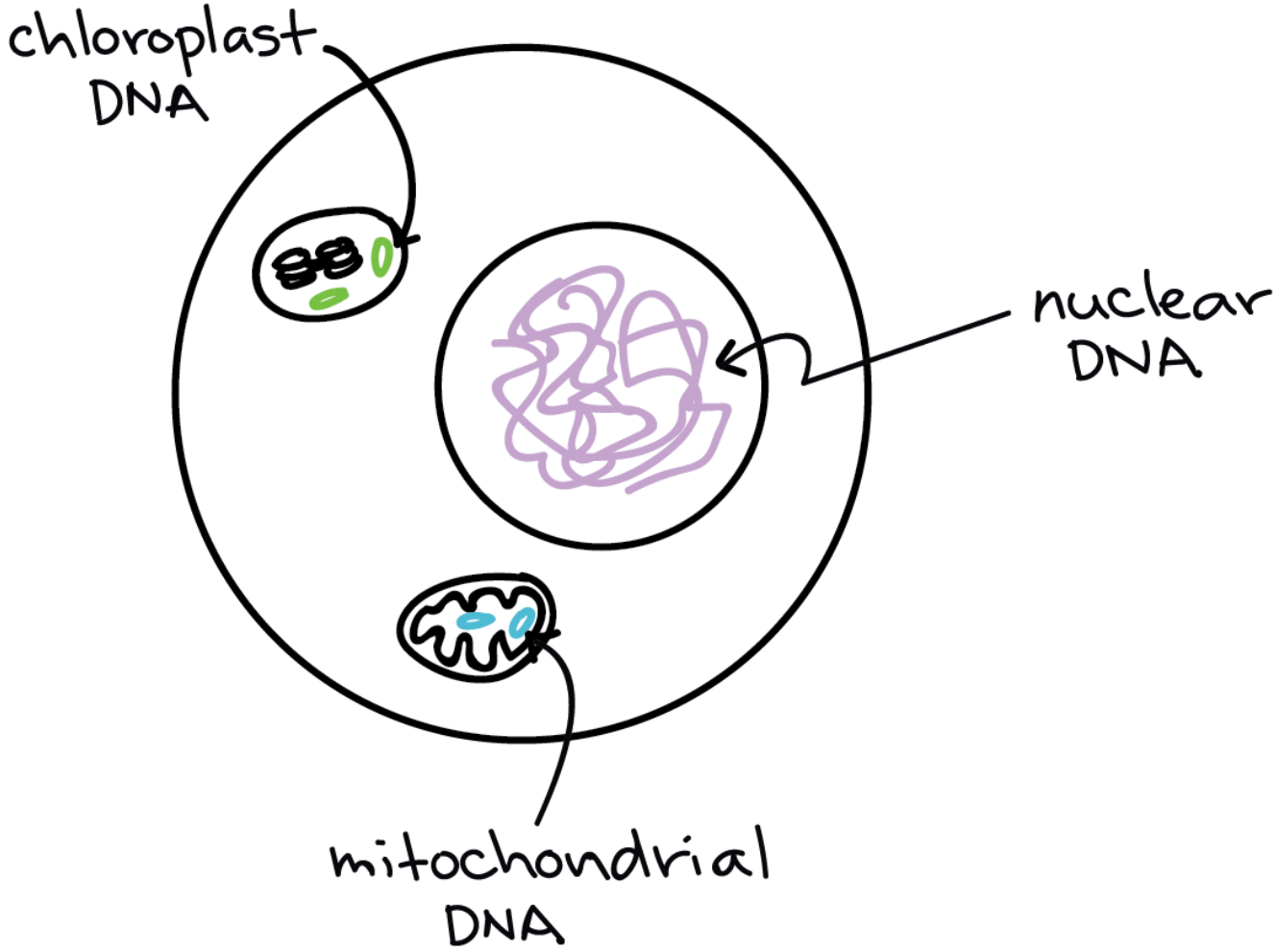
CHROMOSOMES

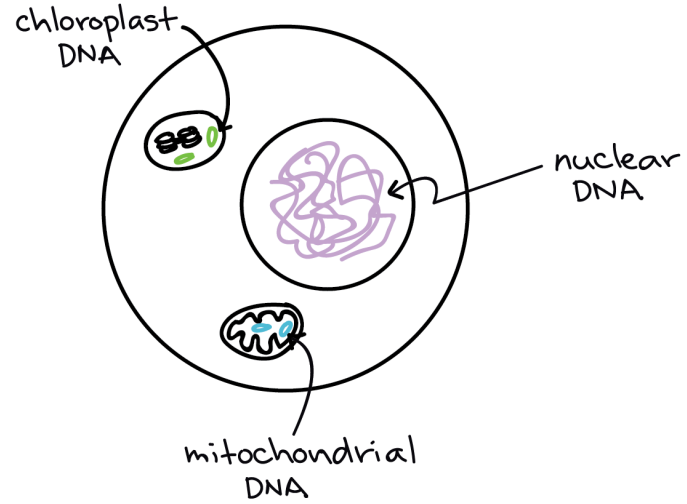
- Introduction
- When a cell divides, one of its main jobs is to make sure that each of the two new cells gets a full, perfect copy of genetic material. Mistakes during copying, or unequal division of the genetic material between cells, can lead to cells that are unhealthy or dysfunctional (and may lead to diseases such as cancer).

- But what exactly is this genetic material, and how does it behave over the course of a cell division?

DNA AND GENOMES

- **DNA** (**deoxyribonucleic acid**) is the genetic material of living organisms. In humans, DNA is found in almost all the cells of the body and provides the instructions they need to grow, function, and respond to their environment.
- When a cell in the body divides, it will pass on a copy of its DNA to each of its daughter cells. DNA is also passed on at the level of organisms, with the DNA in sperm and egg cells combining to form a new organism that has genetic material from both its parents.
- Physically speaking, DNA is a long string of paired chemical units (nucleotides) that come in four different types, abbreviated A, T, C, and G, and it carries information organized into units called **genes**. Genes typically provide instructions for making proteins, which give cells and organisms their functional characteristics


chloroplast DNA
nuclear DNA
mitochondrial DNA



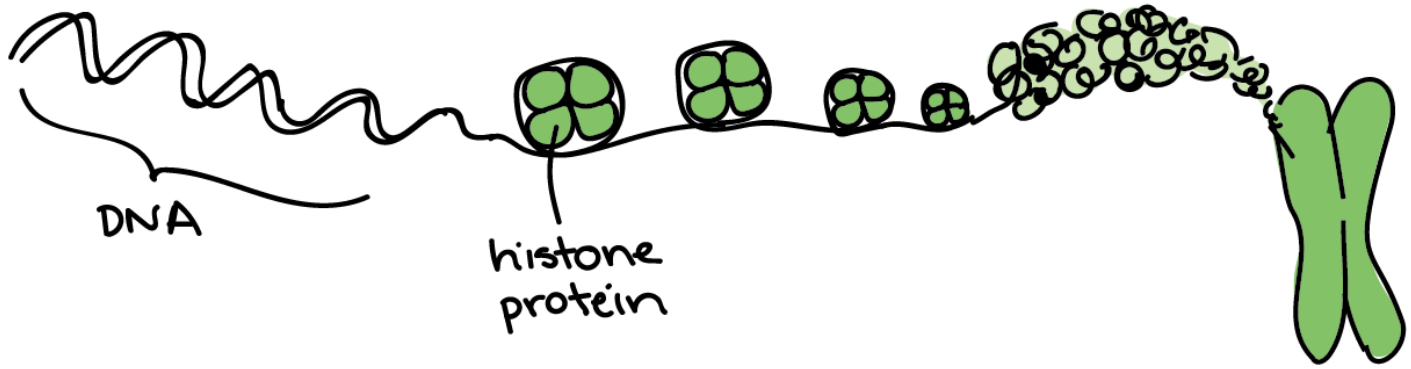
- In eukaryotes such as plants and animals, the majority of DNA is found in the nucleus and is called **nuclear DNA**. Mitochondria, organelles that harvest energy for the cell, contain their own **mitochondrial DNA**, and chloroplasts, organelles that carry out photosynthesis in plant cells, also have **chloroplast DNA**. The amounts of DNA found in mitochondria and chloroplasts are much smaller than the amount found in the nucleus. In bacteria, most of the DNA is found in a central region of the cell called the **nucleoid**, which functions similarly to a nucleus but is not surrounded by a membrane.

DNA AND GENOMES

- A cell's set of DNA is called its **genome**. Since all of the cells in an organism (with a few exceptions) contain the same DNA, you can also say that an organism has its own genome, and since the members of a species typically have similar genomes, you can also describe the genome of a species. In general, when people refer to the human genome, or any other eukaryotic genome, they mean the set of DNA found in the nucleus. Mitochondria and chloroplasts are considered to have their own separate genomes.

CHROMATIN

- In a cell, DNA does not usually exist by itself, but instead associates with specialized proteins that organize it and give it structure. In eukaryotes, these proteins include the **histones**, a group of basic (positively charged) proteins that form "bobbins" around which negatively charged DNA can wrap. In addition to organizing DNA and making it more compact, histones play an important role in determining which genes are active. The complex of DNA plus histones and other structural proteins is called **chromatin**.



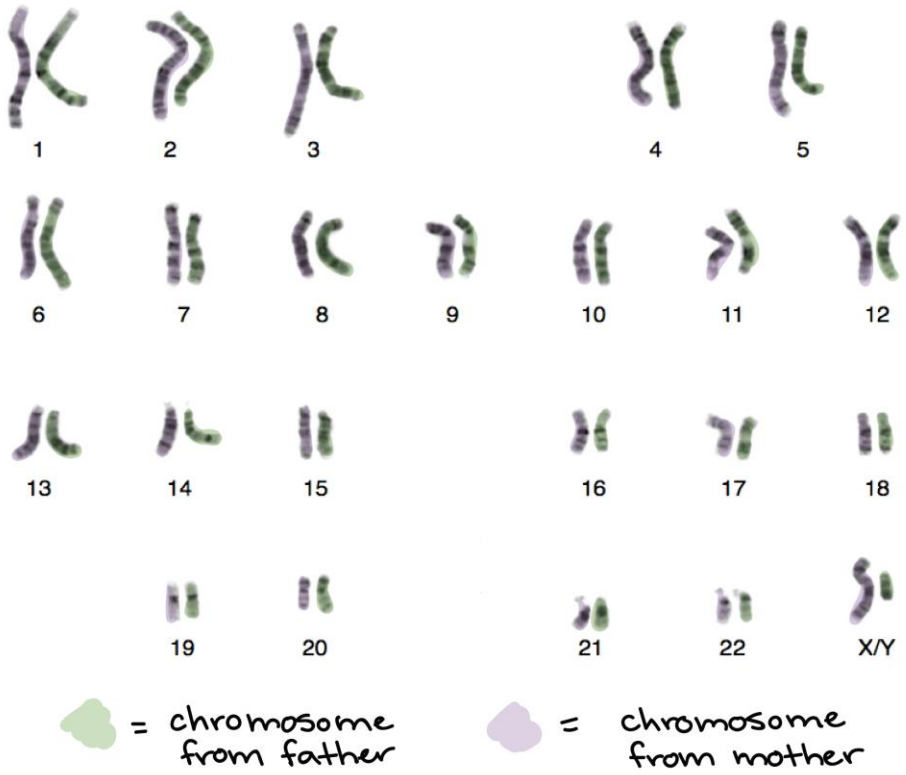
CHROMATIN

- For most of the life of the cell, chromatin is **decondensed**, meaning that it exists in long, thin strings that look like squiggles under the microscope. In this state, the DNA can be accessed relatively easily by cellular machinery (such as proteins that read and copy DNA), which is important in allowing the cell to grow and function.
- *Decondensed* may seem like an odd term for this state – why not just call it "stringy"? – but makes more sense when you learn that chromatin can also **condense**. Condensation takes place when the cell is about to divide. When chromatin condenses, you can see that eukaryotic DNA is not just one long string. Instead, it's broken up into separate, linear pieces called **chromosomes**. Bacteria also have chromosomes, but their chromosomes are typically circular.

CHROMOSOMES

- Each species has its own characteristic number of chromosomes. Humans, for instance, have 46 chromosomes in a typical body cell (somatic cell), while dogs have 78^11start superscript, 1, end superscript. Like many species of animals and plants, humans are **diploid** (**2*n***), meaning that most of their chromosomes come in matched sets known as **homologous pairs**. The 46 chromosomes of a human cell are organized into 23 pairs, and the two members of each pair are said to be **homologues** of one another (with the slight exception of the X and Y chromosomes; see below).
- Human sperm and eggs, which have only one homologous chromosome from each pair, are said to be **haploid** (**1*n***). When a sperm and egg fuse, their genetic material combines to form one complete, diploid set of chromosomes. So, for each homologous pair of chromosomes in your genome, one of the homologues comes from your mom and the other from your dad.

CHROMOSOMES



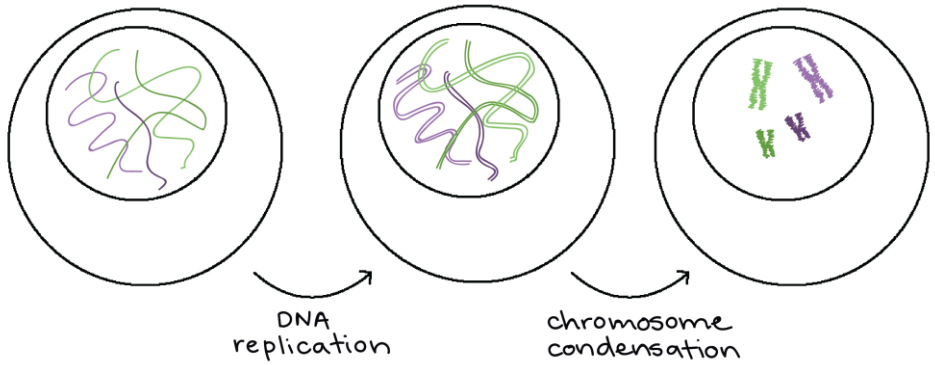
CHROMOSOMES

- The two chromosomes in a homologous pair are very similar to one another and have the same size and shape. Most importantly, they carry the same type of genetic information: that is, they have the same genes in the same locations. However, they don't necessarily have the same versions of genes. That's because you may have inherited two different gene versions from your mom and your dad.
- As a real example, let's consider a gene on chromosome 9 that determines blood type (A, B, AB, or O)^22start superscript, 2, end superscript. It's possible for a person to have two identical copies of this gene, one on each homologous chromosome—for example, you may have a double dose of the gene version for type A. On the other hand, you may have two different gene versions on your two homologous chromosomes, such as one for type A and one for type B (giving AB blood).

CHROMOSOMES

- The **sex chromosomes**, X and Y, determine a person's biological sex: XX specifies female and XY specifies male. These chromosomes are not true homologues and are an exception to the rule of the same genes in the same places. Aside from small regions of similarity needed during meiosis, or sex cell production, the X and Y chromosomes are different and carry different genes. The 44 non-sex chromosomes in humans are called **autosomes**

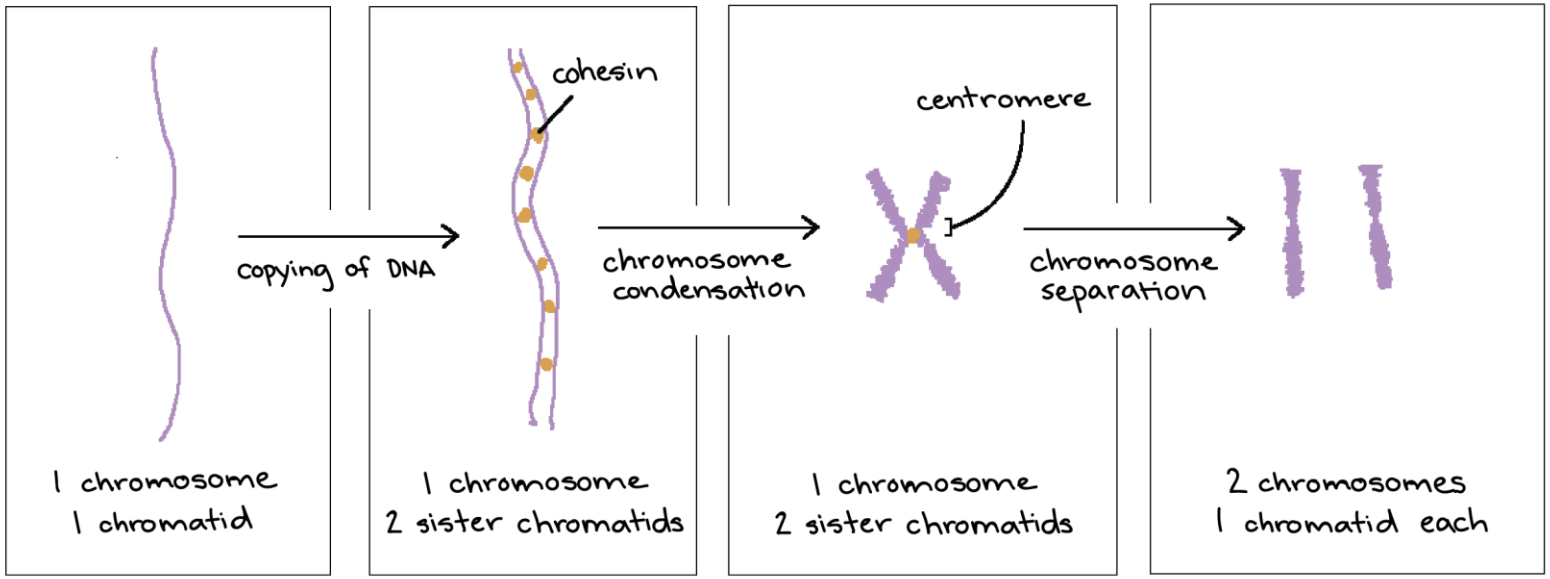
CHROMOSOMES AND CELL DIVISION



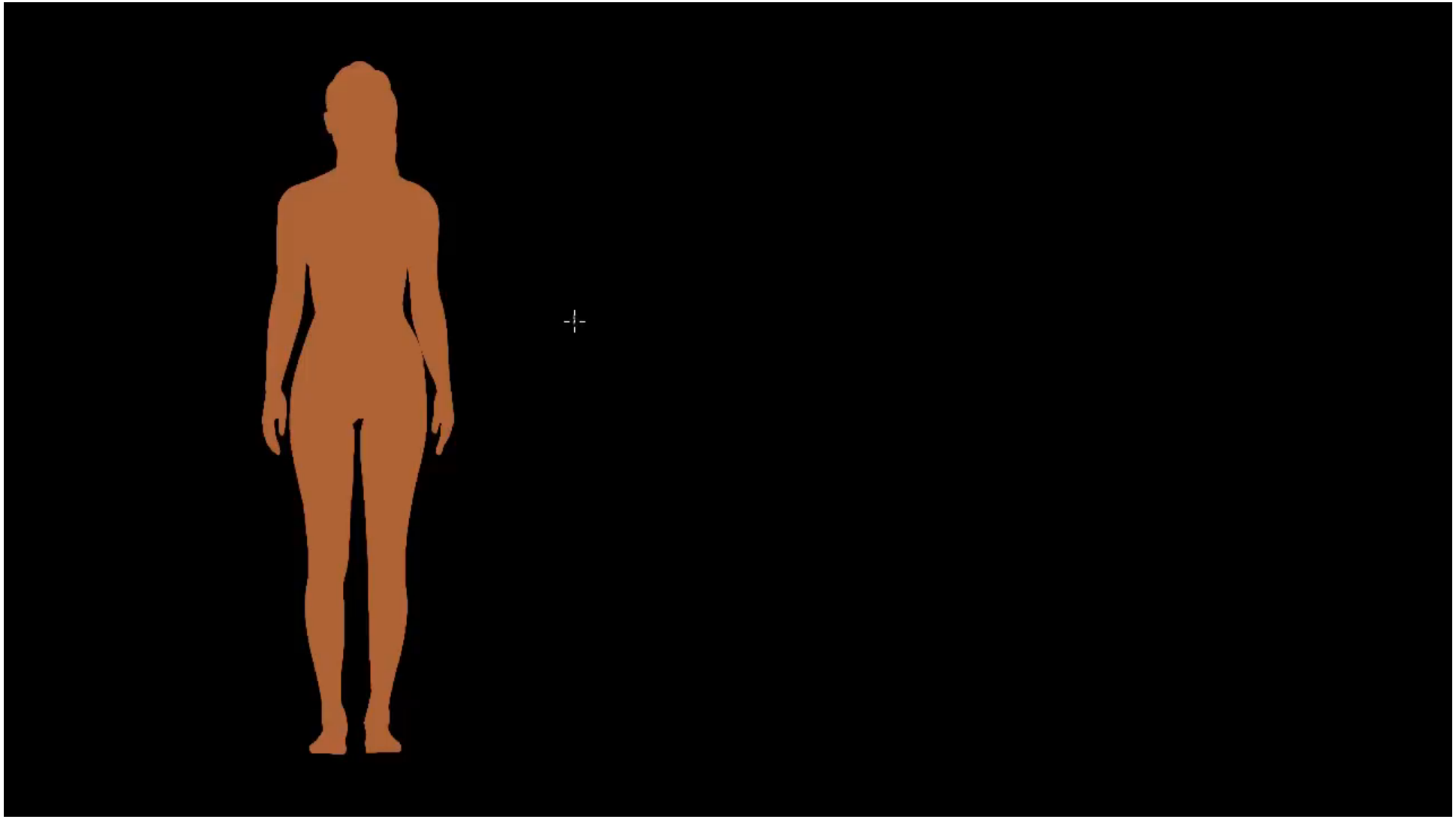
- As a cell prepares to divide, it must make a copy of each of its chromosomes. The two copies of a chromosome are called **sister chromatids**. The sister chromatids are identical to one another and are attached to each other by proteins called **cohesins**. The attachment between sister chromatids is tightest at the **centromere**, a region of DNA that is important for their separation during later stages of cell division

CHROMOSOMES AND CELL DIVISION

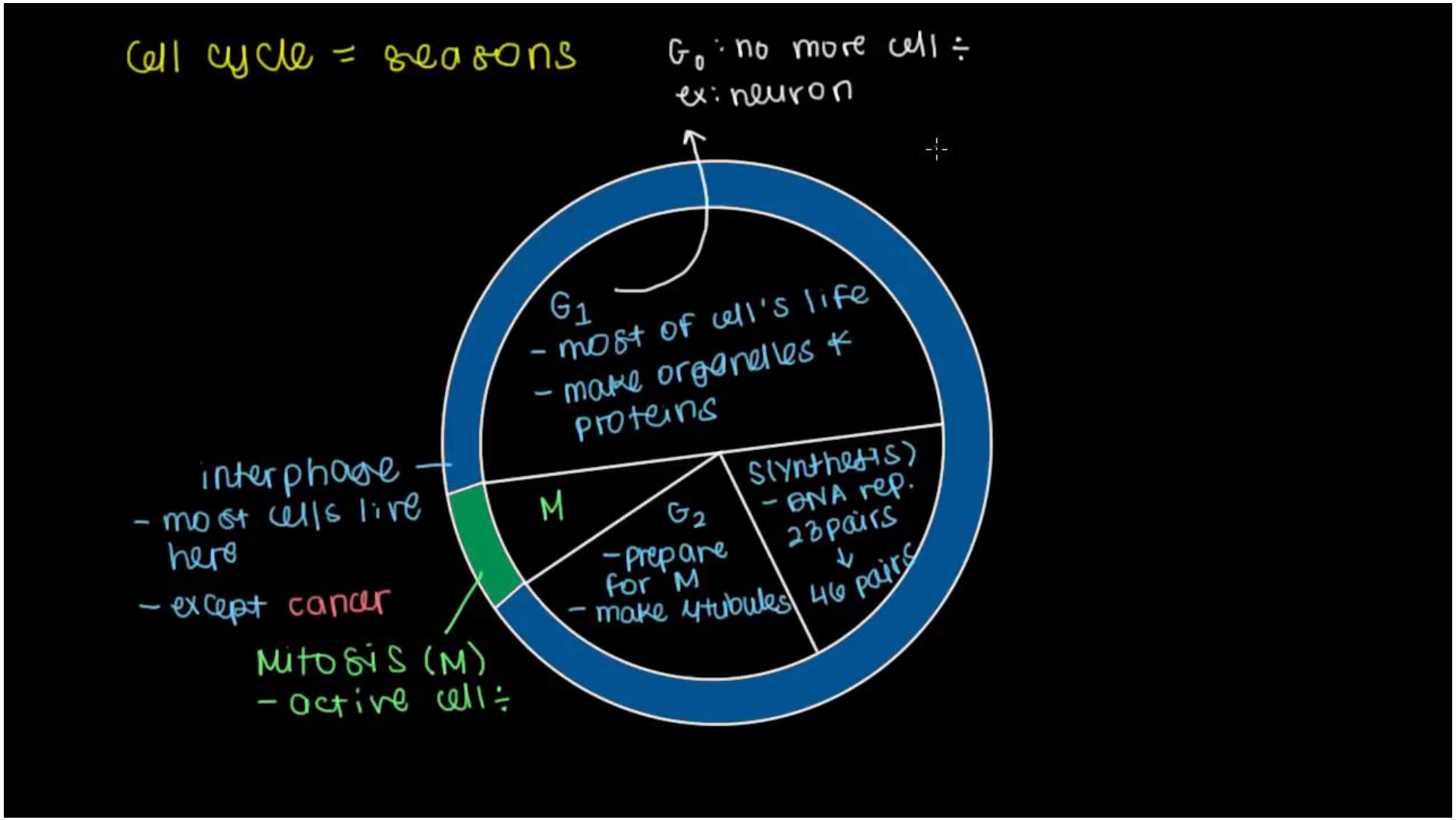
- As long as the sister chromatids are connected at the centromere, they are still considered to be one chromosome. However, as soon as they are pulled apart during cell division, each is considered a separate chromosome



CELL CYCLE PHASES



CELL CYCLE CONTROL



CELL CYCLE CHECKPOINTS

- **Introduction**
- As cells move through the cell cycle, do they breeze through from one phase to the next? If they're cancer cells, the answer might be yes.

- Normal cells, however, move through the cell cycle in a regulated way. They use information about their own internal state and cues from the environment around them to decide whether to proceed with cell division.

- This regulation makes sure that cells don't divide under unfavorable conditions (for instance, when their DNA is damaged, or when there isn't room for more cells in a tissue or organ).

CELL CYCLE CHECKPOINTS

- A **checkpoint** is a stage in the eukaryotic cell cycle at which the cell examines internal and external cues and "decides" whether or not to move forward with division.

- There are a number of checkpoints, but the three most important ones are:
  - The G1 checkpoint, at the G1/S transition.
  - The G2 checkpoint, at the G2/M transition.
  - The spindle checkpoint, at the transition from metaphase to anaphase.

CELL CYCLE CHECKPOINTS

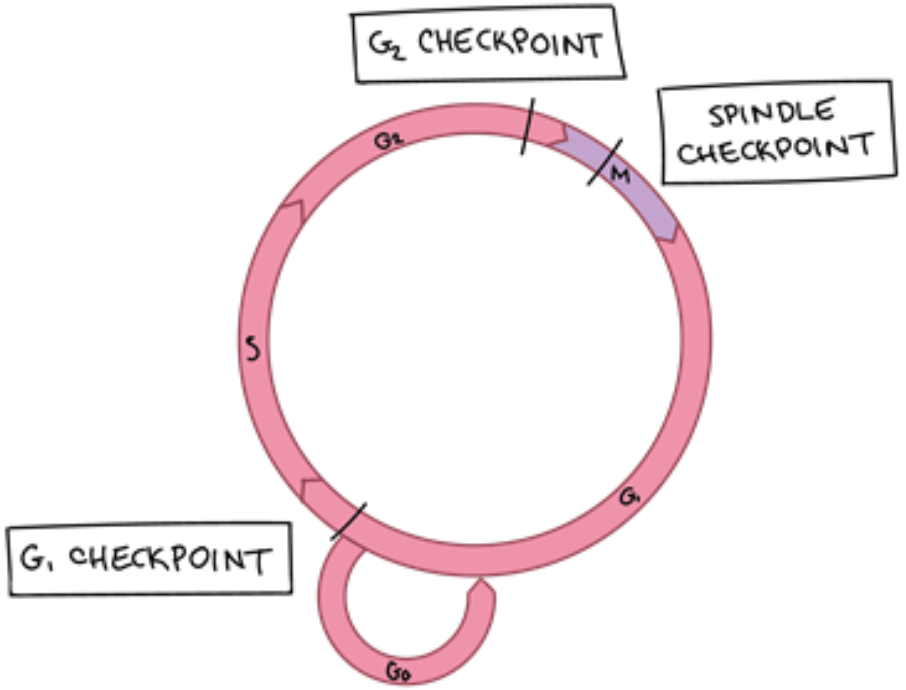


Diagram of cell cycle with checkpoints marked. G1 checkpoint is near the end of G1 (close to the G1/S transition). G2 checkpoint is near the end of G2 (close to the G2/M transition). Spindle checkpoint is partway through M phase, and more specifically, at the metaphase/anaphase transition.

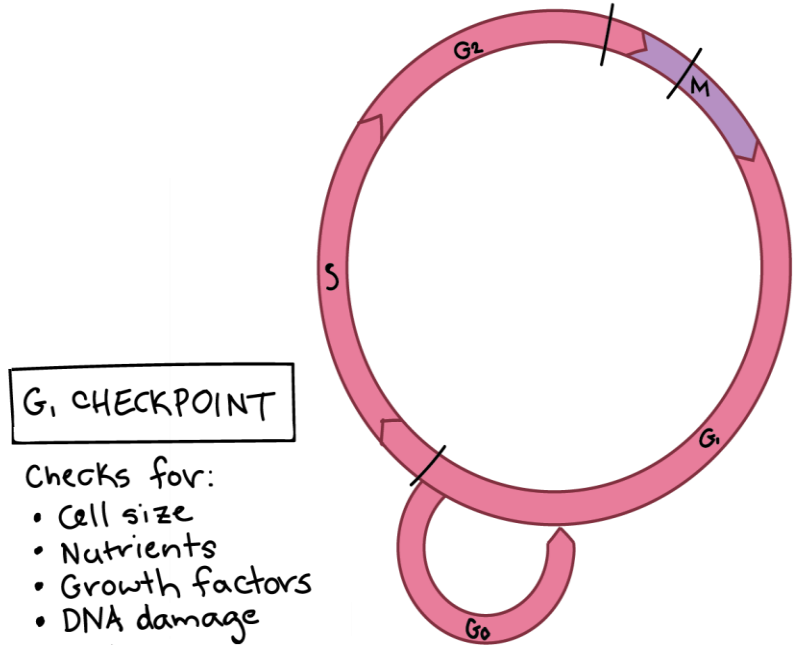
THE G1 CHECKPOINT

- The **G1 checkpoint** is the main decision point for a cell – that is, the primary point at which it must choose whether or not to divide.

- Once the cell passes the G1 checkpoint and enters S phase, it becomes irreversibly committed to division. That is, barring unexpected problems, such as DNA damage or replication errors, a cell that passes the G1 checkpoint will continue the rest of the way through the cell cycle and produce two daughter cells

THE G1 CHECKPOINT

- At the G1 checkpoint, a cell checks whether internal and external conditions are right for division. Here are some of the factors a cell might assess:
- **Size.** Is the cell large enough to divide?
- **Nutrients.** Does the cell have enough energy reserves or available nutrients to divide?
- **Molecular signals.** Is the cell receiving positive cues (such as growth factors) from neighbors?
- **DNA integrity.** Is any of the DNA damaged?



THE G1 CHECKPOINT

- These are not the only factors that can affect progression through the G1checkpoint, and which factors are most important depend on the type of cell. For instance, some cells also need mechanical cues (such as being attached to a supportive network called the extracellular matrix) in order to divide.
- If a cell doesn't get the go-ahead cues it needs at the G1 checkpoint, it may leave the cell cycle and enter a resting stat called **G0 phase**. Some cells stay permanently in G0, while others resume dividing if conditions improve

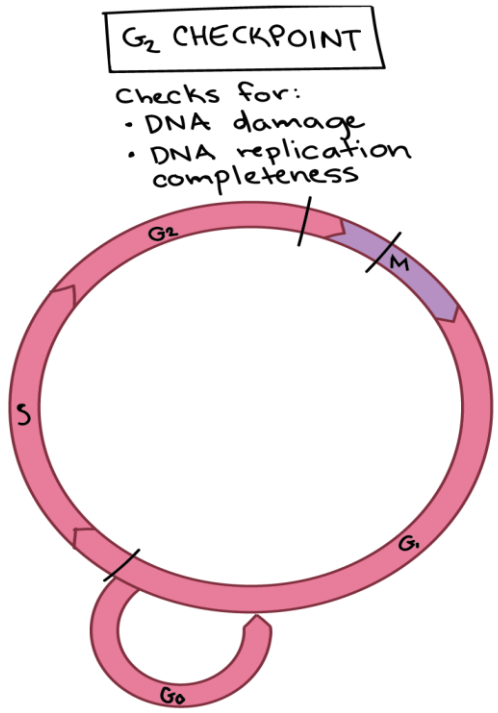
THE G2 CHECKPOINT

- To make sure that cell division goes smoothly (produces healthy daughter cells with complete, undamaged DNA), the cell has an additional checkpoint before M phase, called the **G2 checkpoint**. At this stage, the cell will check:
- **DNA integrity.** Is any of the DNA damaged?
- **DNA replication.** Was the DNA completely copied during S phase?
- If errors or damage are detected, the cell will pause at the G2 checkpoint to allow for repairs. If the checkpoint mechanisms detect problems with the DNA, the cell cycle is halted, and the cell attempts to either complete DNA replication or repair the damaged DNA.

THE G2 CHECKPOINT

- If the damage is irreparable, the cell may undergo apoptosis, or programmed cell death.

- This self-destruction mechanism ensures that damaged DNA is not passed on to daughter cells and is important in preventing cancer.

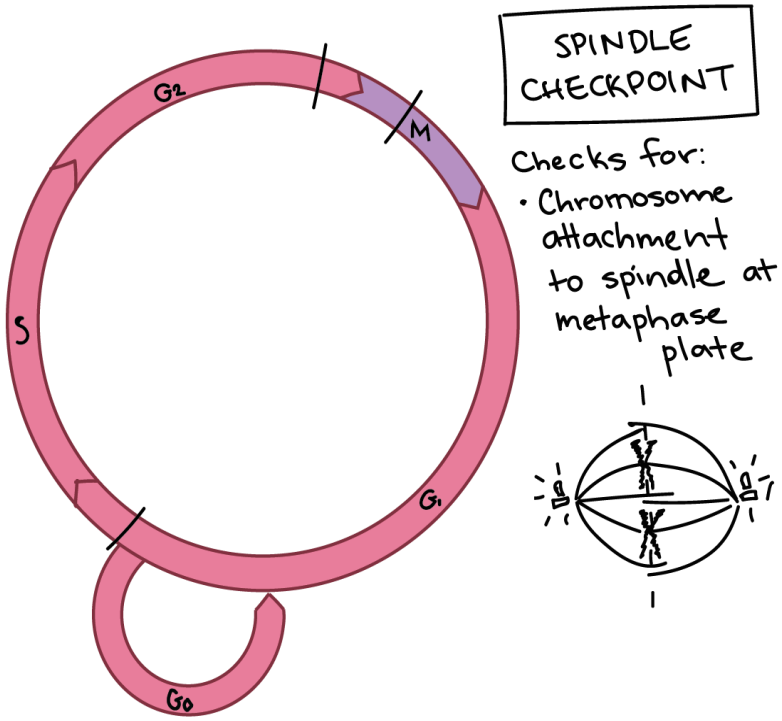


THE SPINDLE CHECKPOINT

- The M checkpoint is also known as the **spindle checkpoint**:

- here, the cell examines whether all the sister chromatids are correctly attached to the spindle microtubules.

- Because the separation of the sister chromatids during anaphase is an irreversible step, the cycle will not proceed until all the chromosomes are firmly attached to at least two spindle fibers from opposite poles of the cell.

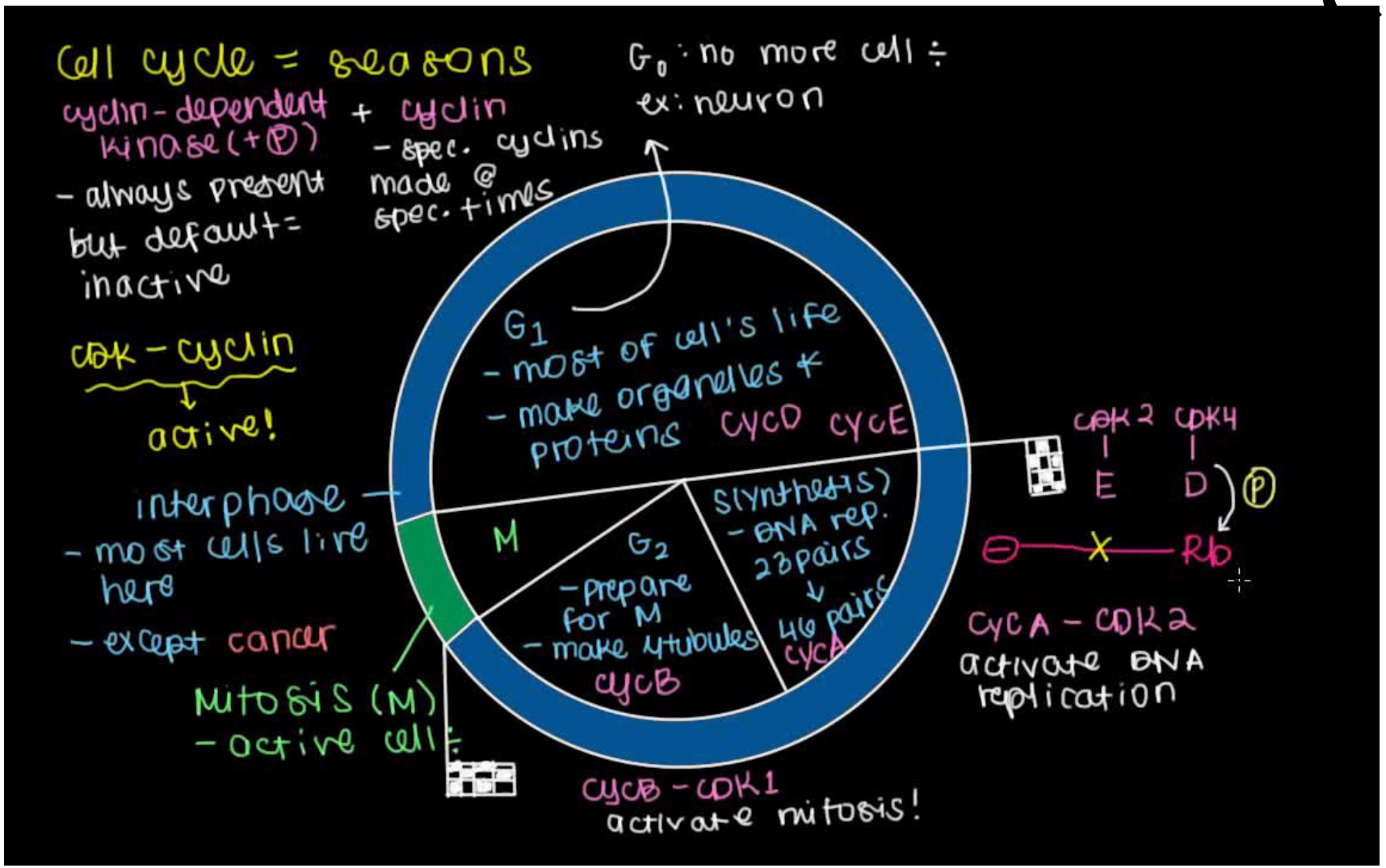


THE SPINDLE CHECKPOINT

- How does this checkpoint work? It seems that cells don't actually scan the metaphase plate to confirm that all of the chromosomes are there.

- Instead, they look for "straggler" chromosomes that are in the wrong place (e.g., floating around in the cytoplasm). If a chromosome is misplaced, the cell will pause mitosis, allowing time for the spindle to capture the stray chromosome.

LOSS OF CELL CYCLE CONTROL IN CANCER



CELL CYCLE REGULATORS

- the factors that a cell considers when deciding whether or not to move forward through the cell cycle. These include both external cues (like molecular signals) and internal cues (like DNA damage).

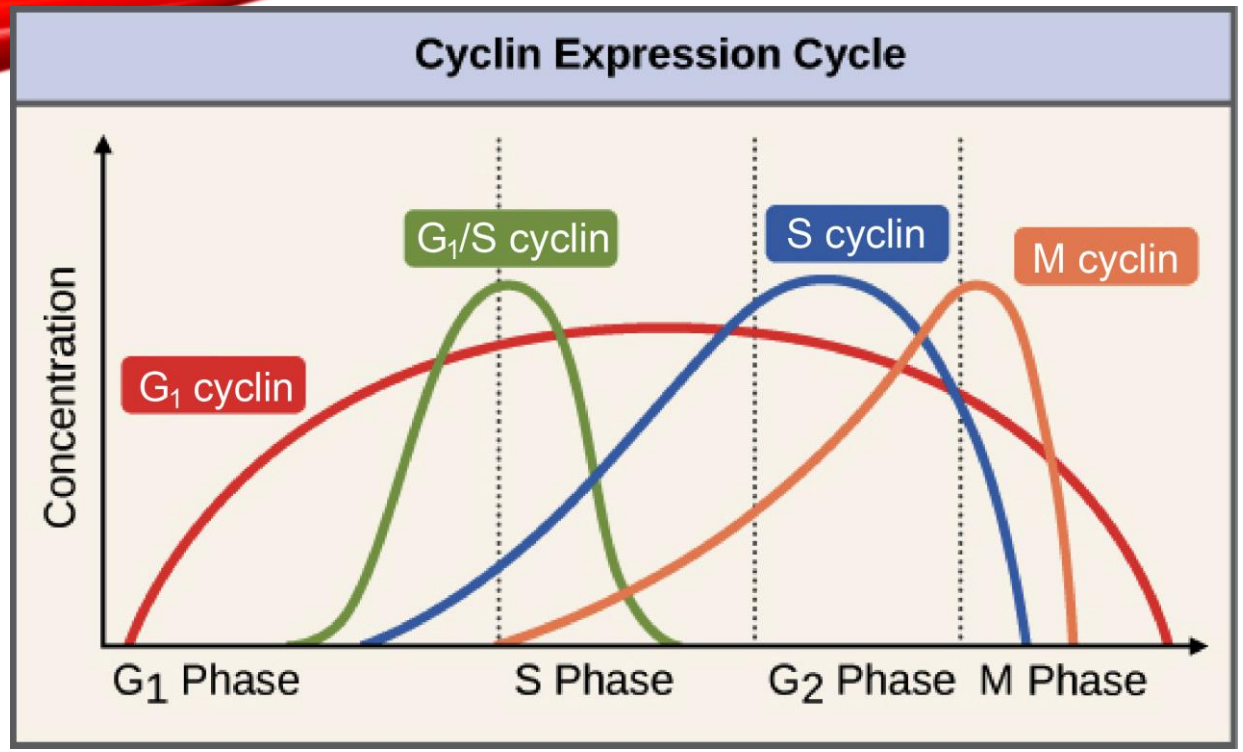
- Cues like these act by changing the activity of core cell cycle regulators inside the cell. These core cell cycle regulators can cause key events, such as DNA replication or chromosome separation, to take place. They also make sure that cell cycle events take place in the right order and that one phase (such as G1) triggers the onset of the next phase (such as S).

CYCLINS

- **Cyclins** are among the most important core cell cycle regulators. Cyclins are a group of related proteins, and there are four basic types found in humans and most other eukaryotes: G1 cyclins, G1/S cyclins, S cyclins, and M cyclins.

- As the names suggest, each cyclin is associated with a particular phase, transition, or set of phases in the cell cycle and helps drive the events of that phase or period. For instance, M cyclin promotes the events of M phase, such as nuclear envelope breakdown and chromosome condensation

CYCLINS



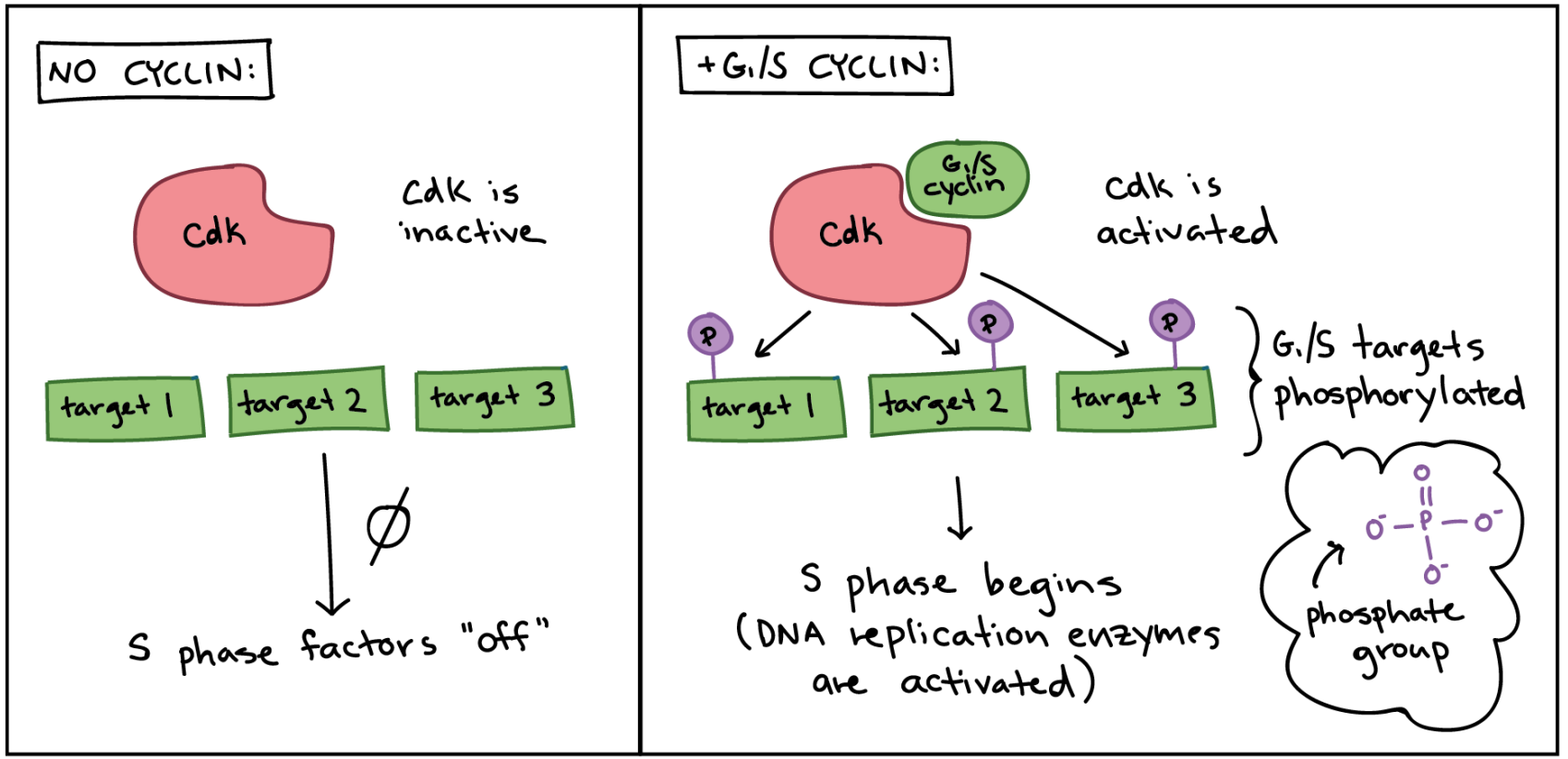
The levels of the different cyclins vary considerably across the cell cycle, as shown in the diagram above. A typical cyclin is present at low levels for most of the cycle, but increases strongly at the stage where it's needed. M cyclin, for example, peaks dramatically at the transition from G2 to M phase. G1cyclins are unusual in that they are needed for much of the cell cycle.

CYCLIN-DEPENDENT KINASES

- In order to drive the cell cycle forward, a cyclin must activate or inactivate many target proteins inside of the cell. Cyclins drive the events of the cell cycle by partnering with a family of enzymes called the **cyclin-dependent kinases** (**Cdks**). A lone Cdk is inactive, but the binding of a cyclin activates it, making it a functional enzyme and allowing it to modify target proteins.

- How does this work? Cdks are **kinases**, enzymes that phosphorylate (attach phosphate groups to) specific target proteins. The attached phosphate group acts like a switch, making the target protein more or less active. When a cyclin attaches to a Cdk, it has two important effects: it activates the Cdk as a kinase, but it also directs the Cdk to a specific set of target proteins, ones appropriate to the cell cycle period controlled by the cyclin. For instance, G1/S cyclins send Cdks to S phase targets (e.g., promoting DNA replication), while M cyclins send Cdks to M phase targets (e.g., making the nuclear membrane break down)

CYCLIN-DEPENDENT KINASES



CYCLIN-DEPENDENT KINASES

- In general, Cdk levels remain relatively constant across the cell cycle, but Cdk activity and target proteins change as levels of the various cyclins rise and fall. In addition to needing a cyclin partner, Cdks must also be phosphorylated on a particular site in order to be active (not shown in the diagrams in this article), and may also be negatively regulated by phosphorylation of other sites

- Cyclins and Cdks are very evolutionarily conserved, meaning that they are found in many different types of species, from yeast to frogs to humans. The details of the system vary a little: for instance, yeast has just one Cdk, while humans and other mammals have multiple Cdks that are used at different stages of the cell cycle. (Yes, this kind of an exception to the "Cdks don't change in levels" rule!) But the basic principles are quite similar, so that Cdks and the different types of cyclins can be found in each species^55

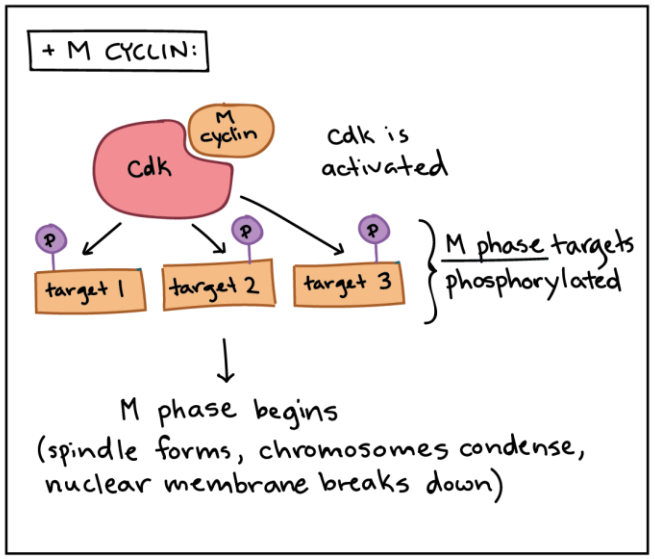
MATURATION-PROMOTING FACTOR (MPF)

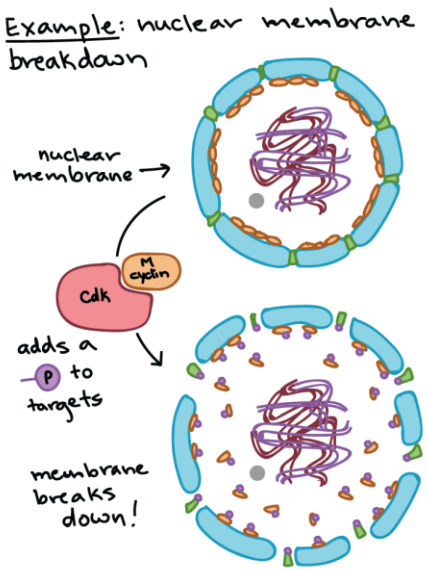
- A famous example of how cyclins and Cdks work together to control cell cycle transitions is that of **maturation-promoting factor** (**MPF**). The name dates back to the 1970s, when researchers found that cells in M phase contained an unknown factor that could force frog egg cells (stuck in G2 phase) to enter M phase. This mystery molecule, called MPF, was discovered in the 1980s to be a Cdk bound to its M cyclin partner

- MPF provides a good example of how cyclins and Cdks can work together to drive a cell cycle transition. Like a typical cyclin, M cyclin stays at low levels for much of the cell cycle, but builds up as the cell approaches the G2/M transition. As M cyclin accumulates, it binds to Cdks already present in the cell, forming complexes that are poised to trigger M phase. Once these complexes receive an additional signal (essentially, an all-clear confirming that the cell's DNA is intact), they become active and set the events of M phase in motion.

MATURATION-PROMOTING FACTOR (MPF)

- The MPF complexes add phosphate tags to several different proteins in the nuclear envelope, resulting in its breakdown (a key event of early M phase), and also activate targets that promote chromosome condensation and other M phase events. The role of MPF in nuclear envelope breakdown is shown in simplified form in the diagram below





THE ANAPHASE-PROMOTING COMPLEX/CYCLOSOME (APC/C)

- In addition to driving the events of M phase, MPF also triggers its own destruction by activating the **anaphase-promoting complex/cyclosome**(**APC/C**), a protein complex that causes M cyclins to be destroyed starting in anaphase.

- The destruction of M cyclins pushes the cell out of mitosis, allowing the new daughter cells to enter G1. The APC/C also causes destruction of the proteins that hold the sister chromatids together, allowing them to separate in anaphase and move to opposite poles of the cell.

THE ANAPHASE-PROMOTING COMPLEX/CYCLOSOME (APC/C)

- How does the APC/C do its job? Like a Cdk, the APC/C is an enzyme, but it has different type of function than a Cdk. Rather than attaching a phosphate group to its targets, it adds a small protein tag called **ubiquitin** (**Ub**).

- When a target is tagged with ubiquitin, it is sent to the **proteasome**, which can be thought of as the recycle bin of the cell, and destroyed. For example, the APC/C attaches a ubiquitin tag to M cyclins, causing them to be chopped up by the proteasome and allowing the newly forming daughter cells to enter G1phase.

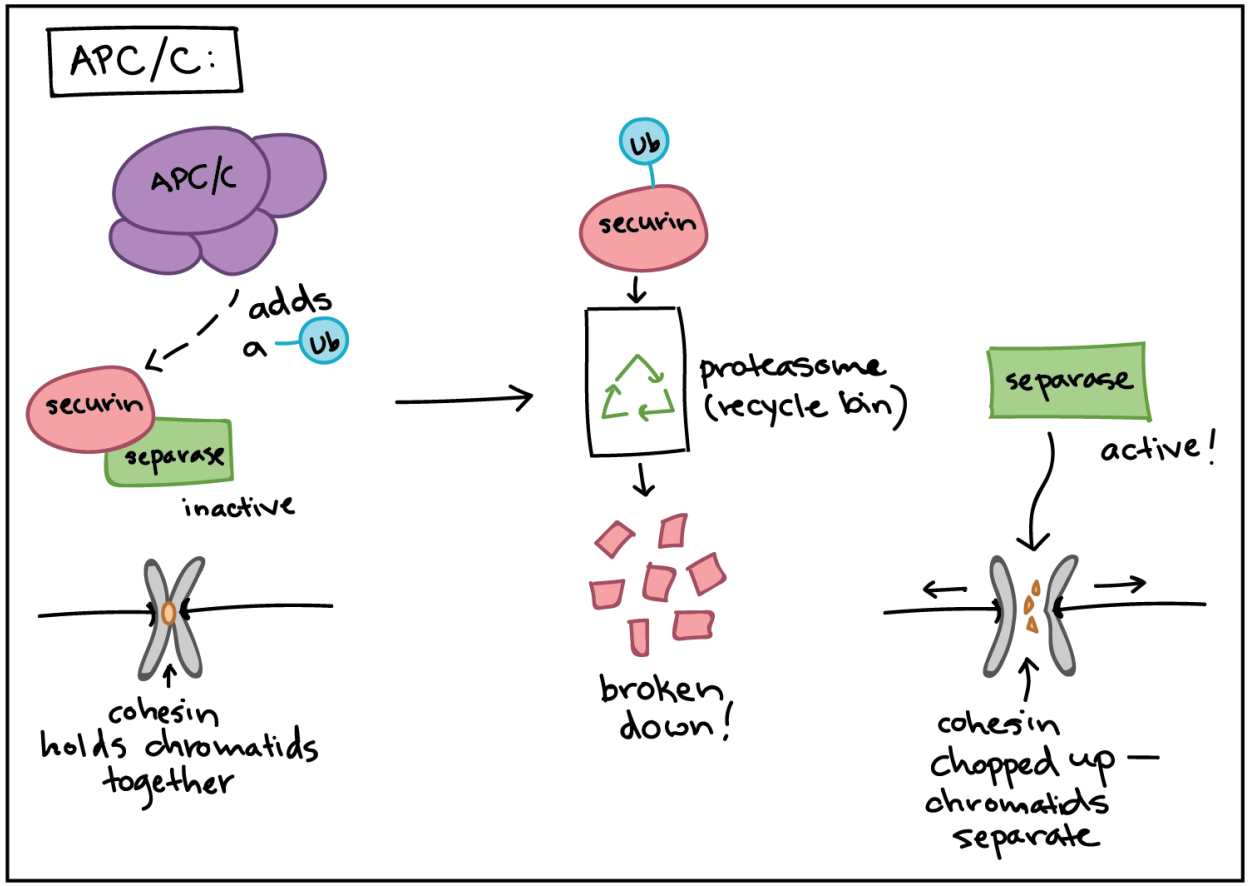
THE ANAPHASE-PROMOTING COMPLEX/CYCLOSOME (APC/C)

- The APC/C also uses ubiquitin tagging to trigger the separation of sister chromatids during mitosis. If the APC/C gets the right signals at metaphase, it sets off a chain of events that destroys **cohesin**, the protein glue that holds sister chromatids together.

- The APC/C first adds a ubiquitin tag to a protein called securin, sending it for recycling. **Securin** normally binds to, and inactivates, a protein called separase.

- When securin is sent for recycling, separase becomes active and can do its job. **Separase** chops up the cohesin that holds sister chromatids together, allowing them to separate.

THE ANAPHASE-PROMOTING COMPLEX/CYCLOSOME (APC/C)



CHECKPOINTS AND REGULATORS

- Cdks, cyclins, and the APC/C are direct regulators of cell cycle transitions, but they aren't always in the driver's seat. Instead, they respond to cues from inside and outside the cell. These cues influence activity of the core regulators to determine whether the cell moves forward in the cell cycle. Positive cues, like growth factors, typically increase activity of Cdks and cyclins, while negative ones, like DNA damage, typically decrease or block activity.

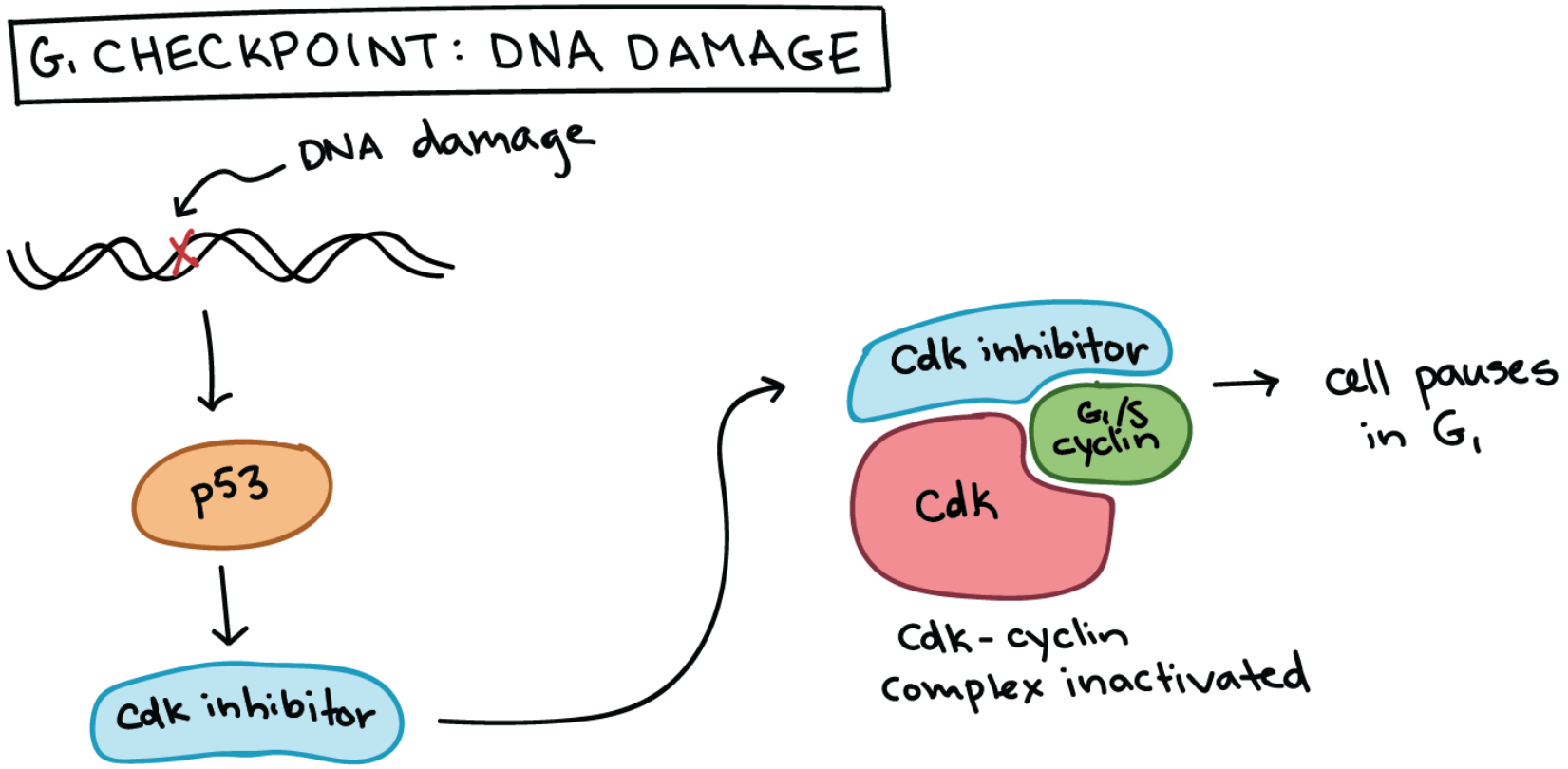
- As an example, let's examine how DNA damage halts the cell cycle in G1. DNA damage can, and will, happen in many cells of the body during a person's lifetime (for example, due to UV rays from the sun). Cells must be able to deal with this damage, fixing it if possible and preventing cell division if not. Key to the DNA damage response is a protein called p53, a famous tumor suppressor often described as "the guardian of the genome.

CHECKPOINTS AND REGULATORS

- p53 works on multiple levels to ensure that cells do not pass on their damaged DNA through cell division. First, it stops the cell cycle at the G1 checkpoint by triggering production of **Cdk inhibitor** (**CKI**) proteins. The CKI proteins bind to Cdk-cyclin complexes and block their activity (see diagram below), buying time for DNA repair.

- p53's second job is to activate DNA repair enzymes. If DNA damage is not fixable, p53 will play its third and final role: triggering programmed cell death so damaged DNA is not passed on.

CHECKPOINTS AND REGULATORS

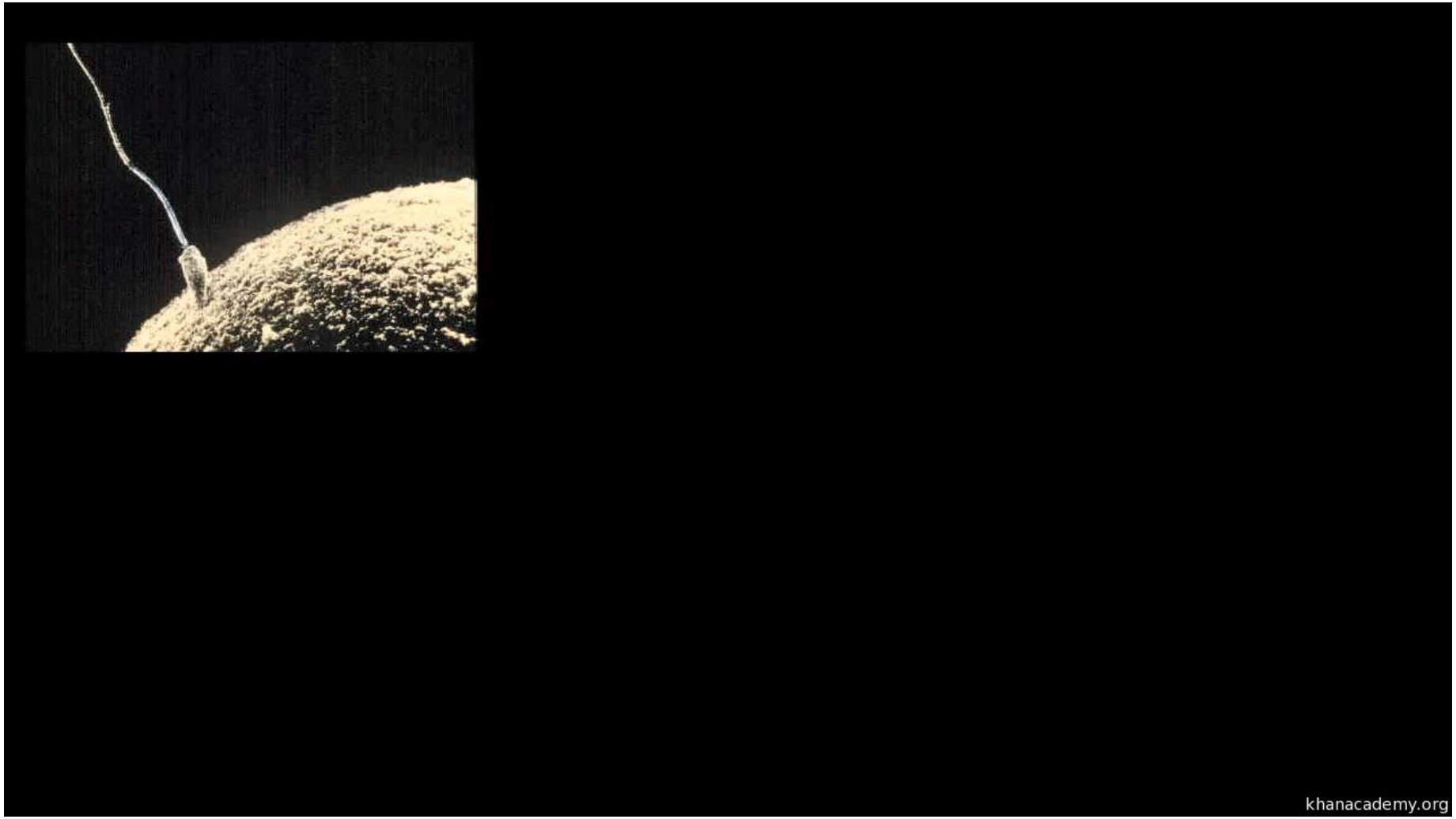


CHECKPOINTS AND REGULATORS

- By ensuring that cells don't divide when their DNA is damaged, p53 prevents mutations (changes in DNA) from being passed on to daughter cells. When p53 is defective or missing, mutations can accumulate quickly, potentially leading to cancer.

- Indeed, out of all the entire human genome, p53 is the single gene most often mutated in cancers. p53 and cell cycle regulation are key topics of study for researchers working on new treatments for cancer.

FERTILIZATION TERMINOLOGY



PHASES OF MITOSIS

PHASES OF MITOSIS

Introduction

What do your intestines, the yeast in bread dough, and a developing frog all have in common? Among other things, they all have cells that carry out mitosis, dividing to produce more cells that are genetically identical to themselves.

Why do these very different organisms and tissues all need mitosis? Intestinal cells have to be replaced as they wear out; yeast cells need to reproduce to keep their population growing; and a tadpole must make new cells as it grows bigger and more complex

WHAT IS MITOSIS?

- **Mitosis** is a type of cell division in which one cell (the **mother**) divides to produce two new cells (the **daughters**) that are genetically identical to itself. In the context of the cell cycle, mitosis is the part of the division process in which the DNA of the cell's nucleus is split into two equal sets of chromosomes.

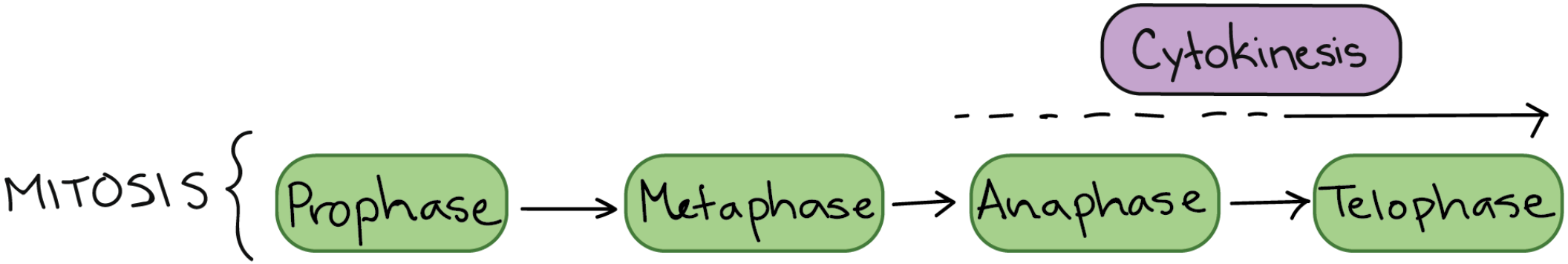
- The great majority of the cell divisions that happen in your body involve mitosis. During development and growth, mitosis populates an organism's body with cells, and throughout an organism's life, it replaces old, worn-out cells with new ones. For single-celled eukaryotes like yeast, mitotic divisions are actually a form of reproduction, adding new individuals to the population.

WHAT IS MITOSIS?

- In all of these cases, the "goal" of mitosis is to make sure that each daughter cell gets a perfect, full set of chromosomes. Cells with too few or too many chromosomes usually don't function well: they may not survive, or they may even cause cancer. So, when cells undergo mitosis, they don't just divide their DNA at random and toss it into piles for the two daughter cells. Instead, they split up their duplicated chromosomes in a carefully organized series of steps.

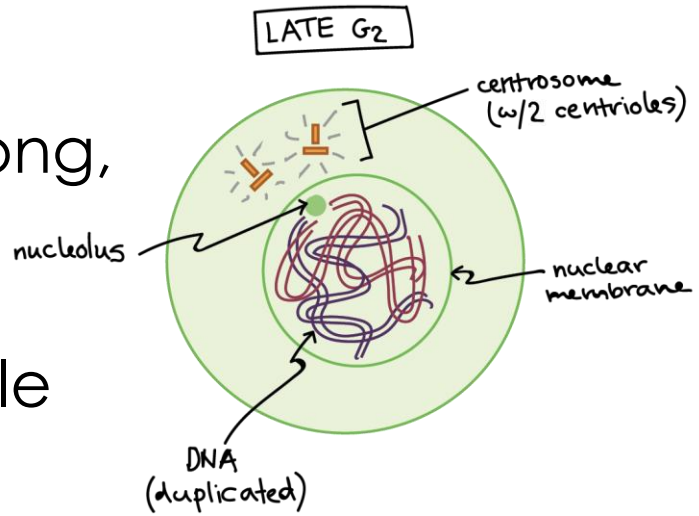
PHASES OF MITOSIS

- Mitosis consists of four basic phases: prophase, metaphase, anaphase, and telophase. Some textbooks list five, breaking prophase into an early phase (called prophase) and a late phase (called prometaphase). These phases occur in strict sequential order, and cytokinesis - the process of dividing the cell contents to make two new cells - starts in anaphase or telophase



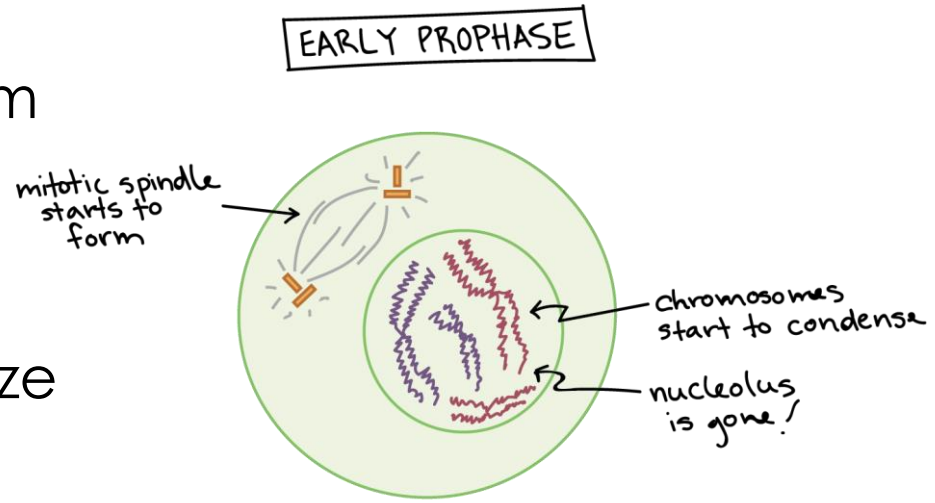
PHASES OF MITOSIS

- Let's start by looking at a cell right before it begins mitosis. This cell is in interphase (late G2start subscript, 2, end subscript phase) and has already copied its DNA, so the chromosomes in the nucleus each consist of two connected copies, called **sister chromatids**. You can't see the chromosomes very clearly at this point, because they are still in their long, stringy, decondensed form.
- This animal cell has also made a copy of its **centrosome**, an organelle that will play a key role in orchestrating mitosis, so there are two centrosomes. (Plant cells generally don't have centrosomes with centrioles, but have a different type of **microtubule organizing center** that plays a similar role.



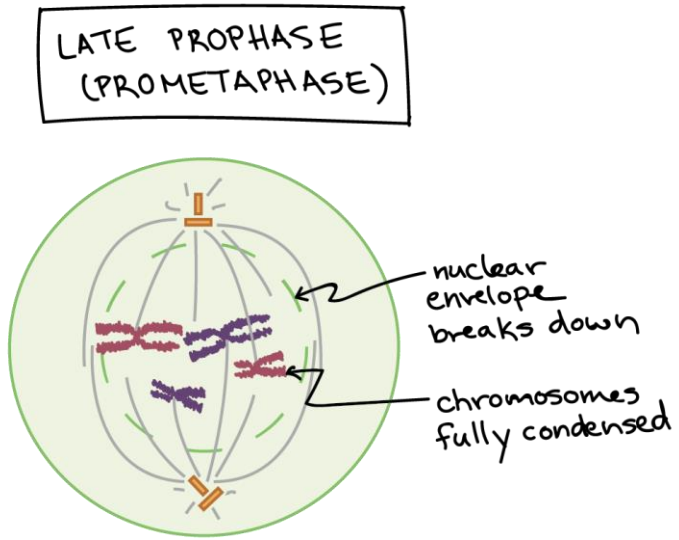
PHASES OF MITOSIS

- In early **prophase**, the cell starts to break down some structures and build others up, setting the stage for division of the chromosomes.
- The chromosomes start to condense (making them easier to pull apart later on).
- The **mitotic spindle** begins to form. The spindle is a structure made of microtubules, strong fibers that are part of the cell's "skeleton." Its job is to organize the chromosomes and move them around during mitosis. The spindle grows between the centrosomes as they move apart.
- The **nucleolus** (or nucleoli, plural), a part of the nucleus where ribosomes are made, disappears. This is a sign that the nucleus is getting ready to break down.



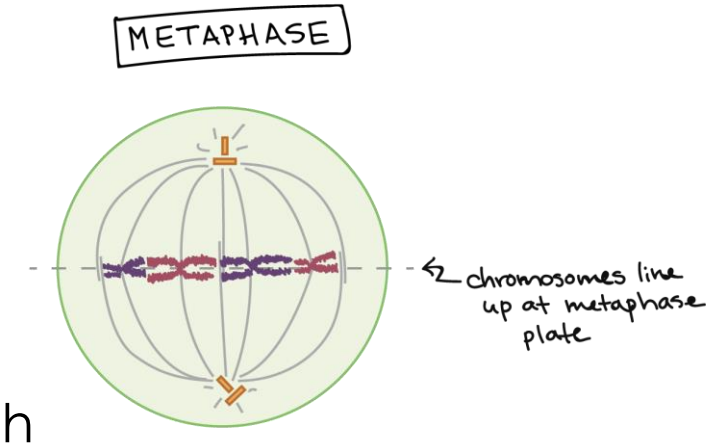
PHASES OF MITOSIS

- In late prophase (sometimes also called **prometaphase**), the mitotic spindle begins to capture and organize the chromosomes.
- The chromosomes finish condensing, so they are very compact.
- The nuclear envelope breaks down, releasing the chromosomes.
- The mitotic spindle grows more, and some of the microtubules start to "capture" chromosomes



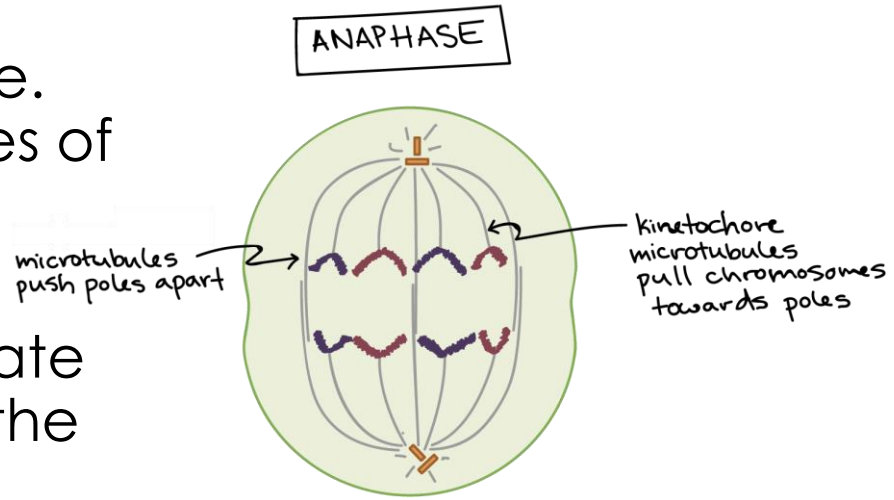
PHASES OF MITOSIS

- In **metaphase**, the spindle has captured all the chromosomes and lined them up at the middle of the cell, ready to divide.
- All the chromosomes align at the **metaphase plate** (not a physical structure, just a term for the plane where the chromosomes line up).
- At this stage, the two kinetochores of each chromosome should be attached to microtubules from opposite spindle poles
- Before proceeding to anaphase, the cell will check to make sure that all the chromosomes are at the metaphase plate with their kinetochores correctly attached to microtubules. This is called the **spindle checkpoint** and helps ensure that the sister chromatids will split evenly between the two daughter cells when they separate in the next step. If a chromosome is not properly aligned or attached, the cell will halt division until the problem is fixed.



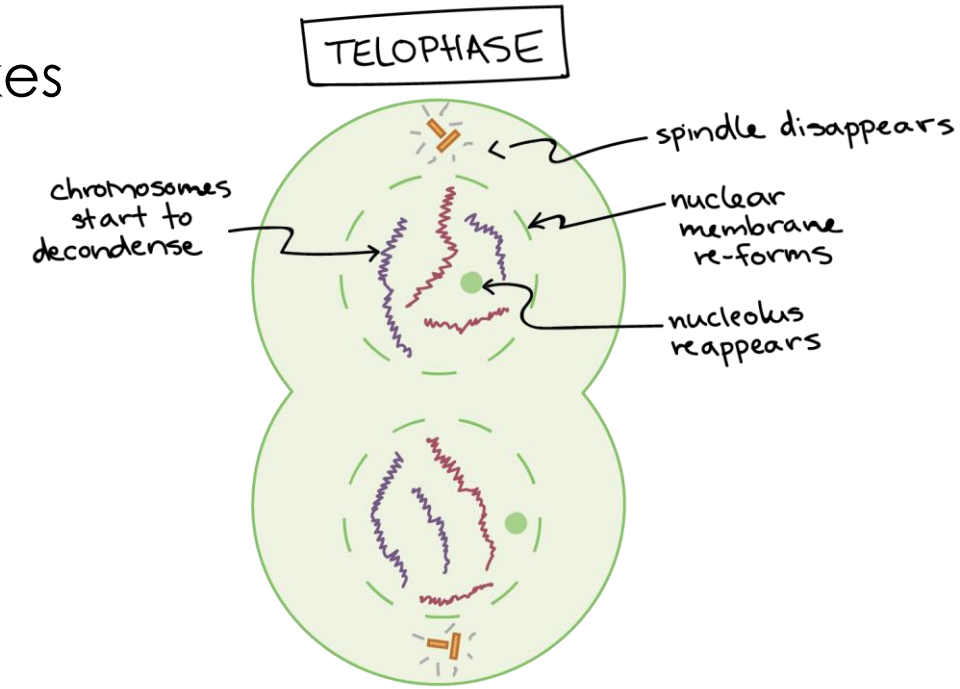
PHASES OF MITOSIS

- In **anaphase**, the sister chromatids separate from each other and are pulled towards opposite ends of the cell.
- The protein "glue" that holds the sister chromatids together is broken down, allowing them to separate. Each is now its own chromosome. The chromosomes of each pair are pulled towards opposite ends of the cell.
- Microtubules not attached to chromosomes elongate and push apart, separating the poles and making the cell longer.
- All of these processes are driven by **motor proteins**, molecular machines that can "walk" along microtubule tracks and carry a cargo. In mitosis, motor proteins carry chromosomes or other microtubules as they walk



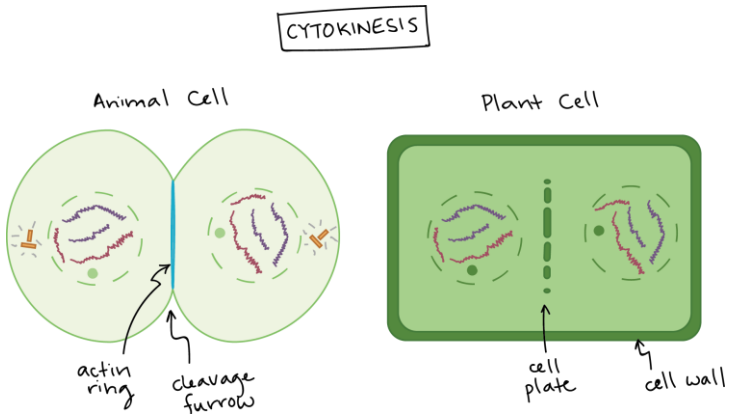
PHASES OF MITOSIS

- In **telophase**, the cell is nearly done dividing, and it starts to re-establish its normal structures as cytokinesis (division of the cell contents) takes place.
- The mitotic spindle is broken down into its building blocks.
- Two new nuclei form, one for each set of chromosomes. Nuclear membranes and nucleoli reappear.
- The chromosomes begin to decondense and return to their "stringy" form



PHASES OF MITOSIS

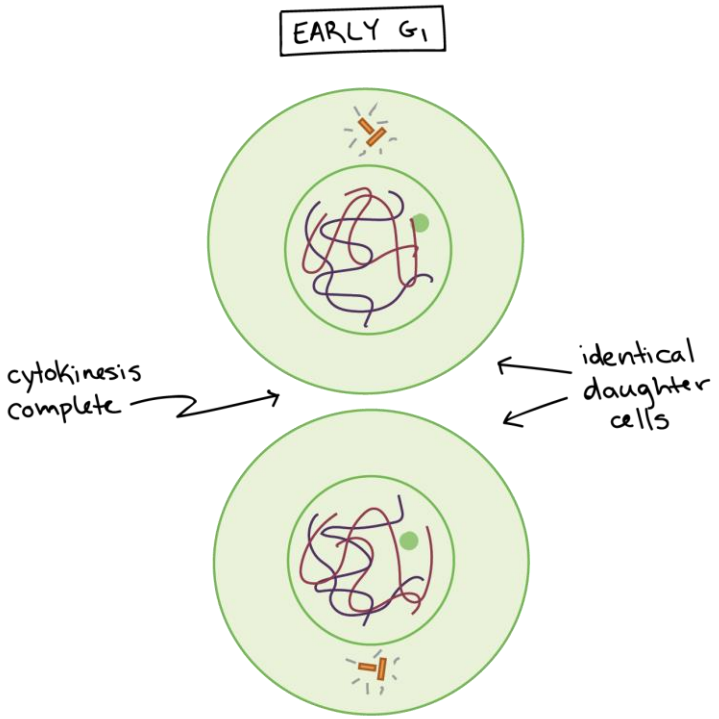
- **Cytokinesis**, the division of the cytoplasm to form two new cells, overlaps with the final stages of mitosis. It may start in either anaphase or telophase, depending on the cell, and finishes shortly after telophase.
- In animal cells, cytokinesis is contractile, pinching the cell in two like a coin purse with a drawstring. The "drawstring" is a band of filaments made of a protein called actin, and the pinch crease is known as the **cleavage furrow**. Plant cells can't be divided like this because they have a cell wall and are too stiff. Instead, a structure called the **cell plate** forms down the middle of the cell, splitting it into two daughter cells separated by a new wall.



PHASES OF MITOSIS

- When cytokinesis finishes, we end up with two new cells, each with a complete set of chromosomes identical to those of the mother cell.

- The daughter cells can now begin their own cellular "lives," and – depending on what they decide to be when they grow up – may undergo mitosis themselves, repeating the cycle.



PHASES OF MEIOSIS

PHASES OF MEIOSIS

- **Introduction**
- Mitosis is used for almost all of your body's cell division needs. It adds new cells during development and replaces old and worn-out cells throughout your life. The goal of mitosis is to produce daughter cells that are genetically identical to their mothers, with not a single chromosome more or less.
- Meiosis, on the other hand, is used for just one purpose in the human body: the production of **gametes**—sex cells, or sperm and eggs. Its goal is to make daughter cells with exactly half as many chromosomes as the starting cell.

- To put that another way, **meiosis** in humans is a division process that takes us from a diploid cell—one with two sets of chromosomes—to haploid cells—ones with a single set of chromosomes. In humans, the haploid cells made in meiosis are sperm and eggs. When a sperm and an egg join in fertilization, the two haploid sets of chromosomes form a complete diploid set: a new genome

PHASES OF MEIOSIS

- In many ways, meiosis is a lot like mitosis. The cell goes through similar stages and uses similar strategies to organize and separate chromosomes. In meiosis, however, the cell has a more complex task. It still needs to separate **sister chromatids** (the two halves of a duplicated chromosome), as in mitosis. But it must also separate **homologous chromosomes**, the similar but nonidentical chromosome pairs an organism receives from its two parents.
- These goals are accomplished in meiosis using a two-step division process. Homologue pairs separate during a first round of cell division, called **meiosis I**. Sister chromatids separate during a second round, called **meiosis II**.
- Since cell division occurs twice during meiosis, one starting cell can produce four gametes (eggs or sperm). In each round of division, cells go through four stages: prophase, metaphase, anaphase, and telophase.

MEIOSIS I

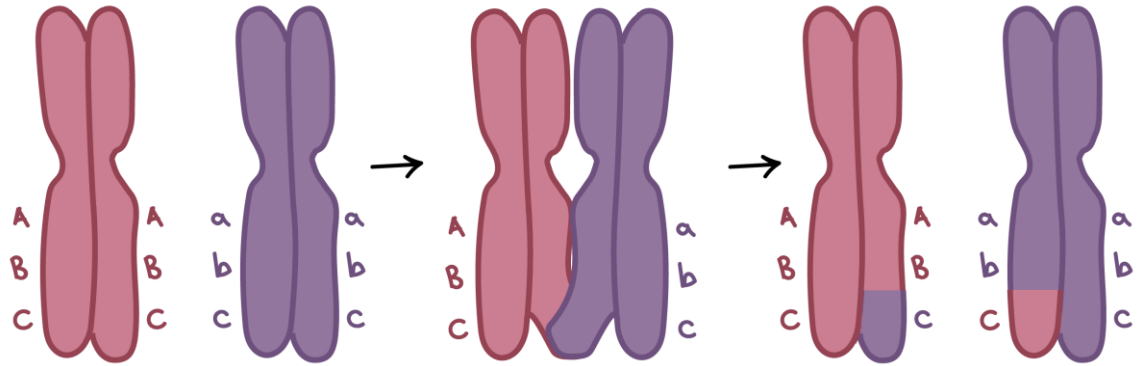
- Before entering meiosis I, a cell must first go through interphase. As in mitosis, the cell grows during G1start subscript, 1, end subscript phase, copies all of its chromosomes during S phase, and prepares for division during G_22start subscript, 2, end subscript phase.

- During **prophase I**, differences from mitosis begin to appear. As in mitosis, the chromosomes begin to condense, but in meiosis I, they also pair up. Each chromosome carefully aligns with its homologue partner so that the two match up at corresponding positions along their full length.

MEIOSIS I

- For instance, in this image, the letters A, B, and C represent genes found at particular spots on the chromosome, with capital and lowercase letters for different forms, or alleles, of each gene.

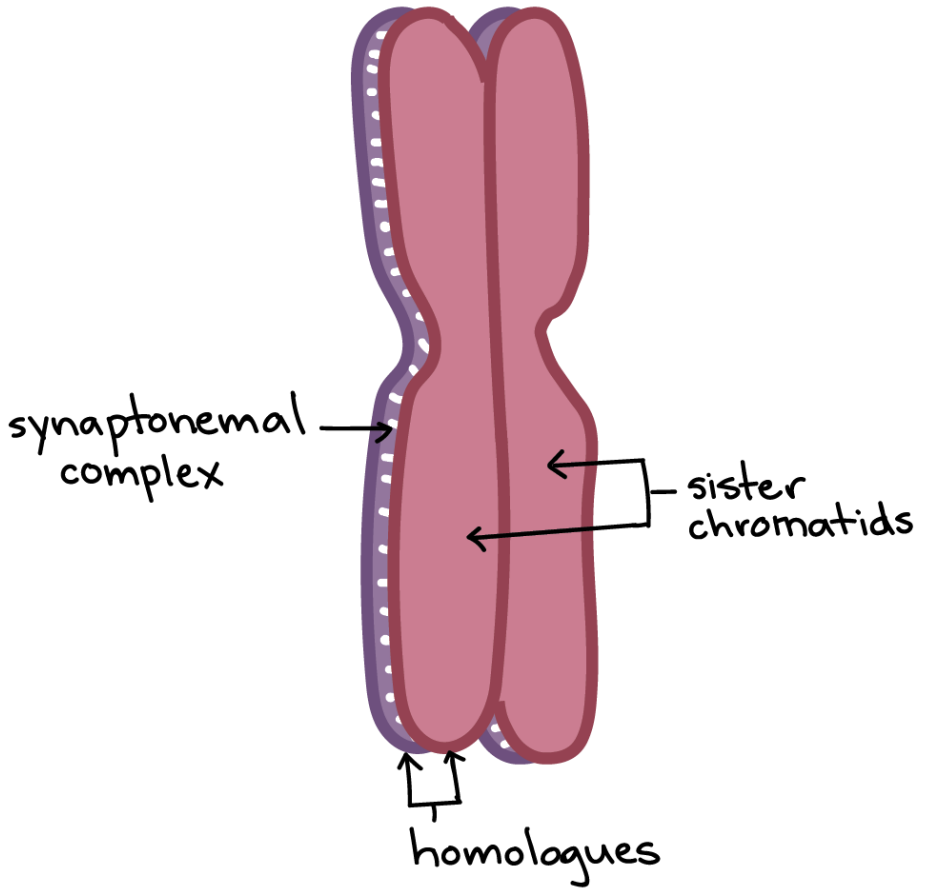
- The DNA is broken at the same spot on each homologue—here, between genes B and C—and reconnected in a criss-cross pattern so that the homologues exchange part of their DNA



MEIOSIS I

- This process, in which homologous chromosomes trade parts, is called **crossing over**. It's helped along by a protein structure called the **synaptonemal complex** that holds the homologues together.

- The chromosomes would actually be positioned one on top of the other—as in the image here—throughout crossing over; they're only shown side-by-side in the last image so that it's easier to see the exchange of genetic material

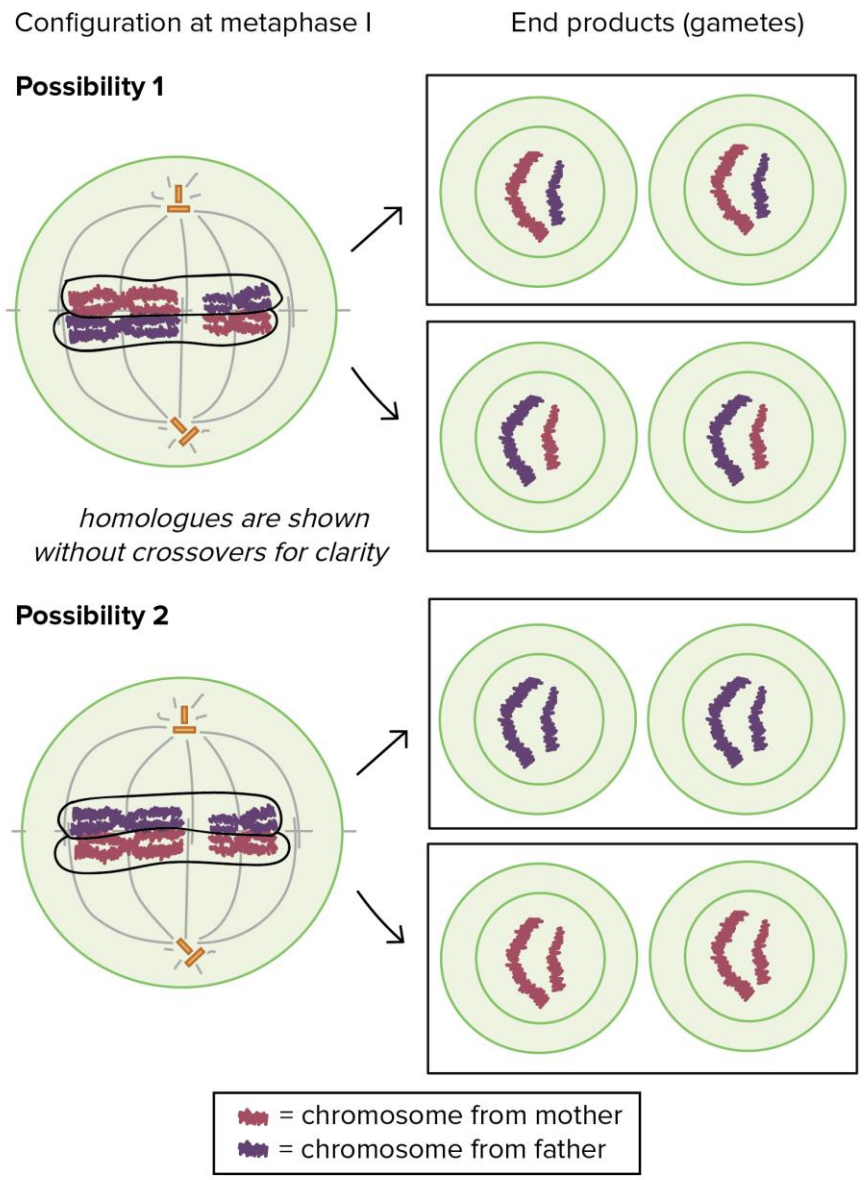


MEIOSIS I

- When the homologous pairs line up at the metaphase plate, the orientation of each pair is random. For instance, in the diagram above, the pink version of the big chromosome and the purple version of the little chromosome happen to be positioned towards the same pole and go into the same cell.

- But the orientation could have equally well been flipped, so that both purple chromosomes went into the cell together. This allows for the formation of gametes with different sets of homologues

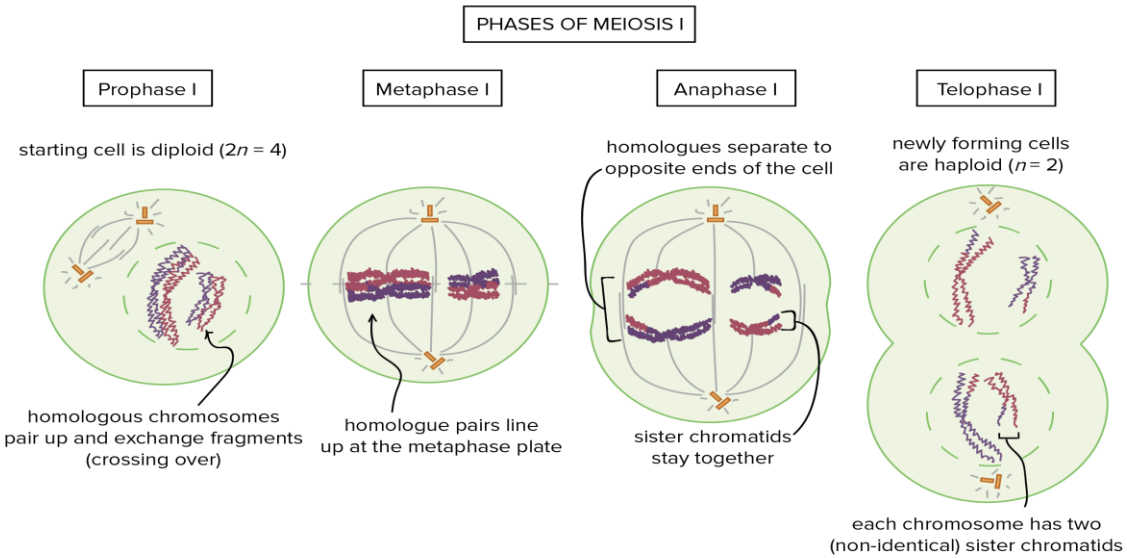
MEIOSIS I


Configuration at metaphase I
End products (gametes)
Possibility 1
homologues are shown without crossovers for clarity
Possibility 2
= chromosome from mother
= chromosome from father

MEIOSIS I

- In **anaphase I**, the homologues are pulled apart and move apart to opposite ends of the cell. The sister chromatids of each chromosome, however, remain attached to one another and don't come apart.

- Finally, in **telophase I**, the chromosomes arrive at opposite poles of the cell. In some organisms, the nuclear membrane re-forms and the chromosomes decondense, although in others, this step is skipped—since cells will soon go through another round of division, meiosis II^{2,3}2,3start superscript, 2, comma, 3, end superscript. Cytokinesis usually occurs at the same time as telophase I, forming two haploid daughter cells.

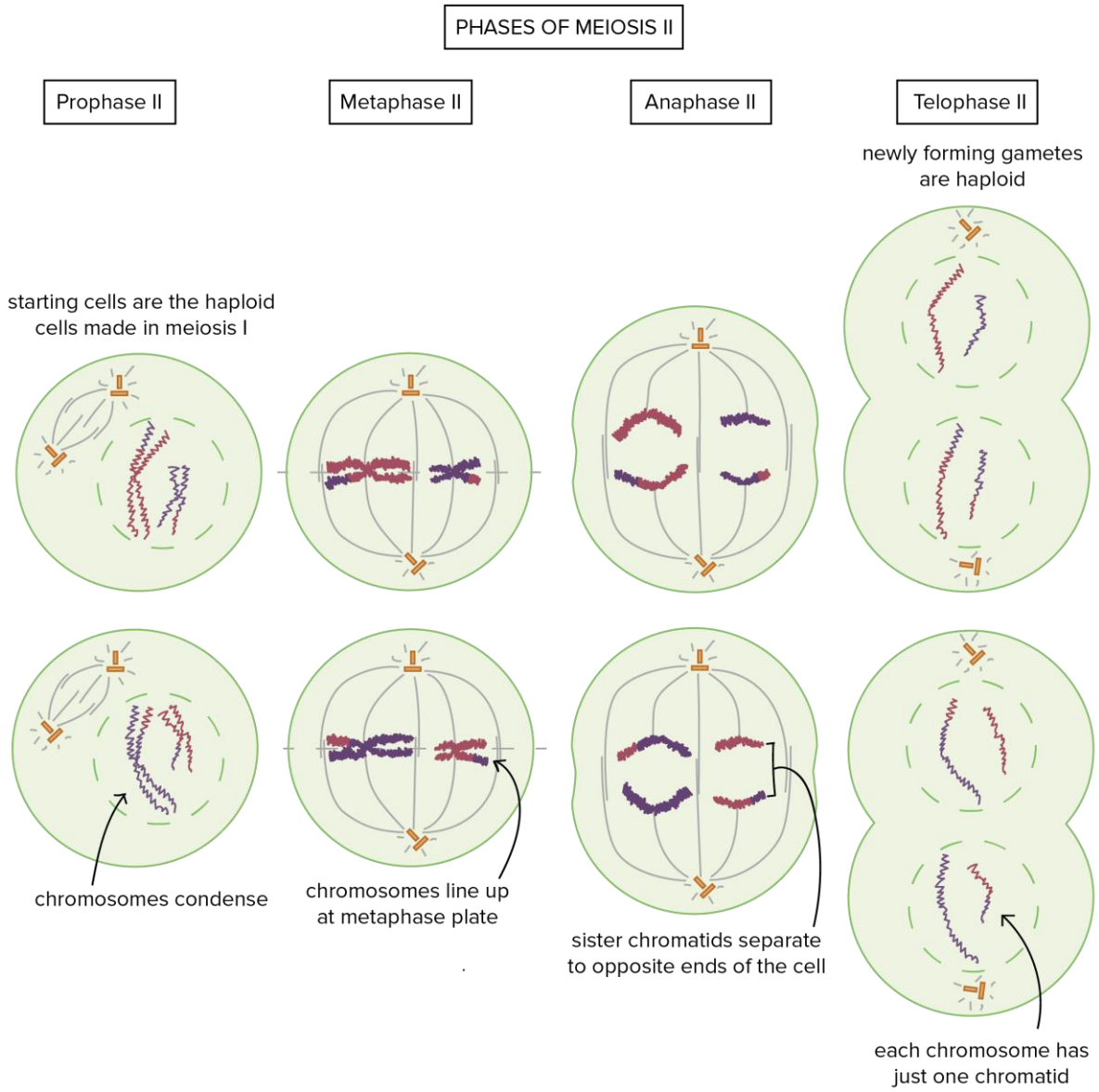


MEIOSIS II

- Cells move from meiosis I to meiosis II without copying their DNA. Meiosis II is a shorter and simpler process than meiosis I, and you may find it helpful to think of meiosis II as “mitosis for haploid cells.“

- The cells that enter meiosis II are the ones made in meiosis I. These cells are haploid—have just one chromosome from each homologue pair—but their chromosomes still consist of two sister chromatids. In meiosis II, the sister chromatids separate, making haploid cells with non-duplicated chromosomes.

MEIOSIS II


PHASES OF MEIOSIS II
Prophase II
Metaphase II
Anaphase II
Telophase II
newly forming gametes are haploid
starting cells are the haploid cells made in meiosis I
chromosomes condense
chromosomes line up at metaphase plate
sister chromatids separate to opposite ends of the cell
each chromosome has just one chromatid

MEIOSIS II

- During **prophase II**, chromosomes condense and the nuclear envelope breaks down, if needed. The centrosomes move apart, the spindle forms between them, and the spindle microtubules begin to capture chromosomes.
- The two sister chromatids of each chromosome are captured by microtubules from opposite spindle poles. In **metaphase II**, the chromosomes line up individually along the metaphase plate. In **anaphase II**, the sister chromatids separate and are pulled towards opposite poles of the cell.
- In **telophase II**, nuclear membranes form around each set of chromosomes, and the chromosomes decondense. Cytokinesis splits the chromosome sets into new cells, forming the final products of meiosis: four haploid cells in which each chromosome has just one chromatid. In humans, the products of meiosis are sperm or egg cells

HOW MEIOSIS "MIXES AND MATCHES" GENES

- The gametes produced in meiosis are all haploid, but they're not genetically identical. For example, take a look the meiosis II diagram above, which shows the products of meiosis for a cell with 2n = 42*n*=4 chromosomes. Each gamete has a unique "sample" of the genetic material present in the starting cell.
- As it turns out, there are many more potential gamete types than just the four shown in the diagram, even for a cell with only four chromosomes. The two main reasons we can get many genetically different gametes are:
  - **Crossing over.** The points where homologues cross over and exchange genetic material are chosen more or less at random, and they will be different in each cell that goes through meiosis. If meiosis happens many times, as in humans, crossovers will happen at many different points.
  - **Random orientation of homologue pairs.** The random orientation of homologue pairs in metaphase I allows for the production of gametes with many different assortments of homologous chromosomes.

MITOSIS VS MEIOSIS

Start	Diploid 46	Diploid 46
End		