

Lecture: Cell Division and Inheritance

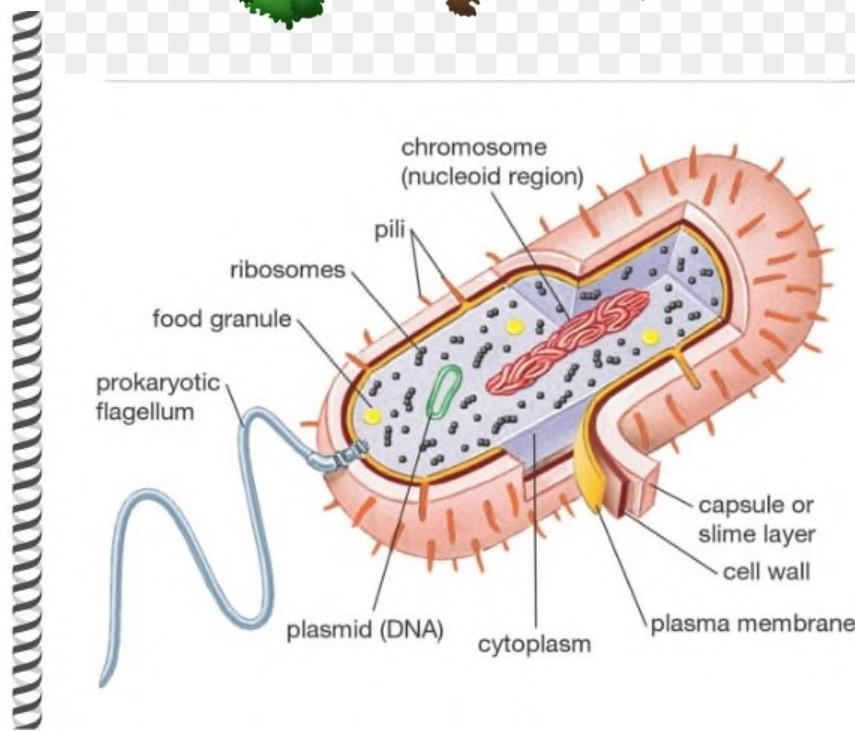
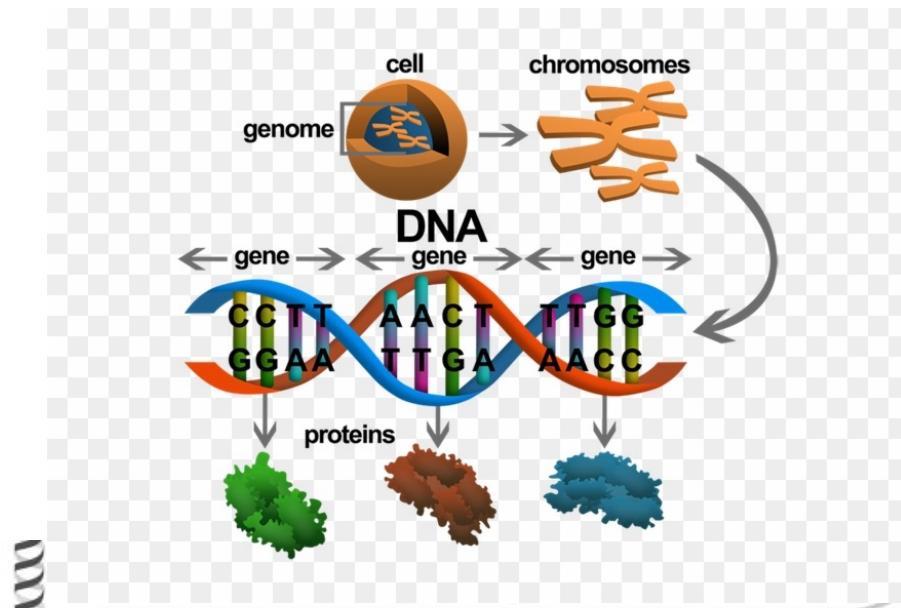
Ref book: Biology for Engineers - Arthur T. Johnson [2nd edition]
Biology for Engineers – G. K. Suraishkumar

Prepared by **Nipa Roy**
Institute of Natural Sciences
United International University

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Introduction: DNA and Genomes

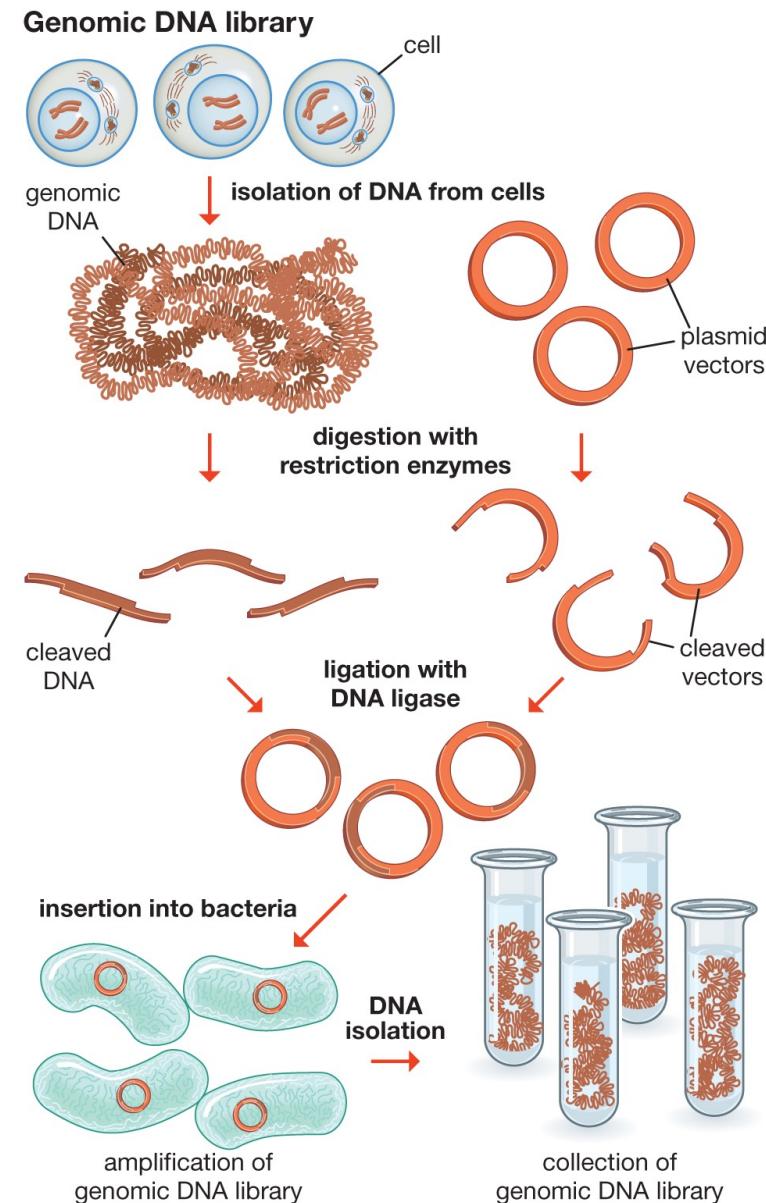
- In eukaryotes such as plants and animals, the great majority of DNA is found in the nucleus and is called **nuclear DNA**. In bacteria and other prokaryotes, most of the DNA is found in a central region of the cell called the **nucleoid**, which functions similarly to a nucleus but is not surrounded by a membrane.
- 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 (that is, the nuclear genome).



Introduction: Chromosomes

Each species has its own characteristic number of chromosomes. Humans, for instance, have 46 chromosomes in a typical body cell, while dogs have 78. Like many species of animals and plants, humans are **diploid ($2n$)**, meaning that most of their chromosomes come in matched sets known as **homologous pairs**. Thus, 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).

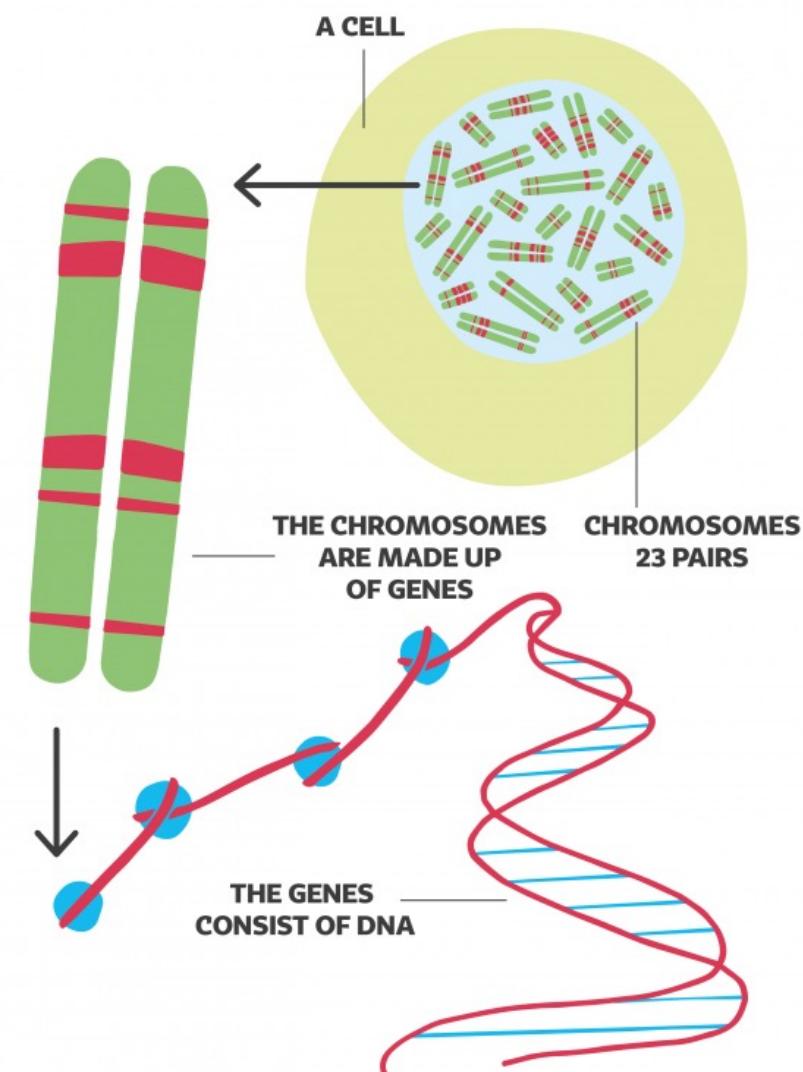
Human sperm and eggs, which have only one homologous chromosome from each pair, are said to be **haploid ($1n$)**. When a sperm and egg fuse, their genetic material combines to form one complete, diploid set of chromosomes. So, for each homologous pair of chromosomes in your genome, one of the homologues comes from your mom and the other from your dad.



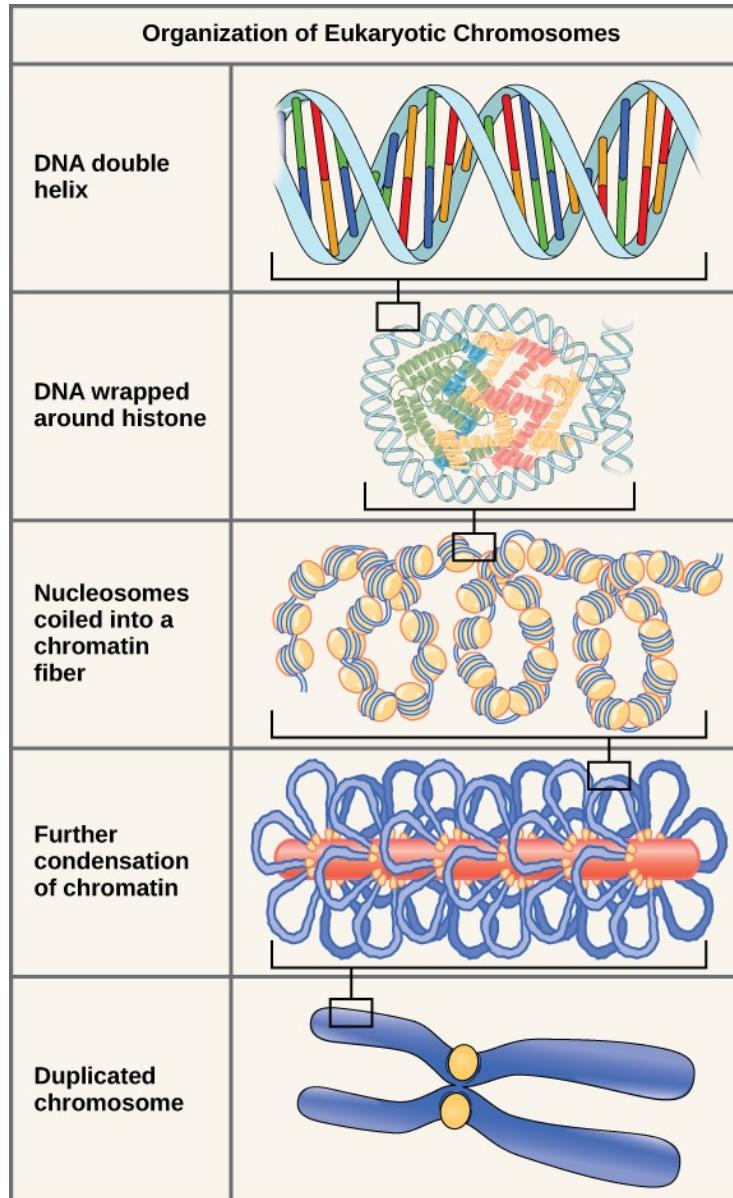
Introduction: Chromosomes

The two chromosomes in a homologous pair are generally very similar to one another. They're the same size and shape, and have the same pattern of light and dark bands, as you can see in the human **karyotype** (image of the chromosomes) shown above. Bands appear when the chromosomes are stained with a dye, and the dark bands mark more compacted DNA (usually, with fewer genes), while the light bands mark less compacted DNA (usually, with more genes). Most importantly, the two homologues in a pair carry the same type of genetic information. For instance, there is a gene found near the bottom of chromosome 15 that affects eye color. A person might have the blue version, or **allele**, of this gene on one homologue, but the brown version on the other. Both homologues have the same type of gene in the same place, but they can (and often do!) have different versions of genes.

In humans, the X and Y chromosomes determine a person's biological sex, with XX for female and XY for male. While the two X chromosomes in a woman's cells are genuinely homologous, the X and Y chromosomes of a man's cells are not. They differ in size and shape, with the X being much larger than the Y, and contain mostly different genes (although they do have small regions of similarity). The X and Y chromosomes are known as **sex chromosomes**, while the other 44 human chromosomes are called **autosomes**.

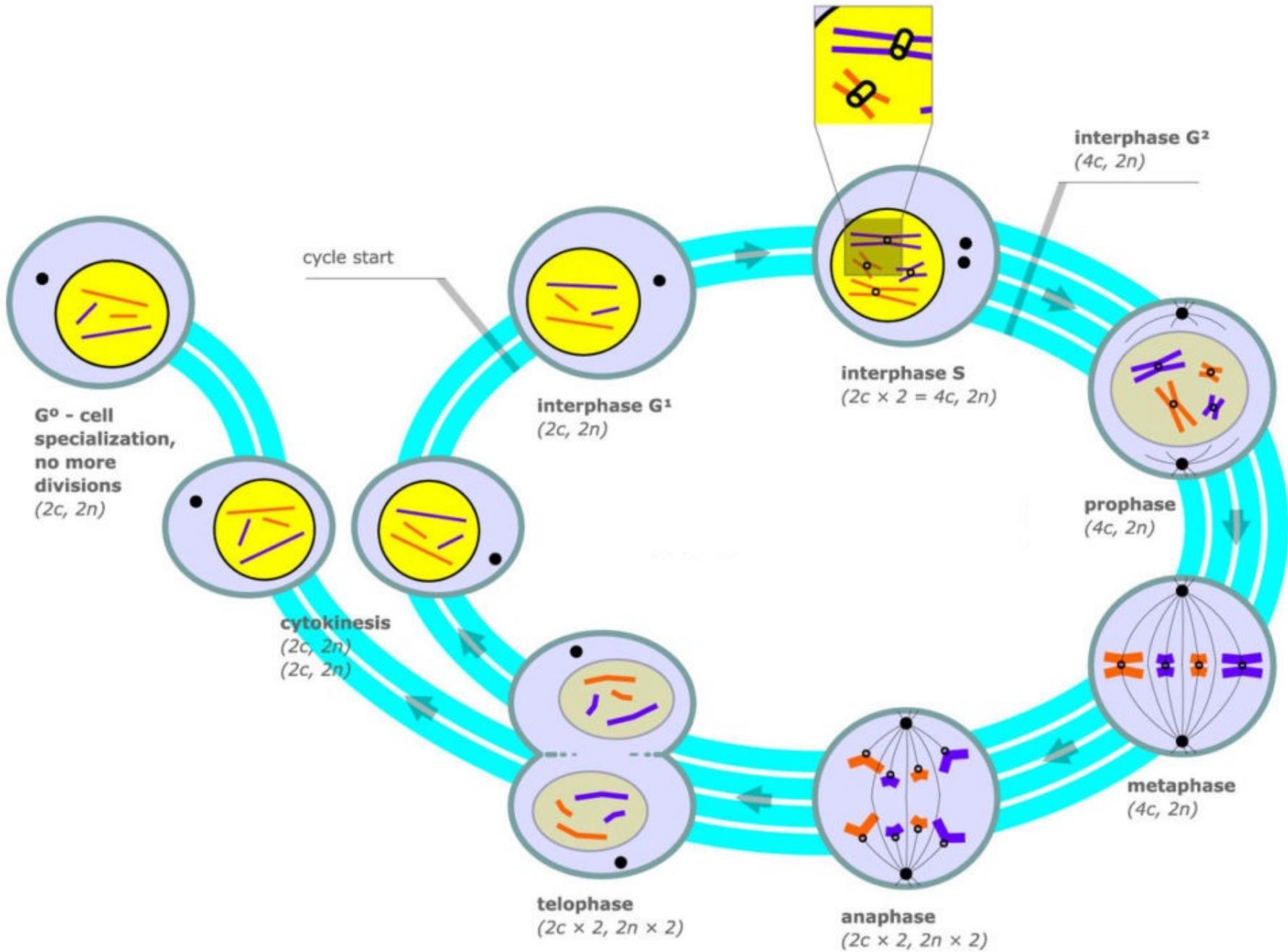


Eukaryotic Chromosomal Structure



Introduction: Cell Cycles

The **cell cycle** is an ordered series of events involving cell growth and cell division that produces two new daughter cells. Cells on the path to cell division proceed through a series of precisely timed and carefully regulated stages of growth, DNA replication, and division that produces two identical (clone) cells. The cell cycle has two major phases: interphase and the mitotic phase. During **interphase**, the cell grows and DNA is replicated. During the **mitotic phase**, the replicated DNA and cytoplasmic contents are separated, and the cell divides.



Interphase

Stages of Interphase

- During interphase, the cell undergoes normal growth processes while also preparing for cell division. It is the longest phase of the cell cycle, cell spends approximately 90% of its time in this phase. In order for a cell to move from interphase into the mitotic phase, many internal and external conditions must be met.
- The three stages of interphase are called G₁, S, and G₂.

G₁ Phase (First Gap)

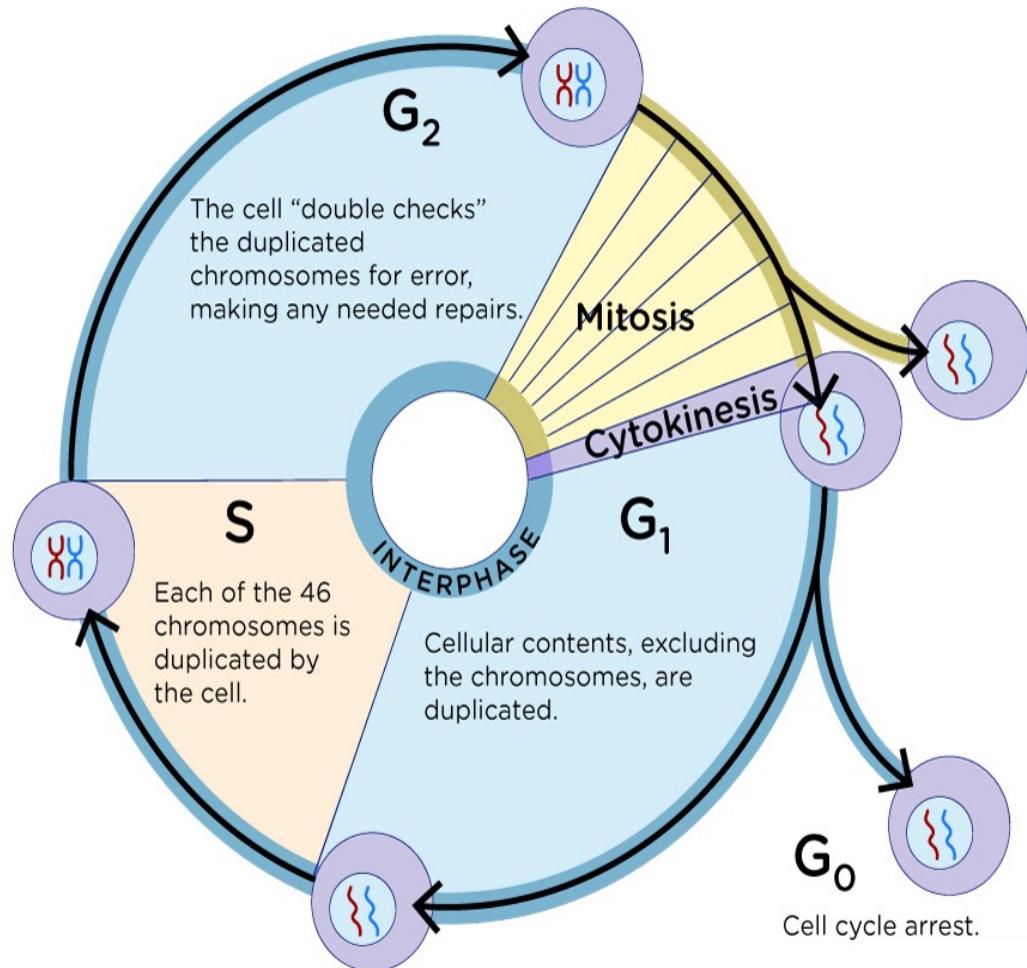
- The first stage of interphase is called the **G₁ phase** (first gap) where the cell is quite active at the biochemical level. The cell is accumulating the building blocks of chromosomal DNA and the associated proteins as well as accumulating sufficient energy reserves to complete the task of replicating each chromosome in the nucleus.

S Phase (Synthesis of DNA)

- In the **S phase**, DNA replication results in the formation of identical pairs of DNA molecules—sister chromatids—that are firmly attached to the centromeric region.

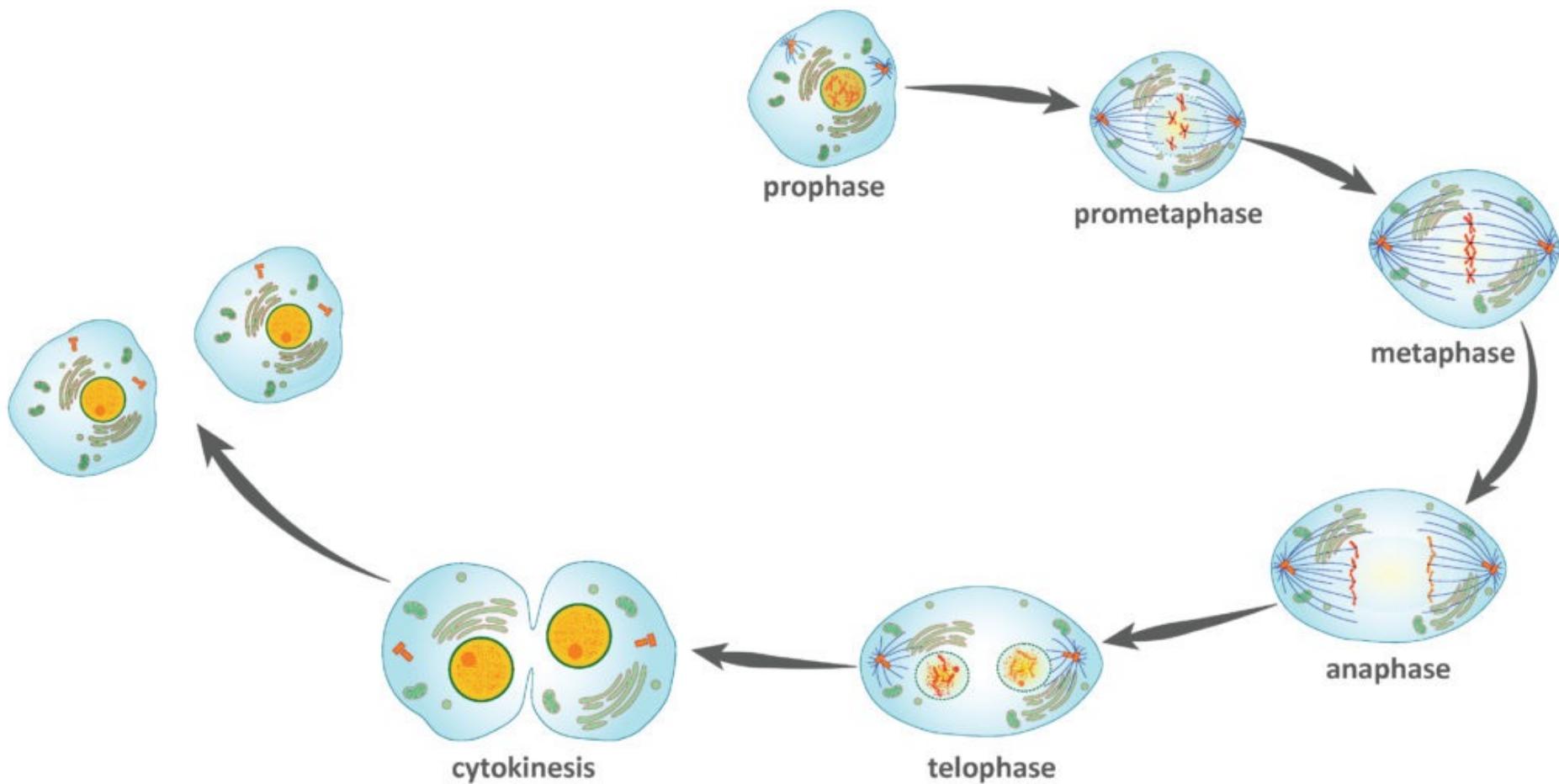
G₂ Phase (Second Gap)

- In the **G₂ phase**, the cell replenishes its energy stores and synthesizes proteins necessary for chromosome manipulation. Some cell organelles are duplicated, and the cytoskeleton is dismantled to provide resources for the mitotic phase.



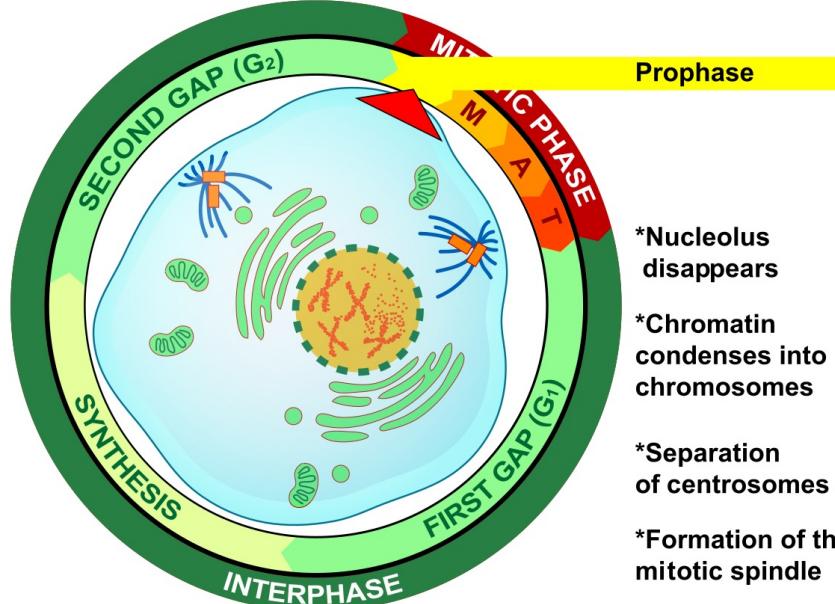
Jack Westin

Introduction: Mitosis

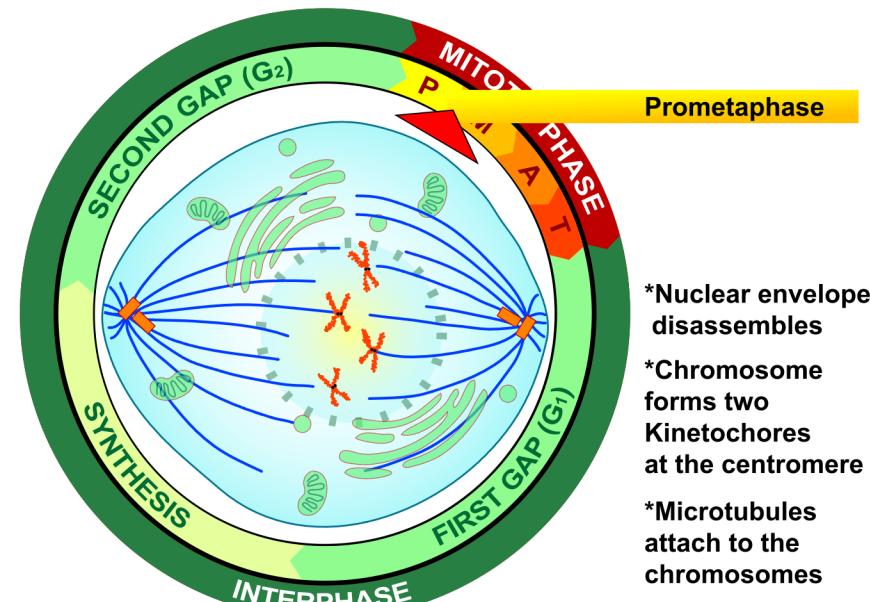


Mitosis

- During **prophase**, the “first phase,” the nuclear envelope starts to dissociate into small vesicles, and the membranous organelles fragment and disperse toward the periphery of the cell. The nucleolus disappears . The centrosomes begin to move to opposite poles of the cell. Microtubules that will form the mitotic spindle extend between the centrosomes, pushing them farther apart as the microtubule fibers lengthen. The sister chromatids begin to coil more tightly and become visible under a light microscope. Each sister chromatid develops a protein structure called a kinetochore in the centromeric region (Figure 2). The proteins of the kinetochore attract and bind mitotic spindle microtubules.
- During **prometaphase**, the nuclear envelope is fully broken down and chromosomes are attached to microtubules from both poles of the mitotic spindle, which begin to move them toward the middle of the cell.



- *Nucleolus disappears
- *Chromatin condenses into chromosomes
- *Separation of centrosomes
- *Formation of the mitotic spindle



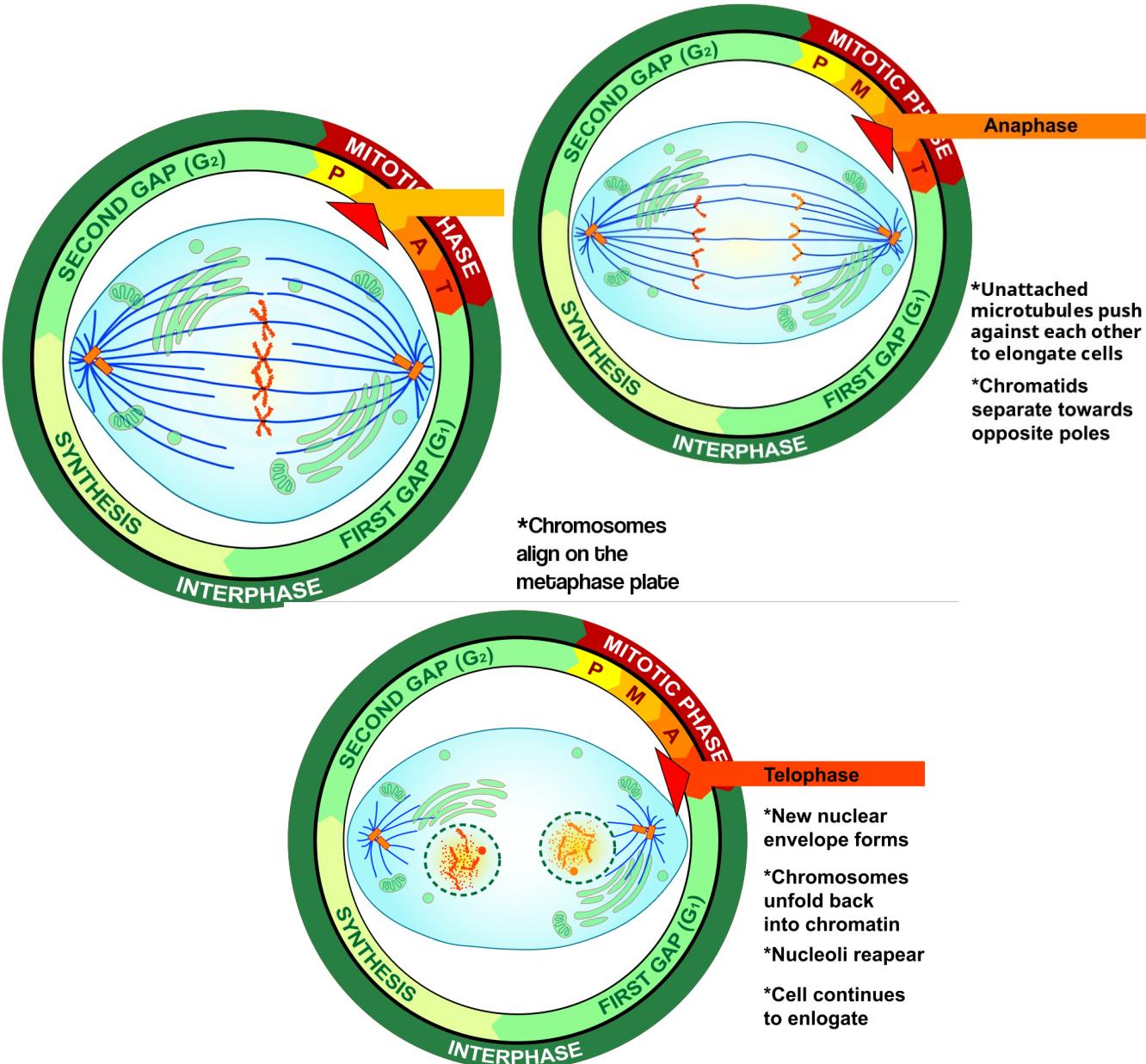
- *Nuclear envelope disassembles
- *Chromosome forms two Kinetochores at the centromere
- *Microtubules attach to the chromosomes

Mitosis

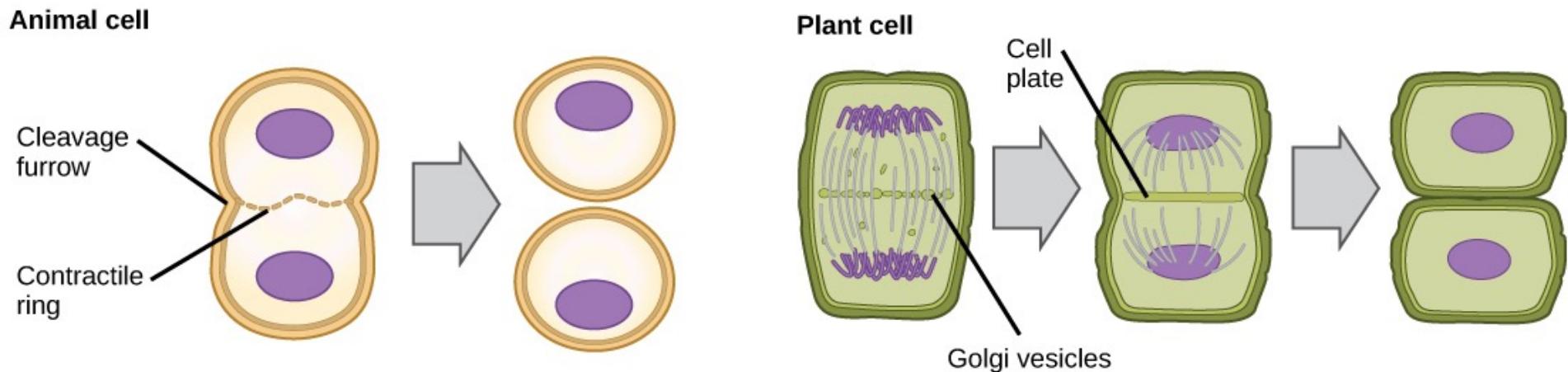
During **metaphase**, all the chromosomes are aligned in a plane called the **metaphase plate**, or the equatorial plane, midway between the two poles of the cell. At this time, the chromosomes are maximally condensed.

During **anaphase**, the sister chromatids separate at the centromere. Each chromatid, now called a chromosome, is pulled rapidly toward the centrosome to which its microtubule is attached. The cell becomes visibly elongated (oval shaped) as the polar microtubules slide against each other at the metaphase plate where they overlap.

During **telophase**, the chromosomes reach the opposite poles and begin to decondense (unravel), relaxing into a chromatin configuration. Nuclear envelopes form around the chromosomes, and nucleosomes appear within the nuclear area.

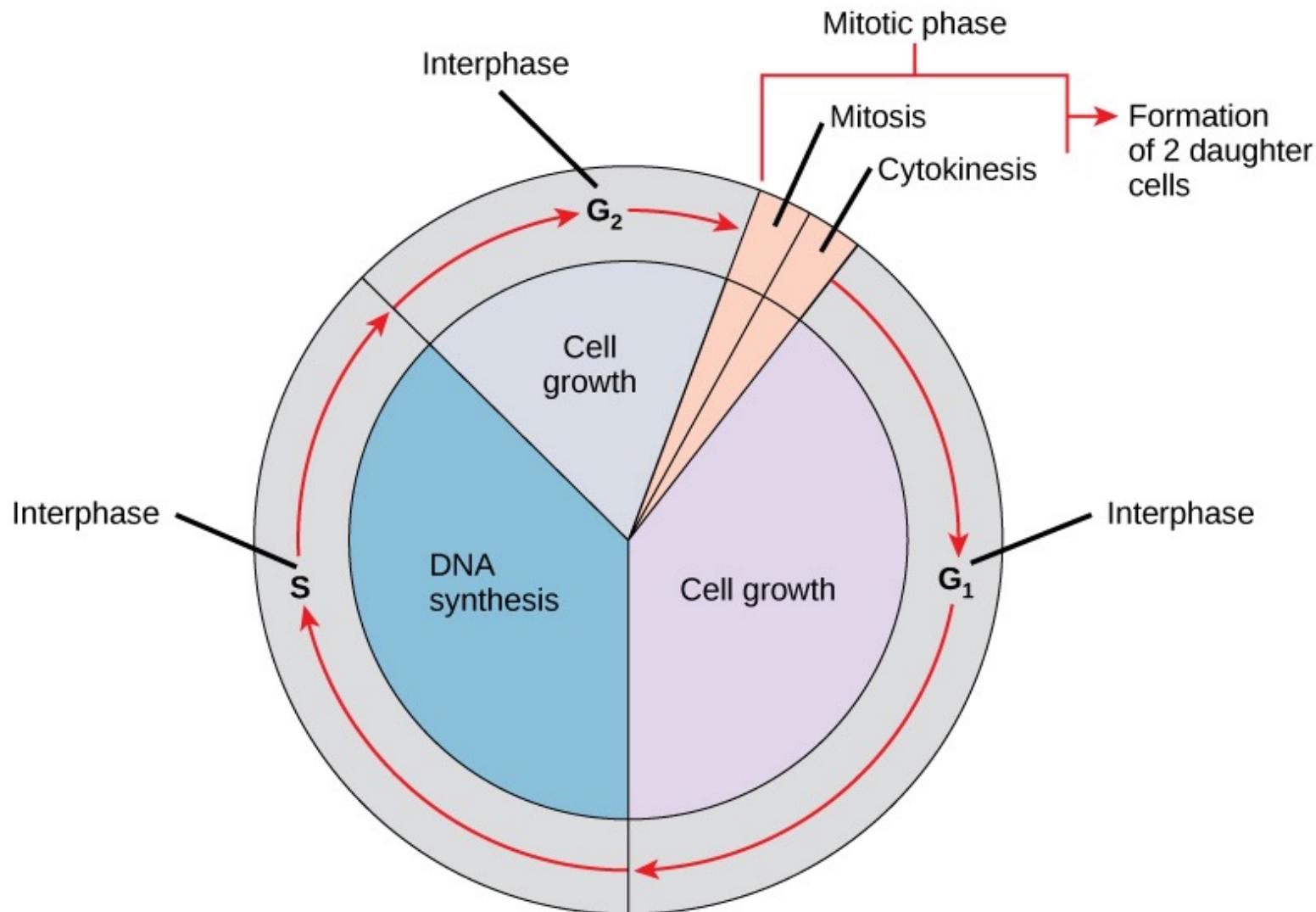


Introduction: Cytokinesis



- **Cytokinesis** is the second main stage of the mitotic phase during which cell division is completed via the physical separation of the cytoplasmic components into two daughter cells. Division is not complete until the cell components have been apportioned and completely separated into the two daughter cells. Although the stages of mitosis are similar for most eukaryotes, the process of cytokinesis is quite different for eukaryotes that have cell walls, such as plant cells.
- In cells such as animal cells that lack cell walls, cytokinesis follows the onset of anaphase. A contractile ring composed of actin filaments forms just inside the plasma membrane at the former metaphase plate. The actin filaments pull the equator of the cell inward, forming a fissure. This fissure, or “crack,” is called the **cleavage furrow**. The furrow deepens as the actin ring contracts, and eventually the membrane is cleaved in two.

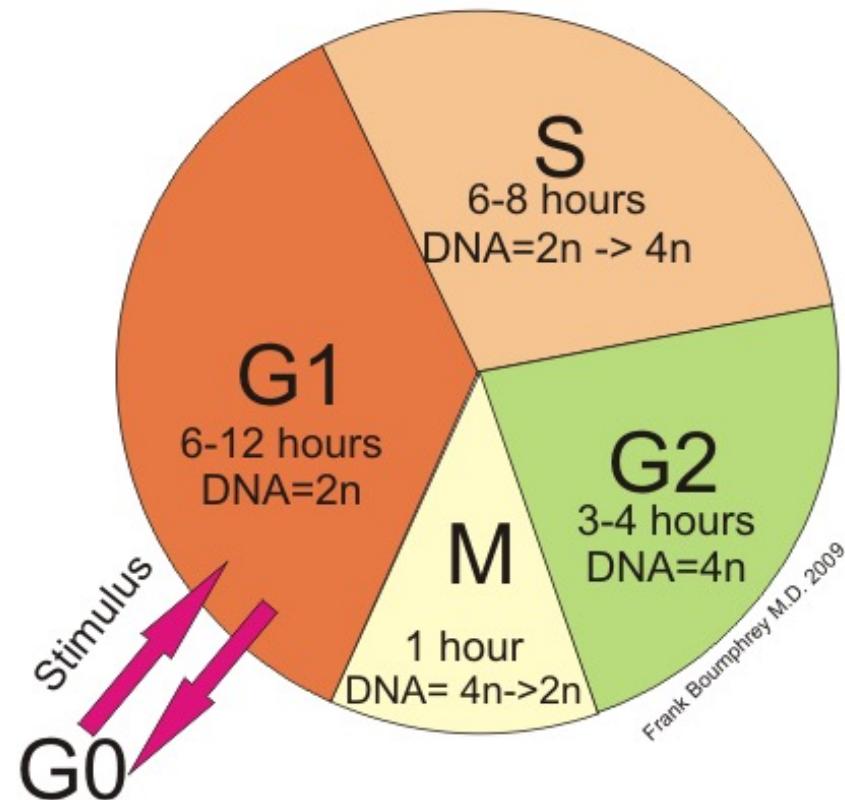
The Complete Cell Cycle



Control of the Cell Cycle

The length of the cell cycle is highly variable, even within the cells of a single organism. In humans, the frequency of cell turnover ranges from a few hours in early embryonic development, to an average of two to five days for epithelial cells, and to an entire human lifetime spent in G_0 by specialized cells, such as cortical neurons or cardiac muscle cells. There is also variation in the time that a cell spends in each phase of the cell cycle. When fast-dividing mammalian cells are grown in culture (outside the body under optimal growing conditions), the length of the cycle is about 24 hours. In rapidly dividing human cells with a 24-hour cell cycle, the G_1 phase lasts approximately nine hours, the S phase lasts 10 hours, the G_2 phase lasts about four and one-half hours, and the M phase lasts approximately one-half hour. In early embryos of fruit flies, the cell cycle is completed in about eight minutes. The timing of events in the cell cycle is controlled by mechanisms that are both internal and external to the cell.

Eukaryotic Replication Cycle (Times are for Cells Growing in Culture)

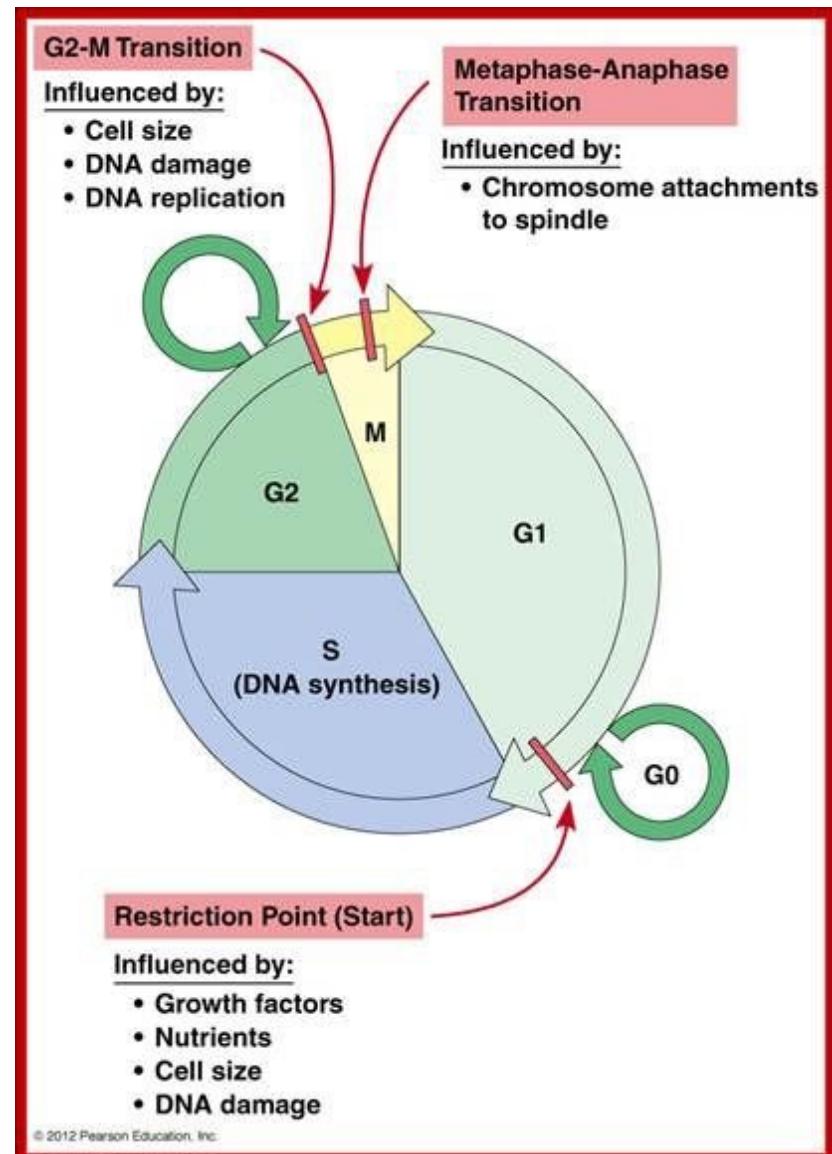


- G_0 : Resting Phase
- G_1 : Growth & Metabolism
- S : DNA Replication
- G_2 : Growth of Structural Elements
- M : Mitosis

Control of the Cell Cycle

Regulation of the Cell Cycle by External Events

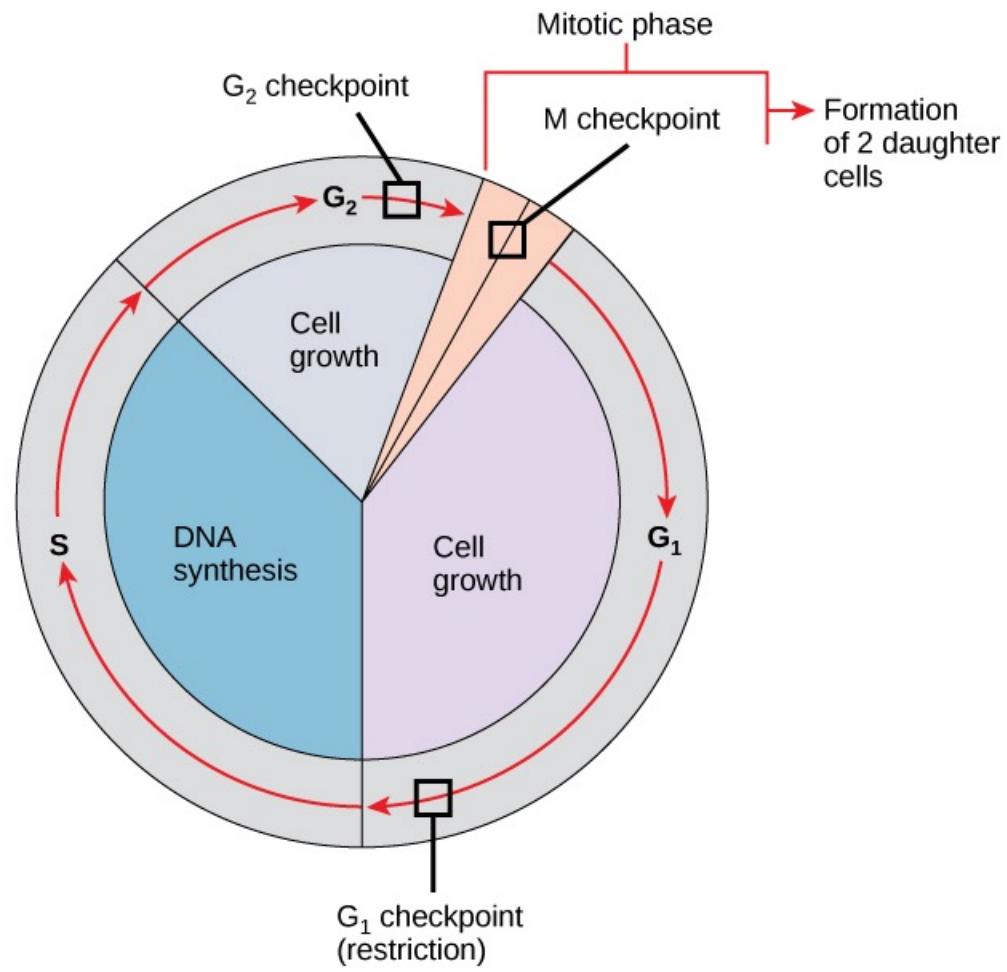
- Both the initiation and inhibition of cell division are triggered by events external to the cell when it is about to begin the replication process. An event may be as simple as the death of a nearby cell or as sweeping as the release of growth-promoting hormones, such as human growth hormone (HGH). A lack of HGH can inhibit cell division, resulting in dwarfism, whereas too much HGH can result in gigantism. Crowding of cells can also inhibit cell division. Another factor that can initiate cell division is the size of the cell; as a cell grows, it becomes inefficient due to its decreasing surface-to-volume ratio. The solution to this problem is to divide.
- Whatever the source of the message, the cell receives the signal, and a series of events within the cell allows it to proceed into mitosis. Moving forward from this initiation point, every parameter required during each cell cycle phase must be met or the cycle cannot progress.



Control of the Cell Cycle

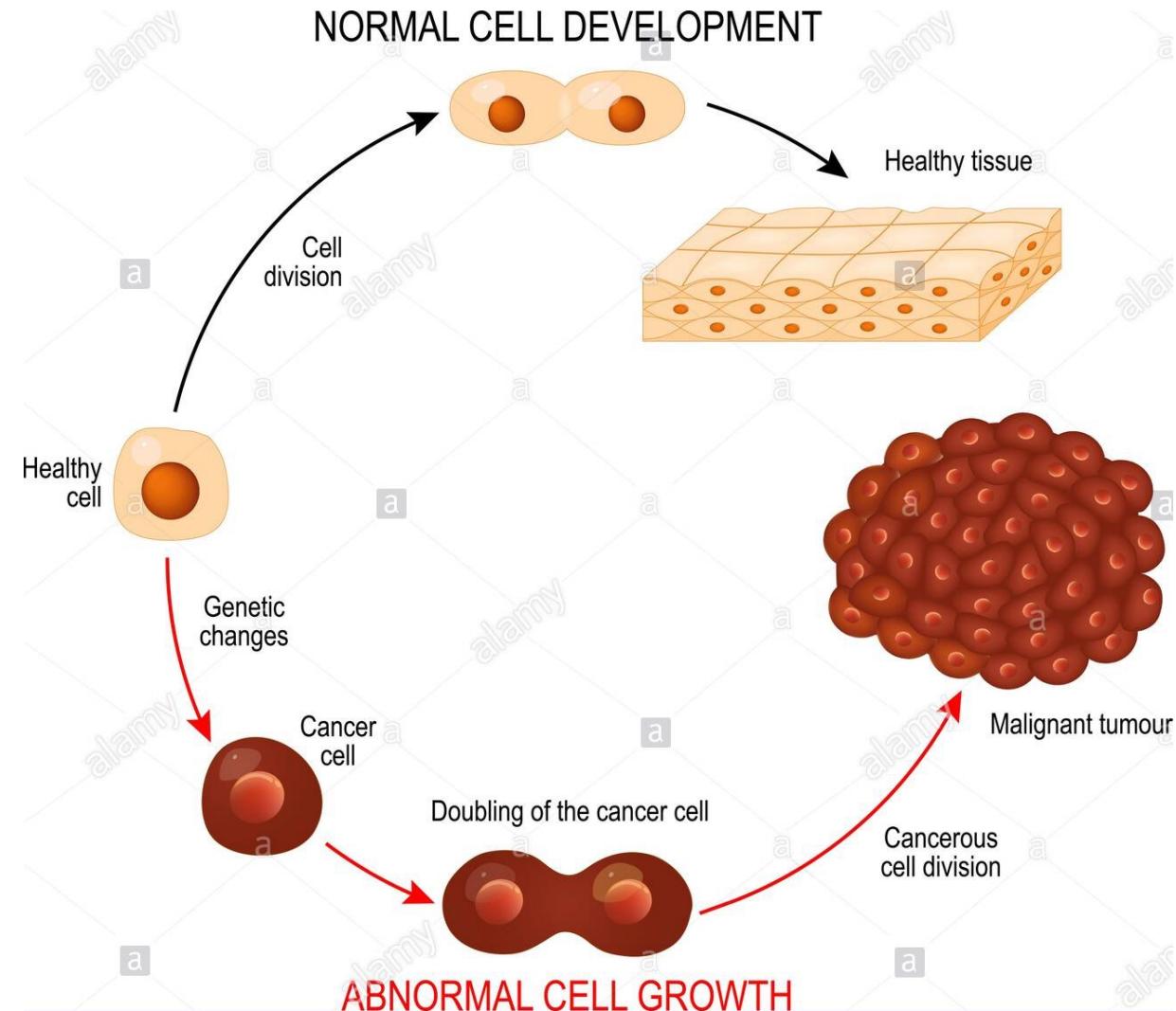
Regulation at Internal Checkpoints

- It is essential that the daughter cells produced be exact duplicates of the parent cell. Mistakes in the duplication or distribution of the chromosomes lead to mutations that may be passed forward to every new cell produced from an abnormal cell. To prevent a compromised cell from continuing to divide, there are internal control mechanisms that operate at three main cell cycle checkpoints. A checkpoint is one of several points in the eukaryotic cell cycle at which the progression of a cell to the next stage in the cycle can be halted until conditions are favorable. These checkpoints occur near the end of G₁, at the G₂/M transition, and during metaphase.



Cancer and the Cell Cycle

Cancer comprises many different diseases caused by a common mechanism: uncontrolled cell growth. Despite the redundancy and overlapping levels of cell cycle control, errors do occur. One of the critical processes monitored by the cell cycle checkpoint surveillance mechanism is the proper replication of DNA during the S phase. Even when all of the cell cycle controls are fully functional, a small percentage of replication errors (mutations) will be passed on to the daughter cells. If changes to the DNA nucleotide sequence occur within a coding portion of a gene and are not corrected, a gene mutation results. All cancers start when a gene mutation gives rise to a faulty protein that plays a key role in cell reproduction. Eventually, the pace of the cell cycle speeds up as the effectiveness of the control and repair mechanisms decreases. Uncontrolled growth of the mutated cells outpaces the growth of normal cells in the area, and a tumor (~oma) can result.



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Cancer and the Cell Cycle

CANCER

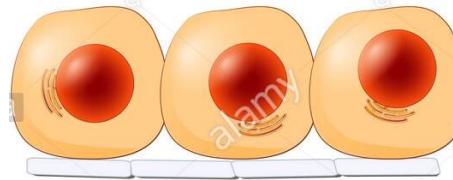
Proto-oncogenes

- The genes that code for the positive cell cycle regulators are called **proto-oncogenes**. Proto-oncogenes are normal genes that, when mutated in certain ways, become **oncogenes**, genes that cause a cell to become cancerous.

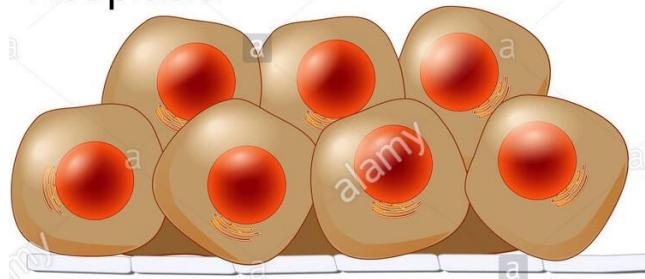
Tumor Suppressor Genes

- Like proto-oncogenes, many of the negative cell cycle regulatory proteins were discovered in cells that had become cancerous. **Tumor suppressor genes** are segments of DNA that code for negative regulator proteins, the type of regulators that, when activated, can prevent the cell from undergoing uncontrolled division. A cell that carries a mutated form of a negative regulator might not be able to halt the cell cycle if there is a problem. Tumor suppressors are similar to brakes in a vehicle: malfunctioning brakes can contribute to a car crash. Mutated p53 genes have been identified in more than one-half of all human tumor cells.

Normal cell



Neoplasia



Abnormal,
and excessive
growth of cells

Dysplasia

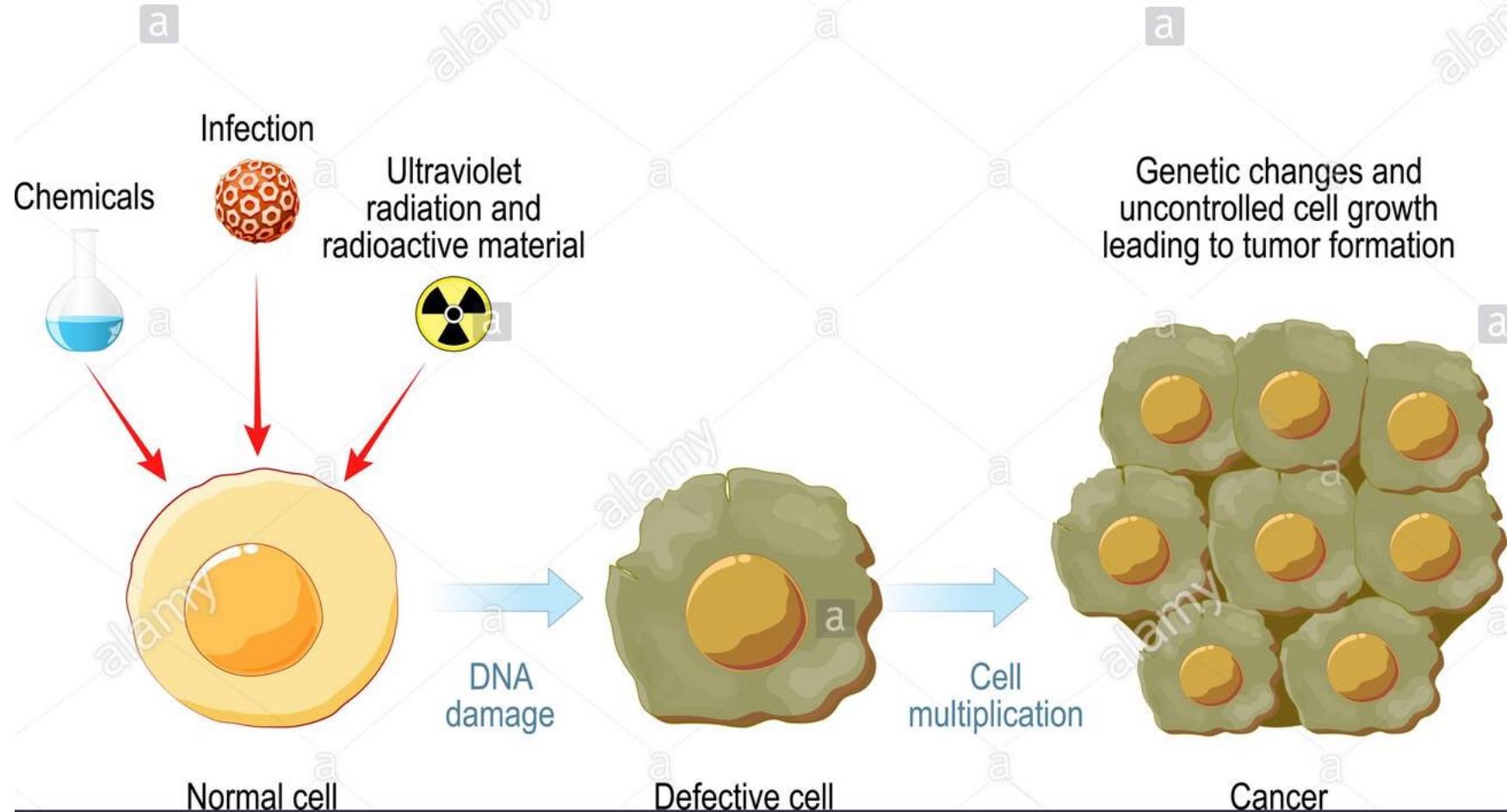


Abnormality
of development,
and differentiation

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Cancer and the Cell Cycle

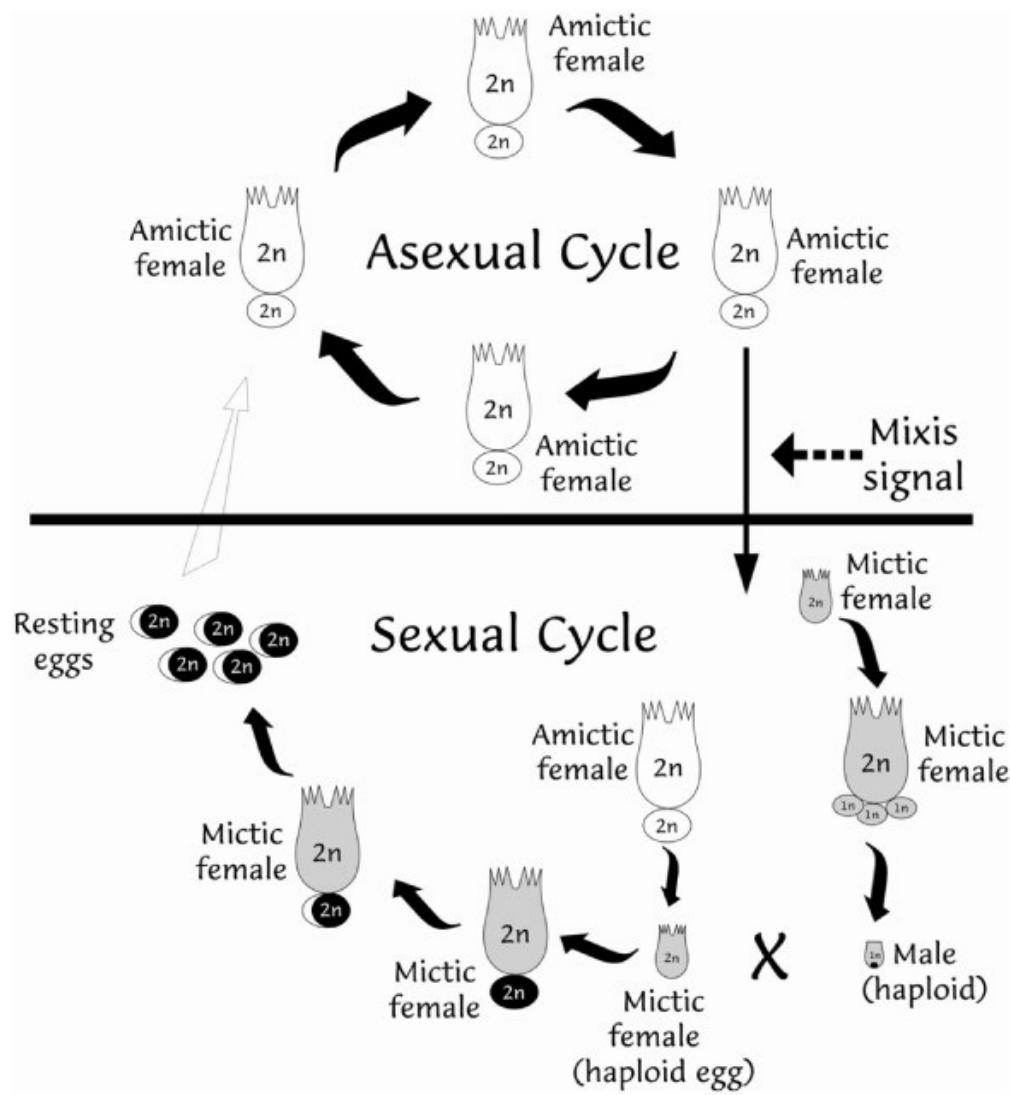
Process of cancer development



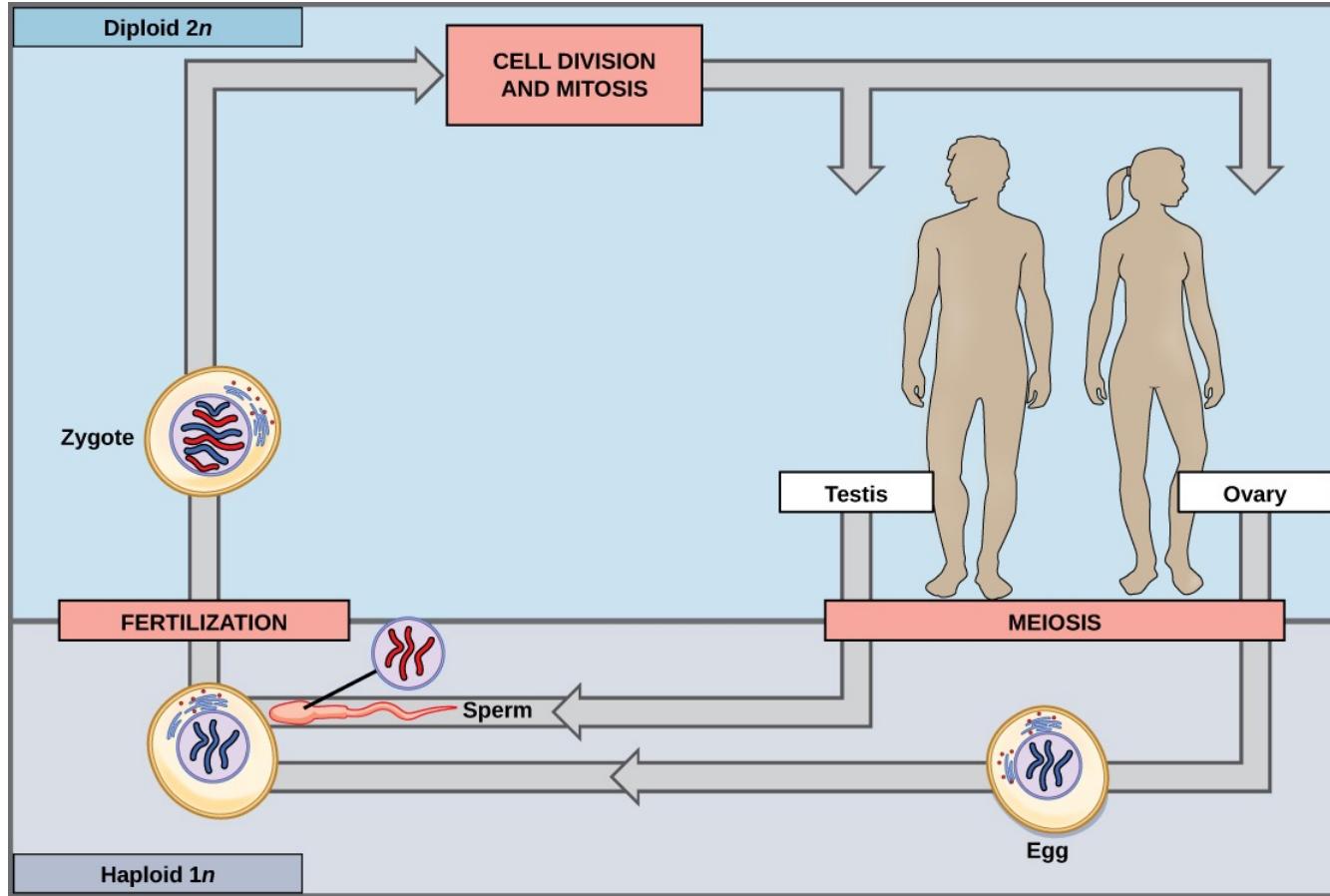
Introduction: Sexual Reproduction

Life Cycles of Sexually Reproducing Organisms

- Fertilization and meiosis alternate in sexual life cycles. What happens between these two events depends on the organism. The process of meiosis reduces the chromosome number by half. Fertilization, the joining of two haploid gametes, restores the diploid condition. There are three main categories of life cycles in multicellular organisms: **diploid-dominant**, in which the multicellular diploid stage is the most obvious life stage, such as with most animals including humans; **haploid-dominant**, in which the multicellular haploid stage is the most obvious life stage, such as with all fungi and some algae; and **alternation of generations**, in which the two stages are apparent to different degrees depending on the group, as with plants and some algae.



Sexual Reproduction



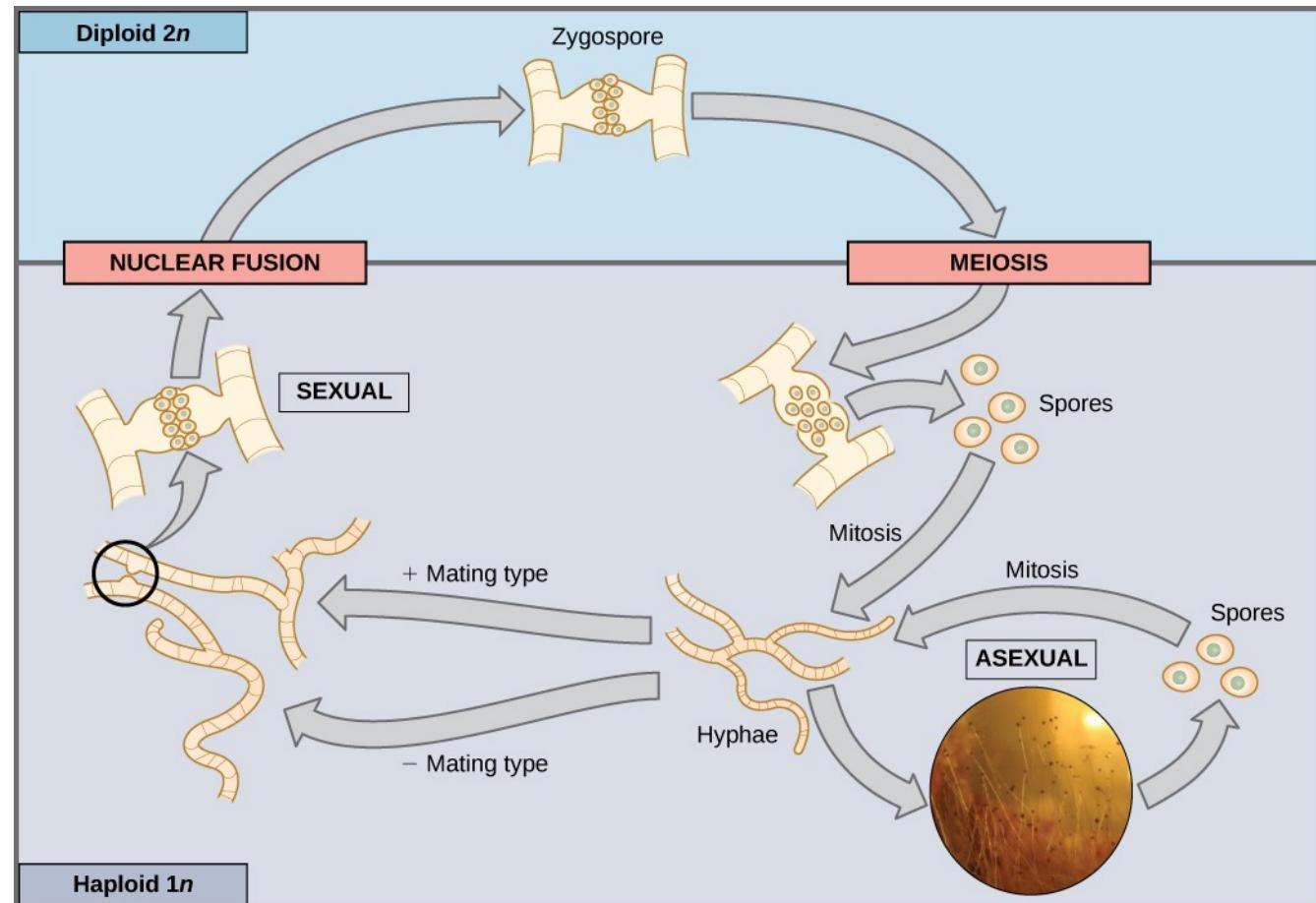
Diploid-Dominant Life Cycle

Nearly all animals employ a diploid-dominant life-cycle strategy in which the only haploid cells produced by the organism are the gametes. Early in the development of the embryo, specialized diploid cells, called **germ cells**, are produced within the gonads, such as the testes and ovaries. Germ cells are capable of mitosis to perpetuate the cell line and meiosis to produce gametes. Once the haploid gametes are formed, they lose the ability to divide again. There is no multicellular haploid life stage. Fertilization occurs with the fusion of two gametes, usually from different individuals, restoring the diploid state.

Sexual Reproduction

Haploid-Dominant Life Cycle

Most fungi and algae employ a life-cycle type in which the “body” of the organism—the ecologically important part of the life cycle—is haploid. The haploid cells that make up the tissues of the dominant multicellular stage are formed by mitosis. During sexual reproduction, specialized haploid cells from two individuals, designated the (+) and (-) mating types, join to form a diploid zygote. The zygote immediately undergoes meiosis to form four haploid cells called spores. Although haploid like the “parents,” these spores contain a new genetic combination from two parents. The spores can remain dormant for various time periods. Eventually, when conditions are conducive, the spores form multicellular haploid structures by many rounds of mitosis.



Introduction: Meiosis



(a)



(b)



(c)

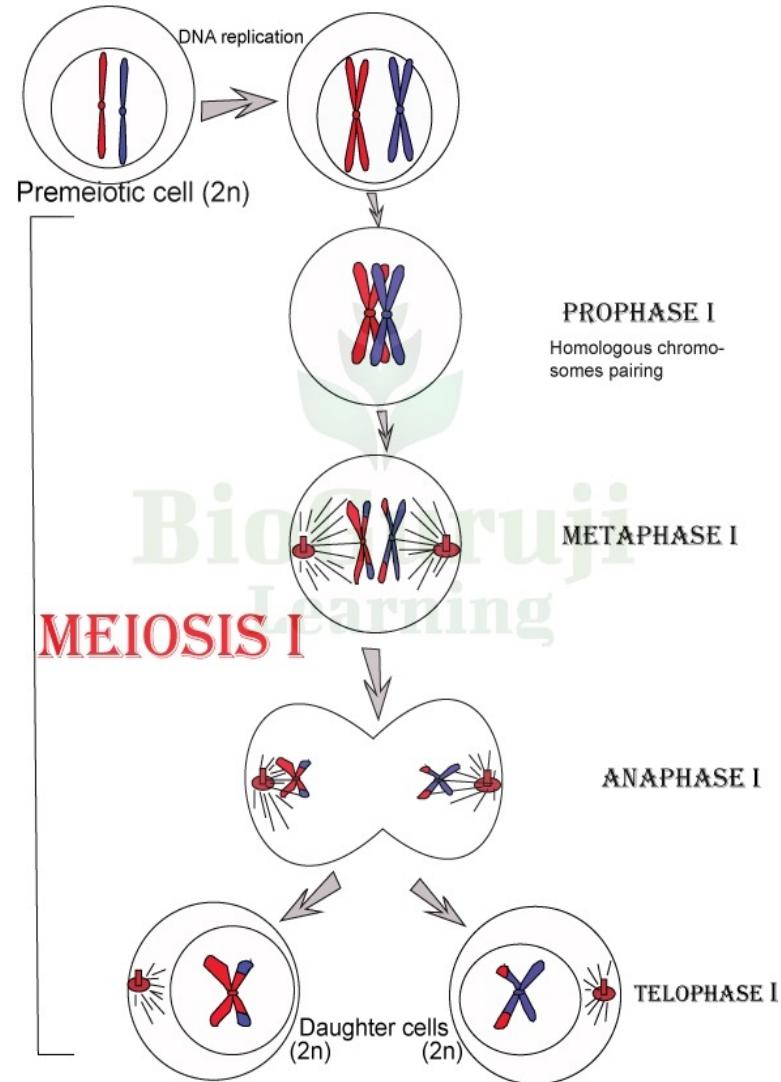
Sexual reproduction, specifically meiosis and fertilization, introduces variation into offspring that may account for the evolutionary success of sexual reproduction. The vast majority of eukaryotic organisms, both multicellular and unicellular, can or must employ some form of meiosis and fertilization to reproduce.

Meiosis employs many of the same mechanisms as mitosis. However, the starting nucleus is always diploid and the nuclei that result at the end of a meiotic cell division are haploid. To achieve this reduction in chromosome number, meiosis consists of one round of chromosome duplication and two rounds of nuclear division.

Because the events that occur during each of the division stages are analogous to the events of mitosis, the same stage names are assigned. However, because there are two rounds of division, the major process and the stages are designated with a “I” or a “II.” Thus, **meiosis I** is the first round of meiotic division and consists of prophase I, prometaphase I, and so on. **Meiosis II**, in which the second round of meiotic division takes place, includes prophase II, prometaphase II, and so on.

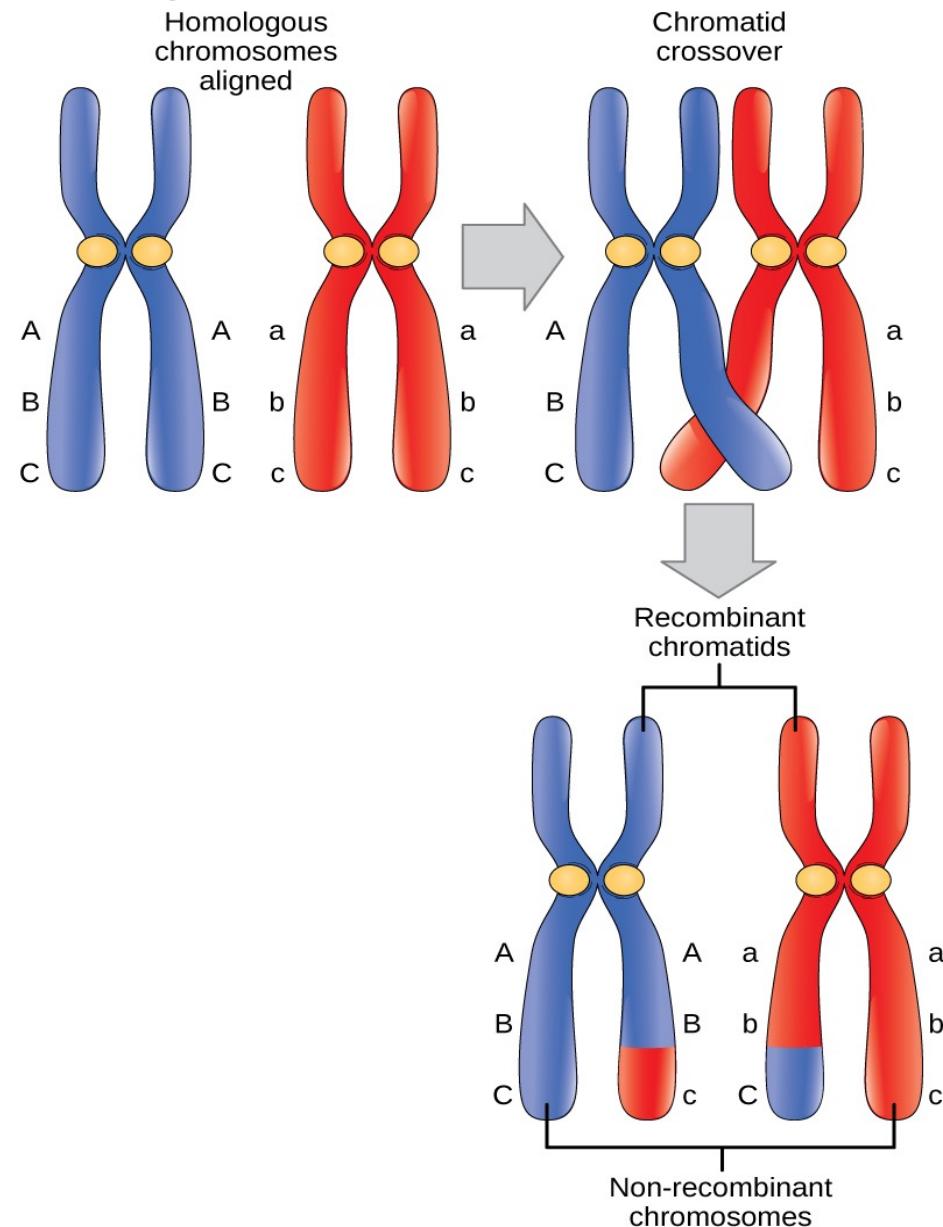
Meiosis I

- Meiosis is preceded by an interphase consisting of the G₁, S, and G₂ phases, which are nearly identical to the phases preceding mitosis. The G₁ phase, which is also called the first gap phase, is the first phase of the interphase and is focused on cell growth. The S phase is the second phase of interphase, during which the DNA of the chromosomes is replicated. Finally, the G₂ phase, also called the second gap phase, is the third and final phase of interphase; in this phase, the cell undergoes the final preparations for meiosis.
- During DNA duplication in the S phase, each chromosome is replicated to produce two identical copies, called sister chromatids, that are held together at the centromere. The centrosomes, which are the structures that organize the microtubules of the meiotic spindle, also replicate. This prepares the cell to enter prophase I, the first meiotic phase.



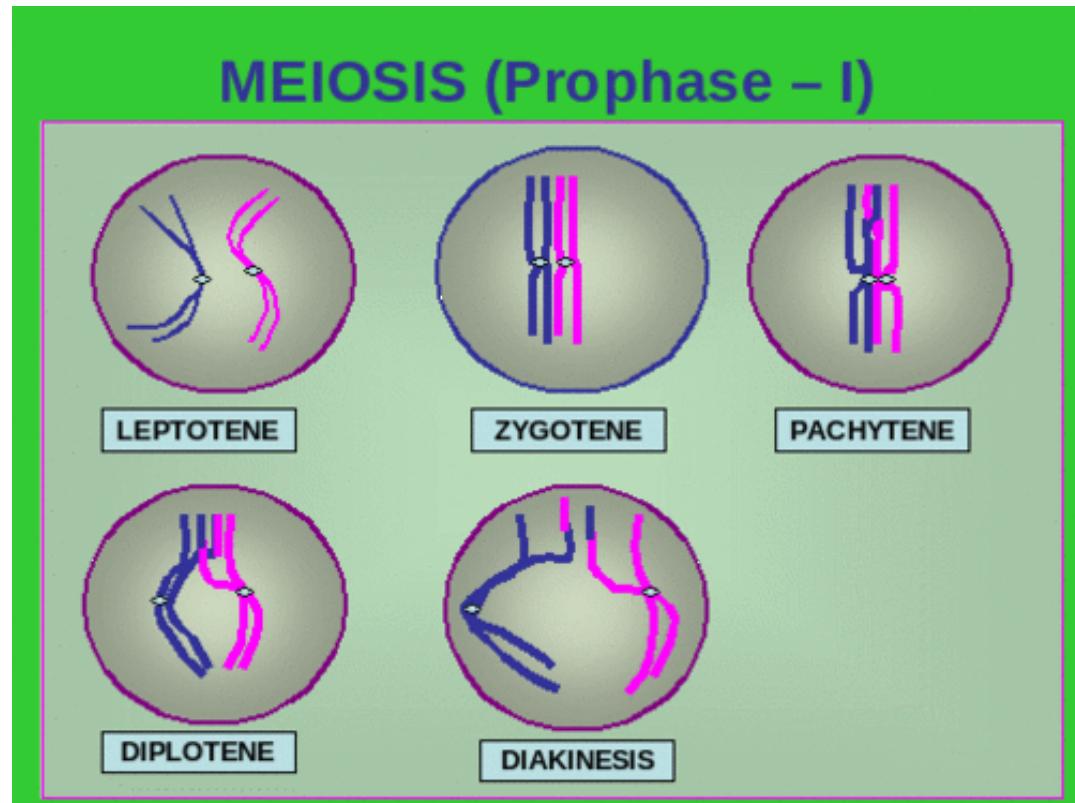
Meiosis I: Prophase I

- As the nuclear envelope begins to break down, the proteins associated with homologous chromosomes bring the pair close to each other. (Recall that, in mitosis, homologous chromosomes do not pair together. In mitosis, homologous chromosomes line up end-to-end so that when they divide, each daughter cell receives a sister chromatid from both members of the homologous pair.) The tight pairing of the homologous chromosomes is called **synapsis**. In synapsis, the genes on the chromatids of the homologous chromosomes are aligned precisely with each other (Figure 1). The synaptonemal complex supports the exchange of chromosomal segments between non-sister homologous chromatids, a process called **crossing over**. Crossing over occurs at **chiasmata** (singular = chiasma), the point of contact between non-sister chromosomes of a homologous pair .
- At the end of prophase I, the pairs are held together only at the chiasmata and are called **tetrads** because the four sister chromatids of each pair of homologous chromosomes are now visible.



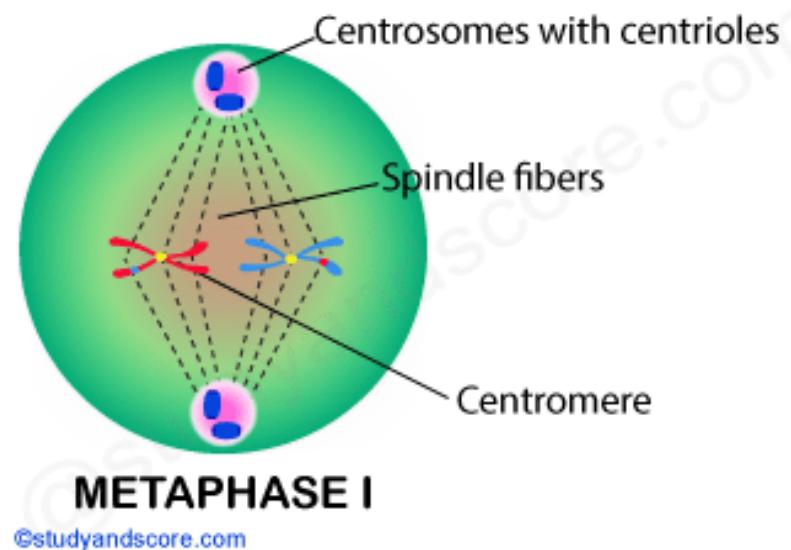
Meiosis I: Prophase I

- The crossover events are the first source of genetic variation in the nuclei produced by meiosis. A single crossover event between homologous non-sister chromatids leads to a reciprocal exchange of equivalent DNA between a maternal chromosome and a paternal chromosome. Now, when that sister chromatid is moved into a gamete cell it will carry some DNA from one parent of the individual and some DNA from the other parent. Multiple crossovers in an arm of the chromosome have the same effect, exchanging segments of DNA to create recombinant chromosomes.
- A second event in Prophase I is the attachment of the spindle fiber microtubules to the kinetochore proteins at the centromeres. At the end of prometaphase I, each tetrad is attached to microtubules from both poles, with one homologous chromosome facing each pole. The homologous chromosomes are still held together at chiasmata.
- In addition, the nuclear membrane has broken down entirely.

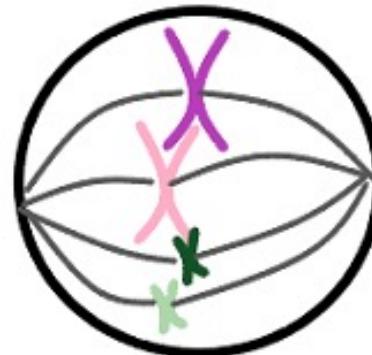


Meiosis I: Metaphase I

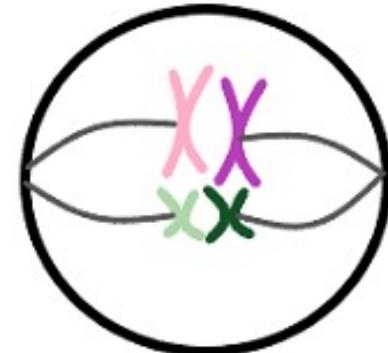
- During metaphase I, the homologous chromosomes are arranged in the center of the cell with the kinetochores facing opposite poles. The homologous pairs orient themselves randomly at the equator. Recall that homologous chromosomes are not identical. They contain slight differences in their genetic information, causing each gamete to have a unique genetic makeup. **This randomness is the physical basis for the creation of the second form of genetic variation in offspring.** The number of variations is dependent on the number of chromosomes making up a set. There are two possibilities for orientation at the metaphase plate; the possible number of alignments therefore equals 2^n , where n is the number of chromosomes per set. Humans have 23 chromosome pairs, which results in over eight million (2^{23}) possible genetically-distinct gametes. This number does not include the variability that was previously created in the sister chromatids by crossover. Given these two mechanisms, it is highly unlikely that any two haploid cells resulting from meiosis will have the same genetic composition.



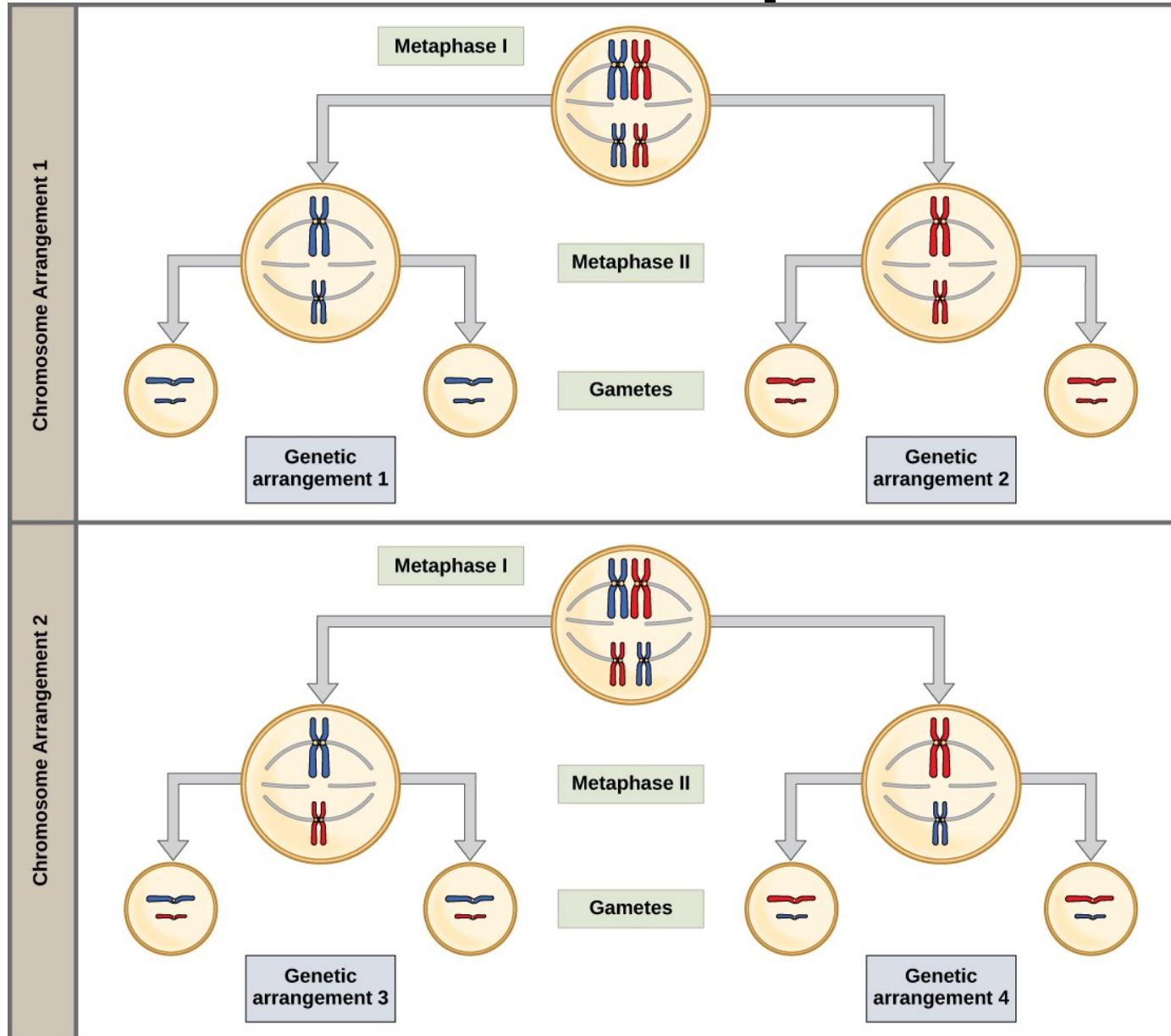
Metaphase of mitosis



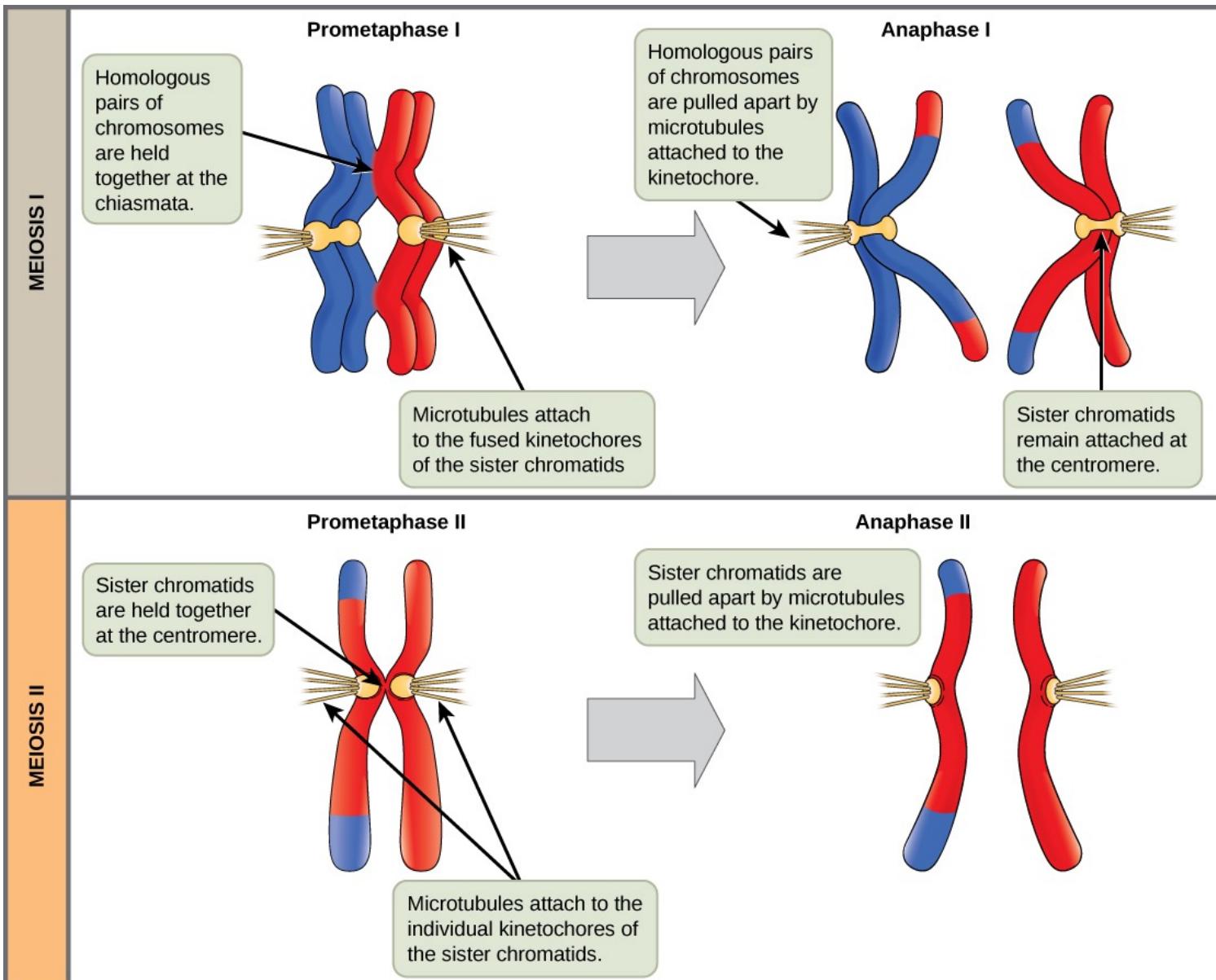
Metaphase I of meiosis



Meiosis I: Metaphase I



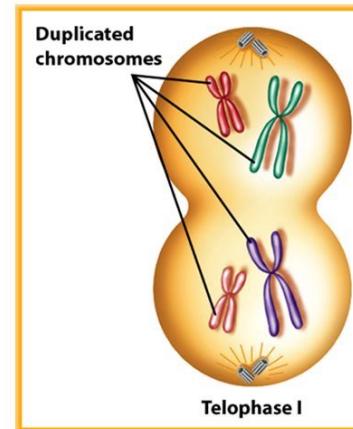
Meiosis I: Anaphase I



Meiosis I: Telophase I and Cytokinesis

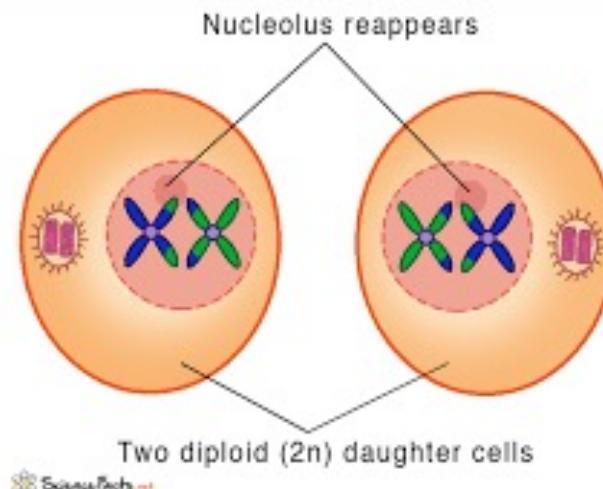
- In telophase, the separated chromosomes arrive at opposite poles. The remainder of the typical telophase events may or may not occur, depending on the species. In some organisms, the chromosomes decondense and nuclear envelopes form around the chromatids in telophase I. In other organisms, cytokinesis—the physical separation of the cytoplasmic components into two daughter cells—occurs without reformation of the nuclei. In nearly all species of animals and some fungi, cytokinesis separates the cell contents via a cleavage furrow (constriction of the actin ring that leads to cytoplasmic division). In plants, a cell plate is formed during cell cytokinesis by Golgi vesicles fusing at the metaphase plate. This cell plate will ultimately lead to the formation of cell walls that separate the two daughter cells.

Telophase I



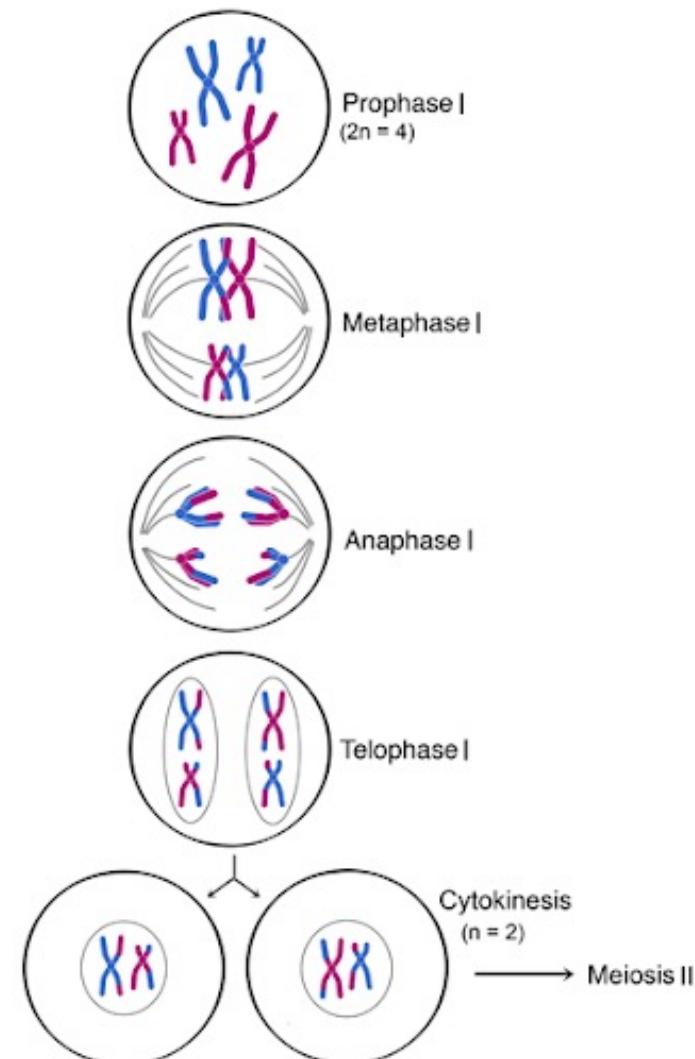
- Chromosomes gather at the poles.
- The cytoplasm divides.

Cytokinesis I of Meiosis



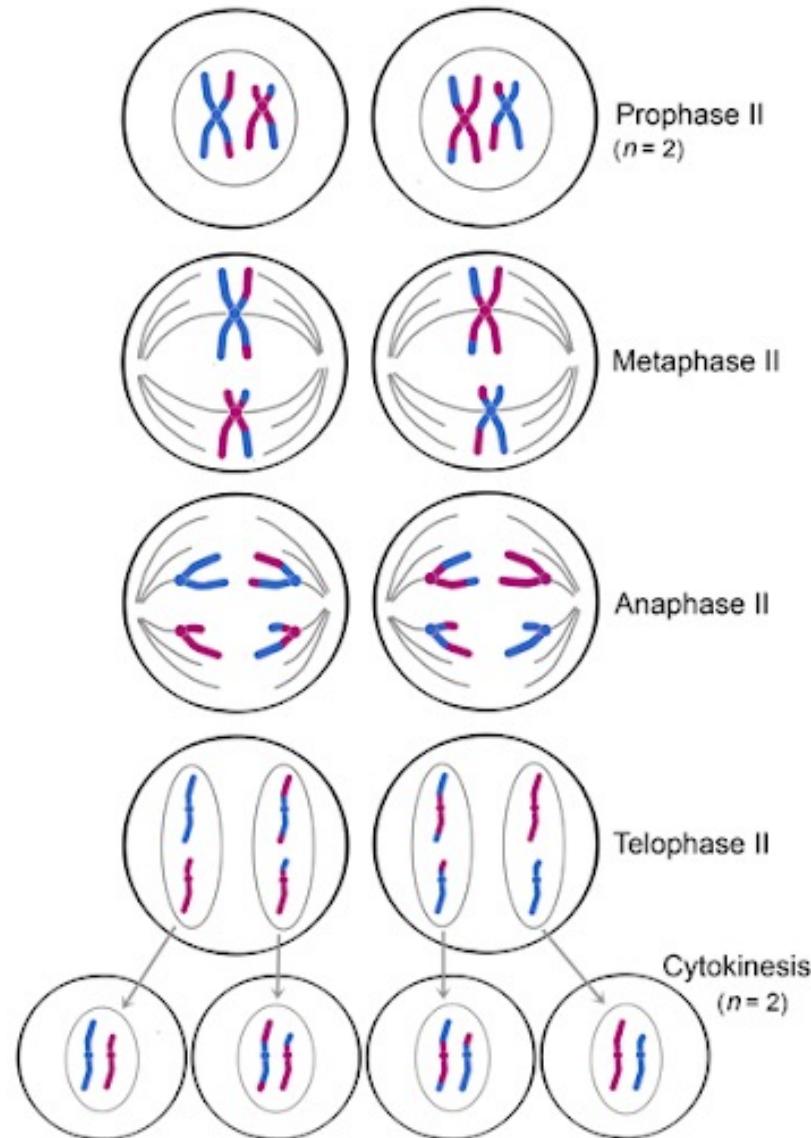
Two haploid cells are the end result of the first meiotic division

- The cells are haploid because at each pole, there is just one of each pair of the homologous chromosomes. Therefore, only one full set of the chromosomes is present. This is why the cells are considered haploid—there is only one chromosome set, even though each homolog still consists of two sister chromatids. Recall that sister chromatids are merely duplicates of one of the two homologous chromosomes (except for changes that occurred during crossing over). In meiosis II, these two sister chromatids will separate, creating four haploid daughter cells.



Meiosis II

- In some species, cells enter a brief interphase, or **interkinesis**, before entering meiosis II. Interkinesis lacks an S phase, so chromosomes are not duplicated. The two cells produced in meiosis I go through the events of meiosis II in synchrony. During meiosis II, the sister chromatids within the two daughter cells separate, forming four new haploid gametes. The mechanics of meiosis II is similar to mitosis, except that each dividing cell has only one set of homologous chromosomes. Therefore, each cell has half the number of sister chromatids to separate out as a diploid cell undergoing mitosis.



Meiosis II

Prophase II

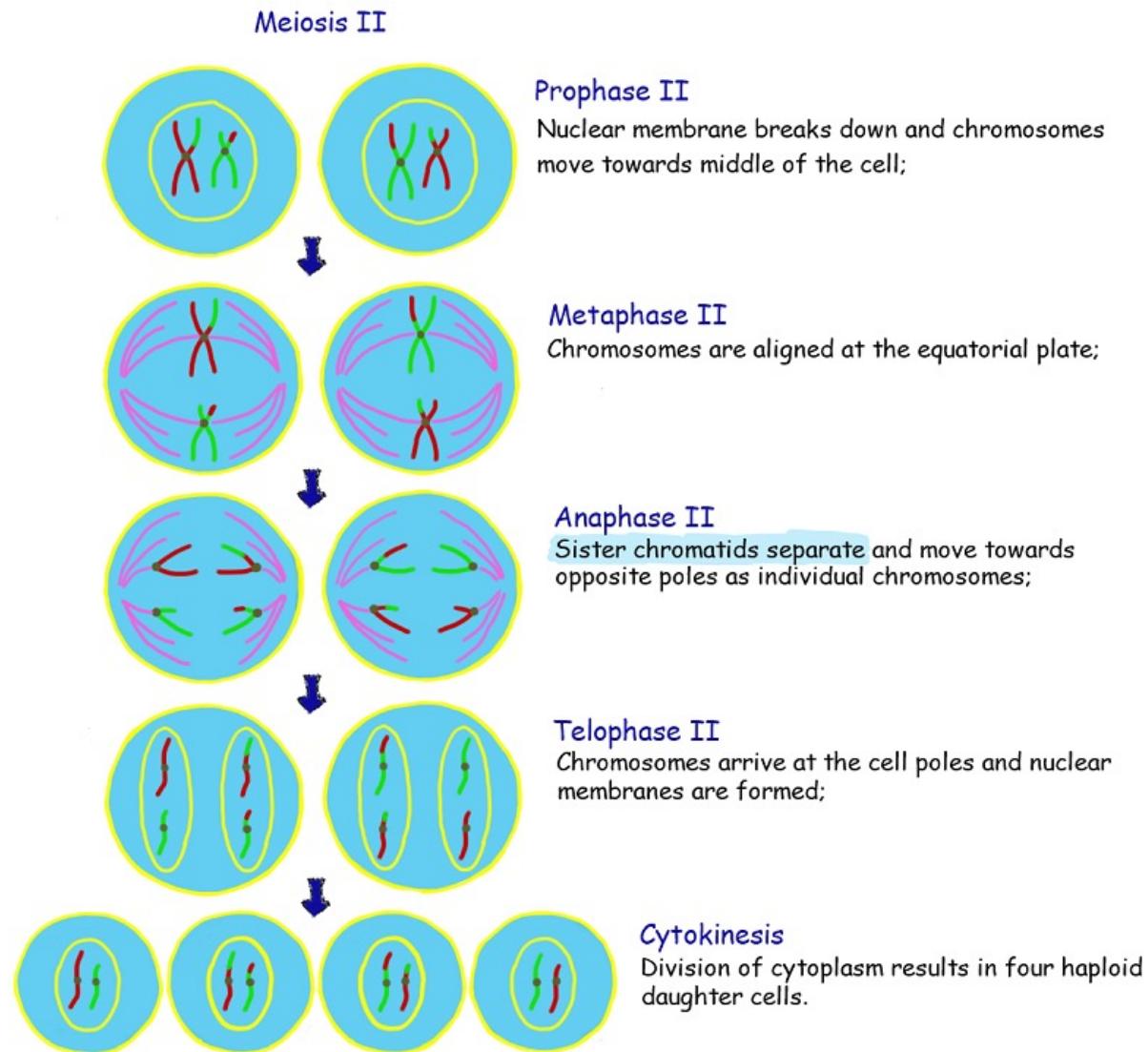
- If the chromosomes decondensed in telophase I, they condense again. If nuclear envelopes were formed, they fragment into vesicles. The centrosomes that were duplicated during interkinesis move away from each other toward opposite poles, and new spindles are formed. The nuclear envelopes are completely broken down, and the spindle is fully formed. Each sister chromatid forms an individual kinetochore that attaches to microtubules from opposite poles.

Metaphase II

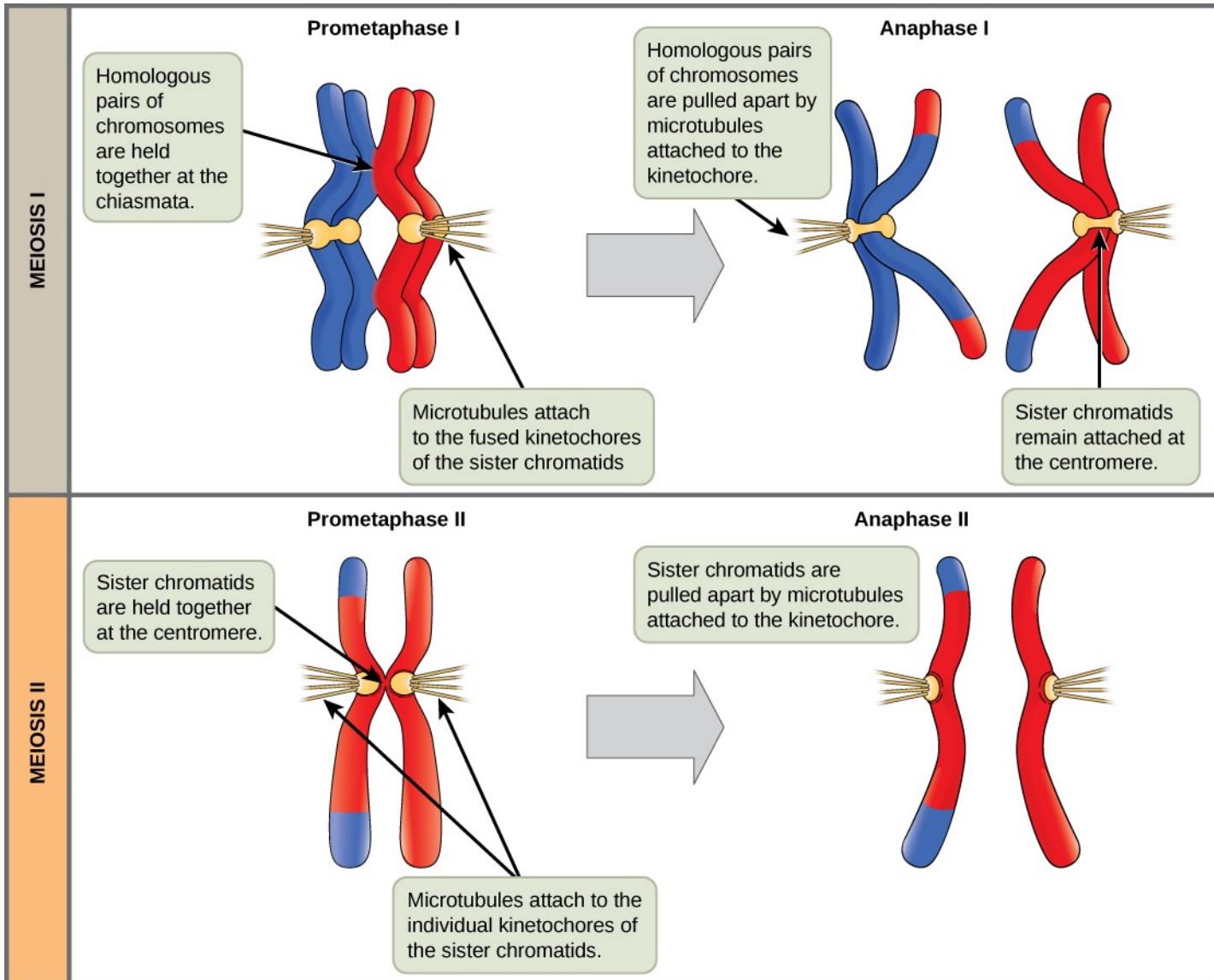
- The sister chromatids are maximally condensed and aligned at the equator of the cell.

Anaphase II

- The sister chromatids are pulled apart by the kinetochore microtubules and move toward opposite poles. Non-kinetochore microtubules elongate the cell.



Meiosis II

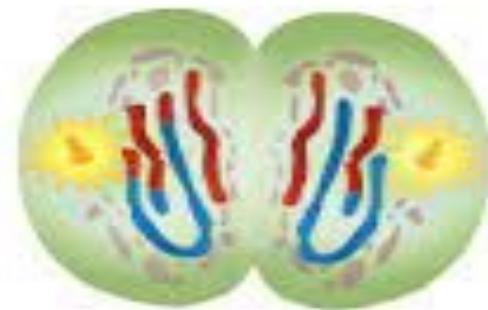


Meiosis II

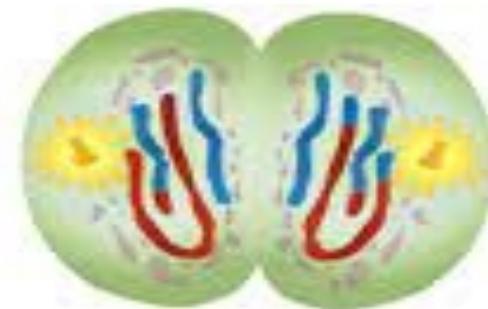
Telophase II and Cytokinesis

- The chromosomes arrive at opposite poles and begin to decondense. Nuclear envelopes form around the chromosomes. Cytokinesis separates the two cells into four unique haploid cells. At this point, the newly formed nuclei are both haploid. The cells produced are genetically unique because of the random assortment of paternal and maternal homologs and because of the recombining of maternal and paternal segments of chromosomes (with their sets of genes) that occurs during crossover. The entire process of meiosis is outlined

Telophase II & cytokinesis



A nuclear envelope forms around each set of chromosomes. The cytoplasm divides.

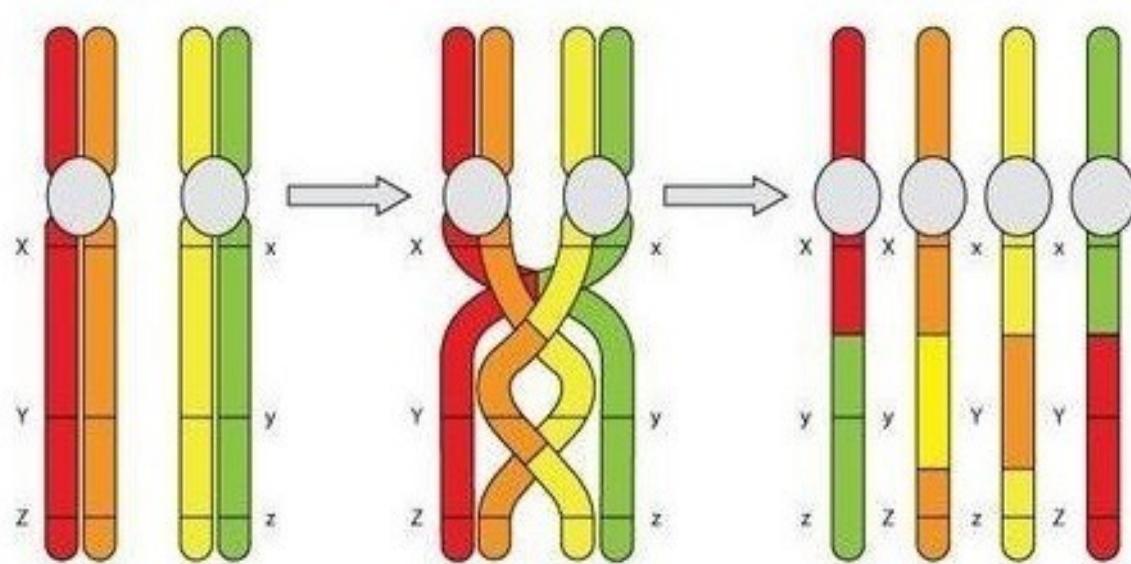


Meiosis: Summary

Stage	Event	Outcome
INTERPHASE	S phase	Nuclear envelope Centrosomes (with centriole pairs) Chromatin
	Prophase I	Spindle Sister chromatids Chiasmata Tetrad
	Prometaphase I	Centromere (with kinetochore)
	Metaphase I	Microtubule attached to kinetochore Metaphase plate
	Anaphase I	Sister chromatids remain attached Homologous chromosomes separate
	Telophase I and Cytokinesis	Cleavage furrow
	Prophase II	
	Prometaphase II	The nuclear envelope disappears, and the spindle fibers engage the individual kinetochores on the sister chromatids.
	Metaphase II	Sister chromatids line up at the metaphase plate.
	Anaphase II	Sister chromatids separate
MEIOSIS II	Telophase II and Cytokinesis	Haploid daughter cells
		Chromosomes arrive at the poles of the cell and decondense. Nuclear envelopes surround the four nuclei. Cleavage furrows divide the two cells into four haploid cells.

Genetic Variation in Meiosis

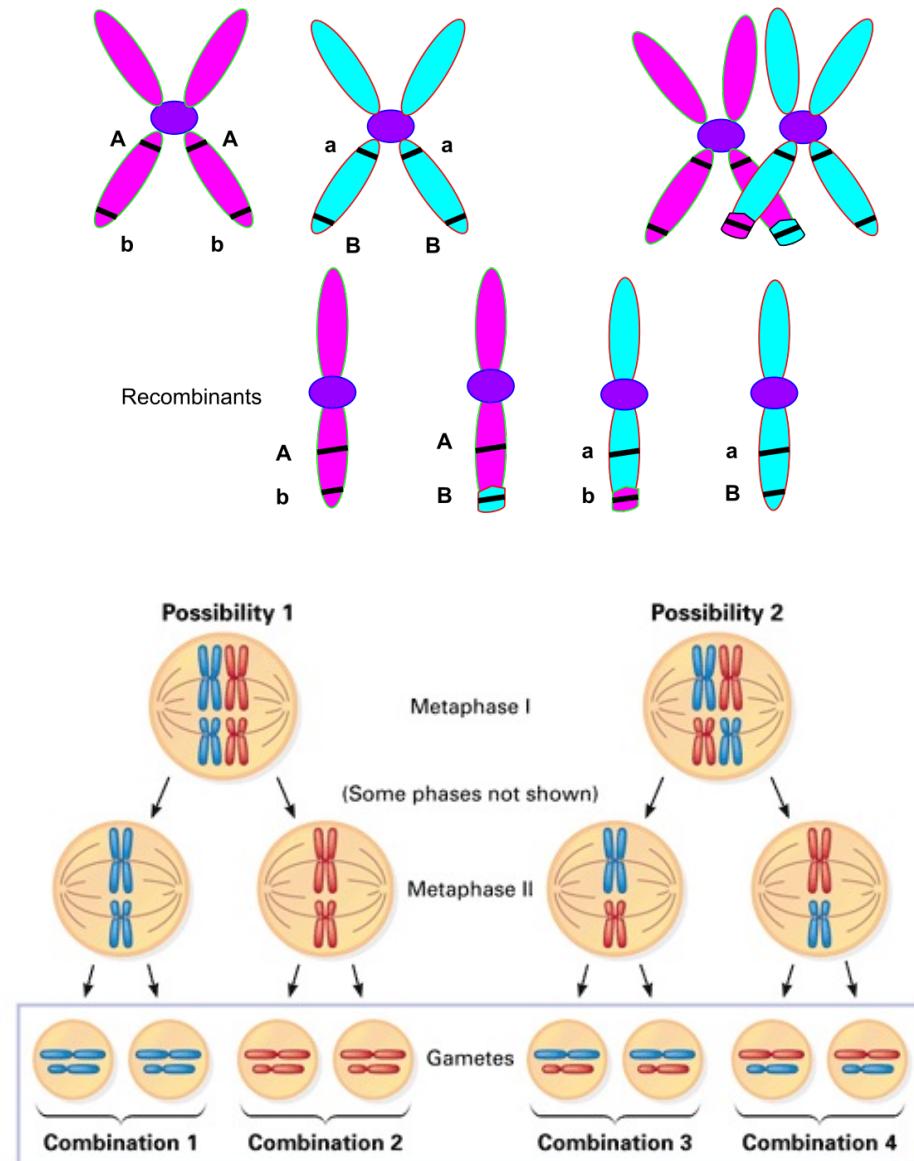
- The gametes produced in meiosis aren't genetically identical to the starting cell, and they also aren't identical to one another. As an example, consider the meiosis II diagram above, which shows the end products of meiosis for a simple cell with a diploid number of $2n = 4$ chromosomes. The four gametes produced at the end of meiosis II are all slightly different, each with a unique combination 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 simple cell with only four chromosomes. This diversity of possible gametes reflects two factors: crossing over and the random orientation of homologue pairs during metaphase of meiosis I.



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Genetic Variation in Meiosis

- **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 it does in human ovaries and testes, crossovers will happen at many different points. This repetition produces a wide variety of recombinant chromosomes, chromosomes where fragments of DNA have been exchanged between homologues.
- **Random orientation of homologue pairs.** The random orientation of homologue pairs during metaphase of meiosis I is another important source of gamete diversity.

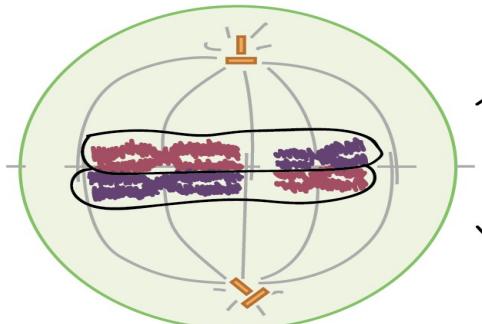


Genetic Variation in Meiosis

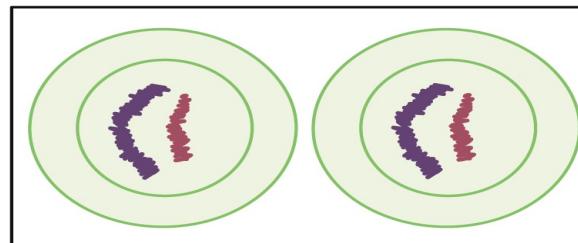
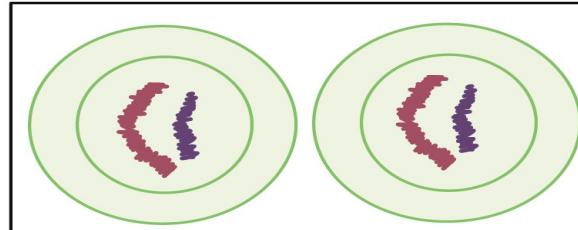
Configuration at metaphase I

End products (gametes)

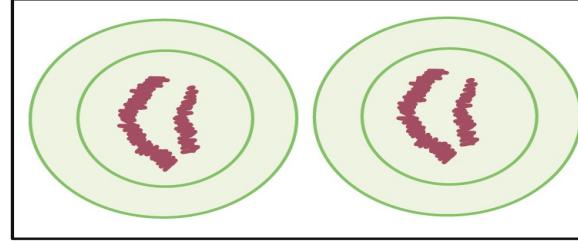
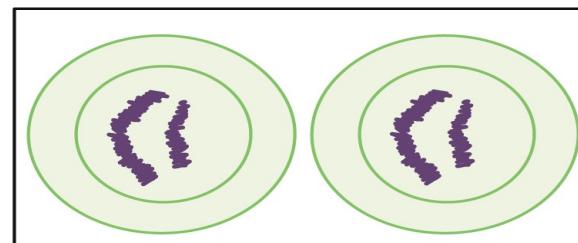
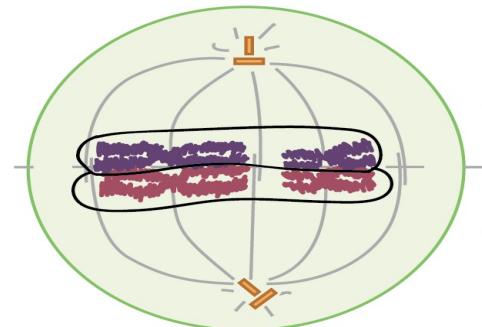
Possibility 1



*homologues are shown
without crossovers for clarity*



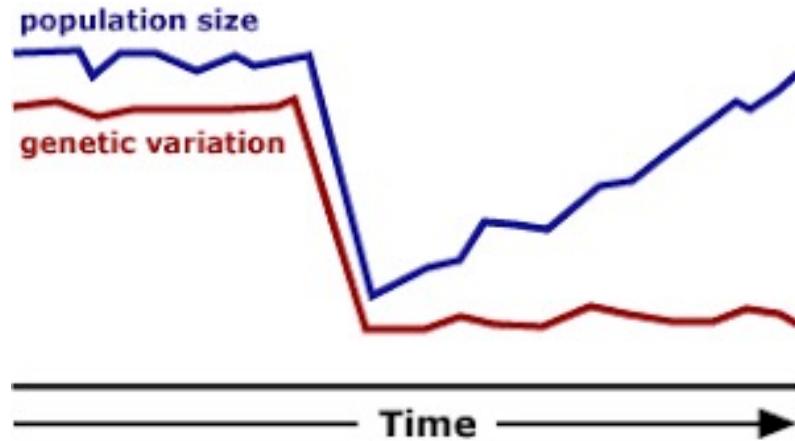
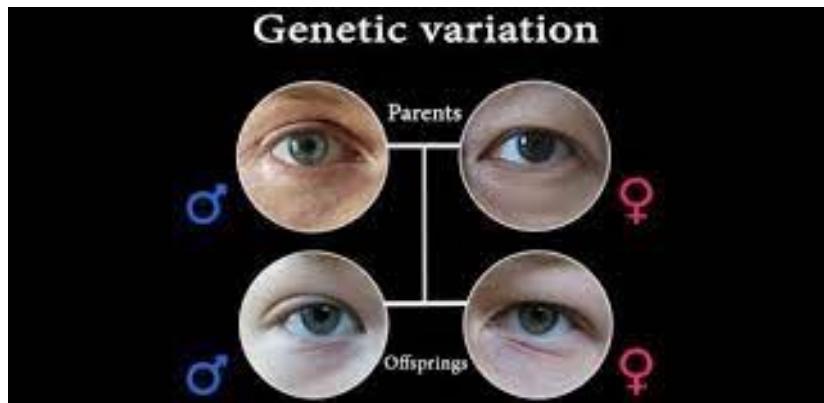
Possibility 2



= chromosome from mother
 = chromosome from father

Genetic Variation in Meiosis

- A homologous pair consists of one homologue from your dad and one from your mom, and you have 23 pairs of homologous chromosomes all together, counting the X and Y as homologous for this purpose. During meiosis I, the homologous pairs will separate to form two equal groups, but it's not usually the case that all the paternal—dad—chromosomes will go into one group and all the maternal—mom—chromosomes into the other.
- Instead, each pair of homologues will effectively flip a coin to decide which chromosome goes into which group. In a cell with just two pairs of homologous chromosomes, like the one at right, random metaphase orientation allows for $2^2 = 4$ different types of possible gametes. In a human cell, the same mechanism allows for $2^{23} = 8,388,608$ different types of possible gametes. And that's not even considering crossovers!

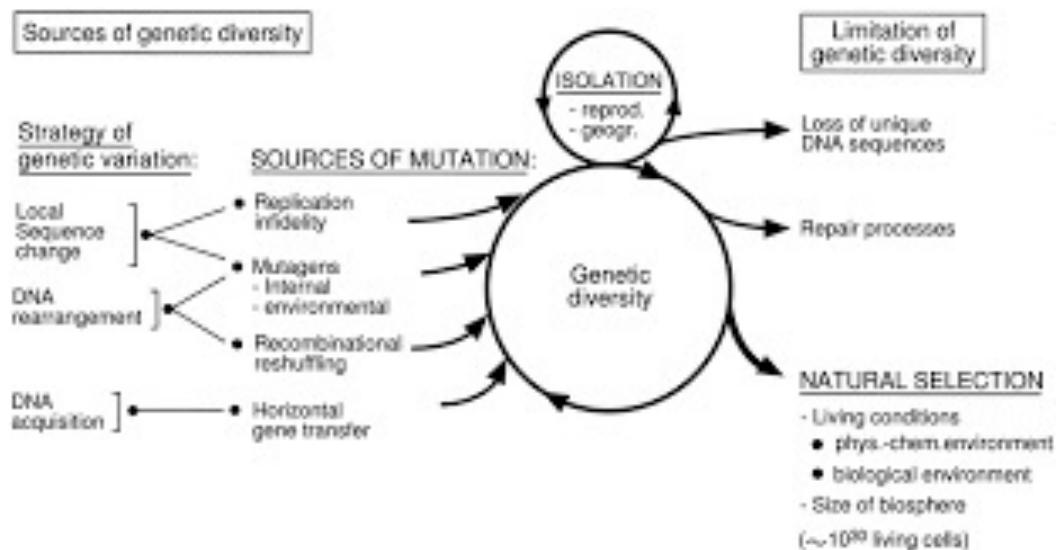
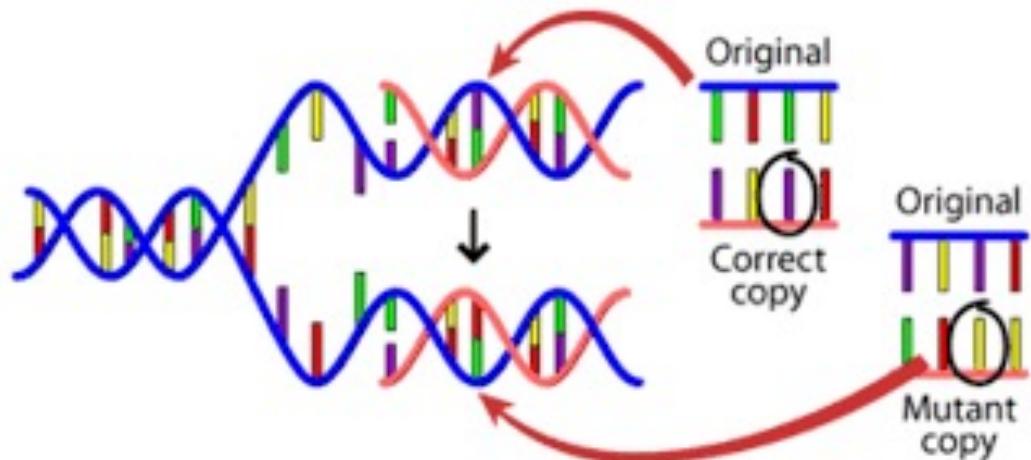


Genetic Variation in Meiosis

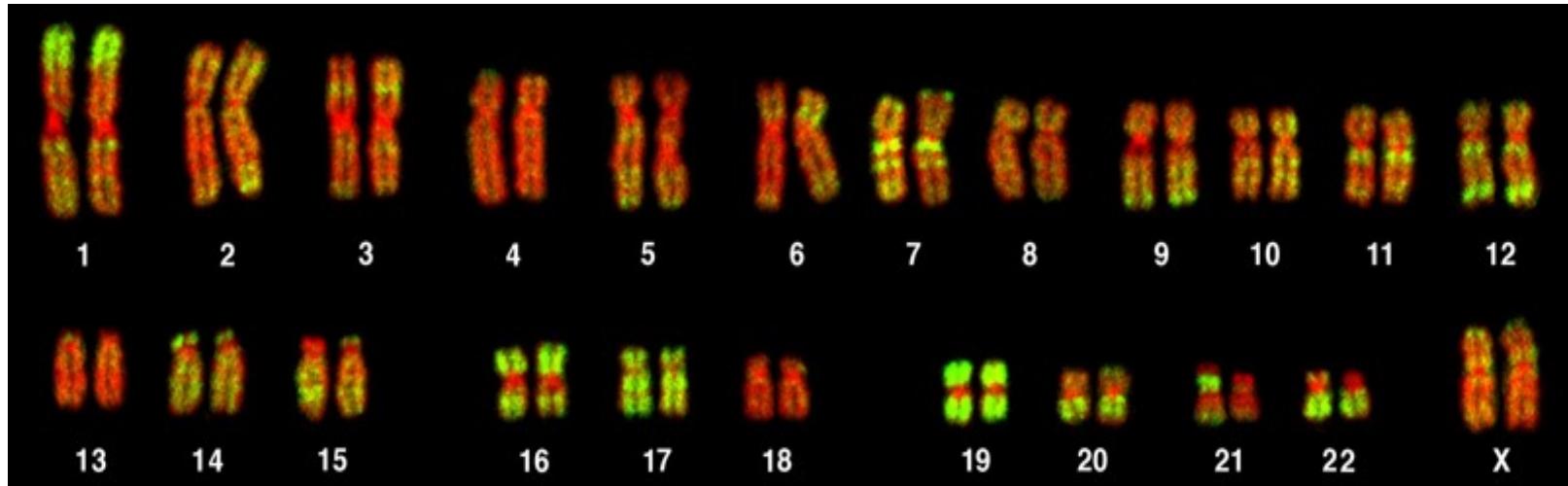
- Given those kinds of numbers, it's very unlikely that any two sperm or egg cells made by a person will be the same. It's even more unlikely that you and your sister or brother will be genetically identical, unless you happen to be identical twins, thanks to the process of fertilization (in which a unique egg from Mom combines with a unique sperm from Dad, making a zygote whose genotype is well beyond one-in-a-trillion!).
- Meiosis and fertilization create genetic variation by making new combinations of gene variants (alleles). In some cases, these new combinations may make an organism more or less fit (able to survive and reproduce), thus providing the raw material for natural selection. Genetic variation is important in allowing a population to adapt via natural selection and thus survive in the long term.

Genetic Variation in Meiosis

- Genetic variation is introduced in multiple ways, including changes in mitosis, crossing over and random orientation in meiosis, and random fertilization. The video below offers you a nice overview of how each contributes to genetic diversity.



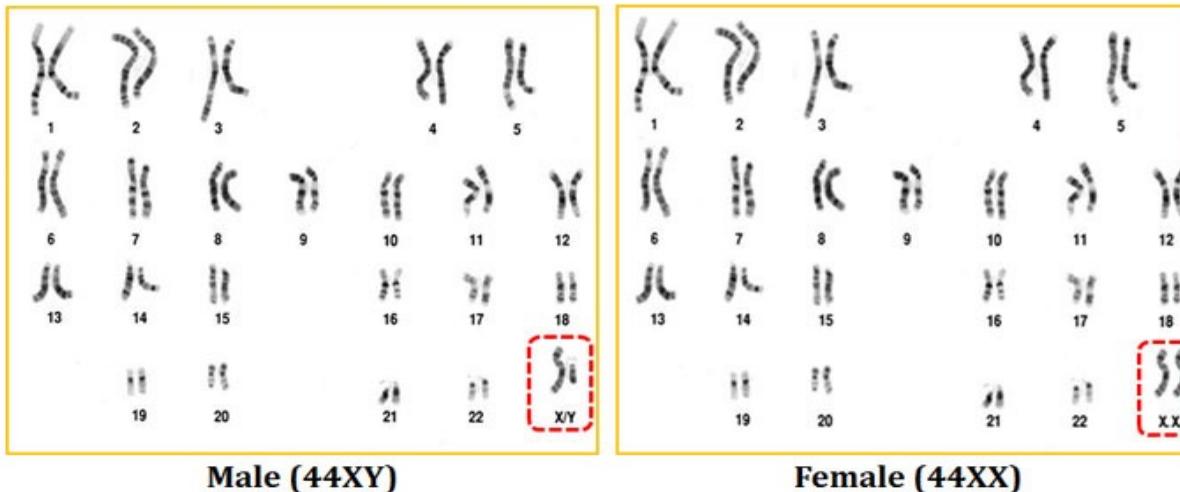
Karyotypes



- The isolation and microscopic observation of chromosomes forms the basis of cytogenetics and is the primary method by which clinicians detect chromosomal abnormalities in humans. A **karyotype** is the number and appearance of chromosomes, and includes their length, banding pattern, and centromere position. To obtain a view of an individual's karyotype, cytologists photograph the chromosomes and then cut and paste each chromosome into a chart, or **karyogram**, also known as an ideogram. The simplest use of a karyotype (or its karyogram image) is to identify abnormal chromosomal numbers.

Karyotypes

HUMAN KARYOTYPE (NORMAL)

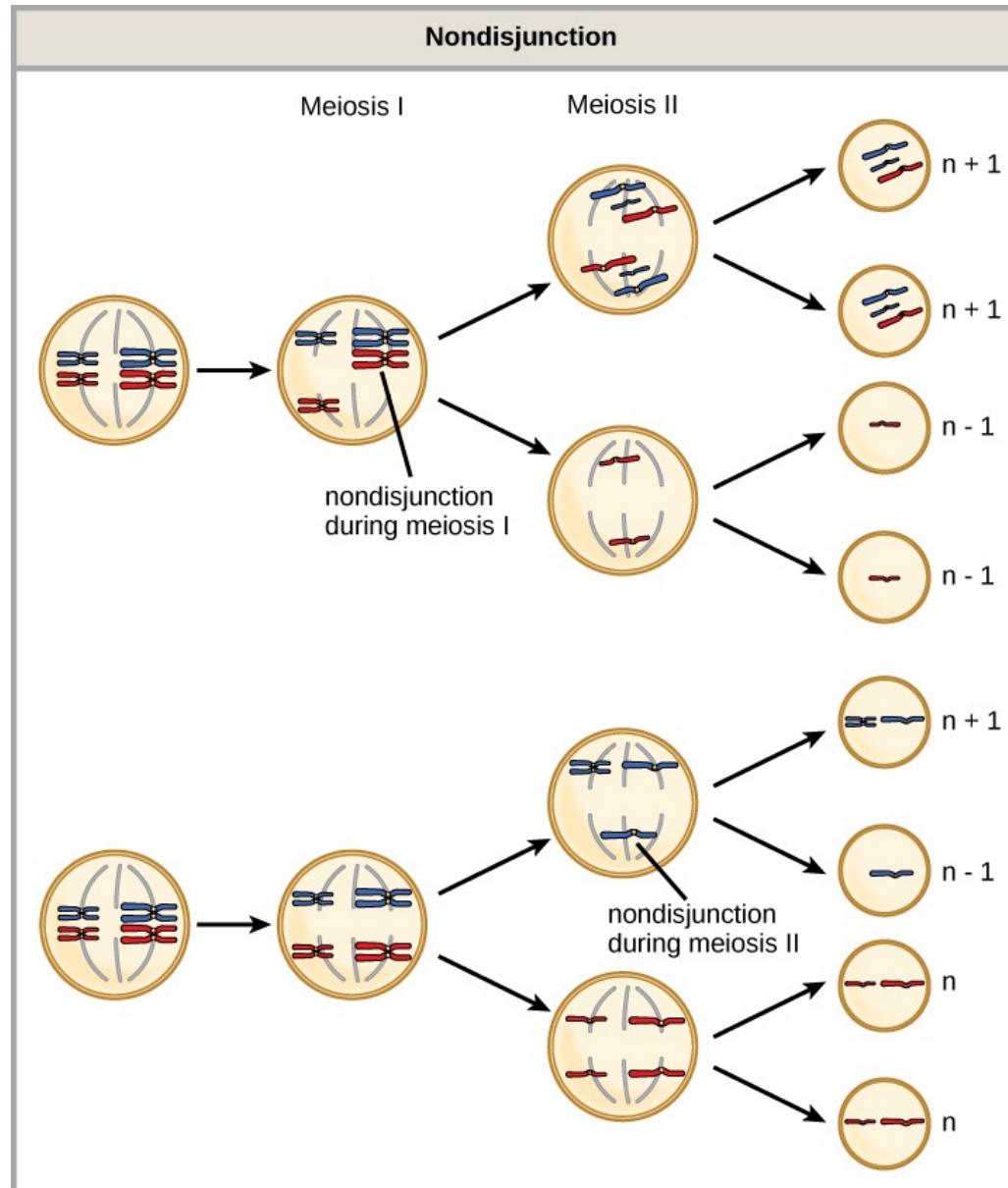


- In a given species, chromosomes can be identified by their number, size, centromere position, and banding pattern. In a human karyotype, **autosomes** or “body chromosomes” (all of the non-sex chromosomes) are generally organized in approximate order of size from largest (chromosome 1) to smallest (chromosome 22). The X and Y chromosomes are not autosomes. However, chromosome 21 is actually shorter than chromosome 22. This was discovered after the naming of Down syndrome as trisomy 21, reflecting how this disease results from possessing one extra chromosome 21 (three total). Not wanting to change the name of this important disease, chromosome 21 retained its numbering, despite describing the shortest set of chromosomes. The chromosome “arms” projecting from either end of the centromere may be designated as short or long, depending on their relative lengths. The short arm is abbreviated *p* (for “petite”), whereas the long arm is abbreviated *q* (because it follows “*p*” alphabetically). Each arm is further subdivided and denoted by a number. Using this naming system, locations on chromosomes can be described consistently in the scientific literature.

Common Disorders

- Of all of the chromosomal disorders, abnormalities in chromosome number are the most obviously identifiable from a karyogram. Disorders of chromosome number include the duplication or loss of entire chromosomes, as well as changes in the number of complete sets of chromosomes. They are caused by **nondisjunction**, which occurs when pairs of homologous chromosomes or sister chromatids fail to separate during meiosis. Misaligned or incomplete synapsis, or a dysfunction of the spindle apparatus that facilitates chromosome migration, can cause nondisjunction. The risk of nondisjunction occurring increases with the age of the parents.
- Nondisjunction can occur during either meiosis I or II, with differing results. If homologous chromosomes fail to separate during meiosis I, the result is two gametes that lack that particular chromosome and two gametes with two copies of the chromosome. If sister chromatids fail to separate during meiosis II, the result is one gamete that lacks that chromosome, two normal gametes with one copy of the chromosome, and one gamete with two copies of the chromosome.

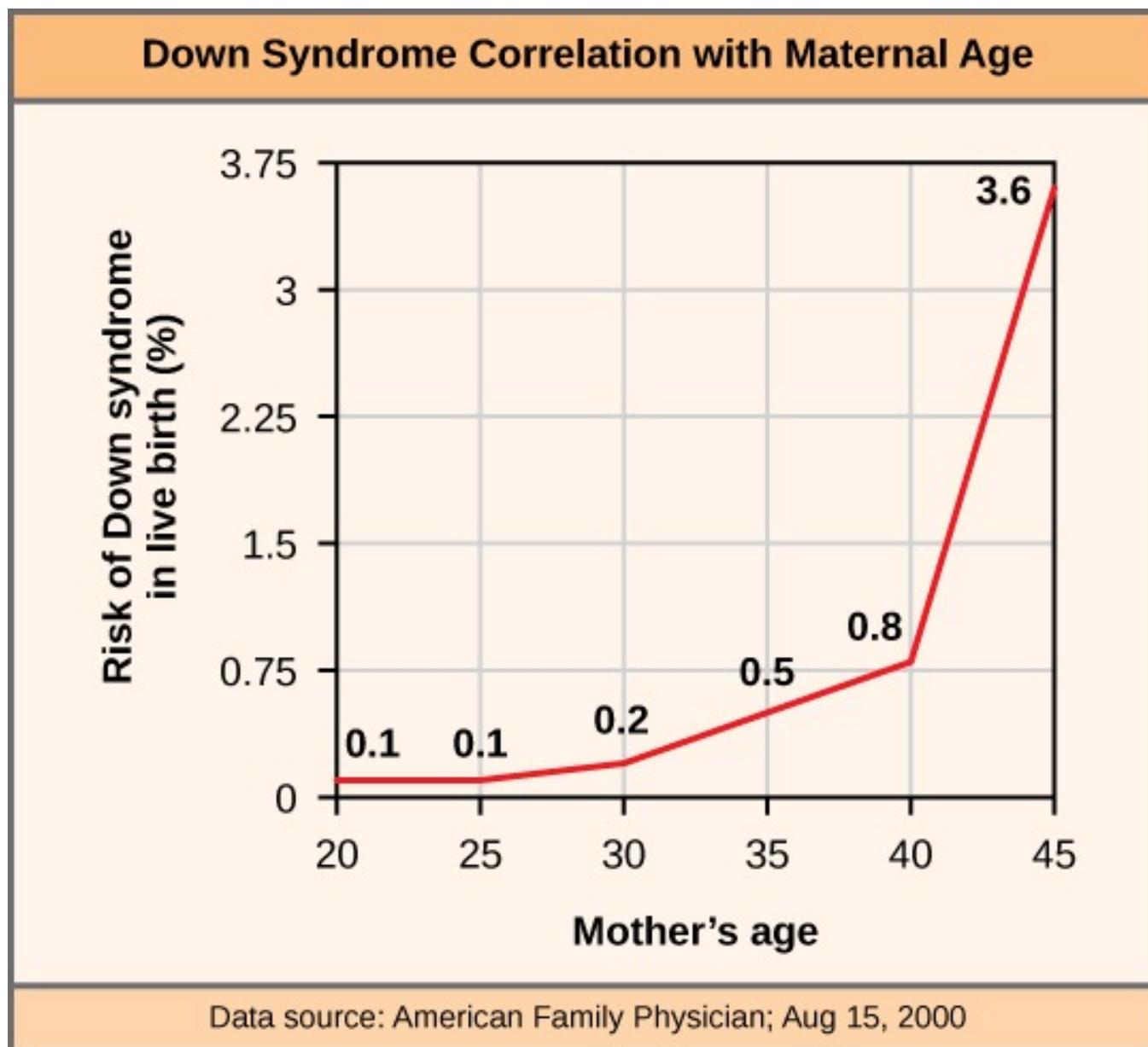
Common Disorders



Common Disorders: Aneuploidy

- An individual with the appropriate number of chromosomes for their species is called **euploid**; in humans, euploidy corresponds to 22 pairs of autosomes and one pair of sex chromosomes. An individual with an error in chromosome number is described as **aneuploid**, a term that includes **monosomy** (loss of one chromosome) or **trisomy** (gain of an extraneous chromosome). Monosomic human zygotes missing any one copy of an autosome invariably fail to develop to birth because they lack essential genes. This underscores the importance of “gene dosage” in humans. Most autosomal trisomies also fail to develop to birth; however, duplications of some of the smaller chromosomes (13, 15, 18, 21, or 22) can result in offspring that survive for several weeks to many years. Trisomic individuals suffer from a different type of genetic imbalance: an excess in gene dose. Individuals with an extra chromosome may synthesize an abundance of the gene products encoded by that chromosome. This extra dose (150 percent) of specific genes can lead to a number of functional challenges and often precludes development. The most common trisomy among viable births is that of chromosome 21, which corresponds to Down Syndrome. Individuals with this inherited disorder are characterized by short stature and stunted digits, facial distinctions that include a broad skull and large tongue, and significant developmental delays. The incidence of Down syndrome is correlated with maternal age; older women are more likely to become pregnant with fetuses carrying the trisomy 21 genotype.

Common Disorders: Aneuploidy



Common Disorders: Polyploidy

- An individual with more than the correct number of chromosome sets (two for diploid species) is called **polyploid**. For instance, fertilization of an abnormal diploid egg with a normal haploid sperm would yield a triploid zygote. Polyploid animals are extremely rare, with only a few examples among the flatworms, crustaceans, amphibians, fish, and lizards. Polyploid animals are sterile because meiosis cannot proceed normally and instead produces mostly aneuploid daughter cells that cannot yield viable zygotes. Rarely, polyploid animals can reproduce asexually by **haplodiploidy**, in which an unfertilized egg divides mitotically to produce offspring. In contrast, polyploidy is very common in the plant kingdom, and polyploid plants tend to be larger and more robust than euploids of their species



Duplications and Deletions



- In addition to the loss or gain of an entire chromosome, a chromosomal segment may be duplicated or lost. Duplications and deletions often produce offspring that survive but exhibit physical and mental abnormalities. Duplicated chromosomal segments may fuse to existing chromosomes or may be free in the nucleus. Cri-du-chat (from the French for “cry of the cat”) is a syndrome associated with nervous system abnormalities and identifiable physical features that result from a deletion of most of 5p (the small arm of chromosome 5) (Figure above). Infants with this genotype emit a characteristic high-pitched cry on which the disorder’s name is based.

This individual with cri-du-chat syndrome is shown at two, four, nine, and 12 years of age.

Trait Inheritance

- For cases in which a single gene controls a single characteristic, a diploid organism has two genetic copies that may or may not encode the same version of that characteristic. Gene variants that arise by mutation and exist at the same relative locations on homologous chromosomes are called **alleles**. Mendel examined the inheritance of genes with just two allele forms, but it is common to encounter more than two alleles for any given gene in a natural population.

Phenotypes and Genotypes

- Two alleles for a given gene in a diploid organism are expressed and interact to produce physical characteristics. The observable traits expressed by an organism are referred to as its **phenotype**. An organism's underlying genetic makeup, consisting of both physically visible and non-expressed alleles, is called its **genotype**. Mendel's hybridization experiments demonstrate the difference between phenotype and genotype. When true-breeding plants in which one parent had yellow pods and one had green pods were cross-fertilized, all of the F_1 hybrid offspring had yellow pods. That is, the hybrid offspring were phenotypically identical to the true-breeding parent with yellow pods. However, we know that the allele donated by the parent with green pods was not simply lost because it reappeared in some of the F_2 offspring. Therefore, the F_1 plants must have been genotypically different from the parent with yellow pods.

Dominant and Recessive Alleles

- Our discussion of homozygous and heterozygous organisms brings us to why the F_1 heterozygous offspring were identical to one of the parents, rather than expressing both alleles. In all seven pea-plant characteristics, one of the two contrasting alleles was dominant, and the other was recessive. Mendel called the dominant allele the expressed unit factor; the recessive allele was referred to as the latent unit factor. We now know that these so-called unit factors are actually genes on homologous chromosome pairs. For a gene that is expressed in a dominant and recessive pattern, homozygous dominant and heterozygous organisms will look identical (that is, they will have different genotypes but the same phenotype). The recessive allele will only be observed in homozygous recessive individuals

Dominant and Recessive Alleles

Human Inheritance in Dominant and Recessive Patterns

Dominant Traits

Achondroplasia

Brachydactyly

Huntington's disease

Marfan syndrome

Neurofibromatosis

Widow's peak

Wooly hair

Recessive Traits

Albinism

Cystic fibrosis

Duchenne muscular dystrophy

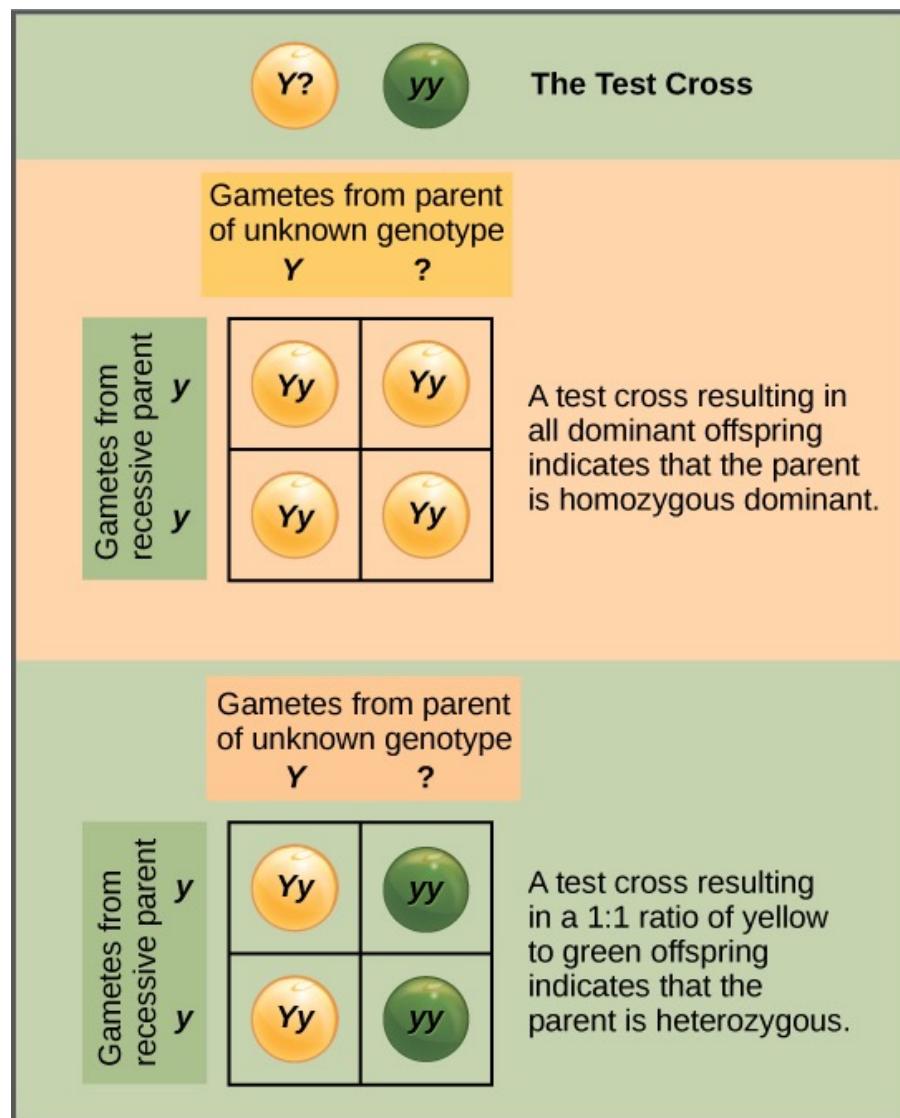
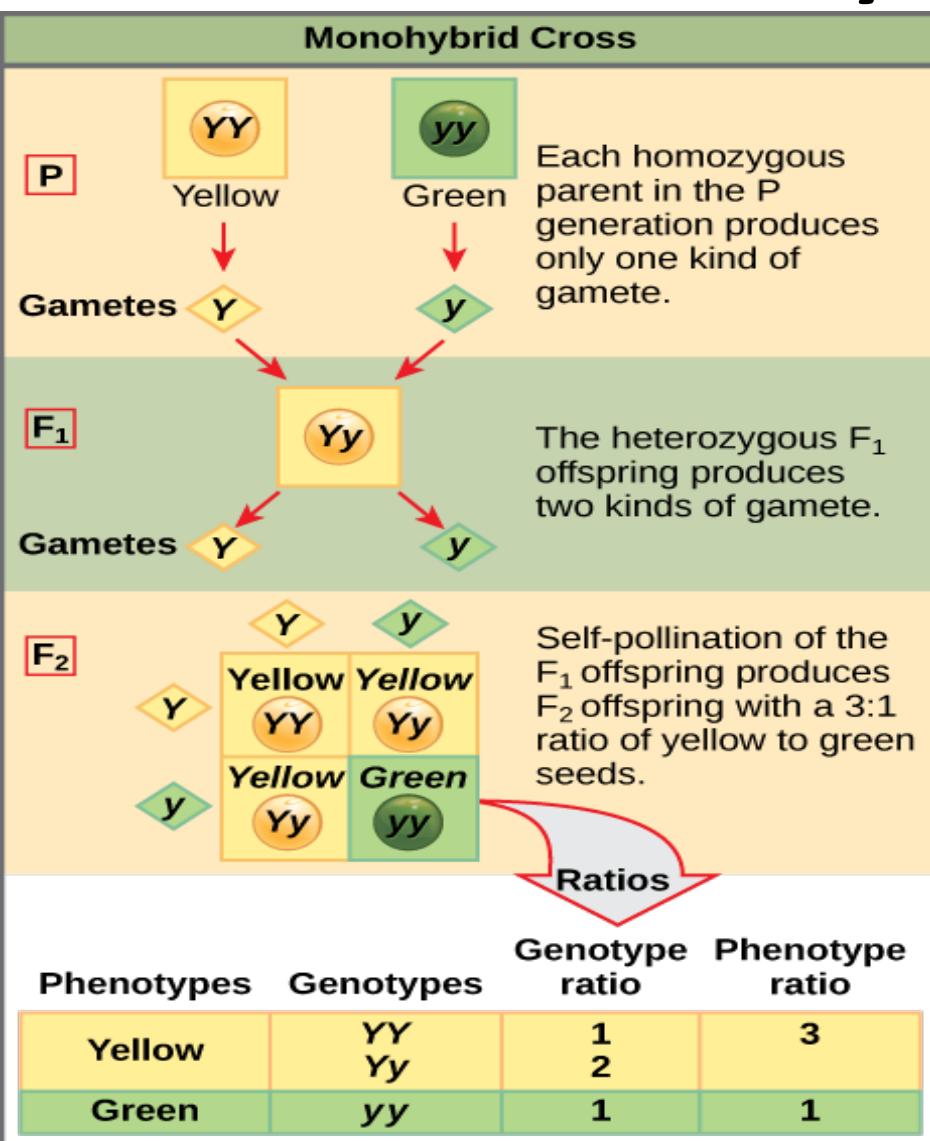
Galactosemia

Phenylketonuria

Sickle-cell anemia

Tay-Sachs disease

The Punnett Square Approach for a Monohybrid Cross



Inheritance: Diseases

- Many human diseases are genetically inherited. A healthy person in a family in which some members suffer from a recessive genetic disorder may want to know if he or she has the disease-causing gene and what risk exists of passing the disorder on to his or her offspring. Of course, doing a test cross in humans is unethical and impractical. Instead, geneticists use pedigree analysis to study the inheritance pattern of human genetic diseases.

Inheritance: Diseases

- Alkaptonuria is a recessive genetic disorder in which two amino acids, phenylalanine and tyrosine, are not properly metabolized. Affected individuals may have darkened skin and brown urine, and may suffer joint damage and other complications. In this pedigree, individuals with the disorder are indicated in blue and have the genotype aa. Unaffected individuals are indicated in yellow and have the genotype AA or Aa. Note that it is often possible to determine a person's genotype from the genotype of their offspring. For example, if neither parent has the disorder but their child does, they must be heterozygous. Two individuals on the pedigree have an unaffected phenotype but unknown genotype. Because they do not have the disorder, they must have at least one normal allele, so their genotype gets the "A?" designation.

Inheritance: Diseases

