BME 1532-CELL BIOLOGY

Sexual Reproduction and Genetics

by Assist. Prof. Görke Gürel Peközer

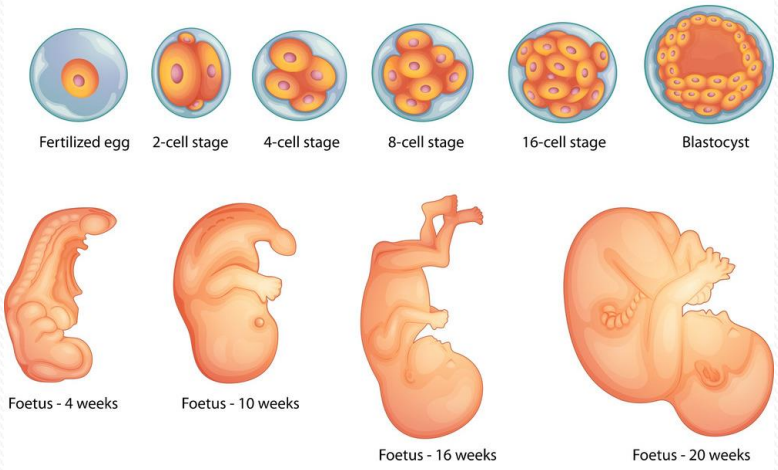
Yıldız Technical University
Biomedical Engineering Department
Spring 2020

Previously on BME 1532

- Cell Cycle
  - G1, S, G2 → Interphase
  - Mitosis and Cytokinesis → M phase
  - Go Phase
- Cell Cycle Control
  - Cyclins and Cyclin dependent kinases
  - G1-S Checkpoint
  - G2-M Checkpoint
  - M Checkpoint
- Mitosis
  - Prophase
  - Prometaphase
  - Metaphase
  - Anaphase
  - Telophase
- Cytokinesis
  - Contractile Ring
- Positive and Negative Regulators of Cell Cycle

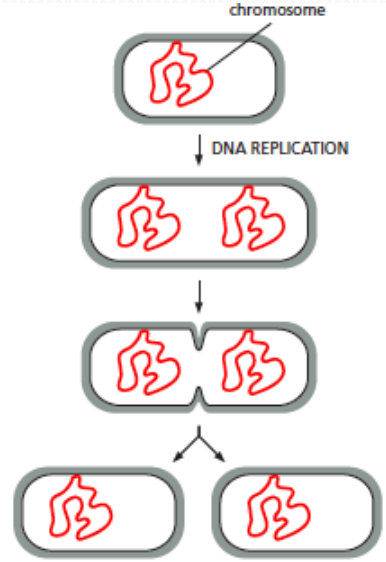
- Individual cells reproduce by replicating their DNA and dividing in two. This basic process of cell proliferation occurs in all living species—in the cells of multicellular organisms and in free-living cells such as bacteria and yeasts—and it allows each cell to pass on its genetic information to future generations.

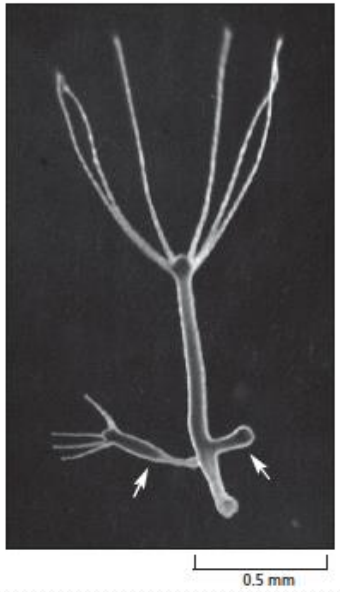
- Yet reproduction in a multicellular organism—in a fish or a fly, a person or a plant—is a much more complicated than this. It entails elaborate developmental cycles, in which all of the organism's cells, tissues, and organs must be generated afresh from a single cell.



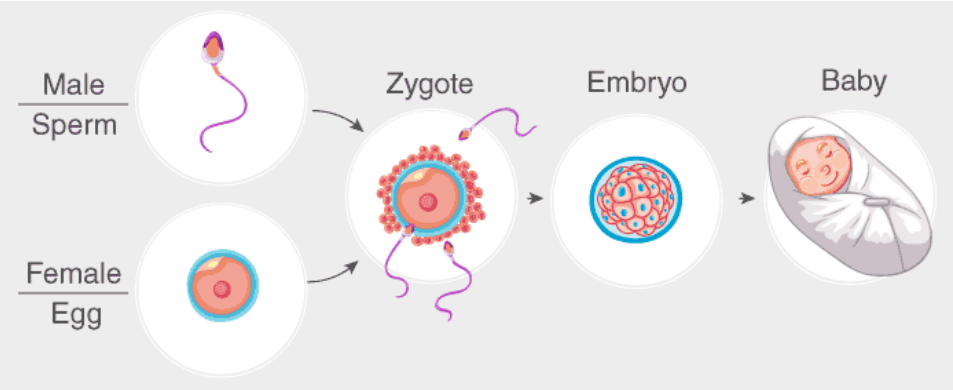
- This starter cell is no ordinary cell. It has a very peculiar origin: for most animal and plant species, it is produced by the union of a pair of cells that hail from two completely separate individuals—a mother and a father.
- As a result of this cell fusion—a central event in ***sexual reproduction***—two genomes merge to form the genome of a new individual. The mechanisms that govern genetic inheritance in sexually reproducing organisms are therefore different, and more complex, than those that operate in organisms that pass on their genetic information asexually—by a straighforward cell division.

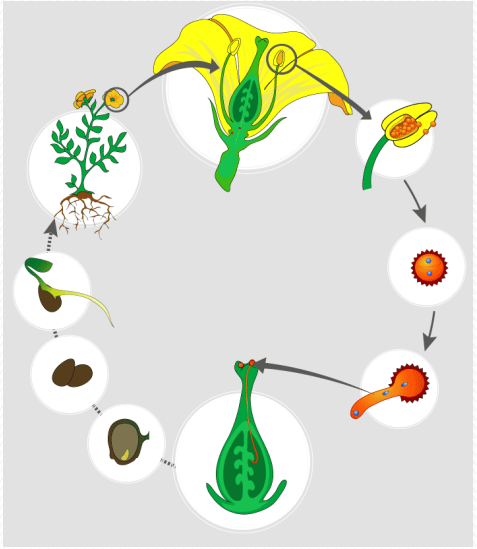
- Most of the creatures we see around us reproduce sexually. However, many organisms, especially those invisible to the naked eye, can produceoffspring without resorting to sex.
- Most bacteria and other single-celled organisms multiply by simple cell division.
- Many plants also reproduce asexually, forming multicellular offshoots that later detach from the parent to make new independent plants. Even in the animal kingdom, there are species that can procreate without sex. Hydra produce young by budding.
- Certain worms, when split in two, can regenerate the "missing halves" to form two complete individuals.
- And in some species of insects, lizards, and even birds, the females can lay eggs that develop parthenogenetically—without the help of males, sperm, or fertilization—into healthy daughters that can also reproduce the same way.



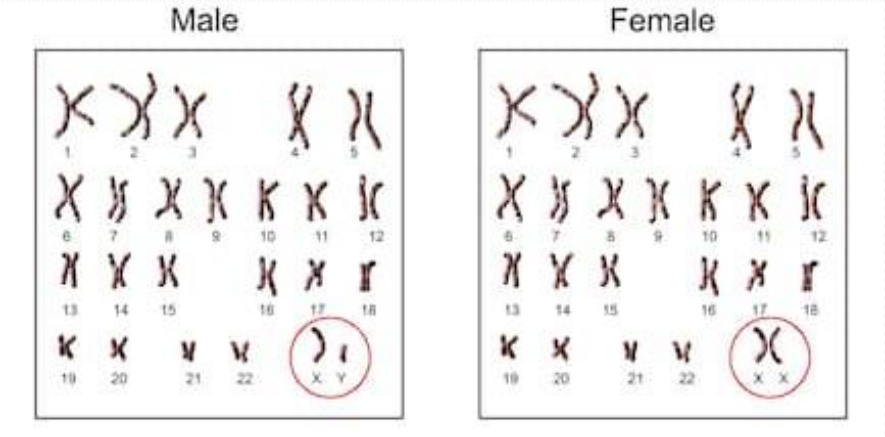


- But while such forms of asexual reproduction are simple and direct, they give rise to offspring that are genetically identical to the parent organism.
- Sexual reproduction, on the other hand, involves the mixing of DNA from two individuals to produce offspring that are genetically distinct from one another and from both their parents.
- This mode of reproduction apparently has great advantages.

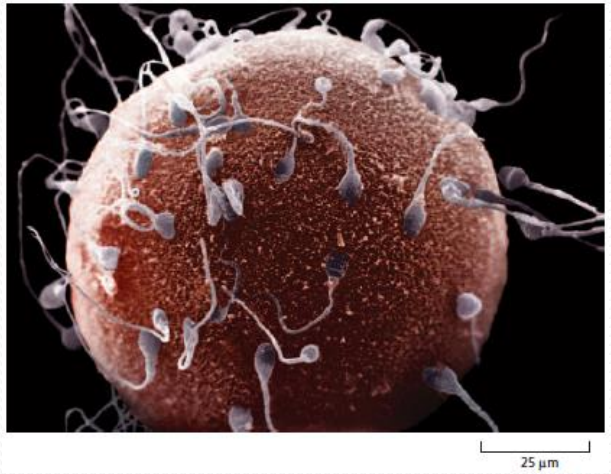


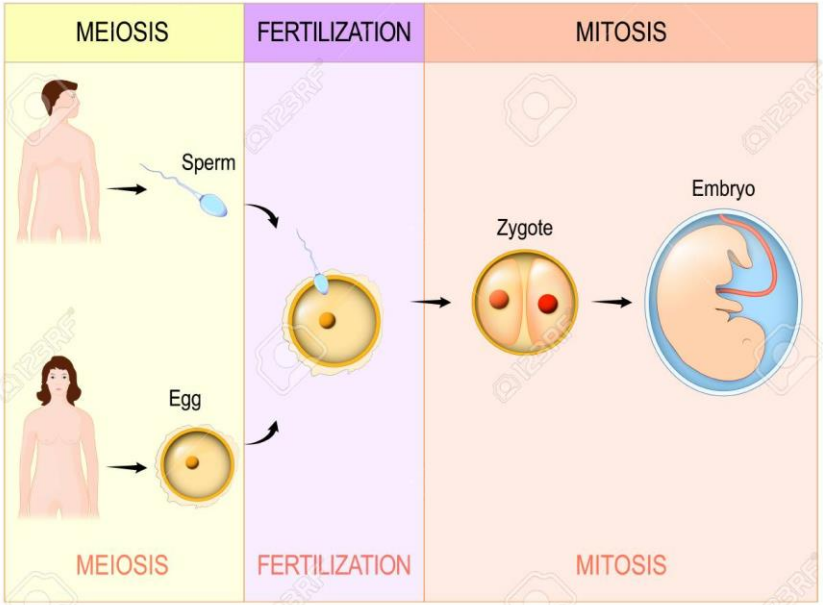


- Organisms that reproduce sexually are generally diploid: each cell contains two sets of chromosomes—one inherited from each parent. Because the two parents are members of the same species, the maternal chromosome set and the paternal chromosome set are very similar.
- The most notable difference between them is the sex chromosomes, which, in some species, distinguish males from females. With the exception of these sex chromosomes, the maternal and paternal versions of every chromosome— called the maternal and paternal homologs—carry the same set of genes.
- Each diploid cell, therefore, carries two copies of every gene (except for those found on the sex chromosomes, which may be present in only one copy).

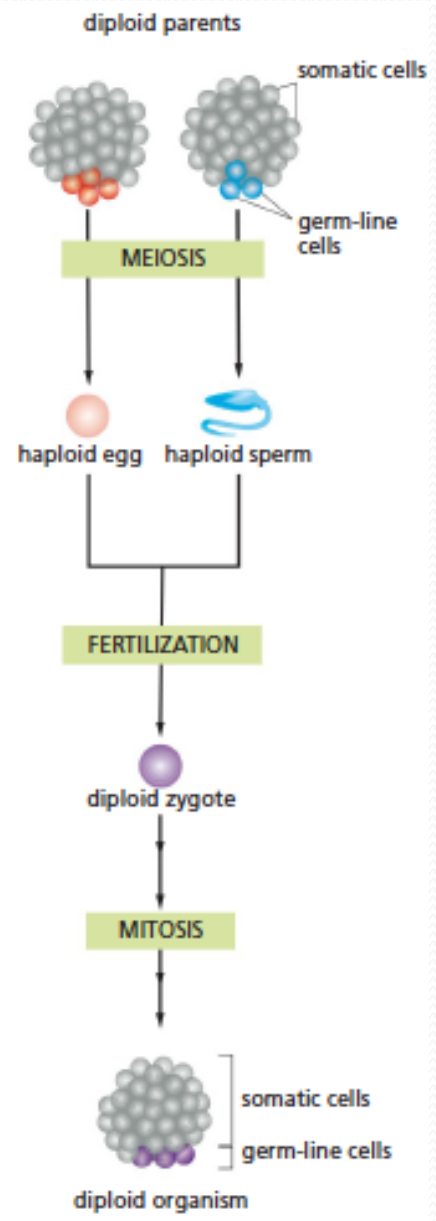


- Unlike the majority of cells in a diploid organism, however, the specialized cells that perform the central process in sexual reproduction—the germ cells, or gametes—are haploid: they each contain only one set of chromosomes.
- For most organisms, the males and females produce different types of gametes. In animals, one is large and nonmotile and is referred to as the egg; the other is small and motile and is referred toas the sperm.
- These two dissimilar haploid gametes join together to regenerate a diploid cell, called the fertilized egg, or ***zygote***, which has chromosomes from both the mother and father.
- The zygote thus produced develops into a new individual with a diploid set of chromosomes that is distinct from that of either parent.



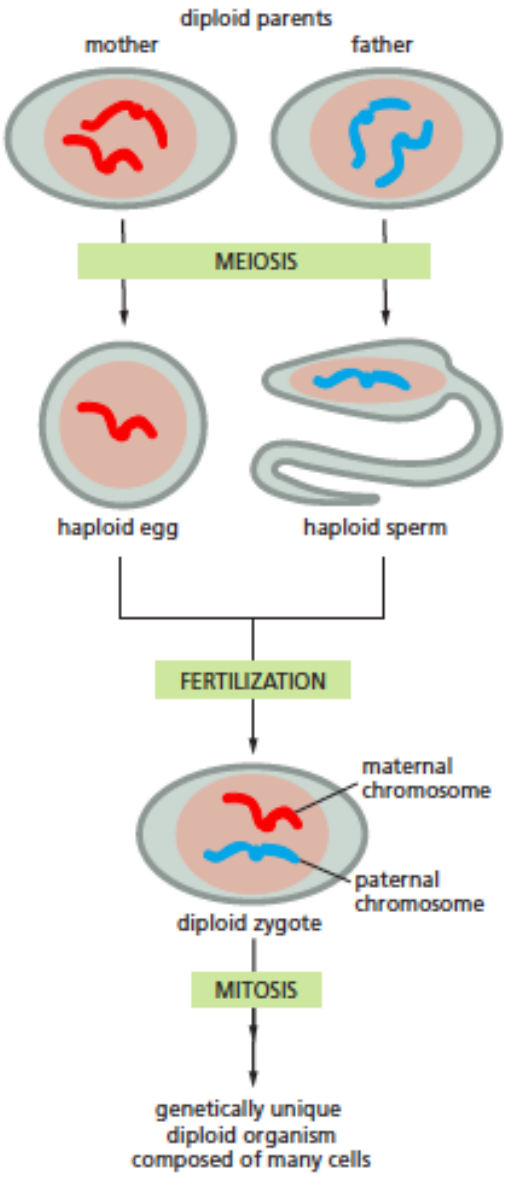


- These haploid gametes are generated from diploid precursor cells by a specialized form of reductive division called meiosis.
- This precursor cell lineage, which is dedicated solely to the production of germ cells, is called the germ line.
- The cells forming the rest of the animal's body—the somatic cells—ultimately leave no progeny of their own.
- They exist, in effect, only to help the cells of the germ line survive and propagate.

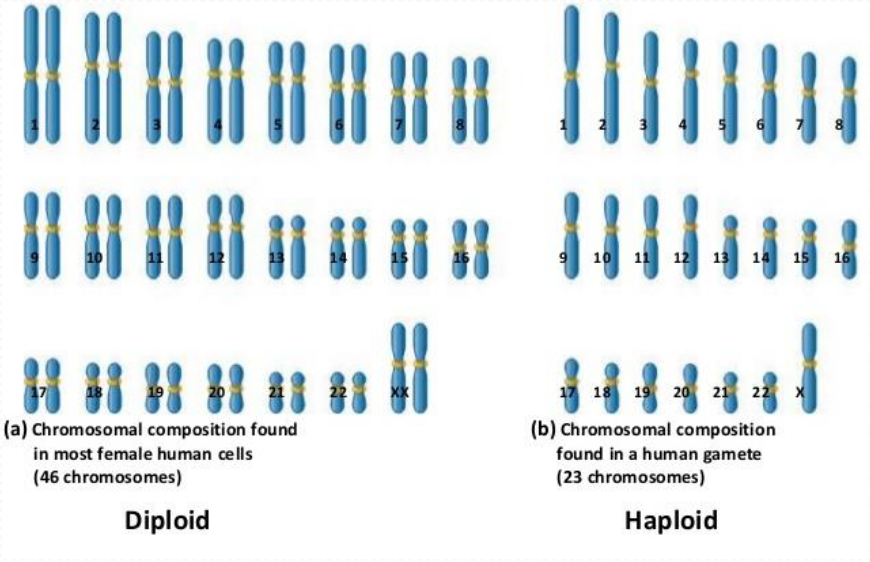


Benefits of Sex

- The sexual reproductive cycle thus involves an alternation of haploid cells, each carrying a single set of chromosomes, with generations of diploid cells, each carrying two sets of chromosomes.
- One benefit of this arrangement is that it allows sexually reproducing organisms to produce offspring that are genetically diverse.



- Sexual reproduction produces novel chromosome combinations. During meiosis, the maternal and paternal chromosome sets present in diploid germ-line cells are partitioned out into the single chromosome sets of the gametes.
- Each gamete will receive a mixture of maternal homologs and paternal homologs; when the genomes of two gametes combine during fertilization, they produce a zygote with a unique chromosomal complement.



- Although maternal and paternal chromosomes contain the same set of genes, genes occur in variant versions, called ***alleles.***
- What makes individuals within a species genetically unique is the inheritance of different combinations of alleles. And with its cycles of diploidy, meiosis, haploidy, and cell fusion, sex breaks up old combinations of alleles and generates new ones.
- Sexual reproduction also generates genetic diversity through a second mechanism—***genetic recombination.***

Benefits of Sexual Reproduction

Different homolog chromosome combinations

Genetic Recombination

Evolutionary Advantages of Sexual Reproduction

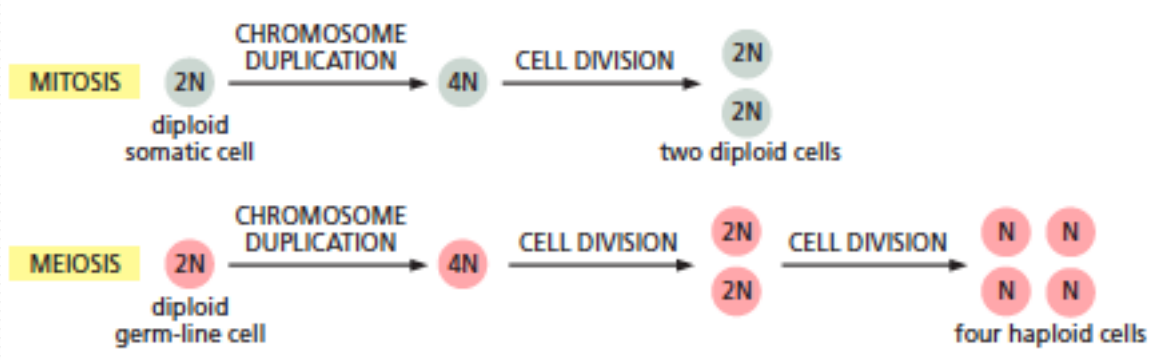
- The processes that generate genetic diversity during meiosis operate at random, as we will shortly discuss.
- That means that the alleles an individual receives from its parents are as likely to represent a change for the worse as they are a change for the better. One advantage seems to be that reshuffling genetic information through sexual reproduction can help a species survive in an unpredictably variable environment.
- If two parents produce many offspring with a wide variety of gene combinations, they increase the odds that at least one of their progeny will have a combination of features necessary for survival in a variety of environmental conditions.
- They are more likely, for example, to survive infections by bacteria, viruses, and parasites, which themselves continually change in a never-ending evolutionary battle.
- This genetic gamble may explain why even unicellular organisms, such as yeasts, intermittently indulge in a simple form of sexual reproduction.
- Typically, they switch on this behavior as an alternative to ordinary cell division when times are hard and starvation looms. Yeasts with a genetic defect that makes them unable to reproduce sexually show a reduced ability to evolve and adapt when they are subjected to harsh conditions.

- Sexual reproduction may also be advantageous for another reason. In any population, new mutations continually occur, giving rise to new alleles— and many of these new mutations may be harmful.
- Sexual reproduction can speed up the elimination of these deleterious alleles and help to prevent them from accumulating in the population.
- By mating with only the fittest males, females select for good combinations of alleles and allow bad combinations to be lost from the population more efficiently than they would otherwise be.
- According to this theory, which is supported by some careful calculations of costs and benefits, sexual reproduction is favored because males can serve as a genetic filtering device: the males who succeed in mating allow the best, and only the best, collections of genes to be passed on, whereas males who fail to mate serve as a genetic "trash can"—a way of discarding bad collections of alleles from the population.
- Whatever its advantages, sex has clearly been favored by evolution.

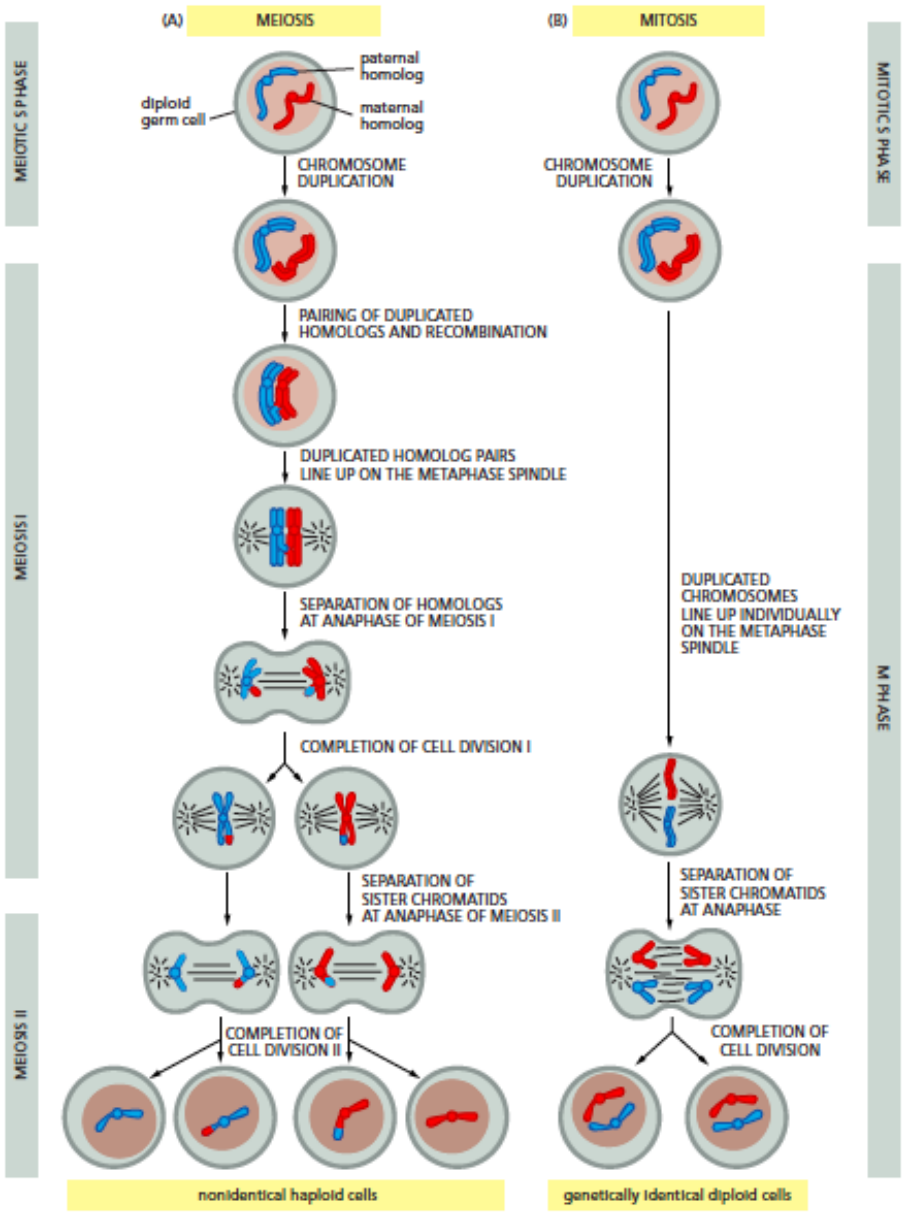
Meiosis

- Gametes are haploid—they carry only a single set of chromosomes.
- All of the other cells of the body, including the germ-line cells that give rise to the gametes, are diploid—they carry two sets of chromosomes, one derived from the mother and the other from the father.
- Therefore, sperm and eggs must be produced by a special kind of "reductive" cell division in which the number of chromosomes is precisely halved.
- This type of cell division is called meiosis.

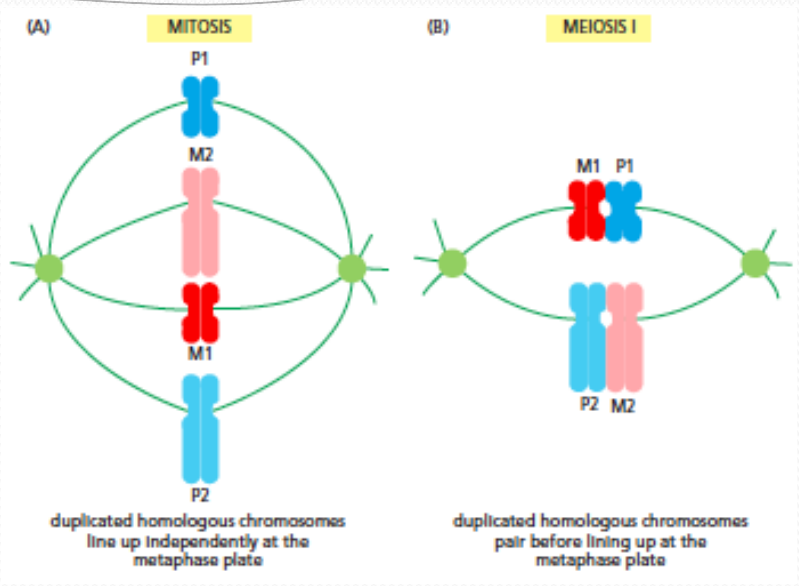
- Before a diploid cell divides by mitosis, it duplicates its two sets of chromosomes. This duplication allows a full set of chromosomes—including a complete maternal set plus a complete paternal set—to be transmitted to each daughter cell.
- Although meiosis ultimately halves this diploid chromosome complement—producing haploid gametes that carry only a single set of chromosomes—it, too, begins with a round of chromosome duplication.
- The subsequent reduction in chromosome number occurs because this single round of duplication is followed by two successive cell divisions without further DNA replication.

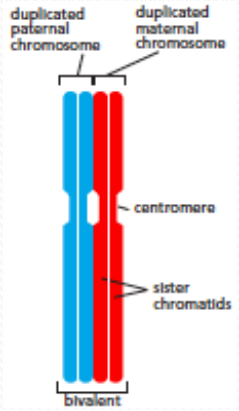


- Together, the two successive meiotic cell divisions, called meiotic division I (meiosis I) and meiotic division II (meiosis II), parcel out one complete set of chromosomes to each of the four haploid cells produced.
- Because the assignment of each homolog to the haploid daughter cells is random, each of the resulting gametes will receive a different mixture of maternal and paternal chromosomes.
- Thus, meiosis produces four cells that are genetically dissimilar and that contain exactly half as many chromosomes as the original parent germline cell.
- Mitosis, in contrast, produces two genetically identical daughter cells.



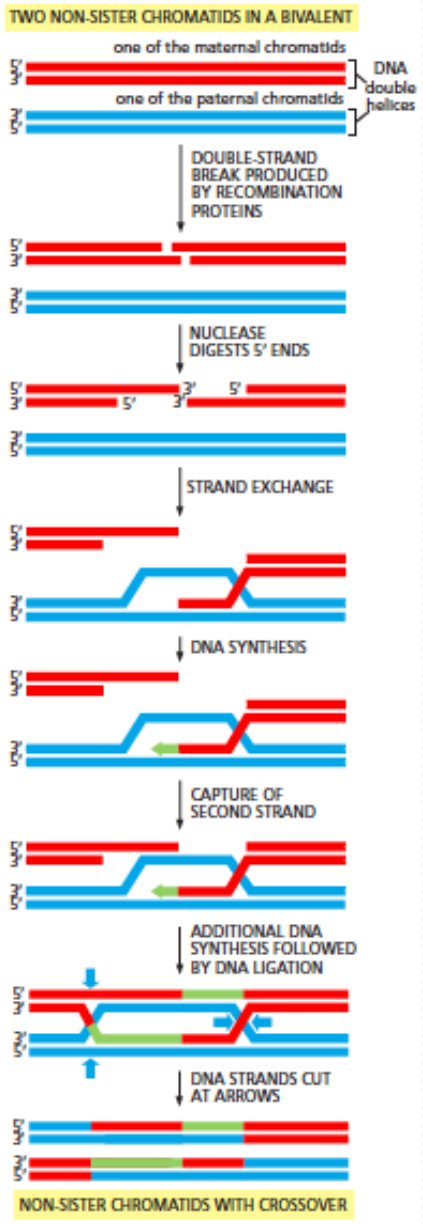
- In meiosis, to ensure that each of the four haploid cells produced by meiosis will receive a single sister chromatid from each chromosome set, a germ-line cell must keep track of both the maternal and paternal homologous chromosomes (homologs). It does so by pairing the duplicated homologs before they line up at the metaphase plate.
- Each pairing forms a structure called a bivalent, in which all four sister chromatids stick together until the cell is ready to divide.
- The maternal and paternal homologs will separate during meiotic division I, and the individual sister chromatids will separate during meiotic division II.



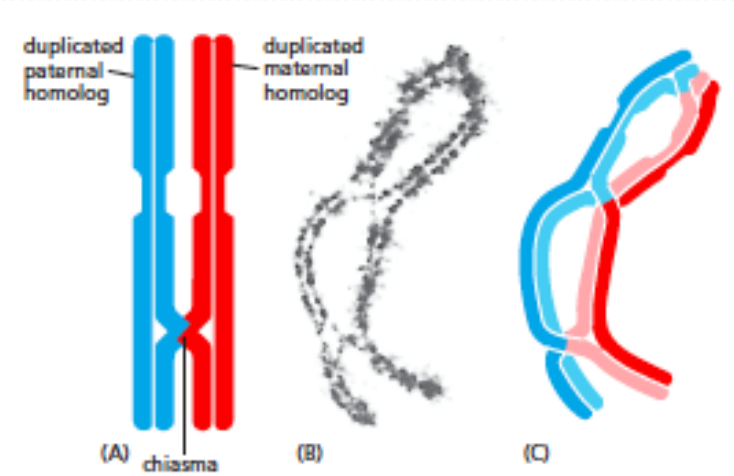


Pairing ensures that the homologs will segregate properly during the two subsequent cell divisions and that each of the final gametes will receive a complete haploid set of chromosomes.

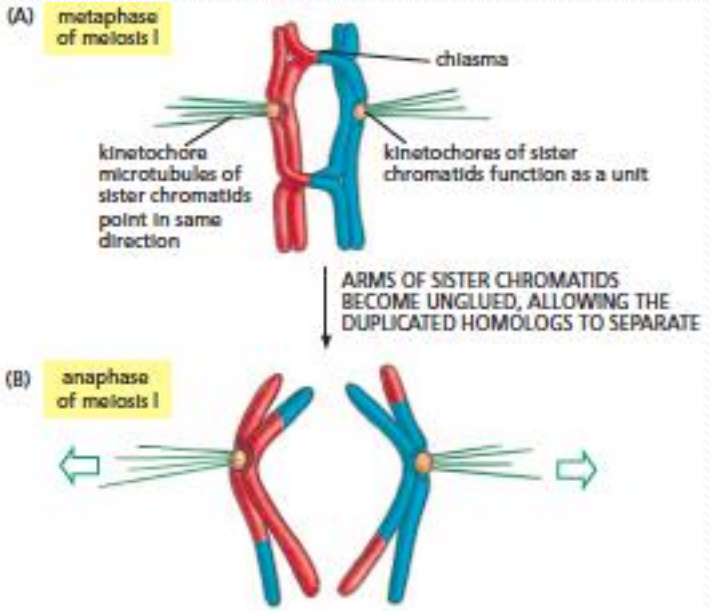
- In sexually reproducing organisms, the pairing of the maternal and paternal chromosomes is accompanied by ***homologous recombination***, a process in which two identical or very similar nucleotide sequences exchange genetic information.
- The recombination occurs between the non-sister chromatids in each bivalent.
- As a result, the maternal and paternal homologs end up physically swapping homologous chromosomal segments in a complex, multistep process called crossing-over.



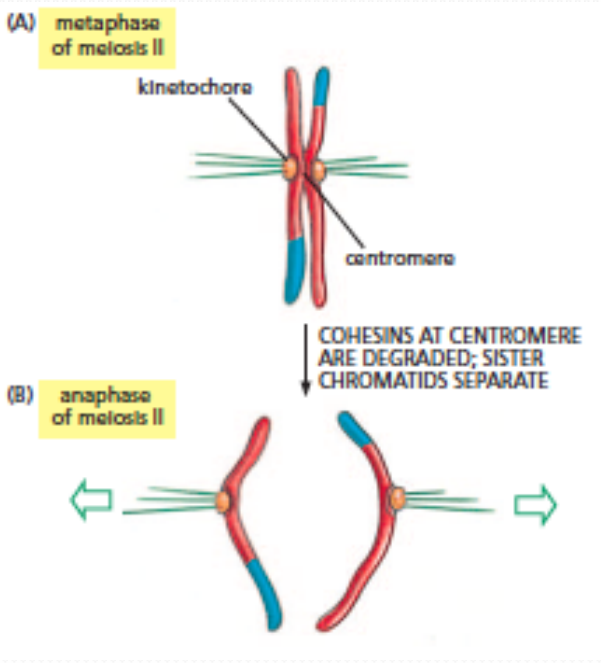
- The point of contact, the physical link, between two (non-sister) chromatids belonging to homologous chromosomes during crossing over is called ***chiasma.***
- Each chiasma corresponds to a crossover between two non-sister chromatids bivalents contain more than one chiasma, indicating that multiple crossovers occur between homologous chromosomes human oocytes—the cells that give rise to the egg—an average of two to three crossover events occur within each bivalent.



- Crossovers that occur during meiosis are a major source of genetic variation in sexually reproducing species. By scrambling the genetic constitution of each of the chromosomes in the gamete, crossing-over helps to produce individuals with novel assortments of alleles.
- Crossing-over also has a second important role in meiosis. By holding homologous chromosomes together during prophase I, the chiasmata help ensure that the maternal and paternal homologs will segregate from one another correctly at the first meiotic division.
- Thus during meiosis I homolog chromosomes are segregated to different daughter cells.

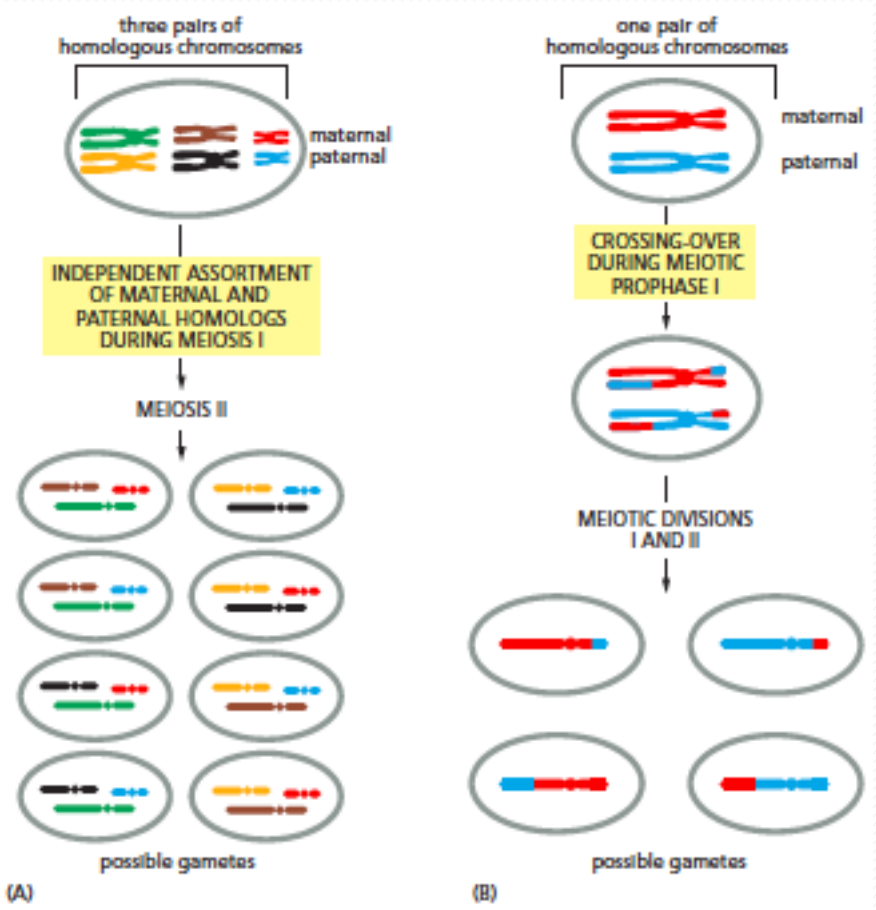


- In meiosis II, a second round of division occurs without further DNA replication or any significant interphase period to separate the sister chromatids and produce cells with a haploid amount of DNA.
- A meiotic spindle forms, and the kinetochores on each pair of sister chromatids now attach to kinetochore microtubules that point in opposite directions, as they would in an ordinary mitotic division.
- At anaphase of meiosis II, the remaining, meiosis-specific cohesins—located in the centromere—are degraded, and the sister chromatids are drawn into different daughter cells.



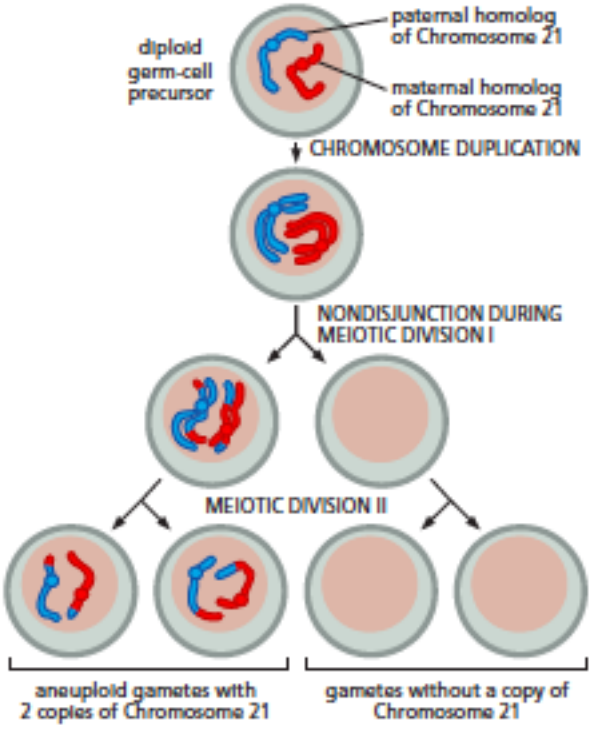
- Even though they share the same parents, no two siblings are genetically the same (unless they are identical twins).
- These genetic differences are initiated long before sperm meets egg, when meiosis I produces two kinds of randomizing genetic reassortment.
- First, as we have seen, the maternal and paternal chromosomes are shuffled and dealt out randomly during meiosis I. Although the chromosomes are carefully distributed so that each cell receives one and only one copy of each chromosome, the choice between the maternal or paternal homolog is made by chance, like the flip of a coin.
- Thus, each gamete contains the maternal versions of some chromosomes and the paternal versions of others.

- Thanks to this random reassortment of maternal and paternal homologs, an individual could in principle produce 2^n genetically different gametes, where n is the haploid number of chromosomes.
- With 23 chromosomes to choose from, each human, for example, could in theory produce 2^{23}—or 8.4×10^6—genetically distinct gametes.
- The actual number of different gametes each person can produce, however, is much greater than that, because the crossing-over that takes place during meiosis provides a second source of randomized genetic reassortment.
- Between two and three crossovers occur on average between each pair of human homologs, generating new chromosomes with novel assortments of maternal and paternal alleles.
- Because crossing-over occurs at more or less random sites along the length of a chromosome, each meiosis will produce four sets of entirely novel chromosomes.



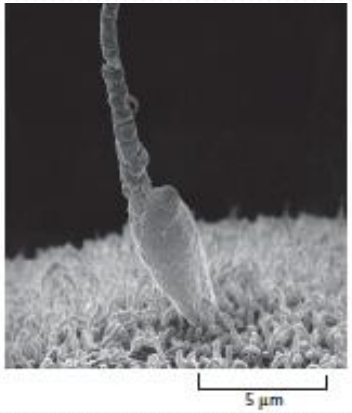
- Taken together, the random reassortment of maternal and paternal chromosomes, coupled with the genetic mixing of crossing-over, provides a nearly limitless source of genetic variation in the gametes produced by a single individual.
- Considering that every person is formed by the fusion of such gametes, produced by two completely different individuals, the richness of human variation that we see around us, even within a single family, is not at all surprising.

- Occasionally, homologs fail to separate properly—a phenomenon known as nondisjunction. As a result, some of the haploid cells that are produced lack a particular chromosome, while others have more than one copy of it.
- Upon fertilization, such gametes form abnormal embryos, most of which die. Some survive, however. Down syndrome, for example—a disorder associated with cognitive disability and characteristic physical abnormalities—is caused by an extra copy of Chromosome 21.
- This error results from nondisjunction of a Chromosome 21 pair during meiosis I, giving rise to a gamete that contains two copies of that chromosome instead of one.
- When this abnormal gamete fuses with a normal gamete at fertilization, the resulting embryo contains three copies of Chromosome 21 instead of two. This chromosome imbalance produces an extra dose of the proteins encoded by Chromosome 21 and thereby interferes with the proper development of the embryo and normal functions in the adult.



Fertilization

- Haploid gametes reunite in the process of fertilization to form a new zygote with a diploid set of chromosomes.
- Of the 300 million human sperm ejaculated during coitus, only about 200 reach the site of fertilization in the oviduct. Sperm are attracted to an ovulated egg by chemical signals released by both the egg and the supporting cells that surround it.
- Once a sperm finds the egg, it must migrate through a protective layer of cells and then bind to, an tunnel through, the egg coat, called the zona pellucida. Finally, the sperm must bind to and fuse with the underlying egg plasma membrane.



- Although many sperm may bind to an egg, only one normally fuses with the egg plasma membrane and introduces its DNA into the egg cytoplasm.
- The control of this step is especially important because it ensures that the fertilized egg—also called a zygote—will contain two, and only two, sets of chromosomes.
- Several mechanisms prevent multiple sperm from entering an egg. In one mechanism, the first successful sperm triggers the release of a wave of Ca^{2+} ions in the egg cytoplasm. This flood of Ca^{2+} in turn triggers the secretion of enzymes that cause a “hardening” of the zona pellucida, which prevents “runner up” sperm from penetrating the egg.

- The process of fertilization is not complete, however, until the two haploid nuclei (called pronuclei) come together and combine their chromosomes into a single diploid nucleus.
- Soon after the pronuclei fuse, the diploid cell begins to divide, forming a ball of cells that—through repeated rounds of cell division and differentiation—will give rise to an embryo and, eventually, an adult organism.
- Fertilization marks the beginning of one of the most remarkable phenomena in all of biology—the process by which a single-celled zygote initiates the developmental program that directs the formation of a new individual.

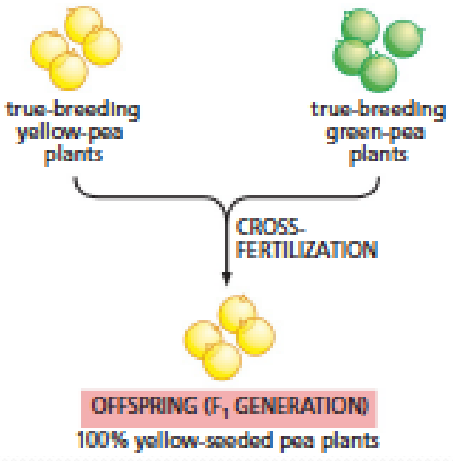
Mendel and the Laws of Inheritance

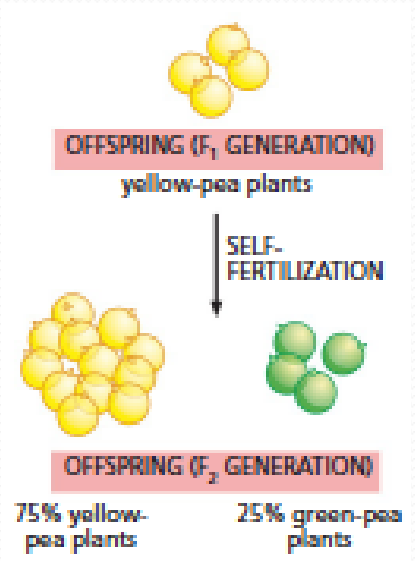
- Mendel, breeding peas in his monastery garden, discovered the laws of inheritance more than 150 years ago.
- Mendel chose to study pea plants because they are easy to cultivate in large numbers and could be raised in a small space—such as an abbey garden. He controlled which plants mated with which by removing sperm (pollen) from one plant and brushing it onto the female structures of another.
- This careful cross-pollination ensured that Mendel could be certain of the parentage of every pea plant he examined.
- Perhaps more important for Mendel's purposes, pea plants were available in many varieties. For example, one variety has purple flowers, another has white.
- One variety produces seeds (peas) with smooth skin, another produces peas that are wrinkled. Mendel chose to follow seven traits—such as flower color and pea shape—that were distinct, easily observable, and, most importantly, inherited in a discrete fashion: for example, the plants have either purple flowers or white flowers—nothing in between.

	pea shape	pea color	flower color	flower position	pod shape	pod color	plant height
one form of trait (dominant)	 round (*R*)	 yellow (*Y*)	 purple	 axial flowers	 inflated	 green	 tall
a second form of trait (recessive)	 wrinkled (*r*)	 green (*y*)	 white	 terminal flowers	 pinched	 yellow	 short

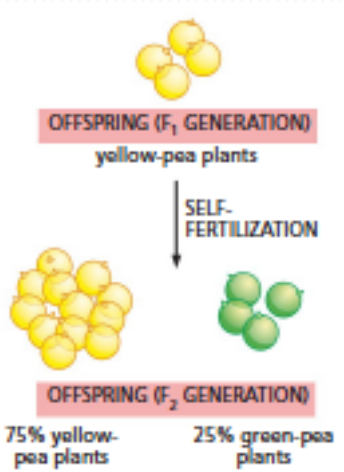
- The breeding experiments that Mendel performed were straightforward.
- He started with stocks of genetically pure, “true-breeding” plants—those that produce offspring of the same variety when allowed to self-fertilize.
- If he followed pea color, for example, he used plants with yellow peas that always produced offspring with yellow peas, and plants with green peas that always produced offspring with green peas.
- Mendel’s predecessors had focused on organisms that varied in multiple traits.
- These investigators often wound up trying to characterize offspring whose appearance differed in such a complex way that they could not easily be compared with their parents.
- But Mendel took the unique approach of studying each trait one at a time. In a typical experiment, he would cross-pollinate two of his true-breeding varieties. He then recorded the inheritance of the chosen trait in the next generation.

- For example, Mendel crossed plants producing yellow peas with plants producing green peas and discovered that the resulting hybrid offspring, called the first filial, or F1, generation, all had yellow peas
- He obtained a similar result for every trait he followed: the F1 hybrids all resembled only one of their two parents.
- Had Mendel stopped there—observing only the F1 generation—he might have developed some mistaken ideas about the nature of heredity: these results appear to support the theory of uniparental inheritance, which states that the appearance of the offspring will match one parent or the other.
- Fortunately, Mendel took his breeding experiments to the next step: he crossed the F1 plants with one another (or allowed them to self-fertilize) and examined the results.





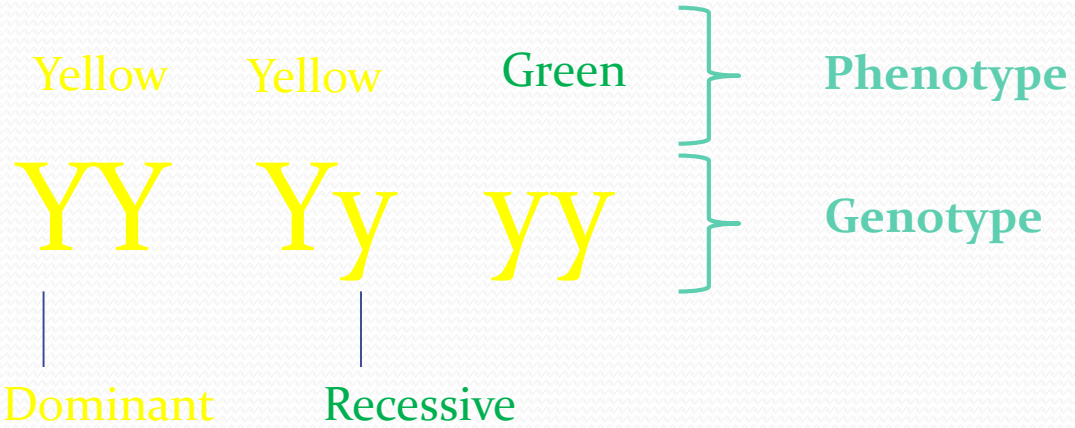
- One look at the offspring of Mendel's initial cross-fertilization experiments, raises an obvious question: what happened to the traits that disappeared in the F1 generation? Did the plants bearing green peas, for example, fail to make a genetic contribution to their offspring? To find out, Mendel allowed the F1 plants to self-fertilize.
- If the trait for green peas had been lost, then the F1 plants would produce only plants with yellow peas in the next, F2, generation.
- Instead, he found that the "disappearing trait" returned: although three quarters of the offspring in the F2 generation had yellow peas, one-quarter had green peas.
- Mendel saw the same type of behavior for each of the other six traits he examined.



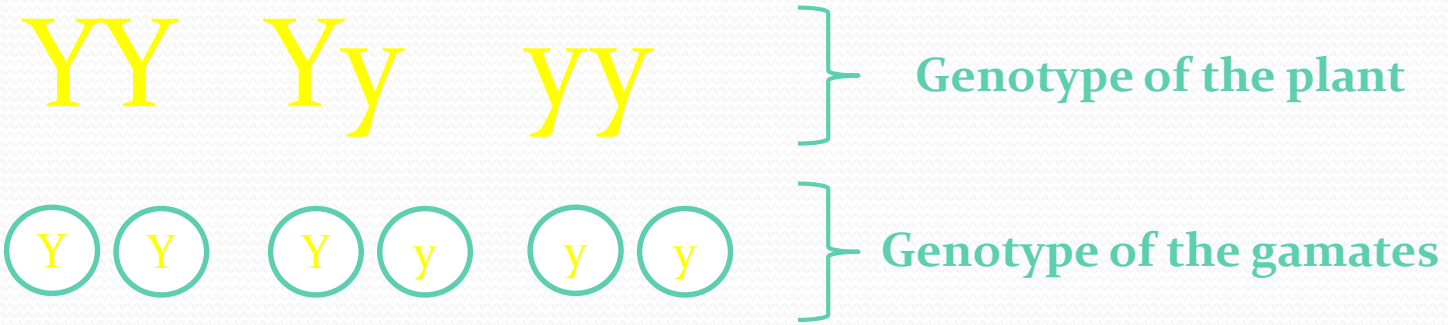
- To account for these observations, Mendel proposed that the inheritance of traits is governed by hereditary factors (which we now call genes) and that these factors come in alternative versions that account for the variations seen in inherited characteristics.
- The gene dictating pea color, for example, exists in two "flavors"—one that directs the production of yellow peas and one that directs production of green peas.
- Such alternative versions of a gene are now called alleles, and the whole collection of alleles possessed by an individual—its genetic makeup—is called its ***genotype.***

YY Yy yy

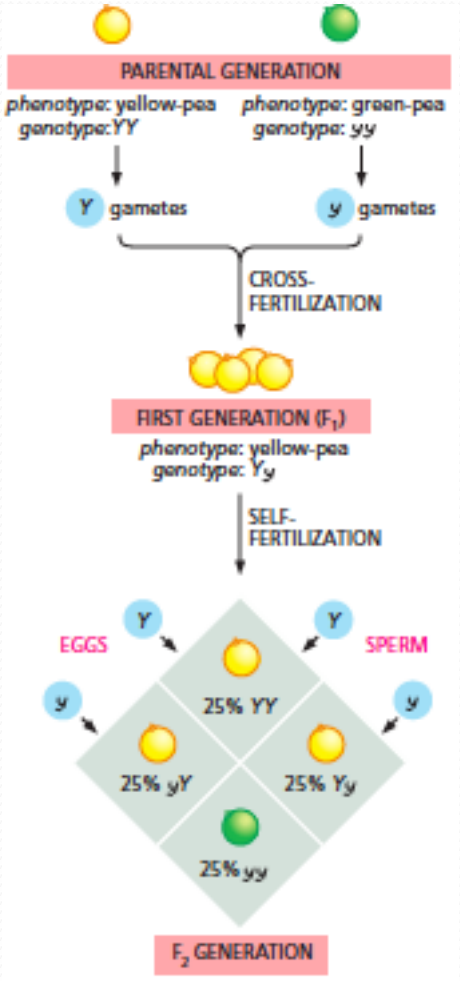
- Mendel's major conceptual breakthrough was to propose that for each characteristic, an organism must inherit two copies, or alleles, of each gene—one from its mother and one from its father.
- The true-breeding parental strains, he theorized, each possessed a pair of identical alleles—the yellow-pea plants possessed two alleles for yellow peas, the green-pea plant two alleles for green peas. An individual that possesses two identical alleles is said to be homozygous for that trait.
- The F1 hybrid plants, on the other hand, had received two dissimilar alleles—one specifying yellow peas and the other green. These plants were heterozygous for the trait of interest.
- The appearance, or phenotype, of the organism depends on which versions of each allele it inherits.
- To explain the disappearance of a trait in the F1 generation—and its reappearance in the F2 generation—Mendel supposed that for any pair of alleles, one allele is ***dominant*** and the other is ***recessive***, or hidden.
- The dominant allele, whenever it is present, would dictate the plant's phenotype. In the case of pea color, the allele that specifies yellow peas is dominant; the green-pea allele is ***recessive.***

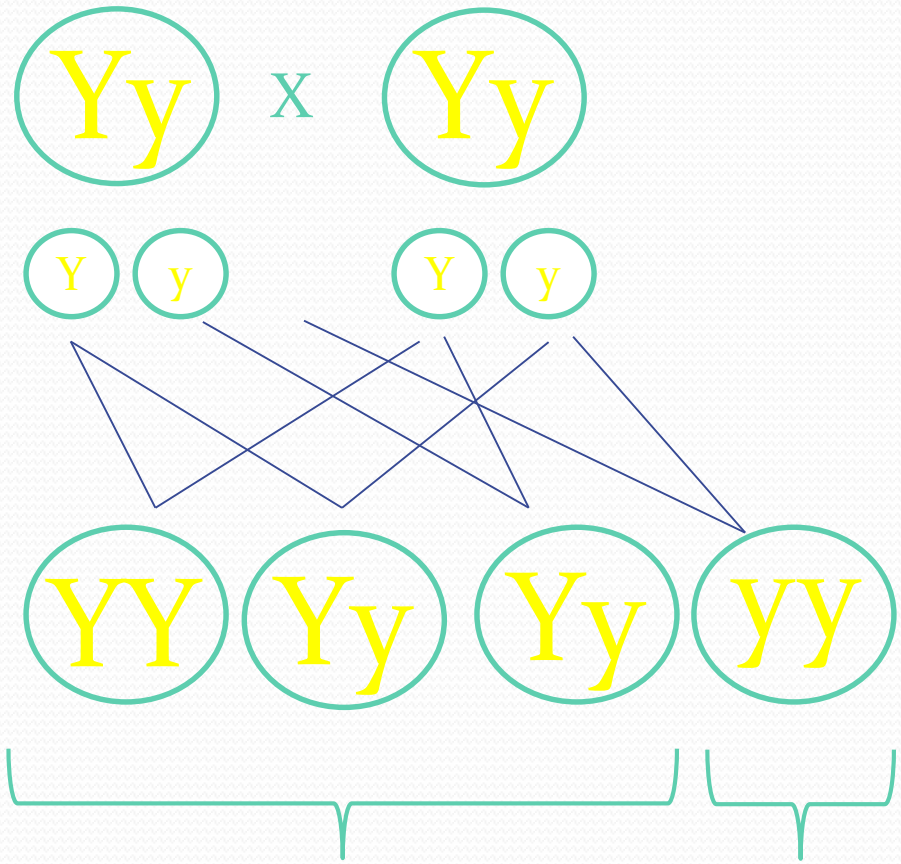


- Mendel's theory—that for every gene, an individual inherits one copy from its mother and one copy from its father—raised some logistical issues. If an organism has two copies of every gene, how does it pass only one copy of each to its progeny? And how do these gene sets come together again in the resulting offspring?
- Mendel postulated that when sperm and eggs are formed, the two copies of each gene present in the parent separate so that each gamete receives only one allele for each trait. For his pea plants, each egg (ovum) and each sperm (pollen) receives only one allele for pea color (either yellow or green), one allele for pea shape (smooth or wrinkled), one allele for flower color (purple or white), and so on. During fertilization, sperm carrying one or other allele unites with an egg carrying one or other allele to produce a fertilized egg or zygote with two alleles. Which type of sperm unites with which type of egg at fertilization is entirely a matter of chance.

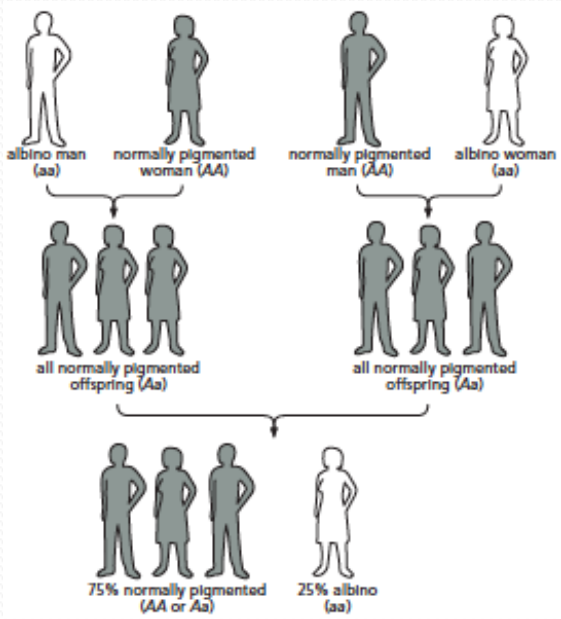


- **This principle of heredity is laid out in Mendel's first law, the law of segregation.**
- It states that the two alleles for each trait separate (or segregate) during gamete formation and then unite at random—one from each parent—at fertilization. According to this law, the F1 hybrid plants with yellow peas will produce two classes of gametes: half the gametes will get a yellow-pea allele and half will get a green-pea allele. When the hybrid plants self-pollinate, these two classes of gametes will unite at random.
- Thus, four different combinations of alleles can come together in the F2 offspring.
  - One-quarter of the F2 plants will receive two alleles specifying green peas; these plants will obviously produce green peas.
  - One-quarter of the plants will receive two yellow-pea alleles and will produce yellow peas.
  - But one-half of the plants will inherit one allele for yellow peas and one allele for green. Because the yellow allele is dominant, these plants—like their heterozygous F1 parents—will all produce yellow peas.
  - All told, three-quarters of the offspring will have yellow peas and one-quarter will have green peas. Thus Mendel's law of segregation explains the 3:1 ratio that he observed in the F2 generation.

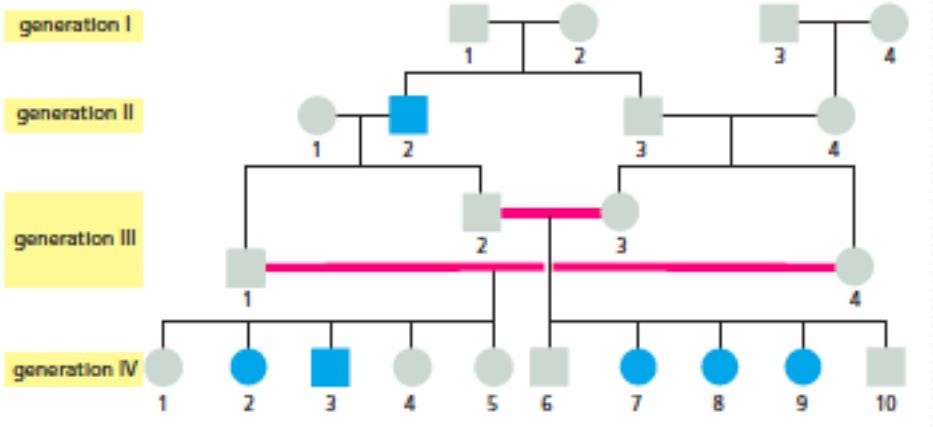



Yy
x
Yy
Y
y
Y
y
YY
Yy
Yy
yy
Yellow
75%
Green
25%

- Mendel's law of segregation applies to all sexually reproducing organisms.
- Consider a phenotype in humans that reflects the action of a single gene. The major form of albinism—Type II albinism—is a rare condition that is inherited in a recessive manner in many animals, including humans.
- Like the pea plants that produce green seeds, albinos are homozygous recessive: their genotype is aa. The dominant allele of the gene (denoted A) encodes an enzyme involved in making melanin, the pigment responsible for most of the brown and black color present in hair, skin, and the retina of the eye.
- Because the recessive allele codes for a version of this enzyme that is only weakly active or completely inactive, albinos have white hair, white skin, and pupils that look pink because a lack of melanin in the eye allows the red color of the hemoglobin in blood vessels in the retina to be visible.
- The trait for albinism is inherited in the same manner as any other recessive trait, including Mendel's green peas. If a Type II albino man (genotype aa) has children with a Type II albino woman (also aa), all of their children will be albino (aa). However, if a nonalbino man (AA) marries and has children with an albino woman (aa), their children will all be heterozygous (Aa) and normally pigmented (Figure 19–25). If two nonalbino individuals with an Aa genotype start a family, each of their children would have a 25% chance of being an albino (aa).



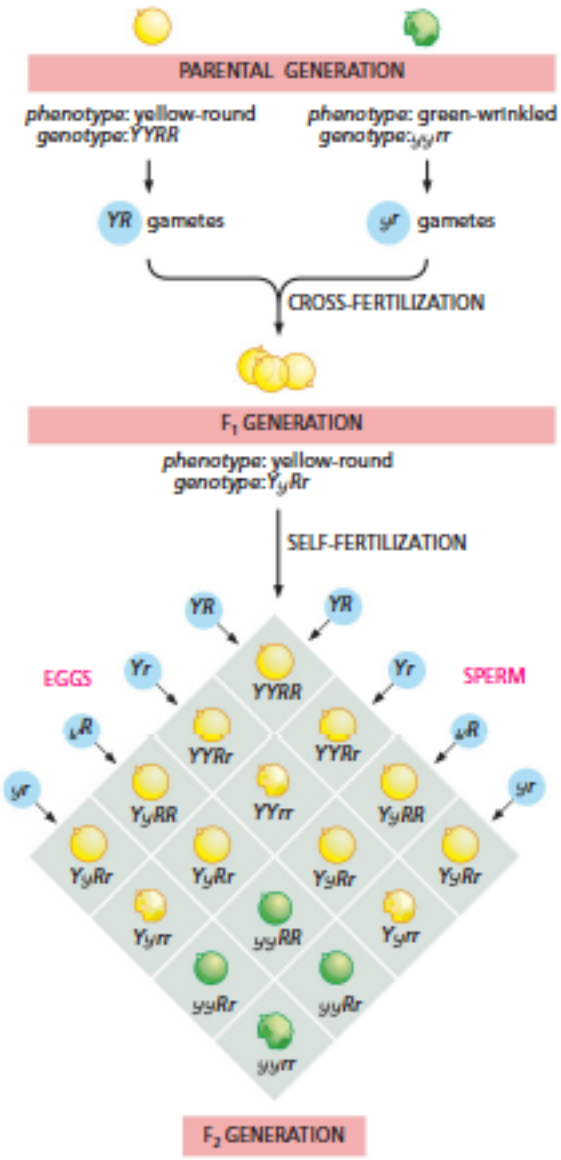
- Of course, humans generally don't have families large enough to guarantee accurate Mendelian ratios. (Mendel arrived at his ratios by breeding and counting thousands of pea plants for most of his crosses.)
- Geneticists that follow the inheritance of specific traits in humans get around this problem by working with large numbers of families—or with several generations of a few large families—and preparing pedigrees that show th phenotype of each family member for the relevant trait.



- **A pedigree shows the risks of first-cousin marriages: Shown here is an actual pedigree for a family that harbors a rare recessive mutation causing deafness.**
- According to convention, squares represent males, circles are females. Here, family members that show the deaf phenotype are indicated by a blue symbol, those that do not by a gray symbol.
- A black horizontal line connecting a male and female represents a mating between unrelated individuals, and a red horizontal line represents a mating between blood relatives.
- The offspring of each mating are shown underneath, in order of their birth from left to right. Individuals within each generation are labeled sequentially from left to right for purposes of identification.
- In the third generation in this pedigree, for example, individual 2, a man who is not deaf, marries his first cousin, individual 3, who is also not deaf. Three out of their five children (individuals 7, 8, and 9 in the fourth generation) are deaf.
- Meanwhile, individual 1, the brother of 2, also marries a first cousin, individual 4, the sister of 3. Two out of their five children are deaf.

- Mendel deliberately simplified the problem of heredity by starting with breeding experiments that focused on the inheritance of one trait at a time, called monohybrid crosses.
- He then turned his attention to multihybrid crosses, examining the simultaneous inheritance of two or more apparently unrelated traits.
- Mendel started with true-breeding parental strains: the dominant strain produced yellow round peas (its genotype is YYRR), the recessive strain produced green wrinkled peas (yyrr).
- The F1 generation of plants all showed the expected phenotype: each produced peas that were yellow and round.
- But this result would ocur whether or not the parental alleles were linked.
- When the F1 plants were then allowed to self-fertilize, the results were clear: the two alleles for seed color segregated independently from the two alleles for seed shape, producing four different pea phenotypes: yellow-round, yellow-wrinkled, green-round, and green-wrinkled.

- Mendel tried his seven pea characters in various pairwise combinations and always observed a characteristic 9:3:3:1 phenotypic ratio in the F2 generation.
- **The independent segregation of each pair of alleles during gamete formation is Mendel's second law—the law of independent assortment.**



- Mendel's "factors"—the things we call genes—are carried on chromosomes that are parceled out during the formation of gametes and then brought together in novel combinations in the zygote at fertilization.
- Together, the meiotic mechanisms that distribute the alleles into gametes and the combining of gametes at fertilization provide the physical foundation for Mendel's law of segregation.
- Because each pair of duplicated homologs attaches to the spindle and lines up at the metaphase plate independently during meiosis, each gamete will inherit a random mixture of paternal and maternal chromosomes.
- Thus the alleles of genes on different chromosomes will segregate independently obeying Mendel's rule of independent assortment.

- However, what about the genes on the same chromosomes? Are they segregated together all the time?
- No, if two genes are far enough away from each other on the same chromosome, they will also sort independently, because of the crossingover that occurs during meiosis.
- If they are not far enough from each other they can not make crossover so that the genes are segregated together. Those genes are called linked genes.