

Chapter 14

Mendel and the Gene Idea

Lecture Outline

Overview

- Every day we observe heritable variations (such as brown, green, or blue eyes) among individuals in a population.
- These traits are transmitted from parents to offspring.
- One possible explanation for heredity is a “blending” hypothesis.
 - This hypothesis proposes that genetic material contributed by each parent mixes in a manner analogous to the way blue and yellow paints blend to make green.
 - With blending inheritance, a freely mating population will eventually give rise to a uniform population of individuals.
 - Everyday observations and the results of breeding experiments tell us that heritable traits do not blend to become uniform.
- An alternative model, “particulate” inheritance, proposes that parents pass on discrete heritable units, genes, that retain their separate identities in offspring.
 - Genes can be sorted and passed on, generation after generation, in undiluted form.
- Modern genetics began in an abbey garden, where a monk named Gregor Mendel documented a particulate mechanism of inheritance.

A. Gregor Mendel’s Discoveries

1. Mendel brought an experimental and quantitative approach to genetics.

- Mendel discovered the basic principles of heredity by breeding garden peas in carefully planned experiments.
- Mendel grew up on a small farm in what is today the Czech Republic.
- In 1843, Mendel entered an Augustinian monastery.
- He studied at the University of Vienna from 1851 to 1853, where he was influenced by a physicist who encouraged experimentation and the application of mathematics to science and by a botanist who stimulated Mendel’s interest in the causes of variation in plants.
- These influences came together in Mendel’s experiments.
- After university, Mendel taught at the Brunn Modern School and lived in the local monastery.
- The monks at this monastery had a long tradition of interest in the breeding of plants, including peas.
- Around 1857, Mendel began breeding garden peas to study inheritance.
- Pea plants have several advantages for genetic study.

- Pea plants are available in many varieties with distinct heritable features, or **characters**, with different variant **traits**.
- Mendel could strictly control which plants mated with which.
- Each pea plant has male (stamens) and female (carpal) sexual organs.
- In nature, pea plants typically self-fertilize, fertilizing ova with the sperm nuclei from their own pollen.
- However, Mendel could also use pollen from another plant for cross-pollination.
- Mendel tracked only those characters that varied in an “either-or” manner, rather than a “more-or-less” manner.
 - For example, he worked with flowers that were either purple or white.
 - He avoided traits, such as seed weight, that varied on a continuum.
- Mendel started his experiments with varieties that were **true-breeding**.
 - When true-breeding plants self-pollinate, all their offspring have the same traits.
- In a typical breeding experiment, Mendel would cross-pollinate (**hybridize**) two contrasting, true-breeding pea varieties.
 - The true-breeding parents are the **P generation**, and their hybrid offspring are the **F₁ generation**.
- Mendel would then allow the F₁ hybrids to self-pollinate to produce an **F₂ generation**.
- It was mainly Mendel’s quantitative analysis of F₂ plants that revealed two fundamental principles of heredity: the law of segregation and the law of independent assortment.

2. By the law of segregation, the two alleles for a character are separated during the formation of gametes.

- If the blending model was correct, the F₁ hybrids from a cross between purple-flowered and white-flowered pea plants would have pale purple flowers.
- Instead, F₁ hybrids all have purple flowers, just as purple as their purple-flowered parents.
- When Mendel allowed the F₁ plants to self-fertilize, the F₂ generation included both purple-flowered and white-flowered plants.
 - The white trait, absent in the F₁, reappeared in the F₂.
- Mendel used very large sample sizes and kept accurate records of his results.
 - Mendel recorded 705 purple-flowered F₂ plants and 224 white-flowered F₂ plants.
 - This cross produced a traits ratio of three purple to one white in the F₂ offspring.
- Mendel reasoned that the heritable factor for white flowers was present in the F₁ plants, but did not affect flower color.
 - Purple flower color is a *dominant* trait, and white flower color is a *recessive* trait.
- The reappearance of white-flowered plants in the F₂ generation indicated that the heritable factor for the white trait was not diluted or “blended” by coexisting with the purple-flower factor in F₁ hybrids.
- Mendel found similar 3-to-1 ratios of two traits among F₂ offspring when he conducted crosses for six other characters, each represented by two different traits.
- For example, when Mendel crossed two true-breeding varieties, one producing round seeds and the other producing wrinkled seeds, all the F₁ offspring had round seeds.
 - In the F₂ plants, 75% of the seeds were round and 25% were wrinkled.

- Mendel developed a hypothesis to explain these results that consisted of four related ideas. We will explain each idea with the modern understanding of genes and chromosomes.
 1. *Alternative versions of genes account for variations in inherited characters.*
 - The gene for flower color in pea plants exists in two versions, one for purple flowers and one for white flowers.
 - These alternate versions are called **alleles**.
 - Each gene resides at a specific locus on a specific chromosome.
 - The DNA at that locus can vary in its sequence of nucleotides.
 - The purple-flower and white-flower alleles are two DNA variations at the flower-color locus.
 2. *For each character, an organism inherits two alleles, one from each parent.*
 - A diploid organism inherits one set of chromosomes from each parent.
 - Each diploid organism has a pair of homologous chromosomes and, therefore, two copies of each gene.
 - These homologous loci may be identical, as in the true-breeding plants of the P generation.
 - Alternatively, the two alleles may differ.
 3. *If the two alleles at a locus differ, then one, the dominant allele, determines the organism's appearance. The other, the recessive allele, has no noticeable effect on the organism's appearance.*
 - In the flower-color example, the F₁ plants inherited a purple-flower allele from one parent and a white-flower allele from the other.
 - They had purple flowers because the allele for that trait is dominant.
 4. **Mendel's law of segregation** states that the two alleles for a heritable character separate and segregate during gamete production and end up in different gametes.
 - This segregation of alleles corresponds to the distribution of homologous chromosomes to different gametes in meiosis.
 - If an organism has two identical alleles for a particular character, then that allele is present as a single copy in all gametes.
 - If different alleles are present, then 50% of the gametes will receive one allele and 50% will receive the other.
- Mendel's law of segregation accounts for the 3:1 ratio that he observed in the F₂ generation.
- The F₁ hybrids produce two classes of gametes, half with the purple-flower allele and half with the white-flower allele.
- During self-pollination, the gametes of these two classes unite randomly.
- This produces four equally likely combinations of sperm and ovum.
- A **Punnett square** predicts the results of a genetic cross between individuals of known genotype.
- Let us describe a Punnett square analysis of the flower-color example.
- We will use a capital letter to symbolize the dominant allele and a lowercase letter to symbolize the recessive allele.
 - *P* is the purple-flower allele, and *p* is the white-flower allele.
- What will be the physical appearance of the F₂ offspring?
 - One in four F₂ offspring will inherit two white-flower alleles and produce white flowers.

- Half of the F₂ offspring will inherit one white-flower allele and one purple-flower allele and produce purple flowers.
- One in four F₂ offspring will inherit two purple-flower alleles and produce purple flowers.
- Mendel's model accounts for the 3:1 ratio in the F₂ generation.
- An organism with two identical alleles for a character is **homozygous** for that character.
- Organisms with two different alleles for a character is **heterozygous** for that character.
- An organism's traits are called its **phenotype**.
- Its genetic makeup is called its **genotype**.
 - Two organisms can have the same phenotype but have different genotypes if one is homozygous dominant and the other is heterozygous.
- For flower color in peas, the only individuals with white flowers are those that are homozygous recessive (*pp*) for the flower-color gene.
- However, *PP* and *Pp* plants have the same phenotype (purple flowers) but different genotypes (homozygous dominant and heterozygous).
- How can we tell the genotype of an individual with the dominant phenotype?
 - The organism must have one dominant allele, but could be homozygous dominant or heterozygous.
- The answer is to carry out a **testcross**.
 - The mystery individual is bred with a homozygous recessive individual.
 - If any of the offspring display the recessive phenotype, the mystery parent must be heterozygous.

3. By the law of independent assortment, each pair of alleles segregates independently into gametes.

- Mendel's first experiments followed only a *single* character, such as flower color.
 - All F₁ progeny produced in these crosses were **monohybrids**, heterozygous for one character.
 - A cross between two heterozygotes is a *monohybrid cross*.
- Mendel identified the second law of inheritance by following *two* characters at the same time.
- In one such **dihybrid cross**, Mendel studied the inheritance of seed color and seed shape.
 - The allele for yellow seeds (*Y*) is dominant to the allele for green seeds (*y*).
 - The allele for round seeds (*R*) is dominant to the allele for wrinkled seeds (*r*).
- Mendel crossed true-breeding plants that had yellow, round seeds (*YYRR*) with true-breeding plants that has green, wrinkled seeds (*yyrr*).
- One possibility is that the two characters are transmitted from parents to offspring as a package.
 - The *Y* and *R* alleles and *y* and *r* alleles stay together.
- If this were the case, the F₁ offspring would produce yellow, round seeds.
- The F₂ offspring would produce two phenotypes (yellow + round; green + wrinkled) in a 3:1 ratio, just like a monohybrid cross.
 - This was not consistent with Mendel's results.

- An alternative hypothesis is that the two pairs of alleles segregate independently of each other.
 - The presence of a specific allele for one trait in a gamete has no impact on the presence of a specific allele for the second trait.
- In our example, the F₁ offspring would still produce yellow, round seeds.
- However, when the F₁s produced gametes, genes would be packaged into gametes with all possible allelic combinations.
 - Four classes of gametes (*YR*, *Yr*, *yR*, and *yr*) would be produced in equal amounts.
- When sperm with four classes of alleles and ova with four classes of alleles combined, there would be 16 equally probable ways in which the alleles can combine in the F₂ generation.
- These combinations produce four distinct phenotypes in a 9:3:3:1 ratio.
- This was consistent with Mendel's results.
- Mendel repeated the dihybrid cross experiment for other pairs of characters and always observed a 9:3:3:1 phenotypic ratio in the F₂ generation.
- Each character appeared to be inherited independently.
- If you follow just one character in these crosses, you will observe a 3:1 F₂ ratio, just as if this were a monohybrid cross.
- The independent assortment of each pair of alleles during gamete formation is now called Mendel's **law of independent assortment**.
- Mendel's law of independent assortment states that *each pair of alleles segregates independently during gamete formation*.
- Strictly speaking, this law applies only to genes located on different, nonhomologous chromosomes.
- Genes located near each other on the same chromosome tend to be inherited together and have more complex inheritance patterns than those predicted for the law of independent assortment.

4. The laws of probability govern Mendelian inheritance.

- Mendel's laws of segregation and independent assortment reflect the same laws of probability that apply to tossing coins or rolling dice.
- The probability scale ranges from 0 (an event with no chance of occurring) to 1 (an event that is certain to occur).
 - The probability of tossing heads with a normal coin is 1/2.
 - The probability of rolling a 3 with a six-sided die is 1/6, and the probability of rolling any other number is $1 - 1/6 = 5/6$.
- When tossing a coin, the outcome of one toss has no impact on the outcome of the next toss.
- Each toss is an independent event, just like the distribution of alleles into gametes.
 - Like a coin toss, each ovum from a heterozygous parent has a 1/2 chance of carrying the dominant allele and a 1/2 chance of carrying the recessive allele.
 - The same odds apply to the sperm.
- We can use the *multiplication rule* to determine the chance that two or more independent events will occur together in some specific combination.
 - Compute the probability of each independent event.

- Multiply the individual probabilities to obtain the overall probability of these events occurring together.
- The probability that two coins tossed at the same time will land heads up is $1/2 \times 1/2 = 1/4$.
- Similarly, the probability that a heterozygous pea plant (Pp) will self-fertilize to produce a white-flowered offspring (pp) is the chance that a sperm with a white allele will fertilize an ovum with a white allele.
- This probability is $1/2 \times 1/2 = 1/4$.
- The rule of multiplication also applies to dihybrid crosses.
 - For a heterozygous parent ($YyRr$) the probability of producing a YR gamete is $1/2 \times 1/2 = 1/4$.
 - We can use this to predict the probability of a particular F_2 genotype without constructing a 16-part Punnett square.
 - The probability that an F_2 plant from heterozygous parents will have a $YYRR$ genotype is $1/16$ ($1/4$ chance for a YR ovum and $1/4$ chance for a YR sperm).
- The rule of addition also applies to genetic problems.
- Under the *rule of addition*, the probability of an event that can occur two or more different ways is the sum of the separate probabilities of those ways.
 - For example, there are two ways that F_1 gametes can combine to form a heterozygote.
 - The dominant allele could come from the sperm and the recessive from the ovum (probability = $1/4$).
 - Or the dominant allele could come from the ovum and the recessive from the sperm (probability = $1/4$).
 - The probability of obtaining a heterozygote is $1/4 + 1/4 = 1/2$.
- We can combine the rules of multiplication and addition to solve complex problems in Mendelian genetics.
- Let's determine the probability of an offspring having two recessive phenotypes for at least two of three traits resulting from a trihybrid cross between pea plants that are $PpYyRr$ and $Ppyyrr$.
 - There are five possible genotypes that fulfill this condition: $ppyyRr$, $ppYyrr$, $Ppyyrr$, $PPyyrr$, and $ppyyrr$.
 - We can use the rule of multiplication to calculate the probability for each of these genotypes and then use the rule of addition to pool the probabilities for fulfilling the condition of at least two recessive traits.
- The probability of producing a $ppyyRr$ offspring:
 - The probability of producing $pp = 1/2 \times 1/2 = 1/4$.
 - The probability of producing $yy = 1/2 \times 1 = 1/2$.
 - The probability of producing $Rr = 1/2 \times 1 = 1/2$.
 - Therefore, the probability of all three being present ($ppyyRr$) in one offspring is $1/4 \times 1/2 \times 1/2 = 1/16$.
- For $ppYyrr$: $1/4 \times 1/2 \times 1/2 = 1/16$.
- For $Ppyyrr$: $1/2 \times 1/2 \times 1/2 = 1/8$ or $2/16$.
- For $PPyyrr$: $1/4 \times 1/2 \times 1/2 = 1/16$.
- For $ppyyrr$: $1/4 \times 1/2 \times 1/2 = 1/16$.

- Therefore, the chance that a given offspring will have at least two recessive traits is $1/16 + 2/16 + 1/16 + 1/16 = 6/16$.

5. Mendel discovered the particulate behavior of genes: a review.

- While we cannot predict with certainty the genotype or phenotype of any particular seed from the F₂ generation of a dihybrid cross, we can predict the probability that it will have a specific genotype or phenotype.
- Mendel's experiments succeeded because he counted so many offspring, was able to discern the statistical nature of inheritance, and had a keen sense of the rules of chance.
- Mendel's laws of independent assortment and segregation explain heritable variation in terms of alternative forms of genes that are passed along according to simple rules of probability.
- These laws apply not just to garden peas, but to all diploid organisms that reproduce by sexual reproduction.
- Mendel's studies of pea inheritance endure not only in genetics, but as a case study of the power of scientific reasoning using the hypothetico-deductive approach.

B. Extending Mendelian Genetics

1. The relationship between genotype and phenotype is rarely simple.

- In the 20th century, geneticists have extended Mendelian principles not only to diverse organisms, but also to patterns of inheritance more complex than Mendel described.
- In fact, Mendel had the good fortune to choose a system that was relatively simple genetically.
 - Each character that Mendel studied is controlled by a single gene.
 - Each gene has only two alleles, one of which is completely dominant to the other.
- The heterozygous F₁ offspring of Mendel's crosses always looked like one of the parental varieties because one allele was dominant to the other.
- The relationship between genotype and phenotype is rarely so simple.
- The inheritance of characters determined by a single gene deviates from simple Mendelian patterns when alleles are not completely dominant or recessive, when a gene has more than two alleles, or when a gene produces multiple phenotypes.
- We will consider examples of each of these situations.
- Alleles show different degrees of dominance and recessiveness in relation to each other.
- One extreme is the **complete dominance** characteristic of Mendel's crosses.
- At the other extreme from complete dominance is **codominance**, in which two alleles affect the phenotype in separate, distinguishable ways.
 - For example, the M, N, and MN blood groups of humans are due to the presence of two specific molecules on the surface of red blood cells.
 - People of group M (genotype MM) have one type of molecule on their red blood cells, people of group N (genotype NN) have the other type, and people of group MN (genotype MN) have both molecules present.
 - The MN phenotype is not intermediate between M and N phenotypes but rather exhibits both the M and the N phenotype.
- Some alleles show **incomplete dominance**, in which heterozygotes show a distinct intermediate phenotype not seen in homozygotes.

- This is not blending inheritance because the traits are separable (particulate), as shown in further crosses.
- Offspring of a cross between heterozygotes show three phenotypes: each parental and the heterozygote.
- The phenotypic and genotypic ratios are identical: 1:2:1.
- A clear example of incomplete dominance is seen in flower color of snapdragons.
 - A cross between a white-flowered plant and a red-flowered plant will produce all pink F₁ offspring.
 - Self-pollination of the F₁ offspring produces 25% white, 25% red, and 50% pink F₂ offspring.
- The relative effects of two alleles range from complete dominance of one allele, through incomplete dominance of either allele, to codominance of both alleles.
- It is important to recognize that a dominant allele does not somehow subdue a recessive allele.
- Alleles are simply variations in a gene's nucleotide sequence.
 - When a dominant allele coexists with a recessive allele in a heterozygote, they do not interact at all.
- To illustrate the relationship between dominance and phenotype, let us consider Mendel's character of round versus wrinkled pea seed shape.
 - Pea plants with wrinkled seeds have two copies of the recessive allele.
 - The seeds are wrinkled due to the accumulation of monosaccharides because of the lack of a key enzyme that converts them to starch.
 - Excess water enters the seed due to the accumulation of monosaccharides.
 - The seeds wrinkle when the excess water dries.
 - Both homozygous dominants and heterozygotes produce enough enzymes to convert all the monosaccharides into starch.
 - As a result, they do not fill with excess water and form smooth seeds as they dry.
- For any character, dominance/recessiveness relationships depend on the level at which we examine the phenotype.
 - For example, humans with **Tay-Sachs disease** lack a functioning enzyme to metabolize certain lipids. These lipids accumulate in the brain, harming brain cells, and ultimately leading to death.
 - Children with two Tay-Sachs alleles (homozygotes) have the disease.
 - Both heterozygotes with one working allele and homozygotes with two working alleles are healthy and normal at the *organismal* level.
 - The activity level of the lipid-metabolizing enzyme is reduced in heterozygotes. At the *biochemical* level, the alleles show incomplete dominance.
 - Heterozygous individuals produce equal numbers of normal and dysfunctional enzyme molecules. At the *molecular* level, the Tay-Sachs and functional alleles are codominant.
- A dominant allele is not necessarily more common in a population than the recessive allele.
 - For example, one baby in 400 is born with polydactyly, a condition in which individuals are born with extra fingers or toes.
 - Polydactyly is due to a dominant allele.
 - However, the recessive allele is far more prevalent than the dominant allele.
 - 399 individuals out of 400 have five digits per appendage.