A Review of Basic Mendelian Genetics

Here is a brief review of material you should have covered in high school biology courses and/or in 1st year University biology courses.

In the nineteenth century, Gregor Mendel, an Augustinian monk living in the former Austro-Hungarian Empire, laid the foundation for a new science - genetics. Prior to Mendel, many scientists had attempted to explain the rules controlling the inheritance of traits, but without much success. Mendel's 1866 paper described the rules governing the transmission of hereditary factors from one generation to another. The rules of hereditary transmission inferred from his results are often referred to as **Mendelian Genetics**. Mendel termed the unit of inheritance a "factor" or "hereditary particle". The hereditary units that are transmitted from one generation to the next are now called **genes**. Genetics is the study of the structure and function of genes and of the transmission of genes between generations.

A gene can have one or more specific effects on the phenotype of the organism.

A gene is a hereditary unit that, in the classical sense, occupies a specific position or **locus** within the genome or chromosome. A gene can have one or more specific effects on the phenotype of the organism. Genes in most organisms consist of DNA and they can mutate to various allelic forms. A gene can recombine with other such units. Some genes are transcribed into mRNAs, which are translated into polypeptides and other genes (RNA-only genes) are transcribed into RNA molecules which are used directly (rRNA, tRNA and many other RNA molecules).

Alleles are different forms of a gene.

Many genes occur in alternate forms called **alleles**. For example, all humans have the same basic genes which control eye colour, hair colour, blood type, and so on. Different individuals, however, may have different forms or alleles of these genes. One individual may have alleles producing blue eyes or type AB blood while another will have alleles producing brown eyes and type O blood. The most common allele of a gene is often designated as the **wildtype** or normal form and the less common allele as the **mutant** form. **Genotype** refers to the genetic makeup of an organism as distinguished from its physical appearance or **phenotype**. Phenotype is the expression of genes in a given environment. **Genome** is the total complement of genes contained in a cell or virus. In eukaryotes, genome usually refers to all genes present in one haploid set of chromosomes. Because many organisms are diploid, they have 2 copies of every gene. An organism inherits one allele of a particular gene from one parent and another allele of the same gene from the other parent. Each parent transmits only one allele of each gene to an offspring. An individual with 2 copies of the same allele is termed a **homozygote**. An individual with 2 non-identical alleles is called a **heterozygote**. If the parent is homozygous, each gamete will be identical for that gene. If the parent is heterozygous, two different gamete types will be produced-----each of equal frequency. This is Mendel's First Law or Principle of Segregation.

Purebred animals are homozygous for genes controlling particular traits.

Purebred or true breeding animals and plants are homozygous for many genes. For example a purebred beagle crossed to another purebred beagle will produce only puppies with the beagle phenotype and not puppies with the collie or dachshund phenotype. These dogs are homozygous for the many genes that produce the beagle phenotype (genes controlling coat length, colour and texture; genes controlling ear posture and tail length etc). On the other hand, a mutt or mongrel is heterozygous for many of the same genes and will not breed true. An individual with non-identical alleles for one gene is termed a **monohybrid**. Similarly an individual with non-identical alleles for two genes is called a **dihybrid**. These hybrids do not breed true.

One allele can completely mask the effect of another allele.

An allele that can phenotypically express itself in the heterozygous condition is called a **dominant allele**. An allele whose phenotypic expression is limited to the homozygous condition is called a **recessive allele**. Upper and lower case letters are commonly used to designate dominant and recessive alleles respectively. A heterozygote could have one copy of a dominant allele and one copy of a recessive allele. The phenotype of the heterozygote would be determined by the dominant allele. **Simple/complete dominance** occurs when the dominant allele completely masks the phenotypic effects of the recessive allele. A heterozygote with a deleterious recessive allele hidden from phenotypic expression by a normal dominant allele is often called a **carrier**.

The phenotype of a heterozygote may be identical to the phenotype of the homozygous dominant individual.

The phenotype of an individual with the genotype *AA* (homozygous dominant) may not be distinguishable from the phenotype of the heterozygote *Aa* due to simple/complete dominance. A **test cross** can be performed to determine the individual's genotype. In a test cross, an individual with an unknown genotype is crossed to a homozygous recessive individual. If the individual with the unknown genotype is homozygous dominant then all progeny will express the dominant trait. If the individual with the unknown genotype is heterozygous, then 50% of the progeny will express the dominant trait and 50% will express the recessive trait.

<u>Problem</u> The wildtype allele for black hair of guinea pigs is dominant to the allele for white hair. If a black female guinea pig is test-crossed and produces at least one white offspring, what is the genotype of the female parent?

<u>Solution</u> The problem indicates that a single trait, hair colour, has two alternative expressions, black and white. The alleles involved show complete dominance, with the

black-hair allele dominant to the white-hair allele. The female is black and the offspring is white. The question asks you to identify the genotype of the female parent. Use the letter *w* as the symbol for the allele that leads to white hair and *W* as the symbol for the allele that leads to black hair.

The male used in the test cross must be homozygous recessive, *ww*. By definition test cross animals are homozygous recessive for the genes under consideration. The female parent has a black phenotype and therefore must have at least one dominant *W* allele. When these two animals were crossed a white offspring resulted. The offspring is *ww* because white is a recessive trait. The offspring must have received one *w* allele from the female parent and one *w* allele from the male parent. Therefore the female parent must be heterozygous.

Problem The lack of pigmentation, called albinism, in humans is caused by a single gene. Two phenotypically normal parents have three albino children. What is the probability that their next child will be an albino?

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Solution The problem indicates that a single trait, pigmentation, has two alternative expressions, normal pigmentation and albinism. Use the letter *a* as the symbol for the albinism allele and *A* as the symbol for the wildtype allele that causes normal pigmentation. The alleles show complete dominance. Both parents are phenotypically normal and therefore they must each have one dominant allele. To produce an albino child, each parent must have contributed a recessive allele and therefore we can conclude that both parents are heterozygous. The chance of a future offspring having a particular genotype is independent of previous offspring. Each parent has a 50% chance of producing a gamete with the recessive allele. All possible random combinations of these eggs and sperm can be shown by completing the Punnett square.

Because the four boxes of the Punnett square represent 100% of the progeny, the box containing *AA* represents 25% of the progeny that are homozygous for the wildtype allele, the two boxes containing *Aa* represent 50% of the progeny that are heterozygous, and the remaining box containing *aa* represents 25% of the progeny that are homozygous for the albinism allele. Therefore the probability that their next child will have albinism is 25%.

Problem A second child is born to the above parents and has normal pigmentation. What is the probability that this second child is a carrier?

<u>Solution</u> A carrier is an individual who is phenotypically normal and genotypically heterozygous. The Punnett square below shows the genotypes of progeny produced by the heterozygous parents. The genotypic ratio is *1 AA : 2 Aa : 1 aa*. The second child is phenotypically normal so she must genotypically be either *Aa* or *AA*. We exclude the possibility that she is homozygous recessive, *aa*, because the question has indicated that she has normal pigmentation.

♂ ♀	A	a
A	AA	Aa
a	Aa	~~aa~~

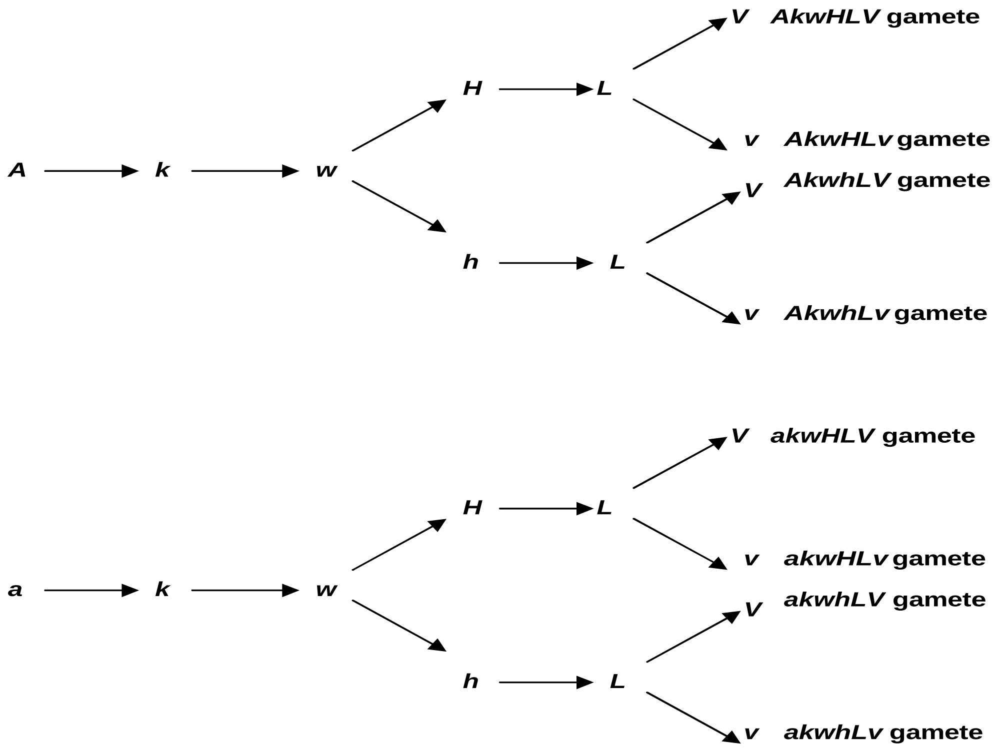
A line has been drawn through the box containing the homozygous recessive genotype in the above Punnett square to remind us that this genotype has been eliminated. Is the child more likely to be *AA* or *Aa*? There are three boxes remaining in the Punnett square. Out of three possible genotypic outcomes two are heterozygous and one is homozygous dominant. In other words the second child has a 2/3 chance of being heterozygous *Aa* (a carrier) and a 1/3 chance of being homozygous dominant, *AA*.

Members of different pairs of alleles assort independently into gametes.

According to Mendel's Principle of independent assortment (Mendel’s Second Law), the segregation of one pair of alleles is independent of the segregation of the second pair of alleles. We now know that independent assortment refers to the behaviour of chromosomes during meiosis. In Mendel's peas, the alleles which control seed shape (*W* and *w*) are located on one homologous pair of chromosomes and the alleles which control seed colour (*G* and *g*) are on another pair of homologous chromosomes. Dihybrids, *WwGg*, form four genetically different gametes with approximately equal frequencies (*WG* and *Wg* and *wG* and *wg*) because of the random orientation of non-homologous chromosome pairs on the first meiotic metaphase plate.

<u>Problem</u> How many kinds of gametes will be produced by plants having the genotype *Aa kk ww Hh LL Vv* ?

<u>Solution</u> If the genes are independently assorting all combinations of alleles are possible. All gametes will carry *k*, *w* and *L*, since the plants are homozygous for these alleles. The gametes will be segregating for all others. The number of different kinds of gametes=2^n, where n is the number of segregating loci. In this example, $2^3 = 8$. There would be 8 different gametes. The branching/forked diagram below indicates the possible allele combinations.



Hybrids (heterozygotes) do not breed true.

When two monohybrids are crossed a proportion of their progeny will not resemble the parents. Three quarters of the progeny will be phenotypically similar to the parents (1/4 homozygous dominant and 1/2 heterozygous) and 1/4 will be phenotypically dissimilar to the parents (1/4 homozygous recessive).

<u>Problem</u> In guinea pigs, two genes which control coat texture and colour are under consideration. The allele for rough coat, *S*, is dominant to the allele for smooth coat, *s*, and the allele for black fur, *W*, is dominant to the allele for white fur, *w*. Two dihybrids are mated. What proportion of the F1 will not resemble the parents? The genes are independently assorting and show simple dominance.

Solution Each parent is heterozygous at both loci and the mating can be represented as *SsWw* X *SsWw*. The phenotypes of both parents will be black in colour with rough-textured coats. Next, we need to identify the types of gametes produced by each dihybrid parent. Each *SsWw* parent will produce four kinds of gametes in equal proportions. The four gametes are *SW, Sw, sW* and *sw*. Notice that if we consider each gene separately, half the gametes carry the *S* allele and half carry the *s* allele and, similarly, half carry *W* and the other half carry *w*. Chance determines the manner in which these independently assorting genes combine in the gametes. The random union of the four different kinds of gametes produced by each parent can be shown in a Punnett square with sixteen boxes.

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The types of gametes are listed across the top and down the side. Determine the genotypes by filling in each box in the square. Under each genotype, write down the animal's phenotype. The phenotypic ratio produced will be as follows: 9/16 will be rough-coated and black, 3/16 will be smooth-coated and black, 3/16 will be rough-coated and white and finally 1/16 will be smooth-coated and white. This gives us the classic Mendelian phenotypic ratio of 9:3:3:1.

The question asked us to determine what proportion of the offspring would not have the same phenotype as the parents. The dihybrid parents are phenotypically rough-coated and black in colour. Progeny that are rough-coated and white or smooth-coated and black or smooth-coated and white differ in phenotype from their parents. Count the number of boxes in the Punnett square which give you those phenotypes. You will find that 7 boxes out of the 16 boxes have genotypes (1-*ssww*, 2-*Ssww*, 1-*SSww*, 1-*ssWW*, 2-*ssWw*) which produce phenotypes that are different from the dihybrid parents.

Another way to solve the same problem is to list the genotypes which will produce phenotypes that are dissimilar to the parents. These are *ssww, S-ww,* and *ssW-*. Then determine the probability of producing these genotypes from crossing dihybrid parents. Remember the cross is *SsWw X SsWw*. If we consider one gene pair at a time we will come up with the following probability calculations:

For *S-ww* the probability would be 3/4 (probability of getting *S-*) multiplied by 1/4 (probability of getting *ww*) = 3/16
For *ssW-* the probability would be 1/4 (probability of getting *ss*) multiplied by 3/4 (probability of getting *W-*) = 3/16
For *ssww* the probability would be 1/4 (probability of getting *ss*) multiplied by 1/4 (probability of getting *ww*) = 1/16
Sum these probabilities and the answer is 7/16. This method is less labourious than using the Punnett square especially when crosses involve 3 or more genes.

<u>Problem</u> In garden peas, tetrahybrid plants are crossed. These tetrahybrid plants have seeds that are yellow and round and pods that are green and inflated. Each trait is controlled by a single gene and all genes show simple dominance and independent assortment. What is the probability that this cross will produce offspring with yellow round seeds and yellow constricted pods?

<u>Solution</u> It far too time consuming to solve this problem using a Punnett square. To indicate every possible genotype generated from the above cross would require a Punnett square with 256 squares. The simplest way to solve this problem is to use the branching/forked diagram method. Let the genes controlling seed colour, seed texture, pod colour and pod shape be represented by the symbols *A*, *B*, *C* and *D* respectively. We know which of the traits are dominant because we know the phenotype of tetrahybrid. Therefore yellow seeds, round seeds, green pods and inflated pods are all dominant traits. Because the genes are independently assorting, single gene crosses, can be considered one at a time. For the first gene the male parent is *Aa* and the female parent is *Aa*. Offspring would be 1/4 *AA*, 1/2 *Aa* and 1/4 *aa*. Because we are just concerned with the phenotypes of the progeny we can simply write 3/4 *A*- and 1/4 *aa*. The slash following *A* indicates that the second allele can be either *A* or *a*. Because allele *A* is completely dominant both *AA* and *Aa* progeny will have the same phenotype (yellow seed colour).
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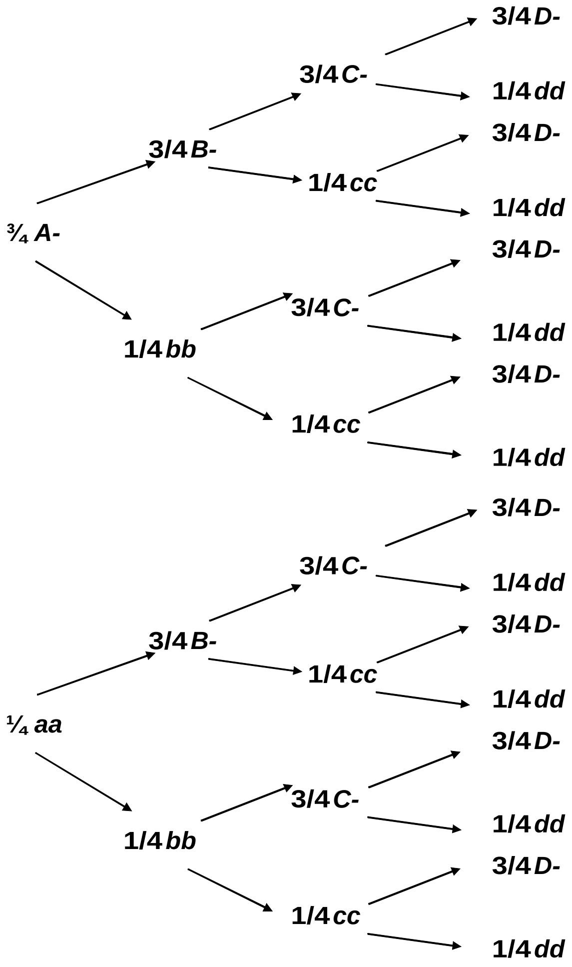

The above branching diagram indicates all the possible phenotypic combinations resulting from the above cross. To calculate the probability that the cross will produce offspring with yellow round seeds and yellow constricted pods, we need only construct one section of this branching diagram. Circle the region in the branching diagram which results in the production of *A-B-ccdd* progeny.

Calculations are as follows: 3/4 (probability of progeny being *A-* yellow seeds) X 3/4 (probability of progeny being *B-* round seeds) X 1/4 (probability of progeny being *cc* yellow pods) X 1/4 (probability of progeny being *dd* constricted pods) = 3/4 X 3/4 X 1/4 X 1/4 = 9/256

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