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Chapter 2 Mendelian Genetics

Synopsis:

The first part of Chapter 2 covers the basic principles of inheritance that can be summarized as Mendel's Laws of Segregation (for one gene) and Independent Assortment (for more than one gene). You will see in chapter 3 how these laws relate to chromosome segregation during meiosis.

In the second part of Chapter 2, we see that the relationship between genotype and phenotype can be more complicated than envisaged by Mendel. Alleles do not have to be completely dominant or recessive with respect to each other. Not all genotypes are equally viable. Genes can have more than two alleles in a population. One gene can govern more than one phenotype. A single phenotype can be influenced by more than one gene, and these genes can interact in a variety of ways.

Despite these complications, the alleles of individual genes still segregate according to Mendel's Law of Segregation, and different pairs of genes still usually behave as dictated by Mendel's Law of Independent Assortment.

Key Terms:

genes and **alleles** of genes – a gene determines a trait; and there are different alleles or forms of a gene. The colour gene in pea has two alleles: the yellow allele and the green allele.

genotype and **phenotype** – genotype is the genetic makeup of an organism (written as alleles of specific genes), while phenotype is what the organism looks like.

homozygous and **heterozygous** – when both alleles of a gene are the same, the individual is homozygous for that gene (or *pure-breeding*). If the two alleles are different, the organism is heterozygous (also called a *hybrid*).

dominant and **recessive** – the dominant allele is the one that controls the phenotype in the heterozygous genotype; the recessive allele controls the phenotype only in a homozygote since its effect is hidden or masked when the dominant allele is present.

monohybrid or **dihybrid cross** – a cross between individuals who are both heterozygous for one gene (monohybrid) or for two genes (dihybrid).

testcross – performed to determine whether or not an individual with the dominant trait is homozygous or heterozygous; an individual with the dominant phenotype but unknown genotype is crossed with an individual with the recessive phenotype.

wild-type alleles – alleles with a frequency equal to or greater than 1 percent in the population. Colloquially, wild-type alleles are the "normal" alleles found most commonly in the population.

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mutant alleles – rare alleles with a frequency of less than 1 percent in the population.

monomorphic gene – a gene with only one common, wild-type allele.

polymorphic gene – a gene with many wild-type alleles. The wild-type alleles of a polymorphic gene are often called **common variants.**

incomplete dominance and **codominance** – cases in which the phenotype of heterozygotes is different than that of either type of homozygote. Incomplete dominance describes alleles where the heterozygote has a phenotype that is in between that of either homozygote, but typically is more similar to one parent than to the other, while heterozygotes for codominant alleles have both of the phenotypes associated with each homozygote. Usually in incomplete dominance one allele is nonfunctional or only partially functional, while in codominance both alleles are fully functional.

recessive lethal allele – an allele (usually a loss-of-function allele) of an **essential gene** necessary to the survival of the individual. A zygote homozygous for a recessive lethal allele cannot survive and thus is not detected among the progeny of a cross.

dominance series of multiple alleles – Although each individual has only two alleles of a gene, many alleles of the gene may exist in the population. These alleles may be completely dominant, incompletely dominant, or codominant with respect to each other as determined by the phenotype of heterozygotes for the particular pair.

pleiotropy – A gene may affect more than one phenotype.

complementary gene action – Function of two different genes is required to produce a phenotype. Nonfunctional recessive alleles of either gene can produce the same abnormal phenotype in homozygotes. Such a phenotype that can be caused by nonfunctional alleles of more than one gene is called a **heterogeneous trait.**

epistasis – An allele of one gene hides the effects of different alleles at a second gene.

redundant genes – Two or more genes provide the same function.

penetrance – the fraction of individuals with a particular genotype who display the genotype's characteristic phenotype.

expressivity – the degree to which an affected individual displays the phenotype associated with that individual's genotype. Expressivity of a genotype can vary due to environment, chance, and alleles of other genes (**modifier genes**).

conditional mutation – a change in the base sequence of a gene that affects gene function only under specific environmental conditions.

continuous (quantitative) trait – a trait whose phenotype varies over a wide range of values that can be measured. Continuous traits are **polygenic** – they are controlled by the combined activities of many genes.

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Key Ratios:

3:1 – Ratio of progeny phenotypes in a cross between monohybrids

[$Aa \times Aa \rightarrow$ 3 A– (dominant phenotype) : 1 aa (recessive phenotype)]

1:2:1 – Ratio of progeny genotypes in a cross between monohybrids

($Aa \times Aa \rightarrow$ 1 AA : 2 Aa : 1aa)

1:1 – Ratio of progeny genotypes in a cross between a heterozygote and a recessive homozygote

($Aa \times aa \rightarrow$ 1 Aa : 1aa)

1:0 – All progeny have the same phenotype. Can result from several cases:

[$AA \times -- \rightarrow$ A– (all dominant phenotype)]

[$aa \times aa \rightarrow$ aa (all recessive phenotype)]

9:3:3:1 – Ratio of progeny phenotypes in a dihybrid cross

($Aa\ Bb \times Aa\ Bb \rightarrow$ 9 A– B– : 3 A– bb : 3 aa B– : 1 aa)

1:2:1 – Ratio of progeny genotypes and phenotypes in a cross between hybrids when there is **incomplete dominance** or **codominance**:

($Aa \times Aa \rightarrow$ 1 AA : 2 Aa : 1aa)

Note that in incomplete dominance and codominance, a new (third) phenotype will appear in the hybrids (Aa) of the F_1 generation. In the F_2 generation, this same phenotype must be the largest component of the 1:2:1 monohybrid ratio.

2:1 – Ratio of progeny phenotypes observed in a cross between hybrids when one allele (A^1) is a **recessive lethal allele** that has a dominant effect on a visible phenotype:

($Aa \times Aa \rightarrow$ 1 A^1A^1 : 2 A^1A^2 : 1 A^2A^2)

Note that in this case, homozygotes for the recessive lethal allele A^1 die (*red colour*), but A^1A^2 heterozygotes have a phenotype different from A^2A^2 homozygotes.

Interactions of Two Genes:

You should be able to recognize traits influenced by two genes as variations on the 9:3:3:1 ratio of genotypic classes resulting from a dihybrid cross. For your convenience, an abbreviated version of Table 2.4 summarizing these gene interactions is presented below. It is particularly useful to understand the concepts of complementary gene action, epistasis, and redundancy.

If you are given the details of a biochemical pathway, you should be able to work out the ratios of phenotypes expected among the progeny of a cross. Note that you cannot go in the opposite

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direction: A particular ratio does not tell much about the underlying biochemistry. Thus, you should NOT try to memorize specific examples relating particular ratios to specific biochemical pathways.

F_2 Genotypic Ratios from an F_1 Dihybrid Cross

Gene interaction	*A- B-*	*A- bb*	*aa B-*	*aa bb*	F_2 Phenotypic Ratio
None: Four distinct F_2 Phenotypes	9	3	3	1	9:3:3:1
Complementary: One dominant allele of each of two genes is necessary to produce the phenotype	9	3	3	1	9:7
Recessive epistasis: Homozygous recessive allele of one gene masks both alleles of another gene	9	3	3	1	9:3:4
Dominant epistasis I: Dominant allele of one gene hides effects of both alleles of another gene	9	3	3	1	12:3:1
Dominant epistasis II: Dominant allele of one gene hides effects of dominant allele of another gene	9	3	3	1	13:3
Redundancy: Only one dominant allele of either of two genes is necessary to produce phenotype	9	3	3	1	15:1

Problem Solving:

The essential component of solving most genetics problems is to DIAGRAM THE CROSS in a consistent manner. In most cases you will be given information about phenotypes, so the diagram would be:

phenotype of one parent x phenotype of the other parent → phenotype(s) of progeny

The goal is to assign genotypes to the parents and then use these predicted genotypes to generate the genotypes, phenotypes, and ratios of progeny. If the predicted progeny match the observed data you were provided, then your genetic explanation is correct.

The points listed below will be particularly helpful in guiding your problem solving:

- Remember that **there are two alleles of each gene when describing the genotypes of individuals.** But if you are describing gametes, remember that **there is only one allele of each gene per gamete.**
- **You will need to determine whether a trait is dominant or recessive.** Two main clues will help you answer this question.

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- First, if the parents of a cross are true-breeding for the alternative forms of the trait, look at the phenotype of the F_1 progeny. Their genotype must be heterozygous, and their phenotype is thus controlled by the dominant allele of the gene.
- Second, look at the F_2 progeny (i.e., the progeny of the F_1 hybrids). The 3/4 portion of the 3:1 phenotypic ratio indicates the dominant phenotype.

- You should **recognize the need to set up a testcross** (to establish the genotype of an individual showing the dominant phenotype by crossing this individual to a recessive homozygote).
- You must **keep in mind the basic rules of probability:**
  - *Product rule*: If two outcomes must occur together as the result of independent events, the probability of one outcome AND the other outcome occurring is the product of the two individual probabilities. So, the probability of getting a 4 on one die AND a 4 on the second die is the product of the two individual probabilities.
  - *Sum rule*: If there is more than one way in which an outcome can be produced, the probability of either one OR the other occurring is the sum of the two mutually exclusive individual probabilities.
- Remember that **Punnett squares are not the only means of analyzing a cross; branched-line diagrams and calculations of probabilities according to the product and sum rules are more efficient ways of looking at complicated crosses** involving more than one or two genes.
- **You should be able to draw and interpret pedigrees.** When the trait is rare, look in particular for vertical patterns of inheritance characteristic of dominant traits, and horizontal patterns that typify recessive traits. Check your work by assigning genotypes to all individuals in the pedigree and verifying that these make sense.
- The vocabulary problem (the first problem in the set) is a useful gauge of how well you know the terms most critical for your understanding of the chapter.

In the first part of Chapter 2, the major goal was to determine which allele of a gene is dominant and which is recessive, and then to ascribe genotypes to various individuals or classes of individuals based on the ratio of progeny types seen in a cross. The challenges become more difficult in the second part of the chapter, but the first step in problem solving remains the same: You need to DIAGRAM THE CROSS in a consistent manner. The next steps are to answer the following questions:

How many genes are involved in determining the phenotype?

How many alleles of each gene are present?

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What phenotypes are associated with which genotypic classes? (The answer to this last question will help you understand the dominance relationships between the alleles of each gene and the interactions between alleles of traits determined by more than one gene.)

The points listed below will be particularly helpful in guiding your problem solving:

- To distinguish between one gene and two gene traits, look for the number of phenotypic classes in the F_2 generation and the ratios in the F_2s among those classes. If a single gene is involved, there will be either two classes (3:1 or 2:1 if an allele is a recessive lethal) or three classes (1:2:1 in the cases of codominance or incomplete dominance). If two genes are involved, you could see two classes (9:7, 13:3, or 15:1) or three classes (9:3:4 or 12:3:1) or four classes (9:3:3:1). [*Note*: These ratios require that the P generation is true-breeding and that the F_1 crosses examined are between hybrids.]
- Understand that when there is codominance or incomplete dominance, a novel phenotype will appear in the F_1 generation. In the F_2 generation, this same phenotype must be the largest component of the 1:2:1 monohybrid ratio.
- If you see a series of crosses involving different phenotypes for a certain trait, for example coat colour, and each individual cross gives a monohybrid ratio (3:1 or 1:2:1), then all the phenotypes are controlled by one gene with many alleles that form an **allelic series**. You should write out the dominance hierarchy for this series (e.g., $a = b > c$) to keep track of the relationships among the alleles. Thus, *a* is codominant or incompletely dominant to *b* and both *a* and *b* are completely dominant to *c*.
- Lethal alleles are almost always recessive because a zygote with a dominant lethal allele could not grow into an adult. (The only exceptions to this rule involve **conditional lethal alleles** that survive in some environments but not others.) On the basis of what you have learned in this chapter, you can recognize recessive lethal alleles if they are pleiotropic and show a dominant visible phenotype such that the monohybrid phenotypic ratio is 2 (dominant phenotype) : 1 (recessive phenotype).
- Remember that the 9:3:3:1 dihybrid F_2 phenotypic ratio and its variants represent various combinations of the genotypic classes 9 *A*– *B*– : 3 *A*– *bb* : 3 *aa B*– : 1 *aa bb*, where the dashed line (–) indicates either a dominant or recessive allele. Based on the observed ratios, you should be able to tell which genotypic classes correspond to which phenotypes. Although you should not memorize the table on the previous page displaying these variants of 9:3:3:1, you should be able to consider whether particular biochemical explanations fit the ratios seen.
- Don't forget to use the product rule of probability to determine the proportions of genotypes or phenotypes for independently assorting genes

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Solutions to Problems:

Vocabulary

2-1a. i. **4**; ii. **3**; iii. **6**; iv. **7**; v. **11**; vi. **13**; vii. **10**; viii. **2**; ix. **14**; x. **9**; xi. **12**; xii. **8**; xiii. **5**; xiv. **1**.

2-1b. i. **2;** ii. **5;** iii. **10;** iv. **7;** v. **6;** vi. **8;** vii. **11;** viii. **3;** ix. **4;** x. **1;** xi. **9**.

Section 2.1 - Background

2-2. Prior to Mendel, **people held two basic misconceptions about inheritance**. First was the common idea of blended inheritance: that the parental traits become mixed and forever changed in the offspring. Second, many thought that one parent contributes the most to an offspring's inherited features (e.g., some people thought they saw a fully formed child in a human sperm).

In addition, **people who studied inheritance did not approach the problem in an organized way**. They did not always control their crosses. They did not look at traits with clear-cut alternative phenotypes. They did not start with pure-breeding lines. They did not count the progeny types in their crosses. For these reasons, they could not develop the same insights as did Mendel.

2-3. There are **several advantages to using peas** for the study of inheritance. **(1) Peas have a fairly rapid generation time** (at least two generations per year if grown in the field, three or four generations per year if grown in greenhouses). **(2) Peas can either self-fertilize or be artificially crossed** by an experimenter. **(3) Peas produce large numbers of offspring** (hundreds per parent). **(4) Peas can be maintained as pure-breeding lines**, simplifying the ability to perform subsequent crosses. **(5) Because peas have been maintained as inbred stocks, two easily distinguished and discrete forms of many traits are known. (6) Peas are easy and inexpensive to grow**.

In contrast, studying **genetics in humans has several disadvantages**. **(1) The generation time of humans is very long** (roughly 20 years). **(2) There is no self-fertilization in humans, and it is not ethical to manipulate crosses. (3) Humans produce only a small number of offspring per mating** (usually one) **or per parent** (almost always fewer than 20). **(4) Although people who are homozygous for a trait do exist (analogous to pure-breeding stocks), homozygosity cannot be maintained** because mating with another individual is needed to produce the next generation. **(5) Because human populations are not inbred, most human traits show a continuum of phenotypes**; only a few traits have two very distinct forms. **(6) People require a lot of expensive care to "grow".**

There is nonetheless one major advantage to the study of genetics in humans: Because many inherited traits result in disease syndromes, and because the world's population now exceeds 7 billion

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people, **a very large number of people with diverse, variant phenotypes can be recognized.** These variations are the raw material of genetic analysis.

Section 2.2 – Genetic Analysis According to Mendel

2-4.

a. **Two phenotypes are seen in the second generation of this cross: normal and albino.** Thus, only one gene is required to control the phenotypes observed.

b. Note that the phenotype of the first generation progeny is normal colour, and that in the second generation, there is a ratio of 3 normal : 1 albino. Both of these observations show that **the allele controlling the normal phenotype (*A*) is dominant to the allele controlling the albino phenotype (*a*).**

c. In a testcross, an individual showing the dominant phenotype but that has an unknown genotype is mated with an individual that shows the recessive phenotype and is therefore homozygous for the recessive allele. The male parent is albino, so **the male parent's genotype is *aa***. The **normal-coloured offspring** must receive an *A* allele from the mother, so **the genotype of the normal offspring is *Aa***. The albino offspring must receive an *a* allele from the mother, so **the genotype of the albino offspring is *aa***. Thus, **the female parent must be heterozygous *Aa***.

2-5. Because two different phenotypes result from the mating of two cats of the same phenotype, the short-haired parent cats must have been heterozygous. The phenotype expressed in the heterozygotes (the parent cats) is the dominant phenotype. Therefore, **short hair is dominant to long hair**.

2-6.

a. Two affected individuals have an affected child and a normal child. This outcome is not possible if the affected individuals were homozygous for a recessive allele conferring piebald spotting, and if the trait is controlled by a single gene. Therefore, **the piebald spotting trait must be the dominant phenotype.**

b. If the trait is dominant, the piebald parents could be either homozygous (*PP*) or heterozygous (*Pp*). However, because the two affected individuals have an unaffected child *(pp)*, **they both must be heterozygous (*Pp*).** A diagram of the cross follows:

piebald x piebald → 1 piebald : 1 normal

Pp x *Pp* → 1 *Pp* : 1 *pp*

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Note that although the apparent ratio is 1:1, this is not a testcross but is instead a cross between two monohybrids. The reason for this discrepancy is that only two progeny were obtained, so this number is insufficient to establish what the true ratio would be (it should be 3:1) if many progeny resulted from the mating.

2-7. You would conduct a testcross between your normal-winged fly (*W*-) and a short-winged fly that must be homozygous recessive (*ww*). The possible results are diagrammed here; the first genotype in each cross is that of the normal-winged fly whose genotype was originally unknown.

***WW* x *ww* → all *Ww* (normal wings)**

***Ww* x *ww* → 1/2 *Ww* (normal wings) : 1/2 *ww* (short wings)**. (1:1 ratio)

2-8. First diagram the crosses:

closed x open → F_1 open → F_2 145 open : 59 closed

F_1 open x closed → 81 open : 77 closed

The results of the crosses fit the pattern of inheritance of a single gene, with the open trait being dominant and the closed trait recessive. The first cross is similar to those Mendel did with pure-breeding plants, although you were not provided with the information that the starting plants were true-breeding. **The phenotype of the F_1 plants is open, indicating that open is dominant. The closed parent must be homozygous for the recessive allele. Because only one phenotype is seen among the F_1 plants, the open parent must be homozygous for the dominant allele**. Thus, the parental cucumber plants were indeed true-breeding homozygotes.

The result of the self-fertilization of the F_1 plants shows a 3:1 ratio of the open : closed phenotypes among the F_2 progeny. **The 3:1 ratio in the F_2 shows that a single gene controls the phenotypes and that the F_1 plants are all hybrids (i.e., they are heterozygotes)**.

The final cross confirms that the F_1 plants from the first cross are heterozygous because **this testcross yields a 1:1 ratio of open: closed progeny**. In summary, all the data are consistent with the trait being determined by one gene with two alleles, and open being the dominant trait.

2-9. The dominant trait (short tail) is easier to eliminate from the population by selective breeding. **The reason is you can recognize every animal that has inherited the short tail allele, because only one such dominant allele is needed to see the phenotype.** If you prevent all the short-tailed animals from mating, then the allele would become extinct.

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On the other hand, the recessive dilute coat colour allele can be passed unrecognized from generation to generation in heterozygous mice (who are *carriers*). The heterozygous mice do not express the phenotype, so they cannot be distinguished from homozygous dominant mice with normal coat colour. You could prevent the homozygous recessive mice with the dilute phenotype from mating, but the allele for the dilute phenotype would remain among the carriers, which you could not recognize.

2-10.

a. The problem already states that only one gene is involved in this trait, and that the dominant allele is dimpled (*D*) while the recessive allele is nondimpled (*d*). Diagram the cross described in this part of the problem:

nondimpled ♂ x dimpled ♀→ proportion of F_1 with dimple?

Note that the dimpled woman in this cross had a *dd* (nondimpled) mother, so the dimpled woman MUST be a heterozygote. We can thus rediagram this cross with genotypes:

dd (nondimpled) ♂ x *Dd* (dimpled) ♀ → **1/2 *Dd* dimpled** : 1/2 *dd* nondimpled

One half of the children produced by this couple would be dimpled.

b. Diagram the cross:

dimpled (*D?*) ♂ x nondimpled (*dd*) ♀ → nondimpled (*dd*) F_1

Because they have a nondimpled child (*dd*), the husband must have a *d* allele to contribute to the offspring. **The husband is thus of genotype *Dd*.**

c. Diagram the cross:

dimpled (*D?*) ♂ x nondimpled (*dd*) ♀ → eight F_1, all dimpled (*D*–)

The *D* allele in the children must come from their father. The father could be either *DD* or *Dd,* but **it is most probable that the father's genotype is *DD***. We cannot rule out completely that the father is a *Dd* heterozygote. However, if this was the case, the probability that all 8 children would inherit the *D* allele from a *Dd* parent is only $(1/2)^8 = 1/256$.

2-11.

a. The only unambiguous cross is:

homozygous recessive x homozygous recessive → all homozygous recessive

The only cross that fits this criteria is: dry x dry → all dry. Therefore, **dry is the recessive phenotype (*ss*) and sticky is the dominant phenotype (*S*–)**.

b. A 1:1 ratio comes from a testcross of heterozygous sticky (*Ss*) x dry (*ss*). However, **the sticky x dry matings here include both the *Ss* x *ss* AND the homozygous sticky (*SS*) x dry (*ss*)**.

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A 3:1 ratio comes from crosses between two heterozygotes, *Ss* x *Ss*. However, the sticky individuals are not only *Ss* heterozygotes but also *SS* homozygotes. Thus the sticky x sticky matings in this human population are a mix of matings between two heterozygotes (*Ss* x *Ss*), between two homozygotes (*SS* x *SS*), and between a homozygote and heterozygote (*SS* x *Ss*). **The 3:1 ratio of the heterozygote cross is therefore obscured by being combined with results of the two other crosses.**

2-12. Diagram the cross:

black x red → 1 black : 1 red

No, **you cannot tell how coat colour is inherited from the results of this one mating.** In effect, this was a testcross – a cross between animals of different phenotypes resulting in offspring of two phenotypes. This does not indicate whether red or black is the dominant phenotype. To determine which phenotype is dominant, remember that an animal with a recessive phenotype must be homozygous. Thus, **if you mate several red horses to each other and also mate several black horses to each other, the crosses that always yield only offspring with the parental phenotype must have been between homozygous recessives.** For example, if all the black x black matings result in only black offspring, black is recessive. Some of the red x red crosses (that is, crosses between heterozygotes) would then result in both red and black offspring in a ratio of 3:1. To establish this point, you might have to do several red x red crosses, because some of these crosses could be between red horses homozygous for the dominant allele. You could of course ensure that you were sampling heterozygotes by using the progeny of black x red crosses (such as that described in the problem) for subsequent black x black or red x red crosses.

2-13.

a. **1/6** because a die has 6 different sides.
b. There are three possible even numbers (2, 4, and 6). The probability of obtaining any one of these is 1/6. Because the 3 events are mutually exclusive, use the sum rule: 1/6 + 1/6 + 1/6 = 3/6 = **1/2**.
c. You must roll either a 3 or a 6, so 1/6 + 1/6 = 2/6 = **1/3**.
d. Each die is independent of the other, thus the product rule is used: 1/6 x 1/6 = **1/36**.
e. The probability of getting an even number on one die is 3/6 = 1/2 (see part *b*). This is also the probability of getting an odd number on the second die. This result could happen either of 2 ways – you could get the odd number first and the even number second, or *vice versa*. Thus the probability of both occurring is 1/2 x 1/2 x 2 = **1/2.**

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f. The probability of any specific number on a die = 1/6. The probability of the same number on the other die =1/6. The probability of both occurring at the same time is 1/6 x 1/6 = 1/36. The same probability is true for the other 5 possible numbers on the dice. Thus the probability of any of these mutually exclusive situations occurring is 1/36 + 1/36 + 1/36 + 1/36 + 1/36 + 1/36 = 6/36 = **1/6**.

g. The probability of getting two numbers both over four is the probability of getting a 5 or 6 on one die (1/6 + 1/6 = 1/3) and 5 or 6 on the other die (1/3). The results for the two dice are independent events, so 1/3 x 1/3 = **1/9**.

2-14. The **probability of drawing a face card** = 12 face cards / 52 cards **= 0.231**. The **probability of drawing a red card** = 26 / 52 **= 0.5**. The **probability of drawing a red face card** = probability of a red card x probability of a face card = 0.231 x 0.5 [or 6 red face cards / 52 cards] **= 0.116**

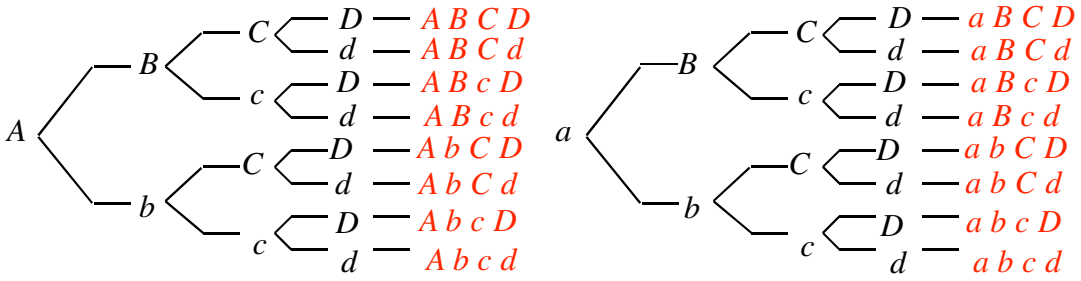
2-15.

a. The *Aa bb CC DD* woman can produce 2 genetically different eggs that vary in their allele of the first gene (*A* or *a*). She is homozygous for the other 3 genes and can only make eggs with the *b C D* alleles for these genes. Thus, using the product rule (because the inheritance of each gene is independent), she can make 2 x 1 x 1 x 1 = **2 different types of gametes**: (*A b C D* and *a b C D*).

b. Using the same logic, an *AA Bb Cc dd* woman can produce 1 x 2 x 2 x 1 = **4 different types of gametes**: *A* (*B* or *b*) (*C* or *c*) *d*.

c. A woman of genotype *Aa Bb cc Dd* can make 2 x 2 x 1 x 2 = **8 different types of gametes**: (*A* or *a*) (*B* or *b*) *c* (*D* or *d*).

d. A woman who is a quadruple heterozygote can make 2 x 2 x 2 x 2 = **16 different types of gametes**: (*A* or *a*) (*B* or *b*) (C or *c*) (*D* or *d*). This problem (like those in parts *a*-*c* above) can also be visualized with a branched-line diagram.



2-16.

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a. The probability of any phenotype in this cross depends only on the gamete from the heterozygous parent. The probability that a child will resemble the quadruply heterozygous parent is thus 1/2 *A* x 1/2 *B* x 1/2 *C* x 1/2 *D* = 1/16. The probability that a child will resemble the quadruply homozygous recessive parent is 1/2 *a* x 1/2 *b* x 1/2 *c* x 1/2 *d* = 1/16. **The probability that a child will resemble either parent is then 1/16 + 1/16 = 1/8**. This cross will produce 2 different phenotypes for each gene or 2 x 2 x 2 x 2 = **16 potential phenotypes.**

b. The probability of a child resembling the recessive parent is 0; the probability of a child resembling the dominant parent is 1 x 1 x 1 x 1 = 1. **The probability that a child will resemble one of the two parents is 0 + 1 = 1**. **Only 1 phenotype is possible in the progeny (dominant for all 4 genes),** as $(1)^4 = 1$.

c. The probability that a child would show the dominant phenotype for any one gene is 3/4 in this sort of cross (remember the 3/4 : 1/4 monohybrid ratio of phenotypes), so the **probability of resembling the parent for all four genes is $(3/4)^4 = 81/256$**. There are 2 phenotypes possible for each gene, so $(2)^4$ = **16 different kinds of progeny.**

d. **All progeny will resemble their parents** because all of the alleles from both parents are identical, so the **probability = 1**. There is only 1 phenotype possible for each gene in this cross; because $(1)^4=1$, the child can have only **one possible phenotype** when considering all four genes.

2-17.

a. The combination of alleles in the egg and sperm allows only one genotype for the zygote: ***aa Bb Cc DD Ee***.

b. Because the inheritance of each gene is independent, you can use the product rule to determine the number of different types of gametes that are possible: 1 x 2 x 2 x 1 x 2 = **8 types of gametes** (as in problem 2-15). To figure out the types of gametes, consider the possibilities for each gene separately and then the possible combinations of genes in a consistent order. For each gene the possibilities are: *a*, (*B* : *b*), (*C* : *c*), *D*, and (*E* : *e*). The possibilities can be determined using the product rule. Thus for the first 2 genes [*a*] x [*B* : *b*] gives [*a B* : *a b*] x [*C* : *c*] gives [*a B C* : *a B c* : *a b C* : *a b c*] x [*D*] gives [*a B C D* : *a B c D* : *a b C D* : *a b c D*] x [*E* : *e*] gives [***a B C D E* : *a B C D e* : *a B c D E* : *a B c D e* : *a b C D E* : *a b C D e* : *a b c D E* : *a b c D e***]. This problem can also be visualized with a branched-line diagram:

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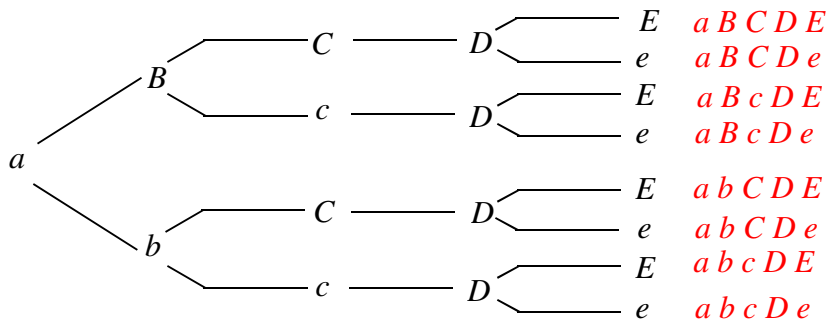

2-18. The first two parts of this problem involve the probability of occurrence of two independent traits: the sex of a child and galactosaemia. The parents are heterozygous for galactosaemia, so there is a 1/4 chance that a child will be affected (that is, homozygous recessive). The probability that a child is a girl is 1/2. The probability of an affected girl is therefore 1/4 x 1/2 = 1/8.

a. Fraternal (non-identical) twins result from two independent fertilization events and therefore the probability that both will be girls with galactosaemia is the product of their individual probabilities (see above); 1/8 x 1/8 = **1/64**.

b. For identical twins, one fertilization event gave rise to two individuals. The probability that both are girls with galactosaemia is **1/8**.

For parts *c*-*g*, remember that each child is an independent genetic event. The sex of the children is not at issue in these parts of the problem.

c. Both parents are carriers (heterozygous), so the probability of having an unaffected child is 3/4. The probability of 4 unaffected children is 3/4 x 3/4 x 3/4 x 3/4 = **81/256**.

d. The probability that at least one child is affected is all outcomes except the one mentioned in part *c*. Thus, the probability is 1 - 81/256 = **175/256**. Note that this general strategy for solving problems, where you first calculate the probability of all events except the one of interest, and then subtract that number from 1, is often useful for problems where direct calculations of the probability of interest appear to be very difficult.

e. The probability of an affected child is 1/4 while the probability of an unaffected child is 3/4. Therefore 1/4 x 1/4 x 3/4 x 3/4 = **9/256**.

f. The probability of 2 affected and 1 unaffected in any one particular birth order is 1/4 x 1/4 x 3/4 = 3/64. There are 3 mutually exclusive birth orders that could produce 2 affected and 1 unaffected – unaffected child first born, unaffected child second born, and unaffected child third born. Thus, there is a 3/64 + 3/64 + 3/64 = **9/64** chance that 2 out of 3 children will be affected.

g. The phenotype of any particular child is independent of all others, so the probability of an affected child is **1/4**.

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2-19. Diagram the cross, where *P* is the normal pigmentation allele and *p* is the albino allele:

normal (*P?*) x normal (*P?*) → albino (*pp*)

An albino must be homozygous recessive *pp*. The parents are normal in pigmentation and therefore could be *PP* or *Pp*. Because they have an albino child, **both parents must be carriers (*Pp*). The probability that their next child will have the *pp* genotype is 1/4**.

2-20. Diagram the cross:

yellow round x yellow round → 156 yellow round : 54 yellow wrinkled

The monohybrid ratio for seed shape is 156 round : 54 wrinkled = 3 round : 1 wrinkled. The parents must therefore have been heterozygous (*Rr*) for the pea shape gene. All the offspring are yellow and therefore have the *Yy* or *YY* genotype. **The parent plants were *Y– Rr* x *YY Rr*** (that is, you know at least one of the parents must have been *YY*).

2-21. Diagram the cross:

smooth black ♂ x rough white ♀ → F_1 rough black

→ F_2 8 smooth white : 25 smooth black : 23 rough white : 69 rough black

a. Since only one phenotype was seen in the first generation of the cross, we can assume that the parents were true-breeding, and that the F_1 generation consists of heterozygous animals. **The phenotype of the F_1 progeny indicates that rough and black are the dominant phenotypes. Four phenotypes are seen in the F_2 generation so there are two genes controlling the phenotypes in this cross**. **Therefore, *R* = rough, *r* = smooth; *B* = black, *b* = white**. In the F_2 generation, consider each gene separately. For the coat texture, there were 8 + 25 = 33 smooth : 23 + 69 = 92 rough, or a ratio of ~1 smooth : ~3 rough. For the coat colour, there were 8 + 23 = 31 white : 25 + 69 = 94 black, or about ~1 white : ~3 black, so the F_2 progeny support the conclusion that the F_1 animals were heterozygous for both genes.

b. An F_1 male is heterozygous for both genes, or *Rr Bb.* The smooth white female must be homozygous recessive; that is, *rr bb*. Thus, *Rr Bb* x *rr bb* → 1/2 *Rr* (rough) : 1/2 *rr* (smooth) and 1/2 *Bb* (black) : 1/2 *bb* (white). The inheritance of these genes is independent, so apply the product rule to find the expected phenotypic ratios among the progeny, or **1/4 rough black : 1/4 rough white : 1/4 smooth black : 1/4 smooth white**.

2-22. Diagram the cross:

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YY rr X *yy RR* → all *Yy Rr* → 9/16 *Y– R–* (yellow round) : 3/16 *Y– rr* (yellow wrinkled) : 3/16 *yy R–* (green round) : 1/16 *yy rr* (green wrinkled).

Each F_2 pea results from a separate fertilization event. The probability of 7 yellow round F_2 peas is $(9/16)^7$ = 4,782,969/268,435,456 = **0.018**.

2-23.

a. First diagram the cross, and then figure out the monohybrid ratios for each gene:

Aa Tt x *Aa Tt* → 3/4 *A–* (achoo) : 1/4 *aa* (non-achoo) and 3/4 *T–* (trembling) : 1/4 *tt* (non-trembling).

The probability that a child will be *A–* (and have achoo syndrome) is independent of the probability that it will lack a trembling chin, so the probability of a child with achoo syndrome but without trembling chin is 3/4 *A–* x 1/4 *tt* = **3/16**.

b. The probability that a child would have neither dominant trait is 1/4 *aa* x 1/4 *tt* = **1/16**.

2-24. The F_1 must be heterozygous for all the genes because the parents were pure-breeding (homozygous). The appearance of the F_1 establishes that the dominant phenotypes for the four traits are tall, purple flowers, axial flowers and green pods.

a. From a heterozygous F_1 x F_1, both dominant and recessive phenotypes can be seen for each gene. Thus, you expect 2 x 2 x 2 x 2 = 16 different phenotypes when considering the four traits together. The possibilities can be determined using the product rule with the pairs of phenotypes for each gene, because the traits are inherited independently. Thus: [tall : dwarf] x [green : yellow] gives [tall green : tall yellow : dwarf green : dwarf yellow] x [purple : white] gives [tall green purple : tall yellow purple : dwarf green purple : dwarf yellow purple : tall green white : tall yellow white : dwarf green white : dwarf yellow white] x [terminal : axial] which gives **tall green purple terminal : tall yellow purple terminal : dwarf green purple terminal : dwarf yellow purple terminal : tall green white terminal : tall yellow white terminal : dwarf green white terminal : dwarf yellow white terminal : tall green purple axial : tall yellow purple axial : dwarf green purple axial : dwarf yellow purple axial : tall green white axial : tall yellow white axial : dwarf green white axial : dwarf yellow white axial**. The possibilities can also be determined using the branched-line method shown below, which might in this complicated problem be easier to track.

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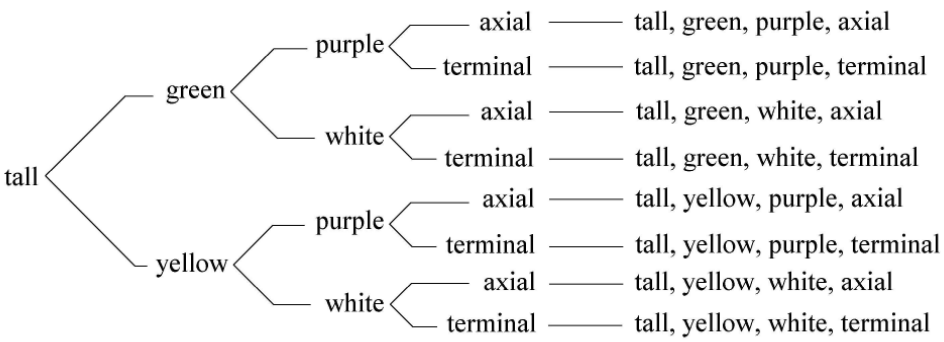

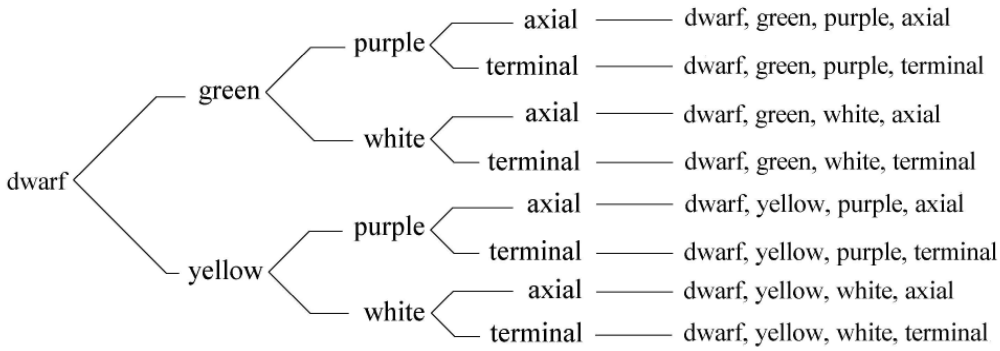

b. Designate the alleles: *T* = tall, *t* = dwarf; *G* = green; *g* = yellow; *P* = purple, *p* = white; *A* = axial, *a* = terminal. The cross *Tt Gg Pp Aa* (an F_1 plant) x *tt gg pp AA* (the dwarf parent) will produce 2 phenotypes for the tall, green and purple genes, but only 1 phenotype (axial) for the fourth gene or 2 x 2 x 2 x 1 = **8 different phenotypes**. The first 3 genes will give a 1/2 dominant : 1/2 recessive ratio of the phenotypes (for example 1/2 *T* : 1/2 *t*) as this is in effect a testcross for each gene. Thus, **the proportion of each phenotype in the progeny will be 1/2 x 1/2 x 1/2 x 1 = 1/8.**

Using either of the methods described in part *a*, the progeny will be **1/8 tall green purple axial : 1/8 tall yellow purple axial : 1/8 dwarf green purple axial : 1/8 dwarf yellow purple axial : 1/8 tall green white axial : 1/8 tall yellow white axial : 1/8 dwarf green white axial : 1/8 dwarf yellow white axial**.

2-25. For each separate cross, determine the number of genes involved. Remember that 4 phenotypic classes in the progeny means that 2 genes control the phenotypes. Next, determine the phenotypic ratio for each gene separately. A 3:1 monohybrid ratio tells you which phenotype is dominant and that both parents were heterozygous for the trait; in contrast, a 1:1 ratio results from a testcross where the dominant parent was heterozygous.

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a. There are 2 genes in this cross (4 phenotypes). One gene controls purple : white with a monohybrid ratio of 94 + 28 = 122 purple : 32 + 11 = 43 white or ~3 purple : ~1 white. The second gene controls spiny : smooth with a monohybrid ratio of 94 + 32 =126 spiny : 28 + 11 = 39 smooth or ~3 spiny : ~1 smooth. Thus, designate the alleles for the flower colour trait as ***P* = purple, *p* = white, with the *P* allele dominant to the *p* allele; and for the pod shape trait as *S* = spiny, *s* = smooth, with the *S* allele dominant to the *s* allele**. This is a straightforward dihybrid cross: ***Pp Ss* x *Pp Ss* → 9 *P– S–* : 3 *P– ss* : 3 *pp S–* : 1 *pp ss***.

b. The 1 spiny : 1 smooth ratio indicates a testcross for the pod shape gene. Because all progeny were purple, at least one parent plant must have been homozygous for the *P* allele of the flower colour gene. The cross was **either *PP Ss* x *P– ss* or *P– Ss* x *PP ss***.

c. This is similar to part *b*, except that here all the progeny were spiny so at least one parent must have been homozygous for the *S* allele. The 1 purple : 1 white testcross ratio indicates that **the parents were either *Pp S–* x *pp SS* or *Pp SS* x *pp S–***.

d. Looking at each trait individually, there are 89 + 31 = 120 purple : 92 + 27 = 119 white. A 1 purple : 1 white monohybrid ratio denotes a testcross. For the other gene, there are 89 + 92 = 181 spiny : 31 + 27 = 58 smooth, or a 3 spiny : 1 smooth ratio indicating that the parents were both heterozygous for the *S* gene. **The genotypes of the parents were *pp Ss* x *Pp Ss***.

e. There is a 3 purple : 1 white ratio among the progeny, so the parents were both heterozygous for the *P* gene. All progeny have smooth pods so the parents were both homozygous recessive *ss*. **The genotypes of the parents were *Pp ss* x *Pp ss***.

f. There is a 3 spiny : 1 smooth ratio, indicative of a cross between heterozygotes (*Ss* x *Ss*). All progeny were white so the parents must have been homozygous recessive *pp*. **The genotypes of the parents were *pp Ss* x *pp Ss***.

2-26. Three characters (genes) are being analyzed in this cross. While we can usually tell which alleles are dominant from the phenotype of the heterozygote, we are not told the phenotype of the heterozygote (that is, the original pea plant that was selfed). Instead, use the monohybrid phenotypic ratios to determine which allele is dominant and which is recessive for each gene. Consider height first. There are 272 + 92 + 88 + 35 = 487 tall plants and 93 + 31 + 29 + 11 = 164 dwarf plants. This is a ratio of ~3 tall : ~1 dwarf, indicating that **tall is dominant**. Next consider pod shape, where there are 272 + 92 + 93 + 31 = 488 inflated pods and 88 + 35 + 29 + 11 = 163 flat pods, or approximately 3 inflated : 1 flat, so **inflated is dominant**. Finally, consider flower colour. There were 272 + 88 + 93 + 29 = 482 purple flowers and 92 + 35 + 31 + 11 = 169 white flowers, or ~3 purple : ~1 white. Thus, **purple is dominant**.

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2-27. Diagram each of these crosses, remember that you were told that tiny wings = *t*, normal wings = *T*, narrow eye = *n* and oval (normal) eye = *N*. You thus know that one gene determines the wing trait and one gene determines the eye trait, and you further know the dominance relationship between the alleles of each gene.

In **cross 1**, all of the parents and offspring show the tiny wing phenotype so there is no variability in the gene controlling this trait, and all flies in this cross are *tt*. Note that the eye phenotypes in the offspring are seen in a ratio of 3 oval : 1 narrow. This phenotypic monohybrid ratio means that both parents are heterozygous for the gene (*Nn*). Thus **the genotypes for the parents in cross 1 are**: ***tt Nn*** ♂ **x** ***tt Nn*** ♀.

In **cross 2** consider the wing trait first. The female parent is tiny (*tt*) so this is a testcross for the wings. The offspring show both tiny and normal in a ratio of 82 : 85 or a ratio of 1 tiny : 1 normal. Therefore the normal male parent must be heterozygous for this gene (*Tt*). For eyes the narrow parent is homozygous recessive (*nn*) so again this is a testcross for this gene. Again both eye phenotypes are seen in the offspring in a ratio of 1 oval : 1 narrow, so the oval female parent is a *Nn* heterozygote. Thus **the genotypes for the parents in cross 2 are**: ***Tt nn*** ♂ **x** ***tt Nn*** ♀.

Consider the wing phenotype in the offspring of **cross 3**. Both wing phenotypes are seen in a ratio of 64 normal flies : 21 tiny or a 3 normal : 1 tiny. Thus both parents are *Tt* heterozygotes. The male parent is narrow (*nn*), so cross 3 is a testcross for eyes. Both phenotypes are seen in the offspring in a 1 normal : 1 narrow ratio, so the female parent is heterozygous for this gene. **The genotypes of the parents in cross 3 are:** ***Tt nn*** ♂ **x** ***Tt Nn*** ♀.

When examining **cross 4** you notice a monohybrid phenotypic ratio of 3 normal : 1 tiny for the wings in the offspring. Thus both parents are heterozygous for this gene (*Tt*). Because the male parent has narrow eyes (*nn*), this cross is a testcross for eyes. All of the progeny have oval eyes, so the female parent must be homozygous dominant for this trait. Thus **the genotypes of the parents in cross 4 are:** ***Tt nn*** ♂ **x** ***Tt NN*** ♀.

2-28.

a. Analyze each gene separately: *Tt* x *Tt* will give 3/4 *T*– (normal wing) offspring. The cross *nn* x *Nn* will give 1/2 *N*– (normal eye) offspring. To calculate the probability of the normal offspring apply the product rule to the normal portions of the monohybrid ratios by multiplying these two fractions: 3/4 *T*– x 1/2 *N*– = 3/8 *T*– *N*–. Thus **3/8 of the offspring of this cross will have normal wings and oval eyes**.

b. Diagram the cross:

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Tt nn ♀ x *Tt Nn* ♂ → ?

Find the phenotypic monohybrid ratio separately for each gene in the offspring. Then multiply these monohybrid ratios to find the phenotypic dihybrid ratio. A cross of *Tt* x *Tt* → 3/4 *T–* (normal wings) : 1/4 *tt* (tiny wings). For the eyes the cross is *nn* x *Nn* → 1/2 *N–* (oval) : 1/2 *nn* (narrow). Applying the product rule gives 3/8 *T– N–* (normal oval) : 3/8 *T– nn* (normal narrow) : 1/8 *tt N–* (tiny oval) : 1/8 *tt nn* (tiny narrow). When you multiply each fraction by 200 progeny you will see **75 normal oval : 75 normal narrow : 25 tiny oval : 25 tiny narrow**.

2-29.

a. **The protein specified by the pea colour gene is an enzyme called Sgr**, which is required for the breakdown of the green pigment chlorophyll. (See Figure A in the Fast Forward box "Genes Encode Proteins").

b. **The *y* allele could be a null allele** because it does not specify the production of any of the Sgr enzyme.

c. The *Y* allele is dominant because in the heterozygote, **the single *Y* allele will lead to the production of some Sgr enzyme**, even if the *y* allele cannot specify any Sgr. **The amount of the Sgr enzyme made in heterozygotes is sufficient for yellow colour.**

d. **In *yy* peas, the green chlorophyll cannot be broken down**, so this pigment stays in the peas, which remain green in colour.

e. If the amount of Sgr protein is proportional to the number of functional copies of the gene, then *YY* homozygotes should have twice the amount of Sgr protein as do *Yy* heterozygotes. Yet both *YY* and *Yy* peas are yellow. These observations suggest that **half the normal amount of Sgr enzyme is sufficient for the pea to break down enough chlorophyll so that the pea will still be yellow.**

f. Just as was seen in part *e*, for many genes (including that for pea colour), half the amount of the protein specified by the gene is sufficient for a normal phenotype. Thus, in most cases, even if the gene is essential, heterozygotes for null alleles will survive. **The advantage of having two copies of essential genes is then that even if one normal allele becomes mutated (changed) so that it becomes a null allele, the organism can survive because half the normal amount of gene product is usually sufficient for survival.**

g. **Yes, a single pea pod could contain peas with different phenotypes because a pod is an ovary that contains several ovules (eggs), and each pea represents a single fertilization event involving one egg and one sperm (from one pollen grain).** If the female plant was *Yy*, or *yy*, then it is possible that some peas in the same pod would be yellow and others green. For example, fertilization of a *y* egg with *Y* pollen would yield a yellow pea, but if the pollen grain was *y*, the pea

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would be green. However, a pea pod could not contain peas with different phenotypes if the female plant was *YY*, because all the peas produced by this plant would be yellow.

h. **Yes, it is possible that a pea pod could be different in colour from a pea growing within it.** One reason is that, as just seen in part *g*, **a single pod can contain green and yellow peas**. But a more fundamental reason is that **one gene controls the phenotype of pea colour, while a different gene controls the separate phenotype of pod colour.**

2-30. If the alleles of the pea colour and pea shape genes inherited from a parent in the P generation always stayed together and never separated, then the gametes produced by the doubly heterozygous F_1 individuals in Figure 2.14 would be either *Y R* or *y r*. (Note that only two possibilities would exist, and these would be in equal frequencies.) On a Punnett square (male gametes shaded in *blue*, female gametes in *pink*):

	Y R ½	*y r* ½
Y R ½	*YY RR* ¼	*Yy Rr* ¼
y r ½	*Yy Rr* ¼	*yy rr* ¼

Thus **the genotypic ratios of the F_2 progeny would be 1/4 *YY RR*, 1/2 *Yy Rr* , and 1/4 *yy rr*. The phenotypic ratios among the F_2 progeny would be 3/4 yellow round and 1/4 green wrinkled.** These results make sense because if the alleles of the two genes were always inherited as a unit, you would expect the same ratios as in a monohybrid cross.

2-31. Similar to what you saw in Figure A in the Fast Forward box "Genes Encode Proteins", **the most likely biochemical explanation is that the dominant allele *L* specifies functional G3βH enzyme, while the recessive allele *l* is incapable of specifying any functional enzyme** (in nomenclature you will see in later chapters, *l* is a *null allele*). The functional enzyme can synthesize the growth hormone gibberellin, so plants with the *L* allele are tall. **Even half the normal amount of this enzyme is sufficient for the tall phenotype, explaining why *Ll* heterozygotes are tall.**

2-32.

a. As in Problem 31 above, **the dominant allele *P* most likely specifies a functional product (in this case, the protein bHLH), while the recessive *p* allele cannot specify any functional protein**. The fact that the hybrid is purple (as shown on Figure 2.7) indicates that half the normal amount of active bHLH protein is sufficient for purple colour.

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b. **Yes, flower colour could potentially be controlled by genes specifying the enzymes DFR, ANS, or 3GT in addition to the gene specifying the bHLH protein.** Alleles specifying functional enzymes would yield purple colour, while those that could not produce functional enzymes would cause white colour. It is likely that the alleles for purple colour would be dominant.

Section 2.3 – Mendelian Inheritance in Humans

2-33.

a. **Recessive** - two unaffected individuals have an affected child— **II-1, V-2** (***aa***). Therefore, the parents in generation I and those involved in the consanguineous marriage must all be carriers – **I-1, I-2, IV-1, IV-2 (*Aa*).**

b. **Dominant** - the trait is seen in each generation and every affected person (***A–***) has an affected parent. Note that III-3 is unaffected (*aa*) even though both his parents are affected; this would not be possible for a recessive trait. The term "carrier" is not applicable, because everyone with a single *A* allele shows the trait.

c. **Recessive** - two unaffected, carrier parents – **II-4, II-5 (*Aa*)** have an affected child— **III-4** (***aa***), as in part *a*. Individual **I-2** is also affected (***aa***) and thus has transmitted a recessive disease allele to all of his children, making individuals **II-1, II-2, and II-3** carriers (***Aa***) also.

2-34.

a. Cutis laxa must be a recessive trait because affected child II-4 has normal parents. Because II-4 is affected she must have received a disease allele (*CL*) from both parents. The mother (I-3) and the father (I-4) are both heterozygous (CL^+ *CL*). **The trait is thus recessive**.

b. You are told that this trait is rare, so unrelated people in the pedigree, like I-2, are almost certainly homozygous normal (CL^+ CL^+). Diagram the cross that gives rise to II-2: *CL CL* (I-1) x CL^+ CL^+ (I-2) → CL^+ *CL*. Thus the **probability that II-2 is a carrier is very close to 100 percent**. (In Chapter 12 you will find the definition of a term called the *allele frequency*; if the value of the allele frequency in the population under study is known, you can calculate the very low likelihood that II-2 is a carrier.)

c. As described in part *a* both parents in this cross are carriers: CL^+ *CL* x CL^+ *CL*. II-3 is <u>not</u> affected so he cannot have the *CL CL* genotype. Therefore there is a 1/3 probability that he has the CL^+ CL^+ genotype and a **2/3 probability that he is a carrier** (CL^+ *CL*).

d. As shown in part *b*, II-2 must be a carrier (CL^+ *CL*). In order to have an affected child II-3 must also be a carrier. The probability of this is 2/3 as shown in part *c*. The probability of two

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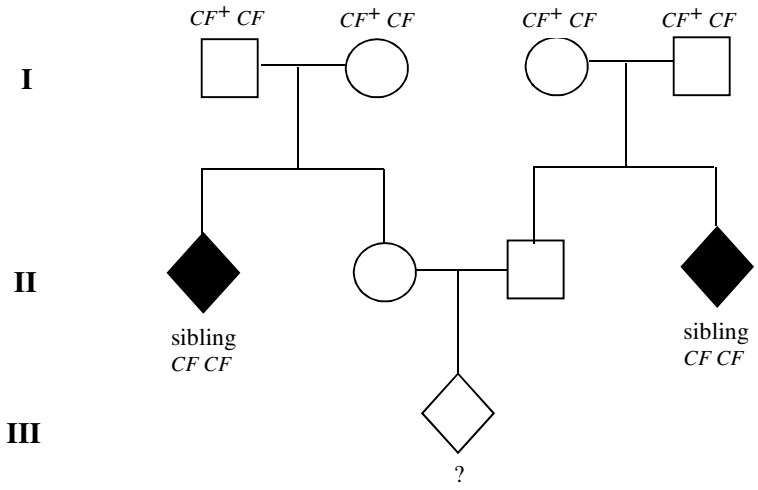
heterozygous parents having an affected child is 1/4. Apply the product rule to these probabilities: (1 probability that II-2 is CL^+ *CL*) x (2/3 probability that II-3 is CL^+ *CL*) x (1/4 probability of an affected child from a mating of two carriers) = 2/12 = **1/6**.

2-35. Diagram the cross! In humans, this is usually done as a pedigree. Remember that the affected siblings must be *CF CF*.



a. **The probability that II-2 is a carrier is 2/3**. Both families have an affected sibling, so both sets of parents (that is, all the people in generation I) must have been carriers. Thus, the expected genotypic ratio in the children is 1/4 affected : 1/2 carrier : 1/4 homozygous normal. II-2 is NOT affected, so she cannot be *CF CF*. Of the remaining possible genotypes, 2 are heterozygous. There is therefore a 2/3 chance that she is a carrier.

b. **The probability that II-2 x II-3 will have an affected child** is 2/3 (the probability that the mother is a carrier as seen in part *a*) x 2/3 (the probability the father is a carrier using the same reasoning) x 1/4 (the probability that two carriers can produce an affected child) = 4/36 = **1/9**.

c. The probability that both parents are carriers and that their child will be a carrier is 2/3 x 2/3 x 1/2 = 2/9 (using the same reasoning as in part *b*, except asking that the child be a carrier instead of affected). However, it is also possible for CF^+ CF^+ x CF^+ *CF* parents to have children that are carriers. Remember that there are 2 possible ways for this particular mating to occur – homozygous father x heterozygous mother or *vice versa*. Thus the probability of this sort of mating is 2 x 1/3 (the probability that a particular parent is CF^+ CF^+) x 2/3 (the probability that the other parent is CF^+ *CF*) x 1/2 (the probability that such a mating could produce a carrier child) = 2/9. **The probability that a child could be a carrier** from either of these two scenarios (where both parents

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are carriers or where only one parent is a carrier) is the sum of these mutually exclusive events, or 2/9 + 2/9 = **4/9**.

2-36.

a. Because the disease is rare the affected father is most likely to be heterozygous (*HD*$^+$ *HD*). **There is a 1/2 chance that the son** inherited the *HD* allele from his father and **will develop the disease.**

b. **The probability of an affected child is:** 1/2 (the probability that Joe is *HD*$^+$ *HD*) x 1/2 (the probability that the child inherits the *HD* allele if Joe is *HD*$^+$ *HD*) = **1/4**.

2-37. The trait is recessive because pairs of unaffected individuals (I-1 x I-2 as well as II-3 x II-4) had affected children (II-1, III-1, and III-2). There are also two cases in which an unrelated individual must have been a carrier (II-4 and either I-1 or I-2), so **the disease allele appears to be common in the population.**

2-38.

a. **The inheritance pattern seen in Figure 2.20 could be caused by a rare dominant mutation**. In this case, the affected individuals would be heterozygous (*HD*$^+$ *HD*) and the normal individuals would be *HD*$^+$ *HD*$^+$. Any mating between an affected individual and an unaffected individual would give 1/2 normal (*HD*$^+$ *HD*$^+$) : 1/2 affected (*HD*$^+$ *HD*) children. **However, the same pattern of inheritance could be seen if the disease were caused by a common recessive mutation**. In the case of a common recessive mutation, all the affected individuals would be *HD HD*. Because the mutant allele is common in the population, most or even all of the unrelated individuals could be assumed to be carriers (*HD*$^+$ *HD*). Matings between affected and unaffected individuals would then also yield phenotypic ratios of progeny of 1/2 normal (*HD*$^+$ *HD*) : 1/2 affected (*HD HD*).

b. **Determine the phenotype of the 14 children of III-6 and IV-6. If the disease is due to a recessive allele**, then III-6 and IV-6 must be homozygous for this recessive allele, and **all their children must have the disease. If the disease is due to a dominant mutation**, then III-6 and IV-6 must be heterozygotes (because they are affected but they each had one unaffected parent), and **1/4 of their 14 children would be expected to be unaffected.**

Alternatively, you could **look at the progeny of matings between unaffected individuals** in the pedigree such as III-1 and an unaffected spouse. **If the disease were due to a dominant mutation**, **these matings** would all be homozygous recessive x homozygous recessive and **would never give affected children**. **If the disease is due to a recessive mutation**, then many of these

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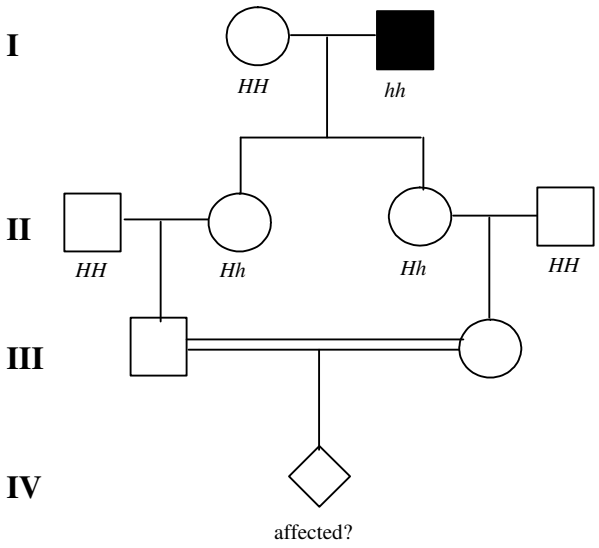
individuals would be carriers, and if the trait is common then at least some of the spouses would also be carriers, so **such matings could give affected children**.

2-39. Diagram the cross by drawing a pedigree:



a. Assuming the disease is very rare, the first generation is *HH* unaffected (I-1) x *hh* affected (I-2). Thus, both of the children (II-2 and II-3) must be carriers (*Hh*). Again assuming this trait is rare in the population, those people marrying into the family (II-1 and II-4) are homozygous normal (*HH*). Therefore, the probability that III-1 is a carrier is 1/2; III-2 has the same chance of being a carrier. **Thus the probability that a child produced by these two first cousins would be affected** is 1/2 (the probability that III-1 is a carrier) x 1/2 (the probability that III-2 is a carrier) x 1/4 (the probability the child of two carriers would have an *hh* genotype) = **1/16 = 0.0625**.

b. If 1/10 people in the population are carriers, then the probability that II-1 and II-4 are *Hh* is 0.1 for each. In this case an affected child in generation IV can only occur if III-1 and III-2 are both carriers. III-1 can be a carrier as the result of 2 different matings: (i) II-1 homozygous normal x II-2 carrier or (ii) II-1 carrier x II-2 carrier. (Note that whether I-1 is *HH* or *Hh*, II-2 must be a carrier because of the normal phenotype (II-2 cannot be *hh*) and the fact that one parent was affected.) The probability of III-1 being a carrier is thus the probability of mating (i) x the probability of generating an *Hh* child from mating (i) + the probability of mating (ii) x the probability of generating an *Hh* child from mating (ii) = 0.9 (the probability II-1 is *HH*, which is the probability for mating [i]) x 1/2 (the probability that III-1 will inherit *h* in mating [i]) + 0.1 (the probability II-1 is *Hh,* which is the probability for mating [ii]) x 2/3 (the probability that III-1 will inherit *h* in mating [ii]; remember that III-1 is known not to be *hh*) = 0.45 + 0.067 = 0.517. The chance that III-2 will inherit *h* is exactly the same. **Thus, the probability that IV-1 is *hh*** = 0.517 (the probability

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III-1 is *Hh*) x 0.517 (the probability that III-2 is *Hh*) x 1/4 (the probability the child of two carriers will be *hh*) **= 0.067**. **This number is slightly higher than the answer to part *a*, which was 0.0625, so the increased likelihood that II-1 or II-4 is a carrier makes it only slightly more likely that IV-1 will be affected.**

2-40.

a. Both diseases are known to be rare, so normal people marrying into the pedigree are assumed to be homozygous normal. **Nail-patella (*N*) syndrome is dominant** because all affected children have an affected parent. **Alkaptonuria (*a*) is recessive** because the affected children are the result of a consanguineous mating between 2 unaffected individuals (III-3 x III-4). Because alkaptonuria is a rare disease, it makes sense to assume that III-3 and III-4 inherited the same *a* allele from a common ancestor. Genotypes: **I-1 *nn Aa*; I-2 *Nn AA* (or I-1 *nn AA* and I-2 *Nn Aa*); II-1 *nn AA*; II-2 *nn Aa*; II-3 *Nn A–*; II-4 *nn A–*; II-5 *Nn Aa*; II-6 *nn AA*; III-1 *nn AA*; III-2 *nn A–*; III-3 *nn Aa*; III-4 *Nn Aa*; III-5 *nn A–*; III-6 *nn A–*; IV-1 *nn A–*; IV-2 *nn A–*; IV-3 *Nn A–*; IV-4 *nn A–*; IV-5 *Nn aa*; IV-6 *nn aa*; IV-7 *nn A–*.**

b. The cross is *nn A–* (IV-2) x *Nn aa* (IV-5). The ambiguity in the genotype of IV-2 is due to the uncertainty of his father's genotype (III-2). His parents' genotypes are *nn AA* (II-1) x *nn Aa* (II-2) so there is a 1/2 chance III-2 is *nn AA* and a 1/2 chance he is *nn Aa*. Thus, for each of the phenotypes below you must consider both possible genotypes for IV-2. For each part below, calculate the probability of the child inheriting the correct gametes from IV-2 x the probability of obtaining the correct gametes from IV-5 to give the desired phenotype. If both the possible IV-2 genotypes can produce the needed gametes, you will need to sum the two probabilities.

- For the child to have **both syndromes** (*N– aa*), IV-2 would have to contribute an *n a* gamete. This could only occur if IV-2 were *nn Aa.* The probability IV-2 is *nn Aa* is 1/4: For IV-2 to be *nn Aa*, III-2 would have had to be *nn Aa* and would also have had to give an *n a* gamete to IV-2. The probability of each of those events is 1/2, so the chance of both of them occurring is 1/2 x 1/2 = 1/4. (Note that we can assume that II-2 is *nn Aa* because III-3 must have given two of her children an *a* allele. Therefore, both II-2 and III-3 must be *nn Aa*). If IV-2 is *nn Aa*, the chance that he would give a child an *n a* gamete is 1/2. The probability that IV-5 would supply an *N a* gamete is also 1/2. Thus, **the probability that the child would have both syndromes is 1/4 x 1/2 x 1/2 = 1/16**. There is no need to sum probabilities in this case because IV-2 cannot produce an *n a* gamete if his genotype is *nn AA*.
- For the child to have only **nail-patella syndrome** (*N– A–*), IV-2 would have to provide an *n A* gamete and IV-5 an *N a* gamete. This could occur if IV-2 were *nn Aa*; the probability is 1/4 (the probability IV-2 is *Aa*) x 1/2 (the probability of an *A* gamete if IV-2 is *Aa*) x 1/2 (the

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probability of an *N a* gamete from IV-5] = 1/16. This could also occur if IV-2 were *nn AA*. Here, the probability is 3/4 (the probability IV-2 is *nn AA*) x 1 (the probability of an *n A* gamete if IV-2 is *nn AA*) x 1/2 (the probability of an *N a* gamete from IV-5) = 3/8. Summing the probabilities for the two mutually exclusive IV-2 genotypes, **the probability that the child of IV-2 and IV-5 would have only nail-patella syndrome is 1/16 + 3/8 = 7/16**.

- For the child to have just alkaptonuria (*nn aa*), IV-2 would have to contribute an *n a* gamete. This could only occur if IV-2 were *nn Aa.* The probability IV-2 is *nn Aa* is 1/4, and the probability of receiving an *n a* gamete from IV-2 if he is *nn Aa* is 1/2. The probability that IV-5 would supply an *n a* gamete is also 1/2. Thus, **the probability that the child of IV-2 and IV-5 would have only alkaptonuria** is 1/4 x 1/2 x 1/2 **= 1/16**. There is no need to sum probabilities in this case because IV-2 cannot produce an *n a* gamete if his genotype is *nn AA*.
- **The probability of neither defect** is 1 – (sum of the first 3) = 1 - (1/16 + 7/16 + 1/16) = 1 - 9/16 **= 7/16**. You can make this calculation because there are only the four possible outcomes and you have already calculated the probabilities of three of them.

2-41. Diagram the cross(es):

midphalangeal x midphalangeal → 1853 midphalangeal : 209 normal

M? x *M*? → *M*? : *mm*

The following crosses are possible:

MM x *MM* → all *MM*

Mm x *MM* → all *M–*

MM x *Mm* → all *M–*

Mm x *Mm* → 3/4 *M–* : 1/4 *mm*

The 209 normal children must have arisen from the last cross, so approximately 3 x 209 = ~630 children should be their *M–* siblings. Thus, about 840 of the children or **~40% came from the last mating** and the other 60% of the children were the result of one or more of the other matings. This problem illustrates that much care in interpretation is required when the results of many matings in mixed populations are reported (as opposed to the results of matings where individuals have defined genotypes).

2-42. Draw a Punnett square (male gametes shaded in *blue*, female gametes in *pink*):

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	HD ½	*HD*⁺ ½
HD⁺ ½	*HD HD*⁺ ¼ **affected**	*HD*⁺ *HD*⁺ ¼ **Unaffected**
HD⁺ ½	*HD HD*⁺ ¼ **affected**	*HD*⁺ *HD*⁺ ¼ **Unaffected**

a. An equally likely possibility exists that any child produced by this couple will be affected (A) or unaffected (U) . For two children, the possibilities are: AA, AU, UA, UU. The case in which only the second child is affected is UA; this is one of the four possibilities so **the probability that only the second child is affected is 1/4.**

b. From the list just presented in part *a*, you can see that there are two possibilities in which only one child is affected: AU and UA. The probability that either of these two mutually exclusive possibilities will occur is the sum of their independent probabilities: 1/4 + 1/4 = **1/2.**

c. From the list just presented in part *a*, you can see that there is only one possibility in which no child is affected: UU. The probability of this event is **1/4.**

d. If this family consisted of 10 children, **the case in which only the second child out of 10 is affected** (that is, UAUUUUUUUU) **has a probability of $1/2^{10}$ = 1/1024 = ~0.00098**. This probability is based on the facts that each birth is an independent event, and that the chance of U and A are each 1/2. We thus use the product rule to determine the chance that each of those 10 independent events will occur in a particular way – a particular birth order.

In a family of ten children, 10 different outcomes (birth orders) exist that satisfy the criterion that only 1 child has the disease. Only the first child could have the disease, only the second child, only the third child, etc. :

1. **A**UUUUUUUUU
2. U**A**UUUUUUUU
3. UU**A**UUUUUUU
4. UUU**A**UUUUUU
5. UUUU**A**UUUUU
6. UUUUU**A**UUUU
7. UUUUUU**A**UUU
8. UUUUUUU**A**UU
9. UUUUUUUU**A**U
10. UUUUUUUUU**A**

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We have already calculated that the chance of one of these outcomes in particular (#2) is 1/1024. As each of the 10 possibilities has the same probability, **the probability that only one child is affected would be 10 x (1/1024) = 10/1024 = ~0.0098.**

Only one possibility exists in which no child would be affected (UUUUUUUUUU), **and just like any other specific outcome, this one has a probability of 1/1024 = ~0.00098.**

e. One way to determine the probability that four children in a family of ten will have the disease is to write down all possible outcomes for the criterion, as we did above for the second answer in part *d*. Then, also as we did above, sum their individual probabilities, each of which is $(1/2)^{10}$ just as before. If you start to do this……

1. **AAAA**UUUUUU
2. **AAA**U**A**UUUUU
3. **AAA**UU**A**UUUU
4. **AAA**UUU**A**UUU
5. **AAA**UUUU**A**UU
6. **AAA**UUUUU**A**U
7. **AAA**UUUUUU**A**
8. **AA**U**AA**UUUUU
9. **AA**U**A**U**A**UUUU
10. **AA**U**A**UU**A**UUU

etc.

…..you will realize fairly quickly that writing down every possible birth order in this case is quite a difficult task and you are likely to miss some outcomes. In short – this is not a good way to find the answer! For questions like this, it is far preferable to use a mathematical tool called the *binomial theorem* in order to determine the number of possible outcomes that satisfy the criterion. The binomial theorem looks like this:

P (**X** will occur **s** times, and **Y** will occur **t** times, in **n** trials) =

$$\frac{\mathbf{n}!}{\mathbf{s}! \times \mathbf{t}!} \quad (\mathbf{p}^{\mathbf{s}} \times \mathbf{q}^{\mathbf{t}})$$

P = the probability of what is in parentheses
p = P(**X**)
q = P(**Y**)

X and **Y** are the only two possibilities, so **p** + **q** = 1.
Also, **s** + **t** = **n**.

Remember that **!** means *factorial*: for example, 5! = 5 × 4 × 3 × 2 × 1.

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To apply the binomial theorem to the question at hand (assuming you can still remember what the question was!), we'll let **X** = a child has the disease (A), and **Y** = a child does not have the disease (U). Then, **s** = 4, **t** = 6, **n** = 10, **p** = 1/2, and **q** = 1/2. The answer to the question is then:

P (4 A and 6 U children out of 10) = (10! / 4! × 6!) ($1/2^4 \times 1/2^6$).

Notice that ($\mathbf{p^s \times q^t}$) = ($1/2^4 \times 1/2^6$) = $1/2^{10}$. This factor of the binomial theorem equation is the probability of each single birth order, as we saw previously in part *d* above. To get the answer to our question, we need to multiply this factor (the probability of each single birth order) by the number of different birth orders that satisfy our criterion. From the equation in the box above, this second factor is [**n!/(s! × t!)**] = (10! / 4! × 6!) = 210. Thus, **the probability (P) of only 4 children having the disease in a family of 10 children is $1/2^{10} \times 210 \approx 21\%$**.

2-43. In the case of cystic fibrosis, the alleles causing the disease do not specify active protein [in this case, the cystic fibrosis transmembrane receptor (CFTR)]. Some *CF* disease alleles specify defective CFTR proteins that do not allow the passage of chloride ions, while other *CF* disease alleles do not specify any CFTR protein at all. As you will learn in a later chapter, such alleles are called *loss-of-function* alleles. In a heterozygote, the normal CF^+ allele still specifies active CFTR protein, which allows for the passage of chloride ions. Because the phenotype of the heterozygote is unaffected, the amount of active CFTR protein allows passage of enough chloride ions for the cells to function normally. Again as you will see, most loss-of-function alleles are recessive to normal alleles for similar reasons. (But it is important to realize that important exceptions are known in which loss-of-function mutations are actually dominant to normal alleles.)

In the case of Huntington disease, the disease-causing allele is dominant. The reason is that **the huntingtin protein specified by this *HD* allele has**, **in addition to its normal function** (which is not entirely understood), **a second function that is toxic to nerve cells.** This makes the *HD* disease allele a *gain-of-function* allele. The reason *HD* is dominant to HD^+ is that the protein specified by the disease allele will be toxic to cells even if the cells have normal huntingtin protein specified by the normal allele. Most (but again not all) gain-of-function mutations are dominant for similar reasons.

Section 2.4 – Extensions to Mendel for Single-Gene Inheritance

2-44. The problem states that the intermediate pink phenotype is caused by incomplete dominance between the alleles of a single gene. We suggest that you employ genotype symbols that can show the lack of complete dominance; the obvious *R* for red and *r* for white does not reflect the complexity of this situation. In such cases we recommend using a base letter as the gene symbol and then employing superscripts to show the different alleles. To avoid any possible misinterpretations, it is always

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advantageous to include a separate statement making the complexities of the dominant/recessive complications clear. Designate the two alleles f^r = red and f^w = white, so the possible genotypes are f^rf^r = red; f^rf^w = pink; and f^wf^w = white. Note that the phenotypic ratio is the same as the genotypic ratio in incomplete dominance.

a. Diagram the cross: f^rf^w x f^rf^w → **1/4 f^rf^r (red) : 1/2 f^rf^w (pink) : 1/4 f^wf^w (white)**.
b. f^wf^w x f^rf^w → **1/2 f^rf^w (pink) : 1/2 f^wf^w (white)**.
c. f^rf^r x f^rf^r → **1 f^rf^r (red)**.
d. f^rf^r x f^rf^w → **1/2 f^rf^r (red) : 1/2 f^rf^w (pink)**.
e. f^wf^w x f^wf^w → **1 f^wf^w (white)**.
f. f^rf^r x f^wf^w → **1 f^rf^w (pink)**.

The cross shown in **part f** is the most efficient way to produce pink flowers, because all the progeny will be pink.

2-45. Diagram the cross: yellow x yellow → 38 yellow : 22 red : 20 white
Three phenotypes in the progeny show that the yellow parents are not true breeding. The ratio of the progeny is close to 1/2 : 1/4 : 1/4. This is the result expected for crosses between individuals heterozygous for incompletely dominant genes. Thus:

c^rc^w x c^rc^w → 1/2 c^rc^w (yellow) : 1/4 c^rc^r (red) : 1/4 c^wc^w (white).

2-46.

a. Diagram the cross: e^+e^+ x e^+e → 1/2 e^+e^+ : 1/2 e^+e. The trident marking is only found in the heterozygotes, so the probability is **1/2**.
b. The offspring with the trident marking are e^+e, so the cross is e^+e x e^+e → 1/4 ee : 1/2 e^+e : 1/4 e^+e^+. Therefore, of 300 offspring, **75 should have ebony bodies, 150 should have the trident marking, and 75 should have honey-coloured bodies**.

2-47. The cross is: white long x purple short → 301 long purple : 99 short purple : 612 long pink : 195 short pink : 295 long white : 98 short white
Deconstruct this dihybrid phenotypic ratio for two genes into separate constituent monohybrid ratios for each of the 2 traits, flower colour and pod length. For flower colour note that there are 3 phenotypes: 301 + 99 purple : 612 +195 pink : 295 + 98 white = 400 purple : 807 pink : 393 white = 1/4 purple : 1/2 pink : 1/4 white. This is a typical monohybrid ratio for incompletely dominant alleles, so **flower colour is caused by incompletely dominant alleles of a gene, with c^p giving purple when homozygous, c^w giving white when homozygous, and the c^pc^w heterozygotes giving pink.** For pod length, the phenotypic ratio is (301 + 612 + 295) long : (99 + 195 + 98) short = 1208 long : 392

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short = 3/4 long : 1/4 short. This 3:1 ratio is that expected for a cross between individuals heterozygous for a gene in which one allele is completely dominant to the other, so **pod shape is controlled by a single gene with the long allele (*L*) completely dominant to the short allele (*l*)**.

2-48. A cross between individuals heterozygous for incompletely dominant alleles of a gene give a ratio of 1/4 (one homozygote) : 1/2 (heterozygote with the same phenotype as the parents) : 1/4 (other homozygote). Because the problem already states which genotypes correspond to which phenotypes, you know that the colour gene will give a monohybrid phenotypic ratio of 1/4 red : 1/2 purple : 1/4 white, while the shape gene will give a monohybrid phenotypic ratio of 1/4 long : 1/2 oval : 1/4 round.

Because the inheritance of these two genes is independent, use the product rule to generate all the possible phenotype combinations (note that there will be 3 x 3 = 9 classes) and their probabilities, thus generating the dihybrid phenotypic ratio for two incompletely dominant genes: **1/16 red long : 1/8 red oval : 1/16 red round : 1/8 purple long : 1/4 purple oval : 1/8 purple round : 1/16 white long : 1/8 white oval : 1/16 white round**. As an example, to determine the probability of red long progeny, multiply 1/4 (probability of red) x 1/4 (probability of long) = 1/16. If you have trouble keeping track of the 9 possible classes, it may be helpful to list the classes in the form of a branched-line diagram or table as follows:

Phenotype	*Probability of phenotype*
red, long	1/4 × 1/4=1/16
red, oval	1/4 × 1/2=1/8
red, round	1/4 × 1/4=1/16
purple, long	1/2 × 1/4=1/8
purple, oval	1/2 × 1/2=1/4
purple, round	1/2 × 1/4=1/8
white, long	1/4 × 1/4=1/16
white, oval	1/4 × 1/2=1/8
white, round	1/4 × 1/4=1/16

2-49. In Mendel's *Pp* heterozygotes, the amount of enzyme leading to purple pigment is sufficient to produce purple colour as intense as the purple colour in *PP* homozygotes. Presumably the heterozygote has enough enzyme P so that the maximal level of purple pigment is produced; more enzyme cannot make more purple pigment.

In the snapdragons in Figure 2.24, the amount of red pigment in the *Aa* heterozygote is less than that in the *AA* homozygote. Presumably here, the amount of enzyme A catalyzing the production of the red pigment in the heterozygotes is insufficient to produce the maximum level of the red pigment seen

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in the *AA* homozygote. That is, in this case **the intensity of the phenotype is proportional to the dosage of functional alleles (1 in the *Aa* heterozygote, 2 in the *AA* homozygote).**

2-50.

a. A person with sickle-cell anaemia is a homozygote for the sickle-cell allele: $\boldsymbol{Hb\beta^S\ Hb\beta^S}$.

b. The child must be homozygous $Hb\beta^S\ Hb\beta^S$ and therefore must have inherited a mutant allele from each parent. Because the parent is phenotypically normal, he/she must be a **carrier with genotype** $\boldsymbol{Hb\beta^S\ Hb\beta^A}$.

c. Each individual has two alleles of every gene, including the β-globin gene. If an individual is heterozygous, he/she has two different alleles. Thus, if each parent is heterozygous for different alleles, there are **four possible alleles** that could be found in the five children. This is the maximum number of different alleles possible (barring the very rare occurrence of a new, novel mutation in a gamete that gave rise to one of the children). If one or both of the parents were homozygous for any one allele, the number of alleles distributed to the children would of course be less than four.

2-51. Remember that the gene determining ABO blood groups has 3 alleles and that $I^A = I^B > i$.

a. The O phenotype means the girl's genotype is *ii*. Each parent contributed an *i* allele, so her parents could be ***ii*** **(O) or** $\boldsymbol{I^Ai}$ **(A) or** $\boldsymbol{I^Bi}$ **(B)**.

b. A person with the B phenotype could have either genotype I^BI^B or genotype I^Bi. The mother is A and thus could not have contributed an I^B allele to this daughter. Instead, because the daughter clearly does not have an I^A allele, the mother must have contributed the *i* allele to this daughter. The mother must have been an I^Ai heterozygote. The father must have contributed the I^B allele to his daughter, so he could be **either** $\boldsymbol{I^BI^B}$**,** $\boldsymbol{I^Bi}$**, or** $\boldsymbol{I^AI^B}$.

c. The genotypes of the girl and her mother must both be I^AI^B. The father must contribute either the I^A or the I^B allele, so there is only one phenotype and genotype which would exclude a man as her father - **the O phenotype (genotype *ii*)**.

2-52. To approach this problem, look at the mother/child combinations to determine what alleles the father must have contributed to each child's genotype.

a. The father had to contribute I^B, *N,* and Rh^- alleles to the child. The only male fitting these requirements is **male d** whose phenotype is B, MN, and Rh^+ (note that the father must be Rh^+Rh^- because the daughter is Rh^-).

b. The father had to contribute *i, N,* and Rh^- alleles. The father could be either male c (O MN Rh^+) or male d (B MN Rh^+). As we saw previously, male c is the only male fitting the requirements for the father in part *a*. Assuming one child per male as instructed by the problem, the father in part *b* must be **male c**.

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c. The father had to contribute I^A, *M,* and Rh^- alleles. Only **male b** (A M Rh^+) fits these criteria.

d. The father had to contribute either I^B or *i, M,* and Rh^-. Three males have the alleles required: these are male a, male c, and male d. However, of these three possibilities, only **male a** remains unassigned to a mother/child pair.

2-53. Designate the alleles: p^m (marbled) > p^s (spotted) = p^d (dotted) > p^c (clear).

a. The expected phenotypes of the F_1 plants from the two original parental crosses are **marbled ($p^m p^s$)** from the first cross **and dotted ($p^d p^c$)** from the second cross.

b. Diagram the crosses:

1. $p^m p^m$ (homozygous marbled) x $p^s p^s$ (spotted) → $p^m p^s$ (marbled F_1)
2. $p^d p^d$ x $p^c p^c$ → $p^d p^c$ (dotted F_1)
3. $p^m p^s$ x $p^d p^c$ → 1/4 $p^m p^d$ (marbled) : 1/4 $p^m p^c$ (marbled) : 1/4 $p^s p^d$ (spotted dotted) : 1/4 $p^s p^c$ (spotted) = **1/4 spotted dotted : 1/2 marbled : 1/4 spotted**.

2-54. Suppose, as maintained by your fellow student, that spotting is due to the action of one gene with alleles *S* (spotting) and *s* (no spots), and that dotting is due to the action of a second gene with alleles *D* (dotting) and *d* (no spots). The cross series shown in Figure 2.25a, starting with true-breeding spotted and true-breeding dotted strains, could be diagrammed as:

SS dd x *ss DD* → *Ss Dd* (spotted and dotted F_1) → F_2 consisting of 9 *S*– *D*– (spotted and dotted) : 3 *S*– *dd* (spotted, not dotted) : 3 *ss D*– (not spotted, dotted) : 1 *ss dd* (not spotted, not dotted)

Thus, the alternative hypothesis suggested by your fellow student would predict that some lentils would be found in the F_2 generation that would be neither spotted nor dotted. The results shown in Figure 2.25 do not include any such lentils. **If you counted a large number of F_2 individuals and you failed to see lentils that were neither spotted nor dotted, you would be able to exclude the hypothesis that two genes were involved.**

2.55.

a. All of the crosses have results that can be explained by one gene - either a 3:1 phenotypic monohybrid ratio showing that one allele is completely dominant to the other, or a 1:1 ratio showing that a testcross was done for a single gene, or all progeny with the same phenotype as the parents. You can thus conclude that all of the coat colours are controlled by the alleles of **one gene, with chinchilla (*C*) > himalaya (c^h) > albino (c^a)**.

b. 1. $c^h c^a$ x $c^h c^a$

2. $c^h c^a$ x $c^a c^a$

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3. $\boldsymbol{Cc^h}$ **x** $\boldsymbol{C(c^h}$ **or** $\boldsymbol{c^a)}$

4. $\boldsymbol{CC}$ **x** $\boldsymbol{c^h}$ $\boldsymbol{(c^h}$ **or** $\boldsymbol{c^a)}$

5. $\boldsymbol{Cc^a}$ **x** $\boldsymbol{Cc^a}$

6. $\boldsymbol{c^hc^h}$ **x** $\boldsymbol{c^ac^a}$

7. $\boldsymbol{Cc^a}$ **x** $\boldsymbol{c^ac^a}$

8. $\boldsymbol{c^ac^a}$ **x** $\boldsymbol{c^ac^a}$

9. $\boldsymbol{Cc^h}$ **x** $\boldsymbol{c^h(c^h}$ **or** $\boldsymbol{c^a)}$ **or** $\boldsymbol{Cc^a}$ **x** $\boldsymbol{c^hc^h}$

10. $\boldsymbol{Cc^a}$ **x** $\boldsymbol{c^hc^a}$.

c. $\boldsymbol{Cc^h}$ **(from cross 9) x** $\boldsymbol{Cc^a}$ **(from cross 10)** → 1/4 *CC* (chinchilla) : 1/4 Cc^a (chinchilla) : 1/4 Cc^h (chinchilla) : 1/4 c^hc^a (himalaya) **= 3/4 chinchilla : 1/4 himalaya**, or $\boldsymbol{Cc^a}$ **(cross 9) x** $\boldsymbol{Cc^a}$ **(cross 10) → 3/4** ***C–*** **chinchilla : 1/4** $\boldsymbol{c^ac^a}$ **albino.**

2-56. There are two keys to this problem: (1) Pollen grains and ovules are gametes that have only one copy of the *S* incompatibility gene, while the stigma (the part of the female plant on which the pollen grains land) has two copies of this gene. (2) Pollen with a particular *S* gene allele cannot fertilize any ovules in a plant whose stigma has the same *S* allele, because the pollen will not grow a tube allowing it to fertilize an ovule.

a. In the cross *S1 S2* x *S1 S2* all of the pollen grains (whether they are *S1* or *S2*) will land on the stigmas of plants that have the same alleles, and therefore **no progeny would be produced at all**.

b. The way this cross was written is ambiguous because the male and female parents were not specified. The cross could be ♂ *S1 S2* x ♀ *S2 S3*, or ♀ *S1 S2* x ♂ *S2 S3*, or both (because the flowers of these plants have both male and female parts). For the cross ♂ *S1 S2* x ♀ *S2 S3*, the pollen grains would be *S1* or *S2*. The *S2* pollen could not fertilize the female plant, but the *S1* pollen could. **The progeny of the ♂** ***S1 S2*** **x ♀** ***S2 S3*** **cross would thus be** ***S1 S2*** **and** ***S1 S3*** **(in a 1:1 ratio).** For the cross written the opposite way (♀ *S1 S2* x ♂ *S2 S3*), the pollen would be *S2* or *S3*. The *S2* pollen would not produce any progeny, but the *S3* pollen could produce both *S1 S3* progeny and *S2 S3* progeny. **The progeny of the ♀** ***S1 S2*** **x ♂** ***S2 S3*** **cross would thus be a 1:1 ratio of** ***S1 S3*** **and** ***S2 S3*****.**

c. Because of the ambiguity in the way the cross was written, there are again two possibilities: The cross could be ♂ *S1 S2* x ♀ *S3 S4*, or ♀ *S1 S2* x ♂ *S3 S4*, or both. Regardless of these possibilities, all pollen grains would be able to fertilize all ovules, because the pollen grains do not share any alleles with the female parent. **As a result, any of these crosses could produce four types of progeny in equal numbers:** ***S1 S3*****,** ***S1 S4*****,** ***S2 S3*****, and** ***S2 S4*****.**

d. **This mechanism would prevent plant self-fertilization because any pollen grain produced by any plant would land on a stigma sharing the same allele.** For example, if an *S1* pollen grain produced by an *S1 S2* plant lands on a stigma from the same plant, the stigma would have the same

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allele and no pollen tube would be able to grow to allow fertilization. The same would be true for an *S2* pollen grain from the same plant. (Of interest, tomato plants in the wild cannot self-fertilize because of this incompatibility mechanism; they proliferate only through cross- fertilization. However, many domesticated cultivars of tomatoes can self-fertilize because they were selected for varieties that have mutations causing the failure of the incompatibility mechanism.)

e. **Plants with functioning incompatibility systems must be heterozygotes because a pollen grain cannot fertilize a female plant sharing the same allele of the *S* incompatibility gene.** For example, an *S1* pollen grain cannot fertilize successfully any female plant that also has an *S1* allele. No way thus exists to create *S1 S1* homozygous progeny.

f. **Peas cannot be governed by this mechanism because you already saw in this chapter that Gregor Mendel routinely self-fertilized his peas in the F_1 generation to produce the F_2 generation.**

g. **The larger the number of different alleles of the *S* gene that are present in the population, the more likely it is that any given pollen grain of any genotype would land on the stigma of a flower that did not share the same allele, and the less likely that the pollen will interact unproductively with flowers that share the same allele.** Within the population, the proportion of matings that could produce progeny would increase with a greater variety in *S* gene alleles; this would clearly increase the fertility (and thus the average evolutionary fitness) of the population as a whole.

2-57.

a. This ratio is approximately **2/3 curly : 1/3 normal**.

b. The expected result for this cross is: Cy^+Cy x Cy^+Cy → 1/4 *Cy Cy* (?): 1/2 Cy^+Cy (curly) : 1/4 Cy^+Cy^+ (normal). If the ***Cy/ Cy*** genotype **is lethal** then the expected ratio will match the observed data.

c. The cross is Cy^+Cy x Cy^+Cy^+ → 1/2 Cy^+Cy : 1/2 Cy^+Cy^+, so there would be approximately **90 curly-winged and 90 normal-winged flies**.

2-58. Designate the gene *p* (for pattern). There are 7 alleles, p^1-p^7, with p^7 being the allele that codes for absence of pattern and $p^1 > p^2 > p^3 > p^4 > p^5 > p^6 > p^7$.

a. There are **7 different patterns** possible. These are associated with the following genotypes: p^1–, p^2p^a (where $p^a = p^2, p^3, p^4 \ldots p^7$), p^3p^b (where $p^b = p^3, p^4, p^5 \ldots p^7$), p^4p^c (where $p^c = p^4, p^5, p^6,$ and p^7), p^5p^d (where $p^d = p^5, p^6,$ and p^7), p^6p^e (where $p^e = p^6$ and p^7), and p^7p^7.

b. The phenotype dictated by the allele p^1 has the greatest number of genotypes associated with it = **7** (p^1p^1, p^1p^2, p^1p^3, etc.). **The absence of pattern** is caused by just one genotype, p^7p^7.

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c. This finding suggests that **the allele determining absence of pattern (p^7) is very common** in these clover plants with the p^7p^7 genotype being the most frequent in the population. The other alleles are present, but are much less common in this population.

2-59.

a. The 2/3 montezuma : 1/3 wild-type phenotypic ratio, and the statement that montezumas are never true-breeding, together suggest that there is a **recessive lethal allele** of this gene. When there is a recessive lethal, crossing two heterozygotes results in a 1:2:1 genotypic ratio, but one of the 1/4 classes of homozygotes do not survive. **The result is the 2:1 phenotypic ratio as seen in this cross. Both the montezuma parents were therefore heterozygous, *Mm*.** The *M* allele must confer the montezuma colouring in a dominant fashion, but homozygosity for *M* is lethal.

b. Designate the alleles: *M* = montezuma, *m* = green; *F* = normal fin, *f* = ruffled fin. Diagram the cross: ***Mm FF* x *mm ff*** → expected monohybrid ratio for the *M* gene alone: 1/2 *Mm* (montezuma) : 1/2 *mm* (wild-type); expected monohybrid ratio for the *F* gene alone: all *Ff*. The expected dihybrid ratio = **1/2 *Mm Ff* (montezuma, normal fin) : 1/2 *mm Ff* (green, normal fin).**

c. ***Mm Ff* x *Mm Ff*** → expected monohybrid ratio for the *M* gene alone: 2/3 montezuma (*Mm*) : 1/3 green (*mm*); expected monohybrid ratio for the *F* gene alone: 3/4 normal fin (*F*–) : 1/4 ruffled fin (*ff*). The expectations when considering both genes together is: **6/12 montezuma normal fin : 2/12 montezuma ruffled fin : 3/12 green normal fin : 1/12 green ruffled fin.**

Section 2.5 – Extensions to Mendel for Gene Interactions

2-60.

a. The mutant plant lacks the function of all three genes, so **its genotype must be *aa bb cc*.**

b. Considering each gene separately, 3/4 of the F_2 progeny will have at least one dominant allele, whereas 1/4 will be homozygous for the recessive allele. As just seen in part *a*, mutant plants must be triply homozygous recessive. The chance that a plant will have the *aa bb cc* genotype is 1/4 x 1/4 x 1/4 = 1/64. All other F_2 plants will be normal for this phenotype, so **the fraction of normal plants = 1 – 1/64 = 63/64.**

c. **The most likely explanation for redundant gene function is that in the relatively recent past, a single gene became duplicated (or in this case, triplicated).** The three copies of the *SEP* gene are nearly identical to each other and thus fulfill the same function. Only if the functions of all three genes are lost does a mutant phenotype result. In fact, these kinds of gene duplication events occur often enough in nature that redundant gene function is a common phenomenon.

2-61. The cross is: black x chestnut → F_1 bay → F_2 black : bay : chestnut : liver

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Four phenotypes in the F_2 generation means there are two genes determining coat colour. The F_1 bay animals produce four phenotypic classes, so they must be doubly heterozygous, *Aa Bb*. Crossing a liver-coloured horse to either of the original parents resulted in the parent's phenotype. The liver horse's alleles do not affect the phenotype, suggesting the recessive genotype *aa bb*. Though it is probable that the original black mare was *AA bb* and the chestnut stallion was *aa BB,* each of these animals only produced 3 progeny, so it cannot be definitively concluded that these animals were homozygous for the dominant allele they carry. Thus, **the black mare was *A– bb*, the chestnut stallion was *aa B–*, and the F_1 bay animals are *Aa Bb*. The F_2 horses were: bay (*A– B–*), liver (*aa bb*), chestnut (*aa B–*), and black (*A– bb*).**

2-62. The cross is: walnut x single → F_1 walnut x F_1 walnut → 93 walnut : 29 rose : 32 pea : 11 single

a. How many genes are involved? The four F_2 phenotypes means there are 2 genes, *A* and *B*. Both genes affect the same structure, the comb. The F_2 phenotypic dihybrid ratio among the progeny is close to 9:3:3:1, so there is no epistasis. Because walnut is the most abundant F_2 phenotype, it must be the phenotype due to the *A– B–* genotype. Single combs are the least frequent class, and are thus *aa bb*. Now assign genotypes to the cross. If the walnut F_2 are *A– B–*, then the original walnut parent must have been *AA BB*:

   ***AA BB* x *aa bb* → *Aa Bb* (walnut) → 9/16 *A– B–* (walnut) : 3/16 *A– bb* (rose) : 3/16 *aa B–* (pea) : 1/6 *aa bb* (single).**

b. Diagram the cross, recalling that the problem states the parents are homozygous:

   ***AA bb* (rose) x *aa BB* (pea) → *Aa Bb* (walnut) → 9/16 *A– B–* (walnut) : 3/16 *A– bb* (rose) : 3/16 *aa B–* (pea) : 1/6 *aa bb* (single).** Notice that this F_2 is in identical proportions as the F_2 generation in part *a*.

c. Diagram the cross: *A– B–* (walnut) x *aa B–* (pea) → 12 *A– B–* (walnut) : 11 *aa B–* (pea) : 3 *A– bb* (rose) : 4 *aa bb* (single). Because there are pea and single progeny, you know that the walnut parent must be *Aa.* The 1 *A–* : 1 *aa* monohybrid ratio in the progeny also tells you the walnut parent must have been *Aa*. Because some of the progeny are single, you know that both parents must be *Bb.* In this case, the monohybrid ratio for the *B* gene is 3 *B–* : 1 *bb*, so both parents were *Bb*. The original cross must have been ***Aa Bb* x *aa Bb***. You can verify that this cross would yield the observed ratio of progeny by multiplying the probabilities expected for each gene alone. For example, you anticipate that 1/2 the progeny would be *Aa* and 3/4 of the progeny would be *Bb,* so 1/2 x 3/4 = 3/8 of the progeny should be walnut; this is close to the 12 walnut chickens seen among 30 total progeny.

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d. Diagram the cross: *A– B–* (walnut) x *A– bb* (rose) → all *A– B–* (walnut). The progeny are all walnut, so **the walnut parent must be *BB***. No pea progeny are seen, so **both parents cannot be *Aa,* so one of the two parents must be *AA***. This could be either the walnut or the rose parent or both.

2-63. green x yellow → F_1 green → F_2 9 green : 7 yellow

a. The 9:7 ratio is a variant of the 9:3:3:1 phenotypic dihybrid ratio arising from complementary gene action, suggesting that **two genes are controlling colour**. The genotypes are:
***AA BB* (green) x *aa bb* (yellow) → F_1 *Aa Bb* (green) → F_2 9/16 *A– B–* (green) : 3/16 *A– bb* (yellow) : 3/16 *aa B–* (yellow) : 1/16 *aa bb* (yellow).**

b. **F_1 *Aa Bb* x *aa bb* → 1/4 *Aa Bb* (green) : 1/4 *aa Bb* (yellow) : 1/4 *Aa bb* (yellow) : 1/4 *aa bb* (yellow) = 1/4 green : 3/4 yellow.**

2-64.

a. Because unaffected individuals had affected children, the **trait is recessive**. From affected individual II-1, you know the mutant allele is present in this generation. The trait was passed on through II-2 who was a carrier. All children of affected individuals III-2 x III-3 are affected, as predicted for a recessive trait. However, generation V seems inconsistent with recessive inheritance of a single gene. This result is consistent with two different genes involved in hearing with a defect in either gene leading to deafness: The trait is polymorphic. **The two family lines shown contain mutations in two separate genes, and the mutant alleles of both genes determining deafness are recessive.**

b. Individuals in generation V are doubly heterozygous (***Aa Bb***), having inherited a dominant and recessive allele of each gene from their parents (*aa BB* x *AA bb*). The people in generation V are not affected because **the product of the dominant allele of each gene is sufficient for normal function.** This is an example of *complementation*: For each gene, the gamete from one parent provided the dominant allele that the gamete from the other parent lacked.

2-65. Dominance relationships are between alleles of the same gene. **Only one gene is involved when considering dominance relationships. Epistasis involves two genes**. The alleles of one gene affect the phenotypic expression of the second gene.

2-66.

a. white x white → F_1 white → F_2 126 white : 33 purple

At first glance this cross seems to involve only one gene, as true-breeding white parents give white F_1s. However, if this were true, then the F_2 MUST be totally white as well. The purple F_2 plants

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show that this cross is NOT controlled by 1 gene. These results may be **due to 2 genes**. To determine if this is the case, it makes sense to ask: Does a ratio of 126 : 33 represent a variant of the 9:3:3:1 dihybrid ratio? Usually when you are given raw numbers of individuals for the classes, you divide through by the smallest number, yielding in this case 3.8 white : 1 purple. This is neither a recognizable monohybrid nor dihybrid ratio. Dividing through by the smallest class is NOT the correct way to convert raw numbers to a ratio. Assuming that the F_1 in this case are dihybrids, there must have been 16 different equally likely fertilization events that produced the F_2 progeny (16 boxes in the 4 x 4 Punnett square), even though the phenotypes may not be distributed in the usual 9/16 : 3/16 : 3/16 : 1/16 ratio. If the 159 F_2 progeny are divided equally into 16 fertilization types, then there are 159/16 = ~10 F_2 plants/fertilization type. The 126 white F_2s therefore represent 126/10 = ~13 of these fertilizations. Likewise the 33 purple plants represent 33/10 = ~3 fertilization types. **The F_2 phenotypic ratio is thus 13 white : 3 purple. The data fit the hypothesis that two genes control colour, and that the F_1 are dihybrids.**

You can now assign genotypes to the parents in the cross. Because the parents are homozygous (true-breeding) and there are 2 genes controlling the phenotypes, there are two

possible ways to set up the genotypes of the parents so that the F_1 dihybrids are heterozygous for dominant and recessive alleles of each gene. One option is: ***AA BB* (white) x *aa bb* (white) → *Aa Bb* (white, same as *AA BB* parent) → 9 *A– B–* (white) : 3 *A– bb* (unknown phenotype) : 3 *aa B–* (unknown phenotype) : 1 *aa bb* (white, same as *aa bb* parent)**. If you assume that *A– bb* is white and *aa B–* is purple (or *vice versa*), then this is a match for the observed data presented in the cross above [(9 + 3 + 1) = 13 white : 3 purple].

Alternatively, you could try to diagram the cross as *AA bb* (white) x *aa BB* (white) → *Aa Bb* (whose phenotype is unknown as this is NOT a genotype seen in the parents) → 9 *A– B–* (same unknown phenotype as in the F_1) : 3 *A– bb* (white like the *AA bb* parent) : 3 *aa B–* (white like the *aa BB* parent) : 1 *aa bb* (unknown phenotype). Such a cross cannot give an F_2 phenotypic ratio of 13 white : 3 purple. The only F_2 classes that could be purple are *A– B–* , but this is impossible because this class is larger than the number of purple plants observed and because the F_1 plants must then have been purple; or the *aa bb* class which is smaller than the number of purple plants observed. Therefore, the first set of possible genotypes (written in bold above) is the best fit for the observed data.

Assume that *A– bb* plants are white, and *aa B–* plants are purple. Our model above states that in order to be purple, a plant must have a *B* allele and no *A* allele. Thus, we can say that *A* is epistatic to *B*.

b. white F_2 x white F_2 (self-cross) → 3/4 white : 1/4 purple. Assume again that the *aa B–* class is purple in part *a* above. A 3:1 monohybrid ratio means the parents are both heterozygous for one

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gene with purple due to the recessive allele. The second gene is not affecting the ratio, so both parents must be homozygous for the same allele of that gene. Thus the cross must be: ***Aa BB* (white)** x *Aa BB* (white self-cross) → 3/4 *A– BB* (white) : 1/4 *aa BB* (purple).

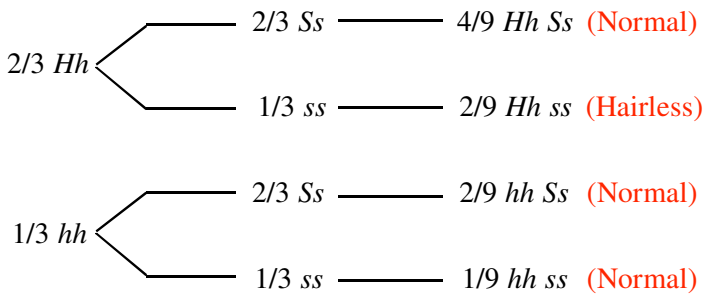
c. purple F_2 x self → 3 purple : 1 white. Again, the selfed parent must be heterozygous for one gene and homozygous for the other gene. Because purple is *aa B–*, the genotype of the purple F_2 plant must be ***aa Bb***.

d. white F_2 x white F_2 (not a self-cross) → 1/2 purple : 1/2 white. The 1:1 monohybrid ratio means a testcross was done for one of the genes. The second gene is not altering the ratio in the progeny, so the parents must be homozygous for that gene. If purple is *aa B–*, then the genotypes of the parents must be ***aa bb* (white) x *Aa BB* (white)** → 1/2 *Aa Bb* (white) : 1/2 *aa Bb* (purple).

2-67. I^AI^B *Ss* x I^AI^A *Ss* → expected monohybrid ratio for the *I* gene of 1/2 I^AI^A : 1/2 I^AI^B; expected ratio for the *S* gene considered alone of 3/4 *S–* : 1/4 *ss*. Use the product rule to generate the phenotypic ratio for both genes considered together and then assign phenotypes, remembering that all individuals with the *ss* genotype **look like type O**. The apparent phenotypic ratio for both genes is: 3/8 I^AI^A *S–* : 3/8 I^AI^B *S–* : 1/8 I^AI^A *ss* : 1/8 I^AI^B *ss* = 3/8 A : 3/8 AB : 1/8 O : 1/8 O = **3/8 Type A : 3/8 Type AB : 2/8 Type O**.

2-68.

a. The cross is between two normal flies that carry *H* and *S*. These individuals cannot be homozygous for *H* or for *S*, because we are told that both are lethal in homozygotes. Thus, the mating described is a dihybrid cross: *Hh Ss* x *Hh Ss*. The genotypic classes among the progeny zygotes should be 9 *H– S–*, 3 *H– ss*, 3 *hh S–*, and 1 *hh ss*. However, all zygotes that are *HH* or *SS* or both will die before they hatch into adult flies. You could do this problem as a branched-line diagram as shown in the following figure, in which the progeny should be 2/3 *Hh* and 1/3 *hh* (considering the *H* gene alone) and 2/3 *Ss* and 1/3 *ss* (considering the *S* gene alone). As can be seen from the diagram, **7/9 of the adult progeny will be normal, and 2/9 will be hairless.**



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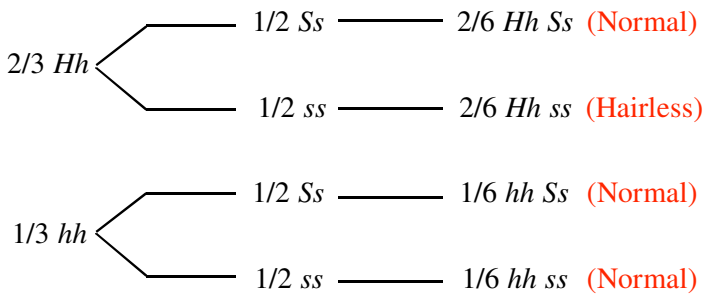
b. As just seen in the diagram, the hairless progeny of the cross in part *a* are *Hh ss*, and these are mated with parental flies that are *Hh Ss*. You could again portray the results of this cross as a branched-line diagram. For the *H* gene, again 2/3 of the viable adult progeny will be *Hh* and 1/3 will be *hh*. The cross involving the *S* gene is a testcross, and all the progeny will be viable, so 1/2 the progeny will be *Ss* and 1/2 will be *ss*. As seen in the diagram that follows, **2/6 = 1/3 of the progeny will be hairless and the remaining 2/3 will be normal.**



2-69.

a. blood types: **I-1 AB; I-2 A; I-3 B; I-4 AB; II-1 O; II-2 O; II-3 AB; III-1 A; III-2 O**.

b. genotypes: **I-1 *Hh* I^AI^B; I-2 *Hh* I^Ai (or I^AI^A); I-3 *H–* I^Bi (or $I^B\,I^B$); I-4 *H–* I^AI^B; II-1 *H– ii*; II-2 *hh* I^AI^A (or I^Ai or I^AI^B); II-3 *Hh* I^AI^B; III-1 *Hh* I^Ai; III-2 *hh* I^AI^A (or I^AI^B or I^Ai or I^bi or I^BI^B)**

At first glance, you find inconsistencies between expectations and what could be inherited from a parent. For example, I-1 (AB) × I-2 (A) could not have an O child (II-2). The epistatic *h* allele (which causes the Bombay phenotype) could explain these inconsistencies. If II-2 has an O phenotype because she is *hh*, her parents must both have been *Hh*. The Bombay phenotype would also explain the second seeming inconsistency of two O individuals (II-1 and II-2) having an A child. II-2 could have received an I^A allele from one of her parents and passed this on to III-1 together with one *h* allele. Parent II-1 would have to contribute the *H* allele so that the I^A allele would be expressed; the presence of *H* means that II-1 must also be *ii* in order to be type O. A third inconsistency is that individuals II-2 and II-3 could not have an *ii* child since II-3 has the I^AI^B genotype, but III-2 has the O phenotype. This could also be explained if II-3 is *Hh* and III-2 is *hh*.

2-70. The difference between traits determined by a single pleiotropic gene and traits determined by several genes would be seen if crosses were done using pure-breeding plants (wild-type x mutant), then selfing the F_1 progeny. If **several genes** were involved there **would be several different**

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combinations of the petal colour, markings, and stem position phenotypes in the F_2 generation. If all 3 traits were due to an allele present at **one gene**, the **three phenotypes would always be inherited together** and the F_2 plants would be either yellow, dark brown, and erect OR white, no markings, and prostrate.

2-71. Diagram the cross. Figure out an expected monohybrid ratio for each gene separately, then apply the product rule to generate the expected dihybrid ratio.

$A^yA\ Cc$ x $A^yA\ cc$ → monohybrid ratio for the *A* gene alone: 1/4 A^yA^y (dead) : 1/2 A^yA (yellow) : 1/4 *AA* (agouti) = 2/3 A^yA (yellow) : 1/3 *AA* (agouti); monohybrid ratio for the *C* gene: 1/2 *Cc* (non-albino) : 1/2 *cc* (albino).

Overall there will be 2/6 $A^yA\ Cc$ (yellow) : 2/6 $A^yA\ cc$ (albino) : 1/6 *AA Cc* (agouti) : 1/6 *AA cc* (albino) = **2/6 $A^yA\ Cc$ (yellow) : 3/6 – – *cc* (albino) : 1/6 *AA Cc* (agouti)**. Note that the $A^yA\ cc$ animals must be albino because the albino parent had exactly the same genotype; this indicates that *cc* is epistatic to all alleles of gene *A*. Although you were not explicitly told that the *AA cc* animals are also albino, this makes sense because in Figure 2.44, *cc* is epistatic to all alleles of another gene *B* in animals that must have been *AA*. (Another way to think of this is that the *cc* albino colour must be epistatic to alleles of all genes that confer colour because no pigments are produced.)

2-72.

a. Diagram one of the crosses:

white-1 x white-2 → red F_1 → F_2 9 red : 7 white

Even though there are only 2 phenotypes in the F_2, colour is not controlled by one gene - the 9:7 ratio is a variation of 9:3:3:1, so there are 2 genes controlling these phenotypes. Individuals must have at least one dominant allele of each gene in order to get the red colour; this is an example of *complementary gene action*. Thus the genotypes of the two pure-breeding white parents in this cross are *aa BB* x *AA bb*. The same conclusions hold for the other 2 crosses.

If white-1 is *aa BB* and white-2 is *AA bb*, then white-3 must be *AA BB cc*. The reason is that if white-3 had the same genotype as white-1 or white-2, then one of the three crosses would have produced an all white F_1 (no complementation). Because none of the crosses had an all white F_1, we can conclude that **three genes are involved**.

b. **white-1 is *aa BB CC*; white-2 is *AA bb CC;* and white-3 is *AA BB cc***.

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c. ***aa BB CC* (white-1) x *AA bb CC* (white-2) → *Aa Bb CC* (red) → 9/16 *A– B– CC* (red) : 3/16 *A– bb CC* (white) : 3/16 *aa B– CC* (white) : 1/6 *aa bb CC* (white). Red colour requires a dominant, functional allele of each of the three genes (*A– B– C–*).**

2-73. You know about the alleles of the *A* gene (*A* for agouti, a^t for black/yellow, *a* for black, and A^y for recessive lethal yellow) from Figure 2.28 and Figure 2.29. You know about the interaction of the *B* and *C* genes governing the variation in black, brown, and albino colours from Figure 2.44.

a. The yellow parent must have an A^y allele, but we don't know the second allele of the *A* gene (A^y–). We don't know at the outset what alleles this yellow mouse has at the *B* gene, so we'll leave these alleles for the time being as *??*. Since this mouse does show colour we know it is not *cc* (albino), so it must have at least one *C* allele (*C*–). The brown agouti parent has at least one *A* allele (*A*–); it must be *bb* at the *B* gene; and since there is colour it must also be *C*–. The mating between these two can thus be represented as A^y– *?? C–* x *A– bb C–*.

   Now consider the progeny. Because one pup was albino (*cc*), the parents must both be *Cc*. A brown pup (*bb*) indicates that both parents had to be able to contribute a *b* allele, so we now know the first mouse (the yellow parent) must have had at least one *b* allele. The fact that this brown pup was non-agouti means both parents carried an *a* allele. The black agouti progeny tells us that the first mouse must have also had a *B* allele. This latter fact also clarifies that A^y is epistatic to *B* because this parent was yellow rather than black. The complete genotypes of the mice are therefore: ***A^ya Bb Cc* x *Aa bb Cc***.

b. Think about each gene individually, then the effect of the other genes in combination with that phenotype. *C*– leads to a phenotype with colour; *cc* gives albino (which is epistatic to all colours determined by the other genes because no pigments are produced). The possible genotypes of the progeny of this cross for the *A* gene are A^yA, A^ya, *Aa,* and *aa*, giving yellow, yellow, agouti, and non-agouti phenotypes, respectively. Since yellow (A^y) is epistatic to *B*, non-albino mice with A^y will be yellow regardless of the genotype of the *B* gene. *Aa* is agouti; with the *aa* genotype there is no yellow on the hair (non-agouti). The type of colouration depends on the *B* gene. For *B* the offspring could be *Bb* (black) or *bb* (brown). In total, **six different coat colour phenotypes are possible: albino (*– – – – cc*), yellow (*A^y*(*A* or *a*) *– – C–*), brown agouti (*A– bb C–*), black agouti (*A– B– C–*), brown (*aa bb C–*), and black (*aa B– C–*).** [Note: Although A^y (yellow colour) is in fact epistatic to *B* (black) or *bb* (brown) colours governed by the *B* gene, you were not explicitly

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told this. Thus, based on the information provided, you might have included an additional colour phenotype if you considered that A^y (*A* or *a*) *bb C*– had a lighter colour than the yellow of A^y (*A* or *a*) *Bb C*– animals.]

2-74.

a. **No**, a single gene cannot account for this result. While the 1:1 ratio seems like a testcross, the fact that **the phenotype of one class of offspring (linear) is not the same as either of the parents** argues against this being a testcross.

b. The appearance of four phenotypes means **two genes** are controlling the phenotypes.

c. The 3:1 ratio suggests that **two alleles of one gene** determine the difference between the wild-type and scattered patterns.

d. The true-breeding wild-type fish are homozygous by definition, and the scattered fish have to be homozygous recessive according to the ratio seen in part *c*, so the cross is: ***bb* (scattered) x *BB* (wild-type) → F_1 *Bb* (wild-type) → 3/4 *B*– (wild-type) : 1/4 *bb* (scattered)**.

e. The inability to obtain a true-breeding nude stock suggests that the nude fish are heterozygous (*Aa*) and that the ***AA* genotype dies**. Thus ***Aa* (nude) x *Aa* (nude) → 2/3 *Aa* (nude) : 1/3 *aa* (scattered)**.

f. Going back to the linear cross from part *b*, the fact that there are four phenotypes led us to propose two genes were involved. The 6:3:2:1 ratio looks like an altered 9:3:3:1 ratio in which some genotypes may be missing, as predicted from the result in part *e* that *AA* animals do not survive. The 9:3:3:1 ratio results from crossing double heterozygotes, so **the linear parents are doubly heterozygous *Aa Bb*. The lethal phenotype associated with the *AA* genotype produces the 6:3:2:1 ratio. The phenotypes and corresponding genotypes of the progeny of the linear x linear cross are: 6 linear, *Aa B*– : 3 wild-type, *aa B*– : 2 nude, *Aa bb* : 1 scattered, *aa bb*.** Note that the *AA BB, AA Bb, AA Bb,* and *AA bb* genotypes are missing due to lethality.

2-75.

a. *Aa Bb Cc* x *Aa Bb Cc* → 9/16 *A*– *B*– x 3/4 *C*– : 9/16 *A*– *B*– x 1/4 *cc* : 3/16 *A*– *bb* x 3/4 *C*– : 3/16 *A*– *bb* x 1/4 *cc*: 3/16 *aa B*– x 3/4 *C*– : 3/16 *aa B*– x 1/4 *cc* : 1/16 *aa bb* x 3/4 *C*– : 1/16 *aa bb* x 1/4 *cc* = 27/64 *A*– *B*– *C*– (wild-type) : 9/64 *A*– *B*– *cc* : 9/64 *A*– *bb C*– : 3/64 *A*– *bb cc* : 9/64 *aa B*– *C*– : 3/64 *aa B*– *cc* : 3/64 *aa bb C*– : 1/64 *aa bb cc* = **27/64 wild-type : 37/64 mutant**.

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b. Diagram the crosses:

1. unknown male x *AA bb cc* → 1/4 wild-type (*A– B– C–*) : 3/4 mutant
2. unknown male x *aa BB cc* → 1/2 wild-type (*A– B– C–*) : 1/2 mutant
3. unknown male x *aa bb CC* → 1/2 wild-type (*A– B– C–*) : 1/2 mutant

The 1:1 ratio in testcrosses 2 and 3 is expected if the unknown male is heterozygous for one of the genes that are recessive in the testcross parent. The 1 wild-type : 3 mutant ratio arises when the male is heterozygous for two of the genes that are homozygous recessive in the testcross parent. (If you apply the product rule to 1/2 *B–* : 1/2 *bb* and 1/2 *C–* : 1/2 *cc* in the first cross, then you find 1/4 *B– C–,* 1/4 *B– cc,* 1/4 *bb C–,* and 1/4 *bb cc.* Only *B– C–* will be wild-type, the other 3 classes will be mutant.) Thus the unknown male must be *Bb Cc*. In testcross 1 the male could be either *AA* or *aa*. Crosses 2 and 3 show that the male is only heterozygous for one of the genes in each case: gene *C* in testcross 2 and gene *B* in testcross 3. In order to get wild-type progeny in both crosses, the male must be *AA*. Therefore the genotype of the unknown male is ***AA Bb Cc***.

2-76. In **Figure 2.48b** the A^1 and B^1 alleles each have the same effect on the phenotype (plant height in this example), while the A^0 and B^0 alleles are non-functional. Thus, the shortest plants are $A^0A^0B^0B^0$, and the tallest plants are $A^1A^1B^1B^1$. **The phenotypes are determined by the total number of A^1 and B^1 alleles in the genotype**. Thus, $A^1A^0B^0B^0$ plants are the same phenotype as $A^0A^0B^0B^1$. In total there will be 5 different phenotypes: 4 '0' alleles (total = 0); 1 '1' allele + 3 '0' alleles (total = 1); 2 '1' alleles + 2 '0' alleles (total = 2); 3 '1' alleles + 1 '0' allele (total = 3); and 4 '1' alleles (total = 4).

In **Figure 2.43** the *a* allele = *b* allele = no function (in this case no colour = white). If the *A* allele has the same level of function as a *B* allele then you would see 5 phenotypes as was the case for **Figure 2.48b**. But since there are a total of 9 phenotypes, this cannot be true so $A \neq B$. Notice that *aa Bb* is lighter than *Aa bb* even though both genotypes have the same number of dominant alleles. Thus, **in Figure 2.43 an *A* allele has more effect on colouration than a *B* allele**. If you assume, for example, that *B* = 1 unit of colour and *A* = 1.5 units of colour, then 16 genotypes lead to 9 phenotypes.

2-77.

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a. Analyze each cross by determining how many genes are involved in the phenotypes and the relationships between the alleles of these genes. In cross 1, there are 2 genes because there are 3 classes in the F_2 showing a modified 9:3:3:1 ratio (12:1:3), and LR is the doubly homozygous recessive class. In cross 2, only 1 gene is involved because there are 2 phenotypes in a 3:1 ratio; WR>DR. In cross 3, there is again only 1 gene involved (2 phenotypes in a 1:3 ratio); DR>LR. In cross 4, there is 1 gene (2 phenotypes, with a 3:1 ratio); WR>LR. In cross 5, there are again 2 genes (and as in cross 1, there is a 12:1:3 ratio of three classes); LR is the double homozygous recessive. In total, **there are 2 genes controlling these phenotypes in foxgloves**.

b. Remember that all four starting strains are true-breeding. In cross 1 the parents can be assigned the following genotypes: ***AA BB* (WR-1)** x ***aa bb* (LR)** → *Aa Bb* (WR) → 9 *A*– *B*– (WR) : 3 *A*– *bb* (WR; this class displays the epistatic interaction) : 3 *aa B*– (DR) : 1 *aa bb* (LR). The results of cross 2 suggested that DR differs from WR-1 by one gene, so **DR is *aa BB***; cross 3 confirms these genotypes for DR and LR. Cross 4 introduces WR-2, which differs from LR by one gene and differs from DR by 2 genes, so **WR-2 is *AA bb***. Cross 5 would then be *AA bb* (WR-2) x *aa BB* (DR) → *Aa Bb* (WR) → 9 *A*– *B*– (WR) : 3 *A*– *bb* (WR) : 3 *aa B*– (DR) : 1 *aa bb* (LR) = 12 WR : 3 DR : 1 LR.

c. WR from the F_2 of cross 1 x LR → 253 WR : 124 DR : 123 LR. Remember from part *b* that LR is *aa bb* and DR is *aa B*– while WR can be either *A*– *B*– or *A*– *bb* = *A*– *??*. The experiment is essentially a testcross for the WR parent. The observed monohybrid ratio for the *A* gene is 1/2 *Aa* : 1/2 *aa* (253 *Aa* : 124 + 123 *aa*), so the WR parent must be *Aa*. The DR and LR classes of progeny show that the WR parent is also heterozygous for the *B* gene (DR is *Bb* and LR is *bb* in these progeny). Thus, the cross is ***Aa Bb* (WR) x *aa bb* (LR)**.

2-78.

a. For all 5 crosses, determine the number of genes involved in the trait and the dominance relationships between the alleles. Cross 1: 1 gene, red > blue. Cross 2: 1 gene, lavender > blue. Cross 3: 1 gene, codominance/incomplete dominance (1:2:1), bronze is the phenotype of the heterozygote. Cross 4: 2 genes with epistasis (9 red : 4 yellow : 3 blue). Cross 5: 2 genes with epistasis (9 lavender : 4 yellow : 3 blue). **In total there are 2 genes. One gene controls blue (c^b), red (c^r), and lavender (c^l), where $c^r = c^l > c^b$. The second gene controls the yellow phenotype: *Y* seems to be colourless (or has no effect on colour), so the phenotype is**

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determined by the alleles of the *c* gene. The *y* allele makes the flower yellow, and is epistatic to all alleles of the *c* gene.

b. **cross 1: $c^r c^r$ *YY* (red) x $c^b c^b$ *YY* (blue) → $c^r c^b$ *YY* (red) → 3/4 c^r– *YY* (red) : 1/4 $c^b c^b$ *YY* (blue)**

cross 2: $c^l c^l$ *YY* (lavender) x $c^b c^b$ *YY* (blue) → $c^l c^b$ *YY* (lavender) → 3/4 c^l– *YY* (lavender) : 1/4 $c^b c^b$ *YY* (blue)

cross 3: $c^l c^l$ *YY* (lavender) x $c^r c^r$ *YY* (red) → $c^l c^r$ *YY* (bronze) → 1/4 $c^l c^l$ *YY* (lavender) : 1/2 $c^l c^r$ *YY* (bronze) : 1/4 $c^r c^r$ *YY* (red)

cross 4: $c^r c^r$*YY* (red) x $c^b c^b$ *yy* (yellow) → $c^r c^b$ *Yy* (red) → 9/16 c^r– *Y*– (red) : 3/16 c^r– *yy* (yellow) : 3/16 $c^b c^b$ *Y*– (blue): 1/16 $c^b c^b$ *yy* (yellow)

cross 5: $c^l c^l$ *yy* (yellow) x $c^b c^b$ *YY* (blue) → $c^l c^b$ *Yy* (lavender) → 9/16 c^l– *Y*– (lavender) : 3/16 c^l– *yy* (yellow) : 3/16 $c^b c^b$ *Y*– (blue) : 1/16 $c^b c^b$ *yy* (yellow)

c. $c^r c^r$ *yy* (yellow) x $c^l c^l$ *YY* (lavender) → $c^r c^l$ *Yy* (bronze) → monohybrid ratio for the *c* gene is 1/4 $c^r c^r$: 1/2 $c^r c^l$: 1/4 $c^l c^l$ and monohybrid ratio for the *Y* gene is 3/4 *Y*– : 1/4 *yy*. Using the product rule, these generate a dihybrid ratio of **3/16 $c^r c^r$ *Y*– (red) : 3/8 $c^r c^l$ *Y*– (bronze) : 3/16 $c^l c^l$ *Y*– (lavender) : 1/16 $c^r c^r$ *yy* (yellow) : 1/8 $c^r c^l$ *yy* (novel genotype) : 1/16 $c^l c^l$ *yy* (yellow).** You expect the $c^r c^l$ *yy* genotype to be yellow as *y* is normally epistatic to the *c* gene. However, you have no direct evidence from the data in any of these crosses that this will be the case, so it is possible that this genotype could cause a different and perhaps completely new phenotype.

2-79. This problem shows that gene interactions producing variations of the 9:3:3:1 ratio in addition to those shown in Table 2.5 are possible though rare.

a. Using the information provided, it is clear that one of the pure-breeding white strains must be homozygous for recessive alleles of gene *A* and the other pure-breeding white strain must be homozygous for recessive alleles of gene *B*. That is, the cross was ***AA bb* (white) x *aa BB* (white) → F_1 *Aa Bb* (all blue).**

b. In the F_2 generation produced by self-mating of the F_1 plants, you would find a genotypic ratio of 9 *A*– *B*– : 3 *A*– *bb* : 3 *aa B*– : 1 *aa bb*. The *A*– *B*– plants would have blue flowers because colourless precursor 1 would be converted into blue pigment. (Colourless precursor 2 would not produce blue pigment in these flowers because the pathway is suppressed by the proteins specified by the dominant alleles of the two genes.) The *A*– *bb* plants would be white because the

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first pathway could not produce blue pigment in the absence of the protein specified by *B*, while the second pathway would be shut off by the protein specified by *A*. The *aa B*– plants would be white because the first pathway could not produce blue pigment in the absence of the protein specified by *A*, while the second pathway would be shut off by the protein specified by *B*. Interestingly, the *aa bb* plants would be blue because even though the first pathway would not function, the second would as it is not suppressed. **You would thus expect in the F_2 generation a ratio of 10 blue (9 *A*– *B*– + 1 *aa bb*) : 6 white (3 *A*– *bb* + 3 *aa B*–).**

2-80. The answers are presented in the table below. Different colours in the table represent different phenotypes; these colours are chosen arbitrarily and do not signify anything. The numbers in parentheses indicate the compounds that are present to produce the colours.

Part	9 *A*– *B*–	3 *A*– *bb*	3 *aa B*–	1 *aa bb*	Ratio
A	(2 + 4)	(2 + 3)	(1 + 4)	(1 + 3)	9:3:3:1
B	(2)	(2)	(2)	(1)	15:1
C	(3)	(2)	(1)	(1)	9:3:4
D	(2)	(1)	(1)	(1)	9:7
E	(2 + 3)	(2)	(3)	(1)	9:3:3:1
F	(2 + 4) = (2)	(2 + 3) = (2)	(1 + 4)	(1 + 3)	12:3:1
G	(3)	(2) = (1)	(1) = (2)	(1) = (2)	9:7
H	(2)	(1)	(2)	(2)	13:3

[Note: In part *e*, you could have interpreted a limitless supply of compound 1 to mean that compound 1 would be present in all the phenotypes (for example, the *A*– *B*– genotype would have compounds 1 + 2 + 3, etc.). The ratio would still be the same under this assumption as the ratio listed in the table.]

2-81. A particular phenotypic ratio does not allow you to infer the operation of a specific biochemical mechanism because as can be seen from the answers to Problem 80, **different biochemical mechanisms can produce the same ratio of phenotypes** (for example, the pathways in parts *d* and *g* are different yet both yield 9:7 ratios). The particular ratio seen in a cross may nonetheless provide information about types of biochemical pathways you could exclude from consideration because those pathways could not produce the observed ratio.

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In contrast, **if you know the biochemical mechanism behind a gene interaction** and you also know the dominance relationships of the alleles, you can then trace out the consequences of each genotypic class and thus **you can predict the ratios of phenotypes you would see among the F_2 progeny.**

2-82.

a. There are actually **two different phenotypes** mentioned in this problem. One phenotype is the shape of the erythrocytes. All people with the genotype *SPH SPH*$^+$ have **spherical erythrocytes**. Therefore this phenotype **is fully penetrant and shows no variation in expression**. The second **phenotype is anaemia. Here the expressivity among anaemic patients varies from severe to mild**. There are even **some people with the *SPH SPH*$^+$ genotype (150/2400) with no symptoms of anaemia at all. Thus the penetrance of the anaemic phenotype is 2250/2400 or 0.94**.

b. The disease-causing phenotype is the anaemia and the severity of the anaemia is greatly reduced when the spleen functions poorly and does not "read" the spherical erythrocytes. Therefore **treatment might involve removing the spleen (an organ which is not essential to survival). The more efficiently the spleen functions, the earlier in a patient's life it should be removed**. *SPH SPH*$^+$ individuals with no symptoms of anaemia should not be subjected to this drastic treatment.

2-83.

a. The most likely mode of inheritance is a **single gene with incomplete dominance** such that $f^n f^n$ = normal (<250 mg/dl), $f^n f^a$ = intermediate levels of serum cholesterol (250-500 mg/dl), and $f^a f^a$ homozygotes = elevated levels (>500 mg/dl). Some of the individuals in the pedigrees do not fit this hypothesis. In 2 of the families (Families 2 and 4), two normal parents have a child with intermediate levels of serum cholesterol. **One possibility is that in each family, at least one of these normal parents (I-3 and/or I-4 in Family 2; I-1 and/or I-2 in Family 4) was actually a $f^n f^a$ heterozygote who did not have elevated cholesterol in excess of 250 mg/dl. In this scenario, familial hypercholesterolaemia is a trait with incomplete penetrance**, so that some unaffected people have a genotype that causes the disease in other people. It is also possible that the affected children of these parents do not have an f^a allele associated with elevated serum

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cholesterol, but they show the trait for other reasons such as diet, level of exercise, or other genes. This explanation is reasonable, but perhaps less likely because multiple children would have to have the trait but not the f^a allele.

b. **Familial hypercholesterolaemia also shows variable expressivity**, meaning that people with the same genotype have the condition, but to different extents. This suggests that factors other than just the genotype are involved in the expression of the phenotype. Such factors could again include diet, level of exercise, and other genes.

2-84. If polycystic kidney disease is dominant, then the child is *Pp* and inherited the *P* disease allele from one parent or the other, yet phenotypically the parents appear to be *pp*. Perhaps one of the parents is indeed *Pp,* but this parent does not show the disease phenotype for some reason. Such situations are not uncommon: the unexpressed dominant allele is said to have **incomplete penetrance** in these cases. Alternatively, it could be that both parents are indeed *pp* and the *P* allele inherited by the child was due to a **spontaneous mutation** during the formation of the gamete in one of the parents; we will discuss this topic in Chapter 8. It is also possible that the **father of the child is not the male parent of the couple**. In this case the biological father must have the disease.

2-85.

a. The pattern in both families **looks like a recessive trait** since unaffected individuals have affected progeny and the trait skips generations. For example, in the Smiths II-3 must be a carrier, but in order for III-5 to be affected II-4 must also be a carrier. **If the trait is rare (as is this one) you wouldn't expect two heterozygotes to marry by chance as many times as required by these pedigrees. The alternative explanation is that the trait is dominant but not 100% penetrant.**
b. Assuming this is a dominant but not completely penetrant trait, **individuals II-3 and III-6 in the Smiths' pedigree and individual II-6 in the Jeffersons' pedigree** must carry the dominant allele but not express it in their phenotypes.
c. If the trait were common, **recessive inheritance** is the more likely mode of inheritance.

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d. **None**; in cases where two unaffected parents have an affected child, both parents would be carriers of the recessive trait.

2-86. The hairy x hairy → 2/3 hairy : 1/3 normal cross described in the first paragraph of the problem tells us that the hairy flies are heterozygous, that the hairy phenotype is dominant to normal, and that the homozygous hairy progeny are lethal (that is, hairy is a recessive lethal). Thus, hairy wings is *Hh*, normal wings is *hh,* and the lethal genotype is *HH*. Normal flies therefore should be ***hh*** **(normal-1)** and a cross with hairy (*Hh*) would be expected to always give 1/2 *Hh* (hairy) : 1/2 *hh* (normal) as seen in cross 1.

In cross 2, the progeny MUST for the same reasons be 1/2 *Hh* : 1/2 *hh*, yet they ALL appear normal. This suggests the normal-2 stock has another mutation that suppresses the hairy wing phenotype in the *Hh* progeny. The hairy parent must have the recessive alleles of this suppressor gene (*ss*), while the normal-2 stock must be homozygous for the dominant allele (*SS*) that suppresses the hairy phenotype. Thus cross 2 is ***hh SS*** **(normal-2)** x *Hh ss* (hairy) → 1/2 *Hh Ss* (normal because hairy is suppressed) : 1/2 *hh Ss* (normal).

In cross 3, the normal-3 parent is heterozygous for the suppressor gene: ***hh Ss*** **(normal-3)** x *Hh ss* (hairy) → the expected ratios for each gene alone are 1/2 *Hh* : 1/2 *hh*, and 1/2 *Ss* : 1/2 *ss*, so the expected ratio for the two genes together is 1/4 *Hh Ss* (normal) : 1/4 *Hh ss* (hairy) : 1/4 *hh Ss* (normal) : 1/4 *hh ss* (normal) = 3/4 normal : 1/4 hairy.

In cross 4 you see a 2/3 : 1/3 ratio again, as if you were crossing hairy x hairy. After a bit of trial-and-error examining the remaining possibilities for these two genes, you will be able to demonstrate that this cross was ***Hh Ss*** **(normal-4)** x *Hh ss* (hairy) → expected ratio for the individual genes are 2/3 *Hh* : 1/3 *hh*, and 1/2 *Ss* : 1/2 *ss*, so the expected ratio for the two genes together from the product rule is 2/6 *Hh Ss* (normal) : 2/6 *Hh ss* (hairy) : 1/6 *hh Ss* (normal) : 1/6 *hh ss* (normal) = 2/3 normal : 1/3 hairy.

2-87. The Black Lab: A solid black dog must: deposit eumelanin (*E*–); not be brown (*B*–); have no pheomelanin striping in the hairs [(K^B– and any *A* gene alleles) or (*aa* and any *K* gene alleles)]; must not be diluted to gray (*D*–); no spotting (*S*–); and no merle (M^2M^2). Because Labs always breed true for solid colours (black, brown, or some light yellow colour), the black Lab cannot be heterozygous at

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any gene for recessive alleles that specify non-solid colours. So **the Black Lab is most likely: *EE* or *Ee*, *BB or Bb*, (K^B K^B and any gene *A* alleles) or (K^B k^y *aa*), *DD*, *SS*, M^2M^2.**

The Chocolate Lab: A solid chocolate brown dog would be the same genotype as solid black, except *bb*.

The Yellow Lab: A solid yellow dog must not deposit eumelanin (*ee*). Any alleles of gene *B* are possible, and as above, the dog must be *DD*, *SS*, and M^2M^2. The same considerations for genes *A* and *K* apply as for the other Labs above. The yellow dog pictured cannot be *aa*, however, or it would be white. Therefore, **yellow labs are *ee*, *B–* or *bb*, K^B K^B, any gene *A* alleles except *aa*, *DD*, *SS*, M^2M^2.**

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Reference B *Arabidopsis thaliana*: Genetic Portrait of a Model Plant

Synopsis:

Arabidopsis thaliana serves as a useful plant model for genetic and molecular analyses. While many of the basic cellular mechanisms are the same in plants and animal cells, the events during development in plants are quite different from animals. Even so, the unique developmental events in plants often have underlying mechanisms that are analogous to those found in animals, fungi, etc. The following list of characteristics of *Arabidopsis* indicates why it is a useful model for plant development, and points out some genetic characteristics and manipulations that are unique to this plant.

- *Arabidopsis* has a fast generation time compared to other plants.
- Each plant can produce a large number of seeds, which is advantageous for mutant screening.
- Researchers can manipulate whether a plant undergoes self-fertilization or an outcross.
- Mutant screens can be done using T-DNA or other transposable elements to create mutations. This facilitates the identification of the altered gene at the DNA level.
- Very little repetitive DNA is present in *Arabidopsis,* so the genome is very small for a plant. Most other plants have very large genome, mostly because they contain massive amounts of repetitive DNA.

Significant Elements:

After reading the chapter and thinking about the concepts, you should be able to:

- think about how genetic analysis is done in this organism including: mutagenesis, isolation of mutants, characterization of mutations (complementation and epistasis analyses), study of mutant phenotypes, and gene
- understand how to interpret data obtained with molecular methods such as gene cloning, PCR, nucleic acid hybridization, the use of DNA markers for mapping, the use of fusions to study gene expression, and making a mutant copy of a cloned gene for reintroduction into the genome
- describe the steps that would be involved in a search for the gene affected by a T-DNA induced mutation

Problem Solving Tips:

- Remember that a seed contains a plant embryo. When seeds are mutagenized you are NOT mutagenizing gametes. Gametes are produced in the reproductive structures of an adult plant.

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- Some of the longer problems in this chapter are real research problems that were carried out essentially as described to you. They require that you integrate your knowledge of classical genetics, molecular genetics, and genome analysis. This is a good time to try out thinking like a geneticist. Consider how you would discover the genes involved, and how you would determine how the products of these genes might act - whether as regulators, messengers in a signal transduction system, structural components, etc.

Solutions to Problems:

B-1. a. **3**; b. **1**; c. **4**; d. **5**; e. **2.**

B-2.

a. The shorter generation time of *Arabidopsis* **allows the geneticist to study many more generations in less time.** In corn or peas, a researcher would be able to generate at most a few generations in a year.

b. The very large number of seeds produced is **an advantage for a geneticist searching for rare mutations.**

c. The small genome size is **advantageous for molecular analysis,** in particular for cloning genes. There is very little repetitive DNA to have to deal with. Historically, the small genome size made it feasible to determine the complete DNA sequence of the genome; *Arabidposis* is the first plant for which this goal was achieved.

B-3. Most of the extra DNA in tobacco and pea is repetitive DNA which presumably is not necessary for the physiology of the plant. **Most repetitive DNA does not encode genes**, so it does not contribute to the proteins made in the organism. In large part due to the paucity of repetitive DNA, genes in *Arabidposis* are packed more closely together (less intervening DNA) and the number and sizes of introns are smaller than in other plant species.

B-4.

a. **Plants of different strains that show the extreme phenotypes (the largest compared to the smallest seed set) could be crossed to produce hybrid F_1 plants that are then self-fertilized to produce the F_2 generation.** If the plants in the F_2 generation show three discrete phenotypes then there is a single gene that determines the trait. The three phenotypes would be associated

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with the *AA, Aa,* and *aa* genotypes. If these plants instead displayed a few more clear-cut phenotypic classes then two or three genes would be involved. If the F_2 plants have a range of phenotypes in a continuum, the trait is determined by several genes and might also have an environmental component.

b. **Different strains contain different alleles of molecular markers** that can be used to identify regions containing genes involved in determination of the phenotype. One would look for genetic linkage to molecular markers and use this linkage information to aid in cloning the gene of interest. **See Chapter 21** for a discussion of quantitative trait analysis.

B-5.

a. **Endosperm is 3*n* and is formed by fertilization of one sperm nucleus and two 1*n* nuclei in the ovule.** The genotype of the endosperm will be similar that of the embryo, in the sense that the endosperm produced from an outcross will yield a combination of genetic information from both parents.

b. **The zygote is 2*n* and is formed by fertilization of one sperm nucleus with the 1*n* egg; the genotype will again be a combination of genetic information from both parents.**

c. **The embryo sac cells are 1*n* and they are derived from the female parent plant.** The embryo sac cells will have the genotype derived from the female parent plant on which they are found, and thus have a very different genotype than the embryo.

B-6. A geneticist usually wants to study mutations that are in the germ cells and can therefore be transmitted to progeny and maintained as stocks for further study. The cells that were mutagenized are the embryonic cells in the seed that will divide and develop into the plant. **If the mutagen were applied very early, soon after fertilization, it might only affect one of the two DNA strands on a chromosome in the original zygotic cell, in which case one daughter cell would be mutant and the other would be normal.** Alternatively, **if the mutagen were applied later in embryonic development the mutation causing the phenotype might have occurred in only one of many embryonic cells present at that time. In either case, the plant growing from the mutagenized seed would be a mosaic, with some cells carrying the mutation, and others being wild type.** The first generation mutations might only affect tissues that could not become germ cells, and the trait would therefore not be transmissible.

B-7. a. **2**; b. **3**; c. **1**.

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B-8. The technique you would use is summarized in **Figure B.11.** **The DNA transformed into *Arabidopsis* would have an inverted duplication of the entire gene of interest or even of a part of the gene**. This inverted duplication would be under the control of a promoter that can be expressed in all or most *Arabidopsis* tissues. **Cells bearing the transgene will express an RNA molecule that will fold on itself to form a double-stranded RNA (dsRNA) with a hairpin loop between the inverted repeats. The *Dicer* complex within *Arabidopsis* cells will cleave this long dsRNA into 21 bp fragments of dsRNA. Target mRNAs are recognized by the RISC carrying RNA fragments and cleaved into smaller, non-coding fragments**. Thus, the expression of the gene of interest will be silenced, even though a true mutation in that gene is not available.

B-9. You could do manipulated crosses where you collect pollen from the sterile plant and use it to fertilize a wild-type plant. The reciprocal cross would also be done: pollen from a wild-type plant crossed with the sterile mutant. From the results you would know if the defect was in the male or female reproductive structures (assuming that one of the crosses would produce progeny while the other cross could not).

B-10. To look for an homolog for a gene in other plants, you would **perform a whole genome Southern blot**. You would first make genomic DNA from the petunias, snapdragons, and potatoes; cut these genomic DNAs with restriction enzymes, separate the resultant restriction fragments by gel electrophoresis according to their size, and then transfer the DNA fragments to nitrocellulose filter paper. You would then do a Southern blot hybridization using the *APETALA* gene from *Arabidopsis* as a probe. Two other approaches are also conceivable. First, if other investigators have determined the sequences of parts of the genomes of these other plants, or EST sequences from individual cDNA clones from these organisms, you could perform computerized BLAST searches to see if any of these nucleic acid sequences could encode a protein related to that encoded by *APETALA*. Second, you could try to amplify *APETELA*-like sequences from the genomes or cDNA libraries of the other species using PCR. However, this would only work if the protein were highly conserved in evolution; even if all the amino acids encoded by the sequences in the PCR primers were identical to those in the *Arabidopsis* protein, you would still have to account for the degeneracy of the genetic code and devise sets of primers that could account for all the possible codons for those amino acids.

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B-11.

a. **You could examine the gravitropic response in an auxin mutant** (defective in auxin production). If the gravitropic response is lacking in an auxin mutant, the response must be either directly or indirectly mediated by auxin.

b. There are a several different ways you could examine the distribution. You could **perform a Northern blot** analyzing the expression of each auxin-regulated mRNA. You would cut the plant up into different parts (such as the hypocotyls, flowering stalk, and root), and then grind up each tissue sample in order to isolate its RNAs. You would then fractionate these RNAs according to their sizes on a gel, transfer the RNAs to nitrocellulose filter paper, and hybridize using an auxin-regulated gene as a probe. For a more accurate picture, you could use DNA for an auxin-regulated gene as a probe against preparations of tissue from the plant (that is, **an *in situ* hybridization**). Or, you could make a fusion between an auxin-regulated gene and a reporter gene such as GUS or luciferase (which emits light when given substrate luciferin), transform the fusion back into the plant, and look at the distribution of where the reporter gene is expressed in the intact plant.

B-12.

a. The *ctr1*$^-$ constitutive mutation in a signaling pathway should not be affected by what is happening in the ethylene biosynthesis. This is because in mutant plants, the pathway is turned on independently of the production of ethylene. Thus, **there would still be expression of the ethylene response** in *ctr1*$^-$ mutants even if ethylene biosynthesis were inhibited.

b. Because inhibitors of biosynthesis affect these mutants, the **mutations are in genes in the biosynthetic pathway**.

c. **You could look for additional copies of the *ETR1* gene by Southern hybridization using the *ETR1* gene to probe in a blot containing genomic *Arabidopsis* genomic DNA.** Because the complete genome sequence of *Arabidopsis* is available, one could also perform a BLAST search to search for similar sequences.

d. The protein encoded by *APETALA2* is known to be a transcription factor, and the information provided indicates that the EREBP proteins are also transcription factors that bind to bases in the promoter region of several ethylene-responsive genes. **These proteins might thus share some similar features (types of motifs) that would allow DNA binding or transcriptional activation/repression.**

e. **To control expression of the ethylene response genes, you would need to make a fusion of an inducible regulatory region with the ethylene response gene you want to induce. The**

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inducible regulatory region would have to be one that you could turn on in the plant cells where you wanted expression. Identifying a suitable inducible regulatory region might take some effort. For example, you might want to look at many plants transformed with a modified T-DNA that carries a promoterless *GUS* gene reporter. In each transformed plant line, *GUS* will be expressed in specific parts of the plant based upon regulatory regions in the vicinity of the T-DNA insertion. This "enhancer-trapping" methodology is shown in **Figure B.10**. Look for a plant that displays *GUS* expression in the tissues in which you wanted to induce the ethylene response gene. You would then take the regulatory region near the T-DNA insertion, fuse it with the ethylene response gene, and transform the construct back into *Arabidopsis.*

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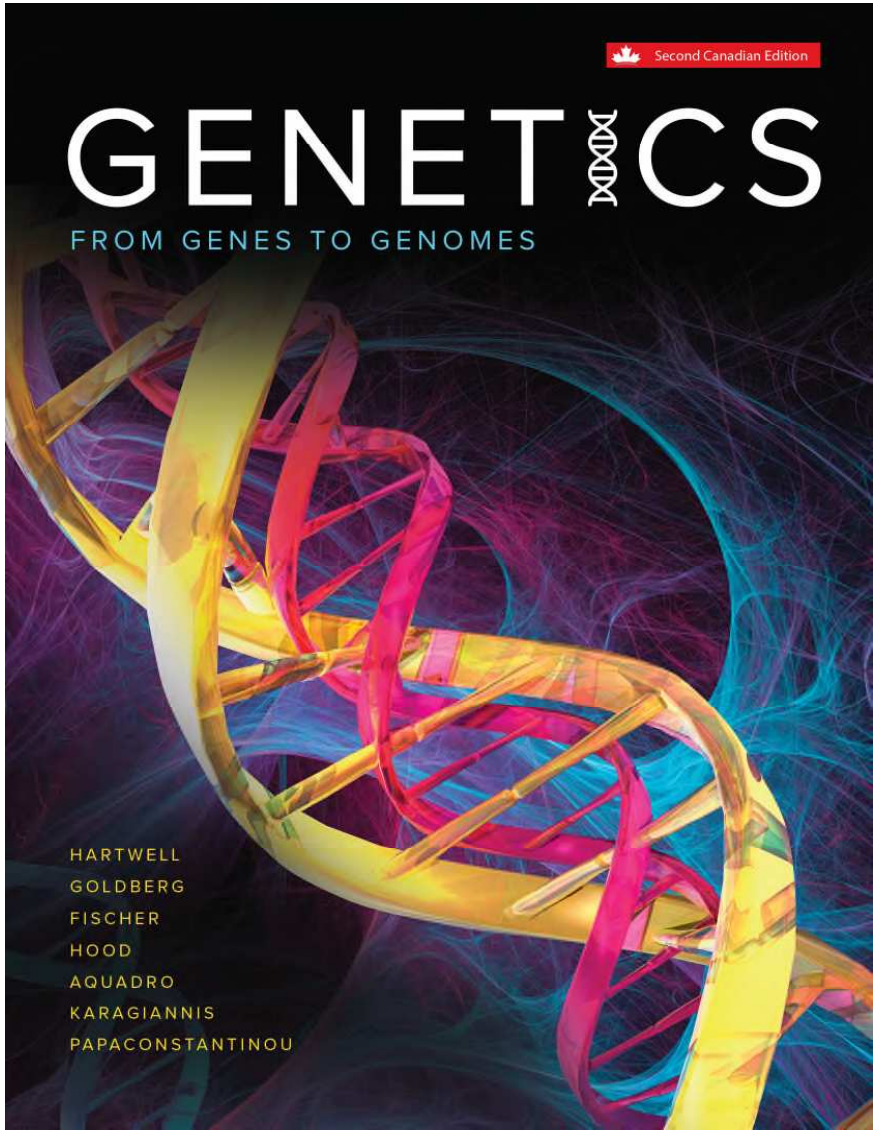
Hartwell, Genetics: From Genes to Genomes. Second Canadian Edition

Prepared by Bassam Nyaeme,
University of The Fraser Valley,
British Columbia Institute of Technology



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Mendelian Genetics

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CHAPTER 2 Learning Objectives

1. Explain how monohybrid crosses led Mendel to infer the law of segregation.

2. Distinguish between the terms *gene* and *allele* and contrast dominant alleles with recessive alleles.

3. Explain Mendel's law of segregation.

4. Differentiate between the terms *homozygous, heterozygous, genotype,* and *phenotype.*

5. Analyze Mendel's law of independent assortment, and explain how Mendel proposed the law from dihybrid crosses.

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CHAPTER 2 Learning Objectives

6. Compare and contrast complete dominance, incomplete dominance, and codominance relationships, and demonstrate how a dominance series can be established.

7. Explain the terms *wild-type allele, mutant allele, monomorphic,* and *polymorphic.*

8. Describe pleiotropy and how it arises.

9. Compare and contrast complementary gene action, recessive epistasis, dominant epistasis, and redundancy.

10. Evaluate the significance of the complementation test as a tool for genetic analysis.

11. Distinguish between penetrance and expressivity.

12. Explain the inheritance of continuous traits.

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CHAPTER 2 OUTLINE

- 2.1 Background: The Historical Puzzle of Inheritance
- 2.2 Genetic Analysis According to Mendel
- 2.3 Mendelian Inheritance in Humans
- 2.4 Extensions to Mendel for Single-Gene Inheritance
- 2.5 Extensions to Mendel for Gene Interactions

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A family portrait with members of four generations

Why do some of the children look like only one of the parents, while some of the other children don't look like any of the assembled relatives and instead look more like the great, great grandparents?

What causes the similarities and differences of appearance and the skipping of generations?

Fig. 2.1

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Gregor Mendel discovered the basic principles of genetics

Mendel was the first scientist to combine data collection, analysis, and theory to understand heredity.

He inferred genetic laws about the appearance and disappearance of traits during different generations.

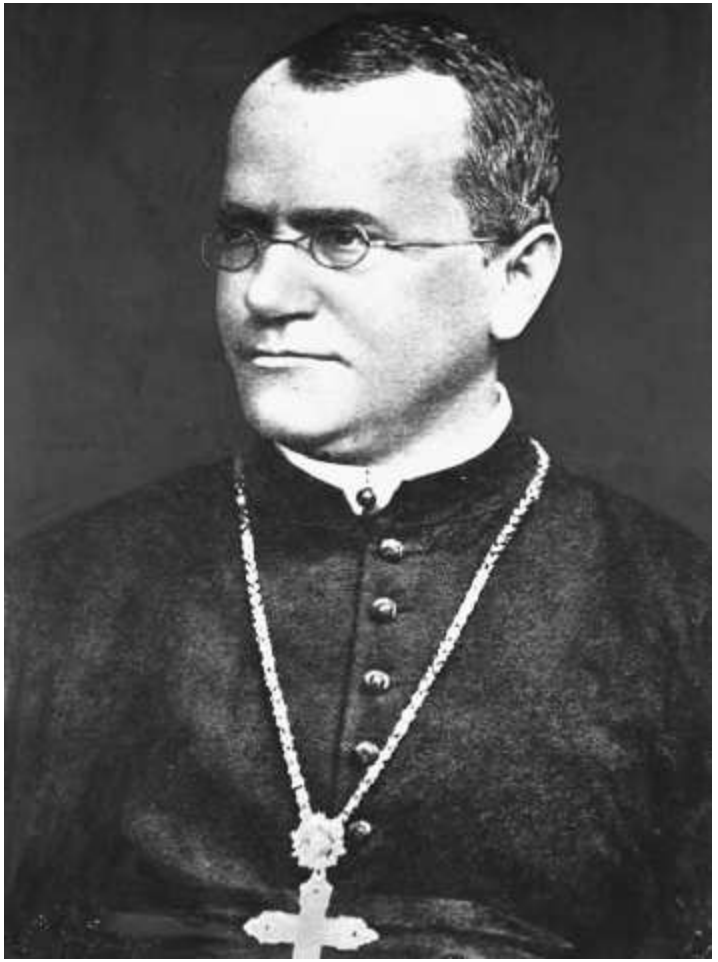

Fig. 2.2

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Genetics explains the mechanisms that determine the inheritance of traits

Genes are the basic units of **heredity**

- Heredity is the way that genes transmit traits from parents to offspring
- Genes are passed from one generation to the next

Genes underlie the formation of every heritable trait, e.g., cleft chin, hair loss, colour of hair, skin, and eyes

- Some traits are causes by a single change in a single gene, e.g., sickle-cell anaemia
- Some traits are caused by complex interactions between many genes, e.g., facial features

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Four general themes of Mendel's work

1. Variation is widespread in nature and provides for continuously evolving diversity.

2. Observable variation is essential for following genes from one generation to another.

3. Variation is inherited by genetic laws, which can explain why like begets like and unlike.

4. Mendel's laws apply to all sexually reproducing organisms.

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Genetic variation exists even within dog breeds

Mendel's laws explain why two black Labradors could have a litter of black, brown, and golden puppies

Fig. 2.3

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Background: The Historical Puzzle of Inheritance

Artificial selection was the first applied genetic technique.

- Purposeful control of mating by choice of parents for the next generation.

Domestication of plants and animals was a key transition in human civilization.

- Domestication of dogs (*Canis lupus familiaris*) from wolves (*Canis lupus*).
- Domestication of rice, wheat, barley, lentils, and dates from weed like plants.

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Critical questions about selective breeding before Mendel's studies

Concluding remarks by Abbot Cyril Napp at the 1837 annual meeting of the Moravian Sheep Breeders Society:

Three basic questions must be answered

- What is inherited?
- How is it inherited?
- What is the role of chance in heredity?

Abbot Napp presided over the monastery where Mendel began his seminal genetic experiments in 1864

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Two key misconceptions about inheritance existed at the time of Mendel's studies

Before Mendel, several misconceptions clouded people's thinking about heredity:

- Inherited features of offspring are contributed mainly by only one parent (e.g., a "homunculus" inside the sperm)

- Parental traits become mixed and changed in the offspring (i.e., "blended inheritance")

Neither idea could explain why some traits would appear, disappear, and then reappear.

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Mendel studied the inheritance of alternative traits in pea plants

Mendel inferred laws of genetics that allowed predictions about which traits would appear, disappear, and then reappear.

- This work was done in his garden at a monastery

Mendel's paper "Experiments in plant hybrids" was published in 1866 and became the cornerstone of modern genetics.

(a)

Fig. 2.4a

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Keys to the success of Mendel's experiments

Pure-breeding lines of peas (*Pisum sativum*)

- Breeding could be done by cross-fertilization or selfing
- Large numbers of progeny produced within a short time
- Traits remained constant in crosses within a line

Inheritance of alternative forms of traits

- Antagonistic pairs of "either-or" traits: e.g., purple or white, yellow or green

Brilliant experimentalist

- Planned experiments carefully
- Controlled the plant breeding
- Analyzed results mathematically

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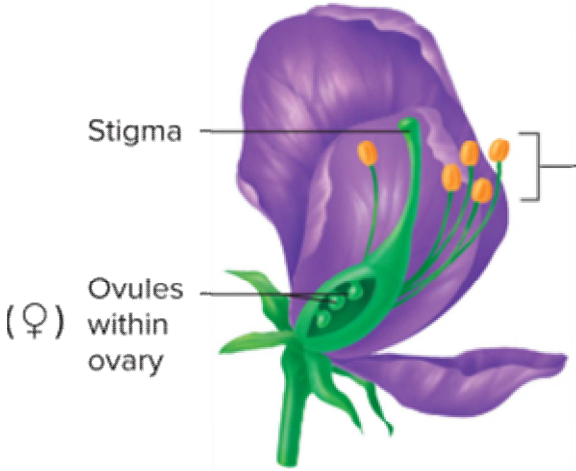
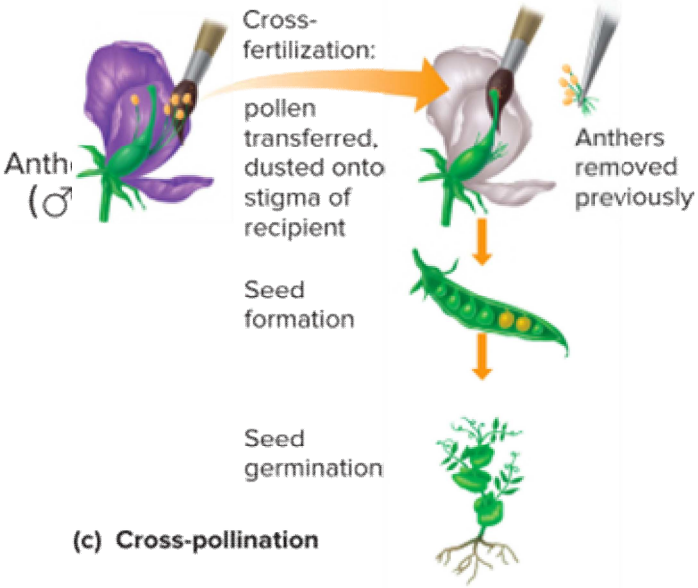
Mendel's experimental organism: The garden pea

(a) *Pisum sativum*



(b) Pea flower anatomy



(c) Cross-pollination

Fig. 2.6

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Mendel studied seven antagonistic pairs of traits in peas

Three antagonistic pairs of traits are shown at right.

Note that each hybrid resembles only one of the parents:
the dominant trait.

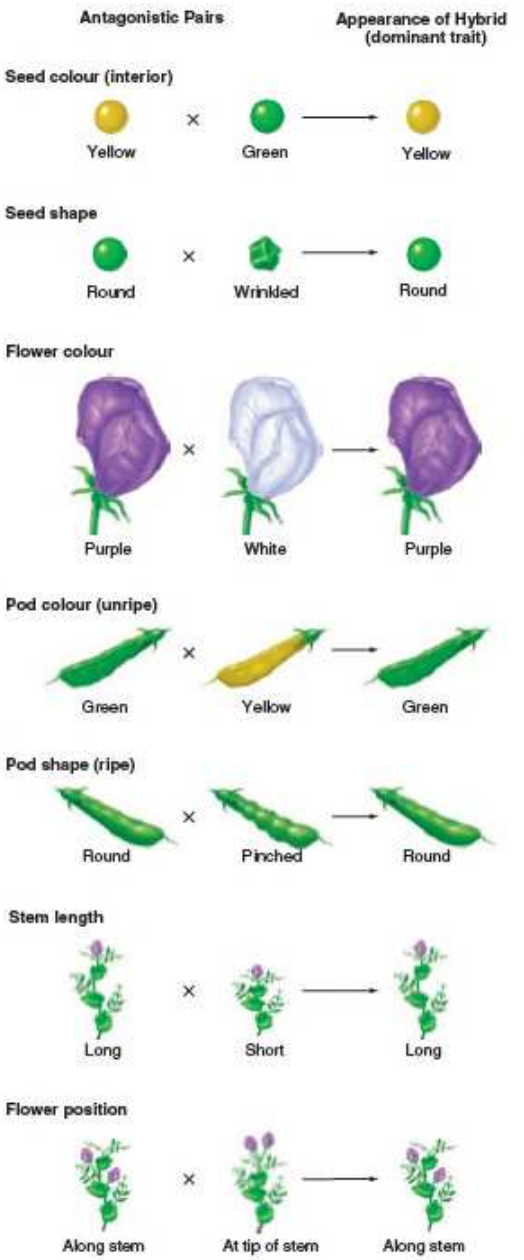

Fig. 2.7

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Monohybrid crosses revealed units of inheritance and the law of segregation

Mendel crossed pure-breeding lines that differed in only one trait, e.g., seed colour.

Examined phenotypes of F_1 progeny and F_2 progeny

- F_1 progeny have only one of the parental traits
- Both parental traits reappear in F_2 progeny in a 3:1 ratio

These results disproved the blending hypothesis

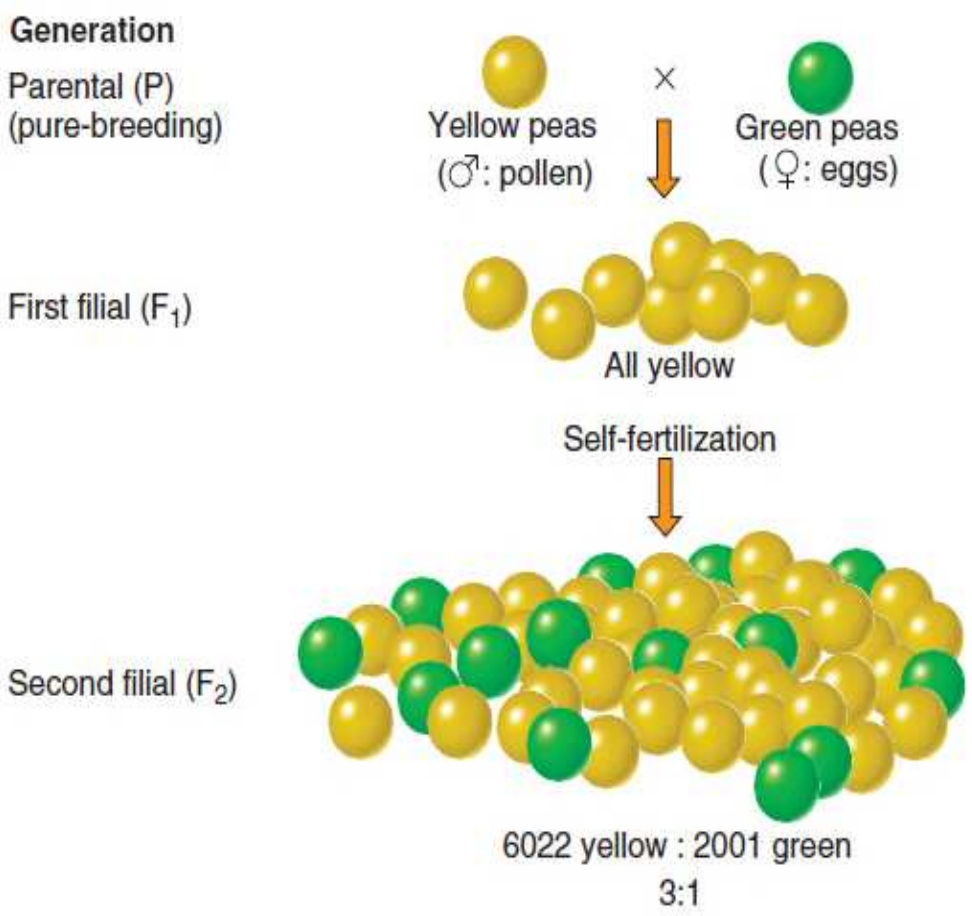

Fig. 2.8

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Mendel proposed that each plant carries two copies of a unit of inheritance

Traits have two forms that can each breed true

- Trait that appears in F_1 progeny is the **dominant** form
- Trait that is hidden in the F_1 progeny is the **recessive** form
- Progeny inherit one unit from the maternal parent and the other unit from the paternal parent

Units of inheritance are now known as "genes"

- Alternative forms of a single gene are "**alleles**"
- Individuals with two different alleles for a single trait are "**monohybrids**"

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Mendel's law of segregation

The two alleles for each trait separate during gamete formation

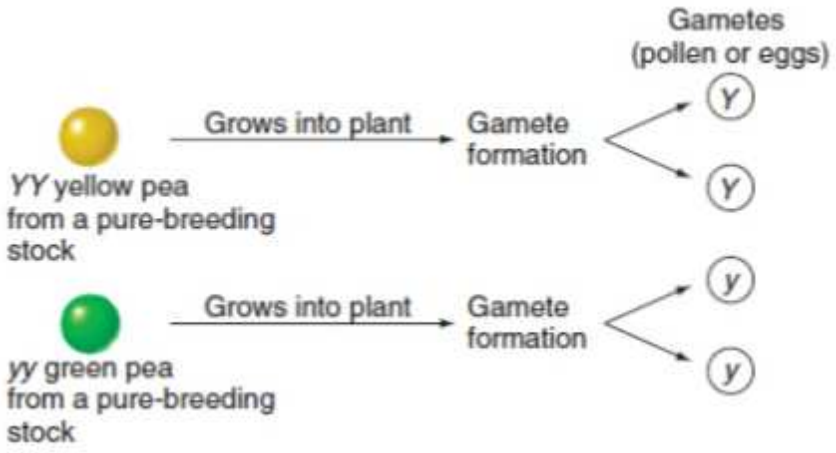

Fig. 2.9a

Two gametes, one from each parent, unite at random at fertilization

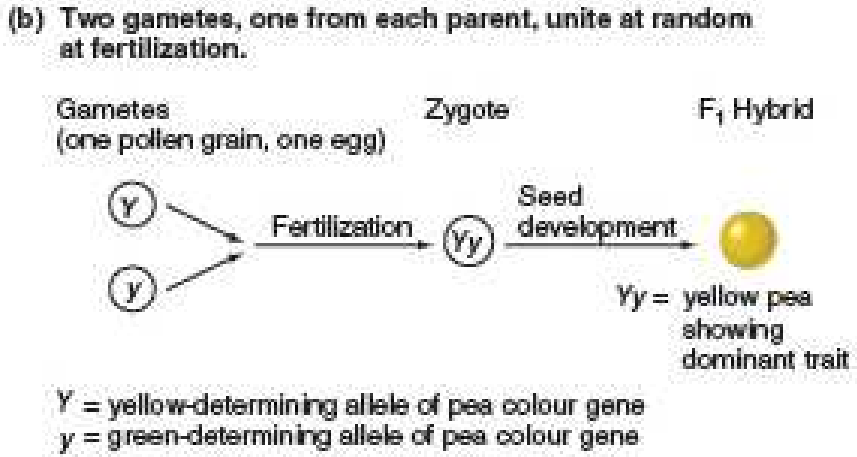

Fig. 2.9b

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Genes Encode Proteins

Genes encode the proteins that cells produce and depend on for structure and function.

- In 1989, scientists from the Hospital for Sick Children in Toronto and the University of Michigan found that the normal allele of the cystic fibrosis gene encodes a chloride channel, called the **c**ystic **f**ibrosis **t**ransmembrane **c**onductance **r**egulator (CFTR). They discovered how a mutant allele causes unusually sticky mucus.

CFTR

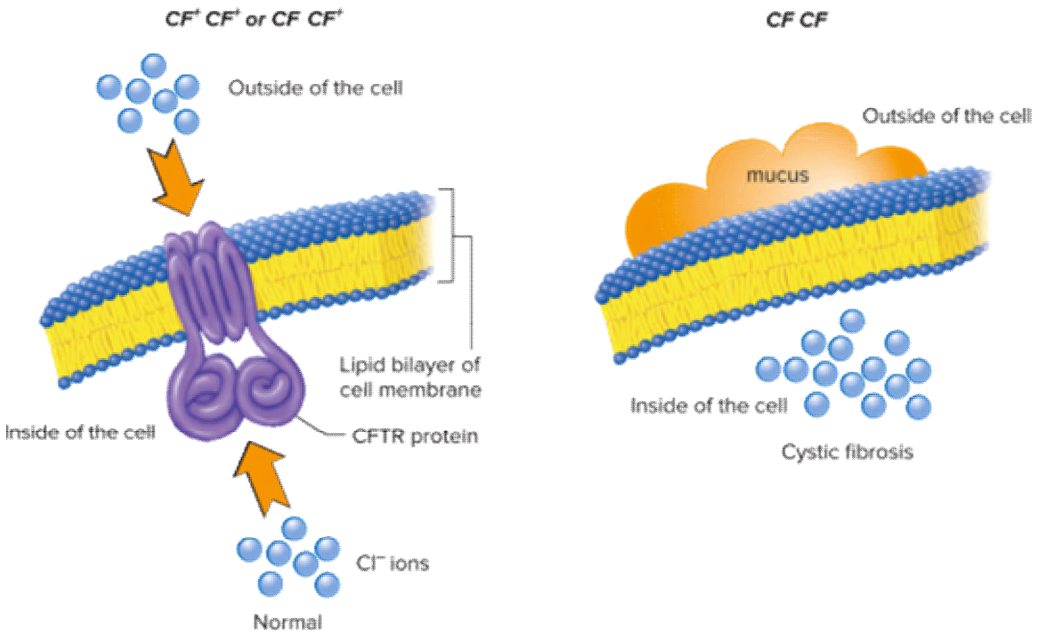

Fig. B

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The Punnett square is a simple way to visualize the segregation and random union of alleles

Each F_1 hybrid produces two kinds of gametes in a 1:1 ratio

F_2 progeny

- 3:1 ratio of phenotypes
- 1/4 will breed true for the dominant trait
- 1/2 will be hybrids
- 1/4 will breed true for the recessive trait

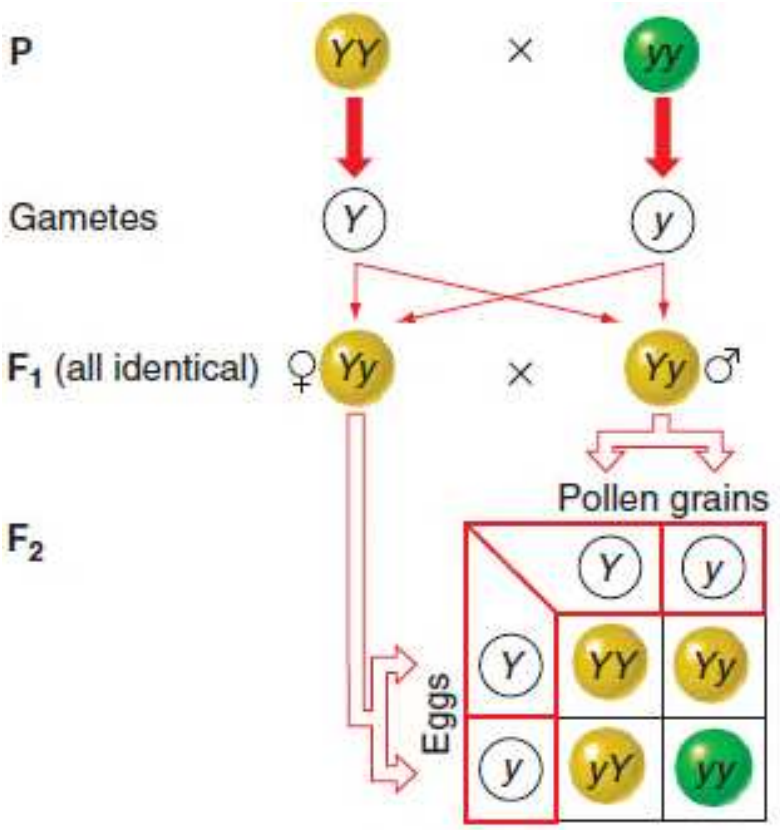

Fig. 2.10

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Mendel's results and the Punnett square reflect the basic rules of probability

Product rule: probability of two independent events occurring together is the product of their individual probabilities

- What is the probability that event 1 AND event 2 will occur?

  P(1 and 2) = probability of event 1 X probability of event 2

Sum rule: probability of either of two mutually exclusive events occurring is the sum of their individual probabilities

- What is the probability that event 1 OR event 2 will occur?

  P(1 or 2) = probability of event 1 + probability of event 2

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Applying probability to Mendel's crosses

From a cross of *Yy* x *Yy* peas

- What is the chance of getting *YY* offspring?
  - Chance of *Y* pollen is 1/2
  - Chance of *Y* ovule is 1/2
  - Chance of *Y* pollen and *Y* ovule uniting is 1/2 x 1/2 = 1/4
- What is the chance of getting *Yy* offspring?
  - Chance of *Y* pollen uniting with *y* ovule is 1/2 x 1/2 = 1/4
  - Chance of *y* pollen uniting with *Y* ovule is 1/2 x 1/2 = 1/4
  - Chance of either event happening is 1/4 + 1/4 = 1/2

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Mendel did further crosses to verify the law of segregation

F_2 plants were selfed to produce F_3 progeny

- All of the green F_2 peas were pure breeding
- 1/3 of the yellow F_2 peas were pure breeding
- 2/3 of the yellow F_2 peas were hybrids

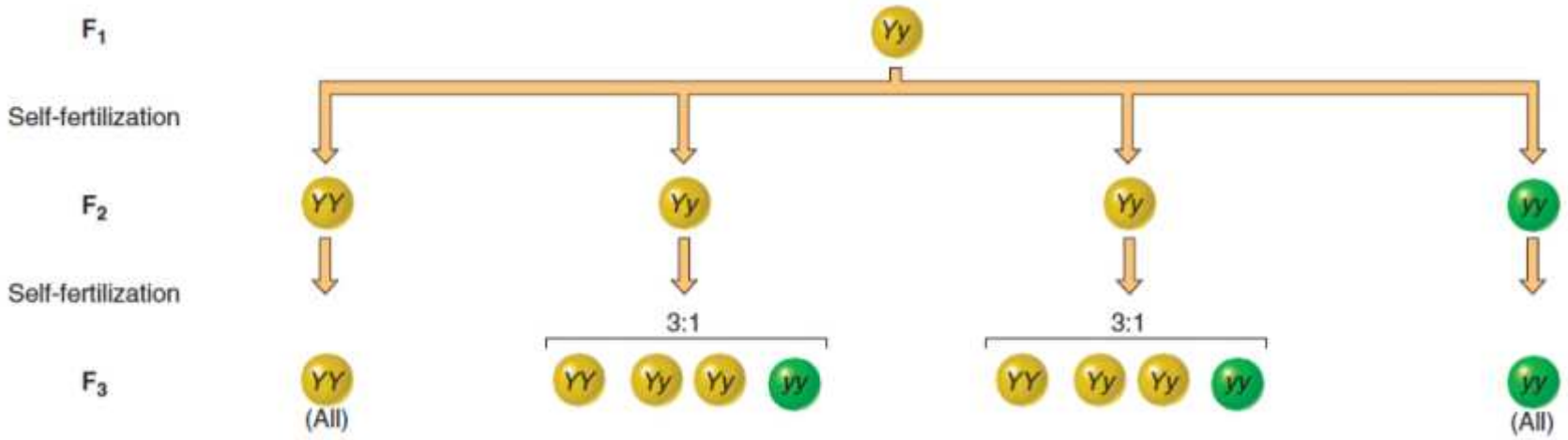

Fig. 2.11

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Definitions of commonly used terms

Phenotype is an observable characteristic (e.g., yellow or green pea seeds)

Genotype is a pair of alleles in an individual (e.g., *YY* or *Yy*)

Homozygote has two identical alleles (e.g., *YY* or *yy*)

Heterozygote has two different alleles (e.g., *Yy*)

- The heterozygous phenotype defines the dominant allele (e.g., *Yy* peas are yellow, so the yellow *Y* allele is dominant to the green *y* allele)
- A dominant allele with a dash represents an unknown genotype (e.g., *Y*− stands for either *YY* or *Yy*)

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Genotype vs phenotype in homozygotes and heterozygotes

From a cross of *Yy* x *Yy* peas

Genotypes in F_2 progeny are in 1:2:1 ratio (1/4 *YY*, 1/2 *Yy*, 1/4 *yy*)

Phenotypes in F_2 progeny are in 3:1 ratio (3/4 yellow, 1/4 green)

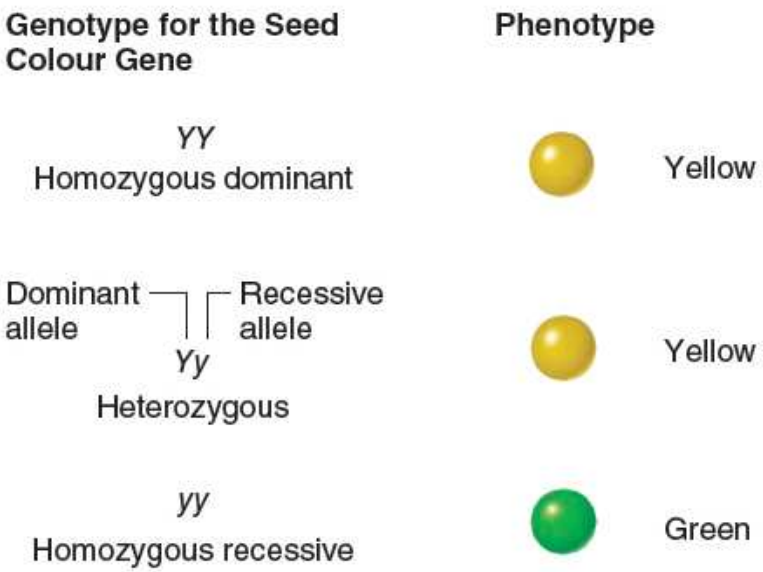

Fig. 2.12

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A testcross can reveal an unknown genotype

Is the genotype of an individual with a dominant phenotype (e.g., *Y*−) heterozygous (*Yy*) or homozygous (*YY*)?

- Solution: Testcross to homozygous recessive (*yy*) and examine progeny

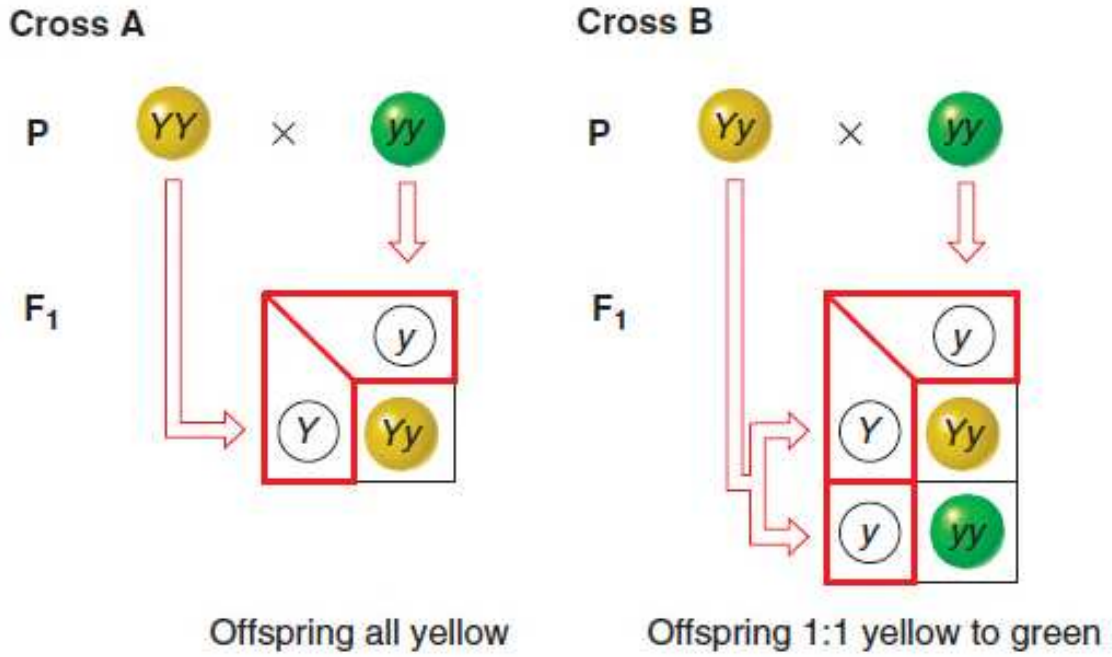

Fig. 2.13

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Mendel's dihybrid crosses revealed the law of independent assortment

Mendel tested whether two genes in dihybrids would segregate independently

First, he crossed true-breeding yellow round peas with true-breeding green wrinkled peas to obtain dihybrid F_1 plants:

YY RR x *yy rr* → F_1 *Yy Rr*

Then, the dihybrid F_1 plants were selfed to obtain F_2 plants:

F_1 *Yy Rr* x F_1 *Yy Rr* → F_2

Mendel asked whether all the F_2 progeny would be **parental types** (yellow round and green wrinkled) or would some be **recombinant types** (yellow wrinkled and green round)?

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A dihybrid cross produces parental types and recombinant types

Each F_1 dihybrid produces four possible gametes in a 1:1:1:1 ratio

Yy Rr → 1/4 *Y R*, 1/4 *Y r*,

1/4 *y R*, 1/4 *y r*

Four phenotypic classes occurred in the F_2 progeny:

- Two are like parents
- Two are recombinant

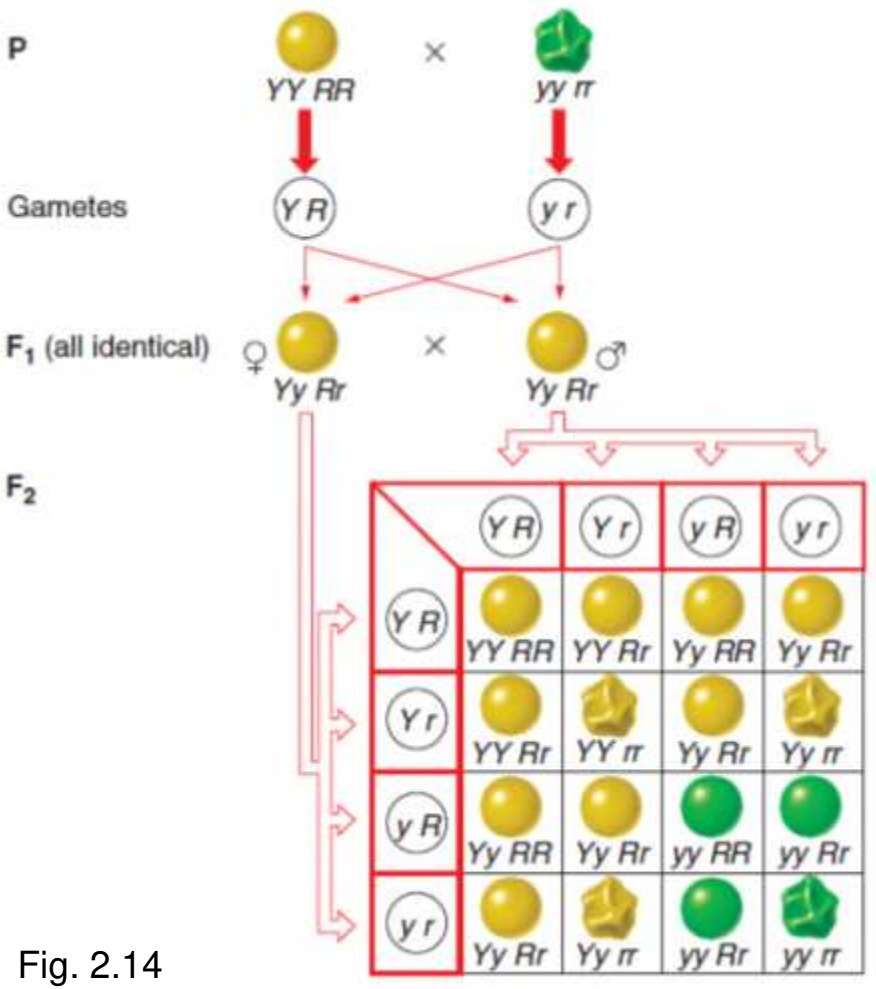

Fig. 2.14

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Independent assortment in crosses of F_1 dihybrids produces a 9:3:3:1 phenotype ratio

Note that in these F_2 progeny, there is a 3:1 phenotype ratio of dominant to recessive forms

Type	Genotype	Phenotype	Number	Phenotypic Ratio
Parental	*Y– R–*	yellow round	315	9/16
Recombinant	*yy R–*	green round	108	3/16
Recombinant	*Y– rr*	yellow wrinkled	101	3/16
Parental	*yy rr*	green wrinkled	32	1/16

Ratio of yellow (dominant) to green (recessive) = 12:4 or 3:1

Ratio of round (dominant) to wrinkled (recessive) = 12:4 or 3:1

Fig. 2.14

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Mendel's law of independent assortment

During gamete formation, different pairs of alleles segregate independently of each other

- *Y* is just as likely to assort with *R* as it is with *r*
- *y* is just as likely to assort with *R* as it is with *r*

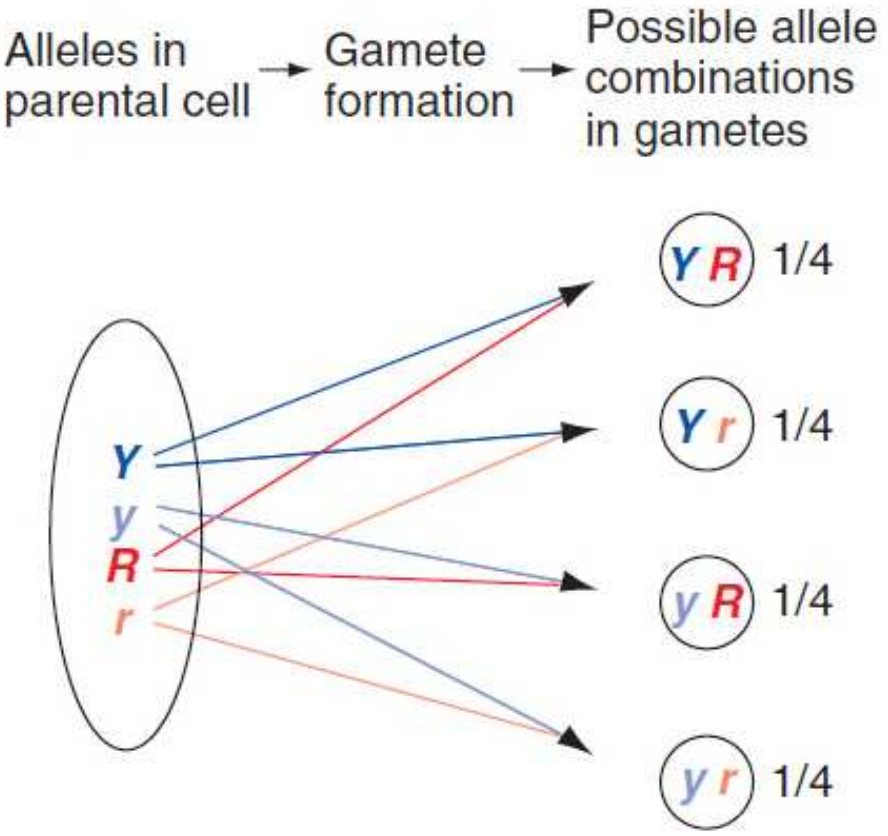

Fig. 2.15

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Following crosses with branched-line diagrams

Progeny phenotypes for each gene are shown in different columns

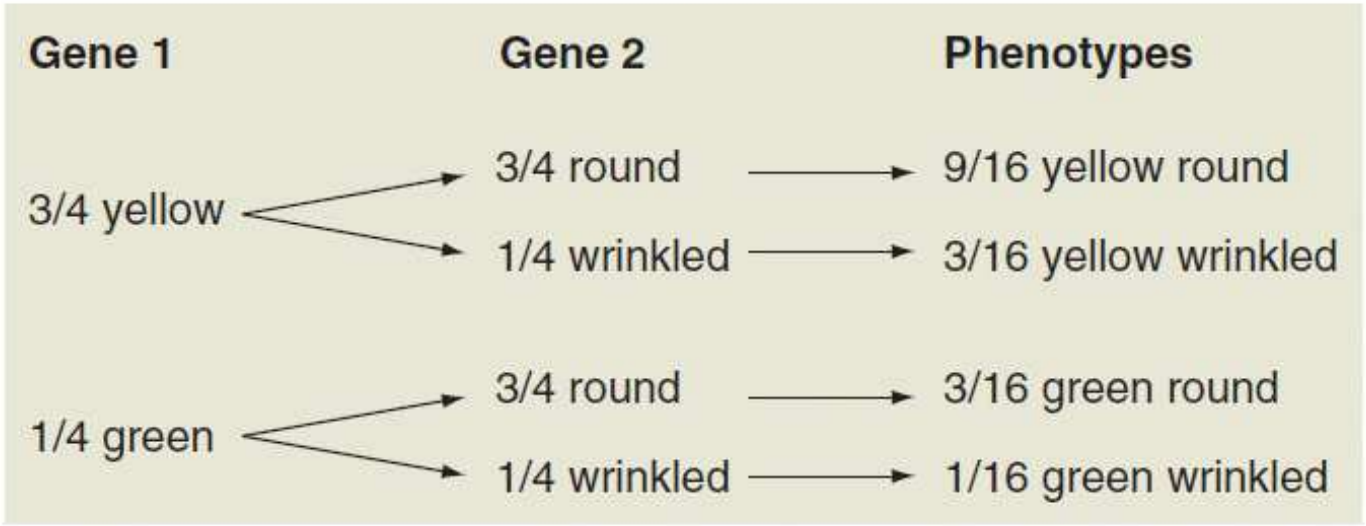

Fig. 2.16

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Testcrosses on dihybrids

Testcross dihybrids to individuals that are homozygous for both recessive traits

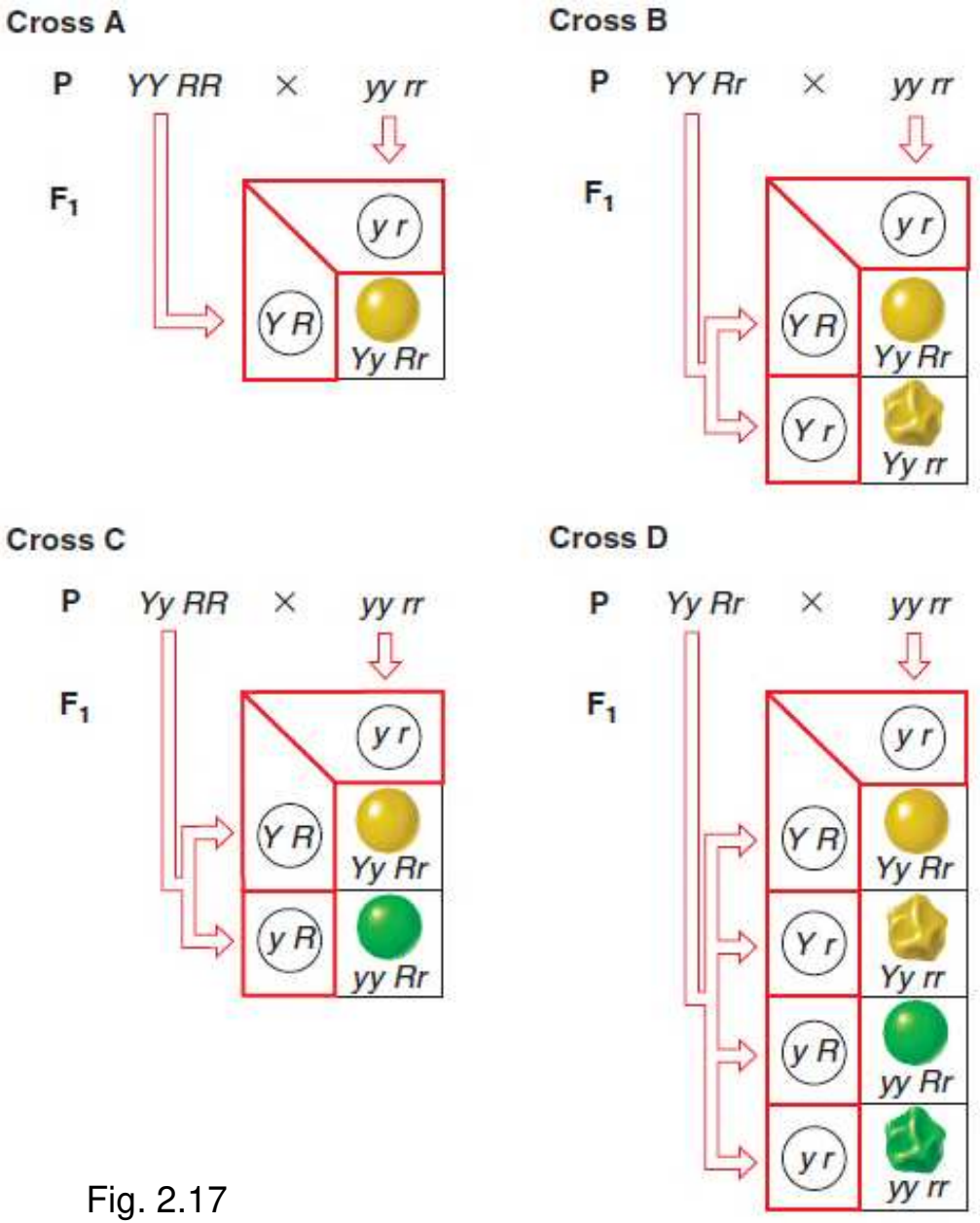

Fig. 2.17

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Mendel's laws can be used to predict offspring from complicated crosses

To calculate the possible number of gamete genotypes from a hybrid, raise 2 to the power of the number of different traits

- *Aa Bb Cc Dd* → 2^4 = 16 kinds of gametes
- *Aa Bb Cc Dd* x *Aa Bb Cc Dd* → 16 x 16 = 256 genotypes
- To do a Punnett square with this cross involving four genes, you would need 16 columns and 16 rows
- An easier way is to break down a multihybrid cross into independently assorting monohybrid crosses

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Predicting proportions of progeny from multihybrid crosses – example 1

Cross *Aa Bb Cc Dd* x *Aa Bb Cc Dd*

What proportion of progeny will be *AA bb Cc Dd*?

- *Aa* x *Aa* → 1/4 *AA*
- *Bb* x *Bb* → 1/4 *bb*
- *Cc* x *Cc* → 1/2 *Cc*
- *Dd* x *Dd* → 1/2 *Dd*

So, the expected proportion of *AA bb Cc DD* progeny is:

1/4 x 1/4 x 1/2 x 1/2 = 1/64

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Predicting proportions of progeny from multihybrid crosses – example 2

Cross *Aa Bb Cc Dd* x *Aa Bb Cc Dd*

How many progeny will show the dominant traits for *A*, *C*, and *D* and the recessive trait for *B*?

- *Aa* x *Aa* → 3/4 *A*−
- *Bb* x *Bb* → 1/4 *bb*
- *Cc* x *Cc* → 3/4 *C*−
- *Dd* x *Dd* → 3/4 *D*−

So, expected proportion of *A*− *bb C*− *D*− progeny is:

3/4 x 1/4 x 3/4 x 3/4 = 27/256

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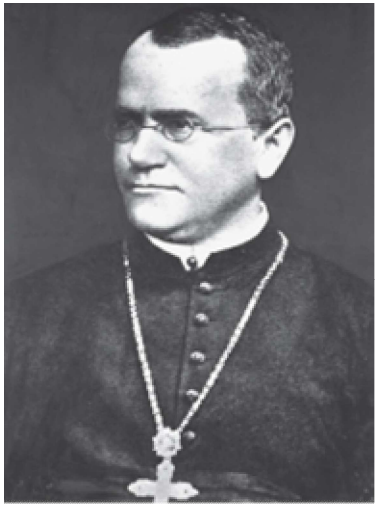
The science of genetics began with the rediscovery of Mendel's work

Mendel published his monumental breakthrough in understanding heredity in 1866, but hardly anyone paid attention to his work!

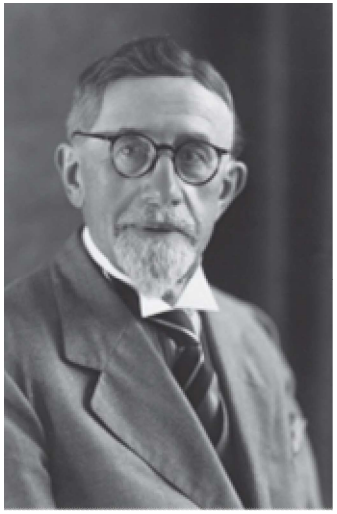
In 1900, three scientists independently rediscovered and acknowledged Mendel's work.



(a) Gregor Mendel

(b) Carl Correns

(c) Hugo de Vries



(d) Erich von Tschermak

Fig. 2.18

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Mendelian inheritance in humans

Many heritable traits in humans are caused by interaction of multiple genes and thus don't show simple Mendelian inheritance patterns.

In 2013, there were ~ 10,000 single-gene traits known in humans.

- See Table 2.1 for some of the common single-gene traits

Even with single-gene traits, determining inheritance pattern in humans can be tricky.

- Long generation time
- Small numbers of progeny
- No controlled matings
- No pure-breeding lines

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Some of the most common single-gene traits caused by recessive alleles in humans

Disease	Effect	Incidence of Disease
Thalassemia (chromosome 16 or 11)	Reduced amounts of haemoglobin; anaemia, bone, and spleen enlargement	1/10 in parts of Italy
Sickle-cell anaemia (chromosome 11)	Abnormal haemoglobin; sickle-shaped red cells, anaemia, blocked circulation; increased resistance to malaria	1/625 African-Americans
Cystic fibrosis (chromosome 7)	Defective cell membrane protein; excessive mucus production; digestive and respiratory failure	1/2000 Caucasians
Tay-Sachs disease (chromosome 15)	Missing enzyme; buildup of fatty deposit in brain; buildup disrupts mental development	1/3000 Eastern European Jews
Phenylketonuria (PKU) (chromosome 12)	Missing enzyme; mental deficiency	1/10,000 Caucasians

Table 2.1

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Some of the most common single-gene traits caused by dominant alleles in humans

Disease	Effect	Incidence of Disease
Hypercholesterolemia (chromosome 19)	Missing protein that removes cholesterol from the blood; heart attack by age 50	1/122 French Canadians
Huntington disease (chromosome 4)	Progressive mental and neurological damage; neurologic disorders by ages 40 - 70	1/25,000 Caucasians

Table 2.1

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In humans, pedigrees can be used to study inheritance

Pedigrees are orderly diagrams of a family's relevant genetic features.

Pedigrees include as many generations as possible (ideally, at least both sets of grandparents of an affected person).

Pedigrees can be analyzed using Mendel's laws:

- Is a trait determined by alternate alleles of a single gene?
- Is a trait dominant or recessive?

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Symbols used in pedigree analysis

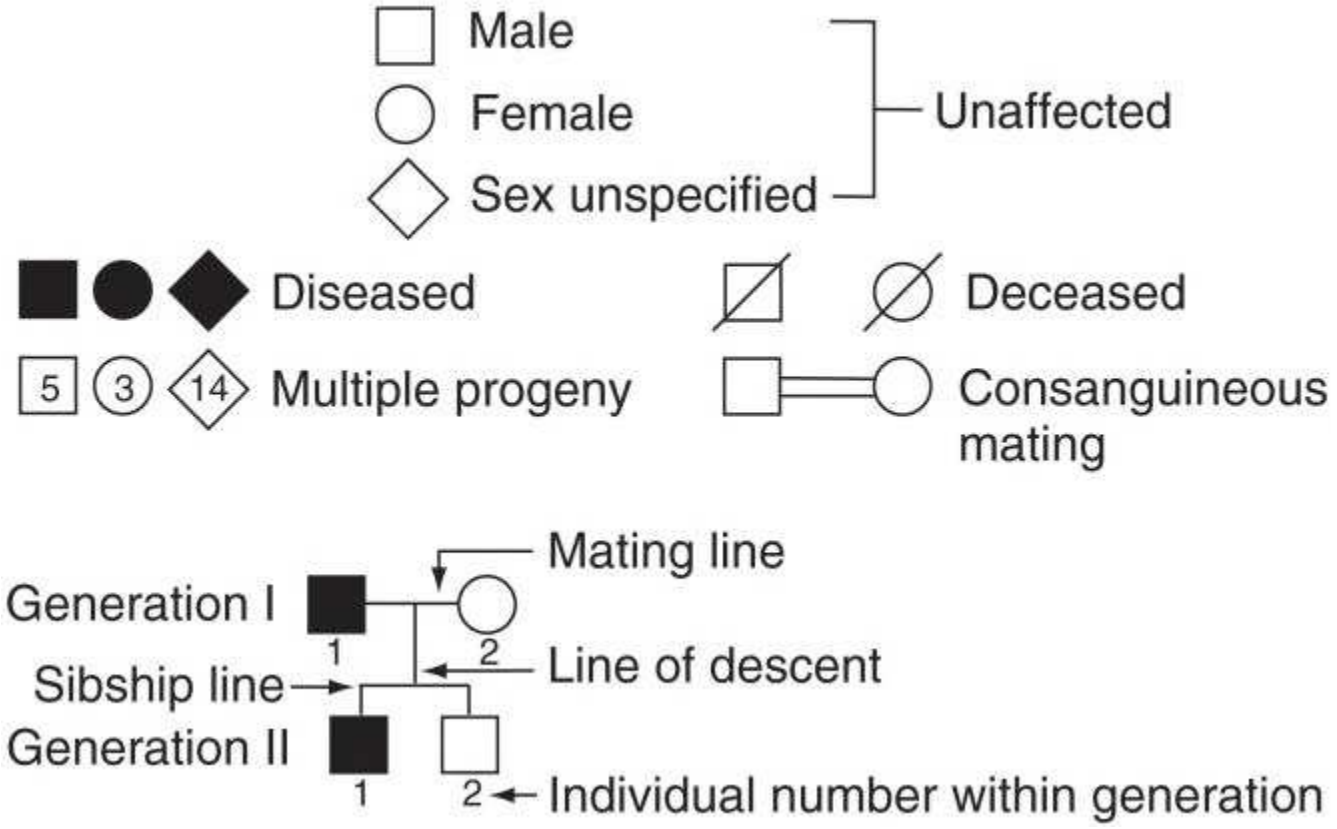

Fig. 2.19

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A vertical pattern of inheritance indicates a rare dominant trait; e.g., Huntington disease

Every affected person has at least one affected parent

Mating between affected person and unaffected person is effectively a testcross

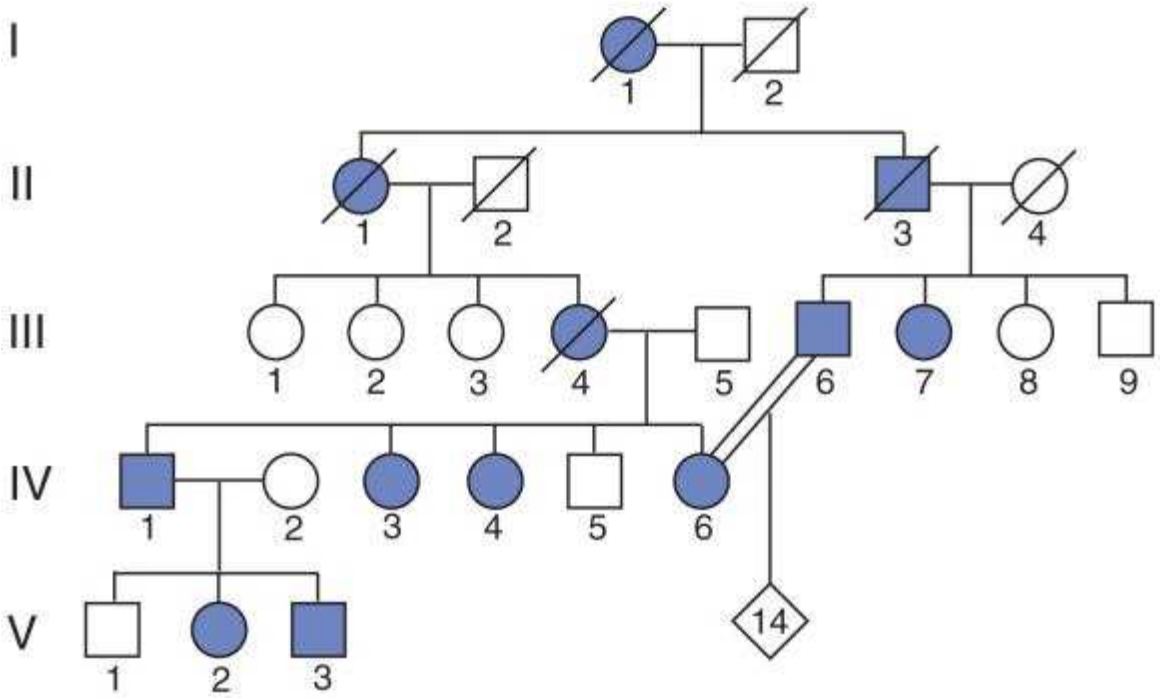

Fig. 2.20

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A horizontal pattern of inheritance indicates a rare recessive trait; e.g., cystic fibrosis

Parents of affected individuals are unaffected but are heterozygous (carriers) for the recessive allele

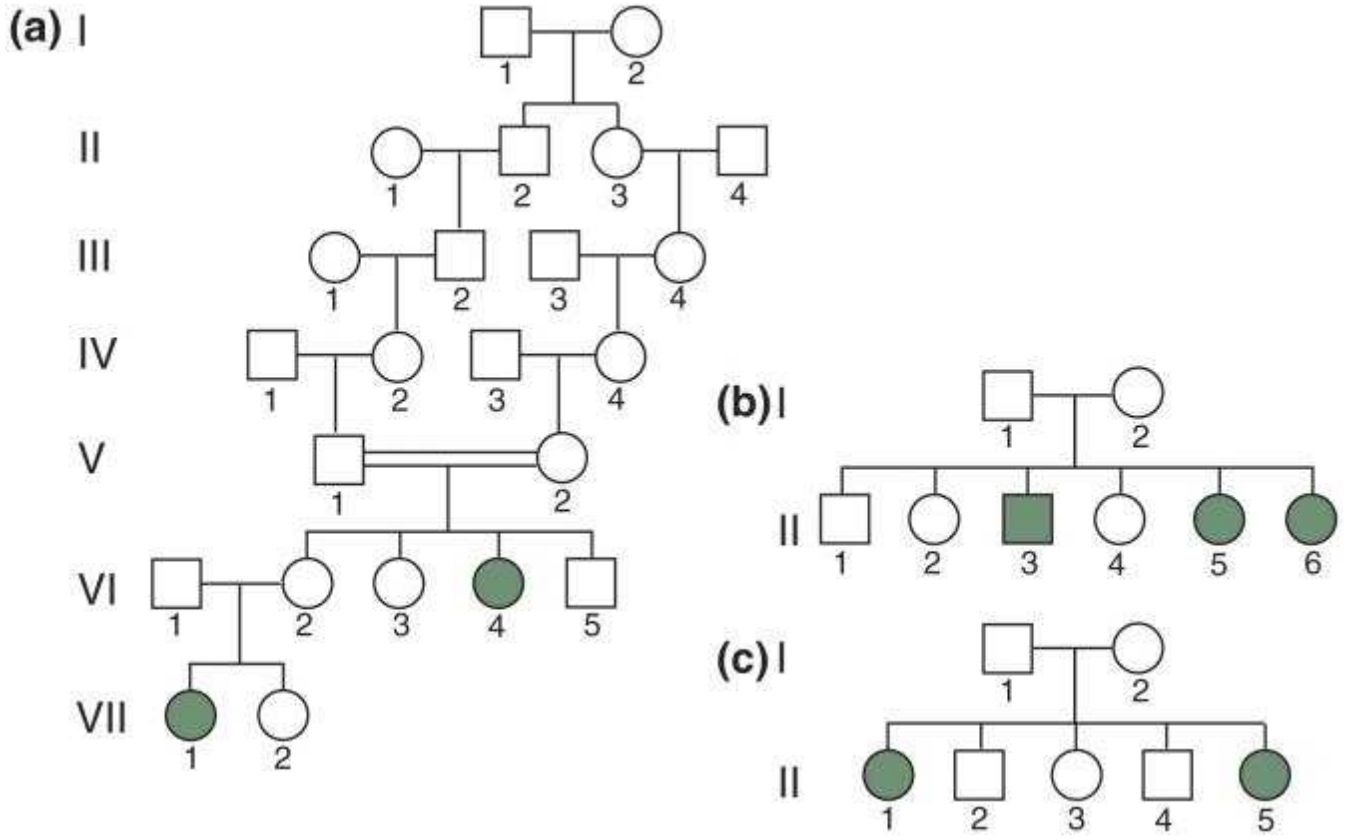

Fig. 2.21

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How to recognize dominant traits in pedigrees

Three key aspects of pedigrees with dominant traits:

1. Affected children always have at least one affected parent.
2. As a result, dominant traits show a **vertical pattern** of inheritance.
3. Two affected parents can produce unaffected children, if both parents are heterozygotes.

Table 2.2

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How to recognize recessive traits in pedigrees

Four keys aspects of pedigrees with recessive traits:

1. Affected individuals can be the children of two unaffected carriers, particularly as a result of consanguineous matings.
2. All the children of two affected parents should be affected.
3. Rare recessive traits show a **horizontal pattern** of inheritance.
4. Recessive traits may show a **vertical pattern** of inheritance if the trait is extremely common in the population.

Table 2.2

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Some phenotypic variation poses a challenge to Mendelian analysis

Crosses of pure-breeding lines can result in progeny phenotypes that don't appear to follow Mendel's rules

- Example: Lentils show complex speckling patterns that are controlled by a gene that has more than two alleles.

Fig. 2.22

Explanations for some traits:

- No definitively dominant or recessive allele
- More than two alleles exist
- Multiple genes are involved
- Gene-environment interactions

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Extensions to Mendel for single-gene inheritance

Dominance is not always complete

- Incomplete dominance – e.g., snapdragon flower colour
- Codominance – e.g., lentil coat patterns, AB blood group in humans

A gene may have >2 alleles – e.g., lentil coat patterns, ABO blood groups in humans, histocompatibility in humans

Pleiotropy - one gene may contribute to several characteristics

- Recessive lethal alleles – e.g., A^Y allele in mice
- Delayed lethality

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Summary of different dominance relationships

The phenotype of the heterozygote defines the dominance relationship of two alleles.

Complete dominance: Hybrid resembles one of the two parents

Incomplete dominance: Hybrid resembles neither parent

Codominance: Hybrid shows traits from both parents

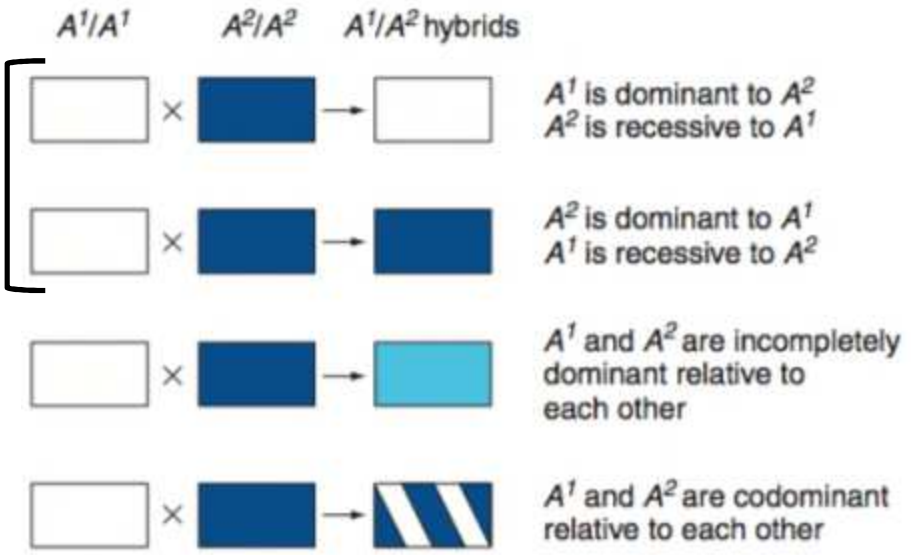

Figure 2.23

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Flower colour in snapdragons is an example of incomplete dominance

Crosses of pure-breeding red with pure-breeding white results in <u>all</u> pink F_1 progeny

(a) *Antirrhinum majus* (snapdragons)

Figure 2.24a

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Pink flowers in snapdragons are the result of incomplete dominance

F_2 progeny ratios:

- 1 red (R^1R^1)
- 2 pink (R^1R^2)
- 1 white (R^2R^2)

Phenotype ratios reflect the genotype ratios

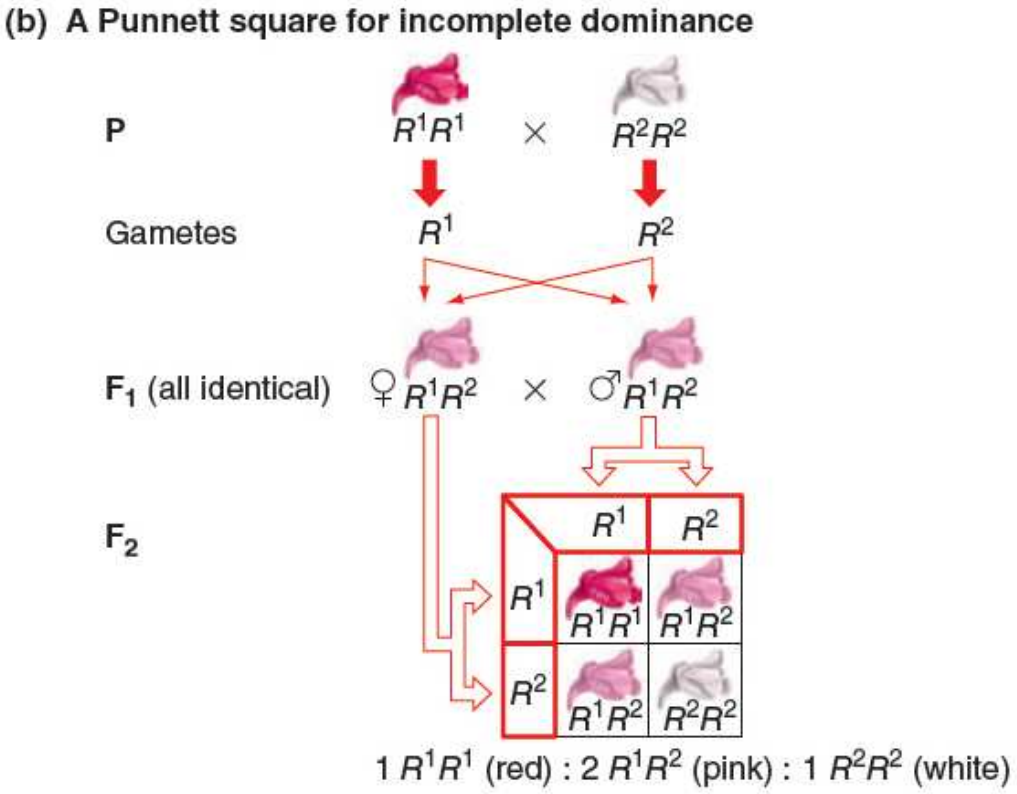

Figure 2.24b

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In codominance, the F_1 hybrids display traits of both parents: e.g., lentil coat patterns

Spotted (C^SC^S) x dotted (C^DC^D)

All F_1 progeny are spotted and dotted (C^SC^D)

F_2 progeny ratios:

- 1 spotted (C^SC^S)
- 2 spotted and dotted (C^SC^D)
- 1 dotted (C^DC^D)

Phenotype ratios reflect the genotype ratios.

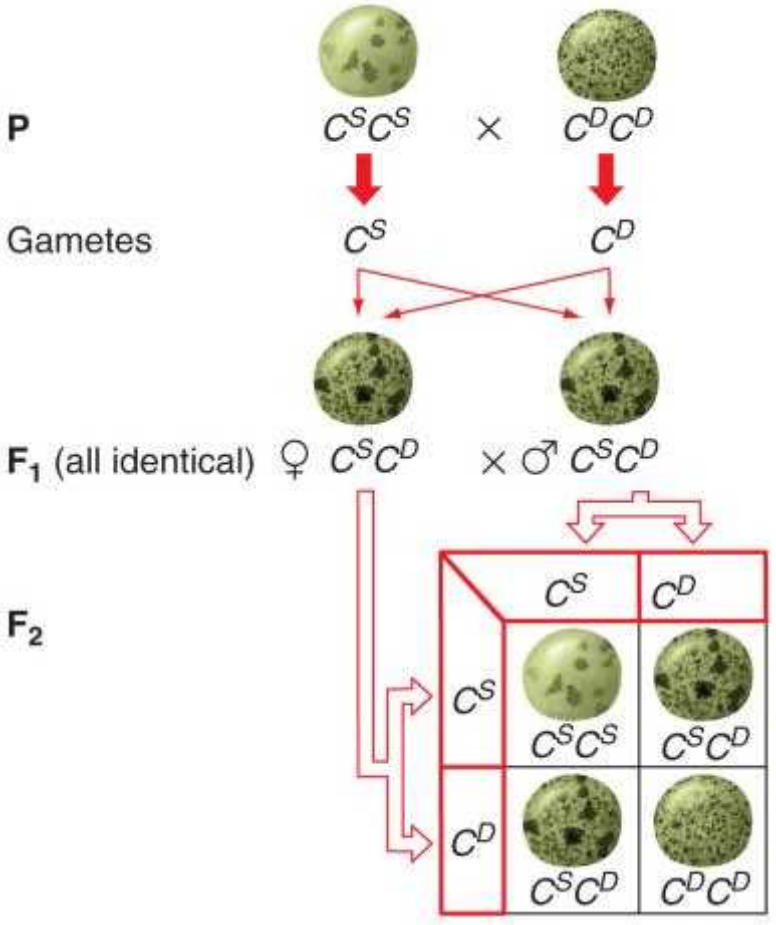

Figure 2.25a

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In codominance, the F_1 hybrids display traits of both parents: e.g., AB blood group

Gene *I* controls the type of sugar polymer on the surface of RBCs

Two alleles, I^A and I^B, result in different sugars

- I^A I^A individuals have A sugar
- I^B I^B individuals have B sugar
- I^A I^B individuals have both A and B sugars

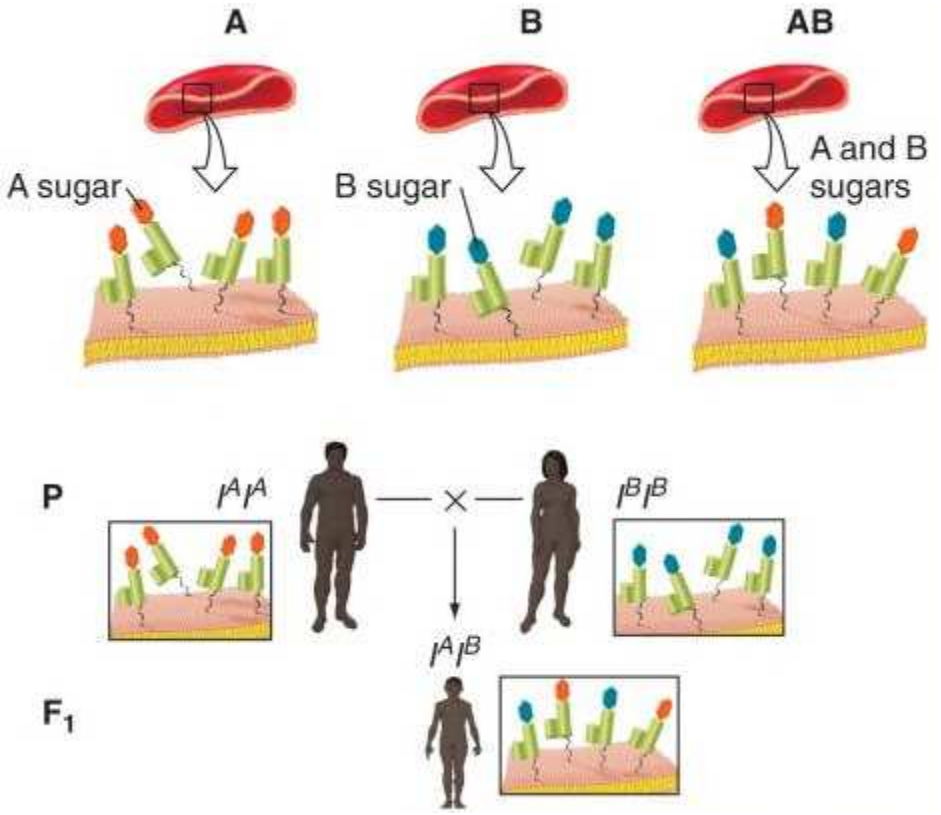

Figure 2.25b

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Dominance relations between alleles do not affect transmission of alleles

Type of dominance (complete, incomplete dominance, codominance) depends on the type of proteins encoded and by the biochemical functions of the proteins.

Variation in dominance relations do not negate Mendel's laws of segregation.

Alleles still segregate randomly.

Interpretation of phenotype/genotype relations is more complex.

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A gene may have more than two alleles

Multiple alleles of a gene can segregate in populations.

Each individual can carry only two alleles.

Dominance relations are always relative to a second allele and are unique to a pair of alleles.

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ABO blood types in humans are determined by three alleles of one gene

I^A allele → A type sugar

I^B allele → B type sugar

i allele → no sugar

Genotypes	Corresponding Phenotypes: Type(s) of Molecule on Cell
$I^A I^A$ $I^A i$	A
$I^B I^B$ $I^B i$	B
$I^A I^B$	AB
ii	O

Six genotypes produce four blood types

Fig. 2.26a

Dominance relations are relative to a second allele

- I^A and I^B are codominant
- I^A and I^B are dominant to *i*

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Medical and legal implications of ABO blood group genetics

Antibodies are made against type A and type B sugars

- Successful blood transfusions occur only with matching blood types.
- Type AB are universal recipients, type O are universal donors

Blood Type	Antibodies in Serum
A	Antibodies against B
B	Antibodies against A
AB	No antibodies against A or B
O	Antibodies against A and B

Blood Type of Recipient	Donor Blood Type (Red Cells) A	B	AB	O
A	+	−	−	+
B	−	+	−	+
AB	+	+	+	+
O	−	−	−	+

Figure 2.26b,c

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Seed coat patterns in lentils are determined by a gene with five alleles

Five alleles for *C* gene: spotted (C^S), dotted (C^D), clear (C^C), marbled-1 (C^{M1}), and marbled-2 (C^{M2})

Reciprocal crosses between pairs of pure-breeding lines is used to determine dominance relations.

Fig. 2.27

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Dominance relations are established between pairs of alleles

Three examples:

1. marbled-1 ($C^{M1}C^{M1}$) x clear ($C^{C}C^{C}$) → all F_1 marbled-1 ($C^{M1}C^{C}$)
   F_2 progeny: 798 marbled-1 (C^{M1}—) and 296 clear ($C^{C}C^{C}$)

2. marbled-2 ($C^{M2}C^{M2}$) x clear ($C^{C}C^{C}$) → all F_1 marbled-2 ($C^{M2}C^{C}$)
   F_2 progeny: 123 marbled-1 (C^{M2}—) and 46 clear ($C^{C}C^{C}$)

3. marbled-1 ($C^{M1}C^{M1}$) x marbled-2 ($C^{M2}C^{M2}$) → all F_1 marbled-1
   F_2 progeny: 272 marbled-1 (C^{M1}—) and 72 marbled-2 ($C^{M2}C^{M2}$)

A 3:1 ratio in each cross indicates that different alleles of the same gene are involved.

Dominance series: $C^{M1} > C^{M2} > C^{C}$

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Mutations are the source of new alleles

Chance alterations of genetic material arise spontaneously.

If mutations occur in gamete-producing cells, they can be transmitted to offspring.

The frequency of gametes with mutations is 10^{-4}-10^{-6}.

Mutations that result in phenotypic variants can be used by geneticists to follow gene transmission.

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Nomenclature for alleles in populations

Allele frequency is the percentage of the total number of gene copies for one allele in a population.

The most common allele is usually the wild-type (+) allele.

A rare allele is considered to be a mutant allele.

Gene w/ only one common wild-type allele is **monomorphic**

- *Agouti* gene in mice – only one allele in wild populations, many alleles in lab mice.

Gene w/ more than one common allele is **polymorphic**

- High-frequency alleles of polymorphic genes are referred to as common variants.

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The mouse *agouti* gene controls hair colour: One wild-type allele, many mutant alleles

Wild-type agouti allele (*A*) produces yellow and black pigment in hair

14 different *agouti* alleles in lab mice, but only *A* allele in wild mice

e.g., mutant alleles *a* and a^t

- *a* recessive to *A*
  - *aa* has black only
- a^t dominant to *a* but recessive to *A*
  - $a^t a^t$ mouse has black on back and yellow on belly

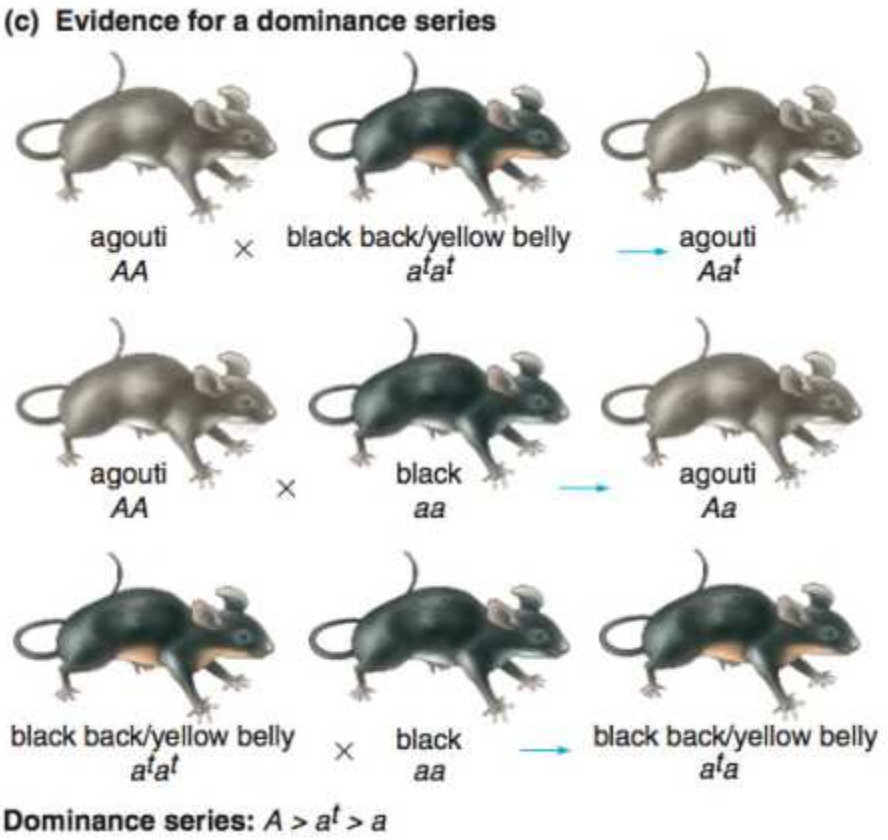

Fig. 2.28c

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One gene may contribute to several characteristics

Pleiotropy is the phenomenon of a single gene determining several distinct and seemingly unrelated characteristics.

- e.g., Many aboriginal Maori men have respiratory problems and are sterile.
  - Defects due to mutations in a gene required for functions of cilia (failure to clear lungs) and flagella (immotile sperm)

With some pleiotropic genes:

- Heterozygotes can have a visible phenotype.
- Homozygotes can be inviable (e.g., A^Y allele of agouti gene in mice).

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The A^Y allele produces a dominant coat colour phenotype in mice

A^Y allele of *agouti* gene causes yellow hairs with no black

Cross agouti x yellow mice

- Progeny in 1:1 ratio of agouti to yellow
- Yellow mice must be heterozygous for *A* and A^Y
- A^Y is dominant to *A*

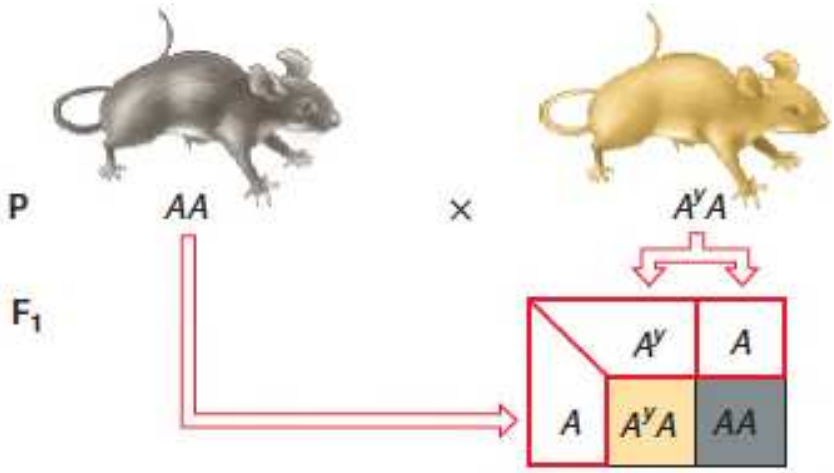

Fig. 2.29a

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The A^Y allele is a recessive lethal allele

A^Y is dominant to A for hair colour, but is recessive to A for lethality.

Cross yellow x yellow mice

- F_1 mice are 2/3 yellow and 1/3 agouti

2:1 ratio is indicative of a recessive lethal allele

- Pure-breeding yellow (A^YA^Y) mice cannot be obtained because they are not viable.

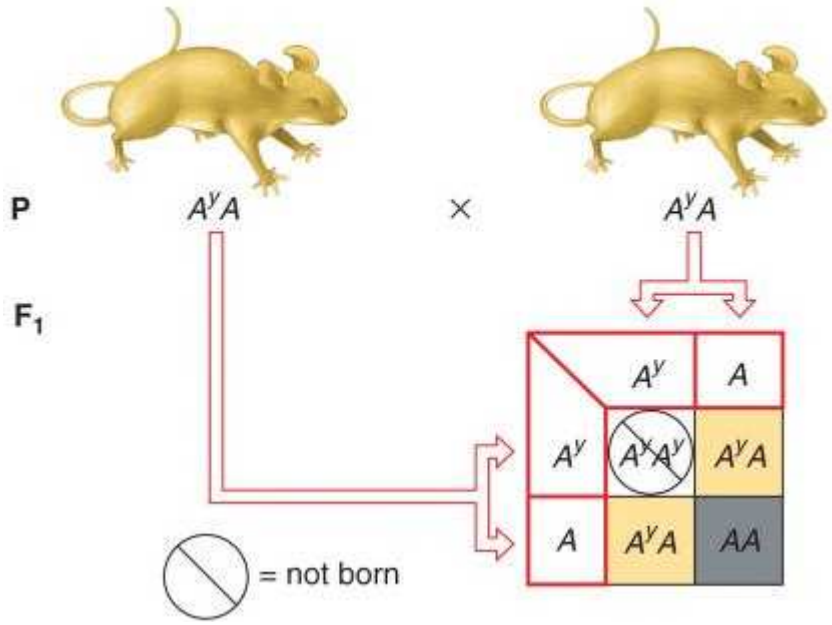

Figure 2.29b

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Extensions to Mendel's analysis explain alterations of the 3:1 monohybrid ratio

What Mendel Described	Extension	Extension's Effect on Heterozygous Phenotype	Extension's Effect on Ratios Resulting from an $F_1 \times F_1$ Cross
Complete dominance	Incomplete dominance Codominance	Unlike either homozygote	Phenotypes coincide with genotypes in a ratio of 1:2:1
Two alleles	Multiple alleles	Multiplicity of phenotypes	A series of 3:1 ratios
All alleles are equally viable	Recessive lethal alleles	No effect	2:1 instead of 3:1
One gene determines one trait	Pleiotropy: one gene influences several traits	Several traits affected in different ways, depending on dominance relations	Different ratios, depending on dominance relations for each affected trait

Table 2.3

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A comprehensive example: Sickle-cell disease

Haemoglobin transports oxygen in RBCs

- Two subunits – alpha (α) globin and beta (β) globin

Mutations in the β-globin gene cause β-thalassemia.

Most common mutation of β-globin ($Hb\beta^S$) causes sickle-cell disease.

- Pleiotropic – affects >1 trait (deformed RBCs, anaemia, heart failure, resistance to malaria)
- Recessive lethality – heart failure
- Different dominance relations for different phenotypic aspects of sickle-cell disease.

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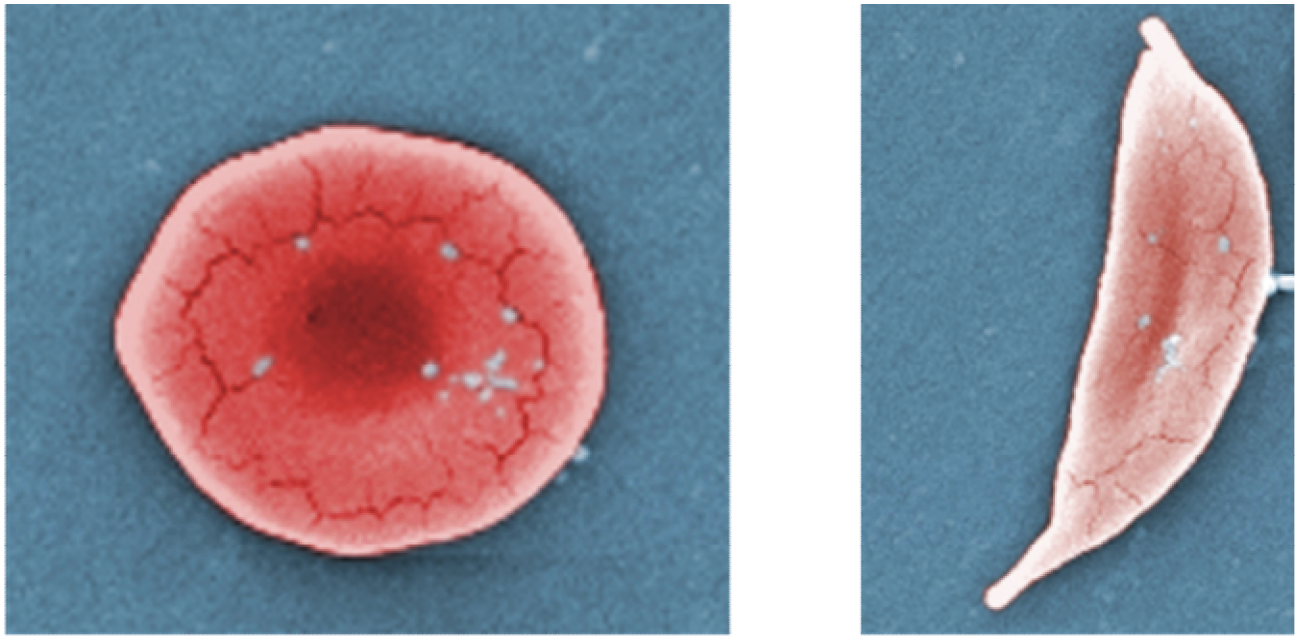
Pleiotropy of sickle-cell anaemia: Dominance relations vary with the phenotype under consideration



(a)

Fig. 2.30a

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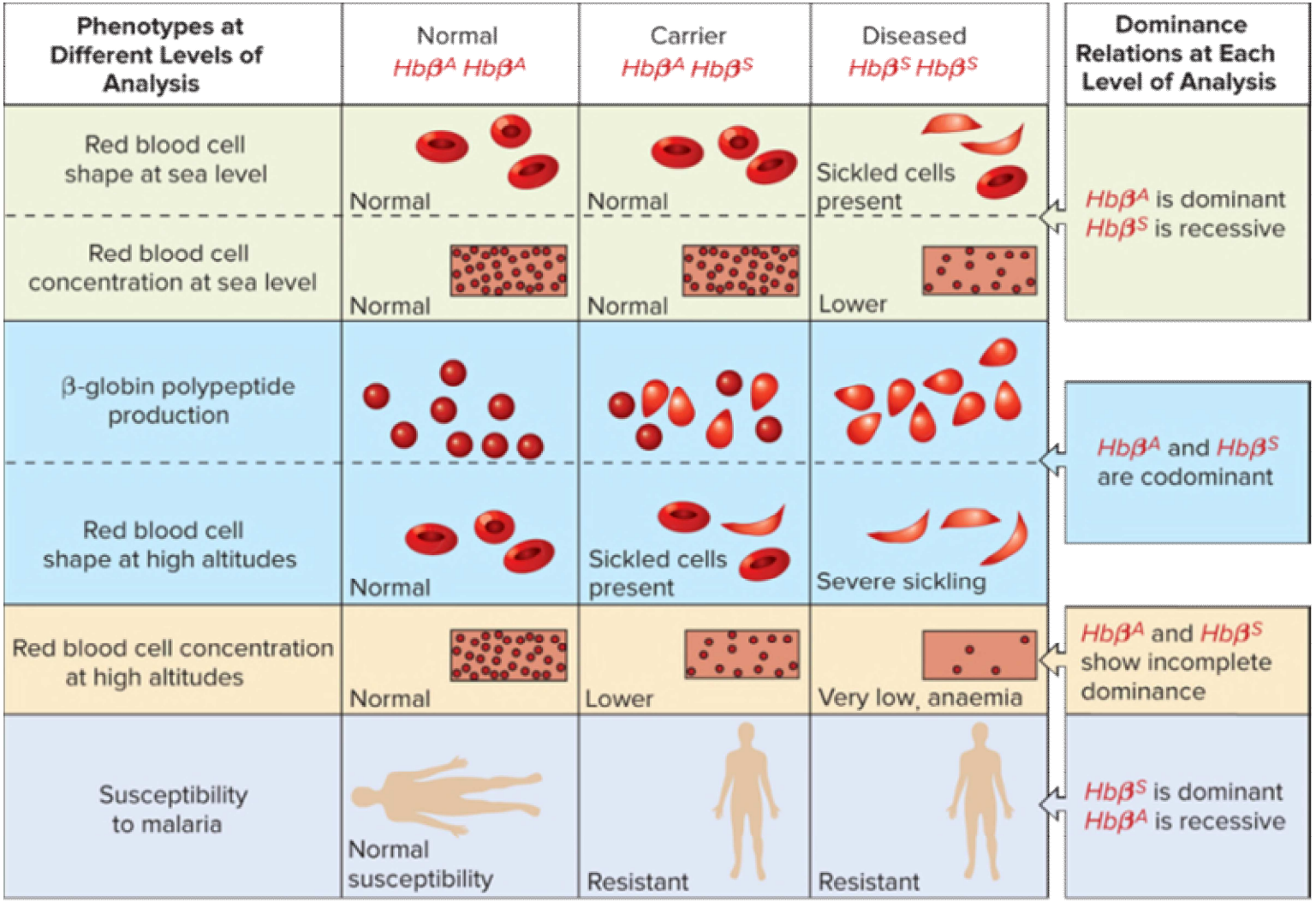
Pleiotropy of sickle-cell anaemia: Dominance relations vary with the phenotype under consideration



(b)

Fig. 2.30b

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Extensions to Mendel for Gene Interaction

Two genes can interact to determine one trait.

- **Novel phenotypes** can result from gene interactions, e.g., seed coat in lentils
- **Complementary gene action**, e.g., flower colour
- **Epistasis**, e.g., dog fur, Bombay phenotype in humans, squash colour, chicken feather colour

In all of these cases, F_2 phenotypes from dihybrid crosses are in a **variation of the 9:3:3:1 ratio** expected for independently assorting genes.

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Novel phenotypes resulting from gene interactions, e.g., seed coat in lentils

Dihybrid cross of lentils, tan x grey

All F_1 seeds are brown

F_2 progeny:

- 9/16 brown
- 3/16 tan
- 3/16 grey
- 1/16 green

9:3:3:1 ratio in F_2 suggests two independently assorting genes for seed coat colour

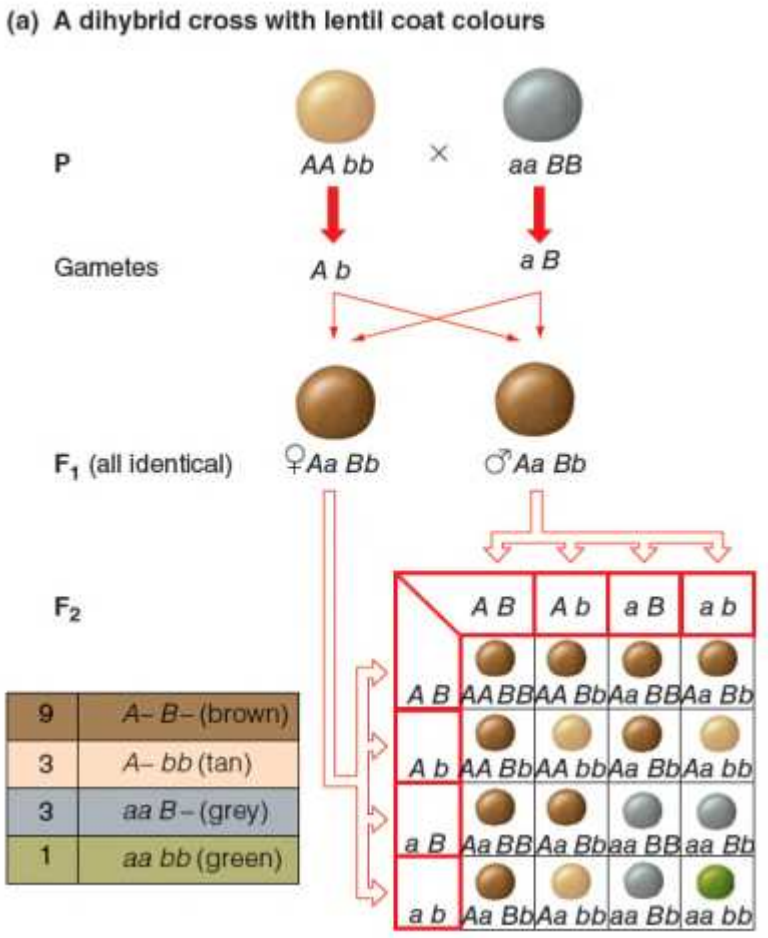

Fig. 2.31a

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Results of self-crosses of F_2 lentils supports the two-gene hypothesis

(b) Self-pollination of the F_2 to produce an F_3

Phenotypes of F_2 Individual	Observed F_3 Phenotypes	Expected Proportion of F_2 Population*
Green	Green	1/16
Tan	Tan	1/16
Tan	Tan, green	2/16
Grey	Grey, green	2/16
Grey	Grey	1/16
Brown	Brown	1/16
Brown	Brown, tan	2/16
Brown	Brown, grey	2/16
Brown	Brown, grey, tan, green	4/16

*This 1 : 1 : 2 : 2 : 1 : 1 : 2 : 2 : 4 F_2 genotypic ratio corresponds to a 9 brown : 3 tan : 3 grey : 1 green F_2 phenotypic ratio.

Figure 2.31b

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Sorting out the dominance relations by select crosses of lentils

F_2 phenotypes from dihybrid crosses will be in 9:3:3:1 ratio only when dominance of alleles at both genes is complete

(c) Sorting out the dominance relations by select crosses

Seed Coat Colour of Parents	F_2 Phenotypes and Frequencies	Ratio
Tan × green	231 tan, 85 green	3:1
Grey × green	2586 grey, 867 green	3:1
Brown × grey	964 brown, 312 grey	3:1
Brown × tan	255 brown, 76 tan	3:1
Brown × green	57 brown, 18 grey, 13 tan, 4 green	9:3:3:1

Figure 2.31c

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A biochemical model for the inheritance of lentil seed coat colours

- The seed has an opaque outer layer (the seed coat) and an inner layer (the cotyledon).
- The green chlorophyll in the cotyledon is not visible if the seed coat is coloured.
- Allele *A* encodes enzyme A.
- Allele *a* does not produce this enzyme.
- Allele *B* of a second gene encodes a different enzyme; *b* produces none of this enzyme. Seeds appear brown if the tan and grey pigments are both present.

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The 9:3:3:1 ratio implies that the *A* and *B* genes operate in independent biochemical pathways.

In the absence of both enzymes (*aa bb*), the seed coat is unpigmented, so the green chlorophyll in the cotyledon will show through. The 9:3:3:1 ratio implies that the *A* and *B* genes operate in independent biochemical pathways.

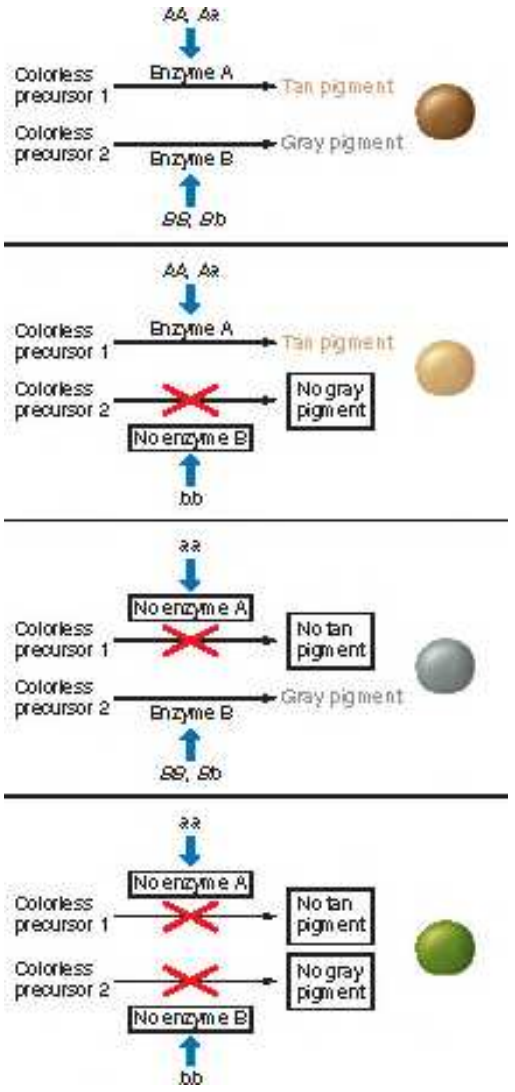

Figure 2.32

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Complementary gene action in sweet peas

Purple F_1 progeny of sweet peas are produced by crossing two pure-breeding white lines.

(a) *Lathyrus odoratus* (sweet peas)

Figure 2.33 a

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Complementary gene action generates purple flower colour in sweet peas

Dihybrid cross generates 9:7 ratio in F_2 progeny

9/16 purple (*A*—*B*—)

7/16 white (*A*— *bb*, *aa B*—, *aa bb*)

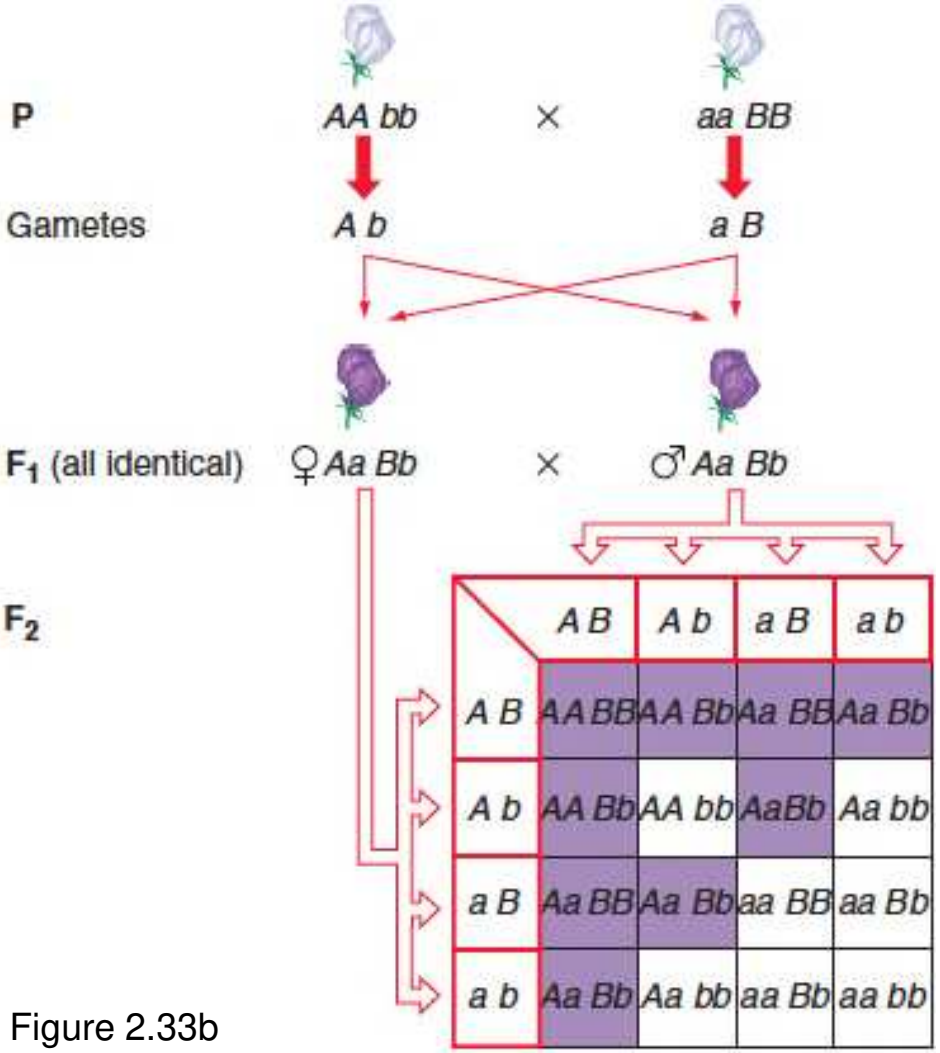

Figure 2.33b

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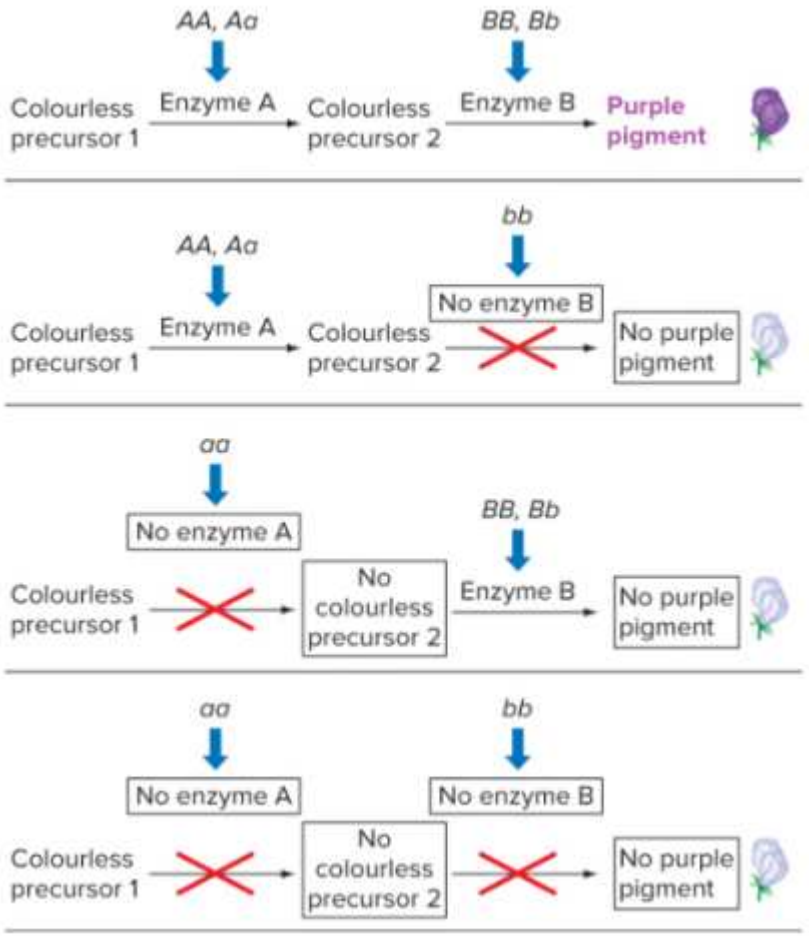
Possible biochemical explanation for complementary gene action for flower colour in sweet peas



One pathway has two reactions catalyzed by different enzymes

- At least one dominant allele of both genes is required for purple pigment
- Homozygous recessive for either or both genes results in no pigment

Figure 2.34

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Epistasis results from the effects of an allele at one gene masking the effects of another gene

The gene that does the masking is **epistatic** to the other gene.

The gene that is masked is **hypostatic** to the other gene.

Epistasis can be recessive or dominant

- Recessive – epistatic gene must be homozygous recessive (e.g., *ee*)
- Dominant – epistatic gene must have at least one dominant allele present (e.g., *E*—)

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Recessive epistasis in Golden Labrador dogs

9:3:4 ratio in F_2 progeny of dihybrid crosses indicates recessive epistasis

9/16 black (*B*— *E*—)

3/16 brown (*bb E*—)

4/16 yellow (*B*— *ee*, *bb ee*)

Genotype *ee* masks the effect of all *B* genotypes

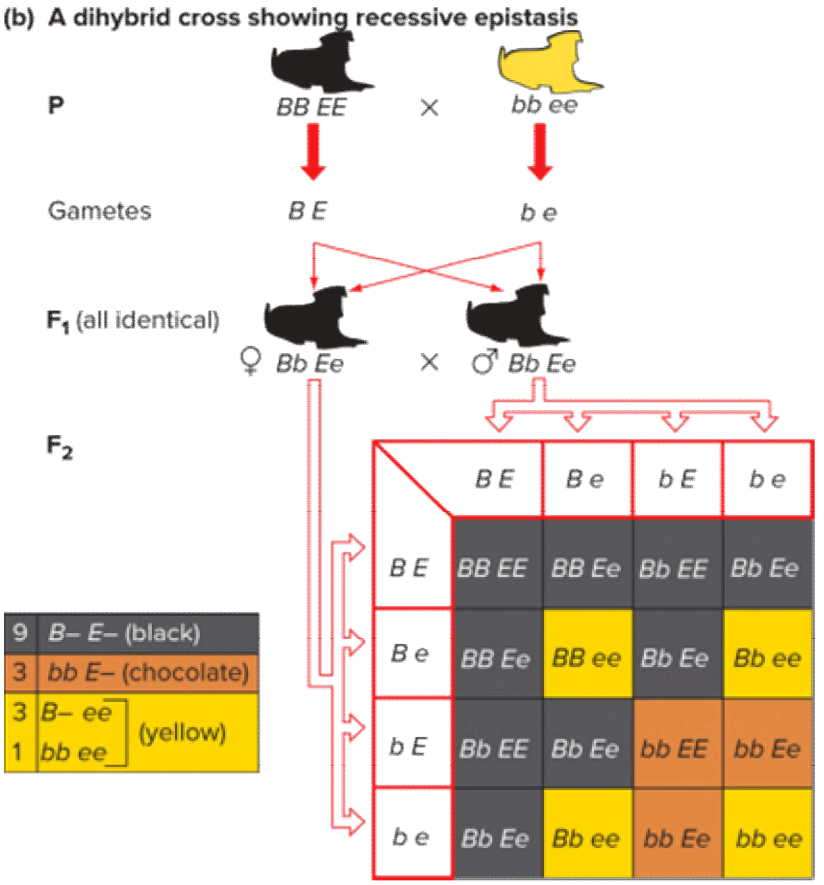

Figure 2.35

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A developmental explanation for coat colour in Labrador retrievers.

- Protein B activates an enzyme that generates eumelanin from a colourless precursor.
- When protein B is present, only black eumelanin is produced so that the hair is black.
- Protein b produces less dense brown eumelanin, resulting in brown (chocolate) hair.
- In the absence of protein E, no eumelanin is deposited in the hair shaft, and instead, pheomelanin (yellow pigment) is synthesized and deposited.

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Homozygous *ee* dogs are always yellow regardless of the gene *B* genotype

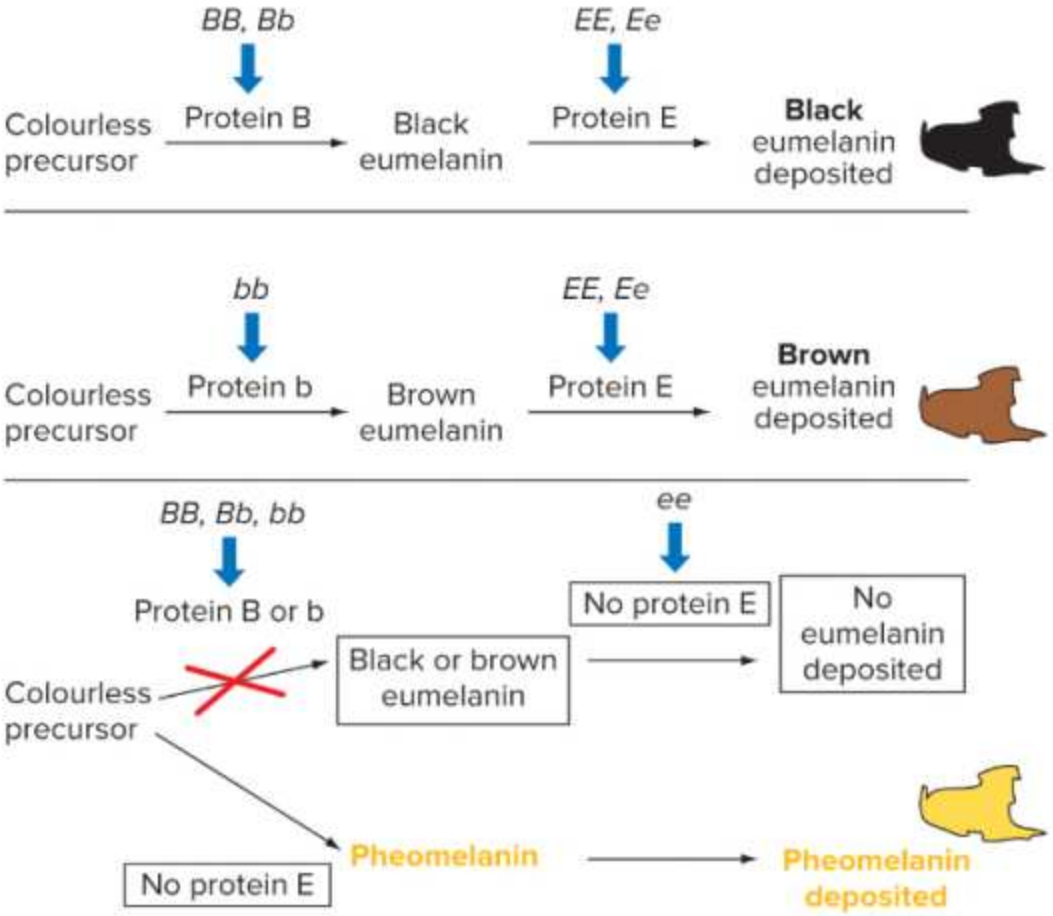

Figure 2.36

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Recessive epistasis in humans with a rare blood type

Gene for substance H is epistatic to the ABO gene

- Without the H substance, there is nothing for the A or B sugar to attach to

All type A, type AB, type B, and type O people are *H*—

People with *hh* genotype will <u>appear</u> to be type O

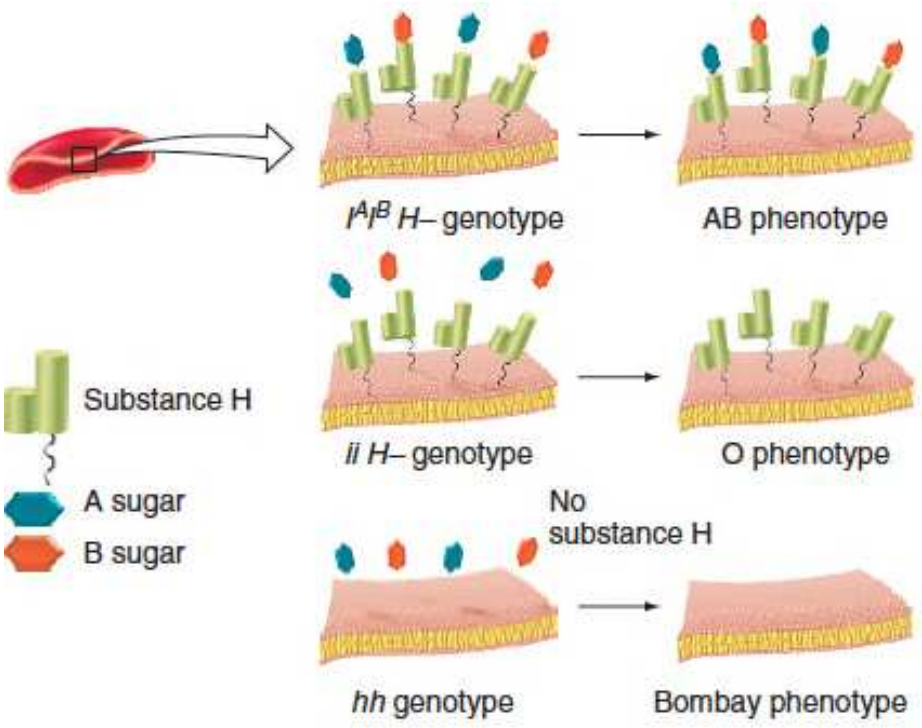

Figure 2.37

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Dominant epistasis I in summer squash

12:3:1 ratio in F_2 progeny of dihybrid crosses indicates dominant epistasis I

12/16 white (*A— B—, aa B—*)

3/16 yellow (*A— bb*)

1/16 green (*aa bb*)

The dominant allele of one gene masks both alleles of another gene.

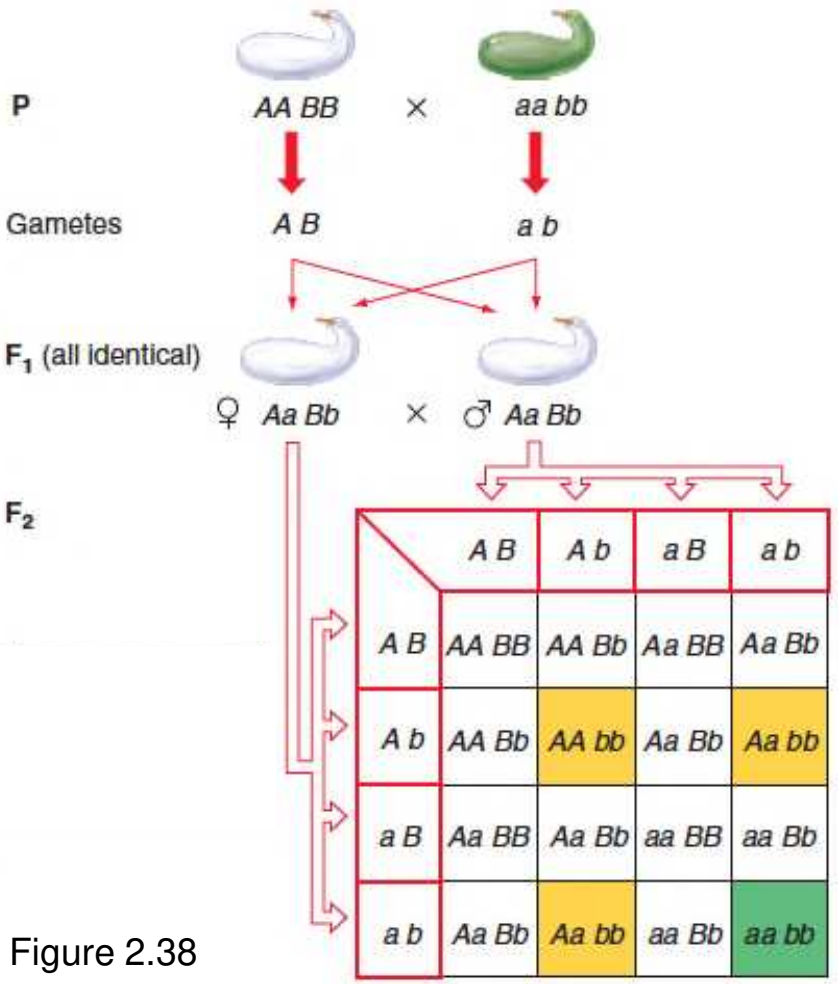

Figure 2.38

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Dominant epistasis II in chickens

13:3 ratio in F_2 progeny of dihybrid crosses indicates dominant epistasis II

13/16 white (*A— B—*, *aa B—*, *aa bb*)

3/16 coloured (*A— bb*)

The dominant allele of one gene masks the dominant allele of another gene.

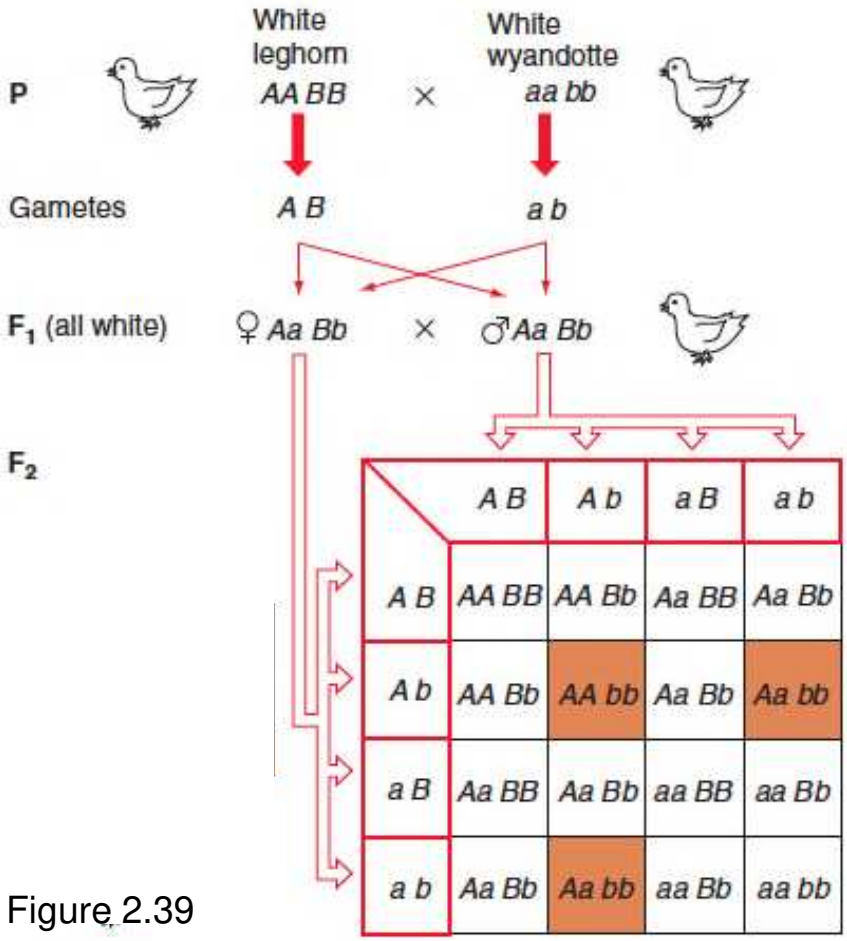

Figure 2.39

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Summary of gene interactions discussed in this chapter

Observing the F_2 ratios below is diagnostic of the type of gene interaction.

- These F_2 ratios occur only in dihybrid crosses where there is complete dominance.

Table 2.4 Summary of Discussed Gene Interactions

Gene Interaction	Example	F_2 Genotypic Ratios from an F_1 Dihybrid Cross				F_2 Phenotypic Ratio
		A– B–	*A– bb*	*aa B–*	*aa bb*	
None: Four distinct F_2 phenotypes	Lentil: seed coat colour (see Figure 2.31a)	9	3	3	1	9:3:3:1
Complementary: One dominant allele of each of two genes is necessary to produce phenotype	Sweet pea: flower colour (see Figure 2.32b)	9	3	3	1	9:7
Recessive epistasis: Homozygous recessive of one gene masks both alleles of another gene	Retriever coat colour (see Figure 2.34a)	9	3	3	1	9:3:4
Dominant epistasis I: Dominant allele of one gene hides effects of both alleles of another gene	Summer squash: colour (see Figure 2.35a)	9	3	3	1	12:3:1
Dominant epistasis II (also referred to as dominant suppression): Dominant allele of one gene hides effects of dominant allele of another gene	Chicken: feather colour (see Figure 2.35b)	9	3	3	1	13:3

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Heterogeneous traits and the complementation test

Heterogeneous traits have the same phenotype but are caused by mutations in different genes.

- e.g., deafness in humans can be caused by mutations in ~ 50 different genes

Complementation testing is used to determine if a particular phenotype arises from mutations in the same or separate genes.

- Can be applied only with recessive, not dominant, phenotypes

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Genetic heterogeneity in humans: Mutations in many genes can cause deafness

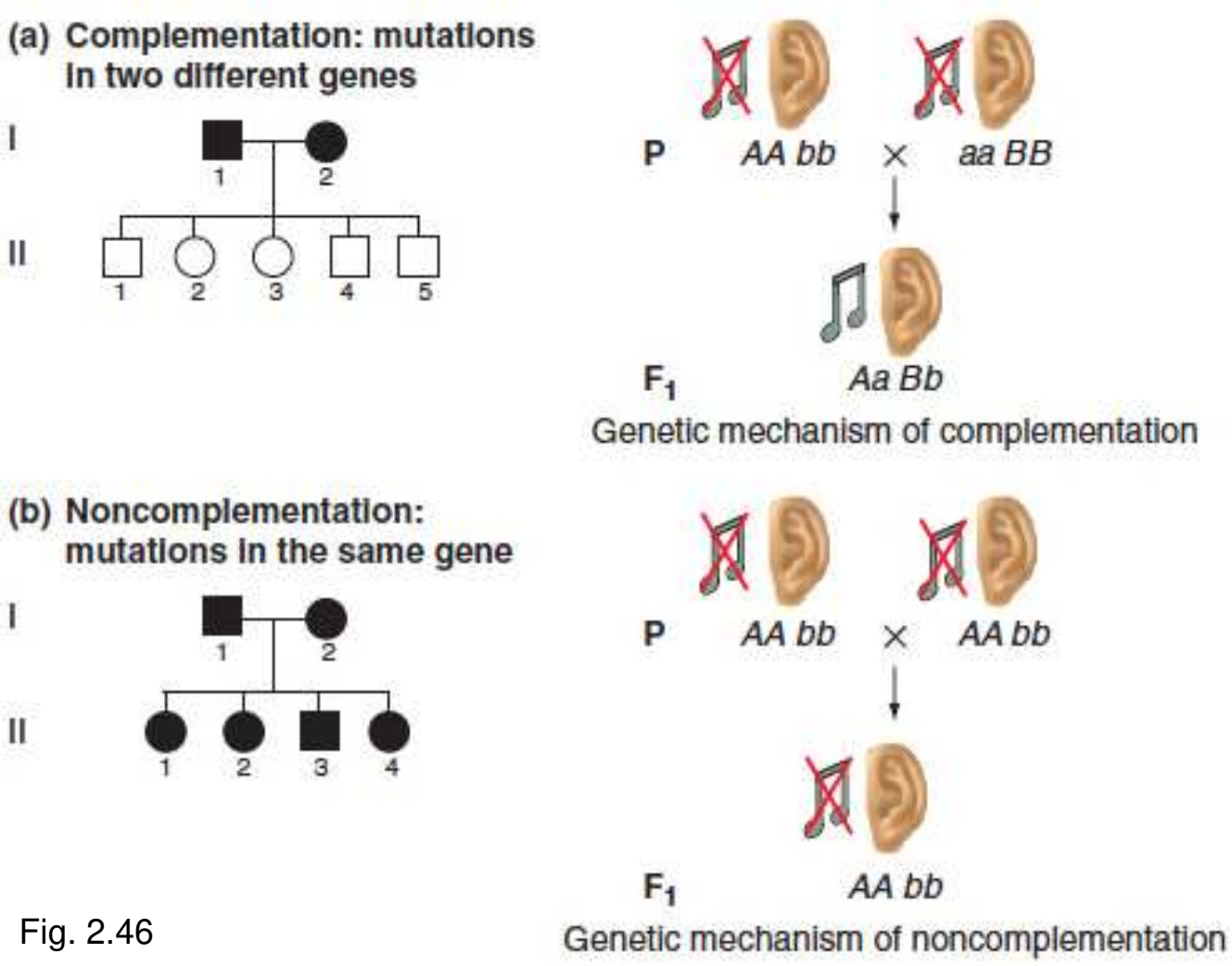

Fig. 2.46

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Variations on the theme of gene interactions and genetic heterogeneity

1. Genes can interact to generate novel phenotypes.
2. The dominant alleles of two interacting genes can both be necessary for the production of a particular phenotype.
3. One gene's alleles can mask the effects of alleles at another gene.
4. Different genes may have redundant functions so that a dominant allele of either gene is sufficient for the production of a particular wild-type phenotype.
5. Mutant alleles at one of two or more different genes can result in the same phenotype.

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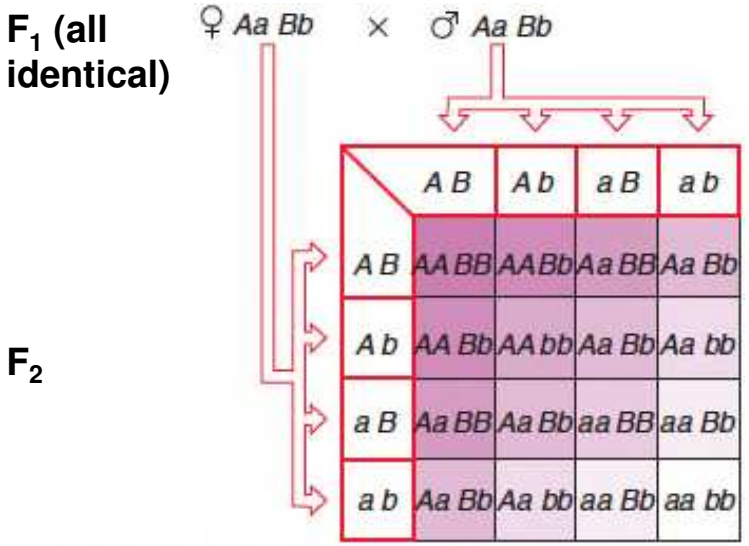
Interaction of two incompletely dominant genes can produce nine phenotypes

Example, two genes A and B:

- Allele *A* is incompletely dominant to allele *a*
- Allele *B* is incompletely dominant to allele *b*

For each gene, two alleles generate three phenotypes

- F_2 progeny have 3^2 phenotypes



1	*AA BB*	purple shade 9
2	*AA Bb*	purple shade 8
2	*Aa BB*	purple shade 7
1	*AA bb*	purple shade 6
4	*Aa Bb*	purple shade 5
1	*aa BB*	purple shade 4
2	*Aa bb*	purple shade 3
2	*aa Bb*	purple shade 2
1	*aa bb*	purple shade 1 (white)

Fig. 2.43

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Breeding studies help determine inheritance of a trait

How do we know if a trait is caused by one gene or by two genes that interact?

Example: dihybrid cross of pure-breeding parents produces three phenotypes in F_2 progeny

- If single gene with incomplete dominance, then F_2 progeny should be in 1:2:1 ratio
- If two independently assorting genes and recessive epistasis, then F_2 progeny should be in 9:3:4 ratio
- Further breeding studies can reveal which hypothesis is correct

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Two hypotheses to explain phenotypes in F2 progeny of mice with different coat colours

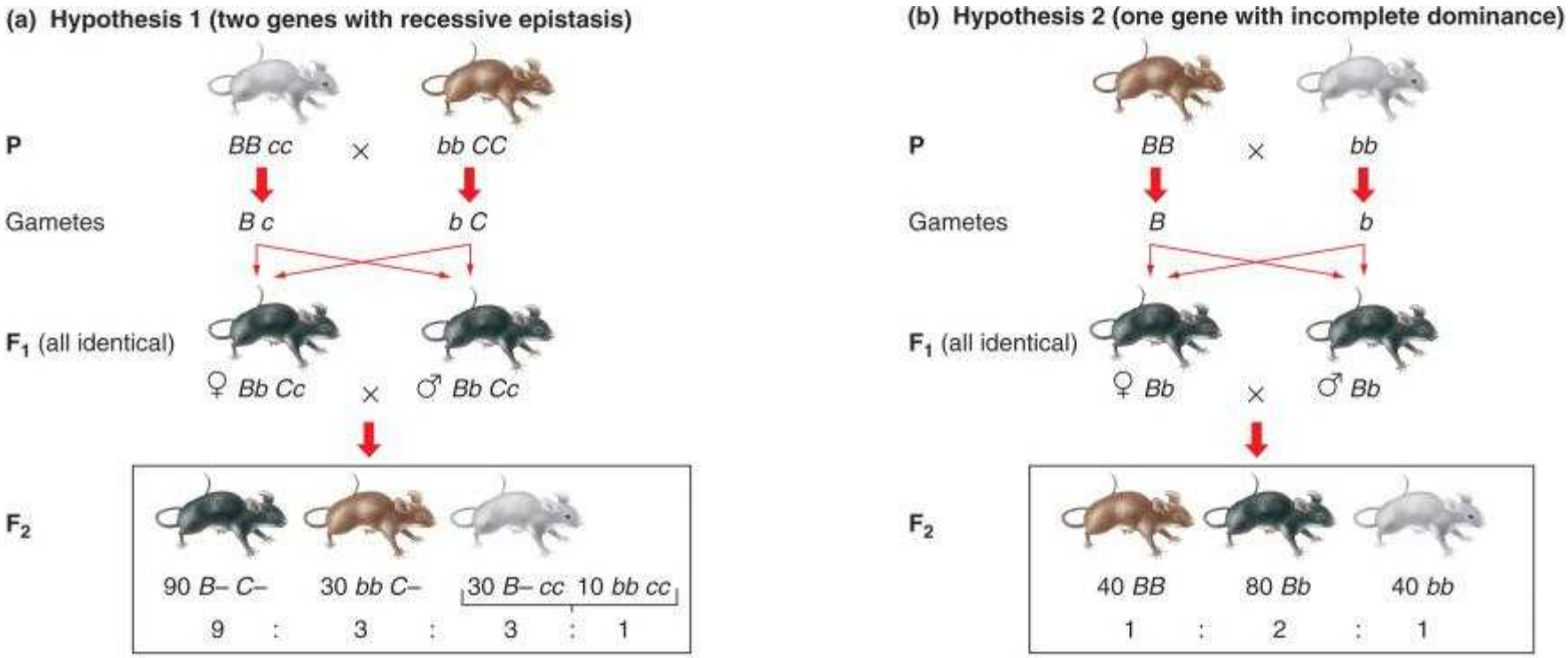

Fig. 2.44 (top)

Are these F_2 progeny in a ratio of 9:3:4 or 1:2:1?

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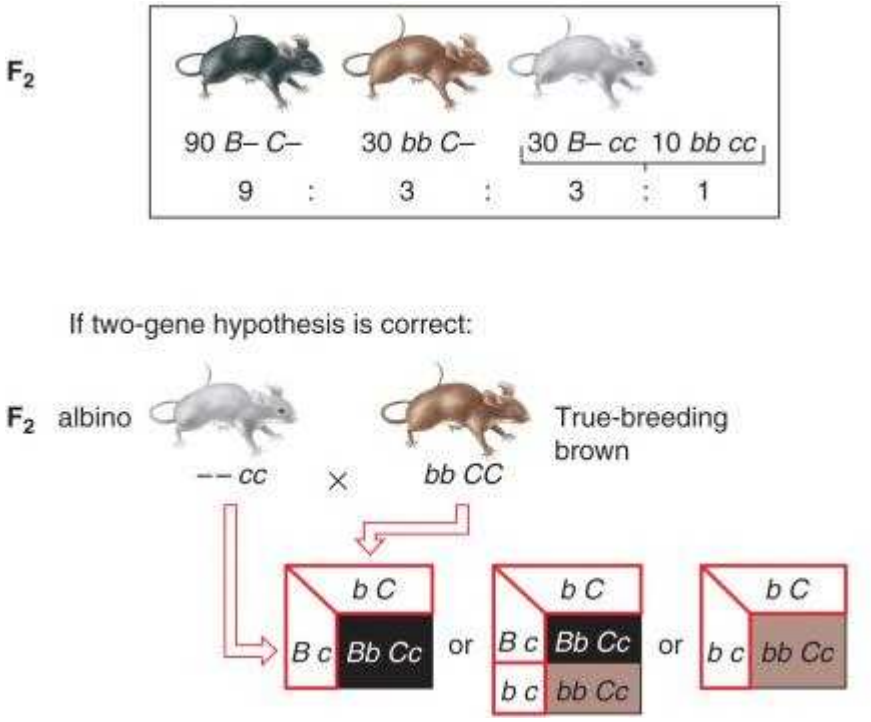
Specific breeding tests can help decide between two hypotheses

Hypothesis 1 – two genes with recessive epistasis



Hypothesis 2 – one gene with incomplete dominance

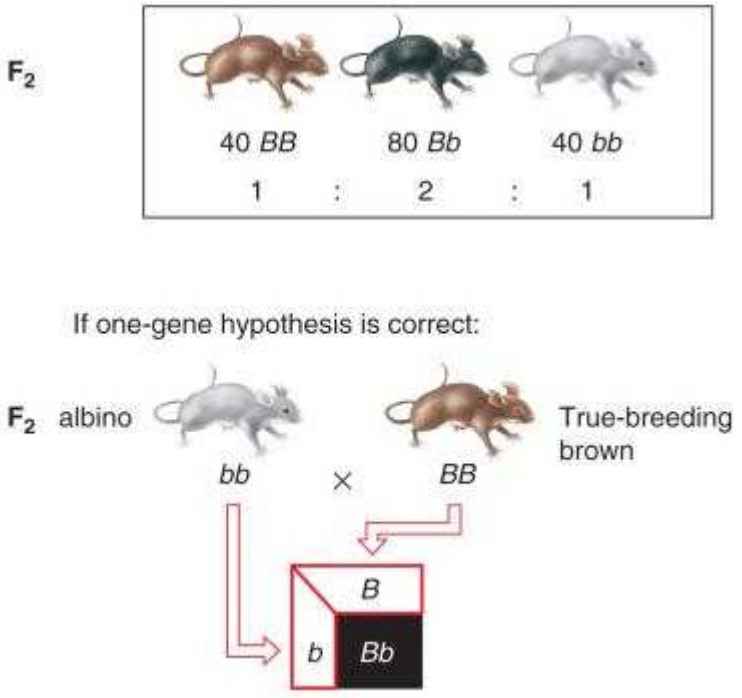


Figure 2.44 (bottom)

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Family pedigrees help unravel the genetic basis of ocular-cutaneous albinism (OCA)

OCA is another example of heterogeneity

(a) Ocular-cutaneous albinism (OCA)

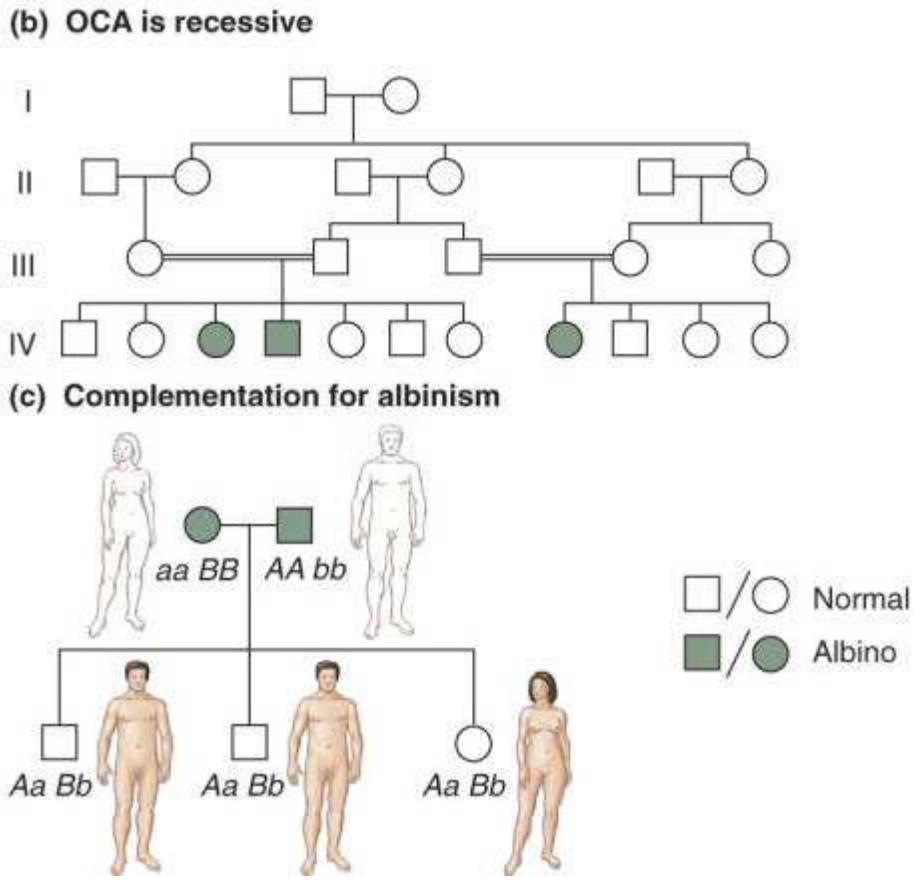

Fig. 2.45 a,b,c

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The same genotype does not always produce the same phenotype

In all of the traits discussed so far, the relationship between a specific genotype and its corresponding phenotype has been absolute.

Phenotypic variation for some traits can occur because of:

- Differences in penetrance and/or expressivity
- Effects of modifier genes
- Effects of environment
- Pure chance

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Phenotype often depends on penetrance and/or expressivity

Penetrance is the percentage of a population with a particular genotype that shows the expected phenotype.

- Can be complete (100%) or incomplete (e.g., penetrance of retinoblastoma is 75%)

Expressivity is the degree or intensity with which a particular genotype is expressed in a phenotype.

- Can be variable or unvarying

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Some traits result from different genes that do not contribute equally to the phenotype

Modifier genes alter the phenotypes produced by alleles of other genes.

- Can have major effect or more subtle effects

Example: T locus of mice

- Mutant *T* allele causes abnormally short tail
- In some inbred strains, mice with *T* allele have tails that are 75% the length of normal tails
- In other inbred strains, mice with the same *T* mutation have tails that are 10% the length of normal tails
- Different inbred strains must carry alternative alleles of a modifier gene for the *T* mutant phenotype

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Environmental effects on phenotype

Temperature is a common element of the environment that can affect phenotype

- Example 1: Coat colour in Siamese cats
  - Extremities are darker than body because of a temperature sensitive allele
- Example 2: Survivability of a Drosophila mutant
  - *Shibire* mutants develop normally at < 29°C but are inviable at temperatures > 29°C

Conditional lethal mutations are lethal only under some conditions

- **Permissive** conditions - mutant allele has wild-type functions
- **Restrictive** conditions - mutant allele has defective functions

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A temperature sensitive mutation affects coat colour in Siamese cats

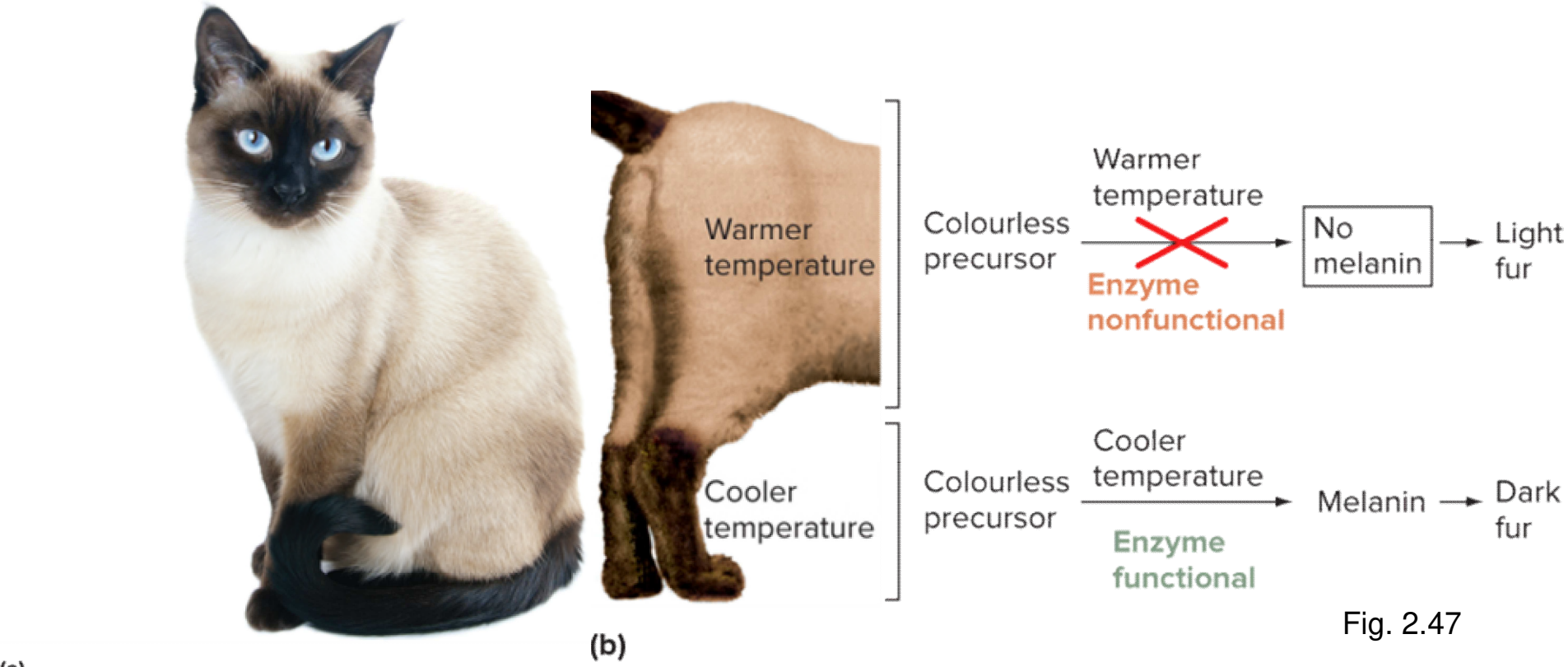

Fig. 2.47

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- You may know **Dr. David Suzuki** for his work as an environmentalist, broadcaster, and a world leader in sustainable ecology
- He is also an award-winning scientist. While at UBC, he conducted large-scale genetic screens in *Drosophila*, with his main focus being the study of **temperature-sensitive** (ts) mutations.
- These ts mutants are useful as tools for investigations into the nature of genetic lesions. By manipulating the conditional and restrictive conditions, one could determine at what developmental stage(s) lethality occurs, as well as any phenotypically distinct (or pleiotropic) defects that may arise upon brief exposure to the restrictive temperature at various stages of development.

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Mendelian principles can also explain continuous variation

Discontinuous traits give clear-cut, "either-or" phenotypic differences between alternative alleles

- Example: All of the traits Mendel studied in peas were discontinuous

Continuous traits are determined by segregating alleles of many genes that interact together and with the environment

- Examples in humans: height, weight, skin colour
- Often appear to blend and "unblend"
- Also called **quantitative traits** because the traits vary over a range that can be measured
- Usually **polygenic** – controlled by multiple genes

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Mendelian explanation of continuous variation

The more genes or alleles, the more possible phenotypic classes and the greater the similarity to continuous variation.

In these examples, all of the alleles are incompletely dominant and have additive effects.

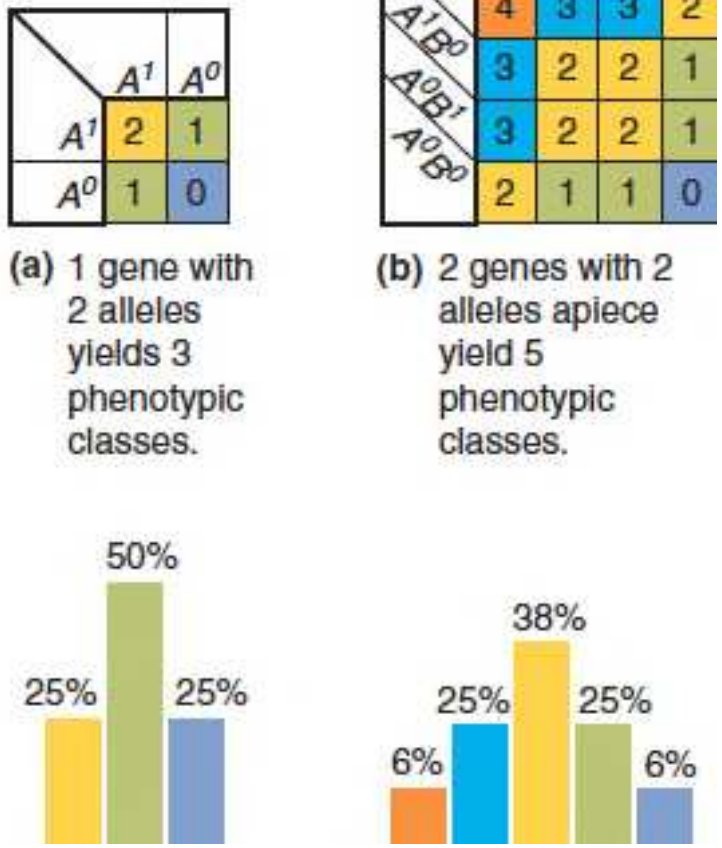

Fig. 2.48 (partial)

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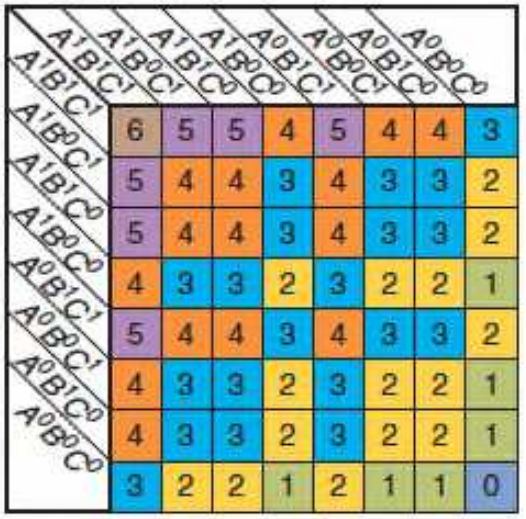
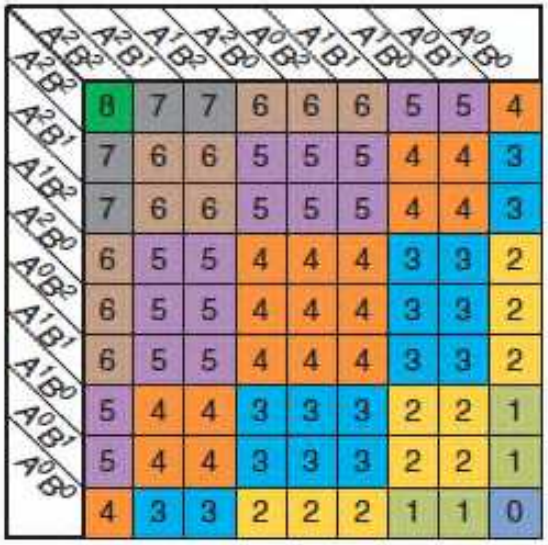
Mendelian explanation of continuous variation (cont.)

The more genes or alleles, the more possible phenotypic classes and the greater the similarity to continuous variation.

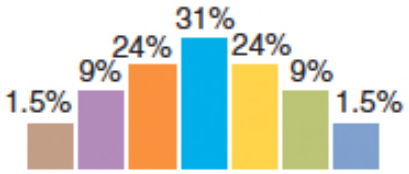
In these examples, all of the alleles are incompletely dominant and have additive effects.



(c) 3 genes with 2 alleles yield 7 phenotypic classes.



(d) 2 genes with 3 alleles apiece yield 9 phenotypic classes.



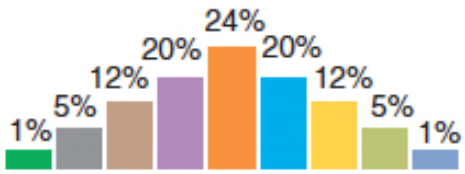


Fig. 2.48 (partial)

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A comprehensive example: Mouse coat colour is determined by multiple alleles of several genes

Gene 1: Agouti or other colour patterns

Wild-type (*A*) allele specifies bands of yellow and black on each hair

- A^Y allele specifies solid yellow (no black)
- *a* allele specifies solid black (no yellow)
- a^t allele specifies black on the back and yellow on the belly
- Dominance series for coat colour: $A^Y > A > a^t > a$
- Dominance series for survivability: $A = a^t = a > A^Y$

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A comprehensive example: Mouse coat colour is determined by multiple alleles of several genes

Gene 2: Black or brown with yellow bands

Gene that specifies dark colour in hair has two alleles: *B* specifies black and *b* specifies brown

- A^Y acts in dominant epistatic manner to *B* gene
- *A*— *B*— genotype gives wild-type agouti colour (black and yellow bands)
- *A*— *bb* genotype gives cinnamon colour (brown and yellow bands)
- *aa bb* gives solid brown (no yellow bands)
- $a^t a^t$ *bb* has brown on back and yellow on belly

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A comprehensive example: Mouse coat colour is determined by multiple alleles of several genes

Gene 2: Black or brown with yellow bands (continued)

Progeny of dihybrid cross of *A^Ya Bb* (yellow) x *A^Ya Bb* (yellow) is an example of dominant epistasis and recessive lethality

- 8/12 yellow (*A^Ya BB*, *A^Ya Bb*, and *A^Ya bb*)
- 3/12 black (*aa B*—)
- 1/12 brown (*aa bb*)
- 4/16 of total progeny will be inviable (*A^YA^Y* ——)

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A comprehensive example: Mouse coat colour is determined by multiple alleles of several genes

Gene 3: Albino or pigmented

C gene controls function of enzyme required for pigment synthesis

C gene acts in a recessive epistatic manner to all other genes that control coat colour.

- Homozygous recessive (*cc*) are pure white, regardless of *A* or *B* genes (or other colours)
- *C*— mice are agouti, black, brown, yellow, or black and yellow depending on alleles at *A* and *B* genes

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1. Discrete units called genes control the appearance of inherited traits.

2. Genes come in alternative forms called alleles that are responsible for the expression of different forms of a trait.

3. Body cells of sexually reproducing organisms carry two copies of each gene. When the two copies of a gene are the same allele, the individual is homozygous for that gene. When the two copies of a gene are different alleles, the individual is heterozygous for that gene.

4. The genotype is a description of the allelic combination of the two copies of a gene present in an individual. The phenotype is the observable form of the trait that the individual expresses.

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5. A cross between two parental lines (P) that are pure-breeding for alternative alleles of a gene will produce a first filial (F_1) generation of hybrids that are heterozygous. The phenotype expressed by these hybrids is determined by the dominant allele of the pair, and this phenotype is the same as that expressed by individuals homozygous for the dominant allele. The phenotype associated with the recessive allele will reappear only in the F_2 generation in individuals homozygous for this allele. In crosses between F_1 heterozygotes, the dominant and recessive phenotypes will appear in the F_2 generation in a ratio of 3:1.

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6. The two copies of each gene segregate during the formation of gametes. As a result, each egg and each sperm or pollen grain contains only one copy, and thus, only one allele, of each gene. Male and female gametes unite at random at fertilization. Mendel described this process as the law of segregation.

7. The segregation of alleles of any one gene is independent of the segregation of the alleles of other genes. Mendel described this process as the law of independent assortment. According to this law, crosses between *Aa Bb* F_1 dihybrids will generate F_2 progeny with a phenotypic ratio of 9 (*A*– *B*–) : 3 (*A*– *bb*) : 3 (*aa B*–) : 1 (*aa bb*).

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8. The F_1 phenotype defines the dominance relationship between each pair of alleles. With complete dominance, heterozygotes resemble the homozygous dominant parent. With incomplete dominance, the F_1 hybrid phenotype resembles neither parent. With codominance, the F_1 hybrid phenotype includes aspects derived from both parents. Many allele pairs are codominant at the level of protein production.

9. A single gene may have any number of alleles, each of which can cause the appearance of different phenotypes. New alleles arise by mutation. Alleles with a frequency equal to or greater than 1 percent in a population are wild-type; alleles that are less frequent are mutant. When two or more wild-type alleles (common variants) exist for a gene, the gene is polymorphic; a gene with only one wild-type allele is monomorphic.

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10. In pleiotropy, one gene contributes to multiple traits. For such a gene, the dominance relationship between any two alleles can vary depending on the trait under consideration.

11. Two or more genes may interact to affect the production of a single trait. These interactions may be understood by observing characteristic deviations from traditional Mendelian phenotypic ratios.

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12. In epistasis, the action of an allele at one gene can hide traits otherwise caused by the expression of alleles at another gene. In complementary gene action, dominant and normally functioning alleles of two or more genes are required to generate a wild-type phenotype. When genes are redundant for a trait, one dominant and normally functioning allele of either gene is sufficient to generate the wild-type phenotype. In heterogeneity, mutant alleles at any one of two or more genes are sufficient to elicit a mutant phenotype. The complementation test can reveal whether a particular phenotype seen in two individuals arises from mutations in the same or separate genes.

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13. In many cases, the route from genotype to phenotype can be modified by the environment, chance, or other genes. A phenotype shows incomplete penetrance when it is expressed in fewer than 100 percent of individuals with the same genotype. A phenotype shows variable expressivity when it is expressed at different levels among individuals with the same genotype.

14. A continuous trait can have any value of expression between two extremes. Traits of this type are polygenic; that is, determined by the interactions of multiple genes.

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