5.6 Genetics

Describing heredity and how genetic diagrams work

Genotype, phenotype, alleles and dominance

In the previous chapter, you learned about the creation of gametes by *meiosis* from parent cells, producing **haploid** cells with half the total number of chromosomes in the original cell. This chapter will take you through how heredity works and how to use genetic cross diagrams, but firstly you need to know about *genotype* and *phenotype*.

The **genotype** refers to the precise *genetic makeup* of the organism, in terms of the **alleles** it contains. This is usually described in terms of a particular characteristic, where the outcome – attributes expressed in the organism – is the **phenotype**. A genotype for a characteristic where the organism has two identical alleles is **homozygous**, and where the organism has two different alleles, the genotype is described as **heterozygous**.

For example, for the disorder *cystic fibrosis*, someone who has the disorder (caused by a mutation to the chromosomes) must have the genotype **cfcf** (they must have the **recessive** allele for cystic fibrosis twice – being homozygous – in order for the phenotype to be cystic fibrosis). Any person with at least one **dominant** allele, i.e. no cystic fibrosis, so either **CFcf** or **CFCF** does not have the disorder, because of the dominance of this allele. A recessive allele is only expressed when accompanied by another identical recessive allele, and when the opposing dominant allele is absent.

DRAWING DIAGRAMS

In pea plants, the allele for purple flowers is dominant **P** and the allele for white flowers is recessive **p**. We can use a genetic cross diagram to show the **F_1 hybrid** – that is the possible genotypes of the first generation of offspring from two parents. Take a cross between a pure-breeding homozygous purple flower and a homozygous white flower:

					White flower	
parental phenotype:	purple	x	white		**p**	**p**
parental genotype:	PP	x	pp	**P**	Pp	Pp
gamete opportunities:	**P**	x	**p**			
F_1 genotypes:	Pp + Pp + Pp + Pp			**P**	Pp	Pp

(Purple flower on left of the grid)

By all outcomes, the first generation of offspring of these two homozygous parents are **Pp** and as the purple allele is dominant, all the offspring from these parents *must* be purple (this is their phenotype)

Codominance in alleles

When an organism has two different alleles (so their gene is heterozygous) which are both expressed in the phenotype, the alleles are described as being **codominant**. Codominant alleles *both* contribute towards the phenotype. Generally, alleles which are codominant are written using one common letter followed by a superscript letter representing that allele, for example: with ABO blood groups, the allele I^O is recessive, and the alleles I^B and I^A are codominant.

DRAWING DIAGRAMS

Red poll cattle are homozygous for an allele which gives them their red coat colour (C^R), and white shorthorn cattle are homozygous for the white coat allele (C^W). When a cattle has both alleles, they have a mixture of red and white hairs, giving them a coat colour called roan. Let's see what happens if we cross one red poll cattle with one roan cattle:

					Roan cattle	
parental phenotype:	red	x	roan		C^R	C^W
parental genotype:	$C^R C^R$	x	$C^R C^W$	C^R	R, R	R, W
gamete opportunities:	C^R	x	$C^R C^W$			
F_1 genotypes:	$C^R C^R$ + $C^R C^R$ + $C^R C^W$ + $C^R C^W$			C^R	R, R	R, W

(Red poll cattle on left of the grid)

The cross diagram shows clearly that half the offspring will have $C^R C^R$ and the other half $C^R C^W$ and so it can be predicted that the F_1 generation will be approximately half red poll and half roan

Dihybrid crosses

A *monohybrid* cross involves one gene, and therefore only involves one characteristic (or, phenotype). But where the inheritance of *two genes* determining two different characteristics is considered, a **dihybrid cross** will be used.

For example, in pea plants, colour is controlled by one gene whereby yellow, **Y**, is dominant to green, **y**. Pea shape is controlled by a different gene, determining either a rounded pea shape, **R**, which is dominant to wrinkled, **r**. There are nine different possible genotypes of a pea plant (YYRR, YyRr, yyRr, etc) but only four possible phenotypes (yellow and round, yellow and wrinkled, green and round, and green and wrinkled).

DRAWING DIAGRAMS

Using the example of the pea plants above, what would happen if we crossed a pure-breeding homozygous yellow and round pea plant with a pure-breeding homozygous green and wrinkled pea plant? Let's cross to work out the proportion of offspring with each phenotype for both the F_1 and F_2 generations:

parental phenotype	yellow, round	x	green, wrinkled
parental genotype:	YYRR	x	yyrr
gamete opportunities:	**YR**	x	**yr**
F_1 genotypes:	All offspring are YyRr		

F_1 generation	Green and wrinkled	
	yr	yr
Yellow and round — YR	YyRr	YyRr
YR	YyRr	YyRr

The first generation all share the phenotype **YyRr** which gives them all the phenotype of yellow and round, as those are the dominant alleles. Therefore, the F_2 generation must be a cross between two YyRr pea plants:

parental phenotype	yellow, round	x	yellow, round
parental genotype:	YyRr	x	YyRr
gamete opportunities:	**YR Yr yR yr**	x	**YR Yr yR yr**
F_2 genotypes:	(see table)		

Looking at the dihybrid cross for the second generation, we see a ratio of 9:3:3:1 of yellow/round : yellow/wrinkled : green/round : green/wrinkled

F_2 generation	Heterozygous offspring			
	YR	Yr	yR	yr
Heterozygous offspring — YR	YYRR	YYRr	YyRR	YyRr
Yr	YYRr	YYrr	YyRr	Yyrr
yR	YyRR	YyRr	yyRR	yyRr
yr	YyRr	Yyrr	yyRr	yyrr

Linked and sex-linked genes

Linkage refers to two or more genes located on the same chromosome, essentially **linked genes** are genes found on the same pair of homologous chromosomes. Most linked genes are found on the **autosomes** (these are all the chromosomes which are not responsible for determining sex, so there are 22 pairs of autosomes in humans), although some genes can be **sex-linked genes**, which are linked on the X chromosome, usually – although some are linked on the Y chromosome.
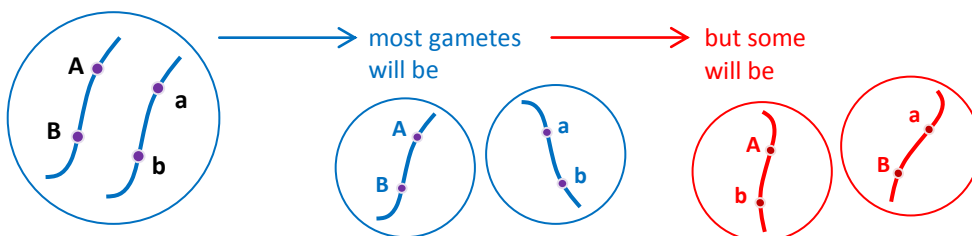
Take the example shown in the diagram: an organism has two alleles on each chromosome for linked genes, **AB** and **ab**. Most of its gametes produced by meiosis will obviously be **AB** or **ab**.

Usually, linked genes do not allow alleles to independently assort as unlinked genes can do, so most of the gametes stay either AB or ab. However, where **chiasmata** form cross-links between the two genes on a chromosome, and crossing-over takes place, **recombinants** are produced: cells which contain genotypes which don't belong to either of their parents. The recombinants are shown in the red meiotic cells above, although in reality linked genes prevent this happening too often. Linkage therefore reduces the number of phenotypes of the organism.

A characteristic is sex-linked when the gene coded for it is found on a sex chromosome. Most are on the X chromosome, as it is bigger, there are few genes on the Y chromosome. Sex-linked characteristics include *red-green colour blindness*.

DRAWING DIAGRAMS

One of the genes for coat colour in cats is sex-linked on the X chromosome. The allele C^O gives orange fur, while C^B gives black fur. The two are codominant, and when both are present a cat's fur appears tortoiseshell.

Question: Explain why male cats cannot be tortoiseshell.

We know this because the alleles are linked to genes on the X chromosome, so in order to be tortoiseshell, a cat needs to have two X chromosomes to have both C^O and C^B – which is not possible for males, as they are heterogametic (have different sex chromosomes, XY) – only possible in females, who have two X chromosomes to be tortoiseshell

Let's see what happens if we do a cross between an orange-coated male and a tortoiseshell female cat:
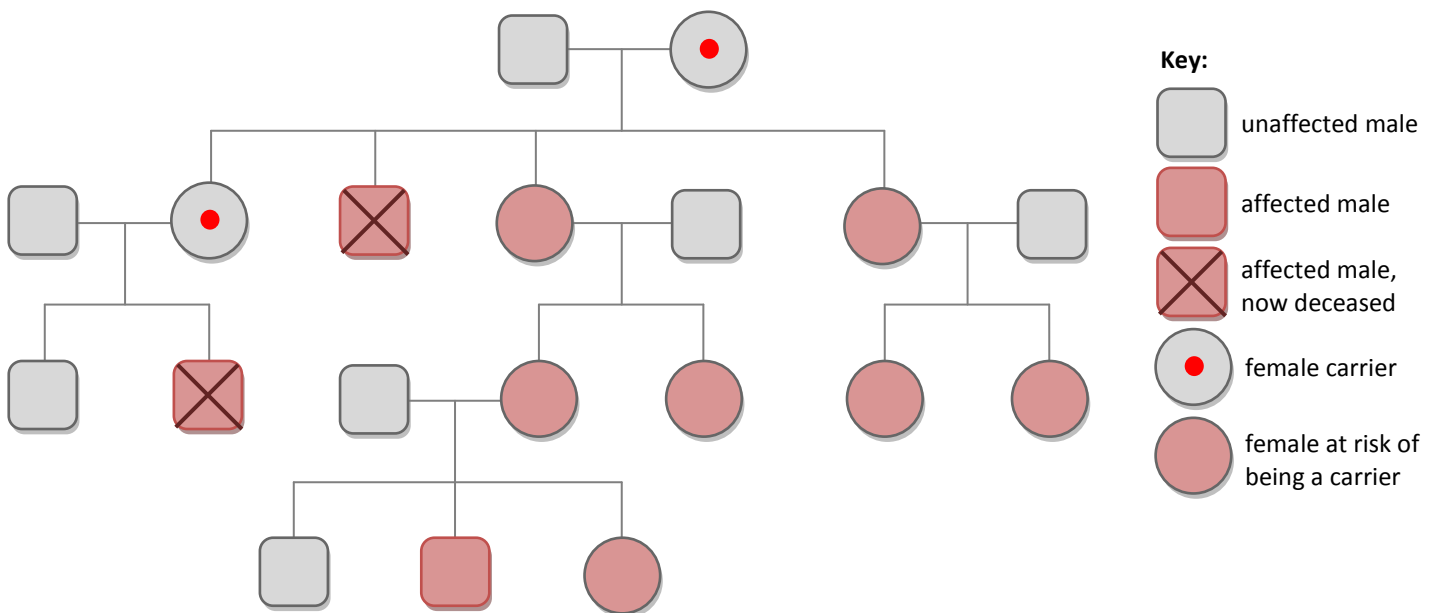
					Tortoiseshell female	
parental phenotype	orange male	x	tortoiseshell female		XC^O	XC^B
parental genotype:	XC^O, Y	x	XC^O, XC^B	Orange male / XC^O	$XC^O XC^O$	$XC^O XC^B$
gamete opportunities:	XC^O (Y)	x	XC^O XC^B	Y	$XC^O Y$	$XC^B Y$

parental phenotype   orange male   x   tortoiseshell female

parental genotype: XC^O, Y   x XC^O, XC^B

gamete opportunities: **XC^O (Y)**   x   **XC^O XC^B**

F_1 genotypes: $XC^O XC^O$ + $XC^O XC^B$ + $XC^O Y$ + $XC^B Y$

The table and the above cross demonstrates that the cross will produce males around half the time and females equally. Half of those males will have an orange coat, and the others black; we can also tell that half the potential females would have an orange coat ($C^O C^O$) and half would be tortoiseshell ($C^O C^B$).

Family pedigrees

Until now, the examples that have been used have solved problems using genetic crosses in tables. These are known as **Punnett squares**. However, an alternative genetic diagram is the **family pedigree**. One example is shown below, using DMD (Duchenne muscular dystrophy) as the disorder. The DMD gene for a muscle protein called dystrophin is on the X chromosome in humans. Mutations of this gene result in a deficiency of dystrophin and is production. Boys with the disease develop muscle weakness in early childhood and are usually wheelchair-bound by the age of ten. Death often occurs due to skeletal and cardiac muscle degeneration by the early 20s. An example family pedigree for DMD is shown. Such family pedigrees can be used to work out the genotypes of particular family members.

Key:

☐	unaffected male
☐	affected male
☒	affected male, now deceased
●	female carrier
●	female at risk of being a carrier

Epistasis

Previously explained was the idea of dominant and recessive alleles, which do not interact in any way, shape or form. Simply, if an organism has a dominant allele (say, for eye colour), that phenotype will be expressed. Alternatively, some alleles share *codominance*, where having two codominant alleles means that the phenotypic characteristic is expressed from *both* alleles. Different from codominance is **epistasis**, which instead occurs where one gene masks or suppresses the expression of another gene.

Epistasis frequently occurs where two different genes both affect the same characteristic (phenotype), because the genes code for two proteins – usually enzymes – that help to control the same metabolic pathway. For example, a particular plant might produce the pigments that colour its petals in a two-step pathway:

colourless substance → *enzyme 1* → yellow pigment → *enzyme 2* → orange pigment

The gene coding for enzyme 1, which is required to produce the yellow pigment, may have two versions (alleles). Allele **A** codes for the enzyme, whereas **a** does not produce a working enzyme. Similarly, **B** produces enzyme 2, **b** does not.

A plant cannot produce any colour pigment at all without enzyme 1, as shown. Even if a plant owns allele **B** to produce orange pigment from the yellow pigment, if it doesn't have **A** to firstly make that yellow pigment, no colour can be produced. If it has the genotype **aa** there is no pigment produced and petals will contain only colourless substances and be white, regardless of the B/b allele, as there is no yellow pigment to work on. This is an example of epistasis working in a 'complementary' fashion.

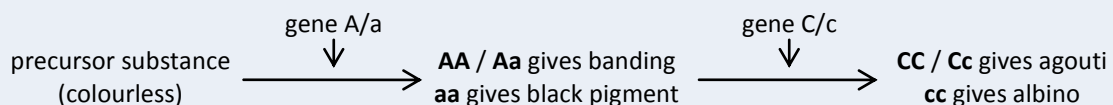## Dominant and recessive 'antagonistic' epistasis

Alternatively, epistasis can work antagonistically, whereby the homozygous presence of a *recessive* allele can prevent the expression of another allele at another **locus** (a locus, plural *loci*, is a specific point in the DNA where a gene or allele is). **Recessive epistasis** occurs where neither a dominant or recessive allele for one gene can be expressed due to the lack of a dominant allele of another gene, which is epistatic to the other gene. **Dominant epistasis** occurs when a dominant allele *is* present on the first gene, which masks the expression of alleles at a second gene locus.

Using phenotypic ratios to solve problems involving epistasis

Mice and coat colour

Coat colour is often determined by epistatic genes in animals. For example, the colours of mice's coats are determined by a gene, **A** or **a** which codes for the distribution of the pigment **melanin** in the hairs. Allele **a** is a mutation, which produces black fur in mice with homozygous **aa** alleles, and the gene for *agouti* (alternate banding of black and white on each hair, to give a grey appearance) has two alleles: A/a. Allele A determines the presence of the agouti banding, whilst allele a determines the uniform black colour of the hair of black mice

A second gene, C/c, determines the production of melanin. The dominant allele **C** allows colour to develop, while a mouse with the genotype **cc** (recessive homozygous) does not make melanin and so is albino

	gene A/a		gene C/c	
precursor substance (colourless)	→	**AA** / **Aa** gives banding **aa** gives black pigment	→	**CC** / **Cc** gives agouti **cc** gives albino

Eye colour in humans

The colour of the iris in humans is determined by at least two genes, D/d and E/e, that are found at separate loci, but interact with one another. Both have dominant alleles that cause the pigment *melanin* to be produced. The recessive alleles do not express melanin. There are two layers of pigment in the iris, one in front of the other. No melanin in either gives the **albino** condition. The iris looks pink as blood vessels within it can be seen. When the rear layer contains melanin, but the front does not, the iris is blue. As more and more melanin is produced in the front layer, the iris looks darker blue, then green, brown and finally almost black

Examples of genotypes	Nº of **D** & **E** alleles	Colour of iris
DDEE	4	dark brown/black
DDEe or DdEE	3	brown
DdEe, ddEE or DDee	2	light brown
Ddee or ddEe	1	dark blue
ddee	0	pale blue

If two people who were heterozygous at both gene loci with light brown eyes were to reproduce, we can work out the possible genotypes, phenotypes and phenotypic ratio of their offspring. We know that we can safely assume they are to each be **DdEe**

The potential phenotypes (once the dihybrid cross has been completed, although not shown in here it is completed simply as with the pea plant example earlier on) are any of the five above, with a ratio of 1:4:6:4:1 from dark brown down through to pale blue. If asked if it was possible for two blue-eyed parents to produce a child with brown eyes, the answer is evidently 'yes' as two dark blue parents can produce offspring with two dominant alleles (light brown)