GENE LINKAGE

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D3.2.17 Punnett grids for predicting genotypic and phenotypic ratios in dihybrid crosses involving pairs of unlinked autosomal genes

D3.2.18 Loci of human genes and their polypeptide products

D3.2.19 Autosomal gene linkage

D3.2.20 Recombinants in crosses involving two linked or unlinked genes

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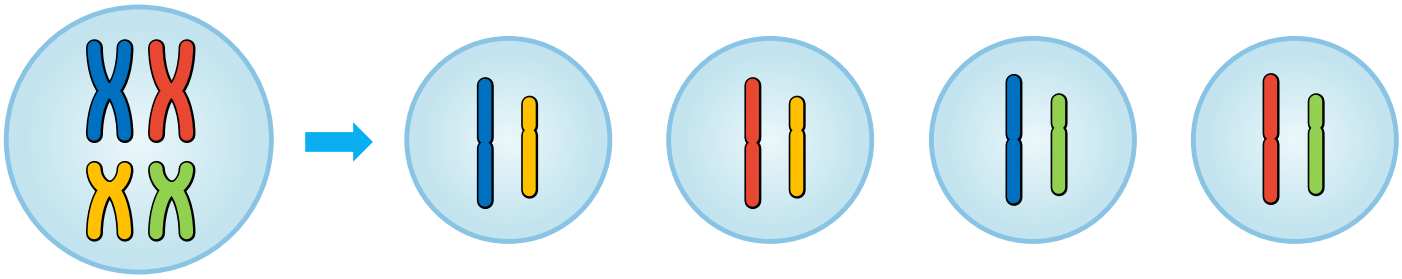
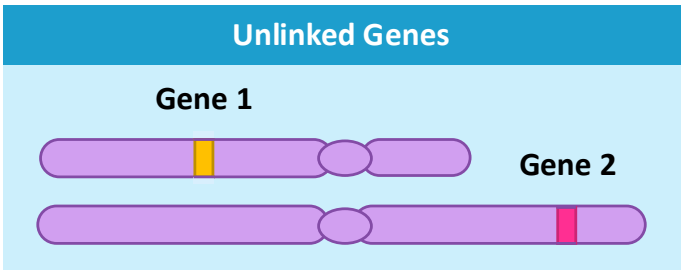
GENETIC ASSORTMENT

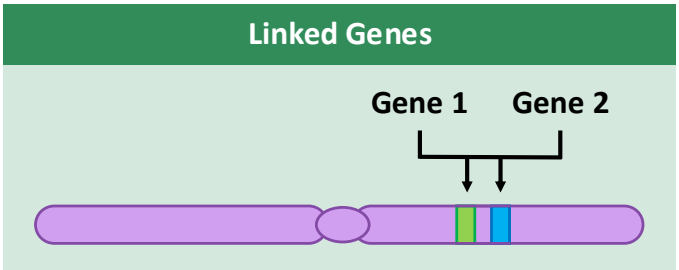
During meiosis, homologous chromosomes are separated to produce cells that are haploid (i.e. one copy of each chromosome). The separation of homologous chromosomes (and their alleles) during anaphase I of meiosis is called **segregation**. The segregation of each homologous pair is random and is not affected by the segregation of any other pair. This random segregation is referred to as the **law of independent assortment** and means an allele on one chromosome has an equal chance of being paired with, or separated from, any allele on another chromosome. The randomness of chromosome segregation creates variability in potential gametes (due to greater numbers of possible allele combinations), but only holds true for **unlinked genes**.



GENE LOCI

The specific position of a gene on a chromosome is called the **gene locus** (plural = loci). Any locus can be identified via three points of reference. The first point of reference is a number (or letter) which denotes the chromosome. The second point of reference is a letter to denote which arm the locus is positioned on, while the third point of reference is a number corresponding to centromere proximity. For example, the human hemoglobin beta gene is located on the p arm of chromosome 11 at a longitudinal position of 15.4 (locus = 11p15.4). The locus of a gene and its polypeptide product can be identified using online databases. **Unlinked genes** are located on *different chromosomes*, while **linked genes** are on the *same chromosome*.





DIHYBRID CROSSES

A dihybrid cross can be used to determine the genotypic and phenotypic combinations of offspring for any two genes that are **unlinked**. As there are two genes, there can be up to four different gamete combinations (established via **FOIL method** in table below). A dihybrid cross involves the following steps:

- Assign characters to represent dominant / recessive alleles
- Identify parent genotypes and potential alleles (via FOIL)
- Use a Punnett grid to determine the ratio of phenotypes

	First	Outside	Inside	Last
Parent	Aa Bb	Aa Bb	Aa Bb	Aa Bb
Gamete	AB	Ab	aB	ab

	YR	Yr	yR	yr
YR	YYRR	YYRr	YyRR	YyRr
Yr	YYRr	YYrr	YyRr	Yyrr
yR	YyRR	YyRr	yyRR	yyRr
yr	YyRr	Yyrr	yyRr	yyrr

Cross: YyRr × YyRr — 9 : 3 : 3 : 1

LINKED GENES

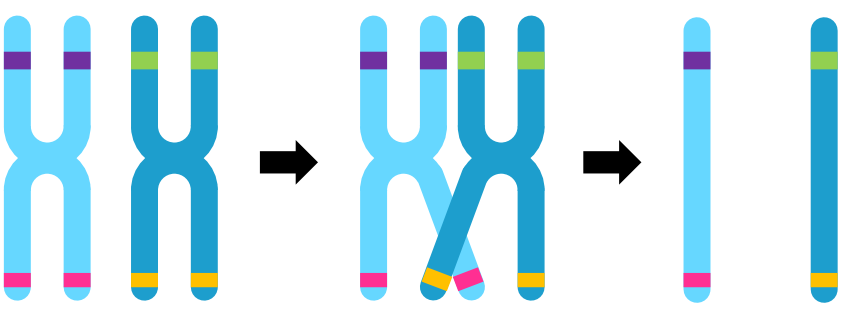
Linked genes are shown as a single entity with the allele pairs being separated by vertical lines representing homologous chromosomes (e.g. AB // ab). Because linked genes are on the same chromosome they must be inherited as a **single unit**. This means that the law of independent assortment does **not** apply to linked genes – instead, inheritance patterns will resemble a monohybrid cross. Two linked alleles will only assort independently if they become unlinked via **crossing over**. This may occur in prophase I of meiosis during the process of synapsis (when the homologous chromosomes form a bivalent). Non-sister chromatids may exchange genetic material at the points of attachment (**chiasma**). This act of recombination will separate the alleles and allow them to be inherited independently of one another (the frequency of recombination is typically low).

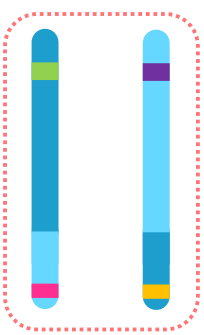
	YR	yr
YR	YR // YR	YR // yr
yr	YR // yr	yr // yr

$\frac{YR}{yr} \times \frac{YR}{yr}$ — 3 : 0 : 0 : 1

RECOMBINANTS

Recombinants are the combinations of alleles not found in the parents. Recombinants are seen in crosses between unlinked genes due to segregation and independent assortment of homologous chromosomes. Linked genes do not undergo independent assortment, but recombination still occurs via crossing over. This is a **random occurrence**, meaning recombinant phenotype frequencies will be lower than non-recombinant phenotype frequencies. The frequency of recombination increases when the linked genes are further apart.



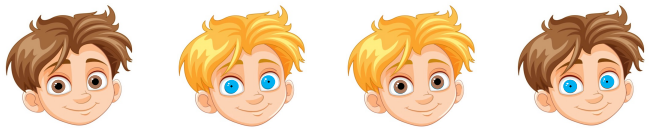


Recombination of linked genes occurs at points called **chiasma** and happens via *crossing over*

UNLINKED VERSUS LINKED

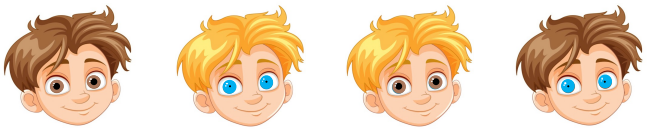
Recombinant phenotypes occur **less frequently** when genes are linked because crossing over will not occur in every gamete. Statistical tests can be used to determine if outcomes represent linked or unlinked genes.

Unlinked: AaBb × aabb



25% 25% 25% 25%

Linked: AB / ab × ab / ab



49% 49% 1% 1%

CHI-SQUARED TEST

A dihybrid cross was conducted using two pea plants heterozygous for pod colour and shape. Phenotypic ratios were recorded and compared against the predicted ratios for **unlinked genes** (using a Punnett grid):

Key:

Y	yellow
y	green
R	round
r	wrinkled

Raw Data:

	701
	204
	243
	68

	YR	Yr	yR	yr
YR				
Yr				
yR				
yr				

Predicted:

	$^{9}/_{16}$
	$^{3}/_{16}$
	$^{3}/_{16}$
	$^{1}/_{16}$

Step 1: Construct a table of frequencies

Expected frequencies are calculated as follows: **Expected = predicted ratio × total number of offspring**
The data is then processed to work out chi-squared values based on both observed and expected numbers.

	Observed Data (O)	Expected Data (E)	$(O - E)^2 \div E$
Yellow, Round	701	9/16 × 1216 = **684**	$(701 - 684)^2 \div 684$ = **0.42**
Green, Round	204	3/16 × 1216 = **228**	$(204 - 228)^2 \div 228$ = **2.53**
Yellow, Wrinkled	243	3/16 × 1216 = **228**	$(243 - 228)^2 \div 228$ = **0.99**
Green, Wrinkled	68	1/16 × 1216 = **76**	$(68 - 76)^2 \div 76$ = **0.84**

Step 3: Determine statistical significance

The chi-squared test can be used to determine a critical value via the following formula: $\chi^2 = \sum(O - E)^2 \div E$
This value is then used to identify a **p value**, which indicates the probability the results are due to chance. The results are considered to be statistically significant (suggesting that the genes are linked) if **p<0.05***.

Data: $\chi^2 = 0.42 + 2.53 + 0.99 + 0.84 =$ **4.76** (this value must be larger than the critical value when p<0.05)

p value (% chance)	0.25	0.1	**0.05**	0.01
Critical value (df = 3)	4.11	6.25	7.82	11.35

The χ^2 value of **4.76** is below the critical value at p<0.05 (7.82), so results are **not** significant

* The degree of freedom (designates the range at which values will be considered significant) will always be **3** for this type of test