Cambridge Assessment International Education

Chapter 16
A2 Level

Inherited Change

Chapter Outline

4 Parts!

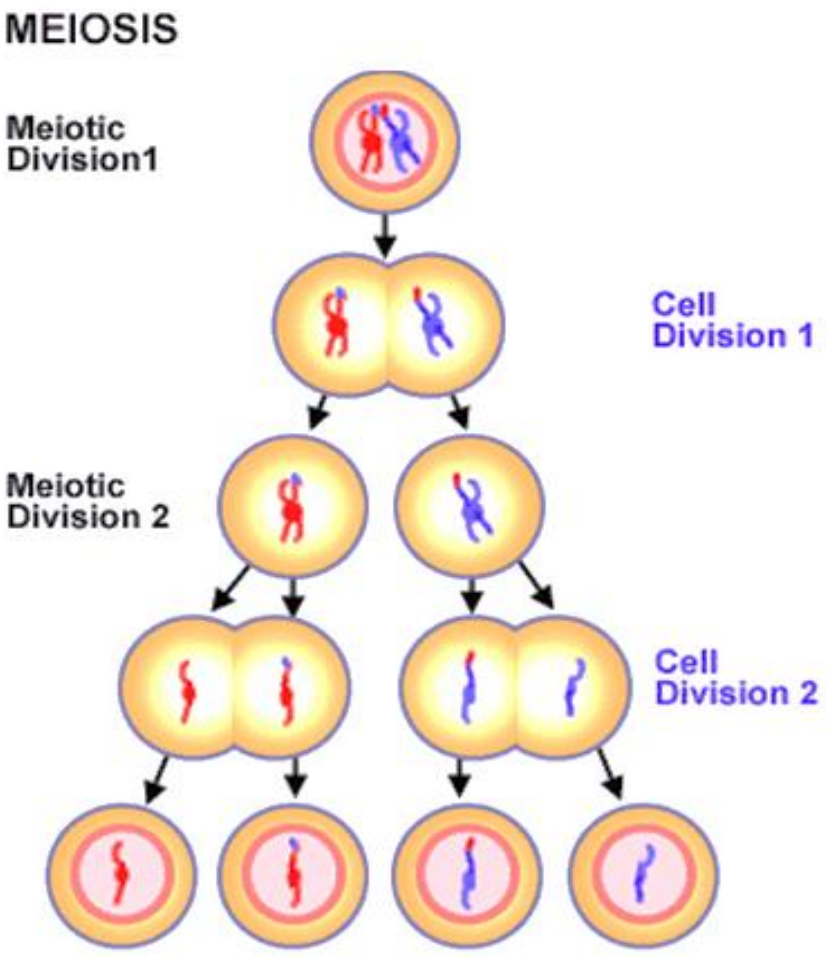
1. Meiosis
2. Mendelian Inheritance + Chi-squared test
3. More Patterns of Inheritance
4. Gene Control

Chapter Outline

Part I: Meiosis

- Meiosis
- Genetic variation due to
  - Crossing over
  - Random assortment of homologous chromosomes
  - Random fusion of gametes

- Role in gametogenesis in humans
- Role in formation of pollen grains and embryo sacs in flowering plants

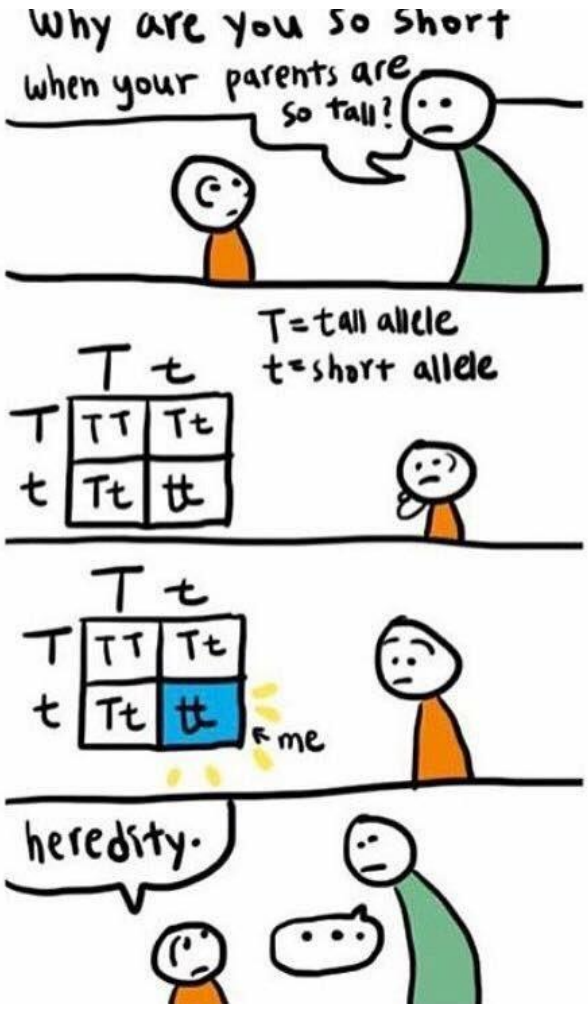


Chapter Outline

Part II: Mendelian Inheritance

- Monohybrid cross
- Dihybrid cross
- Test crosses

- **P5:** Chi-squared test



Chapter Outline

Part III: More Patterns of Inheritance

- Sex linkage
- Codominance
- Multiple alleles
- Epistasis
- Autosomal linkage

- Mutations
  - Important examples of mutations: sickle cell anemia, albinism, haemophilia, Huntington's disease, cystic fibrosis

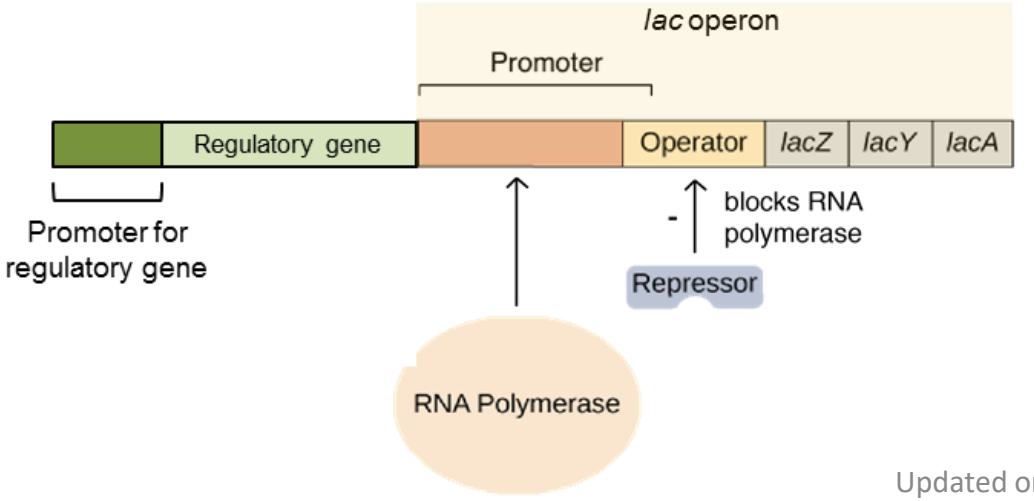
Chapter Outline

Part IV: Gene Control

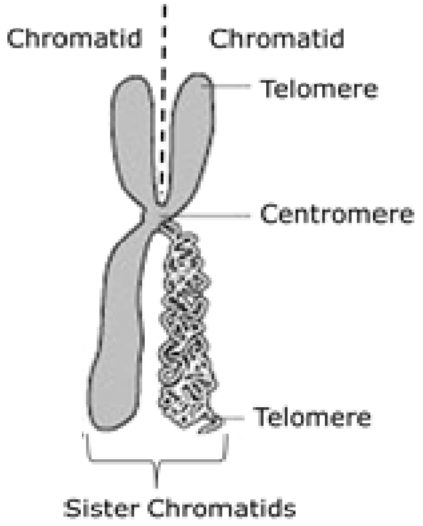
- Structural vs regulatory genes
- Repressible vs inducible enzymes

- Prokaryotes: The *lac* operon
- Eukaryotes: Function of transcription factors in gene expression

- Gibberellin breaks down DELLA protein repressors to activate genes



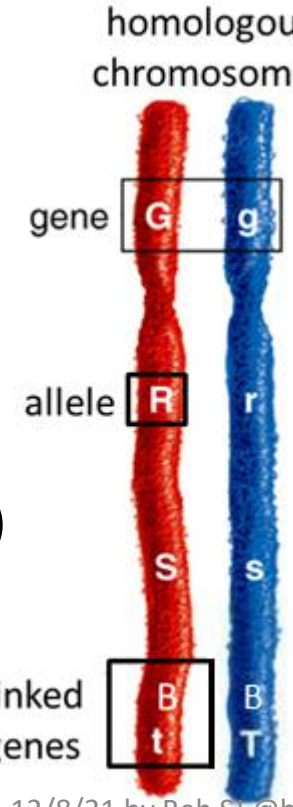
Important Terms



- **Homologous chromosomes** = A pair of chromosomes in diploid cells. One inherited from mother, one from father. Same size, same genes, but may have diff alleles.

- **Sex chromosomes** = X and Y chromosome
- **Autosomes** = All chromosomes except sex chromosomes

- **Gene = a specific DNA seq that codes for polypeptide**
  - Sex-linked genes = genes on sex chromosome
  - Autosomal-linked genes = genes on autosomes
  - **Linked genes** = all genes on the same chromosome. They are in a **linkage group**. Likely to be inherited together. (Not the same with sex/autosomal-linked genes)



- **Allele = a form of gene** → result of mutation
- **Locus** (plural: loci) = position of gene on chromosome

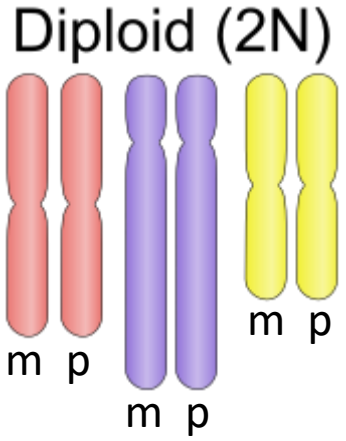
Important Terms

Diploid cells have two sets of chromosomes (2n)

= 2 copies of each gene = **2 alleles**

- 1 maternal, 1 paternal
- **Somatic cells** = all cells except for gametes
- In humans: **2n = 46**

→ Result of **mitosis**

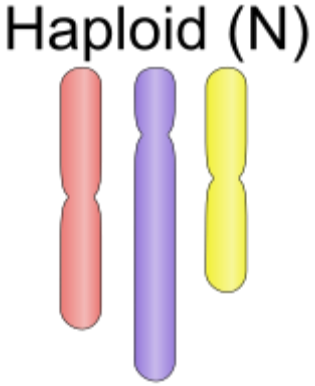


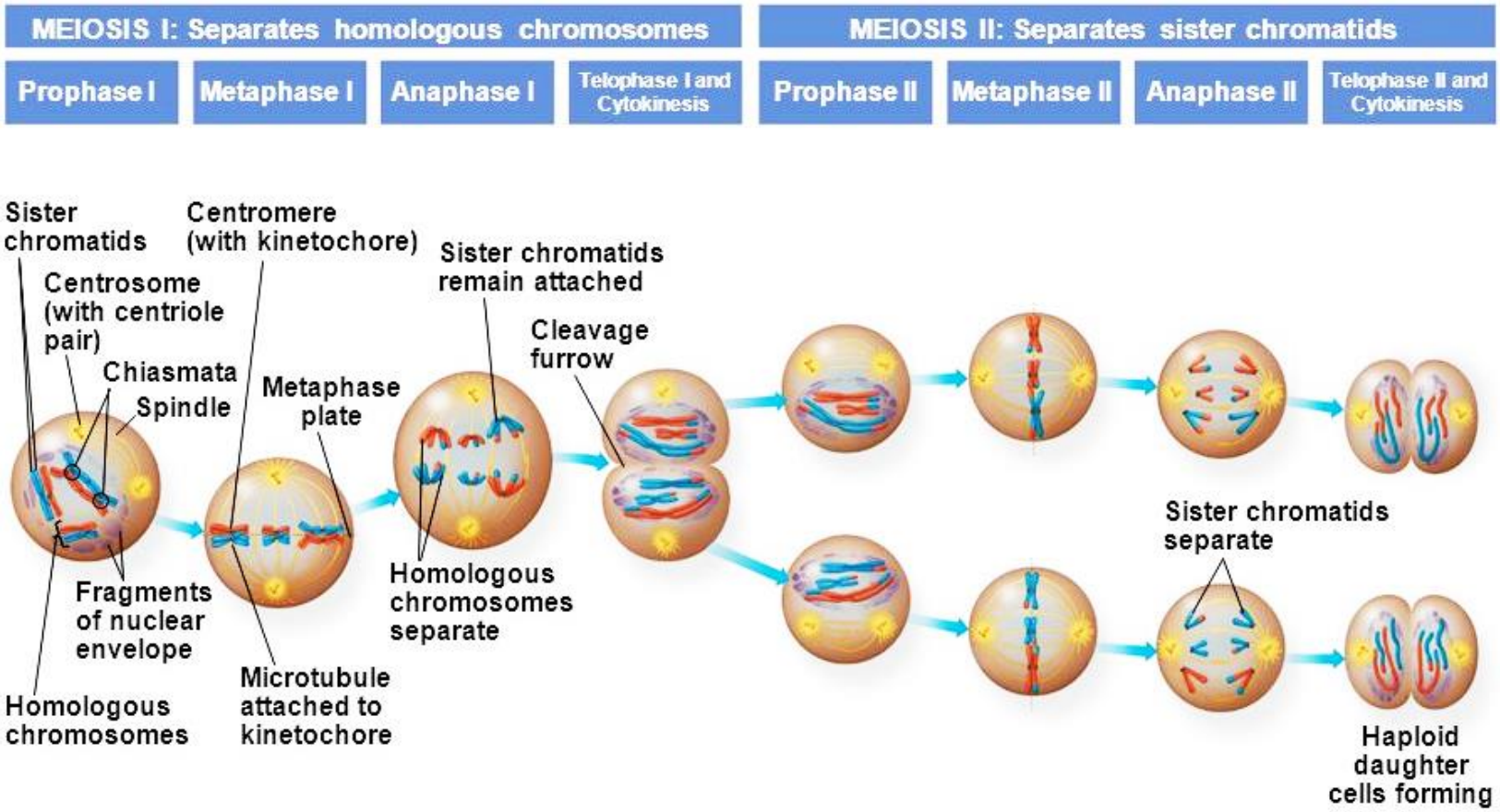
Haploid cells have only one set of chromosomes (n)

= Only one copy of each gene = **1 allele**

- **Gametes / germ cells**
- In humans: **n = 23**

→ Result of **meiosis**





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Excellence in education

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Part 1: Meiosis

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Part I: Meiosis

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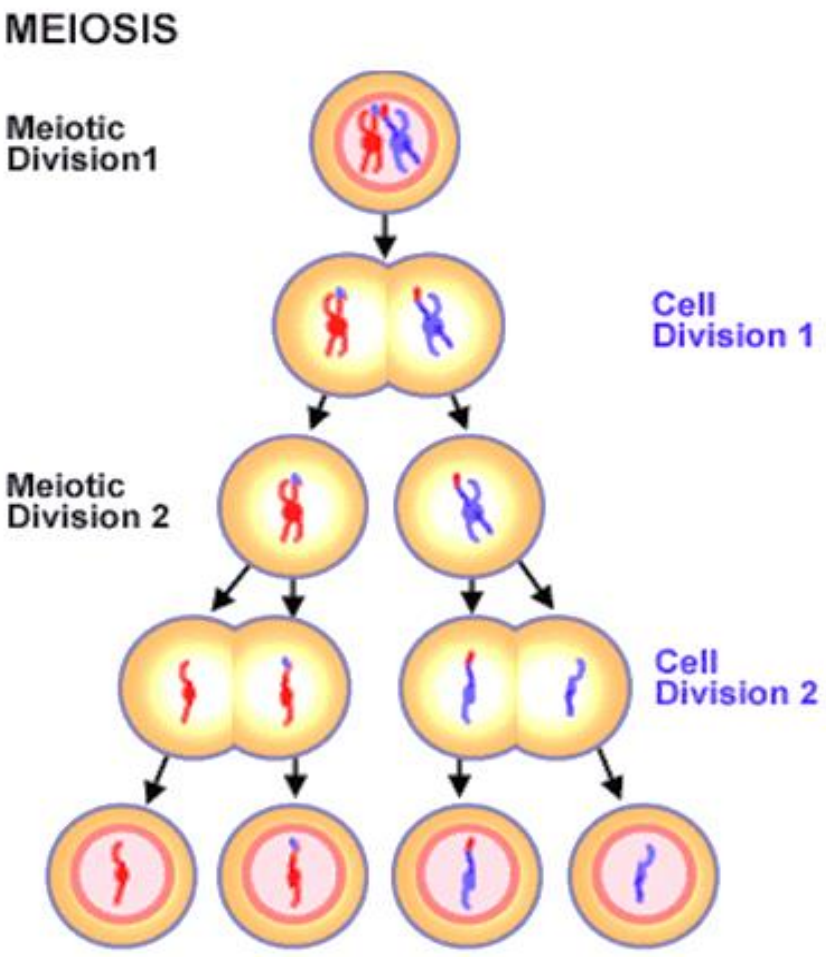
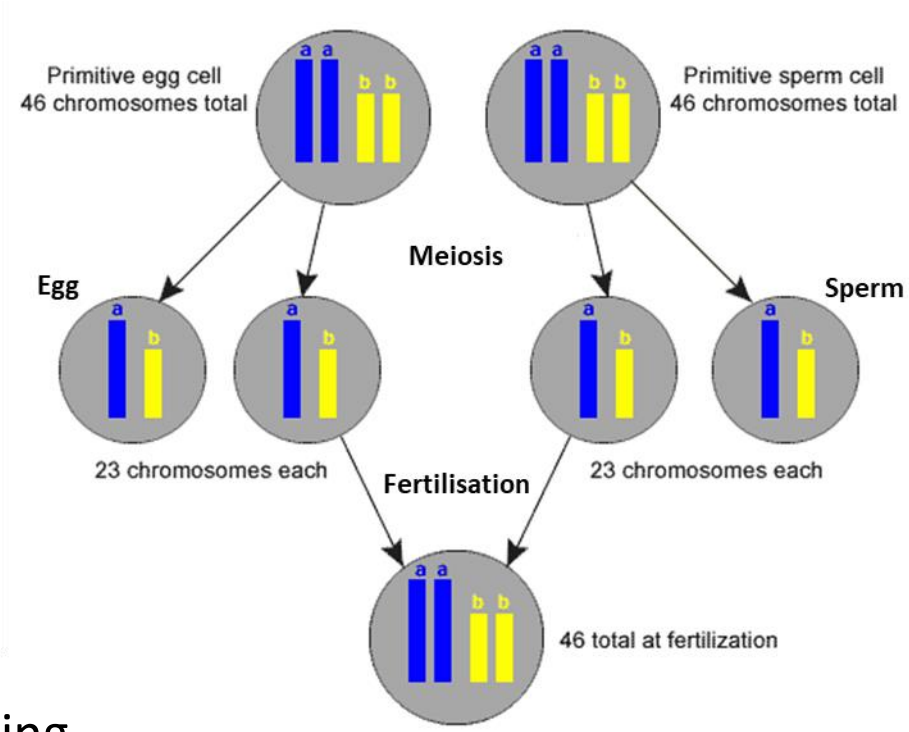


Meiosis

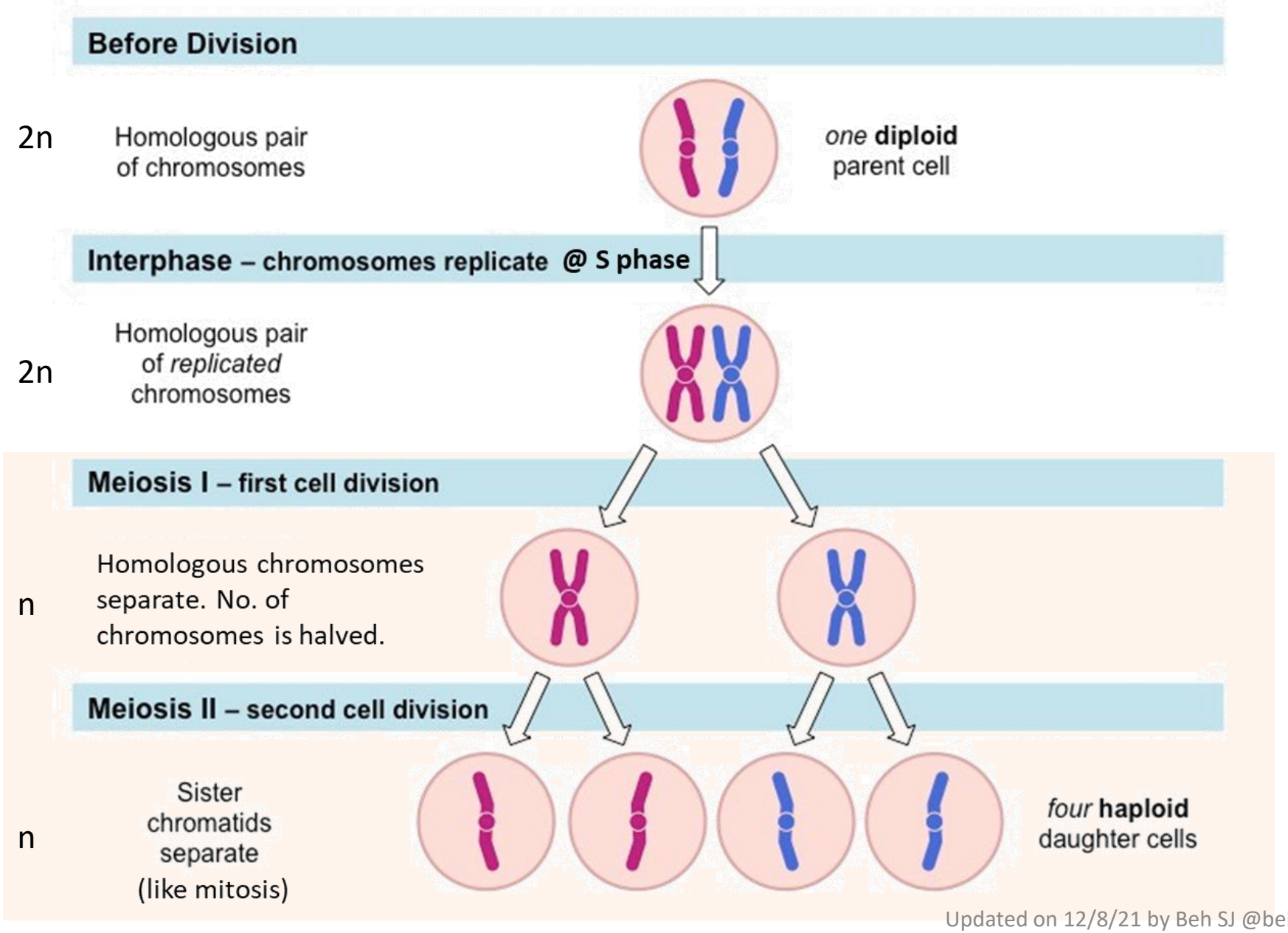
- Aka reduction division
- Before fertilisation in sexual reproduction



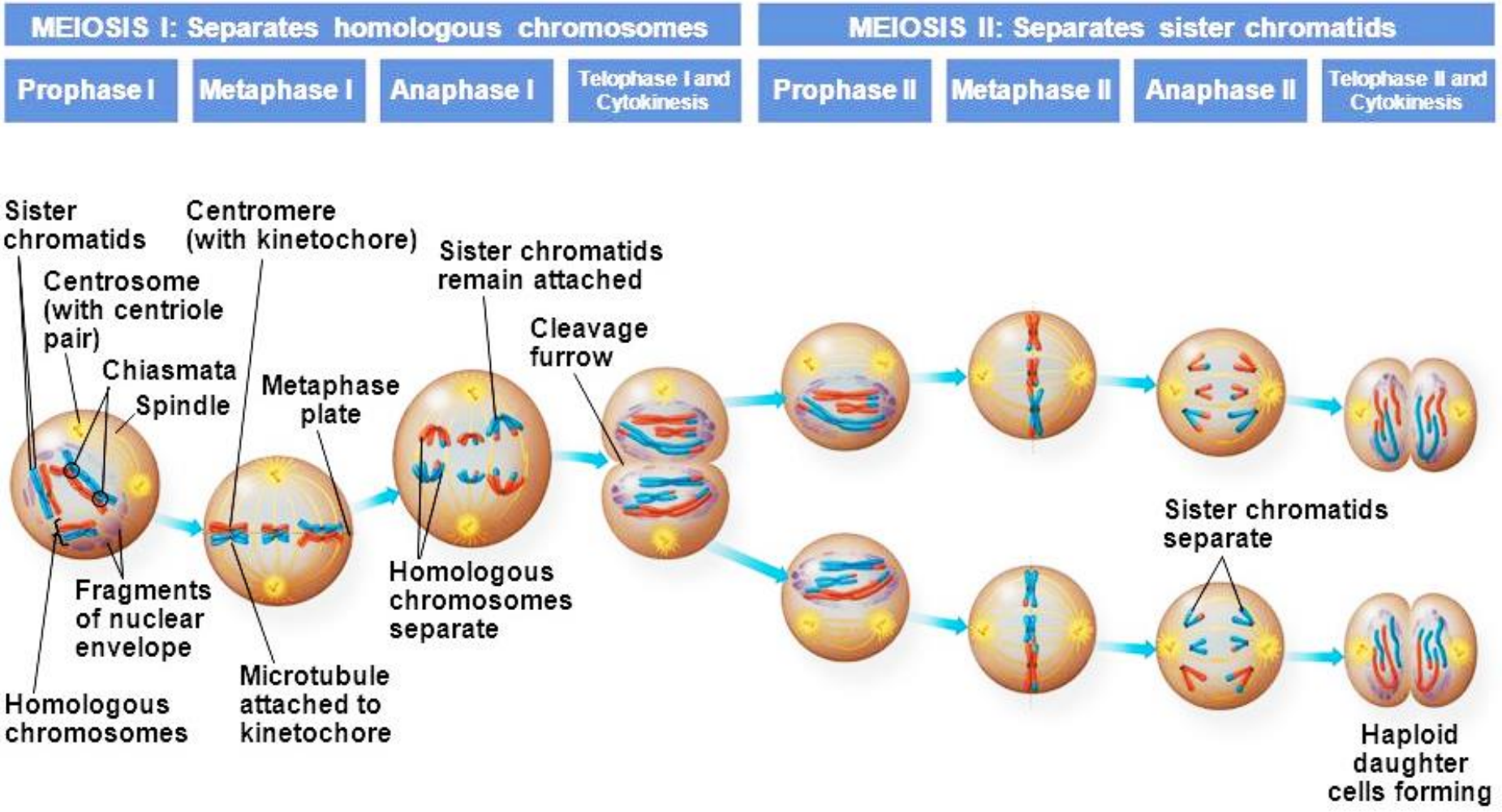
Importance of meiosis:

- To produce **gametes / sex cells** with **half the no. of chromosomes**
- Maintain the **diploid** no. of chromosomes in each generation
- To produce **genetic variation** in offspring

Meiosis


Before Division
2n
Homologous pair of chromosomes
one diploid parent cell
Interphase – chromosomes replicate @ S phase
2n
Homologous pair of replicated chromosomes
Meiosis I – first cell division
n
Homologous chromosomes separate. No. of chromosomes is halved.
Meiosis II – second cell division
n
Sister chromatids separate (like mitosis)
four haploid daughter cells

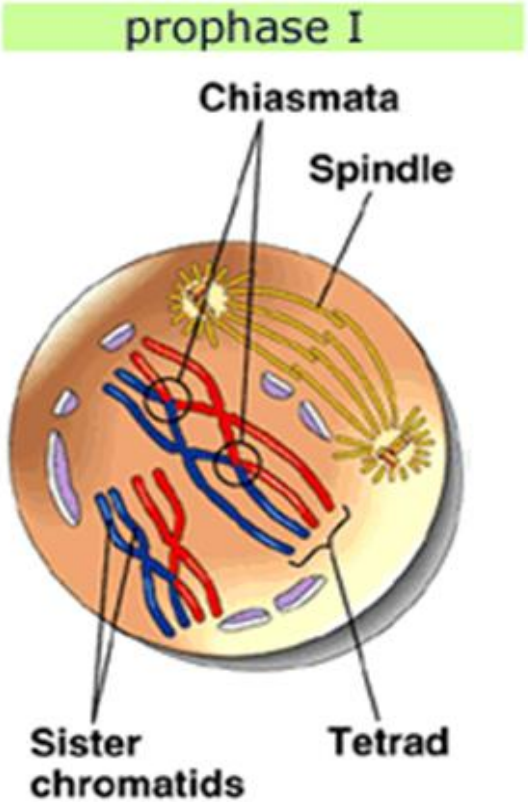
Stages in Meiosis



Prophase I

- Condensation of chromatin/chromosome
- Centrosomes move to opposite poles
- Nuclear envelope breaks down
- Nucleolus disappears
- Spindle fibres form

→ Start attaching to centromere and pull



- **Synapsis** occurs

→ Process where **homologous chromosomes pair up**

→ Each pair is called a **bivalent/tetrad**

- **Crossing over** takes place between non-sister chromatids

→ At **chiasmata** (singular: chiasma)

→ Result in **exchange of genetic material**

Prophase I: Crossing over

- During synapsis, homologous chromosomes coil around each other intimately
- Remain in contact at chiasmata
- Site of crossing over: **chiasma**

- Part of chromatids break
- Reconnect to another non-sister chromatid

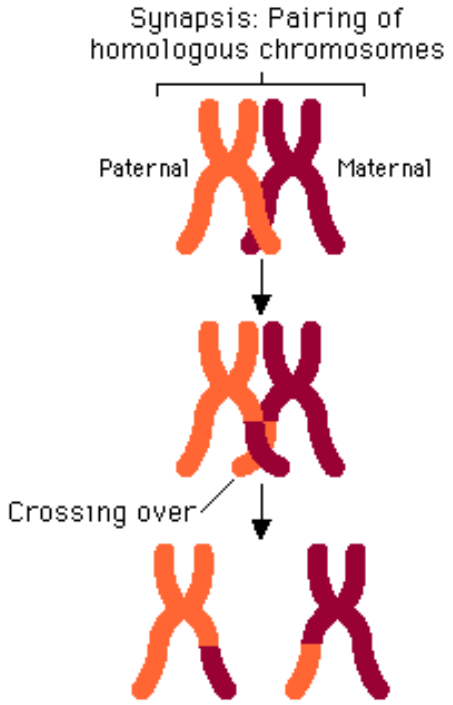
Result in:

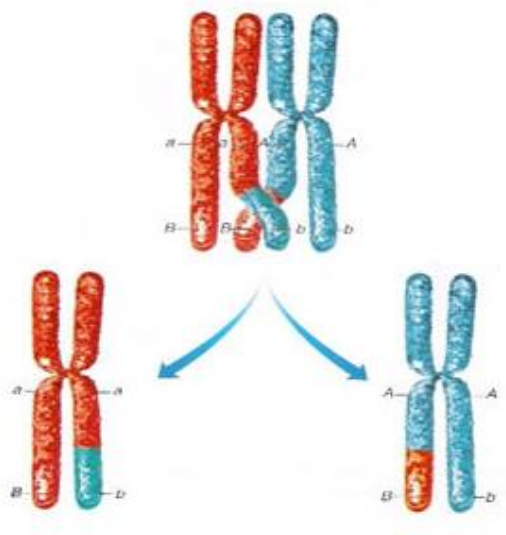
→ **Exchange of genetic material** [NOT genes]

→ **Linkage groups broken** / linked genes on same chromosome are separated

→ **New combination of alleles** within each chromosome

→ **Genetic variation**





Metaphase I

- Centrosomes reach opposite poles
- Spindle fibres are fully formed

→ Attached to chromosomes at centromeres

- **Bivalents / tetrads** line up across **equator / metaphase plate**

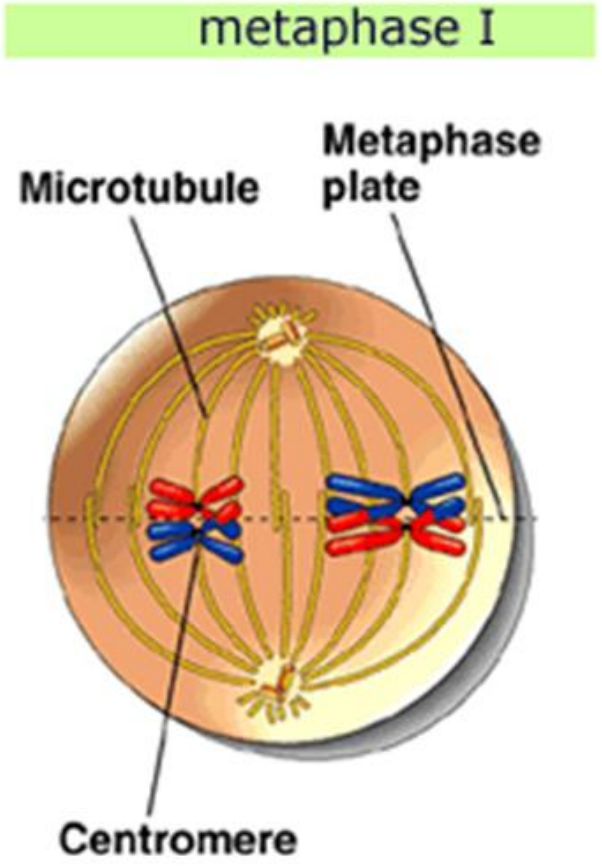
→ Chromosomes line up in **pairs**

- **Independent assortment** of homologous chromosome pairs occurs

→ Each pair lines up independently of others on equator

→ E.g. could be red-blue, or blue-red

→ Results in gametes that are genetically unique



Anaphase I

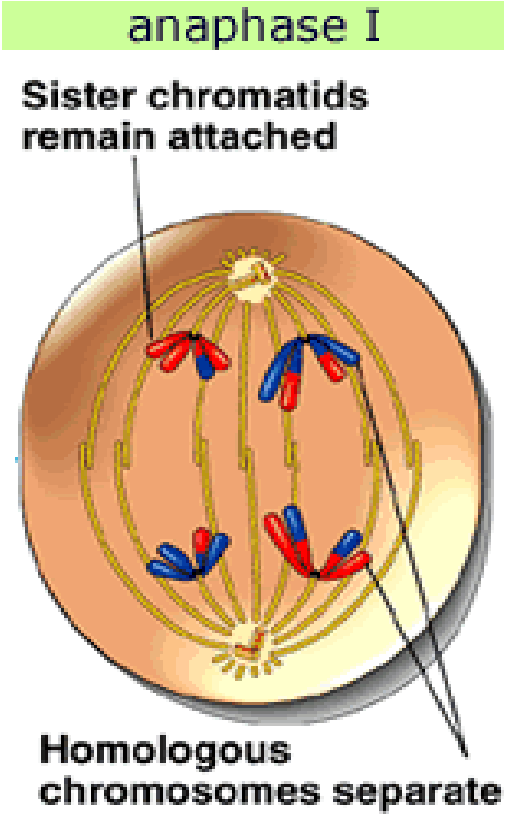
- Spindle microtubules shorten

- **Homologous chromosomes separate**

→ **Chromosomes of each pair pulled to opposite poles**

→ with centromeres leading towards poles

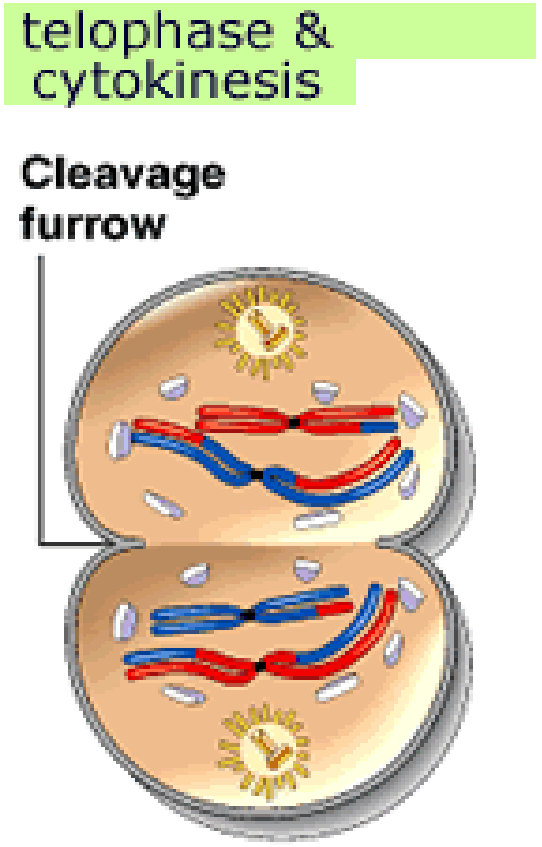
- Centromeres DO NOT divide



Telophase I & Cytokinesis

- Chromosomes reach the poles
- Chromosome ***partially*** **decondenses**
- Nucleolus reforms
- Nuclear envelope reassembles
- Spindle fibres breaks down
- **Cytokinesis** occurs
- Number of chromosomes in each daughter cell are now halved

→ **2 haploid cells formed**



Chap 5 Recap

Cytokinesis

- Division of the cell's cytoplasm

In animal cells:

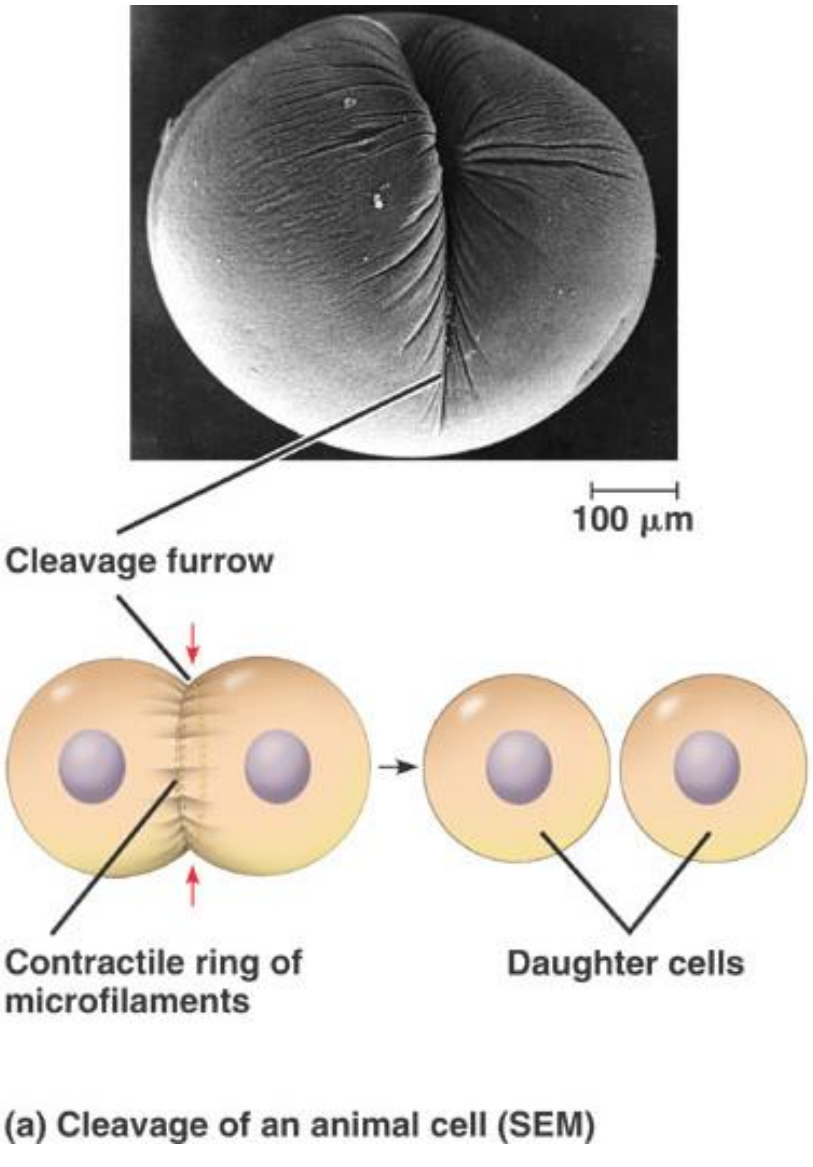
- **Cell membrane drawn together**

→ By contractile ring of microfilaments

→ Forms a **cleavage furrow**

→ Creating a drawstring effect

- **Cell membrane fuses**
- To divide cell into two
- Organelles are shared out



(a) Cleavage of an animal cell (SEM)

Chap 5 Recap

Cytokinesis

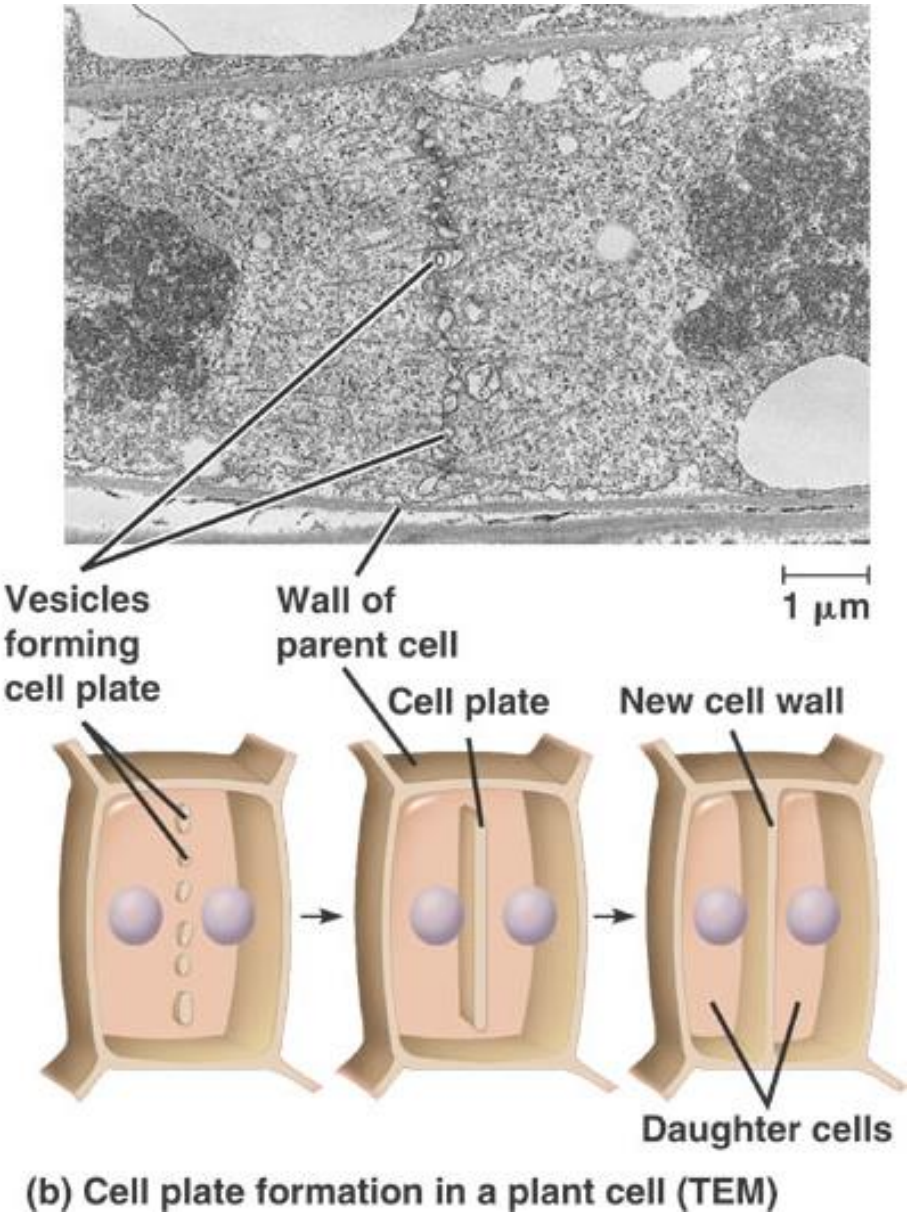
In plants:

- **Vesicles** transported to equator

→ To form **cell plate** at equator

- **Cell wall** laid down

- So cytoplasm divided into two
- Organelles are shared out

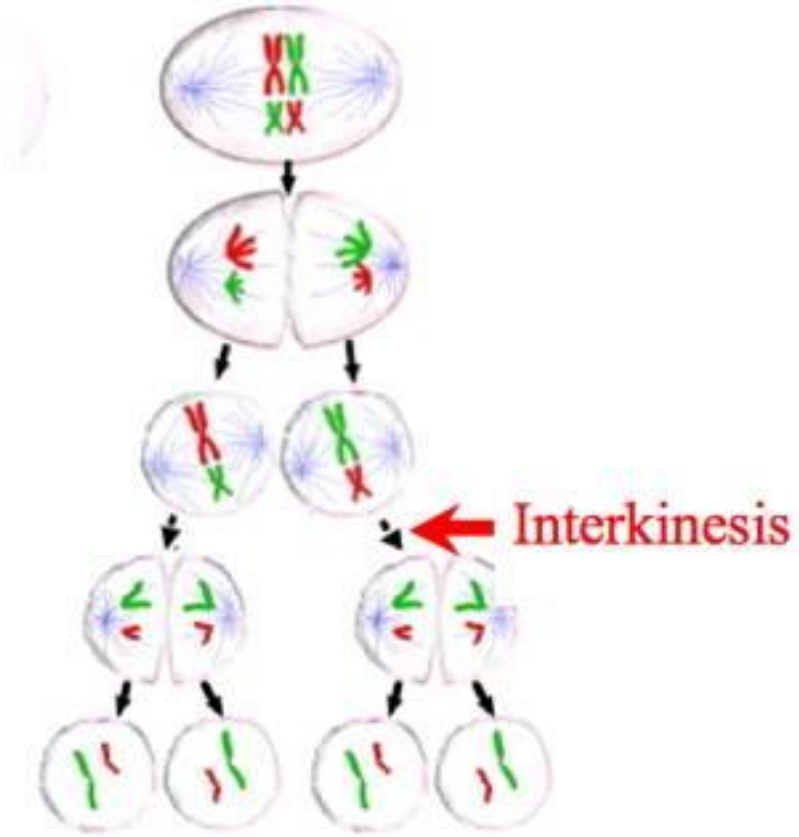


(b) Cell plate formation in a plant cell (TEM)

Brief interphase between Meiosis I and Meiosis II

- Called interphase II / interkinesis
- Growth
- Synthesis of protein & other substances
- **No DNA replication**

- Plant cells go straight into meiosis II
- No reformation of nucleolus and nuclear envelope



Prophase II

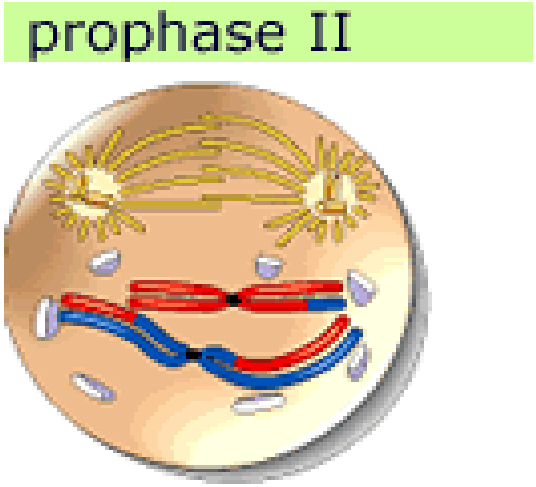
P/S: Meiosis ll is just like mitosis!

- **Condensation** of chromatin

- **Spindle fibres** form

→ Start attaching to centromere

- Centrosomes move to opposite poles
- Nuclear envelope breaks down
- Nucleolus breaks down



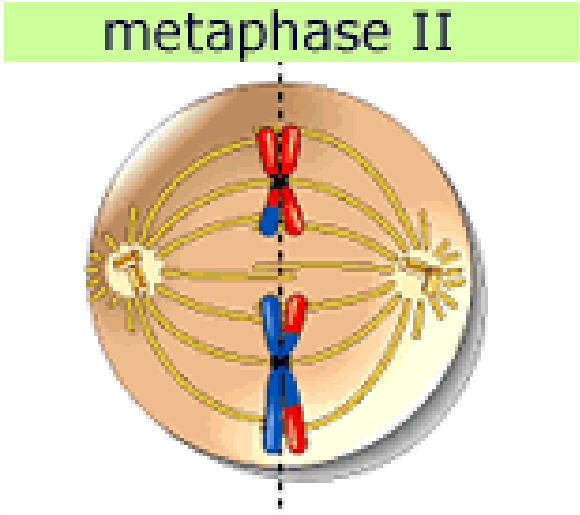
Metaphase II

- Centrosomes reach opposite poles
- Spindle fibres are fully formed

- Chromosomes line up at the **metaphase plate** / equator
- At right angles to first equator

- Chromosomes **attached to spindle fibres at centromere** / kinetochore

- **Independent assortment** of sister chromatids occurs



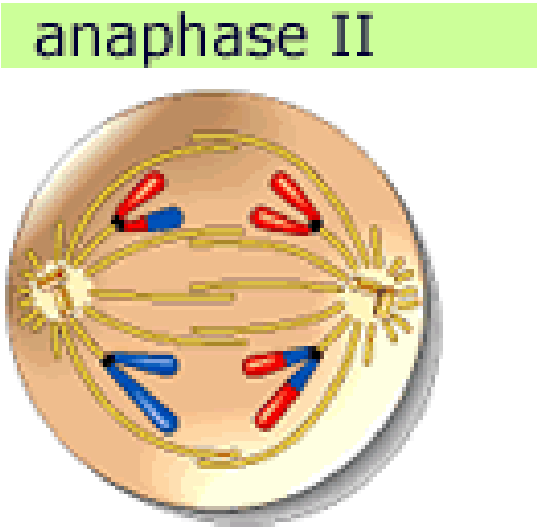
Anaphase II

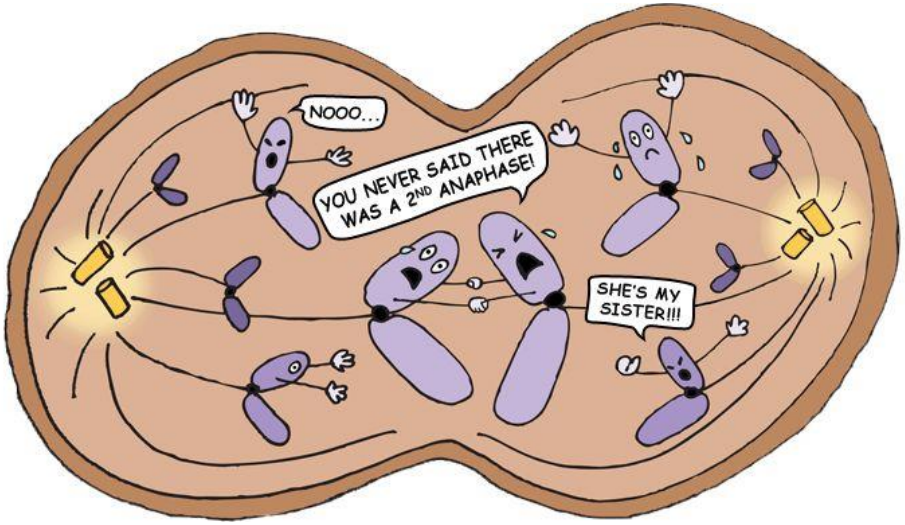
- **Centromere** of each chromosome **divides**
- Sister chromatids split at the centromere

- Spindle microtubules **shorten**

- **Chromatids pulled to opposite poles**

→ with **centromeres leading** towards poles





Telophase II & Cytokinesis

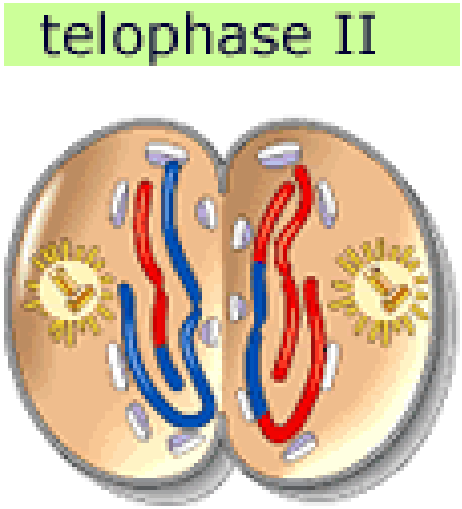
- Chromatids reach the poles
- **Chromosomes decondense**

→ Become long and thin

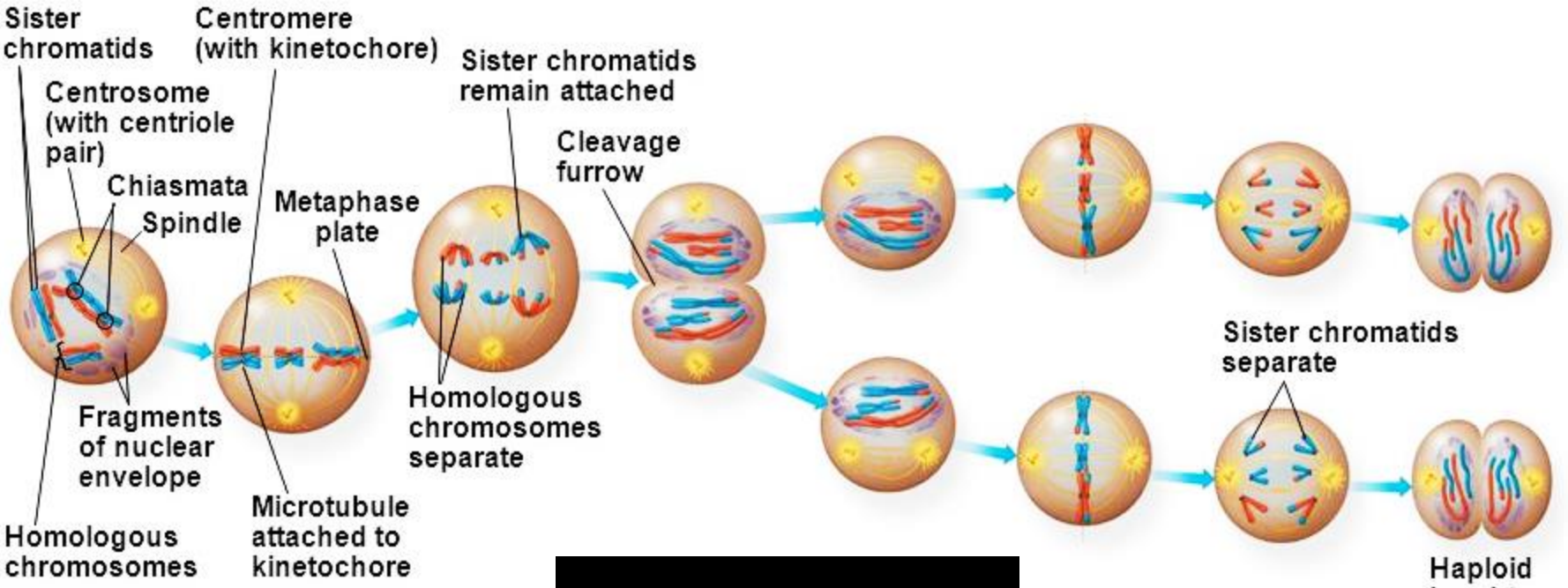
- **Nucleolus** reforms
- **Nuclear envelope** reassembles
- Spindle fibres breaks down

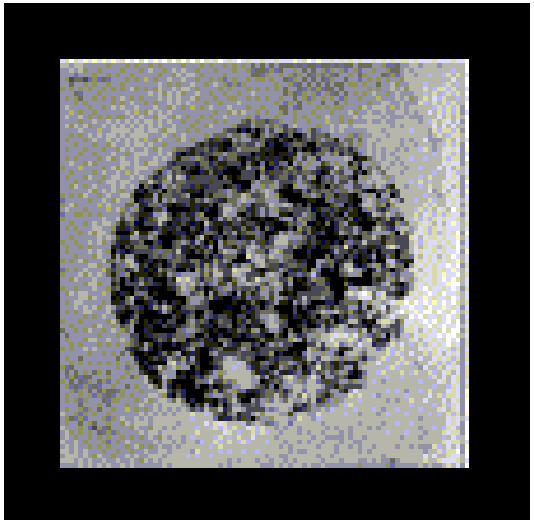
- Cytokinesis occurs

→ **4 haploid cells formed**



MEIOSIS I: Separates homologous chromosomes				MEIOSIS II: Separates sister chromatids			
Prophase I	Metaphase I	Anaphase I	Telophase I and Cytokinesis	Prophase II	Metaphase II	Anaphase II	Telophase II and Cytokinesis

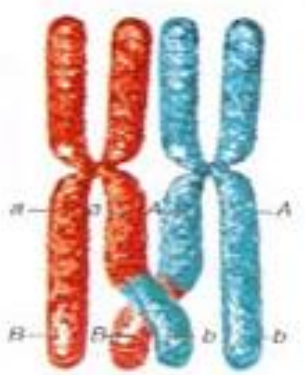




How does meiosis cause genetic variation?

1. <u>Crossing over</u> @ Prophase I

- Between **non-sister chromatids** of homologous chromosomes
- At **chiasma**

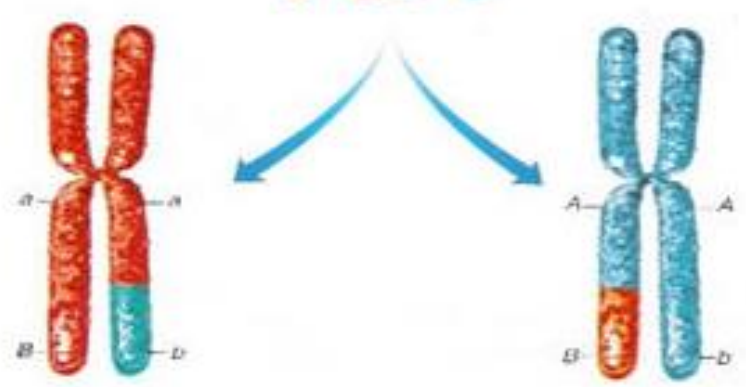


→ **Exchange of genetic material** [NOT genes]

→ **Linkage groups broken** / linked genes on same chromosome are separated

→ **New combination of alleles** within each chromosome

→ Genetic variation

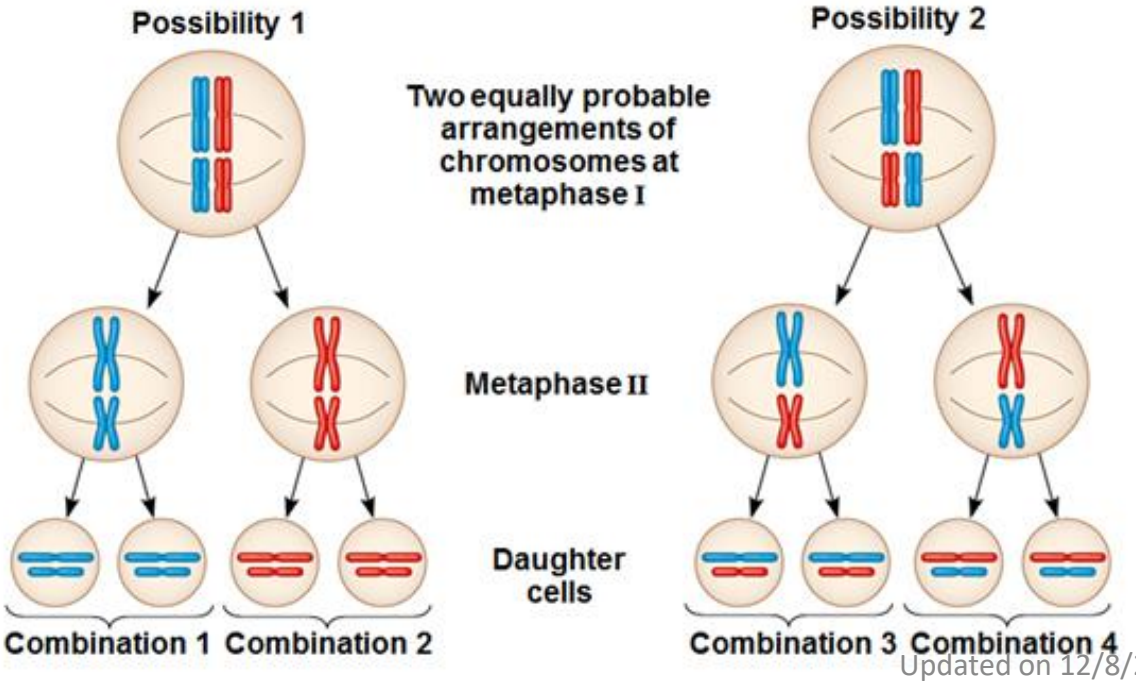


How does meiosis cause genetic variation?

2. Random / <u>Independent Assortment</u> of Homologous Chromosomes @ Metaphase I

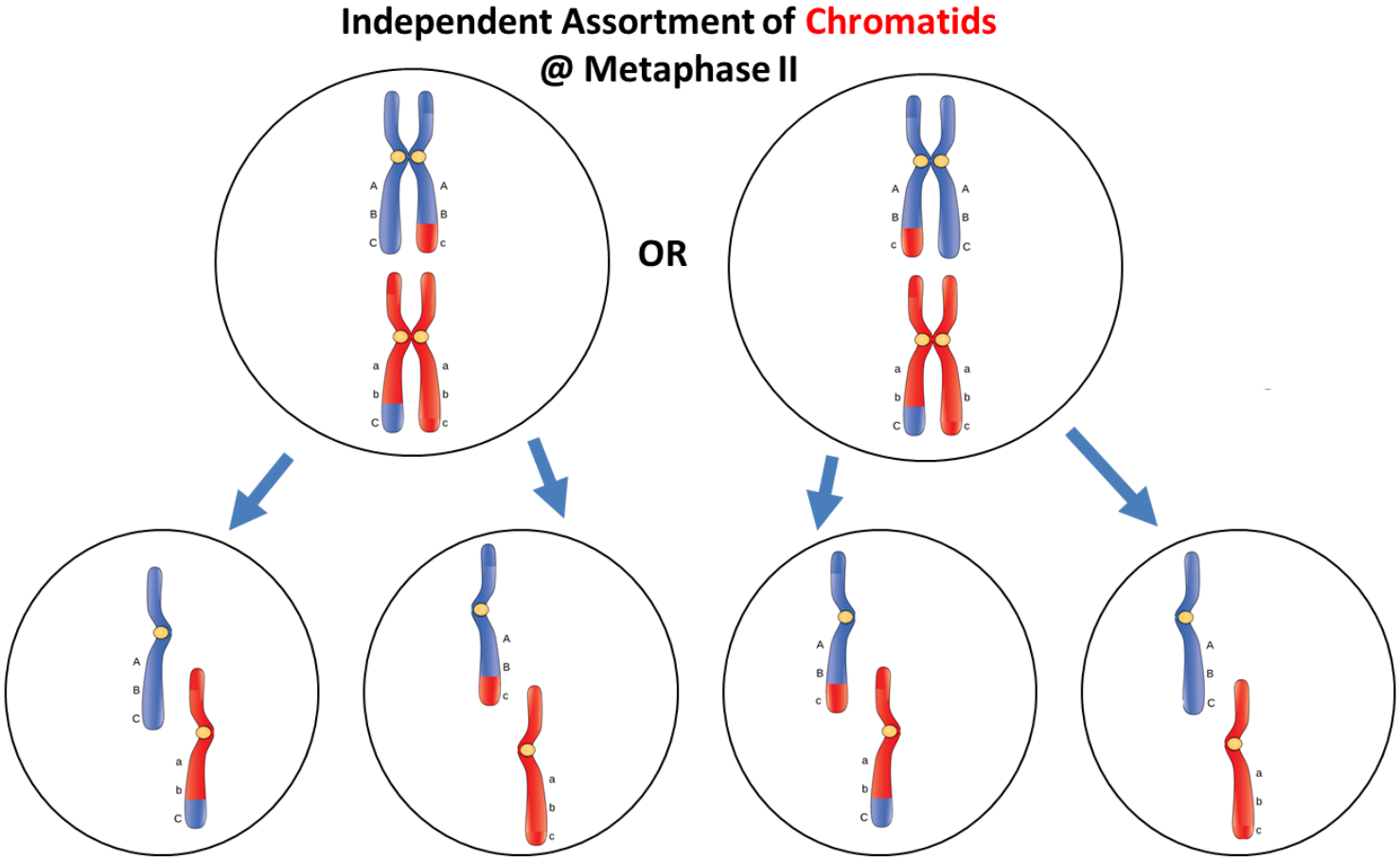
- **Each pair lines up independently of others on equator**
- Possible combinations = 2^n

→ Results in **gametes that are genetically unique**



How does meiosis cause genetic variation?

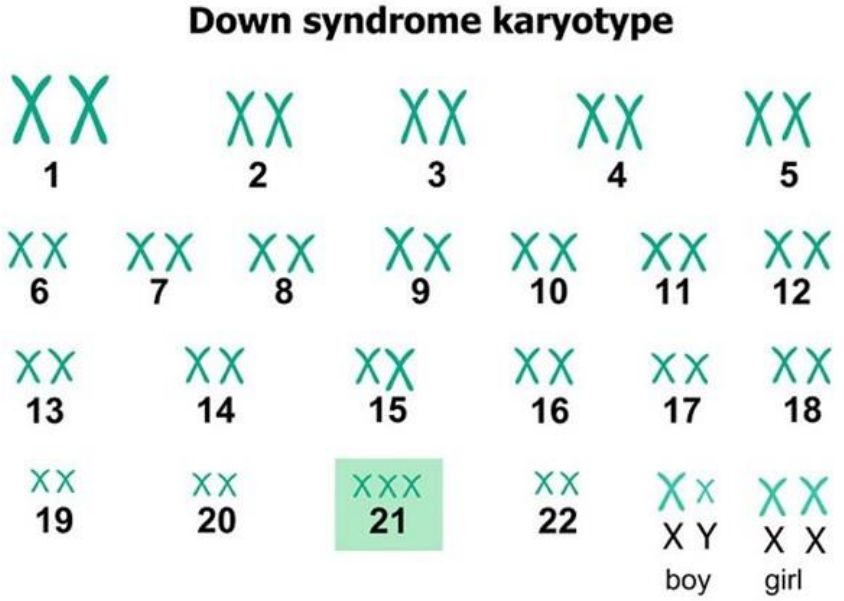
3. Independent assortment of chromatids @ Metaphase II



How does meiosis cause genetic variation?

4. Possible chromosome mutation

• Faulty meiosis may cause changes to chromosome number or structure → New alleles



P/S: Besides meiosis, **fertilisation** can also cause genetic variation! This is due to:

1. Random mating

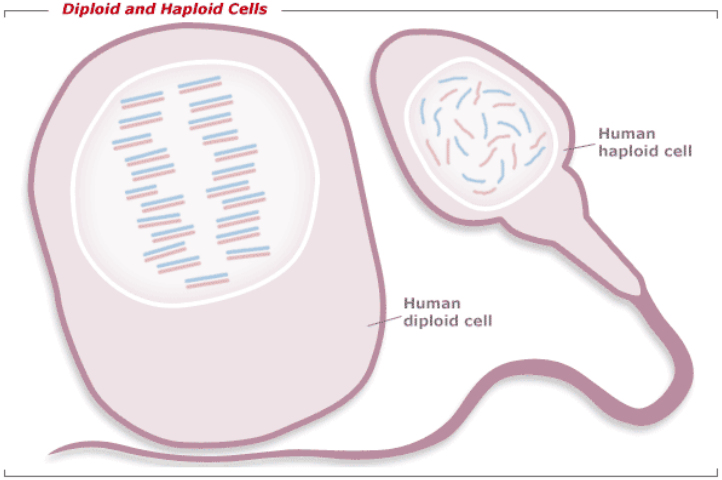
2. Random fusion of gametes

Role of meiosis in gametogenesis in humans

- Somatic cells are **diploid (2n)**
- Gametes are **haploid (n)**

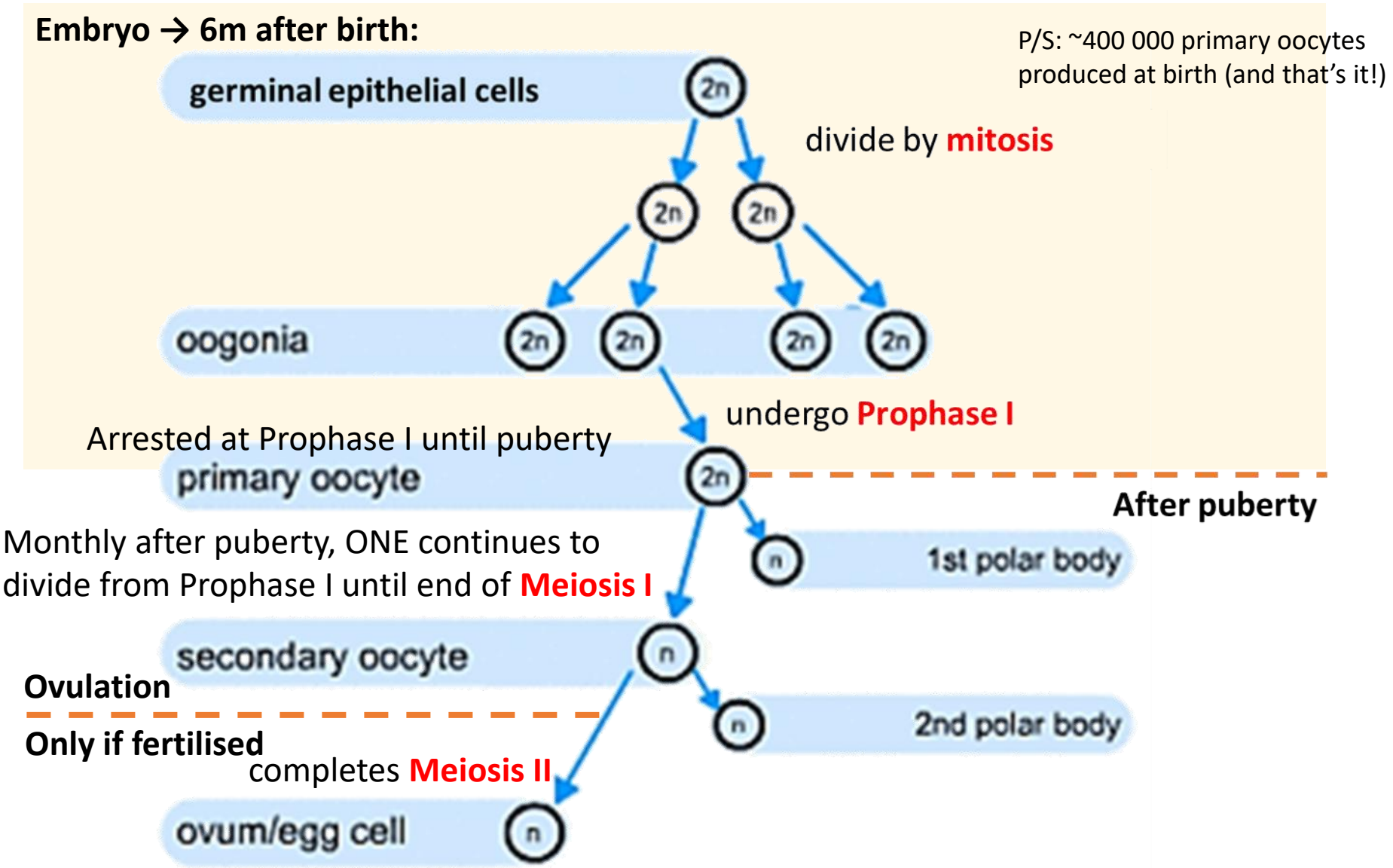
→ Half the number of chromosomes

→ Formed by **meiosis** in testes/ovaries



- **Oogenesis** = production of female gametes
- **Spermatogenesis** = production of male gametes

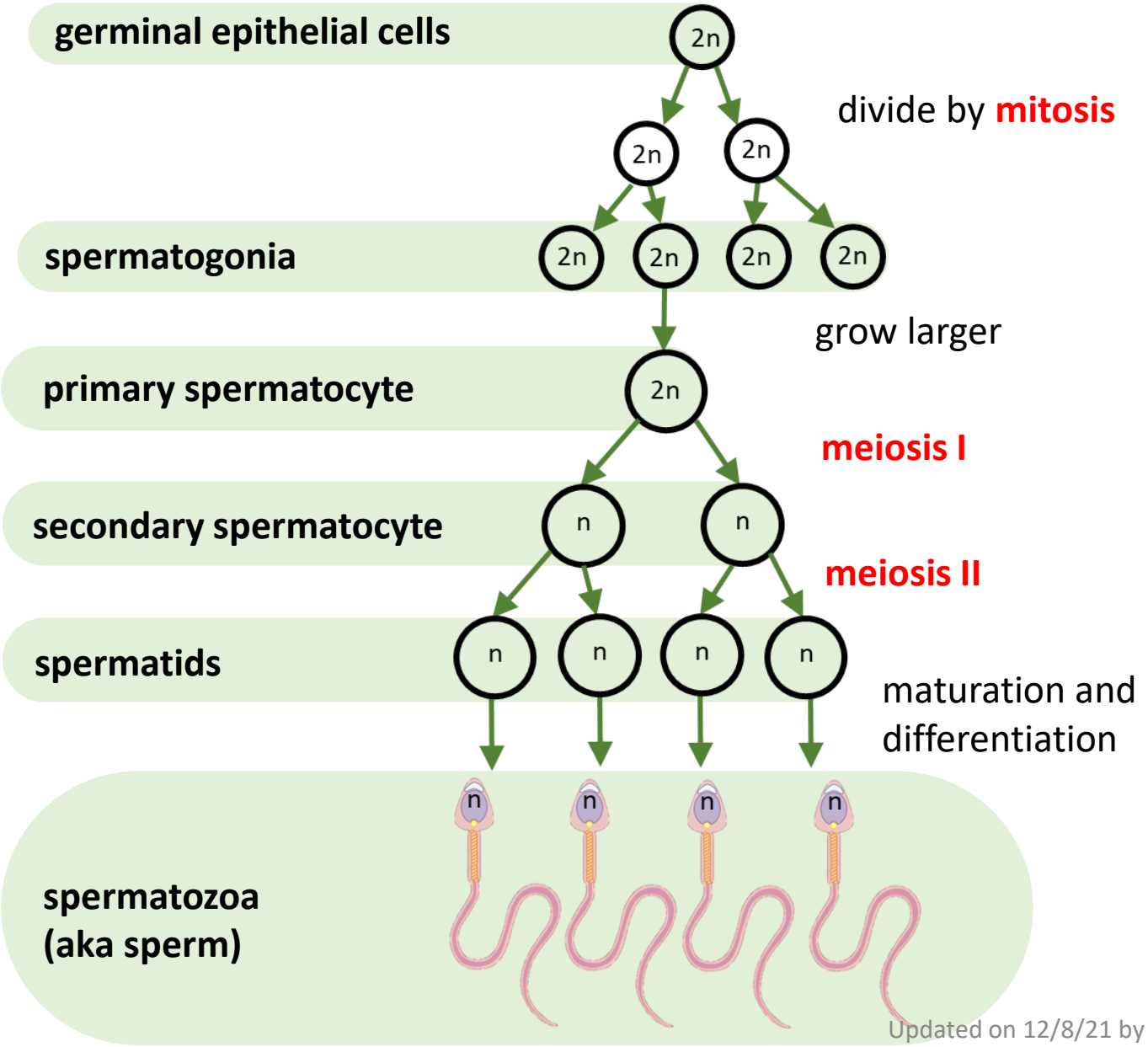
Oogenesis


Embryo → 6m after birth:
P/S: ~400 000 primary oocytes produced at birth (and that's it!)
germinal epithelial cells
2n
divide by mitosis
2n
2n
oogonia
2n
2n
2n
2n
undergo Prophase I
Arrested at Prophase I until puberty
primary oocyte
2n
After puberty
Monthly after puberty, ONE continues to divide from Prophase I until end of Meiosis I
n
1st polar body
secondary oocyte
n
Ovulation
Only if fertilised
n
2nd polar body
completes Meiosis II
ovum/egg cell
n

Spermatogenesis

At puberty (~11-15yo) and throughout lifetime:

100 - 200 mil produced <u>daily</u>



Spermatogenesis vs Oogenesis

Spermatogenesis	Oogenesis
Begins at puberty	Begins before birth
4 spermatids / spermatozoa produced	1 ovum produced
Meiosis is a continuous process / not interrupted	Meiosis is interrupted
Greater number of gametes produced in males	Smaller number of gametes produced
Males can produce gametes to a greater age	Females only till menopause

Role of meiosis in formation of pollen grains and embryo sacs in flowering plants

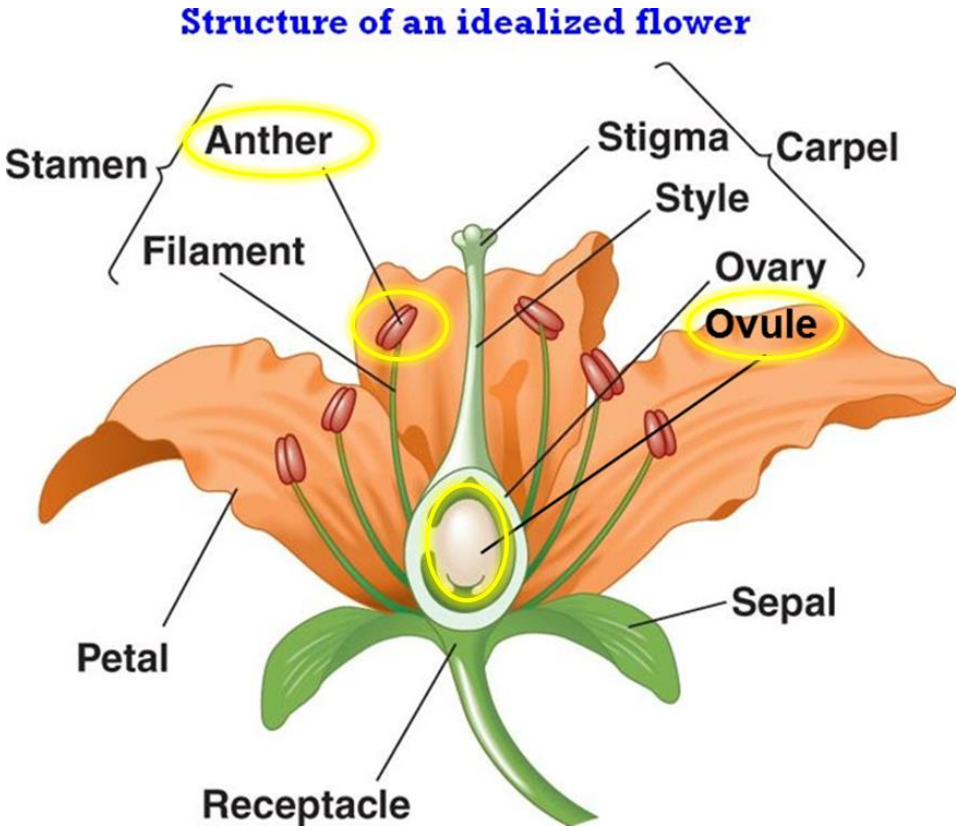
In plants, gametes are formed by meiosis AND mitosis

Inside anthers:

- **Formation of pollen grain**
- Male gamete formed in pollen grain
- From pollen mother cells

Inside ovule:

- **Formation of embryo sac**
- Female gamete formed in embryo sac
- From spore mother cells



Pollen grain formation @ anthers

Pollen mother cell (2n)

→ Divide by **meiosis**

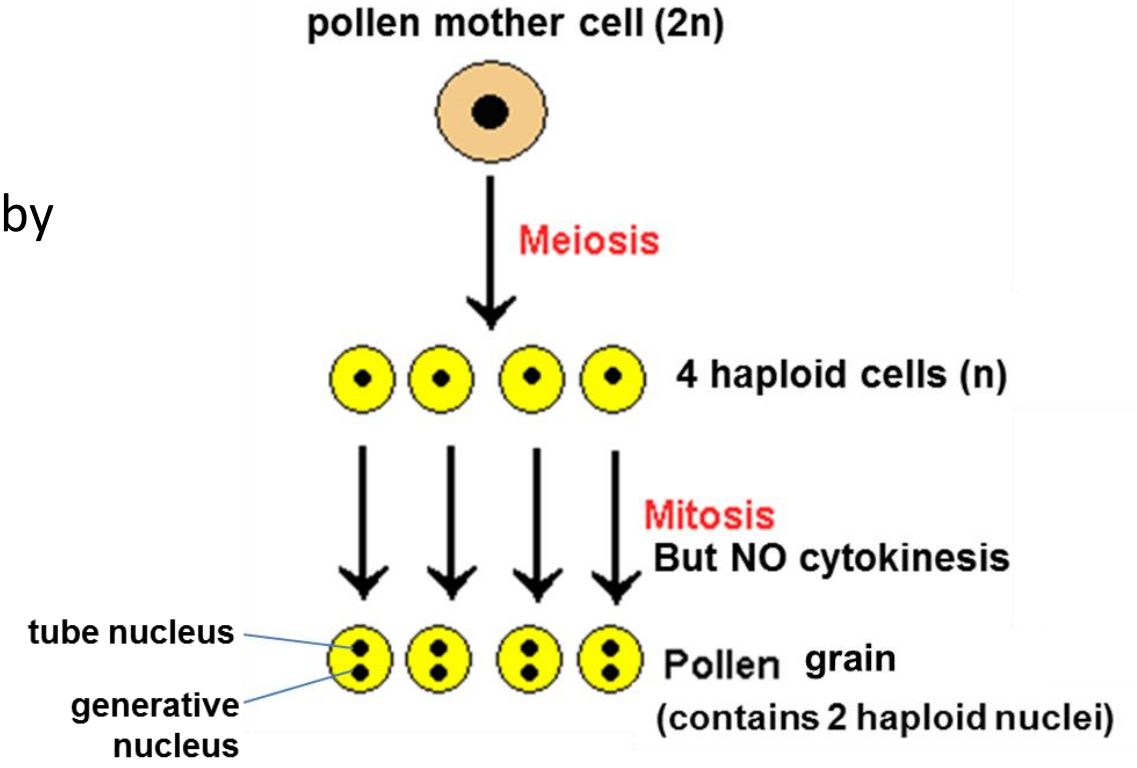
→ Form **4 haploid cells**

→ Nuclei of haploid cell divide by **mitosis**

→ **But cell does not divide / no cytokinesis**

→ Result in **cells that contain 2 haploid nuclei**

→ Mature into **pollen grains** with protective wall



Formation of embryo sacs @ ovules

Spore mother cell (2n)

→ Divide by **meiosis**

→ Form **4 haploid cells**

→ **3 haploid cells degenerate**

→ Nuclei of 1 haploid cell divide by **mitosis 3 TIMES**

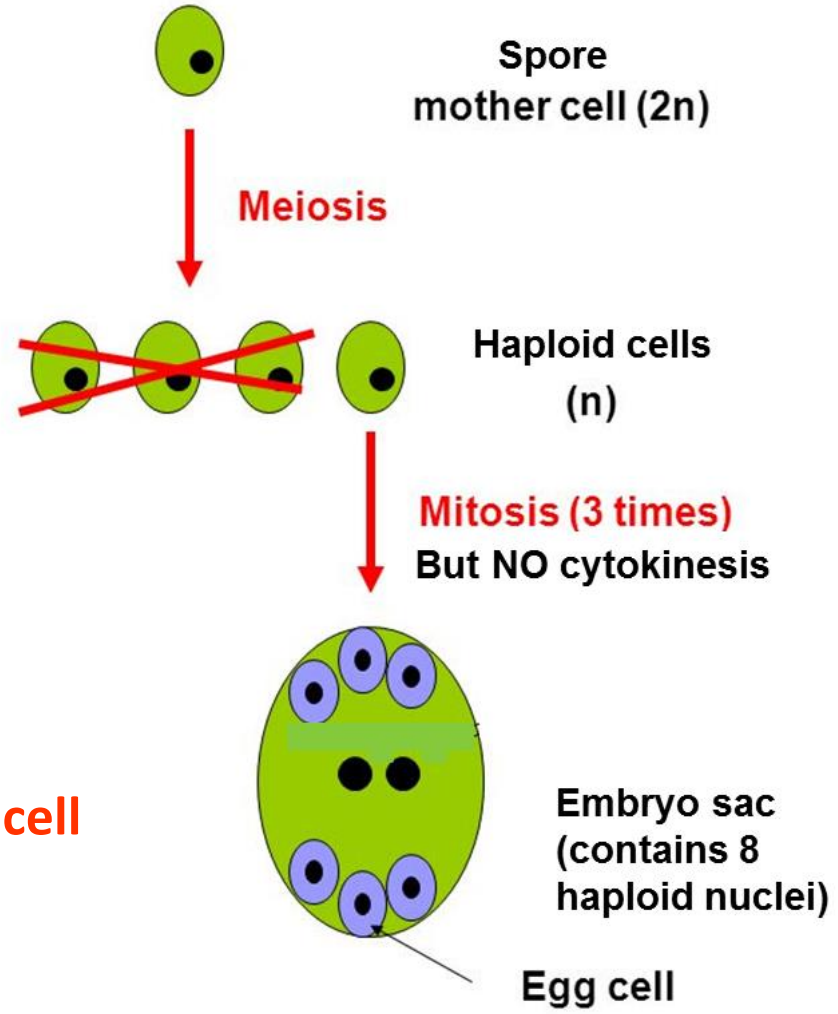
→ **But cell does not divide / no cytokinesis**

→ Cell grows larger

→ Result in a **cell that contain 8 haploid nuclei**

→ 1 of them is the **female gamete/egg cell**

→ Develops into **embryo sac**

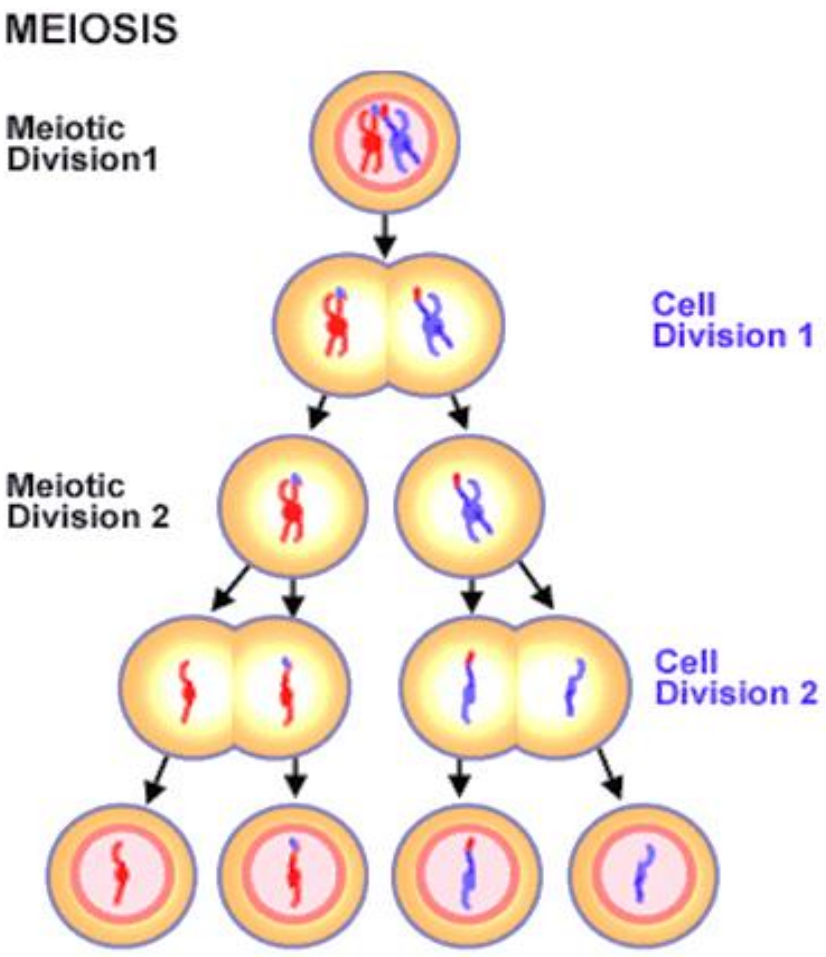


Chapter Outline

Part I: Meiosis

- Meiosis
- Genetic variation due to
  - Crossing over
  - Random assortment of homologous chromosomes
  - Random fusion of gametes

- Role in gametogenesis in humans
- Role in formation of pollen grains and embryo sacs in flowering plants



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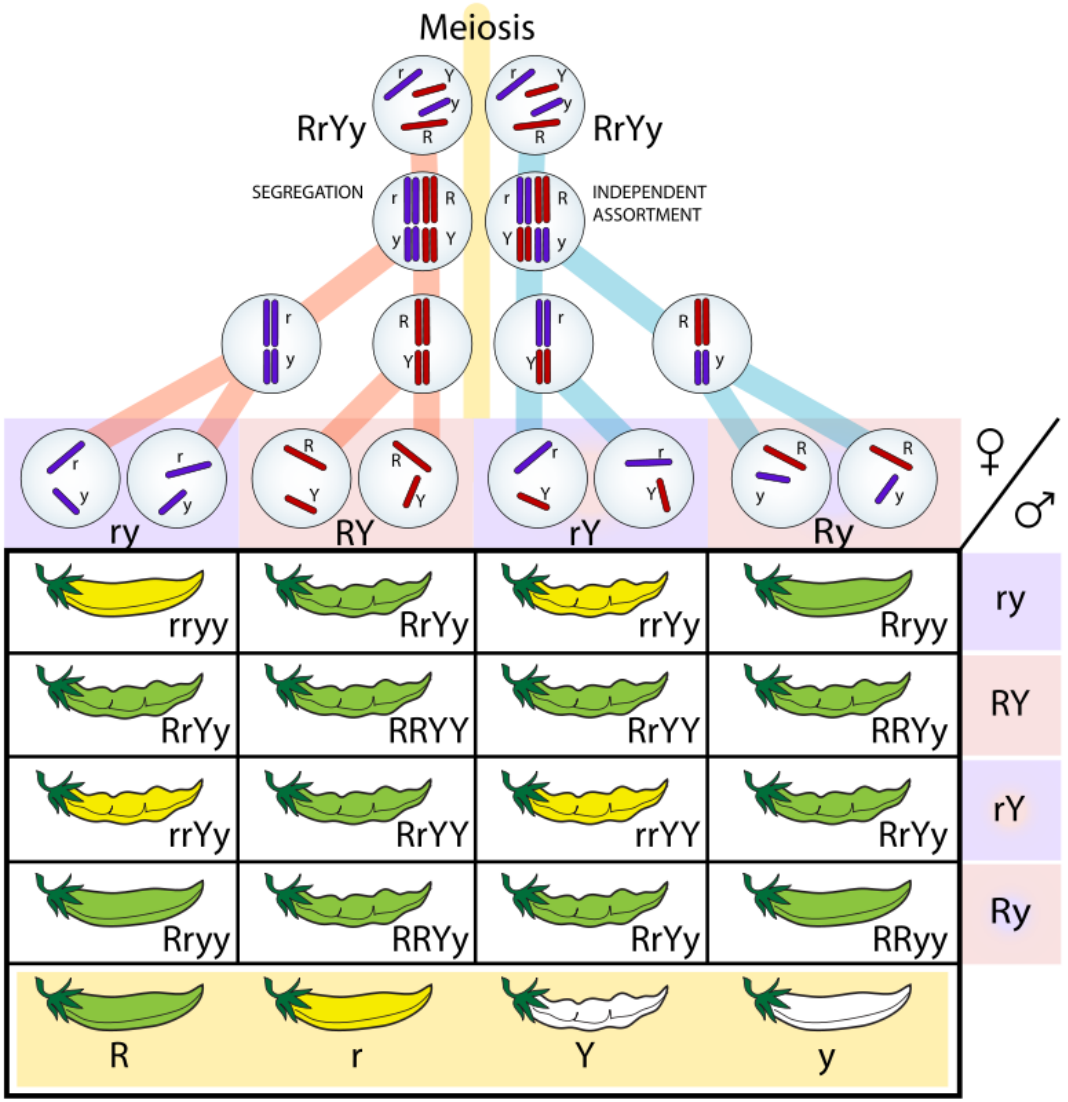
Chapter 16
A2 Level

Inherited Change

Part 2: Mendelian Inheritance

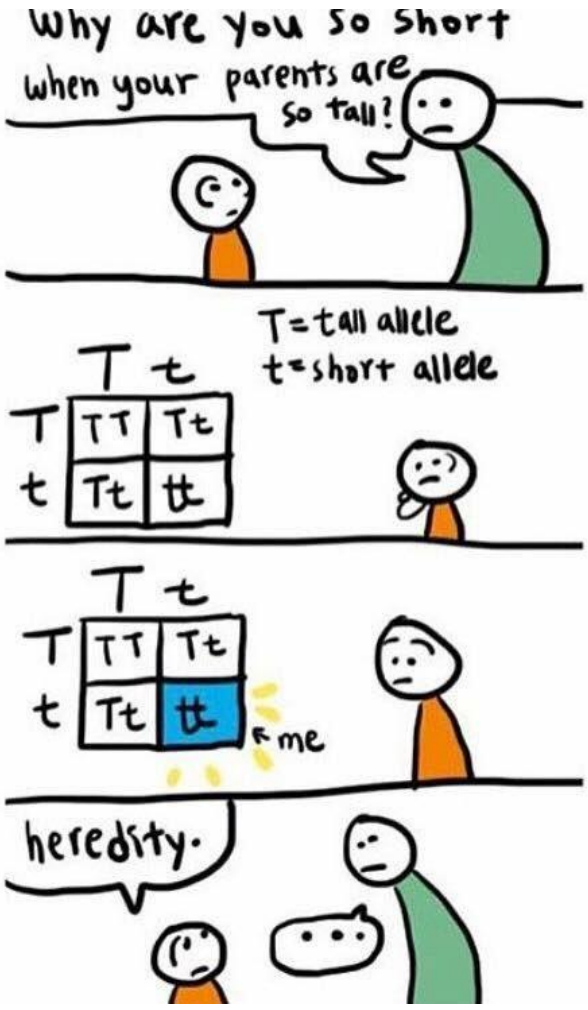


Chapter Outline

Part II: Mendelian Inheritance

- Monohybrid cross
- Dihybrid cross
- Test crosses

- **P5:** Chi-squared test



Important Terms

- **Genotype** = the alleles possessed by an organism
- **Phenotype** = the observable characteristics of an organism

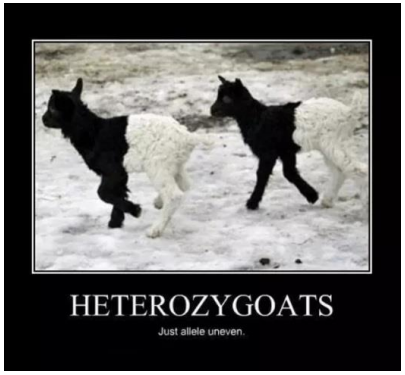
→ Can be influenced by genotype, environment

Genotype

- **Gene = a specific DNA seq that codes for polypeptide**
  - Represented by same alphabet (e.g. **B** and **b** = same gene, different allele)
  - Gene short form name is usually in italics, whereas gene full name and protein is not italicized (e.g. *HBB* = haemoglobin beta gene → codes for beta globin protein)

- **Allele = a form of gene** → result of mutation
  - Dominant allele represented by capital letter and always placed in front (e.g. **B**)
  - Recessive allele represented by small letter and always placed behind (e.g. **b**)

Important Terms



Diploid cells: 2 sets of chromosomes, so 2 alleles

- **Homozygous** = Have two identical alleles of a gene
  - Can be **homozygous dominant** *(e.g. **BB**)* OR **homozygous recessive** *(e.g. **bb**)*
- **Heterozygous** = Have two different alleles of a gene *(e.g. **Bb**, NEVER bB)*

Dominant allele

- Expressed in the phenotype even when **only one copy** of the allele is present
- Expressed in heterozygotes and homozygote for the allele *(e.g. **Bb** and **BB**)*

Recessive allele

- Expressed in the phenotype only when **two copies** of the allele are present
- Expressed only in a homozygote for the allele *(e.g. **bb**)*

Important Terms

E.g. Let B = allele for brown hair; b = allele for blonde hair

Genotype	**Phenotype**
BB (homozygous dominant)	Brown hair
Bb (heterozygous)	Brown hair
bb (homozygous recessive)	Blond hair

P/S: Sometimes, symbols could be written this way too….

Hb = haemoglobin gene
Hb^A = normal allele
Hb^S = sickle allele

X = gene on X chromosome
X^+ = normal allele
X^- = recessive allele

I = *ABO* gene for blood group
I^A = A alelle
I^B = B alelle
i = O allele

vg = *vestigial* gene in flies
vg^+ = wild-type allele (normal, long wings)
vg = mutant vestigial wings allele

Mendelian Genetics

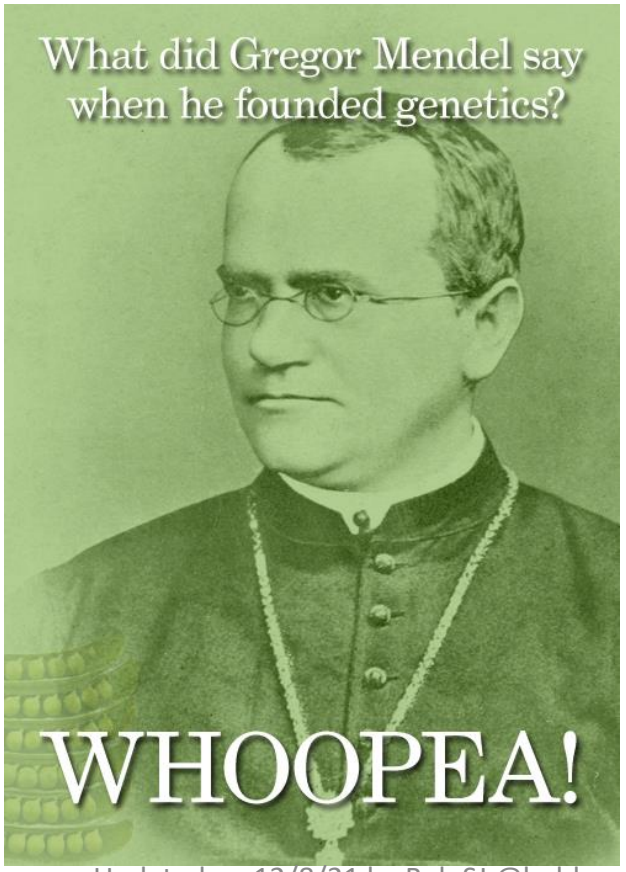
- Gregor Mendel = father of modern genetics
- Didn't even know about chromosomes and genes yet!

- Planted over 28,000 plants in 8 years (1856-1863) …mostly peas
- Studied inheritance in pea plants by observing contrasting traits in pea plants

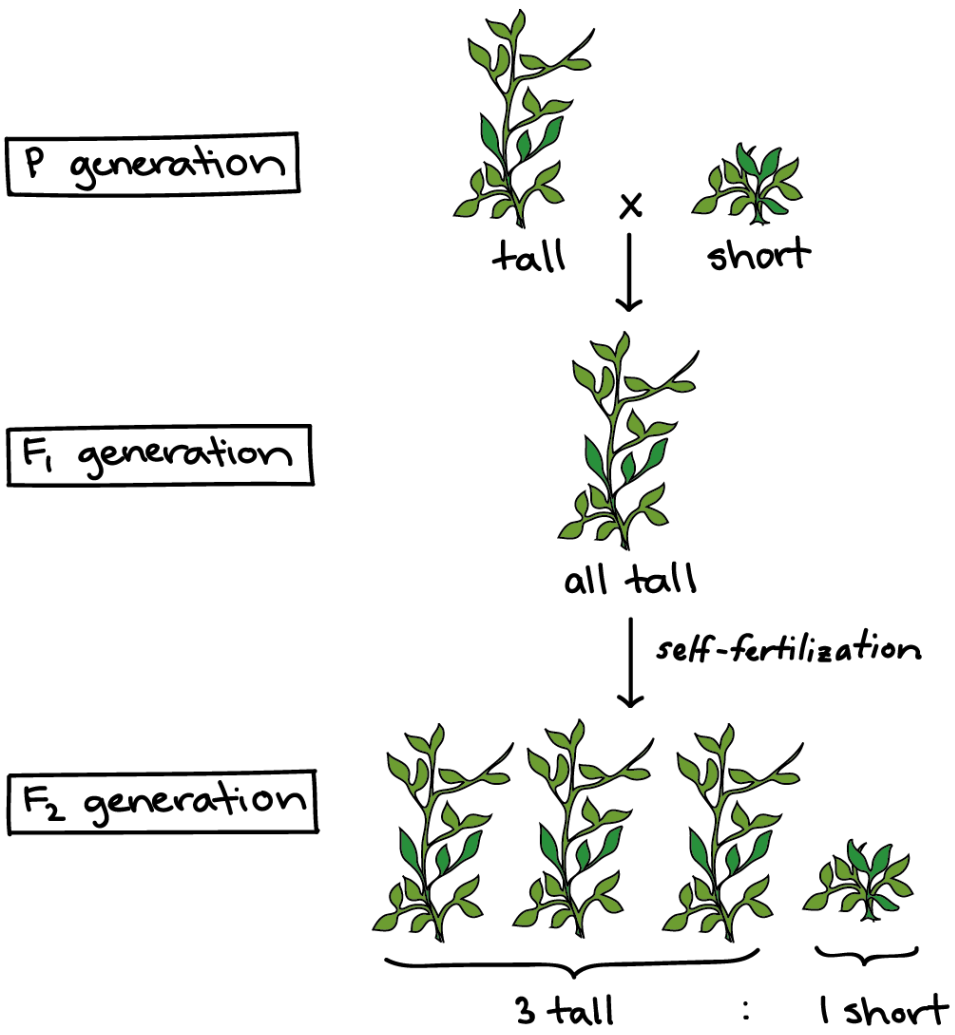
→ E.g. yellow/green pea pods; round/crinkled seeds; tall/short plants etc.

- Two main experiments:

1) **Monohybrid cross**
2) **Dihybrid cross**



Monohybrid inheritance



- Trait is controlled by **1 gene**
- Mendel crossed a **purebred** tall pea plant and a **purebred** short pea plant. Both are homozygous.
- This is the **parental (P) generation**
- All resulting offspring in the **F1 generation** is tall
- Crossed offspring in **F1** with each other (self-fertilisation)
- In the resulting **F2**, he obtained 787 tall and 277 short pea plants
- Approx. a ratio of 3:1

We can represent genetic crosses using a genetic diagram...

Every genetic diagram must have:

Let T = allele for tall plant; t = allele for short plant

Don't forget the x

1. **PARENTAL PHENOTYPES**
2. **PARENTAL GENOTYPES**

Tall TT x Short tt

3. **GAMETES**

T T t t

4. **OFFSPRING (F1) GENOTYPE AND PHENOTYPE**

GAMETES	t
T	Tt tall

You must circle gametes

You MUST draw a Punnett Square

5. **PROBABILITY/RATIO**
Depends on what the question wants

All plants are tall.

Probability of getting a tall plant = 1

F1 PHENOTYPES

F1 GENOTYPES

Tall Tt x Tall Tt

GAMETES

F2 GENOTYPES AND PHENOTYPE

GAMETES	T	t
T	TT tall	Tt tall
t	Tt tall	tt short

PROBABILITY/RATIO

Ratio of tall:short plants is 3:1

Probability of getting a tall plant= ¾

Probability of getting a short plant = ¼

He also found the approx. the same ratio in all 7 traits he studied!
Why isn't it exactly 3:1 for everything?

Pea trait	Dominant trait		Recessive trait		Numbers in second generation (F2)	Ratio
Seeds						
Seed shape	Round		Wrinkled		5474:1850	2.96:1
Seed colour	Yellow		Green		6002:2001	2.99:1
Whole plants						
Flower colour	Purple		White		705:224	3.15:1
Flower position	Axial		Terminal		651:207	3.14:1
Plant height	Tall		Short		787:277	2.84:1
Pod shape	Inflated		Constricted		882:299	2.95:1
Pod colour	Green		Yellow		428:152	2.82:1

You found a tall pea plant. How to determine if its genotype is **TT** or **Tt**?

Test Cross!

- Test cross = method to determine exact genotype of a dominant phenotype organism

→ Is it homozygous dominant or heterozygous for the gene?

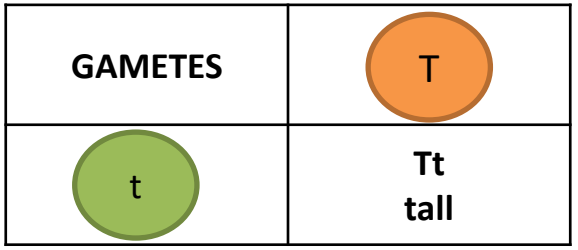
→ **Cross with individual homozygous recessive for the gene**

→ Aka a short plant (tt)

If the tall plant is **TT** :

- TT x tt

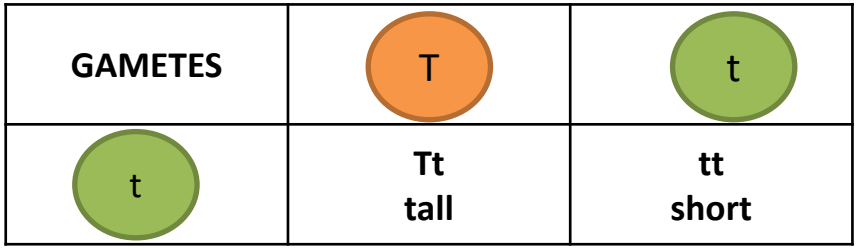
→ All offspring will be tall (Tt)



If tall plant is **Tt**:

- Tt x tt

→ Offspring can be either tall (Tt) or short (tt)



Example Question

In dalmatian dogs, the spots' colour is determined by a gene which has two alleles. Black spot allele is dominant while brown spot allele is recessive.

A breeder wanted to know the exact genotype of her black spot dog. She crossed her with another brown spot dog & the puppies produced, all showed black spots. The breeder did this for multiple times and the same results were produced.

What is the dog's genotype?

Explain your answer by drawing genetic diagrams.

Important Terms

- **Purebred** = A cross of same purebred organisms always produce offspring with same genotype. ***Homozygous*** individuals.

- **Parental (P) generation** = initial generation

- **F1 generation** = stands for first filial generation / first set of offspring. Result of crossing 2 different purebreds (i.e. 2 homozygotes of different phenotype.). ***F1 offspring are all heterozygotes.***

- **F2 generation** = offspring result of self-pollination of F1 plants OR ***cross of 2 heterozygotes.***

- **Test cross** = method to determine exact genotype of a dominant phenotype organism. **Cross with individual homozygous recessive for the gene(s).**

Dihybrid Inheritance

- Involves the crosses of **two genes** at once

→ 2 genes are on **different chromosomes**

→ 2 alleles each

→ Code for **different traits**

E.g. Gene for tall/short plants & gene for purple/white flowers

Flower colour	Purple		White	
Plant height	Tall		Short	

Let T= allele for tall; t = allele for short;
P = allele for purple flower; p = allele for white flowers;

PARENTAL PHENOTYPES Tall, purple flowers x Short, white flowers

PARENTAL GENOTYPES TTPP ttpp *(Diploid)*

Meiosis

GAMETES TP tp *(Haploid)*

F1 GENOTYPES AND PHENOTYPES

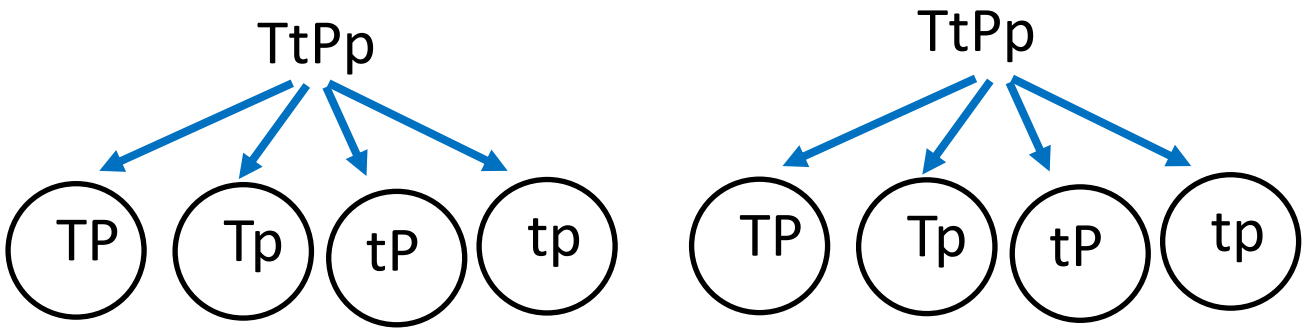
GAMETES	**tp**
TP	**TtPp** tall, purple flowers

PROBABILITY/RATIO **All plants are tall and have purple flowers.**
Probability of tall and purple = 1

Let T= allele for tall; t = allele for short;
P = allele for purple flower; p = allele for white flowers;

F1 PHENOTYPES Tall, purple flowers x Tall, purple flowers

F1 GENOTYPES



GAMETES

F2 GENOTYPES AND PHENOTYPES

GAMETES	TP	Tp	tP	tp
TP				
Tp				
tP				
tp				

Arrange with dominant gametes first to make your life easier

F2 GENOTYPES AND PHENOTYPES

Note: 9:3:3:1 ratio is only produced when **2 heterozygotes for 2 genes are crossed.** AND triangle trick only works if you arranged gametes properly

GAMETES	TP	Tp	tP	tp
TP	**TTPP** Tall, purple flowers	**TTPp** Tall, purple flowers	**TtPP** Tall, purple flowers	**TtPp** Tall, purple flowers
Tp	**TTPp** Tall, purple flowers	**TTpp** Tall, white flowers	**TtPp** Tall, purple flowers	**Ttpp** Tall, white flowers
tP	**TtPP** Tall, purple flowers	**TtPp** Tall, purple flowers	**ttPP** Short, purple flowers	**ttPp** Short, purple flowers
tp	**TtPp** Tall, purple flowers	**Ttpp** Tall, white flowers	**ttPp** Short, purple flowers	**ttpp** Short, white flowers

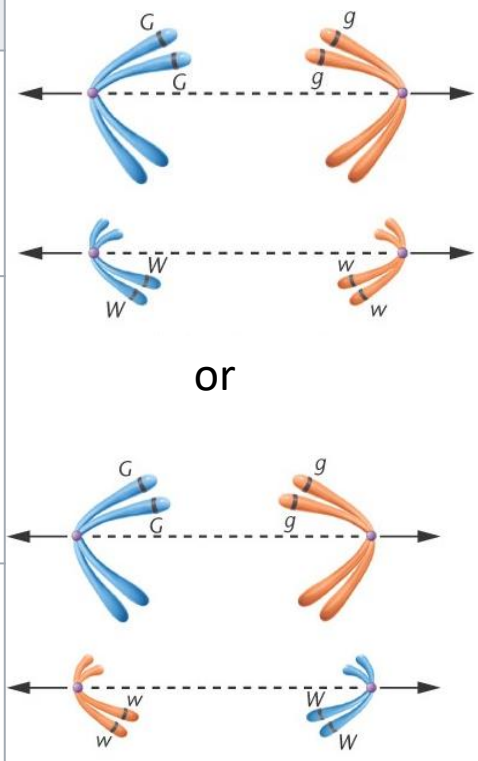
PROBABILITY

Tall, purple flowers: 9/16
Short, purple flowers: 3/16
Tall, white flowers: 3/16
Short, white flowers: 1/16

Mendelian Genetics

- His experiments proved 3 laws in his paper published in 1866

Law	Definition
Law of segregation	During gamete formation, the alleles for each gene segregate from each other (during **anaphase I**) so that **each gamete carries only one allele for each gene**.
Law of independent assortment	**Each pair lines up independently of others on equator** (during **metaphase I**). Genes for different traits can segregate independently during the formation of gametes.
Law of dominance	**Some alleles are dominant while others are recessive**; an organism with at least one dominant allele will display the effect of the dominant allele.

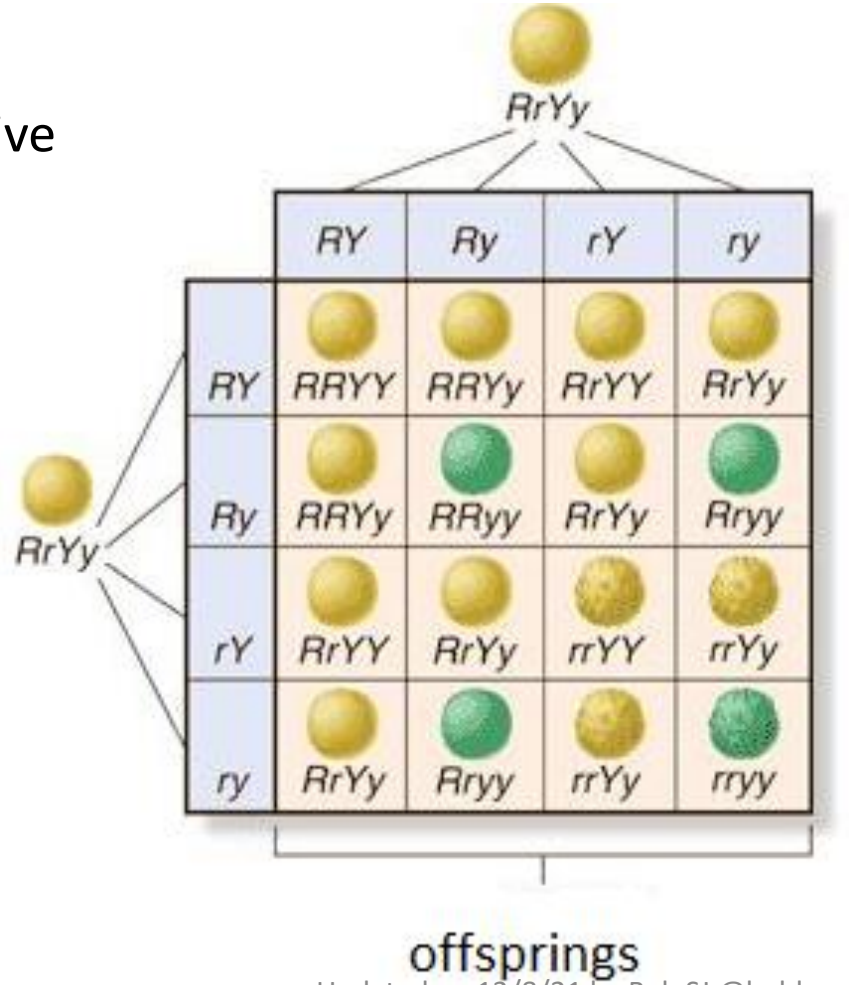


Example Question

- In a pea plant, the inheritance of its pea shape and colour is controlled by two genes.

- Dominant shape is **round** (R), while recessive is **crinkled** (r).
- Dominant colour is **yellow** (Y), while recessive is **green** (y).

- What are the genotypes of the offspring when two heterozygous parents for both traits cross?



Example Question

- What is the probability of getting an offspring with round shape and yellow colour when a plant with heterozygous for both traits and a plant which is homozygous recessive for both traits cross?

- Draw a genetic diagram to show the outcomes with its probability.

You found a tall, purple flower pea plant. How to determine its genotype?

Test Cross!

- **Test cross** = method to determine exact genotype of a dominant phenotype organism

→ **Cross with individual homozygous recessive for both genes**

→ E.g. short, white plant (ttpp)

→ Different ratios of diff phenotypes in offspring will reveal the genotype

- Possible genotypes for tall, purple flower plant = TTPP, TtPp, TTPp, TtPP

If its genotype is TTPP…

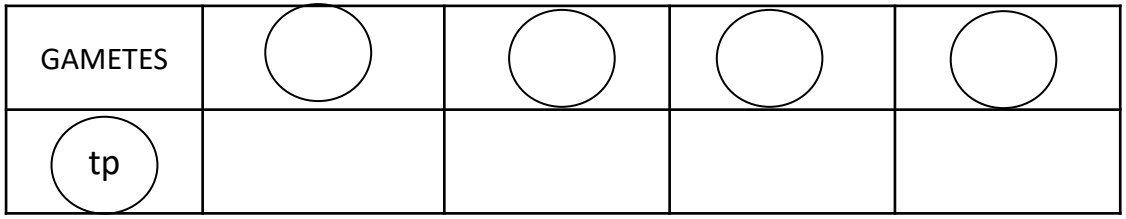
- TTPP x ttpp
- All offspring will be tall, have purple flowers

GAMETES	TP
tp	TtPp Tall, purple

Test Cross!

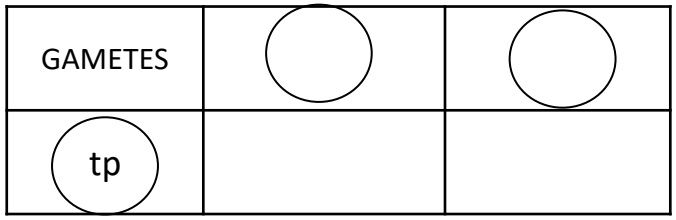
If its genotype is TtPp…

- TtPp x ttpp
- Ratio = 1:1:1:1



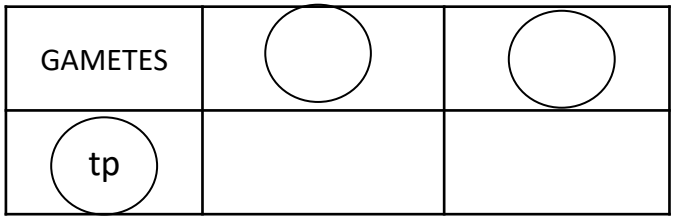
If its genotype is TTPp…

- TTPp x ttpp
- All offspring will be tall
- 50% white, 50% purple



If its genotype is TtPP…

- TtPP x ttpp
- All offspring will have purple flowers
- 50% tall, 50% short



What if 3 genes are involved?

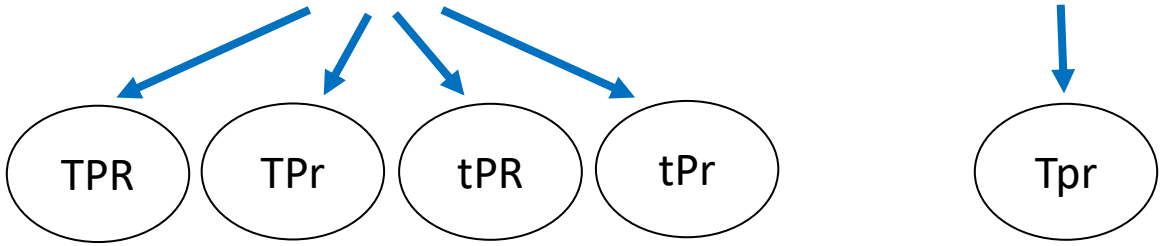
Using the same method and understanding, we should be able to predict the genetic outcome of this cross below:

Let T= allele for tall; t = allele for short;
P = allele for purple flower; p = allele for white flowers;
R = allele for round pea; r = allele for crinkled pea

PARENTAL PHENOTYPES Tall, purple, round x Tall, white, crinkled

PARENTAL GENOTYPES TtPPRr x TTpprr

GAMETES



OFFSPRING GENOTYPES AND PHENOTYPE

GAMETES	TPR	TPr	tPR	tPr
Tpr	TTPpRr Tall, purple, round	TTPprr Tall, purple, crinkled	TtPpRr Tall, purple, round	TtPprr Tall, purple, crinkled

RATIO

All are tall and have purple flowers

50% round, 50% crinkled

1 : 1

P5: Chi-Squared Test (χ^2 Test)

4 Statistical Tests to Learn!

1) t-test

2) Chi-squared

} To test for significance of difference

3) Pearson's linear correlation

4) Spearman's rank correlation

} To test for correlation

Introduction to Statistics in Biology

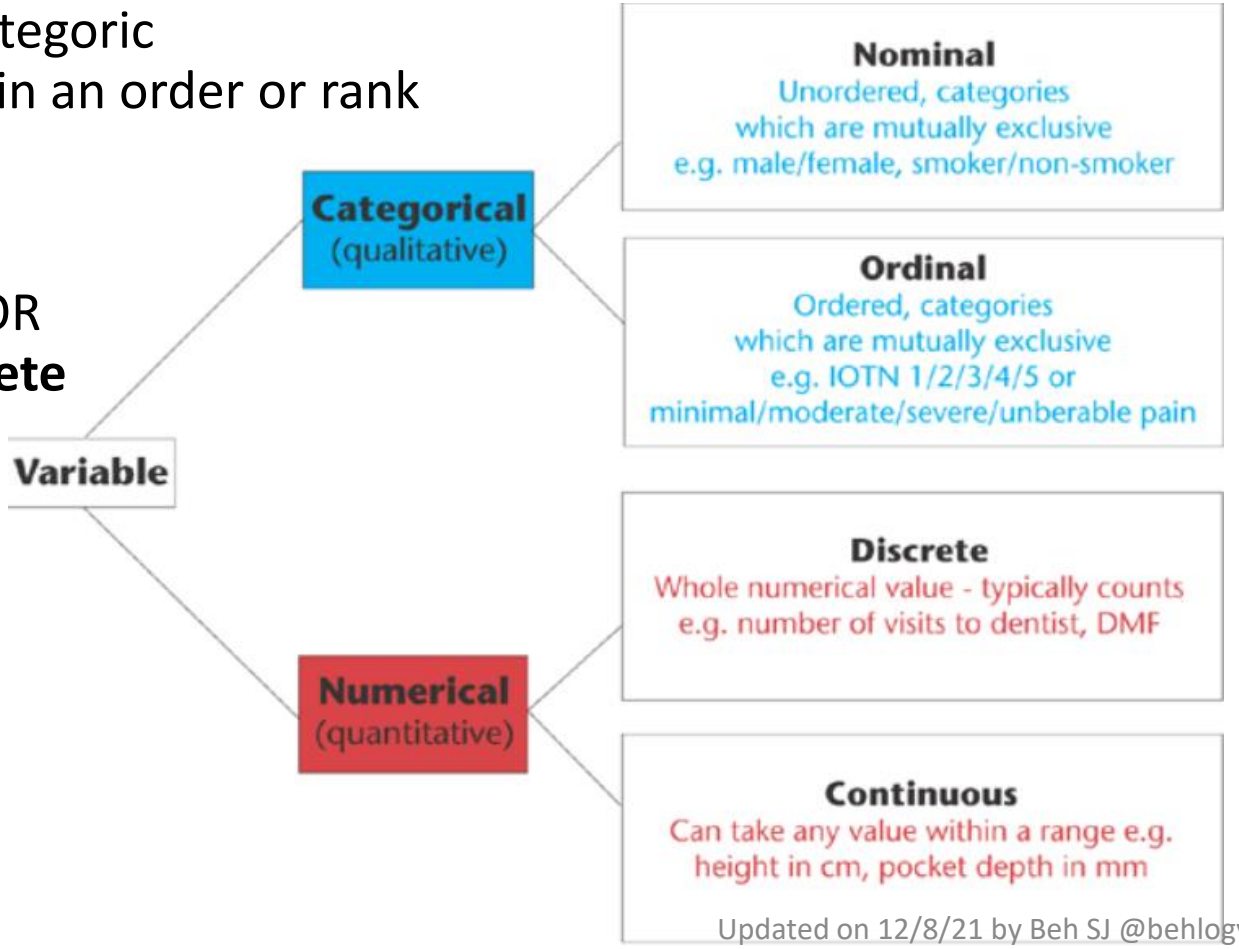
Types of data:

1) Qualitative data

- Can be **nominal** = categoric
  OR **ordinal** = placed in an order or rank

2) Quantitative data:

- Can be **continuous** OR **discontinuous/discrete**

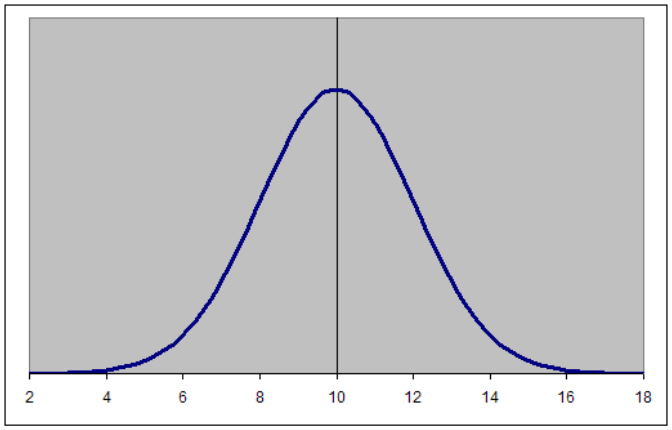


Introduction to Statistics in Biology

Types of distributions:

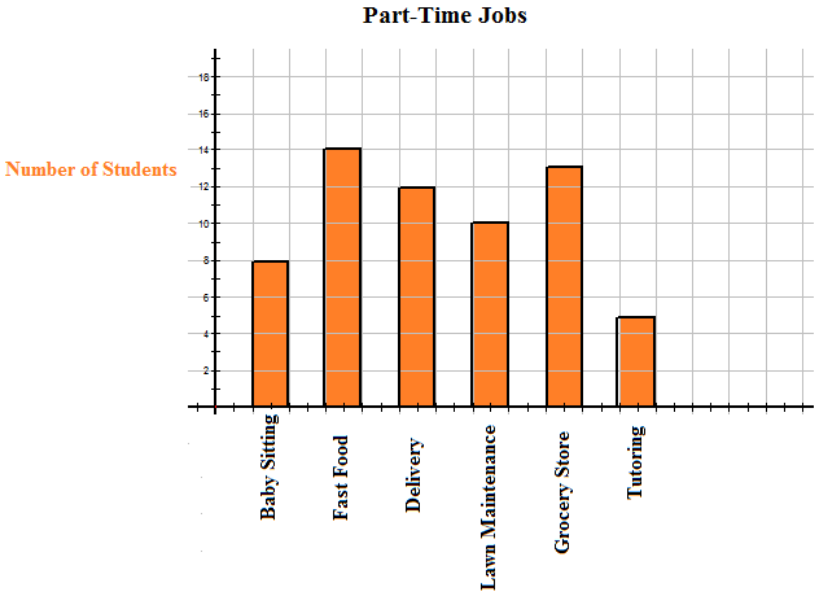
1) Normal distribution

- Continuous data
- Bell-shaped curve
- E.g. mass, height



2) Discontinuous distribution

- Not normally distributed
- E.g. categories, discrete data



Type of data/distribution will influence what stats test can be used

Null Hypothesis

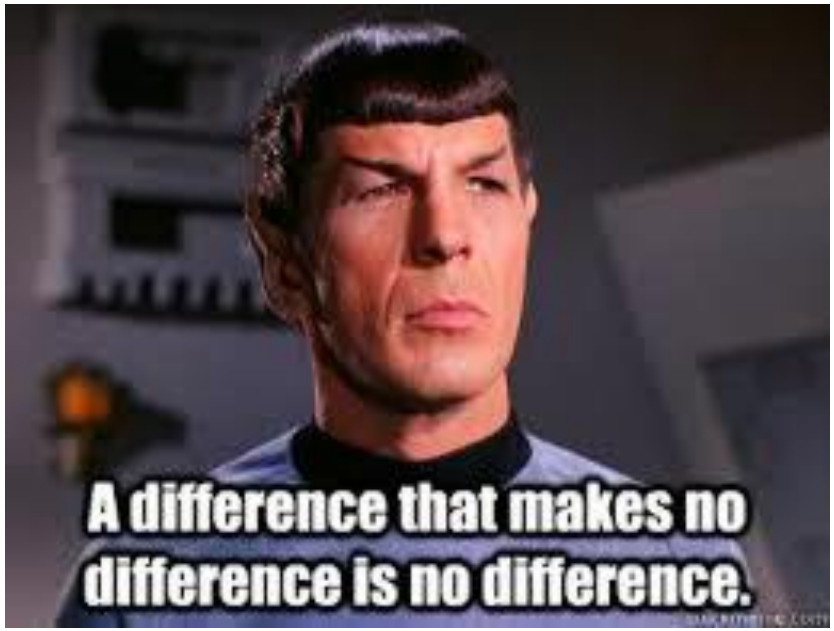
- Statement to assume
- **No significant difference**
- Between two sets of results/data

- Differences present:-

→ **Not significant**

→ Due to random error or chance

→ Can be ignored



E.g. There is no significant difference… <u>between data set A and data set B.</u>

https://www.youtube.com/watch?v=i60wwZDA1CI

Chi-squared Test, χ^2

- To show if the **observed results** are **significantly different** from the **expected results**

Only can be used if:

- **Discrete data / nominal data**
- **Discontinuous distribution**

To test the results of:

a) Breeding experiments

b) Ecological sampling

$$\chi^2 = \sum \frac{(O - E)^2}{E}$$

χ^2 = the test statistic $\sum$ = the sum of

O = Observed E = Expected

Chi-squared Test, χ^2

$$\chi^2 = \sum \frac{(O - E)^2}{E}$$

χ^2 = the test statistic $\sum$ = the sum of

O = Observed E = Expected

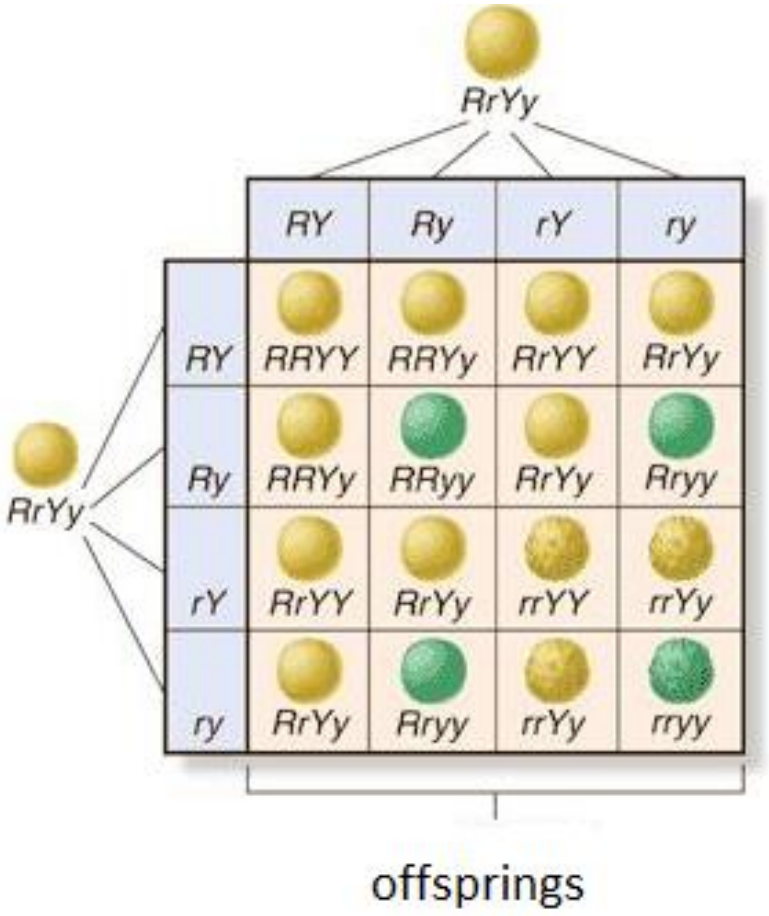
Example #1

- In a pea plant, the inheritance of its pea shape and colour is controlled by two genes.

- Dominant shape is round (R), while recessive is crinkled (r). Dominant colour is yellow (Y), while recessive is green (y).

What are the genotype's ratio of the offspring when two heterozygous parents for both traits cross?

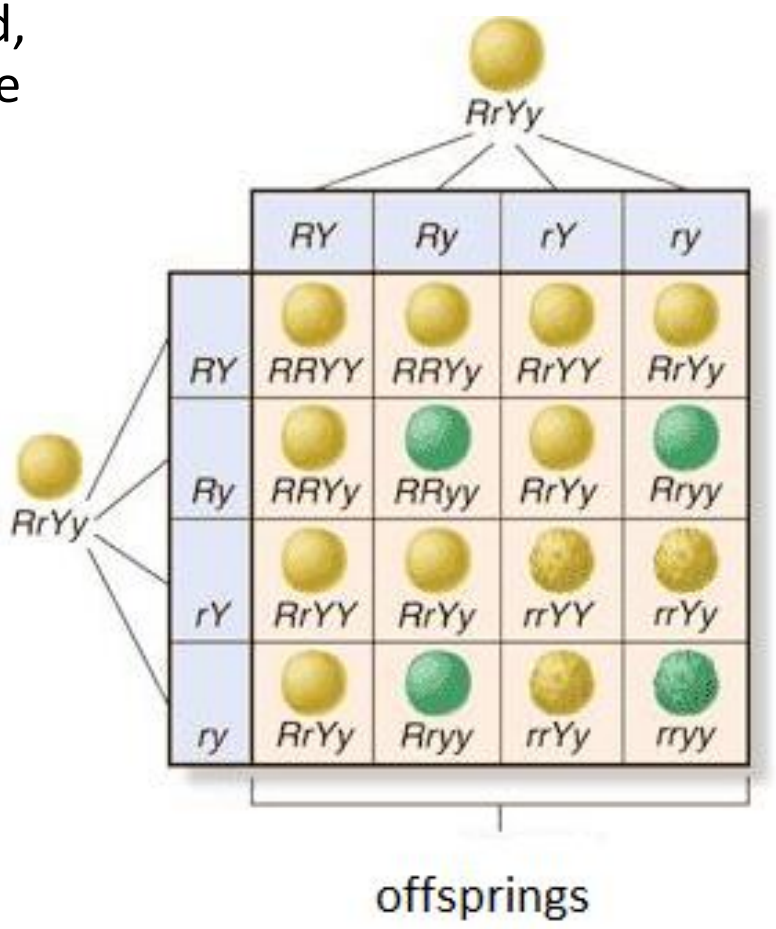
→ 9:3:3:1



Example #1

If there are a total of 144 offspring produced, the **expected** offspring number for each type would be:-

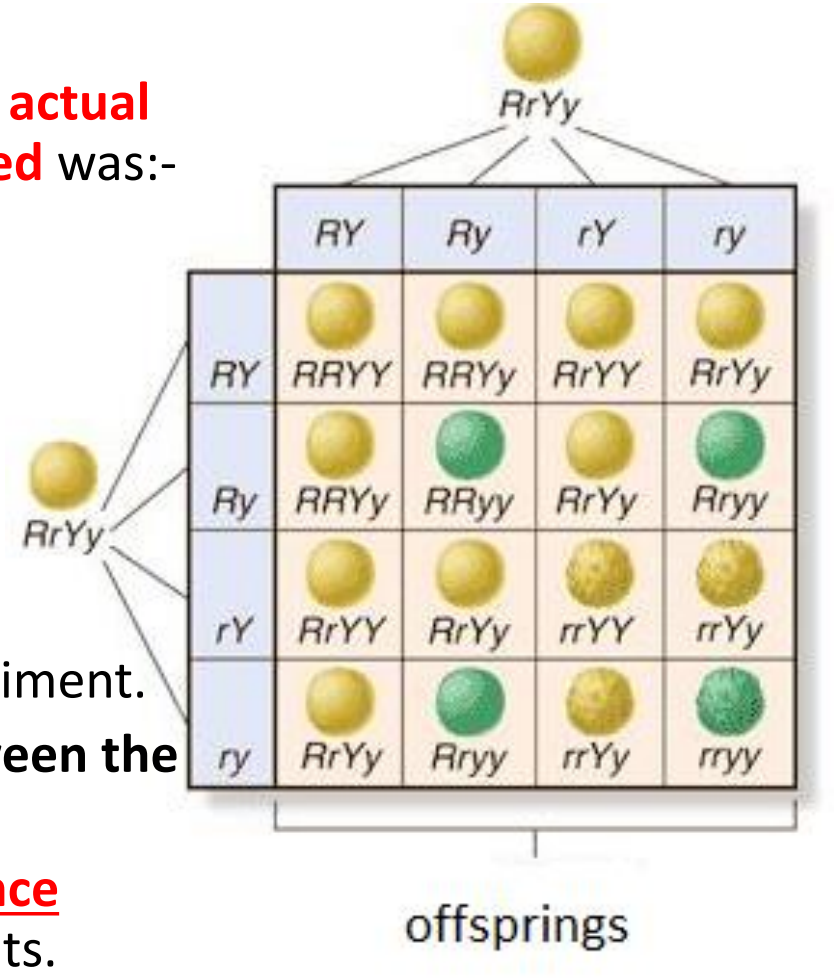
- Round, yellow – 81
- Round, green – 27
- Crinkled, yellow – 27
- Crinkled, green – 9



Example #1

When a cross was done in the lab and the **actual** number of offspring for each type **observed** was:-

- Round, yellow – 88
- Round, green – 25
- Crinkled, yellow – 28
- Crinkled, green – 3



a) Write the **null hypothesis** for this experiment.

→ **There is no significant difference between the observed and expected results.**

b) Find out if there is a **significant difference between observed and expected** results.

→ χ^2 **test**

P5

$$\chi^2 = \sum \frac{(O - E)^2}{E}$$

O	E	(O-E)	(O-E)^2	(O-E)^2 / E
88	81	7		
25	27	2		
28	27	1		
3	9	6		
			χ^2	4.790

How to use the χ^2 table to determine significance of difference?

1) Calculate value of χ^2 test

2) Look for **critical value** at **p = 0.05**

3) Degrees of freedom, v = c-1
(number of classes minus 1)

4) Check if value of χ^2 calculated is higher or lower compared to **critical value** in χ^2 table

Chi-squared Table

DoF = (n-1) Dependent on number of categories In this case, 4-1 = 3

5% probability that differences are not significant/due to chance

Percentage Points of the Chi-Square Distribution

Degrees of Freedom	Probability of a larger value of x^2								
	0.99	0.95	0.90	0.75	0.50	0.25	0.10	0.05	0.01
1	0.000	0.004	0.016	0.102	0.455	1.32	2.71	3.84	6.63
2	0.020	0.103	0.211	0.575	1.386	2.77	4.61	5.99	9.21
3	0.115	0.352	0.584	1.212	2.366	4.11	4.790 6.25	7.81	11.34
4	0.297	0.711	1.064	1.923	3.357	5.39	7.78	9.49	13.28
5	0.554	1.145	1.610	2.675	4.351	6.63	9.24	11.07	15.09
6	0.872	1.635	2.204	3.455	5.348	7.84	10.64	12.59	16.81
7	1.239	2.167	2.833	4.255	6.346	9.04	12.02	14.07	18.48
8	1.647	2.733	3.490	5.071	7.344	10.22	13.36	15.51	20.09
9	2.088	3.325	4.168	5.899	8.343	11.39	14.68	16.92	21.67
10	2.558	3.940	4.865	6.737	9.342	12.55	15.99	18.31	23.21

Calculated chi-squared value < critical value, then there is no sig. diff. btwn observed and expected.

critical value at p=0.05

Making Conclusions from Chi-squared test

1) If chi squared-test value calculated is **higher** than value in table:-

- **Significant difference** in results
- **Reject** null hypothesis

→ Differences are NOT due to random error/chance

2) If chi squared-test value calculated is **lower** than value in table:-

- **No significant difference** in results
- **Accept** null hypothesis

→ Differences are due to random error/chance

Making Conclusions from Chi-squared test

Percentage Points of the Chi-Square Distribution

Degrees of Freedom	Probability of a larger value of x^2								
	0.99	0.95	0.90	0.75	0.50	0.25	0.10	0.05	0.01
1	0.000	0.004	0.016	0.102	0.455	1.32	2.71	3.84	6.63
2	0.020	0.103	0.211	0.575	1.386	2.77	4.61	5.99	9.21
3	0.115	0.352	0.584	1.212	2.366	4.11	6.25	7.81	11.34
4	0.297	0.711	1.064	1.923	3.357	5.39	7.78	9.49	13.28

- Using our example, $\mathcal{X}^2$ value is 4.790
- The degree of freedom, v = 3
- The critical value at p = 0.05 is 7.81
- So the probability of the difference occuring by chance is > 0.05 (5%)
- Null hypothesis is accepted
- There is no sig. diff. btwn the observed and expected results

Chi-squared Test

$$\chi^2 = \sum \frac{(O - E)^2}{E}$$

χ^2 = the test statistic $\sum$ = the sum of

O = Observed E = Expected

Example #2

Round – R Yellow - Y

Crinkled – r Green – y

What is the ratio of offsprings' phenotypes when a plant with **heterozygous for both traits** and a plant which is **homozygous recessive for both traits** cross?

a) Draw a genetic diagram to show the expected outcomes with its ratio.

Example #2

b) If the total number of offspring produced is 124, and the following numbers are actually observed:-

Round, yellow – 28

Round, green – 23

Crinkled, yellow – 35

Crinkled, green – 38

i) Write the null hypothesis.

ii) Find out if there is any significant difference between expected and observed results.

Chi-squared Table

Percentage Points of the Chi-Square Distribution

Degrees of Freedom	Probability of a larger value of x^2								
	0.99	0.95	0.90	0.75	0.50	0.25	0.10	0.05	0.01
1	0.000	0.004	0.016	0.102	0.455	1.32	2.71	3.84	6.63
2	0.020	0.103	0.211	0.575	1.386	2.77	4.61	5.99	9.21
3	0.115	0.352	0.584	1.212	2.366	4.11	6.25	7.81	11.34
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5	0.554	1.145	1.610	2.675	4.351	6.63	9.24	11.07	15.09
6	0.872	1.635	2.204	3.455	5.348	7.84	10.64	12.59	16.81
7	1.239	2.167	2.833	4.255	6.346	9.04	12.02	14.07	18.48
8	1.647	2.733	3.490	5.071	7.344	10.22	13.36	15.51	20.09
9	2.088	3.325	4.168	5.899	8.343	11.39	14.68	16.92	21.67
10	2.558	3.940	4.865	6.737	9.342	12.55	15.99	18.31	23.21

Example #3

P5

(a) Grassland, grazed by goats, was compared to grassland ungrazed for varying amounts of time. Moths were trapped, their numbers counted and then the moths were released. The effect of grazing on a species of rare moth was investigated. A chi-squared (χ^2) test was used to test the significance of the results obtained.

(i) State the null hypothesis.

..... [1]

(ii) Complete Table 3.1 to calculate the value of χ^2 from the equation below.

$$\chi^2 = \sum \frac{(O - E)^2}{E}$$

O = Observed result
E = Expected result

Table 3.1

site	O	E	$(O - E)^2$	$\frac{(O - E)^2}{E}$
grazed for 2 years	36			
ungrazed for 10 years	90			
ungrazed for 30 years	114			

χ^2 = ... [4]

degrees of freedom	probability			
	0.10	0.05	0.01	0.001
1	2.71	3.84	6.64	10.83
2	4.60	5.99	9.21	13.82
3	6.25	7.82	11.34	16.27
4	7.78	9.49	13.28	18.46
10	15.99	18.31	23.21	29.59
20	28.40	31.41	37.57	45.31

P5

Example #3

(b) (i) State the number of degrees of freedom. ..... [1]

(ii) State the probability of the value calculated for χ^2. ..... [1]

(iii) Explain the significance of these results and suggest the consequences to this species of moth if grazing land is increased.

.....

.....

.....

.....

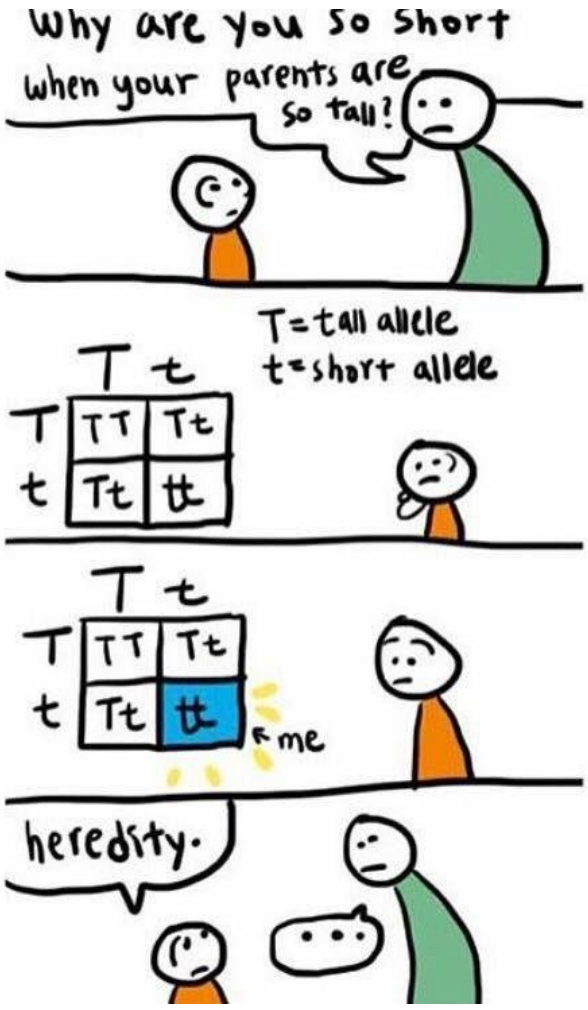
..... [3]

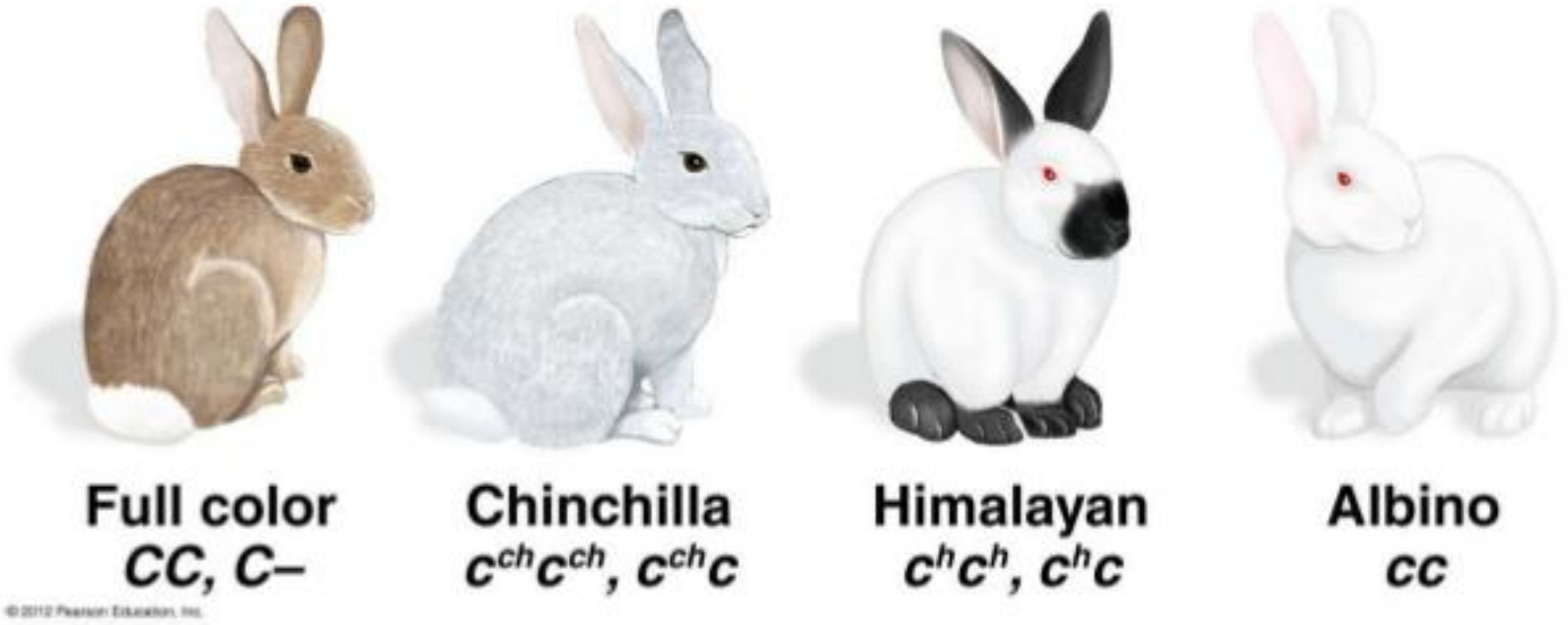
Chapter Outline

Part II: Mendelian Inheritance

- Monohybrid cross
- Dihybrid cross
- Test crosses

- **P5:** Chi-squared test





UNIVERSITY of CAMBRIDGE International Examinations
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Chapter 16
A2 Level

Inherited Change

Part 3: More Patterns of Inheritance

Chapter Outline

Part III: More Patterns of Inheritance

- Sex linkage
- Codominance
- Multiple alleles
- Epistasis
- Autosomal linkage

- Mutations
  - Important examples of mutations: sickle cell anemia, albinism, haemophilia, Huntington's disease, cystic fibrosis

But okay, it doesn't work the same with all alleles and all phenotypes.

What if….

- there are sex chromosomes involved? → **sex-linked**
- it's NOT exactly recessive/dominant? → **codominance**
- more than 2 alleles are involved? → **multiple alleles**
- the expression of some genes affect other genes? → **epistasis**
- the genes are on the same chromosome? → **autosomal linkage**

Sex-Linkage

- **Sex-linkage = Allele / gene carried on the sex chromosomes**
- Usually X chromosome

- Y chromosome is shorter than X

→ Carries fewer genes than X

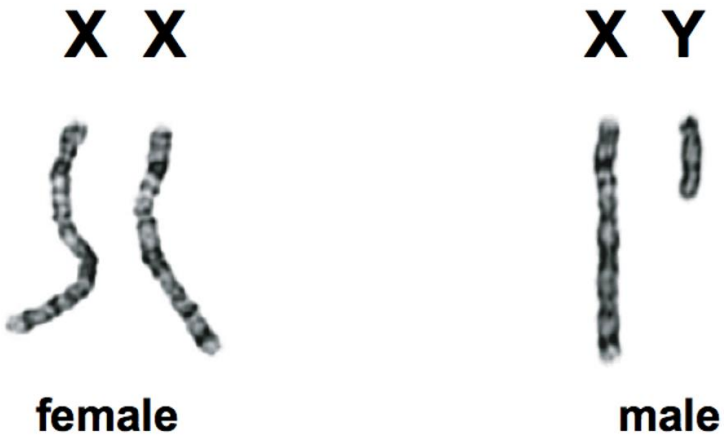
→ Do not have the same genes in the same loci

→ Some different genes from X

→ **Some genes exist as a single copy only** either on X or Y chromosome = hemizygous

Types of sex-linked inheritance patterns:

- **X-linked recessive**
- **X-linked dominant**
- **Y-linked** (not in syllabus)



X-linked Recessive

- **Phenotype determined by recessive allele on X**
- Phenotype will be expressed if there are no dominant alleles of the same gene present
- I.e**. in females with both recessive alleles on X, or males with one recessive allele on X**

- To show genotypes for sex-linked genes:

a) Use symbols for gender (XX, XY)

b) Write alleles as superscripts

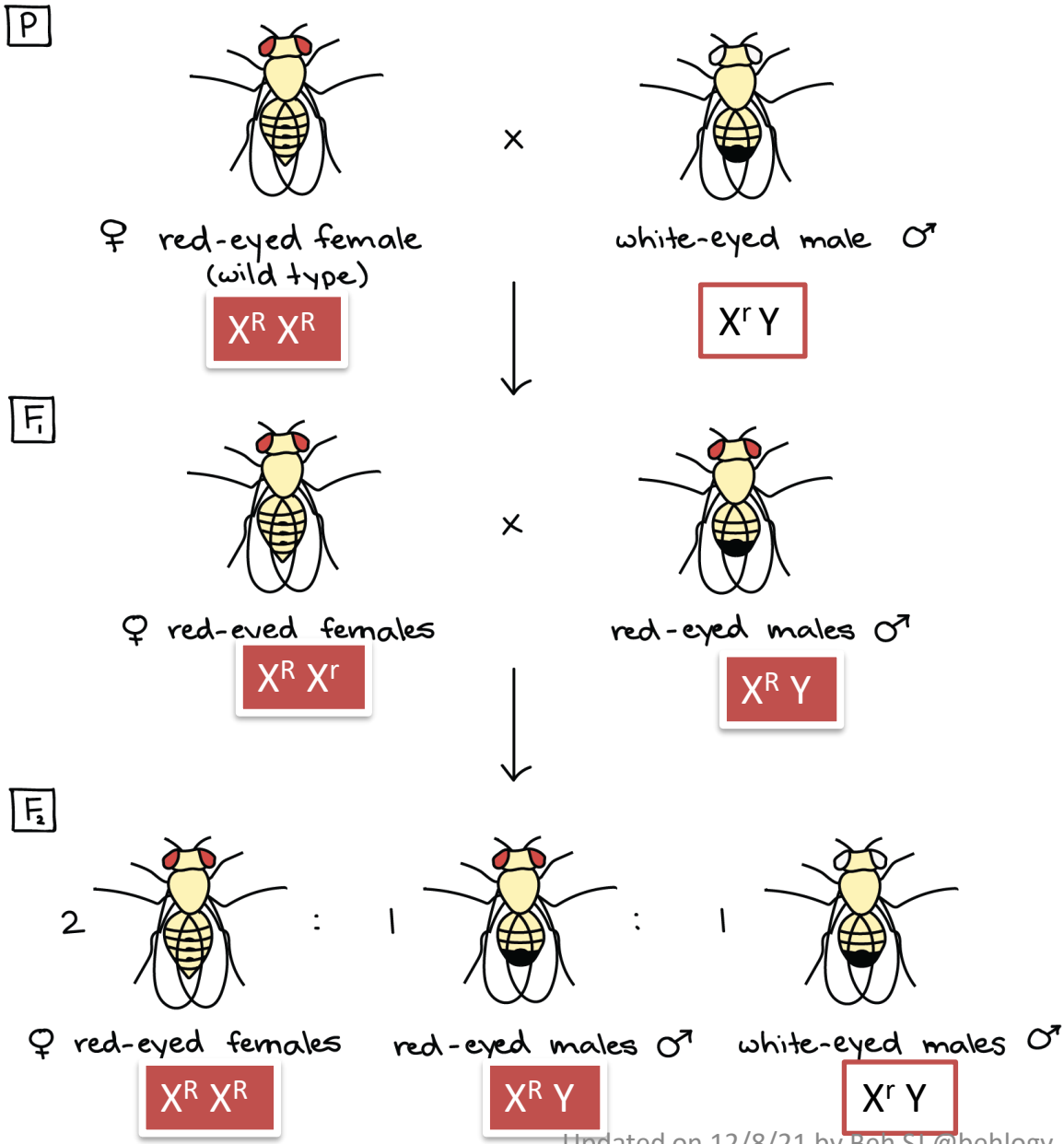
E.g. **gene for eye colour in flies** is on the X chromosome

- X^R = dominant allele for red eyes
- X^r = recessive allele for white eyes
- Possible genotypes:

$X^R X^r$ $X^r X^r$ $X^R X^R$ $X^R Y$ $X^r Y$

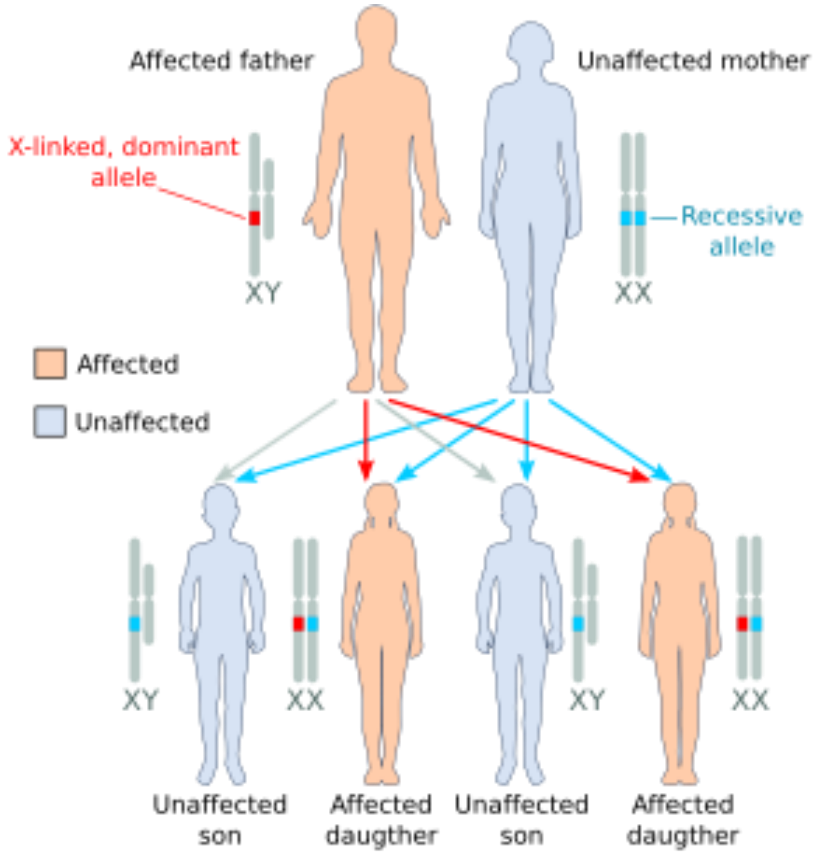
X-linked Recessive

- So…when a white-eyed male is crossed with a red-eyed female, all F1 fruit flies have red eyes
- When F1 is crossed, 75% of F2 have red-eyes and 25% have white-eyes
- AND all white-eyes are male
- How is this so? Draw Punnett squares to prove that the ratio shown is correct!



X-linked Dominant

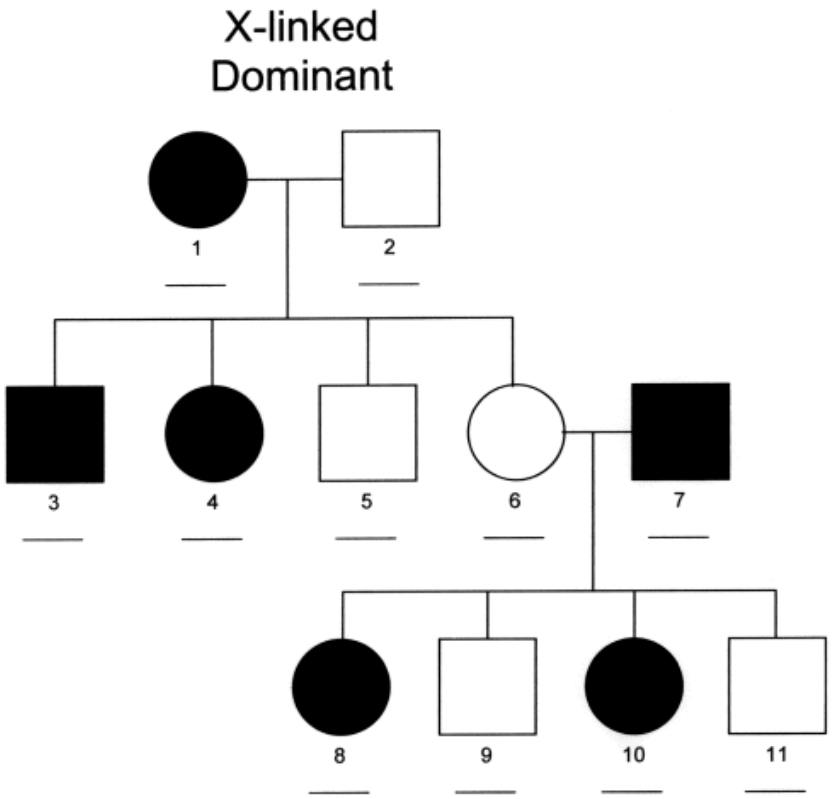
- **Phenotype determined by dominant allele on X**
- Phenotype is shown in **homozygous dominant and heterozygous females, and males with the dominant allele**



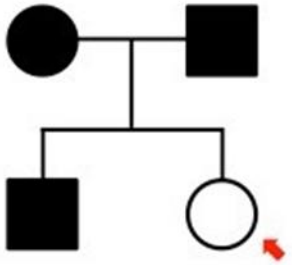
- Affected males will not pass the dominant allele on X to sons (since sons must inherit Y)
- But will pass it on to daughters (daughters must inherit one X from mum and one X from dad)

X-linked Dominant

- In a pedigree diagram…
  - ○ is female
  - □ is male
  - ● and ■ is affected
- Is Female 1 homozygous or heterozygous for the allele? Explain why.
- Why are all females in generation 3 affected?



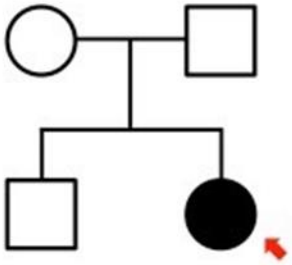
AUTOSOMAL DOMINANT



Cannot be recessive as two affected parents could **not** have an unaffected offspring

Parents MUST be heterozygous

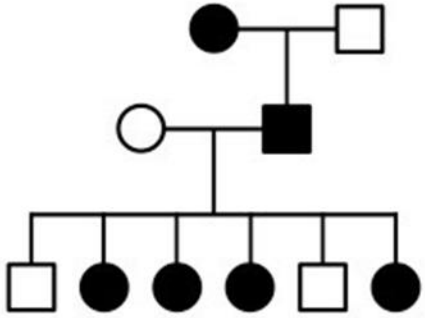
AUTOSOMAL RECESSIVE



Cannot be dominant as two unaffected parents could **not** have an affected offspring

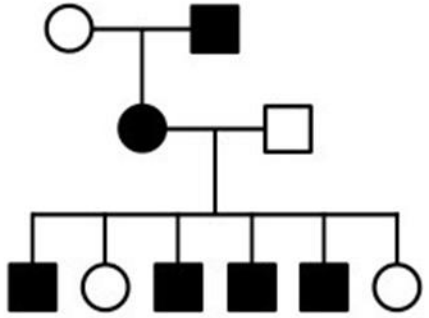
Parents MUST be heterozygous

X-LINKED DOMINANT



100% incidence of affected daughters from an affected father *suggests* X-linked dominance

X-LINKED RECESSIVE



100% incidence of affected sons from an affected mother *suggests* X-linked recessive

Codominance

- Codominance = **when both alleles are fully expressed in the heterozygote**
- More than 2 phenotypes possible
- Phenotype of heterozygote different from either homozygote
- When 2 heterozygotes (F1) are crossed, the resulting phenotype is in a **1:2:1 ratio**

E.g. shorthorn cattle (cows)

- Cows that are heterozygotes have both red and white fur = roan coats

- C^R = allele for red; C^W = allele for white
- *Note: we don't use Rr because it's not dominant/recessive, it's **CO**dominant*

Codominance in Shorthorn Cattle

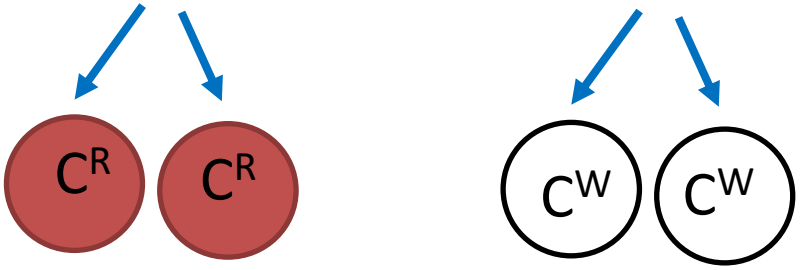
Let C^R = allele for red; C^W = allele for white

PARENTAL PHENOTYPES

PARENTAL GENOTYPES

Red cow $C^R C^R$ x White bull $C^W C^W$

GAMETES



OFFSPRING (F1) GENOTYPES

GAMETES	C^W
C^R	$C^R C^W$

OFFSPRING (F1) PHENOTYPES

All resulting shorthorn cattle have roan coats

Codominance in Shorthorn Cattle

Let C^R = allele for red; C^W = allele for white

F1 PHENOTYPES

Roan bull x Roan cow

F1 GENOTYPES

$C^R\ C^W$ x $C^R\ C^W$

GAMETES

OFFSPRING (F2) GENOTYPES

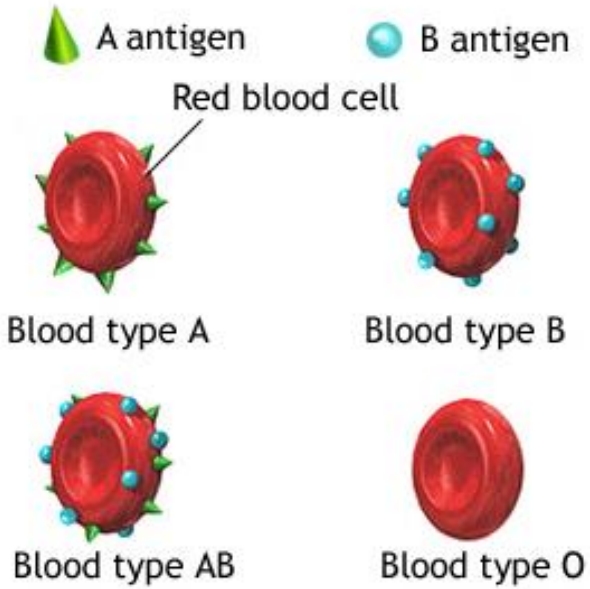
GAMETES	C^R	C^W
C^R	$C^R\ C^R$	$C^R\ C^W$
C^W	$C^W\ C^R$	$C^W\ C^W$

OFFSPRING (F2) PHENOTYPES

Ratio of red:roan:white coats are 1:2:1

Multiple Alleles

- **Genes with more than 2 alleles**



E.g. *ABO* gene for human blood groups

- I^A = A alelle
- I^B = B alelle

} codominant

- i = O allele → recessive to I^A and I^B

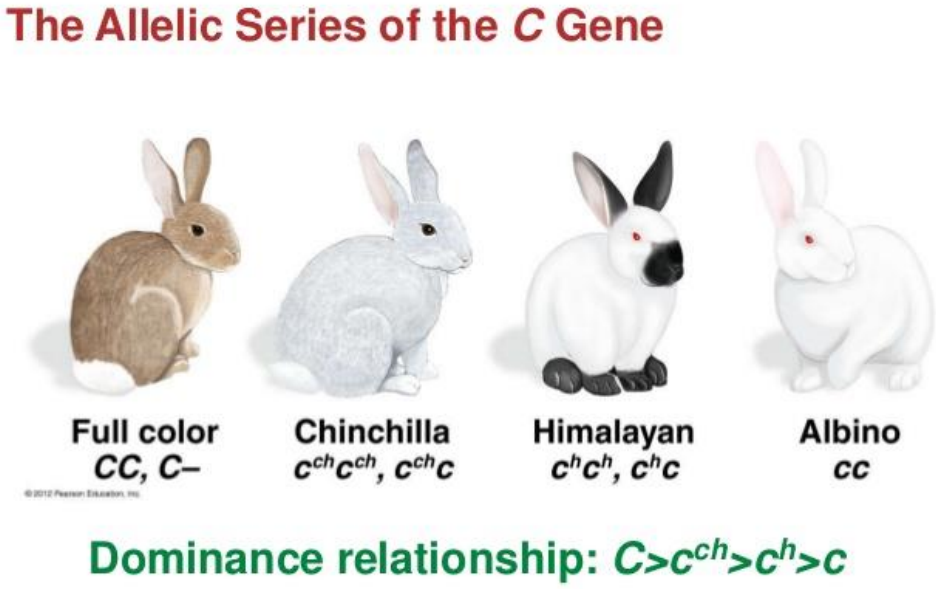
List the possible genotypes for each blood group

Blood group (Phenotype)	Genotype
A	
B	
AB	
O	

Example Question

E.g. Fur colour in rabbits

Draw a genetic diagram to show a cross between rabbits with genotype Cc^{ch} and $c^{ch}c$. What's the probability of obtaining a chinchilla rabbit?



Epistasis

- **When different genes at diff loci**
- **Interact to affect ONE phenotype**

E.g. Feather colour in chickens

- Individuals with dominant allele, **I**, have white feathers even if dominant allele, **C**, for coloured feathers is present
- Only individuals that are homozygous recessive for **i** and have at least one dominant allele , **C**, for coloured feathers, will be coloured

IICC = white

iiCC / iiCc = coloured

iicc = white

PARENTAL PHENOTYPES white x white

PARENTAL GENOTYPES IICC iicc

GAMETES IC ic

F1 GENOTYPES

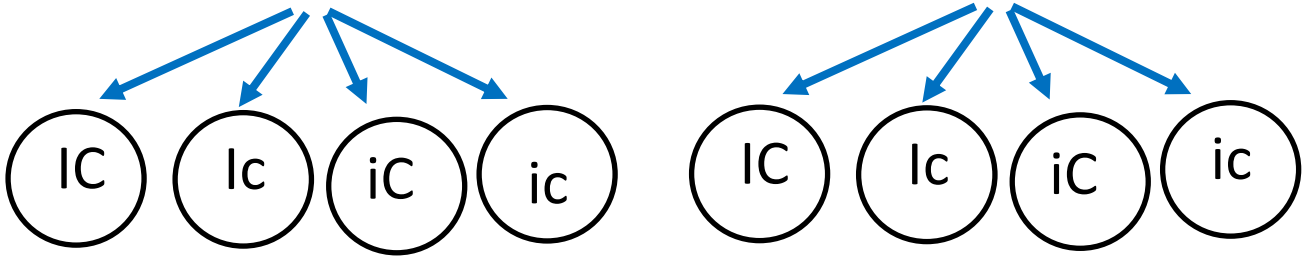
GAMETES	**ic**
IC	**IiCc**

F1 PHENOTYPES **All chickens are white.**

F1 PHENOTYPES white x white

F1 GENOTYPES liCc liCc

GAMETES



F2 GENOTYPES AND PHENOTYPES

GAMETES	IC	Ic	iC	ic
IC				
Ic				
iC				
ic				

F2 GENOTYPES AND PHENOTYPES

GAMETES	IC	Ic	iC	ic
IC	IICC white	IICc white	IiCC white	IiCc white
Ic	IICc white	IIcc white	IiCc white	Iicc white
iC	IiCC white	IiCc white	iiCC coloured	iiCc coloured
ic	IiCc white	Iicc white	iiCc coloured	iicc white

RATIO and PROBABILITY

white:coloured = 13:3

P (white) = (9+3+1)/16

P (coloured) = 3/16

Example Question

- A pure-bred, pink flower variety of *Salvia* was crossed with a pure-bred, white-flowered variety. The offspring had purple flowers.
- Interbreeding these offspring to give another generation resulted in purple, pink and white-flowered plants in a ratio of 9:3:4
- Two loci, A/a and B/b, on diff chromosomes are involved:

Genotype	Phenotype
A–B–	purple
A–bb	pink
aaB–	white
aabb	white

(– indicates that either allele of the gene may be present)

- Draw a genetic diagram of the *Salvia* cross described above to show the 9:3:4 ratio in the 2nd generation.

Autosomal Linkage

- **Linked genes** = 2 genes are on the **same chromosome**

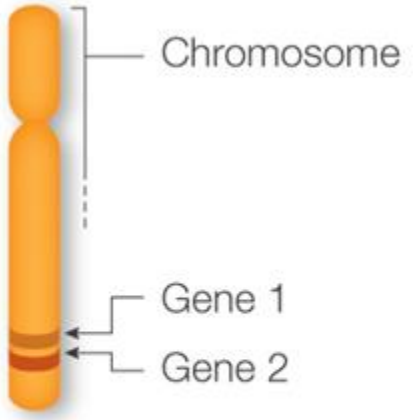
→ They are in an autosomal **linkage group**
(not to be confused with sex/autosomal-linked genes!)

→ Likely to be inherited together

→ **No independent assortment**

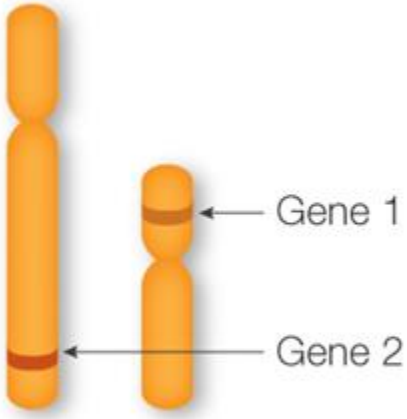
→ No separation during anaphase

- The closer the loci are tgr, **the lower the chance of crossing over**



Linked
(lower chance
of crossing over)

Linked
(higher chance
of crossing over)



Not Linked

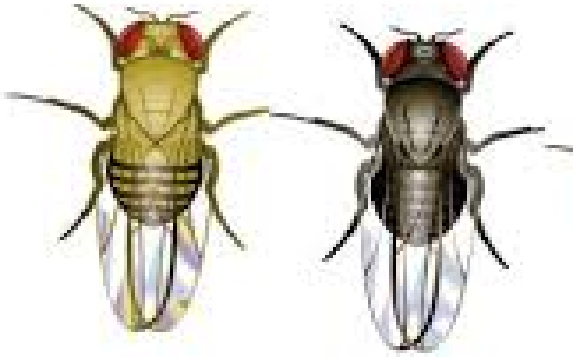
Autosomal Linkage

E.g. body colour and antennal shape of the fruit fly, *Drosophila*

- The gene for body colour and the gene for antennal shape are close together on the same chromosome and so are linked.

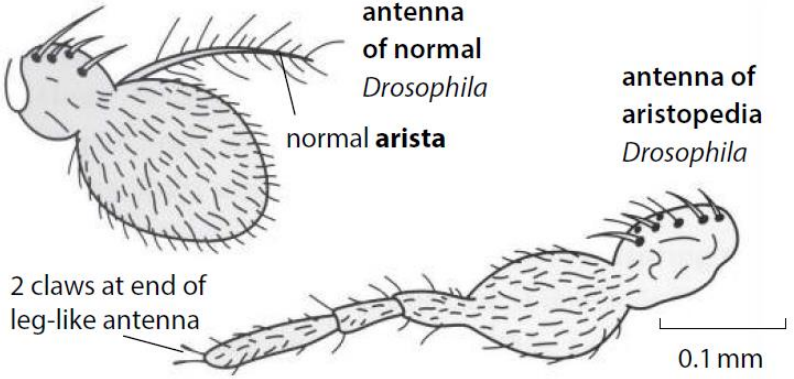
Body colour gene:

- E = allele for striped body
- e = allele for ebony body



Antennal shape gene:

- A = allele for normal antennae
- a = allele for aristopedia antennae (looks more like a leg)



*__We will use brackets in gentotypes (EA)(EA)__ to show they are on the same chromosome. EEAA without brackets indicates that they are on diff chromsomes.

PARENTAL PHENOTYPES

Striped body,
Normal antennae

x

Ebony body,
Aristopedia antennae

PARENTAL GENOTYPES

(EA)(EA)

(ea)(ea)

GAMETES

EA

ea

F1 GENOTYPES

GAMETES	**ea**
EA	**(EA)(ea)**

F1 PHENOTYPES

All *Drosophila* have striped bodies and normal antennae.

F1 looks normal… But how about F2?
Draw a genetic diagram to show F2

How to determine whether the 2 genes are linked or just normal dihybrid?

Test Cross

Cross an individual **heterozygous** for both genes (EA)(ea) with a **homozygous recessive** individual (ea)(ea)

F1 PHENOTYPES

Striped body,
Normal antennae

x

Ebony body,
Aristopedia antennae

F1 GENOTYPES

(EA)(ea)

(ea)(ea)

GAMETES

F2 GENOTYPES AND PHENOTYPES

GAMETES	**EA**	**ea**
ea	**(EA)(ea)** Striped body, Normal antennae	**(ea)(ea)** Ebony body, Aristopedia antennae

RATIO 1 : 1

Autosomal Linkage

- A test cross of (EA)(ea) with (ea)(ea)
- Would give a **1 : 1 ratio**
- Not the 1 : 1 : 1 : 1 ratio expected from a dihybrid cross

- BUT getting a 1:1 ratio is rare
- **1:1 ratio = total linkage**
- Linked genes can be separated by **rare cross over events** during prophase I
- The closer the loci are tgr, **the lower the chance of crossing over**
- Test cross would typically result in:

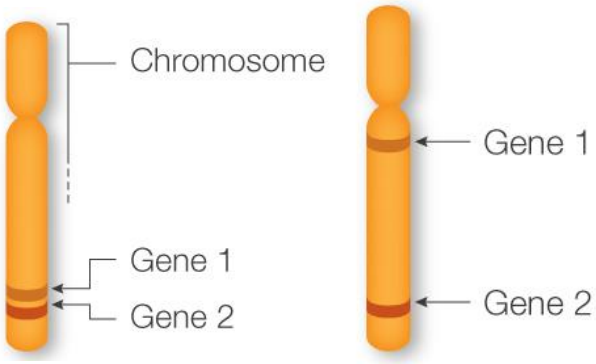
(EA)(ea)	striped body, normal antennae	44%	parental classes
(ea)(ea)	ebony body, aristopedia antennae	44%	
Eeaa	striped body, aristopedia antennae	6%	recombinant classes
eeAa	ebony body, normal antennae	6%	
		(result of crossing over)	

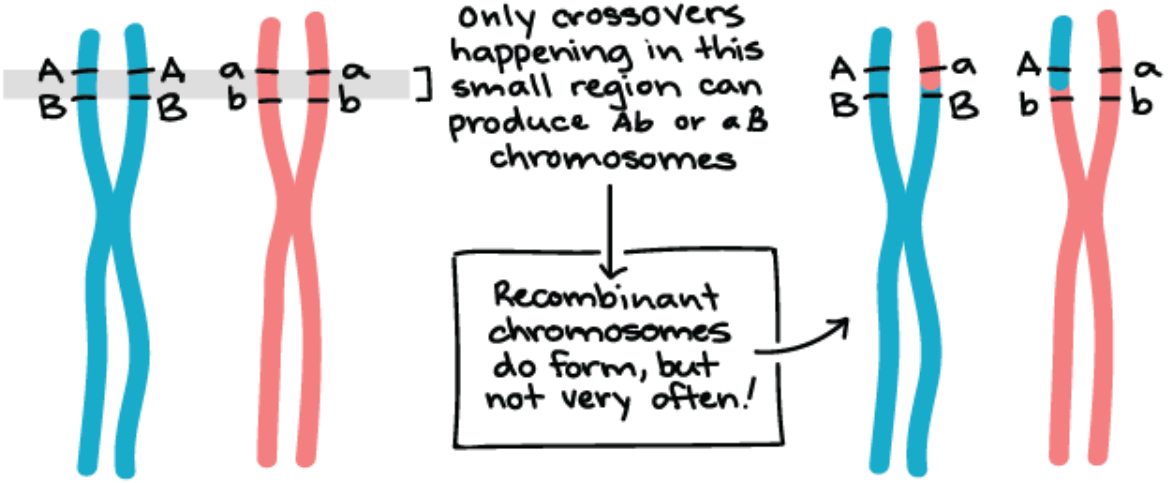
Autosomal Linkage: Cross Over Value

- **Cross over value** = measure of distance btwn 2 gene loci on chromosomes
- This is the percentage that belong to the recombinant class

i.e. 6% + 6% = 12% in this case

- **The smaller the cross over value, the closer the loci are together**
- The closer the loci are tgr, **the lower the chance of crossing over**





Summary

Pattern of inheritance	What is it?	F2 ratio
Monohybrid	1 gene, 2 alleles	3:1
Dihybrid	2 gene on diff chromosomes, 2 alleles each	9:3:3:1
X-linked	Gene on X chromosome, absent on Y	Depends whether allele is recessive or dominant
Codominance	1 gene, 2 alleles, both fully expressed in heterozygotes	1:2:1
Multiple alleles	1 gene, >2 alleles	Depends which alleles are involved
Epistasis	2 genes, both influence 1 phenotype only	Depends on the gene and organism
Autosomal Linkage	2 genes on same chromosome	Depends which alleles are on the same chromosome

Chap 6 Recap

Gene Mutations

- Caused by mutagens (e.g. ionizing radiation, UV radiation, mustard gas)

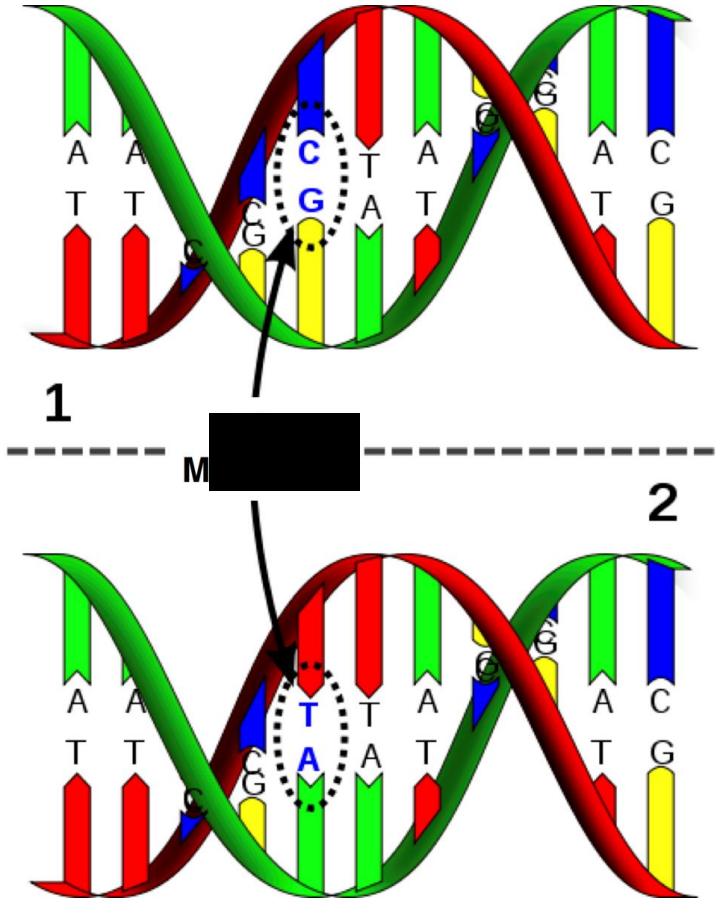
- **Mutations = random change in the DNA sequence** during DNA replication

→ Causes altered **codons** in mRNA seq

→ May alter **amino acid seq** of polypeptide chain

- Can result in **new alleles**
- **Alleles = diff forms of one gene**

→ Affects phenotype (appearance/trait) of organism



Chap 6 Recap

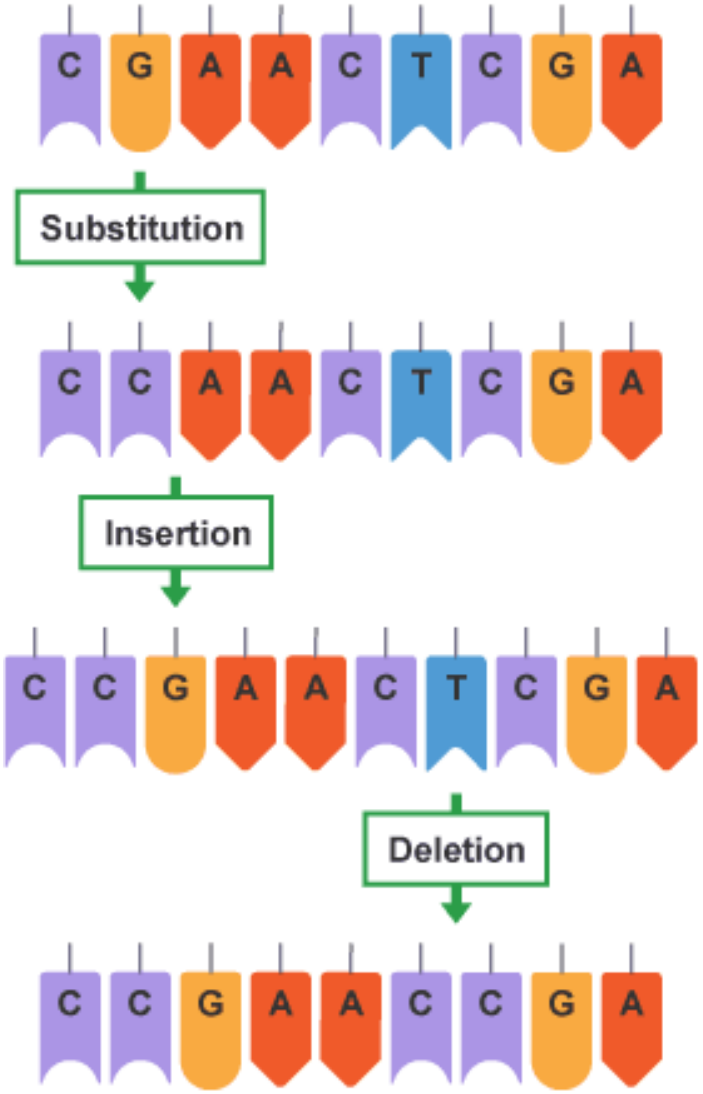
Gene Mutations

Types of gene mutations:

- Substitution
- Insertion/Addition
- Deletion

- The simplest form of mutation involves only **a change of one nucleotide**

→ Point mutations / base mutations



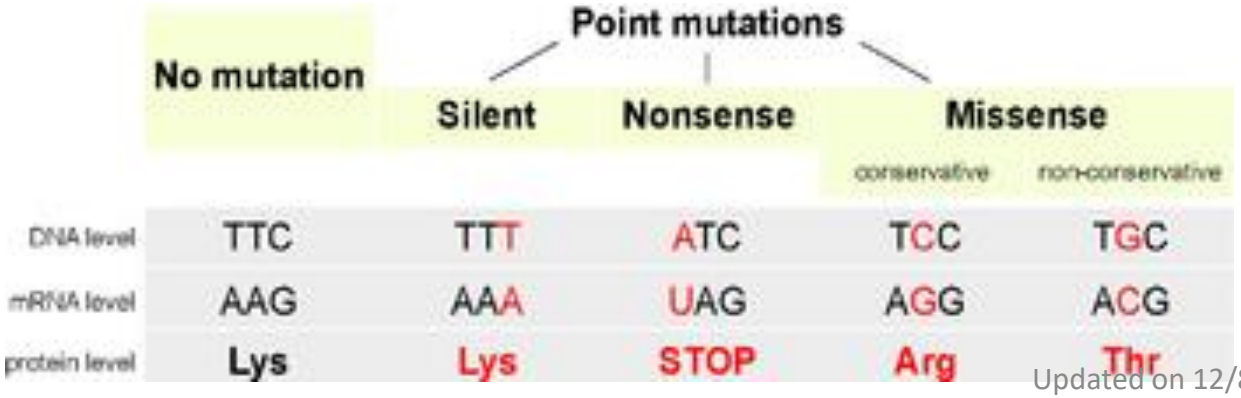
Chap 6 Recap

Base substitution

- Only **one** nucleotide is replaced by another

Can result in one of 3 types of mutations:

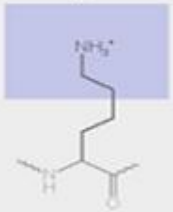
1. **Silent mutation**
   = triplet code / codon still codes for the **same amino acid**
2. **Nonsense mutation**
   = **stop codon** is introduced
3. **Missense mutation**
   = triplet code / codon codes for a **different amino acid**

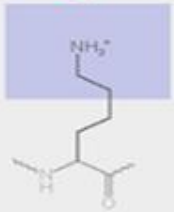


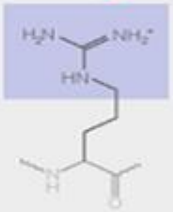
Chap 6 Recap

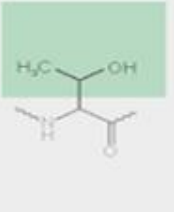
Base substitution

	No mutation	Silent	Nonsense	Missense	
DNA level	TTC	TTT	ATC	TCC	TGC
mRNA level	AAG	AAA	UAG	AGG	ACG
protein level	Lys	Lys	STOP	Arg	Thr









basic
polar

Triplet code changed but amino acid seq is **unaffected**

Normal, functional protein

Result in STOP codon

Premature chain termination

Subsequent amino acids are not formed

Incomplete, non-functional polypeptide

Only **one** amino acid of the polypeptide seq is affected

If amino acid has side chain with different property, tertiary structure is more affected.

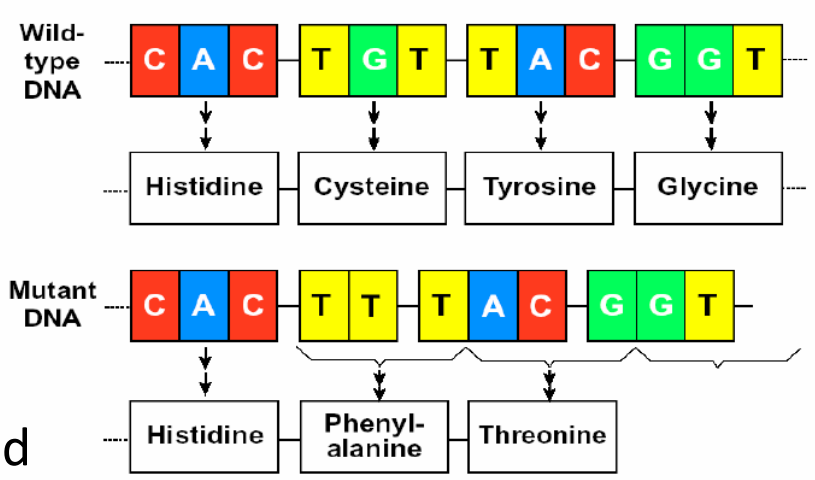
Faulty protein, may be still functional

Base Insertion + Base Deletion

- Results in one of 2 types of mutations:

1. Frameshift mutations

- Deleting/inserting one nucleotide of DNA will change which bases are read together
- **All subsequent codons are affected, all subsequent amino acids affected**
- **Faulty, non-functional protein**



2. Nonsense mutation

- Result in STOP codon
- **Premature chain termination**
- Subsequent amino acids are not formed
- **Incomplete, non-functional polypeptide**

5 Important Disease Examples

Diseases	Pattern of inheritance	Gene	Normal allele	Mutant allele
Sickle Cell Anaemia (SCA)	Codominance	Gene coding for β-globin	Hb^A	Hb^S
Albinism	Autosomal recessive	*TYR* gene coding for tyrosinase	You decide	
Haemophilia	X-linked recessive	Gene coding for factor VIII	X^H	X^h
Huntington's Disease (HD)	Autosomal dominant	Huntingtin (*HTT*) gene	h	H
Cystic fibrosis (CF)	Autosomal recessive	*CFTR* gene	You decide	

Chap 6 Recap

1. Sickle Cell Anaemia

- Inherited blood disorder
- Affects the structure of the haemoglobin
- Cause: **Base substitution** in gene coding for **β-globin**

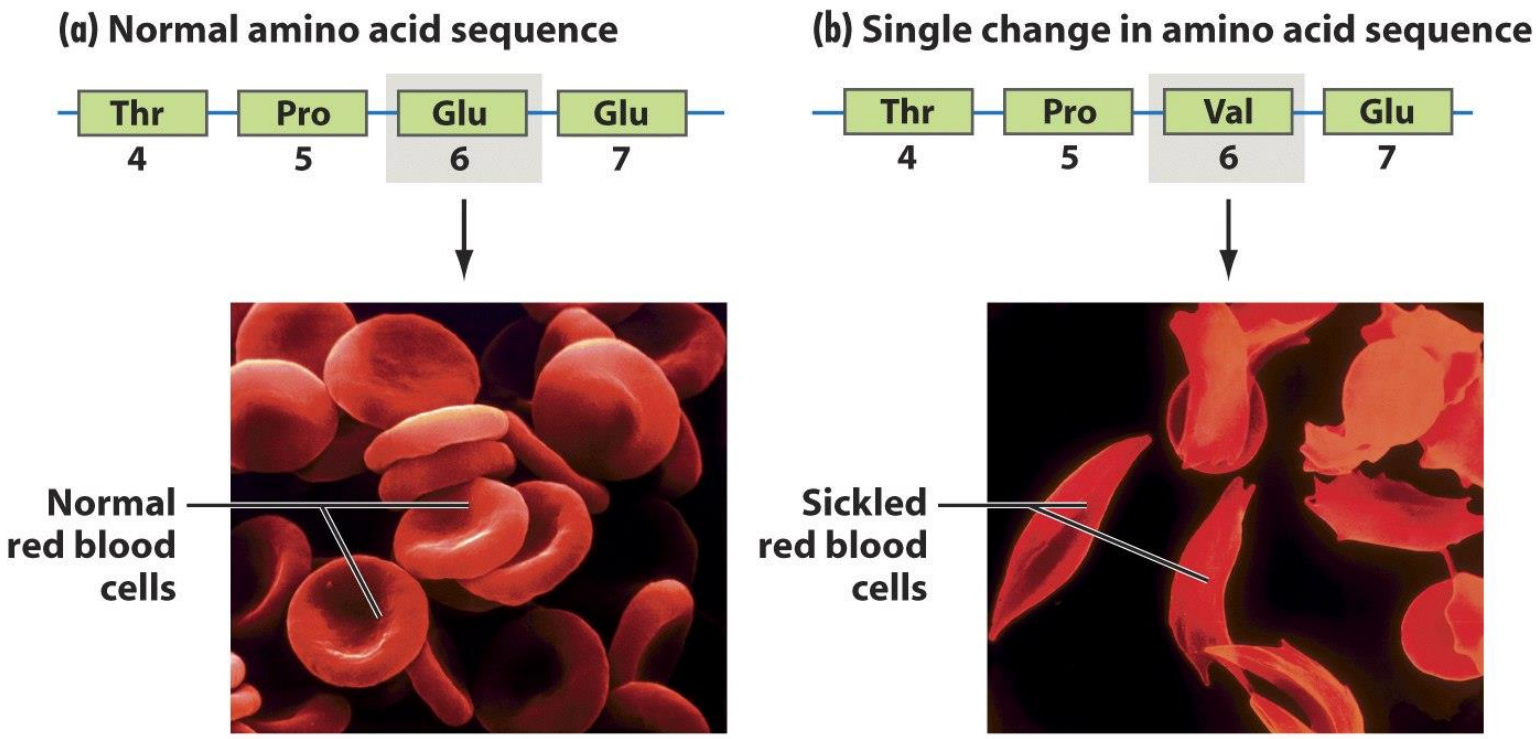
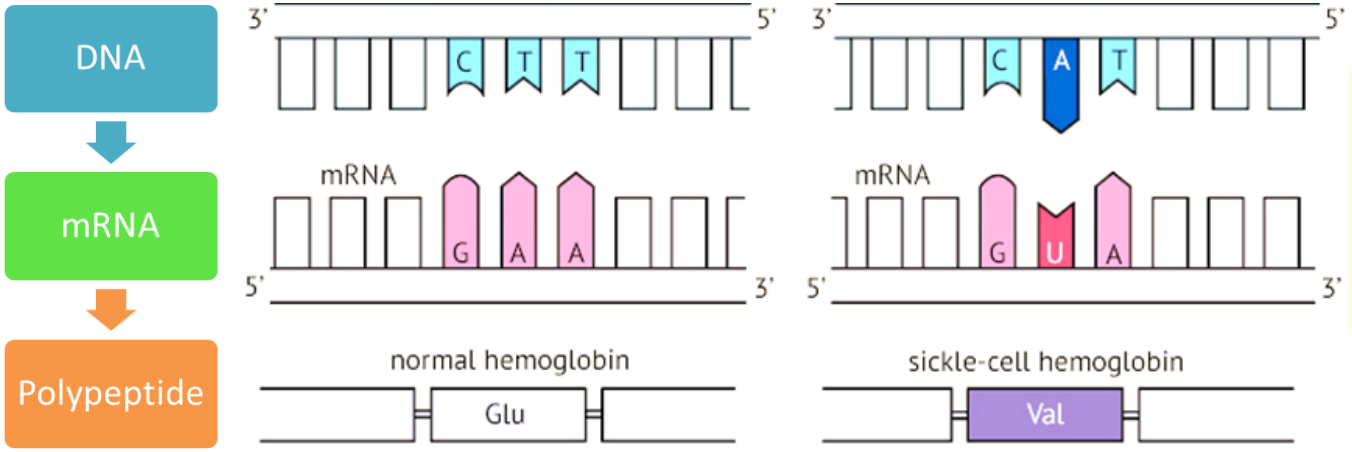


Figure 3-13 Biological Science, 2/e

Chap 6 Recap

1. Sickle Cell Anaemia



P/S: the textbook is wrong and yes, you need to rmb that T is replaced by A.

- Base substitution in **gene** coding for β-globin results in

→ different **mRNA** codon

→ different **tRNA** brings a different **amino acid** to ribosome

→ leads to a change of 6th amino acid in **polypeptide** chain

→ Altered **primary structure**

→ Glutamic acid is polar whereas valine is non-polar

→ Changed **secondary, tertiary and quaternary structure**

1. Sickle Cell Anaemia

Mutated β-globin causes:

- Hb molecule to become **less soluble** in low pO_2
- Stick tgr
- Form long fibres
- Cells become crescent / **sickle-shaped**
- **Carry less oxygen**

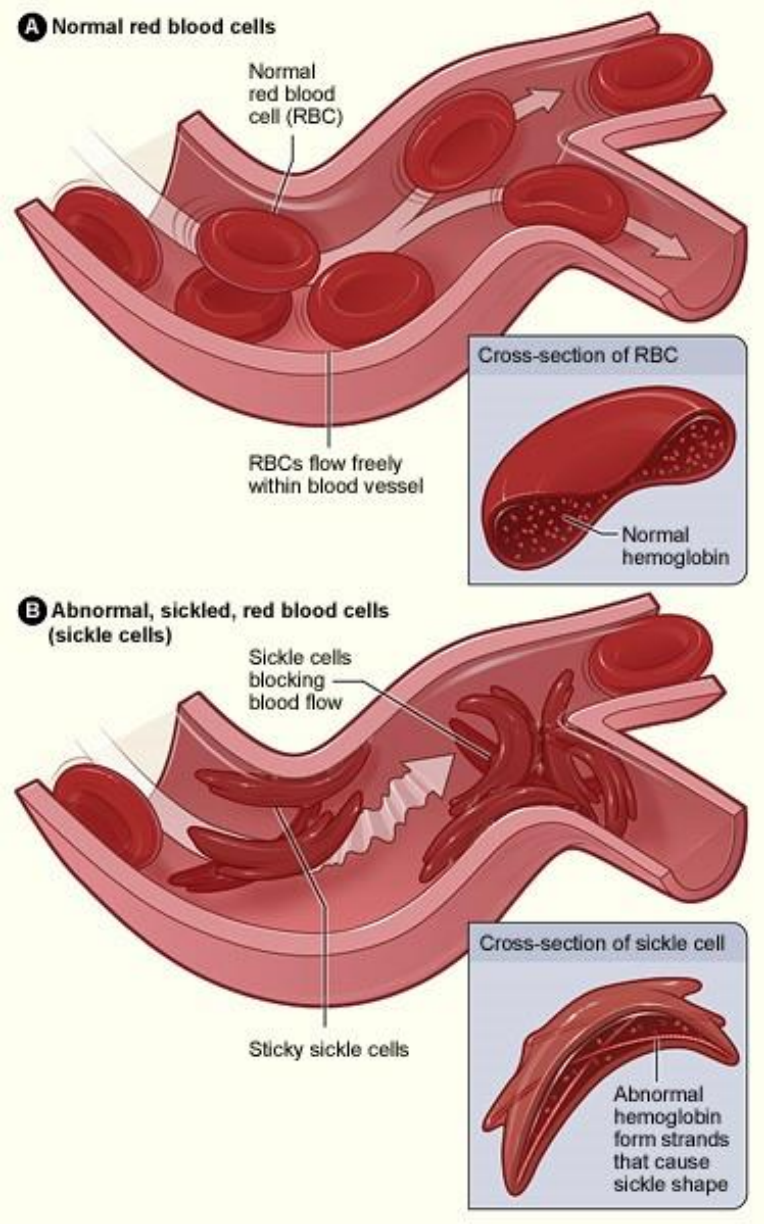
- Sickled red blood cells break down faster

→ cause lack of RBCs

- Sickle cell crisis = RBC get stuck in capillaries and block blood flow

→ Cause pain

- BUT give protection against malaria / Plasmodium infection (more in Chap 17)



1. Sickle Cell Anaemia

- Hb^A = normal β-globin allele
- Hb^S = mutant β-globin allele

- Hb^AHb^A = 2 <u>normal</u> β polypeptide alleles

→ Normal

- Hb^SHb^S = 2 <u>mutant</u> β polypeptide alleles

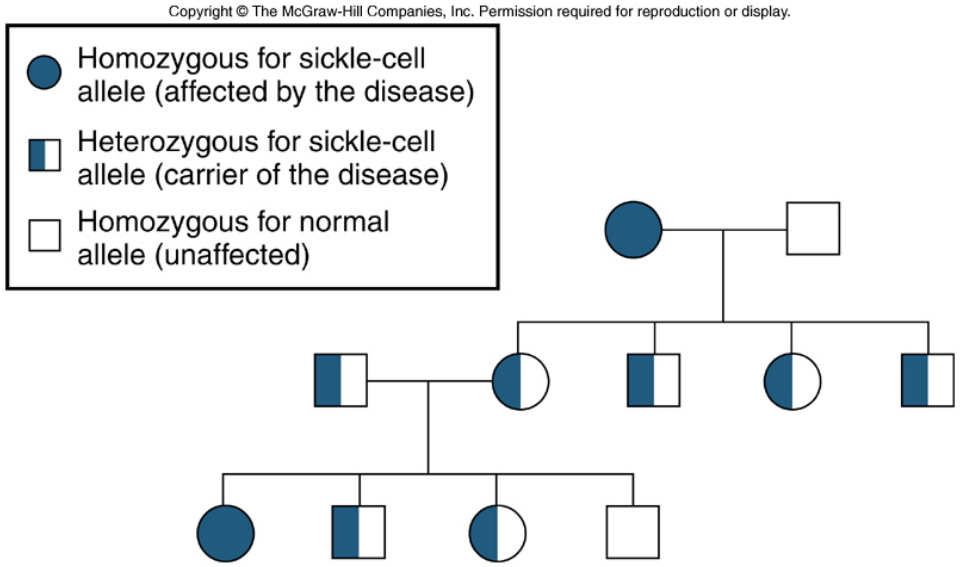
→ sickle cell anaemia

- Hb^AHb^S = 1 normal & 1 mutant

→ Has the sickle cell trait / 'carriers'

→ <u>Half</u> of the haemoglobin is normal

→ **Codominant**



2. Albinism

- Classic form caused by **autosomal recessive** mutation
- **Melanin** is missing from eyes, skin and hair

Symptoms:

- **Pale / white skin and hair**
- **Pink eyes**
- Increased susceptibility to sunburn / skin cancer

- Rapid, jerky eye movements
- Tend to have poor vision
- Tend to avoid bright light

2. Albinism

- Classic form caused by **autosomal recessive** mutation
- In ***TYR* gene** coding for enzyme **tyrosinase**
- Involved in **conversion of tyrosine to DOPA, which is needed for melanin production** in **melanocytes** (cells that produce melanin)

- Tyrosinase is an oxidase enzyme
- Has 2 copper atoms, binds 1 O_2 molecule
- Transmembrane protein found at membrane of melanosomes (large, specialised organelles in melanocytes)

- Mutation results in absence / inactive tyrosinase

3. Haemophilia

- **Sex-linked**
- Gene for blood clotting protein (factor VIII) is carried on X chromosome
- Caused by **X-linked recessive** mutation

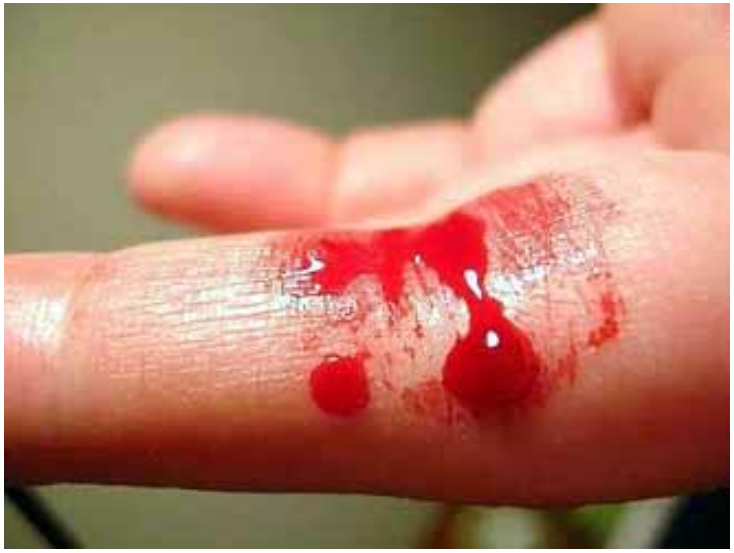
- X^H = normal allele
- X^h = haemophilia allele

→ **Factor VIII is not produced**

→ This **reduces clotting of blood**

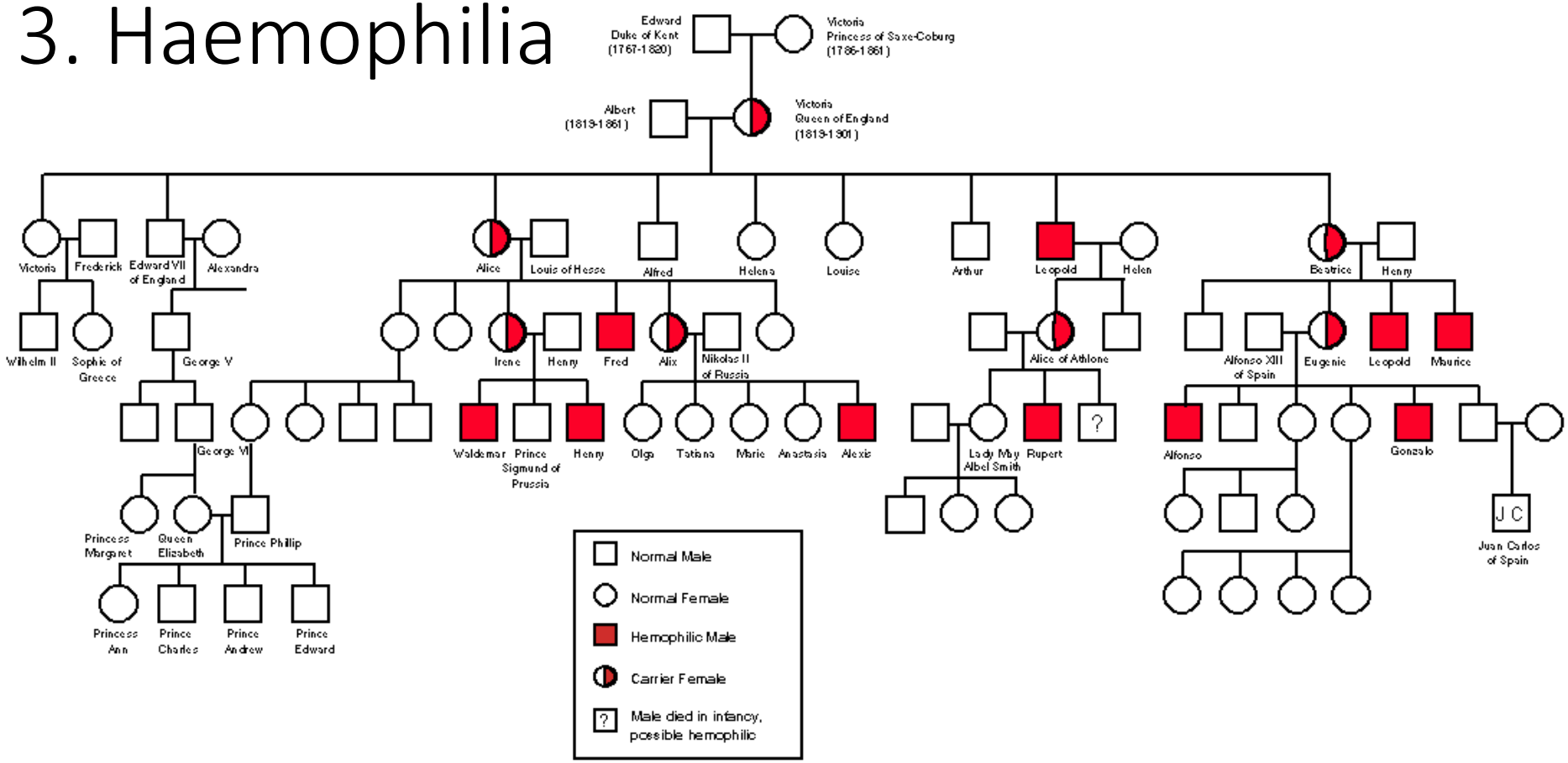
Symptoms:

- Excessive bleeding
- Bleeding into joints
- Large bruises
- Internal bleeding



Haemophilia in the British Monarch

3. Haemophilia



Possible genotypes:

$X^H X^h$	$X^h X^h$	$X^H X^H$	$X^h Y$	$X^H Y$
female carrier	female affected	female normal	male affected	male normal

All carriers must be female

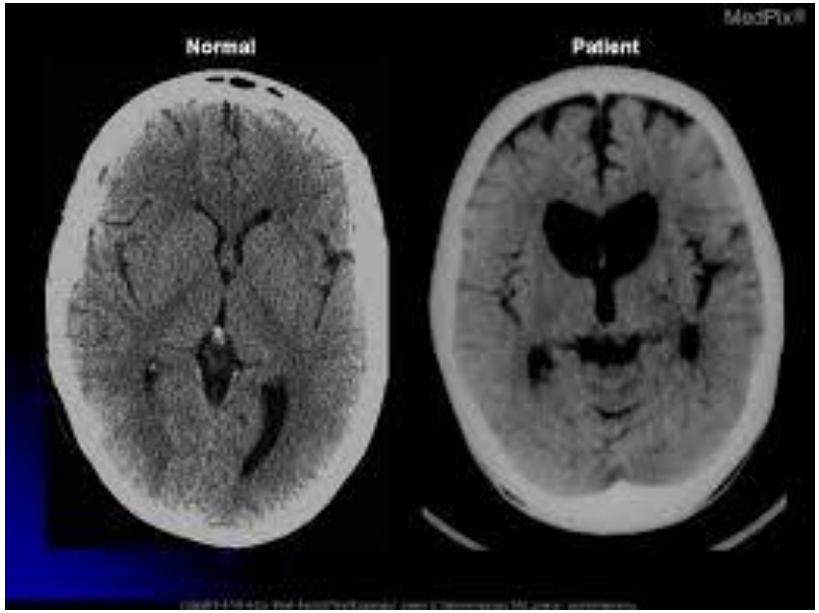
Male with carrier mother has 50% chance of having haemophilia

4. Huntington's disease (HD)

- Neurological disorder (i.e. neurones die)
- Usual onset in middle age btwn 28-65yo
- Caused by an **autosomal dominant** mutated allele
- Mutation at the **huntingtin (*HTT*) gene** on chromosome 4

Symptoms:

- Involuntary movements / uninhibited motor control
- Mood changes
- Progressive mental deterioration
- Brain cells lost



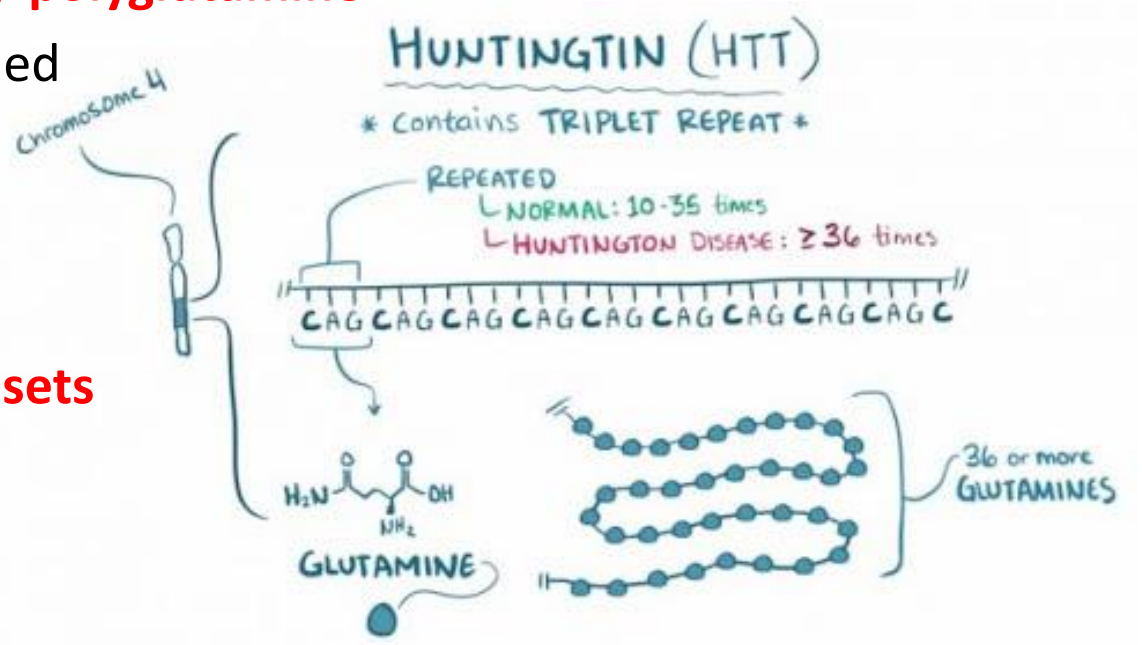
4. Huntington's disease (HD)

- Normal recessive allele has 10–35 repeats of CAG
- Mutant dominant allele has **>= 36 repeats of CAG**

→ CAG codes for glutamine

→ Result in **extra glutamine / polyglutamine**

→ Huntingtin protein misfolded

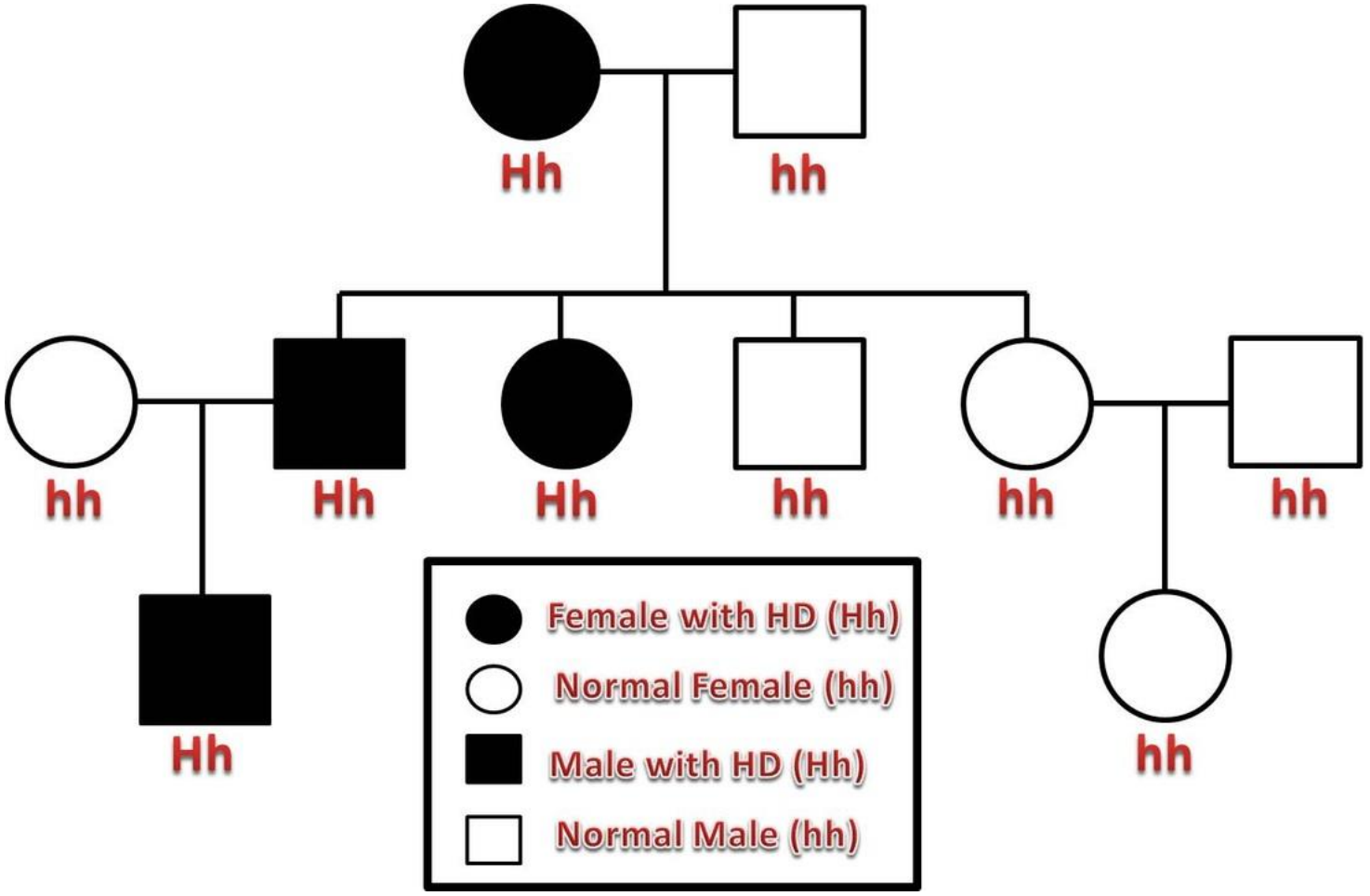


- **More repeats = earlier onsets**

→ E.g. onset even in babies if many repeats

4. Huntington's disease (HD)

Pedigree diagram for Huntington's Disease



Most people with HD are heterozygous
Have 50% chance of passing it to child

5. Cystic Fibrosis

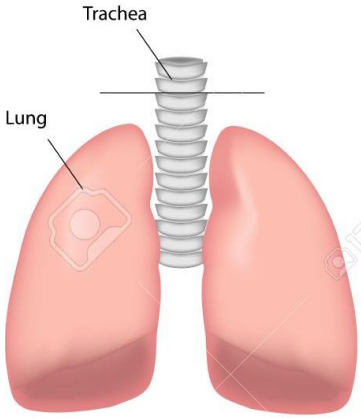
- Inherited genetic disease
- Faulty, **autosomal recessive** allele of the ***CFTR* gene**

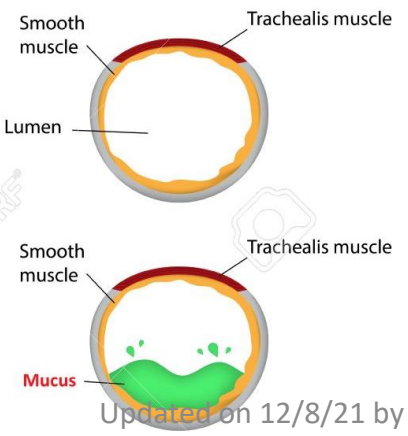
Normal CFTR protein :

- Transmembrane protein at cell surface membrane
- Acts as **chloride channel**
- Has binding site for ATP
- **Cl^- moves out of cell via active transport**
- Water is drawn out from cell

→ **Normal / less viscous mucus** formed

→ Easy removal by cilia





5. Cystic Fibrosis

Faulty *CFTR* allele:

a) Base deletion → faulty CFTR (most common)

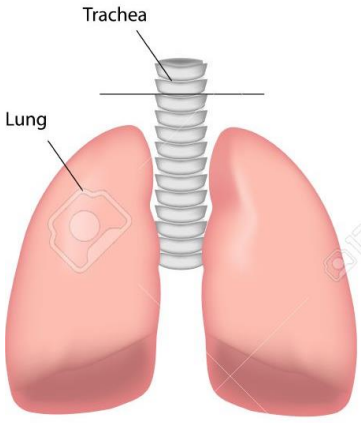
b) Base substitution → STOP codon → incomplete CFTR

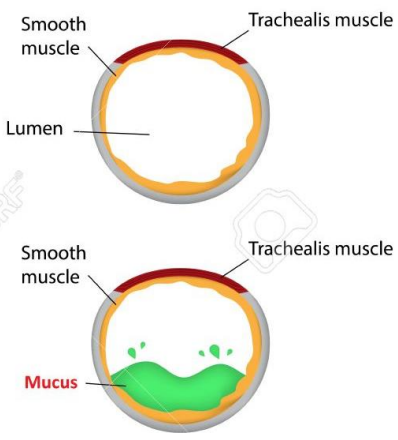
Faulty CFTR protein:

- No functional channels for Cl^- ions
- **Cl^- ions do not move out**
- **Less water leaves cell**

→ Formation of **thick, sticky mucus** on cell surface membrane

→ Cannot be removed by cilia



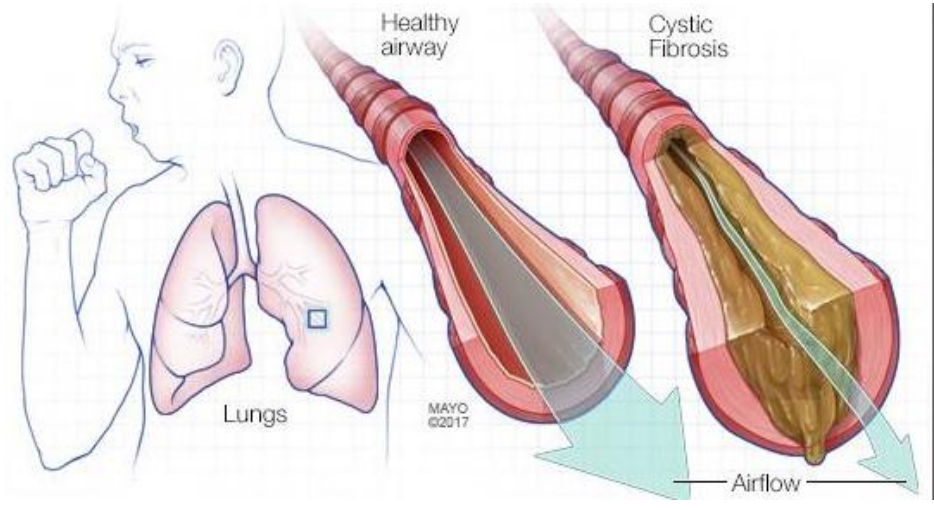


5. Cystic Fibrosis

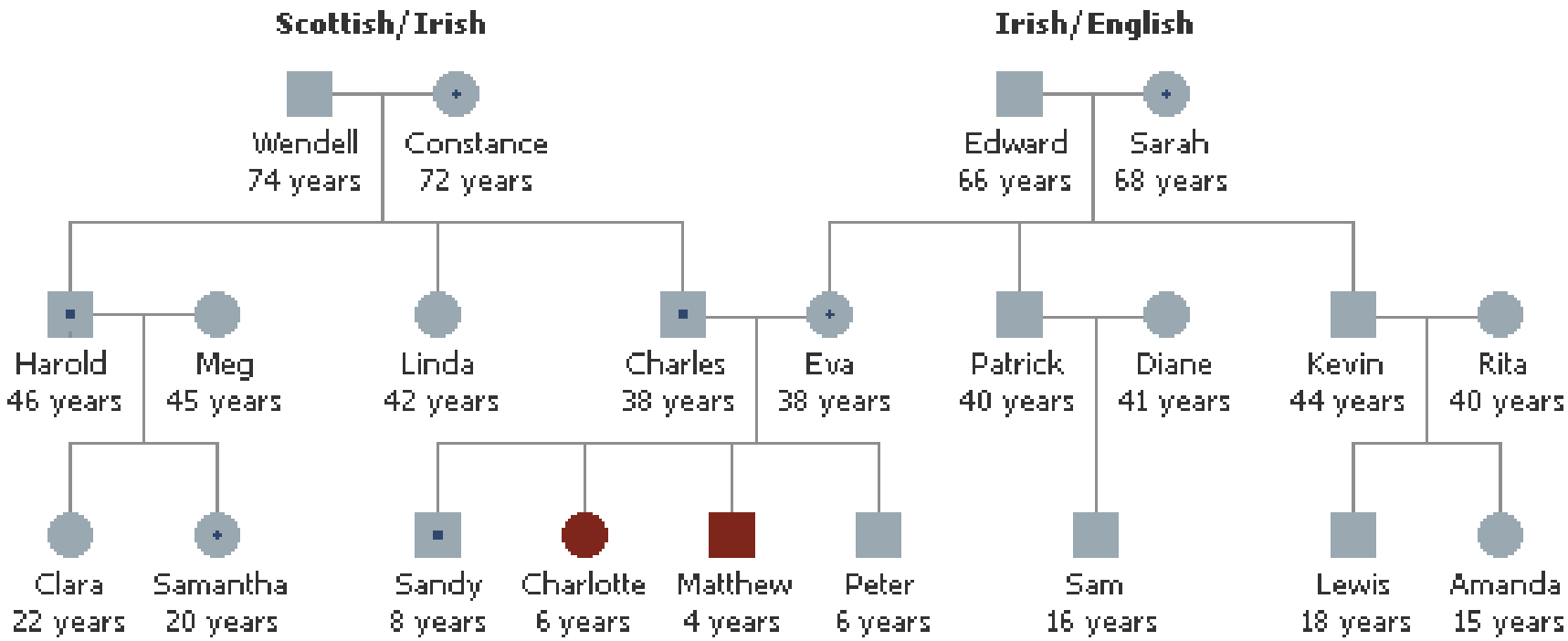
Symptoms:

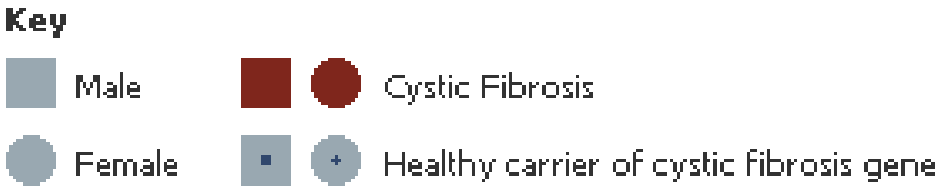
- **thick and sticky mucus** produced at **lungs**
- mucus not moved effectively by **cilia** → mucus accumulates
- mucus traps bacteria → **more infections**
- **reduced gaseous exchange** → due to longer diffusion pathway
- difficulty in breathing, wheezing
- coughing → cause lungs to be scarred

- blocked **pancreatic duct** → reduced digestion, damage of pancreatic tissues causes diabetes
- blocked **sperm ducts / oviducts** → reduced fertility



5. Cystic Fibrosis



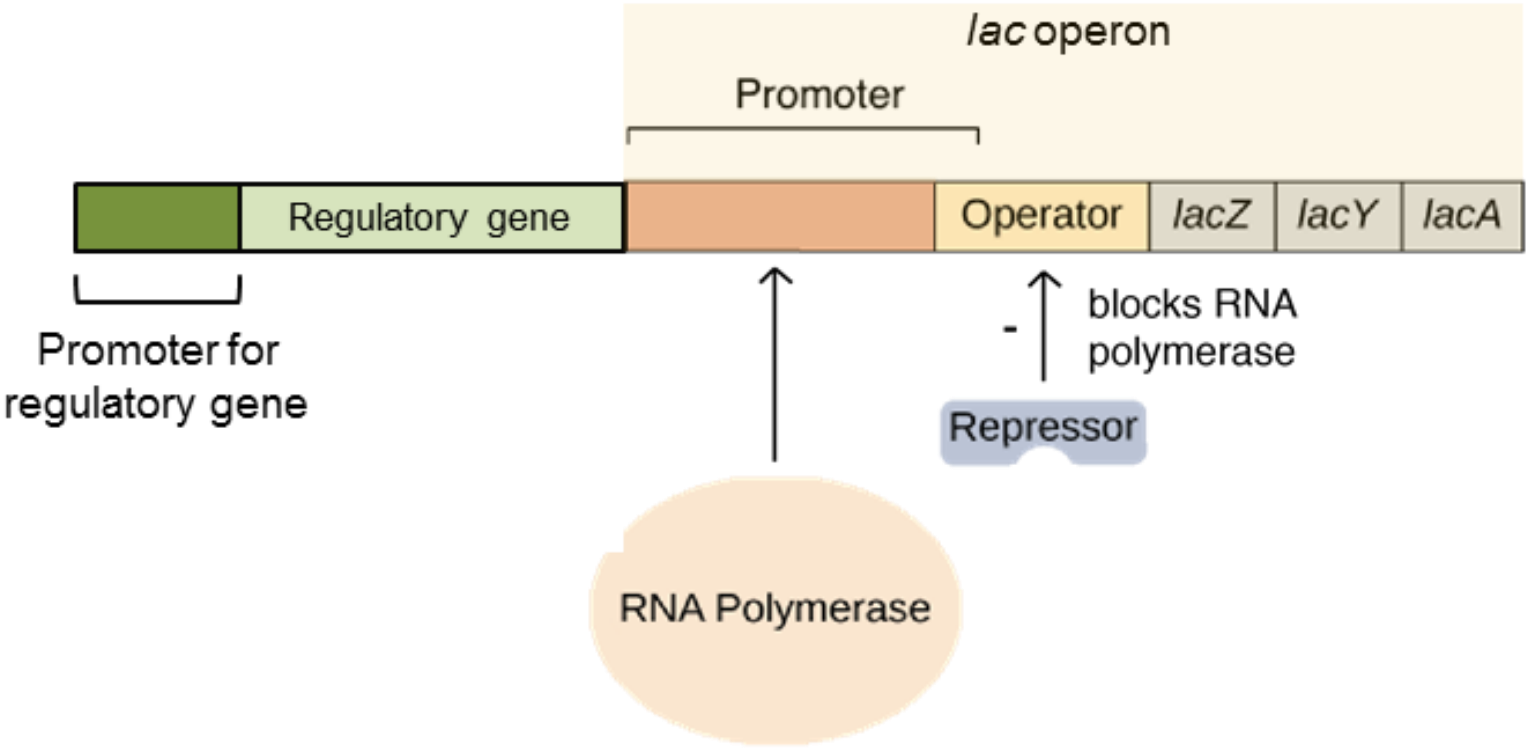


Chapter Outline

Part III: More Patterns of Inheritance

- Sex linkage
- Codominance
- Multiple alleles
- Epistasis
- Autosomal linkage

- Mutations
  - Important examples of mutations: sickle cell anemia, albinism, haemophilia, Huntington's disease, cystic fibrosis



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Chapter 16
A2 Level

Inherited Change

Part 4: Gene Control

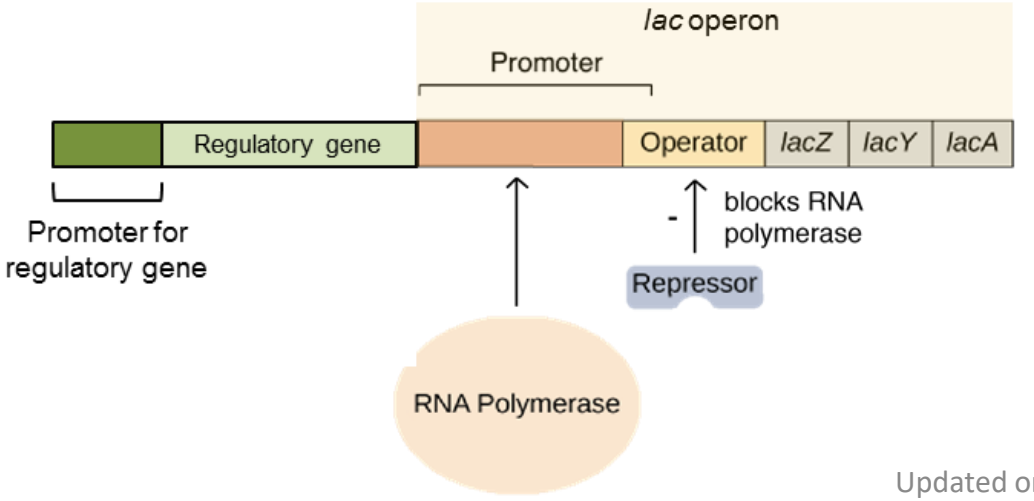
Chapter Outline

Part IV: Gene Control

- Structural vs regulatory genes
- Repressible, inducible enzymes

- Prokaryotes: The *lac* operon
- Eukaryotes: Function of transcription factors in gene expression

- Gibberellin breaks down DELLA protein repressors to activate genes



Regulation of Gene Expression

- **Gene expression** = process where gene is being transcribed to mRNA and then translated to protein

- **Gene regulation** = process that enable gene expression in specific cells and specific time

→ To ensure gene is expressed in correct cell at the correct time in the correct context

→ Some genes are transcribed all the time to produce **constitutive proteins**

→ Others are only 'switched on' when their protein products are required

→ Why?

  - No wastage of energy and resources
  - No expression of protein that may interfere with cell function

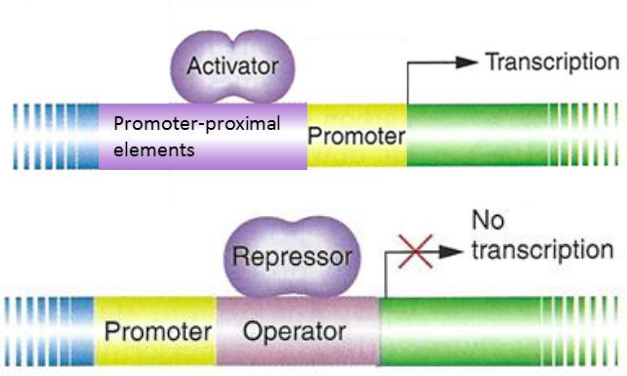
Structural vs Regulatory Genes

Structural genes

- Gene that code for **proteins needed for cell structure or function**
- E.g. proteins that form part of cellular structure, enzymes, rRNA etc.

Regulatory genes

- Genes that code for **regulatory proteins that controls gene expression/transcription**
- **E.g. transcription factors**, including repressors and activators
- Transcription factors can **bind to a specific DNA seq** and control transcription
- **Activators** = increases gene expression
- **Repressor** = reduce / inhibit gene expression



Repressible, inducible enzymes

Repressible enzymes

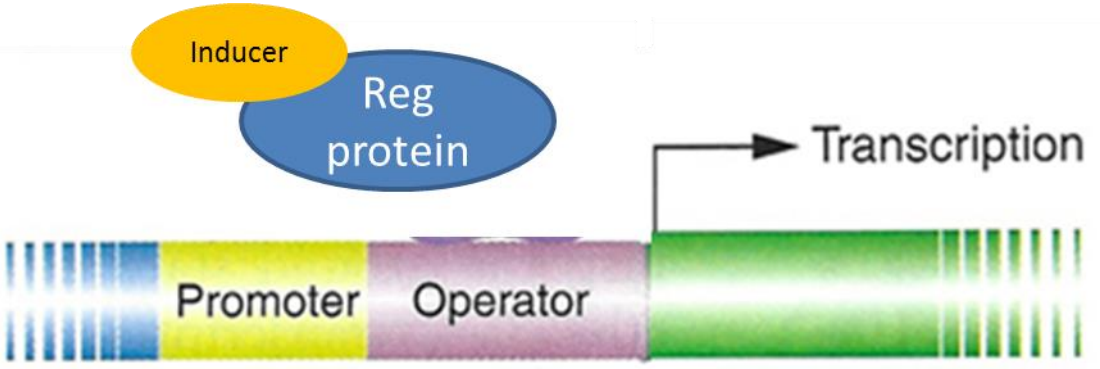
- Synthesis can be prevented when a **repressor** protein binds to an **operator**, a specific seq of DNA
- Repressor **stops binding of RNA polymerase**

Inducible enzymes

- Synthesis only occurs when substrate is present
- **Inducer** that binds to **regulatory protein**

→ Gene is switched on

E.g. the lac enzymes



Gene Control in Prokaryotes: Operons

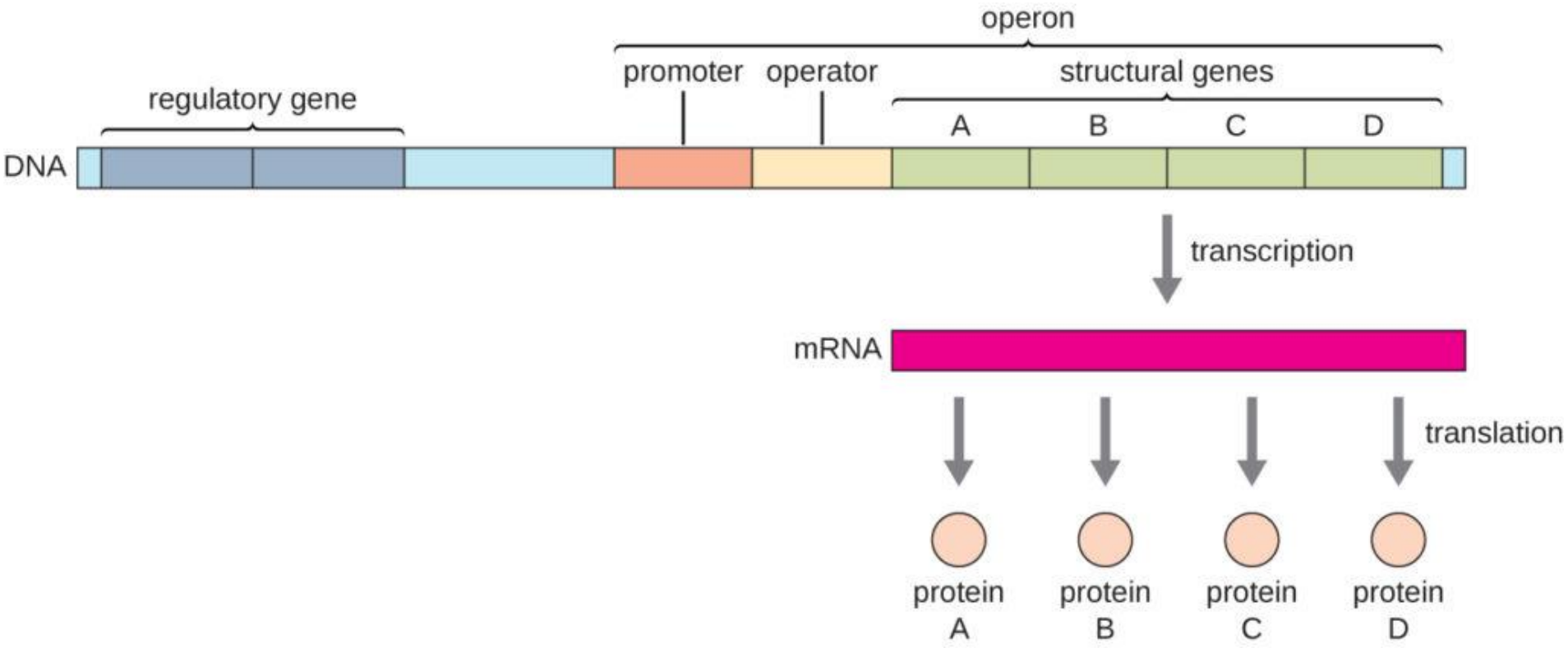
- Found in **prokaryotic** DNA
- Makes up a unit of gene expression in bacterium
- Regulatory gene is close to the operon

Operons consist of:

- **One or more structural genes**, under control of a single promoter

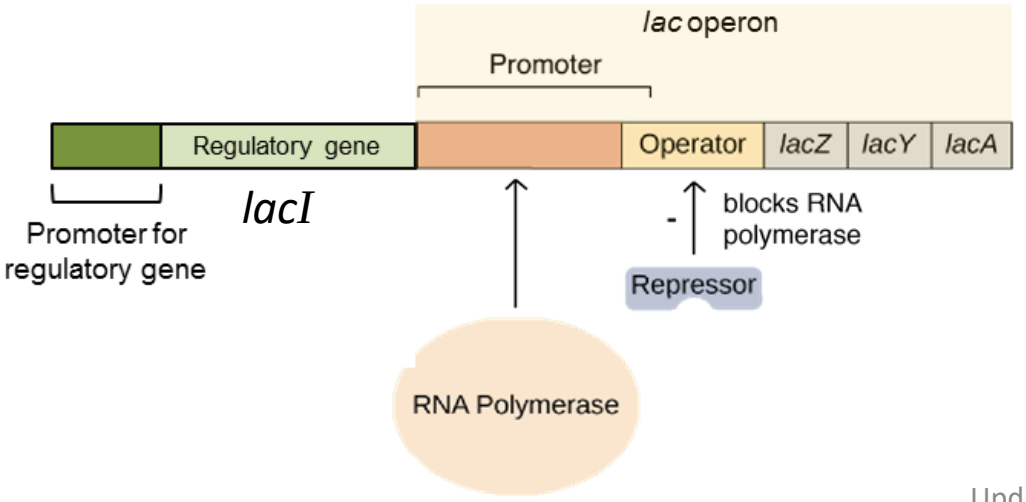
- Control region of DNA, which are specific seq recognised by regulatory proteins and enzymes
  - **Promoter** = where **RNA polymerase** binds
  - **Operator** = where **repressor** binds

Gene Control in Prokaryotes: Operons



The *lac* operon

- Found in *Escherichia coli* bacteria
- The bacteria lives on sugar, i.e. glucose and lactose
- ***Lac* operon = set of 3 genes** next to each other
- Code for **3 repressible, inducible enzymes**
  - *lacZ* = codes for β-galactosidase (breaks down lactose into galactose and glucose)
  - *lacY* = codes for permease (increases lactose uptake)
  - *lacA* = codes for transacetylase

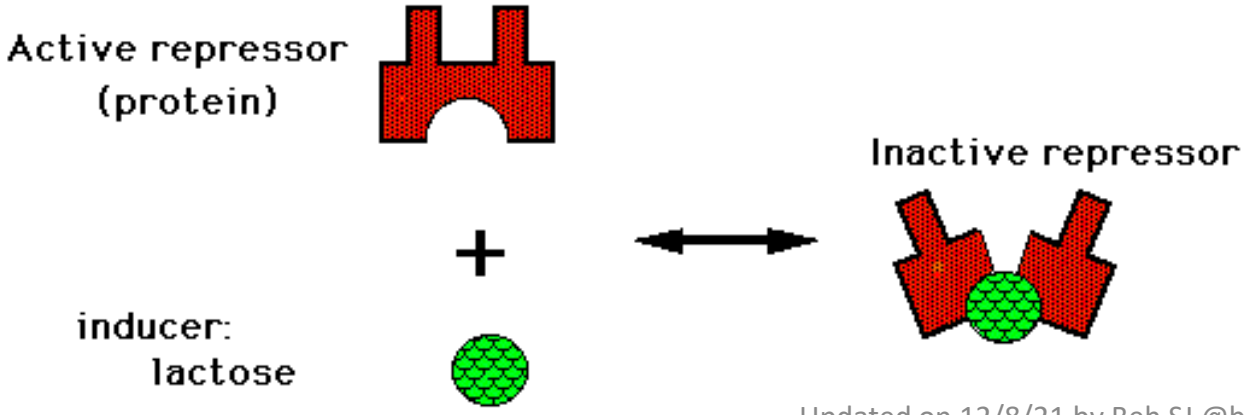


The *lac* operon

- **Regulatory gene, *lacI*** that codes for repressor is close by
- Repressor is a **constitutive protein** = produced all the time

- Repressor protein is an **allosteric protein = has 2 binding sites**
  1. DNA-binding site (to bind to operator region)
  2. Lactose-binding site

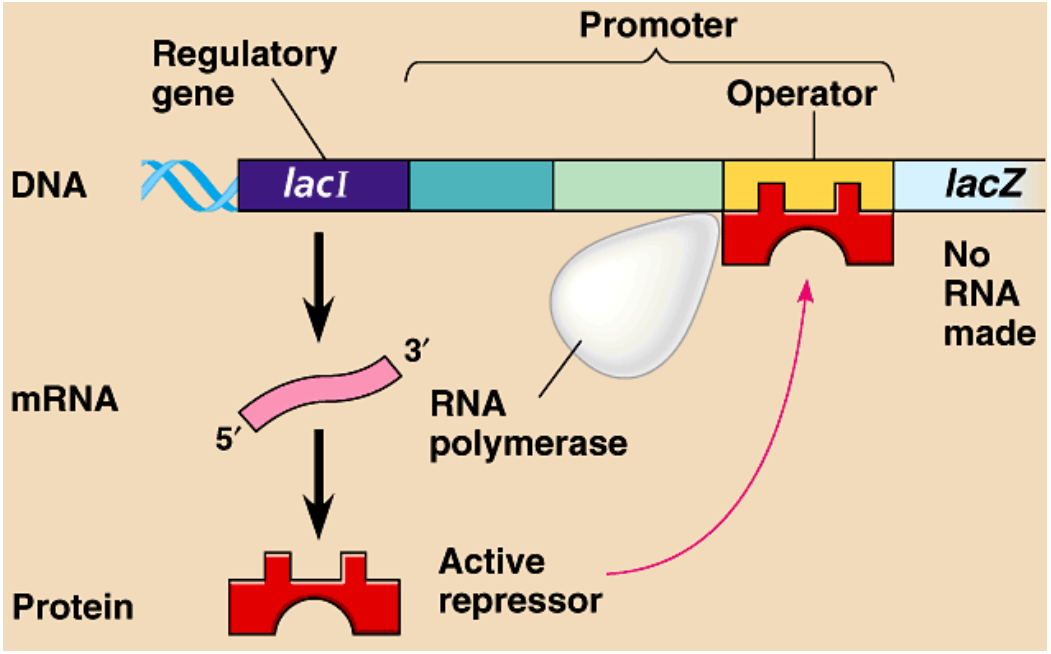
- When **lactose binds** to its site, the shape of protein changes
- **DNA-binding site is closed**
- Repressor is inactivated



The *lac* operon

When there is **no lactose**:

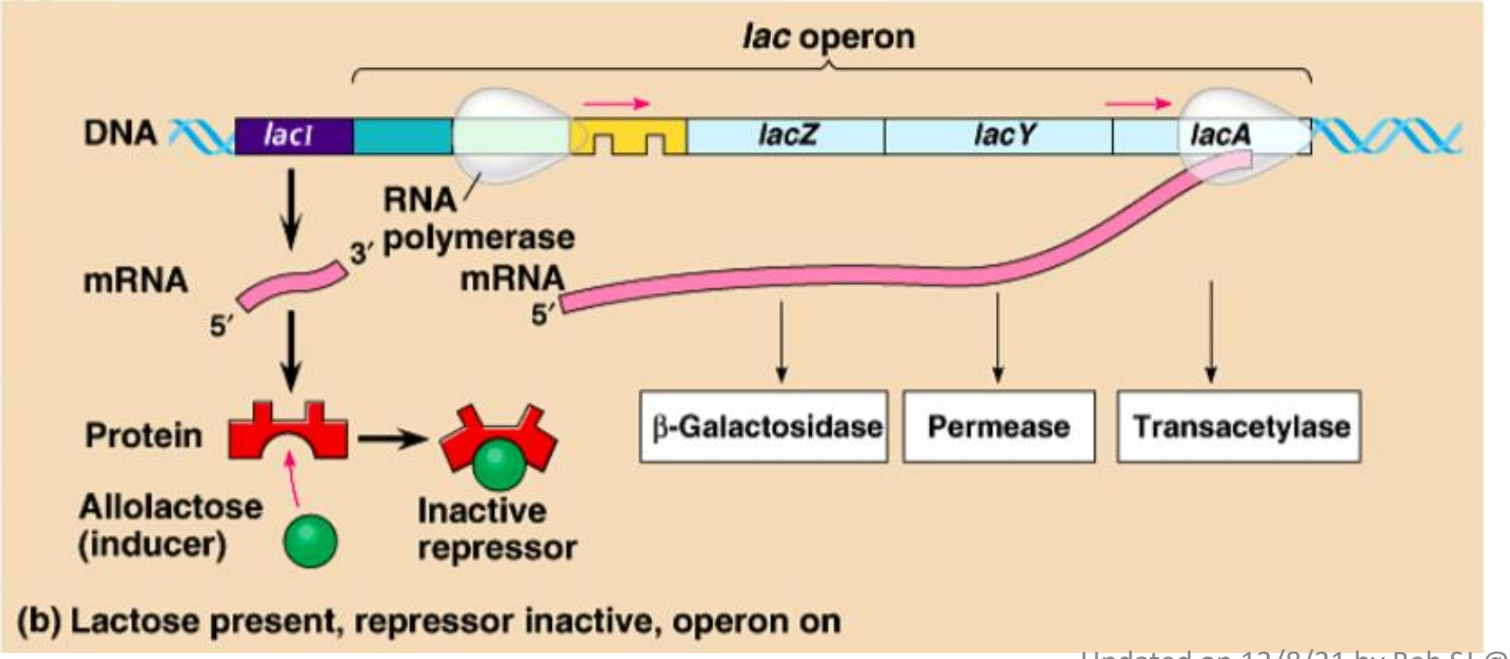
- Regulatory gene codes for repressor
- Repressor not bound to lactose
- **Repressor** binds to the **operator** region
- **RNA polymerase** cannot move to operator and structural genes
- **NO transcription** of the 3 genes
- Genes are switched **OFF**



The *lac* operon

When **lactose is present**:

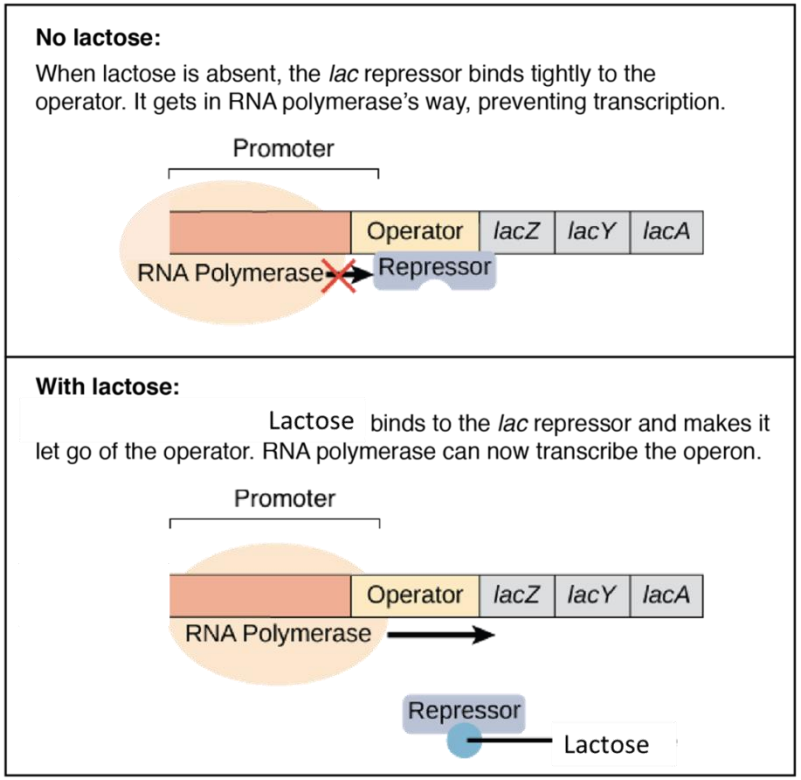
- Lactose is taken up by bacteria
- **Lactose acts as inducer** and binds to **repressor**
- Repressor changes shape, and cannot bind to the **operator** region on DNA
- **RNA polymerase** can bind to promoter and move to operator and genes
- **Transcription occurs**
- Genes are switched **ON**



The *lac* operon

Benefits of this mechanism:

- Allow bacteria to produce the 3 enzymes only when lactose is available
- When both glucose and lactose available, bacteria prefers glucose – can repress the *lac* operon using another transcription factor
- 3 enzymes produced in equal amounts
- Avoids waste of energy and materials



Gene Control in Eukaryotes

- **Genome size is larger than prokaryotes**
- **Have more diff transcription factors and mechanism to regulate gene expression**
- In humans, 10% genes code for transcription factors

Functions of transcription factors:

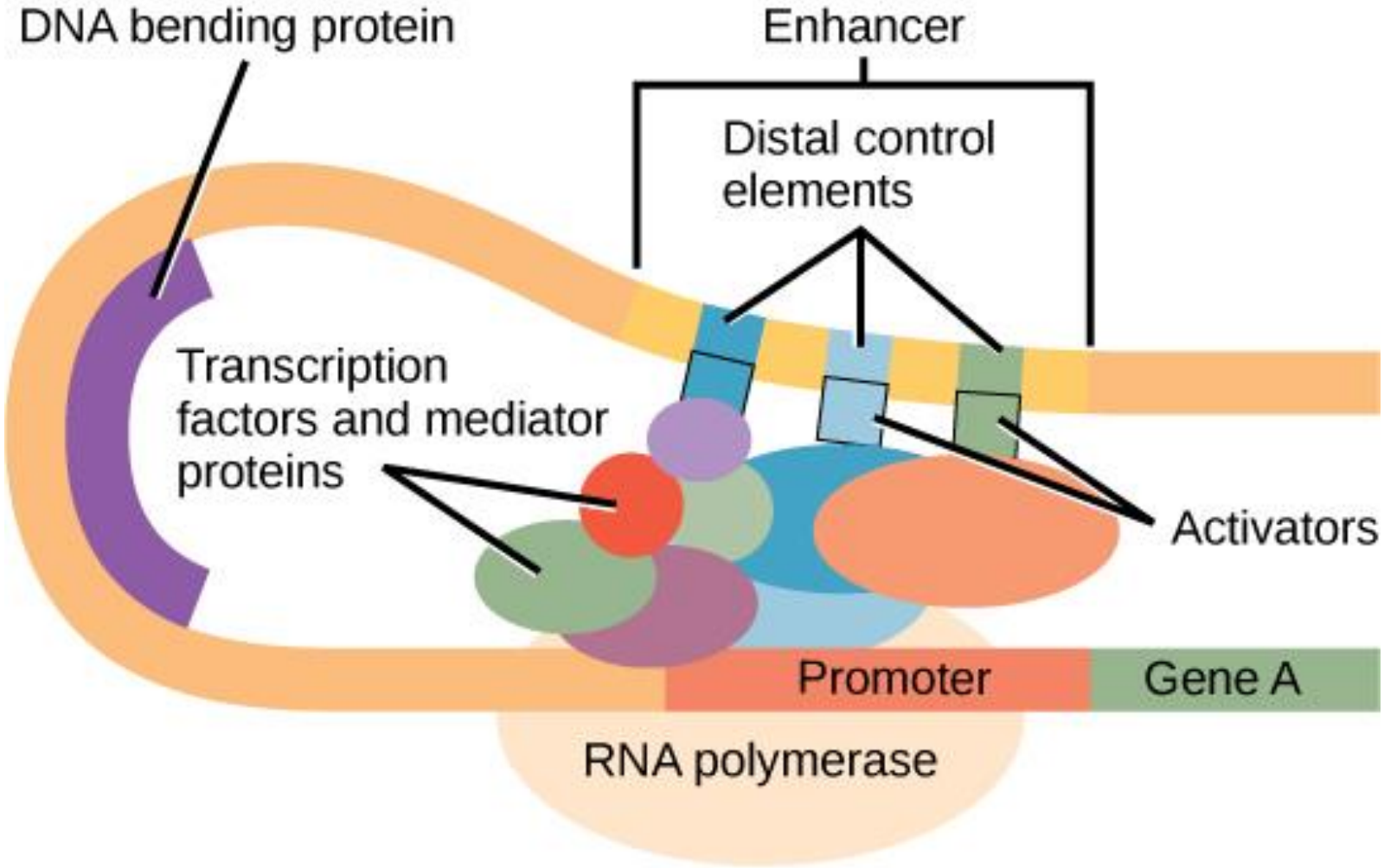
- General TFs = form part of the protein complex that binds to the promoter region with RNA polymerase

→ **transcription**

- Activate appropriate gene in sequence

→ allow correct **pattern of development** of body regions

- **Determination of sex** in mamals
- Allow **responses to environmental stimuli** e.g. temp
- Products of proto-oncogenes and tumour suppressor genes and other TFs, **regulate the cell cycle, growth and apoptosis**
- TFs carry out the effect in **response to hormones**


DNA bending protein
Enhancer
Distal control elements
Transcription factors and mediator proteins
Activators
Promoter
Gene A
RNA polymerase

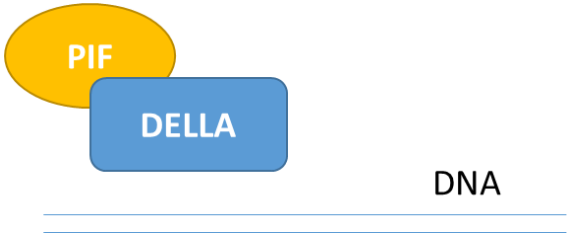
Chap 15 Recap

Gene Control in Plants

Role of Gibberellin in Stem Elongation

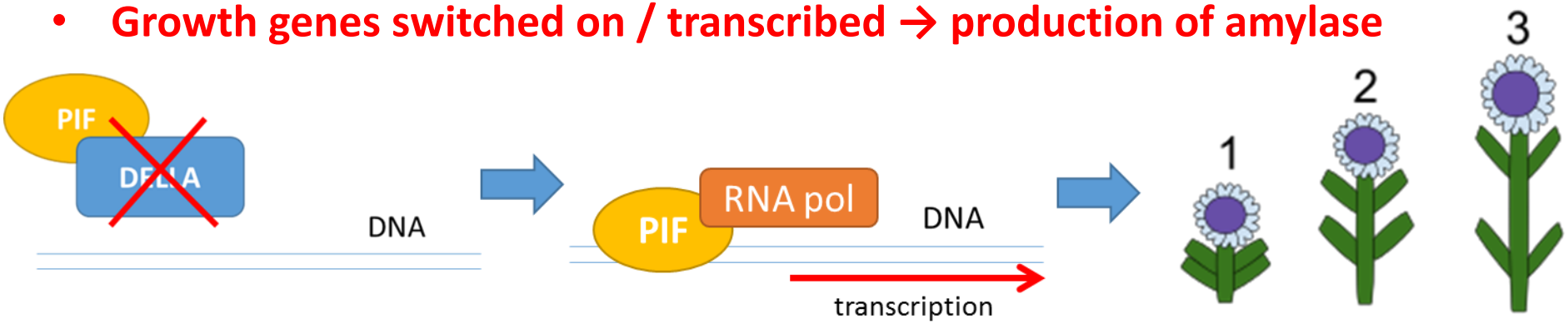
Without GA:

- Transcription factor (i.e. PIF) attached to DELLA protein
- TF cannot bind to DNA



When GA binds to receptor:

- **causes DELLA protein destruction**
- inhibition of transcription removed
- TF **binds to DNA**
- TF recruits **RNA polymerase to bind to DNA**
- **Growth genes switched on / transcribed → production of amylase**



Chapter Outline

4 Parts!

1. Meiosis
2. Mendelian Inheritance + Chi-squared test
3. More Patterns of Inheritance
4. Gene Control