Chapter V

Genetics of diploïds

Overview:

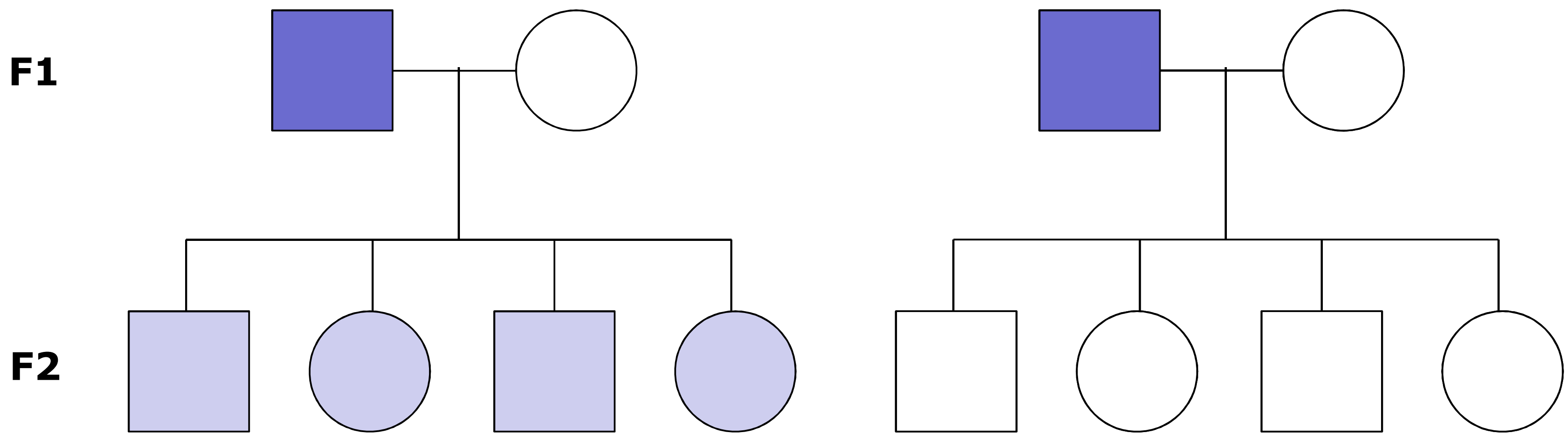
- What genetic principles explain the transmission of traits (characteristics) from parents to offspring ?

Is inheritance blending or particulate?

1. In the mid 19th century,biologists believed that inheritance was blending, that is, traits of offspring were the average of their parents.

2. Problematic because new genetic variations would quickly be diluted and could not be accumulated and passed to subsequent generations as theory of evolution predicted.

3. Blending inheritance was quickly discredited by Gregor Mendel's experiments, which showed that inheritance is particulate.



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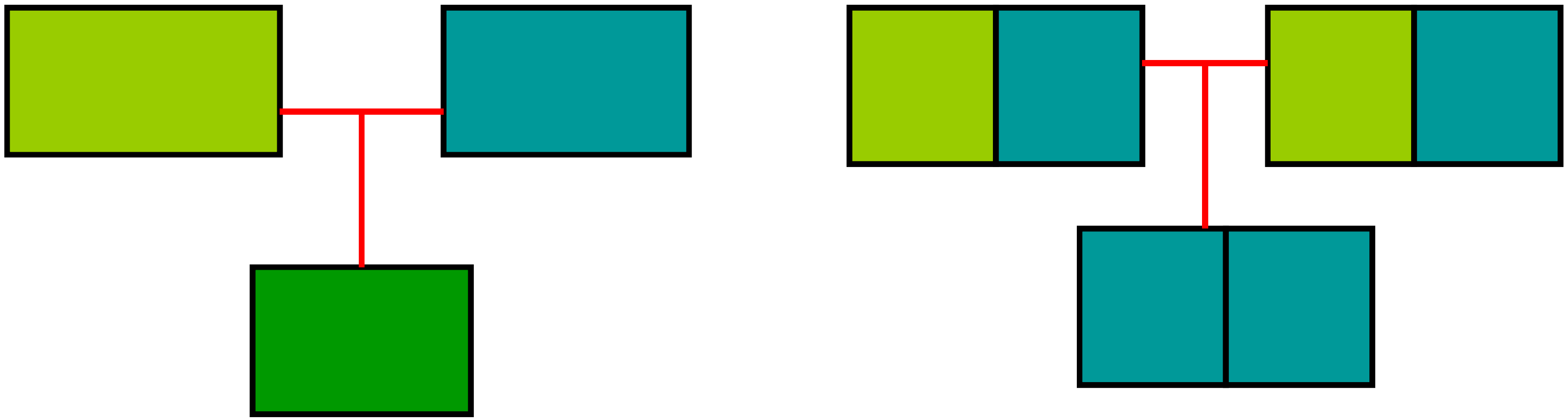


L'héritage se mélange-t-il ou il est particulaire?

- L'hypothèse «particulaire» est l'idée que les parents transmettent des unités héréditaires distinctes (gènes)

- Mendel a documenté un mécanisme particulaire à travers ses expériences

- Il a découvert les principes fondamentaux de l'hérédité en cultivant des pois dans des expériences

Genetic Vocabulary

- **Character**: a heritable feature, such as flower color
- **Trait**: a variant of a character, such as purple or white flowers
- Each trait carries two copies of a unit of inheritance, one inherited from the mother and the other from the father
- Alternative forms of traits are called alleles

Terminology

- **Gene** = fundamental unit of heredity, 2 copies/cell
- **Allele** = a different version of a gene (derived from the Greek allel = another)
- **Wild allele** = most frequent/non-pathological.
- **Zygote** = product of the fusion of 2 gametes
- **Genotype** = allelic constitution of an individual's genes (at a given locus).
- **Phenotype** = aspect of the organism
- **Locus** = physical site where a DNA sequence (coding or not) is located on a chromosome
- **Loci** = multiple loci.

Terminology

Pure lineage: being pure lineage for a trait means that the two homologous chromosomes possess at the same locus the same two alleles for the gene in question.

Homozygous: an individual who has two identical alleles of the same gene (AA or aa).

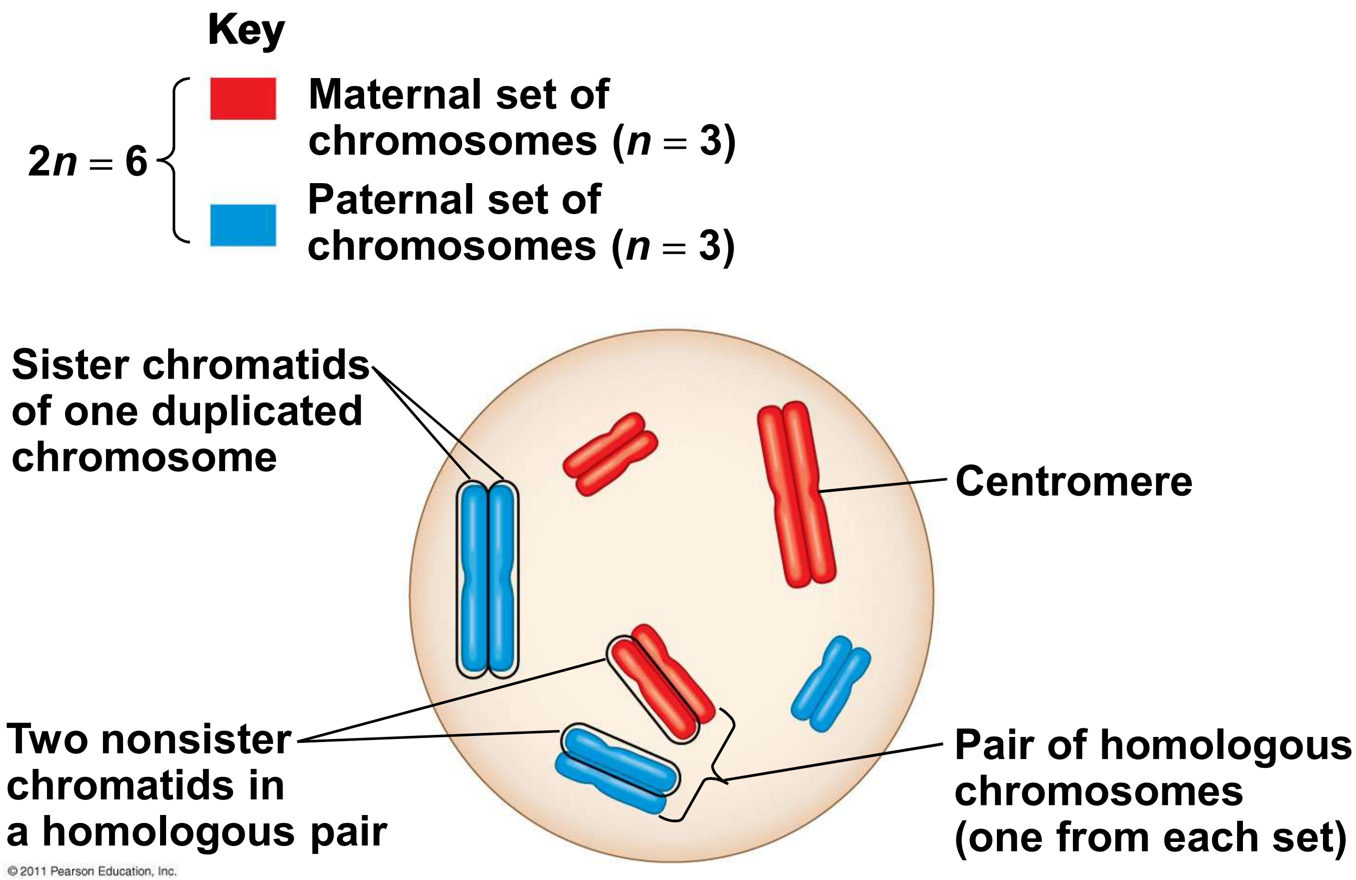
Heterozygous: an individual who has two different alleles for the same gene (Aa)

Phenotype: visible manifestation of the genotype. More generally, it is the set of observable characteristics of an individual, depending on the genotype in interaction with the environment.

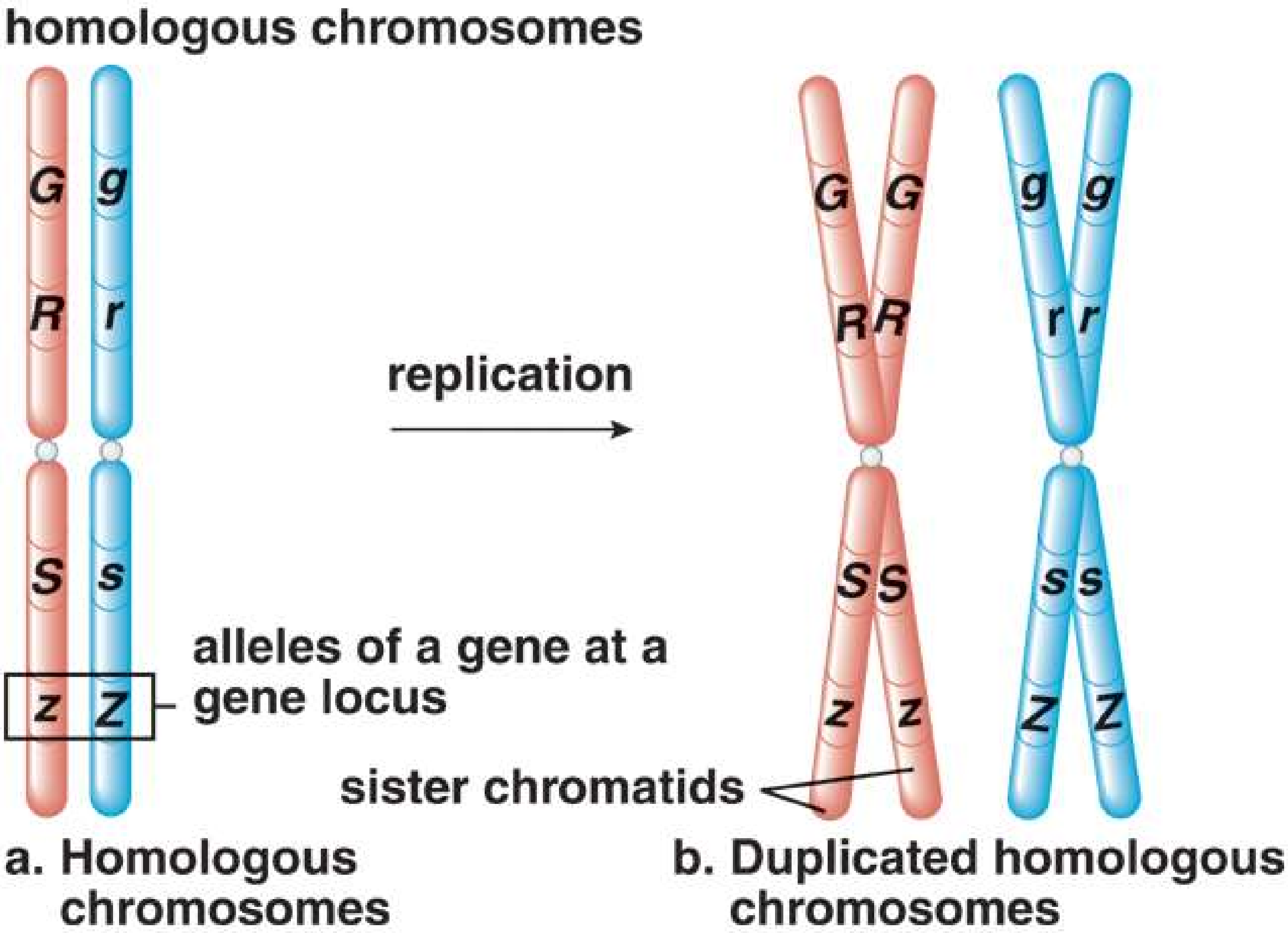
Terminology

- **Generations:**
  - P = parental generation
  - F1 = First filial generation, the offspring of generation P
  - F2 = 2nd filial generation, the descendants of the F1 generation (same for F3 and so on)
- **Crossing :**
  - Mating between a male and a female

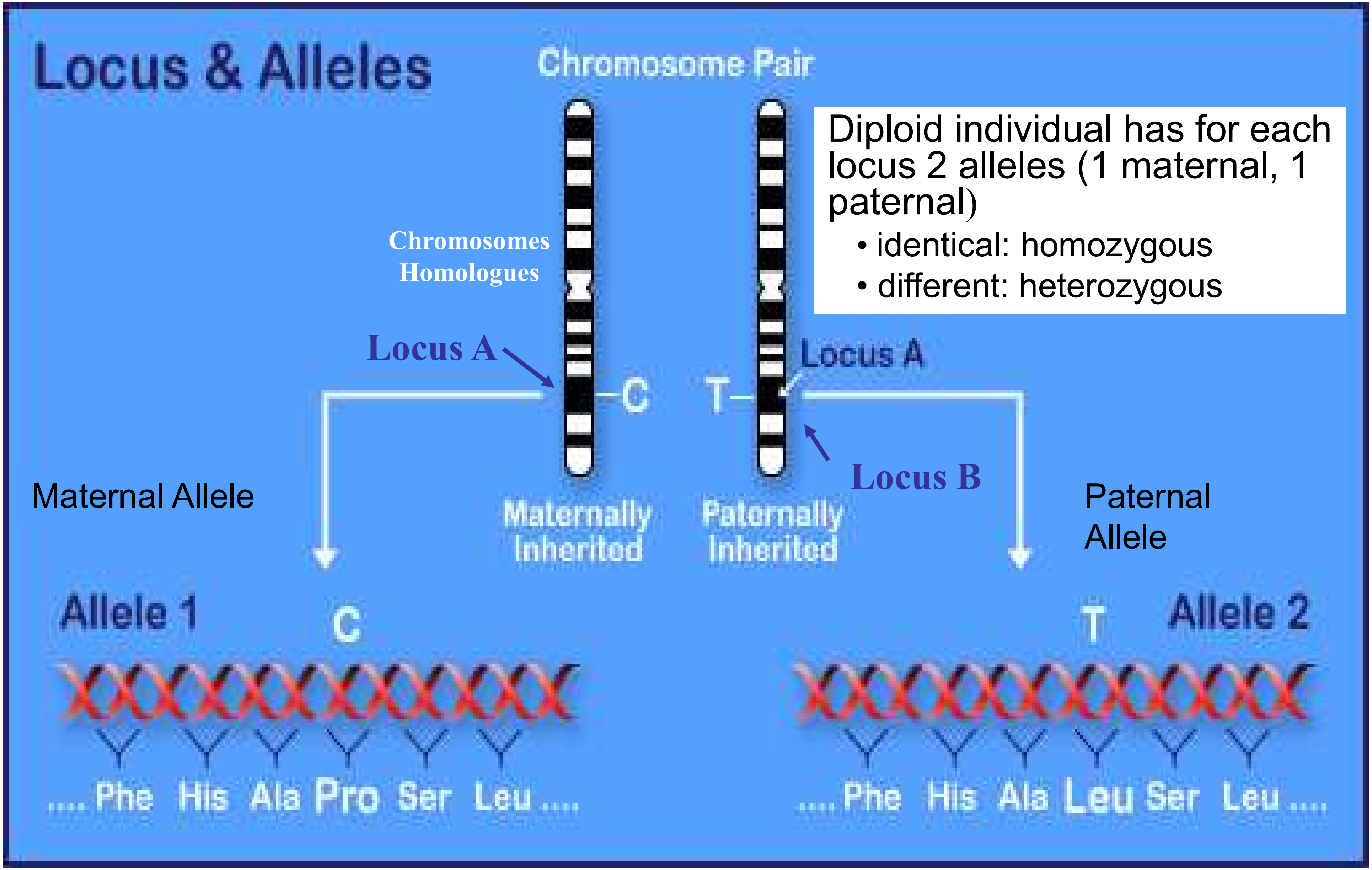
- in a cell in which DNA synthesis has occurred - each chromosome has been replicated
- each **duplicated chromosome** consists of two identical **sister chromatids** joined at a **centromere**



Locus & alleles



Locus et allèles



Wild allele: most frequent/non-pathological.

Dominance – Recessivity

Phenotypic expression of different alleles

- **Dominance :** the dominant allele A always manifests its character

	Genotype	Phenotype
Homozygous	AA	[A]
Heterozygous	Aa	[A]

  - **Co-dominance** : **Aa** expresses both AA and aa genotype (eg: Blood groups A and B)
  - **Incomplete dominance** : Aa phenotype is intermediate between AA and aa

- **Recessivity**
  - Allèle récessif **a** ne se manifeste pas en présence de **A,** ne s'exprime qu'à l'état homozygote

	Genotype	Phenotype
Heterozygous	Aa	[A]
Homozygous	aa	[a]

Conventional writing

- **Phenotype** : it's in brackets [ ]
- **Génotype** : it's in parentheses ( )

- **Dominant Character** : first letter of the character is capitalized, ex: L , G .

  It is expressed in the phenotype when it is present in only **one version**.

- **Recessive character**: first letter of the character put into tiny, ex : vg , e .

  It is expressed in the phenotype when he is present in **two versions**.

Gene transmission diploids(2n)

1) The transmission of a single character
(animals with only one difference):
- It’s **monohybridism** ex: Hair color in mice (wild mouse: gray, mutant mouse: white)

2) The transmission of two characters:
- It’s **dihybridism** Ex: In Drosophils (wings length, eye color, body color etc ...)

3) The transmission of three and more characters:
- it is **multihybridism**

Monohybrid Crossing

(study of a single character)

Mendel’s Experiments - Monohybrid Crossing

- A crossing between two parents who have different forms of a gene designated under the name of **Monohybridism**.
- Ex: Involve plants that differ for a single character: Large x Short, purple flower x white flower, round seed x seed wrinkled.

Mendel's Contributions

Mendel's Life:

- Born July 20, 1822 in Czech Rep.

- Entered Augustinian Abbey in Brno – 1843

Mendel's Contributions

Mendel's Life:

- 1856-63: tested 29,000 pea plants

- 1866: Published "Experiments on Plant Hybridization", which was only cited 3 times in 35 yrs

- Died Jan 6, 1884 in Brno.

Mendel’s Experiments

- In a typical experiment, Mendel mated two contrasting, true-breeding varieties, a process called **hybridization**
- The true-breeding parents are the **P generation**
- The hybrid offspring of the P generation are called the **F_1 generation**
- When F_1 individuals self-pollinate, the **F_2 generation** is produced

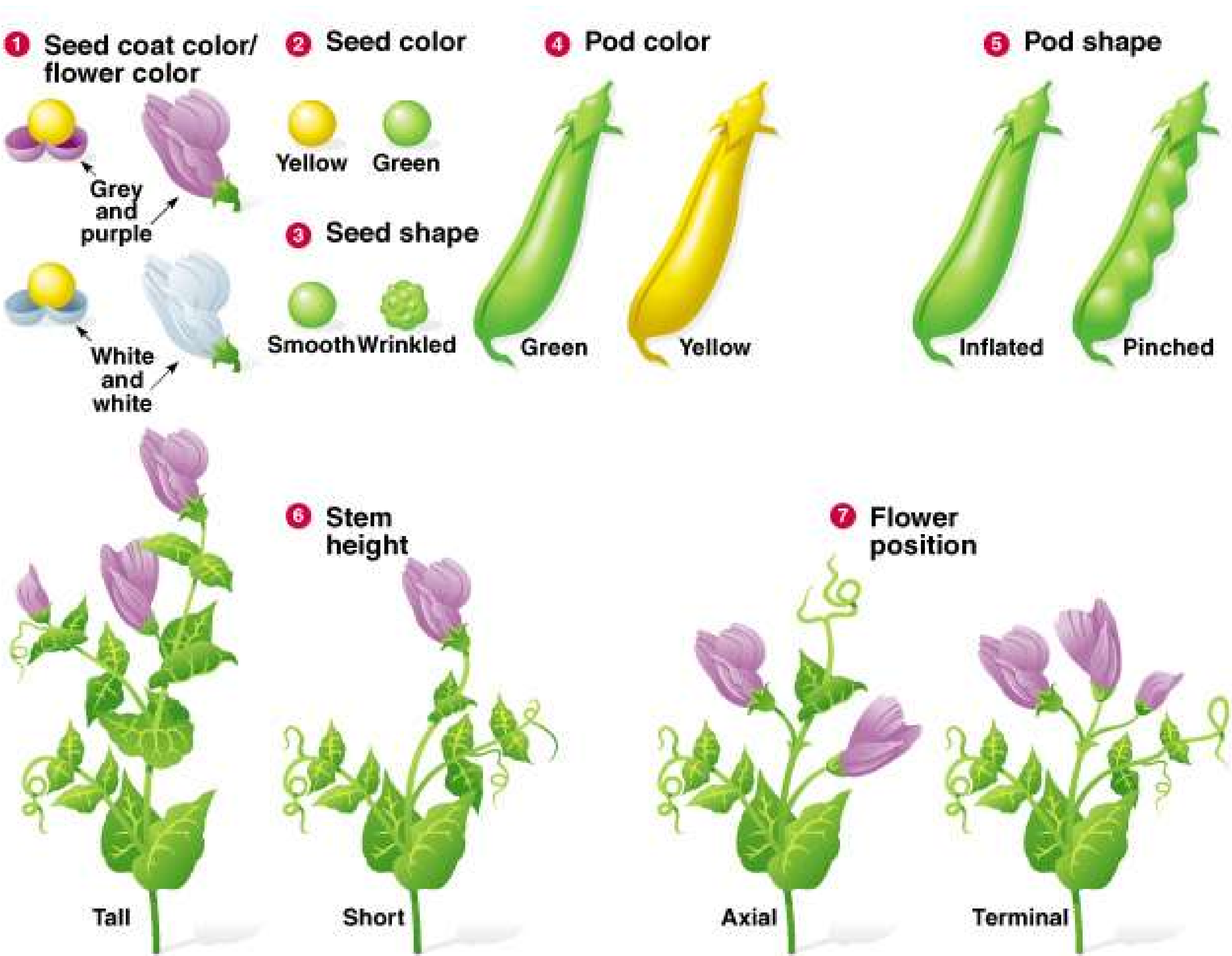
Mendel's Experiments:

1. Began by self-fertilizing 34 different pea strains (phenotypes) so that they bred true (selfing, the opposite of cross-fertilization).

2. Focused on 7 well-defined garden pea traits by crossing different phenotypes one at a time:

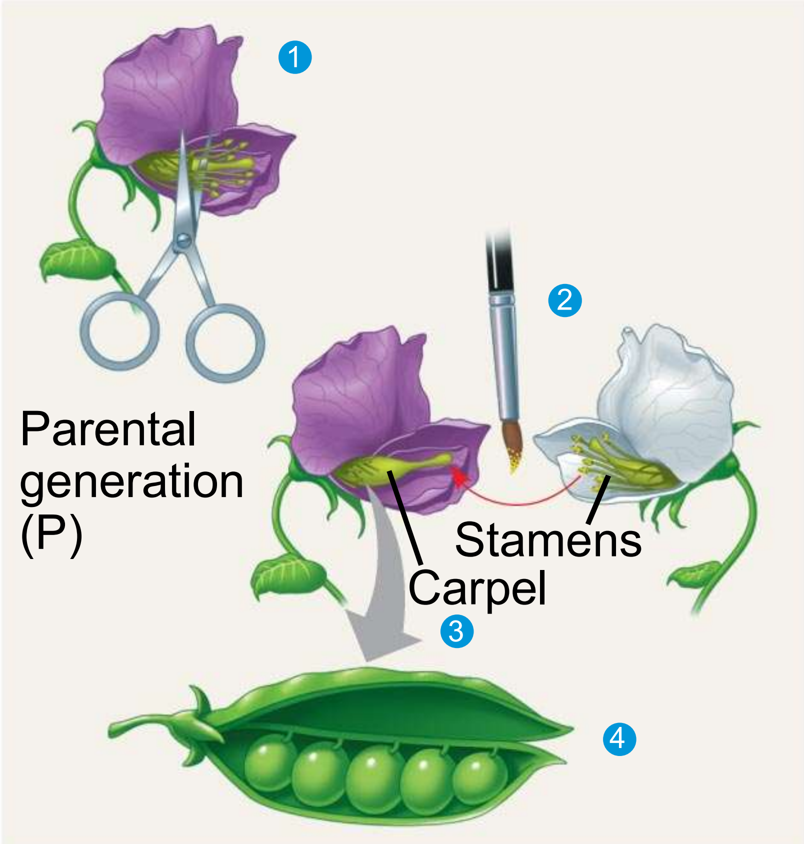
Flower/seed coat color:	purple vs. white flowers grey vs. white seed coats (*controlled by single gene)
Seed color:	yellow vs. green
Seed shape:	smooth vs. wrinkled
Pod color:	green vs. yellow
Pod shape:	inflated vs. pinched
Stem height:	tall vs. short
Flower position:	axial vs. terminal

3. Counted offspring of each phenotype and analyzed the results mathematically.

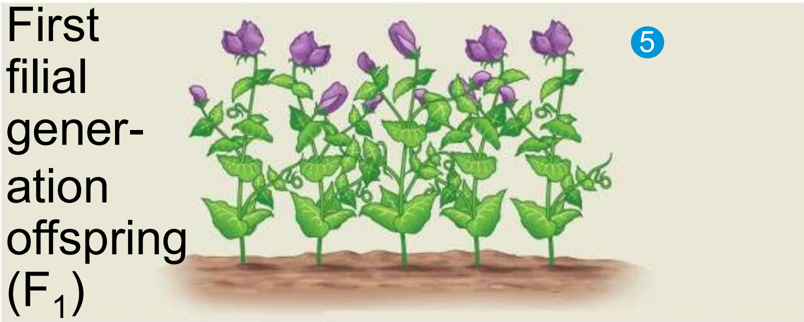


Mendel's 7 garden pea characters.

TECHNIQUE



RESULTS



Mendel’s Experimental, Quantitative Approach

- Advantages of pea plants for genetic study:
  - There are many varieties with distinct heritable features, or **characters** (such as flower color); character variants (such as purple or white flowers) are called **traits**
  - Each character has only 2 forms "2 variations"
  - Mating of plants can be controlled
  - Each pea plant has sperm-producing organs (stamens) and egg-producing organs (carpels)
  - Cross-pollination (fertilization between different plants) can be achieved by dusting one plant with pollen from another

Mendel’s Experiments:

- Mendel chose to track only those characters that varied in an either-or manner

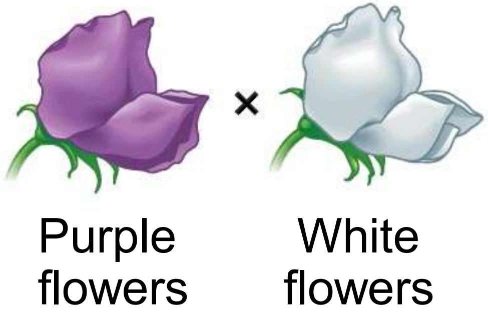
- He also used varieties that were **true-breeding** (plants that produce offspring of the same variety when they self-pollinate)

The Law of Segregation

- When Mendel crossed contrasting, true-breeding white and purple flowered pea plants, all of the F_1 hybrids were purple
- When Mendel crossed the F_1 hybrids, many of the F_2 plants had purple flowers, but some had white
- Mendel discovered a ratio of about three to one (1:3), purple to white flowers, in the F_2 generation

EXPERIMENT

P Generation
(true-breeding
parents)



EXPERIMENT True-breeding purple-flowered pea plants and white-flowered pea plants were crossed (symbolized by ×). The resulting F_1 hybrids were allowed to self-pollinate or were cross- pollinated with other F_1 hybrids. Flower color was then observed in the F_2 generation.

RESULTS Both purple-flowered plants and white-flowered plants appeared in the F_2 generation. In Mendel's experiment, 705 plants had purple flowers, and 224 had white flowers, a ratio of about 3 purple : 1 white.

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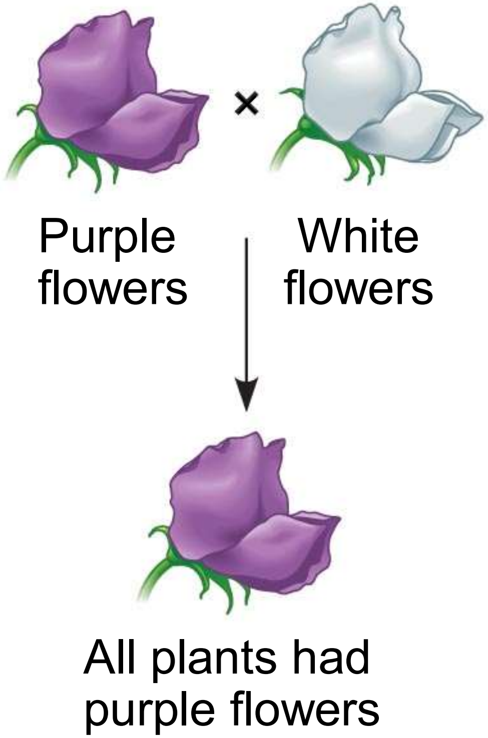
P Generation (true-breeding parents)

F_1 Generation (hybrids)



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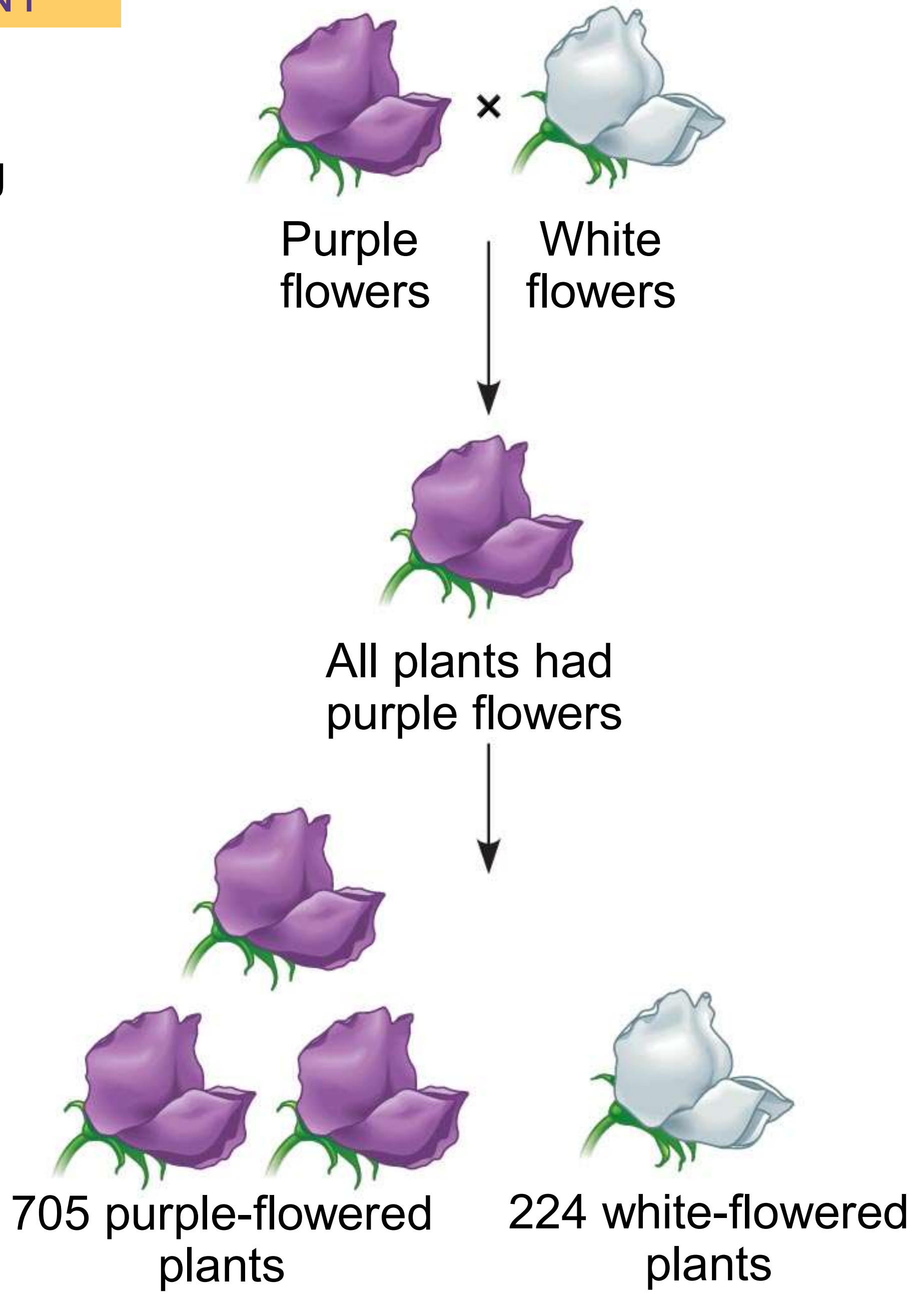
P Generation (true-breeding parents)

F_1 Generation (hybrids)

F_2 Generation



- Mendel reasoned that only the purple flower factor was affecting flower color in the F_1 hybrids
- Mendel called the purple flower color a dominant trait and the white flower color a recessive trait
- Mendel observed the same pattern of inheritance in six other pea plant characters, each represented by two traits
- What Mendel called a “heritable factor” is what we now call a gene

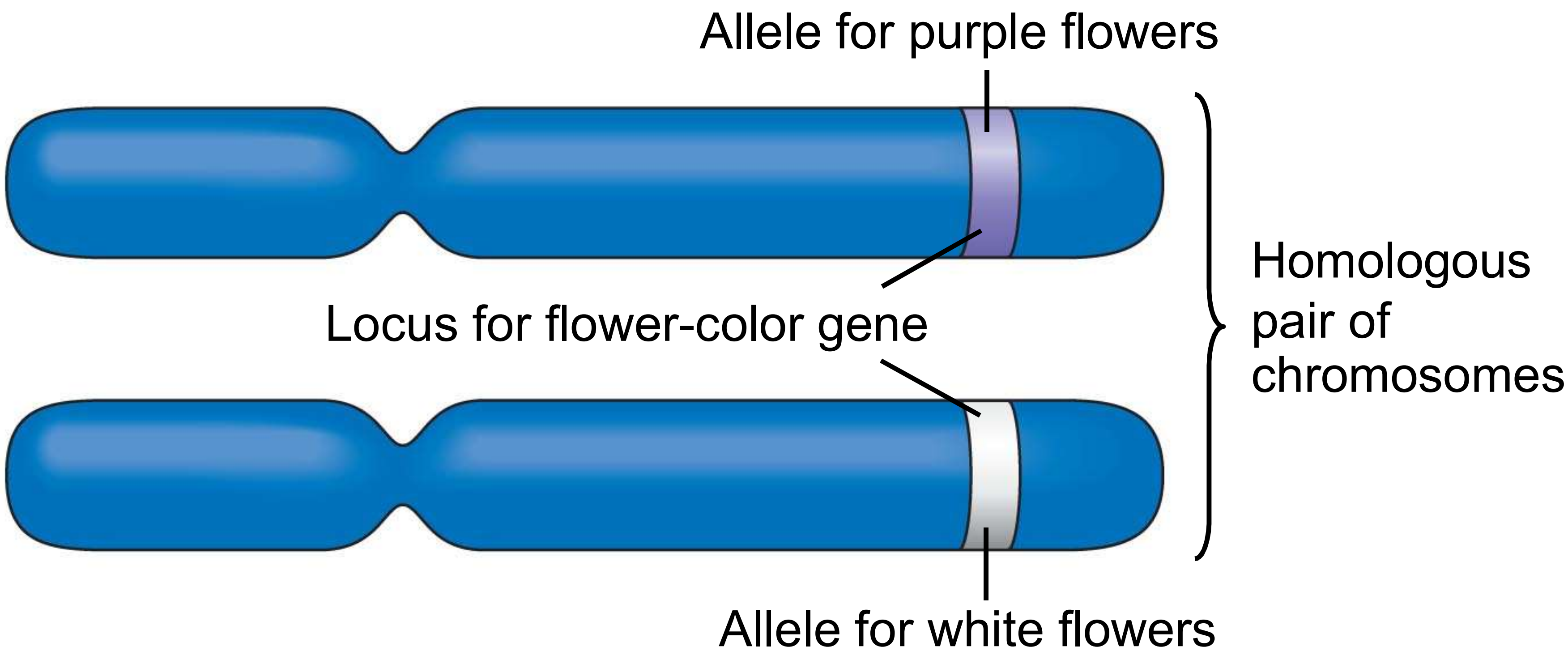
Table 14-1

Table 14.1 The Results of Mendel's F_1 Crosses for Seven Characters in Pea Plants

Character	Dominant Trait	x	Recessive Trait	F_2 Generation Dominant:Recessive	Ratio
Flower color	Purple 	×	White 	705:224	3.15:1
Flower position	Axial 	×	Terminal 	651:207	3.14:1
Seed color	Yellow 	×	Green 	6,022:2,001	3.01:1
Seed shape	Round 	×	Wrinkled 	5,474:1,850	2.96:1
Pod shape	Inflated 	×	Constricted 	882:299	2.95:1
Pod color	Green 	×	Yellow 	428:152	2.82:1
Stem length	Tall 	×	Dwarf 	787:277	2.84:1

- Mendel developed a hypothesis to explain the 3:1 inheritance pattern he observed in F_2 offspring
- Four related concepts make up this model
- These concepts can be related to what we now know about genes and chromosomes

- The first concept is that alternative versions of genes account for variations in inherited characters
- For example, the gene for flower color in pea plants exists in two versions, one for purple flowers and the other for white flowers
- These alternative versions of a gene are now called **alleles**
- Each gene resides at a specific locus on a specific chromosome


Allele for purple flowers
Locus for flower-color gene
Homologous
pair of
chromosomes
Allele for white flowers

- The second concept is that for each character an organism inherits two alleles, one from each parent
- Mendel made this deduction without knowing about the role of chromosomes
- The two alleles at a locus on a chromosome may be identical, as in the true-breeding plants of Mendel’s P generation
- Alternatively, the two alleles at a locus may differ, as in the F_1 hybrids

- The third concept is that if the two alleles at a locus differ, then one (the **dominant allele**) determines the organism's appearance, and the other (the **recessive allele**) has no noticeable effect on appearance
- In the flower-color example, the F_1 plants had purple flowers because the allele for that trait is dominant

The Law of Segregation

- The fourth concept, now known as the **law of segregation**, states that the two alleles for a heritable character separate (segregate) during gamete formation and end up in different gametes
- Thus, an egg or a sperm gets only one of the two alleles that are present in the somatic cells of an organism
- This segregation of alleles corresponds to the distribution of homologous chromosomes to different gametes in meiosis

The Law of Segregation

- Mendel's segregation model accounts for the 3:1 ratio he observed in the F_2 generation of his numerous crosses
- The possible combinations of sperm and egg can be shown using a **Punnett square**, a diagram for predicting the results of a genetic cross between individuals of known genetic makeup
- A capital letter represents a dominant allele, and a lowercase letter represents a recessive allele

Fig. 14-5-1

Each true-breeding plant of the parental generation has identical alleles, *PP* or *pp*.

Gametes (circles) each contain only one allele for the flower-color gene. In this case, every gamete produced by one parent has the same allele.

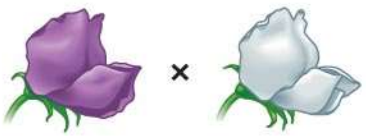
Union of the parental gametes produces F_1 hybrids having a *Pp* combination. Because the purple-flower allele is dominant, all these hybrids have purple flowers.

When the hybrid plants produce gametes, the two alleles segregate, half the gametes receiving the *P* allele and the other half the *p* allele.

This box, a Punnett square, shows all possible combinations of alleles in offspring that result from an $F_1 \times F_1$ (*Pp* × *Pp*) cross. Each square represents an equally probable product of fertilization. For example, the bottom left box shows the genetic combination resulting from a *p* egg fertilized by a *P* sperm.

Random combination of the gametes results in the 3:1 ratio that Mendel observed in the F_2 generation.

P Generation



Appearance:	Purple flowers	White flowers
Genetic makeup:	*PP*	*pp*
Gametes:	*P*	*p*

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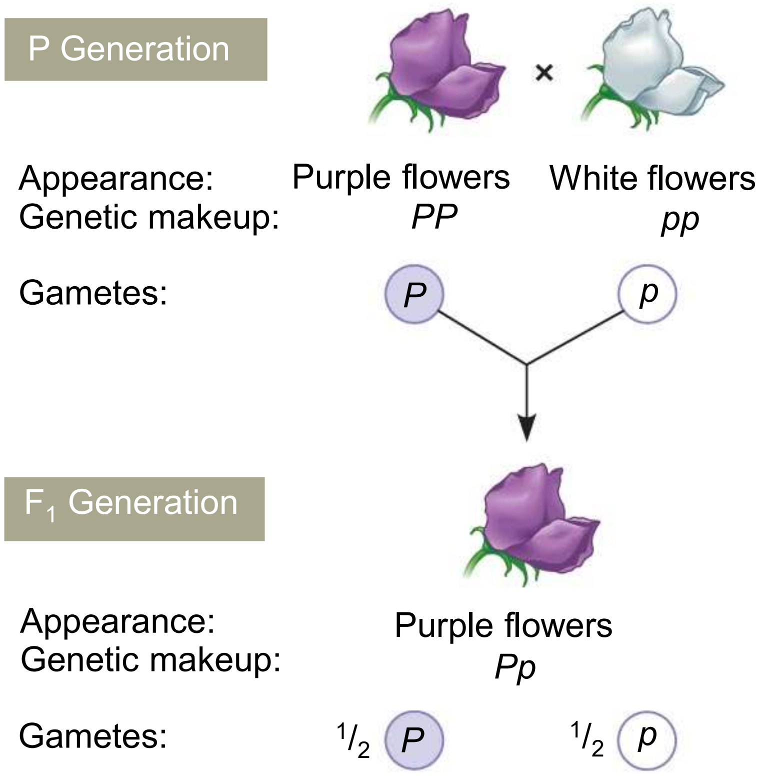

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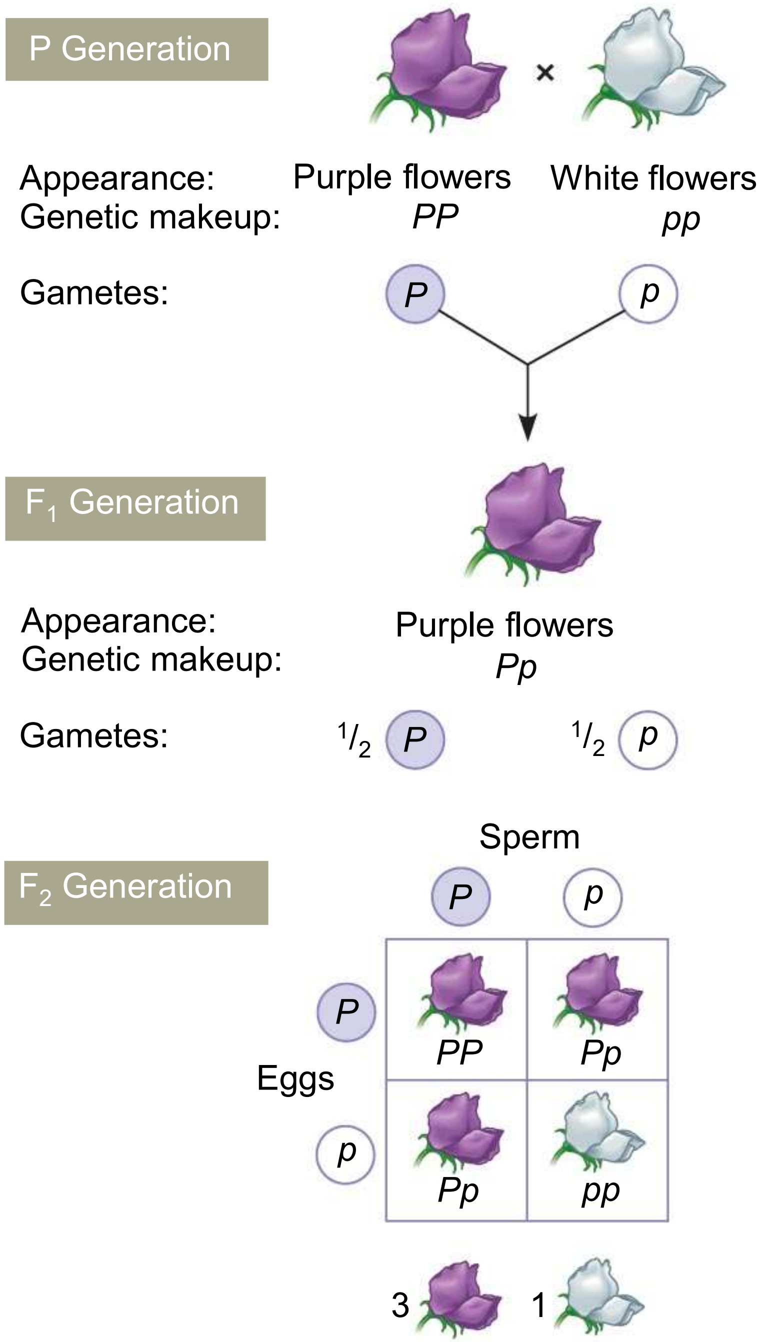
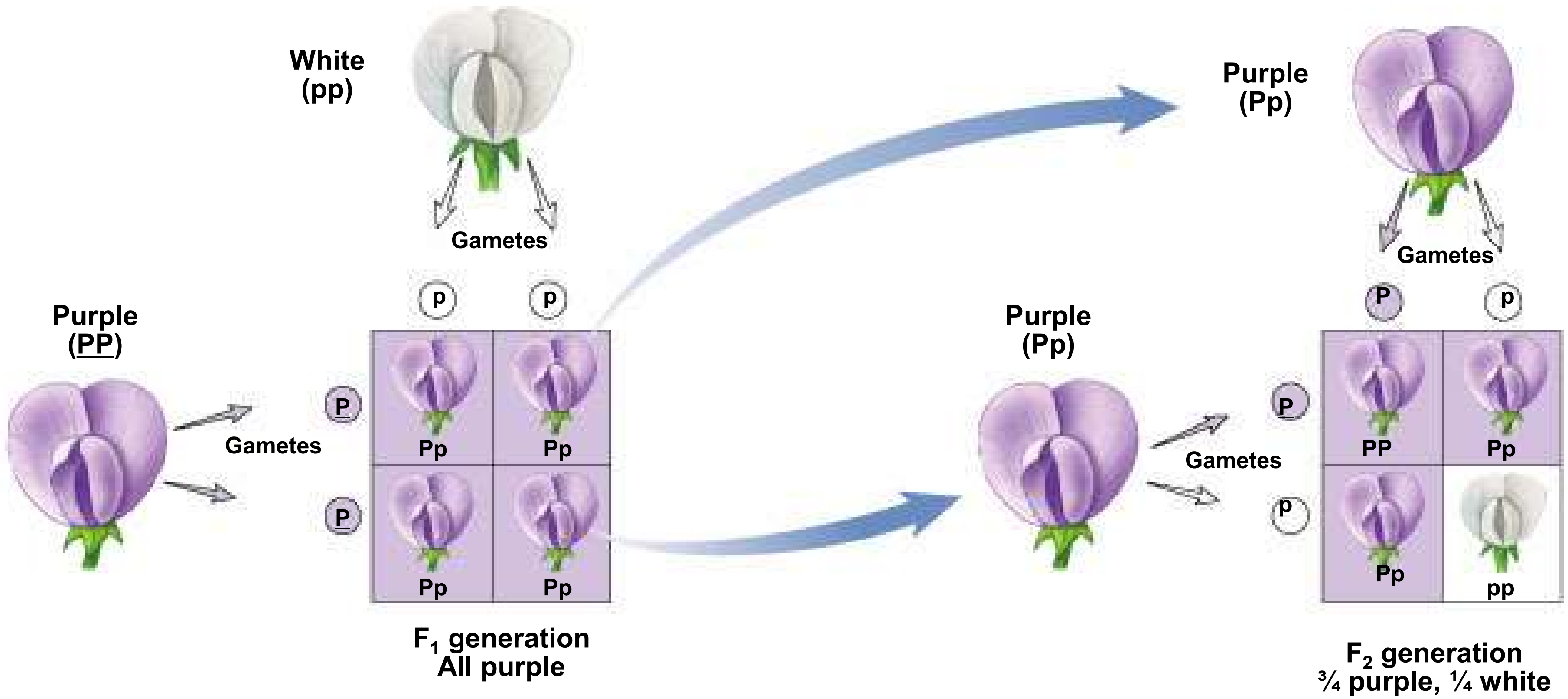
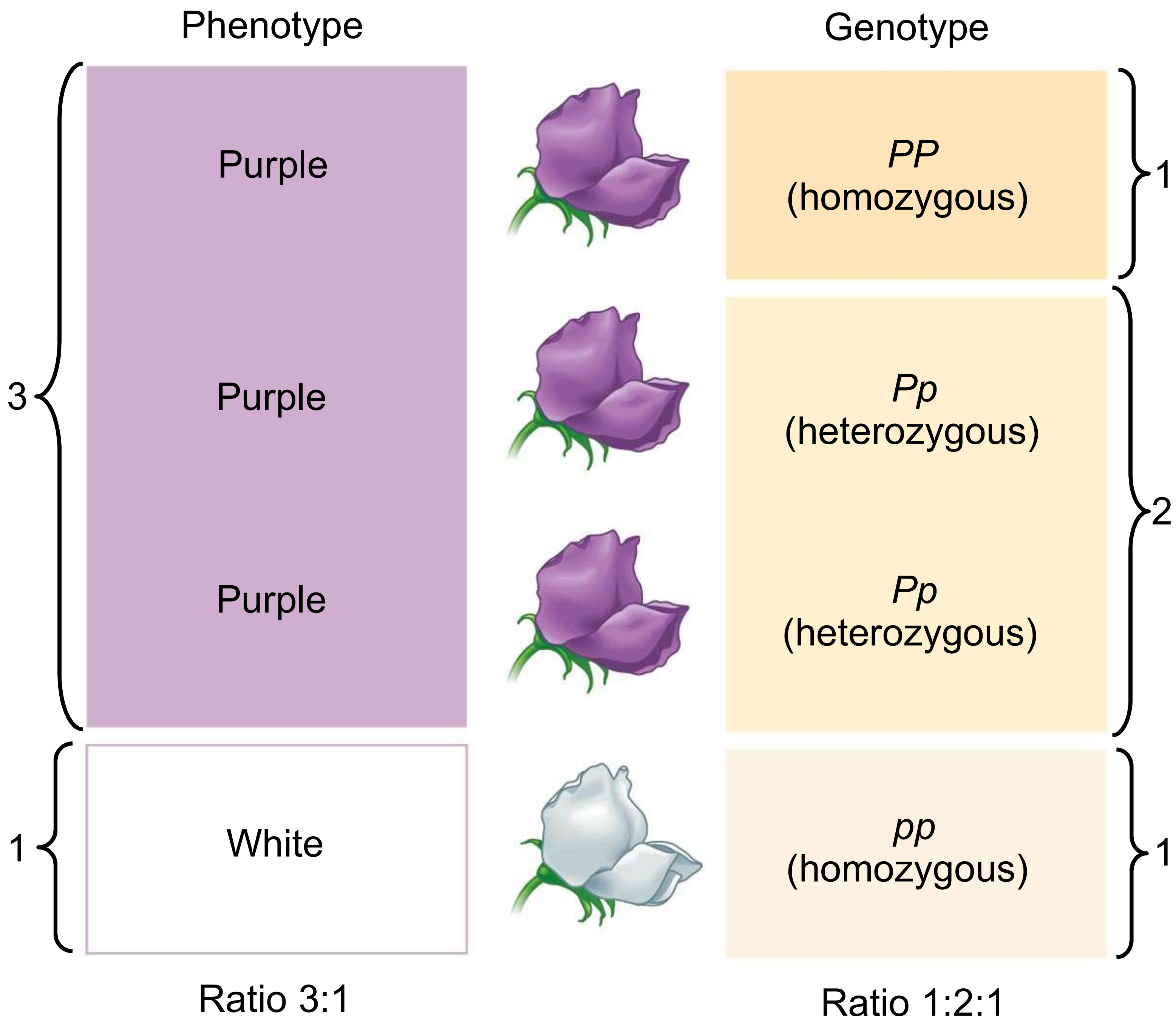


Mendel's Monohybrid Cross

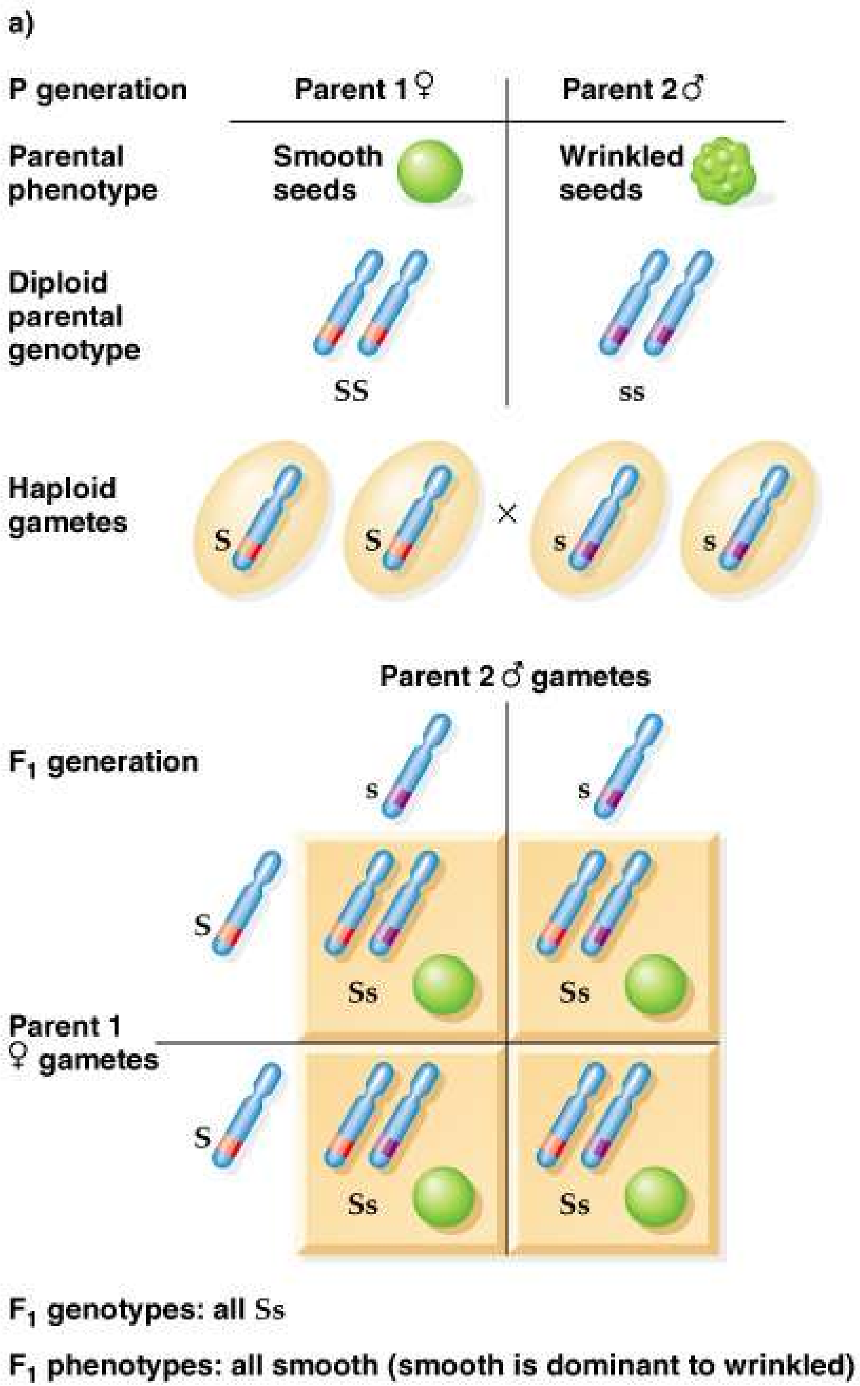



Phenotype
Genotype
Purple
Purple
Purple
White
3
1
PP
(homozygous)
Pp
(heterozygous)
Pp
(heterozygous)
pp
(homozygous)
1
2
1
Ratio 3:1
Ratio 1:2:1

Chromosomes representation

Smooth and wrinkled parental seed strains crossed.

- **Punnett square**
  - **F1 genotypes: 4/4 Ss**
  - **F1 phenotypes: 4/4 smooth**



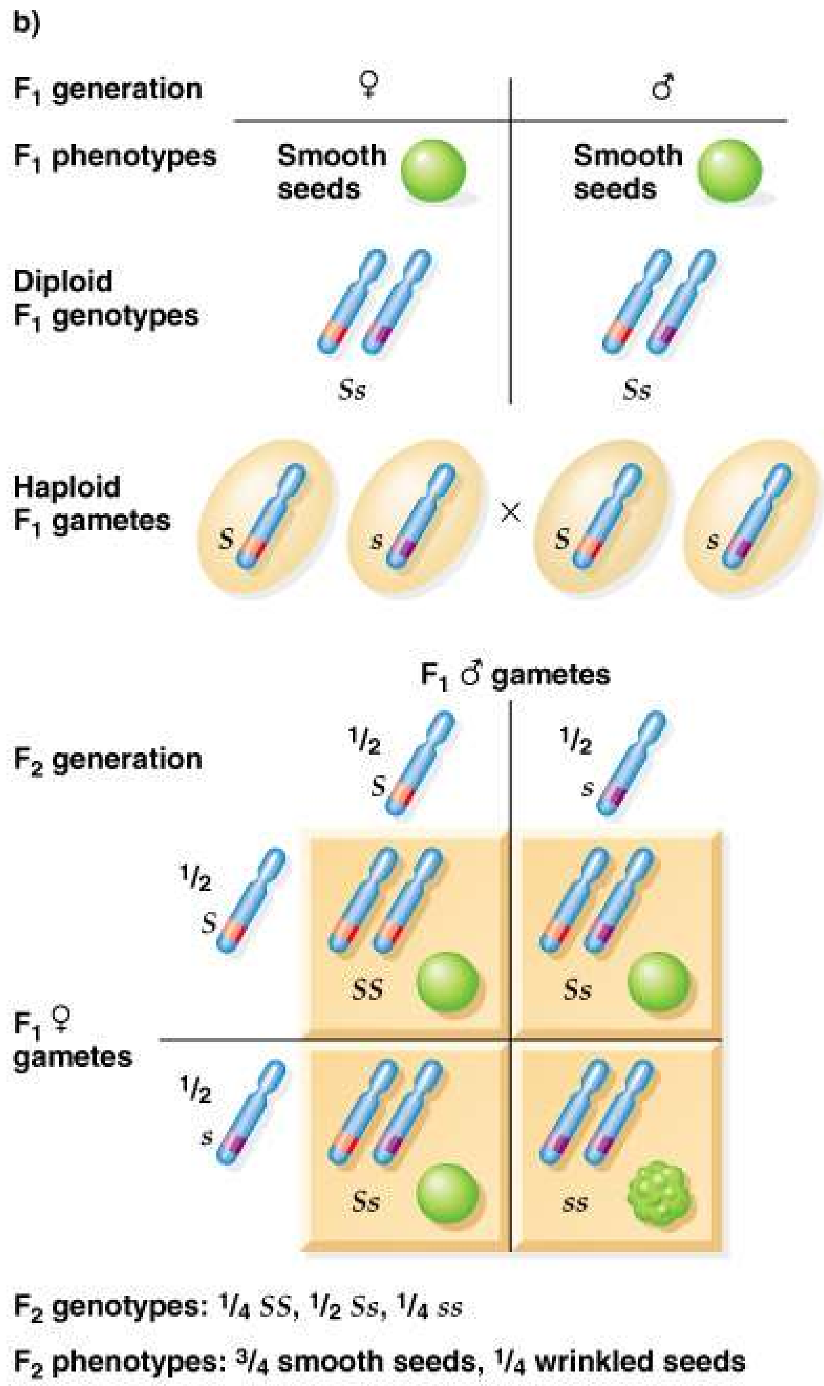
F_1 x F_1 Punnett square:

F_2 genotypes

1/4 SS
1/2 Ss
1/4 ss

F_2 phenotypes

3/4 lisses
1/4 ridées

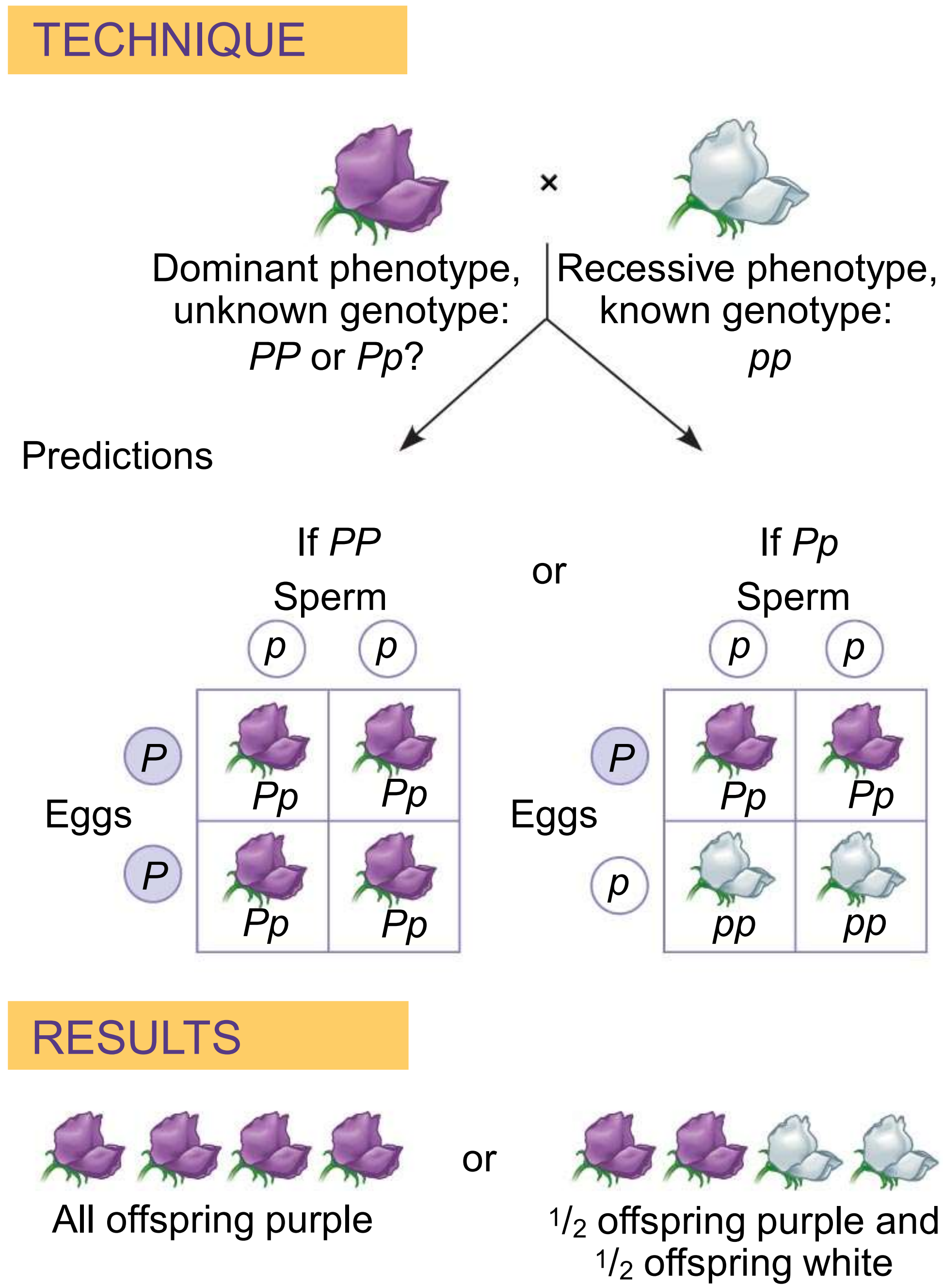


The Testcross

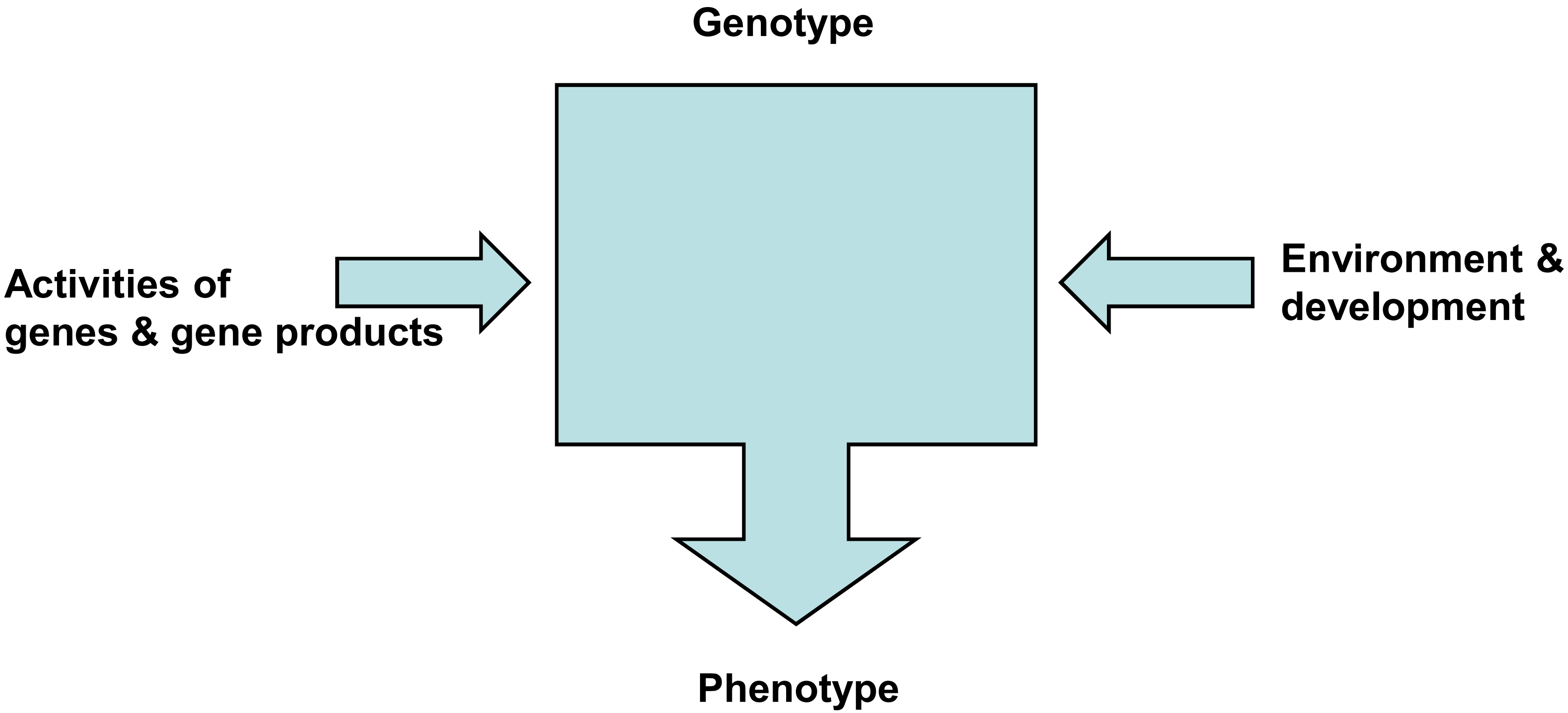
- How can we tell the genotype of an individual with the dominant phenotype?
- Such an individual must have one dominant allele, but the individual could be either homozygous dominant or heterozygous
- The answer is to carry out a **testcross**: breeding the mystery individual with a homozygous recessive individual
- If any offspring display the recessive phenotype, the mystery parent must be heterozygous

An organism that exhibits a dominant trait, such as purple flowers in pea plants, can be either homozygous for the dominant allele or heterozygous. To determine the organism's genotype, geneticists can perform a testcross.

In a testcross, the individual with the unknown genotype is crossed with a homozygous individual expressing the recessive trait (white flowers in this example).
By observing the phenotypes of the offspring resulting from this cross, we can deduce the genotype of the purple-flowered parent.



Numerous factors contribute to the phenotype:



<u>Genotype</u> = collection of genes (and alleles) in an organism

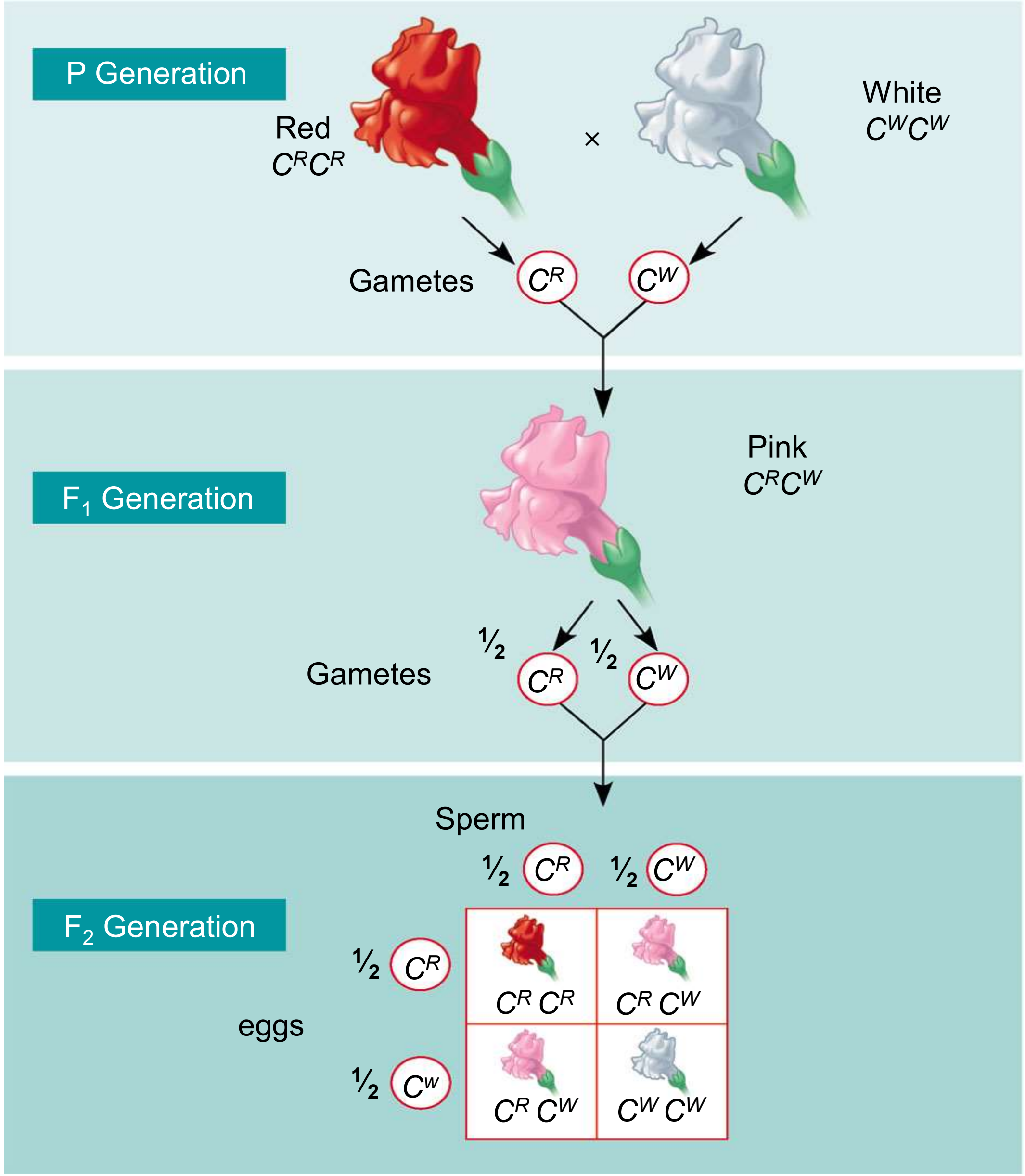
<u>Phenotype</u> = observable properties of an organism

Exceptions (extension) to Mendel's Laws

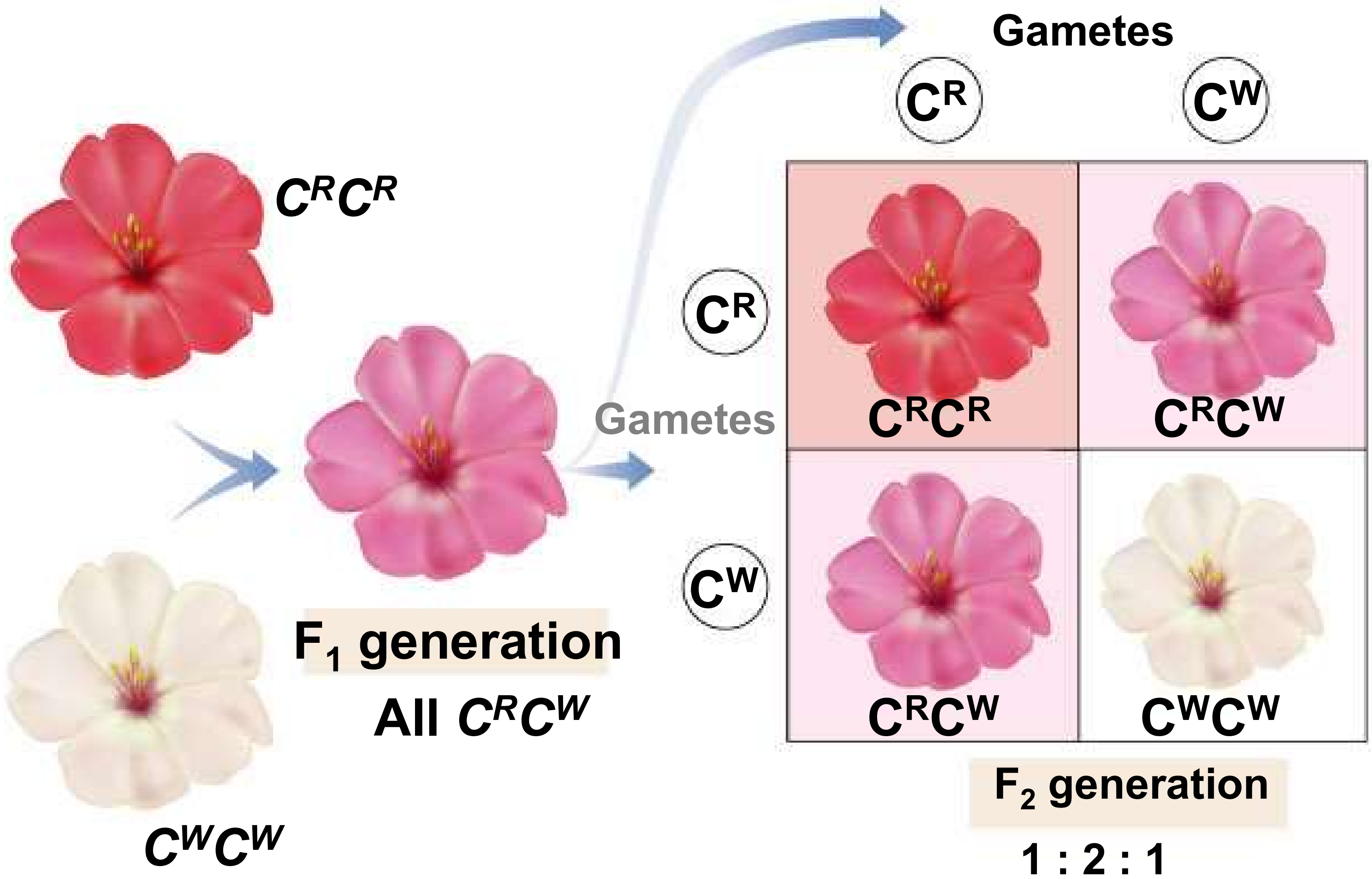
- Incomplete dominance
- Codominance
- Multiple alleles
- Polygenic traits
- Epistasis
- Penetrance
- Germinal mosaicism
- Mutation *de novo*
- Pleiotropy
- Environmental effects on gene expression
- Linked genes
- Sex-linked inheritance
- ……

Incomplete dominance

- Neither allele is dominant and heterozygous individuals have an intermediate phenotype
- For example, in Japan “Four o'clock” plants, with one red allele and one white allele have pink flowers.



Incomplete Dominance



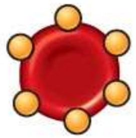
Codominance

•Neither allele is dominant and both alleles are expressed in heterozygous individuals

•Example of ABO blood groups

Allele	Carbohydrate
I^A	A
I^B	B
i	none

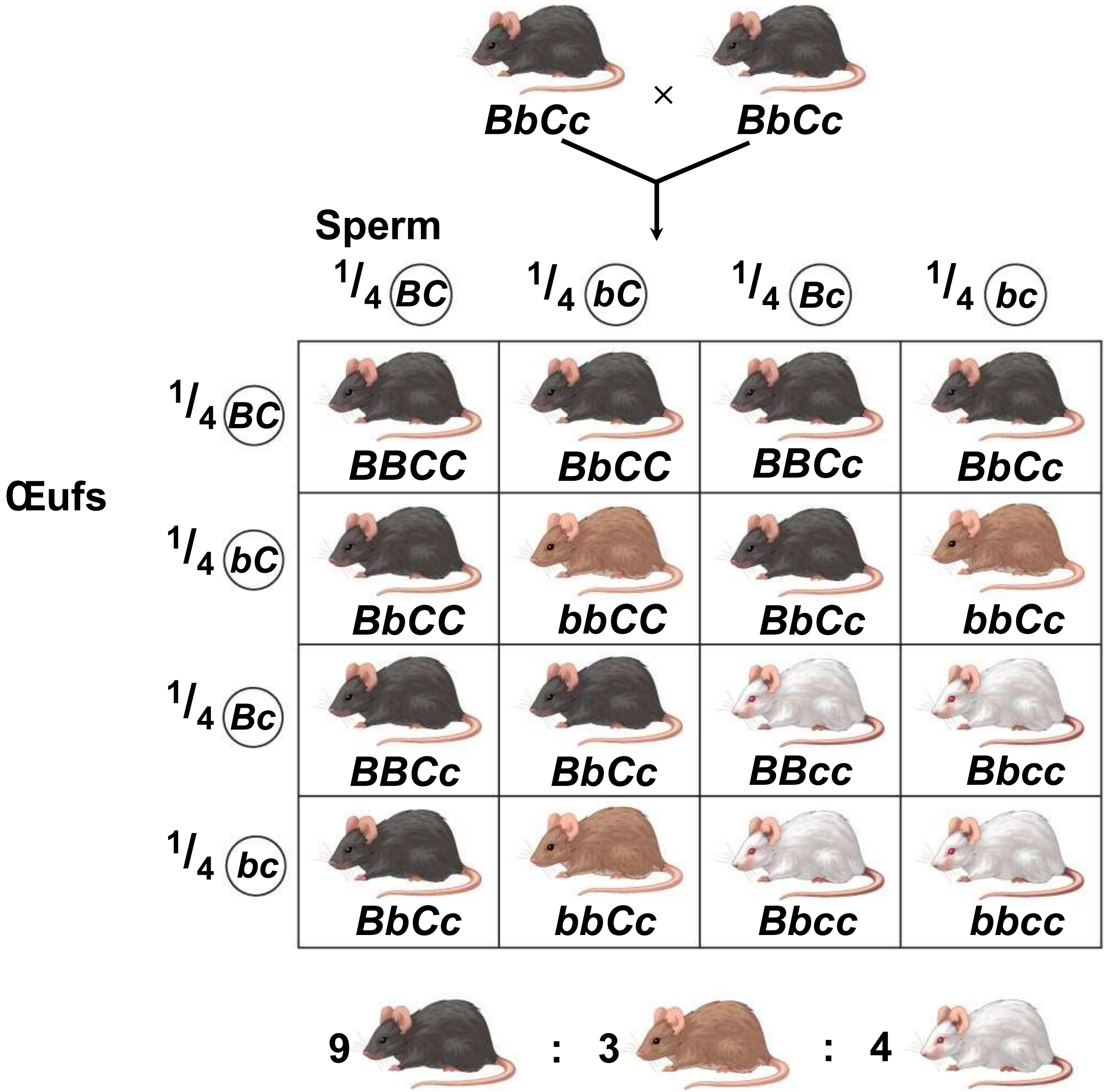
(a) The three alleles for ABO blood groups and their associated carbohydrates

Genotype	Appearance of red blood cells	Phenotype (blood groups)
I^AI^A ou $I^A i$		A
I^BI^B ou $I^B i$		B
I^AI^B		AB
ii		O

(b) blood groups: genotypes and phenotypes

Epistasie

- En épistasie, un gène à un locus peut altérer l'expression phénotypique d'un autre gène différent à un second locus
- Par exemple, chez les souris et de nombreux autres mammifères, la couleur du pelage dépend de deux gènes
- Un gène détermine la couleur du pigment (avec les allèles B pour le noir et b pour le brun)
- L'autre gène (avec les allèles C pour la couleur et c pour aucune couleur) détermine si le pigment sera déposé dans les cheveux


BbCc
×
BbCc
Sperm
1/4 BC
1/4 bC
1/4 Bc
1/4 bc
Œufs
1/4 BC
1/4 bC
1/4 Bc
1/4 bc
BBCC
BbCC
BBCc
BbCc
BbCC
bbCC
BbCc
bbCc
BBCc
BbCc
BBcc
Bbcc
BbCc
bbCc
Bbcc
bbcc
9
:
3
:
4

Pleiotropie

- C'est lorsqu'un gène unique affecte plus d'un trait.
- Par exemple, chez les labradors le locus du gène qui contrôle la façon dont le pigment noir se dépose dans les cheveux peut affecter également la couleur du nez, les lèvres et les yeux.

Traits polygéniques

- La plupart des traits ne sont pas contrôlés par un locus de gène unique, mais par l'interaction combinée de beaucoup de loci géniques. Ceux-ci sont appelés traits polygéniques.

- Les traits polygéniques montrent souvent des variations continues, plutôt que quelques formes discrètes:

- La couleur de la peau chez les humains est un exemple de l’hérédité polygénique

Environmental effects

- Another exception to Mendelian genetics occurs when the phenotype of a trait depends on the environment as well as the genotype.
- Phenotypic variation of a genotype is influenced by the environment
- For example, hydrangea flowers of the same genotype range from blue-purple to pink, depending on the acidity of the soil.

Chromosomal bases of Mendelian inheritance

- 1879: Walter Flemming discovers chromosomes in living cells.
- 1900: DeVries, Correns, and Tschermak repeat Mendel's discoveries.
- 1902: Sutton and Boveri and others link chromosome behavior to Mendelian segregation and independent assortment and propose the Chromosomal Theory of Inheritance.

Exceptions to the Chromosome Theory

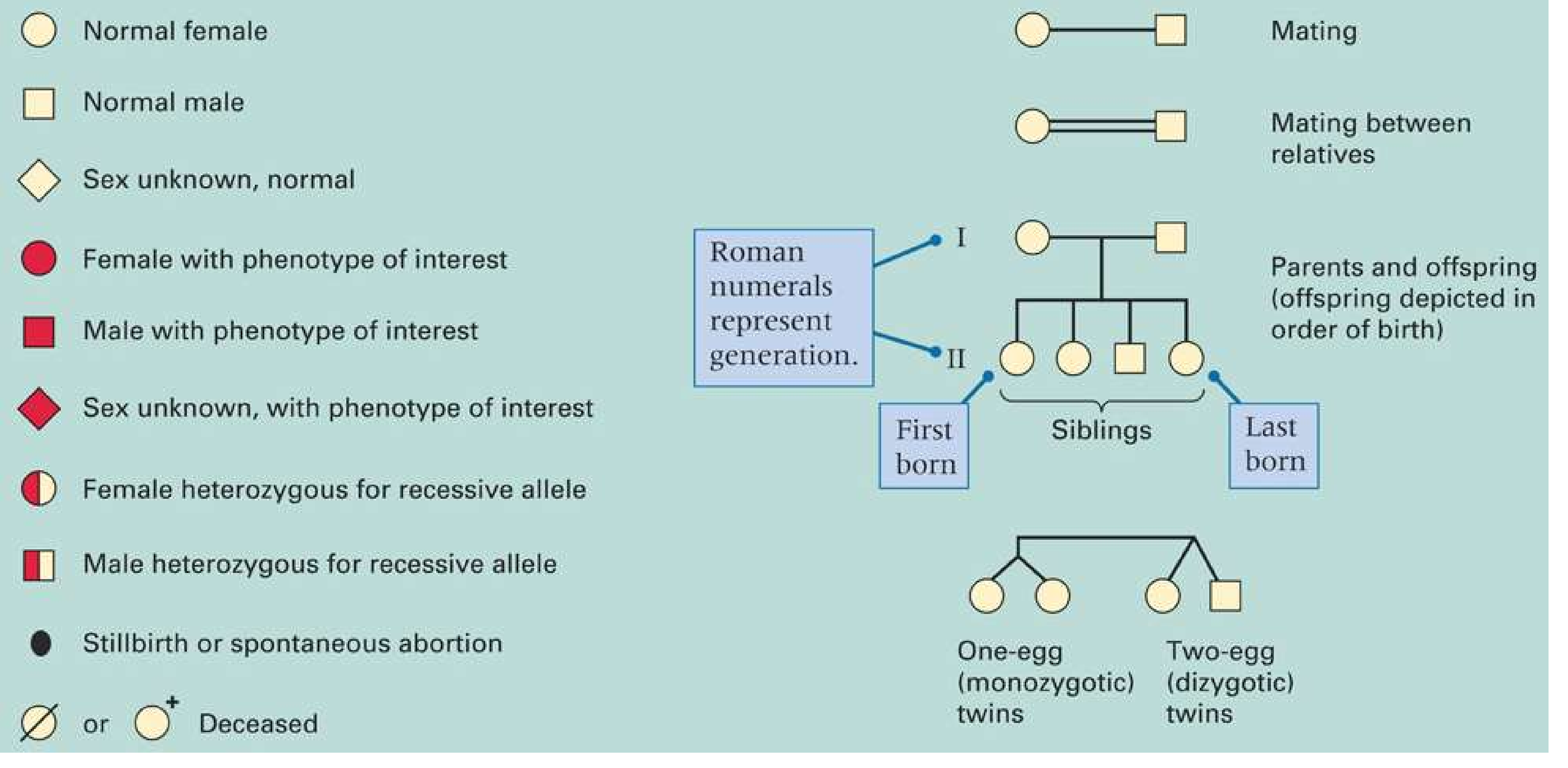
- Mitochondria and chloroplasts contain genes.
  - The traits controlled by these genes do not follow the chromosomal theory of inheritance
  - Mitochondrial and chloroplast genes are often passed on to offspring by only one parent (the mother)

Pedigree Analysis

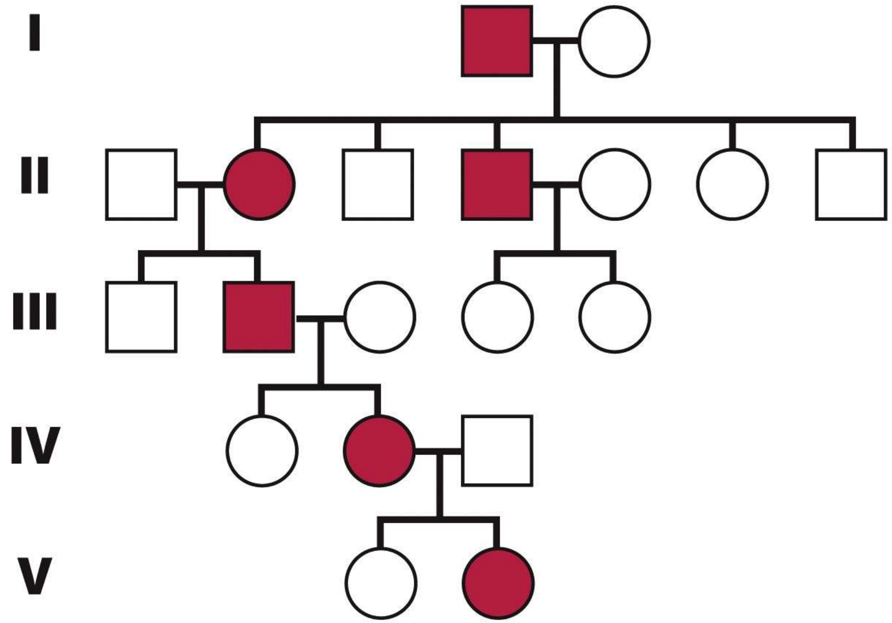
- A family tree (pedigrees) is a tree that describes the relationships of parents and children across generations
- The inheritance of particular traits can be traced and described using pedigrees
- Pedigrees can also be used to make predictions about future offspring
- We can use the rules of multiplication and addition to predict the probability of specific phenotypes

Pedigree Analysis

- In humans, pedigree analysis is used to determine individual genotypes and to predict the mode of transmission of single gene traits

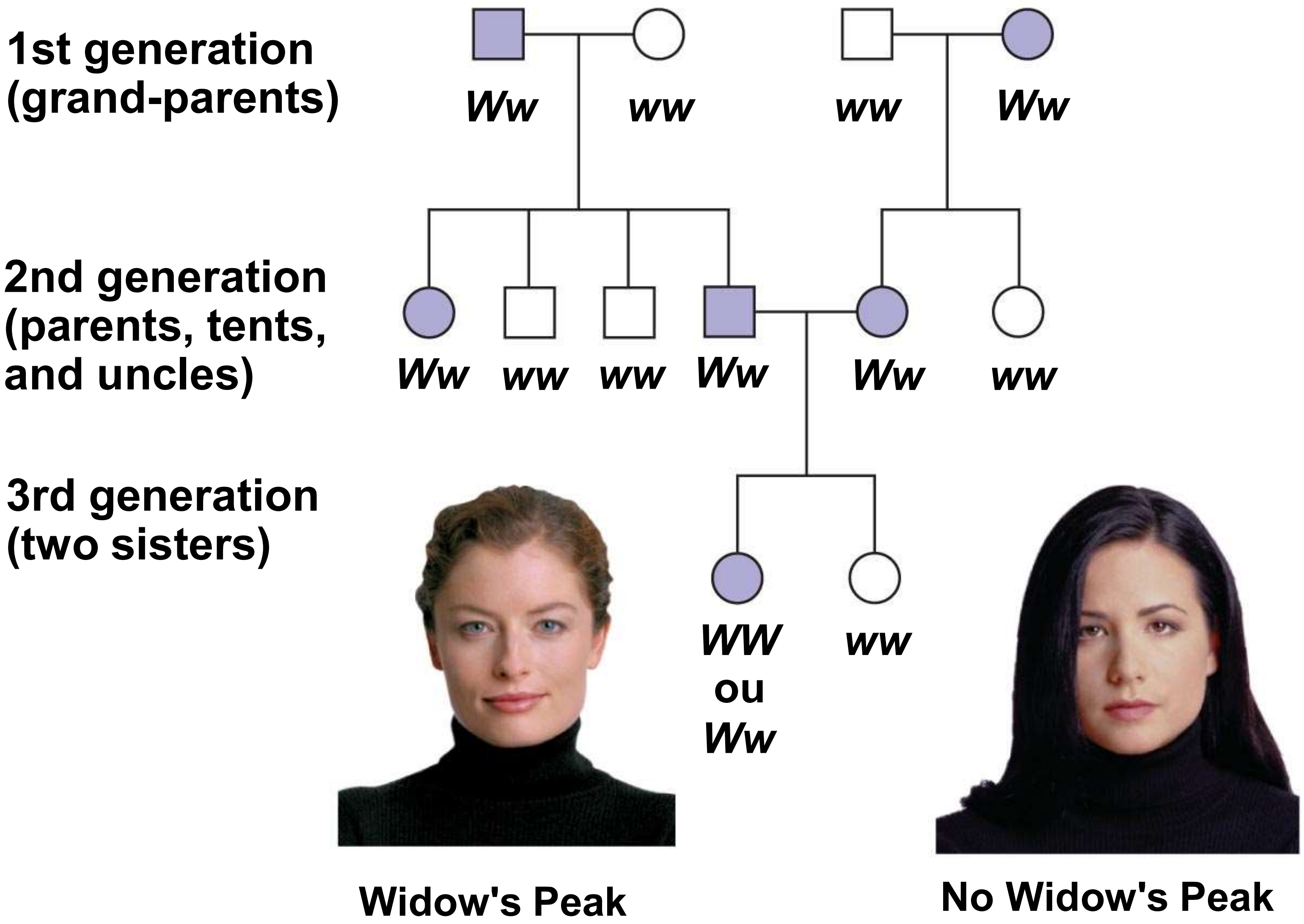


Autosomal dominant trait



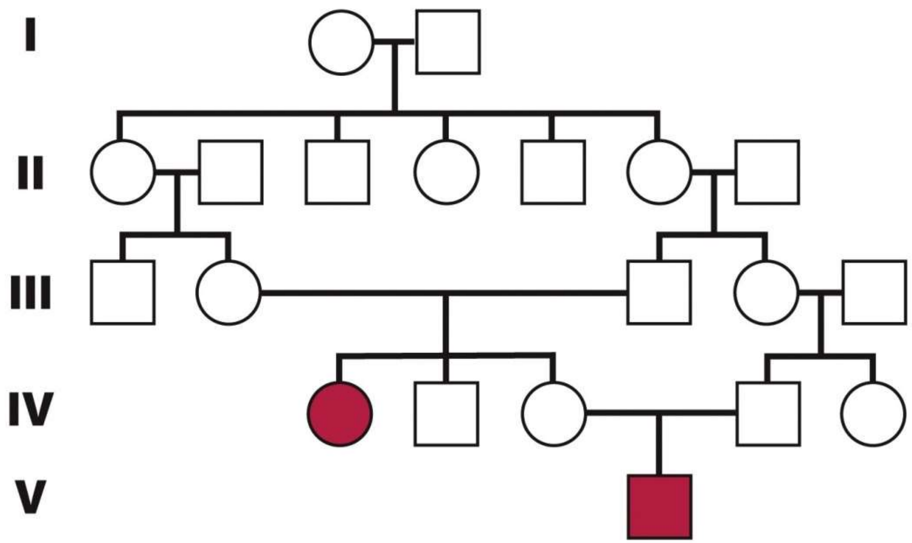
Dominant trait

- Each individual who carries the dominant allele manifests the trait.
- Each affected person must have at least one affected parent.
- Most people who show the trait are heterozygous, and they have a ½ chance of passing the trait to their children..



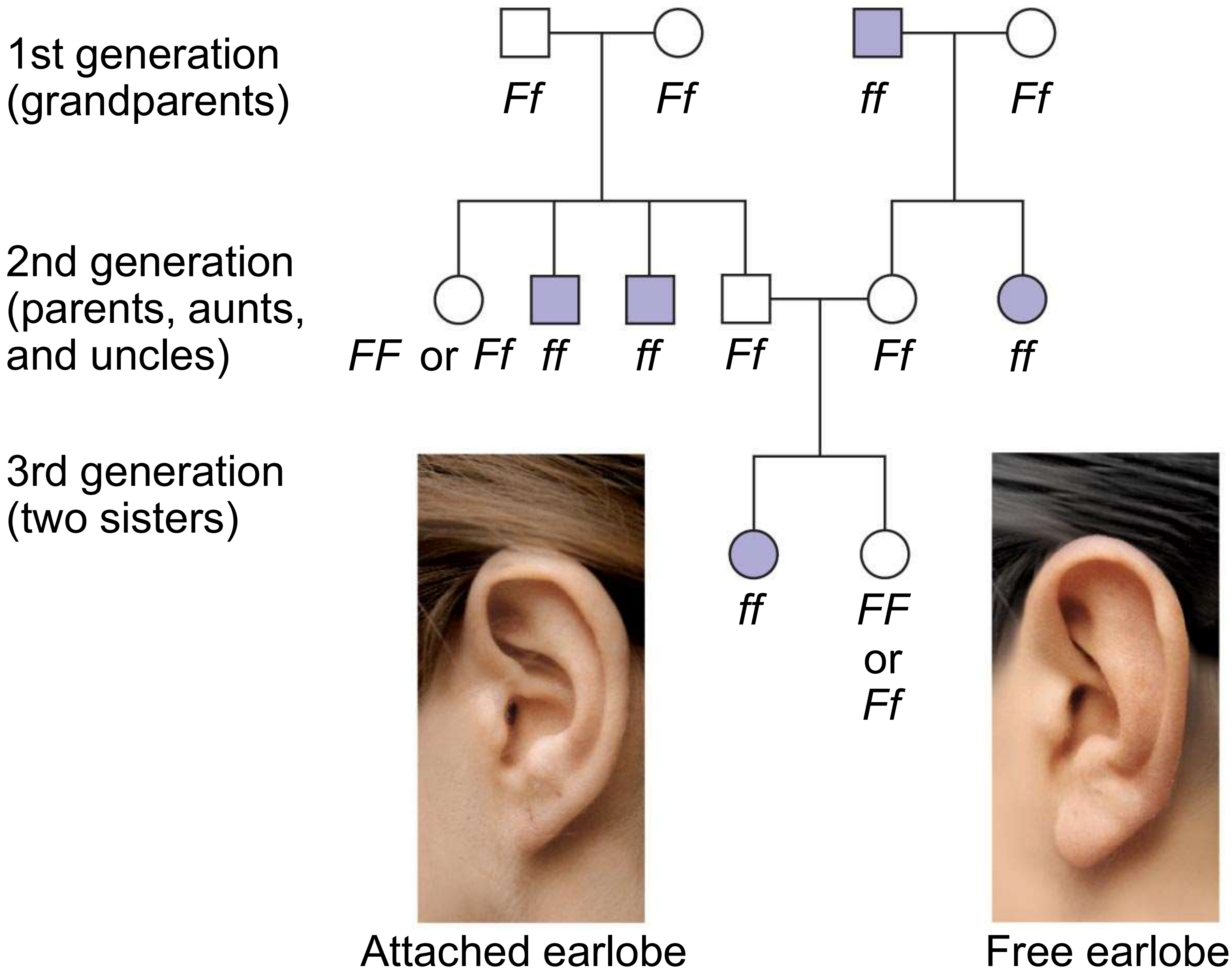
(a) Is widow's peak a dominant trait?

Autosomal recessive trait



Recessive trait

- Recessive traits can occur in individuals whose parents are not affected.
- The parents are heterozygous for the recessive allele and are called carriers
- Carriers' have about 1/4 chance to get affected children
- Affected individuals are homozygous for the trait



(b) Is an attached earlobe a dominant or recessive trait?

Hereditary diseases

1) Autosomal recessive hereditary disorders

2) Autosomal dominant hereditary disorders

Autosomal recessive disorders

- Many genetic disorders are inherited in a recessive manner
- Recessively inherited disorders show up only in individuals homozygous for the allele
- **Carriers** are heterozygous individuals who carry the recessive allele but are phenotypically normal (i.e., pigmented)
- Albinism is a recessive condition characterized by a lack of pigmentation in skin and hair
- If two parents are asymptomatic carriers, they have a one in four (1/4) chance of having a sick child.

Autosomal recessive disorders

- If a recessive allele that causes a disease is rare, then the chance of two carriers meeting and mating is low
- Consanguineous matings (i.e., matings between close relatives) increase the chance of mating between two carriers of the same rare allele
- Most societies and cultures have laws or taboos against marriages between close relatives

Albinism is a recessive condition characterized by a lack of pigmentation in skin and hair

Parents

Normal *Aa* × Normal *Aa*

Sperm

Eggs	*A*	*a*
A	*AA* Normal	*Aa* Normal (carrier)
a	*Aa* Normal (carrier)	*aa* Albino

Cystic Fibrosis

- **Cystic fibrosis** is the most common lethal genetic disease in the United States,striking one out of every 2,500 people of European descent
- The cystic fibrosis allele results in defective or absent chloride transport channels in plasma membranes
- Symptoms include mucus buildup in some internal organs and abnormal absorption of nutrients in the small intestine

Cystic Fibrosis

If two parents carry the recessive gene for Cystic Fibrosis (c), that is to say they are heterozygous (C c), they have a one in four (1/4) chance of having a child who is homozygous for the morbid (recessive) allele and therefore sick; a one in two (1/2) chance of having a carrier child.

C C = normal
C *c* = Carrier
c c = malade

	½ C	1/2 *c*
½ C	1/4C C	1/4C *c*
½ *c*	1/4C *c*	1/4*C c*

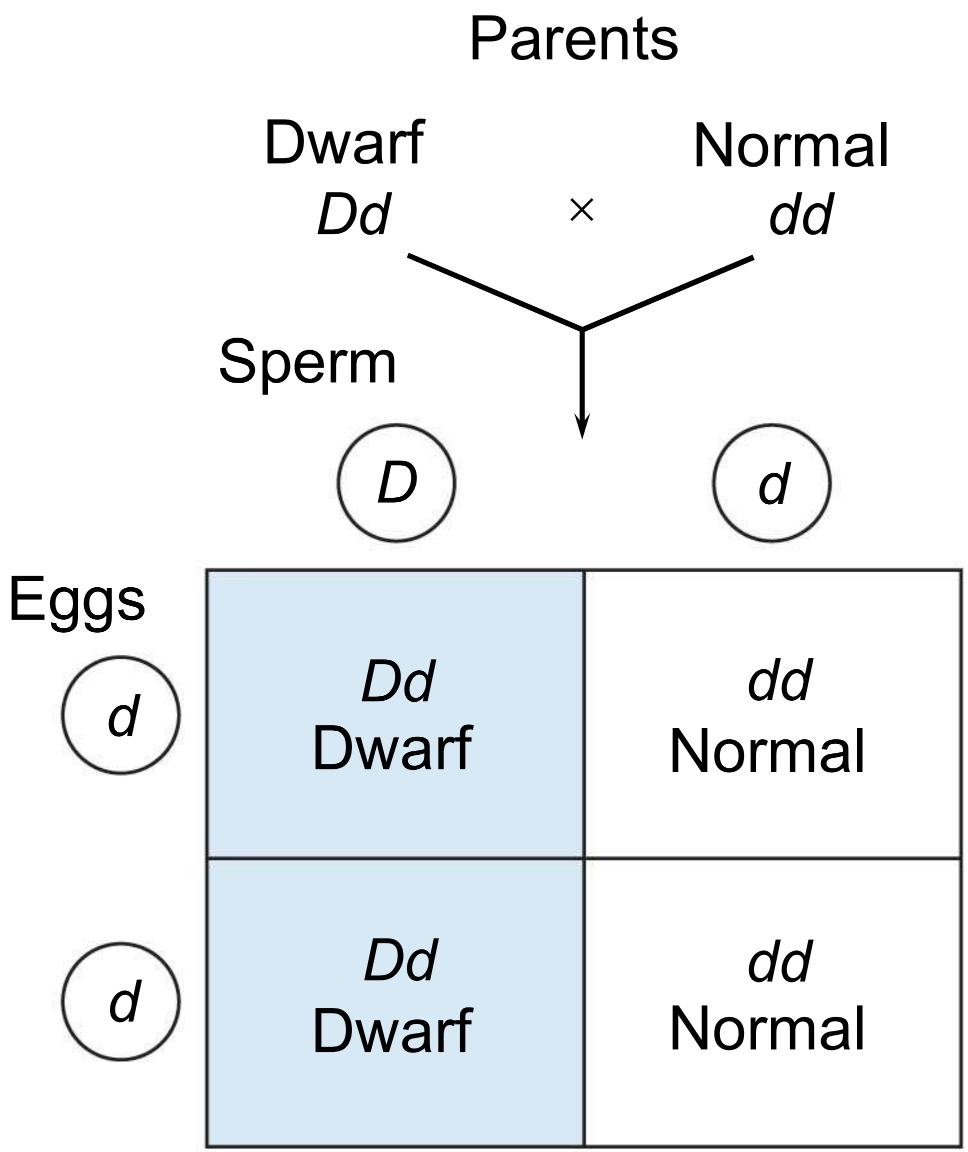
Probabilité…

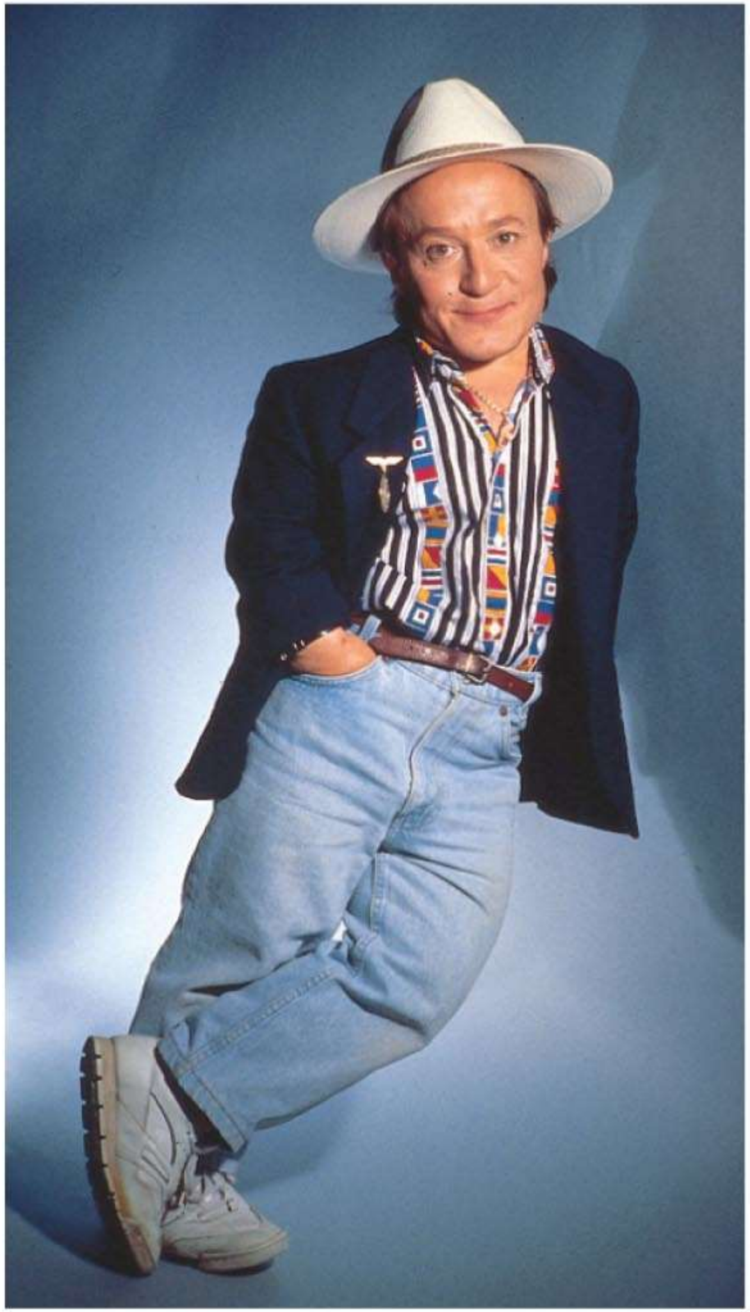
- Bien sûr, la probabilité 1 sur 4 d'obtenir la maladie est juste une prédiction, et en réalité, deux transporteurs sains peuvent avoir des enfants normaux.
- Cependant, la plus grande probabilité est qu’il y’ait 1 enfant sur 4 soit atteint (si le couple a 4 enfants).
- Exp:
  - Probabilité pour un couple porteur d’avoir enfant atteint = 1/4
  - Probabilité pour un couple porteur d’avoir 3 enfants atteints = 1/4 x 1/4 x 1/4 = 1/64

Autosomal dominant disorders

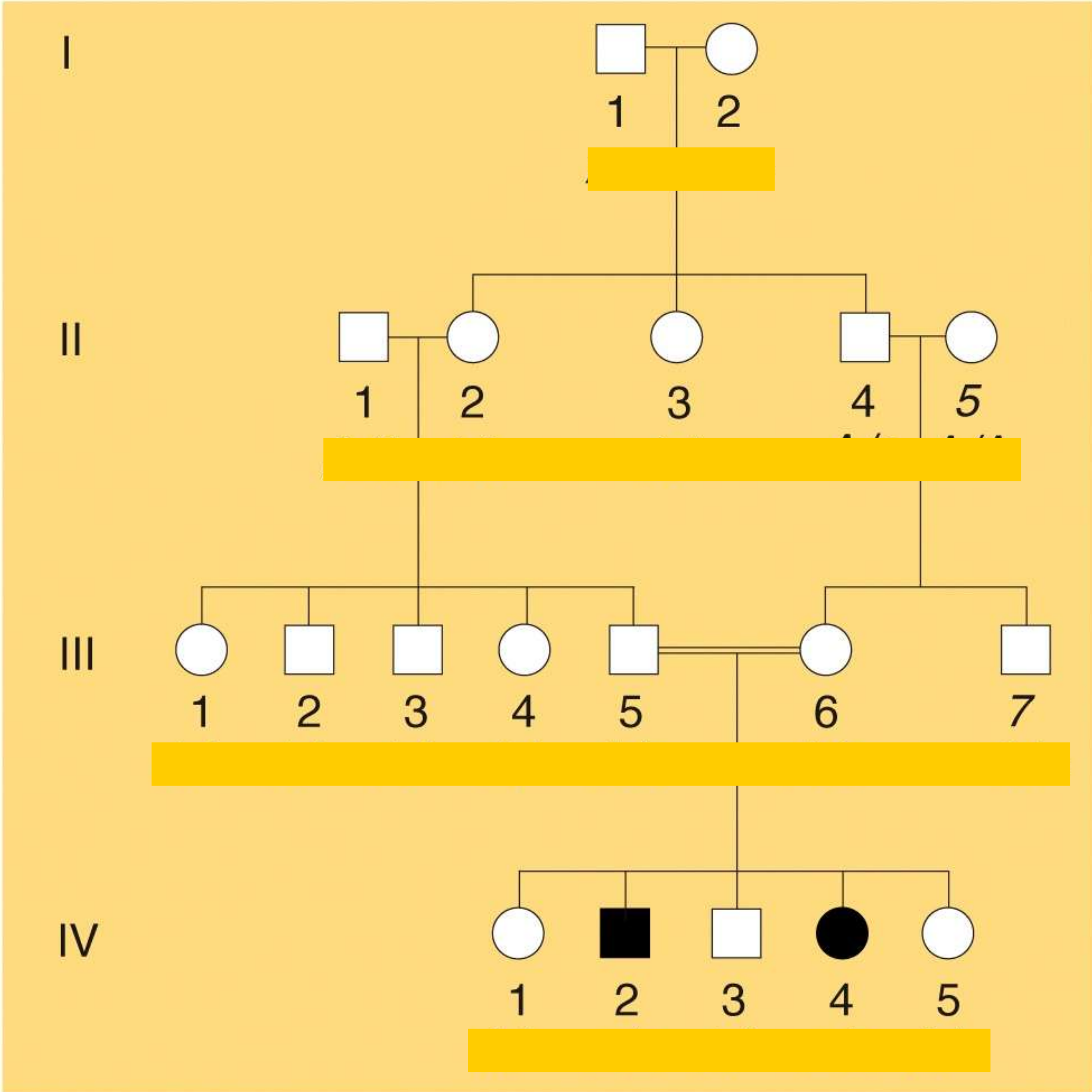
- Some human disorders are caused by dominant alleles
- Dominant alleles that cause a lethal disease are rare and arise by mutation
- Dominant hereditary diseases occur in individuals who are homozygous for the morbid allele (severe form of the disease) and in individuals who are heterozygous for the morbid allele.
- If one of the two parents is heterozygous for the morbid allele, there is a one in two (1/2) chance of having a sick child.
- *Achondroplasia* is a form of dwarfism caused by a rare dominant allele

Achondroplasia is a form of dwarfism caused by a rare dominant allele





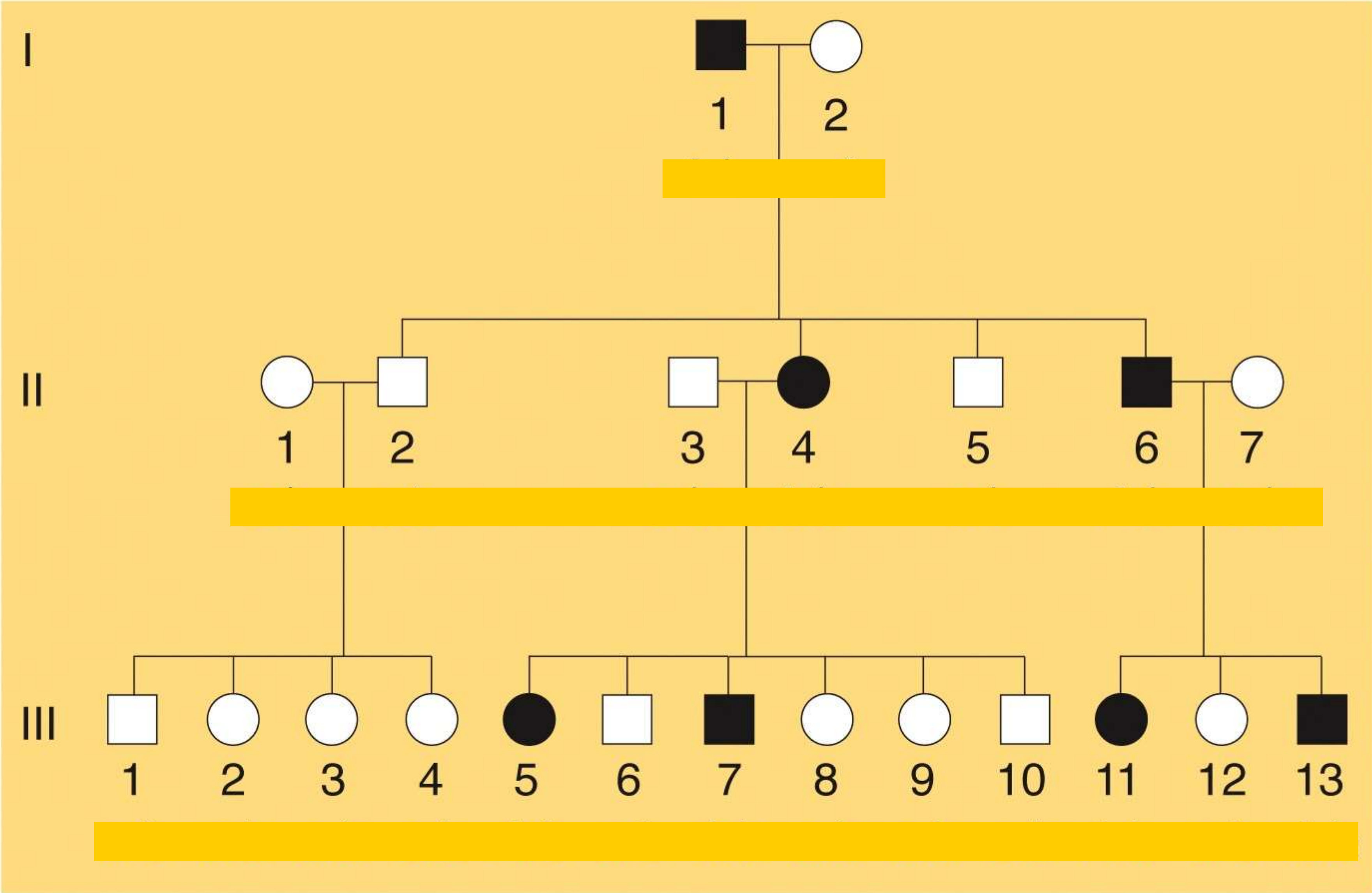
How is this disorder transmitted?



If individuals III5 and III6 decide to have another child, what is the probability that the child will be affected?

How is this disorder transmitted?

If individual III4 and III6 marry and have a child, what is the probability that the child will be affected?



Dihybrid cross

(study of two characters)

Case of independent genes

The Law of Independent Assortment

- Mendel identified his second law of inheritance by following two characters at the same time
- Crossing two true-breeding parents differing in two characters produces **dihybrids** in the F_1 generation, heterozygous for both characters
- A dihybrid cross, a cross between F_1 dihybrids, can determine whether two characters are transmitted to offspring as a package or independently

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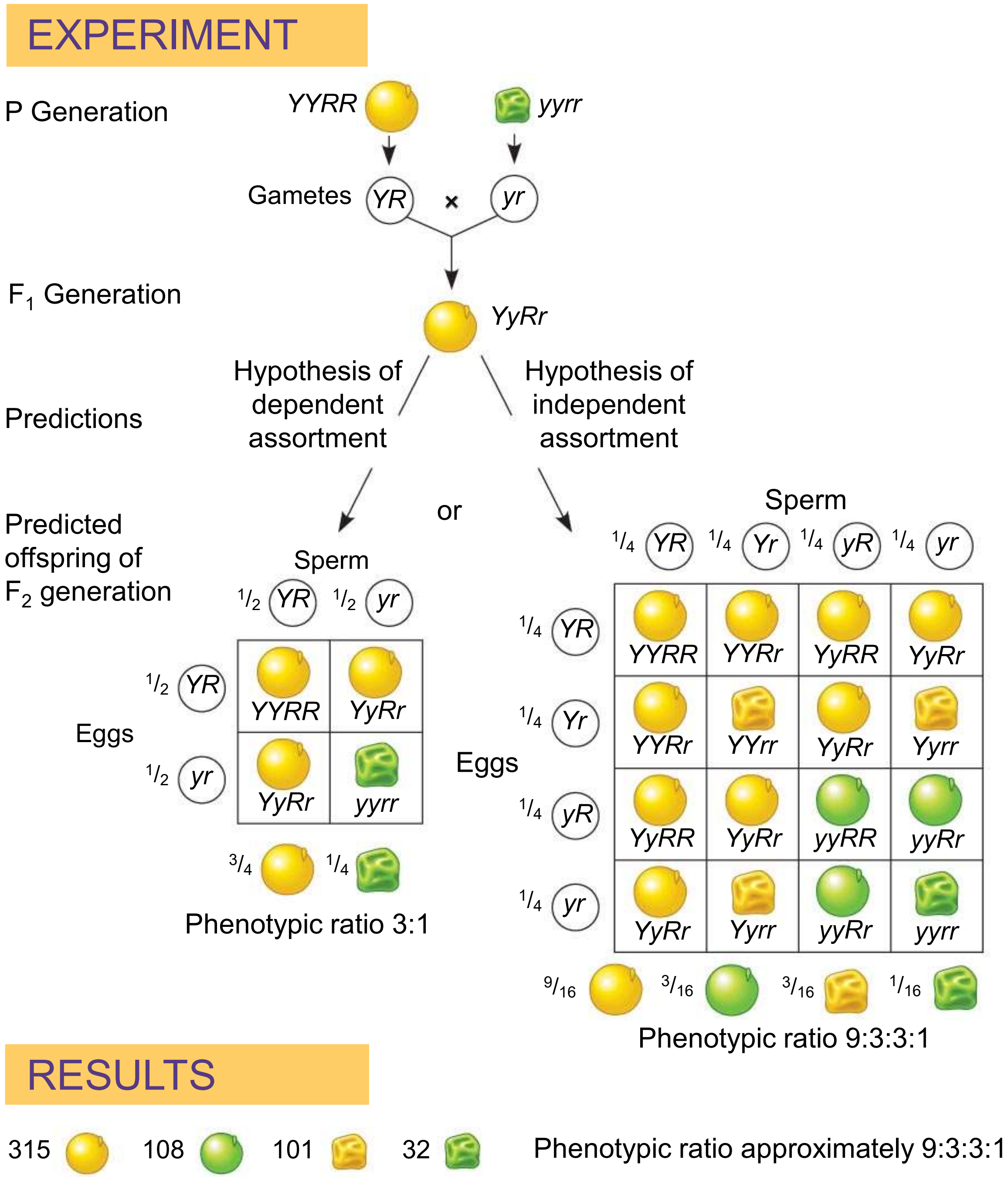
Fig. 14-8



EXPERIMENT
P Generation
YYRR
yyrr
Gametes
YR
×
yr
F1 Generation
YyRr
Predictions
Hypothesis of dependent assortment
or
Hypothesis of independent assortment
Predicted offspring of F2 generation
Sperm
1/2 YR
1/2 yr
Eggs
1/2 YR
1/2 yr
YYRR
YyRr
YyRr
yyrr
3/4
1/4
Phenotypic ratio 3:1
Sperm
1/4 YR
1/4 Yr
1/4 yR
1/4 yr
Eggs
1/4 YR
1/4 Yr
1/4 yR
1/4 yr
YYRR
YYRr
YyRR
YyRr
YYRr
YYrr
YyRr
Yyrr
YyRR
YyRr
yyRR
yyRr
YyRr
Yyrr
yyRr
yyrr
9/16
3/16
3/16
1/16
Phenotypic ratio 9:3:3:1
RESULTS
315
108
101
32
Phenotypic ratio approximately 9:3:3:1

Origins of Genetic Variation Among Offspring

- The behavior of chromosomes during meiosis and fertilization is responsible for most of the variation that arises in each generation
- Three mechanisms contribute to genetic variation:
  – Independent assortment of chromosomes
  – Crossing over
  – Random fertilization

Mendel's Experiments - Dihybrid Crossing

Independent Assortment of Chromosomes

Dihybridism is the study of the transmission of 2 pairs of alleles (two characteristics).

Independent Assortment of Chromosomes (recombination) corresponds to the independent disjunction of pairs of alleles carried by different homologous chromosomes (case of independent genes).

Independent Assortment of Chromosomes occurs during metaphase 1/anaphase 1 of meiosis and leads to the appearance of recombinant phenotypes in quantities equal to the parental phenotypes.

Independent Assortment of Chromosomes

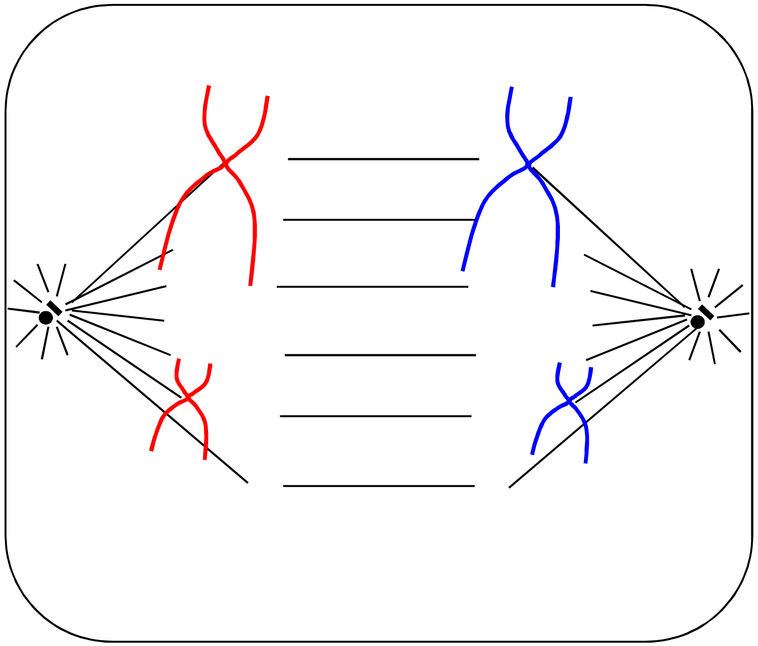
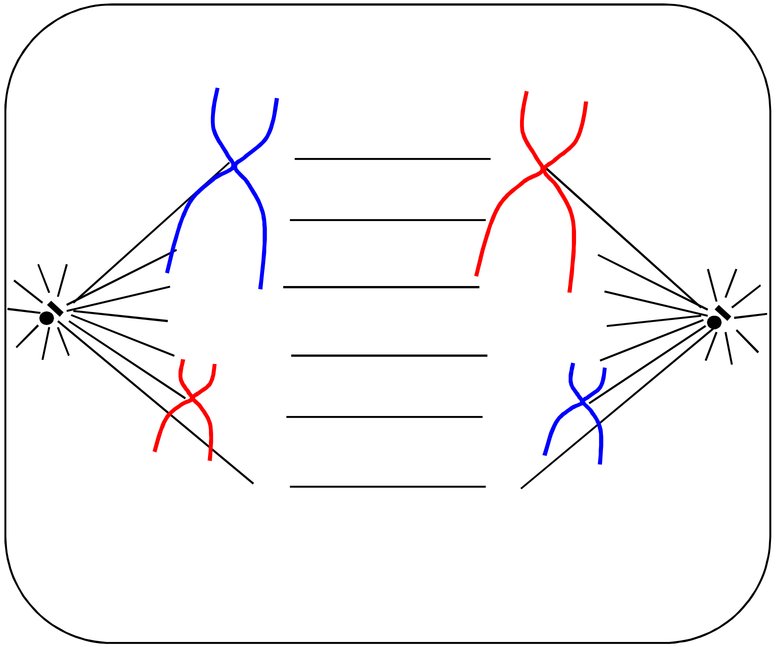
- Homologous pairs of chromosomes orient randomly at metaphase I of meiosis
- In independent assortment, each pair of chromosomes sorts maternal and paternal homologues into daughter cells independently of the other pairs
- The number of combinations possible when chromosomes assort independently into gametes is 2^n, where n is the haploid number
- For humans ($n = 23$), there are more than 8 million ($2^{23} = 8,388,608$) possible combinations of chromosomes

Dihybrid Cross:

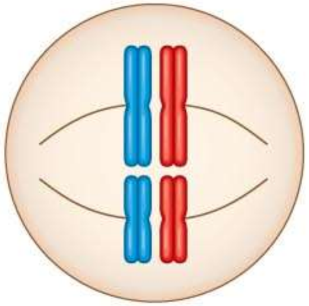
Mendel & Meiosis:

Independent Assortment of Chromosomes

- Chromosome pairs would be oriented differently in metaphase 1 and anaphase 1

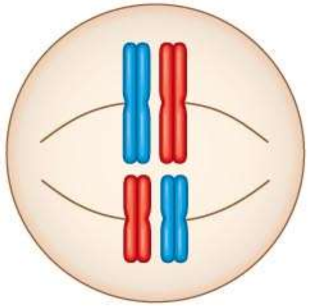



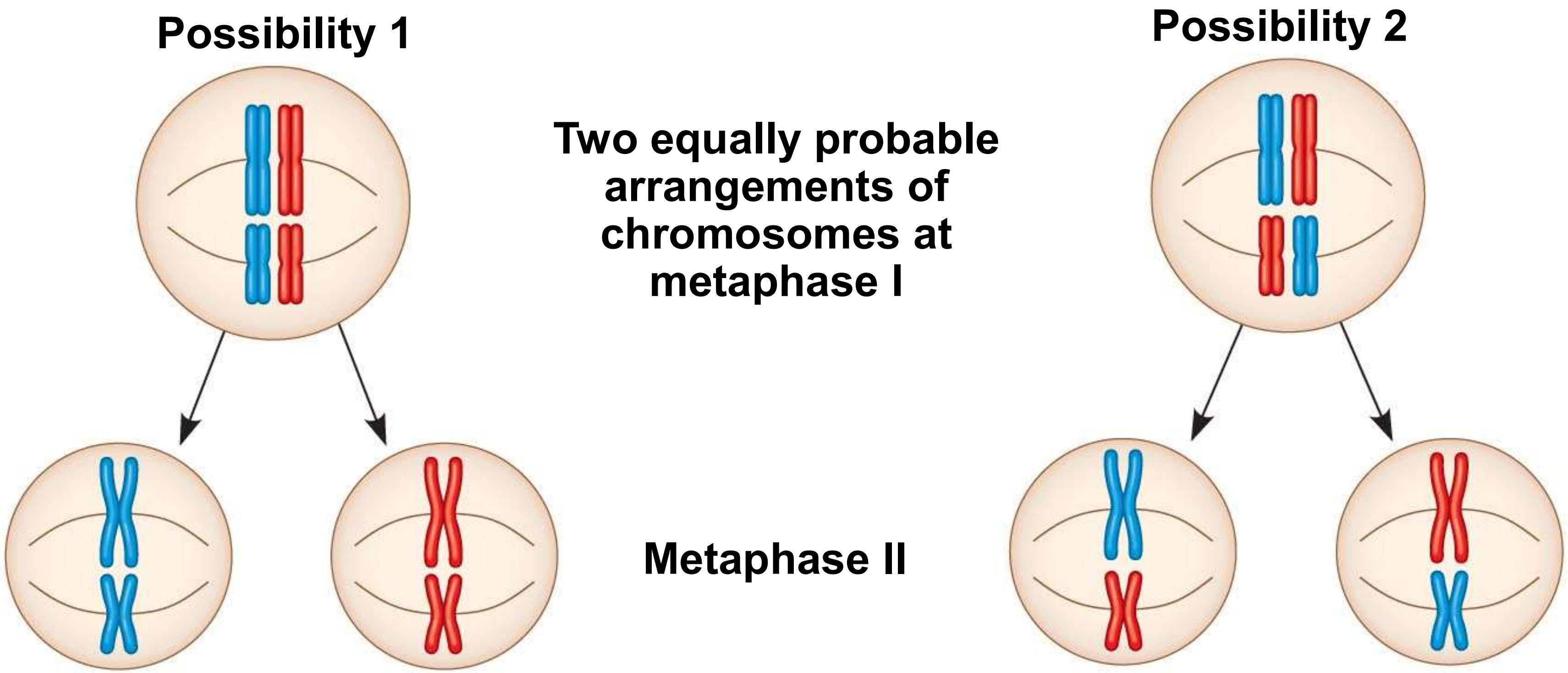
Possibility 1

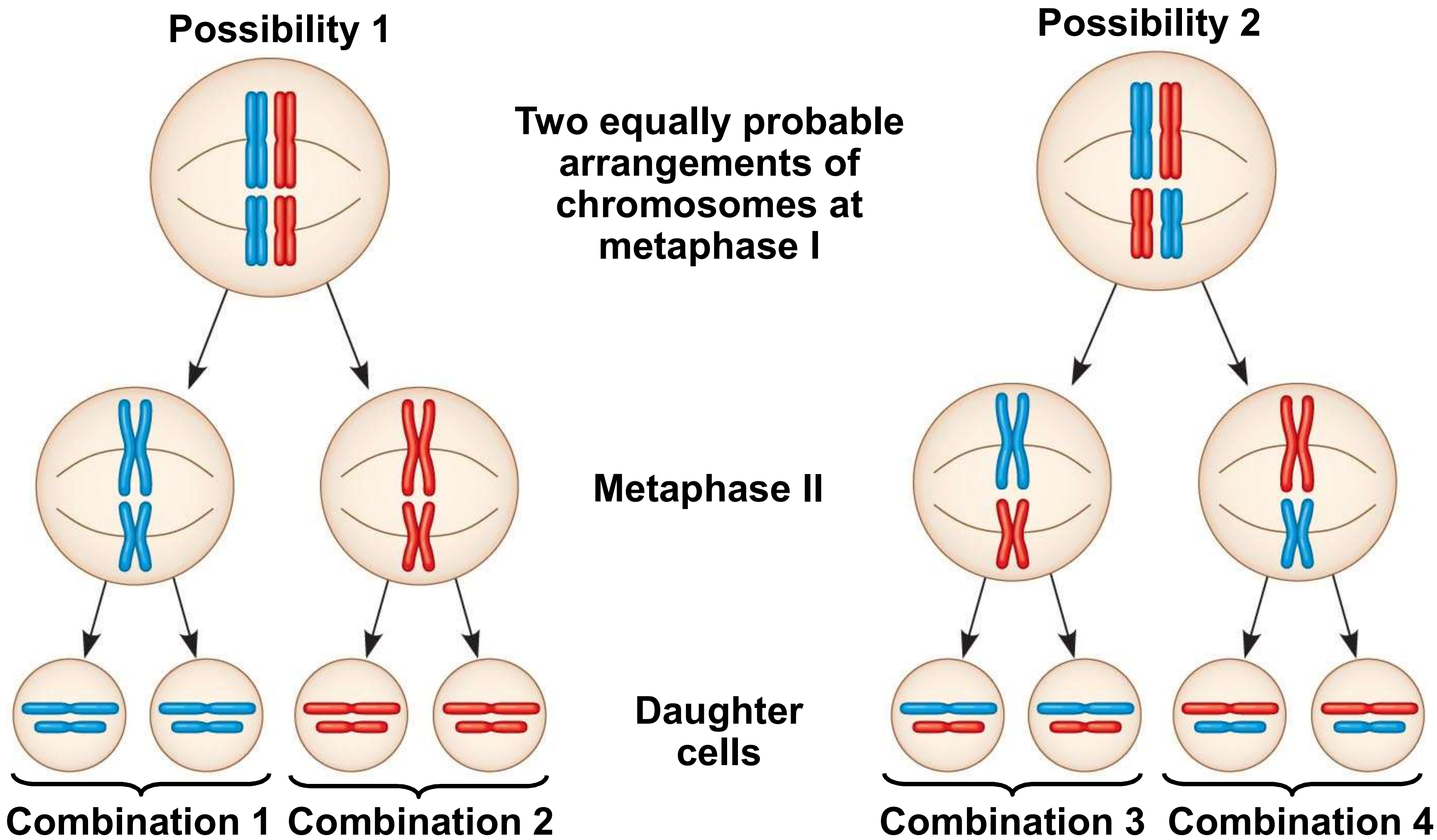


Two equally probable arrangements of chromosomes at metaphase I

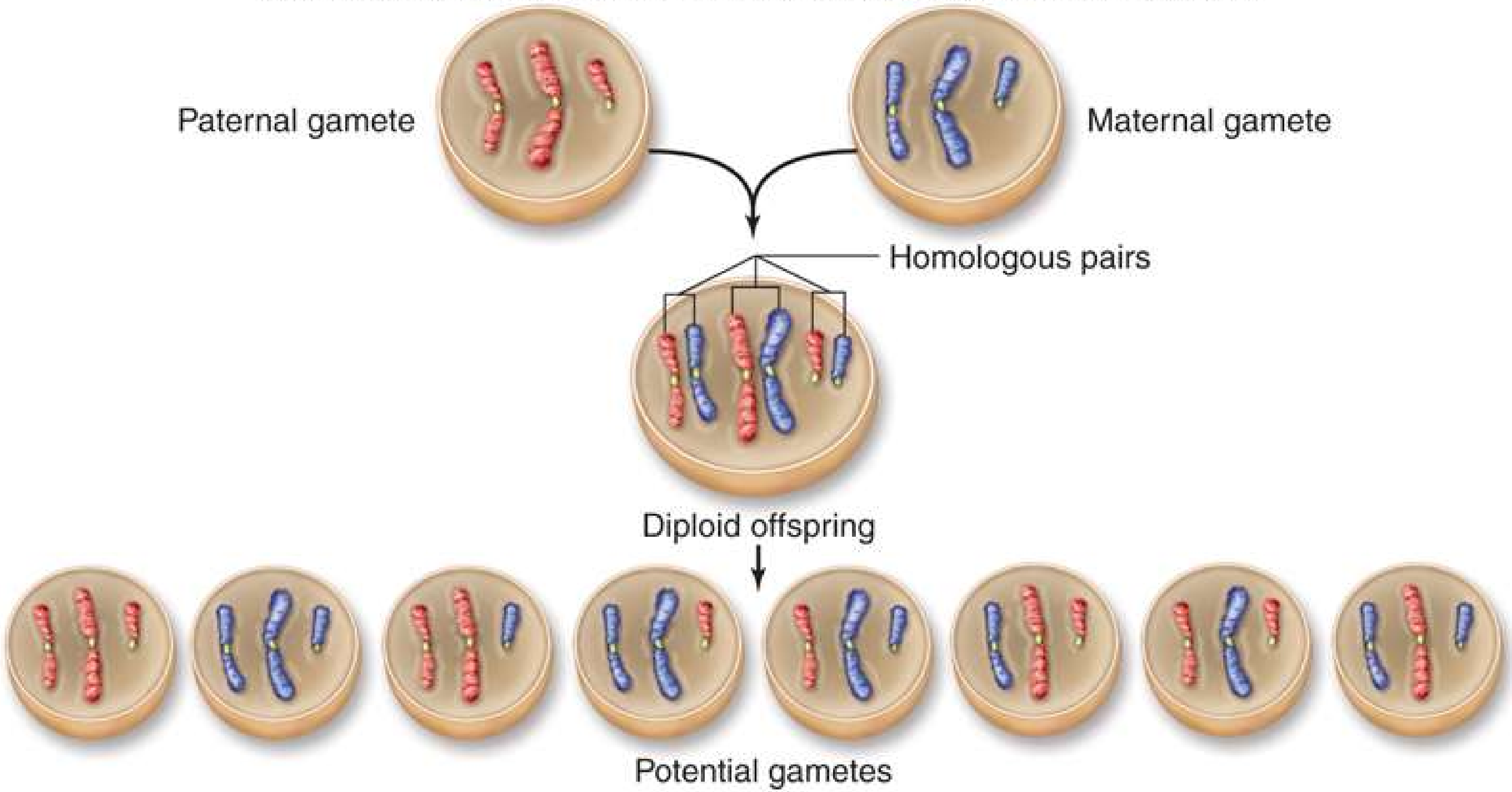
Possibility 2




Possibility 1
Possibility 2
Two equally probable arrangements of chromosomes at metaphase I
Metaphase II



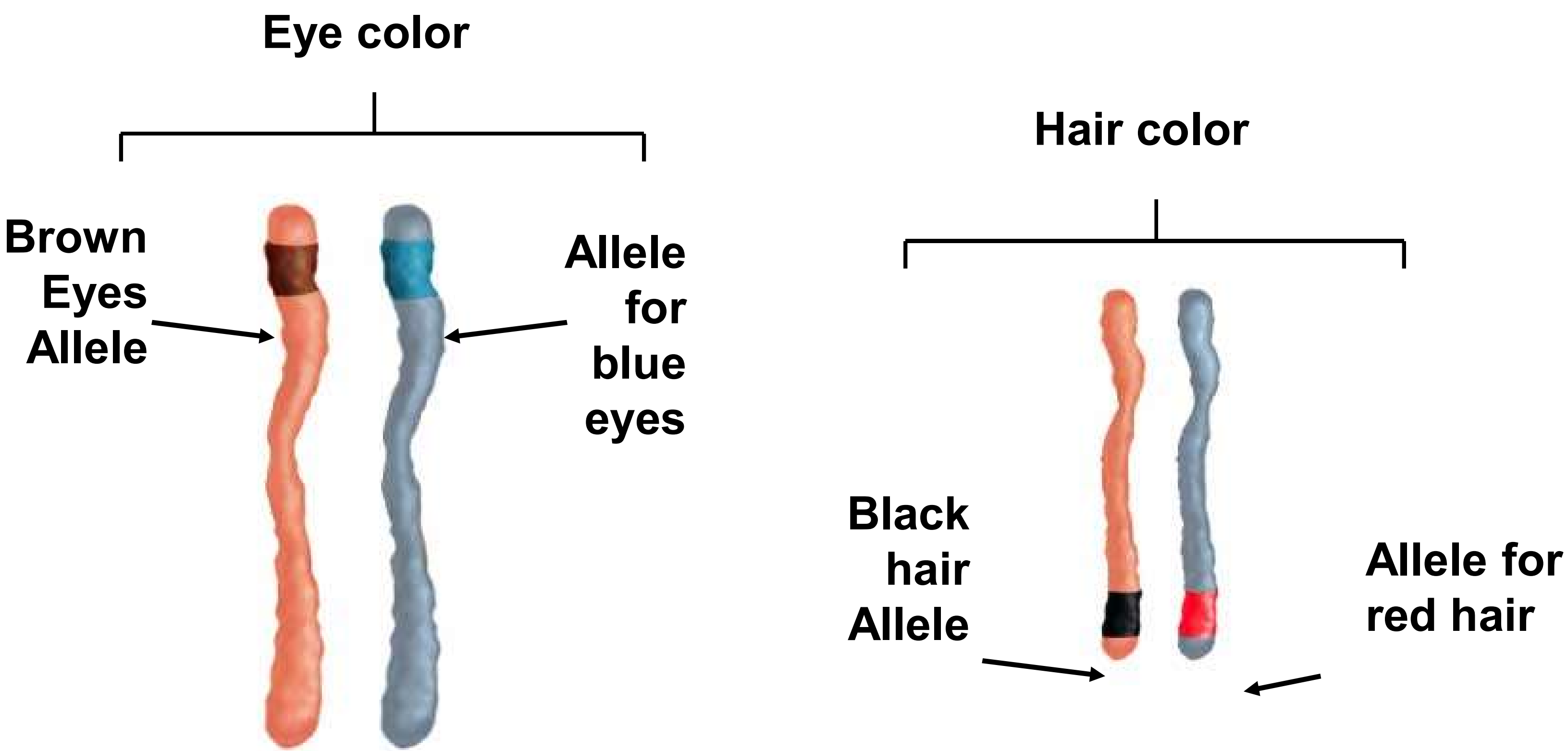
Possibility 1
Possibility 2
Two equally probable arrangements of chromosomes at metaphase I
Metaphase II
Daughter cells
Combination 1
Combination 2
Combination 3
Combination 4


Paternal gamete
Maternal gamete
Homologous pairs
Diploid offspring
Potential gametes

Random Fertilization

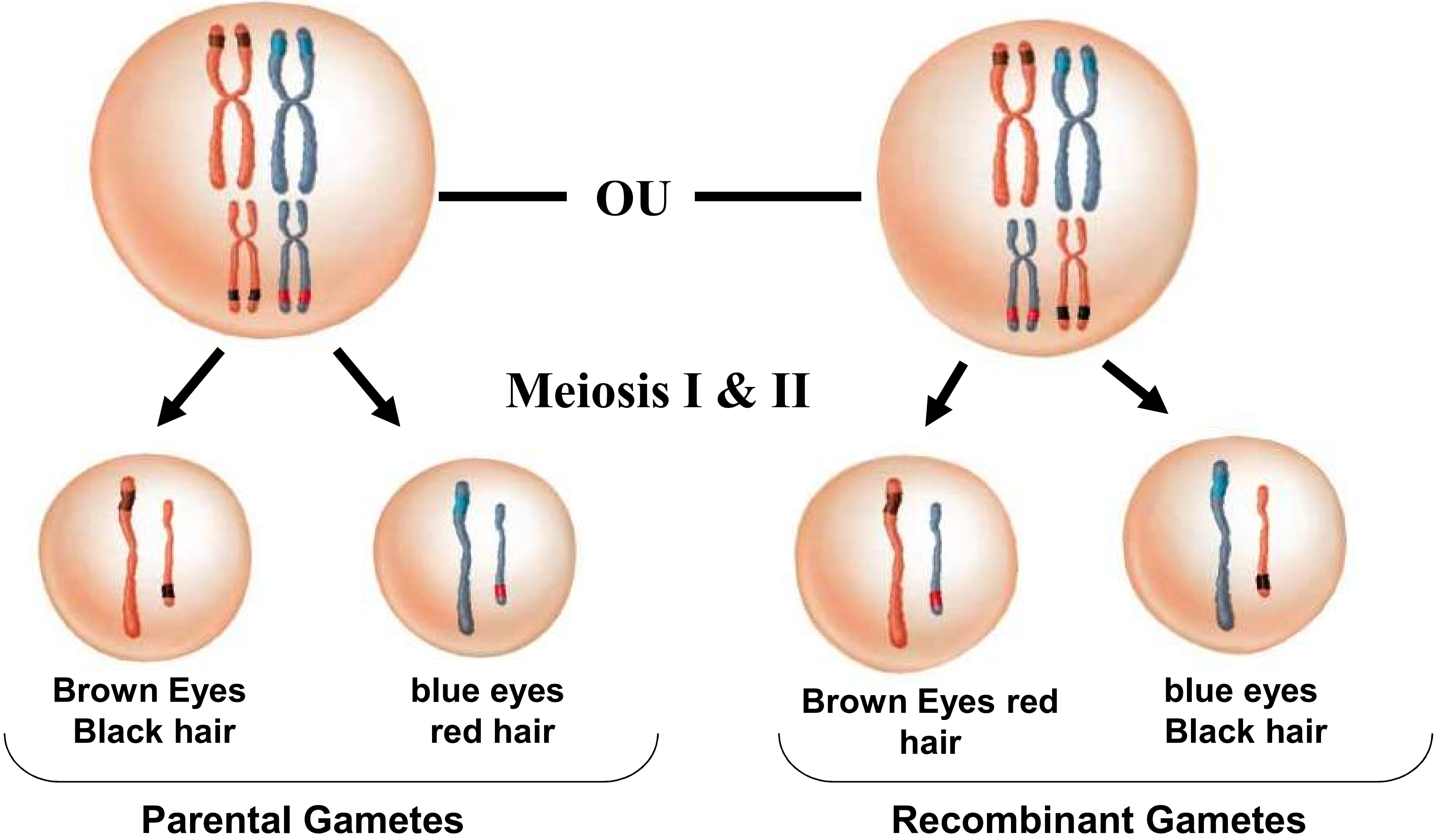
- Random fertilization adds to genetic variation because any sperm can fuse with any ovum (unfertilized egg)
- The fusion of two gametes (each with 8.4 million possible chromosome combinations from independent assortment) produces a zygote with any of about 70 trillion diploid combinations

Segregation and independent assortment



Segregation and independent assortment

During meiosis I, tetrads can appear in 2n different ways



Independent Assortment of Chromosomes

- Using a dihybrid cross, Mendel developed the law of independent assortment
- The law of independent assortment states that each pair of alleles separates independently of the other pair of alleles during gamete formation
- Strictly speaking, this law only applies to genes on different non-homologous chromosomes
- Genes located near each other on the same chromosome tend to be inherited together

How are two characters transmitted from parents to children?

- As a package?
- Independently?

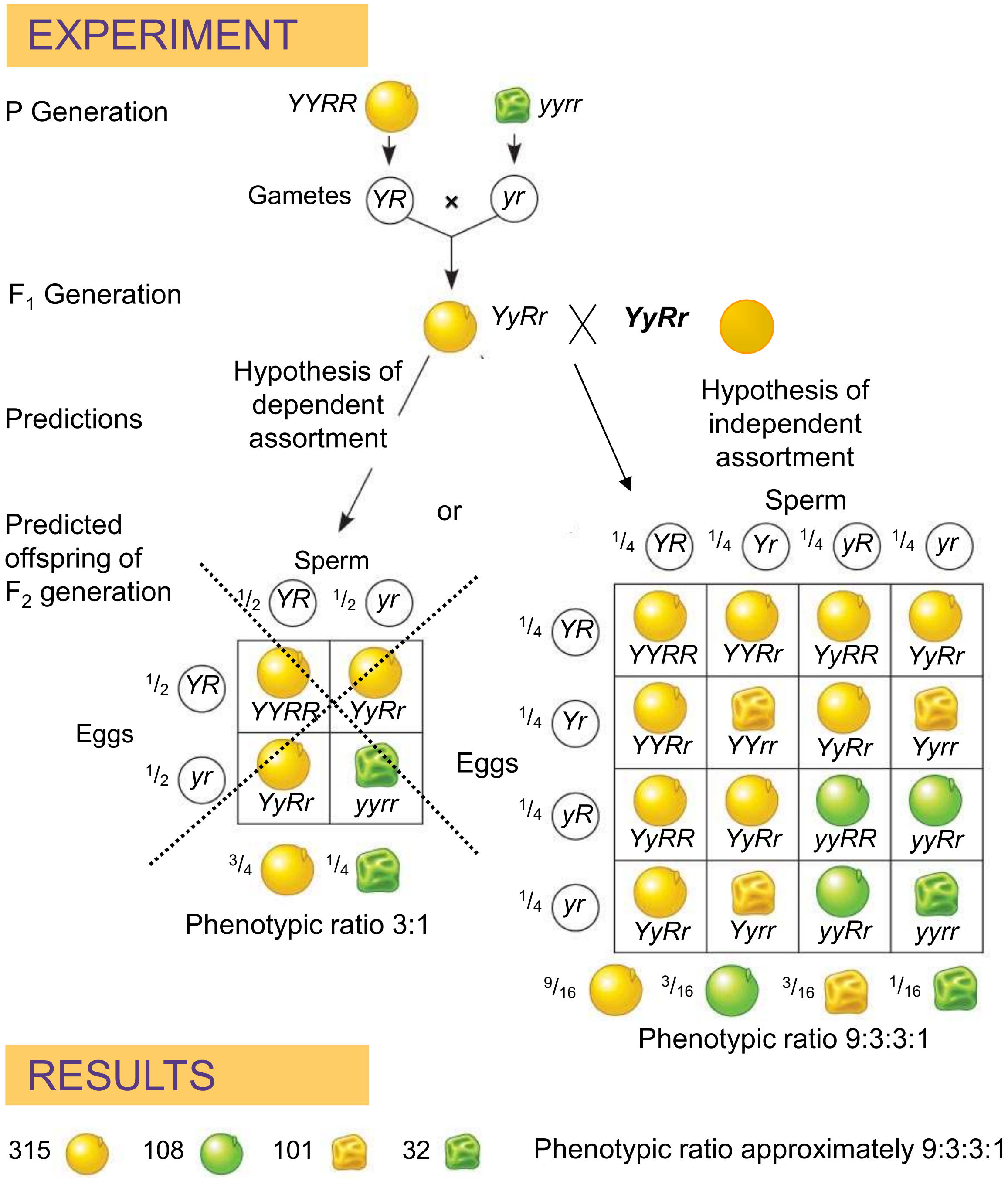
A dihybrid cross:

Illustrates the transmission of two traits

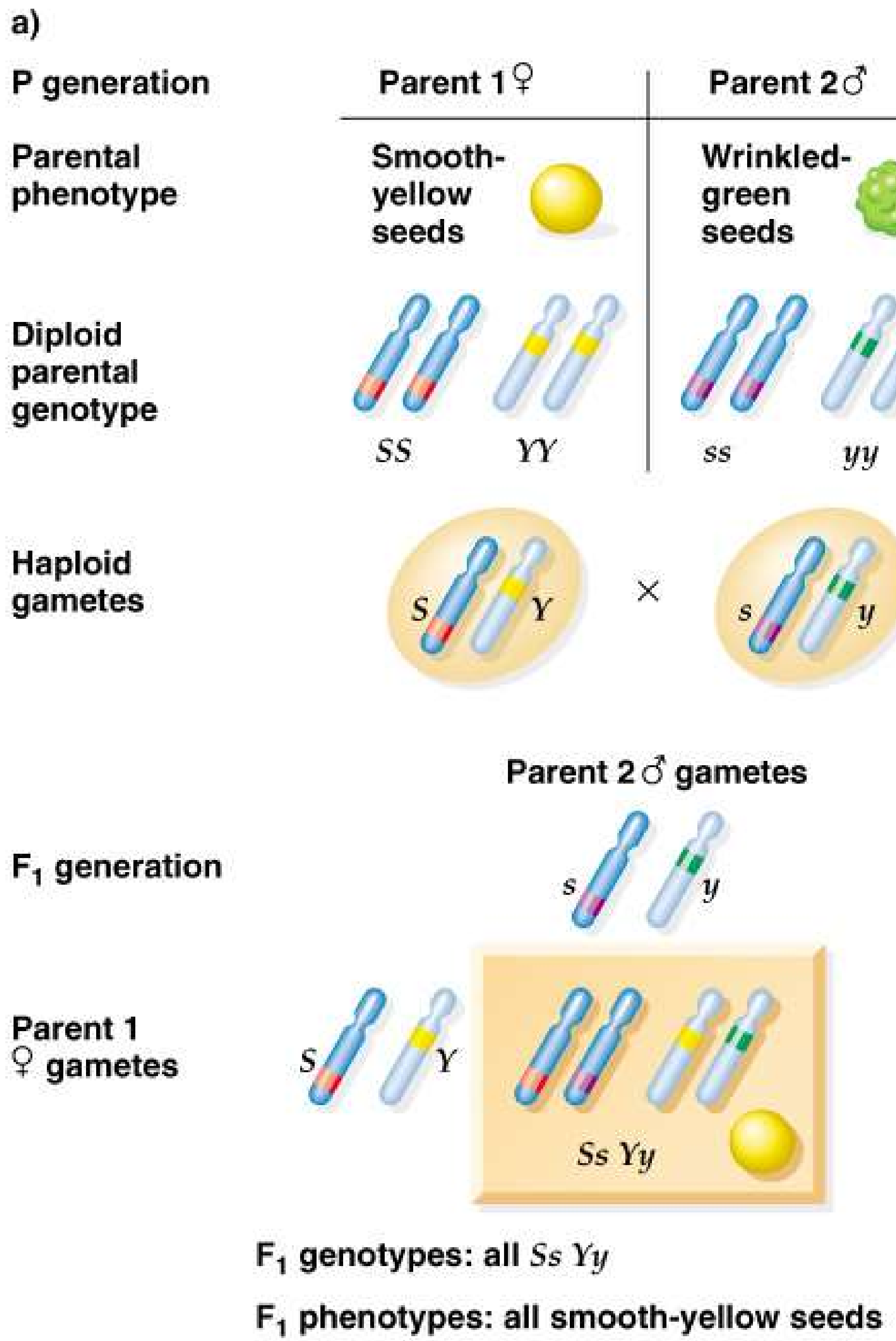
produces four phenotypes in the F2 generation

EXPERIMENT Two purebred pea plants, one with yellow-round seeds and the other with green-wrinkled seeds, were crossed, producing dihybrid F1 plants. Self-fertilization of the F1 hybrids, which were heterozygous for both traits, produced the F2 generation. The two hypotheses predict different phenotypic ratios. Note that yellow color (Y) and round shape (R) are dominant. Green color (y) and wrinkled shape (r) are recessive.

CONCLUSION The results support the hypothesis of independent assortment. Alleles for seed color and seed shape segregate into gametes independently of each other.



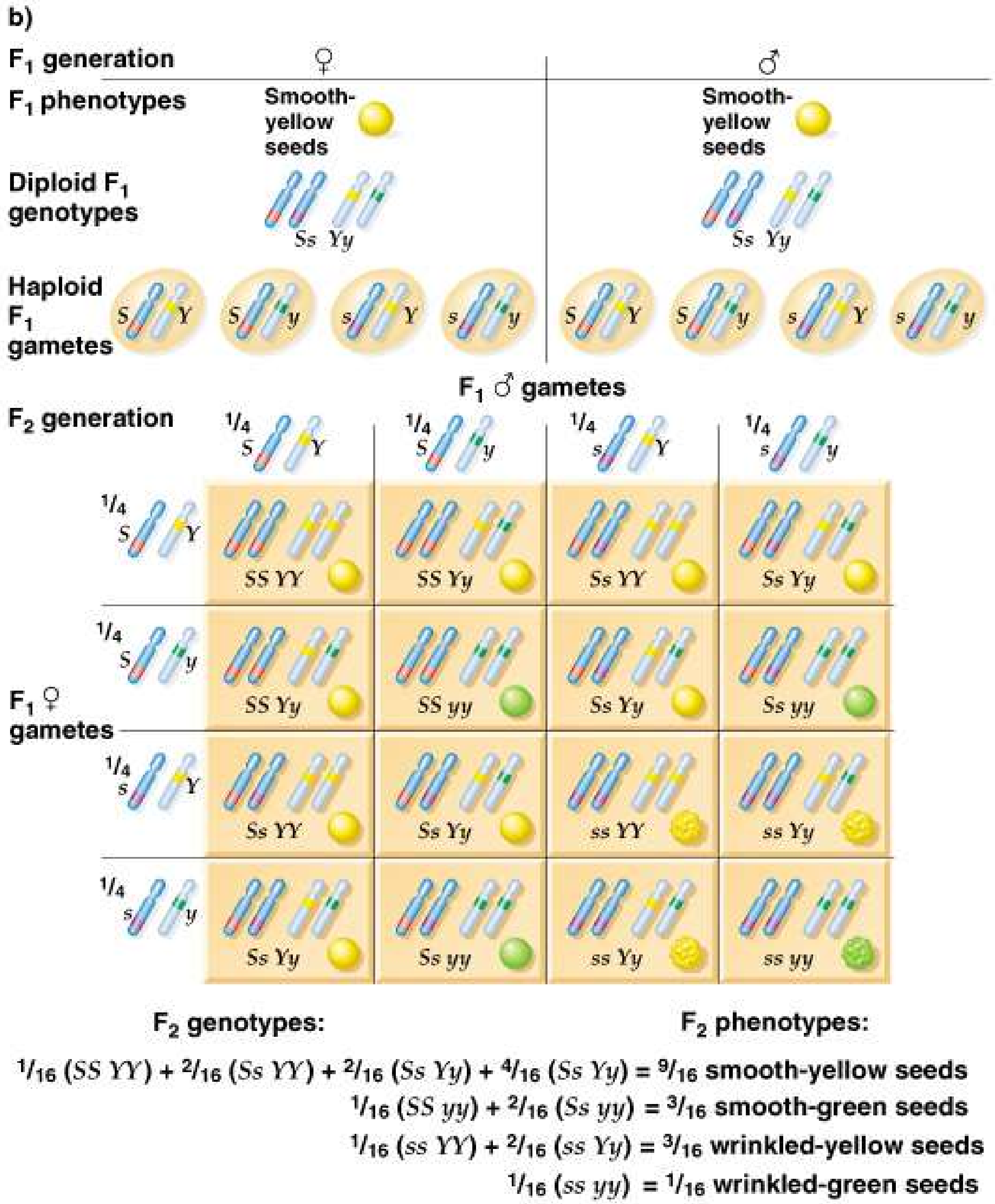
Dihybrid Croiss:
F_1 generation



Dihybrid Croiss:
F_2 generation

<u>Ratio</u>:

9:3:3:1



Dihybrid Croiss:

P	**Phenotypes**	Yellow color Smouth seed	X	Wrinkled green seed	(purbred)
	Genotypes	YYSS		yyss	
		meiosis		*meiosis*	
	Gametes	YS		ys	
			fertilization		
F_1	**Phenotypes**		YySs		
	Genotypes		Yellow color Smouth seed		
	Proportions		100%		

Dihybrid Croiss:

F1 X F1 self fertilization

F1 Genotypes YySs X YySs

Phenotypes Yellow color
Smouth seed

Proportions 100%

Meiosis

↓

Gametes 1/4*YR* 1/4*Yr* 1/4*yR* 1/4*yr* X 1/4*YR* 1/4*Yr* 1/4*yR* 1/4*yr*

F1: Yellow color Smouth seeds:

YySs

Each gamete will have one gene for each trait :

Y or y **S or s**

YS **Ys** **yS** **ys**

If the genes for these traits are passed on to gametes independently of each other, then each F1 parent should produce four types of gametes, at equal frequencies

Dihybrid Test-cross

- In monohybrid crosses, to know if a dominant trait is homozygous or heterozygous, it is necessary to perform a test-cross

- This is done with a recessive homozygote

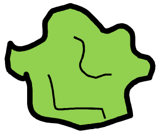
- The same is true for a dihybrid cross where the test-cross is done with an individual who is homozygous recessive for both traits (double recessive homozygote)

Dihybrid Test-cross

Mendel Experiments

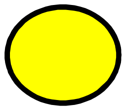
Cross with a double recessive that can give only recessive alleles for both traits to all offspring

yyss



All gametes = **ys**

F1 phenotypes



YySs

¼ YS	**¼ YySs**	**25% YS Yellow Smouth**
¼ yS	**¼ yySs**	**25% yS Green Smouth**
¼ Ys	**¼ Yyss**	**25% Ys Yellow Wrinkled**
¼ ys	**¼ yyss**	**25% ys Green Wrinkled**

And the phenotypes of the offspring reflect the gametes donated by the YySs parent.

Genotypic frequencies in offspring

Cross interpretation:

There are 4 types of descendants in equiprobable proportions with as many parental phenotypes as recombinant phenotypes.

However, the double recessive male produces only one type of gamete.

We deduce that the F1 female produces 4 types of gametes, therefore each trait is coded by a different gene (therefore 2 genes here)

The equiprobability of the parental and recombinant phenotypes shows that the F1 female produces as many parental gametes as recombinant gametes and therefore the genes in question behave independently during meiosis (there are therefore no privileged allelic associations).

The genes in question are therefore independent, i.e. carried by different pairs of chromosomes (it is the interchromosomal mixing that is at the origin of the different phenotypes observed in the offspring of the test-cross)

Dihybrid cross

(study of two characters)

Case of Linked genes

Crossing Over

- Crossing over produces **recombinant chromosomes**, which combine genes inherited from each parent
- Crossing over begins very early in prophase I, as homologous chromosomes pair up gene by gene
- In crossing over, homologous portions of two nonsister chromatids trade places
- Crossing over contributes to genetic variation by combining DNA from two parents into a single chromosome

Crossing Over

- In crossing over, homologous portions of two nonsister chromatids trade places
- Crossing over contributes to genetic variation by combining DNA from two parents into a single chromosome

Fig. 13-12-1

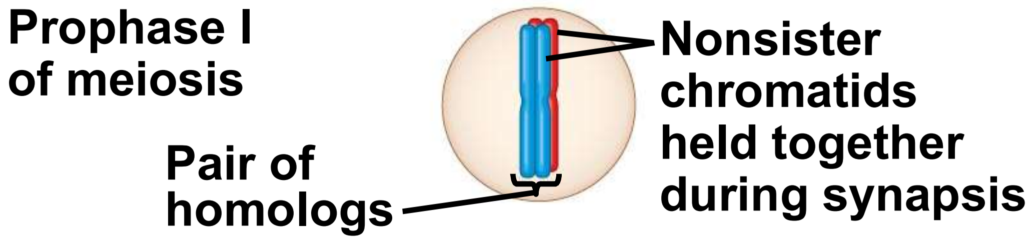

Prophase I
of meiosis
Pair of
homologs
Nonsister
chromatids
held together
during synapsis

Fig. 13-12-2

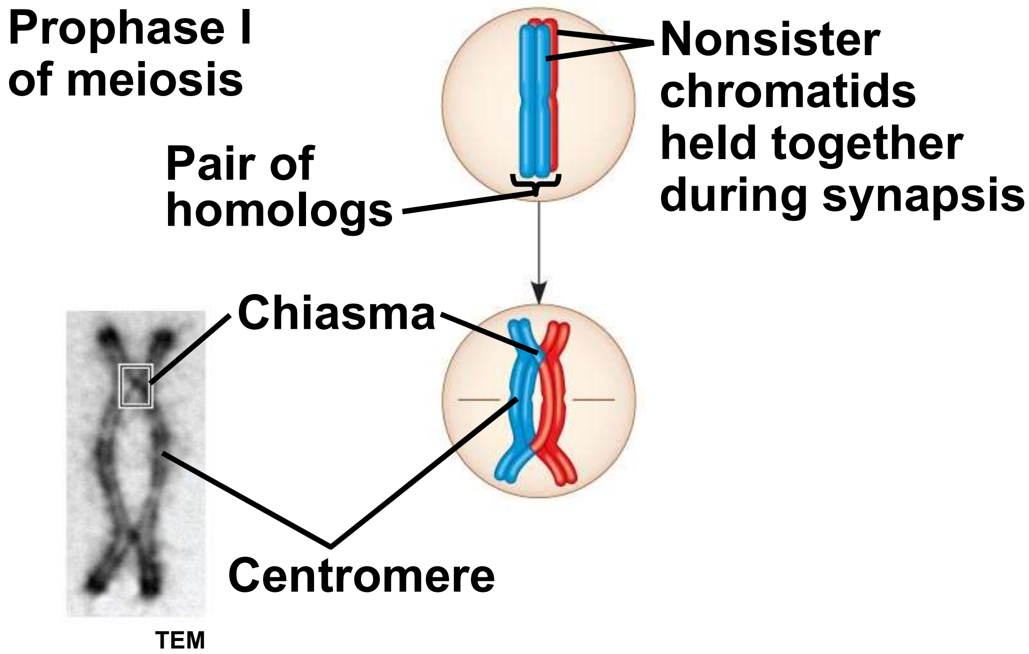

Prophase I
of meiosis
Pair of
homologs
Nonsister
chromatids
held together
during synapsis
Chiasma
Centromere
TEM

Fig. 13-12-3

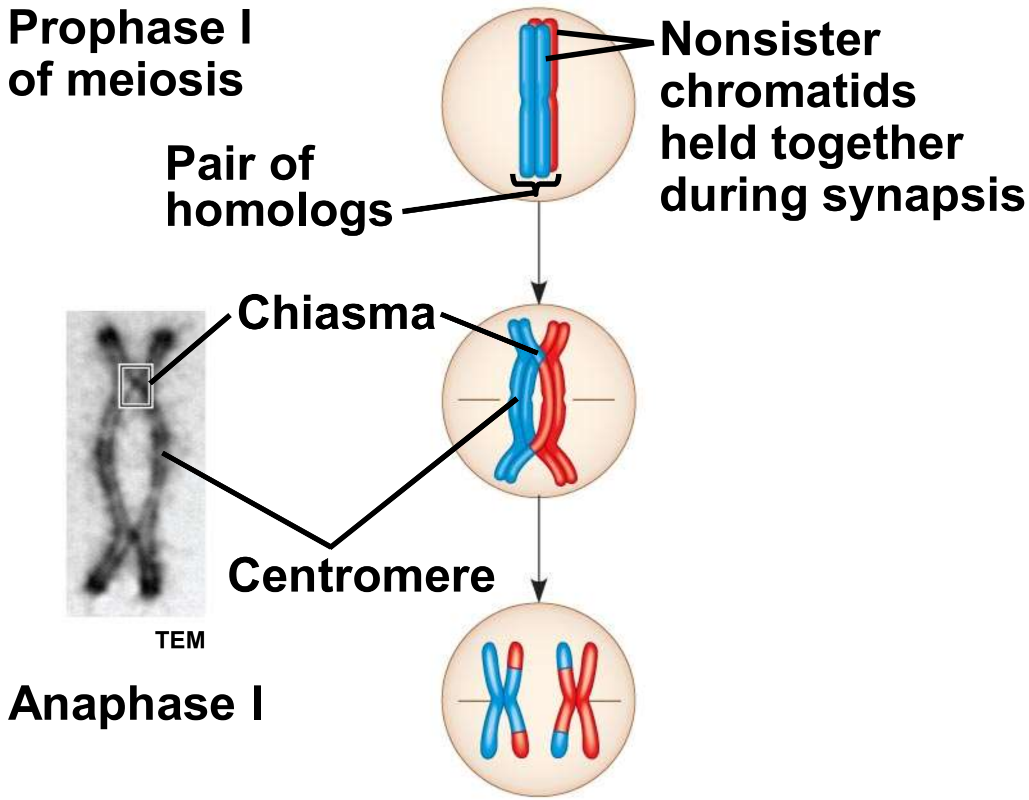

Prophase I
of meiosis
Nonsister
chromatids
held together
during synapsis
Pair of
homologs
Chiasma
Centromere
TEM
Anaphase I

Fig. 13-12-4

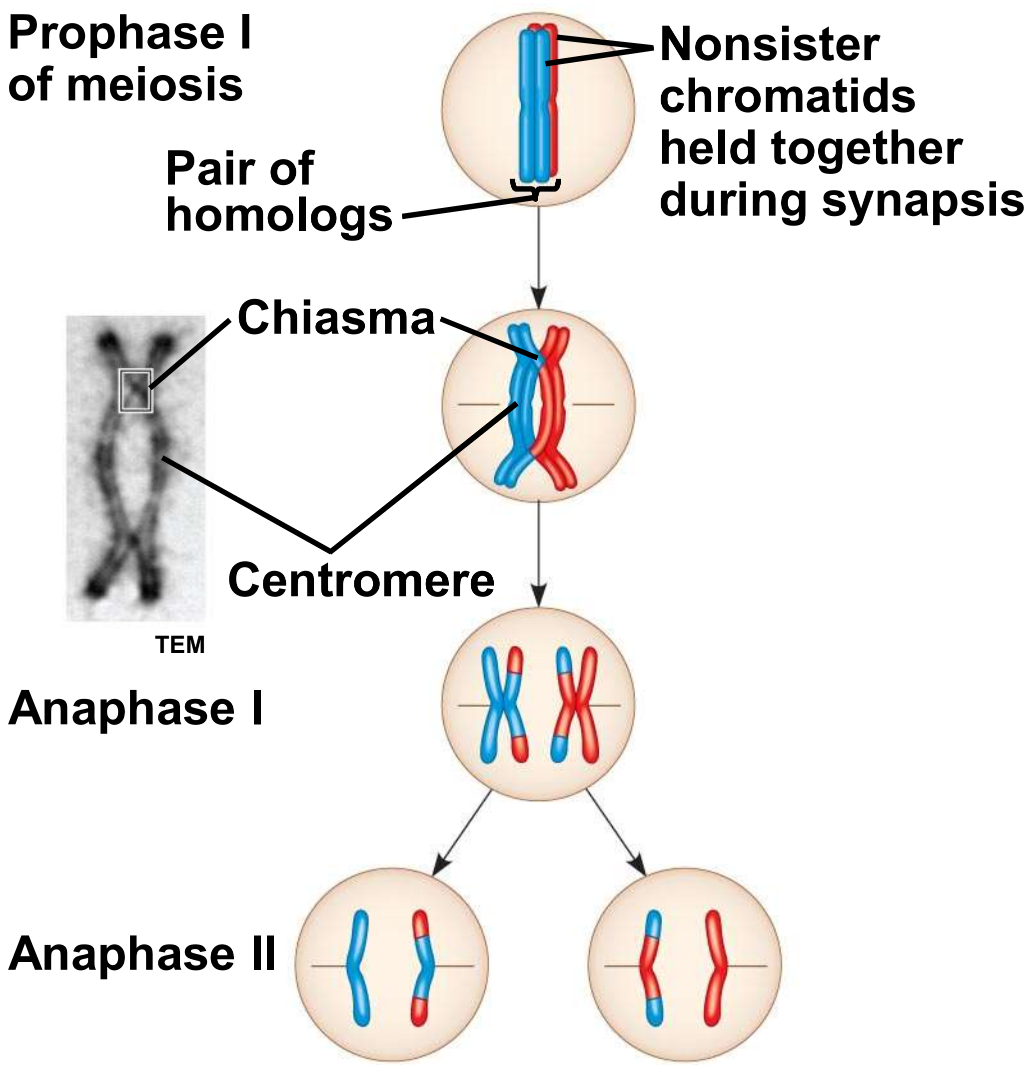
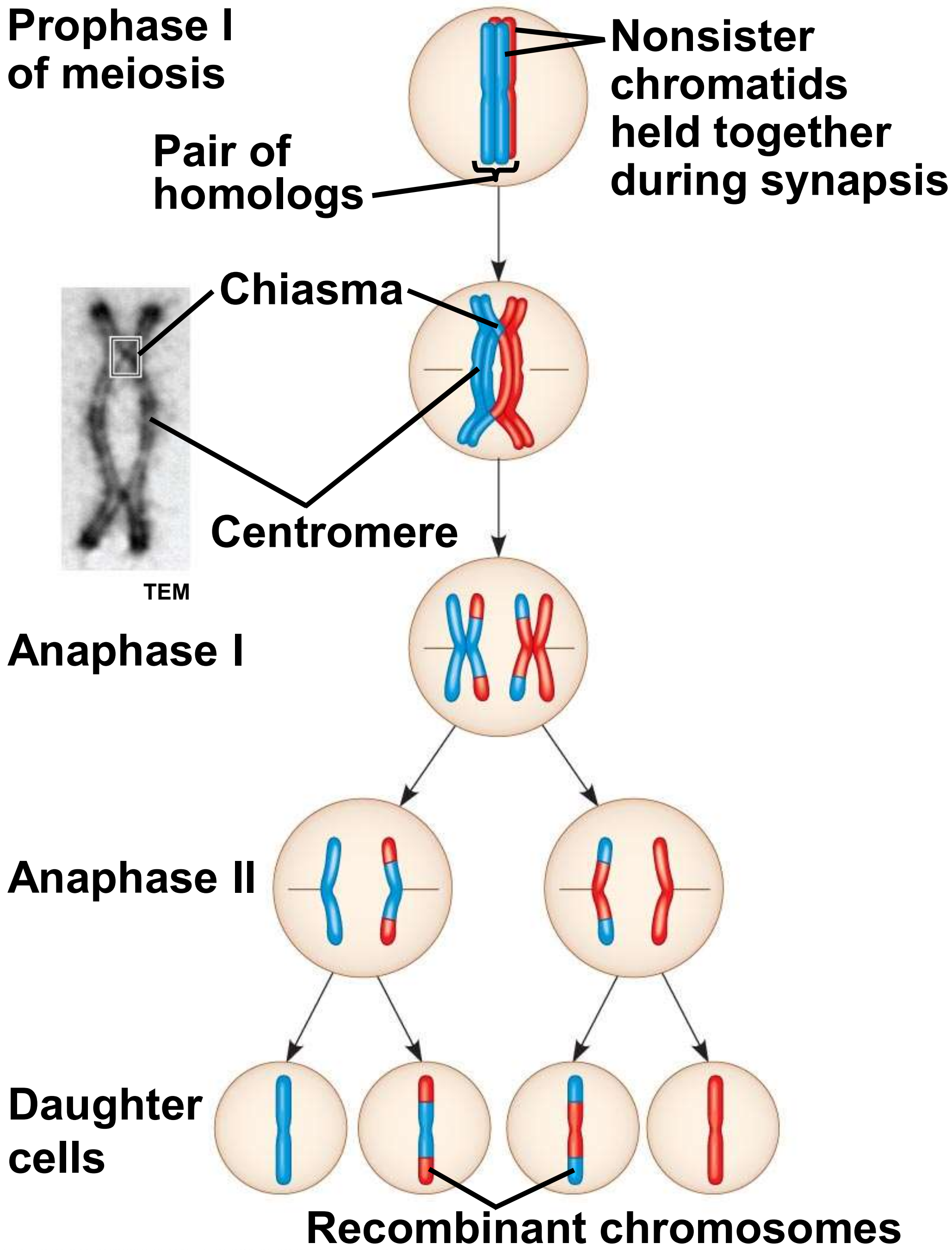

Prophase I
of meiosis
Pair of
homologs
Nonsister
chromatids
held together
during synapsis
Chiasma
Centromere
TEM
Anaphase I
Anaphase II

Fig. 13-12-5


Prophase I
of meiosis
Nonsister
chromatids
held together
during synapsis
Pair of
homologs
Chiasma
Centromere
TEM
Anaphase I
Anaphase II
Daughter
cells
Recombinant chromosomes

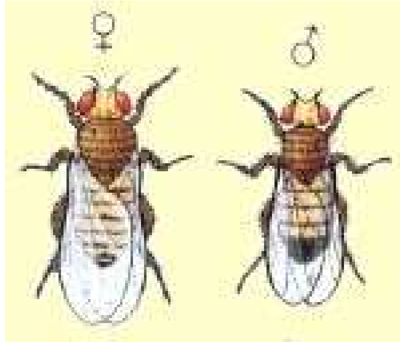
Discovery of gene linkage

<u>Thomas Hunt Morgan</u>

<u>Morgan's experiment:</u>

- **Early 1900s**
- **First to associate a specific gene with a specific chromosome**
- **Experiments conducted on fruit flies (drosophila)**

Morgan's experiment: fruit flies (drosophila)



Why drosophila ?

- Little harmful fly
- Prolific (about 100 individuals every 15 days)
- The sex can be easily identified by the abdomen
- Has only 8 chromosomes → less material to study
- Its giant chromosomes are visible under an optical microscope. We can therefore follow their movement as well as that of the genes they carry under a microscope.
- Sex determination resembles that of humans
  - 3 pairs of autosomes and 1 pair of XX in females
  - 3 pairs of autosomes and 1 pair of XY in males
- Morgan raised flies for a year while subjecting them to X-rays to induce mutations. The first mutant he found was a male fly with white eyes..

Morgan's Dihybrid Cross

Crossing two characters

Gray body character (b^+, dominant) or black (b, recessive)

Normal Wings Character (vg^+, dominant) or vestigial (vg, recessive)

The presence of crossing overv can be deduced cross results

Croisement A :

drosophila ♂ [Normal Wings ; Gray body]
(vg+b+//vg+ b+)

drosophile♀ [Vestigial Wings ; Black body]
(vg b//vg b)

→ 100 % F1 [Normal Wings ; Gray body]
→ (vg+b+//vg b)

Croisement B :

♂ double recessive x ♀ F1 (test cross)
(vg b//vg b) (vg+b+//vg b)

Forecast crossing table:

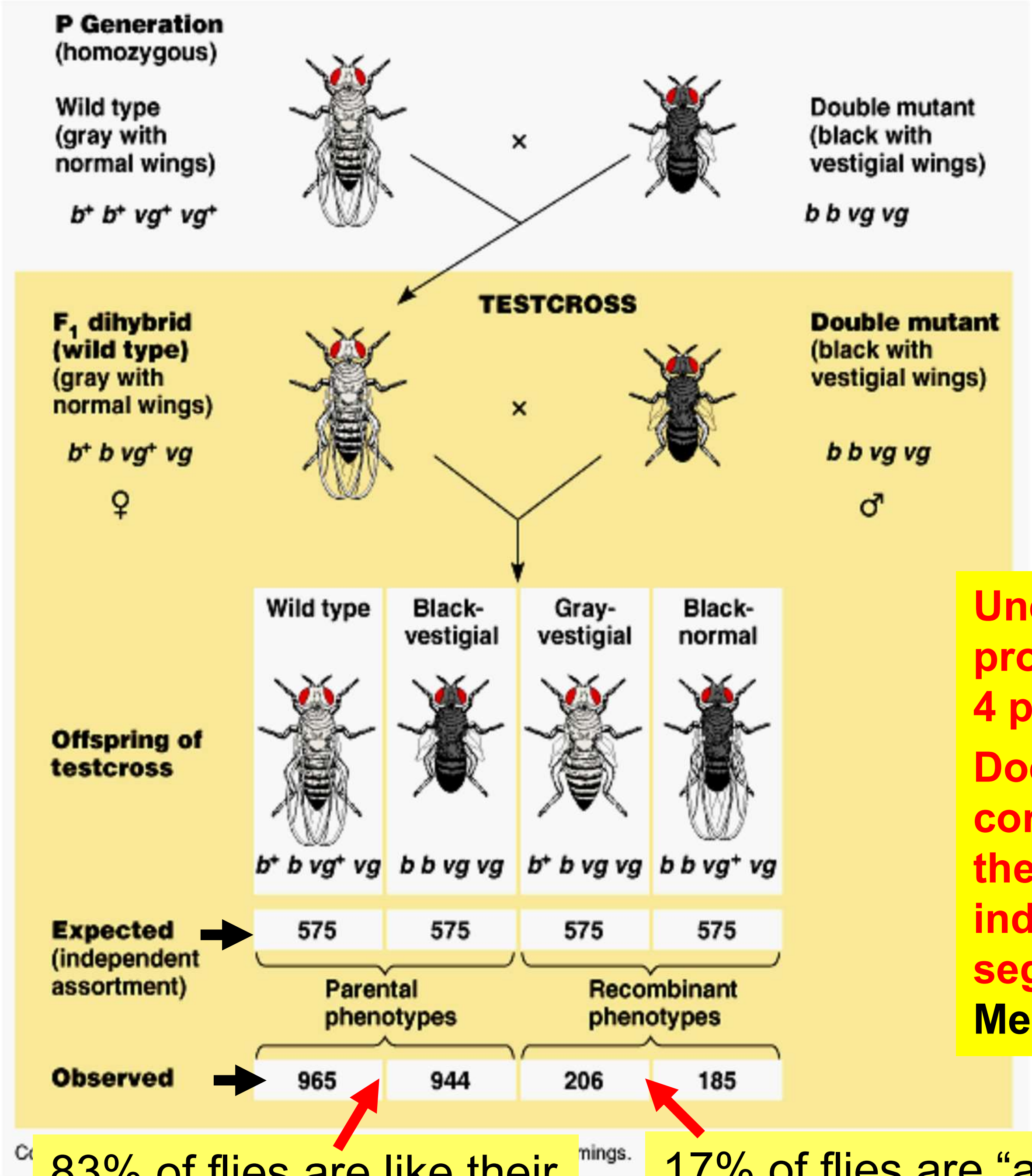
Parental Gametes	(Vg + b+)	(Vg b)	(Vg + b)	(Vg b+)
(Vg b)	**(vg+b+//vg b)** **[Vg+; b+]** 965	**(vg b//vg b)** **[Vg-; b-]** 944	**(vg+ b//vg b)** **[Vg+; b]** 185	**(vg b+//vg b)** **[Vg; b+]** 206

$$\underbrace{\text{Parental Types } 83\%}\ >\ \underbrace{\text{Recombinant Types } 17\%}$$

Parental Types
83%

Recombinant Types
17%

Morgan observes 4 phenotypes in F1 as predicted by Mendel's law of segregation



Unequal proportion of the 4 phenotypes

Does not correspond to the law of independent segregation of Mendel.

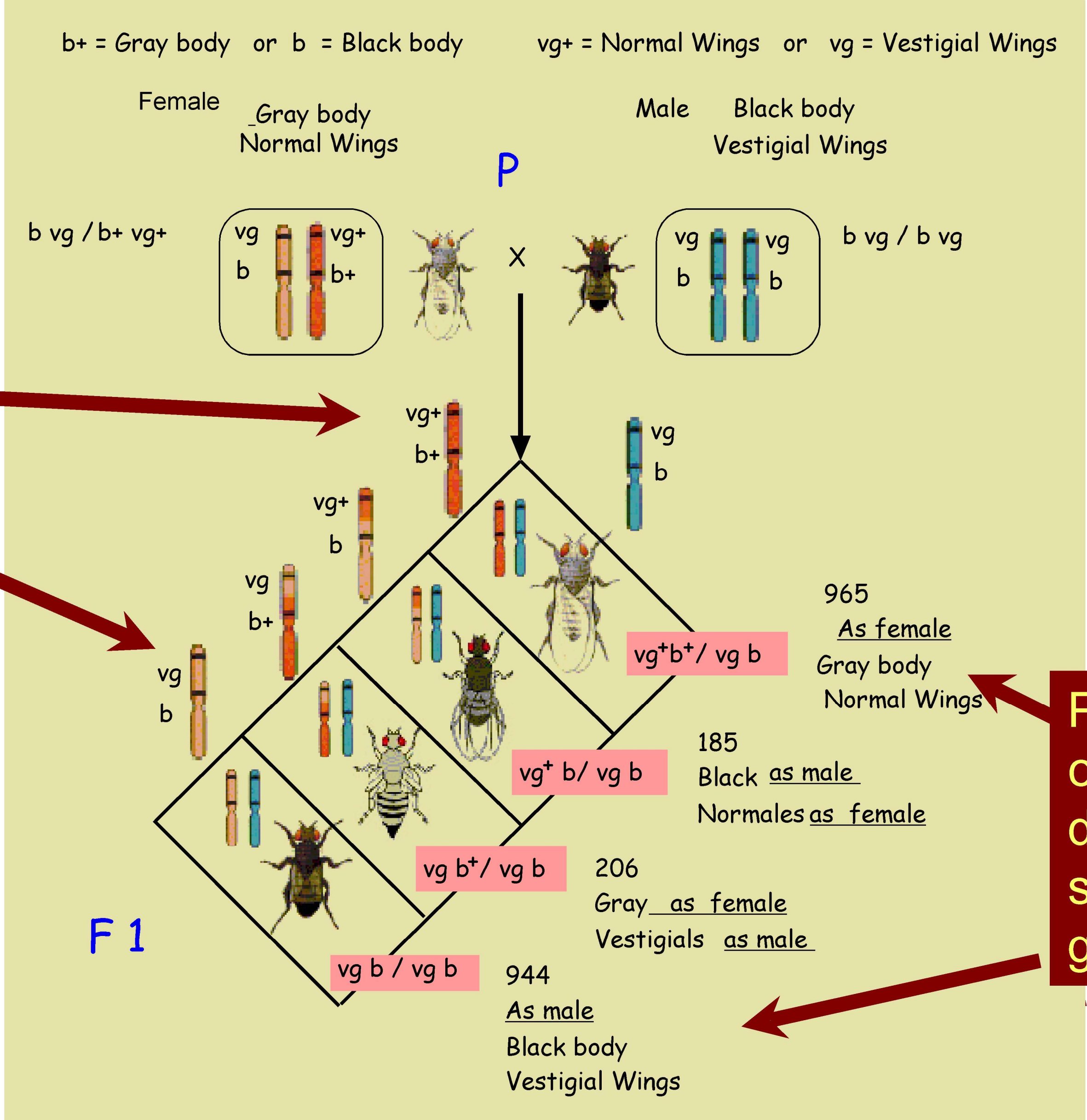
83% of flies are like their parents

17% of flies are "a mixture of parents"

Campbell : 293 (2ᵉéd. Fr)
Figure 15.4

Morgan's first hypothesis to explain his results :

The genes studied (body/wings) are carried by the same chromosome and are transmitted together (most often) in a gamete.

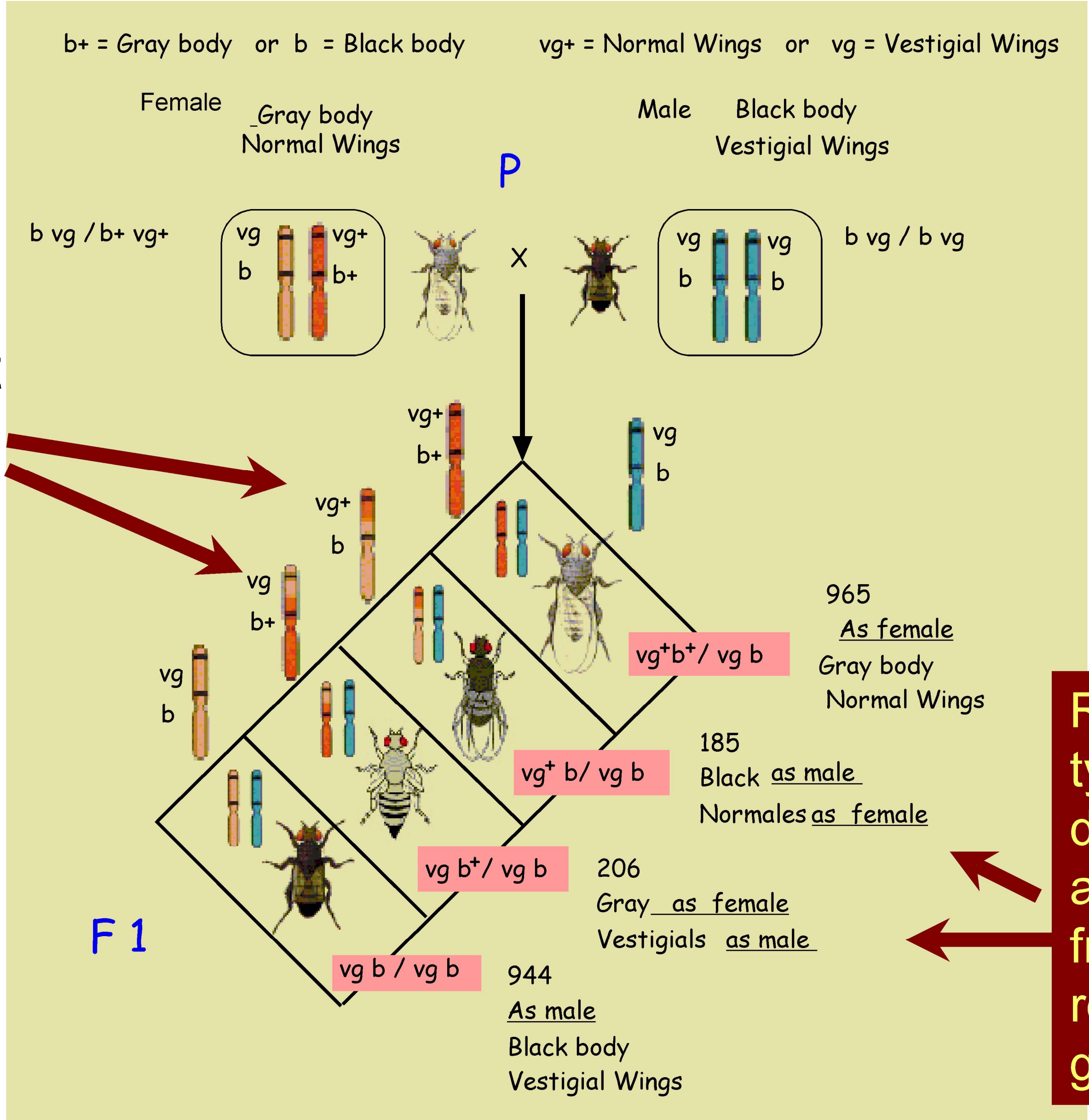


Standard (majority) gametes have the parental allelic combination

Parental type offspring are derived from standard gametes

Morgan's first hypothesis to explain his results :

The genes studied (body/wings) are carried by the same chromosome and are transmitted together (most often) in a gamete.



Recombinant gametes are a mixture of the parental allelic combination

Recombinant type descendants are derived from recombinant gametes

Interpretation of cross A:

The parents are purebred so the F1 generation is heterozygous for the genes considered.

However, only the alleles coding for the long wings and gray body phenotype are expressed

We deduce that the allele coding for the long wings is dominant over the allele coding for the vestigial wings and that the allele coding for the gray body is dominant over the allele coding for the black body.

Interpretation of the test-cross (cross B):

The 2 characters studied in the Morgan dihybrid cross did not undergo independent assortment of chromosomes since the 4 phenotypes are not in equal proportion

There are 4 types of descendants in non-equiprobable proportions with many more parental phenotypes than recombinant phenotypes.

However, the double recessive male produces only one type of gamete.

We deduce that the F1 female produces 4 types of gametes, therefore each character is coded by a different gene (therefore 2 genes here)

The non-equiprobability of the parental and recombinant phenotypes shows that the F1 female produces more parental gametes than recombinant gametes and therefore that the genes in question behave in a linked manner during meiosis (therefore there are privileged allelic associations).

The genes in question are therefore linked, that is to say carried by the same pair of chromosomes.

Notes:

In a given organism containing a large number of linked and independent genes the effect of crossing over is added to the effect of independent assortment of chromosomes

$\rightarrow$ leads to a much higher number of allelic combinations in the gametes formed.

GENETIC MAPPING

There are two main types of maps:

- genetic maps

distances are expressed in centimorgan (cM)

- physical maps

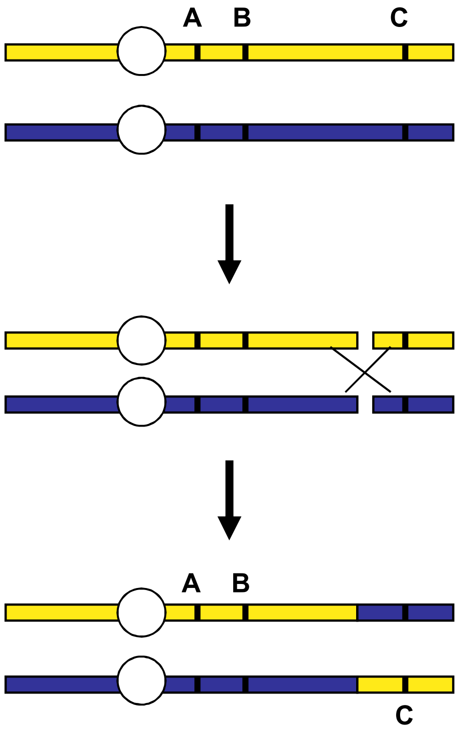
distances are expressed in base pairs (bp)
kilobases (kb) = 1000 bp
Megabases (Mb) = 1000 kb

Genetic maps

Genetic distances are a reflection of the recombination frequency (RF).

During meiosis, "crossing-over" causes the exchange of genetic material between homologous chromosomes.

When two genes are close enough to be separated only once in 100 (1% recombination frequency), the genetic distance between them is set at 1 centimorgan (1 cM).



Recombination frequency (RF)

Recombination frequency is **a measure of genetic linkage** and is used in the creation of a genetic linkage map. Recombination frequency (θ) is the frequency with which a single chromosomal crossover will take place between two genes during meiosis.

In Morgan's dihybrid cross there are 17% recombinant individuals.

$$\text{RF} = \left[\frac{206 + 185}{2300} \times 100 = 17\% \right]$$

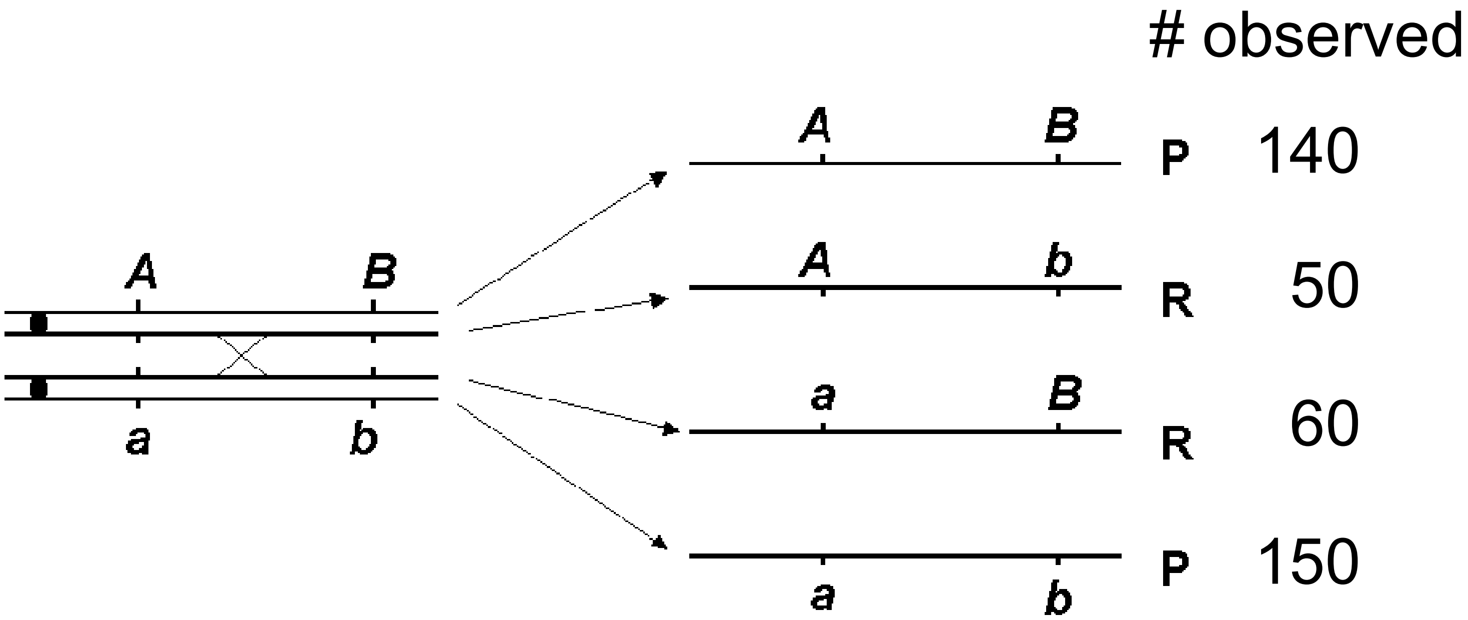
Mapping unit:
In the Morgan dihybrid cross there are 17% recombinant individuals, therefore there are 17 cM between the two genes b and vg.

Value of the centimorgan
Centimorgans have no absolute dimension.

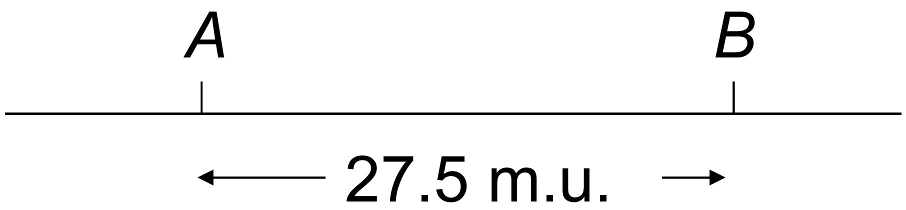
Recombination frequency (RF)

- Experimentally determined from frequency of recombinant phenotypes in testcrosses
- Roughly proportional to physical length of DNA between loci
- Greater physical distance between two loci, greater chance of recombination by crossing-over
- 1% recombinants = 1 map unit (m.u.)
- 1 m.u. = 1 centiMorgan (cM)

Linkage maps



- RF is (60+50)/400=27.5%, clearly less than 50%
- Map is given by:

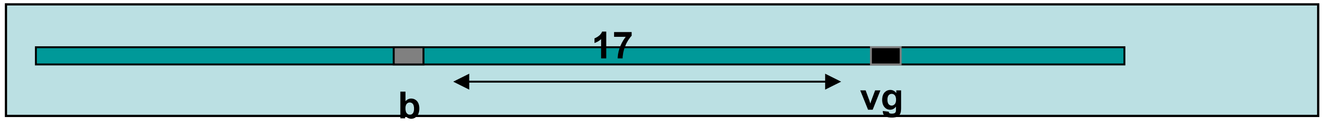


Mapping

- RF analysis determines relative gene order
- RF between same two loci may be different in different strains or sexes
- RF values are roughly additive up to 50%
  - multiple crossovers essentially uncouple loci, mimicking independent assortment
- Maps based on RF can be combined with molecular and cytological analyses to provide more precise locations of genes

Construction of a genetic map for the b, vg and cn alleles

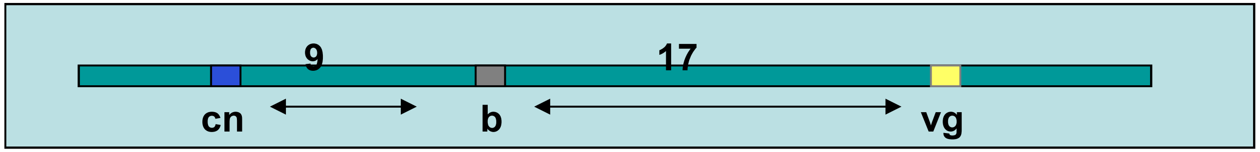
A cross between 2 drosophila for the b and vg characters produces 17% of recombinants → 17 cM between the b and vg genes



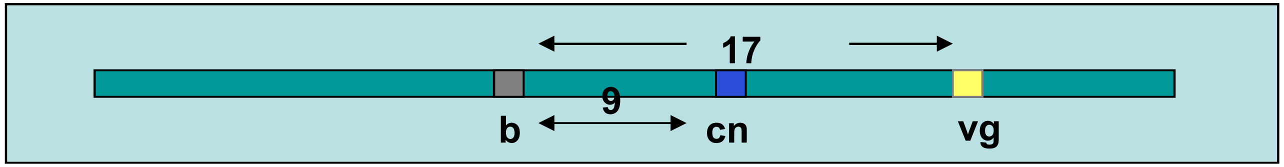
•A cross between 2 drosophila for the b and cn characters (vermilion eyes) produces 9% of recombinants → 9 cM between the b and cn genes

What is the genetic map of the three genes? map A ou map B ?

A



B

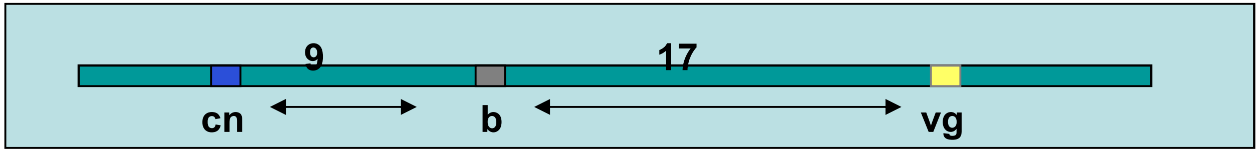


We can't answer with these data, we need another cross. A student of Morgan, made this cross. He found 9.5% recombinants for the cn and vg characters.

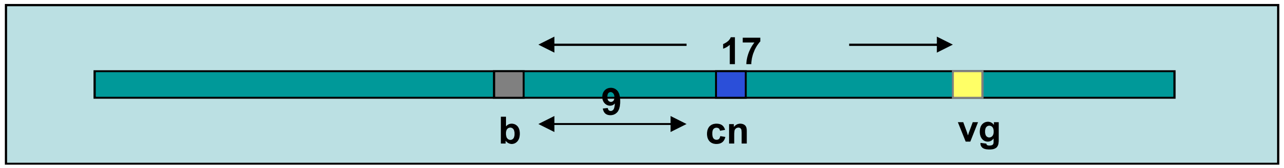
→ 9 cM between cn and vg genes

What is the genetic map of the three genes? map B

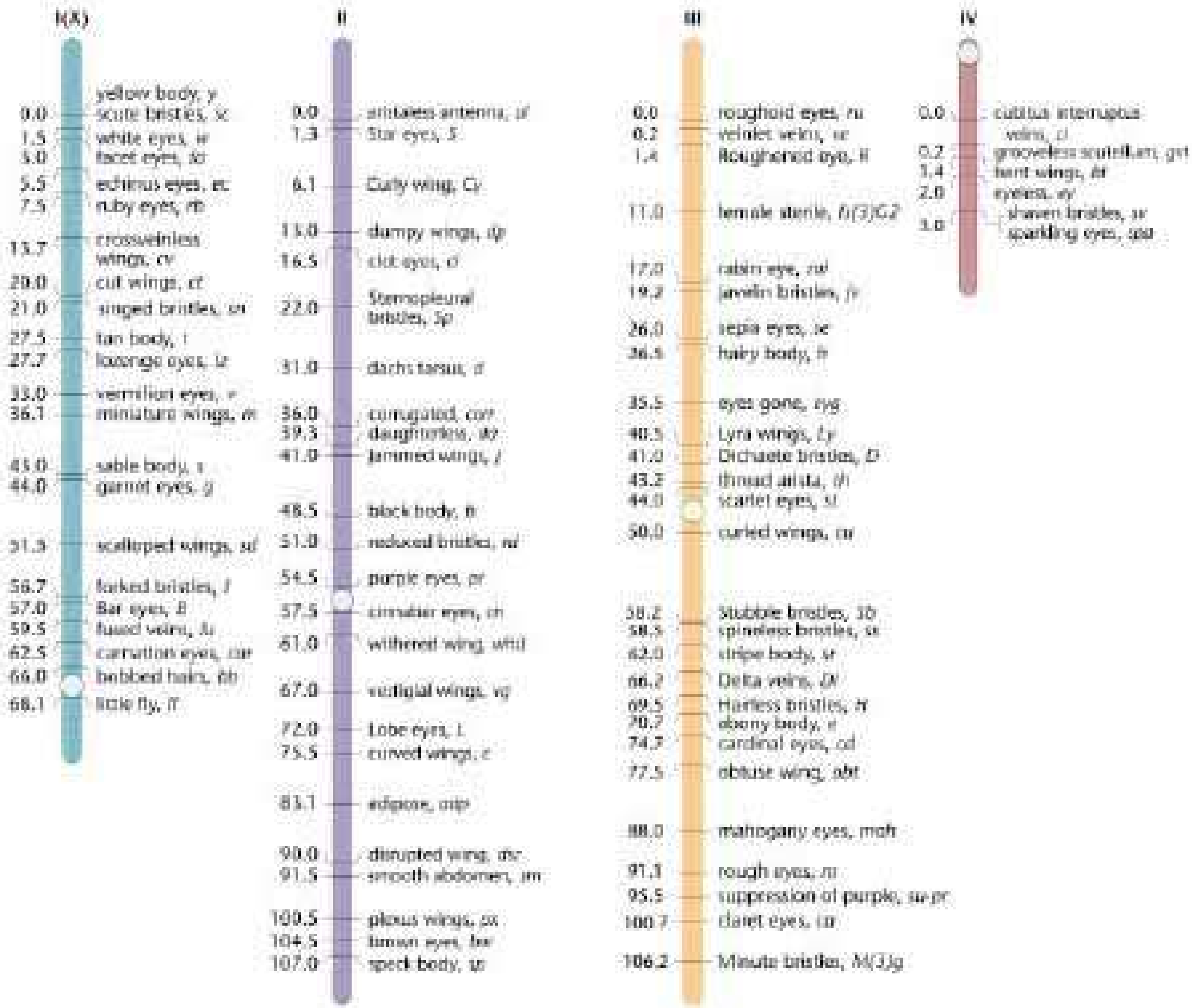
A



B



Genetic mapping of *Drosophila melanogaster*



Sex chromosomes and sex-linked inheritance

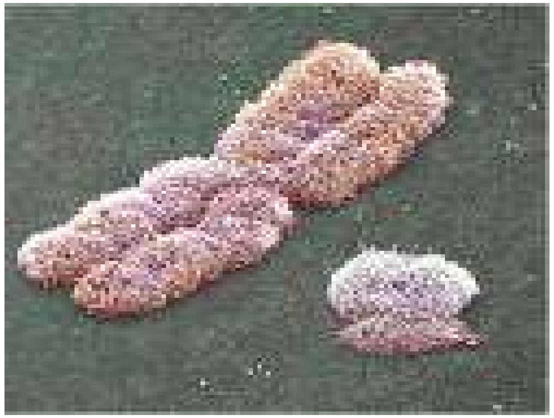
Sex chromosomes and sex-linked inheritance

In humans, there are 23 pairs of chromosomes:

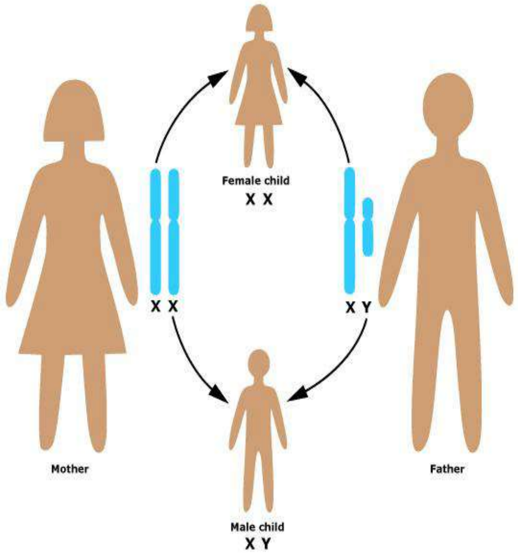
Autosomes = 22 pairs of chromosomes that are identical in both sexes.

Gonosomes = sex chromosomes (X chromosome and Y chromosome).

Sex chromosomes and sex-linked inheritance



♀ \ ♂	X	Y
X	XX	XY
X	XX	XY



Sex chromosomes and sex-linked inheritance

- In humans

-Y chromosome : It is much smaller than the X chromosome and contains around 50 to 200 genes. Its main role is to determine male sex, in particular through the SRY gene (Sex-determining Region Y), which initiates the development of male characteristics in embryos

-Chromosome X : This is a relatively large chromosome containing about 1,100 genes. These genes play a role in various aspects of human biology, in addition to sex determination.

-Genes carried by x are hemizygous (sex-linked characteristics)

Sex determination is variable in nature !

Oiseaux

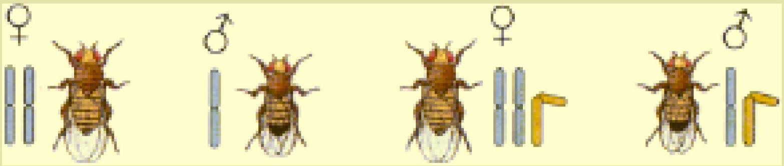
Système Z W

Z W

Z Z

Drosophiles

Système X <u>quantitatif</u>



XX Fertile

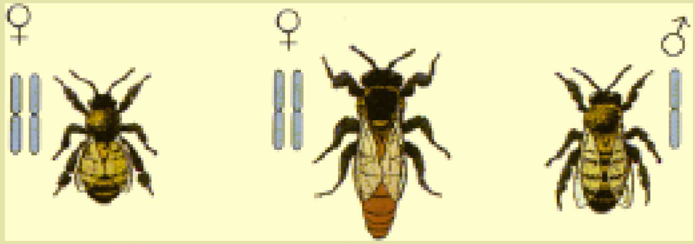
XO Stérile

XXY Fertile

XY Fertile

Abeilles

Système haploïde-diploïde



Ouvrière diploïde

Reine diploïde

Bourdon haploïde

Sex Chromosomes in Other Organisms

1. Sex chromosome composition in birds, butterflies, moths and some fish is opposite that of mammals, with the male the homogametic sex (ZZ) and the female heterogametic (ZW). Z-linked genes behave like X-linked genes in mammals, but the sexes are reversed.
2. In plants, the arrangement of sex organs varies:
    a. Dioecious species (e.g., ginkgo) have plants of separate sexes, one with male parts, the other with female.
    b. Monoecious species have male and female parts on the same plant.
        i. Perfect flowers (e.g., rose, buttercup) have both types of parts in the same flower.
        ii. Imperfect flowers (e.g., corn) have male and female parts in different flowers on the same plant.
3. Some dioecious plants have sex chromosomes and use an X-chromosome-autosome balance system, but many other sex determination systems also occur in dioecious plants.
4. Other eukaryotes use a genic system instead of entire sex chromosomes. A single allele determines the mating type (e.g., *MATa* and *MATα* in *Saccharomyces cerevisiae*).

Sex Linkage

X-Linked Inheritance

1. Morgan (1910) found a mutant white-eyed male fly, and used it in a series of experiments that showed a gene for eye color located on the X chromosome.
   a. First, he crossed the white-eyed male with a wild-type (red-eyed) female. All F_1 flies had red eyes. Therefore, the white-eyed trait is recessive.
   b. Next, F_1 were interbred. They produced an F_2 with:
      i. 3,470 red-eyed flies.
      ii. 782 white-eyed flies.
   c. The recessive number is too small to fit Mendelian ratios (explanation discovered later is that white-eyed flies have lower viability).
   d. All of the F_2 white-eyed flies were male.

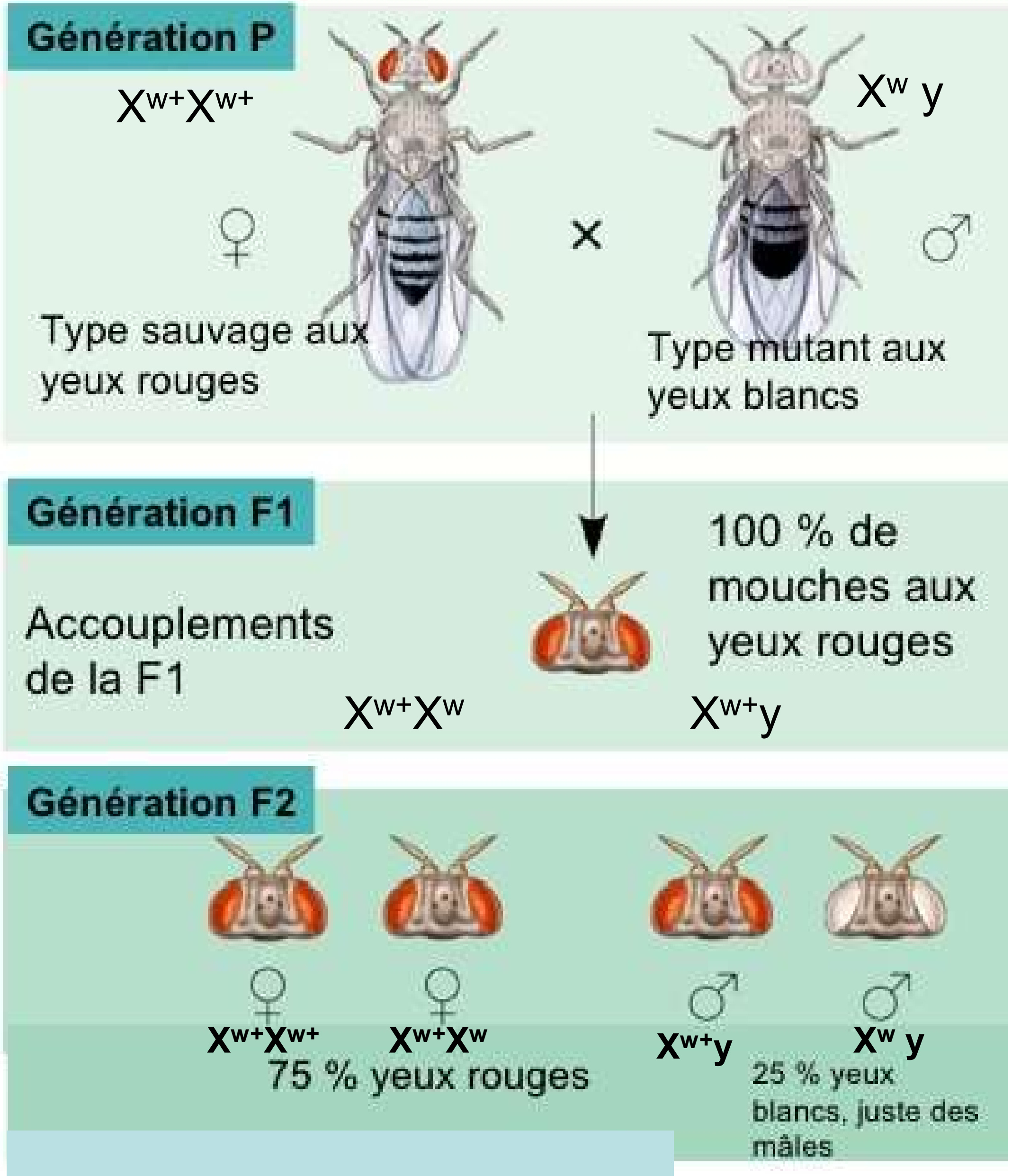
Le croisement monohybride de Morgan — yeux rouges (w^+) ou yeux blancs (w) — et sa principale déduction

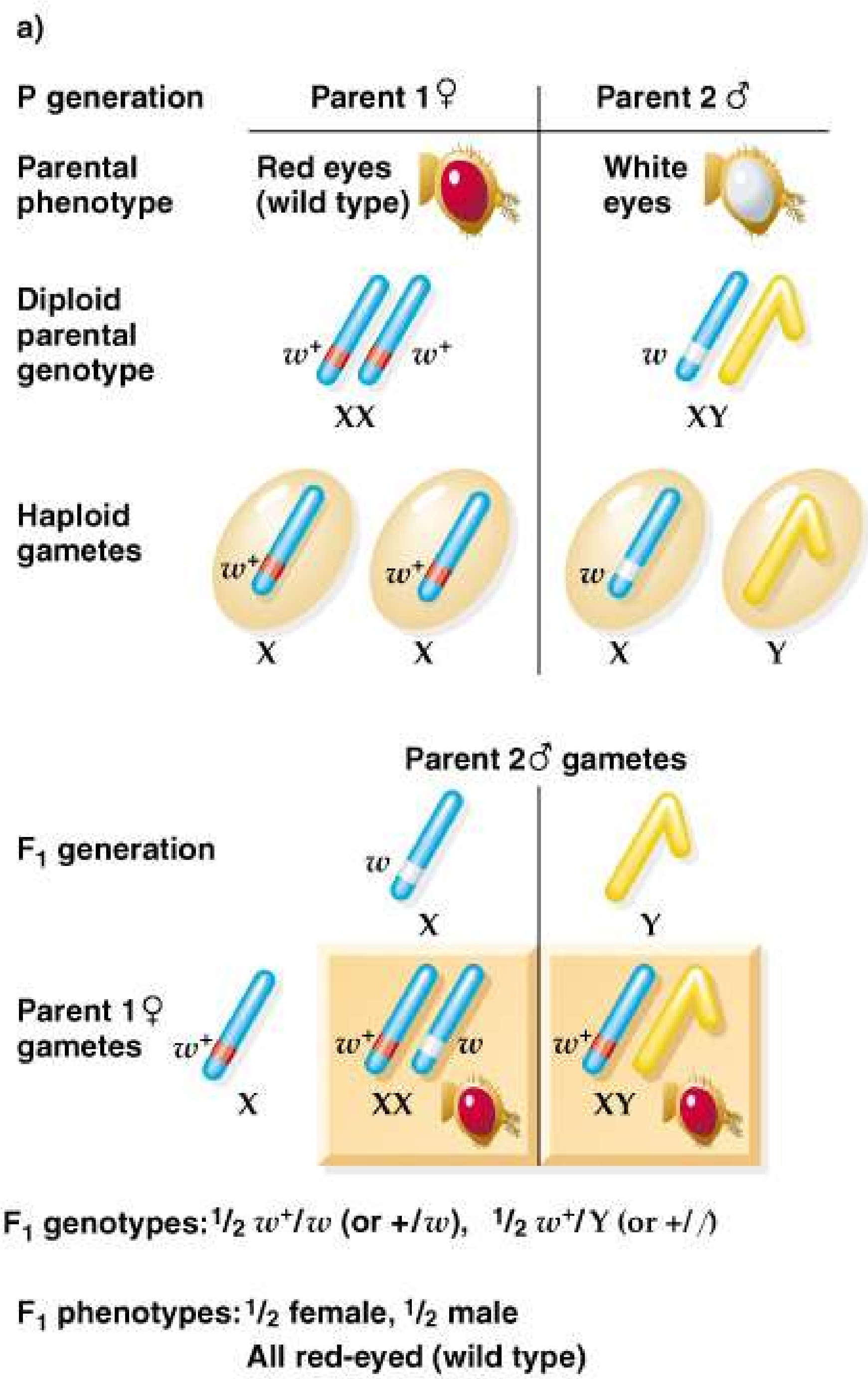
A- Son croisement

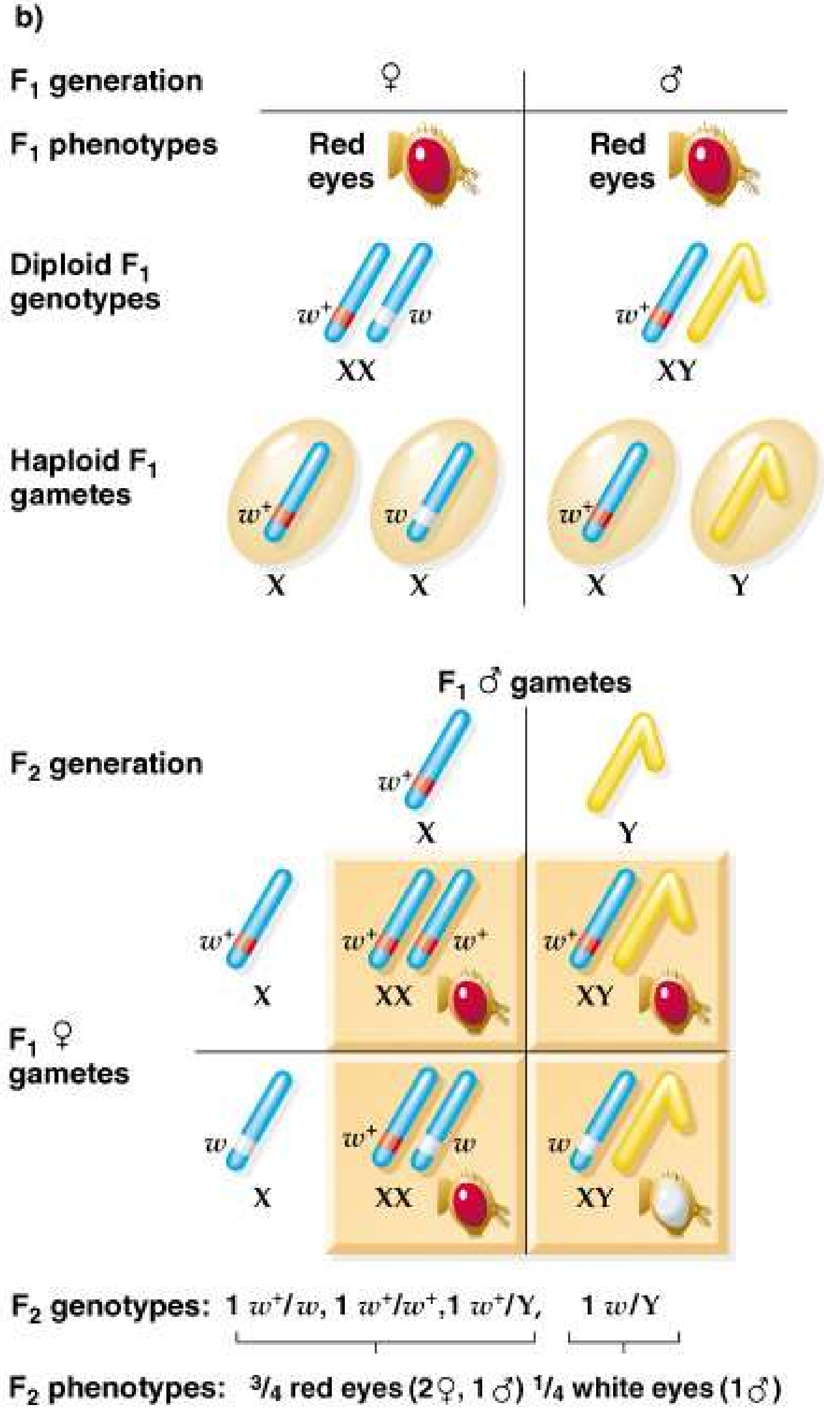
Morgan croise deux lignées pures : une femelle aux yeux rouges «type sauvage » avec un mâle aux yeux blancs «type mutant»

En F1, il observe :
La disparition d'un caractère parental *(comme pour Mendel)*
Déduction : les yeux blancs sont récessifs.

En F2, il observe :
La réapparition du caractère parental disparu chez 25 % des descendants *(comme pour Mendel)*
Les mouches aux yeux blancs sont tous des mâles (*pas comme Mendel)*
Comment expliquer cela ?




a)
P generation
Parent 1♀
Parent 2♂
Parental phenotype
Red eyes (wild type)
White eyes
Diploid parental genotype
w^+
w^+
XX
w
XY
Haploid gametes
w^+
X
w^+
X
w
X
Y
Parent 2♂ gametes
F₁ generation
w
X
Y
Parent 1♀ gametes
w^+
X
w^+
w
XX
w^+
XY
F₁ genotypes: 1/2 w^+/w (or $+/w$), 1/2 w^+/Y (or +/ /)
F₁ phenotypes: 1/2 female, 1/2 male
All red-eyed (wild type)


b)
F1 generation
♀
♂
F1 phenotypes
Red eyes
Red eyes
Diploid F1 genotypes
w+
w
XX
w+
XY
Haploid F1 gametes
w+
X
w
X
w+
X
Y
F1 ♂ gametes
F2 generation
w+
X
Y
F1 ♀ gametes
w+
X
w+ w+
XX
w+
XY
w
X
w+ w
XX
w
XY
F2 genotypes: 1 w+/w, 1 w+/w+, 1 w+/Y, 1 w/Y
F2 phenotypes: 3/4 red eyes (2♀, 1♂) 1/4 white eyes (1♂)

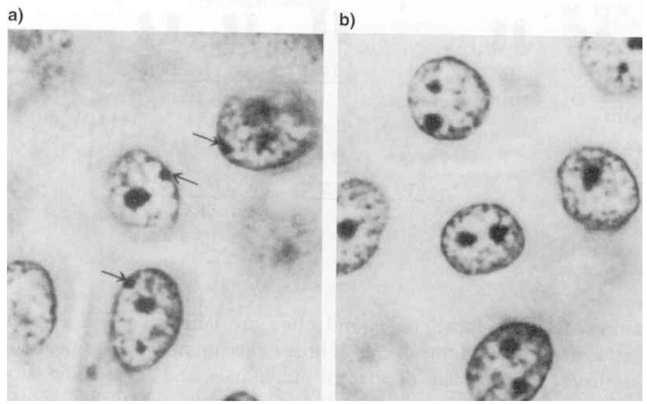
Morgan's hypothesis to explain his results

The (Mendelian trait) gene for eye color is carried on the X chromosome and has no equivalent on the Y chromosome (Sex-linked gene)

Several genes are believed to be linked to the sex chromosomes

Dosage Compensation Mechanism for X-Linked Genes in Mammals

1. Gene dosage varies between the sexes in mammals, because females have two copies of X while males have one. Early in development, gene expression from the X chromosome must be equalized to avoid death. Different dosage compensation systems have evolved in different organisms.
2. In mammals, female somatic cell nuclei contain a Barr body (highly condensed chromatin) while male nuclei do not. The Lyon hypothesis explains the phenomenon:
   a. Barr body is a condensed and (mostly) inactivated X chromosome. Lyonization of one chromosome leaves one transcriptionally active X, equalizing gene dose between the sexes.
   b. An X is randomly chosen in each cell for inactivation early in development (in humans, day 16 postfertilization).



c. Descendants of that cell will have the same X inactivated, making female mammals genetic mosaics. Examples are:

   i. Calico cats, in which differing descendant cells produce patches of different color on the animal

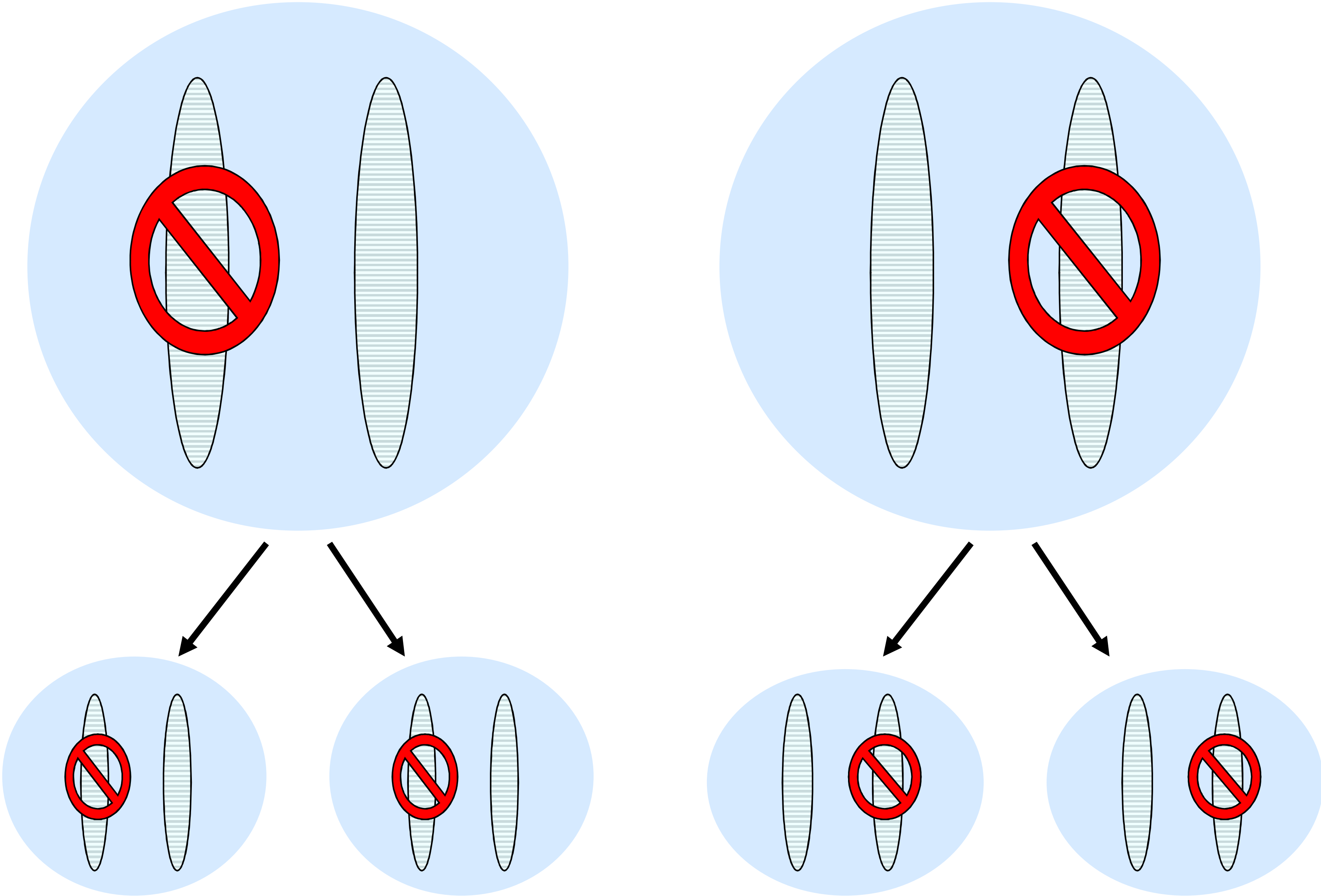
   ii. Women heterozygous for an X-linked allele responsible for sweat glands, who have a mosaic of normal skin and patches lacking sweat glands (anhidrotic ectodermal displasia).

d. Lyonization allows extra sex chromosomes to be tolerated well. No such mechanism exists for autosomes, and so an extra autosome is usually lethal.

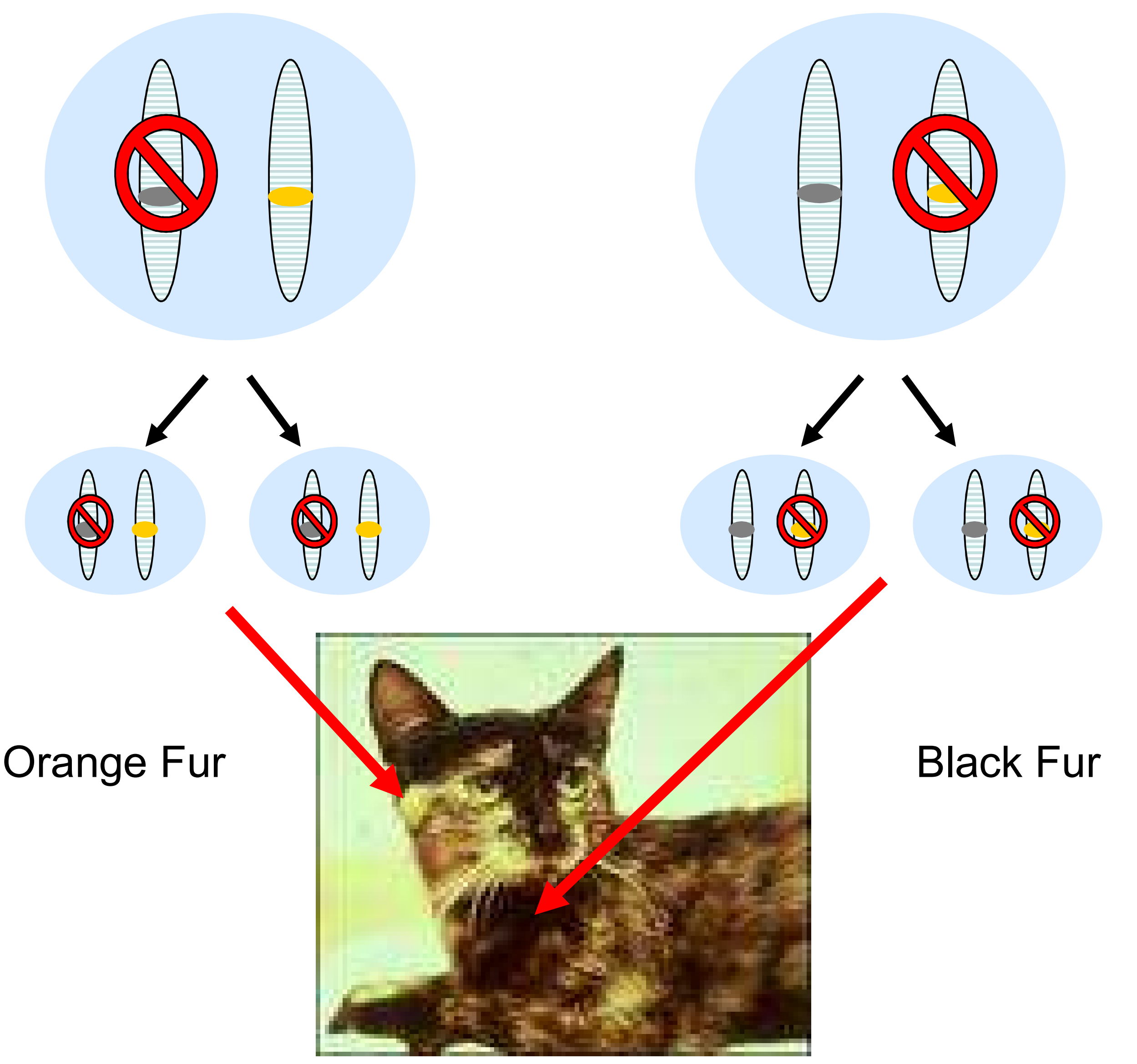
e. The number of Barr bodies is the number of X chromosomes minus one (Table 11.2).

Figure 11.12
A calico kitten.

X Chromosome Inactivation



Fur Color in Tortoiseshell Cats



Sex- Influence Inheritance

- Modes of gene expression differ between males and females
- An allele may be expressed as a dominant in one sex and a recessive in the other

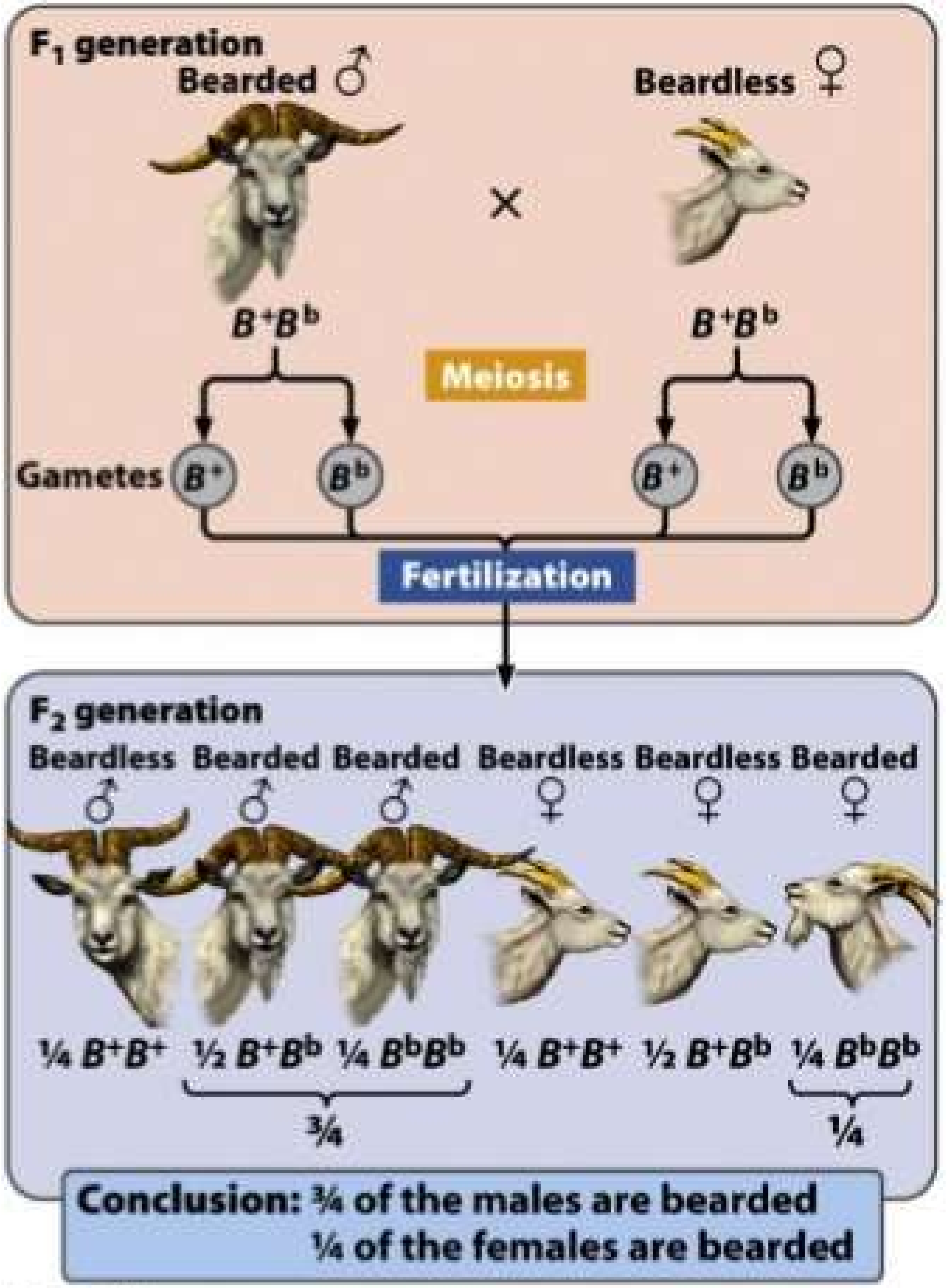


Figure 5-12b
Genetics: A Conceptual Approach, Third Edition

Sex-Limited inheritance

- Phenotypic expression is limited to one sex
- Ex. Milk production, and scrotal circumference
- These genes are not necessarily on the sex chromosomes but are only expressed in the male or female
- Thought to be hormonally conditioned

Maladies héréditaires liées au sexe chez l'humain

- Maladies héréditaires liées à l'X dues à un allèle récessif

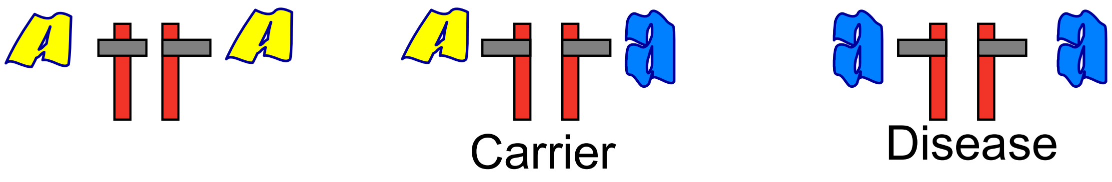
- Maladies héréditaires liées à l'X dues à un allèle dominant

X-linked hereditary diseases

Differences in gene expression between men and women

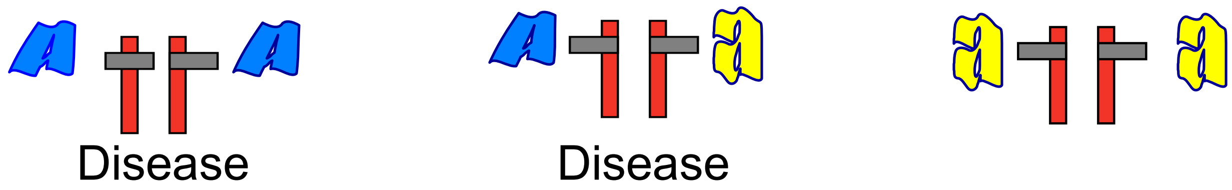
Yellow Gene = Health
Blue Gene = Disease

Woman-recessive disease



2 copies of the recessive gene are needed to trigger the disease

Woman-dominant disease



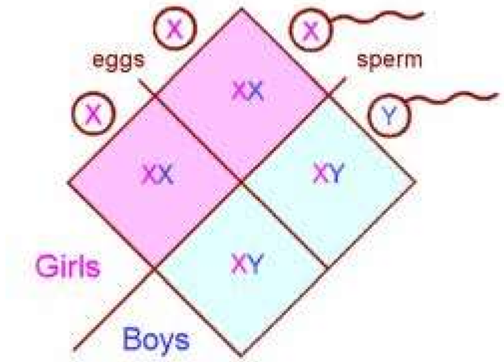
1 copy of the dominant gene is needed to trigger the disease

Man

1 copy of the gene is needed to trigger the disease, regardless of whether it is a dominant gene or a recessive gene

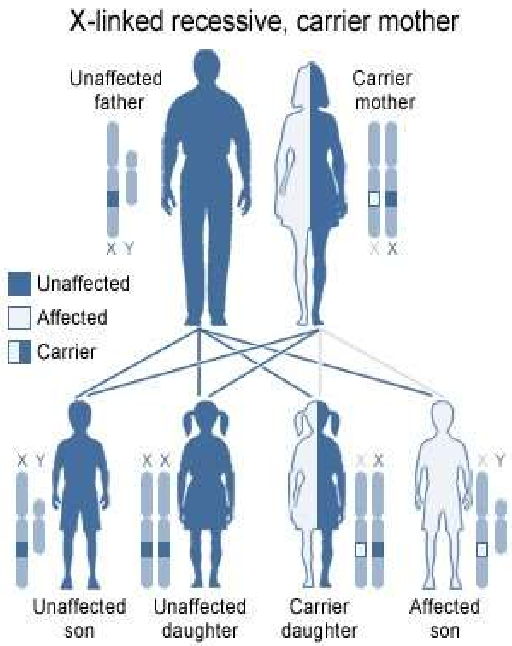
Who is affected by Sex-Linked Disorders?

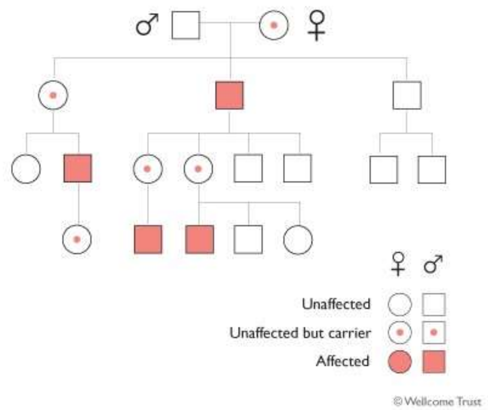
- Genes for certain traits are on the X **chromosome only…**
  - Since **<u>Men</u>** only receive **one X** chromosome then they are <u>more likely</u> to inherit these types of disorders.
    - Who gives men the X Chromosome?
  - **<u>Women</u>** are somewhat protected since they receive two X chromosomes and are less likely to inherit these types of disorders.
    - What do you think happens when they get only one defective copy of an X chromosome?



Sex-Linked Disorders

- The vast majority of affected individuals are **male**.
- **Affected males never pass the disease to their sons** because there is no male-to-male transmission of the X chromosome.
- Affected males pass the defective X chromosome to **all of their daughters**, who are described as **carriers**.
  - This means they carry the disease-causing allele but generally show no disease symptoms since a functional copy of the gene is present on the other chromosome.
- Female carriers pass the defective X chromosome to…
  - **half their sons** (who are affected by the disease)
  - **half their daughters** (who are therefore also carriers).
  - The other children inherit the normal copy of the chromosome.
- The overall pattern of the disease is therefore characterized by the transmission of the disease from affected males to male grandchildren through carrier daughters, a pattern sometimes described as a '**knight's move**'.
- **Affected females,** with two deficient X chromosomes, are the rare products of a marriage between an **affected male and a carrier (or affected) female.**





How do you solve Sex-linked Problems?

If Red eyes are dominant and sex-linked, show the cross between a homozygous red eyed female and a white eyed male.

White-Eyed Male

Red-Eyed Female	X^r	Y
X^R	X^RX^r	X^RY
X^R	X^RX^r	X^RY

<u>Genotypes</u>: X^RX^r , X^RY

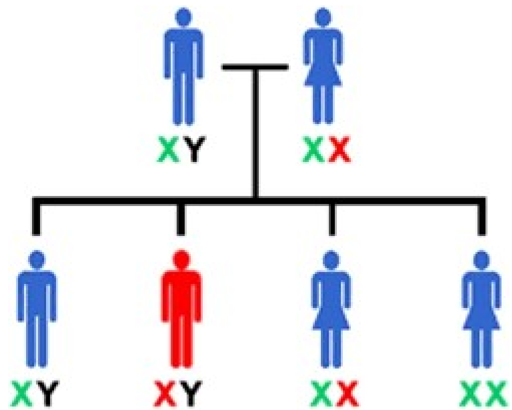
<u>Phenotypes</u>: All offspring have red eyes.

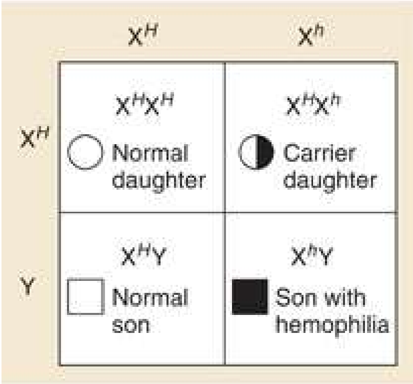
- You determine which trait (or disorder) is **dominant** or **recessive**.
- Set up a punnett square using <u>XX for females</u> and <u>XY for males</u>.
  - **Assign alleles for X only**!
- Solve as usual, keeping in mind that the Y chromosome has <u>**no**</u> **allele**!

X-linked hereditary disorders due to a recessive allele

- In this mode of inheritance, the morbid allele behaves as a recessive trait. Heterozygous women are not affected but can transmit the disease; they are said to be carriers of the disease.

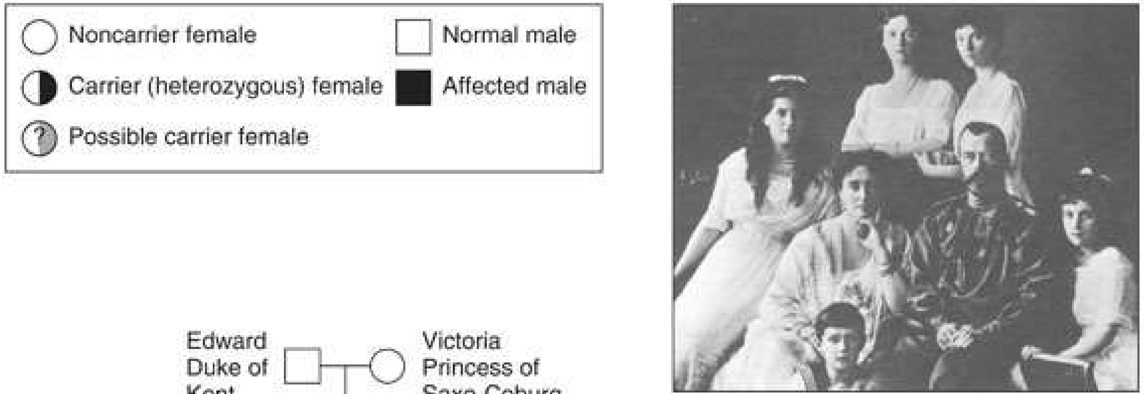
- The disease often occurs in males (XY) who have only one copy of the lethal gene (hemizygous subjects).



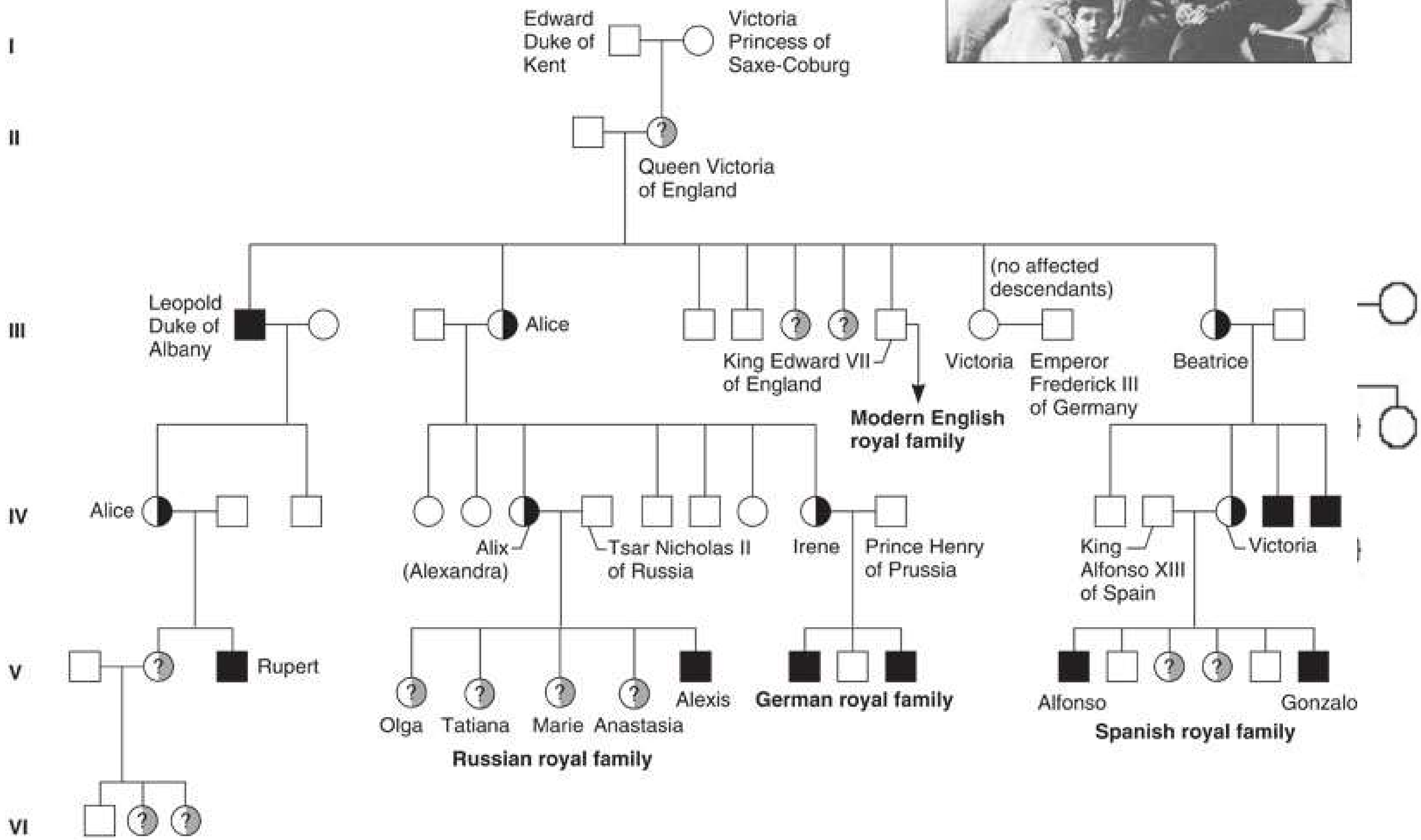


X^H
X^h
X^H
Y
X^H X^H
Normal daughter
X^H X^h
Carrier daughter
X^H Y
Normal son
X^h Y
Son with hemophilia

a.



Noncarrier female
Normal male
Carrier (heterozygous) female
Affected male
Possible carrier female



I
II
III
IV
V
VI
Edward Duke of Kent
Victoria Princess of Saxe-Coburg
Queen Victoria of England
(no affected descendants)
Leopold Duke of Albany
Alice
King Edward VII of England
Modern English royal family
Victoria
Emperor Frederick III of Germany
Beatrice
Alice
Alix (Alexandra)
Tsar Nicholas II of Russia
Irene
Prince Henry of Prussia
King Alfonso XIII of Spain
Victoria
Rupert
Olga
Tatiana
Marie
Anastasia
Alexis
Russian royal family
German royal family
Alfonso
Gonzalo
Spanish royal family

b.

X-linked hereditary disorders due to a recessive allele

- Daltonism (Color blindness):
  - Daltonism is when someone has the inability to recognize the differences between certain colors.

Normal vision

Seen by a color blind person

Daltonism:

d = colorblind
D = normal
Dd = carrier

$X^D X^D$ = normal woman
$X^D X^d$ = carrier woman
$X^d X^d$ = affected woman

$X^D Y$ = normal man
$X^d Y$ = affected man

A mother with normal but conductive vision and a father who is color blind may have :

Father x Mother

X^dY X^DX^d

	X^D	X^d
X^d	X^DX^d	X^dX^d
Y	X^DY	X^dY

a) Colorblind boy

b) Color blind girl

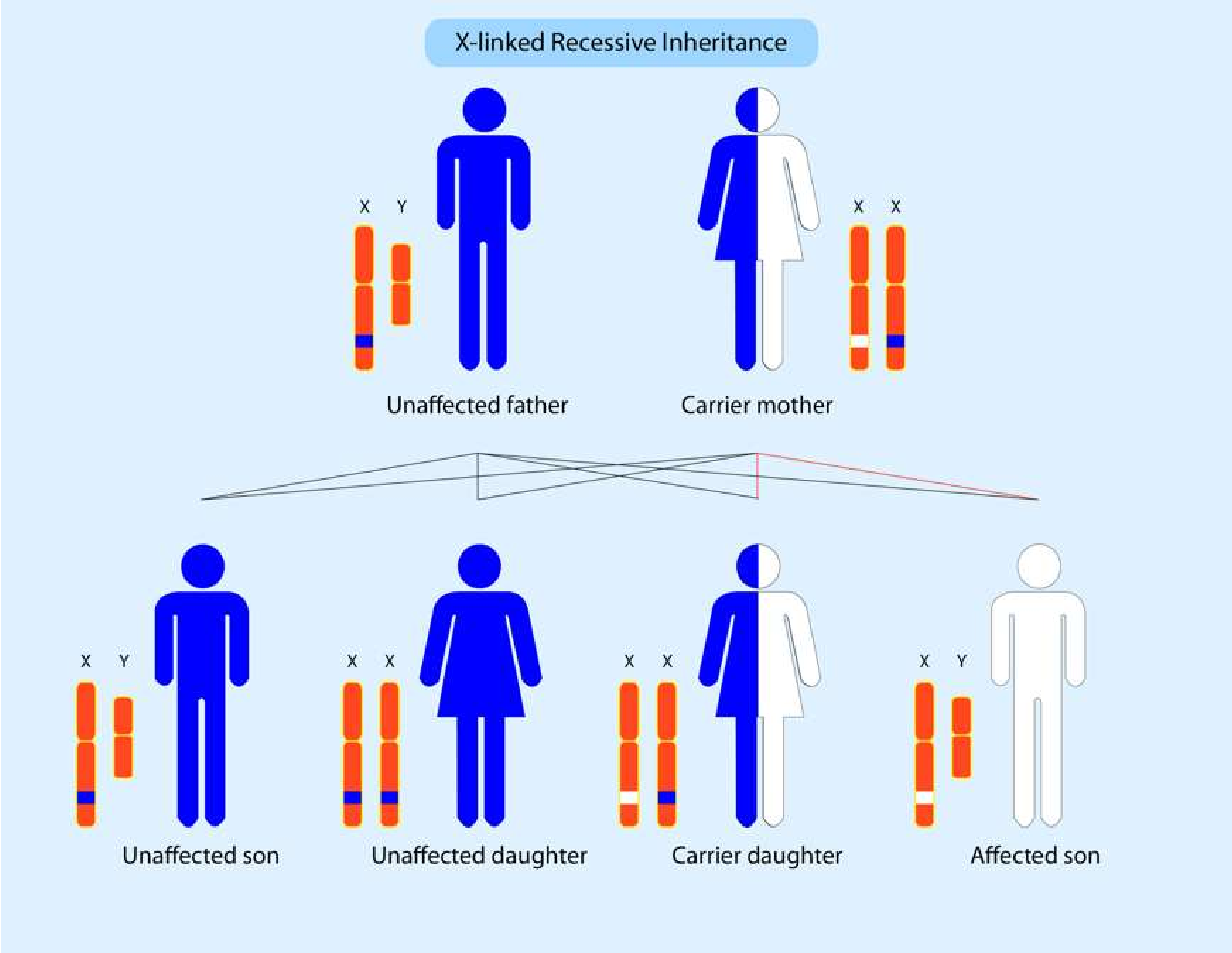
Colorblind boy

Color blind girl X^dX^d.

X-linked hereditary disorders due to a recessive allele

- Duchenne muscular dystrophy :
  - Muscle atrophy (poor muscle development).
  - Muscle cells of sick individuals are unable to produce a protein: dystrophin, which is essential for muscle function.

- Duchenne muscular dystrophy :



X-linked hereditary disorders due to a recessive allele

- Haemophilia :
  - Hereditary hemorrhagic disease with sex-linked recessive transmission.
    - **Coagulation factor VIII deficiency = Hemophilia A.**
    - **Coagulation factor IX deficiency = Hemophilia B.**

Carrier Mother X Normal Father

$X^H X^h$ & $X^H y$

	X^H	y
X^H	$X^H X^H$	$X^H y$
X^h	$X^H X^h$	$X^h y$

Offspring

If woman
1/2 = normal
1/2 = normal but Carrier

If man
1/2 = normal
1/2 = hemophilia

X-linked hereditary disorders due to a dominant allele

- In X-linked dominant transmission, the morbid allele behaves as a dominant trait and occurs in both hemizygous boys and heterozygous girls (often to a lesser degree of severity).

X-linked hereditary disorders due to a dominant allele

- **X-linked dominant inheritance characteristic**

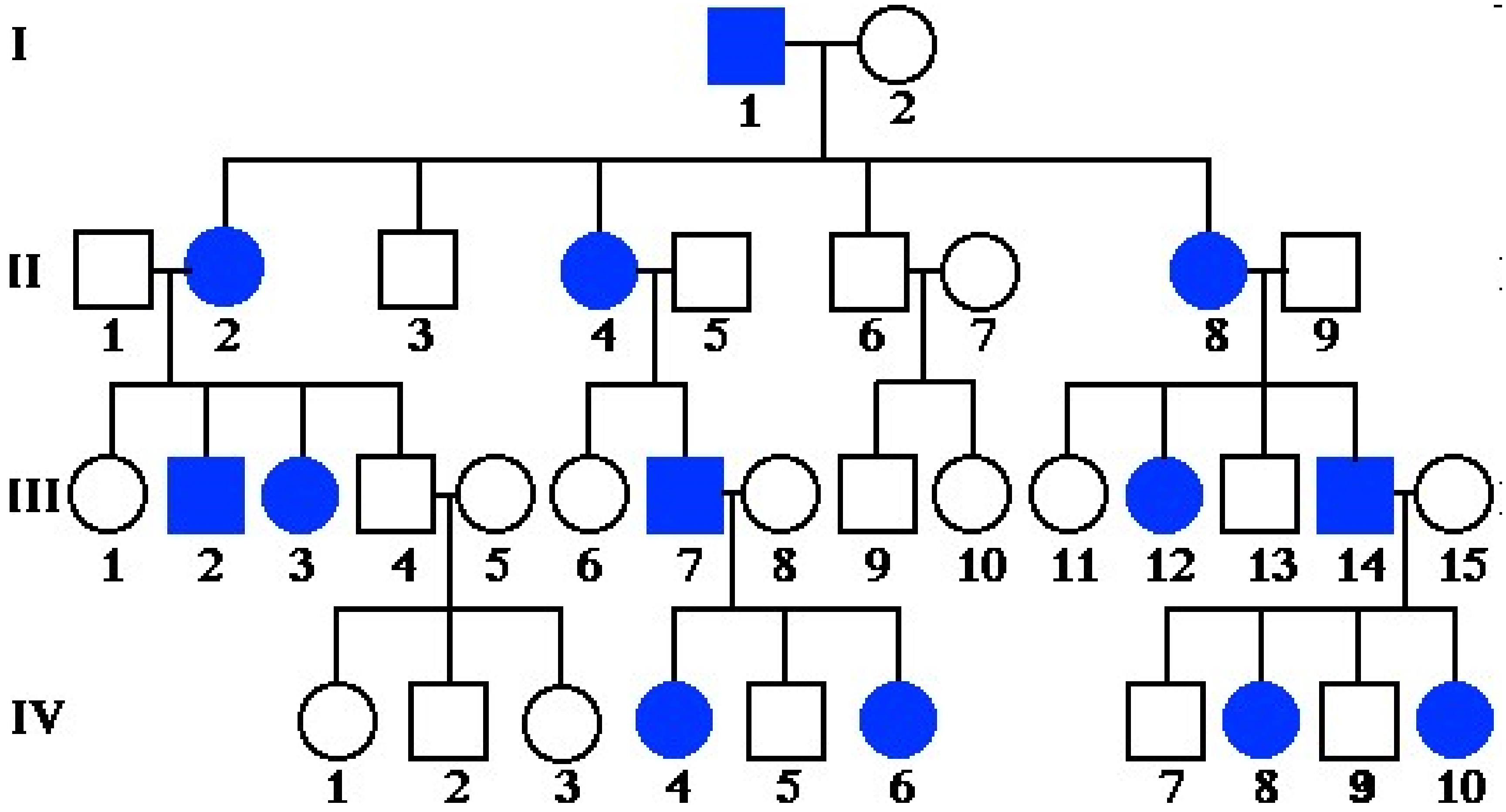
- Both sexes can be affected by the disease

- In general, heterozygous girls are less severely ill than boys

- Affected women can transmit their disease to children of both sexes with a risk of 1/2

- In the offspring of an affected man, all girls receive the mutated gene; on the other hand, there is never an affected boy (no father-son transmission)

Hérédité dominante lié à l'X



Pedigree 5. X-linked dominant inheritance.