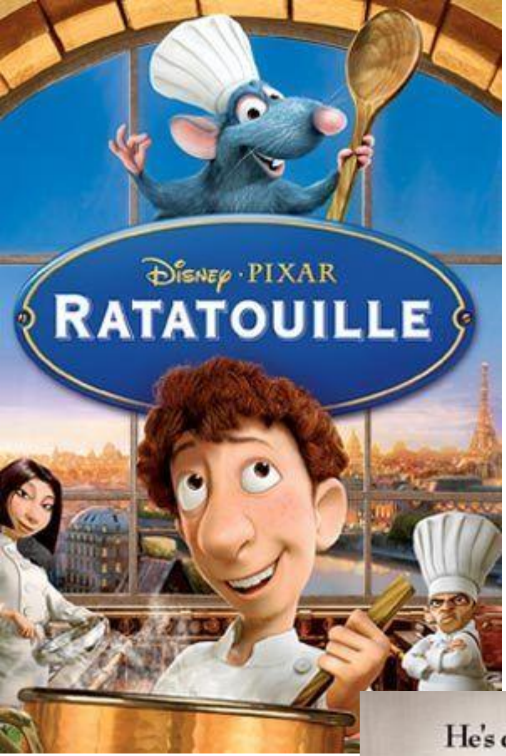
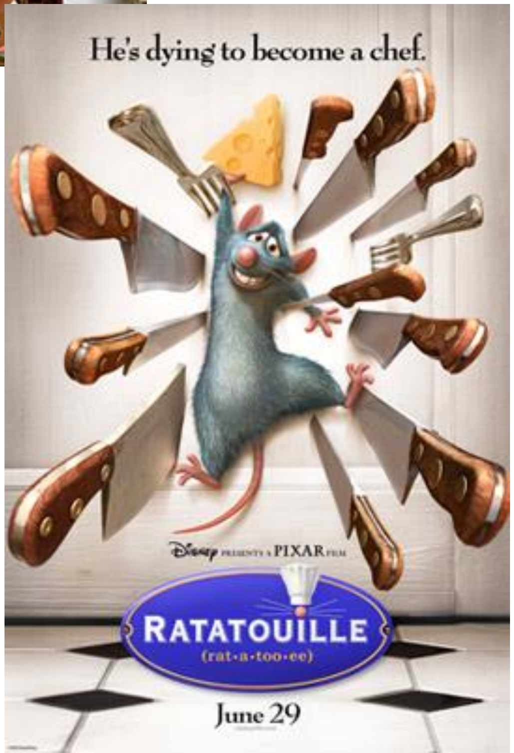




Combine one favor with another,
and something new was created!

Chapter I

Mendel’s Law of Inheritance

I. Mendel’s breakthrough

Patterns, particles, and principles of heredity

II. Extension to Mendel’s laws

Complexities in relating genotype to phenotype

1. **Single-gene inheritance**
2. **Multifactorial inheritance**

Chapters in reference books：H2-H3, D3

II.2. Extensions to Mendel for Multifactorial inheritance

The action of two or more genes

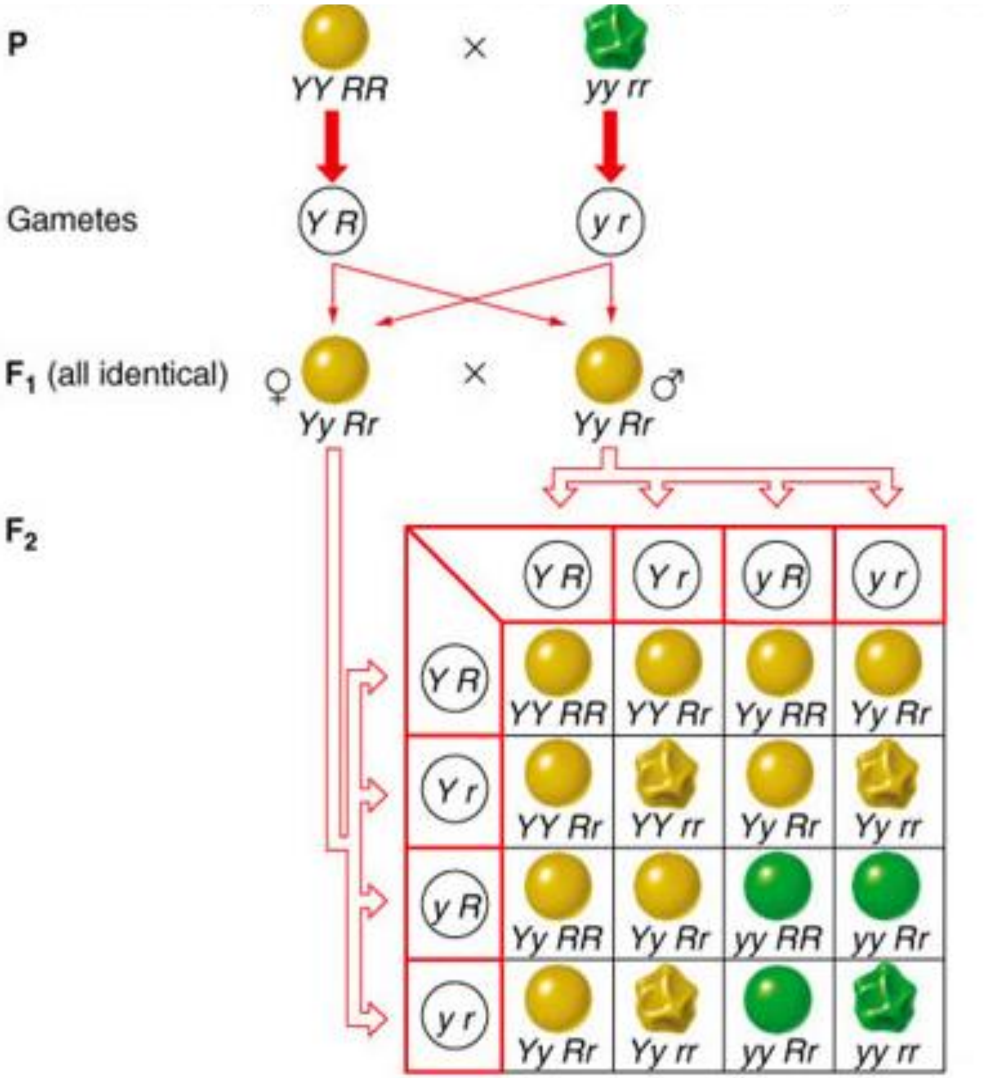
- Additive gene interactions 基因互作
- Complementary gene action 基因互补
- Epistasis 上位效应
- Duplicate effect 叠加效应

Interactions between genes and the environment

Key Words

gene interactions（基因互作）
complementary gene action（基因互补）
complementary gene（互补基因）
complementation（互补作用）
complementation test（互补测验）
heterogeneity（异质性）
duplicate effect（叠加效应/重叠效应）
redundancy（基因冗余）
redundant gene（冗余基因）
epistasis, epistatic effect（上位效应/上位性）
epistatic gene（上位基因）
hypostatic gene（下位基因）
recessive epistasis（隐性上位）
dominant epistasis（显性上位）

A dihybrid cross by Mendel



Genotype	Phenotype	Phenotypic ratio
Y– R–	yellow round	9/16
yy R–	green round	3/16
Y– rr	yellow wrinkled	3/16
yy rr	green wrinkled	1/16

9 genotypes； 4 phenotypes

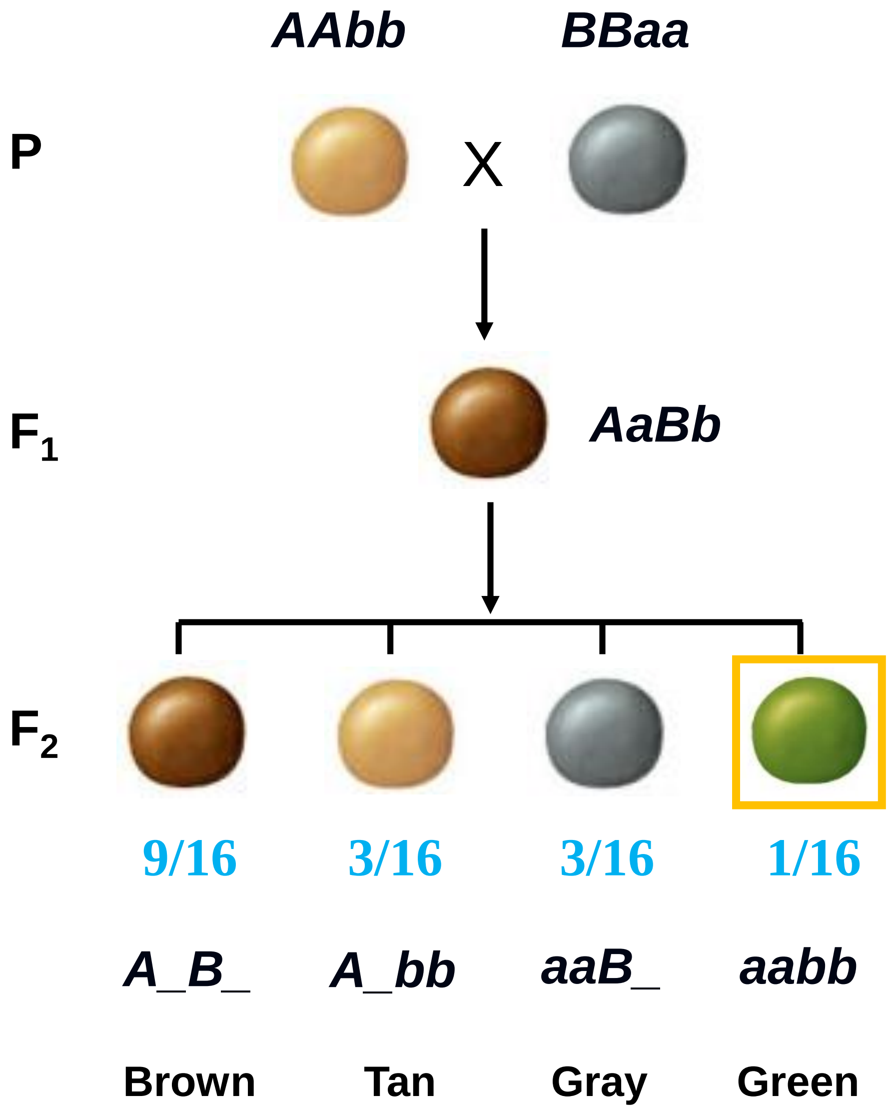
II.2. Extensions to Mendel for Multifactorial inheritance

The action of two or more genes

Additive gene interactions	基因互作
Complementary gene action	基因互补
Epistasis	上位效应
Duplicate effect	叠加效应

Two genes can interact to determine one trait

Lentil coat color



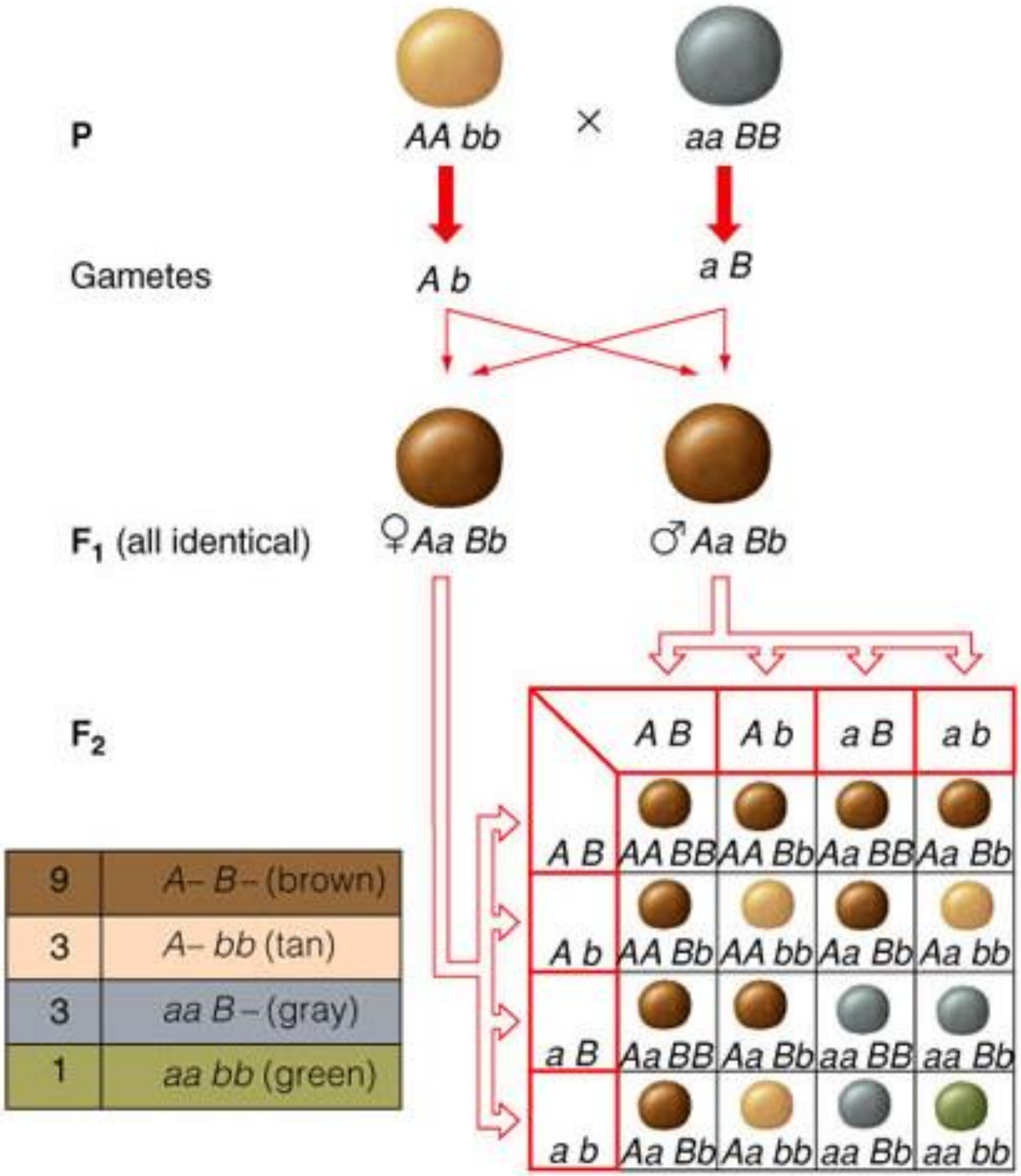
Cross of F_1 produces F_2 with

9 brown : 3 tan : 3 gray : 1 green

→ two independently sorted genes

Novel phenotypes can emerge from the combination of alleles of two genes.

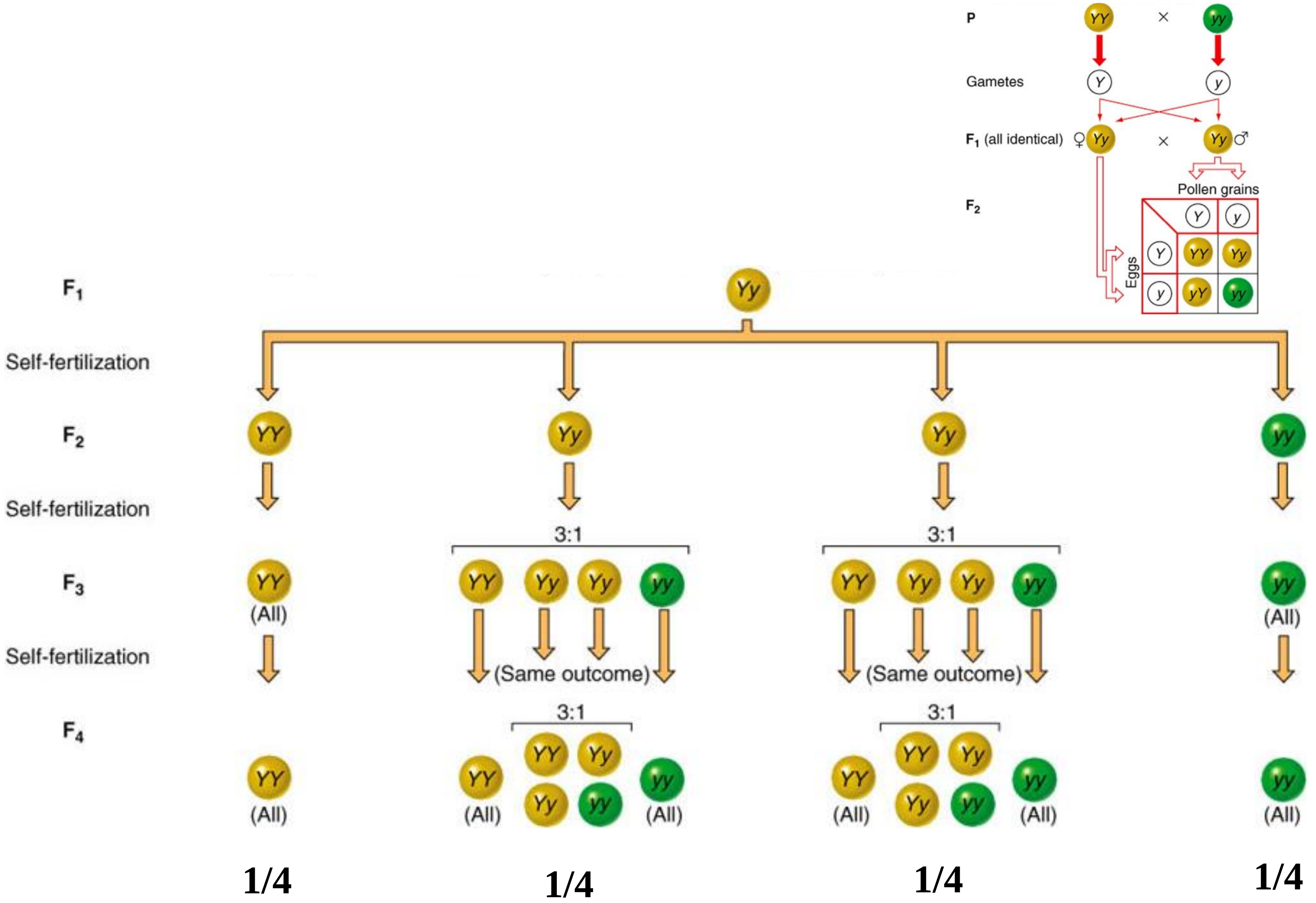
(a) A dihybrid cross with lentil coat colors



How to confirm?

gene interactions
（基因互作）

Further crosses confirm predicted ratios



Further crosses confirm predicted ratios

9	*A– B–* (brown)
3	*A– bb* (tan)
3	*aa B–* (gray)
1	*aa bb* (green)

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

	Phenotypes of F_2 Individual	Observed F_3 Phenotypes	Expected Proportion of F_2 Population*	
aabb	Green	Green	1/16	**1/16**
AAbb	Tan	Tan	1/16	**3/16**
Aabb	Tan	Tan, green	2/16	
aaBb	Gray	Gray, green	2/16	**3/16**
aaBB	Gray	Gray	1/16	
AABB	Brown	Brown	1/16	**9/16**
AABb	Brown	Brown, tan	2/16	
AaBB	Brown	Brown, gray	2/16	
AaBb	Brown	Brown, gray, tan, green	4/16	

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

Self pollination of F_2 to produce F_3 shows interaction between two genes.

gene interactions
（基因互作）

(c) Sorting out the dominance relations by select crosses

Seed Coat Color of Parents	F_1	F_2 Phenotypes and Frequencies	Ratio
Tan × green	***Aabb***	231 tan, 85 green	3:1
Gray × green	***aaBb***	2586 gray, 867 green	3:1
Brown × gray	***AaBB***	964 brown, 312 gray	3:1
Brown × tan	***AABb***	255 brown, 76 tan	3:1
Brown × green	***AaBb***	57 brown, 18 gray, 13 tan, 4 green	9:3:3:1

Each genotypic class (defined in terms of the presence or absence of the dominant allele of two genes) determines a particular phenotype:

1) both present

2) one present

3) the other present

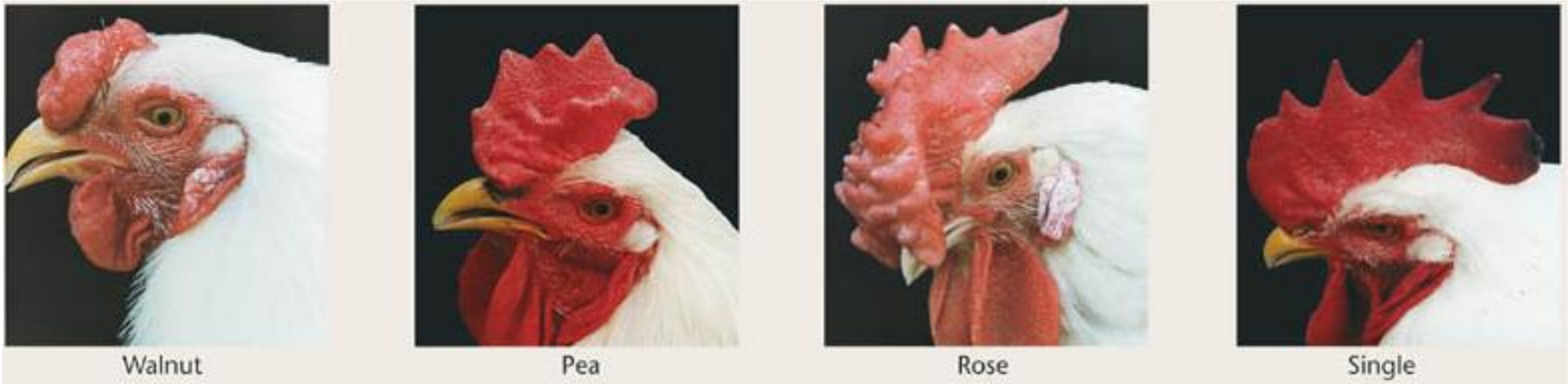
4) neither present

9	*A– B–* (brown)
3	*A– bb* (tan)
3	*aa B–* (gray)
1	*aa bb* (green)

gene interactions
（基因互作）

The shape of cockscombs

鸡冠



Cross 1: Single × Single → Single

Cross 2: Walnut X Walnut → Walnut

Cross 3: Rose × Pea → Walnut （F_1）

$F_1 \times F_1 \rightarrow$ 93 Walnut: 28 Rose: 32 Pea: 10 Single

9 : 3 : 3 : 1

II.2. Extensions to Mendel for Multifactorial inheritance

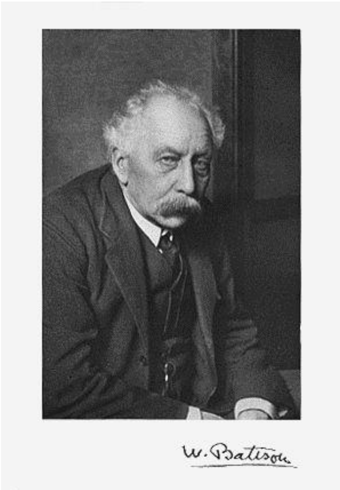
The action of two or more genes

Additive gene interactions	基因互作
Complementary gene action	基因互补
Epistasis	上位效应
Duplicate effect	叠加效应



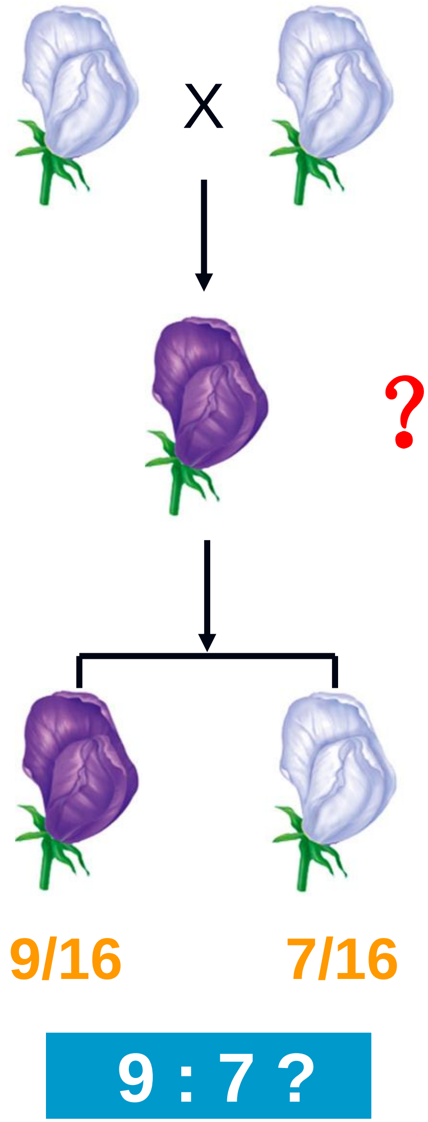
Complementation makes perfect

Complementary gene action – color in sweet peas

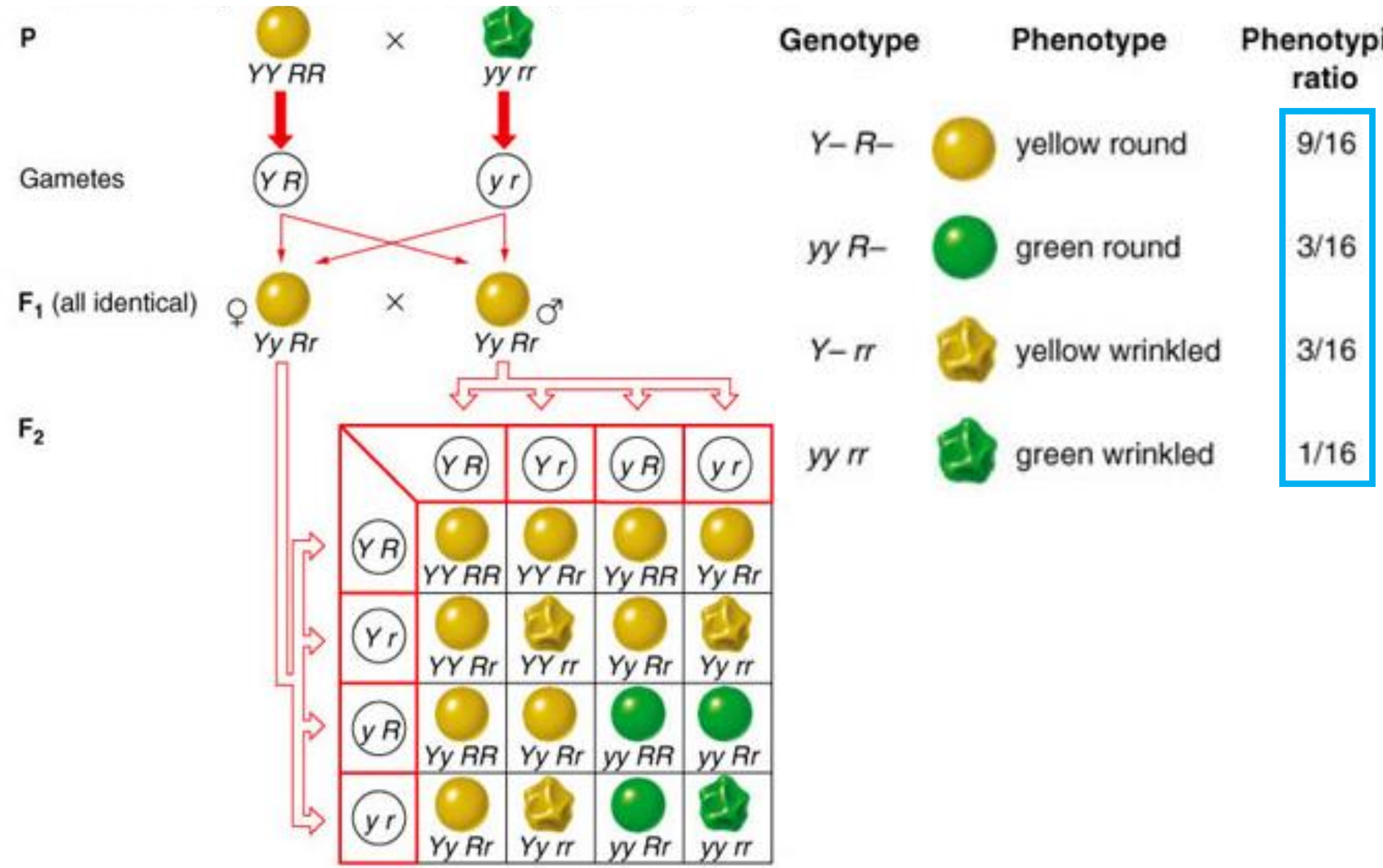


William Bateson

(a) *Lathyrus odoratus* (sweet peas)



A dihybrid cross by Mendel

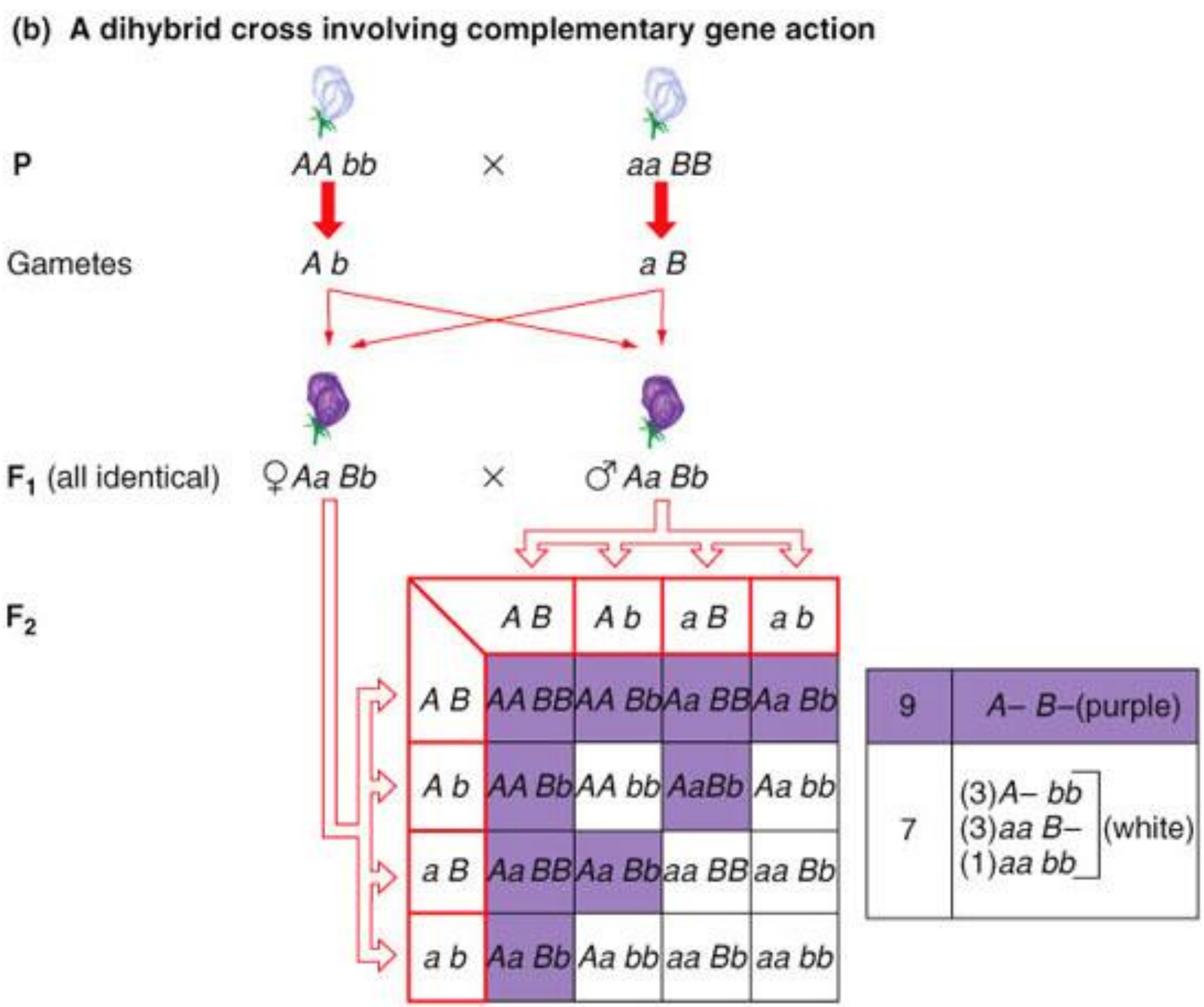


9/16

7/16

Complementary gene action - color in sweet peas

9:7 ratio hints that one dominant allele of each gene must be present to produce purple flowers.



No pigment

$\downarrow$ **A**

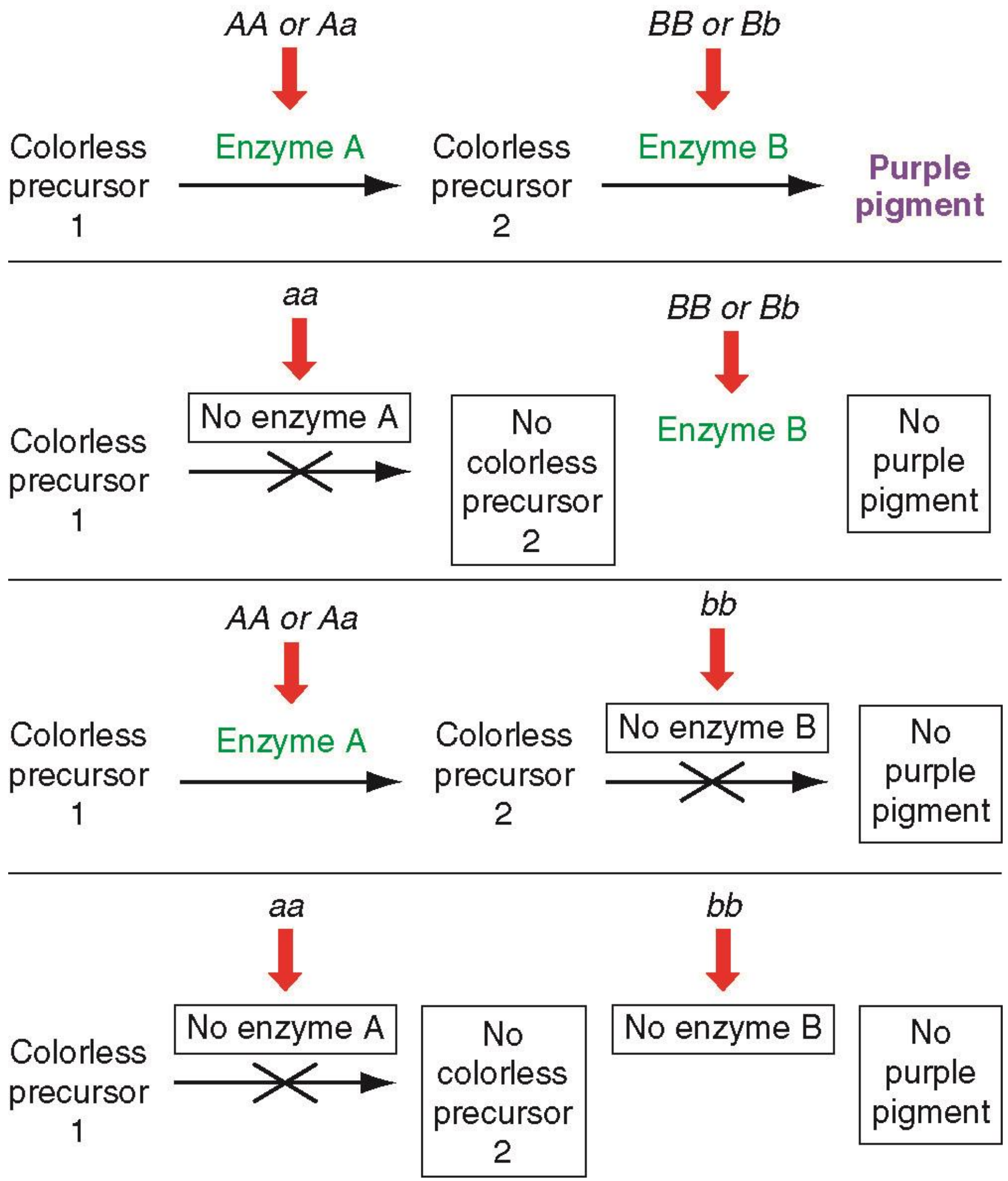
No pigment

$\downarrow$ **B**

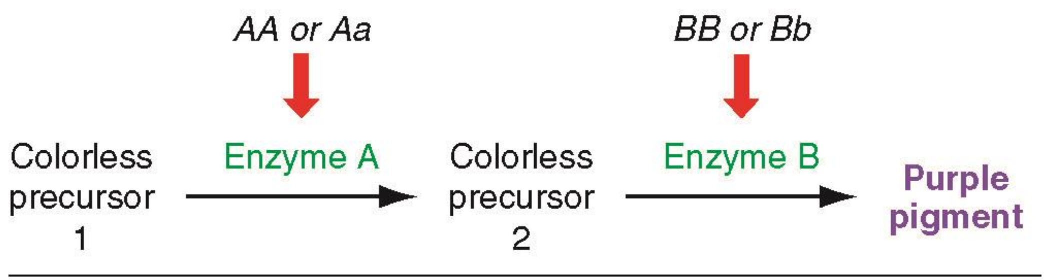
Purple pigment

complementary gene action （基因互补）

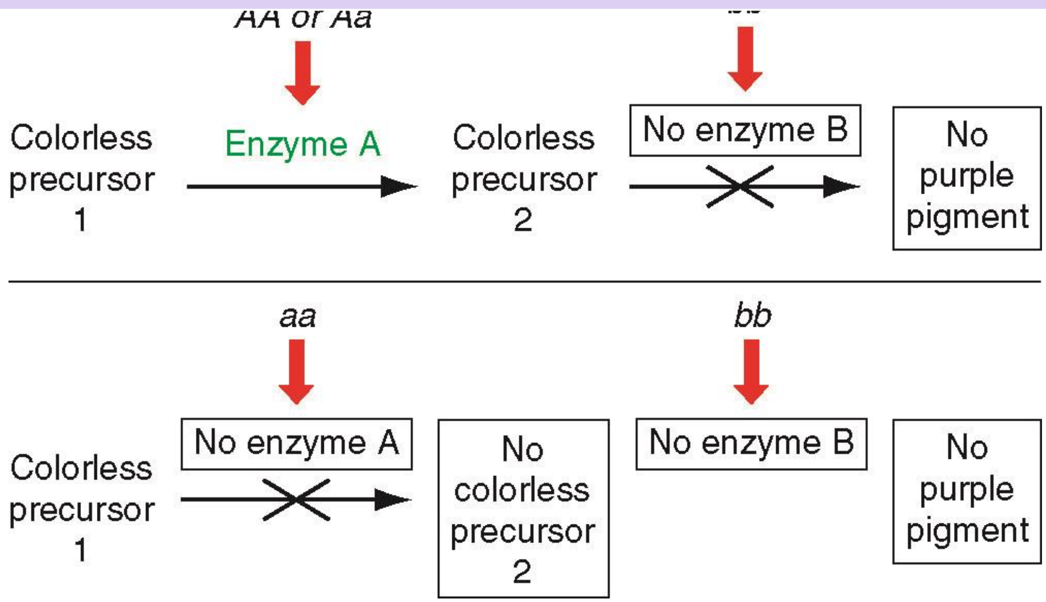
A possible biochemical explanation



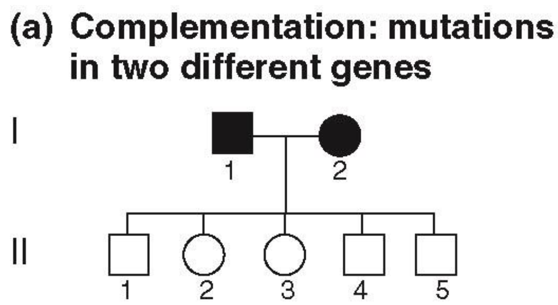
A possible biochemical explanation

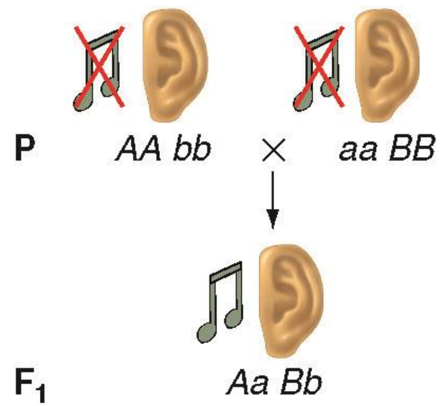


9:7 ratio is a phenotypic signature of complementary gene interaction where dominant alleles of two genes act together (A_B_) to produce a trait while other three genotypic classes do not.



Genetic heterogeneity in human deafness





Genetic mechanism of complementation

Complementation: if offspring receiving two mutations - one from each parent - express the wild-type phenotype, complementation has occurred.

Complementation test can determine if mutations arise from the same or different genes.

Close to 50 different genes have mutant alleles that can cause deafness in humans

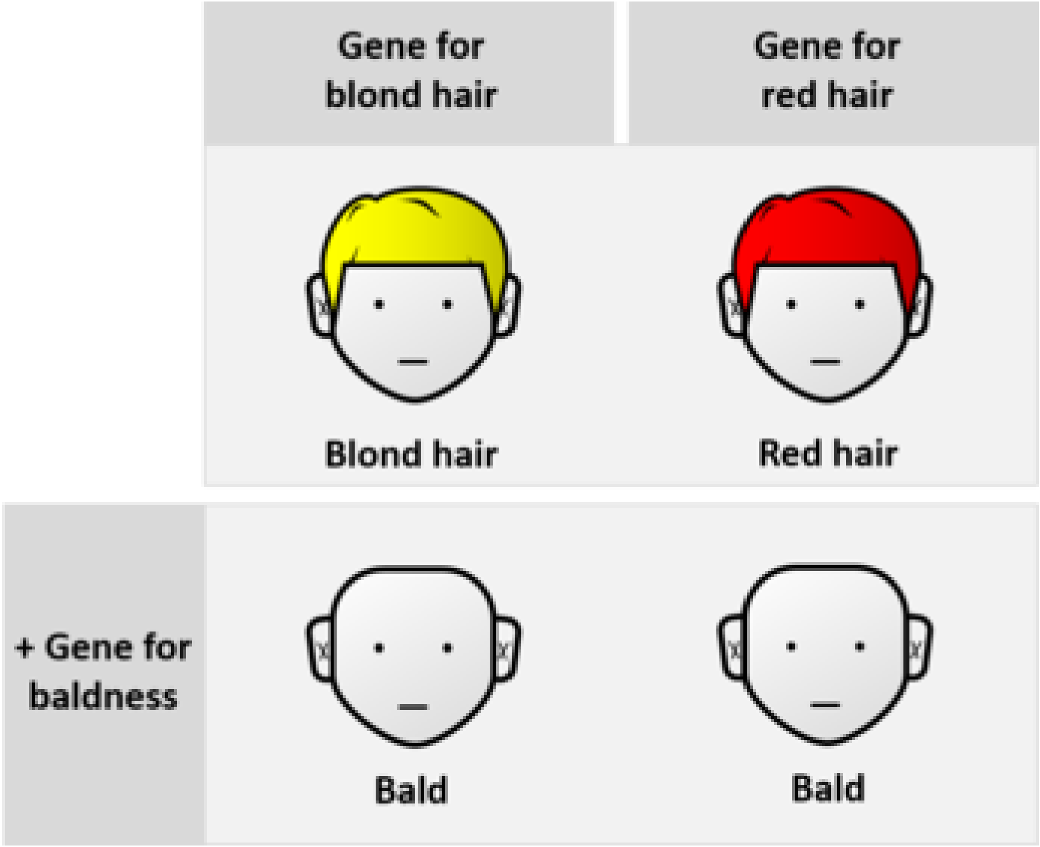
II.2. Extensions to Mendel for Multifactorial inheritance

The action of two or more genes

Additive gene interactions	基因互作
Complementary gene action	基因互补
Epistasis	上位效应
Duplicate effect	叠加效应

Epistasis

皮之不存，毛将焉附？



[Hypostatic]

[Epistatic]

Epistasis - coat color in Labrador retriever dog

Golden yellow

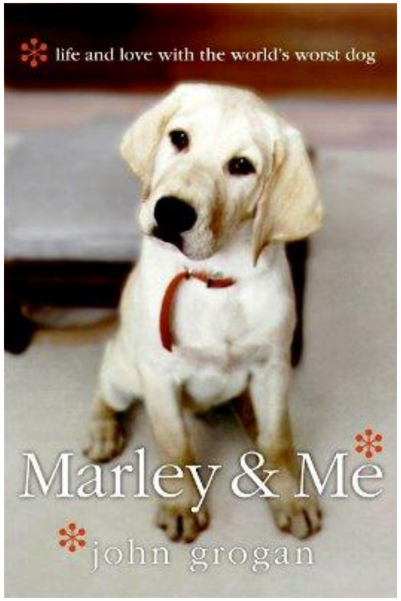
B_ee **or** ***bbee***

Brown

bbE_

Black

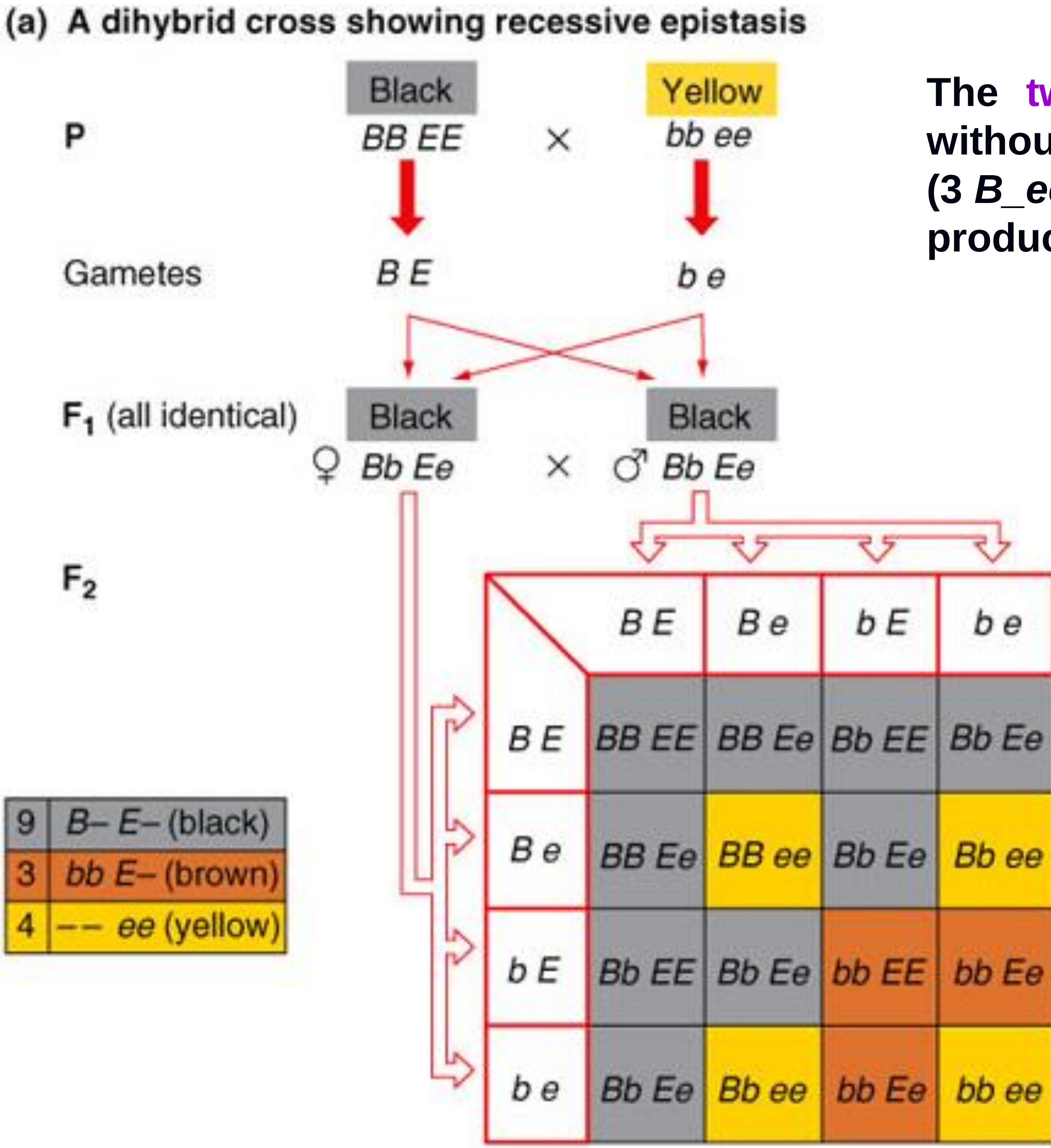
B_E_



Epistasis:

A gene interaction in which the effects of an allele at one gene masks the effects of alleles at another gene

4 Mendelian genotypic classes → < 4 phenotypes



The two genotypic classes without a dominant E allele (3 *B_ee* + 1 *bbee*) combine to produce yellow phenotype

B E

$\frac{3}{4} \times \frac{3}{4} = 9/16$

$\frac{1}{4} \times \frac{3}{4} = 3/16$

$1 \times \frac{1}{4} = 4/16$

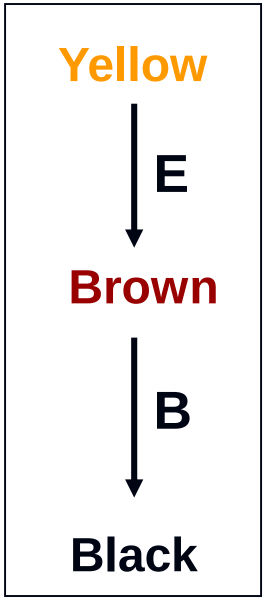
recessive epistasis
（隐性上位）

Recessive epistasis

隐性上位

Labrador retriever example – recessive epistasis

- **At the presence of *E* allele, *B* allele is dominant and determines black; *b* allele is recessive and determines brown if homozygous.**
- **However, *e* allele is recessive and if homozygous, hides effects of black or brown alleles.**
- **9:3:4 is a telltale ratio of recessive epistasis at F2 generation.**



Recessive epistasis: the homozygosity for a recessive allele of a gene is required to hide the effects of another gene

An intriguing puzzle - Bombay blood type

孟买

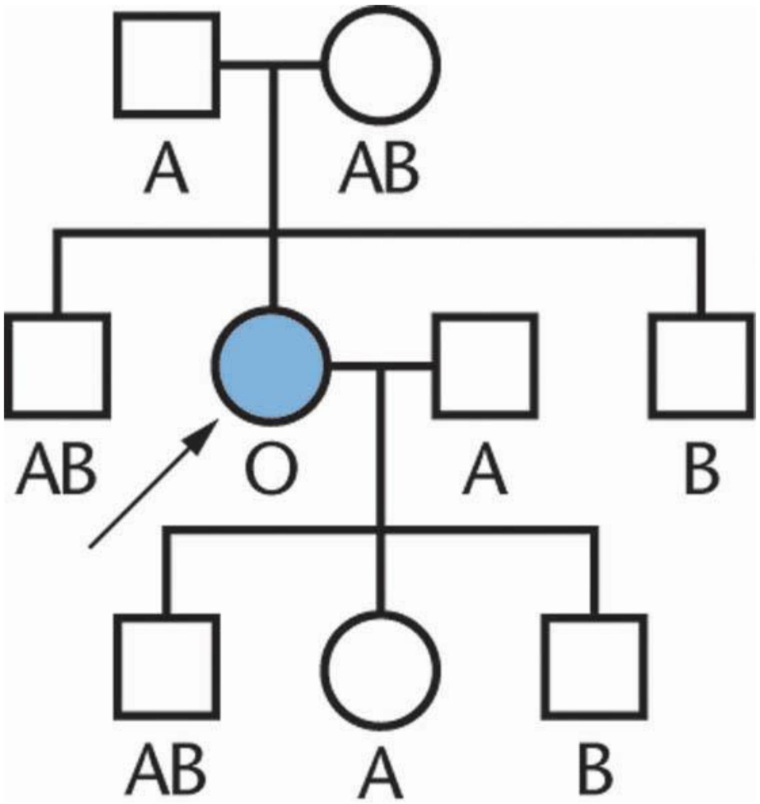
This was first discovered in Bombay, now known as Mumbai, in India, by Dr. Y. M. Bhende in 1952.

A woman was blood type O.
However,

Her mother was blood type AB

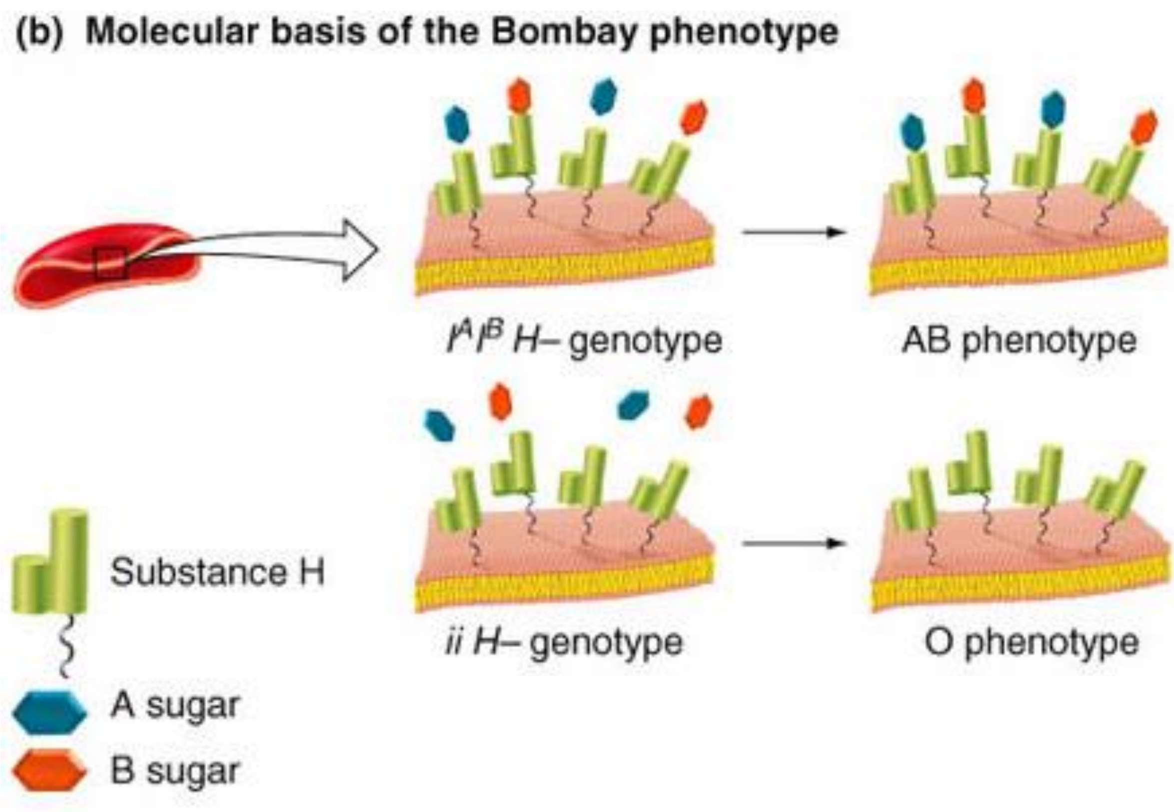
Her husband was blood type A. Yet they produced children who were blood type B or blood type AB!

?



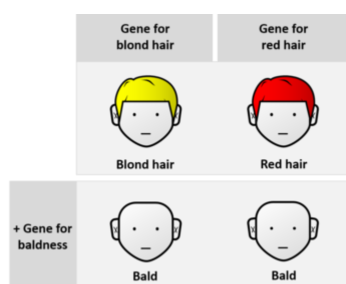
Molecular explanation for recessive epistasis in human blood groups

Bombay phenotype: a mutant recessive allele at a second gene (*hh*) masks effects of any ABO alleles.



Substance H: a base consisting of a sugar polymer

***hh* is epistatic to any combinations of I^A, I^B and *i* alleles**



皮之不存，毛将焉附？

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A woman was blood type O.
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Her mother was blood type AB

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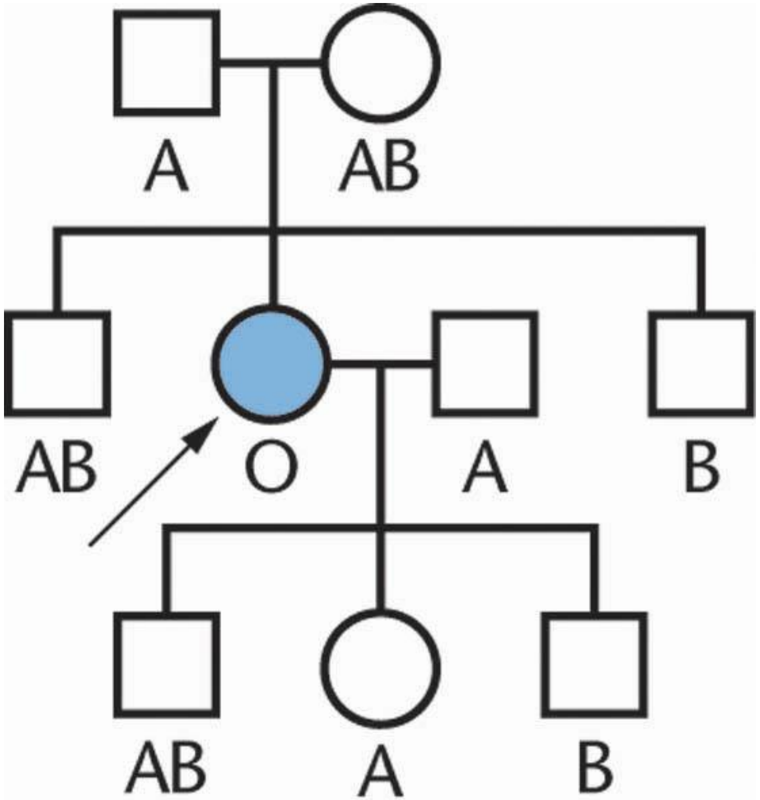
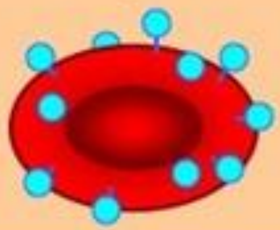
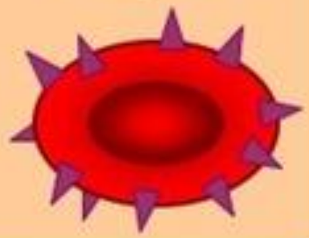
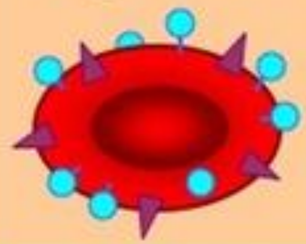
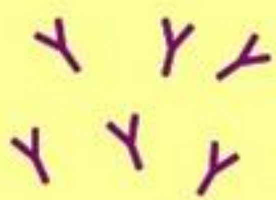
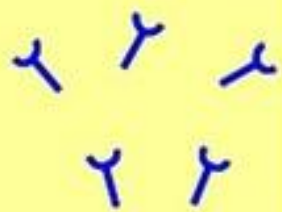
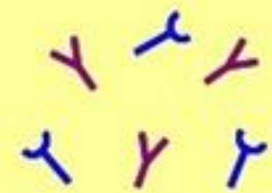


Q1: $I^{B}i\ \ hh \qquad I^{A}I^{B}\ \ hh$

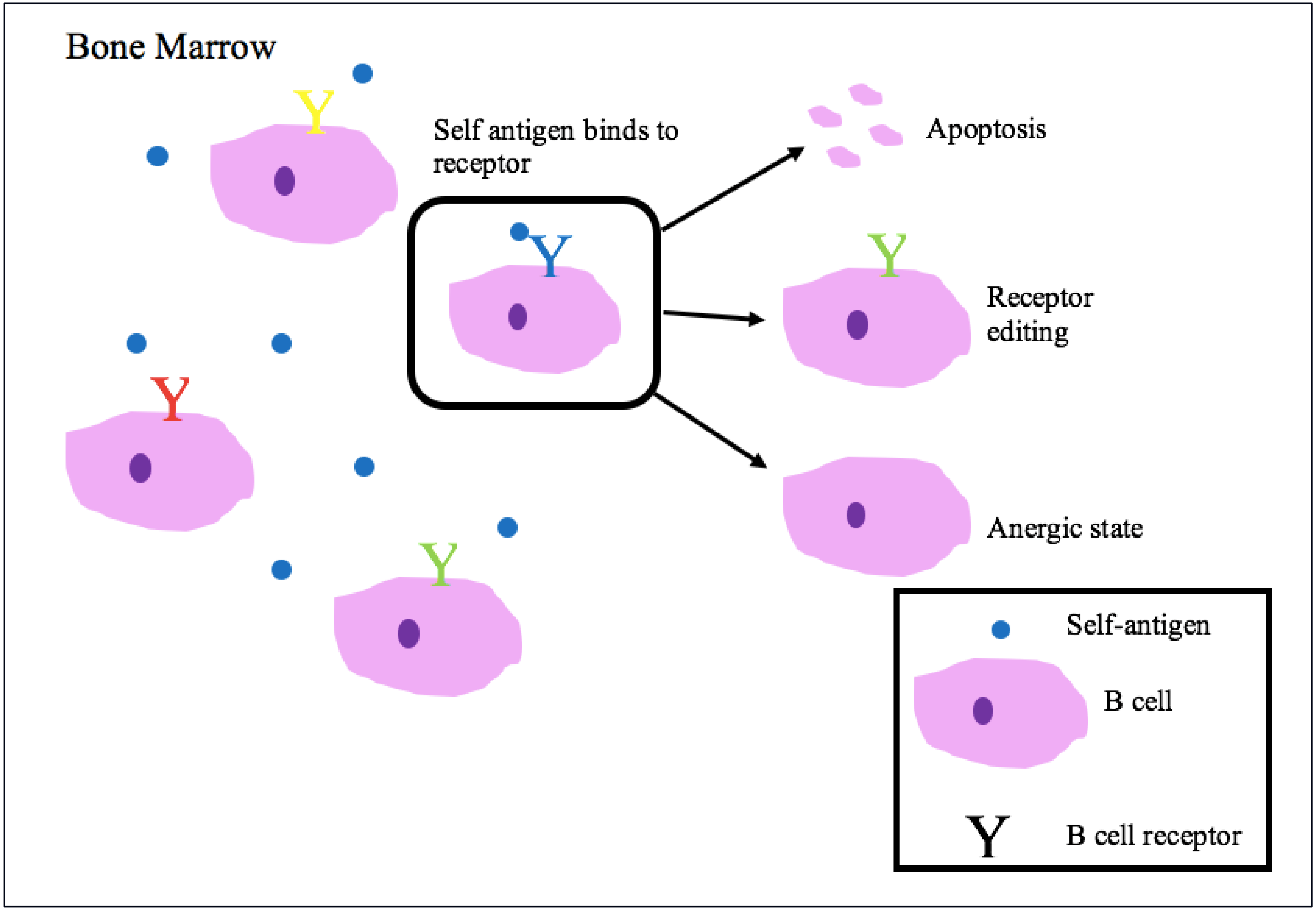
Q2: **Bombay blood type - blood transfusion?**

People who carry Bambay blood type, about 1 in 10, 000 Indians, can accept blood only from another Bombay blood type individual, and not from anyone who is O, A, B or AB type. But these people are universal donors

Human ABO Blood Group

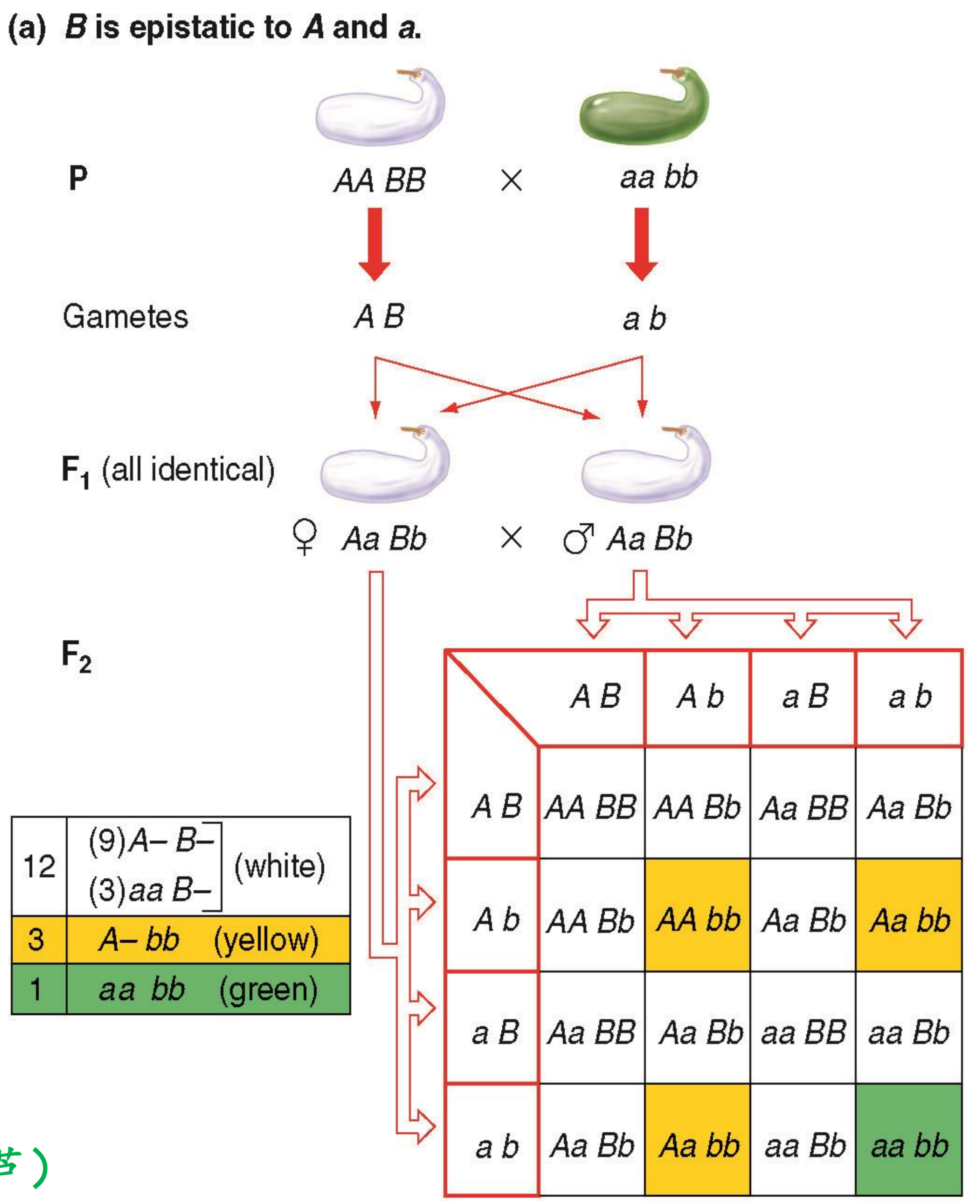
ABO Blood Groups				
Antigen (on RBC)	Antigen A 	Antigen B 	Antigens A + B 	Neither A or B 
Antibody (in plasma)	Anti-B Antibody 	Anti-A Antibody 	Neither Antibody	Both Antibodies 
Blood Type	**Type A** Cannot have B or AB blood Can have A or O blood	**Type B** Cannot have A or AB blood Can have B or O blood	**Type AB** Can have any type of blood Is the universal recipient	**Type O** Can only have O blood Is the universal donor

B cell tolerance



补充内容

Dominant epistasis in summer squash



	A B	A b	a B	a b
A B	AA BB	AA Bb	Aa BB	Aa Bb
A b	AA Bb	AA bb	Aa Bb	Aa bb
a B	Aa BB	Aa Bb	aa BB	aa Bb
a b	Aa Bb	Aa bb	aa Bb	aa bb

12	(9) A– B– (3) aa B–	(white)
3	A– bb	(yellow)
1	aa bb	(green)

B_ is epistatic to any genotype of the Aa gene

Dominant epistasis: the dominant allele of one gene hides the effects of another gene

?

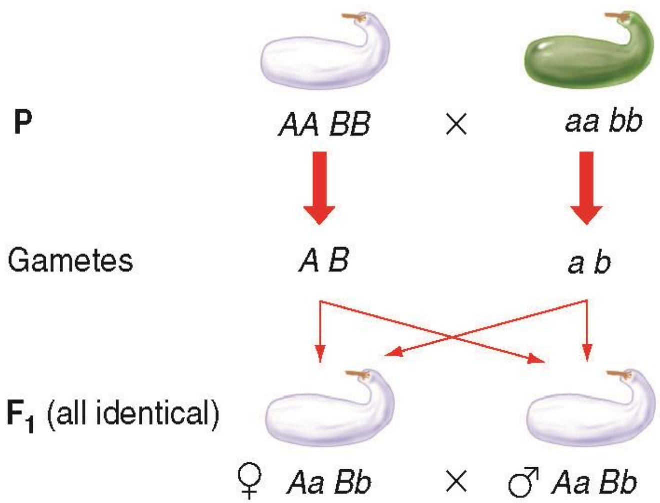
12:3:1

dominant epistasis
（显性上位）

（西葫芦）

Dominant epistasis in summer squash

(a) *B* is epistatic to *A* and *a*.



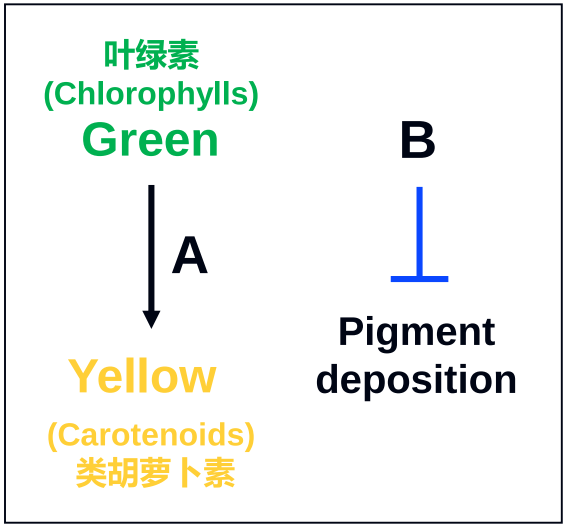
F_2

	A B	A b	a B	a b
A B	AA BB	AA Bb	Aa BB	Aa Bb
A b	AA Bb	AA bb	Aa Bb	Aa bb
a B	Aa BB	Aa Bb	aa BB	aa Bb
a b	Aa Bb	Aa bb	aa Bb	aa bb

12	(9) A– B– (3) aa B–	(white)
3	A– bb	(yellow)
1	aa bb	(green)

（西葫芦）

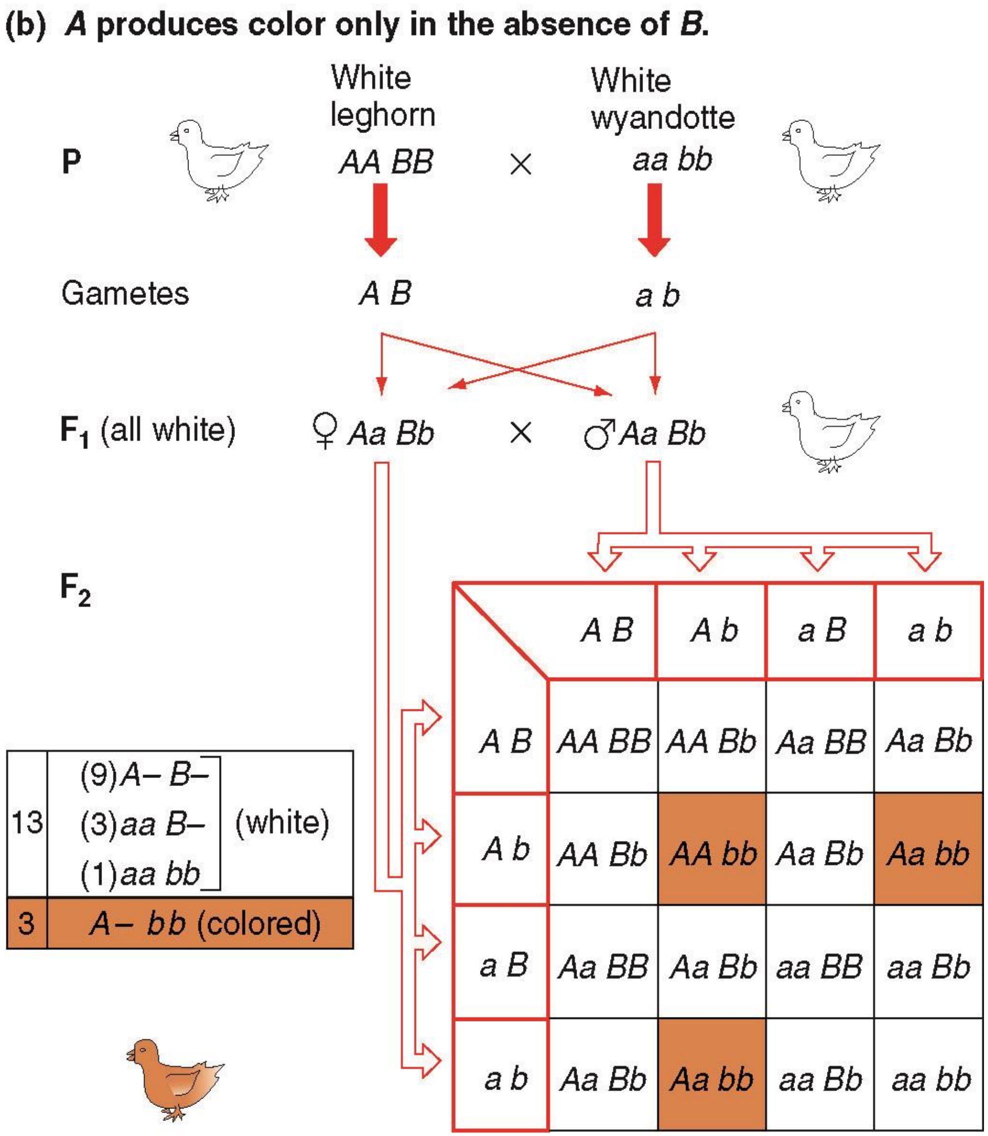
B_ is epistatic to any genotype of the Aa gene



12:3:1

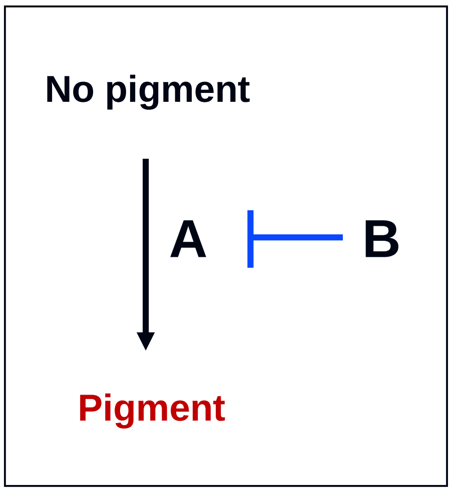
dominant epistasis
（显性上位）

Dominant epistasis in chicken feather



A_ produces color

only in the absence of B



?

13:3

dominant epistasis
（显性上位）

Dominant epistasis

显性上位

- **Presence of dominant allele at second gene hides effects of alleles at a gene.**

- **12:3:1 and 13:3 are telltale ratios for dominant epistasis.**

dominant epistasis
（显性上位）

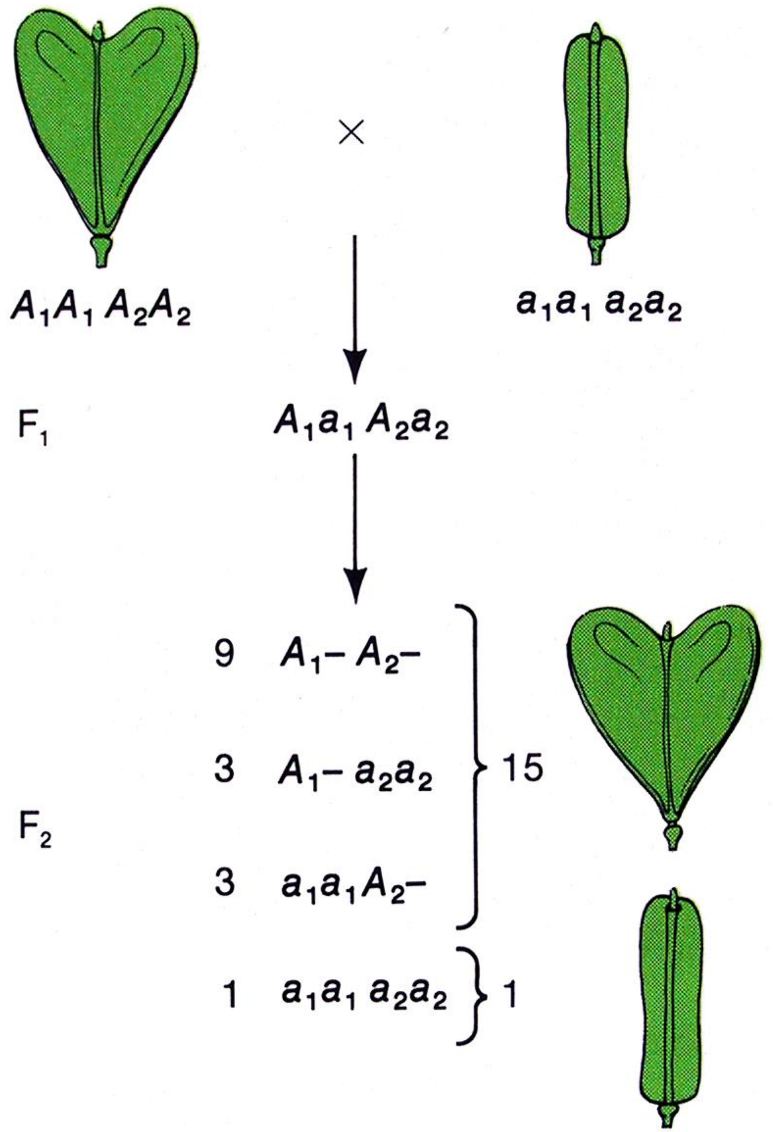
II.2. Extensions to Mendel for Multifactorial inheritance

The action of two or more genes

Additive gene interactions	基因互作
Complementary gene action	基因互补
Epistasis	上位效应
Duplicate effect	叠加效应

Duplicate effect in shepherd’s purse

荠菜

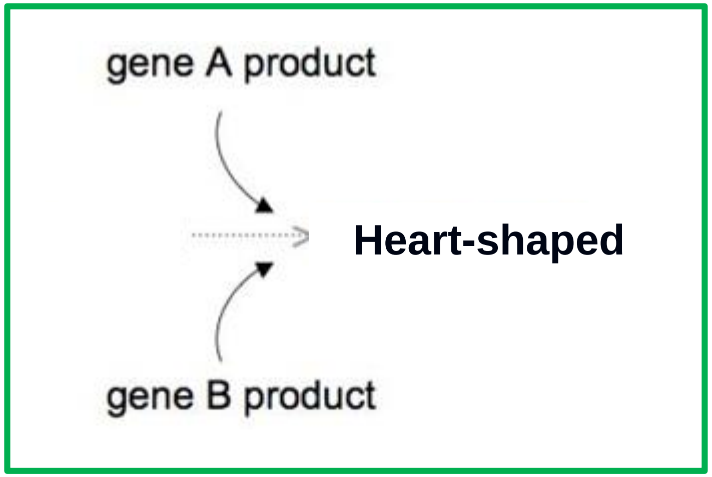


15:1

Fruit shape: heart-shaped or narrow

Duplicate genes provide alternative genetic determination of a specific phenotype.

Redundancy



Summary of discussed gene interactions

TABLE 3.2 **Summary of Discussed Gene Interactions**

Gene Interaction	F$_2$ Genotypic Ratios from an F$_1$ Dihybrid Cross					F$_2$ Phenotypic Ratio
	Example	*A– B–*	*A– bb*	*aa B–*	*aa bb*	
None: Four distinct F$_2$ phenotypes	Lentil: seed coat color (see Fig. 3.11)	9	3	3	1	9:3:3:1
Complementary: One dominant allele of each of two genes is necessary to produce phenotype	Sweet pea: flower color (see Fig. 3.12b)	9	3	3	1	9:7
Recessive epistasis: Homozygous recessive of one gene masks both alleles of another gene	Retriever: coat color (see Fig. 3.13a)	9	3	3	1	9:3:4
Dominant epistasis I: Dominant allele of one gene hides effects of both alleles of another gene	Summer squash: color (see Fig. 3.14a)	9	3	3	1	12:3:1
Dominant epistasis II: Dominant allele of one gene hides effects of dominant allele of another gene	Chicken: feather color (see Fig. 3.14b)	9	3	3	1	13:3

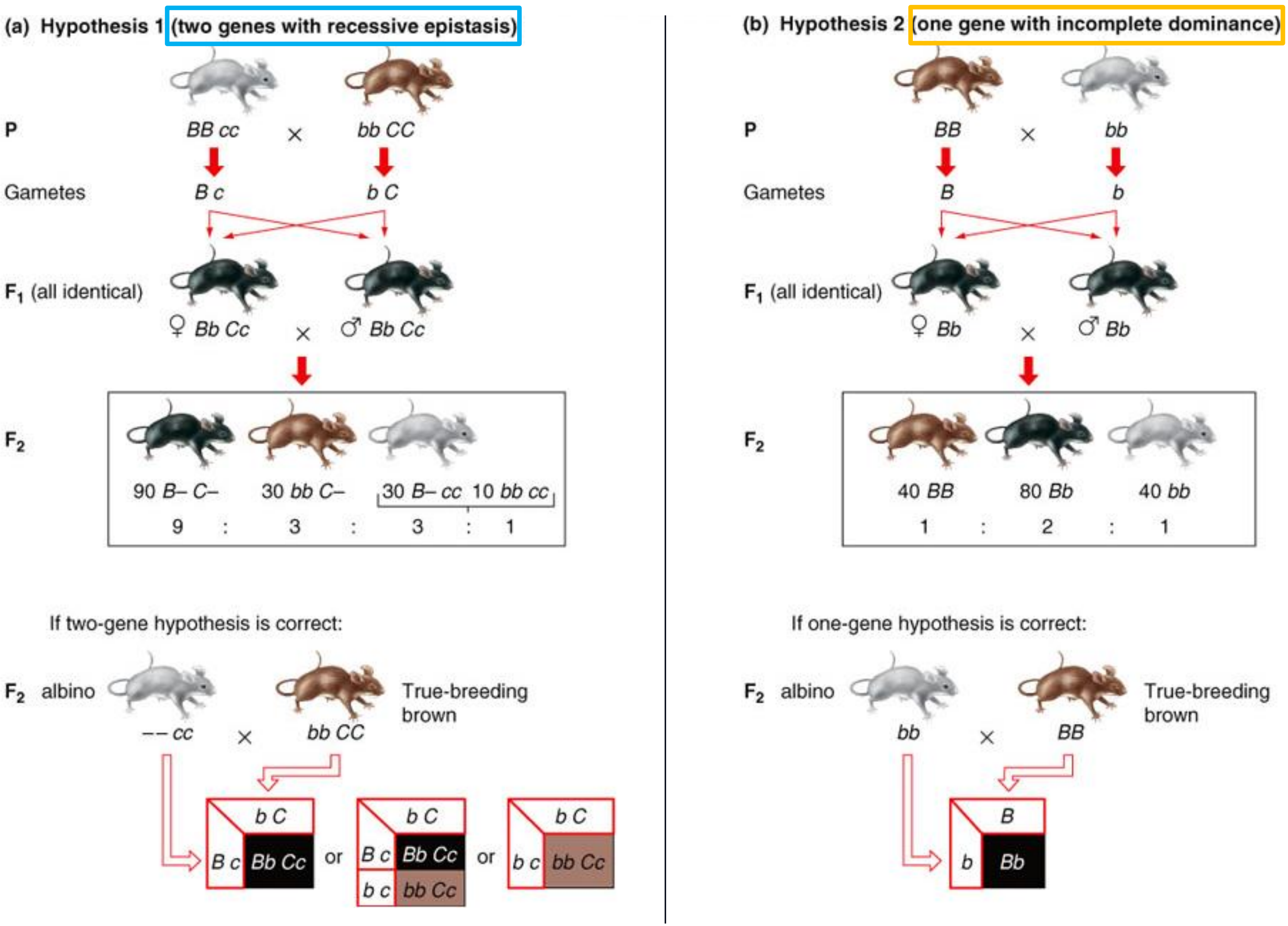
Summary of discussed gene interactions

Gene interaction	9 *A_B_*	3 *A_bb*	3 *aaB_*	1 *aabb*	F2 phenotypic ratio
None	9	3	3	1	9:3:3:1
Complementary	9	7			9:7
Recessive epistasis	9	3	4		9:3:4
Dominant epistasis	12		3	1	12:3:1
Duplicate	15			1	15:1

Breeding studies help determine inheritance of a trait

- How do we know if a trait is caused by one gene or two genes that interact?
  - Ratios such as 9:3:3:1, 9:7, 9:3:4, 12:3:1, 13:3 or 15:1 indicate potential gene interaction.
  - Further breeding studies can confirm the hypotheses.

Testing two gene and one gene hypothesis



Pedigree analysis can be used to test trait inheritance hypotheses in humans

OCA (ocular-cutaneous albinism)

produces little or no pigmentation in skin, hair, and eyes.

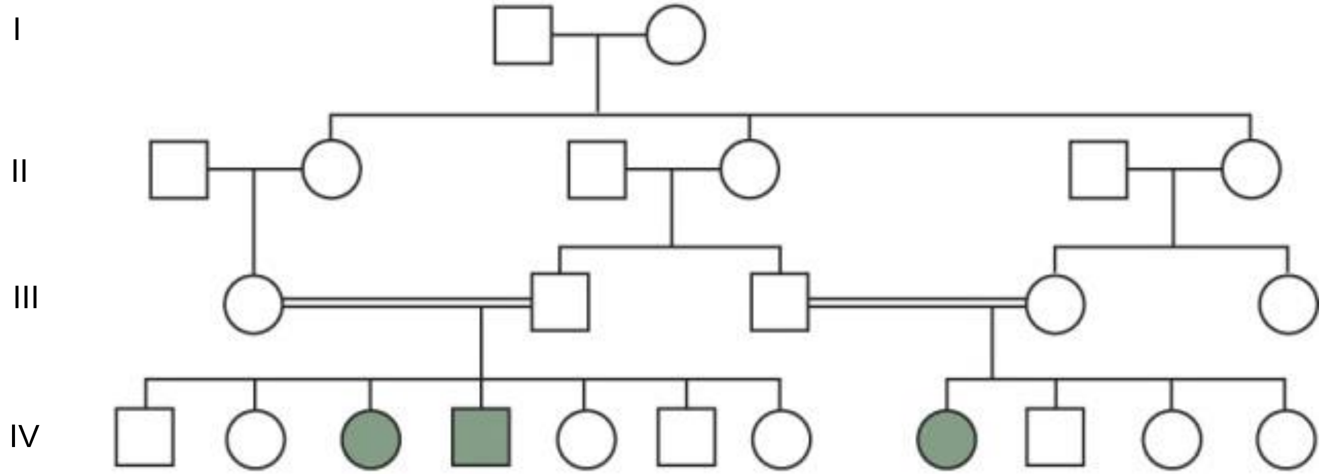
Can you determine the inheritance from pedigrees?

(a) Ocular-cutaneous albinism (OCA)

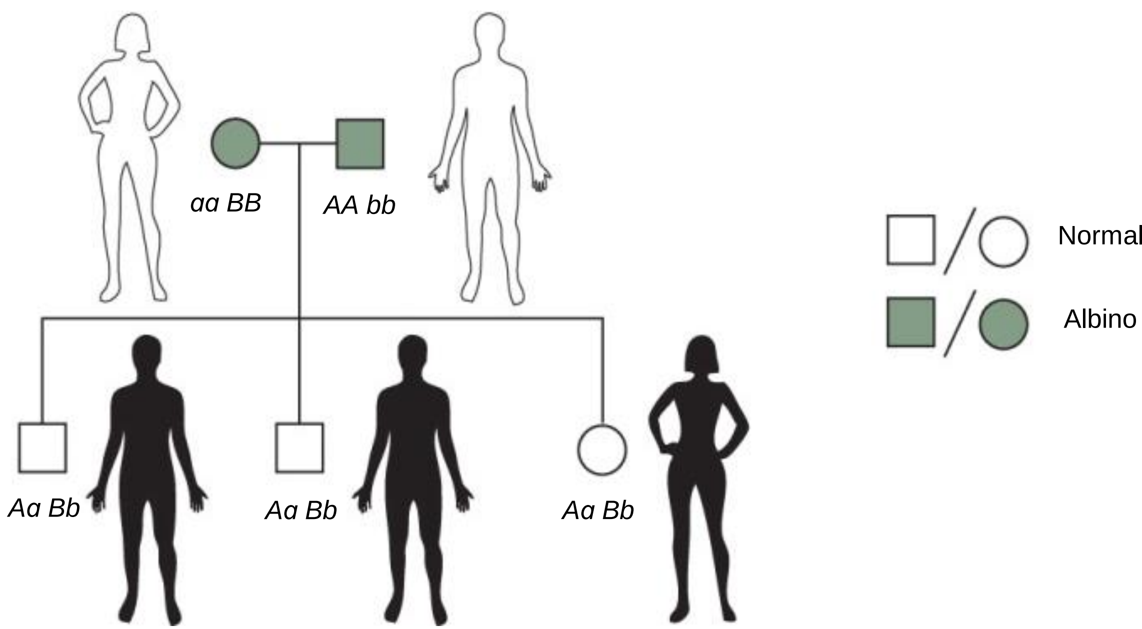
An albino Nigerian girl

尼日利亚

OCA is dominant or recessive?



Complementation for albinism



II.2. Extensions to Mendel for Multifactorial inheritance

The action of two or more genes

Interactions between genes and the environment

Penetrance（外显率）
Expressivity（表现度）

Modifier gene（修饰基因）
Major gene（主要基因）

Phenocopy（表型模拟）

Key Words

penetrance（外显率）
expressivity（表现度）
incomplete penetrance
variable expressivity
discrete trait（不连续性状）
discontinuous trait

quantitative trait（数量性状）
continuous trait（连续性状
modifier gene（修饰基因）
major gene（主要基因）

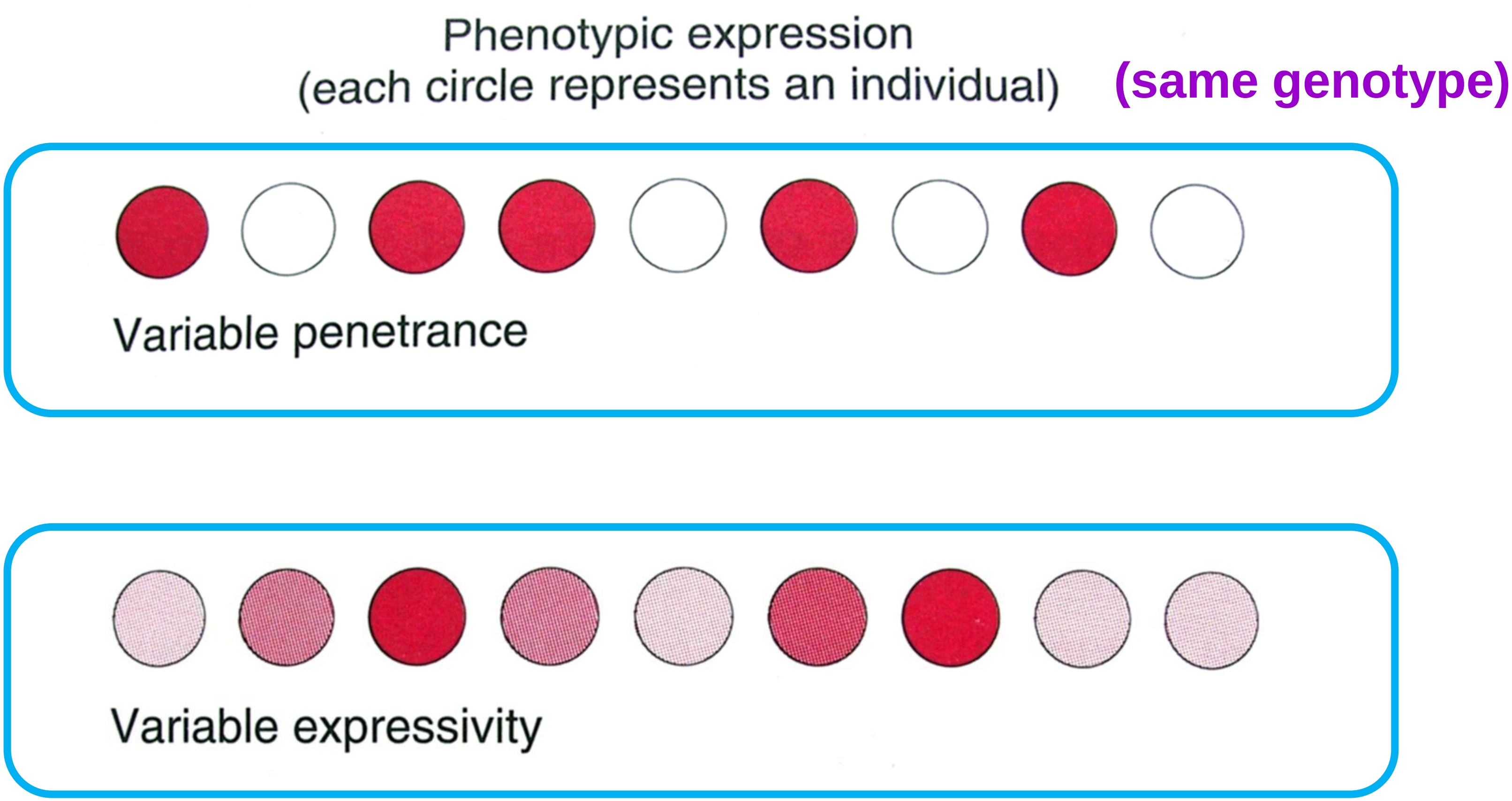
temperature sensitive（温度敏感）
permissive [许可（温度、条件）**]**
restrictive [限制性（温度、条件）**]**
conditional lethal（条件致死）
phenocopy（拟表型，表型模拟）

The same genotype does not always produce the same phenotype

Phenotype often depends on penetrance and expressivity:

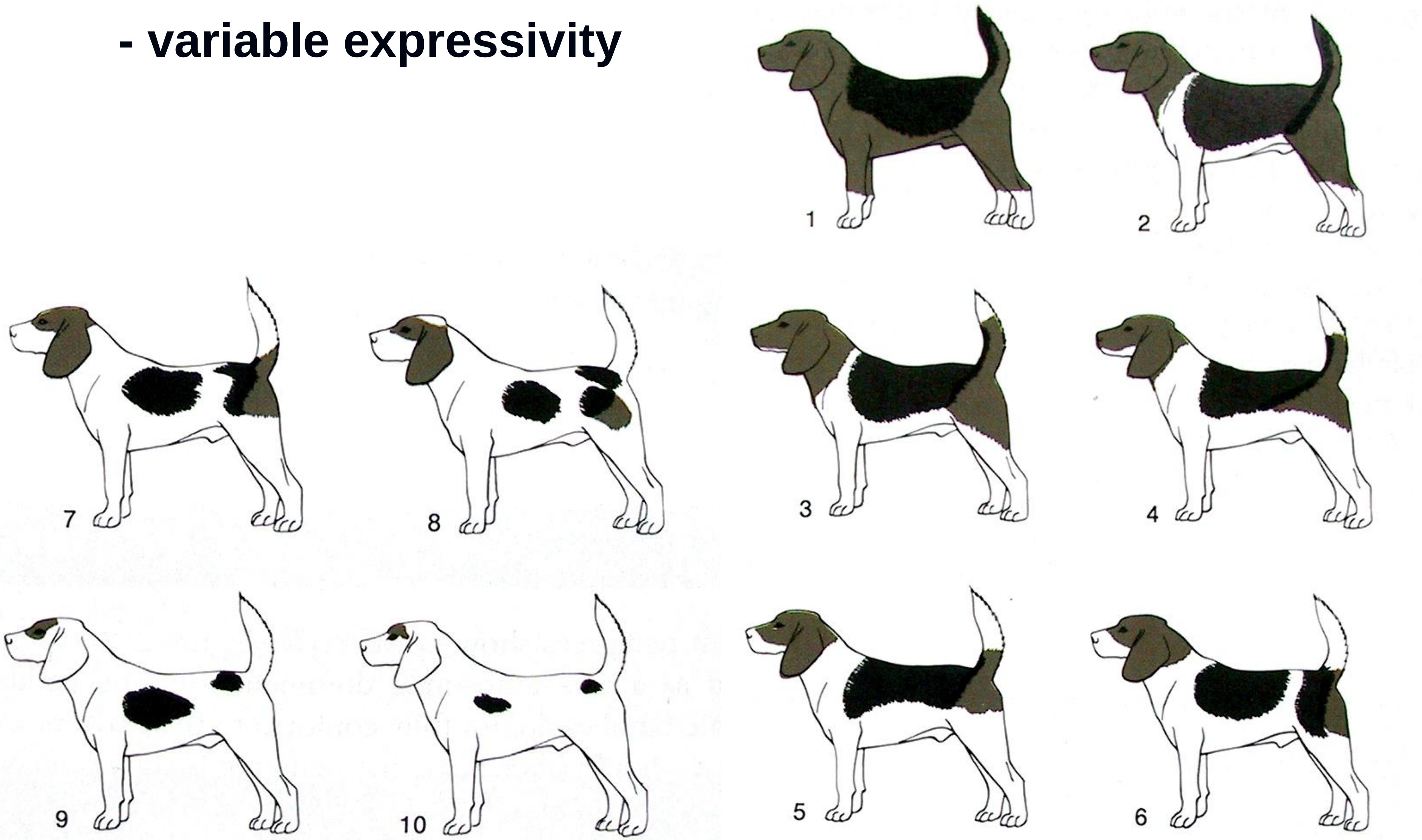
- Penetrance - percentage of a population with a particular genotype that show the expected phenotype
  - Penetrance can be complete (100%) or incomplete (*e.g.*, retinoblastoma penetrance is 75%).
- Expressivity - degree or intensity with which a particular genotype is expressed in a phenotype
  - Expressivity can be variable or unvarying.

Penetrance vs. expressivity



Piebald spotting in dogs

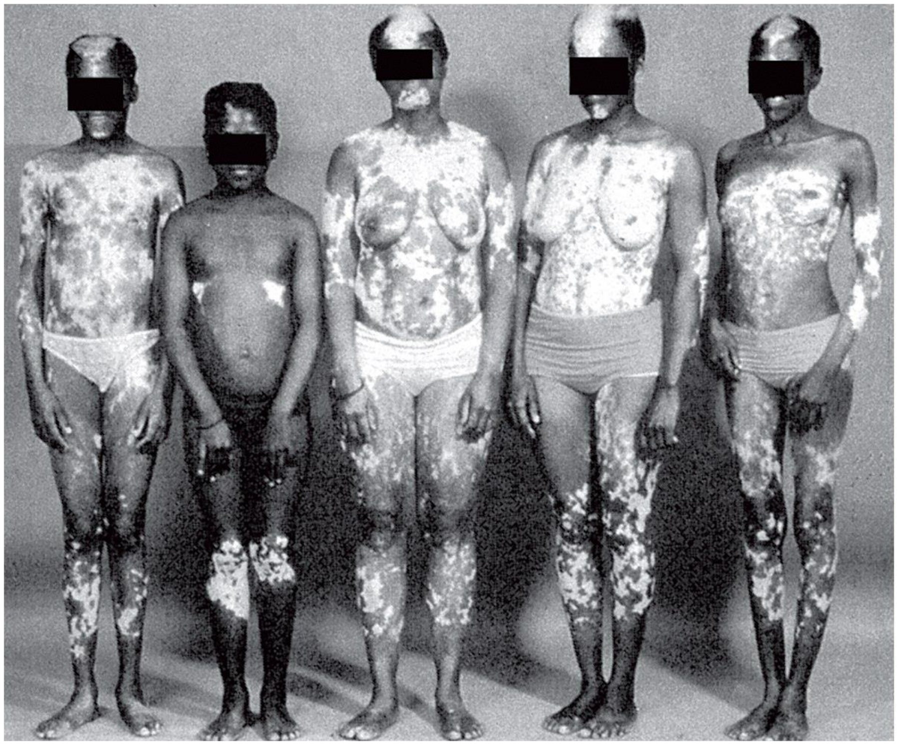
- variable expressivity



Piebald spotting in humans (piebaldism)

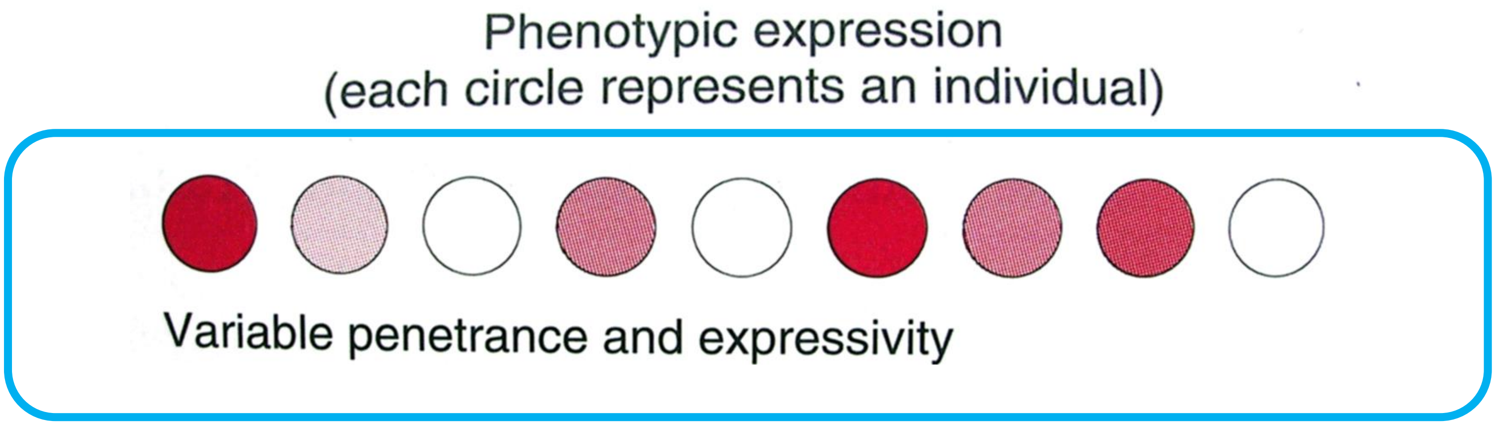
- variable expressivity

人类的白斑病



Dominant inheritance

Variable penetrance and expressivity



The trait caused by a genotype is expressed to various degrees or in a variety of ways in different individuals.

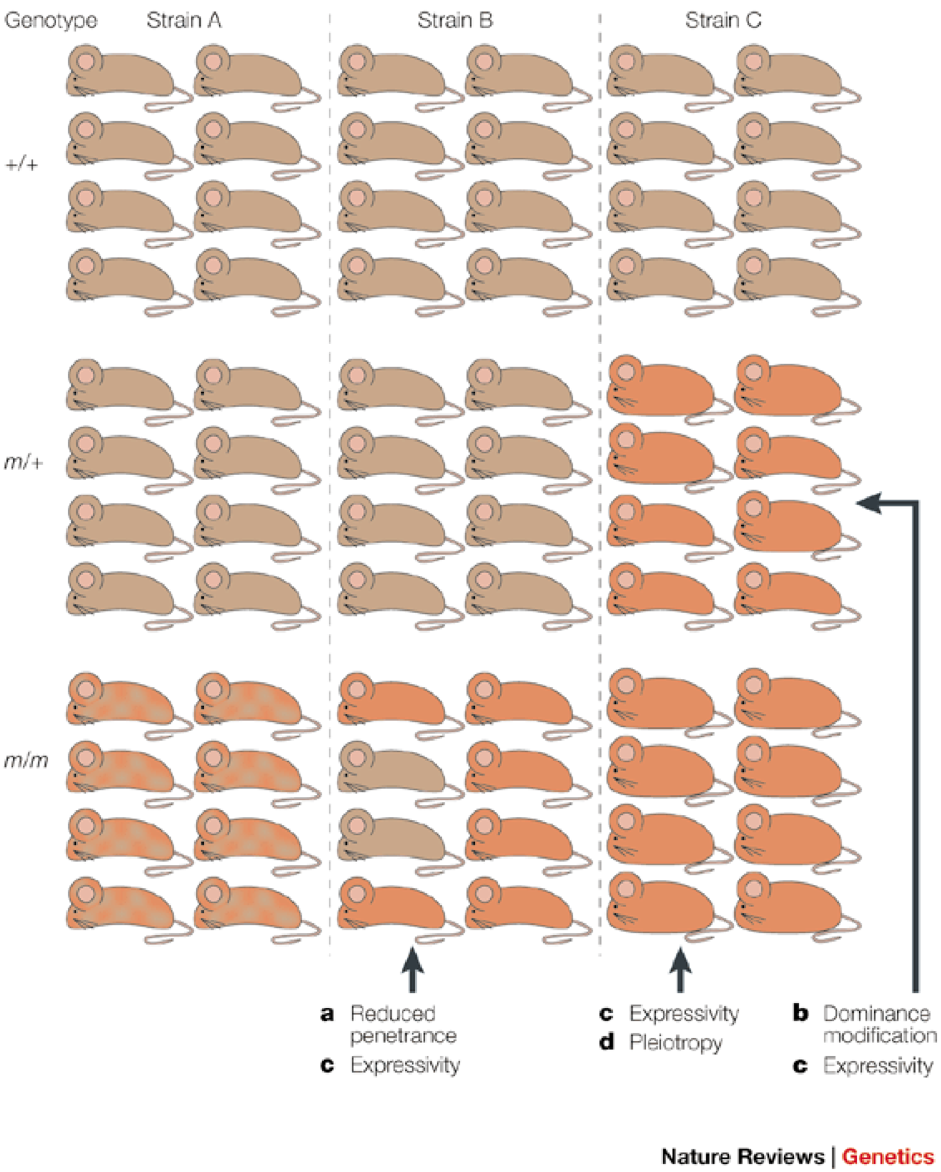
Factors that alter the phenotypic expression of genotype include:

- **Modifier genes**
- **The environment (temperature, diet, exercise, etc.)**
- **Chance**

Modifier genes

Not all genes that influence the appearance of a trait contribute equally to the phenotypes

Modifier genes have a more subtle, secondary effect, while major genes have a large influence.



(Joseph H. Nadeau, 2001)

Environmental effects on phenotype

- Temperature
- Chemicals or other environmental agents
- Diet and exercise

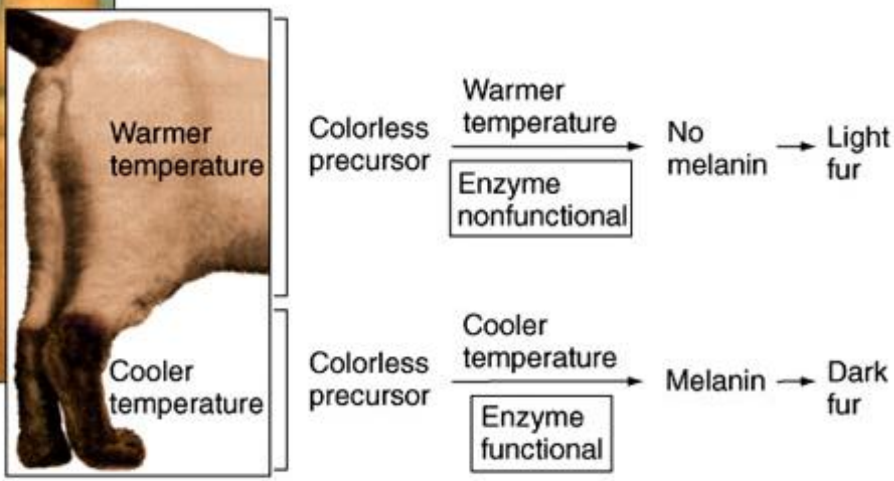
Hydrangea （绣球花)

The more alkaline the soil, the pinker the flowers

Siamese cat - temperature sensitive pigmentation

暹罗猫

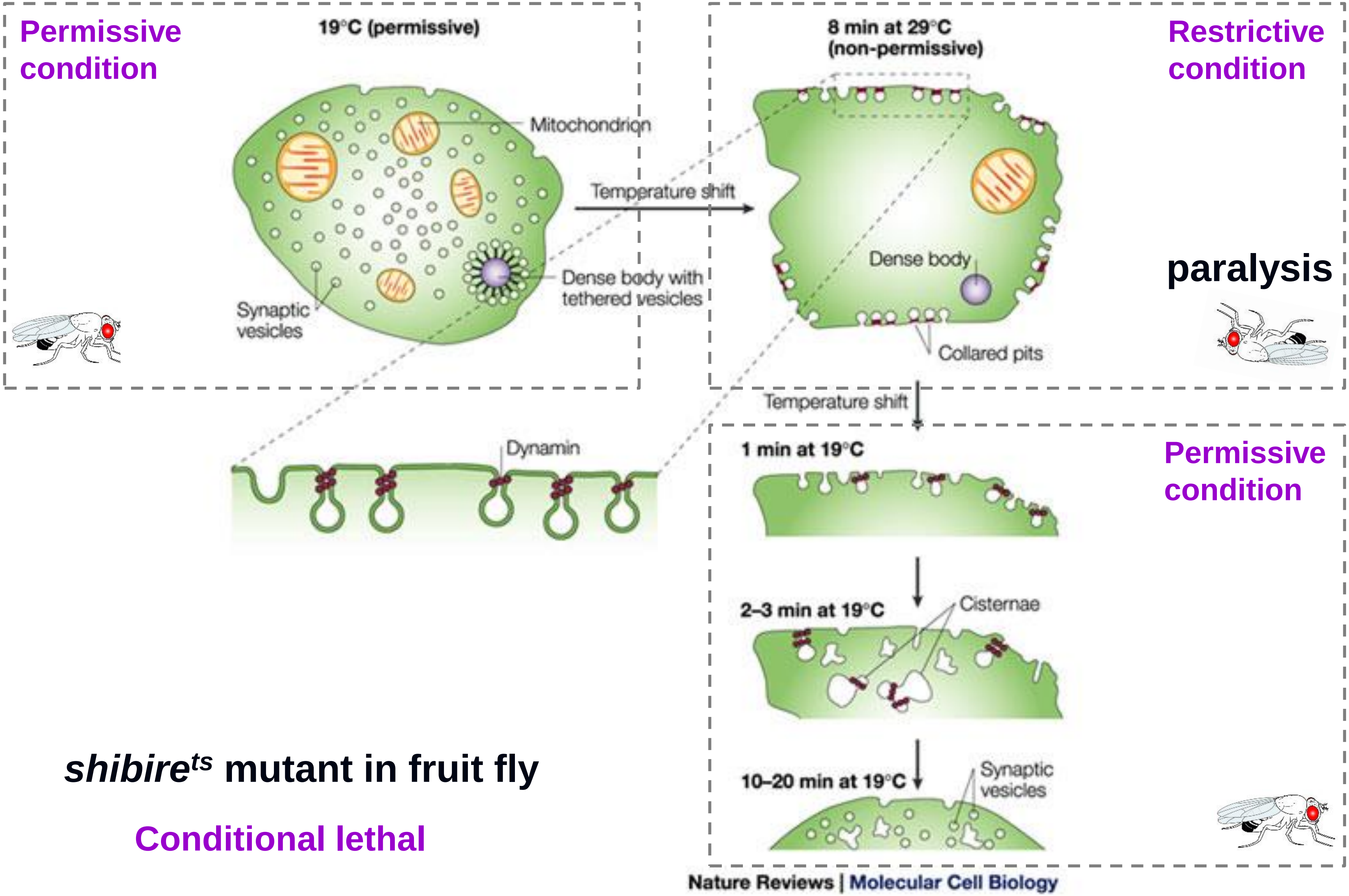

(a)



(b)

Melanin is produced only in the cooler extremities.

Temperature and viability

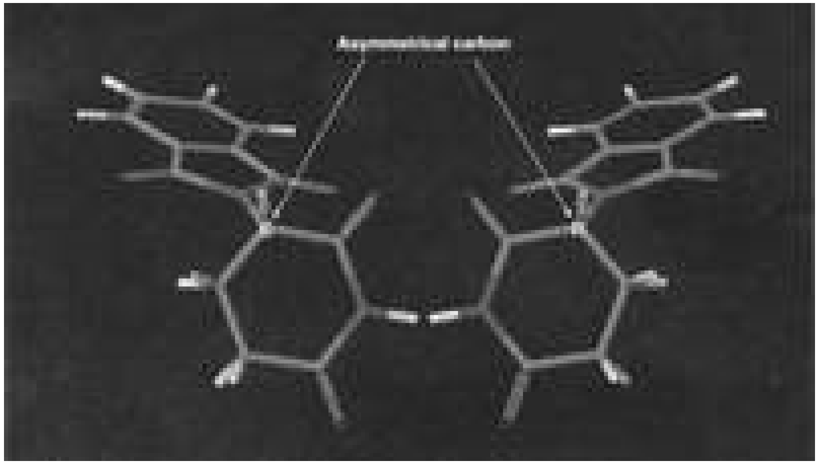


***shibire*^{ts} mutant in fruit fly**

Conditional lethal

Phocomelia – chemical exposure

Phocomelia（短肢畸形）

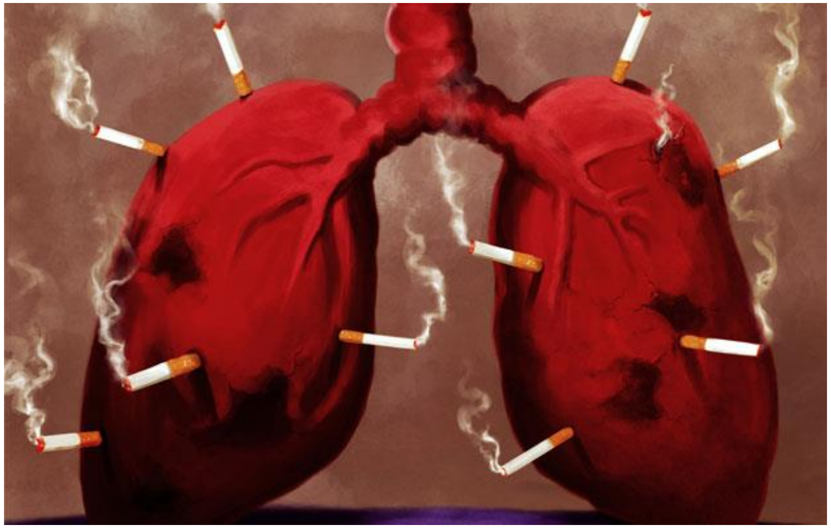


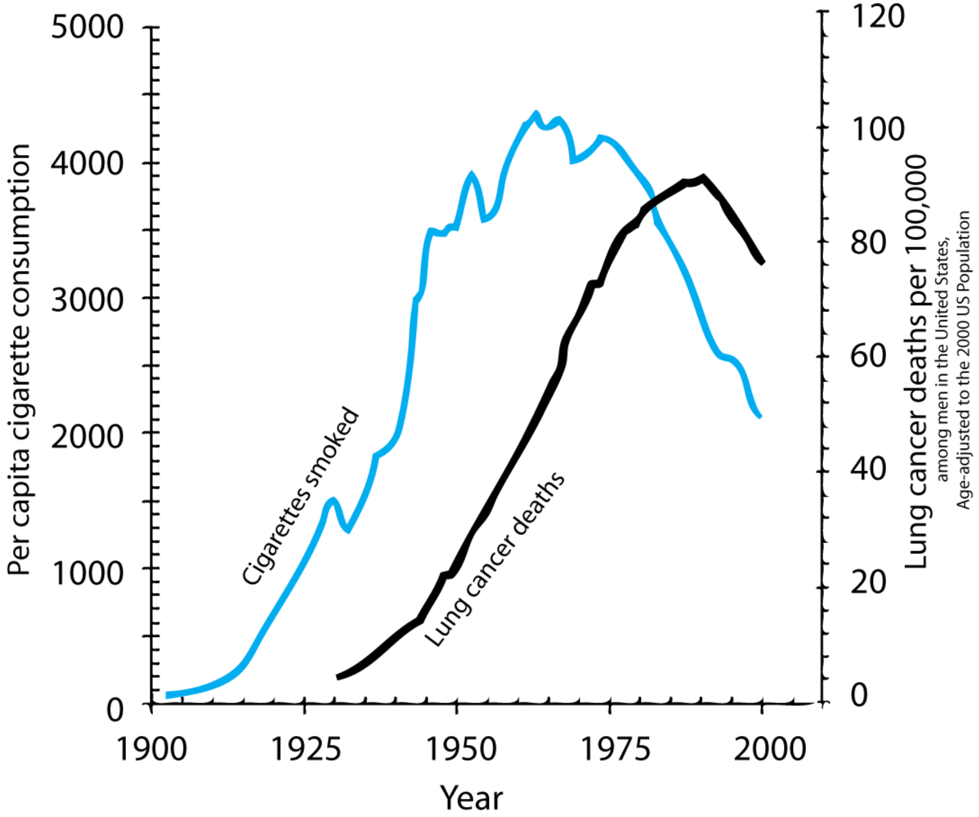
Thalidomide - sedative（反应停）

In the early 1960s, ingestion of Thalidomide by pregnant women led to disrupting of limb development in fetuses.

Phenocopy: a change in phenotype arising from environmental agents that mimics the effect of a mutation at a gene

Smoking and lung cancer





Chapter I

Mendel's Law of Inheritance

I. Mendel's breakthrough

Patterns, particles, and principles of heredity

II. Extension to Mendel's laws

Complexities in relating genotype to phenotype

1. **Single-gene inheritance**
2. **Multifactorial inheritance**

Chapters in reference books：H2-H3, D3