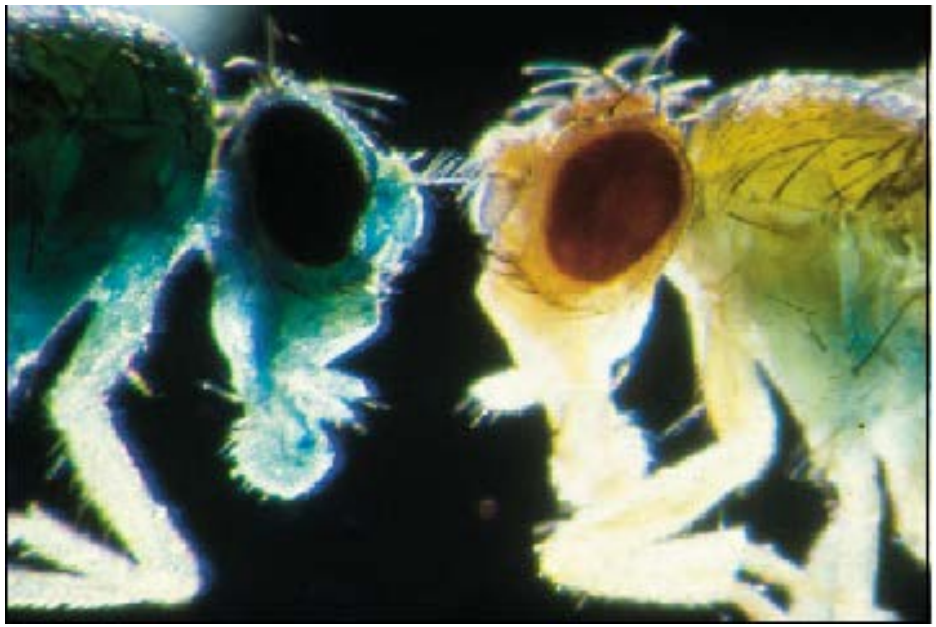
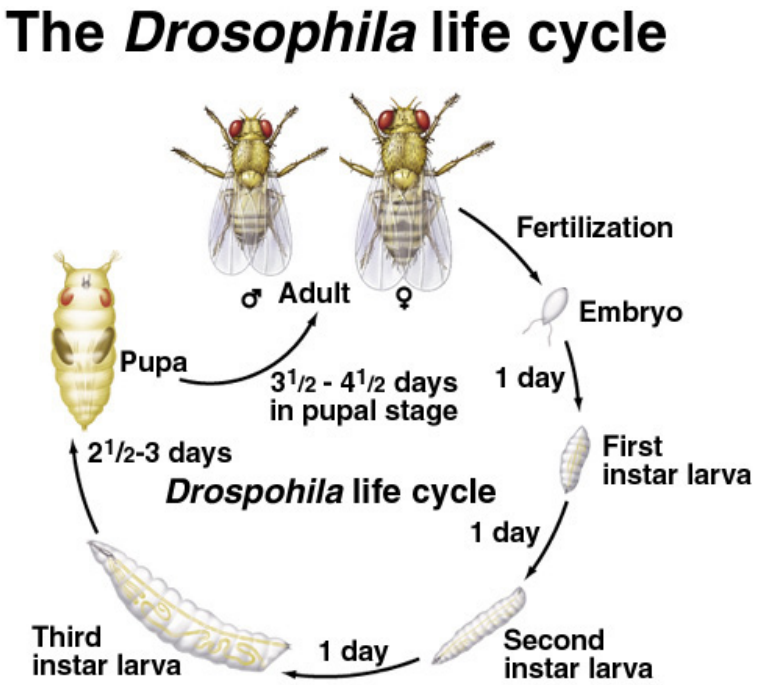
第二章　连锁分析与染色体作图
Linkage and Chromosome Mapping



The chromosomal basis of Mendelism

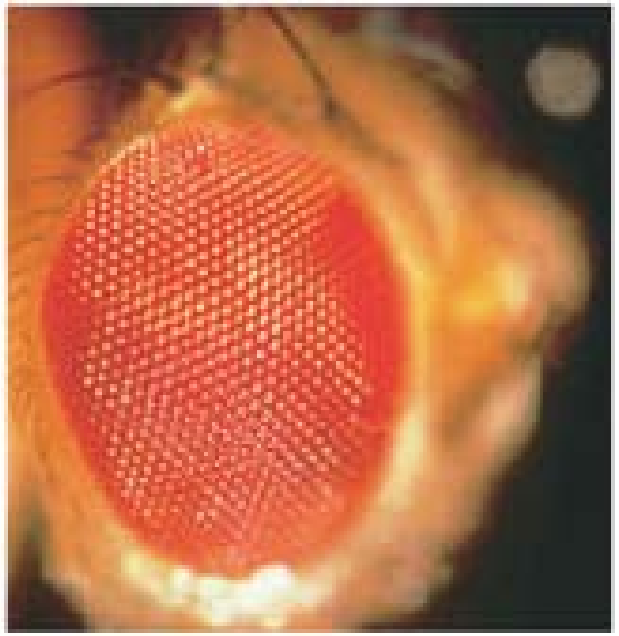
- T.H.Morgan

Thomas H. Morgan (1866-1945)

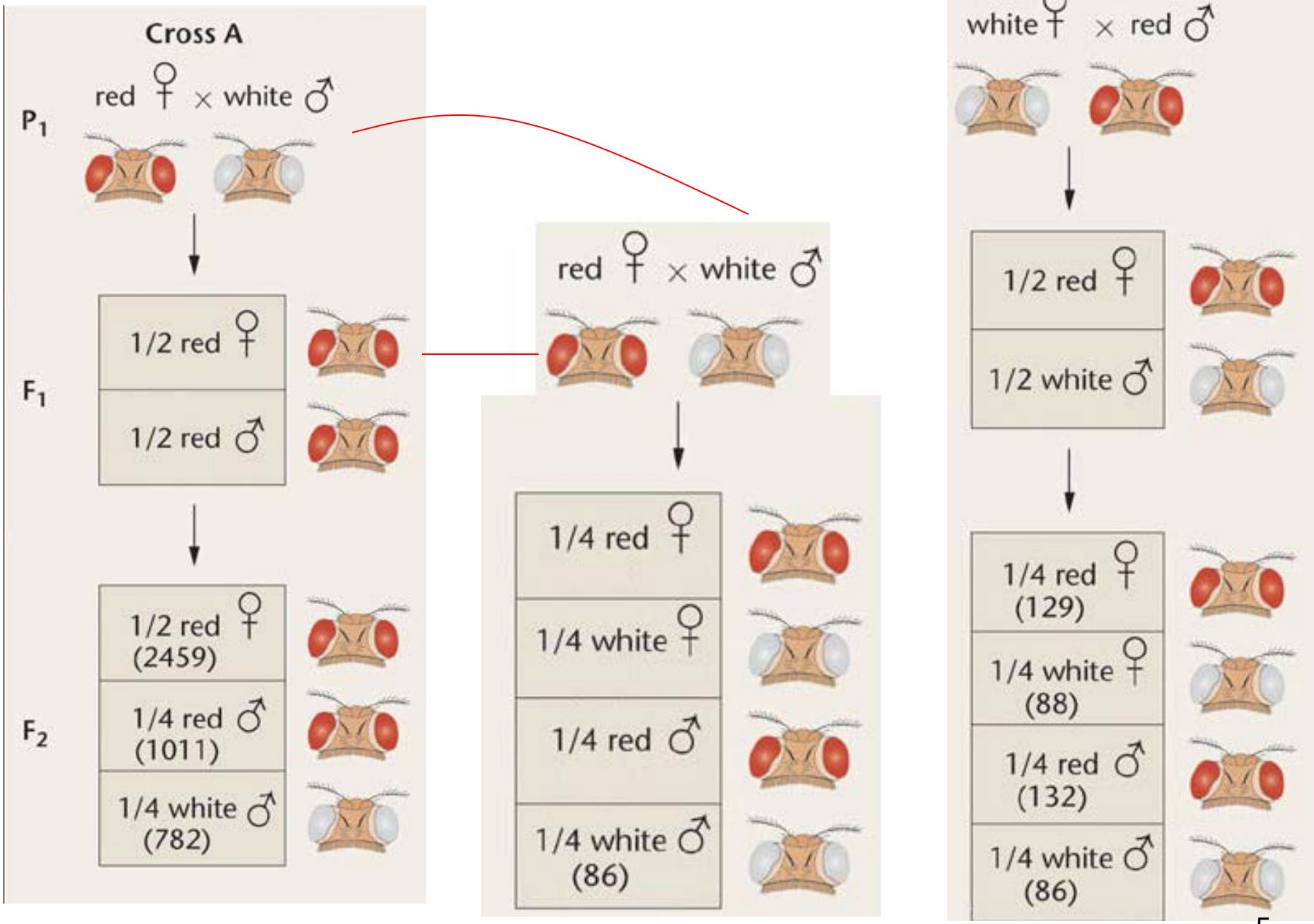


Morgan found a mutant white eye fruit fly

What would you do on this fly?

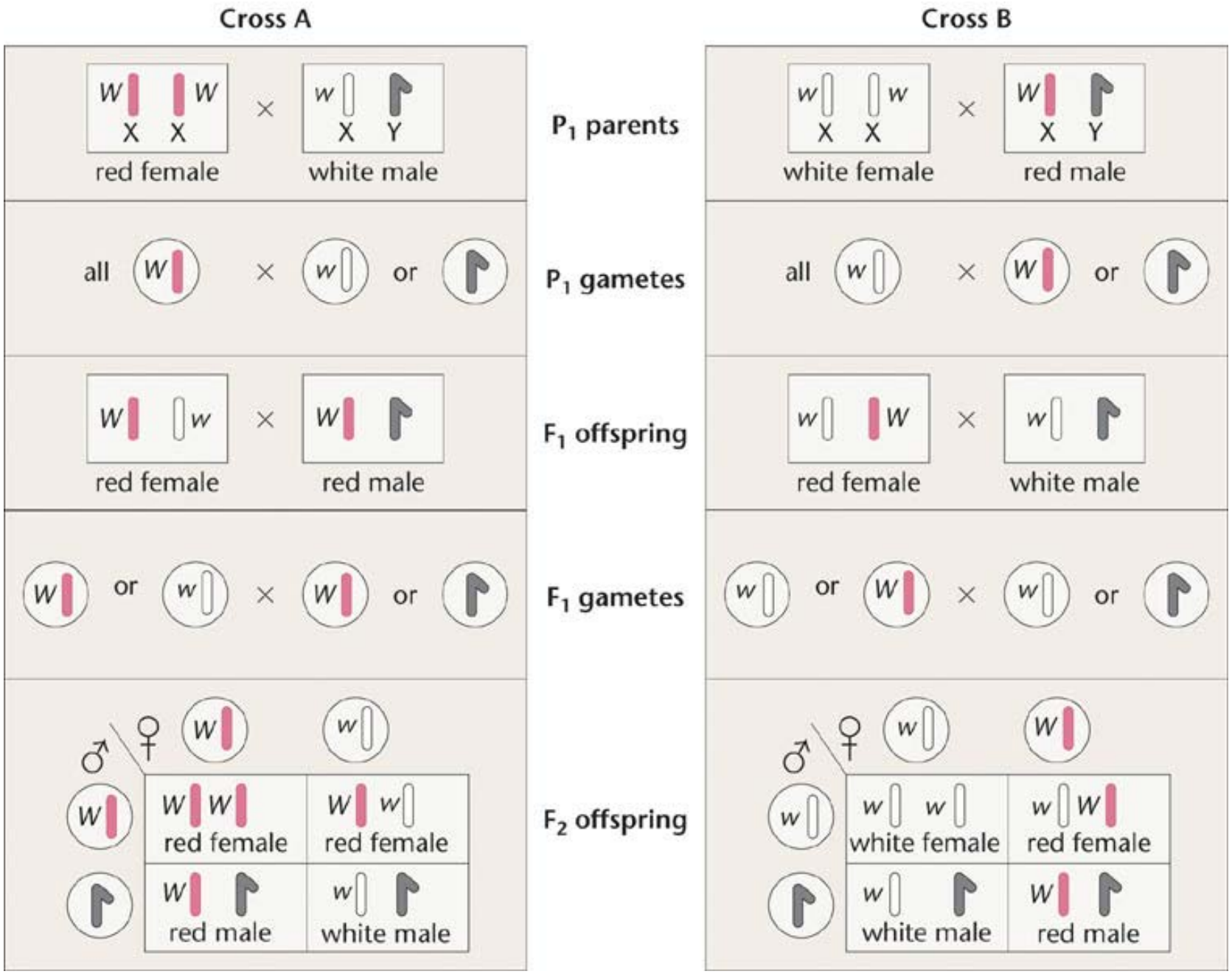


1910


Cross A
red ♀ × white ♂
P1
F1
1/2 red ♀
1/2 red ♂
F2
1/2 red ♀ (2459)
1/4 red ♂ (1011)
1/4 white ♂ (782)
red ♀ × white ♂
1/4 red ♀
1/4 white ♀
1/4 red ♂
1/4 white ♂ (86)
Cross B
white ♀ × red ♂
1/2 red ♀
1/2 white ♂
1/4 red ♀ (129)
1/4 white ♀ (88)
1/4 red ♂ (132)
1/4 white ♂ (86)

- The **reciprocal cross** gave different results with the **original cross**.

- Morgan hypothesized that the recessive white allele of the first white eye fly located on the **X chromosome**.


Cross A
Cross B
P1 parents
red female
white male
white female
red male
P1 gametes
all
or
F1 offspring
red female
red male
white female
white male
F1 gametes
F2 offspring
red female
red female
red male
white male
white female
red female
white male
red male

The fountainhead of *Drosophila* genetics. Thomas Hunt Morgan and his students in the fly room at Columbia University, at a party in 1919 celebrating the return of Alfred Sturtevant from military service in World War I. Individuals whose work is discussed in this book include Morgan (back row, far left), Sturtevant (front row, third from the right), Calvin Bridges (back row, third from the right), and Herman J. Muller (back row, second from the left). The "honored guest" between Muller and Bridges has clearly seen better days.

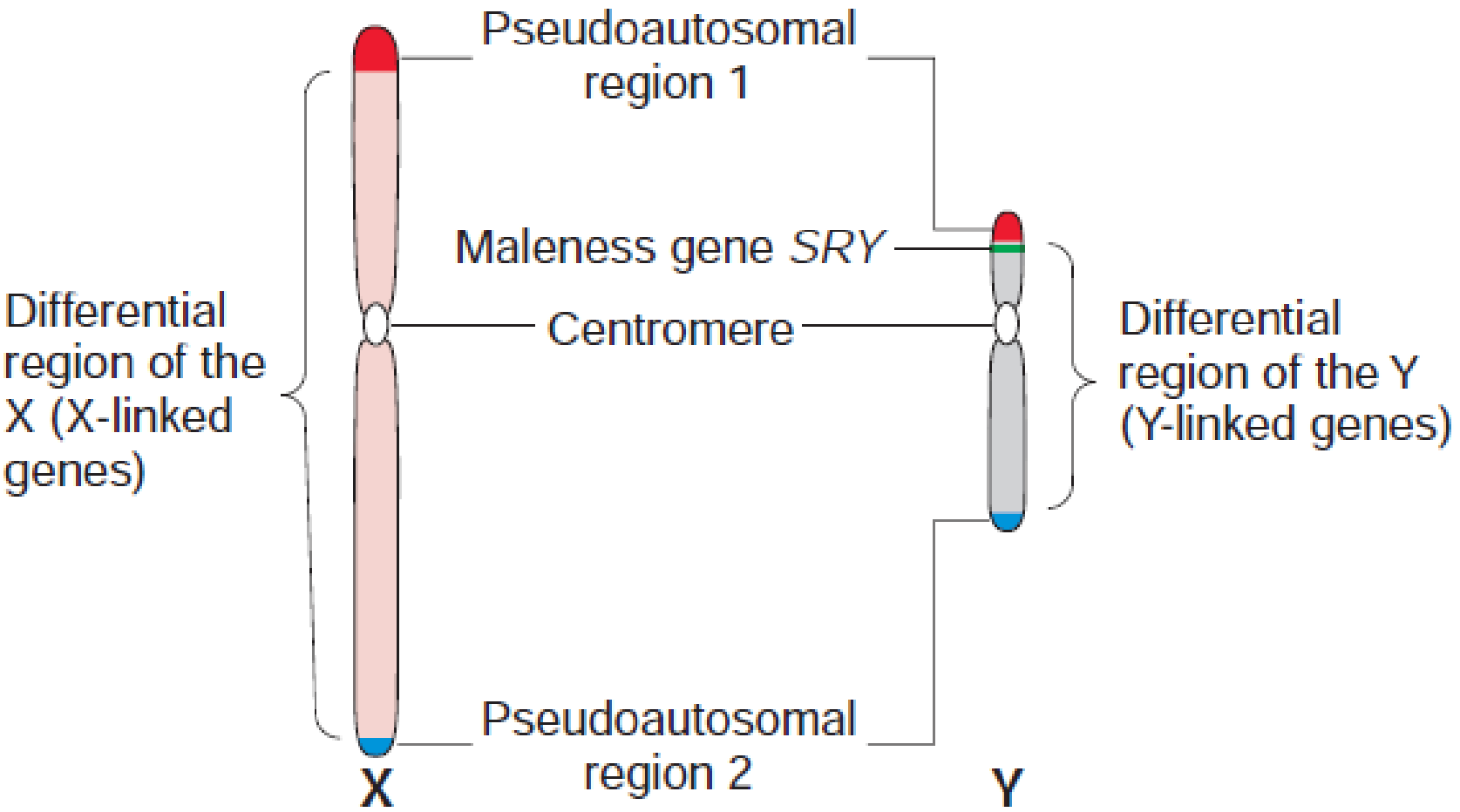
第一节　伴性遗传
(Sex chromosomes and sex-linked inheritance)

一、性染色体 Sex Chromosomes

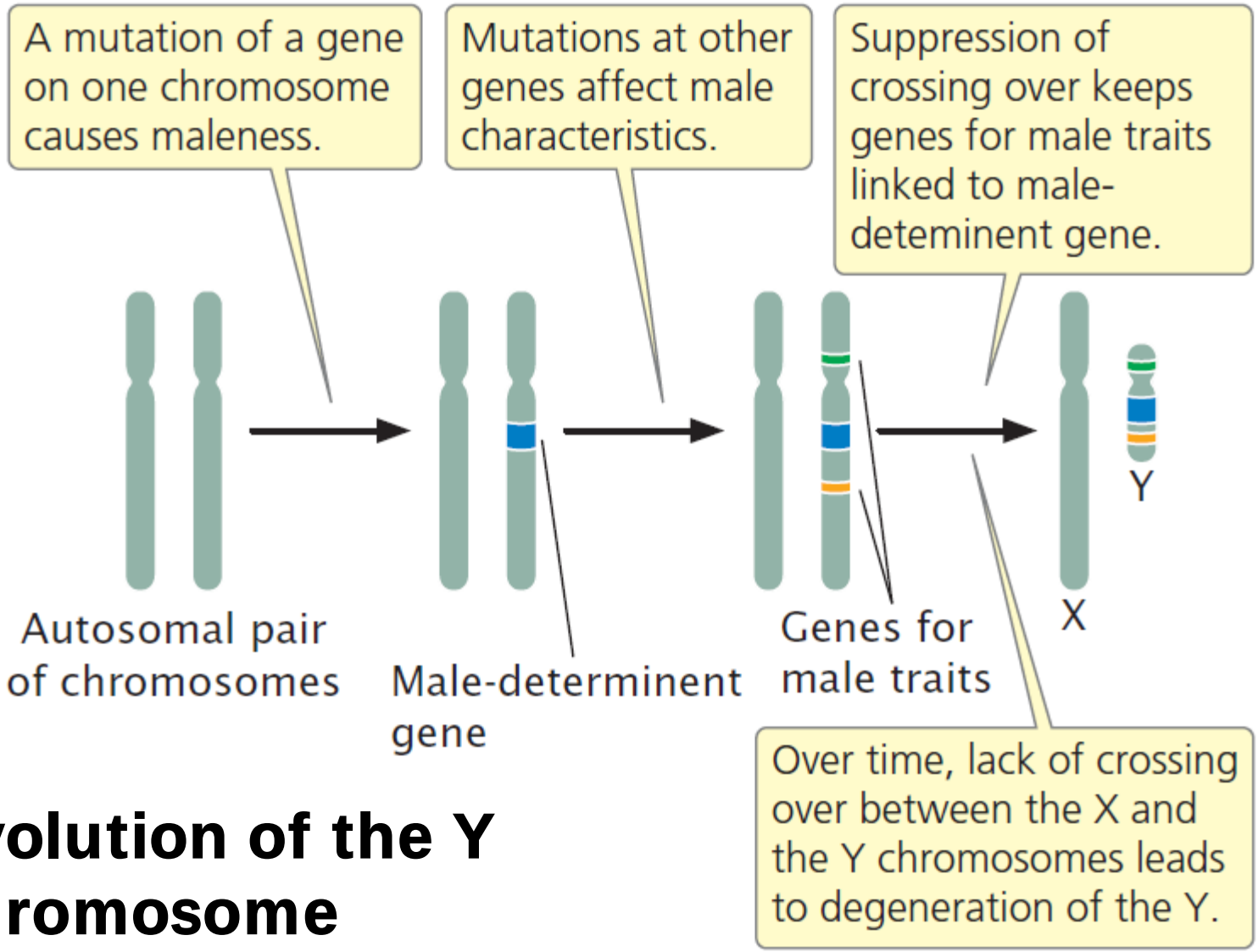
Sex chromosomes: Chromosomes that are connected with the determination of sex (XY & ZW)

All the other chromosomes in the genome are called **autosomes** (A)

Human sex chromosomes



Hemizygous (半合子): Genes in the differential regions of sex chromosomes



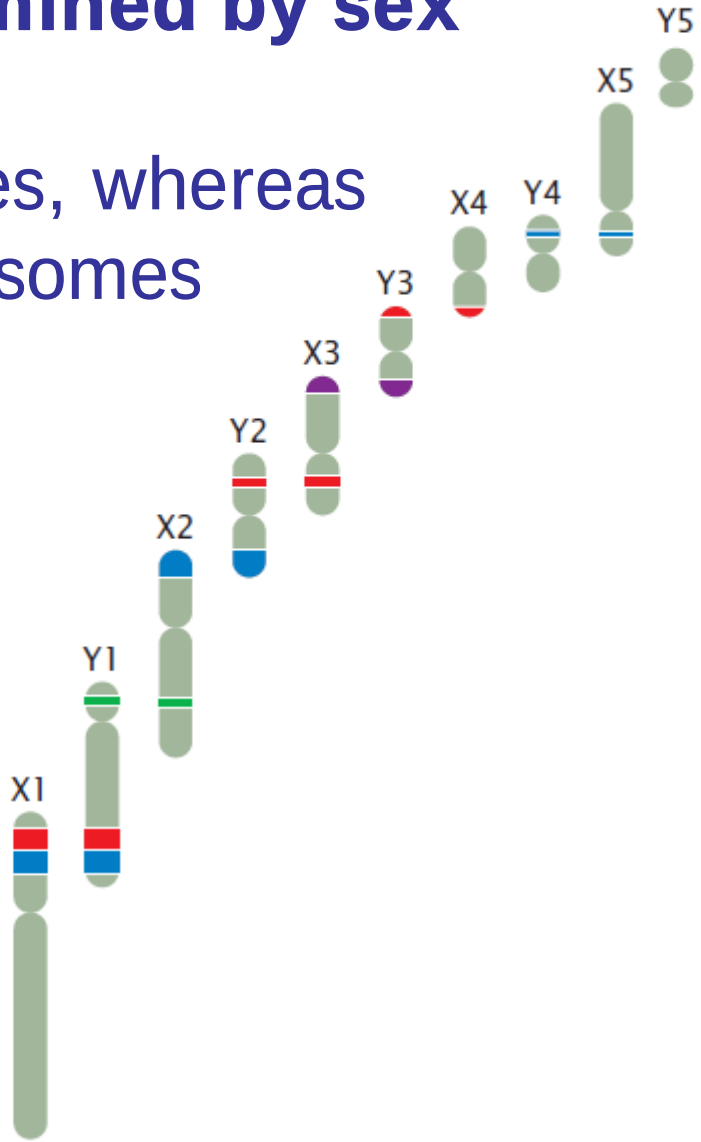
Evolution of the Y chromosome

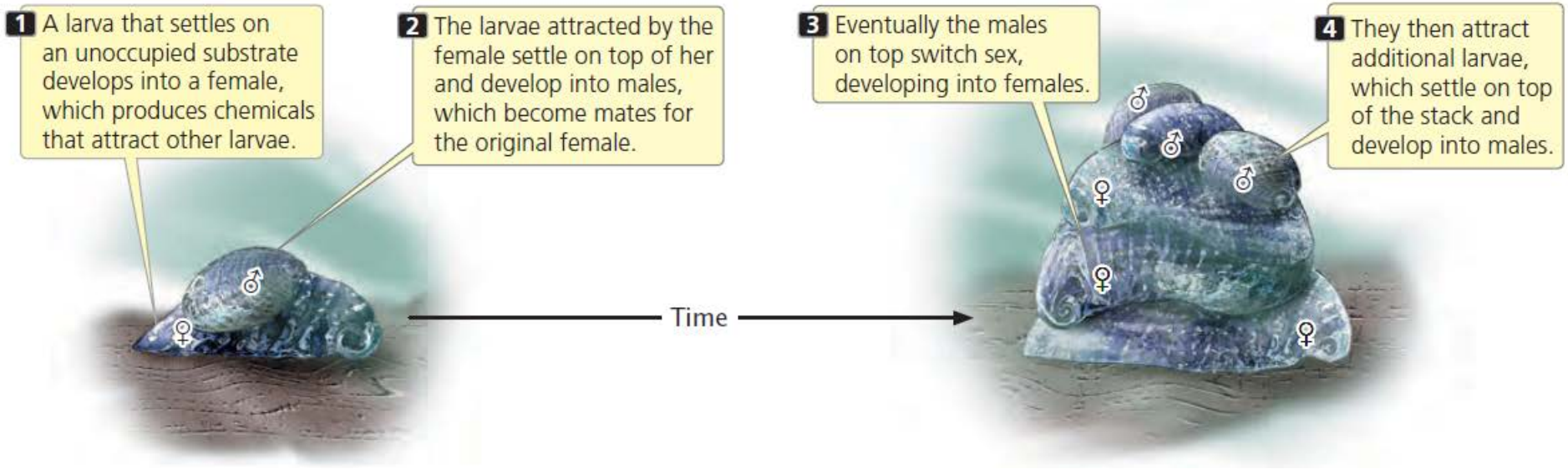
Sex Is Determined by a Number of Different Mechanisms

- Chromosomal Sex-Determining Systems
  - **XX-XY**:
  - **ZZ-ZW**: birds, snakes, butterflies, some amphibians, and some fishes.
  - **XX-XO**: grasshoppers, *C.elegans*
- Genic Sex Determination
  - some plants, fungi, and protozoans
- Environmental Sex Determination

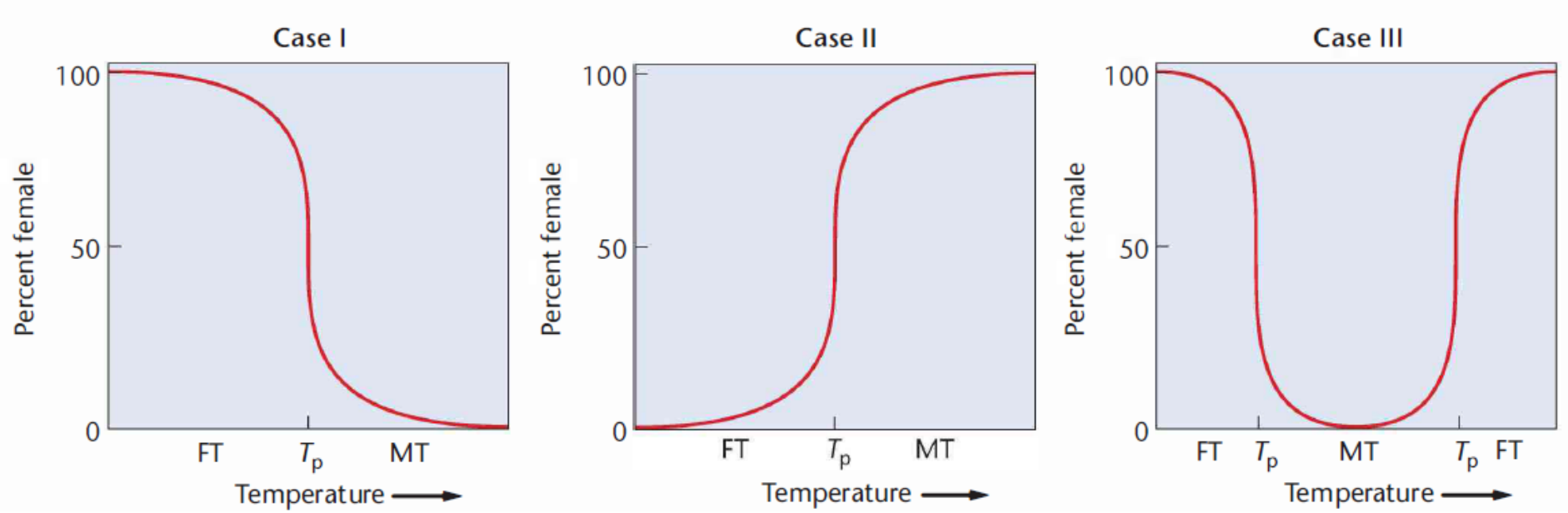
Sex in the platypus is determined by sex chromosomes.

Females have 10 X chromosomes, whereas males have 5 X and 5 Y chromosomes





In *Crepidula fornicata*, the common slipper limpet, sex is determined by an environmental factor—the limpet's position in a stack of limpets.



Three different patterns of temperature-dependent sex determination (TSD) in reptiles

二、伴性遗传
Sex-linked patterns of inheritance

- 决定性状的基因在性染色体上
- 性状的遗传与性别有关
- 正交与反交结果不同
- 表现特殊的交叉遗传和隔代遗传现象

X-Linkage in Human

- Red-green color blindness
- Hemophilia A & B (血友病)
- G-6-PD deficiency
- HGPRT
- ……

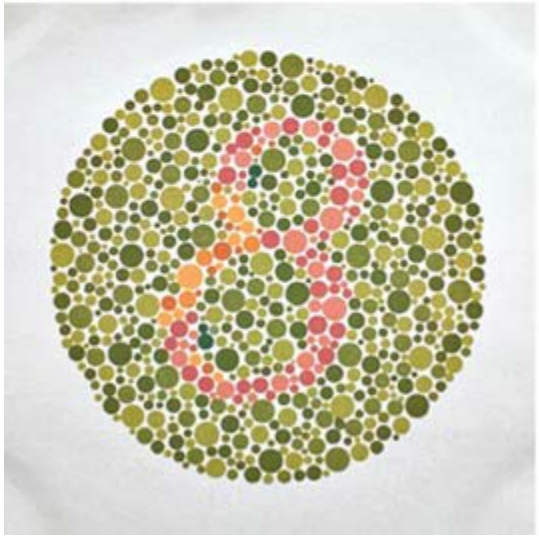
Human Red-green color blindness

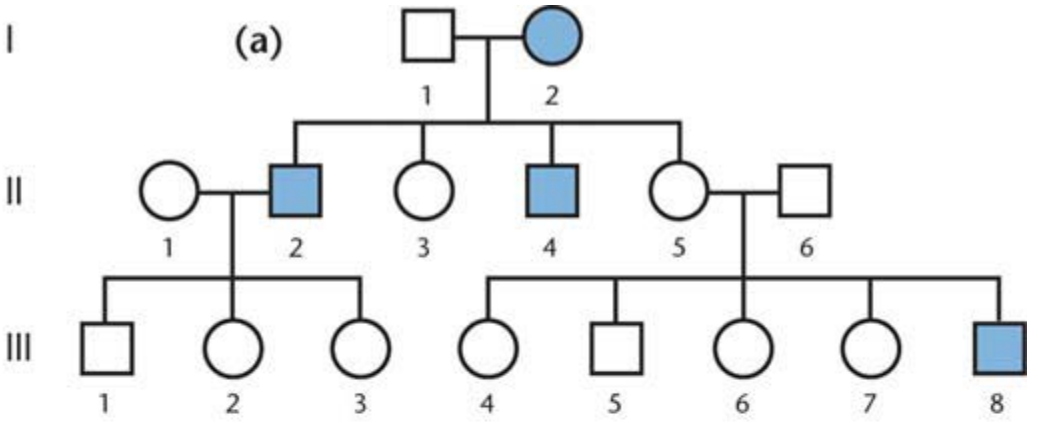
Symbols

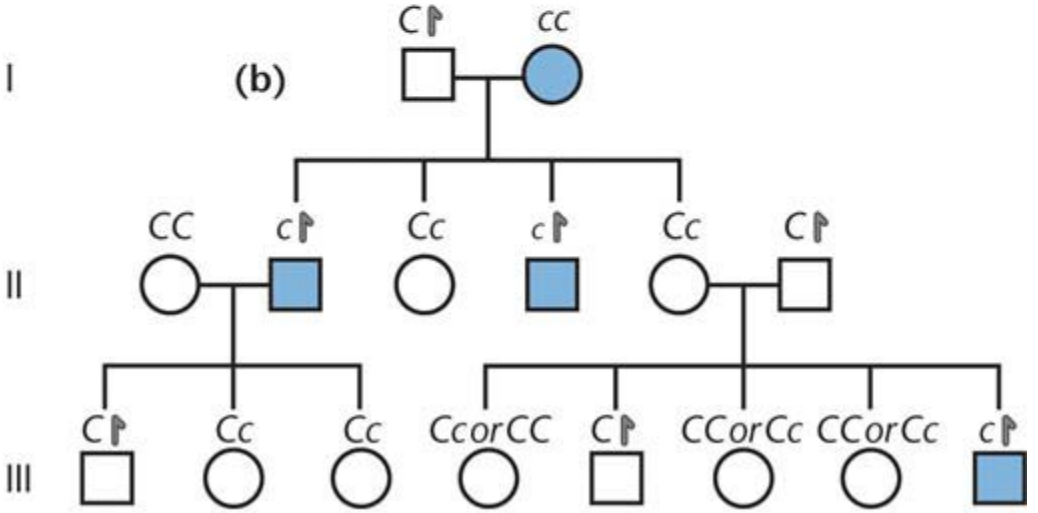
c = color blindness

C = normal vision

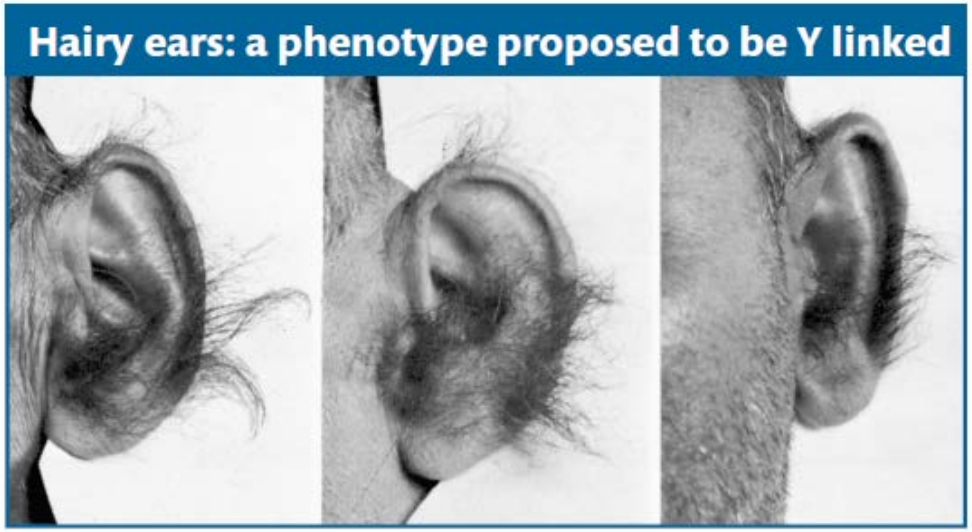
♂ = Y chromosome







Y-Linked Traits in Human



- Very few genes have been localized to the human Y chromosome
  - According to HGP, 397 genes on Y, while less than 100 are functional
  - For X, 900-1400 genes
- Determination of maleness
- Nonsexual phenotypic variants

三、限性遗传与从性遗传
Sex-limited and sex-influenced inheritance

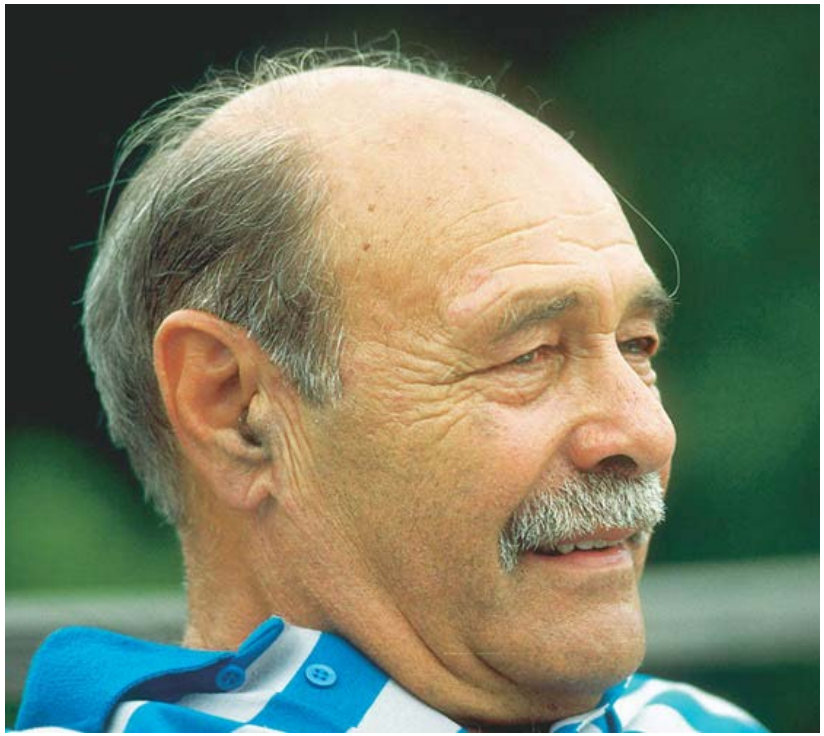
- **Sex-limited inheritance**, the expression of a specific phenotype is absolutely limited to one sex.
- **Sex-influenced inheritance**, the sex of an individual influences the way a phenotype is expressed.
- In both types of inheritance, **autosomal genes** are responsible for the contrasting phenotypes, but the expression of these genes is dependent on the hormone constitution of the individuals.

Sex-limited inheritance

Hen feathering: H

Genotype	Phenotype	
	♀	♂
HH	Hen-feathered	Hen-feathered
Hh	Hen-feathered	Hen-feathered
hh	Hen-feathered	Cock-feathered

Sex-influenced inheritance



Pattern baldness is a complex trait that can be affected by many genes

The phenotypic extent is different between male and female

Genotype	Phenotype ♀	♂
BB	Bald	Bald
Bb	Not bald	Bald
bb	Not bald	Not bald

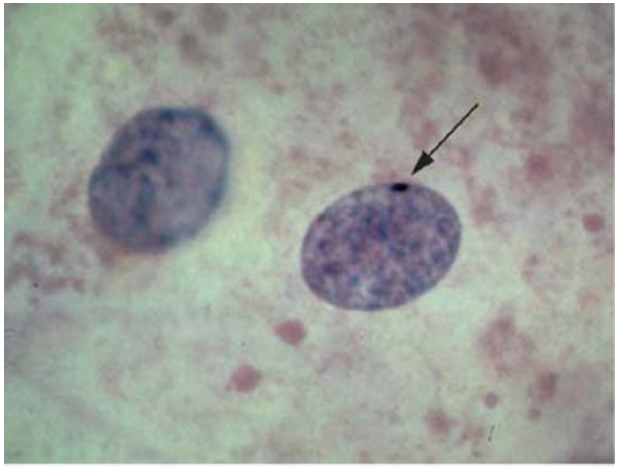
The heterozygous genotype exhibits one phenotype in one sex and the contrasting one in the other

The presence of a beard on some goats is determined by an autosomal gene (B^b) that is dominant in males and recessive in females

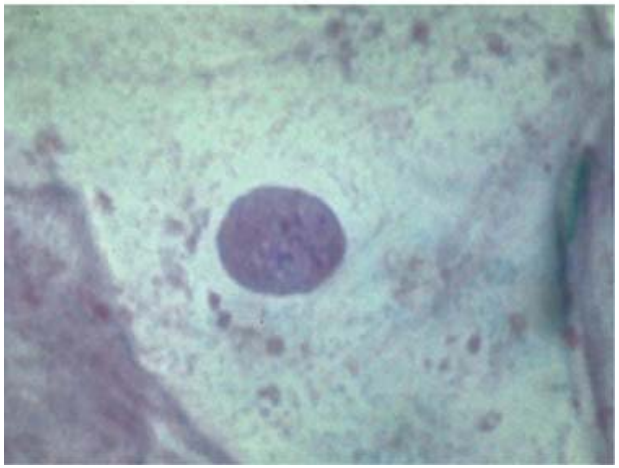
Genotype	Males	Females
B^+B^+	beardless	beardless
B^+B^b	bearded	beardless
B^bB^b	bearded	bearded

四、剂量补偿效应
(Dosage compensation of X-linked genes)

- **Barr body**
  巴氏小体



Barr body test



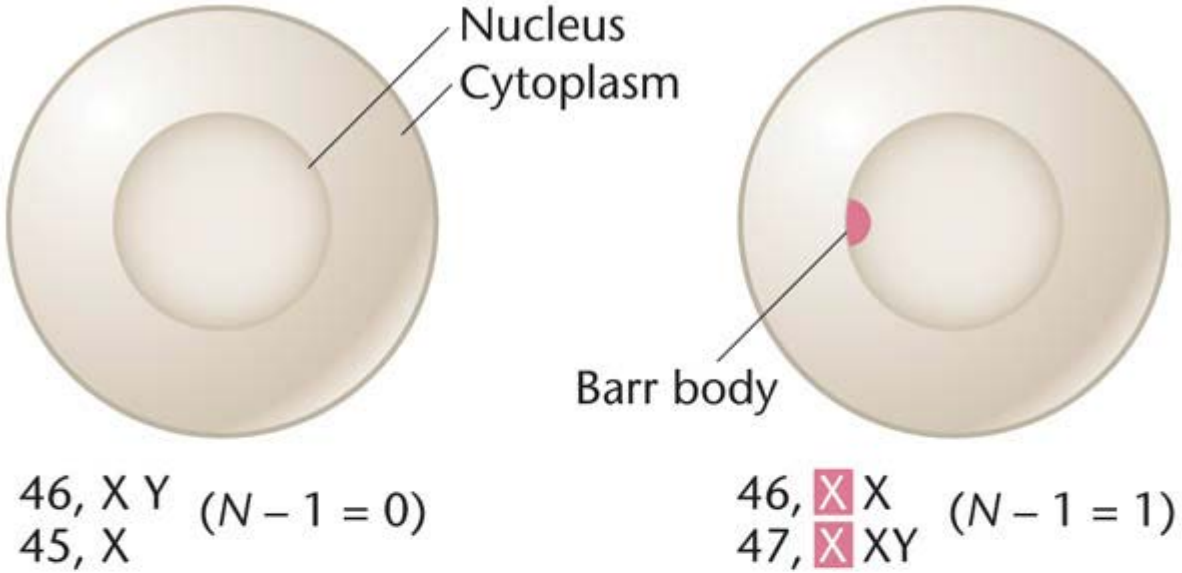
Nature, 1949, 163(4148): 676–677

Dosage compensation effect

In **humans and other mammals**, one of the two X chromosomes is inactivated in the cells of females

In ***Drosophila***, male X-linked genes are transcribes at twice the level of the comparable genes in females

In ***C.elegans*** (XX, XO), female X-linked genes are transcribes at half the level of the comparable genes in males

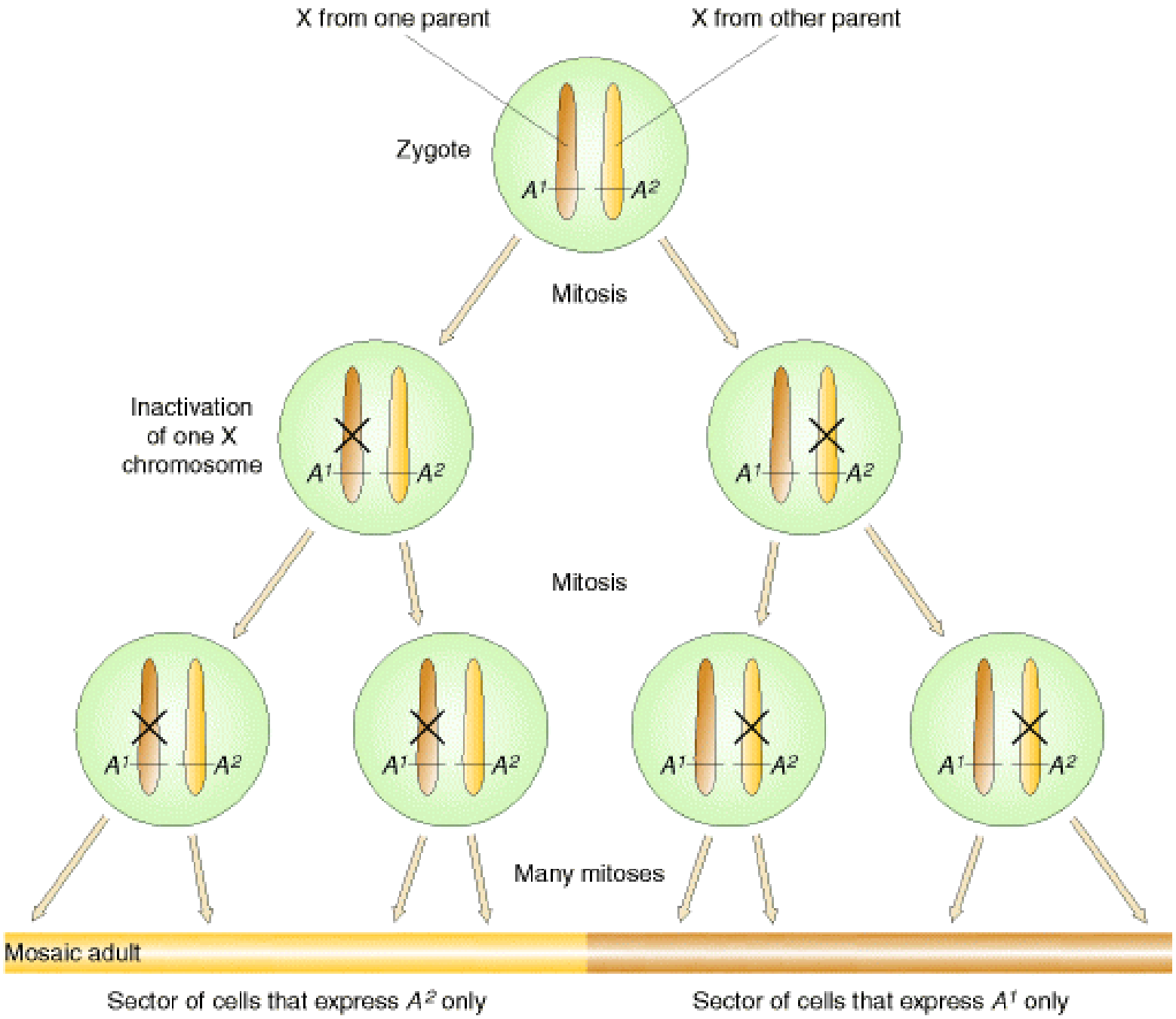

Nucleus
Cytoplasm
Barr body
46, X Y
45, X
(N – 1 = 0)
46, X X
47, X XY
(N – 1 = 1)
47, X X X
48, X X XY
(N – 1 = 2)
48, X X X X
49, X X X XY
(N – 1 = 3)

Lyon Hypothesis (Lyon 假说) (1961)

◇**The inactivation of X chromosomes occurs randomly in somatic cells at a point early in embryonic development (in human, 16d, about 5000~6000 cells)**

◇**Once inactivation has occurred, all progeny cells have the same X chromosome inactivated.**

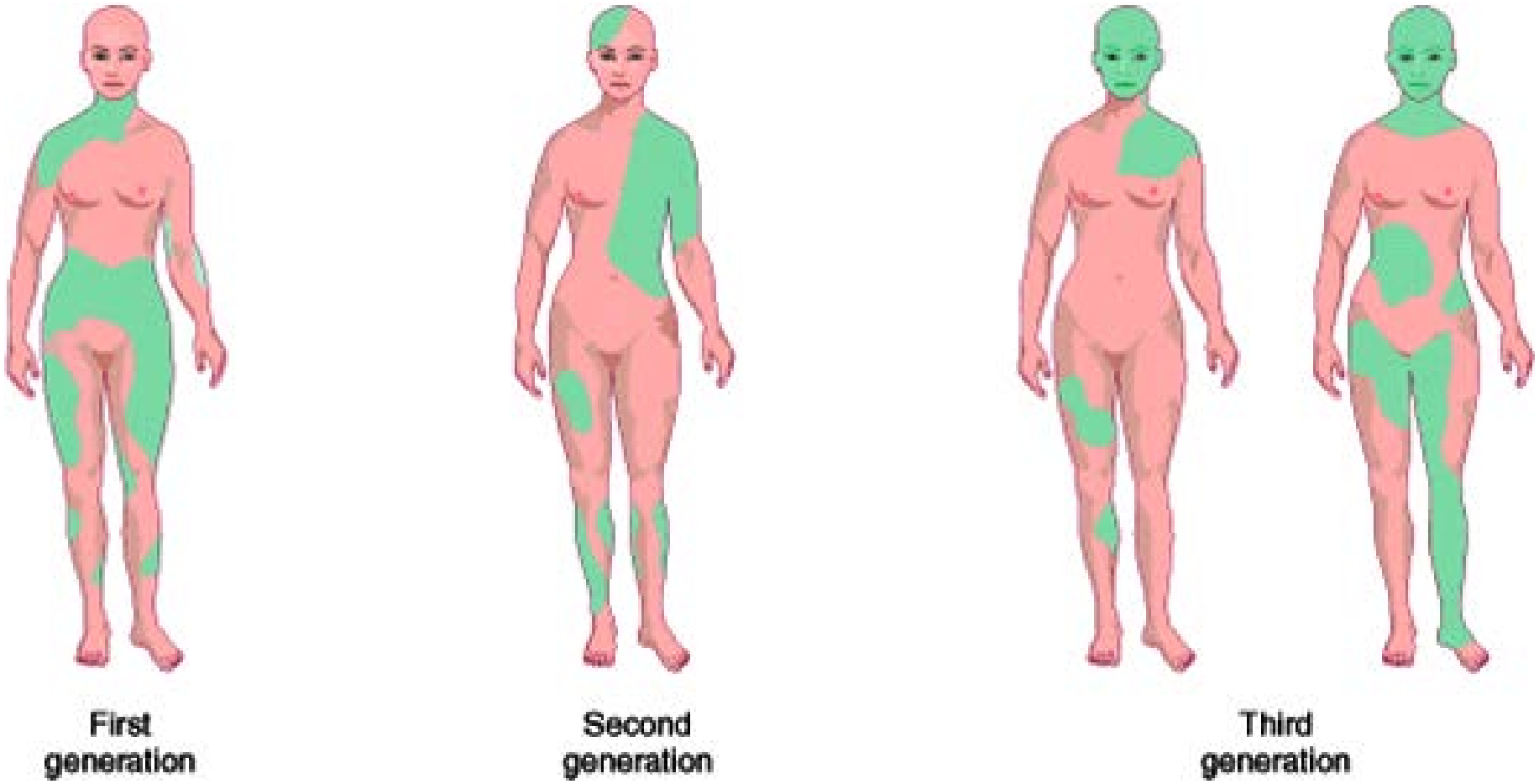
◇**The inactivated X chromosome is re-activated during the formation of germ-line cells**


X from one parent
X from other parent
Zygote
A1
A2
Mitosis
Inactivation of one X chromosome
Mitosis
Many mitoses
Mosaic adult
Sector of cells that express A2 only
Sector of cells that express A1 only

(a)

(b)

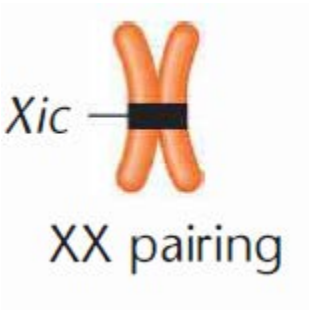
如果发现一只玳瑁雄猫，可能是什么原因？



Anhidrotic ectodermal displasia 无汗性外胚层发育不良

The Mechanism of Inactivation

- **哺乳动物X染色体失活过程**
  - 印记失活，随机失活
- **X染色体随机失活机制**
  - **Xic** (X-chromosome inactivation center)
    - ***Xist***, *Tsix*, *Jpx*, *Xite* → Non-coding RNA
  - *Xist* RNA包裹X染色体, DNA甲基化和组蛋白修饰随即发生
  - 失活逃逸（15%）



Jeannie T. Lee

第二节　连锁与交换
Linkage and Crossing over

I. The discovery of linkage

Bateson-Punnet: Sweet Pea (1906)

Flower color: purple and red

Shape of pollen grains: long and round

P: purple/long × red/round

↓

F1: purple/long

↓

F2:	purple/long	purple/round	red/long	red/round
	4831	**390**	**393**	**1338**

Chi square test

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

O：observed　E：expected

	purple/long	purple/round	red/long	red/round
observed	4831	390	393	1338
expected	3910.5	1303.5	1303.5	434.5

$$\chi^2 = \frac{(4831-3910.5)^2}{3910.5} + \frac{(390-1303.5)^2}{1303.5} + \frac{(393-1303.5)^2}{1303.5}$$

$$+ \frac{(1338-434.5)^2}{434.5}$$

$$= 3371.58$$

Chi square values

Table 4.1 Critical Chi Square Values

Degrees of Freedom	*P* values						
	Null Hypothesis Accepted				Null Hypothesis Rejected		
	0.99	0.90	0.50	0.10	0.05	0.01	0.001
	x^2 calculations						
1	—	0.02	.45	2.71	3.84	6.64	10.83
2	0.02	0.21	1.39	4.61	5.99	9.21	13.82
3	0.11	0.58	2.37	6.25	7.81	11.35	16.27
4	0.30	1.06	3.36	7.78	9.49	13.28	18.47
5	0.55	1.61	4.35	9.24	11.07	15.09	20.52

$$d_f = \mathrm{n} - 1 = 3$$

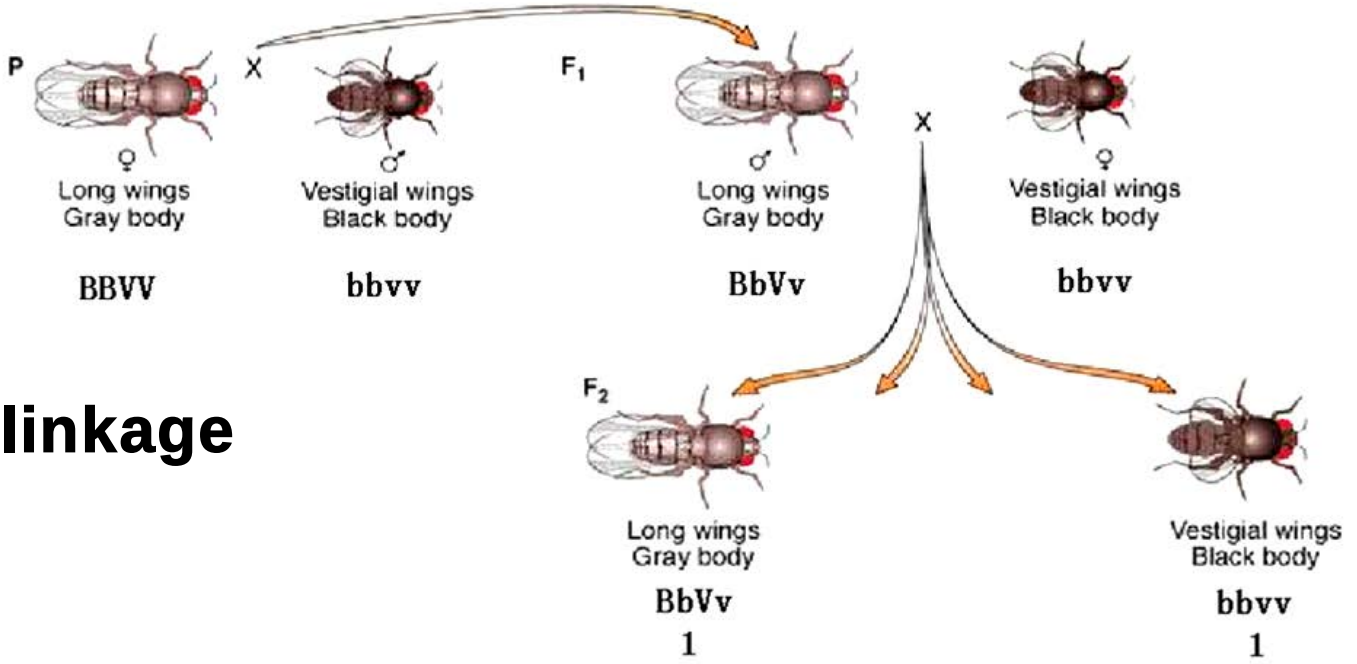
显著性标准

- P>0.05　结果与理论数无显著差异
- P<0.05　结果与理论数有显著差异
- P<0.01　结果与理论数有极显著差异

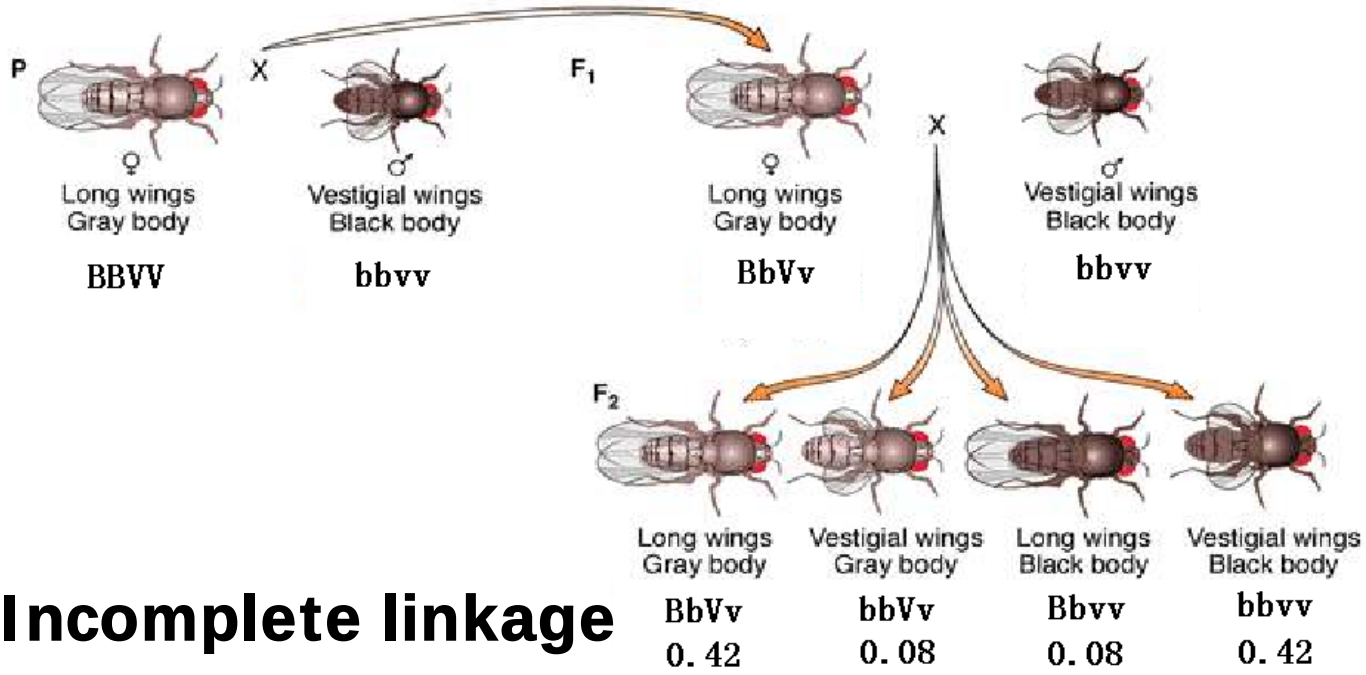
X^2= 3371.58　　P<<0.01

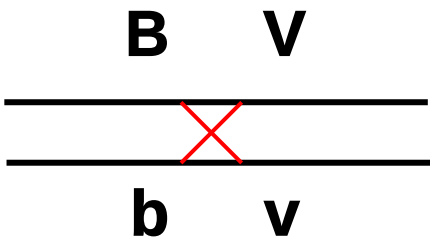
说明实验结果不符合自由组合定律

T.H.Morgan's Experiment



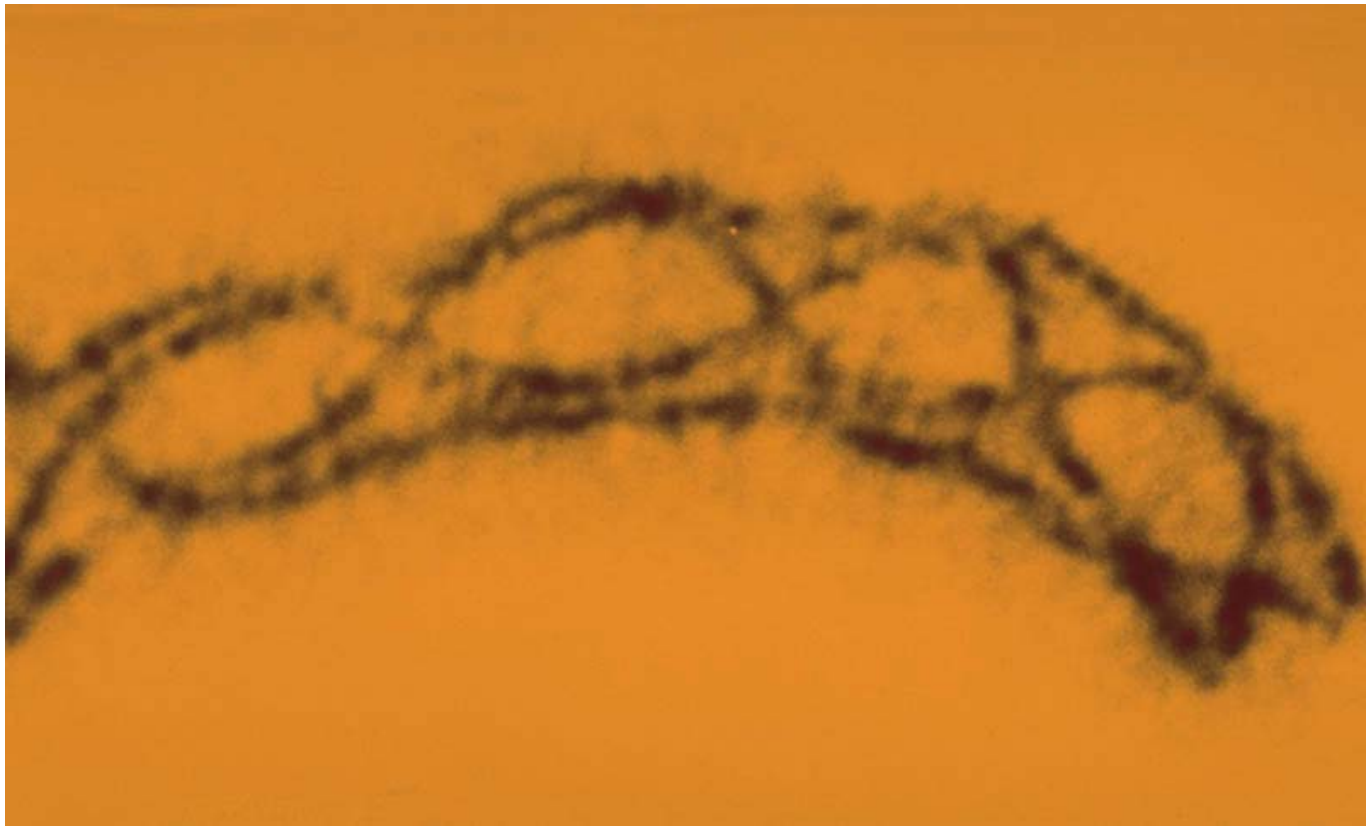
Complete linkage





Incomplete linkage

II. Crossing over as the physical basis of recombination



Chiasmata are the sites of crossing over

减数分裂 I 前期 5个阶段
（示非姊妹染色单体间的交换）

Leptonema

- Chromosomes are already duplicated.
- Synaptinemal complex begins to appear.

Zygonema

- Pairing is initiated.
- Synaptinemal complex develops more fully.

Pachynema

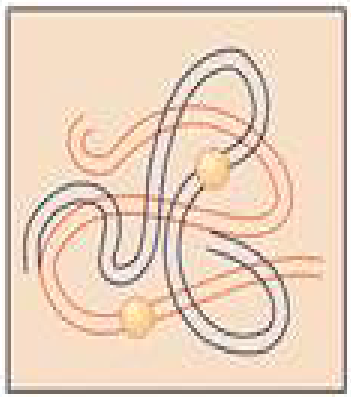
- Pairing is completed.
- Chromosomes thicken.
- Crossing over occurs.
- Chromosome bouquet forms.

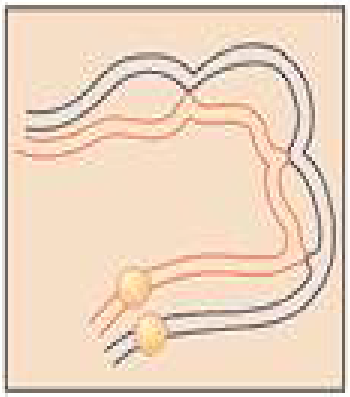
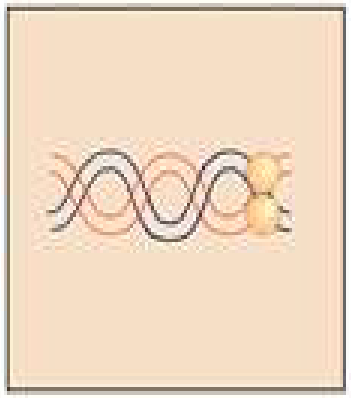
Diplonema

- Repulsion between homologs begins.
- Chiasmata are clearly visible.
- Chromosomes are held together at chiasmata and centromere.

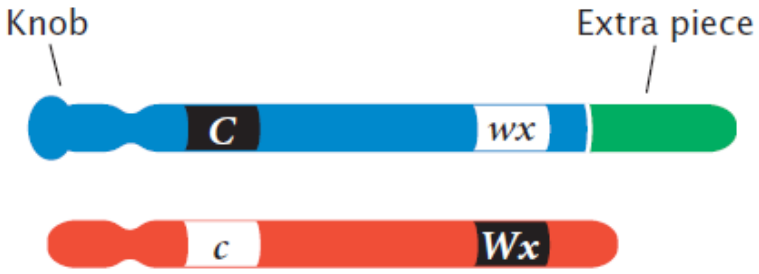
Diakinesis

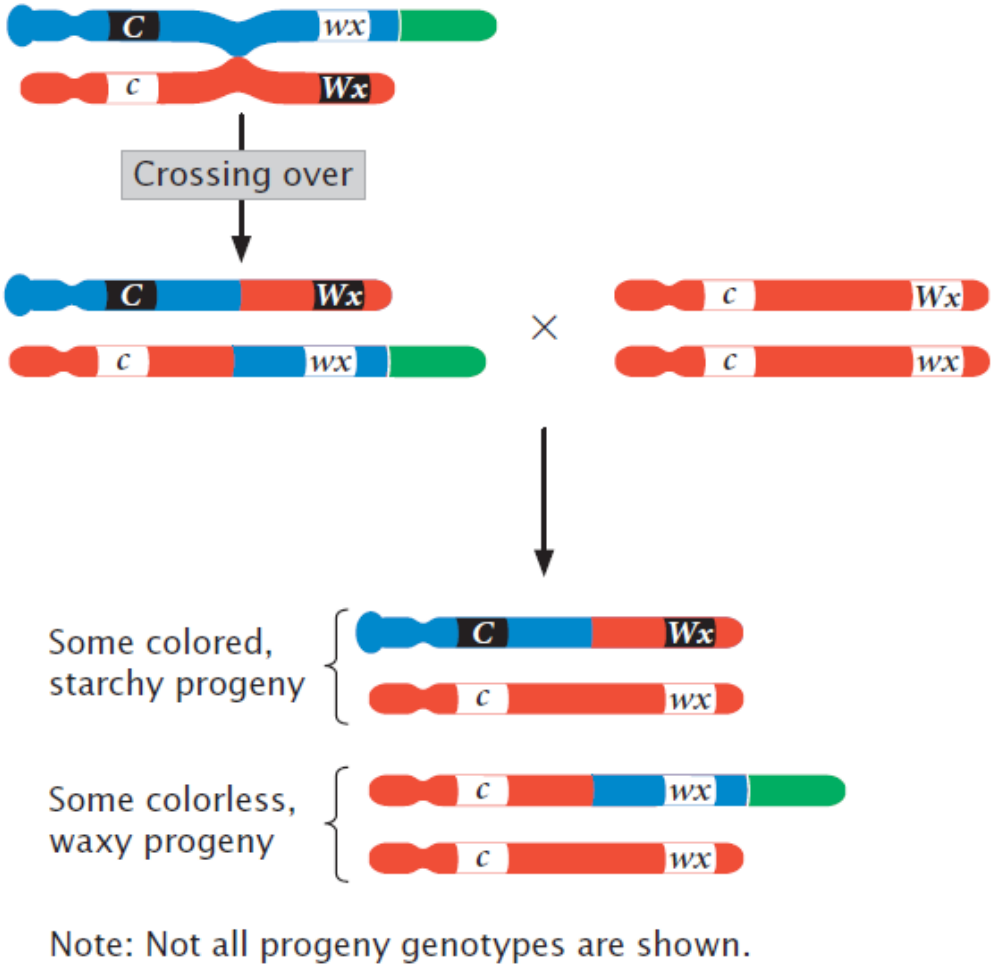
- Maximum chromosome thickening occurs.
- Chiasmata disappear.
- Chromosomes move to equatorial plane.




Evidence that crossing over causes recombination

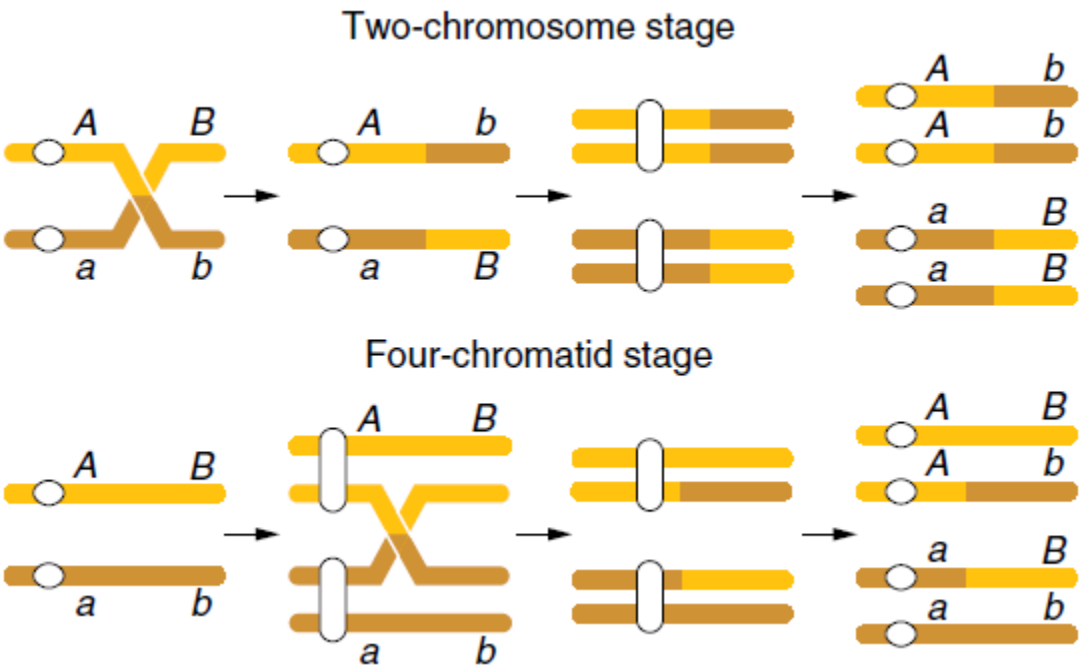




C: colored kernels
c: colorless kernels

Wx: starchy kernels
wx: waxy kernels

Evidence that crossing-over occurs at the four-chromatid stage



A B × a b

A B

A b

a B

a b

Multiple crossovers can involve more than two chromatids

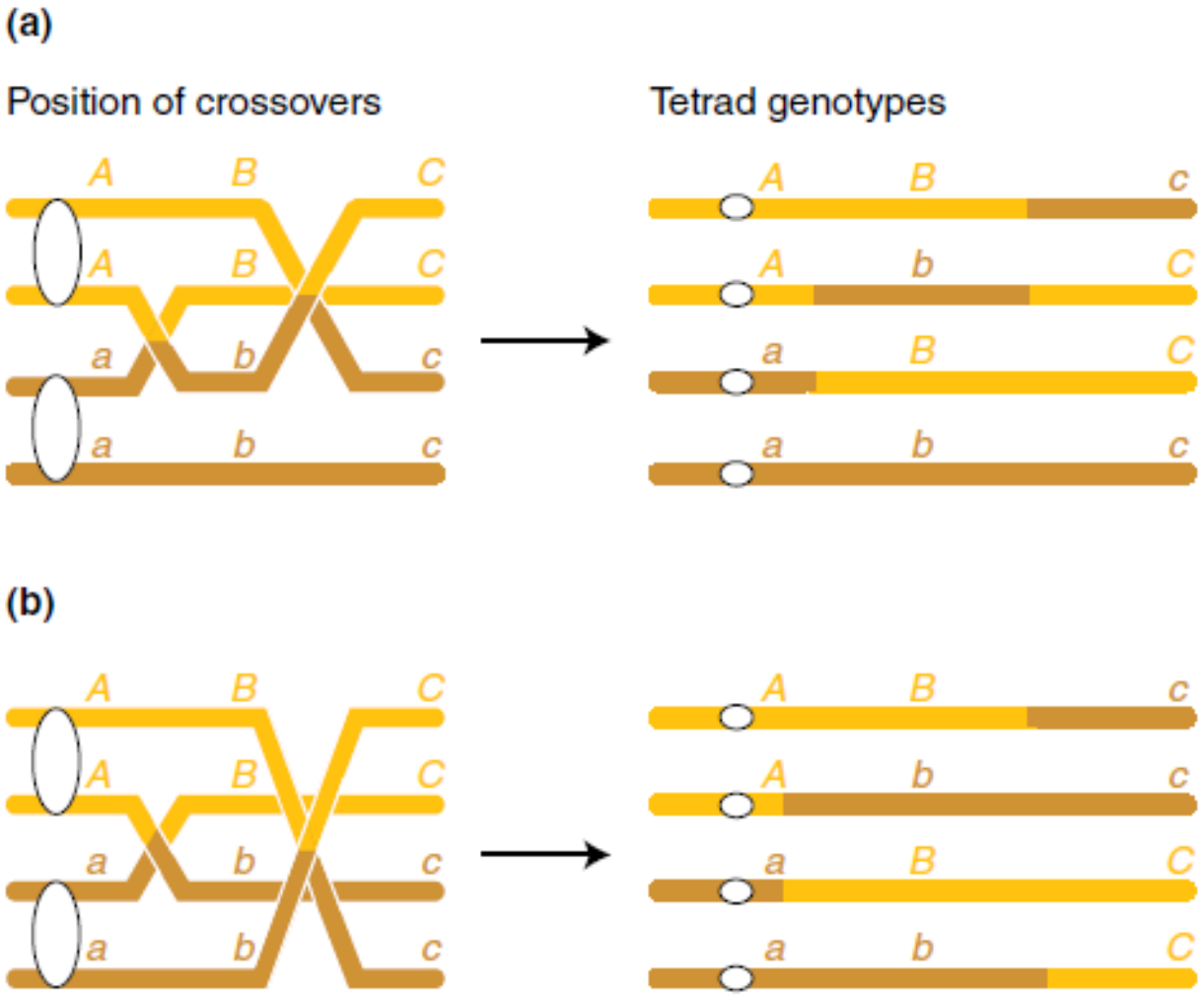
A B C × a b c

A B c

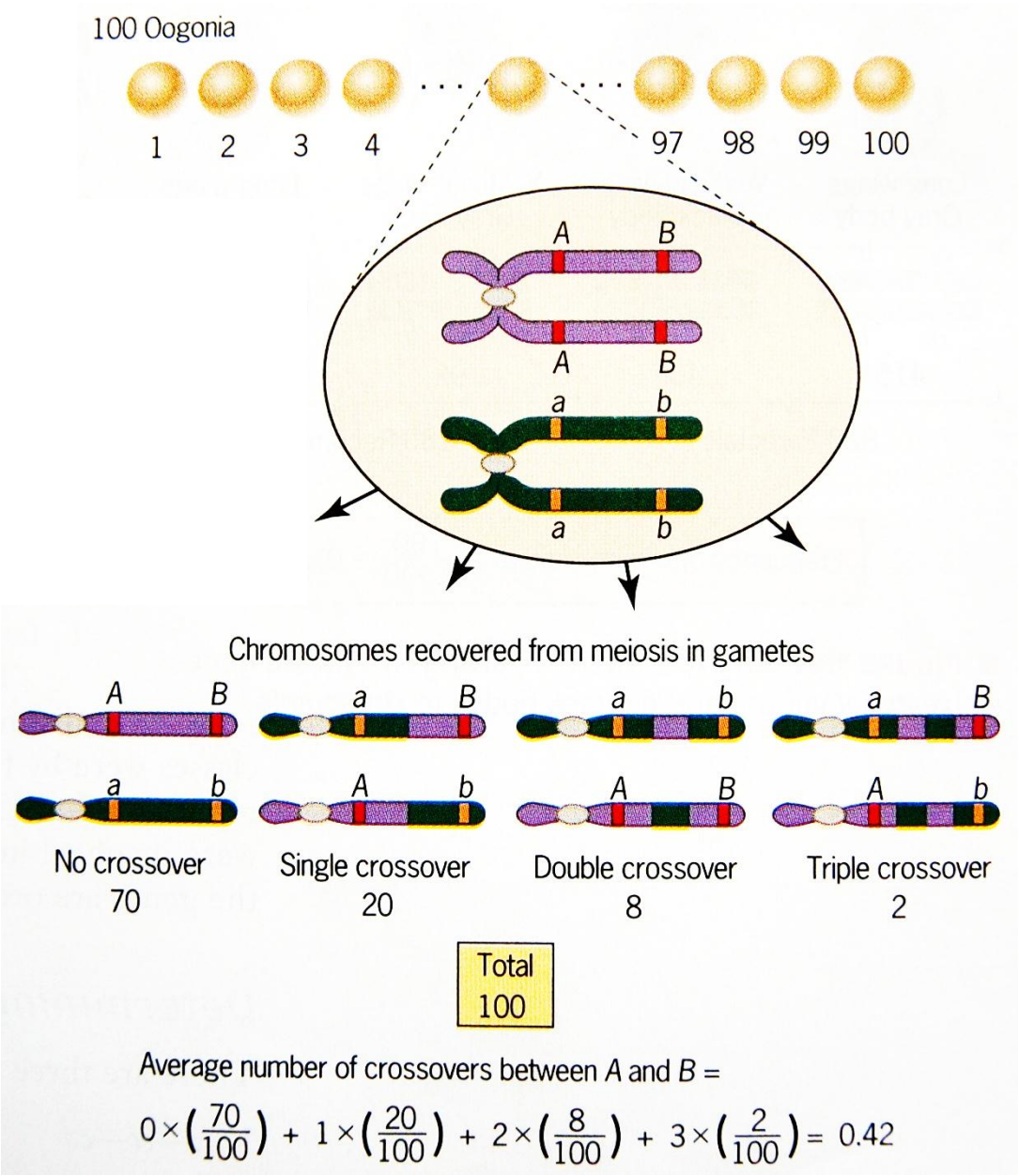
A b c

a B C

a b C

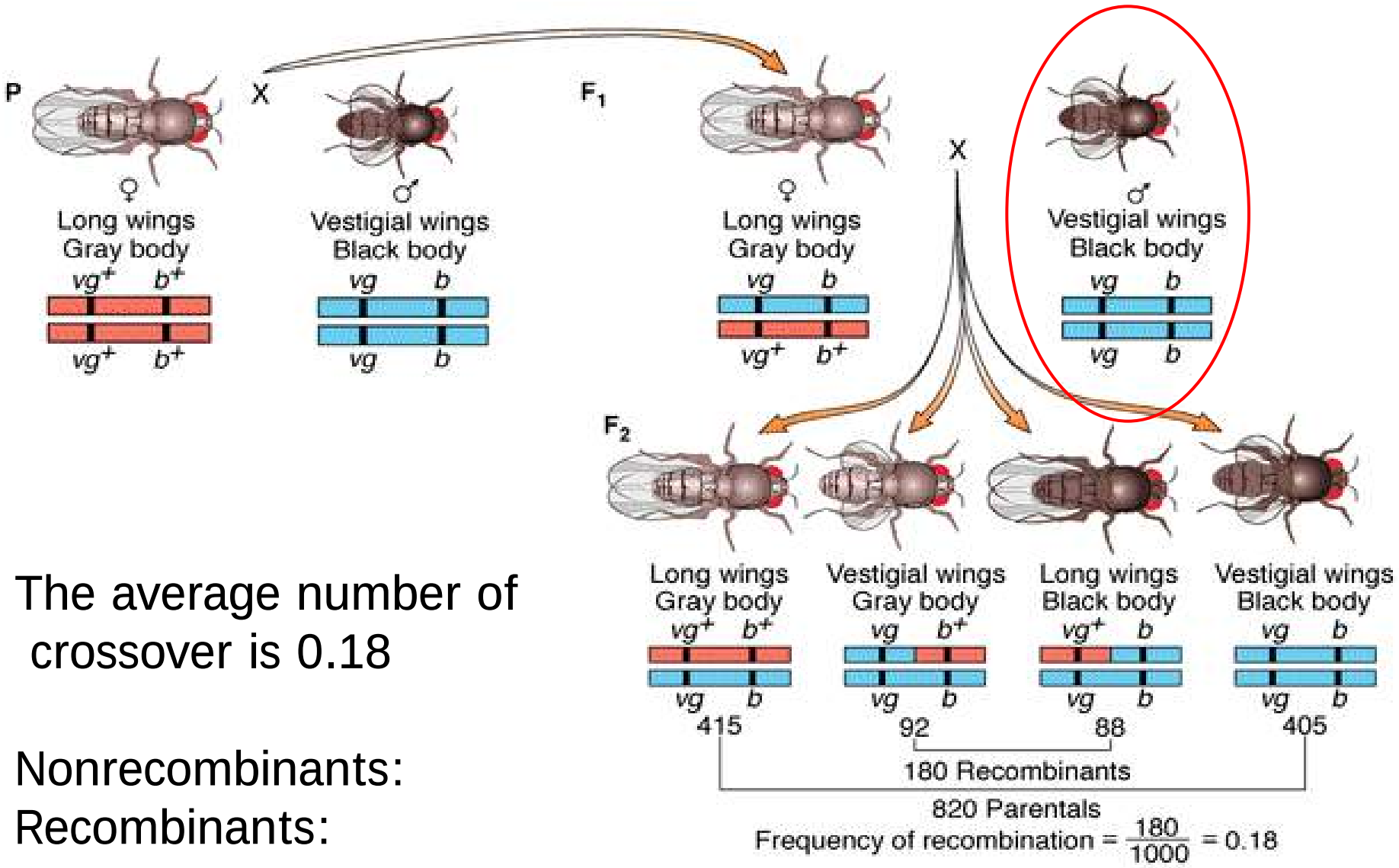


Crossing over as a measure of genetic distance



The distance between two points on the genetic map of a chromosome is the average number of crossovers between them

However, we cannot "**see**" each of the chromosomes coming out of meiosis



The average number of crossover is 0.18

Nonrecombinants:

Recombinants:

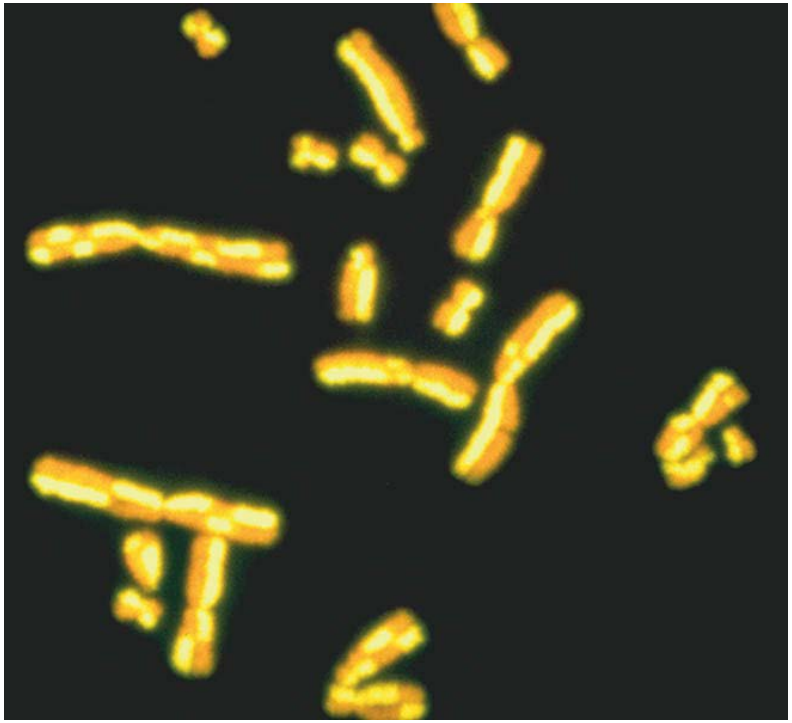
- **Map distance**（图距）

Map distance is equal to **the frequency of recombination**

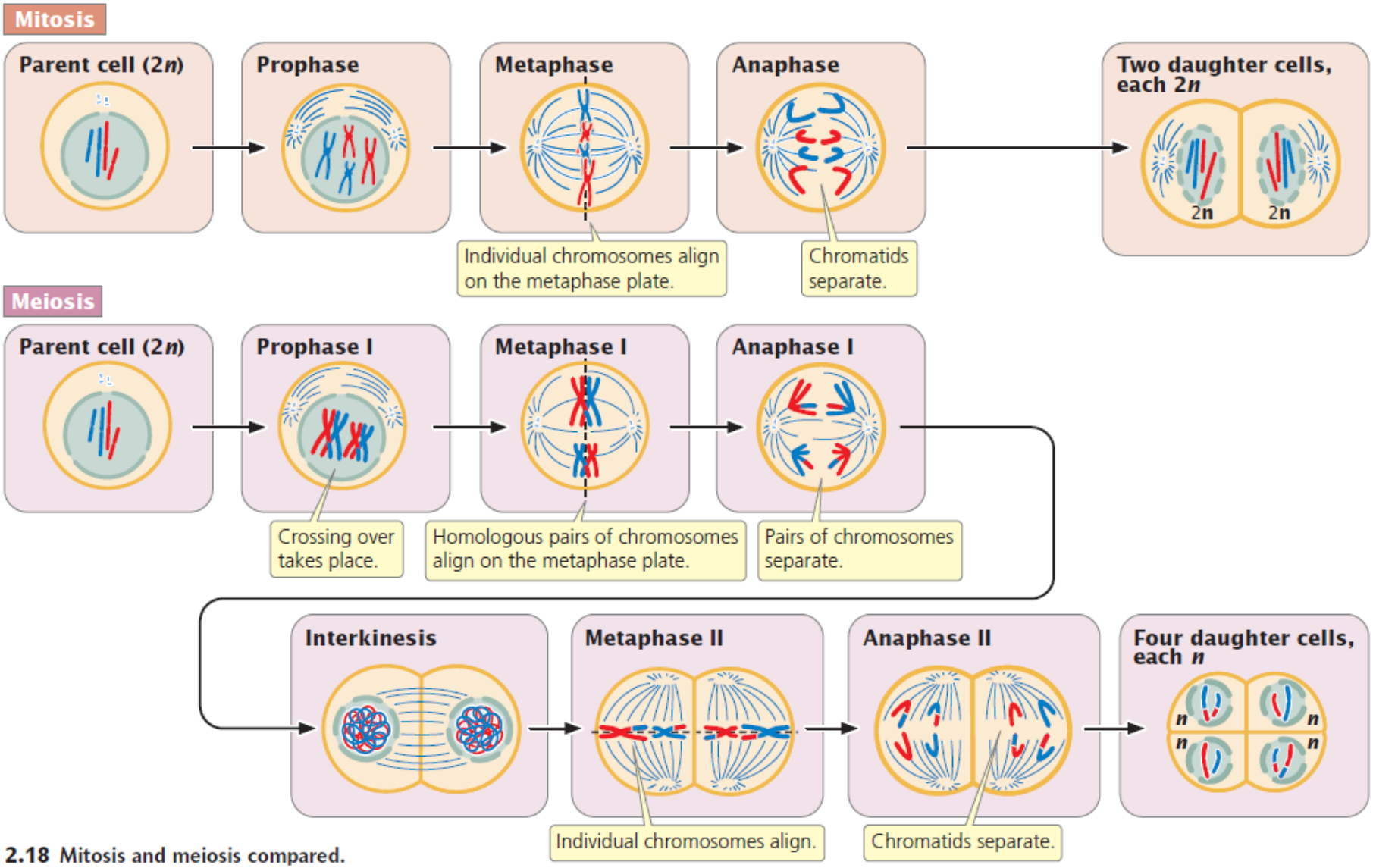
In honor of T.H.Morgan，map unit is called **centiMorgan**（**cM**）

Exchanges also occur between sister chromatids

- Sister chromatic exchanges (SCEs)
  - Do not produce new allelic combinations
- The significance of SCEs is still uncertain



Does crossing over occur in mitosis?

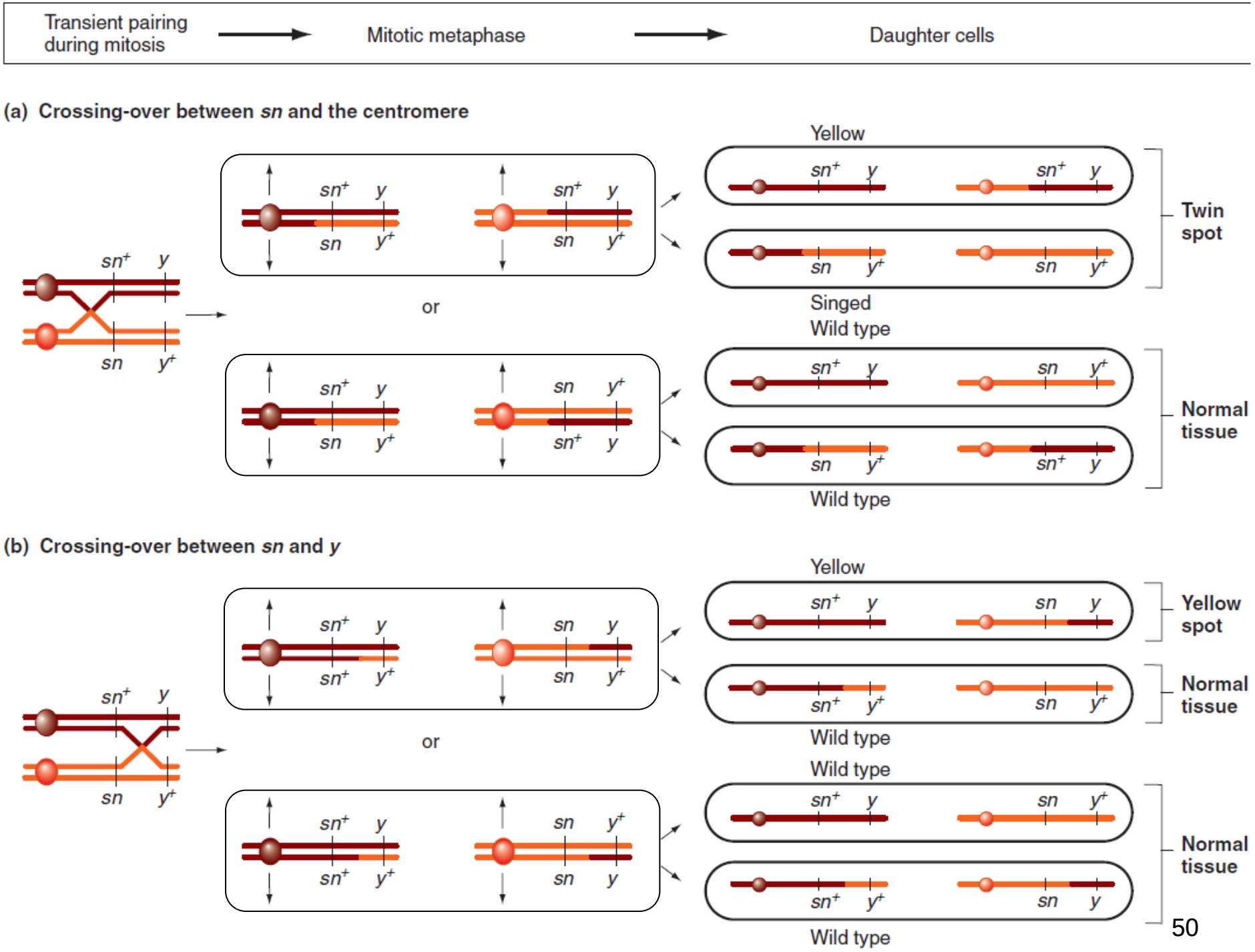


2.18 Mitosis and meiosis compared.

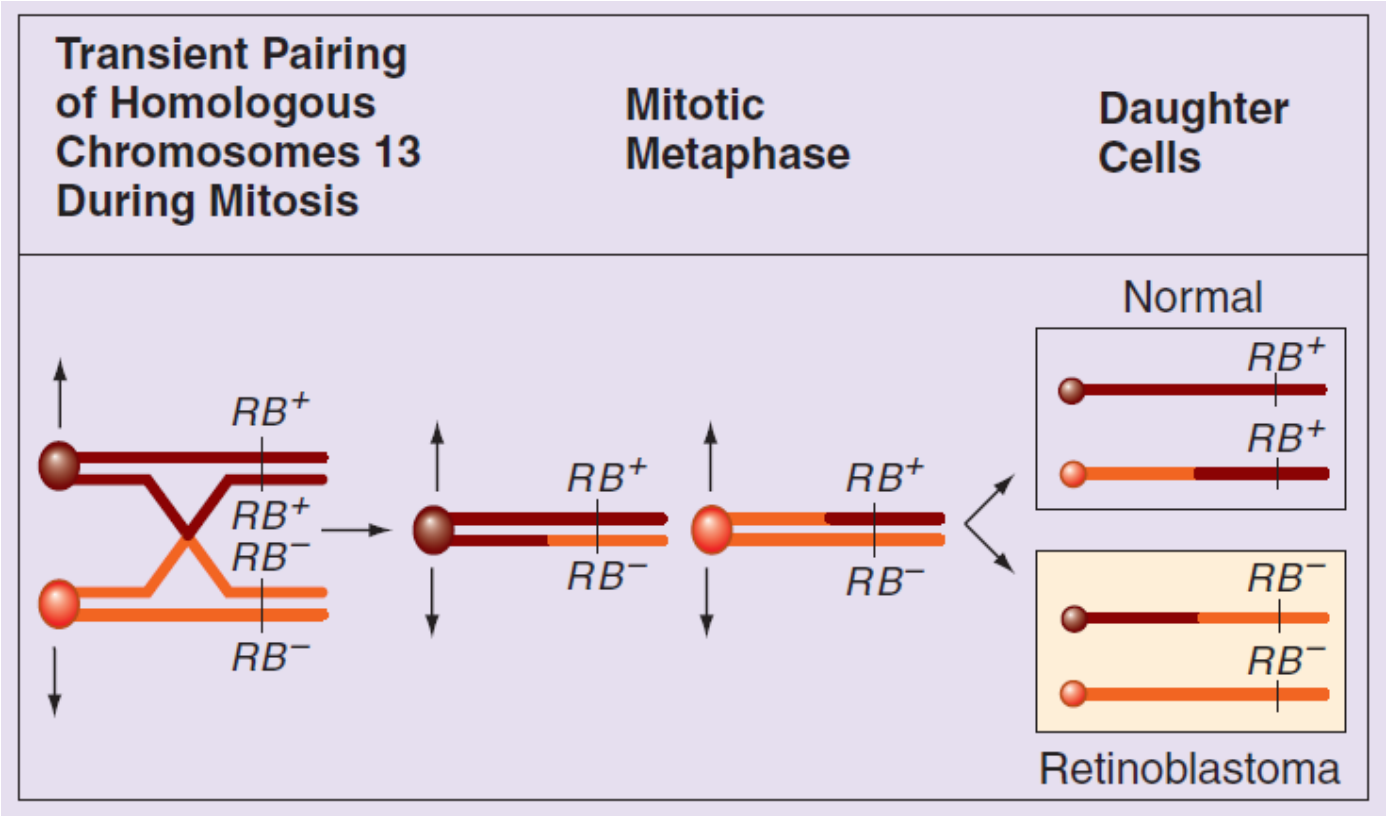
Crossing over occurs between mitotic chromosomes

y+/+sn ♀

Single yellow spot | Twin spot | Single singed spot


Transient pairing during mitosis
Mitotic metaphase
Daughter cells
(a) Crossing-over between sn and the centromere
Yellow
Singed
Wild type
Twin spot
or
Wild type
Normal tissue
(b) Crossing-over between sn and y
Yellow
Yellow spot
Normal tissue
or
Wild type
Wild type
Normal tissue
Wild type

The retinoblastoma gene (RB) encodes a protein that regulates retinal growth and differentiation, and is known as a tumor-suppressor gene.
Cells in the eye need at least one copy of the normal wild-type allele to maintain control over cell division.



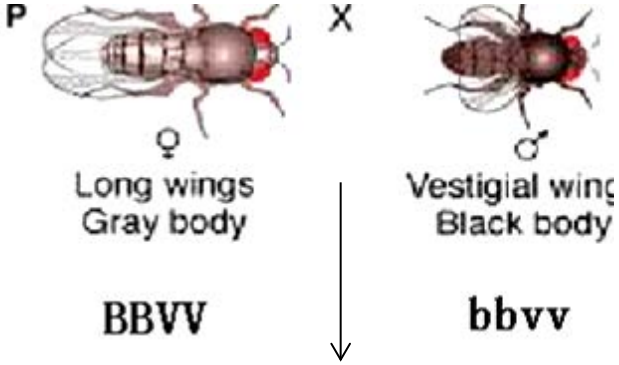
RB^+/RB^-: incomplete penetrance and variable expressivity

Factors influence crossing over

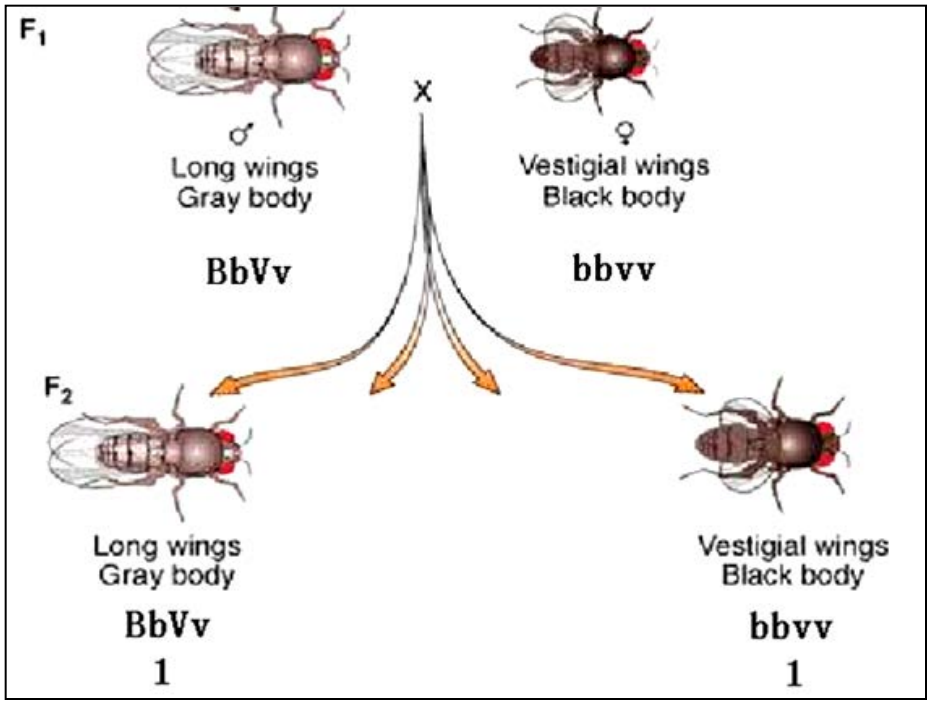
- Distance between two genes
- Environments: temperature, radiation, chemical mutagens...
- Locations on the chromosome
- **Sex differences**

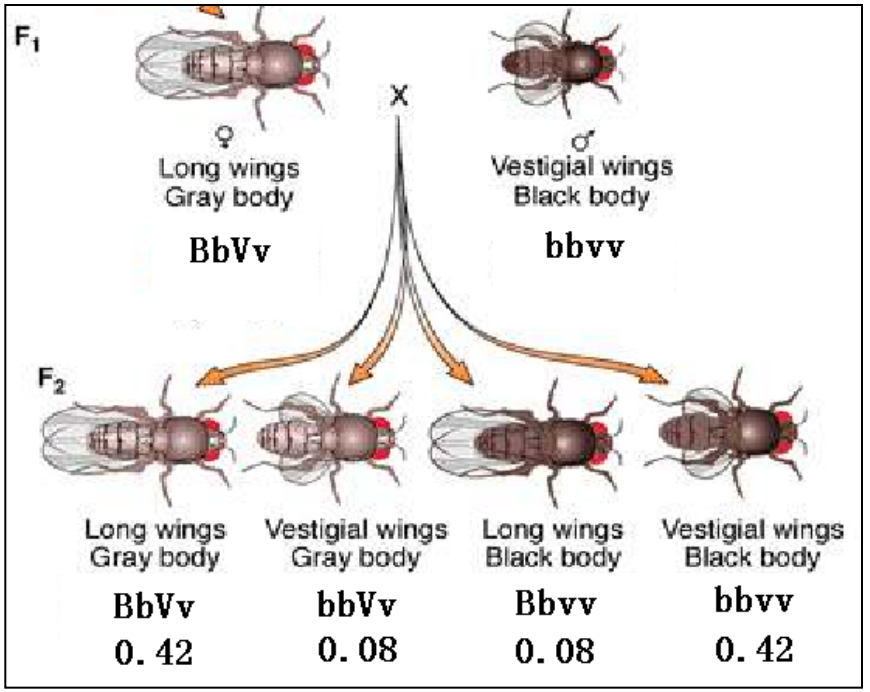
Haldane's (1922) **rule** that crossing-over is reduced or prevented in the heterogametic sex.

Drosophila

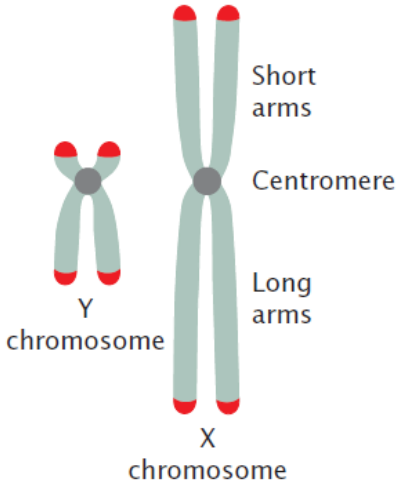

P
X
♀
♂
Long wings
Gray body
Vestigial wing
Black body
BBVV
bbvv

F1


F1
X
♂
♀
Long wings
Gray body
Vestigial wings
Black body
BbVv
bbvv
F2
Long wings
Gray body
BbVv
1
Vestigial wings
Black body
bbvv
1

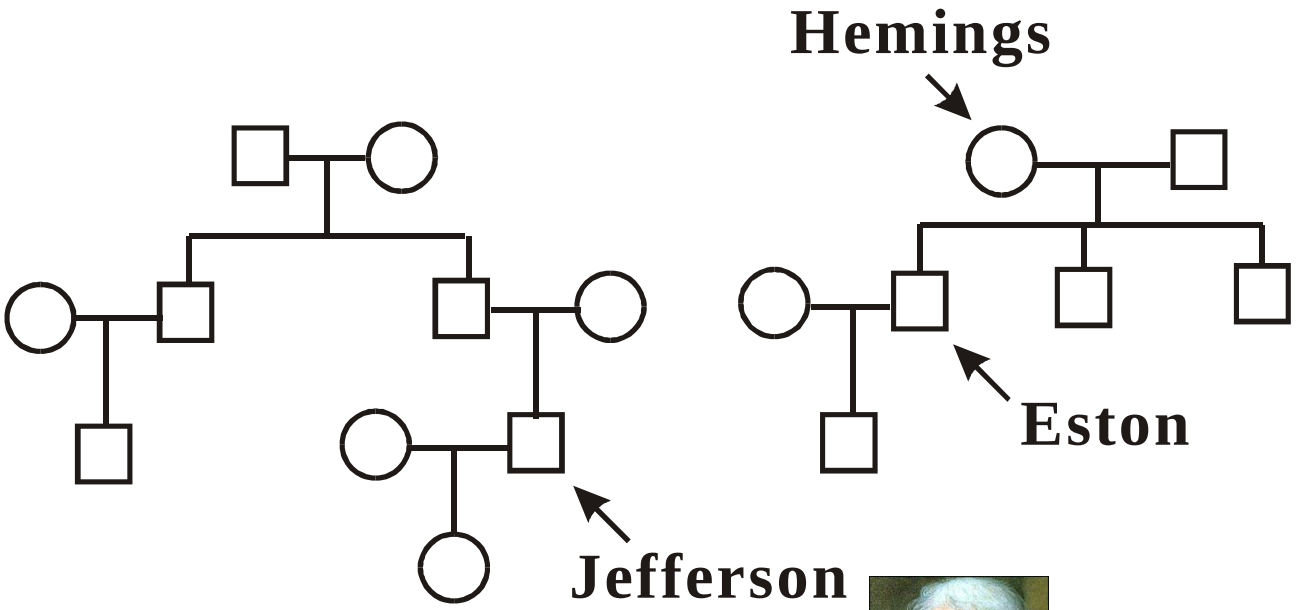

F1
X
♀
♂
Long wings
Gray body
Vestigial wings
Black body
BbVv
bbvv
F2
Long wings
Gray body
BbVv
0. 42
Vestigial wings
Gray body
bbVv
0. 08
Long wings
Black body
Bbvv
0. 08
Vestigial wings
Black body
bbvv
0. 42

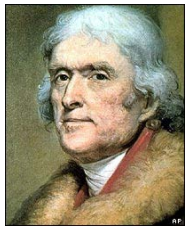
Y染色体很少发生交换



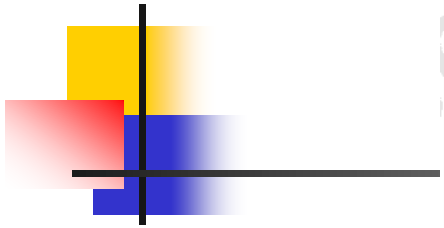
Meiosis：

- Autosomes and X chromosome
- Y chromosome



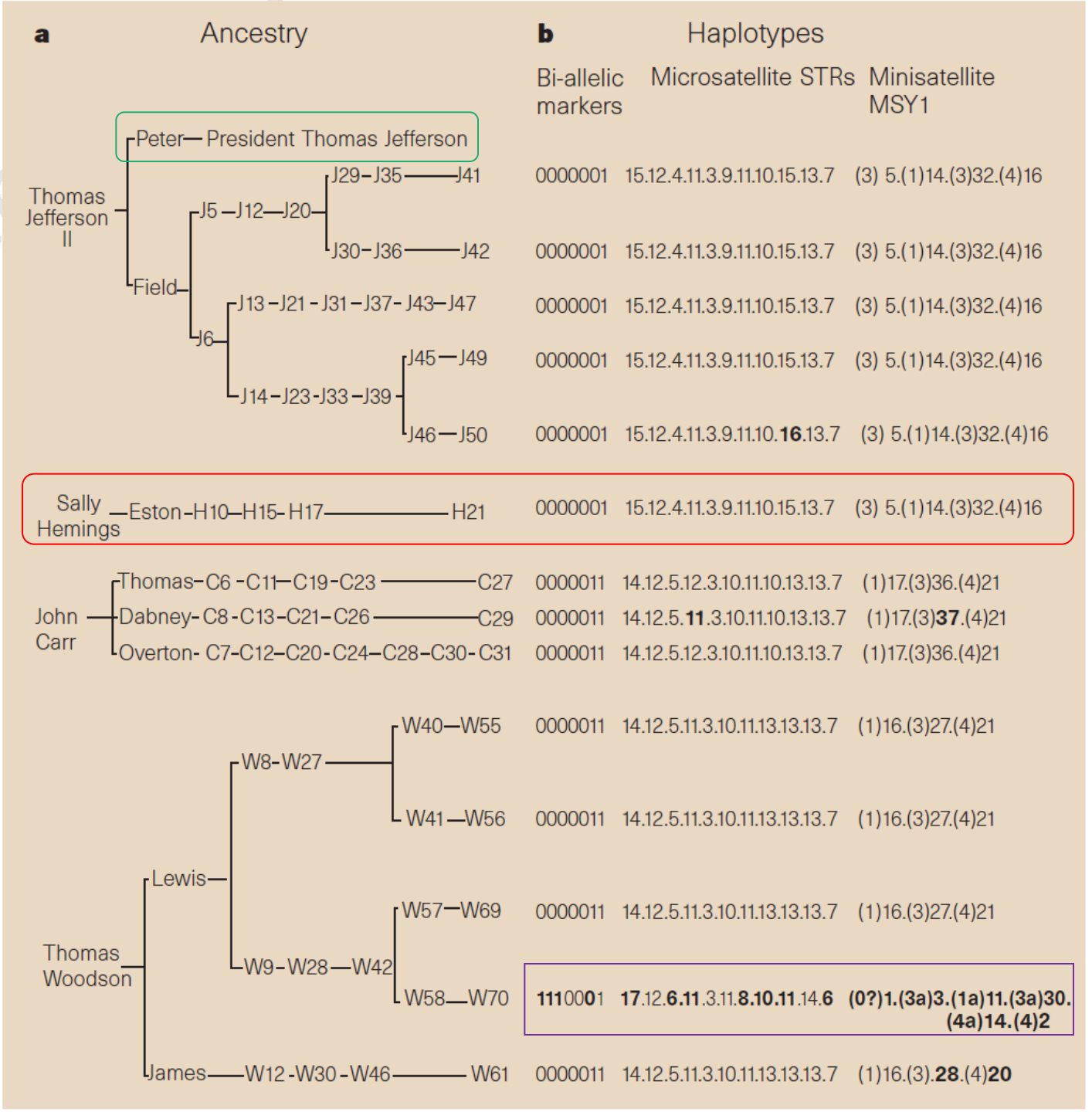


"Founding father"
"Jefferson fathered slave's last child"
***Nature* 396**, 13-14, 27-28 , 1998



Grandfather of Samuel and Peter Carr, two were sons of Jefferson's sister

The first son of Hemings



Out of Africa——走出非洲

African Origin of Modern Humans in East Asia: A Tale of 12,000 Y Chromosomes

Science 2001 Vol292(5519):1151

中美科学家的一项对东亚的163个人群(populations)的12,000多位男性的Y染色体标记的新研究，有力地证明了现代人(modern humans)起源的"走出非洲"假说。这个理论认为，一个起源于非洲的现代人的人群出现在大约十万年前，他们取代了全球的所有原始人(archaic humans)群体。Yeuhai Ke和同事们分析了从伊朗到新几内亚岛的不同个人的染色体，来寻找三个特殊的Y染色体突变，这些突变都源于非洲人群中的一个更早的突变。他们采样的所有12,127位男性都携带这三个突变中的一个。作者说，这些数据表明东亚的原始人群对该地区的现代人的起源没有贡献。

第三节　染色体作图
Chromosome Mapping

Chromosome maps calculated by using the genetic recombination are called **genetic maps**

Chromosome maps calculated by using physical distances along the chromosome (often expressed as numbers of base pairs) are called **physical maps**

一、两点测交(two-point testcross)

- 以两对基因为基本单位来计算重组频率，求得基因间的距离从而进行定位
- 二倍体生物中，以杂种F_1进行测交

- *Drosophila* X chromosome

白眼（**w**） 黄体（**y**） 粗脉翅（**bi**）

♀ ♂

w bi/+ + × w bi/**Y** bi-w: 5.3%

w y /+ + × w y /**Y** w-y: 1.1%

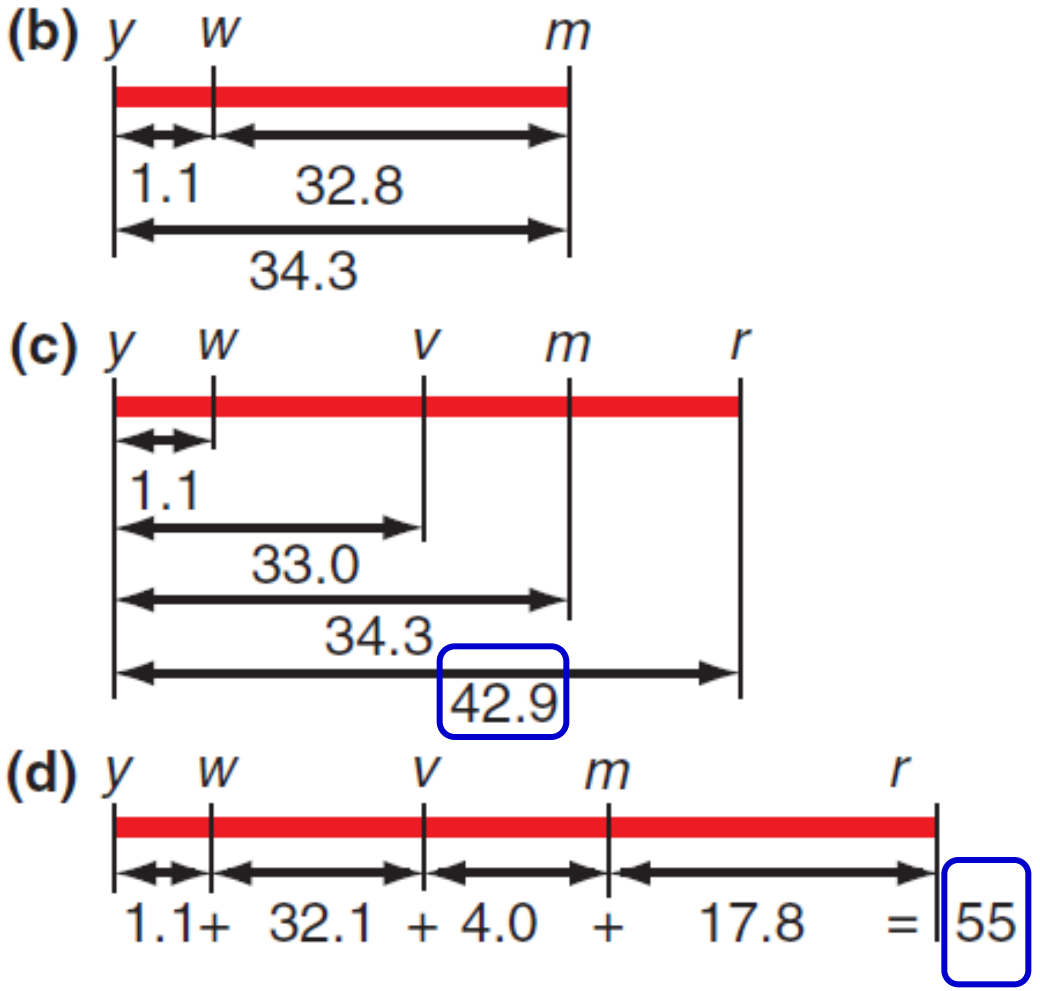
(1) w-y----bi (2) y-w-----bi

y bi/+ + × y bi/**Y** y-bi: 5.5%

y-w-----bi

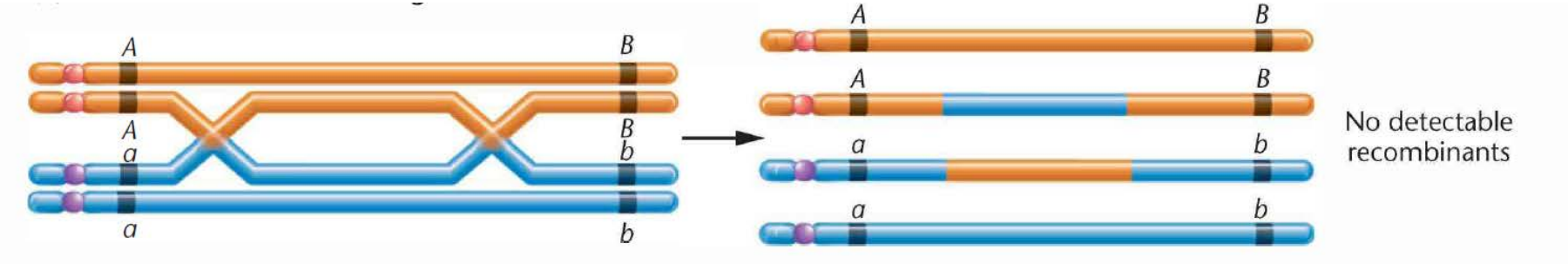
(a)

Gene pair	RF
y-*w*	1.1
y-*v*	33.0
y-*m*	34.3
y-*r*	42.9
w-*v*	32.1
w-*m*	32.8
w-*r*	42.1
v-*m*	4.0
v-*r*	24.1
m-*r*	17.8



Two-point crosses have their **limitations**

- The actual distances between genes do not always add up
  - The **double crossover** is overlooked



The distance between two points on the genetic map of a chromosome is **the average number of crossovers** between them

- Difficult to determine gene order if some genes lie very close together

二、三点测交（three-point testcross）

- 定义：根据同一染色体上三个非等位基因间的交换行为测定它们之间排列顺序的杂交试验。**1913**年由**Morgan**的学生**Sturtevant**首创。一般用三杂合体与三隐性个体进行测交
- 优点：通过一次杂交(测交)确定相关三个基因在染色体上的位置和顺序；可测出双交换值
- 以果蝇**X**染色体上的三个基因，黄体（**y**）、白眼（**w**）和棘眼（**ec**）为例

ec ct + / + + cv × ec ct cv / Y

表型			个体数目
ec	ct	+	2125
+	+	cv	2207
ec	+	cv	273
+	ct	+	265
ec	+	+	217
+	ct	cv	223
+	+	+	5
ec	ct	cv	3

合计 5318

- 计算**ct-cv**的重组值

  RF(ct-cv)

=(217+223+5+3)/5318

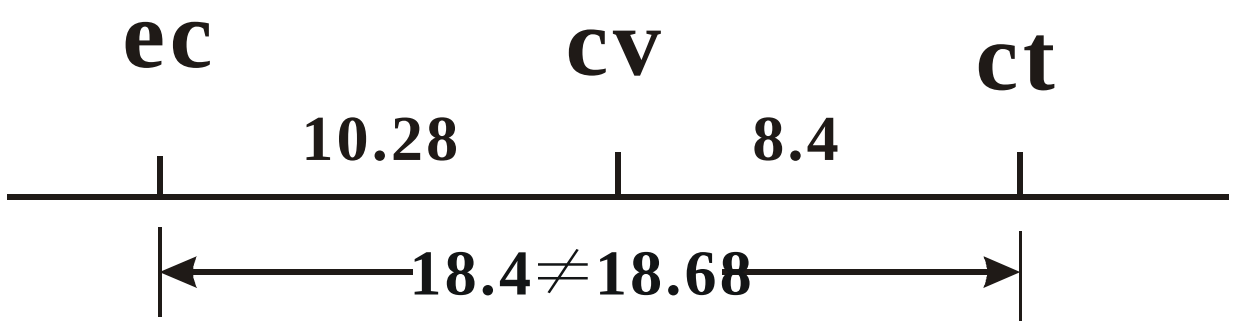
=8.4%

- 计算**ec-cv**的重组值

  RF(cv-cv)=10.28%

- 计算**ec-ct**的重组值

  RF(ec-ct)=18.4%



亲本

ec	cv	ct	3	ec	+	ct
+	+	+	5	+	cv	+

18.4%+2×(5+3)/5318=18.7%

三点测交结果总结

表型			实得数	比例	重组发生在		
					ec-cv	cv-ct	ec-ct
ec	+	ct	2125	81.5%			
+	cv	+	2207				
ec	cv	+	273	10.1%	√		√
+	+	ct	265				
ec	+	+	217	8.3%		√	√
+	cv	ct	223				
+	+	+	5	0.1%	√	√	
ec	cv	ct	3				
总计			5318	1	10.2%	8.4%	18.4%

Deducing Gene Order

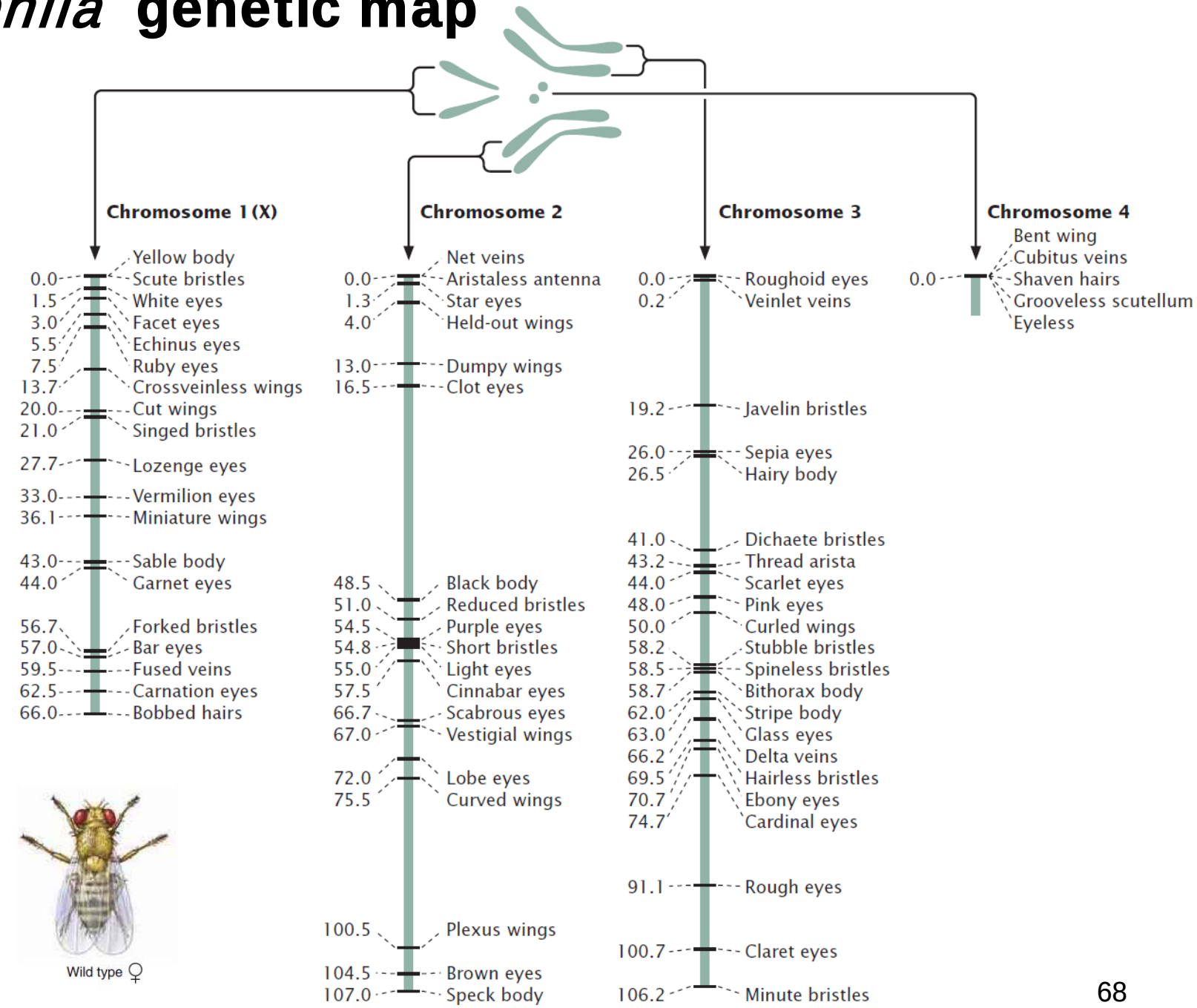
- 当三点测交出现8种表型时，数目最少的两类一定是双交换型。用双交换型与亲本型比较，位置发生改变的那个基因一定位于中间
- 当三点测交出现8种表型时，表明末端两个基因之间必定有双交换发生，因此其重组值需要用两倍双交换值作校正
- 若相距较近的3个基因的三点测交，往往不出现双交换类型，测交后代只有6种表型，无需校正

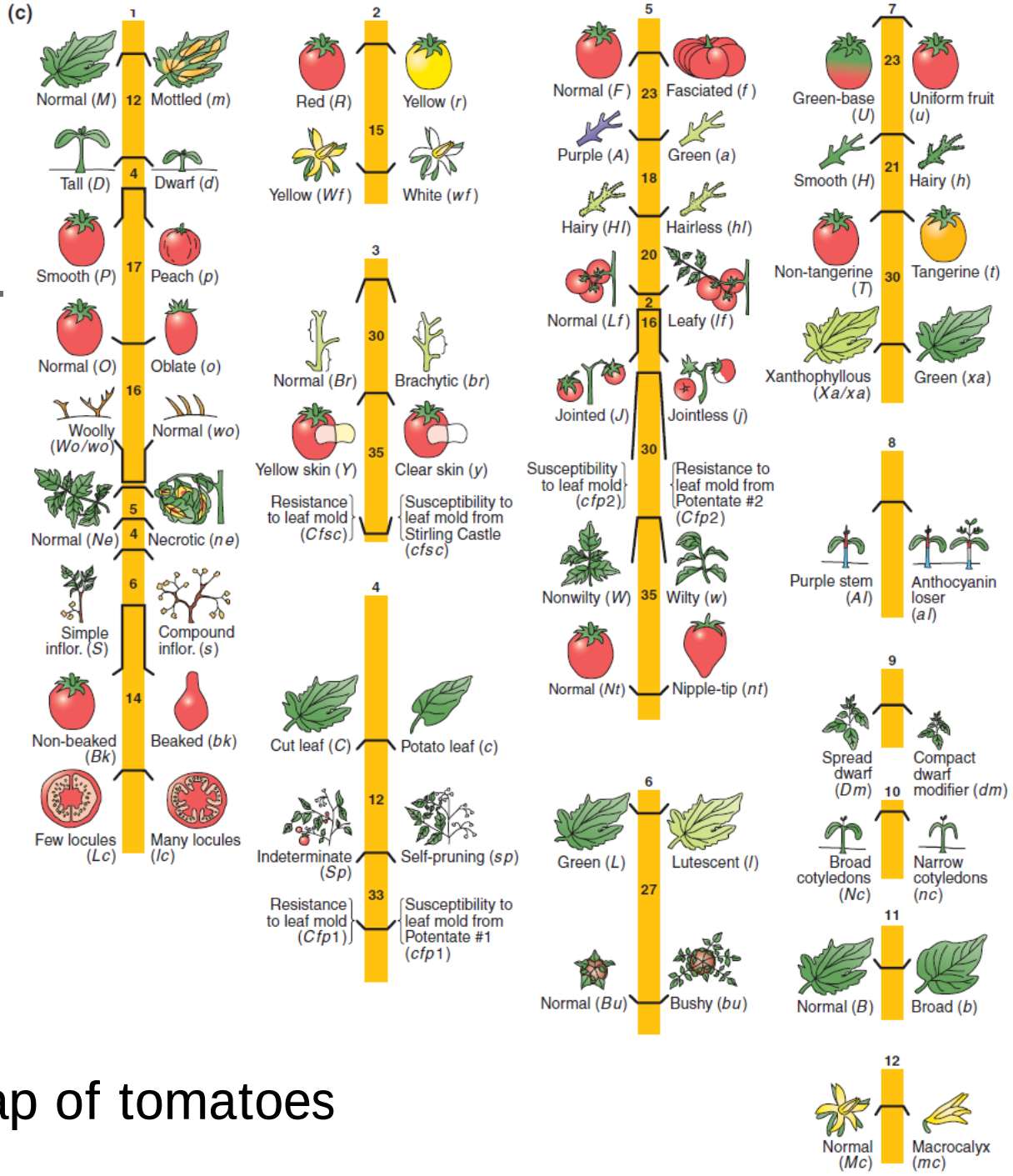
♀ + *v bm* / *pr* + + × ♂ *pr v bm* / *pr v bm*

♀ *pr v bm* / *pr v bm* × ♂ + *v bm* / *pr* + +

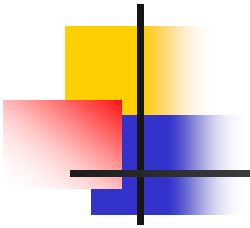
Phenotypes of offspring			Number	Total and percentage	Exchange classification
+	*v*	*bm*	230	467 42.1%	Noncrossover (NCO)
pr	+	+	237		
+	+	*bm*	82	161 14.5%	Single crossover (SCO)
pr	*v*	+	79		
+	*v*	+	200	395 35.6%	Single crossover (SCO)
pr	+	*bm*	195		
pr	*v*	*bm*	44	86 7.8%	Double crossover (DCO)
+	+	+	42		

Drosophila genetic map





1952 genetic map of tomatoes



Emphasize :

- Two genes that are far apart on the same chromosome tends to underestimate the true physical distance
- If genes exhibit 50% recombination, they are on different chromosomes or far apart on the same chromosome
- Recombination frequencies between two genes never exceed 50%

三、干涉（Interference，I）与并发系数(Coefficient of coincidence，C)

$DCO_{expected}=0.1028\times0.084=0.86\%$

$DCO_{observed}=(3+5)/5318=0.15\%$

Coefficient of coincidence, C

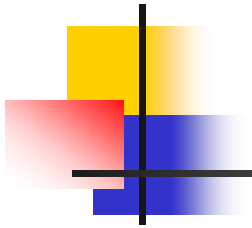
- The ratio of observed to expected double recombinants

$$\text{Coefficient of coincidence} = \frac{\text{frequency observed}}{\text{frequency expected}}$$

Interference, I

- The inhibition of further crossover events by a crossover event in a nearby region of the chromosome, cause this reduction.

- $I = 1 - C = 1 - \dfrac{\text{frequency observed}}{\text{frequency expected}}$

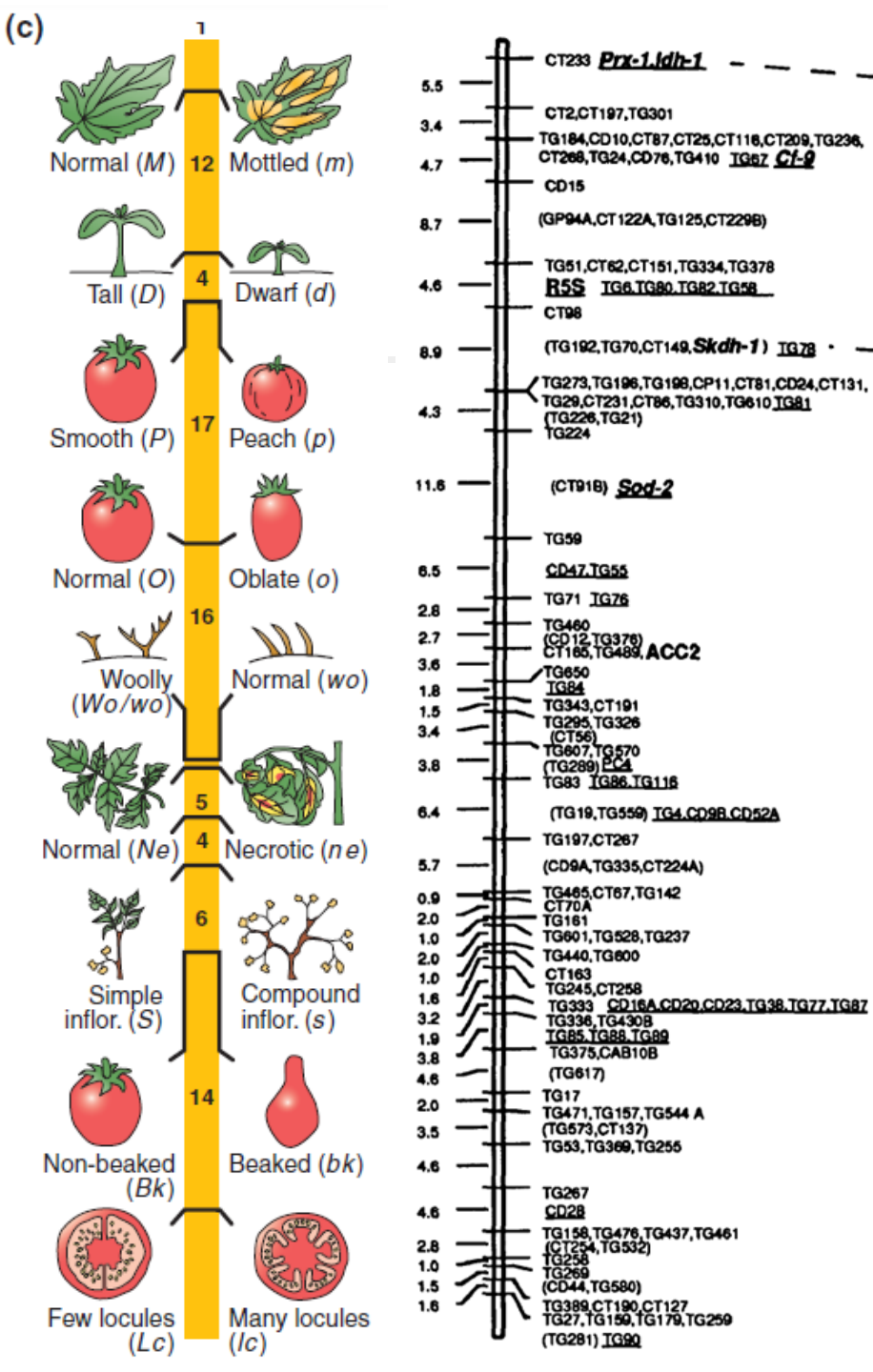


- 正干涉(positive interference)：一个单交换的发生减少另一个单交换发生的概率，此时实际双交换值<理论双交换值 (**Positive interference is most often observed in eukaryotic systems).**

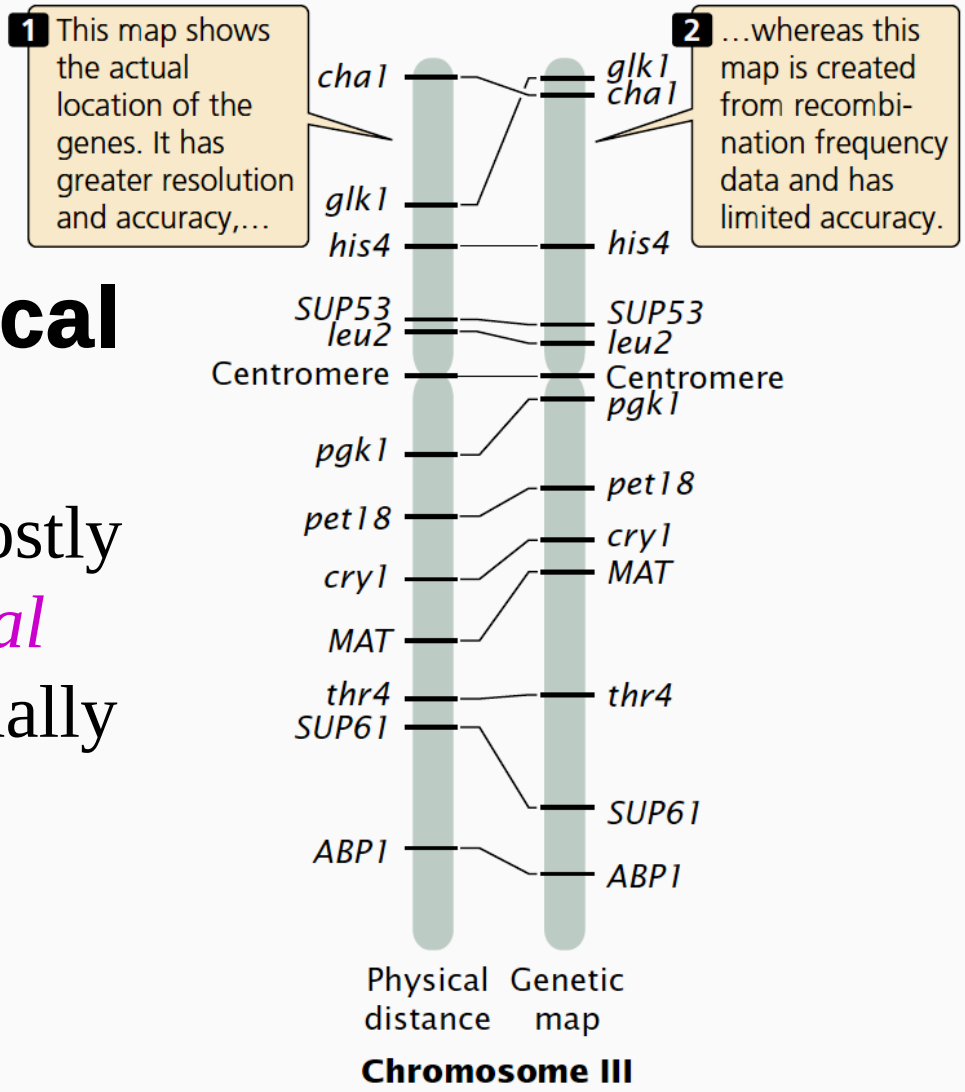
- 负干涉(negative interference)：一个单交换的发生增加另一个单交换发生的频率。

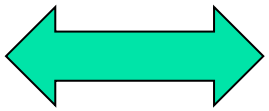
Others:

- **Mapping with molecular markers**



- **Do genetic maps correlate with physical reality?**
  - The *order of genes* are mostly consistent, while the *actual physical distances* are usually imprecise
  - Complicate factors act on recombination: locations, species……
    - 1% RF ≈ 1,000,000 bp in human
    - 1% RF ≈ 2,500 bp in yeast



交换率？  重组率？

第四节　顺序四分子分析
Ordered Tetrad Analysis

一、粗糙脉胞菌（*Neurospora crassa*）

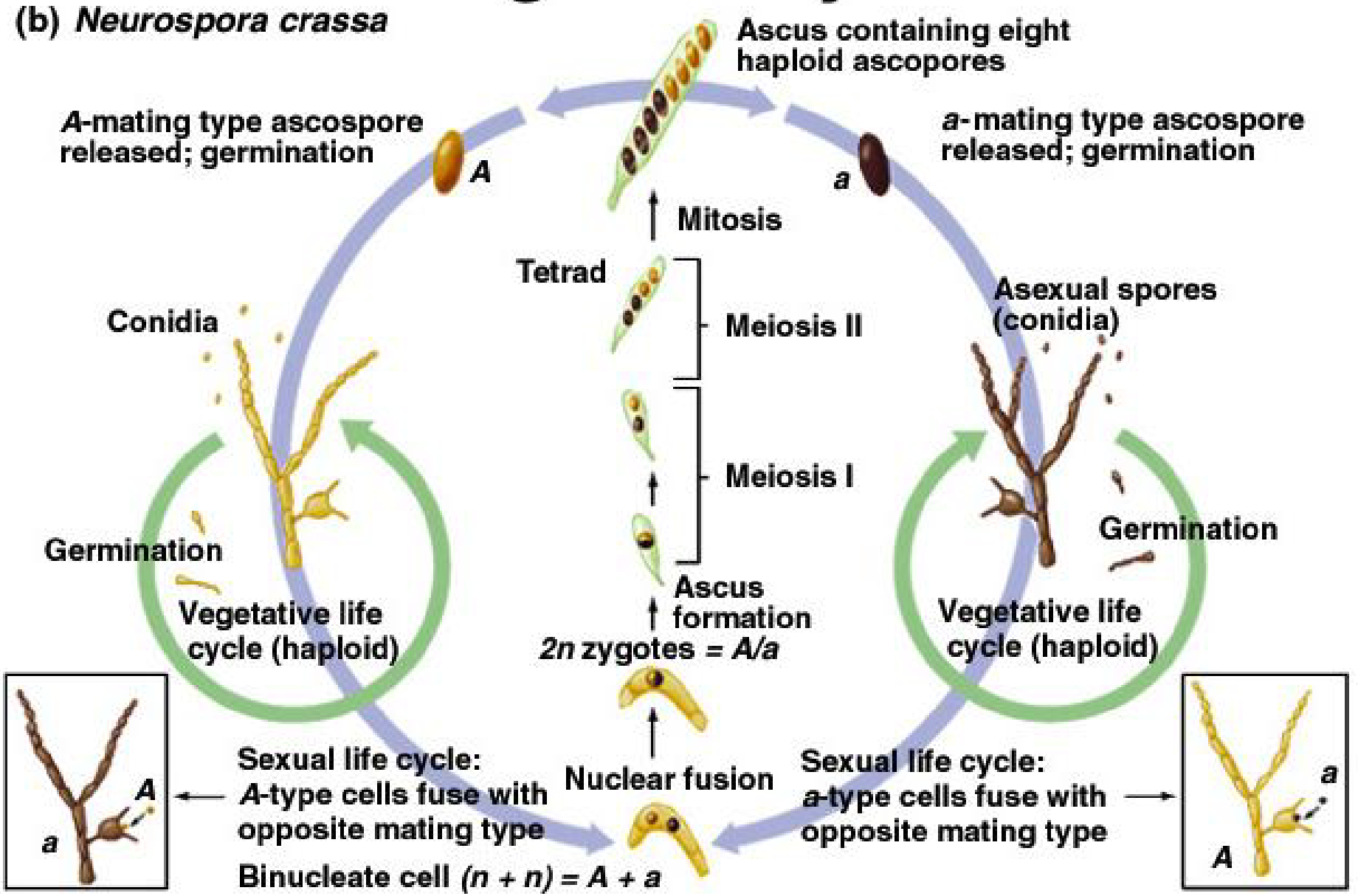
◇粗糙脉胞霉的生活史

（**The life cycles of *Neurospora crassa***）

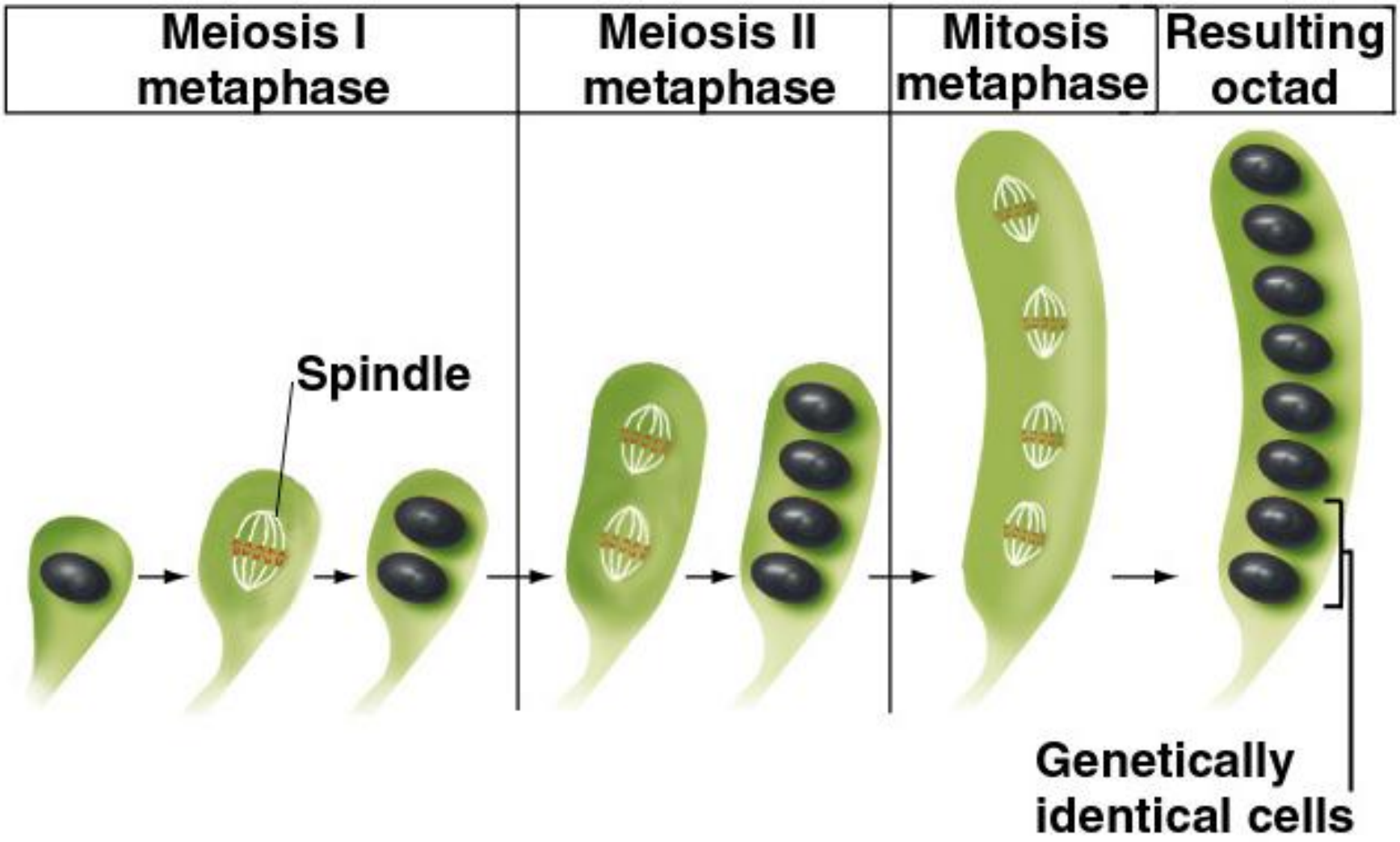
◇顺序四分子的形成

(The formation of ordered tetrads)

Fungal life cycles



Formation of ordered tetrads



◇粗糙脉胞菌是遗传分析的好材料

Neurospora crassa is good material for genetic analysis

- 子囊孢子是单倍体
- 一次只分析一个减数分裂的产物
- 体积小，易增殖，易于培养
- 进行有性生殖，染色体的结构和功能类似于高等动、植物

二、顺序四分子分析（Ordered Tetrad Analysis）

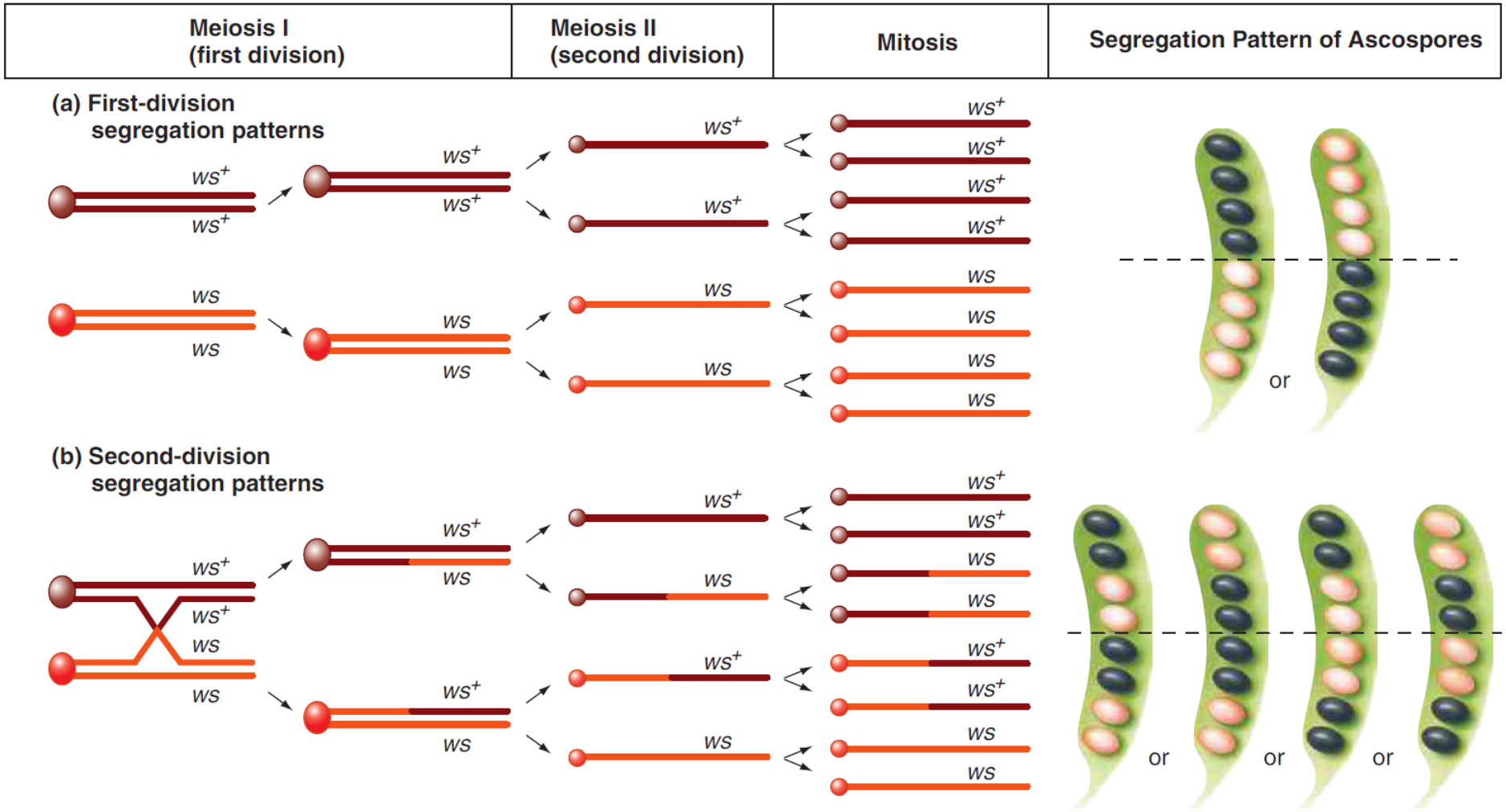
1. 着丝粒作图 （centromere mapping)

利用四分子分析法，测定基因与着丝粒间的距离

第一次分裂分离(first-division segregation，M_I)

第二次分裂分离(second-division segregation，M_{II})

Two segregation patterns in ordered asci



lys^+ × lys^-

	Tetrad group	Number	Segregation pattern	
1.	++−−	105	M_I	●●●●○○○○
2.	−−++	129	M_I	○○○○●●●●
3.	+−+−	9	M_{II}	●●○○●●○○
4.	−+−+	5	M_{II}	○○●●○○●●
5.	+−−+	10	M_{II}	●●○○○○●●
6.	−++−	16	M_{II}	○○●●●●○○

$$RF = \frac{M_{II}}{M_I + M_{II}} \times \frac{1}{2} \times 100\%$$

$$= \frac{9+5+10+16}{105+129+9+5+10+16} \times \frac{1}{2} \times 100\%$$

$$= 7.3\% = 7.3cM$$

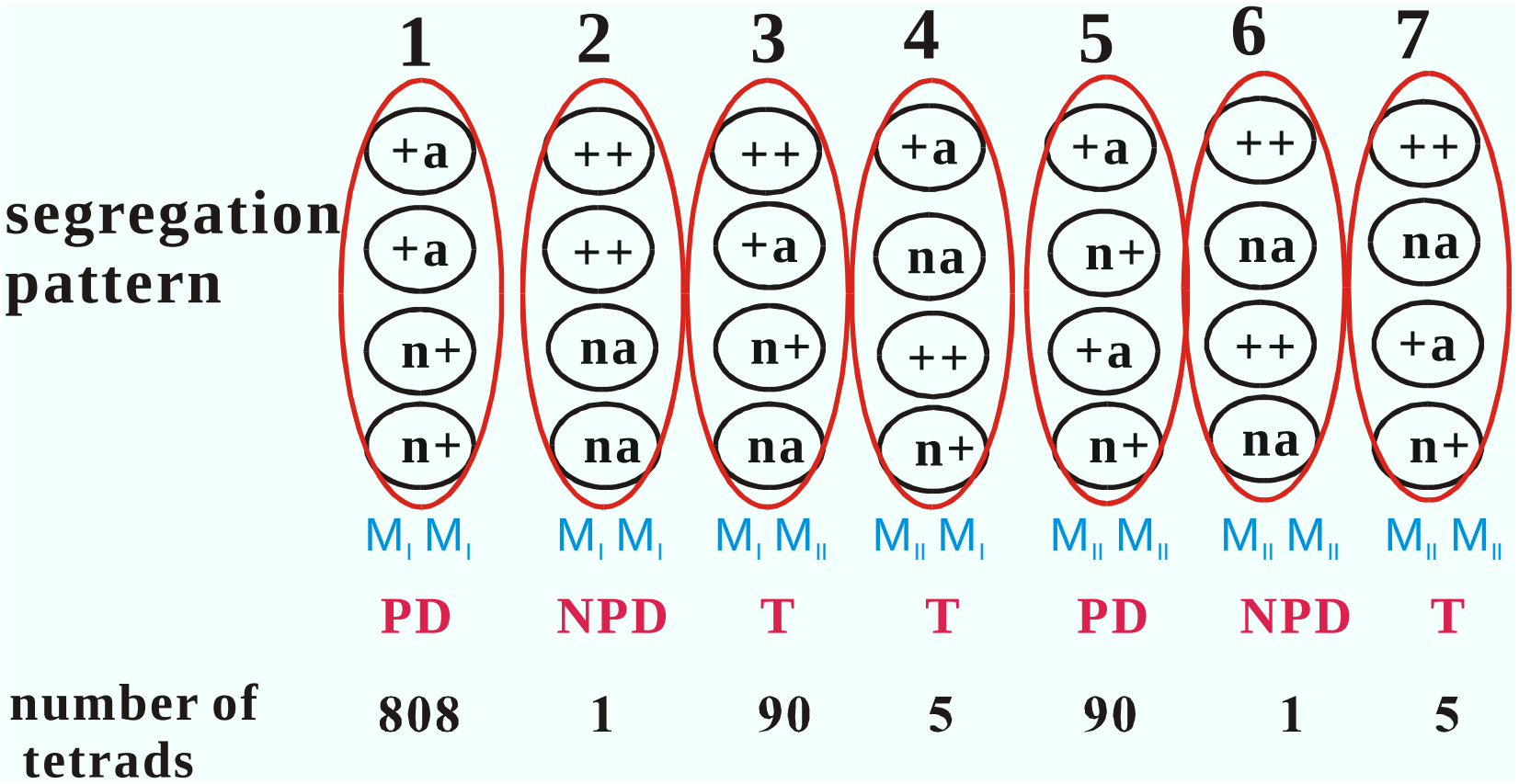
2. 两个连锁基因作图
（two linked genes mapping）

nic ＋　×　＋ ade

nic: cannot grow in the absence of nicotinic acid烟酸

ade: cannot grow in the absence of adenine腺嘌呤

n + × + a



PD (parental ditype)：亲二型

NPD (non-parental ditype)：非亲二型

T (tetratype)： 四型

- 首先判断**n**、**a**基因是自由组合的还是连锁的

PD：four spores are parental

NPD：four recombinant spores

T：two parental and two recombinant

- PD=NPD　　two genes are unlinked
- PD＞＞ NPD　　linkage

Calculate the recombination frequency

$$RF(\bullet\!-\!n)=\frac{M_{II}}{M_I+M_{II}}\times\frac{1}{2}\times 100\%$$

$$=\frac{5+90+1+5}{1000}\times\frac{1}{2}\times 100\%$$

$$=5.05\% \qquad 5.05cM$$

$$RF(\bullet\!-\!a)=\frac{90+90+1+5}{1000}\times\frac{1}{2}\times 100\%$$

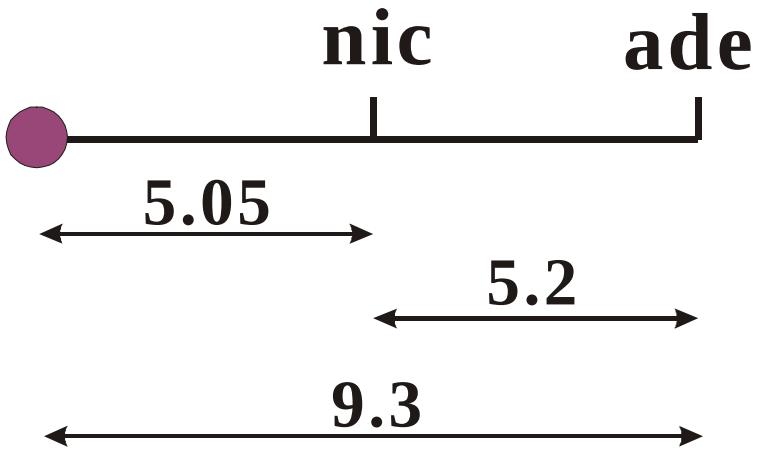
$$=9.3\% \qquad 9.3cM$$

$$RF(n\!-\!a)=\frac{NPD+1/2T}{T+NPD+PD}\times 100\%$$

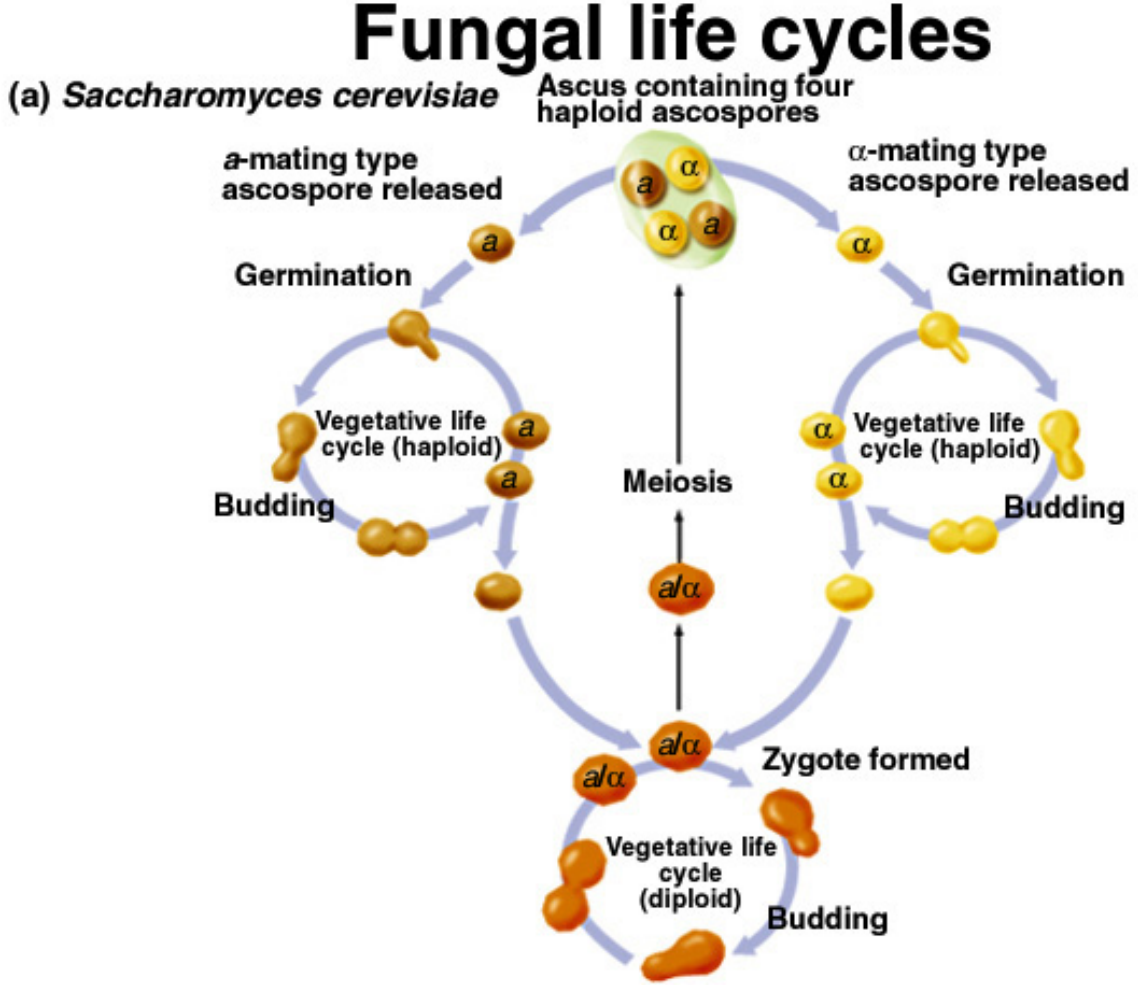
$$=\frac{(1+1)+1/2(90+5+5)}{1000}\times 100\%$$

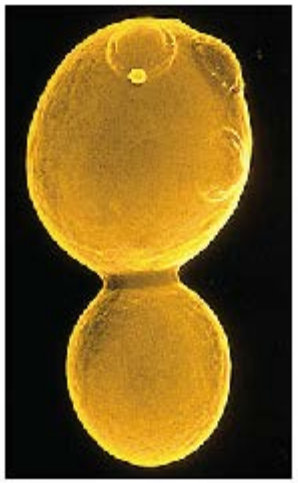
$$=5.2\% \qquad 5.2cM$$

- **Genetic map**



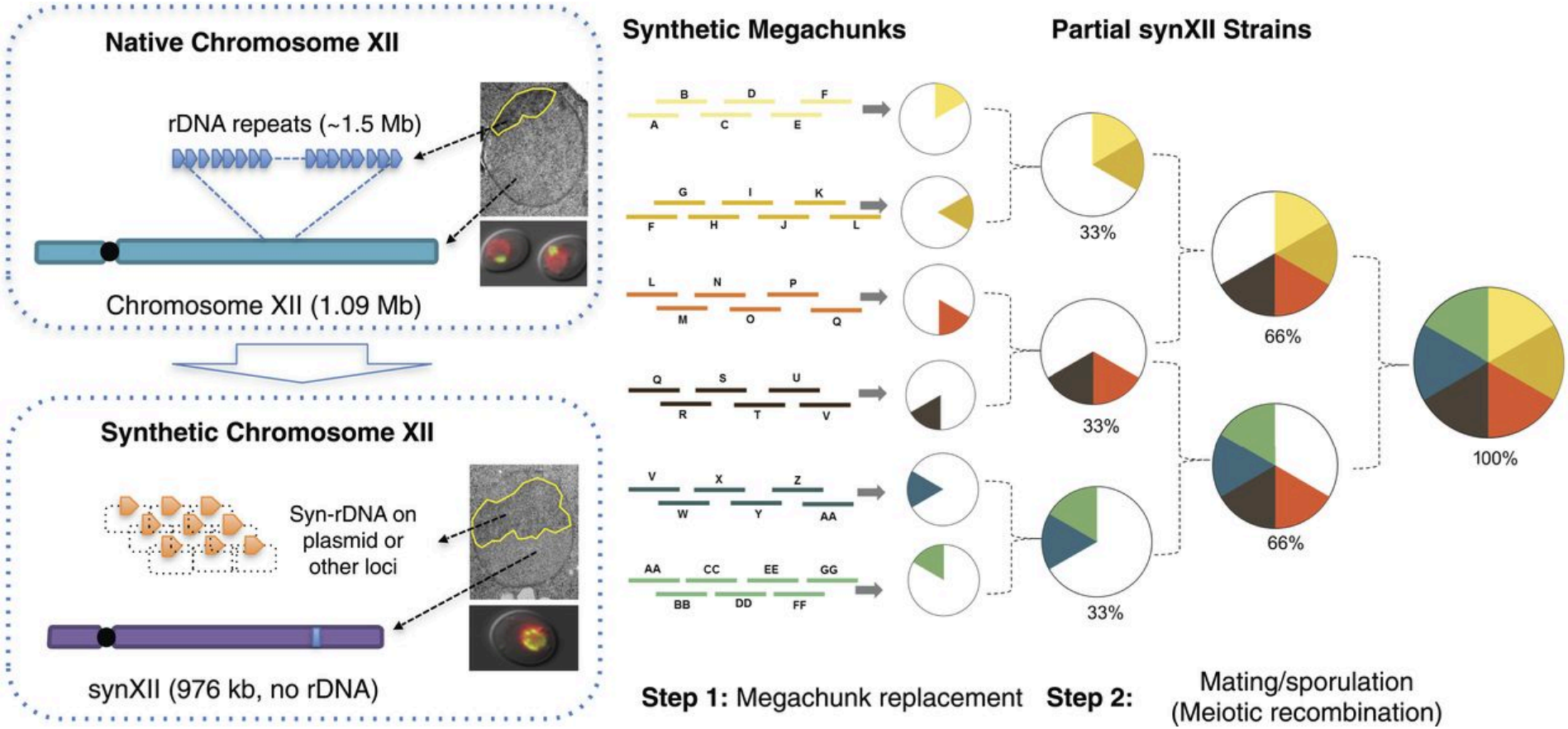
三、非顺序四分子分析
Unordered Tetrad Analysis





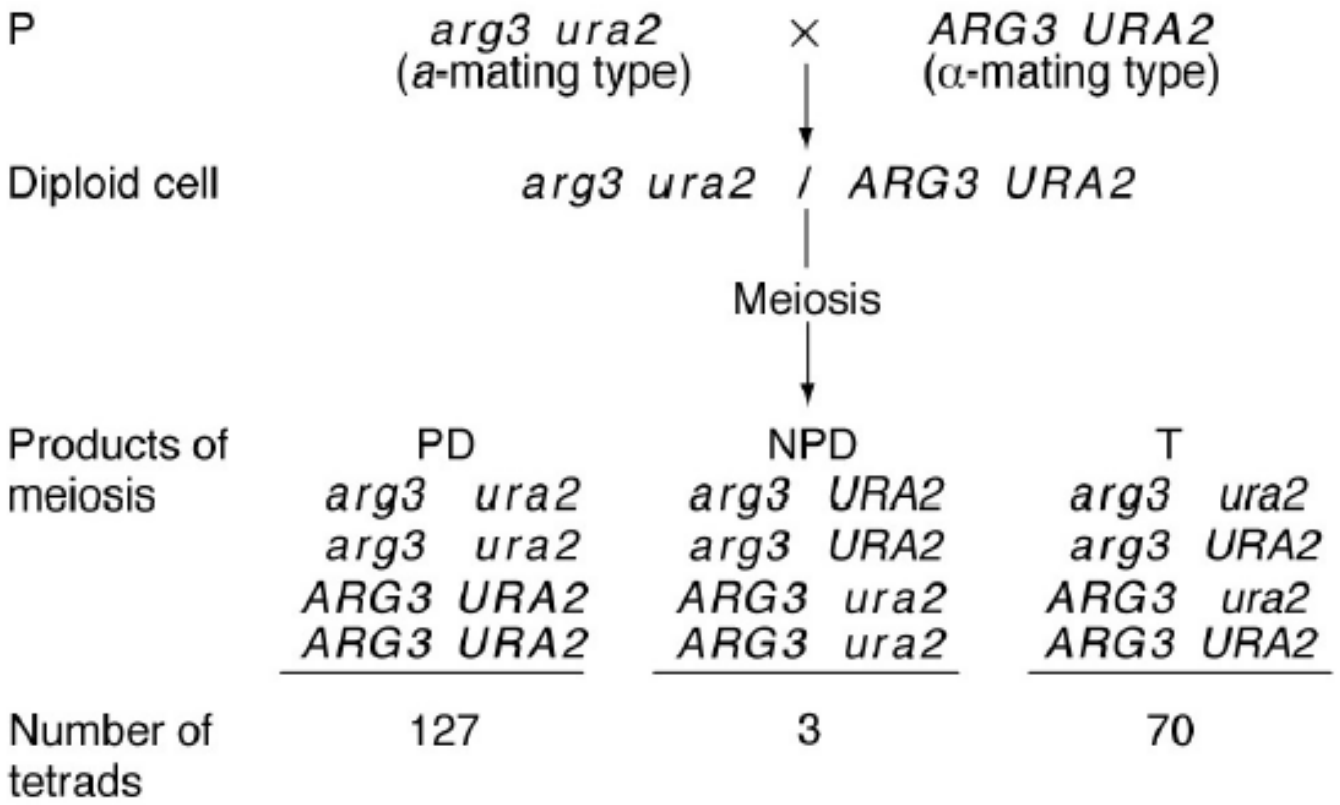
酵母基因组合成国际计划（Sc2.0）

The design and hierarchical assembly of synXII.



Engineering the ribosomal DNA in a megabase synthetic chromosome.
Weimin Zhang et al. Science 2017;355:eaaf3981

Science
AAAS



$$\text{RF} = \frac{\text{NPD} + 1/2\text{T}}{\text{Total tetrads}} \times 100$$

$$\text{RF} = \frac{3 + (1/2)70}{200} \times 100 = 19 \text{ m.u.}$$

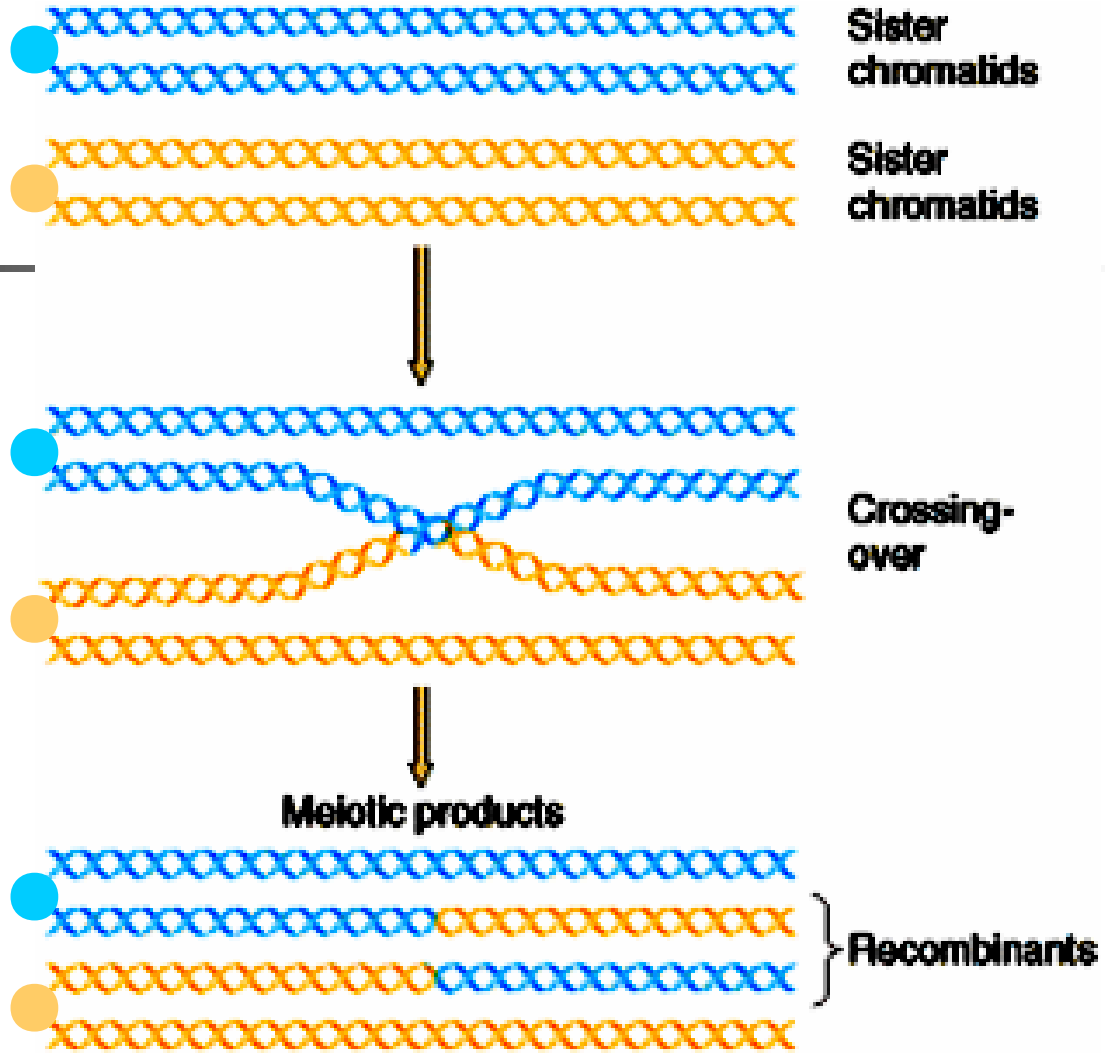
Ordered *verse* Unordered Tetrad Analysis

Ordered tetrad is essential for two types of analysis

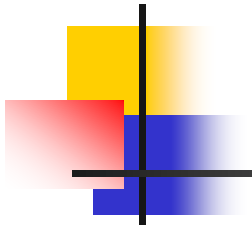
- Map the centromere
- Reveal the Gene Conversion (基因转变）

第五节　同源重组的分子机制

Molecular Basis of Homologous Recombination



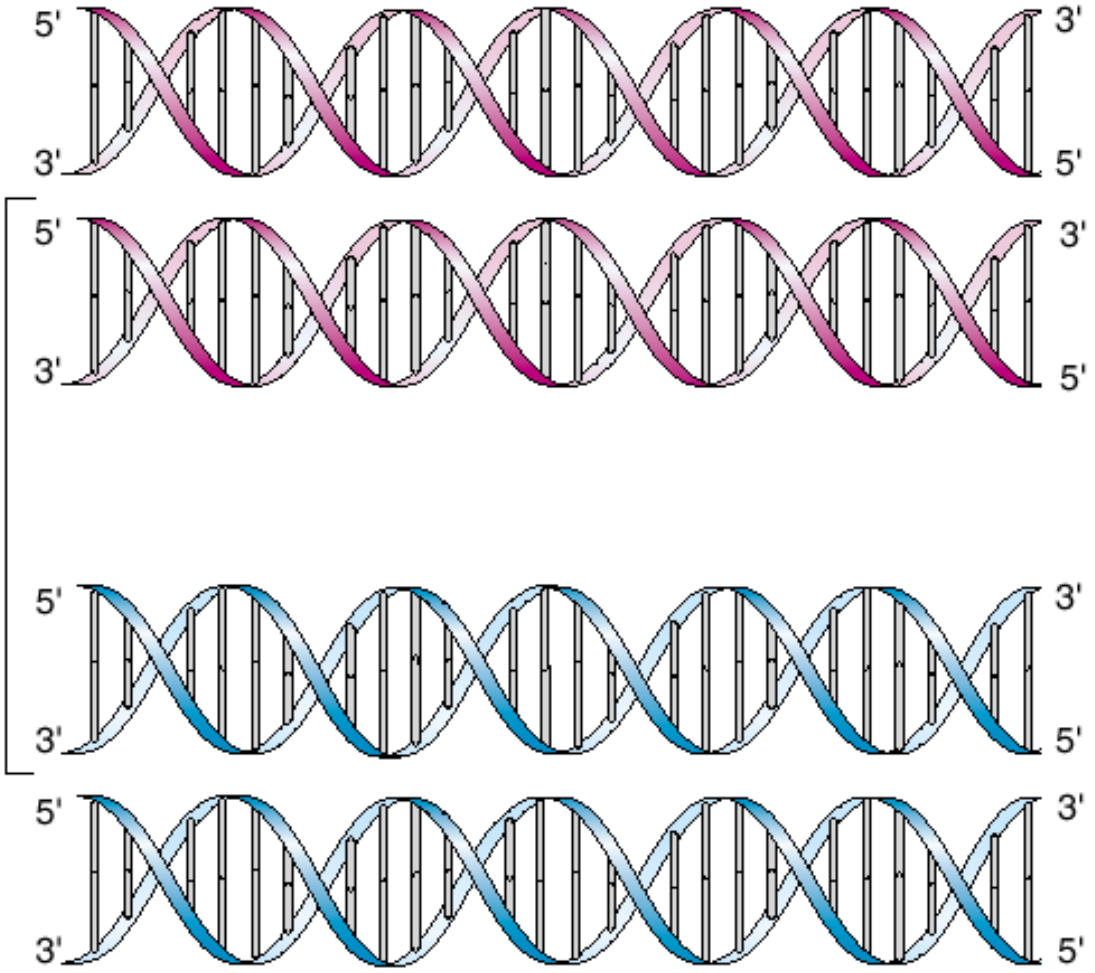
Homologous recombination can take place through several different pathways



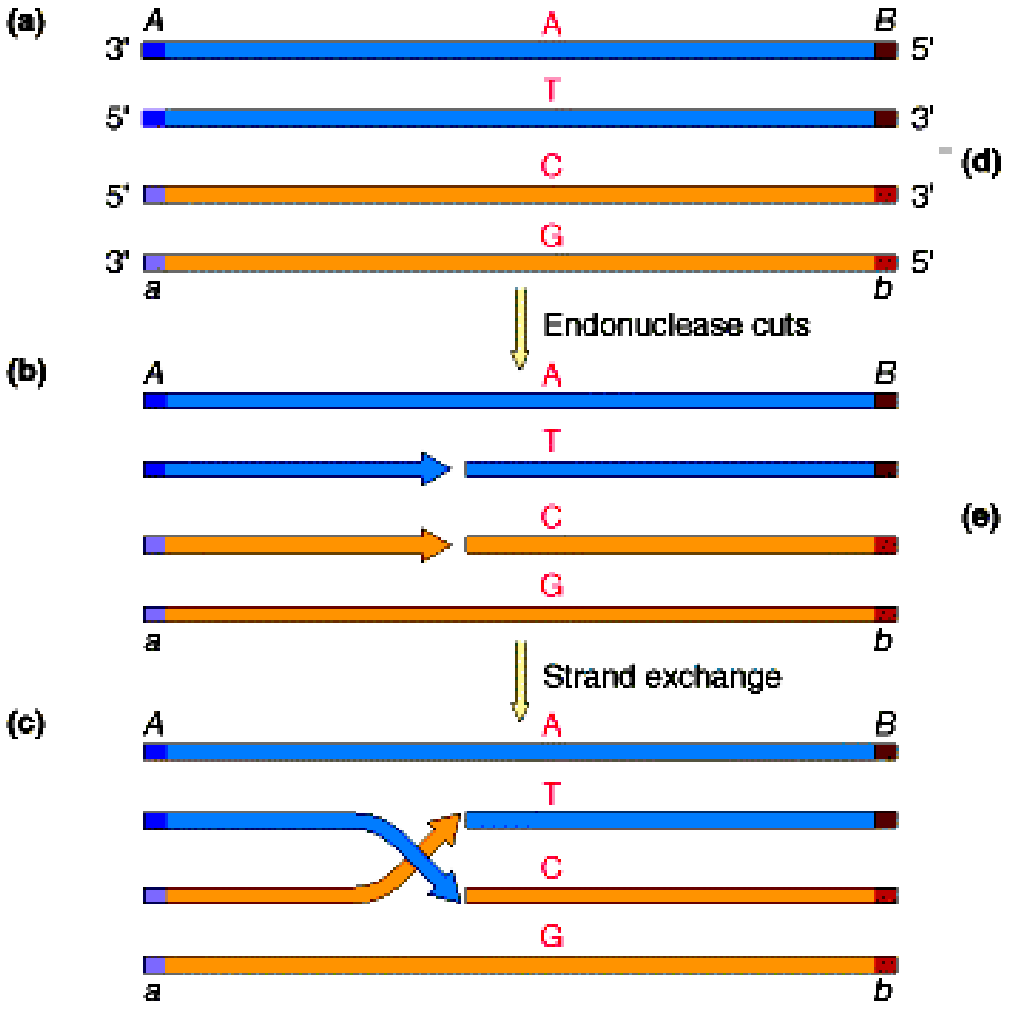
1. The Holliday Model

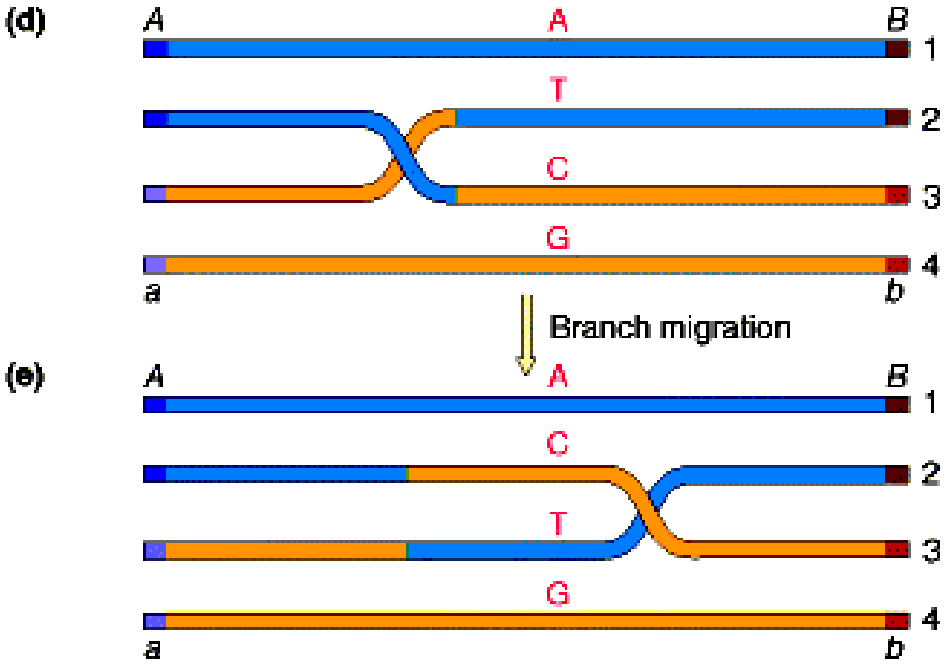
1964，R.Holliday

The structure of chromatids in meiotic prophase



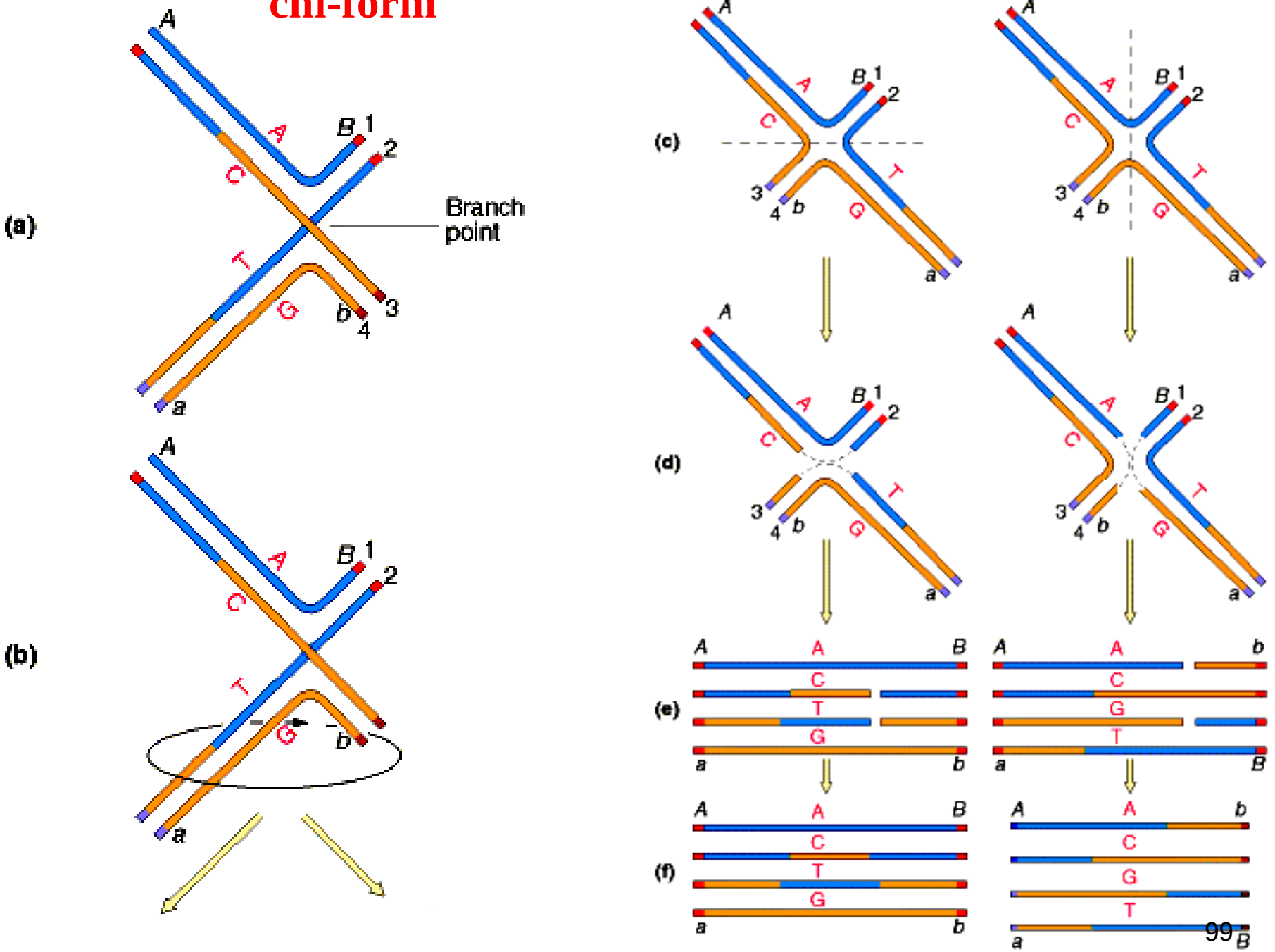
Holliday model





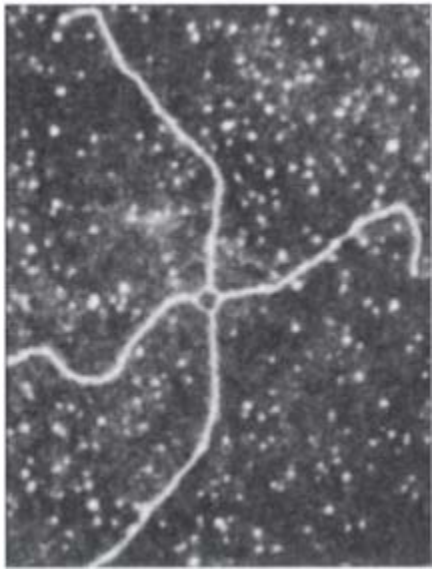
Heteroduplex DNA
Holliday structure

chi-form



Evidence supporting this model

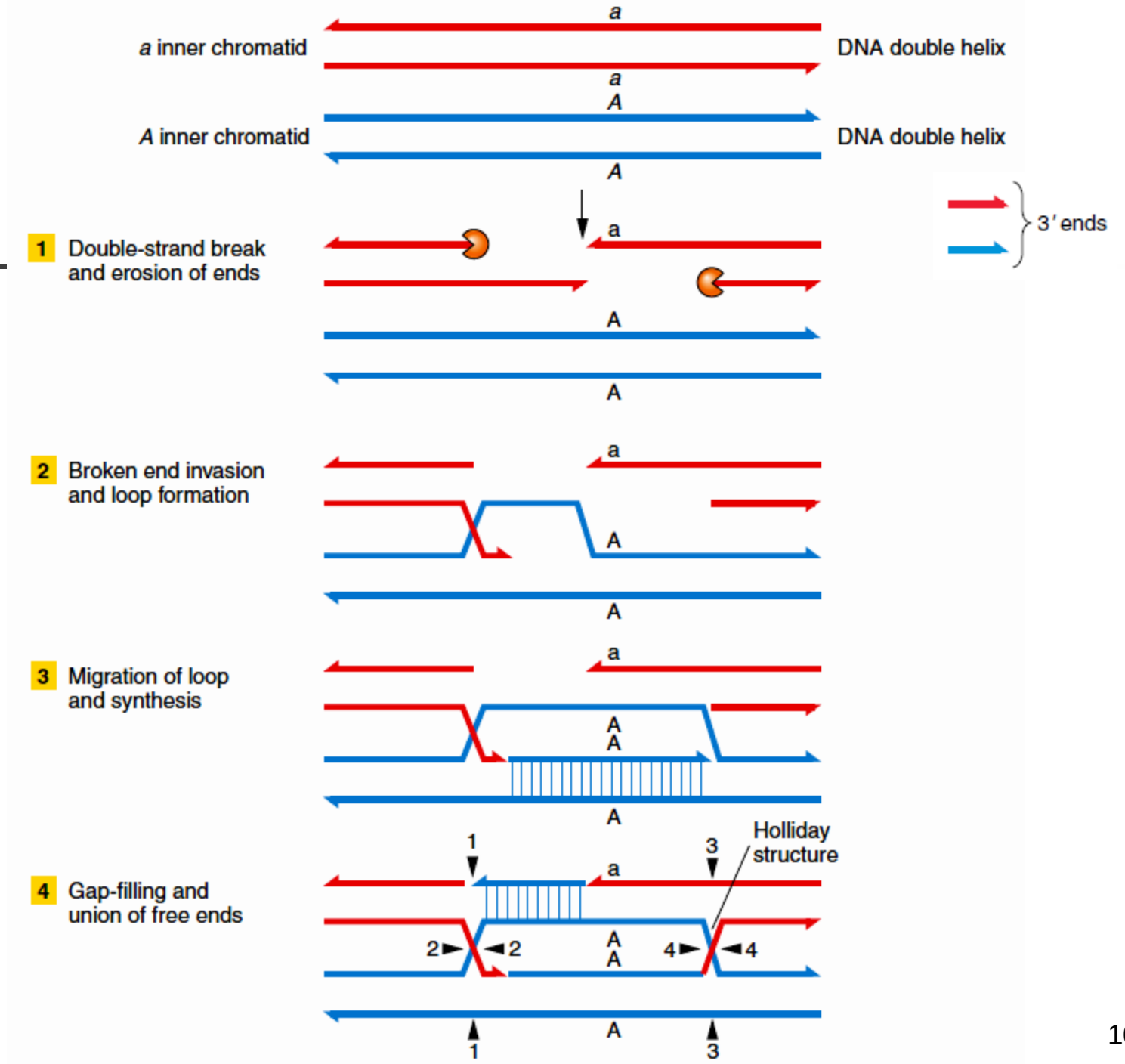
◇ The electron microscopic visualization of chi-form

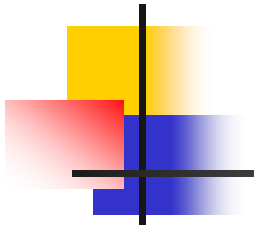


◇ The discovery of RecA protein in *E.coli*

2. The Double-Strand-Break Model (1983)

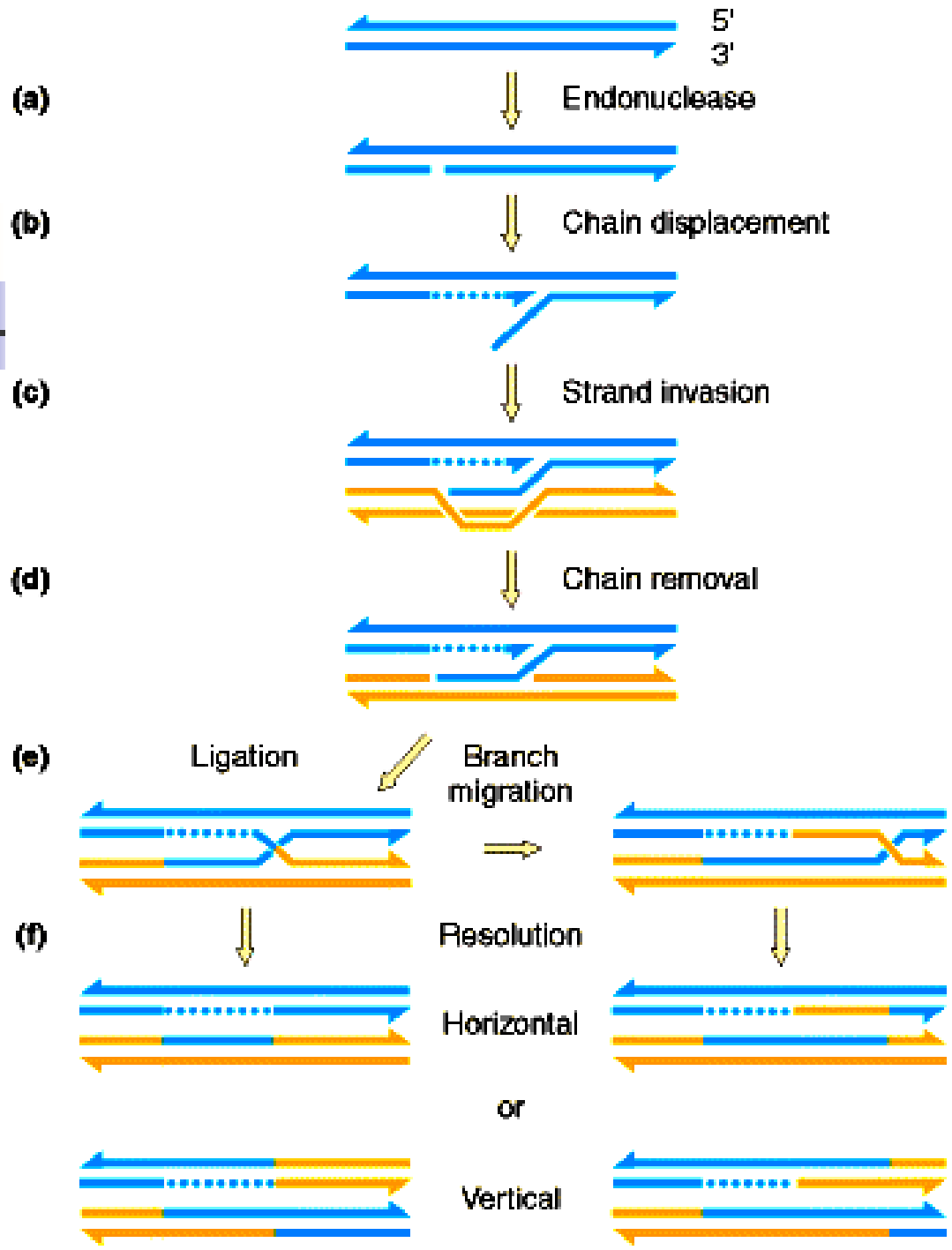
- Recombination starts with double-strand breaks in one of the two aligned DNA molecules


a inner chromatid
DNA double helix
A inner chromatid
DNA double helix
3′ ends
1 Double-strand break and erosion of ends
2 Broken end invasion and loop formation
3 Migration of loop and synthesis
4 Gap-filling and union of free ends
Holliday structure



3. Meselson-Radding model

(single-strand break and repair model)


5'
3'
(a)
Endonuclease
(b)
Chain displacement
(c)
Strand invasion
(d)
Chain removal
(e)
Ligation
Branch migration
(f)
Resolution
Horizontal
or
Vertical

See movie 1

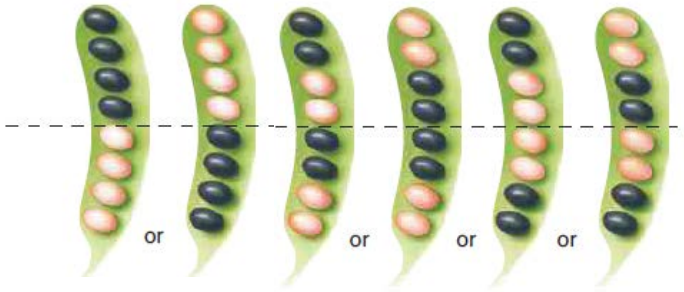
2

4. 基因转变 Gene conversion

g+（black spore）× g⁻（gray spore）

↓

200,000 ascus

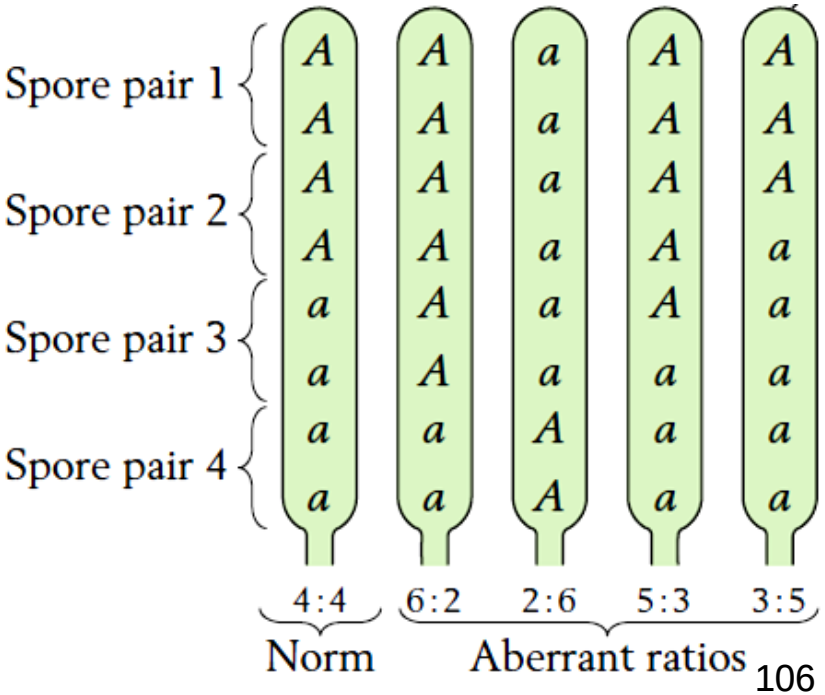


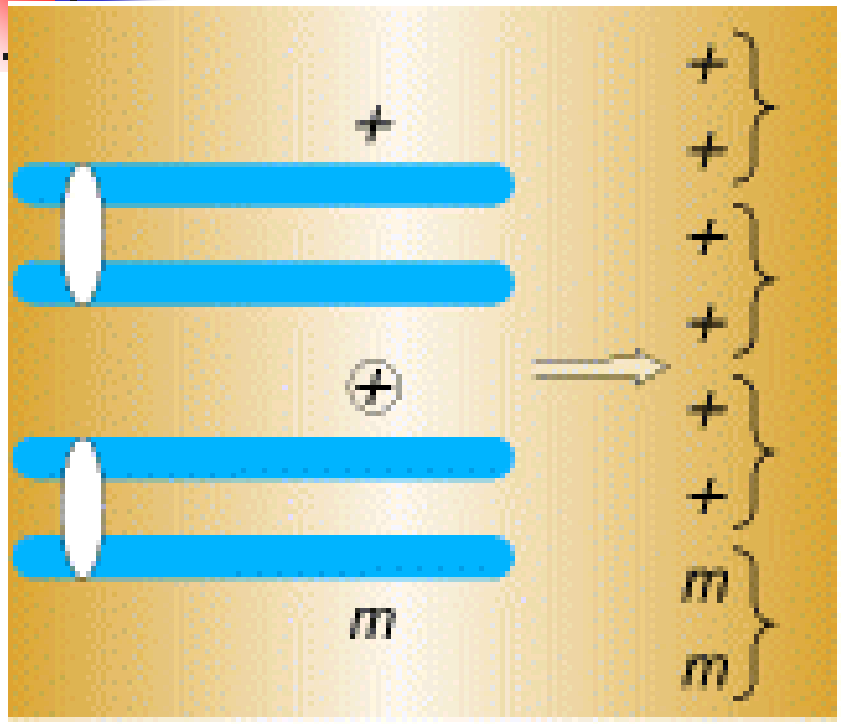
4g+：4g⁻：mostly

5g+：3g⁻：0.06%

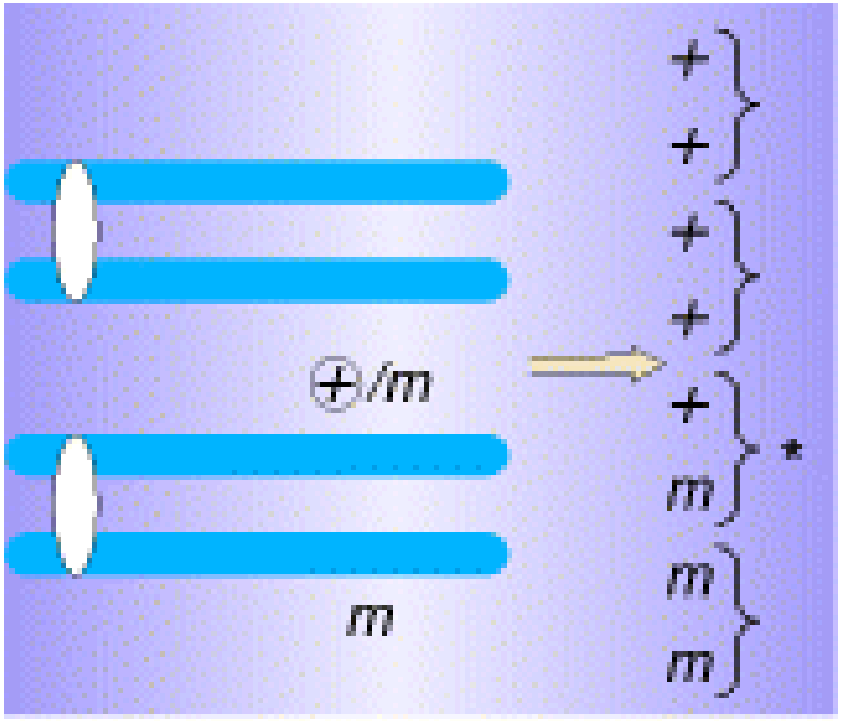
6g+：2g⁻：0.05%

3g+：g⁻：g+：3g⁻：0.008%





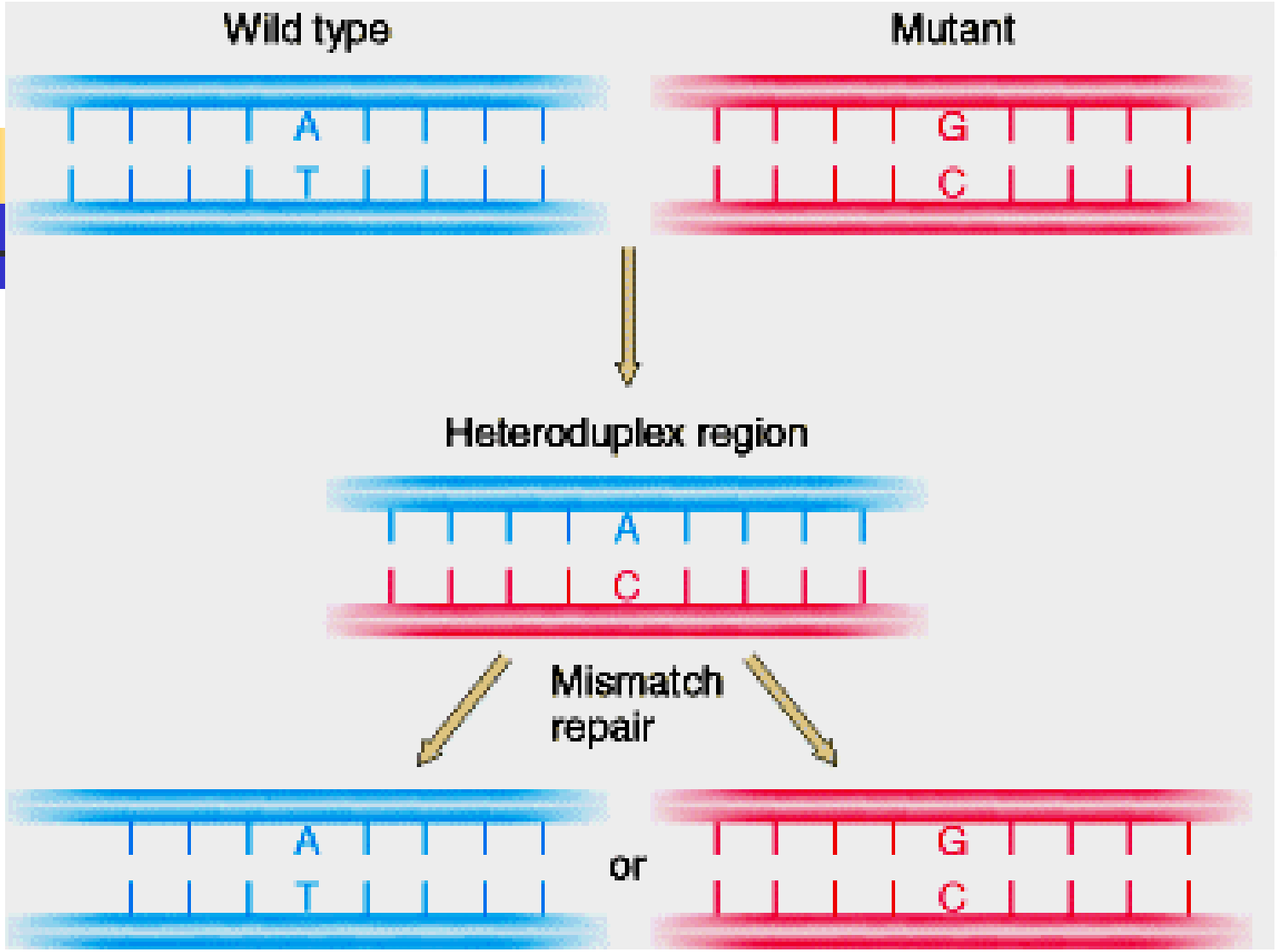
(a) Chromatid conversion

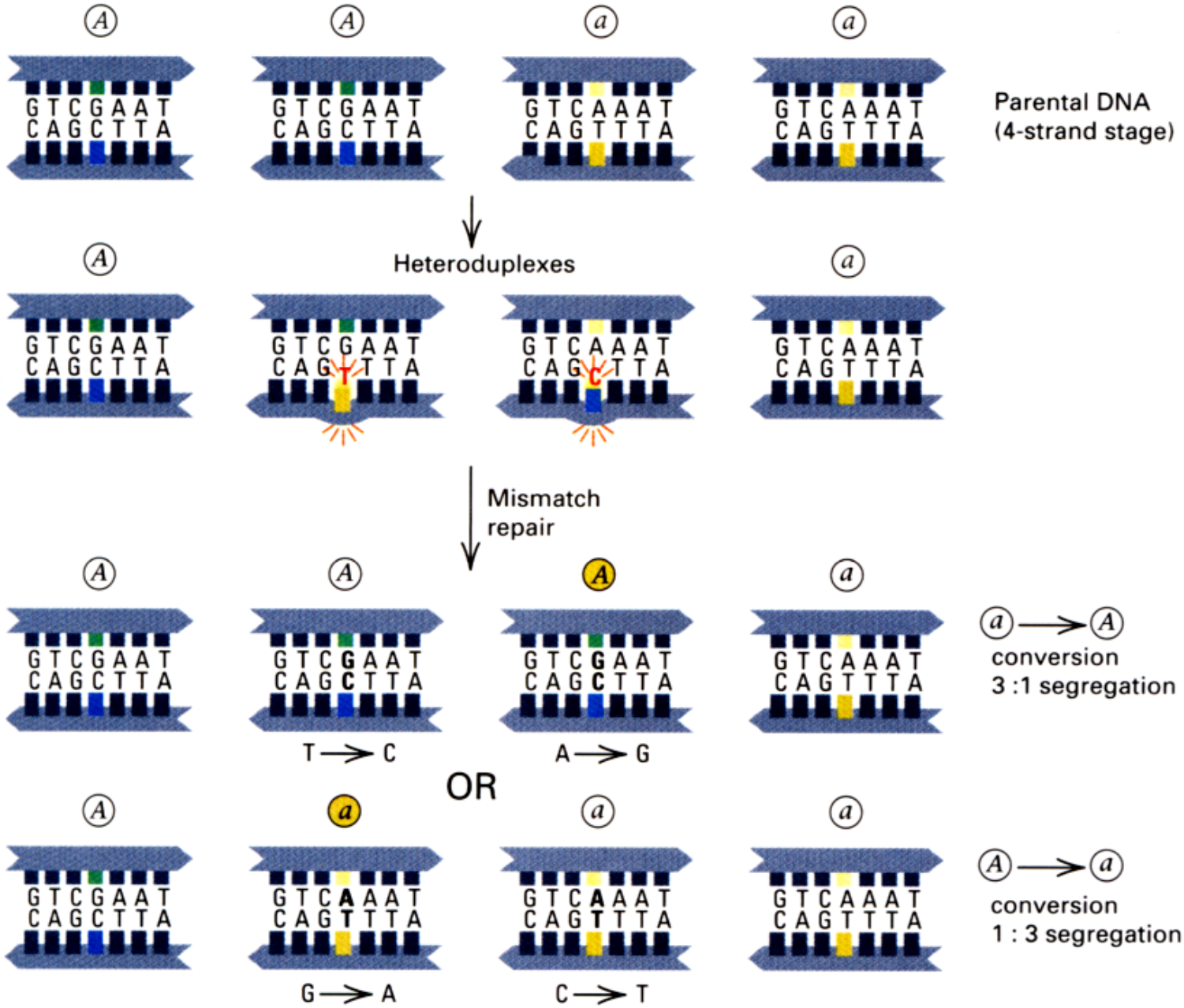


(b) Half-chromatid conversion

- Gene conversion is a consequence of DNA recombination

- It results from the mismatch repair process of heteroduplex DNA


Wild type
Mutant
A
T
G
C
Heteroduplex region
A
C
Mismatch
repair
A
T
or
G
C



gene conversion

- **Gene conversion** is a meiotic process of directed change in which one allele directs the conversion of a partner allele into its own form

The figures and tables are cited from:

- **Genetics (From genes to genomes)**, Leland Hartwell, Mcgraw-Hill Companies, Inc
- **Concept of Genetics**, William S.Klug, Prentice Hall, Inc
- **Introduction to Genetics Analysis**, Anthony J.F. Griffiths, W.H.Freeman, Inc
- **Principle of Genetics**, D.Peter Snustad, John Wiley & Sons, Inc
- **Genetics-A Conceptual Approach**, Benjamin A. Pierce, W. H. Freeman