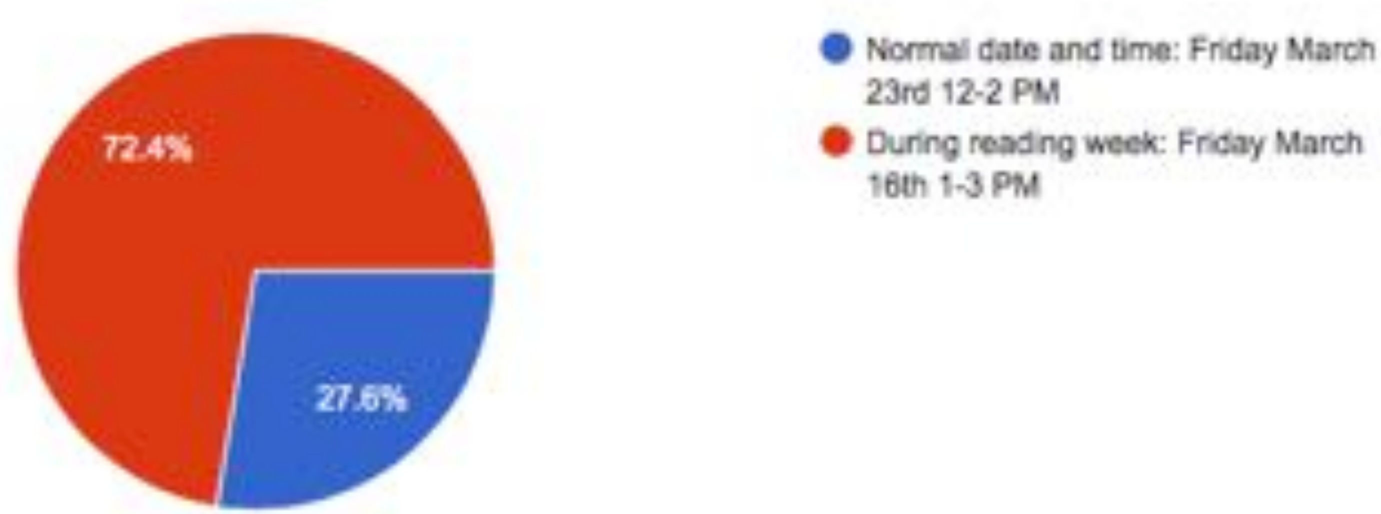
Course website:
bio393.andersenlab.org

Problem set #1 is out.

Genetics terms are online.

Final will be on Friday March 16 1-3 PM

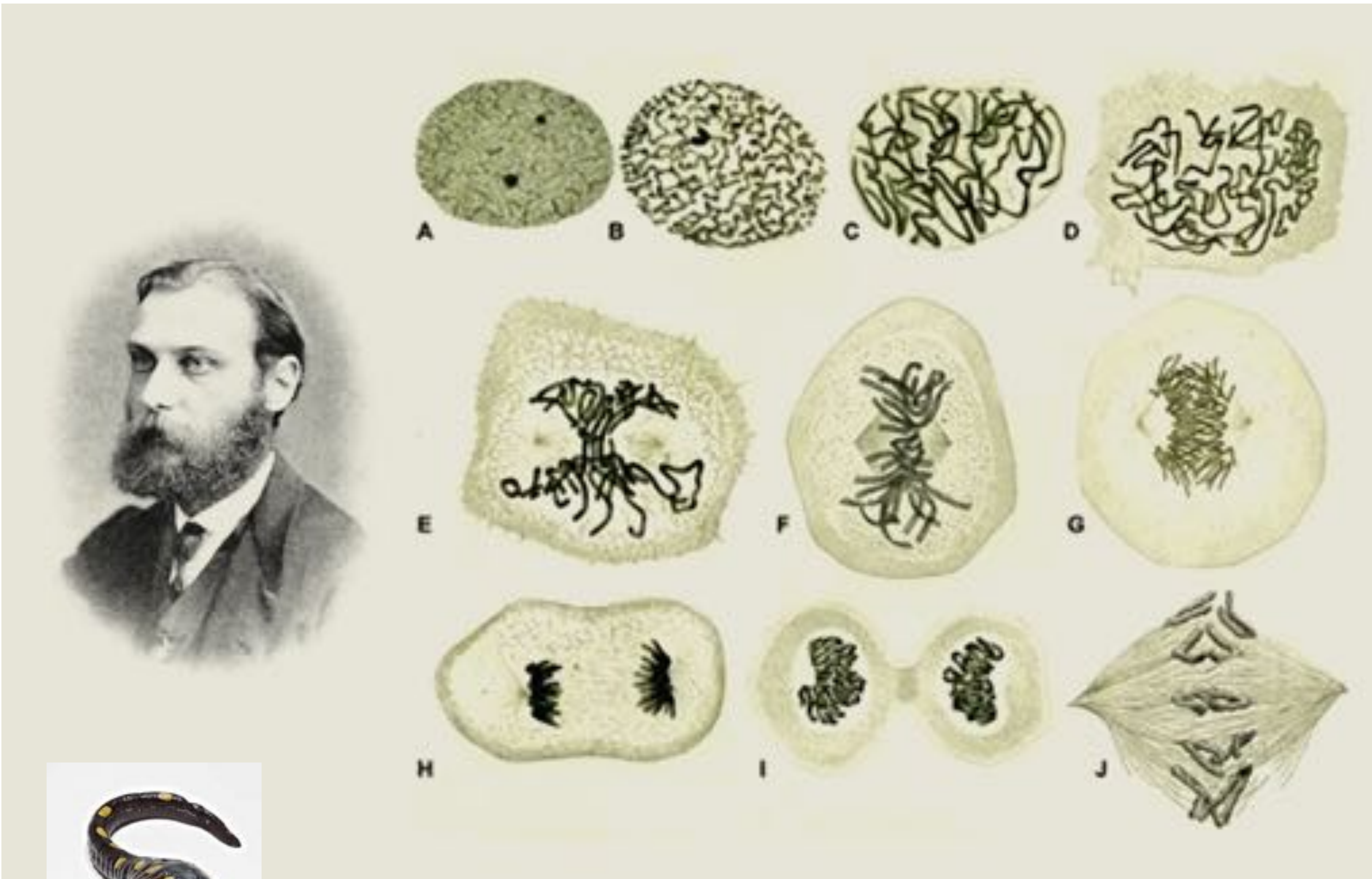


Bio393: Genetic Analysis

Chromosome theory, recombination, and mapping

Lecture 2

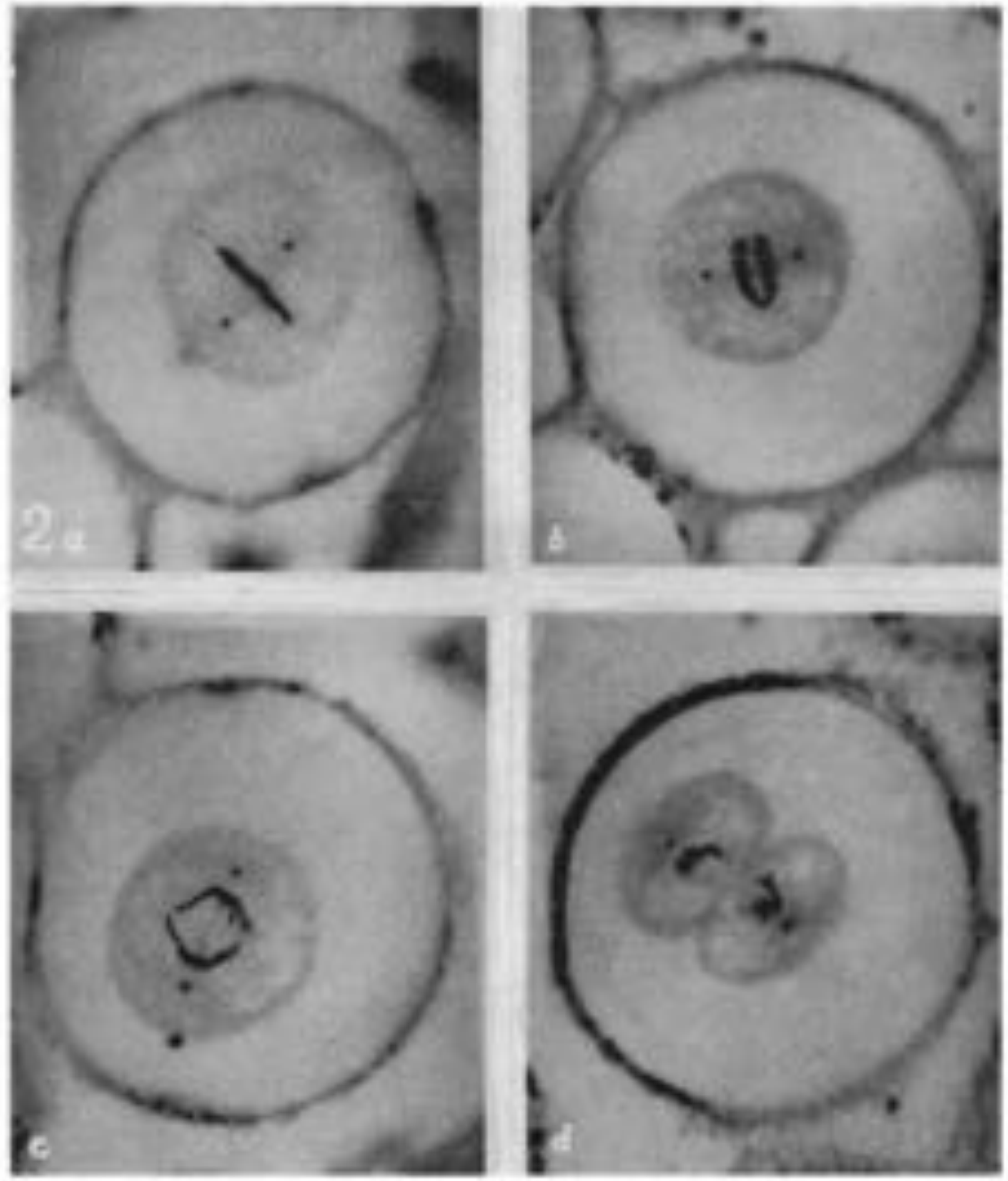
Walther Flemming stained cells



Walther Flemming, 1882

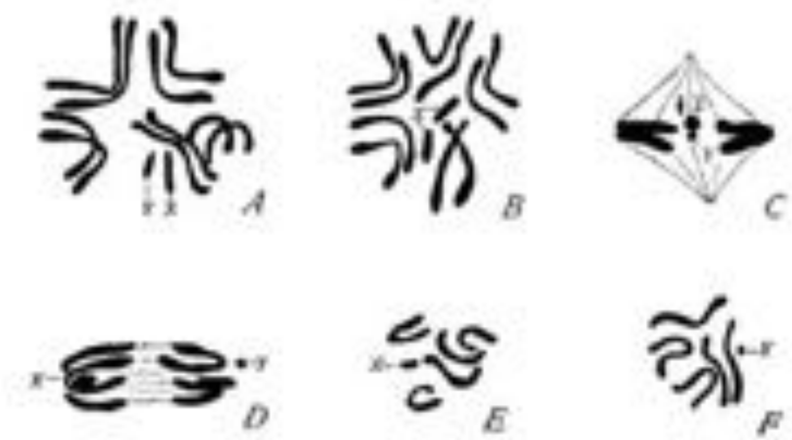
Cells divide their chromosomes with high fidelity

Theodor Boveri



Discovery of sex chromosomes

Nettie Stevens



Tenebrio melitor

then 50 beetle species and nine species of fly!

Gametes have half the chromosomes of the soma


Theodor Boveri

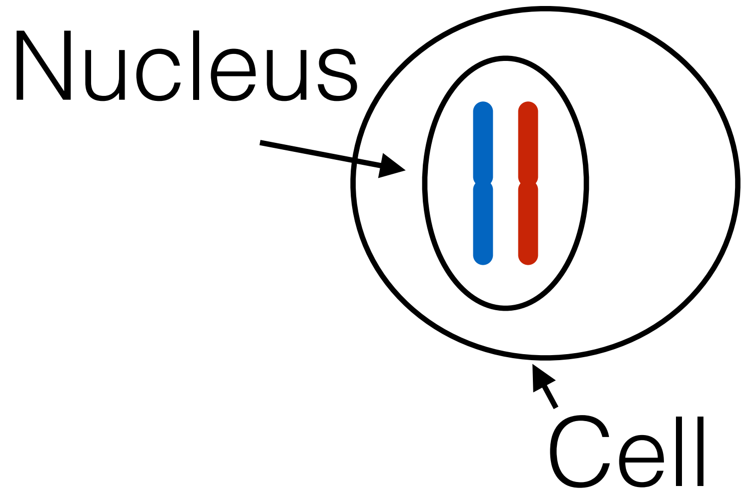

Parascaris equorum

Discovery of a connection to Mendel's principles

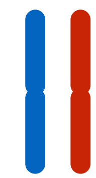
Walter Sutton

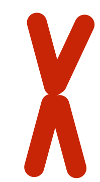
- Gametes have half chromosome complement of somatic cells
- Homolog separation to gamete was random

Terms for mitosis and meiosis



 Chromosome

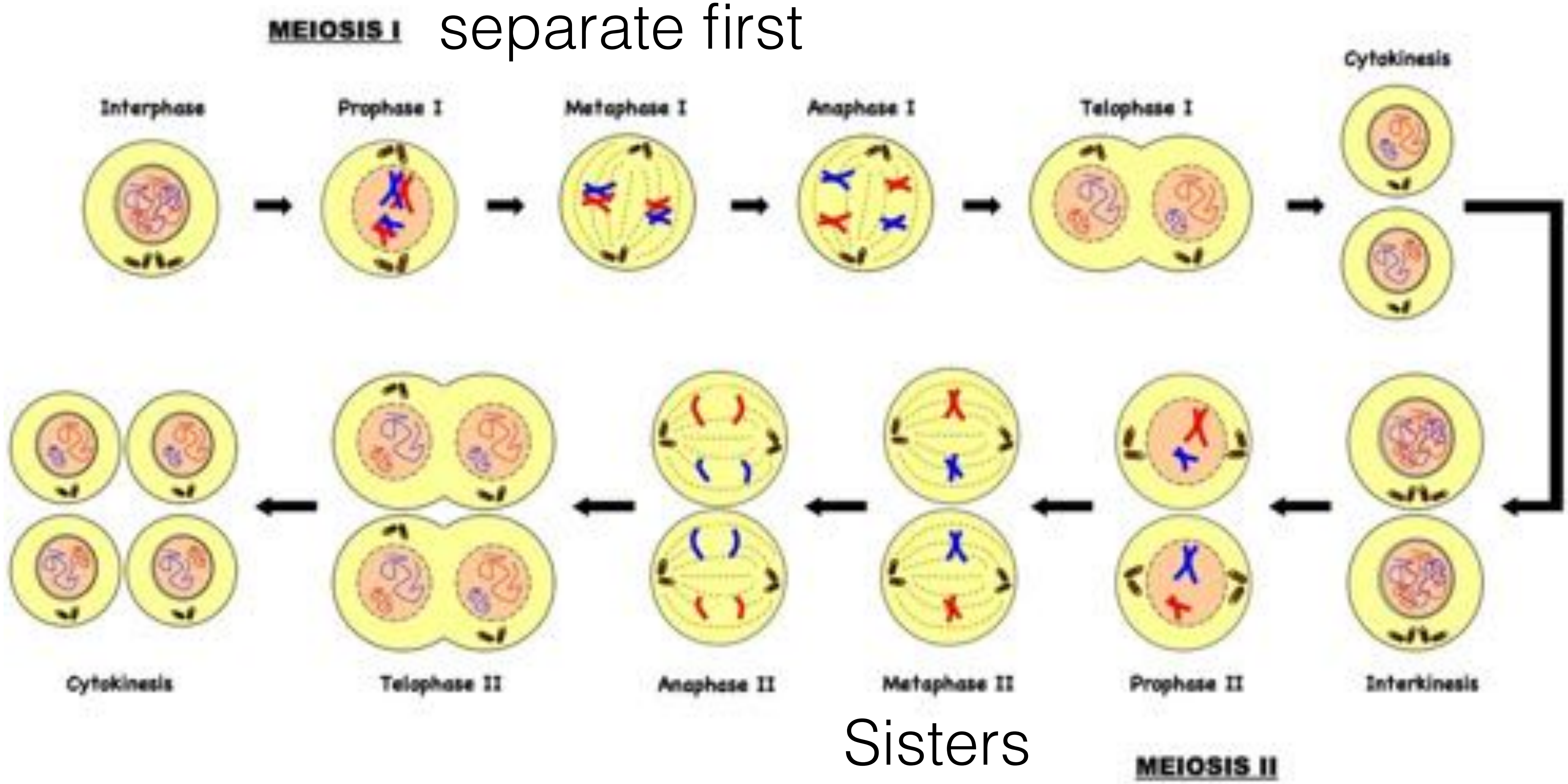
 Pair of homologs (2N)

 Sister chromatids

Ploidy (N)
Diploid (2N)
Haploid (1N)
Polyploid (>2N)
Gamete

Meiosis: A reductional division in two acts

Homologs
separate first



Sisters
separate last

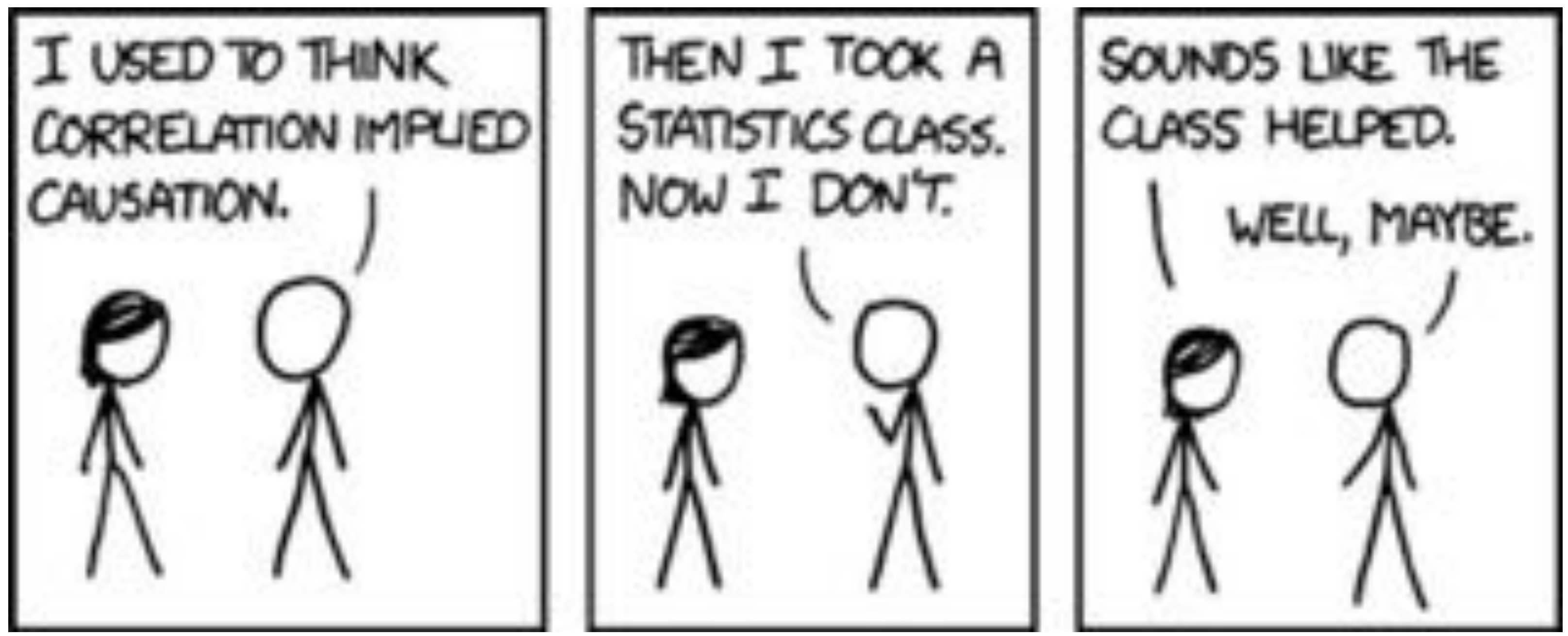
Keep track of
centromere

Discovery of a connection to Mendel's principles

Walter Sutton

- Gametes have half chromosome complement of somatic cells
- Homolog separation to gamete was random

Correlation does not mean causation



xkcd.com

Thomas Hunt Morgan

Drosophila melanogaster: genetics superstar

Nettie Stevens

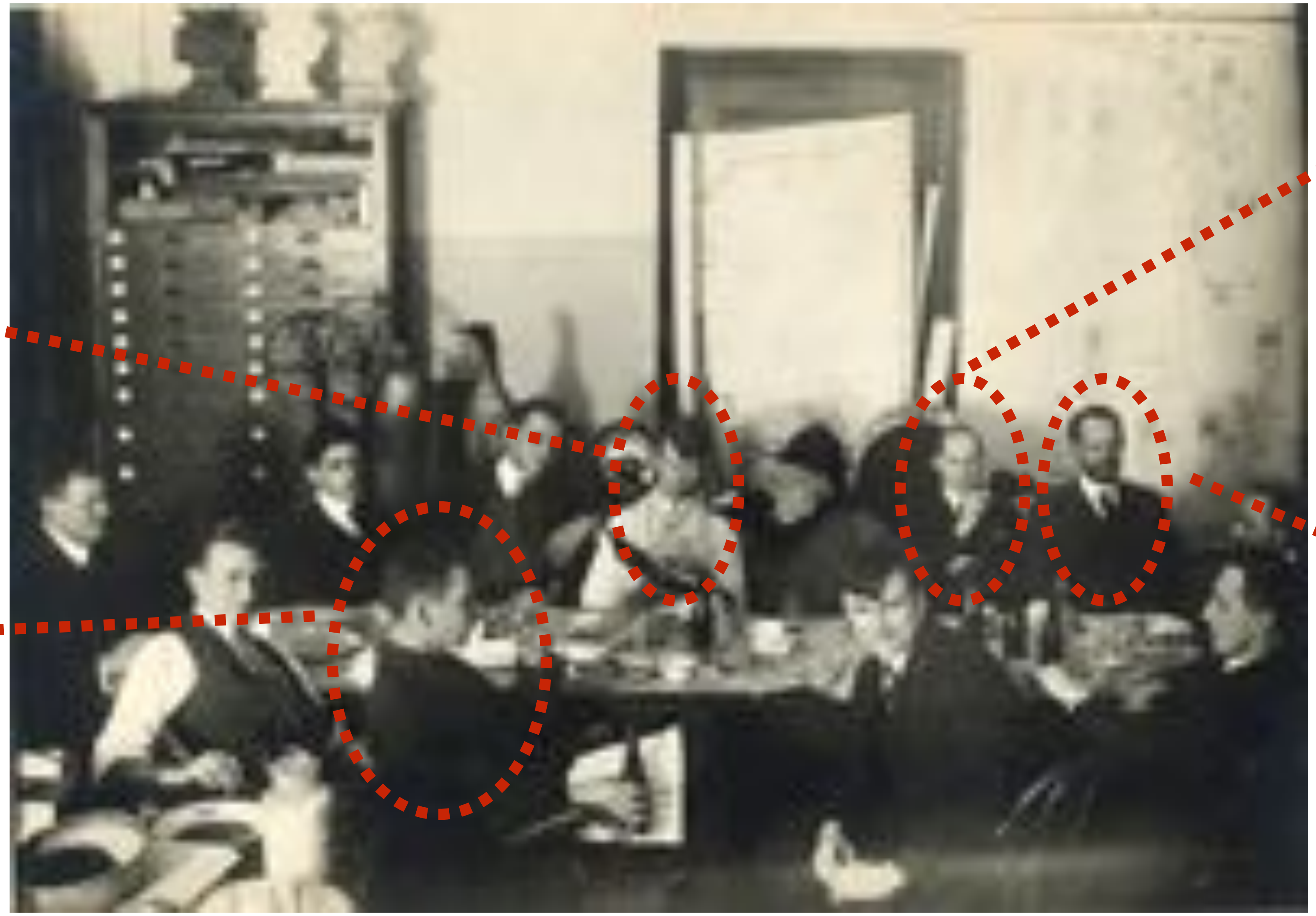
Thomas Hunt Morgan

Drosophila polytene chromosomes allow us to directly visualize genetic principles

The fly room at Columbia

Hermann Muller

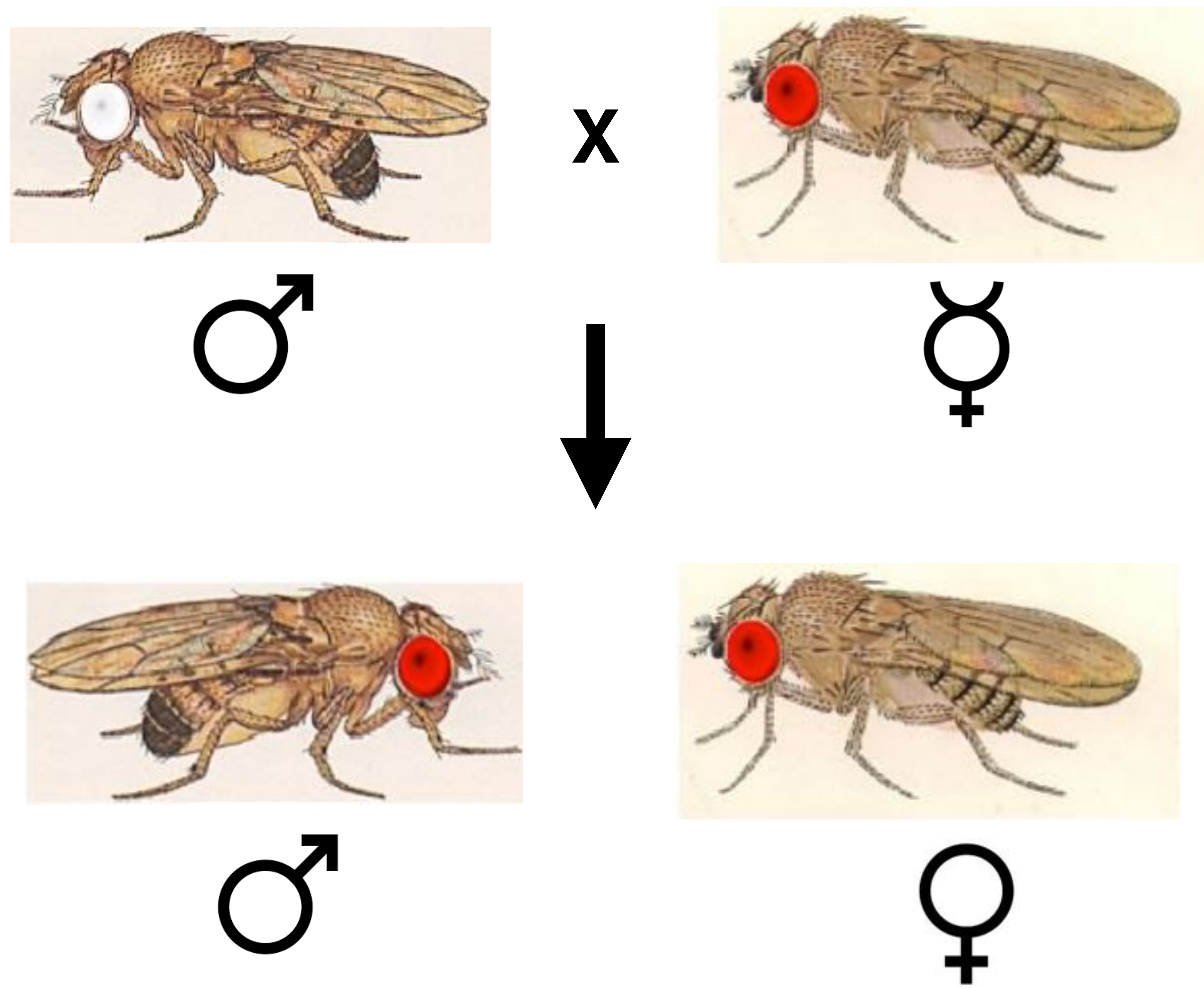
Calvin Bridges



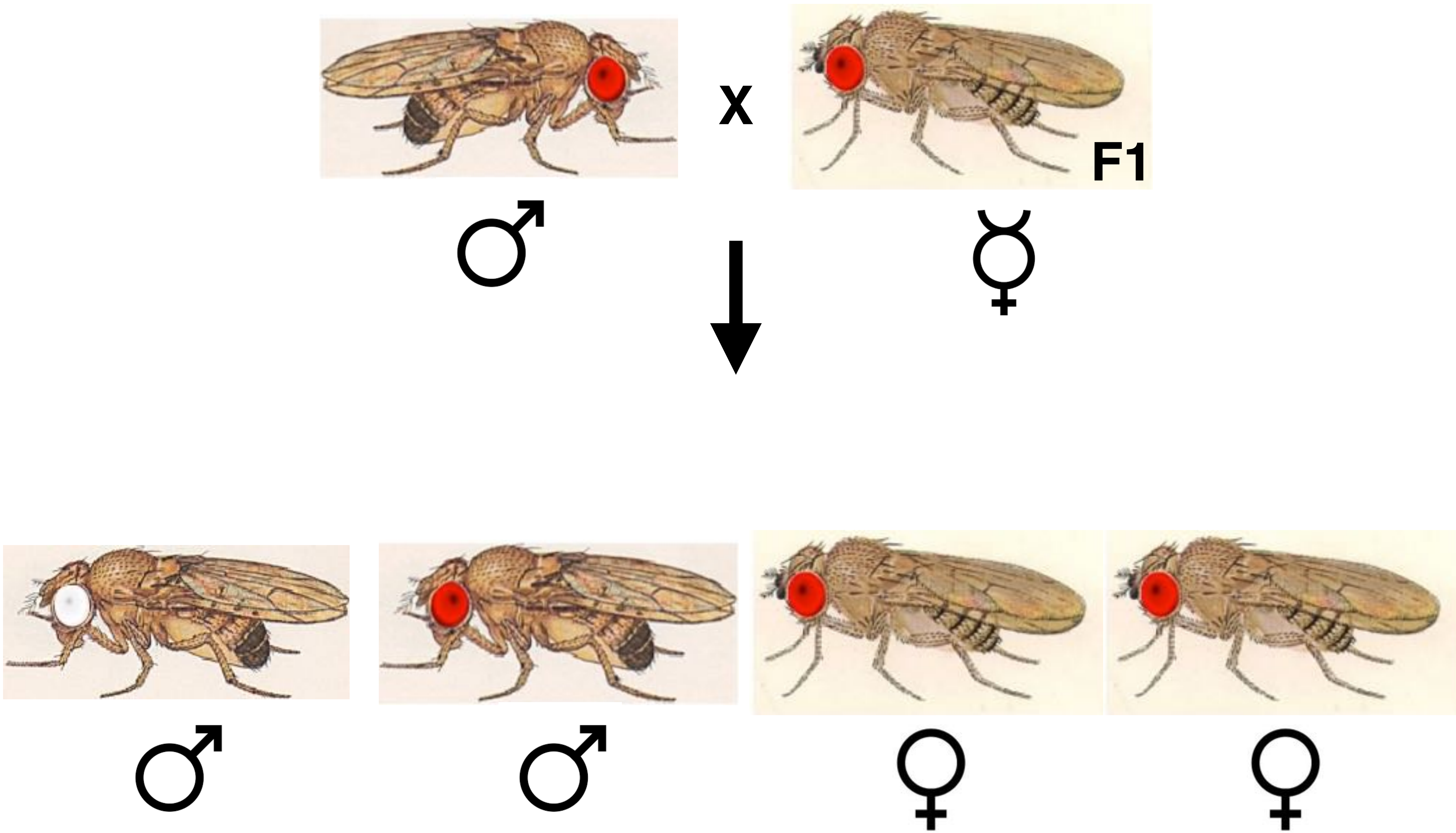
Thomas H. Morgan

Alfred Sturtevant

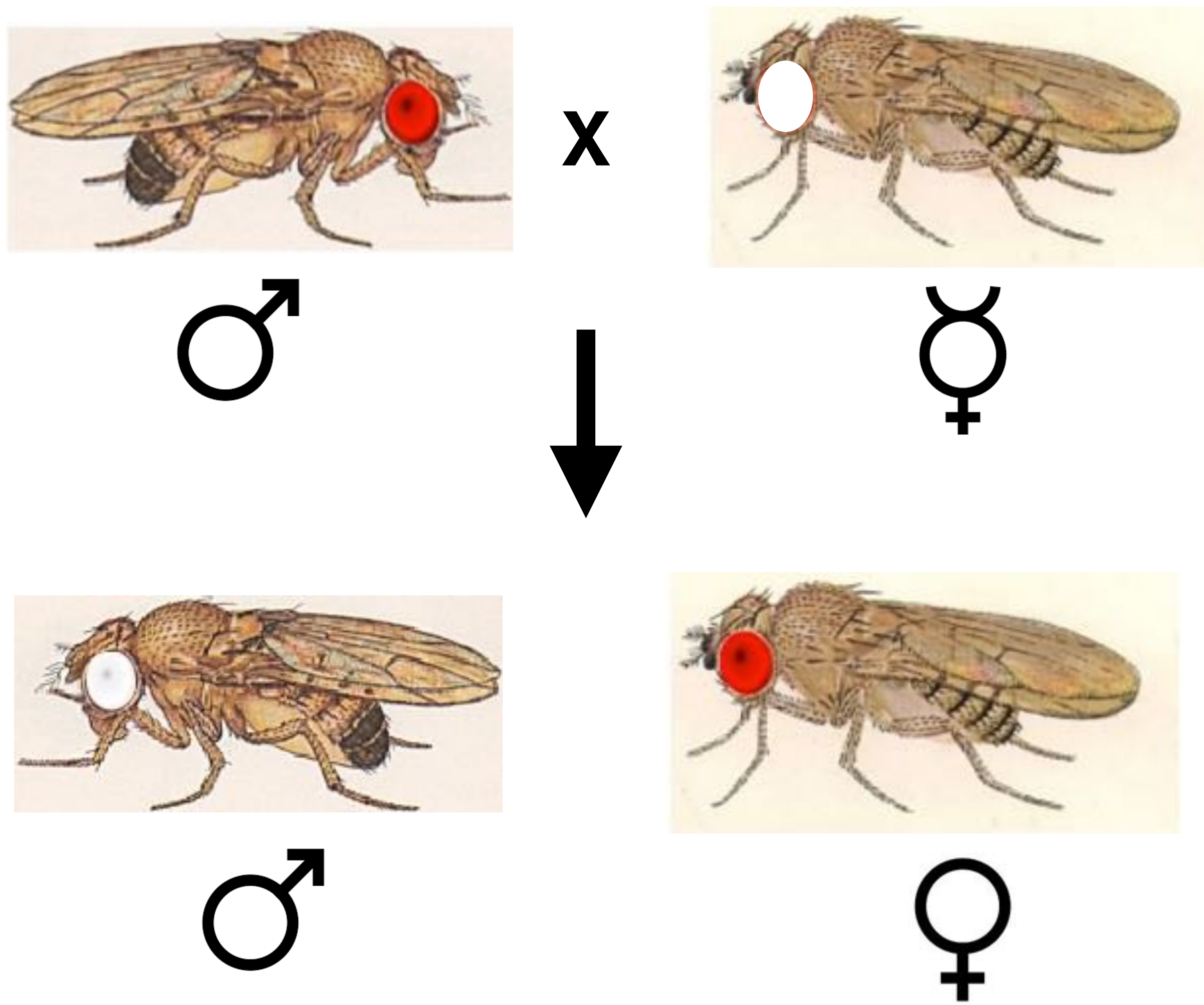
w^+ w

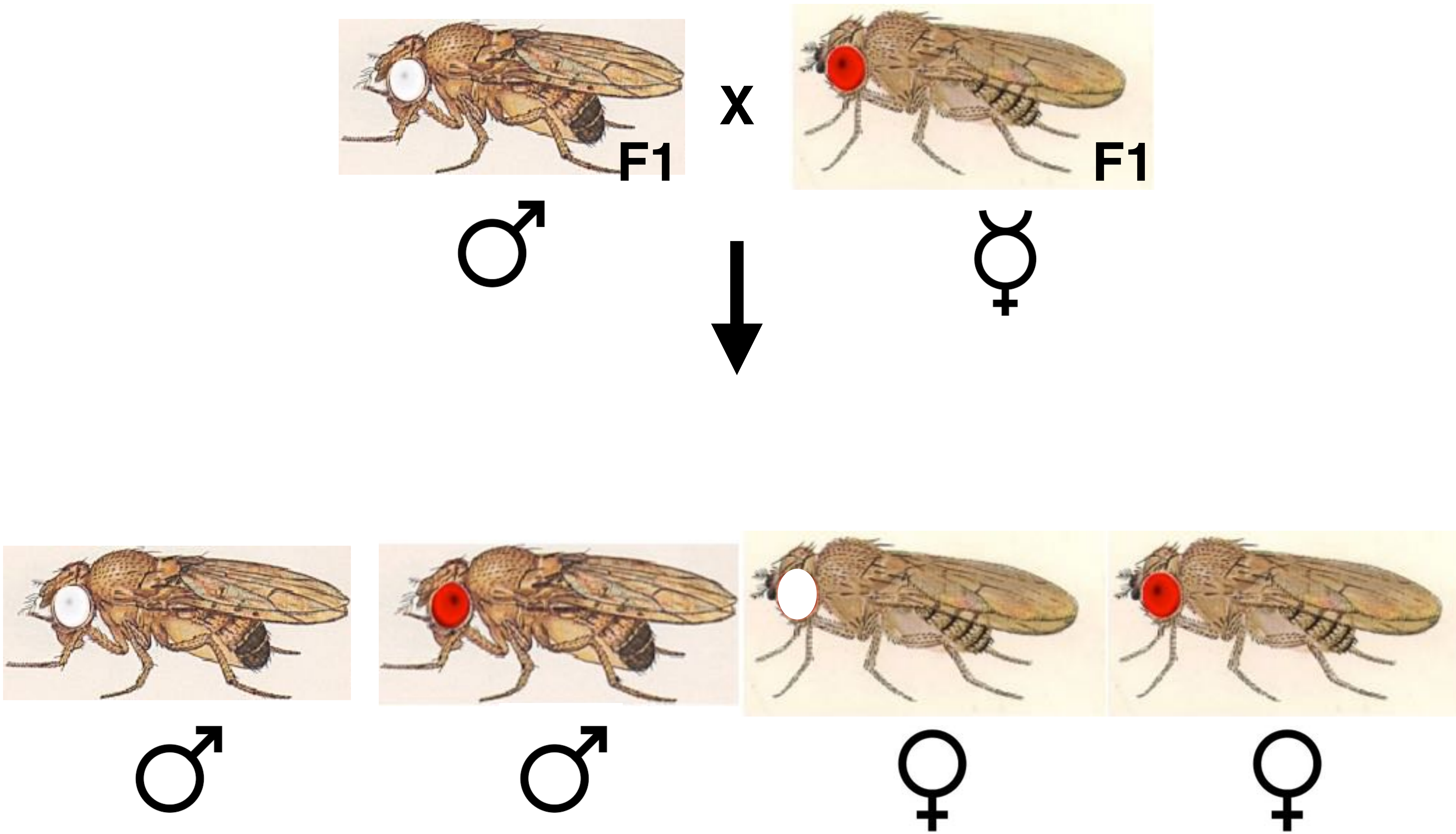


What is dominance relationship of *white* mutant allele?

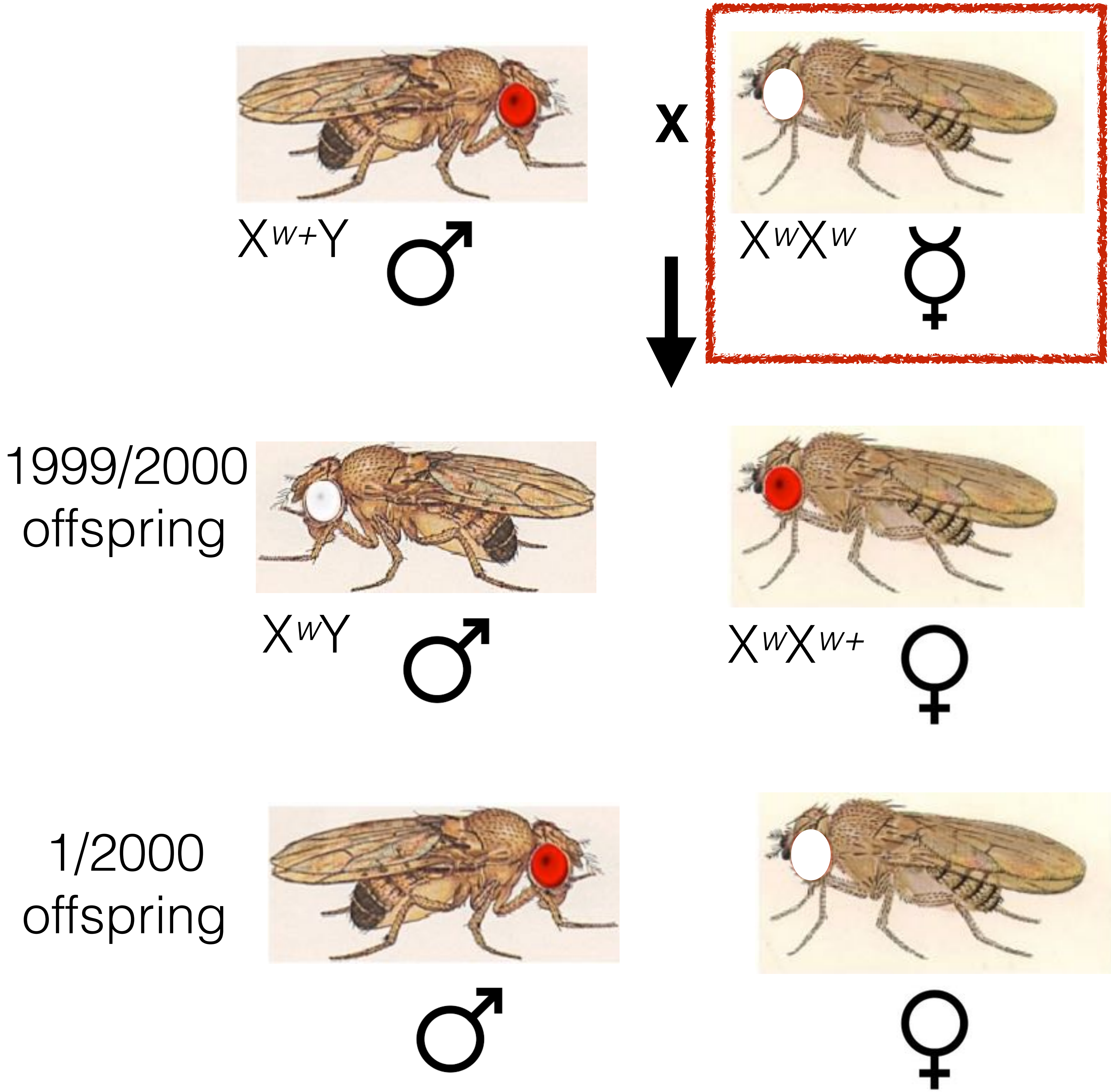

X
F1

The reciprocal cross





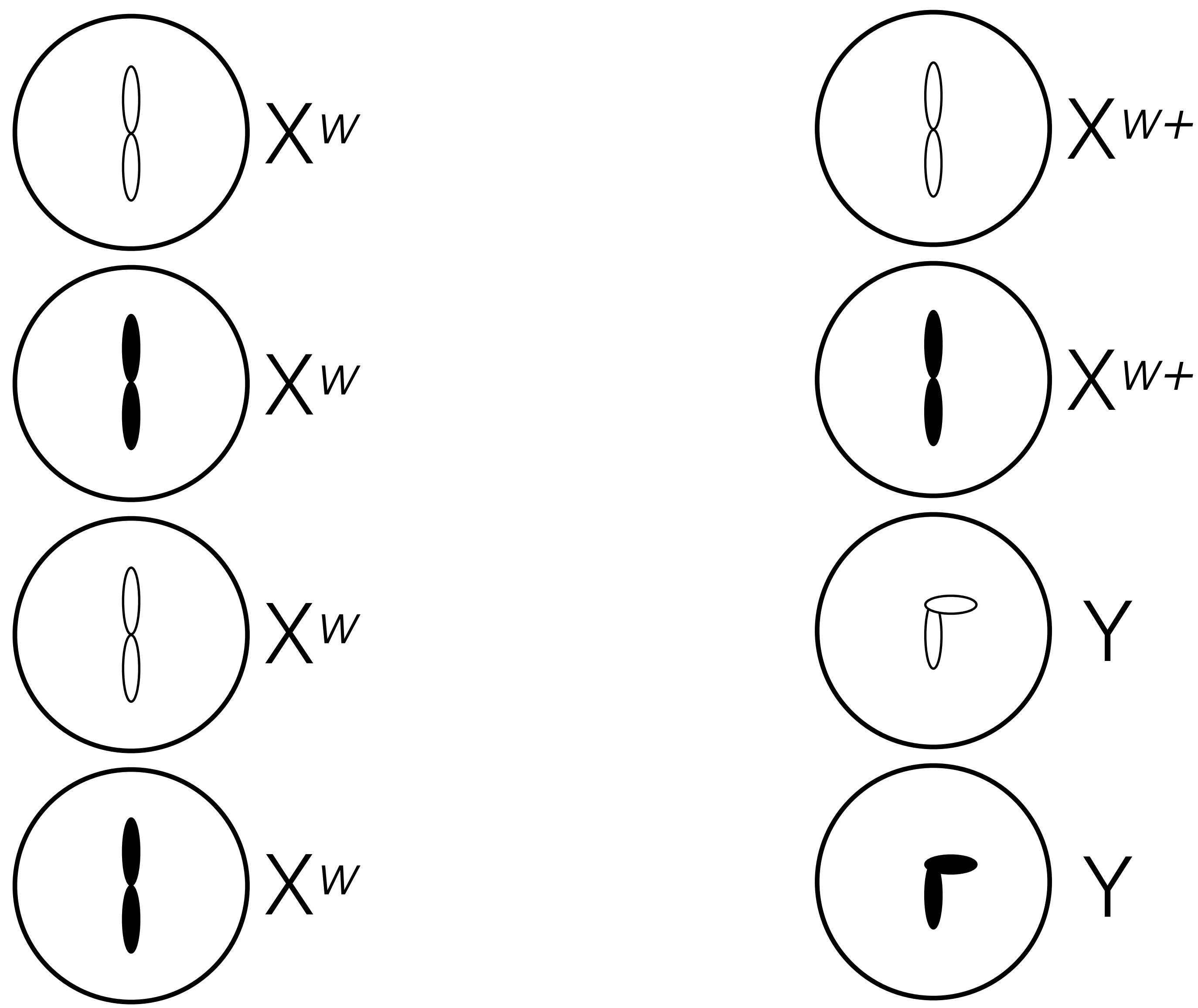
Equal ratios of each sex and eye color



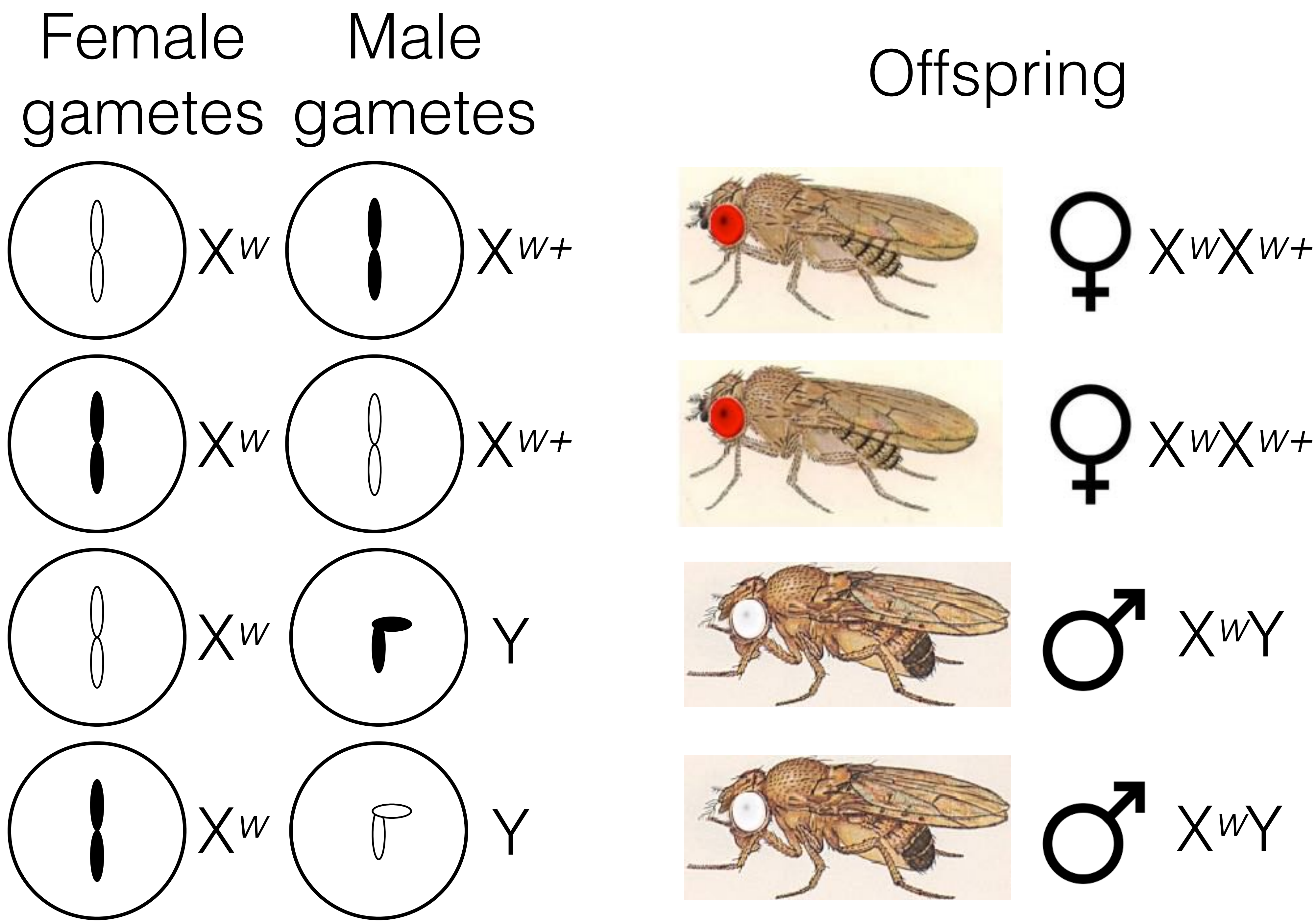
$X^{w+}Y$
♂
x
$X^{w}X^{w}$
☿
1999/2000 offspring
$X^{w}Y$
♂
$X^{w}X^{w+}$
♀
1/2000 offspring
♂
♀

Female gametes

Male gametes

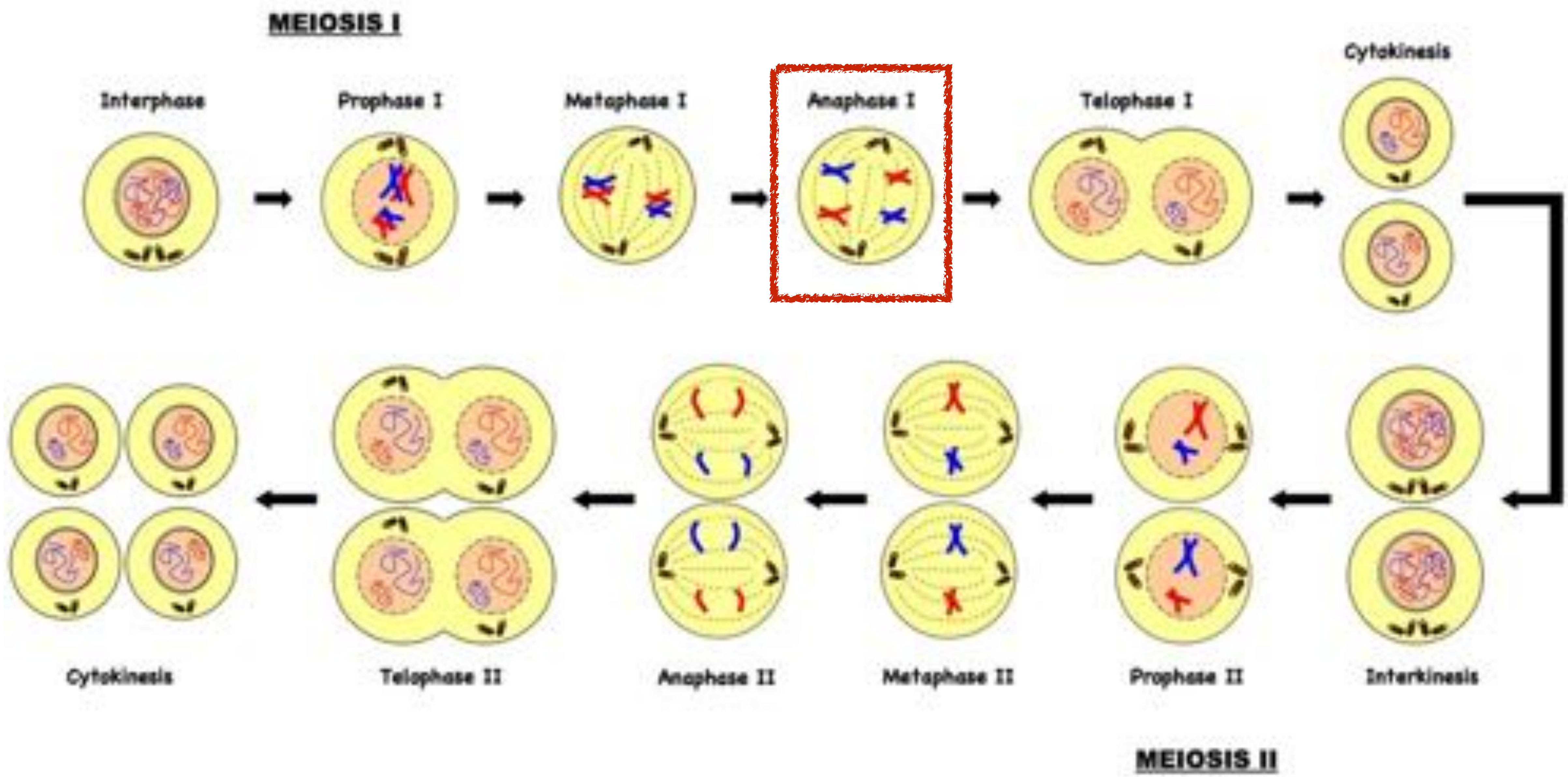


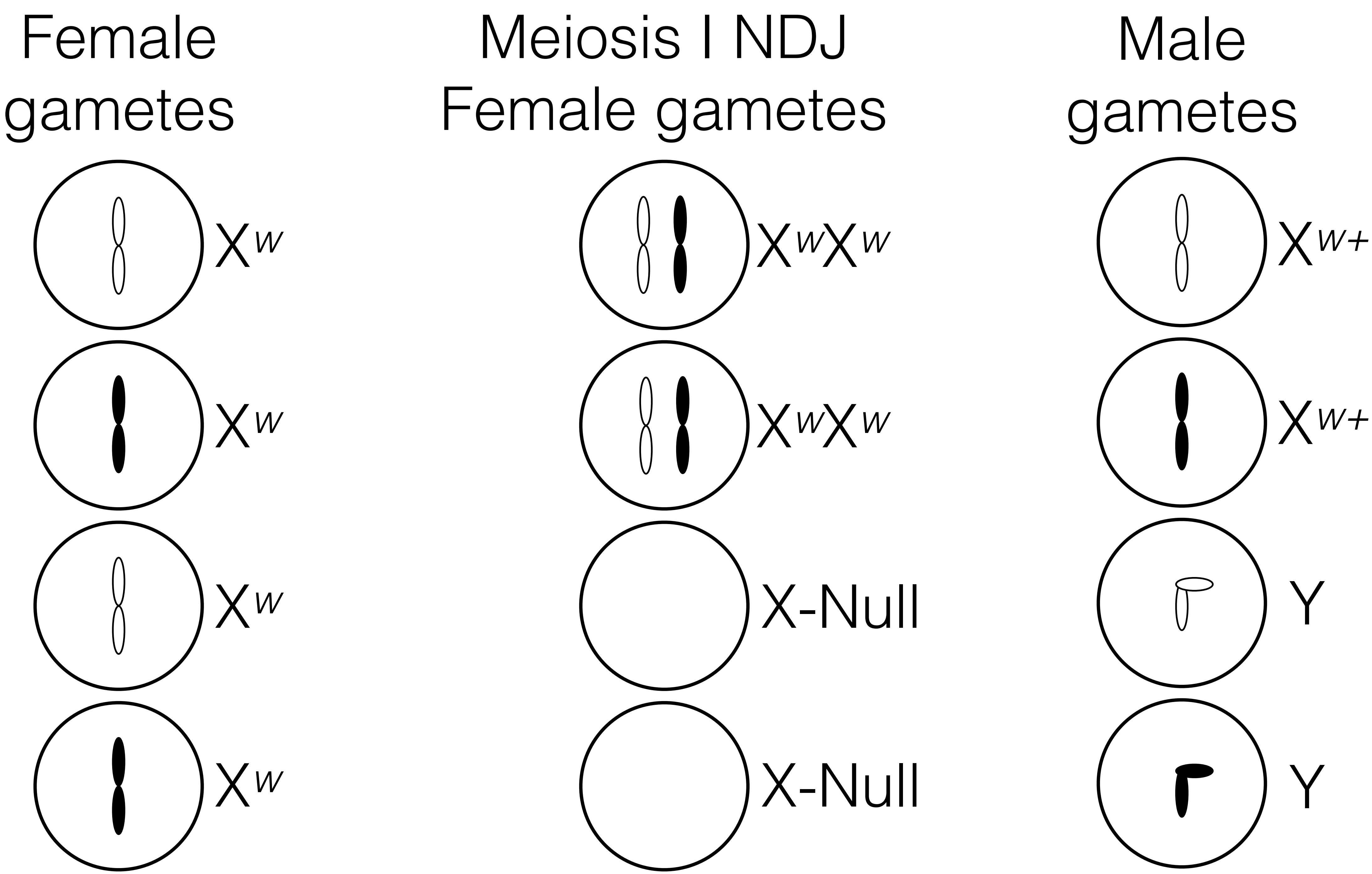
1999/2000 offspring



What is going on with the rare (1/2000) class?

Meiotic non-disjunction I

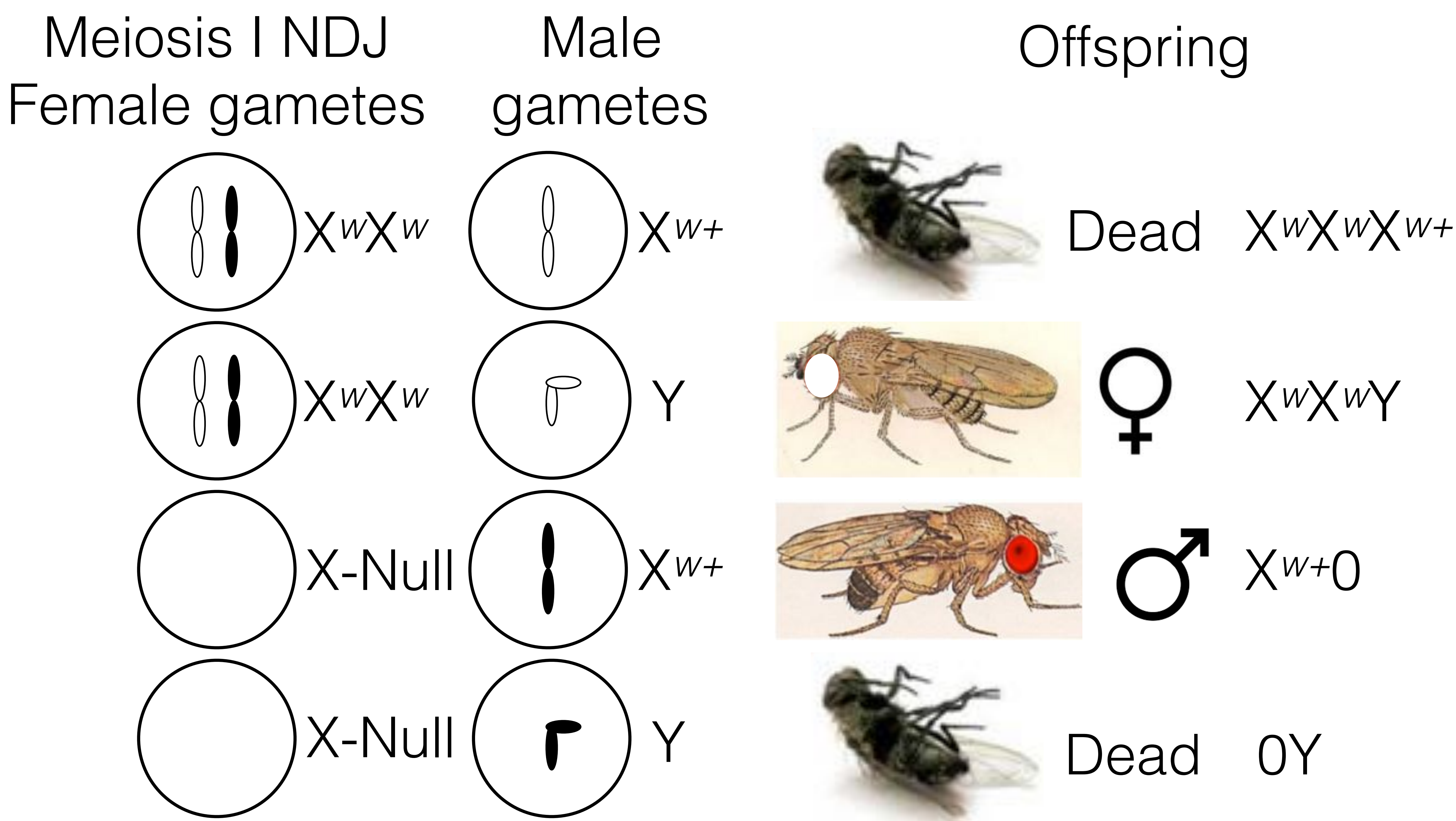




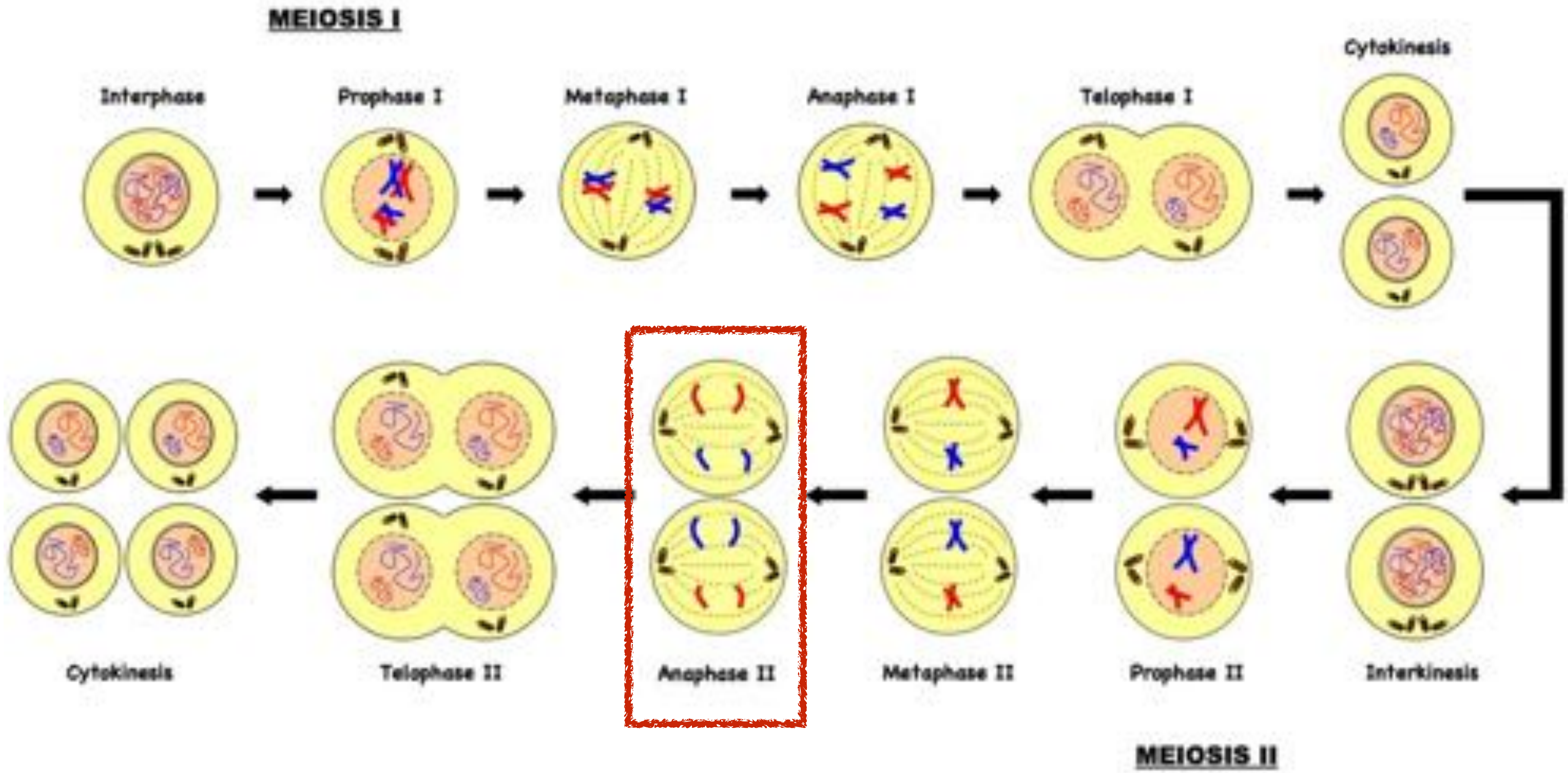
1999/2000 offspring $X^{w+}X^w$ X^wY

1/2000 offspring $X^{w+}0$ red male; X^wX^wY white female

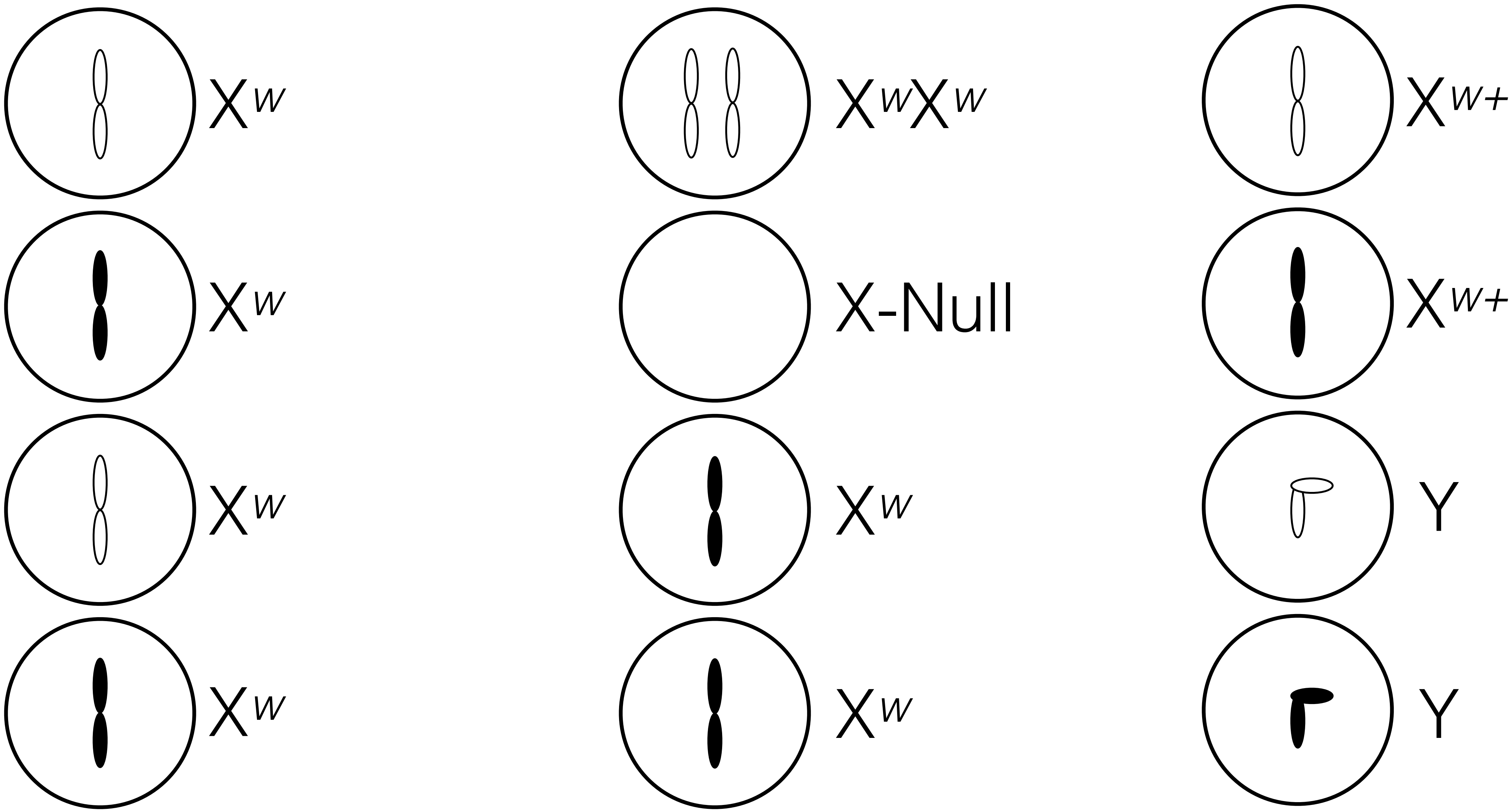
Two different types of female gametes


Meiosis I NDJ
Female gametes
Male
gametes
Offspring
X^wX^w
X^{w+}
Dead
$X^wX^wX^{w+}$
X^wX^w
Y
♀
X^wX^wY
X-Null
X^{w+}
♂
$X^{w+}0$
X-Null
Y
Dead
0Y

Meiotic non-disjunction II



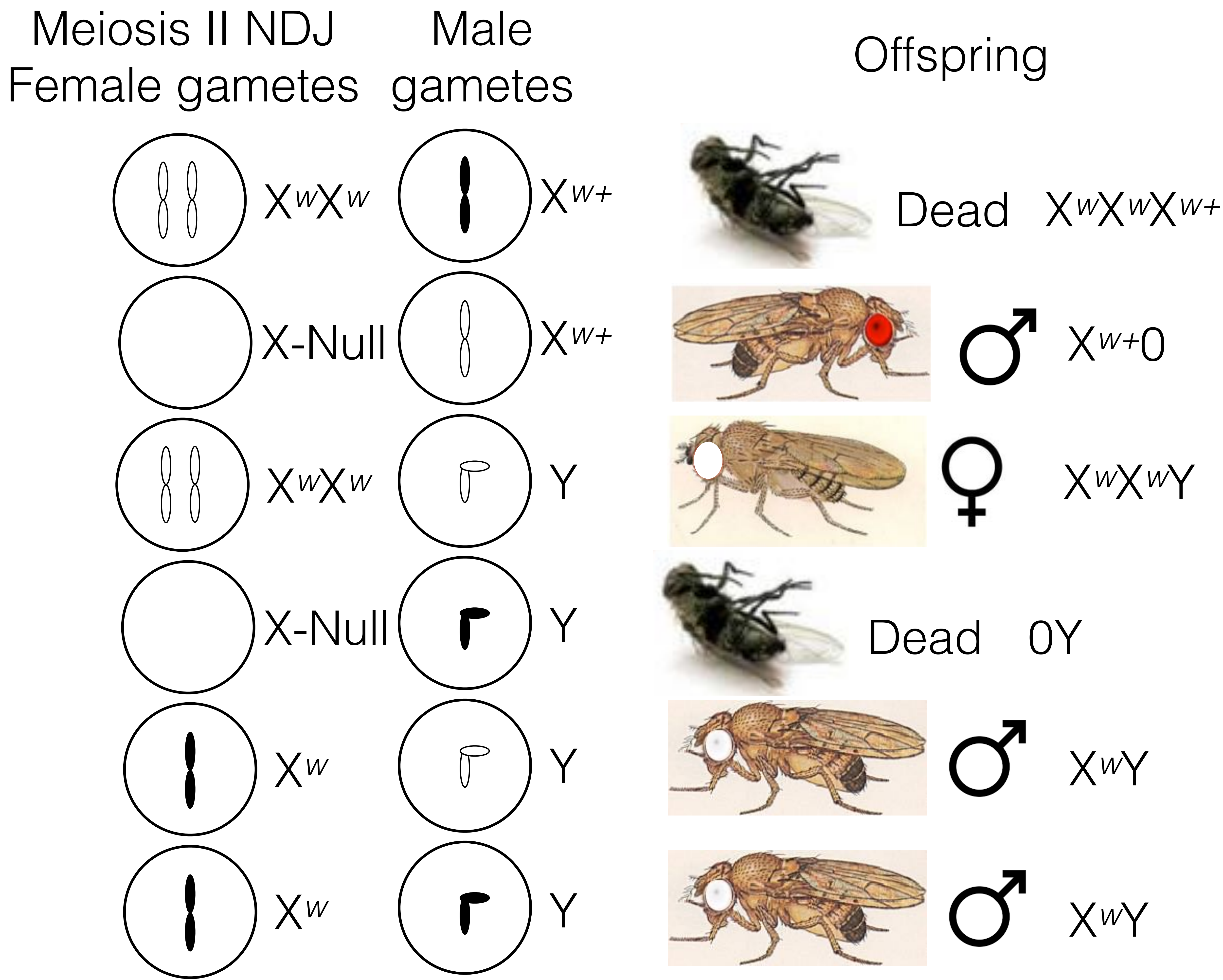
Female gametes | Meiosis II NDJ Female gametes | Male gametes



1999/2000 offspring: $X^{w+}X^{w}$, $X^{w}Y$

1/2000 offspring: $X^{w+}0$ red male; $X^{w}X^{w}Y$ white female

Three different types of female gametes

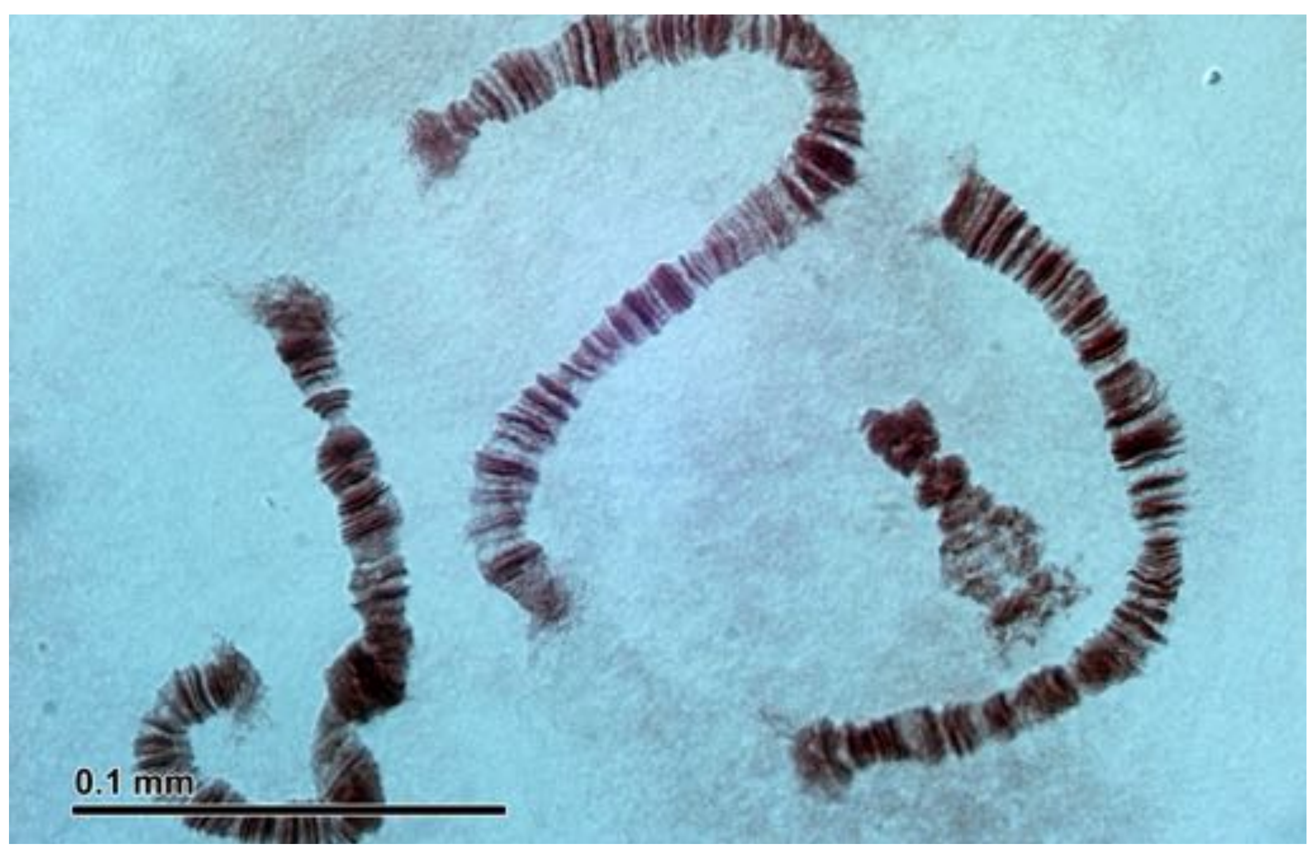

Meiosis II NDJ
Female gametes
Male
gametes
Offspring
$X^{w}X^{w}$
X^{w+}
Dead $X^{w}X^{w}X^{w+}$
X-Null
X^{w+}
♂ $X^{w+}0$
$X^{w}X^{w}$
Y
♀ $X^{w}X^{w}Y$
X-Null
Y
Dead 0Y
X^{w}
Y
♂ $X^{w}Y$
X^{w}
Y
♂ $X^{w}Y$

The connections between chromosome NDJ and a trait was made by Stevens and Bridges

Nettie Stevens

Calvin Bridges

Polytene chromosomes

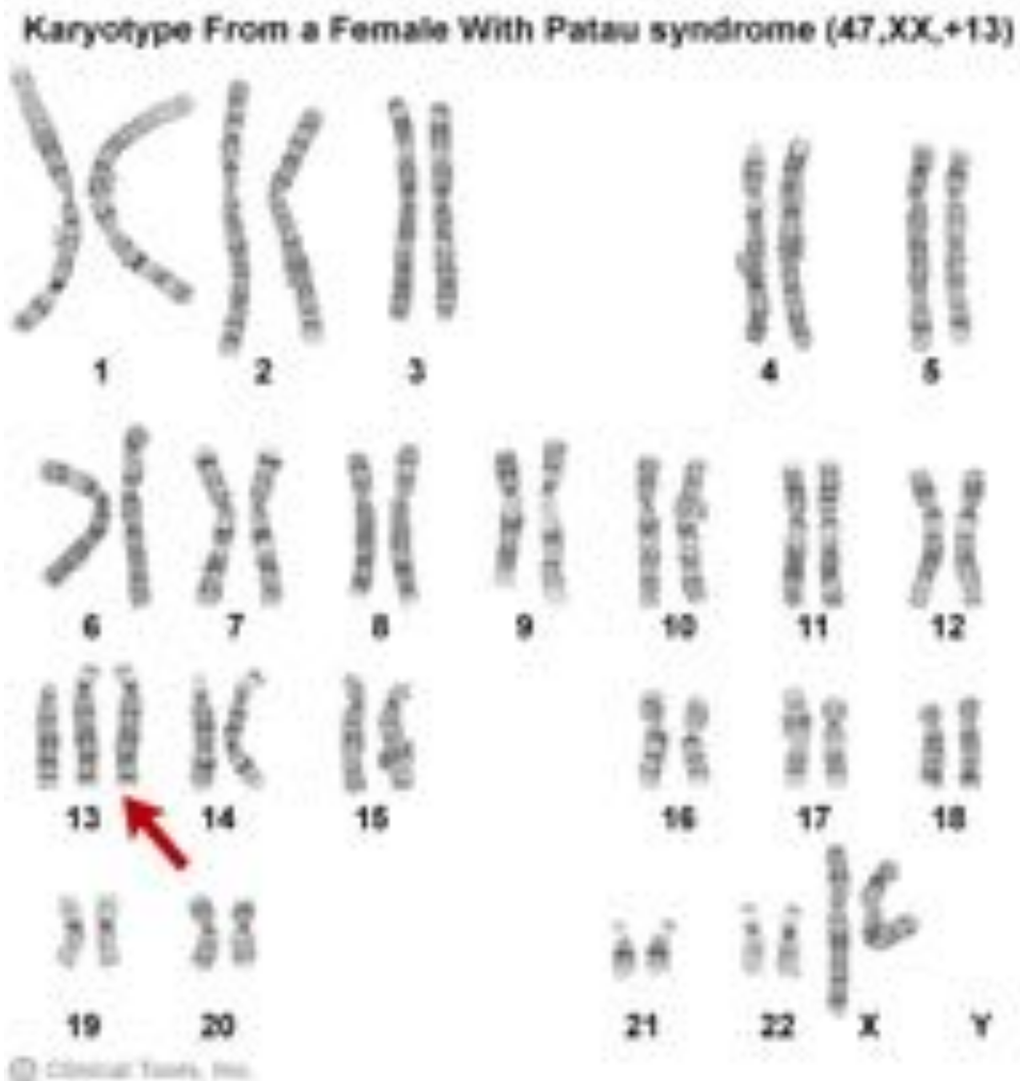


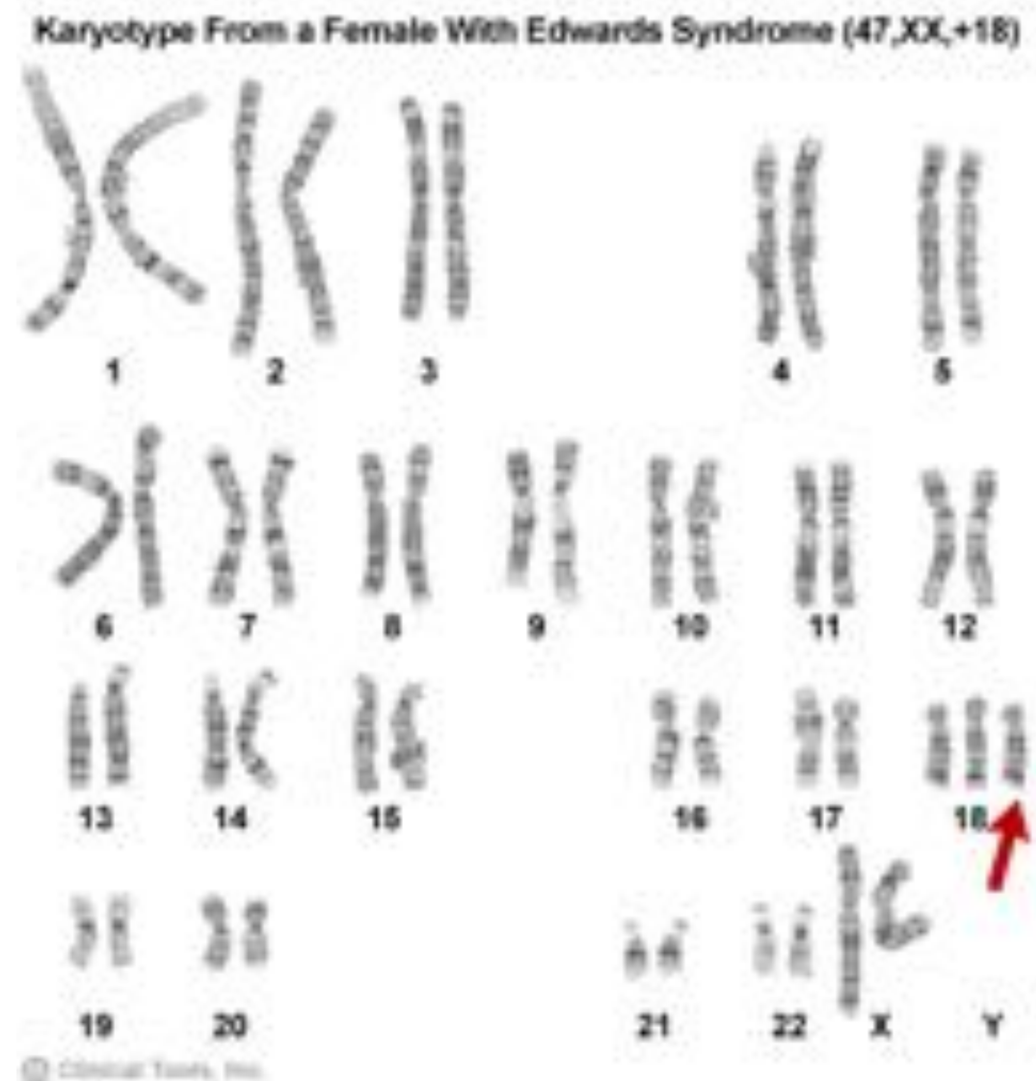
Why did the first cross not indicate to them that something weird was going on?

$X^{w}Y$ **X** $X^{w+}X^{w+}$

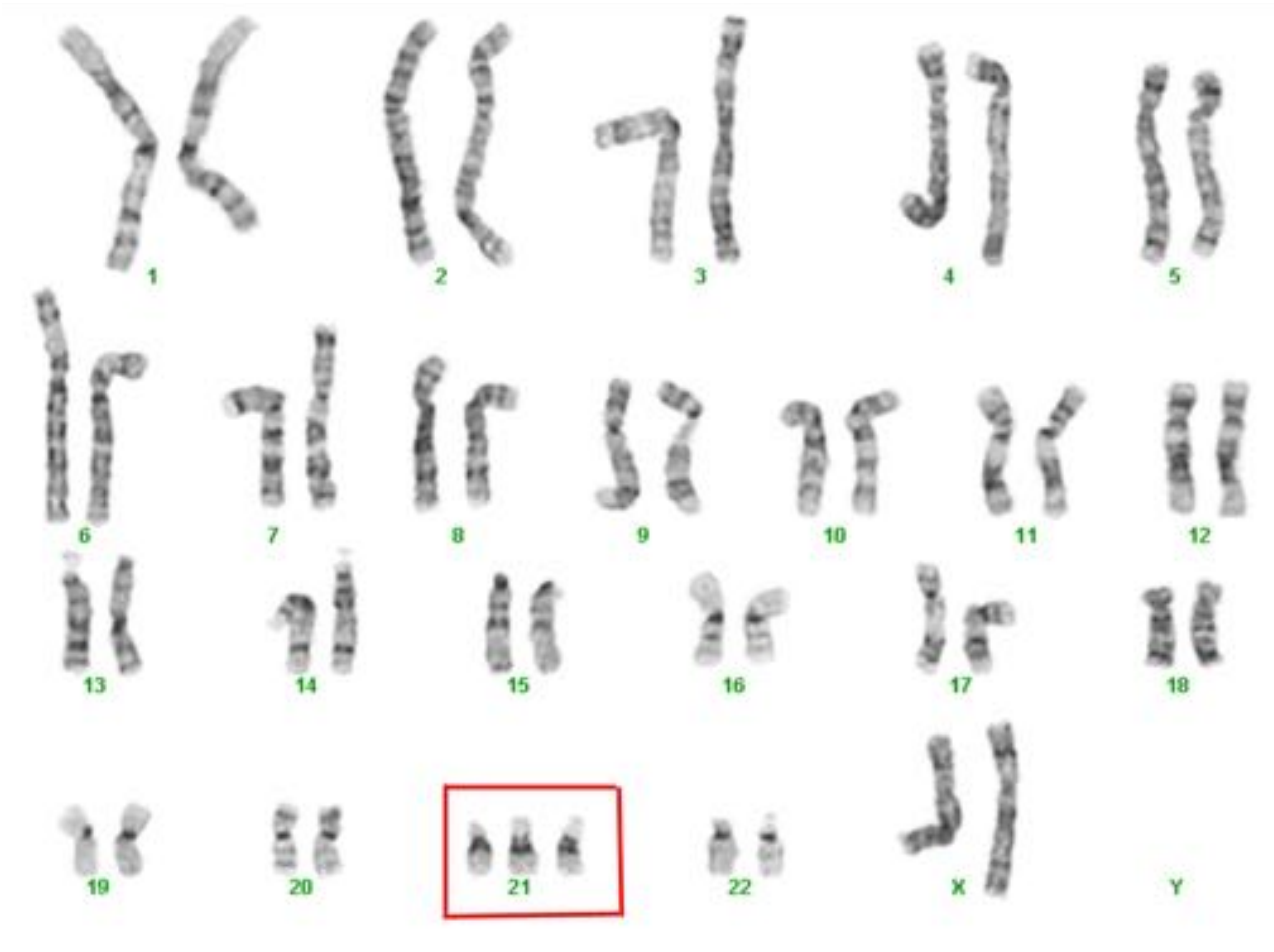
How can you tell the difference between Meiosis I NDJ and Meiosis II NDJ?

Non-disjunction is a relatively common error - not just the X chromosome
aneuploidy





Non-disjunction is a relatively common error - not just the X chromosome aneuploidy



Chromosomal abnormalities

A B C D E F

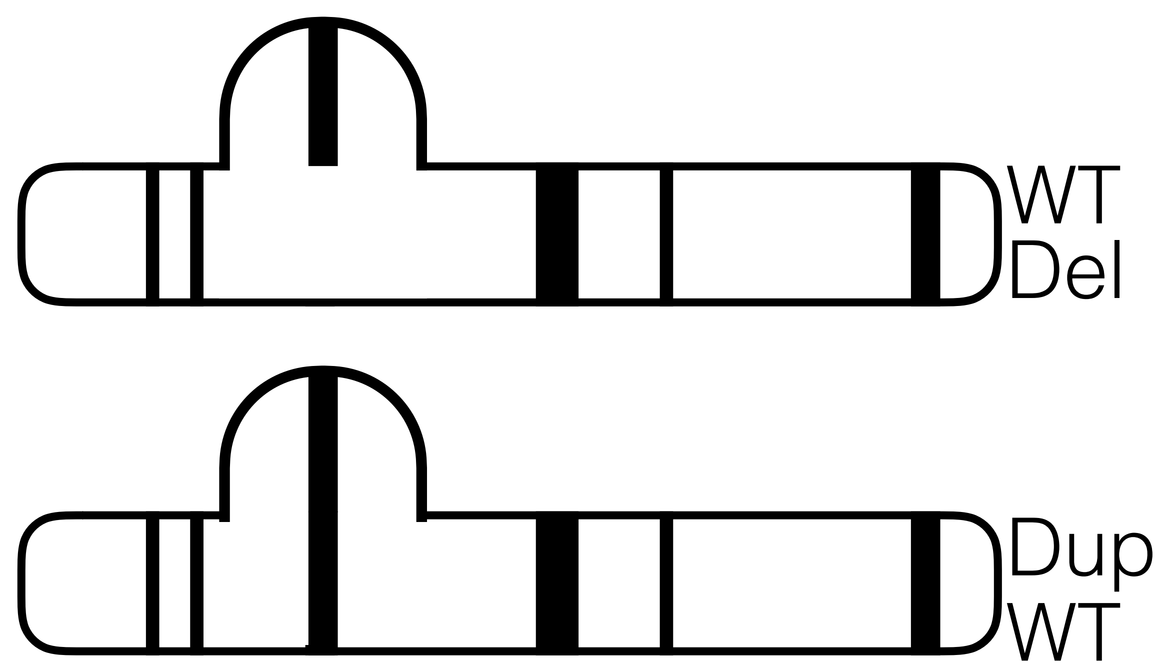
WT

A D E F

Deletion BC

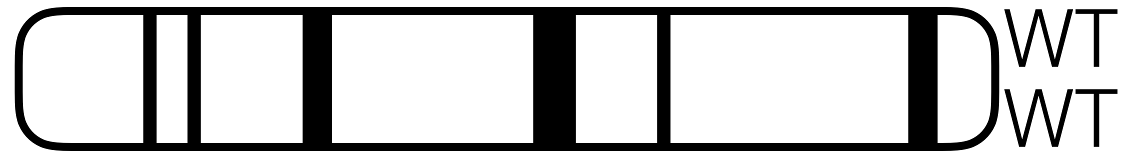
A B C B C D E F

Duplication BC



Chromosomal abnormalities

A B C D E F



WT

A D C B E F

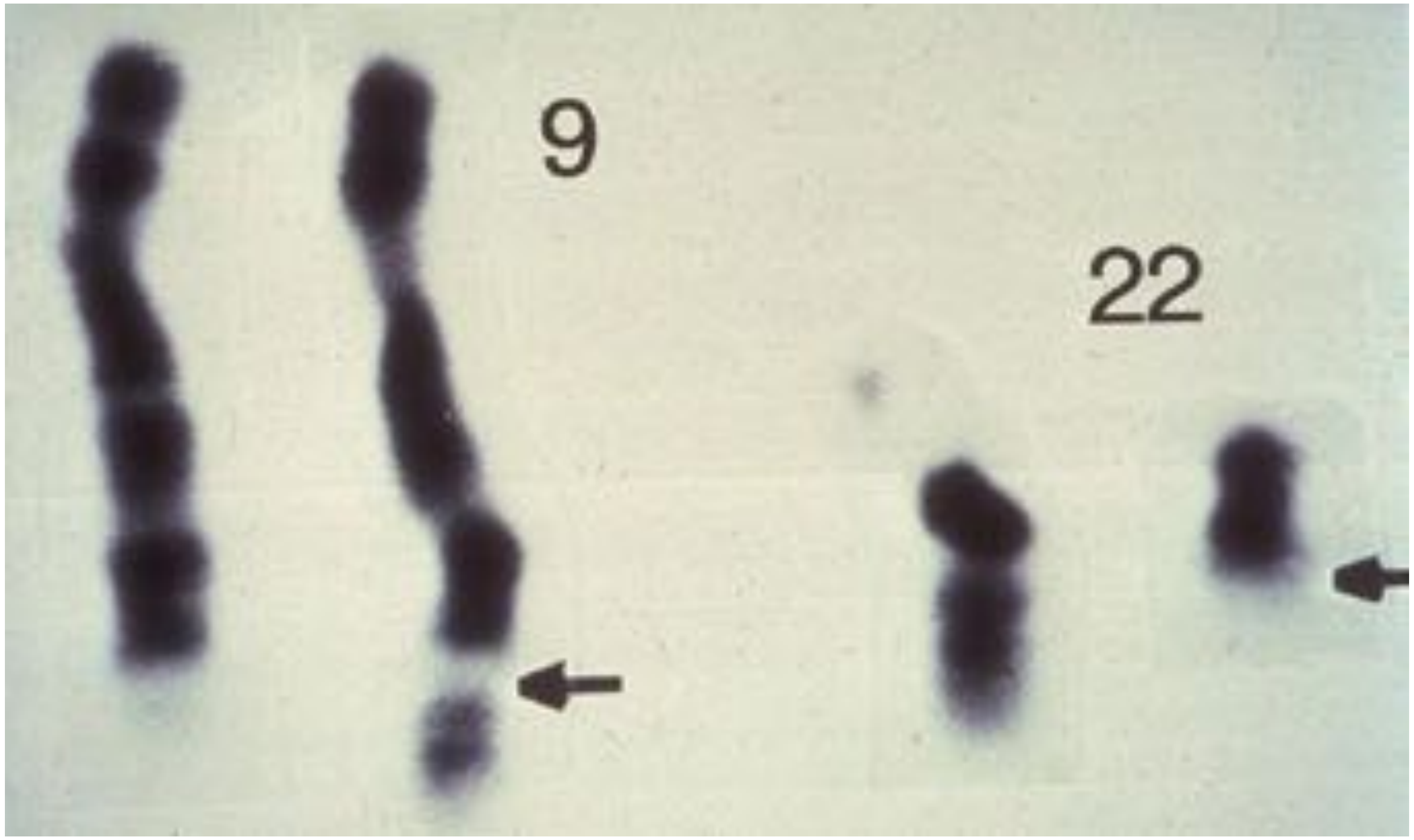
Inversion BCD

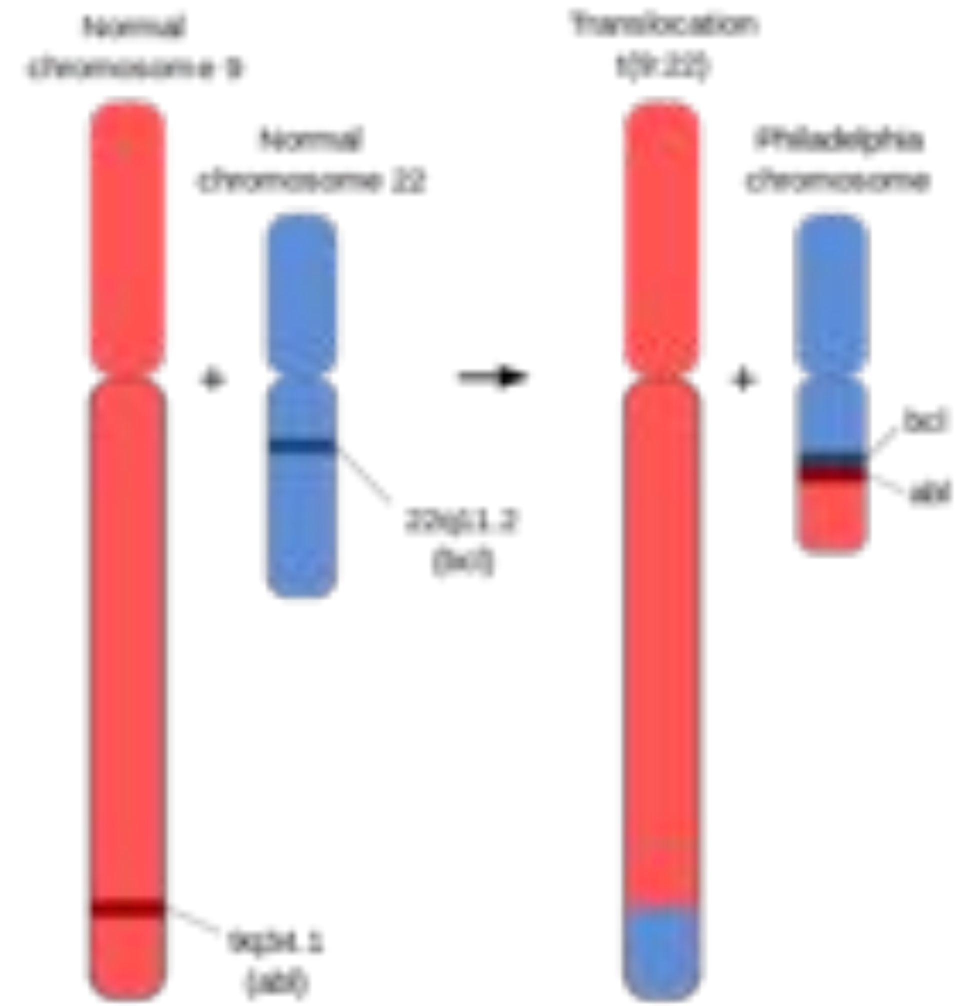
X Y Z D E F

Fusion of two chromosomes

Translocation ABC-XYZ

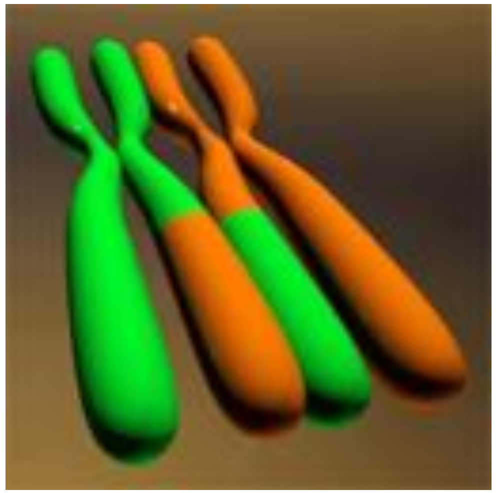
The Philadelphia chromosome: translocation





Janet Rowley

Recombination and mapping



Lecture 2

Reginald Punnett William Bateson

Bateson and Punnett's pea crosses

PPLL X **ppll**

Purple, Long ↓ Red, Short

PpLl

↓

P= purple flower
p= red flower
L= long pollen
l= short pollen

Bateson and Punnett's pea crosses

PPLL X **ppll**

Purple, Long — Red, Short

↓

PpLl

⊗ ↓

Phenotype	**Expected number**	**Expected ratio**
Purple Long	215	9
Purple short	71	3
red Long	71	3
red short	24	1

P= purple flower
p= red flower
L= long pollen
l= short pollen

Bateson and Punnett's pea crosses

PPLL X **ppll**

Purple, Long → Red, Short

PpLl

⊗ ↓

Phenotype	Expected number	Expected ratio	Observed number
Purple Long	215	9	284
Purple short	71	3	21
red Long	71	3	21
red short	24	1	55

P= purple flower
p= red flower
L= long pollen
l= short pollen

Bateson and Punnett's pea crosses

PPLL X **ppll**

Purple, Long ↓ Red, Short

PpLl

Parental = allelic combination found in parents
(most abundant classes, always paired)

Recombinant = allelic combination NOT found in parents
(least abundant classes, always paired)

Bateson and Punnett's pea crosses

PPLL X **ppll**

Purple, Long — Red, Short

↓

PpLl

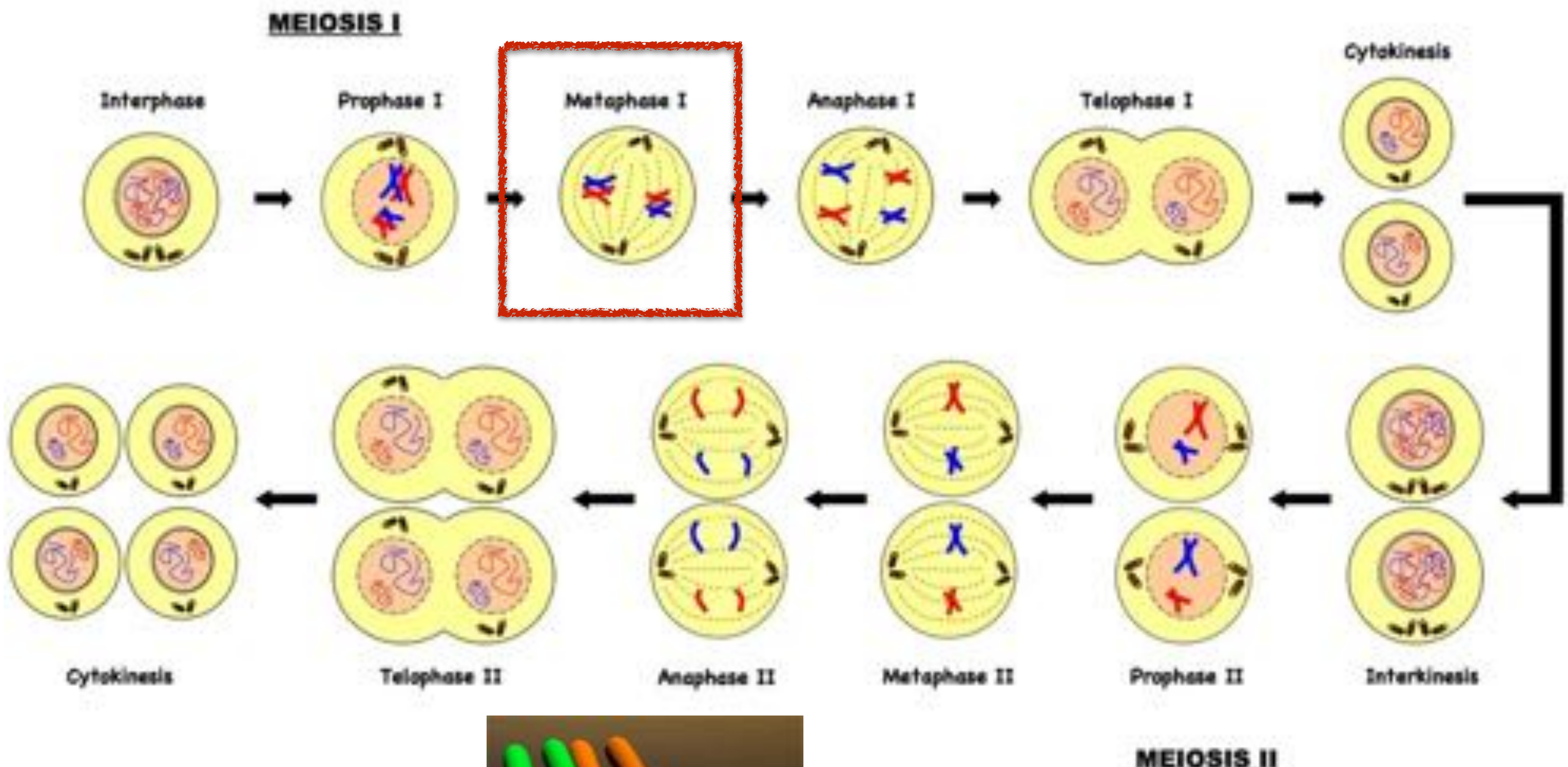
⊗ ↓

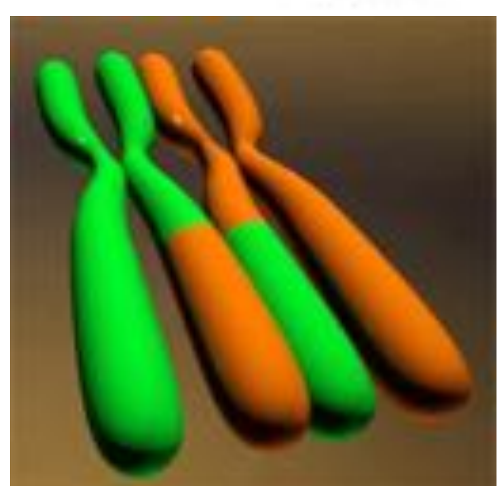
Phenotype	**Expected number**	**Expected ratio**	**Observed number**
Purple Long	215	9	284
Purple short	71	3	21
red Long	71	3	21
red short	24	1	55

P= purple flower
p= red flower
L= long pollen
l= short pollen

Which are recombinant and parental offspring?

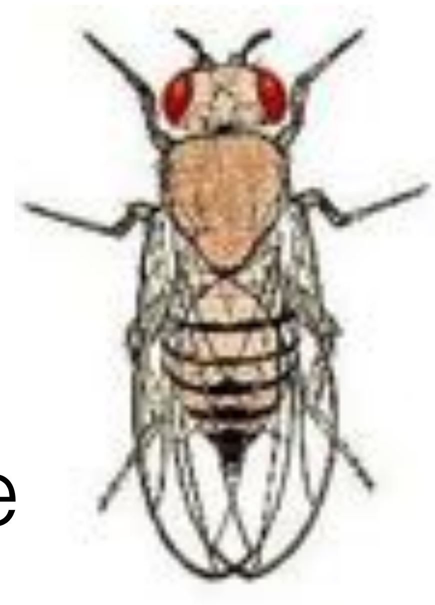
Meiosis: A reductional division in two acts





The fly room at Columbia

Wild-type



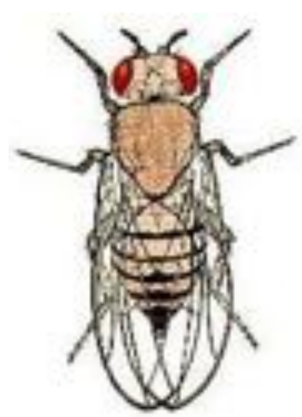
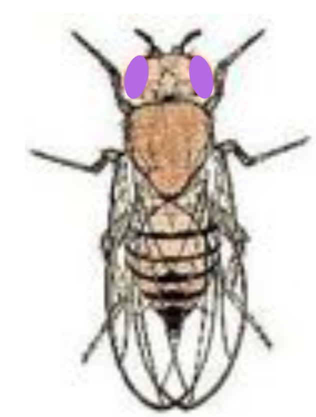
+ +

Purple eyes, vestigial wings

pr vg

☿ $\dfrac{pr\quad vg}{+\quad +}$ X $\dfrac{pr\quad vg}{pr\quad vg}$ ♂

↓

$\dfrac{+\quad +}{pr\quad vg}$	$\dfrac{pr\quad vg}{pr\quad vg}$	$\dfrac{+\quad vg}{pr\quad vg}$	$\dfrac{pr\quad +}{pr\quad vg}$
			
P	P	R	R
1339	1195	151	154

Expectation is equal proportion of each class

Total = 2839

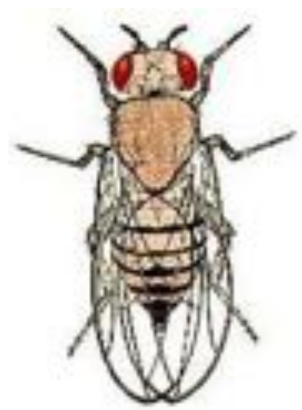
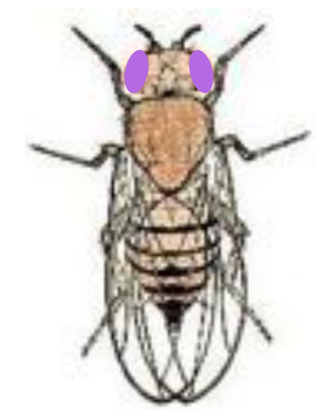
Alfred Sturtevant

$$\frac{\text{Number of recombinants}}{\text{Total progeny}} \times 100 = \text{Recombination frequency}$$

1% RF = 1 map unit = 1 centiMorgan

☿ $\dfrac{pr \quad vg}{+ \quad +}$ X $\dfrac{pr \quad vg}{pr \quad vg}$ ♂

↓

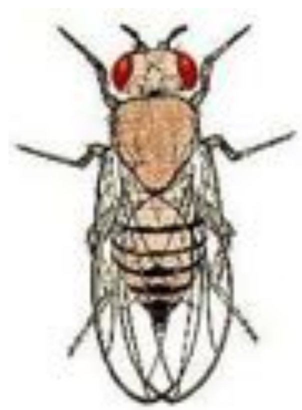
$\dfrac{+ \quad +}{pr \quad vg}$	$\dfrac{pr \quad vg}{pr \quad vg}$	$\dfrac{+ \quad vg}{pr \quad vg}$	$\dfrac{pr \quad +}{pr \quad vg}$
			
P	P	R	R
1339	1195	151	154

$$\frac{\textbf{Number of recombinants}}{\textbf{Total progeny}} \times \textbf{100} = \textbf{Recombination frequency}$$

Total = 2839

☿ $\dfrac{pr \quad vg}{+ \quad +}$ X $\dfrac{pr \quad vg}{pr \quad vg}$ ♂

↓

$\dfrac{+ \quad +}{pr \quad vg}$	$\dfrac{pr \quad vg}{pr \quad vg}$	$\dfrac{+ \quad vg}{pr \quad vg}$	$\dfrac{pr \quad +}{pr \quad vg}$
			
P	P	R	R
1339	1195	151	154

$$\frac{\mathbf{151+154}}{\mathbf{2839}} \times \mathbf{100} = \mathbf{11\%}$$

Total = 2839

Recombination is the exchange of genetic material between homologous chromosomes

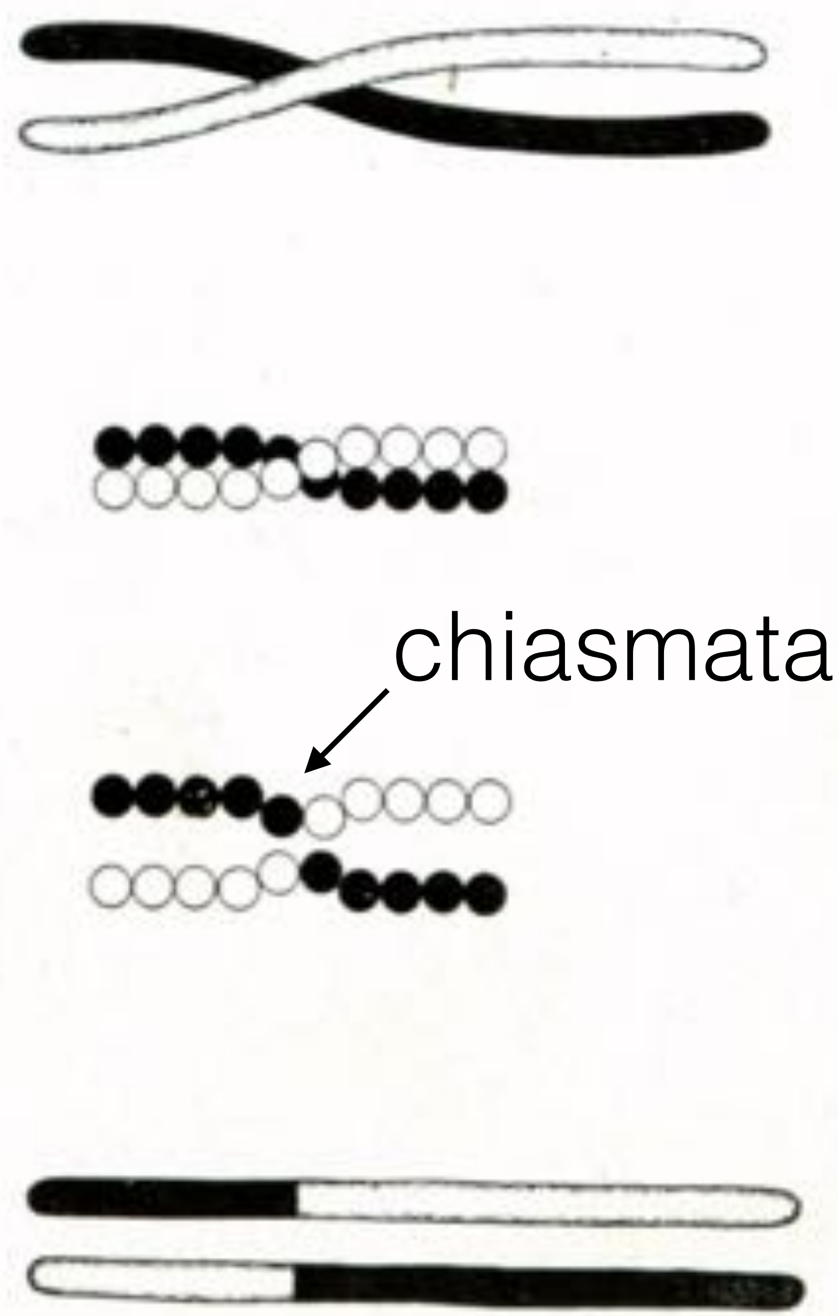
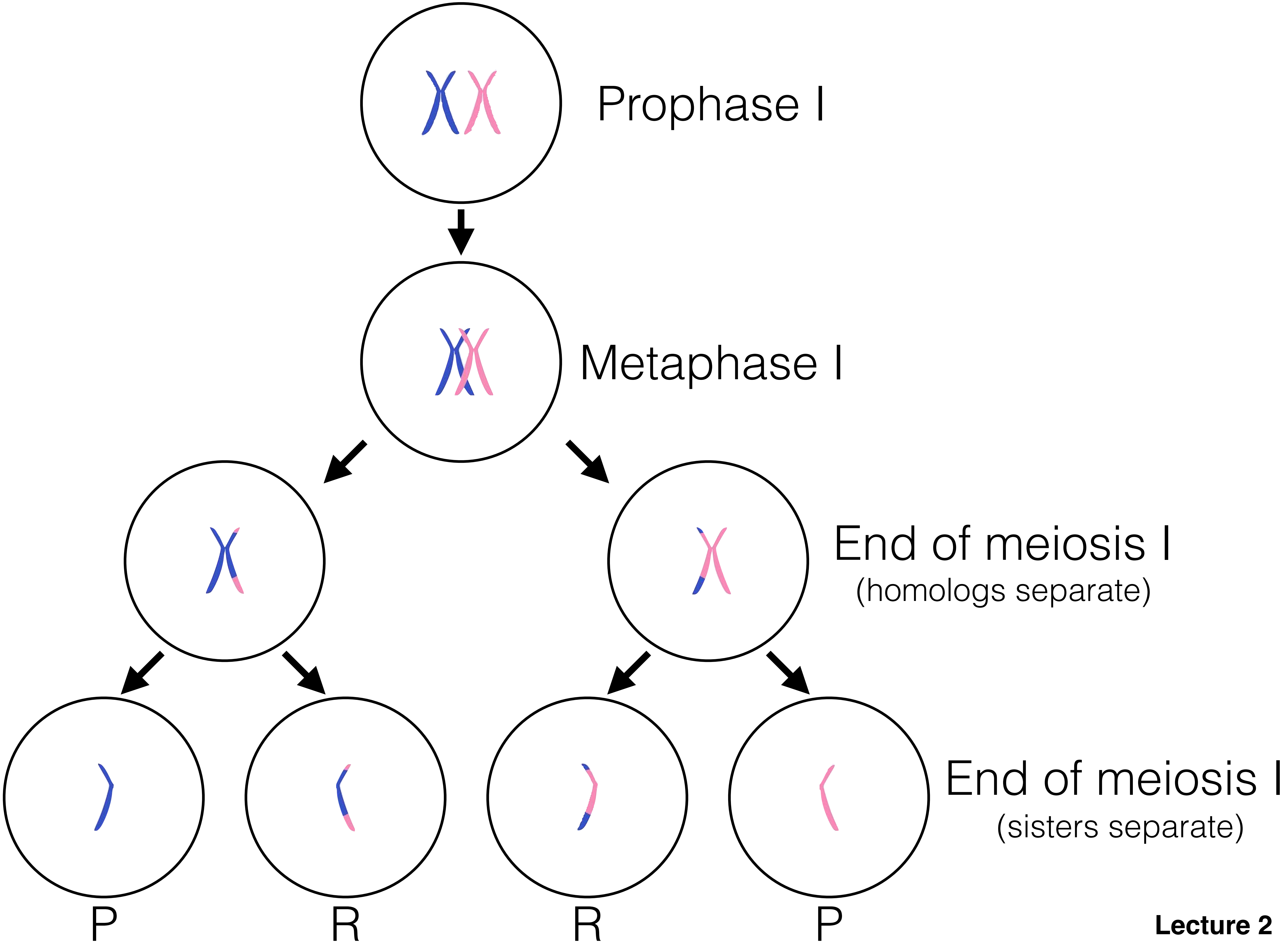


FIG. 64. Scheme to illustrate a method of crossing over of the chromosomes.


Prophase I
Metaphase I
End of meiosis I
(homologs separate)
End of meiosis II
(sisters separate)
P
R
R
P

Independent assortment defines the limit of linkage at 50 cM

AaBb X aabb

↓

AaBb	Aabb	aaBb	aabb
P	R	R	P

All four classes occur in equal ratios

$$\frac{\textbf{Number of recombinants}}{\textbf{Total progeny}} \times \mathbf{100} = \textbf{Recombination frequency}$$

Independent assortment defines the limit of linkage at 50 cM

AaBb X aabb

↓

AaBb	Aabb	aaBb	aabb
P	R	R	P

All four classes occur in equal ratios

$$\frac{\mathbf{2*x}}{\mathbf{2*x + 2*x}} \quad \times \quad \mathbf{100} \quad = \quad \mathbf{50\%}$$

A three-factor cross

$$\frac{v\quad +\quad +}{v\quad +\quad +}\ ♂ \quad \mathbf{x} \quad \frac{+\quad cv\quad ct}{+\quad cv\quad ct}\ ☿$$

$$\downarrow$$

$$\frac{+\quad cv\quad ct}{v\quad +\quad +}\ ☿ \quad \mathbf{x} \quad \frac{v\quad cv\quad ct}{v\quad cv\quad ct}\ ♂$$

$$\downarrow$$

Eye Phenotype	Crossvein Phenotype	Cut Phenotype	Number of offspring
Red	No crossvein	Cut wing	580
Vermillion	Crossvein	Normal wing	592
Red	Crossvein	Cut wing	40
Vermillion	No crossvein	Normal wing	45
Red	Crossvein	Normal wing	94
Vermillion	No crossvein	Cut wing	89
Red	No crossvein	Normal wing	5
Vermillion	Crossvein	Cut wing	3

v = vermillion eyes
ct = cut wings
cv= crossveinless wings
+ = red eyes and normal wings

$$\frac{+\ \ cv\ \ ct}{v\ \ +\ \ +} ♀ \times \frac{v\ \ cv\ \ ct}{v\ \ cv\ \ ct} ♂$$

Eye Phenotype	Crossvein Phenotype	Cut Phenotype	Number of offspring
Red	No crossvein	Cut wing	580
Vermillion	Crossvein	Normal wing	592
Red	Crossvein	Cut wing	40
Vermillion	No crossvein	Normal wing	45
Red	Crossvein	Normal wing	94
Vermillion	No crossvein	Cut wing	89
Red	No crossvein	Normal wing	5
Vermillion	Crossvein	Cut wing	3

$+\ \ cv\ \ ct$ **P**

$v\ \ +\ \ +$ **P**

1. Determine parental class, label

v = vermillion eyes
ct = cut wings
cv= crossveinless wings
+ = red eyes and normal wings

$$\frac{+\quad cv\quad ct}{v\quad +\quad +}\ ☿\quad \mathbf{x}\quad \frac{v\quad cv\quad ct}{v\quad cv\quad ct}\ ♂$$

Eye Phenotype	Crossvein Phenotype	Cut Phenotype	Number of offspring		
Red	No crossvein	Cut wing	580	+ *cv* *ct*	**P**
Vermillion	Crossvein	Normal wing	592	*v* + +	**P**
Red	Crossvein	Cut wing	40		**R**
Vermillion	No crossvein	Normal wing	45		**R**
Red	Crossvein	Normal wing	94		**R**
Vermillion	No crossvein	Cut wing	89		**R**
Red	No crossvein	Normal wing	5		**R**
Vermillion	Crossvein	Cut wing	3		**R**

1. Determine parental class, label
2. Are all classes present?

v = vermillion eyes
ct = cut wings
cv= crossveinless wings
+ = red eyes and normal wings

$$\frac{+\ \ cv\ \ ct}{v\ \ +\ \ +}\ ♀\ \ \mathbf{x}\ \ \frac{v\ \ cv\ \ ct}{v\ \ cv\ \ ct}\ ♂$$

Eye Phenotype	Crossvein Phenotype	Cut Phenotype	Number of offspring		
Red	No crossvein	Cut wing	580	*+ cv ct*	**P**
Vermillion	Crossvein	Normal wing	592	*v + +*	**P**
Red	Crossvein	Cut wing	40		**R**
Vermillion	No crossvein	Normal wing	45		**R**
Red	Crossvein	Normal wing	94		**R**
Vermillion	No crossvein	Cut wing	89		**R**
Red	No crossvein	Normal wing	5	*+ cv +*	**R**
Vermillion	Crossvein	Cut wing	3	*v + ct*	**R**

1. Determine parental class, label
2. Are all classes present?
3. Least abundant class is double recombinant, tells gene in middle

v = vermillion eyes
ct = cut wings
cv= crossveinless wings
\+ = red eyes and normal wings

$$\frac{+\quad cv\quad ct}{v\quad +\quad +}\ ♀\ \times\ \frac{v\quad cv\quad ct}{v\quad cv\quad ct}\ ♂$$

Eye Phenotype	Crossvein Phenotype	Cut Phenotype	Number of offspring
Red	No crossvein	Cut wing	580
Vermillion	Crossvein	Normal wing	592
Red	Crossvein	Cut wing	40
Vermillion	No crossvein	Normal wing	45
Red	Crossvein	Normal wing	94
Vermillion	No crossvein	Cut wing	89
Red	No crossvein	Normal wing	5
Vermillion	Crossvein	Cut wing	3

+	cv	ct	**P**
v	+	+	**P**
+	+	ct	**R**
v	cv	+	**R**
+	+	+	**R**
v	cv	ct	**R**
+	cv	+	**R**
v	+	ct	**R**

1. Determine parental class, label
2. Are all classes present?
3. Least abundant class is double recombinant, tells gene in middle
4. Write out the genotypes of the offspring

v = vermillion eyes
ct = cut wings
cv= crossveinless wings
+ = red eyes and normal wings

$$\frac{+\ \ cv\ \ ct}{v\ \ +\ \ +} ♀ \times \frac{v\ \ cv\ \ ct}{v\ \ cv\ \ ct} ♂$$

Eye Phenotype	Crossvein Phenotype	Cut Phenotype	Number of offspring		
Red	No crossvein	Cut wing	580	+ cv ct	P
Vermillion	Crossvein	Normal wing	592	v + +	P
Red	Crossvein	Cut wing	40	+ + ct	R
Vermillion	No crossvein	Normal wing	45	v cv +	R
Red	Crossvein	Normal wing	94	+ + +	R
Vermillion	No crossvein	Cut wing	89	v cv ct	R
Red	No crossvein	Normal wing	5	+ cv +	R
Vermillion	Crossvein	Cut wing	3	v + ct	R

1448 total progeny

1. Determine parental class, label
2. Are all classes present?
3. Least abundant class is double recombinant, tells gene in middle
4. Write out the genotypes of the offspring
5. Calculate distance from one gene to middle gene ***v* to *ct***

v = vermillion eyes
ct = cut wings
cv= crossveinless wings
\+ = red eyes and normal wings

$$\frac{\mathbf{94+89+5+3}}{\mathbf{1448}} \times \mathbf{100} = \mathbf{13.2\%}$$

$$\frac{+\quad cv\quad ct}{v\quad +\quad +} ♀ \times \frac{v\quad cv\quad ct}{v\quad cv\quad ct} ♂$$

Eye Phenotype	Crossvein Phenotype	Cut Phenotype	Number of offspring
Red	No crossvein	Cut wing	580
Vermillion	Crossvein	Normal wing	592
Red	Crossvein	Cut wing	40
Vermillion	No crossvein	Normal wing	45
Red	Crossvein	Normal wing	94
Vermillion	No crossvein	Cut wing	89
Red	No crossvein	Normal wing	5
Vermillion	Crossvein	Cut wing	3

+ cv ct **P**
v + + **P**
+ + ct **R**
v cv + **R**
+ + + **R**
v cv ct **R**
+ cv + **R**
v + ct **R**

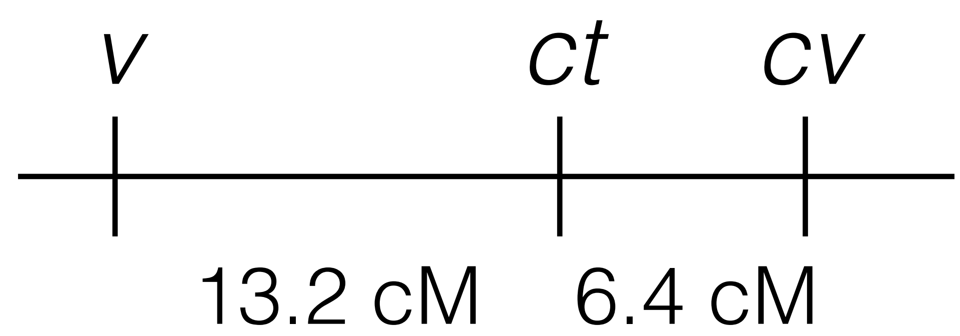
1448 total progeny

1. Determine parental class, label
2. Are all classes present?
3. Least abundant class is double recombinant, tells gene in middle
4. Write out the genotypes of the offspring
5. Calculate distance from one gene to middle gene
6. Calculate distance from the other gene to middle gene ***cv* to *ct***

v = vermillion eyes
ct = cut wings
cv= crossveinless wings
+ = red eyes and normal wings

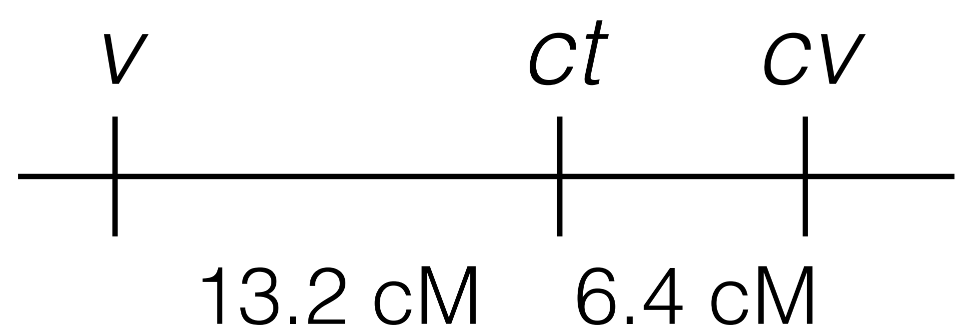
$$\frac{\mathbf{40+45+5+3}}{\mathbf{1448}} \times \mathbf{100} = \mathbf{6.4\%}$$

Our first genetic map



1. Order by least abundant class
2. Arbitrary which genes on ends
3. Class *v* to *cv* undercounts because double recombinants look like parentals

Our first genetic map



1. Order by least abundant class
2. Arbitrary which genes on ends
3. Class *v* to *cv* undercounts because double recombinants look like parentals

We have a better way!