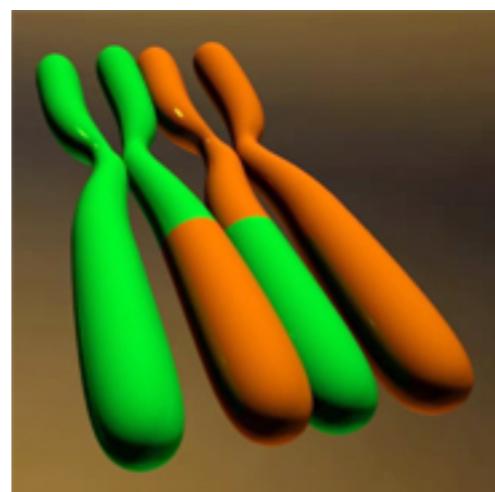


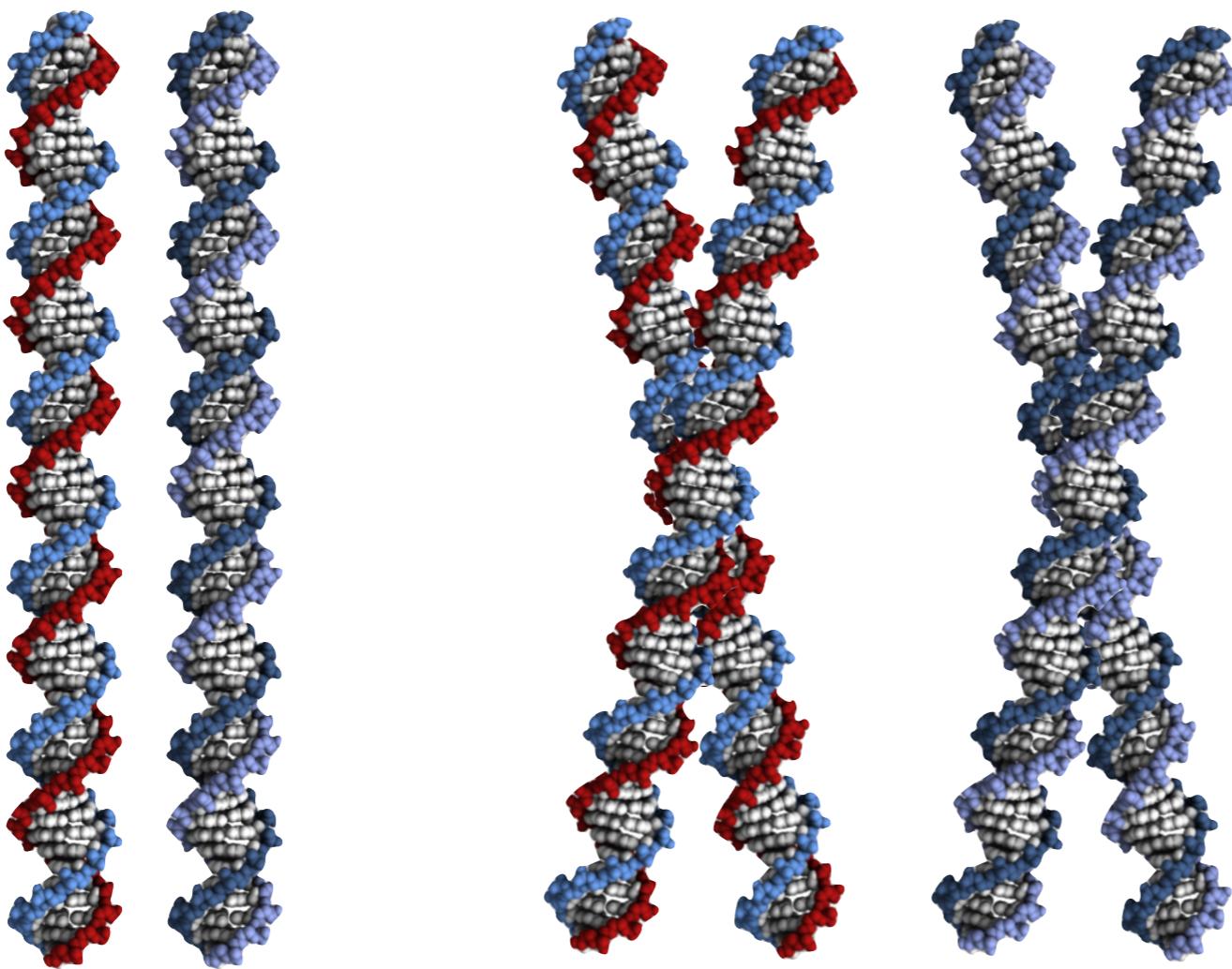
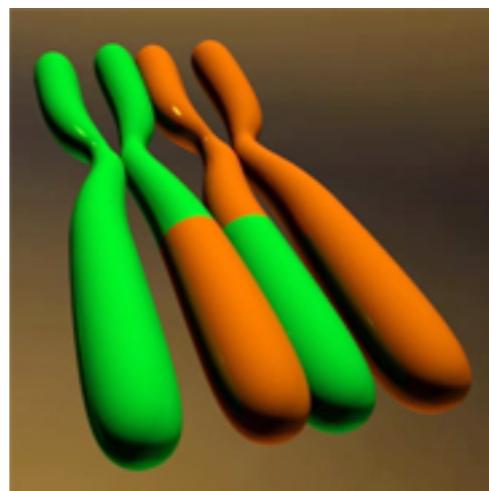
Bio393: Genetic Analysis

Recombination and mapping



What are these depictions?

A + a
b + B

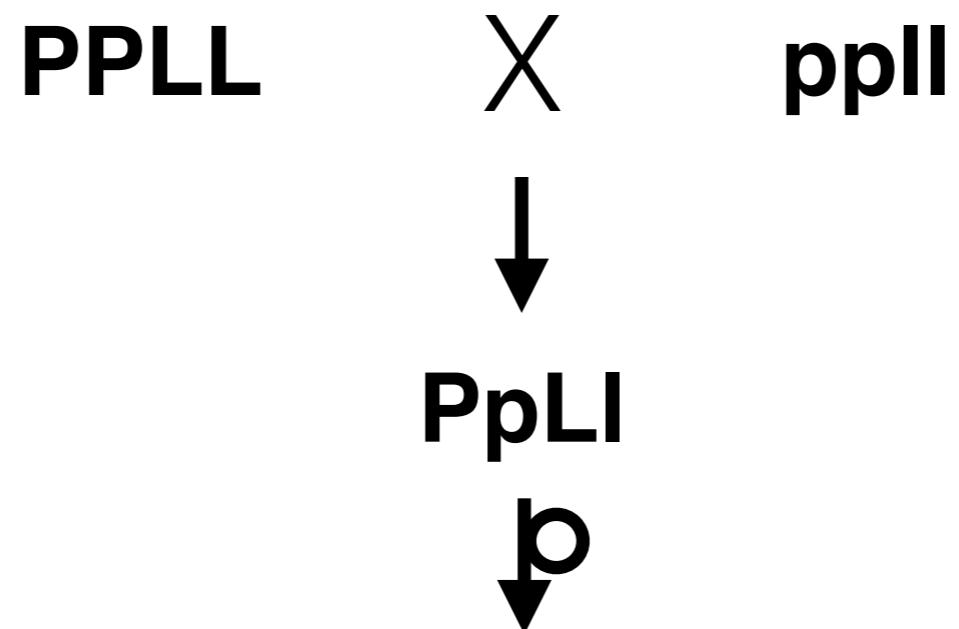




Reginald Punnett William Bateson



Bateson and Punnett's pea crosses



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

Bateson and Punnett's pea crosses

PPLL X ppll



PpLl



| Phenotype | Expected number | Expected ratio |
|--------------|-----------------|----------------|
| Purple Long | 215 | 9 |
| Purple round | 71 | 3 |
| red Long | 71 | 3 |
| red round | 24 | 1 |

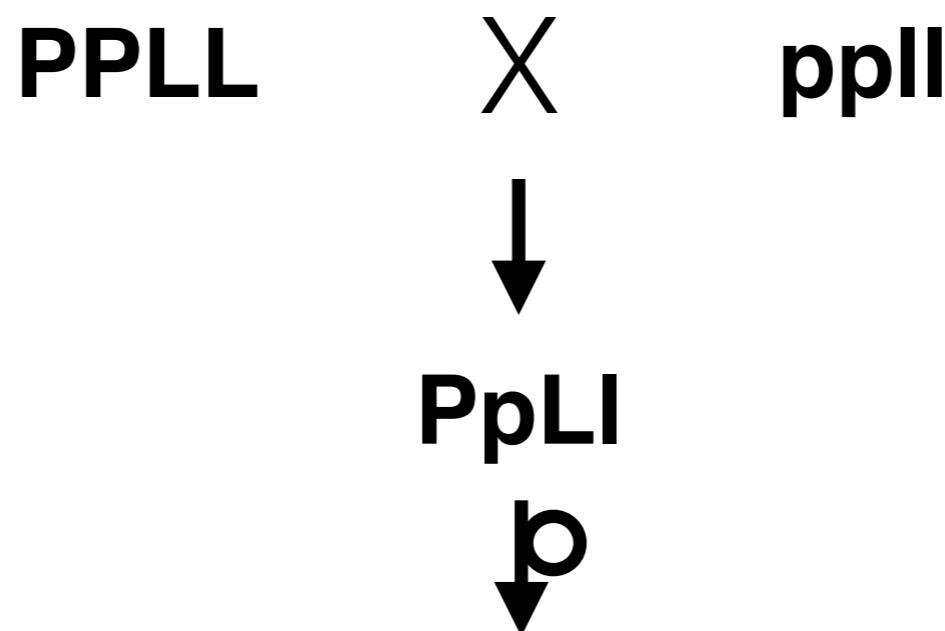
P= purple flower

p= red flower

L= long pollen

l= short pollen

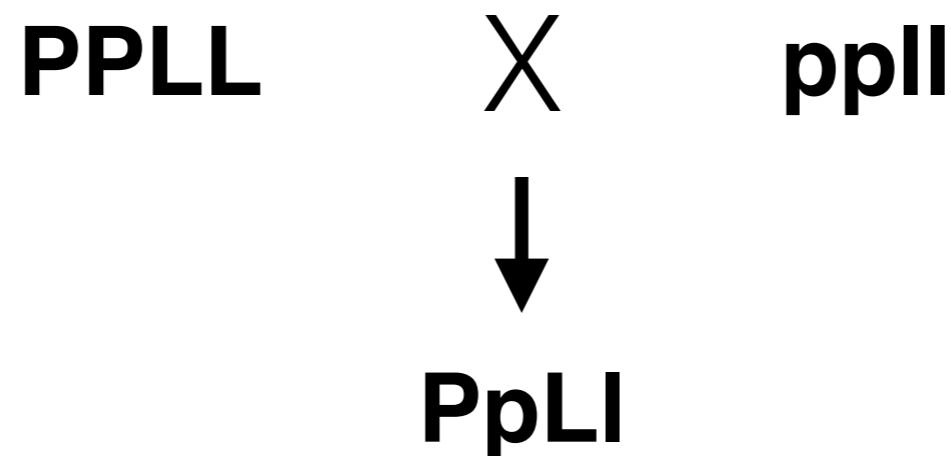
Bateson and Punnett's pea crosses



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

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

Bateson and Punnett's pea crosses



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



PpLl

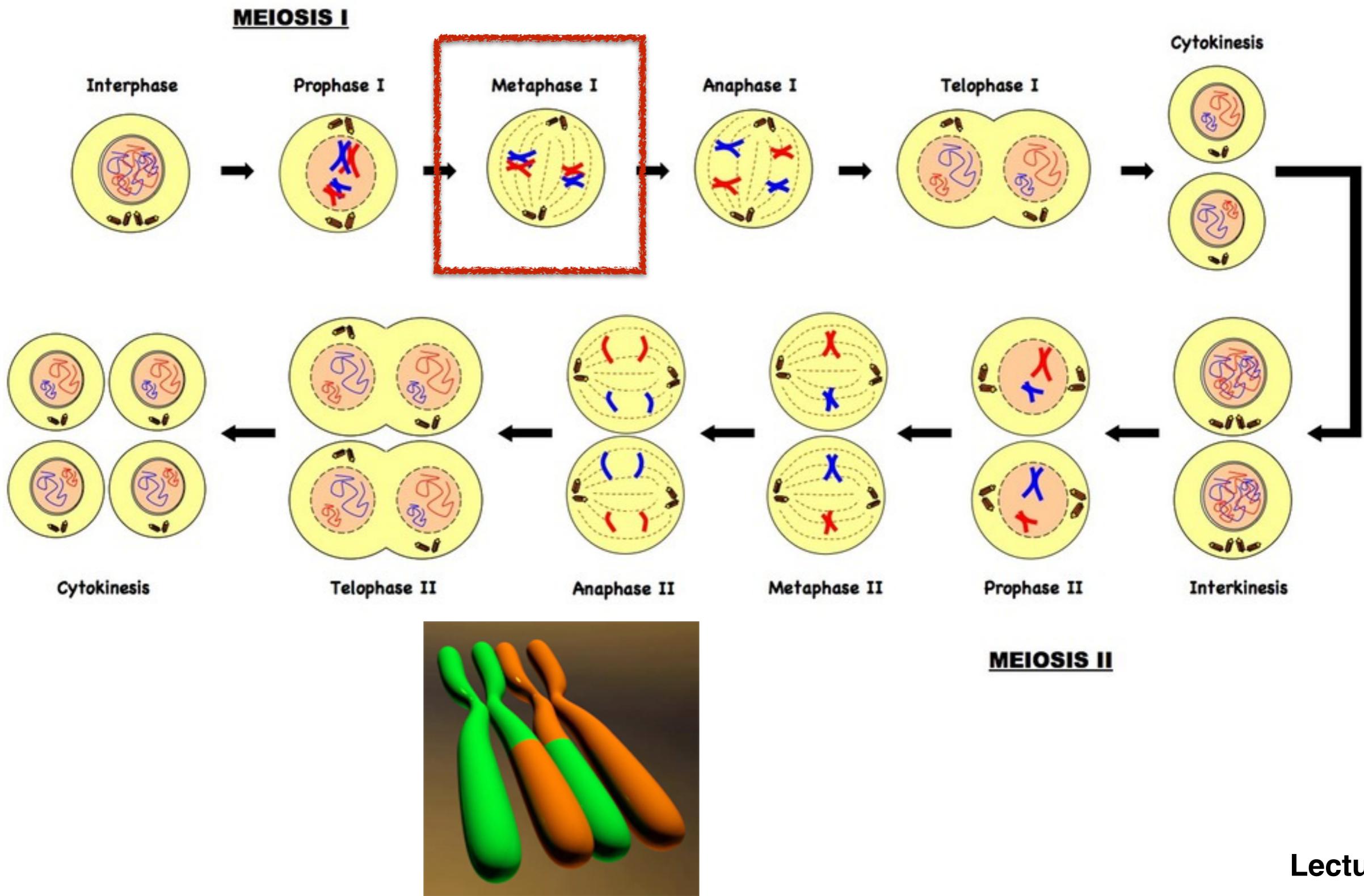


| Phenotype | Expected number | Expected ratio | Observed number |
|--------------|-----------------|----------------|-----------------|
| Purple Long | 215 | 9 | 284 |
| Purple round | 71 | 3 | 21 |
| red Long | 71 | 3 | 21 |
| red round | 24 | 1 | 55 |

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

Which are recombinant
and parental offspring?

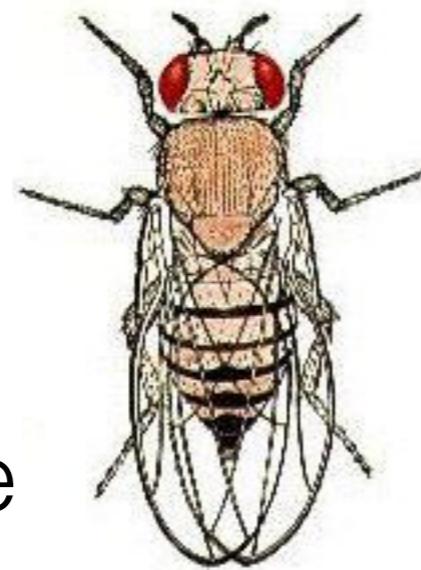
Meiosis: A reductional division in two acts



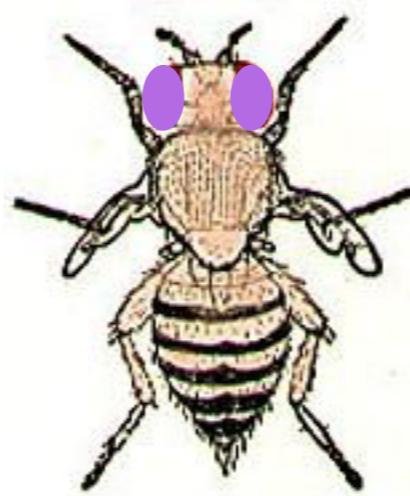
The fly room at Columbia



Wild-type

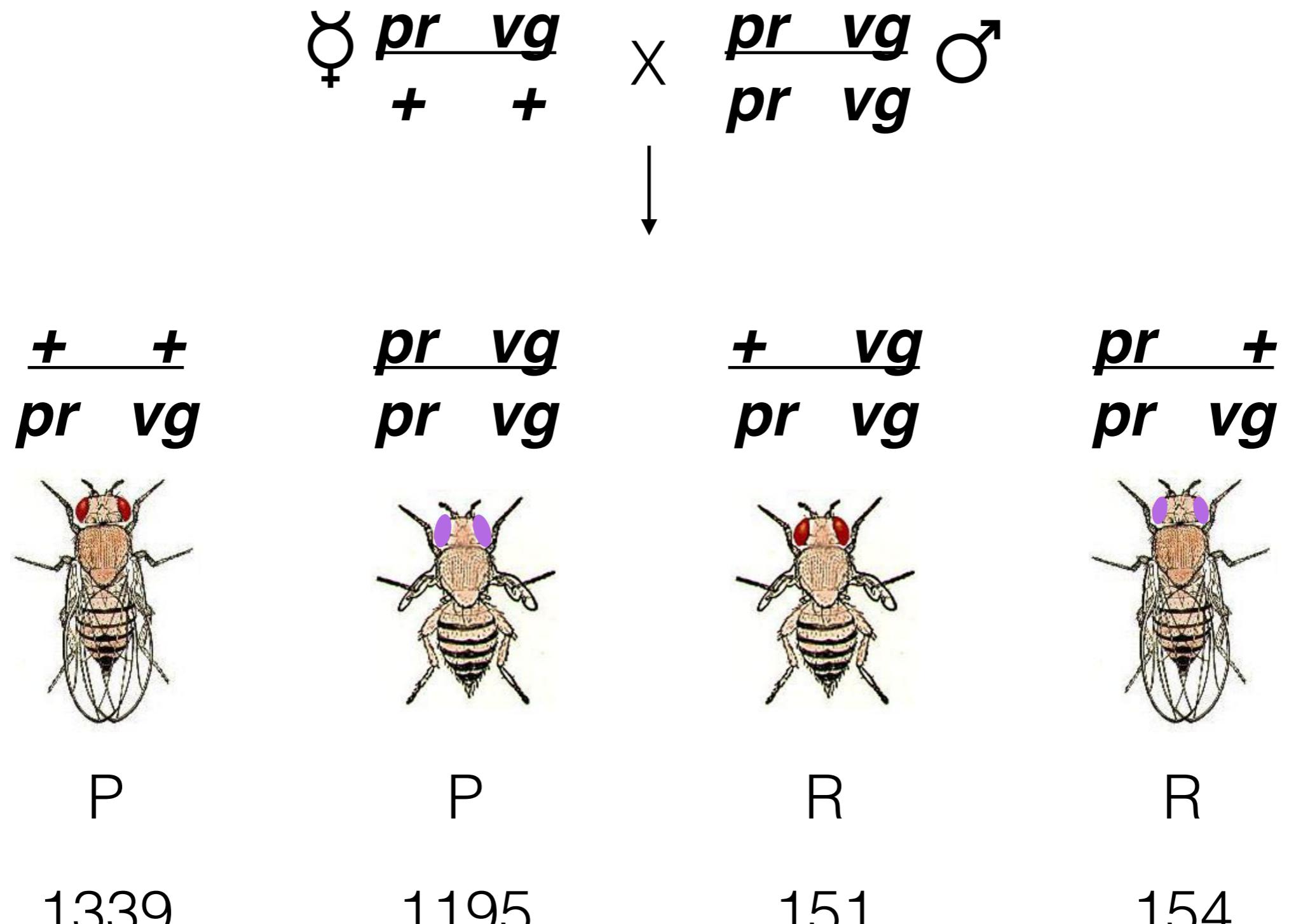


$+$ +



Purple eyes,
vestigial wings

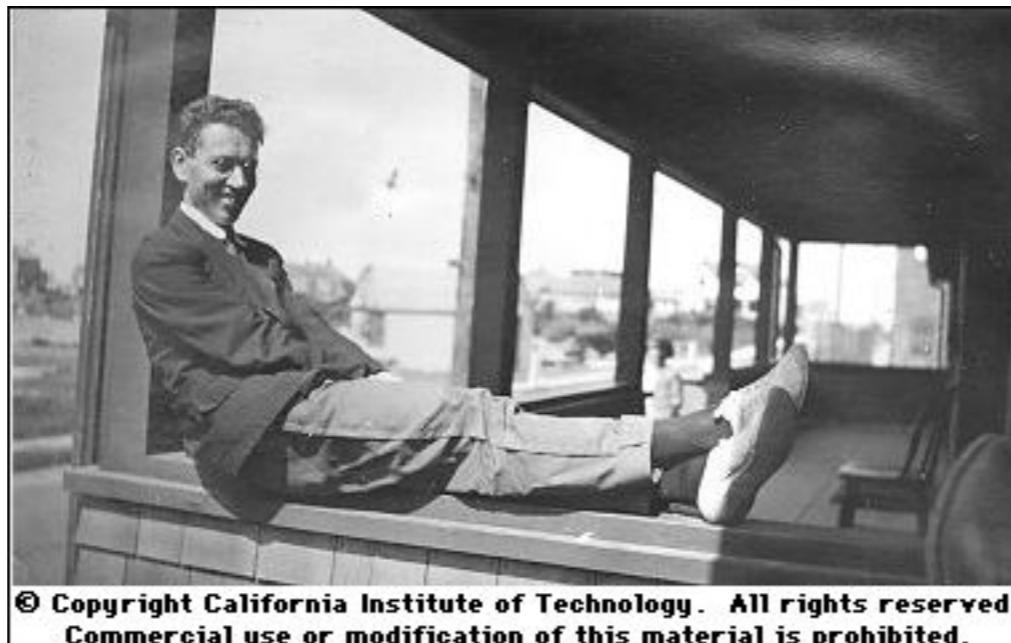
$pr\ vg$



Expectation is equal proportion of each class

Total = 2839

Lecture 3

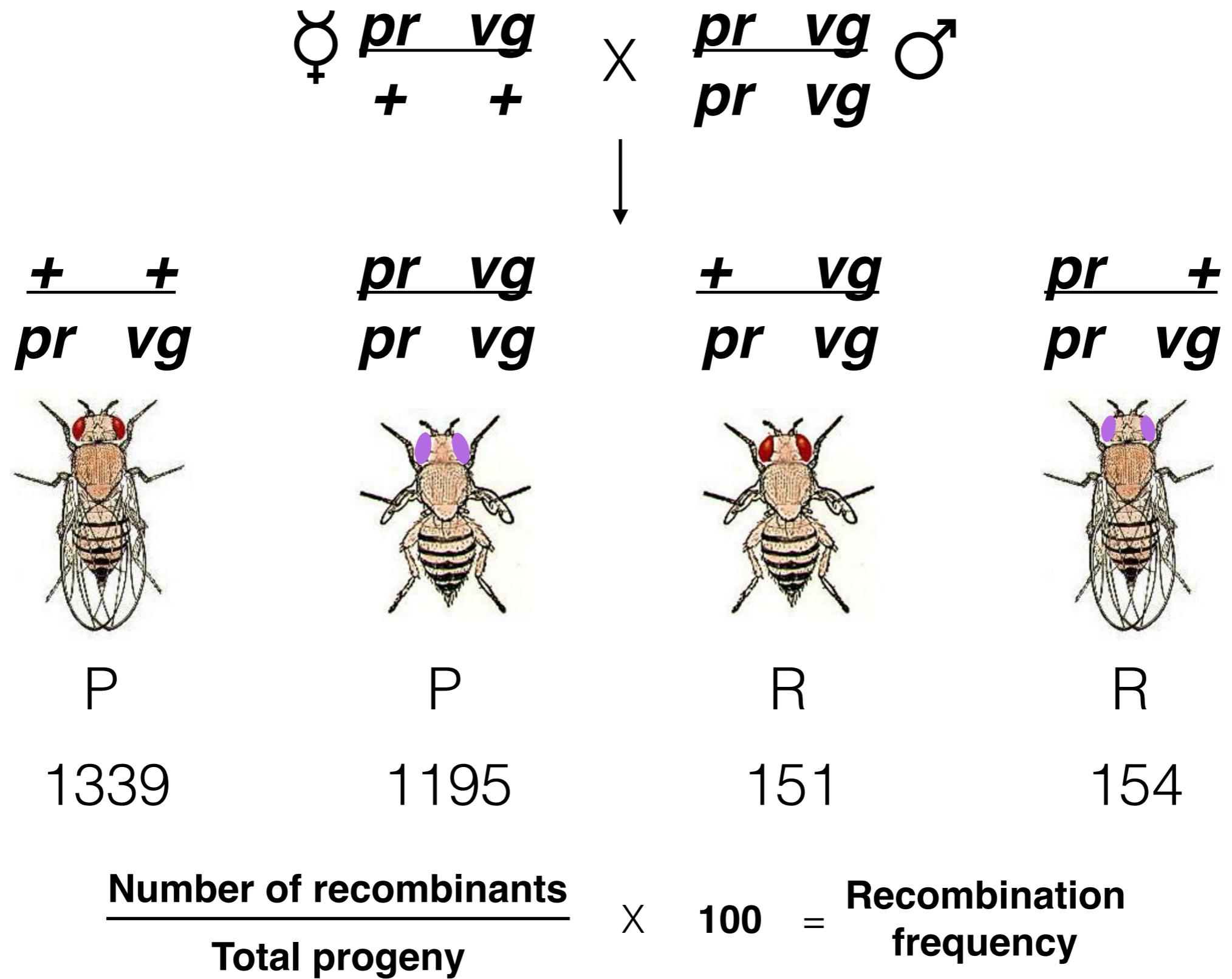


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Alfred Sturtevant

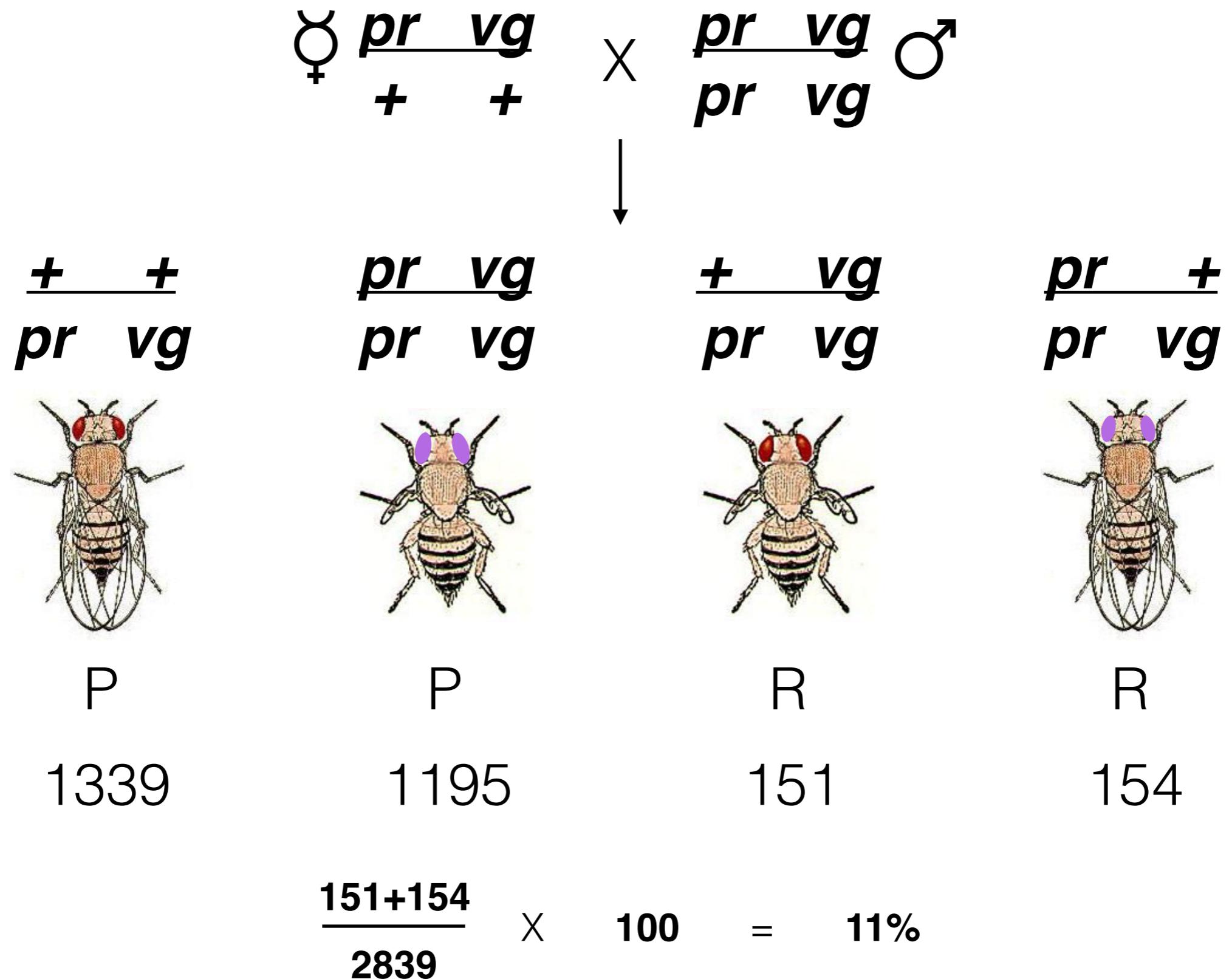
$$\frac{\text{Number of recombinants}}{\text{Total progeny}} \times 100 = \text{Recombination frequency}$$

1% RF = 1 map unit = 1 centiMorgan



Total = 2839

Lecture 3



Total = 2839

Lecture 3

Recombination is the exchange of genetic material between homologous chromosomes

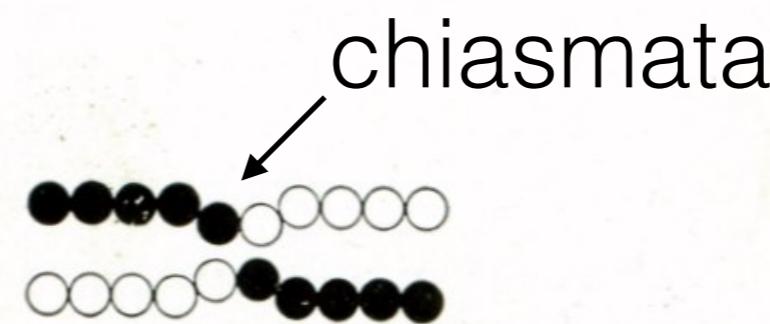
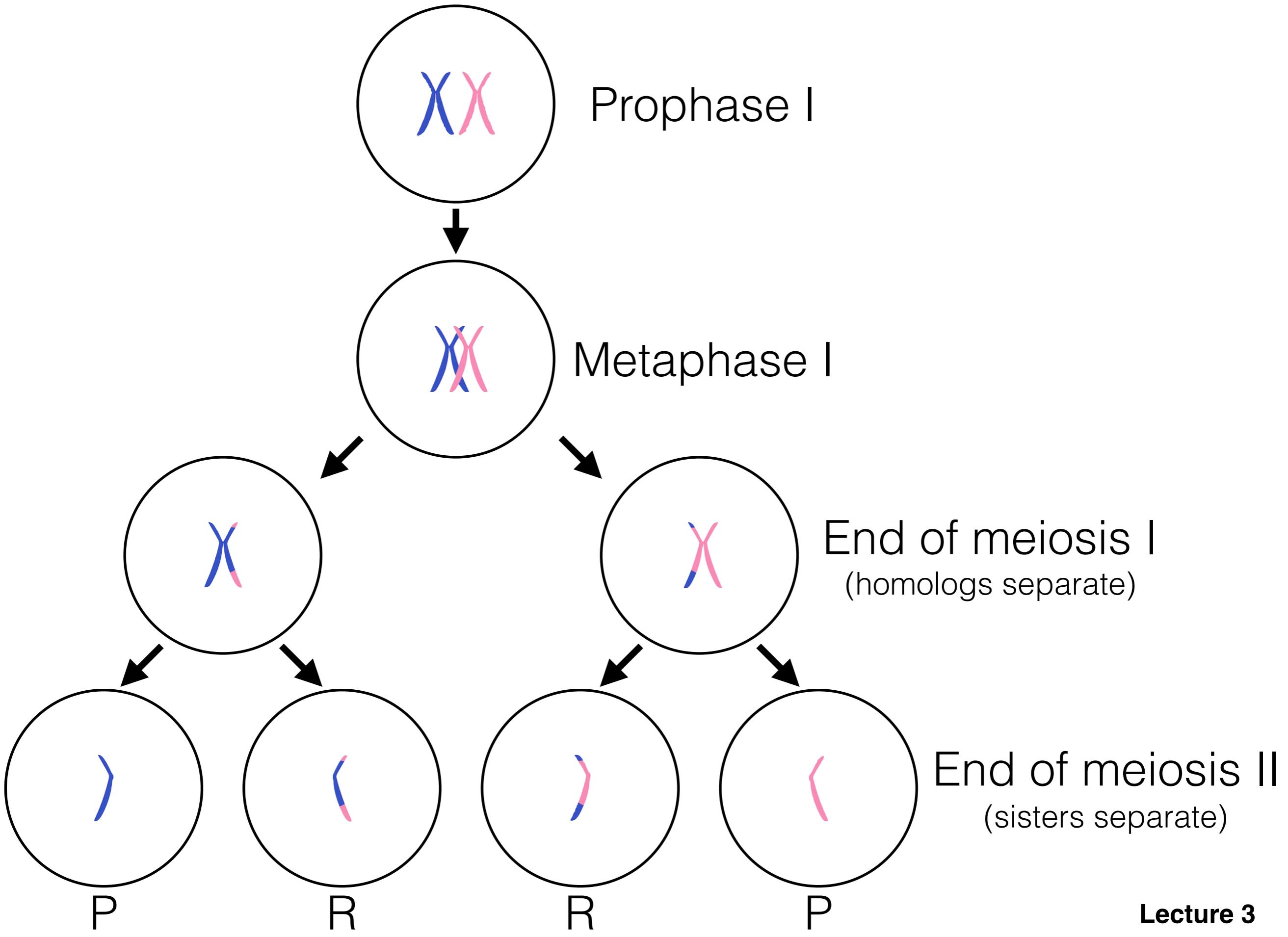
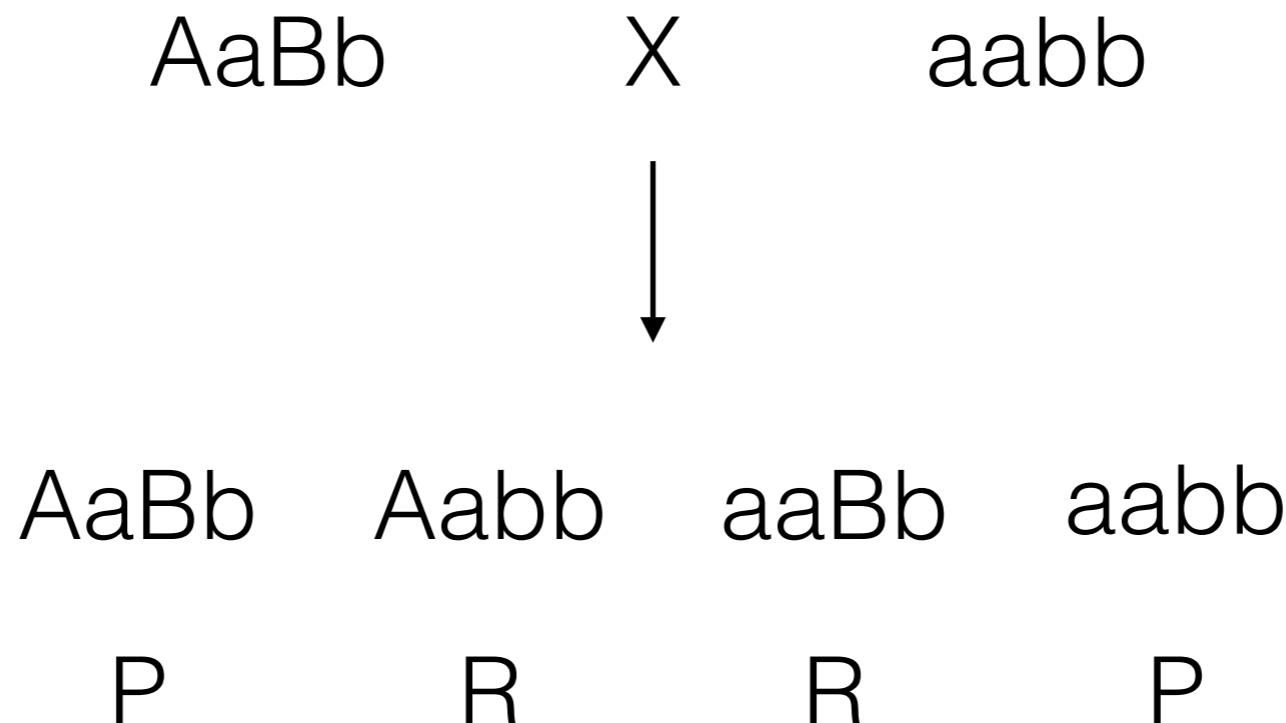


FIG. 64. Scheme to illustrate a method of crossing over of the chromosomes.



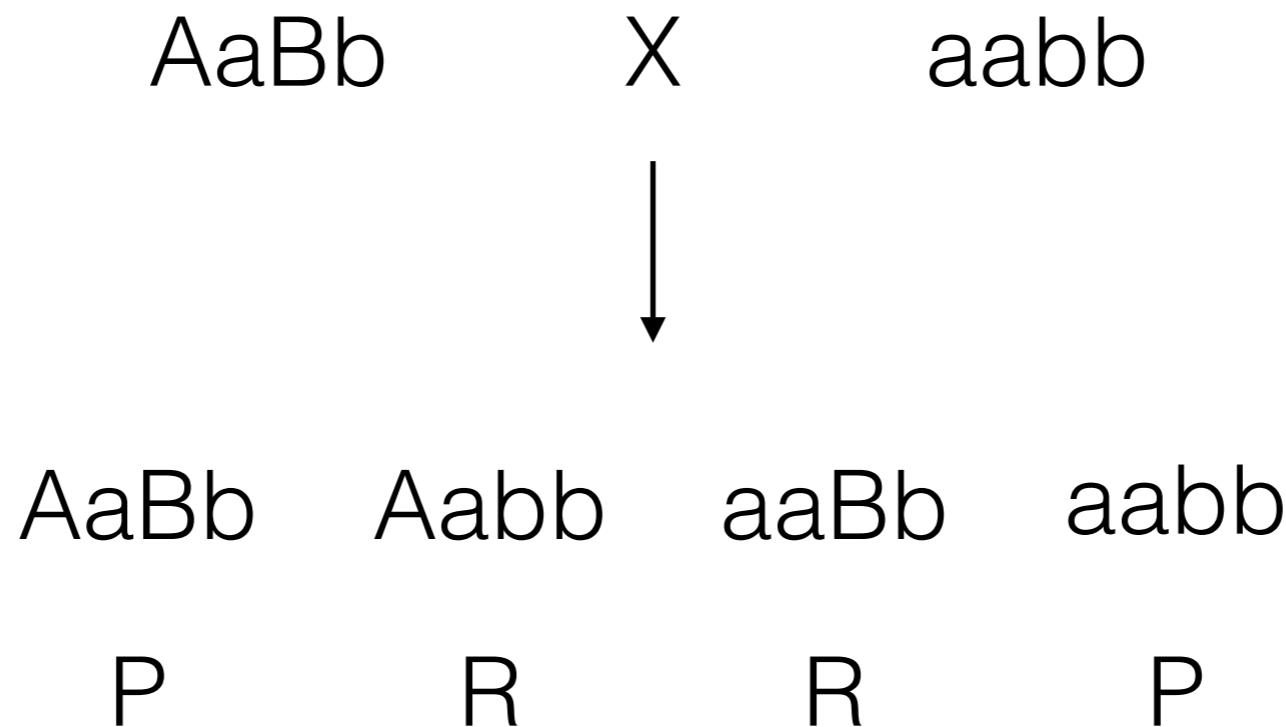
Independent assortment defines the limit of linkage



All four classes occur in equal ratios

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

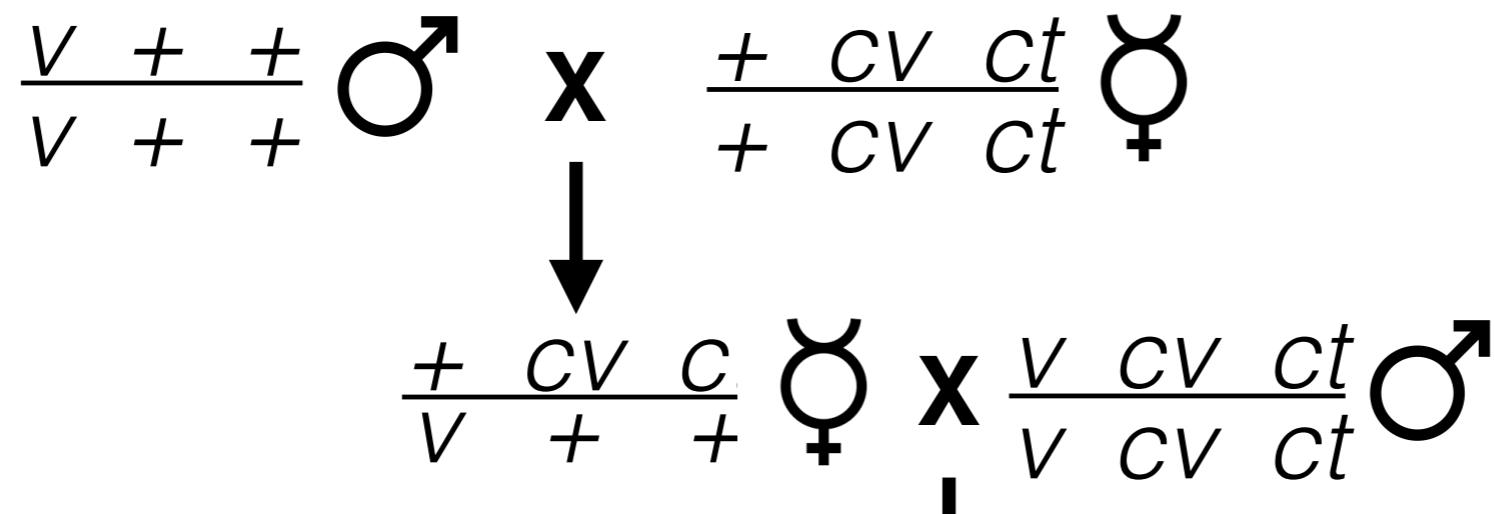
Independent assortment defines the limit of linkage



All four classes occur in equal ratios (R=P)

$$\frac{2^*R}{2^*R + 2^*P} \times 100 = 50\%$$

A three-factor cross



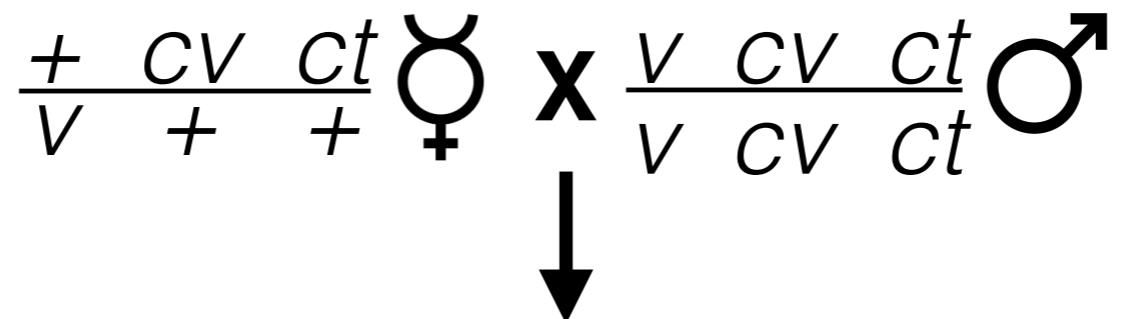
| Eye Phenotype | Crossvein Phenotype | Cut Phenotype | Number of offspring |
|---------------|---------------------|---------------|---------------------|
| Red | No crossvein | Cut wing | 580 |
| Vermillion | Crossvein | Normal wing | 592 |
| Red | Crossvein | Cut wing | 40 |
| Vermillion | No crossvein | 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



| 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 |

$+ \quad CV \quad ct$ **P**
 $V \quad + \quad +$ **P**

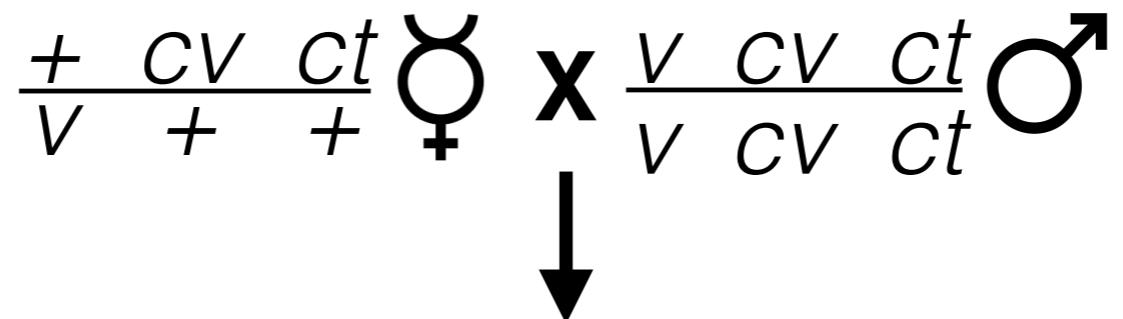
1. Determine parental class, label

v = vermillion eyes

ct = cut wings

cv = crossveinless wings

$+$ = red eyes and normal wings



| 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 |
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| Red | Crossvein | Normal wing | 94 |
| Vermillion | No crossvein | Cut wing | 89 |
| Red | No crossvein | Normal wing | 5 |
| Vermillion | Crossvein | Cut wing | 3 |

$+ \quad CV \quad ct$ **P**
 $V \quad + \quad +$ **P**
R
R
R
R
R
R

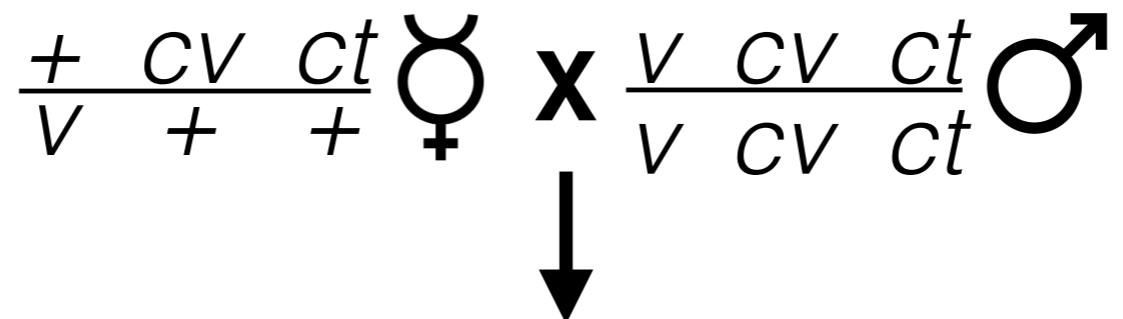
1. Determine parental class, label
2. Are all classes present?

v = vermillion eyes

ct = cut wings

cv= crossveinless wings

+ = red eyes and normal wings



| 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
 R R
 R R
 R R
 + CV + R
 V + ct R

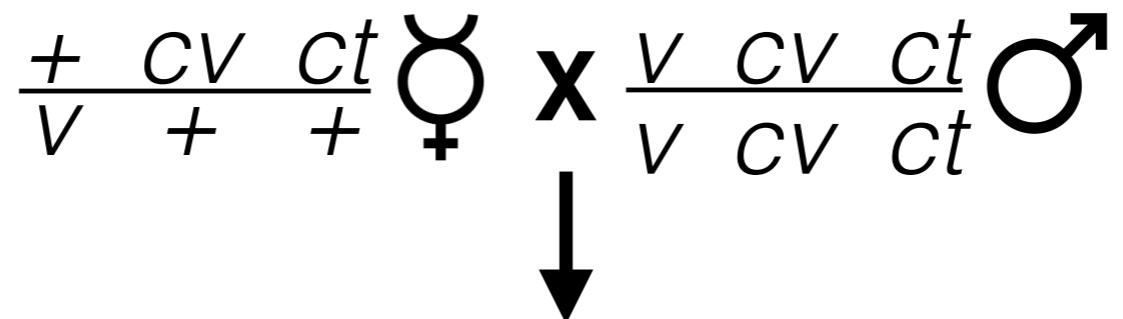
1. Determine parental class, label
2. Are all classes present?
3. Least abundant class is double recombinant, tells gene in middle

v = vermillion eyes

ct = cut wings

cv= crossveinless wings

+ = red eyes and normal wings



| 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 |
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| 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 |

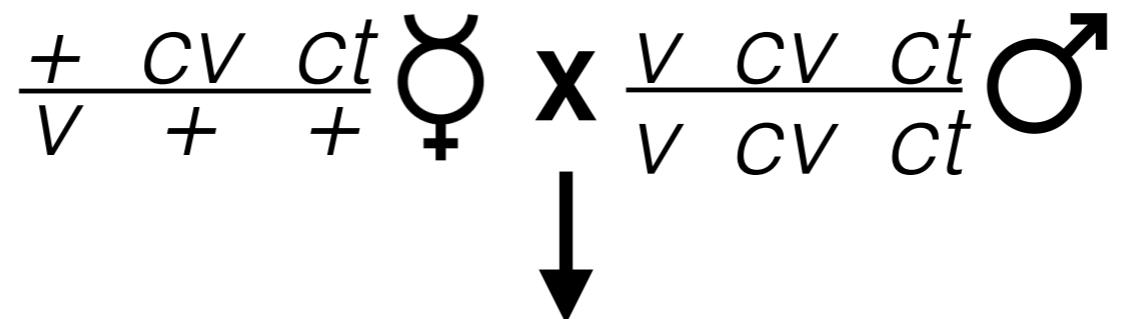
1. Determine parental class, label
2. Are all classes present?
3. Least abundant class is double recombinant, tells gene in middle
4. Write out the genotypes of the offspring

v = vermillion eyes

ct = cut wings

cv= crossveinless wings

+ = red eyes and normal wings



| 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 **v to ct**

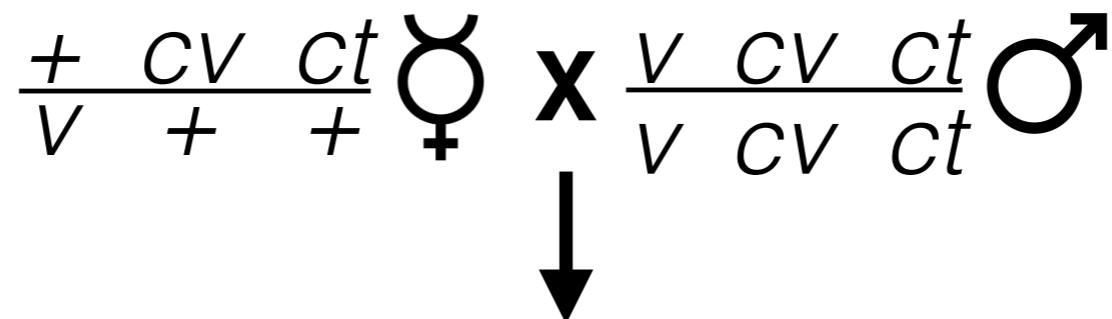
v = vermillion eyes

ct = cut wings

cv= crossveinless wings

+ = red eyes and normal wings

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



| 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

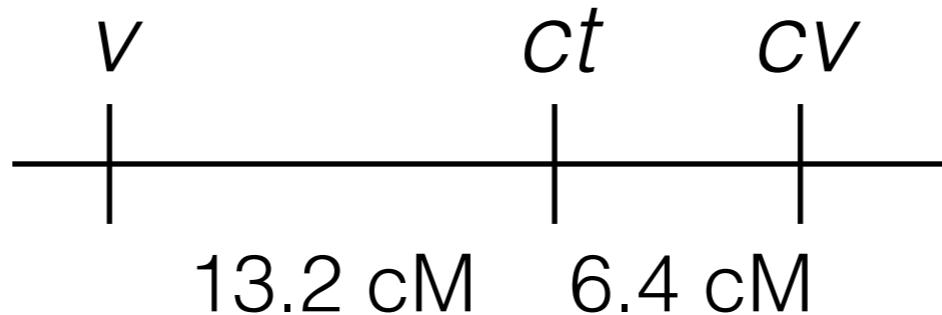
ct = cut wings

cv= crossveinless wings

+ = red eyes and normal wings

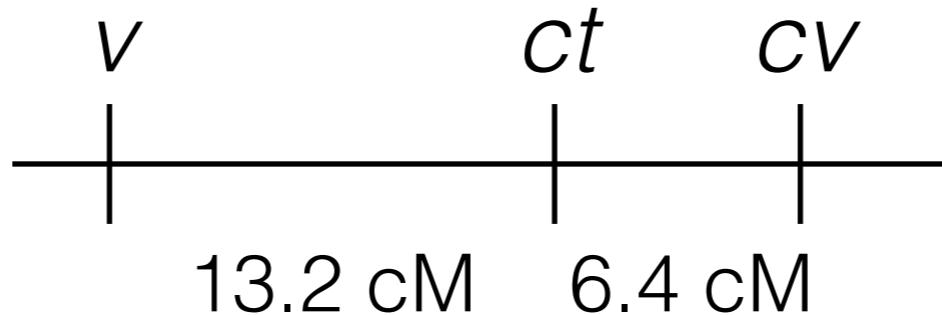
$$\frac{40+45+5+3}{1448} \times 100 = 6.4\%$$

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 (with respect to v and cv)

Our first genetic map

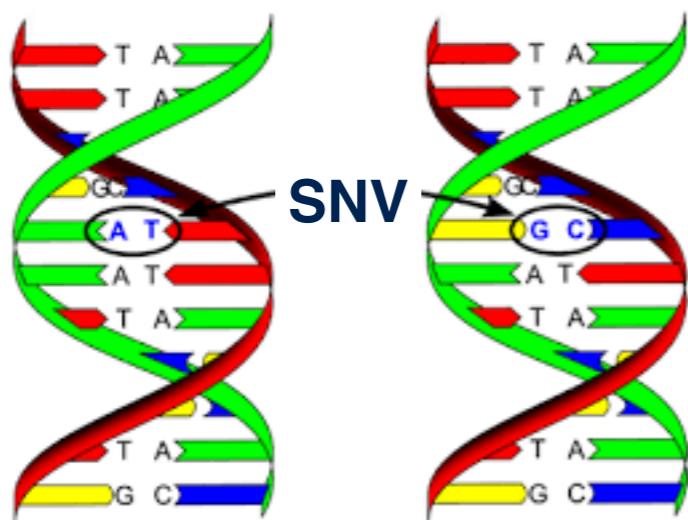


1. Order by least abundant class
2. Arbitrary which genes on ends
3. Class *v* to *cv* undercounts because double recombinants look like parentals (with respect to *v* and *cv*)

We have a better way!

Molecular markers are often used for genetic mapping

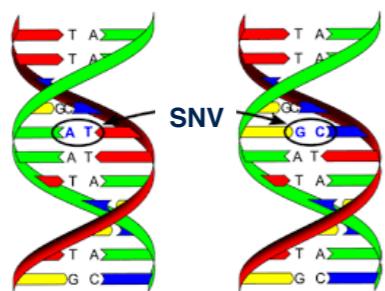
- Single nucleotide variants



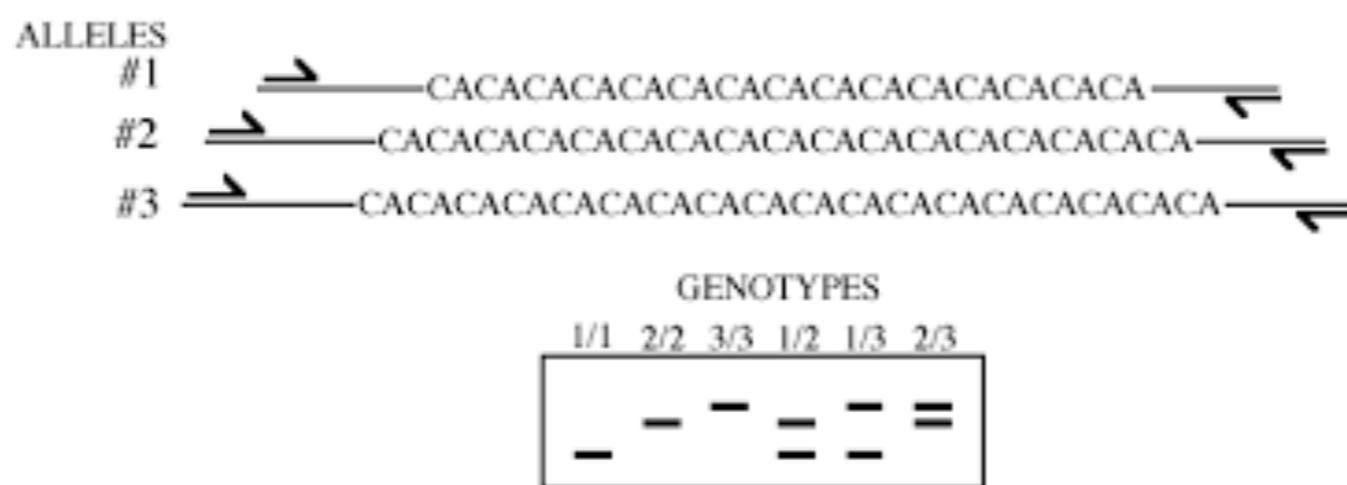
Detected by sequencing,
hybridization (array), or PCR.

Molecular markers are often used for genetic mapping

- Single nucleotide variants

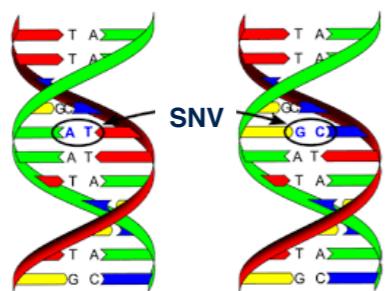


- Microsatellite repeats

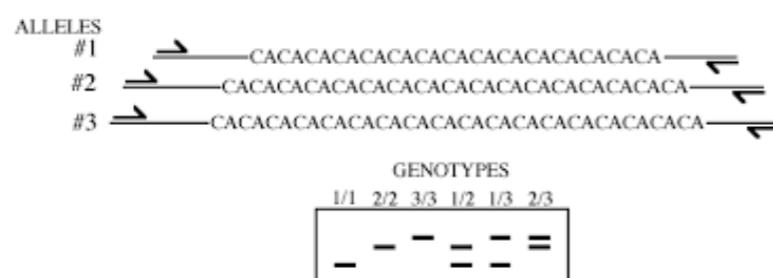


Molecular markers are often used for genetic mapping

- Single nucleotide variants

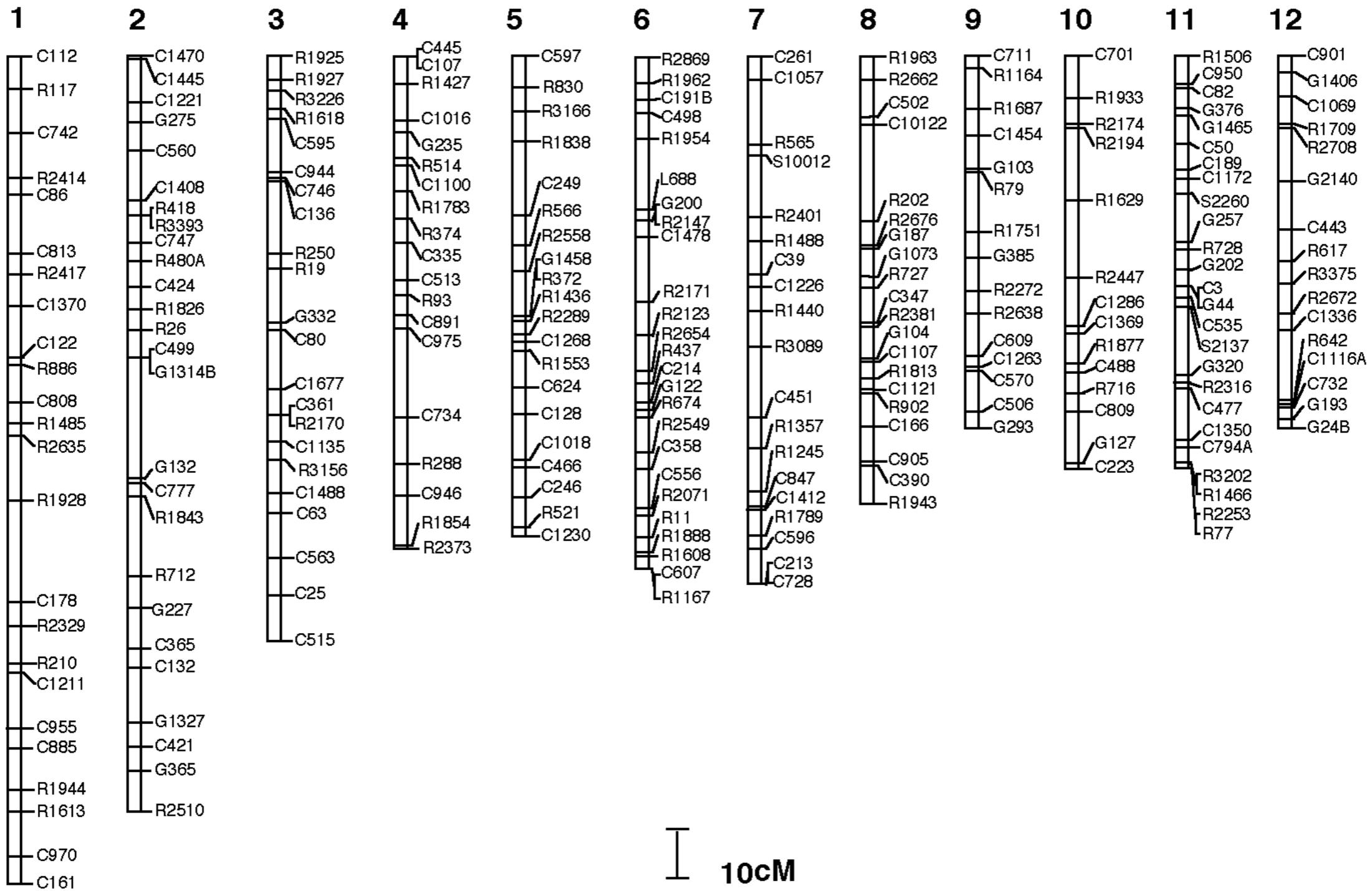


- Microsatellite repeats



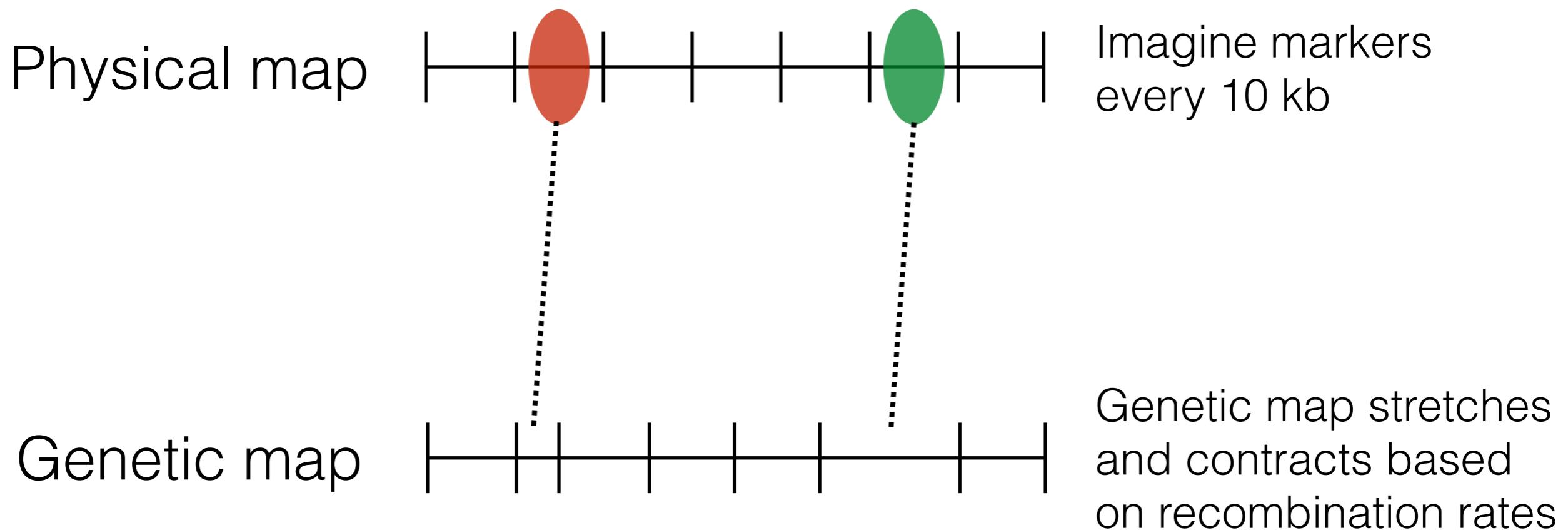
- Insertion/deletion variants

Molecular markers are often used for genetic mapping

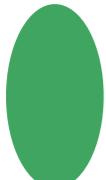


10cM

What do regions of more or less recombination do to the linkage map?

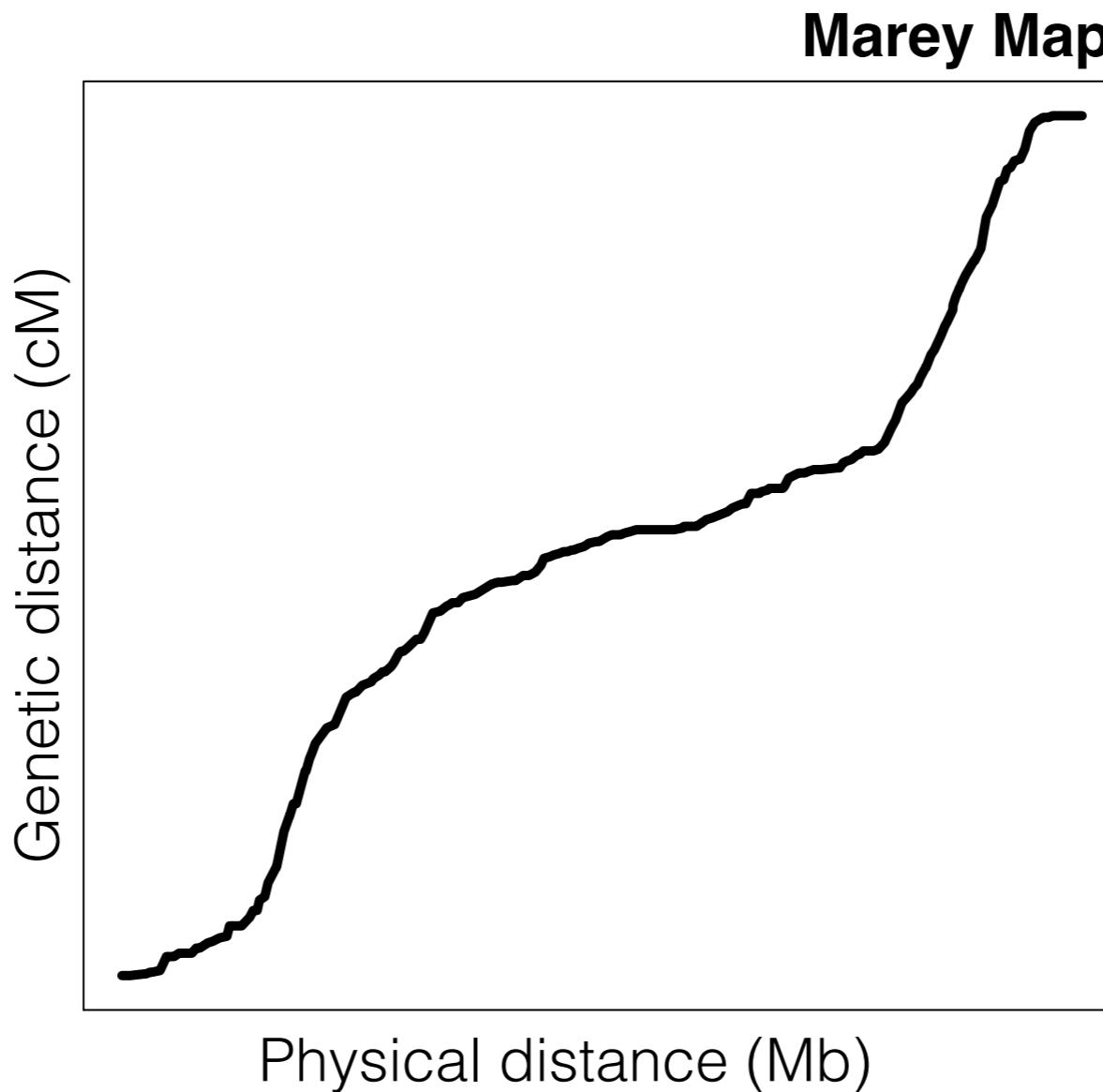


Less recombination (cold spot)



More recombination (hot spot)

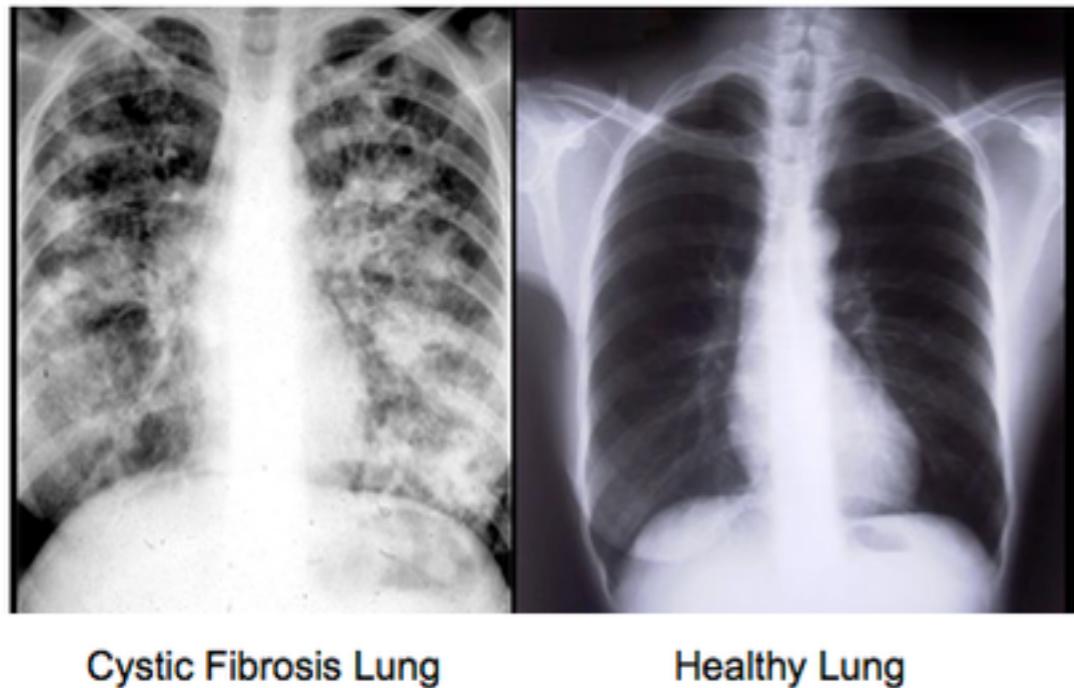
What do regions of more or less recombination do to the linkage map?



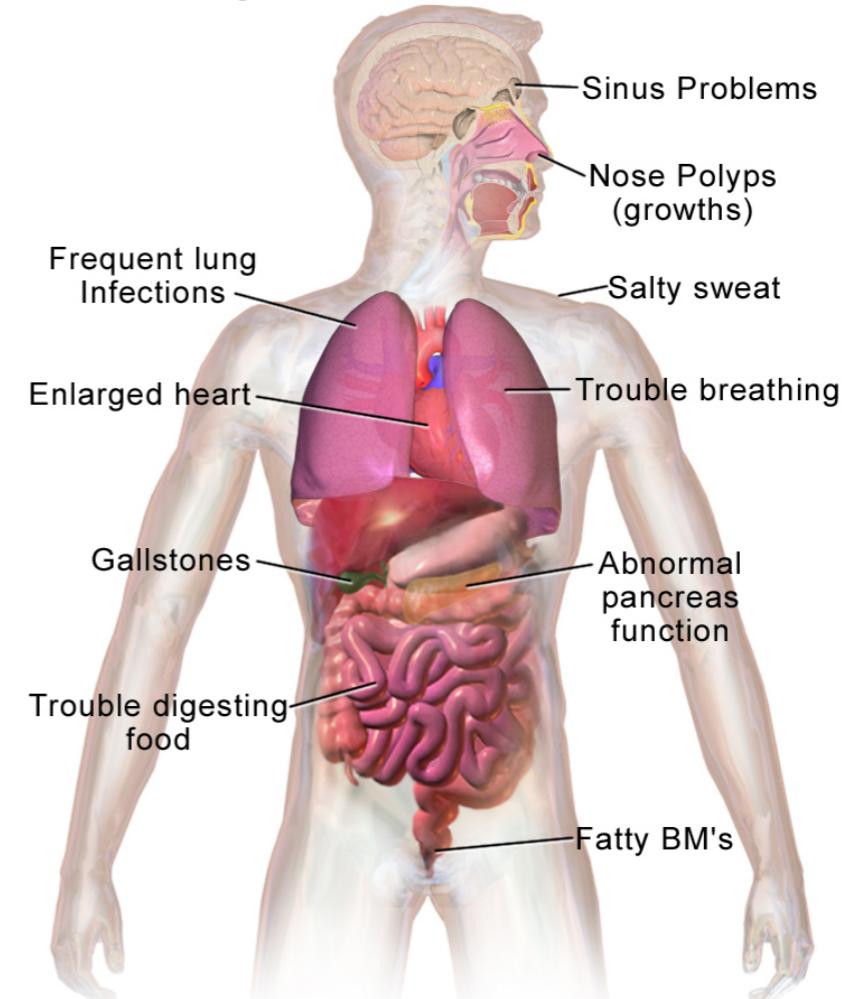
Why do we care?

Is this technique “old-fashioned”?

What about cystic fibrosis and today's topic?



Health Problems with Cystic Fibrosis



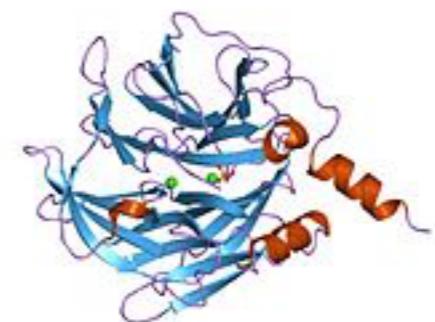
Where is the gene that when mutated causes cystic fibrosis?

How would you map it?

Linkage to allozymes

Allozymes are enzymes with activities that vary from person to person

PON1 is a hydrolase used for detoxifying cells.
Activity varies from person to person.



68 families with at least two children with and without CF were phenotyped for *PON1* activity and CF.

Found linkage to *PON1* and chromosome 7

What have we learned so far?

CF is rare – 1/10,000 births

Autosomal recessive disorder

Not caused by chromosomal aberrations or NDJ

Linked to *PON1* on chromosome 7

