Linkage & Gene Mapping in Eukaryotes

(CHAPTER 5- Brooker Text)

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BIO 184
Dr. Tom Peavy

- Chromosomes are called linkage groups
  - They contain a group of genes that are linked together
- The number of linkage groups is the number of types of chromosomes of the species
  - For example, in humans
    - 22 autosomal linkage groups
    - An X chromosome linkage group
    - A Y chromosome linkage group
- Genes that are far apart on the same chromosome may independently assort from each other
  - This is due to crossing-over

Crossing Over May Produce Recombinant Phenotypes

- In diploid eukaryotic species, linkage can be altered during meiosis as a result of crossing over
- Crossing over
  - Occurs during prophase I of meiosis at the bivalent stage
  - Non-sister chromatids of homologous chromosomes exchange DNA segments

- Genetic maps allow us to estimate the relative distances between linked genes, based on the likelihood that a crossover will occur between them
- Experimentally, the percentage of recombinant offspring is correlated with the distance between the two genes
  - If the genes are far apart → many recombinant offspring
  - If the genes are close → very few recombinant offspring

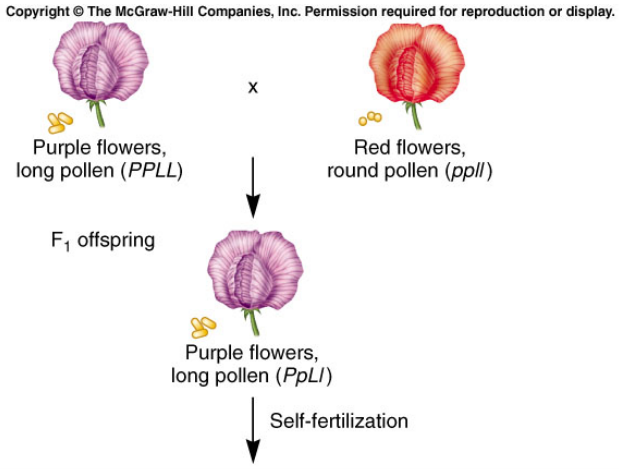
- Map distance = $\frac{\text{Number of recombinant offspring}}{\text{Total number of offspring}}$ X 100
  - The units of distance are called map units (mu)
    - They are also referred to as centiMorgans (cM)
  - One map unit is equivalent to 1% recombination frequency

Trihybrid or 3-Point Crosses

- Data from trihybrid crosses yields information about map distance and gene order
  - Example, we will consider fruit flies that differ in body color, eye color and wing shape
    - *b* = black body color
    - b^+ = gray body color
    - *pr* = purple eye color
    - pr^+ = red eye color
    - *vg* = vestigial wings
    - vg^+ = normal wings

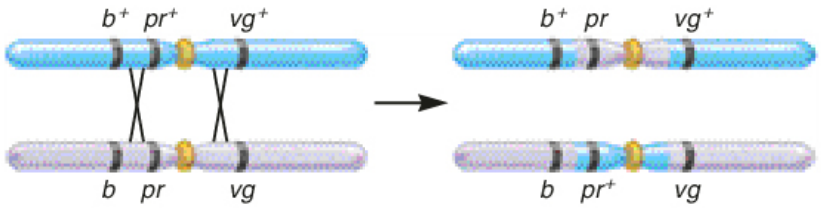
- Analysis of the F_2 generation flies will allow us to map the three genes
  - The three genes exist as two alleles each
  - Therefore, there are $2^3 = 8$ possible combinations of offspring
  - If the genes assorted independently, all eight combinations would occur in equal proportions

- In the offspring of crosses involving linked genes,
  - Parental phenotypes occur most frequently
  - Double crossover phenotypes occur least frequently
  - Single crossover phenotypes occur with “intermediate” frequency

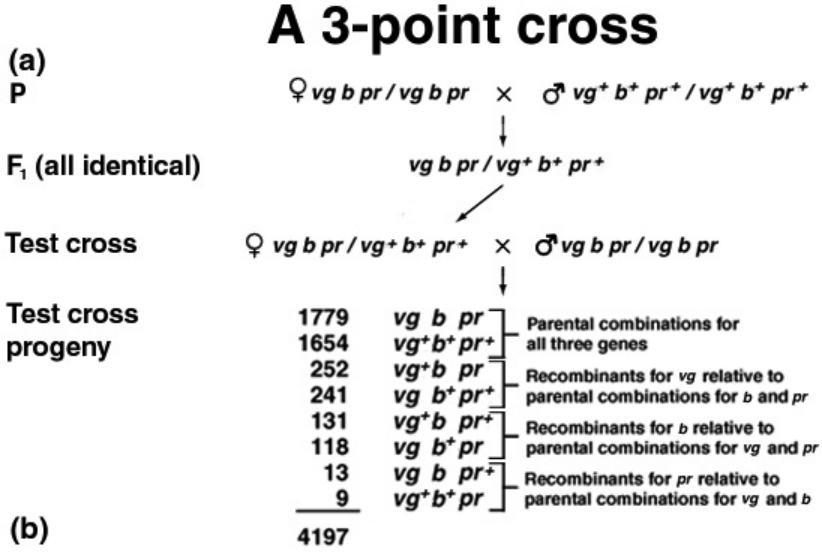


F_2 offspring	Observed number	Ratio	Expected number	Ratio
Purple flowers, long pollen	296	15.6	240	9
Purple flowers, round pollen	19	1.0	80	3
Red flowers, long pollen	27	1.4	80	3
Red flowers, round pollen	85	4.5	27	1

- The combination of traits in the double crossover tells us which gene is in the middle
  - A double crossover separates the gene in the middle from the other two genes at either end



- In the double crossover categories, the recessive purple eye color is separated from the other two recessive alleles
  - Thus, the gene for eye color lies between the genes for body color and wing shape



Which ones are the double crossover recombinants?

- Calculate the map distance between pairs of genes
  - To do this, one strategy is to regroup the data according to pairs of genes
    - From the parental generation, we know that the dominant alleles are linked, as are the recessive alleles
    - This allows us to group pairs of genes into parental and nonparental combinations
      - Parentals have a pair of dominant or a pair of recessive alleles
      - Nonparentals have one dominant and one recessive allele
    - The regrouped data will allow us to calculate the map distance between the two genes

3-Point Mapping

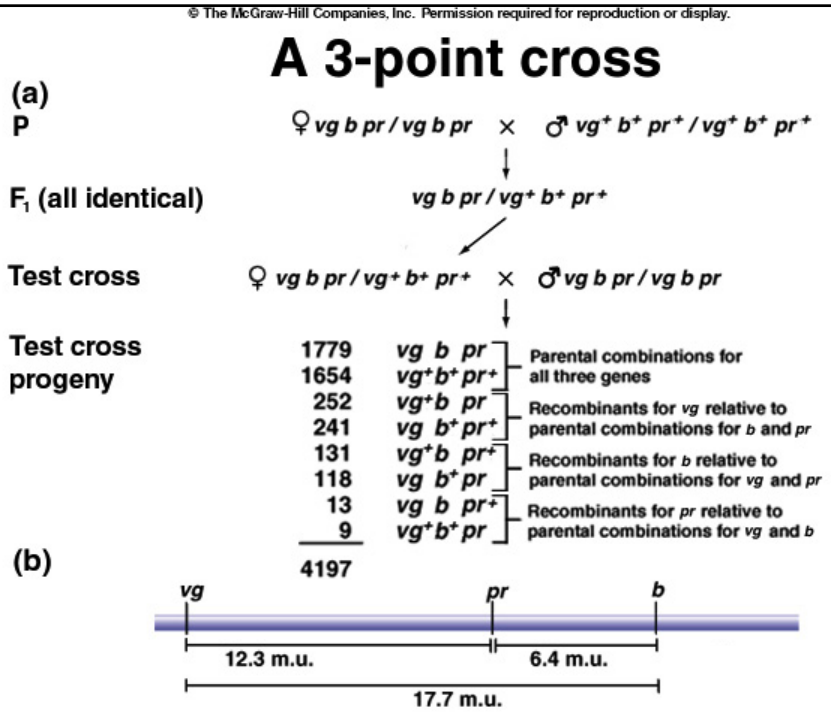
- vg-b recombinants are:
  - vg-b^+
  - vg^+-b

3-Point Mapping

- Now lets look at b-pr, recombinants?
  - b-pr^+
  - b^+-pr

3-Point Mapping

- Now lets look at vg-pr, recombinants?
  - vg-pr$^+$
  - vg$^+$-pr



3-Point Mapping

- Now double check ourselves?

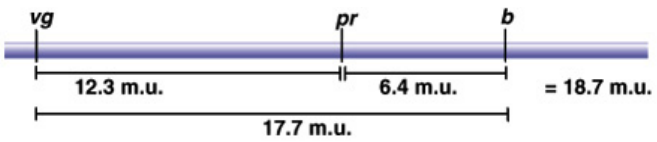
  12.3+6.4=?

  18.7

  But 18.7 does not equal 17.7 why?

3-Point Mapping

- Didn't include the double crossover events in your determination of vg and b:
  - A more accurate distance would be calculated using all numbers of recombinants
    - Need to count double crossover two times WHY?
      - Because in order to get all exchanges between vg and b then would occur twice



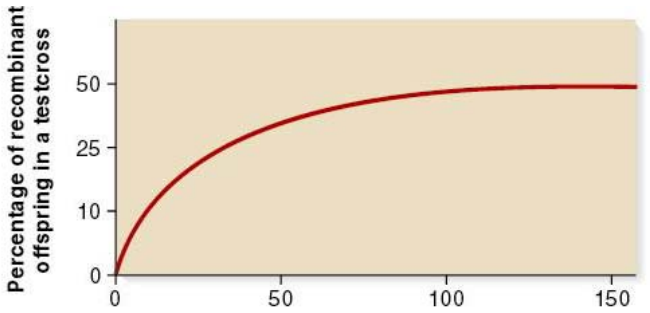


Figure 5.11

- When the distance between two genes is large
  - The likelihood of multiple crossovers increases
  - This causes the observed number of recombinant offspring to underestimate the distance between the two genes

Interference

- The product rule allows us to predict the likelihood of a double crossover from the individual probabilities of each single crossover

$$P_{\text{(double crossover)}} = P_{\text{(single crossover between } b \text{ and } pr\text{)}} \times P_{\text{(single crossover between } pr \text{ and vg)}}$$

$$= 0.064 \times 0.123 = 0.0079$$

- Based on a total of 4,197 offspring
  - The expected number of double crossover offspring is

$$= 4{,}197 \times 0.0079 = 33$$

Interference

- Therefore, we would expect 33 offspring to be produced as a result of a double crossover
- However, the observed number was only (13+9)=22!
  - 9 with gray bodies, purple eyes, and normal wings
  - 13 with black body, red eyes, and vestigial wings
- This lower-than-expected value is due to a common genetic phenomenon, termed positive interference
  - The first crossover decreases the probability that a second crossover will occur nearby

- Interference (I) is expressed as

  I = 1 – C
  - where C is the coefficient of coincidence

$$C = \frac{\text{Observed number of double crossovers}}{\text{Expected number of double crossovers}}$$

$$C = \frac{22}{33} = 0.67$$

I = 1 – C = 1 – 0.67

= 0.33 or 33%

  - This means that 33% or 1/3 of the expected number of crossovers did not occur

- Since I is positive, this interference is positive interference
- Rarely, the outcome of a testcross yields a negative value for interference
  - Negative value would suggest that a first crossover *enhances* the rate of a second crossover
- The molecular mechanisms that cause interference are not completely understood
  - However, most organisms regulate the number of crossovers so that very few occur per chromosome