Chapter 7: Linkage, Recombination, and Eukaryotic Gene Mapping, Parts 1 and 2

1. Linked genes: located close together on same chromosome

Syntenic genes: located on same chromosome

2. Independent assortment versus linkage.
3. Independent assortment versus linkage.

Before: AaCc
Now: AC/ac

4. Genetic maps show the relative locations of genes on chromosomes.
   A. If genes are unlinked, their recombination rate is 50%.
   B. If recombination rate is <50%, the genes can be seen to be linked.

   Before: AaBb x aabb = genotypes in a test cross

   Can write as: ABab x abab

   - If want to look at recomb in 1st individual, 2nd individual's alleles can not
     mask expression of 1st one's alleles.
   - Thus looking at phenotype of offspring lets us "see" what genotype of gametes was in the first individual.
   - Also lets us "see" what alleles are on that chromosome.

   Phenotypes of progeny:

   Unlinked: 1/4 A,B 1/4 a,b 1/4 A,b 1/4 a,B
   (Completely) Linked: 1/2 A,B 1/2 a,b
   (Partially) Linked: >1/4 A,B >1/4 a,b <1/4 a,B <1/4 A,B

5. Map units = % recombination
   One map unit: the distance between gene pairs for which one
   product of meiosis out of 100 is recombinant.
   Map units usually, but not always proportional to physical distance.
   1 mu = 1% recombination = 1cM (centimorgan)

   CD/cd x cd/cd

<table>
<thead>
<tr>
<th>Phenytype</th>
<th>Frequency</th>
</tr>
</thead>
<tbody>
<tr>
<td>c,d</td>
<td>478</td>
</tr>
<tr>
<td>C,D</td>
<td>482</td>
</tr>
<tr>
<td>c,D</td>
<td>19</td>
</tr>
<tr>
<td>C,D</td>
<td>21</td>
</tr>
<tr>
<td>Total</td>
<td>1000</td>
</tr>
</tbody>
</table>

   Recombination frequency = 19+21/1000 - 40/1000 = 0.04 or 4%
   C and D are 4 map units apart on the chromosome.
7. Crossing over between linked genes produces nonrecombinant and recombinant offspring

Recombination frequency:

\[
\frac{\text{# of cross-overs}}{\text{total # of progeny}} = \frac{8 + 7}{55 + 53 + 8 + 7} = 0.12 = 12\%
\]

Two point cross (two loci)

Four kinds of progeny

8. Gene Mapping with Recombination Frequencies

<table>
<thead>
<tr>
<th>Gene Pair</th>
<th>% Recombination</th>
</tr>
</thead>
<tbody>
<tr>
<td>A and D</td>
<td>8</td>
</tr>
<tr>
<td>B and D</td>
<td>13</td>
</tr>
<tr>
<td>C and D</td>
<td>23</td>
</tr>
</tbody>
</table>
9. Linkage and Recombination between Three Genes (three point crosses)


Step 1: Look at the numbers. What do they tell you? Are the genes linked?

Step 2: Determine which phenotypes represent the nonrecombinant chromosomes.

Step 3: Determine which phenotypes represent the double recombinant chromosomes. What is the gene order?

Step 4: Write the phenotypes in their gene order.

Step 4: Calculate the map distances.
1. Phenotypes (=homolog placement)

2. Numbers

<table>
<thead>
<tr>
<th>Phenotype</th>
<th>Frequency</th>
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<tbody>
<tr>
<td>st+ ss+ e+</td>
<td>283</td>
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<tr>
<td>st ss e</td>
<td>278</td>
</tr>
<tr>
<td>st+ ss+</td>
<td>55</td>
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<tr>
<td>st ss+</td>
<td>3</td>
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<tr>
<td>st, ss+</td>
<td>5</td>
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<tr>
<td>scarlet, e</td>
<td>41</td>
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</tbody>
</table>

3. Phenotypes in correct order

<table>
<thead>
<tr>
<th>Phenotype</th>
<th>Frequency</th>
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</thead>
<tbody>
<tr>
<td>st+ ss+ e+</td>
<td>283</td>
</tr>
<tr>
<td>st ss e</td>
<td>278</td>
</tr>
<tr>
<td>st+ ss+</td>
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<tr>
<td>st, ss+</td>
<td>5</td>
</tr>
<tr>
<td>scarlet, e</td>
<td>41</td>
</tr>
</tbody>
</table>

4. Region getting crossover

- none
- st–ss (region 1)
- st–ss (region 1&2)
- ss–e (region 2)
- ss–e (region 2)

Map:

\[ \text{ss–e rec. freq.} = \frac{43+41+5+3}{755} = 0.122 \]
\[ \text{Map distance: 12.2cM} \]
11. Requirements of 3-point crosses:
   A. One parent must be heterozygous for all traits under consideration.
   B. The genotypes of gametes produced by the heterozygote must be evident from phenotypes of the offspring.
   C. Must look at sufficient numbers of progeny.

12. Interference: Usually one cross-over will interfere with formation of another crossover near it.

   Leads to: reduction (or increase) in observed number of double crossovers versus the number expected, when genes are close.

   \[
   \text{observed DCO} = \frac{8}{755} = 0.0105
   \]

   \[
   \text{expected DCO} = (\text{Prob. of st-- CO})(\text{Prob. of ss-- CO}) = 0.146 \times 0.122 = 0.0178
   \]

   A. Coefficient of coincidence = \( C = \frac{\text{observed DCO}}{\text{expected DCO}} \)  
      C usually < 1 = positive interference

   B. Interference: \( I = 1 - C = 1 - \frac{\text{observed DCO}}{\text{expected DCO}} \)  
      Usually positive interference: \( I > 0 \)

13. Linkage can be determined by analyzing pedigrees

   Lod scores: a measure of how likely two loci are to be linked.

   Pedigree linkage was used to locate at least two of the genes involved in familial Alzheimer's.

   Only these children were produced by cross-over events
14. Mapping with molecular markers: later in the course. Variations in the DNA sequence at each allele can be the “phenotypes” that are seen.

15. Deletion mapping: Mapping of the Testis Determining Factor gene. See worked problem 4, p. 192

16. Mapping with somatic cell hybrids

Example: Mouse/human somatic cell hybridization leads to cell lines with mainly mouse chromosomes and only a few human chromosomes.

Which chromosome encodes the gene for the gene product being found?

<table>
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<th>Human chromosomes present</th>
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Use of deletions in somatic cell hybrids

Conclusion: If the gene product is present in a cell line with an intact chromosome but missing from a line with a chromosome deletion, the gene for that product must be located in the deleted region.
17. Mapping by in situ hybridization

FISH: Fluorescence in situ hybridization
DNA probe is labeled with a fluorescent dye.

18. Mapping by DNA sequencing

Chromosome Painting with chromosome-specific FISH probes causes each chromosome to appear a specific color.