MAPPING GENES

A normal woman whose colorblind father had normal blood clotting has a son who has hemophilia. Could she have any normal sons? Is there a risk of having sons with both genetic defects?

Since both of these genes are on the X chromosome, she must carry recessive alleles of the colorblindness and clotting factor genes on different X-chromosomes. That is her X chromosomes have the following gene composition with respect to these two traits:

\[
\begin{align*}
\text{Cb} & \quad \text{h} \\
\text{cb} & \quad \text{H}
\end{align*}
\]

If X chromosomes always segregate "intact" to opposite poles in meiosis I, every son would be either a hemophiliac or colorblind. As it turns out, however, new gene combinations can be created, by a process called crossing-over or recombination.

Crossing-over occurs during prophase of meiosis I.

It occurs after the already duplicated chromosomes have paired (synapsis).

Most paired chromosomes will undergo at least one crossover.

Any one crossover involves only 2 of the 4 chromatids present.

At most, 1/2 of the gametes will show "recombination"

Since crossing over involves a physical exchange along the DNA helixes, the two crossover classes should be reciprocal and equal in frequency

The location of crossovers is random along the chromosome.

There is little chance for a crossover between two genes that are close together.

Crossing over (recombination) results in a reciprocal exchange of chromatids.

In the example given, a crossover between the Cb and H loci on the paired X chromosomes can be represented as:

\[
\begin{align*}
\text{Cb} & \quad \text{h} \\
\text{cb} & \quad \text{H}
\end{align*}
\]
The exchange point, which is sometimes visible in stained chromosome spreads, is called a chiasma.

Crossover gametes in the above figure would be *Cb--H* and *cb--h*.

Map distance between 2 genes is defined as % recombination.

If 5% of the sons from such mothers are *Cb--H*, 5% should also be *cb--h*, and we would say the genes are 10 map units apart.

When we know that genes are linked, we write the genotype showing those on each chromosome together. In this case the mother was *Cb--h/cb--H* rather than *Cbcb, Hh*.

Other than for the X chromosome, it is difficult to do mapping in humans. Mapping in plants and model organisms generally takes advantage of testcrosses.

Given in peas

<table>
<thead>
<tr>
<th>Alleles</th>
<th>Trait</th>
</tr>
</thead>
<tbody>
<tr>
<td>T_</td>
<td>tall</td>
</tr>
<tr>
<td>G_</td>
<td>green</td>
</tr>
<tr>
<td>tt</td>
<td>dwarf</td>
</tr>
<tr>
<td>gg</td>
<td>yellow</td>
</tr>
</tbody>
</table>

two different testcrosses can be made:

**Cross 1**  
*T-G/t-g X t-g/t-g*; the double recessive parent will only produce *t-g* gametes, so the combination of alleles in the gametes from the heterozygous parent can be seen by the phenotypes in the progeny. When a crossover between the *T* and *G* loci occurs, synapsis in *P1* will appear as:

![Diagram of synapsis in P1]

If the following results are observed:

<table>
<thead>
<tr>
<th>Gametes from <em>T-G/t-g</em> parent</th>
<th>Genotype of progeny</th>
<th>Phenotype of progeny</th>
<th>Percentage of progeny</th>
</tr>
</thead>
<tbody>
<tr>
<td><em>T-G</em></td>
<td><em>T-G/t-g</em></td>
<td>Tall, green</td>
<td>43 (Par)</td>
</tr>
<tr>
<td><em>T-g</em></td>
<td><em>T-g/t-g</em></td>
<td>Tall, yellow</td>
<td>7 (Rec)</td>
</tr>
</tbody>
</table>
the genes for height and color are 14 map units apart (7% Rec + 7% Rec = 14). 
Also in this cross, the doubly heterozygous parent is in "coupling" phase, meaning both dominant alleles are on the same chromosome and both recessive are on the other.

**Cross 2**  
T-g/t-G  X  t-g/t-g.  This is actually the same cross, but the heterozygous parent is in "repulsion" phase.  Since the genes are still located at the same sites on the chromosome, we can calculate the expected frequency of gametes and therefore the phenotypic ratio expected in the progeny.  The 14% recombination will be equally divided into T-G and t-g gametes.  In those relatively rare instances where a crossover occurs between genes T and G, the pairing will give:

```
    T-G  :  7%
    T-g  :  43%
    t-G  :  43%
    t-g  :  7%
```

Now the array of gametes will be 7% T-G : 43% T-g, : 43% t-G : 7% t-g.

Note that the arrangement of the genes in the parent has a dramatic effect on the frequency of each class of progeny!

The only formula that is needed for mapping genes or predicting gamete frequencies for linked genes is "map distance = % recombination".

Genes on the same chromosome belong to the same linkage group; although those that are greater than 50 or more map units apart show random segregation just as if they were on different chromosomes, they will show linkage to "in-between" genes.

A chromosome map can be made showing the relative location of the genes:

<table>
<thead>
<tr>
<th>map units</th>
<th>18</th>
<th>5</th>
<th>30</th>
<th>16</th>
<th>3</th>
<th>22</th>
<th>10</th>
<th>14</th>
<th>12</th>
</tr>
</thead>
<tbody>
<tr>
<td>gene</td>
<td>A</td>
<td>B</td>
<td>C</td>
<td>D</td>
<td>E</td>
<td>F</td>
<td>G</td>
<td>H</td>
<td>I</td>
</tr>
</tbody>
</table>