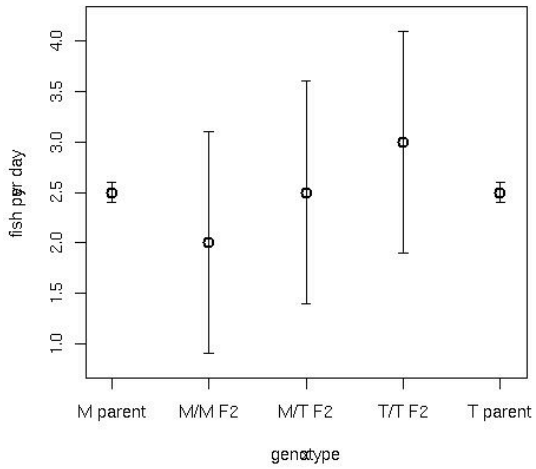
1. We learned in class that most common human diseases are controlled by many loci, each of which has a very subtle effect on disease. What is the value of actually mapping one of these loci? Name two ways that knowing the identity of a subtle causal locus associated with a disease might someday impact human health.

   Someday it will be possible to diagnose people (or predict their susceptibility to a disease) based on genotypes at the causal loci even if there are many such loci, as long as we know most of them. Also, identifying causal variants can single out genes and gene products that can be targeted for rational drug design; even though the effect of a natural variant in the gene may be subtle, blocking the gene product artificially with a drug might turn out to be a very good treatment for the disease.

2. Imagine that you are studying fishing success in kingfisher birds, a quantitative trait. You have two birds, one deriving from a wild bird caught in Micronesia and the other deriving from a Tokyo Bay isolate, that are each inbred to complete homozygosity. You mate them to produce a large family of F2's. From this population you map two additive and incompletely dominant loci that completely explain variation in fishing success between birds in the cross. One locus is on chromosome II and the other is on chromosome X. The effect of the chromosome II locus is shown below, where M stands for Micronesia and T stands for Tokyo:



   (a) What is the effect on phenotype (in units of fish per day) among the F2's of gaining a single T allele at the chromosome II locus?

   On average, inheriting each T allele is associated with catching 0.5 more fish per day among the F2's.

(b) If you made a similar diagram comprising all the possible F2 **genotypes** plus the parents, how many columns (*x* values) would there be?

Eleven. The Punnett square for two loci in a dihybrid cross has 16 squares, of which 9 represent unique genotypes (see for example Figure 3.17 in your book); plus add two for the parents.

(c) The "error bars" in this plot don't all reflect error per se. What do they represent in the middle three data points and why are they wide relative to the parents?

The error bars in the middle three columns represent the variation in phenotype among F2's with the same genotype at the chromosome II locus. They are wide because each group of F2's varies in genotype at the chromosome X locus. For example, individuals homozygote for the M allele at the chromosome II locus could have M/M, M/T, or T/T genotypes at the chromosome X locus. Each of those genotypes could be associated with a different fishing success rate. So there is a wide spread in the data of each column.

(d) What must the phenotype be of F2's that are homozygous for the Micronesian allele at both the chromosome II locus and the X locus? (Hint: look at the first column of the figure and remember that the loci act additively.)

Because the loci act additively, the phenotype on average of the individuals that are M/M at both loci must be the same as the phenotype of the M parent itself: 2.5 fish per day.

(e) Given this, what can you say about the average phenotype be of F2's that are homozygous for the Micronesian allele at the chromosome II locus and homozygous for the Tokyo allele at the chromosome X locus?

The average among all F2's that are M/M at the chromosome II locus is 2 fish per day. Again, this is an average of three genotypes at the chromosome X locus: M/M, M/T, and T/T. We just saw that the phenotype among individuals that are M/M at both loci have mean fishing success of 2.5. So the phenotypes of individuals that are M/T and T/T at chromosome X must be pulling down the average; you can say that F2's that are M/M at chromosome II and T/T at chromosome X must be worse fishers than F2's that are M/M at both loci.