

Homework Assignment #1

Date Assigned: 12 September 2010.

Date Due: 23 September 2010.

1. In some population, the genotype frequencies for two alleles A and a of a given locus were found to be consistent with Hardy-Weinberg (HW) proportions with allele frequencies of 0.3579 for A and 0.6421 for a . Assuming that all of the assumptions of HW model hold, calculate the genotype frequencies expected in the next generation along with the corresponding allele frequencies.
2. Phenylketonuria is a defect in phenylalanine metabolism caused by lack of a functional allele encoding the enzyme phenylalanine hydroxylase. Over 200 defective alleles have been identified, and most affected individuals are actually heterozygous for two different defective alleles. The condition affects about 1 in 10,000 newborn Caucasians. Estimate the frequency of heterozygotes for the normal and a defective allele under the assumption of random mating.
3. In a sample of 1617 individuals, the numbers of A, B, O, and AB blood types observed were 724, 110, 763, and 20, respectively. The best estimates of allele frequency are $\hat{p}_1 = 0.2661$ (for A), $\hat{p}_2 = 0.0411$ (for B), $\hat{p}_3 = 0.6928$ (for O). Calculate the expected numbers of the four phenotypes and carry out a χ^2 test for goodness of fit to the HW expectations.
4. The table below shows the number of individuals affected, per million individuals, for each of several autosomal recessive traits. Assuming random mating proportions in the population, what is the expected frequency of individuals who are heterozygous for each of the recessive alleles?

Trait	# of individuals affected per million individuals
(a)	2786
(b)	658
(c)	287
(d)	160
(e)	102

5. In a population undergoing random mating for a single gene with a dominant and recessive allele, show that the allele frequency of the recessive allele among individuals with the dominant phenotype is $q/(1+q)$, where q is the allele frequency of the recessive in the whole population. Then, show that the frequency of homozygous recessive genotypes from dominant \times dominant matings is $[q/(1+q)]^2$, and from dominant \times recessive matings is $q/(1+q)$.
6. Consider two linked genes that have a frequency of recombination of $r = 0.005$. What types and frequencies of gametes would be produced by an individual of genotype AB/ab ? By an individual of genotype Ab/aB ?
7. To see how population admixture can cause linkage disequilibrium (even for genes in different chromosomes), consider the three situations in the table below. Each example gives the gametic frequencies in two subpopulations, both of which are in linkage equilibrium for the alleles A , a and B , b for two genes. The gametic frequencies in the two populations are denoted $P1$ and $P2$ with appropriate subscripts for the alleles in the gametes. For each example, verify the absence of linkage disequilibrium in each original subpopulation. Then assume that the two subpopulations in each example undergo admixture in equal proportions, and calculate the D' and ρ^2 in the resulting admixed population.

Example	(a)	(b)	(c)
$P1_{AB}$	0.0734	0.7220	0.0277
$P1_{Ab}$	0.6860	0.0082	0.0628
$P1_{aB}$	0.0232	0.2667	0.2786
$P1_{ab}$	0.2174	0.0031	0.6309
$P2_{AB}$	0.4082	0.0132	0.0281
$P2_{Ab}$	0.3380	0.0621	0.2959
$P2_{aB}$	0.1388	0.1622	0.0587
$P2_{ab}$	0.1150	0.7625	0.6173

8. The paper “Population genomic analysis of outcrossing and recombination in yeast,” by Ruderfer *et al.* (Nature Genetics, 38(9): 1077-1081, 2006; posted on the course website) describes a novel HMM-based method for estimating the rate of recombination from sequence data. Describe formally the method that they propose and discuss the assumptions underlying the method. In particular, you need to describe the HMM formally, and discuss its underlying assumptions.