Ecology and Population Biology 314
Data Set 1: Malaria and sickle cell

Background:

As you learned in lecture, a mutation at a single amino acid in the beta chain of the Hemoglobin gene (S) can lead to changes in the structure of red blood cells. The structural changes this mutation produces, however, depend upon whether an individual is homozygous (SS) or heterozygous (AS) for the mutant sickle cell allele, S. If an individual is heterozygous, their red blood cells are mostly normal and, in areas where Malaria is present, receive some level of protection against the parasite. If, instead, an individual is homozygous for the mutant S allele, their red blood cells are "sickled" and break down more quickly than normal red blood cells, frequently resulting in severe anemia and reduced survival. Thus, in regions where Malaria is prevalent, heterozygous individuals may have a greater fitness than both types of homozygote (Hedrick 2011). In contrast, in areas where Malaria is infrequent or absent altogether, the mutant sickle cell allele confers no advantage and individuals homozygous for the normal A allele have the greatest fitness (Hedrick 2011).

Based on geographically widespread genetic studies, we know that the frequency of the mutant sickle cell allele, S, varies across space. One hypothesis for this pattern is that the frequency of the mutant S allele is elevated in areas where infection by malaria causes overdominant selection; in areas where malaria is rare or absent the frequency of the mutant S allele is very low and attributable to the balance between selection and mutation. An alternative hypothesis is that the S allele is at mutation selection balance in all locations, but selection against homozygous SS individuals is stronger in some locations than others. Fortunately, data exists that may help us to distinguish between these possibilities. Specifically, we know that:

- The equilibrium frequency of the S allele at mutation selection balance is given by the following equation:

$$\hat{q} \approx \frac{\mu}{\mu+\sqrt{\mu(\mu+(1-2\mu)s_{ss})}}$$

- The selection coefficient acting against SS individuals, s_{ss}, ranges between 0.7 and 1.0 worldwide (Hedrick 2011).

- The per-generation mutation rate, μ, for the sickle cell locus is almost certainly somewhere between 1×10^{-8} and 1×10^{-5} (Nachman and Crowell 2000).

You task:

Using the background information above and the data on individual genotypes compiled in the file DataSet1.xls, identify the populations in which the malaria hypothesis seems more likely than the mutation selection balance hypothesis. Is your result consistent with what we know about the worldwide distribution of Malaria? Be sure to provide appropriate citations within your report for any additional sources you use to justify your conclusion.

The file, DataSet1.xls contains data collected in three different studies, each conducted within a different geographic region. In each study, the Hemoglobin genotype of individuals was recorded. The first study was conducted in Gambia, and incudes genotypes for a total of 229 individuals (Atkinson et al. 2006). The second study was conducted in Brazil and includes genotypes for 1,965 individuals (Silva et al. 2006). The third study was conducted in Canada and includes genotypes for 2,716 individuals (Yorke et al. 1992). Within the data file, the first column indicates the country, the second column the individual, and the third column the individual's genotype. In order to make progress (e.g., to calculate allele frequencies), you will need to manipulate this data within Excel (highly recommended) or spend an inordinate amount of time playing with your calculator.

References:

Atkinson, S. H., K. Rockett, G. Sirugo, P. A. Bejon, A. Fulford, M. A. O'Connell, R. Bailey et al. 2006. Seasonal childhood anaemia in West Africa is associated with the haptoglobin 2-2 genotype. Plos Medicine 3:652-658.

Hedrick, P. W. 2011. Population genetics of malaria resistance in humans. Heredity 107:283-304.

Nachman, M. W., and S. L. Crowell. 2000. Estimate of the mutation rate per nucleotide in humans. Genetics 156:297-304.

Silva, W. d. S., A. Lastra, S. F. d. Oliveira, N. Klautau-Guimarães, and C. K. Grisolia. 2006. Avaliação da cobertura do programa de triagem neonatal de hemoglobinopatias em populações do Recôncavo Baiano, Brasil hemoglobinopathies in the Recôncavo region of Bahia, Brazil. Cadernos de Saúde Pública 22:2561-2566.

Yorke, D., J. Mitchell, C. Clow, E. Nuguid, R. Cadogan, D. Sinclair, S. Luscombe et al. 1992. NEWBORN SCREENING FOR SICKLE-CELL AND OTHER HEMOGLOBINOPATHIES - A CANADIAN PILOT-STUDY. Clinical and Investigative Medicine-Medecine Clinique Et Experimentale 15:376-383.