Chapter 7 – Additional Models

Selection w/ 3 alleles or 2 loci

Fecundity Selection

Frequency-dependent Selection

Selection and drift (compare to migration and drift)

*Selection and migration (divergence w/ gene flow)

Selection and mutation

Selection in the coalescent

A simple fitness "landscape"

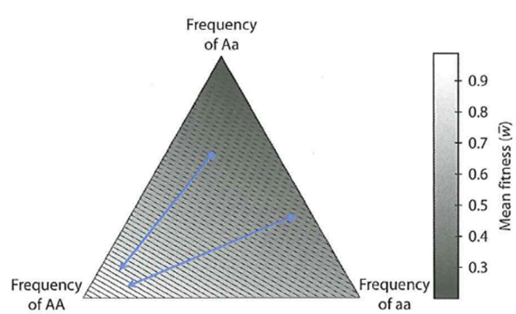


Figure 7.1 A fitness surface made by including mean fitness on a De Finetti plot of the three genotype frequencies for a diallelic locus. The colored lines indicate the possible trajectories of genotype frequencies as natural selection increases the mean fitness of the population. The fitness values are $w_{AA} = 1.0$, $w_{Aa} = 0.6$, and $w_{aa} = 0.2$ so the highest mean fitness is found in the lower left apex when the population is fixed for the AA genotype. This highest fitness point can be reached by continually increasing mean fitness from any initial point on the surface. Gene action is additive because alleles have a constant impact fitness regardless of the allele they are paired with in a genotype. An A allele always contributes 0.5 and an a allele 0.1 toward the fitness of a genotype.

Malaria

- **S** allele codes for a variant form of β-hemoglobin
- **SS** individuals suffer from severe anemia
  - sickle-cell disease
- **AS** individuals appear to be protected from malaria because infected cells undergo sickling and are removed from circulation
- ~fitness where malaria is prevalent
  - $w_{AA} = 0.9$, $w_{AS} = 1$, $w_{SS} = 0.2$
- equilibrium allele frequency of **A** = 0.89

Malaria

- glucose-6-phosphate dehydrogenase (G6PD) is an X-linked gene that helps control oxidative damage in erythrocytes
- **G6PD *A-*** has reduced activity but appears to protect carriers from severe malaria

distribution of sickle-cell allele

distribution of G6PD deficiency allele

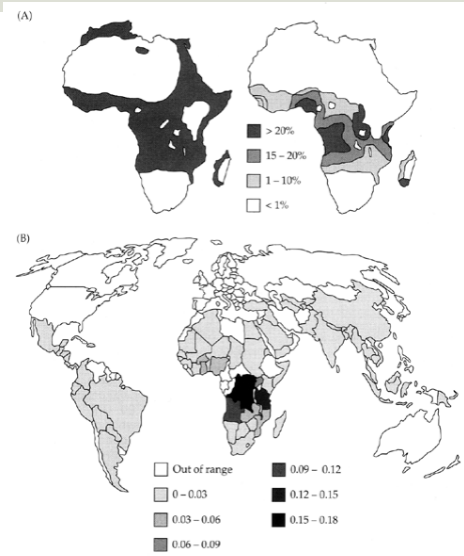
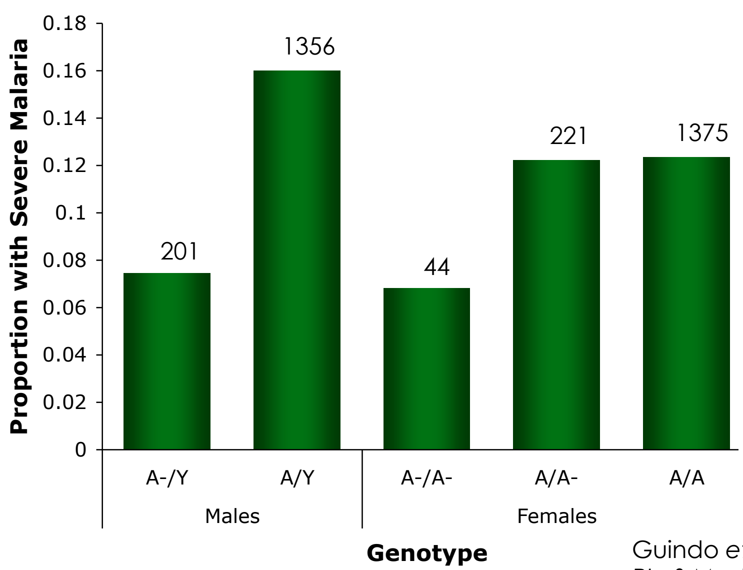


FIGURE 5.5 (A) A map of the distribution of the allele for sickle-cell anemia, and (B) map of the incidence of the *G6PD* deficiency allele. Both mutations are associated with resistance to malaria cause by *Plasmodium falciparum*. (A) The upper left map shows in gray the areas of incidence of falciparum malaria in Africa in the 1920s before mosquito control programs were implemented. The upper right figure shows the distribution of the beta-S globin allele. The global map in (B) shows the frequency of *G6PD* deficiency alleles indicated by the shading. The extensive overlap in the distributions relative to malaria was an early indication that there might be some causal connection.

X-Linked G6PD Deficiency Protects Hemizygous Males but Not Heterozygous Females against Severe Malaria



Guindo *et al*. 2007
PLoS Medicine

The C allele…

- CC homozygote has the highest fitness but is rare… why?

Table 7.1 Relative fitness estimates for the six genotypes of the hemoglobin β gene estimated in Western Africa where malaria is common. Values from Cavallo-Sforza and Bodmer (1971) are based by deviation from Hardy–Weinberg expected genotype frequencies. Values from Hedrick (2004) are estimated from relative risk of mortality for individuals with AA, AC, AS, and CC genotypes and assume 20% overall mortality from malaria.

	Relative fitness (w)					
Genotype . . .	**AA**	**AS**	**SS**	**AC**	**SC**	**CC**
From Cavallo-Sforza and Bodmer (1971)						
Relative to w_{CC}	0.679	0.763	0.153	0.679	0.534	1.0
Relative to w_{AS}	0.89	1.0	0.20	0.89	0.70	1.31
From Hedrick (2004)						
Relative to w_{CC}	0.730	0.954	0.109	0.865	0.498	1.0
Relative to w_{AS}	0.765	1.0	0.114	0.906	0.522	1.048

The C allele…

- CC homozygote has the highest fitness but is rare… why?
  - at equilibrium:

    A frequency $= 8/9$, $S = 1/9$, and $\overline{w} = 0.911$
  - rare **C** allele has mean fitness of:

$$8/9 \times 0.9 + 1/9 \times 0.7 = 0.878$$

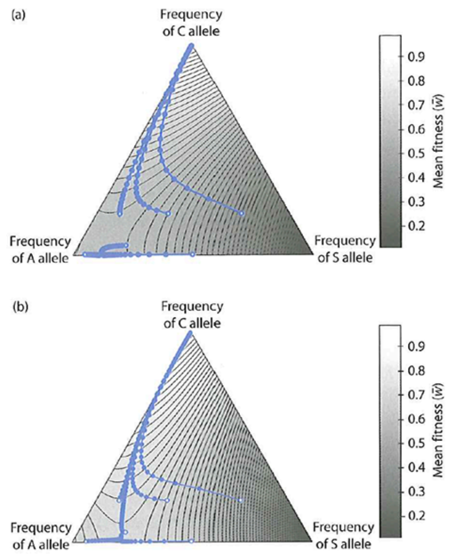


Figure 7.2 Fitness surfaces for the A, S, and C alleles at the human hemoglobin β gene when malaria is common. The surface in (a) corresponds to the top set of fitness values in Table 7.1 and (b) shows the surface for the bottom set of values. The tracks of circles represent generation-by-generation allele frequency trajectories due to natural selection over 50 generations calculated with equation 7.3. In (a), when the initial frequency of the C allele is relatively high, the equilibrium of natural selection is the fixation of the CC genotype. In contrast, when the C allele is initially rare (a frequency of less than about 7%) selection reaches an equilibrium with only the A and S alleles segregating and the C allele going to loss. In (b), selection will eventually fix the CC genotype from any initial frequency of the C allele. However, when the C allele is at low frequencies, the increase in the C allele each generation is extremely small so that selection would take hundreds of generations to fix the CC genotype. The six initial allele frequency points, shown as open circles, are identical for the two surfaces.

$$\Delta p = p\frac{\left(\bar{w}_A - \bar{w}\right)}{\bar{w}} = \frac{\left(w_{AA}p + w_{AB}q + w_{AC}r\right) - \bar{w}}{\bar{w}}$$

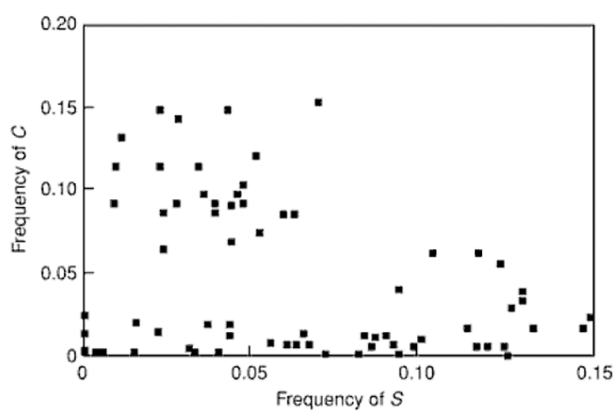


Figure 11.6. Frequencies of *S* and *C* alleles in 72 West African populations. Reprinted with permission from Fig. 4.12 in L. L. Cavalli-Sforza and W. F. Bodmer, *The Genetics of Human Populations*. Copyright ©1971 by W. H. Freeman and Co.

From: Templeton AR (2006) *Population Genetics and Microevolutionary Theory*

Does overdominance (heterozygote advantage) maintain genetic diversity?

ONE LOCUS:

- stable equilibria are generally not expected with multiple alleles
- if w_{ij} > max (w_{ii}, w_{jj}), stability for 4, 5, or 6 alleles is expected in only 12.6, 1.2, and 0.03% of random fitness sets
  - each w_{ij} assigned a random number between 0 and 1
- if w_{ij} > max (w_{ii},…, w_{nn}), stability for 4, 5, or 6 alleles is expected in only 34.3, 10.4, and 1.3% of random fitness sets

Does overdominance (heterzygote advantage) maintain genetic diversity?

MANY LOCI:

- "genetic load" - reduction in fitness compared to the situation if all individuals had the optimal genotype
- if overdominance were important at a large number of loci, most individuals would have less fit homozygous genotypes at many loci
- if fitness is multiplicative across loci, then mean fitness would be very low

Adaptive topography & Drift

- fitness as a function of allele frequencies forms an adaptive topography or landscape

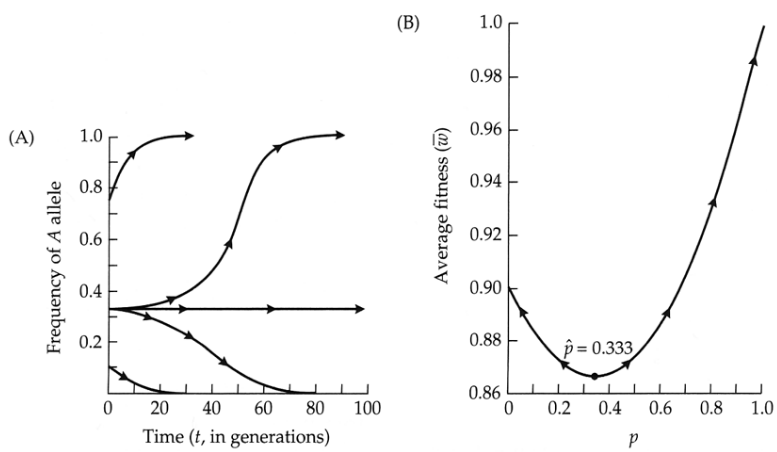
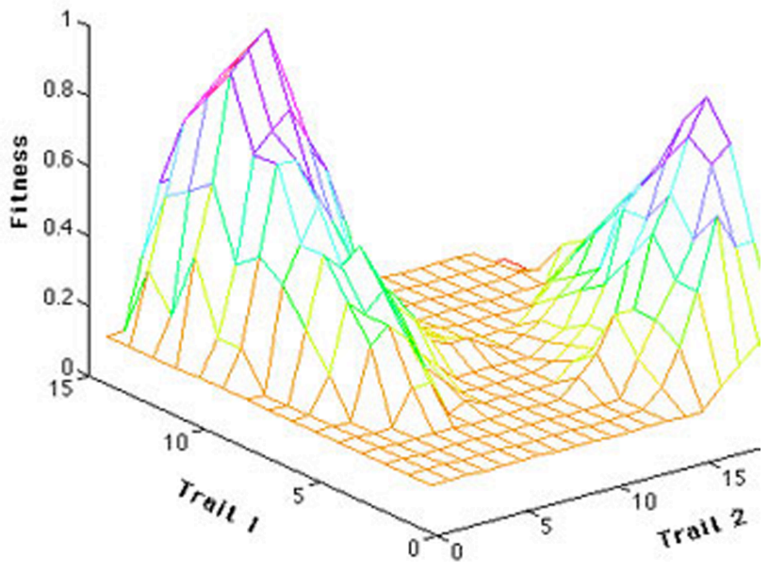
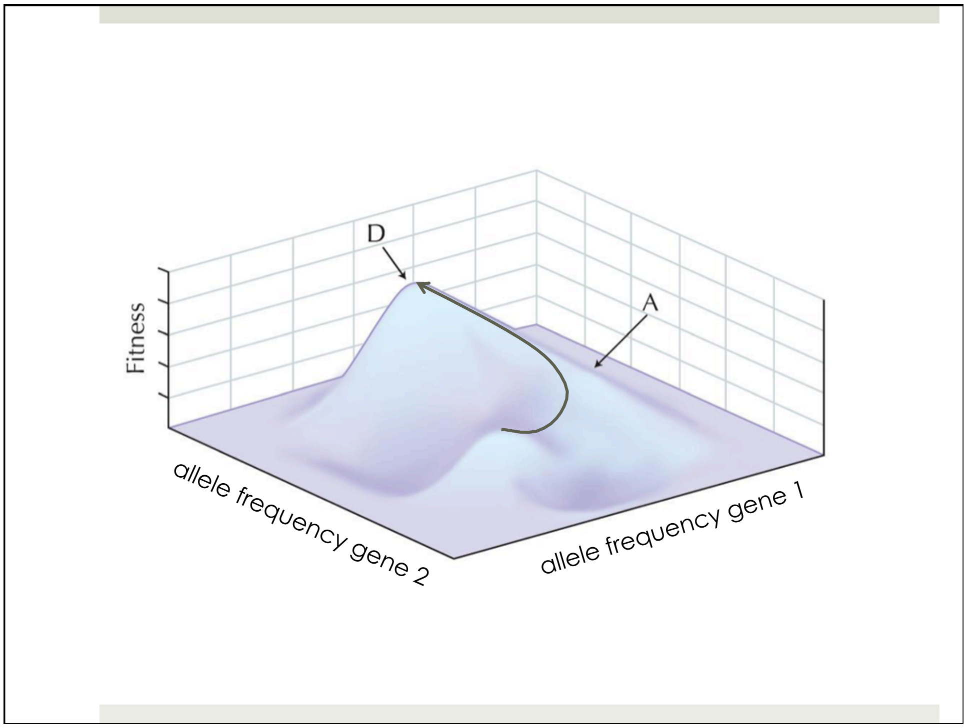


FIGURE 5.7 Selection when there is heterozygote inferiority. (A) The allele frequency goes to 0 or 1 depending on the initial frequency. In this example, $w_{11} = 1$, $w_{12} = 0.8$, and $w_{22} = 0.9$, and there is an unstable equilibrium when the frequency of the *A* allele is $\hat{p} = \frac{1}{3}$. An infinite population with $p = \frac{1}{3}$ maintains this frequency, but any slight upward change in the frequency of *A* results in eventual fixation, and any slight downward change in the frequency of *A* results in ultimate loss. (B) Average fitness $\bar{w}$ against *p* for the same example. The unstable equilibrium represents the minimum of $\bar{w}$.



Adaptive Topography & Drift

- fitness as a function of allele frequencies forms an adaptive topography or landscape
- how can populations escape non-optimal, local equilibria?
  - Wright – "shifting balance theory"
    - important role for genetic drift in moving populations between adaptive peaks
  - the fitness landscape may also change with environmental conditions, population density, etc.


D
A
Fitness
allele frequency gene 2
allele frequency gene 1