Biology 4250 - Principles of Evolution
Dr. Carr

Laboratory #3:
Computer Simulation of Natural Selection

This laboratory uses an **Excel** program to simulate natural selection. You will use it to examine the consequences of **directional selection on dominant and recessive alleles** (Exercise 1), and to examine the conditions under which **incomplete dominance** and **balancing selection** can maintain polymorphism in a population (Exercise 2). Review the lecture discussion of modes of selection.

The emphasis in this lab is how genetic dominance affects the behaviour of alleles subject to (negative) selection. "Real" examples have been chosen to make the population genetics easier to visualize and discuss; the biology of these examples will be discussed in lecture.

Before coming to lab, read through each scenario and write down the initial conditions of **q**, **W0**, **W1**, and **W2** for each part of each exercise. Before running each simulation, check with the instructors to make sure that these values are correct.

Description of Excel spreadsheet GSM

The **Excel** spreadsheet **GSM** simulates natural selection on a one-locus, two-allele (**A** & **B**) model in a *monoecious* population with random union of *gametes* (the '*tide pool*' model). This accurately simulates selection in the *dioecious* species used here. Required input parameters are the initial **allele frequency q0** = f(**B**)) and the **fitness values W0**, **W1**, and **W2** of the *phenotypes* for each of the three *genotypes* **AA**, **AB**, and **BB**, respectively. Recall that ***fitness* is a *phenotype***, but may be assigned to a genotype *iff* each *genotype* has a different *phenotype*. Population size is infinite and is unchanged by selection. The model is therefore **deterministic**, and **q** approaches either **fixation** (**q=1**) or **loss** (**q=0**) **asymptotically**: **q** = 1.0000... or 0.0000... to four decimals can be thought of as such. [The program **NatSel** will explore selection with *finite* populations].

Three graphs of the tabled results are given. All three are plotted on the same **X** axis (time). (1) Change in allele frequency f**(B) = q**. (2) Change in genotype frequencies f(**AA**), f(**AB**), & f(**BB**), and for complete dominance models f("**A**") = f(**AA** + **AB**). (3) Change in population fitness, **W-bar**, calculated as defined, **W-bar** = **W0** x f(**AA**) + **W1** x f(**AB**) + **W2** x f(**BB**).

The spreadsheet program runs as a single continuous scenario, with **W0**, **W1**, and **W2** changing periodically according to the environment. Changes during each scenario alters **q** at the end of each segment, which will affect behavior of the model in the next segment. For example, how does f(**B**) behave when **BB** is favored, but **q** is uncommon, rare, or very rare (**q = 0.1**, **q = 0.01** or **q = 0.001**)? Transitions between different values of **W** can be made smoothly rather than abruptly. For example, a change from **W** = 1.0 to 0.70 in five 5% steps (0.95, 0.90, 0.85. 0.80, & 0.75) (or the reverse) will smooth the change in **q**.

The model follows the behavior of **q** = f(**B**), for example when **B** is recessive to **A**. It is important to realize that this is *exactly* the same model as **p** = **f(A)** with **A** *dominant* to **B**. The only difference is that graph of f(**A**) is *inverted* wrt f(**B**). Avoid thinking of these two scenarios as different.

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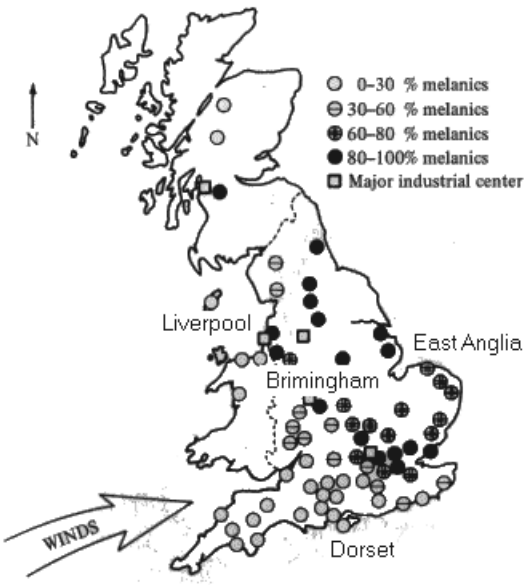
Lab #3, Exercise 1 - Directional & Stabilizing Selection in *Biston betularia*

The phenomenon of **industrial melanism** in *Biston betularia*, the common British pepper moth, is the classic example of **Ecological Genetics,** natural selection in the wild. Research on *B. betularia* ha been carried out for many decades by HBD Kettlewell (1907 - 79). co-workers, and successors.

Pepper moths are nocturnal animals that sit motionless on trees during the day. Their major predators are diurnal predators, such as thrushes and other birds, that detect the moths visually. The species is **polymorphic** for several colour phases. The common form is light grey and speckled, which is highly **cryptic** (camouflaged) when seen against the bark of the lichen-covered trees common in the English Midlands. A second colour phase, a **melanic** (black pigmented) form called "*carbonaria*", is quite conspicuous on the same light-coloured trees [compare phases in the figure, below]. Experiments show that the two colour phases are subject to differential predation by birds, according to degree of **crypsis**. The polymorphism is under genetic control of a single locus with two classes of alleles. The **dominant** alleles corresponds to the **melanic** form and the **recessive** alleles to the **lighter** form.

Changes in the frequency of the two forms are documented in amateur insect collections from the 18th century onward. Melanic forms were initially rare, because the alleles were rapidly eliminated whenever they arose. The melanic form began to increase in numbers in the English Midlands about 1850. This coincided with the onset of the Industrial Revolution, which generated extensive air pollution in the form of vast quantities of black soot from the chimneys of coal-burning factories. In heavily industrialized areas, such as Manchester and Birmingham [right figure, below], forests of previously white, lichen-covered trees became completely blackened. Under these circumstances, the melanic form became *more cryptic* than the lighter form [middle figure, below]. By 1900, the proportion of melanic forms in the Manchester area exceeded 90%. Outside of these industrial areas, trees remained relatively uncontaminated and the lighter form continued more prevalent. In the latter 20th century, the death of older trees and institution of pollution control measures, such as installation of "*scrubbers*" on smokestacks, led to a partial restoration of pre-industrial environmental conditions, so that forests in some previously heavily polluted areas have been restored to their original state. The frequency of the melanic form has declined in these areas.



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Lab #3, Exercise 1 - Directional & stabilizing Selection in *Biston betularia* (cont'd)

Directions

Set the initial frequency of the recessive '***light***' allele [**q0** = f(**B**)] as indicated. Set the relative fitness values of the three genotypes **AA**, **AB**, and **BB** (**W0**, **W1**, **W2**, respectively) as indicated in the first scenario below.

In each of the following five scenarios, **record f(B) at the end of every ten generations**, and **collect the graphs** as directed. Be prepared to explain to the instructors the changes between the '*before*' and '*after*' lines in any one generation.

(a) A r**ural area without pollution**, pre-1850. [**q0** = 0.90, 30% selection against the **dark** phenotype]. Continue for 10 generations, to g = 10, ***OR*** as instructed. [What is the expected initial **f('A')**?]

(b) A **rural area during the Industrial Revolution**. [30% selection against the **light** phenotype]. Continue for an additional 60 generations, to g = 70, ***OR*** as instructed.

(c) A **polluted industrial area**, late 19th century. [30% selection against the **light** phenotype, as in (b)]. Continue for an additional 30 generations, to g = 100, **OR** as instructed.

(d) An **industrial area becoming a "smokeless zone,"** late 20th to early 21st century. [30% selection against the **dark** phenotype. Continue for 100 generations, to g = 200].

Results

Save your Excel Spreadsheet file data: print out the graph at the end of all four scenarios. Label your axes: indicate the points where the scenario changed.

The graphs record

(1) **q = f(B)** over the course of the model,

(2) ***f*[AA+AB]** = *f*['**dark**' phenotype], *f*[**AA**], *f*[**AB**], *f*[**BB**] = *f*['**light**' phenotype], and

(3) **Wbar** = mean fitness of the population.

Lab #3, Exercise 1 - Questions (1.5 pts)

1. How rapidly does s**trong negative selection** modify the frequency of a ***rare dominant*** (scenario **a**) allele as compared with a ***rare recessive*** (scenario **c**) allele? Can either type of allele ever be completely eliminated from the population by selection? Why is there a difference?

2. How rapidly does strong negative selection modify the frequency of a ***common recessive*** (scenario **b**) allele, compared with a ***common dominant*** (scenario **d**) allele? How quickly does the **phenotype of the population** change (***HINT***: how many generations are required for the '*common*' phenotype to become '*uncommon*')? Why is there a difference?

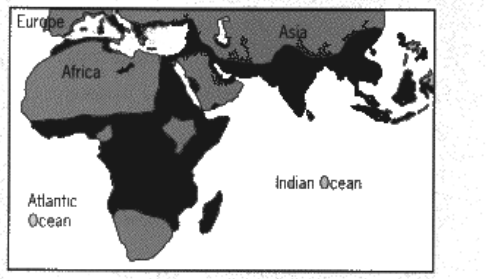
3. What is the difference in the behavior of advantageous phenotypes that are ***very rare*** (**q = 0.001**) as compared with a ***rare*** (**q = 0.01**, as in scenario **d**)? What happens as the phenotype becomes less rare? Why?

Laboratory #3, Exercise 2 - Balancing Selection of Hemoglobin A and S

Standard human hemoglobin (**Hemoglobin A**, **HbA**) is a **tetrameric protein** comprising two **alpha** subunits and two **beta** subunits. **Sickle-cell** hemoglobin (**Hemoglobin S**, **HbS**) differs from **HbA** by a single **DNA** base **SNP** that leads to a single amino acid substitution in the **beta** subunit. Persons homozygous for the **S** beta chain allele (**SS**) have a severe blood disorder called **sickle-cell anemia**. Under conditions of reduced blood oxygen tension, **HbS** molecules form large, crystalline lattices that distort red blood cells into crescent-like "*sickles*." These impede blood flow through capillaries, which causes episodes of severe muscular pain (**infarctive crises**) as well as chronic **hemolytic anemia**. The fitness of **SS** homozygotes in the absence of adequate medical care is close to zero, since few survive to reproductive age. Persons heterozygous for the **S** beta chain (**AS**) allele show a much milder form of anemia, known as "**sickle cell trait**", which is seldom life threatening. [Distinguish '*trait*' from '*anemia*'.] New **CRISPR**-based technologies are effective treatments for sickle-cell anemia.

The sickle-cell allele occurs most commonly in human populations from West and Central Africa, in whom it reaches frequencies as high as f(**S**) = 0.20. These areas are also characterized by high incidence of **malaria**, and several lines of evidence indicate that f(**S**) is maintained by the increased resistance of **AS** heterozygotes to malaria. Besides the geographical correlation, (1) the frequency of sickle-cell trait increases with age among African populations, (2) hospital records indicate increased co-morbidity from malaria among **AA** homozygotes relative to **AS** heterozygotes, and (3) laboratory tests indicate that the malarial plasmodium parasite is less able to infect **AS** red cells. In malarial environments, the relative fitness of **AA** homozygotes seems to be substantially reduced with respect to the **AS** heterozygotes. Thus, **A** & **S** are subject to **balancing selection**.

Sickle-cell anemia is a major health and social problem in Africa and in black communities of North America, most of whose ancestors originated in West Africa. In the absence of malaria, the heterozygous advantage of the sickle-cell trait is lost, and the **S** allele is subject to **directional selection**.

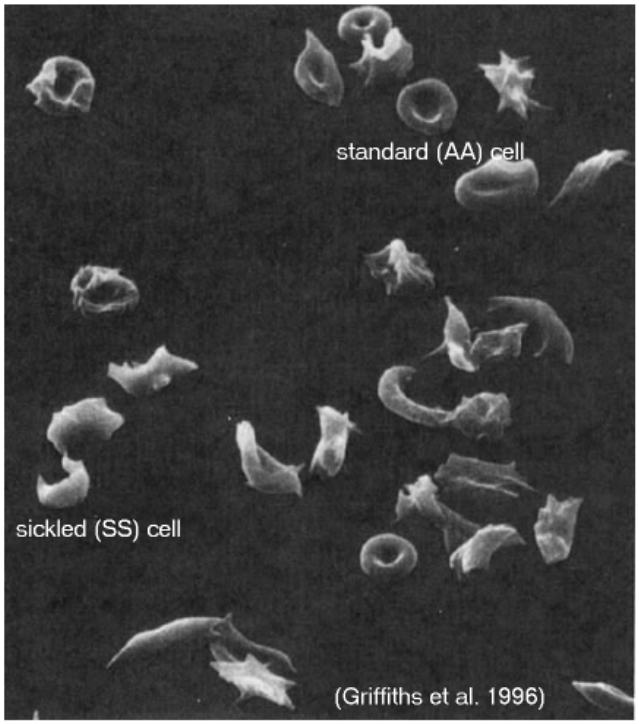


(a) Distribution of Falciparum malaria.

(b) Distribution of sickle-cell anemia allele (Hb^S).

Figure 27.7 Distribution of Falciparum malaria (*a*) and the distribution of the sickle-cell anemia allele (Hb^S) (*b*) in the Old World.

(Snustad et al. 1997)



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Laboratory #3, Exercise 2 - Balancing Selection between Hemoglobin A & S alleles (cont'd)

Directions

The column heads for this exercsie are re-labelled as **AA**, **AS**, & **SS**. Run **GSM** with the following parameters. Let **q** = f(**S**), where **S** is the allele for sickle-cell hemoglobin. The fitness of **AA** homozygotes is **1.00** in a non-malarial environment, or **0.50** in a malarial environment. In either environment, the fitness of **AS** heterozygotes is **1.0** and the fitness of **SS** homozygotes is **0.0**. [These values allow the model to run rapidly, in a more easily analyzed manner. Realistic values for f(**S**) and **W** have been estimated from clinical data, see **Question #6** below. If you like, repeat the exercise with realistic values **GSM** model].

The following scenario is continuous over many generations, and traces a human population as it moves between different selective environments. The number of generations in each environment may be adjusted upward

(a) Consider a population of hunter-gatherers from a non-malarial environment in East Africa that initially carries the allele for sickle-cell hemoglobin at a frequency of f(**S**) = 0.05. [Enter **q**, **N**, and **W0**, **W1**, and **W2** as indicated]. Continue for **20** generations, ***OR*** as instructed.

(b) Suppose this population moves westward and begins farming in a high-malarial environment in West Africa. [Continue from part (a): change the fitness values as indicated, and continue for **40** more generations, ***OR*** as instructed.]

(c) West African blacks were brought to North America beginning about 400 years ago [how many generations is this?]. Assume that North America is a non-malarial environment. [Continue from part (b): change the fitness values as appropriate, and continue for **40** more generations, ***OR*** as instructed.].

(d) How long would it take to eliminate the **S** allele if ***all*** persons with sickle-cell "*trait*" (**AS** individuals) voluntarily choose not to have children? If **50**% or **10**% of carriers restrained? [Start with **q = 0.05,** set **W0**, **W1**, & **W2** as appropriate.] [

Results

Save the Excel Spreadsheet(s). **Copy & Paste graphs** as necessary to answer the questions. Label you axes.

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Laboratory #3, Exercise 2 - Questions

1. In part (b), explain the patterns of deaths due to malaria and sickle-cell anemia after the East African population moves to the malarial West African environment (between generations 20 and 40).

2. CALCULATE the expected frequency of the **S** allele at equilibrium (between generations 30 & 40) (see lecture notes for the formula). Compare this with the observed frequency in this interval. Explain how f(**S**) is maintained in this interval.

3. What happens to the mean fitness (**W**) of the population when the mode of selection changes at 20 generations (Hint: what is the total population size *after* selection in generations 25 and 35)? In the malarial environment, at which value of f(**S**) is the total population size after selection maximized? Explain.

4. Compare the rate of increase of the frequency of the **S** allele between generations 20 & 30 with the rate of decrease between generations 40 & 60 (compare the shape of the curves). Why is there a difference (hint: how does the fitness of the **AA** phenotype change with respect to **AS** in these two intervals)?

5. In part (c), approximately how many generations are required before f(**S**) declines to the original value, f(S) = 0.05) Predict how long it would take to eliminate the **S** allele under these circumstances. How long would it take to eliminate the S allele if ***all*** persons with sickle-cell "*trait*" (**AS** individuals) voluntarily choose not to have children? What if **50%**or **10%** of carriers restrained? What are the social policy and ethical implications of such a solution?

6. In this model of balancing selection, selection against **AA** in malarial environments has been set unrealistically high in order to make the principles clearer.

a. If the actual observed frequency of **S** in West African populations (**q = 0.16**) represents the true equilibrium frequency, calculate the selection coefficient associated with the **A** allele.
b. Repeat the scenarios with ***realistic selections coefficients*** as calculated in [https://www.mun.ca/biology/scarr/NS_07-Box7smc.html].
You will likely need to double the number of generations at each stage.

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Laboratory #1, Exercise 3 - Natural Selection in a Variable Environment