

Evolutionary Mechanisms –Computer Simulations

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We can study many evolutionary processes over a longer time period using computer simulations. Computer simulations offer an excellent opportunity to model some of the processes we will discuss in lecture. Computer models can show how selection and genetic drift affect the frequency of alleles over time. The program we are going to use is freeware developed by ecologists at the University of Minnesota. The program is available on all the computers in the computer labs, and is also available free from the University of Minnesota web site (<http://www.cbs.umn.edu/software/populus.html>).

The Populus software contains a set of simulation models that all share a common format, as follows: After a model is chosen from the menu, the program displays (optionally) several screens of background material which introduce the theory and mathematics, and end with basic references. You should see a window listing all of the input parameters; you can change initial defaults to values specified below or of your own choosing. The program sets permissible maxima and minima for each parameter and filters input values accordingly. Usually there are several possible outputs (e.g., allele frequency, p , vs. generation) which can also be selected from the parameter input screen and appear in a separate window. Alternatively, you can view the different outputs in sequence, by clicking on the appropriate button in turn. Context-sensitive help screens are available from the input and output screens of every model.

Instructions for Using POPULUS: Population Biology Simulations

- Open Populus by double-clicking the icon.

Model Drop-Down Menu (the ones in bold with sub-menus will be the ones we'll use):

- Population Growth:
- Interspecific Interactions:
- Interaction Engine
- **Genetic Drift Models:**
 - **Genetic Drift**
 - Inbreeding
 - Population Structure
 - **Drift and Selection**
- **Selection Models:**
 - **Woozleology**
 - **Selection on a Diallelic Autosomal Locus**
 - Selection on a Sex-Linked Locus
 - Selection on a Multi-Allelic Locus
 - Two Locus Selection
 - Selection and Mutation
 - Group Selection:
 - Sexual Selection:
 - Frequency and Density-Dependent Selection
- Quantitative Genetics Models:
- Differentiation Models:
- Coevolution Models:
- Spatial Dilemmas

- Load Model From File

Woozleology

For over a century now, those who contest evolution have argued that the evolution of complex structures by natural selection is simply too mathematically unlikely. To explore this, we will examine how aspects of brood size, mutation rate, and recombination rate affect the time it takes to “evolve” the phrase “METHINKS IT IS LIKE A WOZLE”.

Open POPULUS. From the Model menu, go to Selection Models and select "Woozleology". Be sure to read the introduction and make sure you know how the program works. For an explanation of the Woozle demonstration, go to the "Help" menu and find the folder for Selection Models - open it and then open the Woozleology file and read the "Background" information and "Parameters" information. Note that in the real world, unlike in Woozleology, natural selection has no long-term goal.

- **BROOD SIZE** this is the number of descendent copies from the original phrase. The one phrase that is most similar to the target phrase will be selected to be the parent phrase for the next generation.
 - Set mutation rate = 0.01; model a diploid, sexual process = no
 - Run 3 simulations at each of the following brood sizes (15 total simulations):
2,10,50,100,500
 - Calculate the mean number of generations it takes to “evolve” the phrase at each brood size.
- **MUTATION RATE** this is the probability that a letter will change or “mutate” to a different letter in the progeny of the parental phrase.
 - Set brood size = 50; model a diploid, sexual process= no
 - Run 3 simulations at each of the following mutation rates (12 total simulations): 0.001, 0.01, 0.1, 0.2
 - Calculate the mean number of generations it takes to “evolve” the phrase at each brood size.

Be prepared to discuss in class the how and why changing your parameter affects the time it takes to evolve the phrase.

(This Woozleology exercise was adapted from one used in the Evolution Laboratory course at the University of Virginia.)

SELECTION and DRIFT

For all simulations and problems below make the following assumptions. Assume that coat color in a certain strain of mice is controlled by one gene with 2 alleles. One allele codes for black coats (*A* allele), and the other codes for white coats (*a* allele). In the population you find 3 coat phenotypes: black (*AA*), gray (heterozygotes – *Aa*), and white (*aa*). Now, assume we have a stable population of mice living on an island with no owls. For convenience, let's assume that there are just as many “*A*” alleles in the population as “*a*” alleles (unless otherwise noted), and the population starts out in Hardy-Weinberg equilibrium.

Simulation A: Here we will assume we have a very large isolated mouse population with no appreciable mutations in coat color alleles and random mating. When owls find their way to the island, it suddenly becomes somewhat more dangerous to be a white mouse. We want to know how the mouse population evolves in response to this selection pressure. How strong does selection have to be in order for there to be a response to it?

1. Open up Populus and go to the Selection Models. Choose Selection on a Diallelic Autosomal Locus (by the way, what is a diallelic autosomal locus?).
2. Set plot options to “genotypic frequencies vs. t.”
3. Choose “Fitness” (rather than “Selection”). Fitness is expressed relative to other genotypes.
 - a. For the fitness of *AA*, enter 1.0.
 - b. For the fitness of *Aa*, enter 1.0.
 - c. For the fitness of *aa*, enter 0.7
4. For initial conditions, choose one initial frequency and enter 0.5. Set number of generations at 130.
5. Hit “view.”
6. If you select “6 Initial Frequencies” the plot shows *p* vs. *t* for 6 computer-generated initial frequencies of the *A* allele. However, you can’t plot genotypic frequencies vs. time for this selection; if you want to examine genotype frequencies for different initial conditions, you must enter them one at a time (see question f below).
7. I’ll print out some sample graphs for you to keep.
8. Answer the following questions.
 - a. Identify the lines representing the 3 genotypes. What happens to each one?
 - b. If *AA* and *Aa* have equal fitness, why does the frequency of *AA* go up and the frequency of *Aa* go down?
 - c. If *aa* is bad, why doesn’t that genotype disappear entirely? Why doesn’t the *a* allele disappear? Now, go back to the Plot Options box and check “*p* vs. *t*”. This shows how the allele frequency (*p* = frequency of allele *A*) changes over time. What do you see?
 - d. What does this simulation tell us about the relationship between fitness and genotypic frequency?
 - e. Natural selection is very good at driving deleterious recessives into rarity, but it’s not so good at eliminating them entirely. What does this say about rare genetic diseases?
 - f. Change the initial frequency of the *A* allele to 0.1 (leave everything else the same). In other words, we’re assuming that for whatever reason, white mice outnumber dark mice on the island prior to the arrival of owls. So, why does the *aa* line start so high and drop so fast? Why does *Aa* increase, then decrease?
 - g. Plot “*p* vs. *t*”. What does this tell you about how selection can work?

Simulation B: Here we will simulate the same large, isolated population of mice with no appreciable mutation in coat color alleles, random mating, and where individuals with white coats are spotted most frequently by predators, individuals with black coats are the next most frequently spotted, and gray individuals are rarely spotted by predators.

1. In the same model, Selection on a Diallelic Autosomal Locus, set everything up as before (*p* = .5), except that this time, set the fitness of the *AA* allele at 0.9 (with *Aa* at 1.0 and *aa* at 0.7).
2. What is the equilibrium condition? What are the major differences between this simulation

and the previous one? Why is the low fitness genotype not eliminated? Why is the high fitness genotype not pushed to fixation?

3. This situation is known as heterozygote advantage. What human disease is the classic example of heterozygote advantage? What causes the low fitness of AA and aa homozygotes in this disease?
4. How would the fitness of the AA genotype vary between areas of sub-Saharan Africa with a serious vs. not so serious malaria problem? Compare genotypic frequencies when $w_{AA} = .9$ vs. $w_{AA} = .8$
5. What is the fitness of the AA genotype in the US today? What effect will this have on the prevalence of sickle-cell disease (model it)? What is the fitness of the aa genotype in the US today? What effect will this have on the prevalence of sickle-cell disease here (model it)?

Simulation C: Now, we'll simulate the same isolated population of mice, but with a small population size. We will assume random mating, no appreciable mutation in coat color alleles, and no differential survival among coat color phenotypes.

1. Open up Populus, then go to the Genetic Drift models. Choose the Monte Carlo tab. Make sure the default settings read:
 - a. Runtime = 100 generations
 - b. Loci = 6
 - c. Initial frequency = 0.5
 - d. Population size = 500
2. Hit view. Each color follows the trajectory through time of the frequency of a particular allele (think of them as six randomly chosen independent loci within the genome). Note that these are neutral alleles (i.e., there is no selection acting on them, and they confer no survival or reproductive advantage relative to other alleles at that locus).
3. Run 18 trials, six with population size of 500, six at $N = 50$, and six at $N = 5$.
4. For each trial, record the following information:
 - a. Trial #
 - b. Population size (N)
 - c. Generations to first fixation (of any allele)
 - d. Color of first to fixation
 - e. Number alleles fixed in trial (note whether to 1.0 or 0.0)
5. Answer the following questions:
 - a. Within each trial, did each of the 6 loci behave similarly? Why or why not?
 - b. Did each color loci behave similarly across the iterations? Why or why not?
 - c. Were particular colors most likely to be the first to go to fixation? Why or why not?
 - d. Within a given population size, how much did time to first fixation vary?
 - e. How does population size affect time to first fixation?
 - f. If these loci are neutral with respect to selection, why are they changing in frequency over time? Why are some alleles winners and others losers?
 - g. Many people confuse small population size effects with drift. Genetic drift is one effect of small population size (see also founder effects and bottleneck effects). One easy way to remember drift is that the colored lines were drifting randomly around on the plot. That random drifting is genetic drift. Note that drift occurs even in large populations, but is more dramatic and consequential in small populations.
 - h. These simulations show changes in gene frequency over time. Isn't that the definition of evolution? Were we watching evolution? Explain your answer.
 - i. What is the probable genetic fate of endangered species? Does a species have to be

- critically endangered to suffer loss of genetic variation? What is the 50:500 rule?
- j. For a given population, can you precisely predict when loss of genetic variation (fixation) will occur?

Simulation D: Drift and Selection - In the real world, drift and selection often operate simultaneously. In fact, drift and selection are probably the two most important agents of evolutionary change. But do they necessarily work hand in hand? Consider again our island mice. With the arrival of owls, the selective regime is against those very common white mice (but note that it's not lethal to be a white mouse – they do 90% as well as darker mice since they hide well in dense island vegetation...).

1. Go to Genetic Drift Models. Choose Drift and Selection. Alter the default settings to read:
 - a. $N = 500$, $p = 0.1$, Generations = 500
 - b. $AA = 1$, $Aa = 1$, $aa = .9$
2. Before you run the simulation, consider: in the absence of drift, do you expect the a allele to go extinct in such a population? Explain your answer.
3. Now hit view and see what happens over 500 generations. Hit view 5 more times, each time seeing what happens. What did happen? Was it the same every time? Why did the A allele go to fixation in this exercise but not in Simulation 1?
4. So ... selection is pushing the frequency of the A allele upwards. But unlike what we saw in Simulation 1, it is not a smooth monotonic increase. The increase is jerky. That drifting line IS genetic drift in action.
5. Now change the population size to 50 and hit view. What happens in this smaller population?
6. Hit view 5 more times. Are your results similar to what you saw in the population of 500?
7. When the population size was 500, you undoubtedly saw the frequency of A make its way upward (jerkily) until it eventually (at least often) became fixed in the population. Remember in our first simulation how the frequency of A went close to fixation but never quite became fixed? How did we explain the persistence of deleterious recessive alleles in the population in that exercise? So what happened here to purge these deleterious alleles from the population? Drift! Natural selection can't weed out rare recessives, but drift can! So drift can take a population to places that natural selection alone can't!! Of course, this is a double-edged sword. Rare recessives aren't necessarily deleterious ... and may be a reservoir of genetic variation within a population. Drift is very effective at eliminating rare alleles, regardless of their "value".
8. Of course, drift doesn't just remove deleterious and neutral alleles. If you keep running the program at population = 50, you'll probably eventually run into a situation where the frequency of A declined and hit zero (that is, a became fixed in the population), EVEN THOUGH "a" WAS BEING SELECTED AGAINST! We saw in earlier trials that natural selection can easily push the frequency of a beneficial allele from 0.1 to 0.99. So why was selection not able to do that in this case? A rare allele is vulnerable to drift, even when beneficial.
9. Were the mice on the island evolving? If so, what mechanism was responsible?
10. What do these results say about the power of selection and drift in small and large populations?