Population Genetics - Notes

An ongoing debate amongst scientists characterized the 19th century.

Uniformitarians or **gradualists** believed that the gradual processes observable daily in the natural world could explain all of the patterns of nature no matter how extreme.

Catastrophists believed that the natural world was formed by periods of sudden, drastic and even catastrophic change followed by long periods of no change.

Darwin was heavily influenced by Malthus's theories regarding overpopulation of the human species and Lyle's uniformitarian view of the making of current geological formations of the earth. Darwin's theory of evolution through natural selection envisioned slow, but steady change in populations over long periods of time due to differences in survival and reproduction between individuals. Characteristics of the successful competitors, if heritable, would become more frequent in the population over time causing constant shifts in population characteristics.

Huxley, Darwin's friend and staunchest defender, believed that natural selection might not work so effectively on minor differences between individuals. He believed that selection would work most effectively on individuals that manifested drastic morphological or behavioral changes - saltations.

Darwinists believed in uniformitarian principles, while saltationists adopted catastrophic mechanisms as their cause for evolutionary changes.

When Mendel was rediscovered at the turn of the last century, his experiments, focusing on alleles with clear dominance-recessive relationships, were interpreted as supporting the catastrophist explanation of evolutionary change. Thus, the catastrophist or saltationist school became known as the Mendelians. The Mendelian school was initially set up in opposition to Darwinists.

Between 1900 and 1925, some biologists determined that Mendelian principles of inheritance could explain apparently continuous variation of characteristics normally associated with Darwinian theorists. The more genes that affected a given trait, the more the expected distribution of phenotypes would resemble a normal distribution, or bell curve. Darwinian natural selection theory and Mendelian genetics began to be synthesized into a new field of evolutionary study - population genetics.

Population genetics seeks to elucidate how populations change over time due to the action of different forces on pools of genes or alleles. Hardy and Weinberg revealed that, under ideal conditions, allele frequencies in a population would not change at all. Thus, the frequency of genotypes in the population would not change from generation to generation, resulting in a *lack of evolutionary change* in the population over time. Those ideal conditions are listed on your Hardy-Weinberg handout, attached.

Two prominent theorists of this synthesis were R. A. Fisher and Sewall Wright. Fisher

elucidated how selection alone could work within large populations to effect evolutionary change over long periods of time. Fisher hypothesized that in large populations, a great diversity of allele types could be harbored without much risk of losing this latent genetic variability. Thus, if the environment changed, large populations would have a store of genetic variability that could then allow the population to adapt to change. Thus evolution would work in large populations which would be able to change slowly over long periods of change in the earth's environment.

Sewall Wright experimented with inbreeding, i.e. very small population sizes. He theorized that small inbred populations would lose genetic variability rapidly, which would usually result in population extinction. However, occasionally small populations would be fixed for very uncommon and very advantageous combinations of alleles. These populations could rapidly adapt to a given new environment and cause rapid speciation events.

The Hardy-Weinberg Principle indicates that populations will not change over time under ideal conditions. Thus, under ideal conditions, populations will not evolve. These ideal conditions include the following:

1. There is no immigration into, or emigration out of, the population

2. There is no mutation.

3. There is no selection.

4. Mating is random.

5. The population is infinitely large.

If these conditions are met, two population level phenomena occur. First, allele frequencies do not change from generation to generation. Second, the frequency of different genotypes within the population is the same from generation to generation.

Let p = frequency of allele "A" in the population, and q = the frequency of the alternative allele "a" in the population. With only these two alleles possible at this gene locus, all of the "A" alleles plus all of the "a" alleles equals all of the alleles for this gene locus in the population total. Thus, (p + q) = all alleles, or "1".

Each individual has a pair of chromosomes at this locus, so each individual has two of the total number of these alleles. To determine how frequently individuals will be of the genotypes "AA" versus "Aa" versus "aa", we simply make use of the mathematical truth that 1 X 1 = 1. Thus, (p + q) X (p + q) = 1. Multiplied out (p + q) X (p + q) = $p^2 + 2pq + q^2 = 1$. Using this second equality,

p^2 = p X p = "A X A" = the frequency of "AA" genotypes in the population.

q^2 = q X q = "a X a" = the frequency of "aa" genotypes in the population.

2pq = 2 X p X q = 2 X "A X a" = the frequency of "Aa" genotypes in the population.

Example:

A population of fruit flies exhibits two possible eye-colors. "R" is a dominant allele determining red eye-color. "r" is the recessive allele and corresponds to brown eye-color.
If the "R" allele has a frequency of 0.7 (i.e. seven of every ten eye-color alleles are "R"), what is the frequency of the recessive allele in this population?

Answer: p + q = 1, so "R" + "r" = 1. 0.7 + "r" = 1. Frequeny of "r" = 0.3.

If I catch 200 flies from this population at random, how many would I expect to be heterozygotes (i.e. have the genotype "Aa")?

Answer: $p^2 + 2pq + q^2 = 1$. The frequency of heterozygotes is equal to the term "2pq" which equals 2(0.7 x 0.3) = 0.42. Out of 200 flies caught randomly then, 0.42 of them would be heterozygotes on average, thus 0.42 x 200 = 84 flies.

Using HWE, continued.

Example:

I go to a different population of fruit flies that have the same two alleles for eye-color. I suspect that the alleles occur in different frequencies in this second population. I sample 1000 flies and discover 10 that have brown eyes. What are the estimated frequencies of the "R" and "r" alleles in this population?

Answer: Again, $p^2 + 2pq + q^2 = 1$. The term q^2 = the relative frequency of homozygous recessive individuals, which corresponds to the ten brown-eyed flies I counted out of 1000 flies sampled. Thus, $q^2 = 10/1000 = 1/100$. q = the square root of 1/100 or 0.1. Thus the frequency of "r" in this second population is 0.1 and the frequency of the "R" allele is 1 – q or 0.9.

Problem 1:

Phenylketonuria (PKU) is a disease caused by the build-up of the byproducts of metabolizing phenylalanine. It is caused by a defective, recessive allele. If a child is homozygous for this recessive allele, it will develop PKU. In the United States, PKU is detected in approximately 1 in 10,000 live births. What is the frequency of the recessive allele in the population? What proportion of people in our country are expected to be carriers (i.e. heterozygotes)?