

Hardy (Castle) Weinberg Equilibrium:

The allele frequency for any characteristic in a stable, non-evolving population will remain the same. For HWE to apply, there are three main assumptions:

1. Random mating
2. No mutation, selection, or migration.
3. A large population (no genetic drift is occurring)

Given two alleles in a population, the frequencies of each (p and q respectively) are $p^2 + 2pq + q^2$ for any population in Hardy-Weinberg Equilibrium (HWE).

This can be used as a “null model” for evolution: if the population is in Hardy-Weinberg Equilibrium, that trait is not evolving (being selected for/against). But if there are deviations, then that means that something interesting is occurring, possibly evolution.

A key result is that if an allele is rare (eg. $p < 0.1$), it occurs most often in heterozygotes rather than homozygotes – i.e. $2pq \gg p^2$

The Hardy-Weinburg Equilibrium can also be used to predict the frequency of heterozygotes in a given population, given the proportion of homozygous recessive phenotype individuals in the population. The heterozygotes are indistinguishable from the dominant homozygous individuals: however, the recessive homozygous individuals are uniquely identifiable. Therefore, $q = \text{square-root}(\text{frequency homozygous recessive})$. Since there are only two alleles, $p = (1-q)$. Once you know p and q , you can solve for the frequency of heterozygotes ($2pq$).

Genotype	Phenotype
AA	A ($p^2 + 2pq$)
AB	
BB	B (q^2)

Frequency $q = \text{square-root of frequency of B}$

Frequency (AB) = $2 * p * q$

Example - Cystic Fibrosis:

Affected individuals in Caucasian population (homozygote recessives) = $4/10000 = 0.0004$

Assuming HWE, the estimated frequency of the CF- allele = $p = 0.02$.

Therefore, $q = 0.98$

The frequency of heterozygotes is $2pq = 2 * (.02) * (.98) = .0392 \sim .04$

What does this tell us? Compare the probabilities. In general, recessive alleles are more likely to be present in heterozygous individuals than in homozygous individuals.

Deviations from Hardy-Weinberg Equilibrium

Inbreeding - How does it affect a population?

Inbreeding is when two relatives produce offspring. Since the inbreeders are related, it's more likely than random mating that for one characteristic they will have matching alleles. This includes recessive alleles. Therefore, the frequency of homozygotes increases (as the genes the offspring receives from both related parents are more likely to be the same) and the frequency of heterozygotes decreases. Consider the following case of self-fertilization, an extreme form of inbreeding:

AA * AA	Homozygote frequency increases
AB * AB	Heterozygote frequency decreases as AB*AB produces both homozygotes and heterozygotes
BB * BB	Homozygote frequency increases

Note that inbreeding changes the proportion of genotypes (increasing homozygotes) but does not in itself change allele frequencies

Small Population Sizes: Genetic Drift

In a small population, the sampling of gametes and fertilization to create zygotes causes random error in allele frequencies. This results in a deviation from the Hardy-Weinberg Equilibrium. This deviation is larger at small sample sizes and smaller at large sample sizes. Think of it like tossing coins - the average result for tossing two coins might be 100% heads. The average for tossing four coins might be 75% heads. But if you take a sample of 10,000 coin tosses, then you are more likely to be close to 50% heads. The direction of this change is random: the dominant or recessive allele might be over or under represented in the next generation relative to the predicted HWE values.

This effect is called **genetic drift**, or that the amplitude of allele frequency fluctuation from one generation to the next increases in small populations. In a small population, genetic drift can result in a loss of variation across the entire genome over time. This even can result in a loss of **polymorphism** (alternate alleles) and driving the frequency of one allele to 1.

How is this relevant to evolution? The fluctuation of allele frequencies in a small isolated population might lead to novel genetic combinations that would not be possibly merely through selection. There are several different situations, which are described below. Alternatively, genetic drift may just reduce genetic diversity (**evolutionary potential**).

Small Population Sizes: Population Bottlenecks

A **population bottleneck** occurs when a population undergoes a severe decrease in size. The effect of genetic drift on this new population is much higher than on the previous population. The new population will be much reduced in genetic diversity: consider the diagram below. Of a population with equal proportions of blue, yellow, and white marbles amongst a population numbering in the 100s, the new population has 5 blue marbles, 1 white marble, and no yellow marbles. This rapid change in allele frequencies could lead to divergence and a new species forming.

Note that a population bottleneck does not involve migration (that's comes later). The most likely causes of a population bottleneck are disease, habitat loss, overharvesting leading to insufficient resources, or climate change.

An example is the prairie chickens of the Illinois plains. Their habitat loss resulted in many smaller populations, rather than a large unified population. The smaller population sizes led to a decrease in diversity and a decrease in the viability (i.e. the number of hatching chicks).

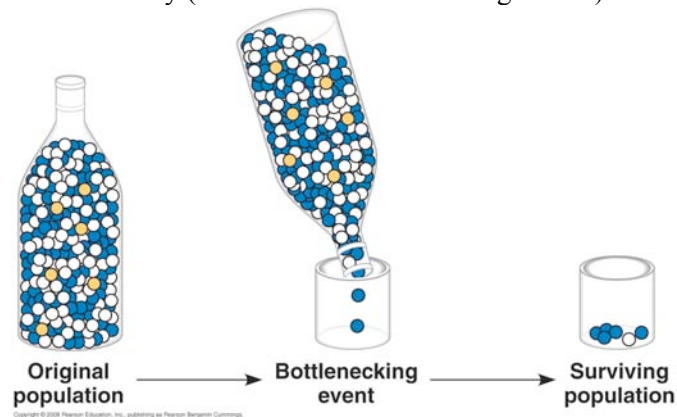


Figure 1: Population Bottlenecks

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Small Population Sizes: Founder Events

In this case, a small population of a species moves to a new habitat. The effects are mostly similar to population bottlenecks (reduced genetic diversity in the new population, rapid change in allele frequency, high potential for divergence and speciation) with the exception that there would be more selection occurring due to the new habitat.

An example would be human colonization. African *Homo sapiens* have the most genetic diversity of any human species, while Europe, Asia, and the Americas have lower genetic diversity. This implies that the wellspring of the human species is in Africa (where the original population with high genetic diversity resided/resides), and the other populations are descendants of smaller migrating populations with lower genetic diversity. (This is what is termed the “Out of Africa” theory of human evolution.)

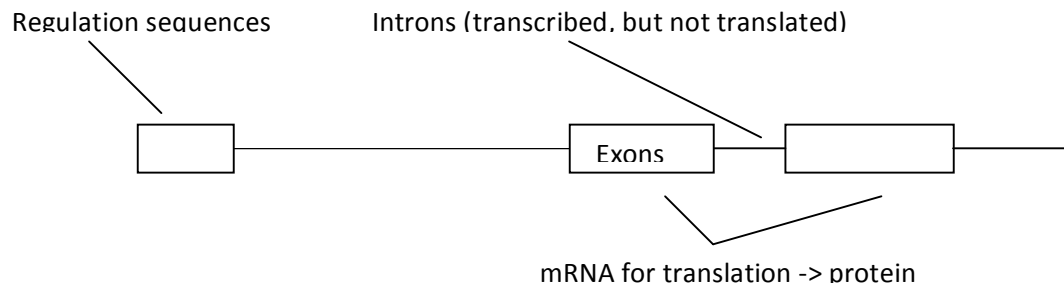
Mutation

The ultimate source of variation in the genome. The process through which DNA is replicated in meiosis is not perfect, and it can produce errors. There are an average of 1 in a hundred million nucleotide-copying errors per base pair gamete per generation – doesn’t sound like much, but the human genome is 3 billion nucleotides long. Therefore, each time the human genome is replicated, it has an average of 30 mutations.

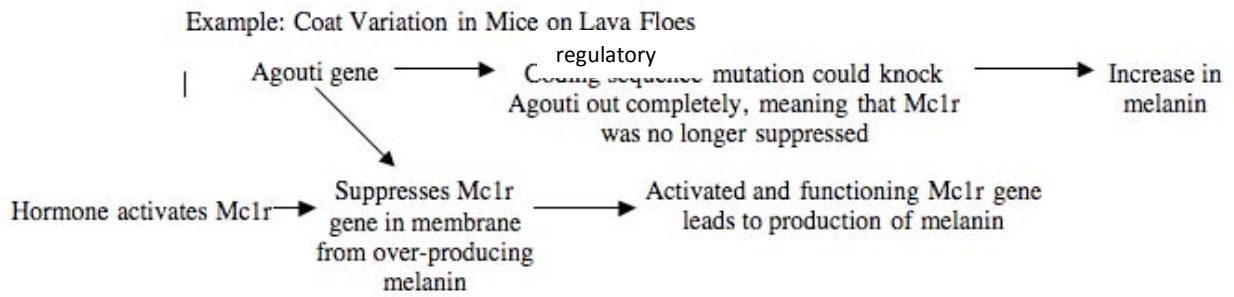
Mutations can arise in either a **somatic** cell line or in the **germ line**. Somatic cells are the cells that make up your body, so mutations in those cells are not passed on to the next generation. Mutations in the germ line, or in gametes, are passed on, so they are the mutations we talk about here.

These errors can be in one of four forms:

1. **Point mutation:** an alteration in the nucleotide coding sequence. For example, from a CTT/GAA sequence, a copy with a point-mutation might read CAT/GTA.
2. **Gene regulation:** a region controlling gene regulation and expression is altered.
3. **Gene copy number error:** a gene is copied more than it should be, so that the copy has multiple copies of the same gene.
4. **Chromosome number and structure:** during meiosis, a gamete receives too many or too few chromosomes, or a chromosome is damaged. Examples include Trisomy 21 (Down’s syndrome) and plant polyploidy, when a plant can have nuclei with genetic material at $2N$, $4N$, $6N$, etc...



Note on basic genetic principles: Definitions of basic genetic terms such as DNA, nucleotide, gene regulation, gene expression, chromosome, etc. were not and will not be covered in lecture. If this material is foreign, you can look them up in the textbook. In Campbell 8th edition, most of the material should be within chapters 15-18. Use the table of contents and the index to find whatever specific material you need clarified.



- Agouti's presence is based on two genes, and both would need to be knocked out to completely stop suppression of Mc1r (recessive)
- Some mutations could increase expression of Agouti, which would lead to a very light colored mouse (paler than normal)
- Mc1r can have dominant mutations that increase the sensitivity to the activation hormone, thus further increasing the production of melanin