Organization of Genetic Variation

I) Random Mating

- **Null model**
- **Basically association of gametes independently of traits**
- **Demographically stable idealized population (common assumption: no overlapping populations, equal sex ratios, not age structured, etc.)**

A) Allele Frequency Estimation

OH 3.1

B) Assumptions of the Hardy-Weinberg Equilibrium Genotype Frequency

1) **Diploid, 2 alleles, autosomal**
2) **Sexually reproducing organism**
3) **Non-overlapping generations**
4) **Large (i.e., infinite) population size**
5) **No migration**
6) **No mutation**
7) **No selection**

C) Hardy-Weinberg Equilibrium by Random Union of Gametes

p = frequency of one allele = F(A)

q = frequency of second allele = F(a)

$$(p + q)^2 = p^2 + 2pq + q^2$$

$$F(AA) = F(A) \times F(A) = F(A)^2 = p^2$$

$$F(Aa) = F(A) \times F(a) + F(a) \times F(A)$$

$$= 2 \times F(A) \times F(a) = 2pq$$

$$= 2p(1 - p)$$

OH 3.2

Allele Frequency	A p	a q
A (p)	AA p^2	Aa pq
a (q)	Aa qp	aa q^2

$$F(A)_{t+1} = p_t^2 + \frac{1}{2}(2p_t q_t) = p_t(p_t + q_t)$$
$$= p_t$$

In words, the allele frequency does not change from one generation to the next under HWE. Also note that regardless of starting condition (i.e., HWE) equilibrium is reached after one generation of random mating.

D) Allele frequencies and Genotype frequencies under HWE.

e.g.,

	Number	Genotype	Frequency
	50	AA	0.050
	878	Aa	0.878
	72	aa	0.073
Total	1000		

$$F(A) = \frac{AA + \frac{1}{2}Aa}{N} \quad \text{OR} \quad F(A) = F(AA) + \frac{1}{2}F(Aa)$$

$$= \frac{50 + \frac{1}{2}(878)}{1000} \quad \text{OR} \quad 0.05 + \frac{1}{2}(0.878)$$

$$= 0.489 \quad \text{OR} \quad 0.489$$

If equal sex ration, random union of gametes and all other HWE assumptions are true then:

Time t			Offspring		
Female	**Male**	**Frequency**	**AA**	**Aa**	**aa**
A	A	p_t^2	p_t^2	—	—
A	a	$p_t q_t$	—	$p_t q_t$	—
a	A	$q_t p_t$	—	$q_t p_t$	—
a	a	q_t^2	—	—	q_t^2
		Time (t + 1)	p_t^2	$2p_t q_t$	q_t^2

$$F(A)_{t+1} = F(p_{t+1}) = p_t^2 + \frac{1}{2}(2p_t q_t)$$

$$= p_t(p_t + q_t)$$

$$= p_t$$

Change in allele frequency over generation is zero

Note: original population

Number	Genotype	Frequency
50	AA	0.050
878	Aa	0.878
72	aa	0.073

$F(A)_t$ == 0.489

Genotype	Observed	Expected
AA	50	239
Aa	878	500
aa	72	261

Clearly the population is not in HWE (can test with χ^2)

But after 1 round of random mating the population will be in HWE i.e.:

$$F(A)_t = 0.489$$

$$F(AA)_{t+1} = F(A)_t^2$$

$$F(Aa)_{t+1} = 2 \times F(A)_t \times F(a)_t$$

$$F(aa)_{t+1} = F(a)_t^2$$

- **Allele frequency does not change from one generation to the next**
- **Populations that start not in HWE will return to HWE after one round of random mating.**

E) Hardy-Weinberg using Individuals – random union of gametes implies random mating of individuals

Define: $F(AA)_t = U$, $F(Aa)_t = V$, and $F(aa)_t = W$

OH 3.1.B

$$F(AA)_{t+1} = U' = U^2 + UV + \frac{1}{4}V^2$$
$$= (U + \frac{1}{2}V)^2$$
$$= [F(AA)_t + \frac{1}{2}F(Aa)_t]^2 = (p^2 + \frac{1}{2}2pq)^2$$
$$= [p(p + q)]^2$$
$$F(AA)_{t+1} = p^2$$

$$V' = 2pq$$

$$W' = q^2$$

Change in genotype frequency is zero and change in allele frequency is zero. This is defined as an equilibrium. Perturbations to this (i.e., deviation in genotype frequencies) return to this state so it is also know as a stable equilibrium. Evolution is defined as the change in allele frequency over time so this system is not evolving.

F) Different frequencies between sexes

1) Autosomal Gene – assume that the frequency of alleles is not the same between the sexes.

$F(A \mid female) = p_f$
$F(A \mid males) = p_m$

$F(a \mid female) = q_f$
$F(a \mid male) = q_m$

The frequency of Genotypes after random union of gametes is:

$$U' = p_f p_m$$

$$V' = p_f q_m + p_m q_f$$

$$W' = q_f q_m$$

The average allele frequency (i.e., expected), however, is:

$$\bar{p} = \frac{1}{2}(p_f + p_m)$$

and the difference between the observed frequency and the expected then is:

$$U' - \bar{p}^2 = p_f p_m - [\frac{1}{2}(p_f + p_m)]^2$$

$$= -\frac{1}{4}(p_f^2 - 2p_f p_m + p_m^2)$$

$$= -\frac{1}{4}(p_f - p_m)^2$$

Similarly:

$$V' - 2\bar{p}\,\bar{q} = \frac{1}{2}(p_f - p_m)^2$$

$$W' - \bar{q}^2 = -\frac{1}{4}(p_f - p_m)^2$$

When allele frequencies are different between the sexes there is an apparent excess of heterozygotes. This effect is removed after one generation of random mating.

The magnitude of this effect depends on the magnitude in the differences in frequencies between the sexes

OH 3.2B

2) **Sex linked genes in haplo-diploid organisms**

a) **Genotype and allele frequencies (allele frequencies are equal between sexes)**

OH 3.3

b) **Genotype frequencies in the next generation (U', V', W')**

$$U' = Up_m + \frac{1}{2}Vp_m$$

$$= p_f^2 p_m + \frac{1}{2}(2p_f q_f)p_m$$

$$= p_f^2 p_m + p_f q_f p_m$$

$$= p_f p_m(p_f + q_f)$$

$$U' = p_f p_m$$

Similarly:

$$V' = p_f q_m + p_m q_f$$

$$W' = q_f q_m$$

c) **Allele frequencies in the next generation**

$$p'_m = Up_m + Uq_m + \frac{1}{2}Vp_m + \frac{1}{2}Vp_m$$

$$= p_f^2 p_m + p_f^2 q_m + \frac{1}{2}(2p_f q_f)p_m + \frac{1}{2}(2p_f q_f)q_m$$

$$= (p_f^2 p_m + p_f q_f p_m) + (p_f^2 q_m + p_f q_f q_m)$$

$$= p_f p_m(p_f + q_f) + p_f q_m(p_f + q_f)$$

$$= p_f p_m + p_f q_m$$

$$p'_m = p_f(p_m + q_m) = p_f$$

Similarly:

$$p'_f = \frac{1}{2}(p_f + p_m)$$

d) If allele frequencies differ between the sexes

Know:

i) $$\bar{p} = \frac{2}{3}p_f + \frac{1}{3}p_m$$

Can be rewritten as:

$$p_m = 3\bar{p} - 2p_f$$

And:

$$p'_f = \frac{1}{2}(p_f + p_m)$$

$$p'_f = \frac{1}{2}(p_f + 3\bar{p} - 2p_f)$$

$$= \frac{1}{2}(3\bar{p} - p_f)$$

$$= 1\bar{p} + \frac{1}{2}\bar{p} - \frac{1}{2}p_f$$

$$p'_f - \bar{p} = -\frac{1}{2}(p_f - \bar{p})$$

The deviation in allele frequency from the average (across sexes) is one half each generation for the females. Since $p'_m = p_f$ it is also one half for the male, but with a one generation time lag. Until the frequencies reach the average, the females are not in HWE Genotype frequencies (heterozygote excesses).

Define:

d_1 = deviation in generation 1

d_0 = deviation in generation 0

$$d_1 = -\frac{1}{2} d_0$$

$$d_t = \left(-\frac{1}{2}\right)^t d_0$$

OH 3.4