

Lecture 2

Population geneticsOutline

1. Definitions
2. HW equilibrium
3. Genetic drift

4. Probability of fixation
5. Rate of fixation
6. Selection,
Wright's equation.

1. Definitions

* Locus A

* Alleles A_1, A_2 * Genotype $A_1A_1, A_1A_2, A_2A_1, A_2A_2$

Locus	Alleles	Genotype	Mut. Rate
Single nucleotide	A, T, G, C	$\begin{matrix} A & T \\ & \end{matrix}$	$\sim 10^{-8}$ per gener.
a gene of L bps	$[\sim 4^L]$ infinite allele single nucl. subs $4L, n$ alleles	gene1 gene2 $\frac{n(n-1)}{2} + n$	$\sim L \cdot 10^{-8} \sim 10^{-5}$ per gener.

2. Hardy - Weinberg equilibrium

$$\begin{array}{ccc}
 \overset{\curvearrowright}{A_1A_1} & \overset{\curvearrowright}{A_1A_2} & \overset{\curvearrowright}{A_2A_2} \\
 x_{11} & x_{12} & x_{22}
 \end{array}
 \leftarrow \text{genotype frequency}$$

$$\begin{array}{cc}
 A_1 & A_2 \\
 p & q=1-p
 \end{array}
 \leftarrow \text{allele frequency}$$

$$(x_{11} + x_{12} + x_{22} = 1)$$

$$p = x_{11} + \frac{1}{2} x_{12}$$

$$q = x_{22} + \frac{1}{2} x_{12}$$

Random mating:

1) $p = \text{const}$

2) After 1-2 rounds of mating the genotype frequencies ~~become~~ and remain constant.

$$x_{11} = p^2$$

$$x_{12} = 2pq$$

$$x_{22} = q^2$$

Consequences of Hardy-Weinberg equilibrium

rare A_2 $q \ll 1$

$$\frac{A_2 \text{ in heterozygotes}}{A_2 \text{ in homozygotes}} = \frac{2pq}{q^2} = \frac{2p}{q} \approx \frac{2}{q} \gg 1 \Rightarrow$$

E.g. $q = 0.01 \Rightarrow 200$ times more in heterozygotes

rare alleles
are
mostly in
heterozyg.

3. Genetic Drift

Consider a randomly mating population of size N

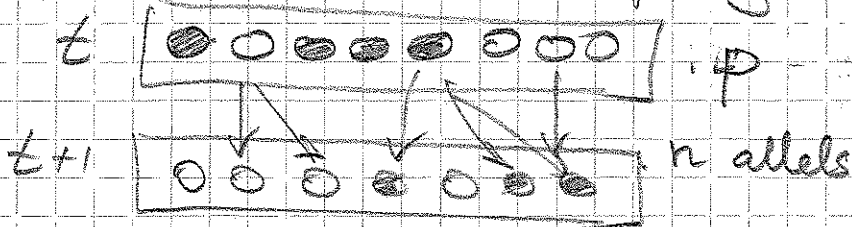
1. Choose an allele at random among $2N$ alleles
2. Make its exact copy
3. Place into new generation
4. Repeat until $2N$ alleles are in the generation

Evolution of p



5. Probability of fixation

Binomial sampling



P_j - prob to have j ● after binomial sampling

$$P_j = p^j (1-p)^{n-j} \binom{n}{j}$$

$$\langle j \rangle = pn$$

$$\text{Var}(j) = \langle j^2 \rangle - \langle j \rangle^2 = p(1-p)n$$

Random mating

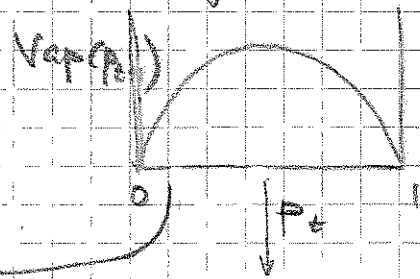
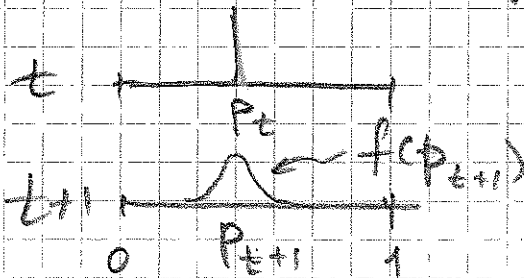
$$n = 2N$$

$$P = P_t$$

$$\frac{j}{n} = \frac{j}{2N} = P_{t+1}$$

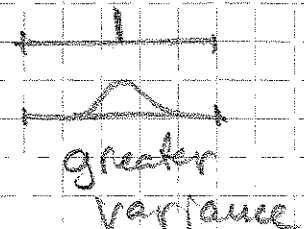
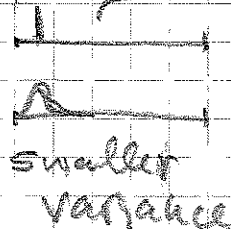
$$\langle P_{t+1} \rangle = P = P_t$$

$$\text{Var}(P_{t+1}) = \frac{p(1-p)}{n} = \frac{P(1-P)}{2N}$$

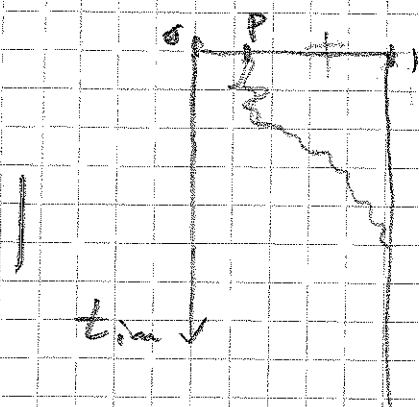


Conclusions

- 1) Doesn't change mean allele freq.
- 2) Variance is larger for smaller populations



$\Pi(p)$ Prob. of fixation, starting at $p = p_0$.



$$\Pi(p_0) = \sum_{\Delta p} \text{Prob}(\Delta p) \Pi(p_0 + \Delta p)$$

Expand: $\Pi(p_0 + \Delta p)$

$$\Pi(p_0 + \Delta p) \approx \Pi(p_0) + \Pi'(p_0) \Delta p + \Pi''(p_0) \frac{\Delta p^2}{2}$$

By plugging into $\Pi(p_0)$ we obtain

$$\Pi(p_0) = \sum_{\Delta p} \text{Prob}(\Delta p) \left[\Pi(p_0) + \Pi'(p_0) \Delta p + \Pi''(p_0) \frac{\Delta p^2}{2} \right]$$

$$= \Pi(p_0) + \Pi'(p_0) \sum_{\Delta p} \text{Prob}(\Delta p) \Delta p + \Pi''(p_0) \sum_{\Delta p} \text{Prob}(\Delta p) \frac{\Delta p^2}{2}$$

$$= \Pi(p_0) + \Pi'(p_0) \langle \Delta p \rangle + \Pi''(p_0) \frac{\langle \Delta p^2 \rangle}{2}$$

$$\boxed{\Pi'(p_0) \langle \Delta p \rangle + \Pi''(p_0) \frac{\langle \Delta p^2 \rangle}{2} = 0}$$

fixation
↓

all have
one common
ancestral

$$\Pi'(p_0) \langle \Delta p \rangle + \Pi''(p_0) \frac{\langle \Delta p^2 \rangle}{2} = 0$$

$$\Pi(0) = 0 ; \Pi(1) = 1$$

Backward
Kolmogorov
equation

Drift (no mutations or selection)

$$\langle \Delta p \rangle = 0$$

$$\langle \Delta p^2 \rangle = \text{Var}(\Delta p) = \frac{p(1-p)}{2N}$$

$$\Pi''(p_0) p_0(1-p_0) = 0$$

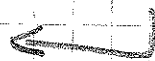
$$\Pi''(p_0) = 0$$

$$\Pi'(p_0) = 0$$

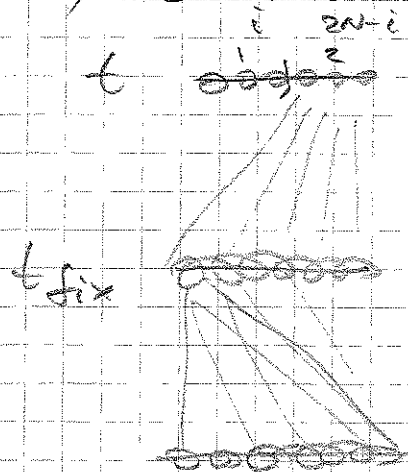
$$\Pi(p_0) = a p_0 + b$$

$$\Pi(p_0) = p_0$$

using boundary
conditions



1) Coalescent argument



all alleles are the offsprings of a single allele at the time of fixation

$$T(p) = p$$

2) Rate of fixation = rate of mutation

$$k = [\text{Rate of acquiring new alleles}] \times [\text{prob of fixation of a new allele}]$$

$\hat{=}$ rate of evolution

$\hat{=}$ rate of fixation of new alleles

$$= [2N \times \mu] \left[\frac{1}{2N} \right] = \mu$$

$$\boxed{k = \mu}$$

Rate of fixation =

$\hat{=}$ rate of mutation