Announcements

Hari’s New Office Hours

- Tues 5–6 pm
- Wed 3–4 pm
- Fri 2–3 pm

In computer lab
3306 LSB
Last Time

- **More Hardy-Weinberg Calculations**
  - Merle Patterning in Dogs: Excel sheet posted

- **First Violation of Hardy-Weinberg assumptions: Random Mating**

- **Effects of Inbreeding on allele frequencies, genotype frequencies, and heterozygosity**
Important Points about Inbreeding

- Inbreeding affects ALL LOCI in genome
- Inbreeding results in a REDUCTION OF HETEROZYGOSITY in the population
- Inbreeding BY ITSELF changes only genotype frequencies, NOT ALLELE FREQUENCIES and therefore has NO EFFECT on overall genetic diversity within populations
- Inbreeding equilibrium occurs when there is a balance between the creation (through outcrossing) and loss of heterozygotes in each generation
Today

- Self-fertilization and mixed mating systems
- Inbreeding equilibrium
- Estimating inbreeding coefficients from pedigrees
- Relatedness and kinship
**Extreme Inbreeding: Self Fertilization**

- Common mode of reproduction in plants: mate only with self
- Assume selfing newly established in a population
- \( \frac{1}{2} \) of heterozygotes become homozygotes each generation
- Homozygotes are NEVER converted to heterozygotes
Self Fertilization

Aa Self-Fertilizations

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<td>a</td>
<td>Aa</td>
<td>aa</td>
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$\frac{1}{2}$ Aa each generation

$\frac{1}{2}$ AA or aa (allele fixed within lineage)

AA Self-Fertilizations

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http://www.life.illinois.edu/ib/335/BreedingSystems/BreedingSystems.html
Decline of Heterozygosity with Self Fertilization

- Steady and rapid decline of heterozygosity to zero

\[
\begin{align*}
H_1 &= \frac{1}{2} H_0 \\
H_t &= \frac{1}{2} H_{t-1} \\
H_t &= \left(\frac{1}{2}\right)^t H_0.
\end{align*}
\]
Partial Self Fertilization

- Mixed mating system: some progeny produced by selfing, others by outcrossing (assumed random)

- Rate of outcrossing = $T$

- Rate of selfing = $S$

- $T + S = 1$

- Heterozygosity declines to equilibrium point

$$H_t = T2pq + S \frac{H_{t-1}}{2}.$$
What determines the equilibrium frequency of heterozygotes in a population with mixed selfing and outcrossing?
Inbreeding Equilibrium

- Production of heterozygotes by outcrossing balances loss of heterozygotes by selfing

- For any value of $p$ and $S$, there is a characteristic equilibrium point, regardless of starting genotype frequencies

- Inbreeding coefficient also reaches equilibrium point, purely a function of selfing rate

\[
D_{eq} = p^2 + \frac{Spq}{2 - S}
\]

\[
H_{eq} = \frac{4pq(1 - S)}{2 - S}
\]

\[
R_{eq} = q^2 + \frac{Spq}{2 - S}
\]

\[
f_{eq} = 1 - \frac{H_{eq}}{2pq} = \frac{S}{2 - S}
\]

See lab notes for derivations
Estimating Selfing in Populations

Level of selfing can be readily estimated from allele frequencies and observed heterozygosity:

\[ F = 1 - \frac{H_O}{H_E} \]

\[ F_{eq} = 1 - \frac{H_O}{H_E} = \frac{S}{2 - S}. \]

\[ S = \frac{2(H_E - H_O)}{2H_E - H_O} \]

What are the assumptions of this calculation?
Estimating Inbreeding from Pedigrees

- Most accurate estimate of $f$ derived from direct assessment of relationships among ancestors

Half First-Cousins
Estimating Inbreeding from Pedigrees

- Probability $P$ contains two $A_1$ alleles IBD

$$P_{A_1,fromD} = \left( \frac{1}{2} \right) \left( \frac{1}{2} \right) \left( \frac{1}{2} \right) = \frac{1}{8}$$

$$P_{A_1,fromE} = \left( \frac{1}{2} \right) \left( \frac{1}{2} \right) \left( \frac{1}{2} \right) = \frac{1}{8}$$

- Overall:

$$P_{A_1,IBD} = \left( \frac{1}{8} \right) \left( \frac{1}{8} \right) = \frac{1}{64}$$

- There are two alleles in the common ancestor, so there are two possibilities to inherit different alleles IBD

- Probability $P$ contains any alleles IBD is therefore:

$$P_{IBD} = f = \frac{1}{64} + \frac{1}{64} = \frac{1}{32}$$
**Chain Counting**

- **Count links to Common Ancestor**
  - Starting with one parent of inbred individual and continuing down to other parent

- **D-B-CA-C-E**
- **N=5 links**

\[
f = \left( \frac{1}{2} \right)^N = \left( \frac{1}{2} \right)^5 = \frac{1}{32}
\]

For multiple common ancestors, \(m\):

\[
f = \sum_{i=1}^{m} \left( \frac{1}{2} \right)^{N_i}.
\]

If common ancestors are inbred as well:

\[
f = \sum_{i=1}^{m} \left( \frac{1}{2} \right)^{N_i} (1 + f_{CA_i})
\]

Where \(f_{CA_i}\) is inbreeding coefficient of common ancestor \(i\)
Kinship Coefficient

- Estimate of relationship between two individuals in a population, D and E
- Probability a randomly selected allele from each is Identical by Descent
- Easiest to estimate as $f$ of hypothetical progeny, p

\[ k_{DE} = f_P = \sum_{i=1}^{m} \left( \frac{1}{2} \right)^{N_i} \left( 1 + f_{CA_i} \right) \]
Relatedness

- Sewall Wright revolutionized study of inbreeding in 1922
- Defined coefficient of relationship \((r)\)
  - Shared alleles between related individuals result in *genetic correlation*
  - Also the fraction of alleles that two individuals share IBD
- Can be estimated as twice the inbreeding coefficient of possible offspring (i.e., twice the kinship)

\[ r = 2f \]
Relatedness

- Relatedness is twice the probability that two alleles, one chosen randomly from each individual, are IBD

\[ r_{DE} = 2k_{DE} = 2f_P \]

- For parent-offspring and full sibs, \( r = 0.5 \)
- For half-sibs, \( r = 0.25 \)
- For first cousins, \( r = 0.125 \)

- Can be estimated from sharing of alleles conditioned on allele frequencies
Estimating Relatedness Without a Pedigree

- Molecular markers provide an indication of relatedness of individuals based on shared alleles.
- More polymorphic markers are preferable: microsatellites.

Source: SilkSatDB

Lowe, Harris, and Ashton 2004
Estimating Relatedness Without a Pedigree

- In many cases, relationships among samples are unknown
- Relationships can be estimated using multiple, highly polymorphic loci
- Queller and Goodnight (1999, *Mol Ecol.* 8:1231) developed a program, KINSHIP, that estimates relatedness based on likelihood ratios (explained in more detail later)

### Number of Microsatellites Required to Distinguish Relationships

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<thead>
<tr>
<th>Null hypothesis</th>
<th>Primary hypothesis (true relationship)</th>
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<tr>
<td></td>
<td>Parent</td>
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<tr>
<td>Parent</td>
<td>—</td>
</tr>
<tr>
<td>Full-sib</td>
<td>5</td>
</tr>
<tr>
<td>Half-sib</td>
<td>5</td>
</tr>
<tr>
<td>Cousin</td>
<td>4</td>
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<tr>
<td>Unrelated</td>
<td>2</td>
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Relatedness in Natural Populations

- White-toothed shrew inbreeding (*Crocidura russula*) (Duarte et al. 2003, Evol. 57:638-645)
- Breeding pairs defend territory
- Some female offspring disperse away from parents
- How much inbreeding occurs?
- 12 microsatellite loci used to calculate relatedness in population and determine parentage
- 17% of matings from inbreeding
Inbreeding and allele frequency

- Inbreeding alone does not alter allele frequencies
- Yet in real populations, frequencies DO change when inbreeding occurs
- What causes allele frequency change?
- Why do so many adaptations exist to avoid inbreeding?
Natural Selection

- Non-random and differential reproduction of genotypes
  - Preserve favorable variants
  - Exclude nonfavorable variants
- Primary driving force behind adaptive evolution of quantitative traits
Fitness

Very specific meaning in evolutionary biology:

- Relative competitive ability of a given genotype

- Usually quantified as the average number of surviving progeny of one genotype compared to a competing genotype, or the relative contribution of one genotype to the next generation

- Heritable variation is the primary focus

- Extremely difficult to measure in practice. Often look at fitness components

- Consider only survival, assume fecundity is equal