Lecture 3
Covariance Between Relatives

• Needed for
  – Estimation of Genetic Parameters
    • Heritabilities
    • Genetic Correlations
  – Estimation of Breeding Values
    • Information on relatives

Ancestral (Parent, grand parents, etc)
measure both parents and offspring
Parent Offspring Regression

Obvious method to determine heritability

\[ b_{o,p} = \frac{Cov(o, p)}{Var(p)} = h^2 \]

Collateral (sibs, measure only sibs, not parents) Full sibs

How does this data give an indication of heritability
What pattern would you expect? Between and within family?
Which Trait has Higher Heritability?

Situation 1

Family
Var(B)=2.5
Var(W)=.5
Vp=Var(B)+Var(W)=3

Situation 2

Family
Var(B)=0
Var(W)=3
Vp=Var(B)+Var(W)=3

Partitioning Variation

Between vs within Family

Case 1

\[
\frac{Var(B)}{V_p} = \frac{2.5}{3} = .83
\]

Case 2

\[
\frac{Var(B)}{V_p} = \frac{0}{3} = 0
\]

Which of these situations is indicative of a high genetic component?

Var(B)=variation among group, group are full sib groups

Var(B)=Cov(full sibs)
Genetic Covariance

- Relatives are more likely to share alleles than non-relatives
  - Sharing Alleles = Identical by Descent (IBD)
    - Identically same allele can be traced to an ancestor
  - Not to be confused with Alike in State
    - Same allele but not IBD

Example IBD alleles

- A\textsubscript{1}A\textsubscript{2}  A\textsubscript{3}A\textsubscript{4}
- A\textsubscript{1}A\textsubscript{3}  A\textsubscript{2}A\textsubscript{4}
Single Parent-offspring Covariance

\[ G_P = \alpha_1 + \alpha_2 + \delta_{12} \]
\[ G_O = \alpha_1 + \alpha_x + \delta_{1x} \]

\[ \text{Cov}(G_P, G_O) = \text{Cov}(\alpha_1 + \alpha_2 + \delta_{12}, \alpha_1 + \alpha_x + \delta_{1x}) \]
\[ = \text{Cov}(\alpha_1, \alpha_1) + \text{Cov}(\alpha_1, \alpha_x) + \text{Cov}(\alpha_1, \delta_{1x}) + \text{Cov}(\alpha_2, \alpha_1) + \text{Cov}(\alpha_2, \alpha_x) + \text{Cov}(\alpha_2, \delta_{1x}) + \text{Cov}(\delta_{12}, \alpha_1) + \text{Cov}(\delta_{12}, \alpha_x) + \text{Cov}(\delta_{12}, \delta_{1x}) \]

In General: Covariance between effects

\[ \text{Cov}(\alpha_i, \alpha_j) = \begin{cases} 
0 & \text{if } i \neq j, \text{ i.e. not IBD} \\
\frac{1}{2} \sigma^2_\alpha & \text{if } i = j, \text{ i.e. IBD} 
\end{cases} \]

Additivity is a function of single alleles

\[ \text{Cov}(\alpha_i, \delta_{ij}) = 0 \quad \text{By construct} \]

\[ \text{Cov}(\delta_{ij}, \delta_{km}) = \begin{cases} 
0 & \text{if } i \neq k \text{ and } j \neq m, \text{ i.e. not IBD} \\
\sigma^2_D & \text{if } i = k \text{ and } j = m, \text{ i.e. both IBD} 
\end{cases} \]

Dominance if a function of both alleles at a locus, it is predicted as the failure of both alleles at that locus to be additive
Single Parent-offspring Covariance

\[ G_P = \alpha_1 + \alpha_2 + \delta_{12} \]

100% of the time, parent and offspring will share one and only one allele.

\[ G_O = \alpha_1 + \alpha_x + \delta_{1x} \]

\[ \text{Cov}(G_P, G_O) = \text{Cov}(\alpha_1 + \alpha_2 + \delta_{12}, \alpha_1 + \alpha_x + \delta_{1x}) \]

\[ = \text{Cov}(\alpha_1, \alpha_1) = \frac{1}{2} \sigma_A^2 \]

Because

\[ \sigma_A^2 = \text{Var}(\alpha_1 + \alpha_2) = \frac{1}{2} \sigma_A^2 + \frac{1}{2} \sigma_A^2 \]

Summary

<table>
<thead>
<tr>
<th>Number of IBD</th>
<th>Probability of Sharing</th>
<th>Contribution to variances</th>
</tr>
</thead>
<tbody>
<tr>
<td>0 IBD alleles</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>1 IBD alleles</td>
<td>1</td>
<td>\frac{1}{2} \sigma_A^2</td>
</tr>
<tr>
<td>2 IBD alleles</td>
<td>0</td>
<td>\sigma_A^2 + \sigma_D^2</td>
</tr>
</tbody>
</table>

Total covariance = Sum Probability x contribution =

\[ (1) \frac{1}{2} \sigma_A^2 + (0)(\sigma_A^2 + \sigma_D^2) = \frac{1}{2} \sigma_A^2 \]
Midparent-Offspring

\[ \text{Cov}(O, MP) = \text{Cov}(o, \frac{P_m + P_f}{2}) \]
\[ = \text{Cov}(o, P_m / 2) + \text{Cov}(o, P_f / 2) \]
\[ = \frac{1}{2} \sigma_A^2 + \frac{1}{2} \sigma_A^2 = \frac{1}{2} \sigma_A^2 \]

Collateral: Half sibs

\[ \text{Cov}(G_{O_1}, G_{O_2}) \]
Collateral: Number of IBD Alleles

Sib O₁ possible genotypes

<table>
<thead>
<tr>
<th></th>
<th>A₁A₃</th>
<th>A₁A₄</th>
<th>A₂A₃</th>
<th>A₂A₄</th>
</tr>
</thead>
<tbody>
<tr>
<td>A₁A₅ ¼</td>
<td>1</td>
<td>1</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>A₁A₆ ¼</td>
<td>1</td>
<td>1</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>A₂A₅ ¼</td>
<td>0</td>
<td>0</td>
<td>1</td>
<td>1</td>
</tr>
<tr>
<td>A₂A₆ ¼</td>
<td>0</td>
<td>0</td>
<td>1</td>
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Collateral: Half sibs

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<tr>
<td>0 IBD alleles</td>
<td>8/16</td>
<td>0</td>
</tr>
<tr>
<td>1 IBD alleles</td>
<td>8/16</td>
<td>1/2 σ²_A + σ²_D</td>
</tr>
<tr>
<td>2 IBD alleles</td>
<td>0</td>
<td>σ²_HS = \left( \frac{8}{16} \right) \frac{1}{2} σ²_A = \frac{1}{4} σ²_A</td>
</tr>
</tbody>
</table>

Cov(G₁, G₂)

Total covariance = Sum Probability x contribution =

σ²_HS = \left( \frac{8}{16} \right) \frac{1}{2} σ²_A = \frac{1}{4} σ²_A
Collateral: Full sibs

Collateral: Number of IBD Alleles

Sib O₁ possible genotypes

<table>
<thead>
<tr>
<th>Sib O₂ possible genotypes</th>
<th>A₁A₃ 1/₄</th>
<th>A₁A₄ 1/₄</th>
<th>A₂A₃ 1/₄</th>
<th>A₂A₄ 1/₄</th>
</tr>
</thead>
<tbody>
<tr>
<td>A₁A₃ 1/₄</td>
<td>2</td>
<td>1</td>
<td>1</td>
<td>0</td>
</tr>
<tr>
<td>A₁A₄ 1/₄</td>
<td>1</td>
<td>2</td>
<td>0</td>
<td>1</td>
</tr>
<tr>
<td>A₂A₃ 1/₄</td>
<td>1</td>
<td>0</td>
<td>2</td>
<td>1</td>
</tr>
<tr>
<td>A₂A₄ 1/₄</td>
<td>0</td>
<td>1</td>
<td>1</td>
<td>2</td>
</tr>
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</table>
Collateral: Full sibs

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<tbody>
<tr>
<td>0 IBD alleles</td>
<td>4/16</td>
<td>0</td>
</tr>
<tr>
<td>1 IBD alleles</td>
<td>8/16</td>
<td>$\frac{1}{2} \sigma_A^2$</td>
</tr>
<tr>
<td>2 IBD alleles</td>
<td>4/16</td>
<td>$\sigma_A^2 + \sigma_D^2$</td>
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$Cov(G_{O_1}, G_{O_2})$  
Total covariance = Sum Probability x contribution =

$$\sigma_{FS} = \left(\frac{4}{16}\right)\left(\frac{1}{2} \sigma_A^2\right) + \left(\frac{4}{16}\right)\left(\sigma_A^2 + \sigma_D^2\right) = \frac{1}{2} \sigma_A^2 + \frac{1}{4} \sigma_D^2$$

Covariance Between Relatives in General

$Cov(G_x, G_y)$

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</thead>
<tbody>
<tr>
<td>1 IBD alleles</td>
<td>$\Pr(1)_{xy}$</td>
<td>$\frac{1}{2} \sigma_A^2$</td>
</tr>
<tr>
<td>2 IBD alleles</td>
<td>$\Pr(2)_{xy}$</td>
<td>$\sigma_A^2 + \sigma_D^2$</td>
</tr>
</tbody>
</table>

Let  
$$r_{xy} = \frac{1}{2} \Pr(1)_{xy} + \Pr(2)_{xy}$$  
$$u_{xy} = \Pr(2)_{xy}$$

Total covariance = Sum Probability x contribution =

$$Cov(G_x, G_y) = r_{xy} \sigma_A^2 + u_{xy} \sigma_D^2$$

With higher order effects (epistasis)

$$Cov(G_x, G_y) = r_{xy} \sigma_A^2 + u_{xy} \sigma_D^2 + r_{xy}^2 \sigma_{AA}^2 + r_{xy} u_{xy} \sigma_{AD}^2 + u_{xy}^2 \sigma_{DD}^2 + ...$$
Covariance Between Relatives
Common Environmental Causes \( Ec \)

Common Farm

Common Maternal

Specific Environmental Effects \( Es \)

Common Cage or Pen

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Environmental Effects

Common Environmental Effects Ec contribute to resemblance of sibs

Specific Environmental effect: Es
Causes correlation among sequential records from same animal

Summary Resemblance Among Relatives

<table>
<thead>
<tr>
<th>Relative Pair</th>
<th>Cov</th>
<th>Relative to Phenotypic Variance</th>
<th>$h^2$</th>
</tr>
</thead>
<tbody>
<tr>
<td>Parent-Offspring</td>
<td>$\frac{1}{2} \sigma^2_a$</td>
<td>$b_{o,p} = \frac{1}{2} \sigma^2_a / \sigma^2_p$</td>
<td>$h^2 = 2b_{o,p}$</td>
</tr>
<tr>
<td>Midparent-Offspring</td>
<td>$\frac{1}{2} \sigma^2_a$</td>
<td>$b_{o,p} = \left( \frac{1}{2} \sigma^2_a \right) / \sigma^2_p$</td>
<td>$h^2 = b_{o,p}$</td>
</tr>
<tr>
<td>Half-Sib</td>
<td>$\frac{1}{4} \sigma^2_a$</td>
<td>$t_{HS} = \left( \frac{1}{4} \sigma^2_a \right) / \sigma^2_p$</td>
<td>$h^2 = 4t_{HS}$</td>
</tr>
<tr>
<td>Full-Sib</td>
<td>$\frac{1}{4} \sigma^2_a + \frac{1}{2} \sigma^2_D + \sigma^2_{Ec}$</td>
<td>$\frac{1}{2} \sigma^2_a + \frac{1}{2} \sigma^2_D + \sigma^2_{Ec}$</td>
<td>$h^2 \leq 2t_{FS}$</td>
</tr>
</tbody>
</table>

$$Var(MP) = Var\left( \frac{P_m + P_f}{2} \right) = \frac{1}{4} \left( Var(P_m + P_f) \right) = \frac{1}{4} \left( \sigma^2_p + \sigma^2_{Ec} \right) = \frac{1}{2} \sigma^2_p$$
Problem set 3

- Recall Problem 1 of Set 2: Falconer (1981) reported a partially dominant gene in the mouse called pg "pygmy." At six weeks of age, they produce the following average weight phenotypes in grams (the actual weight of the heterozygote was 12, but it was reduced to 10 for this example):
  - $+$ / $+$ : 14, $+$ / pg : 10, pg / pg : 6
- If the population of mice is randomly mating with $p^+ = 0.3$, $q^{pg} = 0.7$
- Assume an Environmental variance of 7 and no environmental effects common to families. Compute the regression or intraclass correlation for the following
  - a) one parent-offspring
  - b) half-sib
  - c) Full-sib
  - d) If the frequency of the wild allele (+) increased to .5, would you expect these values to increase, decrease, or remain the same, Why (?)