Genetic Covariance of Trait Values for Relatives
Coefficients of Coancestry

- We previously showed that for a pair of individuals that the kinship coefficient (or coefficient of coancestry) $\theta$ can be written in terms of Jacquard’s 9 condensed coefficients of identity where

$$\theta = \Delta_1 + \frac{1}{2}(\Delta_3 + \Delta_5 + \Delta_7) + \frac{1}{4}\Delta_8$$
Jacquard’s (1970) 9 Condensed Coefficients of Identity

<table>
<thead>
<tr>
<th>Probability</th>
<th>Identity state</th>
<th>Maternal</th>
<th>Paternal</th>
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<tr>
<td>$\Delta_1$</td>
<td>![Diagram]</td>
<td>A’s alleles</td>
<td>B’s alleles</td>
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<tr>
<td>$\Delta_2$</td>
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<td>$\Delta_9$</td>
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</table>
Coefficients of Coancestry

- Consider an outbred population. For outbred populations we have that $\Delta_1$ to $\Delta_6$ are 0.
- It is convenient to let $k_2$, $k_1$ and $k_0$ represent the probability that a pair of outbred individuals sharing 2, 1, or 0 alleles IBD, respectively, in lieu of $\Delta_7$, $\Delta_8$, and $\Delta_9$.
- For outbred populations the kinship coefficient for a pair of individuals can be written as

$$\theta = \frac{1}{2}k_2 + \frac{1}{4}k_1$$

- Note that the kinship coefficient is based on the probability of sharing 0, 1, or 2 alleles IBD. However, at a locus, a pair of individuals actually share either zero, one, or two alleles IBD at a locus.
Coefficients of Coancestry

- Let $k_0^*$, $k_1^*$, and $k_2^*$ be the actual value at the locus.
- Exactly one of these three quantities is one (for that ibd state being true) and the other two are zero (for those ibd states being false).
- Calculate the following
  - $E[k_i^*]$
  - $\text{Var}[k_i^*]$
  - $E[k_i^* k_j^*]$ for $i \neq j$
  - $\text{Cov}[k_i^*, k_j^*]$ for $i \neq j$
Variance of actual Coancestry

- We have the following:
  - $E[k_i^*] = k_i$
  - $\text{Var}[k_i^*] = k_i(1 - k_i)$
  - $E[k_i^* k_j^*] = 0$ for $i \neq j$
  - $\text{Cov}[k_i^*, k_j^*] = -k_i k_j$ for $i \neq j$
Now, the actual coancestry at a locus for two noninbred individuals is

\[ \theta^* = \frac{1}{2} k_2^* + \frac{1}{4} k_1^* \]

Calculate \( \text{Var}(\theta^*) \)
Variance of actual Coancestry

\[ Var(\theta^*) = \frac{1}{4} Var(k_2^*) + \frac{1}{16} Var(k_1^*) + \frac{1}{4} Cov(k_1^*, k_2^*) \]

\[ = \frac{1}{4} k_2(1 - k_2) + \frac{1}{16} k_1(1 - k_1) - \frac{1}{4} k_2 k_1 \]

- First cousins have \( k_2 = 0 \), \( k_1 = .25 \) and \( k_0 = .75 \). Calculate the expected value, variance, and standard deviation of actual coancestry for this relative pair type at a locus.

- What is the variance of actual coancestry for parent-offspring?
Variance of actual Coancestry

\[
Var(\theta^*) = \frac{1}{4} k_2 (1 - k_2) + \frac{1}{16} k_1 (1 - k_1) - \frac{1}{4} k_2 k_1
\]

- First cousins have \( k_2 = 0, k_1 = \frac{1}{4} \) and \( k_0 = \frac{3}{4} \), so \( \theta = \frac{1}{16} = .0625 \).
- The variance of actual coancestry is \( \left( \frac{1}{16} \right) \left( \frac{1}{4} \right) \left( \frac{3}{4} \right) = \frac{3}{256} \).
- The standard deviation is \( \sqrt{\frac{3}{16}} = .10825 \).
- For parent-offspring, the variance of actual coancestry is 0.
We will now focus on obtaining the genetic covariance of trait values for two outbred relatives.

Consider a quantitative trait that is influenced by a single locus.

As before, we denote the genetic value for genotype $A_iA_j$ as

$$G_{ij} = \mu_G + \alpha_i + \alpha_j + \delta_{ij}$$

where

$$\mu_G = \sum_i \sum_j p_i p_j G_{ij} = G..$$

$$\alpha_i = \sum_j p_j G_{ij} - \mu_G = G_i. - G..$$

$$\delta_{ij} = G_{ij} - \mu_G - \alpha_i - \alpha_j = G_{ij} - G_i. - G_j. + G..$$

These imply that $\sum_i p_i \alpha_i = 0$ and $\sum_i p_i \delta_{ij} = 0$.
Genetic Covariance for Two Outbred Relatives

- Consider two individuals $X$ and $Y$. We will calculate the covariance of the genetic values for $X$ and $Y$.
- Let $X_1$ and $X_2$ be the two alleles at the locus for individual $X$, and let $Y_1$ and $Y_2$ be the two alleles for individual $Y$.
- We have the following:

\[
\text{Cov}(G_{X_1X_2}, G_{Y_1Y_2}) = \\
\text{Cov}(\mu_G + \alpha_{X_1} + \alpha_{X_2} + \delta_{X_1X_2}, \mu_G + \alpha_{Y_1} + \alpha_{Y_2} + \delta_{Y_1Y_2}) \\
= \text{Cov}(\alpha_{X_1}, \alpha_{Y_1}) + \text{Cov}(\alpha_{X_1}, \alpha_{Y_2}) + \text{Cov}(\alpha_{X_1}, \delta_{Y_1Y_2}) \\
+ \text{Cov}(\alpha_{X_2}, \alpha_{Y_1}) + \text{Cov}(\alpha_{X_2}, \alpha_{Y_2}) + \text{Cov}(\alpha_{X_2}, \delta_{Y_1Y_2}) \\
+ \text{Cov}(\delta_{X_1X_2}, \alpha_{Y_1}) + \text{Cov}(\delta_{X_1X_2}, \alpha_{Y_2}) + \text{Cov}(\delta_{X_1X_2}, \delta_{Y_1Y_2}) \\
= 4 \text{Cov}(\alpha_{X_1}, \alpha_{Y_1}) + 2 \text{Cov}(\alpha_{X_1}, \delta_{Y_1Y_2}) + 2 \text{Cov}(\delta_{X_1X_2}, \alpha_{Y_1}) \\
+ \text{Cov}(\delta_{X_1X_2}, \delta_{Y_1Y_2})
\]

Since in outbred populations the two alleles within an individual are independent and identically distributed (iid)
Now let’s first focus on the terms involving the covariance of the additive and dominance effects: $2 \text{Cov}(\alpha_{X_1}, \delta_{Y_1} Y_2)$ and $2 \text{Cov}(\delta_{X_1 X_2}, \alpha_{Y_1})$

Let’s consider the covariance when $X$ and $Y$ are the monozygotic twins, or the genetic equivalence of $X = Y$. What do we know about $\text{Cov}(\alpha_{X_1}, \delta_{X_1 X_2})$

\[
\text{Cov}(\alpha_{X_1}, \delta_{X_1 X_2}) = E(\alpha_{X_1} \delta_{X_1 X_2}) - E(\alpha_{X_1})E(\delta_{X_1 X_2})
\]

\[
= E(\alpha_{X_1} \delta_{X_1 X_2}) - 0
\]

\[
= \sum_i \sum_j p_i p_j \alpha_i \delta_{ij} = \sum_i p_i \alpha_i \sum_j p_j \delta_{ij} = \sum_i p_i \alpha_i(0) = 0
\]

We actually already know this to be true since the additive effects and the dominance effects are uncorrelated!
Genetic Covariance for Two Outbred Relatives

- It follows that for any pair of individuals \( X \) and \( Y \), who obviously must have IBD sharing that is less than or equal to monozygotic twins, that the additive and dominance effects must also have a covariance of 0.

- So we have

\[
\text{Cov}(G_{X_1X_2}, G_{Y_1Y_2}) = 4\text{Cov}(\alpha_{X_1}, \alpha_{Y_1}) + 2\text{Cov}(\alpha_{X_1}, \delta_{Y_1Y_2}) + 2\text{Cov}(\delta_{X_1X_2}, \alpha_{Y_1}) \\
+ \text{Cov}(\delta_{X_1X_2}, \delta_{Y_1Y_2})
\]

\[
= 4\text{Cov}(\alpha_{X_1}, \alpha_{Y_1}) + \text{Cov}(\delta_{X_1X_2}, \delta_{Y_1Y_2})
\]

- Now take a moment to calculate \( 4\text{Cov}(\alpha_{X_1}, \alpha_{Y_1}) \). Hint: use the kinship coefficient \( \theta \) for the two individuals for this calculation.
Genetic Covariance for Two Outbred Relatives

We have

$$\text{Cov}(\alpha_{X_1}, \alpha_{Y_1}) = E[\alpha_{X_1} \alpha_{Y_1}] - E[\alpha_{X_1}]E[\alpha_{Y_1}]$$

$$= E[\alpha_{X_1} \alpha_{Y_1}] - 0$$

Now

$$E[\alpha_{X_1} \alpha_{Y_1}] = E[\alpha_{X_1} \alpha_{Y_1} | X_1 \text{and } Y_1 \text{ are IBD}] P(X_1 \text{and } Y_1 \text{ are IBD})$$

$$+ E[\alpha_{X_1} \alpha_{Y_1} | X_1 \text{and } Y_1 \text{ are not IBD}] P(X_1 \text{and } Y_1 \text{ are not IBD})$$

$$= E[\alpha_{X_1}^2] \theta + 0(1 - \theta)$$

$$= \frac{1}{2} \sigma_a^2 \theta$$

where $\sigma_a^2$ is the additive variance for the trait since we previously define $\sigma_a^2 = 2\text{Var}(\alpha_i) = 2 \sum_i p_i \alpha_i^2$
Genetic Covariance for Two Outbred Relatives

So we have

\[ \text{Cov}(G_{X_1X_2}, G_{Y_1Y_2}) = \]
\[ = 4 \text{Cov}(\alpha_{X_1}, \alpha_{Y_1}) + \text{Cov}(\delta_{X_1X_2}, \delta_{Y_1Y_2}) \]
\[ = 4 \left( \frac{1}{2} \sigma_a^2 \right) + \text{Cov}(\delta_{X_1X_2}, \delta_{Y_1Y_2}) = 2\theta \sigma_a^2 + \text{Cov}(\delta_{X_1X_2}, \delta_{Y_1Y_2}) \]

Now take a moment to calculate \( \text{Cov}(\delta_{X_1X_2}, \delta_{Y_1Y_2}) \). Hint: condition of the probabilities of the pair sharing zero, one, or two alleles IBD, i.e., \( k_0, k_1, \) and \( k_2 \)
Genetic Covariance for Two Outbred Relatives

- We have

\[
\text{Cov}(\delta_{X_1X_2}, \delta_{Y_1Y_2}) = E[\delta_{X_1X_2}\delta_{Y_1Y_2}] - E[\delta_{X_1X_2}]E[\delta_{Y_1Y_2}]
\]

\[= E[\delta_{X_1X_2}\delta_{Y_1Y_2}] - 0\]

- Now \(E[\delta_{X_1X_2}\delta_{Y_1Y_2}] = \)

\[
E[\delta_{X_1X_2}\delta_{Y_1Y_2}|X \text{ and } Y \text{ share 2 alleles IBD}] \times P(X \text{ and } Y \text{ share 2 alleles IBD})
\]

\[+ E[\delta_{X_1X_2}\delta_{Y_1Y_2}|X \text{ and } Y \text{ share 1 allele IBD}] \times P(X \text{ and } Y \text{ share 1 alleles IBD})
\]

\[+ E[\delta_{X_1X_2}\delta_{Y_1Y_2}|X \text{ and } Y \text{ share 0 alleles IBD}] \times P(X \text{ and } Y \text{ share 0 alleles IBD})\]
Genetic Covariance for Two Outbred Relatives

- We have that

\[ E[\delta_{X_1X_2}\delta_{Y_1Y_2}|X \text{ and } Y \text{ share 2 alleles IBD}] \times P(X \text{ and } Y \text{ share 2 alleles IBD}) = E[\delta^2_{X_1X_2}]k_2 \]

- We also have that

\[ E[\delta_{X_1X_2}\delta_{Y_1Y_2}|X \text{ and } Y \text{ share 1 allele IBD}] \times P(X \text{ and } Y \text{ share 1 alleles IBD}) = k_1 \sum_l \sum_i \sum_j p_l p_i p_j \delta_{il} \delta_{jl} \]

\[ = k_1 \sum_l p_l \sum_i p_i \delta_{il} \sum_j p_j \delta_{jl} \]

\[ = k_1 \sum_l p_l (0)(0) \]

since \( \sum_i p_i \delta_{ij} = 0. \)
Finally, we have that

\[ E[\delta_{X_1} \delta_{Y_1} | X \text{ and } Y \text{ share 0 alleles IBD}] \times P(X \text{ and } Y \text{ share 0 alleles IBD}) = E[\delta_{X_1} \delta_{Y_1}] E[\delta_{Y_1}] k_0 \]

\[ = (0)(0)k_0 = 0 \]
So, putting the three terms together we have that

$$\text{Cov}(\delta_{X_1 X_2}, \delta_{Y_1 Y_2}) = E[\delta^2_{X_1 X_2}]k_2 + (0)k_1 + (0)k_0 = \sigma_d^2 k_2$$

where $\sigma_d^2$ is the dominance variance for the trait that we previously define as

$$\sigma_d^2 = \text{Var}(\delta_{ij}) = E[\delta^2_{ij}] = \sum_{ij} p_{ij} \delta_{ij}^2$$
Genetic Covariance for Two Outbred Relatives

So we have

\[
\begin{align*}
\text{Cov}(G_{X_1 X_2}, G_{Y_1 Y_2}) &= \\
&= 4 \text{Cov}(\alpha_{X_1}, \alpha_{Y_1}) + \text{Cov}(\delta_{X_1 X_2}, \delta_{Y_1 Y_2}) \\
&= 2\theta\sigma_a^2 + k_2\sigma_d^2
\end{align*}
\]

For inbred individuals, obtaining genetic covariance is a bit more complicated, but one can show that for \(X\) and \(Y\) inbreed we have

\[
\begin{align*}
\text{Cov}(G_{X_1 X_1}, G_{Y_1 Y_2}) &= \\
&= 2\theta\sigma_a^2 + \Delta_7\sigma_d^2 \\
&\quad + D_1(4\Delta_1 + \Delta_3 + \Delta_5) + D_2\Delta_1 + H^2(\Delta_1 + \Delta_2 - F_X F_Y)
\end{align*}
\]
Terminology and Expressions for Variance of Traits

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<th>Components</th>
<th>Multi-allelic</th>
<th>Bi-allelic</th>
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<tr>
<td>Additive Variance</td>
<td>$\sigma_A^2 = 2 \sum_i p_i \alpha_i^2$</td>
<td>$\sigma_A^2 = 2pq \alpha^2$</td>
</tr>
<tr>
<td>Dominance Variance</td>
<td>$\sigma_D^2 = \sum_i \sum_j p_i p_j \delta_{ij}^2$</td>
<td>$\sigma_D^2 = (2pqd)^2$</td>
</tr>
<tr>
<td>Inbreeding depression</td>
<td>$H = \sum_i p_i \delta_{ii}$</td>
<td>$H = -2qpd$</td>
</tr>
<tr>
<td>Covariance of $\alpha_i$’s and $\delta_{ii}$’s</td>
<td>$D_1 = \sum_i p_i \alpha_i \delta_{ii}$</td>
<td>$D_1 = 2pqd \alpha (p - q)$</td>
</tr>
<tr>
<td>Variance of $\delta_{ii}$’s</td>
<td>$D_2 = \sum_i p_i \delta_{ii}^2 - H^2$</td>
<td>$D_2 = 4pq (1 - 4pq) d^2$</td>
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