Quantitative Genetics with X-Chromosomal Loci

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Introduction

The importance of autosomal loci to genetic variation and covariation of quantitative traits is well documented. In contrast, the importance of X-chromosomal loci to these variances and covariances is less well documented.

Lush (1945) suggested that X-chromosomal inheritance accounted for about five percent of total inheritance of farm animals, based on chromosome number. Jerome et al. (1956) and Thomas et al. (1958), however, found evidence of considerable variation for X-chromosomal effects on body weight or weight gain in poultry. Recent evidence (VanRaden, 1987) suggests that five to ten percent of genetic variation for milk production in Holstein cattle is located on the X chromosome. In species with few autosomal chromosomes, such as Drosophila melanogaster, variance from X-chromosomal loci can account for a large proportion of the total genetic variance for some quantitative traits (Cowley et al., 1986). We cannot assume, therefore, that genetic variation from X-chromosomal loci is zero as we do in computing covariance between relatives for use in genetic evaluation.

The early work of Fisher (1918) and Wright (1921) presented formulae for covariance and correlations between relatives for different degrees of dominance, epistasis and environmental variance (see comments by Hill, 1984). Fisher's paper, which dealt with epistasis between pairs of loci, was extended to include an arbitrary number of loci by Cockerham (1954, for two alleles with inbreeding) and by Kempttjorne (1954, for multiple alleles with no inbreeding). Cockerham's (1956) extension included effects of linkage on covariance between relatives. Schnell (1963) corrected errors in Cockerham's (1956) work and gave general formulations, including inbreeding of parents and linkage. Cockerham's formulae for genetic variances and covariances are appropriate to populations in genetic equilibrium. For populations in disequilibrium, such as in populations derived from crosses, these formulae do not hold.

According to Hardy-Weinberg, for a single autosomal locus, a population achieves genotypic equilibrium in one generation of random mating if allelic frequency is the same in the sexes, or in two generations if the frequency is not (Crow and Kimura, 1970). For a single X-chromosomal locus, however, the approach of the population to equilibrium oscillates and is gradual (Jennings, 1916; Crow and Kimura, 1970), reaching equilibrium only in the limit. For X-chromosomal inheritance, therefore, covariances between relatives

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may be complicated because the population is always in disequilibrium, unless of course it starts out in equilibrium.

For autosomal loci, it is well understood how genetic variance and covariance between relatives can be formulated in terms of genetic parameters, such as allelic frequencies and genotypic effects, for a population in equilibrium. Such formulations were not as well understood for X-chromosomal loci, and were not known for a population in disequilibrium.

Correlation between full sibs and between parent and offspring for additive and dominant gene actions at an X-chromosomal locus for a population in equilibrium has been derived by Hogben (1932). Wright (1969) presented correlations between various relatives for an X-chromosomal locus. Commonly-used covariances between relatives for X-chromosomal loci in a random mating population in equilibrium have been derived by Bohidar (1964), James (1973), and Grossman and Eisen (1989). Although assumption of equilibrium is defensible for an autosomal locus, it is less defensible for an X-chromosomal locus.

Grossman and Fernando (1989) derived covariance between collateral and between lineal relatives for X-chromosomal loci in a population not in equilibrium. Collateral relatives, such as sibs or cousins, are of the same generation and lineal relatives, such as parent-offspring or aunt-nephew, are of different generations. Coefficients of coancestry between relatives, based on identity by descent (Malécot, 1969), were derived for X-chromosomal loci (Grossman and Eisen, 1989) and used for their development. Recently, Fernando and Grossman (1990) showed how Best Linear Unbiased Prediction (BLUP) can be used for genetic evaluation in the presence of autosomal and X-chromosomal additive inheritance. In this paper, we shall review our recent work on quantitative genetics with X-chromosomal inheritance.

We shall assume a model for X-chromosomal inheritance, which paradoxically will describe the general case. Remember that results for the homogametic sex are applicable to autosomal inheritance. Therefore, by developing the theory for X-chromosomal inheritance, we develop it for autosomal inheritance simultaneously. Furthermore, results are applicable also to haplo-diploid organisms, such as the honeybee, in which the entire genome is equivalent to being X-chromosomal (Li, 1976).

We assume that the male is the heterogametic sex (XY) and the female is the homogametic sex (XX). The Y chromosome is considered to contain an inert locus and, therefore, will be ignored. For species in which the male is the homogametic sex and the female is the heterogametic sex, such as poultry, results should be interpreted accordingly.
Inbreeding, Coancestry, and Covariance for a Population in Equilibrium

Let U and V denote males and let W and Z denote females. For males, let U contain allele $u_1$ on the X chromosome and let V contain allele $v_1$ on the X chromosome, at a given locus. For females, let W contain alleles $w_1$ and $w_2$ and let Z contain alleles $z_1$ and $z_2$ on the X chromosomes, at the same locus. Let $u$ be the random allele from male U and $v$ be the random allele from male V. Let $w$ be the random allele from female W and $z$ be the random allele from female Z. Individuals and their alleles are summarized below, where $Y$ represents the Y chromosome:

<table>
<thead>
<tr>
<th>Individual</th>
<th>U</th>
<th>V</th>
<th>W</th>
<th>Z</th>
</tr>
</thead>
<tbody>
<tr>
<td>Genotype</td>
<td>$u_1Y$</td>
<td>$v_1Y$</td>
<td>$w_1w_2$</td>
<td>$z_1z_2$</td>
</tr>
<tr>
<td>Random allele</td>
<td>$u$</td>
<td>$v$</td>
<td>$w$</td>
<td>$z$</td>
</tr>
</tbody>
</table>

Coefficient of inbreeding ($f$) of an individual is the probability ($P$) that two homologous alleles, received by that individual from its parents, are identical by descent ($\equiv$) at a given locus (Malécot, 1969):

for a male, say U,

\[ f_U \text{ is undefined ,} \]

which is a consequence of X-chromosomal inheritance; and for a female, say W,

\[ f_W = P(w_1 \equiv w_2) , \]

which is the same as for autosomal inheritance.

Coefficient of coancestry ($r$) between two individuals is the probability that an allele at a given locus on the X chromosome in an individual is identical by descent to an allele at that locus in another individual (Malécot, 1969). For autosomal loci, it is not necessary to distinguish the sex of individuals, but for X-chromosomal loci it is. For females, which have two X chromosomes, the allele is drawn at random so that the probability of obtaining each allele is one-half. For males, which have only one X chromosome, however, the allele is not drawn at random so that the probability of obtaining that allele is unity.

Male-male: The $r$ between males U and V ($r_{UV}$) is the probability that the allele on the X chromosome in U is identical by descent to the allele on the X chromosome in V, or that $u_1$ and $v_1$ are identical by descent:

\[ r_{UV} = P(u_1 \equiv v_1) . \]
Note that $r$ between a male individual, say $U$, and itself, as for monozygous male twins, is found by sampling $U$ twice with replacement:

$$r_{UU} = P(u_1 \equiv u_1) = 1.$$ 

**Female-female:** The $r$ between females $W$ and $Z$ ($r_{wz}$) is the probability that allele $w$ drawn at random from $W$ is identical by descent to allele $z$ drawn at random from $Z$:

$$r_{wz} = P(w \equiv z) = \frac{1}{4} \left[ P(w_1 \equiv z_1) + P(w_1 \equiv z_2) + P(w_2 \equiv z_1) + P(w_2 \equiv z_2) \right].$$

Note that $r$ between a female individual, say $W$, and itself, as for monozygous female twins, is found by sampling $W$ twice with replacement:

$$r_{ww} = P(w \equiv w') = \frac{1}{2} \left( 1 + f_w \right).$$

**Male-female:** The $r$ between male $U$ and female $W$ is the probability that the allele on the X chromosome in $U$ is identical by descent to allele $w$ drawn at random from $W$, or that $u_1$ and $w$ are identical by descent:

$$r_{uw} = P(u_1 \equiv w) = \frac{1}{4} \left[ P(u_1 \equiv w_1) + P(u_1 \equiv w_2) \right].$$

Covariance ($Cov$) between relatives is the covariance between genotypic values of related individuals. For a single X-chromosomal locus in a random mating population at equilibrium (equal gene frequencies in the sexes), it is composed of fractions of components of variance and covariance, depending on the sex of relatives involved: variance of additive genetic values for males ($\sigma_{Am}^2$), variance of additive genetic values ($\sigma_{Af}^2$) and of dominance deviations ($\sigma_{Dr}^2$) for females, and covariance between additive genetic values for a male and a female ($\sigma_{AmAf}$):

$$Cov = a_{11} \sigma_{Am}^2 + a_{22} \sigma_{Af}^2 + d_{22} \sigma_{Dr}^2 + a_{12} \sigma_{AmAf},$$

where $a_{11}$ is additive relationship between males, or fraction of additive genetic variance component for males; $a_{22}$ is additive relationship between females, or fraction of additive genetic component for females; $d_{22}$ is dominance relationship between females, or fraction of dominance variance component for females; and $a_{12}$ is additive genetic relationship between a male and a female, or fraction of additive genetic covariance between a male and a female.

Additive and dominance relationships are functions of coefficient of inbreeding and coefficient of coancestry and, for X-chromosomal loci, are defined for sexes differently. To define additive and dominance relationships, we derive the covariance between relatives following approaches of Kempthorne (1969) and Weir and Cockerham (1977).
**Male-male:** Let $g_i$ be the value of male genotype $s_i$ as a deviation from the mean of males, and let $\beta_i$ be its additive genetic value. Then covariance between males is

$$\text{Cov}(g_i, g_j) = \text{Cov}(\beta_i, \beta_j) = P(s_i \equiv s_j)E(\beta_i^2) = r_{11}\sigma_{Am}^2 = a_{11}\sigma_{Am}^2,$$

where $E(\beta_i^2)$ is covariance between additive genetic values of the same allele in males, such as brothers, or variance of additive genetic values for males ($\sigma_{Am}^2$).

Additive relationship between males ($a_{11}$), therefore, will be defined as the coefficient of coancestry between males ($r_{11}$), which is the probability that the one allele ($s_i$) in a male is identical by descent to the one allele ($s_j$) in the other male. Dominance relationship between males for X-chromosomal loci is undefined. Additive relationship of a male with itself, as for monozygous male twins, is unity.

**Female-female:** Let $g_{jk}$ be the value of female genotype $s_j s_k$, as a deviation from the mean of females, let $\alpha_j$ and $\alpha_k$ be its additive genetic values, and let $\delta_{jk}$ be its dominance deviation. Then covariance between females is

$$\text{Cov}(g_{jk}, g_{j'k'}) = \text{Cov}(\alpha_j + \alpha_k + \delta_{jk}, \alpha_{j'} + \alpha_{k'} + \delta_{j'k'}) = \text{Cov}(\alpha_j, \alpha_{j'}) + \text{Cov}(\alpha_k, \alpha_{k'}) + \text{Cov}(\alpha_j, \alpha_k) + \text{Cov}(\delta_{jk}, \delta_{j'k'})$$

$$= [P(s_j \equiv s_{j'}) + P(s_j \equiv s_k) + P(s_k \equiv s_{j'}) + P(s_k \equiv s_{k'})]E(\alpha_{j'}^2) + P(s_j s_k \equiv s_j s_{k'})E(\delta_{jk}^2)$$

$$= 4r_{22}(\gamma\sigma_{Af}^2) + d_{22}\sigma_{Dr}^2$$

$$= 2r_{22}\sigma_{Af}^2 + d_{22}\sigma_{Dr}^2$$

$$= a_{22}\sigma_{Af}^2 + d_{22}\sigma_{Dr}^2,$$

where $E(\alpha_{j'}^2)$ is covariance between additive genetic values of the same allele in females, such as sisters, or variance of additive genetic values for females ($\sigma_{Af}^2$), and $E(\delta_{jk}^2)$ is covariance between dominance deviations of the same alleles in females or variance of dominance deviations for females ($\sigma_{Dr}^2$).

Additive relationship between females ($a_{22}$), therefore, will be defined as twice the coefficient of coancestry between those females ($r_{22}$), which is the probability that each allele ($s_j$ or $s_k$) in a female is identical by descent to each allele in the other female. Dominance relationship between females ($d_{22}$) will be defined as the probability that both alleles ($s_j$ and $s_k$) in a female are identical by descent to both alleles ($s_{j'}$ and $s_{k'}$) in the other female. These definitions of relationship are equivalent to those for autosomal loci. In a random mating population, additive relationship and dominance relationship of a female with itself, as for monozygous female twins, is unity.

**Male-female:** The covariance between genotypic value $g_i$ for a male and genotypic value $g_{jk}$ for a female is
Cov(gi,gjk) = Cov(βp, αj + αk + δjk)
= Cov(βp,αj) + Cov(βp,αk)
= [P(sj ≡ sj) + P(sj ≡ sk)]E(β,αi)
= 2r_{12}σ_{AmAf}
= a_{12}σ_{AmAf},

where E(β,αi) is covariance between additive genetic values of the same allele expressed in a male and a female, such as father-daughter, the other allele coming at random, or covariance between additive genetic values for a male and a female (σ_{AmAf}).

Additive relationship between a male and a female (a_{12}), therefore, will be defined as twice the coefficient of coancestry between male and female (r_{12}), which is the probability that the one allele (sj) in a male is identical by descent to one allele (sj or sk) in a female. Dominance relationship between male and female is undefined.

Additive and dominance relationships, useful for computing covariances between relatives, are summarized in Table 1 for collateral relatives (of the same generation) and in Table 2 for lineal relatives (of different generations) for a random mating population.

Covariance for a Population in Disequilibrium

For random mating in an infinite population, consider a single X-chromosomal locus with two alleles, s1 and s2, for a population in disequilibrium, i.e., allelic frequency is not the same in the sexes. Results can be extended easily to a single X-chromosomal locus with multiple alleles. The model is described below in generation t:

<table>
<thead>
<tr>
<th>Sex</th>
<th>Male</th>
<th>Female</th>
</tr>
</thead>
<tbody>
<tr>
<td>Genotype</td>
<td>s1</td>
<td>s2</td>
</tr>
<tr>
<td>Frequency</td>
<td>m1^t</td>
<td>m2^t</td>
</tr>
<tr>
<td>Genotypic value</td>
<td>y1</td>
<td>y2</td>
</tr>
</tbody>
</table>

For males, X-chromosomal inheritance determines that a genotype S = s_i (i = 1,2) receives its allele from its maternal parent.

Frequency of genotype s_i in generation t (m_i^t) is that for females in generation t-1 (f_i^{t-1}) (Li, 1976, p. 135) as

P(S = s_i) = m_i^t = f_i^{t-1},

with Σ_i m_i^t = 1.

For females, we will distinguish alleles by parent of origin. Because an allele may differ in its effect depending on parent of origin (Marx, 1988), genotypic value of the heterozygote is y_{12} for s1s2 and y_{21} for s2s1. By our convention a female with genotype
\( S_m S_p = s_j s_k \) receives allele \( s_j (j = 1,2) \) from its maternal parent and allele \( s_k (k = 1,2) \) from its paternal parent.

Frequency of genotype \( s_j s_k \) in generation \( t \) (\( f_{jk}^t \)) is the product of the allelic frequency for females (\( f_j^{t-1} \)) and for males (\( m_k^{t-1} \)) in generation \( t-1 \) (Li, 1976) as

\[
P(S_m = s_j, S_p = s_k) = P[(S_m = s_j), (S_p = s_k)] = f_{jk}^t = f_j^{t-1} m_k^{t-1},
\]
with \( \sum_j f_{jk}^t = 1 \).

For females, we have computed frequencies of alleles by parent of origin. The frequency of a maternal allele in generation \( t \) (\( f_{jm}^t \)) is allelic frequency for females in the previous generation as

\[
P(S_m = s_j) = f_{jm}^t = f_j^{t+1},
\]
with \( \sum_j f_{jm}^t = 1 \). Similarly, the frequency of a paternal allele in generation \( t \) (\( f_{kp}^t \)) is allelic frequency for males in the previous generation as

\[
P(S_p = s_k) = f_{kp}^t = m_k^{t-1},
\]
with \( \sum_k f_{kp}^t = 1 \). Frequency of \( s_j (j = 1,2) \) for females in generation \( t \) (\( f_j^t \)) is the arithmetic mean of allelic frequencies for parents in generation \( t-1 \) (Li, 1976, p. 135) as

\[
f_j^t = \frac{1}{2}(f_{jm}^t + f_{jp}^t) = \frac{1}{2}(f_j^{t-1} + m_j^{t-1}),
\]
with \( \sum_j f_j^t = 1 \).

Allelic frequency for males and for females in generation \( t \) can be expressed also by the arithmetic mean of frequencies in the two previous generations (Li, 1976, p. 136) as

\[
m_j^t = \frac{1}{2}(m_j^{t-1} + m_j^{t-2})
\]
and

\[
f_j^t = \frac{1}{2}(f_j^{t-1} + f_j^{t-2}).
\]

This recurrence relation allows us to express allelic frequency in generation \( t \) in terms of an equilibrium allelic frequency (\( p_i \)) and the deviation from equilibrium in generation \( t \) (\( d_i^t \)) (Li, 1976, pp. 152-156) as

\[
m_j^t = p_i - 2d_j^t
\]
and

\[
f_j^t = p_i + d_j^t,
\]
where \( p_i = (m_j/3) + (2f_j/3) \) in each generation, \( d_j^t = (-\frac{1}{2})^t \delta_j^0 / 3 \) in generation \( t \), and \( \delta_j^0 = f_j^0 - m_j^0 \) in generation zero. Note that as \( t \to \infty \), \( m_j^t \to p_i \) and \( f_j^t \to p_i \); at equilibrium, \( m_i^e = f_i^e = p_i \).
**Genotypic models**

For males, the genotypic value $Y^M = y_i$ for genotype $S = s_i$ in generation $t$ can be modeled as

$$y_i = \mu_m^t + \beta_i^t,$$

where $\mu_m^t$ is the mean genotypic value for males and $\beta^t = \beta_i^t$ is the average effect for allele $s_p$ measured by the average of genotypes with that allele as a deviation from the mean for males:

$$\mu_m^t = E(Y^M) = \Sigma_i m_i^t(y_i)$$

and

$$\beta_i^t = E(Y^M | S = s_i) - \mu_m^t = y_i - \mu_m^t,$$

and where $E()$ is the expectation operator at generation $t$. From the above definition, $E(\beta^t) = \Sigma_i m_i^t \beta_i^t = 0$. Note that the average effect of an allelic substitution for males is $\beta_1^t - \beta_2^t$ (Falconer 1981). At equilibrium, the genotypic mean is $\mu_m^e$ and the average effect is $\beta_i^e$, which are computed as above using the equilibrium allelic frequency ($p_i$).

For females, the genotypic value $Y^F = y_{jk}$ for genotype $S_mS_p = s_js_k$ in generation $t$ can be modeled as

$$y_{jk} = \mu_f^t + \alpha_{jm}^t + \alpha_{kp}^t + \delta_{jk}^t$$

where $\mu_f^t$ is the mean genotypic value for females; $\alpha_m^t = \alpha_{jm}^t$ is the average effect for maternal allele $S_m = s_j$ measured by the average of genotypes with that allele as a deviation from the mean for females; $\alpha_p^t = \alpha_{kp}^t$ is the average effect for paternal allele $S_p = s_k$ measured by the average of genotypes with that allele as a deviation from the mean for females; and $\delta^t = \delta_{jk}^t$ is the dominant deviation for genotype $S_mS_p = s_js_k$ measured by the failure of the average effects to sum to that genotypic value as a deviation from the mean for females:

$$\mu_f^t = E(Y^F) = \Sigma_j \Sigma_k f_{jk} \delta_{jk}(y_{jk})$$

$$\alpha_{jm}^t = E(Y^F | S_m = s_j) - \mu_f^t = \Sigma_k f_{kp}^t(y_{jk}) - \mu_f^t$$

$$\alpha_{kp}^t = E(Y^F | S_p = s_k) - \mu_f^t = \Sigma_j f_{jm}^t(y_{jk}) - \mu_f^t$$

and

$$\delta_{jk}^t = E(Y^F | S_mS_p = s_js_k) - \mu_f^t - \alpha_{jm}^t - \alpha_{kp}^t = (y_{jk} - \mu_f^t) - (\alpha_{jm}^t + \alpha_{kp}^t).$$
From above definitions,

\[
\begin{align*}
E(\alpha^t_m) &= \sum_{j} f_{jm}^t \alpha_{jm}^t = 0 \\
E(\alpha^t_p) &= \sum_{k} f_{kp}^t \alpha_{kp}^t = 0 \\
E(\delta^t) &= \sum_{j} \sum_{k} f_{jk}^t \delta_{jk}^t = 0
\end{align*}
\]

and, from random mating,

\[
E(\alpha^t_m \alpha^t_p) = E(\alpha^t_m \delta^t) = E(\alpha^t_p \delta^t) = 0;
\]

thus covariances between terms in the model are null. Note that the average effect of an allelic substitution for a maternal allele is \(\alpha_{1m}^t - \alpha_{2m}^t\), and that the average effect of an allelic substitution for a paternal allele is \(\alpha_{1p}^t - \alpha_{2p}^t\). At equilibrium, the genotypic mean is \(\mu_f^t\), average effects are \(\alpha_{jm}^c\) and \(\alpha_{kp}^c\), and dominant deviations are \(\delta_{jk}^c\), which are computed as above using the equilibrium allelic frequency (\(p_i\)).

**Variances**

For males, the variance of genotypic values, from (1), is the variance for average effects:

\[
V(Y^M) = V(\beta^t) = \sum_{i} m_i^t (\beta_i^t)^2
\]

\[
= \sum_{i} m_i^t (y_i - \mu_m^t)(y_i - \mu_m^t)
\]

(3)

where \(V()\) is the variance operator at generation \(t\). The variance at equilibrium, \(V(\beta^c)\), can be computed using \(m_i^c\) and \(\beta_i^c\) in (3).

For females, the variance of genotypic values, from (2), is the sum of variances for average effects and dominant deviations:

\[
V(Y^F) = V(\alpha^t_m) + V(\alpha^t_p) + V(\delta^t)
\]

(4)

where

\[
V(\alpha^t_m) = \sum_{j} f_{jm}^t (\alpha_{jm}^t)^2
\]

\[
= \sum_{j} f_{jm}^t (y_{jm}^t - \mu_f^t)(y_{jm}^t - \mu_f^t)
\]

(4.1)

\[
V(\alpha^t_p) = \sum_{k} f_{kp}^t (\alpha_{kp}^t)^2
\]

\[
= \sum_{k} f_{kp}^t (y_{kp}^t - \mu_f^t)(y_{kp}^t - \mu_f^t)
\]

(4.2)

and

\[
V(\delta^t) = \sum_{j} \sum_{k} f_{jk}^t (\delta_{jk}^t)^2
\]

\[
= \sum_{j} \sum_{k} f_{jk}^t (y_{jk}^t - \mu_f^t - \alpha_{jm}^t - \alpha_{kp}^t)(y_{jk}^t - \mu_f^t - \alpha_{jm}^t - \alpha_{kp}^t)
\]

(4.3)

Variances at equilibrium, \(V(\alpha^c_m)\), \(V(\alpha^c_p)\) and \(V(\delta^c)\), can be computed using \(f_j^c\) and \(m_k^c\), and \(\mu_f^c, \alpha_{jm}^c\) and \(\alpha_{kp}^c\) in (4.1), (4.2) and (4.3).
Covariance between relatives

Covariance between relatives is the covariance between genotypic values of related individuals. It is expressed in terms of fractions of components of variance and covariance, depending on the sex of relatives involved.

We shall derive covariance between relatives for X-chromosomal loci following the approaches of Kempthorne (1969) and Weir and Cockerham (1977), depending on the sex of relatives and on whether they are collateral or lineal relatives. Coefficients of coancestry are from Grossman and Eisen (1989).

Male-male: Let \( r = P(S'^tS) \) be the probability that the allele \( S' \) in a male \( M' \) in generation \( t' \) is identical by descent (\( \equiv \)) to the allele \( S \) in another male \( M \) in generation \( t \). This probability is the coefficient of coancestry for males. Also let \( P_i = P(S_i = s_i | S'^tS) \) be the probability that the allele in male \( M' \) is \( s_i \) given alleles in the two males are identical by descent.

Then covariance between genotypic values for males is covariance between the average effect (\( \beta'^t \)) for male \( M' \) and the average effect (\( \beta^t \)) for male \( M \), which must be evaluated depending on male relationships:

\[
C(Y'M', Y'M) = C(\beta'^t, \beta^t) = C(\beta'^t, \beta^t | S'^tS)P(S'^tS) \\
= P(S'^tS)P_i(S_i = s_i | S'^tS)(\beta_i'^t)(\beta_i^t) \\
= rP_i(\beta_i'^t)(\beta_i^t),
\]

where \( C() \) is the covariance operator between generations \( t' \) and \( t \) and \( C(\beta'^t, \beta^t | S'^tS) \) is the covariance between the average effect for alleles in generation \( t' \) and the average effect for alleles in generation \( t \), given the alleles are identical by descent. To compute covariances for commonly used collateral and lineal male relationships, see Table 1 in Grossman and Fernando (1989).

Female-female: Remember that a female with genotype \( S_mS_p \) receives allele \( S_m \) from its maternal parent and allele \( S_p \) from its paternal parent. Therefore, let \( r_{mm} = P(S'_m = S_m) \) be the probability that the allele of maternal origin \( S'_m \) in female \( F' \) in generation \( t' \) is identical by descent to the allele of maternal origin \( S_m \) in female \( F \) in generation \( t \); similarly, let \( r_{mp} = P(S'_m = S_p) \), \( r_{pm} = P(S'_p = S_m) \) and \( r_{pp} = P(S'_p = S_p) \), and let \( d = P(S'_mS'_p) \equiv (S_mS_p) \) be the probability that both alleles in \( F' \) are identical by descent to both alleles in \( F \).

Also let \( P_{ij|mm} = P(S'_m = s_j | S'_m = S_m) \) be the probability that the maternal allele in \( F' \) is \( s_j \) given maternal alleles in the females are identical by descent; similarly, let \( P_{ij|mp} = P(S'_m = s_j | S'_m = S_p) \), \( P_{ik|pm} = P(S'_p = s_k | S'_p = S_m) \) and \( P_{ik|pp} = P(S'_p = s_k | S'_p = S_p) \); and let \( P_{jk|mm} = P(S'_m = s_j | S'_m = S_p) \equiv (S_mS_p) \equiv (S'_mS'_p) \) be the probability that the genotype in \( F' \) is \( s_js_k \) given both alleles in \( F' \) and \( F \) are identical by descent.
Then covariance between genotypic values for females is the sum of covariances between average effects for maternal and paternal alleles and between dominant deviations of females $F'$ and $F$, which must be evaluated depending on female relationships:

\[
C(Y^F,Y^F) = C(\alpha'_m, \alpha'_p) + \delta'_t, \sigma^t_m + \alpha^t_p + \delta^t)
\]

where $C(\alpha'_m, \delta^t) = C(\alpha'_p, \delta^t) = C(\delta'_t, \alpha'_m) = C(\delta'_t, \alpha'_p) = 0$ because of random mating and where

\[
C(\alpha'_m, \alpha'_p) = C(\alpha'_m, \alpha'_p | S'_m = S_m) P(S'_m = S_m)
\]

\[
C(\alpha'_m, \alpha'_p) = P(S'_m = S_m) \sum_j P(S'_m = s_j | S'_m = S_m) (\alpha'_m) (\alpha'_p)
\]

\[
C(\alpha'_p, \alpha'_p) = P(\alpha'_p | S'_p = S_p) P(\alpha'_p | S'_p = S_p)
\]

\[
C(\delta'_t, \delta'_t) = C(\delta'_t, \delta'_t | (S'_m,S'_p) = (S_m,S_p)) P[(S'_m,S'_p) = (S_m,S_p)]
\]

\[
= P((S'_m,S'_p) = (S_m,S_p)) \sum_k P[(S'_m,S'_p) = (S_m,S_p)] (\delta'_t)(\delta'_t)
\]

\[
= d \sum_{jk} \sum_{k} P(\delta'_t)(\delta'_t)
\]

where, for example, $C(\alpha'_m, \alpha'_m | S'_m = S_m)$ is the covariance between the average effect for maternal alleles in generation $t'$ and the average effect for maternal alleles in generation $t$, given the maternal alleles are identical by descent. To compute covariances for commonly used collateral and lineal female relationships, see Table 2 in Grossman and Fernando (1989).

**Male-Female:** Let $r_m = P(S = S_m)$ be the probability that the allele $S$ in male $M$ in generation $t'$ is identical by descent to the maternal allele $S_m$ in female $F$ in generation $t$; similarly, $r_p = P(S = S_p)$.

Also let $p_{ijm} = P(S = s_i | S = S_m)$ be the probability that the allele in $M$ is $s_p$, given the allele in $M$ is identical by descent to the maternal allele in $F$; similarly, $p_{ijp} = P(S = s_i | S = S_p)$.

Covariance between genotypic values for male $M$ in generation $t'$ and female $F$ in generation $t$ is the sum of covariances between the average effect for $M$ and average effects
for maternal and paternal alleles for F, which must be evaluated depending on male-female relationships:

\[ C(Y^M,Y^F) = C(\beta^{t'}_m, \alpha^{t'}_m) + C(\beta^{t'}, \alpha^{t'}_p) \]

(7)

where \( C(\beta^{t'}, \delta^{t'}) = 0 \) and

\[ C(\beta^{t'}, \alpha^{t'}_m) = C(\beta^{t'}, \alpha^{t'}_m \mid S=S_m)P(S=S_m) \]

(7.1)

\[ = P(S=S_m) \Sigma_i P(S=s_i \mid S=S_m) (\beta^{t'}_i) (\alpha^{t'}_m) \]

\[ = r_m \Sigma_i P(s_i \mid S=S_m) (\beta^{t'}_i) (\alpha^{t'}_m) \]

and

\[ C(\beta^{t'}, \alpha^{t'}_p) = C(\beta^{t'}, \alpha^{t'}_p \mid S=S_p)P(S=S_p) \]

(7.2)

\[ = P(S=S_p) \Sigma_i P(S=s_i \mid S=S_p) (\beta^{t'}_i) (\alpha^{t'}_p) \]

\[ = r_p \Sigma_i P(s_i \mid S=S_p) (\beta^{t'}_i) (\alpha^{t'}_p) , \]

where, for example, \( C(\beta^{t'}, \alpha^{t'}_m \mid S=S_m) \) is the covariance between the average effect for males in generation \( t' \) and the average effect for maternal alleles in generation \( t \), given the allele in the male and the maternal allele are identical by descent. To compute covariances for commonly used collateral and lineal male-female relationships, see Table 3 of Grossman and Fernando (1989).

At equilibrium, and for equal genotypic values for heterozygotes, conditional covariances between average effects for male and female (7.1 and 7.2) correspond to half "the covariance between the additive effects of the sex-linked genes in male and female \([\frac{1}{2}C_{As}]\)" of Bohidar (1964) and to \( C_{MF} = \frac{1}{2}C_{As} \) of James (1973):

\[ C(\beta^c, \alpha^c_m \mid S=S_m) = C(\beta^c, \alpha^c_p \mid S=S_p) = \frac{1}{2}C_{As} = C_{MF} . \]

Genetic Evaluation with Autosomal and X-chromosomal Inheritance

Best linear unbiased prediction (BLUP; Henderson, 1973) is widely used for genetic evaluation in livestock for traits with autosomal inheritance (e.g., Benyshek et al., 1988; Wiggans et al., 1988; and Robinson and Chesnais, 1988). BLUP can accommodate models that include X-chromosomal in addition to autosomal inheritance. At present, however, models used for genetic evaluation do not account for X-chromosomal inheritance.

Genetic model

Consider a single X-chromosomal locus. We define the additive genotypic value for a trait in male M to be \( g_M \) and for the same trait in female F to be \( g_F \). Male M receives
its allele x from its maternal parent and female F receives alleles x_m from its maternal parent m and x_p from its paternal parent p. Then, for male M,

\[ g_M = \alpha \]

and, for female F,

\[ g_F = \alpha_m + \alpha_p , \]

where \( \alpha \) is the additive genetic effect for the maternal allele (x) in male M, and where \( \alpha_m \) and \( \alpha_p \) are additive genetic effects for the maternal (x_m) and paternal (x_p) allele in female F. We assume that additive effects for the same allele in males and females are equal. Therefore, because allelic frequency is equal in the sexes,

\[ V(\alpha) = V(\alpha_m) = V(\alpha_p) . \]  

Thus, additive genotypic variance for males, \( V(g_M) \), and for noninbred females, \( V(g_F) \), are

\[ V(g_M) = V(\alpha) \]

and

\[ V(g_F) = V(\alpha_m + \alpha_p) \]
\[ = V(\alpha_m) + V(\alpha_p) \]
\[ = 2V(\alpha) \]
\[ = 2V(g_M) , \]

from (8).

For a trait determined by many such loci, therefore, additive genetic variance for noninbred females (\( \sigma_F^2 \)) is twice additive genetic variance for males (\( \sigma_M^2 \)). Variance for inbred females is \( \sigma_F^2 (1 + f) \), where \( f \) is the coefficient of inbreeding for X-chromosomal loci (Wright, 1933).

Consider again a single X-chromosomal locus. Additive genotypic covariance between two males M and M' is

\[ C(g_M, g_M') = C(\alpha, \alpha') = V(\alpha)P(x \equiv x') \]
\[ = V(\alpha)r_{MM'} \]
\[ = \frac{1}{2}V(g_F)r_{MM'} , \]

where \( P(x \equiv x') \) denotes the probability that allele x is identical by descent to allele x', and where the coancestry between males (\( r_{MM'} \)) is the probability that allele x in M is identical by descent to the allele x' in M' (Grossman and Eisen, 1989).

Additive genotypic covariance between two females F and F' is
Additive genotypic covariance between male M and female F is
\[
C(g_M, g_F) = C(\alpha_M, \alpha_M) + C(\alpha_p, \alpha_p).
\]
Because additive effects for the same allele in the sexes are equal,
\[
C(g_M, g_F) = \sigma_F^2 r_{MP}.
\]
where the coancestry between male and female \(r_{MP}\) is the probability that the allele \(x\) in \(M\) is identical by descent to an allele drawn at random from \(F\) (Grossman and Eisen, 1989).

For a trait determined by many such loci, therefore, additive genetic covariance between males is \(\frac{1}{2}(\sigma_F^2) r_{MM}\), between females is \(2(\sigma_F^2) r_{PP}\), and between male and female is \((\sigma_F^2) r_{MP}\).

**Best Linear Unbiased Prediction**

Total additive genetic effect for animal \(i\) can be written as the sum of its additive genetic effect for autosomal loci \(a_i\) and its additive genetic effect for X-chromosomal loci \(s_i\). To obtain BLUP of \(a_i\) and \(s_i\) we write
\[
y_i = x'_i \beta + a_i + s_i + e_i,
\]
where \(y_i\) is the phenotypic value for individual \(i\), \(x'_i\) is a row vector of constants relating \(y_i\) to fixed effects, \(\beta\) is a column vector of fixed effects, and \(e_i\) is random error.

The covariance matrix of \(a_i\)'s is \(A\sigma_A^2\), where \(A\) is the matrix of twice the coancestries between relatives for autosomal loci (Henderson, 1976) and \(\sigma_A^2\) is the variance of additive genetic values for autosomal loci. The covariance matrix of \(s_i\)'s is \(S\sigma^2\), where \(S\) is a matrix whose elements are functions of coancestries between relatives for X-chromosomal loci. The covariance matrix of \(e_i\)'s is assumed to be \(I\sigma^2\).
Given the covariance matrices of effects $a_i$, $s_i$, and $e_i$, and one record for each individual, BLUP's of autosomal effects ($\hat{\alpha}$) and of X-chromosomal effects ($\hat{s}$) are obtained using mixed model equations (MME's; Henderson, 1973):

$$
\begin{pmatrix}
X'X & X' & X' \\
X & I+\mathbf{A}^{-1}\sigma^2/\sigma^2_a & I \\
X & I & I+\mathbf{S}^{-1}\sigma^2/\sigma^2_p
\end{pmatrix}
\begin{pmatrix}
\beta^* \\
\hat{\alpha} \\
\hat{s}
\end{pmatrix}
= 
\begin{pmatrix}
X'y \\
\hat{y} \\
y
\end{pmatrix}
$$

The inverse of $\mathbf{A}$ can be obtained simply by an algorithm described by Henderson (1976). The construction of $\mathbf{S}$ and the simple, efficient computation of its inverse follow.

**Construction of S via the tabular method**

The tabular method to construct $\mathbf{S}$ is based on the following linear models for additive genotypic values for X-chromosomal loci in male $M$ with a maternal parent $m$ and in female $F$ with a maternal parent $m$ and a paternal parent $p$:

**Male:** $s_M = \frac{1}{2}s_m + \epsilon_M \tag{10}$

**Female:** $s_F = \frac{1}{2}s_m + s_p + \epsilon_p \tag{11}$

[Theorem. For individuals $i$ and $j$, where $i$ is not a direct descendent of $j$, the covariance between $s_i$ and $\epsilon_j$ is null. For proof, see Fernando and Grossman (1990).]

Now, covariance between an individual $i$ and male $M$, where $i$ is not a direct descendent of $M$, can be written as

$$
\begin{align*}
C(s_i s_M) &= C(s_p, \frac{1}{2}s_m + \epsilon_M) \\
&= \frac{1}{2}C(s_p, s_m) + C(s_p, \epsilon_M) \\
&= \frac{1}{2}C(s_p, s_m) , \tag{12}
\end{align*}
$$

because $C(s_p, \epsilon_M)$ is zero from Theorem.

Covariance between individual $i$ and female $F$, where $i$ is not a direct descendent of $F$, can be written as

$$
\begin{align*}
C(s_i s_F) &= C(s_p, \frac{1}{2}s_m + s_p + \epsilon_p) \\
&= \frac{1}{2}C(s_p, s_m) + \hat{C}(s_p, s_p) + C(s_p, \epsilon_p) \\
&= \frac{1}{2}C(s_p, s_m) + C(s_p, s_p) , \tag{13}
\end{align*}
$$
because $C(s_p \epsilon_p)$ is zero from Theorem.

From (12) and (13), recursive rules to construct the $S$ matrix, similar to those given by Henderson (1976), are given below:

1. Number individuals such that progeny follow parents.
2. For females, set diagonal elements to 1.
3. For males, set diagonal elements to $\frac{1}{2}$.
4. For female $i$ with mother $m$ and father $p$, element $j$ of row $i$ ($s_{ij}$) in $S$ is computed as

$$s_{ij} = \frac{1}{2}s_{mj} + s_{pj}, \text{ for } j = 1, ..., i-1.$$  

4.1. Elements in column $i$ are obtained by symmetry.
4.2. Add $s_{mp}$ to $s_{ii}$.
5. For male $i$ with mother $m$, element $s_{ij}$ is computed as

$$s_{ij} = \frac{1}{2}s_{mj}, \text{ for } j = 1, ..., i-1.$$  

5.1. Elements in column $i$ are obtained by symmetry.

A numerical example for constructing $S$ is given in Fernando and Grossman (1990).

**Computation of $S$ inverse**

Following Quaas et al. (1984), (10) and (11) are used to write the vector $(s)$ of additive genetic effects for X-chromosomal loci:

$$s = Ps + \epsilon$$

where $P$ is a matrix in which each row contains one or two non-zero elements, if parents are known, or all zeros, if parents are unknown. From (10), the row for a male contains an element $\frac{1}{2}$ in the column corresponding to its maternal parent. From (11), the row for a female contains an element $\frac{1}{2}$ in the column corresponding to its maternal parent and an element 1 in the column corresponding to its paternal parent.

It is shown below that the covariance matrix of $\epsilon$ is $V \sigma_{\epsilon}^2$, where $V$ is a diagonal matrix of order $n$, the number of individuals in the pedigree. For any two individuals, one will not be a direct descendent of the other. Thus, without loss of generality, let $i$ be an individual that is not a direct descendent of $j$, which has maternal and paternal parents $m$ and $p$. Covariances of $s_i$, $s_m$, and $s_p$ with $\epsilon_j$ are null, from Theorem, because parents $m$ and $p$ are not and cannot be direct descendents of individual $j$. Hence, from (10) and (11), the covariance between $\epsilon_i$ and $\epsilon_j$ is also null and $V$ is diagonal.
To proceed, we need the diagonal elements of V for males and for females when parents are known and unknown. If parents m and p are known, the diagonal element for a male (from (10)) or for a female (from (11)) is \( \frac{1}{2}(1 - f) \), where \( f \) is the coefficient of inbreeding for the maternal parent m. If maternal parent m is unknown, the diagonal element for a male or for a female is \( \frac{1}{2} \). If paternal parent p is unknown, the diagonal element for a male is \( \frac{1}{2}(1 - f) \) and the diagonal element for a female is \( \frac{1}{2}(3 - f) \). If both parents are unknown, the diagonal element for a male is \( -1 \) and for a female is 1.

Again following Quaas et al. (1984), s can be written as

\[ s = (I - P)^{-1}\epsilon \]

and the covariance matrix of s as

\[ V(s) = S\sigma_p^2 = (I - P)^{-1}V(I - P')^{-1}\sigma_p^2 . \]

The inverse of S now can be written as

\[ S^{-1} = (I - P')V^{-1}(I - P) = QV^{-1}Q' , \quad (14) \]

where \( Q = (I - P') \). Because \( V^{-1} \) is diagonal, (14) can be written as

\[ S^{-1} = \Sigma q_i q_i' d_i , \text{ for } i = 1, \ldots, n , \]

where \( q_i \) is column i of Q and \( d_i \) is diagonal element i of \( V^{-1} \).

Thus, to construct the inverse of S directly,

1. Set \( S^{-1} \) to 0.
2. For each individual i, with maternal and paternal parents m and p, add \( d_i \) times the following to the indicated elements of \( S^{-1} \):

   For males, if m is known, \( \frac{1}{2} \) to element (m,m), 1 to element (i,i), and \( -\frac{1}{2} \) to elements (m,i) and (i,m). If m is unknown, omit elements involving m; or

   For females, if m and p are known, \( \frac{1}{2} \) to element (m,m), 1 to elements (p,p) and (i,i), \( \frac{1}{2} \) to elements (m,p) and (p,m), \( -\frac{1}{2} \) to elements (m,i) and (i,m), and \( -1 \) to elements (p,i) and (i,p). If m is unknown, omit elements involving m. If p is unknown, omit elements involving p.

A numerical example for constructing S inverse is given in Fernando and Grossman (1990).
Summary and Discussion

Knowledge of the quantitative genetics with X-chromosomal loci is necessary to compute genetic variances and covariances for use in genetic evaluation of individuals for economically important traits in livestock and poultry. Using a unified approach, we have derived explicitly the coefficient of inbreeding for individuals and the coefficient of coancestry between collateral and lineal relatives of the same or different sex, assuming the male is heterogametic and the female is homogametic. We have also defined additive and dominance relationships to compute genetic covariance between relatives, assuming random mating equilibrium. Results are applicable also to organisms that have few autosomal loci, such as Drosophila, in which X-chromosomal loci can account for a large amount of genetic variance, and to haplo-diploid organisms, such as the honeybee, in which the entire genome is equivalent to being X-chromosomal.

Further, we have derived genetic variances and covariances between common relatives for an X-chromosomal locus in a random mating population in disequilibrium. These variances and covariances deviate from equilibrium to an extent depending on the difference between allelic frequency in the sexes, the disequilibrium changing sign each generation. Results for female relatives can be applied to an autosomal locus in which allelic frequency is not equal in the sexes.

Finally, we have described a tabular method to construct the S matrix for X-chromosomal loci. We also developed a simple and efficient algorithm to compute the inverse of S. This development allows for X-chromosomal inheritance to be accounted for in genetic evaluation by including X-chromosomal additive effects, in addition to autosomal additive effects, in a mixed model. This results in an increase in the number of mixed model equations equal to the number of individuals in the pedigree. Equivalent models, such as the reduced animal model, may be used to reduce the number of equations.

Remember that a population reaches equilibrium in one or two generations for an autosomal locus and only in the limit for an X-chromosomal locus. In cross-breeding programs, where interest is primarily on the first few generations, allelic frequency in the sexes is not expected to be equal and the population, therefore, is in disequilibrium with respect to both autosomal and X-chromosomal loci. Data from such programs are used to estimate genetic parameters under theory developed when the population is in equilibrium. As demonstrated here, when the population is not in equilibrium, variances and covariances between relatives deviate from their equilibrium values. Thus, using equilibrium variances and covariances between relatives yields biased estimates of genetic parameters. For autosomal loci, Melchinger (1988) derived genetic parameters for crossbred populations in which the parent populations consisted of a number of homozygous inbred lines. Results presented here, however, may be useful to assess the deviation from equilibrium for autosomal and X-chromosomal loci when the parent populations are not inbred.

Cross-breeding programs typically involve traits determined by a large number of loci, each locus possibly having a different disequilibrium value, different allelic frequencies and different effects. The situation may be further complicated by finite population size
and overlapping generations. For a proper treatment of disequilibrium in cross breeding, the above conditions must be taken into account.

Acknowledgment

I appreciate very much the collaboration of my colleagues E. J. Eisen and R. L. Fernando.

References


Table 1. Additive and dominance relationships for collateral relatives in a random mating population for X-chromosomal loci

<table>
<thead>
<tr>
<th>Collateral relatives</th>
<th>$a_{11}$</th>
<th>$a_{22}$</th>
<th>$d_{22}$</th>
<th>$a_{12}$</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Male-male</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Monozygous twins</td>
<td>1</td>
<td>-</td>
<td>-</td>
<td>-</td>
</tr>
<tr>
<td>Full brothers</td>
<td>$\frac{1}{2}$</td>
<td>-</td>
<td>-</td>
<td>-</td>
</tr>
<tr>
<td>Paternal half brothers</td>
<td>0</td>
<td>-</td>
<td>-</td>
<td>-</td>
</tr>
<tr>
<td>Maternal half brothers</td>
<td>$\frac{1}{2}$</td>
<td>-</td>
<td>-</td>
<td>-</td>
</tr>
<tr>
<td>1st cousins (full brothers)</td>
<td>0</td>
<td>-</td>
<td>-</td>
<td>-</td>
</tr>
<tr>
<td>1st cousins (full sisters)</td>
<td>$\frac{3}{8}$</td>
<td>-</td>
<td>-</td>
<td>-</td>
</tr>
<tr>
<td>1st cousins (brother-sister)</td>
<td>0</td>
<td>-</td>
<td>-</td>
<td>-</td>
</tr>
<tr>
<td>D’ble 1st cousins (same-sex)</td>
<td>$\frac{3}{8}$</td>
<td>-</td>
<td>-</td>
<td>-</td>
</tr>
<tr>
<td>D’ble 1st cousins (diff-sex)</td>
<td>0</td>
<td>-</td>
<td>-</td>
<td>-</td>
</tr>
<tr>
<td><strong>Female-female</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Monozygous twins</td>
<td>-</td>
<td>1</td>
<td>$\frac{1}{3}$</td>
<td>-</td>
</tr>
<tr>
<td>Full sisters</td>
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<td>$\frac{3}{4}$</td>
<td>$\frac{1}{2}$</td>
<td>-</td>
</tr>
<tr>
<td>Paternal half sisters</td>
<td>-</td>
<td>$\frac{1}{2}$</td>
<td>0</td>
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</tr>
<tr>
<td>Maternal half sisters</td>
<td>-</td>
<td>$\frac{1}{2}$</td>
<td>0</td>
<td>-</td>
</tr>
<tr>
<td>1st cousins (full brothers)</td>
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</tr>
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<td>$\frac{1}{8}$</td>
<td>0</td>
<td>-</td>
</tr>
<tr>
<td>1st cousins (brother-sister)</td>
<td>-</td>
<td>$\frac{1}{8}$</td>
<td>0</td>
<td>-</td>
</tr>
<tr>
<td>D’ble 1st cousins (same-sex)</td>
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<td>$\frac{7}{16}$</td>
<td>$\frac{3}{16}$</td>
<td>-</td>
</tr>
<tr>
<td>D’ble 1st cousins (diff-sex)</td>
<td>-</td>
<td>$\frac{1}{4}$</td>
<td>$\frac{1}{16}$</td>
<td>-</td>
</tr>
<tr>
<td><strong>Male-female</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Full brother-sister</td>
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<td>-</td>
<td>$\frac{1}{2}$</td>
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<td>Paternal half brother-sister</td>
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<td>0</td>
</tr>
<tr>
<td>Maternal half brother-sister</td>
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<td>-</td>
<td>-</td>
<td>$\frac{1}{2}$</td>
</tr>
<tr>
<td>1st cousins (full brothers)</td>
<td>-</td>
<td>-</td>
<td>-</td>
<td>0</td>
</tr>
<tr>
<td>1st cousins (full sisters)</td>
<td>-</td>
<td>-</td>
<td>-</td>
<td>$\frac{3}{8}$</td>
</tr>
<tr>
<td>1st cousins (brother-sister)</td>
<td>-</td>
<td>-</td>
<td>-</td>
<td>0</td>
</tr>
<tr>
<td>1st cousins (sister-brother)</td>
<td>-</td>
<td>-</td>
<td>-</td>
<td>$\frac{1}{4}$</td>
</tr>
<tr>
<td>D’ble 1st cousins (same-sex)</td>
<td>-</td>
<td>-</td>
<td>-</td>
<td>$\frac{3}{8}$</td>
</tr>
<tr>
<td>D’ble 1st cousins (diff-sex)</td>
<td>-</td>
<td>-</td>
<td>-</td>
<td>$\frac{1}{4}$</td>
</tr>
</tbody>
</table>

$^{1}a_{11}$ is additive relationship between males, or the fraction of additive genetic variance component for males; $a_{22}$ is additive relationship between females, or the fraction of additive genetic component for females; $d_{22}$ is dominance relationship between females, or the fraction of dominance variance component for females; and $a_{12}$ is additive genetic relationship between a male and a female, or the fraction of additive genetic covariance component for a male and a female.
Table 2. Additive and dominance relationships for lineal relatives in a random mating population for X-chromosomal loci

<table>
<thead>
<tr>
<th>Relationship</th>
<th>$a_{11}$</th>
<th>$a_{22}$</th>
<th>$d_{22}$</th>
<th>$a_{12}$</th>
</tr>
</thead>
<tbody>
<tr>
<td>Lineal relatives</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Male-male</td>
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<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Father-son</td>
<td>0</td>
<td>-</td>
<td>-</td>
<td>-</td>
</tr>
<tr>
<td>Paternal g’father-g’son</td>
<td>0</td>
<td>-</td>
<td>-</td>
<td>-</td>
</tr>
<tr>
<td>Maternal g’father-g’son</td>
<td>$\frac{1}{2}$</td>
<td>-</td>
<td>-</td>
<td>-</td>
</tr>
<tr>
<td>Paternal uncle-nephew</td>
<td>0</td>
<td>-</td>
<td>-</td>
<td>-</td>
</tr>
<tr>
<td>Maternal uncle-nephew</td>
<td>$\frac{1}{4}$</td>
<td>-</td>
<td>-</td>
<td>-</td>
</tr>
<tr>
<td>Female-female</td>
<td></td>
<td></td>
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<td></td>
</tr>
<tr>
<td>Mother-daughter</td>
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<td>$\frac{1}{2}$</td>
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<td>-</td>
</tr>
<tr>
<td>Paternal g’mother-g’daughter</td>
<td>-</td>
<td>$\frac{1}{2}$</td>
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</tr>
<tr>
<td>Maternal g’mother-g’daughter</td>
<td>-</td>
<td>$\frac{1}{4}$</td>
<td>0</td>
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<tr>
<td>Paternal aunt-niece</td>
<td>-</td>
<td>$\frac{1}{4}$</td>
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<tr>
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<td>$3/8$</td>
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<td>-</td>
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<tr>
<td>Male-female</td>
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<td>Father-daughter</td>
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<tr>
<td>Paternal g’father-g’dughter</td>
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<tr>
<td>Maternal g’father-g’dughter</td>
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<td>-</td>
<td>$\frac{1}{2}$</td>
</tr>
<tr>
<td>Paternal uncle-niece</td>
<td>-</td>
<td>-</td>
<td>-</td>
<td>$\frac{1}{2}$</td>
</tr>
<tr>
<td>Maternal uncle-niece</td>
<td>-</td>
<td>-</td>
<td>-</td>
<td>$\frac{1}{4}$</td>
</tr>
<tr>
<td>Female-male</td>
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<tr>
<td>Mother-son</td>
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<td>-</td>
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<tr>
<td>Paternal g’mother-g’son</td>
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<tr>
<td>Maternal g’mother-g’son</td>
<td>-</td>
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<td>$\frac{1}{2}$</td>
</tr>
<tr>
<td>Paternal aunt-nephew</td>
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<td>0</td>
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<td>Maternal aunt-nephew</td>
<td>-</td>
<td>-</td>
<td>-</td>
<td>$3/4$</td>
</tr>
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</table>

$^1a_{11}$ is additive relationship between males, or the fraction of additive genetic variance component for males; $a_{22}$ is additive relationship between females, or the fraction of additive genetic component for females; $d_{22}$ is dominance relationship between females, or the fraction of dominance variance component for females; and $a_{12}$ is additive genetic relationship between a male and a female, or the fraction of additive genetic covariance component for a male and a female.
Question: A. Freeman

X - chromosome effects are random -- Where do you set priors \( \sigma_\alpha^2/\sigma_\gamma^2 \), say \( \sigma_\alpha^2 \) is the X-chromosome variance, for the traits of interest? More precisely, how do you estimate \( \sigma_\alpha^2 \) in a general sense?

Response: M. Grossman

We can estimate \( \sigma_\alpha^2 \) by REML.

Comment: V. Toelle

You need to be concerned about sex - inactivation in mammals but not in poultry because poultry don't have heterochromatin. Also sire components of variance are potentially always biased by sex - linkage.

Response: M. Grossman

Thank you for your comment.