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Covariance between relatives for X-chromosomal loci in a population in disequilibrium *

M. Grossman and R. L. Fernando

Department of Animal Sciences, 1207 W. Gregory Drive, University of Illinois, Urbana, IL 61801, USA

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Summary. According to Hardy-Weinberg, for a single autosomal locus, a population achieves 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. For a single X-chromosomal locus, however, the approach to equilibrium oscillates and is gradual. Covariances between relatives for autosomal and for X-chromosomal loci are in the literature for a random mating population in equilibrium. Although assumption of equilibrium is defensible for an autosomal locus, it is less defensible for an X-chromosomal locus. Covariances between collateral and between lineal relatives are derived for X-chromosomal loci in a random mating population not in equilibrium. Collateral relatives such as sibs are of the same generation, and lineal relatives such as parent-offspring are of different generations. Coefficient of co-ancestry between relatives, based on identity by descent, was used in this development. Results are applicable to crossbreeding in livestock and poultry, and also to haplo-diploid organisms, such as the honeybee, in which the entire genome is equivalent to being X-chromosomal.

Key words: X-linkage – Covariance – Genetic parameters – Disequilibrium – Crossbreeding

Introduction

The contribution of autosomal loci to genetic variance and covariance between relatives is well-documented. In contrast, the contribution of X-chromosomal loci to such variance and covariance is less well-documented, but may be important and should not be ignored (Grossman and Eisen 1989).

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 are not as well-understood for X-chromosomal loci, and are not known for a population in disequilibrium.

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.

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.

The objective of this paper is to derive 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

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Offprint requests to M. Grossman

same generation and lineal relatives, such as parent-offspring or aunt-nephew, are of different generations. Coefficients of co-ancestry between relatives, based on identity by descent (Malécot 1969), have been derived for X-chromosomal loci (Grossman and Eisen 1989) and will be used for the development in this paper.

Theory

Model

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 (ZZ) and the female is the heterogametic sex (ZW), such as poultry, results should be interpreted accordingly. 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).

For random mating in an infinite population, consider a single X-chromosomal locus with two alleles, s_1 and s_2, 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:

Sex	Male		Female			
Genotype	s_1	s_2	$s_1 s_1$	$s_1 s_2$	$s_2 s_1$	$s_2 s_2$
Frequency	m_1^t	m_2^t	f_{11}^t	f_{12}^t	f_{21}^t	f_{22}^t
Genotypic value	y_1	y_2	y_{11}	y_{12}	y_{21}	y_{22}

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 $\Sigma_i m_i^t = 1$.

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 $s_1 s_2$ and y_{21} for $s_2 s_1$. 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

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

with $\Sigma_j \Sigma_k f_{jk}^t = 1$.

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 $\Sigma_j f_{jm}^t = 1$. 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 $\Sigma_k f_{kp}^t = 1$. 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

$$f_j^t = \tfrac{1}{2}(f_{jm}^t + f_{jp}^t) = \tfrac{1}{2}(f_j^{t-1} + m_j^{t-1}),$$

with $\Sigma_j f_j^t = 1$.

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

$$m_i^t = \tfrac{1}{2}(m_i^{t-1} + m_i^{t-2})$$

and

$$f_i^t = \tfrac{1}{2}(f_i^{t-1} + f_i^{t-2}).$$

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

$$m_i^t = p_i - 2 d_i^t$$

and

$$f_i^t = p_i + d_i^t,$$

where $p_i = (m_i/3) + (2 f_i/3)$ in each generation, $d_i^t = (-\tfrac{1}{2})^t \delta_i^0/3$ in generation t, and $\delta_i^0 = f_i^0 - m_i^0$ in generation zero. Note that as $t \rightarrow \infty$, $m_i^t \rightarrow p_i$ and $f_i^t \rightarrow p_i$; 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

$$y_i = \mu_m^t + \beta_i^t, \tag{1}$$

where μ_m^t is the mean genotypic value for males and $\beta^t = \beta_i^t$ is the average effect for allele s_i, 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 μ_m^e and the average effect is β_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 $S_m S_p = s_j s_k$ in generation t can be modeled as

$$y_{jk} = \mu_f^t + \alpha_{jm}^t + \alpha_{kp}^t + \delta_{jk}^t \tag{2}$$

where μ_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 $S_m S_p = s_j s_k$, measured by the failure of the average effects to sum to that genotypic value as a deviation from the mean for females:

$$\mu_f^t = E(Y^F) = \Sigma_j \Sigma_k f_{jk}^t (y_{jk}) = \Sigma_j \Sigma_k f_j^{t-1} m_k^{t-1} (y_{jk}),$$

$$\begin{aligned} \alpha_{jm}^t &= E(Y^F | S_m = s_j) - \mu_f^t = \Sigma_k f_{kp}^t (y_{jk}) - \mu_f^t \\ &= \Sigma_k m_k^{t-1} (y_{jk}) - \mu_f^t = \bar{y}_{jm}^t - \mu_f^t, \end{aligned}$$

$$\begin{aligned} \alpha_{kp}^t &= E(Y^F | S_p = s_k) - \mu_f^t = \Sigma_j f_{jm}^t (y_{jk}) - \mu_f^t \\ &= \Sigma_j f_j^{t-1} (y_{jk}) - \mu_f^t = \Sigma_j m_j^t (y_{jk}) - \mu_f^t = \bar{y}_{kp}^t - \mu_f^t, \end{aligned}$$

and

$$\begin{aligned} \delta_{jk}^t &= E(Y^F | S_m S_p = s_j s_k) - \mu_f^t - \alpha_{jm}^t - \alpha_{kp}^t \\ &= (y_{jk} - \mu_f^t) - (\alpha_{jm}^t + \alpha_{kp}^t). \end{aligned}$$

From above definitions,

$$\begin{aligned} E(\alpha_m^t) &= \Sigma_j f_{jm}^t \alpha_{jm}^t = \Sigma_j f_j^{t-1} \alpha_{jm}^t = 0 \\ E(\alpha_p^t) &= \Sigma_k f_{kp}^t \alpha_{kp}^t = \Sigma_k m_k^{t-1} \alpha_{kp}^t = 0 \\ E(\delta^t) &= \Sigma_j \Sigma_k f_{jk}^t \delta_{jk}^t = \Sigma_j \Sigma_k f_j^{t-1} m_k^{t-1} \delta_{jk}^t = 0 \end{aligned}$$

and, from random mating,

$$E(\alpha_m^t \alpha_p^t) = E(\alpha_m^t \delta^t) = E(\alpha_p^t \delta^t) = 0;$$

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 μ_f^e, average effects are α_{jm}^e and α_{kp}^e, and dominant deviations are δ_{jk}^e, 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:

$$\begin{aligned} V(Y^M) &= V(\beta^t) = \Sigma_i m_i^t (\beta_i^t)^2 & (3) \\ &= \Sigma_i m_i^t (y_i - \mu_m^t)(y_i - \mu_m^t) = \Sigma_i m_i^t (y_i - \mu_m^t)\, y_i, & (3.1) \end{aligned}$$

where $V(\ )$ is the variance operator at generation t. The variance at equilibrium, $V(\beta^e)$, can be computed using m_i^e and μ_m^e in (3.1).

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

$$V(Y^F) = V(\alpha_m^t) + V(\alpha_p^t) + V(\delta^t) \tag{4}$$

where

$$\begin{aligned} V(\alpha_m^t) &= \Sigma_j f_{jm}^t (\alpha_{jm}^t)^2 = \Sigma_j f_{jm}^t (\bar{y}_{jm}^t - \mu_f^t)(\bar{y}_{jm}^t - \mu_f^t) & (4.1) \\ &= \Sigma_j f_j^{t-1} (\bar{y}_{jm}^t - \mu_f^t)\, \bar{y}_{jm}^t \\ &= \Sigma_j m_j^t (\bar{y}_{jm}^t - \mu_f^t)\, \bar{y}_{jm}^t, & (4.1.1) \end{aligned}$$

$$\begin{aligned} V(\alpha_p^t) &= \Sigma_k f_{kp}^t (\alpha_{kp}^t)^2 = \Sigma_k f_{kp}^t (\bar{y}_{kp}^t - \mu_f^t)(\bar{y}_{kp}^t - \mu_f^t) & (4.2) \\ &= \Sigma_k m_k^{t-1} (\bar{y}_{kp}^t - \mu_f^t)\, \bar{y}_{kp}^t, & (4.2.1) \end{aligned}$$

and

$$\begin{aligned} V(\delta^t) &= \Sigma_j \Sigma_k f_{jk}^t (\delta_{jk}^t)^2 = \Sigma_j \Sigma_k f_{jk}^t (y_{jk} - \mu_f^t - \alpha_{jm}^t - \alpha_{kp}^t) \\ &\quad \cdot (y_{jk} - \mu_f^t - \alpha_{jm}^t - \alpha_{kp}^t) & (4.3) \\ &= \Sigma_j \Sigma_k f_j^{t-1} m_k^{t-1} (y_{jk} - \mu_f^t - \alpha_{jm}^t - \alpha_{kp}^t)\, y_{jk}. & (4.3.1) \end{aligned}$$

Variances at equilibrium, $V(\alpha_m^e)$, $V(\alpha_p^e)$, and $V(\delta^e)$, can be computed using f_j^e and m_k^e, and μ_f^e, α_{jm}^e and α_{kp}^e in (4.1.1), (4.2.1) and (4.3.1).

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 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 (see Sect. A in Appendix). Coefficients of co-ancestry are from Grossman and Eisen (1989).

Male-male. Let $r = P(S' \equiv S)$ 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 co-ancestry for males. Also let $P_i = P(S' = s_i | S' \equiv S)$ 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 (β^t) for male M, which must be evaluated depending on male relationships:

$$C(Y^{M'}, Y^{M}) = C(\beta'^{t'}, \beta^{t}) = C(\beta'^{t'}, \beta^{t} | S' \equiv S)\, P(S' \equiv S) \quad (5)$$

$$= P(S' \equiv S)\ \Sigma_i P(S' = s_i | S' \equiv S)\, (\beta_i^{t'})\, (\beta_i^{t})$$

$$= r\, \Sigma_i P_i\, (\beta_i^{t'})\, (\beta_i^{t}), \quad (5.1)$$

where $C(\,)$ is the covariance operator between generations t' and t and $C(\beta'^{t'}, \beta^{t} | S' \equiv S)$ 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 (see A1 in Appendix).

To compute covariances for commonly used collateral male relationships, Table 1. For full brothers in generation t, for example, $r = \frac{1}{2}$ (Grossman and Eisen 1989), $t' = t$, $\beta_i^{t'} = \beta_i^{t}$ and $P_i = m_i^{t}$. From (5) and (3),

$$C(Y^{M'}, Y^{M}) = \tfrac{1}{2}\, C(\beta'^{t}, \beta^{t} | S' \equiv S) = \tfrac{1}{2}\, \Sigma_i m_i^{t}\, (\beta_i^{t})^2$$

$$= \tfrac{1}{2}\, V(\beta^{t}).$$

Thus covariance between full brothers is half the variance of average effects for males in generation t. Covariance at equilibrium is $\frac{1}{2}\, V(\beta^{e})$.

To compute covariances for commonly used lineal male relationships, Table 1. For maternal uncle-nephew, $r = \frac{1}{4}$, the generation of the uncle $t' = t-1$, $\beta_i^{t'} = \beta_i^{t-1}$ and $P_i = m_i^{t-1}$. From (5) and (3.1),

$$C(Y^{M'}, Y^{M}) = \tfrac{1}{4}\, C(\beta'^{t-1}, \beta^{t} | S' \equiv S)$$

$$= \tfrac{1}{4}\, \Sigma_i m_i^{t-1}\, (\beta_i^{t-1})\, (\beta_i^{t})$$

$$= \tfrac{1}{4}\, \Sigma_i m_i^{t-1}\, (y_i - \mu_m^{t-1})\, (y_i - \mu_m^{t})$$

$$= \tfrac{1}{4}\, \Sigma_i m_i^{t-1}\, (y_i - \mu_m^{t-1})\, y_i = \tfrac{1}{4}\, V(\beta^{t-1}).$$

Thus covariance between maternal uncle-nephew is one-quarter the variance of average effects for males in generation $t-1$. Covariance at equilibrium is $\frac{1}{4}\, V(\beta^{e})$.

Table 1. Probabilities for male relationships in a random mating population for X-chromosomal loci

Male relationship	t'	Probability[1]	
		P_q	r
Collateral			
Monozygous twins	t	m_q^{t}	1
Full brothers	t	m_q^{t}	$\frac{1}{2}$
Maternal half brothers	t	m_4^{t}	$\frac{1}{2}$
Paternal half brothers	t	...	0
Lineal			
Father-son	$t-1$	...	0
Maternal g'father-g'son	$t-2$	m_q^{t-2}	$\frac{1}{4}$
Paternal g'father-g'son	$t-2$	...	0
Maternal uncle-nephew	$t-1$	m_4^{t-1}	$\frac{1}{4}$
Paternal uncle-nephew	$t-1$	...	0

[1] $P_q = P(S = s_q | S' \equiv S)$; $q = 1, 2$; $r = P(S' \equiv S)$

Female-female. Remember that a female with genotype $S_m S_p$ receives allele S_m from its maternal parent and allele S_p from its paternal parent. Therefore, let $r_{mm} = P(S'_m \equiv S_m)$ 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 $r_{mp} = P(S'_m \equiv S_p)$, $r_{pm} = P(S'_p \equiv S_m)$ and $r_{pp} = P(S'_p \equiv S_p)$, and let $d = P[(S'_m, S'_p) \equiv (S_m, S_p)] = r_{mm} r_{pp} + r_{mp} r_{pm}$ be the probability that both alleles in F' are identical by descent to both alleles in F.

Also let $P_{j|mm} = P(S'_m = s_j | S'_m \equiv S_m)$ be the probability that the maternal allele in F' is s_j, given maternal alleles in the females are identical by descent; similarly, let $P_{j|mp} = P(S'_m = s_j | S'_m \equiv S_p)$, $P_{k|pm} = P(S'_p = s_k | S'_p \equiv S_m)$ and $P_{k|pp} = P(S'_p = s_k | S'_p \equiv S_p)$; and let $P_{jk} = P[(S'_m S'_p = s_j s_k) | (S'_m, S'_p) \equiv (S_m, S_p)]$ be the probability that the genotype in F' is $s_j s_k$, 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:

$$C(Y^{F'}, Y^{F}) = C(\alpha_m'^{t'} + \alpha_p'^{t'} + \delta'^{t'}, \alpha_m^{t} + \alpha_p^{t} + \delta^{t})$$

$$= C(\alpha_m'^{t'}, \alpha_m^{t}) + C(\alpha_m'^{t'}, \alpha_p^{t}) + C(\alpha_p'^{t'}, \alpha_m^{t})$$

$$+ C(\alpha_p'^{t'}, \alpha_p^{t}) + C(\delta'^{t'}, \delta^{t}), \quad (6)$$

where

$$C(\alpha_m'^{t'}, \delta^{t}) = C(\alpha_p'^{t'}, \delta^{t}) = C(\delta'^{t'}, \alpha_m^{t}) = C(\delta'^{t'}, \alpha_p^{t}) = 0$$

because of random mating and where

$$C(\alpha_m'^{t'}, \alpha_m^{t}) = C(\alpha_m'^{t'}, \alpha_m^{t} | S'_m \equiv S_m)\, P(S'_m \equiv S_m) \quad (6.1)$$

$$= P(S'_m \equiv S_m)\ \Sigma_j P(S'_m = s_j | S'_m \equiv S_m)\, (\alpha_{jm}^{t'})\, (\alpha_{jm}^{t})$$

$$= r_{mm}\, \Sigma_j P_{j|mm}\, (\alpha_{jm}^{t'})\, (\alpha_{jm}^{t}) \quad (6.1.1)$$

$$C(\alpha_m'^{t'}, \alpha_p^{t}) = C(\alpha_m'^{t'}, \alpha_p^{t} | S'_m \equiv S_p)\, P(S'_m \equiv S_p) \quad (6.2)$$

$$= P(S'_m \equiv S_p)\ \Sigma_j P(S'_m = s_j | S'_m \equiv S_p)\, (\alpha_{jm}^{t'})\, (\alpha_{jp}^{t})$$

$$= r_{mp}\, \Sigma_j P_{j|mp}\, (\alpha_{jm}^{t'})\, (\alpha_{jp}^{t}) \quad (6.2.1)$$

$$C(\alpha_p'^{t'}, \alpha_m^{t}) = C(\alpha_p'^{t'}, \alpha_m^{t} | S'_p \equiv S_m)\, P(S'_p \equiv S_m) \quad (6.3)$$

$$= P(S'_p \equiv S_m)\ \Sigma_k P(S'_p = s_k | S'_p \equiv S_m)\, (\alpha_{kp}^{t'})\, (\alpha_{km}^{t})$$

$$= r_{pm}\, \Sigma_k P_{k|pm}\, (\alpha_{kp}^{t'})\, (\alpha_{km}^{t}) \quad (6.3.1)$$

$$C(\alpha_p'^{t'}, \alpha_p^{t}) = C(\alpha_p'^{t'}, \alpha_p^{t} | S'_p \equiv S_p)\, P(S'_p \equiv S_p) \quad (6.4)$$

$$= P(S'_p \equiv S_p)\ \Sigma_k P(S'_p = s_k | S'_p \equiv S_p)\, (\alpha_{kp}^{t'})\, (\alpha_{kp}^{t})$$

$$= r_{pp}\, \Sigma_k P_{k|pp}\, (\alpha_{kp}^{t'})\, (\alpha_{kp}^{t}) \quad (6.4.1)$$

and

$$C(\delta'^{t'}, \delta^{t}) = C(\delta'^{t'}, \delta^{t} | (S'_m, S'_p) \equiv (S_m, S_p))$$

$$\cdot P[(S'_m, S'_p) \equiv (S_m, S_p)] \quad (6.5)$$

$$= P[(S'_m, S'_p) \equiv (S_m, S_p)]$$

$$\cdot \Sigma_j \Sigma_k P[(S'_m S'_p = s_j s_k) | (S'_m, S'_p) \equiv (S_m, S_p)]$$

$$\cdot (\delta_{jk}^{t'})\, (\delta_{jk}^{t}) = d\, \Sigma_j \Sigma_k P_{jk}\, (\delta_{jk}^{t'})\, (\delta_{jk}^{t}), \quad (6.5.1)$$

Table 2. Probabilities for female relationships in a random mating population for X-chromosomal loci

Female relationship	t'	Probability[1]							
		$P_{q\|mm}$	r_{mm}	$P_{q\|mp}$	r_{mp}	$P_{q\|pm}$	r_{pm}	$P_{q\|pp}$	r_{pp}
Collateral									
Monozygous twins	t	f_q^{t-1}	1	...	0	...	0	m_q^{t-1}	1
Full sisters	t	f_q^{t-1}	$\frac{1}{2}$	...	0	...	0	m_q^{t-1}	1
Maternal half sisters	t	f_q^{t-1}	$\frac{1}{2}$	...	0	...	0	...	0
Paternal half sisters	t	...	0	...	0	...	0	m_q^{t-1}	1
Lineal									
Mother-daughter	$t-1$	f_q^{t-2}	$\frac{1}{4}$	...	0	m_q^{t-2}	$\frac{1}{2}$	...	0
Maternal g'mother-g'daughter	$t-2$	f_q^{t-3}	$\frac{1}{8}$	m_q^{t-3}	$\frac{1}{4}$	...	0	...	0
Paternal g'mother-g'daughter	$t-2$	...	0	f_q^{t-3}	$\frac{1}{4}$	...	0	m_q^{t-3}	$\frac{1}{2}$
Maternal aunt-niece	$t-1$	f_q^{t-2}	$\frac{1}{4}$	...	0	m_q^{t-2}	$\frac{1}{2}$	...	0
Paternal aunt-niece	$t-1$	...	0	f_q^{t-2}	$\frac{1}{2}$	...	0	...	0

[1] $P_{q|mm} = P(S'_m = s_q | S'_m \equiv S_m)$; $P_{q|mp} = P(S'_m = s_q | S'_m \equiv S_p)$; $P_{q|pm} = P(S'_p = s_q | S'_p \equiv S_m)$; $P_{q|pp} = P(S'_p = s_q | S'_p \equiv S_p)$; $q = 1, 2$
$r_{mm} = P(S'_m \equiv S_m)$; $r_{mp} = P(S'_m \equiv S_p)$; $r_{pm} = P(S'_p \equiv S_m)$ and $r_{pp} = P(S'_p \equiv S_p)$

where, e.g., $C(\alpha'^{t'}_m, \alpha^t_m | S'_m \equiv S_m)$ 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 (see A2 in Appendix).

To compute covariances for commonly used collateral female relationships, Table 2. For full sisters in generation t, e.g., $r_{mm} = \frac{1}{2}$, $r_{mp} = r_{pm} = 0$, $r_{pp} = 1$, $d = \frac{1}{2}$, $t' = t$, $\alpha^{t'}_{jm} = \alpha^t_{jm}$, $\alpha^{t'}_{kp} = \alpha^t_{kp}$ and $\delta^{t'}_{jk} = \delta^t_{jk}$, and $P_{j|mm} = f_j^{t-1} = f^t_{jm}$, $P_{k|pp} = m_k^{t-1} = f^t_{kp}$ and $P_{jk} = f_j^{t-1} m_k^{t-1} = f^t_{jk}$ (see Sect. B in Appendix). From (6.1), (6.4) and (6.5), and from (4.1) to (4.3),

$$\begin{aligned} C(Y^{F'}, Y^F) &= \tfrac{1}{2} C(\alpha'^t_m, \alpha^t_m | S'_m \equiv S_m) + 1\, C(\alpha'^t_p, \alpha^t_p | S'_m \equiv S_p) \\ &\quad + \tfrac{1}{2} C(\delta'^t, \delta^t | (S'_m, S'_p) \equiv (S_m, S_p)) \\ &= \tfrac{1}{2} \Sigma_j f^t_{jm} (\alpha^t_{jm})^2 + \Sigma_k f^t_{kp} (\alpha^t_{kp})^2 \\ &\quad + \tfrac{1}{2} \Sigma_j \Sigma_k f^t_{jk} (\delta^t_{jk})^2 \\ &= \tfrac{1}{2} V(\alpha^t_m) + V(\alpha^t_p) + \tfrac{1}{2} V(\delta^t). \end{aligned}$$

Thus covariance between full sisters in the sum of half the variance of the average effect for maternal alleles, the variance of the average effect for paternal alleles, and half the variance of dominant deviations for females in generation t.

At equilibrium, and for equal genotypic values for heterozygotes, $V(\alpha^e_m) = V(\alpha^e_p) = \frac{1}{2} V(\alpha^e)$, so that variance of average effects for maternal and for paternal alleles is half the variance of average effects for females. Then

$$\begin{aligned} C(Y^{F'}, Y^F) &= \tfrac{1}{2}(\tfrac{1}{2} + 1) V(\alpha^e) + \tfrac{1}{2} V(\delta^e) \\ &= (\tfrac{3}{4}) V(\alpha^e) + \tfrac{1}{2} V(\delta^e). \end{aligned}$$

Thus, covariance between full sisters at equilibrium is the sum of three-quarters the variance of average effects and half the variance of dominant deviations for females, a known result (Grossman and Eisen 1989).

To compute covariances for commonly used lineal female relationships, Table 2. For paternal aunt-niece, $r_{mp} = \frac{1}{2}$, $r_{mm} = r_{pm} = r_{pp} = d = 0$, $t' = t-1$, $\alpha'^{t'}_m = \alpha'^{t-1}_m$ and $P_{j|mp} = f_j^{t-2}$. From (6.2),

$$\begin{aligned} C(Y^{F'}, Y^F) &= \tfrac{1}{2} C(\alpha'^{t-1}_m, \alpha^t_p | S'_m \equiv S_p) \\ &= \tfrac{1}{2} \Sigma_j f_j^{t-2} (\alpha^{t-1}_{jm}) (\alpha^t_{jp}). \end{aligned}$$

Thus covariance between paternal aunt-niece is half the covariance between the average effect for maternal alleles in generation $t-1$ and the average effect for paternal alleles in generation t, given the maternal allele is identical by descent to the paternal allele. Covariance at equilibrium can be computed using f_j^e, α^e_{jm} and α^e_{jp}.

Male-female. Let $r_m = P(S \equiv S_m)$ 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, $r_p = P(S \equiv S_p)$.

Also let $P_{i|m} = P(S = s_i | S \equiv S_m)$ be the probability that the allele in M is s_i, given the allele in M is identical by descent to the maternal allele in F; similarly, $P_{i|p} = P(S = s_i | S \equiv S_p)$.

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:

$$\begin{aligned} C(Y^M, Y^F) &= C(\beta^{t'}, \alpha^t_m + \alpha^t_p + \delta^t) \\ &= C(\beta^{t'}, \alpha^t_m) + C(\beta^{t'}, \alpha^t_p) \end{aligned} \quad (7)$$

Table 3. Probabilities for male-female relationships in a random mating population for X-chromosomal loci

Male-female relationship	t'	Probability[1]			
		$P_{q\|m}$	r_m	$P_{q\|p}$	r_p
Collateral					
Full brother-sister	t	f_q^{t-1}	$\frac{1}{2}$	...	0
Maternal half brother-sister	t	f_q^{t-1}	$\frac{1}{2}$	...	0
Paternal half brother-sister	t	...	0	...	0
Lineal					
Father-daughter	$t-1$	...	0	m_q^{t-1}	1
Maternal g'father-g'daughter	$t-2$	m_q^{t-2}	$\frac{1}{2}$	...	0
Paternal g'father-g'daughter	$t-2$	...	0	...	0
Maternal uncle-niece	$t-1$	m_q^{t-1}	$\frac{1}{4}$	...	0
Paternal uncle-niece	$t-1$	...	0	m_q^{t-1}	$\frac{1}{2}$
Mother-son	$t+1$	m_q^t	$\frac{1}{2}$	m_q^{t-1}	$\frac{1}{2}$
Maternal g'mother-g'son	$t+2$	f_q^{t-3}	$\frac{1}{8}$	m_q^{t-3}	$\frac{1}{4}$
Paternal g'mother-g'son	$t+2$	...	0	...	0
Maternal aunt-nephew	$t+1$	f_q^{t-2}	$\frac{1}{4}$	m_q^{t-2}	$\frac{1}{2}$
Paternal aunt-nephew	$t+1$	...	0	...	0

[1] $P_{q|m} = P(S=s_q|S \equiv S_m)$ and $P_{q|p} = P(S=s_q|S \equiv S_p)$; $q=1, 2$
$r_m = P(S \equiv S_m)$ and $r_p = P(S \equiv S_p)$

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

$$C(\beta^{t'}, \alpha_m^t) = C(\beta^{t'}, \alpha_m^t|S \equiv S_m)\, P(S \equiv S_m) \tag{7.1}$$

$$= P(S \equiv S_m)\, \Sigma_i\, P(S=s_i|S \equiv S_m)(\beta_i^{t'})(\alpha_{im}^t)$$

$$= r_m \Sigma_i P_{i|m} (\beta_i^{t'})(\alpha_{im}^t) \tag{7.1.1}$$

and

$$C(\beta^{t'}, \alpha_p^t) = C(\beta^{t'}, \alpha_p^t|S \equiv S_p)\, P(S \equiv S_p) \tag{7.2}$$

$$= P(S \equiv S_p)\, \Sigma_i\, P(S=s_i|S \equiv S_p)(\beta_i^{t'})(\alpha_{ip}^t)$$

$$= r_p \Sigma_i P_{i|p} (\beta_i^{t'})(\alpha_{ip}^t)\,, \tag{7.2.1}$$

where, e.g., $C(\beta^{t'}, \alpha_m^t|S \equiv S_m)$ 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 (see A3 in Appendix).

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):

$$C(\beta^e, \alpha_m^e|S \equiv S_m) = C(\beta^e, \alpha_p^e|S \equiv S_p) = \tfrac{1}{2} C_{As} = C_{MF}\,.$$

To compute covariances for commonly used collateral male-female relationships, Table 3. For brother-sister in generation t, e.g., $r_m = \frac{1}{2}$, $r_p = 0$, $t' = t$, $\beta_i^{t'} = \beta_i^t$ and $P_{i|m} = f_i^{t-1}$. From (7.1),

$$C(Y^M, Y^F) = \tfrac{1}{2} C(\beta^t, \alpha_m^t|S \equiv S_m) = \tfrac{1}{2} \Sigma_i f_i^{t-1} (\beta_i^t)(\alpha_{im}^t)\,.$$

Thus covariance between full borther-sister is half the covariance between the average effect for males and the average effect of maternal alleles for females in generation t, given the alleles are identical by descent. Covariance at equilibrium can be computed using f_i^e, β_i^e and α_{im}^e.

To compute covariance between commonly used lineal male-female relationships, Table 3. For father-daughter, $r_m = 0$, $r_p = 1$, $t' = t-1$, $\beta^{t'} = \beta^{t-1}$ and $P_{i|p} = m_i^{t-1}$. From (7.2),

$$C(Y^M, Y^F) = 1\, C(\beta^{t-1}, \alpha_p^t|S \equiv S_p) = \Sigma_i m_i^{t-1} (\beta_i^{t-1})(\alpha_{ip}^t)\,.$$

Thus covariance between father-daughter is the covariance between the average effect for males in generation $t-1$ and the average effect of paternal alleles for females in generation t, given the alleles are identical by descent.

For mother-son, $r_m = r_p = \frac{1}{2}$, $t' = t+1$, $\beta^{t'} = \beta^{t+1}$, and $P_{i|m} = m_i^t$ and $P_{i|p} = m_i^{t-1}$. From (7.1) and (7.2),

$$C(Y^M, Y^F) = \tfrac{1}{2} C(\beta^{t+1}, \alpha_m^t|S \equiv S_m) + \tfrac{1}{2} C(\beta^{t+1}, \alpha_p^t|\, S \equiv S_p)$$

$$= \tfrac{1}{2} [\Sigma_i m_i^t (\beta_i^{t+1})(\alpha_{im}^t) + \Sigma_i m_i^{t-1} (\beta_i^{t+1})(\alpha_{ip}^t)]\,.$$

Thus covariance between mother-son is the average covariance between the average effect for males in generation $t+1$ and the average effects for the maternal and for the paternal alleles for females in generation t, given the alleles are identical by descent. Covariance at equilibrium can be computed using m_i^e, β_i^e, α_{im}^e and α_{ip}^e.

Discussion

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.

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.

Appendix

A Derivation of covariance between relatives for average effects

Let X be the average effect of allele S_x in an individual and Y be the average effect of allele S_y in a related individual, and let Z be a random variable that has value 1 when $S_x \equiv S_y$ and value 0 when $S_x \not\equiv S_y$. Then from Kempthorne and Folks (1971), covariance between average effects is

$$\begin{aligned} C(X, Y) &= E_z[C(X, Y|Z)] + C_z[E(X|Z), E(Y|Z)] \\ &= C(X, Y|Z=1)\,P(Z=1) + C(X, Y|Z=0)\,P(Z=0) \\ &\quad + C_z[E(X|Z), E(Y|Z)] \\ &= C(X, Y|Z=1)\,P(Z=1) + C_z[E(X|Z), E(Y|Z)] \end{aligned}$$

because the covariance between average effects is null when alleles are not identical by descent.

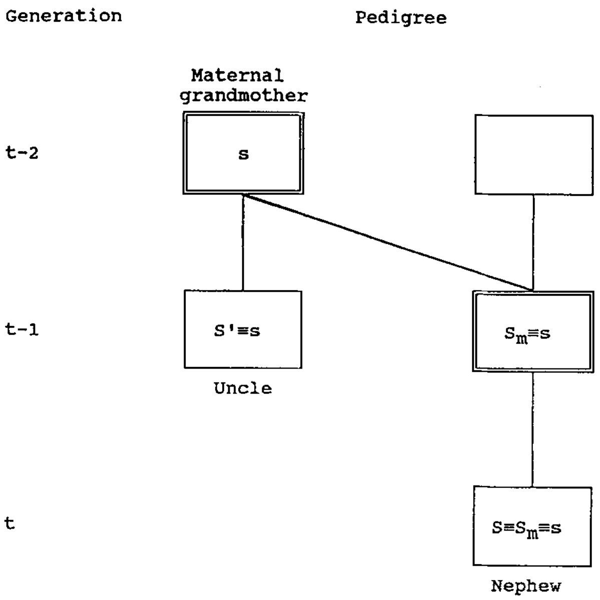

Fig. 1. Pedigree of maternal uncle-nephew relationship; box —— denotes male and box ═══ denotes female, where s is a random allele from the grandmother, S' is the allele in the uncle, S_m is the maternal allele in the female, and S is the allele in the nephew

For relatives considered in this paper, $C_z[E(X|Z), E(Y|Z)]$ is zero because either $E(X|Z)$ or $E(Y|Z)$ is a constant, namely zero. For other relatives, for which $E(X|Z)$ and $E(Y|Z)$ are not constant, such as first cousins whose mothers are full sisters or double first cousins whose parents are members of the same-sex full sibship, $C_z[E(X|Z), E(Y|Z)]$ must be computed explicitly. In the following examples of collateral and lineal relatives considered in this paper, we show that either $E(X|Z)$ or $E(Y|Z)$ is constant with respect to the value of Z and, therefore, $C_z[E(X|Z), E(Y|Z)]$ is zero. In addition, we present the basis for determining allelic frequencies given $Z=1$, which are necessary to compute $E(X, Y|Z=1)\,P(Z=1)$.

A1 Male-male

Collateral. For full brothers, for S' to be identical by descent to S, the alleles must have descended from their mother. Allelic frequency in the mother and thus her son is $f_i^{t-1} = m_i^t$, irrespective of whether the alleles in the brothers are identical by descent, which implies that allelic frequency in the brothers is independent of the condition of identical by descent. Thus,

$$\begin{aligned} P_i &= P(S'=s_i|S'\equiv S) = P(S'=s_i|S'\not\equiv S) = P(S'=s_i) \\ &= P(S=s_i|S'\equiv S) = P(S=s_i|S'\not\equiv S) = P(S=s_i) \\ &= m_i^t\,. \end{aligned}$$

Therefore, $E(X|Z) = E(Y|Z) = E(\beta^t|Z) = \Sigma_i m_i^t \beta_i^t$ is constant with respect to the value of Z because the allelic frequency in the brothers is independent of Z. Thus, $C_z[E(X|Z), E(Y|Z)] = 0$.

Lineal. For maternal uncle-nephew (Fig. 1), for S' to be identical by descent to S, the alleles must have descended from the maternal grandmother. Allelic frequency in the grandmother and thus in the uncle is $f_i^{t-2} = m_i^{t-1}$, irrespective of whether the alleles in the uncle and in the nephew are identical by descent, which implies that allelic frequency in the uncle is independent of

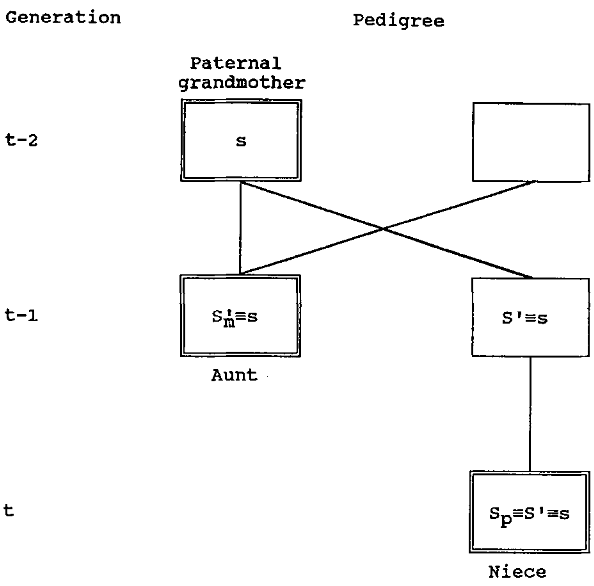

Fig. 2. Pedigree of paternal aunt-niece relationship; box —— denotes male and box ═══ denotes female, where s is the random allele in the grandmother, S_m' is the maternal allele in the aunt, S' is the allele in the male, and S_p is the paternal allele in the niece

the condition of identical by descent. Allelic frequency in the nephew, however, is $f_i^{t-2} = m_i^{t-1}$ when the alleles are identical by descent whereas the unconditional allelic frequency is m_i^t, which implies that allelic frequency in the nephew is not independent of the condition of identical by descent. Thus,

$$\begin{aligned} P_i &= P(S'=s_i|S'\equiv S) = P(S'=s_i|S'\not\equiv S) = P(S'=s_i) \\ &= P(S=s_i|S'\equiv S) \neq P(S=s_i|S'\not\equiv S) \neq P(S=s_i) \\ &= m_i^{t-1}. \end{aligned}$$

Therefore, $E(X|Z) = E(\beta^{t-1}|Z) = \Sigma_i m_i^{t-1} \beta_i^{t-1}$ is constant because the allelic frequency in the uncle is independent of Z. However, $E(Y|Z) = E(\beta^t|Z)$ is not constant because the allelic frequency in the nephew is not independent of Z. Nevertheless, $C_z[E(X|Z), E(Y|Z)] = 0$ because $E(X|Z)$ is a constant.

A2 Female-female

Collateral. For full sisters, for S_m' to be identical by descent to S_m, the maternal alleles must have descended from either the maternal or the paternal allele of their mother. Allelic frequency in the mother and of maternal alleles in the sisters is $\frac{1}{2}(f_{jm}^{t-1} + f_{jp}^{t-1}) = f_j^{t-1} = f_{jm}^t$, irrespective of whether the alleles in the sisters are identical by descent, which implies that allelic frequency in the sisters is independent of the condition of identical by descent. Thus,

$$\begin{aligned} P_{j|mm} &= P(S_m'=s_j|S_m'\equiv S_m) = P(S_m'=s_j|S_m'\not\equiv S_m) = P(S_m'=s_j) \\ &= P(S_m=s_j|S_m'\equiv S_m) = P(S_m=s_j|S_m'\not\equiv S_m) = P(S_m=s_j) \\ &= f_j^{t-1}. \end{aligned}$$

Therefore, $E(X|Z) = E(Y|Z) = E(\alpha_m^t|Z) = \Sigma_j f_j^{t-1} \alpha_{jm}^t$ is constant.

For full sisters also, S_p' is identical by descent to S_p with a probability equal to 1, so that $Z=1$ always. Thus $P_{k|pp} = m_k^{t-1}$, and $E(X|Z) = E(Y|Z)$ is constant because Z is a constant.

Lineal. For paternal aunt-niece (Fig. 2), e.g., for S_m' to be identical by descent to S_p, the maternal allele in the aunt and the paternal allele in the niece must have descended from the paternal grandmother. Frequency of the allele in the grandmother, of maternal alleles in the aunt, and of paternal alleles in the niece is

$$f_j^{t-2} = f_{jm}^{t-1} = m_j^{t-1} = f_{jp}^t,$$

irrespective of whether the alleles in the aunt and niece are identical by descent, which implies that allelic frequency of maternal alleles in the aunt and of paternal alleles in the niece are independent of the condition of identical by descent. Thus,

$$\begin{aligned} P_{j|mp} &= P(S_m'=s_j|S_m'\equiv S_p) = P(S_m'=s_j|S_m'\not\equiv S_p) = P(S_m'=s_j) \\ &= P(S_p=s_j|S_m'\equiv S_p) = P(S_p=s_j|S_m'\not\equiv S_p) = P(S_p=s_j) \\ &= f_j^{t-2} = f_{jm}^{t-1} = f_{jp}^t. \end{aligned}$$

Therefore, $E(X|Z) = E(\alpha_m^{t-1}|Z) = \Sigma_j f_{jm}^{t-1} \alpha_{jm}^{t-1}$ is constant because the allelic frequency of maternal alleles in the aunt is independent of Z, and $E(Y|Z) = E(\alpha_p^t|Z) = \Sigma_j f_{jp}^t \alpha_{jp}^t$ is constant because the allelic frequency of paternal alleles in the niece is independent of Z.

A3 Male-female

Collateral. For brother-sister, for S to be identical by descent to S_m, the allele in the brother and the maternal allele in the sister must have descended from their mother. Frequency of the allele in the mother, of the allele in the brother, and of the maternal alleles in the sisters is

$$f_i^{t-t} = m_i^t = f_{im}^t,$$

irrespective of whether the alleles in the brother and sister are identical by descent, which implies that allelic frequency in the brother and of the maternal alleles in the sister are independent of the condition of identical by descent. Thus,

$$\begin{aligned} P_{i|m} &= P(S=s_i|s\equiv S_m) = P(S=s_i|S\not\equiv S_m) = P(S=s_i) \\ &= P(S_m=s_i|S\equiv S_m) = P(S_m=s_i|S\not\equiv S_m) = P(S_m=s_i) \\ &= f_i^{t-1} = m_i^t. \end{aligned}$$

Therefore, $E(X|Z) = E(\beta^t|Z) = \Sigma_i m_i^t \beta_i^t$ is constant because the allelic frequency in the brother is independent of Z, and $E(Y|Z) = E(\alpha_m^t|Z) = \Sigma_i f_{im}^t \alpha_{im}^t$ is constant because the allelic frequency of the maternal alleles in the sister is independent of Z.

Lineal. For mother-son, the allele in the son must have descended from its mother. Frequency of the maternal allele in the mother is f_{im}^t and of paternal allele is f_{ip}^t, irrespective of whether the son receives the maternal or paternal allele from the mother, which implies that frequency of the maternal allele and of the paternal allele are independent of the condition of identical by descent.

When the son receives the maternal allele ($S\equiv S_m$), allelic frequency in the son is the frequency of the maternal allele in the mother, $f_{im}^t = f_i^{t-1} = m_i^t$, whereas the unconditional allelic frequency in the son is m_i^{t+1}, which implies that allelic frequency in the son is not independent of the condition of identical by descent. Thus,

$$\begin{aligned} P_{i|m} &= P(S_m=s_i)|S\equiv S_m) = P(S_m=s_i)|S\not\equiv S_m) = P(S_m=s_i) \\ &= P(S=s_i|S\equiv S_m) \neq P(S=s_i|S\not\equiv S_m) \neq P(S=s_i) \\ &= f_{im}^{t-1} = m_i^t. \end{aligned}$$

Therefore, $E(X|Z) = E(\alpha_m^t|Z) = \Sigma_i f_{im}^{t-1} \alpha_{im}^t$ is constant because frequency of the maternal allele in the mother is independent of Z. However, $E(Y|Z) = E(\beta^{t+1}|Z)$ is not constant because the allelic frequency in the son is not independent of Z. Nevertheless, $C_z[E(\alpha_m^t|Z), E(\beta^{t+1}|Z)] = 0$ because $E(X|Z)$ is constant.

When the son receives the paternal allele ($S\equiv S_p$), allelic frequency in the son is the frequency of the paternal allele in the mother, $f_{ip}^{t} = m_i^{t-1}$, whereas the unconditional allelic frequency in the son is m_i^{t+1}, which implies that allelic frequency in the son is not independent of the condition of identical by descent. Thus,

$$\begin{aligned} P_{i|p} &= P(S_p = s_i) | S \equiv S_p) = P(S_p = s_i) | S \not\equiv S_p) = P(S_p = s_i) \\ &= P(S = s_i | S \equiv S_p) \neq P(S = s_i | S \not\equiv S_p) \neq P(S = s_i) \\ &= f_{ip}^{t} = m_i^{t-1} . \end{aligned}$$

Therefore, $E(X|Z) = E(\alpha_p^t|Z) = \Sigma_i f_{ip}^t \alpha_{ip}^t$ is constant because frequency of the paternal allele in the mother is independent of Z. However, $E(Y|Z) = E(\beta^{t+1}|Z)$ is not constant because the allelic frequency in the son is not independent of Z. Nevertheless, $C_z[E(\alpha_p^t|Z), E(\beta^{t+1})] = 0$ because $E(X|Z)$ is constant.

B Derivation of covariance between female relatives for dominant deviations

Let X be the dominant deviation of genotype $S_{xm} S_{xp}$ in a female and Y be the dominant deviation of genotype $S_{ym} S_{yp}$ in a related female, and let Z be a random variable that has value 1 when $S_{xm} S_{xp} \equiv S_{ym} S_{yp}$ and value 0 when $S_{xm} S_{xp} \not\equiv S_{ym} S_{yp}$. Then covariance between dominant deviations is

$$C(X, Y) = C(X, Y|Z=1) \, P(Z=1) + C_z[E(X|Z), E(Y|Z)] .$$

For full sisters, for $S'_m S'_p$ to be identical by descent to $S_m S_p$, the maternal allele in both sisters must have descended from either the maternal or the paternal allele of their mother. The paternal alleles in both sisters are always identical by descent. The genotypic frequency in the sisters if f_{jk}^t, irrespective of whether the maternal alleles in the sisters are identical by descent, which implies that allelic frequency in the sisters is independent of the condition of identical by descent. Thus,

$$\begin{aligned} P_{jk} &= P[(S'_m = s_j), (S'_p = s_k) | (S'_m S'_p) \equiv (S_m S_p)] \\ &= P[(S'_m = s_j), (S'_p = s_k) | (S'_m S'_p) \not\equiv (S_m S_p)] \\ &= P(S'_m = s_j | S'_m \equiv S_m) \, P(S'_p = s_k | S'_p \equiv S_p) \\ &= P(S'_m = s_j | S'_m \not\equiv S_m) \, P(S'_p = s_k | S'_p \not\equiv S_p) \\ &= P(S'_m = s_j) \, P(S'_p = s_k) \\ &= f_{jm}^t f_{kp}^t = f_j^{t-1} m_k^{t-1} = f_{jk}^t . \end{aligned}$$

Therefore, $E(X|Z) = E(Y|Z) = E(\delta_{jk}^t|Z) = \Sigma_j \Sigma_k f_{jk}^t \delta_{jk}^t$ is constant because allelic frequency in the sisters is independent of Z. Thus, $C_z[E(X|Z), E(Y|Z)] = 0$.

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