

LINKAGE DISEQUILIBRIUM IN A FINITE POPULATION THAT IS PARTIALLY SELFING

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ABSTRACT

The linkage disequilibrium expected in a finite, partially selfing population is analyzed, assuming the infinite allele model. Formulas for the expected sum of squares of the linkage disequilibria and the squared standard linkage disequilibrium are derived from the equilibrium values of sixteen inbreeding coefficients required to describe the behavior of the system. These formulas are identical to those obtained with random mating if the effective population size $N_e = (1 - \frac{1}{2}S)N$ and the effective recombination value $r_e = (1 - S)r / (1 - \frac{1}{2}S)$, where S is the proportion of selfing, are substituted for the population size and the recombination value. Therefore, the effect of partial selfing at equilibrium is to reduce the population size by a factor $1 - \frac{1}{2}S$ and the recombination value by a factor $(1 - S) / (1 - \frac{1}{2}S)$.

THERE have been several studies on the amount of linkage disequilibrium found in natural populations. Most of these studies found no significant linkage disequilibrium between loci that are not associated with an inversion (LEWONTIN 1974; LANGLEY, ITO and VOELKER 1977). However, in plant populations that are partially selfing, a significant amount of linkage disequilibrium is consistently present (BROWN 1979). This observed linkage disequilibrium could be generated either by selection with epistatic interactions between the loci or by random drift. In order to determine whether or not this observed disequilibrium could be a result of random drift, it is necessary to know the amount of linkage disequilibrium expected in a partially selfing finite population without selection.

The expected amount of linkage disequilibrium in a finite population with random mating has been studied extensively. These studies have assumed two alleles at each locus with no mutation (HILL and ROBERTSON 1968; OHTA and KIMURA 1969) or an infinite number of alleles at each locus with mutant alleles differing from all pre-existing ones (HILL 1975) *i.e.*, the infinite-allele model of KIMURA and CROW (1964). In this paper, the amount of linkage disequilibrium expected in a finite population assuming the infinite allele model and partial selfing is derived using inbreeding coefficients. It is shown that the formulas for the expected sum of squares of the linkage disequilibria and the squared standard linkage disequilibrium are equivalent to those from random mating with a reduced recombination value and a reduced population size.

THEORY

Before considering random drift of two loci in a finite population that is primarily selfing, the one-locus model is developed.

Let the population consist of N diploid individuals that produce offspring by both selfing and outcrossing. Let S be the proportion of the offspring of an individual that are produced by selfing and $1-S$ the proportion of offspring produced by outcrossing. Each of the N individuals in the next generation is the offspring of either one individual selected at random (if it is produced by selfing) or two individuals selected at random without replacement (if it is produced by outcrossing) from the present generation. If $S = 1/N$, then there is random mating.

Two inbreeding coefficients or descent measures are needed to describe the behavior of the system from one generation to the next. One coefficient, $\Psi_{(A/A)}$, is the probability that the two genes of an individual are identical by descent. The other coefficient, $\Phi_{(A)(A)}$, is the probability that two genes selected from two different individuals are identical by descent. (The notation used for the subscripts is explained when considering the two-locus model.) Since the probability of an offspring having its two genes identical by descent is $\frac{1}{2} + \frac{1}{2}\Psi_{(A/A)}$ if it is produced by selfing and $\Phi_{(A)(A)}$ if it is produced by outcrossing,

$$\Psi_{(A/A)}' = (1-\mu)^2 [S(\frac{1}{2} + \frac{1}{2}\Psi_{(A/A)}) + (1-S)\Phi_{(A)(A)}] \quad (1a)$$

$$\Phi_{(A/A)}' = (1-\mu)^2 \left[\frac{1}{N}(\frac{1}{2} + \frac{1}{2}\Psi_{(A/A)}) + \left(1 - \frac{1}{N}\right)\Phi_{(A)(A)} \right] \quad (1b)$$

where μ is the mutation rate to unique alleles.

If $N \gg 1$ and $\mu \approx O\left(\frac{1}{N}\right)$, then these equations can be approximated by

$$\Psi_{(A/A)}' = S(\frac{1}{2} + \frac{1}{2}\Psi_{(A/A)}) + (1-S)\Phi_{(A)(A)} \quad (2a)$$

if terms of $O\left(\frac{1}{N}\right)$ or less are neglected, and

$$\Phi_{(A)(A)}' = \frac{1}{N}(\frac{1}{2} + \frac{1}{2}\Psi_{(A/A)}) + (1 - \frac{1}{N} - 2\mu)\Phi_{(A)(A)} \quad (2b)$$

if terms of $O\left(\frac{1}{N^2}\right)$ or less are neglected. At equilibrium

$$\hat{\Psi}_{(A/A)} = \frac{\frac{1}{2}S + (1-S)\hat{\Phi}_{(A)(A)}}{1 - \frac{1}{2}S}$$

from (2a) and substituting this value into (2b)

$$\hat{\Phi}_{(A)(A)} = \frac{1}{1 + 4N\mu - 2N\mu S} = \frac{1}{1 + 4N_e\mu}, \quad (3a)$$

and therefore

$$\hat{\Psi}_{(A/A)} = \frac{1 + 2N_e\mu S}{1 + 4N_e\mu - 2N_e\mu S} = \frac{1 + 2N_e\mu S}{1 + 4N_e\mu}, \quad (3b)$$

where $N_e = (1 - \frac{1}{2}S)N$. It can be verified that these are the approximate equilibrium values of equations (1a) and (1b) by substitution or from the theory of perturbed matrices (section 5.5, NOBLE and DANIEL 1977). If $\hat{\Phi}_A$ is the probability that two genes chosen randomly from the population without replacement (not necessarily from two different individuals) are identical by descent, then

$$\hat{\Phi}_A = \frac{1}{2N-1} \hat{\Psi}_{(A/A)} + \left(1 - \frac{1}{2N-1}\right) \hat{\Phi}_{(A)(A)} \simeq \hat{\Phi}_{(A)(A)}$$

since $N \gg 1$.

We now turn our attention to the two-locus model. Denote the two loci by A and B , and let r be the recombination value between them. Let N be the number of diploid individuals, S be the proportion of selfing and μ and ν be the mutation rates to unique alleles at the A and B loci, respectively.

Sixteen inbreeding coefficients are required to describe random drift of two loci in a finite population that is partially selfing. These inbreeding coefficients involve randomly choosing chromosomes without replacement from one, two, three or four different individuals and are denoted by Ψ , Φ , Γ and Δ , respectively. The following notation is used in the subscripts: parentheses are used to separate the genes contributed by different individuals, and slashes are used to separate the genes contributed by different chromosomes of an individual. For example, $\Phi_{(AB)(A/B)}$ is the probability of identity by descent at both loci if the genes at the A and B loci are chosen from one chromosome of one individual and from different chromosomes of another individual. If the genes on the two chromosomes of an arbitrary individual are denoted by $a_{i1}b_{i1}$ and $a_{i2}b_{i2}$, respectively, then the sixteen inbreeding coefficients are given in Table 1.

The recursion equations for these sixteen inbreeding coefficients are given in the APPENDIX. At equilibrium,

$$\begin{aligned} \hat{\Psi}_{(A/A)} &= \frac{\frac{1}{2}S + (1-S)\hat{\Phi}_{(A)(A)}}{1 - \frac{1}{2}S} \\ \hat{\Psi}_{(B/B)} &= \frac{\frac{1}{2}S + (1-S)\hat{\Phi}_{(B)(B)}}{1 - \frac{1}{2}S} \\ \hat{\Psi}_{(AB/AB)} &= \frac{\frac{1}{2}S + (1-S)\hat{\Phi}_{(AB)(AB)}}{1 - \frac{1}{2}S} \\ \hat{\Phi}_{(AB)(A/B)} &= \frac{\frac{1}{2}S\hat{\Phi}_{(AB)(AB)} + (1-S)\hat{\Gamma}_{(AB)(A)(B)}}{1 - \frac{1}{2}S} \end{aligned} \quad (4a)$$

TABLE 1

Definitions of the sixteen inbreeding coefficients

$\Psi_{(A/A)} = P(a_{i1} \equiv a_{i2})$	$\Psi_{(B/B)} = P(b_{i1} \equiv b_{i2})$
$\Phi_{(A)(A)} = P(a_{i1} \equiv a_{j1})$	$\Phi_{(B)(B)} = P(b_{i1} \equiv b_{j1})$
$\Psi_{(AB/AB)} = P(a_{i1} \equiv a_{i2} \text{ and } b_{i1} \equiv b_{i2})$	
$\Phi_{(AB)(AB)} = P(a_{i1} \equiv a_{j1} \text{ and } b_{i1} \equiv b_{j1})$	
$\Phi_{(AB)(A/B)} = P(a_{i1} \equiv a_{j1} \text{ and } b_{i1} \equiv b_{j2})$	
$\Phi_{(AB/B)(A)} = P(a_{i1} \equiv a_{j1} \text{ and } b_{i1} \equiv b_{i2})$	
$\Phi_{(AB/A)(B)} = P(a_{i1} \equiv a_{i2} \text{ and } b_{i1} \equiv b_{j1})$	
$\Phi_{(A/A)(B/B)} = P(a_{i1} \equiv a_{i2} \text{ and } b_{j1} \equiv b_{j2})$	
$\Phi_{(A/B)(A/B)} = P(a_{i1} \equiv a_{j2} \text{ and } b_{i1} \equiv b_{j2})$	
$\Gamma_{(AB)(A)(B)} = P(a_{i1} \equiv a_{j1} \text{ and } b_{i1} \equiv b_{k1})$	
$\Gamma_{(B/B)(A)(A)} = P(a_{j1} \equiv a_{k1} \text{ and } b_{i1} \equiv b_{i2})$	
$\Gamma_{(A/A)(B)(B)} = P(a_{i1} \equiv a_{i2} \text{ and } b_{j1} \equiv b_{k1})$	
$\Gamma_{(A/B)(A)(B)} = P(a_{i1} \equiv a_{j1} \text{ and } b_{i2} \equiv b_{k1})$	
$\Delta_{(A)(B)(A)(B)} = P(a_{i1} \equiv a_{k1} \text{ and } b_{j1} \equiv b_{l1})$	

The genes of the two chromosomes of an individual are denoted by $a_{i1}b_{i1}$ and $a_{i2}b_{i2}$, respectively. ("≡" is read "is identical by descent to.")

$$\hat{\Phi}_{(AB/B)(A)} = \frac{1/2 \hat{\Phi}_{(A)(A)} + (1-S) \hat{\Gamma}_{(AB)(A)(B)}}{1 - 1/2 S}$$

$$\hat{\Phi}_{(AB/A)(B)} = \frac{1/2 \hat{\Phi}_{(B)(B)} + (1-S) \hat{\Gamma}_{(AB)(A)(B)}}{1 - 1/2 S} \quad (4a)$$

$$\hat{\Gamma}_{(B/B)(A)(A)} = \frac{1/2 S \hat{\Phi}_{(A)(A)} + (1-S) \hat{\Delta}_{(A)(B)(A)(B)}}{1 - 1/2 S}$$

$$\hat{\Gamma}_{(A/A)(B)(B)} = \frac{1/2 S \hat{\Phi}_{(B)(B)} + (1-S) \hat{\Delta}_{(A)(B)(A)(B)}}{1 - 1/2 S}$$

$$\hat{\Gamma}_{(A/B)(A)(B)} = \frac{1/2 S \hat{\Gamma}_{(AB)(A)(B)} + (1-S) \hat{\Delta}_{(A)(B)(A)(B)}}{1 - 1/2 S}$$

$$\hat{\Phi}_{(AB)(AB)} = \frac{16UV[8(U+V)^2+4(U+V)R+18(U+V)+2R+9]+32(U+V)^4+48(U+V)^2R+16(U+V)R^2+80(U+V)^2+76(U+V)R+8R^2+54(U+V)+26R+9}{(1+4U)(1+4V)[32(U+V)^2+48(U+V)R+16(U+V)R^2+80(U+V)^2+76(U+V)R+8R^2+54(U+V)+26R+9]}$$

$$\hat{\Gamma}_{(AB)(A)(B)} = \frac{16UV[2(U+V)+3]+32(U+V)^2+48(U+V)R+16(U+V)R^2+80(U+V)^2+76(U+V)R+8R^2+54(U+V)+26R+9}{(1+4U)(1+4V)[32(U+V)^2+48(U+V)R+16(U+V)R^2+80(U+V)^2+76(U+V)R+8R^2+54(U+V)+26R+9]}$$

$$\hat{\Delta}_{(A)(B)(A)(B)} = \frac{32UV+32(U+V)^2+48(U+V)R+16(U+V)R^2+80(U+V)^2+76(U+V)R+8R^2+54(U+V)+26R+9}{(1+4U)(1+4V)[32(U+V)^2+48(U+V)R+16(U+V)R^2+80(U+V)^2+76(U+V)R+8R^2+54(U+V)+26R+9]}$$

from (A1) and substituting these values into (A2)

$$\hat{\Phi}_{(A)(A)} = \frac{1}{1+4U}$$

$$\hat{\Phi}_{(B)(B)} = \frac{1}{1+4V} \quad (4b)$$

$$\Phi_{(A/A)(B/B)} = \frac{\frac{1}{4}S^2(1+\frac{1}{2}S) + \frac{3}{4}S^2(1-S)(\hat{\Phi}_{(A)(A)} + \hat{\Phi}_{(B)(B)} + (1-S)^2(1+\frac{3}{2}S)\hat{\Delta}_{(A)(B)(A)(B)}}{(1+\frac{1}{2}S)(1-\frac{1}{2}S)^2}$$

$$\hat{\Phi}_{(A/B)(A/B)} = \frac{\frac{1}{4}S^2(1+\frac{1}{2}S)\hat{\Phi}_{(AB)(AB)} + \frac{3}{2}S^2(1-S)\hat{\Gamma}_{(AB)(A)(B)} + (1-S)^2(1+\frac{3}{2}S)\hat{\Delta}_{(A)(B)(A)(B)}}{(1+\frac{1}{2}S)(1-\frac{1}{2}S)^2} \quad (4b)$$

where

$$U = N(1-\frac{1}{2}S)\mu = N_e\mu$$

$$V = N(1-\frac{1}{2}S)\nu = N_e\nu$$

$$R = N(1-S)r = N(1-\frac{1}{2}S)(1-S)r/(1-\frac{1}{2}S) = N_e r_e .$$

The equilibrium values of the other inbreeding coefficients are obtained by substituting the equilibrium values (4b) into (4a).

In order to compare these results for a partially selfing population to the equivalent results for a random mating population, it is necessary to define five further inbreeding coefficients. Three of these inbreeding coefficients involve choosing at random two chromosomes without replacement from the population; one coefficient, choosing three chromosomes; and one coefficient, choosing four chromosomes. (The chromosomes are not necessarily from different individuals.) If an arbitrary chromosome is denoted by $a_i b_i$, then the five inbreeding coefficients are

$$\Phi_A = P(a_1 \equiv a_2)$$

$$\Phi_B = P(b_1 \equiv b_2)$$

$$\Phi_{AB} = P(a_1 \equiv a_2 \text{ and } b_1 \equiv b_2)$$

$$\Gamma_{AB} = P(a_1 \equiv a_2 \text{ and } b_1 \equiv b_3)$$

$$\Delta_{AB} = P(a_1 \equiv a_3 \text{ and } b_2 \equiv b_4) .$$

(STROBECK and MORGAN 1978). In terms of the previous sixteen inbreeding coefficients,

$$\Phi_A = \frac{1}{2N-1} \Psi_{(A/A)} + \left(1 - \frac{1}{2N-1}\right) \Phi_{(A)(A)} \simeq \Phi_{(A)(A)}$$

$$\Phi_B = \frac{1}{2N-1} \Psi_{(B/B)} + \left(1 - \frac{1}{2N-1}\right) \Phi_{(B)(B)} \simeq \Phi_{(B)(B)}$$

$$\Phi_{AB} = \frac{1}{2N-1} \Psi_{(AB/AB)} + \left(1 - \frac{1}{2N-1}\right) \Phi_{(AB)(AB)} \simeq \Phi_{(AB)(AB)}$$

$$\Gamma_{AB} = \frac{1}{2N-1} (\Phi_{(AB)(A/B)} + \Phi_{(AB/A)(B)} + \Phi_{(AB/B)(A)}) + \frac{2N-4}{2N-1}$$

$$\Gamma_{(AB)(A)(B)} \simeq \Gamma_{(AB)(A)(B)}$$

$$\Delta_{AB} = \frac{1}{(2N-1)(2N-3)} (\Phi_{(A/A)(B/B)} + 2\Phi_{(A/A)(B/B)}) + \frac{2N-4}{(2N-1)(2N-3)} (\Gamma_{(A/A)(B)(B)} + \Gamma_{(B/B)(A)(A)} + 4\Gamma_{(AB)(A)(B)}) + \frac{(2N-4)(2N-6)}{(2N-1)(2N-3)} \Delta_{(A)(B)(A)(B)} \simeq \Delta_{(A)(B)(A)(B)}$$

if $N \gg 1$. Therefore, the equilibrium values of these inbreeding coefficients are given by (4b), which are identical to those obtained assuming random mating with a population size $N_e = (1 - \frac{1}{2}S)N$ and a recombination value $r_e = (1 - S)r / (1 - \frac{1}{2}S)$ (STROBECK and MORGAN 1978). Therefore, the effect of partial selfing at equilibrium is to reduce the population size by a factor $1 - \frac{1}{2}S$ and the recombination value by a factor $(1 - S) / (1 - \frac{1}{2}S)$.

There is a simple relationship between these five inbreeding coefficients and the quantities used by HILL (1975) to measure the amount of linkage disequilibrium expected in a finite population (SERANT 1976; STROBECK and MORGAN 1978). If p_i is the frequency of the i th allele A_i at the A locus, q_j the frequency of the j th allele B_j at the B locus, and $f_{ij} = p_i q_j + D_{ij}$ the frequency of the chromosome $A_i B_j$, where D_{ij} is the linkage disequilibrium between A_i and B_j , then the expected sum of squares of the linkage disequilibria

$$E(\sum_{ij} D_{ij}^2) = \frac{16UV[2(U+V)] + [4(U+V) + 2R + 5]}{(1+4U)(1+4V)[32(U+V)^2 + 48(U+V)^2R + 16(U+V)R^2 + 80(U+V)^2 + 76(U+V)R + 8R^2 + 54(U+V) + 26R + 9]}$$

and the squared standard linkage disequilibrium

$$\sigma_d^2 = \frac{E(\sum_{ij} D_{ij}^2)}{E(\sum_{i \neq k} \sum_{j \neq l} p_i p_k q_j q_l)} = \frac{4(U+V) + 2R + 5}{16(U+V)^2 + 24(U+V)R + 8R^2 + 32(U+V) + 26R + 11}$$

(HILL 1975). In Figures 1 and 2, the equilibrium values of $E(\sum_{ij} D_{ij}^2)$ and σ_d^2 are plotted for $10^{-3} \leq Nr \leq 10^3$ and with $N_\mu = N_\nu = 0.25$ and 1.0 and $S = 0.0, 0.5, 0.9, 0.99$ and 1.0 . It is seen that $E(\sum_{ij} D_{ij}^2)$ and σ_d^2 remain significantly greater than zero for increasingly larger values of Nr as S approaches one and are not functions of the recombination value if $S = 1$. If $r = 0$, $E(\sum_{ij} D_{ij}^2)$ has a maximum value when $U = V \simeq 0.505$, whereas σ_d^2 is a decreasing function of $U + V$. Therefore, increasing the proportion of selfing increases the value of σ_d^2 , but may increase or decrease $E(\sum_{ij} D_{ij}^2)$ when $r = 0$. Thus, the squared standard linkage disequilibrium is probably the better measure of the amount of linkage disequilibrium in a finite population that is partially selfing.

DISCUSSION

The results in the previous section show that there is significant linkage disequilibrium due to random drift in a partially selfing population if

$$N_e r_e = N(1 - S)r \leq 1$$

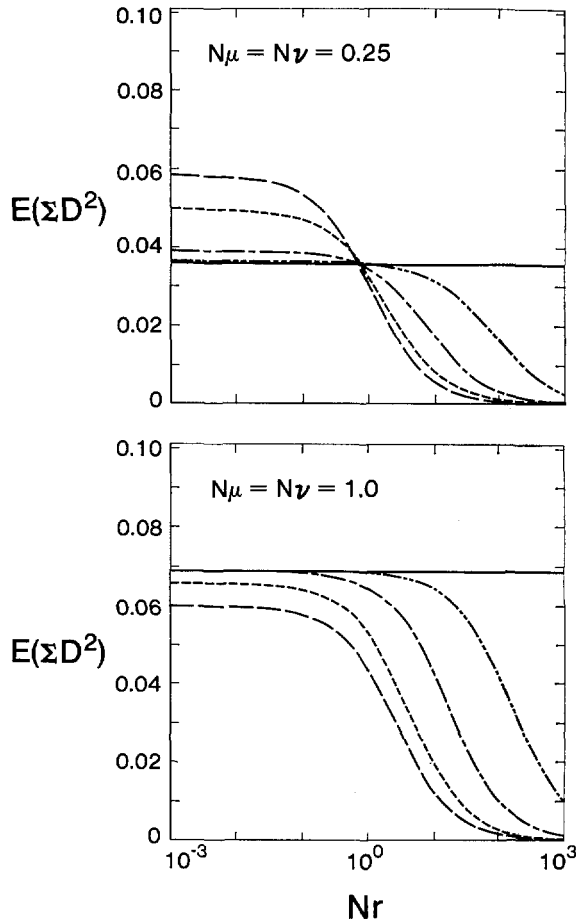


FIGURE 1.—The expected value of the sum of squares of the linkage disequilibria for $N\mu = N\nu = 0.25$ and 1.0 and with $S = 0.0, 0.5, 0.9, 0.99$ and 1.0 (— $S = 0.0$, - - - $S = 0.5$, - · - · $S = 0.9$, · · · · $S = 0.99$, ——— $S = 1.0$).

and the mutation rates μ and ν are of the order of $1/N$. It is, therefore, appropriate to examine the experimental data collected from populations of partially selfing plants to see if the observed linkage disequilibrium can be explained by random drift. The magnitude of $(1-S)r$ will be used as an indicator of whether the observed linkage disequilibrium could be due to random drift. Since the mutation rate is generally assumed to be between 10^{-4} and 10^{-8} , the population size must be larger than approximately 10^4 if the variation is to be maintained in the population. Therefore, $(1-S)r$ must be less than approximately 10^{-4} before the observed linkage disequilibrium is likely to be the result of random drift.

In barley, *Hordeum vulgare*, ALLARD and his co-workers (ALLARD, KAHLER and WEIR 1972; WEIR, ALLARD and KAHLER 1972, 1974) found significant linkage disequilibrium between four esterase loci in Composite Cross \bar{V} . Three

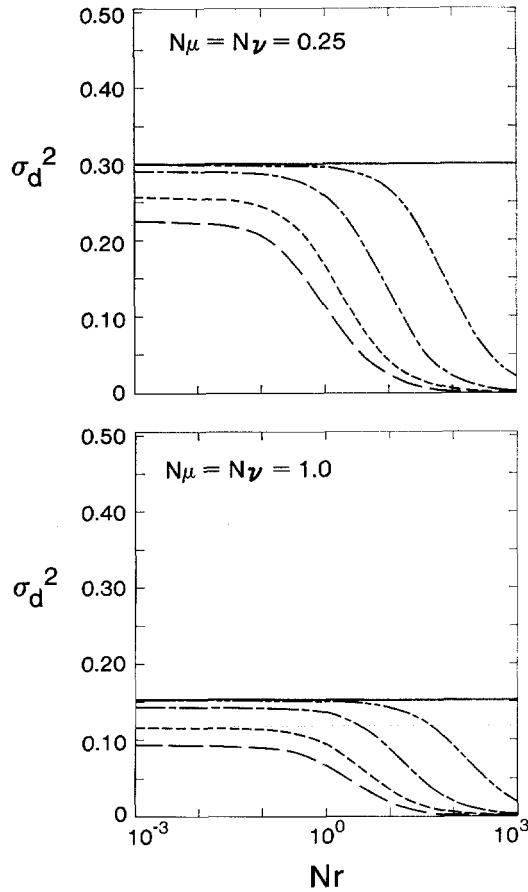


FIGURE 2.—The expected value of the squared standard linkage disequilibrium for $N\mu = N\nu = 0.25$ and 1.0 and with $S = 0.0, 0.5, 0.9, 0.99$ and 1.0 (..... $S = 0.0$, $S = 0.5$, $S = 0.9$, $S = 0.99$, ————— $S = 1.0$).

loci, A , B and C , are closely linked and the fourth locus is unlinked to the other three. The recombination value between the three linked loci are estimated to be $r_{AB} = 0.0023$, $r_{AC} = 0.0048$ and $r_{BC} = 0.0059$ (KAHLER and ALLARD 1970). The estimate of the proportion of selfing is $S = 0.9943$ (ALLARD, KAHLER and WEIR 1972). Therefore, the value of $(1-S)r$ between AB , AC and BC are 0.000013 , 0.000027 and 0.000034 , respectively. These values are in the range such that linkage disequilibria could be generated by random drift. However, since Composite Cross \bar{V} was initiated in 1941, a transient analysis is probably more appropriate than the comparison of the observed sum of squares of the linkage disequilibria or the squared standard linkage disequilibrium to that expected at equilibrium.

Also, the linkage disequilibrium between six loci, four esterase loci E_1 , E_4 , E_9 and E_{10} , a phosphatase P_5 , and an aneodal peroxidase APX_5 , has been analyzed in *Avena barbata*, wild oats, by ALLARD *et al.* (1972). Three loci, P_5 , APX_5

and E_{10} , are linked, and the recombination values are $r_{P_5-APX_5} = 0.04$, $r_{APX_5-E_{10}} = 0.23$ and $r_{P_5-E_{10}} = 0.25$ (MARSHALL and ALLARD 1969). The proportion of selfing has been estimated to be approximately $S = 0.98$ (MARSHALL and ALLARD 1970; HAMRICK and ALLARD 1972). Therefore, the smallest value of $(1 - S)r$, which is between P_5 and APX_5 , is 0.0008. This value is small enough that random drift might have a significant effect if the size of the effective population is relatively small. The actual population size was estimated to be approximately 50,000.

These two examples show that random drift might explain some of the linkage disequilibrium observed in natural populations. However, random drift is unlikely to be the cause of the observed linkage disequilibrium between loosely linked loci.

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APPENDIX

The recursion equations for the sixteen inbreeding coefficients in Table 1 are:

$$\Psi_{(A/A)'} = (1-\mu)^2 [S(1/2 + 1/2\Psi_{(A/A)}) + (1-S)\Phi_{(A)(A)}]$$

$$\Psi_{(B/B)'} = (1-\nu)^2 [S(1/2 + 1/2\Psi_{(B/B)}) + (1-S)\Phi_{(B)(B)}]$$

$$\Phi_{(A)(A)'} = (1-\mu)^2 \left[\frac{1}{N}(1/2 + 1/2\Psi_{(A/A)}) + \left(1 - \frac{1}{N}\right)\Phi_{(A)(A)} \right]$$

$$\Phi_{(B)(B)'} = (1-\nu)^2 \left[\frac{1}{N}(1/2 + 1/2\Psi_{(B/B)}) + \left(1 - \frac{1}{N}\right)\Phi_{(B)(B)} \right]$$

$$\Psi_{(AB/AB)'} = (1-\mu)^2(1-\nu)^2 \left\{ S[(1-r)^2\Lambda_1 + 2r(1-r)\Lambda_2 + r^2\Lambda_1] + (1-S)\Phi_{(AB)(AB)} \right\}$$

$$\Phi_{(AB)(AB)'} = (1-\mu)^2(1-\nu)^2 \left\{ (1-r)^2 \left[\frac{1}{N}\Lambda_1 + \left(1 - \frac{1}{N}\right)\Phi_{(AB)(AB)} \right] + 2r(1-r) \left[\frac{1}{N}\Lambda_2 + \left(1 - \frac{1}{N}\right)\Phi_{(AB)(A/B)} \right] + r^2 \left[\frac{1}{N}\Lambda_1 + \left(1 - \frac{1}{N}\right)\Phi_{(A/B)(A/B)} \right] \right\}$$

$$\Phi_{(AB)(A/B)'} = (1-\mu)^2(1-\nu)^2 \left\{ S \left\{ (1-r) \left[\frac{1}{N}\Lambda_3 + \left(1 - \frac{1}{N}\right)\Omega_1 \right] + r \left[\frac{1}{N}\Lambda_3 + \left(1 - \frac{1}{N}\right)\Omega_2 \right] \right\} + (1-S) \left\{ (1-r) \left[\frac{1}{N}\Omega_3 + \frac{1}{N}\Omega_4 \right] + \left(1 - \frac{2}{N}\right)\Gamma_{(AB)(A)(B)} \right\} + r \left[\frac{1}{N}\Omega_3 + \frac{1}{N}\Omega_4 + \left(1 - \frac{2}{N}\right)\Gamma_{(A/B)(A)(B)} \right] \right\}$$

$$\Phi_{(AB/B)(A)'} = (1-\mu)^2(1-\nu)^2 \left\{ S \left[\frac{1}{N}\Lambda_3 + \left(1 - \frac{1}{N}\right)\Omega_4 \right] + (1-S) \left\{ (1-r) \left[\frac{1}{N}\Omega_1 + \frac{1}{N}\Omega_3 + \left(1 - \frac{2}{N}\right)\Gamma_{(AB)(A)(B)} \right] + r \left[\frac{1}{N}\Omega_2 + \frac{1}{N}\Omega_3 + \left(1 - \frac{2}{N}\right)\Gamma_{(A/B)(A)(B)} \right] \right\} \right\}$$

$$\Phi_{(AB/A)(B)'} = (1-\mu)^2(1-\nu)^2 \left\{ S \left[\frac{1}{N}\Lambda_3 + \left(1 - \frac{1}{N}\right)\Omega_3 \right] + (1-S) \left\{ (1-r) \left[\frac{1}{N}\Omega_1 + \frac{1}{N}\Omega_4 + \left(1 - \frac{2}{N}\right)\Gamma_{(AB)(A)(B)} \right] + r \left[\frac{1}{N}\Omega_2 + \frac{1}{N}\Omega_4 + \left(1 - \frac{2}{N}\right)\Gamma_{(A/B)(A)(B)} \right] \right\} \right\}$$

$$\begin{aligned} \Phi_{(A/A)(B/B)'} &= (1-\mu)^2(1-\nu)^2 \left\{ S \left[\frac{1}{N} \Lambda_3 + \left(1 - \frac{1}{N}\right) \Omega_5 \right] + S(1-S) \left[\frac{2}{N} \Phi_{(AB/A)(B)} \right. \right. \\ &\quad \left. \left. + \left(1 - \frac{2}{N}\right) \Gamma_{(A/A)(B)(B)} \right] + S(1-S) \left[\frac{2}{N} \Phi_{(AB/B)(A)} \right. \right. \\ &\quad \left. \left. + \left(1 - \frac{2}{N}\right) \Gamma_{(B/B)(A)(A)} \right] + (1-S)^2 \left[\frac{2}{N(N-1)} \Omega_6 + \frac{4(N-2)}{N(N-1)} \Pi_3 \right. \right. \\ &\quad \left. \left. + \frac{(N-2)(N-3)}{N(N-1)} \Delta_{(A)(B)(A)(B)} \right] \right\} \end{aligned}$$

$$\begin{aligned} \Phi_{(A/B)(A/B)'} &= (1-\mu)^2(1-\nu)^2 \left\{ S^2 \left[\frac{1}{N} \Lambda_3 + \left(1 - \frac{1}{N}\right) \Omega_6 \right] + 2S(1-S) \left[\frac{1}{N} \Omega_3 + \frac{1}{N} \Omega_4 \right. \right. \\ &\quad \left. \left. + \left(1 - \frac{2}{N}\right) \Gamma_{(A/B)(A)(B)} \right] + (1-S)^2 \left[\frac{1}{N(N-1)} (\Omega_5 + \Omega_6) \right. \right. \\ &\quad \left. \left. + \frac{N-2}{N(N-1)} (\Pi_1 + \Pi_2 + 2\Pi_3) + \frac{(N-2)(N-3)}{N(N-1)} \Delta_{(A)(B)(A)(B)} \right] \right\} \end{aligned}$$

$$\begin{aligned} \Gamma_{(AB)(A)(B)'} &= (1-\mu)^2(1-\nu)^2 \left\{ (1-r) \left[\frac{1}{N^2} \Lambda_3 + \frac{N-1}{N^2} (\Omega_1 + \Omega_3 + \Omega_4) \right. \right. \\ &\quad \left. \left. + \frac{(N-1)(N-2)}{N^2} \Gamma_{(AB)(A)(B)} \right] + r \left[\frac{1}{N^2} \Lambda_3 + \frac{N-1}{N^2} (\Omega_2 + \Omega_3 + \Omega_4) \right. \right. \\ &\quad \left. \left. + \frac{(N-1)(N-2)}{N^2} \Gamma_{(A/B)(A)(B)} \right] \right\} \end{aligned}$$

$$\begin{aligned} \Gamma_{(B/B)(A)(A)'} &= (1-\mu)^2(1-\nu)^2 \left\{ S \left[\frac{1}{N^2} \Lambda_3 + \frac{N-1}{N^2} (2\Omega_4 + \Omega_5) + \frac{(N-1)(N-2)}{N^2} \Pi_2 \right] \right. \\ &\quad \left. + (1-S) \left[\frac{1}{N(N-1)} (\Omega_3 + \Omega_6) + \frac{4(N-2)}{N(N-1)} \Pi_3 \right. \right. \\ &\quad \left. \left. + \frac{(N-2)(N-3)}{N(N-1)} \Delta_{(A)(B)(A)(B)} \right] \right\} \end{aligned}$$

$$\begin{aligned} \Gamma_{(A/A)(B)(B)'} &= (1-\mu)^2(1-\nu)^2 \left\{ S \left[\frac{1}{N^2} \Lambda_3 + \frac{N-1}{N^2} (2\Omega_3 + \Omega_5) + \frac{(N-1)(N-2)}{N^2} \Pi_1 \right] \right. \\ &\quad \left. + (1-S) \left[\frac{1}{N(N-1)} (\Omega_4 + \Omega_6) + \frac{4(N-2)}{N(N-1)} \Pi_3 \right. \right. \\ &\quad \left. \left. + \frac{(N-2)(N-3)}{N(N-1)} \Delta_{(A)(B)(A)(B)} \right] \right\} \end{aligned}$$

$$\begin{aligned} \Gamma_{(A/B)(A)(B)'} &= (1-\mu)^2(1-\nu)^2 \left\{ S \left[\frac{1}{N^2} \Lambda_3 + \frac{N-1}{N^2} (\Omega_3 + \Omega_4 + \Omega_5) \right. \right. \\ &\quad \left. \left. + \frac{(N-1)(N-2)}{N^2} \Pi_3 \right] + (1-S) \left[\frac{1}{N(N-1)} (\Omega_5 + \Omega_6) \right. \right. \\ &\quad \left. \left. + \frac{N-2}{N(N-1)} (\Pi_1 + \Pi_2 + 2\Pi_3) + \frac{(N-2)(N-3)}{N(N-1)} \Delta_{(A)(B)(A)(B)} \right] \right\} \end{aligned}$$

$$\begin{aligned} \Delta_{(A)(B)(A)(B)}' &= (1-\mu)^2(1-\nu)^2 \left[\frac{1}{N^3} \Lambda_3 + \frac{N-1}{N^3} (2\Omega_3 + 2\Omega_4 + \Omega_5 + 2\Omega_6) \right. \\ &\quad + \frac{(N-1)(N-2)}{N^3} (\Pi_1 + \Pi_2 + 4\Pi_3) \\ &\quad \left. + \frac{(N-1)(N-2)(N-3)}{N^3} \Delta_{(A)(B)(A)(B)} \right], \end{aligned}$$

where

$$\begin{aligned} \Lambda_1 &= \frac{1}{2} + \frac{1}{2} \Psi_{(AB/AB)} \\ \Lambda_2 &= \frac{1}{2} \Psi_{(A/A)} + \frac{1}{2} \Psi_{(B/B)} \\ \Lambda_3 &= \frac{1}{4} + \frac{1}{4} \Psi_{(A/A)} + \frac{1}{4} \Psi_{(B/B)} + \frac{1}{4} \Psi_{(AB/AB)} \\ \Omega_1 &= \frac{1}{2} \Phi_{(AB)(AB)} + \frac{1}{2} \Phi_{(AB)(A/B)} \\ \Omega_2 &= \frac{1}{2} \Phi_{(AB)(A/B)} + \frac{1}{2} \Phi_{(A/B)(A/B)} \\ \Omega_3 &= \frac{1}{2} \Phi_{(B)(B)} + \frac{1}{2} \Phi_{(AB/A)(B)} \\ \Omega_4 &= \frac{1}{2} \Phi_{(A)(A)} + \frac{1}{2} \Phi_{(AB/B)(A)} \\ \Omega_5 &= \frac{1}{4} + \frac{1}{4} \Psi_{(A/A)} + \frac{1}{4} \Psi_{(B/B)} + \frac{1}{4} \Phi_{(A/A)(B/B)} \\ \Omega_6 &= \frac{1}{4} \Phi_{(AB)(AB)} + \frac{1}{2} \Phi_{(AB)(A/B)} + \frac{1}{4} \Phi_{(A/B)(A/B)} \\ \Pi_1 &= \frac{1}{2} \Phi_{(B)(B)} + \frac{1}{2} \Gamma_{(A/A)(B)(B)} \\ \Pi_2 &= \frac{1}{2} \Phi_{(A)(A)} + \frac{1}{2} \Gamma_{(B/B)(A)(A)} \\ \Pi_3 &= \frac{1}{2} \Gamma_{(AB)(A)(B)} + \frac{1}{2} \Gamma_{(A/B)(A)(B)}. \end{aligned}$$

If $N \gg 1$, $\mu \approx O\left(\frac{1}{N}\right)$, $\nu \approx O\left(\frac{1}{N}\right)$, and $r \approx O\left(\frac{1}{N}\right)$, then these equations can be approximated by

$$\begin{aligned} \Psi_{(A/A)}' &= S\left(\frac{1}{2} + \frac{1}{2} \Psi_{(A/A)}\right) + (1-S)\Phi_{(A)(A)} \\ \Psi_{(B/B)}' &= S\left(\frac{1}{2} + \frac{1}{2} \Psi_{(B/B)}\right) + (1-S)\Phi_{(B)(B)} \\ \Psi_{(AB/AB)}' &= S\left(\frac{1}{2} + \frac{1}{2} \Psi_{(AB/AB)}\right) + (1-S)\Phi_{(AB)(AB)} \\ \Phi_{(AB)(A/B)}' &= S\left[\frac{1}{2} \Phi_{(AB)(AB)} + \frac{1}{2} \Phi_{(AB)(A/B)}\right] + (1-S)\Gamma_{(AB)(A)(B)} \\ \Phi_{(AB/B)(A)}' &= S\left[\frac{1}{2} \Phi_{(A)(A)} + \frac{1}{2} \Phi_{(AB/B)(A)}\right] + (1-S)\Gamma_{(AB)(A)(B)} \\ \Phi_{(AB/A)(B)}' &= S\left[\frac{1}{2} \Phi_{(B)(B)} + \frac{1}{2} \Phi_{(AB/A)(B)}\right] + (1-S)\Gamma_{(AB)(A)(B)} \\ \Phi_{(A/A)(B/B)}' &= S^2\left[\frac{1}{4} + \frac{1}{4} \Psi_{(A/A)} + \frac{1}{4} \Psi_{(B/B)} + \frac{1}{4} \Phi_{(A/A)(B/B)}\right] \\ &\quad + S(1-S)\left[\Gamma_{(A/A)(B)(B)} + \Gamma_{(B/B)(A)(A)}\right] + (1-S)^2 \Delta_{(A)(B)(A)(B)} \\ \Phi_{(A/B)(A/B)}' &= S^2\left[\frac{1}{4} \Phi_{(AB)(AB)} + \frac{1}{2} \Phi_{(AB)(A/B)} + \frac{1}{4} \Phi_{(A/B)(A/B)}\right] \\ &\quad + 2S(1-S)\Gamma_{(A/B)(A)(B)} + (1-S)^2 \Delta_{(A)(B)(A)(B)} \end{aligned} \tag{A1}$$

$$\Gamma_{(B/B)(A)(A)'} = S[\frac{1}{2}\Phi_{(A)(A)} + \frac{1}{2}\Gamma_{(B/B)(A)(A)}] + (1-S)\Delta_{(A)(B)(A)(B)}$$

$$\Gamma_{(A/A)(B)(B)'} = S[\frac{1}{2}\Phi_{(B)(B)} + \frac{1}{2}\Gamma_{(A/A)(B)(B)}] + (1-S)\Delta_{(A)(B)(A)(B)}$$

$$\Gamma_{(A/B)(A)(B)'} = S[\frac{1}{2}\Gamma_{(AB)(A)(B)} + \frac{1}{2}\Gamma_{(A/B)(A)(B)}] + (1-S)\Delta_{(A)(B)(A)(B)}$$

neglecting terms of $O\left(\frac{1}{N}\right)$ or less, and

$$\Phi_{(A)(A)'} = \frac{1}{N} [\frac{1}{2} + \frac{1}{2}\Psi_{(A/A)}] + (1 - \frac{1}{N} - 2\mu)\Phi_{(A)(A)}$$

$$\Phi_{(B)(B)'} = \frac{1}{N} [\frac{1}{2} + \frac{1}{2}\Psi_{(B/B)}] + (1 - \frac{1}{N} - 2\nu)\Phi_{(B)(B)}$$

$$\Phi_{(AB)(AB)'} = \frac{1}{N} [\frac{1}{2}\Psi_{(AB/AB)}] + (1 - \frac{1}{N} - 2\mu - 2\nu - 2r)\Phi_{(AB)(AB)} + 2r\Phi_{(AB)(A/B)}$$

(A2)

$$\begin{aligned} \Gamma_{(AB)(A)(B)'} &= \frac{1}{N} [\frac{1}{2}\Phi_{(A)(A)} + \frac{1}{2}\Phi_{(AB/B)(A)} + \frac{1}{2}\Phi_{(B)(B)} + \frac{1}{2}\Phi_{(AB/A)(B)} \\ &\quad + \frac{1}{2}\Phi_{(AB)(AB)} + \frac{1}{2}\Phi_{(AB)(A/B)}] \\ &\quad + (1 - \frac{3}{N} - 2\mu - 2\nu - r)\Gamma_{(AB)(A)(B)} + r\Gamma_{(A/B)(A)(B)} \end{aligned}$$

$$\begin{aligned} \Delta_{(A)(B)(A)(B)'} &= \frac{1}{N} [\frac{1}{2} + \frac{1}{2}\Phi_{(A)(A)} + \frac{1}{2}\Gamma_{(B/B)(A)(A)} + \frac{1}{2}\Phi_{(B)(B)} + \frac{1}{2}\Gamma_{(A/A)(B)(B)} \\ &\quad + 2\Gamma_{(AB)(A)(B)} + 2\Gamma_{(A/B)(A)(B)}] + (1 - \frac{6}{N} - 2\mu - 2\nu)\Delta_{(A)(B)(A)(B)} \end{aligned}$$

neglecting terms of $O\left(\frac{1}{N^2}\right)$ or less.