Am J Hum Genet 38:965–970, 1986

Brief Communication

Average Inbreeding or Equilibrium Inbreeding?

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SUMMARY

The equilibrium inbreeding is always higher than the average inbreeding. For human populations with high inbreeding levels, the inbreeding equilibrium is more than 25% higher than the average inbreeding. Assuming no initial inbreeding in the population, the equilibrium inbreeding value is closely approached in 10 generations or less. A secondary effect of this higher inbreeding level is that the equilibrium frequency of recessive detrimental alleles is somewhat lower than expected using average inbreeding.

INTRODUCTION

In human populations, when two or more types of consanguineous matings occur, the inbreeding coefficient is usually calculated as the inbreeding coefficient of the different types of matings weighted by the frequency of each mating type. The inbreeding coefficient calculated in this manner is usually called the average inbreeding coefficient (e.g., [1]) and is defined as

$$\alpha = \sum_{i=1}^{m} p_i f_i \ , \tag{1}$$

where p_i and f_i are the frequency and inbreeding coefficient of the ith mating type. However, some of the individuals in the earlier generations may themselves be the offspring of consanguineous matings. In populations in which there are pedigrees extending over many generations, such matings may be known and incorporated into pedigrees. In many populations, such historical information is not known.

Received September 13, 1985; revised January 6, 1986.

Supported by grant R01 HD 12731 from the National Institutes of Health to Glenys Thomson.

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If it is assumed that the frequencies of different mating types are constant over time, then Hedrick and Cockerham [2] have given the equilibrium inbreeding coefficients as

$$f_e = \frac{\sum_{i=1}^{n} \frac{p_i}{2^i}}{1 - \sum_{i=1}^{n} p_i (1 - ½^i)} , \tag{2}$$

where p_1 is the proportion of selfing; p_2, the proportion of first-degree mating; p_3, second-degree mating, etc., and the remainder of the population, $1 - \Sigma\, p_i$, mates at random. (Note that this expression is an approximation in some cases but its simplicity makes it useful here; for a discussion see [2]). In this model, the population is assumed to be large so that finite population effects can be ignored. Because of the balance between an inbred proportion of the population increasing homozygosity and a random-mating proportion reducing heterozygosity to Hardy-Weinberg proportions, an equilibrium inbreeding coefficient (or heterozygosity proportion) results (see [3] for a discussion of the partial-selfing model). Let us rewrite expression (1) as

$$\alpha = \sum_{i=1}^{n} \frac{p_i}{2^i} \tag{3}$$

by substituting $(½)^i$ for f_i. The ratio of expression (2) over (3) is then

$$\frac{\alpha}{f_e} = 1 - \sum_{i=1}^{n} p_i (1 - ½^i) . \tag{4}$$

In other words, α is less than f_e by the amount given by the summed term on the right. Notice that as i increases to more distant mating types, the term in parentheses becomes larger.

Perhaps a more appropriate term for α would be the immediate inbreeding coefficient. In general, the immediate and equilibrium inbreeding are related as

$$f_e = \alpha + (1 - \alpha) f , \tag{5}$$

where f_e is the total inbreeding, α is the inbreeding coefficient based on current information, and f is the prior inbreeding. The comparison here is between the immediate inbreeding from a particular mating system and the equilibrium that would result if the same mating system had occurred in prior generations.

APPLICATION

To illustrate the difference between α and f_e for some data, the five countries with the highest α given by Cavalli-Sforza and Bodmer ([2], p. 350) were used

TABLE 1

THE PROPORTION OF DIFFERENT MATING TYPES IN FIVE COUNTRIES WITH HIGH INBREEDING (FROM CAVALLI-SFORZA AND BODMER [2])

	p_3 (Uncle-Niece, Aunt-Nephew)	p_4 (First cousin)	p_5 (1½ cousin)	p_6 (Second cousin)
India:				
(a) Andra-Pradesh (1957)...	.0923	.3330	...	...
(b) Andra-Pradesh (1963)...	.0726	.1662	...	...
Guinea....................	...	.1908	.0054	.0622
Japan.....................	...	.0615	.0133	.0228
Brazil....................	.0006	.0263	.0081	.0132
Italy:				
(a) 1916–1920............	.0006	.0217	.0048	.0175
(b) 1921–1925............	.0005	.0185	.0040	.0160

(table 1) (two samples from both Andra-Pradesh, India; and Italy are given). The values of α, f_e and α/f_e for these data are presented in the first three columns of table 2. As expected, the equilibrium inbreeding is always larger than the average inbreeding, the greatest difference occurring for Indian sample (a) where α is only 60.7% of f_e.

The difference between α and f_e is due to two factors: the difference between equilibrium values and the average values that does not account for past generations and the effect of simultaneously having two or more degrees of mating. We can separate these effects by calculating the sum of these individual equilibrium inbreeding effects for comparison. In other words, let us define this as

$$\Sigma f_e = \sum_{i=1}^{n} \frac{p_i}{2^i - p_i(2^i - 1)} \,. \tag{6}$$

The last two columns give these values of Σf_e for the five different countries and the ratio of Σf_e to f_e. Notice that approximately half of the difference between α and f_e is the result of the effect of multiple types of mating.

TABLE 2

THE AVERAGE INBREEDING (α), EQUILIBRIUM INBREEDING (f_e), AND Σf_e FOR THE DATA IN TABLE 1

	α	f_e	α/f_e	Σf_e	$\Sigma f_e/f_e$
India:					
(a)............	.0324	.0533	.607	.0428	.803
(b)............	.0195	.0249	.781	.0220	.884
Guinea..........	.0131	.0173	.757	.0157	.908
Japan...........	.00462	.00509	.907	.00486	.957
Brazil..........	.00218	.00228	.956	.00223	.978
Italy:					
(a)............	.00185	.00194	.954	.00189	.974
(b)............	.00159	.00166	.958	.00162	.976

TIME TO INBREEDING EQUILIBRIUM

How long does it take for a population to reach inbreeding equilibrium? For populations with a significant proportion of self-fertilization, it is known that equilibrium genotypic proportions are approximated in about 5 generations (e.g., [3]). However, here we are concerned with relatively low levels of more remote consanguineous matings. Using the recursion equations of (1), then

$$\begin{aligned} f_{t+4} = {} & \frac{p_3}{2}\left[\tfrac{1}{4}(1 + f_{t+1} + 2f_{t+2}) + f_{t+3}\right] + \frac{p_4}{16}(1 + f_{t+1} + 14f_{t+2}) \\ & + \frac{p_5}{32}(1 + f_t + 2f_{t+1} + 28f_{t+2}) + \frac{p_6}{64}(1 + f_t + 62f_{t+1}) \ , \end{aligned} \tag{7}$$

where the four terms refer to the proportion of uncle-niece and aunt-nephew, first-cousin, 1½-cousin, and second-cousin matings, respectively.

Let us assume that $f_0 = f_1 = f_2 = f_3 = 0$ and then follow the inbreeding coefficient over time. Table 3 gives the number of generations until the inbreeding coefficient is greater than $\alpha + x(f_e - \alpha)$ when x is .5, .95, or .99 using the p_i values in table 1. The generation number given in table 3 is four less than the actual number because the pedigrees need to be extended back 4 generations to allow all four types of inbreeding to occur. Using this assumption, in generation 1, the inbreeding coefficient is α and the inbreeding coefficient quickly increases to the equilibrium value. The increase is fastest for low levels of breeding but only takes 9 generations to reach .95 for the increment in inbreeding to India sample (a). In other words, it only takes a few generations to reach inbreeding equilibrium levels for these amounts of inbreeding.

EFFECT ON ALLELIC FREQUENCY

How much difference is there in equilibrium allelic frequency of a recessive disease using f_e instead of α (the equilibrium genotypic frequencies are the same)? There is some indication that deleterious alleles have lower frequencies

TABLE 3

THE INBREEDING COEFFICIENT IS $\alpha + x\,(f_e - \alpha)$ WHERE x IS .5, .95, OR .99

	x		
	.5	.95	.99
India:			
(a)	3	9	12
(b)	3	6	12
Guinea	3	7	10
Japan	3	7	7
Brazil	3	4	4
Italy:			
(a)	3	4	5
(b)	3	4	6

in populations with long-term inbreeding (e.g., [4]). Haldane [5] gave the equilibrium frequency as

$$q_e = \frac{-f + \left[f^2 + 4(1-f)\frac{u}{s}\right]^{1/2}}{2\,(1-f)}\,, \tag{8}$$

where f is the inbreeding coefficient, u is the mutation rate to the recessive allele, and s is the selective disadvantage of the recessive genotype. To obtain a general impression of the difference between f_e and α, let us substitute them in the above expression for the different populations using u/s ratios of 10^{-5} and 10^{-6} and solve for q_e. Table 4 gives the q_e values and their ratios, showing that the higher level of inbreeding due to inbreeding equilibrium greatly decreases the equilibrium allelic frequency. For example, q_e in India sample (a) when $u/s = 10^{-5}$ using the α value from table 2 is .00031. Using the f_e value from table 2 gives a much lower q_e, only .00019, one that is only 61% of that calculated using the α value. However, for the less inbred populations, the effect is quite small.

CONCLUSION

Average inbreeding values may greatly underestimate the real inbreeding coefficient in a population. Inbreeding equilibrium values for some highly inbred human populations were more than 25% greater than that calculated using the formula for average inbreeding. Furthermore, these equilibrium values are reached in only a few generations. As a result, it seems prudent to use inbreeding equilibrium values rather than average inbreeding to describe inbreeding levels in a population in which the breeding structure has remained constant for several generations.

A further complication arises due to variation in inbreeding over time. However, if there is zero autocorrelation among inbreeding proportions over time, the expected inbreeding is the same as the equilibrium inbreeding [6]. On the

TABLE 4

THE EQUILIBRIUM FREQUENCY OF A RECESSIVE ALLELE WITH AN INBREEDING COEFFICIENT OF α OR f_e FOR TWO VALUES OF u/s

$\frac{u}{s}$	10^{-5}			10^{-6}		
	$q_e(\alpha)$	$q_e(f_e)$	Ratio	$q_e(\alpha)$	$q_e(f_e)$	Ratio
India:						
(a)........	.00031	.00019	.61	.000031	.000019	.61
(b)........	.00050	.00040	.79	.000051	.000040	.78
Guinea......	.00073	.00056	.77	.000076	.000058	.76
Japan.......	.00161	.00152	.94	.000207	.000189	.91
Brazil.......	.00226	.00222	.99	.000389	.000377	.97
Italy:						
(a)........	.00237	.00234	.99	.000437	.000423	.97
(b)........	.00247	.00244	.99	.000483	.000470	.97

other hand, if there is a positive autocorrelation of inbreeding levels over time, then the expected inbreeding is slightly higher than the equilibrium inbreeding [6].

ACKNOWLEDGMENTS

I appreciate the comments of L. L. Cavalli-Sforza, C. C. Cockerham, and J. F. Crow.

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