Letters to the Editor

Am. J. Hum. Genet. 62:000, 1998

On the Probability of Identity States in Permutable Populations: Reply to Cannings

To the Editor:

To extend the affected-sib-pair method to consanguineous populations, we derived the probabilities of the nine condensed identity states as a function of the probability, α, that two genes, drawn at random from the population, will be identical by descent (IBD) (Génin and Clerget-Darpoux 1996). Cannings (1998 [in this issue]) criticizes our derivations and argues that they are correct only in certain very restricted and uninteresting models of populations. He proposes another treatment, which requires three coefficients, α_2, α_3, and α_4. These coefficients represent the probability that two, three, and four genes, respectively, drawn at random from the population, will be IBD (table 1). He compares this model to ours. It should be noted that his comparison was performed with incorrect formulas that we have since corrected in a letter (Génin and Clerget-Darpoux 1998 [in this issue]); unfortunately, our letter had not been published at the time when Cannings (1998) wrote his article. The corrections explain the inconsistencies he notes in our derivations; these inconsistencies are no longer present in the corrected formulas (table 1).

First of all, we would like to emphasize that our derivations were approximations. We agree that Cannings's (1998) derivations of the probabilities of the condensed identity states are more correct, in the sense that they are not approximations. Cannings's coefficient α_2 is equivalent to the kinship coefficient, α, that we have used, but Cannings's other two coefficients, α_3 and α_4, were approximated in our model by α^2 and α^3, respectively. Of course, if either the coefficients α_3 and α_4 or genealogies are available, it is better to use them. However, in most situations, accurate estimates of these two coefficients are either unavailable or very difficult to obtain, and this is also true of genealogies. Weir (1994) reported this difficulty elsewhere and suggested the use of approximations that depend only on the probability α that two genes will be IBD (θ, in his article); these are, in fact, the same approximations that we used. Hence, he proposed to approximate α_3 by α^2, assuming that three genes, a, b, and c, are IBD if a and b are IBD, if b and c are IBD, and if these two events are independent. He further showed that, for the purpose of forensic calculations, these approximations are fairly accurate and that they have the advantage of being analytically simpler. The problem now is to determine whether, for our purpose, the approximations were or were not correct.

To answer this question, we must further describe the population model that we used in our paper (Génin and Clerget-Darpoux 1996); we admit that the model was not discussed in sufficient detail. We considered a population in which mating was random but that derived from a few founders. Consequently, even if the population was in Hardy-Weinberg equilibrium, there was some random inbreeding (Allen 1982). This is exactly the same population model considered by Cannings (1998). The only further assumption in our model was that the F initial founders were assumed to be unrelated and heterozygous for different alleles at the locus under consideration (which means that, in the initial population, α was assumed to be zero). Therefore, a total of $2F$ distinct alleles were present in the population, both at the beginning and across generations. The probability α that two alleles, taken at random in the population, are IBD was thus $\frac{1}{2F}$ (after the first generation). Under these conditions, α can take on only discrete values—for example, $\frac{1}{2}$, $\frac{1}{4}$, or $\frac{1}{6}$, for one, two, or three founders, respectively (the identity-state probabilities are then always greater than or equal to zero). The model assumes that all of the alleles present in the founders are maintained in the population, across generations; this is not true for a small population, because of genetic drift, but it is expected for an infinite population, as in the first model considered by Cannings (1998). The assumption that alleles are unique in the first generation is the only way, in our view, to ensure that two alleles observed to be identical are in fact IBD—and is therefore not a major assumption of the model. Under these conditions, each allele is expected to have the same frequency, and, therefore, as shown by Cannings (1998) himself, α_3 exactly equals α^2, and α_4 equals α^3, which makes our approximations correct. If the population is of finite size and the number of generations is not too large, then allele frequencies will not differ significantly from the original

frequencies in the founder population (i.e., alleles are also expected to have approximately the same frequencies, and approximations would also hold). This can be shown by simulations: if we assume that there are 10 founder genes and a population size of 100 genes at each generation, after 10 generations of random mating, the expected distribution of identity states for the 100 genes, computed with our approximations, is significantly different, from the one computed with Cannings's model, in only 6/1,000 replicates (when the mutation rate is zero) and in 2/1,000 replicates (when the mutation rate is 10^{-5}). Of course, if the population has diverged for only 10 generations, the stability of the inbreeding coefficient α and of the kinship coefficient ϕ is not reached; but, in most situations, the variation of these coefficients from one generation to the next is expected to be small, so that $\alpha \approx \phi$. In conclusion, we think that our approximations are correct in most situations that involve a population that is diverging from a few unrelated founders and is expanding rapidly.

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0002-9297/98/6203-0032$02.00