of the various populations studied by this method, it is difficult to have confidence in estimates of ϕd or a, the intercept in the Malécot formulation.

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To the Editor: The treatment of random phenotype pairs by Harpending is simpler and more accurate than our approximation. To compare the two results, we must include the scalar factor L to which Harpending refers. He considers that it measures kinship of random pairs within the region and is not readily estimable. We consider that it represents kinship of random pairs at large distances, which includes differentiation due to disruptive selection (clines) as well as random kinship, and can be estimated from kinship of the class at greatest distance (or from mean kinship if the region is large). We assumed that, as in [1],

$$\varphi_d = (1 - L)\, ae^{-bd} + L. \tag{1}$$

If D represents the class at greatest distance, we have $ae^{-bD} \doteq 0$. Letting $\varphi'(d) \equiv (\varphi_d - \varphi_D)/(1 - \varphi_D)$ be the adjusted value of φ_d, we see that $\varphi'_d = ae^{-bd}$. Harpending shows that it is better to take

$$\varphi_d = (1 - L)a[1 + 2e^{-bd}]/3 + L, \tag{2}$$

where for the class at greatest distance $\varphi_D \doteq (1 - L)a/3 + L$. Again letting $\varphi'_d \equiv (\varphi_d - \varphi_D)/(1 - \varphi_D)$, we find that for Harpending's formula

$$\varphi'_d = \frac{2ae^{-bd}(1 - L)}{3(1 - \varphi_D)} \doteq \frac{2ae^{-bd}}{3}.$$

Thus the estimate of b is unchanged, but the estimate of a from equation (1) should be multiplied by 1.5.

Would that this were the only problem in bioassay of phenotype pairs. At least two other difficulties are encountered. First, if samples of size N_i and N_j are drawn from populations I and J, the number of different phenotype pairs that can be formed without replacement is $N_i(N_i - 1)/2$ within I, $N_j(N_j - 1)/2$ within J, and N_iN_j between I and J. As a result, a sample contributes to the estimate of kinship within populations (φ_0) in proportion to $N(N - 1)$, giving too much weight to large samples. Second, even the Harpending formula is approximate, primarily because of ignoring terms in φ^2. This limits the usefulness of phenotype pairs to cases where the smallest gene frequency is greater than φ_0.

For the past year we have been using a method which pairs gene frequencies rather than phenotypes, and therefore does not suffer from the above two problems

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[7]. In addition, it lends itself to estimation of kinship between each pair of populations, making kinship an ideal metric for genetic distance. As expected, the unbiased estimates of a and b by this method tend to be higher than for phenotype pairs, even by equation (2). Probably in the future, phenotype pairs will be used only for mates and for random pairs from regions very sparsely sampled, so that the sample size from a locality is often too small to give reliable estimates of gene frequencies—then equation (2) applies.

The history of kinship bioassay has spanned phenotypes [8], which require enormous samples and are easily biased by selection and other factors; phenotype pairs, first crudely and now more exactly treated; and finally gene-frequency pairs, which at present seem most promising. The importance of bioassay can hardly be overestimated for studies of kinship, since it is the only test of predictions from pedigrees, migration, or Monte Carlo simulation, which are extrapolated from a much smaller number of generations than were required to establish kinship.

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