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Genetic structure of forensic populations

(population structure/DNA typing/forensic science/genetic identity)

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ABSTRACT **DNA-based identification depends on the probability that two different individuals have the same phenotype, which is given by kinship theory. Together with the large and consistent body of evidence on human population structure, kinship theory provides a sound basis for forensic use of DNA markers.**

Recent years have seen a debate on the validity of DNA-based identification in forensic science. Opponents cite general principles that would apply with equal force were the suspect a *Drosophila* or other organism whose population structure is little known, neglecting the large body of evidence in humans (1, 2). Proponents defend current procedures to calculate matching probabilities, without noting that these procedures are a special case of a more general theory that places useful limits on their results (3, 4). Because there is now general agreement on the technical reliability of DNA testing in competent hands, the principal constraint on the forensic use of matching probabilities is in the evaluation of evidence from population genetics (5). This constraint is all the more remarkable because both theory and data are the fruit of a generation of research on population structure, which ended only when the major problems of general significance appeared solved (6). Here I shall recall the theory, make extensions required for forensic populations, and recapitulate the evidence on which legal use of matching probabilities should be based.

Definitions

The basic calculation deals with phenotype i from system j in population k ($i = 1, \ldots, I; j = 1, \ldots, J; k = 1, \ldots, K$). The phenotype may or may not have a 1:1 correspondence to genotype, the system may or may not be a single locus, and the population may or may not be an aggregation of subpopulations with different phenotype frequencies. A population is assumed to be formed by indefinitely many gametes and, therefore, to be infinite. We are concerned with two diploid individuals, which I shall call the "suspect" and the "culprit" although in a significant proportion of cases the suspect is a victim and the culprit is DNA from the victim or another person. I shall not explicitly consider paternity trials in which the suspect is a defendant and two other individuals, a child and his mother, complete the evidence, but the same considerations of population structure apply.

If the suspect and the culprit do not match, no issue of population structure arises. However, if they do match, we must assess the weight of evidence favoring their identity, which depends on two probabilities. P_i^{jk} is the probability of drawing phenotype i from system j when population k is sampled at random. C_i^{jk} is the conditional probability that the culprit has the same phenotype at system j as the suspect, given that the suspect has phenotype i, the culprit is a different individual, and both are drawn from population k under a specified sampling rule. Current applications are entirely in terms of P_i^{jk}, but it is C_i^{jk} that defines the weight of evidence. They are interrelated as

$$C_i^{jk} = M_i^{jk}/P_i^{jk},$$

where M_i^{jk} is the probability of drawing two individuals with phenotype i at system j from population k under a specified sampling rule.

From these basic parameters the average matching probability M^{jk} may be derived, which is the probability of the same phenotype (not otherwise specified) where two individuals are drawn from system j in population k under a specified sampling rule,

$$M^{jk} = \sum_i P_i^{jk} C_i^{jk} = \sum_i M_i^{jk}.$$

The power of the jth system to exclude identity in population k is $1 - M^{jk}$, the exclusion probability.

Models for P_i^{jk}

To specify P_i^{jk} there are two nonparametric models (empirical and Laplace) and four parametric models (Hardy–Weinberg, endogamy, null allele, and binning). The empirical model takes

$$P_i^{jk} = n_i^{jk}/n^{jk}, \qquad [1]$$

where n_i^{jk} is the number of individuals of phenotype i at system j in a random sample from population k, and $n^{jk} = \Sigma_i n_i^{jk}$ is the number of individuals typed for system j in that sample. While appealingly simple, this model overestimates frequencies with $n_i^{jk} > 0$ and underestimates frequencies with $n_i^{jk} = 0$. A polymorphism with R alleles generates $R(R + 1)/2$ genotypes, and so some phenotypes are likely not to be observed if n^{jk} is small and R is large. We hesitate to assume that P_i^{jk} is zero and, therefore, may adopt the law of succession of Laplace, which supposes a uniform prior probability for P_i^{jk}. If the ith phenotype is thought to exist in population k,

$$P_i^{jk} = \begin{cases} 1/(n^{jk} + 1) & \text{if } n_i^{jk} = 0 \\ n_i^{jk}/(n^{jk} + 1) & \text{if } n_i^{jk} > 0. \end{cases} \qquad [2]$$

This method has with justice been critically discussed (e.g., ref. 7), but it gives a consistent estimator that is conservative in the sense of overestimating the frequency of rare phenotypes at the expense of common phenotypes, retaining the fundamental property that $\Sigma_i P_i^{jk} = 1$.

Both the empirical and Laplace models can be applied to systems that are not factor-union (8) or that involve two or more loci, and to populations that are stratified. Parametric models, when their assumptions are valid, are more informative. All interpret the system j as a single locus (which I shall take to be autosomal) and the phenotype i as either a

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heterozygote $G_r^j G_s^j$ or a homozygote $G_r^j G_r^j$ with observed numbers n_{rs}^{jk} and n_{rr}^{jk}, respectively. A 1:1 correspondence between genotype and phenotype is assumed unless otherwise stated.

The Hardy–Weinberg model of panmixia assumes that

$$P_i^{jk} = \begin{cases} 2q_r^{jk}q_s^{jk} & \text{if } i = G_r^jG_s^j,\ r \neq s \\ (q_r^{jk})^2 & \text{if } i = G_r^jG_r^j \end{cases}. \quad [3]$$

The maximum likelihood estimate of q_r^{jk} is

$$q_r^{jk} = (2n_{rr}^{jk} + \sum_{s\neq r} n_{rs}^{jk})/2n^{jk}.$$

If this value is zero for m^{jk} alleles thought to be present in population k, the Laplace estimate may be used:

$$q_r^{jk} = \begin{cases} (2n_{rr}^{jk} + \sum_{s\neq r} n_{rs}^{jk} + 1)/(2n^{jk} + m^{jk}) & \text{if } n_{rs} = 0 \\ (2n_{rr}^{jk} + \sum_{s\neq r} n_{rs}^{jk})/(2n^{jk} + m^{jk}) & \text{if } n_{rs} > 0 \end{cases}. \quad [4]$$

However, missing alleles are less of a problem for parametric models than are missing phenotypes for nonparametric models, except for small samples from hypervariable loci, a combination that should be avoided as far as possible.

If population k is made up of subpopulations that tend to marry endogamously, Wright's generalization of panmixia is parsimonious and appropriate (9). The endogamy model is

$$P_i^{jk} = \begin{cases} 2\,q_r^{jk}q_s^{jk}(1-\alpha^{jk}) & \text{if } i = G_r^j\,G_s^j,\ r \neq s \\ q_r^{jk}\,[q_r^{jk} + \alpha^{jk}\,(1-q_r^{jk})] & \text{if } i = G_r^j\,G_r^j \end{cases}, \quad [5]$$

where α^{jk} is the inbreeding coefficient for system j in population k. The effect of endogamy is to create a positive value of α^{jk} in the 0, 1 interval. The practice in forensics of taking the frequency of $G_r^jG_r^j$ as $2q_r^{jk}$ corresponds to the logically impossible value $\alpha^{jk} = (2 - q_r^{jk})/(1 - q_r^{jk})$, which gives negative frequencies if applied to heterozygotes or $\Sigma_i P_i^{jk} > 1$ otherwise (10).

In some systems there may be a recessive null (or silent) allele G_0^j with a fragment so small that it migrates off the gel or so large that its movement from the origin is not detected. Then the phenotype frequencies under panmixia are

$$P_i^{jk} = \begin{cases} 2q_r^{jk}q_s^{jk} & \text{if } i = G_r^jG_s^j,\ r \neq s \neq 0 \\ q_r^{jk}\,(q_r^{jk} + 2q_0^{jk}) & \text{if } i = G_r^jG_r^j,\ r \neq 0 \\ (q_0^{jk})^2 & \text{if } i = G_0^jG_0^j \end{cases} \quad [6]$$

If the null allele is uncommon, the homozygote $G_0^jG_0^j$ may not be observed or may be misinterpreted as a denatured and, therefore, unclassifiable sample. In that event the presence of a null allele will go undetected and q_r^{jk} for $r > 0$ will be incorrectly estimated by maximum likelihood as

$$q_r^{jk*} = q_r^{jk}/\,(1 - q_0^{jk}).$$

Then the apparent frequency of heterozygotes involving G_r^j is

$$2q_r^{jk}\,(1 - q_r^{jk} - q_0^{jk}) = 2q_r^{jk*}\,(1 - q_r^{jk*})\,(1 - \lambda^{jk}), \quad [7]$$

which implies that $\lambda^{jk} = q_0^{jk}\,(2 - q_0^{jk})$ is indistinguishable from an inbreeding coefficient α^{jk} in a population sample, although the segregation of G_0^j may be apparent in families. Moreover, if the existence of a null allele is suspected, and its frequency is estimated simultaneously, there is virtually no information about α^{jk} even in an enormous sample (11–13).

At a hypervariable locus, or more generally when two bands migrate to nearly the same position, a heterozygote between two similar alleles may be misclassified as a homozygote. Let a bin be defined as an interval within which bands are not distinguished and let ε^{jk} be the proportion of heterozygotes that are consequently misclassified. Then under panmixia the expected frequency of recognized heterozygotes is

$$2\sum_r q_r^{jk}\,(1 - q_r^{jk})\,(1 - \varepsilon^{jk}). \quad [8]$$

Therefore ε^{jk} enters into phenotype probabilities in much the same way as an inbreeding coefficient, although there are slight variations among alleles, the estimated gene frequencies of which will be distorted so as to make discrimination from endogamy impractical.

The effects of endogamy, binning, and null alleles are independent, generating an apparent inbreeding coefficient

$$F^{jk} = 1 - (1 - \alpha^{jk})\,(1 - \varepsilon^{jk})\,(1 - \lambda^{jk}) \doteq \alpha^{jk} + \varepsilon^{jk} + \lambda^{jk}, \quad [9]$$

in which all components are positive, and $0 \leq F^{jk} \leq 1$. It is F^{jk} rather than α^{jk} that can be bioassayed from the phenotype distribution P_i^{jk} in Eq. 5 on the assumption of a 1:1 correspondence between phenotype and genotype (11). The maximum likelihood score for F^{jk} under the null hypothesis is

$$u = \sum_{r=1} \left(\frac{1 - q_r^{jk}}{q_r^{jk}}\right) n_{rr}^{jk} - \sum_{s\neq r} n_{rs}$$

with information

$$w = (R - 1)n^{jk}.$$

A system with 10 alleles and a sample size of 10,000 estimates F^{jk} with a SE of 0.003. The requirement for very large samples favors sharing of records on DNA typing over regions and countries, which would provide more efficient estimation of genetic diversity (14).

Models for M_i^{jk}

There are three models for the matching probability (independent, cognate, and affinal). In the independent model the culprit is randomly drawn from population k. Therefore $M_i^{jk} = (P_i^{jk})^2$ and so $C_i^{jk} = P_i^{jk}$. This is the only model appropriate assuming the culprit to belong to a different population from the suspect, which tends to minimize the matching probability. Therefore the assumption of the same population is less controversial.

In the cognate model the culprit is a regular relative of the suspect with probability c_p of having p genes identical by descent (15). (Relatives are regular if their parents are not inbred.) Then

$$M_i^{jk} = \begin{cases} c_2 + c_1\,q_r^{jk} + c_0\,(q_r^{jk})^2 & \text{if } i = G_r^jG_r^j \\ c_2 + c_1(q_r^{jk} + q_s^{jk})/2 + 2c_0\,q_r^{jk}q_s^{jk} & \text{if } i = G_r^jG_s^j \text{ for } r \neq s \end{cases}. \quad [10]$$

In the affinal model the culprit is related to the suspect as closely as a spouse would be. This removes the restriction to regular relatives (16). The probabilities up to linear terms in α^{jk} are

$$M_i^{jk} = \begin{cases} (q_r^{jk})^4 + 6\,(q_r^{jk})^3\,(1 - q_r^{jk})\,\alpha^{jk} & \text{if } i = G_r^jG_r^j \\ 4\,(q_r^{jk})^2\,(q_s^{jk})^2 + 4\,q_r^{jk}q_s^{jk}\,(q_r^{jk} + q_s^{jk} - 6\,q_r^{jk}q_s^{jk})\,\alpha^{jk} & \text{if } i = G_r^jG_s^j,\ r \neq s \end{cases}.$$

Therefore

$$C_i^{jk} = \begin{cases} (q_r^{jk})^2 + 5q_r^{jk}(1 - q_r^{jk})\alpha^{jk} \\ 2q_r^{jk}q_s^{jk}\left[1 + \dfrac{q_r^{jk} + q_s^{jk} - 5\,q_r^{jk}q_s^{jk}}{q_r^{jk}q_s^{jk}}\alpha^{jk}\right] \end{cases} \quad \begin{matrix} \text{if } i = G_r^j G_r^j \\ \text{if } i = G_r^j G_s^j,\ r \neq s' \end{matrix} \quad [11]$$

ignoring terms in $(\alpha^{jk})^2$. The coefficient 6 reflects the $\binom{4}{2}$ ways in which the four alleles of suspect and culprit may be related. The coefficient 5 indicates that one of these paths has been removed by conditioning on two alleles of the suspect. Binning and null alleles do not contribute to kinship between suspect and culprit, and so the apparent inbreeding coefficient that replaces α^{jk} in Eq. 11 is

$$F^{jk} = \alpha^{jk} + (\varepsilon^{jk} + \lambda^{jk})/5. \quad [12]$$

Combination of Systems

There are three models to combine matching probabilities over systems (empirical, independent, and pairwise dependent). The empirical model notes that n^k random individuals in population k have been tested for all J systems, none of whom has the same phenotypes as the suspect. Then a confidence interval of strength P is given by

$$C^k < (-\ln P)/n^k. \quad [13]$$

For example, with $n^k = 1000$ and $P = 0.01$, we would be confident that the matching probability is <0.005, but we could not say how much less, whereas parametric models would indicate a much smaller limit. Therefore, the empirical frequency of a combined match is a necessary but not sufficient part of the evidence.

The independent model takes

$$C^k = \prod_j C_i^{jk}. \quad [14]$$

This simple approach has been attacked on the grounds that independence has not been proven (1, 2). Because highly polymorphic systems are preferred, most values of C_i^{jk} will be small and their product infinitesimal. In such a sparse contingency table a general test of independence is impractical, even in an enormous sample. However, we are concerned only with the probability of a complete match, and for this there is a feasible approach. Let x and y represent the matching probabilities C_i^{jk} and $C_{i'}^{j'k}$ for systems j and j', respectively. Table 1 shows how to test for pairwise independence by maximum likelihood scores u and their information w in a model that gives

$$C^k = \prod_j C_i^{jk} e^z, \quad [15]$$

where

$$z = (J - 1)\sum u/\sum w,$$

and the summation is taken over all $\binom{J}{2}$ pairs of loci. Available evidence favors z near zero and, therefore, little effect of this refinement on matching probabilities (17).

If γ is the proportion of suspects who are guilty, the conditional probability that the suspect is the culprit, given a match with probability C^k, is

$$\rho = \frac{\gamma}{\gamma + (1 - \gamma)C^k}, \quad [16]$$

Table 1. Probability of a match by chance on two systems

	j' match	j' no match
j match		
Expected	xye^θ/Σ	$x(1 - y)/\Sigma$
Observed	a	b
j no match		
Expected	$(1 - x)y/\Sigma$	$(1 - x)(1 - y)/\Sigma$
Observed	c	d

$\Sigma = 1 - xy + xye^\theta$, $n = a + b + c + d$; H_0, $\theta = 0$; *ML* score, $u = (ad - bc)/n$; information, $w = (a + b)(c + d)(a + c)(b + d)/n^3$; $\chi^2 = u^2/w$.

where the frequency of conviction might be taken as a rough estimate of γ. This Bayesian calculation may be presented as an alternative way of looking at C^k, but it should not be emphasized because it requires an assumption about γ that may well depend on time, location, social class, population, age, ancillary evidence, circumstances of the offence, and other factors.

In the above equations the average matching probability M^{jk} may be substituted for C_i^{jk} if it is desired to calculate expected matching probabilities, averaged over all phenotypes.

Definition of Populations

Reliable gene frequencies require large samples, especially for hypervariable loci. Therefore, only major populations are of interest, their stratification being represented by inbreeding coefficients α^{jk}. A major population is called a race in the vernacular and an ethnic group by the fastidious. Race may be defined in three ways (genealogical, phenotypic, and testimonial). The genealogical definition specifies the populations of all close ancestors. It is precise but impractical. The phenotypic definition, often influenced by name, costume, or social status, is unreliable, except for categories like Caucasian, Oriental, or Black. Even these can be misinterpreted if there is racial admixture or brief observation. In the United Kingdom Caucasoids from the Indian subcontinent may be confounded with Orientals as "Asians." The Hispanic population of the United States is a favorite target for critics of DNA testing, because it subsumes a Caribbean element on the East coast with more African than American Indian ancestry and a southwestern subpopulation in which this admixture is reversed. Samples classified by region of residence are especially suitable to test models of genetic structure for forensic populations.

Much racial classification is by testimony of the suspect, which is usually more detailed and sometimes more fanciful than phenotypic classification. Mixed or ambiguous race requires samples from two or more populations. Let f_k be the prior probability of the kth race. There is a synthetic population in which the frequency of G_r^j is $\Sigma_k f_k q_r^{jk}$ with equilibrium inbreeding $\Sigma f_k F^{jk}$. If a matching probability is calculated for each putative race and the synthetic race, the largest of these values might be used. Interracial crosses, which may have negative values of α^{jk}, have been treated in some detail (18).

Estimates of α^k

The three most important models of population structure relate to islands, isolation by distance, and hierarchical structure. The island model (9) states that kinship φ_k within population k is a balance between evolutionary size N_k and effective migration rate m_k,

$$\varphi_k = 1/(4N_k m_k + 1). \quad [17]$$

The isolation by distance model (19) states that kinship $\varphi(d)$ at distance d in an array of local populations within a region is approximately

$$\varphi(d) = (1 - L)ae^{-bd} + L. \quad [18]$$

The hierarchical model (9) states that

$$F_{IT} = F_{ST}(1 - F_{IS}) + F_{IS}, \quad [19]$$

where I denotes a local population belonging to a subpopulation (region) S within a major population T. In terms of Eq. 18,

$$F_{IT} = ae^{-bd}$$

$$F_{ST} = -L/(1 - L). \quad [20]$$

These models assume that $\alpha^{jk} = \alpha^k$ as for drift without selection. This is certainly not true among races but appears to hold within a major population. On the condition that the major population is panmictic, $\alpha^k = 0$. On the condition that the major population is divided into endogamous regions, within which there is panmixia, and that the suspect and culprit are randomly and independently drawn from the major population, α^k should be equated to F_{ST}, and the independent model should be used for M_i^{jk}. On the condition that the major population is divided into endogamous regions within which there is panmixia, and the suspect and culprit are randomly and independently drawn from the same region, α^k should be equated to F_{ST}, and the affinal model should be used for M_i^{jk}.

The expert witness who bases his calculations solely on the first condition obtains the smallest matching probabilities and the most painful crossexamination. The counsel for the defense who prefers the third condition must explain why both individuals are credibly drawn from the same subpopulation unless the suspect is the culprit. In exceptional cases it may be asserted that the suspect comes from the same local population and, therefore, F_{IT} should be substituted for F_{ST}. The effect of these assumptions is to increase the matching probability and, therefore, to decrease the weight of evidence. This can be compensated by more DNA testing, and so the evidence required by the court will be a balance between cost and credibility.

It remains to summarize the available evidence on α^k. Unfortunately many studies of population structure are directed solely to inferring phylogeny and use a metric of the type F_{IT}/a that gives no information about α^k (20, 21). Even with this waste, the population structure of humans is better known than for any other organism. In most of the world isolation by distance is reinforced by preferential consanguineous marriage, difficult and hazardous travel, bigotry, and xenophobia. We are concerned with the more homogeneous populations in which forensic science is practiced. Information comes from genealogies, migration, isonymy, rare genes, and polymorphisms (Table 2).

The genealogical method uses the frequencies of close consanguineous marriages to estimate inbreeding at equilibrium. Typically first cousin marriages account for half of the total inbreeding (22). Frequencies of consanguineous marriages have declined dramatically in developed countries, and to that extent the estimates in Table 2 are too large. However, events in the past, including small population size and selection, are not allowed for in the genealogical method, which underestimates α^k for polymorphisms. Migration gives F_{ST} as $\Sigma_h \Sigma_{h'} f_h f_{h'} \varphi_{hh'}$, where $f_{h,h'}$ is the proportion of the regional population born in locality h, and $\varphi_{hh'}$ is kinship between localities h and h'. Isonymy estimates F_{ST} as $\Sigma q_r^2/4$, where q_r is the regional frequency of the rth surname. Bioassay of kinship best reflects drift and selection in the past but is inflated by mistyping and sampling errors. The large body of evidence in Table 2 indicates that $F_{ST} < 0.01$ for nearly all forensic situations and, therefore, dominated in many systems by effects of null alleles and binning even in populations with more local differentiation than the United States. F_{IT} is much more variable and in the most extreme isolates (seldom encountered in court) approaches the value of 0.15 observed for major races (39).

Table 2. Kinship F_{ST} in contemporary populations

Source	Region	F_{ST}	Reference
Genealogy	Belgium	0.0019	22
	United States	0.0001	22
	Norway	0.0022	22
	Japan	0.0043	22
	England	0.0004	22
	Switzerland	0.0010	22
	Mexico	0.0008	22
Migration	Ireland	0.0004	23
	Aland Islands	0.0009	24
Isonymy	Ireland	0.0003	25
	Brazil	0.0012	26
	Switzerland	0.0004	27
	Caucasians	0.0003	28
	Japan	0.0005	28
Rare genes	Cystic fibrosis	0.0043	29
	Minor race	0.0005	17
	Major race	0.0009	17
Polymorphisms	Aland Islands	0.0020	30
	Northern England	0.0022	31
	Ireland	0.0006	25
	Ferrara Province	0.0029	32
	Belgium	0.0002	33
	Japan	0.0001	26
	Sweden	0.0006	26
	Switzerland	0.0006	27
	Brazil	0.0010	26
	Finland	0.0022	34
	Sardinia	0.0013	35
	United Kingdom	0.0014	36
	Iceland	0.0012	23
	France	0.0006	37
	Europe	0.0010	38
	Jews	0.0040	38

Discussion

The theory of this paper covers a wide range of genetic structures but does not specify the models or parameters to be used for a particular case. This treatment gives ample scope for prosecution and defense to present different arguments on the same evidence, on the condition that samples of major forensic populations are the basis of inference. However, this condition may be attacked by the defense in three ways. (*i*) The Cohen defense (1) is that forensic samples are not randomly drawn from a precisely specified universe, but neither are suspects or culprits, and precise definition does not assure relevance. The forensic sample for each race is sufficient, without requiring that the sample be representative of a general population at liberty. Therefore, this argument has not been entertained for blood groups, dermatoglyphics, ballistics, or other evidence.

(*ii*) The Lander defense insists that "regardless of the defendant's ethnic background, each allele frequency used (should) be the maximum observed in various ethnic samples" (2). The latter are not specified, except that they be "a dozen or so well-separated ethnic population samples," not necessarily including the population of the suspect. At a single locus the culprit might be assumed to be a Lapp for

allele G_r and a Hottentot for G_s. The resulting calculations are not even probabilities because $\Sigma q_{max} > 1$. However extensively our species might be sampled, an ethnic sample could always be found with an apparently higher gene frequency, either through drift, mistyping, or sampling error. The Lander defense is certainly conservative (of culprits), but few courts could follow his logic.

(*iii*) The Lewontin–Hartl defense is similar in intent, but very different in logic (40). It insists that k must be chosen to match the suspect's subpopulation, not assumed to be endogamous, however narrowly defined and however poorly supported his claim to that subpopulation may be, and in the absence of any evidence that the culprit belongs to that subpopulation. Were this principle accepted by the court, the defense could try to define the subpopulation so that no reliable sample is available. "When does population gathering stop, and how is it used?" (3). If the suspect pleads the Fifth Amendment, there is no information on testimonial race (41). Because the suspect cannot be assigned to a subpopulation, the Lewontin–Hartl defense is that no matching probability can be calculated. Case law will determine whether such argument, unsupported by genetic evidence, is permissible.

To protect the suspect, the Lander and Lewontin–Hartl defenses argue that the calculation of matching probability should be absurdly conservative. The methods of this paper allow a court to be conservative without being absurd.

1. Cohen, J. E. (1990) *Am. J. Hum. Genet.* **46,** 358–368.
2. Lander, E. S. (1991) *Am. J. Hum. Genet.* **48,** 819–823.
3. Caskey, C. T. (1991) *Am. J. Hum. Genet.* **49,** 893–894.
4. Cotton, R. W., Forman, L. & Word, C. J. (1991) *Am. J. Hum. Genet.* **49,** 898–899.
5. Lander, E. S. (1991) *Am. J. Hum. Genet.* **49,** 899–903.
6. Morton, N. E. (1982) *Outline of Genetic Epidemiology* (Karger, Basel), pp. 105–146.
7. Feller, W. (1957) *An Introduction to Probability Theory and Its Applications* (Wiley, New York), Vol. 1, pp. 113–114.
8. Cotterman, C. W. (1969) in *Computer Applications in Genetics*, ed. Morton, N. E. (Univ. of Hawaii Press, Honolulu), pp. 1–19.
9. Wright, S. (1969) *Evolution and the Genetics of Populations* (Univ. of Chicago Press, Chicago), Vol. 2.
10. Budowle, B., Giusti, A. M., Waye, J. S., Baechtel, F. S., Fourney, R. M., Adams, D. E., Presley, L. A., Deadman, H. A. & Monson, K. L. (1991) *Am. J. Hum. Genet.* **48,** 841–855.
11. Yasuda, N. (1968) *Biometrics* **24,** 915–935.
12. Morton, N. E. & Yee, S. (1970) *Am. J. Hum. Genet.* **22,** 112–113.
13. Edwards, A. W. F. (1971) *Am. J. Hum. Genet.* **23,** 97–98.
14. Morton, N. E. (1975) *Theor. Pop. Biol.* **7,** 246–255.
15. Cotterman, C. W. (1940) *A Calculus for Statistical Genetics* (Ohio State Univ., Columbus).
16. Yasuda, N. (1968) *Am. J. Hum. Genet.* **20,** 1–23.
17. Mi, M. P. & Morton, N. E. (1966) *Vox Sang.* **11,** 434–449.
18. Morton, N. E., Chung, C. S. & Mi, M. P. (1967) *Genetics of Interracial Crosses in Hawaii* (Karger, New York).
19. Malecot, G. (1975) *Theor. Pop. Biol.* **8,** 212–241.
20. Nei, M. (1974) in *Genetic Distance*, eds. Crow, J. F. & Denniston, C. (Plenum, New York), pp. 63–76.
21. Sokal, R. R. & Wartenberg, D. E. (1983) *Genetics* **105,** 219–237.
22. Morton, N. E. (1982) in *Current Developments in Anthropological Genetics*, eds. Crawford, M. H. & Mielke, J. H. (Plenum, New York), Vol. 2, pp. 449–466.
23. Jorde, L. B. (1980) in *Current Developments in Anthropological Genetics*, eds. Mielke, J. H. & Crawford, M. H. (Plenum, New York), Vol. 1, pp. 135–208.
24. Workman, P. L. & Jorde, L. B. (1980) in *Population Structure and Genetic Disorders*, eds. Eriksson, A. W., Forsius, H., Nevanlinna, H. R., Workman, P. L. & Norio, R. K. (Academic, London), pp. 487–508.
25. Lees, F. C. & Relethford, J. H. (1982) in *Current Developments in Anthropological Genetics*, eds. Crawford, M. H. & Mielke, J. H. (Plenum, New York), Vol. 2, pp. 385–428.
26. Imaizumi, Y. & Morton, N. E. (1969) *Hum. Hered.* **19,** 433–443.
27. Morton, N. E., Klein, D., Hussels, I. E., Dodinval, P., Todorov, A., Lew, R. & Yee, S. (1973) *Am. J. Hum. Genet.* **25,** 347–361.
28. Yasuda, N. & Morton, N. E. (1967) in *Proceeding of the Third International Congress of Human Genetics*, eds. Crow, J. F. & Neel, J. V. (Johns Hopkins Press, Baltimore), pp. 249–265.
29. Wright, S. W. & Morton, N. E. (1968) *Am. J. Hum. Genet.* **20,** 157–169.
30. Jorde, L. B., Workman, P. L. & Eriksson, A. W. (1982) in *Current Developments in Anthropological Genetics*, eds. Crawford, M. H. & Mielke, J. H. (Plenum, New York), Vol. 2, pp. 333–366.
31. Roberts, D. F. (1982) in *Current Developments in Anthropological Genetics*, eds. Crawford, M. H. & Mielke, J. H. (Plenum, New York), Vol. 2, pp. 367–384.
32. Zanardi, P., Dell'Acqua, G., Menini, C. & Barrai, I. (1977) *Am. J. Hum. Genet.* **29,** 169–177.
33. Dodinval, P. (1970) *Hum. Hered.* **20,** 169–177.
34. Workman, P. L., Mielke, J. H. & Nevanlinna, H. R. (1976) *Am. J. Phys. Anthropol.* **44,** 341–368.
35. Workman, P. L., Lucarelli, P., Agostino, R., Scarabino, R., Scacchi, R., Carapella, E., Palmarino, R. & Bottini, E. (1975) *Am. J. Phys. Anthropol.* **43,** 165–176.
36. Imaizumi, Y. (1974) *Hum. Hered.* **24,** 151–159.
37. Ohayon, E. & Cambon-Thomsen, A. (1986) *Genetique des Populations Humaines* (Institut National de la Santé et de la Recherche Médicale, Paris).
38. Morton, N. E., Kenett, R., Yee, S. & Lew, R. (1982) *Curr. Anthropol.* **23,** 157–167.
39. Morton, N. E. & Keats, B. (1976) in *Human Biology*, Series 6, Australian Institute of Aboriginal Studies, eds. Kirk, R. L. & Thorne, A. G. (Humana, Clifton, NJ), pp. 379–399.
40. Lewontin, R. C. & Hartl, D. L. (1991) *Science* **254,** 1745–1750.
41. Wooley, J. R. (1991) *Am. J. Hum. Genet.* **49,** 892–893.