

Inference of Population Structure Using Multilocus Genotype Data: Linked Loci and Correlated Allele Frequencies

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ABSTRACT

We describe extensions to the method of Pritchard *et al.* for inferring population structure from multilocus genotype data. Most importantly, we develop methods that allow for linkage between loci. The new model accounts for the correlations between linked loci that arise in admixed populations ("admixture linkage disequilibrium"). This modification has several advantages, allowing (1) detection of admixture events farther back into the past, (2) inference of the population of origin of chromosomal regions, and (3) more accurate estimates of statistical uncertainty when linked loci are used. It is also of potential use for admixture mapping. In addition, we describe a new prior model for the allele frequencies within each population, which allows identification of subtle population subdivisions that were not detectable using the existing method. We present results applying the new methods to study admixture in African-Americans, recombination in *Helicobacter pylori*, and drift in populations of *Drosophila melanogaster*. The methods are implemented in a program, *structure*, version 2.0, which is available at <http://pritch.bsd.uchicago.edu>.

THE study of admixed populations arises in many contexts in population genetics: for example, in the study of hybrid zones (BARTON and HEWITT 1989), in methods that use admixed populations for gene mapping (CHAKRABORTY and WEISS 1988; STEPHENS *et al.* 1994; McKEIGUE 1998), in studying the ancestry of ethnic groups such as Icelanders and Finns (THOMPSON 1973; GUGLIELMINO *et al.* 1990), and in association mapping (KNOWLER *et al.* 1988; THORNSBERRY *et al.* 2001). In many of these problems we would like to identify the extent of admixture of individuals, or to infer the origin of particular loci in the sampled individuals (McKEIGUE *et al.* 2000). These problems can be difficult if good estimates of the allele frequencies in the parental populations are not available.

In this article, we develop methods for studying the ancestry of both individuals and specific loci within admixed populations. Much of the previous work on population admixture has aimed to estimate *average* admixture proportions in an entire population (*e.g.*, LONG 1991; BERTORELLE and EXCOFFIER 1998; CHIKHI *et al.* 2001) or to study geographic clines in admixture (*e.g.*, SITES *et al.* 1995). However, the *distribution* of ancestry proportions can provide additional information about the admixture process (McKEIGUE *et al.* 2000; BEAUMONT *et al.* 2001; ANDERSON and THOMPSON 2002; FALUSH *et al.* 2003). It can also be of interest to determine whether specific parts of the genome are inherited

at a higher than normal rate from one of the parental populations, as in admixture mapping or in studying selection across hybrid zones (RIESEBERG *et al.* 1999).

We consider a situation in which we have multilocus genotype data from a sample of individuals collected from a population with (possibly) unknown structure. PRITCHARD *et al.* (2000) introduced a method to identify the presence of different subpopulations, if any, and to estimate the ancestry of the sampled individuals. That article considered two models for the ancestry of individuals. In the first, the "no-admixture model," individuals are assumed to be drawn purely from one of K populations. In the second, the "admixture model," individuals are allowed to have mixed ancestry: that is, a fraction q_k of an individual's genome comes from subpopulation k (where $\sum_k q_k = 1$). Both of those models assume that all the markers are unlinked and provide independent information on an individual's ancestry. In this article we introduce a third model, the "linkage model," which extends the admixture model to account for the correlations between linked markers that arise as the result of admixture ("admixture linkage disequilibrium"; STEPHENS *et al.* 1994). As we show, the linkage model allows estimation of the origin of chromosomal regions within individuals and provides better resolution to study the historical process of admixture.

We also discuss a new prior model for the allele frequencies within each population, which can be used in conjunction with any of the three ancestry models. This model, while still relatively simple, is more accurate in many situations and sometimes allows much more information to be extracted from the data. These and a number

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of other extensions to the original model described by Pritchard *et al.* have been implemented in a computer program, *structure* version 2.0, available at <http://pritch.bsd.uchicago.edu>.

SUMMARY OF OLD AND NEW MODELS

Consider a sample of N individuals, each genotyped at L loci. PRITCHARD *et al.* (2000) began by assuming that the individuals represent a mixture from K unobserved populations. All of the calculations are conditional on a particular value of K ; Pritchard *et al.* suggested performing the analysis for a range of values of K and described a heuristic that provides a guide toward the most appropriate value (or values).

In the no-admixture model, each individual comes from one of the K populations. We let $z^{(i)}$ denote the population of origin of individual i and Z denote the vector $(z^{(1)} \dots z^{(N)})$. Each of the K populations is characterized by a set of allele frequencies at each locus. Let p_{klj} refer to the frequency of allele j at locus l in population k , and let P denote the full multidimensional vector of allele frequencies for all k, l , and j . A key modeling assumption is that there is linkage equilibrium and Hardy-Weinberg equilibrium (HWE) within populations. Hence, the likelihood of the genotype of individual i , conditional on its population-of-origin $z^{(i)}$, is simply a product of the frequencies of its alleles in that population.

An obvious limitation of the no-admixture model is that in practice individuals may have recent ancestors in more than one population. To model this, Pritchard *et al.* introduced an admixture model, in which each individual is assumed to have inherited some proportion of its ancestry from each population. Let $q_k^{(i)}$ denote the proportion of individual i 's genome that is derived from population k (where $\sum_k q_k^{(i)} = 1$), and let Q be the multidimensional vector of ancestry proportions for all the members of the sample. It is now possible for the different allele copies in an individual to come from different populations. (We use the term "allele copy" to refer to an allele carried at a particular locus by a particular individual.) To reflect this, the vector Z now records the population of origin of every allele copy in each individual, with $z_l^{(i,a)}$ denoting the origin of the a th allele copy at locus l in individual i . PRITCHARD *et al.* (2000) discussed only the case of diploid individuals (so $a = 1$ or 2), but the model is easily extended to data of any ploidy, and we have now done this in the updated implementation of *structure* (version 2). Under Pritchard *et al.*'s admixture model, the z 's for individual i are assumed to be drawn independently from $\{1, \dots, K\}$ according to the probability vector $q^{(i)}$, so that

$$\Pr[z_l^{(i,a)} = k] = q_k^{(i)}. \quad (1)$$

This admixture model also assumes linkage equilibrium and HWE within populations.

Inference is performed in a Bayesian framework, which

offers a number of practical advantages in this context. Among these, it allows a straightforward assessment of the statistical uncertainty in each estimate of interest. It also allows us to make use of any prior information that we might have regarding population membership for some members of the sample. See PRITCHARD *et al.* (2000) for further discussion.

The Bayesian approach requires priors for P and Q . Following BALDING and NICHOLS (1997), Pritchard *et al.* assumed that the vector of allele frequencies at locus l in population k is drawn from a symmetric Dirichlet distribution parameterized by a single hyperparameter λ , independently for each k . Some modifications of this prior are described below. The admixture proportions $q^{(i)}$ for individual i were also modeled as draws from a symmetric Dirichlet distribution, in this case with a hyperparameter α . The assumption of symmetry in the prior for the q 's corresponds intuitively to an assumption that the K populations contribute roughly equal amounts of genetic material to the sample. To better model situations where this is not the case, the updated implementation of *structure* allows different values of α to be estimated for each population (so α becomes a vector of K values, with α_k representing the relative contribution of population k to the genetic material in the sample). Otherwise the prior for q is unchanged. Alternative models for q are considered by ANDERSON (2001) and ANDERSON and THOMPSON (2002).

In practice we may not know either the allele frequencies P or the populations of origin Z in advance. Pritchard *et al.* described a Markov chain Monte Carlo (MCMC) scheme that estimates these jointly. This procedure clusters individuals into populations and estimates the probability of membership (or, for the admixture model, the proportion of membership) in each population for each individual.

A number of related population genetic methods have been described, including DAWSON and BELKHIR (2001), SILLANPÄÄ *et al.* (2001), and SATTEN *et al.* (2001). Further, it has recently come to our attention that the admixture model belongs to a class of models known as "grade of membership" models, which have been used in other literatures, including medical classification and machine learning (EROSHEVA 2002).

The linkage model: A deficiency of the admixture model is that by assuming that the z 's within each individual are independent, it ignores the correlations in ancestry that one would expect to see along each chromosome. In this context, it is helpful to distinguish between three sources of linkage disequilibrium (LD). The first source is variation in ancestry (q) among the sampled individuals. Variation in q leads to correlations among markers across the genome, even if they are unlinked, because individuals with a large component of ancestry in population k have an excess of alleles that are common in k . We call this LD "mixture LD." The second source is correlations in ancestry along each

chromosome, which cause additional LD between linked markers. We visualize this LD as occurring because each chromosome is composed of a set of “chunks” that are derived, as unbroken units, from one or another of the ancestral populations. In our terminology, this second source is “admixture LD.” The third source is “background LD” within populations, which usually decays on a much shorter scale (tens of kilobases in humans). The admixture model in PRITCHARD *et al.* (2000) models only mixture LD; here we extend the model to include admixture LD. However, we continue to ignore background LD, and so our model is best suited to data on markers that are linked, but not so tightly linked that one would expect to see substantial background LD (we return to this point in our discussion).

To make inference computationally tractable, we use a simple model that incorporates the notion of discrete chromosomal chunks inherited from ancestral populations. Whereas in the “admixture” model of PRITCHARD *et al.* (2000), each allele copy is derived independently from one of the K populations, in the new “linkage” model chunks of chromosomes are derived as intact units from one or another of the K populations, and all allele copies on the same chunk derive from the same population. We assume that the breakpoints between successive chunks occur at random (*i.e.*, as a Poisson process), at a rate r per unit of genetic distance, and that the population of origin of each chunk in individual i is independently drawn according to the vector $q^{(i)}$, which continues to represent the overall (expected) ancestry proportions of the individual.

Formally, the above assumptions translate into replacing the admixture model assumption that the z 's along each chromosome are *independent* with the assumption that z 's along each chromosome are *dependent*, forming a Markov chain. Specifically, for haploid data, independently for each individual i ,

$$\Pr(z_l^{(i)} = k | r, Q) = q_k^{(i)}, \quad (2)$$

and

$$\Pr(z_{l+1}^{(i)} = k' | z_l^{(i)} = k, r, Q) = \begin{cases} \exp(-dr) + (1 - \exp(-dr))q_{k'}^{(i)} & \text{if } k' = k \\ (1 - \exp(-dr))q_k^{(i)} & \text{otherwise,} \end{cases} \quad (3)$$

where d_l denotes the genetic distance from locus l to locus $l + 1$, assumed known. For diploid (or polyploid) data, independently for each individual i , the z 's along each of i 's two (or more) chromosomes form independent Markov chains satisfying Equations 2 and 3.

Note that the linkage model includes the admixture model as a limiting case: as r tends to infinity in (3), all loci become independent, returning us to the original admixture model (Equation 1). Note also that we assume that r is the same for all individuals, although this assumption

could be relaxed at the cost of an increase in the number of parameters.

Interpretation of the linkage model: To provide some motivation for the linkage model, consider the following idealized scenario. Suppose that our sample comes from a diploid population that experienced a single “admixture event” followed by t_2 generations of subsequent random mating within postadmixture populations. In the generation of the admixture event, individuals are formed by mating of individuals between two or more ancestral populations. These individuals inherit their DNA intact (*i.e.*, without intervening recombination) from the ancestral populations. In the subsequent generation, the boundaries delineating these intact chunks will correspond to crossover events in a single meiosis and so (assuming no interference) will form a Poisson process of rate 1 per morgan. Chromosomes in each subsequent generation will inherit chunks of DNA from chromosomes in the previous generation in a similar manner, and it follows from standard results on the superposition of Poisson processes that, in chromosomes in the current generation, the boundaries between the chunks of DNA inherited intact since the admixture event will form a Poisson process of rate t_2 per morgan.

This reasoning provides some justification for the form of the transition rates in Equation 3. However, it falls short of providing a complete justification for all assumptions of the linkage model and in particular for the assumption that the ancestral populations of origin of the chunks are independent draws from some (individual-specific) vector q . Furthermore, in real populations, biological details such as crossover interference and gene conversion events (or transformation in bacteria) will cause deviations from the assumed model. Nevertheless, the linkage model captures, in a parsimonious and computationally convenient way, the correlations in ancestry between linked loci that we would expect to see in admixed individuals from real populations.

The discussion above also suggests an interpretation of the parameter r in terms of the number of generations since admixture first occurred. Specifically, if the genetic distances d_l between adjacent markers are measured in morgans, then r can be interpreted as an estimate of t_2 , the number of generations since the admixture event (although inevitable deviations from the model assumptions mean that it would be wise to treat any such estimate with a degree of caution). Similarly, if the genetic distances are measured in centimorgans, then r can be interpreted as an estimate of $100t_2$. In some situations the genetic distances between loci may not be known, but a proxy such as physical distance may be available. If the physical distance between loci, measured in nucleotides, is used in place of the genetic distance for d_l , then r can instead be interpreted as an estimate of the product of t_2 and the recombination rate (expected number of crossovers per base pair per meiosis). If there is no

information on map positions, then the linkage model is not applicable.

For many data sets, we will have little prior knowledge concerning the time since admixture (and perhaps also the recombination rate). We have therefore implemented a uniform prior for $\log r$. The bounds of the prior should generally be set to include all biologically plausible values of r , which may range over several orders of magnitude (partly explaining the attraction of working with $\log r$).

Computations for the linkage model: Because in practice the z 's for each chromosome are not observed, the Markov model for the z 's used by the linkage model (Equations 2 and 3) results in a hidden Markov model (HMM) for the observed genotype data. Standard HMM methods (see RABINER 1989 for a review) can be used to sample efficiently from the conditional distribution of the z 's and compute the probability of the observed genotype data, given all other parameters. Both these procedures are used in our MCMC algorithm to fit the model, including Metropolis-Hastings updates for Q and r (see the APPENDIX for details). The necessary computations are relatively straightforward when considering haploid data, or if phase relationships among all linked loci are known, as the computations for each chromosome can then be performed separately. If the data are unphased then individual allele copies may be inherited on the same chunk as any one of the allele copies at the preceding locus. This ambiguity leads to a reduction in the amount of information provided by the data on the population of origin of each allele copy and on the value of r , in comparison with a completely phased data set. It also increases the complexity of the algorithm required to fit the model. If relatives have been genotyped, then pedigree information may indicate that particular loci have been inherited together from the same parent, restoring some of the lost information. In the APPENDIX we describe algorithms that can handle unphased data for diploids and that can also incorporate simple pedigree information when available (but note that the individuals analyzed by *structure* should all be unrelated).

Although the linkage model was developed with computational tractability in mind, it is nevertheless more computationally intensive than the admixture model. This can make the linkage model less convenient for particularly large or complicated data sets. For the African-American data set described below (626 diploid individuals and 252 loci) and $K = 2$ populations, a run consisting of 10,000 burn-in iterations followed by 50,000 further iterations took 3 hr using the admixture model, 7 hr for the linkage model if it was (incorrectly) assumed that the data were fully phased, and 11 hr for the linkage model assuming (correctly) that the data were unphased (calculations were performed on a DEC Alpha of 2001 vintage). Performance differentials will increase for larger K : the computation scales linearly

with K for the admixture model and for the linkage model with phased data, but scales with K^2 for the linkage model with unphased or partially phased data.

Models of allele frequencies: As described above, PRITCHARD *et al.* (2000) assumed a model in which the allele frequencies in the different populations are independent. Under that model, the allele frequencies in one population provide no information about what the allele frequencies might be in another population. In practice, however, we often expect the allele frequencies in closely related populations to be very similar. This suggests that a prior model that accounts for such correlations would be more accurate in many cases and may therefore lead to improved performance on "difficult" problems, where distinct populations are quite similar. Indeed, PRITCHARD *et al.* (2000) remarked briefly that they had found some cases of rather subtle population structure where the model of independent allele frequencies was less successful than an alternative model that allowed for correlations in allele frequencies among different populations. Here, we describe the implementation of an improved model of allele frequency correlations, which has fewer parameters and is more interpretable than the model for correlated allele frequencies in PRITCHARD *et al.* (2000).

The new model is based on ideas in NICHOLSON *et al.* (2002), who present a model for correlated frequencies for biallelic loci [specifically, single-nucleotide polymorphisms (SNPs)] in different populations. The model assumes that the populations all diverged from a common ancestral population at the same time, but allows that the populations may have experienced different amounts of drift (due to different effective population sizes) since this divergence event. The assumption of simultaneous divergence, while unrealistic, is appealing in its simplicity. One alternative, which might be more realistic in some settings, would be to assume that the populations are related to one another by a tree.

The new model for correlated allele frequencies that we describe here is based on the same implicit assumptions as the model of NICHOLSON *et al.* (2002), but applies to allele frequencies at multiallelic loci. [This extension to multiallelic loci was also suggested independently by MARCHINI and CARDON (2002) and is related to the parameterization of BALDING and NICHOLS (1997).] We introduce a new (multidimensional) vector, P_A , which records the allele frequencies in a hypothetical "ancestral" population. With a slight abuse of notation we denote the frequency of allele j at locus l in the ancestral population by p_{Ajl} . It is assumed that the K populations represented in our sample have each undergone independent drift away from the ancestral allele frequencies, at rates parameterized by $F_1, F_2, F_3, \dots, F_K$, respectively. The allele frequencies in P_A are assumed to have Dirichlet priors of the same form as that used in the original model for the (uncorrelated) population frequencies,

$$p_{Al} \sim \mathcal{D}(\lambda_1, \lambda_2, \dots, \lambda_{J_l}), \quad (4)$$

independently for each l . Here, λ may be fixed or estimated within the MCMC scheme. Conditional on P_A , the frequencies in each population k have a prior distribution

$$p_{kl} \sim \mathcal{D}\left(p_{Al1} \frac{1 - F_k}{F_k}, p_{Al2} \frac{1 - F_k}{F_k}, \dots, p_{AlJ_l} \frac{1 - F_k}{F_k}\right), \quad (5)$$

independently for each k and l . The size of F_k tells us about the effective population size of population k during the time since divergence, with large values of F_k indicating a smaller effective population size (NICHOLSON *et al.* 2002).

We refer to this new model for correlated allele frequencies as the “ F ” model. The name is chosen to reflect the fact that there are close connections between the model and the classical measure of correlations between populations, Wright’s F_{ST} (WRIGHT 1951). NICHOLSON *et al.* (2002) describe the connections in some detail; here we give a brief summary. Traditionally, F_{ST} is estimated as a single value that summarizes the average deviation of a collection of populations away from the mean. Although definitions vary, it is commonly written as $F_{ST} = \text{Var}(p_k) / \bar{p}(1 - \bar{p})$, where p_k is the frequency of an allele in population k , and \bar{p} is the overall frequency of that allele across all subpopulations (EXCOFFIER 2001). In our parameterization (Equations 4 and 5) $E(p_{klj}) = p_{Alj}$, and $\text{Var}(p_{klj}) = F_k p_{Alj}(1 - p_{Alj})$. Hence, p_{Alj} plays a role analogous to that of \bar{p} , and F_k plays a role like that of F_{ST} in the classical model, except that we use a generalized model with different drift rates for each population. Using a different value of F for each population, rather than a single common value for all populations, introduces a considerable amount of extra flexibility into the model at the expense of only a few additional parameters.

The prior distribution that we have implemented for F assumes that the F_k are *a priori* independent, with a density proportional to a gamma distribution truncated at 1 (so that $\text{Pr}[0 < F_k < 1] = 1$). Depending on the parameters of the distribution, the prior can be “harsh”—putting most of its weight on low values of F , or “permissive”—not discriminating strongly against any value of F_k . A harsh prior on low values of F corresponds to strong prior information that the allele frequencies in the different populations are similar to one another, and this seems generally to give the best performance in detecting subtle admixture in problems that are difficult for the independent frequencies model. However, if the values of F_k are being used to make evolutionary inferences, a permissive prior is more appropriate. In the APPENDIX, we present Metropolis-Hastings updates for P_A , P_b , and F_k .

MODEL RESULTS USING SIMULATED DATA SETS

To assess the uses and limitations of the new *structure* features, we have performed Wright-Fisher simulations,

based on the seven demographic scenarios (I–VII) shown in Figure 1. Mutation parameters differ among the simulations and are specified separately for each one. Under each scenario, the goal is first to identify the current populations and second to reconstruct elements of their history: for example, the amount of genetic drift, the degree of admixture, and the time since admixture occurred.

Differentiating between closely related populations—

The F model: One advantage of the new F model is that it can sometimes detect population subdivision that is invisible to *structure* when the gene frequencies of the populations are modeled without correlations. An example is shown in Figure 2, where a single randomizing population splits into two (scenario II). Eight generations after the split, the uncorrelated model is unable to distinguish between the two populations, while the F model distinguishes them quite accurately, with the exception of a few individuals that are not assigned with high probability to either population. After 16 generations of separate evolution, the uncorrelated model becomes able to distinguish reasonably accurately between the two populations and the F model provides little improvement in clustering. Further simulations (not shown) indicate that the F model is less likely to improve performance when the number of loci is small; rather, it can allow accurate clustering of individuals from extremely closely related populations when large numbers of markers are used (*e.g.*, ROSENBERG *et al.* 2002). However, even with very many markers, it is unlikely to be possible in practice to differentiate between biological populations that have split <20 generations ago unless there has been little subsequent admixture and genetic drift has been strong.

Estimation of K : Simulations presented by PRITCHARD *et al.* (2000) and further experience with other data sets suggest that the value of K that maximizes the estimated model log-likelihood, $\log(P(X|K))$, is often a sensible choice for the number of populations. However, the value of K estimated by this procedure can sometimes depend on the model used. The F model is in general more permissive of additional populations being fitted to a data set, as it permits the existence of two or more populations with very similar allele frequencies (particularly if the prior on F is chosen to favor small values). Consequently, $P(X|K)$ is sometimes maximized for a higher value of K than under the uncorrelated model. This cuts to the heart of one of the principal reasons why inferring K is so difficult and why estimates for K should be treated with caution: the number of populations supported by the data may depend on how different one would expect allele frequencies in the different populations to be *a priori*, which is often difficult to specify.

For some data sets, higher estimates of K obtained using the F model may reflect deviations from random assortment that are not caused by genuine population subdivision. Table 1A shows model likelihoods estimated for a single panmictic population (scenario I).

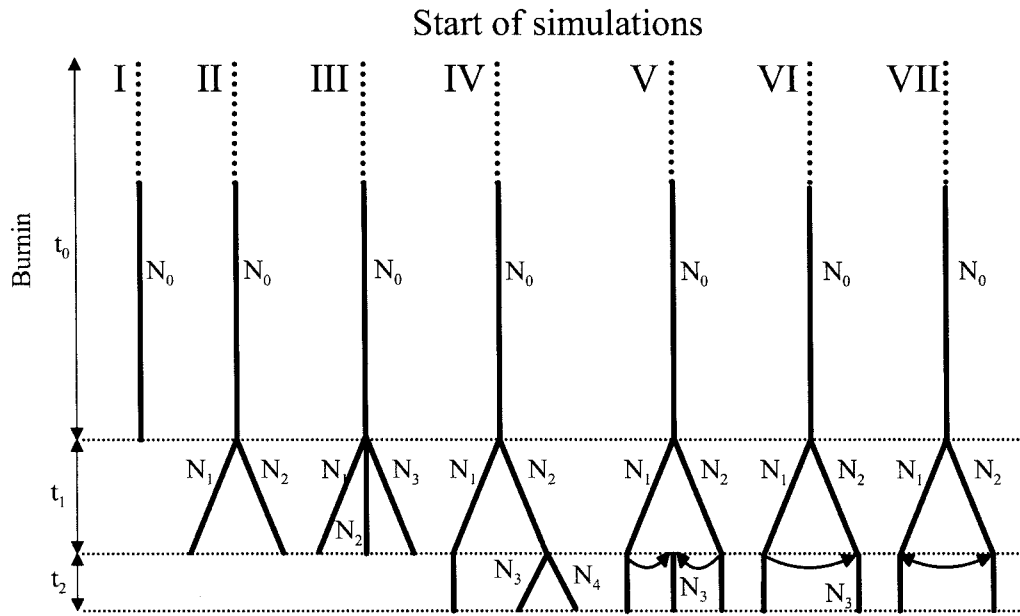


FIGURE 1.—Scenarios simulated using the Wright-Fisher model. $N_0 \dots N_4$ indicate haploid population sizes, while t_0 , t_1 , and t_2 indicate time in generations. In each case $t_0 > 5N_0$, so that the population is close to mutation-drift equilibrium at the end of the burn-in. (I) Sample from a single random-mating population. (II) Population bifurcation. (III) Population trifurcation. (IV) Hierarchical subdivision. (V) Admixture creates an additional population. (VI) Unidirectional admixture leaves one population unchanged. (VII) Bidirectional admixture between two populations. In V, VI, and VII the diverged populations undergo an admixture event in which individuals are formed by the union of gametes from preadmixture populations, before undergoing t_2 generations of subsequent evolution. The ancestry of the postadmixture populations is determined by a matrix u , where u_{ij} is the proportion of gametes in population j that come from preadmixture population i .

ture event in which individuals are formed by the union of gametes from preadmixture populations, before undergoing t_2 generations of subsequent evolution. The ancestry of the postadmixture populations is determined by a matrix u , where u_{ij} is the proportion of gametes in population j that come from preadmixture population i .

Whether or not the F model is used, the highest value of $P(X|K)$ is given by $K = 1$. In Table 1B the evolutionary parameters are identical but there is a 50% selfing rate. In this case, the F model gives higher probabilities for $K = 2$, while the original model continues to give the highest model likelihood for $K = 1$. Other situations that might cause additional populations to be inferred by *structure* (with or without the F model) include a significant frequency of inbreeding, cryptic relatedness within the sample, or the presence of null alleles.

Inference of demographic history: The F model can also be used to estimate the amount of genetic drift undergone by the different populations under study. In Figure 3A, estimates of F are shown for a population that trifurcated (scenario III). For a substantial time period after the trifurcation, the estimated values of F are approximately proportional to the time since the split and inversely proportional to the population sizes. When the values of F start to exceed ~ 0.2 , F no longer increases linearly but the ranking of the values of F continues to reflect the relative degrees of drift that the populations have undergone.

The use of the F model to estimate drift is subject to a caveat, which is that contrary to the model assumption, drift may not have occurred independently in each population. For example, Figure 3B shows results based on scenario IV, in which a single population divides into two and one of the populations subsequently subdivides. The *structure* algorithm interprets the similarity of the two subpopulations as evidence that their gene frequencies are close to those of the ancestor of all three populations and estimates lower values of F for them than for their common ancestor prior to subdivision.

In principle it should be possible to generalize the model to allow for the possibility of hierarchical subdivision but we do not attempt this here. Rather, we suggest testing for deviations from the model by estimating values of F while excluding one or more of the populations in turn. If the assumption that all of the populations evolved independently from a single common ancestral population is correct, then this should leave the F values estimated for the other populations approximately unchanged. If the F values decrease, then this suggests that one of the excluded populations diverged first, so that the remaining populations share a more recent common ancestor than shared by the whole sample considered together. If F values of one or more of the populations increase, then it may indicate that the original F values were artificially reduced by the presence of closely related subpopulations in the sample. Other diagnostics are discussed by NICHOLSON *et al.* (2002).

Inference in admixed populations—the linkage model: Inference of demographic history becomes more difficult if admixture has occurred subsequent to population divergence (*e.g.*, BEAUMONT *et al.* 2001). In these situations, it may be very difficult to estimate allele frequencies in the original “pure” populations, as required for standard population genetic analyses. When analyzing data using *structure*, such populations can also be problematic. The algorithm estimates P and Q jointly, so the model can either simultaneously underestimate the degree of admixture and the genetic distance between pairs of populations or simultaneously overestimate the same quantities.

Linkage information can help to resolve the ambiguity. Informally, admixed individuals contain chromosomal

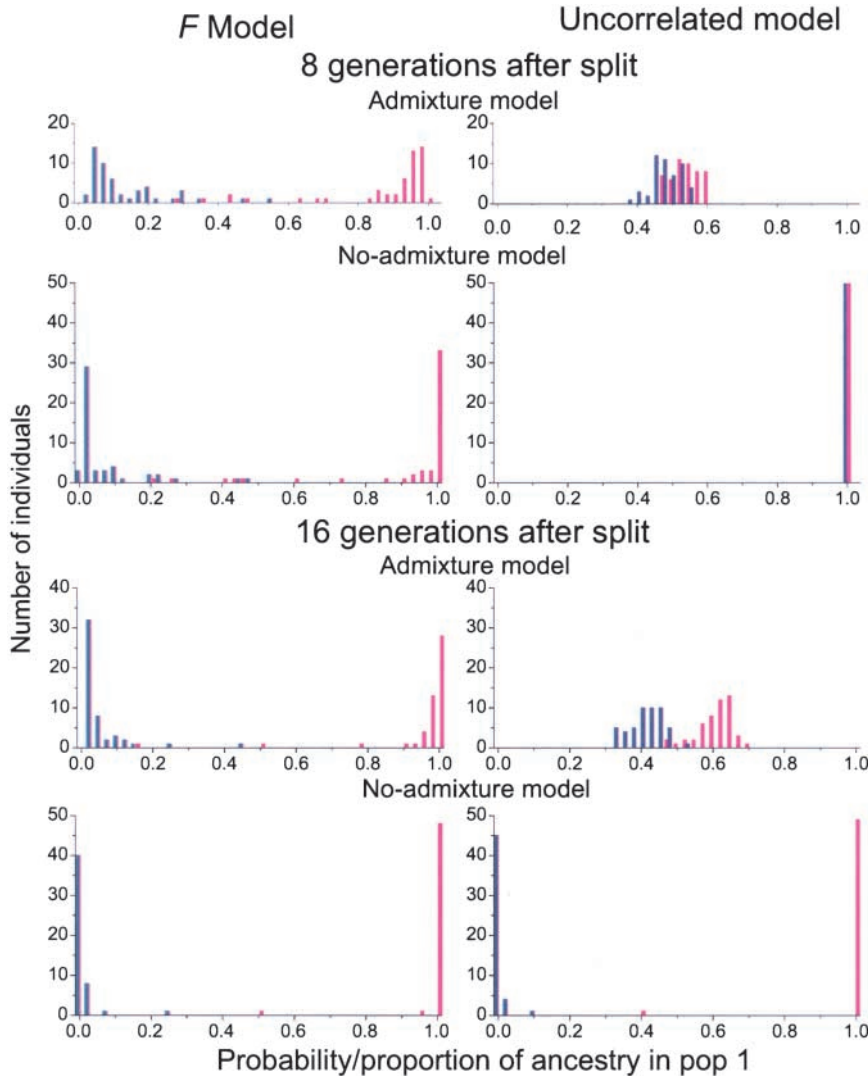


FIGURE 2.—Performance of different models in distinguishing recently diverged populations (scenario II). *Structure* was run with 50 diploid individuals sampled from each of two populations. A total of 400 unlinked microsatellite loci were simulated according to the stepwise mutation model with mutation rate $\mu = 2 \times 10^{-4}$; haploid population sizes were $N_0 = 2N_1 = 2N_2 = 2500$. Here, the prior for F was chosen to put most of its weight on low values (specifically, we used a gamma distribution with mean 0.01 and standard deviation 0.05).

chunks that derive from one population or another. Using closely linked markers, the linkage model aims to detect the chromosomal chunks and can potentially reconstruct the ancestral populations accurately even if no pure members exist.

To explore the properties of the new method, we have performed extensive simulations. We consider individuals genotyped at L^* loci on each of C chromosomes (*i.e.*, typed at a total of CL^* loci). The loci are equidistant, with a recombination rate R per generation between adjacent genotyped sites. The genetic map is assumed known. We analyzed the simulated data using the uncorrelated model for allele frequencies.

Estimation of allele frequencies: One measure of whether *structure* is performing well is if it can accurately estimate the population allele frequencies in the ancestral populations. To visualize this, we have constructed neighbor-joining trees based on the posterior mean allele frequencies. When the allele frequencies are accurately estimated, the branch tips lie close to the large black dots (which represent the “correct” frequencies).

We focus on scenario VI, “unidirectional” admixture. In three out of the four cases shown (Figure 4, A–C), *structure* is highly consistent in its inference of gene frequencies for ancestral population 1, reflecting the continuous presence of pure individuals in the sample. The accuracy of this inference provides a baseline from which to judge the performance of *structure* in disentangling the gene frequencies of ancestral population 2, which ceases to have any pure descendants a few generations after admixture.

In the first simulated example (Table 2A, Figure 4A), as the number of generations after admixture (t_2) increases, the admixture model becomes increasingly biased, underestimating the divergence between the populations (shown by the intermediate position of the inferred populations in the gene frequency tree) and underestimating the amount of admixture (H_2 in Table 2A). In contrast, the linkage model estimates gene frequencies and the degree of admixture accurately for many generations after the admixture event.

The performance of the admixture model is im-

TABLE 1

Estimates for model log-likelihood ($\log P(X|K)$) for 100 diploid individuals taken from a simulated random-mating population (scenario I) with $N_0 = 2500$

<i>K</i>	Uncorrelated model	<i>F</i> model
A.		
1	<u>−81404</u>	<u>−81404</u>
2	—	−81819
3	—	−82657
4	—	−82470
B.		
1	<u>−76855</u>	<u>−76855</u>
2	<u>−77169</u>	−76780
3	<u>−77059</u>	−77099
4	—	−78171

In B there is a 50% selfing rate. (—) One of the populations was empty in all of the simulated runs. A total of 400 microsatellites were simulated according to the stepwise mutation model with $\mu = 2 \times 10^{-4}$. Each model log-likelihood is the average from two *structure* runs with 5000 generations burn-in and 50,000 iterations. The prior for *F* (gamma distribution with mean 0.01 and standard deviation 0.05) puts most of its weight on low values of *F*. The highest likelihood run in each group is underlined.

proved by increasing the number of chromosomal regions studied (Table 2B, Figure 4B) but the linkage model continues to prolong the number of generations after admixture for which accurate ancestry estimates can be obtained.

In another example (Table 2C, Figure 4C), the admixture model shows the opposite bias for a number of generations, overestimating rather than underestimating admixture and the degree of divergence between ancestral populations. The linkage model again uses linkage information to resolve the ambiguity and it performs well up to eight generations after the admixture event. However, in this example, the marker density is low enough that in later generations, the linkage information is lost, and the admixture and linkage models produce almost identical (and similarly biased) results.

By contrast, Figure 4D (see also Table 2D) shows the situation where the marker density is very high. In this case, background LD is substantial, leading the linkage model to consistently overestimate the divergence between the two populations. Further, substantial admixture is estimated for population 1, which is in fact pure. The admixture model actually does rather better in the populations it infers, but a few generations after the admixture event it also produces misleading results. These results illustrate the problems that can arise when there is substantial background LD, a point to which we return in the DISCUSSION.

Estimating the time since admixture: In addition to improving estimates of the degree of admixture, the linkage model also provides an indication of the time since

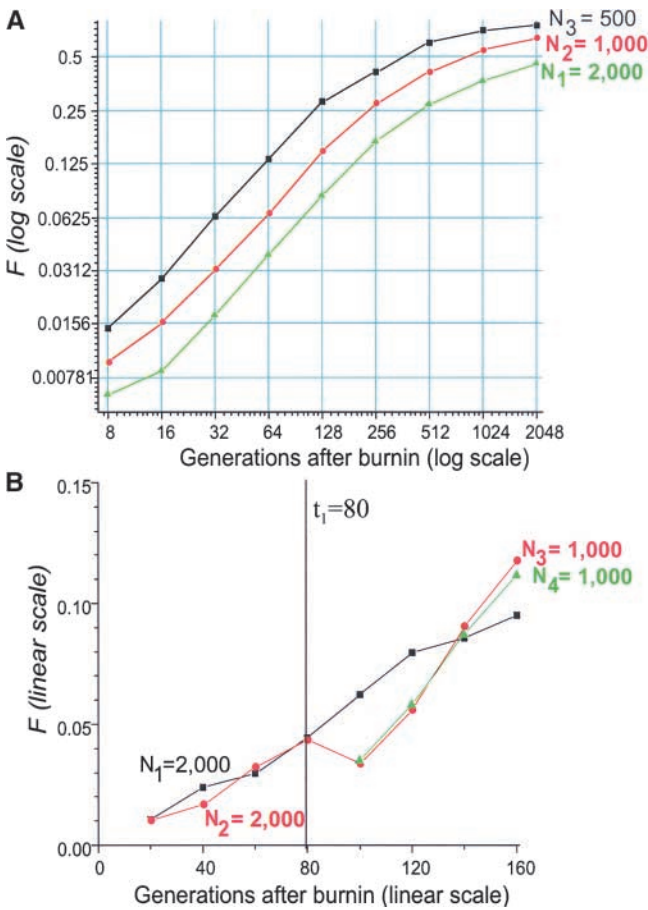


FIGURE 3.—Estimates of *F* under two evolutionary scenarios. (A) Scenario III (population trifurcation). (B) Scenario IV (hierarchical subdivision). *Structure* was run with 50 diploid individuals from each of the populations. The no-admixture model was used throughout. Mutational parameters were as in Figure 2. Population sizes are shown on the graph. The vertical line in B indicates the time at which population 2 split into populations 3 and 4.

admixture. For examples A–C the value of *r* (Table 2) provides good estimates of the number of generations since admixture, except immediately after the admixture event (when little admixture has occurred, so that there is not yet much admixture LD and the posterior for *r* is uninformative) and >100 generations after admixture, when the number of generations is underestimated. The time of admixture may be considerably overestimated by *r* if there is substantial background LD in the sample (Table 2D).

Population-of-origin assignments for chromosomal regions: A further advantage of the linkage model is that if the marker density is high enough, it can provide accurate population-of-origin assignments for chromosomal regions, as required in applications such as admixture mapping. For example, Figure 5 shows population-of-origin assignments for the two allele copies at each locus of a single diploid individual. The Markov structure of the data is clearly evident from the *structure*

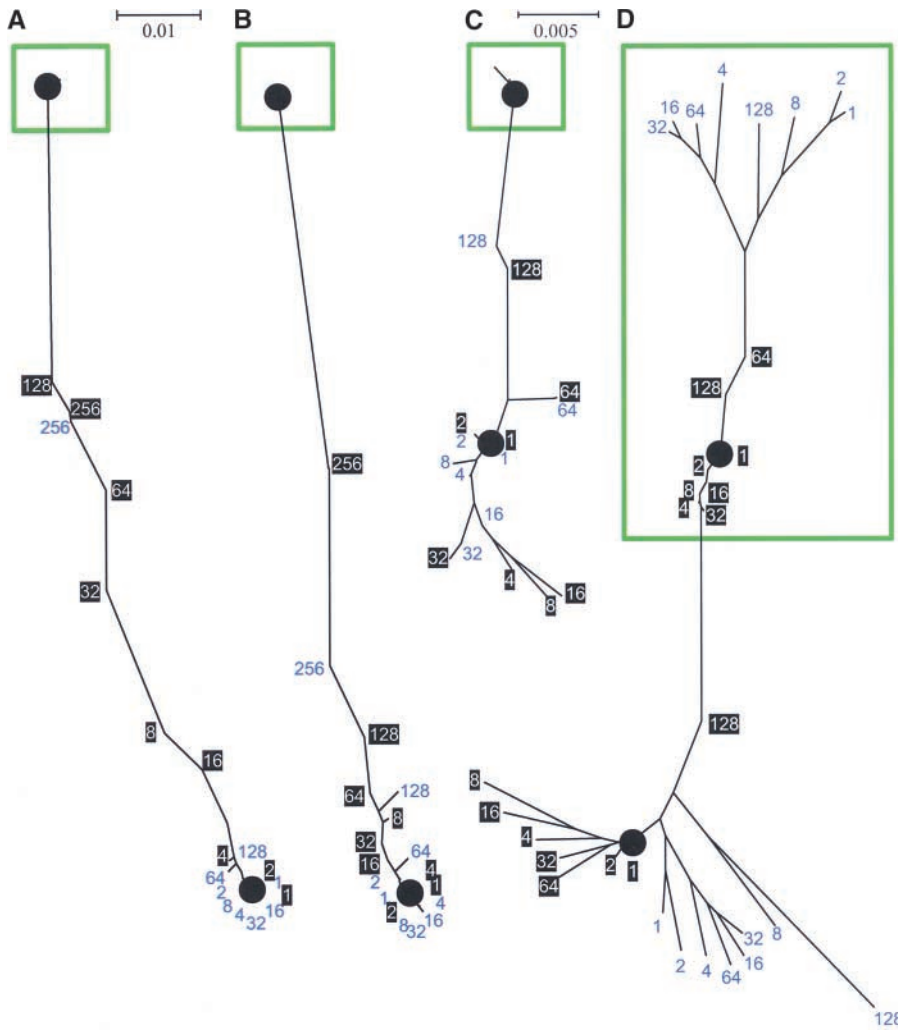


FIGURE 4.—Population allele frequencies estimated using the linkage (blue) and admixture (white on black) models in the generations following an admixture event, as visualized using neighbor-joining trees of genetic distances (KUMAR *et al.* 2001). The simulations were performed according to scenario VI, in which ancestral population 2 receives one-half of its gametes from ancestral population 1 (in boxes) in a single, one-way admixture event. The positions of the true ancestral populations in the trees are indicated by the large black dots. The labels give the number of generations after admixture (t_2) at which the sample was taken. When the allele frequencies are estimated accurately, the corresponding labels lie close to the black dots. Labels are not shown for population 1 in A–C as they all fall close together on the top black dot. In each of the simulations, $L^* = 50$, $N_0 = 2N_1 = N_2 = 5000$. (A) $C = 5$, $t_1 = 5000$, $R = 0.001$, $N_2 = 2500$. (B) As in A except $C = 50$ (10-fold more chromosomes). (C) $C = 50$, $t_1 = 500$, $R = 0.01$, $N_2 = 100$ (resulting in strong drift in the recipient population). (D) As in C except $R = 0.0001$ (tighter linkage). Biallelic markers were simulated with $\mu = 10^{-5}$. In each case, *structure* was run with $K = 2$, using 100 haploid individuals from both of the postadmixture populations. In the notation of Figure 1, $u_{11} = 1$, $u_{12} = 0.5$. The trees were constructed using the Nei and Li (1979) distance δ_{PP_j} between allele frequency vectors P_i and P_j as $\delta_{PP_j} = d_{PP_j} - (d_{PP_i} + d_{PP_j})/2$, where $d_{PP_j} = \sum_{l=1}^L (1 - \sum_j p_{lj} p_{kj})/L$ and p_{kj} is the frequency of allele j at locus l in population k .

output, in that nearby loci typically have similar assignment probabilities. When the data are phased, individual loci are often assigned with very high probability to the correct ancestral population, especially in the middle of a large chunk inherited from one population. At boundaries between chunks, the assignment probabilities typically change rapidly, giving a good indication of the position of the recombination event that brought the chunks from different populations together.

For unphased diploids, the data contain somewhat less information about the population of origin of individual allele copies, particularly in regions of the genome where the two homologous chromosomes are spanned by chunks inherited from different ancestral populations. In these regions, neighboring loci do not provide information concerning which of the two allele copies at a particular locus comes from one population and which comes from the other. For many problems (such as in admixture mapping) we are mainly interested in inferring the number of allele copies from

each population, and this information can be extracted from the data, given sufficiently dense markers (as in Figure 5).

Coverage properties: A final advantage of the linkage model is that it gives more accurate estimates of the statistical uncertainty of admixture proportions. This property is illustrated in Figure 6, which shows 90% credibility regions for q for a sample of individuals from two populations partially admixed with each other in an admixture event (scenario VII) 32 generations before the sample was taken. After 32 generations of random mating within each postadmixture population, the ancestry coefficients of each individual are almost identical (differing by <0.001) and are shown by the red horizontal lines in the figure. Ancestry estimates were made by both the admixture and linkage models, for markers at a variety of genetic distances. Tightly linked markers give nonindependent information and are therefore less informative about the value of q for each individual than are the same

TABLE 2
Estimates for model log-likelihood, ancestry, and other parameters for the *structure* runs shown in Figure 4

	Admixture model				Linkage model				
	H_1	H_2	$\text{Log } P(X K)$	α	H_1	H_2	$\text{Log } P(X K)$	α	r
A.									
1	0.999	0.999	-4306	0.026	0.995	0.515	-4304	0.0286	3.5
2	0.995	0.512	-5414	0.1042	0.966	0.523	-4694	0.1897	2.4
4	0.991	0.533	-5728	0.1944	0.940	0.522	-4676	0.3711	5.3
8	0.990	0.400	-5965	0.1785	0.932	0.505	-4872	0.4368	7.3
16	0.990	0.419	-5957	0.191	0.937	0.492	-4961	0.4353	14.2
32	0.993	0.221	-6153	0.1144	0.956	0.479	-5428	0.4021	36.4
64	0.990	0.169	-5970	0.0985	0.961	0.476	-5433	0.3886	62.1
128	0.995	0.044	-5935	0.038	0.962	0.450	-5781	0.3977	106.7
256	0.997	0.016	-5836	0.0303	0.995	0.026	-5856	0.0345	114.3
B.									
1	1.000	0.470	-39362	0.0231	1.000	0.471	-39219	0.0247	39.3
2	0.999	0.501	-49602	0.0907	0.998	0.501	-42360	0.0918	2.5
4	0.999	0.531	-55770	0.1786	0.996	0.472	-43881	0.2032	3.9
8	0.999	0.508	-57284	0.16	0.996	0.510	-44938	0.2103	7.4
16	0.999	0.490	-57299	0.1895	0.997	0.507	-46542	0.2047	15.3
32	0.999	0.468	-56969	0.1893	0.997	0.505	-48755	0.1962	32.2
64	0.999	0.452	-56558	0.1879	0.998	0.487	-50787	0.1855	62.2
128	0.998	0.366	-56027	0.1918	0.998	0.443	-52857	0.1805	110.4
256	0.999	0.006	-54832	0.0321	0.998	0.327	-54373	0.1784	199.6
C.									
1	0.998	0.412	-62175	0.03	0.999	0.411	-62141	0.025	0.00
2	0.989	0.493	-64033	0.1669	0.993	0.486	-63491	0.1152	2.46
4	0.987	0.641	-66179	0.2827	0.987	0.570	-65363	0.2661	4.97
8	0.990	0.683	-66145	0.2769	0.984	0.592	-65464	0.3061	8.82
16	0.991	0.667	-66213	0.2459	0.985	0.592	-65878	0.3016	18.3
32	0.989	0.598	-65657	0.2641	0.985	0.578	-65689	0.3097	40.81
64	0.982	0.453	-65429	0.3425	0.985	0.456	-65343	0.3041	58.37
128	0.995	0.024	-64370	0.054	0.997	0.014	-64393	0.0314	97.46
D.									
1	0.993	0.526	-58517	0.0579	0.575	0.450	-53428	6.25	423
2	0.976	0.488	-60928	0.2256	0.573	0.450	-54267	8.65	439
4	0.979	0.639	-61922	0.3278	0.541	0.441	-54570	10.71	373
8	0.986	0.703	-63055	0.3022	0.556	0.455	-54130	10.79	377
16	0.987	0.634	-62297	0.2708	0.605	0.481	-54419	9.62	402
32	0.970	0.566	-62248	0.3924	0.602	0.470	-54324	8.63	426
64	0.980	0.551	-61368	0.348	0.604	0.459	-53901	9.1	437
128	0.969	0.261	-62590	0.3239	0.621	0.440	-53029	7.69	465

The first column gives the number of generations after the admixture event, T_2 . H_1 and H_2 are the average estimated ancestry from ancestral population 1 for individuals in the two postadmixture populations (true values are 1.000 and 0.500). r is measured in generations. The highest log-likelihood in each row gives a heuristic guide to which model fits better.

number of unlinked markers, leading to higher variation in estimates between individuals. The admixture model does not take these correlations into account. Consequently, the sizes of the estimated credibility regions are approximately independent of the actual degree of linkage and are much too narrow for tightly linked markers. Under the linkage model, the credibility regions for q become wider as linkage between mark-

ers increases and continue to reflect the true degree of statistical uncertainty even for tightly linked markers.

APPLICATIONS TO DATA

Recombination between distinct populations of *Helicobacter pylori*: The bacterium *Helicobacter pylori* colonizes the human stomach lining. When multiple strains infect

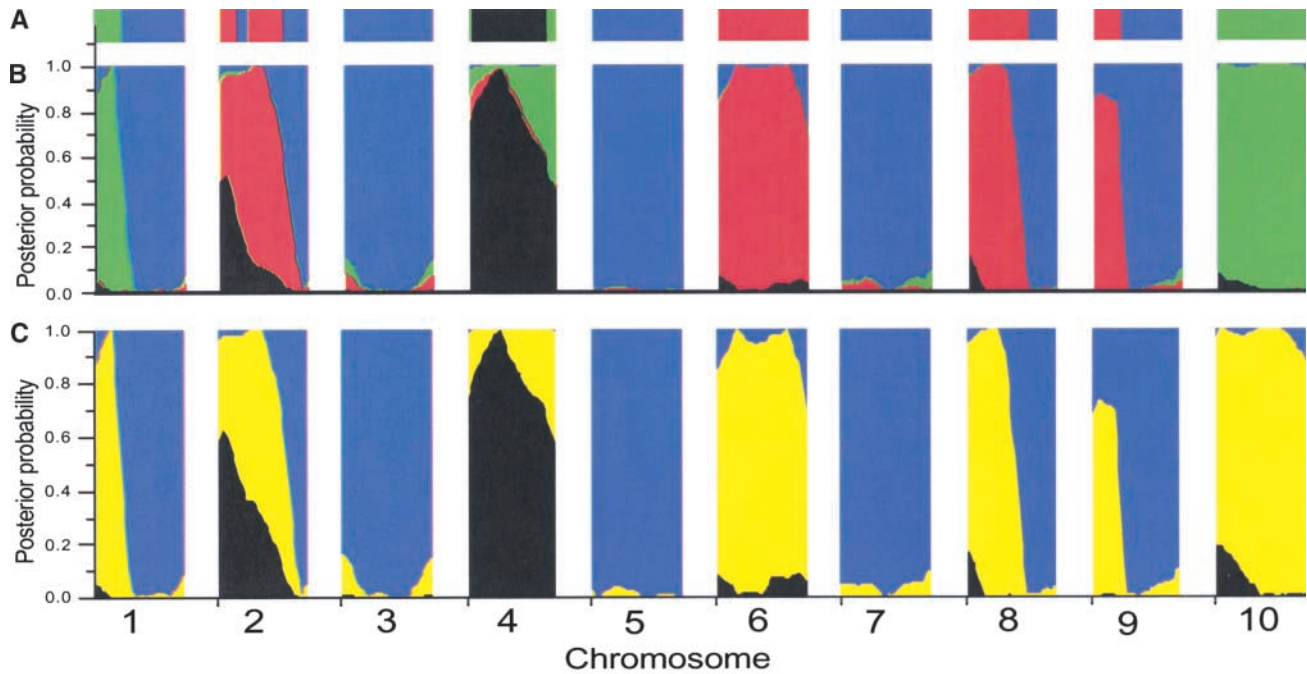


FIGURE 5.—Population-of-origin assignments for maternal and paternal strands from 10 chromosomes of a single diploid individual. The loci are shown in map order, with 50 loci per chromosome. (A) True population-of-origin combinations for each chromosomal region; (B) posterior assignment probabilities (proportion occupied by each color) calculated using the linkage model with phased data; (C) as in B but for unphased data. The colors indicate different assignment combinations: both allele copies inherited from population 1 (black) or population 2 (blue), maternal from population 1 and paternal from population 2 (red), maternal from population 1 and paternal from population 2 (green), and an unspecified copy from population 1 and the other from population 2 (yellow). In B the assignment probabilities for each strand can be inferred by summing over the different combinations for the other strand. So, for example, the probability that the maternal copy is inherited from population 1 is given by the proportion that is either black or red. In C individual allele copies are not assigned separately, so if the true population of origin is either red or green, the correct assignment for that locus is yellow. *Structure* was run with $K = 2$ and 50 individuals from each population. Wright-Fisher simulations were performed according to scenario VI with $C = 10$, $L^* = 50$, $R = 0.001$, $t_1 = 5000$, $t_2 = 32$, $u_{11} = 1$, and $u_{21} = 0.3$. $N_0 = 2N_1 = 2N_2 = 5000$ and mutational parameters as in Figure 4.

the same stomach, they recombine rapidly through the import of fragments of DNA that are typically a few hundred base pairs in length (FALUSH *et al.* 2001). FALUSH *et al.* (2003) used the no-admixture model on multilocus sequence data from a global collection of strains to show that there are four major modern populations of bacteria, which they named “hpAfrica1,” “hpAfrica2,” “hpEastAsia,” and “hpEurope,” on the basis of their geographical distributions. Here, we use results from that analysis to illustrate site-by-site (in this case nucleotide-by-nucleotide) population-of-origin assignment in haploid organisms.

Figure 7 shows results for a typical isolate from South Africa. South Africa contained isolates from hpAfrica1, hpAfrica2, and hpEurope populations, reflecting the ethnic diversity of the region. The particular isolate we consider here was assigned to the Africa1 (blue) population by the no-admixture model. The top plot (Figure 7A) shows the posterior assignment probabilities for each individual nucleotide based purely on the estimated population allele frequencies (*i.e.*, not using information from q). The plot shows that most sites provide little information about ancestry, with assignment prob-

abilities to all four populations being ~ 0.25 . The remaining nucleotides are mostly assigned with high probability to Africa1 or, less frequently, Africa2 (red). The Africa2 nucleotides appear to come in runs, suggesting import of specific DNA fragments into a bacterium from the Africa1 population. This conclusion was confirmed by further exploratory analysis (Figure 7B). For each population, the sum of the log of the assignment probabilities was computed within a 100-nucleotide moving window. For most of the sequence, the value of the sum was positive for the Africa1 population (indicating higher probabilities than those under random assignment) and negative for the other three populations. However, in three stretches the sum for the Africa2 population gives positive values, suggesting DNA import into those regions.

The linkage model provides a formal method to make population-of-origin assignments that take the linkage relationships into account (Figure 7C). Nucleotides in the three regions identified by the exploratory analysis were assigned to the Africa2 population with probabilities close to 1.0, providing statistical support for the conclusion that there have been (at least) three imports

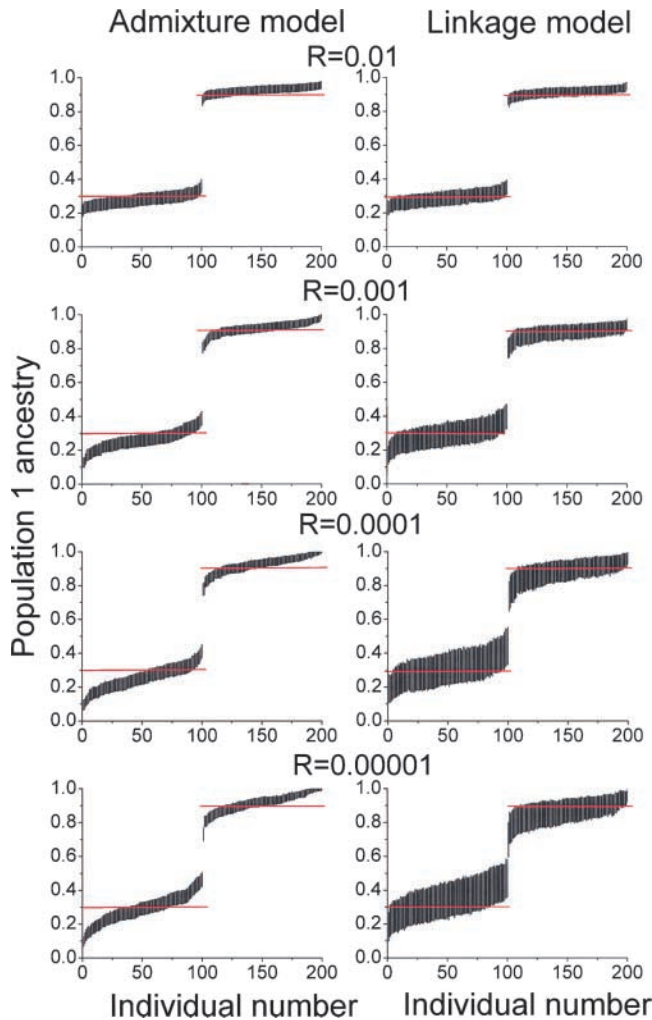


FIGURE 6.—Coverage properties of ancestry estimates for individuals sampled from two postadmixture populations (scenario VII). In each plot, the 90% credibility region for q for each individual is drawn as a thin vertical line. Within each population the true ancestry coefficients are essentially the same for all individuals and are indicated by a red horizontal line. The individuals are ordered according to their point estimates for q . When the inference is performed correctly, $\sim 90\%$ of the individual credibility regions should cross the red line. Details are 100 haploid individuals from each population, $C = 50$, $L^* = 100$. Wright-Fisher simulations were performed with R as shown; $t_1 = 5000$, $t_2 = 32$, $u_{11} = 0.9$, and $u_{21} = 0.3$. $N_0 = 2N_1 = 2N_2 = 5000$ and mutational parameters are as in Figure 4.

of Africa2 DNA into these fragments. This example shows that given highly differentiated populations and enough informative sites, it can be possible in practice to make accurate population-of-origin assignments for individual loci. Further, because of the large amount of information provided by linkage, it is also possible to reconstruct ancestral populations in the absence of pure individuals, using the linkage model. See FALUSH *et al.* (2003) for details of this analysis.

Admixture LD in African-Americans: We used the new linkage model to study the extent of admixture linkage

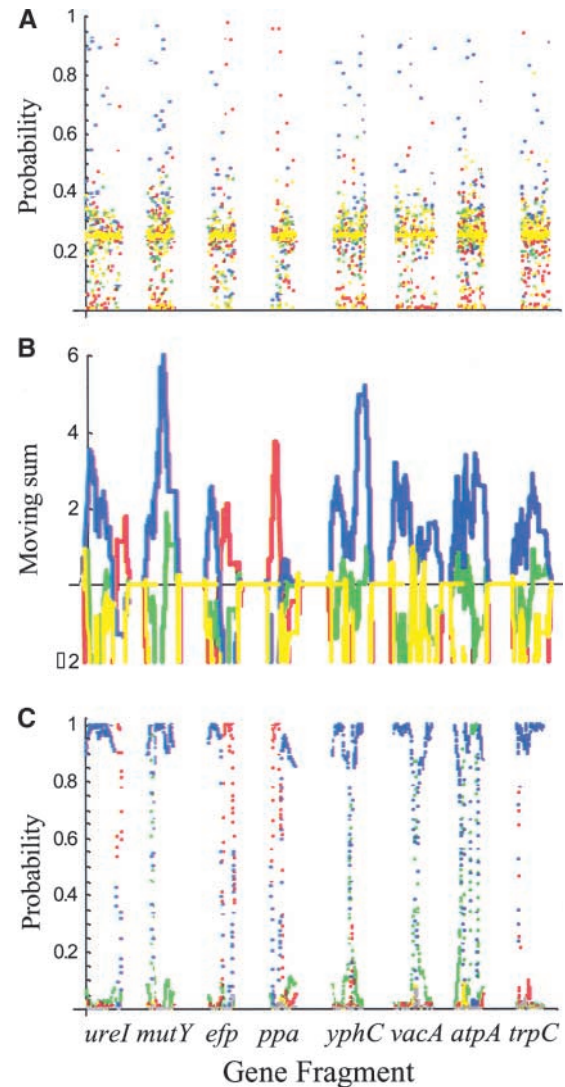


FIGURE 7.—Hybrid ancestry of a *Helicobacter pylori* isolate, showing import of Africa2 fragments (red) into an isolate that is mostly of Africa1 origin (blue). Data are for eight gene fragments of between 398 and 623 nucleotides in length. (A) Posterior assignment probabilities of polymorphic nucleotides to populations, based on the nucleotide frequencies P estimated by the no-admixture model; (B) 100-nucleotide moving sum of the log of four times the assignment probabilities shown in A; (C) assignment of nucleotides using the linkage model. The colors green and yellow indicate European and East Asian contributions, respectively.

disequilibrium in a Chicago-based population of African-Americans. Previous work on African-Americans has shown significant levels of European admixture in the range of $\sim 5\text{--}25\%$, with substantial variation across studies and across study populations (summarized by PARRA *et al.* 1998). Since the admixture is quite recent (primarily in the last 200 years or so; PARRA *et al.* 1998; PFAFF *et al.* 2001), it is likely that admixture LD extends over large distances and hence could be useful for gene mapping (CHAKRABORTY and WEISS 1988; STEPHENS *et al.* 1994; McKEIGUE 1998). Indeed, PARRA *et al.* (1998) de-

tected admixture LD across 22 cM between two markers that have extremely large frequency differences between Africans and Europeans, in several African-American populations.

The data set that we used consists of 247 microsatellites genotyped in samples of unrelated individuals including 210 African-Americans (from Maywood, Illinois), 158 European-Americans (from Michigan), and 308 Nigerians (Yoruba; COOPER *et al.* 2002; THIEL *et al.* 2003). The data were kindly provided by R. Cooper, A. Chakravarti, N. Schork, and A. Weder. We analyzed the data using the linkage model described above, without haplotype phase information. Genetic distances between markers were estimated using the Marshfield linkage map (BROMAN *et al.* 1998). The average spacing between adjacent markers on the same chromosome was 13 cM with a minimum of 2.14 and a maximum of 42.66. While the markers are not especially close together, this density should still be informative about admixture that occurred on the order of 10 generations ago, because under those conditions, adjacent markers would frequently be inherited on the same ancestral chunk.

When run with $K = 2$, both the admixture and linkage models gave very similar ancestry estimates and both suggested that Nigerians and American whites were almost pure representatives of the respective preadmixture populations, with average estimated admixture rates of 1.4% for both populations. The African-Americans were substantially admixed, having a mean of 17.8% European ancestry (the range of point estimates for individuals' values of q was 2–59%, using the admixture model). Similar results were obtained if we used the USEPOPINFO = 1 option to specify the population of origin of the American whites and Nigerians. Our estimate of 17.8% European ancestry is very similar to the estimate of 18.8% obtained by PARRA *et al.* (1998) for their sample from this population.

The posterior distribution for the parameter r under the linkage model is shown in Figure 8A. The posterior mean of r was 0.098 chromosome chunk breakpoints per centimorgan, with a 90% credible region of 0.07–0.13. Under the simplifying assumption that the African-American population was created by a single hypothetical admixture event (scenario V), this event is estimated to have taken place 7–13 generations ago. This is consistent with what one might expect, on the basis of the history of African-Americans, who were mostly exported from Africa during the late eighteenth century (PARRA *et al.* 1998) and have undergone some degree of continuous admixture with the European-American population since then.

We repeated our analysis using information provided by map distances from the recently published deCODE map (KONG *et al.* 2002) and obtained similar answers (data not shown). To assess the potential impact of map misspecification more generally, we applied *structure* to a series of simulated data sets with inaccurately specified

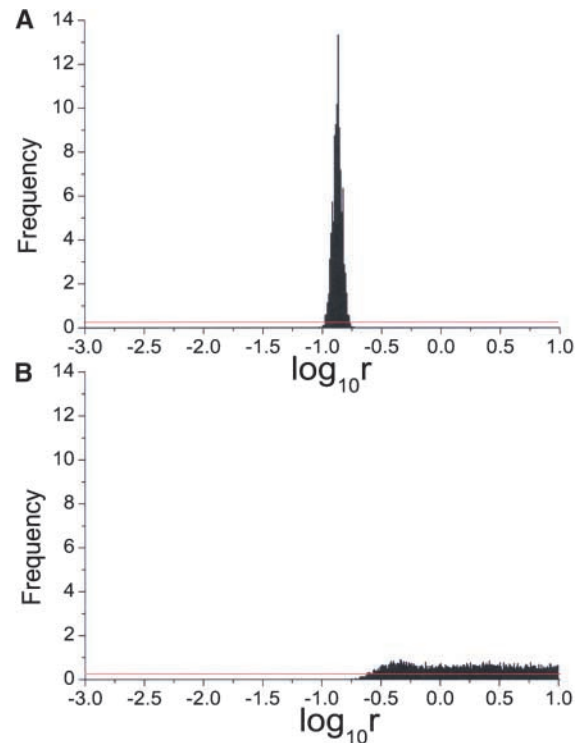


FIGURE 8.—Posterior distribution of the chunk size parameter r , per centimorgan, for the data set of African-Americans, European Americans, and Nigerians. (A) Genetic distances estimated from the Marshfield map; (B) using Marshfield map distances but with the order of the loci randomized. The prior distribution of $\log_{10} r$ is uniform on $(-3, 1)$ and is shown by the red line on each graph.

maps (Figure 9). The simulations assumed that the estimated distances between markers are unbiased on average, but may be inaccurate. The results indicate that as long as the chromosome chunks are typically larger than the intermarker distances, then even highly inaccurate maps do not lead to biases in r .

The posterior distribution of r (Figure 8A) clearly excludes large values of r , indicating that we are detecting a significant signal of admixture LD. Recall that as r gets large the linkage model becomes equivalent to the admixture model, so the fact that the posterior for r excludes large values shows that the linkage model provides a better fit to the data than does the admixture model in this case. For comparison, Figure 8B shows the posterior for r for the same data and map distances, but with the order of the loci randomized. The posterior for r has considerable support all the way up to the maximum value of r permitted by the prior and would clearly have extended to still larger values had the prior allowed this. Three further randomizations produced similar results, supporting the effectiveness of the posterior for r in summarizing the extent of admixture LD.

Although we detected a definite signal of admixture LD in our sample, most of the LD present in the African-Americans is actually due to variation in q : *i.e.*, “mixture

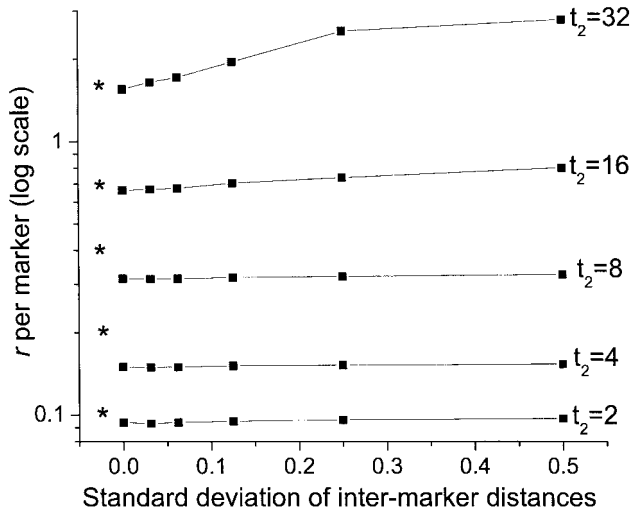


FIGURE 9.—Effect of genetic map-distance errors on estimates of r . Simulations were performed according to scenario V, in which an additional population is formed by mixture of two ancestral populations, t_2 generations before sampling. The intermarker distances used to simulate the data were all equal (5 cM), but *structure* was given distances with errors (mean of 1 unit; standard deviation as shown on x -axis). The asterisks show the correct estimates of r for each value of t_2 . Map errors had a substantial effect on estimates of r only when the average chunk size was smaller than the intermarker distances. Details are $L^* = 100$, $C = 25$, $N_0 = 7500$, $N_1 = N_2 = N_3 = 2500$. $t_1 = 50$, $R = 0.05$, $N_2 = 2500$. Markers were simulated according to the stepwise mutation model with $\mu = 10^{-4}$. In each case, *structure* was run with $K = 2$, using 50 haploid individuals from each of the three populations. The genetic map distances entered into the program were simulated as Poisson(n)/ n , for a range of values of n (corresponding to different levels of accuracy). In the notation of Figure 1, $u_{11} = 1$, $u_{22} = 1$, $u_{31} = 0.5$, $u_{32} = 0.5$.

LD” in the terminology we introduced earlier. To differentiate between mixture and admixture LD, we examined the correlations of ancestry estimates (from the admixture model) between adjacent loci. The first measure that we used (Figure 10A) measures the correlation between the estimated probability of African ancestry (averaged over the two allele copies at each locus) for pairs of neighboring loci. The correlations were positive on average (mean 0.041 with standard error 0.009), albeit with a great deal of variation between different locus pairs. These correlations reflect the total LD in the sample. The second measure (Figure 10B) shows the correlations that remain when variation in q among African-Americans is accounted for. For each individual, at each locus, we computed a “residual” by subtracting the individual’s estimated $q^{(i)}$ from the estimated probability of African ancestry (averaged over the two allele copies at each locus). The figure shows the correlations of these residuals. The correlations are slightly but not significantly negative on average (mean -0.001 with standard error 0.007), implying that most of the LD in the sample can be accounted for by variation in q (i.e., mixture LD). Further, a regression of the correlations

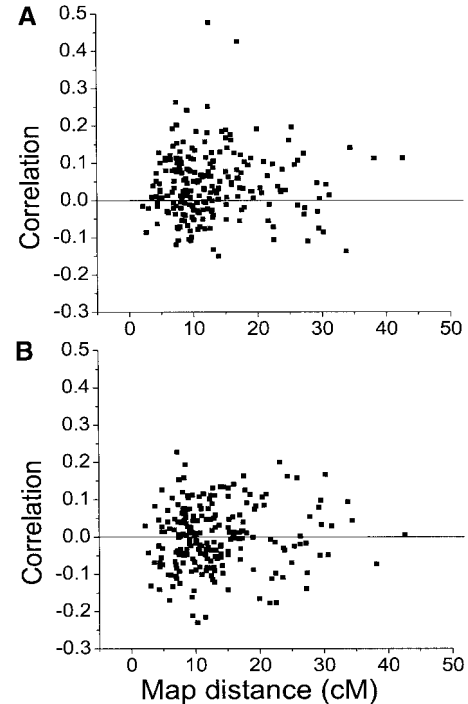


FIGURE 10.—Most of the LD present in African-Americans is mixture LD, not admixture LD. The figure shows two different measures of correlation between adjacent markers, plotted as a function of the genetic distance between the markers. (A) Correlation of ancestry probabilities for allele copies at pairs of adjacent markers. (B) Residual correlation of ancestry probabilities, corrected for variation in q across individuals. The correlations in the top plot are the result of both mixture and admixture LD and are clearly positive on average, albeit noisy. The correlations in the bottom plot result from admixture LD only, and the average is not significantly different from zero. However, the more powerful *structure*-based analysis does detect a strong signal of admixture LD. See text for further explanation.

with the genetic distance between the loci does not have a significant slope under either measure, presumably because the trend has been obscured by the high degree of variation in correlation values at each genetic distance. The fact that the linkage model obtains plausible estimates of r and rejects large values of r indicates that the linkage model extracts much more information from the data than the pairwise comparisons do.

Our results also highlight an important feature of human genetic data, which is that there is a great deal of noise in raw LD estimates for individual locus pairs, even when the admixture involves populations that, by human standards, are relatively highly differentiated. Thus, our description of admixture LD in this population would be enhanced by using a denser set of markers, and for applications such as admixture mapping where one needs to estimate the population of origin for the sampled chromosomes, a denser marker set would be critical. In admixed populations where loci have been chosen specifically to have large frequency

differences between the putative parental populations (PARRA *et al.* 1998), these loci may be more informative for studying admixture than microsatellites were here.

Genetic drift in *Drosophila melanogaster*: To illustrate some of the possible ways of using the F model in historical inference, we have reanalyzed the data set of AGIS and SCHLÖTTERER (2001). Their data set consisted of 48 microsatellite loci typed in samples of flies from Israel (1 sampling location, 58 genotypes), New South Wales, Australia (8 sampling locations, 190 genotypes), and Tasmania (2 sampling locations, 53 genotypes). Some of the genotypes came from isofemale lines, so we haplo-dized the data set by randomly discarding an allele copy at each locus. In the original analysis, Agis and Schlötterer found that the Tasmanian population had similar high pairwise F_{ST} values with both Australian and Israeli populations. In contrast, F_{ST} between Australian and Israeli flies was quite low (though statistically significant), as is typical for populations of *Drosophila melanogaster*. Tasmanian flies had lower genetic diversity than the other groups, but statistical tests for bottlenecks based on the allelic distribution in individual locations were inconclusive, not providing clear evidence for stronger drift within the Tasmanian lineage. Since their analysis did not establish any particular connection between the Australian and Tasmanian populations, Agis and Schlötterer could not rule out the possibility that Tasmanian flies might have come from an entirely different source population with distinct gene frequencies.

We started the analysis without making any assumption about geographical clustering. Using the no-admixture and F models, $K = 3$ gave the highest model likelihood. The three inferred populations correlated well with the land masses Israel, Tasmania, and Australia, although many flies were not clearly allocated to one population and 50 Australian flies, 2 Tasmanian flies, and 7 Israeli flies were assigned to their home population with $<50\%$ probability. These inconsistencies are due to limited statistical power rather than to identifiable admixture events because an analysis under the migration model with the USEPOPINFO option (PRITCHARD *et al.* 2000), in which each genotype was assigned a 5% prior probability of being admixed, did not identify any evidence for admixture. The value of F inferred for the Tasmanian population was high, consistent with a strong episode of genetic drift (Figure 11A). The much lower values of F for the other two populations and the weaker correlation of assignments with geography indicate that there has been no comparable episode of genetic drift separating Israeli and Australian flies.

Where did the Tasmanian flies come from? We estimated F values when analyzing Tasmanian and Israeli flies together (Figure 11C) and Tasmanian and Australian flies together (Figure 11D). The value of F inferred for the Australian population was close to zero, much lower than that for the Israeli population, while a high value of F was estimated for the Tasmanian population

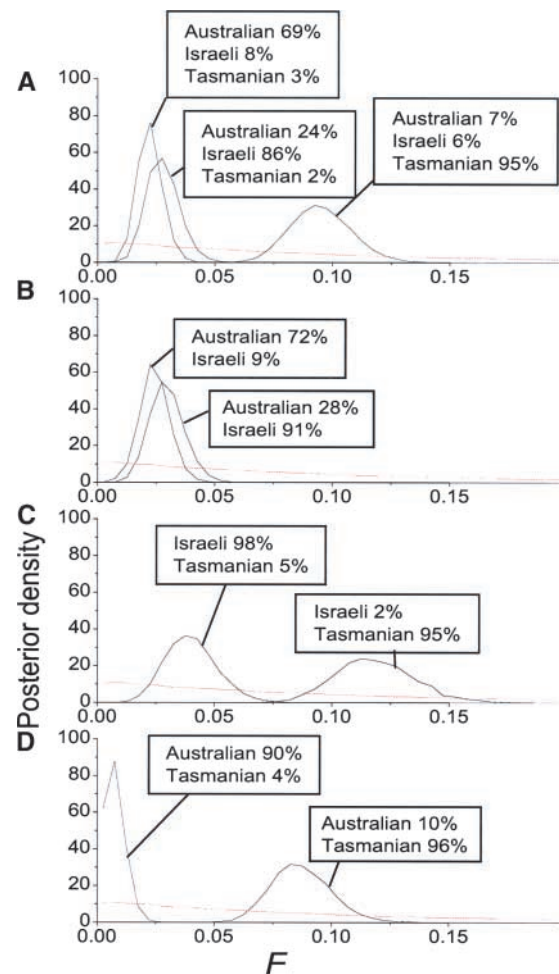


FIGURE 11.—Posterior for F for *D. melanogaster* populations identified by *structure*. The prior (a gamma distribution with a mean and standard deviation of 0.1) is shown as a red dotted line. (A) Values of F estimated using the whole data set, with $K = 3$. (B–D) Values estimated with $K = 2$, excluding data from Tasmania, Australia, and Israel, respectively. The proportions of genotypes from the three land masses assigned to each *structure* population are shown in boxes.

in both cases. This analysis suggests that Tasmanian and Australian flies share a more recent common ancestor with each other than with the Israeli flies. Further, the amount of drift that the Australian flies have undergone since splitting with the Tasmanian flies is very low, implying that Tasmania was colonized from Australia and underwent a bottleneck in the process. A possible technical objection to our analysis is that flies were sampled in several locations in Australia and that this might somehow account for the particularly low estimated value of F . We tested for this possibility using the five sampling locations in Australia that had >25 genotypes. We ran *structure* separately for each one, using all of the Tasmanian genotypes in every case. The analysis gave a consistently high value of F for the Tasmanian population (0.100–0.125) and a low value for the Australian population (0.004–0.023)—lower than that for the Israeli

population in the equivalent analysis (0.039). Our inference therefore appears to be robust to the exact combination of populations chosen for analysis.

The approach we have taken is similar to that used by NICHOLSON *et al.* (2002), who calculated drift parameters for populations that were defined on the basis of geographical labels (this type of analysis can be performed using *structure* by using the program option USEPOPINFO). For this data set utilizing geographical labels does not change the conclusions concerning the origin of the Tasmanian flies, although it does lead to different estimates for the extent of genetic drift, estimating higher values of F for the Israeli population (0.055 *vs.* 0.026) and lower values of F for the Australian one (0.015 *vs.* 0.022) when all three populations are included in the analysis. These results show that when clustering is inaccurate due to limited divergence between populations, this can significantly affect F estimates. The advantage of the approach taken here is that no assumption is made at the outset about the likely patterns of geographical partitioning. If either the actual population structure is independent of geography, for example, because of cryptic speciation, or the boundaries to gene flow are unexpected, then this will be picked up by the analysis. In the *Drosophila* example, the most likely cause of differentiation is one that might have been expected at the outset—a founder effect during the colonization of an island from a mainland source.

DISCUSSION

We have presented two major modifications of the *structure* approach, namely the linkage model and the F model. Both can significantly improve the technical quality of the inference, giving better clustering, more realistic confidence limits, and more accurate admixture estimates. For some data sets, these improvements are critical, allowing the detection of population substructure or admixture that was invisible using the earlier algorithm. The new models are also an important step in making *structure* into a tool for performing detailed historical inference.

The linkage model allows *structure* to analyze data sets containing markers with admixture LD between them, significantly expanding the range of data sets for which it is an appropriate tool. For data sets with weak admixture LD (*e.g.*, the African-American example), the linkage model gives similar clustering and ancestry estimates to the admixture model, but also estimates a chunk size parameter r that provides information on the average rate of decay of admixture LD in the sample. The rate of decay reflects the amount of time that has elapsed since populations admixed. For very informative data sets (*e.g.*, the *H. pylori* data), the linkage model also allows accurate assignment of chromosomal chunks to ancestral populations. One consequence is that ancestral populations can be reconstructed even if admixture

has been so extensive that no pure individuals remain in the sample. In highly informative data sets, it might also be useful to relax the assumption of a single value for r . Possible ways forward include using a different r for each individual or geographical location and/or allowing the expected chunk size to depend on the population of origin of the chunk. In this way, it might be possible to extract additional information about the timing of admixture between different subpopulations.

Although the linkage model takes into account the correlations between markers that occur due to admixture, *structure* will always need data from several unlinked or weakly linked genetic regions from each individual to make meaningful inferences. We strongly recommend against using the model for a data set consisting of human Y chromosome or mitochondrial haplotypes, for example. As well as having markers from several genomic regions, it is also important that none of the markers be too strongly linked. Background linkage disequilibrium arises through genetic drift within populations, and in some scenarios this can lead *structure* to produce misleading results.

Background LD causes problems when particular allele combinations are overrepresented in two or more of the populations before admixture takes place. Such LD can arise through genetic drift before the populations separate (*i.e.*, during the burn-in phase in scenarios V, VI, and VII in Figure 1). If the markers are tightly linked, then this LD can persist throughout the period of divergence and subsequent admixture. Suppose that for this reason, allele combinations ab and AB are overrepresented in both of the populations, compared to Ab and aB . The linkage model tries to attribute this LD to admixture and hence tends to overestimate the frequency of alleles a and b in one population and the frequency of alleles A and B in the other. In this manner, *structure* can both overestimate the divergence between ancestral populations and infer spurious admixture. Because background LD decays over short distances, this also leads to overestimation of the time since admixture.

In designing a data set to be used by the linkage model, it is therefore desirable to ensure that the markers are sufficiently closely linked to allow for admixture LD, yet sufficiently far apart that there is not substantial background LD between them. Historical information about the likely time of admixture, combined with knowledge of intermarker recombination rates, can be used to help select an appropriate marker spacing.

An alternative, post hoc, approach is to rely on inspection of *structure* output. One observation that we have made from simulations (based on a variety of demographic scenarios; data not shown) is that when background LD is a problem, *structure* infers that *all individuals* from *both* populations are admixed. Genuine admixture, by contrast, is often asymmetrical, affecting some populations much more than others. For example, if a predefined subpopulation in the sample has substantial ances-

try from one *structure* population without corresponding ancestry from a second, then this is an indication that background LD is not a serious bias. Further when $K > 2$, background LD causes admixture to be inferred preferentially between the most closely related *structure* populations; thus if admixture is inferred between distantly related populations, this result is unlikely to result from background LD.

In future, it should be possible to specifically model the background LD present in the data. Full coalescent approaches to this type of problem are computationally daunting, and so models that simplify the structure of the data may be suitable. One approach would be to use a Markov formulation of haplotype structure, perhaps like that used by DALY *et al.* (2001). This model would split each chromosome into segments that contained background LD, so that any LD between segments would be due to admixture. Another, more ambitious, approach would be to approximate patterns of LD using the kinds of ideas applied in a quite different setting by STEPHENS *et al.* (2001).

This article also introduced the new *F* model for correlated allele frequencies. This update improves clustering for some data sets where populations are very weakly differentiated and also allows inference of the pattern of drift. We used the model to show that Tasmania was almost certainly colonized by Australian *D. melanogaster* and that a significant bottleneck occurred in the process. A weakness of the current model is that it assumes that all populations have evolved by independent drift from a single ancestral source population, which may not always be a good approximation. This framework could potentially be generalized to incorporate, and differentiate between, more complicated scenarios, with populations splitting from each other sequentially.

The new implementation of *structure* (version 2) also contains other new options that can be useful for some data sets. In the earlier version, the gene frequencies P and admixture proportions Q were drawn from symmetric Dirichlet distributions with parameters λ and α , respectively. λ was normally fixed at 1.0, which corresponds to a uniform prior on allele frequencies. For some types of markers (*e.g.*, sequence polymorphisms and SNPs, depending on the process of ascertainment), the frequency spectrum may be skewed toward rare alleles. In this situation, the data are better modeled by smaller values of λ (smaller values of λ place more prior weight on configurations where all but one allele at a locus is rare). Therefore, we have implemented a Metropolis-Hastings update for λ . We have found that for data where most alleles are rare, updating λ can lead to more accurate estimates of P . We now also allow different values of α for each population. This generalized prior for Q allows for the fact that in practice not all populations are equally represented in the sample, which may lead to more accurate ancestry estimates, particularly in situations of highly asymmetric admix-

ture. The no-admixture model assumes a prior probability that each individual is drawn from one of the K populations is $1/K$. It would also be possible to generalize this prior to allow for differences in frequency between populations but this option has not yet been implemented.

The large number of model options that have now been implemented might lead to concerns about overparameterization. However, provided that there are a reasonable number of loci (>10), the number of model parameters added by each model option is small in comparison with both the number of elements in the data set and the total number of parameters estimated by *structure* (which include all the elements of P and Q). Indeed, although the *F* model may appear to increase the number of parameters to be estimated by the model, in some sense it *decreases* the effective number of parameters, by introducing correlations among the allele frequencies in the different populations.

Nevertheless, there may not be enough information in a particular data set to estimate all of the parameters, in which case a simpler model would be more appropriate. The linkage model adds only a single parameter, r , but for some data sets little or no admixture LD may be present (indicated by posterior support for large values of r), in which case the admixture model should provide essentially the same answers (and be faster to run). It is also possible that certain parameter combinations could lead to problems. For example, our experience with simulated data suggests that it is sometimes difficult to estimate both λ and F jointly (perhaps because estimated values for λ are sensitive to the estimates for the ancestral allele frequencies P_A , which in turn are sensitive to estimates of F). In such cases we have found it useful to first estimate λ using the old independent model for population allele frequencies and then to fix λ at its estimated value while using the *F* model for correlated allele frequencies.

In many cases, symptoms that might be attributed to overparameterization in fact provide useful indicators of genuine biological uncertainty. For example, the model used for gene frequencies sometimes has a large effect on the estimates of admixture proportions that are obtained. In Figure 2 the estimates of admixture between the populations (in fact, 0) are much more accurate under the *F* model than under the uncorrelated model. However, neither model makes accurate estimates for the proportion of European ancestry of the African-Americans if Nigerians are excluded from the sample. The uncorrelated model overestimates admixture (28%) while the *F* model underestimates it (3%). For both of these data sets, the large difference in admixture estimates between models provides an indication that there is limited information on the true degree of admixture. In contrast, when Nigerians are added to the latter data set, both models give very similar estimates (18 and 17%) for the European ancestry of African-

Americans, reflecting the additional information about African gene frequencies provided by the unadmixed individuals.

Despite the many complexities in the demography of species, their genetic structure can often be approximated by a division into discrete (or semidiscrete) populations. This approximation greatly simplifies statistical inference, allowing assignment of individuals to populations, with modest computational requirements even for large data sets. Here, we have extended the approach to gain greater information on the history of the populations themselves. In effect, we are approximating a complex history by a narrative of population fissions and fusions. The resulting algorithms remain computationally tractable and can potentially help resolve the major events in the history of the species under study.

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APPENDIX

Here we provide the computational details for the new MCMC updates. Recall that our goal is to sample from the joint posterior distribution of

$$\Pr(P, Q, Z, r, F, \alpha, \lambda | X, K). \quad (\text{A1})$$

MCMC methods provide an approach for doing this. We start by making arbitrary initial choices for each parameter and then propose updates that change a subset of these, conditional on the other parameters and the data. One full iteration of our Markov chain proposes changes to each parameter. This algorithm results in a Markov chain whose stationary distribution is the joint posterior distribution of interest. For background on these methods in the present context see PRITCHARD *et al.* (2000) or a general text such as GILKS *et al.* (1996).

PRITCHARD *et al.* (2000) described updates for P , Q , Z , and α . Here, we describe updates for r , F , and λ , as well as modified updates for Q and Z under the linkage model, and for P under the F model.

MCMC update for the F model: The update for p_{kl} is similar to that for the original (independent frequencies) model (Equation A6, PRITCHARD *et al.* 2000), but substitute $p_{\Delta l}(F_k^{-1} - 1)$ in place of λ_j .

The update for the “ancestral” allele frequencies P_A is more complicated. The algorithm that we have implemented is as follows. Start with initial guesses for P_A (*e.g.*, based on the overall sample frequencies). Then, at each step of the Markov chain, propose the following update once for each locus. Select at random two alleles m and n , such that $1 \leq m < n \leq J_l$, where J_l is the total number of alleles observed at locus l . Simulate a value δ from a normal with mean 0 and some small (fixed) standard deviation (we used 0.05) and propose changing the allele frequencies $p_{\Delta lm}$ and $p_{\Delta ln}$ to $p'_{\Delta lm} = p_{\Delta lm} + \delta$ and $p'_{\Delta ln} = p_{\Delta ln} - \delta$, respectively. Reject the proposal if either of the proposed allele frequencies is outside (0, 1). Otherwise, accept the updated allele frequencies according to the appropriate Metropolis-Hastings probability, that is, the minimum of 1 and

$$\frac{\Pr(P'_A)\Pr(P_1, \dots, P_K | P'_A, F)}{\Pr(P_A)\Pr(P_1, \dots, P_K | P_A, F)}, \quad (\text{A2})$$

where $\Pr(P_A)$ is the prior probability of P_A , assumed to be symmetric Dirichlet with parameter λ . Expression (A2) can be rewritten as

$$\left(\frac{p'_{\Delta lm} p'_{\Delta ln}}{p_{\Delta lm} p_{\Delta ln}} \right)^{\lambda-1} \prod_{k=1}^K \frac{\Gamma(f_k p_{\Delta lm}) \Gamma(f_k p_{\Delta ln})}{\Gamma(f_k p'_{\Delta lm}) \Gamma(f_k p'_{\Delta ln})} p_{klm}^{\delta} p_{kln}^{-\delta}, \quad (\text{A3})$$

where $f_k \equiv (1 - F_k)/F_k$.

Finally, to update each value of F_k , we start from an initial value $F_k^{(0)}$ (the prior mean, say) and then update it as follows. Conditional on the current value, F_k , we propose a new value, F'_k , from a normal distribution with mean F_k and some fixed standard deviation (0.05, say). If the new value F'_k is outside the interval (0, 1), we reject the proposal. Otherwise, we accept it with the Metropolis-Hastings probability, namely, the minimum of 1 and

$$\frac{\Pr(F'_k)\Pr(P_k | P_A, F'_k)}{\Pr(F_k)\Pr(P_k | P_A, F_k)}, \quad (\text{A4})$$

where $\Pr(F_k)$ is the prior probability of F_k , assumed to be proportional to a gamma distribution with mean μ and variance σ^2 (see main text). Expression (A4) can be rewritten as

$$\exp\left[\frac{\mu(F_k - F'_k)}{\sigma^2}\right] \left(\frac{F'_k}{F_k}\right)^{\mu^2/\sigma^2-1} \prod_{l=1}^L \left[\frac{\Gamma(f'_l) \prod_j \Gamma(f_j p_{\Delta lj}) p_{klj}^{p_{\Delta lj}}}{\Gamma(f_l) \prod_j \Gamma(f_j p_{\Delta lj}) p_{klj}^{p_{\Delta lj}}} \right], \quad (\text{A5})$$

where f' and f are $(F'_k - 1)/F'_k$ and $(F_k - 1)/F_k$, respectively. If we assume a single value F for all populations, the update is much the same, except that the posterior ratio is given by a product over both k and l .

Full description of the linkage model, including unphased data: The following describes an MCMC scheme for simulating from a Markov chain with stationary distribution $\Pr(P, Z, r, Q|X, K)$.

1. Sample from $\Pr(Z|P, r, Q, X)$.
2. Sample from $\Pr(P|Z, r, Q, X) = \Pr(P|X)$.
3. Update r by Metropolis-Hastings update.
4. Update Q by Metropolis-Hastings update.

Step 2 is exactly the same as in PRITCHARD *et al.* (2000). Step 1 can be done separately for each individual, using the forward-backward algorithm (*e.g.*, RABINER 1989), as follows. We start by assuming that individuals are haploid or that phase is known. For each chromosome from one individual (and omitting the individual's superscript i for clarity), we let $\beta_{lk} = \Pr(x_1, \dots, x_l, z_l = k|P, r, Q)$. Then, recalling that p_{klj} is the frequency of allele j at locus l in population k , we have

$$\beta_{1k} = q_k p_{k1x_1} \quad (\text{A6})$$

for $k = 1, \dots, K$ and

$$\beta_{(l+1)k'} = \sum_{k=1}^K \beta_{lk} \Pr(z_{l+1} = k' | z_l = k) p_{k'(l+1)x_{l+1}}. \quad (\text{A7})$$

This allows us to compute β_{lk} for $k = 1, \dots, K$ and $l = 1, \dots, L$ (the “forward” part of the algorithm). This computation can be made linear in K rather than quadratic, following a simple rearrangement. After substituting Equation 3 for $\Pr(z_{l+1} = k' | z_l = k)$, we get

$$\beta_{(l+1)k'} = \left[\sum_{k=1}^K \beta_{lk} \right] p_{k'(l+1)x_{l+1}} q_{k'} (1 - \exp(-d_l r)) + \beta_{lk'} p_{k'(l+1)x_{l+1}} \exp(-d_l r). \quad (\text{A8})$$

Note that the sum in brackets is independent of k' and therefore needs to be calculated only once for each l .

Having done this, the “backward” part allows us to simulate Z , starting from z_L , using Gibbs sampling based on

$$\Pr(z_L = k|X, P, r, Q) \propto \beta_{Lk} \quad (\text{A9})$$

and

$$\begin{aligned} \Pr(z_l = k | z_{l+1}, \dots, z_L, X, P, r, Q) &\propto \Pr(z_l = k, x_1, \dots, x_l | P, r, Q) \Pr(z_{l+1}, \dots, z_L, x_{l+1}, \dots, x_L | P, r, Q) \\ &\propto \beta_{lk} \Pr(z_{l+1} | z_l = k, r, Q), \end{aligned} \quad (\text{A10})$$

where $\Pr(z_{l+1} | z_l = k, r, Q)$ is given by (3).

For unphased or partially phased diploids, we have implemented two algorithms. The two algorithms can incorporate different types of phase information and produce equivalent results for unphased data. The first algorithm is based on a Markov formulation for phase information. For each pair of adjacent linked loci we have an estimate of the probability b_l that the first alleles of loci l and $l+1$ are on the same chromosome. Information that adjacent allele copies were inherited together from the same (unspecified) parent is often available from sib-pair pedigree data. For unphased data the order of the allele copies is random so that $b_l = 0.5$ for all loci. We define

$$\beta_{lk^1k^2} = \Pr(x_1^1, x_1^2, \dots, x_l^1, x_l^2, z_l^1 = k^1, z_l^2 = k^2 | P, r, Q), \quad (\text{A11})$$

where superscript $(^1)$ refers to the first allele copy and $(^2)$ refers to the second allele copy at each locus. Denote the quantity in the right-hand side of Equation 3 by $P_{k'k}$. In the forward part of the algorithm we calculate

$$\beta_{1k^1k^2} = q_{k^1} q_{k^2} p_{k^1 1x_1^1} p_{k^2 1x_1^2} \quad (\text{A12})$$

for $k^1 = 1, \dots, K$; $k^2 = 1, \dots, K$; and

$$\beta_{(l+1)k^1k^2} = \sum_{k^1=1}^K \sum_{k^2=1}^K \beta_{lk^1k^2} p_{k^1(l+1)x_{l+1}^1} p_{k^2(l+1)x_{l+1}^2} \{b_l P_{k^1k^1} P_{k^2k^2} + (1 - b_l) P_{k^1k^2} P_{k^2k^1}\}. \quad (\text{A13})$$

In the backward part we jointly simulate z^1 and z^2 using

$$\Pr(z_L^1 = k^1, z_L^2 = k^2 | X, P, r, Q) \propto \beta_{Lk^1k^2} \quad (\text{A14})$$

and

$$\Pr(z_L^1 = k^1, z_L^2 = k^2 | z_{l+1}^1, z_{l+1}^2, \dots, z_L^1, z_L^2, X, P, r, Q) \propto \beta_{lk^1k^2} \{b_l P_{z_{l+1}^1k^1} P_{z_{l+1}^2k^2} + (1 - b_l) P_{z_{l+1}^1k^2} P_{z_{l+1}^2k^1}\}. \quad (\text{A15})$$

The model for maternal and paternal phase information is similar; here

$$\beta_{lk^mk^p} = \Pr(x_1^1, x_1^2, \dots, x_l^1, x_l^2, z_l^m = k^m, z_l^p = k^p | P, r, Q), \quad (\text{A16})$$

where superscripts m and p refer to the maternal and paternal allele copies at each locus,

$$\beta_{lk^mk^p} = q_{k^m} q_{k^p} \{M_l p_{k^m1x_l^1} p_{k^p1x_l^2} + (1 - M_l) p_{k^m1x_l^2} p_{k^p1x_l^1}\} \quad (\text{A17})$$

and

$$\beta_{(l+1)k^mk^p} = \sum_{k^m=1}^K \sum_{k^p=1}^K \beta_{lk^mk^p} P_{k^mk^p} P_{k^mk^p} \{M_l p_{k^m(l+1)x_{l+1}^1} p_{k^p(l+1)x_{l+1}^2} + (1 - M_l) p_{k^m(l+1)x_{l+1}^2} p_{k^p(l+1)x_{l+1}^1}\}, \quad (\text{A18})$$

where M_l is the probability that allele 1 at locus l is inherited maternally, assumed known. In the backward step, we simulate the population of origin of maternal and paternal chromosomes.

$$\Pr(z_L^m = k^m, z_L^p = k^p | X, P, r, Q) \propto \beta_{Lk^mk^p} \quad (\text{A19})$$

and

$$\Pr(z_l^m = k^m, z_l^p = k^p | z_{l+1}^m, z_{l+1}^p, \dots, z_L^m, z_L^p, X, P, r, Q) \propto \beta_{lk^mk^p} P_{z_{l+1}^mk^m} p_{z_{l+1}^pk^p}. \quad (\text{A20})$$

We then simulate the population of origin for the two allele copies at each locus, conditional on maternal and paternal assignments, using

$$\Pr(z_l^1 = k^m, z_l^2 = k^p | z_l^m = k^m, z_l^p = k^p) \propto M_l p_{k^mk^p} p_{k^pk^m}. \quad (\text{A21})$$

For both of these diploid models, a rearrangement analogous to that described for the haploid case leads to the computation in the forward part being proportional to K^2 rather than to K^4 .

For each of these models, the updates for r and Q use the random-walk Metropolis algorithm. In haploids, for example (with the individual superscript i reinstated),

$$\Pr(x_1^{(i)} \dots x_L^{(i)} | P, r, q^{(i)}) = \sum_{k=1}^K \beta_{Lk}^{(i)}; \quad (\text{A22})$$

r is updated using a Metropolis-Hastings step, by comparing this sum for proposed and current values of r . We have implemented a uniform prior for $\log_{10}(r)$; the proposed value of $\log_{10}(r)$ differs from the current value according to a normal distribution with mean of 0.05.

Last, we perform step 4, the Metropolis-Hastings update for Q , as follows. For each individual i , we simulate a proposal value $q^{(i)*}$ from the prior distribution, which is $D(\alpha_1, \alpha_2, \dots, \alpha_K)$. The proposed value $q^{(i)*}$ is accepted with probability that is equal to the ratio of the likelihoods.

MCMC updates for λ and α : We begin by placing independent uniform priors in the range (0, 10) on λ_k for each population k . We start the Markov chain at arbitrary initial values, $\lambda_k^{(0)} = 1$, for instance, and then update each λ_k as follows. Conditional on the current value of λ_k , we propose a new value λ'_k from a normal distribution with mean λ_k and some standard deviation (0.3, say). If λ'_k is outside (0, 10), we reject the new proposal; otherwise, we accept it according to the standard Metropolis-Hastings ratio. That is, we accept it with a probability that is the minimum of 1 and

$$\frac{\prod_{l=1}^L \Gamma(J_l \lambda'_k) \Gamma(\lambda_k)^{J_l}}{\prod_{l=1}^L \Gamma(J_l \lambda_k) \Gamma(\lambda'_k)^{J_l}} (p_{k1} p_{k2} \dots p_{kL})^{\lambda'_k - \lambda_k}. \quad (\text{A23})$$

The latter expression is the ratio of the density function for the Dirichlet distribution given the proposed and current values of λ_k , respectively, multiplied across all loci. If we assume that the same value of λ holds for all K populations, then the analogous update ratio is

$$\frac{\prod_{l=1}^L \prod_{k=1}^K \Gamma(J_l \lambda') \Gamma(\lambda)^{J_l}}{\prod_{l=1}^L \prod_{k=1}^K \Gamma(J_l \lambda) \Gamma(\lambda')^{J_l}} (p_{k1} p_{k2} \dots p_{kL})^{\lambda' - \lambda}. \quad (\text{A24})$$

The full update used for α is closely analogous to that for λ , except that the products are over individuals, not loci, and over ancestry coefficients, q , not allele frequencies, p .

