

1 **UNDERSTANDING ADMIXTURE FRACTIONS**

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ABSTRACT. Estimation of admixture fractions has become one of the most commonly used computational tools in population genomics. However, there is remarkably little population genetic theory on their statistical properties. We develop theoretical results that can accurately predict means and variances of admixture proportions within a population using models with recombination and genetic drift. Based on established theory on measures of multilocus disequilibrium, we show that there is a set of recurrence relations that can be used to derive expectations for higher moments of the admixture fraction distribution. We obtain closed form solutions for some special cases. Using these results, we develop a method for estimating admixture parameters from estimated admixture proportion obtained from programs such as *Structure* or *Admixture*. We apply this method to HapMap data and find that the population history of African Americans, as expected, is not best explained by a single admixture event between people of European and African ancestry. A model of constant gene flow for the past 11 generations until 2 generations ago gives a better fit.

3 INTRODUCTION

4 It is common in population genetic analyses to consider individuals as
5 belonging fractionally to two or more discrete source populations. The pro-
6 portion of an individual's genome that belongs to a population is called
7 that individual's 'admixture fraction' or 'admixture proportion'. Programs
8 such as *Structure* (Pritchard et al., 2000), *Eigenstrat* (Price et al., 2006),
9 *Frappe* (Tang et al., 2005), or *Admixture* (Alexander et al., 2009) can jointly
10 estimate these admixture fractions for multiple individuals in a sample, along
11 with the corresponding allele frequencies in each of the source populations.
12 These admixture fractions are often presented in a 'structure plot,' an ex-
13 ample of which is shown in Figure 1. We will henceforth refer to these
14 methods as 'structure analyses'. This approach has proven highly useful for
15 understanding genetic relationships in many different species, e.g. humans

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16 (Rosenberg et al., 2002), cats (Menotti-Raymond et al., 2008), or pandas
17 (Zhang et al., 2007). Other analyses reconstruct admixture tracts for each
18 genome in the sample, by inferring the local ancestry of every position, or
19 window, in each sampled genome (Tang et al., 2006; Maples et al., 2013). In
20 this context, the admixture fraction for a genome is the fraction of its total
21 length that is inherited from a particular source population.

22 Although structure analyses are not tied to any particular mechanistic
23 model of population history and demography, the admixture fractions and
24 admixture tracts are commonly interpreted to be the result of past admix-
25 ture events in which modern populations were formed by admixture (or
26 introgression) between ancestral source populations. The distribution of
27 admixture tract lengths has been related to specific mechanistic models of
28 admixture (Falush et al., 2003; Tang et al., 2006; Pool and Nielsen, 2009),
29 and has been used to estimate times of admixture (Gravel, 2012). However,
30 the admixture proportions themselves also contain information regarding
31 admixture times. Following an admixture event, the variance in admixture
32 proportions within a population will be high, but will thereafter decrease,
33 and will eventually converge to zero in the limit of large genomes. The
34 variance in admixture fractions among individuals contains substantial in-
35 formation about the time since admixture that can be used in addition to
36 the tract length distribution. In some cases, this may be more robust than
37 inferences based on tract lengths, because the length distribution of tracts
38 is often difficult to infer, and is often not modeled accurately by the hid-
39 den Markov model (HMM) methods used to infer tract lengths (Liang and
40 Nielsen, 2014). Even in cases where tract lengths can be accurately inferred,
41 studies aimed at estimating admixture times should benefit from using both
42 variance in admixture proportions among individuals and overall admixture
43 tract lengths distributions.

44 Verdu and Rosenberg (2011) developed a method for computing moments
45 of admixture proportions in a model in which admixed population is formed
46 as a mixture between multiple source populations, allowing for arbitrary
47 gene-flow from the source populations over a number of generations (g).
48 They establish recursions for the moments of the admixture fractions and
49 use these equations to determine how the mean and the variance changes
50 through time in particular admixture scenarios. These moments are expec-
51 tations for *single* individual's admixture fraction and are averaged over the
52 possible genealogical histories of the population. As a result, they can be

53 difficult to relate to data because replicates from multiple identical popula-
54 tions rarely are available. In this paper, we consider a different problem, the
55 problem of calculating sample moments for admixture proportions obtained
56 from individuals in one population.

57 We extend the model model in Verdu and Rosenberg (2011) to incorporate
58 the effects of recombination and genetic drift by adding a a random union of
59 zygotes component. Recombination is important because even if one half of
60 a chromosome's ancestors are from the first source population, it is unlikely
61 that exactly one half of that chromosome's genetic material is inherited
62 from that population. Genetic drift is important because the individuals in
63 a sample might share ancestors and, therefore, have more similar admixture
64 fractions than expected by chance in a model without drift. The results
65 developed in this paper should be directly applicable for quantifying the
66 results of a structure analysis.

67

THE GENERAL MECHANISTIC MODEL

68 We start by considering admixture fractions in haploid genomes. These
69 haploid admixture fractions can later be paired up to create diploid admix-
70 ture fractions. The admixture fraction of a (haploid) genome H_i , is the
71 proportion of H_i that is inherited from a particular source population. For
72 notational simplicity, we only consider gene-flow only from one population
73 into another. We will later discuss how to extend this model to multiple ad-
74 mixing source populations. We use the same mechanistic admixture model
75 of Verdu and Rosenberg (2011), and will use its notation where possible.
76 Finally, we use the random union of zygotes model, with a diploid popula-
77 tion size of N ($2N$ chromosomes), for genetic drift and recombination, and
78 assume a sample size of n chromosomes from a single population.

79 In this model, a hybrid population of N diploid individuals forms in gen-
80 eration 1 from two previously isolated source populations. In this first
81 generation, individuals in the hybrid population are from the first source
82 population with probability s_0 or from the second source population with
83 probability $1 - s_0$. In generation $g + 1$, each chromosome is, independently,
84 from the first source population with introgression probability s_g , or from
85 the hybrid population with probability $1 - s_g$. Chromosomes inherited from
86 the hybrid population are the product of the recombination of the two chro-
87 mosomes of one individual (zygote), chosen uniformly at random. Finally,

88 these $2N$ chromosomes are paired up to form the N individuals in generation
89 $g + 1$.

90 Finally, we let the stochastic process $A(\ell)$ represent the local ancestry
91 along a chromosome as a function of ℓ , the physical position:

$$A(\ell) = \begin{cases} 0 & : \ell \text{ is descended from first source population} \\ 1 & : \ell \text{ is descended from second source population} \end{cases} .$$

92 The fraction of the chromosome descended from the second source popu-
93 lation is given by

$$H = \frac{1}{L} \int_0^L A(\ell) d\ell,$$

94 where L is the total length of the chromosome.

95 Assume that g generations after the start of admixture we have randomly
96 sampled n chromosomes from the hybrid population and determined their
97 corresponding admixture fractions, $H_{1(g)}, H_{2(g)}, \dots, H_{n(g)}$. We are inter-
98 ested in the joint distribution of these n random variables. When $n = 1$
99 and as $L \rightarrow \infty$, this is the admixture fraction considered by Verdu and
100 Rosenberg (2011).

101 Because the n chromosomes have possibly overlapping genealogies, the
102 admixture fractions are not independent. However, the joint distribution
103 of the admixture fractions does not depend on their ordering, so they are
104 exchangeable. As a result, they can be viewed as being identically and
105 independently (*iid*) drawn from a random distribution \mathcal{G} . This random
106 distribution can be interpreted as a function of the random genealogy of
107 the entire hybrid population up to g generations in the past. When g is
108 small, the genealogies of the n samples will be unlikely to differ from n non-
109 overlapping binary trees, so \mathcal{G} will be approximately constant. If g is large
110 however, these genealogies are likely to overlap, and this will no longer be
111 true.

112 Verdu and Rosenberg (2011) focus on moments of $H_{1(g)}$, in particular on
113 the mean and variance. However, because the admixture fractions are not
114 independent, even as $n \rightarrow \infty$, the sample mean and sample variance will
115 converge to the mean and variance of \mathcal{G} , which are random quantities. For
116 example,

$$\mathbb{E}(H_{1(g)}) \neq \mathbb{E}(H_{1(g)}|\mathcal{M}) = \lim_{n \rightarrow \infty} \frac{1}{n} \sum_{i=1}^n H_{i(g)}$$

$$\text{var}(H_{1(g)}) \neq \text{var}(H_{1(g)}|\mathcal{M}) = \lim_{n \rightarrow \infty} \frac{1}{n-1} \sum_{i=1}^n \left(H_{i(g)} - \frac{1}{n} \sum_{j=0}^n H_{j(g)} \right)^2,$$

117 and similarly for higher-order moments. The moments of the admixture
 118 factions have two components: randomness from sampling the population
 119 genealogy, and randomness from the sampling of chromosomes. The ex-
 120 pressions to left account for both, while the expressions to the right only
 121 account for the latter. Variances among individuals within one popula-
 122 tion correspond to $\text{var}(H_{1(g)}|\mathcal{G})$, while variances over replicate populations
 123 correspond to $\text{var}(H_{1(g)})$. This latter value will be larger than the expected
 124 sample variance calculated from multiple individuals sampled from the same
 125 population, and will rarely be useful for inference purposes.

126 In the following sections, we will show how the constants on the left-hand
 127 side, as well as expectations of the random variables on the right-hand side,
 128 can be derived for mechanistic models of introgression. By comparing these
 129 expectations to the observed admixture parameters from a sample, we will
 130 be able to construct a method of moments estimator for the parameters of
 131 the model.

132 Let k_1 be the sample mean:

$$k_1 \equiv \frac{1}{n} \sum_{i=1}^n H_{i(g)}.$$

133 We can express its expectation in terms of the 1-point correlation function
 134 of A :

$$\begin{aligned} \mathbb{E}(k_1) &= \mathbb{E}(H_{1(g)}) \\ &= \frac{1}{L} \int_0^L \mathbb{P}\{A_{1(g)}(\ell) = 1\} d\ell \\ &= \mathbb{P}\{A_{1(g)}(0) = 1\}. \end{aligned}$$

135 Similarly, let k_2 be the unbiased estimator of the sample variance:

$$k_2 \equiv \frac{1}{n-1} \sum_{i=1}^n (H_{i(g)} - k_1)^2.$$

136 Its expectation is given by

$$\begin{aligned} \mathbb{E}(k_2) &= \frac{1}{n-1} \sum_{i=1}^n \mathbb{E}(H_{i,g}^2) - \frac{1}{n(n-1)} \sum_{i,j=1}^n \mathbb{E}(H_{i,g}H_{j,g}) \\ &= \mathbb{E}(H_{1,g}^2) - \mathbb{E}(H_{1,g}H_{2,g}). \end{aligned}$$

137 These expectations can be written in terms of two-point correlation func-
138 tions of A :

$$\begin{aligned} \mathbb{E}(H_{1(g)}^2) &= \frac{1}{L^2} \mathbb{E} \left(\int_0^L A_{1(g)}(\ell) d\ell \int_0^L A_{1(g)}(\ell') d\ell' \right) \\ &= \frac{1}{L^2} \int_0^L \int_0^L \mathbb{E} (A_{1(g)}(\ell) A_{1(g)}(\ell')) d\ell d\ell' \\ &= \frac{1}{L^2} \int_0^L \int_0^L \mathbb{P} \{ A_{1(g)}(\ell) = 1, A_{1(g)}(\ell') = 1 \} d\ell d\ell'. \end{aligned}$$

139 Similarly,

$$\mathbb{E}(H_{1(g)}H_{2(g)}) = \frac{1}{L^2} \int_0^L \int_0^L \mathbb{P} \{ A_{1(g)}(\ell) = 1, A_{2(g)}(\ell') = 1 \} d\ell d\ell'.$$

140 Writing these two correlation functions as

$$\mathbf{v}_{2(g)} = \begin{pmatrix} \mathbb{P} \{ A_{1(g)}(\ell) = 1, A_{1(g)}(\ell') = 1 \} \\ \mathbb{P} \{ A_{1(g)}(\ell) = 1, A_{2(g)}(\ell') = 1 \} \end{pmatrix},$$

141 we find that

$$(1) \quad \mathbb{E}(k_2) = \frac{1}{L^2} \int_0^L \int_0^L \begin{pmatrix} 1 & -1 \end{pmatrix} \mathbf{v}_{2(g)} d\ell d\ell'.$$

142 In general, the i^{th} k -statistic is an unbiased estimator of the i^{th} cumulant
143 of \mathcal{G} , and its expectation can be written as an integral over $[0, L]^i$ of a linear
144 combinations of i -point correlation functions. For example,

$$\begin{aligned} \mathbb{E}(k_3) &= \frac{1}{L^3} \int_0^L \int_0^L \int_0^L \begin{pmatrix} 1 & -1 & -1 & -1 & 2 \end{pmatrix} \mathbf{v}_{3(g)} d\ell d\ell' d\ell'' \\ \mathbb{E}(k_4) &= \frac{1}{L^4} \int_{[0,L]^4} \begin{pmatrix} 1 & \underbrace{-1}_{4 \text{ times}} & \underbrace{-1}_{3 \text{ times}} & \underbrace{2}_{6 \text{ times}} & 6 \end{pmatrix} \mathbf{v}_{4(g)} d\ell d\ell' d\ell'' d\ell''' \\ &\dots \end{aligned}$$

145 Remarkably, the linear combinations required to compute the expecta-
 146 tions of the k -statistics correspond exactly to the higher-order disequilibria
 147 as defined by Bennett (1952). Furthermore, if instead we choose to
 148 compute the expectations of the h -statistics, which estimate the central
 149 moments, the linear combinations would correspond to the higher-order dis-
 150 equilibria as defined by Slatkin (1972).

151 We next find the recurrence relations these correlation functions satisfy
 152 and solve them in the some special cases. In particular we will consider the
 153 case of a single admixture event g generations ago and the case of constant
 154 gene-flow starting g generations ago.

155 **A Single Admixture Event.** We start with a simple case, where intro-
 156 gression only occurs in the founding generation, i.e. $s_g = 0$ for $g > 0$. Using
 157 the random union of zygotes model, we can compute $\mathbf{v}_{2(g)}$ in terms of the
 158 probabilities from the previous generation:

159 If two sites at ℓ and ℓ' are on the same chromosome in generation $g + 1$,
 160 then they were inherited from one chromosome from generation g with prob-
 161 ability $[\ell\ell']$ and from two chromosomes from generation g with probability
 162 $[\ell|\ell']$. If they are on different chromosomes, then the probability that they
 163 are descended from one chromosome in generation g is $\frac{1}{2N}[\ell\ell']$ and the prob-
 164 ability that they are descended from two chromosomes is $\frac{1}{2N}[\ell|\ell'] + (1 - \frac{1}{2N})$
 165 In matrix notation,

$$\mathbf{v}_{2(g+1)} = (\mathbf{L}_2 \mathbf{U}_2) \mathbf{v}_{2(g)} = (\mathbf{L}_2 \mathbf{U}_2)^g \mathbf{v}_{2(0)},$$

166 where the recombination and drift matrices are given by

$$\mathbf{L}_2 = \begin{pmatrix} 1 & 0 \\ \frac{1}{2N} & 1 - \frac{1}{2N} \end{pmatrix}$$

$$\mathbf{U}_2 = \begin{pmatrix} [\ell\ell'] & [\ell|\ell'] \\ 0 & 1 \end{pmatrix}.$$

167 This is the the same matrix equation (Wright 1933 and Hill and Robertson
 168 1966) derived for the decay of two-locus linkage disequilibrium. The ‘alleles’
 169 we consider are the local ancestry at ℓ and ℓ' . To the extent possible, our
 170 notation will follow (Hill 1974), whose results for measures of multi-locus
 171 linkage disequilibria we use. The matrices \mathbf{L}_2 and \mathbf{U}_2 share $(1 \ -1)$ as a
 172 left-eigenvector, with corresponding eigenvalues $1 - \frac{1}{2N}$ and $[\ell\ell']$. As a result,

$$\begin{aligned} \mathbb{E}(k_2) &= \frac{1}{L^2} \int_0^L \int_0^L \begin{pmatrix} 1 & -1 \end{pmatrix} \cdot (\mathbf{L}_2 \mathbf{U}_2)^g \mathbf{v}_{2(0)} d\ell d\ell' \\ (2) \quad &= \frac{1}{L^2} \left(1 - \frac{1}{2N}\right)^g (s_0 - s_0^2) \int_0^L \int_0^L [\ell\ell']^g d\ell d\ell'. \end{aligned}$$

173 For a model using the Haldane map function, $[\ell|\ell'] = \frac{1 - \exp(-2|\ell - \ell'|)}{2}$, this
 174 equation becomes

$$\begin{aligned} \mathbb{E}(k_2) &= \frac{1}{L^2} \left(1 - \frac{1}{2N}\right)^g (s_0 - s_0^2) \int_0^L \int_0^L \left(\frac{1 + \exp(-2|\ell - \ell'|)}{2}\right)^g d\ell d\ell' \\ &= \frac{2}{L^2} \left(1 - \frac{1}{2N}\right)^g (s_0 - s_0^2) \int_0^L (L - \ell) \left(\frac{1 + \exp(-2\ell)}{2}\right)^g d\ell d\ell', \end{aligned}$$

175 while for a model of complete crossover interference on a chromosome of
 176 length 1 Morgan, we can get a closed form solution:

$$\begin{aligned} \mathbb{E}(k_2) &= \left(1 - \frac{1}{2N}\right)^g (s_0 - s_0^2) \int_0^1 \int_0^1 (1 - |\ell - \ell'|)^g d\ell d\ell' \\ &= \left(1 - \frac{1}{2N}\right)^g (s_0 - s_0^2) \frac{2}{2 + g}. \end{aligned}$$

177 For predicting the expected sample variance, the difference between these
 178 two models is not large, as shown in figure 4. For the simulations and
 179 inference in this paper, we will ignore crossover interference, and use the
 180 Haldane map function. However, none of the mathematical results of this
 181 paper will require this assumption.

182 For computing higher-order correlation functions, we find a similar equa-
183 tion

$$(3) \quad \mathbf{v}_{i(g)} = (\mathbf{L}_i \mathbf{U}_i)^g \mathbf{v}_{i(0)}.$$

184 Bennett's coefficients for higher-order linkage are left-eigenvectors of the
185 recombination matrix \mathbf{U}_i . For $i = 3$, it is also a left-eigenvector of the drift
186 matrix, so we immediately get that

$$\mathbb{E}(k_3) = \frac{s_0(1-s_0)(2-s_0)}{L^3} \left(1 - \frac{1}{2N}\right)^T \left(1 - \frac{2}{2N}\right)^T \int_{[0,L]^3} [\ell \ell' \ell'']^G d\ell d\ell' d\ell''.$$

187 For $i \geq 4$, this is no longer true, but the results of (Hill, 1974) can be
188 used to compute $\mathbf{v}_i(g)$ without having to exponentiate the entire drift and
189 recombination matrices. For example, for k_4 , the drift and recombination
190 matrices are 15×15 , but using the technique in (Hill, 1974), we only need
191 to exponentiate a 4×4 matrix to compute $\mathbb{E}(k_4)$.

192 **Varying Migration.** If $s_g > 0$ for $s \geq 1$, we obtain a modified version of
193 Equation 3:

$$(4) \quad \mathbf{v}_{i(g)} = \mathbf{L}_i \mathbf{D}_{i(g)} \mathbf{U}_i \mathbf{v}_{i(g-1)},$$

194 where the diagonal matrix $\mathbf{D}_{i(g)}$ has entries giving the probabilities the
195 set of chromosomes, p , in a correlation function are all from the hybrid
196 population in the previous generation:

$$d_{p,p(g)} = (1 - s_g)^{|p|}.$$

197 Note that if $s_{(g)}$ is fixed, then equation (4) is linear, and can be solved
198 using a Laplace transform.

199 INFERENCE OF ADMIXTURE TIMES

200 The equations in the previous section can be used to develop a method
201 of moments-estimators for admixture parameters by numerically solving the
202 admixture parameters in terms of the expectations for the k -statistics. Sub-
203 stituting in the observed values for the k -statistics gives estimates for the
204 admixture parameter(s).

205 However, with real data, we only have estimates of the admixture frac-
206 tions, so some of the variability seen in the distribution of admixture frac-
207 tions will be due to estimation variability. To account for this, we assume
208 that the estimations errors are additive and *iid*:

$$\hat{H}_{i(g)} = H_{i(g)} + \epsilon_i.$$

209 Because cumulants are additive,

$$\begin{aligned}\mathbb{E}(k_n) &= \mathbb{E}(\kappa_n(H_{i(g)} + \epsilon_i | \mathcal{G})) \\ &= \mathbb{E}(\kappa_n(H_{i(g)} | \mathcal{G})) + \kappa_n(\epsilon_i).\end{aligned}$$

210 The expectations we have computed are just the term of this sum. To correct
211 for the variability in the estimates, we need to subtract off the second term.
212 We use a block bootstrap to estimate these effects.

213 One additional complication arises in dealing with genotyping data. We
214 have assumed that we have the ancestry fractions for each haplotype in the
215 sample, but with genotyping data, we instead have their pairwise means:
216 $(H_{1(g)} + H_{2(g)})/2 \dots$. This results in a decrease in the expectations of
217 the k -statistics. Conditional on the random distribution \mathcal{G} , $H_{1(g)}, H_{2(g)}, \dots$
218 are *iid* drawn from \mathcal{G} . Cumulants are additive, so we use the law of total
219 expectation to find that

$$\begin{aligned}\kappa_i\left(\frac{H_{1(g)} + H_{2(g)}}{2}\right) &= \mathbb{E}\left(\kappa_i\left(\frac{H_{1(g)} + H_{2(g)}}{2} \middle| \mathcal{G}\right)\right) \\ &= \mathbb{E}\left(\kappa_i\left(\frac{H_{1(g)}}{2} \middle| \mathcal{G}\right) + \kappa_i\left(\frac{H_{2(g)}}{2} \middle| \mathcal{G}\right)\right) \\ &= 2^{-i+1} \mathbb{E}(\kappa_i(H_{1(g)} | \mathcal{G})) \\ &= 2^{-i+1} \kappa_i(H_{1(g)}).\end{aligned}$$

220 **Comparison to Verdu and Rosenberg.** The recursion equations given
221 by Verdu and Rosenberg (2011) are different from the ones we have derived.
222 This is partly because we have accounted for the effects of genetic drift and
223 recombination, but also because we are computing the moments of slightly
224 different quantities.

225 In figure 2, we have shown the admixture fractions for five replicate pop-
226 ulations 5, 50, and 500 generations after an admixture pulse. The variance
227 that (Verdu and Rosenberg, 2011) compute variance over all the replicate

228 populations, while the variance we have computed in this paper is the ex-
 229 pectation of the variance within a single population. When g is small, these
 230 similar, but when g is large, the variance within a population goes to zero,
 231 but the variance across the replicate populations does not. This effect is
 232 shown in Figure 3. Initially, both quantities decline exponentially in g , but
 233 after $2^g > nLg$, the variance we predict begins to decline linearly instead.
 234 This is because variance is inversely proportional to the number of genetic
 235 ancestors of the sample. When g is small, the number of genetic ancestors
 236 is approximately 2^g . However, the approximate number of recombination
 237 events in the sample is approximately bounded by nLg , so when this quan-
 238 tity is smaller than 2^g , it provides a better approximation for the number
 239 of genetic ancestors. In this regime, the variance will decline linearly in g .

240 It is also possible to compute the variance over all population replicates
 241 under our model, which allows a direct comparison to Verdu and Rosenberg
 242 (2011). In the case of one pulse of admixture, we can now solve equations 1
 243 for $\mathbb{P}\{A_{1,g}(\ell) = 1, A_{1,g}(\ell') = 1\}$ to get

$$\begin{aligned}
 \text{var}(H_{1(g)}) &= \mathbb{E}(H_{1,g}^2) - s_0^2 \\
 &= \frac{1}{L^2} \int_0^L \int_0^L \mathbb{P}\{A_{1,g}(\ell) = 1, A_{1,g}(\ell') = 1\} d\ell d\ell' - s_0^2 \\
 (5) \quad &= \frac{1}{L^2} (s_0 - s_0^2) \int_0^L \int_0^L 1 - (1 - [\ell\ell']) \frac{1 - [\ell\ell']^g (1 - \frac{1}{2N})^g}{1 - [\ell\ell'] (1 - \frac{1}{2N})} d\ell d\ell'.
 \end{aligned}$$

244 This variance and the expectation of the second k -statistic have the same
 245 limit as $N \rightarrow \infty$, but for finite N , the variance is larger. This is because

$$\text{var}(H_{1(g)}) = \text{var}[\mathbb{E}(H_{1(g)}|\mathcal{G})] + \mathbb{E}[\text{var}(H_{1(g)}|\mathcal{G})] = \text{var}[k_1] + \mathbb{E}[k_2].$$

246 The first variance is small when N is large, but is always non-negative.
 247 The difference between this equation and equation 1 only becomes significant
 248 on a coalescent time scale. In the absence of genetic drift, the admixture
 249 fractions are approximately independent, because the samples do not share
 250 ancestors.

251 **Application to African American Data.** We applied this method to a
 252 subset of the ASW, CEU, and YRI data from the HapMap 3 project (Con-
 253 sortium et al., 2010). After excluding children from trios, there were the
 254 genotypes for 49 ASW, 113 YRI, and 112 CEU individuals. We estimated

255 the admixture fractions using the supervised learning mode of **Admixture**,
256 with the CEU and YRI individuals assigned to separate clusters. The sam-
257 pling distribution of the admixture fractions was estimated using the block
258 bootstrap with 10^4 replicates and 2678 blocks, giving a block size of approx-
259 imately 10 CM. The admixture fractions for the 49 ASW samples are shown
260 in Figure 1 and the observed k -statistics are given in table 6.

261 We assumed a 3-parameter model of constant admixture. For $g_{start} \leq$
262 $g \leq g_{stop}$, $s_g = s$ with $s_g = 0$ elsewhere. By matching the block-bootstrap
263 corrected k_2 and k_3 to the predictions of equation 1, we obtained a point
264 estimates of

$$\begin{aligned}\hat{s} &= 0.0277 \\ \hat{g}_{start} &= 2 \\ \hat{g}_{stop} &= 11.\end{aligned}$$

265 We obtained confidence intervals, shown in Figure 5, by simulation. For
266 each cell in the grid, we simulated 10^3 replicates under the corresponding
267 g_{start} and g_{stop} , with $s = 1 - k_1^{1/(g_{stop}-g_{start}+1)}$. For each replicate, we com-
268 puted the k_2 , k_3 , and k_4 statistics. A cell was then included in the confidence
269 interval if and only if the corrected k_2 , k_3 , and k_4 statistics from the HapMap
270 data fall inside a centered interval containing 98.7% of the probability mass
271 of the simulated distribution. This mass was chosen so that under the Bon-
272 ferroni correction for three tests, there is at least a 95% chance of including
273 the true parameter values in the confidence region.

274 The point estimates for g_{start} and g_{stop} correspond to the values for which
275 the observed k -statistics are closest to their simulated medians.

DISCUSSION

277 We have extended the mechanistic model of Verdu and Rosenberg (2011)
278 to account for recombination and genetic drift. Doing so allows us to apply
279 the predictions of this model to data. This mechanistic model allows for a
280 large number of parameters. For the purposes of inference, it seems that
281 imposing constraints, i.e. a small number of pulses or constant admixture,
282 will be needed to narrow the search space.

283 In this paper, we have assumed that admixture only comes from one
284 source population, this need not be the case. To account for admixture
285 from multiple source populations, equation 1 must be modified to account

286 for the probability that haplotypes trace their descent to multiple source
287 populations. Algorithmically, this is feasible, but the notation is cumber-
288 some. The resulting equations are given in the appendix, along with the
289 equations for computing expectations of higher-order k -statistics.

290 Applications of the method to African-American HapMap data provides
291 estimates of the time since admixture between people of Europe and
292 African descent in America. Notice that the confidence set for the admix-
293 ture parameters does not include values of $g_s top = 0$. We interpret this as
294 evidence that admixture rates have declined the last few generations. The
295 point estimate of time gene-flow stopped is $g_s top = 2$. This probably reflects
296 a more gradual reduction in gene-flow within the last 5 generations or so,
297 rather than a discrete stop in gene-flow 2 generations ago. The discreteness
298 is enforced by the model. Also notice that admixture before 15 generations
299 ago can be rejected. With a generation time of 25-30 years, this corresponds
300 to 325-400 years, and is in good accordance with the historical record. The
301 point estimate of the time of first admixture is 11 generations, or approx.
302 275-330 years ago.

303 Structure analyses have become one of the most commonly applied tools
304 in population genomic analyses. The theory developed in this paper allows
305 users of structure analyses to interpret their data in the context of a model of
306 admixture between populations, and should find use in many studies aimed
307 at understanding the history of populations.

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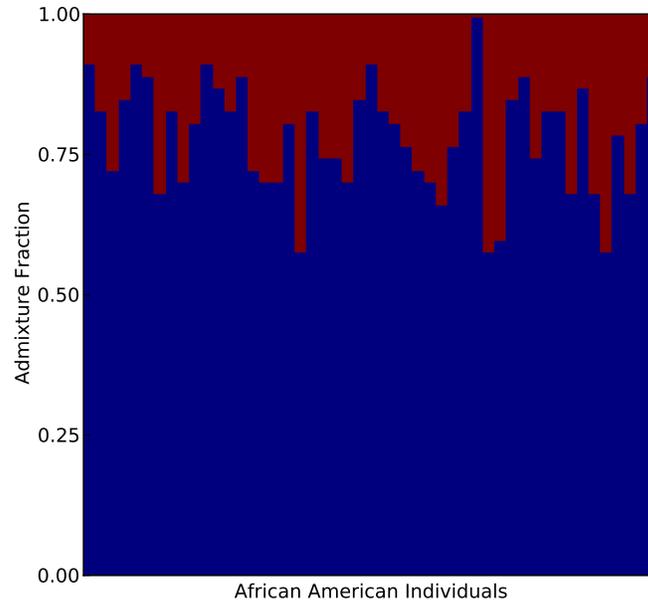


FIGURE 1. Admixture fractions for 49 African American individuals in the HapMap 3 data. Source population allele frequencies were estimated using 113 Yoruban and 111 European individuals.

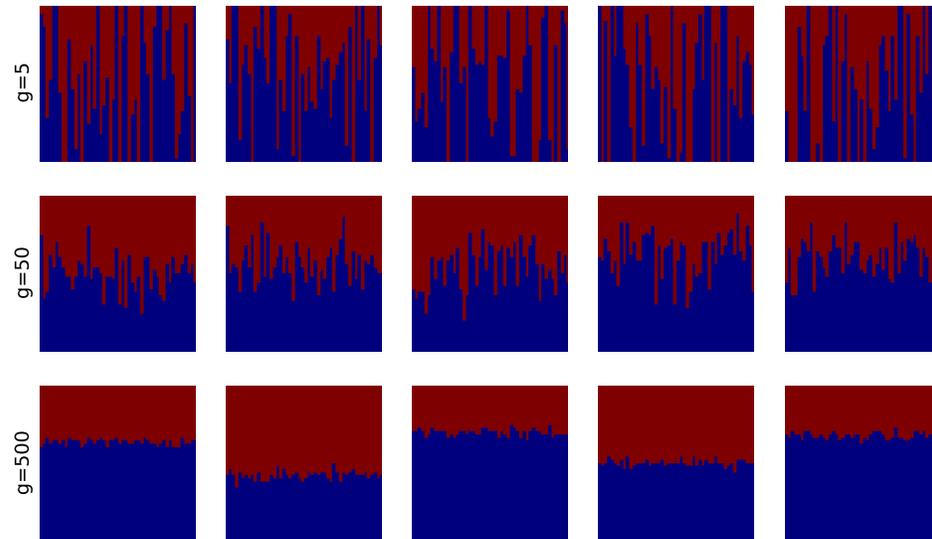


FIGURE 2. The admixture fractions of five replicate populations (each column) 5, 50, and 500 generations after an admixture pulse. As the admixture event grows more ancient, the variability within a replicate population decreases, but some variability is still maintained across the populations.

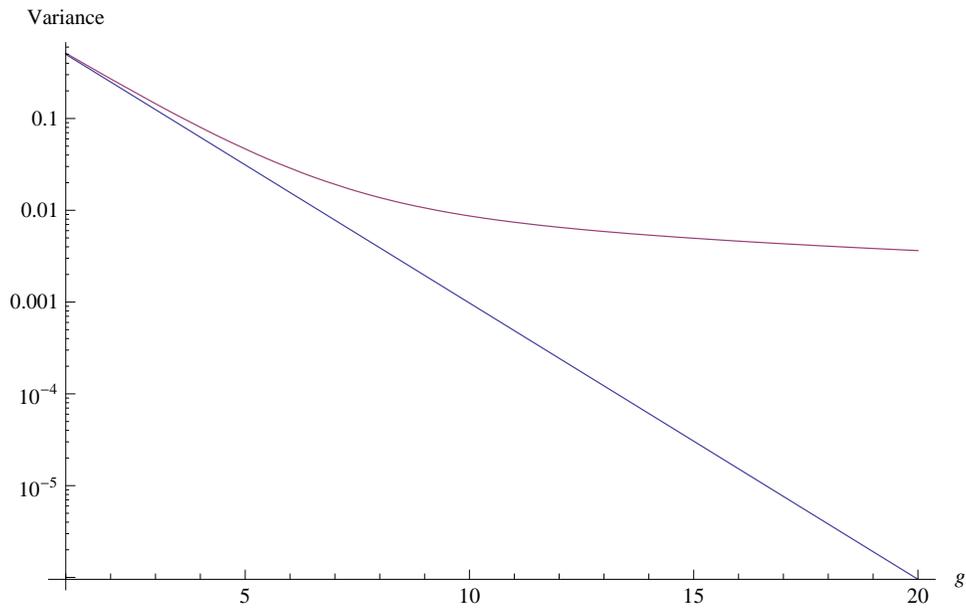


FIGURE 3. The variance predicted by Verdu and Rosenberg (2011) and equation 5, plotted on a logarithmic scale. The variance we predict (red) is always larger, but the two are very similar when g is small.

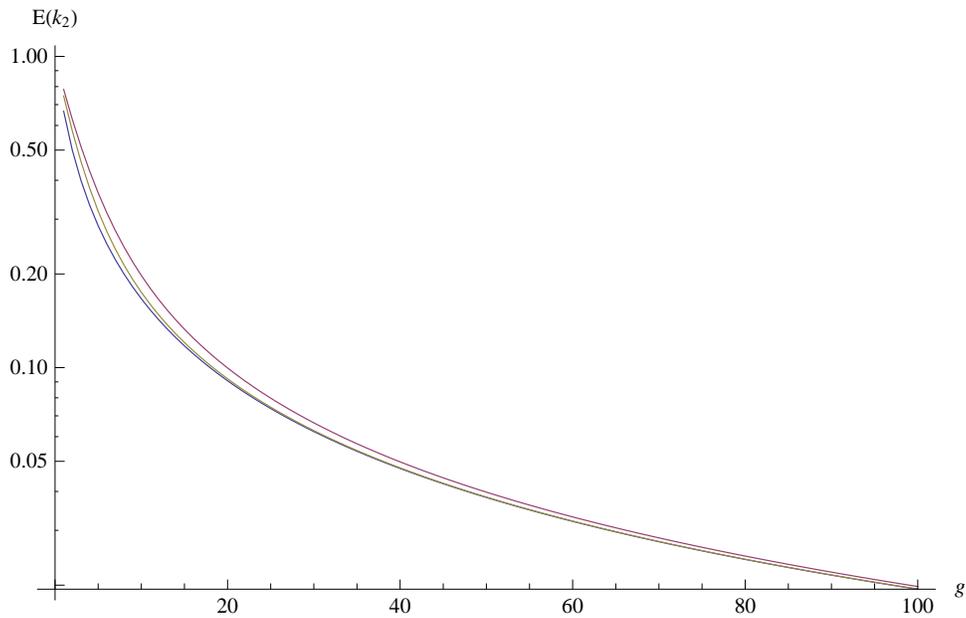


FIGURE 4. The expected sample variance given by equation 1 plotted on a logarithmic scale, for a three different map functions. We used a map distance of $L = 1$ Morgan and $N = 10^4$. The Haldane map function $(1/2 - e^{-2x}/2)$ is in red, the Kosambi map function $(\tanh(2x)/2)$ is in yellow, and the complete interence map function (x) is in blue. For all values of g , the expectations are ordered in the same order as the map functions, but the difference between the three disappears by $g = 100$.

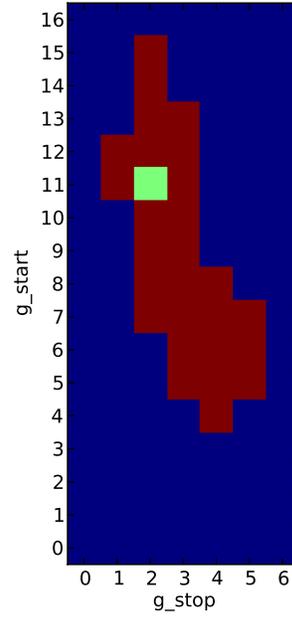


FIGURE 5. 95% confidence region for a model with constant admixture from generations g_{start} to g_{stop} . The point estimate of $g_{start} = 11$ and $g_{stop} = 2$ generations ago is colored green.

	Observed	Bootstrap	Corrected
k_1	0.777	-2.22×10^{-15}	0.777
k_2	9.00×10^{-3}	2.59×10^{-4}	8.75×10^{-3}
k_3	2.98×10^{-4}	1.60×10^{-5}	2.82×10^{-4}
k_4	-3.99×10^{-5}	-1.41×10^{-6}	-3.85×10^{-5}

FIGURE 6. k -statistics

363

APPENDIX

364 These are the matrices for computing $\mathbb{E}(k_3)$. The matrices for computing
 365 $\mathbb{E}(k_4)$ are 15×15 and not given here, but can be found in (Hill, 1974).

$$\begin{aligned}
 \mathbf{v}_{3(g)} &= \begin{pmatrix} \mathbb{P}\{A_{1(g)}(\ell) = A_{1(g)}(\ell') = A_{1(g)}(\ell'') = 1\} \\ \mathbb{P}\{A_{1(g)}(\ell) = A_{1(g)}(\ell') = A_{2(g)}(\ell'') = 1\} \\ \mathbb{P}\{A_{1(g)}(\ell) = A_{2(g)}(\ell') = A_{2(g)}(\ell'') = 1\} \\ \mathbb{P}\{A_{1(g)}(\ell) = A_{2(g)}(\ell') = A_{1(g)}(\ell'') = 1\} \\ \mathbb{P}\{A_{1(g)}(\ell) = A_{2(g)}(\ell') = A_{3(g)}(\ell'') = 1\} \end{pmatrix} \\
 \mathbf{U}_3 &= \begin{pmatrix} [\ell\ell'\ell''] & [\ell\ell'|\ell''] & [\ell|\ell'\ell''] & [\ell\ell''|\ell'] & 0 \\ 0 & [\ell\ell'] & 0 & 0 & [\ell|\ell'] \\ 0 & 0 & [\ell'\ell''] & 0 & [\ell|\ell''] \\ 0 & 0 & 0 & [\ell\ell''] & [\ell'|\ell''] \\ 0 & 0 & 0 & 0 & 1 \end{pmatrix} \\
 \mathbf{L}_3 &= \frac{1}{4N^2} \begin{pmatrix} 4N^2 & 0 & 0 & 0 & 0 \\ 2N & 2N-1 & 0 & 0 & 0 \\ 2N & 0 & 2N-1 & 0 & 0 \\ 2N & 0 & 0 & 2N-1 & 0 \\ 1 & 2N-1 & 2N-1 & 2N-1 & (2N-1)(2N-2) \end{pmatrix} \\
 \mathbf{D}_{3(g)} &= \begin{pmatrix} 1-s_g & 0 & 0 & 0 & 0 \\ 0 & (1-s_g)^2 & 0 & 0 & 0 \\ 0 & 0 & (1-s_g)^2 & 0 & 0 \\ 0 & 0 & 0 & (1-s_g)^2 & 0 \\ 0 & 0 & 0 & 0 & (1-s_g)^3 \end{pmatrix}
 \end{aligned}$$

366 When there is migration from both source populations, the recursion re-
 367 lations for the i -point correlation functions will depend on $i-1$ -point, $i-2$ -
 368 point, \dots correlations functions as well. As an example, consider the case of
 369 $\mathbf{v}_{2(g)}$. Let the introgression probability from the second source population
 370 be given by t_g . The recursion equation for $\mathbf{v}_{2(g)}$ now also depends on $\mathbf{v}_{1(g)}$.

$$\begin{aligned}\mathbf{v}_{2(g+1)} &= \mathbf{L}_2 \begin{pmatrix} 1 - s_g - t_g & 0 \\ 0 & (1 - s_g - t_g)^2 \end{pmatrix} \mathbf{U}_2 \mathbf{v}_{2(g)} + \begin{pmatrix} t_g \\ t_g^2 + 2t_g \mathbb{P}\{A_{1(g)}(\ell) = 1\} \end{pmatrix} \\ &= \mathbf{L}_2 \begin{pmatrix} 1 - s_g - t_g & 0 \\ 0 & (1 - s_g - t_g)^2 \end{pmatrix} \mathbf{U}_2 \mathbf{v}_{2(g)} + \begin{pmatrix} t_g \\ t_g^2 + 2t_g \mathbf{v}_{1(g)} \end{pmatrix}.\end{aligned}$$

371 Similarly, the recursion equation for $\mathbf{v}_{3(g)}$ depends on $\mathbf{v}_{2(g)}$ and $\mathbf{v}_{1(g)}$.