Inference of recent admixture using genotype data

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Abstract

For inference of individual genetic histories, admixture barplots are being used abundantly in forensic genetics. The underlying admixture-model (as e.g. implemented in the software STRUCTURE and ADMIXTURE) assumes parameters for individual ancestry (IA). Further, every allele in the individual's genome originates in one of several ancestral populations with the same probability. Here, we introduce the recent-admixture model. In this model, we assume that the two homologous copies of each allele originate from the ancestral populations independently for the mother's and the father's copy. Estimates for IA in absence of recent admixture are almost identical for the admixture and recent admixture model. However, they are more accurate for the recent-admixture model in individuals which are in fact recently admixed. Moreover, we develop a likelihood ratio test for recent admixture, which has a high power to find recently admixed individuals. We analyse data from the 1000 genomes dataset with our methods and find some recently admixed individuals.

1 Introduction

xxx Start with forensics

xxx Make a good case, e.g. Philippino and Italian located in Afghanistan

Inference of the geographical ancestry of a trace using genetic markers is today a well-established research field in forensic genetics (see e.g. [11, 4, 5]). Either the trace is classified into one of several groups of different origin (e.g. Africa, Europe, East Asia, Native America, and Oceania; see e.g. [10, 8], or it is assumed that it consists of a mixture of ancestral genetic material originating in several groups. For this task, STRUCTURE [13] has become the de-facto standard to estimate individual ancestry (IA) proportions of a trace among several continental groups. (This Bayesian approach using MCMC was complemented by the faster, likelihood based approach, implemented in the software ADMIXTURE [2]; see also [14] for the same model.).

When using STRUCTURE or ADMIXTURE for estimating continental (or other scales of geography) IA of a trace, allelic frequencies for all continents from a reference database must be used. A main assumption for estimating IAs is that all allelic states have the same independent chance to share a

copy from some continent, implying Hardy-Weinberg equilibrium at each site. When using a (small) set of ancestry informative markers, this assumption is justified by the large genomic distance which makes loci almost independent by recombination. However, the assumption that homologous alleles at the same locus have the same probability for carrying some allele – also known as Hardy-Weinberg equilibrium – may not always hold. For example, consider an individual whose parents have different continental backgrounds, and an allele which separates perfectly between the two continents. Then, the individual will certainly be a heterozygote at this marker. This increase in frequency for heterozygotes under admixture is known for a long time and usually called the Wahlund effect [17]. However, STRUCTURE and ADMIXTURE will estimate that the chance for some allele to come from one of the two continents to be 50%, which is then also be the estimate for a heterozygote at the locus (due to the assumption of independence of allelic states in the admixture model).

Inference of recent admixture is often based on an excess of heterozygotes. For example, [7] uses a statistical test by simply counting the number of heterozygous positions in an individual in order to infer recent admixture. Extending work of [16], a likelihood-ratio test for first-order admixed individuals versus outside-of-reference-database is given in [15]. Here, we extend the likelihood-model behind STRUCTURE or ADMIXTURE in order to account for recent admixture. In our approach, IA consists of two vectors, one for each parent. As a result, we obtain estimates of IA for the two parents and can give a likelihood ratio test for recent admixture versus non-admixture of a trace.

xxx some more detail for our approach

xxx Mention Tvedebrink2019, Cheung2018.

xxx explain exchangeability of q^M, q^P.

xxx p-value when our error is better (admixture, recent-admixture);

xxx Figure in Supplement: AFR, EAS, EUR, SAS not worse in recent-admixture

2 Materials and Methods

More details on the derivations in the admixture and recent-admiture model can be found in the SI. Moreover, the implementation of our methods can be downloaded from `https://github.com/pfaffelh/recent-admixture`, and is described in detail in the SI.

2.1 The admixture model

We briefly recall the admixture model, which is the basis for the sofware STRUCTURE [13], ADMIXTURE [2] and FRAPPE [14]. Here and below, we assume to have reference database of M bi-allelic markers from K populations. We denote by p_{mk} the frequency of allele 1 at marker m in population k. We have a trace with $G_m \in \{0, 1, 2\}$ copies of allele 1 at marker m for $m = 1, ..., M$. Assuming that each allele observed in the trace comes from population k with probability q_k, the probability to observe allele 1 at marker m is

$$\beta_m(q) := \sum_k p_{mk} q_k, \tag{1}$$

and the log-likelihood of $q = (q_k)_{k=1,...,K}$ is (see also (S1) in the SI)

$$\ell(q|G) = \sum_{m=1}^{M} \log\Big(\binom{2}{G_m}\beta_m(q)^{G_m}(1-\beta_m(q))^{2-G_m}\Big). \tag{2}$$

Assuming that all p_{mk}'s are known, this function can be maximized over q by computing $\hat{q} = (\hat{q}_k)_{k=1,...,K}$ such that $\hat{q}_k = f_k(\hat{q})$ for (see also (S10) in the SI)

$$f_k(q) = \frac{1}{2M}\sum_{m=1}^{M}\Big(G_m\frac{p_{mk}}{\beta_m(q)} + (2-G_m)\frac{1-p_{mk}}{1-\beta_m(q)}\Big)q_k, \qquad k = 1, ..., K. \tag{3}$$

This can be done numerically by iterating $q_{n+1} = (f_k(q_n))_{k=1,...,K}$ until convergence. (In our implementation, we continue the iteration until $|q_{n+1} - q_n| < 10^{-6}$.) We note that this approach is essentially the same as in the EM-algorithm from [14], but combining the expectation and maximization steps. In addition, although maximizing (2) could also be handled using a Newton method as in [**?**], this approach has the advantage that q_n's are positive in all steps, and the sum of all entries in q_n is always 1. Moreover, the iteration is computationally fast if only a small or moderat number of alleles is considered.

2.2 The recent-admixture model

When mother and father of an individual come with their own vectors of admixture proportions, q^M and q^P, the log-likelihood from (2) changes to (see also (S14) in the SI)

$$\ell(q^M, q^P|G) = \sum_{m=1}^{M}\log(\gamma_m(q^M, q^P, G_m)), \tag{4}$$

$$\gamma_m(q^M, q^P, g) = \begin{cases} \beta_m(q^M)\beta_m(q^P), & \text{if } g = 2, \\ (\beta_m(q^M)(1-\beta_m(q^P)) + (1-\beta_m(q^M))\beta_m(q^P)), & \text{if } g = 1, \\ (1-\beta_m(q^M))(1-\beta_m(q^P)), & \text{if } g = 0. \end{cases}$$

As carried out in the SI, this function can be maximized by computing $\hat{q}^M, \hat{q}^P$ such that $\hat{q}^P = f(\hat{q}^M, \hat{q}^P)$ and $\hat{q}^M = f(\hat{q}^P, \hat{q}^M)$ for $f(q, q') = (f_k(q, q'))_{k=1,...,K}$ with (see (S15) in the SI)

$$f_k(q, q') := \frac{1}{M}\sum_{m=1}^{M}\delta_k(q, q', G_m)q'_k, \tag{5}$$

$$\delta_k(q^M, q^P, g) = \begin{cases} \dfrac{p_{mk}}{\beta_m(q')}, & \text{if } g = 2, \\ \dfrac{(p_{mk}(1-\beta_m(q)) + (1-p_{mk})\beta_m(q))}{\beta_m(q)(1-\beta_m(q')) + (1-\beta_m(q))\beta_m(q')}, & \text{if } g = 1, \\ \dfrac{(1-p_{mk})}{1-\beta_m(q')}, & \text{if } g = 0. \end{cases}$$

In our implementation, we iteratively compute $q^P_{n+1} = f(q^M_n, q^P_n)$ and $q^M_{n+1} = f(\tilde{q}^P_{n+1}, q^M_n)$ until convergence.

2.3 Obtaining admixed individuals in silico

In order to test our method, we created admixed individuals from a reference database. (We use the 1000 genomes dataset, but excluding Admixed Americans, AMR; see below.) For example, we obtain an individual admixed from populations k and k' by choosing a genome $\tilde{G} = (\tilde{G}_m)_{m=1,\ldots,M}$ from population k and $\bar{G} = (\bar{G}_m)_{m=1,\ldots,M}$ from population k' as the parents. Then, $G_m = X_m + Y_m$ where $X_m = 1$ with probability $\tilde{G}_m/2$, $X_m = 0$ with probability $(2 - \tilde{G}_m)/2$ and $Y_m = 1$ with probability $\bar{G}_m/2$, $Y_m = 0$ with probability $(2 - \bar{G}_m)/2$. When iterating this procedure, we can also model second-order admixed individuals etc. in silico.

Using AFR, EAS, EUR, SAS as population labels (as in the 1000 genomes dataset), all cases for second generation admixed individuals fall into one of seven categories. Writing up the ancestries of the four grand-parents (Mother of mother, father of mother / mother of father, father of father), we have the following cases for second generation admixed individuals (the full list of all resulting 55 cases is given in the SI; note that [3] come up with only 35 cases, since they do not distinguish between maternal and paternal ancestry, e.g. they count AFR, AFR / EAS, EAS and AFR, EAS / AFR, EAS as one case):

(A) 4 non-admixed cases, e.g. AFR, AFR/ AFR, AFR;

(B) 6 admixed cases with admixture ratio 50:50, where both parents are non-admixed, e.g. AFR, AFR/ EAS, EAS;

(C) 6 admixed cases with admixture ratio 50:50, where both parents are admixed, e.g. AFR, EAS/ AFR, EAS;

(D) 12 admixed cases with admixture ratio 75:25, e.g. AFR, AFR/ AFR, EAS;

(E) 12 admixed cases with admixture ratio 50:25:25, where one parent is non-admixed, e.g. AFR, AFR/ EAS, EUR;

(F) 12 admixed with admixture ratio 50:25:25, where both parents are admixed, e.g. AFR, EAS/ AFR, EUR;

(G) 3 admixed with admixture ratio 25:25:25:25, e.g. AFR, EAS/ EUR, SAS;

For each of the other 55 cases, we simulated 500 individuals in silico by picking four grand-parents at random from the populations, creating mother and father from the grand-parents, and creating a new individual from the parents, as described above.

2.4 Comparing results from admixture and recent-admixture

For a reference database from which we compute (or estimate) allele frequencies p_{mk} (which is the allele frequency of allele 1 at marker m in population k), we can estimate q from the admixture model as well as q^M, q^P from the recent-admixture model, as described in (3) and (5). In order to

compare the results from the admixture and recent-admixture model, we compute $q_k^{MP} := \frac{1}{2}(q_k^M + q_k^P)$ for $k = 1, ..., K$, which give the fractions of the genome coming from populations $1, ..., K$. Then, for a non-admixed individual, we have $q_k^{\text{TRUE}} = 1$ for some k, and for an admixed individual with parents from populations k and k' we have $q_k^{\text{TRUE}} = q_{k'}^{\text{TRUE}} = 0.5$, and similarly for individuals with grandparents from three or four different populations. Computing the estimation error, i.e. the distance to the true IA for the admixture model, results in

$$\sum_k |q_k - q_k^{\text{TRUE}}| \text{ and } \sum_k |q_k^{MP} - q_k^{\text{TRUE}}| \tag{6}$$

for the recent-admixture model. We stress that in the recent-admixture model, we in fact obtain results for q^M and q^P separately, such that even more information than q^{MP} is contained in the estimates for this model.

2.5 A likelihood-ratio test for recent admixture

We want to test if data $G = (G_m)_{m=1,...,M}$ from a new trace fits significantly better to the recent-admixture model than to the admixture model. Since the admixutre model is identical to the recent-admixture model for $q^M = q^P = q$, we are testing the hypothesis $H_0 : q^M = q^P$ against $H_1 : q^M \neq q^P$. For this, we take the estimators $\hat{q}$ of q from iteration of (3), and $\hat{q}^M, \hat{q}^P$ of q^M and q^P from iteration of (5) and compute $\Delta\ell := \ell(\hat{q}^M, \hat{q}^P|G) - \ell(\hat{q}|G)$ with $\ell(q^M, q^P|G)$ from (4) and $\ell(q|G)$ from (2). If $\Delta\ell > x$ for some x (which needs to be specified), the recent-admixture model fits significantly better and we reject H_0. If $\Delta\ell \leq x$, we accept H_0. In order to find x, we fix a p-value (1%, say), and take x to be the p-quantile of the empirical distribution for data in the reference database. (This means, if $p = 1\%$ and the reference dataset contains 1000 samples, we compute all values for $\Delta\ell$ for all samples, and set x to be the 10th-smallest value we obtained.)

2.6 Human data

We downloaded 1000 Genomes data (phase 3) from `ftp://ftp.1000genomes.ebi.ac.uk/vol1/ftp/release/20130502/`, as well as information on the sampling locations from `ftp://ftp.1000genomes.ebi.ac.uk/vol1/ftp/release/20130502/integrated_call_samples_v3.20130502.ALL.panel` [1]. This is data from 661 individuals from Africa (AFR), 347 Admixed Americans (AMR), 504 East Asians (EAS), 503 Europeans (EUR) and 489 South-East Asians (SAS).

xxx Explain why we use EUROFORGEN, Kidd

The dataset comes with approximately 80 million SNPs. However, we use only a few of them known as the EUROFORGENE AIMset [9] and Kidd AIMset [6], respectively. The EUROFORGENE AIMset comes with 128 SNPs able to distinguish between continental groups. Here, we ignore tri-allelic SNPs (rs17287498, rs2069945, rs2184030, rs433342, rs4540055, rs5030240), as well as rs12402499, which is not available in the 1000 genomes dataset. The Kidd AIMset consists of 55 bi-allelic SNPs, all of which are available in the 1000 genomes dataset.

3 Results

xxx compare runtimes

3.1 Estimation accuracy

Both, the admixture model and the recent-admixture model give estimates of IA. Using data from the 1000 genomes, but excluding all Admixed Americans (AMRs) since they are known to have an admixed background [4, 8], we use the SNPs from the EUROFORGENE and Kidd AIMsets. We use the continental origins as described in the dataset, i.e. we have AFR (African), EAS (East-Asia), EUR (European) and SAS (South-Asian) samples. As described in MM, we average estimates $\hat{q}^M$ and $\hat{q}^P$ from the recent-admixture model, in order to compare to the true IAs. As can be seen in Figure 1.A, the recent-admixture estimates outperform admixture estimates in all cases (which were created in silico as described in MM) for first generation admixed individuals. For second generation admixed individuals, the situation is similar, but depending on the type of admixture; see cases (B)–(G) as defined in Section 2.3 above. (A full list of 55 cases is displayed in Figure S4 in the SI.) In Figure 1.B, note that column A gives non-admixed samples, and we see that estimates of IA are essentially as accurate in the admixture model and the recent-admixture model. All results for the Kidd AIMset are similar and found in the SI.

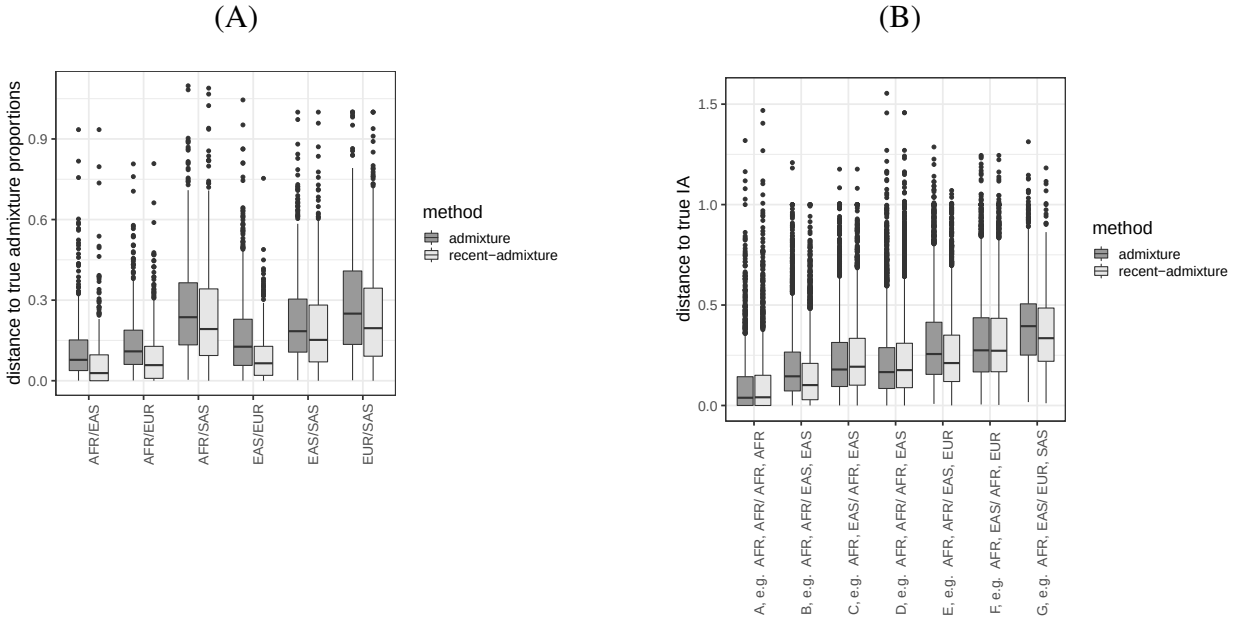


Figure 1: For all first generation admixed samples (A) and second generation admixed samples (B), we computed IA from the admixture and recent-admixture model. The distance to the true IA is computed as in (6). The cases in (B) are as described above. xxx add p-values xxx put a figure for the non-admixed scenario in the SI.

3.2 Power of the Likelihood-ratio test for recent admixture

When fixing the maximal p-value for significance of the likelihood-ration test for recent admixture (as described in MM), we obtain the power of the test for all cases of recent admixture. Displaying the false positives (i.e. positively tested non-admixed) against true positives (i.e. positively tested admixed) in cases (B)–(G) for all possible values of p, we obtain the Receiver-Operation-Characteristic (ROC) curve (xxx ref). The optimal curve nearly hits 0 false positives with 100% true positives and has an AUC (Area Under the Curve) of 1. As we see in Figure 2, the power of the test differs with the kind of admixture. For first generation admixed (case (B)), one non-admixed parent (case (E)) and all grand-parents from different continents (case (G)), the test is nearly perfect in distinguishing recent-admixture from admixture. If only half of the genome has two different ancestries (cases (D) and (F)), the power is reduced. If the individual is not recently-admixed in first generation, but both parents are (case (C)), power drops even more. In fact, the latter case is not recent-admixture as in our definition, since $q^M = q^P$ should technically hold. For the overall performance of the test, we give some examples in Table 1, in particular the power at $p = 1\%$ and AUC in all cases. Results for the EUROFORGEN AIMset are marginalle better than for the Kidd AIMset, which are given in the SI in Figure S7 and Table S2.

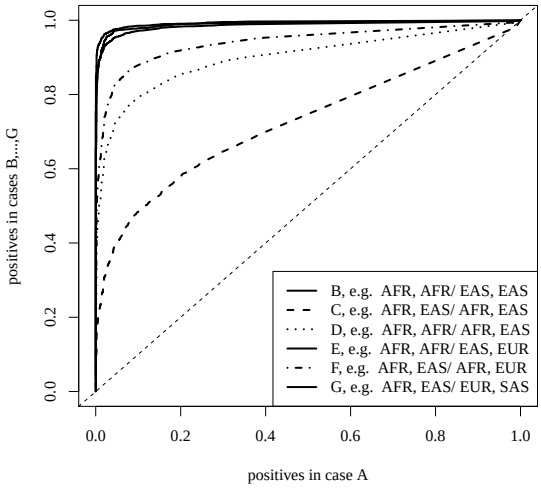


Figure 2: Using the EUROFORGEN AIMset, we plot false positives (i.e. positive non-admixed individuals, as in case (A) above, againts positives for all cases of admixture in second generation.

xxx compare with Tvedebrink

3.3 Recent admixture in the 1000 genomes dataset

From the 1000 genomes dataset, we highlight individuals which give significant results for the test of recent admixture for both AIMsets. We exclude AMRs from our analysis, and give in Table 3

Case	B	C	D	E	F	G
AUC	0.99	0.637	0.872	0.983	0.928	0.99
Power at $p = 0.01$	0.94	0.23	0.51	0.9	0.62	0.9

Table 1: Using the same data as in Figure 2, we e.g. see that the test for recent admixture turns out to have a p-value below 1% in 94% cases of first generation admixed individuals. xxx add false positives to x-axis, add true positives to y-axis.

the eight most extreme cases, which show highly significant results for recent admixture for both AIMsets. There are six Africans from population ASW (Americans from Southwest USA), and two from South Asia, one from GIH (Gujarati Indian from Houston, Texas) and one from BEB (Bengali from Bangladesh). We note that it is known that the ASW population is admixed [4], but until now, it has not been tested if admixture is recent.

- NA20278: Giving the most significant results for both datasets, this male has most probably parents of African and European ancestry. Note also that q^{MP} and q are very similar for both AIMsets.
- NA20342, NA19625, NA20355: Clearly, one parent has African ancestry. The other parent is most likely partly European.
- NA20274: Our test indicates two parents of different ancestry, one mostly African, the other mostly East-Asian.
- NA20299: Interestingly, the results for both AIMsets differ in this example. One parent has most likely African ancestry, the other is European according to the EUROFORGEN AIMset and South-Asian according to the Kidd AIMset.
- HG03803: Most likely, one parent is of South-Asian, the other has East-Esian ancestry.
- NA20864: Most likely, one parent is of South-Asian, the other has European ancestry.

In order to get a clearer picture about *true* ancestries in these individuals, we examined local ancestry in the genome. xxx

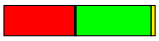
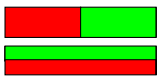
4 Discussion

xxx add references, write some more paragraphs

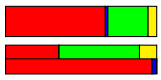
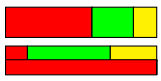
xxx Mention [12].

We address the inference of recent admixture in estimating individual admixture (IA), when data from Ancestry Informative Markers is available. The well-known admixture model assumes that in each individual for some $q = (q_k)_{k=1,\dots,K}$, every allele has ancestry within population k with probability q_k. We extend this model by distinguishing between maternally and paternally inherited

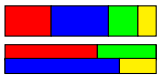
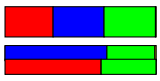
NA20278, AFR, ASW

EURO	ad	q	
$\Delta\ell = 6.69$	r-ad	q^{MP} q^M, q^P	
Kidd	ad	q	
$\Delta\ell = 9.98$	r-ad	q^{MP} q^M, q^P	

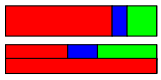
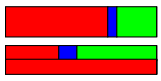
NA20342, AFR, ASW

EURO	ad	q	
$\Delta\ell = 1.82$	r-ad	q^{MP} q^M, q^P	
Kidd	ad	q	
$\Delta\ell = 3.66$	r-ad	q^{MP} q^M, q^P	

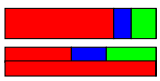
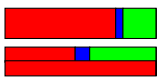
NA20274, AFR, ASW

EURO	ad	q	
$\Delta\ell = 6.56$	r-ad	q^{MP} q^M, q^P	
Kidd	ad	q	
$\Delta\ell = 2.68$	r-ad	q^{MP} q^M, q^P	

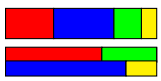
NA19625, AFR, ASW

EURO	ad	q	
$\Delta\ell = 1.52$	r-ad	q^{MP} q^M, q^P	
Kidd	ad	q	
$\Delta\ell = 1.6$	r-ad	q^{MP} q^M, q^P	

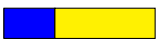
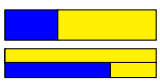
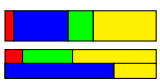
NA20355, AFR, ASW

EURO	ad	q	
$\Delta\ell = 1.11$	r-ad	q^{MP} q^M, q^P	
Kidd	ad	q	
$\Delta\ell = 1.55$	r-ad	q^{MP} q^M, q^P	

NA20299, AFR, ASW

EURO	ad	q	
$\Delta\ell = 6.31$	r-ad	q^{MP} q^M, q^P	
Kidd	ad	q	
$\Delta\ell = 1.52$	r-ad	q^{MP} q^M, q^P	

HG03803, SAS, BEB

EURO	ad	q	
$\Delta\ell = 1.01$	r-ad	q^{MP} q^M, q^P	
Kidd	ad	q	
$\Delta\ell = 1.12$	r-ad	q^{MP} q^M, q^P	

NA20864, SAS, GIH

EURO	ad	q	
$\Delta\ell = 0.87$	r-ad	q^{MP} q^M, q^P	
Kidd	ad	q	
$\Delta\ell = 0.95$	r-ad	q^{MP} q^M, q^P	

Figure 3: The most extreme individuals in the 1000 genomes dataset in terms of a signal for recent admixture. For all individuals, we give IA from the admixture model (ad), given by q, the recent-admixture model (r-ad) $q^M, q^P, q^{MP} = \frac{1}{2}(q^M + q^P)$, for the analysis with the EUROFORGEN and Kidd AIMset. Difference in log-likelihoods for both models is given by $\Delta\ell$. Colors are AFR ■, EAS ■, EUR ■, SAS ■. xxx explain $\Delta\ell$, order recent-admixture barplots.

alleles (but still consider only autosomes). The maternally inherited alleles come with IA q^M, and the paternally inherited alleles with q^P, which extends the admixture model if $q^M \neq q^P$. Within this model, q^P and q^M can be estimated by the same methods as in the admixture model. Taking the average of q^M and q^P, we obtain IA which is highly similar to q in the admixture model in non-admixed and admixed individuals. In addition, the IA estimated from the recent-admixture model in recently admixed individuals, in particular if the two parents come from different populations, is more accurate than for the admixture model. Moreover, and in contrast to the admixture model, we also estimate the form of recent admixture. A resulting likelihood ratio test for recent admixture has high power to detect recent admixture in many relevant scenarios, in particular if the two parents come from different populations.

In many applications, STRUCTURE still seems to be the gold-standard for estimating the IA of traces. STRUCTURE uses the same admixture model as we do, it is computationally much more demanding. The same holds for ADMIXTURE and FRAPPE. The reason is that these programs aim to simultaneously estimate the IA of the new trace, as well as allele frequencies in ancestral populations. In other words, in these programs, the new trace changes allelic frequencies in ancestral populations during the runtime. However, as in forensics we mostly have a large reference database and only one (or a few) new traces, the impact on the allelic frequencies are negligible. Therefore, we take the computationally easier way and take allele frequencies for ancestral populations as fixed, and only change the IAs of the new traces during the runtime. The result is that the analysis is fast. E.g. the $500 \cdot 55 = 27500$ individuals which need to be analysed for Figure 1, and which are created in silico, takes about five hours on a standard laptop computer using the statistical language R.

Not included the GDA from Cheung 2019. In addition, we also only need frequencies from the reference database (or some external source, e.g. from Frog-kb), although we use the same model as structure. Reason is that we do not update frequencies. Updating frequencies would mean that the trace can alter ancestral allelic frequencies.

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Supporting Information: Inference of recent admixture using genotype data

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S1 Theory

We write down the admixture model and derive a method to estimate Individual Admixture (IA) in the case when allele frequencies within populations are not updated. In addition, we write down the recent-admixture model, where an individual is allowed to have parents with different admixture proportions. We take the following notation for the reference database:

K : number of ancestral populations,
M : number of markers,
p_{mk} : frequency of allele 1 at (bi-allelic) marker m in population k.

In addition, we consider one additional diploid genome $(G_{m1}, G_{m2})_{m=1,\dots,M}$, or $(G_m)_{m=1,\dots,M}$ with $G_m = G_{m1} + G_{m2}$ if phase is not known. The goal is to estimate admixture proportions $(q_k)_{k=1,\dots,K}$ (or $(q_k^M)_{k=1,\dots,K}, (q_k^P)_{k=1,\dots,K}$) of this additional genome.

S1.1 The admixture model

In Tang et al (2005) and elsewhere, the main goal is to maximize the log-likelihood (see also (1) and (2) of Tang et al)

$$\ell(q|G) = \sum_{m=1}^{M} \sum_{a=1,2} \log\Big(\sum_{k=1}^{K} \alpha_{mak} q_k\Big),$$

where

$$\alpha_{mak} := \begin{cases} p_{mk}, & \text{if } G_{ma} = 1, \\ 1 - p_{mk}, & \text{if } G_{ma} = 0. \end{cases}$$

is the frequency of the observed allele in copy a of marker m in population k. (Note that $e^{\ell(q|G)}$ is the probabiltiy of observing $(G_{ma})_{m=1,\dots,M;a=1,2}$, if every allele is picked independently from population $k$with probability q_k.)

Assuming that phase is not known, and with

$$\alpha_{mkl} := \alpha_{m1k}\alpha_{m2l} = \begin{cases} p_{mk}p_{ml}, & \text{if } G_{m1}+G_{m2}=2, \\ p_{mk}(1-p_{ml})+(1-p_{mk})p_{ml}, & \text{if } G_{m1}+G_{m2}=1, \\ (1-p_{mk})(1-p_{ml}), & \text{if } G_{m1}+G_{m2}=0, \end{cases} \tag{S7}$$

note that the log-likelihood can as well be written as

$$\ell(q|G) = \sum_{m=1}^{M} \log\Big(\sum_{k,l=1}^{K} \alpha_{mkl}q_kq_l\Big). \tag{S8}$$

We set $\beta_m(q) := \sum_{k=1}^{K} p_{mk}q_k$ and analyse the last sum by distinguishing the case $G_m = 2$, where

$$\sum_{k,l=1}^{K} \alpha_{mkl}q_kq_l = \Big(\sum_{k=1}^{k} p_{mk}q_k\Big)^2 = \beta_m(q)^2$$

while for $G_m = 1$ we find

$$\sum_{k,l=1}^{K} \alpha_{mkl}q_kq_l = 2\Big(\sum_{k=1}^{k} p_{mk}q_k\Big)\Big(1-\sum_{k=1}^{k} p_{mk}q_k\Big) = 2\beta_m(q)(1-\beta_m(q))$$

and for $G_m = 0$

$$\sum_{k,l=1}^{K} \alpha_{mkl}q_kq_l = \Big(1-\sum_{k=1}^{k} p_{mk}q_k\Big)^2 = (1-\beta_m(q))^2,$$

such that

$$\ell(q|G) = \sum_{m=1}^{M} \log\Big(\binom{2}{G_m}\beta_m(q)^{G_m}(1-\beta_m(q))^{2-G_m}\Big) \tag{S9}$$

Lemma S1.1. *The maximum of $q \mapsto \ell(q|G)$ under the constraint $\sum_{k=1}^{K} q_k = 1$ solves*

$$\frac{1}{M}\sum_{m=1}^{M}\sum_{l=1}^{K} \frac{\alpha_{mkl}q_l}{\sum_{k',l'=1}^{K}\alpha_{mk'l'}q_{k'}q_{l'}} = 1, \qquad k = 1, ..., K. \tag{$*$}$$

Remark S1.1. 1. Assume we add a set of *Ancestry Uninformative Markers*, i.e. a set of markers $\tilde{m} = 1, ..., \tilde{M}$, with frequencies not depending on the population, i.e. $\alpha_{\tilde{m}kl} = \alpha_{\tilde{m}k'l'}$ for $k, l, k, l'' = 1, ..., K$. For these markers,

$$\sum_{\tilde{m}=1}^{\tilde{M}}\sum_{l=1}^{K} \frac{\alpha_{\tilde{m}kl}q_l}{\sum_{k',l'=1}^{K}\alpha_{\tilde{m}k'l'}q_{k'}q_{l'}} = \tilde{M}.$$

This implies that q is a solution of $(*)$ without these markers iff q is a solution of $(*)$ if these markers are included. This might be reassuring.

2. Let us have a closer look at the left hand side of $(*)$. We set $\beta_m := \sum_{k=1}^K p_{mk}q_k$. For $G_m = 2$,

$$\sum_{l=1}^K \frac{\alpha_{mkl}q_l}{\sum_{k',l'}\alpha_{mk'l'}q_{k'}q_{l'}} = \sum_{l=1}^K \frac{p_{mk}p_{ml}q_l}{\sum_{k',l'}p_{mk'}p_{ml'}q_{k'}q_{l'}} = \frac{p_{mk}}{\beta_m}.$$

For $G_m = 1$, we have

$$\begin{aligned}\sum_{l=1}^K \frac{\alpha_{mkl}q_l}{\sum_{k',l'}\alpha_{mk'l'}q_{k'}q_{l'}} &= \sum_{l=1}^K \frac{(p_{mk}(1-p_{ml}) + (1-p_{mk})p_{ml})q_l}{\sum_{k',l'}(p_{mk'}(1-p_{ml'}) + (1-p_{mk'})p_{ml'})q_{k'}q_{l'}} \\ &= \frac{p_{mk}(1-\beta_m) + (1-p_{mk})\beta_m}{2\beta_m(1-\beta_m)} = \frac{1}{2}\Big(\frac{p_{mk}}{\beta_m} + \frac{1-p_{mk}}{1-\beta_m}\Big)\end{aligned}$$

and for $G_m = 0$

$$\sum_{l=1}^K \frac{\alpha_{mkl}q_l}{\sum_{k',l'}\alpha_{mk'l'}q_{k'}q_{l'}} = \sum_{l=1}^K \frac{(1-p_{mk})(1-p_{ml})q_l}{\sum_{k',l'}(1-p_{mk'})(1-p_{ml'})q_{k'}q_{l'}} = \frac{1-p_{mk}}{1-\beta_m}.$$

In total, this gives that q needs to solve

$$\frac{1}{2M}\sum_{m=1}^M \Big(G_m\frac{p_{mk}}{\beta_m} + (2-G_m)\frac{1-p_{mk}}{1-\beta_m}\Big) = 1$$

3. In order to find a solution of $(*)$, we reformulate as the fixed point equation

$$q_k = f_k(q) \text{ for } f_k(q) = \frac{1}{2M}\sum_{m=1}^M \Big(G_m\frac{p_{mk}}{\beta_m} + (2-G_m)\frac{1-p_{mk}}{1-\beta_m}\Big)q_k, \qquad k = 1,...,K. \tag{S10}$$

A solution can be computed by iteratively computing $q' = (f_k(q))_{k=1,...,K}$.

Proof. We use the theory of Lagrange multipliers, since we need to maximize ℓ over q under the constraint $\sum_k q_k = 1$. Since

$$\frac{\partial \ell(q|G)}{\partial q_k} = \sum_{m=1}^M\sum_{l=1}^K \frac{\alpha_{mkl}q_l}{\sum_{k',l'=1}^K \alpha_{mk'l'}q_{k'}q_{l'}},$$

we have to solve the system of equations

$$\lambda = \sum_{m=1}^M\sum_{l=1}^K \frac{\alpha_{mkl}q_l}{\sum_{k',l'=1}^K \alpha_{mk'l'}q_{k'}q_{l'}}, \qquad k = 1,...,K, \tag{S11}$$

$$1 = \sum_{k=1}^K q_k. \tag{S12}$$

It is easy to eliminate λ, since using (S19) gives

$$\lambda = \lambda\sum_{k=1}^K q_k = \sum_{m=1}^M\sum_{k,l=1}^K \frac{\alpha_{mkl}q_kq_l}{\sum_{k',l'=1}^K \alpha_{mk'l'}q_{k'}q_{l'}} = M.$$

So, we are left with finding $q = (q_k)_{k=1,...,K}$ such that

$$\frac{1}{M}\sum_{m=1}^{M}\sum_{l=1}^{K}\frac{\alpha_{mkl}q_l}{\sum_{k',l'=1}^{K}\alpha_{mk'l'}q_{k'}q_{l'}} = 1, \qquad k = 1, ..., K. \tag{S13}$$

□

S1.2 The recent-admixture model

For the recent-admixture-version, we want to estimate $q^M = (q_k^M)_{k=1,...,K}, q^P = (q_k^P)_{k=1,...,K}$, where q_k^M and q_k^P are the fractions of the genomes of the mother and father, respectively, which come from population k. This assumption implies that the log-likelihood changes to

$$\ell(q^M, q^P|G) = \sum_{m=1}^{M}\log\Big(\sum_{k,l=1}^{K}\alpha_{mkl}q_k^M q_l^P\Big),$$

where α_{mkl} is given as in (S7).

As is apparent from the log-Likelihood function, the recent-admixture model generalizes the admixture model. Put differently, choosing $q^M = q^P = q$ in the recent-admixture model gives the admixture model. This will later pave the way to write down a likelihood ratio test. With the Akaike Information Criterion, we vote for the recent-admixture model if the difference in the log-likelihood is at least $2 \cdot 4 = 8$.

We note that again, the log-likelihood can be written differently,

$$\begin{aligned}\ell(q^M, q^P|G) = \sum_{m=1}^{M}\log\Big(&1_{G_m=2}\beta_m(q^M)\beta_m(q^P)\\ &+ 1_{G_m=1}(\beta_m(q^M)(1-\beta_m(q^P)) + (1-\beta_m(q^M))\beta_m(q^P))\\ &+ 1_{G_m=0}(1-\beta_m(q^M))(1-\beta_m(q^P))\Big).\end{aligned} \tag{S14}$$

Lemma S1.2. *The maximum of $q \mapsto \ell(q^P, q^M, G)$ under the constraint $\sum_{k=1}^{K} q_k^M = \sum_{k=1}^{K} q_k^P = 1$ solves*

$$\frac{1}{M}\sum_{m=1}^{M}\sum_{l=1}^{K}\frac{\alpha_{mkl}q_l^M}{\sum_{k',l'=1}^{K}\alpha_{mk'l'}q_{k'}^M q_{l'}^P} = \frac{1}{M}\sum_{m=1}^{M}\sum_{l=1}^{K}\frac{\alpha_{mkl}q_l^P}{\sum_{k',l'=1}^{K}\alpha_{mk'l'}q_{k'}^P q_{l'}^M} = 1, \qquad k = 1, ..., K. \quad (*)$$

Again, we have a closer look at the left hand side of $(*)$. For $\beta_m(q) := \sum_k p_{mk}q_k$, we have for $G_m = 2$

$$\sum_{l=1}^{K}\frac{\alpha_{mkl}q_l^M}{\sum_{k',l'=1}^{K}\alpha_{mk'l'}q_{k'}^M q_{l'}^P} = \frac{p_{mk}\beta_m(q^M)}{\beta_m(q^M)\beta_m(q^P)} = \frac{p_{mk}}{\beta_m(q^P)},$$

for $G_m = 1$

$$\sum_{l=1}^{K}\frac{\alpha_{mkl}q_l^M}{\sum_{k',l'=1}^{K}\alpha_{mk'l'}q_{k'}^M q_{l'}^P} = \frac{p_{mk}(1-\beta_m(q^M)) + (1-p_{mk})\beta_m(q^M)}{\beta_m(q^M)(1-\beta_m(q^P)) + (1-\beta_m(q^M))\beta_m(q^P)}$$

and for $G_m = 0$

$$\sum_{l=1}^{K} \frac{\alpha_{mkl} q_l^M}{\sum_{k',l'=1}^{K} \alpha_{mk'l'} q_{k'}^M q_{l'}^P} = \frac{(1-p_{mk})(1-\beta_m(q^M))}{(1-\beta_m(q^M))(1-\beta_m(q^P))} = \frac{1-p_{mk}}{1-\beta_m(q^P)}.$$

Remark S1.2. 1. Note that $(*)$ is symmetric in q^M and q^P, i.e. if (q^M, q^P) solve $(*)$, another solution is given by (q^P, q^M).

2. Again, we can turn $(*)$ into fixed point equations. Here, we suggest to iteratively compute

$$\tilde{q}^P = f(q^M, q^P) \text{ and } \tilde{q}^M = f(\tilde{q}^P, q^M) \tag{S15}$$

for $f(q, q') = (f_k(q, q'))_{k=1,\dots,K}$ with

$$\begin{aligned} f_k(q, q') := \frac{1}{M} \sum_{m=1}^{M} \Big(& 1_{G_m=2} \frac{p_{mk}}{\beta_m(q')} \\ & + 1_{G_m=1} \frac{(p_{mk}(1-\beta_m(q)) + (1-p_{mk})\beta_m(q))}{\beta_m(q)(1-\beta_m(q')) + (1-\beta_m(q))\beta_m(q')} \\ & + 1_{G_m=0} \frac{(1-p_{mk})}{1-\beta_m(q')} \Big) q'_k. \end{aligned} \tag{S16}$$

Proof. Again, we use Lagrange multipliers. Since

$$\begin{aligned} \frac{\partial \ell(q^P, q^M | G)}{\partial q_k^P} &= \sum_{m=1}^{M} \sum_{l} \frac{\alpha_{mak} q_l^M}{\sum_{k',l'} \alpha_{mk'l'} q_{k'}^P q_{k'}^M}, \\ \frac{\partial \ell(q^P, q^M | G)}{\partial q_k^M} &= \sum_{m=1}^{M} \sum_{l} \frac{\alpha_{mak} q_l^P}{\sum_{k',l'} \alpha_{mk'l'} q_{k'}^P q_{k'}^M}, \end{aligned}$$

we have to solve the system of equations

$$\lambda = \sum_{m=1}^{M} \sum_{l} \frac{\alpha_{mak} q_l^M}{\sum_{k',l'} \alpha_{mk'l'} q_{k'}^P q_{k'}^M}, \qquad k = 1, ..., K, \tag{S17}$$

$$\rho = \sum_{m=1}^{M} \sum_{l} \frac{\alpha_{mak} q_l^P}{\sum_{k',l'} \alpha_{mk'l'} q_{k'}^P q_{k'}^M}, \qquad k = 1, ..., K, \tag{S18}$$

$$1 = \sum_{k=1}^{K} q_k^P = \sum_{k=1}^{K} q_k^M. \tag{S19}$$

It is easy to eliminate λ and ρ, since

$$\begin{aligned} \lambda = \lambda \sum_{k=1}^{K} q_k^P &= \sum_{m=1}^{M} \sum_{k,l} \frac{\alpha_{mkl} q_k^P q_l^M}{\sum_{k',l'} \alpha_{mk'l'} q_{k'}^P q_{l'}^M} = M, \\ \rho = \rho \sum_{k=1}^{K} q_k^M &= \sum_{m=1}^{M} \sum_{k,l} \frac{\alpha_{mkl} q_k^P q_l^M}{\sum_{k',l'} \alpha_{mk'l'} q_{k'}^P q_{l'}^M} = M. \end{aligned}$$

So, we are left with finding q^P and q^M such that

$$\frac{1}{M}\sum_{m=1}^{M}\frac{\alpha_{mkl}q_l^P}{\sum_{k',l'}^{K}\alpha_{mk'l'}q_{k'}^P q_{l'}^M}=1, \qquad k=1,...,K, \tag{S20}$$

$$\frac{1}{M}\sum_{m=1}^{M}\frac{\alpha_{mkl}q_l^M}{\sum_{k',l'}^{K}\alpha_{mk'l'}q_{k'}^P q_{l'}^M}=1, \qquad k=1,...,K. \tag{S21}$$

□

S2 Description of downloadable software

Our methods are based on R-scripts and are available via `https://github.com/pfaffelh/recent-admixture`.

xxx

S3 Additional results

S3.1 Estimation accuracy

For first generation admixed individuals, all cases (non-admixed and parents come from different continents) are described in the main text. For second generation admixed individuals, we have several cases, depending on the origin of the grand-parents. When data from four populations (AFR, EAS, EUR, SAS; see below) is available, we have the following cases:

(A) 4 non-admixed cases (with IA 100:0): (AFR, AFR/ AFR, AFR), (EAS, EAS/ EAS, EAS), (EUR, EUR/ EUR, EUR), (SAS, SAS/ SAS, SAS);

(B) 6 admixed cases with admixture ratio 50:50, where both parents are non-admixed: (AFR, AFR/ EAS, EAS), (AFR, AFR/ EUR, EUR), (AFR, AFR/ SAS, SAS), (EAS, EAS/ EUR, EUR), (EAS, EAS/ SAS, SAS), (EUR, EUR/ SAS, SAS);

(C) 6 admixed cases with admixture ratio 50:50, where both parents are admixed: (AFR, EAS/ AFR, EAS), (AFR, EUR/ AFR, EUR), (AFR, SAS/ AFR, SAS), (EAS, EUR/ EAS, EUR), (EAS, SAS/ EAS, SAS), (EUR, SAS/ EUR, SAS);

(D) 12 admixed cases with admixture ratio 75:25: (AFR, AFR/ AFR, EAS), (AFR, AFR/ AFR, EUR), (AFR, AFR/ AFR, SAS), (EAS, EAS/ EAS, AFR), (EAS, EAS/ EAS, EUR), (EAS, EAS/ EAS, SAS), (EUR, EUR/ EUR, AFR), (EUR, EUR/ EUR, EAS), (EUR, EUR/ EUR, SAS), (SAS, SAS/ SAS, AFR), (SAS, SAS/ SAS, EAS), (SAS, SAS/ SAS, EUR);

(E) 12 second generation admixed with admixture ratio 50:25:25, where one parent is non-admixed: (AFR, AFR/ EAS, EUR), (AFR, AFR/ EAS, SAS), (AFR, AFR/ EUR, SAS), (EAS, EAS/ AFR,

Case	B	C	D	E	F	G
AUC	0.982	0.655	0.855	0.983	0.921	0.982
Power at $p = 0.01$	0.92	0.29	0.5	0.89	0.65	0.89

Table S2: Same as Table 1, but using the Kidd AIMset.

EUR), (EAS, EAS/ AFR, SAS), (EAS, EAS/ EUR, SAS), (EUR, EUR/ AFR, EAS), (EUR, EUR/ AFR, SAS), (EUR, EUR/ EAS, SAS), (SAS, SAS/ AFR, EAS), (SAS, SAS/ AFR, EUR), (SAS, SAS/ EAS, EUR);

(F) 12 second generation admixed with admixture ratio 50:25:25, where both parents are admixed: (AFR, EAS/ AFR, EUR), (AFR, EAS/ AFR, SAS), (AFR, EUR/ AFR, SAS), (EAS, AFR/ EAS, EUR), (EAS, AFR/ EAS, SAS), (EAS, EUR/ EAS, SAS), (EUR, AFR/ EUR, EAS), (EUR, AFR/ EUR, SAS), (EUR, EAS/ EUR, SAS), (SAS, AFR/ SAS, EAS), (SAS, AFR/ SAS, EUR), (SAS, EAS/ SAS, EUR);

(G) 3 second generation admixed with admixture ratio 25:25:25:25: (AFR, EAS/ EUR, SAS), (AFR, EUR/ EAS, SAS), (AFR, SAS/ EAS, EUR);

As can be seen in Figure S4, the recent-admixture model never gives worse estimates than the admixture model, and outperforms the admixture-model in several cases; see also Figure 1 in the main text. For the Kidd AIMset, see Figures S5 and S6.

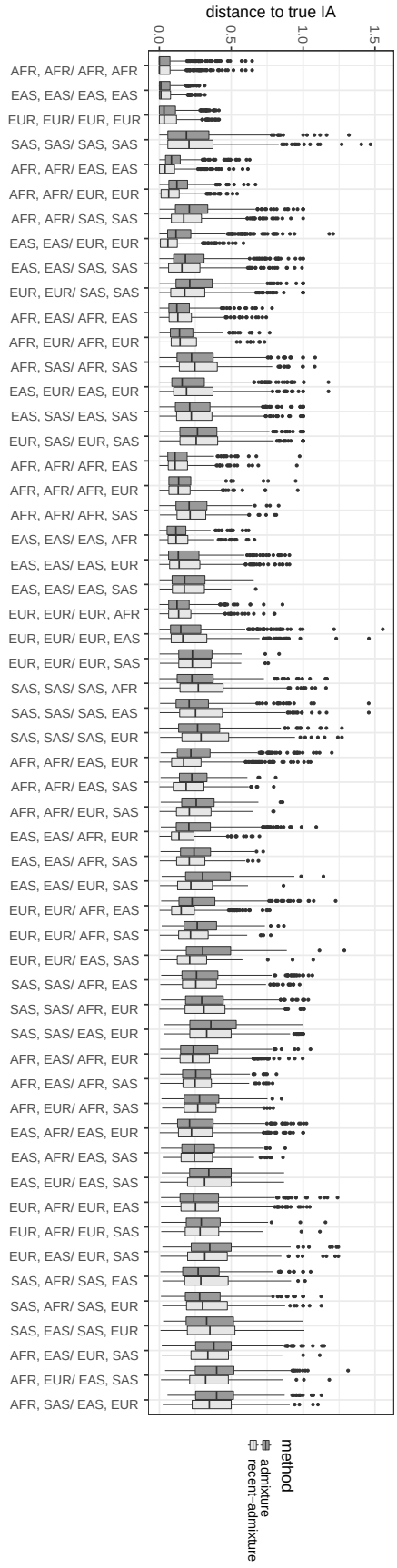

Figure S4: For all cases of second generation admixed individuals, we compare estimation accuracy of IA using the EUROFORGEN AIMset.

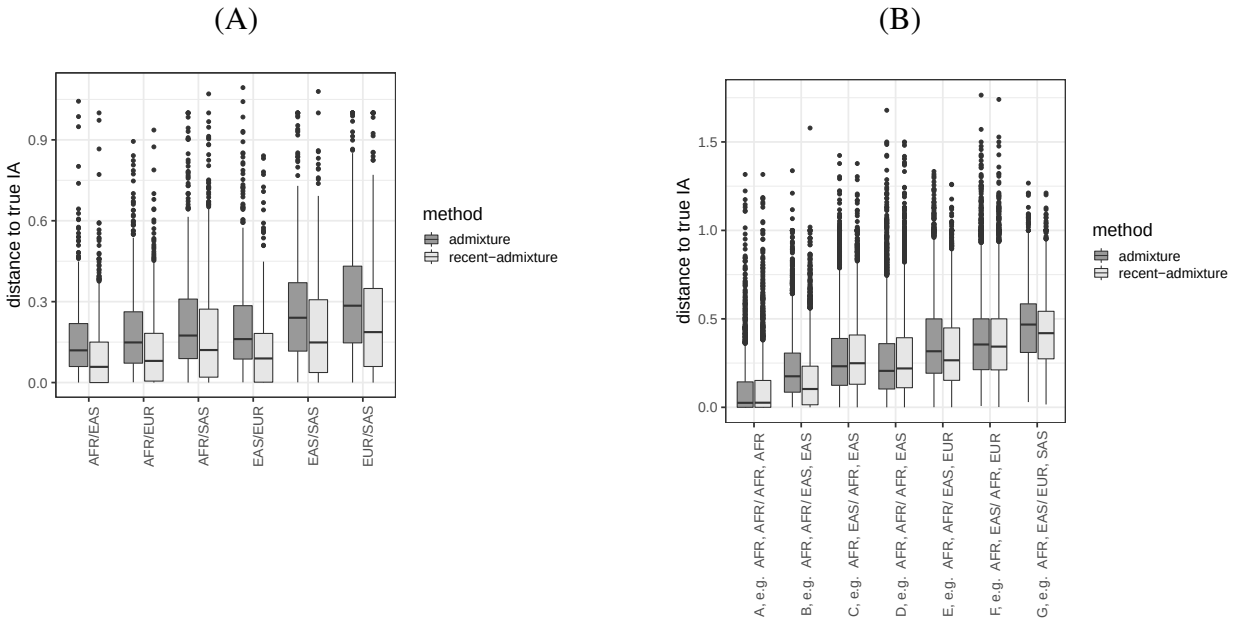

Figure S5: Same as in Figure 1, but using the Kidd AIMset.

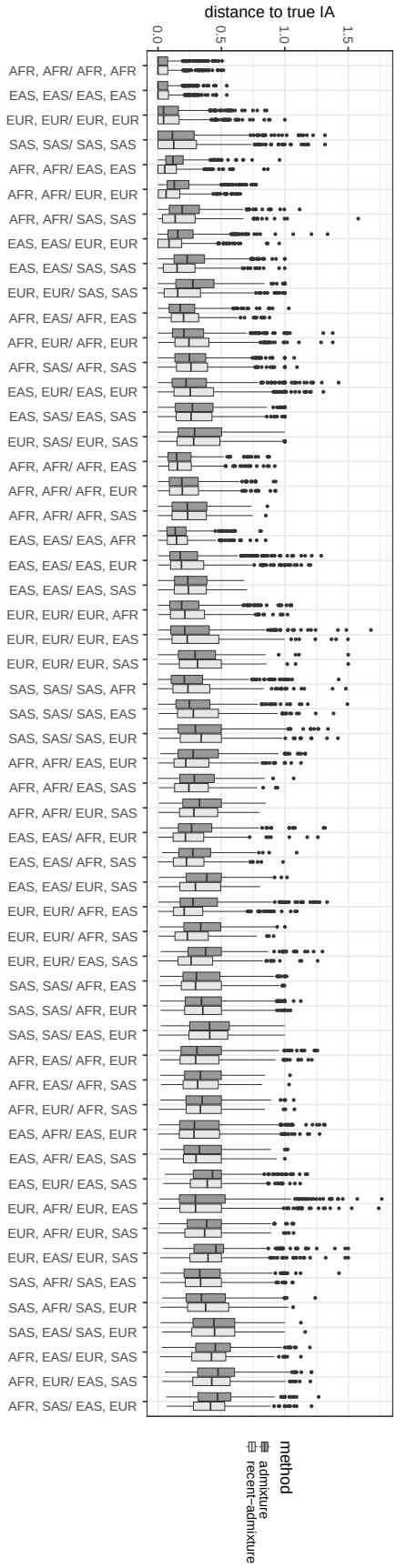

Figure S6: Same as in Figure S4, but using the Kidd AIMset.

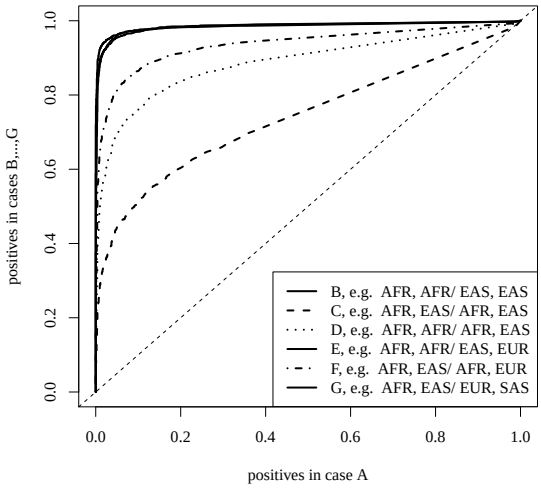

Figure S7: Same as in Figure 2, but using the Kidd AIMset.