Simulate Admixed Populations with `bnpsd`

Alejandro Ochoa and John D. Storey

2017-08-24

1 Introduction

The `bnpsd` package simulates the genotypes of an admixed population. In the PSD model (Pritchard, Stephens, and Donnelly 2000), admixed individuals draw their alleles with individual-specific probabilities (admixture proportions) from K intermediate subpopulations. We impose the BN model (Balding and Nichols 1995) to the intermediate subpopulation allele frequency, which thus evolve independently with subpopulation-specific inbreeding coefficients ($F_{\rm ST}$ values) from a common ancestral population T. The kinship coefficients and generalized $F_{\rm ST}$ of the admixed individuals were derived in recent work (Ochoa and Storey 2016a). A simulated admixed population was used to benchmark kinship and $F_{\rm ST}$ estimators in the accompaning paper (Ochoa and Storey 2016b). Here we briefly summarize the notation and intuition behind the key parameters (see (Ochoa and Storey 2016a) for precise definitions).

1.1 The BN-PSD population structure

The population structure determines how individuals are related to each other. The key parameters are the inbreeding coefficients of the intermediate subpopulations ($f^T_{S_u}$ below) and the admixture proportions of each individual for each subpopulation (q_{ju}), which are treated as fixed variables.

Each intermediate subpopulation S_u ($u \in \{1, ..., K\}$) evolved independently from a shared ancestral population T with an inbreeding coefficient denoted by $f^T_{S_u}$. Each admixed individual $j \in \{1, ..., n\}$ draws each allele from S_u with probability given by the admixture proportion q_{ju} ($\sum_{u=1}^K q_{ju} = 1 \forall j$). In this case the coancestry coefficients θ^T_{jk} between individuals j, k (including $j = k$ case) and the $F_{\rm ST}$ of the admixed individuals are given by:

$$\theta^T_{jk} = \sum_{u=1}^K q_{ju} q_{ku} f^T_{S_u}, \qquad F_{\rm ST} = \sum_{j=1}^n \sum_{u=1}^K w_j q^2_{ju} f^T_{S_u},$$

where $0 < w_j < 1, \sum_{j=1}^n w_j = 1$ are user-defined weights for individuals (default $w_j = \frac{1}{n} \forall j$). Note θ^T_{jk} equals the kinship coefficient for $j \neq k$ and the inbreeding coefficient for $j = k$.

The bias coefficient s is defined by

$$s = \frac{\bar{\theta}^T}{F_{\rm ST}}$$

where $\bar{\theta}^T = \sum_{j=1}^n \sum_{k=1}^n w_j w_k \theta^T_{jk}$. This $0 < s \leq 1$ approximates the proportional bias of $F_{\rm ST}$ estimators that assume independent subpopulations, and one `bnpsd` function below fits its parameters to yield a desired s.

1.2 Random allele frequencies and genotypes

This section details the distributions of the allele frequencies and genotypes of the various populations or individuals of the BN-PSD model.

Every biallelic locus i in the ancestral population T has an ancestral reference allele frequency denoted by p^T_i. By default the `bnpsd` code draws

$$p^T_i \sim \text{Uniform}(a, b)$$

with $a = 0.01, b = 0.5$, but the code accepts p^T_i from arbitrary distributions (see below).

The distribution of the allele frequency at locus i in subpopulation S_u, denoted by $p_i^{S_u}$, is the BN distribution:

$$p_i^{S_u}|T \sim \text{Beta}\left(\nu_s p_i^T, \nu_s\left(1-p_i^T\right)\right),$$

where $\nu_s = \frac{1}{f_{S_u}^T} - 1$. Allele frequencies for different loci and different subpopulations $(S_u, S_v, u \neq v)$ are drawn independently.

Each admixed individual j at each locus i draws alleles from a mixture of Bernoulli distributions from each intermediate subpopulation, which is mathematically equivalent to assigning what we call "individual-specific allele frequencies" (IAFs) π_{ij} constructed as:

$$\pi_{ij} = \sum_{u=1}^{K} p_i^{S_u} q_{ju}.$$

The unphased genotype x_{ij} (encoded to count the number of reference alleles) is drawn as:

$$x_{ij}|\pi_{ij} \sim \text{Binomial}(2, \pi_{ij}).$$

2 Simulation examples

2.1 Population structure: 1D geography

Let's generate the same population structure used in the simulation of (Ochoa and Storey 2016b).

```
library(RColorBrewer) # for nice colors
# load this package (bnpsd) and a related popgen package (popkin)
# since both packages have an "fst" function, load "bnpsd" last so its function isn't masked
library(popkin) # for visualizing coancestry matrix with plotPopkin
library(bnpsd)
```

```
##
## Attaching package: 'bnpsd'
```

```
## The following object is masked from 'package:popkin':
##
##     fst
```

```
# dimensions of data/model
n <- 1000 # number of individuals
k <- 10 # number of intermediate subpops

# define population structure
F <- 1:k # subpopulation FST vector, up to a scalar
s <- 0.5 # desired bias coefficient
Fst <- 0.1 # desired FST for the admixed individuals
obj <- q1d(n, k, s=s, F=F, Fst=Fst) # admixture proportions from 1D geography
Q <- obj$Q
F <- obj$F

# get pop structure parameters of the admixed individuals
Theta <- coanc(Q,F) # the coancestry matrix
# verify that we got the desired Fst!
Fst2 <- fst(Q,F)
Fst2
```

```
## [1] 0.1
```

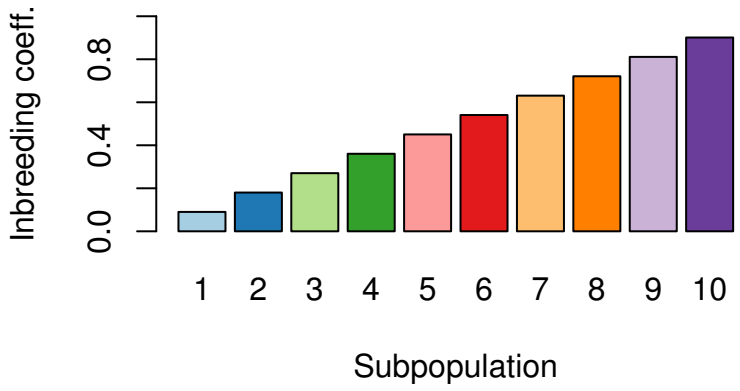
```
# this should also equal Fst
inbr <- diag(Theta)
popkin::fst(inbr)
```

```
## [1] 0.1
```

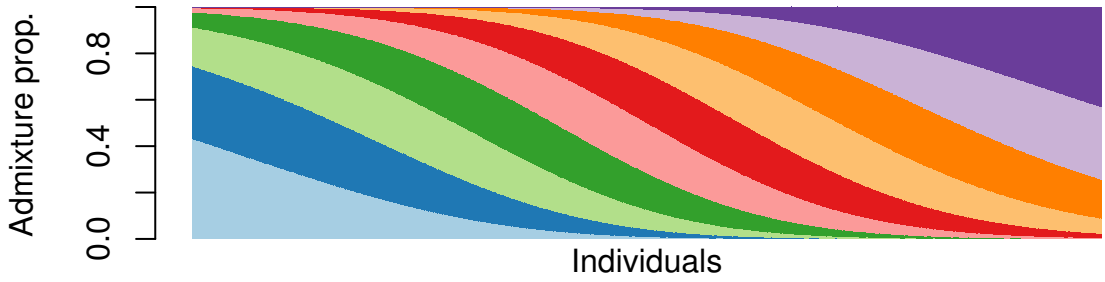
```
# verify that we got the desired s too!
s2 <- mean(Theta)/Fst
s2
```

```
## [1] 0.5
```

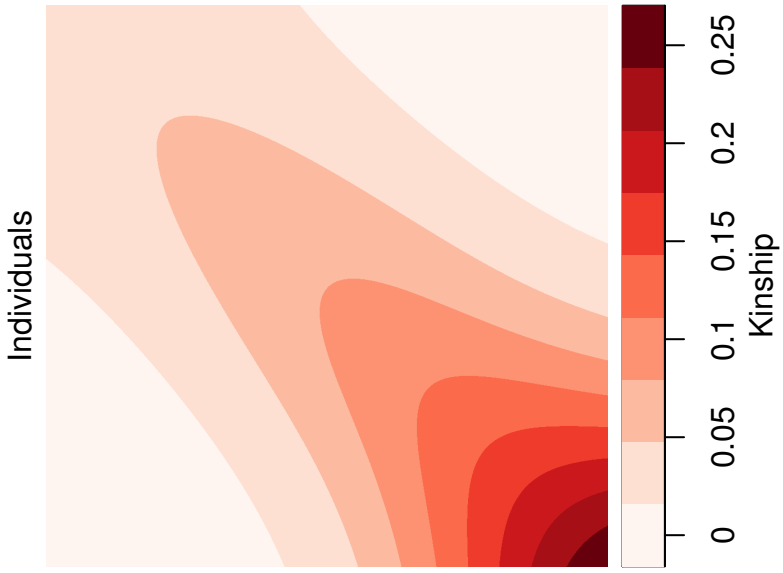
```
# visualize the per-subpopulation inbreeding coefficients (FSTs)
par(mar=c(4,4,0,0)+0.2) # shrink default margins
colIS <- brewer.pal(k, "Paired") # indep. subpop. colors
barplot(F, col=colIS, names.arg=1:k, ylim=c(0,1),
    xlab='Subpopulation', ylab='Inbreeding coeff.')
```




```
# visualize the admixture proportions
par(mar=c(1,4,0,0)+0.2) # shrink default margins
barplot(t(Q), col=colIS, border=NA, space=0, ylab='Admixture prop.')
mtext('Individuals', 1)
```




```
# Visualize the coancestry matrix using "popkin"!
# set outer margin for axis labels (left and right are non-zero)
par(oma=c(0,1.5,0,3))
# zero inner margin (plus padding) because we have no individual or subpopulation labels
par(mar=c(0,0,0,0)+0.2)
# now plot!
plotPopkin(Theta)
```

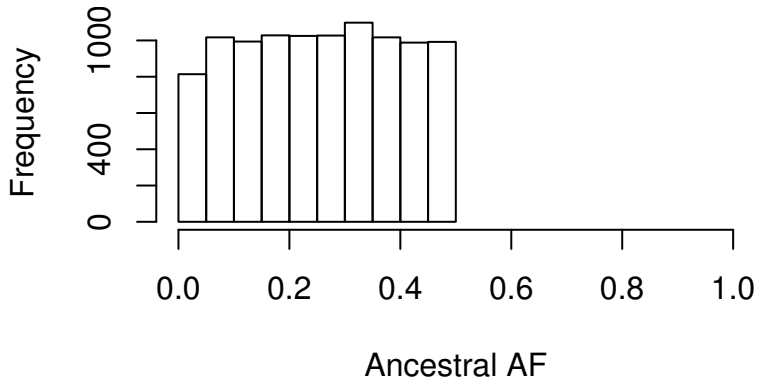


2.2 Draw random allele frequencies and genotypes

Now let's draw all the random allele frequencies and genotypes from the population structure. The easiest way is to use `rbnpsd` (the initial `r` is for drawing "random" samples in this and the following functions, in analogy to the `runif`, `rnorm`, `rbeta`, etc. functions from the `stats` R package).

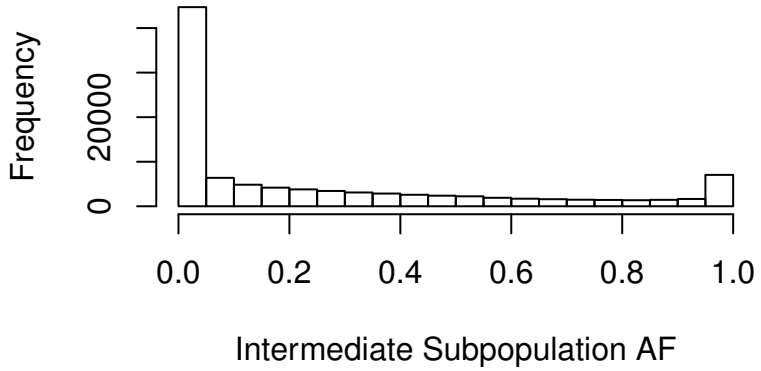
```
m <- 10000 # number of loci in simulation (NOTE this is 30x less than in publication!)
# draw all random Allele Freqs (AFs) and genotypes
# reuse the previous F,Q
out <- rbnpsd(Q, F, m)
X <- out$X # genotypes
P <- out$P # IAFs (individual-specific AFs)
B <- out$B # intermediate AFs
pAnc <- out$Pa # ancestral AFs
```

```
# inspect distribution of ancestral AFs (~ Uniform(0.01,0.5))
par(mar=c(4,4,0,0)+0.2) # shrink default margins for these figures
hist(pAnc, xlab='Ancestral AF', main='', xlim=c(0,1))
```

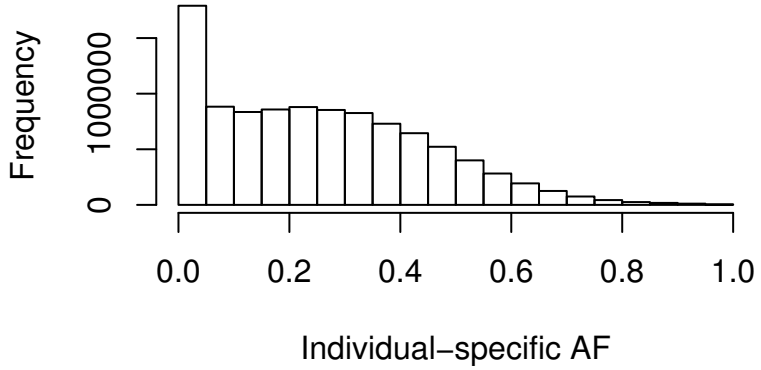



```
# distribution of intermediate population AFs
# (all subpopulations combined)
# (will be more dispersed toward 0 and 1 than ancestral AFs)
```

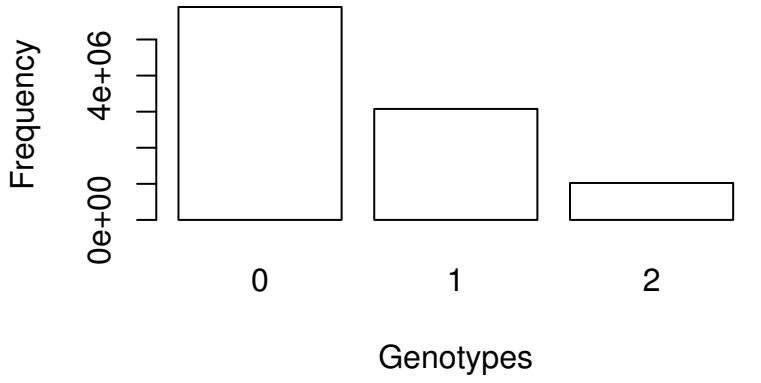
```r
hist(B, xlab='Intermediate Subpopulation AF', main='', xlim=c(0,1))
```




```r
# distribution of IAFs (admixed individuals)
# (admixture reduces differentiation, so these resemble ancestral AFs a bit more)
hist(P, xlab='Individual-specific AF', main='', xlim=c(0,1))
```




```r
# genotype distribution of admixed individuals
barplot(table(X), xlab='Genotypes', ylab='Frequency', col='white')
```



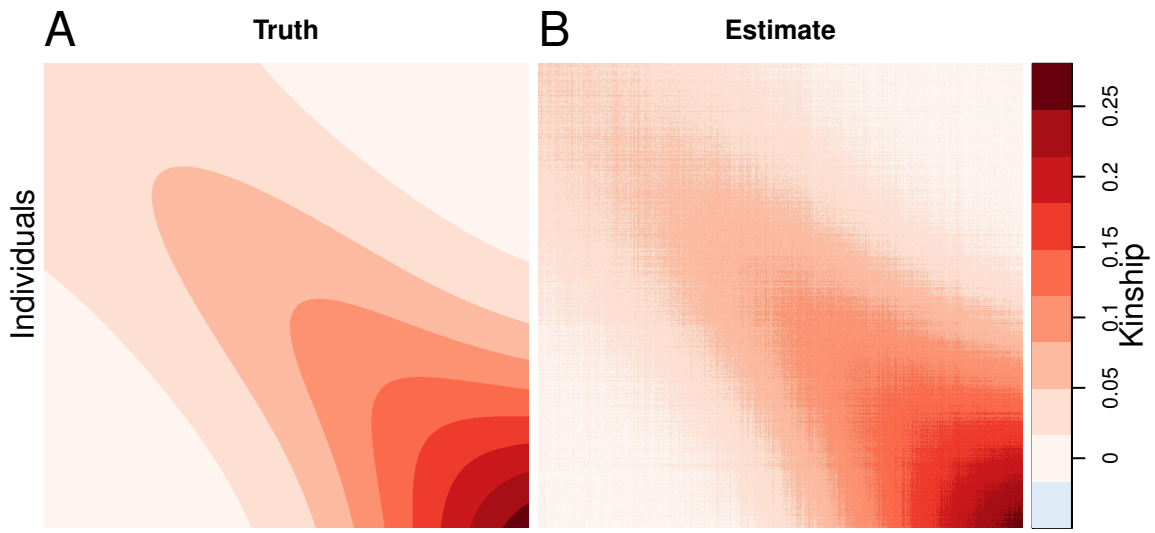
Lastly, let's verify that the correlation structure of the genotypes matches the theoretical coancestry matrix we constructed earlier. For this we use the `popkin` function of the package with the same name.

```r
# for best estimates, group individuals into subpopulations using the geography
# this averages more individuals in estimating the minimum kinship
subpops <- ceiling( (1:n)/n*k )
table(subpops) # got k=10 subpops with 100 individuals each
```

```
## subpops
##   1   2   3   4   5   6   7   8   9  10
## 100 100 100 100 100 100 100 100 100 100
```

```
# now estimate kinship using popkin
PhiHat <- popkin(X, subpops)
# replace diagonal with inbreeding coeffs. to match coancestry matrix
ThetaHat <- inbrDiag(PhiHat)

# Visualize the coancestry matrix using "popkin"!
# set outer margin for axis labels (left and right are non-zero)
par(oma=c(0,1.5,0,3))
# increase inner top margin for panel titles
par(mar=c(0,0,2.5,0)+0.2)
# now plot!
x <- list(Theta, ThetaHat)
titles <- c('Truth', 'Estimate')
plotPopkin(x, titles)
```



2.3 Customizing the allele frequency and genotype pipeline

The random variables generated by `rbnpsd` above can also be generated separately using the following functions (where p is the usual variable symbol for allele frequencies):

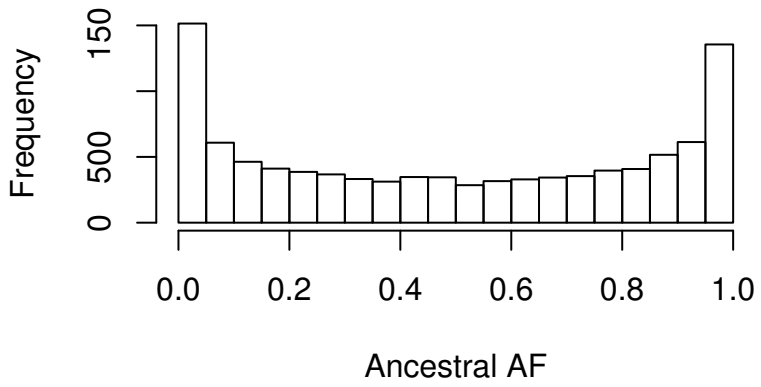
- `rpanc` (Random p ANCestral)
- `rpint` (Random p INTermediate)
- `rpiaf` (Random p Individual-specific Allele Frequency)
- `rgeno` (Random GENOtypes)

Here is the step-by-step procedure for drawing AFs and genotypes in `rbnpsd`:

```
# reuse the previous m,F,Q
pAnc <- rpanc(m) # draw ancestral AFs
B <- rpint(pAnc, F) # draw intermediate AFs
P <- rpiaf(B, Q) # draw IAFs (individual-specific AFs)
X <- rgeno(P) # draw genotypes
```

We provide functions for these separate steps to allow for more flexibility. For example, the ancestral allele frequencies could be drawn from a Symmetric Beta:

```
alpha <- 1/2 # this increases rare alleles
pAnc <- rbeta(m, alpha, alpha)
par(mar=c(4,4,0,0)+0.2) # shrink default margins for these figures
hist(pAnc, xlab='Ancestral AF', main='', xlim=c(0,1))
```



You could also draw genotypes from the ancestral population or the intermediate populations:

```
# draw genotypes for one individual from the ancestral population
# use "cbind" to turn the vector pAnc into the column matrix "rgeno" expects
Xanc <- rgeno(cbind(pAnc))
# returns a column matrix:
dim(Xanc)
```

```
## [1] 10000     1
```

```
# draw genotypes from intermediate populations
# draws one individual per intermediate population
Xint <- rgeno(B)
```

2.4 Low-memory genotype simulation algorithm

If you desire to simulate a very large number of individuals (n) and loci (m), you might run out of memory while running `rbnpsd`. Memory consumption is reduced by passing the `lowMem=TRUE` option to `rbnpsd`, which draws the genotypes `X` directly fromm the subpopulation AF matrix `B` and the admixture coefficients `Q`, without storing the whole IAF matrix `P` at any given time. However, this algorithm is much slower than the default one (`lowMem=FALSE`).

```
out <- rbnpsd(Q, F, m, lowMem=TRUE)
X <- out$X # genotypes
B <- out$B # intermediate AFs
pAnc <- out$Pa # ancestral AFs
# NOTE: out$P is not computed in this mode!
```

The same option exists for `rgeno`, which instead of accepting the IAF matrix `P` as input requires both `B` and `Q` as above:

```
X <- rgeno(B, Q, lowMem=TRUE)
```

3 Additional population structures

Here we show examples for functions that create admixture matrices for various population structures.

3.1 Independent subpopulations

The independent subpopulations model, where individuals are actually unadmixed, is the most trivial form of the BN-PSD admixture model.

```
# define population structure
# we'll have k=3 subpopulations, each with these sizes:
k <- 3
n1 <- 100; n2 <- 50; n3 <- 20
# here's the labels (for simplicity, list all individuals of S1 first, then S2, then S3)
labs <- c( rep.int('S1', n1), rep.int('S2', n2), rep.int('S3', n3) )
# data dimensions infered from labs:
length(labs) # number of individuals "n"
```

```
## [1] 170
```

```
length(unique(labs)) # number of subpopulations "k"
```

```
## [1] 3
```

```
# desired admixture matrix ("is" stands for "Independent Subpopulations")
Q <- qis(labs)
# got a boolean matrix with a single TRUE value per row
# (denoting the sole subpopulation from which each individual draws its ancestry)
head(Q, 2)
```

```
##        S1    S2    S3
## [1,] TRUE FALSE FALSE
## [2,] TRUE FALSE FALSE
```

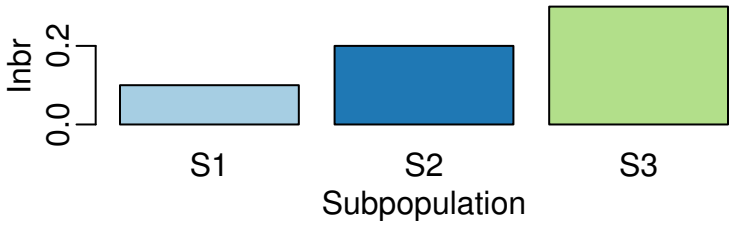
```
# construct the intermediate subpopulation FST vector
Fst <- 0.2 # the desired final FST
F <- 1:k # subpopulation FST vector, unnormalized so far
F <- F/popkin::fst(F)*Fst # normalized to have the desired Fst
popkin::fst(F) # verify FST for the intermediate subpopulations
```

```
## [1] 0.2
```

```
# get coancestry of the admixed individuals
Theta <- coanc(Q,F) # the coancestry matrix
# before getting FST for individuals, weigh then inversely proportional to subpop sizes
w <- weightsSubpops(labs) # function from 'popkin' package
# verify Fst for individuals (same as for intermediate subpops for this pop structure)
fst(Q, F, w)
```

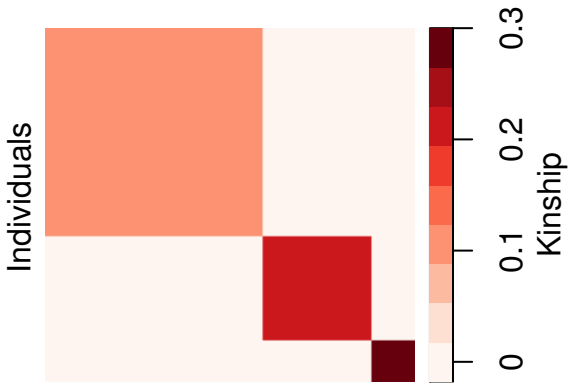
```
## [1] 0.2
```

```
# visualize the per-subpopulation inbreeding coefficients (FSTs)
par(mar=c(2.5,2.5,0,0)+0.2, lab=c(2,1,7), mgp=c(1.5,0.5,0)) # tweak margins/etc
colIS <- brewer.pal(k, "Paired") # indep. subpop. colors
barplot(F, col=colIS, names.arg=colnames(Q), xlab='Subpopulation', ylab='Inbr')
```




```
# visualize the admixture proportions
par(mar=c(1,4,0.4,0)+0.2, lab=c(2,2,7)) # tweak margins/etc
barplot(t(Q), col=colIS, border=NA, space=0, ylab='Admix prop')
mtext('Individuals', 1)
```


```
# Visualize the coancestry matrix using "popkin"!
par(oma=c(0,1.5,0,3), mar=c(0,0,0.4,0)+0.2) # tweak margins/etc
plotPopkin(Theta, nPretty=3)
```



References

Balding, D. J., and R. A. Nichols. 1995. "A Method for Quantifying Differentiation Between Populations at Multi-Allelic Loci and Its Implications for Investigating Identity and Paternity." *Genetica* 96 (1-2): 3–12.

Ochoa, Alejandro, and John D. Storey. 2016a. "F_{ST} And Kinship for Arbitrary Population Structures I: Generalized Definitions." *bioRxiv* doi:10.1101/083915. Cold Spring Harbor Labs Journals. doi:10.1101/083915.

———. 2016b. "F_{ST} And Kinship for Arbitrary Population Structures II: Method of Moments Estimators." *bioRxiv* doi:10.1101/083923. Cold Spring Harbor Labs Journals. doi:10.1101/083923.

Pritchard, J. K., M. Stephens, and P. Donnelly. 2000. "Inference of Population Structure Using Multilocus Genotype Data." *Genetics* 155 (2): 945–59.