

# practical 3: Inbreeding and kinship

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```
library(gaston)
library(hierfstat)
library(JGTeach)
```

For this practical we will use both simulated pedigrees, simulated genetic data on these pedigrees and the small chunk of chromosome 22 from the 1000 genomes.

## Kinship and inbreeding from pedigrees

1. load a pedigree from a monogamous population

(<https://www2.unil.ch/popgen/teaching/SISGData/pedmono.txt>) using `read.table`. Explore the pedigree: what are the first, second and third column? How many founders in this pedigree? Find at least two families with sibships of four (just inspect the pedigree).

```
ped<-read.table("https://www2.unil.ch/popgen/teaching/SISGData/pedmono.txt",header=TRUE)
str(ped)
dim(ped)

# number of founders
# founders are individuals with missing sires and dams

sum(is.na(ped$sire) & is.na(ped$dam))

# families: 28:32; 59:62

#first inds of gen 1:5 : c(21,47,77,117,159)
```

- Calculate the additive relationship matrix of individuals from this pedigree using `JGTeach::pedARM`. What is the pedigree relatedness among the sibship previously identified? and of these individuals with their parents? Examine sibship 92:95. What is special about it?

```
ARM<-JGTeach::pedARM(ped$sire,ped$dam)

ARM[28:32,28:32]
ped[28:32,]
ARM[28:32,c(ped[28,2],ped[28,3])]
ARM[59:62,59:62]
ARM[59:62,c(ped[59,2],ped[59,3])]

#relatedness higher than 0.5 with their sibs
ARM[92:95,92:95]

#and their parents
ARM[92:95,c(ped[92,2],ped[92,3])]

#their parents are related
ARM[c(ped[92,2],ped[92,3]),c(ped[92,2],ped[92,3])]
```

- Plot a histogram of the relatedness using only off diagonal elements. The function `hierfstat::mat2vec` will be useful. Comments? Transform the relatedness matrix into a kinship and inbreeding matrix using `hierfstat::GRM2kinship`. Plot a heatmap of resulting matrix using `image` and `interpret`

```
hist(mat2vec(ARM))

ped.kin<-hierfstat::grm2kinship(ARM)
image(1:195,1:195,ped.kin)

#add vertical and horizontal lines between generations
genlim<-c(21,47,77,117,159)
abline(h=genlim-.5,v=genlim-.5)
```

## Kinship and inbreeding from markers, compared to pedigrees

2. We have generated genotypes dosage from these individuals ([https://www2.unil.ch/popgen/teaching/SISGData/geno\\_mono.RDS](https://www2.unil.ch/popgen/teaching/SISGData/geno_mono.RDS)). First download, then load this file using `readRDS`, and compute
  - Allele sharing kinship using `hierfstat::beta.dosage`
  - Standard GRM (average of ratios) as computed in e.g. GCTA using `gaston::GRM`;
  - Standard GRM (ratio of averages) using `JGTeach::Kc0`. Compare each to the expected values obtained from the pedigree and discuss.

```

genoped<-readRDS("geno_mono.RDS")
genoped.Kas<-hierfstat::beta.dosage(genoped,inb=FALSE,Mb=TRUE)
genoped.M<-with(genoped.Kas,betas*(1-MB)+MB)
genoped.Kc0<-JGTeach::Kc0(genoped.M,matching=TRUE)
bed.genoped<-gaston::as.bed.matrix(genoped)
genoped.std.GRM<-gaston::GRM(bed.genoped,autosome.only=FALSE)

par(mfrow=c(1,3))
plot(mat2vec(ARM)/2,mat2vec(genoped.Kas$betas),
     cex=0.5,col="red",main=expression(K[AS]),
     xlab="ped kinship",ylab="est. kinship")
abline(c(0,1))
plot(mat2vec(ARM)/2,mat2vec(genoped.Kc0),
     cex=0.5,col="red",main=expression(K[c0]),
     xlab="ped kinship",ylab="est. kinship")
abline(c(0,1))

# gaston::GRM reports relatedness rather than kinship, hence the /2

plot(mat2vec(ARM)/2,mat2vec(genoped.std.GRM)/2,
     cex=0.5,col="red",main="standard kinship",
     xlab="ped kinship",ylab="est. kinship")
abline(c(0,1))
par(mfrow=c(1,1))

```

- Redo these comparisons after having “rescaled” the pedigree kinship such that mean expected kinship is 0 and discuss

```

#we divide by two because we want kinships rather than relatedness
mARM<-mean(mat2vec(ARM)/2)
ARMc<-(ARM/2-mARM)/(1-mARM)

par(mfrow=c(1,3))
plot(mat2vec(ARMc),mat2vec(genoped.Kas$betas),
     cex=0.5,col="red",main=expression(K[AS]),
     xlab="ped kinship",ylab="est. kinship")
abline(c(0,1))
plot(mat2vec(ARMc),mat2vec(genoped.Kc0),
     cex=0.5,col="red",main=expression(K[c0]),
     xlab="ped kinship",ylab="est. kinship")
abline(c(0,1))
plot(mat2vec(ARMc),mat2vec(genoped.std.GRM)/2,
     cex=0.5,col="red",main="standard kinship",
     xlab="ped kinship",ylab="est. kinship")
abline(c(0,1))
par(mfrow=c(1,1))

```

For a discussion of these issues, see Weir and Goudet, 2017 Genetics  
<https://www.genetics.org/content/206/4/2085#sec-16>, Fig. 5 and followings

## kinship and inbreeding in the 1000 genomes

3. We will now compare these three estimators of genomic kinship using the subset of Chromosome 22 we used in previous practical. Start by computing the three estimators:

```
ch22<-read.VCF("chr22_Mb0_20.recode.vcf.gz")
ch22.M<-readRDS("matching.ch22.RDS")
Mb<-mean(mat2vec(ch22.M))

ch22.Kas<-(ch22.M-Mb)/(1-Mb)
ch22.Kc0<-JGTeach::Kc0(ch22.M,matching=TRUE)
ch22.std.GRM<-gaston::GRM(ch22)
```

- Produce a heat map for each (this may take some times, you might want to save the results to an external file for future inspection, hence the commented call to `png`), after having removed the main diagonal (which contains the self kinships), and arranging samples according to `super_population` first, and then population.

```
#extract self kinship and convert it to inbreeding
ch22.Kas.inb<-diag(ch22.Kas)*2-1/2
diag(ch22.Kas)<-NA
ch22.Kc0.inb<-diag(ch22.Kc0)*2-1/2
diag(ch22.Kc0)<-NA
ch22.std.Inb<-diag(ch22.std.GRM)-1
diag(ch22.std.GRM)<-NA

samp.desc<-read.table("ftp://ftp-trace.ncbi.nih.gov/1000genomes/ftp/release/20130502/integrated_
call_samples_v3.20130502.ALL.panel",header=TRUE,stringsAsFactors = TRUE)

#to order samples
ospp<-with(samp.desc,order(super_pop,pop))
lsp<-cumsum(table(samp.desc$super_pop))

#png("1kg_ch22chunk_Kas.png")
image(1:2504,1:2504,ch22.Kas[ospp,ospp])
abline(h=lsp,v=lsp)
#dev.off()
#png("1kg_ch22chunk_Kc0.png")
image(1:2504,1:2504,ch22.Kc0[ospp,ospp])
abline(h=lsp,v=lsp)
#dev.off()
#png("1kg_ch22chunk_Kstdk.png")
image(1:2504,1:2504,ch22.std.GRM[ospp,ospp]/2)
abline(h=lsp,v=lsp)
#dev.off()
```

- Discuss the resulting heatmaps, in the light of what you know about human population demographic history.