imputeR Documentation

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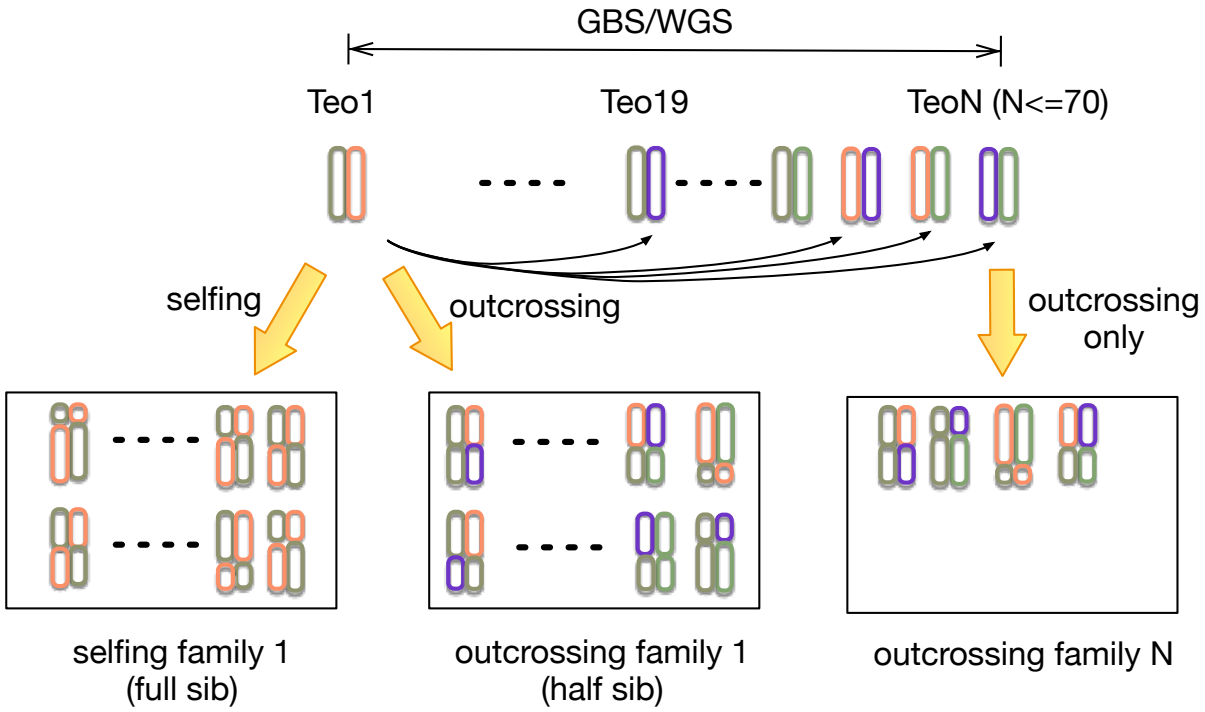
Contents

1 Introduction

1.1 Crossing Scheme and Experimental Design



In this experiment, we selfed and outcrossed a set of ~70 teosinte landraces to get a progeny array composed of 4,875 individuals. The ~70 founders and all the progeny were genotyped using GBS. We also re-sequenced 20/70 founder lines (the others will be re-sequenced soon). Because of the high error rate of the GBS data, especially problematic for calling heterozygous sites, we employed a phasing and imputation strategy to infer the expected genotypes by combining parentage and GBS information.

This file is to document the `R` package we developed to solve the problems step by step.

1.2 Install and Usage

Install devtools first, and then use devtools to install imputeR from github.

```
# install and load devtools
devtools::install_github("hadley/devtools")
library(devtools)
# install and load imputeR
install_github("yangjl/imputeR")
library(imputeR)
```

1.3 How to find help.

Within "R" console, type `?impute_mom` or `help(impute_mom)` to find help information about the function.

```
library(imputeR)
?impute_mom
```

2 Infer mom's genotype from GBS data

If we got mom's WGS data, this step can be skipped.

We have observed mom and observed (selfed) kids. We want to know $P(G|\theta)$, or the probability of mom's genotype given observed data θ. And according to Bayes' theorem,

$P(G|\theta) \propto P(\theta|G) \times P(G)$,

where $P(G)$ is the probability of the genotype according to the Hardy-Weinberg equilibrium estimated from the population. This consists of observed genotypes (G') of both mom and kids. So:

$$P(G|\theta) \propto \left(\prod_{i=1}^{k} P(G'_k|G) \right) \times P(G'_{mom}|G) \times P(G),$$

where $P(G'_{mom}|G)$ is the probability of mom's observed genotype given a true genotype G by considering error rates, i.e. GBS homozygote error = 0.02 and heterozygote error = 0.8.
And $P(G'_k|G)$ is the probability of the k th kid's observed genotype given genotype G by considering error rates and Mendelian segregation rate. The function `impute_mom` was implemented to compute mom's genotype probabilities.

2.1 Toy example

In the below toy example, we simulated a full sib family with 12 kids for 3 loci. Mom GBS genotype is `0 0 0` and kids are all `0 0 0`. In the resulting table, the first three columns are the probabilities of genotype `0, 1, 2`. The 4th column is the odd ratio of the highest divided by the 2nd highest probability. `gmax` mom's genotype with the highest probability. `gor` mom's genotype with the highest probability and `OR` bigger than your threshould.

```
# mom's GBS data is a vector
obs_mom <- c(0, 0, 0)
# kids GBS data is a list of vectors
obs_kids <- list(c(0, 0, 0), c(0, 0, 0), c(0, 0, 0), c(0, 0, 0), c(0, 0, 0), c(0, 0, 0),
c(0, 0, 0), c(0, 0, 0), c(0, 0, 0), c(0, 0, 0), c(0, 0, 0), c(0, 0, 0))

# run impute_mom to get the probabilities of mom's genotype of all loci
geno <- impute_mom(obs_mom, obs_kids, hom.error=0.02, het.error=0.8)
```

```
## ###>>> impute mom's genotype using [ 12 ] kids in a full sib family ...
```

```
# find the most likely genotype of mom
momgeno(geno, oddratio=0.5, returnall=TRUE)
```

```
##           g0        g1        g2        OR gmax gor
## 1  -4.533885 -13.40911 -30.63523 8.8752203    0   0
## 2 -13.683307 -14.48731 -23.64221 0.8040017    0   0
## 3 -13.683307 -14.48731 -23.64221 0.8040017    0   0
```

2.2 Simulated Data

```
set.seed(123456)
sim <- SimSelfer(size.array=10, het.error=0.8, hom.error=0.002, numloci=100, rec=1.2, imiss=0.3)
```

2.3 Real Data

To load `hdf5` file, you could install Vince's tasselr and ProgenyArray packages. And then, following the below instructions.

```
# install tasselr and ProgenyArray, if you fail to install it, checking all the dependencies.
library(devtools)
install_github("vsbuffalo/tasselr")
install_github("vsbuffalo/ProgenyArray")

library(parallel)
options(mc.cores=NULL)
# you need to specify the location where the packages were installed.
load_all("~/bin/tasselr")
load_all("~/bin/ProgenyArray")

# Note: at least 64G memory was needed to load the hdf5 file
loading_h5_recode(h5file="largedata/teo.h5", save.file="largedata/out.RData")
```

---

3 Phasing Founder Genotypes

$$P(H|\theta) \propto P(\theta|H) \times P(H)$$
$$P(H|\theta) \propto \left(\prod_{i=1}^{k} P(H'_k|H) \right) \times P(H)$$
$$P(H|\theta) \propto \left(\prod_{i=1}^{k} \prod_{l=1}^{n} P(G'_{i,l}|H) \right) \times P(H)$$

- Where θ denotes observed data.
- $P(H)$ is the probability of the haplotype for a given window size of n.
- $P(G'_{i,l}|H)$ is the probability of kid i at locus l for a given haplotype H.
- The prior $P(H)$ is that all possible haplotypes of a given window size are equally likely.

---

4 Imputing and Phasing Kids

$$P(H_k|\theta) \propto P(\theta|H_k) \times P(H_k)$$
$$P(H_k|\theta) \propto \left(\prod_{i=k} P(H'_k|H_k) \right) \times P(H_k)$$
$$P(H_k|\theta) \propto \left(\prod_{i=k} \prod_{l=1}^{n} P(G'_{i,l}|H_k) \right) \times P(H_k)$$

- Where θ denotes observed data.
- $P(H)$ is the probability of the haplotype for a given window size of n.
- $P(G'_{i,l}|H)$ is the probability of kid i at locus l for a given haplotype H.
- The prior $P(H)$ is that all possible haplotypes of a given window size are equally likely.

```
phase <- read.csv("../data/sim_phasing_res.csv")

hist(phase$er, breaks=30, main="Simulation (N=100)",col="#faebd7", xlab="Phasing Error Rate")
abline(v=mean(phase$er), col="red", lwd=2)
abline(v=median(phase$er), col="darkblue", lwd=2)
```

---

5 Phasing Dad of outcrossing progeny array

$$P(H_d|\theta) \propto P(\theta|H_d) \times P(H_d)$$
$$P(H_d|\theta) \propto \left(\prod_{i=1}^{k} P(H'_k|H_d, H_m) \right) \times P(H_m) \times P(H_d)$$
$$P(H|\theta) \propto \left(\prod_{i=1}^{k} \prod_{l=1}^{n} P(G'_{i,l}|H) \right) \times P(H)$$

- Where θ denotes observed data.
- $P(H_d)$ is the probability of the dad's haplotype for a given window size of n.
- $P(G'_{i,l}|H)$ is the probability of kid i at locus l for a given haplotype H.
- The prior $P(H)$ is that all possible haplotypes of a given window size are equally likely.
