# Genetic linkage map construction:R/qtl

## PLPTH813 Bioinformatics Application

Ying Hu

2017/03/07

# R/qtl introduction

QTL analysis package R/qtl (Broman & Wu, 2014) is a very popular package for the linkage map construction of a simple Backcross (BC), Doubled Haploid (DH), intercrossed F2 (F2), 4-way crosses and advanced Recombinant Inbred Lines (RIL).

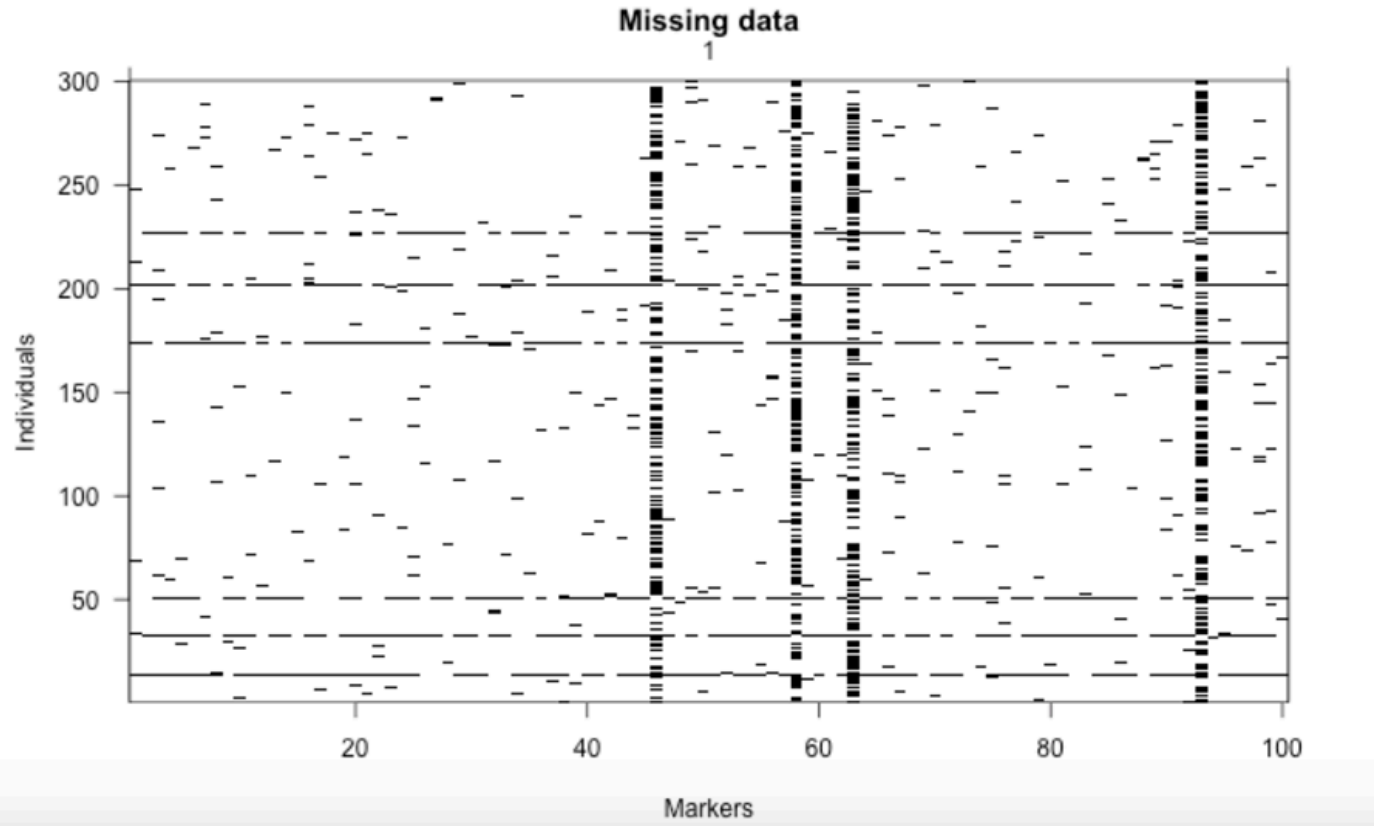
**install.packages("qtl")**

```
library(qtl)
data(mapthis)
summary(mapthis)

## F2 intercross
##
## No. individuals: 300
##
## No. phenotypes: 1
## Percent phenotyped: 100
##
## No. chromosomes: 1
## Autosomes: 1
##
## Total markers: 100
## No. markers: 100
## Percent genotyped: 95.4
## Genotypes (%): AA:26.2 AB:48.2 BB:25.6 not BB:0.0 not AA:0.0
```

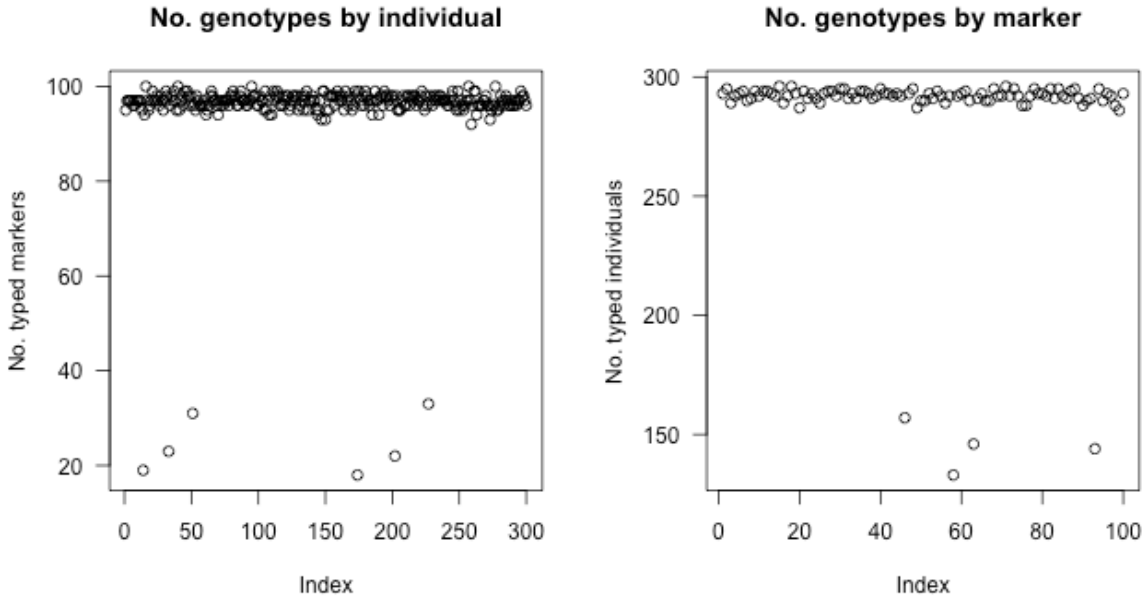
# Omit individuals and markers with lots of missing data

plotMissing(mapthis, main="Missing data")



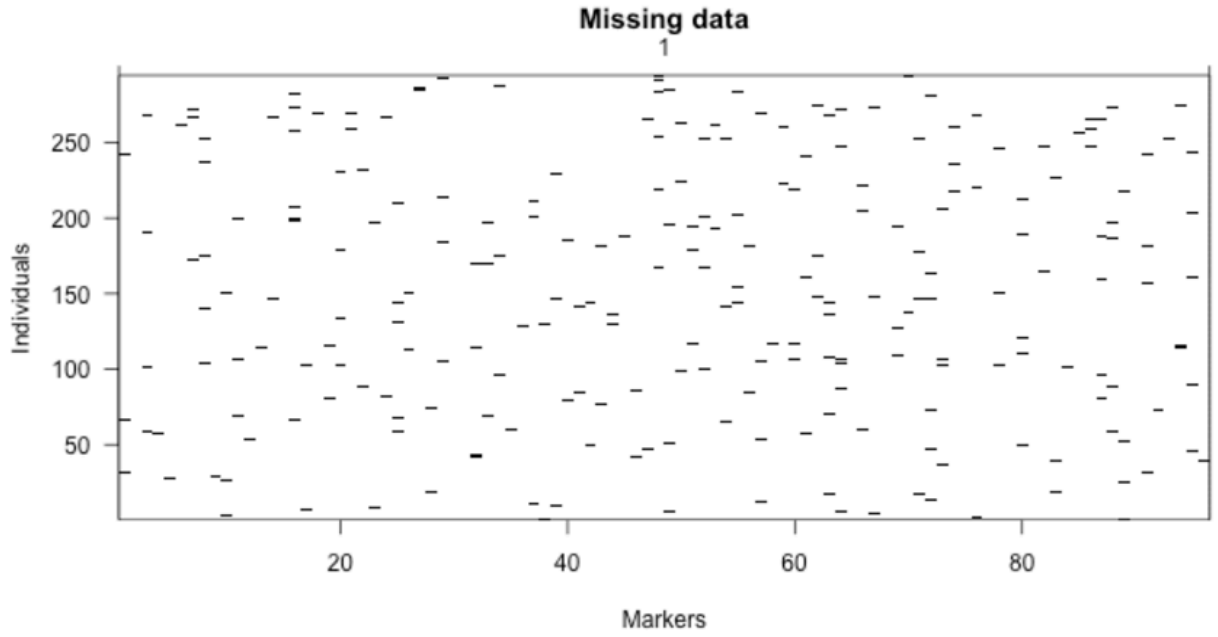
# Omit individuals and markers with lots of missing data

```
par(mfrow=c(1,2), las=1)
plot(ntyped(mapthis), ylab="No. typed markers", main="No. genotypes by individual")
plot(ntyped(mapthis, "mar"), ylab="No. typed individuals",
main="No. genotypes by marker")
```



# Drop individuals and markers with lots of missing data

```
mapthis <- subset(mapthis, ind=(ntyped(mapthis)>50))
nt.bymar <- ntyped(mapthis, "mar")
todrop <- names(nt.bymar[nt.bymar < 200])
mapthis <- drop.markers(mapthis, todrop)
plotMissing(mapthis, main="Missing data")
```



# Look for markers with distorted segregation patterns

We expect the genotypes to appear with the frequencies 1:2:1. The function geno.table is used to inspect the segregation patterns.We will focus on those markers that show significant distortion at the 5% level, after a Bonferroni correction for the multiple tests.

```
gt <- geno.table(mapthis)
gt[gt$P.value < 0.05/totmar(mapthis),]
```

```
##        chr missing  AA  AB  BB not.BB not.AA       P.value
## C4M2     1       1  99 144  50      0      0  2.646238e-04
## C1M4     1       4   8 209  73      0      0  2.539267e-19
## C2M9     1       2 287   3   2      0      0 2.318765e-182
## C1M21    1       5 199  10  80      0      0  2.235412e-76
## C2M15    1       3   0   1 290      0      0 1.455993e-188
## C2M27    1       4   2 217  71      0      0  2.204480e-23
```

```
todrop <- rownames(gt[gt$P.value < 0.05/totmar(mapthis), ])
mapthis <- drop.markers(mapthis, todrop)
```

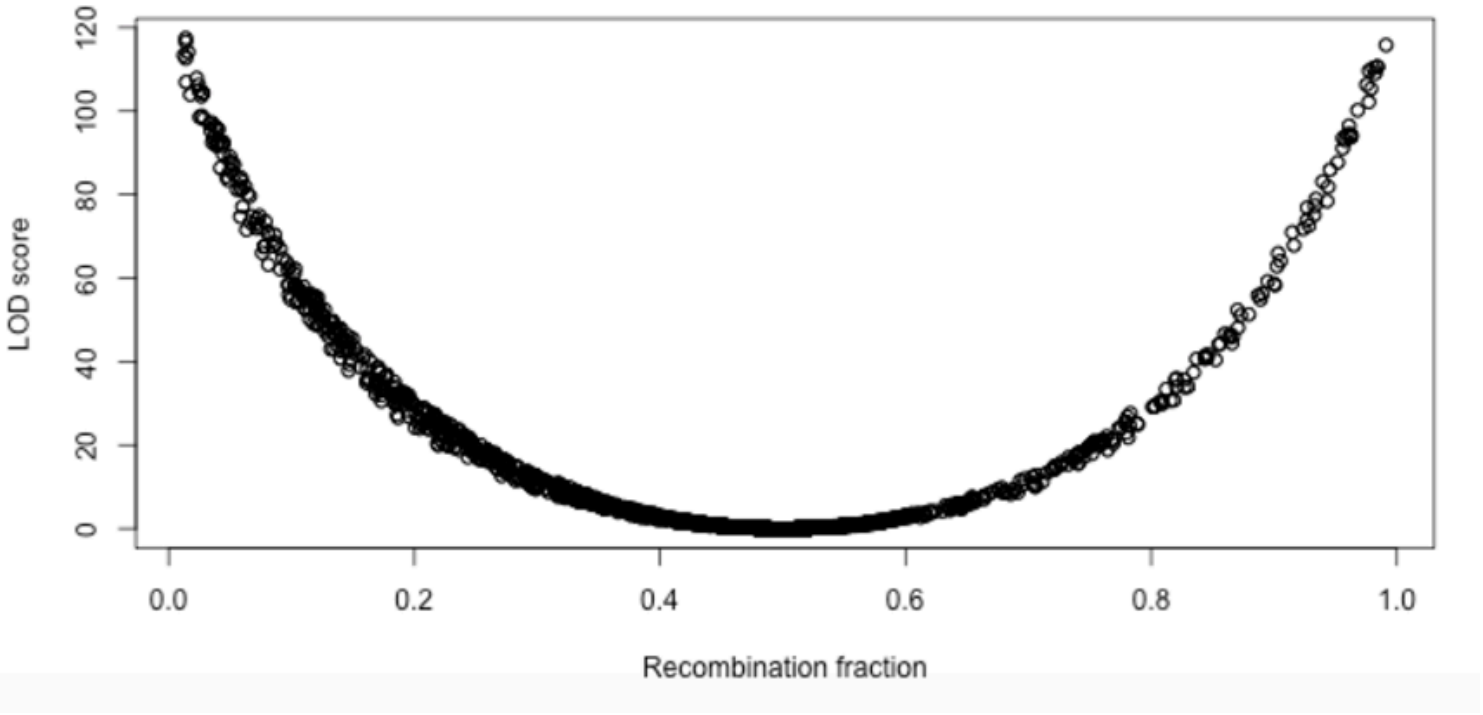
# Study pairwise marker linkages; look for switched alleles

```
mapthis <- est.rf(mapthis)

## Warning in est.rf(mapthis): Alleles potentially switched at markers
## C3M16 C2M16 C1M2 C3M9 C2M14 C1M24 C1M1 C2M12 C1M36 C3M1
C2M25 C1M22
```

# Plot of LOD scores versus estimated recombination fractions for all markers pairs

```
rf <- pull.rf(mapthis)
lod <- pull.rf(mapthis, what="lod")
plot(as.numeric(rf), as.numeric(lod), xlab="Recombination fraction", ylab="LOD score")
```



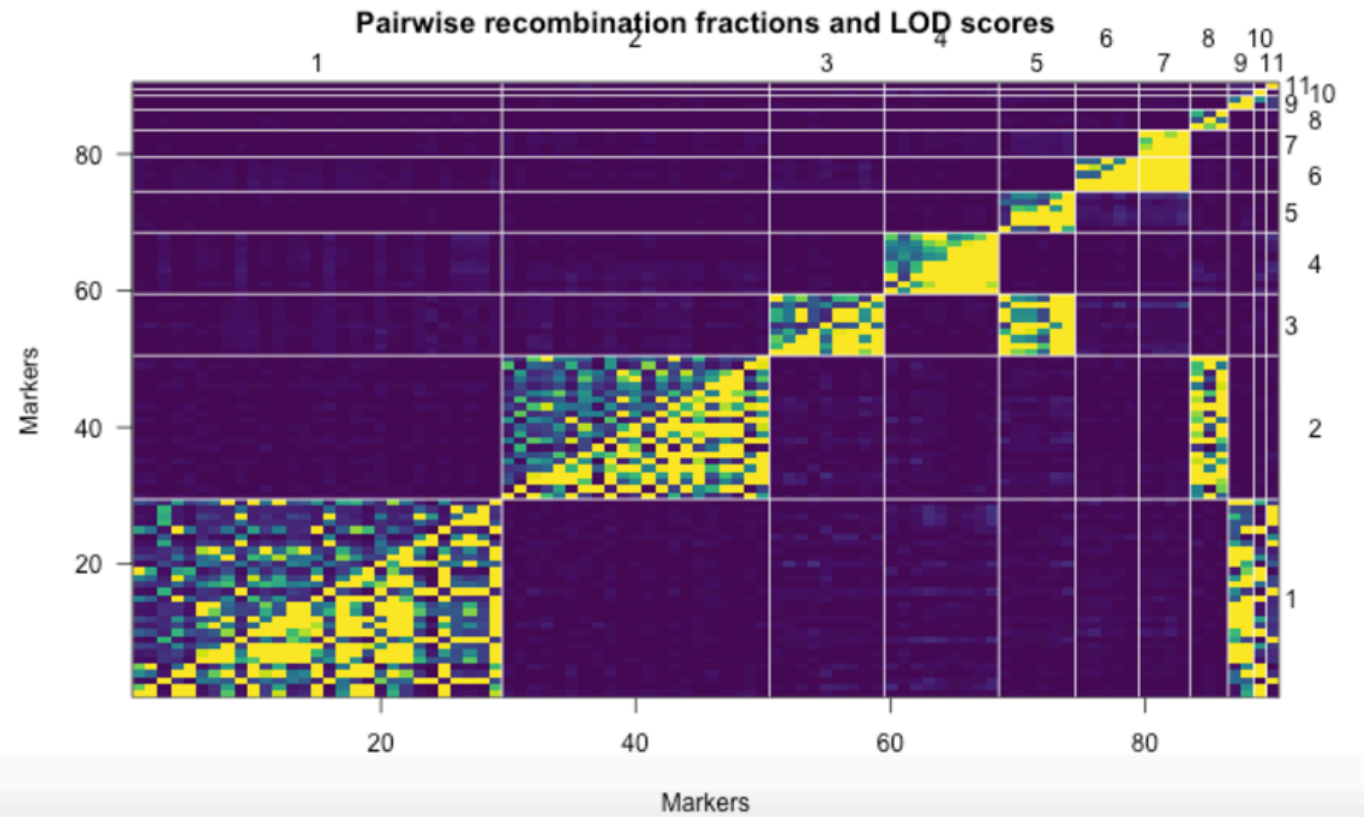
# Look for switched alleles

One solution to this problem is to form initial linkage groups, ensuring that markers with rf > 1/2 are placed in different groups. If all goes well, each chromosome will come out as a pair of linkage groups: one containing markers with correct alleles and another containing markers with switched alleles.

```
mapthis <- formLinkageGroups(mapthis, max.rf=0.35, min.lod=6, reorgMarkers = T)
```

# Plot of estimated recombinant fractions (Upper-left triangle) and LOD scores (lower-right triangle)

plotRF(mapthis, alternate.chrid=TRUE)

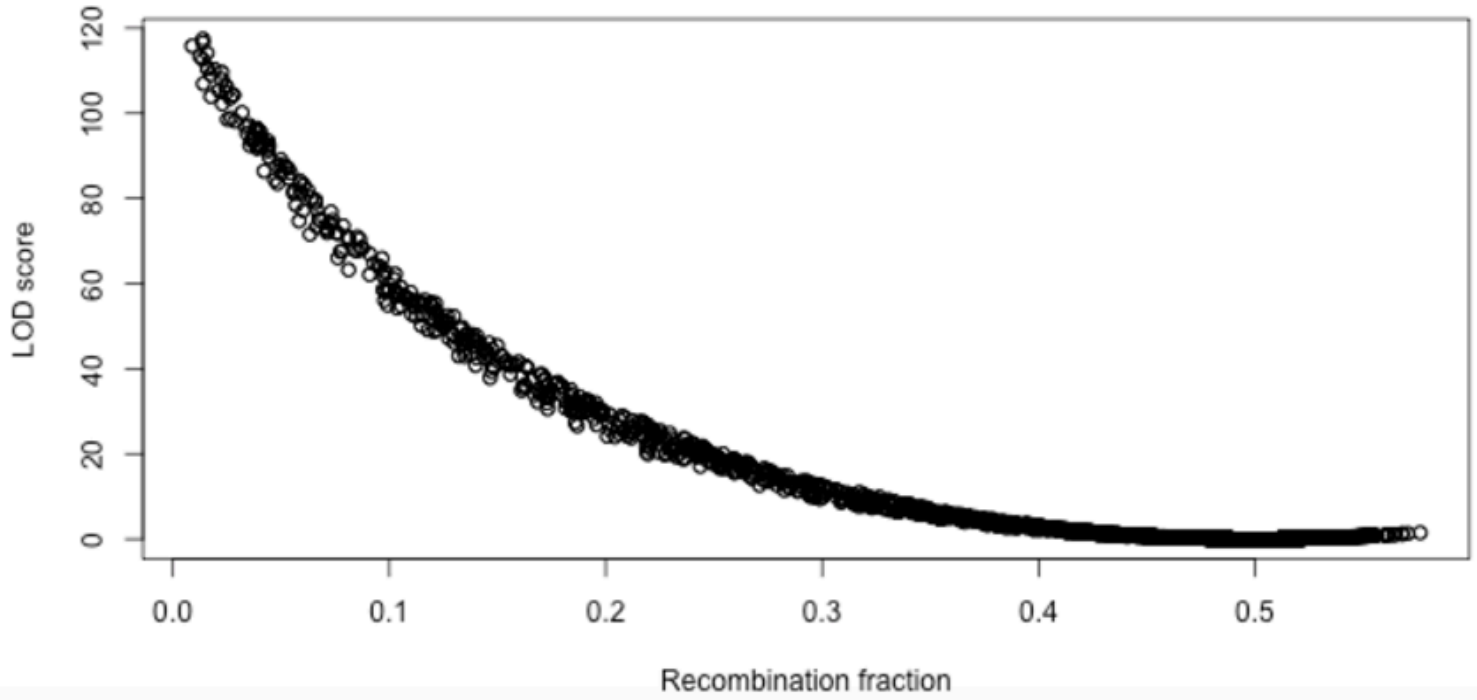


# Switch alleles

```
toswitch <- markernames(mapthis, chr=c(5, 7:11))
mapthis <- switchAlleles(mapthis, toswitch)
```

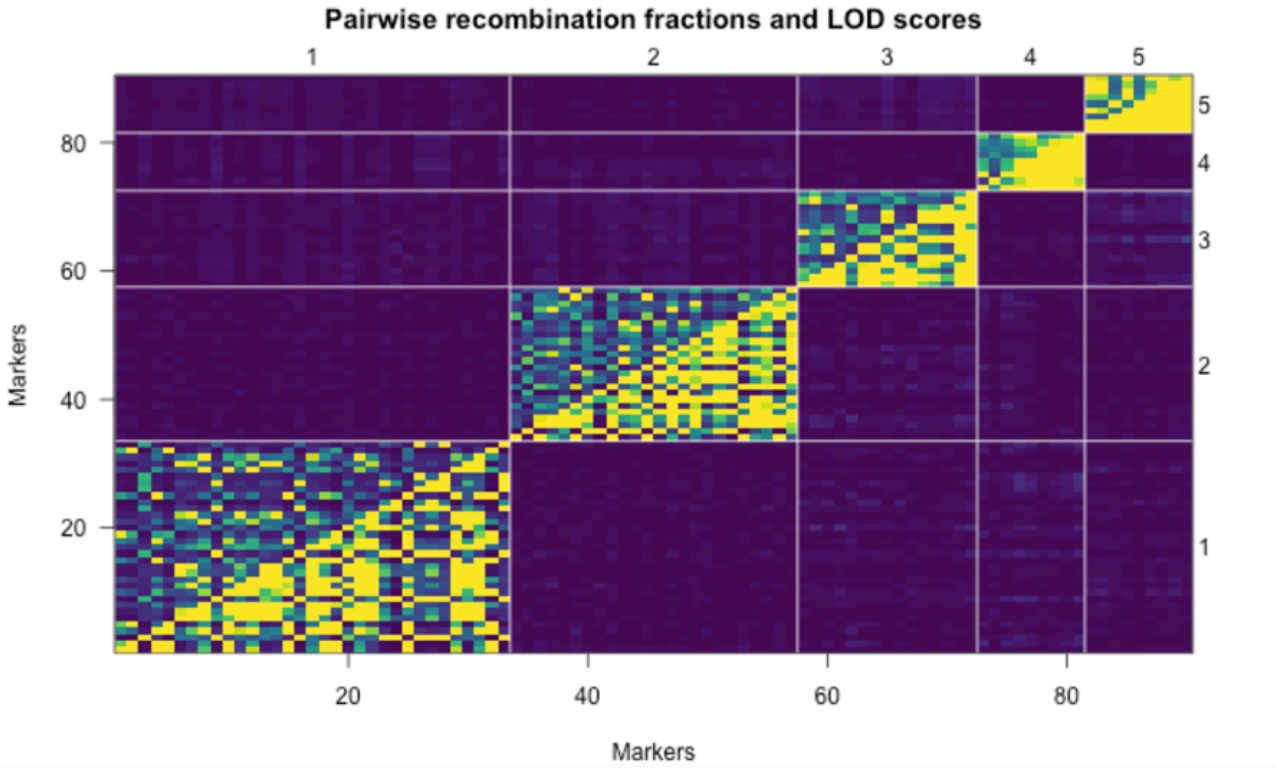
# Revisit the plot of LOD scores versus recombinaion fractions

```
rf <- pull.rf(mapthis)
lod <- pull.rf(mapthis, what="lod")
plot(as.numeric(rf), as.numeric(lod), xlab="Recombination fraction",
ylab="LOD score")
```



# Form modifed linkage groups

```
mapthis <- formLinkageGroups(mapthis, max.rf=0.35, min.lod=6,
reorgMarkers=TRUE)
plotRF(mapthis)
```



# Order markers of each linkage group

```
mapthis <- orderMarkers(mapthis, use.ripple=TRUE, window = 7, chr=1)
mapthis <- orderMarkers(mapthis, use.ripple=TRUE, window = 7, chr=2)
mapthis <- orderMarkers(mapthis, use.ripple=TRUE, window = 7, chr=3)
mapthis <- orderMarkers(mapthis, use.ripple=TRUE, window = 7, chr=4)
mapthis <- orderMarkers(mapthis, use.ripple=TRUE, window = 7, chr=5)
```

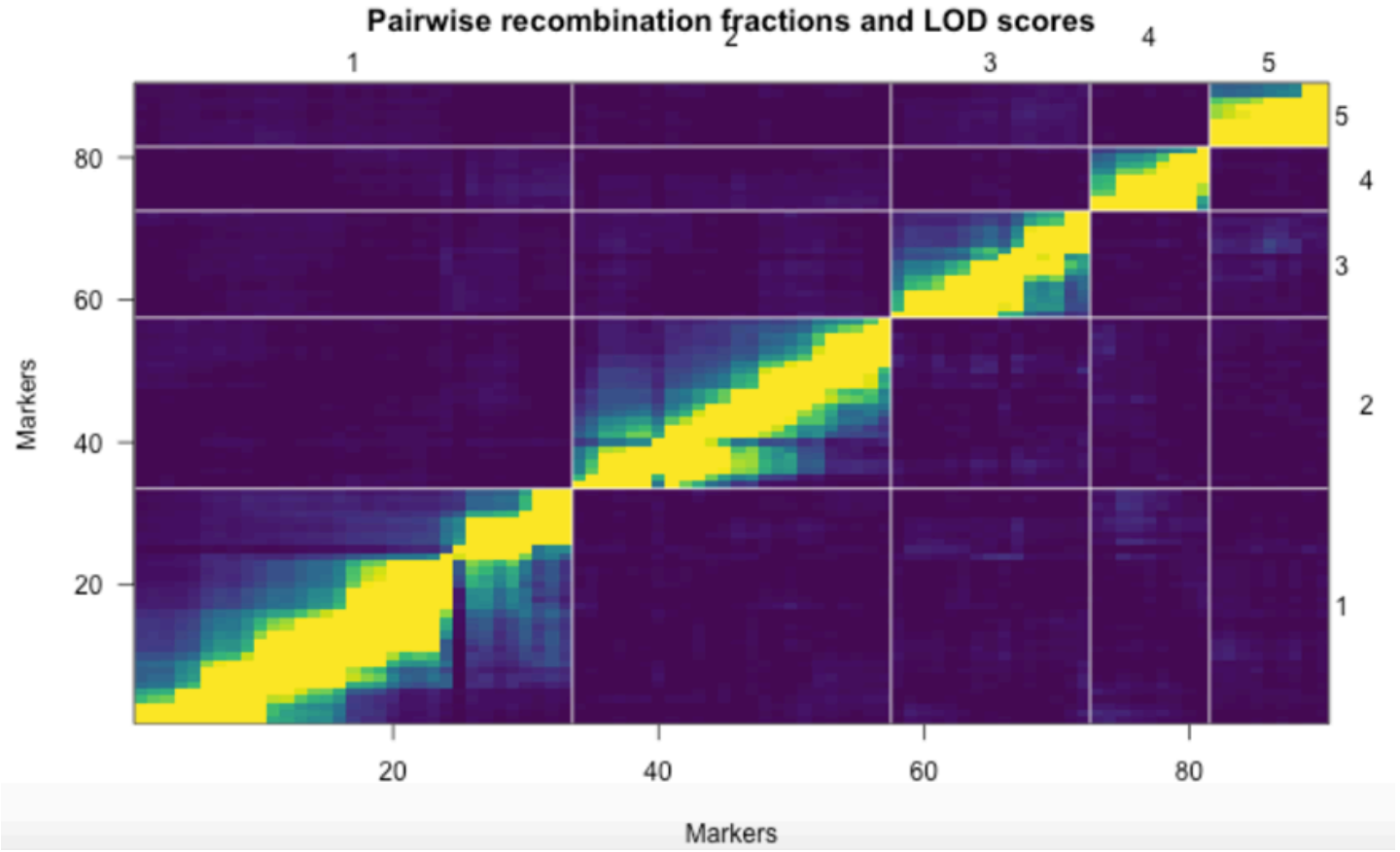
# Summary

summaryMap(mapthis)

```
##           n.mar length ave.spacing max.spacing
## 1            33  239.9         7.5         46.2
## 2            24  188.2         8.2         22.6
## 3            15  126.6         9.0         20.9
## 4             9   60.4         7.6         20.9
## 5             9   41.9         5.2         24.7
## overall      90  657.1         7.7         46.2
```

# Plot of estimated recombinant fractions (Upper-left triangle) and LOD scores (lower-right triangle)

plotRF(mapthis, alternate.chrid=TRUE)



# Plot genetic linkage map

plotMap(mapthis, main="Genetic linkage map")