

R-programında Synbreed Paketini Kullanarak Genomik Seleksiyon Uygulaması

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http://synbreed.r-forge.r-project.org/



Welcome to synbreed project!

Collection of statistical and genetic methods developed for the synbreed project for synergistic plant and animal breeding.

Description:

- The R-package synbreed provides a framework for the analysis of genomic prediction data (Genomic Selection, GWAS, QTL-mapping) within an open source software.
- Features
- Data processing
 - Combining raw data sources to a gpData object
 - Conversion from and to class cross in package qtl
 - Coding marker data into number of copies of the minor allele
 - Preselection of markers according to MAF, % missing values and LD
 - Imputation of missing genotypes by marginal allele distribution, family structure for fully homozygous inbred individuals or flanking markers using Beagle
 - Data visualization and analysis
 - Summary method for classes gpData, pedigree and relationshipMatrix
 - Marker map representation for low and high density maps
 - LD computation as r2 and LD decay visualization as as scatterplot or stacked histogram
 - Pedigree tree and kinship visualization of relatedness between individuals
 - Statistical models
 - Estimation of pedigree based relationship (additive and dominance)
 - Marker based relationship
 - Cross-validation for BLUP, Ridge Regression and Bayesian methods
- The package comes with ABSOLUTELY NO WARRANTY; for details see http://www.gnu.org/copyleft/gpl.html (GPL).

Download:

To install the latest development version of package synbreed from R-Forge (if you are running a recent R version), use

install.packages("synbreed",repos="http://r-forge.r-project.org")

You can also manually download the source code from https://r-forge.r-project.org/R/?group_id=710

A stable release is available from **CRAN**



http://synbreed.r-forge.r-project.org/

Documentation:

- Publication in Bioinformatics
- Citation information:

```
citation(package="synbreed")
```

- pdf version of the manual
- package vignette with detailed background information and examples:

```
library(symbreed)
vignette("IntroSym")
```

- · overview over the functions
- Poster presented at the 4th International Conference on Quantitative Genetics, June 2012, Edinburgh

Workshop: Introduction to the synbreed R package, November 2012, TUM:

- Course slides (2012 11 08)
- Code of the slides (2012 11 08)

Developers:

- Valentin Wimmer, Chair of Plant Breeding, Technische Universität München
- Theresa Albrecht, Chair of Plant Breeding, Technische Universität München
- Hans-Juergen Auinger, Chair of Plant Breeding, Technische Universität München

Financial support:

The development of the package was financially supported by the German Federal Ministry of Education and Research (BMBF) within the AgroClustEr "Synbreed Synergistic plant and animal breeding" (FKZ 0315528A)



Synbreed Paketinden Önce Yüklenmesi Gereken Paketler

- lattice
 - install.packages("lattice")
- igraph
 - install.packages("igraph")
- MASS
 - install.packages("MASS")
- LDheatmap
 - install.packages("LDheatmap")

- qtl
 - install.packages("qtl")
- doBy
 - install.packages("doBy")
- BLR
 - install.packages("BLR")
- Regress
 - install.packages("regress")

install.packages("synbreed",repos="http://r-forge.r-project.org")



Synbreed Paketi – Veri Setleri

```
    Synbreed paketinin aktifleştirilmesi

   library("synbreed")

    Synbreed paketinde mevcut veri setleri

  # Maize (Mısır) veri seti
     data(maize)
     str(maize)
  # Mice (Fare) veri seti
     data(mice)
     str(mice)
  # Cattle (Sigir) veri seti
    data(cattle)
     str(cattle)
```



Synbreed – Cattle Veri Seti

```
# Cattle (Sigir) veri seti
 data(cattle)
  str(cattle)
List of 7
              :'data.frame': 1929 obs. of 3 variables:
 $ covar
                : chr [1:1929] "ID10001" "ID10002" "ID10003" "ID10004"
  ..$ id
  ... phenotyped: logi [1:1929] FALSE FALSE FALSE FALSE FALSE ...
  ..$ genotyped : logi [1:1929] FALSE FALSE FALSE FALSE FALSE ...
             : num [1:500, 1:2, 1] -23.4 15.5 -19.2 -10.4 -14.1 ...
 $ pheno
  ..- attr(*, "dimnames")=List of 3
  ...$ : chr [1:500] "ID11430" "ID11431" "ID11432" "ID11433" ...
  ....$ : chr [1:2] "Phenotype1" "Phenotype2"
  .. ..$ : chr "1"
```



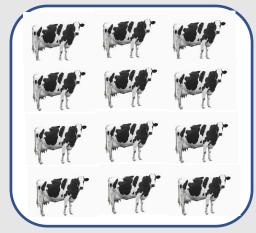
Synbreed – Cattle Veri Seti

```
$ geno : chr [1:500, 1:7250] "AB" "BB" "BB" "BB" ...
  ..- attr(*, "dimnames")=List of 2
  ....$ : chr [1:500] "ID11430" "ID11431" "ID11432" "ID11433" ...
  ....$ : chr [1:7250] "SNP_1" "SNP_2" "SNP_3" "SNP_4" ...
$ map :Classes 'GenMap' and 'data.frame': 7250 obs. of 2 variables:
  ..$ chr: int [1:7250] 1 1 1 1 1 1 1 1 1 1 ...
  ..$ pos: num [1:7250] 0.000001 0.20258 0.279809 0.668932 0.763913 ...
$ pedigree :Classes 'pedigree' and 'data.frame': 1929 obs. of 4 variables:
  ..$ ID : chr [1:1929] "ID10001" "ID10002" "ID10003" "ID10004" ...
  ..$ Par1 : chr [1:1929] "0" "0" "0" "0" ...
  ..$ Par2 : chr [1:1929] "0" "0" "0" "0" ...
  ..$ gener: num [1:1929] 0 0 0 0 0 0 0 0 0 ...
$ phenoCovars: NULL
$ info :List of 2
  ..$ map.unit: chr "Mb"
  ..$ codeGeno: logi FALSE
 - attr(*, "class")= chr "gpData"
```



Synbreed – Genomik Seleksiyon

Uygulama Popülasyonu (Veriseti) Training – Referance Population

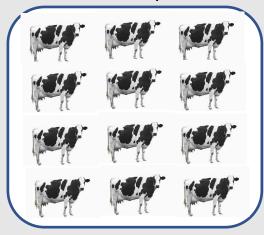


Veriseti

- Özellikler:
 - Fenotipik değerler (Süt veya et verimi, canlı ağırlık)
- Kovaryet:
 - Sabit veya şansa bağlı faktör (Sürü, Yıl, Mevsim, Laktasyon sırası vb)
- Pedigri:
 - Soy kütüğü (baba, ana ve doğum yılı kayıtları)
- Genotip:
 - SNP markır verileri (700 K, 50 K veya 3 K)
- SNP markır harita kayıtları

Model: GBLUP, BayesA, B, C veya LASSO

SNP markır etkileri tahmin edilir Seleksiyon Uygulanacak Adaylar (Veriseti)
Validation Population



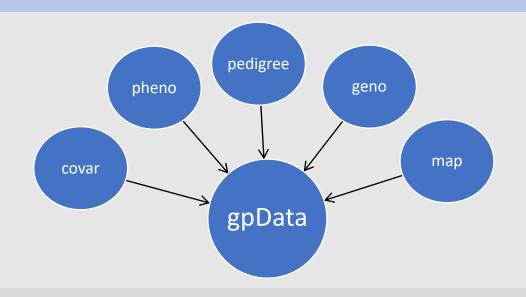
Veriseti

- Genotip:
 - SNP markir verileri (700 K, 50 K veya 3 K)

Adayların genomik damızlık değer tahmininde ve buna bağlı olarak seçiminde kullanılır



Synbreed -gpData Veri Yapısının Oluşturulması



gpData:

covar, phone, pedigree, geno, map nesnelerinin birey ID'lerine ve SNP markır ID'lerine göre birleştirilmesiyle oluşturulur



covar:

Veri analizinde yer alacak kesikli-sürekli kovaryet değişkenlere ait değerleri içerir

phone:

Analiz edilecek değişkenlere (özelliklere) ait değerleri içerir

• pedigree:

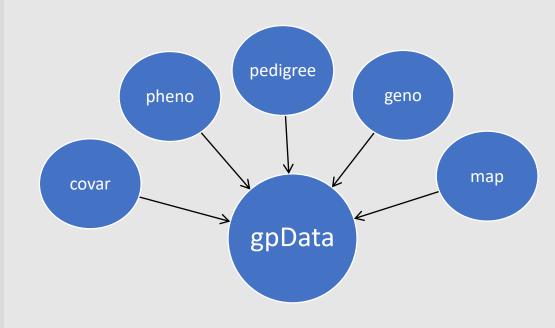
Analizde yer alan bireylerin pedigri (soy kütüğü) kayıtlarını içerir

• geno:

Analizde yer alacak SNP markır değerlerini içerir

• map:

Analizde yer alacak SNP markırları haritalamak için gerekli değerleri içerir





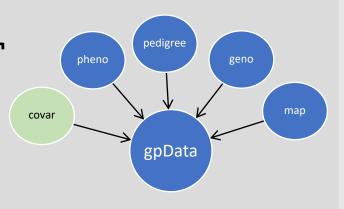
Sığır (cattle) Veri Seti covar – data.frame

Kesikli-Sürekli Kovaryet Değişkenler

Analizde yer alacak kovaryet değişkenler mevcut ise data.frame veri yapısında R'a yüklenir.

Kovaryet değişkenler yüklenirken hayvan numaraları rownames olarak aktarılmalıdır.

Sığır veri setinde kovaryet değişkenler yoktur





Sığır Veri Seti pheno – data.frame

```
Fenotipik Değerler – Özelliklere Ait Gözlem Değerleri
```

```
Dosya adı: cattle_pheno.txt
```

Sütun-1: Hayvanların numarası, ID

Sütun-2: Özellik 1 için gözlem değerleri, Trait1

Sütun-3: Özellik 2 için gözlem değerleri, Trait2

ID Trait1 Trait2

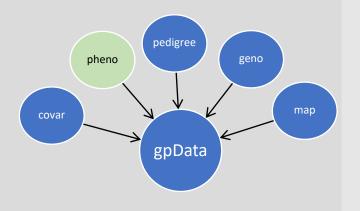
ID11430 -23.43 263.9

ID11431 15.48 182.22

ID11432 -19.18 6.64

ID11433 -10.43 42.55

ID11434 -14.07 326.41





ID11433 -10.43 42.55

ID11434 -14.07 326.41

ID11435 -6.62 -34.01

Sığır Veri Seti pheno – data.frame

```
# Fenotipik degerler - Ozelliklere ait degerler
pheno = read.table(file = "cattle_pheno.txt", header = TRUE, row.names = 1)
str(pheno)
'data.frame': 500 obs. of 2 variables:
 $ Trait1: num -23.4 15.5 -19.2 -10.4 -14.1 ...
 $ Trait2: num 263.9 182.22 6.64 42.55 326.41 ...
head(pheno)
        Trait1 Trait2
ID11430 -23.43 263.90
ID11431 15.48 182.22
                                                                gpData
ID11432 -19.18 6.64
```



ID10004

Sığır Veri Seti pedigree – data.frame

```
# Pedigri degerleri
pedigree = read.table(file = "cattle_pedigree.txt", header = TRUE)
str(pedigree)
'data.frame': 1929 obs. of 4 variables:
  ID : chr "ID10001" "ID10002" "ID10003" "ID10004" ...
              "0" "0" "0" "0"
 $ Par1 : chr
              "0" "0" "0" "0"
 $ Par2 : chr
              0000000000...
 $ gener: int
                                                             pedigree
head(pedigree)
      ID Par1 Par2 gener
 ID10001
                                                             gpData
 ID10002 0 0
 ID10003
```



Sığır Veri Seti pedigree – data.frame - create.pedigree

```
create.pedigree(ID, Par1, Par2, gener=NULL,sex=NULL,add.ancestors=FALSE,unknown=0)
# create.pedigree() fonksiyonu ile pedigri formatını olustur
  ped = create.pedigree(pedigree$ID, pedigree$Par1, pedigree$Par2, pedigree$gener)
  str(ped)
                                                                          ped
Classes 'pedigree' and 'data.frame': 1929 obs. of 4 variables:
        : chr "ID10001" "ID10002" "ID10003" "ID10004" ...
                                                                          create.pedigree()
$ Par1 : chr "0" "0" "0" "0"
$ Par2 : chr "0" "0" "0" "0"
                                                                       pedigree
$ gener: int 0000000000...
                                                                       gpData
```



Sığır Veri Seti pedigree – data.frame - create.pedigree

summary(ped)

\$nID

[1] 1929

\$nPar1

[1] 376

\$nPar2

[1] 1053

\$nGener

[1] 6

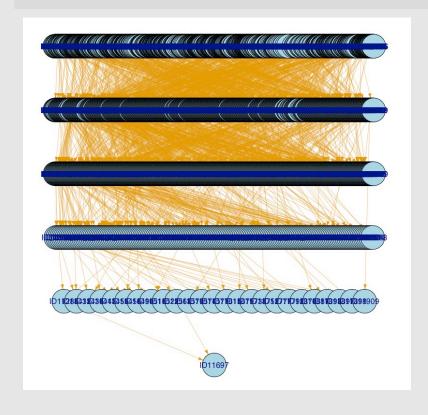
\$nUnknownParents

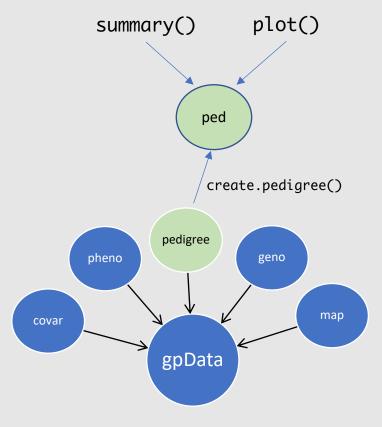
[1] 1512

attr(,"class")

[1] "summary.pedigree"

plot(ped)





Sığır Veri Seti geno – matrix

SNP markir degerleri

```
Dosya adı: cattle_geno012.txt
```

Sütun-1: Hayvanların numarası, ID

Sütun-2: SNP 1 için gözlem değerleri, SNP_1 Sütun-3: SNP 2 için gözlem değerleri, SNP_2

٠

Sütun-7250: SNP 7250 için gözlem değerleri, SNP_7250

pedigree geno geno map

ID	SNP_1	SNP_2	SNP_3	SNP_4	SNP_5
ID11430	1	2	0	2	0
ID11431	2	1	0	0	0
ID11432	2	2	0	2	0
ID11433	2	1	0	1	0
ID11434	2	2	0	2	1

R

Sığır Veri Seti geno – matrix

```
# SNP markir degerleri
geno = read.table(file = "cattle_geno012.txt", header = TRUE, row.names = 1)
geno = as.matrix(geno)
str(geno)
 int [1:500, 1:7250] 1 2 2 2 2 2 2 2 2 2 ...
 - attr(*, "dimnames")=List of 2
  ..$ : chr [1:500] "ID11430" "ID11431" "ID11432" "ID11433" ...
  ..$ : chr [1:7250] "SNP_1" "SNP_2" "SNP_3" "SNP_4" ...
                                                                              gpData
geno[1:5,1:10]
        SNP_1 SNP_2 SNP_3 SNP_4 SNP_5 SNP_6 SNP_7 SNP_8 SNP_9 SNP_10
ID11430
ID11431
ID11432
ID11433
ID11434
```

Sığır mar

Sığır Veri Seti map – data.frame

```
SNP markir haritasi
```

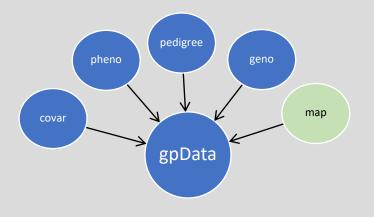
```
Dosya ad1: cattle_map.txt
```

Sütun-1: SNP markır numarası, SNP_ID

Sütun-2: Kromozom numarası, chr

Sütun-3: SNP markırın kromozom üzerindeki yeri, pos

```
SNP_ID chr pos
SNP_1 1 1e-06
SNP_2 1 0.20258
SNP_3 1 0.279809
SNP_4 1 0.668932
SNP_5 1 0.763913
```



R

SNP_3 1 0.279809

SNP_4 1 0.668932

SNP_5 1 0.763913

SNP_6 1 0.828652

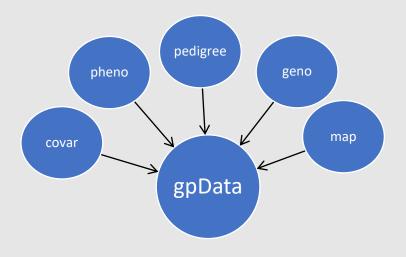
Sığır Veri Seti map – data.frame

```
# Map degerleri
map = read.table(file = "cattle_map.txt", header = TRUE, row.names = 1)
str(map)
'data.frame': 7250 obs. of 2 variables:
 $ chr: int 1 1 1 1 1 1 1 1 1 ...
 $ pos: num 0.000001 0.20258 0.279809 0.668932 0.763913 ...
head(map)
                                                                   geno
      chr
              pos
SNP_1 1 0.000001
SNP_2 1 0.202580
```

gpData

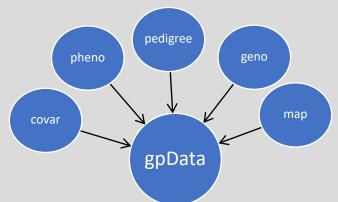


gpData olustur
gpData <- create.gpData(pheno=pheno, geno=geno,
map=map, pedigree=ped)</pre>



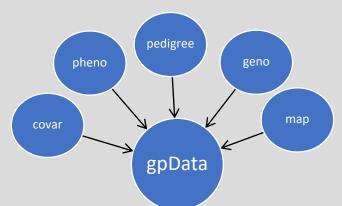


```
# apData olustur
  gpData <- create.gpData(pheno = pheno, geno = geno, map = map, pedigree = ped)</pre>
  str(gpData)
List of 7
             :'data.frame': 1929 obs. of 4 variables:
 $ covar
  ..$ id
          : chr [1:1929] "ID10001" "ID10002" "ID10003" "ID10004" ...
  ... phenotyped: logi [1:1929] FALSE FALSE FALSE FALSE FALSE ...
  ... genotyped : logi [1:1929] FALSE FALSE FALSE FALSE FALSE ...
  ...$ family : logi [1:1929] NA NA NA NA NA NA ...
 $ pheno : num [1:500, 1:2, 1] -23.4 15.5 -19.2 -10.4 -14.1 ...
  ..- attr(*, "dimnames")=List of 3
  ....$ : chr [1:500] "ID11430" "ID11431" "ID11432" "ID11433" ...
  .. ..$ : chr [1:2] "Trait1" "Trait2"
  ....$ : chr "1"
       : int [1:500, 1:7250] 1 2 2 2 2 2 2 2 2 2 ...
 $ geno
  ..- attr(*, "dimnames")=List of 2
  ....$ : chr [1:500] "ID11430" "ID11431" "ID11432" "ID11433" ...
  ....$ : chr [1:7250] "SNP_1" "SNP_2" "SNP_3" "SNP_4" ...
             :Classes 'GenMap' and 'data.frame': 7250 obs. of 2 variables:
 $ map
  ..$ chr: int [1:7250] 1 1 1 1 1 1 1 1 1 1 ...
  ...$ pos: num [1:7250] 0.000001 0.20258 0.279809 0.668932 0.763913 ...
 $ pedigree :Classes 'pedigree' and 'data.frame': 1929 obs. of 4 variables:
  ..$ ID : chr [1:1929] "ID10001" "ID10002" "ID10003" "ID10004" ...
  ..$ Par1 : chr [1:1929] "0" "0" "0" "0"
  ..$ Par2 : chr [1:1929] "0" "0" "0" "0"
  ..$ gener: int [1:1929] 0 0 0 0 0 0 0 0 0 ...
 $ phenoCovars: NULL
 $ info
             :List of 4
  ..$ map.unit: chr "cM"
  ..$ codeGeno: logi FALSE
  ..$ version : chr "apData object was created by symbreed version 0.12-14"
  ...$ Call : language create.gpData(pheno = pheno, geno = geno, map = map, pedigree = ped)
 - attr(*, "class")= chr "apData"
```





```
# apData olustur
  gpData <- create.gpData(pheno = pheno, geno = geno, map = map, pedigree = ped)</pre>
  str(gpData)
List of 7
             :'data.frame': 1929 obs. of 4 variables:
 $ covar
  ..$ id
          : chr [1:1929] "ID10001" "ID10002" "ID10003" "ID10004" ...
  ... phenotyped: logi [1:1929] FALSE FALSE FALSE FALSE FALSE ...
  ... genotyped : logi [1:1929] FALSE FALSE FALSE FALSE FALSE ...
  ...$ family : logi [1:1929] NA NA NA NA NA NA ...
 $ pheno : num [1:500, 1:2, 1] -23.4 15.5 -19.2 -10.4 -14.1 ...
  ..- attr(*, "dimnames")=List of 3
  ....$ : chr [1:500] "ID11430" "ID11431" "ID11432" "ID11433" ...
  .. ..$ : chr [1:2] "Trait1" "Trait2"
  ....$ : chr "1"
       : int [1:500, 1:7250] 1 2 2 2 2 2 2 2 2 2 ...
 $ geno
  ..- attr(*, "dimnames")=List of 2
  ....$ : chr [1:500] "ID11430" "ID11431" "ID11432" "ID11433" ...
  ....$ : chr [1:7250] "SNP_1" "SNP_2" "SNP_3" "SNP_4" ...
             :Classes 'GenMap' and 'data.frame': 7250 obs. of 2 variables:
 $ map
  ..$ chr: int [1:7250] 1 1 1 1 1 1 1 1 1 1 ...
  ...$ pos: num [1:7250] 0.000001 0.20258 0.279809 0.668932 0.763913 ...
 $ pedigree :Classes 'pedigree' and 'data.frame': 1929 obs. of 4 variables:
  ..$ ID : chr [1:1929] "ID10001" "ID10002" "ID10003" "ID10004" ...
  ..$ Par1 : chr [1:1929] "0" "0" "0" "0"
  ..$ Par2 : chr [1:1929] "0" "0" "0" "0"
  ..$ gener: int [1:1929] 0 0 0 0 0 0 0 0 0 0 ...
 $ pbenoCovars: NULL
 $/info
              :List of 4
  .$ map.unit: chr "cM"
  ... codeGeno: logi FALSE
  ..$ version : chr "apData object was created by symbreed version 0.12-14"
  ...$ Call : language create.gpData(pheno = pheno, geno = geno, map = map, pedigree = ped)
 - attr(*, "class")= chr "apData"
```



Map birimi olarak "Mb" tanımla

gpData\$info\$map.unit <- "Mb"</pre>

- attr(*, "class")= chr "gpData"

..\$ Call : language create.gpData(pheno = pheno, geno = geno, map = map, pedigree = ped)



Sığır Veri Seti - gpData - list summary(gpData)

```
# gpData icin Ozet bilgiler
summary(gpData)
$covar
```

\$covar\$n

[1] 1929

\$covar\$nphenotyped

[1] 500

\$covar\$ngenotyped

[1] 500

\$pheno

Trait1 Trait2

Min. :-50.07000 Min. :-424.43

1st Qu.:-10.25750 1st Qu.: -94.40

Median : 0.13500 Median : -0.84

Mean : -0.00104 Mean : 0.05

3rd Qu.: 10.35250 3rd Qu.: 96.99

Max. : 49.41000 Max. : 422.63



summary(gpData)

```
$geno
```

\$geno\$nMarkers

[1] 7250

\$geno\$genotypes

geno

0 1

0.2889283 0.3483592 0.3627126

\$geno\$nNA

[1] 0

\$geno\$markerChr

1 2 3 4 5 6 7 8 9 10 11 12 13 14 15 16 17 18 19 20 21

22 23 24 25 26 27 28 29

250 250 250 250 250 250 250

\$geno\$mappedMarkers

[1] 7250



Sığır Veri Seti - gpData – list summary(gpData)

```
$pedigree
$nID
[1] 1929
$nPar1
[1] 376
$nPar2
[1] 1053
$nGener
[1] 6
$nUnknownParents
[1] 1512
```

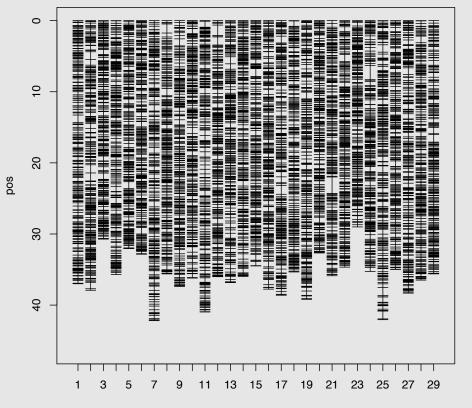
```
$nUnknownParents
[1] 1512
attr(,"class")
[1] "summary.pedigree"
attr(,"class")
[1] "summary.gpData"
```



SNP Markır Haritası

plotGenMap(gpData\$map) # plot ekranda oluşturulur

plotGenMap(gpData\$map, file="CattleMap1") # plot dosyaya kaydedilir

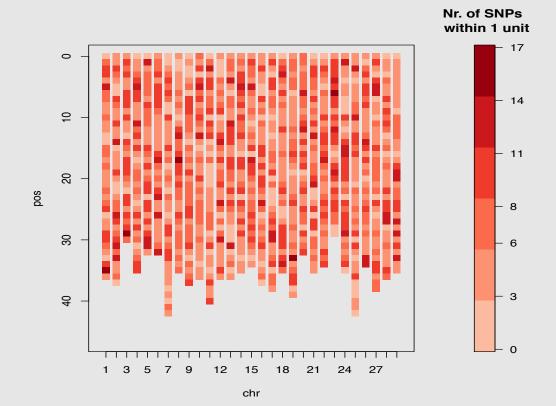




SNP Markır Haritası

```
# plot ekranda oluşturulur
plotGenMap(gpData$map, dense=TRUE, nMarker=FALSE)

# plot dosyaya kaydedilir
plotGenMap(gpData$map, dense=TRUE, nMarker=FALSE, file="CattleMap2")
```





SNP Markır – Kodlama - Eksik Markır Tahmini (Imputation) - Markır Ayıklama

```
codeGeno(apData,
         impute=FALSE,
         impute.type=c("random","family","beagle","beagleAfterFamily","beagleNoRand",
                       "beagleAfterFamilyNoRand", "fix"),
         replace.value=NULL,
         maf=NULL,
         nmiss=NULL,
         label.heter="alleleCoding",
         reference.allele="minor",
         keep.list=NULL.
         keep.identical=TRUE,
         verbose=FALSE,
         minFam=5,
         showBeagleOutput=FALSE,
         tester=NULL,
         print.report=FALSE,
         check=FALSE,
         ploidy=2,
         cores=1)
```



SNP Markır – Kodlama - Eksik Markır Tahmini (Imputation) - Markır Ayıklama (Sığır SNP markır)

```
# SNP kodlama, impute ve kalite kontrol
  gpCode <- codeGeno(gpData, label.heter="1", impute=TRUE, impute.type="random",</pre>
                     verbose=TRUE)
   step 1 : No markers removed due to fraction of missing values
   step 2 : Recoding alleles
   step 4 : No markers discarded due to minor allele frequency
   step 7 : Imputing of missing values
   step 7d : Random imputing of missing values
   step 8 : No recoding of alleles necessary after imputation
   step 9 : No markers discarded due to minor allele frequency
   step 10 : No duplicated markers removed
           : 7250 marker(s) remain after the check
   End
```

Summary of imputation total number of missing values : 0 number of random imputations : 0



$$r^2 = \frac{D_{AB}^2}{p_A p_B p_a p_b}$$

$$D_{AB} = p_{AB} - p_A p_B$$

 p_{AB} : AB halotipin frekansı

 $p_A = 1 - p_a$: bir lokustaki A alelin frekansı

 $p_B = 1 - p_b$: diğer lokustaki B alelin frekansı



```
# Kromozom-1 için LD hesaplama
chr1 <- pairwiseLD(gpCode, chr=1, type="data.frame")</pre>
> str(chr1)
List of 1
 $ chr_1:'data.frame': 31125 obs. of 5 variables:
  ..$ marker1: chr [1:31125] "SNP_1" "SNP_1" "SNP_1" "SNP_1" ...
  ..$ marker2: chr [1:31125] "SNP_2" "SNP_3" "SNP_4" "SNP_5" ...
  ..$ r : num [1:31125] -0.08286 0.19335 0.00712 -0.12762 -0.42093 ...
  ..$ r2 : num [1:31125] 6.87e-03 3.74e-02 5.07e-05 1.63e-02 1.77e-01 ...
  ..$ dist : num [1:31125] 0.203 0.28 0.669 0.764 0.829 ...
 - attr(*, "class")= chr "LDdf"
> chr1
$chr 1
   marker1 marker2
                                          r2 dist
     SNP_1 SNP_2 -0.0828573035 6.865333e-03 0.202579
2
3
4
5
     SNP_1 SNP_3 0.1933493688 3.738398e-02
                                             0.279808
     SNP_1
            SNP_4
                    0.0071181940 5.066869e-05 0.668931
     SNP 1
            SNP_5 -0.1276181342 1.628639e-02 0.763912
     SNP 1 SNP 6 -0.4209317562 1.771835e-01 0.828651
```



```
# Kromozom-1 için LD hesaplama
chr1mat <- pairwiseLD(gpCode, chr=1, type="matrix")</pre>
```

```
> str(chr1mat)
List of 3
$ LD :List of 1
  ..$ chr_1: num [1:250, 1:250] 1.00 6.87e-03 3.74e-02 5.07e-05 1.63e-02 ...
  ....- attr(*, "dimnames")=List of 2
  ....$ : chr [1:250] "SNP_1" "SNP_2" "SNP_3" "SNP_4" ...
 ....$ : chr [1:250] "SNP_1" "SNP_2" "SNP_3" "SNP_4" ...
$ distance:List of 1
  ..$ chr_1: num [1:250, 1:250] 0 0.203 0.28 0.669 0.764 ...
  ....- attr(*, "dimnames")=List of 2
  ....$ : chr [1:250] "SNP_1" "SNP_2" "SNP_3" "SNP_4" ...
  ....$ : chr [1:250] "SNP_1" "SNP_2" "SNP_3" "SNP_4" ...
$ LDcor :List of 1
  ...: num [1:250, 1:250] 1 -0.08286 0.19335 0.00712 -0.12762 ...
  ... ..- attr(*, "dimnames")=List of 2
  ....$ : chr [1:250] "SNP_1" "SNP_2" "SNP_3" "SNP_4" ...
  ....$ : chr [1:250] "SNP_1" "SNP_2" "SNP_3" "SNP_4" ...
 - attr(*, "class")= chr "LDmat"
```



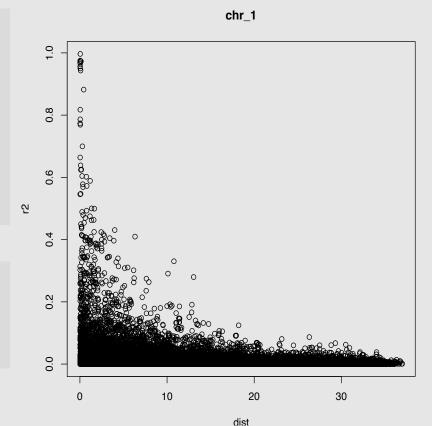
```
# Kromozom-1 için LD değerlerinin SNP markırlar arası mesafeye göre dağılımı
# plot.LDdf
```

plot(chr1, gpCode, plotType="dist", chr=1, file="Chr1_LD", fileFormat="pdf")

```
> chr1
$chr 1
   marker1 marker2
                                           r2
                                                dist
     SNP 1
             SNP_2 -0.0828573035 6.865333e-03
                                              0.202579
2
3
4
     SNP_1 SNP_3 0.1933493688 3.738398e-02
                                              0.279808
     SNP_1
            SNP_4
                    0.0071181940 5.066869e-05
                                              0.668931
            SNP_5 -0.1276181342 1.628639e-02
     SNP_1
                                              0.763912
     SNP_1
             SNP_6 -0.4209317562 1.771835e-01
                                              0.828651
```

> summary(chr1)

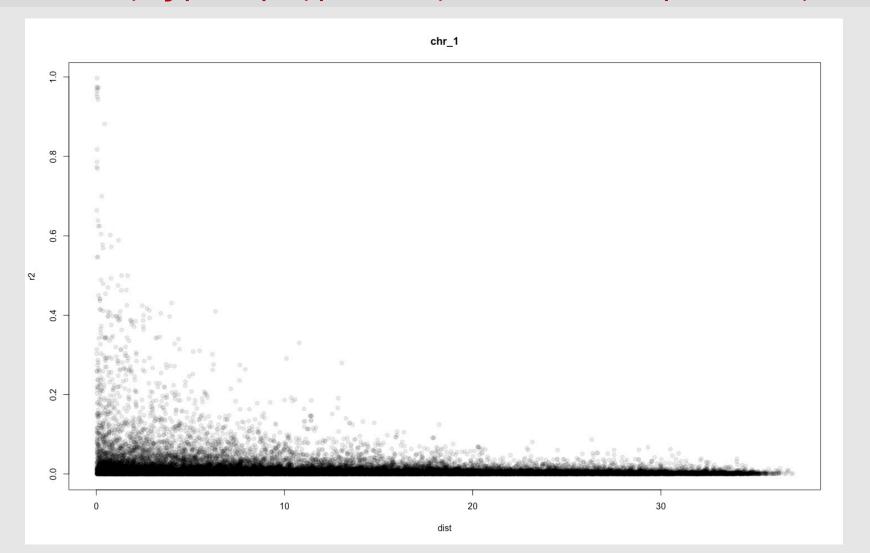
noM avgr2 minr2 maxr2 Pr02 averDist maxDist chr_1 250 0.0124188 0 0.9967143 0.007453815 0.0124188 36.99836





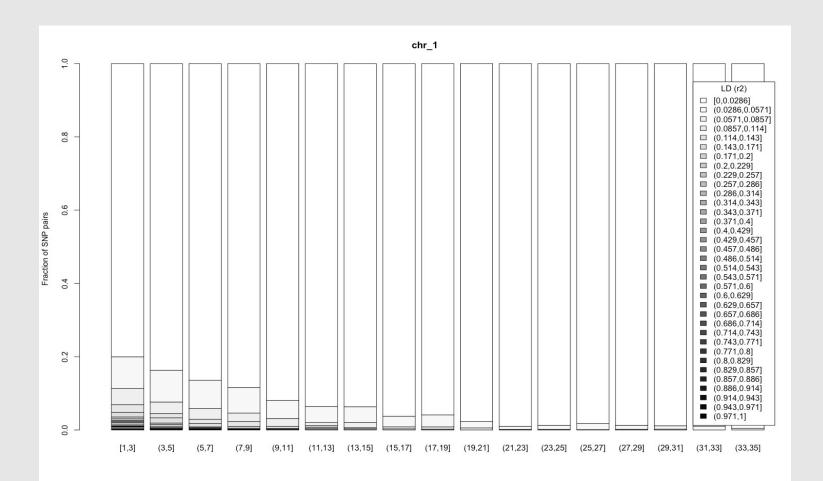
Bağlantı Dengesizliği - Linkage Disequilibrium (LD)

LDDist(chr1, type="p", pch=19, colD=hsv(alpha=0.1, v=0))





Bağlantı Dengesizliği - Linkage Disequilibrium (LD)





Akrabalık İlişkisi – Pedigri - SNP Markır

```
kin(gpCode,
    ret=c("add",
          "kin",
                    Pedigriye göre akrabalık
          "dom",
          "gam",
          "realized",
          "realizedAB"
                           SNP markırlara göre akrabalık
          "sm",
          "sm-smin",
          "gaussian"),
     DH=NULL,
     maf=NULL,
     selfing=NULL,
     lambda=1,
     P=NULL,
     cores=1)
```



Akrabalık İlişkisi – Pedigri - SNP Markır

```
Pedigriye göre akrabalığın hesaplanmasında Pedigri Kayıtlarının bilinmesini gerektirir ret=c("add"): Ekleme genlerden ileri gelen akrabalık (A matrisi) ret=c("kin"): Ekleme genlerden ileri gelen akrabalığın yarısı ret=c("dom"): Dominans ilişkiye göre akrabalık ret=c("gam"): Gametik ilişkiye göre akrabalık
```

Akrabalık İlişkisi – Pedigri (A Matrisi)

ret=c("add"): Ekleme genlerden ileri gelen akrabalık (A matrisi)

```
A <- kin(gpCode, ret="add")
str(A)
 'relationshipMatrix' num [1:1929, 1:1929] 1 0 0 0 0 0 0 0 0
 - attr(*, "dimnames")=List of 2
  ..$ : chr [1:1929] "ID10001" "ID10002" "ID10003" "ID10004" ...
  ..$ : chr [1:1929] "ID10001" "ID10002" "ID10003" "ID10004" ...
 - attr(*, "info")= chr "This relationshipMatrix was calculated
by synbreed version 0.12-14"
 - attr(*, "type")= chr "add"
```



Akrabalık İlişkisi – Pedigri (A Matrisi)

```
summary(A)
$dim
nrow ncol
1929 1929
$rank
[1] 1929
$range.off.diagonal
  min
        max
0.000 0.625
$mean.diag
[1] 1.000194
```

```
$mean.off.diag
[1] 0.002926408
$diag.val
  Min. 1st Qu. Median Mean 3rd Qu.
                                        Max.
 1.000 1.000 1.000
                        1.000 1.000
                                       1.125
$empty
[1] 0
attr(,"class")
[1] "summary.relationshipMatrix"
```



Akrabalık İlişkisi – SNP Markır (*G*)

```
SNP markırlara göre akrabalık
```

ret=c("realized"), Habier et al. (2007) veya vanRaden (2008)'e göre genomik akrabalık matrisini (G) oluşturu.

$$G = \frac{ZZ'}{2\sum p_i(1-p_i)} = \frac{(W-P)(W-P)'}{2\sum p_i(1-p_i)}$$

W: SNP markır değerlerini içeren matris,

P: 2 ile çarpılmış allel frekans değerlerini içeren matris

 p_i : SNP markir i nin allel frekansi

Akrabalık İlişkisi – SNP Markır (G)

ret=c("realized) SNP markirlara göre akrabalik

```
# SNP markırlara göre Akrabalık (G) Matrisini olustur
  G <- kin(gpCode, ret="realized")</pre>
  str(G)
 'relationshipMatrix' num [1:500, 1:500] 24.345 4.546 0.857 0.388 -1.234 ...
 - attr(*, "dimnames")=List of 2
  ..$ : chr [1:500] "ID11430" "ID11431" "ID11432" "ID11433" ...
  ..$ : chr [1:500] "ID11430" "ID11431" "ID11432" "ID11433" ...
 - attr(*, "alleleFrequencies")= Named num [1:7250] 0.132 0.376 -0.986 0.934 -0.584 0.88
0.866 -0.602 0.9 0.008 ...
  ..- attr(*, "names")= chr [1:7250] "SNP_1" "SNP_2" "SNP_3" "SNP_4" ...
 - attr(*, "expectedMAX")= num 168
 - attr(*, "SNPs")= chr [1:7250] "SNP_1" "SNP_2" "SNP_3" "SNP_4" ...
 - attr(*, "info")= chr "This relationshipMatrix was calculated by synbreed version 0.12-14"
 - attr(*, "type")= chr "realized"
```



Akrabalık İlişkisi – SNP Markır (G)

ret=c("realized) SNP markirlara göre akrabalik

```
$mean.off.diag
summary(G)
$dim
                                           [1] -0.04067172
nrow ncol
                                           $diag.val
 500 500
                                              Min. 1st Qu. Median Mean 3rd Qu.
                                                                                     Max.
$rank
                                             17.41 19.91 20.23
                                                                    20.30 20.60
                                                                                    24.35
Γ1 | 499
                                           $empty
$range.off.diagonal
                                           [1] 0
     min
               max
-1.980661 7.483978
                                           attr(,"class")
                                           [1] "summary.relationshipMatrix"
$mean.diag
[1] 20.29519
```



Tahmin Modeli

Pedigri-BLUP (PBLUP)

$y = X\beta + Za + e$

y: gözlem değerleri vektörü

β: sabit etkiler vektörü

a: şans balığı etkiler (damızlık değer)

vektörü $a \sim N(\mathbf{0}, A\sigma_a^2)$

A: eklemeli akrabalık matrisi

 σ_a^2 : eklemeli genetik varyans

e: şansa bağlı hata vektörü $e \sim N(\mathbf{0}, I\sigma_e^2)$

I: Birim matrisi

 σ_e^2 : hata varyansı

X: sabit etkilere ait desen matrisi

z: şansa bağlı etkilere ait desen matrisi

Genomik-BLUP (GBLUP)

$$y = X\beta + Zu + e$$

y: gözlem değerleri vektörü

β: sabit etkiler vektörü

u: şans balığı etkiler (genomik damızlık değer)

vektörü $\boldsymbol{u} \sim N(\boldsymbol{0}, \boldsymbol{U}\sigma_u^2)$

U: genomik akrabalık matrisi

 σ_u^2 : genomik varyans

e: şansa bağlı hata vektörü $e \sim N(\mathbf{0}, I\sigma_e^2)$

I: Birim matrisi

 σ_e^2 : hata varyansı

X: sabit etkilere ait desen matrisi

z: şansa bağlı etkilere ait desen matrisi



Tahmin Modeli

Pedigri-BLUP (PBLUP)

$$y = X\beta + Z\alpha + e$$

$$E\begin{bmatrix} \boldsymbol{a} \\ \boldsymbol{e} \end{bmatrix} = \begin{bmatrix} 0 \\ 0 \end{bmatrix}$$
$$Var\begin{bmatrix} \boldsymbol{a} \\ \boldsymbol{e} \end{bmatrix} = \begin{bmatrix} \boldsymbol{G} & \mathbf{0} \\ \mathbf{0} & \boldsymbol{R} \end{bmatrix} = \begin{bmatrix} \boldsymbol{A}\sigma_a^2 & \mathbf{0} \\ \mathbf{0} & \boldsymbol{I}\sigma_e^2 \end{bmatrix}$$

$$E[y] = X\beta$$
$$Var[y] = V = ZGZ' + R$$

Karışık Model Eşitlikleri
$$\begin{bmatrix} \widehat{\boldsymbol{\beta}} \\ \widehat{\boldsymbol{a}} \end{bmatrix} = \begin{bmatrix} X'R^{-1}X & X'R^{-1}Z \\ Z'R^{-1}X & Z'R^{-1}Z + G^{-1} \end{bmatrix}^{-} \begin{bmatrix} X'R^{-1}y \\ Z'R^{-1}y \end{bmatrix}$$

Genomik-BLUP (GBLUP)

$$y = X\beta + Zu + e$$

$$E\begin{bmatrix} \mathbf{u} \\ \mathbf{e} \end{bmatrix} = \begin{bmatrix} \mathbf{0} \\ \mathbf{0} \end{bmatrix}$$
$$Var\begin{bmatrix} \mathbf{u} \\ \mathbf{e} \end{bmatrix} = \begin{bmatrix} \mathbf{G} & \mathbf{0} \\ \mathbf{0} & R \end{bmatrix} = \begin{bmatrix} \mathbf{U}\sigma_a^2 & \mathbf{0} \\ \mathbf{0} & I\sigma_e^2 \end{bmatrix}$$

$$E[y] = X\beta$$
$$Var[y] = V = ZGZ' + R$$

Karışık Model Eşitlikleri
$$\begin{bmatrix} \widehat{\boldsymbol{\beta}} \\ \widehat{\boldsymbol{u}} \end{bmatrix} = \begin{bmatrix} X'R^{-1}X & X'R^{-1}Z \\ Z'R^{-1}X & Z'R^{-1}Z + G^{-1} \end{bmatrix}^{-} \begin{bmatrix} X'R^{-1}y \\ Z'R^{-1}y \end{bmatrix}$$



$$y = X\beta + Z\alpha + e$$

$$\begin{bmatrix} \widehat{\boldsymbol{\beta}} \\ \widehat{\boldsymbol{a}} \end{bmatrix} = \begin{bmatrix} X'R^{-1}X & X'R^{-1}Z \\ Z'R^{-1}X & Z'R^{-1}Z + G^{-1} \end{bmatrix}^{-} \begin{bmatrix} X'R^{-1}y \\ Z'R^{-1}y \end{bmatrix}$$

PBLUP_Trait1 <- gpMod(gpCode, model="BLUP", kin=A, trait="Trait1")</pre>

summary(PBLUP_Trait1)

	Length	Class	Mode
fit	24	regress	list
model	1	-none-	character
у	500	-none-	numeric ⇒ Gözlem değerleri vektörü
g	500	-none-	numeric \Rightarrow Damızlık değer tahminleri (\hat{a})
prediction	0	-none-	NULL
markerEffects	0	-none-	NULL
kin	3721041	relationshipMatrix	numeric



$$y = X\beta + Z\alpha + e$$

$$\begin{bmatrix} \widehat{\boldsymbol{\beta}} \\ \widehat{\boldsymbol{a}} \end{bmatrix} = \begin{bmatrix} \boldsymbol{X}'\boldsymbol{R}^{-1}\boldsymbol{X} & \boldsymbol{X}'\boldsymbol{R}^{-1}\boldsymbol{Z} \\ \boldsymbol{Z}'\boldsymbol{R}^{-1}\boldsymbol{X} & \boldsymbol{Z}'\boldsymbol{R}^{-1}\boldsymbol{Z} + \boldsymbol{G}^{-1} \end{bmatrix}^{-} \begin{bmatrix} \boldsymbol{X}'\boldsymbol{R}^{-1}\boldsymbol{y} \\ \boldsymbol{Z}'\boldsymbol{R}^{-1}\boldsymbol{y} \end{bmatrix} = \begin{bmatrix} \boldsymbol{X}'(\boldsymbol{I}\sigma_{e}^{2})^{-1}\boldsymbol{X} & \boldsymbol{X}'(\boldsymbol{I}\sigma_{e}^{2})^{-1}\boldsymbol{Z} \\ \boldsymbol{Z}'(\boldsymbol{I}\sigma_{e}^{2})^{-1}\boldsymbol{X} & \boldsymbol{Z}'(\boldsymbol{I}\sigma_{e}^{2})^{-1}\boldsymbol{Z} + (\boldsymbol{A}\sigma_{a}^{2})^{-1} \end{bmatrix}^{-} \begin{bmatrix} \boldsymbol{X}'\boldsymbol{R}^{-1}\boldsymbol{y} \\ \boldsymbol{Z}'\boldsymbol{R}^{-1}\boldsymbol{y} \end{bmatrix}$$

PBLUP_Trait1 <- gpMod(gpCode, model="BLUP", kin=A, trait="Trait1")</pre>

summary(PBLUP_Trait1\$fit)

Likelihood kernel: K = (Intercept)

Maximized log likelihood with kernel K is -1613.348

Linear Coefficients:

Estimate Std. Error

(Intercept) 0.526 1.009

Variance Coefficients:

Estimate Std. Error

kinTS 99.552 40.605

In 142.800 37.399

 $\hat{\sigma}_a^2 = 99.552$ $\hat{\sigma}_e^2 = 142.800$

$$h^2 = \frac{\sigma_a^2}{\sigma_a^2 + \sigma_e^2} = \frac{99.552}{99.552 + 142.800} = 0.41$$



$$y = X\beta + Z\alpha + e$$

$$\begin{bmatrix} \widehat{\boldsymbol{\beta}} \\ \widehat{\boldsymbol{a}} \end{bmatrix} = \begin{bmatrix} X'R^{-1}X & X'R^{-1}Z \\ Z'R^{-1}X & Z'R^{-1}Z + G^{-1} \end{bmatrix}^{-} \begin{bmatrix} X'R^{-1}y \\ Z'R^{-1}y \end{bmatrix}$$

PBLUP_Trait1 <- gpMod(gpCode, model="BLUP", kin=A, trait="Trait1")
summary(PBLUP_Trait1)</pre>

Length Class Mode fit 24 regress list

model 1 -none- character

y 500 -none- numeric ⇒ Gözlem değerleri vektörü

g 500 -none- numeric \Rightarrow Damızlıkdeğere tahminleri (\hat{a})

Korelasyon $r(y, \hat{a}) = 0.9560781$

> cor(PBLUP_Trait1\$y, PBLUP_Trait1\$g)

[1] 0.9560781



```
y = X\beta + Z\alpha + e
     PBLUP_Trait1 <- gpMod(gpCode, model="BLUP", kin=A, trait="Trait1")</pre>
> data.frame(PBLUP_Trait1$y, PBLUP_Trait1$g)
        PBLUP_Trait1.y PBLUP_Trait1.g
ID11430
                -23.43 -11.774060986
ID11431
                15.48 0.264133336
                -19.18 -6.861402741
ID11432
               -10.43 -4.943506739
ID11433
ID11434
                -14.07 -3.295750040
Korelasyon r(y, \hat{a}) = 0.9560781
> cor(PBLUP_Trait1$y, PBLUP_Trait1$g)
[1] 0.9560781
```



```
y = X\beta + Zu + e
                                   \begin{bmatrix} \widehat{\boldsymbol{\beta}} \\ \widehat{\boldsymbol{\imath}} \end{bmatrix} = \begin{bmatrix} X'R^{-1}X & X'R^{-1}Z \\ Z'R^{-1}X & Z'R^{-1}Z + G^{-1} \end{bmatrix}^{-1} \begin{bmatrix} X'R^{-1}y \\ Z'R^{-1}y \end{bmatrix}
       GBLUP_Trait1 <- gpMod(gpCode, model="BLUP", kin=G, trait="Trait1")</pre>
  summary(GBLUP_Trait1)
                    Length Class
                                               Mode
fit
                           24 regress
                                             list
model
                            1 -none- character
                                               numeric ⇒ Gözlem değerleri vektörü
y
                         500 -none-
                         500 -none-
                                               numeric \Rightarrow Genomik damızlık değere tahminleri (\hat{u})
g
prediction 0 -none-
                                               NULL
markerEffects 0 -none-
                                               NULL
kin
                    250000 relationshipMatrix numeric
```



$$y = X\beta + Zu + e$$

$$\begin{bmatrix} \widehat{\beta} \\ \widehat{u} \end{bmatrix} = \begin{bmatrix} X'R^{-1}X & X'R^{-1}Z \\ Z'R^{-1}X & Z'R^{-1}Z + G^{-1} \end{bmatrix}^{-} \begin{bmatrix} X'R^{-1}y \\ Z'R^{-1}y \end{bmatrix} = \begin{bmatrix} X'(I\sigma_e^2)^{-1}X & X'(I\sigma_e^2)^{-1}Z \\ Z'(I\sigma_e^2)^{-1}X & Z'(I\sigma_e^2)^{-1}Z + (U\sigma_a^2)^{-1} \end{bmatrix}^{-} \begin{bmatrix} X'R^{-1}y \\ Z'R^{-1}y \end{bmatrix}$$

GBLUP_Trait1 <- gpMod(gpCode, model="BLUP", kin=G, trait="Trait1")</pre>

summary(GBLUP_Trait1\$fit)

Likelihood kernel: K = (Intercept)

Maximized log likelihood with kernel K is -1615.298

Linear Coefficients:

Estimate Std. Error

(Intercept) -0.001 0.585

Variance Coefficients:

Estimate Std. Error

kinTS 3.503 1.474

In 171.030 28.834

 $\hat{\sigma}_a^2 = 3.503$ $\hat{\sigma}_e^2 = 171.030$

$$h^2 = \frac{\sigma_u^2}{\sigma_u^2 + \sigma_e^2} = \frac{3.503}{3.503 + 171.030} = 0.02$$



```
y = X\beta + Zu + e
                                    \begin{bmatrix} \widehat{\boldsymbol{\beta}} \\ \widehat{\boldsymbol{y}} \end{bmatrix} = \begin{bmatrix} X'R^{-1}X & X'R^{-1}Z \\ Z'R^{-1}X & Z'R^{-1}Z + G^{-1} \end{bmatrix}^{-} \begin{bmatrix} X'R^{-1}y \\ Z'R^{-1}y \end{bmatrix}
       GBLUP_Trait1 <- gpMod(gpCode, model="BLUP", kin=G, trait="Trait1")</pre>
   summary(GBLUP_Trait1)
                                               Mode
                    Length Class
                                              list
fit
                           24 regress
                             1 -none- character
model
                          500 -none- numeric ⇒ Gözlem değerleri vektörü
                          500 -none-
                                                numeric \Rightarrow Genomik damızlık değere tahminleri (\hat{u})
g
Korelasyon r(y, \hat{u}) = 0.9127231
> cor(GBLUP_Trait1$y, GBLUP_Trait1$g)
[1] 0.9127231
```



```
y = X\beta + Zu + e
         GBLUP_Trait1 <- qpMod(qpCode, model="BLUP", kin=G, trait="Trait1")
  data.frame(GBLUP_Trait1$y, GBLUP_Trait1$g)
        GBLUP_Trait1.y GBLUP_Trait1.g
ID11430
                -23.43 -8.52562829
                15.48 0.21847379
ID11431
                -19.18 -5.04440346
ID11432
                -10.43 -2.01580621
ID11433
                -14.07
ID11434
                          0.53287980
Korelasyon r(y, \hat{u}) = 0.9127231
> cor(GBLUP_Trait1$y, GBLUP_Trait1$g)
[1] 0.9127231
```



Çapraz-Doğrulama (Genomik-BLUP - GBLUP)

```
# Son 50 birey Çapraz Doğrulama için belirlendi
 son50 <- rownames(gpCode$pheno)[451:500]</pre>
# Son 50 birey veri setinden çıkartıldı
# İlk 450 birey Uygulama (Training) veri seti olarak oluşturuldu
 gpCode2 <- discard.individuals(gpCode, son50)</pre>
# GBLUP ile Uygulama veri setinin analizi
 GBLUP450 <- qpMod(qpCode2, model="BLUP", kin=G)
# Son 50 bireyin genomik damızlık degerlerinin tahmini
 g50 <- predict(GBLUP450, son50)</pre>
 cor(data.frame(g50, gpCode$pheno[451:500]))
                             q50 qpCode.pheno.451.500.
q50
                                             0.2081486
                       1.0000000
gpCode.pheno.451.500. 0.2081486
                                             1.0000000
```



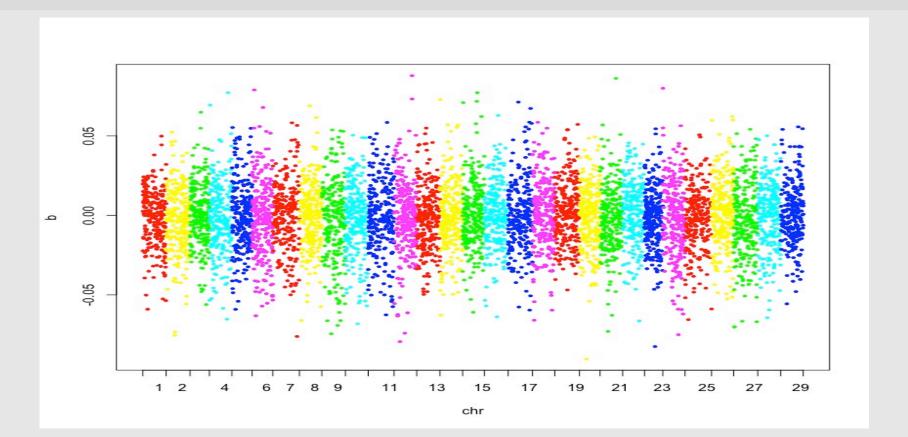
Çapraz-Doğrulama (Genomik-BLUP - GBLUP) — crossVal()

```
# Çapraz doğrulama Replication:1 ve Validasyon:2
  cv.GBLUP_Trait1 <- crossVal(gpCode, cov.matrix=list(G), k=2, Rep=1,
                              Seed=123, sampling="random",
                              varComp=GBLUP_Trait1$fit$sigma,
                              VC.est="commit")
Validayon gruplarına ait korelasyonlar
  cv.GBLUP_Trait1$PredAbi
         rep1
fold1 -0.0564
fold2 -0.0658
Validayon gruplarına ait hata kareler ortalaması
  cv.GBLUP_Trait1$mse
          rep1
fold1 213.5414
fold2 273.1165
```



Genomik-BLUP – RRBLUP

manhattanPlot(RRBLUP_Trait1, gpCode, colored=TRUE, pch=19, cex=0.5)





Teşekkürler