Package 'SummaryLasso'

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Type Package

Title Building Polygenic Risk Score Using GWAS Summary Statistics

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Description
Shrinkage estimator for polygenic risk prediction models based on summary statistics of genome-wide association studies.

License GPL-3

NeedsCompilation yes

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R topics documented:

funcIndex *Inputs for the functional annotations of SNPs.*

Description

A 3614 x 3 matrix with (0,1) entry with 3614 SNPs and 3 functional annotations. For the element at i-th row, j-th column, the entry 0 means SNP i without j-th functional annotation; entry 1 means otherwise. follows:

- f1: The binary index for functional annotation 1.
- f2: The binary index for functional annotation 2.
- f3: The binary index for functional annotation 3.

Usage

```
data(summaryZ)
```

Format

A matrix with 3614 rows for the 3614 SNPs and 3 columns for functional annotations.

gsfPEN *SummaryLasso incorporating multiple traits and functional annotations of SNPs.*

Description

SummaryLasso to model pleiotropy by introducing a group-Lasso type penalty, which is sensitive to select SNPs modestly associated with multiple traits and to incorporate functional annotations of SNPs simultaneously.

Usage

```
gsfPEN(summaryZ, Nvec, plinkLD, NumIter = 1000, RupperVal = NULL,
breaking = 1, numChrs = 22, ChrIndexBeta = 0, Init_summaryBetas = 0,
Zscale = 1, tuningMatrix = NULL, penalty = "mixLOG", funcIndex,
numfunc, p.Threshold = NULL, p.Thresholdpara = c(0.5, 10^-4, 4),
taufactor = c(1/25, 1, 3), llim_length = 4, subtuning = 4,
Lambda_limit = c(0.5, 0.9), Lenlam = 4, lambdavec_func = NULL,
lambdavec_func_limit_len = c(1.5, 3), dfMax = NULL, outputAll = 0,
warmStart = 0, customed = 0, AllTuningMatrix = NULL, SDvec = NULL,
IniBeta = 0)
```

Arguments

summaryZ	The Z statistics of p SNPs from q GWA studies. A matrix with dimension p x q for p SNPs and q traits. The first column corresponds to the primary trait and the rest columns correspond to the secondary traits.
Nvec	A vector of length q for the sample sizes of q GWA studies.
plinkLD	.ld file obtained from the LD calculation from plink.
NumIter	The number of maximum iterations for the estimation procedure.
RupperVal	The maximum tolerable magnitude of the estimates of coefficients during the iterations. This is to avoid certain estimates of coefficients to diverge during the iterations. This may happen when the signs of the correlation coefficients were estimated incorrectly. The default value is 50 times the maximum of coefficients from the input in absolute values.
breaking	A binary (0,1) variable to check if there are some certain estimates of coefficients to diverge during the iterations. This may happen when the signs of the correlation coefficients were estimated incorrectly. The default value is 1.
numChrs	The number of chromosomes used in the analysis. Current version of package does not use this argument.
ChrIndexBeta	The chromosome index for each SNP. Current version of packge does not use this argument.
Init_summaryBetas	Can be used to set the initial values of the coefficients for the iterative estimation.
Zscale	A binary (0,1) variable to make the coefficients from different GWA studies with unequal sample sizes comparable. The default value is 1.
tuningMatrix	Inputs for the tuning values of the tuning parameters. Default is null and it will be generated automatically.
penalty	Current version of pacakge does not use this argument.
funcIndex	Inputs for the functional annotations of SNPs. A p x k matrix with (0,1) entry; p is the number of SNPs and k is the number of functional annotations. For the element at i-th row, j-th column, the entry 0 means SNP i without j-th functional annotation; entry 1 means otherwise.
numfunc	The number of functional annotations.
p.Threshold	The p-values threshold to set up the tuning values of the baseline tuning parameter.
p.Thresholdpara	When p.Threshold is null, p.Threshold will be generated automatically based on the values of p.Thresholdpara. The default values are c(0.5, 10^4, 5), where the first element is the maximum of the p-value threshold, the second element is the minimum, and the third element is total number of p-value thresholds to be generated from the minimum to the maximum.
taufactor	The weights to generate the tuning values for the tuning paramter "tau" and the default is c(1/25, 1, 10) times the median of the p summation of the coefficients for each SNP across q traits.
llim_length	The argument to set up the number of tuning values for lambdas between the lower and upper bound. The default value is 10.

`subtuning` The argument to set up the number of tuning values for lambdas between the lower and upper bound. The default value is 50.

`Lambda_limit` The quantiles to set up the tuning values of lambda. The default value is c(0.5, 0.9).

`Lenlam` The number of tuning values for lambda parameter without using the Log penalty. In other words, the initial `Lenlam` rows of the tuningMatrix are for summayLasso single trait analysis.

`lambdavec_func` The tuning values for the tuning parameters associated with the functional annotations.

`lambdavec_func_limit_len`
When lambdavec_func is null, lambdavec_func will be generated automatically based on the arguments of `lambdavec_func_limit_len`. The default values are c(1.5, 4). The first element is the maximum of the tuning value and the second element is the total number of the tuning values to be generated from 0 to the maximum.

`dfMax` The upper bound of the number of non-zero estimates of coefficients for the primary trait.

`outputAll` For internal checking usage. The default value is 0.

`warmStart` For internal checking usage. The default value is 0.

`customed` For internal checking usage. The default value is 0.

`AllTuningMatrix`
For internal checking usage. The default value is NULL.

`SDvec` The matrix of the standard error for regression coefficients. When the input of SummaryZ is at Z scale, let SDvec = NULL and it will be computed internally.

`IniBeta` A binary (0,1) variable to indicate if the regression coefficients need to be initialized or not. 1 is for yes.

Details

Note that the tuning values for the tuning parameters may need to be modified manually when the selected optimal tuning parameters are at the boundary of the inputs.

Value

`BetaMatrix` The output of the coefficients matrix with dimensions (total number of combinations of the tuning values times (pq)). Each column represents the vectorization of the p x q coefficients matrix given a particular combination of the tuning values (stacking its columns into a column vector).

`Numitervec` This vector shows the number of iterations to converge for each combination of the tuning values.

`AllTuningMatrix`
This matrix shows all combination of tuning values used in the estimation process. Its dimension is that total number of combinations of the tuning values times total number of tuning parameters.

Author(s)

Ting-Huei Chen

References

This R packages is based on the method introduced in the manuscript "A comprehensive statistical framework for building polygenic risk prediction models based on summary statistics of genome-wide association studies."

Examples

```
data("summaryZ")
data("Nvec")
data("plinkLD")
data("funcIndex")
output = gsfPEN(summaryZ=summaryZ, Nvec=Nvec, plinkLD=plinkLD,funcIndex=funcIndex,
numfunc=ncol(funcIndex))
```

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gsPEN *SummaryLasso incorporating multiple traits*

Description

SummaryLasso to model pleiotropy by introducing a group-Lasso type penalty, which is sensitive to select SNPs modestly associated with multiple traits.

Usage

```
gsPEN(summaryZ, Nvec, plinkLD, NumIter = 100, breaking = 1, numChrs = 22,
ChrIndexBeta = 0, Init_summaryBetas = 0, Zscale = 1, RupperVal = NULL,
tuningMatrix = NULL, penalty = c("mixLOG"), taufactor = c(1/25, 1, 10),
llim_length = 10, subtuning = 50, Lambda_limit = c(0.5, 0.9),
Lenlam_singleTrait = 200, dfMax = NULL, IniBeta = 0, inverseTuning = 0,
outputAll = 0, warmStart = 1)
```

Arguments

summaryZ	The Z statistics of p SNPs from q GWA studies. A matrix with dimension p x q for p SNPs and q traits. The first column corresponds to the primary trait and the rest columns correspond to the secondary traits.
Nvec	A vector of length q for the sample sizes of q GWA studies.
plinkLD	.ld file of the LD calculation from plink.
NumIter	The number of maximum iteraions for the estimation procedure.
breaking	A binary (0,1) variable to check if there are some certain estimates of coefficients to diverge during the iterations. This may happen when the signs of the correlation coefficinets were estimated incorrectly. The default value is 1.

`numChrs` The number of chromosomes used in the analysis. Current version of pacakge does not use this argument.

`ChrIndexBeta` The chromosome index for each SNP. Current version of pacakge does not use this argument.

`Init_summaryBetas` Can be used to set the initial values of the coefficients for the iterative estimation.

`Zscale` A binary (0,1) variable to make the coefficients from different GWA studies with unequal sample sizes comparable. The default value is 1.

`RupperVal` The maximum tolerable magnitude of the estimates of coefficients during the iterations. This is to avoid a certain estimates of coefficients to diverge during the iterations. This may happen when the signs of the correlation coefficinets were estimated incorrectly. The default value is 50 times the maximum of coeffcients from the input in absolute values.

`tuningMatrix` Inputs for the tuning values of the tuning parameters. Default is null and it will be generated automatically.

`penalty` Current version of pacakge does not use this argument.

`taufactor` The weights to generate the tuning values for the tuning paramter "tau" and the default is c(1/25, 1, 10) times the median of the p summation of the coefficients for each SNP across q traits.

`llim_length` The argument to set up the number of tuning values for lambdas between the lower and upper bound. The default value is 10.

`subtuning` The argument to set up the number of tuning values for lambdas between the lower and upper bound. The default value is 50.

`Lambda_limit` The quantiles to set up the tuning values of lambda. The default value is c(0.5, 0.9).

`Lenlam_singleTrait` The quantiles to set up the tuning values of lambda for single trait analysis.

`dfMax` The upper bound of the number of non-zero estimates of coefficients for the primary trait.

`IniBeta` A binary (0,1) variable to indicate if the regression coefficients need to be initialized or not. 1 is for yes.

`inverseTuning` For internal checking usage. The default value is 0.

`outputAll` For internal checking usage. The default value is 0.

`warmStart` For analysis with single trait or multiple traits without functional annotations, it is recommended to use warmStart = 1 to enhance computations.

Details

Note that the tuning values for the tuning parameters may need to be modified manually when the selected optimal tuning parameters are at the boundary of the inputs.

Value

`BetaMatrix` The output of the coefficients matrix with dimensions (total number of combinations of the tuning values times (pq)). Each column represents the vectorization of the p x q coefficients matrix given a particular combination of the tuning values (stacking its columns into a column vector).

`Numitervec` This vector shows the number of iterations to converge for each combination of the tuning values.

`AllTuningMatrix` This matrix shows all combination of tuning values used in the estimation process. Its dimension is that total number of combinations of the tuning values times total number of tuning parameters.

Author(s)

Ting-Huei Chen

References

This R packages is based on the method introduced in the manuscript "A comprehensive statistical framework for building polygenic risk prediction models based on summary statistics of genome-wide association studies."

Examples

```
data("summaryZ")
data("Nvec")
data("plinkLD")
output = gsPEN(summaryZ=summaryZ, Nvec=Nvec, plinkLD=plinkLD)
```

Nvec *A vector of sample sizes for the q traits of the* `summaryZ`.

Description

A vector of q sample sizes for the q set of Z statistics corresponding to the q columns of `summaryZ`.

Usage

```
data(Nvec)
```

Format

A vector with q elements, where q is the number of columns of `summaryZ`.

plinkLD *The LD info from output of the software (plink)*

Description

The LD information is crucial for the analysis by SummaryLasso. The reference alleles used to obtained for the Z statsitics or the regression coefficients have to be the sames as those used for the LD calculation. This file can be obtained directly from the output of the LD calculation by the software (plink); for example the output can be like plink.ld. On the other hand, the user can calcuate the LD based on their prefered tools. The variables are as follows:

- CHR_A: The chromosome of SNP_A
- BP_A: The positions of SNP_A
- SNP_A: The names of SNP_A
- CHR_B: The chromosome of SNP_B
- BP_B: The positions of SNP_B
- SNP_B: The names of SNP_B
- R: The correlation between SNP_A and SNP_B

Usage

```
data(plinkLD)
```

Format

A data frame with 205959 rows and 7 columns

References

- Purcell S, et al. (2007) PLINK: a toolset for whole-genome association and population-based linkage analysis. *American Journal of Human Genetics*, **81**.

summaryZ *The Z statistics from the univariate analysis of the association between 3614 SNPs and three traits respectively.*

Description

These Z statsitics are obtained from simulated datasets. The variables are as follows:

- Z1: The Z statistics from trait 1; the primary trait.
- Z2: The Z statistics from trait 2; the secondary trait.
- Z2: The Z statistics from trait 3; the secondary trait.

Usage

```
data(summaryZ)
```

Format

A matrix with 3614 rows for the 3614 SNPs and 3 columns for 3 traits.

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