Package 'interep'

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Type Package

Title Interaction Analysis of Repeated Measure Data

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Description Extensive penalized variable selection methods have been developed in the past two decades for analyzing high dimensional omics data, such as gene expressions, single nucleotide polymorphisms (SNPs), copy number variations (CNVs) and others. However, lipidomics data have been rarely investigated by using high dimensional variable selection methods. This package incorporates our recently developed penalization procedures to conduct interaction analysis for high dimensional lipidomics data with repeated measurements. The core module of this package is developed in C++. The development of this software package and the associated statistical methods have been partially supported by an Innovative Research Award from Johnson Cancer Research Center, Kansas State University.

Depends R (>= 3.5.0)

License GPL-2

Encoding UTF-8

LazyData true

Imports Rcpp, MASS

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`cv.interep` *k-folds cross-validation for interep*

Description

This function does k-fold cross-validation for interep and returns the optimal value of lambda.

Usage

```
cv.interep(e, g, y, beta0, lambda1, lambda2, nfolds, corre, pmethod, maxits)
```

Arguments

`e`	matrix of environment factors.
`g`	matrix of omics factors. In the case study, the omics measurements are lipidomics data.
`y`	the longitudinal response.
`beta0`	the intial value for the coefficient vector.
`lambda1`	a user-supplied sequence of λ_1 values, which serves as a tuning parameter for individual predictors.
`lambda2`	a user-supplied sequence of λ_2 values, which serves as a tuning parameter for interactions.
`nfolds`	the number of folds for cross-validation.
`corre`	the working correlation structure that is used in the estimation algorithm. interep provides three choices for the working correlation structure: "a" as AR-1", "i" as "independence" and "e" as "exchangeable".
`pmethod`	the penalization method. "mixed" refers to MCP penalty to individual main effects and group MCP penalty to interactions; "individual" means MCP penalty to all effects.
`maxits`	the maximum number of iterations that is used in the estimation algorithm.

Details

When dealing with predictors with both main effects and interactions, this function returns two optimal tuning parameters, λ_1 and λ_2; when there are only main effects in the predictors, this function returns λ_1, which is the optimal tuning parameter for individual predictors containing main effects.

Value

an object of class "cv.interep" is returned, which is a list with components:

`lam1`	the optimal λ_1.
`lam2`	the optimal λ_2.

References

Zhou, F., Ren, J., Li, G., Jiang, Y., Li, X., Wang, W.and Wu, C. (2019). Penalized variable selection for Lipid–environment interactions in a longitudinal lipidomics study. *Genes*, 10(12), 1002

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Wu, C., and Ma, S. (2015). A selective review of robust variable selection with applications in bioinformatics. doi: 10.1093/bib/bbu046*Briefings in Bioinformatics*, 16(5), 873–883

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Wu, C., Cui, Y., and Ma, S. (2014). Integrative analysis of gene–environment interactions under a multi–response partially linear varying coefficient model. doi: 10.1002/sim.6287*Statistics in Medicine*, 33(28), 4988–4998

Wu, C. and Cui, Y. (2013). A novel method for identifying nonlinear gene–environment interactions in case–control association studies. doi: 10.1007/s004390131350z*Human Genetics*, 132(12):1413–1425

Wu, C. and Cui, Y. (2013). Boosting signals in gene–based association studies via efficient SNP selection. doi: 10.1093/bib/bbs087*Briefings in Bioinformatics*, 15(2):279–291

Wu, C., Zhong, P.S. and Cui, Y. (2013). High dimensional variable selection for gene-environment interactions. *Technical Report*, Michigan State University.

Wu, C., Li, S., and Cui, Y. (2012). Genetic Association Studies: An Information Content Perspective. doi: 10.2174/138920212803251382*Current Genomics*, 13(7), 566–573

`dat` *simulated data for demonstrating the features of interep*

Description

Simulated data for demonstrating the features of interep.

Usage

```
data("dat")
```

Format

Each data consists of six components: e, z, x, y, coef and index; index shows the location of the true coefficients used to generate y.

Examples

```
data("dat")
```

dmcp *This function obtains the first derivative function of MCP (Minimax Concave Penalty)*

Description

This function obtains the first derivative function of MCP (Minimax Concave Penalty)

Usage

```
dmcp(theta, lambda, gamma = 3)
```

Arguments

theta	a coefficient vector.
lambda	the tuning parameter.
gamma	the regularization parameter in MCP (Minimax Concave Penalty). It balances between the unbiasedness and concavity of MCP.

Details

Rigorously speaking, the regularization parametre γ needs to be obtained via a data-driven approach. Published studies suggest experimenting with a few values, such as 1.8, 3, 4.5, 6, and 10, then fixing its value. In our numerical study, we have examined this sequence and found that the results are not sensitive to the choice of value of γ, and set the value at 3. In practice, to be prudent, values other than 3 should also be investigated. Similar discussions can be found in the references below.

Value

the first derivative of MCP function.

References

Ren, J., Du, Y., Li, S., Ma, S., Jiang, Y. and Wu, C. (2019). Robust network-based regularization and variable selection for high-dimensional genomic data in cancer prognosis. doi: 10.1002/gepi.22194*Genetic epidemiology*, 43(3), 276-291

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Wu, C., Zhang, Q., Jiang, Y. and Ma, S. (2018). Robust network-based analysis of the associations between (epi) genetic measurements. doi: 10.1016/j.jmva.2018.06.009*Journal of multivariate analysis*, 168, 119-130

Ren, J., He, T., Li, Y., Liu, S., Du, Y., Jiang, Y. and Wu, C. (2017). Network-based regularization for high dimensional SNP data in the case–control study of Type 2 diabetes. doi: 10.1186/s12863-01704955*BMC genetics*, 18(1), 44

Examples

```
theta=runif(20,-5,5)
lambda=1
dmcp(theta,lambda,gamma=3)
```

`interep` *fit generalized estimaitng equations with given tuning parameters*

Description

This function makes predictions for generalized estimating equation with a given value of lambda. Typical usage is to have the cv.interep function compute the optimal lambda, then provide it to the interep function.

Usage

```
interep(e, g, y, beta0, corre, pmethod, lam1, lam2, maxits)
```

Arguments

`e`	matrix of environment factors.
`g`	matrix of omics factors. In the case study, the omics measurements are lipidomics data.
`y`	the longitudinal response.
`beta0`	the inital coefficient vector.
`corre`	the working correlation structure that is used in the estimation algorithm. interep provides three choices for the working correlation structure: "a" as AR-1", "i" as "independence" and "e" as "exchangeable".
`pmethod`	the penalization method. "mixed" refers to MCP penalty to individual main effects and group MCP penalty to interactions; "individual" means MCP penalty to all effects.
`lam1`	the tuning parameter lambda1 for individual predictors.
`lam2`	the tuning parameter lambda2 for interactions.
`maxits`	the maximum number of iterations that is used in the estimation algorithm. The default value is 30

Value

`coef`	the coefficient vector.

References

Zhou, F., Ren, J., Li, G., Jiang, Y., Li, X., Wang, W.and Wu, C. (2019). Penalized variable selection for Lipid–environment interactions in a longitudinal lipidomics study. *Genes*, 10(12), 1002

Zhou, F., Ren, J., Lu, X., Ma, S. and Wu, C. (2020) Gene–Environment Interaction: a Variable Selection Perspective. *Epistasis*, Methods in Molecular Biology. Humana Press. (Accepted)

Examples

```
data("dat")
e=dat$e
g=dat$z
y=dat$y
beta0=dat$coef
index=dat$index
b = interep(e, g, y,beta0,corre="e",pmethod="mixed",lam1=dat$lam1, lam2=dat$lam2,maxits=30)
b[abs(b)<0.05]=0
pos = which(b != 0)
tp = length(intersect(index, pos))
fp = length(pos) - tp
list(tp=tp, fp=fp)
```

`penalty` *This function gives the penalty functions*

Description

This function gives the penalty functions

Usage

```
penalty(x, n, p, q, beta, lam1, pmethod, p1, lam2)
```

Arguments

`x`	matrix of covariates.
`n`	the sample size.
`p`	the number of predictors.
`q`	the number of environment factors.
`beta`	the coefficient vector.
`lam1`	the tuning parameter lambda1 for individual penalty.
`pmethod`	the penalization method. "mixed" refers to MCP penalty to individual main effects and group MCP penalty to interactions; "individual" means MCP penalty to all effects.
`p1`	the number of gene factors.
`lam2`	the tuning parameter lambda2 for group penalty.

Value

`E`	the penalty function.

`reformat` *This function changes the format of the longitudinal data from wide format to long format*

Description

This function changes the format of the longitudinal data from wide format to long format

Usage

```
reformat(k, y, x)
```

Arguments

`k`	the number of repeated measurement.
`y`	the longitudinal response.
`x`	a matrix of predictors, consisting of omics and environment factors, as well as their interactions. In the case study, the omics measurements are lipidomics data.

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