Package ‘GGPA’

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Type Package

Title graph-GPA: A graphical model for prioritizing GWAS results and investigating pleiotropic architecture

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Author Dongjun Chung, Hang J. Kim, Carter Allen

Maintainer Dongjun Chung <dongjun.chung@gmail.com>

Description Genome-wide association studies (GWAS) is a widely used tool for identification of genetic variants associated with phenotypes and diseases, though complex diseases featuring many genetic variants with small effects present difficulties for traditional these studies. By leveraging pleiotropy, the statistical power of a single GWAS can be increased. This package provides functions for fitting graph-GPA, a statistical framework to prioritize GWAS results by integrating pleiotropy. 'GGPA' package provides user-friendly interface to fit graph-GPA models, implement association mapping, and generate a phenotype graph.

License GPL (>= 2)

URL https://github.com/dongjunchung/GGPA/

Depends R (>= 4.0.0), stats, methods, graphics, GGally, network, sna, scales, matrixStats

Suggests BiocStyle

Imports Rcpp (>= 0.11.3)

LinkingTo Rcpp, RcppArmadillo

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SystemRequirements GNU make

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Description

This package provides functions for fitting graph-GPA, a statistical framework to prioritize GWAS results by integrating pleiotropy.

Details

Package: GGPA
Type: Package
Version: 0.99.11
Date: 2018-01-15
License: GPL (>= 2)
LazyLoad: yes

This package contains a main class, GGPA, which represents graph-GPA model fit. This package contains four main methods, GGPA, assoc, and plot. GGPA method fits the graph-GPA model and assoc method implements association mapping. plot method provides a graph representing genetic relationship among phenotypes.

Author(s)

Hang J. Kim and Dongjun Chung
Maintainer: Hang J. Kim <hang.kim@uc.edu>, Dongjun Chung <dongjun.chung@gmail.com>
References

See Also
GGPA, assoc, plot, GGPA.

Examples
# load simulation data
data(simulation)

# fit graph-GPA model
fit <- GGPA( simulation$pmat, nBurnin=200, nMain=200 )
fit

# fit graph-GPA model using a prior phenotype graph
# as an example, edge 6-7 added & edge 2-3 removed in pgraph
pgraph <- matrix( 0, ncol(simulation$pmat), ncol(simulation$pmat) )
fit.pg <- GGPA( simulation$pmat, pgraph, nBurnin=200, nMain=200 )
fit.pg

# association mapping for each phenotype
head(assoc( fit, FDR=0.1, fdrControl="global" ))

# hypothesis testing for 1st and 2nd phenotype pair
head(assoc( fit, FDR=0.1, fdrControl="global", i=1, j=2 ))

# plot phenotype graph
plot(fit)
plot(fit.pg)

##

assoc Association mapping

Description
Association mapping.
Usage

assoc( object, ... )

## S4 method for signature 'GGPA'
assoc( object, FDR=0.05, fdrControl="global", i=NULL, j=NULL )

Arguments

- **object**: A GGPA model fit as obtained by GGPA().
- **FDR**: The desired FDR level.
- **fdrControl**: Method to control FDR. Possible values are "global" (global FDR control) and "local" (local FDR control). Default is "global".
- **i**: Index for the first phenotype used in association mapping. See the details about how users can specify the pattern.
- **j**: Index for the second phenotype used in association mapping. See the details about how users can specify the pattern.
- **...**: Other parameters to be passed through to generic assoc.

Details

assoc uses the direct posterior probability approach of Newton et al. (2004) to control global FDR in association mapping.

By default (i.e., i=NULL, j=NULL), assoc implements association mapping for each phenotype. If users are interested in identifying SNPs associated with a pair of phenotypes, users can specify indices of phenotypes of interest using the arguments i and j. Note that both i and j should be either NULL or numeric.

Value

If i=NULL, j=NULL, returns a binary matrix indicating association of SNPs for each phenotype, where its rows and columns match those of input p-value matrix for function GGPA. Otherwise, returns a binary vector indicating association of SNPs for i-th and j-th phenotype pair.

Author(s)

Hang J. Kim and Dongjun Chung

References


Kim H, Yu Z, Lawson A, Zhao H, and Chung D (2017), "Improving SNP prioritization and pleiotropic architecture estimation by incorporating prior knowledge using graph-GPA."

GGPA

See Also
GGPA, GGPA.

Examples

# Load the included simulation data
data(simulation)

# fit GGPA model with 200 iterations and a burn-in of 200 iterations
# Note that we recommend more than 200 iterations in practice
fit <- GGPA(simulation$pmat, nMain = 200, nBurnin = 200)

# Association mapping with FDR of 0.1 and global control
head(assoc( fit, FDR=0.1, fdrControl="global" ))

# We may specify i = 1 and j = 2 if we are interested in that specific phenotype
head(assoc( fit, FDR=0.1, fdrControl="global", i=1, j=2 ))

GGPA  Fit graph-GPA model

Description

Fit graph-GPA model.

Usage

GGPA( gwasPval, pgraph=NULL, nBurnin=10000, nMain=40000, lbPval=1e-10, verbose=1 )

Arguments

gwasPval p-value matrix from GWAS data, where row and column correspond to SNP and phenotype, respectively.
pgraph A binary matrix representing the prior phenotype graph, where its rows and columns match the columns of gwasPval.
nBurnin Number of burn-in iterations. Default is 10000.
nMain Number of main MCMC iterations. Default is 40000.
lbPval Lower bound for GWAS p-value. Any GWAS p-values smaller than lbPval are set to lbPval. Default is 1e-10.
verbose Amount of progress report during the fitting procedure. Possible values are 0 (minimal output), 1, 2, or 3 (maximal output). Default is 1.

Details

GGPA fits the graph-GPA model. It requires to provide GWAS p-value to gwasPval. If a phenotype graph is provided in pgraph, it is utilized to guide the phenotype graph estimation. Based on this GGPA fit, assoc implements association mapping and plot provides a phenotype graph.
**Value**
Construct GGPA class object.

**Author(s)**
Hang J. Kim and Dongjun Chung

**References**

**See Also**
assoc, GGPA.

**Examples**
```r
# Load the included simulation data
data(simulation)

# fit GGPA model with 200 iterations and a burn-in of 200 iterations
# Note that we recommend more than 200 iterations in practice
fit <- GGPA( simulation$pmat, nMain = 200, nBurnin = 200)

# Association mapping with FDR of 0.1 and global control
head(assoc( fit, FDR=0.1, fdrControl="global" ))

# We may specify i = 1 and j = 2 if we are interested in that specific phenotype
head(assoc( fit, FDR=0.1, fdrControl="global", i=1, j=2 ))

# plot the GGPA model fit
plot(fit)
```

---

**GGPA-class Class “GGPA”**

**Description**
This class represents graph-GPA model fit.

**Objects from the Class**
Objects can be created by calls of the form `new("GGPA", ...).`
Slots

- **fit**: Object of class "list", representing the MCMC draws.
- **summary**: Object of class "list", representing the summary statistics.
- **setting**: Object of class "list", representing the setting for graph-GPA model fitting.
- **gwasPval**: Object of class "matrix", representing the p-value matrix from GWAS data.
- **pgraph**: Object of class "matrix", representing the prior phenotype graph.

Methods

- **show** signature(object = "GGPA"): provide brief summary of the object.
- **plot** signature(x = "GGPA", y = "missing", pCutoff = 0.5, betaCI = 0.95): plot a phenotype graph. Nodes i and j are connected if the posterior probability of $E_{ij} > pCutoff$ and the posterior probability of $beta_{ij} > betaCI$.
- **fdr** signature(object = "GGPA", i=NULL, j=NULL): provide local FDR. By default (i.e., i=NULL, j=NULL), it returns a matrix of local FDR that a SNP is not associated with each phenotype (i.e., marginal FDR), where the order of columns is same as that in input GWAS data. If phenotype indices i and j are specified, a vector of corresponding local FDR is provided.
- **estimates** signature(object = "GGPA"): extract parameter estimates from graph-GPA model fit.

Author(s)

Hang J. Kim, Dongjun Chung

References


See Also

GGPA.

Examples

```
showClass("GGPA")

# Load the included simulation data
data(simulation)

# fit GGPA model with 200 iterations and a burn-in of 200 iterations
# Note that we recommend more than 200 iterations in practice
fit <- GGPA( simulation$pmat, nMain = 200, nBurnin = 200)

# Plot GGPA model fit
plot(fit)
```
head(fdr( fit ))
head(fdr( fit, i=1, j=2 ))
str(estimates( fit ))

---

GGPA-internal | Internal GGPA objects

Description

Internal GGPA objects.

Details

These are not to be called by the user.

Examples

# Load the included simulation data
data(simulation)

# fit GGPA model with 200 iterations and a burn-in of 200 iterations
# Note that we recommend more than 200 iterations in practice
fit <- GGPA( simulation$pmat, nMain = 200, nBurnin = 200)

# Association mapping with FDR of 0.1 and global control
head(assoc( fit, FDR=0.1, fdrControl="global" ))

# We may specify i = 1 and j = 2 if we are interested in that specific phenotype
head(assoc( fit, FDR=0.1, fdrControl="global", i=1, j=2 ))

# Plot model fit
plot(fit)

---

simulation | Simulation data for graph-GPA

Description

This is an simulation dataset.

Usage

data(simulation)
**simulation**

### Format

*simulation* list object containing simulation data (element Y) and its simulation setting (the remaining elements).

### Author(s)

Hang J. Kim, Dongjun Chung

### References


Kim H, Yu Z, Lawson A, Zhao H, and Chung D (2017), "Improving SNP prioritization and pleiotropic architecture estimation by incorporating prior knowledge using graph-GPA."

### Examples

```r
# The simulation data set is included with the GGPA package
data(simulation)
head(t(simulation$pmat))
```
Index

* classes
  GGPA-class, 6
* datasets
  simulation, 8
* internal
  GGPA-internal, 8
* methods
  assoc, 3
  GGPA, 5
* models
  assoc, 3
  GGPA, 5
* package
  GGPA-package, 2
  assoc, 3, 6
  assoc,GGPA-method (assoc), 3
  cGGPA (GGPA-internal), 8
  estimates (GGPA-class), 6
  estimates,GGPA-method (GGPA-class), 6
  fdr (GGPA-class), 6
  fdr,GGPA-method (GGPA-class), 6
  GGPA, 3, 5, 6, 7
  GGPA-class, 6
  GGPA-internal, 8
  GGPA-package, 2
  Gibbs_e_it_no_ann (GGPA-internal), 8
  plot, 3
  plot,GGPA,missing-method (GGPA-class), 6
  plot,GGPA-method (GGPA-class), 6
  Rcpp_cGGPA-class (GGPA-internal), 8
  show,GGPA-method (GGPA-class), 6
  simulation, 8