

Package: hJAM (via r-universe)

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Type Package

Title Hierarchical Joint Analysis of Marginal Summary Statistics

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Author Lai Jiang <jian848@usc.edu>

Maintainer Lai Jiang <jian848@usc.edu>

Description Provides functions to implement a hierarchical approach which is designed to perform joint analysis of summary statistics using the framework of Mendelian Randomization or transcriptome analysis. Reference: Lai Jiang, Shujing Xu, Nicholas Mancuso, Paul J. Newcombe, David V. Conti (2020). "A Hierarchical Approach Using Marginal Summary Statistics for Multiple Intermediates in a Mendelian Randomization or Transcriptome Analysis."
<bioRxiv><doi:10.1101/2020.02.03.924241>.

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LazyData true

RoxygenNote 6.1.1

Suggests knitr, rmarkdown

VignetteBuilder knitr

URL <https://github.com/lailylajiang/hJAM>

BugReports <https://github.com/lailylajiang/hJAM/issues>

Imports ggplot2, ggpubr, dplyr, reshape2

NeedsCompilation no

Config/pak/sysreqs cmake make libicu-dev

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betas.Gy

Example beta list of hJAM

Description

Example beta list of hJAM

Usage

betas.Gy

Format

The betas.Gy is the beta vector in the hJAM model: the association estimates between 210 SNPs and myocardial infarction. The summary data was collected from UK Biobank (n=459,324).

References

Sudlow C, Gallacher J, Allen N, et al. UK biobank: an open access resource for identifying the causes of a wide range of complex diseases of middle and old age. PLoS Med 2015; 12: e1001779.

conditional_A	<i>Example conditional A matrix of hJAM</i>
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Description

Example conditional A matrix of hJAM

Usage

```
conditional_A
```

Format

The conditional_A is the conditional estimates alpha matrix in the hJAM model: the association estimates between 210 SNPs and body mass index (BMI) and type 2 diabetes (T2D). The summary data was collected from GIANT consortium (n=339,224) and DIAGRAM+GERA+UKB (n=659316) for BMI and T2D, respectively. We converted it from marginal_A, using get_cond_A function in hJAM package.

References

1. Locke AE, Kahali B, Berndt SI, et al. Genetic studies of body mass index yield new insights for obesity biology. *Nature* 2015; 518: 197-206. 2. Xue A, Wu Y, Zhu Z, et al. Genome-wide association analyses identify 143 risk variants and putative regulatory mechanisms for type 2 diabetes. *Nat Commun* 2018; 9: 2941.

get_cond_A	<i>Compute conditional Z matrix</i>
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Description

The get_cond_A function is to get the conditional A matrix by using marginal A matrix

Usage

```
get_cond_A(marginal_A, G1, N.Gx, ridgeTerm = FALSE)
```

Arguments

marginal_A	the marginal effects of SNPs on the exposures (Gx).
G1	the reference panel (G1), such as 1000 Genome
N.Gx	the sample size of each Gx. It can be a scalar or a vector. If there are multiple X's from different Gx, it should be a vector including the sample size of each Gx. If all alphas are from the same Gx, it could be a scalar.
ridgeTerm	ridgeTerm = TRUE when the matrix L is singular. Matrix L is obtained from the cholesky decomposition of $G0'G0$. Default as FALSE.

Value

A matrix with conditional estimates which are converted from marginal estimates using the JAM model.

Author(s)

Lai Jiang

Examples

```
data(G1)
data(betas.Gy)
data(marginal_A)
get_cond_A(marginal_A = marginal_A, G1 = G1, N.Gx = c(339224, 659316), ridgeTerm = TRUE)
```

<code>get_cond_alpha</code>	<i>Compute conditional alphas</i>
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Description

The `get_cond_alpha` function is to compute the conditional alpha vector for each X. If only one X in the model, please use `get_cond_alpha` instead of `get_cond_A`. A sub-step in the `get_cond_A` function.

Usage

```
get_cond_alpha(alphas, G1, N.Gx, ridgeTerm = FALSE)
```

Arguments

<code>alphas</code>	the marginal effects of SNPs on one exposure (Gx).
<code>G1</code>	the reference panel (G1), such as 1000 Genome
<code>N.Gx</code>	the sample size of the Gx. It can be a scalar.
<code>ridgeTerm</code>	<code>ridgeTerm = TRUE</code> when the matrix L is singular. Matrix L is obtained from the cholesky decomposition of $G0'G0$. Default as <code>FALSE</code>

Value

A vector with conditional estimates which are converted from marginal estimates using the JAM model.

Author(s)

Lai Jiang

References

Lai Jiang, Shujing Xu, Nicholas Mancuso, Paul J. Newcombe, David V. Conti (2020). A Hierarchical Approach Using Marginal Summary Statistics for Multiple Intermediates in a Mendelian Randomization or Transcriptome Analysis. *bioRxiv* <https://doi.org/10.1101/2020.02.03.924241>.

Examples

```
data(G1)
data(betas.Gy)
data(marginal_A)
get_cond_alpha(alphas = marginal_A[, 1], G1 = G1, N.Gx = 339224, ridgeTerm = TRUE)
```

G1	<i>Example reference data of hJAM</i>
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Description

The real data example from hJAM paper

Usage

G1

Format

The G1 object is a data matrix with 2467 individual of 210 SNPs from 1000 Genome project.

References

Consortium GP. A global reference for human genetic variation. *Nature* 2015; 526: 68.

hJAM_egger	<i>Fit hJAM with Egger regression</i>
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Description

The hJAM_egger function is to get the results from the hJAM model with Egger regression. It is for detecting potential pleiotropy

Usage

```
hJAM_egger(betas.Gy, N.Gy, G1, A, ridgeTerm = FALSE)
```

Arguments

betas.Gy	The betas in the paper: the marginal effects of SNPs on the phenotype (Gy)
N.Gy	The sample size of Gy
G1	The reference panel (G1), such as 1000 Genome
A	The A matrix in the paper: the marginal/conditional effects of SNPs on the exposures (Gx)
ridgeTerm	ridgeTerm = TRUE when the matrix L is singular. Matrix L is obtained from the cholesky decomposition of $G0'G0$. Default as FALSE.

Value

An object of the hJAM with egger regression results.

Exposure The intermediates, such as the modifiable risk factors in Mendelian Randomization and gene expression in transcriptome analysis.

numSNP The number of SNPs that the user use in the instrument set.

Estimate The conditional estimates of the associations between intermediates and the outcome.

StdErr The standard error of the conditional estimates of the associations between intermediates and the outcome.

Lower.CI The lower bound of the 95% confidence interval of the estimates.

Upper.CI The upper bound of the 95% confidence interval of the estimates.

Pvalue The p value of the estimates with a type-I error equals 0.05.

Est.Int The intercept of the regression of intermediates on the outcome.

StdErr.Int The standard error of the intercept of the regression of intermediates on the outcome.

Lower.CI.Int The lower bound of the 95% confidence interval of the intercept.

Upper.CI.Int The upper bound of the 95% confidence interval of the intercept.

Pvalue.Int The p value of the intercept with a type-I error equals 0.05.

An object of hJAM with egger regression results.

Author(s)

Lai Jiang

References

Lai Jiang, Shujing Xu, Nicholas Mancuso, Paul J. Newcombe, David V. Conti (2020). A Hierarchical Approach Using Marginal Summary Statistics for Multiple Intermediates in a Mendelian Randomization or Transcriptome Analysis. *bioRxiv* <https://doi.org/10.1101/2020.02.03.924241>.

Examples

```
data(G1)
data(betas.Gy)
data(conditional_A)
hJAM_egger(betas.Gy = betas.Gy, G1 = G1, N.Gy = 459324, A = conditional_A, ridgeTerm = TRUE)
```

hJAM_Inreg	<i>Fit hJAM with linear regression</i>
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Description

The hJAM function is to get the results from the hJAM model using input data

Usage

```
hJAM_Inreg(betas.Gy, N.Gy, G1, A, ridgeTerm = FALSE)
```

Arguments

betas.Gy	The betas in the paper: the marginal effects of SNPs on the phenotype (Gy)
N.Gy	The sample size of Gy
G1	The reference panel (G1), such as 1000 Genome
A	The A matrix in the paper: the marginal/conditional effects of SNPs on the exposures (Gx)
ridgeTerm	ridgeTerm = TRUE when the matrix L is singular. Matrix L is obtained from the cholesky decomposition of $G0'G0$. Default as FALSE.

Value

An object of the hJAM with linear regression results.

Exposure The intermediates, such as the modifiable risk factors in Mendelian Randomization and gene expression in transcriptome analysis.

numSNP The number of SNPs that the user use in the instrument set.

Estimate The conditional estimates of the associations between intermediates and the outcome.

StdErr The standard error of the conditional estimates of the associations between intermediates and the outcome.

Lower.CI The lower bound of the 95% confidence interval of the estimates.

Upper.CI The upper bound of the 95% confidence interval of the estimates.

Pvalue The p value of the estimates with a type-I error equals 0.05.

Author(s)

Lai Jiang

References

Lai Jiang, Shujing Xu, Nicholas Mancuso, Paul J. Newcombe, David V. Conti (2020). A Hierarchical Approach Using Marginal Summary Statistics for Multiple Intermediates in a Mendelian Randomization or Transcriptome Analysis. *bioRxiv* <https://doi.org/10.1101/2020.02.03.924241>.

Examples

```
data(G1)
data(betas.Gy)
data(conditional_A)
hJAM_lgreg(betas.Gy = betas.Gy, G1 = G1, N.Gy = 459324, A = conditional_A, ridgeTerm = TRUE)
```

marginal_A

Example marginal A matrix of hJAM

Description

Example marginal A matrix of hJAM

Usage

```
marginal_A
```

Format

The marginal_A is the marginal estimates alpha matrix in the hJAM model: the association estimates between 210 SNPs and body mass index (BMI) and type 2 diabetes (T2D). The summary data was collected from GIANT consortium (n=339,224) and DIAGRAM+GERA+UKB (n=659316) for BMI and T2D, respectively.

References

1. Locke AE, Kahali B, Berndt SI, et al. Genetic studies of body mass index yield new insights for obesity biology. *Nature* 2015; 518: 197-206.
2. Xue A, Wu Y, Zhu Z, et al. Genome-wide association analyses identify 143 risk variants and putative regulatory mechanisms for type 2 diabetes. *Nat Commun* 2018; 9: 2941.

output.format

Keep the output as three digits

Description

Keep the output as three digits

Usage

```
output.format(x, ...)
```

Arguments

x	input
...	other options you want to put in

Author(s)

Lai Jiang

print.hJAM_egger *Print out for hJAM_egger*

Description

Print out for hJAM_egger

Usage

```
## S3 method for class 'hJAM_egger'  
print(x, ...)
```

Arguments

x input
... other options you want to put in

Author(s)

Lai Jiang

print.hJAM_lgreg *Print out for hJAM_lgreg*

Description

Print out for hJAM_lgreg

Usage

```
## S3 method for class 'hJAM_lgreg'  
print(x, ...)
```

Arguments

x input
... other options you want to put in

Author(s)

Lai Jiang

SNPs_heatmap

Heatmap for all the SNPs used in the analysis

Description

To generate the heatmap of all the SNPs that the user use in the analysis

Usage

```
SNPs_heatmap(G1)
```

Arguments

G1 The reference panel (G1) of the SNPs that the user use in the analysis, such as 1000 Genome

Author(s)

Lai Jiang

Examples

```
data(G1)
t = SNPs_heatmap(G1 = G1)
t
```

SNPs_info

Example SNPs' information of hJAM

Description

Example SNPs' information of hJAM

Usage

```
SNPs_info
```

Format

The SNPs_info is the information of the 210 SNPs that we used in this data example. It includes three columns: the rsID, major allele, and minor allele frequency of each SNP. The minor allele frequencies were calculated in the 503 European-ancestry subjects in 1000 Genome project.

References

Consortium GP. A global reference for human genetic variation. Nature 2015; 526: 68.

SNPs_scatter_plot	<i>Scatter plot for all the SNPs used in the analysis</i>
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Description

To generate the scatter plot of all the SNPs that the user use in the analysis

Usage

```
SNPs_scatter_plot(A, betas.Gy, num_X)
```

Arguments

A	The effects of SNPs on the exposures (Gx).
betas.Gy	The betas in the paper: the marginal effects of SNPs on the phenotype (Gy)
num_X	The number of intermediates in the research question.

Value

A set of scatter plots with x-axis being the conditional α estimates for each intermediate and y-axis being the β estimates.

Author(s)

Lai Jiang

Examples

```
data(conditional_A)
data(betas.Gy)
t = SNPs_scatter_plot(A = conditional_A, betas.Gy = betas.Gy, num_X = 2)
t
```

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