

Package ‘CINOEDV’

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Type Package

Title Co-Information based N-Order Epistasis Detector and Visualizer

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Author Junliang Shang

Maintainer Junliang Shang <shangjunliang110@163.com>

Description Detecting and visualizing nonlinear interaction effects of single nucleotide polymorphisms or epistatic interactions, especially high-order epistatic interactions, are important topics in bioinformatics because of their significant mathematical and computational challenges. We present CINOEDV (Co-Information based N-Order Epistasis Detector and Visualizer) for detecting, visualizing, and analyzing high-order epistatic interactions by introducing virtual vertices into the construction of a hypergraph. CINOEDV was developed as an alternative to existing software to build a global picture of epistatic interactions and unexpected high-order epistatic interactions, which might provide useful clues for understanding the underlying genetic architecture of complex diseases.

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CINOEDV-package	<i>Co-Information based N-Order Epistasis Detector and Visualizer</i>
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Description

Detecting and visualizing nonlinear interaction effects of single nucleotide polymorphisms or epistatic interactions, especially high-order epistatic interactions, are important topics in bioinformatics because of their significant mathematical and computational challenges. We present CINOEDV (Co-Information based N-Order Epistasis Detector and Visualizer) for detecting, visualizing, and analyzing high-order epistatic interactions by introducing virtual vertices into the construction of a hypergraph. CINOEDV was developed as an alternative to existing software to build a global picture of epistatic interactions and unexpected high-order epistatic interactions, which might provide useful clues for understanding the underlying genetic architecture of complex diseases.

Details

Package: CINOEDV
 Type: Package
 Version: 1.0
 Date: 2014-05-02
 License: GPL-2

```
##### ## Normal Using type ## #####
result <- CINOEDV_Main()
#### Please input the file name with its format (.mat) that saves SNP data. # test.mat
#### Please input the maximum order (1/2/3/4/5), and 3 is the Recommendation Option. # 3
#### Please input the 1 ratio threshold. # 1
#### Please input the 2 ratio threshold. # 0.5
#### Please input the 3 ratio threshold. # 0.8
#### Please input the 1 number threshold. # 10
#### Please input the 2 number threshold. # 20
#### Please input the 3 number threshold. # 8
#### Please select the evaluation measure (1/2/3), and 1 is the Recommendation Option. # 1
#### Please input the name of such file with (.mat) format. # NA
```

Author(s)

Junliang Shang <shangjunliang110@163.com>

Examples

```
rm(list=ls())

File1 <- system.file("extdata","test.mat",package="CINOEDV")
File2 <- system.file("extdata","test1.mat",package="CINOEDV")
File3 <- system.file("extdata","test_Name.mat",package="CINOEDV")
File4 <- system.file("extdata","test1_Name.mat",package="CINOEDV")

FileName <- c(File1,File2)
MaxOrder <- 2
RThreshold <- c(1,1)
NThreshold <- c(10,10)
measure <- 1
SNFName <- c(File3,File4)
Stra <- 1
Pop <- 100
Iter <- 10
```



```

SingleEffect <- Effect$SingleEffect
TwoEffect <- Effect$TwoEffect
ThreeEffect <- Effect$ThreeEffect
FourEffect <- Effect$FourEffect
FiveEffect <- Effect$FiveEffect

# SNP Name Notation
Effect <- NotationName(MaxOrder,SingleEffect,TwoEffect,ThreeEffect,FourEffect
                      ,FiveEffect,SNPNames)

SingleEffect <- Effect$SingleEffect
TwoEffect <- Effect$TwoEffect
ThreeEffect <- Effect$ThreeEffect
FourEffect <- Effect$FourEffect
FiveEffect <- Effect$FiveEffect

# Collect Vertices and Edges
GraphData <- NetworkData(SingleEffect,TwoEffect,ThreeEffect,FourEffect,
                        FiveEffect,RatioThreshold,NumberThreshold)
Edges <- GraphData$edges
Vertices <- GraphData$vertices

# Construct Complete Graph
ConstructCompleteGraph(Vertices,Edges,6,SaveFileName)

# Plot Top Effects
TpEffect <- PlotTopEffects(Vertices,20,SaveFileName)
TopEffect <- TpEffect$TopEffect
CombinationEffect <- TpEffect$CombinationEffect

# Degree Analysis
Degrees <- DegreeAnalysis(Vertices,Edges,SaveFileName)
Degrees <- Degrees$Degrees
print(Degrees)

# Split subgraphs
SubgraphSNPs <- SubgraphSplit(Vertices,Edges)
SubgraphSNPs <- SubgraphSNPs$SubgroupSNPs

# heatmap Factor
HeatMapFactors <- HeatMapFactor(pts,class,factor = c(5, 8),SaveFileName,Title = "")
HeatMapFactors <- HeatMapFactors$HeatMapFactors

```

BatCINOEDV

Batch mode for using CINOEDV

Description

Batch mode for using CINOEDV function.

Usage

```
BatCINOEDV(FileName, MaxOrder, RatioThreshold,
           NumberThreshold, measure, Strategy, Population, Iteration, SNPNameFileName)
```

Arguments

FileName	character. The file name with its format (.mat) that saves SNP data. It has two variables, i.e., pts and class. For pts, Row -> Sample, Column -> SNP, 1 -> AA, 2 -> Aa, 3 -> aa. For class, Row -> 1, Column -> class label, 1 -> case, 2-> control.
MaxOrder	numeric. The considered maximum order of epistatic interactions. It must be setted as 1, 2, 3, 4, or 5.
RatioThreshold	character. It controls the numbers of detected SNPs or SNP-combinations with the help of NumberThreshold. The length of RatioThreshold is equal to Max-Order. Each element is a decimal in [0,1].
NumberThreshold	character. It controls the numbers of detected SNPs or SNP-combinations with the help of RatioThreshold. The length of NumberThreshold is equal to Max-Order. Each element is an integer.
measure	numeric. The used evaluation measure. 1 -> the classic co-information measure; 2 -> the normalized co-information measure; 3 -> TingHu's co-informationn measure.
Strategy	The search strategy, 1 -> The exhaustive search strategy, 2 -> The PSO search strategy
Population	numeric. The number of particles. For example, Population=1000.
Iteration	numeric. The number of iterations. For example, Iteration=100.
SNPNameFileName	character. The file name with its format (.mat) that saves the names of SNPs. The file has only one variable, i.e., Name. In Name, Row -> 1, Column -> SNP Name, and the length is equal to RowNum. If not exist such file (default), SNPNameFileName <- NA.

Value

None

Note

The returned values save in files with (.mat) or (.RData) formats respectively.

Author(s)

Junliang Shang <shangjunliang110@163.com>

References

None

Examples

```
File1 <- system.file("extdata","test.mat",package="CINOEDV")
File2 <- system.file("extdata","test1.mat",package="CINOEDV")
File3 <- system.file("extdata","test1_Name.mat",package="CINOEDV")
FileName <- c(File1,File2)
SNFName <- c(NA,File3)
MaxOrder <- 2
RThreshold <- c(1, 1)
NThreshold <- c(10, 10)
measure <- 1
Stra <- 1
Pop <- 10
Iter <- 10
BatCINOEDV(FileName, MaxOrder, RThreshold, NThreshold, measure, Stra, Pop, Iter, SNFName)
```

CheckVerticeType	<i>Test Vertice Type</i>
------------------	--------------------------

Description

This function check a vertice whether belongs to a real vertice or a virtual one.

Usage

```
CheckVerticeType(Vertice)
```

Arguments

Vertice character. A vertice in the network, namely, the graph.

Value

Whether: logical. Whether the checked vertice belongs to a real vertice or a virtual one.

Author(s)

Junliang Shang <shangjunliang110@163.com>

References

None

Examples

```
Vertice <- "rs1366208"
Whether <- CheckVerticeType(Vertice)
Whether <- Whether$Whether
Vertice <- "rs2801008:rs4763023"
Whether <- CheckVerticeType(Vertice)
Whether <- Whether$Whether
```

CINOEDV_Main

Co-Information based N-Order Epistasis Detector and Visualizer

Description

This function integrates almost all functions of the package for providing one stop service.

Usage

```
CINOEDV_Main()
```

Details

No input parameters

Value

parameters	list. It returns six parameters, including FileName, MaxOrder, RatioThreshold, NumberThreshold, SNPNameFileName, and measure. FileName: character. The file name with its format (.mat) that saves SNP data. MaxOrder: numeric. The considered maximum order of epistatic interactions. RatioThreshold: numeric. It controls the numbers of detected SNPs or SNP-combinations with the help of NumberThreshold. NumberThreshold: numeric. It controls the numbers of detected SNPs or SNP-combinations with the help of RatioThreshold. SNPNameFileName: character or logical (NA). The file name with its format (.mat) that saves the names of SNPs. measure: numeric. The used evaluation measure.
data	list. It returns used data, including pts, class, and SNPNames. pts: matrix. SNP data. class: matrix. Class labels of samples. SNPNames: character or logical (NA). Names of SNPs.
results	list. It returns detected results, including SingleEffect, TwoEffect, ThreeEffect, FourEffect, and FiveEffect. SingleEffect: matrix. main Effects of SNPs. TwoEffect: matrix. interaction Effects of two-SNP combinations. ThreeEffect: matrix. interaction Effects of three-SNP combinations. FourEffect: matrix. interaction Effects of four-SNP combinations. FiveEffect: matrix. interaction Effects of five-SNP combinations.
graphs	list. It returns observed results from the constructed graph, including Edges, Vertices, TopEffect, Degrees, SubgraphSNPs, CombinationEffect and HeatMapFactors. Edges: matrix. Edges of constructed graphs. Vertices: matrix. Vertices of constructed graphs, including real vertices and virtual vertices. TopEffect: numeric. Top independent effects of SNPs or SNP-combinations. Degrees: matrix. Degrees of real vertices. SubgraphSNPs: list. SNPs in each subgraph of the graph. CombinationEffect: numeric. Top combination effects of SNPs or SNP-combinations. HeatMapFactors: data.frame. The heatmap data for observing how a SNP or a SNP-combination influencing the phenotype.

Note

The returned values also save in files with (.mat) or (.RData) formats respectively.

Author(s)

Junliang Shang <shangjunliang110@163.com>

References

None

Examples

```
# See details of package CINOEDV
```

class	<i>Class labels of samples</i>
-------	--------------------------------

Description

Class labels of samples

Usage

```
data(class)
```

Format

The format is: num [1, 1:4000] 2 1 1 2 1 1 1 1 1 ... - attr(*, "dimnames")=List of 2 ..\$: NULL ..\$
: chr [1:4000] "Sample1" "Sample2" "Sample3" "Sample4" ...

References

None

Examples

```
data(class)
```

CoInformation

Co-Information Computation

Description

This function compute co-information value of a given SNP combination.

Usage

```
CoInformation(pts, class, factor)
```

Arguments

pts	matrix. SNP data. Each row represents a sample. Each column represents a SNP. For the element, 1 -> AA, 2 -> Aa, 3 -> aa.
class	matrix. Class labels of samples. It only has one row. Each column represents a class label. For the element, 1 -> case, 2-> control.
factor	numeric. The considered SNP or SNP-combination. For example, factor <- 5, or factor <- c(2,5)

Value

Co_Information_Value: matrix. co-information value of a give SNP combination.

Author(s)

Junliang Shang <shangjunliang110@163.com>

References

None

Examples

```
data(pts)
data(class)
factor <- c(2,5)
V <- CoInformation(pts, class, factor)
Co_Information_Value <- V$Co_Information_Value
```

CombinationEntropy *Combination Entropy Computation*

Description

This function compute combination entropy of given variables. These variables can be one SNP, the class label, SNP-combination, or SNP-combination-class label.

Usage

```
CombinationEntropy(data)
```

Arguments

data matrix. The given variables, for example, `data <- cbind(pts[,factor],t(class))`

Value

Combination_Entropy_Value: matrix. combination entropy value.

Author(s)

Junliang Shang <shangjunliang110@163.com>

References

None

Examples

```
data(pts)
data(class)
factor <- c(2, 5)
data <- cbind(pts[,factor],t(class))
V <- CombinationEntropy(data)
Combination_Entropy_Value <- V$Combination_Entropy_Value
```

`ConstructCompleteGraph`*Construct complete graph*

Description

This function construct complete graph by using all vertices and edges.

Usage

```
ConstructCompleteGraph(Vertices, Edges, BaseSize = 6, SaveFileName = "")
```

Arguments

Vertices	matrix. Vertices of constructed graphs, including real vertices and virtual vertices. The first column represents SNP ID or SNP-combination ID. The second column represents effect value. The third column represents the class of vertices, "1" -> real vertice, others -> virtual vertice.
Edges	matrix. Edges of constructed graphs.
BaseSize	numeric. Basic size of vertices in the graph. By default, BaseSize <- 6.
SaveFileName	character. Basic file name for saving figure. By default, SaveFileName <- "".

Value

None

Author(s)

Junliang Shang <shangjunliang110@163.com>

References

None

Examples

```
data(Vertices)
data(Edges)
ConstructCompleteGraph(Vertices, Edges, BaseSize = 6, SaveFileName = "")
```

DegreeAnalysis	<i>Degree analysis of real vertices</i>
----------------	---

Description

Degree analysis of real vertices.

Usage

```
DegreeAnalysis(Vertices, Edges, SaveFileName = "")
```

Arguments

Vertices	matrix. Vertices of constructed graphs, including real vertices and virtual vertices. The first column represents SNP ID or SNP-combination ID. The second column represents effect value. The third column represents the class of vertices, "1" -> real vertice, others -> virtual vertice.
Edges	matrix. Edges of constructed graphs.
SaveFileName	character. Basic file name for saving figure. By default, SaveFileName <- "".

Value

Degrees: matrix. Degrees of real vertices.

Author(s)

Junliang Shang <shangjunliang110@163.com>

References

None

Examples

```
data(Vertices)
data(Edges)
Degrees <- DegreeAnalysis(Vertices, Edges, SaveFileName = "")
Degrees <- Degrees$Degrees
```

Edges *Edges of constructed graphs*

Description

Edges of constructed graphs

Usage

```
data(Edges)
```

Format

The format is: chr [1:45, 1:2] "rs00008:rs00019" "rs00005:rs00017" ... - attr(*, "dimnames")=List of 2 ..\$: NULL ..\$: chr [1:2] "From" "To"

References

None

Examples

```
data(Edges)
```

EvaluationMeasure *Evaluation Measure*

Description

This function provides several co-information based measures for measuring main or interaction effect of a SNP or SNP-combination.

Usage

```
EvaluationMeasure(factor, pts, class, measure = 1)
```

Arguments

pts	matrix. SNP data. Each row represents a sample. Each column represents a SNP. For the element, 1 -> AA, 2 -> Aa, 3 -> aa.
class	matrix. Class labels of samples. It only has one row. Each column represents a class label. For the element, 1 -> case, 2-> control.
factor	numeric. The considered SNP or SNP-combination. For example, factor <- 5, or factor <- c(2,5)
measure	numeric. The used evaluation measure. 1 -> the classic co-information measure; 2 -> the normalized co-information measure; 3 -> TingHu's co-informatiomm measure.

Value

Value: matrix. The main or interaction effect value corresponding to a sing SNP or a SNP combination.

Author(s)

Junliang Shang <shangjunliang110@163.com>

References

None

Examples

```
factor <- c(2,5)
data(pts)
data(class)
V <- EvaluationMeasure(factor, pts, class, measure = 1)
Value <- V$Value
```

ExhaustiveSearch

Exhaustive Search

Description

This function exhaustively compute main effects of all SNPs and interaction effects of all SNP-combinations within the maximum order.

Usage

```
ExhaustiveSearch(pts, class, MaxOrder = 3, measure = 1, alpha = 0)
```

Arguments

pts	matrix. SNP data. Each row represents a sample. Each column represents a SNP. For the element, 1 -> AA, 2 -> Aa, 3 -> aa.
class	matrix. Class labels of samples. It only has one row. Each column represents a class label. For the element, 1 -> case, 2-> control.
MaxOrder	numeric. The considered maximum order of epistatic interactions. It must be setted as 1, 2, 3, 4, or 5.
measure	numeric. The used evaluation measure. 1 -> the classic co-information measure; 2 -> the normalized co-information measure; 3 -> TingHu's co-informationn measure.
alpha	numeric. The lower threshold of effects, either main effects or interaction effects, which must be higher or equal to 0, By default, alpha <- 0.

Value

SingleEffect	matrix. main Effects of SNPs. There are 2 columns. The first column saves all SNPs, and the second column saves their corresponding effects. Descending save according to their effects.
TwoEffect	matrix. interaction Effects of two-SNP combinations. There are three columns. The first two columns save all two-SNP combinations, and the last column saves their corresponding effects. Descending save according to their interaction effects.
ThreeEffect	matrix. interaction Effects of three-SNP combinations. There are four columns. The first three columns save all three-SNP combinations, and the last column saves their corresponding effects. Descending save according to their interaction effects.
FourEffect	matrix. interaction Effects of four-SNP combinations. There are five columns. The first four columns save all four-SNP combinations, and the last column saves their corresponding effects. Descending save according to their interaction effects.
FiveEffect	matrix. interaction Effects of five-SNP combinations. There are six columns. The first five columns save all five-SNP combinations, and the last column saves their corresponding effects. Descending save according to their interaction effects.

Author(s)

Junliang Shang <shangjunliang110@163.com>

References

None

Examples

```
data(pts)
data(class)
Effect <- ExhaustiveSearch(pts, class, MaxOrder = 2, measure = 1, alpha = 0)
SingleEffect <- Effect$SingleEffect
TwoEffect <- Effect$TwoEffect
ThreeEffect <- Effect$ThreeEffect
FourEffect <- Effect$FourEffect
FiveEffect <- Effect$FiveEffect
```

FiveEffect

Interaction Effects of five-SNP combinations

Description

Interaction Effects of five-SNP combinations

Usage

```
data(FiveEffect)
```

Format

The format is: num [1, 1] 0

References

None

Examples

```
data(FiveEffect)
```

FourEffect

Interaction Effects of four-SNP combinations

Description

Interaction Effects of four-SNP combinations

Usage

```
data(FourEffect)
```

Format

The format is: num [1, 1] 0

References

None

Examples

```
data(FourEffect)
```

HeatMapFactor	<i>Heatmap function</i>
---------------	-------------------------

Description

This function create a heatmap figure for visualizing how a SNP or a SNP-combination influencing the phenotype.

Usage

```
HeatMapFactor(pts, class, factor, SaveFileName = "", Title = "")
```

Arguments

pts	matrix. SNP data. Each row represents a sample. Each column represents a SNP. For the element, 1 -> AA, 2 -> Aa, 3 -> aa.
class	matrix. Class labels of samples. It only has one row. Each column represents a class label. For the element, 1 -> case, 2-> control.
factor	numeric. The considered SNP or SNP-combination. For example, factor <- 5, or factor <- c(2,5)
SaveFileName	character. Basic file name for saving figure. By default, SaveFileName <- "".
Title	character. Title of the heatmap figure. By default, Title <- "".

Value

HeatMapFactors: data.frame. The heatmap data for observing how a SNP or a SNP-combination influencing the phenotype.

Author(s)

Junliang Shang <shangjunliang110@163.com>

References

None

Examples

```
data(pts)
data(class)
factor <- c(2,5)
H <- HeatMapFactor(pts, class, factor, SaveFileName = "", Title = "")
HeatMapFactors <- H$HeatMapFactors
```

InputData

Input data

Description

Input SNP data from a file with (.mat) format.

Usage

```
InputData(FileName)
```

Arguments

FileName character. The file name with its format (.mat) that saves SNP data. It has two variables, i.e., pts and class. For pts, Row -> Sample, Column -> SNP, 1 -> AA, 2 -> Aa, 3 -> aa. For class, Row -> 1, Column -> class label, 1 -> case, 2-> control.

Value

pts matrix. Each row represents a sample. Each column represents a SNP. For the element, 1 -> AA, 2 -> Aa, 3 -> aa.

class matrix. It only has one row. Each column represents a class label. For the element, 1 -> case, 2-> control.

Author(s)

Junliang Shang <shangjunliang110@163.com>

References

None

Examples

```
# The files (test.mat) should be downloaded from http://sourceforge.net/projects/cinoedv/files/.

FileName <- system.file("extdata", "test.mat", package="CINOEDV")
Data <- InputData(FileName)
pts <- Data$pts
class <- Data$class
```

InstallPackage	<i>Install CINOEDV used packages</i>
----------------	--------------------------------------

Description

Install CINOEDV used packages, including R.matlab, igraph, ggplot2, and reshape2.

Usage

```
InstallPackage()
```

Value

None

Author(s)

Junliang Shang <shangjunliang110@163.com>

References

None

Examples

```
InstallPackage()
```

NetworkData	<i>Collect vertices and edges for network construction</i>
-------------	--

Description

Collect vertices and edges from effect data (SingleEffect, TwoEffect, ThreeEffect, FourEffect, FiveEffect) for network construction.

Usage

```
NetworkData(SingleEffect, TwoEffect, ThreeEffect,  
            FourEffect, FiveEffect, RatioThreshold, NumberThreshold)
```

Arguments

SingleEffect	matrix. main Effects of SNPs. There are 2 columns. The first column saves all SNPs, and the second column saves their corresponding effects. Descending save according to their effects.
TwoEffect	matrix. interaction Effects of two-SNP combinations. There are three columns. The first two columns save all two-SNP combinations, and the last column saves their corresponding effects. Descending save according to their interaction effects.
ThreeEffect	matrix. interaction Effects of three-SNP combinations. There are four columns. The first three columns save all three-SNP combinations, and the last column saves their corresponding effects. Descending save according to their interaction effects.
FourEffect	matrix. interaction Effects of four-SNP combinations. There are five columns. The first four columns save all four-SNP combinations, and the last column saves their corresponding effects. Descending save according to their interaction effects.
FiveEffect	matrix. interaction Effects of five-SNP combinations. There are six columns. The first five columns save all five-SNP combinations, and the last column saves their corresponding effects. Descending save according to their interaction effects.
RatioThreshold	character. It controls the numbers of detected SNPs or SNP-combinations with the help of NumberThreshold. The length of RatioThreshold is equal to Max-Order. Each element is a decimal in [0,1].
NumberThreshold	character. It controls the numbers of detected SNPs or SNP-combinations with the help of RatioThreshold. The length of NumberThreshold is equal to Max-Order. Each element is an integer.

Details

Parameters 'RatioThreshold' and 'NumberThreshold' are used together to control the numbers of vertices and edges. That is, $\min(\text{NumberThreshold}[1], \text{RatioThreshold}[1] * \text{nrow}(\text{SingleEffect}))$, $\min(\text{NumberThreshold}[2], \text{RatioThreshold}[2] * \text{nrow}(\text{TwoEffect}))$, $\min(\text{NumberThreshold}[3], \text{RatioThreshold}[3] * \text{nrow}(\text{ThreeEffect}))$, $\min(\text{NumberThreshold}[4], \text{RatioThreshold}[4] * \text{nrow}(\text{FourEffect}))$, $\min(\text{NumberThreshold}[5], \text{RatioThreshold}[5] * \text{nrow}(\text{FiveEffect}))$. Using above settings, the numbers of virtual vertexes denoting high order epistatic interactions in the graph are clear. Nevertheless, the number of Real Vertexes (i.e., the number of SNPs) is unclear, which is obviously more than the above set, since some of them must be included to connect virtual vertexes.

Value

Vertices	matrix. Vertices of constructed graphs, including real vertices and virtual vertices. The first column represents SNP ID or SNP-combination ID. The second column represents effect value. The third column represents the class of vertices, "1" -> real vertice, others -> virtual vertice.
Edges	matrix. Edges of constructed graphs.

Author(s)

Junliang Shang <shangjunliang110@163.com>

References

None

Examples

```
data(SingleEffect)
data(TwoEffect)
data(ThreeEffect)
data(FourEffect)
data(FiveEffect)
RatioThreshold <- c(1,1,1,1,1)
NumberThreshold <- c(10,10,10,10,10)
Net <- NetworkData(SingleEffect, TwoEffect, ThreeEffect, FourEffect,
  FiveEffect, RatioThreshold, NumberThreshold)
Vertices <- Net$Vertices
Edges <- Net$Edges
```

NormalizationEffect *Normalization Effect*

Description

Normalization of main effects, and n-order interaction effects in SingleEffect, TwoEffect, ThreeEffect, FourEffect and FiveEffect respectively.

Usage

```
NormalizationEffect(MaxOrder, SingleEffect, TwoEffect,
  ThreeEffect, FourEffect, FiveEffect, SaveFileName = "")
```

Arguments

MaxOrder	numeric. The considered maximum order of epistatic interactions. It must be setted as 1, 2, 3, 4, or 5.
SingleEffect	matrix. main Effects of SNPs. There are 2 columns. The first column saves all SNPs, and the second column saves their corresponding effects. Descending save according to their effects.
TwoEffect	matrix. interaction Effects of two-SNP combinations. There are three columns. The first two columns save all two-SNP combinations, and the last column saves their corresponding effects. Descending save according to their interaction effects.

ThreeEffect	matrix. interaction Effects of three-SNP combinations. There are four columns. The first three columns save all three-SNP combinations, and the last column saves their corresponding effects. Descending save according to their interaction effects.
FourEffect	matrix. interaction Effects of four-SNP combinations. There are five columns. The first four columns save all four-SNP combinations, and the last column saves their corresponding effects. Descending save according to their interaction effects.
FiveEffect	matrix. interaction Effects of five-SNP combinations. There are six columns. The first five columns save all five-SNP combinations, and the last column saves their corresponding effects. Descending save according to their interaction effects.
SaveFileName	character. Basic file name for saving figure. By default, SaveFileName <- "".

Value

SingleEffect	matrix. main Effects of SNPs. There are 2 columns. The first column saves all SNPs, and the second column saves their corresponding effects. Descending save according to their effects.
TwoEffect	matrix. interaction Effects of two-SNP combinations. There are three columns. The first two columns save all two-SNP combinations, and the last column saves their corresponding effects. Descending save according to their interaction effects.
ThreeEffect	matrix. interaction Effects of three-SNP combinations. There are four columns. The first three columns save all three-SNP combinations, and the last column saves their corresponding effects. Descending save according to their interaction effects.
FourEffect	matrix. interaction Effects of four-SNP combinations. There are five columns. The first four columns save all four-SNP combinations, and the last column saves their corresponding effects. Descending save according to their interaction effects.
FiveEffect	matrix. interaction Effects of five-SNP combinations. There are six columns. The first five columns save all five-SNP combinations, and the last column saves their corresponding effects. Descending save according to their interaction effects.

Author(s)

Junliang Shang <shangjunliang110@163.com>

References

None

Examples

```

data(pts)
data(class)
MaxOrder <- 2
measure <- 1
SaveFileName <- ""

# Search Strategies
Effect <- ExhaustiveSearch(pts,class,MaxOrder,measure,0)
SingleEffect <- Effect$SingleEffect
TwoEffect <- Effect$TwoEffect
ThreeEffect <- Effect$ThreeEffect
FourEffect <- Effect$FourEffect
FiveEffect <- Effect$FiveEffect

# Normalization
Effect <- NormalizationEffect(MaxOrder,SingleEffect,TwoEffect,ThreeEffect,FourEffect
                              ,FiveEffect,SaveFileName)

SingleEffect <- Effect$SingleEffect
TwoEffect <- Effect$TwoEffect
ThreeEffect <- Effect$ThreeEffect
FourEffect <- Effect$FourEffect
FiveEffect <- Effect$FiveEffect

```

NotationName	<i>Notation of real SNP Name</i>
--------------	----------------------------------

Description

If there are real SNP names which will be used for constructing graphs and further analysis, this function then replaces SNP indexes by real SNP names.

Usage

```

NotationName(MaxOrder, SingleEffect, TwoEffect,
              ThreeEffect, FourEffect, FiveEffect, SNPNames = NA)

```

Arguments

MaxOrder	numeric. The considered maximum order of epistatic interactions. It must be setted as 1, 2, 3, 4, or 5.
SingleEffect	matrix. main Effects of SNPs. There are 2 columns. The first column saves all SNPs, and the second column saves their corresponding effects. Ddescending save according to their effects.

TwoEffect	matrix. interaction Effects of two-SNP combinations. There are three columns. The first two columns save all two-SNP combinations, and the last column saves their corresponding effects. Descending save according to their interaction effects.
ThreeEffect	matrix. interaction Effects of three-SNP combinations. There are four columns. The first three columns save all three-SNP combinations, and the last column saves their corresponding effects. Descending save according to their interaction effects.
FourEffect	matrix. interaction Effects of four-SNP combinations. There are five columns. The first four columns save all four-SNP combinations, and the last column saves their corresponding effects. Descending save according to their interaction effects.
FiveEffect	matrix. interaction Effects of five-SNP combinations. There are six columns. The first five columns save all five-SNP combinations, and the last column saves their corresponding effects. Descending save according to their interaction effects.
SNPNames	character or logical (NA). Names of SNPs. Row -> 1, Column -> SNP Name

Value

SingleEffect	matrix. main Effects of SNPs. There are 2 columns. The first column saves all SNPs, and the second column saves their corresponding effects. Ddescending save according to their effects.
TwoEffect	matrix. interaction Effects of two-SNP combinations. There are three columns. The first two columns save all two-SNP combinations, and the last column saves their corresponding effects. Descending save according to their interaction effects.
ThreeEffect	matrix. interaction Effects of three-SNP combinations. There are four columns. The first three columns save all three-SNP combinations, and the last column saves their corresponding effects. Descending save according to their interaction effects.
FourEffect	matrix. interaction Effects of four-SNP combinations. There are five columns. The first four columns save all four-SNP combinations, and the last column saves their corresponding effects. Descending save according to their interaction effects.
FiveEffect	matrix. interaction Effects of five-SNP combinations. There are six columns. The first five columns save all five-SNP combinations, and the last column saves their corresponding effects. Descending save according to their interaction effects.

Author(s)

Junliang Shang <shangjunliang110@163.com>

References

None

Examples

```

data(pts)
data(class)
MaxOrder <- 2
measure <- 1
SaveFileName <- ""
SNPNames <- c("rs1366208","rs1950123","rs10485136","rs1484673",
              "rs1484433","rs1795462","rs10501558","rs2018041",
              "rs10489495","rs3846302","rs2801008","0","rs1773409",
              "rs4786670","rs2260614","rs1326298","rs9315726",
              "rs1582545","rs10505084","rs4763023")

# Search Strategies
Effect <- ExhaustiveSearch(pts,class,MaxOrder,measure,0)
SingleEffect <- Effect$SingleEffect
TwoEffect <- Effect$TwoEffect
ThreeEffect <- Effect$ThreeEffect
FourEffect <- Effect$FourEffect
FiveEffect <- Effect$FiveEffect

# Normalization
Effect <- NormalizationEffect(MaxOrder,SingleEffect,TwoEffect,ThreeEffect,FourEffect
                              ,FiveEffect,SaveFileName)

SingleEffect <- Effect$SingleEffect
TwoEffect <- Effect$TwoEffect
ThreeEffect <- Effect$ThreeEffect
FourEffect <- Effect$FourEffect
FiveEffect <- Effect$FiveEffect

# SNP Name Notation
Effect <- NotationName(MaxOrder,SingleEffect,TwoEffect,ThreeEffect,FourEffect
                      ,FiveEffect,SNPNames)

SingleEffect <- Effect$SingleEffect
TwoEffect <- Effect$TwoEffect
ThreeEffect <- Effect$ThreeEffect
FourEffect <- Effect$FourEffect
FiveEffect <- Effect$FiveEffect

```

PlotTopEffects

Plot top n effects with their corresponding SNPs or SNP-combinations

Description

Effects can be respectively considered as independent effects and combination effects. Independent Effect: Effect that only the SNP or SNP-combination has. Combination Effect: Effect is the addition of all effects of SNP-combination and its sub-combinations. This function plots top n

effects (including Independent Effect and Combination Effect) with their corresponding SNPs or SNP-combinations.

Usage

```
PlotTopEffects(Vertices, Top = 20, SaveFileName = "")
```

Arguments

Vertices matrix. Vertices of constructed graphs, including real vertices and virtual vertices. The first column represents SNP ID or SNP-combination ID. The second column represents effect value. The third column represents the class of vertices, "1" -> real vertice, others -> virtual vertice.

Top numeric. Top n Effects. By default, Top <- 20.

SaveFileName character. Basic file name for saving figure. By default, SaveFileName <- "".

Value

TopEffect numeric. Top independent effects of SNPs or SNP-combinations.

CombinationEffect numeric. Top combination effects of SNPs or SNP-combinations.

Author(s)

Junliang Shang <shangjunliang110@163.com>

References

None

Examples

```
data(Vertices)
data(Edges)
TP <- PlotTopEffects(Vertices, Top = 20, SaveFileName = "")
TopEffect <- TP$TopEffect
CombinationEffect <- TP$CombinationEffect
```

Description

PSO based method for computing main effects of selected SNPs and interaction effects of selected SNP-combinations within the maximum order.

Usage

```
PSOsearch(pts,class,MaxOrder=3,Population=1000,Iteration=100,
          c1=2,c2=2,TopSNP=10,measure=1,alpha=0)
```

Arguments

pts	matrix. SNP data. Each row represents a sample. Each column represents a SNP. For the element, 1 -> AA, 2 -> Aa, 3 -> aa.
class	matrix. Class labels of samples. It only has one row. Each column represents a class label. For the element, 1 -> case, 2-> control.
MaxOrder	numeric. The considered maximum order of epistatic interactions. It must be setted as 1, 2, 3, 4, or 5.
Population	numeric. The number of particles. For example, Population=1000.
Iteration	numeric. The number of iterations. For example, Iteration=100.
c1	numeric. The acceleration factor of individual experience. For example, c1=2.
c2	numeric. The acceleration factor of global experience. For example, c2=2.
TopSNP	numeric. The selected SNPs with top indexes. For example, TopSNP=10.
measure	numeric. The used evaluation measure. 1 -> the classic co-information measure; 2 -> the normalized co-information measure; 3 -> TingHu's co-informationn measure.
alpha	numeric. The lower threshold of effects, either main effects or interaction effects, which must be higher or equal to 0, By default, alpha <- 0.

Value

SingleEffect	matrix. main Effects of SNPs. There are 2 columns. The first column saves all SNPs, and the second column saves their corresponding effects. Ddescending save according to their effects.
TwoEffect	matrix. interaction Effects of two-SNP combinations. There are three columns. The first two columns save all two-SNP combinations, and the last column saves their corresponding effects. Descending save according to their interaction effects.
ThreeEffect	matrix. interaction Effects of three-SNP combinations. There are four columns. The first three columns save all three-SNP combinations, and the last column saves their corresponding effects. Descending save according to their interaction effects.
FourEffect	matrix. interaction Effects of four-SNP combinations. There are five columns. The first four columns save all four-SNP combinations, and the last column saves their corresponding effects. Descending save according to their interaction effects.
FiveEffect	matrix. interaction Effects of five-SNP combinations. There are six columns. The first five columns save all five-SNP combinations, and the last column saves their corresponding effects. Descending save according to their interaction effects.

Author(s)

Junliang Shang <shangjunliang110@163.com>

References

None

Examples

```
data(pts)
data(class)
MaxOrder <- 2
Pop <- 10
Iter <- 10
c1 <- 2
c2 <- 2
TopSNP <- 10
measure <- 1
alpha <- 0
Effect <- PS0Search(pts, class, MaxOrder, Pop, Iter, c1, c2, TopSNP, measure, alpha)
SingleEffect <- Effect$SingleEffect
TwoEffect <- Effect$TwoEffect
ThreeEffect <- Effect$ThreeEffect
FourEffect <- Effect$FourEffect
FiveEffect <- Effect$FiveEffect
```

pts

SNP data

Description

SNP data

Usage

data(pts)

Format

The format is: int [1:4000, 1:20] 1 2 1 3 1 2 2 1 1 1 ... - attr(*, "dimnames")=List of 2 ..\$: chr [1:4000] "Sample1" "Sample2" "Sample3" "Sample4"\$: chr [1:20] "SNP1" "SNP2" "SNP3" "SNP4" ...

References

None

Examples

data(pts)

SingleEffect	<i>Main Effects of SNPs</i>
--------------	-----------------------------

Description

Main Effects of SNPs

Usage

```
data(SingleEffect)
```

Format

The format is: chr [1:20, 1:2] "rs00013" "rs00010" "rs00006" "rs00001" ... - attr(*, "dimnames")=List of 2 ..\$: NULL ..\$: chr [1:2] "SNP" "Value"

References

None

Examples

```
data(SingleEffect)
```

SubgraphSplit	<i>Split subgraphs</i>
---------------	------------------------

Description

Split subgraphs using walktrap.community algorithm

Usage

```
SubgraphSplit(Vertices, Edges)
```

Arguments

Vertices	matrix. Vertices of constructed graphs, including real vertices and virtual vertices. The first column represents SNP ID or SNP-combination ID. The second column represents effect value. The third column represents the class of vertices, "1" -> real vertice, others -> virtual vertice.
Edges	matrix. Edges of constructed graphs.

Value

SubgroupSNPs: list. SNPs in each subgraph of the graph.

Author(s)

Junliang Shang <shangjunliang110@163.com>

References

None

Examples

```
data(Vertices)
data(Edges)
SubgroupSNPs <- SubgraphSplit(Vertices, Edges)
SubgroupSNPs <- SubgroupSNPs$SubgroupSNPs
```

TestMaxOrder

Test the parameter MaxOrder

Description

This function check the parameter MaxOrder. MaxOrder is the maximum order of epistatic interactions that CINOEDV considered.

Usage

```
TestMaxOrder(MaxOrder)
```

Arguments

MaxOrder character. It must be setted as "1", "2", "3", "4", or "5".

Value

None

Author(s)

Junliang Shang <shangjunliang110@163.com>

References

None

Examples

```
MaxOrder <- "2"
TestMaxOrder(MaxOrder)
```

TestNumberThreshold *Test the parameter NumberThreshold*

Description

This function check the parameter NumberThreshold

Usage

```
TestNumberThreshold(MaxOrder, NumberThreshold)
```

Arguments

MaxOrder numeric. The considered maximum order of epistatic interactions. It must be setted as 1, 2, 3, 4, or 5.

NumberThreshold character. It controls the numbers of detected SNPs or SNP-combinations with the help of RatioThreshold. The length of NumberThreshold is equal to Max-Order. Each element is an integer with the character format.

Value

None

Author(s)

Junliang Shang <shangjunliang110@163.com>

References

None

Examples

```
MaxOrder <- 3
NumberThreshold <- c("5", "20", "10")
TestNumberThreshold(MaxOrder, NumberThreshold)
```

TestPSOParameters *Check the PSO parameters*

Description

This function Check the PSO parameters 'Population' and 'Iteration'.

Usage

```
TestPSOParameters(Population, Iteration)
```

Arguments

Population numeric. The number of particles.
Iteration numeric. The number of iterations.

Value

None

Author(s)

Junliang Shang <shangjunliang110@163.com>

References

None

Examples

```
Population <- 1000  
Iteration <- 50  
TestPSOParameters(Population, Iteration)
```

TestRatioThreshold *Test the parameter RatioThreshold*

Description

This function check the parameter RatioThreshold.

Usage

```
TestRatioThreshold(MaxOrder, RatioThreshold)
```

Arguments

- MaxOrder numeric. The considered maximum order of epistatic interactions. It must be setted as 1, 2, 3, 4, or 5.
- RatioThreshold character. It controls the numbers of detected SNPs or SNP-combinations with the help of NumberThreshold. The length of RatioThreshold is equal to Max-Order. Each element is a decimal in [0,1] with the character format.

Value

None

Author(s)

Junliang Shang <shangjunliang110@163.com>

References

None

Examples

```
MaxOrder <- 3
RatioThreshold <- c("1.0", "0.5", "0.2")
TestRatioThreshold(MaxOrder, RatioThreshold)
```

TestSNPNameFile	<i>Test the parameter TestSNPNameFile</i>
-----------------	---

Description

This function check the parameter TestSNPNameFile. If there are real SNP names which will be used for constructing graphs and further analysis, the name of file that saves real SNP names should be provided.

Usage

```
TestSNPNameFile(RowNum, SNPNameFileName = NA)
```

Arguments

- RowNum numeric. It is the number of considered SNPs.
- SNPNameFileName character or logical (NA). The file name with its format (.mat) that saves the names of SNPs. The file has only one variable, i.e., Name. In Name, Row -> 1, Column -> SNP Name, and the length is equal to RowNum. If not exist such file (default), SNPNameFileName <- NA.

Value

SNPNames: character or logical (NA). Names of SNPs.

Author(s)

Junliang Shang <shangjunliang110@163.com>

References

None

Examples

```
RowNum <- 10
SNPNameFileName <- NA
SNPNames <- TestSNPNameFile(RowNum, SNPNameFileName)
SNPNames <- SNPNames$SNPNames
```

ThreeEffect

Interaction Effects of three-SNP combinations

Description

Interaction Effects of three-SNP combinations

Usage

```
data(ThreeEffect)
```

Format

The format is: chr [1:1137, 1:4] "rs00002" "rs00008" "rs00004" "rs00001" ... - attr(*, "dim-names")=List of 2 ..\$: NULL ..\$: chr [1:4] "SNP1" "SNP2" "SNP3" "Value"

References

None

Examples

```
data(ThreeEffect)
```

tic *Start stopwatch timer*

Description

tic starts a stopwatch timer to measure performance. The function records the internal time at execution of the tic command. Display the elapsed time with the toc function.

Usage

```
tic(gcFirst = TRUE, type = c("elapsed", "user.self", "sys.self"))
```

Arguments

```
gcFirst      gcFirst <- TRUE
type         type <- c("elapsed", "user.self", "sys.self")
```

Value

None

Author(s)

Junliang Shang <shangjunliang110@163.com>

References

None

Examples

```
tic()
Sys.sleep(2)
toc()
```

toc *Read elapsed time from stopwatch*

Description

toc reads the elapsed time from the stopwatch timer started by the tic function. The function reads the internal time at the execution of the toc command, and displays the elapsed time since the most recent call to the tic function that had no output, in seconds.

Usage

```
toc()
```

Value

None

Author(s)

Junliang Shang <shangjunliang110@163.com>

References

None

Examples

```
tic()  
Sys.sleep(2)  
toc()
```

TwoEffect

Interaction Effects of two-SNP combinations

Description

interaction Effects of two-SNP combinations

Usage

```
data(TwoEffect)
```

Format

The format is: chr [1:187, 1:3] "rs00008" "rs00005" "rs00013" "rs00005" ... - attr(*, "dimnames")=List of 2 ..\$: NULL ..\$: chr [1:3] "SNP1" "SNP2" "Value"

References

None

Examples

```
data(TwoEffect)
```

Vertices

Vertices of constructed graphs

Description

Vertices of constructed graphs, including real vertices and virtual vertices.

Usage

```
data(Vertices)
```

Format

The format is: chr [1:37, 1:3] "rs00002" "rs00008" "rs00004" "rs00001" ... - attr(*, "dimnames")=List of 2 ..\$: NULL ..\$: chr [1:3] "id" "value" "label"

References

None

Examples

```
data(Vertices)
```

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