Package 'Lheuristic'

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Title Detection of scatterplots with L-shaped pattern

Version 1.3.0

Description The Lheuristic package identifies scatterpots that follow and L-shaped, negative distribution. It can be used to identify genes regulated by methylation by integration of an expression and a methylation array. The package uses two different methods to detect expression and methyaltion L-shapped scatterplots. The parameters can be changed to detect other scatterplot patterns.

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`binScore` *binScore*

Description

`binScore` can be used to score scatterplots by directly comparing the sample counts with a matrix of minimal or maximal percentages/counts to be found in each cell. It implements the three bands rule implicitly by setting threshold values.

Usage

```
binScore(aGrid, aReq)
```

Arguments

`aGrid`	A matrix of counts as computed by 'calcFreqs' function.
`aReq`	A matrix of minimum or maximum counts to be found in each cell if L-shape is TRUE.

Value

a score value for each scatterplot

Examples

```
# Generate some example data
aGrid <- matrix(c(20, 3, 0, 10, 2, 2, 20, 10, 20),
    nrow = 3, ncol = 3, byrow = TRUE
)
aReq <- matrix(c(15, 5, 0, 0, 5, 5, 10, 10, 15),
    nrow = 3, ncol = 3, byrow = TRUE
)

# Calculate the bin score
binScore(aGrid, aReq)
```

`calcFreqs` *calcFreqs*

Description

`calcFreqs` Given a MultiAssayExperiment with methylation and expression data, the function overlays a grid on a YMet ~ Xmet scatterplot and returns a 3x3 matrix with point counts per grid cell based on the vertical and horizontal lines.

Usage

```
calcFreqs(
  mae,
  geneNum,
  x1,
  x2,
  y1 = NULL,
  y2 = NULL,
  percY1 = 1/3,
  percY2 = 2/3
)
```

Arguments

`mae`	MultiAssayExperiment object containing methylation and expression matrices.
`geneNum`	row of expression/methylation matrix for which the frequencies will be computed.
`x1, x2`	Coordinates of vertical points in the X axis. Because it is expected to contain. methylation values that vary between 0 and 1, default values are 1/3 and 2/3.
`y1, y2`	Coordinates of vertical points on the Y-axis. If set to NULL, they will be automatically assigned as the percentiles of ‘y‘ defined by ‘percY1‘ and ‘percY2‘.
`percY1, percY2`	Default values for ‘y1‘ and ‘y2‘ when set to ‘NULL‘

Value

a matrix with calculated frequencies

Examples

```
# Methylation data
methylData <- matrix(runif(50), nrow = 10)
colnames(methylData) <- paste0(
    "samp",
    1:ncol(methylData)
)
rownames(methylData) <- paste0(
    "gene",
    1:nrow(methylData)
)
# Expression data
expresData <- matrix(rnorm(50), nrow = 10)
colnames(expresData) <- paste0(
    "samp",
    1:ncol(methylData)
)
rownames(expresData) <- paste0(
    "gene",
    1:nrow(methylData)
)
# ColData
colDat <- data.frame(
    sampleID = colnames(methylData),
    name = letters[1:ncol(methylData)]
)

rownames(colDat) <- colDat$sampleID
mae <- MultiAssayExperiment::MultiAssayExperiment(
    experiments = list(
        methylation = methylData,
        expression = expresData
    ),
    colData = colDat
)
geneRow <- 1
x1 <- 1 / 3
x2 <- 2 / 3
y1 <- NULL
y2 <- NULL
percY1 <- 1 / 3
percY2 <- 2 / 3

calcFreqs(
    mae = mae, geneNum = geneRow,
    x1, x2, y1, y2, percY1, percY2
)
```

checkPairing *checkPairing*

Description

checkPairing function to check if two matrices have the same dimensions row and column names.

Usage

```
checkPairing(X, Y)
```

Arguments

X	matrix
Y	matrix

Value

a logical value indicating if the two matrices have the same row and column names.

Examples

```
(X <- round(matrix(rnorm(30) * 10, ncol = 6), 1)) + 1:10
(Y <- round(X + matrix(rnorm(30) * 10, ncol = 6), 1)) - 10:1
(rownames(X) <- rownames(Y) <- letters[1:nrow(X)])
(m1 <- checkPairing(X, Y))
```

---

correlationSelection *correlationSelection: A vector correlation function calculator*

Description

correlationSelection Uses the function matCorrs; given two matrices X (m,n), Y (m,n) this function computes Pearson and Spearman correlation coefficients and their significance p-values for every pair of row vectors.

Usage

```
correlationSelection(
  mae,
  type = "Spearman",
  adj = TRUE,
  pValCutoff = 0.05,
  rCutoff = 0,
  sortByCorrs = FALSE
)
```

Arguments

mae	a MultiAssayExperiment object containing the methylation
type	specifies the correlation to choose between Spearman and Pearson. Default is Spearman.
adj	logical variable indicating if the p-value returned should be adjusted or not. Default is TRUE, it returns an adjusted p-value.
pValCutoff	the upper limit used for the p-value. Default is 0.05.
rCutoff	the upper limit used for the correlation coefficient. Default is 0, no cut off.
sortByCorrs	logical; if TRUE, results are ordered by ascending p-value. Default set to FALSE.

Value

dataframe with the correlations selected

Examples

```
# Methylation data
methylData <- matrix(runif(50), nrow = 10)
colnames(methylData) <- paste0("samp", 1:ncol(methylData))
rownames(methylData) <- paste0("gene", 1:nrow(methylData))
# Expression data
expresData <- matrix(rnorm(50), nrow = 10)
colnames(expresData) <- paste0("samp", 1:ncol(methylData))
rownames(expresData) <- paste0("gene", 1:nrow(methylData))
# ColData
colDat <- data.frame(
    sampleID = colnames(methylData),
    name = letters[1:ncol(methylData)]
)

rownames(colDat) <- colDat$sampleID
mae <- MultiAssayExperiment::MultiAssayExperiment(
    experiments = list(
        methylation = methylData,
        expression = expresData
    ),
    colData = colDat
)
correlationSelection(mae, pValCutoff = 0.25, rCutoff = 0.1,
type = "Spearman", sortByCorrs = TRUE)
```

---

lhCreateMAE *lhCreateMAE: Create a MultiAssayExperiment with Methylation and Expression Data*

Description

This function constructs a MultiAssayExperiment object using methylation and expression data, automatically ensuring consistency in sample names, feature names, and exposing dataset names. It internally uses `checkPairing` to validate that the provided datasets have matching row and column names.

Usage

```
lhCreateMAE(
  xDat,
  yDat,
  xName = "methylation",
  yName = "expression",
  colData = NULL
)
```

Arguments

`xDat`	A numeric matrix containing methylation data (features in rows, samples in columns).
`yDat`	A numeric matrix containing expression data (features in rows, samples in columns).
`xName`	A string specifying the name of the methylation dataset. Default: "methylation".
`yName`	A string specifying the name of the expression dataset. Default: "expression".
`colData`	(Optional) A DataFrame containing sample-level metadata. Default: NULL.

Value

A MultiAssayExperiment object containing the provided datasets with sample metadata.

Examples

```
library(MultiAssayExperiment)

# Create synthetic methylation and expression data
methylData <- matrix(runif(50), nrow = 10)
colnames(methylData) <- paste0("samp", 1:ncol(methylData))
rownames(methylData) <- paste0("gene", 1:nrow(methylData))

expresData <- matrix(rnorm(50), nrow = 10)
colnames(expresData) <- colnames(methylData)
rownames(expresData) <- rownames(methylData)

# Create sample metadata
colDat <- data.frame(sampleID = colnames(methylData),
name = letters[1:ncol(methylData)])
rownames(colDat) <- colDat$sampleID

# Construct MultiAssayExperiment
mae <- lhCreateMAE(methylData, expresData, colData = colDat)
```

```
# Display dataset names
names(experiments(mae))
```

---

matCorrs *A row-wise correlation function calculator*

Description

matCorrs Given a MultiAssayExperiment object, the function computes Pearson and Spearman correlation coefficients and their significance p-values for every pair of row vectors.

Usage

```
matCorrs(mae)
```

Arguments

mae	A MultiAssayExperiment object containing the methylation and expression data.

Value

matrix with a correlation value for each gene

Examples

```
# Methylation data
methylData <- matrix(runif(50), nrow = 10)
colnames(methylData) <- paste0("samp", 1:ncol(methylData))
rownames(methylData) <- paste0("gene", 1:nrow(methylData))
# Expression data
expresData <- matrix(rnorm(50), nrow = 10)
colnames(expresData) <- paste0("samp", 1:ncol(methylData))
rownames(expresData) <- paste0("gene", 1:nrow(methylData))
# ColData
colDat <- data.frame(
    sampleID = colnames(methylData),
    name = letters[1:ncol(methylData)]
)

rownames(colDat) <- colDat$sampleID
mae <- MultiAssayExperiment::MultiAssayExperiment(
    experiments = list(
        methylation = methylData,
        expression = expresData
    ),
    colData = colDat
)
matCorrs(mae)
```

messageTitle *messageTitle*

Description

messageTitle A wrapper function for sending messages to console.

Usage

```
messageTitle(aMessage, underChar = "-")
```

Arguments

aMessage	text of the message.
underChar	character to use for underlining the message.

Value

a message to console

Examples

```
messageTitle("Hello world", "$")
```

numScore *numScore*

Description

numScore A function to score scatterplot using a weight matrix. The scoring does not incorporate logical conditions such as 'if xij < C ...'

Usage

```
numScore(aGrid, LShaped, aWeightMifL, aWeightMifNonL)
```

Arguments

aGrid	A matrix of counts computed by the 'calcFreqs' function.
LShaped	A boolean indicating whether the scatterplot can be classified as "L-shaped".
aWeightMifL	A matrix of weights applied to score counts if the scatterplot is classified as "L".
aWeightMifNonL	A matrix of weights applied to score counts if the scatterplot is classified as "non-L".

Value

a numeric score for each scatterplot

Examples

```
# Methylation data
methylData <- matrix(runif(50), nrow = 10)
colnames(methylData) <- paste0("samp", 1:ncol(methylData))
rownames(methylData) <- paste0("gene", 1:nrow(methylData))
# Expression data
expresData <- matrix(rnorm(50), nrow = 10)
colnames(expresData) <- paste0("samp", 1:ncol(methylData))
rownames(expresData) <- paste0("gene", 1:nrow(methylData))
# ColData
colDat <- data.frame(
    sampleID = colnames(methylData),
    name = letters[1:ncol(methylData)]
)

rownames(colDat) <- colDat$sampleID
mae <- MultiAssayExperiment::MultiAssayExperiment(
    experiments = list(
        methylation = methylData,
        expression = expresData
    ),
    colData = colDat
)
trueFreq <- calcFreqs(mae, x1 = 1 / 3, x2 = 2 / 3)
LShaped <- FALSE
weightsIfL <- matrix(c(2, -1, -99, 1, 0, -1, 1, 1, 2),
    nrow = 3, byrow = TRUE
)
weightsIfNonL <- matrix(c(0, -1, -99, 0, 0, -1, 0, 0, 0),
    nrow = 3, byrow = TRUE
)
numScore(
    trueFreq, LShaped,
    weightsIfL, weightsIfNonL
)
```

---

plotGeneByName *plotGeneByName*

Description

plotGeneByName plots points on a scatterplot with a 3x3 grid superimposed. The name of a the gene is provided jointly with the MultiAssayExperiment object and used to select the row to be plotted.

Usage

```
plotGeneByName(
  geneName,
  mae,
  filename = NULL,
  text4Title = NULL,
  plotGrid = TRUE,
  figs = c(2, 2)
)
```

Arguments

geneName	The name of the gene to be plotted.
mae	A MultiAssayExperiment object containing the methylation and expression data for the specified gene.
filename	If provided, the name of the file to save the results as a PDF; defaults to NULL.
text4Title	A string used as the main title for the plot. Defaults to 'geneName' if set to NULL.
plotGrid	A boolean parameter indicating whether to pass the grid option to the 'plotGeneSel' function.
figs	A two-component vector defining the 2-dimensional structure of the plots to be generated.

Value

a pdf with scatterplots of selected by gene name

Examples

```
# Plot gene by name based on example data
# Methylation data
methylData <- matrix(runif(50), nrow = 10)
colnames(methylData) <- paste0("samp", 1:ncol(methylData))
rownames(methylData) <- paste0("gene", 1:nrow(methylData))
# Expression data
expresData <- matrix(rnorm(50), nrow = 10)
colnames(expresData) <- paste0("samp", 1:ncol(methylData))
rownames(expresData) <- paste0("gene", 1:nrow(methylData))
# ColData
colDat <- data.frame(
    sampleID = colnames(methylData),
    name = letters[1:ncol(methylData)]
)

rownames(colDat) <- colDat$sampleID
mae <- MultiAssayExperiment::MultiAssayExperiment(
    experiments = list(
        methylation = methylData,
        expression = expresData
```

```
    ),
    colData = colDat
)
plotGeneByName(gene = "gene7", mae = mae)
```

---

plotGeneSel *plotGeneSel*

Description

plotGeneSel plots points on a scatterplot with a 3x3 grid overimposed.

Usage

```
plotGeneSel(
  mae,
  genePos,
  titleText,
  x1 = 1/3,
  x2 = 2/3,
  y1 = NULL,
  y2 = NULL,
  percY1 = 1/3,
  percY2 = 2/3,
  plotGrid = TRUE
)
```

Arguments

mae	A MultiAssayExperiment object containing the methylation and expression data for the specified gene.
genePos	The index of the gene to be plotted within the MultiAssayExperiment object.
titleText	plot title.
x1, x2	Coordinates of vertical points in the X axis. Because it is expected to contain methylation values that vary between 0 and 1. The default values are 1/3 and 2/3.
y1, y2	Coordinates of vertical points in the Y axis. Leaving them as NULL assigns them the percentiles of yVec defined by 'percY1' and 'percY2'.
percY1, percY2	Values used to act as default for 'y1'and 'y2' when these are set to 'NULL'
plotGrid	logical. Defautl to TRUE will plot gridlines over the scatterplot.

Value

a pdf with scatterplots for selected genes

Examples

```
# Methylation data
methylData <- matrix(runif(50), nrow = 10)
colnames(methylData) <- paste0("samp", 1:ncol(methylData))
rownames(methylData) <- paste0("gene", 1:nrow(methylData))
# Expression data
expresData <- matrix(rnorm(50), nrow = 10)
colnames(expresData) <- paste0("samp", 1:ncol(methylData))
rownames(expresData) <- paste0("gene", 1:nrow(methylData))
# ColData
colDat <- data.frame(
    sampleID = colnames(methylData),
    name = letters[1:ncol(methylData)]
)

rownames(colDat) <- colDat$sampleID
mae <- MultiAssayExperiment::MultiAssayExperiment(
    experiments = list(
        methylation = methylData,
        expression = expresData
    ),
    colData = colDat
)

plotGeneSel(mae, genePos = 7, titleText = "L-shaped gene")
```

---

plotGenesMat *plotGenesMat*

Description

plotGenesMat wrapper function for plotting the scatterplots associated with two matrices.

Usage

```
plotGenesMat(
  mae,
  geneNames = NULL,
  fileName = "Scatplot_Sel_Genes.pdf",
  text4Title = NULL,
  x1 = 1/3,
  x2 = 2/3,
  y1 = NULL,
  y2 = NULL,
  percY1 = 1/3,
  percY2 = 2/3,
  plotGrid = TRUE,
```

```
  logicSc = NULL,
  saveToPDF = FALSE,
  plotsPerPage = 9
)
```

Arguments

mae	A MultiAssayExperiment object containing the methylation and expression data.
geneNames	A character vector of gene names to plot. If NULL, all genes are plotted.
fileName	The name of the file used to save the results as a PDF. If NULL, the plot is displayed on the screen.
text4Title	An optional title for the plot, incorporating the gene name and L-shape score. Defaults to NULL.
x1	The x-coordinate of vertical points on the X-axis. Expected to contain methylation values ranging between 0 and 1, with default values set to 1/3 and 2/3.
x2	The x-coordinate of vertical points on the X-axis. Expected to contain methylation values ranging between 0 and 1, with default values set to 1/3 and 2/3.
y1	The y-coordinate of vertical points on the Y-axis. If NULL, these are set to the percentiles of yVec defined by percY1 and percY2.
y2	The y-coordinate of vertical points on the Y-axis. If NULL, these are set to the percentiles of yVec defined by percY1 and percY2.
percY1	Values used as defaults for y1 when it is set to NULL.
percY2	Values used as defaults for y2 when it is set to NULL.
plotGrid	A logical value; defaults to TRUE, indicating whether to plot gridlines on the graph.
logicSc	A numeric score representing the L-shape score. Defaults to NULL.
saveToPDF	Logical, if TRUE, saves the plots to a PDF file specified by fileName. If FALSE (default), plots are displayed interactively without saving.
plotsPerPage	A numeric value indicating the number of plots to be printed in each page. Default set to 9.

Value

a pdf with scatterplots for all genes

Examples

```
# Methylation data
methylData <- matrix(runif(50), nrow = 10)
colnames(methylData) <- paste0("samp", 1:ncol(methylData))
rownames(methylData) <- paste0("gene", 1:nrow(methylData))
# Expression data
expresData <- matrix(rnorm(50), nrow = 10)
colnames(expresData) <- paste0("samp", 1:ncol(methylData))
rownames(expresData) <- paste0("gene", 1:nrow(methylData))
# ColData
```

```
colDat <- data.frame(
sampleID = colnames(methylData),
name = letters[1:ncol(methylData)])

rownames(colDat) <- colDat$sampleID
mae <- MultiAssayExperiment::MultiAssayExperiment(
    experiments = list(
        methylation = methylData,
        expression = expresData
    ),
    colData = colDat
)
selectedGenes <- c("gene1", "gene5")
plotGenesMat(mae, geneNames = selectedGenes,
saveToPDF = FALSE)
```

---

scoreGenesMat *scoreGenesMat*

Description

scoreGenesMat scores scatterplots using a binary and a numeric schemes row-wise.

Usage

```
scoreGenesMat(
  mae,
  x1 = 1/3,
  x2 = 2/3,
  y1 = NULL,
  y2 = NULL,
  percY1 = 1/3,
  percY2 = 2/3,
  aReqPercentsMat,
  aWeightMifL = 0.5,
  aWeightMifNonL = 0.25
)
```

Arguments

mae	MultiAssayExperiment object containing methylation and expression matrices.
x1, x2	Coordinates of vertical points on the X-axis. Expected to contain methylation values ranging between 0 and 1, with default values set to 1/3 and 2/3.
y1, y2	Coordinates of vertical points on the Y-axis. If set to NULL, they default to the percentiles of yVec as defined by 'percY1' and 'percY2'.
percY1, percY2	Values used to act as default for 'y1'and 'y2' when these are set to 'NULL'.

aReqPercentsMat
: A matrix specifying the minimum and maximum percentage counts required in each cell.

aWeightMifL
: A matrix of weights applied to score counts when the scatterplot is classified as "L".

aWeightMifNonL
: A matrix of weights applied to score counts when the scatterplot is classified as "non-L".

Value

A data frame with two columns: 'logicSc' (logical score indicating if the gene is 'active') and 'numericSc' (a numerical score).

Examples

```
# Score genes based on example data

# Methylation data
methylData <- matrix(runif(50), nrow = 10)
colnames(methylData) <- paste0("samp", 1:ncol(methylData))
rownames(methylData) <- paste0("gene", 1:nrow(methylData))
# Expression data
expresData <- matrix(rnorm(50), nrow = 10)
colnames(expresData) <- paste0("samp", 1:ncol(methylData))
rownames(expresData) <- paste0("gene", 1:nrow(methylData))
# ColData
colDat <- data.frame(
    sampleID = colnames(methylData),
    name = letters[1:ncol(methylData)]
)

rownames(colDat) <- colDat$sampleID
mae <- MultiAssayExperiment::MultiAssayExperiment(
    experiments = list(
        methylation = methylData,
        expression = expresData
    ),
    colData = colDat
)
sampleSize <- ncol(MultiAssayExperiment::experiments(mae)[[1]])
reqPercentages <- matrix(c(3, 20, 5, 5, 40, 20, 4, 1, 2),
    nrow = 3, byrow = TRUE
)
(theWeightMifL <- matrix(c(2, -2, -sampleSize / 5, 1, 0, -2, 1, 1, 2),
    nrow = 3, byrow = TRUE
))
(theWeightMifNonL <- matrix(c(0, -2, -sampleSize / 5, 0, 0, -2, 0, 0, 0),
    nrow = 3, byrow = TRUE
))
scoreGenesMat(mae,
    x1 = 1 / 3, x2 = 2 / 3,
    y1 = NULL, y2 = NULL, percY1 = 1 / 3, percY2 = 2 / 3,
```

```
    aReqPercentsMat = reqPercentages,
    aWeightMifL = theWeightMifL,
    aWeightMifNonL = theWeightMifNonL
)
```

TCGAexpression *Expression data matrix obtained from TCGA, TCGA-COAD dataset*

Description

A mxn matrix containing normalized gene expressions from TCGA

Usage

```
data(TCGAexpression)
```

Format

An object of class `matrix` (inherits from `array`) with 1000 rows and 30 columns.

Value

data matrix with gene expression data

Source

TCGA.org

TCGAmethylation *Methylation data matrix obtained from TCGA, TCGA-COAD dataset*

Description

A mxn matrix containing normalized methylation values from TCGA

Usage

```
data(TCGAmethylation)
```

Format

An object of class `matrix` (inherits from `array`) with 1000 rows and 30 columns.

Value

data matrix with gene methylation data

Source

TCGA.org

---

toReqMat *toReqMat*

Description

toReqMat can be used to turn a matrix of required percentages into a matrix of required counts to facilitate its scoring.

Usage

```
toReqMat(numPoints, aReqPercentMat)
```

Arguments

numPoints	Number of points in a scatterplot. Used to turn the required percentages into required counts.
aReqPercentMat	Matrix of required percentages.

Value

a counts matrix

Examples

```
reqPercentages <- matrix(
    c(
        3, 20, 5,
        5, 40, 20,
        4, 1, 2
    ),
    nrow = 3, byrow = TRUE
)
numberOfPoints <- 100
reqMat <- toReqMat(
    numPoints = numberOfPoints,
    aReqPercentMat = reqPercentages
)
```

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