Package 'gatom'

April 29, 2025

Title Finding an Active Metabolic Module in Atom Transition Network

Version 1.7.0

Description This package implements a metabolic network analysis pipeline to identify an active metabolic module based on high throughput data. The pipeline takes as input transcriptional and/or metabolic data and finds a metabolic subnetwork (module) most regulated between the two conditions of interest. The package further provides functions for module post-processing, annotation and visualization.

biocViews GeneExpression, DifferentialExpression, Pathways, Network

Depends R (>= 4.3.0)

Imports data.table, igraph, BioNet, plyr, methods, XML, sna, intergraph, network, GGally, grid, ggplot2, mwcsr, pryr, htmlwidgets, htmltools, shinyCyJS (>= 1.0.0)

Suggests testthat, knitr, rmarkdown, KEGGREST, AnnotationDbi, org.Mm.eg.db, reactome.db, fgsea, readr, BiocStyle, R.utils

License MIT + file LICENCE

Encoding UTF-8

LazyData true

RoxygenNote 7.2.3

VignetteBuilder knitr

URL https://github.com/ctlab/gatom/

BugReports https://github.com/ctlab/gatom/issues

git_url https://git.bioconductor.org/packages/gatom

git_branch devel

git_last_commit 6509ada

git_last_commit_date 2025-04-15

Repository Bioconductor 3.22

Date/Publication 2025-04-29

Author Anastasiia Gainullina [aut],
Mariia Emelianova [aut],
Alexey Sergushichev [aut, cre]

Maintainer Alexey Sergushichev <alsergbox@gmail.com>

Contents

abbreviateLabels . . . 2
addHighlyExpressedEdges . . . 3
collapseAtomsIntoMetabolites . . . 3
connectAtomsInsideMetabolite . . . 4
createShinyCyJSWidget . . . 4
gatom . . . 5
gene.de.rawEx . . . 6
getGeneDEMeta . . . 6
getMetabolicPathways . . . 7
getMetDEMeta . . . 8
gEx . . . 9
gsEx . . . 9
makeMetabolicGraph . . . 9
makeOrgGatomAnnotation . . . 10
met.de.rawEx . . . 12
met.kegg.dbEx . . . 12
mEx . . . 12
networkEx . . . 12
org.Mm.eg.gatom.annoEx . . . 13
prepareDE . . . 13
saveModuleToDot . . . 14
saveModuleToHtml . . . 14
saveModuleToPdf . . . 15
saveModuleToXgmml . . . 16
scoreGraph . . . 16
styleWidget . . . 17

Index **18**

`abbreviateLabels` *Abbreviate lipid labels for lipid module*

Description

Abbreviate lipid labels for lipid module

Usage

```
abbreviateLabels(module, orig.names, abbrev.names)
```

Arguments

`module`	Module to prepare
`orig.names`	whether to use original names from the dataset
`abbrev.names`	whether to use abbreviated names for all lipids

Value

module object with abbreviated labels

addHighlyExpressedEdges

Add reactions without highly changing genes but with high average expression

Description

Add reactions without highly changing genes but with high average expression

Usage

```
addHighlyExpressedEdges(m, g, top = 3000)
```

Arguments

m	Metabolic module
g	Scored graph
top	Maximum rank value for the gene to be considered highly expressed

Value

module with added edges that correspond to high average expression

Examples

```
data(mEx)
data(gEx)
m <- addHighlyExpressedEdges(m = mEx, g = gEx)
```

collapseAtomsIntoMetabolites

Collapse atoms belonging to the same metabolite into one vertex

Description

Collapse atoms belonging to the same metabolite into one vertex

Usage

```
collapseAtomsIntoMetabolites(m)
```

Arguments

m	Metabolic module

Value

module in which atoms of the same metabolite are collapsed into one

Examples

```
data(mEx)
m <- collapseAtomsIntoMetabolites(m = mEx)
```

`connectAtomsInsideMetabolite` *Connect atoms belonging to the same metabolite with edges*

Description

Connect atoms belonging to the same metabolite with edges

Usage

```
connectAtomsInsideMetabolite(m)
```

Arguments

`m`	Metabolic module

Value

module in which atoms of the same metabolite are connected

Examples

```
data(mEx)
m <- connectAtomsInsideMetabolite(m = mEx)
```

`createShinyCyJSWidget` *Creates shinyCyJS widget from module*

Description

Creates shinyCyJS widget from module

Usage

```
createShinyCyJSWidget(
  module,
  layout = list(name = "cose-bilkent", animate = FALSE, randomize = FALSE,
    nodeDimensionsIncludeLabels = TRUE),
  ...
)
```

Arguments

module	Module
layout	Layout for the module
...	Other parameters

Value

html widget of input module

Examples

```
data(mEx)
hw <- createShinyCyJSWidget(module = mEx)
```

---

gatom *gatom: a package for finding an active metabolic module in atom transition network*

Description

This package implements a metabolic network analysis pipeline to identify an active metabolic module based on high throughput data. The pipeline takes as input transcriptional and/or metabolic data and finds a metabolic subnetwork (module) most regulated between the two conditions of interest. The package further provides functions for module post-processing, annotation and visualization.

Functions

Data preprocessing: prepareDE, getMetDEMeta, getGeneDEMeta

Graph creation: makeMetabolicGraph

Graph scoring: scoreGraph

Module postprocessing: collapseAtomsIntoMetabolites, connectAtomsInsideMetabolite, addHighlyExpressedE
abbreviateLabels

Plotting module: createShinyCyJSWidget

Exporting module: saveModuleToHtml, saveModuleToDot, saveModuleToPdf, saveModuleToXgmml

For detailed pipeline analysis, see gatom vignette: `vignette("gatom-tutorial", package = "gatom")`

Example Data

Example data provided by gatom consists of: metabolite differential abundance data (met.de.rawEx), gene differential expression data (gene.de.rawEx), KEGG-based network object (networkEx), KEGG-based metabolite database object (met.kegg.dbEx), Example organism annotation object (org.Mm.eg.gatom.annoEx), metabolic graph with atom topology (gEx), scored metabolic graph with atom topology (gsEx), and metabolic module (mEx).

gene.de.rawEx *Example gene differential expression data.*

Description

See file https://github.com/ctlab/gatom/blob/master/inst/scripts/example.R for details.

Format

tibble/data.frame object

getGeneDEMeta *Finds columns in gene differential expression table required for gatom analysis*

Description

Default values for all columns are NULL which mean they are determined automatically.

Usage

```
getGeneDEMeta(
  gene.de.raw,
  org.gatom.anno,
  idColumn = NULL,
  idType = NULL,
  pvalColumn = NULL,
  logPvalColumn = NULL,
  log2FCColumn = NULL,
  baseMeanColumn = NULL,
  signalColumn = NULL,
  signalRankColumn = NULL
)
```

Arguments

gene.de.raw	A table with differential expression results, an object convertable to data.frame.
org.gatom.anno	Organsim-specific annotation obtained from makeOrgGatomAnnotation function.
idColumn	Specifies column name with gene identifiers.
idType	Specifies type of gene IDs (one of the supported by annotation).
pvalColumn	Specifies column with p-values.
logPvalColumn	Specifies column with log p-values, if there is no such column one will be generated automatically.
log2FCColumn	Specifies column with log2-fold changes.
baseMeanColumn	Specifies column with average expression across samples.

signalColumn Specifies column with identifier of the measured entity (such as gene ID for RNA-seq and probe ID for microarrays). Could be NULL (automatic, set from based on pval and log2FC columns), character (column name), or function (evaluated in a scope of original data frame)

signalRankColumn
Specifies how the genes are ranked from highly to lowly expressed, used in 'addHighlyExpressedEdgues' function. Could be NULL (automatic), character (column name) function (evaluated in a scope of original data frame).

Value

object with prepared columns for the analysis for gene data

Examples

```
data("org.Mm.eg.gatom.annoEx")
data("gene.de.rawEx")
de.meta <- getGeneDEMeta(gene.de.rawEx, org.gatom.anno = org.Mm.eg.gatom.annoEx)
```

---

getMetabolicPathways *Generate list of metabolic pathways from Reactome and KEGG databases*

Description

Generate list of metabolic pathways from Reactome and KEGG databases

Usage

```
getMetabolicPathways(
  universe,
  metGenes,
  keggOrgCode,
  threshold = 0.01,
  includeReactome = TRUE,
  includeKEGG = TRUE
)
```

Arguments

universe	list of genes
metGenes	list of metabolic genes
keggOrgCode	KEGG organism code, like mmu or hsa
threshold	threshold for Fisher test to filter out non-metabolic pathways
includeReactome	whether to include Reactome pathways (only works for Entrez ID universe)
includeKEGG	whether to include KEGG pathways and modules

Value

list of metabolic pathways for given organism and list of genes

getMetDEMeta *Finds columns in differential expression table for metabolites required for gatom analysis*

Description

Finds columns in differential expression table for metabolites required for gatom analysis

Usage

```
getMetDEMeta(
  met.de.raw,
  met.db,
  idColumn = NULL,
  idType = NULL,
  pvalColumn = NULL,
  logPvalColumn = NULL,
  log2FCColumn = NULL,
  signalColumn = NULL
)
```

Arguments

met.de.raw	A table with differential expression results, an object convertable to data.frame.
met.db	Metabolite database
idColumn	Specifies column name with metabolite identifiers.
idType	Specifies type of metabolite IDs (one of the supported by annotation).
pvalColumn	Specifies column with p-values.
logPvalColumn	Specifies column with log p-values, if there is no such column one will be generated automatically.
log2FCColumn	Specifies column with log2-fold changes.
signalColumn	Specifies column with identifier of the measured entity Could be NULL (automatic, set from based on pval and log2FC columns), character (column name), or function (evaluated in a scope of original data frame)

Value

object with prepared columns for the analysis for metabolite data

Examples

```
data("met.kegg.dbEx")
data("met.de.rawEx")
de.meta <- getMetDEMeta(met.de.rawEx, met.db = met.kegg.dbEx)
```

gEx *Example metabolic graph with atom topology.*

Description

See file https://github.com/ctlab/gatom/blob/master/inst/scripts/example.R for details.

Format

igraph object

gsEx *Example scored metabolic graph with atom topology.*

Description

See file https://github.com/ctlab/gatom/blob/master/inst/scripts/example.R for details.

Format

igraph object

makeMetabolicGraph *Creates metabolic graph based on specified data*

Description

Creates metabolic graph based on specified data

Usage

```
makeMetabolicGraph(
  network,
  topology = c("atoms", "metabolites"),
  org.gatom.anno,
  gene.de,
  gene.de.meta = getGeneDEMeta(gene.de, org.gatom.anno),
  gene.keep.top = 12000,
  met.db,
  met.de,
  met.de.meta = getMetDEMeta(met.de, met.db),
 met.to.filter = fread(system.file("extdata", "mets2mask.lst", package = "gatom"))$ID,
  gene2reaction.extra = NULL,
  keepReactionsWithoutEnzymes = FALSE,
  largest.component = TRUE
)
```

Arguments

network	Network object
topology	Way to determine network vertices
org.gatom.anno	Organism annotation object
gene.de	Table with the differential gene expression, set to NULL if absent
gene.de.meta	Annotation of ‘gene.de‘ table
gene.keep.top	Only the ‘gene.keep.top‘ of the most expressed genes will be kept for the network
met.db	Metabolite database
met.de	Table with the differential expression for metabolites, set to NULL if absent
met.de.meta	Annotation of ‘met.de‘ table
met.to.filter	List of metabolites to filter from the network
gene2reaction.extra	Additional gene to reaction mappings. Should be a data.table with ‘gene‘ and ‘reaction‘ columns
keepReactionsWithoutEnzymes	If TRUE, keep reactions that have no annotated enzymes, thus expanding the network but including some reactions which are not possible in the considered species.
largest.component	If TRUE, only the largest connected component is returned

Value

igraph object created from input data

Examples

```
data("gene.de.rawEx")
data("met.de.rawEx")
data("met.kegg.dbEx")
data("networkEx")
data("org.Mm.eg.gatom.annoEx")
g <- makeMetabolicGraph(network = networkEx, topology = "atoms",
                    org.gatom.anno = org.Mm.eg.gatom.annoEx,
                    gene.de = gene.de.rawEx, met.db = met.kegg.dbEx,
                    met.de = met.de.rawEx)
```

---

makeOrgGatomAnnotation

Create an organism annotation object for network analysis

Description

Create an organism annotation object for network analysis

Usage

```
makeOrgGatomAnnotation(
  org.db,
  idColumns = c(Entrez = "ENTREZID", RefSeq = "REFSEQ", Ensembl = "ENSEMBL", Symbol =
    "SYMBOL"),
  nameColumn = "SYMBOL",
  enzymeColumn = "ENZYME",
  appendEnzymesFromKegg = TRUE,
  appendOrthologiesFromKegg = TRUE,
  filterNonSpecificEnzymes = TRUE,
  keggOrgCode = NULL
)
```

Arguments

org.db	Bioconductor org.db object, e.g. org.Mm.eg.db
idColumns	vector of column names from ‘org.db‘ object to creat ID mappings. First ID will be used as a base identifier, should be compatible with KEGG and Reactome databases.
nameColumn	column with a human readable gene symbol. Default to "SYMBOL".
enzymeColumn	column with an Enzyme Commission ID. Default to "ENZYME".
appendEnzymesFromKegg	if TRUE, KEGG databases will be sued to extend gene to enzyme mappings obtained from org.db package.
appendOrthologiesFromKegg	if TRUE, KEGG database will be sued to extend gene to orthology mappings obtained from org.db package
filterNonSpecificEnzymes	if TRUE, will filter out non-specific enzymes from gene to enzyme mappings obtained from org.db package
keggOrgCode	KEGG organism code, e.g. "mmu". If set to NULL, the code is determined automatically.

Value

organism annotation object that will be used for network analysis

Examples

```
library(org.Mm.eg.db)
org.Mm.eg.gatom.anno <- makeOrgGatomAnnotation(org.db = org.Mm.eg.db)
```

met.de.rawEx *Example metabolite differential abundance data.*

Description

See file https://github.com/ctlab/gatom/blob/master/inst/scripts/example.R for details.

Format

tibble/data.frame object

met.kegg.dbEx *Example KEGG-based metabolite database object*

Description

See file https://github.com/ctlab/gatom/blob/master/inst/scripts/example.R for details.

Format

list object

mEx *Example metabolic module.*

Description

See file https://github.com/ctlab/gatom/blob/master/inst/scripts/example.R for details.

Format

igraph object

networkEx *Example KEGG-based network object*

Description

See file https://github.com/ctlab/gatom/blob/master/inst/scripts/example.R for details.

Format

list object

org.Mm.eg.gatom.annoEx *Example organism annotation object*

Description

See file https://github.com/ctlab/gatom/blob/master/inst/scripts/example.R for details.

Format

list object

prepareDE *Makes data.table with differential expression results containing all columns required for gatom and in the expected format based on metadata object*

Description

Makes data.table with differential expression results containing all columns required for gatom and in the expected format based on metadata object

Usage

```
prepareDE(de.raw, de.meta)
```

Arguments

de.raw	Table with differential expression results, an object convertable to data.frame
de.meta	Object with differential expression table metadata acquired with getGeneDEMeta or getMetDEMeta functions

Value

data.table object with converted differential expression table

Examples

```
data("org.Mm.eg.gatom.annoEx")
data("gene.de.rawEx")
de.meta <- getGeneDEMeta(gene.de.rawEx, org.gatom.anno = org.Mm.eg.gatom.annoEx)
de <- prepareDE(gene.de.rawEx, de.meta)
```

saveModuleToDot *Save module to a graphviz dot file*

Description

Save module to a graphviz dot file

Usage

```
saveModuleToDot(
  module,
  file,
  name = NULL,
  extra.node.attrs = NULL,
  extra.edge.attrs = NULL
)
```

Arguments

module	Module to save
file	File to save to
name	Name of the module
extra.node.attrs	Table with additional node attributes to be written to the dot file as is
extra.edge.attrs	Table with additional edge attributes to be written to the dot file as is

Value

Returns NULL

Examples

```
data(mEx)
saveModuleToDot(module = mEx, file = "module.dot")
```

saveModuleToHtml *Save module to a html widget*

Description

Save module to a html widget

Usage

```
saveModuleToHtml(
  module,
  file,
  name = "",
 sizingPolicy = htmlwidgets::sizingPolicy(defaultWidth = "100%", defaultHeight =
    "90vh", padding = 10),
  ...
)
```

Arguments

module	Module to save
file	File to save to
name	Name of the module
sizingPolicy	A widget sizing policy
...	Other parameters

Value

Returns NULL

Examples

```
data(mEx)
saveModuleToHtml(module = mEx, file = "module.html")
```

---

saveModuleToPdf *Save module to a nice pdf file*

Description

Save module to a nice pdf file

Usage

```
saveModuleToPdf(module, file, name = NULL, n_iter = 100, force = 1e-05)
```

Arguments

module	Module to save
file	File to save to
name	Name of the module
n_iter	Number of repel algorithm iterations
force	Value of repel force

Value

Returns NULL

Examples

```
data(mEx)
saveModuleToPdf(module = mEx, file = "module.pdf")
```

`saveModuleToXgmml` *Save module to an XGMML file*

Description

Save module to an XGMML file

Usage

```
saveModuleToXgmml(module, file, name = NULL)
```

Arguments

`module`	Module to save
`file`	File to save to
`name`	Name of the module

Value

Returns NULL

Examples

```
data(mEx)
saveModuleToXgmml(module = mEx, file = "module.xgmml")
```

`scoreGraph` *Score metabolic graph*

Description

Score metabolic graph

Usage

```
scoreGraph(
  g,
  k.gene,
  k.met,
  vertex.threshold.min = 0.1,
  edge.threshold.min = 0.1,
  met.score.coef = 1,
  show.warnings = TRUE,
  raw = FALSE
)
```

Arguments

g	Metabolic graph obtained with makeMetabolic graph function
k.gene	Number of gene signals to be scored positively, the higher is the number, the larger will be the resulting module. If set to NULL, genes will not be used for scoring.
k.met	Number of metabolite signals to be scored positively, the higher is the number, the larger will be the resulting module. If set to NULL, metabolites will not be used for scoring.
vertex.threshold.min	The worst acceptable estimated FDR for vertices. If necessary number of positive metabolite signals will be decreased from 'k.met' to reach this threshold. Default value is 0.1.
edge.threshold.min	The worst acceptable estimated FDR for vertices. If necessary number of positive metabolite signals will be decreased from 'k.gene' to reach this threshold. Default value is 0.1.
met.score.coef	Coefficient on which all vertex weights are multiplied. Can be used to balance vertex and edge weights. Default values is 1.
show.warnings	whether to show warnings
raw	whether to return raw scored graph, not a SGMWCS instance. Default to FALSE.

Value

SGMWCS instance or scored igraph object

Examples

```
data("gEx")
gs <- scoreGraph(g = gEx, k.gene = 25, k.met = 25)
```

---

styleWidget *code adopted from https://github.com/ramnathv/htmlwidgets/issues/231*

Description

code adopted from https://github.com/ramnathv/htmlwidgets/issues/231

Usage

```
styleWidget(hw, style = "", addl_selector = "", elementId = NULL)
```

Value

styled html widget

Index

∗ **internal**
styleWidget, 17

abbreviateLabels, 2, *5*
addHighlyExpressedEdges, 3, *5*

collapseAtomsIntoMetabolites, 3, *5*
connectAtomsInsideMetabolite, 4, *5*
createShinyCyJSWidget, 4, *5*

gatom, 5
gene.de.rawEx, *5*, 6
getGeneDEMeta, *5*, 6
getMetabolicPathways, 7
getMetDEMeta, *5*, 8
gEx, *5*, 9
gsEx, *5*, 9

makeMetabolicGraph, *5*, 9
makeOrgGatomAnnotation, 10
met.de.rawEx, *5*, 12
met.kegg.dbEx, *5*, 12
mEx, *5*, 12

networkEx, *5*, 12

org.Mm.eg.gatom.annoEx, *5*, 13

prepareDE, *5*, 13

saveModuleToDot, *5*, 14
saveModuleToHtml, *5*, 14
saveModuleToPdf, *5*, 15
saveModuleToXgmml, *5*, 16
scoreGraph, *5*, 16
styleWidget, 17