Package ‘gep2pep’

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Description Pathway Expression Profiles (PEPs) are based on the expression of pathways (defined as sets of genes) as opposed to individual genes. This package converts gene expression profiles to PEPs and performs enrichment analysis of both pathways and experimental conditions, such as "drug set enrichment analysis" and "gene2drug" drug discovery analysis respectively.
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gep2pep-package  gep2pep: creation and analysis of Pathway Expression Profiles

Description

Pathway Expression Profiles (PEPs) are based on the expression of pathways (or generic gene sets) belonging to a collection, as opposed to individual genes. gep2pep supports the conversion of gene expression profiles (GEPs) to PEPs and performs enrichment analysis of both pathways and conditions.
gep2pep-package

Details

gep2pep creates a local repository of gene sets, which can also be imported from the MSigDB [1] database. The local repository is in the repo format. When a GEP, defined as a ranked list of genes, is passed to buildPEPs, the stored database of pathways is used to convert the GEP to a PEP and permanently store the latter.

One type of analysis that can be performed on PEPs and that is directly supported by gep2pep is the Drug-Set Enrichment Analysis (DSEA [2]). It finds pathways that are consistently dysregulated by a set of drugs, as opposed to a background of other drugs. Of course PEPs may refer to non-pharmacological conditions (genetic perturbations, disease states, cell types, etc.) for analogous analyses. See CondSEA function.

A complementary approach is that of finding conditions that consistently dysregulate a set of pathways. This is the pathway-based version of the Gene Set Enrichment Analysis (GSEA). As an application example, this approach can be used to find drugs mimicking the dysregulation of a gene by looking for drugs dysregulating pathways involving the gene (this has been published as the gene2drug tool [3]). See PathSEA.

Both DSEA and gene2drug analyses can be performed using preprocessed data from http://dsea.tigem.it/downloads.php. The data include Connectivity Map [4] GEPs (drug-induced gene expression profiles) converted to PEPs in the form of a gep2pep repository.

Naming conventions:

- pathway: any set of gene identifiers (not necessarily representing a molecular pathway).
- pathway collection: a set of pathways.
- pathway database: a set of pathway collections, like the MSigDB.
- Gene Expression Profile (GEP): a named vector where names are gene identifiers of the same type as those in the pathway database and elements are ranks ranging from 1 to the number of genes.
- Pathway Expression Profile (PEP): a ranked list of pathways, as converted from a GEP according to a pathway collection.
- condition: any transcriptomic-modelled biological state (drug treatment, gene knock-out, disease state, cell type, etc.) characterized by an induced GEP and therefore a PEP.
- gep2pep repository: a pathway database and possibly a related database of PEPs as created by the gep2pep package. It is implemented in repo format.

Author(s)

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References


addSingleGeneSets

Add a collection of single-gene pseudo-sets.

Description

This function can be used to add single-gene (as opposed to pathway)-based collections. Sets including a single gene don’t need to go through normal Kolmogorov-Smirnov statistic computation and are treated differently for performance.

Usage

addSingleGeneSets(rp, genes, organism = "Homo Sapiens")

Arguments

- **rp**: A repository created by createRepository.
- **genes**: A character vector containing the gene names. For each of them a single-gene GeneSet will be created.
- **organism**: Character vector used to annotate the created sets. "Homo Sapiens" by default.

Details

Enrichment Scores and p-values for sets including a single gene are computed with dedicated (fast) routines. Although a statistic based on a single gene is not efficient per se, it is useful to have data in the same format as pathway-based profiles. buildPEPs internally calls single gene dedicated routines whenever a gene set collection is tagged (see repo function tag) with "SGE" ("Single Gene Expression"), which is done automatically by addSingleGeneSets. In that case, the min_size parameter is ignored.

Value

Nothing, used for side effects.

See Also

buildPEPs

Examples

```r
db <- loadSamplePWS()
repo_path <- file.path(tempdir(), "gep2pepTemp")

rp <- createRepository(repo_path, db)

## The following will create PEPs in 2 separate files
```
as.CategorizedCollection

Converts GeneSetCollection objects to CategorizedCollection objects.

Usage

as.CategorizedCollection(GScollection, category = "uncategorized",
subCategory = "uncategorized")

Arguments

GScollection An object of class GeneSetCollection.
category The name of the category that all the gene sets will be assigned to (see details).
subCategory The name of the subcategory that all the gene sets will be assigned to (see details).

Details

This function sets the CollectionType for each set in the collection to CategorizedCollection. If
GScollection contains BroadCollection gene sets, their fields category and subcategory will
be used. Otherwise the category and subcategory fields will be used.

Value

A CategorizedCollection object

Examples

## Not run:

## To run this example, first obtain the MSigDB database in XML
## format (see
## http://software.broadinstitute.org/gsea/downloads.jsp). It is
## assumed that the database is locally available as the file
## "msigdb_v6.0.xml".

The \code{importMSigDB.xml} function is just a shortcut to the following:

```r
geps <- loadSampleGEP()
addSingleGeneSets(rp, rownames(geps))
unlink(repo_path, TRUE)
```
buildPEPs

Build PEPs from GEPs and stores them in the repository.

Description

Given a matrix of ranked lists of genes (GEPs) and a gep2pep repository, converts GEPs to PEPs and stores the latter in the repository.

Usage

buildPEPs(rp, geps, min_size = 3, max_size = 500, parallel = FALSE,
buildPEPs

collections = "all", replace_existing = FALSE, donotstore = FALSE,
progress_bar = TRUE, rawmode_id = NULL,
rawmode_outdir = file.path(rp$root(), "raw")

Arguments

rp
A repository created by createRepository.

geps
A matrix of ranks where each row corresponds to a gene and each column to a
collection. Each column must include all ranks from 1 to the number of rows.
Row and column names must be defined. Row names will be matched against
gene identifiers in the pathways collections, and unrecognized gene names will
not be used.

min_size
An integer representing the minimum number of genes that must be included in
a set before the KS statistic is computed. Smaller gene sets will get ES=NA and
p=NA. Default is 3. Ignored for SGE mode (see addSingleGeneSets).

max_size
An integer representing the maximum number of genes that must be included in
a set before the KS statistic is computed. Larger gene sets will get ES=NA and
p=NA. Default is 500.

parallel
If TRUE, gene sets will be processed in parallel. Requires a parallel backend.

collections
A subset of the collection names returned by getCollections. If set to "all"
(default), all the collections in rp will be used.

replace_existing
What to do if PEPs, identified by column names of geps are already present
in the repository. If set to TRUE, they will be replaced, otherwise they will be
skipped and only PEPs of new conditions will be computed and added. Either
ways, will throw a warning.

donotstore
Just compute and return the pathway-based profiles without storing them in the
repository. The repository is still required to load pathway data, however it will
not be modified.

progress_bar
If set to TRUE (default) will show a progress bar updated after conversion of each
column of geps.

rawmode_id
An integer to be appended to files produced in raw mode (see details). If set to
NULL (default), raw mode is turned off.

rawmode_outdir
A character vector specifying the destination path for files produced in raw mode
(by fault it is ROOT/raw, where ROOT is the root of the repository). Ignored
if rawmode_id is NULL.

Details

By default, output is written to the repository as new items named using the collection name. How-
ever, it is possible to avoid the repository and write the output to regular files turning 'raw mode' on
through the rawmode_id and rawmode_outdir parameters. This is particularly useful when deal-
ing with very large corpora of GEPs, and conversions are split into independent jobs submitted to
a scheduler. At the end, the data will need to be reconstructed and put into the repository using
importFromRawMode in order to perform CondSEA or PathSEA analysis.
Value

Nothing. The computed PEPs will be available in the repository.

See Also

buildPEPs

Examples

```r
db <- loadSamplePWS()
repo_path <- file.path(tempdir(), "gep2pepTemp")

rp <- createRepository(repo_path, db)
## Repo root created.
## Repo created.
## [15:45:06] Storing pathway data for collection: c3_TFT
## [15:45:06] Storing pathway data for collection: c3_MIR
## [15:45:06] Storing pathway data for collection: c4_CGN

rp
## ID   Dims  Size
## c3_TFT_sets 10 18.16 kB
## c3_MIR_sets 10 17.25 kB
## c4_CGN_sets 10 6.9 kB

## Loading sample gene expression profiles
geps <- loadSampleGEP()

geps[1:3,1:3]
## (+)_chelidonine (+)_isoprenaline (+/_)_catechin
## AKT3 88 117 417
## MED6 357 410 34
## NR2E3 383 121 453

buildPEPs(rp, geps)

rp
## ID   Dims  Size
## c3_TFT_sets 10 18.16 kB
## c3_MIR_sets 10 17.25 kB
## c4_CGN_sets 10 6.9 kB
## c3_TFT 2 1.07 kB
## c3_MIR 2 1.07 kB
## c4_CGN 2 1.04 kB

unlink(repo_path, TRUE)
```
CategorizedCollection

Constructor method for objects of class CategorizedCollection.

Description

See CategorizedCollection-class.

Usage

CategorizedCollection(category = "uncategorized",
                      subCategory = "uncategorized")

Arguments

category  A character defining the main category that the gene set belongs to.
subCategory  A character defining the secondary category that the gene set belongs to.

Value

An object of class CategorizedCollection.

Examples

library(GSEABase)
gs1 <- GeneSet(setName="set1", setIdentifier="101")
collectionType(gs1) <- CategorizedCollection()

CategorizedCollection-class

A class to contain categorized gene set collection

Description

This class is a simple generalization of the BroadCollection function of GSEABase to store gene sets having assigned categories and subcategories that can be different from those of the MSigDB.

Slots

category  A character defining the main category that the gene set belongs to.
subCategory  A character defining the secondary category that the gene set belongs to.
checkRepository  

Check an existing repository for consistency

Description

Check both repository data consistency (see repo_check from the repo package) and specific gep2pep data consistency.

Usage

checkRepository(rp)

Arguments

rp  
A repository created by createRepository.

Value

Nothing.

Examples

db <- loadSamplePWS()
repo_path <- file.path(tempdir(), "gep2pepTemp")

rp <- createRepository(repo_path, db)
checkRepository(rp)
unlink(repo_path, TRUE)

clearCache  

Clear cached ranked matrices

Description

Clear cached ranked matrices

Usage

clearCache(rp_peps)

Arguments

rp_peps  
A repository created with createRepository, and containing PEPs created with buildPEPs.
Details

This will clear everything in the repository tagged with "stashed", which by default includes only matrices ranked by some gep2pep functions such as CondSEA.

Value

Nothing, used for side effects

See Also

CondSEA

Examples

```r
db <- loadSamplePWS()
repo_path <- file.path(tempdir(), "gep2pepTemp")

rp <- createRepository(repo_path, db)
geps <- loadSampleGEP()
buildPEPs(rp, geps)

pgset <- c("(+)_chelidonine", "(+/_)_catechin")
psea <- CondSEA(rp, pgset, usecache=TRUE)
## the repository contains cached data
print(rp, all=TRUE)

clearCache(rp)

unlink(repo_path, TRUE)
```

---

**CondSEA**

Performs Condition Set Enrichment Analysis

Description

Condition Set Enrichment Analysis (CondSEA) can be seen as a Gene-SEA performed over rows (as opposed to columns) of a matrix of GEPs. It tells how much a pathway is consistently dysregulated under a set of conditions (such as a set of drug treatments, disease states, cell types, etc.) when compared to a statistical background of other conditions.

Usage

```r
CondSEA(rp_peps, pgset, bgset = "all", collections = "all",
details = TRUE, rankingFun = rankPEPsByRows.ES, usecache = FALSE,
sortoutput = TRUE)
```
Arguments

\textbf{rp\_peps} A repository created with \texttt{createRepository}, and containing PEPs created with \texttt{buildPEPs}.

\textbf{pgset} A vector of names of conditions. Corresponding PEPs must exist in all the pathway collections currently in \texttt{rp}.

\textbf{bgset} The background against which to compare \texttt{pgset}. If set to all (default), all the remaining PEPs will be used. If provided, the corresponding PEPs must exist in all the pathway collections currently in \texttt{rp}.

\textbf{collections} A subset of the collection names returned by \texttt{getCollections}. If set to "all" (default), all the collections in \texttt{rp} will be used.

\textbf{details} If TRUE (default) rank details will be reported for each condition in \texttt{pgset}.

\textbf{rankingFun} The function used to rank PEPs column-wise. By default \texttt{rankPEPsByRows.ES} is used, which ranks using gene set enrichment scores (see details).

\textbf{usecache} If set to TRUE, the computed ranked matrix will be stored in the the repository (see details). FALSE by default.

\textbf{sortoutput} If TRUE (default) the output gene sets will be sorted in order of increasing p-value.

Details

For each pathway, all conditions are ranked by how much they dysregulate it (from the most UP-regulating to the most DOWN-regulating). Then, a Kolmogorov-Smirnov (KS) test is performed to compare the ranks assigned to conditions in \texttt{pgset} against the ranks assigned to conditions in \texttt{bgset}. A positive (negative) Enrichment Score (ES) of the KS test indicates whether each pathway is UP- (DOWN-) regulated by \texttt{pgset} as compared to \texttt{bgset}. A p-value is associated to the ES.

When PEPs are obtained from drug-induced gene expression profiles, \texttt{PathSEA} is the Drug-Set Enrichment Analysis [1].

The \texttt{rankingFun} must take in input PEPs like those loaded from the repository and return a matrix of row-wise ranks. Each row must contains ranks from 1 to the number of PEPs minus the number of NAs in the row.

When \texttt{usecache}=TRUE, the ranked matrix is permanently stored in HDF5 format, and subsequent calls to \texttt{CondSEA} will load from the disk the necessary ranks (not the whole matrix). The correct cached data is identified by the alphabetically sorted set \texttt{union(pgset, bgset)}, by the collection name, and by the ranking function. Additional alls to \texttt{CondSEA} with variations of these inputs will create additional cache. Cached data is hidden in the repository by default and can be printed with \texttt{rp\_peps$print(all=TRUE)}, and cleared with \texttt{clearCache(rp\_peps)}.

Value

A list of 2, by names "CondSEA" and "details". The "CondSEA" entry is a 2-columns matrix including ESs and p-values (see details) for each pathway database and condition. The "details" entry reports the rank of each condition in \texttt{pgset} for each pathway.

References

createMergedRepository

See Also

getResults, getDetails, clearCache

Examples

db <- loadSamplePWS()
repo_path <- file.path(tempdir(), "gep2pepTemp")

rp <- createRepository(repo_path, db)
geps <- loadSampleGEP()
buildPEPs(rp, geps)

pgset <- c("(+)_chelidonine", "(+/_)_catechin")
psea <- CondSEA(rp, pgset)

res <- getResults(psea, "c3_TFT")

## getting the names of the top pathways
setId2setName(loadCollection(rp, "c3_TFT"), rownames(res))

unlink(repo_path, TRUE)

createMergedRepository

Merge multiple PEPs to build a repository of consensus PEPs

Description

Merge multiple PEPs to build a repository of consensus PEPs

Usage

createMergedRepository(rpIn_path, rpOut_path, mergestr,
progressBar = TRUE, collections = "all")

Arguments

<table>
<thead>
<tr>
<th>Argument</th>
<th>Description</th>
</tr>
</thead>
<tbody>
<tr>
<td>rpIn_path</td>
<td>path to existing gep2pep repository</td>
</tr>
<tr>
<td>rpOut_path</td>
<td>path where the new merged repository will be created</td>
</tr>
<tr>
<td>mergestr</td>
<td>a named list of character vectors, each one including a set of PEP names. For each list entry, a consensus PEP will be created and assigned the entry name.</td>
</tr>
<tr>
<td>progressBar</td>
<td>if TRUE, show a progress bar</td>
</tr>
<tr>
<td>collections</td>
<td>A subset of the collection names returned by getCollections. If set to &quot;all&quot; (default), all the collections in rp will be used.</td>
</tr>
</tbody>
</table>
createRepository

Description

Given a database of collections, stores them in a local repository to be used by gep2pep functions.

Usage

createRepository(path, sets, name = NULL, description = NULL)

Arguments

<table>
<thead>
<tr>
<th>Argument</th>
<th>Description</th>
</tr>
</thead>
<tbody>
<tr>
<td>path</td>
<td>Path to a non-existing directory where the repository will be created.</td>
</tr>
<tr>
<td>sets</td>
<td>An object of class CategorizedCollection.</td>
</tr>
<tr>
<td>name</td>
<td>Name of the repository. Defaults to NULL (a generic name will be given).</td>
</tr>
<tr>
<td>description</td>
<td>Description of the repository. If NULL (default), a generic description will be given.</td>
</tr>
</tbody>
</table>
Details

Sets can be created by `importMSigDB.xml` or using GSEABase GeneSetCollection class and then converting it to CategorizedCollection. See examples.

Value

An object of class `repo` that can be passed to `gep2pep` functions.

See Also

buildPEPs

Examples

db <- loadSamplePWS()
repo_path <- file.path(tempdir(), "gep2pepTemp")

rp <- createRepository(repo_path, db)
## Repo root created.
## Repo created.
## [15:45:06] Storing pathway data for collection: c3_TFT
## [15:45:06] Storing pathway data for collection: c3_MIR
## [15:45:06] Storing pathway data for collection: c4_CGN

rp
## ID Dims Size
## c3_TFT_sets 10 18.16 kB
## c3_MIR_sets 10 17.25 kB
## c4_CGN_sets 10 6.9 kB

unlink(repo_path, TRUE)

Description

The XLS output includes the full CondSEA or PathSEA results, together with additional gene set information for the CondSEA. If the PathSEA or CondSEA analysis was performed with `details=TRUE`, details will be reported in the XLS file. This function requires the WriteXLS library.

Usage

`exportSEA(rp, results, outname = NULL)`

Arguments

- `rp`: A repository created by `createRepository`.
- `results`: The output of CondSEA or PathSEA.
- `outname`: Name of the XLS file to be created.
gene2pathways

Value
Nothing.

See Also
CondSEA, PathSEA

Examples

```r
db <- loadSamplePWS()
repo_path <- file.path(tempdir(), "gep2pepTemp")

rp <- createRepository(repo_path, db)
geps <- loadSampleGEP()
bruilPPEFs(rp, geps)

pgset <- c("(+)_chelidonine", "(+/_)_catechin")
psea <- CondSEA(rp, pgset)

## Not run:
exportSEA(rp, psea)
## End(Not run)
unlink(repo_path, TRUE)
```

gene2pathways

*Finds pathways including a given gene.*

Description

Given a gene, find the set of pathways that involve it in each collection of the repository. This can be used to define a set of pathways for the PathSEA.

Usage

gene2pathways(rp, genes, and = TRUE)

Arguments

<table>
<thead>
<tr>
<th>Argument</th>
<th>Description</th>
</tr>
</thead>
<tbody>
<tr>
<td>rp</td>
<td>A repository created by createRepository.</td>
</tr>
<tr>
<td>genes</td>
<td>A vector of gene identifiers of the same type as that used to create the repository.</td>
</tr>
<tr>
<td>and</td>
<td>If set to TRUE (default), will return sets containing all of genes. Otherwise will return the sets containing any of genes.</td>
</tr>
</tbody>
</table>

Value

A database of pathways suitable as input to PathSEA.
getCollections

Returns the names of the pathway collections in a repository.

description

Given a gep2pep repository, returns the names of the stored collections by looking at appropriate repository item names.

usage

getcollections(rp)

arguments

rp A repository created by createRepository.

details

Each collection in a database has a "category" and a "subcategory" assigned, which are used to build the collection identifier as "category_subcategory". This function obtains the identifiers by looking at data stored in the repository rp (entries that are tagged with "sets").

value

Vector of collection names (see details).
getDetails

Examples

db <- loadSamplePWS()
repo_path <- file.path(tempdir(), "gep2pepTemp")

rp <- createRepository(repo_path, db)
## Repo root created.
## Repo created.
## [15:45:06] Storing pathway data for collection: c3_TFT
## [15:45:06] Storing pathway data for collection: c3_MIR
## [15:45:06] Storing pathway data for collection: c4_CGN

collections(rp)
## [1] "c3_TFT" "c3_MIR" "c4_CGN"

unlink(repo_path, TRUE)

getDetails

Extracts the details matrix from CondSEA or PathSEA output

Description

Extracts the details matrix from CondSEA or PathSEA output

Usage

getDetails(analysis, collection)

Arguments

analysis The output of either CondSEA or PathSEA.
collection One of the names returned by getCollections.

Value

A matrix including the ranks of each pathway (over rows) and each condition (over columns) used as input to CondSEA or PathSEA.

See Also

CondSEA, PathSEA
getResults

Examples

db <- loadSamplePWS()
repo_path <- file.path(tempdir(), "gep2pepTemp")

rp <- createRepository(repo_path, db)
geps <- loadSampleGEP()
buildPEPs(rp, geps)

pgset <- c("(+)_chelidonine", "(+/-)_catechin")
psea <- CondSEA(rp, pgset)

details <- getDetails(psea, "c3_TFT")

unlink(repo_path, TRUE)

getResults

Extracts the results matrix from CondSEA or PathSEA output

Description

Extracts the results matrix from CondSEA or PathSEA output

Usage

getResults(analysis, collection)

Arguments

analysis The output of either CondSEA or PathSEA.
collection One of the names returned by getCollections.

Value

A 2-columns matrix including ESs and p-values (see details) for each pathway database and condition.

See Also

CondSEA, PathSEA

Examples

db <- loadSamplePWS()
repo_path <- file.path(tempdir(), "gep2pepTemp")

rp <- createRepository(repo_path, db)
geps <- loadSampleGEP()
buildPEPs(rp, geps)
importFromRawMode <- c("(+)_chelidonine", "(+/_)_catechin")
psea <- CondSEA(rp, pgset)

getResult(psea, "c3_TFT")
unlink(repo_path, TRUE)

---

**importFromRawMode**

*Imports PEPs created in raw mode*

**Description**

Raw mode is meant to deal with large collections of PEPs (like hundreds of thousands). In this case, problems may arise while trying to convert GEPs by loading all of them in memory at once. Raw mode is meant to be used with HDF5 format, which allows to load subsets of GEPs from the disk. buildPEPs, when used in raw mode, can create the corresponding subsets of PEPs, so that the job can be distributed on a computer cluster. importFromRawMode is meant to join the chunks into HDF5 matrices, which are than stored into the repository. The .loadPEPs function can seamlessly load PEPs stored in normal (RDS) or HDF5 format.

**Usage**

importFromRawMode(rp, path = file.path(rp$root(), "raw"),
                  collections = "all")

**Arguments**

- **rp**: A repository created by createRepository.
- **path**: Path were raw PEPs are stored (default is a "raw" directory under the repository root folder).
- **collections**: A subset of the collection names returned by getCollections. If set to "all" (default), all the collections in rp will be used.

**Details**

PEPs are expect to be found at the specified path and follow the naming convention as generated by buildPEPs. According to such convention, each file is named using the format category_subcategory#chunknumber.RDS. All non-alphanumeric characters from the original category and subcategory names are replace with an underscore (in rare cases this could create ambiguity that should be manually prevented). All chunks for the same subcategory are joined together following the chunk numbers into a single HDF5 matrix and stored in the repository as an "attachment" (see repo documentation).

Note that raw PEPs (by default everything at repository_root/raw) can be safely removed once they have been imported.
Value
Nothing, used for side effects.

See Also
buildPEPs

Examples

```r
db <- loadSamplePWS()
repo_path <- file.path(tempdir(), "gep2pepTemp")

rp <- createRepository(repo_path, db)

## The following will create PEPs in 2 separate files
geps <- loadSampleGEP()
buildPEPs(rp, geps[,1:2], progress_bar=FALSE, rawmode_id=1)
buildPEPs(rp, geps[,3:5], progress_bar=FALSE, rawmode_id=2)

## The separate files are then merged into one (possibly big) file
## in HDF5 format
importFromRawMode(rp)

## Now most operations (excluding the addition of new PEPs to
## existing collections) will be available as usual.
unlink(repo_path, TRUE)
```

importMSigDB.xml

Imports pathways data from an MSigDB XML file.

Description

Creates a `GeneSetCollection` object using the XML distribution of the MSigDB (see references). The returned object can be passed to `createRepository`.

Usage

`importMSigDB.xml(fname, organism = "Homo Sapiens")`

Arguments

- `fname` Path to an XML file downloaded from MSigDB.
- `organism` Select only gene sets for a given organism. Default is "Homo Sapiens".
Details

This function now just calls getBroadSets(fname) from the GSEABase package. However, it is left for backward compatibility and as an entry point to package functionalities.

Value

A CategorizedCollection object

References

http://software.broadinstitute.org/gsea/downloads.jsp

Examples

## Not run:

## To run this example, first obtain the MSigDB database in XML
## format (see
## http://software.broadinstitute.org/gsea/downloads.jsp). It is
## assumed that the database is locally available as the file
## "msigdb_v6.0.xml".

db <- importMSigDB.xml("msigdb_v6.0.xml")

## The database is now in an acceptable format to create a local
## repository using createRepository

## End(Not run)

## A small excerpt from the MSigDB is included in gep2pep. The
## following creates (and then deletes) a gep2pep repository.

db_sample <- loadSamplePWS()

repo_path <- file.path(tempdir(), "gep2pepTemp")
rp <- createRepository(repo_path, db_sample)

## removing temporary repository
unlink(repo_path, TRUE)

loadCollection

Loads a collection of pathways from the repository

Description

Loads a collection of pathways from the repository

Usage

loadCollection(rp, collection)
loadESmatrix

Arguments

rp A repository created by createRepository.
collection One of the names returned by getCollections.

Value

a GeneSetCollection object loaded from the repository rp.

Examples

db <- loadSamplePWS()
repo_path <- file.path(tempdir(), "gep2pepTemp")

rp <- createRepository(repo_path, db)
geps <- loadSampleGEP()

loadCollection(rp, "c3_TFT")

unlink(repo_path, TRUE)

loadESmatrix

Loads the matrix of Enrichment Scores for a collection

Description

Loads the matrix of Enrichment Scores for a collection

Usage

loadESmatrix(rp, collection)

Arguments

rp A repository created by createRepository.
collection One of the names returned by getCollections.

Value

The matrix of Enrichment Scores (ES) of the Kolmogorov-Smirnov statistic for the pathway collection, if previously computed with buildPEPs. The entry i, j reports the ES for the pathway i, condition j. If buildPEPs was not run, throws an error.
### loadPVmatrix

**Loads the matrix of p-values for a collection**

**Description**

Loads the matrix of p-values for a collection

**Usage**

```r
loadPVmatrix(rp, collection)
```

**Arguments**

- **rp**: A repository created by `createRepository`
- **collection**: One of the names returned by `getCollections`

**Value**

The matrix of p-values (PV) of the Kolmogorov-Smirnov statistic for the pathway collection, if previously computed with `buildPEPs`. The entry `i,j` reports the PV for the pathway `i`, condition `j`. If `buildPEPs` was not run, throws an error.

**Examples**

```r
db <- loadSamplePWS()
repo_path <- file.path(tempdir(), "gep2pepTemp")

rp <- createRepository(repo_path, db)
geps <- loadSampleGEP()
buildPEPs(rp, geps)

loadESmatrix(rp, "c3_TFT")[1:5,1:2]

unlink(repo_path, TRUE)
```

```r
db <- loadSamplePWS()
repo_path <- file.path(tempdir(), "gep2pepTemp")

rp <- createRepository(repo_path, db)
geps <- loadSampleGEP()
buildPEPs(rp, geps)

loadPVmatrix(rp, "c3_TFT")

unlink(repo_path, TRUE)
```
loadSampleGEP

Description
Loads sample Gene Expression Profiles

Usage
loadSampleGEP()

Value
Sample gene expression data

Examples
geps <- loadSampleGEP()

loadSamplePWS

Description
Loads sample pathway collections

Usage
loadSamplePWS()

Value
Sample pathway collections in GeneSetCollection format

Examples
geps <- loadSampleGEP()
makeCollectionIDs  

*Creates a collection label for each pathway.*

**Description**

Given a database, uses "category" and "subcategory" entries to create a vector of collection identifiers. Useful to extract a collection from a database.

**Usage**

```r
makeCollectionIDs(sets)
```

**Arguments**

- `sets`  
  A pathway database in the same format as output by `importMSigDB.xml`.

**Value**

A vector of identifiers, one per pathway, with the format: "category_subcategory".

**See Also**

`importMSigDB.xml`

**Examples**

```r
db <- loadSamplePWS()
ids <- makeCollectionIDs(db)

unique(ids)
## [1] "c3_TFT" "c3_MIR" "c4_CGN"

db <- db[ids=="c3_MIR"]

length(db)
## [1] 10
```

---

openRepository  

*Opens an existing repository of pathway collections.*

**Description**

The repository must have been created by `createRepository`. Provides an R object to interact with the repository.
PathSEA

Usage

openRepository(path)

Arguments

path Path to a directory where the repository has been created with createRepository.

Details

This function only calls the repo_open function from the repo package on path. It is meant to allow users not to explicitly load the repo library, unless they want to access advanced features.

Value

An object of class repo that can be passed to gep2pep functions.

See Also

createRepository

Examples

db <- loadSamplePWS()
repo_path <- file.path(tempdir(), "gep2pepTemp")

rp <- createRepository(repo_path, db)
rp2 <- openRepository(repo_path)

## rp and rp2 point to the same data:
identical(rp$entries(), rp2$entries())
## > [1] TRUE

unlink(repo_path, TRUE)

PathSEA Performs Pathway Set Enrichment Analysis (PSEA)

Description

PathSEA is analogous to the Gene Set Enrichment Analysis (GSEA), but for pathways instead of single genes. It can therefore be used to look for conditions under which a given set of pathways is consistently UP- or DOWN-regulated.

Usage

PathSEA(rp_peps, pathways, bgsets = "all", collections = "all",
        subset = "all", details = TRUE, rankingFun = rankPEPsByCols.SPV)
Arguments

rp_peps A repository created with createRepository, and containing PEPs created with buildPEPs.

pathways A database of pathways in the same format as input to createRepository. PSEA will be performed for each database separately.

bgsets Another list like pathways, representing the statistical background for each database. If set to "all" (the default), all pathways that are in the repository and not in pathways will be used.

collections A subset of the collection names returned by getCollections. If set to "all" (default), all the collections in rp will be used.

subset Character vector including PEP names to be considered (all by default, which may take time).

details If TRUE (default) details will be reported for each condition in pgset.

rankingFun The function used to rank PEPs column-wise. By default rankPEPsByCols.ES is used, which uses gene set enrichment scores (see details).

Details

For each condition, all pathways are ranked by how much they are dysregulated by it (from the most UP-regulated to the most DOWN-regulated, according to the corresponding p-values). Then, a Kolmogorov-Smirnov (KS) test is performed to compare the ranks assigned to pathways in pathways against the ranks assigned to pathways in bgsets. A positive (negative) Enrichment Score (ES) of the KS test indicates whether each pathway is UP- (DOWN-) regulated by pgset as compared to bgset. A p-value is associated to the ES.

When PEPs are obtained from drug-induced gene expression profiles, PathSEA can be used together with gene2pathways to perform gene2drug [1] analysis, which predicts which drugs may target a gene of interest (or mimick such effect).

The rankingFun must take in input PEPs like those loaded from the repository and return a matrix of column-wise ranks. Each column must contain ranks from 1 to the number of gene sets minus the number of NAs in the column.

Value

A list of 2, by names "PathSEA" and "details". The "PathSEA" entry is a 2-columns matrix including ESs and p-values for each collection and condition. The "details" entry reports the rank of each pathway in pathways for each condition.

References


See Also

getResults, getDetails
Examples

```r
library(GSEABase)

db <- loadSamplePWS()
repo_path <- file.path(tempdir(), "gep2pepTemp")

rp <- createRepository(repo_path, db)
geps <- loadSampleGEP()
buildPEPs(rp, geps)

w <- sapply(db, setIdentifier) %in% pathways

psea <- PathSEA(rp, db[w])

getResults(psea, "c3_TFT")
```

```
## ES   PV
## (_)_mk_801  0.7142857 0.1666667
## (_)_atenolol 0.7142857 0.1666667
## (+)_isoprenaline 0.5714286 0.4000000
## (+/_)_catechin  0.5714286 0.4000000
## (+)_chelidonine 0.3333333 0.9333333
```

unlink(repo_path, TRUE)


---

**setId2setName**

*Converts gene set IDs to gene set names*

### Description

Converts gene set IDs to gene set names

### Usage

```r
setId2setName(sets, ids)
```
Arguments

sets        An object of class GeneSetCollection
ids        character vector of gene set IDs to be converted to set names

Value

A vector of gene set names

See Also

CondSEA, PathSEA

Examples

collection <- loadSamplePWS()
setId2setName(collection, c("M3128", "M11607"))
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