Package 'R3CPET'

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Type Package

Title 3CPET: Finding Co-factor Complexes in Chia-PET experiment using a Hierarchical Dirichlet Process

Description The package provides a method to infer the set of proteins that are more probably to work together to maintain chormatin interaction given a ChIA-PET experiment results.

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`R3CPET-package` *3CPET: Finding Co-factor Complexes in Chia-PET experiment using a Hierarchical Dirichlet Process*

Description

The main goal of 3CPET is to try to infer the set of protein networks that are likely to work together inorder to maintain chromatin loops obtained by a ChIA-PET experiment. It is based on an idea silimar to the one used for document classification. It starts first by building a PPI network for each chromatin interaction, then uses an HDLA (Hierarchical Dirichlet Latent Allocation) model to infer the set of networks that are enriched together.

Details

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Type:	Package
Version:	1.0
Date:	2013-11-23
License:	GPL (>= 3.0)

Author(s)

Written by M.N.Djekidel Maintainer: Mohamed Nadhir Djekidel <nde12@mails.tsinghua.edu.cn>

References

M.N Djekidel et al,*3CPET: Finding Co-factor Complexes in Chia-PET experiment using a Hierarchical Dirichlet Process*, in press, 2015

See Also

`ChiapetExperimentData`, `ChromMaintainers` , `HLDAResult`

`annotateExpression-methods`

Add the gene expression attribute to the graph nodes

Description

This method is a kinda of helper method, it helps the user to add for each node in the inferred chromatin maintainer network the `RPKM` attributes. It is useful if the user want to save the networks as `".gml"` files and visualize them using software such as Gephi or Cytoscape. Or maybe if he wants to know which networks are highly expressed then others.

Usage

```
## S4 method for signature 'ChromMaintainers,data.frame'
annotateExpression(object, RPKMS)
```

Arguments

object	a ChromMaintainers object in which the networks are already present
RPKMS	a two columns data.frame, where the first column contains the name of the gene and the second contains the expression values

Value

A ChromMaintainers object in which the networks are annotated.

Author(s)

Mohamed Nadhir Djekidel (<nde12@mails.tsinghua.edu.cn>)

See Also

ChromMaintainers, InferNetworks

Examples

```
  ## get the different datasets path
  petFile <- file.path(system.file("example",package="R3CPET"),"HepG2_interactions.txt")
  tfbsFile <- file.path(system.file("example",package="R3CPET"),"HepG2_TF.txt.gz")

## Not run:
 x <- ChiapetExperimentData(pet = petFile, tfbs=  tfbsFile, IsBed = FALSE, ppiType="HPRD", filter= TRUE)
  ## build the diffrent indexes
  x <- createIndexes(x)
  x

## build the different indexes
x <- createIndexes(x)

## build networks connecting each interacting regions
nets<- buildNetworks(x)

## infer the networks
hlda<- InferNetworks(nets)

networks(hlda)

## Annotate networks
hlda<- annotateExpression(hlda,as.data.frame(RPKMS))

## Notice the addition of the RPKM attribute to each network
networks(hlda)

## End(Not run)
```

Biogrid *Biogrid Network*

Description

loads an igraph object that contains the Biogrid V 2.0.49 PPI .

Usage

```
data(Biogrid)
```

Value

an igraph named PPI.Biogrid.

Source

http://thebiogrid.org/

Examples

```
data(Biogrid)
PPI.Biogrid
```

buildNetworks *Building interaction networks connecting interacting regions*

Description

This methods uses the background PPI to try to build an interaction network that connects each interacting regions. If a regionA interacts with a regionB and if TF_A is the list of TF in regionA and TF_B is the list of TF in regionB, than we use the loaded PPI as a background network to connect each TF from TF_A to each TF in TF_B.

We suppose that a minimum number of physical interactions (minimum energy) are needed to connection each TF to the other. Thus, we take the shortest path in the PPI. at this stage, each network is a collection of edges.

Usage

```
## S4 method for signature 'ChiapetExperimentData'
buildNetworks(object, minFreq = 0.25, maxFreq = 0.75)
```

Arguments

object	a ChiapetExperimentData object in which the interactions and TFBS and PPI are already loaded. Check loadPETs, loadTFBS, loadPPI for more info.
minFreq	After constructing the networks for all the interacting regions all edges that appear in less than minFreq of the networks are considered to be outliers.
maxFreq	After constructing the networks for all the interacting regions all edges that appear in more than maxFreq of the networks are considered to be interactions involving general TF and are removed.

Value

A NetworkCollection object that contain the list of all the constructed networks and their sizes.

NOTE: interactions for which no TF was bound or no networks could be constructed or which was empty after filtering will not be considered.

Author(s)

Mohamed Nadhir Djekidel (<nde12@mails.tsinghua.edu.cn>)

References

Mohamed Nadhir D, Yang C et al *3CPET: Finding Co-factor Complexes in Chia-PET experiment using a Hierarchical Dirichlet Process*, ...

See Also

ChiapetExperimentData, loadTFBS , loadPETs, loadPPI, createIndexes

Examples

```
## get the different datasets path
petFile <- file.path(system.file("example",package="R3CPET"),"HepG2_interactions.txt")
tfbsFile <- file.path(system.file("example",package="R3CPET"),"HepG2_TF.txt.gz")


 ## Not run:
x <- ChiapetExperimentData(pet = petFile, tfbs=  tfbsFile, IsBed = FALSE, ppiType="HPRD", filter= TRUE)
## build the diffrent indexes
x <- createIndexes(x)

## build networks connecting each interacting regions
nets<- buildNetworks(x)
nets

## End(Not run)
```

ChiapetExperimentData-class
3CPET used raw data

Description

The ChiapetExperimentData class is a container for storing the set of raw data used by 3CPET to do the prediction.

Usage

```
ChiapetExperimentData(pet='', tfbs='', ppi=NULL,
                      ## loadPETs options
                      IsBed=TRUE, petHasHeader=FALSE, dist=1000,
                      ## loadTFBS options
                      tfbsHasHeader=FALSE,
                      ## loadPPI options
                      ppiType=c("HPRD","Biogid"),
                      filter=FALSE, term="GO:0005634", annot=NULL,
                      RPKM= NULL, threshold=1
                      )
```

Arguments

pet	(*optional*) a ChIAP-PET interactions file path or a GRanges object. The GRanges object should have a column named PET_ID. details on the file format can be found on the loadPETs help page.
tfbs	(*optional*) a file path to a BED file containing transcription factors binding site or a GRanges object. The GRanges object should have a metadata column named TF.
ppi	(*optional*) an igraph object that contains a user defined protein-protein interaction network. if this parameter is not specified, the ppiType paramter will be used.
IsBed	(*optional*) considered only if the pet parameter is a file path. More info about this paramters can be found in the loadPETs help page.
petHasHeader	(*optional*) logical. Indicates if the ChIA-PET interactions file has a header or not.
dist	(*optional*) The size of the region to consider arround the center of the interacting regions.
tfbsHasHeader	(*optional*) logical. Indicates if the TFBS file has a header or not.
ppiType	(*optional*) considered only if the ppi paramter is not specified. This paramter tell the pakage to load one of the PPI (HPRD or Biogrid) shiped with the package.
filter	(*optional*) logical. whether of not to filter the PPI network. if the RPKM paramter is specified then the RPKM dataset incorporated with the package will be used. if you want to to your own way of filtering, you ca set filter = FALSE and pass an already processed PPI to the ppi paramterer.

`term` (*optional*) the GO term used to filter the nodes of the PPI. this is different from the `filter` parameter. in the `filter` parameter the PPI nodes are filtered by their gene expression, while in the `term` parameter they are filtered by their genomic location. by default `"GO:0005634"` is used for filtering.

`annot` (*optional*) the annotation dataset used for filtering by default the `geneLocations` is used. The user can pass a custom `data.frame`. For more details check the `loadPPI` help page.

`RPKM` (*optional*) a `data.frame` object that contains the expression value of each genes. by default the `RPKMS` dataset will be used (expression value in K562 celline). For more information about the format of the data passed to this parameter please check the `loadPPI`

`threshold` (*optional*) threshold value used to filter gene expression. default: 1.

Details

The `ChiapetExperimentData` class stores the genomic coordinates of the ChIA-PET interactions, the binding sites of the different transcription factor (TFBS) and the background protein-protein interaction (PPI) network used to infer the final chromatin maintainer networks.

Value

Constructs a `ChiapetExperimentData` object with the specified fields populated.

Slots

pet : Object of class `GRanges` that stores the genomic coordinated of the interactions. it can be populated using the method `loadPETs`

tfbs : Object of class `GRanges` that stores the TF binding site. it can be populated using the method `loadTFBS`. NOTE: the TFBS locations can be obtained from a ChIP-Seq experiment or a motif finding software. for more information on the format of the provided data check `loadTFBS`

ppi Object of class `"igraph"` used as the background PPI for further analysis. it can be populated using the method `loadPPI`

.dt Object of class `"list"` contains a collection of `data.table` serving as indexes used internally by the package (not expected to be manipulated by the user). it can be populated using the method `createIndexes`

Accessors

The following methods can be used to get the content of a `ChiapetExperimentData` object `x` :

`pet(x)`, `pet(x) <- value`: Get ChIA-PET interactions encoded as a `GRanges` object in `x`. The returned `GRanges` objects contains an attribute `PET_ID` in which the left side have an id of the form `PET#\d+\.1` and the right side interaction have an id of the form `PET#\d+\.2`. for more information check `loadPETs`

```
          seqnames             ranges strand |      PET_ID
             <Rle>          <IRanges>  <Rle> | <character>
      [1]     chr1 [1240734, 1242734]      * |     PET#1.1
```

```
[2]     chr1 [1242224, 1244224]      * |     PET#1.2
[3]     chr1 [1282208, 1284208]      * |     PET#2.1
[4]     chr1 [1283334, 1285334]      * |     PET#2.2
[5]     chr1 [1370371, 1372371]      * |     PET#3.1
[6]     chr1 [1371822, 1373822]      * |     PET#3.2
```

`tfbs(x)`, `tfbs(x) <- value`: Get the GRanges storing the transcription factor binding sites.

`ppi(x)`, `ppi(x) <- value`: Returns an igraph object used as a background PPI. check the loadPPI for more information.

Author(s)

Mohamed Nadhir Djekidel (<nde12@mails.tsinghua.edu.cn>)

References

Li G, Fullwood MJ, Xu H et al.*ChIA-PET tool for comprehensive chromatin interaction analysis with paired-end tag sequencing*. Genome Biology 2010, 11(2):R22

Mohamed Nadhir D, Yang C et al *3CPET: Finding Co-factor Complexes in Chia-PET experiment using a Hierarchical Dirichlet Process*, ...

See Also

loadPETs, loadTFBS , loadPPI

Examples

```
## for example Reading ChIA-PET interaction results generated from ChIA-PET tool
## it should be formatted as follow:

## ------------------------------------------------------------------------------------------
## chromleft startleft endleft chromright startright endright counts     pvalue     qvalue
##      chr1    872113  879175       chr1     933836   938416     12 1.84529e-30 6.90983e-28
##      chr1    874165  879175       chr1     933340   938306     10 1.23139e-25 3.58932e-23
##      chr1    889676  896594       chr1     933897   938982     13 4.91311e-36 2.33753e-33
##      chr1    898753  907581       chr1     931133   939571     19 0.00000e+00 0.00000e+00
##      chr1    910103  918775       chr1     930834   938627     15 2.20004e-43 1.32812e-40
##      chr1    919314  922154       chr1     934212   937864      6 3.70292e-21 7.88551e-19
##------------------------------------------------------------------------------------------

## The counts, pvalue and qvalue fields are not considered in our case
## it is up to the user to filter the interactions.

## The TFBS should be a BED file that contain the chromosome, start, end and the TF name

## Not run:

  ## load the different datasets
  petFile <- file.path(system.file("example",package="R3CPET"),"HepG2_interactions.txt")
  tfbsFile <- file.path(system.file("example",package="R3CPET"),"HepG2_TF.txt.gz")
```

```
x <- ChiapetExperimentData(pet = petFile, tfbs= tfbsFile, IsBed = FALSE, ppiType="HPRD", filter= TRUE)
 ## build the diffrent indexes
 x <- createIndexes(x)
 x

 ## Pass objects instead of files.
 pet <- sample(pet(x),size = 20,replace = TRUE )
 tfbs <- sample(tfbs(x), size=300, replace=TRUE)
 ppi <- ppi(x)
 tst <- ChiapetExperimentData(pet = pet, tfbs= tfbs, ppi=ppi)
 tst <- createIndexes(tst)
 tst

## End(Not run)
```

`ChromMaintainers-class`

Chomatin maintainer networks

Description

The `ChromMaintainers` holds information about the inferred network by the method `InferNetworks`. It contains the list of inferred networks as `igraph` object, a list of edges and a list of proteins. In addition to an `HLDAResult` object that contains the final probabilities calculated by the HLDA algorithm.

Usage

```
ChromMaintainers( maintainers,topEdges,topNodes, clusRes = NULL, networks = list())
```

Arguments

`maintainers`	Object of class `"HLDAResult"` that contains the HLDA results.
`topEdges`	a `"matrix"` containing the list the top edges per network.
`topNodes`	a `"matrix"` containing the list the top proteins per network.
`networks`	the list of infered networks as an `igraph` objects list
`clusRes`	Object of class `"cluesOrSota"` describing the assignment of each DNA-interaction to a chromatin-maintainer network according to their enrichment.

Value

a `ChromMaintainers` object.

Accesors

if x is a ChromMaintainers object the following accessors can be applied :

networks(x) gets the list of networks as igraph objects

topNodes(x) gets a matrix object that contains the list of top proteins per network

topEdges(x) gets a matrix object that contains the list of top proteins per network

getClusters(x) returns the clustering results of DNA-interaction into groups according to their partnership enrichment profile to the set of inferred chromatin maintainer networks.

Methods

Many plotting and annotation methods are associated with this class.

annotateExpression(object, RPKMS) To add the gene expression attribute to the igraph objects

clusterInteractions(object, method, nbClus) To cluster the DNA-interactions according to their partnership enrichment profile.

GenerateGmlNetworks(object,...) Creates the list of igraph object from the topEdges matrix

outputGenesPerClusterToDir(hdaRes,data,path, ...) get the list genes belonging to each DNA-interaction cluster.

getRegionsIncluster(hdaRes,data, cluster, ...) returns the coordinates of the DNA interactions for a given cluster.

GOEnrich.networks(object, pval=0.05, GOlimit= 5,path="") do a GO enrichment of the elements of each inferred network.

plot3CPETRes(object, path, W, H, type,byEdge, netPerRow, layoutfct, ...) provide different type of plots to visualize the results

visualizeCircos(object, data, cluster, chrLenghts) Draws a circos plot of the DNA interactions in a given cluster.

Author(s)

Mohamed Nadhir Djekidel (<nde12@mails.tsinghua.edu.cn>)

References

https://www.cs.princeton.edu/~blei/topicmodeling.html (C. Wang's hdp code)

Chong Wang, John Paisley and David M. Blei, *Online variational inference for the hierarchical Dirichlet process* .In AISTATS 2011

Mohamed Nadhir D, Yang C et al *3CPET: Finding Co-factor Complexes in Chia-PET experiment using a Hierarchical Dirichlet Process*, ...

See Also

InferNetworks, ChromMaintainers , HLDAResult

Examples

```
showClass("ChromMaintainers")
```

chromosoms *Human chromosom lenghts*

Description

This dataset contains the human chromosoms lengths

Examples

```
data(chromosoms)
Chromosoms
```

cluesOrSota-class *Wrapper for* clues *and* sota *S3 classes*

Description

This is an S4 virtual union class that defines a new object that can be a sota or a clues class. Now that the clues method is deprecated, only the sota method is supported.

Definition

```
setClassUnion("cluesOrSota", c("sota","NULL"))
```

Objects from the Class

A virtual Class: No objects may be created from it.

Methods

No methods defined with class "cluesOrSota" in the signature.

Author(s)

Mohamed Nadhir Djekidel (<djek.nad@gmail.com>)

References

Herrero, J., Valencia, A, and Dopazo, J. (2005).*A hierarchical unsupervised growing neural network for clustering gene expression patterns*. Bioinformatics, 17, 126-136.

See Also

ChromMaintainers

Examples

```
showClass("cluesOrSota")
```

clusterInteractions-methods

Grouping DNA interactions by enrichment profile

Description

This method aims at clustering the DNA interactions according to their partnership probability to the inferred chromatin maintainer networks.

Usage

```
## S4 method for signature 'ChromMaintainers'
clusterInteractions(object, method="sota", nbClus=20 )
```

Arguments

`object`	(**Required**) a non-empty `ChromMaintainers` object
`method`	(*optional*)used to specify the method to use. Only the `method = "sota"` is supported for the moment, the `method='clues'` is deprecated. The user needs to specify the number of clusters by setting the parameter `nbClus`, by default it is set to 20.
`nbClus`	(*optional*) The user-specified number of clusters. It is taken into consideration only if `method = sota`.

Value

A `ChromMaintainers` object in which the `clusRes` is populated as a `sota`.

Author(s)

Mohamed Nadhir Djekidel (<nde12@mails.tsinghua.edu.cn>)

References

Herrero, J., Valencia, A, and Dopazo, J. (2005). *A hierarchical unsupervised growing neural network for clustering gene expression patterns*. Bioinformatics, 17, 126-136.

See Also

`ChromMaintainers`, `sota`, `InferNetworks`

Examples

```
 data(RPKMS)

  ## get the different datasets path
  petFile <- file.path(system.file("example",package="R3CPET"),"HepG2_interactions.txt")
  tfbsFile <- file.path(system.file("example",package="R3CPET"),"HepG2_TF.txt.gz")

## Not run:
 x <- ChiapetExperimentData(pet = petFile, tfbs=  tfbsFile, IsBed = FALSE, ppiType="HPRD", filter= TRUE)
  ## build the diffrent indexes
  x <- createIndexes(x)
  x

  ## build networks connecting each interacting regions
  nets<- buildNetworks(x)

  ## infer the networks
  hlda<- InferNetworks(nets)

  #cluster
  hlda<- clusterInteractions(hlda)

  #Display heatmap
  plot3CPETRes(hlda,type="heatmap")
  hlda

## End(Not run)
```

`CreateCenteredBED-methods`

Create centered interactions

Description

This helper method can be used to create a "bed" file in which the coordinates of the regions are the centre of the interactions in the raw data. in **R3CPET** we suppose that the centre of the interactions are the most enriched when doing read mapping ,thus, we consider just the region around the centre to detect the TFBS.

Usage

```
## S4 method for signature 'character'
CreateCenteredBED(file, header=TRUE,dist=1000)
```

Arguments

`file`	a `character` indicating the location of the rawdata file. the file should be a six column "bed" file in which the fist 3 columns indicate the left side interaction (chr, start, stop) and the other 3 columns indicate the right side interaction.

header	logical, indicates if the first line in the file is a header.
dist	numeric, indicated the distance around the center of the region to take.

Value

A 4 columns data.frame object, in which the first 3 columns indicate the location of the region and the 4th on indicate its name. The names are of the format PET#\w+.1 for the left side regions and PET#\w+.2 for the right side ones.

Author(s)

Mohamed Nadhir Djekidel (<nde12@mails.tsinghua.edu.cn>)

References

Mohamed Nadhir D, Yang C et al *3CPET: Finding Co-factor Complexes in Chia-PET experiment using a Hierarchical Dirichlet Process*, ...

See Also

ChiapetExperimentData, loadTFBS , loadPETs, loadPPI, createIndexes.

Examples

```
## get interactions file location
petFile <- file.path(system.file("example",package="R3CPET"),"HepG2_interactions.txt")

res <- CreateCenteredBED(petFile, header=TRUE, dist=1000)
head(res)
```

---

createIndexes-methods *Preparing TF indexes per region*

Description

After loading the interactions and the TFBS, the createIndexes method can be used to build indexes for fast look-up for which which TF are located in which region. This method is an intermediate step needed for further analysis.

Usage

```
## S4 method for signature 'ChiapetExperimentData'
createIndexes(object, minOverlap = 50)
```

Arguments

object	a ChiapetExperimentData object in which the interactions and TFBS are already loaded. Check loadPETs and loadTFBS for more info.
minOverlap	The minimum overlap between a TF binding site and a region, to consider a TF as binding to that region. The default value is 50.

Value

A ChiapetExperimentData object in which the .dt slot is populated as a data.table object.

Author(s)

Mohamed Nadhir Djekidel (<nde12@mails.tsinghua.edu.cn>)

References

Mohamed Nadhir D, Yang C et al *3CPET: Finding Co-factor Complexes in Chia-PET experiment using a Hierarchical Dirichlet Process*, ...

See Also

ChiapetExperimentData, loadTFBS , loadPETs, loadPPI

Examples

```
  ## get the different datasets path
  petFile <- file.path(system.file("example",package="R3CPET"),"HepG2_interactions.txt")
  tfbsFile <- file.path(system.file("example",package="R3CPET"),"HepG2_TF.txt.gz")

## Not run:
 x <- ChiapetExperimentData(pet = petFile, tfbs=  tfbsFile, IsBed = FALSE, ppiType="HPRD", filter= TRUE)
  ## build the diffrent indexes
  x <- createIndexes(x)
  x

## End(Not run)
```

---

createServer-methods *Explore results in a web browser*

Description

To facilitate the interaction of the user with the package, we added an additional web interface using the **shiny** package. The user can check some basic statistics about the row data and he can explore the results and generate some graphs.

Usage

```
## S4 method for signature
## 'ChiapetExperimentData,NetworkCollection,ChromMaintainers'
createServer(x,nets,hlda)
```

Arguments

x	a ChiapetExperimentData object in which the interactions, TFBS and the index tables are already created.
nets	a NetworkCollection object containing the list of the used TF and the initial interaction networks.
hlda	a ChromMaintainers object in which the results are already calculated.

Value

A webpage is opened.

Author(s)

Mohamed Nadhir Djekidel (<nde12@mails.tsinghua.edu.cn>)

See Also

NetworkCollection, ChiapetExperimentData, ChromMaintainers

Examples

```
  ## get the different datasets path
  petFile <- file.path(system.file("example",package="R3CPET"),"HepG2_interactions.txt")
  tfbsFile <- file.path(system.file("example",package="R3CPET"),"HepG2_TF.txt.gz")

## Not run:
  data(RPKMS)
 x <- ChiapetExperimentData(pet = petFile, tfbs=  tfbsFile, IsBed = FALSE, ppiType="HPRD", filter= TRUE)
  ## build the diffrent indexes
  x <- createIndexes(x)

  ## build networks connecting each interacting regions
  nets<- buildNetworks(x)

  ## infer the networks and do the clustering
  hlda<- InferNetworks(nets)
  hlda<- clusterInteractions(hlda)

  ## Run the server
  createServer(x, nets, hlda)


## End(Not run)
```

EnsemblToHGNC *Ensemble to HGNC conversion*

Description

This helper method uses the biomaRt package to convert Ensembl ids to HGNC ids.

Usage

```
EnsemblToHGNC(EnsemblIDs)
```

Arguments

EnsemblIDs	a character vector with Ensembl IDs.

Value

returns a data.frame containing the Ensembl ID and his corresponding HGNC gene id and Name plus a description of the gene.

Author(s)

Mohamed Nadhir Djekidel (<nde12@mails.tsinghua.edu.cn>)

See Also

EntrezToHGNC

Examples

```
## Not run:
EnsemblIDs<-c("ENSG00000164548","ENSG00000118515","ENSG00000105705",
        "ENSG00000177414","ENSG00000108179")

EnsemblToHGNC(EnsemblIDs)

## End(Not run)
```

EntrezToHGNC *Entrez to HGNC conversion*

Description

This helper method uses the biomaRt package to convert Entrez ids to HGNC icS.

Usage

```
EntrezToHGNC(EntrezID)
```

Arguments

EntrezID	a character vector with Entrez IDs.

Value

returns a data.frame containing the Entrez ID and his corresponding HGNC gene id and Name plus a description of the gene.

Author(s)

Mohamed Nadhir Djekidel (<nde12@mails.tsinghua.edu.cn>)

See Also

EnsemblToHGNC

Examples

```
## Not run:
EntrezID <-c("2114","9757","5886","9373","6921",
        "4088","7006","6196","10054","10945")

EntrezToHGNC(EntrezID)

## End(Not run)
```

geneLocations *Nucleus located genes*

Description

This dataset contains a data.frame containing the set of genes that are located in the nucleus "GO:0005634".

Usage

```
data(geneLocations)
```

Value

data.frame containing genes located at the nucleus.

Examples

```
data(geneLocations)
head(geneLocations.nucleus)
```

GenerateNetworks-methods *Generate a list of* igraph *networks*

Description

This methods converts the networks slot of a ChromMaintainers object, it reads the topEdge slot and convert it into a list of igraph objectts.

Usage

```
## S4 method for signature 'ChromMaintainers'
GenerateNetworks(object,...)
```

Arguments

object	a ChromMaintainers object
...	future options not considered for the moment.

Value

Returns ChromMaintainers object in which the networks slot is populated.

Author(s)

Mohamed Nadhir Djekidel (<nde12@mails.tsinghua.edu.cn>)

See Also

ChromMaintainers, InferNetworks

Examples

```
  ## get the different datasets path
  petFile <- file.path(system.file("example",package="R3CPET"),"HepG2_interactions.txt")
  tfbsFile <- file.path(system.file("example",package="R3CPET"),"HepG2_TF.txt.gz")

## Not run:
  data(RPKMS)
 x <- ChiapetExperimentData(pet = petFile, tfbs=  tfbsFile, IsBed = FALSE, ppiType="HPRD", filter= TRUE)
  ## build the diffrent indexes
  x <- createIndexes(x)
  ## build networks connecting each interacting regions
  nets<- buildNetworks(x)

  ## infer the networks
  hlda<- InferNetworks(nets)

  hlda <- GenerateNetworks(hlda)
  networks(hlda)

## End(Not run)
```

---

getRegionsIncluster-methods

list of interactions per cluster

Description

This method can be used to retrieve the genomic coordinated of the DNA-interactions in each cluster.

Usage

```
## S4 method for signature 'ChromMaintainers,ChiapetExperimentData,numeric'
getRegionsIncluster(hdaRes,data, cluster=1, ...)
```

Arguments

hdaRes	a ChromMaintainers object in which the clusters are already calculated
data	a ChiapetExperimentData object that contains the genomic location of all the interactions.
cluster	The ID of the cluster for which we want to get the list of the involved regions.
...	additional parameters not used for the moment.

Value

a GRanges object is returned

Author(s)

Mohamed Nadhir Djekidel (<nde12@mails.tsinghua.edu.cn>)

See Also

clusterInteractions, InferNetworks, ChiapetExperimentData, ChromMaintainers

Examples

```
    ## get the different datasets path
   petFile <- file.path(system.file("example",package="R3CPET"),"HepG2_interactions.txt")
    tfbsFile <- file.path(system.file("example",package="R3CPET"),"HepG2_TF.txt.gz")
## Not run:
    data(RPKMS)
   x <- ChiapetExperimentData(pet = petFile, tfbs=  tfbsFile, IsBed = FALSE, ppiType="HPRD", filter= TRUE)
    ## build the different indexes
    x <- createIndexes(x)
    ## build networks connecting each interacting regions
    nets<- buildNetworks(x)

    ## infer the networks and do the clustering
    hlda<- InferNetworks(nets)
    hlda<- clusterInteractions(hlda)

    ## return the DNA-interactions in cluster 3
    getRegionsIncluster(hlda,x,cluster=3)


## End(Not run)
```

---

getRegionsInNetwork-methods

list of interactions per network

Description

This method can be used to retrieve the genomic coordinated of the DNA-interactions enriched for each network given a certain threshold.

Usage

```
## S4 method for signature 'ChromMaintainers,ChiapetExperimentData,numeric'
getRegionsInNetwork(hdaRes,data, net=1, thr=0.5, ...)
```

Arguments

hdaRes	a ChromMaintainers object which already contains the calculated results
data	a ChiapetExperimentData object that contains the genomic location of all the interactions.
net	The ID of the network for which we want to get the list of the involved regions.
thr	Specify the minimum enrichment value to consider an interaction to be controlled by the network. by default it is 0.5
...	additional parameters not used for the moment.

Value

a GRanges object is returned

Author(s)

Mohamed Nadhir Djekidel (<nde12@mails.tsinghua.edu.cn>)

See Also

InferNetworks, ChiapetExperimentData, ChromMaintainers

Examples

```
    ## get the different datasets path
   petFile <- file.path(system.file("example",package="R3CPET"),"HepG2_interactions.txt")
    tfbsFile <- file.path(system.file("example",package="R3CPET"),"HepG2_TF.txt.gz")

## Not run:
    data(RPKMS)
   x <- ChiapetExperimentData(pet = petFile, tfbs=  tfbsFile, IsBed = FALSE, ppiType="HPRD", filter= TRUE)
    ## build the different indexes
    x <- createIndexes(x)

    ## build networks connecting each interacting regions
    nets<- buildNetworks(x)

    ## infer the networks and do the clustering
    hlda<- InferNetworks(nets)

    ## return the DNA-interactions in cluster 3
    getRegionsIncluster(hlda,x,net=3)


## End(Not run)
```

GOEnrich.folder-methods

GO enrichment methods

Description

This helper methods can be called to do GO enrichment by using the DAVID web service.

GOEnrich.networks can be used to do a GO enrichment of the chromatin maintainer networks.

GOEnrich.folder can be called to do a GO enrichment on the gene-list files generated by the method outputGenesPerClusterToDir.

There is a 5 secs delay between each request to not avoid being rejected by the server.

Usage

```
## S4 method for signature 'character'
GOEnrich.folder(folder, fdr=0.05,GOlimit=20)

## S4 method for signature 'ChromMaintainers'
GOEnrich.networks(object, fdr=0.05, GOlimit= 5,path="")
```

Arguments

folder	name of the folder that contains the gene-list files. The files are supposed to have a .txt extension. The first column of each file is supposed to contain the genes EntrezID.
object	a "ChromMaintainers" objects with the topNodes already calculated.
fdr	cut-off value GO terms with fdr value <= fdr will be considered. Benjamini-Hochberg FDR is used.
GOlimit	the number of top GO terms to return.
path	the path where to store the generated plot (*pdf file*). if not specified the plot will be displayed.

Value

Returns a list of data.frame that contain the GO results for each file (or network).

Author(s)

Mohamed Nadhir Djekidel (<nde12@mails.tsinghua.edu.cn>)

References

http://david.abcc.ncifcrf.gov/ (DAVID website)

Huang DW, Sherman BT, Lempicki RA. *Systematic and integrative analysis of large gene lists using DAVID Bioinformatics Resources*. Nature Protoc. 2009;4(1):44-57.

See Also

outputGenesPerClusterToDir

Examples

```
  ## get the different datasets path
 petFile <- file.path(system.file("example",package="R3CPET"),"HepG2_interactions.txt")
  tfbsFile <- file.path(system.file("example",package="R3CPET"),"HepG2_TF.txt.gz")

## Not run:

 x <- ChiapetExperimentData(pet = petFile, tfbs=  tfbsFile, IsBed = FALSE, ppiType="HPRD", filter= TRUE)
  ## build the different indexes
  x <- createIndexes(x)

  ## build networks connecting each interacting regions
  nets<- buildNetworks(x)

  ## infer the networks
  hlda<- InferNetworks(nets)

  ## Get the list of genes in each cluster by default
  ## a folder ClustersGenes will be created
  outputGenesPerClusterToDir(hlda,x)

  ## GO enrichment
  GOEnrich.folder(folder="ClustersGenes/")


## End(Not run)
```

HLDAResult-class *Class* "HLDAResult"

Description

This class is a container for the results generated by the HLDA algorithm

Usage

```
HLDAResult(docPerTopic,wordsPerTopic ,betas)
```

Arguments

docPerTopic	Object of class "matrix" describing the partnership of each document in a topic. In our case a documents is the protein interaction networks associated with each DNA interaction and the topics are the inferred chromatin maintainer networks.
wordsPerTopic	Object of class "matrix" describing the partnership of each word to a topic. In our case a word is an edge and the topics are the chromatin maintainer networks.

betas	Object of class "numeric" the beta values for each network. Basically, it shows how popular is the network.

Value

an HLDAResult object.

Accessors

For a given HLDAResult object the following accesor functions can be used:

docPerTopic(x) gets the content of the docPerTopic matrix.

wordsPerTopic(x) gets the content of the wordsPerTopic matrix.

betas(x) gets the betas values.

Author(s)

Mohamed Nadhir Djekidel (<nde12@mails.tsinghua.edu.cn>)

References

Chong Wang, John Paisley and David M. Blei, *Online variational inference for the hierarchical Dirichlet process* .In AISTATS 2011

Mohamed Nadhir D, Yang C et al, *3CPET: Finding Co-factor Complexes in Chia-PET experiment using a Hierarchical Dirichlet Process*, ...

See Also

NetworkCollection, ChromMaintainers , InferNetworks

Examples

```
showClass("HLDAResult")
```

HPRD *HPRD protein interaction Network*

Description

loads an igraph object that contains the HRPD PPI release 9.

Usage

```
data(HPRD)
```

Value

an igraph object named PPI.HPRD.

Source

http://hprd.org/

Examples

```
data(HPRD)
PPI.HPRD
```

`InferNetworks-methods` *Network construction using Hierarchical Dirichlet Process*

Description

This methods applies a Hierarchical Dirichlet Process (HDP) algorithm on the collection of proteins networks to infer the set of chromatin loop-maintainer proteins. HDP are non-parametric Bayesian models widely used in document classification as it enables us to model datasets with a mixtures of classes. In our case, we suppose that different kinds of networks are involved in maintaining the different loops. Thus, to make an analogy with topic modeling, we each DNA-interaction maintaining protein network as a document and each edge in this network as word. Thus, the task is to say which word (*edge*) belongs to which topic (*chromatin-maintainer family*). The method implementation is based on the C++ code of Chong Wang and David Blei with adaptation to Rcpp and removal of the dependency on the Gnu Scientific Library.

Usage

```
## S4 method for signature 'NetworkCollection'
InferNetworks(object,thr =0.5,max_iter = 500L, max_time = 3600L, ...)
```

Arguments

`object`	a `NetworkCollection` object in which the list of protein interactions associated with each DNA interaction is already populated.
`thr`	Used to select the top protein interaction in each inferred chromatin-maintainer family. In HDP each topic (*Chromatin-maintainer family*) is considered as a distribution over words (*edges*), thus, for each topic we consider the words that capture `threshold` percent of the topic to be the top words. For example, in topic1, we first rank edges by partnership probability to topic1 in a decreasing order, and we take the top edges that capture 50% of the partnership.
`max_iter`	maximum number of iterations (befault 500).
`max_time`	maximum runing time (3600 sec).
`...`	You can pass additional paramters to control the behaviour of the HDP model. The possible paramters are *eta*, *alpha* and *gamma*. *eta* controls how edges are assigned to CMNs on the global level. smaller *eta* values will lead to sparce edge-to-CMN assignment, which *eta* >1 leads to more uniform assignments. *gamma* on the other hand, controls the number of CMNs, smaller *gamma* values will produce a small number of CMNs and *gamma*>1 will favor the generation

of more. *alpha* controls the sparcity at the local PPI. smaller *alpha* value force edges to be conrolled by a small number of CMNs, while lagrger values leads to more uniform distribution. By default *eta = 0.01*, *gamma =1* and *alpha =1*.

Value

Returns a ChromMaintainers object that contains the list of inferred networks and the probability of each edge in each network.

Author(s)

Mohamed Nadhir Djekidel (<nde12@mails.tsinghua.edu.cn>)

References

https://www.cs.princeton.edu/~blei/topicmodeling.html (C. Wang's hdp code)

Chong Wang, John Paisley and David M. Blei, *Online variational inference for the hierarchical Dirichlet process* .In AISTATS 2011

Mohamed Nadhir D, Yang C et al *3CPET: Finding Co-factor Complexes in Chia-PET experiment using a Hierarchical Dirichlet Process*, ...

See Also

NetworkCollection, ChromMaintainers

Examples

```
    ## get the different datasets path
   petFile <- file.path(system.file("example",package="R3CPET"),"HepG2_interactions.txt")
    tfbsFile <- file.path(system.file("example",package="R3CPET"),"HepG2_TF.txt.gz")
## Not run:
   x <- ChiapetExperimentData(pet = petFile, tfbs=  tfbsFile, IsBed = FALSE, ppiType="HPRD", filter= TRUE)
    ## build the different indexes
    x <- createIndexes(x)
    ## build networks connecting each interacting regions
    nets<- buildNetworks(x)

    ## infer the networks
    hlda<- InferNetworks(nets)
    hlda

## End(Not run)
```

loadPETs-methods *Parsing ChIA-PET interaction data*

Description

This method loads the ChIA-PET interactions data into a GRanges object from a file generated by ChIA-PET tool or an already formatted BED file.

Usage

```
## S4 method for signature 'ChiapetExperimentData,character'
loadPETs(object, petFile, IsBed=TRUE, header=TRUE, dist=1000)
```

Arguments

object	(**Required**) a ChiapetExperimentData object
petFile	(**Required**) path to the file to parse. two types of formats are accepted. If the file comes from the ChIA-PET tool or has the same format used in the ENCODE project

```
chromleft startleft endleft chromright startright endright
    chr1    872113  879175       chr1     933836   938416
    chr1    874165  879175       chr1     933340   938306
    chr1    889676  896594       chr1     933897   938982
    chr1    898753  907581       chr1     931133   939571
    chr1    910103  918775       chr1     930834   938627
    chr1    919314  922154       chr1     934212   937864
```

only the the coordinates of the left and the right regions are considered (which means the first 6 columns), The additional columns are just ignored. We suppose that the user has already selected the interactions that sound significant for him.

if this kind of file is provided the IsBed parameter should be set to FASLE. if the file has no header the user needs to set header=FALSE.

if IsBed parameter is provided, the provided file should have 4 columns, three to describe the region location and the forth column to indicate the ID of the interaction and its position (1: for left and 2: for right), according to following pattern PET#\d\.1 or PET#\d\.2.

```
chr1   1241234   1242234 PET#1.1
chr1   1242724   1243724 PET#1.2
chr1   1282708   1283708 PET#2.1
chr1   1283834   1284834 PET#2.2
chr1   1370871   1371871 PET#3.1
chr1   1372322   1373322 PET#3.2
```

IsBed	(*optional*) The flag indicates whether the provided file has a 4 columns BED (when IsBed = TRUE) format or has the ChIA-PET tool format (when IsBed = FALSE). By default, IsBed = TRUE

header (*optional*) Indicates whether or not the first line of the file should be considered as a header. by default it is TRUE

dist (*optional*) This parameter indicates the size of the up- and down-stream regions *(in bp)* to consider around the center of each region. 3CPET is based on the assumption that the real ChIP-Seq signal is more enriched around the center of the regions and get more depleted when moving further in both directions. Thus, when the user provides a file that has a ChIA-PET tool format (IsBed = TRUE), 3CPET will first center the regions and consider only distance bp up- and down-stream of the center of each region. A default value of 1000bp is used.

Value

A ChiapetExperimentData object in which the ppi is populated as a GRanges object.

Author(s)

Mohamed Nadhir Djekidel (<nde12@mails.tsinghua.edu.cn>)

References

Li G, Fullwood MJ, Xu H et al.*ChIA-PET tool for comprehensive chromatin interaction analysis with paired-end tag sequencing*. Genome Biology 2010, 11(2):R22

Mohamed Nadhir D, Yang C et al *3CPET: Finding Co-factor Complexes in Chia-PET experiment using a Hierarchical Dirichlet Process*, ...

See Also

ChiapetExperimentData, loadTFBS , loadPPI, createIndexes

Examples

```
## Create a ChiapetExperimentData object
x <- ChiapetExperimentData(ppiType= "HPRD")

## load the different datasets (where the file has a Chia-PET tool format )
petFile <- file.path(system.file("example",package="R3CPET"),"HepG2_interactions.txt")
x <- loadPETs(x, petFile=petFile, IsBed=FALSE)

## when loading an already formatted BED file
petFile <- file.path(system.file("example",package="R3CPET"),"HepG2_centered.bed")
x <- loadPETs(x, petFile=petFile, IsBed=TRUE, header=FALSE)

pet(x)
```

loadPPI-methods *Setting the background protein-protein interaction*

Description

This method enables the user to define the PPI network as a background network. The user can provide his own PPI or use the HPRD or the Biogrid PPI incorporated in the package.

Usage

```
## S4 method for signature 'ChiapetExperimentData'
loadPPI(object,type=c("HPRD","Biogid"),customPPI= NULL,
              filter=FALSE, term ="GO:0005634", annot=NULL,
              RPKM= NULL, threshold=1 )
```

Arguments

object	a ChiapetExperimentData to load the PPI into as an igraph object
type	if customPPI = NULL, this parameter indicats which of the available PPI to use HPRD or Biogrid (*build 3.2.100*). by default, the HPRD network is used.
customPPI	If the user wants to use his own PPI interaction network (for example for another species), he can provide an igraph object or a path to an "ncol" formatted graph (a file with two columns indicating the interacting parts and an optional third column to indicate the weight). It is preferred that the user provides an igraph object, to avoid any problems when parsing the "ncol" file.
filter	This parameter indicates whether the user want to filter the selected PPI or not. filter = FALSE means that the PPI (provided by the user or by the HPRD and Biogrid networks) will be used as is. if filter = TRUE,the proteins in the PPI will be filtered according to their position in cell (by default proteins located in the nucleus are kept and the other removed). In addition to the filtering by location, if the user wants just to keep the proteins that show a certain amount of expression he can provide a gene expression table to the RPKM parameter and set the threshold for filtering.
term	The GO term used to for filtering. By default, only protein that are located in the nucleus are kept (term = "GO:0005634"). If the user want to use another annotation table he can pass a data.frame object to the parameter annot.
annot	If the user wants to provide his own annotation data-set, he can pass a data.frame object to this parameter. The passed data.frame should have at least two columns named respectively: geneSymbol that contains the gene names, and cellular_component_term that contain the term.

```
geneSymbol                    cellular_component_term
FAU Ribosome      (GO:0005840); Nucleolus (GO:0005730)
ALDH3A1   Cytoplasm (GO:0005737); Nucleus (GO:0005634)
ASCL1     Nucleus (GO:0005634); Cytoplasm (GO:0005737)
```

RPKM — A data.frame that contains the expression of each gene in the PPI. The data.frame should at least have 2 columns. The first one contains the gene symbol (should be the same as the one used in the PPI) and the second gives the expression.

threshold — Threshold value used to filter gene expression. All genes with expression value less than threshold are removed.

Value

A ChiapetExperimentData object in which the ppi slot is populated as an igraph object filtered according to the specified conditions.

Author(s)

Mohamed Nadhir Djekidel (<nde12@mails.tsinghua.edu.cn>)

References

Prasad, T. S. K. et al. (2009) *Human Protein Reference Database - 2009 Update*. Nucleic Acids Research. 37, D767-72.

Chatr-Aryamontri A, Breitkreutz BJ et al. *The BioGRID Interaction Database: 2013 update*. Nucleic Acids Res. 2012 Nov 30

M.N Djekidel et al,*3CPET: Finding Co-factor Complexes in Chia-PET experiment using a Hierarchical Dirichlet Process*, in press, 2015

See Also

ChiapetExperimentData, loadTFBS , loadPETs, createIndexes

Examples

```
## Create a ChiapetExperimentData object
x <- ChiapetExperimentData(ppiType= "HPRD")

## Loading the default HPRD network without filtering

x <- loadPPI(x,type="HPRD")
ppi(x)

## Using the HPRD network and filtering using the GO:0005634
x <- loadPPI(x,type="HPRD", filter=TRUE)
ppi(x)

data(RPKMS)
x <- loadPPI(x,type="HPRD",filter=TRUE,annot= NULL, RPKM= RPKMS, threshold = 5)
ppi(x)
```

loadTFBS-methods *Loading TF binding sites*

Description

This methods reads a BED file that contains the peak positions of different TF. All the TF peaks should be merged into one BED file that contains 4 columns that respectively contain the chromosome name, peak start, peak end, TF name.

Usage

```
## S4 method for signature 'ChiapetExperimentData,character'
loadTFBS(object, tfbsFile,header=FALSE, ...)
```

Arguments

object	(**Required**) a ChiapetExperimentData object
tfbsFile	(**Required**): path the BED file containing the position of the different TF binding site All the TF binding sites should be merged in this file as showed in this example:

```
 chr1  569820  569998 BHLHE40
 chr1  936071  936346 BHLHE40
 chr1 1014795 1015082 BHLHE40
 ........................
 ........................
chrY 13485240 13485769 ZBTB33
chrY 13488718 13489030 ZBTB33
chrY 15016340 15016848 ZBTB33
chrY 58843918 58844104 ZBTB33
```

header	*(optional)* indicates if the provided BED file has a header or node. by default header=FALSE
,	
...	reserved for later use.

Value

A ChiapetExperimentData object in which the tfbs slot is populated as a GRanges object.

Author(s)

Mohamed Nadhir Djekidel (<nde12@mails.tsinghua.edu.cn>)

References

Mohamed Nadhir D, Yang C et al *3CPET: Finding Co-factor Complexes in Chia-PET experiment using a Hierarchical Dirichlet Process*, ...

See Also

ChiapetExperimentData, loadTFBS , loadPPI, createIndexes

Examples

```
## Create a ChiapetExperimentData object
x <- ChiapetExperimentData(ppiType= "HPRD")

## load TFBS
tfbsFile <- file.path(system.file("example",package="R3CPET"),"HepG2_TF.txt.gz")
x <- loadTFBS(x,tfbsFile=tfbsFile)
tfbs(x)
```

NetworkCollection-class

protein interaction networks maintaining DNA loops

Description

The class NetworkCollection stores information about the set of protein networks that maintains DNA interactions.

Usage

```
NetworkCollection(networks, sizes,  TFCollection)
```

Arguments

networks	a list of list, each list contains the set of edges in each network
sizes	the sizes of each network. The should correspond to the sizes of the networks
TFCollection	the set of all the TF involved in all the interactions.

Details

The NetworkCollection contains three main information: *(i)* the set of edges in each network maintaining each DNA loop, *(ii)* the number of edges in each network and *(iii)* the set of TF involved in all the networks.

Value

a NetworkCollection object.

Accesors

networks gets the list of networks

sizes gets the vector containing the size of each network

TF gets the list of involved TF (after filtering)

Author(s)

Mohamed Nadhir Djekidel (<nde12@mails.tsinghua.edu.cn>)

References

Mohamed Nadhir D, Yang C et al *3CPET: Finding Co-factor Complexes in Chia-PET experiment using a Hierarchical Dirichlet Process*, ...

See Also

InferNetworks, ChiapetExperimentData, buildNetworks

Examples

```
showClass("NetworkCollection")
```

---

outputGenesPerClusterToDir-methods

List of genes in each cluster

Description

This helper methods get the set of genes located in the DNA-regions in each cluster. A folder that contain a bunch of `.txt` files (one for each cluster) is generated. We consider a gene to be part of a cluster if the (-1500bp, +500bp) around its TSS intersects with one of the DNA regions of the cluster.

Usage

```
## S4 method for signature 'ChromMaintainers,ChiapetExperimentData'
outputGenesPerClusterToDir(hdaRes,data,path="ClustersGenes", ...)
```

Arguments

hdaRes	a ChromMaintainers object in which the DNA-interaction are already clustered.
data	a ChiapetExperimentData object containing information about the interactions.
path	path of the folder to create. by default a folder named ClustersGenes is created in the current working directory.
...	additional parameters, not used for the moment.

Value

The specified folder is created with a list `.txt` files that contain the list of genes.

Author(s)

Mohamed Nadhir Djekidel (<nde12@mails.tsinghua.edu.cn>)

See Also

ChromMaintainers, InferNetworks, ChiapetExperimentData, clusterInteractions

Examples

```
   petFile <- file.path(system.file("example",package="R3CPET"),"HepG2_interactions.txt")
    tfbsFile <- file.path(system.file("example",package="R3CPET"),"HepG2_TF.txt.gz")

## Not run:
   x <- ChiapetExperimentData(pet = petFile, tfbs=  tfbsFile, IsBed = FALSE, ppiType="HPRD", filter= TRUE)
    ## build the different indexes
    x <- createIndexes(x)

    ## build networks connecting each interacting regions
    nets<- buildNetworks(x)

    ## infer the networks
    hlda<- InferNetworks(nets)
    hlda<- clusterInteractions(hlda)

    ## get the list of genes per cluster.
    outputGenesPerClusterToDir(hlda,x)


## End(Not run)
```

`outputGenesPerNetworkToDir`

List of genes controlled by each network

Description

This helper methods get the set of genes located in the DNA-regions controlled by each network. A folder that contains a bunch of `.txt` files (one for each network) is generated. We consider (-2500bp, +2500bp) around the TSS of gene located in a region showing 0.5 or more enrichment for the network.

Usage

```
## S4 method for signature 'ChromMaintainers,ChiapetExperimentData'
outputGenesPerNetworkToDir(hdaRes,data,path="NetworksGenes", ...)
```

Arguments

hdaRes	a ChromMaintainers object containing the enrichment values.
data	a ChiapetExperimentData object containing information about the interactions.
path	path of the folder to create. by default a folder named NetworksGenes is created in the current working directory.
...	additional parameters, not used for the moment.

Value

The specified folder is created with a list .txt files each for each network that contain the list of genes.

Author(s)

Mohamed Nadhir Djekidel (<nde12@mails.tsinghua.edu.cn>)

See Also

ChromMaintainers, InferNetworks, ChiapetExperimentData

Examples

```
  ## get the different datasets path
  petFile <- file.path(system.file("example",package="R3CPET"),"HepG2_interactions.txt")
  tfbsFile <- file.path(system.file("example",package="R3CPET"),"HepG2_TF.txt.gz")
## Not run:
    data(RPKMS)
   x <- ChiapetExperimentData(pet = petFile, tfbs=  tfbsFile, IsBed = FALSE, ppiType="HPRD", filter= TRUE)
    ## build the different indexes
    x <- createIndexes(x)

    ## build networks connecting each interacting regions
    nets<- buildNetworks(x)

    ## infer the networks
    hlda<- InferNetworks(nets)

    ## get the list of genes per network.
    outputGenesPerNetworkToDir(hlda,x)


## End(Not run)
```

`plot3CPETRes-methods` *Plotting clustering results*

Description

This method enables the user the generate different types of plots to visualize the results.

Usage

```
## S4 method for signature 'ChromMaintainers'
plot3CPETRes(object, path="", W=14, H=7 ,
          type=c("heatmap","clusters","curve","avgCurve","netSim", "networks"),
          byEdge=TRUE, layoutfct=layout.kamada.kawai, ...)
```

Arguments

`object`	*(***Required***)* a `ChromMaintainers` object that contains the results
`path`	*(optional)* path where to save the plots *should be* `".pdf"`. if not provided the plot will be displayed on the screen.
`W`	*(optional)* The width of the plot in the pdf file.by default it is 14 inch
`H`	*(optional)* The Height of the plot in the pdf file.by default it is 7 inch
`type`	type of the plot to generate. It can support the following values (*(default: "heatmap")*):

- `"heatmap"` : Generates a heatmap of the partnership of each DNA interaction to a chromatin maintainer network. Each column is a DNA interaction and each row a chromatin maintainer network.
- `"clusters"` : generates a pair-wise scatter plots of all clusters. *Note:* only supported if the `sota` method was applied.
- `"curve"` : for each cluster plots the enrichment profile of all the elements.
- `"avgCurve"` : draws the average curve of the enrichment profile for each clusters.
- `"netSim"` : plots a heatmap showing the percentage of common proteins or edges between the chromatin maintainer networks. *Note:* generally the similarity between networks is so small so the user can set the value in the diagonal to zero and then re-plot or plot the dissimilarity plot. if `byEdge = TRUE` a similarity based on the common edges is calculated otherwise by common nodes.
- `"networks"` : plots all the networks. if this option is chosen a pdf file named `"AllGraphs.pdf"` is generated in the current working unless the `path` parameter is explicitly determined. To get a finer control, the user can specify the type of layout to use, by default the `layout.kamada.kawai` is used. For additional layout functions you can check the `igraph` package. The reason we generate a pdf file because there is a lot of networks and it will not be convenient to display them in one plot, or generating multiple plots.

byEdge	*(optional)* if TRUE and type = "netSim" then the a heatmap showing the similarity between the chromatin maintainer networks by common edges. if FALSE the similarity is calculated based on the number of common nodes.
layoutfct	*(optional)* The graph layout algorithm to use. by default the layout.kamada.kawai is used. Additional functions are available in the igraph package.
...	options for future use.

Value

Different types of values are returned depending on the type of the plot selected.

"heatmap" returns a list generated by the pheatmap method, however it is always empty.

"clusters","curve","avgCurve" returns a list describing the number of plots per row and column.

"netSim" returns a list that contains a ggplot2 object and the similarity matrix

"networks" returns a list of ggplot2 objects, one per network.

Author(s)

Mohamed Nadhir Djekidel (<nde12@mails.tsinghua.edu.cn>)

See Also

cluster, igraph, sota

Examples

```
    ## get the different datasets path
   petFile <- file.path(system.file("example",package="R3CPET"),"HepG2_interactions.txt")
    tfbsFile <- file.path(system.file("example",package="R3CPET"),"HepG2_TF.txt.gz")

## Not run:
    data(RPKMS)
   x <- ChiapetExperimentData(pet = petFile, tfbs=  tfbsFile, IsBed = FALSE, ppiType="HPRD", filter= TRUE)
    ## build the different indexes
    x <- createIndexes(x)

    ## build networks connecting each interacting regions
    nets<- buildNetworks(x)

    ## infer the networks
    hlda<- InferNetworks(nets)

    ## cluster results
    hlda<- clusterInteractions(hlda)

    ## plot a heatmap
    plot3CPETRes(hlda,type="heatmap")

    ## plot clusters pair-wise scatter plots
```

```
plot3CPETRes(hlda,type="clusters")

## enrichment plot for the elements in each network
plot3CPETRes(hlda,type="curve")

##  average enrichment plot for the elements in each network
plot3CPETRes(hlda,type="avgCurve")

## heatmap showing the similarity between the different network
plot3CPETRes(hlda,type="netSim")

## plot all the networks in the file "AllGraphs.pdf"
nets_plot <- plot3CPETRes(hlda,type="networks")

## plot one of the networks
plot(nets_plot[[3]])


## End(Not run)
```

`plotTrack-methods` *Plot interaction on a genomic track*

Description

This helper method can be used to display a genomic track for a certain location that contains the chromosome and the related interactions if any.

Usage

```
## S4 method for signature 'ChiapetExperimentData,GRanges'
plotTrack(object, range)
```

Arguments

`object`	a `ChiapetExperimentData` object which contains the raw data.
`range`	The genomic coordinates of the location to display

Value

a `ggbio::track` object

Author(s)

Mohamed Nadhir Djekidel (<nde12@mails.tsinghua.edu.cn>)

See Also

`ChiapetExperimentData`

Examples

```
petFile <- file.path(system.file("example",package="R3CPET"),"HepG2_interactions.txt")
 tfbsFile <- file.path(system.file("example",package="R3CPET"),"HepG2_TF.txt.gz")

 ## Not run:
x <- ChiapetExperimentData(pet = petFile, tfbs= tfbsFile, IsBed = FALSE, ppiType="HPRD", filter= TRUE)
 gr <- GRanges("chr1",IRanges(start=100000,end=300000))
 plotTrack(x,gr)

## End(Not run)
```

`PrepareData-methods` *Loading the raw data all at once*

Description

Instead of loading the data one at a time and then creating the index using the methods `loadPETs`,`loadTFBS` and `createIndexes`. The user can directly use the method `PrepareData` to do that.

Usage

```
## S4 method for signature 'character,character,logical'
PrepareData(petFile,tfbsFile, petIsBed=TRUE)
```

Arguments

`petFile`	a `character` specifying the path to the interaction file. it the file is in a "bed" format `petIsBed` should be `TRUE`. The data should be formated as described in `loadPETs`.
`tfbsFile`	a `character` specifying the path to the transcription factors binding site file. The data should be formated as described in `loadTFBS`.
`petIsBed`	a logical value specifying if the interaction file is in a "bed" format or not.

Value

A `ChiapetExperimentData` object in which the `pet`,`tfbs` and `.dt` slots populated .

Author(s)

Mohamed Nadhir Djekidel (<nde12@mails.tsinghua.edu.cn>)

References

Mohamed Nadhir D, Yang C et al *3CPET: Finding Co-factor Complexes in Chia-PET experiment using a Hierarchical Dirichlet Process*, ...

See Also

ChiapetExperimentData, loadTFBS , loadPETs, loadPPI, createIndexes.

Examples

```
  ## get interactions file location
petFile <- file.path(system.file("example",package="R3CPET"),"HepG2_interactions.txt")

  ## get the TFBS file location
  tfFile <- file.path(system.file("example",package="R3CPET"),"HepG2_TF.txt.gz")

  ## Not run:
  ## load the data
  x<- PrepareData(petFile, tfFile, FALSE)
  x

## End(Not run)
```

RPKMS *A gene expression dataset*

Description

A gene expression dataset for the K562 cell line.

Usage

```
data(RPKMS)
```

Value

a `data.frame` containing genes expression in K562 cells.

Examples

```
data(RPKMS)
head(RPKMS)
```

updateResults-methods *update top maintain networks elements*

Description

This helper method can be used to update the list of interactions constituting the chromatin maintainer networks by changing the threshold.

Usage

```
## S4 method for signature 'ChromMaintainers,NetworkCollection,numeric'
updateResults(object,nets,thr=0.5)
```

Arguments

object	a ChromMaintainers object in which the clusters are already calculated
nets	a NetworkCollection used to get the vocabulary list.
thr	The cut-off threshold. the top edges that have an enrichment value that sum up to a value >= thr are considered.

Value

a ChromMaintainers object in which the topNodes and topEdges tables are updated.

Author(s)

Mohamed Nadhir Djekidel (<nde12@mails.tsinghua.edu.cn>)

See Also

InferNetworks, NetworkCollection, ChromMaintainers

Examples

```
petFile <- file.path(system.file("example",package="R3CPET"),"HepG2_interactions.txt")
 tfbsFile <- file.path(system.file("example",package="R3CPET"),"HepG2_TF.txt.gz")

 ## Not run:
 data(RPKMS)

x <- ChiapetExperimentData(pet = petFile, tfbs=  tfbsFile, IsBed = FALSE, ppiType="HPRD", filter= TRUE)
 ## build the different indexes
 x <- createIndexes(x)
 ## build networks connecting each interacting regions
 nets<- buildNetworks(x)

 ## infer the networks
 hlda<- InferNetworks(nets)
```

```
topNodes(hlda)

hlda <- updateResults(hlda, nets, 0.4)
topNodes(hlda)

## End(Not run)
```

---

visualizeCircos-methods

Generate circos plot per cluster

Description

This method generates a basic circos plot of the chromatin interaction in a given cluster.

Usage

```
## S4 method for signature 'ChromMaintainers,ChiapetExperimentData,numeric'
visualizeCircos(object, data, cluster = 1, chrLenghts = NULL)
```

Arguments

object	a ChromMaintainers object in which the clusters are already calculated.
data	a ChiapetExperimentData containing the interaction data.
cluster	the number of the cluster to display
chrLenghts	the chromatin lengths. if not provided the package suppose it is a human chromatin and uses the corresponding lengths. Change it if you are using another species.

Value

circos a GRanges object that contains the coordinate of the left side interactions. The right side interactions can be accessed by writing circos\$to.gr.

plot a ggplot object

Author(s)

Mohamed Nadhir Djekidel (<nde12@mails.tsinghua.edu.cn>)

See Also

NetworkCollection, ChromMaintainers

Examples

```
      ## get the different datasets path
     petFile <- file.path(system.file("example",package="R3CPET"),"HepG2_interactions.txt")
      tfbsFile <- file.path(system.file("example",package="R3CPET"),"HepG2_TF.txt.gz")

## Not run:
    data(RPKMS)
   x <- ChiapetExperimentData(pet = petFile, tfbs=  tfbsFile, IsBed = FALSE, ppiType="HPRD", filter= TRUE)
    ## build the different indexes
    x <- createIndexes(x)

    ## build networks connecting each interacting regions
    nets<- buildNetworks(x)

    ## infer the networks
    hlda<- InferNetworks(nets)
    hlda<- clusterInteractions(hlda)

    visualizeCircos(hlda,x, cluster=3)

## End(Not run)
```

`visualizeInteractions` *Display a Circos plot of ChIA-pet interactions*

Description

This method can be used to draw a circos plot of the chromatin interactions located in the given genomic range.

Usage

```
## S4 method for signature 'ChiapetExperimentData,GRanges'
visualizeInteractions(object, range)
```

Arguments

`object`	a `ChiapetExperimentData` in which the interactions are already loaded. Check `loadPETs` for more info.
`range`	a `GRanges` object containing the genomic region of interest.

Value

A ciros plot of the selected region is displayed and a list containing the following objects is returned.

`circos :` a `GRanges` object that contains the involved chromatin interactions.

`plot :` a `ggplot` object containing plot.

Author(s)

Mohamed Nadhir Djekidel (<nde12@mails.tsinghua.edu.cn>)

See Also

ChiapetExperimentData, loadPETs, ggbio, GRanges

Examples

```
petFile <- file.path(system.file("example",package="R3CPET"),"HepG2_interactions.txt")
tfbsFile <- file.path(system.file("example",package="R3CPET"),"HepG2_TF.txt.gz")


## Not run:
x <- ChiapetExperimentData(pet = petFile, tfbs= tfbsFile, IsBed = FALSE, ppiType="HPRD", filter= TRUE)
## plot intractions in the region of interest
gr <- GRanges("chr1", IRanges(1240000,10300000))
p <- visualizeInteractions(x, gr)
p

## End(Not run)
```

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