Package 'R3CPET'

October 12, 2016

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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URL https://github.com/sirusb/R3CPET

BugReports https://github.com/sirusb/R3CPET/issues

License GPL (>=2)

Depends R (>= 3.2), Rcpp (>= 0.10.4), methods

Imports methods, parallel, clues, ggplot2, pheatmap, clValid, igraph, data.table, reshape2, Hmisc, RCurl, BiocGenerics, S4Vectors, IRanges, GenomeInfoDb, GenomicRanges, ggbio

LinkingTo Rcpp

VignetteBuilder knitr

Suggests BiocStyle, knitr, TxDb.Hsapiens.UCSC.hg19.knownGene, biovizBase, biomaRt, AnnotationDbi, org.Hs.eg.db, shiny, ChIPpeakAnno

biocViews NetworkInference, GenePrediction, Bayesian, GraphAndNetwork, Network, GeneExpression

NeedsCompilation yes

R topics documented:

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

Package:	R3CPET
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.

Definition

```
setClassUnion("cluesOrSota", c("clues", "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 (<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. Wang, S., Qiu, W., and Zamar, R. H. (2007). *CLUES: A non-parametric clustering method based on local shrinking. Computational Statistics & Data Analysis*, Vol. 52, issue 1, pages 286-298.

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.

Two kinds of clustering are supported supervised and un-supervised. In the first one the function sota from the clValid package. In the second case the clues method from the clues package is used.

Usage

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

Arguments

object   (**Required***)* a non-empty ChromMaintainers object

method   (*optional*)used to specify the method to use. if clues is specified, the number
                of clusters will be determined automatically. if method = "sota", the user can
                specify the number of clusters by setting the parameter nbClus, by default it is
                set to 20. by default method = "clues".

                Another option is that user can first do an automatic clustering using "clues"
                and then if judges that more or less clusters are required he can recall the
                clusterInteractions method and specify the number the number of clusters.

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 or clues object.

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.

Wang, S., Qiu, W., and Zamar, R. H. (2007). *CLUES: A non-parametric clustering method based on local shrinking*. Computational Statistics & Data Analysis, Vol. 52, issue 1, pages 286-298

See Also

ChromMaintainers, clues , 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).
...	not used for the moment, left for additional parameters.

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)
```

Index