

Package ‘LOLA’

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Title Location overlap analysis for enrichment of genomic ranges

Description Provides functions for testing overlap of sets of genomic regions with public and custom region set (genomic ranges) databases.

This make is possible to do automated enrichment analysis for genomic region sets, thus facilitating interpretation of functional genomics and epigenomics data.

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Imports BiocGenerics, S4Vectors, IRanges, GenomicRanges, data.table

Suggests knitr, parallel, testthat

Enhances simpleCache, qvalue

VignetteBuilder knitr

License GPL-3

biocViews GeneSetEnrichment, GeneRegulation, GenomeAnnotation,
SystemsBiology, FunctionalGenomics, ChIPSeq, MethylSeq,
Sequencing

URL <http://databio.org/lola>

BugReports <http://github.com/sheffien/LOLA>

NeedsCompilation no

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buildRestrictedUniverse

If you want to test for differential enrichment within your usersets, you can restrict the universe to only regions that are covered in at least one of your sets. This function helps you build just such a restricted universe

Description

If you want to test for differential enrichment within your usersets, you can restrict the universe to only regions that are covered in at least one of your sets. This function helps you build just such a restricted universe

Usage

```
buildRestrictedUniverse(userSets)
```

Arguments

userSets The userSets you will pass to the enrichment calculation.

Value

A restricted universe

Examples

```
data("sample_input", package="LOLA") # load userSets
restrictedUniverse = buildRestrictedUniverse(userSets)
```

```
checkUniverseAppropriateness
      Check universe appropriateness
```

Description

Checks to see if the universe is appropriate for the userSets. Anything in the userSets should be present in the universe. In addition, 2 different regions in the userSets should not overlap the same region in the universe.

Usage

```
checkUniverseAppropriateness(userSets, userUniverse, cores = 1,
                             fast = FALSE)
```

Arguments

userSets	Regions of interest
userUniverse	Regions tested for inclusion in userSets
cores	Number of processors
fast	Skip the (slow) test for many-to-many relationships

Value

No return value.

Examples

```
data("sample_input", package="LOLA") # load userSet
data("sample_universe", package="LOLA") # load userUniverse
checkUniverseAppropriateness(userSets, userUniverse)
```

```
cleanws      cleanws takes multi-line, code formatted strings and just formats them
              as simple strings
```

Description

cleanws takes multi-line, code formatted strings and just formats them as simple strings.

Usage

```
cleanws(string)
```

Arguments

string string to clean

Value

A string with all consecutive whitespace characters, including tabs and newlines, merged into a single space.

countOverlapsAnyRev *Just a reverser. Reverses the order of arguments and passes them untouched to countOverlapsAny – so you can use it with lapply.*

Description

Just a reverser. Reverses the order of arguments and passes them untouched to countOverlapsAny – so you can use it with lapply.

Usage

```
countOverlapsAnyRev(subj, quer)
```

Arguments

subj Subject
quer Query

Value

Results from countOverlaps

extractEnrichmentOverlaps
Given a single row from an enrichment table calculation, finds the set of overlaps between the user set and the test set. You can then use these, for example, to get sequences for those regions.

Description

Given a single row from an enrichment table calculation, finds the set of overlaps between the user set and the test set. You can then use these, for example, to get sequences for those regions.

Usage

```
extractEnrichmentOverlaps(locResult, userSets, regionDB)
```

Arguments

locResult Results from runLOLA function
userSets User sets passed to the runLOLA function
regionDB Region database used

Value

userSets overlapping the supplied database entry.

Examples

```
dbPath = system.file("extdata", "hg19", package="LOLA")
regionDB = loadRegionDB(dbLocation=dbPath)
data("sample_universe", package="LOLA")
data("sample_input", package="LOLA")

getRegionSet(regionDB, collections="ucsc_example", filenames="vistaEnhancers.bed")
getRegionSet(dbPath, collections="ucsc_example", filenames="vistaEnhancers.bed")

res = runLOLA(userSets, userUniverse, regionDB, cores=1)
locResult = res[2,]
extractEnrichmentOverlaps(locResult, userSets, regionDB)
writeCombinedEnrichment(locResult, "temp_outfolder")

userSetsRedefined = redefineUserSets(userSets, userUniverse)
resRedefined = runLOLA(userSetsRedefined, userUniverse, regionDB, cores=1)
```

getRegionSet

Grab a single region set from a database, specified by filename.

Description

If you want to work with a LOLA regionDB region set individually, this function can help you. It can extract individual (or subsets of) region sets from either loaded regionDBs, loaded with loadRegionDB(), or from a database on disk, where only the region sets of interest will be loaded.

Usage

```
getRegionSet(regionDB, filenames, collections = NULL)
```

Arguments

regionDB	A region database loaded with loadRegionDB().
filenames	Filename(s) of a particular region set to grab.
collections	(optional) subset of collections to list

Value

A GRanges object derived from the specified file in the regionDB.

Examples

```
dbPath = system.file("extdata", "hg19", package="LOLA")
regionDB = loadRegionDB(dbLocation=dbPath)
data("sample_universe", package="LOLA")
data("sample_input", package="LOLA")

getRegionSet(regionDB, collections="ucsc_example", filenames="vistaEnhancers.bed")
```

```

getRegionSet(dbPath, collections="ucsc_example", filenames="vistaEnhancers.bed")

res = runLOLA(userSets, userUniverse, regionDB, cores=1)
locResult = res[2,]
extractEnrichmentOverlaps(locResult, userSets, regionDB)
writeCombinedEnrichment(locResult, "temp_outfolder")

userSetsRedefined = redefineUserSets(userSets, userUniverse)
resRedefined = runLOLA(userSetsRedefined, userUniverse, regionDB, cores=1)

```

lapplyAlias	<i>Function to run lapply or mclapply, depending on the option set in getOption("mc.cores"), which can be set with setLapplyAlias().</i>
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Description

Function to run lapply or mclapply, depending on the option set in getOption("mc.cores"), which can be set with setLapplyAlias().

Usage

```
lapplyAlias(..., mc.preschedule = TRUE)
```

Arguments

... Arguments passed lapply() or mclapply()
mc.preschedule Argument passed to mclapply

Value

Result from lapply or parallel::mclapply

listRegionSets	<i>Lists the region sets for given collection(s) in a region database on disk.</i>
----------------	------------------------------------------------------------------------------------

Description

Lists the region sets for given collection(s) in a region database on disk.

Usage

```
listRegionSets(regionDB, collections = NULL)
```

Arguments

regionDB File path to region database
collections (optional) subset of collections to list

Value

a list of files in the given collections

Examples

```
dbPath = system.file("extdata", "hg19", package="LOLA")
listRegionSets(dbPath)
```

listToGRangesList	<i>converts a list of GRanges into a GRangesList; strips all metadata.</i>
-------------------	----------------------------------------------------------------------------

Description

converts a list of GRanges into a GRangesList; strips all metadata.

Usage

```
listToGRangesList(lst)
```

Arguments

lst a list of GRanges objects

Value

a GRangesList object

loadRegionDB	<i>Helper function to annotate and load a regionDB, a folder with subfolder collections of regions.</i>
--------------	---------------------------------------------------------------------------------------------------------

Description

Helper function to annotate and load a regionDB, a folder with subfolder collections of regions.

Usage

```
loadRegionDB(dbLocation, useCache = TRUE, limit = NULL,
             collections = NULL)
```

Arguments

dbLocation folder where your regionDB is stored, or list of such folders
 useCache uses simpleCache to cache and load the results
 limit You can limit the number of regions for testing. Default: NULL (no limit)
 collections Restrict the database loading to this list of collections

Value

regionDB list containing database location, region and collection annotations, and regions GRanges-List

Examples

```
dbPath = system.file("extdata", "hg19", package="LOLA")
regionDB = loadRegionDB(dbLocation=dbPath)
```

LOLA

Provides functions for genome location overlap analysis.

Description

Run, Lola!

Author(s)

Nathan Sheffield

References

<http://github.com/sheffien>

mergeRegionDBs

Given two regionDBs, (lists returned from loadRegionDB()), This function will combine them into a single regionDB. This will enable you to combine, for example, LOLA Core databases with custom databases into a single analysis.

Description

Given two regionDBs, (lists returned from loadRegionDB()), This function will combine them into a single regionDB. This will enable you to combine, for example, LOLA Core databases with custom databases into a single analysis.

Usage

```
mergeRegionDBs(dbA, dbB)
```

Arguments

dbA First regionDB database.
dbB Second regionDB database.

Value

A combined regionDB.

Examples

```
dbPath = system.file("extdata", "hg19", package="LOLA")
regionDB = loadRegionDB(dbPath)
combinedRegionDB = mergeRegionDBs(regionDB, regionDB)
```

nlist	<i>Named list function.</i>
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Description

This function is a drop-in replacement for the base `list()` function, which automatically names your list according to the names of the variables used to construct it. It seamlessly handles lists with some names and others absent, not overwriting specified names while naming any unnamed parameters. Took me awhile to figure this out.

Usage

```
nlist(...)
```

Arguments

... arguments passed to `list()`

Value

A named list object.

readBed	<i>Imports bed files and creates GRanges objects, using the <code>fread()</code> function from <code>data.table</code>.</i>
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Description

Imports bed files and creates GRanges objects, using the `fread()` function from `data.table`.

Usage

```
readBed(file)
```

Arguments

file File name of bed file.

Value

GRanges Object

Examples

```
a = readBed(system.file("extdata", "examples/combined_regions.bed",
package="LOLA"))
```

readCollection	<i>Given a bunch of region set files, read in all those flat (bed) files and create a GRangesList object holding all the region sets. This function is used by readRegionGRL to process annotation objects.</i>
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Description

Given a bunch of region set files, read in all those flat (bed) files and create a GRangesList object holding all the region sets. This function is used by readRegionGRL to process annotation objects.

Usage

```
readCollection(filesToRead, limit = NULL)
```

Arguments

filesToRead	a vector containing bed files
limit	for testing purposes, limit the number of files read. NULL for no limit (default).

Value

A GRangesList with the GRanges in the filesToRead.

Examples

```
files = list.files(system.file("extdata", "hg19/ucsc_example/regions",
  package="LOLA"), pattern="*.bed")
regionAnno = readCollection(files)
```

readCollectionAnnotation	<i>Read collection annotation</i>
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Description

Read collection annotation

Usage

```
readCollectionAnnotation(dbLocation, collections = NULL)
```

Arguments

dbLocation	Location of the database
collections	Restrict the database loading to this list of collections. Leave NULL to load the entire database (Default).

Value

Collection annotation data.table

Examples

```
dbPath = system.file("extdata", "hg19", package="LOLA")
collectionAnno = readCollectionAnnotation(dbLocation=dbPath)
```

readCollectionFiles	<i>Given a database and a collection, this will create the region annotation data.table; either giving a generic table based on file names, or by reading in the annotation data.</i>
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Description

Given a database and a collection, this will create the region annotation data.table; either giving a generic table based on file names, or by reading in the annotation data.

Usage

```
readCollectionFiles(dbLocation, collection, refreshSizes = FALSE)
```

Arguments

dbLocation	folder where your regionDB is stored.
collection	Collection folder to load
refreshSizes	should I recreate the sizes files documenting how many regions (lines) are in each region set?

Value

A data.table annotating the regions in the collections.

Examples

```
dbPath = system.file("extdata", "hg19", package="LOLA")
regionAnno = readCollectionFiles(dbLocation=dbPath, "ucsc_example")
```

readRegionGRL	<i>This function takes a region annotation object and reads in the regions, returning a GRangesList object of the regions.</i>
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Description

This function takes a region annotation object and reads in the regions, returning a GRangesList object of the regions.

Usage

```
readRegionGRL(dbLocation, annoDT, refreshCaches = FALSE, useCache = TRUE,
  limit = NULL)
```

Arguments

dbLocation	folder of regionDB
annoDT	output of readRegionSetAnnotation().
refreshCaches	should I recreate the caches?
useCache	uses simpleCache to cache and load the results
limit	for testing purposes, limit the number of files read. NULL for no limit (default).

Value

GRangesList object

Examples

```
dbPath = system.file("extdata", "hg19", package="LOLA")
regionAnno = readRegionSetAnnotation(dbLocation=dbPath)
regionGRL = readRegionGRL(dbLocation= dbPath, regionAnno, useCache=FALSE)
```

readRegionSetAnnotation

Given a folder containing region collections in subfolders, this function will either read the annotation file if one exists, or create a generic annotation file.

Description

Given a folder containing region collections in subfolders, this function will either read the annotation file if one exists, or create a generic annotation file.

Usage

```
readRegionSetAnnotation(dbLocation, collections = NULL,
  refreshCaches = FALSE, useCache = TRUE)
```

Arguments

dbLocation	folder where your regionDB is stored.
collections	Restrict the database loading to this list of collections Leave NULL to load the entire database (Default).
refreshCaches	should I recreate the caches?
useCache	Use simpleCache to store results and load them?

Value

Region set annotation (data.table)

Examples

```
dbPath = system.file("extdata", "hg19", package="LOLA")
regionAnno = readRegionSetAnnotation(dbLocation=dbPath)
```

redefineUserSets	<i>This function will take the user sets, overlap with the universe, and redefine the user sets as the set of regions in the user universe that overlap at least one region in user sets. this makes for a more appropriate statistical enrichment comparison, as the user sets are actually exactly the same regions found in the universe otherwise, you can get some weird artifacts from the many-to-many relationship between user set regions and universe regions.</i>
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Description

This function will take the user sets, overlap with the universe, and redefine the user sets as the set of regions in the user universe that overlap at least one region in user sets. this makes for a more appropriate statistical enrichment comparison, as the user sets are actually exactly the same regions found in the universe otherwise, you can get some weird artifacts from the many-to-many relationship between user set regions and universe regions.

Usage

```
redefineUserSets(userSets, userUniverse, cores = 1)
```

Arguments

userSets	Regions of interest
userUniverse	Regions tested for inclusion in userSets
cores	Number of processors

Value

userSets redefined in terms of userUniverse

Examples

```
dbPath = system.file("extdata", "hg19", package="LOLA")
regionDB = loadRegionDB(dbLocation=dbPath)
data("sample_universe", package="LOLA")
data("sample_input", package="LOLA")

getRegionSet(regionDB, collections="ucsc_example", filenames="vistaEnhancers.bed")
getRegionSet(dbPath, collections="ucsc_example", filenames="vistaEnhancers.bed")

res = runLOLA(userSets, userUniverse, regionDB, cores=1)
locResult = res[2,]
extractEnrichmentOverlaps(locResult, userSets, regionDB)
writeCombinedEnrichment(locResult, "temp_outfolder")

userSetsRedefined = redefineUserSets(userSets, userUniverse)
resRedefined = runLOLA(userSetsRedefined, userUniverse, regionDB, cores=1)
```

replaceFileExtension *This will change the string in filename to have a new extension*

Description

This will change the string in filename to have a new extension

Usage

```
replaceFileExtension(filename, extension)
```

Arguments

filename	string to convert
extension	new extension

Value

Filename with original extension deleted, replaced by provided extension

runLOLA *Enrichment Calculation*

Description

Workhorse function that calculates overlaps between userSets, and then uses a fisher's exact test rank them by significance of the overlap.

Usage

```
runLOLA(userSets, userUniverse, regionDB, minOverlap = 1, cores = 1,
        redefineUserSets = FALSE)
```

Arguments

userSets	Regions of interest
userUniverse	Regions tested for inclusion in userSets
regionDB	Region DB to check for overlap, from loadRegionDB()
minOverlap	(Default:1) Minimum bases required to count an overlap
cores	Number of processors
redefineUserSets	run redefineUserSets() on your userSets?

Value

Data.table with enrichment results. Rows correspond to individual pairwise fisher's tests comparing a single userSet with a single databaseSet. The columns in this data.table are: userSet and dbSet: index into their respective input region sets. pvalueLog: $-\log_{10}(\text{pvalue})$ from the fisher's exact result; logOddsRatio: result from the fisher's exact test; support: number of regions in userSet overlapping databaseSet; rnkPV, rnkLO, rnkSup: rank in this table of p-value, logOddsRatio, and Support respectively. The $-\text{value}$ is the negative natural log of the p-value returned from a one-sided fisher's exact test. maxRnk, meanRnk: max and mean of the 3 previous ranks, providing a combined ranking system. b, c, d: 3 other values completing the 2x2 contingency table (with support). The remaining columns describe the dbSet for the row.

If you have the qvalue package installed from bioconductor, runLOLA will add a q-value transformation to provide FDR scores automatically.

Examples

```
dbPath = system.file("extdata", "hg19", package="LOLA")
regionDB = loadRegionDB(dbLocation=dbPath)
data("sample_universe", package="LOLA")
data("sample_input", package="LOLA")

getRegionSet(regionDB, collections="ucsc_example", filenames="vistaEnhancers.bed")
getRegionSet(dbPath, collections="ucsc_example", filenames="vistaEnhancers.bed")

res = runLOLA(userSets, userUniverse, regionDB, cores=1)
locResult = res[,2,]
extractEnrichmentOverlaps(locResult, userSets, regionDB)
writeCombinedEnrichment(locResult, "temp_outfolder")

userSetsRedefined = redefineUserSets(userSets, userUniverse)
resRedefined = runLOLA(userSetsRedefined, userUniverse, regionDB, cores=1)
```

sampleGRL

Function to sample regions from a GRangesList object, in specified proportion

Description

Function to sample regions from a GRangesList object, in specified proportion

Usage

```
sampleGRL(GRL, prop)
```

Arguments

GRL	GRangesList from which to sample
prop	vector with same length as GRL, of values between 0-1, proportion of the list to select

Value

A sampled subset of original GRangesList object.

setLapplyAlias	<i>To make parallel processing a possibility but not required, I use an lapply alias which can point at either the base lapply (for no multicore), or it can point to mclapply, and set the options for the number of cores (what mclapply uses). With no argument given, returns instead the number of cpus currently selected.</i>
----------------	--------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------

Description

To make parallel processing a possibility but not required, I use an lapply alias which can point at either the base lapply (for no multicore), or it can point to mclapply, and set the options for the number of cores (what mclapply uses). With no argument given, returns instead the number of cpus currently selected.

Usage

```
setLapplyAlias(cores = 0)
```

Arguments

cores Number of cpus

Value

None

setSharedDataDir	<i>setSharedDataDir Sets global variable specifying the default data directory.</i>
------------------	-------------------------------------------------------------------------------------

Description

setSharedDataDir Sets global variable specifying the default data directory.

Usage

```
setSharedDataDir(sharedDataDir)
```

Arguments

sharedDataDir directory where the shared data is stored.

Value

No return value.

Examples

```
setSharedDataDir("project/data")
```

splitDataTable	<i>Efficiently split a data.table by a column in the table</i>
----------------	----------------------------------------------------------------

Description

Efficiently split a data.table by a column in the table

Usage

```
splitDataTable(DT, splitFactor)
```

Arguments

DT	Data.table to split
splitFactor	Column to split, which can be a character vector or an integer.

Value

List of data.table objects, split by column

splitFileIntoCollection

This function will take a single large bed file that is annotated with a column grouping different sets of similar regions, and split it into separate files for use with the LOLA collection format.

Description

This function will take a single large bed file that is annotated with a column grouping different sets of similar regions, and split it into separate files for use with the LOLA collection format.

Usage

```
splitFileIntoCollection(filename, splitCol)
```

Arguments

filename	the file to split
splitCol	factor column that groups the lines in the file by set

Value

No return value.

Examples

```
combFile = system.file("extdata", "examples/combined_regions.bed", package="LOLA")
splitFileIntoCollection(combFile, 4)
```

userSets	<i>An example set of regions, sampled from the example database.</i>
----------	----------------------------------------------------------------------

Description

A dataset containing a few sample regions.

Usage

```
data(sample_input)
```

Format

A GRangesList object

Value

No return value.

Examples

```
## Not run:
  This is how I produced the sample data sets:
  dbPath = system.file("extdata", "hg19", package="LOLA")
  regionDB = loadRegionDB(dbLocation= dbPath)
  userSetA = reduce(do.call(c, (sampleGRL(regionDB$regionGRL,
  prop=c(.1,.25,.05,.05,0)))))
  userSetB = reduce(do.call(c, (sampleGRL(regionDB$regionGRL,
  prop=c(.2,.05,.05,.05,0)))))

  userSets = GRangesList(setA=userSetA, setB=userSetB)
  userUniverse = reduce(do.call(c, regionDB$regionGRL))
  save(userSets, file="sample_input.RData")
  save(userUniverse, file="sample_universe.RData")

## End(Not run)
```

userUniverse	<i>A reduced GRanges object from the example regionDB database</i>
--------------	--------------------------------------------------------------------

Description

A reduced GRanges object from the example regionDB database

Usage

```
data(sample_universe)
```

Format

A GRanges object

Value

No return value.

write.tsv	<i>Wrapper of write.table that provides defaults to write a simple .tsv file. Passes additional arguments to write.table</i>
-----------	------------------------------------------------------------------------------------------------------------------------------

Description

Wrapper of write.table that provides defaults to write a simple .tsv file. Passes additional arguments to write.table

Usage

```
write.tsv(...)
```

Arguments

... Additional arguments passed to write.table

Value

No return value

writeCombinedEnrichment	<i>Function for writing output all at once: combinedResults is an table generated by "locationEnrichment()" or by rbinding category/location results. Writes all enrichments to a single file, and also spits out the same data divided into groups based on userSets, and Databases, just for convenience. disable this with an option.</i>
-------------------------	----------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------

Description

Function for writing output all at once: combinedResults is an table generated by "locationEnrichment()" or by rbinding category/location results. Writes all enrichments to a single file, and also spits out the same data divided into groups based on userSets, and Databases, just for convenience. disable this with an option.

Usage

```
writeCombinedEnrichment(combinedResults, outFolder = NULL,
  includeSplits = TRUE)
```

Arguments

combinedResults	enrichment results object
outFolder	location to write results on disk
includeSplits	also include individual files for each user set and database?

Value

No return value.

Examples

```
dbPath = system.file("extdata", "hg19", package="LOLA")
regionDB = loadRegionDB(dbLocation=dbPath)
data("sample_universe", package="LOLA")
data("sample_input", package="LOLA")

getRegionSet(regionDB, collections="ucsc_example", filenames="vistaEnhancers.bed")
getRegionSet(dbPath, collections="ucsc_example", filenames="vistaEnhancers.bed")

res = runLOLA(userSets, userUniverse, regionDB, cores=1)
locResult = res[2,]
extractEnrichmentOverlaps(locResult, userSets, regionDB)
writeCombinedEnrichment(locResult, "temp_outfolder")

userSetsRedefined = redefineUserSets(userSets, userUniverse)
resRedefined = runLOLA(userSetsRedefined, userUniverse, regionDB, cores=1)
```

writeDataTableSplitByColumn

Given a data table and a factor variable to split on, efficiently divides the table and then writes the different splits to separate files, named with filePrepend and numbered according to split.

Description

Given a data table and a factor variable to split on, efficiently divides the table and then writes the different splits to separate files, named with filePrepend and numbered according to split.

Usage

```
writeDataTableSplitByColumn(DT, splitFactor, filePrepend = "",
  orderColumn = NULL)
```

Arguments

DT	data.table to split
splitFactor	column of DT to split on
filePrepend	notation string to prepend to output files
orderColumn	column of DT to order on (defaults to the first column)

Value

number of splits written

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