Package ‘LOLA’

March 22, 2017

Version 1.4.0

Date 2015-05-18

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

R topics documented:

buildRestrictedUniverse ........................................... 2
checkUniverseAppropriateness ...................................... 3
cleanws ............................................................... 3
countOverlapsAnyRev ............................................... 4
evaluateEnrichmentOverlaps ....................................... 4
getRegionSet ......................................................... 5
lapplyAlias .................................................................. 6
listRegionSets .......................................................... 6
listToGRangesList ...................................................... 7
loadRegionDB .......................................................... 7
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

```r
buildRestrictedUniverse(userSets)
```

Arguments

- `userSets`: The userSets you will pass to the enrichment calculation.

Value

A restricted universe
Examples

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

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

```r
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

```r
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

```r
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
getRegionSet

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")
listRegionSets

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

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

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

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

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
listToGRangesList

Value

a list of files in the given collections

Examples

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

listToGRangesList(lst)

Arguments

lst

a list of GRanges objects

Value

a GRangesList object

loadRegionDB

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

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
### 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.

#### Usage

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

#### Arguments

- `dbA` First regionDB database.
- `dbB` Second regionDB database.

#### Value

A combined regionDB.
Examples

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

---

**nlist**

*Named list function.*

**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**

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

**Arguments**

... arguments passed to `list()`

**Value**

A named list object.

---

**readBed**

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

**Description**

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

**Usage**

```r
readBed(file)```

**Arguments**

- `file` File name of bed file.

**Value**

GRanges Object

**Examples**

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

readCollection  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.

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

Read collection annotation

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**

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

**readCollectionFiles**

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.

**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**

```r
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**

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

**readRegionGRL**

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

**Description**

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

**Usage**

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

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)
redefineUserSets

**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**

```r
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: -log10(pvalue) from the Fisher's exact result; logOddsRatio: result from the Fisher's exact test; support: number of regions in userSet overlapping databaseSet; mkPV, mkLO, mkSup: rank in this table of p-value, logOddsRatio, and Support respectively. The –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
```r
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
```r
sampleGRL(GRL, prop)
```

### Arguments

<table>
<thead>
<tr>
<th>Argument</th>
<th>Description</th>
</tr>
</thead>
<tbody>
<tr>
<td>GRL</td>
<td>GRangesList from which to sample</td>
</tr>
<tr>
<td>prop</td>
<td>vector with same length as GRL, of values between 0-1, proportion of the list to select</td>
</tr>
</tbody>
</table>

### Value
A sampled subset of original GRangesList object.
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**

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

**Arguments**

- `cores` Number of cpus

**Value**

None

---

setSharedDataDir

Sets global variable specifying the default data directory.

**Description**

setSharedDataDir Sets global variable specifying the default data directory.

**Usage**

```r
setSharedDataDir(sharedDataDir)
```

**Arguments**

- `sharedDataDir` directory where the shared data is stored.

**Value**

No return value.

**Examples**

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

**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**

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

An example set of regions, sampled from the example database.

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

A reduced GRanges object from the example regionDB database

Description
A reduced GRanges object from the example regionDB database

Usage
data(sample_universe)

Format
A GRanges object
Value

No return value.

---

**write.tsv**

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

**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**

*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.*

**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?
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**

```r
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
Index

*Topic** datasets
  userSets, 18
  userUniverse, 18

buildRestrictedUniverse, 2

checkUniverseAppropriateness, 3
cleans, 3
countOverlapsAnyRev, 4

extractEnrichmentOverlaps, 4

getRegionSet, 5

lapplyAlias, 6
listRegionSets, 6
listToGRangesList, 7
loadRegionDB, 7
LOLA, 8
LOLA-package (LOLA), 8

mergeRegionDBs, 8

nlist, 9

readBed, 9
readCollection, 10
readCollectionAnnotation, 10
readCollectionFiles, 11
readRegionGRL, 11
readRegionSetAnnotation, 12
redefineUserSets, 13
replaceFileExtension, 14
runLOLA, 14

sampleGRL, 15
setLapplyAlias, 16
setSharedDataDir, 16
splitDataTable, 17
splitFileIntoCollection, 17

userSets, 18
userUniverse, 18

write.tsv, 19
writeCombinedEnrichment, 19
writeDataTableSplitByColumn, 20