

# 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>
-------------	--

---

### 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>
-------	-----------------------------

---

**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 fread() function from data.table.</i>
---------	---

---

**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>
----------------	---

---

**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>
--------------------------	-----------------------------------

---

**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>
---------------------	---

---

**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>
---------------	--

---

**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>
------------------	---

---

### 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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