Package ‘rGREAT’

April 13, 2024

Type Package
Title GREAT Analysis - Functional Enrichment on Genomic Regions
Version 2.5.7
Date 2024-03-07
Depends R (>= 4.0.0), GenomicRanges, IRanges, methods
Imports graphics, rjson, GetoptLong (>= 0.0.9), RCurl, utils, stats,
  GlobalOptions, shiny, DT, GenomicFeatures, digest, GO.db,
  progress, circlize, AnnotationDbi,
  TxDb.Hsapiens.UCSC.hg19.knownGene,
  TxDb.Hsapiens.UCSC.hg38.knownGene, org.Hs.eg.db, RColorBrewer,
  S4Vectors, GenomeInfoDb, foreach, doParallel, Rcpp
Suggests testthat (>= 0.3), knitr, rmarkdown, BiocManager,
  org.Mm.eg.db, msigdb, KEGGREST, reactome.db
Enhances BioMartGOGeneSets, UniProtKeywords
VignetteBuilder knitr
biocViews GeneSetEnrichment, GO, Pathways, Software, Sequencing,
  WholeGenome, GenomeAnnotation, Coverage
Description GREAT (Genomic Regions Enrichment of Annotations Tool) is a type of
  functional enrichment analysis directly performed on genomic regions. This package
  implements the GREAT algorithm (the local GREAT analysis), also it supports directly
  interacting with the GREAT web service (the online GREAT analysis). Both analysis
  can be viewed by a Shiny application. rGREAT by default supports more than 600 organisms
  and a large number of gene set collections, as well as self-provided gene sets and
  organisms from users. Additionally, it implements a general method for dealing
  with background regions.
URL https://github.com/jokergoo/rGREAT,
License MIT + file LICENSE
LinkingTo Rcpp
git_url https://git.bioconductor.org/packages/rGREAT
git_branch devel
Contents

availableCategories-GreatJob-method .......................................................... 3
availableOntologies-GreatJob-method ........................................................... 4
extendTSS .......................................................................................................... 5
extendTSSFromDataFrame .................................................................................. 6
extendTSSFromOrgDb ......................................................................................... 7
extendTSSFromTxDb .......................................................................................... 8
getEnrichmentTable-dispatch .......................................................................... 8
getEnrichmentTable-GreatJob-method .............................................................. 9
getEnrichmentTable-GreatObject-method ......................................................... 10
getEnrichmentTables-dispatch ......................................................................... 10
getEnrichmentTables-GreatJob-method ............................................................ 11
getEnrichmentTables-GreatObject-method ....................................................... 12
getGapFromUCSC ............................................................................................... 13
getGeneSetsFromBioMart .................................................................................. 13
getGeneSetsFromOrgDb ...................................................................................... 14
getGenesFromGencode ...................................................................................... 15
getGenomeDataFromNCBI .................................................................................. 15
getGREATDefaultTSS ...................................................................................... 16
getKEGGGenome ............................................................................................... 17
getKEGGPathways ............................................................................................. 17
getRefSeqGenesFromUCSC .............................................................................. 18
getRegionGeneAssociations-dispatch .............................................................. 18
getRegionGeneAssociations-GreatJob-method ............................................... 19
getRegionGeneAssociations-GreatObject-method .......................................... 20
getTSS ............................................................................................................... 20
great .................................................................................................................. 21
GreatJob ............................................................................................................ 24
GreatJob-class .................................................................................................. 25
GreatObject ....................................................................................................... 26
GreatObject-class .............................................................................................. 27
great_opt .......................................................................................................... 27
plotRegionGeneAssociationGraphs-GreatJob-method .................................. 28
plotRegionGeneAssociations-dispatch ............................................................ 28
plotRegionGeneAssociations-GreatJob-method ............................................ 29
plotRegionGeneAssociations-GreatObject-method ....................................... 30
plotVolcano-dispatch ....................................................................................... 31
plotVolcano-GreatJob-method ......................................................................... 31
availableCategories-GreatJob-method

Available ontology categories of the GREAT job

Description

Available ontology categories of the GREAT job

Usage

## S4 method for signature 'GreatJob'
availableCategories(object)

Arguments

object A GreatJob-class object returned by submitGreatJob.

Details

The values of the supported categories sometime change. You should run the function to get the real-time values. The meaning of categories returned is quite self-explained by the name.

Value

The returned value is a vector of categories.

Author(s)

Zuguang gu <z.gu@dkfz.de>

Examples

job = readRDS(system.file("extdata", "GreatJob.rds", package = "rGREAT"))
availableCategories(job)
All available ontology names of the GREAT job

Description

All available ontology names of the GREAT job

Usage

```r
## S4 method for signature 'GreatJob'
availableOntologies(object, category = NULL)
```

Arguments

- `object`: A `GreatJob-class` object returned by `submitGreatJob`.
- `category`: one or multiple categories. All available categories can be got by `availableCategories`.

Details

The values of the supported ontologies sometime change. You should run the function to get the real-time values. The meaning of ontology returned is quite self-explained by the name.

Value

The returned values is a vector of ontologies.

Author(s)

Zuguang gu <z.gu@dkfz.de>

Examples

```r
job = readRDS(system.file("extdata", "GreatJob.rds", package = "rGREAT"))
availableOntologies(job)
```
extendTSS

**Description**

Extend TSS

**Usage**

```
extendTSS(gene, seqlengths = NULL, genome = NULL,
          gene_id_type = NULL, mode = "basalPlusExt", extend_from = c("TSS", "gene"),
          basal_upstream = 5000, basal_downstream = 1000, extension = 1000000,
          verbose = great_opt$verbose, .attr = list())
```

**Arguments**

- **gene**
  A GRanges object of gene (or TSS) coordinates.
- **extend_from**
  Should the gene be extended only from its TSS or the complete gene?
- **seqlengths**
  A named vector of chromosome lengths. If it is not provided, it is taken by seqlengths(gene).
- **genome**
  UCSC genome can be set here, then seqlengths will be automatically retrieved from UCSC server.
- **gene_id_type**
  Gene ID types in gene. You need to set this argument if you use built-in gene sets in great so that genes can be correctly mapped. The value can only be one of "SYMBOL", "ENTREZ", "ENSEMBL" and "REFSEQ".
- **mode**
  The mode to extend TSS. Value should be one of 'basalPlusExt', 'twoClosest' and 'oneClosest'. See "Details" section.
- **basal_upstream**
  In 'basalPlusExt' mode, number of base pairs extending to the upstream of TSS to form the basal domains.
- **basal_downstream**
  In 'basalPlusExt' mode, number of base pairs extending to the downstream of TSS to form the basal domains.
- **extension**
  Extensions from the basal domains. The value can also be a vector of length two which corresponds to extension to upstream and downstream respectively.
- **verbose**
  Whether to print messages.
- **.attr**
  Only used internally.

**Details**

Following are general explanations of the three modes for extending TSS:

1. **basalPlusExt**
   1. TSS are extended into basal domains (e.g. by upstream 5kb, downstream 1kb);
   2. basal domains are sorted by their genomic coordinates;
   3. each basal domain is extended to its both sides until it reaches the next TSS’s basal domain or it reaches the maximal extension (e.g. 1000kb).
extendTSSFromDataFrame

1. TSS are sorted by their genomic coordinates; 2. each TSS is extended to its both sides until it reaches the next TSS or it reaches the maximal extension (e.g. 1000kb).

oneClosest 1. TSS are sorted by their genomic coordinates; 2. each TSS is extended to its both sides until it reaches the middle point of itself and the next TSS or it reaches the maximal extension (e.g. 1000kb).


**Value**

A GRanges object with one meta column 'gene_id'.

**Examples**

```r
# There is no example
NULL
```

---

**extendTSSFromData****Frame**

*Extend TSS*

**Description**

Extend TSS

**Usage**

```r
extendTSSFromDataFrame(df, seqlengths, genome = NULL, strand = NULL, gene_id = NULL, gene_id_type = NULL, verbose = great_opt$verbose, ...)
```

**Arguments**

- **df**
  A bed-like data frame where the first three columns should be chromosomes, start positions, end positions. It does not matter whether regions correspond to genes or TSS.

- **seqlengths**
  A named vector of chromosome lengths.

- **genome**
  UCSC genome can be set here, then seqlengths will be automatically retrieved from UCSC server.

- **strand**
  The strand information can be provided in df as a column named "strand" or as a column with "+"/"-"/"*", or the strand information can be provided as a vector and be assigned to this argument.

- **gene_id**
  The gene ID information can be provided in df as a column named "gene_id", or it can be provided as a vector and be assigned to this argument.
extendTSSFromOrgDb

gene_id_type: Gene ID types in df. You need to set this argument if you use built-in gene sets in great so that genes can be correctly mapped. The value can only be one of "SYMBOL", "ENTREZ", "ENSEMBL" and "REFSEQ".

verbose: Whether to print messages.

Value: A GRanges object with one meta column 'gene_id'.

Examples:

```r
if(FALSE) {
  extendTSSFromOrgDb("Org.Hs.eg.db")
  extendTSSFromOrgDb("hg19")
}
```
extendTSSFromTxDb  

**Description**

Extend TSS

**Usage**

```r
extendTSSFromTxDb(txdb, verbose = great_opt$verbose, ...)
```

**Arguments**

- `txdb` Name of "TxDb.*" packages from Bioconductor. All supported TxDb packages are in `rGREAT::BIOC_ANNO_PKGS$txdb`. Note short genome version can also be used here such as "hg19" or "hg19.knownGene".

- `verbose` Whether to print messages.

- `...` All pass to `extendTSS`.

**Value**

A `GRanges` object with one meta column 'gene_id'.

**Examples**

```r
if(FALSE) {
  extendTSSFromTxDb("TxDb.Hsapiens.UCSC.hg19.knownGene")
  extendTSSFromTxDb("hg19")
}
```

---

getEnrichmentTable-dispatch

**Method dispatch page for getEnrichmentTable**

**Description**

Method dispatch page for `getEnrichmentTable`.

**Dispatch**

`getEnrichmentTable` can be dispatched on following classes:

- `getEnrichmentTable,GreatJob-method,GreatJob-class` class method
- `getEnrichmentTable,GreatObject-method,GreatObject-class` class method
getEnrichmentTable-GreatJob-method

Get a single enrichment table from GREAT web server

Description

Get a single enrichment table from GREAT web server

Usage

## S4 method for signature 'GreatJob'
getEnrichmentTable(object, ontology, ...)

Arguments

- **object**  
  A `GreatJob-class` object returned by `submitGreatJob`.
- **ontology**  
  A single ontology names. Valid values are in `availableOntologies`.
- **...**  
  All pass to `getEnrichmentTables,GreatJob-method`.

Value

A data frame of the enrichment results for a single ontology.

Examples

```r
job = readRDS(system.file("extdata", "GreatJob.rds", package = "rGREAT"))
tb = getEnrichmentTable(job, ontology = "GO Molecular Function")
head(tb)
```
### Description
Get enrichment table

### Usage
```r
## S4 method for signature 'GreatObject'
getEnrichmentTable(object, min_region_hits = 5)
```

#### Arguments
- `object`: A `GreatObject-class` object returned by `great`.
- `min_region_hits`: Minimal number of input regions overlapping to the geneset associated regions.

#### Details
Note: adjusted p-values are re-calculated based on `min_region_hits`.

### Value
A data frame of enrichment results

### Examples
```r
obj = readRDS(system.file("extdata", "GreatObject.rds", package = "rGREAT"))
getEnrichmentTable(obj)
```

---

### Description
Method dispatch page for `getEnrichmentTables`.

### Dispatch
`getEnrichmentTables` can be dispatched on following classes:
- `getEnrichmentTables,GreatObject-method,GreatObject-class` class method
- `getEnrichmentTables,GreatJob-method,GreatJob-class` class method
Examples

```r
# no example
NULL
```

Description

Get enrichment tables from GREAT web server

Usage

```r
## S4 method for signature 'GreatJob'
getEnrichmentTables(object, ontology = NULL, category = "GO",
                     request_interval = 10, max_tries = 100, download_by = c("json", "tsv"),
                     verbose = TRUE)
```

Arguments

- **object**: A `GreatJob-class` object returned by `submitGreatJob`.
- **ontology**: Ontology names. Valid values are in `availableOntologies`. ontology is prior to category argument.
- **category**: Pre-defined ontology categories. One category can contain more than one ontologies. Valid values are in `availableCategories`
- **request_interval**: Time interval for two requests. Default is 300 seconds.
- **max_tries**: Maximal times for automatically reconnecting GREAT web server.
- **download_by**: Internally used. The complete enrichment table is provided as json data on the website, but there is no information of gene-region association. By setting `download_by = 'tsv'`, another URL from GREAT will be envoked which also contains detailed information of which genes are associated with each input region, but due to the size of the output, only top 500 terms will be returned. So if you do not really want the gene-region association column, take the default value of this argument. The columns that contain statistics are identical.
- **verbose**: Whether to print messages.

Value

The structure of the data frames are same as the tables available on GREAT website.
getEnrichmentTables-GreatObject-method

See

availableOntologies, availableCategories

Author(s)

Zuguang gu <z.gu@dkfz.de>

Examples

job = readRDS(system.file("extdata", "GreatJob.rds", package = "rGREAT"))
tbl = getEnrichmentTables(job)
names(tbl)
head(tbl[[1]])
job

tbl = getEnrichmentTables(job, ontology = "GO Molecular Function")
tbl = getEnrichmentTables(job, category = "GO")

getEnrichmentTables-GreatObject-method

Description

Get enrichment table

Usage

## S4 method for signature 'GreatObject'
getEnrichmentTables(object, ...)

Arguments

object A GreatObject-class object returned by great.
... All passed to getEnrichmentTable,GreatObject-method.

Details

Please use getEnrichmentTable,GreatObject-method directly.

Value

A data frame of enrichment results

Examples

# There is no example
NULL
**getGapFromUCSC**

*Get gap regions from UCSC*

---

**Description**

Get gap regions from UCSC

**Usage**

```r
cgapFromUCSC(genome, seqnames = NULL)
```

**Arguments**

- `genome`: UCSC genome, such as "hg19".
- `seqnames`: A vector of chromosome names.

**Value**

A `GRanges` object.

**Examples**

```r
cgapFromUCSC("hg19")
```

---

**getGeneSetsFromBioMart**

*Get GO gene sets from BioMart*

---

**Description**

Get GO gene sets from BioMart

**Usage**

```r
cgeneSetsFromBioMart(dataset, ontology = "bp")
```

**Arguments**

- `dataset`: Name of the dataset.
- `ontology`: Value should be bp, mf or cc.

**Details**

GO gene sets are from `BioMartGOGeneSets::getBioMartGOGeneSets`.
getGeneSetsFromOrgDb

Value

A list of vectors where each vector contains Ensembl IDs annotated to a GO term.

Examples

# There is no example
NULL

getGeneSetsFromOrgDb  Get GO gene sets from OrgDb object

Description

Get GO gene sets from OrgDb object

Usage

geneSetsFromOrgDb(orgdb, ontology = "BP")

Arguments

orgdb An OrgDb object.
ontology Value should be bp, mf or cc.

Value

A list of vectors where each vector contains Entrez IDs annotated to a GO term.

Examples

# There is no example
NULL
getGenesFromGencode  

Get Gencode genes

Description
Get Gencode genes

Usage
getGenesFromGencode(version)

Arguments
version  
Gencode version, e.g. v19 for human, vM21 for mouse.

Details
Only the protein coding genes.

Value
A GRanges object.

Examples
# There is no example
NULL

getGenomeDataFromNCBI  

Get genome data from NCBI

Description
Get genome data from NCBI

Usage
getGenomeDataFromNCBI(refseq_assembly_accession, return_granges = FALSE)

Arguments
refseq_assembly_accession  
The RefSeq accession number for the assembly, such as "GCF_000001405.40" for human.

return_granges  
If the assembly is already on chromosome level, it will directly construct a GRanges object where "chromosomes" are only used and chromosome lengths are corrected fitted in its seqlengths.
getGREATDefaultTSS

Details

Only protein coding genes are used.

Value

If `return_granges` is set to FALSE, it returns a list of two data frames:

- **genome**: A data frame of several columns.
- **gene**: A data frame for genes. The first column contains the RefSeq accession numbers of the corresponding contigs. If the genome is assembled on the chromosome level, the first column corresponds to chromosomes. The contig names can be converted to other names with the information in the genome data frame.

Examples

```r
if(FALSE) {
  getGenomeDataFromNCBI("GCF_000001405.40", return_granges = TRUE)
  getGenomeDataFromNCBI("GCF_000001405.40")
}
```

---

getGREATDefaultTSS  
*Get built-in TSS from GREAT*

Description

Get built-in TSS from GREAT

Usage

```r
getGREATDefaultTSS(genome)
```

Arguments

- **genome**: Only support "hg19", "hg38", "mm10", "mm9". Files are downloaded from [https://great-help.atlassian.net/wiki/spaces/GREAT/pages/655445/Genes](https://great-help.atlassian.net/wiki/spaces/GREAT/pages/655445/Genes).

Value

A `GRanges` object.

Examples

```r
# There is no example
NULL
```
getKEGGGenome

Get the corresponding assembly id for a kegg organism

Description
Get the corresponding assembly id for a kegg organism

Usage
getKEGGGenome(organism)

Arguments
organism The organism code on KEGG.

Value
The Refseq access ID for the genome.

Examples
# There is no example
NULL

getKEGGPathways
Get KEGG pathway gene sets

Description
Get KEGG pathway gene sets

Usage
getKEGGPathways(organism, as_table = FALSE)

Arguments
organism The organism code on KEGG.
as_table Whether to return the gene sets as a two-column table.

Value
A list of a data frame, depends on the value of as_table.
getRefSeqGenesFromUCSC

*Get RefSeq genes from UCSC*

**Description**

Get RefSeq genes from UCSC

**Usage**

```r
getRefSeqGenesFromUCSC(genome, subset = c("RefSeqSelect", "RefSeqCurated"))
```

**Arguments**

- `genome` UCSC genome, such as "hg19".
- `subset` Subset of RefSeq genes. See [https://genome.ucsc.edu/cgi-bin/hgTrackUi?db=hg38&g=refSeqComposite](https://genome.ucsc.edu/cgi-bin/hgTrackUi?db=hg38&g=refSeqComposite).

**Value**

A `GenomicRanges` object.

**Examples**

```r
# There is no example
NULL
```

---

getRegionGeneAssociations-dispatch

*Method dispatch page for getRegionGeneAssociations*

**Description**

Method dispatch page for `getRegionGeneAssociations`.

**Dispatch**

`getRegionGeneAssociations` can be dispatched on following classes:

- `getRegionGeneAssociations,GreatObject-method`, `GreatObject-class` class method
- `getRegionGeneAssociations,GreatJob-method`, `GreatJob-class` class method
getRegionGeneAssociations-GreatJob-method

Description
Get region-gene associations

Usage
## S4 method for signature 'GreatJob'
getRegionGeneAssociations(object, ontology = NULL, term_id = NULL,
request_interval = 10, max_tries = 100, verbose = great_opt$verbose)

Arguments

object  A GreatJob-class object returned by submitGreatJob.
ontology ontology name
term_id  Term id in the selected ontology.
request_interval  Time interval for two requests. Default is 300 seconds.
max_tries  Maximal times for automatically reconnecting GREAT web server.
verbose  Whether to show messages.

Value
A GRanges object. Please the two meta columns are in formats of CharacterList and IntegerList because a region may associate to multiple genes. Please note, the distance is from the middle points of input regions to TSS.

Author(s)
Zuguang gu <z.gu@dkfz.de>

Examples

job = readRDS(system.file("extdata", "GreatJob.rds", package = "rGREAT"))

gr = getRegionGeneAssociations(job)
gr
**getRegionGeneAssociations**

Get region-gene associations

**Description**

Get region-gene associations

**Usage**

```r
## S4 method for signature 'GreatObject'
getRegionGeneAssociations(object, term_id = NULL, by_middle_points = FALSE,
                           use_symbols = TRUE)
```

**Arguments**

- **object**: A `GreatObject-class` object returned by `great`.
- **term_id**: Term ID.
- **by_middle_points**: Whether the distances are calculated from the middle points of input regions?
- **use_symbols**: Whether to use gene symbols

**Value**

A `GRanges` object. Please the two meta columns are in formats of `CharacterList` and `IntegerList` because a region may associate to multiple genes.

**Examples**

```r
obj = readRDS(system.file("extdata", "GreatObject.rds", package = "rGREAT"))
getRegionGeneAssociations(obj)
```

---

**getTSS**

Get the internally used TSS

**Description**

Get the internally used TSS

**Usage**

```r
getTSS(tss_source, biomart_dataset = NULL)
```
Arguments

<table>
<thead>
<tr>
<th>Argument</th>
<th>Description</th>
</tr>
</thead>
<tbody>
<tr>
<td>tss_source</td>
<td>The same format as in great.</td>
</tr>
<tr>
<td>biomart_dataset</td>
<td>The same format as in great.</td>
</tr>
</tbody>
</table>

Value

A GRanges object.

Examples

```r
# There is no example
NULL
```

---

**great**  
*Perform GREAT analysis*

Description

Perform GREAT analysis

Usage

```r
great(gr, gene_sets, tss_source, biomart_dataset = NULL,  
      min_gene_set_size = 5, mode = "basalPlusExt", extend_from = c("TSS", "gene"),  
      basal_upstream = 5000, basal_downstream = 1000, extension = 1000000,  
      extended_tss = NULL, background = NULL, exclude = "gap",  
      cores = 1, verbose = great_opt$verbose)
```

Arguments

<table>
<thead>
<tr>
<th>Argument</th>
<th>Description</th>
</tr>
</thead>
<tbody>
<tr>
<td>gr</td>
<td>A GRanges object. This is the input regions. It is important to keep consistent for the chromosome names of the input regions and the internal TSS regions. Use getTSS to see the format of internal TSS regions.</td>
</tr>
<tr>
<td>gene_sets</td>
<td>A single string of default supported gene sets collections (see the full list in &quot;Genesets&quot; section), or a named list of vectors where each vector correspond to a gene set.</td>
</tr>
<tr>
<td>tss_source</td>
<td>Source of TSS. See &quot;TSS&quot; section.</td>
</tr>
<tr>
<td>biomart_dataset</td>
<td>The value should be in BioMartGOGeneSets::supportedOrganisms.</td>
</tr>
<tr>
<td>min_gene_set_size</td>
<td>Minimal size of gene sets.</td>
</tr>
<tr>
<td>mode</td>
<td>The mode to extend genes. Value should be one of <code>basalPlusExt</code>, <code>twoClosest</code> and <code>oneClosest</code>. See extendTSS for details.</td>
</tr>
<tr>
<td>extend_from</td>
<td>Should the gene be extended only from its TSS or the complete gene?</td>
</tr>
</tbody>
</table>
basal_upstream  In 'basalPlusExt' mode, number of base pairs extending to the upstream of TSS to form the basal domains.

basal_downstream  In 'basalPlusExt' mode, number of base pairs extending to the downstream of TSS to form the basal domains.

extension  Extensions from the basal domains.

extended_tss  If your organism is not defaultly supported, you can first prepare one by `extendTSSFromDataFrame` or `extendTSS`, and set the object to this argument. Please see more examples in the vignette.

background  Background regions. The value can also be a vector of chromosome names.

exclude  Regions that are excluded from analysis such as gap regions (which can be get by `getGapFromUCSC`). The value can also be a vector of chromosome names. It also allows a special character value "gap" so that gap regions for corresponding organism will be removed from the analysis.

cores  Number of cores to use.

verbose  Whether to print messages.

Details

When background or exclude is set, the analysis is restricted in the background regions, still by using Binomial method. Note this is different from the original GREAT method which uses Fisher’s exact test if background regions is set. See `submitGreatJob` for explanations.

By default, gap regions are excluded from the analysis.

Value

A `GreatObject-class` object. The following methods can be applied on it:

- `getEnrichmentTable`, `getRegionGeneAssociations` to retrieve the result table.
- `getRegionGeneAssociations`, `plotRegionGeneAssociations` to get the associations between input regions and genes.
- `shinyReport` to view the results by a shiny application.

Tss

rGREAT supports TSS from many organisms. The value of tss_source should be encoded in a special format:

- Name of TxDb.* packages. Supported packages are in `rGREAT::BIOC_ANNO_PKGS$txdb`.
- Genome version of the organism, e.g. "hg19". Then the corresponding TxDb will be used.
- In a format of `RefSeqCurated:$genome` where $genome is the genome version of an organism, such as hg19. RefSeqCurated subset will be used.
- In a format of `RefSeqSelect:$genome` where $genome is the genome version of an organism, such as hg19. RefSeqSelect subset will be used.
- In a format of Gencode_v$version where $version is gencode version, such as 19 (for human) or M21 for mouse. Gencode protein coding genes will be used.
- In a format of GREAT:$genome, where $genome can only be mm9, mm10, hg19, hg38. The TSS from GREAT will be used.

**Genesets**

rGREAT supports the following built-in GO gene sets for all organisms (note "GO:" can be omitted):

"GO:BP": Biological Process, from GO.db package.
"GO:CC": Cellular Component, from GO.db package.
"GO:MP": Molecular Function, from GO.db package.

rGREAT also supports built-in gene sets collections from MSigDB (note this is only for human, "msigdb:" can be omitted):

"msigdb:H" Hallmark gene sets.
"msigdb:C1" Positional gene sets.
"msigdb:C2" Curated gene sets.
"msigdb:C2:CP:BIOCARTA" C2 subcategory: BioCarta subset of CP.
"msigdb:C2:CP:KEGG" C2 subcategory: KEGG subset of CP.
"msigdb:C2:CP:PID" C2 subcategory: PID subset of CP.
"msigdb:C2:CP:REACTOME" C2 subcategory: REACTOME subset of CP.
"msigdb:C2:CP:WIKIPATHWAYS" C2 subcategory: WIKIPATHWAYS subset of CP.
"msigdb:C3" Regulatory target gene sets.
"msigdb:C3:MIR:MIRDB" miRDB of microRNA targets gene sets.
"msigdb:C3:MIR:MIR_LEGACY" MIR_Legacy of MIRDB.
"msigdb:C3:TFT:GTRD" GTRD transcription factor targets gene sets.
"msigdb:C3:TFT:TFT_LEGACY" TFT_Legacy.
"msigdb:C4" Computational gene sets.
"msigdb:C5" Ontology gene sets.
"msigdb:C5:GO:BP" C5 subcategory: BP subset.
"msigdb:C5:GO:CC" C5 subcategory: CC subset.
"msigdb:C5:GO:MF" C5 subcategory: MF subset.
"msigdb:C5:HPO" C5 subcategory: human phenotype ontology gene sets.
"msigdb:C6" Oncogenic signature gene sets.
"msigdb:C7" Immunologic signature gene sets.
"msigdb:C7:IMMUNESIGDB" ImmuneSigDB subset of C7.
"msigdb:C7:VAX" C7 subcategory: vaccine response gene sets.
"msigdb:C8" Cell type signature gene sets.

If the defaultly supported TxDb is used, Entrez gene ID is always used as the main gene ID. If you provide a self-defined gene_sets or extended_tss, you need to make sure they two have the same gene ID types.

**Biomart**

rGREAT supports a large number of organisms of which the information is retrieved from Ensembl BioMart. The name of a BioMart dataset can be assigned to argument biomart_dataset. All supported organisms can be found with BioMartGOGeneSets::supportedOrganisms.

**Examples**

```r
if(FALSE) {
  gr = randomRegions(genome = "hg19")
  res = great(gr, "MSigDB:H", "txdb:hg19")
  res = great(gr, "MSigDB:H", "TxDb.Hsapiens.UCSC.hg19.knownGene")
  res = great(gr, "MSigDB:H", "RefSeq:hg19")
  res = great(gr, "MSigDB:H", "GREAT:hg19")
  res = great(gr, "MSigDB:H", "Gencode_v19")
  res = great(gr, "GO:BP", "hsapiens_gene_ensembl")
}
```

---

**GreatJob**

*Constructor method for GreatJob class*

**Description**

Constructor method for GreatJob class

**Usage**

`GreatJob(...)`

**Arguments**

... arguments.

**Details**

There is no public constructor method for the `GreatJob-class`.

**Value**

No value is returned.
**GreatJob-class**

**Author(s)**

Zuguang Gu <z.gu@dkfz.de>

**Examples**

```r
# There is no example
NULL
```

---

**GreatJob-class**  
*Class to store and retrieve GREAT results*

**Description**

Class to store and retrieve GREAT results

**Details**

After submitting request to GREAT server, the generated results will be available on GREAT server for some time. The GreatJob-class is defined to store parameters that user has set and result tables what were retrieved from GREAT server.

**Constructor**

Users don’t need to construct by hand, submitGreatJob is used to generate a GreatJob-class instance.

**Workflow**

After submitting request to GREAT server, users can perform following steps:

- `getEnrichmentTables,GreatJob-method` to get enrichment tables for selected ontologies catalogues.
- `plotRegionGeneAssociations,GreatJob-method` to plot associations between regions and genes
- `getRegionGeneAssociations,GreatJob-method` to get a GRanges object which contains associations between regions and genes.
- `shinyReport,GreatJob-method` to view the results by a shiny application.

**Author(s)**

Zuguang Gu <z.gu@dkfz.de>

**Examples**

```r
# There is no example
NULL
```
GreatObject

Description
Constructor method for GreatObject class

Usage
GreatObject(...)

Arguments
... arguments.

Details
There are following methods that can be applied on GreatObject-class object:

- `getEnrichmentTable,GreatObject-method` to retrieve the result table.
- `getRegionGeneAssociations,GreatObject-method` to get the associations between input regions and genes.
- `plotRegionGeneAssociations,GreatObject-method` to plot the associations between input regions and genes.
- `shinyReport,GreatObject-method` to view the results by a shiny application.

Value
No value is returned.

Author(s)
Zuguang Gu <z.gu@dkfz.de>

Examples
# There is no example
NULL
GreatObject-class

Class for local GREAT analysis

Description

Class for local GREAT analysis

Details

great returns a GreatObject-class object.

Examples

# There is no example
NULL

great_opt

Global parameters for rGREAT

Description

Global parameters for rGREAT

Usage

great_opt(..., RESET = FALSE, READ.ONLY = NULL, LOCAL = FALSE, ADD = FALSE)

Arguments

... Arguments for the parameters, see "details" section
RESET Reset to default values.
READ.ONLY Please ignore.
LOCAL Please ignore.
ADD Please ignore.

Details

There are following parameters:

verbose Whether to show messages.

Examples

great_opt
Description

Plot region-gene associations

Usage

## S4 method for signature 'GreatJob'
plotRegionGeneAssociationGraphs(object, ...)

Arguments

- `object` A `GreatJob-class` object returned by `submitGreatJob`.
- `...` All passed to `plotRegionGeneAssociations,GreatJob-method`.

Details

This function will be removed in the future, please use `plotRegionGeneAssociations,GreatJob-method` instead.

Examples

```r
# There is no example
NULL
```

Description

Method dispatch page for `plotRegionGeneAssociations`.

Dispatch

`plotRegionGeneAssociations` can be dispatched on following classes:

- `plotRegionGeneAssociations,GreatObject-method,GreatObject-class` class method
- `plotRegionGeneAssociations,GreatJob-method,GreatJob-class` class method
Examples

```r
# no example
NULL
```

---

**plotRegionGeneAssociations-GreatJob-method**

*Plot region-gene associations*

---

**Description**

Plot region-gene associations

**Usage**

```r
## S4 method for signature 'GreatJob'
plotRegionGeneAssociations(object, ontology = NULL, term_id = NULL, which_plot = 1:3, request_interval = 10, max_tries = 100, verbose = great_opt$verbose)
```

**Arguments**

- `object`: A `GreatJob-class` object returned by `submitGreatJob`.
- `ontology`: A single ontology names. Valid values are in `availableOntologies`.
- `term_id`: Term id in the selected ontology.
- `which_plot`: Which plots to draw? The value should be in 1, 2, 3. See "Details" section for explanation.
- `request_interval`: Time interval for two requests. Default is 300 seconds.
- `max_tries`: Maximal times for automatically reconnecting GREAT web server.
- `verbose`: Whether to show messages.

**Details**

There are following figures:

- Association between regions and genes (`which_plot = 1`).
- Distribution of distance to TSS (`which_plot = 2`).
- Distribution of absolute distance to TSS (`which_plot = 3`).

If `ontology` and `term_id` are set, only regions and genes corresponding to selected ontology term will be used. Valid value for `ontology` is in `availableOntologies` and valid value for `term_id` is from 'id' column in the table which is returned by `getEnrichmentTables`. 
Author(s)
Zuguang gu <z.gu@dkfz.de>

Examples

```r
job = readRDS(system.file("extdata", "GreatJob.rds", package = "rGREAT"))
plotRegionGeneAssociations(job)
plotRegionGeneAssociations(job, which_plot = 1)
# Do not use other term_id for this example, or you need to generate a new `job` object.
plotRegionGeneAssociations(job, ontology = "GO Molecular Function",
   term_id = "GO:0004984")
```

Description
Plot region-gene associations

Usage

```r
## S4 method for signature 'GreatObject'
plotRegionGeneAssociations(object, term_id = NULL, which_plot = 1:3)
```

Arguments

- `object`: A `GreatObject-class` object returned by `great`.
- `term_id`: Term ID.
- `which_plot`: Which plots to draw? The value should be in 1, 2, 3. See "Details" section for explanation.

Details

There are following figures:

- Association between regions and genes (which_plot = 1).
- Distribution of distance to TSS (which_plot = 2).
- Distribution of absolute distance to TSS (which_plot = 3).

Examples

```r
obj = readRDS(system.file("extdata", "GreatObject.rds", package = "rGREAT"))
plotRegionGeneAssociations(obj)
```
plotVolcano-dispatch

Method dispatch page for plotVolcano

Description

Method dispatch page for plotVolcano.

Dispatch

PlotVolcano can be dispatched on following classes:

- `plotVolcano,GreatObject-method, GreatObject-class` class method
- `plotVolcano,GreatJob-method, GreatJob-class` class method

Examples

```r
# no example
NULL
```

plotVolcano-GreatJob-method

Make volcano plot

Description

Make volcano plot

Usage

```r
## S4 method for signature 'GreatJob'
plotVolcano(object, ontology, min_region_hits = 5,
    x_values = c("fold_enrichment", "z-score"),
    y_values = c("p_value", "p_adjust"),
    main = NULL)
```

Arguments

<table>
<thead>
<tr>
<th>Argument</th>
<th>Description</th>
</tr>
</thead>
<tbody>
<tr>
<td><code>object</code></td>
<td>A <code>GreatJob-class</code> object returned by <code>submitGreatJob</code>.</td>
</tr>
<tr>
<td><code>ontology</code></td>
<td>A single ontology names. Valid values are in <code>availableOntologies</code>.</td>
</tr>
<tr>
<td><code>min_region_hits</code></td>
<td>Minimal number of input regions overlapping to the geneset associated regions.</td>
</tr>
<tr>
<td><code>x_values</code></td>
<td>Which values for the x-axis.</td>
</tr>
<tr>
<td><code>y_values</code></td>
<td>Which values for the y-axis.</td>
</tr>
<tr>
<td><code>main</code></td>
<td>Title of the plot.</td>
</tr>
</tbody>
</table>
Details

Since the enrichment is an over-representation test, it is only the half volcano.

Examples

# There is no example
NULL
randomRegions

Generate random regions

Description

Generate random regions

Usage

```
randomRegions(genome = NULL, nr = 1000, seqlengths = NULL,
               width_fun = function(n) runif(n, min = 1000, max = 10000))
```

Arguments

- **genome**  
  UCSC genome version, e.g. "hg19".
- **nr**  
  Number of regions.
- **seqlengths**  
  Alternatively, you can also specify a named vector of seqlengths (chromosome lengths).
- **width_fun**  
  A function which defines the distribution of region widths.

Details

The number of regions per chromosome is proportional to the chromosome length.

Examples

```
gr = randomRegions(genome = "hg19")
quantile(width(gr))
```

randomRegionsFromBioMartGenome

Generate random regions from a BioMart genome

Description

Generate random regions from a BioMart genome

Usage

```
randomRegionsFromBioMartGenome(biomart_dataset, nr = 1000, ...)
```

Arguments

- **biomart_dataset**  
  A BioMart dataset. Values should be in BioMartGOGeneSets::supportedOrganisms.
- **nr**  
  Number of regions.
- **...**  
  Pass to randomRegions.
Details

The number of regions per chromosome is proportional to the chromosome length.

Examples

```r
if(FALSE) {
  # Giant panda
  gr = randomRegionsFromBioMartGenome("amelanoleuca_gene_ensembl")
}
```

---

**read_gmt**

*Read gmt gene sets file*

**Description**

Read gmt gene sets file

**Usage**

```r
read_gmt(x, from = NULL, to = NULL, orgdb = NULL)
```

**Arguments**

- `x`  
The file name of a .gmt file.
- `from`  
  Gene ID type in the original gmt file. Value can only take values in 'ENTREZ/SYMBOL/ENSEMBL/REFSEQ'.
- `to`  
  Gene ID type that you want to convert to. Value can only take values in 'ENTREZ/SYMBOL/ENSEMBL/REFSEQ'.
- `orgdb`  
The name of an OrgDb database.

**Value**

A named list of vectors.

**Examples**

```r
read_gmt(url("http://dsigdb.tanlab.org/Downloads/D2_LINCS.gmt"))
```
reduce_by_start_and_end

Reduce by start and end

Description
Reduce by start and end

Usage
reduce_by_start_and_end(s, e)

Arguments
s    Start positions. Sorted.
e    End positions. Sorted.

Details
Only internally used.

Value
Sum of total widths of the reduced regions.

Examples
# There is no example
NULL

shinyReport-dispatch

Method dispatch page for shinyReport

Description
Method dispatch page for shinyReport.

Dispatch
shinyReport can be dispatched on following classes:

- shinyReport,GreatJob-method, GreatJob-class class method
- shinyReport,GreatObject-method, GreatObject-class class method
shinyReport-GreatObject-method

Shiny app on the GreatObject object

Description

Shiny app on the GreatObject object

Usage

## S4 method for signature 'GreatObject'
shinyReport(object)

Arguments

object  The GreatObject object returned by submitGreatJob.

Value

A shiny app object.

Examples

if(FALSE) {
  # pseudo code
  job = submitGreatJob(...)
  shinyReport(job)
}

shinyReport-GreatJob-method

Shiny app on the GreatJob object

Description

Shiny app on the GreatJob object

Usage

## S4 method for signature 'GreatJob'
shinyReport(object)

Arguments

object  The GreatJob object returned by submitGreatJob.

Value

A shiny app object.

Examples

if(FALSE) {
  # pseudo code
  job = submitGreatJob(...)
  shinyReport(job)
}
submitGreatJob

Arguments

object The GreatObject object returned by great.

Value

A shiny app object.

Examples

if(FALSE) {
  # pseudo code
  obj = great(...)
  shinyReport(obj)
}

submitGreatJob Perform online GREAT analysis

Description

Perform online GREAT analysis

Usage

submitGreatJob(gr, bg = NULL, 
gr_is_zero_based = FALSE, 
species = "hg19", 
genome = species, 
includeCuratedRegDoms = TRUE, 
rule = c("basalPlusExt", "twoClosest", "oneClosest"), 
adv_upstream = 5.0, 
adv_downstream = 1.0, 
adv_span = 1000.0, 
adv_twoDistance = 1000.0, 
adv_oneDistance = 1000.0, 
request_interval = 60, 
max_tries = 10, 
version = DEFAULT_VERSION, 
base_url = "http://great.stanford.edu/public/cgi-bin", 
use_name_column = FALSE, 
verbose = help, help = great_opt$verbose)

Arguments

gr A GRanges object or a data frame which contains at least three columns (chr, start and end).

bg Not supported any more. See explanations in section "When_background_regions_are_set".
submitGreatJob

gr_is_zero_based

Are start positions in gr zero-based?

geno me

Genome. "hg38", "hg19", "mm10", "mm9" are supported in GREAT version 4.x.x, "hg19", "mm10", "mm9", "danRer7" are supported in GREAT version 3.x.x and "hg19", "hg18", "mm9", "danRer7" are supported in GREAT version 2.x.x.

species

The same as genome but it will be deprecated soon.

includeCuratedRegDoms

Whether to include curated regulatory domains, see https://great-help.atlassian.net/wiki/spaces/GREAT/pages/655443/Association+Rules#AssociationRules-CuratedRegulatoryDomains.

rule

How to associate genomic regions to genes. See 'Details' section.

adv_upstream

Unit: kb, only used when rule is basalPlusExt.

adv_downstream

Unit: kb, only used when rule is basalPlusExt.

adv_span

Unit: kb, only used when rule is basalPlusExt.

adv_twoDistance

Unit: kb, only used when rule is twoClosest.

adv_oneDistance

Unit: kb, only used when rule is oneClosest.

request_interval

Time interval for two requests. Default is 300 seconds.

max_tries

Maximal times for automatically reconnecting GREAT web server.

version

Version of GREAT. The value should be "4.0.4", "3.0.0", "2.0.2". Shorten version numbers can also be used, such as using "4" or "4.0" is same as "4.0.4".

base_url

the url of cgi-bin path, only used when it is explicitly specified.

use_name_column

If the input is a data frame, whether to use the fourth column as the "names" of regions?

verbose

Whether to print help messages.

help

Whether to print help messages. This argument will be replaced by verbose in future versions.

Details

Note: On Aug 19 2019 GREAT released version 4(https://great-help.atlassian.net/wiki/spaces/GREAT/pages/655442/Version+History) where it supports hg38 genome and removes some ontologies such pathways. submitGreatJob still takes hg19 as default. hg38 can be specified by the genome = "hg38" argument. To use the older versions such as 3.0.0, specify as submitGreatJob(..., version = "3.0.0").

Note it does not use the standard GREAT API. This function directly send data to GREAT web server by HTTP POST.

Following text is copied from GREAT web site (http://great.stanford.edu/public/html/) Explanation of rule and settings with names started with 'adv_' (advanced settings):
basalPlusExt  Mode 'Basal plus extension'. Gene regulatory domain definition: Each gene is assigned a basal regulatory domain of a minimum distance upstream and downstream of the TSS (regardless of other nearby genes, controlled by \texttt{adv\_upstream} and \texttt{adv\_downstream} argument). The gene regulatory domain is extended in both directions to the nearest gene’s basal domain but no more than the maximum extension in one direction (controlled by \texttt{adv\_span}).

twoClosest  Mode 'Two nearest genes'. Gene regulatory domain definition: Each gene is assigned a regulatory domain that extends in both directions to the nearest gene’s TSS (controlled by \texttt{adv\_twoDistance}) but no more than the maximum extension in one direction.

oneClosest  Mode 'Single nearest gene'. Gene regulatory domain definition: Each gene is assigned a regulatory domain that extends in both directions to the midpoint between the gene’s TSS and the nearest gene’s TSS (controlled by \texttt{adv\_oneDistance}) but no more than the maximum extension in one direction.

Value

A \texttt{GreatJob-class} object which can be used to get results from GREAT server. The following methods can be applied on it:

- \texttt{getEnrichmentTables,GreatObject-method} to retrieve the result tables.
- \texttt{getRegionGeneAssociations,GreatObject-method} to get the associations between input regions and genes.
- \texttt{plotRegionGeneAssociations,GreatObject-method} to plot the associations between input regions and genes.
- \texttt{shinyReport,GreatObject-method} to view the results by a shiny application.

When \texttt{background\_regions\_are\_set}

Note when \texttt{bg} argument is set to a list of background regions, GREAT uses a completely different test!

When \texttt{bg} is set, \texttt{gr} should be exactly subset of \texttt{bg}. For example, let’s say a background region list contains five regions: [1, 10], [15, 23], [34, 38], [40, 49], [54, 63], \texttt{gr} can only be a subset of the five regions, which means \texttt{gr} can take [15, 23], [40, 49], but it cannot take [16, 20], [39, 51]. In this setting, regions are taken as single units and Fisher’s exact test is applied for calculating the enrichment (by testing number of regions in the 2x2 contingency table).


Please note from rGREAT 1.99.0, setting \texttt{bg} is not supported any more and this argument will be removed in the future. You can either directly use GREAT website or use other Bioconductor packages such as "LOLA" to perform the Fisher’s exact test-based analysis.

If you want to restrict the input regions to background regions (by intersections) and still to apply Binomial test there, please consider to use local GREAT by \texttt{great}.

Author(s)

Zuguang gu <z.gu@dkfz.de>
See Also

great for the local implementation of GREAT algorithm.

Examples

```r
set.seed(123)
gr = randomRegions(nr = 1000, genome = "hg19")
job = submitGreatJob(gr)
job

# more parameters can be set for the job
if(FALSE) { # suppress running it when building the package
  # current GREAT version is 4.0.4
  job = submitGreatJob(gr, genome = "hg19")
  job = submitGreatJob(gr, adv_upstream = 10, adv_downstream = 2, adv_span = 2000)
  job = submitGreatJob(gr, rule = "twoClosest", adv_twoDistance = 2000)
  job = submitGreatJob(gr, rule = "oneClosest", adv_oneDistance = 2000)
}
```
Index

availableCategories, 4, 11, 12
availableCategories
  (availableCategories-GreatJob-method), 3
availableCategories-GreatJob-method
  (availableCategories-GreatJob-method), 3
availableCategories-GreatJob-method, 3
availableOntologies, 9, 11, 12, 29, 31
availableOntologies
  (availableOntologies-GreatJob-method), 4
availableOntologies-GreatJob-method
  (availableOntologies-GreatJob-method), 4
availableOntologies-GreatJob-method, 4
extendTSS, 5, 7, 8, 21, 22
extendTSSFromDataFrame, 6, 22
extendTSSFromOrgDb, 7
extendTSSFromTxDb, 8
GenomicRanges, 18
getEnrichmentTable
  (getEnrichmentTable-dispatch), 8
getEnrichmentTable-GreatJob-method
  (getEnrichmentTable-GreatJob-method), 9
getEnrichmentTable-GreatObject-method
  (getEnrichmentTable-GreatObject-method), 10
getEnrichmentTable-dispatch, 8
getEnrichmentTable-GreatJob-method, 9
getEnrichmentTable-GreatObject-method, 10
getEnrichmentTables, 29
getEnrichmentTables
  (getEnrichmentTables-dispatch), 10
getEnrichmentTables-GreatJob-method
  (getEnrichmentTables-GreatJob-method), 11
getEnrichmentTables-GreatObject-method
  (getEnrichmentTables-GreatObject-method), 12
getEnrichmentTables-dispatch, 10
getEnrichmentTables-GreatJob-method, 11
getEnrichmentTables-GreatObject-method, 12
gapFromUCSC, 13, 22
geneSetsFromBioMart, 13
geneSetsFromOrgDb, 14
genesFromGencode, 15
getGenomeDataFromNCBI, 15
greatDefaultTSS, 16
KEGGGenome, 17
KEGGPathways, 17
getRefSeqGenesFromUCSC, 18
geneAssociations
  (geneAssociations-dispatch), 18
geneAssociations-GreatJob-method
  (geneAssociations-GreatJob-method), 19
geneAssociations-GreatObject-method
  (geneAssociations-GreatObject-method), 20
geneAssociations-dispatch, 18
geneAssociations-GreatJob-method, 19
geneAssociations-GreatObject-method, 20
gene, 5, 7, 10, 12, 20, 21, 21, 27, 30, 32, 37,
39, 40
great_opt, 27
GreatJob, 24
GreatJob-class, 25
GreatObject, 26
GreatObject-class, 27

plotRegionGeneAssociationGraphs
(plotRegionGeneAssociationGraphs-GreatJob-method), 28
plotRegionGeneAssociationGraphs,GreatJob-method
(plotRegionGeneAssociationGraphs-GreatJob-method), 28
plotRegionGeneAssociationGraphs-GreatJob-method,
28
plotRegionGeneAssociations
(plotRegionGeneAssociations-dispatch), 28
plotRegionGeneAssociations,GreatJob-method
(plotRegionGeneAssociations-GreatJob-method), 29
plotRegionGeneAssociations,GreatObject-method
(plotRegionGeneAssociations-GreatObject-method), 30
plotRegionGeneAssociations-dispatch,
28
plotRegionGeneAssociations-GreatJob-method,
29
plotRegionGeneAssociations-GreatObject-method,
30
plotVolcano (plotVolcano-dispatch), 31
plotVolcano,GreatJob-method
(plotVolcano-GreatJob-method), 31
plotVolcano,GreatObject-method
(plotVolcano-GreatObject-method), 32
plotVolcano-dispatch, 31
plotVolcano-GreatJob-method, 31
plotVolcano-GreatObject-method, 32

randomRegions, 33, 33
randomRegionsFromBioMartGenome, 33
read_gmt, 34
reduce_by_start_and_end, 35

shinyReport (shinyReport-dispatch), 35
shinyReport,GreatJob-method
(shinyReport-GreatJob-method), 36
shinyReport,GreatObject-method
(shinyReport-GreatObject-method), 36
shinyReport-dispatch, 35
shinyReport-GreatJob-method, 36
shinyReport-GreatObject-method, 36
submitGreatJob, 3, 4, 9, 11, 19, 22, 25, 28, 29, 31, 36, 37, 38