

Package ‘STRINGdb’

September 23, 2026

Type Package

Title STRINGdb - Protein-Protein Interaction Networks and Functional Enrichment Analysis

Version 2.24.0

Date 2024-06-05

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Description The STRINGdb package provides an R interface to STRING, a protein-protein interaction database and functional enrichment analysis tool (<https://string-db.org>).

License GPL-2

Depends R (>= 2.14.0)

Imports png, sqldf, plyr, igraph, httr, methods, RColorBrewer, gplots, hash, plotrix

Suggests RUnit, BiocGenerics

biocViews Network

git_url <https://git.bioconductor.org/packages/STRINGdb>

git_branch RELEASE_3_23

git_last_commit 1c4a249

git_last_commit_date 2026-04-28

Repository Bioconductor 3.23

Date/Publication 2026-09-22

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add_diff_exp_color	<i>add_diff_exp_color</i>
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Description

Take in input a dataframe containing a logFC column that reports the logarithm of the difference in expression level. Add a "color" column to the data frame such that strongly downregulated genes are colored in green and strong upregulated genes are in red. When the down or up-regulation is instead weak the intensity of the color gets weaker as well, accordingly.

Usage

```
## S4 method for signature 'STRINGdb'  
add_diff_exp_color(screen, logFcColStr="logFC" )
```

Arguments

screen	Dataframe containing the results of the experiment (e.g. the analyzed results of a microarray or RNAseq experiment)
logFcColStr	name of the colum that contains the logFC of the expression

Value

vector containing the colors

Author(s)

Andrea Franceschini

add_proteins_description
add_proteins_description

Description

Add description coluns to the proteins that are present in the data frame given in input. The data frame must contain a column named "STRING_id".

Usage

```
## S4 method for signature 'STRINGdb'  
add_proteins_description(screen)
```

Arguments

screen	Dataframe containing the results of the experiment (e.g. the analyzed results of a microarray or RNAseq experiment)
--------	---

Value

returns the same dataframe given in input with an additional columns containing a description of the proteins.

Author(s)

Andrea Franceschini

`coeffOfvar`*coeffOfvar*

Description

coefficient of variation

Usage

```
coeffOfvar(x)
```

Arguments

x input number

Details

coefficient of variation

Value

coefficient of variation

Author(s)

Andrea Franceschini

`delColDf`*delColDf*

Description

delete a column in the data frame

Usage

```
delColDf(df, colName)
```

Arguments

df data frame
colName name of the column to be deleted

Value

data frame

Author(s)

Andrea Franceschini

diff_exp_example1	<i>example of microarray data (data processed from GEO GSE9008)</i>
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Description

example of microarray data (data processed from GEO GSE9008)

Usage`data(diff_exp_example1)`**Format**

Data frames with 20861 observations on the following 3 variables.

gene a character vector

pvalue a numeric vector

logFC a numeric vector

Source

Whyte L, Huang YY, Torres K, Mehta RG. Molecular mechanisms of resveratrol action in lung cancer cells using dual protein and microarray analyses. Cancer Res 2007.

downloadAbsentFile	<i>downloadAbsentFile</i>
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Description

download a file only if it is not present.

Usage`downloadAbsentFile(urlStr, oD = tempdir())`**Arguments**

urlStr url from which to download the file

oD directory where to store the file

Author(s)

Andrea Franceschini

downloadAbsentFileSTRING

downloadAbsentFileSTRING

Description

download a STRING file only if it is not present or if it is corrupted.

Usage

```
downloadAbsentFileSTRING(urlStr, oD = tempdir())
```

Arguments

urlStr	url from which to download the file
oD	directory where to store the file

Author(s)

Andrea Franceschini

get_aliases

get_aliases

Description

Loads and returns STRING aliases. Depending on takeFirst, this returns either all alias mappings or a single preferred mapping for ambiguous aliases.

Usage

```
## S4 method for signature 'STRINGdb'
get_aliases(takeFirst=TRUE, usePreferredSources=TRUE)
```

Arguments

takeFirst	boolean indicating whether ambiguous aliases should be collapsed to a single STRING identifier. If FALSE, all alias mappings are returned. If TRUE, one mapping is returned for each ambiguous alias.
usePreferredSources	boolean indicating whether preferred alias sources should be used to disambiguate aliases when takeFirst=TRUE. This parameter is ignored when takeFirst=FALSE.

Value

a data frame containing STRING aliases. With takeFirst=FALSE, all alias mappings are returned. With takeFirst=TRUE, ambiguous aliases are collapsed to one STRING identifier.

Author(s)

Andrea Franceschini

get_annotations	<i>get_annotations</i>
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Description

Loads and returns STRING annotations (i.e. GO annotations, KEGG pathways, domain databases). The annotations are stored in the "annotations" variable.

Usage

```
## S4 method for signature 'STRINGdb'  
get_annotations( )
```

Value

a data frame containing the annotations to the STRING proteins (e.g. GeneOntology, KEGG pathways, InterPro domains)

Author(s)

Andrea Franceschini

get_annotations_desc	<i>get_annotations_desc</i>
----------------------	-----------------------------

Description

Returns a data frame with the description of every STRING annotation term (it downloads and caches the information the first time that is called).

Usage

```
## S4 method for signature 'STRINGdb'  
get_annotations_desc()
```

Value

data frame with the description of every STRING annotation term.

Author(s)

Andrea Franceschini

get_bioc_graph	<i>get_bioc_graph</i>
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Description

Returns the interaction graph as an object of the graph package in Bioconductor.

Usage

```
## S4 method for signature 'STRINGdb'  
get_bioc_graph()
```

Value

interaction graph as an object of the graph package in Bioconductor.

Author(s)

Andrea Franceschini

get_clusters	<i>get_clusters</i>
--------------	---------------------

Description

Returns a list of clusters of interacting proteins. See the iGraph (<http://igraph.sourceforge.net/>) documentation for additional information on the algorithms.

Usage

```
## S4 method for signature 'STRINGdb'  
get_clusters(string_ids, algorithm="fastgreedy")
```

Arguments

string_ids	a vector of STRING identifiers.
algorithm	algorithm to use for the clustering. You can choose between "fastgreedy", "walk-trap", "spinglass" and "edge.betweenness").

Value

list of clusters of interacting proteins.

Author(s)

Andrea Franceschini

get_enrichment	<i>get_enrichment</i>
----------------	-----------------------

Description

Returns the enrichment in pathways of the vector of STRING proteins that is given in input.

Usage

```
## S4 method for signature 'STRINGdb'  
get_enrichment(string_ids, category = "Process", methodMT = "fdr", iea = TRUE, minScore=NULL)
```

Arguments

string_ids	a vector of STRING identifiers.
category	category for which to compute the enrichment (i.e. "Process", "Component", "Function", "KEGG", "Pfam", "InterPro"). The default category is "Process".
methodMT	method to be used for the multiple testing correction. (i.e. "fdr", "bonferroni"). The default is "fdr".
iea	specify whether you also want to use electronic inference annotations
minScore	with Tissue and Disease categories is possible to filter the annotations having an annotation score higher than this threshold (from 0 to 5)

Value

Data frame containing the enrichment in pathways of the vector of STRING proteins that is given in input.

Author(s)

Andrea Franceschini

get_graph	<i>get_graph</i>
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Description

Return an igraph object with the STRING network (for information about iGraph visit <http://igraph.sourceforge.net>)

Usage

```
## S4 method for signature 'STRINGdb'  
get_graph()
```

Value

igraph object with the STRING network

Author(s)

Andrea Franceschini

References

Csardi G, Nepusz T: The igraph software package for complex network research, InterJournal, Complex Systems 1695. 2006. <http://igraph.sf.net>

See Also

In order to simplify the most common tasks, we do also provide convenient functions that wrap some iGraph functions. `get_interactions(string_ids)` # returns the interactions in between the input proteins `get_neighbors(string_ids)` # Get the neighborhoods of a protein (or of a vector of proteins) that is given in input. `get_subnetwork(string_ids)` # returns a subgraph from the given input proteins

`get_homologs_besthits` *get_homologs_besthits*

Description

Returns the list of closest homologs (as measured by bitscore) of the given input identifiers in all STRING species or single target species.

Usage

```
## S4 method for signature 'STRINGdb'  
get_homologs_besthits(string_ids, target_species_id=NULL)
```

Arguments

`string_ids` a vector of STRING identifiers.
`target_species_id` NCBI taxonomy identifier of the species to query for homologs (the species must be present in the STRING database)

Value

Data frame containing the best blast hits x species of the given input identifiers.

Author(s)

Andrea Franceschini

get_interactions	<i>get_interactions</i>
------------------	-------------------------

Description

Shows the interactions in between the proteins that are given in input.

Usage

```
## S4 method for signature 'STRINGdb'  
get_interactions(string_ids)
```

Arguments

string_ids a vector of STRING identifiers

Value

Data frame containing the interactions in between the input proteins. The leading columns are from, to, combined_score, from_name and to_name, followed by any additional loaded edge attributes.

Author(s)

Damian Szklarczyk

get_interaction_partners	<i>get_interaction_partners</i>
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Description

Returns the interaction partners of the input proteins using the locally loaded STRING graph. The returned data frame preserves the edge attributes available for the current link_data setting.

Usage

```
## S4 method for signature 'STRINGdb'  
get_interaction_partners(string_ids, required_score=NULL, limit=NULL)
```

Arguments

string_ids a vector of STRING identifiers

required_score optional minimum combined score for returned partners. This value cannot be below the score_threshold used to load the local graph.

limit optional maximum number of partner rows returned per query protein

Value

Data frame containing one row per query-partner interaction. The leading columns are from, to, combined_score, from_name and to_name, followed by any additional edge attributes loaded for the current link_data mode. Here from is the queried protein and to is its interaction partner. If limit is used, rows are ordered by combined_score.

Author(s)

Damian Szklarczyk

get_link	<i>get_link</i>
----------	-----------------

Description

Returns a short link to the network page of the STRING website that shows the protein interactions between the given identifiers.

Usage

```
## S4 method for signature 'STRINGdb'
get_link(string_ids=NULL, required_score=NULL, network_flavor="evidence", payload_id=NULL, network_t
```

Arguments

- string_ids a vector of STRING identifiers. Can be omitted when network_term_id is provided.
- required_score minimum STRING combined score of the interactions (if left NULL we get the combined score of the object, which is 400 by default).
- network_flavor specify the flavor of the network ("evidence" or "confidence". Default "evidence").
- payload_id an identifier of payload data on the STRING server (see method post_payload for additional informations).
- network_term_id functional term identifier used by STRING instead of explicit protein identifiers.
- hide_node_labels hides all protein names from the picture. Accepts TRUE/FALSE or 0/1.
- hide_disconnected_nodes hides proteins that are not connected to any other protein in the network. Accepts TRUE/FALSE or 0/1.
- block_structure_pics_in_bubbles disables structure pictures inside the bubbles. Accepts TRUE/FALSE or 0/1.
- flat_node_design disables 3D bubble design. Accepts TRUE/FALSE or 0/1. Default is TRUE.

center_node_labels
 centers protein names on nodes. Accepts TRUE/FALSE or 0/1.

custom_label_font_size
 changes the font size of the protein names (from 5 to 50).

caller_identity
 caller identifier sent to STRING.

Value

short link to the network page of the STRING website that shows the protein interactions between the input identifiers.

Author(s)

Damian Szklarczyk

get_neighbors	<i>get_neighbors</i>
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Description

Get the neighborhoods of a protein (or of a vector of proteins) that is given in input.

Usage

```
## S4 method for signature 'STRINGdb'  
get_neighbors(string_ids)
```

Arguments

string_ids a vector of STRING identifiers

Value

vector containing the neighborhoods of a protein (or of a vector of proteins) that is given in input.

Author(s)

Andrea Franceschini

get_paralogs	<i>get_paralogs</i>
--------------	---------------------

Description

Returns the list of paralogs of the given input in their species.

Usage

```
## S4 method for signature 'STRINGdb'  
get_paralogs(string_ids)
```

Arguments

string_ids a vector of STRING identifiers.

Value

Data frame containing the within-species homology hits of the input identifiers, with columns ncbiTaxonId_A, stringId_A, ncbiTaxonId_B, stringId_B, and bitscore.

Author(s)

Andrea Franceschini

get_png	<i>get_png</i>
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Description

Returns a STRING network image for the given identifiers or for a STRING functional term.

Usage

```
## S4 method for signature 'STRINGdb'  
get_png(string_ids=NULL, required_score=NULL, network_flavor="evidence", file=NULL, payload_id=NULL,
```

Arguments

- string_ids a vector of STRING identifiers. Can be omitted when network_term_id is provided.
- required_score minimum STRING combined score of the interactions (if left NULL we get the combined score of the object, which is 400 by default).
- network_flavor specify the flavor of the network ("evidence" or "confidence". Default "evidence").

file	file where to save the image output.
payload_id	identifier of the payload.
output_format	STRING image output format: "image", "highres_image" or "svg".
network_term_id	functional term identifier used by STRING instead of explicit protein identifiers.
hide_node_labels	hides all protein names from the picture. Accepts TRUE/FALSE or 0/1.
hide_disconnected_nodes	hides proteins that are not connected to any other protein in the network. Accepts TRUE/FALSE or 0/1.
block_structure_pics_in_bubbles	disables structure pictures inside the bubbles. Accepts TRUE/FALSE or 0/1.
flat_node_design	disables 3D bubble design. Accepts TRUE/FALSE or 0/1. Default is TRUE.
center_node_labels	centers protein names on nodes. Accepts TRUE/FALSE or 0/1.
custom_label_font_size	changes the font size of the protein names (from 5 to 50).
caller_identity	caller identifier sent to STRING.

Value

For output_format="image" and output_format="highres_image", returns a PNG image array.
 For output_format="svg", returns the SVG markup as text.

Author(s)

Damian Szklarczyk

get_ppi_enrichment	<i>get_ppi_enrichment</i>
--------------------	---------------------------

Description

Returns a pvalue representing the enrichment in interactions of the list of proteins (i.e. the probability to obtain such a number of interactions by chance).

Usage

```
## S4 method for signature 'STRINGdb'
get_ppi_enrichment(string_ids)
```

Arguments

string_ids a vector of STRING identifiers

Value

Returns a pvalue representing the enrichment in interactions of the list of proteins (i.e. the probability to obtain such a number of interactions by chance).

Author(s)

Andrea Franceschini

get_proteins	<i>get_proteins</i>
--------------	---------------------

Description

Returns the STRING proteins data frame. (it downloads and caches the information the first time that is called).

Usage

```
## S4 method for signature 'STRINGdb'  
get_proteins()
```

Value

STRING proteins data frame.

Author(s)

Andrea Franceschini

get_subnetwork	<i>get_subnetwork</i>
----------------	-----------------------

Description

Returns the subgraph generated by the given input proteins.

Usage

```
## S4 method for signature 'STRINGdb'  
get_subnetwork(string_ids )
```

Arguments

string_ids a vector of STRING identifiers

Value

Returns the subgraph (i.e. an iGraph object) generated by the given input proteins.

Author(s)

Andrea Franceschini

get_summary	<i>get_summary</i>
-------------	--------------------

Description

Returns a summary of the STRING sub-network containing the identifiers provided in input.

Usage

```
## S4 method for signature 'STRINGdb'  
get_summary(string_ids)
```

Arguments

string_ids a vector of STRING identifiers

Value

Returns a summary (i.e. a text description) of the STRING sub-network containing the identifiers provided in input.

Author(s)

Andrea Franceschini

get_term_proteins	<i>get_term_proteins</i>
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Description

Returns the proteins annotated to belong to a given term.

Usage

```
## S4 method for signature 'STRINGdb'  
get_term_proteins(term_ids, string_ids=NULL, enableIEA=TRUE)
```

Arguments

term_ids	vector of terms
string_ids	a vector of STRING identifiers. If the variable is set, the method returns only the proteins that are present in this vector.
enableIEA	whether to consider also Electronic Inferred Annotations

Value

Returns the proteins annotated to belong to a given term.

Author(s)

Andrea Franceschini

interactions_example	<i>example of a protein-protein interactions sorted data frame</i>
----------------------	--

Description

example of a sorted list of protein-protein interactions, resulta our cooccurrence algorithm (SVD_Phy)

Usage

```
data(interactions_example)
```

Format

Data frames with 20861 observations on the following 3 variables.

proteinA a character vector

proteinB a character vector

score a numeric vector

load

*load***Description**

Downloads and returns the STRING network (the network is set also in the graph variable of the STRING_db object). When possible, the download uses the threshold-specific streamed network file matching the current score_threshold.

It makes use of the variables: "backgroundV" vector containing STRING identifiers to be used as background (i.e. the STRING network loaded will contain only the proteins that are present also in this vector) "score_threshold" STRING combined score threshold (the network loaded contains only interactions having a combined score greater than this threshold)

Usage

```
## S4 method for signature 'STRINGdb'
load()
```

Value

STRING network (i.e. an iGraph object. For info look to <http://igraph.sourceforge.net>)

Author(s)

Andrea Franceschini and Damian Szklarczyk

load_all

*load_all***Description**

Force download and loading of all the files (so that you can later store the object on the hard disk if you like). It makes use of the variables: "backgroundV" vector containing STRING identifiers to be used as background (i.e. the STRING network loaded will contain only the proteins that are present also in this vector) "score_threshold" STRING combined score threshold (the network loaded contains only interactions having a combined score greater than this threshold)

Usage

```
## S4 method for signature 'STRINGdb'
load_all()
```

Author(s)

Andrea Franceschini

map	<i>map</i>
-----	------------

Description

Maps the gene identifiers of the input dataframe to STRING identifiers. It returns the input dataframe with the "STRING_id" additional column.

Usage

```
## S4 method for signature 'STRINGdb'  
map(my_data_frame, my_data_frame_id_col_names, takeFirst=TRUE, removeUnmappedRows=FALSE, quiet=FALSE)
```

Arguments

- my_data_frame data frame provided as input.
- my_data_frame_id_col_names
 vector containing the names of the columns of "my_data_frame" that have to be used for the mapping.
- takeFirst boolean indicating what to do in case of multiple STRING proteins that map to the same name. If TRUE, only the first of those is taken. Otherwise all of them are used. (default TRUE)
- removeUnmappedRows
 remove the rows that cannot be mapped to STRING (by default those lines are left and their STRING_id is set to NA).
- quiet Setting this variable to TRUE we can avoid printing the warning relative to the unmapped values.
- usePreferredSources
 when takeFirst=TRUE, prioritize aliases using the preferred source order.

Value

Returns the dataframe that is given in input with the "STRING_id" additional column.

Author(s)

Andrea Franceschini

mp	<i>mp</i>
----	-----------

Description

Maps the gene identifiers of the input vector to STRING identifiers (using a take first approach). It returns a vector with the STRING identifiers of the mapped proteins.

Usage

```
## S4 method for signature 'STRINGdb'  
mp(protein_aliases)
```

Arguments

protein_aliases

vector of protein aliases that we want to convert to STRING identifiers

Value

It returns a vector with the STRING identifiers of the mapped proteins.

Author(s)

Andrea Franceschini

multi_map_df	<i>multi_map_df</i>
--------------	---------------------

Description

mapping function (it add the possibility to map using more than one column of the data frame)

Usage

```
multi_map_df(dfToMap, dfMap, strColsFrom, strColFromDfMap, strColToDfMap, caseSensitive=FALSE)
```

Arguments

dfToMap input data frame (that contains the columns that need to be mapped)

dfMap data frame containing the mapping data

strColsFrom sorted vector containing the names of the columns to be used in the input data frame for the mapping (the order of the elements in the vector defines the priority for the mapping)

strColFromDfMap	name of the column in the mapping data frame to be used as source for the mapping
strColToDfMap	name of the column in the mapping data frame to be used as target for the mapping
caseSensitive	specify whether the mapping should be case sensitive

Value

data frame with an additional column containing the result of the mapping

Author(s)

Andrea Franceschini

plot_network	<i>plot_network</i>
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Description

Plots an image of the STRING network with the given proteins.

Usage

```
## S4 method for signature 'STRINGdb'
plot_network(string_ids, payload_id=NULL, required_score=NULL, add_link=TRUE, add_summary=TRUE)
```

Arguments

string_ids	a vector of STRING identifiers
payload_id	an identifier of payload data on the STRING server (see method post_payload for additional informations)
required_score	a threshold on the score that overrides the default score_threshold, that we use only for the picture
add_link	parameter to specify whether you want to generate and add a short link to the relative page in STRING. As default this option is active but we suggest to deactivate it in case one is generating many images (e.g. in a loop). Deactivating this option avoids to generate and store a lot of short-urls on our server.
add_summary	parameter to specify whether you want to add a summary text to the picture. This summary includes a p-value and the number of proteins/interactions.

Author(s)

Andrea Franceschini

post_payload	<i>post_payload</i>
--------------	---------------------

Description

Posts the input to STRING and returns an identifier that you can use to access the payload when you enter in our website.

Usage

```
## S4 method for signature 'STRINGdb'  
post_payload(stringIds, colors=NULL, comments=NULL, links=NULL, iframe_urls=NULL, logo_imgF=NULL, leg
```

Arguments

stringIds	vector of STRING identifiers.
colors	vector containing the colors to use for a every STRING identifier (the order of the elements must match those in the string_ids vector)
comments	vector containing the comments to use for every STRING identifier (the order of the elements must match those in the string_ids vector)
links	vector containing the links to use for every STRING identifier (the order of the elements must match those in the string_ids vector)
iframe_urls	vector containing the urls of the iframes to use for every STRING identifier (the order of the elements must match those in the string_ids vector).
logo_imgF	path to a file containing the logo image to be display in the STRING website
legend_imgF	path to a file containing a legend image to be display in the STRING website

Value

identifier of the payload.

Author(s)

Andrea Franceschini

```
remove_homologous_interactions
    remove_homologous_interactions
```

Description

With this method it is possible to remove the interactions that are composed by a pair of homologous/similar proteins, having a similarity bitscore between each other higher than a threshold.

Usage

```
## S4 method for signature 'STRINGdb'
remove_homologous_interactions(interactions_dataframe, bitscore_threshold = 60)
```

Arguments

```
interactions_dataframe
    a data frame containing the sorted interactions to be benchmarked. The data
    frame should have the following column names: proteinA, proteinB, score

bitscore_threshold
    filter out pairs of homologous proteins, having a similarity bitscore higher than
    this parameter
```

Value

interactions data frame where the homologous pairs have been removed, from the input interactions' data frame

Author(s)

Andrea Franceschini

```
renameColDf    renameColDf
```

Description

Rename a column of a data frame

Usage

```
renameColDf(df, colOldName, colNewName)
```

Arguments

df	input data frame
colOldName	column name to be changed
colNewName	new column name

Value

data frame with the column name changed

Author(s)

Andrea Franceschini

set_background	<i>set_background</i>
----------------	-----------------------

Description

With this method you can specify a vector of proteins to be used as background. The network is reloaded and only the proteins that are present in the background vector are inserted in the graph. Besides, the background is taken in consideration for all the enrichment statistics. If you already created a STRINGdb object, calling set_background is sufficient and you do not need to instantiate a new object again.

Usage

```
## S4 method for signature 'STRINGdb'
set_background(background_vector )
```

Arguments

background_vector	vector of STRING protein identifiers
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Author(s)

Andrea Franceschini

STRINGdb-class

Class "STRINGdb"

Description

The R package STRINGdb provides a convenient interface to STRING, a protein-protein interaction database and functional enrichment analysis tool, for R/Bioconductor users. Please look at the manual/vignette for additional information and examples on how to use the package. STRING is a database of known and predicted protein-protein interactions. It contains information from numerous sources, including experimental repositories, computational prediction methods, and public text collections. Each interaction is associated with a combined confidence score that integrates the different evidence channels. STRING v12.0 contains information on 59.3 million proteins from 12,535 organisms and more than 20 billion interactions. The STRING web interface is freely accessible at: <https://string-db.org/>

Extends

All reference classes extend and inherit methods from "[envRefClass](#)".

Fields

annotations: Object of class data.frame ~~
 annotations_description: Object of class data.frame ~~
 graph: Object of class igraph ~~
 proteins: Object of class data.frame ~~
 speciesList: Object of class data.frame ~~
 species: Object of class numeric ~~
 version: Object of class character ~~
 input_directory: Object of class character ~~
 backgroundV: Object of class vector ~~
 score_threshold: Object of class numeric ~~

Methods

set_background(background_vector): ~~
 post_payload(stringIds, colors, comments, links, iframe_urls, logo_imgF, legend_imgF):
 ~~
 plot_network(string_ids, payload_id, required_score): ~~
 plot_ppi_enrichment(string_ids, file, sliceWindow, edgeWindow, windowExtendedReferenceThreshold, minVa
 ~~
 map(my_data_frame, my_data_frame_id_col_names, takeFirst, removeUnmappedRows, quiet):
 ~~
 load(): ~~

```

get_term_proteins(term_ids, string_ids, enableIEA): ~~
get_summary(string_ids): ~~
get_subnetwork(string_ids): ~~
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```

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