

Package ‘magrene’

April 2, 2025

Title Motif Analysis In Gene Regulatory Networks

Version 1.9.0

Date 2022-01-21

Description magrene allows the identification and analysis of graph motifs in (duplicated) gene regulatory networks (GRNs), including lambda, V, PPI V, delta, and bifan motifs. GRNs can be tested for motif enrichment by comparing motif frequencies to a null distribution generated from degree-preserving simulated GRNs. Motif frequencies can be analyzed in the context of gene duplications to explore the impact of small-scale and whole-genome duplications on gene regulatory networks. Finally, users can calculate interaction similarity for gene pairs based on the Sorensen-Dice similarity index.

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URL <https://github.com/almeidasilvaf/magrene>

BugReports <https://support.bioconductor.org/t/magrene>

biocViews Software, MotifDiscovery, NetworkEnrichment, SystemsBiology, GraphAndNetwork

Encoding UTF-8

Roxygen list(markdown = TRUE)

RoxygenNote 7.2.0

Imports utils, stats, BiocParallel

Suggests BiocStyle, covr, knitr, rmarkdown, ggplot2, sessioninfo, testthat (>= 3.0.0)

Config/testthat/edition 3

VignetteBuilder knitr

Depends R (>= 4.2.0)

LazyData false

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

git_branch devel

git_last_commit 99513a8

git_last_commit_date 2024-10-29

Repository Bioconductor 3.21

Date/Publication 2025-04-02

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calculate_Z	<i>Calculate Z-score for motif frequencies</i>
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Description

Calculate Z-score for motif frequencies

Usage

```
calculate_Z(observed = NULL, nulls = NULL)
```

Arguments

observed	A list of observed motif frequencies for each motif type. List elements must be named 'lambda', 'bifan', 'V', 'PPI_V', and 'delta' (not necessarily in that order).
nulls	A list of null distributions for each motif type as returned by generate_nulls.

Value

A numeric vector with the Z-score for each motif type.

Examples

```
# Simulating it for test purposes
null <- rnorm(1000, mean = 5, sd = 1)
nulls <- list(
  lambda = null, V = null, PPI_V = null, delta = null, bifan = null
)
observed <- list(lambda = 7, bifan = 13, delta = 9, V = 5, PPI_V = 10)
z <- calculate_Z(observed, nulls)
# Check for motif enrichment (Z > 5)
z[which(z > 5)]
```

find_bifan

*Find bifan motifs***Description**

Find bifan motifs

Usage

```
find_bifan(
  edgelist = NULL,
  paralogs = NULL,
  lambda_vec = NULL,
  count_only = FALSE
)
```

Arguments

edgelist	A 2-column data frame with regulators in column 1 and targets in column 2. It can be ignored if you give lambda motifs to parameter lambda_vec (recommended).
paralogs	A 2-column data frame with gene IDs for each paralog in the paralog pair.
lambda_vec	A character of lambda motifs as returned by <code>find_lambda()</code> . If this is <code>NULL</code> , this function will find lambda motifs from edgelist and paralogs first. Passing previously identified lambda motifs will make this function much faster.
count_only	Logical indicating whether the function should return only motif counts as a numeric scalar. If <code>FALSE</code> , it will return a character vector of motifs. Default: <code>FALSE</code> .

Value

A character vector with bifan motifs represented in the format **regulator1, regulator2->target1, target2**.

Examples

```

data(gma_grn)
data(gma_paralogs)
edgelist <- gma_grn[1:50000, 1:2]
paralogs <- gma_paralogs[gma_paralogs$type == "WGD", 1:2]
paralogs <- rbind(
  paralogs,
  data.frame(duplicate1 = "Glyma.01G177200",
             duplicate2 = "Glyma.08G116700")
)
lambda_vec <- find_lambda(edgelist, paralogs)
bifan <- find_bifan(paralogs = paralogs, lambda_vec = lambda_vec)

```

find_delta

Find delta motifs

Description

Find delta motifs

Usage

```

find_delta(
  edgelist = NULL,
  paralogs = NULL,
  edgelist_ppi = NULL,
  lambda_vec = NULL,
  count_only = FALSE
)

```

Arguments

edgelist	A 2-column data frame with regulators in column 1 and targets in column 2. It can be ignored if you give lambda motifs to parameter lambda_vec (recommended).
paralogs	A 2-column data frame with gene IDs for each paralog in the paralog pair. It can be ignored if you give lambda motifs to parameter lambda_vec (recommended).
edgelist_ppi	A 2-column data frame with IDs of genes that encode each protein in the interacting pair.
lambda_vec	A character of lambda motifs as returned by <code>find_lambda()</code> . If this is NULL, this function will find lambda motifs from edgelist and paralogs first. Passing previously identified lambda motifs will make this function much faster.
count_only	Logical indicating whether the function should return only motif counts as a numeric scalar. If FALSE, it will return a character vector of motifs. Default: FALSE.

Value

A character vector with lambda motifs represented in the format **target1<-regulator->target2**.

Examples

```
data(gma_grn)
data(gma_paralogs)
data(gma_ppi)
edgelist <- gma_grn[500:1000, 1:2] # reducing for test purposes
edgelist <- gma_grn[1:10000, 1:2]
paralogs <- gma_paralogs[gma_paralogs$type == "WGD", 1:2]
edgelist_ppi <- gma_ppi
lambda_vec <- find_lambda(edgelist, paralogs)
motifs <- find_delta(edgelist_ppi = edgelist_ppi, lambda_vec = lambda_vec)
```

find_lambda

Find lambda motifs

Description

Find lambda motifs

Usage

```
find_lambda(edgelist = NULL, paralogs = NULL, count_only = FALSE)
```

Arguments

edgelist	A 2-column data frame with regulators in column 1 and targets in column 2.
paralogs	A 2-column data frame with gene IDs for each paralog in the paralog pair.
count_only	Logical indicating whether the function should return only motif counts as a numeric scalar. If FALSE, it will return a character vector of motifs. Default: FALSE.

Value

A character vector with lambda motifs represented in the format **target1<-regulator->target2**.

Examples

```
data(gma_grn)
data(gma_paralogs)
edgelist <- gma_grn[500:1000, 1:2] # reducing for test purposes
paralogs <- gma_paralogs[gma_paralogs$type == "WGD", 1:2]
motifs <- find_lambda(edgelist, paralogs)
```

find_ppi_v	<i>Find V motifs in protein-protein interactions</i>
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Description

Find V motifs in protein-protein interactions

Usage

```
find_ppi_v(edgelist = NULL, paralogs = NULL, count_only = FALSE)
```

Arguments

edgelist	A 2-column data frame with protein 1 in column 1 and protein 2 in column 2.
paralogs	A 2-column data frame with gene IDs for each paralog in the paralog pair.
count_only	Logical indicating whether the function should return only motif counts as a numeric scalar. If FALSE, it will return a character vector of motifs. Default: FALSE.

Details

This function aims to find the number of paralogous gene pairs that share an interaction partner.

Value

A character vector with V motifs represented in the format **paralog1-partner-paralog2**.

Examples

```
data(gma_ppi)
data(gma_paralogs)
edgelist <- gma_ppi
paralogs <- gma_paralogs[gma_paralogs$type == "WGD", 1:2]
motifs <- find_ppi_v(edgelist, paralogs)
```

find_v	<i>Find V motifs</i>
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Description

Find V motifs

Usage

```
find_v(edgelist = NULL, paralogs = NULL, count_only = FALSE)
```

Arguments

edgelist	A 2-column data frame with regulators in column 1 and targets in column 2.
paralogs	A 2-column data frame with gene IDs for each paralog in the paralog pair.
count_only	Logical indicating whether the function should return only motif counts as a numeric scalar. If FALSE, it will return a character vector of motifs. Default: FALSE.

Value

A character vector with V motifs represented in the format **regulator1->target<-regulator2**.

Examples

```
data(gma_grn)
data(gma_paralogs)
edgelist <- gma_grn[2000:4000, 1:2] # reducing for test purposes
paralogs <- gma_paralogs[gma_paralogs$type == "WGD", 1:2]
motifs <- find_v(edgelist, paralogs)
```

generate_nulls

Generate null distributions of motif counts for each motif type

Description

Generate null distributions of motif counts for each motif type

Usage

```
generate_nulls(
  edgelist = NULL,
  paralogs = NULL,
  edgelist_ppi = NULL,
  n = 1000,
  bp_param = BiocParallel::SerialParam()
)
```

Arguments

edgelist	A 2-column data frame with regulators in column 1 and targets in column 2.
paralogs	A 2-column data frame with gene IDs for each paralog in the paralog pair.
edgelist_ppi	A 2-column data frame with IDs of genes that encode each protein in the interacting pair.
n	Number of degree-preserving simulated networks to generate. Default: 1000.
bp_param	BiocParallel back-end to be used. Default: BiocParallel::SerialParam().

Value

A list of numeric vectors named lambda, delta, V, PPI_V, and bifan, containing the null distribution of motif counts for each motif type.

Examples

```
set.seed(123)
data(gma_grn)
data(gma_paralogs)
data(gma_ppi)
edgelist <- gma_grn[500:1000, 1:2] # reducing for test purposes
paralogs <- gma_paralogs[gma_paralogs$type == "WGD", 1:2]
edgelist_ppi <- gma_ppi
n <- 2 # small n for demonstration purposes
generate_nulls(edgelist, paralogs, edgelist_ppi, n)
```

gma_grn

Sample soybean GRN

Description

The GRN was inferred with BioNERO using expression data from Libault et al., 2010, and Severin et al., 2010.

Usage

```
data(gma_grn)
```

Format

A 3-column data frame with node1, node2, and edge weight.

References

Severin, A. J., Woody, J. L., Bolon, Y. T., Joseph, B., Diers, B. W., Farmer, A. D., ... & Shoemaker, R. C. (2010). RNA-Seq Atlas of Glycine max: a guide to the soybean transcriptome. *BMC plant biology*, 10(1), 1-16.

Libault, M., Farmer, A., Joshi, T., Takahashi, K., Langley, R. J., Franklin, L. D., ... & Stacey, G. (2010). An integrated transcriptome atlas of the crop model Glycine max, and its use in comparative analyses in plants. *The Plant Journal*, 63(1), 86-99.

Examples

```
data(gma_grn)
```

`gma_paralogs`*Soybean (Glycine max) duplicated genes*

Description

The repertoire of soybean paralogs was retrieved from Almeida-Silva et al., 2020.

Usage

```
data(gma_paralogs)
```

Format

A 3-column data frame with duplicate 1, duplicate 2, and duplication type

References

Almeida-Silva, F., Moharana, K. C., Machado, F. B., & Venancio, T. M. (2020). Exploring the complexity of soybean (*Glycine max*) transcriptional regulation using global gene co-expression networks. *Planta*, 252(6), 1-12.

Examples

```
data(gma_paralogs)
```

`gma_ppi`*Sample soybean PPI network*

Description

PPI were retrieved from the STRING database and filtered to keep only medium confidence edges and nodes in the GRN.

Usage

```
data(gma_ppi)
```

Format

A 2-column data frame with node1 and node2.

Examples

```
data(gma_ppi)
```

nulls	<i>Null distribution of motif frequencies for vignette data set</i>
-------	---

Description

Data were filtered exactly as demonstrated in the vignette. Briefly, the top 30k edges from the GRN were kept, and only WGD-derived gene pairs were used.

Usage

```
data(nulls)
```

Format

A list of numeric vectors with the motif frequencies in each simulated network. List elements are named **lambda**, **delta**, **V**, **PPI_V**, and **bifan**, and each element has length 100.

Examples

```
data(nulls)
```

sd_similarity	<i>Calculate Sorensen-Dice similarity between paralogous gene pairs</i>
---------------	---

Description

Calculate Sorensen-Dice similarity between paralogous gene pairs

Usage

```
sd_similarity(edgelist = NULL, paralogs = NULL)
```

Arguments

edgelist	A 2-column data frame with regulators in column 1 and targets in column 2.
paralogs	A 2-column data frame with gene IDs for each paralog in the paralog pair.

Value

A data frame containing the paralogous gene pairs and their Sorensen-Dice similarity scores.

Examples

```
data(gma_ppi)
data(gma_paralogs)
edgelist <- gma_ppi
paralogs <- gma_paralogs
sim <- sd_similarity(edgelist, paralogs)
```

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