

# Package ‘magrene’

December 26, 2024

**Title** Motif Analysis In Gene Regulatory Networks

**Version** 1.8.0

**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.

**License** GPL-3

**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** RELEASE\_3\_20

**git\_last\_commit** 3e6291f

**git\_last\_commit\_date** 2024-10-29

**Repository** Bioconductor 3.20

**Date/Publication** 2024-12-26

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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)]
```

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find_bifan	<i>Find bifan motifs</i>
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**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 <b>lambda_vec</b> (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 find_lambda(). If this is NULL, this function will find lambda motifs from <b>edgelist</b> and <b>paralogs</b> 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 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 <b>lambda_vec</b> (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 <b>lambda_vec</b> (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 find_lambda(). If this is NULL, this function will find lambda motifs from <b>edgelist</b> and <b>paralogs</b> 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	<i>Find lambda motifs</i>
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---

**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)

```

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`find_ppi_v`*Find V motifs in protein-protein interactions*

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**Description**

Find V motifs in protein-protein interactions

**Usage**

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

**Arguments**

<code>edgelist</code>	A 2-column data frame with protein 1 in column 1 and protein 2 in column 2.
<code>paralogs</code>	A 2-column data frame with gene IDs for each paralog in the paralog pair.
<code>count_only</code>	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`*Find V motifs*

---

**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	<i>Generate null distributions of motif counts for each motif type</i>
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---

**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>
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**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>
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---

**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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