

Package ‘BICORN’

July 21, 2025

Title Integrative Inference of De Novo Cis-Regulatory Modules

Version 0.1.0

Description Prior transcription factor binding knowledge and target gene expression data are integrated in a Bayesian framework for functional cis-regulatory module inference. Using Gibbs sampling, we iteratively estimate transcription factor associations for each gene, regulation strength for each binding event and the hidden activity for each transcription factor.

Depends R (>= 3.4)

License GPL-2

Encoding UTF-8

LazyData true

RoxygenNote 6.0.1

Suggests knitr, rmarkdown

Imports stats

VignetteBuilder knitr

NeedsCompilation no

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Repository CRAN

Date/Publication 2018-06-06 10:30:06 UTC

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A	<i>TF-gene regulation strength matrix</i>
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Description

A matrix of TF-gene regulation strength with genes as rows and TFs as columns.

Usage

A

Format

numeric matrix

alpha	<i>Inverse-gamma distribution hyper-parameter alpha</i>
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Description

Hyper-parameter alpha of inverse-gamma distribution.

Usage

alpha

Format

scalar

A_old	<i>TF-gene regulation strength matrix sampled from the previous round</i>
-------	---

Description

A matrix of TF-gene regulation strength with genes as rows and TFs as columns, sampled from the previous round. During the Gibbs sampling process, this matrix is used as prior for a new round of regulation strength sampling.

Usage

A_old

Format

numeric matrix

A_sampling	<i>Regulation Strength Sampling Function</i>
------------	--

Description

Function 'A_sampling' estimates a regulation strength for each sampled binding event in C, according to a posterior Gaussian distribution.

Usage

```
A_sampling(Y, C, A_old, X, base_line, C_prior, sigma_noise, sigma_A,
           sigma_baseline, sigma_X)
```

Arguments

Y	gene expression data matrix
C	sampled TF-gene binding network
A_old	regulatory strength sampled from the previous round, used as a prior in current function
X	sampled transcription factor activity matrix
base_line	sampled gene expression baseline activity
C_prior	prior TF-gene binding network
sigma_noise	variance of gene expression fitting residuals
sigma_A	variance of regulatory strength
sigma_baseline	variance of gene expression baseline activity
sigma_X	variance of transcription factor activity

baseline_sampling	<i>Gene Baseline Expression Sampling Function</i>
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Description

Function 'baseline_sampling' estimates a baseline expression for each gene, according to a posterior Gaussian distribution.

Usage

```
baseline_sampling(Y, C, A, X, base_line_old, C_prior, sigma_noise, sigma_A,
                 sigma_baseline, sigma_X)
```

Arguments

Y	gene expression data matrix
C	sampled TF-gene binding network
A	sampled regulatory strength matrix
X	sampled transcription factor activity matrix
base_line_old	prior gene expression baseline activity
C_prior	prior TF-gene binding network
sigma_noise	variance of gene expression fitting residuals
sigma_A	variance of regulatory strength
sigma_baseline	variance of gene expression baseline activity
sigma_X	variance of transcription factor activity

base_line	<i>Gene baseline expression</i>
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Description

A vector of baseline expression for all genes.

Usage

base_line

Format

numeric vector

base_line_old	<i>Gene baseline expression sampled from the previous round.</i>
---------------	--

Description

A vector of baseline expression for all genes, sampled from the previous round. During the Gibbs Sampling process, this is used as a prior for a new round of gene baseline expression sampling.

Usage

base_line_old

Format

numeric vector

beta	<i>Inverse-gamma distribution hyper-parameter beta</i>
------	--

Description

Hyper-parameter beta of inverse-gamma distribution.

Usage

beta

Format

scalar

BICORN

*BICORN Algorithm Function***Description**

Function 'BICORN' infers a posterior module-gene regulatory network by iteratively sampling regulatory strength, transcription factor activity and several key model parameters.

Usage

```
BICORN(BICORN_input = NULL, L = 100, output_threshold = 10)
```

Arguments

BICORN_input this list structure contains TF symbols, gene symbols and candidate modules
 L total rounds of Gibbs Sampling.
 output_threshold number of rounds after which we start to record results.

Examples

```
# load in the sample data input
data("sample.input")

# Data initialization (Integrate prior binding network and gene expression data)
BICORN_input<-data_integration(Binding_matrix = Binding_matrix, Binding_TFs = Binding_TFs,
Binding_genes = Binding_genes, Exp_data = Exp_data, Exp_genes = Exp_genes,
Minimum_gene_per_module_regulate = 2)

# Infer cis-regulatory modules (TF combinations) and their target genes
BICORN_output<-BICORN(BICORN_input, L = 2, output_threshold = 1)
```

Binding_genes

*Genes in the prior binding network***Description**

A list of official gene symbols in the binary binding network.

Usage

```
Binding_genes
```

Format

character vector

Binding_matrix	<i>Prior TF-gene binding network</i>
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Description

A prior binary TF-gene regulatory network with each unit either 1 (binding) or 0 (non-binding).

Usage

Binding_matrix

Format

numeric matrix

Binding_TFs	<i>TFs in the prior binding network</i>
-------------	---

Description

A list of transcription factors in the prior binding network.

Usage

Binding_TFs

Format

character vector

C	<i>TF-gene binding network</i>
---	--------------------------------

Description

A matrix of TF-gene regulatory network with each unit either 1 (binding) or 0 (non-binding).

Usage

C

Format

numeric matrix

C_old	<i>TF-gene binding network sampled from the previous round</i>
-------	--

Description

A matrix of TF-gene binding network sampled from the previous round, with each unit either 1 (binding) or 0 (non-binding). During the Gibbs sampling process, this is used as a prior for a new round of binding network sampling.

Usage

C_old

Format

numeric matrix

C_prior	<i>Prior TF-gene binding network</i>
---------	--------------------------------------

Description

A matrix of prior TF-gene binding events, with each unit either 1 (binding) or 0 (non-binding). Such a prior network can be obtained from TF-gene binding database, motif searching, ChIP-seq peaks or ATAC-seq peaks.

Usage

C_prior

Format

numeric matrix

C_sampling_cluster	<i>cis-Regulatory Module Sampling Function</i>
--------------------	--

Description

Function 'C_sampling_cluster' samples a candidate cis-regulatory module for each gene, according to a discrete posterior probability distribution.

Usage

```
C_sampling_cluster(Y, C_old, A_old, X_old, base_line_old, C_prior, sigma_noise,
  sigma_A, sigma_baseline, sigma_X, BICORN_input)
```

Arguments

Y	gene expression data matrix
C_old	TF-gene binding network sampled from the previous round
A_old	regulatory strength matrix sampled from the previous round
X_old	transcription factor activity matrix sampled from the previous round
base_line_old	gene expression baseline activity sampled from the previous round
C_prior	prior TF-gene binding network
sigma_noise	variance of gene expression fitting residuals
sigma_A	variance of regulatory strength
sigma_baseline	variance of gene expression baseline activity
sigma_X	variance of transcription factor activity
BICORN_input	this list structure contains TF symbols, Gene symbols and candidate modules

data_integration	<i>Data Initialization for BICORN</i>
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Description

Function 'data_integration' integrates the prior TF-gene binding network and gene expression data together. It will remove any genes missing either TF bindings or gene expression and identify a list of candidate cis-regulatory modules.

Usage

```
data_integration(Binding_matrix = NULL, Binding_TFs = NULL,
  Binding_genes = NULL, Exp_data, Exp_genes = NULL,
  Minimum_gene_per_module_regulate = 2)
```

Arguments

- Binding_matrix loaded prior binding network
- Binding_TFs loaded transcription factors
- Binding_genes loaded genes in the prior binding network
- Exp_data loaded properly normalized gene expression data
- Exp_genes loaded genes in the gene expression data
- Minimum_gene_per_module_regulate
 the minimum number of genes regulated by each module, used for candidate module filtering.

Examples

```
# load in the sample data input
data("sample.input")

# Data initialization (Integrate prior binding network and gene expression data)
BICORN_input<-data_integration(Binding_matrix = Binding_matrix, Binding_TFs = Binding_TFs,
Binding_genes = Binding_genes, Exp_data = Exp_data, Exp_genes = Exp_genes,
Minimum_gene_per_module_regulate = 2)
```

Exp_data	<i>Gene expression data</i>
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Description

A matrix of normalized gene expression data with genes as rows and samples as columns. The gene expression data can be either time-course data measured under multiple time points or steady state data generated from at least two different conditions.

Usage

Exp_data

Format

numeric matrix

Exp_genes	<i>Genes in the expression data</i>
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Description

A list of official gene symbols in the gene expression data set.

Usage

Exp_genes

Format

character vector

sigmanoise_sampling	<i>Fitting Residue Variance Sampling Function</i>
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Description

Function 'sigmanoise_sampling' estimates the variance of overall gene expression fitting residuals, according to an inverse-gamma distribution.

Usage

```
sigmanoise_sampling(Y, C, A, X, base_line, C_prior, sigma_A, sigma_baseline,
  sigma_X, alpha, beta)
```

Arguments

Y	gene expression data matrix
C	sampled TF-gene binding network
A	sampled regulatory strength matrix
X	sampled transcription factor activity matrix
base_line	sampled gene expression baseline activity
C_prior	prior TF-gene binding network
sigma_A	variance of regulatory strength
sigma_baseline	variance of gene expression baseline activity
sigma_X	variance of transcription factor activity
alpha	hyper-parameter for inverse-gamma distribution
beta	hyper-parameter for inverse-gamma distribution

sigma_A	<i>Regulation strength variance</i>
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Description

Variance of regulation strength matrix A.

Usage

sigma_A

Format

scalar

sigma_baseline	<i>Variance of baseline gene expression.</i>
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Description

Variance of baseline gene expression.

Usage

sigma_baseline

Format

scalar

sigma_noise	<i>Variance of gene expression fitting residuals.</i>
-------------	---

Description

Variance of gene expression fitting residuals.

Usage

sigma_noise

Format

scalar

<i>sigma_X</i>	<i>Transcription factor activity variance</i>
----------------	---

Description

Variance of transcription factor activity matrix X.

Usage

sigma_X

Format

scalar

<i>X</i>	<i>Transcription factr activity matrix</i>
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Description

A matrix of hidden transcription factr activity estimated from gene expression data, with transcription factrs as rows and samples as columns.

Usage

X

Format

numeric matrix

<i>X_old</i>	<i>Transcription factr activity matrix sampled from the previous round</i>
--------------	--

Description

A matrix of hidden transcription factr activity estimated from gene expression data, with transcription factrs as rows and samples as columns, sampled from the previous round. During the Gibbs sampling process, this is used as a prior for a new round of transcription factor activity sampling.

Usage

X_old

Format

numeric matrix

X_sampling	<i>Transcription Factor Activity Sampling Function</i>
------------	--

Description

Function 'X_sampling' estimates the hidden activities of each transcription factor, according to a posterior Gaussian random process.

Usage

```
X_sampling(Y, C, A, X_old, base_line, C_prior, sigma_noise, sigma_A,
           sigma_baseline, sigma_X)
```

Arguments

Y	gene expression data matrix
C	sampled TF-gene binding network
A	sampled regulatory strength matrix
X_old	sampled transcription factor activity matrix from the previous round
base_line	sampled gene expression baseline activity
C_prior	prior TF-gene binding network
sigma_noise	variance of gene expression fitting residuals
sigma_A	variance of regulatory strength
sigma_baseline	variance of gene expression baseline activity
sigma_X	variance of transcription factor activity

Y	<i>Gene expression data used for module inference</i>
---	---

Description

A matrix of normalized gene expression for common genes of prior binding input and gene expression input, with genes as rows and samples as columns. Y is the matrix used for cis-regulatory module inference.

Usage

```
Y
```

Format

numeric matrix

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