

Package: mfa (via r-universe)

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Title Bayesian hierarchical mixture of factor analyzers for modelling genomic bifurcations

Version 1.27.0

Description MFA models genomic bifurcations using a Bayesian hierarchical mixture of factor analysers.

Depends R (>= 3.4.0)

Imports methods, stats, ggplot2, Rcpp, dplyr, ggmcmc, MCMCpack, MCMCglmm, coda, magrittr, tibble, Biobase

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Contents

calculate_chi	2
create_synthetic	2
empirical_lambda	3
mfa	4
plot_chi	6
plot_dropout_relationship	6

plot_mfa_autocorr	7
plot_mfa_trace	8
print.mfa	8
summary.mfa	9
to_ggmcmc	10

Index	11
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calculate_chi	<i>Calculate posterior chi precision parameters</i>
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Description

Calculates a data frame of the MAP estimates of χ .

Usage

```
calculate_chi(m)
```

Arguments

m A fit returned from mfa

Value

A data_frame with one entry for the feature names and one for the MAP estimates of chi (using the posterior.mode function from MCMCglm).

Examples

```
synth <- create_synthetic(C = 20, G = 5)
m <- mfa(synth$X)
chi_map <- calculate_chi(m)
```

create_synthetic	<i>Create synthetic data</i>
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Description

Create synthetic bifurcating data for two branches. Optionally incorporate zero inflation and transient gene expression.

Usage

```
create_synthetic(C = 100, G = 40, p_transient = 0, zero_negative = TRUE,
  model_dropout = FALSE, lambda = 1)
```

Arguments

C	Number of cells to simulate
G	Number of genes to simulate
p_transient	Proportion of genes that exhibit transient expression
zero_negative	Logical: should expression generated less than zero be set to zero? This will zero-inflate the data
model_dropout	Logical: if true, expression will be set to zero with the exponential dropout formula dependent on the latent expression using dropout parameter lambda
lambda	The dropout parameter

Value

A list with the following entries:

- X A cell-by-feature expression matrix
- branch A vector of length C assigning cells to branches
- pst A vector of pseudotimes for each cell
- k The k parameters
- phi The ϕ parameters
- delta The δ parameters
- p_transient The proportion of genes simulated as transient according to the original function call

Examples

```
synth <- create_synthetic()
```

empirical_lambda *Estimate the dropout parameter*

Description

Estimate the dropout parameter

Usage

```
empirical_lambda(y, lower_limit = 0)
```

Arguments

y	A cell-by-gene expression matrix
lower_limit	The limit below which expression counts as 'dropout'

Value

The estimated lambda

Examples

```
synth <- create_synthetic(C = 20, G = 5, zero_negative = TRUE, model_dropout = TRUE)
lambda <- empirical_lambda(synth$X)
```

mfa

Fit a MFA object

Description

Perform Gibbs sampling inference for a hierarchical Bayesian mixture of factor analysers to identify bifurcations in single-cell expression data.

Usage

```
mfa(y, iter = 2000, thin = 1, burn = iter/2, b = 2,
    zero_inflation = FALSE, pc_initialise = 1, prop_collapse = 0,
    scale_input = !zero_inflation, lambda = NULL, eta_tilde = NULL,
    alpha = 0.1, beta = 0.1, theta_tilde = 0, tau_eta = 1,
    tau_theta = 1, tau_c = 1, alpha_chi = 0.01, beta_chi = 0.01,
    w_alpha = 1/b, clamp_pseudotimes = FALSE)
```

Arguments

y	A cell-by-gene single-cell expression matrix or an ExpressionSet object
iter	Number of MCMC iterations
thin	MCMC samples to thin
burn	Number of MCMC samples to throw away
b	Number of branches to model
zero_inflation	Logical, should zero inflation be enabled?
pc_initialise	Which principal component to initialise pseudotimes to
prop_collapse	Proportion of Gibbs samples which should marginalise over c
scale_input	Logical. If true, input is scaled to have mean 0 variance 1
lambda	The dropout parameter - by default estimated using the function <code>empirical_lambda</code>
eta_tilde	Hyperparameter
alpha	Hyperparameter
beta	Hyperparameter
theta_tilde	Hyperparameter
tau_eta	Hyperparameter

tau_theta	Hyperparameter
tau_c	Hyperparameter
alpha_chi	Hyperparameter
beta_chi	Hyperparameter
w_alpha	Hyperparameter
clamp_pseudotimes	This clamps the pseudotimes to their initial values and doesn't perform sampling. Should be FALSE except for diagnostics.

Details

The column names of Y are used as feature (gene/transcript) names while the row names are used as cell names. If either of these is undefined then the corresponding names are set to `cell_x` or `feature_y`.

It is recommended the form of Y is analogous to log-expression to mitigate the impact of outliers.

In the absence of prior information, three valid local maxima in the posterior likelihood exist (see manuscript). Setting the initial values to a principal component typically fixes sampling to one of them, analogous to specifying a root cell in similar methods.

The hyper-parameter η represents the expected expression in the absence of any actual expression measurements. While a Bayesian purist might reason this based on knowledge of the measurement technology, simply taking the mean of the input matrix in an Empirical Bayes style seems reasonable.

The degree of shrinkage of the factor loading matrices to a common value is given by the gamma prior on χ . The mean of this is $\alpha_{\chi} / \beta_{\chi}$ while the variance $\alpha_{\chi} / \beta_{\chi}^2$. Therefore, to obtain higher levels of shrinkage increase α_{χ} with respect to β_{χ} .

The collapsed Gibbs sampling option given by `collapse` involves marginalising out c (the factor loading intercepts) when updating the branch assignment parameters γ which tends to soften the branch assignments.

If zero inflation is enabled using the `zero_inflation` parameter then scaling should *not* be enabled.

Value

An S3 structure with the following entries:

- `traces` A list of iteration-by-dim trace matrices for several important variables
- `iter` Number of iterations
- `thin` Thinning applied
- `burn` Burn period at the start of MCMC
- `b` Number of branches modelled
- `prop_collapse` Proportion of updates for γ that are collapsed
- `N` Number of cells
- `G` Number of features (genes/transcripts)
- `feature_names` Names of features
- `cell_names` Names of cells

Examples

```
synth <- create_synthetic(C = 20, G = 5)
m <- mfa(synth$X)
```

plot_chi *Plot posterior precision parameters*

Description

Plot posterior precision parameters

Usage

```
plot_chi(m, nfeatures = m$G)
```

Arguments

m A fit returned from mfa
nfeatures Top number of

Value

A ggplot2 bar-plot showing the map estimates of χ^{-1}

Examples

```
synth <- create_synthetic(C = 20, G = 5)
m <- mfa(synth$X)
plot_chi(m)
```

plot_dropout_relationship
Plot the dropout relationship

Description

Plot the dropout relationship

Usage

```
plot_dropout_relationship(y, lambda = empirical_lambda(y))
```

Arguments

y The input data matrix
lambda The estimated value of lambda

Value

A ggplot2 plot showing the estimated dropout relationship

Examples

```
synth <- create_synthetic(C = 20, G = 5, zero_negative = TRUE, model_dropout = TRUE)
lambda <- empirical_lambda(synth$X)
plot_dropout_relationship(synth$X, lambda)
```

`plot_mfa_autocorr` *Plot MFA autocorrelation*

Description

Plots the autocorrelation of the posterior log-likelihood.

Usage

```
plot_mfa_autocorr(m)
```

Arguments

`m` A fit returned from `mfa`

Value

A ggplot2 plot returned by the `ggmcmc` package plotting the autocorrelation of the posterior log-likelihood.

Examples

```
synth <- create_synthetic(C = 20, G = 5)
m <- mfa(synth$X)
plot_mfa_autocorr(m)
```

plot_mfa_trace	<i>Plot MFA trace</i>
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Description

Plots the trace of the posterior log-likelihood.

Usage

```
plot_mfa_trace(m)
```

Arguments

m A fit returned from mfa

Value

A ggplot2 plot plotting the trace of the posterior log-likelihood.

Examples

```
synth <- create_synthetic(C = 20, G = 5)
m <- mfa(synth$X)
plot_mfa_trace(m)
```

print.mfa	<i>Print an mfa fit</i>
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Description

Print an mfa fit

Usage

```
## S3 method for class 'mfa'
print(x, ...)
```

Arguments

x An MFA fit returned by mfa
... Additional arguments

Value

A string representation of an mfa object.

Examples

```
synth <- create_synthetic(C = 20, G = 5)
m <- mfa(synth$X)
print(m)
```

summary.mfa

Summarise an mfa fit

Description

Returns summary statistics of an mfa fit, including MAP pseudotime and branch allocations along with uncertainties.

Usage

```
## S3 method for class 'mfa'
summary(object, ...)
```

Arguments

object	An MFA fit returned by a call to mfa
...	Additional arguments

Value

A data_frame with the following columns:

- pseudotime The MAP pseudotime estimate
- branch The MAP branch estimate
- branch_certainty The proportion of traces for which the cell is assigned to its MAP branch
- pseudotime_lower The lower bound on the 95 (HPD) credible interval
- pseudotime_upper The upper bound on the 95

Examples

```
synth <- create_synthetic(C = 20, G = 5)
m <- mfa(synth$X)
ms <- summary(m)
```

`to_ggmcmc`*Turn a trace list to a ggmcmc object*

Description

Turn a trace list to a ggmcmc object

Usage

```
to_ggmcmc(g)
```

Arguments

`g` A list of trace matrices

Value

The trace list converted into a ggs object for input to ggmcmc.

Index

`calculate_chi`, [2](#)
`create_synthetic`, [2](#)

`empirical_lambda`, [3](#)

`mfa`, [4](#)

`plot_chi`, [6](#)
`plot_dropout_relationship`, [6](#)
`plot_mfa_autocorr`, [7](#)
`plot_mfa_trace`, [8](#)
`print.mfa`, [8](#)

`summary.mfa`, [9](#)

`to_ggmcmc`, [10](#)