Package ‘mfa’

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Title Bayesian hierarchical mixture of factor analyzers for modelling genomic bifurcations

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

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`calculate_chi` *Calculate posterior chi precision parameters*

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 `MCMCglmm`).

Examples

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

`create_synthetic` *Create synthetic data*

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`	Propotion 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()
```

cs_sigmoid *Sigmoid function for activations - renamed to avoid naming conflict*

Description

Sigmoid function for activations - renamed to avoid naming conflict

Usage

```
cs_sigmoid(t, phi, k, delta)
```

Value

Sigmoid function given the parameters

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)
```

log_sum_exp — *Log sum of exponentials*

Description

Log sum of exponentials

Usage

```
log_sum_exp(x)
```

Arguments

x	Vector of quantities

Value

Log sum of exponentials in a numerically stable manner.

map_branch — *Find the MAP branch and uncertainty*

Description

Find the MAP branch and uncertainty

Usage

```
map_branch(g)
```

Arguments

g	The trace slot from an mfa fit

Value

A data frame with a column corresponding to the MAP branch and a further column corresponding to the proportion of samples assigned to that branch (a measure of uncertainty).

mcmcify — *Turn a matrix's columns into informative names*

Description

Turn a matrix's columns into informative names

Usage

```
mcmcify(m, name)
```

Arguments

m	A fit returned from mfa
name	The name of the parameter

Value

The input with consistent naming.

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 `empirical_lambda`

`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 `eta_tilde` 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 `chi`. 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 `alpha_chi` with respect to `beta_chi`.

The collapsed Gibbs sampling option given by `collapse` involves marginalising out `c` (the factor loading intercepts) when updating the branch assignment parameters `gamma` 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 gamma 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 *Plot MFA trace*

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)
```

---

posterior *Calculate the log-posterior during inference*

Description

Calculate the log-posterior during inference

Usage

```
posterior(y, c, k, pst, tau, gamma, theta, eta, chi, w, tau_c, r, alpha, beta,
  theta_tilde, eta_tilde, tau_theta, tau_eta, alpha_chi, beta_chi,
  zero_inflation = FALSE, lambda = NULL)
```

Arguments

y	Cell-by-gene gene expression matrix
c	Factor loading parameter
k	Factor loading parameter
pst	Pseudotime vector
tau	Precision parameter
gamma	Branch responsibility parameter
theta	Factor loading parameter
eta	Factor loading parameter
chi	ARD-like precision
w	Branch responsibility prior (simplex)
tau_c	Hyperparameter
r	Hyperparameter
alpha	Hyperparamter
beta	Hyperparameter
theta_tilde	Hyperparameter
eta_tilde	Hyperparameter
tau_theta	Hyperparameter
tau_eta	Hyperparameter
alpha_chi	Hyperparameter
beta_chi	Hyperparameter
zero_inflation	Logical - was zero inflation modelled?
lambda	Zero inflation parameter

Value

The posterior log-likelihood.

---

print.mfa *Print an mfa fit*

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.

transient *Transient mean function*

Description

Transient mean function

Usage

```
transient(t, location = 0.5, scale = 0.01, reverse = FALSE)
```

Value

Transient mean function given the parameters.

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