Package ‘MIMOSA’

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MIMOSA-package MIMOSA: Mixture Models for Single Cell Assays

Description

MIMOSA implements mixtures of Dirichlet-multinomial or Beta-binomial models for paired count data from single–cell assays that typically arise in immunological studies. It can be used for ICS (Intracellular Cytokine Staining) assays to detect vaccine responders, for example, or to detect changes in proportions of cells expressing a gene, such as in Fluidigm Biomark Single–cell gene expression.

References


See Also

MIMOSA, ConstructMIMOSAExpressionSet

.fitMCMC Fit the MIMOSA model via MCMC

Description

This is an internal function that fits the MIMOSA model via MCMC. It is called from MIMOSA

Usage

.fitMCMC(data, inits = NULL, iter = 250000, burn = 50000, thin = 1, tune = 100, outfile = basename(tempfile(tmpdir = ".", fileext = ".dat")), alternative = "greater", UPPER = 0.5, LOWER = 0.15, FAST = TRUE, EXPRATE = 1e-04, pXi = c(1, 1), seed = 10)
Arguments

- **data**: a list with elements names 'n.stim' and 'n.unstim', the stimulated and unstimulated counts. Must be at least of dimension 2.
- **inits**: the initialization parameters for the MCMC routine. Can be initialized from MDMix with initonly=TRUE.
- **iter**: the number of Mote Carlo iterations
- **burn**: the number of burn-in iterations
- **thin**: The thinning interval
- **tune**: the number of iterations used for tuning the step size
- **outfile**: the output file name
- **alternative**: either 'greater' or 'not equal' for fitting the one-sided or two-sided MIMOSA model, respectively.
- **UPPER**: tuning parameter for the upper bound on the acceptance ratio of each parameter
- **LOWER**: tuning parameter for the lower bound on the acceptance ratio of each parameter
- **FAST**: TRUE,FALSE. Use the heuristic (FAST=TRUE) for fitting a one-sided model rather than recomputing the normalization constant via MCMC for each step.
- **EXPRATE**: the mean of the prior distribution for the model hyperparameters.
- **pXi**: is the prior on the w, beta(1,1) by default.
- **seed**: numeric random seed

asinh_trans(a)

Arguments

- **c**: numeric cofactor for asinh transform. Default 1.

Details

Arcsinh transform for use with coord_trans in ggplot2

Value

transform

Author(s)

Greg Finak
BetaMixResult-class

The output of fitting Beta-Binomial EM implementation BetaMix.

Description

BetaMix will return an object of this class.

boxplotMIMOSAResultList

Boxplots of MIMOSA

Usage

boxplotMIMOSAResultList(data, title = "A Boxplot", x_axis_category = NULL, cofactor = 5000, line = TRUE, threshold = 0.005)

Arguments

data MIMOSAResultList
title character Title of the plot.
x_axis_category name the column of the phenoData frame for the x-axis of the boxplots.
cofactor integer cofactor of the arcsinhTransform for the y axis.
line logical whether or not to connect points from the same subject
threshold numeric the FDR threshold (q-value) at which to classify responders as a separate category.

Details

Generate boxplots for MIMOSA positivity calls.

Value

ggplot object.

Author(s)

Greg Finak
combine.MIMOSA

Combine MIMOSAResultList objects

Description
Combining two or more MIMOSAResultList objects

Usage
combine.MIMOSA(x, y, ...)

Arguments
x, y MIMOSAResultList
... Additional MIMOSAResultList objects

Details
Combines two or more MIMOSAResultList objects. The method is light on error checking so the results should be from the same MIMOSAExpressionSet object.

Value
a MIMOSAResultList

Author(s)
Greg Finak

ConstructMIMOSAExpressionSet

A wrapper for constructing an Expression Set for MIMOSA

Description
Calls a series of other functions that will reshape and refactor the data frame into the right format for use by MIMOSA. Standardized for use with internal SCHARP data sets. We provide some default arguments as examples. Currently slow, and very much prototype code.

Usage
ConstructMIMOSAExpressionSet(thisdata, reference = quote(STAGE %in% "CTRL" & PROTEIN %in% "Media+cells"), measure.columns = c("Neg", "Pos"), other.annotations = setdiff(colnames(thisdata), measure.columns), default.cast.formula = component ~ ..., .variables = quote(.PTID, TESTDT, ASSAYID, PLATEID)), featureCols = 1, ref.append.replace = "_NEG")
countsTable

Arguments

thisdata
is the input data frame

reference
is an expression that evaluates to a logical vector which specifies the observations in the data frame that are to be used for the negative control or reference set

measure.columns
is a character vector that specifies which columns hold the observed counts

other.annotations
is a character vector that specifies which additional columns in the data frame should be included in the returned data. By default we take everything, but you could specify only relevant phenotypic information.

default.cast.formula
is a formula that tells reshape how to recast the data frame so that rows correspond to different measured components and columns correspond to samples. By default component~... will put the components as the rows (i.e. positive and negative cell counts) and all measured phenotypic information on the columns.

:variables
is a dotted list that specifies the variable names (columns of the data frame) by which to group the data when organizing stimulated and unstimulated observations. i.e. PTID x ANTIGEN x TCELLSUBSET x TESTDT, or something else for your own data.

featureCols
is a numeric vector that specifies the indices of the columns to be used to name the features. If the casting formula is component~... then there is only one feature column (and it is the first one), so featureCols = 1, by default.

ref.append.replace
the terminating character string in the column names of the negative controls. It will be replaces with _REF for 'reference'

Examples

data(ICS)
E <- ConstructMIMOSAExpressionSet(ICS,
  reference=ANTIGEN%in%negctrl, measure.columns=c('CYTNUM', 'NSUB'),
  other.annotations=c('CYTOKINE', 'TCELLSUBSET', 'ANTIGEN', 'UID'),
  default.cast.formula=component~UID+ANTIGEN+CYTOKINE+TCELLSUBSET,
  .variables=(TCELLSUBSET, CYTOKINE, UID),
  featureCols=1, ref.append.replace='_REF')

countsTable

Extract the table of counts from a MIMOSA model

Description

Extract the table of counts from a MIMOSA model
Usage

countsTable(object, proportion = FALSE)

## S4 method for signature 'MIMOSAResult'
countsTable(object, proportion = FALSE)

## S4 method for signature 'MCMCResult'
countsTable(object, proportion = FALSE)

## S4 method for signature 'MDMixResult'
countsTable(object, proportion = FALSE)

## S3 method for class 'MIMOSAResultList'
countsTable(object, proportion = FALSE)

## S4 method for signature 'MIMOSAResultList'
countsTable(object, proportion = FALSE)

Arguments

object a MIMOSAResult
proportion logical return the counts or the proportions

Value

a data.frame of counts to which the model was fit.
a data.frame of counts for the stimulated and unstimulated samples

Examples

data(ICS)
E<-ConstructMIMOSAExpressionSet(ICS,
    reference=ANTIGEN%in%negctrl, measure.columns=c('CYTNUM', 'NSUB'),
    other.annnotations=c('CYTOKINE', 'TECELLSUBSET', 'ANTIGEN', 'UID'),
    default.cast.formula=component~UID+ANTIGEN+CYTOKINE+TECELLSUBSET,
    .variables=(TECELLSUBSET, CYTOKINE, UID),
    featureCols=1, ref.append.replace='_REF')

result<-MIMOSA(NSUB+CYTNUM~UID+TECELLSUBSET+CYTOKINE|ANTIGEN,
    data=E, method='EM',
    subset=RefTreat%in%Treatment & ANTIGEN%in%ENV',
    ref=ANTIGEN%in%ENV & RefTreat%in%Reference')
head(countsTable(result))
head(countsTable(result, proportion=TRUE))

fdr

Compute the fdr (q-value) from posterior probabilities

Description

Given the z’s from a MIMOSA model, calculates the q-values for each observation.
Usage

fdr(z)
## S3 method for class 'matrix'
fdr(z)
## S3 method for class 'MIMOSAResult'
fdr(z)
## S3 method for class 'MIMOSAResultList'
fdr(z)

Arguments

z matrix of posterior probabilities, or a MIMOSAResult, or MIMOSAResultList

Value

a vector of q-values or a list of vectors of q-values.

Examples

data(ICS)
E<-ConstructMIMOSAExpressionSet(ICS,
    reference=ANTIGEN%in%negctrl',measure.columns=c('CYTNUM', 'NSUB'),
    other.annotations=c('CYTOKINE', 'TELLSUBSET', 'ANTIGEN', 'UID'),
    default.cast.formula=component~UID+ANTIGEN+CYTOKINE+TELLSUBSET,
    .variables=.+(TELLSUBSET,CYTOKINE,UID),
    featureCols=1,ref.append.replace='_REF')
result<-MIMOSA(NSUB+CYTNUM~UID+TELLSUBSET+CYTOKINE|ANTIGEN,
    data=E, method='EM',
    subset=RefTreat%in'Treatment'&ANTIGEN%in'ENV',
    ref=ANTIGEN%in'ENV'&RefTreat%in'Reference'
) qvalues<-fdr(result)

getZ

Extract the posterior probabilities of response from a MIMOSA model

Description

Extract the posterior probabilities of response from a MIMOSA model

Usage

getZ(x)
## S3 method for class 'MIMOSAResultList'
getZ(x)
## S3 method for class 'MIMOSAResult'
getZ(x)
getW(x)

## S3 method for class 'MIMOSAResultList'
getW(x)

## S3 method for class 'MIMOSAResult'
getW(x)

Arguments

x
output from a MIMOSA model

Value

a matrix of posterior probabilities
a vector of component weights

Examples

data(ICS)
E<-ConstructMIMOSAExpressionSet(ICS,
  reference=ANTIGEN%in%negctrl, measure.columns=c('CYTNUM', 'NSUB'),
  other.annotations=c('CYTOKINE', 'TCELLSUBSET', 'ANTIGEN', 'UID'),
  default.cast.formula=component~UID+ANTIGEN+CYTOKINE+TCELLSUBSET,
  .variables=(TCELLSUBSET,CYTOKINE,UID),
  featureCols=1, ref.append.replace='_REF')

result<-MIMOSA(NSUB+CYTNUM~UID+TCELLSUBSET+CYTOKINE|ANTIGEN,
  data=E, method='EM',
  subset=RefTreat%in%Treatment &ANTIGEN%in%ENV,
  ref=ANTIGEN%in%ENV &RefTreat%in%Reference)

getZ(result)

data(ICS)
E<-ConstructMIMOSAExpressionSet(ICS,
  reference=ANTIGEN%in%negctrl, measure.columns=c('CYTNUM', 'NSUB'),
  other.annotations=c('CYTOKINE', 'TCELLSUBSET', 'ANTIGEN', 'UID'),
  default.cast.formula=component~UID+ANTIGEN+CYTOKINE+TCELLSUBSET,
  .variables=(TCELLSUBSET,CYTOKINE,UID),
  featureCols=1, ref.append.replace='_REF')

result<-MIMOSA(NSUB+CYTNUM~UID+TCELLSUBSET+CYTOKINE|ANTIGEN,
  data=E, method='EM',
  subset=RefTreat%in%Treatment &ANTIGEN%in%ENV,
  ref=ANTIGEN%in%ENV &RefTreat%in%Reference)

getW(result)

ICS

Stimulated and unstimulated T-cell counts for an ICS assay

Description

A data set containing T-cell counts for various stimulations and cytokines in an ICS assay.
MDMix

Format

A data frame with 3960 rows

Details

- **pos.** The positive cell counts
- **neg.** The negative cell counts
- **fname.** The feature name (cytokine) measured
- **parent.** The parent T-cell population
- **antigen.** The antigen stimulation for this sample
- **ID.** The subject ID

Description

This function fits the multinomial dirichelt MIMOSA model using EM. It can also be used to initialize the model parameters for the MCMC model.

Usage

```r
MDMix(data = NULL, modelmatrix = NULL, alternative = "greater", initonly = FALSE)
```

Arguments

- **data** The observed data
- **modelmatrix** a model matrix specifying which components should be computed
- **alternative** either ‘greater’ or ‘not equal’ to fit the one-sided or two-sided model.
- **initonly** TRUE or FALSE to return just the initialization parameters.

Value

An object of class MDMixResult

Author(s)

Greg Finak TODO filtering of pu>ps needs to be corrected here.
Fit a MIMOSA Model

Description
This method fits a MIMOSA model to count data stored in an ExpressionSet object.

Usage
MIMOSA(formula, data, ...)

Arguments
- formula: describing the features on the lhs and the phenodata on the rhs, supporting extended formula interface with conditioning.
- data: an ExpressionSet object with features on rows and samples (labelled with phenoData) on columns.
- ...: additional arguments

Details
The ExpressionSet should be fully annotated with featureData and phenoData. For ICS data, for example, features would be positive and negative counts for different cytokine producing cell subsets (i.e. IFNg_pos, IFNg_neg) The formula lhs should contain features and the rhs should contain phenotypic variable. See the vignette for an example.

Value
an object of type MIMOSAResult

See Also
MIMOSA-package ConstructMIMOSAExpressionSet MIMOSAResult

Examples
data(ICS)
E<-ConstructMIMOSAExpressionSet(ICS,
  reference=ANTIGEN%in%'negctrl',measure.columns=c('CYTNUM','NSUB'),
  other.annotations=c('CYTOKINE','TCELLSUBSET','ANTIGEN','UID'),
  default.cast.formula=component~UID+ANTIGEN+CYTOKINE+TCELLSUBSET,
  .variables=(TCELLSUBSET,CYTOKINE,UID),
  featureCols=1,ref.append.replace='_REF')

result<-MIMOSA(NSUB+CYTNUM+UID+TCELLSUBSET+CYTOKINE|ANTIGEN,
  data=E, method='EM',
  subset=RefTreat%in'Treatment' & ANTIGEN%in'ENV',
  ref=ANTIGEN%in'ENV' & RefTreat%in'Reference')
MIMOSAExpressionSet  

*Construct an ExpressionSet for MIMOSA*

**Description**

Starting from a reshaped data frame in the correct format, construct an ExpressionSet object that can be used with MIMOSA.

**Usage**

```r
MIMOSAExpressionSet(df, featureCols)
```

**Arguments**

- `df`  
  a data.frame that is in the correct form

- `featureCols`  
  the indices of the columns that identify features.

**Details**

The `featureCols` will be used to construct feature names, and these columns will be dropped from the `exprs` matrix. The column names are assumed to have names that contain `_` characters separating phenotypic characteristics. These would be generated automatically if the data frame was constructed with `reshape`. They are used to construct the `phenoData` for the expression set.

**Examples**

```r
E <- ConstructMIMOSAExpressionSet(ICS,  
  reference=ANTIGEN%in%“negctrl”,measure.columns=c(“CYTNUM”,”NSUB”),  
  other.annotations=c(“CYTOKINE”,’TCELLSUBSET’,”ANTIGEN”,’UID’),  
  default.cast.formula=component~UID+ANTIGEN+CYTOKINE+TCELLSUBSET,  
  .variables=.”(TCELLSUBSET,CYTOKINE,UID),  
  featureCols=1,ref.append.replace='_.REF”)
```

MIMOSAResult  

*Stores the result of a MIMOSA fitted model*

**Description**

MIMOSA returns an object of MIMOSAResult irrespective of which method / implementation is used to fit the data.

MIMOSAResult-class  

*Stores the result of a MIMOSA fitted model*

**Description**

MIMOSA returns an object of MIMOSAResult irrespective of which method / implementation is used to fit the data.
pData,MIMOSAResult-method

pData extract the phenoData table from a MIMOSA result

Description

pData extract the phenoData table from a MIMOSA result

Usage

## S4 method for signature 'MIMOSAResult'
pData(object)

## S4 method for signature 'MDMixResult'
pData(object)

## S4 method for signature 'MCMCResult'
pData(object)

pData.MIMOSAResultList(object)

## S4 method for signature 'MIMOSAResultList'
pData(object)

Arguments

object is the MIMOSAResult returned from a call to MIMOSA

Details

Extracts the phenoData data.frame from a MIMOSAResult object

Value

an object of type data.frame

print.MIMOSAResultList

Print a MIMOSAResultList

Description

Print a summary of the list of results returned by a call to MIMOSA

Usage

## S3 method for class 'MIMOSAResultList'
print(x, ...)
**volcanoPlot**

**Arguments**

- `x`  
  a MIMOSAResultList
- `...`  
  additional arguments passed down

**Description**

Show a MIMOSAResultList

**Usage**

```r
## S4 method for signature 'MIMOSAResult'
show(object)
```

**Arguments**

- `object`  
  MIMOSAResultList

**Details**

Show a summary of a MIMOSAResultList.

---

**volcanoPlot**

*Volcano plot for a MIMOSA model*

**Description**

Plots effect size vs posterior probability of response from a MIMOSAResultList, faceting by the conditioning variables.

**Usage**

```r
volcanoPlot(x, effect_expression = NA, facet_var = NA, threshold = 0.01)
```

**Arguments**

- `x`  
  A MIMOSAResultList
- `effect_expression`  
  an expression that defines the effect size. Usually a function of the stimulated and unstimulated proportions from `countsTable(x, proportion = TRUE)`
- `facet_var`  
  an expression defining the faceting in ggplot parlance. i.e. `~ faceting + variables`
- `threshold`  
  a numeric value between [0,1] for coloring significant observations (based on the q-value)

**See Also**

`countsTable`
**Examples**

```r
data(ICS)
E <- ConstructMIMOSAExpressionSet(ICS, reference = ANTIGEN %in% 'negctrl', measure.columns = c('CYTNUM', 'NSUB'), other.annotations = c('CYTOKINE', 'TCELLSUBSET', 'ANTIGEN', 'UID'), default.cast.formula = component ~ UID + ANTIGEN + CYTOKINE + TCELLSUBSET, .variables = (TCELLSUBSET, CYTOKINE, UID), featureCols = 1, ref.append.replace = '_REF')

result <- MIMOSA(NSUB + CYTNUM ~ UID + TCELLSUBSET + CYTOKINE | ANTIGEN, data = E, method = 'EM', subset = RefTreat %in% 'Treatment' & ANTIGEN %in% 'ENV', ref = ANTIGEN %in% 'ENV' & RefTreat %in% 'Reference')
volcanoPlot(result, CYTNUM - CYTNUM_REF)
```
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