

Package ‘scDDboost’

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Type Package

Title A compositional model to assess expression changes from single-cell rna-seq data

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Description

scDDboost is an R package to analyze changes in the distribution of single-cell expression data between two experimental conditions. Compared to other methods that assess differential expression, scDDboost benefits uniquely from information conveyed by the clustering of cells into cellular subtypes. Through a novel empirical Bayesian formulation it calculates gene-specific posterior probabilities that the marginal expression distribution is the same (or different) between the two conditions. The implementation in scDDboost treats gene-level expression data within each condition as a mixture of negative binomial distributions.

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Imports Rcpp ($\geq 0.12.11$), RcppEigen ($\geq 0.3.2.9.0$), EBSeq, BiocParallel, mclust, SingleCellExperiment, cluster, Oscope, SummarizedExperiment, stats, methods

biocViews SingleCell, Software, Clustering, Sequencing, GeneExpression, DifferentialExpression, Bayesian

Depends R (≥ 4.2), ggplot2

LinkingTo Rcpp, RcppEigen, BH

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VignetteBuilder knitr

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Description

scDDboost is an R package to analyze changes in the distribution of single-cell expression data between two experimental conditions. Compared to other methods that assess differential expression, scDDboost benefits uniquely from information conveyed by the clustering of cells into cellular subtypes. Through a novel empirical Bayesian formulation it calculates gene-specific posterior probabilities that the marginal expression distribution is the same (or different) between the two conditions. The implementation in scDDboost treats gene-level expression data within each condition as a mixture of negative binomial distributions.

Details

The DESCRIPTION file: This package was not yet installed at build time.

Index: This package was not yet installed at build time.

Package used to score evidence of differential distribution in single-cell RNA-seq data

Author(s)

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References

<https://projecteuclid.org/journals/annals-of-applied-statistics/volume-15/issue-2/A-compositional-model-to-assess-expression-changes-from-single-cell/10.1214/20-AOAS1423.short>

See Also

<https://github.com/wiscstatman/scDDboost/blob/master/DESCRIPTION>

Examples

```
data(sim_dat)
dat = extractInfo(sim_dat)
data_counts = dat$count_matrix
cd = dat$condition
bp <- BiocParallel::MulticoreParam(4)
D_c = calD(data_counts,bp)
pDD = pdd(data_counts,cd,bp,D_c)
```

calD

calculate distance matrix

Description

calculate distance matrix

Usage

```
calD(data, bp)
```

Arguments

| | |
|------|-------------------------|
| data | transcripts |
| bp | bioc parallel parameter |

Value

distance matrix

Examples

```
data(sim_dat)
dat <- extractInfo(sim_dat)
data_counts <- dat$count_matrix
bp <- BiocParallel::MulticoreParam(4)
D_c <- calD(data_counts, bp)
```

clusHelper

function to get intra and inter distance for clusters

Description

function to get intra and inter distance for clusters

Usage

```
clusHelper(D, i)
```

Arguments

| | |
|---|--------------------|
| D | distance matrix |
| i | number of clusters |

Value

vector of intra and inter distance

detK *determine the number of clusters*

Description

determine the number of clusters

Usage

```
detK(D, epi = 1)
```

Arguments

D distance matrix
epi threshold for cutting off

Value

number of clusters

Examples

```
data(sim_dat)  
dat <- extractInfo(sim_dat)  
data_counts <- dat$count_matrix  
bp <- BiocParallel::MulticoreParam(4)  
D_c <- calD(data_counts, bp)  
detK(D_c)
```

EBS *accelerated empirical bayesian*

Description

accelerated empirical bayesian

Usage

```
EBS(data, conditions, gclus, sf, iter = 10, hyper, PP, stp1, stp2)
```

Arguments

| | |
|------------|--|
| data | single cell expression matrix, row as genes column as cells |
| conditions | partition of cells |
| gclus | partition of genes |
| sf | size factors |
| iter | maximum iteration step of EM |
| hyper | hyper parameters for beta distributions |
| PP | pattern of partitions |
| stp1 | step size of hyperparameter alpha (shared by all units) in one step EM |
| stp2 | step size of hyperparameter beta (unit specific) in one step EM |

Value

posterior probability of mean expression pattern

| | |
|-------------|--|
| extractInfo | <i>extract count matrix from SingleCellExperiment object</i> |
|-------------|--|

Description

extract count matrix from SingleCellExperiment object

Usage

```
extractInfo(data)
```

Arguments

| | |
|------|-----------------------------|
| data | SingleCellExperiment object |
|------|-----------------------------|

Value

list of count matrix and condition vector

Examples

```
data(sim_dat)
dat <- extractInfo(sim_dat)
```

| | |
|-----|---------------------------|
| gCl | <i>gene_level cluster</i> |
|-----|---------------------------|

Description

gene_level cluster

Usage

```
gCl(data, bp)
```

Arguments

| | |
|------|-------------------------|
| data | transcripts |
| bp | bioc parallel parameter |

Value

return a matrix whose row represent gene specific cluster

| | |
|----------|------------------------------------|
| genRClus | <i>generate random clusterings</i> |
|----------|------------------------------------|

Description

generate random clusterings

Usage

```
genRClus(D, a, K)
```

Arguments

| | |
|---|--------------------------|
| D | distance matrix of cells |
| a | paramter for weights |
| K | number of subtypes |

Value

random generated clustering of cells

| | |
|-------|--|
| getDD | <i>index of DD genes under FDR control</i> |
|-------|--|

Description

index of DD genes under FDR control

Usage

```
getDD(pDD, FDR = 0.01)
```

Arguments

| | |
|-----|-------------------------------|
| pDD | probability of genes being DD |
| FDR | fdr to be controlled |

Value

index of positive genes

Examples

```
p_dd <- c(0.01, 0.99, 0.7, 0.5)
getDD(p_dd)
```

| | |
|-------------|---|
| getSizeofDD | <i>number of DD genes under FDR control</i> |
|-------------|---|

Description

number of DD genes under FDR control

Usage

```
getSizeofDD(pDD, FDR = 0.01)
```

Arguments

| | |
|-----|-----------------------------------|
| pDD | estimated probability of being DD |
| FDR | fdr to be controlled |

Value

number of positive genes

Examples

```
p_dd <- c(0.1, 0.99, 1, 0.05, 0.05)
getSizeofDD(p_dd)
```

| | |
|---------|--|
| getZ1Z2 | <i>function to get counts of cluster sizes at two conditions</i> |
|---------|--|

Description

function to get counts of cluster sizes at two conditions

Usage

```
getZ1Z2(cc1, cd)
```

Arguments

| | |
|-----|------------------|
| cc1 | clustering label |
| cd | condition label |

Value

return list of counts

| | |
|------|----------------------------------|
| gRef | <i>generate reference matrix</i> |
|------|----------------------------------|

Description

generate reference matrix

Usage

```
gRef(Posp)
```

Arguments

| | |
|------|----------------------------|
| Posp | possible partition of data |
|------|----------------------------|

Value

return a matrix indicate the refinement relation between different partitions.

| | |
|-------|---|
| isRef | <i>check refinement relation between two clusters</i> |
|-------|---|

Description

check refinement relation between two clusters

Usage

isRef(x, y)

Arguments

| | |
|---|-----------|
| x | a cluster |
| y | a cluster |

Value

whether x refines y

| | |
|----|---|
| LL | <i>likelihood function for hyperparameters estimation</i> |
|----|---|

Description

likelihood function for hyperparameters estimation

Usage

LL(param, x, d0)

Arguments

| | |
|-------|--|
| param | parameters to be determined by MLE |
| x | distance matrix of cells |
| d0 | rate parameter of prior of 1 / true distance |

Value

return hyperparameteres a.

| | |
|--------|--|
| lpt1t2 | <i>log likelihood of z1,z2 given t1,t2</i> |
|--------|--|

Description

log likelihood of z1,z2 given t1,t2

Usage

lpt1t2(z1, z2, pp, alpha1, alpha2)

Arguments

| | |
|--------|-------------------------------------|
| z1 | counts of each group in condition 1 |
| z2 | counts of each group in condition 2 |
| pp | a partition |
| alpha1 | parameter of double dirichlet prior |
| alpha2 | parameter of double dirichlet prior |

Value

log likelihood of z1,z2 given t1,t2

| | |
|-------|---|
| lpzgt | <i>log likelihood of aggregated multinomial counts z given aggregated proportions t</i> |
|-------|---|

Description

log likelihood of aggregated multinomial counts z given aggregated proportions t

Usage

lpzgt(z, pp, alpha)

Arguments

| | |
|-------|---------------------------------------|
| z | counts of each group in one condition |
| pp | a partition |
| alpha | parameter of double dirichlet prior |

Value

log likelihood of aggregated multinomial counts z given aggregated proportions t

mdd *posterior of proportion change given mixture double dirichlet prior*

Description

posterior of proportion change given mixture double dirichlet prior

Usage

mdd(z1, z2, pat, alpha1, alpha2)

Arguments

| | |
|--------|-------------------------------------|
| z1 | counts of each group in condition 1 |
| z2 | counts of each group in condition 2 |
| pat | partition patterns |
| alpha1 | parameter of double dirichlet prior |
| alpha2 | parameter of double dirichlet prior |

Value

posterior of proportion change

pat *generating partition patterns*

Description

generating partition patterns

Usage

pat(K)

Arguments

| | |
|---|--------------------|
| K | number of elements |
|---|--------------------|

Value

all possible partition of K elements

Examples

pat(3)

pdd *calculate posterior probabilities of a gene to be differential distributed*

Description

calculate posterior probabilities of a gene to be differential distributed

Usage

```
pdd(
  data,
  cd,
  bp,
  D,
  random = TRUE,
  norm = TRUE,
  epi = 1,
  Upper = 1000,
  nrandom = 50,
  iter = 20,
  reltol = 0.001,
  stp1 = 1e-06,
  stp2 = 0.01,
  K = 0
)
```

Arguments

| | |
|---------|---|
| data | normalized preprocessed transcripts |
| cd | conditions label |
| bp | bioc parallel parameter |
| D | distance matrix of cells or cluster of cells or a given clustering |
| random | boolean indicator of whether randomzation has been implemented on distance matrix |
| norm | boolean indicator of whether the input expression data is normalized |
| epi | tol for change of validity score in determining number of clusters |
| Upper | bound for hyper parameters optimization |
| nrandom | number of random generated distance matrix |
| iter | max number of iterations for EM |
| reltol | relative tolerance for optim on weighting paramters |
| stp1 | step size of hyperparameter alpha (shared by all units) in one step EM |
| stp2 | step size of hyperparameter beta (unit specific) in one step EM |
| K | number of subtypes, could be user specified or determined internally(set to 0) |

Value

posterior probabilities of a gene to be differential distributed

Examples

```
data(sim_dat)
dat <- extractInfo(sim_dat)
data_counts <- dat$count_matrix
cd <- dat$condition
bp <- BiocParallel::MulticoreParam(4)
D_c <- calD(data_counts,bp)
pDD <- pdd(data_counts,cd,bp,D_c)
```

pddAggregate

function to aggregate intermediate results and get prob of DD

Description

function to aggregate intermediate results and get prob of DD

Usage

```
pddAggregate(z1, z2, Posp, DE, K, REF)
```

Arguments

| | |
|------|---|
| z1 | counts of cluster sizes in condition 1 |
| z2 | counts of cluster sizes in condition 2 |
| Posp | partition of cells |
| DE | posterior probabilities of DE patterns |
| K | number of clusters |
| REF | reference matrix indicating relation of nested partitions |

Value

return vector of prob of DD

pddRandom *calculate PDD when add random noise in distance matrix*

Description

calculate PDD when add random noise in distance matrix

Usage

pddRandom(data, cd, K, D, a, sz, hp, Posp, iter, REF, stp1, stp2)

Arguments

| | |
|------|--|
| data | normalized preprocessed transcripts |
| cd | condition label |
| K | number of subgroups |
| D | distance matrix of cells |
| a | shape param for weights |
| sz | size factors |
| hp | hyper parameters for EBSeq |
| Posp | partition patterns |
| iter | max number of iterations for EM in EBSeq |
| REF | refinement relation matrix |
| stp1 | step size of hyperparameter alpha (shared by all units) in one step EM |
| stp2 | step size of hyperparameter beta (unit specific) in one step EM |

Value

posterior probabilities under random distance matrix

rwMle *MLE for random weighting parameter*

Description

MLE for random weighting parameter

Usage

rwMle(D, reltol)

Arguments

D distance matrix of cells
reltol tolerance of convergence

Value

MLE of random weighting parameter

sim_dat *scDDboost*

Description

simulated data for demonstration, data are mixture negative binomial distributed

Usage

```
data(sim_dat)
```

Format

An object of class "list".

Examples

```
data(sim_dat)
```


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