

# Package ‘scDDboost’

May 7, 2024

**Type** Package

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

**Version** 1.6.0

**Date** 2018-10-31

**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.

**License** GPL (>= 2)

**Imports** Rcpp (>= 0.12.11), RcppEigen (>= 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

**Suggests** knitr, rmarkdown, BiocStyle, testthat

**SystemRequirements** c++11

**Roxygen** list(wrap=FALSE)

**RoxygenNote** 7.1.2

**VignetteBuilder** knitr

**BugReports** <https://github.com/wiscstatman/scDDboost/issues>

**URL** <https://github.com/wiscstatman/scDDboost>

**git\_url** <https://git.bioconductor.org/packages/scDDboost>

**git\_branch** RELEASE\_3\_19

**git\_last\_commit** cc6alea

**git\_last\_commit\_date** 2024-04-30

**Repository** Bioconductor 3.19

**Date/Publication** 2024-05-06

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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

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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                      *extract count matrix from SingleCellExperiment object*

---

**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                      *check refinement relation between two clusters*

---

**Description**

check refinement relation between two clusters

**Usage**

isRef(x, y)

**Arguments**

x                      a cluster

y                      a cluster

**Value**

whether x refines y

---

LL                      *likelihood function for hyperparameters estimation*

---

**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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weighting, local false discovery  
rate**

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