

# Package: scBFA (via r-universe)

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**Version** 1.19.0

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**Title** A dimensionality reduction tool using gene detection pattern to mitigate noisy expression profile of scRNA-seq

**Description** This package is designed to model gene detection pattern of scRNA-seq through a binary factor analysis model. This model allows user to pass into a cell level covariate matrix X and gene level covariate matrix Q to account for nuisance variance(e.g batch effect), and it will output a low dimensional embedding matrix for downstream analysis.

**URL** <https://github.com/ucdavis/quon-titative-biology/BFA>

**BugReports** <https://github.com/ucdavis/quon-titative-biology/BFA/issues>

**biocViews** SingleCell, Transcriptomics,  
DimensionReduction, GeneExpression, ATACSeq, BatchEffect, KEGG,  
QualityControl

**Depends** R (>= 3.6)

**Imports** SingleCellExperiment, SummarizedExperiment, Seurat, MASS,  
zinbwave, stats, copula, ggplot2, DESeq2, utils, grid, methods,  
Matrix

**Suggests** knitr, rmarkdown, testthat, Rtsne

**VignetteBuilder** knitr

**RoxygenNote** 7.0.2

**License** GPL-3 + file LICENSE

**LazyData** true

**Encoding** UTF-8

**Repository** <https://bioc.r-universe.dev>

**RemoteUrl** <https://github.com/bioc/scBFA>

**RemoteRef** HEAD

**RemoteSha** 96c5a696d014f43a5347f1787df99d8b633c7d61

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BinaryPCA	<i>Performs Binary PCA (as outlined in our paper). This function take the input of gene expression profile and perform PCA on gene detection pattern</i>
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Description

Performs Binary PCA (as outlined in our paper). This function take the input of gene expression profile and perform PCA on gene detection pattern

Usage

```
BinaryPCA(scData, X = NULL, scale. = FALSE, center = TRUE)
```

Arguments

scData	can be a raw count matrix, in which rows are genes and columns are cells; can be a seurat object; can be a SingleCellExperiment object.
X	$N$ by $C$ covariate matrix,e.g batch effect, in which rows are cells,columns are number of covariates. If no such covariates available $X = \text{NULL}$
scale.	Logical value isndicating whether the variables should be scaled to have unit variance before the analysis takes place. In general scaling is not advisable, since we think the variance in the gene detection space is potentially associated with celltypes (e.g cell type specific markers)
center	Logical value indicating whether the variables should be shifted to be zero centered

**Value**

A list with class "prcomp", containing the following components:

sdev: the standard deviations of the principal components (i.e., the square roots of the eigenvalues of the covariance/correlation matrix, though the calculation is actually done with the singular values of the data matrix).

rotation: the matrix of variable loadings (i.e., a matrix whose columns contain the eigenvectors). The function princomp returns this in the element loadings.

x: the rotated data (the centred (and scaled if requested) data multiplied by the rotation matrix) is returned. Hence,  $\text{cov}(x)$  is the diagonal matrix  $\text{diag}(\text{sdev}^2)$ .

center, scale. centering and scaling used, or FALSE.

**Examples**

```
## Working with Seurat or SingleCellExperiment object

library(Seurat)
library(SingleCellExperiment)

## Input expression profile, 5 genes x 3 cells

GeneExpr = matrix(rpois(15,1),nrow = 5,ncol = 3)
rownames(GeneExpr) = paste0("gene",seq_len(nrow(GeneExpr)))
colnames(GeneExpr) = paste0("cell",seq_len(ncol(GeneExpr)))
celltype = as.factor(sample(c(1,2,3),3,replace = TRUE))

## Create cell level technical batches

batch = sample(c("replicate 1","replicate 2","replicate 2"))
X = matrix(NA,nrow = length(batch),ncol = 1)
X[which(batch == "replicate 1"), ] = 0
X[which(batch == "replicate 2"), ] = 1
rownames(X) = colnames(GeneExpr)

##run BFA with raw count matrix

bpca_model = BinaryPCA(scData = GeneExpr,X = scale(X))

## Create Seurat object for input to BFA

scData = CreateSeuratObject(counts = GeneExpr,project = "sc",min.cells = 0)

## Standardize the covariate matrix should be a default operation

bpca_model = BinaryPCA(scData = scData, X = scale(X))

## Build the SingleCellExperiment object for input to BFA

## Set up SingleCellExperiment class

sce <- SingleCellExperiment(assay = list(counts = GeneExpr))
```

```
## Standardize the covariate matrix should be a default operation
bpca_model = BinaryPCA(scData = sce, X = scale(X))
```

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celltype	<i>Cell types as labels of example scRNA-seq dataset(exprdata)</i>
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### Description

A vector contains the cell types as labels for cells in example scRNA-seq dataset(exprdata)

### Usage

```
data(celltype)
```

### References

<https://www.ncbi.nlm.nih.gov/geo/query/acc.cgi?acc=GSE89232>

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celltype_toy	<i>toy cell type vector with 3 cell types generated for 5 cells in toy dataset</i>
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### Description

The cell type vector is generated from the following code

### Usage

```
data(celltype_toy)
```

### Details

```
celltype = as.factor(sample(c(1,2,3),5,replace = TRUE))
```

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diagnose	<i>Perform diagnosis of dispersion on the expression profile to check whether scBFA works on specific dataset</i>
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**Description**

Perform diagnosis of dispersion on the expression profile to check whether scBFA works on specific dataset

**Usage**

```
diagnose(  
  scData,  
  sampleInfo = NULL,  
  disperType = "Fitted",  
  diagnose_feature = "dispersion"  
)
```

**Arguments**

scData	can be a raw count matrix, in which rows are genes and columns are cells; can be a seurat object; can be a SingleCellExperiment object.
sampleInfo	sample level feature matrix,e.g batch effect,experimental conditions in which rows are cells,columns are number of covariates.Default is NULL
disperType	a parameter to tell which dispersion estimate the user can plot DESeq2 offers stepwise dispersion estimate, a gene wise dispersion estimate using "GeneEst", dispersion estimate from fitted disperions ~ mean curve (using "Fitted") And final MAP estimate,using "Map". Default value is "Fitted"
diagnose_feature	a parameter to determine whether the user want to check GDR or dispersion.

**Value**

A Figure to tell the where the input data's dispersion ~ tpm curve align to the 14 benchmark datasets in Figure 2.a or Gene detection rate

**Examples**

```
data(exprdata)  
diagnose(scData = exprdata)
```

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disperPlot	<i>Reference dataset(disperPlot)</i>
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### Description

A dataframe contains all the gene-wise dispersion estimates loess curve for 14 datasets we benchmarked in Figure 2.a

### Usage

```
data(disperPlot)
```

### Details

The variable in the columns are: fitted\_dispersion: the log value of gene-wise dispersion after fitting a loess curve with respect to TPM value. Note that the genes at the top 2.5 meantpm is average tpm value calculated per gene dataset are nams for datasets variance is gene selection method, here is HEG vs HVG

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exprdata	<i>scRNA-seq dataset(exprdata)</i>
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### Description

A matrix contains 950 cells and 500 genes. The source of this dataset is cDC/ pre-DC cells(see supplementary files) We subset most variant 100 genes as example scRNA-seq dataset(exprdata)

### Usage

```
data(exprdata)
```

### References

<https://www.ncbi.nlm.nih.gov/geo/query/acc.cgi?acc=GSE89232>

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getGeneExpr	<i>Function to extract gene expression matrix from input observation matrix</i>
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**Description**

Function to extract gene expression matrix from input observation matrix

**Usage**

```
getGeneExpr(scData)
```

**Arguments**

scData	can be a raw count matrix, in which rows are genes and columns are cells; can be a Seurat object; can be a SingleCellExperiment object
--------	--

**Value**

a raw expression matrix in which rows are genes and columns are cells.

**Examples**

```
scData = matrix(rpois(15,1),3,5)

GeneExpr = getGeneExpr(scData)
```

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getLoading	<i>Function to get low dimensional loading matrix</i>
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**Description**

Function to get low dimensional loading matrix

**Usage**

```
getLoading(modelEnv)
```

**Arguments**

modelEnv	output environment variable
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**Value**

$A$ :  $G$  by  $K$  compressed feature space

**Examples**

```
GeneExpr = matrix(rpois(15,1),3,5)
bfa_model = scBFA(scData = GeneExpr,X = NULL,numFactors =2)
A = getLoading(bfa_model)
```

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getScore	<i>Function to get low dimensional embedding matrix</i>
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**Description**

Function to get low dimensional embedding matrix

**Usage**

```
getScore(modelEnv)
```

**Arguments**

modelEnv	output environment variable
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**Value**

Z:  $N$  by  $K$  low dimensional embedding

**Examples**

```
GeneExpr = matrix(rpois(15,1),3,5)
bfa_model = scBFA(scData = GeneExpr,X = NULL,numFactors =2)
Z = getScore(bfa_model)
```

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gradient	<i>Calculate gradient of the negative log likelihood, used for calls to the optim() function.</i>
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---

**Description**

Calculate gradient of the negative log likelihood, used for calls to the optim() function.

**Usage**

```
gradient(parameters, modelEnv)
```

**Arguments**

parameters	Vectorized parameter space.
modelEnv	Environment variable contains parameter space, and global variables such as N,G,C,detection matrix B, etc



**Value**

Vectorized gradient

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gradient_chunk	<i>Calculate gradient of the negative log likelihood, used for calls to the optim() function.</i>
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**Description**

Calculate gradient of the negative log likelihood, used for calls to the optim() function.

**Usage**

```
gradient_chunk(parameters, modelEnv)
```

**Arguments**

parameters	Vectorized parameter space.
modelEnv	Environment variable contains parameter space, and global variables such as N,G,C,detection matrix B, etc

**Value**

Vectorized gradient

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scBFA	<i>Perform BFA model on the expression profile</i>
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**Description**

Perform BFA model on the expression profile

**Usage**

```
scBFA(  
  scData,  
  numFactors,  
  X = NULL,  
  Q = NULL,  
  maxit = 300,  
  method = "L-BFGS-B",  
  initCellcoef = NULL,  
  updateCellcoef = TRUE,  
  updateGenecoeff = TRUE,  
  NUM_CELLS_PER_CHUNK = 5000,  
  doChunking = FALSE  
)
```

**Arguments**

scData	can be a raw count matrix, in which rows are genes and columns are cells; can be a <code>seurat</code> object; can be a <code>SingleCellExperiment</code> object.
numFactors	Numeric value, number of latent dimensions
X	$N$ by $C$ covariate matrix, e.g. batch effect, in which rows are cells, columns are number of covariates. Default is <code>NULL</code>
Q	$G$ by $T$ gene-specific covariate matrix (e.g. quality control measures), in which rows are genes, columns are number of covariates. If no such covariates are available, then $Q = \text{NULL}$
maxit	Numeric value, parameter to control the Maximum number of iterations in the optimization, default is 300.
method	Method of optimization, default is L-BFGS-B (Limited memory BFGS) approach. Conjugate Gradient (CG) is recommended for larger dataset (number of cells > 10k)
initCellcoef	Initialization of $C$ by $G$ gene-specific coefficient matrix as user-defined coefficient $\beta$ . Such user-defined coefficient can be applied to address confounding batch effect
updateCellcoef	Logical value, parameter to decide whether to update $C$ by $G$ gene-specific coefficient matrix. Again, when the cell types are confounded with technical batches or there is no cell level covariate matrix, the user can keep the initialization of coefficients as known estimate.
updateGenecof	Logical value, parameter to decide whether to update $N$ by $T$ gene-specific coefficient matrix. Again, when there is no gene level covariate matrix, this value should be <code>FALSE</code> by default.
NUM_CELLS_PER_CHUNK	scBFA can run out of memory on large datasets, so we can chunk up computations to avoid this if necessary. <code>NUM_CELLS_PER_CHUNK</code> is the number of cells per 'chunk' computed. Shrink if running out of mem.
doChunking	Use memory-efficient (but slower) chunking. Will do automatically if the chunk size is specified to be smaller than the # of cells in dataset.

**Value**

A model environment containing all parameter space of a BFA model as well as global variables needed for calculation:

$A$ :  $G$  by  $K$  compressed feature space matrix

$Z$ :  $N$  by  $K$  low dimensional embedding matrix

$\beta$ :  $C$  by  $G$  cell level coefficient matrix

$\gamma$ :  $N$  by  $T$  gene level coefficient matrix

$V$ :  $G$  by 1 offset matrix

$U$ :  $N$  by 1 offset matrix

**Examples**

```
## Working with Seurat or SingleCellExperiment object

library(Seurat)
library(SingleCellExperiment)

## Input expression profile, 5 genes x 3 cells

GeneExpr = matrix(rpois(15,1),nrow = 5,ncol = 3)
rownames(GeneExpr) = paste0("gene",seq_len(nrow(GeneExpr)))
colnames(GeneExpr) = paste0("cell",seq_len(ncol(GeneExpr)))
celltype = as.factor(sample(c(1,2,3),3,replace = TRUE))

## Create cell level technical batches

batch = sample(c("replicate 1","replicate 2","replicate 2"))
X = matrix(NA,nrow = length(batch),ncol = 1)
X[which(batch == "replicate 1"), ] = 0
X[which(batch == "replicate 2"), ] = 1
rownames(X) = colnames(GeneExpr)

## run BFA with raw count matrix

bfa_model = scBFA(scData = GeneExpr,X = scale(X),numFactors =2)

## Create Seurat object for input to BFA

scData = CreateSeuratObject(counts = GeneExpr,project="sc",min.cells = 0)

## Standardize the covariate matrix should be a default operation

bfa_model = scBFA(scData = scData, X = scale(X), numFactors = 2)

## Build the SingleCellExperiment object for input to BFA

## Set up SingleCellExperiment class

sce <- SingleCellExperiment(assay = list(counts = GeneExpr))

## Standardize the covariate matrix should be a default operation

bfa_model = scBFA(scData = sce, X = scale(X), numFactors = 2)
```

**Description**

simulation to generate scRNA-seq data with varying level of gene detection noise versus gene count noise

**Usage**

```
scNoiseSim(zinb, celltype, disper, var_dropout = 1, var_count = 1, delta)
```

**Arguments**

zinb	a ZINB-WaVE object representing ZINB-WaVE fit to real data to get realistic simulation parameters
celltype	a factor to specify the ground-truth cell types in the original dataset that the parameter of zinb object is fit to. Since we filter out some simulated cells due to low amount of genes detected in that cell, we subset the ground truth cell types correspondingly
disper	numeric value, parameter to control the size factor $r$ in $NB(\mu, r)$ . $r$ is varied in the set 0.5,1,5 in our simulation(as outlined in our paper)
var_dropout	numeric value, parameter to control the noise level added to a common embedding space for to generate gene detection matrix. This parameter is formulated as $\sigma_\pi$ and in the paper is selected from the set 0.1, 0.5, 1, 2, 3
var_count	numeric value, parameter to control the noise level added to a common embedding space to generate gene count matrix. This parameter is formulated as $\sigma_\mu$ and in the paper is selected from the set 0.1, 0.5, 1, 2, 3
delta	intercept to control the overall gene detection rate. and in the paper is selected from the set -2, -0.5, 1,2.5,4

**Value**

GeneExpr,a count matrix with rows number of genes and columns number of cells  
 celltype,a vector specify the corresponding celltype after QC measures.

**Examples**

```
## raw counts matrix with rows are genes and columns are cells
data("zinb_toy",package = "scBFA", envir = environment())
## a vector specify the ground truth of cell types provided by conquer database
data("celltype_toy",package = "scBFA",envir = environment())

scData = scNoiseSim(zinb = zinb_toy,
  celltype = celltype_toy,
  disper = 1,
  var_dropout =1,
  var_count = 1,
  delta = 1)
```

---

zinb\_toy*example zinb object after fitting a toy dataset with 5 cells and 10 genes*

---

**Description**

The toy dataset is generated from the following code `require(zinbwave)` `GeneExpr = matrix(rpois(50,1),nrow = 10,ncol = 5)` `rownames(GeneExpr) = paste0("gene",seq_len(nrow(GeneExpr)))` `colnames(GeneExpr) = paste0("cell",seq_len(ncol(GeneExpr)))` `celltype = as.factor(sample(c(1,2,3),5,replace = TRUE))` `zinb = zinbFit(Y = GeneExpr,K=2)`

**Usage**`data(zinb_toy)`

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