Package: scINSIGHT (via r-universe)

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Type Package

Title Interpretation of Heterogeneous Single-Cell Gene Expression Data

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Description We develop a novel matrix factorization tool named 'scINSIGHT' to jointly analyze multiple single-cell gene expression samples from biologically heterogeneous sources, such as different disease phases, treatment groups, or developmental stages. Given multiple gene expression samples from different biological conditions, 'scINSIGHT' simultaneously identifies common and condition-specific gene modules and quantify their expression levels in each sample in a lower-dimensional space. With the factorized results, the inferred expression levels and memberships of common gene modules can be used to cluster cells and detect cell identities, and the condition-specific gene modules can help compare functional differences in transcriptomes from distinct conditions. Please also see Qian K, Fu SW, Li HW, Li WV (2022) <doi:10.1186/s13059-022-02649-3>.

License GPL-3

Imports Rcpp, RANN, igraph, parallel, stats, stringr

LinkingTo Rcpp, RcppArmadillo

Depends methods

URL https://github.com/Vivianstats/scINSIGHT, https://genomebiology.biomedcentral.com/articles/10.1186/s13059-022-02649-3

NeedsCompilation yes

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`create_scINSIGHT` *Create an scINSIGHT object.*

Description

This function initializes an scINSIGHT object with normalized data passed in.

Usage

```
create_scINSIGHT(norm.data, condition)
```

Arguments

`norm.data`	List of normalized expression matrices (genes by cells). Gene names should be the same in all matrices.
`condition`	Vector specifying sample conditions.

Value

`scINSIGHT` object with norm.data slot set.

Examples

```
# Demonstration using matrices with randomly generated numbers
S1 <- matrix(runif(50000,0,2), 500,100)
S2 <- matrix(runif(60000,0,2), 500,120)
S3 <- matrix(runif(80000,0,2), 500,160)
S4 <- matrix(runif(75000,0,2), 500,150)
data = list(S1, S2, S3, S4)
sample = c("sample1", "sample2", "sample3", "sample4")
condition = c("control", "activation", "control", "activation")
names(data) = sample
names(condition) = sample
scINSIGHTx <- create_scINSIGHT(data, condition)
```

`run_scINSIGHT` *Perform scINSIGHT on normalized datasets*

Description

Perform INterpreting single cell gene expresSIon bioloGically Heterogeneous daTa (scINSIGHT) to return factorized $W_{\ell 1}$, $W_{\ell 2}$, H and V matrices.

This factorization produces a $W_{\ell 1}$ matrix (cells by K_j), a $W_{\ell 2}$ matrix (cells by K), a shared V matrix (K by genes) for each sample, and a H (K_j by genes) matrix for each condition. $W_{\ell 2}$ are the expression matrices of K common gene modules for all samples, V is the membership matrix of K common gene modules, and it's shared by all samples. $W_{\ell 1}$ are the expression matrices of K_j condition-specific gene modules for all samples, and H are the membership matrices of K_j condition-specific gene modules for all conditions.

Usage

```
run_scINSIGHT(
  object,
  K = seq(5, 15, 2),
  K_j = 2,
  LDA = c(0.001, 0.01, 0.1, 1, 10),
  thre.niter = 500,
  thre.delta = 0.01,
  num.cores = 1,
  B = 5,
  out.dir = NULL,
  method = "increase"
)
```

Arguments

`object`	`scINSIGHT` object.
`K`	Number of common gene modules. (default `c(5, 7, 9, 11, 13, 15)`)
`K_j`	Number of dataset-specific gene modules. (default 2)
`LDA`	Regularization parameters. (default `c(0.001, 0.01, 0.1, 1, 10)`)
`thre.niter`	Maximum number of block coordinate descent iterations to perform. (default 500)
`thre.delta`	Stop iteration when the reduction of objective function is less than the threshold. (default 0.01)
`num.cores`	Number of cores used for optimizing factorizations in parallel (default 1).
`B`	Number of repeats with random seed from 1 to B. (default 5)
`out.dir`	Output directory of scINSIGHT results. (default NULL)

`method` Method of updating the factorization (default "increase"). If provide multiple K, user can choose method between "increase" and "decrease".

For "increase", the algorithm will first perform factorization with the least $K = K_1$. Then initialize $K_2 - K_1$ facotrs, where K_2 is the K sightly larger than K_1, and perform facotrization with these new facotrs. Continue this process until the largest K.

For "increase", the algorithm will first perform factorization with the largest $K = K_1$. Then choose K_2 facotrs, where K_2 is the K sightly less than K_1, and perform facotrization with these new facotrs. Continue this process until the least K.

Value

`scINSIGHT` object with W_1, W_2, H, V and parameters slots set.

`scINSIGHT-class` *The scINSIGHT Class*

Description

The scINSIGHT object is created from two or more single cell datasets. To construct a scINSIGHT object, the user needs to provide at least two normalized expression (or another single-cell modality) matrices and the condition vector.

Details

The key slots used in the scINSIGHT object are described below.

Slots

`norm.data` List of normalized expression matrices (genes by cells). Each matrix should have the same number and name of genes.

`condition` Vector specifying each sample's condition name.

`W_1` List of $W_{\ell 1}$ estimated by scINSIGHT, names correspond to sample names.

`W_2` List of $W_{\ell 2}$ estimated by scINSIGHT, names correspond to sample names.

`H` List of H estimated by scINSIGHT, names correspond to condition names.

`V` Matrix V estimated by scINSIGHT.

`norm.W_2` List of $W_{\ell 2}$ after normalization. Recommended for downstream analysis.

`clusters` List of cluster results.

`parameters` List of selected parameters, including K and λ.

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