Package 'GeneNMF'

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Type Package

Title Non-Negative Matrix Factorization for Single-Cell Omics

Version 0.4.0

Description A collection of methods to extract gene programs from single-cell gene expression data using non-negative matrix factorization (NMF). 'GeneNMF' contains functions to directly interact with the 'Seurat' toolkit and derive interpretable gene program signatures.

biocViews

Depends R (>= 4.3.0)

Imports RcppML, NMF, stats, Seurat (>= 4.3.0), cluster, pheatmap, viridis

Suggests knitr, rmarkdown, fgsea, dplyr, msigdbr

VignetteBuilder knitr

URL https://github.com/carmonalab/GeneNMF

BugReports https://github.com/carmonalab/GeneNMF/issues

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R topics documented:

`findVariableFeatures_wfilters` *Find variable features*

Description

Select highly variable genes (HVG) from an expression matrix. Genes from a blocklist (e.g. cell cycling genes, mitochondrial genes) can be excluded from the list of variable genes, as well as genes with very low or very high average expression

Usage

```
findVariableFeatures_wfilters(
  obj,
  nfeatures = 2000,
  genesBlockList = NULL,
  min.exp = 0.01,
  max.exp = 3
)
```

Arguments

`obj`	A Seurat object containing an expression matrix
`nfeatures`	Number of top HVG to be returned
`genesBlockList`	Optionally takes a vector or list of vectors of gene names. These genes will be ignored for HVG detection. This is useful to mitigate effect of genes associated with technical artifacts or batch effects (e.g. mitochondrial, heat-shock response). If set to 'NULL' no genes will be excluded
`min.exp`	Minimum average normalized expression for HVG. If lower, the gene will be excluded
`max.exp`	Maximum average normalized expression for HVG. If higher, the gene will be excluded

Value

Returns the input Seurat object `obj` with the calculated highly variable features accessible through `VariableFeatures(obj)`

Examples

```
data(sampleObj)
sampleObj <- findVariableFeatures_wfilters(sampleObj, nfeatures=100)
```

`getDataMatrix` *Extract data matrix from Seurat object*

Description

Get the gene expression matrix from a Seurat object, optionally centered and/or subset on highly variable genes

Usage

```
getDataMatrix(
  obj,
  assay = "RNA",
  slot = "data",
  hvg = NULL,
  do_centering = TRUE
)
```

Arguments

`obj`	Seurat object
`assay`	Get data matrix from this assay
`slot`	Get data matrix from this slot (=layer)
`hvg`	List of variable genes to subset the matrix. If NULL, uses all genes
`do_centering`	Whether to center the data matrix

Value

Returns a sparse data matrix (cells per genes), subset according to the given parameters

Examples

```
data(sampleObj)
matrix <- getDataMatrix(sampleObj)
```

getMetaPrograms *Extract consensus gene programs (meta-programs)*

Description

Run it over a list of NMF models obtained using multiNMF; it will determine gene programs that are consistently observed across samples and values of k.

Usage

```
getMetaPrograms(
  nmf.res,
  method = 0.5,
  max.genes = 200,
  hclust.method = "ward.D2",
  nprograms = 10,
  min.confidence = 0.2,
  remove.empty = TRUE
)
```

Arguments

nmf.res	A list of NMF models obtained from multiNMF
method	Parameter passed to extractFeatures to obtain top genes for each program
max.genes	Max number of genes for each programs
hclust.method	Method to build similarity tree between individual programs
nprograms	Total number of meta-programs
min.confidence	Percentage of programs in which a gene is seen (out of programs in the corresponding program tree branch/cluster), to be retained in the consensus metaprograms
remove.empty	Whether to remove meta-programs with no genes above confidence threshold

Value

Returns a list with i) 'metaprograms.genes' top genes for each meta-program; ii) 'metaprograms.metrics' dataframe with meta-programs statistics: a) freq. of samples where the MP is present, b) average silhouette width, c) mean Jaccard similarity, d) number of genes in MP, e) number of gene programs in MP; iii) 'programs.jaccard': matrix of Jaccard similarities between meta-programs; iv) 'programs.tree': hierarchical clustering of meta-programs (hclust tree); v) 'programs.clusters': meta-program identity for each program

Examples

```
library(Seurat)
data(sampleObj)
geneNMF_programs <- multiNMF(list(sampleObj), k=5)
geneNMF_metaprograms <- getMetaPrograms(geneNMF_programs, nprograms=3)
```

`getNMFgenes` *Get list of genes for each NMF program*

Description

Run it over a list of NMF models obtained using `multiNMF()`

Usage

```
getNMFgenes(nmf.res, method = 0.5, max.genes = 200)
```

Arguments

`nmf.res`	A list of NMF models obtained using `multiNMF()`
`method`	Parameter passed to `extractFeatures` to obtain top genes for each program. When 'method' is a number between 0 and 1, it indicates the minimum relative basis contribution above which the feature is selected, i.e. how specific is a gene for a given program.
`max.genes`	Max number of genes for each program

Value

Returns a list of top genes for each gene program found by `multiNMF()`

Examples

```
library(Seurat)
data(sampleObj)
geneNMF_programs <- multiNMF(list(sampleObj), k=5)
geneNMF_genes <- getNMFgenes(geneNMF_programs)
```

`multiNMF` *Run NMF on a list of Seurat objects*

Description

Given a list of Seurat objects, run non-negative matrix factorization on each sample individually, over a range of target NMF components (k).

Usage

```
multiNMF(
  obj.list,
  assay = "RNA",
  slot = "data",
  k = 5:6,
  hvg = NULL,
  nfeatures = 2000,
  L1 = c(0, 0),
  min.exp = 0.01,
  max.exp = 3,
  do_centering = TRUE,
  min.cells.per.sample = 10,
  hvg.blocklist = NULL,
  seed = 123
)
```

Arguments

`obj.list`	A list of Seurat objects
`assay`	Get data matrix from this assay
`slot`	Get data matrix from this slot (=layer)
`k`	Number of target components for NMF (can be a vector)
`hvg`	List of pre-calculated variable genes to subset the matrix. If hvg=NULL it calculates them automatically
`nfeatures`	Number of HVG, if calculate_hvg=TRUE
`L1`	L1 regularization term for NMF
`min.exp`	Minimum average log-expression value for retaining genes
`max.exp`	Maximum average log-expression value for retaining genes
`do_centering`	Whether to center the data matrix
`min.cells.per.sample`	Minimum numer of cells per sample (smaller samples will be ignored)

hvg.blocklist	Optionally takes a vector or list of vectors of gene names. These genes will be ignored for HVG detection. This is useful to mitigateeffect of genes associated with technical artifacts and batch effects (e.g. mitochondrial), and to exclude TCR and BCR adaptive immune(clone-specific) receptors. If set to 'NULL' no genes will be excluded
seed	Random seed

Value

Returns a list of NMF programs, one for each sample and for each value of 'k'. The format of each program in the list follosw the structure of nmf factorization models.

Examples

```
library(Seurat)
data(sampleObj)
geneNMF_programs <- multiNMF(list(sampleObj), k=5)
```

---

plotMetaPrograms *Visualizations for meta-programs*

Description

Generates a clustered heatmap for meta-program similarities (by Jaccard index). This function is intended to be run on the object generated by getMetaPrograms, which contains a pre-calculated tree of pairwise similarities between clusters (as a 'hclust' object).

Usage

```
plotMetaPrograms(
  mp.res,
  jaccard.cutoff = c(0, 0.8),
  scale = "none",
  palette = viridis(100, option = "A", direction = -1),
  annotation_colors = NULL,
  main = "Clustered Heatmap",
  show_rownames = FALSE,
  show_colnames = FALSE,
  ...
)
```

Arguments

mp.res	The meta-programs object generated by getMetaPrograms
jaccard.cutoff	Min and max values for plotting the Jaccard index
scale	Heatmap rescaling (passed to pheatmap as 'scale')

palette	Heatmap color palette (passed to pheatmap as 'color')
annotation_colors	Color palette for MP annotations
main	Heatmap title
show_rownames	Whether to display individual program names as rows
show_colnames	Whether to display individual program names as cols
...	Additional parameters for pheatmap

Value

Returns a clustered heatmap of MP similarities, in ggplot2 format

Examples

```
library(Seurat)
data(sampleObj)
geneNMF_programs <- multiNMF(list(sampleObj), k=5)
geneNMF_metaprograms <- getMetaPrograms(geneNMF_programs, nprograms=3)
plotMetaPrograms(geneNMF_metaprograms)
```

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runGSEA *Run Gene set enrichment analysis*

Description

Utility function to run Gene set enrichment analysis (GSEA) against gene sets from MSigDB.

Usage

```
runGSEA(
  genes,
  universe = NULL,
  category = "H",
  subcategory = NULL,
  species = "Homo sapiens",
  pval.thr = 0.05
)
```

Arguments

genes	A vector of genes
universe	Background universe of gene symbols (passed on to `fgsea::fora`)
category	GSEA main category (e.g. "H" or "C5")
subcategory	GSEA subcategory
species	Species for GSEA analysis. For a list of the available species, type `msigdbr::msigdbr_species()`
pval.thr	Min p-value to include results

Value

Returns a table of enriched gene programs from GSEA

Examples

```
data(sampleObj)
geneset <- c("BANK1","CD22","CD79A","CD19","IGHD","IGHG3","IGHM")
gsea_res <- runGSEA(geneset, universe=rownames(sampleObj), category = "C8")
```

---

runNMF *Compute NMF as a low-dim embedding for Seurat*

Description

Compute NMF embeddings for single-cell dataset, and store them in the Seurat data structure. They can be used as an alternative to PCA for downstream analyses.

Usage

```
runNMF(
  obj,
  assay = "RNA",
  slot = "data",
  k = 10,
  new.reduction = "NMF",
  seed = 123,
  L1 = c(0, 0),
  hvg = NULL,
  do_centering = TRUE
)
```

Arguments

obj	A seurat object
assay	Get data matrix from this assay
slot	Get data matrix from this slot (=layer)
k	Number of components for low-dim representation
new.reduction	Name of new dimensionality reduction
seed	Random seed
L1	L1 regularization term for NMF
hvg	Which genes to use for the reduction
do_centering	Whether to center the data matrix

Value

Returns a Seurat object with a new dimensionality reduction (NMF)

Examples

```
data(sampleObj)
sampleObj <- runNMF(sampleObj, k=8)
```

`sampleObj` *Sample dataset to test GeneNMF installation*

Description

A Seurat object containing single-cell transcriptomes (scRNA-seq) for 50 cells and 20729 genes. Single-cell UMI counts were normalized using a standard log-normalization: counts for each cell were divided by the total counts for that cell and multiplied by 10,000, then natural-log transformed using 'log1p'.

This a subsample of 25 predicted B cells and 25 predicted NK cells from the large scRNA-seq PBMC dataset published by Hao et al. (doi:10.1016/j.cell.2021.04.048) and available as UMI counts at `https://atlas.fredhutch.org/data/nygc/multimodal/pbmc_multimodal.h5seurat`

Usage

```
sampleObj
```

Format

A sparse matrix of 50 cells and 20729 genes.

Source

doi:10.1016/j.cell.2021.04.048

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