Package 'UCell'

October 2, 2025

```
UCell signature scores, based on the Mann-
      Whitney U statistic, are robust to dataset size and heterogeneity, and their calculation
      demands less computing time and memory than other available methods, enabling the process-
      ing of large datasets in a few minutes even
      on machines with limited computing power. UCell can be applied to any single-
      cell data matrix, and includes functions to directly
      interact with SingleCellExperiment and Seurat objects.
Depends R(>= 4.3.0)
Imports methods, data.table(>= 1.13.6), Matrix, stats, BiocParallel,
      BiocNeighbors, SingleCellExperiment, SummarizedExperiment
Suggests scater, scRNAseq, reshape2, patchwork, ggplot2, BiocStyle,
      Seurat(>= 5.0.0), SeuratObject(>= 5.0.0), knitr, rmarkdown
biocViews SingleCell, GeneSetEnrichment, Transcriptomics,
      GeneExpression, CellBasedAssays
VignetteBuilder knitr
BugReports https://github.com/carmonalab/UCell/issues
URL https://github.com/carmonalab/UCell
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```

Title Rank-based signature enrichment analysis for single-cell data

Description UCell is a package for evaluating gene signatures in single-cell datasets.

Type Package

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AddModuleScore_UCell Calculate module enrichment scores from single-cell data (Seurat interface)

Description

Given a Seurat object, calculates module/signature enrichment scores at single-cell level using the Mann-Whitney U statistic. UCell scores are normalized U statistics (between 0 and 1), and they are mathematically related to the Area under the ROC curve (see Mason and Graham)

```
AddModuleScore_UCell(
  obj,
  features,
  maxRank = 1500,
  chunk.size = 100,
  BPPARAM = NULL,
  ncores = 1,
  storeRanks = FALSE,
  w_neg = 1,
  assay = NULL,
  slot = "counts",
  ties.method = "average",
  missing_genes = c("impute", "skip"),
  force.gc = FALSE,
```

```
name = "_UCell"
)
```

Arguments

obj	Seurat object
features	A list of signatures, for example: list(Tcell_signature = c("CD2", "CD3E", "CD3D"), Myeloid_signature = c("SPI1", "FCER1G", "CSF1R")) You can also specify positive and negative gene sets by adding a + or - sign to genes in the signature; see an example below
maxRank	Maximum number of genes to rank per cell; above this rank, a given gene is considered as not expressed.
chunk.size	Number of cells to be processed simultaneously (lower size requires slightly more computation but reduces memory demands)
BPPARAM	A BiocParallel::bpparam() object that tells UCell how to parallelize. If provided, it overrides the ncores parameter.
ncores	Number of processors to parallelize computation. If BPPARAM = NULL, the function uses BiocParallel::MulticoreParam(workers=ncores)
storeRanks	Store ranks matrix in Seurat object ('UCellRanks' assay) for fast subsequent computations. This option may demand large amounts of RAM.
w_neg	Weight on negative genes in signature. e.g. w_neg=1 weighs equally up- and down-regulated genes, w_neg=0.5 gives 50% less importance to negative genes
assay	Pull out data from this assay of the Seurat object (if NULL, use DefaultAssay(obj))
slot	Pull out data from this slot (layer in v5) of the Seurat object
ties.method	How ranking ties should be resolved - passed on to data.table::frank
missing_genes	How to handle missing genes in matrix: "impute": impute expression to zero; "skip": remove missing genes from signature
force.gc	Explicitly call garbage collector to reduce memory footprint
name	Name tag that will be appended at the end of each signature name, "_UCell" by default (e.g. signature score in meta data will be named: Myeloid_signature_UCell)

Details

In contrast to Seurat's AddModuleScore, which is normalized by binning genes of similar expression at the population level, UCell scores depend only on the gene expression ranks of individual cell, and therefore they are robust across datasets regardless of dataset composition.

Value

Returns a Seurat object with module/signature enrichment scores added to object meta data; each score is stored as the corresponding signature name provided in features followed by the tag given in name (or "_UCell" by default)

Examples

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calculate_Uscore

Calculate rankings and scores for query data and given signature set

Description

Calculate rankings and scores for query data and given signature set

Usage

```
calculate_Uscore(
  matrix,
  features,
  maxRank = 1500,
  chunk.size = 100,
  BPPARAM = NULL,
  ncores = 1,
  w_neg = 1,
  ties.method = "average",
  missing_genes = c("impute", "skip"),
  storeRanks = FALSE,
  force.gc = FALSE,
  name = "_UCell"
)
```

Arguments

matrix	Input data matrix
features	List of signatures
maxRank	Rank cutoff (1500)
chunk.size	Cells per sub-matrix (100)
BPPARAM	A BioParallel object to instruct UCell how to parallelize
ncores	Number of cores to use for parallelization
w_neg	Weight on negative signatures
ties.method	How to break ties, for data.table::frankv method ("average")
missing_genes	How to handle missing genes in matrix: "impute": impute expression to zero; "skip": remove missing genes from signature

check_signature_names 5

storeRanks Store ranks? (FALSE)

force.gc Force garbage collection? (FALSE)
name Suffix for metadata columns ("_UCell")

Value

A list of signature scores

Description

Check signature names and add standard names is missing

Usage

```
check_signature_names(features)
```

Arguments

features List of signatures for scoring

Value

The input list of signatures, with standard names if provided un-named

```
data_to_ranks_data_table
```

Calculate per-cell feature rankings

Description

Calculate per-cell feature rankings

Usage

```
data_to_ranks_data_table(data, ties.method = "average")
```

Arguments

data Expression data matrix

ties.method How to break ties (passed on to data.table::frankv)

Value

A data.table of ranks

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get_gene_idx Get indices for genes in data matrix	
---------------------------------------------------	--

Description

Transform gene names into indices. Handle missing genes either by imputing or by skipping them.

Usage

```
get_gene_idx(all_genes, signature, missing_genes = "impute")
```

Arguments

all_genes Dictionary of all accepted gene names

signature A gene signature

missing_genes How to handle missing genes in dictionary: "impute": impute expression to

zero; "skip": remove missing genes from signature

Value

List of indices for genes in signatures

knn_smooth_scores Smoothing scores by KNN

Description

Smoothing scores by KNN

Usage

```
knn_smooth_scores(matrix = NULL, nn = NULL, decay = 0.1, up.only = FALSE)
```

Arguments

matrix Input data matrix

nn A nearest neighbor object returned by findKNN

decay Exponential decay for nearest neighbor weight: (1-decay)^n

up.only If set to TRUE, smoothed scores will only be allowed to increase by smoothing

Value

A dataframe of knn-smoothed scores

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rankings2Uscore

Get signature scores from pre-computed rank matrix

Description

Get signature scores from pre-computed rank matrix

Usage

```
rankings2Uscore(
  ranks_matrix,
  features,
  chunk.size = 100,
  w_neg = 1,
  BPPARAM = NULL,
  ncores = 1,
  force.gc = FALSE,
  missing_genes = c("impute", "skip"),
  name = "_UCell"
)
```

Arguments

ranks_matrix	A rank matrix
features	List of signatures
chunk.size	How many cells per matrix chunk
w_neg	Weight on negative signatures
BPPARAM	A BioParallel object to instruct UCell how to parallelize
ncores	How many cores to use for parallelization?
force.gc	Force garbage collection to recover RAM? (FALSE)
missing_genes	How to handle missing genes in matrix: "impute": impute expression to zero; "skip": remove missing genes from signature
name	Name suffix for metadata columns ("_UCell")

Value

A list of signature scores

sample.matrix

Sample dataset to test UCell installation

Description

A sparse matrix (class "dgCMatrix") of single-cell transcriptomes (scRNA-seq) for 30 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 T cells from the large scRNA-seq PBMC dataset published by Hao et al. and available as UMI counts at https://atlas.fredhutch.org/data/nygc/multimodal/pbmc_multimodal.h5seurat

Usage

```
sample.matrix
```

Format

A sparse matrix of 30 cells and 20729 genes.

Source

```
https://doi.org/10.1016/j.cell.2021.04.048
```

ScoreSignatures_UCell Calculate module enrichment scores from single-cell data

Description

Given a gene vs. cell matrix, calculates module/signature enrichment scores on single-cell level using Mann-Whitney U statistic. UCell scores are normalized U statistics (between 0 and 1), and they are mathematically related to the Area under the ROC curve (see Mason and Graham) These scores only depend on the gene expression ranks of individual cell, and therefore they are robust across datasets regardless of dataset composition.

```
ScoreSignatures_UCell(
  matrix = NULL,
  features,
  precalc.ranks = NULL,
  maxRank = 1500,
  w_neg = 1,
  name = "_UCell",
  assay = "counts",
  chunk.size = 100,
  missing_genes = c("impute", "skip"),
  BPPARAM = NULL,
```

```
ncores = 1,
ties.method = "average",
force.gc = FALSE
)
```

Arguments

matrix	Input matrix, either stored in a SingleCellExperiment::SingleCellExperiment object or as a raw matrix. dgCMatrix format supported.
features	A list of signatures, for example: list(Tcell_signature = c("CD2", "CD3E", "CD3D"), Myeloid_signature = c("SPI1", "FCER1G", "CSF1R")) You can also specify positive and negative gene sets by adding a + or - sign to genes in the signature; see an example below
precalc.ranks	If you have pre-calculated ranks using StoreRankings_UCell, you can specify the pre-calculated ranks instead of the gene vs. cell matrix.
maxRank	Maximum number of genes to rank per cell; above this rank, a given gene is considered as not expressed. Note: this parameter is ignored if precalc.ranks are specified
w_neg	Weight on negative genes in signature. e.g. w_neg=1 weighs equally up- and down-regulated genes, w_neg=0.5 gives 50% less importance to negative genes
name	Name suffix appended to signature names
assay	The sce object assay where the data is to be found
chunk.size	Number of cells to be processed simultaneously (lower size requires slightly more computation but reduces memory demands)
missing_genes	How to handle missing genes in matrix: "impute": impute expression to zero; "skip": remove missing genes from signature
BPPARAM	A BiocParallel::bpparam() object that tells UCell how to parallelize. If provided, it overrides the ncores parameter.
ncores	Number of processors to parallelize computation. If BPPARAM = NULL, the function uses BiocParallel::MulticoreParam(workers=ncores)
ties.method	How ranking ties should be resolved - passed on to data.table::frank

Explicitly call garbage collector to reduce memory footprint

Value

force.gc

Returns input SingleCellExperiment object with UCell scores added to altExp

Examples

10 SmoothKNN.Seurat

SmoothKNN.Seurat

Smooth signature scores by kNN

Description

This function performs smoothing of single-cell scores by weighted average of the k-nearest neighbors. It can be useful to 'impute' scores by neighboring cells and partially correct data sparsity. While this function has been designed to smooth UCell scores, it can be applied to any numerical metadata contained in SingleCellExperiment or Seurat objects

```
## S3 method for class 'Seurat'
SmoothKNN(
  obj = NULL,
  signature.names = NULL,
  reduction = "pca",
  k = 10,
  decay = 0.1,
  up.only = FALSE,
  BNPARAM = AnnoyParam(),
  BPPARAM = SerialParam(),
  suffix = "_kNN",
  assay = NULL,
  slot = "data"
  sce.expname = NULL,
  sce.assay = NULL
)
## S3 method for class 'SingleCellExperiment'
SmoothKNN(
  obj = NULL,
  signature.names = NULL,
  reduction = "PCA",
  k = 10,
  decay = 0.1,
  up.only = FALSE,
  BNPARAM = AnnoyParam(),
  BPPARAM = SerialParam(),
  suffix = "_kNN",
  assay = NULL,
  slot = "data",
  sce.expname = c("UCell", "main"),
  sce.assay = NULL
```

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```
)
SmoothKNN(
  obj = NULL,
  signature.names = NULL,
  reduction = "pca",
  k = 10,
  decay = 0.1,
  up.only = FALSE,
  BNPARAM = AnnoyParam(),
  BPPARAM = SerialParam(),
  suffix = "_kNN",
  assay = NULL,
  slot = "data",
  sce.expname = c("UCell", "main"),
  sce.assay = NULL
)
```

Arguments

obj	Input object - either a SingleCellExperiment::SingleCellExperiment object or a Seurat object.
signature.name	s
	The names of the signatures (or any numeric metadata column) for which to calculate kNN-smoothed scores
reduction	Which dimensionality reduction to use for kNN smoothing. It must be already present in the input object.
k	Number of neighbors for kNN smoothing
decay	Exponential decay for nearest neighbor weight: (1-decay)^n
up.only	If set to TRUE, smoothed scores will only be allowed to increase by smoothing
BNPARAM	A BiocNeighbors::BiocNeighborParam object specifying the algorithm to use for kNN calculation.
BPPARAM	A BiocParallel::bpparam() object for parallel computing, e.g. BiocParallel::MulticoreParam or BiocParallel::SnowParam
suffix	Suffix to append to metadata columns for the new knn-smoothed scores
assay	For Seurat objects only - do smoothing on expression data from this assay. When NULL, only looks in metadata
slot	For Seurat objects only - do smoothing on expression data from this slot
sce.expname	For sce objects only - which experiment stores the signatures to be smoothed. Set to 'main' for smoothing gene expression stored in the main sce experiment.
sce.assay	For sce objects only - pull data from this assay

Value

An augmented obj with the smoothed signatures. If obj is a Seurat object, smoothed signatures are added to metadata; if obj is a SingleCellExperiment object, smoothed signatures are returned in a new altExp. See the examples below.

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Examples

```
#### Using Seurat ####
library(Seurat)
gene.sets <- list(Tcell = c("CD2","CD3E","CD3D"),
                Myeloid = c("SPI1","FCER1G","CSF1R"))
data(sample.matrix)
obj <- Seurat::CreateSeuratObject(sample.matrix)</pre>
# Calculate UCell scores
obj <- AddModuleScore_UCell(obj,features = gene.sets, name=NULL)</pre>
# Run PCA
obj <- FindVariableFeatures(obj) |> NormalizeData() |> ScaleData() |> RunPCA(npcs=5)
# Smooth signatures
obj <- SmoothKNN(obj, k=3, signature.names=names(gene.sets))</pre>
head(obj[[]])
#### Using SingleCellExperiment ####
library(SingleCellExperiment)
library(scater)
data(sample.matrix)
sce <- SingleCellExperiment(list(counts=sample.matrix))</pre>
gene.sets <- list( Tcell = c("CD2","CD3E","CD3D"),</pre>
                   Myeloid = c("SPI1","FCER1G","CSF1R"))
# Calculate UCell scores
sce <- ScoreSignatures_UCell(sce, features=gene.sets, name=NULL)</pre>
# Run PCA
sce <- logNormCounts(sce)</pre>
sce <- runPCA(sce, scale=TRUE, ncomponents=5)</pre>
# Smooth signatures
sce <- SmoothKNN(sce, k=3, signature.names=names(gene.sets))</pre>
# See results
altExp(sce, 'UCell')
assays(altExp(sce, 'UCell'))
# Plot on UMAP
sce <- runUMAP(sce, dimred="PCA")</pre>
plotUMAP(sce, colour_by = "Tcell_kNN", by_exprs_values = "UCell_kNN")
```

split_data.matrix

Split data matrix into smaller sub-matrices ('chunks')

Description

Split data matrix into smaller sub-matrices ('chunks')

Usage

```
split_data.matrix(matrix, chunk.size = 100)
```

Arguments

matrix Input data matrix

chunk.size How many cells to include in each sub-matrix

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Value

A list of sub-matrices, each with size (n_features x chunk_size)

StoreRankings_UCell Calculate and store gene rankings for a single-cell dataset

Description

Given a gene vs. cell matrix, calculates the rankings of expression for all genes in each cell.

Usage

```
StoreRankings_UCell(
  matrix,
  maxRank = 1500,
  chunk.size = 100,
  BPPARAM = NULL,
  ncores = 1,
  assay = "counts",
  ties.method = "average",
  force.gc = FALSE
)
```

Arguments

matrix	Input matrix, either stored in a SingleCellExperiment::SingleCellExperiment object or as a raw matrix. dgCMatrix format supported.
maxRank	Maximum number of genes to rank per cell; above this rank, a given gene is considered as not expressed
chunk.size	Number of cells to be processed simultaneously (lower size requires slightly more computation but reduces memory demands)
BPPARAM	A BiocParallel::bpparam() object that tells UCell how to parallelize. If provided, it overrides the ncores parameter.
ncores	Number of processors to parallelize computation. If BPPARAM = NULL, the function uses BiocParallel::MulticoreParam(workers=ncores)
assay	Assay where the data is to be found (for input in 'sce' format)
ties.method	How ranking ties should be resolved - passed on to data.table::frank
force.gc	Explicitly call garbage collector to reduce memory footprint

Details

While ScoreSignatures_UCell can be used 'on the fly' to evaluate signatures in a query dataset, it requires recalculating gene ranks at every execution. If you have a large dataset and plan to experiment with multiple signatures, evaluating the same dataset multiple times, this function allows you to store pre-calculated ranks so they do not have to be recomputed every time. Pre-calculated ranks can then be applied to the function ScoreSignatures_UCell to evaluate gene signatures in a significantly faster way on successive iterations.

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Value

Returns a sparse matrix of pre-calculated ranks that can be used multiple times to evaluate different signatures

Examples

UCell

UCell: Robust and scalable single-cell gene signature scoring

Description

UCell is an R package for scoring gene signatures in single-cell datasets. UCell scores, based on the Mann-Whitney U statistic, are robust to dataset size and heterogeneity, and their calculation demands relatively less computing time and memory than most other methods, enabling the processing of large datasets (> 10^5 cells). UCell can be applied to any cell vs. gene data matrix, and includes functions to directly interact with Seurat and SingleCellExperiment objects.

UCell functions

- ScoreSignatures_UCell Calculate module enrichment scores from single-cell data. Given a gene vs. cell matrix (either as sparse matrix or stored in a SingleCellExperiment object), it calculates module/signature enrichment scores. This score depends only on the gene activity ranks of individual cell, and therefore is robust across datasets.
- AddModuleScore_UCell A wrapper for UCell to interact directly with Seurat objects. Given
 a Seurat object and a set of signatures, it calculates enrichment scores on single-cell level and
 returns them into the meta.data of the input Seurat object.
- StoreRankings_UCell Calculates and stores gene rankings for a single-cell dataset. Given a gene vs. cell matrix and a set of signatures, it calculates the rankings of expression for all genes in each cell. It can then be applied to the function ScoreSignatures_UCell to evaluate gene signatures on the gene expression ranks of individual cells.
- SmoothKNN Perform signature score smoothing using a weighted average of the scores of the first k nearest neighbors (kNN). It can be useful to 'impute' scores by neighboring cells and partially correct data sparsity. While this function has been designed to smooth UCell scores, it can be applied to any numerical metadata contained in SingleCellExperiment or Seurat objects

Gene signatures

UCell evaluates the strength of gene signatures (or gene sets) in individual cells of your dataset. You may specify positive and negative (up- or down-regulated) genes in signatures. See the examples below:

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If you don't specify +/- for genes, they are assumed to be all as a positive set. The UCell score is calculated as:

$$U = max(0, U^+ - w_{neg} * U^-)$$

where U^+ and U^- are respectively the UCell scores for the positive and negative set, and $w_n eg$ is a weight on the negative set. When no negative set of genes is present, $U=U^+$

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References

UCell: robust and scalable single-cell gene signature scoring. Massimo Andreatta & Santiago J Carmona (2021) CSBJ https://doi.org/10.1016/j.csbj.2021.06.043

See Also

Useful links:

- https://github.com/carmonalab/UCell
- Report bugs at https://github.com/carmonalab/UCell/issues

u_stat

Calculate Mann Whitney U from a vector of ranks

Description

Maximum sum of ranks, rank_sum_max: len_sig * max_Rank Minimum sum of ranks, rank_sum_min: len_sig * (len_sig + 1)/2 Maximum U statistic, Umax: Maximum sum of ranks - Minimum sum of ranks Minimum U statistic, Umin: 0 Normalized U statistic (0 to 1), Unorm: (U - Umin)/(Umax-Umin) = U/Umax UCell score (0 to 1): 1 - Unorm

```
u_stat(ranks_matrix, gene_idx, maxRank = 1500, sparse = FALSE)
```

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Arguments

ranks_matrix A matrix of ranks gene_idx A list of gene indices

maxRank Max number of features to include in ranking sparse Whether the vector of ranks is in sparse format

Details

Any rank > maxRank is set to maxRank

Value

Normalized U statistic for the vector of ranks

Description

Calculate U scores for a list of signatures, given a rank matrix

Usage

```
u_stat_signature_list(
    sig_list,
    ranks_matrix,
    maxRank = 1500,
    sparse = FALSE,
    w_neg = 1,
    missing_genes = "impute"
)
```

Arguments

sig_list A list of signatures

ranks_matrix Matrix of pre-computed ranks

maxRank Max number of features to include in ranking, for u_stat function

sparse Whether the vector of ranks is in sparse format

w_neg Weight on negative signatures

missing_genes How to handle missing genes in signatures

Value

A matrix of U scores

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