Package 'MetaNeighbor'

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Type Package

Title Single cell replicability analysis

Version 1.28.0

Description MetaNeighbor allows users to quantify cell type replicability across datasets using neighbor voting.

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Contents

`extendClusterSet` *Extend cluster set to nearest neighbors on cluster graph.*

Description

Note that the graph is directed, i.e. neighbors are retrieved by following arrows that start from the initial clusters.

Usage

```
extendClusterSet(graph, initial_set, max_neighbor_distance = 2)
```

Arguments

graph	Graph in igraph format generated by makeClusterGraph.
initial_set	Vector of cluster labels
max_neighbor_distance	Include more distantly related nodes by performing neigbor extension max_neighbor_distance rounds.

Value

Character vector including initial cluster set and all neighboring clusters (if any).

---

extractMetaClusters *Extracts groups of reciprocal top hits from a 1-vs-best AUROC matrix.*

Description

Note that meta-clusters are *not* cliques, but connected components, e.g., if 1<->2 and 1<->3 are reciprocal top hits, 1, 2, 3 is a meta-cluster, independently from the relationship between 2 and 3.

Usage

```
extractMetaClusters(best_hits, threshold = 0)
```

Arguments

best_hits	Matrix of AUROCs produced by MetaNeighborUS.
threshold	AUROC threshold. Two clusters belong to the same meta-cluster if they are reciprocal top hits and their similarity exceeds the threshold *both* ways (AUROC(1->2) > threshold *AND* AUROC(2->1) > threshold).

Value

A named list, where names are default meta-cluster names, and values are vectors of cluster names, one vector per meta-cluster. The last element of the list is called "outliers" and contains all clusters that had no match in any other dataset.

getCellType *Return cell type from a label in format 'study_id|cell_type'*

Description

Return cell type from a label in format 'study_id|cell_type'

Usage

```
getCellType(cluster_name)
```

Arguments

cluster_name	Character vector containing cluster names in the format study_id|cell_type.

Value

Character vector containing all cell type names.

getStudyId *Return study ID from a label in format 'study_id|cell_type'*

Description

Return study ID from a label in format 'study_id|cell_type'

Usage

```
getStudyId(cluster_name)
```

Arguments

cluster_name	Character vector containing cluster names in the format study_id|cell_type.

Value

Character vector containing all study ids.

ggPlotHeatmap *Plots symmetric AUROC heatmap, clustering cell types by similarity.*

Description

This function is a ggplot alternative to plotHeatmap (without the cell type dendrogram).

Usage

```
ggPlotHeatmap(aurocs, label_size = 10)
```

Arguments

aurocs	A square AUROC matrix as returned by MetaNeighborUS.
label_size	Font size of cell type labels along the heatmap (default is 10).

Value

A ggplot object.

See Also

plotHeatmap

GOhuman *GOhuman*

Description

List containing gene symbols for 71 GO function

Usage

```
GOhuman
```

Format

genesets List containing gene symbols for 71 GO function (GO slim terms containing between 50 and 1,000 genes) downloaded from the Gene Ontology Consortium August 2015 http://www.geneontology.org/page/download-annotations

Source

Dataset: https://github.com/mm-shah/MetaNeighbor/tree/master/data | Paper: https://www.biorxiv.org/content/early/2017/06/16/150524

GOmouse *GOmouse*

Description

List containing gene symbols for 10 GO function

Usage

```
GOmouse
```

Format

genesets List containing gene symbols for 10 GO function (GO:0016853 , GO:0005615, GO:0005768, GO:0007067, GO:0065003, GO:0042592, GO:0005929, GO:0008565, GO:0016829, GO:0022857) downloaded from the Gene Ontology Consortium August 2015 http://www.geneontology.org/page/download-annotations

Source

Dataset: https://github.com/mm-shah/MetaNeighbor/tree/master/data | Paper: https://www.biorxiv.org/content/early/2017/06/16/150524

makeClusterGraph *Convert AUROC matrix into a graph.*

Description

This representation is a useful alternative for heatmaps for large datasets and sparse AUROC matrices (MetaNeighborUS with one_vs_best = TRUE)

Usage

```
makeClusterGraph(best_hits, low_threshold = 0, high_threshold = 1)
```

Arguments

best_hits	Matrix of AUROCs produced by MetaNeighborUS.
low_threshold	AUROC threshold value. An edge is drawn between two clusters only if their similarity exceeds low_threshold.
high_threshold	AUROC threshold value. An edge is drawn between two clusters only if their similarity is lower than high_threshold (enables focusing on close calls).

Value

A graph in igraph format, where nodes are clusters and edges are AUROC similarities.

makeClusterName *Make cluster names in format 'study_id|cell_type'*

Description

Make cluster names in format 'study_id|cell_type'

Usage

```
makeClusterName(study_id, cell_type)
```

Arguments

study_id	Character vector containing study ids.
cell_type	Character vector containing cell type names

Value

Character vector containing cluster names in the format study_id|cell_type.

mergeSCE *Merge multiple SingleCellExperiment objects.*

Description

Merge multiple SingleCellExperiment objects.

Usage

```
mergeSCE(sce_list)
```

Arguments

sce_list	A *named* list, where values are SingleCellExperiment objects and names are SingleCellExperiment objects.

Value

A SingleCellExperiment object containing the input datasets with the following limitations: (i) only genes common to all datasets are kept, (ii) only colData columns common to all datasets are kept, (iii) only assays common to all datasets (i.e., having the same name) are kept, (iv) all other slots (e.g., reducedDims or rowData) will be ignored and left empty. The SingleCellExperiment object contains a "study_id" column, mapping each cell to its original dataset (names in "sce_list").

`MetaNeighbor` *Runs MetaNeighbor*

Description

For each gene set of interest, the function builds a network of rank correlations between all cells. Next,It builds a network of rank correlations between all cells for a gene set. Next, the neighbor voting predictor produces a weighted matrix of predicted labels by performing matrix multiplication between the network and the binary vector indicating cell type membership, then dividing each element by the null predictor (i.e., node degree). That is, each cell is given a score equal to the fraction of its neighbors (including itself), which are part of a given cell type. For cross-validation, we permute through all possible combinations of leave-one-dataset-out cross-validation, and we report how well we can recover cells of the same type as area under the receiver operator characteristic curve (AUROC). This is repeated for all folds of cross-validation, and the mean AUROC across folds is reported. Calls `neighborVoting`.

Usage

```
MetaNeighbor(
  dat,
  i = 1,
  experiment_labels,
  celltype_labels,
  genesets,
  bplot = TRUE,
  fast_version = FALSE,
  node_degree_normalization = TRUE,
  batch_size = 10,
  detailed_results = FALSE
)
```

Arguments

`dat`	A SummarizedExperiment object containing gene-by-sample expression matrix.
`i`	default value 1; non-zero index value of assay containing the matrix data
`experiment_labels`	A vector that indicates the source/dataset of each sample.
`celltype_labels`	A character vector or one-hot encoded matrix (cells x cell type) that indicates the cell type of each sample.
`genesets`	Gene sets of interest provided as a list of vectors.
`bplot`	default true, beanplot is generated
`fast_version`	default value FALSE; a boolean flag indicating whether to use the fast and low memory version of MetaNeighbor

node_degree_normalization
: default value TRUE; a boolean flag indicating whether to normalize votes by dividing through total node degree.

batch_size
: Optimization parameter. Gene sets are processed in groups of size batch_size. The count matrix is first subset to all genes from these groups, then to each gene set individually.

detailed_results
: Should the function return the average AUROC across all test datasets (default) or a detailed table with the AUROC for each test dataset?

Value

A matrix of AUROC scores representing the mean for each gene set tested for each celltype is returned directly (see neighborVoting). If detailed_results is set to TRUE, the function returns a table of AUROC scores in each test dataset for each gene set.

See Also

neighborVoting

Examples

```
data("mn_data")
data("GOmouse")
library(SummarizedExperiment)
AUROC_scores = MetaNeighbor(dat = mn_data,
                            experiment_labels = as.numeric(factor(mn_data$study_id)),
                           celltype_labels = metadata(colData(mn_data))[["cell_labels"]],
                            genesets = GOmouse,
                            bplot = TRUE)
```

MetaNeighborUS *Runs unsupervised version of MetaNeighbor*

Description

When it is difficult to know how cell type labels compare across datasets this function helps users to make an educated guess about the overlaps without requiring in-depth knowledge of marker genes

Usage

```
MetaNeighborUS(
  var_genes = c(),
  dat,
  i = 1,
  study_id,
  cell_type,
  trained_model = NULL,
```

```
  fast_version = FALSE,
  node_degree_normalization = TRUE,
  one_vs_best = FALSE,
  symmetric_output = TRUE
)
```

Arguments

var_genes	vector of high variance genes.
dat	SummarizedExperiment object containing gene-by-sample expression matrix.
i	default value 1; non-zero index value of assay containing the matrix data
study_id	a vector that lists the Study (dataset) ID for each sample
cell_type	a vector that lists the cell type of each sample
trained_model	default value NULL; a matrix containing a trained model generated from MetaNeighbor::trainModel. If not NULL, the trained model is treated as training data and dat is treated as testing data. If a trained model is provided, fast_version will automatically be set to TRUE and var_genes will be overridden with genes used to generate the trained_model
fast_version	default value FALSE; a boolean flag indicating whether to use the fast and low memory version of MetaNeighbor
node_degree_normalization	default value TRUE; a boolean flag indicating whether to use normalize votes by dividing through total node degree.
one_vs_best	default value FALSE; a boolean flag indicating whether to compute AUROCs based on a best match against second best match setting (default version is one-vs-rest). This option is currently only relevant when fast_version = TRUE.
symmetric_output	default value TRUE; a boolean flag indicating whether to average AUROCs in the output matrix.

Value

The output is a cell type-by-cell type mean AUROC matrix, which is built by treating each pair of cell types as testing and training data for MetaNeighbor, then taking the average AUROC for each pair (NB scores will not be identical because each test cell type is scored out of its own dataset, and the differential heterogeneity of datasets will influence scores). If symmetric_output is set to FALSE, the training cell types are displayed as columns and the test cell types are displayed as rows. If trained_model was provided, the output will be a cell type-by-cell type AUROC matrix with training cell types as columns and test cell types as rows (no swapping of test and train, no averaging).

Examples

```
data(mn_data)
var_genes = variableGenes(dat = mn_data, exp_labels = mn_data$study_id)
celltype_NV = MetaNeighborUS(var_genes = var_genes,
                             dat = mn_data,
```

```
                                study_id = mn_data$study_id,
                                cell_type = mn_data$cell_type)
celltype_NV
```

`mn_data` *mn_data*

Description

A SummarizedExperiment object containing: a gene matrix, cell type labels, experiment labels, sets of genes, sample ID, study id and cell types.

Usage

```
mn_data
```

Format

Gene matrix A gene-by-sample expression matrix consisting of 3157 rows (genes) and 1051 columns (cell types)

cell_labels 1051x1 binary matrix that indicates whether a cell belongs to the SstNos cell type (1=yes, 0 = no)

sample_id A character vector of length 1051 that indicates the sample_id of each sample

study_id A character vector of length 1051 that indicates the study_id of each sample ("GSE60361" = Zeisel et al, "GSE71585" = Tasic et al)

cell_type A character vector of length 1051 that indicates the cell-type of each sample

Source

Dataset:https://github.com/mm-shah/MetaNeighbor/tree/master/data 1. Zeisal et al. http://science.sciencemag.org/content/347/6226/1138 2. Tasic et al. http://www.nature.com/neuro/journal/v19/n2/full/nn.4216.html

---

`neighborVoting` *Runs the neighbor voting algorithm.*

Description

The function performs cell type identity prediction based on 'guilt by association' using cross validation. Performance is evaluated by calculating the AUROC for each cell type.

Usage

```
neighborVoting(
  exp_labels,
  cell_labels,
  network,
  means = TRUE,
  node_degree_normalization = TRUE
)
```

Arguments

exp_labels	A vector that indicates the dataset source of each sample
cell_labels	sample by cell type matrix that indicates the cell type of each sample (0-absent; 1-present)
network	sample by sample adjacency matrix, ranked and standardized between 0-1
means	default TRUE, determines output formatting
node_degree_normalization	default TRUE, should predictions be divided by node degree?

Value

If means = TRUE (default) a vector containing the mean of AUROC values across cross-validation folds will be returned. If FALSE a list is returned containing a cell type by dataset matrix of AUROC scores, for each fold of cross-validation. Default is over-ridden when more than one cell type is assessed.

See Also

MetaNeighbor

Examples

```
data("mn_data")
data("GOmouse")
library(SummarizedExperiment)
AUROC_scores = MetaNeighbor(dat = mn_data,
                            experiment_labels = as.numeric(factor(mn_data$study_id)),
                           celltype_labels = metadata(colData(mn_data))[["cell_labels"]],
                            genesets = GOmouse,
                            bplot = TRUE)
AUROC_scores
```

`orderCellTypes` *Order cell types based on AUROC similarity matrix.*

Description

Order cell types based on AUROC similarity matrix.

Usage

```
orderCellTypes(M, na_value = 0)
```

Arguments

`M`	A square AUROC matrix as returned by MetaNeighborUS.
`na_value`	Replace NA values with this value (default is 0).

Value

A hierarchical clustering object as returned by stats::hclust.

`plotBPlot` *Plot Bean Plot, showing how replicability of cell types depends on gene sets.*

Description

Plot Bean Plot, showing how replicability of cell types depends on gene sets.

Usage

```
plotBPlot(nv_mat, hvg_score = NULL, cex = 1)
```

Arguments

`nv_mat`	A rectangular AUROC matrix as returned by MetaNeighbor, where each row is a gene set and each column is a cell type.
`hvg_score`	Named vector with AUROCs obtained from a set of Highly Variable Genes (HVGs). The names must correspond to cell types from nv_mat. If specified, the HVG score is highlighted in red.
`cex`	Size factor for row and column labels.

Examples

```
data("mn_data")
data("GOmouse")
library(SummarizedExperiment)
AUROC_scores = MetaNeighbor(dat = mn_data,
                            experiment_labels = as.numeric(factor(mn_data$study_id)),
                           celltype_labels = metadata(colData(mn_data))[["cell_labels"]],
                            genesets = GOmouse,
                            bplot = FALSE)
plotBPlot(AUROC_scores)
```

`plotClusterGraph` *Plot cluster graph generated with makeClusterGraph.*

Description

In this visualization, edges are colored in black when AUROC > 0.5 and orange when AUROC < 0.5, edge width scales linearly with AUROC. Edges are oriented from training cluster towards test cluster. A black bidirectional edge indicates that two clusters are reciprocal top matches. Node radius reflects cluster size (small: up to 10 cells, medium: up to 100 cells, large: all other clusters).

Usage

```
plotClusterGraph(
  graph,
  study_id = NULL,
  cell_type = NULL,
  size_factor = 1,
  label_cex = 0.2 * size_factor,
  legend_cex = 2,
  study_cols = NULL
)
```

Arguments

`graph`	Graph in igraph format generated by makeClusterGraph.
`study_id`	Vector with study IDs provided to MetaNeighborUS to compute AUROCs stored in graph (used to compute cluster size). If NULL, all nodes have medium size.
`cell_type`	Vector with cell type labels provided to MetaNeighborUS to compute AUROCs stored in graph (used to compute cluster size). If NULL, all nodes have medium size.
`size_factor`	Numeric value controling the size of nodes and edges.
`label_cex`	Numeric value controling the size of cell type labels.
`legend_cex`	Numeric value controling the size of the legend.
`study_cols`	Named vector where values are RGB colors and names are unique study identifiers. If NULL, a default color palette is used.

plotDotPlot *Plot dot plot showing expression of a gene set across cell types.*

Description

The size of each dot reflects the number of cell that express a gene, the color reflects the average expression. Expression of genes is first average and scaled in each dataset independently. The final value is obtained by averaging across datasets.

Usage

```
plotDotPlot(
  dat,
  experiment_labels,
  celltype_labels,
  gene_set,
  i = 1,
  normalize_library_size = TRUE,
  alpha_row = 10,
  average_expressing_only = FALSE
)
```

Arguments

dat	A SummarizedExperiment object containing gene-by-sample expression matrix.
experiment_labels	A vector that indicates the source/dataset of each sample.
celltype_labels	A character vector that indicates the cell type of each sample.
gene_set	Gene set of interest provided as a vector of genes.
i	Default value 1; non-zero index value of assay containing the matrix data.
normalize_library_size	Whether to apply library size normalization before computing average expression (set this value to FALSE if data are already normalized).
alpha_row	Parameter controling row ordering: a higher value of alpha_row gives more weight to extreme AUROC values (close to 1).
average_expressing_only	Whether average expression should be computed based only on expressing cells (Seurat default) or taking into account zeros.

Value

a ggplot object.

plotHeatmap *Plots symmetric AUROC heatmap, clustering cell types by similarity.*

Description

Plots symmetric AUROC heatmap, clustering cell types by similarity.

Usage

```
plotHeatmap(aurocs, cex = 1, margins = c(8, 8), ...)
```

Arguments

aurocs	A square AUROC matrix as returned by MetaNeighborUS.
cex	Size factor for row and column labels.
margins	Size of margins (for row and column labels).
...	Additional graphical parameters that are passed on to gplots::heatmap.2 (allows customization of the heatmap).

See Also

ggPlotHeatmap

Examples

```
data(mn_data)
var_genes = variableGenes(dat = mn_data, exp_labels = mn_data$study_id)
celltype_NV = MetaNeighborUS(var_genes = var_genes,
                             dat = mn_data,
                             study_id = mn_data$study_id,
                             cell_type = mn_data$cell_type)
plotHeatmap(celltype_NV)
```

plotHeatmapPretrained *Plots rectangular AUROC heatmap, clustering train cell types (columns) by similarity, and ordering test cell types (rows) according to similarity to train cell types..*

Description

Plots rectangular AUROC heatmap, clustering train cell types (columns) by similarity, and ordering test cell types (rows) according to similarity to train cell types..

Usage

```
plotHeatmapPretrained(
  aurocs,
  alpha_col = 1,
  alpha_row = 10,
  cex = 1,
  margins = c(8, 8)
)
```

Arguments

aurocs	A rectangular AUROC matrix as returned by MetaNeighborUS,
alpha_col	Parameter controling column clustering: a higher value of alpha_col gives more weight to extreme AUROC values (close to 1).
alpha_row	Parameter controling row ordering: a higher value of alpha_row gives more weight to extreme AUROC values (close to 1).
cex	Size factor for row and column labels.
margins	Size of margins (for row and column labels).

Examples

```
data(mn_data)
var_genes = variableGenes(dat = mn_data, exp_labels = mn_data$study_id)
celltype_NV = MetaNeighborUS(var_genes = var_genes,
                             dat = mn_data,
                             study_id = mn_data$study_id,
                             cell_type = mn_data$cell_type,
                             symmetric_output = FALSE)
keep_col = getStudyId(colnames(celltype_NV)) == "GSE71585"
keep_row = getStudyId(rownames(celltype_NV)) != "GSE71585"
plotHeatmapPretrained(celltype_NV[keep_row, keep_col])
```

---

plotMetaClusters *Plot meta-cluster badges, each badge is a small AUROC heatmap restricted to a specific meta-cluster.*

Description

Plot meta-cluster badges, each badge is a small AUROC heatmap restricted to a specific meta-cluster.

Usage

```
plotMetaClusters(
  meta_clusters,
  best_hits,
  reorder = FALSE,
  cex = 1,
  study_cols = NULL,
  auroc_breaks = c(0, 0.5, 0.7, 0.9, 0.95, 0.99, 1),
 auroc_cols = (grDevices::colorRampPalette(c("white", "blue")))(length(auroc_breaks) -
    1)
)
```

Arguments

meta_clusters	Meta-cluster list generated by extractMetaClusters.
best_hits	Matrix of AUROCs used to extract meta-clusters.
reorder	Reorder datasets by similarity for each badge? By default, the same dataset ordering is used for each badge.
cex	Size factor controling label size.
study_cols	Named vector where values are RGB colors and names are unique study identifiers (corresponding to study_id). If NULL, a default color palette is used.
auroc_breaks	Numeric vector used to bin AUROC values for color coding.
auroc_cols	Vector containing RGB colors used to encode AUROC levels. The length of auroc_cols must correspond to the length of auroc_breaks - 1.

---

plotUpset *Plot Upset plot showing how replicability depends on input dataset.*

Description

Plot Upset plot showing how replicability depends on input dataset.

Usage

```
plotUpset(metaclusters, min_recurrence = 2, outlier_name = "outliers")
```

Arguments

metaclusters	Metaclusters extracted from MetaNeighborUS analysis.
min_recurrence	Only show replicability structure for metaclusters that are replicable across at least min_recurrence datasets.
outlier_name	In metaclusters, name assigned to outliers (clusters that did not match with any other cluster)

Examples

```
data(mn_data)
var_genes = variableGenes(dat = mn_data, exp_labels = mn_data$study_id)
celltype_NV = MetaNeighborUS(var_genes = var_genes,
                             dat = mn_data,
                             study_id = mn_data$study_id,
                             cell_type = mn_data$cell_type,
                             fast_version = TRUE, one_vs_best = TRUE)
mclusters = extractMetaClusters(celltype_NV)
plotUpset(mclusters)
```

---

scoreMetaClusters *Summarize meta-cluster information in a table.*

Description

Summarize meta-cluster information in a table.

Usage

```
scoreMetaClusters(meta_clusters, best_hits, outlier_label = "outliers")
```

Arguments

meta_clusters	Meta-cluster list generated by extractMetaClusters.
best_hits	Matrix of AUROCs used to extract meta-clusters.
outlier_label	Element of meta-cluster list containing outlier clusters.

Value

A data.frame. Column "meta_cluster" contains meta-cluster names, "clusters" lists the clusters belonging to each meta-cluster, "n_studies" is the number of studies spanned by the meta-cluster, "score" is the average similarity between meta-cluster members (average AUROC, NAs are treated as 0).

`splitClusters` *Split clusters according to symmetric AUROC similarity.*

Description

This function computes hierarchical clustering to group similar clusters, interpreting the AUROC matrix as a similarity matrix, then uses a standard tree cutting algorithm to obtain groups of similar clusters. Note that the cluster hierarchy corresponds exactly to the dendrogram shown when using the plotHeatmap function.

Usage

```
splitClusters(mn_scores, k)
```

Arguments

`mn_scores`	A symmetric AUROC matrix as generated by MetaNeighborUS.
`k`	The number of desired cluster sets.

Value

A list of cluster sets, each cluster set is a character vector containg cluster labels.

See Also

`plotHeatmap`

`splitTestClusters` *Split test clusters according to AUROC similarity to train clusters.*

Description

This function computes hierarchical clustering to group similar test clusters, using similarity to train clusters as features, then uses a standard tree cutting algorithm to obtain groups of similar clusters. Note that the cluster hierarchy does *not* correspond to the row ordering of plotHeatmapPretrained function, which uses a different heuristic.

Usage

```
splitTestClusters(mn_scores, k)
```

Arguments

`mn_scores`	An AUROC matrix as generated by MetaNeighborUS, usually with the "trained_model" option.
`k`	The number of desired cluster sets.

Value

A list of cluster sets, each cluster set is a character vector containg cluster labels.

See Also

plotHeatmapPretrained

`splitTrainClusters` *Split train clusters according to AUROC similarity to test clusters.*

Description

This function computes hierarchical clustering to group similar train clusters, using similarity to test clusters as features, then uses a standard tree cutting algorithm to obtain groups of similar clusters. Note that the cluster hierarchy corresponds exactly to the column dendrogram shown when using the plotHeatmapPretrained function.

Usage

```
splitTrainClusters(mn_scores, k)
```

Arguments

`mn_scores`	An AUROC matrix as generated by MetaNeighborUS, usually with the "trained_model" option.
`k`	The number of desired cluster sets.

Value

A list of cluster sets, each cluster set is a character vector containg cluster labels.

See Also

plotHeatmapPretrained

standardizeLabel *Remove special characters ("\|") from labels to avoid later conflicts*

Description

Remove special characters ("|") from labels to avoid later conflicts

Usage

```
standardizeLabel(labels, replace = "|", with = ".")
```

Arguments

labels	Character vector containing study ids or cell type names.
replace	Special character to replace
with	Character to use instead of special character

Value

Character vector with replaced special characters.

subsetClusterGraph *Subset cluster graph to clusters of interest.*

Description

Subset cluster graph to clusters of interest.

Usage

```
subsetClusterGraph(graph, vertices)
```

Arguments

graph	Graph in igraph format generated by makeClusterGraph.
vertices	Vector of cluster labels

Value

Graph in igraph format, where nodes have been restricted to clusters of interests.

See Also

extendClusterSet

topHits *Find reciprocal top hits*

Description

Identifies reciprocal top hits and high scoring cell type pairs. This function only look for the overall top hit for each cell type. We strongly recommend using topHitsByStudy instead, which looks for top hits in each target study, providing a more comprehensive view of replicability.

Usage

```
topHits(cell_NV, dat, i = 1, study_id, cell_type, threshold = 0.95)
```

Arguments

cell_NV	matrix of celltype-to-celltype AUROC scores (output from MetaNeighborUS)
dat	a SummarizedExperiment object containing gene-by-sample expression matrix.
i	default value 1; non-zero index value of assay containing the matrix data
study_id	a vector that lists the Study (dataset) ID for each sample
cell_type	a vector that lists the cell type of each sample
threshold	default value 0.95. Must be between [0,1]

Value

Function returns a dataframe with cell types that are either reciprocal best matches, and/or those with AUROC values greater than or equal to threshold value

See Also

topHitsByStudy

Examples

```
data(mn_data)
var_genes = variableGenes(dat = mn_data, exp_labels = mn_data$study_id)
celltype_NV = MetaNeighborUS(var_genes = var_genes,
                             dat = mn_data,
                             study_id = mn_data$study_id,
                             cell_type = mn_data$cell_type)
top_hits = topHits(cell_NV = celltype_NV,
                   dat = mn_data,
                   study_id = mn_data$study_id,
                   cell_type = mn_data$cell_type,
                   threshold = 0.9)
top_hits
```

topHitsByStudy *Find reciprocal top hits, stratifying results by study.*

Description

This function looks for reciprocal top hits in each target study separately, allowing for as many reciprocal top hits as target studies. This is the recommended function for extracting top hits.

Usage

```
topHitsByStudy(
  auroc,
  threshold = 0.9,
  n_digits = 2,
  collapse_duplicates = TRUE
)
```

Arguments

auroc	matrix of celltype-to-celltype AUROC scores (output from MetaNeighborUS)
threshold	AUROC threshold, must be between [0,1]. Default is 0.9. Only top hits above this threshold are included in the result table.
n_digits	Number of digits for AUROC values in the result table. Set to "Inf" to skip rounding.
collapse_duplicates	Collapse identical pairs of cell types (by default), effectively averaging AUROCs when reference and target roles are reversed. Setting this option to FALSE makes it easier to filter results by study or cell type. If collapse_duplicates is set to FALSE, "Celltype_1" is the reference cell type and "Celltype_2" is the target cell type (relevant if MetaNeighborUS was run with symmetric_output = FALSE).

Value

Function returns a dataframe with cell types that are either reciprocal best matches, and/or those with AUROC values greater than or equal to threshold value

See Also

topHits

Examples

```
data(mn_data)
var_genes = variableGenes(dat = mn_data, exp_labels = mn_data$study_id)
aurocs = MetaNeighborUS(var_genes = var_genes,
                        dat = mn_data,
```

```
                        study_id = mn_data$study_id,
                        cell_type = mn_data$cell_type)
top_hits = topHitsByStudy(aurocs)
top_hits
```

`trainModel` *Pretrains model for the unsupervised version of MetaNeighbor*

Description

When comparing clusters to a large reference dataset, this function summarizes the gene-by-cell matrix into a much smaller highly variable gene-by-cluster matrix which can be fed as training data into MetaNeighborUS, resulting in substantial time and memory savings.

Usage

```
trainModel(var_genes, dat, i = 1, study_id, cell_type)
```

Arguments

`var_genes`	vector of high variance genes.
`dat`	SummarizedExperiment object containing gene-by-sample expression matrix.
`i`	default value 1; non-zero index value of assay containing the matrix data
`study_id`	a vector that lists the Study (dataset) ID for each sample
`cell_type`	a vector that lists the cell type of each sample

Value

The output is a gene-by-cluster matrix that contains all the information necessary to run MetaNeighborUS from a pre-trained model.

Examples

```
data(mn_data)
var_genes = variableGenes(dat = mn_data, exp_labels = mn_data$study_id)
trained_model = trainModel(var_genes = var_genes,
                           dat = mn_data,
                           study_id = mn_data$study_id,
                           cell_type = mn_data$cell_type)
celltype_NV = MetaNeighborUS(trained_model = trained_model,
                             dat = mn_data,
                             study_id = mn_data$study_id,
                             cell_type = mn_data$cell_type)
celltype_NV
```

variableGenes *Identify a highly variable gene set*

Description

Identifies genes with high variance compared to their median expression (top quartile) within each experimentCertain function

Usage

```
variableGenes(
  dat,
  i = 1,
  exp_labels,
  min_recurrence = length(unique(exp_labels)),
  downsampling_size = 10000
)
```

Arguments

dat	SummarizedExperiment object containing gene-by-sample expression matrix.
i	default value 1; non-zero index value of assay containing the matrix data
exp_labels	character vector that denotes the source (Study ID) of each sample.
min_recurrence	Number of studies across which a gene must be detected as highly variable to be kept. By default, only genes that are variable across all studies are kept (intersection).
downsampling_size	Downsample each study to downsampling_size samples without replacement. If set to 0 or value exceeds dataset size, no downsampling is applied.

Value

The output is a vector of gene names that are highly variable in every experiment (intersect)

Examples

```
data(mn_data)
var_genes = variableGenes(dat = mn_data, exp_labels = mn_data$study_id)
var_genes
```

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