Package 'ssPATHS'

November 9, 2024

Type Package

Title ssPATHS: Single Sample PATHway Score

Version 1.20.0

Author Natalie R. Davidson

Maintainer Natalie R. Davidson <natalie.davidson@inf.ethz.ch>

Description This package generates pathway scores from expression data for single samples after training on a reference cohort. The score is generated by taking the expression of a gene set (pathway) from a reference cohort and performing linear discriminant analysis to distinguish samples in the cohort that have the pathway augmented and not. The separating hyperplane is then used to score new samples.

License MIT + file LICENSE

Encoding UTF-8

LazyData true

Imports ROCR, dml, MESS

Suggests ggplot2, testthat (>= 2.1.0)

Depends SummarizedExperiment

RoxygenNote 6.1.1

biocViews Software, GeneExpression, BiomedicalInformatics, RNASeq, Pathways, Transcriptomics, DimensionReduction, Classification

git_url https://git.bioconductor.org/packages/ssPATHS

git_branch RELEASE_3_20

git_last_commit 37a0886

git_last_commit_date 2024-10-29

Repository Bioconductor 3.20

Date/Publication 2024-11-08

Contents

`expected_score_output` *Gene Expression Values for PDAC Cancer Cell Lines exposed to Hypoxia*

Description

Gene Expression Values for PDAC Cancer Cell Lines exposed to Hypoxia

Usage

```
data(expected_score_output)
```

Format

A data frame with columns:

sample_id String. The name of the sample. Samples with "hyp" or "norm" in the sample id are cell lines that were exposed to hypoxic or normoxic conditions respectively. Samples with "ctrl" or "noHIF" were samples that were able to produce a HIF-mediated hypoxic response or not, respectively.

pathway_score Float. The estimated hypoxia score for this sample.

Source

Derived Data

Examples

```
## Not run:
 expected_score_output

## End(Not run)
```

`gene_weights_reference` *Gene Expression Values for PDAC Cancer Cell Lines exposed to Hypoxia*

Description

Gene Expression Values for PDAC Cancer Cell Lines exposed to Hypoxia

Usage

```
data(gene_weights_reference)
```

Format

A data frame with columns:

gene_weight Float. Gene weighting learned from reference data.

gene_id String. The ensembl id of the gene.

Source

Derived data

Examples

```
## Not run:
 gene_weights_reference

## End(Not run)
```

---

get_classification_accuracy *Get Classification Accuracy*

Description

Get the AUC-ROC, AUC-PR, and ROC/PR curves for plotting.

Usage

```
get_classification_accuracy(sample_scores, positive_val)
```

Arguments

sample_scores	This is a data.frame containing the sample id, score, and true label Y. This object is returned by the method get_gene_weights.
positive_val	This is the value that will denote a true positive. It must be one of the two values in the Y column in sample_scores.

Value

This returns a list of performance metrics

auc_pr	Area under the PR-curve
auc_roc	Area under the ROC-curve
perf_pr	ROCR object for plotting the PR-curve
perf_roc	ROCR object for plotting the ROC-curve

Author(s)

Natalie R. Davidson

Examples

```
data(tcga_expr_df)

# transform from data.frame to SummarizedExperiment
tcga_se <- SummarizedExperiment(t(tcga_expr_df[ , -(1:4)]),
                                colData=tcga_expr_df[ , 2:4])
colnames(tcga_se) <- tcga_expr_df$tcga_id
colData(tcga_se)$sample_id <- tcga_expr_df$tcga_id

hypoxia_gene_ids <- get_hypoxia_genes()
hypoxia_gene_ids <- intersect(hypoxia_gene_ids, rownames(tcga_se))

colData(tcga_se)$Y <- ifelse(colData(tcga_se)$is_normal, 0, 1)

# now we can get the gene weightings
res <- get_gene_weights(tcga_se, hypoxia_gene_ids, unidirectional=TRUE)
sample_scores <- res[[2]]

# check how well we did
training_res <- get_classification_accuracy(sample_scores, positive_val=1)
print(training_res[[2]])

plot(training_res[[3]], col="orange", ylim=c(0, 1))
legend(0.1,0.8,c(training_res$auc_pr,"\n"), border="white", cex=1.7,
        box.col = "white")

plot(training_res[[4]], col="blue", ylim=c(0, 1))
legend(0.1,0.8,c(training_res$auc_roc,"\n"),border="white",cex=1.7,
        box.col = "white")
```

`get_gene_weights` *Get Gene Weights from Reference Data*

Description

This method performs linear discriminant analysis on a reference dataset using a pre-defined set of genes related to a pathway of interest.

Usage

```
get_gene_weights(expression_se, gene_ids, unidirectional)
```

Arguments

`expression_se`	This is an SummarizedExperiment object of the reference samples. Rows are genes and columns are samples. The colData component must contain a `sample_id` column. Within this method, there is a normalization step where each sample is scaled across all genes in the SummarizedExperiment assay. For this to be stable and consistent, we recommend that the assay contain at least 500 genes that are consistently expressed across all samples in addition to the genes in the pathway of interest.

`gene_ids` This is a vector of strings, where each element is a `gene_id` in the pathway of interest. The `gene_ids` must be present in `rownames(expression_se)`.

`unidirectional` This is a boolean, `default=TRUE`. Most genesets are unidirectional, meaning that most genes are either increasing or decreasing together. If this is set to `TRUE`, then the learned weights will be clipped such that the dominant directionality is kept, and the other gene weights are set to zero.

Value

A list containing the gene weights and estimated scores of the reference samples.

`proj_vector_df` A dataframe containing the gene weights and gene ids

`dca_proj` A dataframe containing the sample scores and sample ids.

Author(s)

Natalie R. Davidson

References

Steven C.H. Hoi, W. Liu, M.R. Lyu and W.Y. Ma (2006). Learning Distance Metrics with Contextual Constraints for Image Retrieval. Proceedings IEEE Conference on Computer Vision and Pattern Recognition (CVPR2006).

Examples

```
data(tcga_expr_df)

# transform from data.frame to SummarizedExperiment
tcga_se <- SummarizedExperiment(t(tcga_expr_df[ , -(1:4)]),
                                colData=tcga_expr_df[ , 2:4])
colnames(tcga_se) <- tcga_expr_df$tcga_id
colData(tcga_se)$sample_id <- tcga_expr_df$tcga_id

# get related genes, for us hypoxia
hypoxia_gene_ids <- get_hypoxia_genes()
hypoxia_gene_ids <- intersect(hypoxia_gene_ids, rownames(tcga_se))

# setup labels for classification
colData(tcga_se)$Y <- ifelse(colData(tcga_se)$is_normal, 0, 1)

# now we can get the gene weightings
res <- get_gene_weights(tcga_se, hypoxia_gene_ids, unidirectional=TRUE)
gene_weights_test <- res[[1]]
sample_scores <- res[[2]]
```

get_hypoxia_genes *Get Ensembl ids of hypoxia related genes.*

Description

Returns a vector of Ensembl ids of hypoxia related genes.

Usage

```
get_hypoxia_genes()
```

Value

Vector of ensembl ids.

Author(s)

Natalie R. Davidson

Examples

```
# read in the reference expression data for hypoxia score generation
data(tcga_expr_df)

# transform from data.frame to SummarizedExperiment
tcga_se <- SummarizedExperiment(t(tcga_expr_df[ , -(1:4)]),
                                colData=tcga_expr_df[ , 2:4])
colnames(tcga_se) <- tcga_expr_df$tcga_id
colData(tcga_se)$sample_id <- tcga_expr_df$tcga_id

# let's get the expression of hypoxia associated genes
hypoxia_gene_ids <- get_hypoxia_genes()
hypoxia_gene_ids <- intersect(hypoxia_gene_ids, rownames(tcga_se))
hypoxia_se <- tcga_se[hypoxia_gene_ids,]
```

get_new_samp_score *Get a pathway score for an unseen sample*

Description

Using the gene weights learned from the reference cohort, we apply the weightings to new samples to estimate their pathway activity.

Usage

```
get_new_samp_score(gene_weights, expression_se, gene_ids, run_normalization = TRUE)
```

Arguments

gene_weights	This is a data.frame containing gene ids and gene weights, output by get_gene_weights. The gene ids must be in the column ids of expression_matr.
expression_se	This is an SummarizedExperiment object of the reference samples. Rows are genes and columns are samples. The colData component must contain columns Y and sample_id. The former indicates whether this is a positive or negative sample and the latter is the unique sample id. Within this method, there is a normalization step where each sample is scaled across all genes in the SummarizedExperiment assay. For this to be stable and consistent, we recommend that the assay contain at least 500 genes that are consistently expressed across all samples in addition to the genes in the pathway of interest.
gene_ids	This is a vector of strings, where each element is a gene_id in the pathway of interest. The gene_ids must be present in rownames(expression_se).
run_normalization	Boolean value. If TRUE, the data will be log-transformed, centered and scaled. This is recommended since this is done to the reference set when learning the gene weights.

Value

A data.frame containing the sample id, sample score, and associated Y value if it was included in expression_se.

Author(s)

Natalie R. Davidson

Examples

```
data(tcga_expr_df)

# transform from data.frame to SummarizedExperiment
tcga_se <- SummarizedExperiment(t(tcga_expr_df[ , -(1:4)]),
                                colData=tcga_expr_df[ , 2:4])
colnames(tcga_se) <- tcga_expr_df$tcga_id
colData(tcga_se)$sample_id <- tcga_expr_df$tcga_id

# get the genes of interest, here hypoxia genes
hypoxia_gene_ids <- get_hypoxia_genes()
hypoxia_gene_ids <- intersect(hypoxia_gene_ids, rownames(tcga_se))

# label the samples for classification
colData(tcga_se)$Y <- ifelse(colData(tcga_se)$is_normal, 0, 1)

# now we can get the gene weightings
res <- get_gene_weights(tcga_se, hypoxia_gene_ids, unidirectional=TRUE)
gene_weights <- res[[1]]
sample_scores <- res[[2]]

# get the new data so we can apply our score to it
data(new_samp_df)
new_samp_se <- SummarizedExperiment(t(new_samp_df[ , -(1)]),
                                    colData=new_samp_df[ , 1, drop=FALSE])
colnames(colData(new_samp_se)) <- "sample_id"
```

```
new_score_df_calculated <- get_new_samp_score(gene_weights, new_samp_se)
```

`new_samp_df` *Gene Expression Values for PDAC Cancer Cell Lines exposed to Hypoxia*

Description

A data frame with columns:

sample_id String. The name of the sample. Samples with "hyp" or "norm" in the sample id are cell lines that were exposed to hypoxic or normoxic conditions respectively. Samples with "ctrl" or "noHIF" were samples that were able to produce a HIF-mediated hypoxic response or not, respectively.

ENSG00000074410 Int. Gene expression value for this gene.

Usage

```
data(new_samp_df)
```

Format

An object of class `data.frame` with 12 rows and 27 columns.

Source

Generated by Philipp Markolin, files will be uploaded on GEO

Examples

```
## Not run:
 new_samp_df

## End(Not run)
```

`tcga_expr_df` *Gene Expression Values for PDAC Cancer Cell Lines exposed to Hypoxia*

Description

A data frame with columns:

tcga_id String. TCGA aliquot barcode

study String. TCGA study abbreviation

is_normal Boolean. TRUE if sample is adjacent normal, FALSE if tumor.

libsize_75percent Float. Library size as estimated by the 75th quartile.

ENSG00000070831 String. Library size normalized gene expression value for this gene.

Usage

```
data(tcga_expr_df)
```

Format

An object of class `data.frame` with 9461 rows and 54 columns.

Source

This data is generated by the TCGA Research Network: https://www.cancer.gov/tcga and downloaded from the NCI Genomic Data Commons.

Examples

```
## Not run:
 tcga_expr_df

## End(Not run)
```

Index