

Package ‘SVMDO’

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Title Identification of Tumor-Discriminating mRNA Signatures via Support Vector Machines Supported by Disease Ontology

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Imports shinyFiles (>= 0.9.3), shinytitle (>= 0.1.0), golem (>= 0.3.5), nortest (>= 1.0-4), e1071 (>= 1.7-12), BSDA (>= 1.2.1), data.table (>= 1.14.6), sjmisc (>= 2.8.9), klaR (>= 1.7-1), caTools (>= 1.18.2), caret (>= 6.0-93), survival (>= 3.4-0), DOSE (>= 3.24.2), AnnotationDbi (>= 1.60.0), org.Hs.eg.db (>= 3.16.0), dplyr (>= 1.0.10), SummarizedExperiment (>= 1.28.0), grDevices, graphics, stats, utils

Description It is an easy-to-use GUI using disease information for detecting tumor/normal sample discriminating gene sets from differentially expressed genes. Our approach is based on an iterative algorithm filtering genes with disease ontology enrichment analysis and wilk and wilk’s lambda criterion connected to SVM classification model construction. Along with gene set extraction, SVMDO also provides individual prognostic marker detection. The algorithm is designed for FPKM and RPKM normalized RNA-Seq transcriptome datasets.

biocViews GeneSetEnrichment, DifferentialExpression, GUI, Classification, RNASeq, Transcriptomics, Survival

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classification_server *SVMDO*

Description

SVMDO

Usage

innerServer_7(input, output, session)

Arguments

input	server input
output	server output
session	server session

Value

Server section of wilks lambda filtration and SVM classification of disease filtered differentially expressed gene set

classification_ui *SVMDO*

Description

SVMDO

Usage

innerUI_classification(id)

Arguments

id	connection input
----	------------------

Value

UI section of wilks lambda filtration and SVM classification of disease filtered differentially expressed gene set

clinic_data_input_server
SVMDO

Description

SVMDO

Usage

innerServer_clinic(input, output, session)

Arguments

input	server input
output	server output
session	server session

Value

Server section of loading clinical data

clinic_data_input_ui *SVMDO*

Description

SVMDO

Usage

innerUI_clinic_data(id)

Arguments

id	connection input
----	------------------

Value

UI section of loading clinical data

deg_server

SVMDO

Description

SVMDO

Usage

```
innerServer_3(input, output, session, rawData, rval)
```

Arguments

input	server input
output	server output
session	server session
rawData	expression dataset provided from innerServer_exp_server
rval	Selected radio button information provided from innerServer_rad_server

Value

Server section of differential gene expression analysis

deg_ui

SVMDO

Description

SVMDO

Usage

```
innerUI_deg_analysis(id)
```

Arguments

id	connection input
----	------------------

Value

UI section of differential gene expression analysis

disc_gene_download_ui *SVMDO*

Description

SVMDO

Usage

disc_gene_download_ui(id)

Arguments

id connection input

Value

UI section of discriminative gene set download button

disc_gene_dw_server *SVMDO*

Description

SVMDO

Usage

disc_gene_dw_server(input, output, session, gene_list_val)

Arguments

input server input
output server output
session server session
gene_list_val discriminative gene set list variable

Value

Server section of discriminative gene set download button

do_based_gene_filtration_server
SVMDO

Description

SVMDO

Usage

innerServer_6(input, output, session)

Arguments

input	server input
output	server output
session	server session

Value

Server section of disease ontology based filtration of differentially expressed genes

do_based_gene_filtration_ui
SVMDO

Description

SVMDO

Usage

innerUI_disease_ont_class(id)

Arguments

id	connection input
----	------------------

Value

UI section of disease ontology based filtration of differentially expressed genes

expression_dataset_input_server
SVMDO

Description

SVMDO

Usage

innerServer_exp(input, output, session)

Arguments

input	server input
output	server output
session	server session

Value

Server section of providing expression dataset

gene_directory_selection_server
SVMDO

Description

SVMDO

Usage

innerServer(input, output, session)

Arguments

input	server input
output	server output
session	server session

Value

Server section of entering output/working for gene list directory

gene_directory_selection_ui
SVMDO

Description

SVMDO

Usage

innerUI_path(id)

Arguments

id connection input

Value

UI section of entering output/working for gene list directory

gene_list_name_server SVMDO

Description

SVMDO

Usage

innerServer_10(input, output, session)

Arguments

input server input
output server output
session server session

Value

Server section of entering final gene list name

gene_list_name_ui *SVMDO*

Description

SVMDO

Usage

innerUI_gene_names(id)

Arguments

id connection input

Value

UI section of entering top gene value

gene_list_table_visualization_ui
SVMDO

Description

SVMDO

Usage

deg_data_table_ui(id)

Arguments

id connection input

Value

Providing table form of discriminative gene sets in GUI

globals	<i>SVMDO</i>
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Description

SVMDO

Value

Including script files and global variables of GUI required to be initiated at the runApp file execution

gui_obj_removal_server	<i>SVMDO</i>
------------------------	--------------

Description

SVMDO

Usage

innerServer_9(input, output, session)

Arguments

input	server input
output	server output
session	server session

Value

Server section of workspace clearance

gui_obj_removal_ui *SVMDO*

Description

SVMDO

Usage

innerUI_clear_env(id)

Arguments

id connection input

Value

UI section of workspace clearance

innerServer_exp_ui *SVMDO*

Description

SVMDO

Usage

innerUI_exp_data(id)

Arguments

id connection input

Value

UI section of providing expression dataset into GUI

package_req_list	<i>SVMDO</i>
------------------	--------------

Description

SVMDO

Value

List of packages involved in SVMDO

plot_list_server	<i>SVMDO</i>
------------------	--------------

Description

SVMDO

Usage

```
plot_list_server(input, output, session)
```

Arguments

input	server input
output	server output
session	server session

Value

Server section of preparing plot list to be visualized in GUI page

plot_list_ui	<i>SVMDO</i>
--------------	--------------

Description

SVMDO

Usage

```
innerUI_collect_plot_data(id)
```

Arguments

id	connection output
----	-------------------

Value

UI section of preparing plot list to be visualized in GUI page

plot_push_server	<i>SVMDO</i>
------------------	--------------

Description

SVMDO

Usage

```
plot_push_server(input, output, session)
```

Arguments

input	server input
output	server output
session	server session

Value

Server section of providing information about total number of survival plots for visualization

plot_push_ui	<i>SVMDO</i>
--------------	--------------

Description

SVMDO

Usage

innerUI_plot_inject(id)

Arguments

id	connection input
----	------------------

Value

UI section of providing information about total number of survival plots for visualization

plot_show_server	<i>SVMDO</i>
------------------	--------------

Description

SVMDO

Usage

plot_show_server(input, output, session, max_data)

Arguments

input	server input
output	server output
session	server session
max_data	Information of total number of survival plots prepared with discriminative gene set

Value

Server section of providing information about total number of survival plots for visualization

plot_show_ui *SVMDO*

Description

SVMDO

Usage

```
innerUI_plot_show(id)
```

Arguments

id connection input

Value

UI section of providing information about total number of survival plots for visualization

runGUI *SVMDO*

Description

SVMDO

Usage

```
linebreaks(n)
```

Arguments

n linebreak function variable

Value

Returning GUI window screen

Examples

```
#SVMDO::runGUI() Calling GUI without activating library
#runGUI() Calling GUI after activating library
# Disease Ontology Enrichment of a differentially expressed gene (entrez id):
a_1<-DOSE::enrichDO(2981,ont="DO")
```

survival_analysis_server
SVMDO

Description

SVMDO

Usage

```
innerServer_8(input, output, session, rawData_2, rval)
```

Arguments

input	server input
output	server output
session	server session
rawData_2	Clinical data provided from clinic_data_input_server
rval	Selected radio button information provided from innerServer_rad_server

Value

Server section of survival analysis of final discriminative gene set

survival_analysis_ui *SVMDO*

Description

SVMDO

Usage

```
innerUI_surv(id)
```

Arguments

id	connection input
----	------------------

Value

UI section of survival analysis of final discriminative gene set

surv_plot_dw_server *SVMDO*

Description

SVMDO

Usage

```
surv_plot_dw_server(input, output, session)
```

Arguments

input	server input
output	server output
session	server session

Value

Server section of downloading survival plots of discriminative gene set

surv_plot_dw_ui *SVMDO*

Description

SVMDO

Usage

```
surv_plots_download_ui(id)
```

Arguments

id	connection input
----	------------------

Value

UI section of downloading survival plots of discriminative gene set

Description

Package Description: It is an easy-to-use GUI using disease information for detecting tumor/normal sample discriminating gene sets from differentially expressed genes. Our approach is based on an iterative algorithm filtering genes with disease ontology enrichment analysis and wilk's lambda criterion connected to SVM classification model construction. Along with gene set extraction, SVMDO also provides individual prognostic marker detection among the discriminative genes. The algorithm is designed for FPKM and RPKM normalized RNA-Seq transcriptome datasets. To provide experience about the GUI usage, a test section involving dummy example using SummarizedExperiment objects of transcriptome (small form) and clinical datasets is also included.

Value

Providing package-level manual page

Package Sections

1. **Analysis:** Acquiring discriminative gene sets and further detecting the gene subset with prognostic characteristics
2. **Result:** Visualization and Download of discriminative gene sets and survival plot list of prognostic genes

Steps of Analysis Screen

1. To search your transcriptome dataset, use the file detection in Choose Your Expression Dataset section. The file will be automatically uploaded into the GUI.
2. To prevent clashing with test datasets, "None" option has to be selected from the radio button section.
3. By clicking on DEG Analysis button you further apply differential expression analysis. Labels of tissue_type column in dataset must contain "Nor" and "Tum" for determining normal/tumour (or tumor) samples. A message window saying Process Completed will appear if there is not any problem.
4. When the differential expression process is completed, a user-defined input size (n) is selected to filter the initial gene list (i.e., n number of upregulated and downregulated genes) by entering a number in Input Size section. It is predetermined as 50 in GUI which can be changed based on the user. If there is problem with the value of input size, you will get a warning about inappropriate input size selection. If the input size remains, algorithm selects all of the differentially expressed genes to be used in the next process.
5. To apply disease ontology-based gene filtration, click on DO Analysis button. A message window saying process completed will appear if there is not any problem.
6. To further apply the following feature selection and classification processes, click on the Classification button. A message window saying process completed will appear if there is not any problem.

7. Acquired discriminative gene set can be further used for survival analysis to detect individual prognostic genes. To apply this process, use the file detection in Choose Clinical Data section for searching clinical data about patient survival followed by clicking on Survival Analysis button.

Steps of Result Screen

1. To visualize discriminative gene sets inside GUI screen, click on Show Gene Results button. When you click this button, a table of gene set will appear. If there is a problem in the analysis, an error message will appear.
2. To visualize survival plots of individual genes, two steps have to be applied. First of all, click on Prepare Plot Lists button to feed plot information to the visualization system. After that, click on Show Plots button to visualize survival plots.
3. Before downloading files, you can adjust the output directory with Choose Directory button. It can be used for separating files by selecting a destination before clicking download buttons. If it is desired, files can be downloaded to the same folder by selecting an output directory just one time before the download steps. If you do not select any output directory, files will be downloaded to your working directory.
4. To download the resulting discriminative gene set, it is obligatory to define a filename in the Enter Final Gene Set Filename section. After that, you can click on Download Gene List button to complete the process.
5. To download survival plots, you have to click on Download Plot List button. Names of plot files are automatically done by assigning gene names.

Application of Test Datasets

SVMDO includes test datasets providing dummy examples for gaining experience on the GUI usage. Test datasets consist of simplified forms of TCGA-COAD (COAD) and TCGA-LUSC (LUSC) with 400 genes along with clinical datasets loaded into summarized experiment objects. When test datasets are used, predetermined expression and clinical datasets are automatically uploaded into the GUI. A test-based analysis is done with predefined input size ($n=50$). Therefore, users have to continue with DO Analysis after DEG Analysis.

Workspace Clearance

When the user task is completed, click on the Clear Environment button to remove the global variables created during the algorithm sections. To prevent error in the next usages of GUI, it is a necessary process. It can be applied at any moment without the necessity of completing all of the steps of algorithm.

table_server	SVMDO
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Description

SVMDO

Usage

```
table_server(input, output, session)
```

Arguments

input	server input
output	server output
session	server session

Value

Server section of providing discriminative gene set for preparing table

table_ui	<i>SVMDO</i>
----------	--------------

Description

SVMDO

Usage

```
innerUI_table_show(id)
```

Arguments

id	connection input
----	------------------

Value

UI section of providing discriminative gene set for preparing table

test_data_selection_server	<i>SVMDO</i>
----------------------------	--------------

Description

SVMDO

Usage

```
innerServer_rad(input, output, session)
```

Arguments

input	server input
output	server output
session	server session

Value

Server section of providing information about selected radio button

test_data_selection_ui
SVMDO

Description

SVMDO

Usage

innerUI_test_data(id)

Arguments

id	connection input
----	------------------

Value

UI section of providing information about selected radio button

top_val_based_deg_filtration
SVMDO

Description

SVMDO

Usage

innerServer_5(input, output, session, top_val)

Arguments

input	server input
output	server output
session	server session
top_val	top gene number value provided from top_val_server

Value

Server section of selecting differentially expressed genes based on top gene value

top_val_based_deg_filtration_ui
SVMDO

Description

SVMDO

Usage

innerUI_top_gene_selection(id)

Arguments

id	connection input
----	------------------

Value

UI section of selecting differentially expressed genes based on top gene value

top_val_server *SVMDO*

Description

SVMDO

Usage

innerServer_4(input, output, session)

Arguments

input	server input
output	server output
session	server session

Value

Server section of entering top gene value

top_val_ui

SVMDO

Description

SVMDO

Usage

innerUI_top_gene_val(id)

Arguments

id connection input

Value

UI section of entering top gene value

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