Package ‘HPiP’

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Type Package

Title Host-Pathogen Interaction Prediction

Version 1.8.0

Description HPiP (Host-Pathogen Interaction Prediction) uses an ensemble learning algorithm for prediction of host-pathogen protein-protein interactions (HP-PPIs) using structural and physicochemical descriptors computed from amino acid-composition of host and pathogen proteins. The proposed package can effectively address data shortages and data unavailability for HP-PPI network reconstructions. Moreover, establishing computational frameworks in that regard will reveal mechanistic insights into infectious diseases and suggest potential HP-PPI targets, thus narrowing down the range of possible candidates for subsequent wet-lab experimental validations.

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BugReports https://github.com/mrbakhsh/HPiP/issues

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**calculateAAC**

**Calculate Amino Acid Composition (AAC) Descriptor**

This function calculates Amino Acid Composition (AAC) descriptor for the data input.

**Description**

This function calculates Amino Acid Composition (AAC) descriptor for the data input.

**Usage**

```r
calculateAAC(x)
```

**Arguments**

- `x` A data.frame containing gene/protein names and their fasta sequences.

**Details**

`calculateAAC`

**Value**

A length 20 named vector for the data input.

**Author(s)**

Matineh Rahmatbakhsh, <matinerb.94@gmail.com>

**References**


**See Also**

See `calculateDC` and `calculateTC` for Dipeptide Composition and Tripeptide Composition descriptors.

**Examples**

```r
data(UP000464024_df)
x_df <- calculateAAC(UP000464024_df)
head(x_df, n = 2L)
```
**Description**

This function calculates autocorrelation descriptors:

- **moran** - moran autocorrelation, (Dim: length(target.props) * nlag).
- **geary** - geary autocorrelation, (Dim: length(target.props) * nlag).
- **moreaubroto** - moreau-broto autocorrelation, (Dim: length(target.props) * nlag).

**Usage**

```r
calculateAutocor(
  x,
  target.props = c("CIDH920105", "BHAR880101", "CHAM820101", "CHAM820102",
                   "CHOC760101", "BIGC670101", "CHAM810101", "DAYM780201"),
  nlag = 30L,
  type = c("moran", "geary", "moreaubroto")
)
```

**Arguments**

- **x** A data.frame containing gene/protein names and their fasta sequences.
- **target.props** A character vector, specifying the accession number of the target properties. 8 properties are used by default, as listed below:
  - **AccNo. CIDH920105** Normalized average hydrophobicity scales (Cid et al., 1992)
  - **AccNo. BHAR880101** Average flexibility indices (Bhaskaran-Ponnuswamy, 1988)
  - **AccNo. CHAM820101** Polarizability parameter (Charton-Charton, 1982)
  - **AccNo. CHAM820102** Free energy of solution in water, kcal/mole (Charton-Charton, 1982)
  - **AccNo. CHOC760101** Residue accessible surface area in tripeptide (Chothia, 1976)
  - **AccNo. BIGC670101** Residue volume (Bigelow, 1967)
  - **AccNo. CHAM810101** Steric parameter (Charton, 1981)
  - **AccNo. DAYM780201** Relative mutability (Dayhoff et al., 1978b)
- **nlag** Maximum value of the lag parameter. Default is 30.
- **type** The autocorrelation type: moran, geary, or moreaubroto.

**Details**

`calculateAutocor`
**Description**

This function transforms each residue in a peptide into 20 coding values.

**Usage**

```
calculateBE(x)
```

**Arguments**

- `x` A data.frame containing gene/protein names and their fasta sequences.

**Details**

`calculateBE`

**Value**

A length 400 named vector for the data input.
Author(s)
Matineh Rahmatbakhsh, <matinerb.94@gmail.com>

References

---

**calculateCTDC**  
*Calculate CTD Descriptors - Composition (C)*

**Description**
This function calculates Composition (C) descriptor for data input.

**Usage**
calculateCTDC(x)

**Arguments**
- `x` A data.frame containing gene/protein names and their fasta sequences.

**Details**
calculateCTDC

**Value**
A length 21 named vector for the data input.

**Author(s)**
Matineh Rahmatbakhsh, <matinerb.94@gmail.com>

**References**

**See Also**
See `calculateCTDT` and `calculateCTDD` for Transition and Distribution descriptors.

**Examples**
```r
data(UP000464024_df)
x_df <- calculateCTDC(UP000464024_df)
head(x_df, n = 2L)
```
calculateCTDD

Calculate CTD Descriptors - Distribution (D)

Description

This function calculates Distribution (D) descriptor for data input.

Usage

calculateCTDD(x)

Arguments

x A data.frame containing gene/protein names and their fasta sequences.

Details

calculateCTDD

Value

A length 105 named vector for the data input.

Author(s)

Matineh Rahmatbakhsh, <matinerb.94@gmail.com>

References


See Also

See `calculateCTDC` and `calculateCTDT` for Composition and Transition descriptors.

Examples

data(UP000464024_df)
x_df <- calculateCTDD(UP000464024_df)
head(x_df, n = 1L)
calculateCTDT

*Calculate CTD Descriptors - Transition (T)*

**Description**

This function calculates Transition (T) descriptor for data input.

**Usage**

```r
calculateCTDT(x)
```

**Arguments**

- `x`: A data.frame containing gene/protein names and their fasta sequences.

**Details**

`calculateCTDT` values

**Value**

A length 21 named vector for the data input.

**Author(s)**

Matineh Rahmatbakhsh, <matinerb.94@gmail.com>

**References**


**See Also**

See `calculateCTDC` and `calculateCTDD` for Composition and Distribution descriptors.

**Examples**

```r
data(UP000464024_df)
x_df <- calculateCTDT(UP000464024_df)
head(x_df, n = 2L)
```
calculateCTriad \hspace{1cm} \textit{Calculate Conjoint Triad Descriptor}

\textbf{Description}

This function calculates Conjoint Triad descriptor for data input.

\textbf{Usage}

calculateCTriad(x)

\textbf{Arguments}

\begin{itemize}
  \item \textbf{x} \hspace{1cm} A data.frame containing gene/protein names and their fasta sequences.
\end{itemize}

\textbf{Details}

\textbf{Value}

A length 343 named vector for the data input.

\textbf{Author(s)}

Matineh Rahmatbakhsh, <matinerb.94@gmail.com>

\textbf{References}


\textbf{Examples}

data(UP000464024_df)
x_df <- calculateCTriad(UP000464024_df)
head(x_df, n = 2L)
calculateDC  

*Calculate Dipeptide Composition (DC) Descriptor*

**Description**

This function calculates Dipeptide Composition (DC) descriptor for data input.

**Usage**

```r
calculateDC(x)
```

**Arguments**

- `x` A data.frame containing gene/protein names and their fasta sequences.

**Details**

`calculateDC`

**Value**

A length 400 named vector for the data input.

**Author(s)**

Matineh Rahmatbakhsh, <matinerb.94@gmail.com>

**References**


**See Also**

See `calculateAAC` and `calculateTC` for Amino Acid Composition and Tripeptide Composition descriptors.

**Examples**

```r
data(UP000464024_df)
x_df <- calculateDC(UP000464024_df)
head(x_df, n = 2L)
```
Description

This function calculates F1 or F2 descriptors:

- **F1** - sum of squared length of Single Amino Acid Repeats (SARs) in the entire protein sequence.
- **F2** - maximum of the sum of Single Amino Acid Repeats (SARs) in a window of 6 residues.

Usage

```r
calculateF(x, type = c("F1", "F2"))
```

Arguments

- **x** A data.frame containing gene/protein names and their fasta sequences.
- **type** The descriptor type: F1 or F2.

Details

`calculateF`

Value

A length 20 named vector for the data input.

Author(s)

Matineh Rahmatbakhsh, <matinerb.94@gmail.com>

References


Examples

```r
data(UP000464024_df)
x_df <- calculateF(UP000464024_df, type = "F1")
head(x_df, n = 2L)
```
**calculateKSAAP**  
*Calculate k-spaced Amino Acid Pairs (KSAAP) Descriptor*

**Description**

This function calculates k-spaced Amino Acid Pairs (KSAAP) Descriptor for data input. This function is adapted from the CkSAAppair function in the ftrCOOL package.

**Usage**

```r
calculateKSAAP(x, spc = 3)
```

**Arguments**

- `x`  
  A data.frame containing gene/protein names and their fasta sequences.

- `spc`  
  A number of spaces separating two adjacent residues by a distance of spc, which can be any number up to two less than the length of the peptide; default to 3.

**Details**

```r
calculateKSAAP
```

**Value**

A length 400 named vector for the data input.

**Author(s)**

Matineh Rahmatbakhsh, <matinerb.94@gmail.com>

**References**


**Examples**

```r
data(UP000464024_df)
x_df <- calculateKSAAP(UP000464024_df)
head(x_df, n = 2L)
```
**calculateQD_Sm**

| calculateQD_Sm | Calculate Quadruples Composition (QC) Descriptor from Biochemical Similarity Classes |

**Description**

This function calculates Quadruples Composition (QC) descriptor from biochemical similarity classes.

**Usage**

```r
calculateQD_Sm(x)
```

**Arguments**

- `x` A data.frame containing gene/protein names and their fasta sequences.

**Details**

calculateQD_Sm

**Value**

A length 1296 named vector for the data input.

**Author(s)**

Matineh Rahmatbakhsh, <matinerb.94@gmail.com>

**References**


**Examples**

```r
data(UP000464024_df)
x_df <- calculateQD_Sm(UP000464024_df)
head(x_df, n = 2L)
```
**Function**

**calculateTC**

*Calculate Tripeptide Composition (TC) Descriptor*

**Description**

This function calculates Tripeptide Composition (TC) descriptor for data input.

**Usage**

`calculateTC(x)`

**Arguments**

- `x` A data.frame containing gene/protein names and their fasta sequences.

**Details**

`calculateTC`

**Value**

A length 8,000 named vector for the data input.

**Author(s)**

Matineh Rahmatbakhsh, <matinerb.94@gmail.com>

**References**


**See Also**

See `calculateAAC`, `calculateDC` and `calculateTC_Sm` for Amino Acid Composition, Dipeptide Composition and Tripeptide Composition (TC) Descriptor from Biochemical Similarity Classes.

**Examples**

```r
data(UP000464024_df)
x_df <- calculateTC(UP000464024_df)
head(x_df, n = 2L)
```
**calculateTC_Sm**

**Calculate Tripeptide Composition (TC) Descriptor from Biochemical Similarity Classes**

**Description**

This function calculates Tripeptide Composition (TC) descriptor from biochemical similarity classes.

**Usage**

```r
calculateTC_Sm(x)
```

**Arguments**

- `x` A data.frame containing gene/protein names and their fasta sequences.

**Details**

`calculateTC_Sm`

**Value**

A length 216 named vector for the data input.

**Author(s)**

Matineh Rahmatbakhsh, <matinerb.94@gmail.com>

**References**


**See Also**

See `calculateTC` for Tripeptide Composition descriptor.

**Examples**

```r
data(UP000464024_df)
x_df <- calculateTC_Sm(UP000464024_df)
head(x_df, n = 2L)
```
Description

A graphical display of a correlation matrix.

Usage

```
corr_plot(cormat, method = "number", cex = 0.9)
```

Arguments

- `cormat`: A correlation matrix.
- `method`: The visualization method of correlation matrix; defaults to number. See `corrplot` for more details.
- `cex`: The size of x/y axis label.

Details

`corr_plot`

Value

A correlation plot.

Author(s)

Matineh Rahmatbakhsh, <matinerb.94@gmail.com>.

Examples

```
data('example_data')
x <- na.omit(example_data)
# perform feature selection
s <- FSmethod(x, type = 'both',
cor.cutoff = 0.7, resampling.method = "repeatedcv",
iter = 5, repeats = 3, metric = "ROC", verbose = TRUE)
corr_plot(s$cor.result$corProfile, method = 'square', cex = 0.5)
```
enrich.df

<table>
<thead>
<tr>
<th>enrich.df</th>
<th>Enrichment Result</th>
</tr>
</thead>
</table>

**Description**

Input data for *enrichplot*

**Usage**

data(enrich.df)

**Details**

To construct this dataset, predicted interactions, generated from *pred_ensembl* was used as data input for *enrichplot*.

enrichfindP

Functional Enrichment Analysis for Pathogen Interactors in the High-Confidence Network.

**Description**

This function uses *gost* function in *gprofiler2* package to perform functional enrichment analysis for pathogen interactors in the high-confidence network.

**Usage**

enrichfindP(
  ppi,
  threshold = 0.05,
  sources = c("GO", "KEGG"),
  p.correction.method = "bonferroni",
  org = "hsapiens"
)

**Arguments**

- **ppi**
  A data.frame containing pathogen proteins in the first column and host proteins in the second column.
- **threshold**
  Custom p-value threshold for significance.
- **sources**
  A vector of data sources to use. See *gost* for more details.
- **p.correction.method**
  The algorithm used for multiple testing correction; defaults to 'bonferroni'. See *gost* for more details.
- **org**
  An organism name; defaults to 'hsapiens'. See *gost* for more details.
Details

enrichfindP

Value

A data.frame with the enrichment analysis results.

Author(s)

Matineh Rahmatbakhsh, <matinerb.94@gmail.com>

See Also

See enrichplot for plotting enrichment analysis.

Examples

data('predicted_PPIs')
#perform enrichment
enrich.df <- enrichfindP(predicted_PPIs, 
threshold = 0.05, 
sources = c("GO", "KEGG"), 
p.correction.method = "bonferroni", 
org = "hsapiens")

---

enrichfind_cpx  
Functional Enrichment Analysis for Predicted Modules

Description

This function uses gost function in gprofiler2 package to perform functional enrichment analysis for predicted modules.

Usage

enrichfind_cpx( 
predcpx, 
threshold = 0.05, 
sources = c("GO", "KEGG"), 
p.correction.method = "bonferroni", 
org = "hsapiens" )
enrichfind_hp

**Arguments**

- **ppi**: A data.frame containing pathogen proteins in the first column and host proteins in the second column.
- **threshold**: Custom p-value threshold for significance.
- **sources**: A vector of data sources to use. See `gost` for more details.
- **p.correction.method**: The algorithm used for multiple testing correction; defaults to ‘bonferroni’. See `gost` for more details.
- **org**: An organism name; defaults to ‘hsapiens’. See `gost` for more details.

**Details**

enrichfind_cpx

**Value**

A data.frame with the enrichment analysis results.

**Author(s)**

Matineh Rahmatbakhsh, <matinerb.94@gmail.com>

---

**Description**

This function uses `gost` function in `gprofiler2` package to perform functional enrichment analysis for all predicted host proteins in the high-confidence network.

**Usage**

```r
enrichfind_hp(
  ppi,
  threshold = 0.05,
  sources = c("GO", "KEGG"),
  p.correction.method = "bonferroni",
  org = "hsapiens"
)
```

**Arguments**

- **ppi**: A data.frame containing pathogen proteins in the first column and host proteins in the second column.
- **threshold**: Custom p-value threshold for significance.
- **sources**: A vector of data sources to use. See `gost` for more details.
p.correction.method

The algorithm used for multiple testing correction; defaults to 'bonferroni'. See gost for more details.

org

An organism name; defaults to 'hsapiens'. See gost for more details.

Details

enrichfind_hp

Value

A data.frame with the enrichment analysis results.

Author(s)

Matineh Rahmatbakhsh, <matinerb.94@gmail.com>

See Also

See enrichplot for plotting enrichment analysis.

Examples

data('predicted_PPIs')
# perform enrichment
enrich.df <- enrichfind_hp(predicted_PPIs, threshold = 0.05, sources = c("GO", "KEGG"), p.correction.method = "bonferroni", org = "hsapiens")

enrichplot low = "blue", high = "red", cex.size = 15

Description

This function plots the enrichment result.

Usage

enrichplot(x, low = "blue", high = "red", cex.size = 15)

Arguments

x A data.frame with the enrichment analysis results.
low Colours for low.
high Colours for high.
cex.size Text size.
example_data

Details

enrichplot

Value

An enrichment plot.

Author(s)

Matineh Rahmatbakhsh, <matinerb.94@gmail.com>

See Also

See enrichfindP for functional enrichment analysis.

Examples

data('enrich.df')
# select enrichment for one of the example (e.g., E protein)
enrich.df <-
enrich.df[enrich.df$id == "E:P0DTC4", ]
enrichplot(enrich.df, low = "blue", high = "red", cex.size = 10)

example_data

Input Data for Prediction Algorithm

Description

Input data for pred_ensembel

Usage

data(example_data)

Format

a data.frame containing unlabeled or labeled HP-PPIs and pre-computed numerical features.
**filter_missing_values**  
*Drop the Missing Values Above a Certain Threshold*

**Description**
Given an input matrix, compute the missingness rate for each features and keep only features with missing rate more than user-defined percentage.

**Usage**
```
filter_missing_values(x, max_miss_rate = 20)
```

**Arguments**
- `x`: A numeric matrix as input.
- `max_miss_rate`: Maximal missing rate allowed for a feature; default is 20.

**Details**
- `filter_missing_values`

**Value**
A dataframe with features with missingness rate of more than user-defined threshold.

**Author(s)**
Matineh Rahmatbakhsh, <matinerb.94@gmail.com>

**Examples**
```
x <- matrix(1:10, ncol = 2)
x[, 2] <- NA
filter_missing_values(x, 30)
```

---

**FreqInteractors**  
*Plot the Pathogen Proteins’ frequency of Interactions with Host Proteins*

**Description**
This function plots the pathogen proteins’ Frequency of interactions with host proteins

**Usage**
```
FreqInteractors(ppi, cex.size = 12)
```
Arguments

ppi   A data.frame containing pathogen proteins in the first column and host proteins in the second column.
cex.size Text size.

Details
FreqInteractors

Value
A frequency plot.

Author(s)
Matineh Rahmatbakhsh, <matinerb.94@gmail.com>

Examples

```r
ppi <- data.frame(
  node2 = c("C", "E", "D", "F", "G", "H", "I")
)
FreqInteractors(ppi)
```

Description

This function performs feature selections via two approaches

- filter.corr - compute matrix correlation between features and filter using a threshold.
- rfeFS - perform recursive feature elimination (RFE) method wrapped with a Random Forest (RF) algorithm for feature importance evaluation.

Usage

```r
FSmethod(
  x, 
  type = c("cor", "rfe", "both"),
  cor.cutoff = 0.7,
  resampling.method = "cv",
  iter = 2,
  repeats = 3,
  metric = "Accuracy",
  verbose = TRUE
)
```
Arguments

x          A data.frame containing protein-protein interactions, class labels and features.
type       The feature selection type, one or two of filter.corr and rfeFS.
cor.cutoff Correlation coefficient cutoff used for filtering. See filter.corr for more details.
resampling.method
            The resampling method for RFE : 'boot', 'boot632', optimism_boot',boot_all',
            'cv', 'repeatedcv', 'LOOCV', 'LGOCV'; defaults to cv. See rfeFS and rfeControl
            for more details.
iter       Number of partitions for cross-validation; defaults to 2. See rfeFS and rfeControl
            for more details.
repeats    For repeated k-fold cross validation only; defaults to 3. See rfeFS and rfeControl
            for more details.
metric     A string that specifies what summary metric will be used to select the optimal
            feature ; default to ROC. See rfeFS and rfe for more details.
verbose    Make the output verbose. See rfeFS and rfeControl for more details.

Details

FSmethod

Value

If the type set to filter.corr, the output includes the following elements:

• corProfile - A correlation matrix.
• corSelectedFeatures - Name of features that retained after the correlation analysis.
• cordf - A data.frame filtered.

If the type set to rfeFS, the output includes the following elements:

• rfProfile - A list of elements. See rfe for more details.
• rfSelectedFeatures - Name of features that retained in the feature selection process.
• rfdf - A data.frame filtered.

If type set to both the output includes the following elements:

• rfdf - The final data.frame that includes the selected features retained after both filter.corr
          and rfeFS analysis.

Author(s)

Matineh Rahmatbakhsh, <matinerb.94@gmail.com>.
getFASTA

Examples

data('example_data')
x <- na.omit(example_data)
s <- FSmethod(x, type = 'both',
cor.cutoff = 0.7, resampling.method = "repeatedcv",
iter = 5, repeats = 3, metric = "ROC", verbose = TRUE)

getFASTA

Fetch FASTA Sequence from the UniProt Database

Description

This function retrieves protein sequences in FASTA format directly from the UniProt database via UniProt protein IDs. This function also checks if the amino-acid composition of protein sequences is in the 20 default types.

Usage

getFASTA(uniprot.id, filename = "FASTA.RData", path = "FASTASeq")

Arguments

uniprot.id A character vector of UniProt identifiers.
filename A character string, indicating the output filename as an RData object to store the retrieved sequences.
path A character string indicating the path to the project directory that contains the interaction data. If the directory is missing, it will be stored in the current directory. Default is FASTASeq.

Details

getFASTA

Value

A list containing protein FASTA sequences.

Author(s)

Matineh Rahmatbakhsh, <matinerb.94@gmail.com>

Examples

# get fasta sequences for three proteins of SARS-Cov-2
local = tempfile()
uniprot.id <- c("P0DTC4", "P0DTC5", "P0DTC9")
fasta_df <- getFASTA(uniprot.id, filename = "FASTA.RData", path = local)
head(fasta_df)
getHPI

Generating Host-Pathogen Protein-Protein Interaction (HP-PPI) Descriptors

Description

This function calculates Host-Pathogen Protein-Protein Interaction (HP-PPI) descriptors via two approaches

- **combine** - combine the two descriptor matrix, result has \((p1 + p2)\) columns
- **kron.prod** - if A has \(m \times n\) matrix and B is \(q \times p\) matrix, then the Kronecker product is the code\((pm \times qn)\) block matrix

Usage

getHPI(pathogenData, hostData, type = c("combine", "kron.prod"))

Arguments

- **pathogenData** The pathogen descriptor matrix.
- **hostData** The host descriptor matrix.
- **type** The interaction type, one or two of "combine" and "kron.prod".

Details

getHPI

Value

A matrix containing the Host-Pathogen Protein-Protein Interaction (HP-PPI) descriptors.

Author(s)

Matineh Rahmatbakhsh <matinerb.94@gmail.com>

Examples

```r
x <- matrix(c(1, 2, 3, 1), nrow = 2, ncol = 2, byrow = TRUE)
y <- matrix(c(0, 3, 2, 1), nrow = 2, ncol = 2, byrow = TRUE)
getHPI(x, y, "combine")
getHPI(x, y, "kron.prod")
```
Construct Negative Reference Host-Pathogen Protein-Protein Interactions (HP-PPIs)

Description

Construct true negative protein-protein interactions from the positive interactions. In the context of PPI prediction, a negative interaction is a pair of proteins that unlikely to interact. Since there is no experimentally verified non-interacting pair, the negative sampling can be used to construct the negative reference set. The negative sampling can be constructed from a set of host proteins, a set of pathogen proteins, and a list of positive reference interactions between members of host and pathogen proteins (Eid et al., 2016).

Usage

get_negativePPI(prot1, prot2, TPset)

Arguments

prot1 A character vector containing pathogen proteins.
prot2 A character vector containing host proteins.
TPset A character vector containing positive reference interactions.

Details

get_negativePPI

Value

A Data.frame containing true negative interactions.

Author(s)

Matineh Rahmatbakhsh, <matinerb.94@gmail.com>

References


See Also

See get_positivePPI for generating positive protein-protein interaction.
Examples

prot1 <- c("P0DTC4", "P0DTC5", "P0DTC9")
prot2 <- c("Q9Y679", "Q9NW15", "Q9NXF8")
TPset <- c("P0DTC4~P31948", "P0DTC8~Q13438")
TN_PPI <- get_negativePPI(prot1, prot2, TPset)
head(TN_PPI)

get_positivePPI

Fetch Positive Reference Host-Pathogen Protein-Protein Interactions (HP-PPIs) from the BioGRID Database

Description

This function retrieves positive reference host-pathogen protein-protein interactions directly from BioGRID database.

Usage

get_positivePPI(
  organism.taxID,
  access.key,
  filename = "PositiveInt.RData",
  path = "PositiveInt"
)

Arguments

organism.taxID Taxonomy identifier for the pathogen.
access.key Access key for using BioGRID webpage. To retrieve interactions from the BioGRID database, the users are first required to register for access key at https://webservice.thebiogrid.org/.
filename A character string, indicating the output filename as an RData object to store the retrieved interactions.
path A character string indicating the path to the project directory that contains the interaction data. If the directory is missing, it will be stored in the current directory. Default is PositiveInt.

Details

get_positivePPI

Value

A Data.frame containing true positive protein-protein interactions for the selected pathogen.
Description

This dataset consists of experimentally validated human-SARS-CoV-2 interactions (positive set) and non-interacting pairs (negative set). The following data consists of:

- PPI: SARS-CoV-2-human protein-protein interactions (PPIs)
- Official Symbol Interactor A: SARS-CoV-2 gene names
- official Symbol Interactor B: human host gene names
- Pathogen_Protein: UniProt identifiers for SARS-CoV-2 virus
- Host_Protein: UniProt identifiers for human proteins
- class: labeled examples (both positive and negative)

Usage

data(Gold_ReferenceSet)

Format

a data.frame containing 500 validated pairs (i.e., positive set) and 500 non-interacting pairs (i.e., negative set).

Details

To construct this dataset, validated interactions (positive set) were retrieved from BioGrid database and were further filtered to only include those interactions provided by (Samavarchi-Tehrani et al., 2020). In this study, the authors mapped interaction between 27 SARS-CoV-2 and human proteins via the proximity-dependent biotinylation (BioID) approach. 500 SARS-CoV-2-host interaction pairs then randomly selected from all pairs to serve as positive examples. To construct negative examples, negative sampling were used using get_positivePPI.
Source
https://www.biorxiv.org/content/10.1101/2020.09.03.282103v1

References

---

`host_se`  
*Host SummarizedExperiment object*

Description
SummarizedExperiment object of numerical features for host proteins.

Usage
`data(host_se)`

Details
To construct this object, first protein sequences were converted to numerical features using (CTD) descriptors provided in the HPiP package, followed by converting each numerical features matrix to SummarizedExperiment object. Each object is then merged into one object using `cbind()`.

---

`impute_missing_data`  
*Impute missing Values per Features (i.e., Columns)*

Description
Given an input matrix, impute the missing values via three approaches including mean, median or zero.

Usage
`impute_missing_data(x, method = c("mean", "median", "zero"))`

Arguments
- `x`: A numeric matrix as input.
- `method`: Imputation method for missing values (mean, median or zero).

Details
`impute_missing_data`
Value

Imputed matrix.

Author(s)

Matineh Rahmatbakhsh <matinerb.94@gmail.com>

Examples

```r
x <- matrix(1:10, ncol = 2)
x[1:3, 2] <- NA
row.names(x) <- c("A", "B", "C", "D", "E")
colnames(x) <- c("col1", "col2")
impute_missing_data(x, method = "mean")
impute_missing_data(x, method = "median")
impute_missing_data(x, method = "zero")
```

---

**plotPPI**

*Plot the Predicted PPI*

Description

Plot the predicted PPIs. This function uses the plot function of the igraph.

Usage

```r
plotPPI(
  ppi,
  edge.name = "ensemble_score",
  node.color = "grey",
  edge.color = "orange",
  cex.node = 4,
  node.label.dist = 1.5
)
```

Arguments

- **ppi**: A data.frame containing protein-protein interactions with edge score.
- **edge.name**: A character string giving an edge attribute name.
- **node.color**: The fill color of the node.
- **edge.color**: The color of the edge.
- **cex.node**: The size of the node.
- **node.label.dist**: The distance of the label from the center of the node.
Details

plotPPI

Value

A PPI plot.

Author(s)

Matineh Rahmatbakhsh, <matinerb.94@gmail.com>

Examples

```r
df <- data.frame(
    node1 = c("A", "B", "C", "D", "E"),
    node2 = c("C", "E", "E", "E", "A"),
    edge.scores = c(0.5, 0.4, 0.3, 0.2, 0.7)
)
plotPPI(df, edge.name = "edge.scores")
```

---

### predicted_PPIs

**Predicted HP-PPIs**

---

**Description**

Input data for `enrichfindP`.

**Usage**

```r
data(predicted_PPIs)
```

---

### pred_ensembl

**Predict Interactions via Ensemble Learning Method**

---

**Description**

This function uses an ensemble of classifiers to predict interactions from the sequence-based dataset. This ensemble algorithm combines different results generated from individual classifiers within the ensemble via average to enhance prediction.
pred_ensemble

Usage

```r
pred_ensemble(
  features,
  gold_standard,
  classifier = c("avNNet", "svmRadial", "ranger"),
  resampling.method = "cv",
  ncross = 2,
  repeats = 2,
  verboseIter = TRUE,
  plots = TRUE,
  filename = "plots.pdf"
)
```

Arguments

- **features**: A data frame with host-pathogen protein-protein interactions (HP-PPIs) in the first column, and features to be passed to the classifier in the remaining columns.
- **gold_standard**: A data frame with gold_standard HP-PPIs and class label indicating if such PPIs are positive or negative.
- **classifier**: The type of classifier to use. See caret for the available classifiers.
- **resampling.method**: The resampling method: 'boot', 'boot632', 'optimism_boot', boot_all', 'cv', 'repeatedcv', 'LOOCV', 'LGOCV'; defaults to cv. See trainControl for more details.
- **ncross**: Number of partitions for cross-validation; defaults to 5. See trainControl for more details.
- **repeats**: for repeated k-fold cross validation only; defaults to 3. See rfeControl for more details.
- **verboseIter**: Logical value, indicating whether to check the status of training process; defaults to FALSE.
- **plots**: Logical value, indicating whether to plot the performance of ensemble learning algorithm as compared to individual classifiers; defaults to TRUE. If the argument set to TRUE, plots will be saved in the current working directory. These plots are:
  - pr_plot: Precision-recall plot of ensemble classifier vs selected individual classifiers.
  - roc_plot: ROC plot of ensemble classifier vs selected individual classifiers.
  - points_plot: Plot accuracy, F1-score, positive predictive value (PPV), sensitivity (SE), and Matthews correlation coefficient (MCC) of ensemble classifier vs selected individual classifiers.
- **filename**: A character string, indicating the output filename as a pdf object.

Details

pred_ensemble
Value

Ensemble_training_output

- prediction score - Prediction scores for whole dataset from each individual classifier.
- Best - Selected hyper parameters.
- Parameter range - Tested hyper parameters.
- prediction_score_test - Scores probabilities for test data from each individual classifier.
- class_label - Class probabilities for test data from each individual classifier.

classifier_performance

- cm - A confusion matrix.
- ACC - Accuracy.
- SE - Sensitivity.
- SP - Specificity.
- PPV - Positive Predictive Value.
- F1 - F1-score.
- MCC - Matthews correlation coefficient.
- Roc_Object - A list of elements. See roc for more details.
- PR_Object - A list of elements. See pr.curve for more details.

predicted_interactions - The input data frame of pairwise interactions, including classifier scores averaged across all models.

Author(s)

Matineh Rahmatbakhsh, <matinerb.94@gmail.com>

Examples

data('example_data')
features <- example_data[, -2]
gd <- example_data[, c(1,2)]
gd <- na.omit(gd)
ppi <- pred_ensembel(features, gd,
classifier = c("avNNet", "svmRadial", "ranger"),
resampling.method = "cv", n.cross = 2, verboseIter = FALSE, plots = FALSE,
filename = "plots.pdf")
#extract predicted interactions
pred_interaction <- ppi[["predicted_interactions"]]

run_clustering

**Module Detection**

**Description**

This function contains five module detection algorithms including fast-greedy algorithm (FC), walktrap algorithm (RW), multi-level community algorithm (ML), label propagation algorithm (clp), and markov clustering (MCL).

**Usage**

```r
run_clustering(
  ppi,
  method = c("FC", "RW", "ML", "clp", "MCL"),
  expan = 2,
  infla = 5,
  iter = 50
)
```

**Arguments**

- **ppi**
  A data.frame containing pathogen proteins in the first column, host proteins in the second column, and edge weight in the third column.

- **method**
  Module detection algorithms including:
  - FC - fast-greedy algorithm.
  - RW - walktrap algorithm.
  - ML - multi-level community algorithm.
  - clp - label propagation algorithm.
  - MCL - markov clustering.

- **expan**
  Numeric value > 1 for the expansion parameter. See `mcl` for more details.

- **infla**
  Numeric value > 0 for the inflation power coefficient. See `mcl` for more details.

- **iter**
  An integer, the maximum number of iterations for the MCL. See `mcl` for more details.

**Details**

run_clustering

**Value**

A data.frame with the enrichment analysis results.

**Author(s)**

Matineh Rahmatbakhsh, <matinerb.94@gmail.com>
**unlabel_data**
*HP-PPIs with Unknown Class Labels*

**Description**
This dataset consists of interactions between SARS-CoV-2 and human proteins, achieved by AP-MS (affinity purification mass spectrometry).

**Usage**
```r
data(unlabel_data)
```

**Format**
A data.frame containing 700 SARS-CoV-2-Human protein-protein interactions (PPIs) with pre-computed numerical features using CTD (composition/transition/distribution) descriptors.

**Details**
To construct this dataset, data (supplementary table 1) containing SARS-CoV-2-human PPIs was retrieved from (Gordon et al., 2020) and 700 pairs were randomly selected from total pairs, followed by converting protein sequences of host or viral proteins to numerical features and finally concatenating the computed features in order to construct host-pathogen PPIs.

**Source**
https://www.nature.com/articles/s41586-020-2286-9#Sec36

**References**

---

**UP000464024_df**
*Data.frame Containing SARS-CoV-2 FASTA Sequences*

**Description**
This data includes one protein sequence per SARS-CoV-2 gene, retrieved directly from UniProt database using `getFASTA`.

**Usage**
```r
data(UP000464024_df)
```
**var_imp**

**Format**

A data.frame with two columns: (1) UniprotKBID, UniProt identifier. (2) FASTASEQ, sequences per SARS-CoV-2 gene.

**Source**

https://www.uniprot.org/uniprot/?query=proteome:UP000464024

---

| var_imp | Variable Importance Plot |

**Description**

A graphical display of variable importance of selected features.

**Usage**

```r
var_imp(x, cex.x = 1, cex.y = 2)
```

**Arguments**

- `x` A list of elements returned from RFE analysis. See `rfe` for more details
- `cex.x` The size of x axis label.
- `cex.y` The size of y axis label.

**Details**

`var_imp`

**Value**

Variable Importance Plot.

**Author(s)**

Matineh Rahmatbakhsh, <matinerb.94@gmail.com>.

**Examples**

```r
data('example_data')
x <- na.omit(example_data)
# perform feature selection
s <- FSmethod(x, type = 'both',
cor.cutoff = 0.7, resampling.method = "repeatedcv",
iter = 5, repeats = 3, metric = "ROC", verbose = TRUE)
var_imp(s$rf.result$rfProfile, cex.x = 10, cex.y = 10)
```
viral_se

Viral SummarizedExperiment object

Description

SummarizedExperiment object of numerical features for SARS-CoV-2 proteins.

Usage

data(viral_se)

Details

To construct this object, first protein sequences were converted to numerical features using (CTD) descriptors provided in the HPiP package, followed by converting each numerical features matrix to SummarizedExperiment object. Each object is then merged into one object using `cbind()`.
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