

Package ‘PheVis’

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Type Package

Title Automatic Phenotyping of Electronic Health Record at Visit Resolution

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Description Using Electronic Health Record (EHR) is difficult because most of the time the true characteristic of the patient is not available. Instead we can retrieve the International Classification of Disease code related to the disease of interest or we can count the occurrence of the Unified Medical Language System. None of them is the true phenotype which needs chart review to identify. However chart review is time consuming and costly. 'PheVis' is an algorithm which is phenotyping (i.e identify a characteristic) at the visit level in an unsupervised fashion. It can be used for chronic or acute diseases. An example of how to use 'PheVis' is available in the vignette. Basically there are two functions that are to be used: ``train_phevis()`` which trains the algorithm and ``test_phevis()`` which get the predicted probabilities. The detailed method is described in preprint by Ferté et al. (2020) <[doi:10.1101/2020.06.15.20131458](https://doi.org/10.1101/2020.06.15.20131458)>.

License GPL (>= 2)

Depends R (>= 3.5.0)

Imports dplyr, ggplot2, glmnet, knitr, lme4, purrr, randomForest, Rcpp (>= 1.0.3), stats, tidyr, viridis, zoo

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boot_df	<i>boot_df</i>
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Description

Sample rows with replacement from a matrix

Usage

```
boot_df(x_matrix, y_sur, ID = NULL, size = 10^5, seed = 1, prob = NULL)
```

Arguments

x_matrix	matrix to perform sampling on
y_sur	The numeric vector of the qualitative surrogate.
ID	The patient ID
size	size of matrix returned
seed	seed for sampling
prob	Vector for weight sampling

Value

A list with the sampled explanatory matrix and the sampled qualitative surrogate (y_sur)

build_qantsur	<i>build_qantsur</i>
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Description

build quantile threshold based on icd variables and omega constant

Usage

```
build_qantsur(df, var.icd, omega)
```

Arguments

df	the dataframe containing the icd codes.
var.icd	the main icd codes
omega	the constant to define the extrema populations

Value

A numeric vector with the thresholds for the extrema populations.

build_quali	<i>build_quali</i>
-------------	--------------------

Description

build_quali

Usage

```
build_quali(x, p, q)
```

Arguments

x	A numeric vector
p	The lower quantile
q	The upper quantile

Value

The qualitative surrogate (x in three categories) defining the extrema populations

check_arg_test_phevis *check_arg_test_phevis*

Description

Function to check arguments passed to test_phevis()

Usage

```
check_arg_test_phevis(  
  train_param,  
  df_test,  
  surparam,  
  model,  
  START_DATE,  
  PATIENT_NUM,  
  ENCOUNTER_NUM  
)
```

Arguments

train_param	Parameters for the model training (variables used, main ICD and CUIS, half_life, gold standard, omega). Usually obtained from train_phevis() function.
df_test	The dataframe on which to make the prediction.
surparam	The parameters used to compute the surrogate. Usually obtained by train_phevis() function.
model	The random intercept logistic regression. Usually obtained by train_phevis() function.
START_DATE	Column name of the time column. The time column should be numeric
PATIENT_NUM	Column name of the patient id column.
ENCOUNTER_NUM	Column name of the encounter id column.

Value

No return value, stop the code execution if one condition is not met.

```
check_arg_train_phevis
      check_arg_train_phevis
```

Description

Function to check arguments passed to train_phevis()

Usage

```
check_arg_train_phevis(
  half_life,
  df,
  START_DATE,
  PATIENT_NUM,
  ENCOUNTER_NUM,
  var_vec,
  main_icd,
  main_cui,
  rf,
  p.noise,
  bool_SAFE,
  omega,
  GS
)
```

Arguments

half_life	Duration of cumulation. For a chronic disease you might chose Inf, for acute disease you might chose the duration of the disease.
df	data.frame containing all the variables.
START_DATE	Column name of the time column. The time column should be numeric
PATIENT_NUM	Column name of the patient id column.
ENCOUNTER_NUM	Column name of the encounter id column.
var_vec	Explanatory variables used for the prediction, including the main variables.
main_icd	Character vector of the column names of the main ICD codes.
main_cui	Character vector of the column names of the main CUIs.
rf	should pseudo-labellisation with random forest be used (default is true)
p.noise	percentage of noise introduced during the noising step (default is 0.3)
bool_SAFE	A boolean. If TRUE, SAFE selection is done, else it is not (default is TRUE)
omega	Constant for the extrema population definition (default is 2)
GS	Character string corresponding to the name of the gold-standard variable (default is null for which a vector of 0 will be taken).

Value

No return value, stop the code execution if one condition is not met.

cum_lag	<i>cum_lag</i>
---------	----------------

Description

helpful function to cumulate information.

Usage

```
cum_lag(x, n_lag)
```

Arguments

x	numeric vector for which lag variable should be computed
n_lag	size of lag window

Value

return numeric vector.

data_perf	<i>Control data for test</i>
-----------	------------------------------

Description

Simulated dataset for PheVis phenotyping.

Usage

```
data(data_perf)
```

Format

An object of class `numeric` of length 2.

data_phevis	<i>PheVis simulated dataset</i>
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Description

Simulated dataset for PheVis phenotyping.

Usage

```
data(data_phevis)
```

Format

An object of class `data.frame` with 19659 rows and 15 columns.

expcorrectC	<i>expcorrectC</i>
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Description

c++ function to compute exponential cumulation of information.

Usage

```
expcorrectC(mat, diffdate, lambda)
```

Arguments

mat	A matrix where each column is a variable to be cumulated.
diffdate	Number of days between each sojourn. NA for switch of patient and restart cumulation.
lambda	A double to set the exponential cumulation.

Details

```
expcorrectC
```

Value

A matrix corresponding to the `mat` argument with cumulated exponential decay

fct_surrogate_quanti *fct_surrogate_quanti*

Description

Compute the quantitative surrogate and then apply thresholds to get the qualitative surrogate.

Usage

```
fct_surrogate_quanti(
  main_icd,
  main_cui,
  df,
  half_life,
  date,
  patient_id,
  encounter_id,
  omega = 2,
  param = NULL
)
```

Arguments

main_icd	Character vector of the column names of the main ICD codes.
main_cui	Character vector of the column names of the main CUIs.
df	Dataframe containing all variables.
half_life	Duration of accumulation. For a chronic disease you might chose Inf, for acute disease you might chose the duration of the disease.
date	Column name of the time column. The time column should be numeric
patient_id	Column name of the patient id column.
encounter_id	Column name of the encounter id column.
omega	Constant for the extrema population definition.
param	param of a previous train_phevis() result.

Value

A list

- table - Main result: data.frame with the rolling variables and the surrogates
- param - the parameters for the standardisation of ICD and CUI
- roll_all - a subset of table with the rolling variables only
- quantile_vec - the quantile defining the extrema populations

ggindividual_plot *ggindividual_plot*

Description

Plot individual predictions.

Usage

```
ggindividual_plot(subject, time, gold_standard, prediction)
```

Arguments

subject	numeric vector subject id
time	numeric vector time or date
gold_standard	numeric vector of gold standard
prediction	numeric vector of prediction

Value

a ggplot graph

Examples

```
ggindividual_plot(subject = rep(1,10),  
  time = 1:10,  
  gold_standard = c(0,0,1,1,0,0,1,1,0,0),  
  prediction = runif(n = 10, min = 0, max = 1))
```

matrix_exp_smooth *matrix_exp_smooth*

Description

Function to accumulate the information with exponential decay.

Usage

```
matrix_exp_smooth(half_life, df, date, patient_id, encounter_id)
```

Arguments

half_life	Duration of accumulation. For a chronic disease you might chose Inf, for acute disease you might chose the duration of the disease.
df	Dataframe of the explanatory variables.
date	Vector of date. The date should be in a numeric format.
patient_id	The vector of patient id
encounter_id	The vector of visit id

Value

A data.frame object with both the raw variables and the accumulated ones.

noising	<i>noising</i>
---------	----------------

Description

Noise a matrix

Usage

```
noising(X_boot, p = 0.3)
```

Arguments

X_boot	matrix to perform noise on
p	amount of noise

Value

A noised matrix

norm_var	<i>norm_var</i>
----------	-----------------

Description

Standardize a numeric variable

Usage

```
norm_var(x)
```

Arguments

x A numeric variable

Value

The standardized variable

phenorm_longit_fit *phenorm_longit_fit*

Description

Apply simplified 'PheNorm' algorithm on longitudinal data with bootstrap and noise.

Usage

```
phenorm_longit_fit(
  x_matrix,
  y_sur,
  ID,
  size = 10^5,
  seed = 1,
  p.noise = 0.3,
  do_sampling = TRUE,
  do_noise = TRUE,
  prob = NULL,
  calc.prob = TRUE,
  nAGQ = 0,
  glmer.control = glmerControl(optimizer = "bobyqa", optCtrl = list(maxfun = 2e+05))
)
```

Arguments

x_matrix	x matrix to sample, noise and predict on
y_sur	surrogate with 3 values (0 and 1 the extremes and 3 middle patients)
ID	Vector of patient ID
size	size of sampling. default is 10^5
seed	seed. default is 1.
p.noise	noise probability parameter. default is .3.
do_sampling	should algorithm do sampling. default is TRUE.
do_noise	should algorithm do noise. default is TRUE.
prob	sampling probability during noising denoising step
calc.prob	should the 'prob' argument be calculated
nAGQ	glmer parameter
glmer.control	glmer parameter

Value

A list with the fixed effects, the predicted responses and the model used (mixed effect or logistic regression)

phenorm_longit_simpl *phenorm_longit_simpl*

Description

'PheNorm' like function adapted to longitudinal data.

Usage

```
phenorm_longit_simpl(
  df,
  var_surrogate,
  surrogates_quali,
  id_rnd,
  rf = FALSE,
  ntree = 100,
  bool_weight = FALSE,
  p.noise = 0.3,
  bool_SAFE = TRUE,
  size = 10^5
)
```

Arguments

<code>df</code>	dataframe
<code>var_surrogate</code>	variables used for building the surrogates
<code>surrogates_quali</code>	numeric vector of the qualitative surrogate
<code>id_rnd</code>	ID for random effect
<code>rf</code>	should pseudo-labellisation with random forest be used (default is FALSE)
<code>ntree</code>	number of tree for randomforest (default is 100)
<code>bool_weight</code>	should the sampling probability balance the number of positive and negative extrema.
<code>p.noise</code>	percentage of noise introduced during the noising step
<code>bool_SAFE</code>	A boolean. If TRUE, SAFE selection is done, else it is not (default is TRUE)
<code>size</code>	minimum size of sampling

Value

A list with the logistic model, the random forest model, the variables selected for prediction and the predictions

```
pred_lme4model      pred_lme4model
```

Description

function to predict probability from 'lme4' or 'glm' objects

Usage

```
pred_lme4model(model = NULL, fe.model = NULL, df)
```

Arguments

model	lme4 model
fe.model	the fixed effect of a model
df	dataframe for prediction

Value

A vector of the predictions

```
pretty_cv.glmnet      pretty_cv.glmnet
```

Description

Train a 'glmnet' with cross validation (cv) model and return convenient results (model and results with non zero coefficients)

Usage

```
pretty_cv.glmnet(
  x_glmnet,
  y,
  alpha = 1,
  family = "binomial",
  s = "lambda.1se",
  weights = rep(1, nrow(x_glmnet)),
  ...
)
```

Arguments

<code>x_glmnet</code>	Independent variable matrix (X)
<code>y</code>	Dependent variable vector (Y)
<code>alpha</code>	alpha parameter of glmnet (default = 1)
<code>family</code>	family parameter of glmnet (default = "binomial")
<code>s</code>	lambda chosen from cv.glmnet (default = "lambda.1se")
<code>weights</code>	glmnet parameter
<code>...</code>	additional parameters passed to glmnet

Value

A list with the model, the coefficient associated with variables and the selected variables.

<code>rolling_var</code>	<i>rolling_var</i>
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Description

Compute rolling variables (last visit, last 5 visits, last month and last year)

Usage

```
rolling_var(id, var, start_date, id_encounter)
```

Arguments

<code>id</code>	Patient id numeric vector
<code>var</code>	Variable numeric vector
<code>start_date</code>	Time numeric vector
<code>id_encounter</code>	Encounter id vector

Value

A dataframe containing the rolling variables.

roll_time_sum	<i>roll_time_sum</i>
---------------	----------------------

Description

Compute the cumulated information of what happened in past month and past year.

Usage

```
roll_time_sum(  
  id,  
  id_encounter,  
  var,  
  start_date,  
  win_size1 = 30,  
  win_size2 = 365,  
  name1 = "cum_month",  
  name2 = "cum_year"  
)
```

Arguments

id	Patient id numeric vector
id_encounter	Encounter id vector
var	Variable numeric vector
start_date	Time numeric vector
win_size1	First window size (default is 30)
win_size2	Second window size (default is 365)
name1	name of first rolling var (default is "cum_month")
name2	name of second rolling var (default is "cum_year")

Value

A dataframe containing the rolling variables.

safe_selection	<i>safe_selection</i>
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Description

Select the variables from dataframe by removing the rare variables and apply 'SAFE' on it.

Usage

```
safe_selection(
  df,
  var_surrogate,
  surrogate_quali,
  threshold = 0.05,
  alpha = 0.5,
  remove_var_surrogate = TRUE,
  bool_weight = FALSE,
  ...
)
```

Arguments

df	dataframe
var_surrogate	variables used for building the surrogates
surrogate_quali	surrogate with 3 values (0 and 1 the extremes and 3 middle patients)
threshold	rareness threshold (default = 0.05).
alpha	glmnet parameter (default is 0.5 elastic net)
remove_var_surrogate	does the glmnet algorithm should learn on features in var_surrogate (default is TRUE).
bool_weight	Should the glmnet function be weighted to balance the extrema populations (default is FALSE).
...	arguments to pass to pretty_cv.glmnet

Value

A list

- `glmnet_model` - A list of three elements: the `cv.glmnet` fitted model, the coefficients of non zero variables and the vector of non zero coefficient variables.
- `important_var` - A vector with the variables used for the surrogate and the non zero variables.
- `surrogate_quali` - The `surrogate_quali` argument.

sur_exp_smooth	<i>sur_exp_smooth</i>
----------------	-----------------------

Description

Function to cumulate surrogate with exponential decay

Usage

```
sur_exp_smooth(half_life, sur, date, patient_id, encounter_id)
```

Arguments

half_life	Duration of cumulation. For a chronic disease you might chose Inf, for acute disease you might chose the duration of the disease.
sur	The quantitative surrogate.
date	A numeric vector of time of days unit.
patient_id	Vector of patient ID
encounter_id	Vector of encounter ID

Value

A dataframe with the cumulated surrogate.

test_phevis	<i>test_phevis</i>
-------------	--------------------

Description

test_phevis

Usage

```
test_phevis(
  train_param,
  df_test,
  surparam,
  model,
  START_DATE,
  PATIENT_NUM,
  ENCOUNTER_NUM
)
```



```

test_perf <- PheVis::test_phevis(train_param = train_model$train_param,
                                df_test = df_test,
                                START_DATE = "time",
                                PATIENT_NUM = "subject",
                                ENCOUNTER_NUM = "ENCOUNTER_NUM",
                                surparam = train_model$surparam,
                                model = train_model$model)

pr_curve <- PRROC::pr.curve(scores.class0 = test_perf$df_result$PREDICTION,
                             weights.class0 = df_test$PR_state)

roc_curve <- PRROC::roc.curve(scores.class0 = test_perf$df_result$PREDICTION,
                               weights.class0 = df_test$PR_state)

```

train_phevis

train_phevis

Description

Global function to train phevis model.

Usage

```

train_phevis(
  half_life,
  df,
  START_DATE,
  PATIENT_NUM,
  ENCOUNTER_NUM,
  var_vec,
  main_icd,
  main_cui,
  rf = TRUE,
  p.noise = 0.3,
  bool_SAFE = TRUE,
  omega = 2,
  GS = NULL
)

```

Arguments

half_life	Duration of cumulation. For a chronic disease you might chose Inf, for acute disease you might chose the duration of the disease.
df	data.frame containing all the variables.
START_DATE	Column name of the time column. The time column should be numeric
PATIENT_NUM	Column name of the patient id column.

ENCOUNTER_NUM	Column name of the encounter id column.
var_vec	Explanatory variables used for the prediction, including the main variables.
main_icd	Character vector of the column names of the main ICD codes.
main_cui	Character vector of the column names of the main CUIs.
rf	should pseudo-labellisation with random forest be used (default is true)
p.noise	percentage of noise introduced during the noising step (default is 0.3)
bool_SAFE	A boolean. If TRUE, SAFE selection is done, else it is not (default is TRUE)
omega	Constant for the extrema population definition (default is 2)
GS	Character string corresponding to the name of the gold-standard variable (default is null for which a vector of 0 will be taken).

Value

A list

- surparam - the parameters used to compute the surrogate
- model - the random intercept logistic regression
- df_train_result - the data.frame containing the output predictions
- train_param - parameters for the model training (variables used, main ICD and CUIS, half_life, gold standard)

Examples

```
library(dplyr)
PheVis::data_phevis
df <- data_phevis %>%
  mutate(ENCOUNTER_NUM = row_number(),
         time = round(as.numeric(time)))
model <- PheVis::train_phevis(half_life = Inf,
                             df = df,
                             START_DATE = "time",
                             PATIENT_NUM = "subject",
                             ENCOUNTER_NUM = "ENCOUNTER_NUM",
                             var_vec = c(paste0("var",1:10), "mainCUI", "mainICD"),
                             main_icd = "mainICD",
                             main_cui = "mainCUI")
```

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