Package ‘vimp’

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Type Package

Title Perform Inference on Algorithm-Agnostic Variable Importance

Version 2.3.3

Description Calculate point estimates of and valid confidence intervals for nonparametric, algorithm-agnostic variable importance measures in high and low dimensions, using flexible estimators of the underlying regression functions. For more information about the methods, please see Williamson et al. (Biometrics, 2020), Williamson et al. (JASA, 2021), and Williamson and Feng (ICML, 2020).

Depends R (>= 3.1.0)

Imports SuperLearner, stats, dplyr, magrittr, ROCR, tibble, rlang, MASS, boot, data.table

Suggests knitr, rmarkdown, xgboost, glmnet, ranger, polspline, quadprog, covr, testthat, ggplot2, cowplot, cvAUC, tidyselect, WeightedROC, purrr

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BugReports https://github.com/bdwilliamson/vimp/issues

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Description

Average the output from multiple calls to `vimp_regression`, for different independent groups, into a single estimate with a corresponding standard error and confidence interval.

Usage

```r
average_vim(..., weights = rep(1/length(list(...)), length(list(...))))
```

Arguments

- `...` an arbitrary number of `vim` objects.
- `weights` how to average the vims together, and must sum to 1; defaults to 1/(number of vims) for each vim, corresponding to the arithmetic mean

Value

an object of class `vim` containing the (weighted) average of the individual importance estimates, as well as the appropriate standard error and confidence interval. This results in a list containing:

- `s` - a list of the column(s) to calculate variable importance for
- `SL.library` - a list of the libraries of learners passed to SuperLearner
- `full_fit` - a list of the fitted values of the chosen method fit to the full data
- `red_fit` - a list of the fitted values of the chosen method fit to the reduced data
- `est` - a vector with the corrected estimates
- `naive` - a vector with the naive estimates
- `update` - a list with the influence curve-based updates
- `mat` - a matrix with the estimated variable importance, the standard error, and the \((1 - \alpha) \times 100\%\) confidence interval
• full_mod - a list of the objects returned by the estimation procedure for the full data regression (if applicable)
• red_mod - a list of the objects returned by the estimation procedure for the reduced data regression (if applicable)
• alpha - the level, for confidence interval calculation
• y - a list of the outcomes

Examples

# generate the data
p <- 2
n <- 100
x <- data.frame(replicate(p, stats::runif(n, -5, 5)))

# apply the function to the x's
smooth <- (x[,1]/5)^2*(x[,1]+7)/5 + (x[,2]/3)^2

# generate Y ~ Normal (smooth, 1)
y <- smooth + stats::rnorm(n, 0, 1)

# set up a library for SuperLearner; note simple library for speed
library("SuperLearner")
learners <- c("SL.glm", "SL.mean")

# get estimates on independent splits of the data
samp <- sample(1:n, n/2, replace = FALSE)
est_2 <- vimp_regression(Y = y[samp], X = x[samp, ], indx = 2, V = 2,
run_regression = TRUE, alpha = 0.05,
SL.library = learners, cvControl = list(V = 2))
est_1 <- vimp_regression(Y = y[-samp], X = x[-samp, ], indx = 2, V = 2,
run_regression = TRUE, alpha = 0.05,
SL.library = learners, cvControl = list(V = 2))
est <- average_vim(est_1, est_2, weights = c(1/2, 1/2))
Usage

```
bootstrap_se(
  Y = NULL,
  f1 = NULL,
  f2 = NULL,
  cluster_id = NULL,
  clustered = FALSE,
  type = "r_squared",
  b = 1000,
  boot_interval_type = "perc",
  alpha = 0.05
)
```

Arguments

- `Y` the outcome.
- `f1` the fitted values from a flexible estimation technique regressing `Y` on `X`. A vector of the same length as `Y`; if sample-splitting is desired, then the value of `f1` at each position should be the result of predicting from a model trained without that observation.
- `f2` the fitted values from a flexible estimation technique regressing either (a) `f1` or (b) `Y` on `X` withholding the columns in `indx`. A vector of the same length as `Y`; if sample-splitting is desired, then the value of `f2` at each position should be the result of predicting from a model trained without that observation.
- `cluster_id` vector of the same length as `Y` giving the cluster IDs used for the clustered bootstrap, if `clustered` is `TRUE`.
- `clustered` should the bootstrap resamples be performed on clusters rather than individual observations? Defaults to `FALSE`.
- `type` the type of importance to compute; defaults to `r_squared`, but other supported options are `auc`, `accuracy`, `deviance`, and `anova`.
- `b` the number of bootstrap replicates (only used if `bootstrap = TRUE` and `sample_splitting = FALSE`); defaults to 1000.
- `boot_interval_type` the type of bootstrap interval (one of "norm", "basic", "stud", "perc", or "bca", as in `boot(boot.ci)`) if requested. Defaults to "perc".
- `alpha` the level to compute the confidence interval at. Defaults to 0.05, corresponding to a 95% confidence interval.

Value

a bootstrap-based standard error estimate
check_fitted_values  

Check pre-computed fitted values for call to vim, cv_vim, or sp_vim

Description

Check pre-computed fitted values for call to vim, cv_vim, or sp_vim

Usage

```r
check_fitted_values(
  Y = NULL,
  f1 = NULL,
  f2 = NULL,
  cross_fitted_f1 = NULL,
  cross_fitted_f2 = NULL,
  sample_splitting_folds = NULL,
  cross_fitting_folds = NULL,
  cross_fitted_se = TRUE,
  V = NULL,
  ss_V = NULL,
  cv = FALSE
)
```

Arguments

- **Y**: the outcome
- **f1**: estimator of the population-optimal prediction function using all covariates
- **f2**: estimator of the population-optimal prediction function using the reduced set of covariates
- **cross_fitted_f1**: cross-fitted estimator of the population-optimal prediction function using all covariates
- **cross_fitted_f2**: cross-fitted estimator of the population-optimal prediction function using the reduced set of covariates
- **sample_splitting_folds**: the folds for sample-splitting (used for hypothesis testing)
- **cross_fitting_folds**: the folds for cross-fitting (used for point estimates of variable importance in cv_vim and sp_vim)
- **cross_fitted_se**: logical; should cross-fitting be used to estimate standard errors?
- **V**: the number of cross-fitting folds
- **ss_V**: the number of folds for CV (if sample_splitting is TRUE)
- **cv**: a logical flag indicating whether or not to use cross-fitting
check_inputs

Details

Ensure that inputs to `vim`, `cv_vim`, and `sp_vim` follow the correct formats.

Value

None. Called for the side effect of stopping the algorithm if any inputs are in an unexpected format.

---

### check_inputs

Check inputs to a call to `vim`, `cv_vim`, or `sp_vim`

#### Description

Check inputs to a call to `vim`, `cv_vim`, or `sp_vim`

#### Usage

```r
check_inputs(Y, X, f1, f2, indx)
```

#### Arguments

- **Y**: the outcome
- **X**: the covariates
- **f1**: estimator of the population-optimal prediction function using all covariates
- **f2**: estimator of the population-optimal prediction function using the reduced set of covariates
- **indx**: the index or indices of the covariate(s) of interest

#### Details

Ensure that inputs to `vim`, `cv_vim`, and `sp_vim` follow the correct formats.

#### Value

None. Called for the side effect of stopping the algorithm if any inputs are in an unexpected format.
create_z

Create complete-case outcome, weights, and Z

Description
Create complete-case outcome, weights, and Z

Usage
create_z(Y, C, Z, X, ipc_weights)

Arguments
Y       the outcome
C       indicator of missing or observed
Z       the covariates observed in phase 1 and 2 data
X       all covariates
ipc_weights   the weights

Value
a list, with the complete-case outcome, weights, and Z matrix

cv_vim

Nonparametric Intrinsic Variable Importance Estimates and Inference using Cross-fitting

Description
Compute estimates and confidence intervals using cross-fitting for nonparametric intrinsic variable importance based on the population-level contrast between the oracle predictiveness using the feature(s) of interest versus not.

Usage
cv_vim(
    Y = NULL,
    X = NULL,
    cross_fitted_f1 = NULL,
    cross_fitted_f2 = NULL,
    f1 = NULL,
    f2 = NULL,
    indx = 1,
    V = ifelse(is.null(cross_fitting_folds), 5, length(unique(cross_fitting_folds)))),
sample_splitting = TRUE,
final_point_estimate = "split",
sample_splitting_folds = NULL,
cross_fitting_folds = NULL,
stratified = FALSE,
type = "r_squared",
run_regression = TRUE,
SL.library = c("SL.glmnet", "SL.xgboost", "SL.mean"),
alpha = 0.05,
delta = 0,
scale = "identity",
na.rm = FALSE,
C = rep(1, length(Y)),
Z = NULL,
ipc_scale = "identity",
ipc_weights = rep(1, length(Y)),
ipc_est_type = "aipw",
scale_est = TRUE,
nuisance_estimators_full = NULL,
nuisance_estimators_reduced = NULL,
exposure_name = NULL,
cross_fitted_se = TRUE,
bootstrap = FALSE,
b = 1000,
boot_interval_type = "perc",
clustered = FALSE,
cluster_id = rep(NA, length(Y)),
...
)

Arguments

Y 
the outcome.

X 
the covariates. If type = "average_value", then the exposure variable should be part of X, with its name provided in exposure_name.

cross_fitted_f1 
the predicted values on validation data from a flexible estimation technique regressing Y on X in the training data. Provided as either (a) a vector, where each element is the predicted value when that observation is part of the validation fold; or (b) a list of length V, where each element in the list is a set of predictions on the corresponding validation data fold. If sample-splitting is requested, then these must be estimated specially; see Details. However, the resulting vector should be the same length as Y; if using a list, then the summed length of each element across the list should be the same length as Y (i.e., each observation is included in the predictions).

cross_fitted_f2 
the predicted values on validation data from a flexible estimation technique regressing either (a) the fitted values in cross_fitted_f1, or (b) Y, on X with-
holding the columns in indx. Provided as either (a) a vector, where each element is the predicted value when that observation is part of the validation fold; or (b) a list of length V, where each element in the list is a set of predictions on the corresponding validation data fold. If sample-splitting is requested, these must be estimated specially; see Details. However, the resulting vector should be the same length as Y; if using a list, then the summed length of each element across the list should be the same length as Y (i.e., each observation is included in the predictions).

f1 the fitted values from a flexible estimation technique regressing Y on X. If sample-splitting is requested, then these must be estimated specially; see Details. If cross_fitted_se = TRUE, then this argument is not used.

f2 the fitted values from a flexible estimation technique regressing either (a) f1 or (b) Y on X withholding the columns in indx. If sample-splitting is requested, then these must be estimated specially; see Details. If cross_fitted_se = TRUE, then this argument is not used.

indx the indices of the covariate(s) to calculate variable importance for; defaults to 1.

V the number of folds for cross-fitting, defaults to 5. If sample_splitting = TRUE, then a special type of V-fold cross-fitting is done. See Details for a more detailed explanation.

sample_splitting should we use sample-splitting to estimate the full and reduced predictiveness? Defaults to TRUE, since inferences made using sample_splitting = FALSE will be invalid for variables with truly zero importance.

final_point_estimate if sample splitting is used, should the final point estimates be based on only the sample-split folds used for inference ("split", the default), or should they instead be based on the full dataset ("full") or the average across the point estimates from each sample split ("average")? All three options result in valid point estimates – sample-splitting is only required for valid inference.

sample_splitting_folds the folds used for sample-splitting; these identify the observations that should be used to evaluate predictiveness based on the full and reduced sets of covariates, respectively. Only used if run_regression = FALSE.

cross_fitting_folds the folds for cross-fitting. Only used if run_regression = FALSE.

stratified if run_regression = TRUE, then should the generated folds be stratified based on the outcome (helps to ensure class balance across cross-validation folds)

type the type of importance to compute; defaults to r_squared, but other supported options are auc, accuracy, deviance, and anova.

run_regression if outcome Y and covariates X are passed to vimp_accuracy, and run_regression is TRUE, then Super Learner will be used; otherwise, variable importance will be computed using the inputted fitted values.

SL.library a character vector of learners to pass to SuperLearner, if f1 and f2 are Y and X, respectively. Defaults to SL.glmnet, SL.xgboost, and SL.mean.

alpha the level to compute the confidence interval at. Defaults to 0.05, corresponding to a 95% confidence interval.
**cv_vim**

- **delta**: the value of the $\delta$-null (i.e., testing if importance < $\delta$); defaults to 0.
- **scale**: should CIs be computed on original ("identity") or another scale? (options are "log" and "logit")
- **na.rm**: should we remove NAs in the outcome and fitted values in computation? (defaults to FALSE)
- **C**: the indicator of coarsening (1 denotes observed, 0 denotes unobserved).
- **Z**: either (i) NULL (the default, in which case the argument $C$ above must be all ones), or (ii) a character vector specifying the variable(s) among Y and X that are thought to play a role in the coarsening mechanism. To specify the outcome, use "Y"; to specify covariates, use a character number corresponding to the desired position in X (e.g., "1").
- **ipc_scale**: what scale should the inverse probability weight correction be applied on (if any)? Defaults to "identity". (other options are "log" and "logit")
- **ipc_weights**: weights for the computed influence curve (i.e., inverse probability weights for coarsened-at-random settings). Assumed to be already inverted (i.e., ipc_weights = 1 / [estimated probability weights]).
- **ipc_est_type**: the type of procedure used for coarsened-at-random settings; options are "ipw" (for inverse probability weighting) or "aipw" (for augmented inverse probability weighting). Only used if C is not all equal to 1.
- **scale_est**: should the point estimate be scaled to be greater than or equal to 0? Defaults to TRUE.
- **nuisance_estimators_full**: (only used if type = "average_value") a list of nuisance function estimators on the observed data (may be within a specified fold, for cross-fitted estimates). Specifically: an estimator of the optimal treatment rule; an estimator of the propensity score under the estimated optimal treatment rule; and an estimator of the outcome regression when treatment is assigned according to the estimated optimal rule.
- **nuisance_estimators_reduced**: (only used if type = "average_value") a list of nuisance function estimators on the observed data (may be within a specified fold, for cross-fitted estimates). Specifically: an estimator of the optimal treatment rule; an estimator of the propensity score under the estimated optimal treatment rule; and an estimator of the outcome regression when treatment is assigned according to the estimated optimal rule.
- **exposure_name**: (only used if type = "average_value") the name of the exposure of interest; binary, with 1 indicating presence of the exposure and 0 indicating absence of the exposure.
- **cross_fitted_se**: should we use cross-fitting to estimate the standard errors (TRUE, the default) or not (FALSE)?
- **bootstrap**: should bootstrap-based standard error estimates be computed? Defaults to FALSE (and currently may only be used if sample_splitting = FALSE).
- **b**: the number of bootstrap replicates (only used if bootstrap = TRUE and sample_splitting = FALSE); defaults to 1000.
boot_interval_type

the type of bootstrap interval (one of "norm", "basic", "stud", "perc", or "bca", as in `boot(boot.ci)`) if requested. Defaults to "perc".

clustered

should the bootstrap resamples be performed on clusters rather than individual observations? Defaults to FALSE.

cluster_id

vector of the same length as Y giving the cluster IDs used for the clustered bootstrap, if clustered is TRUE.

... other arguments to the estimation tool, see "See also".

Details

We define the population variable importance measure (VIM) for the group of features (or single feature) \( s \) with respect to the predictiveness measure \( V \) by

\[
\psi_{0,s} := V(f_0, P_0) - V(f_{0,s}, P_0),
\]

where \( f_0 \) is the population predictiveness maximizing function, \( f_{0,s} \) is the population predictiveness maximizing function that is only allowed to access the features with index not in \( s \), and \( P_0 \) is the true data-generating distribution.

Cross-fitted VIM estimates are computed differently if sample-splitting is requested versus if it is not. We recommend using sample-splitting in most cases, since only in this case will inferences be valid if the variable(s) of interest have truly zero population importance. The purpose of cross-fitting is to estimate \( f_0 \) and \( f_{0,s} \) on independent data from estimating \( P_0 \); this can result in improved performance, especially when using flexible learning algorithms. The purpose of sample-splitting is to estimate \( f_0 \) and \( f_{0,s} \) on independent data; this allows valid inference under the null hypothesis of zero importance.

Without sample-splitting, cross-fitted VIM estimates are obtained by first splitting the data into \( K \) folds; then using each fold in turn as a hold-out set, constructing estimators \( f_{n,k} \) and \( f_{n,k,s} \) of \( f_0 \) and \( f_{0,s} \), respectively on the training data and estimator \( P_{n,k} \) of \( P_0 \) using the test data; and finally, computing

\[
\psi_{n,s} := K^{-1} \sum_{k=1}^{K} \{ V(f_{n,k}, P_{n,k}) - V(f_{n,k,s}, P_{n,k}) \}.
\]

With sample-splitting, cross-fitted VIM estimates are obtained by first splitting the data into \( 2K \) folds. These folds are further divided into 2 groups of folds. Then, for each fold \( k \) in the first group, estimator \( f_{n,k} \) of \( f_0 \) is constructed using all data besides the kth fold in the group (i.e., \( (2K-1)/(2K) \) of the data) and estimator \( P_{n,k} \) of \( P_0 \) is constructed using the held-out data (i.e., \( 1/2K \) of the data); then, computing

\[
v_{n,k} = V(f_{n,k}, P_{n,k}).
\]

Similarly, for each fold \( k \) in the second group, estimator \( f_{n,k,s} \) of \( f_{0,s} \) is constructed using all data besides the kth fold in the group (i.e., \( (2K-1)/(2K) \) of the data) and estimator \( P_{n,k} \) of \( P_0 \) is constructed using the held-out data (i.e., \( 1/2K \) of the data); then, computing

\[
v_{n,k,s} = V(f_{n,k,s}, P_{n,k}).
\]

Finally,

\[
\psi_{n,s} := K^{-1} \sum_{k=1}^{K} \{ v_{n,k} - v_{n,k,s} \}.
\]
See the paper by Williamson, Gilbert, Simon, and Carone for more details on the mathematics behind the cv_vim function, and the validity of the confidence intervals.

In the interest of transparency, we return most of the calculations within the vim object. This results in a list including:

- \texttt{s} the column(s) to calculate variable importance for
- \texttt{SL.library} the library of learners passed to \texttt{SuperLearner}
- \texttt{full_fit} the fitted values of the chosen method fit to the full data (a list, for train and test data)
- \texttt{red_fit} the fitted values of the chosen method fit to the reduced data (a list, for train and test data)
- \texttt{est} the estimated variable importance
- \texttt{naive} the naive estimator of variable importance
- \texttt{eif} the estimated efficient influence function
- \texttt{eif_full} the estimated efficient influence function for the full regression
- \texttt{eif_reduced} the estimated efficient influence function for the reduced regression
- \texttt{se} the standard error for the estimated variable importance
- \texttt{ci} the \((1 - \alpha) \times 100\%\) confidence interval for the variable importance estimate
- \texttt{test} a decision to either reject (TRUE) or not reject (FALSE) the null hypothesis, based on a conservative test
- \texttt{p_value} a p-value based on the same test as \texttt{test}
- \texttt{full_mod} the object returned by the estimation procedure for the full data regression (if applicable)
- \texttt{red_mod} the object returned by the estimation procedure for the reduced data regression (if applicable)
- \texttt{alpha} the level, for confidence interval calculation
- \texttt{sample_splitting_folds} the folds used for hypothesis testing
- \texttt{cross_fitting_folds} the folds used for cross-fitting
- \texttt{y} the outcome
- \texttt{ipc_weights} the weights
- \texttt{cluster_id} the cluster IDs
- \texttt{mat} a tibble with the estimate, SE, CI, hypothesis testing decision, and p-value

\textbf{Value}

An object of class \texttt{vim}. See Details for more information.

\textbf{See Also}

\texttt{SuperLearner} for specific usage of the \texttt{SuperLearner} function and package.
Examples

```r
n <- 100
p <- 2
# generate the data
x <- data.frame(replicate(p, stats::runif(n, -5, 5)))

# apply the function to the x's
smooth <- (x[,1]/5)^2*(x[,1]+7)/5 + (x[,2]/3)^2

# generate Y ~ Normal (smooth, 1)
y <- as.matrix(smooth + stats::rnorm(n, 0, 1))

# set up a library for SuperLearner; note simple library for speed
library("SuperLearner")
learners <- c("SL.glm")

# using Super Learner (with a small number of folds, for illustration only)
set.seed(4747)
est <- cv_vim(Y = y, X = x, indx = 2, V = 2,
type = "r_squared", run_regression = TRUE,
SL.library = learners, cvControl = list(V = 2), alpha = 0.05)

# doing things by hand, and plugging them in
# (with a small number of folds, for illustration only)
# set up the folds
indx <- 2
V <- 2
Y <- matrix(y)
set.seed(4747)
# Note that the CV.SuperLearner should be run with an outer layer
# of 2*V folds (for V-fold cross-fitted importance)
full_cv_fit <- suppressWarnings(SuperLearner::CV.SuperLearner(
  Y = Y, X = x, SL.library = learners, cvControl = list(V = 2 * V),
innerCvControl = list(list(V = V))
))
full_cv_preds <- full_cv_fit$SL.predict
# use the same cross-fitting folds for reduced
reduced_cv_fit <- suppressWarnings(SuperLearner::CV.SuperLearner(
  Y = Y, X = x[, -indx, drop = FALSE], SL.library = learners,
cvControl = SuperLearner::SuperLearner.CV.control( 
  V = 2 * V, validRows = full_cv_fit$folds 
),
innerCvControl = list(list(V = V))
))
reduced_cv_preds <- reduced_cv_fit$SL.predict
# for hypothesis testing
cross_fitting_folds <- get_cv_sl_folds(full_cv_fit$folds)
set.seed(1234)
```
```r
sample_splitting_folds <- make_folds(unique(cross_fitting_folds), V = 2)
set.seed(5678)
est <- cv_vim(Y = y, cross_fitted_f1 = full_cv_preds,
cross_fitted_f2 = reduced_cv_preds, indx = 2, delta = 0, V = V, type = "r_squared",
cross_fitting_folds = cross_fitting_folds,
sample_splitting_folds = sample_splitting_folds,
run_regression = FALSE, alpha = 0.05, na.rm = TRUE)
```

---

**estimate**

*Estimate a Predictiveness Measure*

**Description**

Generic function for estimating a predictiveness measure (e.g., R-squared or classification accuracy).

**Usage**

```r
estimate(x, ...)
```

**Arguments**

- **x**: An R object. Currently, there are methods for `predictiveness_measure` objects only.
- **...**: further arguments passed to or from other methods.

---

**estimate.predictiveness.measure**

*Obtain a Point Estimate and Efficient Influence Function Estimate for a Given Predictiveness Measure*

**Description**

Obtain a Point Estimate and Efficient Influence Function Estimate for a Given Predictiveness Measure

**Usage**

```r
## S3 method for class 'predictiveness_measure'
estimate(x, ...)
```

**Arguments**

- **x**: an object of class "predictiveness_measure"
- **...**: other arguments to type-specific predictiveness measures (currently unused)
Value

A list with the point estimate, naive point estimate (for ANOVA only), estimated EIF, and the predictions for coarsened data EIF (for coarsened data settings only)

---

**estimate_eif_projection**

*Estimate projection of EIF on fully-observed variables*

---

Description

Estimate projection of EIF on fully-observed variables

Usage

```r
estimate_eif_projection(
  obs_grad = NULL,
  C = NULL,
  Z = NULL,
  ipc_fit_type = NULL,
  ipc_eif_preds = NULL,
  ...
)
```

Arguments

- `obs_grad` the estimated (observed) EIF
- `C` the indicator of coarsening (1 denotes observed, 0 denotes unobserved).
- `Z` either `NULL` (if no coarsening) or a matrix-like object containing the fully observed data.
- `ipc_fit_type` if "external", then use `ipc_eif_preds`; if "SL", fit a SuperLearner to determine the IPC correction to the efficient influence function.
- `ipc_eif_preds` if `ipc_fit_type = "external"`, the fitted values from a regression of the full-data EIF on the fully observed covariates/outcome; otherwise, not used.
- `...` other arguments to SuperLearner, if `ipc_fit_type = "SL"`.

Value

the projection of the EIF onto the fully-observed variables
Estimate nuisance functions for average value-based VIMs

Usage

```r
estimate_nuisances(
  fit,
  X,
  exposure_name,
  V = 1,
  SL.library,
  sample_splitting,
  sample_splitting_folds,
  verbose,
  weights,
  cross_fitted_se,
  split = 1,
  ...
)
```

Arguments

- `fit` the fitted nuisance function estimator
- `X` the covariates. If `type = "average_value"`, then the exposure variable should be part of `X`, with its name provided in `exposure_name`.
- `exposure_name` (only used if `type = "average_value"`) the name of the exposure of interest; binary, with 1 indicating presence of the exposure and 0 indicating absence of the exposure.
- `V` the number of folds for cross-fitting, defaults to 5. If `sample_splitting = TRUE`, then a special type of `V`-fold cross-fitting is done. See Details for a more detailed explanation.
- `SL.library` a character vector of learners to pass to SuperLearner, if `f1` and `f2` are `Y` and `X`, respectively. Defaults to `SL.glmnet`, `SL.xgboost`, and `SL.mean`.
- `sample_splitting` should we use sample-splitting to estimate the full and reduced predictiveness? Defaults to `TRUE`, since inferences made using `sample_splitting = FALSE` will be invalid for variables with truly zero importance.
- `sample_splitting_folds` the folds used for sample-splitting; these identify the observations that should be used to evaluate predictiveness based on the full and reduced sets of covariates, respectively. Only used if `run_regression = FALSE`.

Description

Estimate nuisance functions for average value-based VIMs
est_predictiveness

Estimate a nonparametric predictiveness functional

Description

Compute nonparametric estimates of the chosen measure of predictiveness.

verbose should we print progress? defaults to FALSE
weights weights to pass to estimation procedure
cross_fitted_se should we use cross-fitting to estimate the standard errors (TRUE, the default) or not (FALSE)?
split the sample split to use
... other arguments to the estimation tool, see "See also".

Value

nuisance function estimators for use in the average value VIM: the treatment assignment based on the estimated optimal rule (based on the estimated outcome regression); the expected outcome under the estimated optimal rule; and the estimated propensity score.

estimate_type_predictiveness

Estimate Predictiveness Given a Type

Description

Estimate the specified type of predictiveness

Usage

estimate_type_predictiveness(arg_lst, type)

Arguments

arg_lst a list of arguments; from, e.g., predictiveness_measure
type the type of predictiveness, e.g., "r_squared"
Usage

```r
est_predictiveness(
  fitted_values,
  y,
  a = NULL,
  full_y = NULL,
  type = "r_squared",
  C = rep(1, length(y)),
  Z = NULL,
  ipc_weights = rep(1, length(C)),
  ipc_fit_type = "external",
  ipc_eif_preds = rep(1, length(C)),
  ipc_est_type = "aipw",
  scale = "identity",
  na.rm = FALSE,
  nuisance_estimators = NULL,
  ...
)
```

Arguments

- **fitted_values**: fitted values from a regression function using the observed data.
- **y**: the observed outcome.
- **a**: the observed treatment assignment (may be within a specified fold, for cross-fitted estimates). Only used if `type = "average_value"`.
- **full_y**: the observed outcome (from the entire dataset, for cross-fitted estimates).
- **type**: which parameter are you estimating (defaults to `"r_squared"`, for R-squared-based variable importance)?
- **C**: the indicator of coarsening (1 denotes observed, 0 denotes unobserved).
- **Z**: either `NULL` (if no coarsening) or a matrix-like object containing the fully observed data.
- **ipc_weights**: weights for inverse probability of coarsening (e.g., inverse weights from a two-phase sample) weighted estimation. Assumed to be already inverted (i.e., `ipc_weights = 1 / [estimated probability weights]`).
- **ipc_fit_type**: if "external", then use `ipc_eif_preds`; if "SL", fit a SuperLearner to determine the correction to the efficient influence function.
- **ipc_eif_preds**: if `ipc_fit_type = "external"`, the fitted values from a regression of the full-data EIF on the fully observed covariates/outcome; otherwise, not used.
- **ipc_est_type**: IPC correction, either "ipw" (for classical inverse probability weighting) or "aipw" (for augmented inverse probability weighting; the default).
- **scale**: if doing an IPC correction, then the scale that the correction should be computed on (e.g., "identity"; or "logit" to logit-transform, apply the correction, and back-transform).
- **na.rm**: logical; should NA’s be removed in computation? (defaults to `FALSE`)
est_predictiveness_cv

 nuisances_estimators
 (only used if type = "average_value") a list of nuisance function estimators on the observed data (may be within a specified fold, for cross-fitted estimates). Specifically: an estimator of the optimal treatment rule; an estimator of the propensity score under the estimated optimal treatment rule; and an estimator of the outcome regression when treatment is assigned according to the estimated optimal rule.

 ... other arguments to SuperLearner, if ipc_fit_type = "SL".

Details

See the paper by Williamson, Gilbert, Simon, and Carone for more details on the mathematics behind this function and the definition of the parameter of interest.

Value

A list, with: the estimated predictiveness; the estimated efficient influence function; and the predictions of the EIF based on inverse probability of censoring.

description

Estimate a nonparametric predictiveness functional using cross-fitting

Usage

est_predictiveness_cv(
  fitted_values,
  y,
  full_y = NULL,
  folds,
  type = "r_squared",
  C = rep(1, length(y)),
  Z = NULL,
  folds_Z = folds,
  ipc_weights = rep(1, length(C)),
  ipc_fit_type = "external",
  ipc_eif_preds = rep(1, length(C)),
  ipc_est_type = "aipw",
  scale = "identity",
  na.rm = FALSE,
  ...
)
Arguments

- **fitted_values**: Fitted values from a regression function using the observed data; a list of length \( V \), where each object is a set of predictions on the validation data, or a vector of the same length as \( y \).
- **y**: The observed outcome.
- **full_y**: The observed outcome (from the entire dataset, for cross-fitted estimates).
- **folds**: The cross-validation folds for the observed data.
- **type**: Which parameter are you estimating (defaults to \( r_{squared} \), for R-squared-based variable importance)?
- **C**: The indicator of coarsening (1 denotes observed, 0 denotes unobserved).
- **Z**: Either `NULL` (if no coarsening) or a matrix-like object containing the fully observed data.
- **folds_Z**: Either the cross-validation folds for the observed data (no coarsening) or a vector of folds for the fully observed data \( Z \).
- **ipc_weights**: Weights for inverse probability of coarsening (e.g., inverse weights from a two-phase sample) weighted estimation. Assumed to be already inverted (i.e., \( \text{ipc_weights} = 1 / \text{[estimated probability weights]} \)).
- **ipc_fit_type**: If "external", then use \( \text{ipc_eif_preds} \); if "SL", fit a SuperLearner to determine the correction to the efficient influence function.
- **ipc_eif_preds**: If \( \text{ipc_fit_type} = "external" \), the fitted values from a regression of the full-data EIF on the fully observed covariates/outcome; otherwise, not used.
- **ipc_est_type**: IPC correction, either "ipw" (for classical inverse probability weighting) or "aipw" (for augmented inverse probability weighting; the default).
- **scale**: If doing an IPC correction, then the scale that the correction should be computed on (e.g., "identity"; or "logit" to logit-transform, apply the correction, and back-transform).
- **na.rm**: Logical; should NA's be removed in computation? (defaults to `FALSE`)
- **...**: Other arguments to SuperLearner, if \( \text{ipc_fit_type} = "SL" \).

Details

See the paper by Williamson, Gilbert, Simon, and Carone for more details on the mathematics behind this function and the definition of the parameter of interest. If sample-splitting is also requested (recommended, since in this case inferences will be valid even if the variable has zero true importance), then the prediction functions are trained as if \( 2K \)-fold cross-validation were run, but are evaluated on only \( K \) sets (independent between the full and reduced nuisance regression).

Value

The estimated measure of predictiveness.
extract_sampled_split_predictions

*Extract sampled-split predictions from a CV.SuperLearner object*

**Description**

Use the cross-validated Super Learner and a set of specified sample-splitting folds to extract cross-fitted predictions on separate splits of the data. This is primarily for use in cases where you have already fit a CV.SuperLearner and want to use the fitted values to compute variable importance without having to re-fit. The number of folds used in the CV.SuperLearner must be even.

**Usage**

```r
evaluate_sampled_split_predictions(
  cvsl_obj = NULL,
  sample_splitting = TRUE,
  sample_splitting_folds = NULL,
  full = TRUE,
  preds = NULL,
  cross_fitting_folds = NULL,
  vector = TRUE
)
```

**Arguments**

- `cvsl_obj`: An object of class "CV.SuperLearner"; must be entered unless `preds` is specified.
- `sample_splitting`: logical; should we use sample-splitting or not? Defaults to `TRUE`.
- `sample_splitting_folds`: A vector of folds to use for sample splitting.
- `full`: logical; is this the fit to all covariates (`TRUE`) or not (`FALSE`)?
- `preds`: a vector of predictions; must be entered unless `cvsl_obj` is specified.
- `cross_fitting_folds`: a vector of folds that were used in cross-fitting.
- `vector`: logical; should we return a vector (where each element is the prediction when the corresponding row is in the validation fold) or a list?

**Value**

The predictions on validation data in each split-sample fold.

**See Also**

`CV.SuperLearner` for usage of the `CV.SuperLearner` function.
**format.predictiveness_measure**

*Format a predictiveness_measure object*

**Description**

Nicely formats the output from a `predictiveness_measure` object for printing.

**Usage**

```r
## S3 method for class 'predictiveness_measure'
format(x, ...)
```

**Arguments**

- `x` the `predictiveness_measure` object of interest.
- `...` other options, see the generic `format` function.

---

**format.vim**

*Format a vim object*

**Description**

Nicely formats the output from a `vim` object for printing.

**Usage**

```r
## S3 method for class 'vim'
format(x, ...)
```

**Arguments**

- `x` the `vim` object of interest.
- `...` other options, see the generic `format` function.
get.cv.sl_folds Get a numeric vector with cross-validation fold IDs from CV.SuperLearner

Description
Get a numeric vector with cross-validation fold IDs from CV.SuperLearner

Usage
get.cv.sl_folds(cv.sl_folds)

Arguments
cv.sl_folds The folds from a call to CV.SuperLearner; a list.

Value
A numeric vector with the fold IDs.

get.full_type Obtain the type of VIM to estimate using partial matching

Description
Obtain the type of VIM to estimate using partial matching

Usage
get.full_type(type)

Arguments
type the partial string indicating the type of VIM

Value
the full string indicating the type of VIM
get_test_set

Description

Return test-set only data

Usage

get_test_set(arg_lst, k)

Arguments

arg_lst a list of estimates, data, etc.
k the index of interest

Value

the test-set only data

make_folds

Create Folds for Cross-Fitting

Description

Create Folds for Cross-Fitting

Usage

make_folds(y, V = 2, stratified = FALSE, C = NULL, probs = rep(1/V, V))

Arguments

y the outcome
V the number of folds
stratified should the folds be stratified based on the outcome?
C a vector indicating whether or not the observation is fully observed; 1 denotes yes, 0 denotes no
probs vector of proportions for each fold number

Value

a vector of folds
**make_kfold**

*Turn folds from 2K-fold cross-fitting into individual K-fold folds*

**Description**

Turn folds from 2K-fold cross-fitting into individual K-fold folds

**Usage**

```r
make_kfold(
  cross_fitting_folds,
  sample_splitting_folds = rep(1, length(unique(cross_fitting_folds))),
  C = rep(1, length(cross_fitting_folds))
)
```

**Arguments**

- `cross_fitting_folds`: the vector of cross-fitting folds
- `sample_splitting_folds`: the sample splitting folds
- `C`: vector of whether or not we measured the observation in phase 2

**Value**

the two sets of testing folds for K-fold cross-fitting

---

**measure_accuracy**

*Estimate the classification accuracy*

**Description**

Compute nonparametric estimate of classification accuracy.

**Usage**

```r
measure_accuracy(
  fitted_values,
  y,
  full_y = NULL,
  C = rep(1, length(y)),
  Z = NULL,
  ipc_weights = rep(1, length(y)),
  ipc_fit_type = "external",
  ipc_eif_preds = rep(1, length(y)),
)```
measure_accuracy

ipc_est_type = "aipw",
scale = "logit",
na.rm = FALSE,
nuisance_estimators = NULL,
a = NULL,
...
)

Arguments

fitted_values  fitted values from a regression function using the observed data (may be within a specified fold, for cross-fitted estimates).
y  the observed outcome (may be within a specified fold, for cross-fitted estimates).
full_y  the observed outcome (not used, defaults to NULL).
C  the indicator of coarsening (1 denotes observed, 0 denotes unobserved).
Z  either NULL (if no coarsening) or a matrix-like object containing the fully observed data.
ipc_weights  weights for inverse probability of coarsening (IPC) (e.g., inverse weights from a two-phase sample) weighted estimation. Assumed to be already inverted. (i.e., ipc_weights = 1 / [estimated probability weights]).
ipc_fit_type  if "external", then use ipc_eif_preds; if "SL", fit a SuperLearner to determine the IPC correction to the efficient influence function.
ipc_eif_preds  if ipc_fit_type = "external", the fitted values from a regression of the full-data EIF on the fully observed covariates/outcome; otherwise, not used.
ipc_est_type  IPC correction, either "ipw" (for classical inverse probability weighting) or "aipw" (for augmented inverse probability weighting; the default).
scale  if doing an IPC correction, then the scale that the correction should be computed on (e.g., "identity"; or "logit" to logit-transform, apply the correction, and back-transform).
na.rm  logical; should NAs be removed in computation? (defaults to FALSE)
nuisance_estimators  not used; for compatibility with measure_average_value.
a  not used; for compatibility with measure_average_value.
...  other arguments to SuperLearner, if ipc_fit_type = "SL".

Value

A named list of: (1) the estimated classification accuracy of the fitted regression function; (2) the estimated influence function; and (3) the IPC EIF predictions.
**measure_anova**

Estimate ANOVA decomposition-based variable importance.

**Description**

Estimate ANOVA decomposition-based variable importance.

**Usage**

```r
measure_anova(
  full,
  reduced,
  y,
  full_y = NULL,
  C = rep(1, length(y)),
  Z = NULL,
  ipc_weights = rep(1, length(y)),
  ipc_fit_type = "external",
  ipc_eif_preds = rep(1, length(y)),
  ipc_est_type = "aipw",
  scale = "logit",
  na.rm = FALSE,
  nuisance_estimators = NULL,
  a = NULL,
  ...
)
```

**Arguments**

- **full**: fitted values from a regression function of the observed outcome on the full set of covariates.
- **reduced**: fitted values from a regression on the reduced set of observed covariates.
- **y**: the observed outcome (may be within a specified fold, for cross-fitted estimates).
- **full_y**: the observed outcome (not used, defaults to NULL).
- **C**: the indicator of coarsening (1 denotes observed, 0 denotes unobserved).
- **Z**: either NULL (if no coarsening) or a matrix-like object containing the fully observed data.
- **ipc_weights**: weights for inverse probability of coarsening (IPC) (e.g., inverse weights from a two-phase sample) weighted estimation. Assumed to be already inverted. (i.e., ipc_weights = 1 / [estimated probability weights]).
- **ipc_fit_type**: if "external", then use ipc_eif_preds; if "SL", fit a SuperLearner to determine the IPC correction to the efficient influence function.
- **ipc_eif_preds**: if ipc_fit_type = "external", the fitted values from a regression of the full-data EIF on the fully observed covariates/outcome; otherwise, not used.
ipc_est_type
IPC correction, either "ipw" (for classical inverse probability weighting) or "aipw" (for augmented inverse probability weighting; the default).

scale
if doing an IPC correction, then the scale that the correction should be computed on (e.g., "identity"; or "logit" to logit-transform, apply the correction, and back-transform).

na.rm
logical; should NAs be removed in computation? (defaults to FALSE)

nuisance_estimators
not used; for compatibility with measure_average_value.

a
not used; for compatibility with measure_average_value.

... other arguments to SuperLearner, if ipc_fit_type = "SL".

Value
A named list of: (1) the estimated ANOVA (based on a one-step correction) of the fitted regression functions; (2) the estimated influence function; (3) the naive ANOVA estimate; and (4) the IPC EIF predictions.

measure_auc
Estimate area under the receiver operating characteristic curve (AUC)

Description
Compute nonparametric estimate of AUC.

Usage
measure_auc(
  fitted_values,
  y,
  full_y = NULL,
  C = rep(1, length(y)),
  Z = NULL,
  ipc_weights = rep(1, length(y)),
  ipc_fit_type = "external",
  ipc_eif_preds = rep(1, length(y)),
  ipc_est_type = "aipw",
  scale = "logit",
  na.rm = FALSE,
  nuisance_estimators = NULL,
  a = NULL,
  ...
)
measure_average_value

Arguments

- **fitted_values**: fitted values from a regression function using the observed data (may be within a specified fold, for cross-fitted estimates).
- **y**: the observed outcome (may be within a specified fold, for cross-fitted estimates).
- **full_y**: the observed outcome (may be within a specified fold, for cross-fitted estimates).
- **C**: the indicator of coarsening (1 denotes observed, 0 denotes unobserved).
- **Z**: either NULL (if no coarsening) or a matrix-like object containing the fully observed data.
- **ipc_weights**: weights for inverse probability of coarsening (IPC) (e.g., inverse weights from a two-phase sample) weighted estimation. Assumed to be already inverted. (i.e., ipc_weights = 1 / [estimated probability weights]).
- **ipc_fit_type**: if "external", then use ipc_eif_preds; if "SL", fit a SuperLearner to determine the IPC correction to the efficient influence function.
- **ipc_eif_preds**: if ipc_fit_type = "external", the fitted values from a regression of the full-data EIF on the fully observed covariates/outcome; otherwise, not used.
- **ipc_est_type**: IPC correction, either "ipw" (for classical inverse probability weighting) or "aipw" (for augmented inverse probability weighting; the default).
- **scale**: if doing an IPC correction, then the scale that the correction should be computed on (e.g., "identity"; or "logit" to logit-transform, apply the correction, and back-transform).
- **na.rm**: logical; should NAs be removed in computation? (defaults to FALSE)
- **nuisance_estimators**: not used; for compatibility with measure_average_value.
- **a**: not used; for compatibility with measure_average_value.
- **...**: other arguments to SuperLearner, if ipc_fit_type = "SL".

Value

A named list of: (1) the estimated AUC of the fitted regression function; (2) the estimated influence function; and (3) the IPC EIF predictions.

---

**measure_average_value** Estimate the average value under the optimal treatment rule

Description

Compute nonparametric estimate of the average value under the optimal treatment rule.
**Usage**

```r
measure_average_value(
  nuisance_estimators,
  y,
  a,
  full_y = NULL,
  C = rep(1, length(y)),
  Z = NULL,
  ipc_weights = rep(1, length(y)),
  ipc_fit_type = "external",
  ipc_eif_preds = rep(1, length(y)),
  ipc_est_type = "aipw",
  scale = "identity",
  na.rm = FALSE,
  ...
)
```

**Arguments**

- `nuisance_estimators`: a list of nuisance function estimators on the observed data (may be within a specified fold, for cross-fitted estimates). Specifically: an estimator of the optimal treatment rule; an estimator of the propensity score under the estimated optimal treatment rule; and an estimator of the outcome regression when treatment is assigned according to the estimated optimal rule.
- `y`: the observed outcome (may be within a specified fold, for cross-fitted estimates).
- `a`: the observed treatment assignment (may be within a specified fold, for cross-fitted estimates).
- `full_y`: the observed outcome (not used, defaults to `NULL`).
- `C`: the indicator of coarsening (1 denotes observed, 0 denotes unobserved).
- `Z`: either `NULL` (if no coarsening) or a matrix-like object containing the fully observed data.
- `ipc_weights`: weights for inverse probability of coarsening (IPC) (e.g., inverse weights from a two-phase sample) weighted estimation. Assumed to be already inverted. (i.e., `ipc_weights = 1 / [estimated probability weights]).`
- `ipc_fit_type`: if "external", then use `ipc_eif_preds`; if "SL", fit a SuperLearner to determine the IPC correction to the efficient influence function.
- `ipc_eif_preds`: if `ipc_fit_type = "external"`, the fitted values from a regression of the full-data EIF on the fully observed covariates/outcome; otherwise, not used.
- `ipc_est_type`: IPC correction, either "ipw" (for classical inverse probability weighting) or "aipw" (for augmented inverse probability weighting; the default).
- `scale`: if doing an IPC correction, then the scale that the correction should be computed on (e.g., "identity"; or "logit" to logit-transform, apply the correction, and back-transform).
- `na.rm`: logical; should NAs be removed in computation? (defaults to `FALSE`)
- `...`: other arguments to SuperLearner, if `ipc_fit_type = "SL"`.
**Value**

A named list of: (1) the estimated classification accuracy of the fitted regression function; (2) the estimated influence function; and (3) the IPC EIF predictions.

---

***measure_cross_entropy***  
*Estimate the cross-entropy*

---

**Description**

Compute nonparametric estimate of cross-entropy.

**Usage**

```r
measure_cross_entropy(
  fitted_values,  
  y,  
  full_y = NULL,  
  C = rep(1, length(y)),  
  Z = NULL,  
  ipc_weights = rep(1, length(y)),  
  ipc_fit_type = "external",  
  ipc_eif_preds = rep(1, length(y)),  
  ipc_est_type = "aipw",  
  scale = "identity",  
  na.rm = FALSE,  
  nuisance_estimators = NULL,  
  a = NULL,  
  ...
)
```

**Arguments**

- `fitted_values`: fitted values from a regression function using the observed data (may be within a specified fold, for cross-fitted estimates).
- `y`: the observed outcome (may be within a specified fold, for cross-fitted estimates).
- `full_y`: the observed outcome (not used, defaults to `NULL`).
- `C`: the indicator of coarsening (1 denotes observed, 0 denotes unobserved).
- `Z`: either `NULL` (if no coarsening) or a matrix-like object containing the fully observed data.
- `ipc_weights`: weights for inverse probability of coarsening (IPC) (e.g., inverse weights from a two-phase sample) weighted estimation. Assumed to be already inverted. (i.e., `ipc_weights = 1 / [estimated probability weights]).
- `ipc_fit_type`: if "external", then use `ipc_eif_preds`; if "SL", fit a SuperLearner to determine the IPC correction to the efficient influence function.
measure_deviance

ipc_eif_preds  if ipc_fit_type = "external", the fitted values from a regression of the full-data EIF on the fully observed covariates/outcome; otherwise, not used.

ipc_est_type  IPC correction, either "ipw" (for classical inverse probability weighting) or "aipw" (for augmented inverse probability weighting; the default).

scale  if doing an IPC correction, then the scale that the correction should be computed on (e.g., "identity"; or "logit" to logit-transform, apply the correction, and back-transform).

na.rm  logical; should NAs be removed in computation? (defaults to FALSE)

nuisance_estimators  not used; for compatibility with measure_average_value.

a  not used; for compatibility with measure_average_value.

...  other arguments to SuperLearner, if ipc_fit_type = "SL".

Value

A named list of: (1) the estimated cross-entropy of the fitted regression function; (2) the estimated influence function; and (3) the IPC EIF predictions.

measure_deviance  Estimate the deviance

Description

Compute nonparametric estimate of deviance.

Usage

measure_deviance(
  fitted_values,
  y,
  full_y = NULL,
  C = rep(1, \text{length}(y)),
  Z = NULL,
  ipc_weights = rep(1, \text{length}(y)),
  ipc_fit_type = "external",
  ipc_eif_preds = rep(1, \text{length}(y)),
  ipc_est_type = "aipw",
  scale = "logit",
  na.rm = FALSE,
  nuisance_estimators = NULL,
  a = NULL,
  ...
)

)
Arguments

- **fitted_values**: fitted values from a regression function using the observed data (may be within a specified fold, for cross-fitted estimates).
- **y**: the observed outcome (may be within a specified fold, for cross-fitted estimates).
- **full_y**: the observed outcome (not used, defaults to `NULL`).
- **C**: the indicator of coarsening (1 denotes observed, 0 denotes unobserved).
- **Z**: either `NULL` (if no coarsening) or a matrix-like object containing the fully observed data.
- **ipc_weights**: weights for inverse probability of coarsening (IPC) (e.g., inverse weights from a two-phase sample) weighted estimation. Assumed to be already inverted. (i.e., `ipc_weights = 1 / [estimated probability weights]`).
- **ipc_fit_type**: if "external", then use `ipc_eif_preds`; if "SL", fit a SuperLearner to determine the IPC correction to the efficient influence function.
- **ipc_eif_preds**: if `ipc_fit_type = "external"`, the fitted values from a regression of the full-data EIF on the fully observed covariates/outcome; otherwise, not used.
- **ipc_est_type**: IPC correction, either "ipw" (for classical inverse probability weighting) or "aipw" (for augmented inverse probability weighting; the default).
- **scale**: if doing an IPC correction, then the scale that the correction should be computed on (e.g., "identity"; or "logit" to logit-transform, apply the correction, and back-transform).
- **na.rm**: logical; should NAs be removed in computation? (defaults to FALSE)
- **nuisance_estimators**: not used; for compatibility with `measure_average_value`.
- **a**: not used; for compatibility with `measure_average_value`.
- **...**: other arguments to SuperLearner, if `ipc_fit_type = "SL"`.

Value

A named list of: (1) the estimated deviance of the fitted regression function; (2) the estimated influence function; and (3) the IPC EIF predictions.

---

**measure_mse**

*Estimate mean squared error*

Description

Compute nonparametric estimate of mean squared error.
Usage

```
measure_mse(
  fitted_values,  # fitted values from a regression function using the observed data (may be within a specified fold, for cross-fitted estimates).
  y,              # the observed outcome (may be within a specified fold, for cross-fitted estimates).
  full_y = NULL,  # the observed outcome (not used, defaults to NULL).
  C = rep(1, length(y)),
  Z = NULL,       # either NULL (if no coarsening) or a matrix-like object containing the fully observed data.
  ipc_weights = rep(1, length(y)),
  ipc_fit_type = "external",  # if "external", then use ipc_eif_preds; if "SL", fit a SuperLearner to determine the IPC correction to the efficient influence function.
  ipc_eif_preds = rep(1, length(y)),  # if ipc_fit_type = "external", the fitted values from a regression of the full-data EIF on the fully observed covariates/outcome; otherwise, not used.
  ipc_est_type = "aipw",  # IPC correction, either "ipw" (for classical inverse probability weighting) or "aipw" (for augmented inverse probability weighting; the default).
  scale = "identity",  # if doing an IPC correction, then the scale that the correction should be computed on (e.g., "identity"; or "logit" to logit-transform, apply the correction, and back-transform).
  na.rm = FALSE,  # logical; should NAs be removed in computation? (defaults to FALSE)
  nuisance_estimators = NULL,  # not used; for compatibility with measure_average_value.
  a = NULL,       # not used; for compatibility with measure_average_value.
  ...             # other arguments to SuperLearner, if ipc_fit_type = "SL".
)
```

Arguments

- `fitted_values`: fitted values from a regression function using the observed data (may be within a specified fold, for cross-fitted estimates).
- `y`: the observed outcome (may be within a specified fold, for cross-fitted estimates).
- `full_y`: the observed outcome (not used, defaults to NULL).
- `C`: the indicator of coarsening (1 denotes observed, 0 denotes unobserved).
- `Z`: either NULL (if no coarsening) or a matrix-like object containing the fully observed data.
- `ipc_weights`: weights for inverse probability of coarsening (IPC) (e.g., inverse weights from a two-phase sample) weighted estimation. Assumed to be already inverted. (i.e., `ipc_weights = 1 / [estimated probability weights]`).
- `ipc_fit_type`: if "external", then use `ipc_eif_preds`; if "SL", fit a SuperLearner to determine the IPC correction to the efficient influence function.
- `ipc_eif_preds`: if `ipc_fit_type = "external"`, the fitted values from a regression of the full-data EIF on the fully observed covariates/outcome; otherwise, not used.
- `ipc_est_type`: IPC correction, either "ipw" (for classical inverse probability weighting) or "aipw" (for augmented inverse probability weighting; the default).
- `scale`: if doing an IPC correction, then the scale that the correction should be computed on (e.g., "identity"; or "logit" to logit-transform, apply the correction, and back-transform).
- `na.rm`: logical; should NAs be removed in computation? (defaults to FALSE)
- `nuisance_estimators`: not used; for compatibility with `measure_average_value`.
- `a`: not used; for compatibility with `measure_average_value`.
- `...`: other arguments to SuperLearner, if `ipc_fit_type = "SL"`. 
Value

A named list of: (1) the estimated mean squared error of the fitted regression function; (2) the estimated influence function; and (3) the IPC EIF predictions.

---

**measure_r_squared**

**Estimate R-squared**

Description

Estimate R-squared

Usage

```r
measure_r_squared(
  fitted_values,
  y,
  full_y = NULL,
  C = rep(1, length(y)),
  Z = NULL,
  ipc_weights = rep(1, length(y)),
  ipc_fit_type = "external",
  ipc_eif_preds = rep(1, length(y)),
  ipc_est_type = "aipw",
  scale = "logit",
  na.rm = FALSE,
  nuisance_estimators = NULL,
  a = NULL,
  ...
)
```

Arguments

- **fitted_values**: fitted values from a regression function using the observed data (may be within a specified fold, for cross-fitted estimates).
- **y**: the observed outcome (may be within a specified fold, for cross-fitted estimates).
- **full_y**: the observed outcome (not used, defaults to `NULL`).
- **C**: the indicator of coarsening (1 denotes observed, 0 denotes unobserved).
- **Z**: either `NULL` (if no coarsening) or a matrix-like object containing the fully observed data.
- **ipc_weights**: weights for inverse probability of coarsening (IPC) (e.g., inverse weights from a two-phase sample) weighted estimation. Assumed to be already inverted. (i.e., `ipc_weights = 1 / [estimated probability weights]`).
- **ipc_fit_type**: if "external", then use `ipc_eif_preds`; if "SL", fit a SuperLearner to determine the IPC correction to the efficient influence function.
merge_vim

ipc_eif preds if ipc_fit_type = "external", the fitted values from a regression of the full-data EIF on the fully observed covariates/outcome; otherwise, not used.
ipc_est_type IPC correction, either "ipw" (for classical inverse probability weighting) or "aipw" (for augmented inverse probability weighting; the default).
scale if doing an IPC correction, then the scale that the correction should be computed on (e.g., "identity"; or "logit" to logit-transform, apply the correction, and back-transform).
na.rm logical; should NAs be removed in computation? (defaults to FALSE)
nuisance_estimators not used; for compatibility with measure_average_value.
a not used; for compatibility with measure_average_value.
... other arguments to SuperLearner, if ipc_fit_type = "SL".

Value
A named list of: (1) the estimated R-squared of the fitted regression function; (2) the estimated influence function; and (3) the IPC EIF predictions.

merge_vim

Merge multiple vim objects into one

Description
Take the output from multiple different calls to vimp_regression and merge into a single vim object; mostly used for plotting results.

Usage
merge_vim(...)

Arguments
...

an arbitrary number of vim objects, separated by commas.

Value
an object of class vim containing all of the output from the individual vim objects. This results in a list containing:

- s - a list of the column(s) to calculate variable importance for
- SL.library - a list of the libraries of learners passed to SuperLearner
- full_fit - a list of the fitted values of the chosen method fit to the full data
- red_fit - a list of the fitted values of the chosen method fit to the reduced data
- est- a vector with the corrected estimates
- naive- a vector with the naive estimates
predictiveness_measure

Construct a Predictiveness Measure

**Description**

Construct a Predictiveness Measure

- eif - a list with the influence curve-based updates
- se - a vector with the standard errors
- ci - a matrix with the CIs
- mat - a tibble with the estimated variable importance, the standard errors, and the \((1 - \alpha) \times 100\%\) confidence intervals
- full_mod - a list of the objects returned by the estimation procedure for the full data regression (if applicable)
- red_mod - a list of the objects returned by the estimation procedure for the reduced data regression (if applicable)
- alpha - a list of the levels, for confidence interval calculation

**Examples**

```r
# generate the data
# generate X
p <- 2
n <- 100
x <- data.frame(replicate(p, stats::runif(n, -5, 5)))

# apply the function to the x's
smooth <- (x[,1]/5)^2*(x[,1]+7)/5 + (x[,2]/3)^2

# generate Y ~ Normal (smooth, 1)
y <- smooth + stats::rnorm(n, 0, 1)

# set up a library for SuperLearner; note simple library for speed
library("SuperLearner")
learners <- c("SL.glm", "SL.mean")

# using Super Learner (with a small number of folds, for illustration only)
est_2 <- vimp_regression(Y = y, X = x, indx = 2, V = 2,
run_regression = TRUE, alpha = 0.05,
SL.library = learners, cvControl = list(V = 2))
est_1 <- vimp_regression(Y = y, X = x, indx = 1, V = 2,
run_regression = TRUE, alpha = 0.05,
SL.library = learners, cvControl = list(V = 2))
ests <- merge_vim(est_1, est_2)
```
predictiveness_measure

Usage

predictiveness_measure(
  type = character(),
  y = numeric(),
  a = numeric(),
  fitted_values = numeric(),
  cross_fitting_folds = rep(1, length(fitted_values)),
  full_y = NULL,
  nuisance_estimators = list(),
  C = rep(1, length(y)),
  Z = NULL,
  folds_Z = cross_fitting_folds,
  ipc_weights = rep(1, length(y)),
  ipc_fit_type = "SL",
  ipc_eif_preds = numeric(),
  ipc_est_type = "aipw",
  scale = "identity",
  na.rm = TRUE,
  ...
)

Arguments

type the measure of interest (e.g., "accuracy", "auc", "r_squared")
y the outcome of interest
a the exposure of interest (only used if type = "average_value")
fitted_values fitted values from a regression function using the observed data (may be within a specified fold, for cross-fitted estimates).
cross_fitting_folds folds for cross-fitting, if used to obtain the fitted values. If not used, a vector of ones.
full_y the observed outcome (not used, defaults to NULL).
nuisance_estimators a list of nuisance function estimators on the observed data (may be within a specified fold, for cross-fitted estimates). For the average value measure: an estimator of the optimal treatment rule (f_n); an estimator of the propensity score under the estimated optimal treatment rule (g_n); and an estimator of the outcome regression when treatment is assigned according to the estimated optimal rule (q_n).
C the indicator of coarsening (1 denotes observed, 0 denotes unobserved).
Z either NULL (if no coarsening) or a matrix-like object containing the fully observed data.
folds_Z either the cross-validation folds for the observed data (no coarsening) or a vector of folds for the fully observed data Z.
print.predictiveness_measure

ipc_weights  weights for inverse probability of coarsening (IPC) (e.g., inverse weights from a two-phase sample) weighted estimation. Assumed to be already inverted. (i.e., ipc_weights = 1 / estimated probability weights).

ipc_fit_type  if "external", then use ipc_eif_preds; if "SL", fit a SuperLearner to determine the IPC correction to the efficient influence function.

ipc_eif_preds  if ipc_fit_type = "external", the fitted values from a regression of the full-data EIF on the fully observed covariates/outcome; otherwise, not used.

ipc_est_type  IPC correction, either "ipw" (for classical inverse probability weighting) or "aipw" (for augmented inverse probability weighting; the default).

scale  if doing an IPC correction, then the scale that the correction should be computed on (e.g., "identity"; or "logit" to logit-transform, apply the correction, and back-transform).

na.rm  logical; should NAs be removed in computation? (defaults to FALSE)

...  other arguments to SuperLearner, if ipc_fit_type = "SL".

Value

An object of class "predictiveness_measure", with the following attributes:

print.predictiveness_measure

Print predictiveness_measure objects

Description

Prints out a table of the point estimate and standard error for a predictiveness_measure object.

Usage

## S3 method for class 'predictiveness_measure'
print(x, ...)

Arguments

x  the predictiveness_measure object of interest.

...  other options, see the generic print function.
print.vim

---

print.vim  \hspace{1cm} \textit{Print vim objects}

---

**Description**

Prints out the table of estimates, confidence intervals, and standard errors for a \texttt{vim} object.

**Usage**

```r
## S3 method for class 'vim'
print(x, ...)
```

**Arguments**

- \texttt{x} \hspace{1cm} the \texttt{vim} object of interest.
- \texttt{...} \hspace{1cm} other options, see the generic \texttt{print} function.

---

process_arg_lst  \hspace{1cm} \textit{Process argument list for Super Learner estimation of the EIF}

---

**Description**

Process argument list for Super Learner estimation of the EIF

**Usage**

```r
process_arg_lst(arg_lst)
```

**Arguments**

- \texttt{arg_lst} \hspace{1cm} the list of arguments for Super Learner

**Value**

- a list of modified arguments for EIF estimation
Run a Super Learner for the provided subset of features

Arguments

Y the outcome
X the covariates
V the number of folds
SL.library the library of candidate learners
univariate_SL.library the library of candidate learners for single-covariate regressions
s the subset of interest
cv_folds the CV folds
sample_splitting logical; should we use sample-splitting for predictiveness estimation?
ss_folds the sample-splitting folds; only used if sample_splitting = TRUE
split the split to use for sample-splitting; only used if sample_splitting = TRUE
sample_subsets

Verbose:
should we print progress? defaults to FALSE

Progress_bar:
the progress bar to print to (only if verbose = TRUE)

Index:
the index to pass to progress bar (only if verbose = TRUE)

Weights:
weights to pass to estimation procedure

Cross_fitted_se:
if TRUE, uses a cross-fitted estimator of the standard error; otherwise, uses the entire dataset

Full:
should this be considered a "full" or "reduced" regression? If NULL (the default), this is determined automatically; a full regression corresponds to \( s \) being equal to the full covariate vector. For SPVIMs, can be entered manually.

Vector:
should we return a vector (TRUE) or a list (FALSE)?

... other arguments to Super Learner

Value

a list of length \( V \), with the results of predicting on the hold-out data for each \( v \) in 1 through \( V \)

Value

Create necessary objects for SPVIMs

Description

Creates the \( Z \) and \( W \) matrices and a list of sampled subsets, \( S \), for SPVIM estimation.

Usage

\function{sample_subsets}{p, gamma, n}

Arguments

\begin{itemize}
\item \texttt{p} the number of covariates
\item \texttt{gamma} the fraction of the sample size to sample (e.g., \texttt{gamma = 1} means sample \texttt{n} subsets)
\item \texttt{n} the sample size
\end{itemize}

Value

a list, with elements \( Z \) (the matrix encoding presence/absence of each feature in the uniquely sampled subsets), \( S \) (the list of unique sampled subsets), \( W \) (the matrix of weights), and \( z \_counts \) (the number of times each subset was sampled)

Examples

```r
p <- 10
gamma <- 1
n <- 100
set.seed(100)
subset_lst <- sample_subsets(p, gamma, n)
```
**scale_est**

*Return an estimator on a different scale*

**Description**

Return an estimator on a different scale

**Usage**

```r
scale_est(obs_est = NULL, grad = NULL, scale = "identity")
```

**Arguments**

- `obs_est`: the observed VIM estimate
- `grad`: the estimated efficient influence function
- `scale`: the scale to compute on

**Details**

It may be of interest to return an estimate (or confidence interval) on a different scale than originally measured. For example, computing a confidence interval (CI) for a VIM value that lies in (0,1) on the logit scale ensures that the CI also lies in (0, 1).

**Value**

the scaled estimate

---

**spvim_ics**

*Influence function estimates for SPVIMs*

**Description**

Compute the influence functions for the contribution from sampling observations and subsets.

**Usage**

```r
spvim_ics(Z, z_counts, W, v, psi, G, c_n, ics, measure)
```
Arguments

- \( Z \): the matrix of presence/absence of each feature (columns) in each sampled subset (rows).
- \( z_{\text{counts}} \): the number of times each unique subset was sampled.
- \( W \): the matrix of weights.
- \( v \): the estimated predictiveness measures.
- \( \psi \): the estimated SPVIM values.
- \( G \): the constraint matrix.
- \( c_n \): the constraint values.
- \( \text{ics} \): a list of influence function values for each predictiveness measure.
- \( \text{measure} \): the type of measure (e.g., "r_squared" or "auc").

Details

The processes for sampling observations and sampling subsets are independent. Thus, we can compute the influence function separately for each sampling process. For further details, see the paper by Williamson and Feng (2020).

Value

A named list of length 2; \( \text{contrib}_v \) is the contribution from estimating \( V \), while \( \text{contrib}_s \) is the contribution from sampling subsets.

Description

Compute standard error estimates based on the estimated influence function for a SPVIM value of interest.

Usage

\[
\text{spvim}_\text{se}(\text{ics}, \text{idx} = 1, \text{gamma} = 1, \text{na_rm} = \text{FALSE})
\]

Arguments

- \( \text{ics} \): the influence function estimates based on the contributions from sampling observations and sampling subsets: a list of length two resulting from a call to \( \text{spvim}_\text{ics} \).
- \( \text{idx} \): the index of interest.
- \( \text{gamma} \): the proportion of the sample size used when sampling subsets.
- \( \text{na_rm} \): remove NAs?
Details

Since the processes for sampling observations and subsets are independent, the variance for a given SPVIM estimator is simply the sum of the variances based on sampling observations and on sampling subsets.

Value

The standard error estimate for the desired SPVIM value

See Also

spvim_ics for how the influence functions are estimated.

Description

Compute estimates and confidence intervals for the SPVIMs, using cross-fitting.

Usage

```r
sp_vim(
  Y = NULL,
  X = NULL,
  V = 5,
  type = "r_squared",
  SL.library = c("SL.glmnet", "SL.xgboost", "SL.mean"),
  univariate_SL.library = NULL,
  gamma = 1,
  alpha = 0.05,
  delta = 0,
  na.rm = FALSE,
  stratified = FALSE,
  verbose = FALSE,
  sample_splitting = TRUE,
  final_point_estimate = "split",
  C = rep(1, length(Y)),
  Z = NULL,
  ipc_scale = "identity",
  ipc_weights = rep(1, length(Y)),
  ipc_est_type = "aipw",
  scale = "identity",
  scale_est = TRUE,
  cross_fitted_se = TRUE,
  ...
)
```
Arguments

Y  the outcome.
X  the covariates. If type = "average_value", then the exposure variable should be part of X, with its name provided in exposure_name.
V  the number of folds for cross-fitting, defaults to 5. If sample_splitting = TRUE, then a special type of V-fold cross-fitting is done. See Details for a more detailed explanation.
type  the type of importance to compute; defaults to r_squared, but other supported options are auc, accuracy, deviance, and anova.
SL.library  a character vector of learners to pass to SuperLearner, if f1 and f2 are Y and X, respectively. Defaults to SL.glmnet, SL.xgboost, and SL.mean.
univariate_SL.library  (optional) a character vector of learners to pass to SuperLearner for estimating univariate regression functions. Defaults to SL.polymars
gamma  the fraction of the sample size to use when sampling subsets (e.g., gamma = 1 samples the same number of subsets as the sample size)
alpha  the level to compute the confidence interval at. Defaults to 0.05, corresponding to a 95% confidence interval.
delta  the value of the δ-null (i.e., testing if importance < δ); defaults to 0.
na.rm  should we remove NAs in the outcome and fitted values in computation? (defaults to FALSE)
stratified  if run_regression = TRUE, then should the generated folds be stratified based on the outcome (helps to ensure class balance across cross-validation folds)
verbose  should sp_vim and SuperLearner print out progress? (defaults to FALSE)
sample_splitting  should we use sample-splitting to estimate the full and reduced predictiveness? Defaults to TRUE, since inferences made using sample_splitting = FALSE will be invalid for variables with truly zero importance.
final_point_estimate  if sample splitting is used, should the final point estimates be based on only the sample-split folds used for inference ("split", the default), or should they instead be based on the full dataset ("full") or the average across the point estimates from each sample split ("average")? All three options result in valid point estimates – sample-splitting is only required for valid inference.
C  the indicator of coarsening (1 denotes observed, 0 denotes unobserved).
Z  either (i) NULL (the default, in which case the argument C above must be all ones), or (ii) a character vector specifying the variable(s) among Y and X that are thought to play a role in the coarsening mechanism. To specify the outcome, use "Y"; to specify covariates, use a character number corresponding to the desired position in X (e.g., "1").
ipc_scale  what scale should the inverse probability weight correction be applied on (if any)? Defaults to "identity". (other options are "log" and "logit")
**sp_vim**

- **ipc_weights**: weights for the computed influence curve (i.e., inverse probability weights for coarsened-at-random settings). Assumed to be already inverted (i.e., \(ipc\_weights = 1 / \text{[estimated probability weights]}\)).

- **ipc_est_type**: the type of procedure used for coarsened-at-random settings; options are "ipw" (for inverse probability weighting) or "aipw" (for augmented inverse probability weighting). Only used if \(C\) is not all equal to 1.

- **scale**: should CIs be computed on original ("identity") or another scale? (options are "log" and "logit")

- **scale_est**: should the point estimate be scaled to be greater than or equal to 0? Defaults to TRUE.

- **cross_fitted_se**: should we use cross-fitting to estimate the standard errors (TRUE, the default) or not (FALSE)?

- **Details**: We define the SPVIM as the weighted average of the population difference in predictiveness over all subsets of features not containing feature \(j\).

This is equivalent to finding the solution to a population weighted least squares problem. This key fact allows us to estimate the SPVIM using weighted least squares, where we first sample subsets from the power set of all possible features using the Shapley sampling distribution; then use cross-fitting to obtain estimators of the predictiveness of each sampled subset; and finally, solve the least squares problem given in Williamson and Feng (2020).

See the paper by Williamson and Feng (2020) for more details on the mathematics behind this function, and the validity of the confidence intervals.

In the interest of transparency, we return most of the calculations within the *vim* object. This results in a list containing:

- **SL.library**: the library of learners passed to SuperLearner
- **v**: the estimated predictiveness measure for each sampled subset
- **fit_lst**: the fitted values on the entire dataset from the chosen method for each sampled subset
- **preds_lst**: the cross-fitted predicted values from the chosen method for each sampled subset
- **est**: the estimated SPVIM value for each feature
- **ics**: the influence functions for each sampled subset
- **var_v_contribs**: the contributions to the variance from estimating predictiveness
- **var_s_contribs**: the contributions to the variance from sampling subsets
- **ic_lst**: a list of the SPVIM influence function contributions
- **se**: the standard errors for the estimated variable importance
- **ci**: the \((1 - \alpha) \times 100\%\) confidence intervals based on the variable importance estimates
- **p_value**: p-values for the null hypothesis test of zero importance for each variable
- **test_statistic**: the test statistic for each null hypothesis test of zero importance
test  a hypothesis testing decision for each null hypothesis test (for each variable having zero importance)

gamma  the fraction of the sample size used when sampling subsets

alpha  the level, for confidence interval calculation

delta  the delta value used for hypothesis testing

y  the outcome

ipc_weights  the weights

scale  the scale on which CIs were computed

mat  - a tibble with the estimates, SEs, CIs, hypothesis testing decisions, and p-values

Value

An object of class \texttt{vim}. See Details for more information.

See Also

\texttt{SuperLearner} for specific usage of the \texttt{SuperLearner} function and package.

Examples

```r
n <- 100
p <- 2
# generate the data
x <- data.frame(replicate(p, stats::runif(n, -5, 5)))

# apply the function to the x's
smooth <- (x[,1]/5)^2*(x[,1]+7)/5 + (x[,2]/3)^2

# generate Y ~ Normal (smooth, 1)
y <- as.matrix(smooth + stats::rnorm(n, 0, 1))

# set up a library for SuperLearner; note simple library for speed
library("SuperLearner")
learners <- c("SL.glm")

# using Super Learner (with a small number of CV folds, # for illustration only)
# -----------------------------------------
set.seed(4747)
est <- sp_vim(Y = y, X = x, V = 2, type = "r_squared",
SL.library = learners, alpha = 0.05)
```
Nonparametric Intrinsic Variable Importance Estimates and Inference

Description

Compute estimates of and confidence intervals for nonparametric intrinsic variable importance based on the population-level contrast between the oracle predictiveness using the feature(s) of interest versus not.

Usage

```r
vim(
  Y = NULL,
  X = NULL,
  f1 = NULL,
  f2 = NULL,
  indx = 1,
  type = "r_squared",
  run_regression = TRUE,
  SL.library = c("SL.glmnet", "SL.xgboost", "SL.mean"),
  alpha = 0.05,
  delta = 0,
  scale = "identity",
  na.rm = FALSE,
  sample_splitting = TRUE,
  sample_splitting_folds = NULL,
  final_point_estimate = "split",
  stratified = FALSE,
  C = rep(1, length(Y)),
  Z = NULL,
  ipc_scale = "identity",
  ipc_weights = rep(1, length(Y)),
  ipc_est_type = "aipw",
  scale_est = TRUE,
  nuisance_estimators_full = NULL,
  nuisance_estimators_reduced = NULL,
  exposure_name = NULL,
  bootstrap = FALSE,
  b = 1000,
  boot_interval_type = "perc",
  clustered = FALSE,
  cluster_id = rep(NA, length(Y)),
  ...
)
```

Arguments

- `Y` the outcome.
the covariates. If type = "average_value", then the exposure variable should be part of X, with its name provided in exposure_name.

f1 the fitted values from a flexible estimation technique regressing Y on X. A vector of the same length as Y; if sample-splitting is desired, then the value of f1 at each position should be the result of predicting from a model trained without that observation.

f2 the fitted values from a flexible estimation technique regressing either (a) f1 or (b) Y on X withholding the columns in indx. A vector of the same length as Y; if sample-splitting is desired, then the value of f2 at each position should be the result of predicting from a model trained without that observation.

indx the indices of the covariate(s) to calculate variable importance for; defaults to 1.

type the type of importance to compute; defaults to r_squared, but other supported options are auc, accuracy, deviance, and anova.

run_regression if outcome Y and covariates X are passed to vimp_accuracy, and run_regression is TRUE, then Super Learner will be used; otherwise, variable importance will be computed using the inputted fitted values.

SL.library a character vector of learners to pass to SuperLearner, if f1 and f2 are Y and X, respectively. Defaults to SL.glmnet, SL.xgboost, and SL.mean.

alpha the level to compute the confidence interval at. Defaults to 0.05, corresponding to a 95% confidence interval.

delta the value of the \( \delta \)-null (i.e., testing if importance < \( \delta \)); defaults to 0.

scale should CIs be computed on original ("identity") or another scale? (options are "log" and "logit")

na.rm should we remove NAs in the outcome and fitted values in computation? (defaults to FALSE)

sample_splitting should we use sample-splitting to estimate the full and reduced predictiveness? Defaults to TRUE, since inferences made using sample_splitting = FALSE will be invalid for variables with truly zero importance.

sample_splitting_folds the folds used for sample-splitting; these identify the observations that should be used to evaluate predictiveness based on the full and reduced sets of covariates, respectively. Only used if run_regression = FALSE.

final_point_estimate if sample splitting is used, should the final point estimates be based on only the sample-split folds used for inference ("split", the default), or should they instead be based on the full dataset ("full") or the average across the point estimates from each sample split ("average")? All three options result in valid point estimates – sample-splitting is only required for valid inference.

stratified if run_regression = TRUE, then should the generated folds be stratified based on the outcome (helps to ensure class balance across cross-validation folds)

C the indicator of coarsening (1 denotes observed, 0 denotes unobserved).

Z either (i) NULL (the default, in which case the argument C above must be all ones), or (ii) a character vector specifying the variable(s) among Y and X that are
thought to play a role in the coarsening mechanism. To specify the outcome, use "Y"; to specify covariates, use a character number corresponding to the desired position in X (e.g., "1").

ipc_scale what scale should the inverse probability weight correction be applied on (if any)? Defaults to "identity". (other options are "log" and "logit")

ipc_weights weights for the computed influence curve (i.e., inverse probability weights for coarsened-at-random settings). Assumed to be already inverted (i.e., ipc_weights = 1 / [estimated probability weights]).

ipc_est_type the type of procedure used for coarsened-at-random settings; options are "ipw" (for inverse probability weighting) or "aipw" (for augmented inverse probability weighting). Only used if C is not all equal to 1.

scale_est should the point estimate be scaled to be greater than or equal to 0? Defaults to TRUE.

nuisance_estimators_full (only used if type = "average_value") a list of nuisance function estimators on the observed data (may be within a specified fold, for cross-fitted estimates). Specifically: an estimator of the optimal treatment rule; an estimator of the propensity score under the estimated optimal treatment rule; and an estimator of the outcome regression when treatment is assigned according to the estimated optimal rule.

nuisance_estimators_reduced (only used if type = "average_value") a list of nuisance function estimators on the observed data (may be within a specified fold, for cross-fitted estimates). Specifically: an estimator of the optimal treatment rule; an estimator of the propensity score under the estimated optimal treatment rule; and an estimator of the outcome regression when treatment is assigned according to the estimated optimal rule.

exposure_name (only used if type = "average_value") the name of the exposure of interest; binary, with 1 indicating presence of the exposure and 0 indicating absence of the exposure.

bootstrap should bootstrap-based standard error estimates be computed? Defaults to FALSE (and currently may only be used if sample_splitting = FALSE).

b the number of bootstrap replicates (only used if bootstrap = TRUE and sample_splitting = FALSE); defaults to 1000.

boot_interval_type the type of bootstrap interval (one of "norm", "basic", "stud", "perc", or "bca", as in boot\{boot.ci\}) if requested. Defaults to "perc".

clustered should the bootstrap resamples be performed on clusters rather than individual observations? Defaults to FALSE.

cluster_id vector of the same length as Y giving the cluster IDs used for the clustered bootstrap, if clustered is TRUE.

... other arguments to the estimation tool, see "See also".
Details

We define the population variable importance measure (VIM) for the group of features (or single feature) $s$ with respect to the predictiveness measure $V$ by

$$\psi_{0,s} := V(f_0, P_0) - V(f_{0,s}, P_0),$$

where $f_0$ is the population predictiveness maximizing function, $f_{0,s}$ is the population predictiveness maximizing function that is only allowed to access the features with index not in $s$, and $P_0$ is the true data-generating distribution. VIM estimates are obtained by obtaining estimators $f_n$ and $f_{n,s}$ of $f_0$ and $f_{0,s}$, respectively; obtaining an estimator $P_n$ of $P_0$; and finally, setting $\psi_{n,s} := V(f_n, P_n) - V(f_{n,s}, P_n)$.

In the interest of transparency, we return most of the calculations within the `vim` object. This results in a list including:

- `s` the column(s) to calculate variable importance for
- `SL.library` the library of learners passed to `SuperLearner`
- `type` the type of risk-based variable importance measured
- `full_fit` the fitted values of the chosen method fit to the full data
- `red_fit` the fitted values of the chosen method fit to the reduced data
- `est` the estimated variable importance
- `naive` the naive estimator of variable importance (only used if `type = "anova"`)
- `eif` the estimated efficient influence function
- `eif_full` the estimated efficient influence function for the full regression
- `eif_reduced` the estimated efficient influence function for the reduced regression
- `se` the standard error for the estimated variable importance
- `ci` the $(1 - \alpha) \times 100\%$ confidence interval for the variable importance estimate
- `test` a decision to either reject (TRUE) or not reject (FALSE) the null hypothesis, based on a conservative test
- `p_value` a p-value based on the same test as `test`
- `full_mod` the object returned by the estimation procedure for the full data regression (if applicable)
- `red_mod` the object returned by the estimation procedure for the reduced data regression (if applicable)
- `alpha` the level, for confidence interval calculation
- `sample_splitting_folds` the folds used for sample-splitting (used for hypothesis testing)
- `y` the outcome
- `ipc_weights` the weights
- `cluster_id` the cluster IDs
- `mat` a tibble with the estimate, SE, CI, hypothesis testing decision, and p-value

Value

An object of classes `vim` and the type of risk-based measure. See Details for more information.
See Also

SuperLearner for specific usage of the SuperLearner function and package.

Examples

```r
# generate the data
# generate X
p <- 2
ten <- 100
x <- data.frame(replicate(p, stats::runif(n, -1, 1)))

# apply the function to the x's
f <- function(x) 0.5 + 0.3*x[1] + 0.2*x[2]
smooth <- apply(x, 1, function(z) f(z))

# generate Y ~ Bernoulli (smooth)
y <- matrix(rbinom(n, size = 1, prob = smooth))

# set up a library for SuperLearner; note simple library for speed
library("SuperLearner")
learners <- c("SL.glm")

# using Y and X; use class-balanced folds
est_1 <- vim(y, x, indx = 2, type = "accuracy",
              alpha = 0.05, run_regression = TRUE,
              SL.library = learners, cvControl = list(V = 2),
              stratified = TRUE)

# using pre-computed fitted values
set.seed(4747)
V <- 2
full_fit <- SuperLearner::CV.SuperLearner(Y = y, X = x,
                                          SL.library = learners,
                                          cvControl = list(V = 2),
                                          innerCvControl = list(list(V = V)))
full_fitted <- SuperLearner::predict.SuperLearner(full_fit)$pred
# fit the data with only X1
reduced_fit <- SuperLearner::CV.SuperLearner(Y = full_fitted,
                                          X = x[, -2, drop = FALSE],
                                          SL.library = learners,
                                          cvControl = list(V = 2, validRows = full_fit$folds),
                                          innerCvControl = list(list(V = V)))
reduced_fitted <- SuperLearner::predict.SuperLearner(reduced_fit)$pred

est_2 <- vim(Y = y, f1 = full_fitted, f2 = reduced_fitted,
              indx = 2, run_regression = FALSE, alpha = 0.05,
              stratified = TRUE, type = "accuracy",
              sample_splitting_folds = get_cv_sl_folds(full_fit$folds))
```
vimp_accuracy

Nonparametric Intrinsic Variable Importance Estimates: Classification accuracy

Description

Compute estimates of and confidence intervals for nonparametric difference in classification accuracy-based intrinsic variable importance. This is a wrapper function for cv_vim, with type = "accuracy".

Usage

vimp_accuracy(
  Y = NULL,
  X = NULL,
  cross_fitted_f1 = NULL,
  cross_fitted_f2 = NULL,
  f1 = NULL,
  f2 = NULL,
  indx = 1,
  V = 10,
  run_regression = TRUE,
  SL.library = c("SL.glmnet", "SL.xgboost", "SL.mean"),
  alpha = 0.05,
  delta = 0,
  na.rm = FALSE,
  final_point_estimate = "split",
  cross_fitting_folds = NULL,
  sample_splitting_folds = NULL,
  stratified = TRUE,
  C = rep(1, length(Y)),
  Z = NULL,
  ipc_weights = rep(1, length(Y)),
  scale = "logit",
  ipc_est_type = "aipw",
  scale_est = TRUE,
  cross_fitted_se = TRUE,
  ...
)

Arguments

Y the outcome.
X the covariates. If type = "average_value", then the exposure variable should be part of X, with its name provided in exposure_name.
cross_fitted_f1 the predicted values on validation data from a flexible estimation technique regressing Y on X in the training data. Provided as either (a) a vector, where each
element is the predicted value when that observation is part of the validation fold; or (b) a list of length $V$, where each element in the list is a set of predictions on the corresponding validation data fold. If sample-splitting is requested, then these must be estimated specially; see Details. However, the resulting vector should be the same length as $Y$; if using a list, then the summed length of each element across the list should be the same length as $Y$ (i.e., each observation is included in the predictions).

cross_fitted_f2
the predicted values on validation data from a flexible estimation technique regressing either (a) the fitted values in cross_fitted_f1, or (b) $Y$, on $X$ withholding the columns in indx. Provided as either (a) a vector, where each element is the predicted value when that observation is part of the validation fold; or (b) a list of length $V$, where each element in the list is a set of predictions on the corresponding validation data fold. If sample-splitting is requested, then these must be estimated specially; see Details. However, the resulting vector should be the same length as $Y$; if using a list, then the summed length of each element across the list should be the same length as $Y$ (i.e., each observation is included in the predictions).

f1
the fitted values from a flexible estimation technique regressing $Y$ on $X$. If sample-splitting is requested, then these must be estimated specially; see Details. If cross_fitted_se = TRUE, then this argument is not used.

f2
the fitted values from a flexible estimation technique regressing either (a) f1 or (b) $Y$ on $X$ withholding the columns in indx. If sample-splitting is requested, then these must be estimated specially; see Details. If cross_fitted_se = TRUE, then this argument is not used.

indx
the indices of the covariate(s) to calculate variable importance for; defaults to 1.

V
the number of folds for cross-fitting, defaults to 5. If sample_splitting = TRUE, then a special type of $V$-fold cross-fitting is done. See Details for a more detailed explanation.

run_regression
if outcome $Y$ and covariates $X$ are passed to vimp_accuracy, and run_regression is TRUE, then Super Learner will be used; otherwise, variable importance will be computed using the inputted fitted values.

SL.library
a character vector of learners to pass to SuperLearner, if f1 and f2 are $Y$ and $X$, respectively. Defaults to SL.glmnet, SL.xgboost, and SL.mean.

alpha
the level to compute the confidence interval at. Defaults to 0.05, corresponding to a 95% confidence interval.

delta
the value of the $\delta$-null (i.e., testing if importance < $\delta$); defaults to 0.

na.rm
should we remove NAs in the outcome and fitted values in computation? (defaults to FALSE)

final_point_estimate
if sample splitting is used, should the final point estimates be based on only the sample-split folds used for inference ("split", the default), or should they instead be based on the full dataset ("full") or the average across the point estimates from each sample split ("average")? All three options result in valid point estimates – sample-splitting is only required for valid inference.
Cross-fitting folds

the folds for cross-fitting. Only used if run_regression = FALSE.

Sample-splitting folds

the folds used for sample-splitting; these identify the observations that should be
used to evaluate predictiveness based on the full and reduced sets of covariates,
respectively. Only used if run_regression = FALSE.

stratified

if run_regression = TRUE, then should the generated folds be stratified based on
the outcome (helps to ensure class balance across cross-validation folds)

C

the indicator of coarsening (1 denotes observed, 0 denotes unobserved).

Z

either (i) NULL (the default, in which case the argument C above must be all
ones), or (ii) a character vector specifying the variable(s) among Y and X that are
thought to play a role in the coarsening mechanism. To specify the outcome, use
"Y"; to specify covariates, use a character number corresponding to the desired
position in X (e.g., "1").

ipc_weights

weights for the computed influence curve (i.e., inverse probability weights for
coarsened-at-random settings). Assumed to be already inverted (i.e., ipc_weights
= 1 / [estimated probability weights]).

scale

should CIs be computed on original ("identity") or another scale? (options are
"log" and "logit")

ipc_est_type

the type of procedure used for coarsened-at-random settings; options are "ipw"
(for inverse probability weighting) or "aipw" (for augmented inverse probability
weighting). Only used if C is not all equal to 1.

scale_est

should the point estimate be scaled to be greater than or equal to 0? Defaults to
TRUE.

cross_fitted_se

should we use cross-fitting to estimate the standard errors (TRUE, the default) or
not (FALSE)?

... other arguments to the estimation tool, see "See also".

Details

We define the population variable importance measure (VIM) for the group of features (or single
feature) s with respect to the predictiveness measure V by

\[ \psi_{0,s} := V(f_0, P_0) - V(f_{0,s}, P_0), \]

where \( f_0 \) is the population predictiveness maximizing function, \( f_{0,s} \) is the population predictiveness
maximizing function that is only allowed to access the features with index not in \( s \), and \( P_0 \) is the
true data-generating distribution.

Cross-fitted VIM estimates are computed differently if sample-splitting is requested versus if it is
not. We recommend using sample-splitting in most cases, since only in this case will inferences
be valid if the variable(s) of interest have truly zero population importance. The purpose of cross-
fitting is to estimate \( f_0 \) and \( f_{0,s} \) on independent data from estimating \( P_0 \); this can result in improved
performance, especially when using flexible learning algorithms. The purpose of sample-splitting
is to estimate \( f_0 \) and \( f_{0,s} \) on independent data; this allows valid inference under the null hypothesis
of zero importance.
Without sample-splitting, cross-fitted VIM estimates are obtained by first splitting the data into $K$ folds; then using each fold in turn as a hold-out set, constructing estimators $f_{n,k}$ and $f_{n,k,s}$ of $f_0$ and $f_{0,s}$, respectively on the training data and estimator $P_{n,k}$ of $P_0$ using the test data; and finally, computing
\[
\psi_{n,s} := K^{(-1)} \sum_{k=1}^{K} \{ V(f_{n,k}, P_{n,k}) - V(f_{n,k,s}, P_{n,k}) \}.
\]

With sample-splitting, cross-fitted VIM estimates are obtained by first splitting the data into $2K$ folds. These folds are further divided into 2 groups of folds. Then, for each fold $k$ in the first group, estimator $f_{n,k}$ of $f_0$ is constructed using all data besides the $k$th fold in the group (i.e., $(2K-1)/(2K)$ of the data) and estimator $P_{n,k}$ of $P_0$ is constructed using the held-out data (i.e., $1/2K$ of the data); then, computing
\[
v_{n,k} = V(f_{n,k}, P_{n,k}).
\]

Similarly, for each fold $k$ in the second group, estimator $f_{n,k,s}$ of $f_{0,s}$ is constructed using all data besides the $k$th fold in the group (i.e., $(2K-1)/(2K)$ of the data) and estimator $P_{n,k}$ of $P_0$ is constructed using the held-out data (i.e., $1/2K$ of the data); then, computing
\[
v_{n,k,s} = V(f_{n,k,s}, P_{n,k}).
\]

Finally,
\[
\psi_{n,s} := K^{(-1)} \sum_{k=1}^{K} \{ v_{n,k} - v_{n,k,s} \}.
\]

See the paper by Williamson, Gilbert, Simon, and Carone for more details on the mathematics behind the cv_vim function, and the validity of the confidence intervals.

In the interest of transparency, we return most of the calculations within the vim object. This results in a list including:

s the column(s) to calculate variable importance for
SL.library the library of learners passed to SuperLearner
full_fit the fitted values of the chosen method fit to the full data (a list, for train and test data)
red_fit the fitted values of the chosen method fit to the reduced data (a list, for train and test data)
est the estimated variable importance
naive the naive estimator of variable importance
eif the estimated efficient influence function
eif_full the estimated efficient influence function for the full regression
eif_reduced the estimated efficient influence function for the reduced regression
se the standard error for the estimated variable importance
ci the $(1 - \alpha) \times 100\%$ confidence interval for the variable importance estimate
test a decision to either reject (TRUE) or not reject (FALSE) the null hypothesis, based on a conservative test
p_value a p-value based on the same test as test
full_mod the object returned by the estimation procedure for the full data regression (if applicable)
**vimp_accuracy**

- **red_mod** the object returned by the estimation procedure for the reduced data regression (if applicable)
- **alpha** the level, for confidence interval calculation
- **sample_splitting_folds** the folds used for hypothesis testing
- **cross_fitting_folds** the folds used for cross-fitting
- **y** the outcome
- **ipc_weights** the weights
- **cluster_id** the cluster IDs
- **mat** a tibble with the estimate, SE, CI, hypothesis testing decision, and p-value

**Value**

An object of classes `vim` and `vim_accuracy`. See Details for more information.

**See Also**

`SuperLearner` for specific usage of the SuperLearner function and package.

**Examples**

```r
# generate the data
# generate X
p <- 2
n <- 100
x <- data.frame(replicate(p, stats::runif(n, -1, 1)))

# apply the function to the x's
f <- function(x) 0.5 + 0.3*x[1] + 0.2*x[2]
smooth <- apply(x, 1, function(z) f(z))

# generate Y \sim Normal (smooth, 1)
y <- matrix(rbinom(n, size = 1, prob = smooth))

# set up a library for SuperLearner; note simple library for speed
library("SuperLearner")
learners <- c("SL.glm", "SL.mean")

# estimate (with a small number of folds, for illustration only)
est <- vimp_accuracy(y, x, indx = 2,
                     alpha = 0.05, run_regression = TRUE,
                     SL.library = learners, V = 2, cvControl = list(V = 2))
```
Description

Compute estimates of and confidence intervals for nonparametric ANOVA-based intrinsic variable importance. This is a wrapper function for cv_vim, with type = “anova”. This type has limited functionality compared to other types; in particular, null hypothesis tests are not possible using type = "anova". If you want to do null hypothesis testing on an equivalent population parameter, use vimp_rsquared instead.

Usage

vimp_anova(
  Y = NULL,
  X = NULL,
  cross_fitted_f1 = NULL,
  cross_fitted_f2 = NULL,
  indx = 1,
  V = 10,
  run_regression = TRUE,
  SL.library = c("SL.glmnet", "SL.xgboost", "SL.mean"),
  alpha = 0.05,
  delta = 0,
  na.rm = FALSE,
  cross_fitting_folds = NULL,
  stratified = FALSE,
  C = rep(1, length(Y)),
  Z = NULL,
  ipc_weights = rep(1, length(Y)),
  scale = "logit",
  ipc_est_type = "aipw",
  scale_est = TRUE,
  cross_fitted_se = TRUE,
  ...
)

Arguments

Y the outcome.

X the covariates. If type = "average_value", then the exposure variable should be part of X, with its name provided in exposure_name.

cross_fitted_f1 the predicted values on validation data from a flexible estimation technique regressing Y on X in the training data. Provided as either (a) a vector, where each element is the predicted value when that observation is part of the validation
fold; or (b) a list of length V, where each element in the list is a set of predictions on the corresponding validation data fold. If sample-splitting is requested, then these must be estimated specially; see Details. However, the resulting vector should be the same length as Y; if using a list, then the summed length of each element across the list should be the same length as Y (i.e., each observation is included in the predictions).

cross_fitted_f2
the predicted values on validation data from a flexible estimation technique regressing either (a) the fitted values in cross_fitted_f1, or (b) Y, on X witholding the columns in indx. Provided as either (a) a vector, where each element is the predicted value when that observation is part of the validation fold; or (b) a list of length V, where each element in the list is a set of predictions on the corresponding validation data fold. If sample-splitting is requested, then these must be estimated specially; see Details. However, the resulting vector should be the same length as Y; if using a list, then the summed length of each element across the list should be the same length as Y (i.e., each observation is included in the predictions).

indx
the indices of the covariate(s) to calculate variable importance for; defaults to 1.

V
the number of folds for cross-fitting, defaults to 5. If sample_splitting = TRUE, then a special type of V-fold cross-fitting is done. See Details for a more detailed explanation.

run_regression
if outcome Y and covariates X are passed to vimp_accuracy, and run_regression is TRUE, then Super Learner will be used; otherwise, variable importance will be computed using the inputted fitted values.

SL.library
a character vector of learners to pass to SuperLearner, if f1 and f2 are Y and X, respectively. Defaults to SL.glmnet, SL.xgboost, and SL.mean.

alpha
the level to compute the confidence interval at. Defaults to 0.05, corresponding to a 95% confidence interval.

delta
the value of the \( \delta \)-null (i.e., testing if importance < \( \delta \)); defaults to 0.

na.rm
should we remove NAs in the outcome and fitted values in computation? (defaults to FALSE)

cross_fitting_folds
the folds for cross-fitting. Only used if run_regression = FALSE.

stratified
if run_regression = TRUE, then should the generated folds be stratified based on the outcome (helps to ensure class balance across cross-validation folds)

C
the indicator of coarsening (1 denotes observed, 0 denotes unobserved).

Z
either (i) NULL (the default, in which case the argument C above must be all ones), or (ii) a character vector specifying the variable(s) among Y and X that are thought to play a role in the coarsening mechanism. To specify the outcome, use "Y"; to specify covariates, use a character number corresponding to the desired position in X (e.g., "1").

ipc_weights
weights for the computed influence curve (i.e., inverse probability weights for coarsened-at-random settings). Assumed to be already inverted (i.e., ipc_weights = 1 / [estimated probability weights]).
scale should CIs be computed on original ("identity") or another scale? (options are "log" and "logit")

ipc_est_type the type of procedure used for coarsened-at-random settings; options are "ipw" (for inverse probability weighting) or "aipw" (for augmented inverse probability weighting). Only used if C is not all equal to 1.

scale_est should the point estimate be scaled to be greater than or equal to 0? Defaults to TRUE.

cross_fitted_se should we use cross-fitting to estimate the standard errors (TRUE, the default) or not (FALSE)?

Details

We define the population ANOVA parameter for the group of features (or single feature) \( s \) by

\[
\psi_{0,s} := E_0\{f_0(X) - f_{0,s}(X)\}^2/\text{var}_0(Y),
\]

where \( f_0 \) is the population conditional mean using all features, \( f_{0,s} \) is the population conditional mean using the features with index not in \( s \), and \( E_0 \) and \( \text{var}_0 \) denote expectation and variance under the true data-generating distribution, respectively.

Cross-fitted ANOVA estimates are computed by first splitting the data into \( K \) folds; then using each fold in turn as a hold-out set, constructing estimators \( f_{n,k} \) and \( f_{n,k,s} \) of \( f_0 \) and \( f_{0,s} \), respectively on the training data and estimator \( E_{n,k} \) of \( E_0 \) using the test data; and finally, computing

\[
\psi_{n,s} := K^{(-1)} \sum_{k=1}^{K} E_{n,k}\{f_{n,k}(X) - f_{n,k,s}(X)\}^2/\text{var}_n(Y),
\]

where \( \text{var}_n \) is the empirical variance. See the paper by Williamson, Gilbert, Simon, and Carone for more details on the mathematics behind this function.

Value

An object of classes \texttt{vim} and \texttt{vim_anova}. See Details for more information.

See Also

\texttt{SuperLearner} for specific usage of the \texttt{SuperLearner} function and package.

Examples

```r
# generate the data
# generate X
p <- 2
n <- 100
x <- data.frame(replicate(p, stats::runif(n, -5, 5)))

# apply the function to the x's
smooth <- (x[,1]/5)^2*(x[,1]+7)/5 + (x[,2]/3)^2
```
# generate Y ~ Normal (smooth, 1)
y <- smooth + stats::rnorm(n, 0, 1)

# set up a library for SuperLearner; note simple library for speed
library("SuperLearner")
learners <- c("SL.glm", "SL.mean")

# estimate (with a small number of folds, for illustration only)
est <- vimp_anova(y, x, indx = 2,
                   alpha = 0.05, run_regression = TRUE,
                   SL.library = learners, V = 2, cvControl = list(V = 2))

---

**vimp_auc**

**Nonparametric Intrinsic Variable Importance Estimates: AUC**

**Description**

Compute estimates of and confidence intervals for nonparametric difference in \$\text{AUC}\$-based intrinsic variable importance. This is a wrapper function for `cv_vim`, with `type = "auc"`.

**Usage**

```r
vimp_auc(
  Y = NULL,
  X = NULL,
  cross_fitted_f1 = NULL,
  cross_fitted_f2 = NULL,
  f1 = NULL,
  f2 = NULL,
  indx = 1,
  V = 10,
  run_regression = TRUE,
  SL.library = c("SL.glmnet", "SL.xgboost", "SL.mean"),
  alpha = 0.05,
  delta = 0,
  na.rm = FALSE,
  final_point_estimate = "split",
  cross_fitting_folds = NULL,
  sample_splitting_folds = NULL,
  stratified = TRUE,
  C = rep(1, length(Y)),
  Z = NULL,
  ipc_weights = rep(1, length(Y)),
  scale = "logit",
  ipc_est_type = "aipw",
  scale_est = TRUE,
)```

Arguments

Y the outcome.

X the covariates. If type = "average_value", then the exposure variable should be part of X, with its name provided in exposure_name.

cross_fitted_f1 the predicted values on validation data from a flexible estimation technique regressing Y on X in the training data. Provided as either (a) a vector, where each element is the predicted value when that observation is part of the validation fold; or (b) a list of length V, where each element in the list is a set of predictions on the corresponding validation data fold. If sample-splitting is requested, then these must be estimated specially; see Details. However, the resulting vector should be the same length as Y; if using a list, then the summed length of each element across the list should be the same length as Y (i.e., each observation is included in the predictions).

cross_fitted_f2 the predicted values on validation data from a flexible estimation technique regressing either (a) the fitted values in cross_fitted_f1, or (b) Y, on X withholding the columns in indx. Provided as either (a) a vector, where each element is the predicted value when that observation is part of the validation fold; or (b) a list of length V, where each element in the list is a set of predictions on the corresponding validation data fold. If sample-splitting is requested, then these must be estimated specially; see Details. However, the resulting vector should be the same length as Y; if using a list, then the summed length of each element across the list should be the same length as Y (i.e., each observation is included in the predictions).

f1 the fitted values from a flexible estimation technique regressing Y on X. If sample-splitting is requested, then these must be estimated specially; see Details. If cross_fitted_se = TRUE, then this argument is not used.

f2 the fitted values from a flexible estimation technique regressing either (a) f1 or (b) Y on X withholding the columns in indx. If sample-splitting is requested, then these must be estimated specially; see Details. If cross_fitted_se = TRUE, then this argument is not used.

indx the indices of the covariate(s) to calculate variable importance for; defaults to 1.

V the number of folds for cross-fitting, defaults to 5. If sample_splitting = TRUE, then a special type of V-fold cross-fitting is done. See Details for a more detailed explanation.

run_regression if outcome Y and covariates X are passed to vimp_accuracy, and run_regression is TRUE, then Super Learner will be used; otherwise, variable importance will be computed using the inputted fitted values.

SL.library a character vector of learners to pass to SuperLearner, if f1 and f2 are Y and X, respectively. Defaults to SL.glmnet, SL.xgboost, and SL.mean.
alpha the level to compute the confidence interval at. Defaults to 0.05, corresponding to a 95% confidence interval.
delta the value of the $\delta$-null (i.e., testing if importance < $\delta$); defaults to 0.
na.rm should we remove NAs in the outcome and fitted values in computation? (defaults to FALSE)
final_point_estimate if sample splitting is used, should the final point estimates be based on only the sample-split folds used for inference ("split", the default), or should they instead be based on the full dataset ("full") or the average across the point estimates from each sample split ("average")? All three options result in valid point estimates – sample-splitting is only required for valid inference.
cross_fitting_folds the folds for cross-fitting. Only used if run_regression = FALSE.
sample_splitting_folds the folds used for sample-splitting; these identify the observations that should be used to evaluate predictiveness based on the full and reduced sets of covariates, respectively. Only used if run_regression = FALSE.
stratified if run_regression = TRUE, then should the generated folds be stratified based on the outcome (helps to ensure class balance across cross-validation folds)
C the indicator of coarsening (1 denotes observed, 0 denotes unobserved).
Z either (i) NULL (the default, in which case the argument C above must be all ones), or (ii) a character vector specifying the variable(s) among Y and X that are thought to play a role in the coarsening mechanism. To specify the outcome, use "Y"; to specify covariates, use a character number corresponding to the desired position in X (e.g., "1").
ipc_weights weights for the computed influence curve (i.e., inverse probability weights for coarsened-at-random settings). Assumed to be already inverted (i.e., ipc_weights = 1 / [estimated probability weights]).
scale should CIs be computed on original ("identity") or another scale? (options are "log" and "logit")
ipc_est_type the type of procedure used for coarsened-at-random settings; options are "ipw" (for inverse probability weighting) or "aipw" (for augmented inverse probability weighting). Only used if C is not all equal to 1.
scale_est should the point estimate be scaled to be greater than or equal to 0? Defaults to TRUE.
cross_fitted_se should we use cross-fitting to estimate the standard errors (TRUE, the default) or not (FALSE)?

Details

We define the population variable importance measure (VIM) for the group of features (or single feature) $s$ with respect to the predictiveness measure $V$ by

$$
\psi_{0,s} := V(f_0, P_0) - V(f_{0,s}, P_0),
$$
where $f_0$ is the population predictiveness maximizing function, $f_{0,s}$ is the population predictiveness maximizing function that is only allowed to access the features with index not in $s$, and $P_0$ is the true data-generating distribution.

Cross-fitted VIM estimates are computed differently if sample-splitting is requested versus if it is not. We recommend using sample-splitting in most cases, since only in this case will inferences be valid if the variable(s) of interest have truly zero population importance. The purpose of cross-fitting is to estimate $f_0$ and $f_{0,s}$ on independent data from estimating $P_0$; this can result in improved performance, especially when using flexible learning algorithms. The purpose of sample-splitting is to estimate $f_0$ and $f_{0,s}$ on independent data; this allows valid inference under the null hypothesis of zero importance.

Without sample-splitting, cross-fitted VIM estimates are obtained by first splitting the data into $K$ folds; then using each fold in turn as a hold-out set, constructing estimators $f_{n,k}$ and $f_{n,k,s}$ of $f_0$ and $f_{0,s}$, respectively on the training data and estimator $P_{n,k}$ of $P_0$ using the test data; and finally, computing

$$
\psi_{n,s} := K^{-1} \sum_{k=1}^{K} \{ V(f_{n,k}, P_{n,k}) - V(f_{n,k,s}, P_{n,k}) \}.
$$

With sample-splitting, cross-fitted VIM estimates are obtained by first splitting the data into $2K$ folds. These folds are further divided into 2 groups of $K$ folds. Then, for each fold $k$ in the first group, estimator $f_{n,k}$ of $f_0$ is constructed using all data besides the $k$th fold in the group (i.e., $(2K - 1)/(2K)$ of the data) and estimator $P_{n,k}$ of $P_0$ is constructed using the held-out data (i.e., $1/2K$ of the data); then, computing

$$
v_{n,k} = V(f_{n,k}, P_{n,k}).
$$

Similarly, for each fold $k$ in the second group, estimator $f_{n,k,s}$ of $f_{0,s}$ is constructed using all data besides the $k$th fold in the group (i.e., $(2K - 1)/(2K)$ of the data) and estimator $P_{n,k}$ of $P_0$ is constructed using the held-out data (i.e., $1/2K$ of the data); then, computing

$$
v_{n,k,s} = V(f_{n,k,s}, P_{n,k}).
$$

Finally,

$$
\psi_{n,s} := K^{-1} \sum_{k=1}^{K} \{ v_{n,k} - v_{n,k,s} \}.
$$

See the paper by Williamson, Gilbert, Simon, and Carone for more details on the mathematics behind the cv_vim function, and the validity of the confidence intervals.

In the interest of transparency, we return most of the calculations within the vim object. This results in a list including:

- **s** the column(s) to calculate variable importance for
- **SL.library** the library of learners passed to SuperLearner
- **full_fit** the fitted values of the chosen method fit to the full data (a list, for train and test data)
- **red_fit** the fitted values of the chosen method fit to the reduced data (a list, for train and test data)
- **est** the estimated variable importance
- **naive** the naive estimator of variable importance
eif  the estimated efficient influence function

eif_full  the estimated efficient influence function for the full regression

eif_reduced  the estimated efficient influence function for the reduced regression

se  the standard error for the estimated variable importance

ci  the \((1 - \alpha) \times 100\%\) confidence interval for the variable importance estimate

test  a decision to either reject (TRUE) or not reject (FALSE) the null hypothesis, based on a conservative test

p_value  a p-value based on the same test as test

full_mod  the object returned by the estimation procedure for the full data regression (if applicable)

red_mod  the object returned by the estimation procedure for the reduced data regression (if applicable)

alpha  the level, for confidence interval calculation

sample_splitting_folds  the folds used for hypothesis testing

cross_fitting_folds  the folds used for cross-fitting

y  the outcome

ipc_weights  the weights

cluster_id  the cluster IDs

mat  a tibble with the estimate, SE, CI, hypothesis testing decision, and p-value

Value

An object of classes \texttt{vim} and \texttt{vim_auc}. See Details for more information.

See Also

\texttt{SuperLearner} for specific usage of the SuperLearner function and package, and \texttt{performance} for specific usage of the ROCR package.

Examples

# generate the data
# generate X
p <- 2
n <- 100
x <- data.frame(replicate(p, stats::runif(n, -1, 1)))

# apply the function to the x's
f <- function(x) 0.5 + 0.3*x[1] + 0.2*x[2]
smooth <- apply(x, 1, function(z) f(z))

# generate Y ~ Normal (smooth, 1)
y <- matrix(rbinom(n, size = 1, prob = smooth))

# set up a library for SuperLearner; note simple library for speed
library("SuperLearner")
learners <- c("SL.glm", "SL.mean")
# estimate (with a small number of folds, for illustration only)
est <- vimp_auc(y, x, indx = 2,
alpha = 0.05, run_regression = TRUE,
SL.library = learners, V = 2, cvControl = list(V = 2))

---

**vimp_ci**  
*Confidence intervals for variable importance*

**Description**

Compute confidence intervals for the true variable importance parameter.

**Usage**

```r
vimp_ci(est, se, scale = "identity", level = 0.95, truncate = TRUE)
```

**Arguments**

- `est`: estimate of variable importance, e.g., from a call to `vimp_point_est`.
- `se`: estimate of the standard error of `est`, e.g., from a call to `vimp_se`.
- `scale`: scale to compute interval estimate on (defaults to "identity": compute Wald-type CI).
- `level`: confidence interval type (defaults to 0.95).
- `truncate`: truncate CIs to have lower limit at (or above) zero?

**Details**

See the paper by Williamson, Gilbert, Simon, and Carone for more details on the mathematics behind this function and the definition of the parameter of interest.

**Value**

The Wald-based confidence interval for the true importance of the given group of left-out covariates.
Nonparametric Intrinsic Variable Importance Estimates: Deviance

Description

Compute estimates of and confidence intervals for nonparametric deviance-based intrinsic variable importance. This is a wrapper function for cv_vim, with type = "deviance".

Usage

vimp_deviance(
  Y = NULL,
  X = NULL,
  cross_fitted_f1 = NULL,
  cross_fitted_f2 = NULL,
  f1 = NULL,
  f2 = NULL,
  indx = 1,
  V = 10,
  run_regression = TRUE,
  SL.library = c("SL.glmnet", "SL.xgboost", "SL.mean"),
  alpha = 0.05,
  delta = 0,
  na.rm = FALSE,
  final_point_estimate = "split",
  cross_fitting_folds = NULL,
  sample_splitting_folds = NULL,
  stratified = TRUE,
  C = rep(1, length(Y)),
  Z = NULL,
  ipc_weights = rep(1, length(Y)),
  scale = "logit",
  ipc_est_type = "aipw",
  scale_est = TRUE,
  cross_fitted_se = TRUE,
  ...
)

Arguments

Y the outcome.
X the covariates. If type = "average_value", then the exposure variable should be part of X, with its name provided in exposure_name.
cross_fitted_f1 the predicted values on validation data from a flexible estimation technique regressing Y on X in the training data. Provided as either (a) a vector, where each
element is the predicted value when that observation is part of the validation fold; or (b) a list of length V, where each element in the list is a set of predictions on the corresponding validation data fold. If sample-splitting is requested, then these must be estimated specially; see Details. However, the resulting vector should be the same length as Y; if using a list, then the summed length of each element across the list should be the same length as Y (i.e., each observation is included in the predictions).

cross_fitted_f2

the predicted values on validation data from a flexible estimation technique regressing either (a) the fitted values in cross_fitted_f1, or (b) Y, on X withholding the columns in indx. Provided as either (a) a vector, where each element is the predicted value when that observation is part of the validation fold; or (b) a list of length V, where each element in the list is a set of predictions on the corresponding validation data fold. If sample-splitting is requested, then these must be estimated specially; see Details. However, the resulting vector should be the same length as Y; if using a list, then the summed length of each element across the list should be the same length as Y (i.e., each observation is included in the predictions).

f1

the fitted values from a flexible estimation technique regressing Y on X. If sample-splitting is requested, then these must be estimated specially; see Details. If cross_fitted_se = TRUE, then this argument is not used.

f2

the fitted values from a flexible estimation technique regressing either (a) f1 or (b) Y on X withholding the columns in indx. If sample-splitting is requested, then these must be estimated specially; see Details. If cross_fitted_se = TRUE, then this argument is not used.

indx

the indices of the covariate(s) to calculate variable importance for; defaults to 1.

V

the number of folds for cross-fitting, defaults to 5. If sample_splitting = TRUE, then a special type of V-fold cross-fitting is done. See Details for a more detailed explanation.

run_regression

if outcome Y and covariates X are passed to vimp_accuracy, and run_regression is TRUE, then Super Learner will be used; otherwise, variable importance will be computed using the inputted fitted values.

SL.library

a character vector of learners to pass to SuperLearner, if f1 and f2 are Y and X, respectively. Defaults to SL.glmnet, SL.xgboost, and SL.mean.

alpha

the level to compute the confidence interval at. Defaults to 0.05, corresponding to a 95% confidence interval.

delta

the value of the δ-null (i.e., testing if importance < δ); defaults to 0.

na.rm

should we remove NAs in the outcome and fitted values in computation? (defaults to FALSE)

final_point_estimate

if sample splitting is used, should the final point estimates be based on only the sample-split folds used for inference ("split", the default), or should they instead be based on the full dataset ("full") or the average across the point estimates from each sample split ("average")? All three options result in valid point estimates – sample-splitting is only required for valid inference.
cross_fitting_folds
the folds for cross-fitting. Only used if run_regression = FALSE.

sample_splitting_folds
the folds used for sample-splitting; these identify the observations that should be
used to evaluate predictiveness based on the full and reduced sets of covariates,
respectively. Only used if run_regression = FALSE.

stratified
if run_regression = TRUE, then should the generated folds be stratified based on
the outcome (helps to ensure class balance across cross-validation folds)

C
the indicator of coarsening (1 denotes observed, 0 denotes unobserved).

Z
either (i) NULL (the default, in which case the argument C above must be all
ones), or (ii) a character vector specifying the variable(s) among Y and X that are
thought to play a role in the coarsening mechanism. To specify the outcome, use
"Y"; to specify covariates, use a character number corresponding to the desired
position in X (e.g., "1").

ipc_weights
weights for the computed influence curve (i.e., inverse probability weights for
coarsened-at-random settings). Assumed to be already inverted (i.e., ipc_weights
= 1 / [estimated probability weights]).

scale
should CIs be computed on original ("identity") or another scale? (options are
"log" and "logit")

ipc_est_type
the type of procedure used for coarsened-at-random settings; options are "ipw"
(for inverse probability weighting) or "aipw" (for augmented inverse probability
weighting). Only used if C is not all equal to 1.

scale_est
should the point estimate be scaled to be greater than or equal to 0? Defaults to
TRUE.

cross_fitted_se
should we use cross-fitting to estimate the standard errors (TRUE, the default) or
not (FALSE)?

... other arguments to the estimation tool, see "See also".

Details

We define the population variable importance measure (VIM) for the group of features (or single
feature) s with respect to the predictiveness measure V by

$$\psi_{0,s} := V(f_0, P_0) - V(f_{0,s}, P_0),$$

where $f_0$ is the population predictiveness maximizing function, $f_{0,s}$ is the population predictiveness
maximizing function that is only allowed to access the features with index not in s, and $P_0$ is the
true data-generating distribution.

Cross-fitted VIM estimates are computed differently if sample-splitting is requested versus if it is
not. We recommend using sample-splitting in most cases, since only in this case will inferences
be valid if the variable(s) of interest have truly zero population importance. The purpose of cross-
fitting is to estimate $f_0$ and $f_{0,s}$ on independent data from estimating $P_0$; this can result in improved
performance, especially when using flexible learning algorithms. The purpose of sample-splitting
is to estimate $f_0$ and $f_{0,s}$ on independent data; this allows valid inference under the null hypothesis
of zero importance.
Without sample-splitting, cross-fitted VIM estimates are obtained by first splitting the data into $K$ folds; then using each fold in turn as a hold-out set, constructing estimators $f_{n,k}$ and $f_{n,k,s}$ of $f_0$ and $f_{0,s}$, respectively on the training data and estimator $P_{n,k}$ of $P_0$ using the test data; and finally, computing

$$\psi_{n,s} := K^{-1} \sum_{k=1}^{K} \{ V(f_{n,k}, P_{n,k}) - V(f_{n,k,s}, P_{n,k}) \}.$$  

With sample-splitting, cross-fitted VIM estimates are obtained by first splitting the data into $2K$ folds. These folds are further divided into 2 groups of folds. Then, for each fold $k$ in the first group, estimator $f_{n,k}$ of $f_0$ is constructed using all data besides the $k$th fold in the group (i.e., $(2K - 1)/(2K)$ of the data) and estimator $P_{n,k}$ of $P_0$ is constructed using the held-out data (i.e., $1/2K$ of the data); then, computing

$$v_{n,k} = V(f_{n,k}, P_{n,k}).$$

Similarly, for each fold $k$ in the second group, estimator $f_{n,k,s}$ of $f_{0,s}$ is constructed using all data besides the $k$th fold in the group (i.e., $(2K - 1)/(2K)$ of the data) and estimator $P_{n,k}$ of $P_0$ is constructed using the held-out data (i.e., $1/2K$ of the data); then, computing

$$v_{n,k,s} = V(f_{n,k,s}, P_{n,k}).$$

Finally,

$$\psi_{n,s} := K^{-1} \sum_{k=1}^{K} \{ v_{n,k} - v_{n,k,s} \}.$$  

See the paper by Williamson, Gilbert, Simon, and Carone for more details on the mathematics behind the cv_vim function, and the validity of the confidence intervals.

In the interest of transparency, we return most of the calculations within the vim object. This results in a list including:

- `s` the column(s) to calculate variable importance for
- `SL.library` the library of learners passed to SuperLearner
- `full_fit` the fitted values of the chosen method fit to the full data (a list, for train and test data)
- `red_fit` the fitted values of the chosen method fit to the reduced data (a list, for train and test data)
- `est` the estimated variable importance
- `naive` the naive estimator of variable importance
- `eif` the estimated efficient influence function
- `eif_full` the estimated efficient influence function for the full regression
- `eif_reduced` the estimated efficient influence function for the reduced regression
- `se` the standard error for the estimated variable importance
- `ci` the $(1 - \alpha) \times 100\%$ confidence interval for the variable importance estimate
- `test` a decision to either reject (TRUE) or not reject (FALSE) the null hypothesis, based on a conservative test
- `p_value` a p-value based on the same test as `test`
- `full_mod` the object returned by the estimation procedure for the full data regression (if applicable)
red_mod  the object returned by the estimation procedure for the reduced data regression (if applicable)
alpha  the level, for confidence interval calculation
sample_splitting_folds  the folds used for hypothesis testing
cross_fitting_folds  the folds used for cross-fitting
y  the outcome
ipc_weights  the weights
cluster_id  the cluster IDs
mat  a tibble with the estimate, SE, CI, hypothesis testing decision, and p-value

Value

An object of classes vim and vim_deviance. See Details for more information.

See Also

SuperLearner for specific usage of the SuperLearner function and package.

Examples

# generate the data
# generate X
p <- 2
n <- 100
x <- data.frame(replicate(p, stats::runif(n, -1, 1)))

# apply the function to the x's
f <- function(x) 0.5 + 0.3*x[1] + 0.2*x[2]
smooth <- apply(x, 1, function(z) f(z))

# generate Y ~ Normal (smooth, 1)
y <- matrix(stats::rbinom(n, size = 1, prob = smooth))

# set up a library for SuperLearner; note simple library for speed
library("SuperLearner")
learners <- c("SL.glm", "SL.mean")

# estimate (with a small number of folds, for illustration only)
est <- vimp_deviance(y, x, indx = 2,
  alpha = 0.05, run_regression = TRUE,
  SL.library = learners, V = 2, cvControl = list(V = 2))
vimp_hypothesis_test  Perform a hypothesis test against the null hypothesis of \( \delta \) importance

Description

Perform a hypothesis test against the null hypothesis of zero importance by: (i) for a user-specified level \( \alpha \), compute a \((1 - \alpha) \times 100\%\) confidence interval around the predictiveness for both the full and reduced regression functions (these must be estimated on independent splits of the data); (ii) if the intervals do not overlap, reject the null hypothesis.

Usage

vimp_hypothesis_test(
    predictiveness_full, predictiveness_reduced, se, delta = 0, alpha = 0.05
)

Arguments

predictiveness_full
    the estimated predictiveness of the regression including the covariate(s) of interest.

predictiveness_reduced
    the estimated predictiveness of the regression excluding the covariate(s) of interest.

se
    the estimated standard error of the variable importance estimator

delta
    the value of the \( \delta \)-null (i.e., testing if importance < \( \delta \)); defaults to 0.

alpha
    the desired type I error rate (defaults to 0.05).

Details

See the paper by Williamson, Gilbert, Simon, and Carone for more details on the mathematics behind this function and the definition of the parameter of interest.

Value

a list, with: the hypothesis testing decision (TRUE if the null hypothesis is rejected, FALSE otherwise); the p-value from the hypothesis test; and the test statistic from the hypothesis test.
vimp_regression

Nonparametric Intrinsic Variable Importance Estimates: ANOVA

Description

Compute estimates of and confidence intervals for nonparametric ANOVA-based intrinsic variable importance. This is a wrapper function for cv_vim, with type = "anova". This function is deprecated in vimp version 2.0.0.

Usage

vimp_regression(
  Y = NULL,
  X = NULL,
  cross_fitted_f1 = NULL,
  cross_fitted_f2 = NULL,
  indx = 1,
  V = 10,
  run_regression = TRUE,
  SL.library = c("SL.glmnet", "SL.xgboost", "SL.mean"),
  alpha = 0.05,
  delta = 0,
  na.rm = FALSE,
  cross_fitting_folds = NULL,
  stratified = FALSE,
  C = rep(1, length(Y)),
  Z = NULL,
  ipc_weights = rep(1, length(Y)),
  scale = "identity",
  ipc_est_type = "aipw",
  scale_est = TRUE,
  cross_fitted_se = TRUE,
  ...
)

Arguments

Y
  the outcome.
X
  the covariates. If type = "average_value", then the exposure variable should be part of X, with its name provided in exposure_name.
cross_fitted_f1
  the predicted values on validation data from a flexible estimation technique regressing Y on X in the training data. Provided as either (a) a vector, where each element is the predicted value when that observation is part of the validation fold; or (b) a list of length V, where each element in the list is a set of predictions on the corresponding validation data fold. If sample-splitting is requested,
then these must be estimated specially; see Details. However, the resulting vector should be the same length as \( Y \); if using a list, then the summed length of each element across the list should be the same length as \( Y \) (i.e., each observation is included in the predictions).

cross_fitted_f2

the predicted values on validation data from a flexible estimation technique regressing either (a) the fitted values in cross_fitted_f1, or (b) \( Y \), on \( X \) withholding the columns in indx. Provided as either (a) a vector, where each element is the predicted value when that observation is part of the validation fold; or (b) a list of length \( V \), where each element in the list is a set of predictions on the corresponding validation data fold. If sample-splitting is requested, then these must be estimated specially; see Details. However, the resulting vector should be the same length as \( Y \); if using a list, then the summed length of each element across the list should be the same length as \( Y \) (i.e., each observation is included in the predictions).

indx

the indices of the covariate(s) to calculate variable importance for; defaults to 1.

\( V \)

the number of folds for cross-fitting, defaults to 5. If \( \text{sample_splitting} = \text{TRUE} \), then a special type of \( V \)-fold cross-fitting is done. See Details for a more detailed explanation.

run_regression

if outcome \( Y \) and covariates \( X \) are passed to vimp_accuracy, and run_regression is \( \text{TRUE} \), then Super Learner will be used; otherwise, variable importance will be computed using the inputted fitted values.

SL.library

a character vector of learners to pass to SuperLearner, if \( f1 \) and \( f2 \) are \( Y \) and \( X \), respectively. Defaults to \( \text{SL.glmnet}, \text{SL.xgboost}, \text{and SL.mean} \).

alpha

the level to compute the confidence interval at. Defaults to 0.05, corresponding to a 95% confidence interval.

delta

the value of the \( \delta \)-null (i.e., testing if importance < \( \delta \)); defaults to 0.

na.rm

should we remove NAs in the outcome and fitted values in computation? (defaults to \( \text{FALSE} \))

cross_fitting_folds

the folds for cross-fitting. Only used if run_regression = \( \text{FALSE} \).

stratified

if run_regression = \( \text{TRUE} \), then should the generated folds be stratified based on the outcome (helps to ensure class balance across cross-validation folds)

\( C \)

the indicator of coarsening (1 denotes observed, 0 denotes unobserved).

\( Z \)

either (i) NULL (the default, in which case the argument \( C \) above must be all ones), or (ii) a character vector specifying the variable(s) among \( Y \) and \( X \) that are thought to play a role in the coarsening mechanism. To specify the outcome, use \( "Y" \); to specify covariates, use a character number corresponding to the desired position in \( X \) (e.g., \( "1" \)).

ipc_weights

weights for the computed influence curve (i.e., inverse probability weights for coarsened-at-random settings). Assumed to be already inverted (i.e., ipc_weights = \( 1 / \) [estimated probability weights]).

scale

should CIs be computed on original ("identity") or another scale? (options are "log" and "logit")
vimp_regression

**ipc_est_type** the type of procedure used for coarsened-at-random settings; options are "ipw" (for inverse probability weighting) or "aipw" (for augmented inverse probability weighting). Only used if \( C \) is not all equal to 1.

**scale_est** should the point estimate be scaled to be greater than or equal to 0? Defaults to TRUE.

**cross_fitted_se** should we use cross-fitting to estimate the standard errors (TRUE, the default) or not (FALSE)?

... other arguments to the estimation tool, see "See also".

**Details**

We define the population ANOVA parameter for the group of features (or single feature) \( s \) by

\[
\psi_{0,s} := E_0 \{ f_0(X) - f_{0,s}(X) \}^2 / \text{var}_0(Y),
\]

where \( f_0 \) is the population conditional mean using all features, \( f_{0,s} \) is the population conditional mean using the features with index not in \( s \), and \( E_0 \) and \( \text{var}_0 \) denote expectation and variance under the true data-generating distribution, respectively.

Cross-fitted ANOVA estimates are computed by first splitting the data into \( K \) folds; then using each fold in turn as a hold-out set, constructing estimators \( f_{n,k} \) and \( f_{n,k,s} \) of \( f_0 \) and \( f_{0,s} \), respectively on the training data and estimator \( E_{n,k} \) of \( E_0 \) using the test data; and finally, computing

\[
\psi_{n,s} := K^{-1} \sum_{k=1}^{K} E_{n,k} \{ f_{n,k}(X) - f_{n,k,s}(X) \}^2 / \text{var}_n(Y),
\]

where \( \text{var}_n \) is the empirical variance. See the paper by Williamson, Gilbert, Simon, and Carone for more details on the mathematics behind this function.

**Value**

An object of classes `vim` and `vim_regression`. See Details for more information.

**See Also**

`SuperLearner` for specific usage of the `SuperLearner` function and package.

**Examples**

```r
# generate the data
# generate X
p <- 2
n <- 100
x <- data.frame(replicate(p, stats::runif(n, -5, 5)))

# apply the function to the x's
smooth <- (x[,1]/5)^2*(x[,1]+7)/5 + (x[,2]/3)^2

# generate Y ~ Normal (smooth, 1)
y <- smooth + stats::rnorm(n, 0, 1)
```
# set up a library for SuperLearner; note simple library for speed
library("SuperLearner")
learners <- c("SL.glm", "SL.mean")

# estimate (with a small number of folds, for illustration only)
est <- vimp_regression(y, x, indx = 2,
                        alpha = 0.05, run_regression = TRUE,
                        SL.library = learners, V = 2, cvControl = list(V = 2))

---

### vimp_rsquared

#### Description

Compute estimates of and confidence intervals for nonparametric $R^2$-based intrinsic variable importance. This is a wrapper function for `cv_vim`, with `type = "r_squared"`.

#### Usage

```r
vimp_rsquared(
  Y = NULL,
  X = NULL,
  cross_fitted_f1 = NULL,
  cross_fitted_f2 = NULL,
  f1 = NULL,
  f2 = NULL,
  indx = 1,
  V = 10,
  run_regression = TRUE,
  SL.library = c("SL.glmnet", "SL.xgboost", "SL.mean"),
  alpha = 0.05,
  delta = 0,
  na.rm = FALSE,
  final_point_estimate = "split",
  cross_fitting_folds = NULL,
  sample_splitting_folds = NULL,
  stratified = FALSE,
  C = rep(1, length(Y)),
  Z = NULL,
  ipc_weights = rep(1, length(Y)),
  scale = "logit",
  ipc_est_type = "aipw",
  scale_est = TRUE,
  cross_fitted_se = TRUE,
  ...
)
```
Arguments

Y
the outcome.

X
the covariates. If type = "average_value", then the exposure variable should be part of X, with its name provided in exposure_name.

cross_fitted_f1
the predicted values on validation data from a flexible estimation technique regressing Y on X in the training data. Provided as either (a) a vector, where each element is the predicted value when that observation is part of the validation fold; or (b) a list of length V, where each element in the list is a set of predictions on the corresponding validation data fold. If sample-splitting is requested, then these must be estimated specially; see Details. However, the resulting vector should be the same length as Y; if using a list, then the summed length of each element across the list should be the same length as Y (i.e., each observation is included in the predictions).

cross_fitted_f2
the predicted values on validation data from a flexible estimation technique regressing either (a) the fitted values in cross_fitted_f1, or (b) Y, on X withholding the columns in indx. Provided as either (a) a vector, where each element is the predicted value when that observation is part of the validation fold; or (b) a list of length V, where each element in the list is a set of predictions on the corresponding validation data fold. If sample-splitting is requested, then these must be estimated specially; see Details. However, the resulting vector should be the same length as Y; if using a list, then the summed length of each element across the list should be the same length as Y (i.e., each observation is included in the predictions).

f1
the fitted values from a flexible estimation technique regressing Y on X. If sample-splitting is requested, then these must be estimated specially; see Details. If cross_fitted_se = TRUE, then this argument is not used.

f2
the fitted values from a flexible estimation technique regressing either (a) f1 or (b) Y on X withholding the columns in indx. If sample-splitting is requested, then these must be estimated specially; see Details. If cross_fitted_se = TRUE, then this argument is not used.

indx
the indices of the covariate(s) to calculate variable importance for; defaults to 1.

V
the number of folds for cross-fitting, defaults to 5. If sample_splitting = TRUE, then a special type of V-fold cross-fitting is done. See Details for a more detailed explanation.

run_regression
if outcome Y and covariates X are passed to vimp_accuracy, and run_regression is TRUE, then Super Learner will be used; otherwise, variable importance will be computed using the inputted fitted values.

SL.library
a character vector of learners to pass to SuperLearner, if f1 and f2 are Y and X, respectively. Defaults to SL.glmnet, SL.xgboost, and SL.mean.

alpha
the level to compute the confidence interval at. Defaults to 0.05, corresponding to a 95% confidence interval.

delta
the value of the δ-null (i.e., testing if importance < δ); defaults to 0.
na.rm should we remove NAs in the outcome and fitted values in computation? (defaults to FALSE)

final_point_estimate
if sample splitting is used, should the final point estimates be based on only the sample-split folds used for inference ("split", the default), or should they instead be based on the full dataset ("full") or the average across the point estimates from each sample split ("average")? All three options result in valid point estimates – sample-splitting is only required for valid inference.

cross_fitting_folds
the folds for cross-fitting. Only used if run_regression = FALSE.

sample_splitting_folds
the folds used for sample-splitting; these identify the observations that should be used to evaluate predictiveness based on the full and reduced sets of covariates, respectively. Only used if run_regression = FALSE.

stratified if run_regression = TRUE, then should the generated folds be stratified based on the outcome (helps to ensure class balance across cross-validation folds)

C the indicator of coarsening (1 denotes observed, 0 denotes unobserved).

Z either (i) NULL (the default, in which case the argument C above must be all ones), or (ii) a character vector specifying the variable(s) among Y and X that are thought to play a role in the coarsening mechanism. To specify the outcome, use "Y"; to specify covariates, use a character number corresponding to the desired position in X (e.g., "1").

ipc_weights weights for the computed influence curve (i.e., inverse probability weights for coarsened-at-random settings). Assumed to be already inverted (i.e., ipc_weights = 1 / [estimated probability weights]).

scale should CIs be computed on original ("identity") or another scale? (options are "log" and "logit")

ipc_est_type the type of procedure used for coarsened-at-random settings; options are "ipw" (for inverse probability weighting) or "aipw" (for augmented inverse probability weighting). Only used if C is not all equal to 1.

scale_est should the point estimate be scaled to be greater than or equal to 0? Defaults to TRUE.

cross_fitted_se should we use cross-fitting to estimate the standard errors (TRUE, the default) or not (FALSE)?

Details
We define the population variable importance measure (VIM) for the group of features (or single feature) s with respect to the predictiveness measure V by

$$\psi_{0,s} := V(f_0, P_0) - V(f_{0,s}, P_0),$$

where $f_0$ is the population predictiveness maximizing function, $f_{0,s}$ is the population predictiveness maximizing function that is only allowed to access the features with index not in s, and $P_0$ is the true data-generating distribution.
Cross-fitted VIM estimates are computed differently if sample-splitting is requested versus if it is not. We recommend using sample-splitting in most cases, since only in this case will inferences be valid if the variable(s) of interest have truly zero population importance. The purpose of cross-fitting is to estimate $f_0$ and $f_{0,s}$ on independent data from estimating $P_0$; this can result in improved performance, especially when using flexible learning algorithms. The purpose of sample-splitting is to estimate $f_0$ and $f_{0,s}$ on independent data; this allows valid inference under the null hypothesis of zero importance.

Without sample-splitting, cross-fitted VIM estimates are obtained by first splitting the data into $K$ folds; then using each fold in turn as a hold-out set, constructing estimators $f_{n,k}$ and $f_{n,k,s}$ of $f_0$ and $f_{0,s}$, respectively on the training data and estimator $P_{n,k}$ of $P_0$ using the test data; and finally, computing

$$\psi_{n,s} := K^{(-1)} \sum_{k=1}^{K} \{V(f_{n,k}, P_{n,k}) - V(f_{n,k,s}, P_{n,k})\}.$$

With sample-splitting, cross-fitted VIM estimates are obtained by first splitting the data into $2K$ folds. These folds are further divided into 2 groups of folds. Then, for each fold $k$ in the first group, estimator $f_{n,k}$ of $f_0$ is constructed using all data besides the $k$th fold in the group (i.e., $(2K - 1)/(2K)$ of the data) and estimator $P_{n,k}$ of $P_0$ is constructed using the held-out data (i.e., $1/2K$ of the data); then, computing

$$v_{n,k} = V(f_{n,k}, P_{n,k}).$$

Similarly, for each fold $k$ in the second group, estimator $f_{n,k,s}$ of $f_{0,s}$ is constructed using all data besides the $k$th fold in the group (i.e., $(2K - 1)/(2K)$ of the data) and estimator $P_{n,k}$ of $P_0$ is constructed using the held-out data (i.e., $1/2K$ of the data); then, computing

$$v_{n,k,s} = V(f_{n,k,s}, P_{n,k}).$$

Finally,

$$\psi_{n,s} := K^{(-1)} \sum_{k=1}^{K} \{v_{n,k} - v_{n,k,s}\}.$$

See the paper by Williamson, Gilbert, Simon, and Carone for more details on the mathematics behind the cv_vim function, and the validity of the confidence intervals.

In the interest of transparency, we return most of the calculations within the vim object. This results in a list including:

- `s` the column(s) to calculate variable importance for
- `SL.library` the library of learners passed to SuperLearner
- `full_fit` the fitted values of the chosen method fit to the full data (a list, for train and test data)
- `red_fit` the fitted values of the chosen method fit to the reduced data (a list, for train and test data)
- `est` the estimated variable importance
- `naive` the naive estimator of variable importance
- `eif` the estimated efficient influence function
- `eif_full` the estimated efficient influence function for the full regression
- `eif_reduced` the estimated efficient influence function for the reduced regression
se  the standard error for the estimated variable importance
ci  the $(1 - \alpha) \times 100\%$ confidence interval for the variable importance estimate
test a decision to either reject (TRUE) or not reject (FALSE) the null hypothesis, based on a conservative test
p_value a p-value based on the same test as test
full_mod the object returned by the estimation procedure for the full data regression (if applicable)
red_mod the object returned by the estimation procedure for the reduced data regression (if applicable)
alpha the level, for confidence interval calculation
sample_splitting_folds the folds used for hypothesis testing
cross_fitting_folds the folds used for cross-fitting
y the outcome
ipc_weights the weights
cluster_id the cluster IDs
mat a tibble with the estimate, SE, CI, hypothesis testing decision, and p-value

Value
An object of classes `vim` and `vim_rsquared`. See Details for more information.

See Also
`SuperLearner` for specific usage of the `SuperLearner` function and package.

Examples

```r
# generate the data
# generate X
p <- 2
n <- 100
x <- data.frame(replicate(p, stats::runif(n, -5, 5)))

# apply the function to the x's
smooth <- (x[,1]/5)^2*(x[,1]+7)/5 + (x[,2]/3)^2

# generate Y ~ Normal (smooth, 1)
y <- smooth + stats::rnorm(n, 0, 1)

# set up a library for SuperLearner; note simple library for speed
library("SuperLearner")
learners <- c("SL.glm", "SL.mean")

# estimate (with a small number of folds, for illustration only)
est <- vimp_rsquared(y, x, indx = 2,
alpha = 0.05, run_regression = TRUE,
SL.library = learners, V = 2, cvControl = list(V = 2))
```
vimp_se

Estimate variable importance standard errors

Description

Compute standard error estimates for estimates of variable importance.

Usage

vimp_se(
  eif_full,
  eif_reduced,
  cross_fit = TRUE,
  sample_split = TRUE,
  na.rm = FALSE
)

Arguments

eif_full
  the estimated efficient influence function (EIF) based on the full set of covariates.
eif_reduced
  the estimated EIF based on the reduced set of covariates.
cross_fit
  logical; was cross-fitting used to compute the EIFs? (defaults to TRUE)
sample_split
  logical; was sample-splitting used? (defaults to TRUE)
na.rm
  logical; should NA’s be removed in computation? (defaults to FALSE).

Details

See the paper by Williamson, Gilbert, Simon, and Carone for more details on the mathematics behind this function and the definition of the parameter of interest.

Value

The standard error for the estimated variable importance for the given group of left-out covariates.

vrc01

Neutralization sensitivity of HIV viruses to antibody VRC01

Description

A dataset containing neutralization sensitivity – measured using inhibitory concentration, the quantity of antibody necessary to neutralize a fraction of viruses in a given sample – and viral features including: amino acid sequence features (measured using HXB2 coordinates), geographic region of origin, subtype, and viral geometry. Accessed from the Los Alamos National Laboratory’s (LANL’s) Compile, Analyze, and tally Neutralizing Antibody Panels (CATNAP) database.
Usage

data("vrc01")

Format

A data frame with 611 rows and 837 variables:

- seqname: Viral sequence identifiers
- subtype.is.01_AE: Dummy variables encoding the viral subtype as 0/1. Possible subtypes are 01_AE, 02_AG, 07_BC, A1, A1C, A1D, B, C, D, O, Other.
- subtype.is.02_AG: Dummy variables encoding the viral subtype as 0/1. Possible subtypes are 01_AE, 02_AG, 07_BC, A1, A1C, A1D, B, C, D, O, Other.
- subtype.is.07_BC: Dummy variables encoding the viral subtype as 0/1. Possible subtypes are 01_AE, 02_AG, 07_BC, A1, A1C, A1D, B, C, D, O, Other.
- subtype.is.A1: Dummy variables encoding the viral subtype as 0/1. Possible subtypes are 01_AE, 02_AG, 07_BC, A1, A1C, A1D, B, C, D, O, Other.
- subtype.is.A1C: Dummy variables encoding the viral subtype as 0/1. Possible subtypes are 01_AE, 02_AG, 07_BC, A1, A1C, A1D, B, C, D, O, Other.
- subtype.is.A1D: Dummy variables encoding the viral subtype as 0/1. Possible subtypes are 01_AE, 02_AG, 07_BC, A1, A1C, A1D, B, C, D, O, Other.
- subtype.is.B: Dummy variables encoding the viral subtype as 0/1. Possible subtypes are 01_AE, 02_AG, 07_BC, A1, A1C, A1D, B, C, D, O, Other.
- subtype.is.C: Dummy variables encoding the viral subtype as 0/1. Possible subtypes are 01_AE, 02_AG, 07_BC, A1, A1C, A1D, B, C, D, O, Other.
- subtype.is.D: Dummy variables encoding the viral subtype as 0/1. Possible subtypes are 01_AE, 02_AG, 07_BC, A1, A1C, A1D, B, C, D, O, Other.
- subtype.is.O: Dummy variables encoding the viral subtype as 0/1. Possible subtypes are 01_AE, 02_AG, 07_BC, A1, A1C, A1D, B, C, D, O, Other.
- subtype.is.Other: Dummy variables encoding the viral subtype as 0/1. Possible subtypes are 01_AE, 02_AG, 07_BC, A1, A1C, A1D, B, C, D, O, Other.
- geographic.region.of.origin.is.Asia: Dummy variables encoding the geographic region of origin as 0/1. Regions are Asia, Europe/Americas, North Africa, and Southern Africa.
- geographic.region.of.origin.is.Europe.Americas: Dummy variables encoding the geographic region of origin as 0/1. Regions are Asia, Europe/Americas, North Africa, and Southern Africa.
- geographic.region.of.origin.is.N.Africa: Dummy variables encoding the geographic region of origin as 0/1. Regions are Asia, Europe/Americas, North Africa, and Southern Africa.
- geographic.region.of.origin.is.S.Africa: Dummy variables encoding the geographic region of origin as 0/1. Regions are Asia, Europe/Americas, North Africa, and Southern Africa.
- ic50.censored: A binary indicator of whether or not the IC-50 (the concentration at which 50 Right-censoring is a proxy for a resistant virus).
- ic80.censored: A binary indicator of whether or not the IC-80 (the concentration at which 80 Right-censoring is a proxy for a resistant virus).
**ic50.geometric.mean.imputed** Continuous IC-50. If neutralization sensitivity for the virus was assessed in multiple studies, the geometric mean was taken.

**ic80.geometric.mean.imputed** Continuous IC-90. If neutralization sensitivity for the virus was assessed in multiple studies, the geometric mean was taken.

**hxb2.46.E.1mer** Amino acid sequence features denoting the presence (1) or absence (0) of a residue at the given HXB2-referenced site. For example, hxb2.46.E.1mer records the presence of an E at HXB2-referenced site 46.

**hxb2.46.K.1mer** Amino acid sequence feature denoting the presence (1) or absence (0) of a residue at the given HXB2-referenced site.

**hxb2.46.Q.1mer** Amino acid sequence feature denoting the presence (1) or absence (0) of a residue at the given HXB2-referenced site.

**hxb2.46.R.1mer** Amino acid sequence feature denoting the presence (1) or absence (0) of a residue at the given HXB2-referenced site.

**hxb2.46.T.1mer** Amino acid sequence feature denoting the presence (1) or absence (0) of a residue at the given HXB2-referenced site.

**hxb2.61.H.1mer** Amino acid sequence feature denoting the presence (1) or absence (0) of a residue at the given HXB2-referenced site.

**hxb2.61.Q.1mer** Amino acid sequence feature denoting the presence (1) or absence (0) of a residue at the given HXB2-referenced site.

**hxb2.61.T.1mer** Amino acid sequence feature denoting the presence (1) or absence (0) of a residue at the given HXB2-referenced site.

**hxb2.61.Y.1mer** Amino acid sequence feature denoting the presence (1) or absence (0) of a residue at the given HXB2-referenced site.

**hxb2.97.E.1mer** Amino acid sequence feature denoting the presence (1) or absence (0) of a residue at the given HXB2-referenced site.

**hxb2.97.K.1mer** Amino acid sequence feature denoting the presence (1) or absence (0) of a residue at the given HXB2-referenced site.

**hxb2.97.N.1mer** Amino acid sequence feature denoting the presence (1) or absence (0) of a residue at the given HXB2-referenced site.

**hxb2.97.R.1mer** Amino acid sequence feature denoting the presence (1) or absence (0) of a residue at the given HXB2-referenced site.

**hxb2.124.F.1mer** Amino acid sequence feature denoting the presence (1) or absence (0) of a residue at the given HXB2-referenced site.

**hxb2.124.P.1mer** Amino acid sequence feature denoting the presence (1) or absence (0) of a residue at the given HXB2-referenced site.

**hxb2.125.I.1mer** Amino acid sequence feature denoting the presence (1) or absence (0) of a residue at the given HXB2-referenced site.

**hxb2.125.L.1mer** Amino acid sequence feature denoting the presence (1) or absence (0) of a residue at the given HXB2-referenced site.

**hxb2.127.I.1mer** Amino acid sequence feature denoting the presence (1) or absence (0) of a residue at the given HXB2-referenced site.

**hxb2.127.V.1mer** Amino acid sequence feature denoting the presence (1) or absence (0) of a residue at the given HXB2-referenced site.
**hxb2.130.D.1mer** Amino acid sequence feature denoting the presence (1) or absence (0) of a residue at the given HXB2-referenced site.

**hxb2.130.E.1mer** Amino acid sequence feature denoting the presence (1) or absence (0) of a residue at the given HXB2-referenced site.

**hxb2.130.H.1mer** Amino acid sequence feature denoting the presence (1) or absence (0) of a residue at the given HXB2-referenced site.

**hxb2.130.I.1mer** Amino acid sequence feature denoting the presence (1) or absence (0) of a residue at the given HXB2-referenced site.

**hxb2.130.K.1mer** Amino acid sequence feature denoting the presence (1) or absence (0) of a residue at the given HXB2-referenced site.

**hxb2.130.L.1mer** Amino acid sequence feature denoting the presence (1) or absence (0) of a residue at the given HXB2-referenced site.

**hxb2.130.N.1mer** Amino acid sequence feature denoting the presence (1) or absence (0) of a residue at the given HXB2-referenced site.

**hxb2.130.Q.1mer** Amino acid sequence feature denoting the presence (1) or absence (0) of a residue at the given HXB2-referenced site.

**hxb2.130.R.1mer** Amino acid sequence feature denoting the presence (1) or absence (0) of a residue at the given HXB2-referenced site.

**hxb2.130.S.1mer** Amino acid sequence feature denoting the presence (1) or absence (0) of a residue at the given HXB2-referenced site.

**hxb2.130.T.1mer** Amino acid sequence feature denoting the presence (1) or absence (0) of a residue at the given HXB2-referenced site.

**hxb2.132.A.1mer** Amino acid sequence feature denoting the presence (1) or absence (0) of a residue at the given HXB2-referenced site.

**hxb2.132.E.1mer** Amino acid sequence feature denoting the presence (1) or absence (0) of a residue at the given HXB2-referenced site.

**hxb2.132.G.1mer** Amino acid sequence feature denoting the presence (1) or absence (0) of a residue at the given HXB2-referenced site.

**hxb2.132.H.1mer** Amino acid sequence feature denoting the presence (1) or absence (0) of a residue at the given HXB2-referenced site.

**hxb2.132.I.1mer** Amino acid sequence feature denoting the presence (1) or absence (0) of a residue at the given HXB2-referenced site.

**hxb2.132.K.1mer** Amino acid sequence feature denoting the presence (1) or absence (0) of a residue at the given HXB2-referenced site.

**hxb2.132.N.1mer** Amino acid sequence feature denoting the presence (1) or absence (0) of a residue at the given HXB2-referenced site.

**hxb2.132.Q.1mer** Amino acid sequence feature denoting the presence (1) or absence (0) of a residue at the given HXB2-referenced site.

**hxb2.132.R.1mer** Amino acid sequence feature denoting the presence (1) or absence (0) of a residue at the given HXB2-referenced site.

**hxb2.132.S.1mer** Amino acid sequence feature denoting the presence (1) or absence (0) of a residue at the given HXB2-referenced site.
hxb2.132.T.1mer  Amino acid sequence feature denoting the presence (1) or absence (0) of a residue at the given HXB2-referenced site.

hxb2.132.V.1mer  Amino acid sequence feature denoting the presence (1) or absence (0) of a residue at the given HXB2-referenced site.

hxb2.132.X.1mer  Amino acid sequence feature denoting the presence (1) or absence (0) of a residue at the given HXB2-referenced site.

hxb2.132.Y.1mer  Amino acid sequence feature denoting the presence (1) or absence (0) of a residue at the given HXB2-referenced site.

hxb2.138.A.1mer  Amino acid sequence feature denoting the presence (1) or absence (0) of a residue at the given HXB2-referenced site.

hxb2.138.C.1mer  Amino acid sequence feature denoting the presence (1) or absence (0) of a residue at the given HXB2-referenced site.

hxb2.138.D.1mer  Amino acid sequence feature denoting the presence (1) or absence (0) of a residue at the given HXB2-referenced site.

hxb2.138.E.1mer  Amino acid sequence feature denoting the presence (1) or absence (0) of a residue at the given HXB2-referenced site.

hxb2.138.G.1mer  Amino acid sequence feature denoting the presence (1) or absence (0) of a residue at the given HXB2-referenced site.

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hxb2.138.K.1mer  Amino acid sequence feature denoting the presence (1) or absence (0) of a residue at the given HXB2-referenced site.

hxb2.138.L.1mer  Amino acid sequence feature denoting the presence (1) or absence (0) of a residue at the given HXB2-referenced site.

hxb2.138.M.1mer  Amino acid sequence feature denoting the presence (1) or absence (0) of a residue at the given HXB2-referenced site.

hxb2.138.N.1mer  Amino acid sequence feature denoting the presence (1) or absence (0) of a residue at the given HXB2-referenced site.

hxb2.138.P.1mer  Amino acid sequence feature denoting the presence (1) or absence (0) of a residue at the given HXB2-referenced site.

hxb2.138.Q.1mer  Amino acid sequence feature denoting the presence (1) or absence (0) of a residue at the given HXB2-referenced site.

hxb2.138.R.1mer  Amino acid sequence feature denoting the presence (1) or absence (0) of a residue at the given HXB2-referenced site.

hxb2.138.S.1mer  Amino acid sequence feature denoting the presence (1) or absence (0) of a residue at the given HXB2-referenced site.

hxb2.138.T.1mer  Amino acid sequence feature denoting the presence (1) or absence (0) of a residue at the given HXB2-referenced site.

hxb2.138.V.1mer  Amino acid sequence feature denoting the presence (1) or absence (0) of a residue at the given HXB2-referenced site.
hxb2.138.Y.1mer Amino acid sequence feature denoting the presence (1) or absence (0) of a residue at the given HXB2-referenced site.
hxb2.138.gap.1mer Amino acid sequence feature denoting the presence (1) or absence (0) of a residue at the given HXB2-referenced site.
hxb2.139.A.1mer Amino acid sequence feature denoting the presence (1) or absence (0) of a residue at the given HXB2-referenced site.
hxb2.139.C.1mer Amino acid sequence feature denoting the presence (1) or absence (0) of a residue at the given HXB2-referenced site.
hxb2.139.D.1mer Amino acid sequence feature denoting the presence (1) or absence (0) of a residue at the given HXB2-referenced site.
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hxb2.139.G.1mer Amino acid sequence feature denoting the presence (1) or absence (0) of a residue at the given HXB2-referenced site.
hxb2.139.I.1mer Amino acid sequence feature denoting the presence (1) or absence (0) of a residue at the given HXB2-referenced site.
hxb2.139.K.1mer Amino acid sequence feature denoting the presence (1) or absence (0) of a residue at the given HXB2-referenced site.
hxb2.139.L.1mer Amino acid sequence feature denoting the presence (1) or absence (0) of a residue at the given HXB2-referenced site.
hxb2.139.N.1mer Amino acid sequence feature denoting the presence (1) or absence (0) of a residue at the given HXB2-referenced site.
hxb2.139.Q.1mer Amino acid sequence feature denoting the presence (1) or absence (0) of a residue at the given HXB2-referenced site.
hxb2.139.R.1mer Amino acid sequence feature denoting the presence (1) or absence (0) of a residue at the given HXB2-referenced site.
hxb2.139.S.1mer Amino acid sequence feature denoting the presence (1) or absence (0) of a residue at the given HXB2-referenced site.
hxb2.139.T.1mer Amino acid sequence feature denoting the presence (1) or absence (0) of a residue at the given HXB2-referenced site.
hxb2.139.V.1mer Amino acid sequence feature denoting the presence (1) or absence (0) of a residue at the given HXB2-referenced site.
hxb2.139.gap.1mer Amino acid sequence feature denoting the presence (1) or absence (0) of a residue at the given HXB2-referenced site.
hxb2.143.A.1mer Amino acid sequence feature denoting the presence (1) or absence (0) of a residue at the given HXB2-referenced site.
hxb2.143.D.1mer Amino acid sequence feature denoting the presence (1) or absence (0) of a residue at the given HXB2-referenced site.
hxb2.143.E.1mer Amino acid sequence feature denoting the presence (1) or absence (0) of a residue at the given HXB2-referenced site.
hxb2.143.F.1mer Amino acid sequence feature denoting the presence (1) or absence (0) of a residue at the given HXB2-referenced site.
**hxb2.143.G.1mer**  Amino acid sequence feature denoting the presence (1) or absence (0) of a residue at the given HXB2-referenced site.

**hxb2.143.I.1mer**  Amino acid sequence feature denoting the presence (1) or absence (0) of a residue at the given HXB2-referenced site.

**hxb2.143.K.1mer**  Amino acid sequence feature denoting the presence (1) or absence (0) of a residue at the given HXB2-referenced site.

**hxb2.143.N.1mer**  Amino acid sequence feature denoting the presence (1) or absence (0) of a residue at the given HXB2-referenced site.

**hxb2.143.P.1mer**  Amino acid sequence feature denoting the presence (1) or absence (0) of a residue at the given HXB2-referenced site.

**hxb2.143.Q.1mer**  Amino acid sequence feature denoting the presence (1) or absence (0) of a residue at the given HXB2-referenced site.

**hxb2.143.S.1mer**  Amino acid sequence feature denoting the presence (1) or absence (0) of a residue at the given HXB2-referenced site.

**hxb2.143.T.1mer**  Amino acid sequence feature denoting the presence (1) or absence (0) of a residue at the given HXB2-referenced site.

**hxb2.143.V.1mer**  Amino acid sequence feature denoting the presence (1) or absence (0) of a residue at the given HXB2-referenced site.

**hxb2.143.Y.1mer**  Amino acid sequence feature denoting the presence (1) or absence (0) of a residue at the given HXB2-referenced site.

**hxb2.143.gap.1mer**  Amino acid sequence feature denoting the presence (1) or absence (0) of a residue at the given HXB2-referenced site.

**hxb2.144.A.1mer**  Amino acid sequence feature denoting the presence (1) or absence (0) of a residue at the given HXB2-referenced site.

**hxb2.144.D.1mer**  Amino acid sequence feature denoting the presence (1) or absence (0) of a residue at the given HXB2-referenced site.

**hxb2.144.E.1mer**  Amino acid sequence feature denoting the presence (1) or absence (0) of a residue at the given HXB2-referenced site.

**hxb2.144.G.1mer**  Amino acid sequence feature denoting the presence (1) or absence (0) of a residue at the given HXB2-referenced site.

**hxb2.144.H.1mer**  Amino acid sequence feature denoting the presence (1) or absence (0) of a residue at the given HXB2-referenced site.

**hxb2.144.I.1mer**  Amino acid sequence feature denoting the presence (1) or absence (0) of a residue at the given HXB2-referenced site.

**hxb2.144.K.1mer**  Amino acid sequence feature denoting the presence (1) or absence (0) of a residue at the given HXB2-referenced site.

**hxb2.144.L.1mer**  Amino acid sequence feature denoting the presence (1) or absence (0) of a residue at the given HXB2-referenced site.

**hxb2.144.N.1mer**  Amino acid sequence feature denoting the presence (1) or absence (0) of a residue at the given HXB2-referenced site.

**hxb2.144.P.1mer**  Amino acid sequence feature denoting the presence (1) or absence (0) of a residue at the given HXB2-referenced site.
hxb2.144.R.1mer  Amino acid sequence feature denoting the presence (1) or absence (0) of a residue at the given HXB2-referenced site.

hxb2.144.S.1mer  Amino acid sequence feature denoting the presence (1) or absence (0) of a residue at the given HXB2-referenced site.

hxb2.144.T.1mer  Amino acid sequence feature denoting the presence (1) or absence (0) of a residue at the given HXB2-referenced site.

hxb2.144.V.1mer  Amino acid sequence feature denoting the presence (1) or absence (0) of a residue at the given HXB2-referenced site.

hxb2.144.Y.1mer  Amino acid sequence feature denoting the presence (1) or absence (0) of a residue at the given HXB2-referenced site.

hxb2.144.gap.1mer Amino acid sequence feature denoting the presence (1) or absence (0) of a residue at the given HXB2-referenced site.

hxb2.150.A.1mer  Amino acid sequence feature denoting the presence (1) or absence (0) of a residue at the given HXB2-referenced site.

hxb2.150.D.1mer  Amino acid sequence feature denoting the presence (1) or absence (0) of a residue at the given HXB2-referenced site.

hxb2.150.E.1mer  Amino acid sequence feature denoting the presence (1) or absence (0) of a residue at the given HXB2-referenced site.

hxb2.150.G.1mer  Amino acid sequence feature denoting the presence (1) or absence (0) of a residue at the given HXB2-referenced site.

hxb2.150.I.1mer  Amino acid sequence feature denoting the presence (1) or absence (0) of a residue at the given HXB2-referenced site.

hxb2.150.K.1mer  Amino acid sequence feature denoting the presence (1) or absence (0) of a residue at the given HXB2-referenced site.

hxb2.150.L.1mer  Amino acid sequence feature denoting the presence (1) or absence (0) of a residue at the given HXB2-referenced site.

hxb2.150.M.1mer  Amino acid sequence feature denoting the presence (1) or absence (0) of a residue at the given HXB2-referenced site.

hxb2.150.N.1mer  Amino acid sequence feature denoting the presence (1) or absence (0) of a residue at the given HXB2-referenced site.

hxb2.150.P.1mer  Amino acid sequence feature denoting the presence (1) or absence (0) of a residue at the given HXB2-referenced site.

hxb2.150.Q.1mer  Amino acid sequence feature denoting the presence (1) or absence (0) of a residue at the given HXB2-referenced site.

hxb2.150.R.1mer  Amino acid sequence feature denoting the presence (1) or absence (0) of a residue at the given HXB2-referenced site.

hxb2.150.S.1mer  Amino acid sequence feature denoting the presence (1) or absence (0) of a residue at the given HXB2-referenced site.

hxb2.150.T.1mer  Amino acid sequence feature denoting the presence (1) or absence (0) of a residue at the given HXB2-referenced site.

hxb2.150.V.1mer  Amino acid sequence feature denoting the presence (1) or absence (0) of a residue at the given HXB2-referenced site.
**hxb2.150.Y.1mer** Amino acid sequence feature denoting the presence (1) or absence (0) of a residue at the given HXB2-referenced site.

**hxb2.150.gap.1mer** Amino acid sequence feature denoting the presence (1) or absence (0) of a residue at the given HXB2-referenced site.

**hxb2.156.D.1mer** Amino acid sequence feature denoting the presence (1) or absence (0) of a residue at the given HXB2-referenced site.

**hxb2.156.I.1mer** Amino acid sequence feature denoting the presence (1) or absence (0) of a residue at the given HXB2-referenced site.

**hxb2.156.K.1mer** Amino acid sequence feature denoting the presence (1) or absence (0) of a residue at the given HXB2-referenced site.

**hxb2.156.N.1mer** Amino acid sequence feature denoting the presence (1) or absence (0) of a residue at the given HXB2-referenced site.

**hxb2.156.Q.1mer** Amino acid sequence feature denoting the presence (1) or absence (0) of a residue at the given HXB2-referenced site.

**hxb2.156.S.1mer** Amino acid sequence feature denoting the presence (1) or absence (0) of a residue at the given HXB2-referenced site.

**hxb2.156.T.1mer** Amino acid sequence feature denoting the presence (1) or absence (0) of a residue at the given HXB2-referenced site.

**hxb2.156.V.1mer** Amino acid sequence feature denoting the presence (1) or absence (0) of a residue at the given HXB2-referenced site.

**hxb2.156.Y.1mer** Amino acid sequence feature denoting the presence (1) or absence (0) of a residue at the given HXB2-referenced site.

**hxb2.179.A.1mer** Amino acid sequence feature denoting the presence (1) or absence (0) of a residue at the given HXB2-referenced site.

**hxb2.179.I.1mer** Amino acid sequence feature denoting the presence (1) or absence (0) of a residue at the given HXB2-referenced site.

**hxb2.179.L.1mer** Amino acid sequence feature denoting the presence (1) or absence (0) of a residue at the given HXB2-referenced site.

**hxb2.179.P.1mer** Amino acid sequence feature denoting the presence (1) or absence (0) of a residue at the given HXB2-referenced site.

**hxb2.179.Q.1mer** Amino acid sequence feature denoting the presence (1) or absence (0) of a residue at the given HXB2-referenced site.

**hxb2.179.S.1mer** Amino acid sequence feature denoting the presence (1) or absence (0) of a residue at the given HXB2-referenced site.

**hxb2.179.T.1mer** Amino acid sequence feature denoting the presence (1) or absence (0) of a residue at the given HXB2-referenced site.

**hxb2.179.V.1mer** Amino acid sequence feature denoting the presence (1) or absence (0) of a residue at the given HXB2-referenced site.

**hxb2.181.I.1mer** Amino acid sequence feature denoting the presence (1) or absence (0) of a residue at the given HXB2-referenced site.

**hxb2.181.L.1mer** Amino acid sequence feature denoting the presence (1) or absence (0) of a residue at the given HXB2-referenced site.

**hxb2.181.M.1mer** Amino acid sequence feature denoting the presence (1) or absence (0) of a residue at the given HXB2-referenced site.

**hxb2.181.V.1mer** Amino acid sequence feature denoting the presence (1) or absence (0) of a residue at the given HXB2-referenced site.
**hxb2.186.A.1mer**  Amino acid sequence feature denoting the presence (1) or absence (0) of a residue at the given HXB2-referenced site.

**hxb2.186.D.1mer**  Amino acid sequence feature denoting the presence (1) or absence (0) of a residue at the given HXB2-referenced site.

**hxb2.186.E.1mer**  Amino acid sequence feature denoting the presence (1) or absence (0) of a residue at the given HXB2-referenced site.

**hxb2.186.G.1mer**  Amino acid sequence feature denoting the presence (1) or absence (0) of a residue at the given HXB2-referenced site.

**hxb2.186.K.1mer**  Amino acid sequence feature denoting the presence (1) or absence (0) of a residue at the given HXB2-referenced site.

**hxb2.186.N.1mer**  Amino acid sequence feature denoting the presence (1) or absence (0) of a residue at the given HXB2-referenced site.

**hxb2.186.P.1mer**  Amino acid sequence feature denoting the presence (1) or absence (0) of a residue at the given HXB2-referenced site.

**hxb2.186.R.1mer**  Amino acid sequence feature denoting the presence (1) or absence (0) of a residue at the given HXB2-referenced site.

**hxb2.186.S.1mer**  Amino acid sequence feature denoting the presence (1) or absence (0) of a residue at the given HXB2-referenced site.

**hxb2.186.T.1mer**  Amino acid sequence feature denoting the presence (1) or absence (0) of a residue at the given HXB2-referenced site.

**hxb2.186.gap.1mer**  Amino acid sequence feature denoting the presence (1) or absence (0) of a residue at the given HXB2-referenced site.

**hxb2.187.A.1mer**  Amino acid sequence feature denoting the presence (1) or absence (0) of a residue at the given HXB2-referenced site.

**hxb2.187.D.1mer**  Amino acid sequence feature denoting the presence (1) or absence (0) of a residue at the given HXB2-referenced site.

**hxb2.187.E.1mer**  Amino acid sequence feature denoting the presence (1) or absence (0) of a residue at the given HXB2-referenced site.

**hxb2.187.G.1mer**  Amino acid sequence feature denoting the presence (1) or absence (0) of a residue at the given HXB2-referenced site.

**hxb2.187.K.1mer**  Amino acid sequence feature denoting the presence (1) or absence (0) of a residue at the given HXB2-referenced site.

**hxb2.187.N.1mer**  Amino acid sequence feature denoting the presence (1) or absence (0) of a residue at the given HXB2-referenced site.

**hxb2.187.Q.1mer**  Amino acid sequence feature denoting the presence (1) or absence (0) of a residue at the given HXB2-referenced site.

**hxb2.187.R.1mer**  Amino acid sequence feature denoting the presence (1) or absence (0) of a residue at the given HXB2-referenced site.

**hxb2.187.S.1mer**  Amino acid sequence feature denoting the presence (1) or absence (0) of a residue at the given HXB2-referenced site.

**hxb2.187.T.1mer**  Amino acid sequence feature denoting the presence (1) or absence (0) of a residue at the given HXB2-referenced site.
hxb2.187.gap.1mer  Amino acid sequence feature denoting the presence (1) or absence (0) of a residue at the given HXB2-referenced site.

hxb2.190.D.1mer  Amino acid sequence feature denoting the presence (1) or absence (0) of a residue at the given HXB2-referenced site.

hxb2.190.E.1mer  Amino acid sequence feature denoting the presence (1) or absence (0) of a residue at the given HXB2-referenced site.

hxb2.190.F.1mer  Amino acid sequence feature denoting the presence (1) or absence (0) of a residue at the given HXB2-referenced site.

hxb2.190.G.1mer  Amino acid sequence feature denoting the presence (1) or absence (0) of a residue at the given HXB2-referenced site.

hxb2.190.I.1mer  Amino acid sequence feature denoting the presence (1) or absence (0) of a residue at the given HXB2-referenced site.

hxb2.190.K.1mer  Amino acid sequence feature denoting the presence (1) or absence (0) of a residue at the given HXB2-referenced site.

hxb2.190.L.1mer  Amino acid sequence feature denoting the presence (1) or absence (0) of a residue at the given HXB2-referenced site.

hxb2.190.M.1mer  Amino acid sequence feature denoting the presence (1) or absence (0) of a residue at the given HXB2-referenced site.

hxb2.190.N.1mer  Amino acid sequence feature denoting the presence (1) or absence (0) of a residue at the given HXB2-referenced site.

hxb2.190.Q.1mer  Amino acid sequence feature denoting the presence (1) or absence (0) of a residue at the given HXB2-referenced site.

hxb2.190.R.1mer  Amino acid sequence feature denoting the presence (1) or absence (0) of a residue at the given HXB2-referenced site.

hxb2.190.S.1mer  Amino acid sequence feature denoting the presence (1) or absence (0) of a residue at the given HXB2-referenced site.

hxb2.190.T.1mer  Amino acid sequence feature denoting the presence (1) or absence (0) of a residue at the given HXB2-referenced site.

hxb2.190.V.1mer  Amino acid sequence feature denoting the presence (1) or absence (0) of a residue at the given HXB2-referenced site.

hxb2.190.Y.1mer  Amino acid sequence feature denoting the presence (1) or absence (0) of a residue at the given HXB2-referenced site.

hxb2.197.D.1mer  Amino acid sequence feature denoting the presence (1) or absence (0) of a residue at the given HXB2-referenced site.

hxb2.197.K.1mer  Amino acid sequence feature denoting the presence (1) or absence (0) of a residue at the given HXB2-referenced site.

hxb2.197.N.1mer  Amino acid sequence feature denoting the presence (1) or absence (0) of a residue at the given HXB2-referenced site.

hxb2.198.A.1mer  Amino acid sequence feature denoting the presence (1) or absence (0) of a residue at the given HXB2-referenced site.

hxb2.198.S.1mer  Amino acid sequence feature denoting the presence (1) or absence (0) of a residue at the given HXB2-referenced site.
**hxb2.198.T.1mer**  Amino acid sequence feature denoting the presence (1) or absence (0) of a residue at the given HXB2-referenced site.

**hxb2.198.V.1mer**  Amino acid sequence feature denoting the presence (1) or absence (0) of a residue at the given HXB2-referenced site.

**hxb2.241.D.1mer**  Amino acid sequence feature denoting the presence (1) or absence (0) of a residue at the given HXB2-referenced site.

**hxb2.241.K.1mer**  Amino acid sequence feature denoting the presence (1) or absence (0) of a residue at the given HXB2-referenced site.

**hxb2.241.N.1mer**  Amino acid sequence feature denoting the presence (1) or absence (0) of a residue at the given HXB2-referenced site.

**hxb2.241.S.1mer**  Amino acid sequence feature denoting the presence (1) or absence (0) of a residue at the given HXB2-referenced site.

**hxb2.276.D.1mer**  Amino acid sequence feature denoting the presence (1) or absence (0) of a residue at the given HXB2-referenced site.

**hxb2.276.K.1mer**  Amino acid sequence feature denoting the presence (1) or absence (0) of a residue at the given HXB2-referenced site.

**hxb2.276.N.1mer**  Amino acid sequence feature denoting the presence (1) or absence (0) of a residue at the given HXB2-referenced site.

**hxb2.276.S.1mer**  Amino acid sequence feature denoting the presence (1) or absence (0) of a residue at the given HXB2-referenced site.

**hxb2.278.A.1mer**  Amino acid sequence feature denoting the presence (1) or absence (0) of a residue at the given HXB2-referenced site.

**hxb2.278.E.1mer**  Amino acid sequence feature denoting the presence (1) or absence (0) of a residue at the given HXB2-referenced site.

**hxb2.278.N.1mer**  Amino acid sequence feature denoting the presence (1) or absence (0) of a residue at the given HXB2-referenced site.

**hxb2.278.S.1mer**  Amino acid sequence feature denoting the presence (1) or absence (0) of a residue at the given HXB2-referenced site.

**hxb2.278.T.1mer**  Amino acid sequence feature denoting the presence (1) or absence (0) of a residue at the given HXB2-referenced site.

**hxb2.279.D.1mer**  Amino acid sequence feature denoting the presence (1) or absence (0) of a residue at the given HXB2-referenced site.

**hxb2.279.E.1mer**  Amino acid sequence feature denoting the presence (1) or absence (0) of a residue at the given HXB2-referenced site.

**hxb2.279.K.1mer**  Amino acid sequence feature denoting the presence (1) or absence (0) of a residue at the given HXB2-referenced site.

**hxb2.279.N.1mer**  Amino acid sequence feature denoting the presence (1) or absence (0) of a residue at the given HXB2-referenced site.

**hxb2.279.S.1mer**  Amino acid sequence feature denoting the presence (1) or absence (0) of a residue at the given HXB2-referenced site.

**hxb2.280.D.1mer**  Amino acid sequence feature denoting the presence (1) or absence (0) of a residue at the given HXB2-referenced site.
**hxb2.280.N.1mer** Amino acid sequence feature denoting the presence (1) or absence (0) of a residue at the given HXB2-referenced site.

**hxb2.280.S.1mer** Amino acid sequence feature denoting the presence (1) or absence (0) of a residue at the given HXB2-referenced site.

**hxb2.280.T.1mer** Amino acid sequence feature denoting the presence (1) or absence (0) of a residue at the given HXB2-referenced site.

**hxb2.281.A.1mer** Amino acid sequence feature denoting the presence (1) or absence (0) of a residue at the given HXB2-referenced site.

**hxb2.281.E.1mer** Amino acid sequence feature denoting the presence (1) or absence (0) of a residue at the given HXB2-referenced site.

**hxb2.281.G.1mer** Amino acid sequence feature denoting the presence (1) or absence (0) of a residue at the given HXB2-referenced site.

**hxb2.281.I.1mer** Amino acid sequence feature denoting the presence (1) or absence (0) of a residue at the given HXB2-referenced site.

**hxb2.281.S.1mer** Amino acid sequence feature denoting the presence (1) or absence (0) of a residue at the given HXB2-referenced site.

**hxb2.281.T.1mer** Amino acid sequence feature denoting the presence (1) or absence (0) of a residue at the given HXB2-referenced site.

**hxb2.281.V.1mer** Amino acid sequence feature denoting the presence (1) or absence (0) of a residue at the given HXB2-referenced site.

**hxb2.282.G.1mer** Amino acid sequence feature denoting the presence (1) or absence (0) of a residue at the given HXB2-referenced site.

**hxb2.282.K.1mer** Amino acid sequence feature denoting the presence (1) or absence (0) of a residue at the given HXB2-referenced site.

**hxb2.282.N.1mer** Amino acid sequence feature denoting the presence (1) or absence (0) of a residue at the given HXB2-referenced site.

**hxb2.282.Q.1mer** Amino acid sequence feature denoting the presence (1) or absence (0) of a residue at the given HXB2-referenced site.

**hxb2.282.R.1mer** Amino acid sequence feature denoting the presence (1) or absence (0) of a residue at the given HXB2-referenced site.

**hxb2.282.Y.1mer** Amino acid sequence feature denoting the presence (1) or absence (0) of a residue at the given HXB2-referenced site.

**hxb2.283.I.1mer** Amino acid sequence feature denoting the presence (1) or absence (0) of a residue at the given HXB2-referenced site.

**hxb2.283.N.1mer** Amino acid sequence feature denoting the presence (1) or absence (0) of a residue at the given HXB2-referenced site.

**hxb2.283.T.1mer** Amino acid sequence feature denoting the presence (1) or absence (0) of a residue at the given HXB2-referenced site.

**hxb2.283.V.1mer** Amino acid sequence feature denoting the presence (1) or absence (0) of a residue at the given HXB2-referenced site.

**hxb2.289.A.1mer** Amino acid sequence feature denoting the presence (1) or absence (0) of a residue at the given HXB2-referenced site.
hxbl.289.D.1mer Amino acid sequence feature denoting the presence (1) or absence (0) of a residue at the given HXB2-referenced site.
hxbl.289.K.1mer Amino acid sequence feature denoting the presence (1) or absence (0) of a residue at the given HXB2-referenced site.
hxbl.289.N.1mer Amino acid sequence feature denoting the presence (1) or absence (0) of a residue at the given HXB2-referenced site.
hxbl.289.R.1mer Amino acid sequence feature denoting the presence (1) or absence (0) of a residue at the given HXB2-referenced site.
hxbl.289.S.1mer Amino acid sequence feature denoting the presence (1) or absence (0) of a residue at the given HXB2-referenced site.
hxbl.289.T.1mer Amino acid sequence feature denoting the presence (1) or absence (0) of a residue at the given HXB2-referenced site.
hxbl.289.V.1mer Amino acid sequence feature denoting the presence (1) or absence (0) of a residue at the given HXB2-referenced site.
hxbl.290.D.1mer Amino acid sequence feature denoting the presence (1) or absence (0) of a residue at the given HXB2-referenced site.
hxbl.290.E.1mer Amino acid sequence feature denoting the presence (1) or absence (0) of a residue at the given HXB2-referenced site.
hxbl.290.G.1mer Amino acid sequence feature denoting the presence (1) or absence (0) of a residue at the given HXB2-referenced site.
hxbl.290.K.1mer Amino acid sequence feature denoting the presence (1) or absence (0) of a residue at the given HXB2-referenced site.
hxbl.290.L.1mer Amino acid sequence feature denoting the presence (1) or absence (0) of a residue at the given HXB2-referenced site.
hxbl.290.N.1mer Amino acid sequence feature denoting the presence (1) or absence (0) of a residue at the given HXB2-referenced site.
hxbl.290.Q.1mer Amino acid sequence feature denoting the presence (1) or absence (0) of a residue at the given HXB2-referenced site.
hxbl.290.R.1mer Amino acid sequence feature denoting the presence (1) or absence (0) of a residue at the given HXB2-referenced site.
hxbl.290.S.1mer Amino acid sequence feature denoting the presence (1) or absence (0) of a residue at the given HXB2-referenced site.
hxbl.290.T.1mer Amino acid sequence feature denoting the presence (1) or absence (0) of a residue at the given HXB2-referenced site.
hxbl.290.X.1mer Amino acid sequence feature denoting the presence (1) or absence (0) of a residue at the given HXB2-referenced site.
hxbl.321.D.1mer Amino acid sequence feature denoting the presence (1) or absence (0) of a residue at the given HXB2-referenced site.
hxbl.321.E.1mer Amino acid sequence feature denoting the presence (1) or absence (0) of a residue at the given HXB2-referenced site.
hxbl.321.G.1mer Amino acid sequence feature denoting the presence (1) or absence (0) of a residue at the given HXB2-referenced site.
hxbl.321.K.1mer Amino acid sequence feature denoting the presence (1) or absence (0) of a residue at the given HXB2-referenced site.
hxbl.321.L.1mer Amino acid sequence feature denoting the presence (1) or absence (0) of a residue at the given HXB2-referenced site.
**hxb2.321.N.1mer** Amino acid sequence feature denoting the presence (1) or absence (0) of a residue at the given HXB2-referenced site.

**hxb2.321.R.1mer** Amino acid sequence feature denoting the presence (1) or absence (0) of a residue at the given HXB2-referenced site.

**hxb2.321.T.1mer** Amino acid sequence feature denoting the presence (1) or absence (0) of a residue at the given HXB2-referenced site.

**hxb2.321.V.1mer** Amino acid sequence feature denoting the presence (1) or absence (0) of a residue at the given HXB2-referenced site.

**hxb2.321.Y.1mer** Amino acid sequence feature denoting the presence (1) or absence (0) of a residue at the given HXB2-referenced site.

**hxb2.321.gap.1mer** Amino acid sequence feature denoting the presence (1) or absence (0) of a residue at the given HXB2-referenced site.

**hxb2.328.A.1mer** Amino acid sequence feature denoting the presence (1) or absence (0) of a residue at the given HXB2-referenced site.

**hxb2.328.E.1mer** Amino acid sequence feature denoting the presence (1) or absence (0) of a residue at the given HXB2-referenced site.

**hxb2.328.I.1mer** Amino acid sequence feature denoting the presence (1) or absence (0) of a residue at the given HXB2-referenced site.

**hxb2.328.K.1mer** Amino acid sequence feature denoting the presence (1) or absence (0) of a residue at the given HXB2-referenced site.

**hxb2.328.L.1mer** Amino acid sequence feature denoting the presence (1) or absence (0) of a residue at the given HXB2-referenced site.

**hxb2.328.N.1mer** Amino acid sequence feature denoting the presence (1) or absence (0) of a residue at the given HXB2-referenced site.

**hxb2.328.Q.1mer** Amino acid sequence feature denoting the presence (1) or absence (0) of a residue at the given HXB2-referenced site.

**hxb2.328.R.1mer** Amino acid sequence feature denoting the presence (1) or absence (0) of a residue at the given HXB2-referenced site.

**hxb2.339.D.1mer** Amino acid sequence feature denoting the presence (1) or absence (0) of a residue at the given HXB2-referenced site.

**hxb2.339.E.1mer** Amino acid sequence feature denoting the presence (1) or absence (0) of a residue at the given HXB2-referenced site.

**hxb2.339.G.1mer** Amino acid sequence feature denoting the presence (1) or absence (0) of a residue at the given HXB2-referenced site.

**hxb2.339.H.1mer** Amino acid sequence feature denoting the presence (1) or absence (0) of a residue at the given HXB2-referenced site.

**hxb2.339.I.1mer** Amino acid sequence feature denoting the presence (1) or absence (0) of a residue at the given HXB2-referenced site.

**hxb2.339.K.1mer** Amino acid sequence feature denoting the presence (1) or absence (0) of a residue at the given HXB2-referenced site.

**hxb2.339.N.1mer** Amino acid sequence feature denoting the presence (1) or absence (0) of a residue at the given HXB2-referenced site.
**hxb2.339.Q.1mer** Amino acid sequence feature denoting the presence (1) or absence (0) of a residue at the given HXB2-referenced site.

**hxb2.339.R.1mer** Amino acid sequence feature denoting the presence (1) or absence (0) of a residue at the given HXB2-referenced site.

**hxb2.339.S.1mer** Amino acid sequence feature denoting the presence (1) or absence (0) of a residue at the given HXB2-referenced site.

**hxb2.339.T.1mer** Amino acid sequence feature denoting the presence (1) or absence (0) of a residue at the given HXB2-referenced site.

**hxb2.339.V.1mer** Amino acid sequence feature denoting the presence (1) or absence (0) of a residue at the given HXB2-referenced site.

**hxb2.339.Y.1mer** Amino acid sequence feature denoting the presence (1) or absence (0) of a residue at the given HXB2-referenced site.

**hxb2.354.E.1mer** Amino acid sequence feature denoting the presence (1) or absence (0) of a residue at the given HXB2-referenced site.

**hxb2.354.G.1mer** Amino acid sequence feature denoting the presence (1) or absence (0) of a residue at the given HXB2-referenced site.

**hxb2.354.H.1mer** Amino acid sequence feature denoting the presence (1) or absence (0) of a residue at the given HXB2-referenced site.

**hxb2.354.I.1mer** Amino acid sequence feature denoting the presence (1) or absence (0) of a residue at the given HXB2-referenced site.

**hxb2.354.K.1mer** Amino acid sequence feature denoting the presence (1) or absence (0) of a residue at the given HXB2-referenced site.

**hxb2.354.L.1mer** Amino acid sequence feature denoting the presence (1) or absence (0) of a residue at the given HXB2-referenced site.

**hxb2.354.N.1mer** Amino acid sequence feature denoting the presence (1) or absence (0) of a residue at the given HXB2-referenced site.

**hxb2.354.P.1mer** Amino acid sequence feature denoting the presence (1) or absence (0) of a residue at the given HXB2-referenced site.

**hxb2.354.Q.1mer** Amino acid sequence feature denoting the presence (1) or absence (0) of a residue at the given HXB2-referenced site.

**hxb2.354.R.1mer** Amino acid sequence feature denoting the presence (1) or absence (0) of a residue at the given HXB2-referenced site.

**hxb2.354.S.1mer** Amino acid sequence feature denoting the presence (1) or absence (0) of a residue at the given HXB2-referenced site.

**hxb2.354.T.1mer** Amino acid sequence feature denoting the presence (1) or absence (0) of a residue at the given HXB2-referenced site.

**hxb2.354.gap.1mer** Amino acid sequence feature denoting the presence (1) or absence (0) of a residue at the given HXB2-referenced site.

**hxb2.355.D.1mer** Amino acid sequence feature denoting the presence (1) or absence (0) of a residue at the given HXB2-referenced site.

**hxb2.355.G.1mer** Amino acid sequence feature denoting the presence (1) or absence (0) of a residue at the given HXB2-referenced site.
hxb2.355.1mer  Amino acid sequence feature denoting the presence (1) or absence (0) of a residue at the given HXB2-referenced site.

hxb2.355.K.1mer  Amino acid sequence feature denoting the presence (1) or absence (0) of a residue at the given HXB2-referenced site.

hxb2.355.N.1mer  Amino acid sequence feature denoting the presence (1) or absence (0) of a residue at the given HXB2-referenced site.

hxb2.355.Q.1mer  Amino acid sequence feature denoting the presence (1) or absence (0) of a residue at the given HXB2-referenced site.

hxb2.355.T.1mer  Amino acid sequence feature denoting the presence (1) or absence (0) of a residue at the given HXB2-referenced site.

hxb2.355.gap.1mer  Amino acid sequence feature denoting the presence (1) or absence (0) of a residue at the given HXB2-referenced site.

hxb2.362.A.1mer  Amino acid sequence feature denoting the presence (1) or absence (0) of a residue at the given HXB2-referenced site.

hxb2.362.D.1mer  Amino acid sequence feature denoting the presence (1) or absence (0) of a residue at the given HXB2-referenced site.

hxb2.362.E.1mer  Amino acid sequence feature denoting the presence (1) or absence (0) of a residue at the given HXB2-referenced site.

hxb2.362.G.1mer  Amino acid sequence feature denoting the presence (1) or absence (0) of a residue at the given HXB2-referenced site.

hxb2.362.K.1mer  Amino acid sequence feature denoting the presence (1) or absence (0) of a residue at the given HXB2-referenced site.

hxb2.362.N.1mer  Amino acid sequence feature denoting the presence (1) or absence (0) of a residue at the given HXB2-referenced site.

hxb2.362.Q.1mer  Amino acid sequence feature denoting the presence (1) or absence (0) of a residue at the given HXB2-referenced site.

hxb2.362.R.1mer  Amino acid sequence feature denoting the presence (1) or absence (0) of a residue at the given HXB2-referenced site.

hxb2.362.S.1mer  Amino acid sequence feature denoting the presence (1) or absence (0) of a residue at the given HXB2-referenced site.

hxb2.362.T.1mer  Amino acid sequence feature denoting the presence (1) or absence (0) of a residue at the given HXB2-referenced site.

hxb2.363.A.1mer  Amino acid sequence feature denoting the presence (1) or absence (0) of a residue at the given HXB2-referenced site.

hxb2.363.E.1mer  Amino acid sequence feature denoting the presence (1) or absence (0) of a residue at the given HXB2-referenced site.

hxb2.363.G.1mer  Amino acid sequence feature denoting the presence (1) or absence (0) of a residue at the given HXB2-referenced site.

hxb2.363.H.1mer  Amino acid sequence feature denoting the presence (1) or absence (0) of a residue at the given HXB2-referenced site.

hxb2.363.K.1mer  Amino acid sequence feature denoting the presence (1) or absence (0) of a residue at the given HXB2-referenced site.
**hxb2.363.N.1mer**  Amino acid sequence feature denoting the presence (1) or absence (0) of a residue at the given HXB2-referenced site.

**hxb2.363.P.1mer**  Amino acid sequence feature denoting the presence (1) or absence (0) of a residue at the given HXB2-referenced site.

**hxb2.363.Q.1mer**  Amino acid sequence feature denoting the presence (1) or absence (0) of a residue at the given HXB2-referenced site.

**hxb2.363.R.1mer**  Amino acid sequence feature denoting the presence (1) or absence (0) of a residue at the given HXB2-referenced site.

**hxb2.363.S.1mer**  Amino acid sequence feature denoting the presence (1) or absence (0) of a residue at the given HXB2-referenced site.

**hxb2.363.T.1mer**  Amino acid sequence feature denoting the presence (1) or absence (0) of a residue at the given HXB2-referenced site.

**hxb2.363.X.1mer**  Amino acid sequence feature denoting the presence (1) or absence (0) of a residue at the given HXB2-referenced site.

**hxb2.365.A.1mer**  Amino acid sequence feature denoting the presence (1) or absence (0) of a residue at the given HXB2-referenced site.

**hxb2.365.L.1mer**  Amino acid sequence feature denoting the presence (1) or absence (0) of a residue at the given HXB2-referenced site.

**hxb2.365.N.1mer**  Amino acid sequence feature denoting the presence (1) or absence (0) of a residue at the given HXB2-referenced site.

**hxb2.365.P.1mer**  Amino acid sequence feature denoting the presence (1) or absence (0) of a residue at the given HXB2-referenced site.

**hxb2.365.Q.1mer**  Amino acid sequence feature denoting the presence (1) or absence (0) of a residue at the given HXB2-referenced site.

**hxb2.365.V.1mer**  Amino acid sequence feature denoting the presence (1) or absence (0) of a residue at the given HXB2-referenced site.

**hxb2.369.A.1mer**  Amino acid sequence feature denoting the presence (1) or absence (0) of a residue at the given HXB2-referenced site.

**hxb2.369.L.1mer**  Amino acid sequence feature denoting the presence (1) or absence (0) of a residue at the given HXB2-referenced site.

**hxb2.369.P.1mer**  Amino acid sequence feature denoting the presence (1) or absence (0) of a residue at the given HXB2-referenced site.

**hxb2.369.Q.1mer**  Amino acid sequence feature denoting the presence (1) or absence (0) of a residue at the given HXB2-referenced site.

**hxb2.369.V.1mer**  Amino acid sequence feature denoting the presence (1) or absence (0) of a residue at the given HXB2-referenced site.
**hxb2.371.I.1mer**  Amino acid sequence feature denoting the presence (1) or absence (0) of a residue at the given HXB2-referenced site.

**hxb2.371.L.1mer**  Amino acid sequence feature denoting the presence (1) or absence (0) of a residue at the given HXB2-referenced site.

**hxb2.371.T.1mer**  Amino acid sequence feature denoting the presence (1) or absence (0) of a residue at the given HXB2-referenced site.

**hxb2.371.V.1mer**  Amino acid sequence feature denoting the presence (1) or absence (0) of a residue at the given HXB2-referenced site.

**hxb2.374.F.1mer**  Amino acid sequence feature denoting the presence (1) or absence (0) of a residue at the given HXB2-referenced site.

**hxb2.374.H.1mer**  Amino acid sequence feature denoting the presence (1) or absence (0) of a residue at the given HXB2-referenced site.

**hxb2.374.L.1mer**  Amino acid sequence feature denoting the presence (1) or absence (0) of a residue at the given HXB2-referenced site.

**hxb2.386.D.1mer**  Amino acid sequence feature denoting the presence (1) or absence (0) of a residue at the given HXB2-referenced site.

**hxb2.386.N.1mer**  Amino acid sequence feature denoting the presence (1) or absence (0) of a residue at the given HXB2-referenced site.

**hxb2.386.S.1mer**  Amino acid sequence feature denoting the presence (1) or absence (0) of a residue at the given HXB2-referenced site.

**hxb2.386.X.1mer**  Amino acid sequence feature denoting the presence (1) or absence (0) of a residue at the given HXB2-referenced site.

**hxb2.386.Y.1mer**  Amino acid sequence feature denoting the presence (1) or absence (0) of a residue at the given HXB2-referenced site.

**hxb2.389.A.1mer**  Amino acid sequence feature denoting the presence (1) or absence (0) of a residue at the given HXB2-referenced site.

**hxb2.389.D.1mer**  Amino acid sequence feature denoting the presence (1) or absence (0) of a residue at the given HXB2-referenced site.

**hxb2.389.E.1mer**  Amino acid sequence feature denoting the presence (1) or absence (0) of a residue at the given HXB2-referenced site.

**hxb2.389.G.1mer**  Amino acid sequence feature denoting the presence (1) or absence (0) of a residue at the given HXB2-referenced site.

**hxb2.389.H.1mer**  Amino acid sequence feature denoting the presence (1) or absence (0) of a residue at the given HXB2-referenced site.

**hxb2.389.I.1mer**  Amino acid sequence feature denoting the presence (1) or absence (0) of a residue at the given HXB2-referenced site.

**hxb2.389.K.1mer**  Amino acid sequence feature denoting the presence (1) or absence (0) of a residue at the given HXB2-referenced site.

**hxb2.389.N.1mer**  Amino acid sequence feature denoting the presence (1) or absence (0) of a residue at the given HXB2-referenced site.

**hxb2.389.P.1mer**  Amino acid sequence feature denoting the presence (1) or absence (0) of a residue at the given HXB2-referenced site.
hxb2.389.Q.1mer  Amino acid sequence feature denoting the presence (1) or absence (0) of a residue at the given HXB2-referenced site.
hxb2.389.R.1mer  Amino acid sequence feature denoting the presence (1) or absence (0) of a residue at the given HXB2-referenced site.
hxb2.389.S.1mer  Amino acid sequence feature denoting the presence (1) or absence (0) of a residue at the given HXB2-referenced site.
hxb2.389.T.1mer  Amino acid sequence feature denoting the presence (1) or absence (0) of a residue at the given HXB2-referenced site.
hxb2.392.D.1mer  Amino acid sequence feature denoting the presence (1) or absence (0) of a residue at the given HXB2-referenced site.
hxb2.392.H.1mer  Amino acid sequence feature denoting the presence (1) or absence (0) of a residue at the given HXB2-referenced site.
hxb2.392.K.1mer  Amino acid sequence feature denoting the presence (1) or absence (0) of a residue at the given HXB2-referenced site.
hxb2.392.N.1mer  Amino acid sequence feature denoting the presence (1) or absence (0) of a residue at the given HXB2-referenced site.
hxb2.392.Q.1mer  Amino acid sequence feature denoting the presence (1) or absence (0) of a residue at the given HXB2-referenced site.
hxb2.392.S.1mer  Amino acid sequence feature denoting the presence (1) or absence (0) of a residue at the given HXB2-referenced site.
hxb2.392.T.1mer  Amino acid sequence feature denoting the presence (1) or absence (0) of a residue at the given HXB2-referenced site.
hxb2.392.Y.1mer  Amino acid sequence feature denoting the presence (1) or absence (0) of a residue at the given HXB2-referenced site.
hxb2.392.gap.1mer  Amino acid sequence feature denoting the presence (1) or absence (0) of a residue at the given HXB2-referenced site.
hxb2.394.A.1mer  Amino acid sequence feature denoting the presence (1) or absence (0) of a residue at the given HXB2-referenced site.
hxb2.394.D.1mer  Amino acid sequence feature denoting the presence (1) or absence (0) of a residue at the given HXB2-referenced site.
hxb2.394.E.1mer  Amino acid sequence feature denoting the presence (1) or absence (0) of a residue at the given HXB2-referenced site.
hxb2.394.I.1mer  Amino acid sequence feature denoting the presence (1) or absence (0) of a residue at the given HXB2-referenced site.
hxb2.394.K.1mer  Amino acid sequence feature denoting the presence (1) or absence (0) of a residue at the given HXB2-referenced site.
hxb2.394.N.1mer  Amino acid sequence feature denoting the presence (1) or absence (0) of a residue at the given HXB2-referenced site.
hxb2.394.R.1mer  Amino acid sequence feature denoting the presence (1) or absence (0) of a residue at the given HXB2-referenced site.
hxb2.394.S.1mer  Amino acid sequence feature denoting the presence (1) or absence (0) of a residue at the given HXB2-referenced site.
**hxb2.394.T.1mer** Amino acid sequence feature denoting the presence (1) or absence (0) of a residue at the given HXB2-referenced site.

**hxb2.394.V.1mer** Amino acid sequence feature denoting the presence (1) or absence (0) of a residue at the given HXB2-referenced site.

**hxb2.394.gap.1mer** Amino acid sequence feature denoting the presence (1) or absence (0) of a residue at the given HXB2-referenced site.

**hxb2.396.A.1mer** Amino acid sequence feature denoting the presence (1) or absence (0) of a residue at the given HXB2-referenced site.

**hxb2.396.D.1mer** Amino acid sequence feature denoting the presence (1) or absence (0) of a residue at the given HXB2-referenced site.

**hxb2.396.E.1mer** Amino acid sequence feature denoting the presence (1) or absence (0) of a residue at the given HXB2-referenced site.

**hxb2.396.F.1mer** Amino acid sequence feature denoting the presence (1) or absence (0) of a residue at the given HXB2-referenced site.

**hxb2.396.G.1mer** Amino acid sequence feature denoting the presence (1) or absence (0) of a residue at the given HXB2-referenced site.

**hxb2.396.H.1mer** Amino acid sequence feature denoting the presence (1) or absence (0) of a residue at the given HXB2-referenced site.

**hxb2.396.I.1mer** Amino acid sequence feature denoting the presence (1) or absence (0) of a residue at the given HXB2-referenced site.

**hxb2.396.K.1mer** Amino acid sequence feature denoting the presence (1) or absence (0) of a residue at the given HXB2-referenced site.

**hxb2.396.L.1mer** Amino acid sequence feature denoting the presence (1) or absence (0) of a residue at the given HXB2-referenced site.

**hxb2.396.M.1mer** Amino acid sequence feature denoting the presence (1) or absence (0) of a residue at the given HXB2-referenced site.

**hxb2.396.N.1mer** Amino acid sequence feature denoting the presence (1) or absence (0) of a residue at the given HXB2-referenced site.

**hxb2.396.P.1mer** Amino acid sequence feature denoting the presence (1) or absence (0) of a residue at the given HXB2-referenced site.

**hxb2.396.Q.1mer** Amino acid sequence feature denoting the presence (1) or absence (0) of a residue at the given HXB2-referenced site.

**hxb2.396.R.1mer** Amino acid sequence feature denoting the presence (1) or absence (0) of a residue at the given HXB2-referenced site.

**hxb2.396.S.1mer** Amino acid sequence feature denoting the presence (1) or absence (0) of a residue at the given HXB2-referenced site.

**hxb2.396.T.1mer** Amino acid sequence feature denoting the presence (1) or absence (0) of a residue at the given HXB2-referenced site.

**hxb2.396.W.1mer** Amino acid sequence feature denoting the presence (1) or absence (0) of a residue at the given HXB2-referenced site.

**hxb2.396.Y.1mer** Amino acid sequence feature denoting the presence (1) or absence (0) of a residue at the given HXB2-referenced site.
**hxb2.396.gap.1mer**  Amino acid sequence feature denoting the presence (1) or absence (0) of a residue at the given HXB2-referenced site.

**hxb2.397.A.1mer**  Amino acid sequence feature denoting the presence (1) or absence (0) of a residue at the given HXB2-referenced site.

**hxb2.397.C.1mer**  Amino acid sequence feature denoting the presence (1) or absence (0) of a residue at the given HXB2-referenced site.

**hxb2.397.D.1mer**  Amino acid sequence feature denoting the presence (1) or absence (0) of a residue at the given HXB2-referenced site.

**hxb2.397.E.1mer**  Amino acid sequence feature denoting the presence (1) or absence (0) of a residue at the given HXB2-referenced site.

**hxb2.397.F.1mer**  Amino acid sequence feature denoting the presence (1) or absence (0) of a residue at the given HXB2-referenced site.

**hxb2.397.G.1mer**  Amino acid sequence feature denoting the presence (1) or absence (0) of a residue at the given HXB2-referenced site.

**hxb2.397.H.1mer**  Amino acid sequence feature denoting the presence (1) or absence (0) of a residue at the given HXB2-referenced site.

**hxb2.397.I.1mer**  Amino acid sequence feature denoting the presence (1) or absence (0) of a residue at the given HXB2-referenced site.

**hxb2.397.K.1mer**  Amino acid sequence feature denoting the presence (1) or absence (0) of a residue at the given HXB2-referenced site.

**hxb2.397.L.1mer**  Amino acid sequence feature denoting the presence (1) or absence (0) of a residue at the given HXB2-referenced site.

**hxb2.397.N.1mer**  Amino acid sequence feature denoting the presence (1) or absence (0) of a residue at the given HXB2-referenced site.

**hxb2.397.P.1mer**  Amino acid sequence feature denoting the presence (1) or absence (0) of a residue at the given HXB2-referenced site.

**hxb2.397.Q.1mer**  Amino acid sequence feature denoting the presence (1) or absence (0) of a residue at the given HXB2-referenced site.

**hxb2.397.R.1mer**  Amino acid sequence feature denoting the presence (1) or absence (0) of a residue at the given HXB2-referenced site.

**hxb2.397.S.1mer**  Amino acid sequence feature denoting the presence (1) or absence (0) of a residue at the given HXB2-referenced site.

**hxb2.397.T.1mer**  Amino acid sequence feature denoting the presence (1) or absence (0) of a residue at the given HXB2-referenced site.

**hxb2.397.V.1mer**  Amino acid sequence feature denoting the presence (1) or absence (0) of a residue at the given HXB2-referenced site.

**hxb2.397.W.1mer**  Amino acid sequence feature denoting the presence (1) or absence (0) of a residue at the given HXB2-referenced site.

**hxb2.397.X.1mer**  Amino acid sequence feature denoting the presence (1) or absence (0) of a residue at the given HXB2-referenced site.

**hxb2.397.Y.1mer**  Amino acid sequence feature denoting the presence (1) or absence (0) of a residue at the given HXB2-referenced site.
hxb2.397.gap.1mer Amino acid sequence feature denoting the presence (1) or absence (0) of a residue at the given HXB2-referenced site.
hxb2.406.A.1mer Amino acid sequence feature denoting the presence (1) or absence (0) of a residue at the given HXB2-referenced site.
hxb2.406.D.1mer Amino acid sequence feature denoting the presence (1) or absence (0) of a residue at the given HXB2-referenced site.
hxb2.406.E.1mer Amino acid sequence feature denoting the presence (1) or absence (0) of a residue at the given HXB2-referenced site.
hxb2.406.F.1mer Amino acid sequence feature denoting the presence (1) or absence (0) of a residue at the given HXB2-referenced site.
hxb2.406.G.1mer Amino acid sequence feature denoting the presence (1) or absence (0) of a residue at the given HXB2-referenced site.
hxb2.406.H.1mer Amino acid sequence feature denoting the presence (1) or absence (0) of a residue at the given HXB2-referenced site.
hxb2.406.I.1mer Amino acid sequence feature denoting the presence (1) or absence (0) of a residue at the given HXB2-referenced site.
hxb2.406.K.1mer Amino acid sequence feature denoting the presence (1) or absence (0) of a residue at the given HXB2-referenced site.
hxb2.406.L.1mer Amino acid sequence feature denoting the presence (1) or absence (0) of a residue at the given HXB2-referenced site.
hxb2.406.M.1mer Amino acid sequence feature denoting the presence (1) or absence (0) of a residue at the given HXB2-referenced site.
hxb2.406.N.1mer Amino acid sequence feature denoting the presence (1) or absence (0) of a residue at the given HXB2-referenced site.
hxb2.406.P.1mer Amino acid sequence feature denoting the presence (1) or absence (0) of a residue at the given HXB2-referenced site.
hxb2.406.Q.1mer Amino acid sequence feature denoting the presence (1) or absence (0) of a residue at the given HXB2-referenced site.
hxb2.406.R.1mer Amino acid sequence feature denoting the presence (1) or absence (0) of a residue at the given HXB2-referenced site.
hxb2.406.S.1mer Amino acid sequence feature denoting the presence (1) or absence (0) of a residue at the given HXB2-referenced site.
hxb2.406.T.1mer Amino acid sequence feature denoting the presence (1) or absence (0) of a residue at the given HXB2-referenced site.
hxb2.406.V.1mer Amino acid sequence feature denoting the presence (1) or absence (0) of a residue at the given HXB2-referenced site.
hxb2.406.W.1mer Amino acid sequence feature denoting the presence (1) or absence (0) of a residue at the given HXB2-referenced site.
hxb2.406.Y.1mer Amino acid sequence feature denoting the presence (1) or absence (0) of a residue at the given HXB2-referenced site.
hxb2.406.gap.1mer Amino acid sequence feature denoting the presence (1) or absence (0) of a residue at the given HXB2-referenced site.
**hxb2.408.A.1mer** Amino acid sequence feature denoting the presence (1) or absence (0) of a residue at the given HXB2-referenced site.

**hxb2.408.D.1mer** Amino acid sequence feature denoting the presence (1) or absence (0) of a residue at the given HXB2-referenced site.

**hxb2.408.E.1mer** Amino acid sequence feature denoting the presence (1) or absence (0) of a residue at the given HXB2-referenced site.

**hxb2.408.F.1mer** Amino acid sequence feature denoting the presence (1) or absence (0) of a residue at the given HXB2-referenced site.

**hxb2.408.G.1mer** Amino acid sequence feature denoting the presence (1) or absence (0) of a residue at the given HXB2-referenced site.

**hxb2.408.H.1mer** Amino acid sequence feature denoting the presence (1) or absence (0) of a residue at the given HXB2-referenced site.

**hxb2.408.I.1mer** Amino acid sequence feature denoting the presence (1) or absence (0) of a residue at the given HXB2-referenced site.

**hxb2.408.K.1mer** Amino acid sequence feature denoting the presence (1) or absence (0) of a residue at the given HXB2-referenced site.

**hxb2.408.L.1mer** Amino acid sequence feature denoting the presence (1) or absence (0) of a residue at the given HXB2-referenced site.

**hxb2.408.M.1mer** Amino acid sequence feature denoting the presence (1) or absence (0) of a residue at the given HXB2-referenced site.

**hxb2.408.N.1mer** Amino acid sequence feature denoting the presence (1) or absence (0) of a residue at the given HXB2-referenced site.

**hxb2.408.P.1mer** Amino acid sequence feature denoting the presence (1) or absence (0) of a residue at the given HXB2-referenced site.

**hxb2.408.Q.1mer** Amino acid sequence feature denoting the presence (1) or absence (0) of a residue at the given HXB2-referenced site.

**hxb2.408.R.1mer** Amino acid sequence feature denoting the presence (1) or absence (0) of a residue at the given HXB2-referenced site.

**hxb2.408.S.1mer** Amino acid sequence feature denoting the presence (1) or absence (0) of a residue at the given HXB2-referenced site.

**hxb2.408.T.1mer** Amino acid sequence feature denoting the presence (1) or absence (0) of a residue at the given HXB2-referenced site.

**hxb2.408.V.1mer** Amino acid sequence feature denoting the presence (1) or absence (0) of a residue at the given HXB2-referenced site.

**hxb2.408.Y.1mer** Amino acid sequence feature denoting the presence (1) or absence (0) of a residue at the given HXB2-referenced site.

**hxb2.408.gap.1mer** Amino acid sequence feature denoting the presence (1) or absence (0) of a residue at the given HXB2-referenced site.

**hxb2.410.A.1mer** Amino acid sequence feature denoting the presence (1) or absence (0) of a residue at the given HXB2-referenced site.

**hxb2.410.C.1mer** Amino acid sequence feature denoting the presence (1) or absence (0) of a residue at the given HXB2-referenced site.
**hxb2.410.D.1mer**  Amino acid sequence feature denoting the presence (1) or absence (0) of a residue at the given HXB2-referenced site.

**hxb2.410.E.1mer**  Amino acid sequence feature denoting the presence (1) or absence (0) of a residue at the given HXB2-referenced site.

**hxb2.410.G.1mer**  Amino acid sequence feature denoting the presence (1) or absence (0) of a residue at the given HXB2-referenced site.

**hxb2.410.H.1mer**  Amino acid sequence feature denoting the presence (1) or absence (0) of a residue at the given HXB2-referenced site.

**hxb2.410.I.1mer**  Amino acid sequence feature denoting the presence (1) or absence (0) of a residue at the given HXB2-referenced site.

**hxb2.410.K.1mer**  Amino acid sequence feature denoting the presence (1) or absence (0) of a residue at the given HXB2-referenced site.

**hxb2.410.L.1mer**  Amino acid sequence feature denoting the presence (1) or absence (0) of a residue at the given HXB2-referenced site.

**hxb2.410.N.1mer**  Amino acid sequence feature denoting the presence (1) or absence (0) of a residue at the given HXB2-referenced site.

**hxb2.410.P.1mer**  Amino acid sequence feature denoting the presence (1) or absence (0) of a residue at the given HXB2-referenced site.

**hxb2.410.R.1mer**  Amino acid sequence feature denoting the presence (1) or absence (0) of a residue at the given HXB2-referenced site.

**hxb2.410.S.1mer**  Amino acid sequence feature denoting the presence (1) or absence (0) of a residue at the given HXB2-referenced site.

**hxb2.410.T.1mer**  Amino acid sequence feature denoting the presence (1) or absence (0) of a residue at the given HXB2-referenced site.

**hxb2.410.V.1mer**  Amino acid sequence feature denoting the presence (1) or absence (0) of a residue at the given HXB2-referenced site.

**hxb2.410.Y.1mer**  Amino acid sequence feature denoting the presence (1) or absence (0) of a residue at the given HXB2-referenced site.

**hxb2.410.gap.1mer**  Amino acid sequence feature denoting the presence (1) or absence (0) of a residue at the given HXB2-referenced site.

**hxb2.415.E.1mer**  Amino acid sequence feature denoting the presence (1) or absence (0) of a residue at the given HXB2-referenced site.

**hxb2.415.I.1mer**  Amino acid sequence feature denoting the presence (1) or absence (0) of a residue at the given HXB2-referenced site.

**hxb2.415.K.1mer**  Amino acid sequence feature denoting the presence (1) or absence (0) of a residue at the given HXB2-referenced site.

**hxb2.415.L.1mer**  Amino acid sequence feature denoting the presence (1) or absence (0) of a residue at the given HXB2-referenced site.

**hxb2.415.M.1mer**  Amino acid sequence feature denoting the presence (1) or absence (0) of a residue at the given HXB2-referenced site.

**hxb2.415.N.1mer**  Amino acid sequence feature denoting the presence (1) or absence (0) of a residue at the given HXB2-referenced site.
**hxb2.415.R.1mer** Amino acid sequence feature denoting the presence (1) or absence (0) of a residue at the given HXB2-referenced site.

**hxb2.415.T.1mer** Amino acid sequence feature denoting the presence (1) or absence (0) of a residue at the given HXB2-referenced site.

**hxb2.415.V.1mer** Amino acid sequence feature denoting the presence (1) or absence (0) of a residue at the given HXB2-referenced site.

**hxb2.415.X.1mer** Amino acid sequence feature denoting the presence (1) or absence (0) of a residue at the given HXB2-referenced site.

**hxb2.415.Y.1mer** Amino acid sequence feature denoting the presence (1) or absence (0) of a residue at the given HXB2-referenced site.

**hxb2.415.Z.1mer** Amino acid sequence feature denoting the presence (1) or absence (0) of a residue at the given HXB2-referenced site.

**hxb2.425.N.1mer** Amino acid sequence feature denoting the presence (1) or absence (0) of a residue at the given HXB2-referenced site.

**hxb2.425.R.1mer** Amino acid sequence feature denoting the presence (1) or absence (0) of a residue at the given HXB2-referenced site.

**hxb2.426.L.1mer** Amino acid sequence feature denoting the presence (1) or absence (0) of a residue at the given HXB2-referenced site.

**hxb2.426.M.1mer** Amino acid sequence feature denoting the presence (1) or absence (0) of a residue at the given HXB2-referenced site.

**hxb2.426.R.1mer** Amino acid sequence feature denoting the presence (1) or absence (0) of a residue at the given HXB2-referenced site.

**hxb2.426.S.1mer** Amino acid sequence feature denoting the presence (1) or absence (0) of a residue at the given HXB2-referenced site.

**hxb2.426.T.1mer** Amino acid sequence feature denoting the presence (1) or absence (0) of a residue at the given HXB2-referenced site.

**hxb2.428.I.1mer** Amino acid sequence feature denoting the presence (1) or absence (0) of a residue at the given HXB2-referenced site.

**hxb2.428.M.1mer** Amino acid sequence feature denoting the presence (1) or absence (0) of a residue at the given HXB2-referenced site.

**hxb2.428.Q.1mer** Amino acid sequence feature denoting the presence (1) or absence (0) of a residue at the given HXB2-referenced site.

**hxb2.429.A.1mer** Amino acid sequence feature denoting the presence (1) or absence (0) of a residue at the given HXB2-referenced site.

**hxb2.429.E.1mer** Amino acid sequence feature denoting the presence (1) or absence (0) of a residue at the given HXB2-referenced site.

**hxb2.429.G.1mer** Amino acid sequence feature denoting the presence (1) or absence (0) of a residue at the given HXB2-referenced site.

**hxb2.429.K.1mer** Amino acid sequence feature denoting the presence (1) or absence (0) of a residue at the given HXB2-referenced site.

**hxb2.429.Q.1mer** Amino acid sequence feature denoting the presence (1) or absence (0) of a residue at the given HXB2-referenced site.

**hxb2.429.R.1mer** Amino acid sequence feature denoting the presence (1) or absence (0) of a residue at the given HXB2-referenced site.

**hxb2.429.T.1mer** Amino acid sequence feature denoting the presence (1) or absence (0) of a residue at the given HXB2-referenced site.
Amino acid sequence feature denoting the presence (1) or absence (0) of a residue at the given HXB2-referenced site.

- hxb2.430.A.1mer  
- hxb2.430.G.1mer  
- hxb2.430.I.1mer  
- hxb2.430.T.1mer  
- hxb2.430.V.1mer  
- hxb2.431.E.1mer  
- hxb2.431.G.1mer  
- hxb2.432.K.1mer  
- hxb2.432.Q.1mer  
- hxb2.432.R.1mer  
- hxb2.432.S.1mer  
- hxb2.442.A.1mer  
- hxb2.442.E.1mer  
- hxb2.442.H.1mer  
- hxb2.442.I.1mer  
- hxb2.442.K.1mer  
- hxb2.442.L.1mer  
- hxb2.442.N.1mer  
- hxb2.442.P.1mer  
- hxb2.442.Q.1mer  
- hxb2.442.R.1mer
**hb2.442.S.1mer**  Amino acid sequence feature denoting the presence (1) or absence (0) of a residue at the given HXB2-referenced site.

**hb2.442.T.1mer**  Amino acid sequence feature denoting the presence (1) or absence (0) of a residue at the given HXB2-referenced site.

**hb2.442.V.1mer**  Amino acid sequence feature denoting the presence (1) or absence (0) of a residue at the given HXB2-referenced site.

**hb2.448.D.1mer**  Amino acid sequence feature denoting the presence (1) or absence (0) of a residue at the given HXB2-referenced site.

**hb2.448.E.1mer**  Amino acid sequence feature denoting the presence (1) or absence (0) of a residue at the given HXB2-referenced site.

**hb2.448.I.1mer**  Amino acid sequence feature denoting the presence (1) or absence (0) of a residue at the given HXB2-referenced site.

**hb2.448.K.1mer**  Amino acid sequence feature denoting the presence (1) or absence (0) of a residue at the given HXB2-referenced site.

**hb2.448.N.1mer**  Amino acid sequence feature denoting the presence (1) or absence (0) of a residue at the given HXB2-referenced site.

**hb2.448.Q.1mer**  Amino acid sequence feature denoting the presence (1) or absence (0) of a residue at the given HXB2-referenced site.

**hb2.448.S.1mer**  Amino acid sequence feature denoting the presence (1) or absence (0) of a residue at the given HXB2-referenced site.

**hb2.448.T.1mer**  Amino acid sequence feature denoting the presence (1) or absence (0) of a residue at the given HXB2-referenced site.

**hb2.455.E.1mer**  Amino acid sequence feature denoting the presence (1) or absence (0) of a residue at the given HXB2-referenced site.

**hb2.455.I.1mer**  Amino acid sequence feature denoting the presence (1) or absence (0) of a residue at the given HXB2-referenced site.

**hb2.455.L.1mer**  Amino acid sequence feature denoting the presence (1) or absence (0) of a residue at the given HXB2-referenced site.

**hb2.455.Q.1mer**  Amino acid sequence feature denoting the presence (1) or absence (0) of a residue at the given HXB2-referenced site.

**hb2.455.T.1mer**  Amino acid sequence feature denoting the presence (1) or absence (0) of a residue at the given HXB2-referenced site.

**hb2.455.V.1mer**  Amino acid sequence feature denoting the presence (1) or absence (0) of a residue at the given HXB2-referenced site.

**hb2.456.H.1mer**  Amino acid sequence feature denoting the presence (1) or absence (0) of a residue at the given HXB2-referenced site.

**hb2.456.I.1mer**  Amino acid sequence feature denoting the presence (1) or absence (0) of a residue at the given HXB2-referenced site.

**hb2.456.M.1mer**  Amino acid sequence feature denoting the presence (1) or absence (0) of a residue at the given HXB2-referenced site.

**hb2.456.R.1mer**  Amino acid sequence feature denoting the presence (1) or absence (0) of a residue at the given HXB2-referenced site.
**hxb2.456.S.1mer**  Amino acid sequence feature denoting the presence (1) or absence (0) of a residue at the given HXB2-referenced site.

**hxb2.456.W.1mer**  Amino acid sequence feature denoting the presence (1) or absence (0) of a residue at the given HXB2-referenced site.

**hxb2.456.Y.1mer**  Amino acid sequence feature denoting the presence (1) or absence (0) of a residue at the given HXB2-referenced site.

**hxb2.457.D.1mer**  Amino acid sequence feature denoting the presence (1) or absence (0) of a residue at the given HXB2-referenced site.

**hxb2.458.E.1mer**  Amino acid sequence feature denoting the presence (1) or absence (0) of a residue at the given HXB2-referenced site.

**hxb2.458.G.1mer**  Amino acid sequence feature denoting the presence (1) or absence (0) of a residue at the given HXB2-referenced site.

**hxb2.458.Q.1mer**  Amino acid sequence feature denoting the presence (1) or absence (0) of a residue at the given HXB2-referenced site.

**hxb2.458.Y.1mer**  Amino acid sequence feature denoting the presence (1) or absence (0) of a residue at the given HXB2-referenced site.

**hxb2.459.D.1mer**  Amino acid sequence feature denoting the presence (1) or absence (0) of a residue at the given HXB2-referenced site.

**hxb2.459.E.1mer**  Amino acid sequence feature denoting the presence (1) or absence (0) of a residue at the given HXB2-referenced site.

**hxb2.459.G.1mer**  Amino acid sequence feature denoting the presence (1) or absence (0) of a residue at the given HXB2-referenced site.

**hxb2.459.P.1mer**  Amino acid sequence feature denoting the presence (1) or absence (0) of a residue at the given HXB2-referenced site.

**hxb2.459.S.1mer**  Amino acid sequence feature denoting the presence (1) or absence (0) of a residue at the given HXB2-referenced site.

**hxb2.459.gap.1mer**  Amino acid sequence feature denoting the presence (1) or absence (0) of a residue at the given HXB2-referenced site.

**hxb2.460.A.1mer**  Amino acid sequence feature denoting the presence (1) or absence (0) of a residue at the given HXB2-referenced site.

**hxb2.460.D.1mer**  Amino acid sequence feature denoting the presence (1) or absence (0) of a residue at the given HXB2-referenced site.

**hxb2.460.E.1mer**  Amino acid sequence feature denoting the presence (1) or absence (0) of a residue at the given HXB2-referenced site.

**hxb2.460.G.1mer**  Amino acid sequence feature denoting the presence (1) or absence (0) of a residue at the given HXB2-referenced site.

**hxb2.460.I.1mer**  Amino acid sequence feature denoting the presence (1) or absence (0) of a residue at the given HXB2-referenced site.

**hxb2.460.K.1mer**  Amino acid sequence feature denoting the presence (1) or absence (0) of a residue at the given HXB2-referenced site.

**hxb2.460.N.1mer**  Amino acid sequence feature denoting the presence (1) or absence (0) of a residue at the given HXB2-referenced site.
**hxb2.460.P.1mer**  Amino acid sequence feature denoting the presence (1) or absence (0) of a residue at the given HXB2-referenced site.

**hxb2.460.Q.1mer**  Amino acid sequence feature denoting the presence (1) or absence (0) of a residue at the given HXB2-referenced site.

**hxb2.460.R.1mer**  Amino acid sequence feature denoting the presence (1) or absence (0) of a residue at the given HXB2-referenced site.

**hxb2.460.S.1mer**  Amino acid sequence feature denoting the presence (1) or absence (0) of a residue at the given HXB2-referenced site.

**hxb2.460.T.1mer**  Amino acid sequence feature denoting the presence (1) or absence (0) of a residue at the given HXB2-referenced site.

**hxb2.460.V.1mer**  Amino acid sequence feature denoting the presence (1) or absence (0) of a residue at the given HXB2-referenced site.

**hxb2.460.gap.1mer**  Amino acid sequence feature denoting the presence (1) or absence (0) of a residue at the given HXB2-referenced site.

**hxb2.461.A.1mer**  Amino acid sequence feature denoting the presence (1) or absence (0) of a residue at the given HXB2-referenced site.

**hxb2.461.D.1mer**  Amino acid sequence feature denoting the presence (1) or absence (0) of a residue at the given HXB2-referenced site.

**hxb2.461.E.1mer**  Amino acid sequence feature denoting the presence (1) or absence (0) of a residue at the given HXB2-referenced site.

**hxb2.461.G.1mer**  Amino acid sequence feature denoting the presence (1) or absence (0) of a residue at the given HXB2-referenced site.

**hxb2.461.H.1mer**  Amino acid sequence feature denoting the presence (1) or absence (0) of a residue at the given HXB2-referenced site.

**hxb2.461.I.1mer**  Amino acid sequence feature denoting the presence (1) or absence (0) of a residue at the given HXB2-referenced site.

**hxb2.461.K.1mer**  Amino acid sequence feature denoting the presence (1) or absence (0) of a residue at the given HXB2-referenced site.

**hxb2.461.N.1mer**  Amino acid sequence feature denoting the presence (1) or absence (0) of a residue at the given HXB2-referenced site.

**hxb2.461.P.1mer**  Amino acid sequence feature denoting the presence (1) or absence (0) of a residue at the given HXB2-referenced site.

**hxb2.461.Q.1mer**  Amino acid sequence feature denoting the presence (1) or absence (0) of a residue at the given HXB2-referenced site.

**hxb2.461.R.1mer**  Amino acid sequence feature denoting the presence (1) or absence (0) of a residue at the given HXB2-referenced site.

**hxb2.461.S.1mer**  Amino acid sequence feature denoting the presence (1) or absence (0) of a residue at the given HXB2-referenced site.

**hxb2.461.T.1mer**  Amino acid sequence feature denoting the presence (1) or absence (0) of a residue at the given HXB2-referenced site.

**hxb2.461.V.1mer**  Amino acid sequence feature denoting the presence (1) or absence (0) of a residue at the given HXB2-referenced site.
hxb2.461.gap.1mer  Amino acid sequence feature denoting the presence (1) or absence (0) of a residue at the given HXB2-referenced site.

hxb2.462.A.1mer  Amino acid sequence feature denoting the presence (1) or absence (0) of a residue at the given HXB2-referenced site.

hxb2.462.D.1mer  Amino acid sequence feature denoting the presence (1) or absence (0) of a residue at the given HXB2-referenced site.

hxb2.462.E.1mer  Amino acid sequence feature denoting the presence (1) or absence (0) of a residue at the given HXB2-referenced site.

hxb2.462.G.1mer  Amino acid sequence feature denoting the presence (1) or absence (0) of a residue at the given HXB2-referenced site.

hxb2.462.I.1mer  Amino acid sequence feature denoting the presence (1) or absence (0) of a residue at the given HXB2-referenced site.

hxb2.462.K.1mer  Amino acid sequence feature denoting the presence (1) or absence (0) of a residue at the given HXB2-referenced site.

hxb2.462.N.1mer  Amino acid sequence feature denoting the presence (1) or absence (0) of a residue at the given HXB2-referenced site.

hxb2.462.P.1mer  Amino acid sequence feature denoting the presence (1) or absence (0) of a residue at the given HXB2-referenced site.

hxb2.462.Q.1mer  Amino acid sequence feature denoting the presence (1) or absence (0) of a residue at the given HXB2-referenced site.

hxb2.462.R.1mer  Amino acid sequence feature denoting the presence (1) or absence (0) of a residue at the given HXB2-referenced site.

hxb2.462.S.1mer  Amino acid sequence feature denoting the presence (1) or absence (0) of a residue at the given HXB2-referenced site.

hxb2.462.T.1mer  Amino acid sequence feature denoting the presence (1) or absence (0) of a residue at the given HXB2-referenced site.

hxb2.462.X.1mer  Amino acid sequence feature denoting the presence (1) or absence (0) of a residue at the given HXB2-referenced site.

hxb2.462.gap.1mer  Amino acid sequence feature denoting the presence (1) or absence (0) of a residue at the given HXB2-referenced site.

hxb2.463.A.1mer  Amino acid sequence feature denoting the presence (1) or absence (0) of a residue at the given HXB2-referenced site.

hxb2.463.D.1mer  Amino acid sequence feature denoting the presence (1) or absence (0) of a residue at the given HXB2-referenced site.

hxb2.463.E.1mer  Amino acid sequence feature denoting the presence (1) or absence (0) of a residue at the given HXB2-referenced site.

hxb2.463.G.1mer  Amino acid sequence feature denoting the presence (1) or absence (0) of a residue at the given HXB2-referenced site.

hxb2.463.K.1mer  Amino acid sequence feature denoting the presence (1) or absence (0) of a residue at the given HXB2-referenced site.

hxb2.463.M.1mer  Amino acid sequence feature denoting the presence (1) or absence (0) of a residue at the given HXB2-referenced site.
**hxb2.463.N.1mer**  Amino acid sequence feature denoting the presence (1) or absence (0) of a residue at the given HXB2-referenced site.

**hxb2.463.P.1mer**  Amino acid sequence feature denoting the presence (1) or absence (0) of a residue at the given HXB2-referenced site.

**hxb2.463.Q.1mer**  Amino acid sequence feature denoting the presence (1) or absence (0) of a residue at the given HXB2-referenced site.

**hxb2.463.R.1mer**  Amino acid sequence feature denoting the presence (1) or absence (0) of a residue at the given HXB2-referenced site.

**hxb2.463.S.1mer**  Amino acid sequence feature denoting the presence (1) or absence (0) of a residue at the given HXB2-referenced site.

**hxb2.463.T.1mer**  Amino acid sequence feature denoting the presence (1) or absence (0) of a residue at the given HXB2-referenced site.

**hxb2.465.A.1mer**  Amino acid sequence feature denoting the presence (1) or absence (0) of a residue at the given HXB2-referenced site.

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**hxb2.465.E.1mer**  Amino acid sequence feature denoting the presence (1) or absence (0) of a residue at the given HXB2-referenced site.

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**hxb2.476.R.1mer**  Amino acid sequence feature denoting the presence (1) or absence (0) of a residue at the given HXB2-referenced site.
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hxb2.677.S.1mer Amino acid sequence feature denoting the presence (1) or absence (0) of a residue at the given HXB2-referenced site.

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hxb2.407.sequon_actual.1mer  Amino acid sequence feature denoting the presence (1) or absence (0) of a residue at the given HXB2-referenced site.

hxb2.408.sequon_actual.1mer  Amino acid sequence feature denoting the presence (1) or absence (0) of a residue at the given HXB2-referenced site.

hxb2.409.sequon_actual.1mer  Amino acid sequence feature denoting the presence (1) or absence (0) of a residue at the given HXB2-referenced site.

hxb2.410.sequon_actual.1mer  Amino acid sequence feature denoting the presence (1) or absence (0) of a residue at the given HXB2-referenced site.

hxb2.411.sequon_actual.1mer  Amino acid sequence feature denoting the presence (1) or absence (0) of a residue at the given HXB2-referenced site.

hxb2.412.sequon_actual.1mer  Amino acid sequence feature denoting the presence (1) or absence (0) of a residue at the given HXB2-referenced site.

hxb2.413.sequon_actual.1mer  Amino acid sequence feature denoting the presence (1) or absence (0) of a residue at the given HXB2-referenced site.

hxb2.442.sequon_actual.1mer  Amino acid sequence feature denoting the presence (1) or absence (0) of a residue at the given HXB2-referenced site.
sequons.total.env  The total number of sequons in various areas of the HIV viral envelope protein.

sequons.total.gp120  The total number of sequons in various areas of the HIV viral envelope protein.
sequons.total.v5 The total number of sequons in various areas of the HIV viral envelope protein.
sequons.total.loop.d The total number of sequons in various areas of the HIV viral envelope protein.
sequons.total.loop.e The total number of sequons in various areas of the HIV viral envelope protein.
sequons.total.vrc01 The total number of sequons in various areas of the HIV viral envelope protein.
sequons.total.cd4 The total number of sequons in various areas of the HIV viral envelope protein.
sequons.total.sj.fence The total number of sequons in various areas of the HIV viral envelope protein.
sequons.total.sj.trimer The total number of sequons in various areas of the HIV viral envelope protein.
cysteines.total.env The number of cysteines in various areas of the HIV viral envelope protein.
cysteines.total.gp120 The number of cysteines in various areas of the HIV viral envelope protein.
cysteines.total.v5 The number of cysteines in various areas of the HIV viral envelope protein.
cysteines.total.vrc01 The number of cysteines in various areas of the HIV viral envelope protein.
length.env The length of various areas of the HIV viral envelope protein.
length.gp120 The length of various areas of the HIV viral envelope protein.
length.v5 The length of various areas of the HIV viral envelope protein.
length.v5.outliers The length of various areas of the HIV viral envelope protein.
length.loop.e The length of various areas of the HIV viral envelope protein.
length.loop.e.outliers The length of various areas of the HIV viral envelope protein.
taylor.small.total.v5 The steric bulk of residues at critical locations.
taylor.small.total.loop.d The steric bulk of residues at critical locations.
taylor.small.total.cd4 The steric bulk of residues at critical locations.

Source

https://github.com/benkeser/vrc01/blob/master/data/fulldata.csv
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