# Package: vimp (via r-universe)

September 9, 2024

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)

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

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http://bdwilliamson.github.io/vimp/

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

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|          |  |

Average multiple independent importance estimates

#### 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

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)))</pre>
# 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)</pre>
# set up a library for SuperLearner; note simple library for speed
library("SuperLearner")
learners <- c("SL.glm", "SL.mean")</pre>
# get estimates on independent splits of the data
samp <- sample(1:n, n/2, replace = FALSE)</pre>
# using Super Learner (with a small number of folds, for illustration only)
est_2 <- vimp_regression(Y = y[samp], X = x[samp, ], indx = 2, V = 2,</pre>
           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,</pre>
           run_regression = TRUE, alpha = 0.05,
           SL.library = learners, cvControl = list(V = 2))
ests <- average_vim(est_1, est_2, weights = c(1/2, 1/2))</pre>
```

| bootstrap_se | Compute bootstrap-based standard error estimates for variable im- |
|--------------|---|
|              | portance  |

# Description

Compute bootstrap-based standard error estimates for variable importance

### 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<br>(b) Y on X withholding the columns in indx. A vector of the same length as Y;<br>if sample-splitting is desired, then the value of f2 at each position should be the<br>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 boot-<br>strap, 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

```
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

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# 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

### Description

Check inputs to a call to vim, cv\_vim, or sp\_vim

# Usage

check\_inputs(Y, X, f1, f2, indx)

### Arguments

| Υ    | the outcome   |
|------|---|
| Х    | 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)

| Y           | the outcome                                   |
|-------------|---|
| С           | indicator of missing or observed              |
| Z           | the covariates observed in phase 1 and 2 data |
| Х           | all covariates                                |
| ipc_weights | the weights                                   |

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

| CV       | VIM    |  |
|----------|--------|--|
| <u> </u> | V TIII |  |

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,
  f_2 = 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,
```

#### cv\_vim

```
bootstrap = FALSE,
b = 1000,
boot_interval_type = "perc",
clustered = FALSE,
cluster_id = rep(NA, length(Y)),
...
```

#### Arguments

Y X the outcome.

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.

| sample_splittir            | Ig   |
|----------------------------|--|
|                            | should we use sample-splitting to estimate the full and reduced predictiveness?<br>Defaults to TRUE, since inferences made using sample_splitting = FALSE will<br>be invalid for variables with truly zero importance.   |
| final_point_est            |  |
|                            | if sample splitting is used, should the final point estimates be based on only<br>the sample-split folds used for inference ("split", the default), or should they<br>instead be based on the full dataset ("full") or the average across the point<br>estimates from each sample split ("average")? All three options result in valid<br>point estimates – sample-splitting is only required for valid inference. |
| <pre>sample_splittir</pre> | ng_folds   |
|                            | the folds used for sample-splitting; these identify the observations that should be<br>used to evaluate predictiveness based on the full and reduced sets of covariates,<br>respectively. Only used if run_regression = FALSE.   |
| cross_fitting_f            | 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.   |
| 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)  |
| С                          | 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]).   |

| <pre>ipc_est_type</pre>    | 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_estima            |  |
|                            | (only used if type = "average_value") a list of nuisance function estimators<br>on the observed data (may be within a specified fold, for cross-fitted estimates).<br>Specifically: an estimator of the optimal treatment rule; an estimator of the<br>propensity score under the estimated optimal treatment rule; and an estimator of<br>the outcome regression when treatment is assigned according to the estimated<br>optimal rule. |
| nuisance_estima            |  |
|                            | (only used if type = "average_value") a list of nuisance function estimators<br>on the observed data (may be within a specified fold, for cross-fitted estimates).<br>Specifically: an estimator of the optimal treatment rule; an estimator of the<br>propensity score under the estimated optimal treatment rule; and an estimator of<br>the outcome regression when treatment is assigned according to the estimated<br>optimal rule. |
| exposure_name              | (only used if type = "average_value") the name of the exposure of interest;<br>binary, with 1 indicating presence of the exposure and 0 indicating absence of<br>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.   |
| <pre>boot_interval_t</pre> | уре  |
|                            | 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 boot-<br>strap, 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 crossfitting 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:

**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

#### cv\_vim

- 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 class vim. See Details for more information.

#### See Also

SuperLearner for specific usage of the SuperLearner function and package.

#### Examples

```
n <- 100
p <- 2
# generate the data
x <- data.frame(replicate(p, stats::runif(n, -5, 5)))</pre>
# apply the function to the x's
smooth <- (x[,1]/5)^2*(x[,1]+7)/5 + (x[,2]/3)^2</pre>
# generate Y ~ Normal (smooth, 1)
y <- as.matrix(smooth + stats::rnorm(n, 0, 1))</pre>
# set up a library for SuperLearner; note simple library for speed
library("SuperLearner")
learners <- c("SL.glm")</pre>
# ------
# 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,
```

#### estimate

```
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(</pre>
Y = Y, X = x, SL.library = learners, cvControl = list(V = 2 * V),
innerCvControl = list(list(V = V))
))
full_cv_preds <- full_cv_fit$SL.predict</pre>
# use the same cross-fitting folds for reduced
reduced_cv_fit <- suppressWarnings(SuperLearner::CV.SuperLearner(</pre>
   Y = Y, X = x[, -indx, drop = FALSE], SL.library = learners,
   cvControl = SuperLearner::SuperLearner.CV.control(
       V = 2 * V, validRows = full_cv_fit$folds
   ),
    innerCvControl = list(list(V = V))
))
reduced_cv_preds <- reduced_cv_fit$SL.predict</pre>
# for hypothesis testing
cross_fitting_folds <- get_cv_sl_folds(full_cv_fit$folds)</pre>
set.seed(1234)
sample_splitting_folds <- make_folds(unique(cross_fitting_folds), V = 2)</pre>
set.seed(5678)
est <- cv_vim(Y = y, cross_fitted_f1 = full_cv_preds,</pre>
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

estimate(x, ...)

#### Arguments

| Х | An R object. Currently, there are methods for predictiveness_measure objects only. |
|---|--|
|   | jects 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

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

### Arguments

| Х | 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

```
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  |
|--------------------------|---|
| С                        | 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.  |
| <pre>ipc_fit_type</pre>  | if "external", then use ipc_eif_preds; if "SL", fit a SuperLearner to determine the IPC correction to the efficient influence function.                   |
| <pre>ipc_eif_preds</pre> | if ipc_fit_type = "external", the fitted values from a regression of the full-<br>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\_nuisances Estimate nuisance functions for average value-based VIMs

# Description

Estimate nuisance functions for average value-based VIMs

# Usage

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

| fit | the fitted nuisance function estimator                                       |
|-----|--|
| Х   | 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.  |  |
| <pre>sample_splittin</pre> | lg   |  |
|                            | 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. |  |
| 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".  |  |

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)

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

est\_predictiveness Estimate a nonparametric predictiveness functional

# Description

Compute nonparametric estimates of the chosen measure of predictiveness.

# Usage

```
est_predictiveness(
  fitted_values,
  у,
  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,
  . . .
)
```

| fitted_values           | fitted values from a regression function using the observed data.   |
|-------------------------|---|
| У                       | the observed outcome.   |
| а                       | the observed treatment assignment (may be within a specified fold, for cross-<br>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)?  |
| С                       | 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-<br>phase sample) weighted estimation. Assumed to be already inverted (i.e., ipc_weights<br>= 1 / [estimated probability weights]). |
| <pre>ipc_fit_type</pre> | if "external", then use ipc_eif_preds; if "SL", fit a SuperLearner to determine the correction to the efficient influence function.   |

| <pre>ipc_eif_preds</pre> | if ipc_fit_type = "external", the fitted values from a regression of the full-<br>data EIF on the fully observed covariates/outcome; otherwise, not used.  |
|--------------------------|--|
| <pre>ipc_est_type</pre>  | 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<br>on (e.g., "identity"; or "logit" to logit-transform, apply the correction, and back-<br>transform).   |
| na.rm                    | logical; should NA's be removed in computation? (defaults to FALSE)  |
| nuisance_estim           | ators  |
|                          | (only used if type = "average_value") a list of nuisance function estimators<br>on the observed data (may be within a specified fold, for cross-fitted estimates).<br>Specifically: an estimator of the optimal treatment rule; an estimator of the<br>propensity score under the estimated optimal treatment rule; and an estimator of<br>the outcome regression when treatment is assigned according to the estimated<br>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.

est\_predictiveness\_cv Estimate a nonparametric predictiveness functional using cross-fitting

# Description

Compute nonparametric estimates of the chosen measure of predictiveness.

# 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

| hts |
|-----|
|     |
|     |
|     |
|     |
|     |
|     |
| 30  |

# 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).

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 crossfitted 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

```
extract_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 speci-   |  |
|---------------------|---|--|
|                     | fied.   |  |
| sample_splittir     | Ig  |  |
|                     | logical; should we use sample-splitting or not? Defaults to TRUE.   |  |
| sample_splittir     | ng_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.

# Description

Nicely formats the output from a predictiveness\_measure object for printing.

# Usage

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

# Arguments

| х | the predictiveness_measure object of interest.  |
|---|---|
|   | other options, see the generic format function. |

|--|

# Description

Nicely formats the output from a vim object for printing.

# Usage

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

| х | 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

# Description

Create Folds for Cross-Fitting

# Usage

make\_folds(y, V = 2, stratified = FALSE, C = NULL, probs = rep(1/V, V))

# Arguments

| У          | the outcome   |
|------------|---|
| V          | the number of folds   |
| stratified | should the folds be stratified based on the outcome?  |
| С          | 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

### Description

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

### Usage

```
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

```
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)),
```

```
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<br>a specified fold, for cross-fitted estimates).   |  |
|--------------------------|---|--|
| У                        | the observed outcome (may be within a specified fold, for cross-fitted estimates).  |  |
| full_y                   | the observed outcome (not used, defaults to NULL).  |  |
| С                        | 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]). |  |
| <pre>ipc_fit_type</pre>  | if "external", then use ipc_eif_preds; if "SL", fit a SuperLearner to determine the IPC correction to the efficient influence function.   |  |
| <pre>ipc_eif_preds</pre> | if ipc_fit_type = "external", the fitted values from a regression of the full-<br>data EIF on the fully observed covariates/outcome; otherwise, not used.   |  |
| <pre>ipc_est_type</pre>  | 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<br>on (e.g., "identity"; or "logit" to logit-transform, apply the correction, and back-<br>transform).                            |  |
| na.rm                    | logical; should NAs be removed in computation? (defaults to FALSE)  |  |
| nuisance_estimators      |   |  |
|                          | not used; for compatibility with measure_average_value.   |  |
| а                        | 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

# Description

Estimate ANOVA decomposition-based variable importance.

# Usage

```
measure_anova(
  full,
  reduced,
  у,
  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,
  . . .
)
```

| 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.  |
| У                        | the observed outcome (may be within a specified fold, for cross-fitted estimates).  |
| full_y                   | the observed outcome (not used, defaults to NULL).  |
| С                        | 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]). |
| <pre>ipc_fit_type</pre>  | if "external", then use ipc_eif_preds; if "SL", fit a SuperLearner to determine the IPC correction to the efficient influence function.   |
| <pre>ipc_eif_preds</pre> | if ipc_fit_type = "external", the fitted values from a regression of the full-<br>data EIF on the fully observed covariates/outcome; otherwise, not used.   |

| <pre>ipc_est_type</pre> | 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<br>on (e.g., "identity"; or "logit" to logit-transform, apply the correction, and back-<br>transform). |
| na.rm                   | logical; should NAs be removed in computation? (defaults to FALSE)   |
| nuisance_estima         | tors   |
|                         | not used; for compatibility with measure_average_value.  |
| а                       | not used; for compatibility with measure_average_value.  |
|                         | other arguments to SuperLearner, if ipc_fit_type = "SL".   |

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,
 у,
  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).  |  |
|--------------------------|---|--|
| У                        | the observed outcome (may be within a specified fold, for cross-fitted estimates).  |  |
| full_y                   | the observed outcome (not used, defaults to NULL).  |  |
| С                        | 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]). |  |
| <pre>ipc_fit_type</pre>  | if "external", then use ipc_eif_preds; if "SL", fit a SuperLearner to determine the IPC correction to the efficient influence function.   |  |
| <pre>ipc_eif_preds</pre> | if ipc_fit_type = "external", the fitted values from a regression of the full-<br>data EIF on the fully observed covariates/outcome; otherwise, not used.   |  |
| <pre>ipc_est_type</pre>  | 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<br>on (e.g., "identity"; or "logit" to logit-transform, apply the correction, and back-<br>transform).                            |  |
| na.rm                    | logical; should NAs be removed in computation? (defaults to FALSE)  |  |
| nuisance_estimators      |   |  |
|                          | not used; for compatibility with measure_average_value.   |  |
| а                        | 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

```
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 spec-<br>ified fold, for cross-fitted estimates). Specifically: an estimator of the optimal<br>treatment rule; an estimator of the propensity score under the estimated optimal<br>treatment rule; and an estimator of the outcome regression when treatment is<br>assigned according to the estimated optimal rule. |
|--------------------------|---|
| У                        | the observed outcome (may be within a specified fold, for cross-fitted estimates).  |
| а                        | the observed treatment assignment (may be within a specified fold, for cross-fitted estimates).   |
| full_y                   | the observed outcome (not used, defaults to NULL).  |
| С                        | 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]).   |
| <pre>ipc_fit_type</pre>  | if "external", then use ipc_eif_preds; if "SL", fit a SuperLearner to determine<br>the IPC correction to the efficient influence function.  |
| <pre>ipc_eif_preds</pre> | if ipc_fit_type = "external", the fitted values from a regression of the full-<br>data EIF on the fully observed covariates/outcome; otherwise, not used.   |
| <pre>ipc_est_type</pre>  | 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<br>on (e.g., "identity"; or "logit" to logit-transform, apply the correction, and back-<br>transform).  |
| na.rm                    | logical; should NAs be removed in computation? (defaults to FALSE)  |
|                          | other arguments to SuperLearner, if ipc_fit_type = "SL".  |

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

```
measure_cross_entropy(
  fitted_values,
 у,
  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,
  . . .
)
```

| fitted_values           | fitted values from a regression function using the observed data (may be within a specified fold, for cross-fitted estimates).  |
|-------------------------|---|
| У                       | the observed outcome (may be within a specified fold, for cross-fitted estimates).  |
| full_y                  | the observed outcome (not used, defaults to NULL).  |
| С                       | 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]). |
| <pre>ipc_fit_type</pre> | if "external", then use ipc_eif_preds; if "SL", fit a SuperLearner to determine the IPC correction to the efficient influence function.   |

| <pre>ipc_eif_preds</pre> | if ipc_fit_type = "external", the fitted values from a regression of the full-<br>data EIF on the fully observed covariates/outcome; otherwise, not used.                                |  |
|--------------------------|--|--|
| <pre>ipc_est_type</pre>  | 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<br>on (e.g., "identity"; or "logit" to logit-transform, apply the correction, and back-<br>transform). |  |
| na.rm                    | logical; should NAs be removed in computation? (defaults to FALSE)   |  |
| nuisance_estimators      |  |  |
|                          | not used; for compatibility with measure_average_value.  |  |
| а                        | not used; for compatibility with measure_average_value.  |  |
|                          | other arguments to SuperLearner, if ipc_fit_type = "SL".   |  |
|                          |  |  |

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.

| timate the deviance | asure_deviance |
|---------------------|----------------|
|---------------------|----------------|

# Description

Compute nonparametric estimate of deviance.

# Usage

```
measure_deviance(
  fitted_values,
 у,
  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\_mse

# Arguments

| fitted_values            | fitted values from a regression function using the observed data (may be within a specified fold, for cross-fitted estimates).  |  |  |
|--------------------------|---|--|--|
| У                        | the observed outcome (may be within a specified fold, for cross-fitted estimates).  |  |  |
| full_y                   | the observed outcome (not used, defaults to NULL).  |  |  |
| С                        | 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]). |  |  |
| <pre>ipc_fit_type</pre>  | if "external", then use ipc_eif_preds; if "SL", fit a SuperLearner to determine the IPC correction to the efficient influence function.   |  |  |
| <pre>ipc_eif_preds</pre> | if ipc_fit_type = "external", the fitted values from a regression of the full-<br>data EIF on the fully observed covariates/outcome; otherwise, not used.   |  |  |
| <pre>ipc_est_type</pre>  | 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<br>on (e.g., "identity"; or "logit" to logit-transform, apply the correction, and back-<br>transform).                            |  |  |
| na.rm                    | logical; should NAs be removed in computation? (defaults to FALSE)  |  |  |
| nuisance_estimators      |   |  |  |
|                          | not used; for compatibility with measure_average_value.   |  |  |
| а                        | 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,
 у,
 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<br>a specified fold, for cross-fitted estimates).   |
|-------------------------|---|
| У                       | the observed outcome (may be within a specified fold, for cross-fitted estimates).  |
| full_y                  | the observed outcome (not used, defaults to NULL).  |
| С                       | 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]). |
| <pre>ipc_fit_type</pre> | 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-<br>data EIF on the fully observed covariates/outcome; otherwise, not used.   |
| <pre>ipc_est_type</pre> | 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<br>on (e.g., "identity"; or "logit" to logit-transform, apply the correction, and back-<br>transform).                            |
| na.rm                   | logical; should NAs be removed in computation? (defaults to FALSE)  |
| nuisance_estima         | ators   |
|                         | not used; for compatibility with measure_average_value.   |
| а                       | not used; for compatibility with measure_average_value.   |
|                         | other arguments to SuperLearner, if ipc_fit_type = "SL".  |
|                         |   |

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

```
measure_r_squared(
  fitted_values,
 у,
  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,
  . . .
)
```

| fitted_values           | fitted values from a regression function using the observed data (may be within a specified fold, for cross-fitted estimates).  |
|-------------------------|---|
| У                       | the observed outcome (may be within a specified fold, for cross-fitted estimates).  |
| full_y                  | the observed outcome (not used, defaults to NULL).  |
| С                       | 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., $ipc\_weights = 1 / [estimated probability weights])$ . |
| <pre>ipc_fit_type</pre> | if "external", then use ipc_eif_preds; if "SL", fit a SuperLearner to determine the IPC correction to the efficient influence function.   |

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

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

- 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

```
# generate the data
# generate X
p <- 2
n <- 100
x <- data.frame(replicate(p, stats::runif(n, -5, 5)))</pre>
# apply the function to the x's
smooth <- (x[,1]/5)^2*(x[,1]+7)/5 + (x[,2]/3)^2</pre>
# generate Y ~ Normal (smooth, 1)
y <- smooth + stats::rnorm(n, 0, 1)</pre>
# set up a library for SuperLearner; note simple library for speed
library("SuperLearner")
learners <- c("SL.glm", "SL.mean")</pre>
# 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,</pre>
           run_regression = TRUE, alpha = 0.05,
           SL.library = learners, cvControl = list(V = 2))
ests <- merge_vim(est_1, est_2)</pre>
```

predictiveness\_measure

Construct a Predictiveness Measure

#### Description

Construct a 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")  |  |
|---------------------|---|--|
| У                   | the outcome of interest   |  |
| а                   | 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_f     | olds  |  |
|                     | 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 $(q_n)$ . |  |
| С                   | 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.   |  |

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| 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]). |
|-------------------------|---|
| <pre>ipc_fit_type</pre> | 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-<br>data EIF on the fully observed covariates/outcome; otherwise, not used.   |
| <pre>ipc_est_type</pre> | 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<br>on (e.g., "identity"; or "logit" to logit-transform, apply the correction, and back-<br>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:

# 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 | $the \ {\tt predictiveness\_measure} \ object \ of \ interest.$ |
|---|---|
|   | other options, see the generic print function.                  |

print.vim

# Description

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

## Usage

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

# Arguments

| х | the vim object of interest.                    |
|---|--|
|   | other options, see the generic print function. |

| process_arg_lst | Process argument list for Super Learner estimation of the EIF |
|-----------------|---|
|                 |   |

# Description

Process argument list for Super Learner estimation of the EIF

#### Usage

```
process_arg_lst(arg_lst)
```

## Arguments

arg\_lst the list of arguments for Super Learner

# Value

a list of modified arguments for EIF estimation

run\_sl

# Description

Run a Super Learner for the provided subset of features

# Usage

```
run_sl(
 Y = NULL,
 X = NULL,
 V = 5,
 SL.library = "SL.glm",
  univariate_SL.library = NULL,
  s = 1,
  cv_folds = NULL,
  sample_splitting = TRUE,
  ss_folds = NULL,
  split = 1,
  verbose = FALSE,
 progress_bar = NULL,
  indx = 1,
 weights = rep(1, nrow(X)),
  cross_fitted_se = TRUE,
  full = NULL,
  vector = TRUE,
  . . .
)
```

# Arguments

| Y                     | the outcome   |  |
|-----------------------|---|--|
| Х                     | 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 |  |

| verbose         | should we print progress? defaults to FALSE  |
|-----------------|--|
| progress_bar    | the progress bar to print to (only if verbose = TRUE)  |
| indx            | 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

sample\_subsets Create necessary objects for SPVIMs

#### Description

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

## Usage

sample\_subsets(p, gamma, n)

## Arguments

| р     | the number of covariates  |
|-------|---|
| gamma | the fraction of the sample size to sample (e.g., gamma = 1 means sample n sub-<br>sets) |
| n     | the sample size   |

## 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)

```
p <- 10
gamma <- 1
n <- 100
set.seed(100)
subset_lst <- sample_subsets(p, gamma, n)</pre>
```

scale\_est

## Description

Return an estimator on a different scale

## Usage

```
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

```
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_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  |
| ics      | a list of influence function values for each predictiveness measure                    |
| 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; contrib\_v is the contribution from estimating V, while contrib\_s is the contribution from sampling subsets.

| SDV1M_ | se |
|--------|----|

Standard error estimate for SPVIM values

#### Description

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

#### Usage

```
spvim_se(ics, idx = 1, gamma = 1, na_rm = FALSE)
```

## Arguments

| ics   | the influence function estimates based on the contributions from sampling ob-<br>servations and sampling subsets: a list of length two resulting from a call to<br>spvim_ics. |
|-------|---|
| idx   | the index of interest   |
| gamma | the proportion of the sample size used when sampling subsets  |
| na_rm | remove NAs?   |

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### sp\_vim

## 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.

| sp_vim | Shapley Population Variable Importance Measure (SPVIM) Estimates |
|--------|--|
|        | and Inference  |

#### Description

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

#### Usage

)

```
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.   |
|-----------------|--|
| Х               | 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 $\delta$ -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)  |
| 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_splittin | ng   |
|                 | should we use sample-splitting to estimate the full and reduced predictiveness?<br>Defaults to TRUE, since inferences made using sample_splitting = FALSE will<br>be invalid for variables with truly zero importance.   |
| final_point_es  | timate   |
|                 | if sample splitting is used, should the final point estimates be based on only<br>the sample-split folds used for inference ("split", the default), or should they<br>instead be based on the full dataset ("full") or the average across the point<br>estimates from each sample split ("average")? All three options result in valid<br>point estimates – sample-splitting is only required for valid inference. |
| С               | 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 / [estimated probability weights]).          |  |
|-------------------------|---|--|
| <pre>ipc_est_type</pre> | 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)?   |  |
|                         | other arguments to the estimation tool, see "See also".   |  |

## 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 contibutions 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 vim. See Details for more information.

### See Also

SuperLearner for specific usage of the SuperLearner function and package.

```
n <- 100
p <- 2
# generate the data
x <- data.frame(replicate(p, stats::runif(n, -5, 5)))</pre>
# apply the function to the x's
smooth <- (x[,1]/5)^2*(x[,1]+7)/5 + (x[,2]/3)^2</pre>
# generate Y ~ Normal (smooth, 1)
y <- as.matrix(smooth + stats::rnorm(n, 0, 1))</pre>
# set up a library for SuperLearner; note simple library for speed
library("SuperLearner")
learners <- c("SL.glm")</pre>
# ------
# 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)
```

#### Description

vim

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

```
vim(
  Y = NULL,
  X = NULL,
  f1 = NULL,
  f_2 = 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.

vim

| Х               | 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<br>(b) Y on X withholding the columns in indx. A vector of the same length as Y;<br>if sample-splitting is desired, then the value of f2 at each position should be the<br>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? (de-faults to FALSE)   |
| sample_splittir |  |
|                 | should we use sample-splitting to estimate the full and reduced predictiveness?<br>Defaults to TRUE, since inferences made using sample_splitting = FALSE will<br>be invalid for variables with truly zero importance.   |
| sample_splittir |  |
|                 | the folds used for sample-splitting; these identify the observations that should be<br>used to evaluate predictiveness based on the full and reduced sets of covariates,<br>respectively. Only used if run_regression = FALSE.   |
| final_point_est | timate   |
|                 | if sample splitting is used, should the final point estimates be based on only<br>the sample-split folds used for inference ("split", the default), or should they<br>instead be based on the full dataset ("full") or the average across the point<br>estimates from each sample split ("average")? All three options result in valid<br>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)   |
| С               | 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]).   |  |
| <pre>ipc_est_type</pre> | 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_estima         | ators_full   |  |
|                         | (only used if type = "average_value") a list of nuisance function estimators<br>on the observed data (may be within a specified fold, for cross-fitted estimates).<br>Specifically: an estimator of the optimal treatment rule; an estimator of the<br>propensity score under the estimated optimal treatment rule; and an estimator of<br>the outcome regression when treatment is assigned according to the estimated<br>optimal rule. |  |
| nuisance_estima         | ators reduced  |  |
|                         | (only used if type = "average_value") a list of nuisance function estimators<br>on the observed data (may be within a specified fold, for cross-fitted estimates).<br>Specifically: an estimator of the optimal treatment rule; an estimator of the<br>propensity score under the estimated optimal treatment rule; and an estimator of<br>the outcome regression when treatment is assigned according to the estimated<br>optimal rule. |  |
| exposure_name           | (only used if type = "average_value") the name of the exposure of interest;<br>binary, with 1 indicating presence of the exposure and 0 indicating absence of<br>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 boot-<br>strap, 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.

vim

## See Also

SuperLearner for specific usage of the SuperLearner function and package.

```
# generate the data
# generate X
p <- 2
n <- 100
x <- data.frame(replicate(p, stats::runif(n, -1, 1)))</pre>
# apply the function to the x's
f \le function(x) 0.5 + 0.3 \times x[1] + 0.2 \times x[2]
smooth <- apply(x, 1, function(z) f(z))
# generate Y ~ Bernoulli (smooth)
y <- matrix(rbinom(n, size = 1, prob = smooth))</pre>
# set up a library for SuperLearner; note simple library for speed
library("SuperLearner")
learners <- c("SL.glm")</pre>
# using Y and X; use class-balanced folds
est_1 <- vim(y, x, indx = 2, type = "accuracy",</pre>
           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,</pre>
                                            SL.library = learners,
                                            cvControl = list(V = 2),
                                            innerCvControl = list(list(V = V)))
full_fitted <- SuperLearner::predict.SuperLearner(full_fit)$pred</pre>
# fit the data with only X1
reduced_fit <- SuperLearner::CV.SuperLearner(Y = full_fitted,</pre>
                                               X = x[, -2, drop = FALSE],
                                               SL.library = learners,
                                       cvControl = list(V = 2, validRows = full_fit$folds),
                                                innerCvControl = list(list(V = V)))
reduced_fitted <- SuperLearner::predict.SuperLearner(reduced_fit)$pred</pre>
est_2 <- vim(Y = y, f1 = full_fitted, f2 = reduced_fitted,</pre>
            indx = 2, run_regression = FALSE, alpha = 0.05,
            stratified = TRUE, type = "accuracy",
            sample_splitting_folds = get_cv_sl_folds(full_fit$folds))
```

vimp\_accuracy

## Description

Compute estimates of and confidence intervals for nonparametric difference in classification accuracybased 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,
  f_2 = 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

| Υ               | the outcome.  |
|-----------------|---|
| Х               | 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 re-  |

gressing 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<br>fold; or (b) a list of length V, where each element in the list is a set of predic-<br>tions on the corresponding validation data fold. If sample-splitting is requested,<br>then these must be estimated specially; see Details. However, the resulting vec-<br>tor should be the same length as Y; if using a list, then the summed length of each<br>element across the list should be the same length as Y (i.e., each observation is<br>included in the predictions).   |
|-----------------|--|
| cross_fitted_f2 |  |
|                 | the predicted values on validation data from a flexible estimation technique re-<br>gressing either (a) the fitted values in cross_fitted_f1, or (b) Y, on X with-<br>holding the columns in indx. Provided as either (a) a vector, where each element<br>is the predicted value when that observation is part of the validation fold; or (b)<br>a list of length V, where each element in the list is a set of predictions on the<br>corresponding validation data fold. If sample-splitting is requested, then these<br>must be estimated specially; see Details. However, the resulting vector should<br>be the same length as Y; if using a list, then the summed length of each element<br>across the list should be the same length as Y (i.e., each observation is included<br>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<br>(b) Y on X withholding the columns in indx. If sample-splitting is requested,<br>then these must be estimated specially; see Details. If cross_fitted_se =<br>TRUE, then this argument is not used.  |
| indx            | the indices of the covariate(s) to calculate variable importance for; defaults to 1.   |
| ٧               | 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<br>is TRUE, then Super Learner will be used; otherwise, variable importance will be<br>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_est |  |
|                 | if sample splitting is used, should the final point estimates be based on only<br>the sample-split folds used for inference ("split", the default), or should they<br>instead be based on the full dataset ("full") or the average across the point<br>estimates from each sample split ("supress")? All three estimates result is uslid   |

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_splittin     | g_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)  |  |
| С                   | 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 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:

**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\_accuracy. See Details for more information.

### See Also

SuperLearner for specific usage of the SuperLearner function and package.

```
# generate the data
# generate X
p <- 2
n <- 100
x <- data.frame(replicate(p, stats::runif(n, -1, 1)))</pre>
# apply the function to the x's
f \le function(x) 0.5 + 0.3 \times x[1] + 0.2 \times x[2]
smooth <- apply(x, 1, function(z) f(z))</pre>
# generate Y ~ Normal (smooth, 1)
y <- matrix(rbinom(n, size = 1, prob = smooth))</pre>
# set up a library for SuperLearner; note simple library for speed
library("SuperLearner")
learners <- c("SL.glm", "SL.mean")</pre>
# estimate (with a small number of folds, for illustration only)
est <- vimp_accuracy(y, x, indx = 2,</pre>
            alpha = 0.05, run_regression = TRUE,
            SL.library = learners, V = 2, cvControl = list(V = 2))
```

vimp\_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 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

| Υ              | the outcome.   |
|----------------|--|
| Х              | the covariates. If type = "average_value", then the exposure variable should be part of X, with its name provided in exposure_name.                                      |
| cross_fitted_f | 1  |
|                | the predicted values on validation data from a flexible estimation technique re-<br>grassing $X$ on $X$ in the training data. Provided as either (a) a vector where each |
|                | gressing 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 predic-<br>tions on the corresponding validation data fold. If sample-splitting is requested,<br>then these must be estimated specially; see Details. However, the resulting vec-<br>tor should be the same length as Y; if using a list, then the summed length of each<br>element across the list should be the same length as Y (i.e., each observation is<br>included in the predictions).   |
|-----------------|--|
| cross_fitted_f2 |  |
|                 | the predicted values on validation data from a flexible estimation technique re-<br>gressing either (a) the fitted values in cross_fitted_f1, or (b) Y, on X with-<br>holding the columns in indx. Provided as either (a) a vector, where each element<br>is the predicted value when that observation is part of the validation fold; or (b)<br>a list of length V, where each element in the list is a set of predictions on the<br>corresponding validation data fold. If sample-splitting is requested, then these<br>must be estimated specially; see Details. However, the resulting vector should<br>be the same length as Y; if using a list, then the summed length of each element<br>across the list should be the same length as Y (i.e., each observation is included<br>in the predictions). |
| indx            | the indices of the covariate(s) to calculate variable importance for; defaults to 1.   |
| ٧               | 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<br>is TRUE, then Super Learner will be used; otherwise, variable importance will be<br>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_f |  |
|                 | 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)   |
| С               | 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")   |  |
|-------------------------|---|--|
| <pre>ipc_est_type</pre> | 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

$$\psi_{0,s} := E_0 \{ f_0(X) - f_{0,s}(X) \}^2 / var_0(Y),$$

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  $var_0$  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

$$\psi_{n,s} := K^{(-1)} \sum_{k=1}^{K} E_{n,k} \{ f_{n,k}(X) - f_{n,k,s}(X) \}^2 / var_n(Y),$$

where  $var_n$  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\_anova. See Details for more information.

#### See Also

SuperLearner for specific usage of the SuperLearner function and package.

```
# 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</pre>
```

vimp\_auc

Nonparametric Intrinsic Variable Importance Estimates: AUC

### Description

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

#### Usage

```
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,
```

```
cross_fitted_se = TRUE,
...
```

# Arguments

| rguments        |  |
|-----------------|--|
| Y               | the outcome.   |
| Х               | 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 re-<br>gressing Y on X in the training data. Provided as either (a) a vector, where each<br>element is the predicted value when that observation is part of the validation<br>fold; or (b) a list of length V, where each element in the list is a set of predic-<br>tions on the corresponding validation data fold. If sample-splitting is requested,<br>then these must be estimated specially; see Details. However, the resulting vec-<br>tor should be the same length as Y; if using a list, then the summed length of each<br>element across the list should be the same length as Y (i.e., each observation is<br>included in the predictions).  |
| cross_fitted_f2 |  |
|                 | the predicted values on validation data from a flexible estimation technique re-<br>gressing either (a) the fitted values in cross_fitted_f1, or (b) Y, on X with-<br>holding the columns in indx. Provided as either (a) a vector, where each element<br>is the predicted value when that observation is part of the validation fold; or (b)<br>a list of length V, where each element in the list is a set of predictions on the<br>corresponding validation data fold. If sample-splitting is requested, then these<br>must be estimated specially; see Details. However, the resulting vector should<br>be the same length as Y; if using a list, then the summed length of each element<br>across the list should be the same length as Y (i.e., each observation is included<br>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<br>(b) Y on X withholding the columns in indx. If sample-splitting is requested,<br>then these must be estimated specially; see Details. If cross_fitted_se =<br>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<br>is TRUE, then Super Learner will be used; otherwise, variable importance will be<br>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_est         | imate  |  |
|                         | if sample splitting is used, should the final point estimates be based on only<br>the sample-split folds used for inference ("split", the default), or should they<br>instead be based on the full dataset ("full") or the average across the point<br>estimates from each sample split ("average")? All three options result in valid<br>point estimates – sample-splitting is only required for valid inference. |  |
| cross_fitting_f         | olds   |  |
| sample_splittin         | the folds for cross-fitting. Only used if run_regression = FALSE.  |  |
| Sampre_Sprictin         | 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)   |  |
| С                       | 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")  |  |
| <pre>ipc_est_type</pre> | 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 crossfitting 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:

**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\_auc. See Details for more information.

#### See Also

SuperLearner for specific usage of the SuperLearner function and package, and performance for specific usage of the ROCR package.

```
# 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")</pre>
```

vimp\_ci

## Confidence intervals for variable importance

## Description

Compute confidence intervals for the true variable importance parameter.

# Usage

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.

vimp\_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.   |
|-----------------|--|
| Х               | 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 predic- |
| tions on the corresponding validation data fold. If sample-splitting is requested,  |
| then these must be estimated specially; see Details. However, the resulting vec-    |
| tor 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 De-tails. 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_splittin         | lg_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)  |  |
| С                       | 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")   |  |
| <pre>ipc_est_type</pre> | 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 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:

**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.

```
# generate the data
# generate X
p <- 2
n <- 100
x <- data.frame(replicate(p, stats::runif(n, -1, 1)))</pre>
# apply the function to the x's
f \le function(x) 0.5 + 0.3 \times x[1] + 0.2 \times x[2]
smooth <- apply(x, 1, function(z) f(z))</pre>
# generate Y ~ Normal (smooth, 1)
y <- matrix(stats::rbinom(n, size = 1, prob = smooth))</pre>
# set up a library for SuperLearner; note simple library for speed
library("SuperLearner")
learners <- c("SL.glm", "SL.mean")</pre>
# estimate (with a small number of folds, for illustration only)
est <- vimp_deviance(y, x, indx = 2,</pre>
            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 inter-                    |  |
|                        | est.   |  |
| 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 $\langle \delta \rangle$ ; 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

### 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

Х

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 re-<br>gressing either (a) the fitted values in cross_fitted_f1, or (b) Y, on X with-<br>holding the columns in indx. Provided as either (a) a vector, where each element<br>is the predicted value when that observation is part of the validation fold; or (b)<br>a list of length V, where each element in the list is a set of predictions on the<br>corresponding validation data fold. If sample-splitting is requested, then these<br>must be estimated specially; see Details. However, the resulting vector should<br>be the same length as Y; if using a list, then the summed length of each element<br>across the list should be the same length as Y (i.e., each observation is included<br>in the predictions). |
|-----------------|--|
| indx            | the indices of the covariate(s) to calculate variable importance for; defaults to 1.   |
| ٧               | 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? (de-faults to FALSE)   |
| cross_fitting_f |  |
|                 | 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)   |
| С               | 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 ANOVA parameter for the group of features (or single feature) s by

 $\psi_{0,s} := E_0 \{ f_0(X) - f_{0,s}(X) \}^2 / var_0(Y),$ 

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  $var_0$  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

$$\psi_{n,s} := K^{(-1)} \sum_{k=1}^{K} E_{n,k} \{ f_{n,k}(X) - f_{n,k,s}(X) \}^2 / var_n(Y),$$

where  $var_n$  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

```
# 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)</pre>
```

vimp\_rsquared

Nonparametric Intrinsic Variable Importance Estimates: R-squared

### 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

```
vimp_rsquared(
 Y = NULL,
 X = NULL,
 cross_fitted_f1 = NULL,
  cross_fitted_f2 = NULL,
  f1 = NULL,
  f_2 = 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

| Arguments       |  |
|-----------------|--|
| Y               | the outcome.   |
| Х               | 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 re-<br>gressing Y on X in the training data. Provided as either (a) a vector, where each<br>element is the predicted value when that observation is part of the validation<br>fold; or (b) a list of length V, where each element in the list is a set of predic-<br>tions on the corresponding validation data fold. If sample-splitting is requested,<br>then these must be estimated specially; see Details. However, the resulting vec-<br>tor should be the same length as Y; if using a list, then the summed length of each<br>element across the list should be the same length as Y (i.e., each observation is<br>included in the predictions).  |
| cross_fitted_f2 |  |
|                 | the predicted values on validation data from a flexible estimation technique re-<br>gressing either (a) the fitted values in cross_fitted_f1, or (b) Y, on X with-<br>holding the columns in indx. Provided as either (a) a vector, where each element<br>is the predicted value when that observation is part of the validation fold; or (b)<br>a list of length V, where each element in the list is a set of predictions on the<br>corresponding validation data fold. If sample-splitting is requested, then these<br>must be estimated specially; see Details. However, the resulting vector should<br>be the same length as Y; if using a list, then the summed length of each element<br>across the list should be the same length as Y (i.e., each observation is included<br>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<br>(b) Y on X withholding the columns in indx. If sample-splitting is requested,<br>then these must be estimated specially; see Details. If cross_fitted_se =<br>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_est            | imate  |  |
|                            | if sample splitting is used, should the final point estimates be based on only<br>the sample-split folds used for inference ("split", the default), or should they<br>instead be based on the full dataset ("full") or the average across the point<br>estimates from each sample split ("average")? All three options result in valid<br>point estimates – sample-splitting is only required for valid inference. |  |
| cross_fitting_f            | olds   |  |
|                            | the folds for cross-fitting. Only used if run_regression = FALSE.  |  |
| <pre>sample_splittin</pre> | g_folds  |  |
|                            | the folds used for sample-splitting; these identify the observations that should be<br>used to evaluate predictiveness based on the full and reduced sets of covariates,<br>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)   |  |
| С                          | 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")  |  |
| <pre>ipc_est_type</pre>    | 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 crossfitting 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:

**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

```
# generate the data
# generate X
p <- 2
n <- 100
x <- data.frame(replicate(p, stats::runif(n, -5, 5)))</pre>
# apply the function to the x's
smooth <- (x[,1]/5)^2*(x[,1]+7)/5 + (x[,2]/3)^2</pre>
# generate Y ~ Normal (smooth, 1)
y <- smooth + stats::rnorm(n, 0, 1)</pre>
# set up a library for SuperLearner; note simple library for speed
library("SuperLearner")
learners <- c("SL.glm", "SL.mean")</pre>
# estimate (with a small number of folds, for illustration only)
est <- vimp_rsquared(y, x, indx = 2,</pre>
           alpha = 0.05, run_regression = TRUE,
           SL.library = learners, V = 2, cvControl = list(V = 2))
```

vimp\_se

### 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 covari-<br>ates. |
|--------------|--|
|              | ates.  |
| 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. vrc01

### 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 Rightcensoring is a proxy for a resistant virus.
- **ic80.censored** A binary indicator of whether or not the IC-80 (the concentration at which 80 Rightcensoring 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.
- **hxb2.138.H.1mer** Amino acid sequence feature denoting the presence (1) or absence (0) of a residue at the given HXB2-referenced site.
- **hxb2.138.I.1mer** Amino acid sequence feature denoting the presence (1) or absence (0) of a residue at the given HXB2-referenced site.
- **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.
- **hxb2.139.E.1mer** Amino acid sequence feature denoting the presence (1) or absence (0) of a residue at the given HXB2-referenced site.
- **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.
- **hxb2.179.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.
- **hxb2.179.Y.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.

- **hxb2.289.D.1mer** Amino acid sequence feature denoting the presence (1) or absence (0) of a residue at the given HXB2-referenced site.
- **hxb2.289.K.1mer** Amino acid sequence feature denoting the presence (1) or absence (0) of a residue at the given HXB2-referenced site.
- **hxb2.289.N.1mer** Amino acid sequence feature denoting the presence (1) or absence (0) of a residue at the given HXB2-referenced site.
- **hxb2.289.R.1mer** Amino acid sequence feature denoting the presence (1) or absence (0) of a residue at the given HXB2-referenced site.
- **hxb2.289.S.1mer** Amino acid sequence feature denoting the presence (1) or absence (0) of a residue at the given HXB2-referenced site.
- **hxb2.289.T.1mer** Amino acid sequence feature denoting the presence (1) or absence (0) of a residue at the given HXB2-referenced site.
- **hxb2.289.V.1mer** Amino acid sequence feature denoting the presence (1) or absence (0) of a residue at the given HXB2-referenced site.
- **hxb2.290.D.1mer** Amino acid sequence feature denoting the presence (1) or absence (0) of a residue at the given HXB2-referenced site.
- **hxb2.290.E.1mer** Amino acid sequence feature denoting the presence (1) or absence (0) of a residue at the given HXB2-referenced site.
- hxb2.290.K.1mer Amino acid sequence feature denoting the presence (1) or absence (0) of a residue at the given HXB2-referenced site.
- **hxb2.290.N.1mer** Amino acid sequence feature denoting the presence (1) or absence (0) of a residue at the given HXB2-referenced site.
- **hxb2.290.Q.1mer** Amino acid sequence feature denoting the presence (1) or absence (0) of a residue at the given HXB2-referenced site.
- **hxb2.290.R.1mer** Amino acid sequence feature denoting the presence (1) or absence (0) of a residue at the given HXB2-referenced site.
- **hxb2.290.S.1mer** Amino acid sequence feature denoting the presence (1) or absence (0) of a residue at the given HXB2-referenced site.
- **hxb2.290.T.1mer** Amino acid sequence feature denoting the presence (1) or absence (0) of a residue at the given HXB2-referenced site.
- **hxb2.290.X.1mer** Amino acid sequence feature denoting the presence (1) or absence (0) of a residue at the given HXB2-referenced site.
- **hxb2.321.D.1mer** Amino acid sequence feature denoting the presence (1) or absence (0) of a residue at the given HXB2-referenced site.
- **hxb2.321.E.1mer** Amino acid sequence feature denoting the presence (1) or absence (0) of a residue at the given HXB2-referenced site.
- **hxb2.321.G.1mer** Amino acid sequence feature denoting the presence (1) or absence (0) of a residue at the given HXB2-referenced site.
- **hxb2.321.K.1mer** Amino acid sequence feature denoting the presence (1) or absence (0) of a residue at the given HXB2-referenced site.
- **hxb2.321.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.I.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.R.1mer** Amino acid sequence feature denoting the presence (1) or absence (0) of a residue at the given HXB2-referenced site.
- **hxb2.365.S.1mer** Amino acid sequence feature denoting the presence (1) or absence (0) of a residue at the given HXB2-referenced site.
- **hxb2.365.T.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.I.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.
- **hxb2.425.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.

- **hxb2.430.A.1mer** Amino acid sequence feature denoting the presence (1) or absence (0) of a residue at the given HXB2-referenced site.
- **hxb2.430.G.1mer** Amino acid sequence feature denoting the presence (1) or absence (0) of a residue at the given HXB2-referenced site.
- **hxb2.430.I.1mer** Amino acid sequence feature denoting the presence (1) or absence (0) of a residue at the given HXB2-referenced site.
- **hxb2.430.T.1mer** Amino acid sequence feature denoting the presence (1) or absence (0) of a residue at the given HXB2-referenced site.
- **hxb2.430.V.1mer** Amino acid sequence feature denoting the presence (1) or absence (0) of a residue at the given HXB2-referenced site.
- **hxb2.431.E.1mer** Amino acid sequence feature denoting the presence (1) or absence (0) of a residue at the given HXB2-referenced site.
- **hxb2.431.G.1mer** Amino acid sequence feature denoting the presence (1) or absence (0) of a residue at the given HXB2-referenced site.
- **hxb2.432.K.1mer** Amino acid sequence feature denoting the presence (1) or absence (0) of a residue at the given HXB2-referenced site.
- **hxb2.432.Q.1mer** Amino acid sequence feature denoting the presence (1) or absence (0) of a residue at the given HXB2-referenced site.
- **hxb2.432.R.1mer** Amino acid sequence feature denoting the presence (1) or absence (0) of a residue at the given HXB2-referenced site.
- **hxb2.432.S.1mer** Amino acid sequence feature denoting the presence (1) or absence (0) of a residue at the given HXB2-referenced site.
- **hxb2.442.A.1mer** Amino acid sequence feature denoting the presence (1) or absence (0) of a residue at the given HXB2-referenced site.
- **hxb2.442.E.1mer** Amino acid sequence feature denoting the presence (1) or absence (0) of a residue at the given HXB2-referenced site.
- **hxb2.442.H.1mer** Amino acid sequence feature denoting the presence (1) or absence (0) of a residue at the given HXB2-referenced site.
- **hxb2.442.I.1mer** Amino acid sequence feature denoting the presence (1) or absence (0) of a residue at the given HXB2-referenced site.
- hxb2.442.K.1mer Amino acid sequence feature denoting the presence (1) or absence (0) of a residue at the given HXB2-referenced site.
- **hxb2.442.L.1mer** Amino acid sequence feature denoting the presence (1) or absence (0) of a residue at the given HXB2-referenced site.
- **hxb2.442.N.1mer** Amino acid sequence feature denoting the presence (1) or absence (0) of a residue at the given HXB2-referenced site.
- **hxb2.442.P.1mer** Amino acid sequence feature denoting the presence (1) or absence (0) of a residue at the given HXB2-referenced site.
- **hxb2.442.Q.1mer** Amino acid sequence feature denoting the presence (1) or absence (0) of a residue at the given HXB2-referenced site.
- **hxb2.442.R.1mer** Amino acid sequence feature denoting the presence (1) or absence (0) of a residue at the given HXB2-referenced site.

- **hxb2.442.S.1mer** Amino acid sequence feature denoting the presence (1) or absence (0) of a residue at the given HXB2-referenced site.
- **hxb2.442.T.1mer** Amino acid sequence feature denoting the presence (1) or absence (0) of a residue at the given HXB2-referenced site.
- **hxb2.442.V.1mer** Amino acid sequence feature denoting the presence (1) or absence (0) of a residue at the given HXB2-referenced site.
- **hxb2.448.D.1mer** Amino acid sequence feature denoting the presence (1) or absence (0) of a residue at the given HXB2-referenced site.
- **hxb2.448.E.1mer** Amino acid sequence feature denoting the presence (1) or absence (0) of a residue at the given HXB2-referenced site.
- **hxb2.448.I.1mer** Amino acid sequence feature denoting the presence (1) or absence (0) of a residue at the given HXB2-referenced site.
- **hxb2.448.K.1mer** Amino acid sequence feature denoting the presence (1) or absence (0) of a residue at the given HXB2-referenced site.
- **hxb2.448.N.1mer** Amino acid sequence feature denoting the presence (1) or absence (0) of a residue at the given HXB2-referenced site.
- **hxb2.448.Q.1mer** Amino acid sequence feature denoting the presence (1) or absence (0) of a residue at the given HXB2-referenced site.
- **hxb2.448.S.1mer** Amino acid sequence feature denoting the presence (1) or absence (0) of a residue at the given HXB2-referenced site.
- **hxb2.448.T.1mer** Amino acid sequence feature denoting the presence (1) or absence (0) of a residue at the given HXB2-referenced site.
- **hxb2.455.E.1mer** Amino acid sequence feature denoting the presence (1) or absence (0) of a residue at the given HXB2-referenced site.
- **hxb2.455.I.1mer** Amino acid sequence feature denoting the presence (1) or absence (0) of a residue at the given HXB2-referenced site.
- **hxb2.455.L.1mer** Amino acid sequence feature denoting the presence (1) or absence (0) of a residue at the given HXB2-referenced site.
- **hxb2.455.Q.1mer** Amino acid sequence feature denoting the presence (1) or absence (0) of a residue at the given HXB2-referenced site.
- **hxb2.455.T.1mer** Amino acid sequence feature denoting the presence (1) or absence (0) of a residue at the given HXB2-referenced site.
- **hxb2.455.V.1mer** Amino acid sequence feature denoting the presence (1) or absence (0) of a residue at the given HXB2-referenced site.
- **hxb2.456.H.1mer** Amino acid sequence feature denoting the presence (1) or absence (0) of a residue at the given HXB2-referenced site.
- **hxb2.456.L.1mer** Amino acid sequence feature denoting the presence (1) or absence (0) of a residue at the given HXB2-referenced site.
- **hxb2.456.M.1mer** Amino acid sequence feature denoting the presence (1) or absence (0) of a residue at the given HXB2-referenced site.
- **hxb2.456.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.
- **hxb2.465.D.1mer** Amino acid sequence feature denoting the presence (1) or absence (0) of a residue at the given HXB2-referenced site.
- **hxb2.465.E.1mer** Amino acid sequence feature denoting the presence (1) or absence (0) of a residue at the given HXB2-referenced site.
- **hxb2.465.I.1mer** Amino acid sequence feature denoting the presence (1) or absence (0) of a residue at the given HXB2-referenced site.
- **hxb2.465.K.1mer** Amino acid sequence feature denoting the presence (1) or absence (0) of a residue at the given HXB2-referenced site.
- **hxb2.465.N.1mer** Amino acid sequence feature denoting the presence (1) or absence (0) of a residue at the given HXB2-referenced site.
- **hxb2.465.P.1mer** Amino acid sequence feature denoting the presence (1) or absence (0) of a residue at the given HXB2-referenced site.
- **hxb2.465.R.1mer** Amino acid sequence feature denoting the presence (1) or absence (0) of a residue at the given HXB2-referenced site.
- **hxb2.465.S.1mer** Amino acid sequence feature denoting the presence (1) or absence (0) of a residue at the given HXB2-referenced site.
- **hxb2.465.T.1mer** Amino acid sequence feature denoting the presence (1) or absence (0) of a residue at the given HXB2-referenced site.
- **hxb2.466.A.1mer** Amino acid sequence feature denoting the presence (1) or absence (0) of a residue at the given HXB2-referenced site.
- **hxb2.466.D.1mer** Amino acid sequence feature denoting the presence (1) or absence (0) of a residue at the given HXB2-referenced site.
- **hxb2.466.E.1mer** Amino acid sequence feature denoting the presence (1) or absence (0) of a residue at the given HXB2-referenced site.
- **hxb2.466.Q.1mer** Amino acid sequence feature denoting the presence (1) or absence (0) of a residue at the given HXB2-referenced site.
- **hxb2.466.S.1mer** Amino acid sequence feature denoting the presence (1) or absence (0) of a residue at the given HXB2-referenced site.

- **hxb2.466.T.1mer** Amino acid sequence feature denoting the presence (1) or absence (0) of a residue at the given HXB2-referenced site.
- **hxb2.466.V.1mer** Amino acid sequence feature denoting the presence (1) or absence (0) of a residue at the given HXB2-referenced site.
- **hxb2.467.I.1mer** Amino acid sequence feature denoting the presence (1) or absence (0) of a residue at the given HXB2-referenced site.
- **hxb2.467.T.1mer** Amino acid sequence feature denoting the presence (1) or absence (0) of a residue at the given HXB2-referenced site.
- **hxb2.467.V.1mer** Amino acid sequence feature denoting the presence (1) or absence (0) of a residue at the given HXB2-referenced site.
- **hxb2.469.R.1mer** Amino acid sequence feature denoting the presence (1) or absence (0) of a residue at the given HXB2-referenced site.
- **hxb2.471.A.1mer** Amino acid sequence feature denoting the presence (1) or absence (0) of a residue at the given HXB2-referenced site.
- **hxb2.471.E.1mer** Amino acid sequence feature denoting the presence (1) or absence (0) of a residue at the given HXB2-referenced site.
- **hxb2.471.G.1mer** Amino acid sequence feature denoting the presence (1) or absence (0) of a residue at the given HXB2-referenced site.
- **hxb2.471.I.1mer** Amino acid sequence feature denoting the presence (1) or absence (0) of a residue at the given HXB2-referenced site.
- **hxb2.471.Q.1mer** Amino acid sequence feature denoting the presence (1) or absence (0) of a residue at the given HXB2-referenced site.
- **hxb2.471.S.1mer** Amino acid sequence feature denoting the presence (1) or absence (0) of a residue at the given HXB2-referenced site.
- **hxb2.471.T.1mer** Amino acid sequence feature denoting the presence (1) or absence (0) of a residue at the given HXB2-referenced site.
- **hxb2.471.V.1mer** Amino acid sequence feature denoting the presence (1) or absence (0) of a residue at the given HXB2-referenced site.
- **hxb2.474.D.1mer** Amino acid sequence feature denoting the presence (1) or absence (0) of a residue at the given HXB2-referenced site.
- **hxb2.474.E.1mer** Amino acid sequence feature denoting the presence (1) or absence (0) of a residue at the given HXB2-referenced site.
- **hxb2.474.N.1mer** Amino acid sequence feature denoting the presence (1) or absence (0) of a residue at the given HXB2-referenced site.
- **hxb2.475.I.1mer** Amino acid sequence feature denoting the presence (1) or absence (0) of a residue at the given HXB2-referenced site.
- **hxb2.475.M.1mer** Amino acid sequence feature denoting the presence (1) or absence (0) of a residue at the given HXB2-referenced site.
- **hxb2.476.K.1mer** Amino acid sequence feature denoting the presence (1) or absence (0) of a residue at the given HXB2-referenced site.
- **hxb2.476.R.1mer** Amino acid sequence feature denoting the presence (1) or absence (0) of a residue at the given HXB2-referenced site.

- **hxb2.477.D.1mer** Amino acid sequence feature denoting the presence (1) or absence (0) of a residue at the given HXB2-referenced site.
- **hxb2.477.N.1mer** Amino acid sequence feature denoting the presence (1) or absence (0) of a residue at the given HXB2-referenced site.
- **hxb2.544.L.1mer** Amino acid sequence feature denoting the presence (1) or absence (0) of a residue at the given HXB2-referenced site.
- **hxb2.544.V.1mer** Amino acid sequence feature denoting the presence (1) or absence (0) of a residue at the given HXB2-referenced site.
- **hxb2.569.S.1mer** Amino acid sequence feature denoting the presence (1) or absence (0) of a residue at the given HXB2-referenced site.
- **hxb2.569.T.1mer** Amino acid sequence feature denoting the presence (1) or absence (0) of a residue at the given HXB2-referenced site.
- **hxb2.569.X.1mer** Amino acid sequence feature denoting the presence (1) or absence (0) of a residue at the given HXB2-referenced site.
- **hxb2.589.D.1mer** Amino acid sequence feature denoting the presence (1) or absence (0) of a residue at the given HXB2-referenced site.
- **hxb2.589.N.1mer** Amino acid sequence feature denoting the presence (1) or absence (0) of a residue at the given HXB2-referenced site.
- **hxb2.655.E.1mer** Amino acid sequence feature denoting the presence (1) or absence (0) of a residue at the given HXB2-referenced site.
- **hxb2.655.I.1mer** Amino acid sequence feature denoting the presence (1) or absence (0) of a residue at the given HXB2-referenced site.
- **hxb2.655.K.1mer** Amino acid sequence feature denoting the presence (1) or absence (0) of a residue at the given HXB2-referenced site.
- **hxb2.655.N.1mer** Amino acid sequence feature denoting the presence (1) or absence (0) of a residue at the given HXB2-referenced site.
- **hxb2.655.Q.1mer** Amino acid sequence feature denoting the presence (1) or absence (0) of a residue at the given HXB2-referenced site.
- **hxb2.655.R.1mer** Amino acid sequence feature denoting the presence (1) or absence (0) of a residue at the given HXB2-referenced site.
- **hxb2.655.S.1mer** Amino acid sequence feature denoting the presence (1) or absence (0) of a residue at the given HXB2-referenced site.
- **hxb2.655.T.1mer** Amino acid sequence feature denoting the presence (1) or absence (0) of a residue at the given HXB2-referenced site.
- **hxb2.668.D.1mer** Amino acid sequence feature denoting the presence (1) or absence (0) of a residue at the given HXB2-referenced site.
- **hxb2.668.G.1mer** Amino acid sequence feature denoting the presence (1) or absence (0) of a residue at the given HXB2-referenced site.
- **hxb2.668.N.1mer** Amino acid sequence feature denoting the presence (1) or absence (0) of a residue at the given HXB2-referenced site.
- **hxb2.668.S.1mer** Amino acid sequence feature denoting the presence (1) or absence (0) of a residue at the given HXB2-referenced site.

- **hxb2.668.T.1mer** Amino acid sequence feature denoting the presence (1) or absence (0) of a residue at the given HXB2-referenced site.
- **hxb2.675.I.1mer** Amino acid sequence feature denoting the presence (1) or absence (0) of a residue at the given HXB2-referenced site.
- **hxb2.675.L.1mer** Amino acid sequence feature denoting the presence (1) or absence (0) of a residue at the given HXB2-referenced site.
- **hxb2.677.H.1mer** Amino acid sequence feature denoting the presence (1) or absence (0) of a residue at the given HXB2-referenced site.
- **hxb2.677.K.1mer** Amino acid sequence feature denoting the presence (1) or absence (0) of a residue at the given HXB2-referenced site.
- **hxb2.677.N.1mer** Amino acid sequence feature denoting the presence (1) or absence (0) of a residue at the given HXB2-referenced site.
- **hxb2.677.Q.1mer** Amino acid sequence feature denoting the presence (1) or absence (0) of a residue at the given HXB2-referenced site.
- **hxb2.677.R.1mer** Amino acid sequence feature denoting the presence (1) or absence (0) of a residue at the given HXB2-referenced site.
- **hxb2.677.S.1mer** Amino acid sequence feature denoting the presence (1) or absence (0) of a residue at the given HXB2-referenced site.
- **hxb2.680.W.1mer** Amino acid sequence feature denoting the presence (1) or absence (0) of a residue at the given HXB2-referenced site.
- **hxb2.681.Y.1mer** Amino acid sequence feature denoting the presence (1) or absence (0) of a residue at the given HXB2-referenced site.
- **hxb2.683.K.1mer** Amino acid sequence feature denoting the presence (1) or absence (0) of a residue at the given HXB2-referenced site.
- **hxb2.683.Q.1mer** Amino acid sequence feature denoting the presence (1) or absence (0) of a residue at the given HXB2-referenced site.
- **hxb2.683.R.1mer** Amino acid sequence feature denoting the presence (1) or absence (0) of a residue at the given HXB2-referenced site.
- **hxb2.688.I.1mer** Amino acid sequence feature denoting the presence (1) or absence (0) of a residue at the given HXB2-referenced site.
- **hxb2.688.V.1mer** Amino acid sequence feature denoting the presence (1) or absence (0) of a residue at the given HXB2-referenced site.
- **hxb2.702.F.1mer** Amino acid sequence feature denoting the presence (1) or absence (0) of a residue at the given HXB2-referenced site.
- **hxb2.702.I.1mer** Amino acid sequence feature denoting the presence (1) or absence (0) of a residue at the given HXB2-referenced site.
- **hxb2.702.L.1mer** Amino acid sequence feature denoting the presence (1) or absence (0) of a residue at the given HXB2-referenced site.
- **hxb2.702.V.1mer** Amino acid sequence feature denoting the presence (1) or absence (0) of a residue at the given HXB2-referenced site.
- hxb2.29.sequon\_actual.1mer Amino acid sequence feature denoting the presence (1) or absence (0) of a residue at the given HXB2-referenced site.

- **hxb2.49.sequon\_actual.1mer** Amino acid sequence feature denoting the presence (1) or absence (0) of a residue at the given HXB2-referenced site.
- hxb2.59.sequon\_actual.1mer Amino acid sequence feature denoting the presence (1) or absence (0) of a residue at the given HXB2-referenced site.
- hxb2.88.sequon\_actual.1mer Amino acid sequence feature denoting the presence (1) or absence (0) of a residue at the given HXB2-referenced site.
- hxb2.130.sequon\_actual.1mer Amino acid sequence feature denoting the presence (1) or absence (0) of a residue at the given HXB2-referenced site.
- hxb2.132.sequon\_actual.1mer Amino acid sequence feature denoting the presence (1) or absence (0) of a residue at the given HXB2-referenced site.
- hxb2.133.sequon\_actual.1mer Amino acid sequence feature denoting the presence (1) or absence (0) of a residue at the given HXB2-referenced site.
- hxb2.134.sequon\_actual.1mer Amino acid sequence feature denoting the presence (1) or absence (0) of a residue at the given HXB2-referenced site.
- hxb2.135.sequon\_actual.1mer Amino acid sequence feature denoting the presence (1) or absence (0) of a residue at the given HXB2-referenced site.
- hxb2.136.sequon\_actual.1mer Amino acid sequence feature denoting the presence (1) or absence (0) of a residue at the given HXB2-referenced site.
- hxb2.137.sequon\_actual.1mer Amino acid sequence feature denoting the presence (1) or absence (0) of a residue at the given HXB2-referenced site.
- hxb2.138.sequon\_actual.1mer Amino acid sequence feature denoting the presence (1) or absence (0) of a residue at the given HXB2-referenced site.
- hxb2.139.sequon\_actual.1mer Amino acid sequence feature denoting the presence (1) or absence (0) of a residue at the given HXB2-referenced site.
- hxb2.140.sequon\_actual.1mer Amino acid sequence feature denoting the presence (1) or absence (0) of a residue at the given HXB2-referenced site.
- hxb2.141.sequon\_actual.1mer Amino acid sequence feature denoting the presence (1) or absence (0) of a residue at the given HXB2-referenced site.
- hxb2.142.sequon\_actual.1mer Amino acid sequence feature denoting the presence (1) or absence (0) of a residue at the given HXB2-referenced site.
- hxb2.143.sequon\_actual.1mer Amino acid sequence feature denoting the presence (1) or absence (0) of a residue at the given HXB2-referenced site.
- hxb2.144.sequon\_actual.1mer Amino acid sequence feature denoting the presence (1) or absence (0) of a residue at the given HXB2-referenced site.
- hxb2.145.sequon\_actual.1mer Amino acid sequence feature denoting the presence (1) or absence (0) of a residue at the given HXB2-referenced site.
- hxb2.146.sequon\_actual.1mer Amino acid sequence feature denoting the presence (1) or absence (0) of a residue at the given HXB2-referenced site.
- hxb2.147.sequon\_actual.1mer Amino acid sequence feature denoting the presence (1) or absence (0) of a residue at the given HXB2-referenced site.
- hxb2.148.sequon\_actual.1mer Amino acid sequence feature denoting the presence (1) or absence (0) of a residue at the given HXB2-referenced site.

- **hxb2.149.sequon\_actual.1mer** Amino acid sequence feature denoting the presence (1) or absence (0) of a residue at the given HXB2-referenced site.
- **hxb2.150.sequon\_actual.1mer** Amino acid sequence feature denoting the presence (1) or absence (0) of a residue at the given HXB2-referenced site.
- hxb2.156.sequon\_actual.1mer Amino acid sequence feature denoting the presence (1) or absence (0) of a residue at the given HXB2-referenced site.
- hxb2.160.sequon\_actual.1mer Amino acid sequence feature denoting the presence (1) or absence (0) of a residue at the given HXB2-referenced site.
- hxb2.171.sequon\_actual.1mer Amino acid sequence feature denoting the presence (1) or absence (0) of a residue at the given HXB2-referenced site.
- hxb2.185.sequon\_actual.1mer Amino acid sequence feature denoting the presence (1) or absence (0) of a residue at the given HXB2-referenced site.
- hxb2.186.sequon\_actual.1mer Amino acid sequence feature denoting the presence (1) or absence (0) of a residue at the given HXB2-referenced site.
- hxb2.187.sequon\_actual.1mer Amino acid sequence feature denoting the presence (1) or absence (0) of a residue at the given HXB2-referenced site.
- hxb2.188.sequon\_actual.1mer Amino acid sequence feature denoting the presence (1) or absence (0) of a residue at the given HXB2-referenced site.
- hxb2.197.sequon\_actual.1mer Amino acid sequence feature denoting the presence (1) or absence (0) of a residue at the given HXB2-referenced site.
- hxb2.229.sequon\_actual.1mer Amino acid sequence feature denoting the presence (1) or absence (0) of a residue at the given HXB2-referenced site.
- hxb2.230.sequon\_actual.1mer Amino acid sequence feature denoting the presence (1) or absence (0) of a residue at the given HXB2-referenced site.
- hxb2.232.sequon\_actual.1mer Amino acid sequence feature denoting the presence (1) or absence (0) of a residue at the given HXB2-referenced site.
- hxb2.234.sequon\_actual.1mer Amino acid sequence feature denoting the presence (1) or absence (0) of a residue at the given HXB2-referenced site.
- hxb2.241.sequon\_actual.1mer Amino acid sequence feature denoting the presence (1) or absence (0) of a residue at the given HXB2-referenced site.
- hxb2.268.sequon\_actual.1mer Amino acid sequence feature denoting the presence (1) or absence (0) of a residue at the given HXB2-referenced site.
- hxb2.276.sequon\_actual.1mer Amino acid sequence feature denoting the presence (1) or absence (0) of a residue at the given HXB2-referenced site.
- hxb2.278.sequon\_actual.1mer Amino acid sequence feature denoting the presence (1) or absence (0) of a residue at the given HXB2-referenced site.
- hxb2.289.sequon\_actual.1mer Amino acid sequence feature denoting the presence (1) or absence (0) of a residue at the given HXB2-referenced site.
- hxb2.293.sequon\_actual.1mer Amino acid sequence feature denoting the presence (1) or absence (0) of a residue at the given HXB2-referenced site.
- hxb2.295.sequon\_actual.1mer Amino acid sequence feature denoting the presence (1) or absence (0) of a residue at the given HXB2-referenced site.

- **hxb2.301.sequon\_actual.1mer** Amino acid sequence feature denoting the presence (1) or absence (0) of a residue at the given HXB2-referenced site.
- **hxb2.302.sequon\_actual.1mer** Amino acid sequence feature denoting the presence (1) or absence (0) of a residue at the given HXB2-referenced site.
- hxb2.324.sequon\_actual.1mer Amino acid sequence feature denoting the presence (1) or absence (0) of a residue at the given HXB2-referenced site.
- hxb2.332.sequon\_actual.1mer Amino acid sequence feature denoting the presence (1) or absence (0) of a residue at the given HXB2-referenced site.
- hxb2.334.sequon\_actual.1mer Amino acid sequence feature denoting the presence (1) or absence (0) of a residue at the given HXB2-referenced site.
- hxb2.337.sequon\_actual.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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- hxb2.344.sequon\_actual.1mer Amino acid sequence feature denoting the presence (1) or absence (0) of a residue at the given HXB2-referenced site.
- hxb2.350.sequon\_actual.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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- hxb2.386.sequon\_actual.1mer Amino acid sequence feature denoting the presence (1) or absence (0) of a residue at the given HXB2-referenced site.
- hxb2.392.sequon\_actual.1mer Amino acid sequence feature denoting the presence (1) or absence (0) of a residue at the given HXB2-referenced site.
- hxb2.393.sequon\_actual.1mer Amino acid sequence feature denoting the presence (1) or absence (0) of a residue at the given HXB2-referenced site.
- hxb2.394.sequon\_actual.1mer Amino acid sequence feature denoting the presence (1) or absence (0) of a residue at the given HXB2-referenced site.

- hxb2.395.sequon\_actual.1mer Amino acid sequence feature denoting the presence (1) or absence (0) of a residue at the given HXB2-referenced site.
- **hxb2.396.sequon\_actual.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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- hxb2.401.sequon\_actual.1mer Amino acid sequence feature denoting the presence (1) or absence (0) of a residue at the given HXB2-referenced site.
- hxb2.402.sequon\_actual.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.sequon\_actual.1mer Amino acid sequence feature denoting the presence (1) or absence (0) of a residue at the given HXB2-referenced site.
- hxb2.611.sequon\_actual.1mer Amino acid sequence feature denoting the presence (1) or absence (0) of a residue at the given HXB2-referenced site.
- hxb2.616.sequon\_actual.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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- hxb2.619.sequon\_actual.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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- hxb2.637.sequon\_actual.1mer Amino acid sequence feature denoting the presence (1) or absence (0) of a residue at the given HXB2-referenced site.
- hxb2.674.sequon\_actual.1mer Amino acid sequence feature denoting the presence (1) or absence (0) of a residue at the given HXB2-referenced site.
- hxb2.743.sequon\_actual.1mer Amino acid sequence feature denoting the presence (1) or absence (0) of a residue at the given HXB2-referenced site.
- hxb2.750.sequon\_actual.1mer Amino acid sequence feature denoting the presence (1) or absence (0) of a residue at the given HXB2-referenced site.
- hxb2.787.sequon\_actual.1mer Amino acid sequence feature denoting the presence (1) or absence (0) of a residue at the given HXB2-referenced site.
- hxb2.816.sequon\_actual.1mer Amino acid sequence feature denoting the presence (1) or absence (0) of a residue at the given HXB2-referenced site.
- hxb2.824.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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