# Package 'vimp'

August 28, 2023

```
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. (Biomet-
      rics, 2020), Williamson et al. (JASA, 2021), and Williamson and Feng (ICML, 2020).
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average\_vim

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

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• 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 \leftarrow smooth + stats::rnorm(n, 0, 1)
# set up a library for SuperLearner; note simple library for speed
library("SuperLearner")
learners <- c("SL.glm", "SL.mean")</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,
           run_regression = TRUE, alpha = 0.05,
           SL.library = learners, cvControl = list(V = 2))
est_1 <- vimp_regression(Y = y[-samp], X = x[-samp, ], indx = 2, V = 2,
           run_regression = TRUE, alpha = 0.05,
           SL.library = learners, cvControl = list(V = 2))
ests <- average_vim(est_1, est_2, weights = c(1/2, 1/2))
```

 $bootstrap\_se$ 

Compute bootstrap-based standard error estimates for variable importance

#### Description

Compute bootstrap-based standard error estimates for variable importance

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### 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
)
```

the outcome.

### Arguments

Υ

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

the type of bootstrap interval (one of "norm", "basic", "stud", "perc", or

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

"bca", as in boot{boot.ci}) if requested. Defaults to "perc".

### Value

alpha

a bootstrap-based standard error estimate

to a 95% confidence interval.

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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**

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

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

### Description

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

### Usage

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

### **Arguments**

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

### **Details**

Ensure that inputs to vim, cv\_vim, and sp\_vim follow the correct formats.

### Value

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

create\_z

Create complete-case outcome, weights, and Z

### **Description**

Create complete-case outcome, weights, and Z

### Usage

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

### **Arguments**

Υ	the outcome
С	indicator of missing or observed
Z	the covariates observed in phase 1 and 2 data
Χ	all covariates

### Value

ipc\_weights

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

the weights

cv\_vim Nonparametric Intrinsic Variable Importance Estimates and Inference using Cross-fitting

### Description

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

### Usage

```
cv_vim(
    Y = NULL,
    X = NULL,
    cross_fitted_f1 = NULL,
    cross_fitted_f2 = NULL,
    f1 = NULL,
    f2 = NULL,
    indx = 1,
    V = ifelse(is.null(cross_fitting_folds), 5, length(unique(cross_fitting_folds))),
```

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

### **Arguments**

Χ

Y the outcome.

the covariates. If type = "average\_value", then the exposure variable should be part of X, with its name provided in exposure\_name.

cross\_fitted\_f1

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

cross\_fitted\_f2

the predicted values on validation data from a flexible estimation technique regressing either (a) the fitted values in cross\_fitted\_f1, or (b) Y, on X with-

> holding the columns in indx. Provided as either (a) a vector, where each element is the predicted value when that observation is part of the validation fold; or (b) a list of length V, where each element in the list is a set of predictions on the corresponding validation data fold. If sample-splitting is requested, 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. the number of folds for cross-fitting, defaults to 5. If sample\_splitting = TRUE, then a special type of V-fold cross-fitting is done. See Details for a more detailed explanation.

sample\_splitting

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

final\_point\_estimate

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

sample\_splitting\_folds

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

cross\_fitting\_folds

the folds for cross-fitting. Only used if run\_regression = FALSE.

stratified

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

type

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

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

SL.library

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

alpha

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

delta the value of the  $\delta$ -null (i.e., testing if importance  $< \delta$ ); defaults to 0. should CIs be computed on original ("identity") or another scale? (options are scale "log" and "logit") should we remove NAs in the outcome and fitted values in computation? (dena.rm faults to FALSE) С the indicator of coarsening (1 denotes observed, 0 denotes unobserved). Ζ 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]). the type of procedure used for coarsened-at-random settings; options are "ipw" ipc\_est\_type (for inverse probability weighting) or "aipw" (for augmented inverse probability weighting). Only used if C is not all equal to 1. should the point estimate be scaled to be greater than or equal to 0? Defaults to scale\_est TRUE. nuisance\_estimators\_full (only used if type = "average\_value") a list of nuisance function estimators on the observed data (may be within a specified fold, for cross-fitted estimates). Specifically: an estimator of the optimal treatment rule; an estimator of the propensity score under the estimated optimal treatment rule; and an estimator of the outcome regression when treatment is assigned according to the estimated optimal rule. nuisance\_estimators\_reduced (only used if type = "average\_value") a list of nuisance function estimators on the observed data (may be within a specified fold, for cross-fitted estimates). Specifically: an estimator of the optimal treatment rule; an estimator of the propensity score under the estimated optimal treatment rule; and an estimator of the outcome regression when treatment is assigned according to the estimated optimal rule. (only used if type = "average\_value") the name of the exposure of interest; exposure\_name binary, with 1 indicating presence of the exposure and 0 indicating absence of the exposure. cross\_fitted\_se should we use cross-fitting to estimate the standard errors (TRUE, the default) or not (FALSE)? should bootstrap-based standard error estimates be computed? Defaults to FALSE bootstrap (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-

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 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 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 \langle (x[,1]/5)^2 \times (x[,1]+7)/5 + (x[,2]/3)^2 \rangle
# generate Y ~ Normal (smooth, 1)
y <- as.matrix(smooth + stats::rnorm(n, 0, 1))
# set up a library for SuperLearner; note simple library for speed
library("SuperLearner")
learners <- c("SL.glm")</pre>
# using Super Learner (with a small number of folds, for illustration only)
# ------
set.seed(4747)
est \leftarrow cv_vim(Y = y, X = x, indx = 2, V = 2,
type = "r_squared", run_regression = TRUE,
SL.library = learners, cvControl = list(V = 2), alpha = 0.05)
# doing things by hand, and plugging them in
# (with a small number of folds, for illustration only)
# set up the folds
indx <- 2
V <- 2
Y <- matrix(y)
set.seed(4747)
# Note that the CV.SuperLearner should be run with an outer layer
# of 2*V folds (for V-fold cross-fitted importance)
full_cv_fit <- suppressWarnings(SuperLearner::CV.SuperLearner(</pre>
Y = Y, X = x, SL.library = learners, cvControl = list(<math>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)
```

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```
sample_splitting_folds <- make_folds(unique(cross_fitting_folds), V = 2)
set.seed(5678)
est <- cv_vim(Y = y, cross_fitted_f1 = full_cv_preds,
cross_fitted_f2 = reduced_cv_preds, indx = 2, delta = 0, V = V, type = "r_squared",
cross_fitting_folds = cross_fitting_folds,
sample_splitting_folds = sample_splitting_folds,
run_regression = FALSE, alpha = 0.05, na.rm = TRUE)</pre>
```

estimate

Estimate a Predictiveness Measure

### Description

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

### Usage

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

### Arguments

An R object. Currently, there are methods for predictiveness\_measure objects only.

. . . further arguments passed to or from other methods.

estimate.predictiveness\_measure

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

### **Description**

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

#### Usage

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

### Arguments

```
x an object of class "predictiveness_measure"
```

... other arguments to type-specific predictiveness measures (currently unused)

### Value

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

```
estimate\_eif\_projection
```

Estimate projection of EIF on fully-observed variables

### Description

Estimate projection of EIF on fully-observed variables

### Usage

```
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.
ipc_fit_type	if "external", then use ipc_eif_preds; if "SL", fit a SuperLearner to determine the IPC correction to the efficient influence function.
ipc_eif_preds	if ipc_fit_type = "external", the fitted values from a regression of the full-data EIF on the fully observed covariates/outcome; otherwise, not used.
• • •	other arguments to SuperLearner, if ipc_fit_type = "SL".

### Value

the projection of the EIF onto the fully-observed variables

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estimate\_nuisances

Estimate nuisance functions for average value-based VIMs

#### **Description**

Estimate nuisance functions for average value-based VIMs

### Usage

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

#### **Arguments**

fit the fitted nuisance function estimator

Χ the covariates. If type = "average\_value", then the exposure variable should

be part of X, with its name provided in exposure\_name.

(only used if type = "average\_value") the name of the exposure of interest; exposure\_name

binary, with 1 indicating presence of the exposure and 0 indicating absence of

the exposure.

the number of folds for cross-fitting, defaults to 5. If sample\_splitting =

TRUE, then a special type of V-fold cross-fitting is done. See Details for a more detailed explanation.

SL.library a character vector of learners to pass to SuperLearner, if f1 and f2 are Y and

X, respectively. Defaults to SL.glmnet, SL.xgboost, and SL.mean.

sample\_splitting

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

```
sample_splitting_folds
```

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

18 est\_predictiveness

verbose should we print progress? defaults to FALSE weights weights to pass to estimation procedure

cross\_fitted\_se

should we use cross-fitting to estimate the standard errors (TRUE, the default) or

not (FALSE)?

split the sample split to use

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

### Value

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

estimate\_type\_predictiveness

Estimate Predictiveness Given a Type

### Description

Estimate the specified type of predictiveness

### Usage

```
estimate_type_predictiveness(arg_lst, type)
```

### **Arguments**

arg\_lst a list of arguments; from, e.g., predictiveness\_measure

type the type of predictiveness, e.g., "r\_squared"

#### **Description**

Compute nonparametric estimates of the chosen measure of predictiveness.

est\_predictiveness 19

### 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,
)
```

### **Arguments**

fitted_values	fitted values from a regression function using the observed data.
у	the observed outcome.
a	the observed treatment assignment (may be within a specified fold, for cross-fitted estimates). Only used if type = "average_value".
full_y	the observed outcome (from the entire dataset, for cross-fitted estimates).
type	which parameter are you estimating (defaults to r_squared, for R-squared-based variable importance)?
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- phase sample) weighted estimation. Assumed to be already inverted (i.e., ipc_weights = 1 / [estimated probability weights]).
ipc_fit_type	if "external", then use ipc_eif_preds; if "SL", fit a SuperLearner to determine the correction to the efficient influence function.
ipc_eif_preds	if ipc_fit_type = "external", the fitted values from a regression of the full-data EIF on the fully observed covariates/outcome; otherwise, not used.
ipc_est_type	IPC correction, either "ipw" (for classical inverse probability weighting) or "aipw" (for augmented inverse probability weighting; the default).
scale	if doing an IPC correction, then the scale that the correction should be computed on (e.g., "identity"; or "logit" to logit-transform, apply the correction, and backtransform).
na.rm	logical; should NA's be removed in computation? (defaults to FALSE)

20 est\_predictiveness\_cv

nuisance\_estimators

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

... other arguments to SuperLearner, if ipc\_fit\_type = "SL".

#### **Details**

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

#### Value

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

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,
  у,
  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,
)
```

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### **Arguments**

fitted_values	fitted values from a regression function using the observed data; a list of length V, where each object is a set of predictions on the validation data, or a vector of the same length as y.
У	the observed outcome.
full_y	the observed outcome (from the entire dataset, for cross-fitted estimates).
folds	the cross-validation folds for the observed data.
type	which parameter are you estimating (defaults to r_squared, for R-squared-based variable importance)?
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.
ipc_weights	weights for inverse probability of coarsening (e.g., inverse weights from a two-phase sample) weighted estimation. Assumed to be already inverted (i.e., ipc_weights = 1 / [estimated probability weights]).
ipc_fit_type	if "external", then use ipc_eif_preds; if "SL", fit a SuperLearner to determine the correction to the efficient influence function.
ipc_eif_preds	if ipc_fit_type = "external", the fitted values from a regression of the full-data EIF on the fully observed covariates/outcome; otherwise, not used.
ipc_est_type	IPC correction, either "ipw" (for classical inverse probability weighting) or "aipw" (for augmented inverse probability weighting; the default).
scale	if doing an IPC correction, then the scale that the correction should be computed on (e.g., "identity"; or "logit" to logit-transform, apply the correction, and backtransform).
na.rm	logical; should NA's be removed in computation? (defaults to FALSE)
	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. If sample-splitting is also requested (recommended, since in this case inferences will be valid even if the variable has zero true importance), then the prediction functions are trained as if 2K-fold cross-validation were run, but are evaluated on only K sets (independent between the full and reduced nuisance regression).

### Value

The estimated measure of predictiveness.

```
extract_sampled_split_predictions
```

Extract sampled-split predictions from a CV.SuperLearner object

#### **Description**

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

### Usage

```
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**

#### Value

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

### See Also

CV. SuperLearner for usage of the CV. SuperLearner function.

 $format.predictiveness\_measure$ 

 $Format\ a\ {\tt predictiveness\_measure}\ object$ 

### Description

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

### Usage

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

### Arguments

- x the predictiveness\_measure object of interest.
- ... other options, see the generic format function.

format.vim

Format a vim object

### **Description**

Nicely formats the output from a vim object for printing.

### Usage

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

### **Arguments**

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

24 get\_full\_type

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 25

get\_test\_set

Return test-set only data

### **Description**

Return test-set only data

### Usage

```
get_test_set(arg_lst, k)
```

### **Arguments**

arg\_lst a list of estimates, data, etc.
k the index of interest

### Value

the test-set only data

make\_folds

Create Folds for Cross-Fitting

### Description

Create Folds for Cross-Fitting

#### Usage

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

### **Arguments**

y the outcome

V the number of folds

stratified should the folds be stratified based on the outcome?

C a vector indicating whether or not the observation is fully observed; 1 denotes

yes, 0 denotes no

probs vector of proportions for each fold number

### Value

a vector of folds

26 measure\_accuracy

make\_kfold

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

### **Description**

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

### Usage

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

#### Arguments

#### 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)),
```

measure\_accuracy 27

```
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]).	
ipc_fit_type	if "external", then use $ipc\_eif\_preds$ ; if "SL", fit a SuperLearner to determine the IPC correction to the efficient influence function.	
ipc_eif_preds	if ipc_fit_type = "external", the fitted values from a regression of the full-data EIF on the fully observed covariates/outcome; otherwise, not used.	
ipc_est_type	IPC correction, either "ipw" (for classical inverse probability weighting) or "aipw" (for augmented inverse probability weighting; the default).	
scale	if doing an IPC correction, then the scale that the correction should be computed on (e.g., "identity"; or "logit" to logit-transform, apply the correction, and backtransform).	
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.

28 measure\_anova

measure\_anova

Estimate ANOVA decomposition-based variable importance.

### 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,
)
```

### **Arguments**

full	fitted values from a regression function of the observed outcome on the full set of covariates.
reduced	fitted values from a regression on the reduced set of observed covariates.
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-data EIF on the fully observed covariates/outcome; otherwise, not used.

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#### Value

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

measure\_auc

Estimate area under the receiver operating characteristic curve (AUC)

### Description

Compute nonparametric estimate of AUC.

#### Usage

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

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

### Value

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

 ${\tt measure\_average\_value} \ \ \textit{Estimate the average value under the optimal treatment rule}$ 

### Description

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

measure\_average\_value 31

#### 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 specified fold, for cross-fitted estimates). Specifically: an estimator of the optimal treatment rule; an estimator of the propensity score under the estimated optimal treatment rule; and an estimator of the outcome regression when treatment is assigned according to the estimated optimal rule.

y the observed outcome (may be within a specified fold, for cross-fitted estimates).

a the observed treatment assignment (may be within a specified fold, for cross-

fitted estimates).

full\_y the observed outcome (not used, defaults to NULL).

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

Z either NULL (if no coarsening) or a matrix-like object containing the fully ob-

served data.

ipc\_weights weights for inverse probability of coarsening (IPC) (e.g., inverse weights from a

two-phase sample) weighted estimation. Assumed to be already inverted. (i.e.,

ipc\_weights = 1 / [estimated probability weights]).

ipc\_fit\_type if "external", then use ipc\_eif\_preds; if "SL", fit a SuperLearner to determine

the IPC correction to the efficient influence function.

ipc\_eif\_preds if ipc\_fit\_type = "external", the fitted values from a regression of the full-

data EIF on the fully observed covariates/outcome; otherwise, not used.

ipc\_est\_type IPC correction, either "ipw" (for classical inverse probability weighting) or

"aipw" (for augmented inverse probability weighting; the default).

scale if doing an IPC correction, then the scale that the correction should be computed

on (e.g., "identity"; or "logit" to logit-transform, apply the correction, and back-

transform).

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

... other arguments to SuperLearner, if ipc\_fit\_type = "SL".

### Value

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

### Description

Compute nonparametric estimate of cross-entropy.

### Usage

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

#### **Arguments**

fitted_values	fitted values from a regression function using the observed data (may be within a specified fold, for cross-fitted estimates).
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., $ipc\_weights = 1 / [estimated probability weights]$ ).
ipc_fit_type	if "external", then use ipc_eif_preds; if "SL", fit a SuperLearner to determine the IPC correction to the efficient influence function.

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

#### Value

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

measure\_deviance

Estimate the deviance

### Description

Compute nonparametric estimate of deviance.

#### Usage

```
measure_deviance(
   fitted_values,
   y,
   full_y = NULL,
   C = rep(1, 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,
   ...
)
```

34 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]).	
ipc_fit_type	if "external", then use $ipc\_eif\_preds$ ; if "SL", fit a SuperLearner to determine the IPC correction to the efficient influence function.	
ipc_eif_preds	if ipc_fit_type = "external", the fitted values from a regression of the full-data EIF on the fully observed covariates/outcome; otherwise, not used.	
ipc_est_type	IPC correction, either "ipw" (for classical inverse probability weighting) or "aipw" (for augmented inverse probability weighting; the default).	
scale	if doing an IPC correction, then the scale that the correction should be computed on (e.g., "identity"; or "logit" to logit-transform, apply the correction, and backtransform).	
na.rm	logical; should NAs be removed in computation? (defaults to FALSE)	
nuisance_estimators		
	not used; for compatibility with measure_average_value.	
a	not used; for compatibility with measure_average_value.	
• • •	other arguments to SuperLearner, if ipc_fit_type = "SL".	

### Value

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

	measure_mse	Estimate mean squared error	
--	-------------	-----------------------------	--

## Description

Compute nonparametric estimate of mean squared error.

measure\_mse 35

### Usage

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

### Arguments

fitted_values	fitted values from a regression function using the observed data (may be within a specified fold, for cross-fitted estimates).	
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]).	
ipc_fit_type	if "external", then use ipc_eif_preds; if "SL", fit a SuperLearner to determine the IPC correction to the efficient influence function.	
ipc_eif_preds	if ipc_fit_type = "external", the fitted values from a regression of the full-data EIF on the fully observed covariates/outcome; otherwise, not used.	
ipc_est_type	IPC correction, either "ipw" (for classical inverse probability weighting) or "aipw" (for augmented inverse probability weighting; the default).	
scale	if doing an IPC correction, then the scale that the correction should be computed on (e.g., "identity"; or "logit" to logit-transform, apply the correction, and backtransform).	
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".	

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### Value

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

 $measure\_r\_squared$ 

Estimate R-squared

### Description

Estimate R-squared

### Usage

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

### **Arguments**

fitted_values	fitted values from a regression function using the observed data (may be within a specified fold, for cross-fitted estimates).
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]).
ipc_fit_type	if "external", then use ipc_eif_preds; if "SL", fit a SuperLearner to determine the IPC correction to the efficient influence function.

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ipc_eif_preds	if ipc_fit_type = "external", the fitted values from a regression of the full-data EIF on the fully observed covariates/outcome; otherwise, not used.	
ipc_est_type	IPC correction, either "ipw" (for classical inverse probability weighting) or "aipw" (for augmented inverse probability weighting; the default).	
scale	if doing an IPC correction, then the scale that the correction should be computed on (e.g., "identity"; or "logit" to logit-transform, apply the correction, and backtransform).	
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 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
# generate Y ~ Normal (smooth, 1)
y \leftarrow smooth + stats::rnorm(n, 0, 1)
# set up a library for SuperLearner; note simple library for speed
library("SuperLearner")
learners <- c("SL.glm", "SL.mean")</pre>
# using Super Learner (with a small number of folds, for illustration only)
est_2 \leftarrow vimp\_regression(Y = y, X = x, indx = 2, V = 2,
           run_regression = TRUE, alpha = 0.05,
           SL.library = learners, cvControl = list(V = 2))
est_1 <- vimp_regression(Y = y, X = x, indx = 1, V = 2,
           run_regression = TRUE, alpha = 0.05,
           SL.library = learners, cvControl = list(V = 2))
ests <- merge_vim(est_1, est_2)</pre>
```

predictiveness\_measure

Construct a Predictiveness Measure

## **Description**

Construct a Predictiveness Measure

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## 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**

the measure of interest (e.g., "accuracy", "auc", "r\_squared") type the outcome of interest У the exposure of interest (only used if type = "average\_value") fitted\_values fitted values from a regression function using the observed data (may be within a specified fold, for cross-fitted estimates). cross\_fitting\_folds folds for cross-fitting, if used to obtain the fitted values. If not used, a vector of 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

a list of nuisance function estimators on the observed data (may be within a specified fold, for cross-fitted estimates). For the average value measure: an estimator of the optimal treatment rule  $(f_n)$ ; an estimator of the propensity score under the estimated optimal treatment rule  $(g_n)$ ; and an estimator of the outcome regression when treatment is assigned according to the estimated optimal rule  $(q_n)$ .

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

Z either NULL (if no coarsening) or a matrix-like object containing the fully observed data.

folds\_Z either the cross-validation folds for the observed data (no coarsening) or a vector of folds for the fully observed data Z.

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

## Value

An object of class "predictiveness\_measure", with the following attributes:

```
print.predictiveness\_measure \\ Print \ predictiveness\_measure \ objects
```

# Description

Prints out a table of the point estimate and standard error for a predictiveness\_measure object.

# Usage

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

# Arguments

x the predictiveness\_measure object of interest.... other options, see the generic print function.

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print.vim

Print vim objects

# 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

x 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

run\_sl

Run a Super Learner for the provided subset of features

## **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

```
Υ
                  the outcome
                  the covariates
Χ
                  the number of folds
SL.library
                  the library of candidate learners
univariate_SL.library
                  the library of candidate learners for single-covariate regressions
                  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
```

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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**

p the number of covariates

gamma the fraction of the sample size to sample (e.g., gamma = 1 means sample n sub-

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)

## **Examples**

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

spvim\_ics

scale\_est

Return an estimator on a different scale

# 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)
```

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## **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.

spvim_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 observations and sampling subsets: a list of length two resulting from a call to spvim_ics.
idx	the index of interest
gamma	the proportion of the sample size used when sampling subsets
na rm	remove NAs?

## **Details**

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

#### Value

The standard error estimate for the desired SPVIM value

## See Also

spvim\_ics for how the influence functions are estimated.

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**

Ζ

Ę	guments			
	Υ	the outcome.		
	X	the covariates. If type = "average_value", then the exposure variable should be part of X, with its name provided in exposure_name.		
	V	the number of folds for cross-fitting, defaults to 5. If sample_splitting = TRUE, then a special type of V-fold cross-fitting is done. See Details for a more detailed explanation.		
	type	the type of importance to compute; defaults to r_squared, but other supported options are auc, accuracy, deviance, and anova.		
	SL.library	a character vector of learners to pass to SuperLearner, if f1 and f2 are $Y$ and $X$ , respectively. Defaults to SL.glmnet, SL.xgboost, and SL.mean.		
	univariate_SL.l	ibrary		
		(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 $\ensuremath{FALSE})$		
	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	g		
		should we use sample-splitting to estimate the full and reduced predictiveness? Defaults to TRUE, since inferences made using sample_splitting = FALSE will be invalid for variables with truly zero importance.		
	final_point_est	imate		
		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		

y estimates from each sample split ("average")? All three options result in valid point estimates – sample-splitting is only required for valid inference.

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

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

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

ipc\_weights weights for the computed influence curve (i.e., inverse probability weights for coarsened-at-random settings). Assumed to be already inverted (i.e., ipc\_weights = 1 / [estimated probability weights]). ipc\_est\_type the type of procedure used for coarsened-at-random settings; options are "ipw" (for inverse probability weighting) or "aipw" (for augmented inverse probability weighting). Only used if C is not all equal to 1. scale 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 crossfitting 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
```

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

An object of class vim. See Details for more information.

scale the scale on which CIs were computed

#### See Also

Value

SuperLearner for specific usage of the SuperLearner function and package.

# **Examples**

```
n <- 100
p <- 2
# generate the data
x \leftarrow 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 \leftarrow as.matrix(smooth + stats::rnorm(n, 0, 1))
# set up a library for SuperLearner; note simple library for speed
library("SuperLearner")
learners <- c("SL.glm")</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)
```

vim

Nonparametric Intrinsic Variable Importance Estimates and Inference

## Description

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

# Usage

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

## **Arguments**

Υ

the outcome.

X	the covariates. If type = "average_value", then the exposure variable should be part of X, with its name provided in exposure_name.
f1	the fitted values from a flexible estimation technique regressing Y on X. A vector of the same length as Y; if sample-splitting is desired, then the value of f1 at each position should be the result of predicting from a model trained without that observation.
f2	the fitted values from a flexible estimation technique regressing either (a) f1 or (b) Y on X withholding the columns in indx. A vector of the same length as Y; if sample-splitting is desired, then the value of f2 at each position should be the result of predicting from a model trained without that observation.
indx	the indices of the covariate(s) to calculate variable importance for; defaults to 1.
type	the type of importance to compute; defaults to r_squared, but other supported options are auc, accuracy, deviance, and anova.
run_regression	if outcome Y and covariates X are passed to vimp_accuracy, and run_regression is TRUE, then Super Learner will be used; otherwise, variable importance will be computed using the inputted fitted values.
SL.library	a character vector of learners to pass to SuperLearner, if f1 and f2 are $Y$ and $X$ , respectively. Defaults to SL.glmnet, SL.xgboost, and SL.mean.
alpha	the level to compute the confidence interval at. Defaults to 0.05, corresponding to a $95\%$ confidence interval.
delta	the value of the $\delta$ -null (i.e., testing if importance $< \delta$ ); defaults to 0.
scale	should CIs be computed on original ("identity") or another scale? (options are "log" and "logit")
na.rm	should we remove NAs in the outcome and fitted values in computation? (defaults to FALSE)
sample_splitti	
	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_splitti	
	the folds used for sample-splitting; these identify the observations that should be used to evaluate predictiveness based on the full and reduced sets of covariates, respectively. Only used if run_regression = FALSE.
final_point_es	
	if sample splitting is used, should the final point estimates be based on only the sample-split folds used for inference ("split", the default), or should they instead be based on the full dataset ("full") or the average across the point estimates from each sample split ("average")? All three options result in valid point estimates – sample-splitting is only required for valid inference.
stratified	if run_regression = TRUE, then should the generated folds be stratified based on the outcome (helps to ensure class balance across cross-validation folds)
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").

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

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

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

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

#### nuisance\_estimators\_full

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

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

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

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

> 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.

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

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

nuisance\_estimators\_reduced

b

cluster\_id

#### **Details**

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

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

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

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

s the column(s) to calculate variable importance for

**SL.library** the library of learners passed to SuperLearner

type the type of risk-based variable importance measured

full fit the fitted values of the chosen method fit to the full data

red\_fit the fitted values of the chosen method fit to the reduced data

est the estimated variable importance

**naive** the naive estimator of variable importance (only used if type = "anova")

eif the estimated efficient influence function

eif\_full the estimated efficient influence function for the full regression

eif\_reduced the estimated efficient influence function for the reduced regression

se the standard error for the estimated variable importance

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

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

**p\_value** a p-value based on the same test as test

**full\_mod** the object returned by the estimation procedure for the full data regression (if applicable)

red\_mod the object returned by the estimation procedure for the reduced data regression (if applicable)

alpha the level, for confidence interval calculation

sample\_splitting\_folds the folds used for sample-splitting (used for hypothesis testing)

y the outcome

ipc\_weights the weights

cluster\_id the cluster IDs

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

## Value

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

## See Also

SuperLearner for specific usage of the SuperLearner function and package.

#### **Examples**

```
# 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 \leftarrow function(x) 0.5 + 0.3*x[1] + 0.2*x[2]
smooth \leftarrow 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 \leftarrow vim(y, x, indx = 2, type = "accuracy",
           alpha = 0.05, run_regression = TRUE,
           SL.library = learners, cvControl = list(V = 2),
           stratified = TRUE)
# using pre-computed fitted values
set.seed(4747)
V <- 2
full_fit <- SuperLearner::CV.SuperLearner(Y = y, X = x,</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

Nonparametric Intrinsic Variable Importance Estimates: Classification accuracy

# Description

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

## Usage

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

## **Arguments**

```
Y the outcome.
X the covariate
```

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.

> 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.

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

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.

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.

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

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

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.

f2

indx

run\_regression

SL.library

alpha

delta

na.rm

cross\_fitting\_folds

the folds for cross-fitting. Only used if run\_regression = FALSE.

sample\_splitting\_folds

the folds used for sample-splitting; these identify the observations that should be used to evaluate predictiveness based on the full and reduced sets of covariates,

respectively. Only used if run\_regression = FALSE.

stratified if run\_regression = TRUE, then should the generated folds be stratified based on

the outcome (helps to ensure class balance across cross-validation folds)

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

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

 $coarsened-at\text{-}random\ settings).\ Assumed to\ be\ already\ inverted\ (i.e.,\ ipc\_weights)$ 

= 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**

Ζ

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.

## **Examples**

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

vimp\_anova

vimp\_anova

Nonparametric Intrinsic Variable Importance Estimates: ANOVA

## Description

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

## Usage

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

## **Arguments**

```
Y the outcome.

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

cross_fitted_f1
```

the predicted values on validation data from a flexible estimation technique regressing Y on X in the training data. Provided as either (a) a vector, where each element is the predicted value when that observation is part of the validation

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> fold; or (b) a list of length V, where each element in the list is a set of predictions on the corresponding validation data fold. If sample-splitting is requested, then these must be estimated specially; see Details. However, the resulting vector should be the same length as Y; if using a list, then the summed length of each element across the list should be the same length as Y (i.e., each observation is included in the predictions).

### cross\_fitted\_f2

the predicted values on validation data from a flexible estimation technique regressing either (a) the fitted values in cross\_fitted\_f1, or (b) Y, on X withholding the columns in indx. Provided as either (a) a vector, where each element is the predicted value when that observation is part of the validation fold; or (b) a list of length V, where each element in the list is a set of predictions on the corresponding validation data fold. If sample-splitting is requested, then these must be estimated specially; see Details. However, the resulting vector should be the same length as Y; if using a list, then the summed length of each element across the list should be the same length as Y (i.e., each observation is included in the predictions).

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

> 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.

should we remove NAs in the outcome and fitted values in computation? (dena.rm

faults to FALSE)

cross\_fitting\_folds

the folds for cross-fitting. Only used if run\_regression = FALSE.

stratified if run regression = TRUE, then should the generated folds be stratified based on

the outcome (helps to ensure class balance across cross-validation folds)

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

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]).

Ζ

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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\_anova. 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</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**

Υ the outcome.

Χ 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).

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.

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.

f1

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)

final\_point\_estimate

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

cross\_fitting\_folds

the folds for cross-fitting. Only used if run\_regression = FALSE.

sample\_splitting\_folds

the folds used for sample-splitting; these identify the observations that should be used to evaluate predictiveness based on the full and reduced sets of covariates,

respectively. Only used if run\_regression = FALSE.

stratified if run\_regression = TRUE, then should the generated folds be stratified based on

the outcome (helps to ensure class balance across cross-validation folds)

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

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

position in X (e.g., "1").

ipc\_weights weights for the computed influence curve (i.e., inverse probability weights for

coarsened-at-random settings). Assumed to be already inverted (i.e., ipc\_weights

= 1 / [estimated probability weights]).

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

"log" and "logit")

ipc\_est\_type the type of procedure used for coarsened-at-random settings; options are "ipw"

(for inverse probability weighting) or "aipw" (for augmented inverse probability

weighting). Only used if C is not all equal to 1.

scale\_est should the point estimate be scaled to be greater than or equal to 0? Defaults to

TRUE.

cross\_fitted\_se

should we use cross-fitting to estimate the standard errors (TRUE, the default) or

not (FALSE)?

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

#### **Details**

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

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

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

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

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

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

With sample-splitting, cross-fitted VIM estimates are obtained by first splitting the data into 2K folds. These folds are further divided into 2 groups of folds. Then, for each fold k in the first group, estimator  $f_{n,k}$  of  $f_0$  is constructed using all data besides the 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 con-
     servative 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 appli-
     cable)
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.

## **Examples**

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

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

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

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

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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 $\operatorname{CI}$ ).
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

Nonparametric Intrinsic Variable Importance Estimates: Deviance

## **Description**

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

## Usage

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

### **Arguments**

```
Y the outcome.
```

X the covariates. If type = "average\_value", then the exposure variable should be part of X, with its name provided in exposure\_name.

```
cross_fitted_f1
```

the predicted values on validation data from a flexible estimation technique regressing Y on X in the training data. Provided as either (a) a vector, where each

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

#### cross\_fitted\_f2

the predicted values on validation data from a flexible estimation technique regressing either (a) the fitted values in cross\_fitted\_f1, or (b) Y, on X withholding the columns in indx. Provided as either (a) a vector, where each element is the predicted value when that observation is part of the validation fold; or (b) a list of length V, where each element in the list is a set of predictions on the corresponding validation data fold. If sample-splitting is requested, then these must be estimated specially; see Details. However, the resulting vector should be the same length as Y; if using a list, then the summed length of each element across the list should be the same length as Y (i.e., each observation is included in the predictions).

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

> 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.

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

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.

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.

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

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

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

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.

f2

indx

run\_regression

SL.library

delta

alpha

na.rm

final\_point\_estimate

cross\_fitting\_folds

the folds for cross-fitting. Only used if run\_regression = FALSE.

sample\_splitting\_folds

the folds used for sample-splitting; these identify the observations that should be used to evaluate predictiveness based on the full and reduced sets of covariates,

respectively. Only used if run\_regression = FALSE.

stratified if run\_regression = TRUE, then should the generated folds be stratified based on

the outcome (helps to ensure class balance across cross-validation folds)

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

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

 $coarsened-at\text{-}random\ settings).\ Assumed to\ be\ already\ inverted\ (i.e.,\ ipc\_weights)$ 

= 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**

Ζ

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)

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

#### Value

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

#### See Also

SuperLearner for specific usage of the SuperLearner function and package.

### **Examples**

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

vimp\_hypothesis\_test Perform a hypothesis test against the null hypothesis of  $\delta$  importance

## **Description**

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

### Usage

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

## **Arguments**

```
predictiveness_full
```

the estimated predictiveness of the regression including the covariate(s) of inter-

est.

predictiveness\_reduced

the estimated predictiveness of the regression excluding the covariate(s) of in-

terest.

se the estimated standard error of the variable importance estimator

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

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

### **Details**

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

## Value

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

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vimp\_regression

Nonparametric Intrinsic Variable Importance Estimates: ANOVA

### **Description**

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

#### Usage

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

## **Arguments**

Y the outcome.

X the covariates. If type = "average\_value", then the exposure variable should be part of X, with its name provided in exposure\_name.

cross\_fitted\_f1

the predicted values on validation data from a flexible estimation technique regressing Y on X in the training data. Provided as either (a) a vector, where each element is the predicted value when that observation is part of the validation fold; or (b) a list of length V, where each element in the list is a set of predictions on the corresponding validation data fold. If sample-splitting is requested,

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> then these must be estimated specially; see Details. However, the resulting vector should be the same length as Y; if using a list, then the summed length of each element across the list should be the same length as Y (i.e., each observation is included in the predictions).

cross\_fitted\_f2

the predicted values on validation data from a flexible estimation technique regressing either (a) the fitted values in cross\_fitted\_f1, or (b) Y, on X withholding the columns in indx. Provided as either (a) a vector, where each element is the predicted value when that observation is part of the validation fold; or (b) a list of length V, where each element in the list is a set of predictions on the corresponding validation data fold. If sample-splitting is requested, then these must be estimated specially; see Details. However, the resulting vector should be the same length as Y; if using a list, then the summed length of each element across the list should be the same length as Y (i.e., each observation is included in the predictions).

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

> 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.

> 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.

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

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

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

cross\_fitting\_folds

the folds for cross-fitting. Only used if run\_regression = FALSE.

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).

> 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")

V

SL.library

alpha

delta na.rm

stratified

Ζ

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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  $v_vim$ , with type = "r\_squared".

## Usage

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

### **Arguments**

Υ the outcome.

Χ 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).

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.

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.

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

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.

> 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.

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

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

f1

f2

indx

SL.library

alpha

delta

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

final\_point\_estimate

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

cross\_fitting\_folds

the folds for cross-fitting. Only used if run\_regression = FALSE.

sample\_splitting\_folds

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

stratified if run\_regression = TRUE, then should the generated folds be stratified based on

the outcome (helps to ensure class balance across cross-validation folds)

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

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 - α) × 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
# generate Y ~ Normal (smooth, 1)
y \leftarrow smooth + stats::rnorm(n, 0, 1)
# set up a library for SuperLearner; note simple library for speed
library("SuperLearner")
learners <- c("SL.glm", "SL.mean")</pre>
# estimate (with a small number of folds, for illustration only)
est <- vimp_rsquared(y, x, indx = 2,
           alpha = 0.05, run_regression = TRUE,
           SL.library = learners, V = 2, cvControl = list(V = 2))
```

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vimp\_se

Estimate variable importance standard errors

## **Description**

Compute standard error estimates for estimates of variable importance.

## Usage

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

## Arguments

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

## **Details**

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

### Value

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

vrc01

Neutralization sensitivity of HIV viruses to antibody VRC01

# Description

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

#### **Usage**

data("vrc01")

#### **Format**

A data frame with 611 rows and 837 variables:

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

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**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.

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**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.

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**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.

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**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.

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**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.
- hxb2.339.sequon\_actual.1mer Amino acid sequence feature denoting the presence (1) or absence (0) of a residue at the given HXB2-referenced site.
- hxb2.343.sequon\_actual.1mer Amino acid sequence feature denoting the presence (1) or absence (0) of a residue at the given HXB2-referenced site.
- **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.
- hxb2.354.sequon\_actual.1mer Amino acid sequence feature denoting the presence (1) or absence (0) of a residue at the given HXB2-referenced site.
- hxb2.355.sequon\_actual.1mer Amino acid sequence feature denoting the presence (1) or absence (0) of a residue at the given HXB2-referenced site.
- **hxb2.356.sequon\_actual.1mer** Amino acid sequence feature denoting the presence (1) or absence (0) of a residue at the given HXB2-referenced site.
- **hxb2.358.sequon\_actual.1mer** Amino acid sequence feature denoting the presence (1) or absence (0) of a residue at the given HXB2-referenced site.
- **hxb2.360.sequon\_actual.1mer** Amino acid sequence feature denoting the presence (1) or absence (0) of a residue at the given HXB2-referenced site.
- hxb2.362.sequon\_actual.1mer Amino acid sequence feature denoting the presence (1) or absence (0) of a residue at the given HXB2-referenced site.
- **hxb2.363.sequon\_actual.1mer** Amino acid sequence feature denoting the presence (1) or absence (0) of a residue at the given HXB2-referenced site.
- 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.

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**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.
- hxb2.397.sequon\_actual.1mer Amino acid sequence feature denoting the presence (1) or absence (0) of a residue at the given HXB2-referenced site.
- hxb2.398.sequon\_actual.1mer Amino acid sequence feature denoting the presence (1) or absence (0) of a residue at the given HXB2-referenced site.
- **hxb2.399.sequon\_actual.1mer** Amino acid sequence feature denoting the presence (1) or absence (0) of a residue at the given HXB2-referenced site.
- **hxb2.400.sequon\_actual.1mer** Amino acid sequence feature denoting the presence (1) or absence (0) of a residue at the given HXB2-referenced site.
- **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.
- hxb2.403.sequon\_actual.1mer Amino acid sequence feature denoting the presence (1) or absence (0) of a residue at the given HXB2-referenced site.
- **hxb2.404.sequon\_actual.1mer** Amino acid sequence feature denoting the presence (1) or absence (0) of a residue at the given HXB2-referenced site.
- **hxb2.405.sequon\_actual.1mer** Amino acid sequence feature denoting the presence (1) or absence (0) of a residue at the given HXB2-referenced site.
- **hxb2.406.sequon\_actual.1mer** Amino acid sequence feature denoting the presence (1) or absence (0) of a residue at the given HXB2-referenced site.
- **hxb2.407.sequon\_actual.1mer** Amino acid sequence feature denoting the presence (1) or absence (0) of a residue at the given HXB2-referenced site.
- **hxb2.408.sequon\_actual.1mer** Amino acid sequence feature denoting the presence (1) or absence (0) of a residue at the given HXB2-referenced site.
- **hxb2.409.sequon\_actual.1mer** Amino acid sequence feature denoting the presence (1) or absence (0) of a residue at the given HXB2-referenced site.
- **hxb2.410.sequon\_actual.1mer** Amino acid sequence feature denoting the presence (1) or absence (0) of a residue at the given HXB2-referenced site.
- **hxb2.411.sequon\_actual.1mer** Amino acid sequence feature denoting the presence (1) or absence (0) of a residue at the given HXB2-referenced site.
- **hxb2.412.sequon\_actual.1mer** Amino acid sequence feature denoting the presence (1) or absence (0) of a residue at the given HXB2-referenced site.
- **hxb2.413.sequon\_actual.1mer** Amino acid sequence feature denoting the presence (1) or absence (0) of a residue at the given HXB2-referenced site.
- **hxb2.442.sequon\_actual.1mer** Amino acid sequence feature denoting the presence (1) or absence (0) of a residue at the given HXB2-referenced site.
- **hxb2.444.sequon\_actual.1mer** Amino acid sequence feature denoting the presence (1) or absence (0) of a residue at the given HXB2-referenced site.

**hxb2.446.sequon\_actual.1mer** Amino acid sequence feature denoting the presence (1) or absence (0) of a residue at the given HXB2-referenced site.

- **hxb2.448.sequon\_actual.1mer** Amino acid sequence feature denoting the presence (1) or absence (0) of a residue at the given HXB2-referenced site.
- hxb2.460.sequon\_actual.1mer Amino acid sequence feature denoting the presence (1) or absence (0) of a residue at the given HXB2-referenced site.
- **hxb2.461.sequon\_actual.1mer** Amino acid sequence feature denoting the presence (1) or absence (0) of a residue at the given HXB2-referenced site.
- **hxb2.462.sequon\_actual.1mer** Amino acid sequence feature denoting the presence (1) or absence (0) of a residue at the given HXB2-referenced site.
- **hxb2.463.sequon\_actual.1mer** Amino acid sequence feature denoting the presence (1) or absence (0) of a residue at the given HXB2-referenced site.
- **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.
- **hxb2.618.sequon\_actual.1mer** Amino acid sequence feature denoting the presence (1) or absence (0) of a residue at the given HXB2-referenced site.
- **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.
- **hxb2.624.sequon\_actual.1mer** Amino acid sequence feature denoting the presence (1) or absence (0) of a residue at the given HXB2-referenced site.
- **hxb2.625.sequon\_actual.1mer** Amino acid sequence feature denoting the presence (1) or absence (0) of a residue at the given HXB2-referenced site.
- 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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