

# Package ‘PRIMsrc’

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**Type** Package

**Title** PRIM Survival Regression Classification

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**Author**

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**Description** Performs a unified treatment of Bump Hunting by Patient Rule Induction Method (PRIM) in Survival, Regression and Classification settings (SRC). The current version is a development release that only implements the case of a survival response. New features will be added soon as they are available.

**Depends** R (>= 3.0.2), parallel, survival, Hmisc, glmnet, MASS

**Imports** graphics, grDevices, stats

**URL** <https://github.com/jedazard/PRIMsrc>

**Repository** PRIMsrc, GitHub, Inc.

**License** GPL (>= 3) | file LICENSE

**LazyLoad** yes

**LazyData** yes

**Archs** i386, x64

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PRIMsrc-package	<i>Bump Hunting by Patient Rule Induction Method in Survival, Regression and Classification settings</i>
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## Description

Performs a unified treatment of Bump Hunting by Patient Rule Induction Method (PRIM) in Survival, Regression and Classification settings (SRC). The method generates decision rules delineating a region in the predictor space, where the response is larger than its average over the entire space. The region is shaped as a hyperdimensional box or hyperrectangle that is not necessarily contiguous. Assumptions are that the multivariate input variables can be discrete or continuous and the univariate response variable can be discrete (Classification), continuous (Regression) or a time-to event, possibly censored (Survival). It is intended to handle low and high-dimensional multivariate datasets, including the situation where the number of covariates exceeds or dominates that of samples ( $p > n$  or  $p \gg n$  paradigm).

## Details

The current version is a development release that only implements the case of a survival response. At this point, survival bump hunting is also restricted to a directed peeling search of the first box covered by the recursive coverage (outer) loop of our Patient Recursive Survival Peeling (PRSP) algorithm. New features will be added soon as they are available. The main function relies on an internal variable pre-selection procedure before the PRSP algorithm is run. At this point, this is done by cross-validated Elastic-Net regularized Cox-regression.

The following describes only the end-user functions that are needed to run a complete procedure. The other internal subroutines are briefly documented in the manual, but are not to be called by the end-user at any time. For computational efficiency, some end-user functions offer a parallelization option that is done by passing a few parameters needed to configure a cluster. This is indicated by an asterisk (\* = optionally involving cluster usage). The R functions are categorized as follows:

### 1. END-USER FUNCTIONS FOR NEWS, SUMMARY AND PREDICTION

#### [PRIMsrc.news](#) **Display the PRIMsrc Package News**

Function to display the log file NEWS of updates of the **PRIMsrc** package.

#### [summary](#) **Summary Function**

S3 generic summary function to display the main parameters of a PRSP object.

#### [predict](#) **Predict Function**

S3 generic predict function to predict the box membership and box vertices on an independent set from a PRSP object trained by a SBH model.

### 2. END-USER SURVIVAL BUMP HUNTING FUNCTION

#### [sbh](#) (\*) **Cross-Validated Survival Bump Hunting**

Main end-user function for fitting a cross-validated Survival Bump Hunting (SBH) model. It

returns a cross-validated PRSP object, as generated by our Patient Recursive Survival Peeling or PRSP algorithm. The function relies on an internal variable pre-selection procedure before the PRSP algorithm is run. At this point, this is done by regular Cox-regression (from the R package **survival**) or a cross-validated Elasticnet Regularized Cox-Regression (from the R package **glmnet**), depending on whether the number of covariates is less ( $p \leq n$ ) or greater ( $p > n$ ) than the number of samples, respectively. At this point, the main function `sbh` performs the search of the *first* box of the recursive coverage (outer) loop of our Patient Recursive Survival Peeling (PRSP) algorithm. The PRSP object contains cross-validated estimates of all the decision-rules of pre-selected covariates and all other statistical quantities of interest at each iteration of the peeling sequence (inner loop of the PRSP algorithm). It enables the display of results graphically of/for model tuning/selection, all peeling trajectories, covariate traces, and survival distributions (see plotting functions below for more details). The function offers a few options such as the type of  $K$ -fold cross-validation desired ((replicated)-averaged or-combined), the peeling criterion for peeling the next box, the optimization criterion for model tuning and selection and a few more parameters for the PRSP algorithm. The function takes advantage of the R package **parallel** for efficient parallel execution. It allows users to create a cluster of workstations on a local and/or remote machine(s), enabling scaling-up to the number of specified CPU cores.

### 3. END-USER PLOTTING FUNCTIONS FOR MODEL VALIDATION AND VISUALIZATION OF RESULTS

#### [plot\\_profile](#) Visualization for Model Selection/Validation

Function for plotting the cross-validated profiles of a PRSP object. It uses the user's choice of statistics among the Log Hazard Ratio (LHR), Log-Rank Test (LRT) or Concordance Error Rate (CER) as a function of the model tuning parameter, that is, the optimal number of peeling steps of the peeling sequence (inner loop of our PRSP algorithm).

#### [plot\\_scatter](#) 2D Visualization of Data Scatter and Box Vertices

Function for plotting the cross-validated box vertices of a PRSP object. Plot the data scatter and cross-validated box vertices in a plane at a given peeling step of the peeling sequence (inner loop of our PRSP algorithm).

#### [plot\\_boxtraj](#) Visualization of Peeling Trajectories/Profiles

Function for plotting the cross-validated peeling trajectories/profiles of a PRSP object. Applies to the user-specified covariates among the pre-selected ones and all other statistical quantities of interest at each iteration of the peeling sequence (inner loop of our PRSP algorithm).

#### [plot\\_boxtrace](#) Visualization of Covariates Traces

Function for plotting the cross-validated covariates traces of a PRSP object. Plot the cross-validated modal trace curves of covariate importance and covariate usage of the user-specified covariates among the pre-selected ones at each iteration of the peeling sequence (inner loop of our PRSP algorithm).

#### [plot\\_boxkm](#) Visualization of Survival Distributions

Function for plotting the cross-validated survival distributions of a PRSP object. Plot the cross-validated Kaplan-Meier estimates of survival distributions for the highest risk (inbox) versus lower-risk (outbox) groups of samples at each iteration of the peeling sequence (inner loop of our PRSP algorithm).

### 4. END-USER DATASETS

#### [Synthetic.1](#), [Synthetic.2](#), [Synthetic.3](#), [Synthetic.4](#), [Synthetic.5](#) Five Simulated Survival Models Datasets

Modeling survival models #1-5 with censoring as a regression function of some informative predictors, depending on the model used. In models where non-informative noisy covariates were used, these covariates were not part of the design matrix (models #2-3 and #5). In one example, the signal is limited to a box-shaped region  $R$  of the predictor space (model #4). In

the last example, the signal is limited to 10% of the predictors in a  $p > n$  situation (model #5). Survival time was generated from an exponential model with rate parameter  $\lambda$  (and mean  $\frac{1}{\lambda}$ ) according to a Cox-PH model with hazard  $\exp(\eta)$ , where  $\eta(\cdot)$  is the regression function. Censoring indicator were generated from a uniform distribution on  $[0,3]$  (models #1-4) or  $[0,2]$  (model #5). In these synthetic examples, all covariates are continuous, i.i.d. from a multivariate uniform distribution on  $[0,1]$  (models #1-4) or from a multivariate standard normal distribution (model #5).

### Real.1 Clinical Dataset

Publicly available dataset from the Women's Interagency HIV cohort Study (WIHS). Inclusion criteria of the study were that women at enrolment were (i) alive, (ii) HIV-1 infected, and (iii) free of clinical AIDS symptoms. Women were followed until the first of the following occurred: (i) treatment initiation (HAART), (ii) AIDS diagnosis, (iii) death, or administrative censoring. The studied outcomes were the competing risks "AIDS/Death (before HAART)" and "Treatment Initiation (HAART)". However, here, for simplification purposes, only the first of the two competing events (i.e. the time to AIDS/Death), was used in this dataset example. Likewise, the entire study enrolled 1164 women, but only the complete cases were used in this dataset example for simplification. Variables included history of Injection Drug Use ("IDU") at enrollment, African American ethnicity ("Race"), age ("Age"), and baseline CD4 count ("CD4"). The question in this dataset example was whether it is possible to achieve a prognostication of patients for AIDS and HAART.

### Real.2 Large Gene Expression Dataset

Publicly available breast cancer gene expression profiling dataset from the Uppsala cohort study that enrolled 249 women. It is entitled: "Genetic Reclassification of Histologic Grade Delineates New Clinical Subtypes of Breast Cancer". The goal of the study was to provide a more objective measure of grade with prognostic benefit for patients with moderately differentiated grade II (G2) tumors. To that end, expression profiles of primary invasive breast tumors were analyzed on microarrays to find a gene expression signature capable of discerning tumors of grade I (G1) and grade III (G3) histology. In this dataset, only the Uppsala cohort and only the gene expression data was included although other clinical covariates are available as well. It represents a situation where the number of covariates dominates the number of complete observations, or  $p \gg n$  case.

Known Bugs/Problems : None at this time.

### Author(s)

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- "Michael LeBlanc, Ph.D." <mleblanc@fhcrc.org>
- "Alberto Santana, MBA." <ahs4@case.edu>

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Acknowledgments: This project was partially funded by the National Institutes of Health NIH - National Cancer Institute (R01-CA160593) to J-E. Dazard and J.S. Rao.

### References

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- Dazard J-E., Choe M., LeBlanc M. and Rao J.S. (2014). "*Cross-Validation of Survival Bump Hunting by Recursive Peeling Methods*." In JSM Proceedings, Survival Methods for Risk Estimation/Prediction Section. Boston, MA, USA. American Statistical Association IMS - JSM, p. 3366-3380.
- Dazard J-E. and J. S. Rao (2010). "*Local Sparse Bump Hunting*." J. Comp Graph. Statistics, 19(4):900-92.

### See Also

- makeCluster (R package **parallel**)
- plot.survfit (R package **survival**)
- glmnet (R package **glmnet**)

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plot\_boxkm

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Visualization of Survival Distributions

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### Description

Function for plotting the cross-validated survival distributions of a PRSP object. Plot the cross-validated Kaplan-Meier estimates of survival distributions for the highest risk (inbox) versus lower-risk (outbox) groups of samples at each iteration of the peeling sequence (inner loop of our PRSP algorithm).

### Usage

```
plot_boxkm(x,
           main = NULL,
           xlab = "Time",
           ylab = "Probability",
           precision = 1e-3,
           mark = 3,
           col = 2,
           cex = 1,
           steps = 1:x$cvfit$cv.nsteps,
           nr = 3,
           nc = 4,
           device = NULL,
           file = "Survival Plots",
           path=getwd(),
           horizontal = TRUE,
           width = 11.5,
           height = 8.5, ...)
```

### Arguments

x	Object of class PRSP as generated by the main function <a href="#">sbh</a> .
main	Character vector. Main Title. Defaults to NULL.
xlab	Character vector. X axis label. Defaults to "Time".
ylab	Character vector. Y axis label. Defaults to "Probability".

precision	Precision of cross-validated log-rank p-values of separation between two survival curves. Defaults to 1e-3.
mark	Integer scalar of mark parameter, which will be used to label the inbox and out-of-box curves. Defaults to 3.
col	Integer scalar specifying the color of the inbox curve. Defaults to 2.
cex	Numeric scalar specifying the size of the marks. Defaults to 1.
steps	Integer vector. Vector of peeling steps at which to plot the survival curves. Defaults to all the peeling steps of PRSP object x.
nr	Integer scalar of the number of rows in the plot. Defaults to 3.
nc	Integer scalar of the number of columns in the plot. Defaults to 4.
device	Graphic display device in {NULL, "PS", "PDF"}. Defaults to NULL (standard output screen). Currently implemented graphic display devices are "PS" (Postscript) or "PDF" (Portable Document Format).
file	File name for output graphic. Defaults to "Survival Plots".
path	Absolute path (without final (back)slash separator). Defaults to the working directory path.
horizontal	Logical scalar. Orientation of the printed image. Defaults to TRUE, that is potrait orientation.
width	Numeric scalar. Width of the graphics region in inches. Defaults to 11.5.
height	Numeric scalar. Height of the graphics region in inches. Defaults to 8.5.
...	Generic arguments passed to other plotting functions, including plot.survfit (R package <b>survival</b> ).

## Details

Some of the plotting parameters are further defined in the function plot.survfit (R package **survival**). Step #0 always corresponds to the situation where the starting box covers the entire test-set data before peeling. Cross-validated LRT, LHR of inbox samples and log-rank p-values of separation are shown at the bottom of the plot with the corresponding peeling step. P-values are lower-bounded by the precision limit given by  $1/A$ , where  $A$  is the number of permutations.

## Value

Invisible. None. Displays the plot(s) on the specified device.

## Note

End-user plotting function.

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- Dazard J-E. and J. S. Rao (2010). "Local Sparse Bump Hunting." J. Comp Graph. Statistics, 19(4):900-92.

## See Also

- `plot.survfit` (R package **survival**)

## Examples

```
#=====
# Loading the library and its dependencies
#=====
library("PRIMsrc")

#=====
# Simulated dataset #1 (n=250, p=3)
# Replicated Combined Cross-Validation (RCCV)
# Peeling criterion = LRT
# Optimization criterion = LRT
#=====
CVCMBREP.synt1 <- sbh(dataset = Synthetic.1,
                      cvtype = "combined", cvcriterion = "lrt",
                      B = 1, K = 5,
                      vs = TRUE, cpv = FALSE, probval = 0.5,
                      arg = "beta=0.05,
                           alpha=0.1,
                           minn=10,
                           L=NULL,
                           peelcriterion=\"lr\"",
                      parallel = FALSE, conf = NULL, seed = 123)

plot_boxkm(x = CVCMBREP.synt1,
           main = paste("RCCV probability curves for model #1", sep=""),
           xlab = "Time", ylab = "Probability",
           device = NULL, file = "Survival Plots", path=getwd(),
           horizontal = TRUE, width = 11.5, height = 8.5)
```

## Description

S3 generic function for plotting the cross-validated covariates traces of a PRSP object. Plot the cross-validated modal trace curves of covariate importance and covariate usage of the user-specified covariates among the pre-selected ones at each iteration of the peeling sequence (inner loop of our PRSP algorithm).

**Usage**

```
plot_boxtrace(x,
              main = NULL,
              xlab = "Box Mass",
              ylab = "Covariate Range (centered)",
              topplot = x$used,
              center = TRUE,
              scale = FALSE,
              col.cov,
              lty.cov,
              lwd.cov,
              col = 1,
              lty = 1,
              lwd = 1,
              cex = 1,
              add.legend = FALSE,
              text.legend = NULL,
              device = NULL,
              file = "Covariate Trace Plots",
              path=getwd(),
              horizontal = FALSE,
              width = 8.5,
              height = 8.5, ...)
```

**Arguments**

x	Object of class PRSP as generated by the main function <a href="#">sbh</a> .
main	Character vector. Main Title. Defaults to.
xlab	Character vector. X axis label. Defaults to "Box Mass". NULL
ylab	Character vector. Y axis label. Defaults to "Covariate Range (centered)".
topplot	Numeric vector. Which of the pre-selected covariates to plot. Defaults to covariates used for peeling.
center	Logical scalar. Shall the data be centered?. Defaults to TRUE.
scale	Logical scalar. Shall the data be scaled? Defaults to FALSE.
col.cov	Integer vector. Line color for the covariate importance curve of each selected covariate. Defaults to vector of colors of length the number of selected covariates. The vector is reused cyclically if it is shorter than the number of selected covariates.
lty.cov	Integer vector. Line type for the covariate importance curve of each selected covariate. Defaults to vector of 1's of length the number of selected covariates. The vector is reused cyclically if it is shorter than the number of selected covariates.
lwd.cov	Integer vector. Line width for the covariate importance curve of each selected covariate. Defaults to vector of 1's of length the number of selected covariates. The vector is reused cyclically if it is shorter than the number of selected covariates.
col	Integer scalar. Line color for the covariate trace curve. Defaults to 1.
lty	Integer scalar. Line type for the covariate trace curve. Defaults to 1.
lwd	Integer scalar. Line width for the covariate trace curve. Defaults to 1.



cex	Integer scalar. Symbol expansion used for titles, legends, and axis labels. Defaults to 1.
add.legend	Logical scalar. Should the legend be added to the current open graphics device?. Defaults to FALSE.
text.legend	Character vector of legend content. Defaults to NULL.
device	Graphic display device in {NULL, "PS", "PDF"}. Defaults to NULL (standard output screen). Currently implemented graphic display devices are "PS" (Postscript) or "PDF" (Portable Document Format).
file	File name for output graphic. Defaults to "Covariate Trace Plots".
path	Absolute path (without final (back)slash separator). Defaults to working directory path.
horizontal	Logical scalar. Orientation of the printed image. Defaults to FALSE, that is potrait orientation.
width	Numeric scalar. Width of the graphics region in inches. Defaults to 8.5.
height	Numeric scalar. Height of the graphics region in inches. Defaults to 8.5.
...	Generic arguments passed to other plotting functions.

### Details

The trace plots limit the display of traces to those only covariates that are used for peeling. If centered, an horizontal black dotted line about 0 is added to the plot.

Due to the variability induced by cross-validation and replication, it is possible that more than one covariate be used for peeling at a given step. So, for simplicity of the trace plots, only the modal or majority vote trace value (over the folds and replications of the cross-validation) is plotted.

The top plot shows the overlay of covariate importance curves for each covariate. The bottom plot shows the overlay of covariate usage curves for each covariate. It is a discretized view of covariate importance.

Both point to the magnitude and order with which covariates are used along the peeling sequence.

### Value

Invisible. None. Displays the plot(s) on the specified device.

### Note

End-user plotting function.

### Author(s)

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- "Michael Choe, M.D." <mjc206@case.edu>
- "Michael LeBlanc, Ph.D." <mleblanc@fhcrc.org>
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Maintainer: "Jean-Eudes Dazard, Ph.D." <jxd101@case.edu>

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- Dazard J-E. and J. S. Rao (2010). "Local Sparse Bump Hunting." J. Comp Graph. Statistics, 19(4):900-92.

## Examples

```
#####
# Loading the library and its dependencies
#####
library("PRIMsrc")

#####
# Simulated dataset #1 (n=250, p=3)
# Replicated Combined Cross-Validation (RCCV)
# Peeling criterion = LRT
# Optimization criterion = LRT
#####
CVCOMBREP.synt1 <- sbh(dataset = Synthetic.1,
                      cvtype = "combined", cvcriterion = "lrt",
                      B = 1, K = 5,
                      vs = TRUE, cpv = FALSE, probval = 0.5,
                      arg = "beta=0.05,
                          alpha=0.1,
                          minn=10,
                          L=NULL,
                          peelcriterion=\"lr\"",
                      parallel = FALSE, conf = NULL, seed = 123)

plot_boxtrace(x = CVCOMBREP.synt1,
              main = paste("RCCV trace plots for model #1", sep=""),
              xlab = "Box Mass", ylab = "Covariate Range (centered)",
              topplot = CVCOMBREP.synt1$used,
              center = TRUE, scale = FALSE,
              device = NULL, file = "Covariate Trace Plots", path=getwd(),
              horizontal = FALSE, width = 8.5, height = 8.5)
```

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plot\_boxtraj

---

Visualization of Peeling Trajectories/Profiles

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## Description

S3 generic function for plotting the cross-validated peeling trajectories/profiles of a PRSP object. Applies to the user-specified covariates among the pre-selected ones and all other statistical quantities of interest at each iteration of the peeling sequence (inner loop of our PRSP algorithm).

**Usage**

```
plot_boxtraj(x,
             main = NULL,
             xlab = "Box Mass",
             ylab = "Covariate Range",
             topplot = x$used,
             col.cov,
             lty.cov,
             lwd.cov,
             col = 1,
             lty = 1,
             lwd = 1,
             cex = 1,
             add.legend = FALSE,
             text.legend = NULL,
             nr = NULL,
             nc = NULL,
             device = NULL,
             file = "Covariate Trajectory Plots",
             path=getwd(),
             horizontal = FALSE,
             width = 8.5,
             height = 11.5, ...)
```

**Arguments**

x	Object of class PRSP as generated by the main function <a href="#">sbh</a> .
main	Character vector. Main Title. Defaults to NULL.
xlab	Character vector. X axis label. Defaults to "Box Mass".
ylab	Character vector. Y axis label. Defaults to "Covariate Range".
topplot	Numeric vector. Which of the pre-selected covariates to plot. Defaults to covariates used for peeling.
col.cov	Integer vector. Line color for the covariate trajectory curve of each selected covariate. Defaults to vector of colors of length the number of selected covariates. The vector is reused cyclically if it is shorter than the number of selected covariates.
lty.cov	Integer vector. Line type for the covariate trajectory curve of each selected covariate. Defaults to vector of 1's of length the number of selected covariates. The vector is reused cyclically if it is shorter than the number of selected covariates.
lwd.cov	Integer vector. Line width for the covariate trajectory curve of each selected covariate. Defaults to vector of 1's of length the number of selected covariates. The vector is reused cyclically if it is shorter than the number of selected covariates.
col	Integer scalar. Line color for the trajectory curve of each statistical quantity of interest. Defaults to 1.
lty	Integer scalar. Line type for the trajectory curve of each statistical quantity of interest. Defaults to 1.
lwd	Integer scalar. Line width for the trajectory curve of each statistical quantity of interest. Defaults to 1.

cex	Integer scalar. Symbol expansion used for titles, legends, and axis labels. Defaults to 1.
add.legend	Logical scalar. Should the legend be added to the current open graphics device? Defaults to FALSE.
text.legend	Character vector of legend content. Defaults to NULL.
nr	Integer scalar of the number of rows in the plot. If NULL, defaults to 3.
nc	Integer scalar of the number of columns in the plot. If NULL, defaults to 3.
device	Graphic display device in {NULL, "PS", "PDF"}. Defaults to NULL (standard output screen). Currently implemented graphic display devices are "PS" (Postscript) or "PDF" (Portable Document Format).
file	File name for output graphic. Defaults to "Covariate Trajectory Plots".
path	Absolute path (without final (back)slash separator). Defaults to working directory path.
horizontal	Logical scalar. Orientation of the printed image. Defaults to FALSE, that is potrait orientation.
width	Numeric scalar. Width of the graphics region in inches. Defaults to 8.5.
height	Numeric scalar. Height of the graphics region in inches. Defaults to 8.5.
...	Generic arguments passed to other plotting functions.

### Details

The plot limits the display of trajectories to those only covariates that are used for peeling.

The plot includes box descriptive statistics (such as support), survival endpoint statistics (such as Maximum Event-Free Time (MEFT), Minimum Event-Free Probability (MEVP), LHR, LRT) and prediction performance (such as CER).

### Value

Invisible. None. Displays the plot(s) on the specified device.

### Note

End-user plotting function.

### Author(s)

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## Examples

```
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# Loading the library and its dependencies
#####
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#####
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# Replicated Combined Cross-Validation (RCCV)
# Peeling criterion = LRT
# Optimization criterion = LRT
#####
CVCOMBREP.synt1 <- sbh(dataset = Synthetic.1,
                      cvtype = "combined", cvcriterion = "lrt",
                      B = 1, K = 5,
                      vs = TRUE, cpv = FALSE, probval = 0.5,
                      arg = "beta=0.05,
                           alpha=0.1,
                           minn=10,
                           L=NULL,
                           peelcriterion=\"lr\"",
                      parallel = FALSE, conf = NULL, seed = 123)

plot_boxtraj(x = CVCOMBREP.synt1,
             main = paste("RCCV peeling trajectories for model #1", sep=""),
             xlab = "Box Mass", ylab = "Covariate Range",
             topplot = CVCOMBREP.synt1$used,
             device = NULL, file = "Covariate Trajectory Plots", path=getwd(),
             horizontal = FALSE, width = 8.5, height = 8.5)
```

## Description

S3 generic function for plotting the cross-validated profiles of a PRSP object. It uses the user's choice of statistics among the Log Hazard Ratio (LHR), Log-Rank Test (LRT) or Concordance Error Rate (CER) as a function of the model tuning parameter, that is, the optimal number of peeling steps of the peeling sequence (inner loop of our PRSP algorithm).

**Usage**

```
plot_profile(x,
             main = NULL,
             xlab = "Peeling Steps",
             ylab = "Mean Profiles",
             add.sd = TRUE,
             add.legend = TRUE,
             add.profiles = TRUE,
             pch = 20,
             col = 1,
             lty = 1,
             lwd = 2,
             cex = 2,
             device = NULL,
             file = "Profile Plot",
             path=getwd(),
             horizontal = FALSE,
             width = 8.5,
             height = 5.0, ...)
```

**Arguments**

x	Object of class PRSP as generated by the main function <a href="#">sbh</a> .
main	Character vector. Main Title. Defaults to NULL.
xlab	Character vector. X axis label. Defaults to "Peeling Steps".
ylab	Character vector. Y axis label. Defaults to "Mean Profiles".
add.sd	Logical scalar. Shall the standard error bars be plotted? Defaults to TRUE.
add.legend	Logical scalar. Shall the legend be plotted? Defaults to TRUE.
add.profiles	Logical scalar. Shall the individual profiles (for all replicates) be plotted? Defaults to TRUE.
pch	Integer scalar of symbol number for all the profiles. Defaults to 20.
col	Integer scalar of line color of the mean profile. Defaults to 1.
lty	Integer scalar of line type of the mean profile. Defaults to 1.
lwd	Integer scalar of line width of the mean profile. Defaults to 2.
cex	Integer scalar of symbol expansion for all the profiles. Defaults to 2.
device	Graphic display device in {NULL, "PS", "PDF"}. Defaults to NULL (standard output screen). Currently implemented graphic display devices are "PS" (Postscript) or "PDF" (Portable Document Format).
file	File name for output graphic. Defaults to "Profile Plot".
path	Absolute path (without final (back)slash separator). Defaults to working directory path.
horizontal	Logical scalar. Orientation of the printed image. Defaults to FALSE, that is potrait orientation.
width	Numeric scalar. Width of the graphics region in inches. Defaults to 8.5.
height	Numeric scalar. Height of the graphics region in inches. Defaults to 5.
...	Generic arguments passed to other plotting functions.

## Details

Model validation is done by applying the optimization criterion on the user's choice of specific statistic. The goal is to find the optimal value of the K-fold cross-validated number of steps by maximization of LHR or LRT, or minimization of CER.

Currently, this done internally for visualization purposes, but it will ultimately offer the option to do be interactive with the end-user as well for parameter choosing/model selection.

## Value

Invisible. None. Displays the plot(s) on the specified device.

## Note

End-user plotting function.

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- "Michael LeBlanc, Ph.D." <mleblanc@fhcrc.org>
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Acknowledgments: This project was partially funded by the National Institutes of Health NIH - National Cancer Institute (R01-CA160593) to J-E. Dazard and J.S. Rao.

## References

- Dazard J-E., Choe M., LeBlanc M. and Rao J.S. (2015). "*Cross-validation and Peeling Strategies for Survival Bump Hunting using Recursive Peeling Methods*." (Submitted).
- Dazard J-E., Choe M., LeBlanc M. and Rao J.S. (2014). "*Cross-Validation of Survival Bump Hunting by Recursive Peeling Methods*." In JSM Proceedings, Survival Methods for Risk Estimation/Prediction Section. Boston, MA, USA. American Statistical Association IMS - JSM, p. 3366-3380.
- Dazard J-E. and J. S. Rao (2010). "*Local Sparse Bump Hunting*." J. Comp Graph. Statistics, 19(4):900-92.

## Examples

```
#=====
# Loading the library and its dependencies
#=====
library("PRIMsrc")

#=====
# Simulated dataset #1 (n=250, p=3)
# Replicated Combined Cross-Validation (RCCV)
# Peeling criterion = LRT
# Optimization criterion = LRT
#=====
CVCMBREP.synt1 <- sbh(dataset = Synthetic.1,
                      cvtype = "combined", cvcriterion = "lrt",
                      B = 1, K = 5,
```

```

vs = TRUE, cpv = FALSE, probval = 0.5,
arg = "beta=0.05,
      alpha=0.1,
      minn=10,
      L=NULL,
      peelcriterion=\"lr\\\"",
parallel = FALSE, conf = NULL, seed = 123)

plot_profile(x = CVCOMBREP.synt1,
  main = "RCCV tuning profiles for model #1",
  xlab = "Peeling Steps", ylab = "Mean Profiles",
  pch=20, col="black", lty=1, lwd=2, cex=2,
  add.sd = TRUE, add.legend = TRUE, add.profiles = TRUE,
  device = NULL, file = "Profile Plot", path=getwd(),
  horizontal = FALSE, width = 8.5, height = 5)

```

plot\_scatter

*2D Visualization of Data Scatter and Box Vertices***Description**

S3 generic function for plotting the cross-validated box vertices of a PRSP object. Plot the data scatter and cross-validated box vertices in a plane at a given peeling step of the peeling sequence (inner loop of our PRSP algorithm).

**Usage**

```

plot_scatter(x,
  main = NULL,
  proj = c(1,2),
  splom = TRUE,
  boxes = FALSE,
  steps = x$cvfit$cv.nsteps,
  pch = 16,
  cex = 0.5,
  col = 2:(length(steps)+1),
  col.box = 2:(length(steps)+1),
  lty.box = rep(2,length(steps)),
  lwd.box = rep(1,length(steps)),
  add.legend = TRUE,
  device = NULL,
  file = "Scatter Plot",
  path=getwd(),
  horizontal = FALSE,
  width = 5,
  height = 5, ...)

```

**Arguments**

x	Object of class PRSP as generated by the main function <a href="#">sbh</a> .
main	Character vector. Main Title. Defaults to NULL.



proj	Integer vector of length two, specifying the two dimensions of the projection plane. Defaults to c(1,2).
splom	Logical scalar. Shall the scatter plot of points inside the box(es) be plotted? Default to TRUE.
boxes	Logical scalar. Shall the box vertices be plotted or just the scatter of points? Default to FALSE.
steps	Integer vector. Vector of peeling steps at which to plot the in-box samples and box vertices. Defaults to the last peeling step of PRSP object x.
pch	Integer scalar of symbol number for the scatter plot. Defaults to 16.
cex	Integer scalar of symbol expansion. Defaults to 0.5.
col	Integer vector specifying the symbol color for each step. Defaults to vector of colors of length the number of steps. The vector is reused cyclically if it is shorter than the number of steps.
col.box	Integer vector of line color of box vertices for each step. Defaults to vector of colors of length the number of steps. The vector is reused cyclically if it is shorter than the number of steps.
lty.box	Integer vector of line type of box vertices for each step. Defaults to vector of 2's of length the number of steps. The vector is reused cyclically if it is shorter than the number of steps.
lwd.box	Integer vector of line width of box vertices for each step. Defaults to vector of 1's of length the number of steps. The vector is reused cyclically if it is shorter than the number of steps.
add.legend	Logical scalar. Shall the legend of steps numbers be plotted? Defaults to TRUE.
device	Graphic display device in {NULL, "PS", "PDF"}. Defaults to NULL (standard output screen). Currently implemented graphic display devices are "PS" (Postscript) or "PDF" (Portable Document Format).
file	File name for output graphic. Defaults to "Scatter Plot".
path	Absolute path (without final (back)slash separator). Defaults to working directory path.
horizontal	Logical scalar. Orientation of the printed image. Defaults to FALSE, that is potrait orientation.
width	Numeric scalar. Width of the graphics region in inches. Defaults to 5.
height	Numeric scalar. Height of the graphics region in inches. Defaults to 5.
...	Generic arguments passed to other plotting functions.

### Details

The scatterplot is drawn on a graphical device with geometrically equal scales on the  $X$  and  $Y$  axes.

### Value

Invisible. None. Displays the plot(s) on the specified device.

### Note

End-user plotting function.

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Maintainer: "Jean-Eudes Dazard, Ph.D." <jxd101@case.edu>

Acknowledgments: This project was partially funded by the National Institutes of Health NIH - National Cancer Institute (R01-CA160593) to J-E. Dazard and J.S. Rao.

**References**

- Dazard J-E., Choe M., LeBlanc M. and Rao J.S. (2015). "*Cross-validation and Peeling Strategies for Survival Bump Hunting using Recursive Peeling Methods*." (Submitted).
- Dazard J-E., Choe M., LeBlanc M. and Rao J.S. (2014). "*Cross-Validation of Survival Bump Hunting by Recursive Peeling Methods*." In JSM Proceedings, Survival Methods for Risk Estimation/Prediction Section. Boston, MA, USA. American Statistical Association IMS - JSM, p. 3366-3380.
- Dazard J-E. and J. S. Rao (2010). "*Local Sparse Bump Hunting*." J. Comp Graph. Statistics, 19(4):900-92.

**Examples**

```
#####
# Loading the library and its dependencies
#####
library("PRIMsrc")

#####
# Simulated dataset #1 (n=250, p=3)
# Replicated Combined Cross-Validation (RCCV)
# Peeling criterion = LRT
# Optimization criterion = LRT
#####
CVCOMBREP.synt1 <- sbh(dataset = Synthetic.1,
                      cvtype = "combined", cvcriterion = "lrt",
                      B = 1, K = 5,
                      vs = TRUE, cpv = FALSE, probval = 0.5,
                      arg = "beta=0.05,
                          alpha=0.1,
                          minn=10,
                          L=NULL,
                          peelcriterion=\"lr\"",
                      parallel = FALSE, conf = NULL, seed = 123)

plot_scatter(x = CVCOMBREP.synt1,
             main = paste("Scatter plot for model #1", sep=""),
             proj = c(1,2), splom = TRUE, boxes = TRUE,
             steps = CVCOMBREP.synt1$cvfit$cv.nsteps,
             pch = 16, cex = 0.5, col = 2,
             col.box = 2, lty.box = 2, lwd.box = 1,
             add.legend = TRUE,
             device = NULL, file = "Scatter Plot", path=getwd(),
             horizontal = FALSE, width = 5.0, height = 5.0)
```

---

predict.PRSP	<i>Predict Function</i>
--------------	-------------------------

---

**Description**

S3 generic predict function to predict the box membership and box vertices on an independent set from a PRSP object trained by a SBH model.

**Usage**

```
## S3 method for class 'PRSP'
predict(object, newdata, steps, na.action = na.omit, ...)
```

**Arguments**

object	Object of class PRSP as generated by the main function <a href="#">sbh</a> .
newdata	An object containing the new input data: either a numeric matrix or numeric vector. A vector will be transformed to a (#sample x 1) matrix.
steps	Integer vector. Vector of peeling steps at which to predict the box memberships and box vertices. Defaults to the last peeling step only.
na.action	A function to specify the action to be taken if NAs are found. The default action is na.omit, which leads to rejection of incomplete cases.
...	Further generic arguments passed to the predict function.

**Value**

List containing the following 2 fields:

boxind	Logical matrix of predicted box membership indicator (columns) by peeling steps (rows). TRUE = in-box, FALSE = out-of-box.
vertices	List of size the number of chosen peeling steps where each entry is a numeric matrix of predicted box vertices: lower and upper bounds (rows) by covariate (columns).

**Note**

End-user predict function.

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## References

- Dazard J-E., Choe M., LeBlanc M. and Rao J.S. (2015). "*Cross-validation and Peeling Strategies for Survival Bump Hunting using Recursive Peeling Methods.*" (Submitted).
- Dazard J-E., Choe M., LeBlanc M. and Rao J.S. (2014). "*Cross-Validation of Survival Bump Hunting by Recursive Peeling Methods.*" In JSM Proceedings, Survival Methods for Risk Estimation/Prediction Section. Boston, MA, USA. American Statistical Association IMS - JSM, p. 3366-3380.
- Dazard J-E. and J. S. Rao (2010). "*Local Sparse Bump Hunting.*" J. Comp Graph. Statistics, 19(4):900-92.

---

PRIMsrc.news

*Display the **PRIMsrc** Package News*

---

## Description

Function to display the log file NEWS of updates of the **PRIMsrc** package.

## Usage

```
PRIMsrc.news(...)
```

## Arguments

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

## Value

None.

## Note

End-user function.

## Author(s)

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## References

- Dazard J-E., Choe M., LeBlanc M. and Rao J.S. (2015). "Cross-validation and Peeling Strategies for Survival Bump Hunting using Recursive Peeling Methods." (Submitted).
- Dazard J-E., Choe M., LeBlanc M. and Rao J.S. (2014). "Cross-Validation of Survival Bump Hunting by Recursive Peeling Methods." In JSM Proceedings, Survival Methods for Risk Estimation/Prediction Section. Boston, MA, USA. American Statistical Association IMS - JSM, p. 3366-3380.
- Dazard J-E. and J. S. Rao (2010). "Local Sparse Bump Hunting." J. Comp Graph. Statistics, 19(4):900-92.

Real.1

Real Dataset #1: Clinical Dataset ( $p < n$  case)

## Description

Publicly available dataset from the Women's Interagency HIV cohort Study (WIHS). Inclusion criteria of the study were that women at enrolment were (i) alive, (ii) HIV-1 infected, and (iii) free of clinical AIDS symptoms. Women were followed until the first of the following occurred: (i) treatment initiation (HAART), (ii) AIDS diagnosis, (iii) death, or administrative censoring. The studied outcomes were the competing risks "AIDS/Death (before HAART)" and "Treatment Initiation (HAART)". However, here, for simplification purposes, only the first of the two competing events (i.e. the time to AIDS/Death), was used in this dataset example. Likewise, the entire study enrolled 1164 women, but only the complete cases were used in this dataset example for simplification. Variables included history of Injection Drug Use ("IDU") at enrollment, African American ethnicity ("Race"), age ("Age"), and baseline CD4 count ("CD4"). The question in this dataset example was whether it is possible to achieve a prognostication of patients for AIDS and HAART. See Bacon et al. (2005) and the WIHS website for more details.

## Usage

Real.1

## Format

Dataset consists of a numeric `data.frame` containing  $n = 485$  complete observations (samples) by rows and  $p = 6$  clinical variables by columns, including the censoring indicator and (censored) time-to-event variables. It comes as a compressed Rda data file.

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Acknowledgments: This project was partially funded by the National Institutes of Health NIH - National Cancer Institute (R01-CA160593) to J-E. Dazard and J.S. Rao.

## Source

See real clinical data application in Dazard et al., 2015.

## References

- Dazard J-E., Choe M., LeBlanc M. and Rao J.S. (2015). "*Cross-validation and Peeling Strategies for Survival Bump Hunting using Recursive Peeling Methods.*" (Submitted).
- Dazard J-E., Choe M., LeBlanc M. and Rao J.S. (2014). "*Cross-Validation of Survival Bump Hunting by Recursive Peeling Methods.*" In JSM Proceedings, Survival Methods for Risk Estimation/Prediction Section. Boston, MA, USA. American Statistical Association IMS - JSM, p. 3366-3380.
- Dazard J-E. and J. S. Rao (2010). "*Local Sparse Bump Hunting.*" J. Comp Graph. Statistics, 19(4):900-92.
- Bacon M.C, von Wyl V., Alden C. et al. 2005. "*Semi-Supervised Methods to Predict Patient Survival from Gene Expression Data.*" Clin Diagn Lab Immunol 12(9): 1013-1019.

## See Also

<http://statepiaps.jhsph.edu/wihs/>

---

Real.2

*Real Dataset #2: Large Gene Expression Dataset ( $p \gg n$  case)*

---

## Description

Publicly available breast cancer gene expression profiling dataset from the Uppsala cohort study. It is entitled: "Genetic Reclassification of Histologic Grade Delineates New Clinical Subtypes of Breast Cancer". The goal of the study was to provide a more objective measure of grade with prognostic benefit for patients with moderately differentiated grade II (G2) tumors. To that end, expression profiles of primary invasive breast tumors were analyzed on microarrays to find a gene expression signature capable of discerning tumors of grade I (G1) and grade III (G3) histology. In this dataset, only the Uppsala cohort ( $n = 249$ ) and only the gene expression data was included although other clinical covariates are available as well. It contains  $p = 22647$  mRNA measurements from the Affymetrix Human Genome U133A Array platform on  $n = 249$  samples. The data was left after removal of outliers and incomplete observations and after removal of Affymetrix controls. See Ivshina et al. (2005) and Gene Expression Omnibus database repository (Accession number: #GSE4922) for more details.

## Usage

Real.2

## Format

Dataset consists of a numeric `data.frame` containing  $n = 177$  complete observations (samples) by rows and  $p = 22577$  variables by columns, including the censoring indicator and (censored) time-to-event variables. It comes as a compressed Rda data file.

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Acknowledgments: This project was partially funded by the National Institutes of Health NIH - National Cancer Institute (R01-CA160593) to J-E. Dazard and J.S. Rao.

**Source**

See real clinical data application in Dazard et al., 2015.

**References**

- Dazard J-E., Choe M., LeBlanc M. and Rao J.S. (2015). "*Cross-validation and Peeling Strategies for Survival Bump Hunting using Recursive Peeling Methods*." (Submitted).
- Dazard J-E., Choe M., LeBlanc M. and Rao J.S. (2014). "*Cross-Validation of Survival Bump Hunting by Recursive Peeling Methods*." In JSM Proceedings, Survival Methods for Risk Estimation/Prediction Section. Boston, MA, USA. American Statistical Association IMS - JSM, p. 3366-3380.
- Dazard J-E. and J. S. Rao (2010). "*Local Sparse Bump Hunting*." J. Comp Graph. Statistics, 19(4):900-92.
- Ivshina AV, George J, Senko O, Mow B et al. (2006). "*Genetic reclassification of histologic grade delineates new clinical subtypes of breast cancer*." Cancer Res 66(21):10292-301. PMID: 17079448

**See Also**

Gene Expression Omnibus (GEO) database. Accession number: #GSE4922 <http://www.ncbi.nlm.nih.gov/geo/query/acc.cgi?acc=GSE4922>

---

sbh

---

*Cross-Validated Survival Bump Hunting*


---

**Description**

Main end-user function for fitting a cross-validated Survival Bump Hunting (SBH) model. It returns a cross-validated PRSP object, as generated by our Patient Recursive Survival Peeling or PRSP algorithm.

**Usage**

```
sbh(dataset,
      B = 10, K = 5, A = 1000,
      vs = TRUE, cpv = FALSE,
      cvtype=c("combined", "averaged", "none"),
      cvcriterion=c("lrt", "cer", "lhr"),
      arg = "beta=0.05,alpha=0.1,minn=10,L=NULL,peelcriterion=\"lr\"",
      probval = NULL, timeval = NULL,
      parallel = FALSE, conf = NULL, seed = NULL)
```

## Arguments

dataset	data.frame or numeric matrix of input dataset containing the observed survival and status indicator variables in the first two columns, respectively, and all the covariates thereafter. If a data.frame is provided, it will be coerced to a numeric matrix.
B	Positive integer scalar of the number of replications of the cross-validation procedure. Defaults to 10.
K	Positive integer scalar of the number of folds for the cross-validation procedure. Defaults to 5.
A	Positive integer scalar of the number of permutations for the computation of cross-validated p-values. Defaults to 1000.
vs	logical scalar. Flag for optional variable (covariate) pre-selection. Defaults to TRUE.
cpv	logical scalar. Flag for computation of permutation p-values. Defaults to FALSE.
cvtype	Character vector describing the cross-validation technique in {"combined", "averaged", "none"}. If NULL, defaults to "combined".
cvcriterion	character vector describing the cross-validation optimization criterion in {"lrt", "cer", "lhr"}. If NULL, defaults to "lrt". Automatically reset to "none" if cvtype is set to "none".
arg	<p>Character vector describing the PRSP parameters:</p> <ul style="list-style-type: none"> <li>• alpha = fraction to peel off at each step. Defaults to 0.1.</li> <li>• beta = minimum support size resulting from the peeling sequence. Defaults to 0.05.</li> <li>• minn = minimum number of observation in a box. Defaults to 10.</li> <li>• L = fixed peeling length. Defaults to NULL.</li> <li>• peelcriterion in {"hr" for Log-Hazard Ratio (LHR), "lr" for Log-Rank Test (LRT), "ch" for Cumulative Hazard Summary (CHS)}. Defaults to "lr".</li> </ul> <p>Note that the parameters in arg come as a string of charaters between double quotes, where all parameter evaluations are separated by comas (see example).</p>
probval	Numeric scalar of the survival probability at which we want to get the endpoint box survival time. Defaults to NULL.
timeval	Numeric scalar of the survival time at which we want to get the endpoint box survival probability. Defaults to NULL.
parallel	Logical. Is parallel computing to be performed? Optional. Defaults to FALSE.
conf	List of parameters for cluster configuration. Inputs for R package <b>parallel</b> function makeCluster (R package <b>parallel</b> ) for cluster setup. Optional, defaults to NULL. See details for usage.
seed	Positive integer scalar of the user seed to reproduce the results.

## Details

The function relies on an internal variable pre-selection procedure before the PRSP algorithm is run. At this point, this is done by cross-validated Elasticnet Regularized Cox-Regression (from the R package **glmnet**). Both Elasticnet mixing (alpha) and shrinkage (lambda) parameters are simultaneously estimated by `glmnet::cv.glmnet` function internal cross-validation.



Also, at this point, the main function `sbh` performs the search of the *first* box of the recursive coverage (outer) loop of our Patient Recursive Survival Peeling (PRSP) algorithm.

The PRSP object contains cross-validated estimates of all the decision-rules of pre-selected covariates and all other statistical quantities of interest at each iteration of the peeling sequence (inner loop of the PRSP algorithm).

It enables the display of results graphically of/for model tuning/selection, all peeling trajectories, covariate traces and survival distributions (see plotting functions for more details).

The function offers a number of options for the type of cross-validation desired:  $K$ -fold (replicated)-averaged or-combined, as well as peeling and optimization criteria for model fitting, tuning and selectio and a few more parameters for the PRSP algorithm.

The function takes advantage of the R package **parallel**, which allows users to create a cluster of workstations on a local and/or remote machine(s), enabling scaling-up with the number of CPU cores specified and efficient parallel execution.

Discrete (or nominal) covariates should be made (or re-arranged into) ordinal variables.

If the computation of cross-validated p-value is desired, then running with the parallelization option is generally advised as it may take a while. In the case of large ( $p > n$ ) or very large ( $p \gg n$ ) datasets, it is required to use the parallelization option preferably on a hyperperformance cluster of workstations.

To run a parallel session (and parallel RNG) of the PRIMsrc procedures (`parallel=TRUE`), argument `conf` is to be specified (i.e. non `NULL`). It must list the specifications of the following parameters for cluster configuration: "names", "cpus", "type", "homo", "verbose", "outfile". These match the arguments described in function `makeCluster` of the R package **parallel**. All fields are required to properly configure the cluster, except for "names" and "cpus", which are the values used alternatively in the case of a cluster of type "SOCK" (socket), or in the case of a cluster of type other than "SOCK" (socket), respectively. See examples below.

- "names": names : character vector specifying the host names on which to run the job. Could default to a unique local machine, in which case, one may use the unique host name "localhost". Each host name can potentially be repeated to the number of CPU cores available on the corresponding machine.
- "cpus": spec : integer scalar specifying the total number of CPU cores to be used across the network of available nodes, counting the workernodes and masternode.
- "type": type : character vector specifying the cluster type ("SOCK", "PVM", "MPI").
- "homo": homogeneous : logical scalar to be set to `FALSE` for inhomogeneous clusters.
- "verbose": verbose : logical scalar to be set to `FALSE` for quiet mode.
- "outfile": outfile : character vector of the output log file name for the workernodes.

Note that argument `B` is internally reset to `conf$cpus*ceiling(B/conf$cpus)` in case the parallelization is used (i.e. `conf` is non `NULL`), where `conf$cpus` denotes the total number of CPUs to be used (see above).

The actual creation of the cluster, its initialization, and closing are all done internally. In addition, when random number generation is needed, the creation of separate streams of parallel RNG per node is done internally by distributing the stream states to the nodes (For more details see function `makeCluster` (R package **parallel**) and/or <http://www.stat.uiowa.edu/~luke/R/cluster/cluster.html>).

The use of a seed allows to reproduce the results within the same type of session: the same seed will reproduce the same results within a non-parallel session or within a parallel session, but it will not necessarily give the exact same results (up to sampling variability) between a non-parallelized and parallelized session due to the difference of management of the seed between the two (see parallel RNG and value of retuned seed below).

**Value**

Object of class PRSP (Patient Recursive Survival Peeling) List containing the following 20 fields:

x	numeric matrix from original dataset with pre-selected covariates only.
times	numeric vector of observed failure / survival times.
status	numeric vector of observed event indicator in {1,0}.
B	positive integer of the number of replications used in the cross-validation procedure.
K	positive integer of the number of folds used in the cross-validation procedure.
A	positive integer of the number of permutations used for the computation of permutation p-values.
vs	logical scalar of returned flag of optional variable pre-selection.
cpv	logical scalar of returned flag of optional computation of permutation p-values.
cvtype	character vector of the cross-validation technique used.
cvcriterion	character vector of cross-validation optimization criterion used.
varsign	numeric vector in {-1,+1} of directions of peeling for all pre-selected covariates.
selected	numeric vector giving the pre-selected covariates.
used	numeric vector giving the covariates used for peeling.
arg	character vector of the parameters used:
probval	Numeric scalar of survival probability used.
timeval	Numeric scalar of survival time used.
cvfit	List with 7 fields of cross-validated estimates: <ul style="list-style-type: none"> <li>• cv.maxsteps: numeric scalar of maximal ceiled-mean of number of peeling steps over the replicates</li> <li>• cv.nsteps: numeric scalar of optimal number of peeling steps according to the optimization criterion</li> <li>• cv.trace: list of numeric matrix and numeric vector of covariate usage traces or modal trace values at each step</li> <li>• cv.boxind: logical matrix in TRUE, FALSE of sample box membership indicator (columns) by peeling steps (rows)</li> <li>• cv.rules: data.frame of decision rules on the covariate (columns) by peeling steps (rows)</li> <li>• cv.stats: numeric matrix of box quantities of interest (columns) by peeling steps (rows)</li> <li>• cv.pval: numeric vector of log-rank permutation p-values of separation of survival distributions</li> </ul>
cvprofiles	List of ( $B$ ) of numeric vectors, one for each replicate, of the cross-validated statistics used in the optimization criterion (one set by user) as a function of the number of peeling steps.
cvmeanprofiles	List of numeric vectors of the cross-validated mean statistics over the replicates. used in the optimization criterion (one set by user) as a function of the number of peeling steps.
plot	logical scalar of the returned flag for plotting results (TRUE if CV successful).
seed	User seed(s) used: integer of a single value, if parallelization is used integer vector of values, one for each replication, if parallelization is not used.

## Note

Unique end-user function for fitting the Survival Bump Hunting model.

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Acknowledgments: This project was partially funded by the National Institutes of Health NIH - National Cancer Institute (R01-CA160593) to J-E. Dazard and J.S. Rao.

## References

- Dazard J-E., Choe M., LeBlanc M. and Rao J.S. (2015). "*Cross-validation and Peeling Strategies for Survival Bump Hunting using Recursive Peeling Methods*." (Submitted).
- Dazard J-E., Choe M., LeBlanc M. and Rao J.S. (2014). "*Cross-Validation of Survival Bump Hunting by Recursive Peeling Methods*." In JSM Proceedings, Survival Methods for Risk Estimation/Prediction Section. Boston, MA, USA. American Statistical Association IMS - JSM, p. 3366-3380.
- Dazard J-E. and J. S. Rao (2010). "*Local Sparse Bump Hunting*." J. Comp Graph. Statistics, 19(4):900-92.

## See Also

- makeCluster (R package **parallel**)
- cv.glmnet (R package **glmnet**)
- glmnet (R package **glmnet**)

## Examples

```
#=====
# Loading the library and its dependencies
#=====
library("PRIMsrc")

## Not run:
#=====
# PRIMsrc package news
#=====
PRIMsrc.news()

#=====
# PRIMsrc package citation
#=====
citation("PRIMsrc")

#=====
# Demo with a synthetic dataset
# Use help for descriptions
#=====
```

```

data("Synthetic.1", "Synthetic.5", "Real.1", "Real.2", package="PRIMsrc")
?Synthetic.1
?Synthetic.5
?Real.1
?Real.2

## End(Not run)

#=====
# Simulated dataset #1 (n=250, p=3)
# Replicated Combined Cross-Validation (RCCV)
# Peeling criterion = LRT
# Optimization criterion = LRT
# Without parallelization
# Without computation of permutation p-values
#=====
CVCOMBREP.synt1 <- sbh(dataset = Synthetic.1,
                      cvtype = "combined", cvcriterion = "lrt",
                      B = 1, K = 5,
                      vs = TRUE, cpv = FALSE, probval = 0.5,
                      arg = "beta=0.05,
                           alpha=0.1,
                           minn=10,
                           L=NULL,
                           peelcriterion=\"lr\"",
                      parallel = FALSE, conf = NULL, seed = 123)

# selected covariates:
selected <- CVCOMBREP.synt1$selected
selected
# covariates used for peeling:
used <- CVCOMBREP.synt1$used
used
# some output results:
CVCOMBREP.synt1$cvfit$cv.maxsteps
CVCOMBREP.synt1$cvfit$cv.nsteps
CVCOMBREP.synt1$cvfit$cv.trace
CVCOMBREP.synt1$cvfit$cv.rules$frame[,used]
round(CVCOMBREP.synt1$cvfit$cv.stats$mean,2)

## Not run:
#=====
# Examples of parallel backend parametrization
#=====
# Example #1 - 1-Quad (4-core double threaded) PC
# Running WINDOWS
# With SOCKET communication
#=====
if (.Platform$OS.type == "windows") {
  cpus <- detectCores()
  conf <- list("names" = rep("localhost", cpus),
              "cpus" = cpus,
              "type" = "SOCK",
              "homo" = TRUE,
              "verbose" = TRUE,
              "outfile" = "")
}

```

```

#####
# Example #2 - 1 master node + 3 worker nodes cluster
# All nodes equipped with identical setups and multicores
# Running LINUX
# With SOCKET communication
#####
if (.Platform$OS.type == "unix") {
  masterhost <- Sys.getenv("HOSTNAME")
  slavehosts <- c("compute-0-0", "compute-0-1", "compute-0-2")
  nodes <- length(slavehosts) + 1
  cpus <- 8
  conf <- list("names" = c(rep(masterhost, cpus),
                           rep(slavehosts, cpus)),
              "cpus" = nodes * cpus,
              "type" = "SOCK",
              "homo" = TRUE,
              "verbose" = TRUE,
              "outfile" = "")
}
#####
# Example #3 - Multinode multicore per node cluster
# Running LINUX
# with MPI communication
# Here, a file named ".nodes" (e.g. in the home directory)
# contains the list of nodes of the cluster
#####
if (.Platform$OS.type == "unix") {
  hosts <- scan(file=paste(Sys.getenv("HOME"), "/.nodes", sep=""),
               what="",
               sep="\n")
  hostnames <- unique(hosts)
  nodes <- length(hostnames)
  cpus <- length(hosts)/length(hostnames)
  conf <- list("cpus" = nodes * cpus,
              "type" = "MPI",
              "homo" = TRUE,
              "verbose" = TRUE,
              "outfile" = "")
}

#####
# Simulated dataset #1 (n=250, p=3)
# Replicated Combined Cross-Validation (RCCV)
# Peeling criterion = LRT
# Optimization criterion = LRT
# With parallelization
# With computation of permutation p-values
#####
CVCOMBREP.synt1 <- sbh(dataset = Synthetic.1,
                      cvtype = "combined", cvcriterion = "lrt",
                      B = 10, K = 5, A = 1024,
                      vs = TRUE, cpv = TRUE, probval = 0.5,
                      arg = "beta=0.05,
                           alpha=0.1,
                           minn=10,
                           L=NULL,
                           peelcriterion=\"lr\"",

```

```

parallel = TRUE, conf = conf, seed = 123)

# selected covariates:
selected <- CVCOMBREP.synt1$selected
selected
# covariates used for peeling:
used <- CVCOMBREP.synt1$used
used
# some output results:
CVCOMBREP.synt1$cvfit$cv.maxsteps
CVCOMBREP.synt1$cvfit$cv.nsteps
CVCOMBREP.synt1$cvfit$cv.trace
CVCOMBREP.synt1$cvfit$cv.pval
CVCOMBREP.synt1$cvfit$cv.rules$frame[,used]
round(CVCOMBREP.synt1$cvfit$cv.stats$mean,2)

## End(Not run)

```

summary.PRSP

*Summary Function***Description**

S3 generic summary function to display the main parameters of a PRSP object.

**Usage**

```

## S3 method for class 'PRSP'
summary(object, ...)

```

**Arguments**

object	Object of class PRSP as generated by the main function <a href="#">sbh</a> .
...	Further generic arguments passed to the summary function.

**Value**

Displays the main parameters of the passed PRSP object.

**Note**

End-user summary function.

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Acknowledgments: This project was partially funded by the National Institutes of Health NIH - National Cancer Institute (R01-CA160593) to J-E. Dazard and J.S. Rao.

## References

- Dazard J-E., Choe M., LeBlanc M. and Rao J.S. (2015). "*Cross-validation and Peeling Strategies for Survival Bump Hunting using Recursive Peeling Methods.*" (Submitted).
- Dazard J-E., Choe M., LeBlanc M. and Rao J.S. (2014). "*Cross-Validation of Survival Bump Hunting by Recursive Peeling Methods.*" In JSM Proceedings, Survival Methods for Risk Estimation/Prediction Section. Boston, MA, USA. American Statistical Association IMS - JSM, p. 3366-3380.
- Dazard J-E. and J. S. Rao (2010). "*Local Sparse Bump Hunting.*" J. Comp Graph. Statistics, 19(4):900-92.

---

Synthetic.1

---

Synthetic Dataset #1:  $p < n$  case

---

## Description

Modeling survival model #1 as described in Dazard et al. (2015) with censoring. Here, the regression function uses all of the predictors, which are also part of the design matrix. Survival time was generated from an exponential model with rate parameter  $\lambda$  (and mean  $\frac{1}{\lambda}$ ) according to a Cox-PH model with hazard  $\exp(\eta)$ , where  $\eta(\cdot)$  is the regression function. Censoring indicator were generated from a uniform distribution on  $[0, 3]$ . In this synthetic example, all covariates are continuous, i.i.d. from a multivariate uniform distribution on  $[0, 1]$ .

## Usage

Synthetic.1

## Format

Each dataset consists of a numeric matrix containing  $n = 250$  observations (samples) by rows and  $p = 5$  variables by columns, including the censoring indicator and (censored) time-to-event variables. It comes as a compressed Rda data file.

## Author(s)

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Acknowledgments: This project was partially funded by the National Institutes of Health NIH - National Cancer Institute (R01-CA160593) to J-E. Dazard and J.S. Rao.

## Source

See simulated survival model #1 in Dazard et al., 2015.

## References

- Dazard J-E., Choe M., LeBlanc M. and Rao J.S. (2015). "*Cross-validation and Peeling Strategies for Survival Bump Hunting using Recursive Peeling Methods.*" (Submitted).
- Dazard J-E., Choe M., LeBlanc M. and Rao J.S. (2014). "*Cross-Validation of Survival Bump Hunting by Recursive Peeling Methods.*" In JSM Proceedings, Survival Methods for Risk Estimation/Prediction Section. Boston, MA, USA. American Statistical Association IMS - JSM, p. 3366-3380.
- Dazard J-E. and J. S. Rao (2010). "*Local Sparse Bump Hunting.*" J. Comp Graph. Statistics, 19(4):900-92.

---

Synthetic.2

*Synthetic Dataset #2:  $p < n$  case*

---

## Description

Modeling survival model #2 as described in Dazard et al. (2015) with censoring. Here, the regression function uses some informative predictors. The rest represent un-informative noisy covariates, which are not part of the design matrix. Survival time was generated from an exponential model with rate parameter  $\lambda$  (and mean  $\frac{1}{\lambda}$ ) according to a Cox-PH model with hazard  $\exp(\eta)$ , where  $\eta(\cdot)$  is the regression function. Censoring indicator were generated from a uniform distribution on  $[0, 3]$ . In this synthetic example, all covariates are continuous, i.i.d. from a multivariate uniform distribution on  $[0, 1]$ .

## Usage

Synthetic.2

## Format

Each dataset consists of a numeric matrix containing  $n = 250$  observations (samples) by rows and  $p = 5$  variables by columns, including the censoring indicator and (censored) time-to-event variables. It comes as a compressed Rda data file.

## Author(s)

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Acknowledgments: This project was partially funded by the National Institutes of Health NIH - National Cancer Institute (R01-CA160593) to J-E. Dazard and J.S. Rao.

## Source

See simulated survival model #2 in Dazard et al., 2015.



## References

- Dazard J-E., Choe M., LeBlanc M. and Rao J.S. (2015). "*Cross-validation and Peeling Strategies for Survival Bump Hunting using Recursive Peeling Methods.*" (Submitted).
- Dazard J-E., Choe M., LeBlanc M. and Rao J.S. (2014). "*Cross-Validation of Survival Bump Hunting by Recursive Peeling Methods.*" In JSM Proceedings, Survival Methods for Risk Estimation/Prediction Section. Boston, MA, USA. American Statistical Association IMS - JSM, p. 3366-3380.
- Dazard J-E. and J. S. Rao (2010). "*Local Sparse Bump Hunting.*" J. Comp Graph. Statistics, 19(4):900-92.

---

 Synthetic.3

---

 Synthetic Dataset #3:  $p < n$  case
 

---

## Description

Modeling survival model #3 as described in Dazard et al. (2015) with censoring. Here, the regression function does not include any of the predictors. This means that none of the covariates is informative (noisy), and are not part of the design matrix. Survival time was generated from an exponential model with rate parameter  $\lambda$  (and mean  $\frac{1}{\lambda}$ ) according to a Cox-PH model with hazard  $\exp(\eta)$ , where  $\eta(\cdot)$  is the regression function. Censoring indicator were generated from a uniform distribution on  $[0, 3]$ . In this synthetic example, all covariates are continuous, i.i.d. from a multivariate uniform distribution on  $[0, 1]$ .

## Usage

Synthetic.3

## Format

Each dataset consists of a numeric matrix containing  $n = 250$  observations (samples) by rows and  $p = 5$  variables by columns, including the censoring indicator and (censored) time-to-event variables. It comes as a compressed Rda data file.

## Author(s)

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Acknowledgments: This project was partially funded by the National Institutes of Health NIH - National Cancer Institute (R01-CA160593) to J-E. Dazard and J.S. Rao.

## Source

See simulated survival model #3 in Dazard et al., 2015.

## References

- Dazard J-E., Choe M., LeBlanc M. and Rao J.S. (2015). "*Cross-validation and Peeling Strategies for Survival Bump Hunting using Recursive Peeling Methods.*" (Submitted).
- Dazard J-E., Choe M., LeBlanc M. and Rao J.S. (2014). "*Cross-Validation of Survival Bump Hunting by Recursive Peeling Methods.*" In JSM Proceedings, Survival Methods for Risk Estimation/Prediction Section. Boston, MA, USA. American Statistical Association IMS - JSM, p. 3366-3380.
- Dazard J-E. and J. S. Rao (2010). "*Local Sparse Bump Hunting.*" J. Comp Graph. Statistics, 19(4):900-92.

---

Synthetic.4

*Synthetic Dataset #4:  $p < n$  case*

---

## Description

Modeling survival model #4 as described in Dazard et al. (2015) with censoring. Here, the regression function uses all of the predictors, which are also part of the design matrix. In this example, the signal is limited to a box-shaped region  $R$  of the predictor space. Survival time was generated from an exponential model with rate parameter  $\lambda$  (and mean  $\frac{1}{\lambda}$ ) according to a Cox-PH model with hazard  $\exp(\eta)$ , where  $\eta(\cdot)$  is the regression function. Censoring indicator were generated from a uniform distribution on  $[0, 3]$ . In this synthetic example, all covariates are continuous, i.i.d. from a multivariate uniform distribution on  $[0, 1]$ .

## Usage

Synthetic.4

## Format

Each dataset consists of a numeric matrix containing  $n = 250$  observations (samples) by rows and  $p = 5$  variables by columns, including the censoring indicator and (censored) time-to-event variables. It comes as a compressed Rda data file.

## Author(s)

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## Source

See simulated survival model #4 in Dazard et al., 2015.

## References

- Dazard J-E., Choe M., LeBlanc M. and Rao J.S. (2015). "Cross-validation and Peeling Strategies for Survival Bump Hunting using Recursive Peeling Methods." (Submitted).
- Dazard J-E., Choe M., LeBlanc M. and Rao J.S. (2014). "Cross-Validation of Survival Bump Hunting by Recursive Peeling Methods." In JSM Proceedings, Survival Methods for Risk Estimation/Prediction Section. Boston, MA, USA. American Statistical Association IMS - JSM, p. 3366-3380.
- Dazard J-E. and J. S. Rao (2010). "Local Sparse Bump Hunting." J. Comp Graph. Statistics, 19(4):900-92.

---

 Synthetic.5

 Synthetic Dataset #5:  $p > n$  case
 

---

## Description

Modeling survival model #5 as described in Dazard et al. (2015) with censoring. Here, the regression function uses 1/10 of informative predictors in a  $p > n$  situation with  $p = 1000$  and  $n = 100$ . The rest represents non-informative noisy covariates, which are not part of the design matrix. Survival time was generated from an exponential model with rate parameter  $\lambda$  (and mean  $\frac{1}{\lambda}$ ) according to a Cox-PH model with hazard  $\exp(\eta)$ , where  $\eta(\cdot)$  is the regression function. Censoring indicator were generated from a uniform distribution on  $[0, 2]$ . In this synthetic example, all covariates are continuous, i.i.d. from a multivariate standard normal distribution.

## Usage

Synthetic.5

## Format

Each dataset consists of a numeric matrix containing  $n = 100$  observations (samples) by rows and  $p = 1002$  variables by columns, including the censoring indicator and (censored) time-to-event variables. It comes as a compressed Rda data file.

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Acknowledgments: This project was partially funded by the National Institutes of Health NIH - National Cancer Institute (R01-CA160593) to J-E. Dazard and J.S. Rao.

## Source

See simulated survival model #2 in Dazard et al., 2015.

**References**

- Dazard J-E., Choe M., LeBlanc M. and Rao J.S. (2015). "*Cross-validation and Peeling Strategies for Survival Bump Hunting using Recursive Peeling Methods.*" (Submitted).
- Dazard J-E., Choe M., LeBlanc M. and Rao J.S. (2014). "*Cross-Validation of Survival Bump Hunting by Recursive Peeling Methods.*" In JSM Proceedings, Survival Methods for Risk Estimation/Prediction Section. Boston, MA, USA. American Statistical Association IMS - JSM, p. 3366-3380.
- Dazard J-E. and J. S. Rao (2010). "*Local Sparse Bump Hunting.*" J. Comp Graph. Statistics, 19(4):900-92.

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