Package 'PRIMsrc'

March 4, 2015

Type Package

Title PRIM Survival Regression Classification
Version 0.5.0
Date 2015-03-04
Author Jean-Eudes Dazard [aut, cre], Michael Choe [ctb], Michael LeBlanc [ctb], Alberto Santana [ctb] Maintainer Jean-Eudes Dazard <jxd101@case.edu> Description Performs Bump Hunting by Patient Rule Induction Method in Survival, Regression and Classification settings. Depends R (>= 3.0.2), parallel, survival, Hmisc, glmnet, MASS URL https://github.com/jedazard/PRIMsrc Repository PRIMsrc, GitHub, Inc. License GPL (>= 3) file LICENSE</jxd101@case.edu>
LazyLoad yes LazyData yes
Archs i386, x64
R topics documented: PRIMsrc-package
plot.boxkm.PRSP
plot.boxtrace.PRSP
plot.boxtraj.PRSP
plot.profile.PRSP
plot.scatter.PRSP
PRIMsrc.news 17 Real.1 18
Real.2
sbh
summary.PRSP
Synthetic.1
Synthetic.2
Synthetic.3
Synthetic.4
Synthetic.5
Index 35

PRIMsrc-package

PRIMsrc-package Bump Hunting by Patient Rule Induction Method in Survival, Regression and Classification settings

Description

Performs a Bump Hunting search by Patient Rule Induction Method. 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 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 high-dimensional multivariate datasets, where the number of variables far exceeds that of the samples ($p \gg n$ paradigm).

Details

The current version is the initial development release that only includes the case of a survival response in either low $(p \le n)$ or high-dimensional situations (p > n). Ultimately, it will include all the features described above. New features will be added soon as they are available. At this point, the main function sbh depends on a internal cross-validated variable selection procedure by regularized Cox-regression from the R package **glmnet**.

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 FUNCTION

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.

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 model. Returns cross-validated "PRSP" object, as generated by our Patient Recursive Survival Peeling or PRSP algorithm at each iteration of the peeling sequence (inner loop of the PRSP algorithm). The object contains cross-validated estimates of all the decision-rules of covariates and other statistical quantities of interest. It also enables displaying results graphically of/for model tuning/selection, all peeling trajectories, variable traces, and survival distributions (see plotting functions below for more details). The function offers a few options such as the type of cross-validation desired (K-fold (replicated)-averaged or-combined), peeling and optimization critera for model fitting, 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. Discrete (or nominal) variables should be made (or re-arranged into) ordinal variables.

PRIMsrc-package 3

3. END-USER PLOTS FOR MODEL VALIDATION AND VISUALIZATION OF RESULTS plot.profile Visualization for Model Selection/Validation

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).

plot. scatter 2D Visualization of Data Scatter and Box Vertices

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).

plot.boxtraj Visualization of Peeling Trajectories/Profiles

S3 generic function for plotting the cross-validated peeling trajectories/profiles of a "PRSP" object. Applies to the covariates used for peeling only and other statistical quantities of interest at each iteration of the peeling sequence (inner loop of our PRSP algorithm).

plot.boxtrace Visualization of Covariates Traces

S3 generic function for plotting the cross-validated covariates traces of a "PRSP" object. Plot the cross-validated modal trace curves of variable importance and variable usage of covariates used for peeling at each iteration of the peeling sequence (inner loop of our PRSP algorithm).

plot.boxkm Visualization of Survival Distributions

S3 generic function for plotting the cross-validated survival distributions of a "PRSP" object. Plot the cross-validated Kaplan-Meir 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 variables were used, these variables 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 with rate parameter λ (and mean $\frac{1}{\lambda}$) according to a Cox-PH model with hazard exp(eta), where eta(.) 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

4 PRIMsrc-package

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 variables (p = 22645) dominates the number of observations (p = 249), or p >> n case.

Known Bugs/Problems: None at this time.

Author(s)

- "Jean-Eudes Dazard, Ph.D." < jxd101@case.edu>
- "Michael Choe, M.D." <mjc206@case.edu>
- "Michael LeBlanc, Ph.D." <mleblanc@fhcrc.org>
- "Alberto Santana, MBA." <ahs4@case.edu>

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.

See Also

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

plot.boxkm.PRSP 5

plot.boxkm.PRSP	Visualization of Survival Distributions
-----------------	---

Description

S3 generic function for plotting the cross-validated survival distributions of a "PRSP" object. Plot the cross-validated Kaplan-Meir 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

```
## S3 method for class 'PRSP'
plot.boxkm(x,
                            main = NULL,
                            xlab = "Time",
                            ylab = "Probability",
                            precision,
                            mark = 3,
                             col = 1,
                             lty = 1,
                             lwd = 1,
                             cex = 1,
                             only.last = FALSE,
                             nr = NULL,
                             nc = NULL,
                             device = NULL,
                             file = "Survival Plots",
                             path=getwd(),
                             horizontal = TRUE,
                             width = 11.5,
                            height = 8.5, ...)
```

Arguments

Χ	Object of class "PRSP" as generated by the main function sbh.
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. Lower bounded by the value $\frac{1}{A}$ of the number of replication A .
mark	Integer vector of mark parameters, which will be used to label the curves. Defaults to 3.
col	Integer vector of specifying colors for each curve. Defaults to 1.
lty	Integer vector of specifying line types for each curve. Defaults to 1.
lwd	Numeric vector of values for line widths. Defaults to 1.
cex	Numeric scalar specifying the size of the marks. Defaults to 1.

plot.boxkm.PRSP

only.last	Logical scalar defining whether only the last step of the peeling sequence should be plotted. Defaults to FALSE.
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 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 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 $survival$).

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/#number of permutations (A).

Value

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

Note

End-user plotting function.

Author(s)

- "Jean-Eudes Dazard, Ph.D." < jxd101@case.edu>
- "Michael Choe, M.D." <mjc206@case.edu>
- "Michael LeBlanc, Ph.D." <mleblanc@fhcrc.org>
- "Alberto Santana, MBA." <ahs4@case.edu>

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).

plot.boxtrace.PRSP 7

 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

• plot.survfit (R package survival)

Examples

```
# Loading the library and its dependencies
library("PRIMsrc")
## Not run:
   # Simulated dataset #1 (n=250, p=3)
   # Replicated Combined Cross-Validation (RCCV)
   # Peeling criterion = LRT
   # Optimization criterion = LRT
   plot.boxkm(x = CVCOMBREP.synt1,
           main = paste("RCCV probability curves for model #1", sep=""),
           xlab = "Time", ylab = "Probability",
           cex = 1, yscale = 1, precision = 1/CVCOMBREP.synt1$A,
           device = NULL, file = "Survival Plots", path=getwd(),
           horizontal = TRUE, width = 11.5, height = 8.5)
## End(Not run)
```

plot.boxtrace.PRSP

Visualization of Covariates Traces

Description

S3 generic function for plotting the cross-validated covariates traces of a "PRSP" object. Applies to the covariates used for peeling only. Plot the cross-validated modal trace curves of variable importance and variable usage at each iteration of the peeling sequence (inner loop of our PRSP algorithm).

Usage

8 plot.boxtrace.PRSP

```
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

Х

**	as generated by the main randition com
main	Character vector. Main Title. Defaults to NULL.
center	Logical scalar. Shall the data be centered before?
scale	Logical scalar. Shall the data be scaled before?
hline	Numeric scalar of where the data is centred. If specified (i.e. not NULL), an horizontal line about this value is added to the plot.
col	Line color. Defaults to 1.
lty	Line type. Defaults to 1.
lwd	Line width. Defaults to 1.
cex	Symbol expansion. 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.

Object of class "PRSP" as generated by the main function sbh.

Details

The trace plots limit the display of traces to those only covariates that are used for peeling.

Due to the variability induced by cross-validation and replication, it is possible that more than one variable 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.

plot.boxtrace.PRSP 9

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

- "Jean-Eudes Dazard, Ph.D." < jxd101@case.edu>
- "Michael Choe, M.D." <mjc206@case.edu>
- "Michael LeBlanc, Ph.D." <mleblanc@fhcrc.org>
- "Alberto Santana, MBA." <ahs4@case.edu>

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

10 plot.boxtraj.PRSP

```
device = NULL, file = "Covariate Trace Plots", path=getwd(),
horizontal = FALSE, width = 8.5, height = 8.5)
```

plot.boxtraj.PRSP

End(Not run)

Visualization of Peeling Trajectories/Profiles

Description

S3 generic function for plotting the cross-validated peeling trajectories/profiles of a "PRSP" object. Applies to the covariates used for peeling only and other statistical quantities of interest at each iteration of the peeling sequence (inner loop of our PRSP algorithm).

Usage

```
## S3 method for class 'PRSP'
plot.boxtraj(x,
                               main = NULL,
                               xlab = "Box Mass",
                               ylab = "Variable Range",
                               col = 1,
                               1ty = 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 = 8.5, ...)
```

Arguments

X	Object of class "PRSP" as generated by the main function sbh.
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 "Variable Range".
col	Line color. Defaults to 1.
lty	Line type. Defaults to 1.
lwd	Line width. Defaults to 1.
cex	Symbol expansion. Defaults to 1.
add.legend	Logical scalar. Should the legend be added to the current open graphics device?. Defaults to FALSE.

plot.boxtraj.PRSP 11

Character vector of legend content Defaults to NULL

text.legend	character vector of legend content. Defaults to NOLL.
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.

Details

taxt lagand

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

Generic arguments passed to other plotting functions.

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)

- "Jean-Eudes Dazard, Ph.D." < jxd101@case.edu>
- "Michael Choe, M.D." <mjc206@case.edu>
- "Michael LeBlanc, Ph.D." <mleblanc@fhcrc.org>
- "Alberto Santana, MBA." <ahs4@case.edu>

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.

- 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.

12 plot.profile.PRSP

Examples

```
# Loading the library and its dependencies
library("PRIMsrc")
## Not run:
  #-----
  # Simulated dataset #1 (n=250, p=3)
  # Replicated Combined Cross-Validation (RCCV)
  # Peeling criterion = LRT
  # Optimization criterion = LRT
  #-----
  plot.boxtraj(x = CVCOMBREP.synt1,
           main = paste("RCCV peeling trajectories for model #1", sep=""),
            col = 2:4, lty = c(1,1,1),
            device = NULL, file = "Covariate Trajectory Plots", path=getwd(),
            horizontal = FALSE, width = 8.5, height = 8.5)
## End(Not run)
```

plot.profile.PRSP

Visualization for Model Selection/Validation

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

```
## S3 method for class 'PRSP'
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,
                                1wd = 2,
                                cex = 2,
                                device = NULL,
                                file = "Profile Plot",
                                path=getwd(),
                                horizontal = FALSE,
                                width = 8.5,
                                height = 5, \ldots)
```

plot.profile.PRSP

Arguments

x	Object of class "PRSP" as generated by the main function sbh.
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	$\label{logical} Logical scalar. Shall the individual profiles (for all replicates) be plotted? Defaults to TRUE.$
pch	Symbol number for all the profiles. Defaults to 20.
col	Line color of the mean profile. Defaults to 1. If more than eight profiles are plotted, line colors will be recycled.
lty	Line type of the mean profile. Defaults to 1.
lwd	Line width of the mean profile. Defaults to 2.
cex	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	${\sf Logical}$ 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.

14 plot.profile.PRSP

Author(s)

- "Jean-Eudes Dazard, Ph.D." < jxd101@case.edu>
- "Michael Choe, M.D." <mjc206@case.edu>
- "Michael LeBlanc, Ph.D." <mleblanc@fhcrc.org>
- "Alberto Santana, MBA." <ahs4@case.edu>

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")
## Not run:
   # Simulated dataset #1 (n=250, p=3)
   # Replicated Combined Cross-Validation (RCCV)
   # Peeling criterion = LRT
   # Optimization criterion = LRT
   _____
   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)
## End(Not run)
```

plot.scatter.PRSP 15

plot.scatter.PRSP 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

```
## S3 method for class 'PRSP'
plot.scatter(x,
                               main = NULL,
                               proj = c(1,2),
                               splom = TRUE,
                               boxes = FALSE,
                               steps = x$cvfit$cv.nsteps,
                               add.legend = TRUE,
                               pch = 16,
                               cex = 0.7,
                               col = 1,
                               box.col = 2,
                               box.1ty = 2,
                               box.lwd = 1,
                               device = NULL,
                               file = "Scatter Plot",
                               path=getwd(),
                               horizontal = FALSE,
                               width = 5,
                               height = 5, \ldots)
```

Arguments

X	Object of class "PRSP" as generated by the main function sbh.
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 one wants to plot the box vertices. Defaults to the last peeling step only.
add.legend	Logical scalar. Shall the legend of steps numbers be plotted? Defaults to TRUE.
pch	Symbol number for the scatter plot. Defaults to 16.
cex	Symbol expansion. Defaults to 0.7.
col	Symbol color. Defaults to 1.

16 plot.scatter.PRSP

box.col	Line color of the box vertices. Defaults to 2.
box.lty	Line type of box vertices. Defaults to 2.
box.lwd	Line width of box vertices. Defaults to 1.
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	${\sf Logical}$ 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.

Author(s)

- "Jean-Eudes Dazard, Ph.D." < jxd101@case.edu>
- "Michael Choe, M.D." <mjc206@case.edu>
- "Michael LeBlanc, Ph.D." <mleblanc@fhcrc.org>
- "Alberto Santana, MBA." <ahs4@case.edu>

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.

- 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 17

Examples

```
# Loading the library and its dependencies
library("PRIMsrc")
## Not run:
  # Simulated dataset #1 (n=250, p=3)
  # Replicated Combined Cross-Validation (RCCV)
  # Peeling criterion = LRT
  # Optimization criterion = LRT
  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,
           add.legend = TRUE, cex = 0.5,
           box.col = "red", box.lty = 3, box.lwd = 1,
           device = NULL, file = "Scatter Plot", path=getwd(),
           horizontal = FALSE, width = 5, height = 5)
## End(Not run)
```

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.

18 Real.1

Author(s)

- "Jean-Eudes Dazard, Ph.D." < jxd101@case.edu>
- "Michael Choe, M.D." <mjc206@case.edu>
- "Michael LeBlanc, Ph.D." <mleblanc@fhcrc.org>
- "Alberto Santana, MBA." <ahs4@case.edu>

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.

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 (p< n case), including the censoring indicator and (censored) time-to-event variables. It comes as a compressed Rda data file.

Real.2 19

Author(s)

- "Jean-Eudes Dazard, Ph.D." < jxd101@case.edu>
- "Michael Choe, M.D." <mjc206@case.edu>
- "Michael LeBlanc, Ph.D." <mleblanc@fhcrc.org>
- "Alberto Santana, MBA." <ahs4@case.edu>

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.

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 >> 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 with n=177 samples after removal of outliers and incomplete observations and p=22577 variables after removal of Affymetrix controls. See Ivshina et al. (2005) and Gene Expression Omnibus database repository (Accession number: #GSE4922) for more details.

20 Real.2

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 (p>>n case), after including the censoring indicator and (censored) time-to-event variables. It comes as a compressed Rda data file.

Author(s)

- "Jean-Eudes Dazard, Ph.D." < jxd101@case.edu>
- "Michael Choe, M.D." <mjc206@case.edu>
- "Michael LeBlanc, Ph.D." <mleblanc@fhcrc.org>
- "Alberto Santana, MBA." <ahs4@case.edu>

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.

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 model. Returns cross-validated "PRSP" object, as generated by our Patient Recursive Survival Peeling or PRSP algorithm at each iteration of the peeling sequence (inner loop of the PRSP algorithm).

Usage

```
sbh(dataset, discr, B = 10, K = 5, A = 1000, cpv = FALSE,
    cvtype = "combined", cvcriterion = "lrt",
    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.
discr	Logical vector describing what covariates are discrete. Defaults to logical(ncol(dataset)-2).
В	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.
срv	logical scalar. Flag for computation of cross-validated p-values. Defaults to FALSE. If computation of cross-validated p-value is deired, then running with the parallelization option is strongly advised, as it may take a while otherwise.
cvtype	Character vector describing the cross-validation technique in {"none", "averaged", "combined"}. Defaults to "combined".
cvcriterion	character vector describing the cross-validation optimization criterion in {"lhr", "lrt", "cer"}. Defaults to "lrt". Automatically set to NULL if cvtype="none".
arg	Character vector describing the PRSP parameters:

- alpha = fraction to peel off at each step. Defaults to 0.1.
- beta = minimum support size resulting from the peeling sequence. Defaults to 0.05.
- minn = minimum number of observation in a box. Defaults to 10.
- L = fixed peeling length. Defaults to NULL.
- peelcriterion in {"hr" (LHR), "lr" (LRT)}. Defaults to "lr".

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).

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.

List of parameters for cluster configuration. Inputs for R package parallel

function makeCluster (R package **parallel**) for cluster setup. Optional, defaults

to NULL. See details for usage.

seed Positive integer scalar of the user seed to reproduce the results.

Details

conf

The function depends at this point on an internal cross-validated variable selection procedure by regularized Cox-regression from the R package **glmnet**.

The PRSP object contains cross-validated estimates of all the decision-rules of covariates and other statistical quantities of interest. It also enables displaying results graphically of/for model tuning/selection, all peeling trajectories, variable traces, and survival distributions (see plotting functions below 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 critera 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) variables should be made (or re-arranged into) ordinal variables.

It is required to use the parallelization and a hyperperformance cluster of workstations to run the computation of cross-validated p-values in the case of large n and/or large (p > n) or very large (p >> n) datasets.

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 18 fields:

x numeric matrix of original covariates.

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 pro-

cedure.

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

cross-validated p-values.

cpv logical scalar returned flag of computation of cross-validated 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 variables.

selected numeric vector giving the selected variable by regularized (Elastic-Net) Cox-

regression.

used numeric vector giving the variables 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:

- cv.maxsteps: numeric scalar of maximal ceiled-mean of number of peeling steps over the replicates
- cv.nsteps: numeric scalar of optimal number of peeling steps according to the optimization criterion
- cv.trace: list of numeric matrix and numeric vector of variable usage traces or modal trace values at each step
- cv.boxind: logical matrix in TRUE, FALSE of sample box membership indicator (columns) by peeling steps (rows)
- cv.rules: data.frame of decision rules on the variable (columns) by peeling steps (rows)
- cv.stats: numeric matrix of box quantities of interest (columns) by peeling steps (rows)
- cv.pval: numeric vector of cross-validated log-rank p-values of sepraration of survival distributions

List (B) of numeric vectors, one for each replicate, of the cross-validated
statistic used in the optimization criterion (set by user) as 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.

Author(s)

- "Jean-Eudes Dazard, Ph.D." < jxd101@case.edu>
- "Michael Choe, M.D." <mjc206@case.edu>
- "Michael LeBlanc, Ph.D." <mleblanc@fhcrc.org>
- "Alberto Santana, MBA." <ahs4@case.edu>

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.

See Also

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

Examples

```
# PRIMsrc package citation
   citation("PRIMsrc")
   # Use of two synthetic and two real datasets
   # 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 cross-validated p-values
CVCOMBREP.synt1 <- sbh(dataset = Synthetic.1,</pre>
                  cvtype = "combined", cvcriterion = "lrt",
                  B = 5, K = 5, 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 variables:
selected <- CVCOMBREP.synt1$selected</pre>
selected
# variables used for peeling:
used <- CVCOMBREP.synt1$used</pre>
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)
# Simulated dataset #5 (n=100, p=1000)
# Replicated Combined Cross-Validation (RCCV)
# Peeling criterion = LRT
# Optimization criterion = LRT
# Without parallelization
# Without computation of cross-validated p-values
CVCOMBREP.synt5 <- sbh(dataset = Synthetic.5,</pre>
```

```
cvtype = "combined", cvcriterion = "lrt",
                      B = 5, K = 5, 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 variables:
selected <- CVCOMBREP.synt5$selected</pre>
# variables used for peeling:
used <- CVCOMBREP.synt5$used
used
# some output results:
{\tt CVCOMBREP.synt5\$cvfit\$cv.maxsteps}
CVCOMBREP.synt5$cvfit$cv.nsteps
CVCOMBREP.synt5$cvfit$cv.trace
CVCOMBREP.synt5$cvfit$cv.rules$frame[,used]
round(CVCOMBREP.synt5$cvfit$cv.stats$mean,2)
# Real dataset #1 (n=485, p=4)
# Replicated Combined Cross-Validation (RCCV)
# Peeling criterion = LRT
# Optimization criterion = LRT
# Without parallelization
# Without computation of cross-validated p-values
CVCOMBREP.real1 <- sbh(dataset = Real.1,</pre>
                      discr = c(0,1,1,0),
                      cvtype = "combined", cvcriterion = "lrt",
                      B = 5, K = 5, 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 variables:
selected <- CVCOMBREP.real1$selected</pre>
# variables used for peeling:
used <- CVCOMBREP.real1$used
used
# some output results:
CVCOMBREP.real1$cvfit$cv.maxsteps
CVCOMBREP.real1$cvfit$cv.nsteps
CVCOMBREP.real1$cvfit$cv.trace
CVCOMBREP.real1$cvfit$cv.rules$frame[,used]
round(CVCOMBREP.real1$cvfit$cv.stats$mean,2)
## Not run:
```

Examples of parallelization below with

```
# a SOCKET or MPI cluster configuration
# 1- WINDOWS multicores PC with SOCKET communication
   With a 2-Quad (8-CPUs) PC
if (.Platform$OS.type == "windows") {
   cpus <- detectCores()</pre>
   conf <- list("names" = rep("localhost", cpus),</pre>
              "cpus" = cpus.
              "type" = "SOCK",
              "homo" = TRUE,
              "verbose" = TRUE,
              "outfile" = "")
# 2- LINUX multinodes cluster with SOCKET communication
    with 4-nodes (32-CPUs) cluster
    with 1 masternode and 3 workernodes
    All hosts run identical setups
    Same number of core CPUs (8) per node
if (.Platform$OS.type == "unix") {
   masterhost <- Sys.getenv("HOSTNAME")</pre>
   slavehosts <- c("compute-0-0", "compute-0-1", "compute-0-2")</pre>
   nodes <- length(slavehosts) + 1</pre>
   cpus <- 8
   conf <- list("names" = c(rep(masterhost, cpus),</pre>
                       rep(slavehosts, cpus)),
              "cpus" = nodes * cpus,
              "type" = "SOCK",
              "homo" = TRUE,
              "verbose" = TRUE,
              "outfile" = "")
# 3- LINUX multinodes cluster with MPI communication
  Here, a file named ".nodes" (e.g. in the home directory)
   must contain the list of nodes of the cluster
if (.Platform$OS.type == "unix") {
   hosts <- scan(file=paste(Sys.getenv("HOME"), "/.nodes", sep=""),</pre>
               what="",
               sep="\n")
   hostnames <- unique(hosts)</pre>
   nodes <- length(hostnames)</pre>
   cpus <- length(hosts)/length(hostnames)</pre>
   conf <- list("cpus" = nodes * cpus,</pre>
              "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 cross-validated p-values
CVCOMBREP.synt1 <- sbh(dataset = Synthetic.1,</pre>
                     cvtype = "combined", cvcriterion = "lrt",
                     B = 5, K = 5, A = 1024, 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 variables:
selected <- CVCOMBREP.synt1$selected</pre>
selected
# variables used for peeling:
used <- CVCOMBREP.synt1$used</pre>
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)
# Real dataset #2 (n=177, p=22577)
# Replicated Combined Cross-Validation (RCCV)
# Peeling criterion = LRT
# Optimization criterion = LRT
# With parallelization
# Without computation of cross-validated p-values
p <- ncol(Real.2) - 2</pre>
CVCOMBREP.real2 <- sbh(dataset = Real.2,</pre>
                     discr = rep(0,p),
                     cvtype = "combined", cvcriterion = "lrt",
                     B = 5, K = 5, cpv = FALSE, probval = 0.5,
                     arg = "beta=0.05,
                            alpha=0.1,
                            minn=10,
                            L=NULL,
                            peelcriterion=\"lr\"",
                     parallel = TRUE, conf = conf, seed = 123)
# selected variables:
selected <- CVCOMBREP.real2$selected</pre>
selected
# variables used for peeling:
used <- CVCOMBREP.real2$used</pre>
# some output results:
CVCOMBREP.real2$cvfit$cv.maxsteps
CVCOMBREP.real2$cvfit$cv.nsteps
```

summary.PRSP 29

```
CVCOMBREP.real2$cvfit$cv.trace
CVCOMBREP.real2$cvfit$cv.rules$frame[,used]
round(CVCOMBREP.real2$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 sbh.
... Further generic arguments passed to the summary function.

Value

Displays the main parameters of the passed "PRSP" object.

Note

End-user summary function.

Author(s)

- "Jean-Eudes Dazard, Ph.D." < jxd101@case.edu>
- "Michael Choe, M.D." <mjc206@case.edu>
- "Michael LeBlanc, Ph.D." <mleblanc@fhcrc.org>
- "Alberto Santana, MBA." <ahs4@case.edu>

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.

- 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.

30 Synthetic.1

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 λ (and mean $\frac{1}{\lambda}$) according to a Cox-PH model with hazard exp(eta), where eta(.) 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 (p< n case), including the censoring indicator and (censored) time-to-event variables. It comes as a compressed Rda data file.

Author(s)

- "Jean-Eudes Dazard, Ph.D." < jxd101@case.edu>
- "Michael Choe, M.D." <mjc206@case.edu>
- "Michael LeBlanc, Ph.D." <mleblanc@fhcrc.org>
- "Alberto Santana, MBA." <ahs4@case.edu>

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.

Source

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

- 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 31

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 variables, which are not part of the design matrix. Survival time was generated from an exponential model with rate parameter λ (and mean $\frac{1}{\lambda}$) according to a Cox-PH model with hazard exp(eta), where eta(.) 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 (p< n case), including the censoring indicator and (censored) time-to-event variables. It comes as a compressed Rda data file.

Author(s)

- "Jean-Eudes Dazard, Ph.D." < jxd101@case.edu>
- "Michael Choe, M.D." <mjc206@case.edu>
- "Michael LeBlanc, Ph.D." <mleblanc@fhcrc.org>
- "Alberto Santana, MBA." <ahs4@case.edu>

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.

Source

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

- 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.

32 Synthetic.3

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 variables is informative (noisy), and are not part of the design matrix. Survival time was generated from an exponential model with rate parameter λ (and mean $\frac{1}{\lambda}$) according to a Cox-PH model with hazard exp(eta), where eta(.) 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 (p< n case) including the censoring indicator and (censored) time-to-event variables. It comes as a compressed Rda data file.

Author(s)

- "Jean-Eudes Dazard, Ph.D." < jxd101@case.edu>
- "Michael Choe, M.D." <mjc206@case.edu>
- "Michael LeBlanc, Ph.D." <mleblanc@fhcrc.org>
- "Alberto Santana, MBA." <ahs4@case.edu>

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.

Source

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

- 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 33

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 thiss 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 λ (and mean $\frac{1}{\lambda}$) according to a Cox-PH model with hazard exp(eta), where eta(.) 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 (p< n case), including the censoring indicator and (censored) time-to-event variables. It comes as a compressed Rda data file.

Author(s)

- "Jean-Eudes Dazard, Ph.D." < jxd101@case.edu>
- "Michael Choe, M.D." <mjc206@case.edu>
- "Michael LeBlanc, Ph.D." <mleblanc@fhcrc.org>
- "Alberto Santana, MBA." <ahs4@case.edu>

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.

Source

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

- 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.

34 Synthetic.5

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 represent un-informative noisy variables, which are not part of the design matrix. Survival time was generated from an exponential model with rate parameter λ (and mean $\frac{1}{\lambda}$) according to a Cox-PH model with hazard exp(eta), where eta(.) 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=1000 variables by columns (p>n case), including the censoring indicator and (censored) time-to-event variables. It comes as a compressed Rda data file.

Author(s)

- "Jean-Eudes Dazard, Ph.D." < jxd101@case.edu>
- "Michael Choe, M.D." <mjc206@case.edu>
- "Michael LeBlanc, Ph.D." <mleblanc@fhcrc.org>
- "Alberto Santana, MBA." <ahs4@case.edu>

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.

Source

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

- 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.

Index

*Topic AIDS Prognostication	plot.boxkm.PRSP, 5
Real.1, 18	plot.boxtrace.PRSP,7
*Topic Bump Hunting	plot.boxtraj.PRSP, 10
plot.boxkm.PRSP, 5	plot.profile.PRSP, 12
plot.boxtrace.PRSP,7	plot.scatter.PRSP, 15
plot.boxtraj.PRSP, 10	PRIMsrc-package, 2
plot.profile.PRSP, 12	sbh, 21
plot.scatter.PRSP, 15	summary.PRSP, 29
PRIMsrc-package, 2	*Topic Survival/Risk Estimation &
sbh, 21	Prediction
summary.PRSP, 29	plot.boxkm.PRSP, 5
*Topic Cross-Validation	plot.boxtrace.PRSP,7
plot.boxkm.PRSP, 5	plot.boxtraj.PRSP, 10
plot.boxtrace.PRSP,7	plot.profile.PRSP, 12
plot.boxtraj.PRSP, 10	plot.scatter.PRSP, 15
plot.profile.PRSP, 12	PRIMsrc-package, 2
plot.scatter.PRSP, 15	sbh, 21
PRIMsrc-package, 2	summary.PRSP, 29
sbh, 21	*Topic Tumor sample comparisons
summary.PRSP, 29	Real.2, 19
*Topic Exploratory Survival/Risk	*Topic datasets
Analysis	Synthetic.1, 30
plot.boxkm.PRSP, 5	Synthetic.2,31
plot.boxtrace.PRSP,7	Synthetic.3,32
plot.boxtraj.PRSP, 10	Synthetic.4, 33
plot.profile.PRSP, 12	Synthetic.5, 34
plot.scatter.PRSP, 15	*Topic documentation
PRIMsrc-package, 2	PRIMsrc.news, 17
sbh, 21	mlat baylom 2
summary.PRSP, 29	plot.boxkm, 3
*Topic Non-Parametric Method	<pre>plot.boxkm(plot.boxkm.PRSP), 5 plot.boxkm.PRSP, 5</pre>
plot.boxkm.PRSP, 5	plot.boxkiii.FR3F, 3 plot.boxtrace, 3
plot.boxtrace.PRSP,7	plot.boxtrace, 3 plot.boxtrace (plot.boxtrace.PRSP), 7
plot.boxtraj.PRSP, 10	plot.boxtrace(plot.boxtrace.rksr), /
plot.profile.PRSP, 12	plot.boxtrace: RSI; 7 plot.boxtraj; 3
plot.scatter.PRSP, 15	plot.boxtraj, 5 plot.boxtraj.PRSP), 10
PRIMsrc-package, 2	plot.boxtraj.PRSP, 10
sbh, 21	plot.profile, 3
summary.PRSP, 29	plot.profile(plot.profile.PRSP), 12
*Topic Real Dataset	plot.profile.PRSP, 12
Real.1, 18	plot.scatter, 3
Real. 2, 19	plot.scatter(plot.scatter.PRSP), 15
*Topic Rule-Induction Method	plot.scatter.PRSP, 15

36 INDEX

```
PRIMsrc (PRIMsrc-package), 2
PRIMsrc-package, 2
PRIMsrc.news, 2, 17

Real.1, 3, 18
Real.2, 3, 19

sbh, 2, 5, 8, 10, 13, 15, 21, 29
summary, 2
summary, PRSP, 29
Synthetic.1, 3, 30
Synthetic.2, 3, 31
Synthetic.3, 3, 32
Synthetic.4, 3, 33
Synthetic.5, 3, 34
```