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Title Subdistribution Analysis of Competing Risks

Author Bob Gray <gray@jimmy.harvard.edu>

Maintainer Bob Gray <gray@jimmy.harvard.edu>

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Description Estimation, testing and regression modeling of subdistribution functions in competing risks, as described in Gray (1988), A class of K-sample tests for comparing the cumulative incidence of a competing risk, Ann. Stat. 16:1141-1154 <DOI:10.1214/aos/1176350951>, and Fine JP and Gray RJ (1999), A proportional hazards model for the subdistribution of a competing risk, JASA, 94:496-509, <DOI:10.1080/01621459.1999.10474144>.

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crr	<i>Competing Risks Regression</i>
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Description

regression modeling of subdistribution functions in competing risks

Usage

```
crr(ftime, fstatus, cov1, cov2, tf, cengroup, failcode=1, cencode=0,
subset, na.action=na.omit, gtol=1e-06, maxiter=10, init, variance=TRUE)
```

Arguments

ftime	vector of failure/censoring times
fstatus	vector with a unique code for each failure type and a separate code for censored observations
cov1	matrix (nobs x ncovs) of fixed covariates (either cov1, cov2, or both are required)
cov2	matrix of covariates that will be multiplied by functions of time; if used, often these covariates would also appear in cov1 to give a prop hazards effect plus a time interaction
tf	functions of time. A function that takes a vector of times as an argument and returns a matrix whose jth column is the value of the time function corresponding to the jth column of cov2 evaluated at the input time vector. At time tk, the model includes the term $\text{cov2}[, j] * \text{tf}(tk)[, j]$ as a covariate.
cengroup	vector with different values for each group with a distinct censoring distribution (the censoring distribution is estimated separately within these groups). All data in one group, if missing.
failcode	code of fstatus that denotes the failure type of interest
cencode	code of fstatus that denotes censored observations
subset	a logical vector specifying a subset of cases to include in the analysis
na.action	a function specifying the action to take for any cases missing any of ftime, fstatus, cov1, cov2, cengroup, or subset.
gtol	iteration stops when a function of the gradient is < gtol
maxiter	maximum number of iterations in Newton algorithm (0 computes scores and var at init, but performs no iterations)
init	initial values of regression parameters (default=all 0)
variance	If FALSE, then suppresses computation of the variance estimate and residuals

Details

Fits the 'proportional subdistribution hazards' regression model described in Fine and Gray (1999). This model directly assesses the effect of covariates on the subdistribution of a particular type of failure in a competing risks setting. The method implemented here is described in the paper as the weighted estimating equation.

While the use of model formulas is not supported, the `model.matrix` function can be used to generate suitable matrices of covariates from factors, eg `model.matrix(~factor1+factor2)[,-1]` will generate the variables for the factor coding of the factors `factor1` and `factor2`. The final `[,-1]` removes the constant term from the output of `model.matrix`.

The basic model assumes the subdistribution with covariates z is a constant shift on the complementary log log scale from a baseline subdistribution function. This can be generalized by including interactions of z with functions of time to allow the magnitude of the shift to change with follow-up time, through the `cov2` and `tfs` arguments. For example, if z is a vector of covariate values, and `uft` is a vector containing the unique failure times for failures of the type of interest (sorted in ascending order), then the coefficients a , b and c in the quadratic (in time) model $az + bzt + zt^2$ can be fit by specifying `cov1=z`, `cov2=cbind(z,z)`, `tf=function(uft) cbind(uft,uft*uft)`.

This function uses an estimate of the survivor function of the censoring distribution to reweight contributions to the risk sets for failures from competing causes. In a generalization of the methodology in the paper, the censoring distribution can be estimated separately within strata defined by the `cengroup` argument. If the censoring distribution is different within groups defined by covariates in the model, then validity of the method requires using separate estimates of the censoring distribution within those groups.

The residuals returned are analogous to the Schoenfeld residuals in ordinary survival models. Plotting the j th column of `res` against the vector of unique failure times checks for lack of fit over time in the corresponding covariate (column of `cov1`).

If `variance=FALSE`, then some of the functionality in `summary.crr` and `print.crr` will be lost. This option can be useful in situations where `crr` is called repeatedly for point estimates, but standard errors are not required, such as in some approaches to stepwise model selection.

Value

Returns a list of class `crr`, with components

<code>\$coef</code>	the estimated regression coefficients
<code>\$loglik</code>	log pseudo-likelihood evaluated at <code>coef</code>
<code>\$score</code>	derivatives of the log pseudo-likelihood evaluated at <code>coef</code>
<code>\$inf</code>	-second derivatives of the log pseudo-likelihood
<code>\$var</code>	estimated variance covariance matrix of <code>coef</code>
<code>\$res</code>	matrix of residuals giving the contribution to each score (columns) at each unique failure time (rows)
<code>\$uftime</code>	vector of unique failure times
<code>\$bfitj</code>	jumps in the Breslow-type estimate of the underlying sub-distribution cumulative hazard (used by <code>predict.crr()</code>)
<code>\$tfs</code>	the <code>tfs</code> matrix (output of <code>tf()</code> , if used)

\$converged	TRUE if the iterative algorithm converged
\$call	The call to crr
\$n	The number of observations used in fitting the model
\$n.missing	The number of observations removed from the input data due to missing values
\$loglik.null	The value of the log pseudo-likelihood when all the coefficients are 0
\$invinf	- inverse of second derivative matrix of the log pseudo-likelihood

References

Fine JP and Gray RJ (1999) A proportional hazards model for the subdistribution of a competing risk. *JASA* 94:496-509.

See Also

[predict.crr](#) [print.crr](#) [plot.predict.crr](#) [summary.crr](#)

Examples

```
# simulated data to test
set.seed(10)
ftime <- rexp(200)
fstatus <- sample(0:2,200,replace=TRUE)
cov <- matrix(runif(600),nrow=200)
dimnames(cov)[[2]] <- c('x1','x2','x3')
print(z <- crr(ftime,fstatus,cov))
summary(z)
z.p <- predict(z,rbind(c(.1,.5,.8),c(.1,.5,.2)))
plot(z.p,lty=1,color=2:3)
crr(ftime,fstatus,cov,failcode=2)
# quadratic in time for first cov
crr(ftime,fstatus,cov,cbind(cov[,1],cov[,1]),function(Uft) cbind(Uft,Uft^2))
#additional examples in test.R
```

cuminc

Cumulative Incidence Analysis

Description

Estimate cumulative incidence functions from competing risks data and test equality across groups

Usage

```
cuminc(ftime, fstatus, group, strata, rho=0, cencode=0,
subset, na.action=na.omit)
```

Arguments

<code>f_{time}</code>	failure time variable
<code>f_{status}</code>	variable with distinct codes for different causes of failure and also a distinct code for censored observations
<code>group</code>	estimates will be calculated within groups given by distinct values of this variable. Tests will compare these groups. If missing then treated as all one group (no test statistics)
<code>strata</code>	stratification variable. Has no effect on estimates. Tests will be stratified on this variable. (all data in 1 stratum, if missing)
<code>rho</code>	Power of the weight function used in the tests.
<code>cencode</code>	value of <code>f_{status}</code> variable which indicates the failure time is censored.
<code>subset</code>	a logical vector specifying a subset of cases to include in the analysis
<code>na.action</code>	a function specifying the action to take for any cases missing any of <code>f_{time}</code> , <code>f_{status}</code> , <code>group</code> , <code>strata</code> , or <code>subset</code> .

Value

A list with components giving the subdistribution estimates for each cause in each group, and a component `Tests` giving the test statistics and p-values for comparing the subdistribution for each cause across groups (if the number of groups is >1). The components giving the estimates have names that are a combination of the group name and the cause code. These components are also lists, with components

<code>time</code>	the times where the estimates are calculated
<code>est</code>	the estimated sub-distribution functions. These are step functions (all corners of the steps given), so they can be plotted using <code>ordinary lines()</code> commands. Estimates at particular times can be located using the <code>timepoints()</code> function.
<code>var</code>	the estimated variance of the estimates, which are estimates of the asymptotic variance of Aalen (1978).

Author(s)

Robert Gray

References

- Gray RJ (1988) A class of K-sample tests for comparing the cumulative incidence of a competing risk, *ANNALS OF STATISTICS*, 16:1141-1154.
- Kalbfleisch and Prentice (1980) *THE ANALYSIS OF FAILURE TIME DATA*, p 168-9.
- Aalen, O. (1978) Nonparametric estimation of partial transition probabilities in multiple decrement models, *ANNALS OF STATISTICS*, 6:534-545.

See Also

[plot.cuminc](#) [timepoints](#) [print.cuminc](#)

Examples

```

set.seed(2)
ss <- rexp(100)
gg <- factor(sample(1:3,100,replace=TRUE),1:3,c('a','b','c'))
cc <- sample(0:2,100,replace=TRUE)
strt <- sample(1:2,100,replace=TRUE)
print(xx <- cuminc(ss,cc,gg,strt))
plot(xx,lty=1,color=1:6)
# see also test.R, test.out

```

plot.cuminc

Create Labeled Cumulative Incidence Plots

Description

Plot method for cuminc. Creates labeled line plots from appropriate list input, for example, the output from cuminc().

Usage

```

## S3 method for class 'cuminc'
plot(x, main=" ", curvlab, ylim=c(0, 1), xlim, wh=2,
     xlab="Years", ylab="Probability", lty=1:length(x), color=1, lwd=par('lwd'),
     ...)

```

Arguments

x	a list, with each component representing one curve in the plot. Each component of x is itself a list whose first component gives the x values and 2nd component the y values to be plotted. Although written for cumulative incidence curves, can in principle be used for any set of lines.
main	the main title for the plot.
curvlab	Curve labels for the plot. Default is names(x), or if that is missing, 1:nc, where nc is the number of curves in x.
ylim	yaxis limits for plot
xlim	xaxis limits for plot (default is 0 to the largest time in any of the curves)
wh	if a vector of length 2, then the upper right coordinates of the legend; otherwise the legend is placed in the upper right corner of the plot
xlab	X axis label
ylab	y axis label
lty	vector of line types. Default 1:nc (nc is the number of curves in x). For color displays, lty=1, color=1:nc, might be more appropriate. If length(lty)<nc, then lty[1] is used for all.
color	vector of colors. If length(color)<nc, then the color[1] is used for all.
lwd	vector of line widths. If length(lwd)<nc, then lwd[1] is used for all.
...	additional arguments passed to the initial call of the plot function.

Value

No value is returned.

See Also

[cuminc](#)

plot.predict.crr *Plot estimated subdistribution functions*

Description

plot method for predict.crr

Usage

```
## S3 method for class 'predict.crr'  
plot(x, lty=1:(ncol(x)-1), color=1,  
ylim=c(0, max(x[, -1])), xmin=0, xmax=max(x[, 1]), ...)
```

Arguments

x	Output from predict.crr
lty	vector of line types. If length is < number of curves, then lty[1] is used for all.
color	vector of line colors. If length is < number of curves, then color[1] is used for all.
ylim	range of y-axis (vector of length two)
xmin	lower limit of x-axis (often 0, the default)
xmax	upper limit of x-axis
...	Other arguments to plot

Side Effects

plots the subdistribution functions estimated by predict.crr, by default using a different line type for each curve

See Also

[crr.predict.crr](#)

`predict.crr`*Estimate subdistribution functions from crr output*

Description

predict method for crr

Usage

```
## S3 method for class 'crr'  
predict(object, cov1, cov2, ...)
```

Arguments

<code>object</code>	output from crr
<code>cov1, cov2</code>	each row of <code>cov1</code> and <code>cov2</code> is a set of covariate values where the subdistribution should be estimated. The columns of <code>cov1</code> and <code>cov2</code> must be in the same order as in the original call to <code>crr</code> . Each must be given if present in the original call to <code>crr</code> .
<code>...</code>	additional arguments are ignored (included for compatibility with generic).

Details

Computes $1 - \exp(-B(t))$, where $B(t)$ is the estimated cumulative sub-distribution hazard obtained for the specified covariate values, obtained from the Breslow-type estimate of the underlying hazard and the estimated regression coefficients.

Value

Returns a matrix with the unique type 1 failure times in the first column, and the other columns giving the estimated subdistribution function corresponding to the covariate combinations in the rows of `cov1` and `cov2`, at each failure time (the value that the estimate jumps to at that failure time).

See Also

[crr.plot.predict.crr](#)

print.crr	<i>prints summary of a crr object</i>
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Description

print method for crr objects

Usage

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

Arguments

x	crr object (output from <code>crr()</code>)
...	additional arguments to <code>print()</code>

Details

prints the convergence status, the estimated coefficients, the estimated standard errors, and the two-sided p-values for the test of the individual coefficients equal to 0. (If convergence is false everything else may be meaningless.)

See Also

[crr](#)

print.cuminc	<i>Print cuminc objects</i>
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Description

A print method for objects of class `cuminc` (output from `cuminc()`).

Usage

```
## S3 method for class 'cuminc'
print(x, ntp=4, maxtime, ...)
```

Arguments

x	an object of class <code>cuminc</code>
ntp	number of timepoints where estimates are printed
maxtime	the maximum timepoint where values are printed. The default is the maximum time in the curves in x
...	additional arguments to <code>print()</code>

Details

Prints the test statistics and p-values (if present in x), and for each estimated cumulative incidence curve prints its value and estimated variance at a vector of times. The times are chosen between 0 and maxtime using the `pretty()` function.

Author(s)

Robert Gray

See Also

[cuminc](#)

summary.crr

Summary method for crr

Description

Generate and print summaries of crr output

Usage

```
## S3 method for class 'crr'
summary(object, conf.int = 0.95, digits =
max(options()$digits - 5, 2), ...)

## S3 method for class 'summary.crr'
print(x, digits = max(options()$digits - 4, 3), ...)
```

Arguments

<code>object</code>	An object of class <code>crr</code> (output from the <code>crr</code> function)
<code>conf.int</code>	the level for a two-sided confidence interval on the coefficients. Default is 0.95.
<code>digits</code>	In <code>summary.crr</code> , <code>digits</code> determines the number of significant digits retained in the p-values. In <code>print.summary.crr</code> , <code>digits</code> sets the values of the digits option for printing the output.
<code>...</code>	Included for compatibility with the generic functions. Not currently used.
<code>x</code>	An object of class <code>summary.crr</code> (output from the <code>summary</code> method for <code>crr</code>)

Details

The `summary` method calculates the standard errors, subdistribution hazard ratios z-scores, p-values, and confidence intervals on the hazard ratios. The `print` method prints a fairly standard format tabular summary of the results.

The pseudo likelihood ratio test in the printed output is based on the difference in the objective function at the global null and at the final estimates. Since this objective function is not a true likelihood, this test statistic is not asymptotically chi-square.

Value

`summary.crr` returns a list of class `summary.crr`, which contains components

<code>call</code>	The call to <code>crr</code>
<code>converged</code>	TRUE if the iterative algorithm converged
<code>n</code>	The number of observations used in fitting the model
<code>n.missing</code>	The number of observations removed by <code>crr</code> from the input data due to missing values
<code>loglik</code>	The value of the negative of the objective function (the pseudo log likelihood at convergence)
<code>coef</code>	A matrix giving the estimated coefficients, hazard ratios, standard errors, z-scores, and p-values
<code>conf.int</code>	A matrix giving the estimated hazard ratios, inverse hazard ratios and lower and upper confidence limits on the hazard ratios
<code>logtest</code>	Twice the difference in log pseudo likelihood values

Author(s)

The `summary` and `print.summary` methods were provided by Luca Scrucca

See Also

[crr](#)

Examples

```
## see examples in the crr help file
```

timepoints *Calculate Estimates at Specific Timepoints*

Description

Find values at specified timepoints from curves specified as all corners of step functions.

Usage

```
timepoints(w, times)
```

Arguments

<code>w</code>	a list containing the estimates, with points for all corners of the step function. (Usually created by <code>cuminc</code> .) Each component in the list contains the estimate for a different group. Each component has components giving times, function estimates, and variances (see <code>cuminc</code>)
<code>times</code>	vector of times where estimates are needed

Value

A list with components

`$est` a matrix of estimates of the subdistributions with a row for each component in `w` and a column for each time

`$var` a matrix giving the corresponding variances.

See Also

[cuminc](#)

[.cuminc

Subset method for lists of class cuminc

Description

A subset method that preserves the class of objects of class `cuminc`, allowing a subset of the curves to be selected.

Usage

```
## S3 method for class 'cuminc'
x[i,...]
```

Arguments

`x` object of class `cuminc`

`i` elements to extract

`...` not used

Value

A list with selected components of `x`, with the class set to `cuminc` so `cuminc` methods can be applied.

See Also

[cuminc](#) [plot.cuminc](#) [print.cuminc](#)

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