# Package 'hds'

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finda	Estimate the time-varying coefficients from a local-in-time Cox model

# **Description**

finda estimates the time-varying coefficients beta(t) at a single time from a local-in-time Cox model. Think of it as a Cox model where the the coefficients are allowed to vary with time. Further details can be found in Cai and Sun (2003) and Tian et al. (2005).

#### Usage

```
finda(tt, times, status, covars, start = rep(0, ncol(covars)), h = 400, ...)
```

#### **Arguments**

tt	Time to estimate beta(t) at
times	A vector of observed follow up times.
status	A vector of status indicators, usually 0=alive, 1=dead.
covars	A matrix or data frame of numeric covariate values, with a column for each covariate and each observation is on a separate row.
start	A vector of length p of starting values to be passed to optim for the numerical optimization procedure. p is the number of covariates. Defaults to all zeroes.
h	A single value on the time scale representing the bandwidth to use.
	Additional parameters to pass to optim.

#### **Details**

The naming of the function finda stands for "find a(t)", where "a(t)" is the notation used in Cai and Sun (2003) to represent the time-varying Cox model coefficients. We also refer to "a(t)" as "beta(t)" through the documentation.

The user typically will not interact with this function, as finda is wrapped by hdslc.

#### Value

A vector of length p, where p is the number of covariates. The vector is the estimated beta(t) from the local-in-time Cox model at time tt.

# References

Cai Z and Sun Y (2003). Local linear estimation for time-dependent coefficients in Cox's regression models. *Scandinavian Journal of Statistics*, 30: 93-111. doi:10.1111/1467-9469.00320

Tian L, Zucker D, and Wei LJ (2005). On the Cox model with time-varying regression coefficients. *Journal of the American Statistical Association*, 100(469):172-83. doi:10.1198/016214504000000845

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hds	Hazard discrimination summary estimator

# Description

Returns hazard discimination summary (HDS) estimates at all specified evaluation times. See Liang and Heagerty (2016) for details on HDS.

# Usage

```
hds(times, status, m, evaltimes = times[order(times)], se = TRUE)
```

# Arguments

times	A vector of observed follow up times.
status	A vector of status indicators, usually 0=alive, 1=dead.
m	A matrix or data frame of covariate values, with a column for each covariate and each observation is on a separate row. Non-numeric values are acceptable, as the values will be transformed into a numeric model matrix through survival::coxph.
evaltimes	A vector of times at which to estimate HDS. Defaults to all the times specified by the times vector. If there are a lot of observations, then you may want to enter in a sparser vector of times for faster computation.
se	TRUE or FALSE. TRUE: calculate and return standard error estimates. FALSE: do not calculate standard errors estimates and return NAs. Defaults to TRUE. May want to set to FALSE to save computation time if using this function to compute bootstrap standard errors.

# **Details**

A wrapper for hds\_t. Since hds\_t only estimates HDS at one time point, this function calls hds\_t multiple times to estimate the entire HDS curve. hds and hdslc are the main functions the user will interact with in this package.

The covariate values m are centered for numerical stability. This is particularly relevant for the standard error calculations.

#### Value

A data frame with three columns: 1) the evaluation times, 2) the HDS estimates at each evaluation time, and 3) the standard error estimates at each evaluation time

#### References

Liang CJ and Heagerty PJ (2016). A risk-based measure of time-varying prognostic discrimination for survival models. *Biometrics*. doi:10.1111/biom.12628

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#### See Also

hdslc

# **Examples**

```
## Not run:
head(hds(times = survival::pbc[1:312, 2],
         status = (survival::pbc[1:312, 3]==2)*1,
        m = survival::pbc[1:312, 5]))
hdsres <- hds(times=pbc5[,1], status=pbc5[,2], m=pbc5[,3:7])
hdslcres \leftarrow hdslc(times = pbc5[,1], status=pbc5[,2], m = pbc5[,3:7], h = 730)
        <- summary(survival::survfit(survival::Surv(pbc5[,1], pbc5[,2])~1))
Survt
        <- cbind(Survt$time, c(0,diff(1-Survt$surv)))</pre>
Survtd
         <- density(x=Survtd[,1], weights=Survtd[,2], bw=100, kernel="epanechnikov")</pre>
tden
par(mar=c(2.25, 2.25, 0, 0)+0.1, mgp=c(1.25, 0.5, 0))
plot(c(hdslcres[,1], hdslcres[,1]), c(hdslcres[,2] - 1.96*hdslcres[,3],
                                      hdslcres[,2] + 1.96*hdslcres[,3]),
     type="n", xlab="days", ylab="HDS(t)", cex.lab=.75, cex.axis=.75,
     ylim=c(-3,15), xlim=c(0,3650))
polygon(x=c(hdsres[,1], hdsres[312:1,1]), col=rgb(1,0,0,.25), border=NA,
        fillOddEven=TRUE, y=c(hdsres[,2]+1.96*hdsres[,3],
                              (hdsres[,2]-1.96*hdsres[,3])[312:1]))
polygon(x=c(hdslcres[,1], hdslcres[312:1, 1]), col=rgb(0,0,1,.25), border=NA,
        fillOddEven=TRUE, y=c(hdslcres[,2] + 1.96*hdslcres[,3],
                              (hdslcres[,2] - 1.96*hdslcres[,3])[312:1]))
lines(hdsres[,1], hdsres[,2], lwd=2, col="red")
lines(hdslcres[,1], hdslcres[,2], lwd=2, col="blue")
abline(h=1, lty=3)
legend(x=1200, y=14, legend=c("Proportional hazards",
                               "Local-in-time proportional hazards",
                               "Time density"), col=c("red", "blue", "gray"),
       lwd=2, bty="n", cex=0.75)
with(tden, polygon(c(x, x[length(x):1]),
                   c(y*3/max(y)-3.5, rep(-3.5, length(x))),
                   col="gray", border=NA, fillOddEven=TRUE))
## End(Not run)
```

hdslc

Hazard discrimination summary estimator

#### **Description**

Returns local constant HDS estimates at all specified evaluation times. See Liang and Heagerty (2016) for details on HDS.

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#### Usage

```
hdslc(times, status, m, evaltimes = times[order(times)], h = 1.06 \times sd(times) \times (length(times)^{-0.2}), se = TRUE)
```

#### **Arguments**

times	A vector of observed follow up times.
status	A vector of status indicators, usually 0=alive, 1=dead.
m	A matrix or data frame of covariate values, with a column for each covariate and each observation is on a separate row. Non-numeric values are acceptable, as the values will be transformed into a numeric model matrix through survival::coxph.
evaltimes	A vector of times at which to estimate HDS. Defaults to all the times specified by the times vector. If there are a lot of observations, then you may want to enter in a sparser vector of times for faster computation.
h	A single numeric value representing the bandwdith to use, on the time scale. The default bandwidth is a very ad hoc estimate using Silverman's rule of thumb
se	TRUE or FALSE. TRUE: calculate and return standard error estimates. FALSE: do not calculate standard errors estimates and return NAs. Defaults to TRUE. May want to set to FALSE to save computation time if using this function to compute bootstrap standard errors.

#### **Details**

A local constant version of hds. While hds estimates HDS(t) assuming the Cox proportional hazards model, hdslc estimates HDS(t) using a relaxed, local-in-time Cox model. Specifically, the hazard ratios are allowed to vary with time. See Cai and Sun (2003) and Tian Zucker Wei (2005) for details on the local-in-time Cox model.

Point estimates use hdslc.fast and standard errors use hdslcse.fast. hdslc.fast requires an estimate of beta(t) (time-varying hazard ratio), which is estimated using finda(); and subject specific survival, which is estimated using sssf.fast(). hdslcse.fast requires the same and in addition standard error estimates of beta(t), which are estimated using betahatse.fast().

The covariate values m are centered for numerical stability. This is particularly relevant for the standard error calculations.

#### Value

A data frame with three columns: 1) the evaluation times, 2) the HDS estimates at each evaluation time, and 3) the standard error estimates at each evaluation time

#### References

Liang CJ and Heagerty PJ (2016). A risk-based measure of time-varying prognostic discrimination for survival models. *Biometrics*. doi:10.1111/biom.12628

Cai Z and Sun Y (2003). Local linear estimation for time-dependent coefficients in Cox's regression models. *Scandinavian Journal of Statistics*, 30: 93-111. doi:10.1111/1467-9469.00320

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Tian L, Zucker D, and Wei LJ (2005). On the Cox model with time-varying regression coefficients. *Journal of the American Statistical Association*, 100(469):172-83. doi:10.1198/016214504000000845

#### See Also

hds, finda

#### **Examples**

```
## Not run:
head(hdslc(times = survival::pbc[1:312, 2],
           status = (survival::pbc[1:312, 3]==2)*1,
           m = survival::pbc[1:312, 5]))
hdsres <- hds(times=pbc5[,1], status=pbc5[,2], m=pbc5[,3:7])</pre>
hdslcres \leftarrow hdslc(times = pbc5[,1], status=pbc5[,2], m = pbc5[,3:7], h = 730)
         <- summary(survival::survfit(survival::Surv(pbc5[,1], pbc5[,2])~1))</pre>
Survtd
        <- cbind(Survt$time, c(0,diff(1-Survt$surv)))</pre>
         <- density(x=Survtd[,1], weights=Survtd[,2], bw=100, kernel="epanechnikov")</pre>
tden
par(mar=c(2.25, 2.25, 0, 0)+0.1, mgp=c(1.25, 0.5, 0))
plot(c(hdslcres[,1], hdslcres[,1]), c(hdslcres[,2] - 1.96*hdslcres[,3],
                                       hdslcres[,2] + 1.96*hdslcres[,3]),
     type="n", xlab="days", ylab="HDS(t)", cex.lab=.75, cex.axis=.75,
     ylim=c(-3,15), xlim=c(0,3650))
polygon(x=c(hdsres[,1], hdsres[312:1,1]), col=rgb(1,0,0,.25), border=NA,
        fillOddEven=TRUE, y=c(hdsres[,2]+1.96*hdsres[,3],
                               (hdsres[,2]-1.96*hdsres[,3])[312:1]))
polygon(x=c(hdslcres[,1], hdslcres[312:1, 1]), col=rgb(0,0,1,.25), border=NA,
        fillOddEven=TRUE, y=c(hdslcres[,2] + 1.96*hdslcres[,3],
                               (hdslcres[,2] - 1.96*hdslcres[,3])[312:1]))
lines(hdsres[,1], hdsres[,2], lwd=2, col="red")
lines(hdslcres[,1], hdslcres[,2], lwd=2, col="blue")
abline(h=1, lty=3)
legend(x=1200, y=14, legend=c("Proportional hazards",
                               "Local-in-time proportional hazards",
                               "Time density"), col=c("red", "blue", "gray"),
       lwd=2, bty="n", cex=0.75)
with(tden, polygon(c(x, x[length(x):1]),
                   c(y*3/max(y)-3.5, rep(-3.5, length(x))),
                   col="gray", border=NA, fillOddEven=TRUE))
## End(Not run)
```

hdslc.fast

Hazard discrimination summary estimate (local constant) at one time point

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#### **Description**

hdslc.fast estimates HDS at a single time using the local-in-time proportional hazards model. See Cai and Sun (2003, Scandinavian Journal of Statistics) for details on the local-in-time PH model.

#### Usage

```
hdslc.fast(S, betahat, m)
```

# **Arguments**

S	A vector of length nrow(m) (which is typically the number of observations n), where each value is the subject-specific survival at time t where t is implied by
	the choice of betahat.

betahat A p x 1 vector of coefficient estimates at time t of interest from the local-in-time

Cox model. Vector length p is the number of covariates. Typically the output

from hdslc::finda is passed here.

m A numeric n x p matrix of covariate values, with a column for each covariate

and each observation is on a separate row.

#### **Details**

The user typically will not interact with this function. Rather, hdslc wraps this function and is what the user typically will use.

#### Value

The HDS estimate at times t, where t is implied by choice of S and betahat passed to hdslc.fast.

hdslcse.fast	Hazard discrimination summary (local constant) standard error esti-
	mate

# **Description**

hdslcse.fast calculates an estimate of the variance for the local constant hazard discrimination summary estimator at a time t. The time t is implied by S, betahat, and betahatse

# Usage

```
hdslcse.fast(S, betahat, m, betahatse)
```

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#### **Arguments**

S A vector of length nrow(m) (which is typically the number of observations n),

where each value is the subject-specific survival at time t where t is implied by

the choice of betahat.

betahat A p x 1 vector of coefficient estimates at time t of interest from the local-in-time

Cox model. Vector length p is the number of covariates. Typically the output

from hdslc::finda is passed here.

m A numeric n x p matrix of covariate values, with a column for each covariate

and each observation is on a separate row.

betahatse A p x p covariance matrix for betahat at time t

#### **Details**

The use will typically not interact with this function directly. Instead this function is wrapped by hdslc.

#### Value

Variance estimate that has not been normalized. To get a usable standard error estimate, divide the output of this function by the bandwidth and sample size, and then take the square root.

hds\_t Hazard discrimination summary estimate at one time point

#### Description

hds\_t estimates HDS at time t under the PH assumption

#### Usage

```
hds_t(t, L0hat, betahat, m)
```

#### **Arguments**

t The time at which to calculate HDS

L0hat A data frame with variable names of hazard and time. Typically the object

returned by basehaz.

betahat A vector of coefficient estimates from the Cox model. Typically the coefficients

value from the coxph. object object returned by coxph.

m A numeric matrix of covariate values, with a column for each covariate and each

observation is on a separate row.

#### **Details**

The user typically will not interact with this function. Rather, hds is a wrapper for this function and is what the user typically will use.

pbc5

pbc5

Cleaned up version of the Mayo PBC data.

# **Description**

A cleaned up version of the Mayo PBC data from survival::pbc. Only the first 312 observations are used (the cases who participated in the randomized trial). Only five of the covariates (listed below) are used. Further, two of the covariates were log transformed.

# Usage

pbc5

# **Format**

A data frame with 312 rows and 7 variables:

**time** follow up time in days **status** 1=death, 0=censored **age** age in years

edema 0=no edema, 0.5=untreated or successfully treated, 1=edema despite diuretic therapy

bili log serum bilirubin level (original value from survival::pbc is unlogged)

albumin serum albumin

protime log standardized blood clotting time (original value from survival::pbc is unlogged)

#### Source

Cleaned up version of survival::pbc

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