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The Covariate Order Method for Nonparametric Censored Exponential Regression

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GENERAL SETUP – LIFETIME DATA

Underlying random variables:

- Z = lifetime
- X = covariate
- C = censoring time

Basic assumption:

- Z, C are conditionally independent given X (independent censoring)

Observed:

- $T = \min(Z, C)$
- $\delta = I(Z \leq C)$
- X

Data:

- Independent triplets

  $(T_1, \delta_1, X_1), \cdots, (T_n, \delta_n, X_n)$

COVARIATE ORDERING
(single continuous covariate)

Order data $(T_1, \delta_1, X_1), \cdots, (T_n, \delta_n, X_n)$

with $X_1 \leq X_2 \leq \cdots \leq X_n$

COVARIATE ORDER PROCESS:

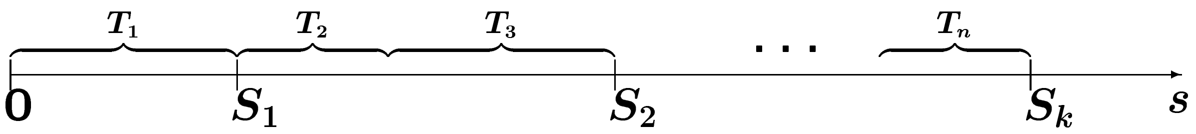
Point process $S_1, S_2, \ldots$ with

$S_i = \sum_{j=1}^{k(i)} T_j$

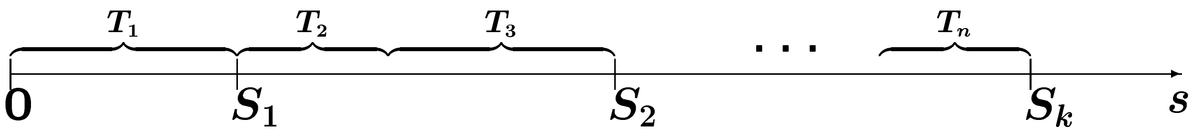
$k(i) = \min\{r | \sum_{j=1}^{r} \delta_j = i\}$.

Example:

$\delta_1 = 1, \delta_2 = 0, \delta_3 = 1, \ldots, , \delta_{n-1} = 0, \delta_n = 1$.



TESTING FOR COVARIATE EFFECT
(Kvaløy 99b)



- NO CENSORING or RANDOM CENSORING (C independent of X)

  $S_1, S_2, \ldots$ is renewal process if lifetime Z is independent of covariate X.

- INDEPENDENT CENSORING (C may depend on X)

  Warning:

  $S_1, S_2, \ldots$ is NOT necessarily a renewal process if lifetime Z independent of covariate X.

  EXCEPTIONAL CASE:

  $Z \sim \exp(\lambda)$, independent of X

  $$\Downarrow$$

  $S_1, S_2, \ldots$ is a homogeneous Poisson process (HPP). under independent censoring.

EXPONENTIAL REGRESSION
(single covariate)

MODEL: Z **given** $X = x$ **is** $\exp(\lambda(x))$;
independent censoring

- $Z|x$ **has density** $f_Z(t|x) = \lambda(x)e^{-\lambda(x)t}$
- $C|x$ **has density** $f_C(t|x)$
- Z, C **independent given** x

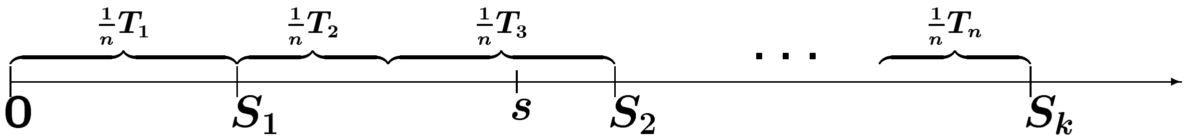
Data:

$(T_1, \delta_1, X_1), \cdots, (T_n, \delta_n, X_n)$

STANDARD NONPARAMETRIC ESTIMATION:

- **Local polynomial regression:**

COVARIATE ORDER METHOD FOR ESTIMATION OF $\lambda(x)$



Define $N(s)$ = number of censored or uncensored events before s

Conditional intensity of process $S_1, S_2, \dots$ at s (see figure) is:

$$\rho(s) = n\lambda(X_{N(s)+1})$$

Idea: Estimate the intensity by kernel estimator ("density estimator") $\hat{\rho}(s)$

Then invert relation

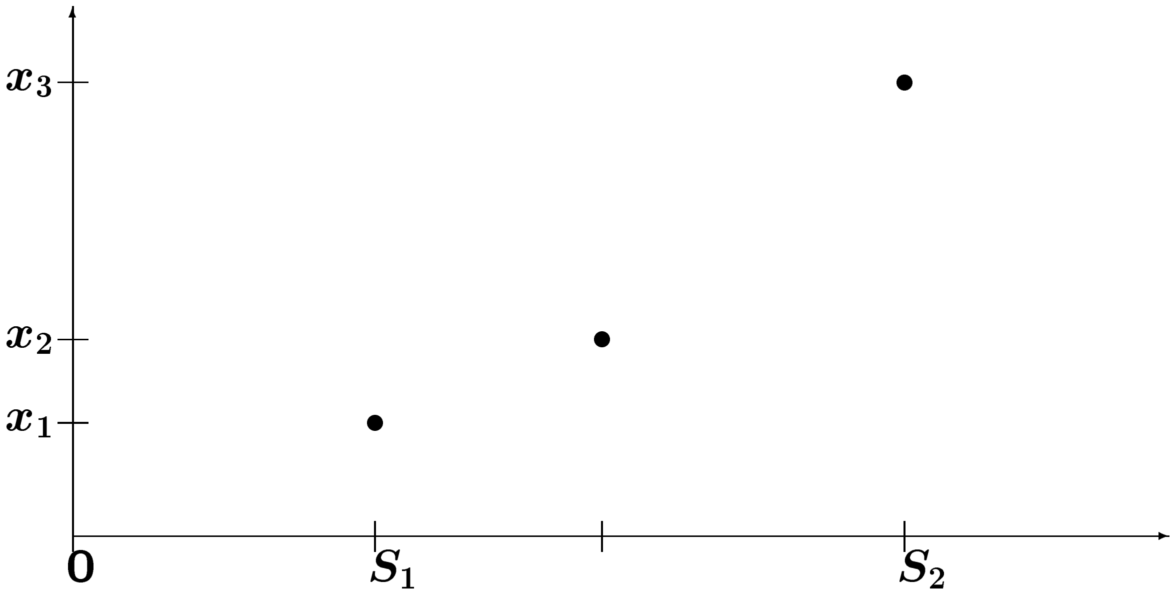
$$\hat{\rho}_n(s) = n\hat{\lambda}(X_{N(s)+1})$$

to obtain $\hat{\lambda}(x)$ at each given x.

Key here: Correspondence between points on s-axis and x-axis.

CORRESPONDENCE FUNCTION

What is the s corresponding to an x?



Step:

$$\bar{s}(x) = (1/n) \sum_{X_i \le x} T_i$$

Piecewise linear:

$$\tilde{s}(x) = \frac{1}{n} \sum_{i=1}^{J-1} T_i + \frac{x - X_{J-1}}{X_J - X_{J-1}} \frac{1}{n} T_J, \quad X_{J-1} < x \le X_J$$

Smooth:

$$\hat{s}(x) = \ldots$$

COVARIATE ORDER ESTIMATOR

$$\hat{\lambda}(x) = \hat{\rho}(\hat{s}(x)) \equiv \frac{1}{nh_s} \sum_{i=1}^{k} K\left(\frac{\hat{s}(x) - S_i}{h_s}\right)$$

is a uniformly consistent estimator for $\lambda(x)$.

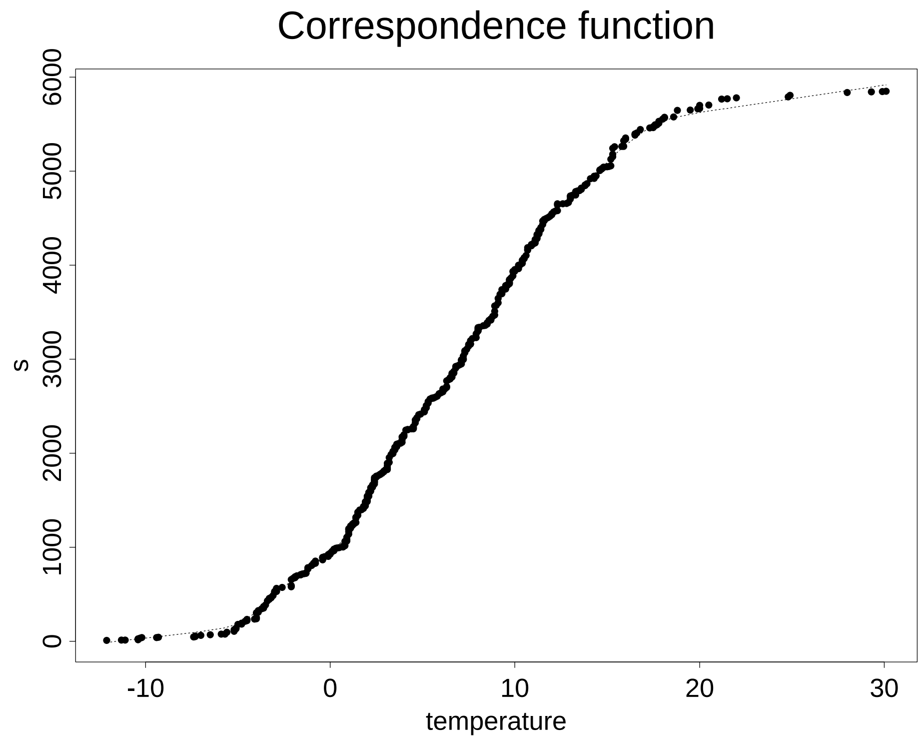
Here:

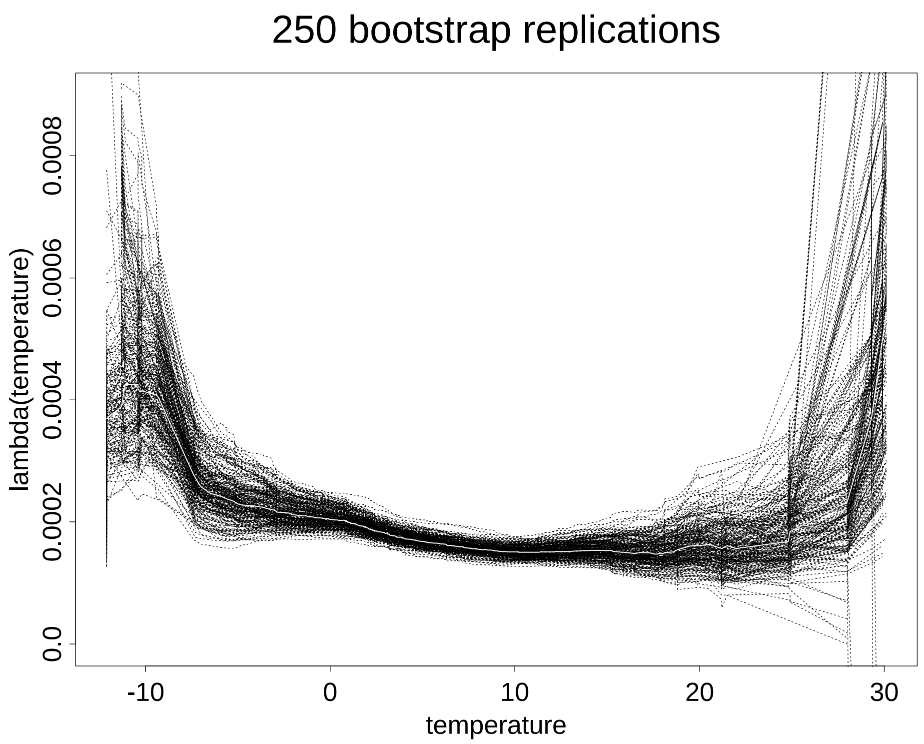
- $K(\cdot)$ is a positive kernel, integral 1
- h_s is a smoothing parameter; may depend on s
- $h_s \to 0$ as $n \to \infty$ for all s.
- There is a sequence h_n such that $h_s \geq h_n$ for all s, n where $nh_n \to \infty$ as $n \to \infty$.

EXAMPLE – CARDIAC ARREST

Times of out-of-hospital cardiac arrests reported to a Norwegian hospital over a 5 years period.

$Z =$ **inter-event times,** $X =$ **temperature.**





SEVERAL COVARIATES

$X = (X_1, \ldots, X_m)$

Local polynomial methods: Generalization in principle immediate

Covariate order method: Generalization less clear without imposing structure

GENERALIZED ADDITIVE MODELS

$$\lambda(x) = e^{\alpha + g_1(x_1) +, \ldots, + g_m(x_m)}$$

$g_1(\cdot), \ldots, g_m(\cdot)$ **estimated iteratively (backfitting)**

Basis:

$Z \sim \exp(e^{\alpha + g_1(x_1) + \ldots + g_m(x_m)})$

$$\Downarrow$$

$Ze^{\alpha + g_1(x_1) + \ldots + g_{j-1}(x_{j-1}) + g_{j+1}(x_{j+1}) + \ldots + g_m(x_m)} \sim \exp(e^{g_j(x_j)})$.

PROPORTIONAL HAZARDS

Basis:

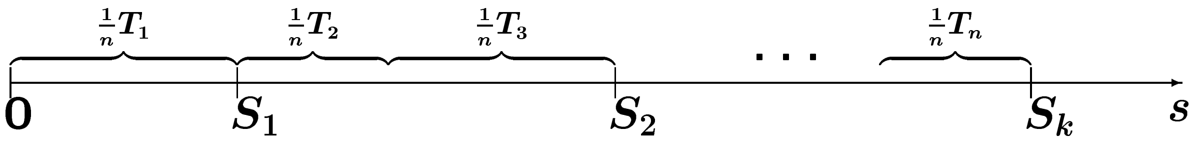
Hazard rate of Z is $\boldsymbol{\lambda}(t|x) = \boldsymbol{\lambda}_0(t)e^{g(\boldsymbol{x})}$

$$\Downarrow$$

$\boldsymbol{\Lambda_0(Z) \sim \exp(e^{g(x)})}$.

CONCLUSIONS

COVARIATE ORDER METHOD FOR NONPARAMETRIC EXPONENTIAL REGRESSION



- Simulations indicate that method is competitive w.r.t. local likelihood methods, in particular for high censoring and few observations.

- Covariate order method is flexible due to "free" choice of density estimation method

- Method is easy to use with existing software

- Method involves informative plots:
  - S-plot contains reconstructed "complete" lifetimes from censored data
  - Correspondence function gives information on covariates and outliers.

- Extension to proportional hazards models is straightforward