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Efficient Semiparametric Estimators via Preliminary Estimators for Kullback-Leibler Minimizers

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OUTLINE

- I. MOTIVATION — Semiparametric Frailty Problems
- II. APPROACH — Finite-Dimensional Version
- III. BACKGROUND LITERATURE —
Profile Likelihood, Semiparametrics, Frailty Models
- IV. Semiparametric Examples
- V. Efficient Estimator in Frailty Case

Survival Models with ‘Frailties’

Variables: T_i Survival times, Discrete Covariates Z_i
 C_i Censoring Times, cond surv fcn $R_z(c)$ given (T_i, C_i)

DATA: iid triples $(\min(T_i, C_i), I_{[T_i \leq C_i]}, Z_i)$

Observable processes:

$$N_z^i(t) = I_{[Z_i=z, T_i \leq \min(C_i, t)]} \quad , \quad Y_z^i(t) = I_{[\min(T_i, C_i) \geq t]}$$

TRANSF. MODEL: $S_{T|Z}(t|z) = \exp(-G(e^{\beta'z} \Lambda))$

G known , $\beta \in \mathbf{R}^m$, Λ cumulative-hazard fcn

PROBLEM: efficient estimation of β .

Special Cases: (1) *Cox 1972:* $G(x) \equiv x$

(2) Frailty: unobserved random intercept $\beta_0 = \xi_i$, $G \equiv x$

$$\implies G(x) = -\log \int_0^\infty e^{-sx} dF(s)$$

(3) *Clayton-Cuzick 1986:* $G(x) \equiv \frac{1}{b} \log(1 + bx)$

Finite-dimensional Case

$X_i, i = 1, \dots, n$ iid $\sim f(x, \beta, \lambda)$,
 $\beta \in \mathbf{R}^m, \lambda \in \mathbf{R}^d$ unknown, with true values (β_0, λ_0)

$$\log Lik(\beta, \lambda) = \sum_{i=1}^n \log f(X_i, \beta, \lambda)$$

Profile Likelihood = $\log Lik(\beta, \hat{\lambda}_\beta)$ with
restricted MLE $\hat{\lambda}_\beta = \arg \max_\lambda \log Lik(\beta, \lambda)$

Min Kullback-Leibler Modified Profile Approach (Severini and Wong 1992)

$$\begin{aligned} \mathcal{K}(\beta, \lambda) &\equiv E_{\beta_0, \lambda_0}(\log f(X_1, \beta, \lambda)) \\ &= \int \{\log f(x, \beta, \lambda)\} f(x, \beta_0, \lambda_0) dx \end{aligned}$$

Define: $\lambda_\beta = \arg \max_\lambda \mathcal{K}(\beta, \lambda)$

Then: $\tilde{\lambda}_\beta$ estimates curve λ_β

Candidate Estimator

$$\tilde{\beta} \equiv \arg \max_\beta \log Lik(\beta, \tilde{\lambda}_\beta)$$

Key mathematical features of this approach are

- the convenience of restricting attention to nuisance parameters such as hazards or density functions which satisfy smoothness restrictions;
- the replacement of operator-inversion within (blocks of) the generalized information operator by differentiation of the restricted Kullback-Leibler minimizer; and
- diminished need for high-order consistency of estimation, when consistent estimators of Kullback-Leibler minimizers *and their derivatives with respect to structural parameters* are available.

NB: Kullback-Leibler Functional = $-\mathcal{K}(\beta, \lambda)$

Sketch of (Finite-dimensional) Theory

Fix β_0, λ_0 and $f_0(x) = f(x, \beta_0, \lambda_0)$.

$$\begin{aligned} \text{Information Matrix: } \mathcal{I}(\beta, \lambda) &= \begin{pmatrix} A_{\beta, \lambda} & B_{\beta, \lambda} \\ B_{\beta, \lambda}^* & C_{\beta, \lambda} \end{pmatrix} \\ &= - \int \begin{pmatrix} \nabla_{\beta}^{\otimes 2} \log f(x, \beta, \lambda) & \nabla_{\beta \lambda}^2 \log f(x, \beta, \lambda) \\ \nabla_{\lambda \beta}^2 \log f(x, \beta, \lambda) & \nabla_{\lambda}^{\otimes 2} \log f(x, \beta, \lambda) \end{pmatrix} f_0(x) dx \end{aligned}$$

$$\lambda_{\beta} = \arg \max_{\lambda} \mathcal{K}(\beta, \lambda) \quad \text{satisfies:} \quad \nabla_{\lambda} \mathcal{K}(\beta, \lambda_{\beta}) = 0$$

Differentiate implicitly (total deriv) wrt β to find:

$$-\nabla_{\beta}^T [\nabla_{\lambda} \mathcal{K}(\beta, \lambda_{\beta})] = B + C \nabla'_{\beta} \lambda_{\beta} = 0$$

This implies $\nabla'_{\beta} \lambda_{\beta} = -C^{-1} B$ and

(β, λ_{β}) is a **least-favorable** nuisance-parameterization

and usual Information about β for this model is

$$\begin{aligned} I_{\beta}^0 &= A_{\beta_0, \lambda_0} - (\nabla'_{\beta} \lambda_{\beta})' C_{\beta_0, \lambda_0} (\nabla'_{\beta} \lambda_{\beta}) \\ &= A_{\beta_0, \lambda_0} - B_{\beta_0, \lambda_0} C_{\beta_0, \lambda_0}^{-1} B_{\beta_0, \lambda_0}^* \end{aligned}$$

Theory, continued

Information Ineq says: $\lambda_{\beta_0} = \lambda_0$, $\nabla_{\beta} \mathcal{K}(\beta_0, \lambda_0) = 0$

Now assume $\tilde{\lambda}_{\beta}$, $\nabla_{\beta}^{\otimes 2} \tilde{\lambda}_{\beta}$ consistent for λ_{β} , $\nabla_{\beta}^{\otimes 2} \lambda_{\beta}$ unif on nbhd of β_0 .

Can check successively:

(A) $(\nabla_{\beta}^T)^{\otimes 2} \log Lik(\beta, \tilde{\lambda}_{\beta})$ neg-def unif on β_0 nbhd

(B) $n^{-1} \log Lik(\beta_0, \tilde{\lambda}_{\beta_0}) \xrightarrow{P} 0$

(C) $\tilde{\beta}$ unique loc sol'n of $\nabla_{\beta}^T \log Lik(\beta, \tilde{\lambda}_{\beta}) = 0$, consistent for β_0 .

(D) $n^{-1} \nabla_{\lambda} \log Lik(\tilde{\beta}, \tilde{\lambda}_{\tilde{\beta}}) = n^{-1} \nabla_{\lambda} \log Lik(\beta_0, \lambda_0) + o_P(\tilde{\beta} - \beta_0)$ [because $-C^{-1}B = \nabla_{\beta} \tilde{\lambda}_{\beta}$]

(E) $n^{-1} \nabla_{\beta} \log Lik(\tilde{\beta}, \tilde{\lambda}_{\tilde{\beta}}) = n^{-1} \nabla_{\beta} \log Lik(\beta_0, \lambda_0) - I_{\beta}^0 \cdot (\tilde{\beta} - \beta_0) + o_P(\tilde{\beta} - \beta_0)$

(F) $\sqrt{n}(\tilde{\beta} - \beta_0) = (I_{\beta}^0)^{-1} \frac{1}{\sqrt{n}} (\nabla_{\beta} \log Lik(\beta_0, \lambda_0) + \nabla'_{\lambda} \log Lik(\beta_0, \lambda_0) \nabla_{\beta} \lambda_{\beta_0})$

(G) $\sqrt{n}(\tilde{\beta} - \beta_0) \stackrel{\mathcal{D}}{\approx} \mathcal{N}(\mathbf{0}, (I_{\beta}^0)^{-1})$

LITERATURE

Profile Likelihood

Cox, D. R. & Reid, N. (1987) **JRSSB**

McCullagh, P. and Tibshirani, R. (1990) **JRSSB**

Severini, T. and Wong, W. (1992) *Ann Stat*

Semiparametrics

Bickel, Klaassen, Ritov, & Wellner: 1993 Book

Cox, D. R. (1972) ‘*Cox-Model*’ paper **JRSSB**

Owen, A. (1988) *Biometrika*: Empirical likelihood

Qin, J. & Lawless, J. (1994) *Ann Stat*: EL & GEE

Murphy & van der Vaart (2000) *JASA*

Transformation/Frailty Models

Cheng, Wei, & Ying (1995) *Biometrika*

Clayton and Cuzick (1986) *ISI Centenary Session*

Slud, E. and Vonta, I. (2002) *submitted*

Parner (1998) *Ann. Stat.*

∞ -dim Examples & Applications

(I). *Mean estimation in the location model*

$$X_i \sim \lambda_0(x - \beta_0), \quad \beta_0 = E(X_1)$$

$\lambda_0 \in L^1(dx)$ compactly supported 0-mean density.

(Easy example, \bar{X} efficient. Owen 1988, Qin & Lawless 1994 studied in connection with *empirical likelihood*.)

$$\text{For } \beta \neq \beta_0, \quad \lambda_\beta(x) = \lambda_0(x + \beta)/(1 - \alpha x)$$

with α solving $\int x \lambda_\beta(x) dx = 0$

Define $\tilde{\lambda}_\beta$ first at β_0 using density estimator

$$\tilde{\lambda}_{\beta_0}(x) = \frac{1}{n h_n} \sum_{i=1}^n \phi((x - X_i + \bar{X})/h_n), \quad h_n \searrow 0$$

$$\tilde{\lambda}_\beta(x) = \frac{\tilde{\lambda}_{\beta_0}(x + \beta)}{1 - \tilde{\alpha}x}, \quad \int \frac{x \tilde{\lambda}_{\beta_0}(x + \beta)}{1 - \tilde{\alpha}x} dx = 0$$

(II). *Cox model.* For $q_z(t) = p_Z(z)R_z(t) \exp(-e^{z'\beta_0}\Lambda_0(t))$,

$$\Lambda_\beta(t) \equiv \int_0^t \lambda_\beta(s) ds = \frac{\sum_z q_z(x) e^{z'\beta_0} \lambda_0(x)}{\sum_z e^{z'\beta} q_z(x)}$$

Example (II), cont'd.

First let $\tilde{\lambda}_0$ be consistent density estimate of $\lambda_0(x) = \Lambda'_0(x)$ (eg by smoothing and differentiating the Kaplan-Meier cumulative-hazard estimator on data in a $z = 0$ data-stratum.) Then estimate elsewhere by

$$\tilde{\lambda}_\beta(t) = \sum_z e^{z' \beta_0} Y_z(t) \tilde{\lambda}_{\beta_0}(t) / \sum_z e^{z' \beta} Y_z(t)$$

NB. In this example, any $\tilde{\beta}$ estimator produced in this way collapses to the usual Cox Max Partial Likelihood Estimator !

(III). *Transformation/Fraily Models*

In the general G transformation model case, must assume for some finite time τ_0 with $\Lambda^0(\tau_0) < \infty$ that all data are censored at τ_0 .

In this model, Slud and Vonta (2002) characterize the \mathcal{K} -optimizing hazard intensity λ_β in its integrated form $L = \Lambda_\beta = \int_0^\cdot \lambda_\beta(x) dx$, through the second order ODE system:

Example (III), cont'd.

$$\frac{dL}{d\Lambda_0}(s) = \frac{\sum_z e^{z'\beta_0} q_z(s) G'(e^{z'\beta_0}\Lambda_0(s))}{\sum_z e^{z'\beta} q_z(s) G'(e^{z'\beta}L(s)) + Q(s)}$$

$$\frac{dQ}{d\Lambda_0}(s) = \sum_z e^{z'\beta} q_z(s) \frac{G''}{G'}|_{e^{z'\beta}L(s)} \cdot$$

$$(e^{z'\beta_0} G'(e^{z'\beta_0}\Lambda_0(s)) - (e^{z'\beta} G'(e^{z'\beta}L(s))) \frac{dL}{d\Lambda_0}(s))$$

subject to the initial/terminal conditions

$$L(0) = 0 \quad , \quad Q(\tau_0) = 0$$

Slud and Vonta (2002) show that these ODE's have unique solutions, smooth with respect to β and differentiable in t , which (with $\lambda_\beta \equiv L'$) maximize the functional $\mathcal{J}(\beta, \lambda_\beta)$ as desired.

Consistent preliminary estimators $\tilde{\lambda}_\beta$ can be developed by substitute for β_0, Λ_0 in those equations (smoothed wrt t) consistent preliminary estimators.

PUNCHLINE: the new estimator $\tilde{\beta} = \arg \max_\beta \log \text{Lik}(\beta, \tilde{\lambda}_\beta)$ is efficient !