A Scalable and Flexible Cox Proportional Hazards Model for High-Dimensional Survival Prediction and Functional Selection

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Background

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"It is extremely unlikely that the true (effect) function f(X) (on the outcome) is actually linear in X."

— Hastie, Tibshirani, and Friedman (2009) PP. 139

Question

How to model nonlinear effects for survival outcome in **high-dimensional** setting?

Additive Cox Proportional Hazards Model

Following all necessary assumptions, a Cox proportional hazards model with event time t_i and predictors $x_{ij}, j = 1, \ldots, p$, is expressed as

$$h(t_i) = h_0(t_i) \exp(\sum_{j=1}^{p} B_j(x_{ij})), \quad i = 1, \ldots, n.$$

- Spline functions

$$B(x) = \sum_{k=1}^{K} \beta_k b_k(x) \equiv \boldsymbol{X}^T \beta$$

$b_k(x)$ are the *basis functions*, possibly truncated power basis and b-spline basis. (Simon N. Wood 2017)

Function Smoothing

- Smoothing penalty $\lambda \int B^{''}(X)^2 dx = \lambda \beta^T \boldsymbol{S} \beta$
  - The smoothing penalty matrix $\boldsymbol{S}$ is known given $\boldsymbol{X}$
  - $\boldsymbol{S}$ is symmetric and positive semi-definite
- Penalized Partial Likelihood Function

$$\hat{h}_0(t_i|\beta) = d_i / \sum_{i' \in R(t_i)} exp(X_{i'}\beta).$$

  - The smoothing parameter λ is a tuning parameter, selected via cross-validation

High-dimensional Additive Cox Model

Primary Challenges:

- Jointly model signal sparsity versus function smoothness
- Adaptive shrinkage
- Bi-level selection that simultaneously answers
    - if a variable is predictive to the outcome, $B_j(X_j) = 0$
    - if a variable has a nonlinear relationship with the outcome, $B_j(X_j) = \beta_j X_j$

Bayesian Hierarchical Additive Model

Bayesian Hierarchical Additive Model

- Two-part spike-and-slab LASSO prior for spline functions
  - Variable selection via inclusion indicator
  - Bi-level selection accounting for effect hierarchy
  - Adaptive shrinkage via Bayesian regularization
- EM-Coordinate Descent algorithm
  - Expedited computation
  - Seamless variable selection via sparse solution

Two-part Spike-and-slab LASSO (SSL) Prior

Follow xxx, a spline function $B(X) = \boldsymbol{X}^T\beta$ can be decomposed to linear and nonlinear components with respect to the smoothing penalty matrix S

$$\boldsymbol{X}^T\beta = X^0\beta + \boldsymbol{X}^*\beta^*$$

- Proposed spike-and-slab LASSO prior

$$\beta_j|\gamma_j, s_0, s_1 \sim DE(0, (1-\gamma_j)s_0 + \gamma_j s_1)$$
$$\beta^*_{jk}|\gamma^*_j, s_0, s_1 \overset{\text{iid}}{\sim} DE(0, (1-\gamma^*_j)s_0 + \gamma^*_j s_1), k = 1, \ldots, K-1$$

  - γ_j controls the inclusion of linear component
  - γ^*_j controls the inclusion of nonlinear component

Effect Hierarchy and Adaptive Shrinkage

Effect hierarchy assumes lower-order effects are more likely to be active than higher-order effects

- Structured prior on latent indicators γ_j and γ_j^*

$$\gamma_j|\theta_j \sim Bin(\gamma_j|1,\theta_j), \quad \gamma_j^*|\gamma_j,\theta_j \sim Bin(1,\gamma_j\theta_j),$$

  - Simplification via analytic integration

$$\gamma_j^*|\theta_j \sim Bin(1,\theta_j^2),$$

- Adaptive shrinkage

$$\theta_j \sim \mathrm{Beta}(a,b)$$

EM-Cooridante Descent Algrithm

We are interested in estimating $\Theta = \{\boldsymbol{\beta}, \boldsymbol{\theta}, \phi\}$ using optimization based algorithm for scalability purpose

- Basic Ideas
  - Treat γs as the "missing data" in the EM procedure
  - Quantify the expectation of log posterior density function of Θ with respect to γ conditioning on $\Theta^{(t-1)}$
  - Maximize two parts of the objective function independently

Decomposition of Objective Function

We aim to maximize the log posterior density of Θ by averaging over all possible values of γ

$$\log f(\Theta, \gamma | \mathbf{y}, \mathbf{X}) = Q_1(\beta, \phi) + Q_2(\boldsymbol{\gamma}, \boldsymbol{\theta}),$$

- L_1-penalized likelihood function of β, ϕ

$$Q_1 \equiv Q_1(\beta, \phi) = \log f(\mathbf{y}|\beta, \phi) + \sum_{j=1}^{p} \left[\log f(\beta_j|\gamma_j) + \sum_{k=1}^{K_j} \log f(\beta^*_{jk}|\gamma^*_j) \right]$$

- Posterior density of θ given data points γs

$$Q_2 \equiv Q_2(\boldsymbol{\gamma}, \boldsymbol{\theta}) = \sum_{j=1}^{p} \left[(\gamma_j + \gamma^*_j) \log \theta_j + (2 - \gamma_j - \gamma^*_j) \log(1 - \theta_j) \right] + \sum_{j=1}^{p} \log f(\theta_j).$$

- Q_1 and Q_2 are independent conditioning on γs

Summary of EM-Coordinate Descent Algorithm

- E-step
  - Formulate $E_{\boldsymbol{\gamma}|\Theta^{(t)}}[Q(\Theta,\boldsymbol{\gamma})] = E(Q_1) + E(Q_2)$
    - $E(Q_1)$ is a l_1 penalized partial likelihood function of β, ϕ
    - $E(Q_2)$ is a posterior density of θ given $E(\gamma)$
    - $E(Q_1)$ and $E(Q_2)$ are conditionally independent
  - Calculate $E(\gamma_j)$, $E(\gamma_j^*)$ and the penalties parameters by Bayes' theorem
- M-step:
  - Use Coordinate Descent to fit the penalized model in $E(Q_1)$ to update β, ϕ
  - Closed form calculation via $E(Q_2)$ to update θ

Numeric Studies

Simulation Study

- $n_{train} = 500$, $n_{test} = 1000$
- $p = 4, 10, 50, 100, 200$
- Survival and censoring time follow Weibull distribution

$$\log \eta = (x_1 + 1)^2/5 + \exp(x_2 + 1)/25 + 3\sin(x_3)/2 + (1.4x_4 + 0.5)/2$$

- Censoring rate is controlled at $\{0.15, 0.3, 0.45\}$
- Splines are constructed using 10 knots
- 50 Iterations

Comparison & Metircs

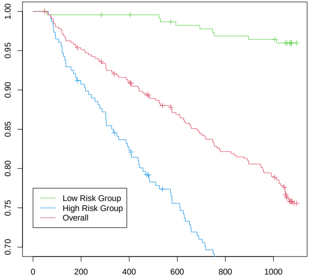
- Methods of comparison
  - Proposed model BHAM
  - Linear LASSO model as the benchmark
  - mgcv (S. N. Wood 2004)
  - COSSO (Zhang and Lin 2006) and adaptive COSSO(Storlie et al. 2011)
- Metrics
  - Out-of-sample deviance & Concordance

Prediction Performance

- Linear LASSO Model performs bad in general
- Low dimensional settings:
  - mgcv performs the best
  - BHAM performs as good as mgcv
- High dimensional setting:
  - BHAM performs better than COSSO models as p increases and more censoring events

Emory Cardiovascular Biobank

- All-cause mortality among patents undergoing cardiac catheterization
- Sample size N=454 and number of features p=200
- 5-knot cubic spline



Conclusion

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- A scalable and flexible Cox Model for high-dimensional survival data analysis
  - Two-part spike-and-slab LASSO prior for spline functions
    - Jointly model signal sparsity and function smoothness with adaptive regularization
    - Bi-level selection that accounts the effect hierarchy principle
  - EM-Coordinate Descent algorithm
    - Computation advantage and sparse solution
- R package: `BHAM`
  - Ancillary functions for high-dimensional formulation
  - Model summary and variable selection
  - Website via *boyiguo1.github.io/BHAM*

References

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