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 $x_{ij}, j = 1, \dots, p$, is expressed as

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

- 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. (Wood 2017)

Function Smoothing

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

$$pl(\beta) = \sum_{i=1}^{n} d_i \log \frac{\exp\left(\beta^T \boldsymbol{x}_i\right)}{\sum_{i' \in R(t_i)} \exp(\beta^T bsx_{i'})} - \sum_{j=1}^{p} \text{pen}_\lambda(B_j(X_j)),$$

  - 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
  - Smooth penalty only overfits the model
  - Sparsity penalty only overshinks the coefficients
  - Damage predictive performance
- Adaptive shrinkage
  - Global shrinkage assumes similar function smoothness
- 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 Marra and Wood (2011), 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

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

Two-part 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

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

EM-Cooridante Descent Algrithm

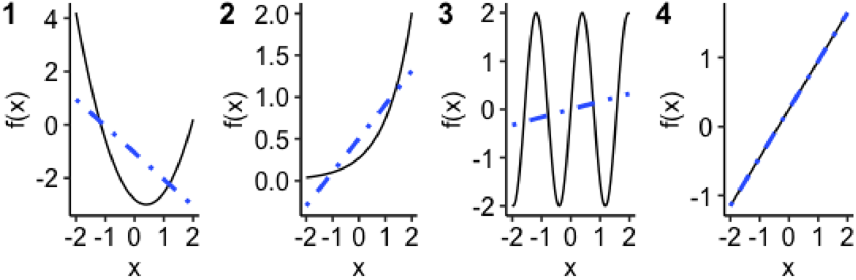
We are interested in estimating $\Theta = \{\boldsymbol{\beta}, \boldsymbol{\theta}\}$ using optimization based algorithm for scalability purpose

- Treat γs as the "missing data" in the EM procedure
  - Construct the conditional expectation of the posterior density function
- Decompose the posterior density function to two pieces
  - L_1 penalized partial likelihood function of β
  - Posterior density function of θ
- Maximize the two pieces independently
  - Optimize β with coordinate descent algorithm
  - Optimize θ with beta-binomial conjugate relationship

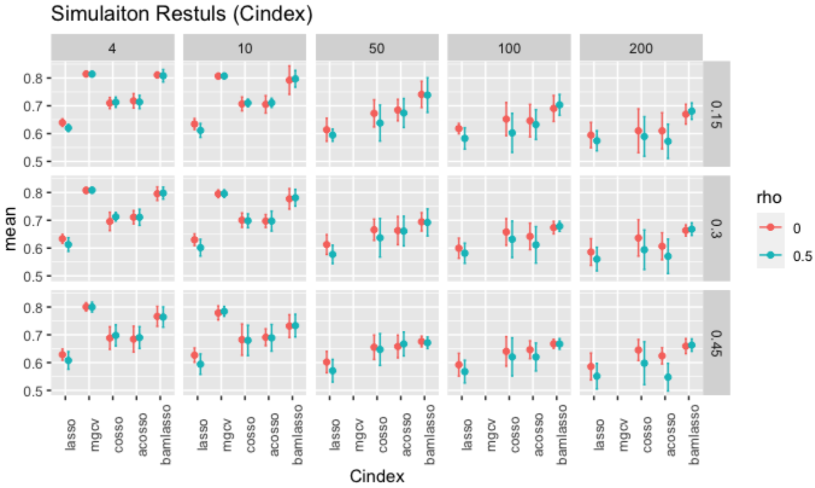
Numeric Studies

Simulation Study

- $n_{train} = 500$, $n_{test} = 1000$
- $p = 4, 10, 50, 100, 200$
- Survival and censoring time follow Weibull distribution
  - Censoring rate is controlled at $\{0.15, 0.3, 0.45\}$

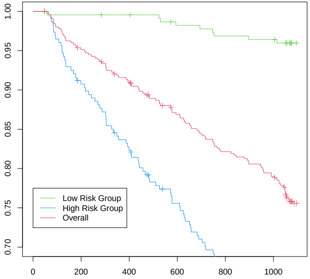


Prediction Performance



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

References I

Hastie, Trevor, Robert Tibshirani, and Jerome Friedman. 2009. *The Elements of Statistical Learning: Data Mining, Inference, and Prediction*. Springer Science & Business Media.

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Wood, Simon N. 2017. *Generalized additive models: An introduction with R, second edition*. https://doi.org/10.1201/9781315370279.