

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

Boyi Guo and Nengjun Yi

Department of Biostatistics
University of Alabama at Birmingham

August 8th, 2022

Background

Background

“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

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

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

Function Smoothing

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

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

- ▶ 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 $B(X) = \mathbf{X}^T \boldsymbol{\beta}$ can be decomposed to linear and nonlinear components with respect to the smoothing penalty matrix S

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

Two-part spike-and-slab LASSO prior

$$\beta_j | \gamma_j, s_0, s_1 \sim DE(0, (1 - \gamma_j)s_0 + \gamma_j s_1)$$

$$\beta_{jk}^* | \gamma_j^*, s_0, s_1 \stackrel{\text{iid}}{\sim} DE(0, (1 - \gamma_j^*)s_0 + \gamma_j^* s_1), k = 1, \dots, K - 1$$

- ▶ 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^*

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

- ▶ Simplification via analytic integration

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

- ▶ Adaptive shrinkage

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

EM-Coordinate Descent Algorithm

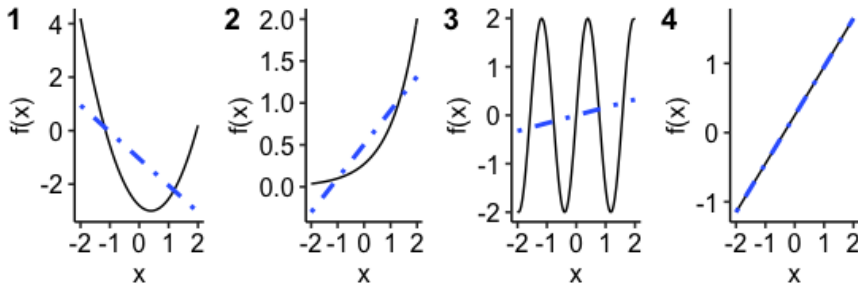
We are interested in estimating $\Theta = \{\beta, \theta\}$ using optimization based algorithm for scalability purpose

- ▶ Treat γ s 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

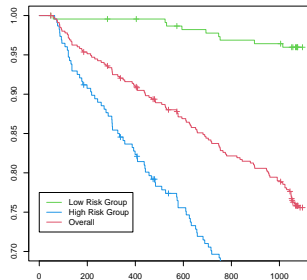
- ▶ $n_{train} = 500$, $n_{test} = 1000$
- ▶ $p = 4, 10, 50, 100, 200$
- ▶ Survival and censoring time follow Weibull distribution
 - ▶ Censoring rate is controlled at $\{0.15, 0.3, 0.45\}$



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

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

Conclusion

- ▶ 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.
- Marra, Giampiero, and Simon N Wood. 2011. "Practical Variable Selection for Generalized Additive Models." *Computational Statistics & Data Analysis* 55 (7): 2372–87.
- Wood, Simon N. 2017. *Generalized additive models: An introduction with R, second edition*. <https://doi.org/10.1201/9781315370279>.