Spike-and-Slab Additive Models And Fast Algorithms For High-Dimensional Data Analysis

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Dissertation Committee

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Outline

- Background
  - Spline Model Development
  - Bayesian Regularization
  - Bayesian Variable Selection
- Dissertation
  - Bayesian Hierarchical Additive Models
  - Additive Cox Proportional Hazards Model
  - R package `BHAM`
- Conclusion
  - Future Research
  - Closing Statement & Acknowledgment
  - Questions & Answers

Background

Spline Model Development

"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

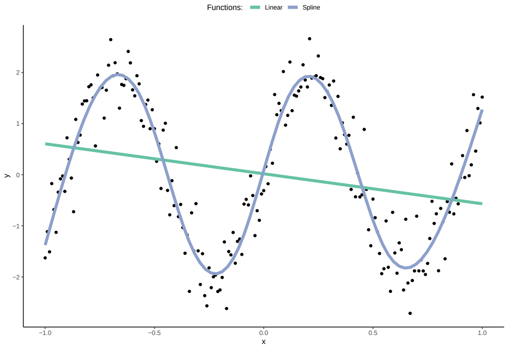
How to model nonlinear effects?

Spline Functions

A *spline* function is a piece-wise polynomial function

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

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



- For simplicity, we assume all functions have K basis functions and knots of functions are equidistance.

Generalized Additive Models with Splines

Generalized additive model (Hastie and Tibshirani 1987) is expressed

$$y_i \overset{\text{iid}}{\sim} EF(\mu_i, \phi), \quad i = 1, \ldots, n$$
$$g(\mu_i) = \beta_0 + B(x_i) = \beta_0 + \boldsymbol{X}_i^T \boldsymbol{\beta}, \quad \mathbb{E}\left[B(X)\right] = 0$$

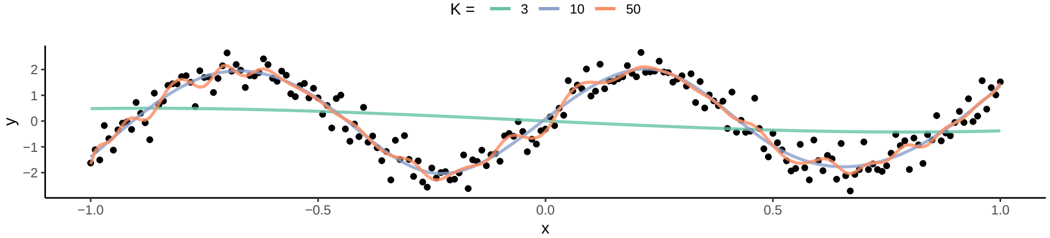
where $B(x_i)$ is the spline function, $g(\cdot)$ is a link function, ϕ is the dispersion parameter

- Model fitting follows the generalized linear models, e.g. ordinary least square for Gaussian outcome
$$\hat{\boldsymbol{\beta}} = \arg\min \sum_{i=1}^{n} \left[y_i - \beta_0 - \boldsymbol{X}_i^T \boldsymbol{\beta}\right]^2$$

Problem: Function Smoothness

Question

How to mathematically define and estimate the smoothness of spline functions?



Smoothing Spline Model

- 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 Least Square for Gaussian Outcome

$$\hat{\beta} = \arg\min \sum_{i=1}^{n} \sum_{i=1}^{n} \left[y_i - \beta_0 - \boldsymbol{X}_i^T \beta \right]^2 + \lambda \beta^T \boldsymbol{S} \beta$$

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

Problem: Multiple Predictor Model

When a model contains multiple spline functions for variables $X_1, \dots, X_p$, the penalized least square estimator is

$$\hat{\beta} = \arg\min \sum_{i=1}^{n} \left[y_i - \beta_0 - \sum_{j=1}^{p} \boldsymbol{X}_{ij}^T \beta_j \right]^2 + \sum_{j=1}^{p} \lambda_j \beta_j^T \boldsymbol{S}_j \beta_j$$

Question

How to choose λ_i for $i = 1, \dots, p$?

- Global smoothing: $\lambda_1 = \cdots = \lambda_p$
- Adaptive smoothing: unique λ_i for $i = 1, \dots, p$

Bayesian Regularization

- Bayesian regularization is the Bayesian analogy of penalized models by using regularizing priors

$$\text{Bayesian ridge:} \quad \beta \sim N(0, \tau^2) \rightarrow \lambda = \sigma^2/\tau^2$$

- Adaptive shrinkage with hierarchical priors

$$\tau_j^2 \overset{\text{iid}}{\sim} IG(a, b)$$

- Adaptive smoothing
  - Random walk prior on b-spline bases with IG hyperprior (Lang and Brezger 2004)
  - Log-normal spline model for τ_k^2 (Baladandayuthapani, Mallick, and Carroll 2005)

Problem: Functional Selection

In the context of variable selection and high-dimensional statistics, we always assume some variables are not effective or predictive of the outcome.

Question

How to statistically detect

- if a variable is predictive to the outcome, $B_j(X_j) = 0$
- if a variable has a nonlinear relationship with the outcome, $B_j(X_j) = \beta_j X_j$

Bi-level selection is the procedure that simultaneously addresses the two questions above

Spike-and-Slab Priors

Spike-and-slab priors are a family of mixture distributions that employs a characterizing structure

$$\beta|\gamma \sim (1-\gamma)f_{spike}(\beta) + \gamma f_{slab}(\beta)$$

- Latent indicator γ follows a Bernoulli distribution with probability θ
- Slab density $f_{slab}(x)$ is a flat density for large effects
- Spike density $f_{spike}(x)$ concentrates around 0 for small effects
- Natural procedure to select variables via posterior distribution of γ
- Markov chain Monte Carlo is not compelling for high-dimensional data analysis

Spike-and-Slab LASSO Priors

- Double exponential distributions as the spike and slab distributions

$$\beta|\gamma \sim (1-\gamma)DE(0, s_0) + \gamma DE(0, s_1), 0 < s_0 < s_1$$

  - Computation advantages via Expectation-Maximization (EM) algorithms
  - Seamless variable selection as coefficients shrink to 0
- Group spike-and-slab LASSO prior
  - Structure among predictors, e.g. gene pathways, bases of a spline function
  - Structured prior $\gamma_k|\theta_j \overset{\text{iid}}{\sim} Binomial(1, \theta_j), k \in j$

Problem: High-dimensional Spline Model

Question

How to jointly model signal sparsity and function smoothness, while capable of bi-level selection?

- Excess shrinkage due to negligence of smooth penalty
  - Group LASSO penalty (Ravikumar et al. 2009; Huang, Horowitz, and Wei 2010), group SCAD penalty (Wang, Chen, and Li 2007; Xue 2009)
- All-in-all-out selection
  - Failed to select function as a whole, e.g. group spike-and-slab LASSO prior
  - Can not detect if a function is linear, e.g. spike-and-slab grouped LASSO prior (Bai et al. 2020; Bai 2021)

Dissertation

Objectives

- To develop statistical models that improve curve interpolation and outcome prediction
  - Adaptive regularization that accounts for signal sparsity and function smoothness
  - Bi-level selection for linear and nonlinear effect
- To develop a fast and scalable algorithm
- To implement a user-friendly statistical software

Projects

- **Guo, B.**, Jaeger, B. C., Rahman, A. F., Long, D. L., Yi, N. (2022). Spike-and-Slab LASSO generalized additive models and scalable algorithms for high-dimensional data analysis. *Statistics in Medicine*. doi: https://doi.org/10.1002/sim.9483
- **Guo, B.**, Jaeger, B. C., Rahman, A. F., Long, D. L., Yi, N. (2022). A scalable and flexible Cox proportional hazards model for high-dimensional survival prediction and functional selection. *arXiv*. doi: https://doi.org/10.48550/arXiv.2205.11600
- **Guo, B.**, Yi, N. (2022). `BHAM`: An R Package to Fit Bayesian Hierarchical Additive Models for High-dimensional Data Analysis. *arXiv*. doi: https://doi.org/10.48550/arXiv.2207.02348

Bayesian Hierarchical Additive Models

Generalized Additive Model

Given the data $\{y_i, x_{i1}, \dots, x_{ip}\}_{i=1}^n$ where $p >> n$

$$y_i \overset{\text{i.i.d.}}{\sim} EF(\mu_i, \phi), \quad i = 1, \dots, n.$$

$$g(\mu_i) = \beta_0 + \sum_{j=1}^{p} B_j(x_{ij}) = \beta_0 + \sum_{j=1}^{p}\sum_{k=1}^{K} \beta_{jk} b_{jk}(x_{ij}) = \beta_0 + \sum_{j=1}^{p} \boldsymbol{X}_{ij}^T \boldsymbol{\beta}_j$$

- Each spline function consists of K bases
- Identifiability constraint: $\mathbb{E}\left[B_j(X)\right] = 0, j = 1, \dots, p$

Spline Function Reparameterization

- Smoothing penalty $\lambda\beta^T \boldsymbol{S}\beta$
  - $\boldsymbol{S}$ is symmetric and positive semi-definite
  - $\boldsymbol{S} = \boldsymbol{U}\boldsymbol{D}\boldsymbol{U}^T$ via eigendecompostion
- Isolate the linear and nonlinear components

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

- Benefits
  - Motivate bi-level selection
  - Implicit modeling of function smoothness
  - Reduce computation load with conditionally independent prior of basis coefficients

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

- SSL prior for the linear coefficient and modified group SSL priors for nonlinear coefficients

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

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

Effect Hierarchy

- *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^*

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

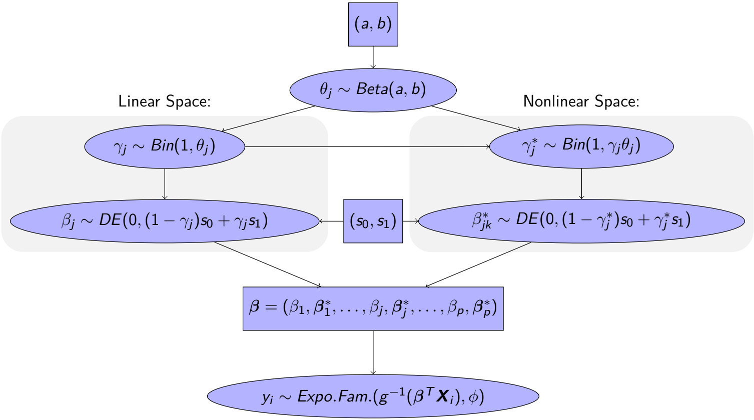
  - Simplification via analytic integration

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

- Adaptive shrinkage

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

Visual Representation



EM-Cooridante Descent Algrithm for Scalable Model Fitting

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
- Previous applications in high-dimensional data analysis
  - EMVS (Ročková and George 2014), Spike-and-slab LASSO (Ročková and George 2018)
  - BhGLM (Yi et al. 2019)

Decomposition of Objective Function

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

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

- L_1-penalized likelihood function of $\boldsymbol{\beta}, \phi$

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

- 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 $E_{\gamma|\Theta^{(t)}}[Q(\Theta,\gamma)] = E(Q_1) + E(Q_2)$
    - $E(Q_1)$ is a penalized 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

Tuning Parameter Selection

- s_0 and s_1 are tuning parameters
- Empirically, s_1 has extremely small effect on changing the estimates
- Focus on tuning s_0
- Consider a sequence of L ordered values $\{s_0^l\} : 0 < s_0^1 < s_0^2 < \cdots < s_0^L < s_1$
- Cross-validation to choose optimal value for s_0

Simulation Study

- Follow the data generating process introduced in Bai et al. (2020).
- $n_{train} = 500,\ n_{test} = 1000$
- $p = 4, 10, 50, 200$

$$g(\mu) = 5\sin(2\pi X_1) - 4\cos(2\pi X_2 - 0.5) + 6(X_3 - 0.5) - 5(X_4^2 - 0.3),$$

- $f_j(x_j) = 0$ for $j = 5, \ldots, p$.
- 2 types of outcome: Gaussian ($\phi = 1$), Binomial
- 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)
  - Sparse Bayesian GAM (Bai 2021)
  - spikeSlabGAM (Scheipl, Fahrmeir, and Kneib 2012)
- Metrics
  - Prediction: R^2 for continuous outcomes, AUC for binary outcomes
  - Variable Selection: positive predictive value (precision), true positive rate (recall), and Matthews correlation coefficient (MCC)

Prediction Performance

- Linear LASSO Model performs bad and mgcv performs well
- BHAM performs better than COSSO, adaptive COSSO and spikeSlabGAM
- BHAM performs better than SB-GAM in low-dimensional case but slightly worse in the high-dimensional setting
- BHAM is much faster than SB-GAM in fitting models

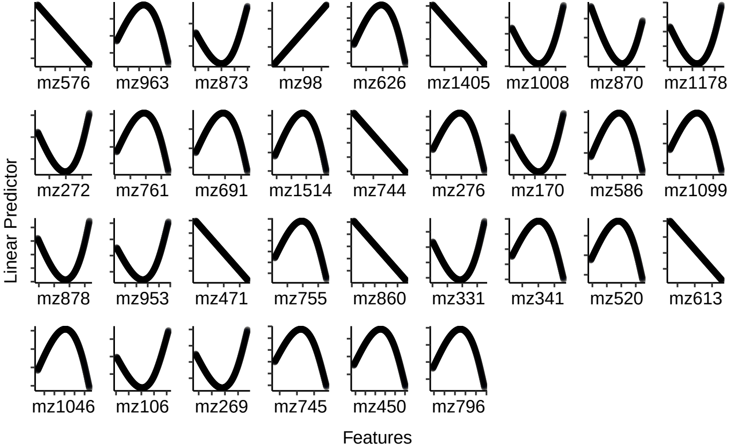
Variable Selection Performance

- SB-GAM has the best variable selection performance
- BHAM has conservative selection
- BHAM and spikeSlabGAM have trade-offs for bi-level selection
    - spikeSlabGAM tends to select only the nonlinear component of the function
    - BHAM is more likely to select both parts

Metabolites Data Applications

- Emory Cardiovascular Biobank
  - Three-year all-cause mortality
  - $p = 200$ and $N = 454$
  - 5-knot cubic spline
- Weight Loss Maintenance Cohort
  - Standardized percent change in insulin resistance
  - $p = 483$ and $N = 237$
  - 5-knot cubic spline
- Compared to SB-GAM, BHAM has better prediction performance and substantial computation advantage

Emory Cardiovascular Biobank



Additive Cox Proportional Hazards Model

Model & Objective Functions

- Cox proportional hazard model with event time t_i

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

  - No intercept term because of the baseline hazard function
- Model fitting
  - Replace likelihood function with partial likelihood function

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

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

- SSL prior for the linear coefficient and group SSL priors for nonlinear coefficients

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

- Effect hierarchy enforced latent inclusion indicators γ_j and γ^*_j for bi-level selection

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

- Local adaptivity of signal sparsity and function smoothness

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

Summary of EM-Coordinate Descent Algorithm

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  - Formulate $E_{\gamma|\Theta^{(t)}}\left[Q(\Theta,\gamma)\right] = E(Q_1) + E(Q_2)$
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  - Calculate $E(\gamma_j)$, $E(\gamma_j^*)$ and the penalties parameters by Bayes' theorem
- M-step:
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  - Closed form calculation via $E(Q_2)$ to update θ

Simulation Study

- Follow the data generating process introduced in Bai et al. (2020).
- $n_{train} = 500, \ n_{test} = 1000$
- $p = 4, 10, 50, 100, 200$
- 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

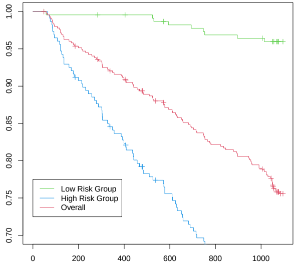
- Methods of comparison
  - Proposed model BHAM
  - Linear LASSO model as the benchmark
  - mgcv (S. N. Wood 2004)
  - COSSO (Zhang and Lin 2006) and adaptive COSSO(Storlie et al. 2011)
- Metrics
  - Out-of-sample deviance & Concordance

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



R Package BHAM

R Package BHAM

- Model formulation for high-dimensional data
- Model fitting and tuning
- Model summary and variable selection
- Spline function visualization
- Website via *boyiguo1.github.io/BHAM*

Design Matrix of Spline Fucntions

- Flexible spline function formulation for high-dimensional data

```
spline_df <- dplyr::tribble(
    ~Var, ~Func, ~Args,
    "X1",  "s", "bs='cr', k=5",
    "X2",  "s", NA,
    "X3",  "s", "")
spline_df <- data.frame(
    Var = setdiff(names(dat), "y"),
    Func = "s",
    Args ="bs='cr', k=7")
train_sm_dat <- BHAM::construct_smooth_data(spline_df, dat)
```

Model Fitting Functions

- Model fitting via `bamlasso`
  - Argument `family` for generalized and survival outcomes
  - Argument `ss` for spike-and-slab LASSO scale parameters
- Model tuning via `tune`
  - Argument `nfolds`, `ncv` for nested cross-validation
  - Argument `s0` for tuning candidates

Post Fitting Functions

- Bi-level selection via `bamlasso_var_selection`
- Make prediction data for splines `make_predict_dat`
- Plot spline functions via `plot_smooth_term`

Conclusion

Future Research

Varying Coefficient Models

- Assume the coefficient of a variable X_j is a function of a covariate Z_j
  - linear model: $\beta(Z_j) = \beta$
  - VC model: $\beta(Z_j) = B(Z_j)$
- Replace each spline function $B(z_{ij})$ with $B(z_{ij})x_{ij} \equiv (x_{ij}\boldsymbol{Z}_{ij}^T)\beta_j$
- Model fitting with EM-Coordinate Descent
- Nonlinear interaction of a continuous variable and a categorical variable

Question

How to model nonlinear interaction of two continuous variables?

Smooth Surface Fitting

- Tensor product of spline functions

$$B_{js}(x_{ij}, x_{is}) = \sum_{P\rho=1}^{K} \sum_{v=1}^{K} \beta_{jspv} b_{j\rho}(x_{ij}) b_{sv}(x_{is})$$

- Smooth Surface

$$B_j(x_{ij}) + B_s(x_{is}) + B_{js}(x_{ij}, x_{is}),$$

Question

Can we have a generalized model that accounts fixed effects, nonlinear curves, smooth surfaces, and random effects?

Structural Additive Model

High-dimensional structural additive model can be formulated as

$$g(\mathbb{E}(y_i)) = \boldsymbol{x}_i^T \boldsymbol{\theta} + \boldsymbol{u}_i^T \gamma + B(z_{i1}) + B(z_{i2}, z_{i3}) + B_{spat}(s_i)$$

- Un-regularized predictors $\boldsymbol{x}_i$
- Regularized predictors $\boldsymbol{u}_i$
- Predictors with nonlinear effects $\boldsymbol{z}_i$
- Spatial random effects with coordinates s_i

Spike-and-slab LASSO prior motivates a seamless process of variable/functional selection and a scalable optimization-based model fitting algorithm

Conclusion

- Identify challenges in high-dimensional GAM with spline functions
  - Balance between signal sparsity and function smoothness
  - Bi-level selection to automatically detect linear and nonlinear effects
- Statistical contribution
  - Two-part spike-and-slab LASSO prior for spline functions
  - Scalable EM-Coordinate Descent algorithms for generalized and survival outcomes
  - R package `BHAM`
- Future Research
  - Extension of spike-and-slab LASSO prior in structured additive model

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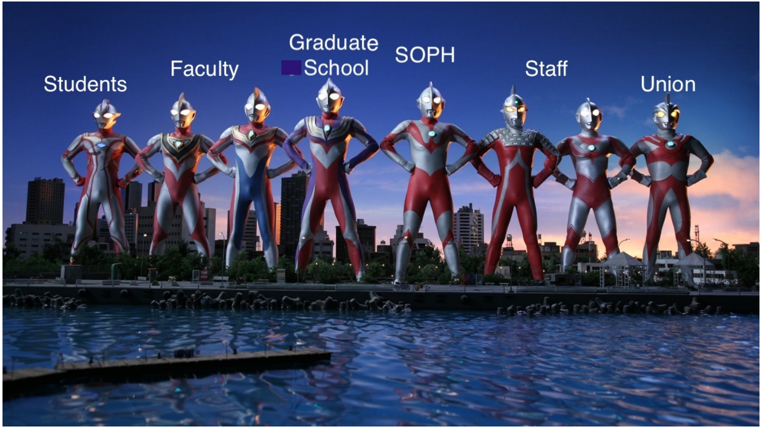
  - PIs
  - Analytic Team
  - Collaborators
- School of Public Health
  - Friends
- Public Health Student Association
- Graduate Student Government

Advocacy

Advocacy



Q & A

Q & A

TODO (Audience): Feel free to ask questions

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