

Generalized Group Lasso for Patient Subgroup Selection

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Overview

1 Introduction

- Prognostic and Predictive Biomarkers
- Why not regression trees?

2 Models

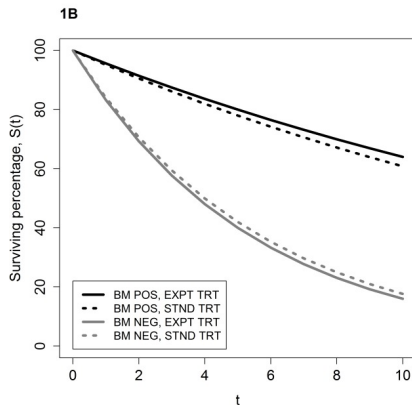
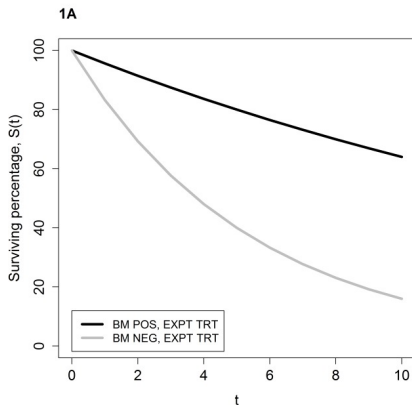
3 Algorithm

4 Criteria

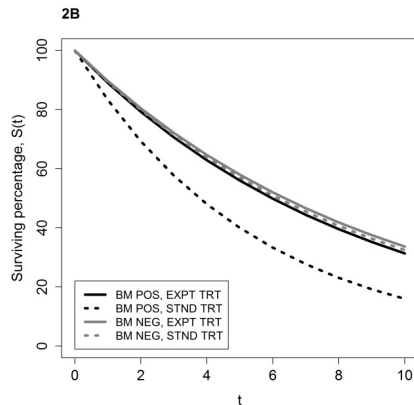
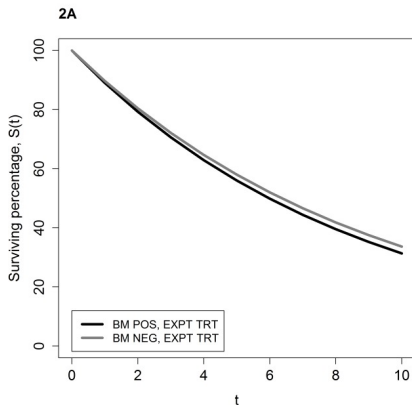
5 Simulation

6 Second Section

Prognostic Biomarkers



Predictive Biomarkers



Regression trees GUIDE[Loh, 2018]:

- piecewise-linear Model
- examine residual patterns for each treatment level

Cannot repeat even the most naive simulation in GUIDE paper.

Reason: limited sample size. Even two splits will results in small sample size in each branch. The results would be highly unstable. Tree-based method is not appropriate to clinical trial dataset and identify prognostic and predictive biomarkers.

Ordinary Linear Model

$$Y = X\beta + W\tau + G\alpha + W \otimes G\gamma + \epsilon$$

- X : Baseline variables
- W : Treatment variables
- G : Main effects of genes, i.e. expression levels, SNP or mutation
- $W \otimes G$: Interaction effects of genes and treatment
- ϵ : Random errors

We choose group lasso for its ability to

- handle high dimensional data
- allow hierarchical structure

However, the current group lasso based methods

- penalize on all parameters
- have no efficient adaptive penalty weights
- do not specifically target on patients treatment subgroup identification

Loss Function

We assume the hierarchical relationship between prognostic biomarkers and predictive biomarkers, that is a predictive biomarker should be a prognostic biomarker.

The loss function is

$$\min_{\theta} f(\theta|Y, X, W, G) + \lambda \sum_i \eta_i^I |\gamma_i| + \lambda \sum_i \eta_i^M \sqrt{\alpha_i^2 + \gamma_i^2}$$

where $f(\theta|Y, X, W, G)$ is L-2 loss function, i.e. sum of squared errors for ordinary linear model.

$\theta = (\beta, \tau, \alpha, \gamma)$ is parameter vector.

Loss function for ordinary linear model

$$\min_{\theta} \| Y - (X\beta + W\tau + G\alpha + W \otimes G\gamma) \|^2 + \lambda \sum_i \eta_i^l |\gamma_i| + \lambda \sum_i \eta_i^M \sqrt{\alpha_i^2 + \gamma_i^2}$$

Denote $X^{(l)} = [G_l, W \otimes G_l]$ is the l th group of the main and interaction effects of gene l . Then we let

$$\eta_i^l = \| X^{(i)} \|_2$$

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Heading

- 1 Statement
- 2 Explanation
- 3 Example

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Table

Treatments	Response 1	Response 2
Treatment 1	0.0003262	0.562
Treatment 2	0.0015681	0.910
Treatment 3	0.0009271	0.296

Table: Table caption

Theorem

Theorem (Mass–energy equivalence)

$$E = mc^2$$

Example (Theorem Slide Code)

```
\begin{frame}  
\frametitle{Theorem}  
\begin{theorem}[Mass--energy equivalence]  
$E = mc^2$  
\end{theorem}  
\end{frame}
```

 Loh, Wei-Yin, Michael Man, and Shuaicheng Wang.

"Subgroups from regression trees with adjustment for prognostic effects and postselection inference."

Statistics in medicine (2018).

The End