# Generalized Group Lasso for Patient Subgroup Selection

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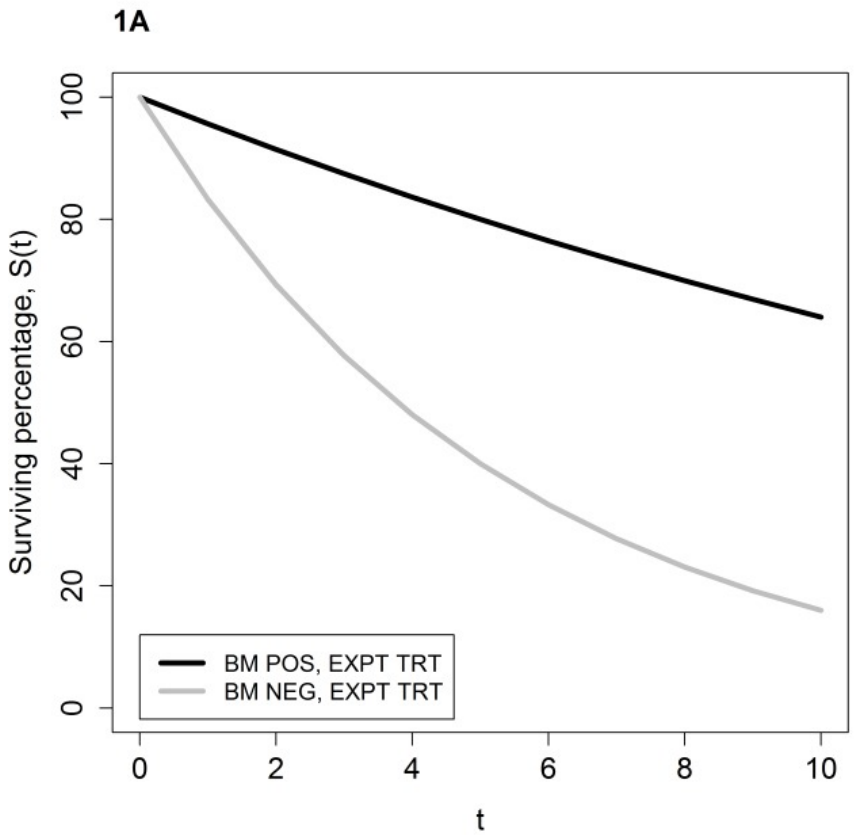
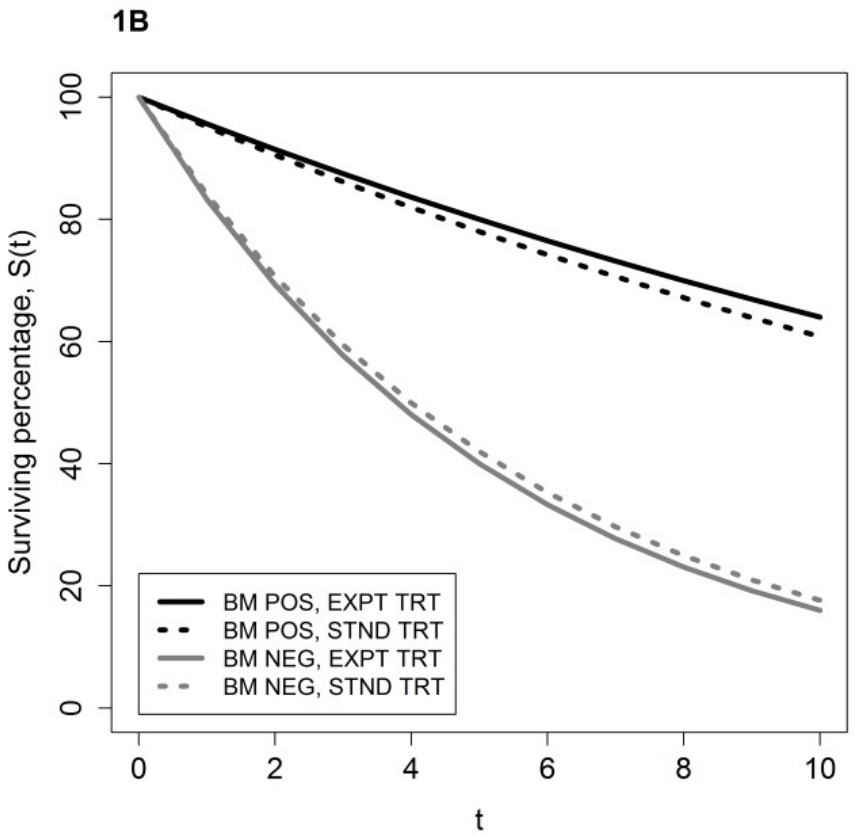
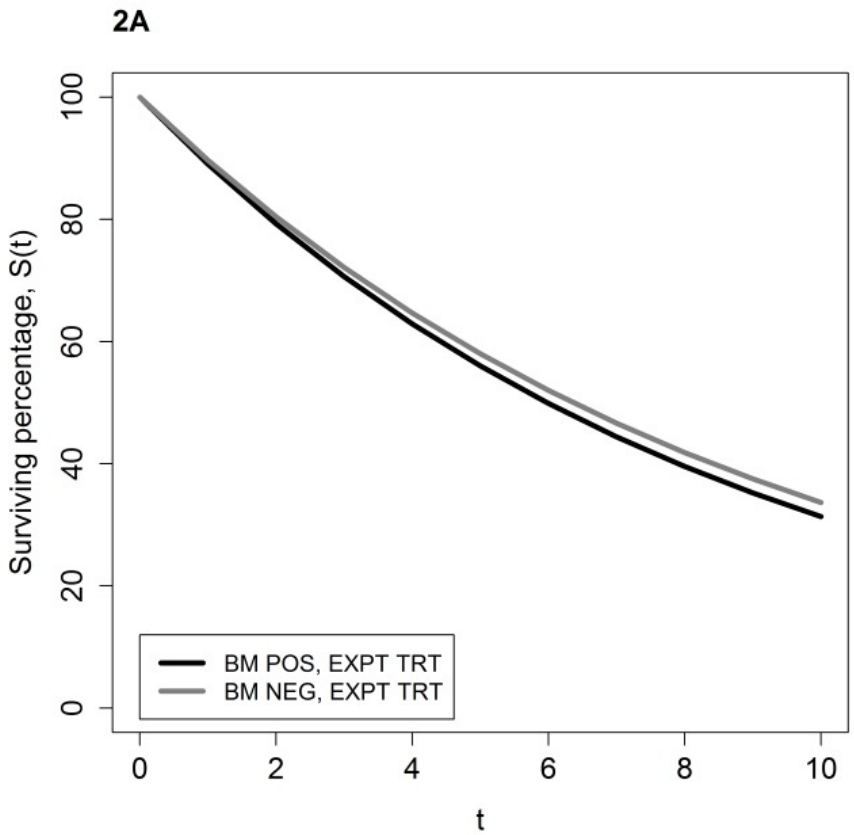
# Overview

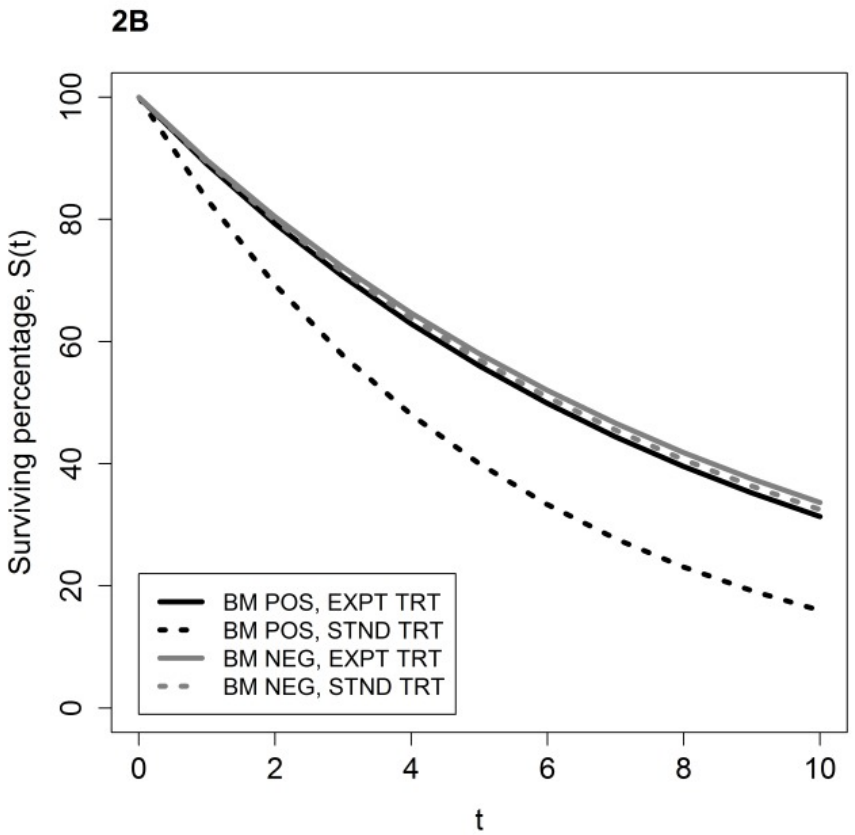
# Prognostic Biomarkers



# Predictive Biomarkers



# Tree-based Methods

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
- $\epsilon$: Random errors

# Group lasso

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

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

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

$$\eta_i^I = \parallel X^{(i)} \parallel_2$$

# Blocks of Highlighted Text

## Block 1

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## Block 2

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# Multiple Columns

**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)

$E = mc^2$

# Verbatim

## Example (Theorem Slide Code)

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

# References

Loh, WeiYin, Michael Man, and Shuaicheng Wang.

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

*Statistics in medicine* (2018).

# The End