

# High-Dimensional Variable Selection for Competing Risks with Cooperative Penalized Regression «CooPeR»

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# Introduction

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- Settings with two competing events  $e \in \{1, 2\}$ , e.g.,
  - (1) Death from bladder cancer
  - (2) Death from other causes

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- Common approach:
  - Fit cause-specific model for event of interest
  - Treats other event as censored  
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**Main goal:** Fit cause-specific model for event 1 **using shared information** from event 2

# Elastic Net



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Objective function with negative log-likelihood contribution for observation  $i$ :

$$\hat{\beta} = \operatorname{argmin}_{\beta} \sum_{i=1}^n \ell(y_i, \mathbf{x}_i^{\top}, \beta) + \lambda \sum_{j=1}^p \left( \alpha |\beta_j| + \frac{1 - \alpha}{2} \beta_j^2 \right)$$

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# Feature-Weighted Elastic Net



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Feature-weighted elastic net<sup>1</sup> extends objective function:

$$\hat{\beta} = \underset{\beta}{\operatorname{argmin}} \quad \sum_{i=1}^n \ell(y_i, \mathbf{x}_i^{\top}, \beta) + \lambda \sum_{j=1}^p w_j(\theta) \left( \alpha |\beta_j| + \frac{1-\alpha}{2} \beta_j^2 \right)$$

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<sup>1</sup>Tay et al. (2023)

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$$w_j(\theta) = \frac{\sum_{l=1}^p \exp(\mathbf{z}_l^{\top} \theta)}{p \exp(\mathbf{z}_j^{\top} \theta)}$$

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Grouping:  $\mathbf{Z} \in \mathbb{R}^{5 \times 2}$

$$\mathbf{Z} = \begin{pmatrix} 1 & 0 \\ 1 & 0 \\ 0 & 1 \\ 0 & 1 \\ 0 & 1 \end{pmatrix}$$

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Individual weighting:  $\mathbf{Z} \in \mathbb{R}^{5 \times 1}$

$$\mathbf{Z} = \begin{pmatrix} 1.5 \\ 1 \\ 1.2 \\ 0.7 \\ 0.3 \end{pmatrix}$$

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- Larger value  $\Rightarrow$  lower  $w_j$

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- $\mathbf{z}_j^\top \theta$ : “Importance score”
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- $\theta \in \mathbb{R}^{K \times 1}$  fit internally
- $\theta = 0 \Rightarrow w_j = 1$

# Individual Feature Weighting

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- Simulation from Tay et al.:  $\mathbf{Z}$  set to noisy version of true  $|\boldsymbol{\beta}|$
- $|\beta_j|$  large  $\Rightarrow$  weaker penalization for  $\hat{\beta}_j$
- $|\beta_j|$  small  $\Rightarrow$  stronger penalization for  $\hat{\beta}_j$

# “Cooperative Penalized Regression” (CooPeR)

Based on multi-task algorithm suggested by Tay et al.

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1. Set  $\hat{\beta}_1^{(0)}, \hat{\beta}_2^{(0)}$  to elastic net solution for  $(\mathbf{X}, \mathbf{y}_1), (\mathbf{X}, \mathbf{y}_2)$  with  $\mathbf{y}_e := (\mathbf{t}_e, \delta_e)$

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2. For  $k = 0, 1, \dots$  until stopped:
  - a) Fit fwelnet  $(\mathbf{X}, \mathbf{y}_2, \mathbf{Z}_2 = |\hat{\beta}_1^{(k)}|)$  to determine  $|\hat{\beta}_2^{(k+1)}|$

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  - b) Fit fwelnet  $(\mathbf{X}, \mathbf{y}_1, \mathbf{Z}_1 = |\hat{\beta}_2^{(k+1)}|)$  to determine  $|\hat{\beta}_1^{(k+1)}|$

# Simulation Study

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- Simulation adapted from Binder et al.<sup>2</sup>
- Mimics gene expression data
- Comparison with CoxBoost<sup>3</sup>, Random Survival Forests<sup>4</sup>

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- Comparison with CoxBoost<sup>3</sup>, Random Survival Forests<sup>4</sup>
- $n = 400$ ,  $p = 5000$ ,
- 4 covariate blocks
- 4 informative variables each

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# Assignment of True Effects

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- Block 1 (**Mutual**): Same effect on both cause-specific hazards
- Block 2 (**Reversed**): Cause 1 (+) Cause 2 (-)
- Block 3 (**Disjoint**): Cause 1 **or** 2

# Assignment of True Effects

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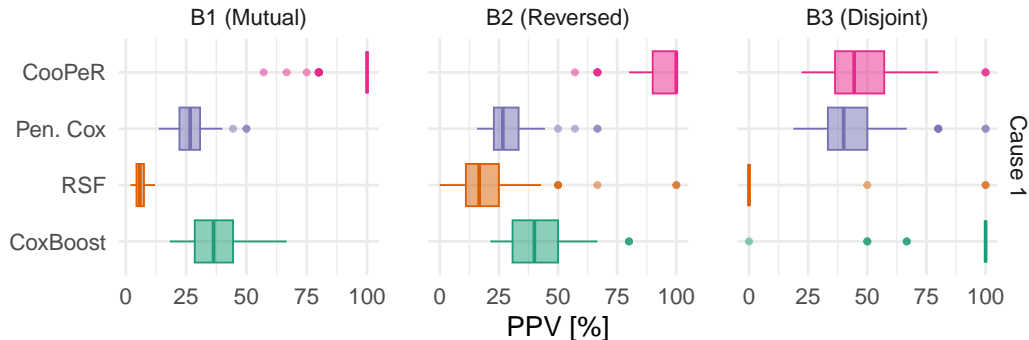


11

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- Block 4 (**Cor. Noise**)
- Rest: Uncorrelated noise

# Positive Predictive Value

Probability a selected variable is informative

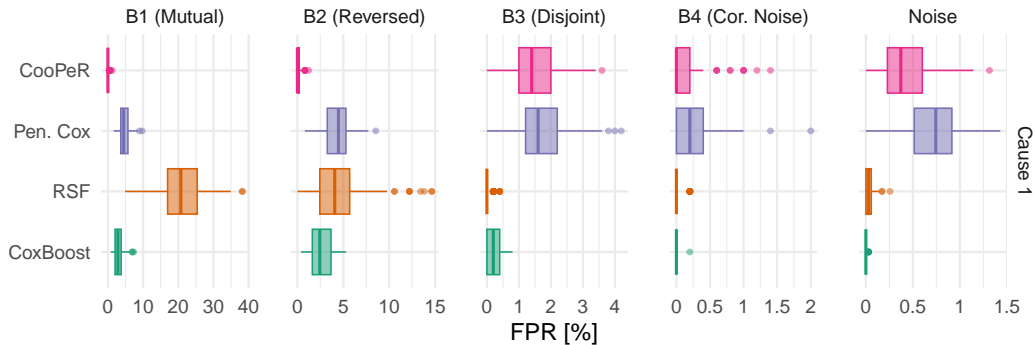




# False Positive Rate

## Proportion of noise variables falsely selected

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# Application on Bladder Cancer Data

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- Clinical & gene expression features <sup>5</sup>

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- Proxy to estimate variable selection performance:
  1. Apply algorithms for variable selection
  2. Fit standard cause-specific Cox model using only selected variables
  3. Evaluate prediction performance (Brier(t), AUC(t))

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- Results:
  - CooPeR-selected variables mostly identical to pen. Cox regression
  - Difference in metrics far from conclusive in either direction

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- Results:
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  - Difference in metrics far from conclusive in either direction
- No shared effects? Effects too small?

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## Conclusion & Outlook

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- So far no promising results on real data
- Lack of readily available high-dimensional data with competing risks



## Conclusion & Outlook

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- Promising variable selection behavior in simulations
- So far no promising results on real data
- Lack of readily available high-dimensional data with competing risks
- Generalization to  $e > 2$  events: Unclear

Thank you for your attention!

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