Nonparametric Bayesian Lomax delegate racing for survival analysis with competing risks

Quan Zhang and Mingyuan Zhou

Mccombs School of Business, University of Texas at Austin

Contact Information:
Department of Information, Risk and Operations Management
2110 Speedway, Austin, TX 78705, US
Email: quan.zhang@mccombs.utexas.edu

Abstract

We propose Lomax delegate racing (LDR) to explicitly model the mechanism of survival under competing risks and to interpret how the covariates accelerate or decelerate the time to event. LDR explains non-monotonic covariate effects by racing a potentially infinite number of sub-risks, and consequently relaxes the ubiquitous proportional-hazards assumption which may be too restrictive. Moreover, LDR is naturally able to model not only censoring, but also missing event times or event types. For inference, we develop a Gibbs sampler under data augmentation for moderately sized data, along with a stochastic gradient descent maximum a posteriori inference algorithm for big data applications. Illustrative experiments are provided on both synthetic and real datasets, and comparison with various benchmark algorithms for survival analysis with competing risks demonstrates distinguished performance of LDR.

Exponential racing and application to survival analysis

Property 1 (Exponential racing)**.** *If* $t_j \sim \text{Exp}(\lambda_j)$, $j = 1, \cdots, J$, *are independent to each other, then the argument of the minimum* $y = \text{argmin}_j\, t_j$ *and* $t = \min\{t_1, \ldots, t_J\}$ *satisfy*

$$y \sim \text{Categorical}\Big(\lambda_1 \Big/ \sum_{j=1}^J \lambda_j, \cdots, \lambda_J \Big/ \sum_{j=1}^J \lambda_j\Big)$$
$$t \sim \text{Exp}\Big(\sum_{j=1}^J \lambda_j\Big), \text{ and } y \perp t.$$

- A race among J teams. Team j's completion time $t_j \sim \text{Exp}(\lambda_j)$.
- The winner is the team with the minimum completion time.
- Property 1 shows the winner's completion time t still follows an exponential distribution and is independent of which team wins the race.
- Fully factorized likelihood $P(y, t \,|\, \{\lambda_j\}_{1,J}) = \lambda_y e^{-t\sum_{j=1}^J \lambda_j}$.

Survival analysis with competing risks

Exponential racing describes a natural mechanism of surviving under competing risks.

- Team $j \to$ competing risk j,
- Compeletion time $t_j \to$ the latent survival time under risk j.
- Winner's completion time $t \to$ the observed time to event (or failure time).
- The winning team $y \to$ the event type (or cause of failure).
- Easy to deal with censoring.
  If we don't observe t but know $t \in \Psi \subseteq \mathbb{R}_+$ with $P(t \in \Psi \,|\, \{\lambda_j\}_{1,J}) = \int_\Psi \lambda e^{-\lambda u} du$, then we draw $t \sim \text{Exp}_\Psi(\sum_j \lambda_j)$ with PDF $f_\Psi(t \,|\, \lambda) = \lambda e^{-\lambda t}\delta_{t\in Psi} / \int_\Psi \lambda e^{-\lambda u} du$, resulting in the likelihood

$$P\left(t, t \in \Psi \,|\, \sum\nolimits_j \lambda_j\right) = f_\Psi\left(t \,|\, \sum\nolimits_j \lambda_j\right) P\left(t \in \Psi \,|\, \sum\nolimits_j \lambda_j\right)$$
$$= \left(\sum\nolimits_j \lambda_j\right) e^{-t\sum_j \lambda_j}.$$

Covariate-dependent Lomax distribution

If $t \sim \text{Exp}(\lambda)$, $\lambda \sim \text{Gamma}(r, 1/b)$ with $\mathbb{E}(\lambda) = r/b$, then $t \,|\, r, b \sim \text{Lomax}(r, b)$ with PDF $f(t \,|\, r, b) = \frac{rb^r}{(t+b)^{r+1}}$, $t \in \mathbb{R}_+$.
We can model covariate dependence of t by assuming

$$t \,|\, r, \boldsymbol{x}, \boldsymbol{\beta} \sim \text{Lomax}(r, e^{-\boldsymbol{x}'\boldsymbol{\beta}}),$$

where $\boldsymbol{\beta}$ and $\boldsymbol{x}$ are the regression-coefficient and covariate vectors, respectively. The ease to infer $\boldsymbol{\beta}$ becomes clear if we express the likelihood as

$$\text{Lomax}(t; r, e^{-\boldsymbol{x}'\boldsymbol{\beta}}) = \frac{re^{-r\boldsymbol{x}'\boldsymbol{\beta}}}{(t + e^{-\boldsymbol{x}'\boldsymbol{\beta}})^{r+1}} = t^{-1}\text{NB}\left(1; r, \frac{e^{\boldsymbol{x}'\boldsymbol{\beta}+\ln t}}{1 + e^{\boldsymbol{x}'\boldsymbol{\beta}+\ln t}}\right)$$

Lomax delegate racing (LDR)

Definition 1 (Lomax delegate racing)**.** *Given a random draw of a gamma process* $G_j \sim \Gamma\text{P}(G_{0j}, 1/c_{0j})$*, expressed as* $G_j = \sum_{k=1}^\infty r_{jk}\delta_{\boldsymbol{\beta}_{jk}}$*, for each* $j \in \{1, \ldots, J\}$*, Lomax delegate racing (LDR) models* y*, the team number of the winner, and* t*, the winner's completion time, given the covariates* $\boldsymbol{x}$ *as*

$$y = \underset{j\in\{1,\ldots,J\}}{\text{argmin}}\ t_j, \quad t = \min_{j\in\{1,\ldots,J\}} t_j, \quad t_j = t_{j\kappa_j},$$
$$\kappa_j = \underset{k\in\{1,\ldots,\infty\}}{\text{argmin}}\ t_{jk}, \quad t_{jk} \sim \text{Lomax}(r_{jk}, e^{-\boldsymbol{x}'\boldsymbol{\beta}_{jk}}).$$

LDR can be interpreted as a two-phase race between multiple teams consisting of countably infinite players.

- In the first phase, the players within a team compete and the completion time of the team is defined as that of its fastest player.
- In the second phase, the teams compete and the winner of the race is the team that has the shortest completion time.

Survival: teams $\to$ competing risks; players $\to$ sub-risks.
t and (or) y are (is) observed but t_j's are not.

Inference

- Gibbs sampler
  Introduce an auxiliary variable $t_i \sim \text{Exp}\left(\sum_{j=1}^J \sum_{k=1}^\infty \lambda_{ijk}\right)$, or $y_i \sim \text{Categorical}(\lambda_1/\sum_{j=1}^J \lambda_j, \cdots, \lambda_J/\sum_{j=1}^J \lambda_j)$ for individual i. Gibbs sampler updates are similar as those for negative binomial regression, since

$$P(t_i, \kappa_{iy_i}, y_i \,|\, \boldsymbol{x}_i, \{\boldsymbol{\beta}_{jk}\}_{jk})$$
$$= t_i^{-1} \prod_j \prod_k \text{NB}\left(\mathbf{1}(\kappa_{iy_i} = k, y_i = j); r_{jk}, \frac{e^{\boldsymbol{x}_i'\boldsymbol{\beta}_{jk}+\ln t_i}}{1 + e^{\boldsymbol{x}_i'\boldsymbol{\beta}_{jk}+\ln t_i}}\right).$$

  - If y_i is observed, we first sample κ_{iy_i} by

$$P(\kappa_{iy_i} = k \,|\, y_i, \cdots) = \frac{\lambda_{iy_i k}}{\sum_{k'=1}^K \lambda_{iy_i k'}}.$$

    If y_i is unobserved which means a missing event type, we sample (y_i, κ_{iy_i}) by

$$P(y_i = j, \kappa_{iy_i} = k \,|\, \cdots) = \frac{\lambda_{ijk}}{\sum_{j'=1}^S \sum_{k'=1}^K \lambda_{ij'k'}}.$$

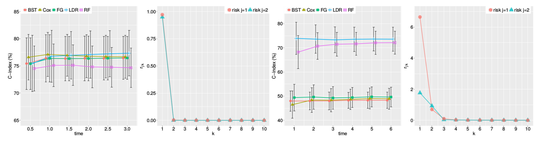
  - Denote $m_{jk} = \sum_{i:y_i=j} \mathbf{1}(\kappa_{iy_i} = k)$. Define $n_{ijk} = 1$ if $y_i = j$ and $\kappa_{iy_i} = k$, and otherwise $n_{ijk} = 0$.
  - Prune redundant capacity. For $j = 1, \cdots, J$ and $k = 1, \cdots, K$, prune sub-risk k of risk j for all observations if $m_{jk} = 0$, by setting $\lambda_{ijk} \equiv 0$ and $t_{ijk} \equiv \infty$ for $\forall i$.
  - Update other parameters by Pólya Gamma and Chinese restaurant table data augmentation.
- Maximum a posteriori (MAP) estimations
  reparameterization: $\lambda_{ijk} \sim \text{Gamma}(r_{jk}, e^{\boldsymbol{x}_i'\boldsymbol{\beta}_{jk}})$
  $\to \lambda_{ijk} = \tilde{\lambda}_{ijk} e^{\boldsymbol{x}_i'\boldsymbol{\beta}_{jk}}$ where $\tilde{\lambda}_{ijk} \sim \text{Gamma}(r_{jk}, 1)$.
  Score function gradients: $\nabla_{\boldsymbol{r}} p(\tilde{\boldsymbol{\lambda}}_i \,|\, \boldsymbol{r}) = p(\tilde{\boldsymbol{\lambda}}_i \,|\, \boldsymbol{r}) \nabla_{\boldsymbol{r}} \log p(\tilde{\boldsymbol{\lambda}}_i \,|\, \boldsymbol{r})$

$$\nabla_{\boldsymbol{\beta}} \log p_i = \frac{\int \left[\nabla_{\boldsymbol{\beta}} \left(p_{t_i} \times p_{y_i}\right)\right] p(\tilde{\boldsymbol{\lambda}}_i \,|\, \boldsymbol{r}) d\tilde{\boldsymbol{\lambda}}_i}{\int \left(p_{t_i} \times p_{y_i}\right) p(\tilde{\boldsymbol{\lambda}}_i \,|\, \boldsymbol{r}) d\tilde{\boldsymbol{\lambda}}_i}$$
$$\approx \frac{\frac{1}{M}\sum_{m=1}^M \nabla_{\boldsymbol{\beta}} \left[p_t(\tilde{\boldsymbol{\lambda}}_i^{(m)} \,|\, \boldsymbol{r}) \times p_y(\tilde{\boldsymbol{\lambda}}_i^{(m)} \,|\, \boldsymbol{r})\right]}{\frac{1}{M}\sum_{m=1}^M \left[p_t(\tilde{\boldsymbol{\lambda}}_i^{(m)} \,|\, \boldsymbol{r}) \times p_y(\tilde{\boldsymbol{\lambda}}_i^{(m)} \,|\, \boldsymbol{r})\right]}$$
$$\nabla_{\boldsymbol{r}} \log p_i = \frac{\int \nabla_{\boldsymbol{r}} \left[\left(p_{t_i} \times p_{y_i}\right) p(\tilde{\boldsymbol{\lambda}}_i \,|\, \boldsymbol{r})\right] d\tilde{\boldsymbol{\lambda}}_i}{\int \left(p_{t_i} \times p_{y_i}\right) p(\tilde{\boldsymbol{\lambda}}_i \,|\, \boldsymbol{r}) d\tilde{\boldsymbol{\lambda}}_i}$$
$$= \frac{\int \left(p_{t_i} \times p_{y_i}\right) \nabla_{\boldsymbol{r}} \log p(\tilde{\boldsymbol{\lambda}}_i \,|\, \boldsymbol{r}) p(\tilde{\boldsymbol{\lambda}}_i \,|\, \boldsymbol{r}) d\tilde{\boldsymbol{\lambda}}_i}{\int \left(p_{t_i} \times p_{y_i}\right) p(\tilde{\boldsymbol{\lambda}}_i \,|\, \boldsymbol{r}) d\tilde{\boldsymbol{\lambda}}_i}$$
$$\approx \frac{\frac{1}{M}\sum_{m=1}^M p_t(\tilde{\boldsymbol{\lambda}}_i^{(m)} \,|\, \boldsymbol{r}) \times p_y(\tilde{\boldsymbol{\lambda}}_i^{(m)} \,|\, \boldsymbol{r}) \nabla_{\boldsymbol{r}} \log p(\tilde{\boldsymbol{\lambda}}_i^{(m)} \,|\, \boldsymbol{r})}{\frac{1}{M}\sum_{m=1}^M \left[p_t(\tilde{\boldsymbol{\lambda}}_i^{(m)} \,|\, \boldsymbol{r}) \times p_y(\tilde{\boldsymbol{\lambda}}_i^{(m)} \,|\, \boldsymbol{r})\right]}.$$

Experimental results

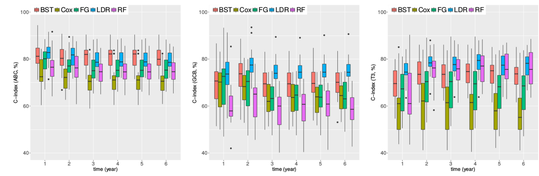
Table 1: Synthetic data generating process.

Synthetic data 1	Synthetic data 2
$t_i = \min(t_{i1}, t_{i2}, 3.5)$, $t_{i1} \sim \text{Exp}(e^{\boldsymbol{x}_i'\boldsymbol{\beta}_1})$, $t_{i2} \sim \text{Exp}(e^{\boldsymbol{x}_i'\boldsymbol{\beta}_2})$	$t_i = \min(t_{i1}, t_{i2}, 6.5)$, $t_{i1} \sim \text{Exp}(1/\cosh(\boldsymbol{x}_i'\boldsymbol{\beta}_1))$, $t_{i2} \sim \text{Exp}(1/\lvert\sinh(\boldsymbol{x}_i'\boldsymbol{\beta}_2)\rvert)$



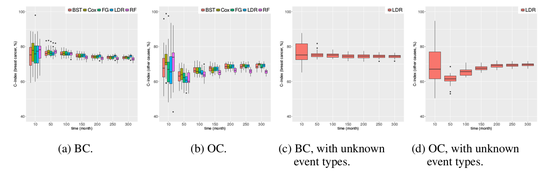
(a) C-index of risk 1 for synthetic data 1. (b) r_{jk} by descending order for synthetic data 1. (c) C-index of risk 1 for synthetic data 2. (d) r_{jk} by descending order for synthetic data 2.

Figure 1: Cause-specific C-indices for synthetic data and shrinkage of r_{jk} by LDR.



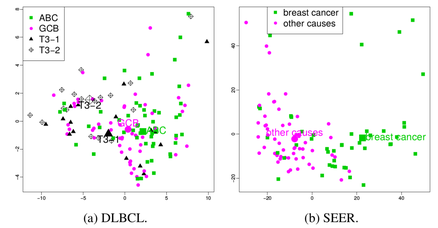
(a) C-index of ABC. (b) C-index of GCB. (c) C-index of T3.

Figure 2: Cause-specific C-indices for the DLBCL data.



(a) BC. (b) OC. (c) BC, with unknown event types. (d) OC, with unknown event types.

Figure 3: Cause-specific C-indices for the SEER breast cancer data.



(a) DLBCL. (b) SEER.

Figure 4: Isomap visualization of the observations and inferred sub-risk representatives.

Table 1: Brier score for T3 of DLBCL.

	$\tau = 1$	$\tau = 2$	$\tau = 3$	$\tau = 4$	$\tau = 5$	$\tau = 6$
Cox	.193±.053	.190±.061	.206±.069	.220±.071	.233±.068	.245±.072
FG	.183±.051	.186±.062	.195±.067	.212±.069	.230±.070	.234±.069
BST	.169±.046	.172±.044	.177±.049	.185±.046	.185±.047	.193±.048
RF	.117±.045	.151±.046	.157±.043	.169±.049	.180±.051	.185±.052
LDR	**.111**±.035	**.137**±.038	**.142**±.036	**.151**±.041	**.165**±.044	**.171**±.046

Conclusions

- Modeling of natural mechanism of surviving under competing risks.
- Interpretable nonlinearity for survival analysis.
- Data mining of sub-risks.
- Introducing covariate dependencies to exponential racing.
- Gibbs sampler by data augmentation.
- Scalability by reparameterization and score function gradients for MAP estimations.