

The negative log-likelihood loss and cross-validation with censored data

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Coffee Talk
Section of Biostatistics

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Outline

Model and hyper-parameter selection for survival models

The least false model in the presence of censoring

Hold-out samples and survival model estimators

Selecting a model from a collection of candidate models

Consider estimation of the parameter

$$\theta(P) := \operatorname{argmin}_{f \in \mathcal{F}} P[L(f, \cdot)], \quad \text{where} \quad P[g] := \int_{\mathcal{O}} g(o) P(\mathrm{d}o),$$

for some loss function $L: \mathcal{F} \times \mathcal{O} \rightarrow \mathbb{R}_+$.

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If \mathcal{F} is a collection of densities on \mathcal{O} and $L(f, O) := -\log(f(O))$, then $\theta(\hat{\mathbb{P}}_n)$ is the MLE for the model \mathcal{F} , where $\hat{\mathbb{P}}_n$ denotes the empirical measure.

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Hyper-parameter selection

For estimation in high-dimensional settings we often introduce a regularization parameter λ (e.g., LASSO, kernel smoothing). To select a value for λ we would typically split the data $\mathcal{D}_n = \{O_1, \dots, O_n\}$ randomly in two, \mathcal{D}_n^1 and \mathcal{D}_n^2 , and calculate

$$\operatorname{argmin}_{\lambda \in \Lambda} \hat{\mathbb{P}}_n^2[L(\hat{f}_\lambda^1, \cdot)],$$

where $\hat{\mathbb{P}}_n^2$ denotes the empirical measure based on the sample \mathcal{D}_n^2 , and \hat{f}_λ^1 denotes an estimator calculated on \mathcal{D}_n^1 with regularization parameter λ .

A loss function for survival data

$O = (\tilde{T}, \Delta, X) \sim P \in \mathcal{P}$ Observed data with $\mathcal{O} = \mathbb{R}_+ \times \{0, 1\} \times \mathbb{R}^p$.

$(T, X) \sim Q \in \mathcal{Q}$ The distribution Q (or a feature of it) is of interest.

Assuming coarsening at random [Gill et al., 1997] we can write

$$\mathcal{P} = \{P_{Q,G} : Q \in \mathcal{Q}, G \in \mathcal{G}\},$$

where \mathcal{G} denotes a collection of conditional distributions for the censoring mechanism, and the likelihood factorizes as

$$\ell(P_{Q,G}, O) = \ell_F(Q, O) \cdot \ell_C(G, O),$$

with

$$\ell_F(Q, O) := q(\tilde{T} | X)^\Delta \bar{Q}(\tilde{T} | X)^{1-\Delta} m(X),$$

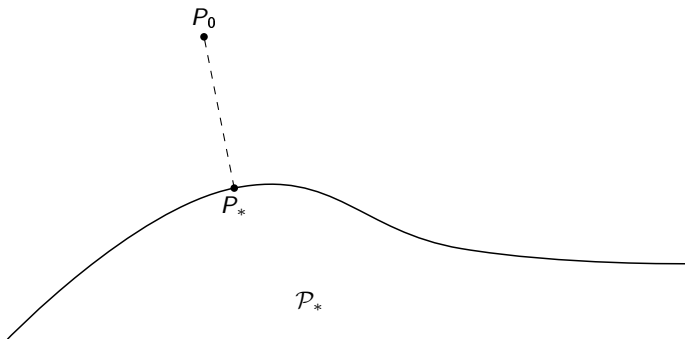
where q and \bar{Q} are the conditional density and survivor function, respectively, and m the marginal distribution of X .

Natural to use the negative partial log-likelihood $-\log \ell_F$ as loss function, or even only the first part concerning the conditional distribution of T given X .

Kullback-Leibler divergence and partial likelihoods

Maximum likelihood estimation is connected to minimizing the Kullback-Leibler divergence and gives an interpretation of the MLE under mis-specified models.

$$D_{\text{KL}}(P_0 \parallel P) := P_0 \left[\log \frac{p_0}{p} \right], \quad \text{where} \quad P_0 = p_0 \cdot \mu, P = p \cdot \mu.$$



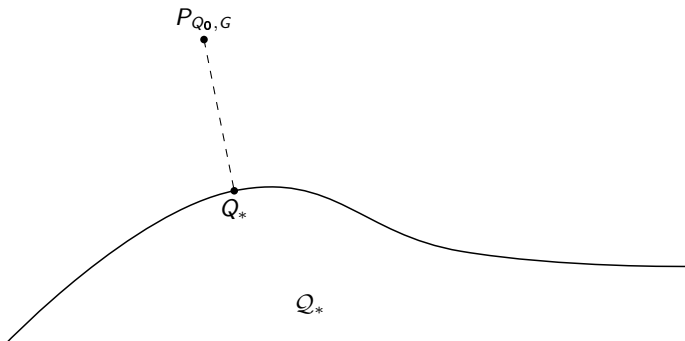
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$$Q \longmapsto D_{\text{KL}}(P_{Q_0, G} \parallel P_{Q, G}), \quad \text{with} \quad Q \in \mathcal{Q}_*.$$



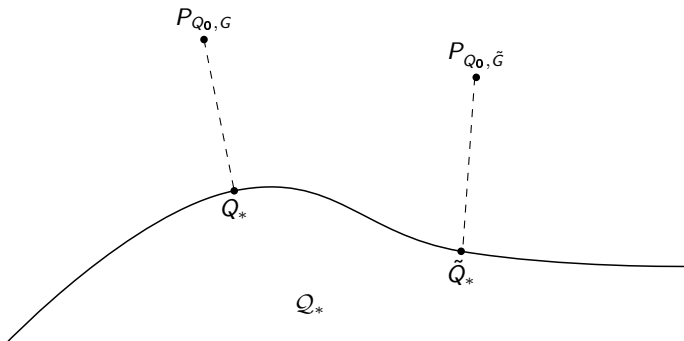
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Least false model depends on the censoring distribution

For any value $G \in \mathcal{G}$ we have that $D_{\text{KL}}(P_{Q_0, G} \parallel P_{Q_0, G}) = 0$, so the correct model Q_0 is ranked better than any other model independently of $G \in \mathcal{G}$. However, if $Q_0 \notin \mathcal{Q}_*$ the minimizer might depend on the value of G .¹

¹This is mentioned in Whitney et al. [2019] and van der Laan and Dudoit [2003], and a similar phenomenon is well studied for the Cox model [Struthers and Kalbfleisch, 1986, Hjort, 1992, Fine, 2002].

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For the simple survival case with no baseline covariates, we have the following result stating that for a mis-specified model Q we can always find an alternative model \tilde{Q} that is ranked better under one censoring regime but worse under another.

Let Q_0 and G be given together with some $Q \neq Q_0$. Then (under regularity conditions) we can find \tilde{Q} and \tilde{G} such that

$$D_{\text{KL}}(P_{Q_0, G} \parallel P_{Q, G}) < D_{\text{KL}}(P_{Q_0, G} \parallel P_{\tilde{Q}, G}),$$

and

$$D_{\text{KL}}(P_{Q_0, \tilde{G}} \parallel P_{Q, \tilde{G}}) > D_{\text{KL}}(P_{Q_0, \tilde{G}} \parallel P_{\tilde{Q}, \tilde{G}}).$$

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Sketch of proof

- Divide $(0, \tau)$ into $(0, \tau_0)$ and $[\tau_0, \tau)$, where $(0, \tau)$ is the support of T .
- Construct \tilde{Q} such that it performs better than Q on $(0, \tau_0)$ but worse on (τ_0, τ) under the censoring regime G .
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Whether the alternative model \tilde{Q} can be constructed such that $\tilde{Q} \in \mathcal{Q}_*$ for some model class \mathcal{Q}_* will depend on the model class and on Q_0 and \mathcal{G} .

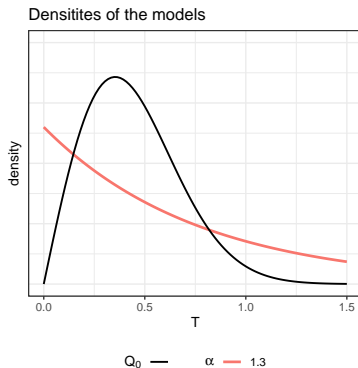
A simple example with mis-specified survival models

Assume the data generating distribution given by

$$Q_0 = \text{Weibull}(2, 0.5), \quad \text{and} \quad G_\gamma = \text{Weibull}(2, \gamma),$$

and consider the four candidate models indexed by α ,

$$Q_\alpha = \text{Exp}(\alpha), \quad \text{with} \quad \alpha \in \{1.3, 1.5, 1.8, 2\}.$$



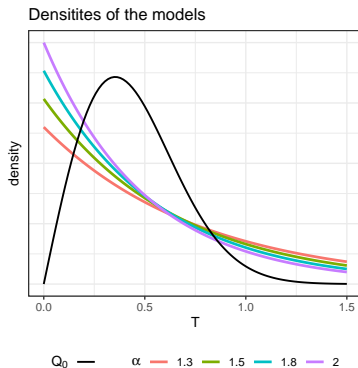
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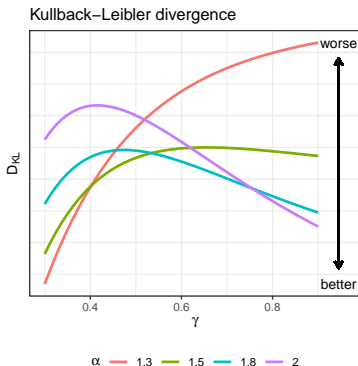
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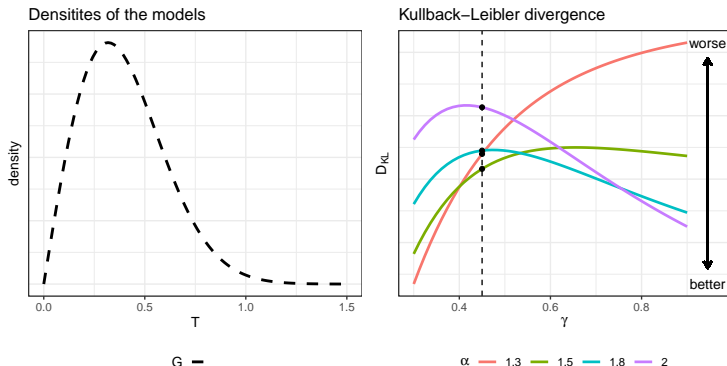
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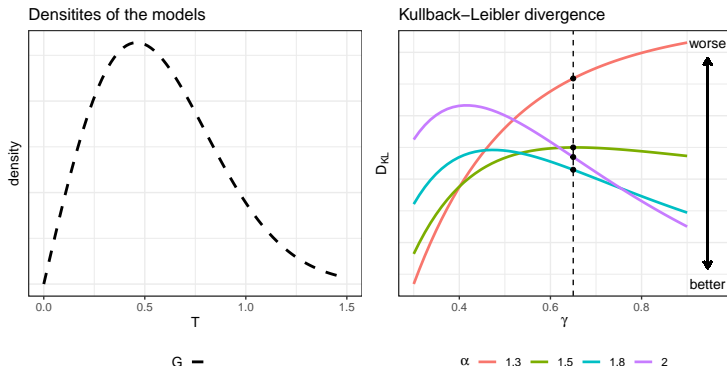
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Survival curve estimators evaluated on hold-out samples

Consider the problem of selecting a hyper-parameter or model using cross-validation. We split the data $\mathcal{D}_n = \{O_1, \dots, O_n\}$ in two, \mathcal{D}_n^1 and \mathcal{D}_n^2 .

On split \mathcal{D}_n^1 Fit models $\{\hat{f}_\lambda : \lambda \in \Lambda\}$ or $\{\hat{f}_1, \hat{f}_2, \dots, \hat{f}_k\}$.

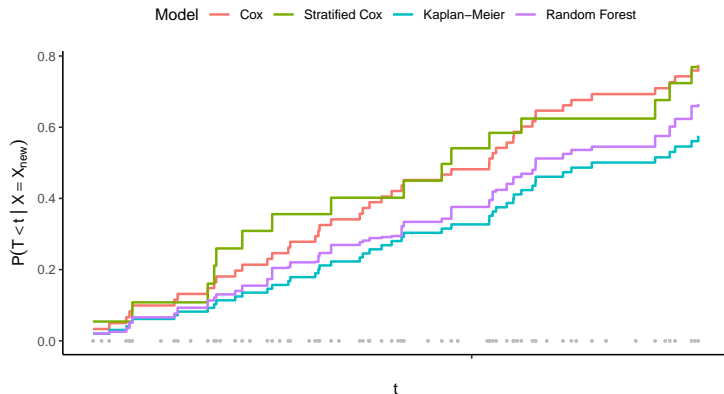
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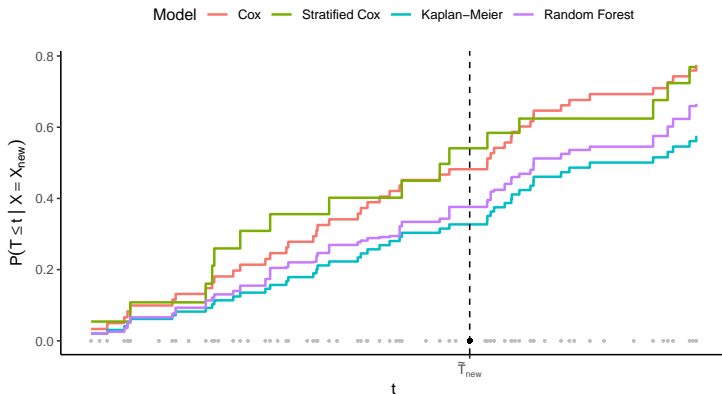


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Taking the censoring distribution into account

To alliviate these problems problems we can reweight the observed outcome or the loss function to account/adjust for the censoring:

- Inverse probability of censoring weighted loss functions [van der Laan and Dudoit, 2003]. For instance, weighted negative log-likelihood or (integrated) Brier score.
- Pseudo-values [Andersen et al., 2003, Mogensen and Gerds, 2013].
- Censoring unbiased transformations [Fan and Gijbels, 1996, Steingrimsson et al., 2019].

These approaches are particularly attractive when we are willing to assume that the censoring does not depend on the baseline covariates.

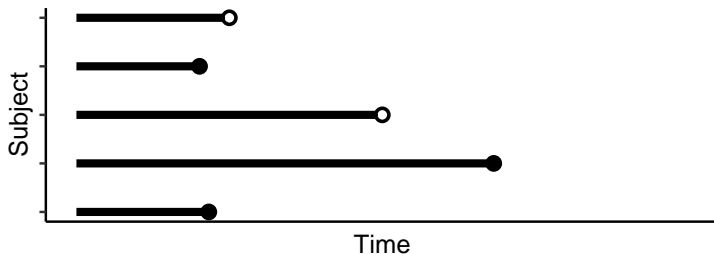
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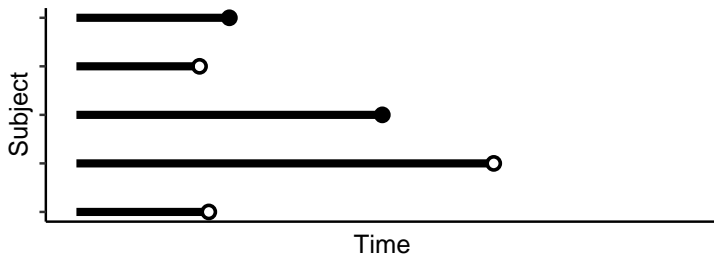
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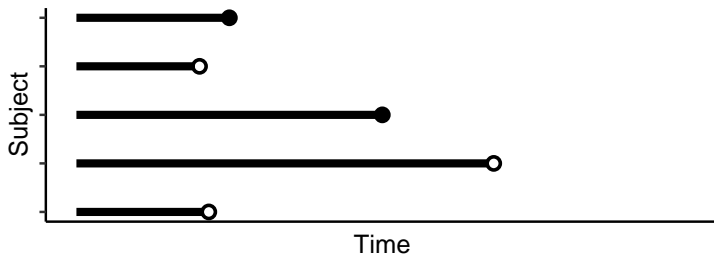
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Inverse-weighted survival games [Han et al., 2021]: Iterate the estimation until convergence (hopefully).

Conclusion

How should we do cross-validation for general survival models?

- Using the negative partial log-likelihood is problematic
 - The least false model is not well-defined (without reference to the censoring regime)
 - For many standard survival estimators, we cannot use it on hold-out samples
- Using loss functions designed to measure the loss for the model of interest is challenging in the presence of complicated censoring
 - We need a model for the censoring ...
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Questions, comments, suggestions?

Thank you!

References

- P. K. Andersen, J. P. Klein, and S. Rosthøj. Generalised linear models for correlated pseudo-observations, with applications to multi-state models. *Biometrika*, 90(1):15–27, 2003.
- J. Fan and I. Gijbels. *Local polynomial modelling and its applications*. Routledge, 1996.
- J. Fine. Comparing nonnested cox models. *Biometrika*, 89(3):635–648, 2002.
- R. D. Gill, M. J. Laan, and J. M. Robins. Coarsening at random: Characterizations, conjectures, counter-examples. In *Proceedings of the First Seattle Symposium in Biostatistics*, pages 255–294. Springer, 1997.
- X. Han, M. Goldstein, A. Puli, T. Wies, A. Perotte, and R. Ranganath. Inverse-weighted survival games. *Advances in Neural Information Processing Systems*, 34, 2021.
- N. L. Hjort. On inference in parametric survival data models. *International Statistical Review/Revue Internationale de Statistique*, pages 355–387, 1992.
- U. B. Mogensen and T. A. Gerds. A random forest approach for competing risks based on pseudo-values. *Statistics in medicine*, 32(18):3102–3114, 2013.
- J. A. Steingrimsson, L. Diao, and R. L. Strawderman. Censoring unbiased regression trees and ensembles. *Journal of the American Statistical Association*, 114(525):370–383, 2019.
- C. A. Struthers and J. D. Kalbfleisch. Misspecified proportional hazard models. *Biometrika*, 73(2):363–369, 1986.
- M. J. van der Laan and S. Dudoit. Unified cross-validation methodology for selection among estimators and a general cross-validated adaptive epsilon-net estimator: Finite sample oracle inequalities and examples. 2003.
- D. Whitney, A. Shojaie, and M. Carone. Comment: Models as (deliberate) approximations. *Statistical science: a review journal of the Institute of Mathematical Statistics*, 34(4):591, 2019.