Random Survival Forests with An Example of Systolic Heart Failure

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A Picture - Forests

Photo by Unilever

Background and Objective

Random forests (RF) has shown to be highly applicable and accurate, comparable to state-of-art methods such as bagging, boosting, and support vector machines.

However, RF have primarily been used for classification and regression tasks. On the other hand, common survival methods rely on assumptions such as proportional hazards that is often too restrictive.

In this paper, Ishwaran et al. (2008) introduce random survival forests (RSF), an extension of Breiman's RF (2001). RSF incorporates survival information and is designed for analysis of right-censored data.

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Pre/Review: Random Forests

Random forests (RF) is made up from a collection of trees, and randomness is introduced in the following tree-growing process.

RF works by

1. first randomly drawing bootstrap sample of data and using it to grow a tree.
2. then at each node of the tree, randomly selecting subsets of predictors for splitting.

The final outcome is based on either majority voting (for classification) or averaging (for regression).

RF is able to approximate rich classes of functions while keeping error low.

Introduction: Random Forests vs Random Survival Forests

RSF adheres to the principle of Breiman's RF (2003). RF is designed such that all aspects of the tree-growing process takes into account the outcome. These have some comprises.

In right-censored survival settings,

- the splitting rule,
- tree node impurity,
- the predicted results,
- the measure of prediction accuracy, etc.

in RSF must incorporate survival and censoring information.

Algorithm (High-Level)

Random survival forests involves the following steps:

1. Randomly draw B bootstrap samples from the original data and grow a survival tree for each bootstrap sample.
2. At each node of the tree, randomly select p predictors.
3. Grow the tree to full size under the constraint that a terminal node shoud have no less than $d_0 > 0$ unique deaths.
4. Calculate CHF (cumulative hazard function) for each tree and average them to obtain the ensemble CHF.
5. Use OOB (out-of-bag) data to calculate prediction error for the ensemble CHF.

Note. OOB data is the number of samples that are NOT drawn, which makes up of ~37% of the original data.

Splitting Rules

Similar to CART (Classification and Regression Trees), survival trees are also binary. Each root node is split to a left and right daughter nodes, and a good split for a node should maximize survival differences.

The log-rank test statistic is used by default in the **R** package `randomForestSRC` uses since log-rank test has traditionally been used for testing two-sample survival data.

Splitting Rules

The best split is decided by finding the predictor X^* and split-value c^* such that, for all X and c,

$$|L(X^*, c^*)| \geq |L(X, c)|,$$

where $|L(X, c)|$ measures node separation and the log-rank split-statistic is given as

$$L(X, c) = \frac{\sum_{j=1}^{m}(d_{j,L} - Y_{j,L}\frac{d_j}{Y_j})}{\sqrt{\sum_{j=1}^{m} d_j(1 - \frac{Y_{j,L}}{Y_j})(\frac{Y_j - d_j}{Y_j - 1})}}.$$

Note. This is the exact same test statistic of long-rank test.

Terminal Node Statistics

The CHF and survival function for each terminal node h are estimated using the bootstrapped Nelson-Aalen and Kaplan-Meier estimators

$$H_h(t) = \sum_{t_{j,h} \leq t} \frac{d_{j,h}}{Y_{j,h}}, \qquad S_h(t) = \prod_{t_{j,h} \leq t} (1 - \frac{d_{j,h}}{Y_{j,h}}),$$

where $d_{j,h}$ is the number of events (e.g. deaths) and $Y_{j,h}$ is the number of individuals at risk at time $t_{j,h}$.

Since the tree is binary, X will fall into a unique terminal node h, which is why the CHF and survival estimators equals to the Nelson-Aalen and Kaplan-Meier estimators for X's terminal node

$$H(t|X)^{IB} = H_h(t), \quad S(t|X)^{IB} = S_h(t), \quad X \in h.$$

Note. $H(t) = -log(S(t))$.

Terminal Node Statistics

The ensemble CHF and survival function for IB (in-bag) and OOB (out-of-bag) are calculated by averaging the tree estimators

$$H(t|X)^{IB} = \frac{1}{ntree}\sum_{b=1}^{ntree} H_b(t|X), \quad S(t|X)^{IB} = \frac{1}{ntree}\sum_{b=1}^{ntree} S_b(t|X),$$

$$H_i^{OOB}(t) = \frac{1}{|O_i|}\sum_{b\in O_i} H_b^{IB}(t|X_i), \quad S_i^{OOB}(t) = \frac{1}{|O_i|}\sum_{b\in O_i} S_b^{IB}(t|X_i),$$

where O_i records the number of OOB case.

Note. IB estimators are used for prediction, whereas OOB estimators are used for inference (on the training data) and prediction error estimation.

Prediction Error: PE & the C-Index

Prediction error (PE) is defined as $1 - C$, where C is Harrell's concordance index (C-index) (Harrell Jr et al., 1982). PE

- is between 0 and 1.
- measures how well the predictor correctly ranks two random individuals in terms of survival. (e.g. PE $= 0.5$: no better than random guessing.)

Harrell's C-index is a popular means for assessing prediction performance in survival settings. The C-index

- estimates the probability that, in a randomly selected pair of cases, the case that fails first had a *worst predicted outcome* (next: mortality).
- is interpreted as a misclassification probability.
- does not depend on choosing a fixed time for evaluation of the model.
- specifically accounts for censoring of individuals.

Prediction Error: Mortality

To compute the C-index, the *worst predicted outcome* is defined using mortality.

Mortality measures the number of deaths expected under a H_0 of similar survival behavior. It is defined as the expected (predicted) value for the CHF summed over time T_j, and, for i,

$$M_i = E_i(\sum_{i=1}^{n} H(T_j|x_i)),$$

where E_i is the expectation under the H_0 that all j are similar to i.

Prediction Error: Ensemble Mortality & the C-Index

The ensemble Mortality for i for OOB is then defined as

$$\bar{M}_i^{OOB} = \sum_{j=1}^{m} \bar{H}_i^{OOB}(t_j), \quad i = 1, ..., n.$$

The OOB ensemble mortality is used to calculate the C-index. Individual i is said to have a *worst (predicted) outcome* than j if

$$\bar{M}_i^{OOB} > \bar{M}_j^{OOB}.$$

Note. Precise steps for calculating the C-Index are omitted here. The idea is to form all possible pairs while omitting pairs whose shorter survival time is censored.

Discussion

1. Other measures such as VIMP (variable importance) can be computed and are useful to uncover complex relationships.
2. The codes took some time to run. It turned out that the recursive `randomForestSRC` algorithm is already parallelized and trees are grown concurrently, not iteratively.
3. Multivariate trees for multivariate outcomes are possible to construct using the package. However, under this setting, correlation has not been taken into account.

A R Example (If Time Allows)

Data `peakVO2` can be loaded from **R** package `randomForestSRC`.

This survival data consists of $n = 2231$ adult patients with systolic heart failure (Hsich et al., 2011).

- All patients underwent cardiopulmonary stress testing, and a total of 742 patients died during a mean follow-up of 5 years (maximum for survivors, 11 years) at the Cleveland Clinic.
- The outcome is all-cause mortality, and a total of $p = 39$ predictors were measured for each patient including demographic, cardiac and noncardiac comorbidity, and stress testing information.

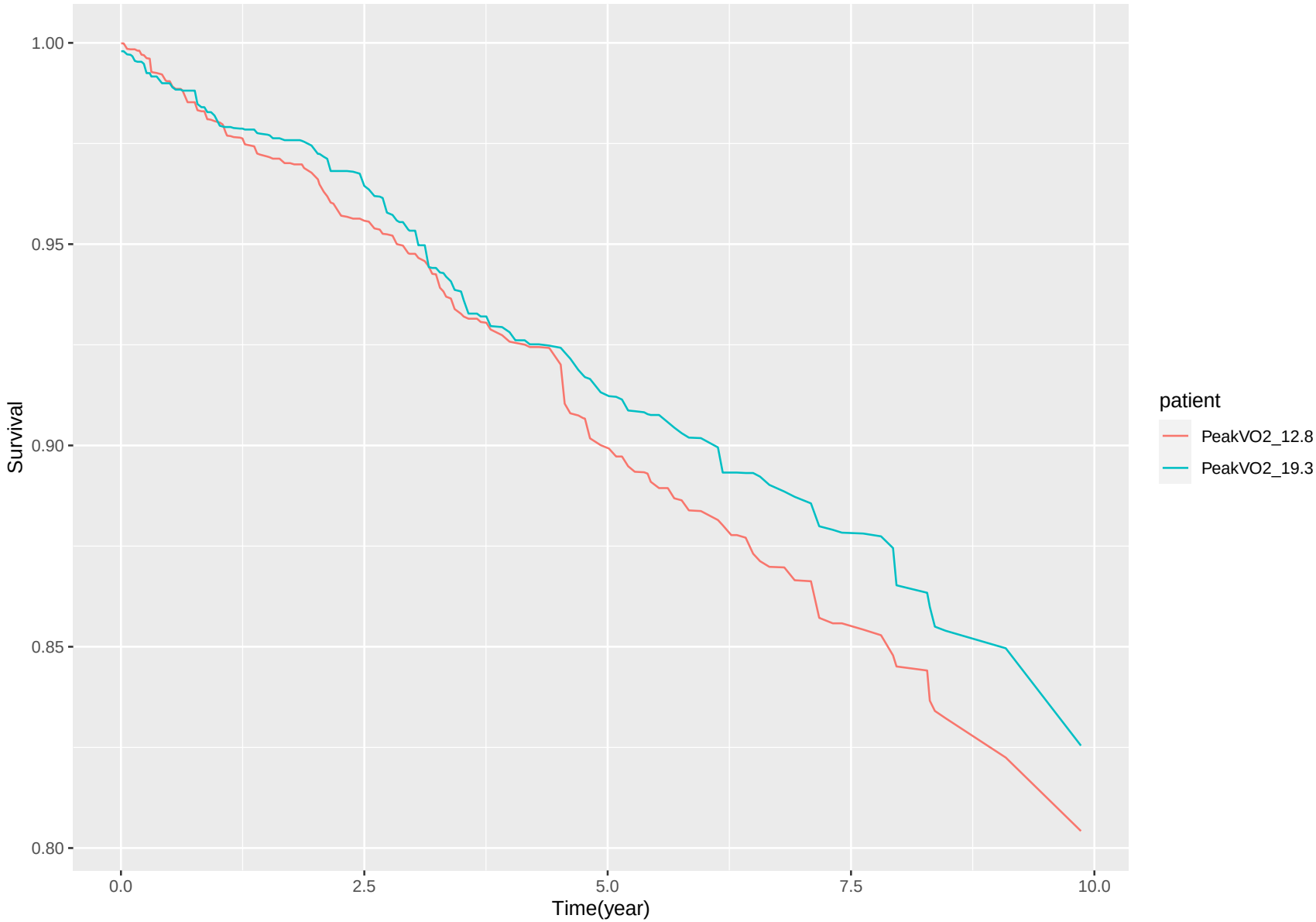
A R Example

RSF results using the `rfsrc` function of **R** package `randomForestSRC`:

```
                                  Sample size: 2231
                          Number of deaths: 726
                           Number of trees: 1000
                Forest terminal node size: 5
            Average no. of terminal nodes: 259.547
No. of variables tried at each split: 7
                    Total no. of variables: 39
            Resampling used to grow trees: swor
         Resample size used to grow trees: 1410
                                  Analysis: RSF
                                    Family: surv
                          Splitting rule: logrank *random*
            Number of random split points: 50
                                (OOB) CRPS: 0.15508379
    (OOB) Requested performance error: 0.29965793
```

A R Example

Plot of predicted survival curves of two hypothetical individuals:



Reference

Ishwaran, H., Kogalur, U. B., Blackstone, E. H., & Lauer, M. S. (2008). Random survival forests. The Annals of Applied Statistics, 2(3), 841–860. JSTOR.

Ishwaran, H., Lauer, M. S., Blackstone, E. H., Lu, M., & Kogalur, U. B. (2021). randomForestSRC: random survival forests vignette. https://luminwin.github.io/randomForestSRC/articles/survival.html.

Thank you!

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