Similarity-based Random Survival Forest

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Abstract Predicting the time to a clinical outcome for patients in intensive care units (ICUs) helps to support critical medical treatment decisions. The time to an event of interest could be, for example, survival time or time to recovery from a disease/ailment observed within the ICU. The massive health datasets generated from the uptake of Electronic Health Records (EHRs) are diverse in variety as patients can be quite dissimilar in their relationship between the feature vector and the outcome, adding more noise than information to prediction. We propose a modified random forest method for survival data that identifies similar cases and improves prediction accuracy. We also introduce an adaptation of our methodology in the case of dependent censoring. Our proposed method is demonstrated in the Medical Information Mart for Intensive Care (MIMIC-III) database, and we also present properties of our methodology through a comprehensive simulation study. Introducing similarity to the random survival forest method indeed provides additional predictive accuracy compared to random survival forest alone in the various analyses we undertook.

Keywords MIMIC database · predictive accuracy · dependent censoring · time-to-event data

1 Introduction

Electronic Health Records (EHRs) have generated health data sets that provide rich and diverse information for modeling and prediction. Survival analysis has been essential in clinical and epidemiological studies, and both parametric and semiparametric modeling have been utilized in the literature. Especially with big datasets, patients can be heterogeneous, which pose challenges to accurate prediction of outcomes of interest. Conditioning on a more relevant subset where the cases are more similar to the point of prediction might improve prediction accuracy. Similarity-based prediction in other prediction contexts has been focused upon by Lee, Maslove & Dubin (2015) [14]. The concept of similarity within the random forest context is seen in Xu, Nettleton & Nordman (2016) [21] paper for regression and classification. Lee (2017) [13] applied the case-specific random forests of Xu, Nettleton & Nordman (2016) [21] to a dataset from the Medical Information Mart for Intensive Care (MIMIC-II) database [19,15].
In survival analysis, one notion of similarity is seen in cure models. These models assume that while some cases will die from a disease or experimental stress, a sub-population will survive for a long time without experiencing the event. Although the term similarity is not specifically mentioned in the literature, the sub-population of long-term survivors can be considered as a group of similar cases. Early studies on such models include Boag (1949) [2], Berkson and Gage (1952) [1], and Haybittle (1965) [5]. Pierce, Stewart & Kopecky (1979) [17] suggested a computationally easy method to deal with grouped survival data based on Cox proportional-hazard model. V. T. Farewell (1982) [4] and Kuk & Chen (1992) [11] used a mixture model representation for the two populations, which models the probability of being a long-term survivor with a logistic regression and the time to event for those that would experience the event with survival models respectively. Many variations of mixture cure models can be seen in literature. Tsodikov, Ibrahim and Yakovlev (2003) [20] provided an alternative to two-component mixture models in estimating cure rate by using bounded cumulative hazard function. These models focus on modeling rather than prediction.

We take a rather different approach to model and predict survival data when there are one or more sub-populations in the dataset, that is, when the relationship between the time-to-event outcome and the explanatory variables are homogeneous within groups and more heterogeneous between groups. This is a more general case than the cure model as there can be more than two groups in the population, and the number of groups is unknown, in general. Note that the similarity is not just based on the grouping of the survival time, or the closeness of the explanatory variables, but depends on the relationship between the two. Tree-based methods such as random forests [3] are a natural way of incorporating both outcome and covariate information, and can be utilized to characterize similarity as cases in the same terminal node can be considered as similar to each other. Random forests methods have been extended to survival data as well, as in Ishwaran et al. [8], and our approach is essentially combining the case-specific random forests model in Xu, Nettleton & Nordman (2016) [21] with random survival forests model [8]. Methods for dealing with dependent right censoring will be discussed as well.

In Section 2, we will discuss the similarity-based random survival forest algorithm with independent right censoring, and methods to adjust for dependent censoring. Time-varying AUC is used as the criterion for evaluating prediction performance. Section 3 and 4 are applications of the algorithm to a simulation study, as well to a real dataset from the MIMIC-III database [10]. In Section 5, we will summarize our methodology and findings from the simulation study and real data analysis.

2 Similarity-based Random Survival Forest

In this section, we will introduce the algorithm for our proposed similarity-based random survival forest (SB-RSF). The idea is to build different random survival forest for prediction for each test case, giving more weights to the training cases that are in closer proximity of the test case, and using less information from those that merely add more noise to prediction. We will discuss independent censoring case in Section 2.1 and dependent censoring in Section 2.2. In Section 2.3, we will talk about using time-varying AUC for model comparison.

2.1 With Independent Censoring

We will assume independent censoring for now. Methods to incorporate dependent censoring will be discussed in Section 2.2.

- 1. Construct a regular random survival forest model for a training dataset that has sample size $N_{train}$.
  - (a) Draw $B$ bootstrap samples from the training data. Uniform sampling is used.
  - (b) Grow a survival tree for each bootstrap sample under the constraint that it should have $d_0 > 0$ unique deaths.
- 2. For each point in the test dataset of size $N_{test}$, obtain a weight vector based on the random survival forest in the first step.
  - (a) Pass a test data point down each tree in the random survival forest, and keep track of how many terminal nodes group a training data point with the test point.
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(b) Assign a weight vector of length $N_{\text{train}}$ to each test data point based on how many terminal nodes group a training data with that test data point.

(c) Iterate through each test data point, and obtain a weight matrix of size $N_{\text{train}} \times N_{\text{test}}$. Normalize each row of the weight matrix so that each row sums to 1.

3. Build a different similarity-based random survival forest for each test data.

(a) For a test data, build a random survival forest model with the weight vector as the sampling probability vector in the bootstrap.

(b) Pass down the test data in each tree, and calculate the CHF of the terminal node to which the test data point belongs.

(c) Average among all trees to get an ensemble CHF for that test data.

(d) Repeat it for each test data. Note that a different survival forest is built for each test data.

2.2 Adjusting for Dependent Censoring

Dependent censoring for right censored data is common in follow-up studies. For right censoring, the event is only known to have occurred after a certain time point. Denoting the censoring time by $C_i$, the observed time $X_i$ will be the minimum of the event time and the censoring time, i.e., $X_i = \min(C_i, T_i)$. Denote the event indicator by $\delta$, which indicates the observed time corresponds to the true event time, then $\delta = I(T_i \leq C_i)$, which is 1 if the event occurs before censoring, and 0 otherwise. For non-informative censoring, the censoring process does not directly depend on the event process, although it can depend on some covariates. With informative censoring, the censoring process directly relates to the expected time to event. Inverse probability-of-censoring weights (IPCW) has been shown to account for the bias that occurs when ignoring informative censoring [7,16]. In this setting, the algorithm is modified as follows.

1. Use K-M estimator with censoring time as the event time to get the probability $P_i(C)$ of getting censored.

2. Calculate the IPC weights for each training case as $IPCW_i = 1/(1 - P_i(C))$, i.e. the weights are equal to the inverse probability of not getting censored.

3. Calculate the similarity weights for a training case $i$ and test case $j$ as $SW_{i,j}$ as described in Section 2.1.

4. The sampling weights for use in the similarity-based random survival forest for $i$ and $j$ will be proportional to $SamplingW_{i,j} = IPCW_i \times SW_{i,j}$.

The intuition behind the multiplication of the weights is that the SB-RSF algorithm now gives greater sampling weights to those data points that are more likely to be censored.

2.3 Prediction Accuracy

We will be using time-varying area-under-the receiver operating characteristic curve (AUC) for model comparison. For binary outcomes, the prediction accuracy can be characterized by ROC, which plots the sensitivity against (1-specificity) for the range of possible threshold. And the area under ROC (AUC) represents a measure of prediction accuracy.

For time-to-event outcome, there are a few proposals to generalize the concept of sensitivity and specificity [6]. One way is to look at sensitivity and specificity at each time of interest $t$. The survival probability up to $t_k$ of a test case $i$, i.e., $S_i(t)$ can be derived from its cumulative hazard $\hat{H}_i(t)$. Then, $AUC(t)$ can be calculated at each $t$. In this paper, we will consider AUC over a dense grid of times.

3 Simulations

We use two simulated examples to further explain what similarity means in the model and demonstrate the prediction performance of the algorithm.
3.1 Example 1

In a simple example, each case has a 3-dimensional covariate \( \{x_1, x_2, x_3\} \) that links directly to the survival outcome. Two of the covariates are linked to similarity as well. In this case, \( S \) is a survival outcome that follows a Weibull distribution with shape=2, and \( \log(\text{scale}) \) mapped to linear predictor \( Y \).

\[
Y = \begin{cases} 
0.2X_1 - 0.1X_2 + 0.5X_3, & \text{if } (X_1 + 7) \cdot (X_3 - 10) > 0 \\
0.3X_1 + 0.1X_2 - 0.3X_3, & \text{otherwise}
\end{cases}
\] (1)

Note that \( (X_1 + 7) \cdot (X_3 - 10) \leq 0 \) and \( (X_1 + 7) \cdot (X_3 - 10) > 0 \) describes a binary tree structure that clusters cases into two subspaces. Within each subspace, the relationship between the survival outcome and the covariates are the same. 1000 cases are generated, where \( X_1, X_2, X_3 \) are independently and uniformly generated from (-15,15). Uniform right censoring (independent for now) is considered. Figure 1 summarizes the comparison between the prediction performance of case-specific random survival forest and the regular random survival forest. The red dots represents the time-varying AUC for the case-specific random survival forest and the black dots are for the regular random survival forest. The AUCs are evaluated at each day from day 1 to day 20. At each day, the time-varying AUC of the case-specific method exceeds the regular random survival forest by roughly 0.02.

3.2 Example 2

In the second model, each case has a 5-dimensional covariate \( \{x_1, x_2, x_3, x_4, x_5\} \), where three of the covariates explain similarity. Again, we will use a binary tree structure to define subspaces. In this case, we will prune the tree until there are four terminal nodes, i.e., four subspaces. Within each subspace, the relationship between \( Y \) and the covariates are the same.
The result in Figure 2 is similar to the first simulation result in Figure 1. Giving more weights in the sampling to similar cases, based on our SB-RSF method, yields better prediction performance in the random survival forest framework.

4 Application to an ICU dataset

4.1 MIMIC-III

MIMIC-III (Medical Information Mart for Intensive Care III) is a freely accessible critical care database for 53423 distinct hospital admissions for adult patients (aged 16 and above). Data includes vital signs, medications, diagnostic code, survival data and high resolution data including lab results and bedside monitoring data [10].

This large dataset provides rich information for modeling and prediction, but the diversity of the patients also poses challenges to accurate prediction of outcome of interest. To illustrate, the goal is to predict ICU patient survival with their age, gender, ICU type, admission type, SAPS II [12] as predictors. ICU type includes CCU (Coronary Care Unit), CSRU (Cardiovascular Intensive Care Unit), MICU (Medical Intensive Care Unit), SICU (Surgical Intensive Care Unit) and TSICU. And admission type includes Elective, Emergency, Urgent. Only the first hospital admission of adult patients (older than 15 years of age) are included in our study. Excluding cases with missing data in one or more of the variables or outcome, the sample size is 38604. In this dataset, 80% of the cases are right censored at 90 days after for de-identification purposes.
4.2 Result

Figure 3(a) compares the time-varying AUC for the algorithm in Section 2.1 with the random survival forests method. The time-varying AUC from our proposed SB-RSF method outperforms that of the regular random survival forest at the beginning of the prediction and after day 20, and the gap between the two lines increases as we predict further into the future.

Figure 3(b) shows the result when considering possible dependency in the censoring. The result is much similar to that in Figure 3(a). It is possible that for this dataset there is not much dependency in the censoring, and thus the calculation of the IPC weights did not have a big impact on the result.

5 Discussion

In this paper we proposed to improve the random survival forests by incorporating the similarity structure between a test data point and training data point. Instead of building a global random survival forests for each test case, we construct similarity-based random survival forests for each one of them, by giving more weights to the training cases that are in closer proximity to the test case. Proximity is measured using a regular random survival forests model. We also developed algorithm to account for dependent censoring which is common in survival data.

Both simulations and a real data example show promising results that, in general, indicate that the similarity-based prediction improves prediction performance of random survival forests in terms of time-varying AUC. This result is also consistent with other findings using similarity structure outside of the random forests model [14].

Our proposed SB-RSF method requires building a random survival forest for every test data point and specification of a few tuning parameters. Specifically, the tuning parameters are the depth of the tree (represented by the number of unique deaths in the terminal nodes), and the number of trees in the forests. This can be computationally intensive when the size of the test data size is large. Future work is necessary to investigate the robustness of their choices. One way of reducing computation time is to use a hard threshold for sampling, that is, giving 0 weights to cases that are too far away from the test case. The tuning parameters for the simulations are selected based on the entire dataset. However, if they are determined from a smaller subset of the dataset, the computational time might be greatly reduced.

For future work, methods other than random forests may be utilized for similarity-based prediction for survival outcomes. One possible extension is the joint modeling of longitudinal covariates and time-to-event
outcome [18]. One might be able to identify similar cases based on longitudinal covariates as well as time-fixed covariates.

In spite of some areas that require future study, we have shown the proposed SB-RSF approach to hold promise for the prediction of survival outcomes. Our investigation shows that our similarity-based algorithm can improve the predictive accuracy of a popular and useful prediction tool, i.e., random survival forest [9], for time-to-event data.

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