Bayesian Nonparametric Modeling of Heterogeneous Groups of Censored Data

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Abstract
Datasets containing large samples of time-to-event data arising from several small heterogeneous groups are commonly encountered in statistics. This presents problems as they cannot be pooled directly due to their heterogeneity or analyzed individually because of their small sample size. Bayesian nonparametric modelling approaches can be used to model such datasets given their ability to flexibly share information across groups. In this paper, we will compare three popular Bayesian nonparametric methods for modelling the survival functions of heterogeneous groups. Specifically, we will first compare the modelling accuracy of the Dirichlet process, the hierarchical Dirichlet process, and the nested Dirichlet process on simulated datasets of different sizes, where group survival curves differ in shape or in expectation. We, then, will compare the models on a real-world injury dataset.

1 Introduction
Survival analysis is widely used in healthcare to model time-to-injury occurrence. Often, the data are stratified in multiple small groups that differ in certain aspects, such as exposure or risk, and cannot be directly pooled to estimate the survival function. Given that the numbers of injuries are often rather small relative to exposure time, and that most individuals do not experience injury during follow-up, it is useful to introduce dependence across group parameters to obtain precise estimates of the injury rates. Bayesian nonparametric methods such as the Dirichlet process (DP) [Ferguson, 1973] and Gaussian process have been widely used in survival analysis, but, surprisingly popular extensions of the DP have yet to be explored in this context. Specifically, we adapted the nested Dirichlet process (NDP) [Rodriguez et al., 2012] and hierarchical Dirichlet process (HDP) [Teh et al., 2012] to model the survival functions of related groups, in which some data has been censored.

The shape of the survival function provides information that cannot be obtained from the parameters alone. In practice, survival functions are unlikely to follow a parametric family and could be better modelled by a mixture of parametric distributions [Farewell, 1982]. Thus, the DP is well-suited to model the survival function since it makes weak assumptions about the shape of the curve, yet provides smooth estimates [Blum and Susarla, 1977, Kuo and Mallick, 1997, Kottas, 2006].

In this paper, we are particularly interested in the case in which the dataset is composed of multiple groups, where each group is a mixture with an unknown number of components, and some components’ parameters might be identical across groups. To take advantage of the structure of such dataset,
2 Adaptation of the Models to Handle Censored Observations

We are interested in modelling a collection of survival functions, where the \( j \)-th group’s survival function is denoted as \( S_j(t) = 1 - F_j(t) = P(X_j > t) \). The \( i \)-th observation of the \( j \)-th group is denoted as \( Y_{ji} = \min\{X_{ji}, Z_{ji}\} \), where \( Z_{ji} \) and \( X_{ji} \) represent the censoring time and event time, respectively. These are mutually independent random variables. In the case where \( Z_{ji} < X_{ji} \), we say that the observation has been censored and we let the indicator variable \( \gamma_{ji} \) be equal to 0, and to 1 otherwise.

The case \( Z_{ji} < X_{ji} \) indicates that the observation has been censored and we let the indicator variable \( \gamma_{ji} \) be equal to 0, and to 1 otherwise.

Censoring makes estimation challenging, because it masks important information about \( P(X_j > t) \). Fortunately, the DP can be modified to handle censored observations by: (1) including the survival function in the likelihood; and (2) using a Gibbs sampling step to augment censored observations.

2.1 Likelihood Function

The likelihood function is used to assign observations to mixture components. Specifically, we assigned the observation \( ji \) to the component \( l \) with probability: \( p(\xi_{ji} = l) \propto w_l f(y_{ji}|\theta_l) \), where \( w_l \) is the weight of the \( l \)-th atom obtained via stick breaking [Sethuraman, 1994], and \( f(y_{ji}|\theta_l) \) is the density of the distribution with parameter \( \theta_l \) evaluated at \( y_{ji} \).

To handle censored observations, we will modify the probability of sampling an indicator variable to: \( p(\xi_{ji} = l) \propto w_l \gamma_{ji} f(y_{ji}|\theta_l) + (1 - \gamma_{ji}) S(y_{ji}|\theta_l) \gamma_{ji} \), where \( S(y_{ji}|\theta_l) \) is the survival function of the distribution with parameter \( \theta_l \) evaluated at \( y_{ji} \), and \( \gamma_{ji} \) is an indicator variable equal to 0 if the observation \( ji \) has been censored, and 1 otherwise. This is intuitive since the survival function is the probability of surviving past time \( y_{ji} \). This modification of the likelihood can easily be performed for the HDP.

This can also be applied to the NDP by assigning group \( j \) to the mixture of distributions \( k \) with probability \( p(\zeta_j = k) \propto \pi_k \prod_{l=1}^{L} lw_k p(y_{ji}|\theta_{lk}) \), where \( I_j \) is the number of observations in group \( j \), and \( \pi_k \) is a weight obtained via the stick breaking construction. [Rodriguez et al., 2012]

2.2 Gibbs Step

Once a censored observation has been assigned to cluster \( l \), it cannot be naively used to update the parameter’s posterior, neither can we ignore the censored observation, since it would bias our estimates. Instead, we can use a Gibbs step to simulate what the observation could have been if it was not censored at time \( y_{ji} \), given that it belongs to cluster \( l \).

Specifically, censored observation \( ji \) assigned to cluster \( l \) can be filled by drawing a value from \( \hat{y}_{ji} \sim p(\theta_l|\hat{y}_{ji} > y_{ji}) \). We can use these simulated values to obtain an unbiased estimate of our parameters. It is straightforward to modify the NDP and HDP algorithm in a similar fashion.

3 Results

We focused on datasets containing small heterogeneous groups of mixtures, where the number of mixtures are unknown and a high proportion of observations are censored. In this case, the groups could not be pooled directly without making strong assumptions about their homogeneity. Further, due to the small sample size it was impractical to fit a different survival curve to each group. Fitting a proportional hazard model would also be difficult for the same reasons. Instead, we took advantage of the BNP methods’ ability to infer clusters from the data, and therefore, estimated their survival function more efficiently. To model the data using BNP, we assumed that the observations were exchangeable within groups and across groups. For instance, observations within groups could be relabeled and groups themselves could also be relabeled.
We will compare the BNP methods to a Weibull Gamma frailty model (GFM) fitted using the parfm R package [Munda et al., 2012]. The GFM confidence interval has been computed using the inverse of the negative hessian as an approximation of the parameters’ covariance matrix.

3.1 Simulation Study

This simulation study aims to demonstrate the statistical pooling power of different models in a commonly occurring situation. The simulated task requires modelling survival functions in an injury dataset that is characterized by high levels of censoring and small, but, numerous heterogeneous groups. To replicate these characteristics, we simulated 600 observations from three mixtures with a censoring rate of approximately 50% using the survsim package [Moriña and Navarro, 2014]. The parameters and weights of the mixtures were chosen so that the curves from mixture one and mixture two had similar shapes, but different expectations, and the curves from mixture one and mixture three had similar expectations, but different shapes, as seen in Figure 1. Furthermore, each group has its own frailty parameter originating from a $\text{Gamma}(1, 1)$.

We will compare the methods on different structures of the dataset e.g. varying the number of groups $J$ and the group size $n_j$ while keeping the overall sample size fixed at 600. To quantify the accuracy of our model, we computed the mean log pointwise predictive density of our model. In addition, to evaluate uncertainty we computed the mean width of our 95% credible interval and the proportion captured by the real survival curve. The results are reported in Figure 2 and Figure 3.

![Figure 1](image1.png)

Figure 1: This displays the mixtures’ parameters and weights that were chosen for this simulation. The curves for mixture 1 and mixture 2 have similar shapes, but differ in expectations, and the curves for mixture 1 and 3 have similar expectation, but different shapes.

3.2 Performance Arts Company

Based on the successful modelling of the synthetic data, the model was applied to a performance art company dataset to determine its performance in real world applications. Similar to the simulation study, this dataset consists of several, clearly related, but heterogeneous groups that cannot be directly pooled without making strong assumptions.

The dataset was structured into shows and roles, both of which could be used as groups. However, it was more reasonable to group the observations by shows, than by roles, because roles vary within shows but also vary across shows in terms of exposure and risk. This resulted in 279 unique groups with a group size ranging from 1 to 69 observations. An overview of the dataset can be seen in the Appendix.
3.3 Discussion

Figure 2: The mean log pointwise predictive density is reported for different structures of the dataset. Note that a higher mean log predictive density implies better modelling of the dataset. The mean width credible interval is also reported in the second panel.

Figure 3: The average proportion of coverage of the true survival curves have been computed at different percentiles of the 3 mixture of survival curves. The percentiles are the same as the identified in Figure 1.

From the results, the BNP methods’ performance depends on the structure of the dataset. On the one hand, based on the mean log predictive density it seems like the HDP is the most adequate method to model small heterogeneous groups, and the complex performance art dataset’s survival curves. On the other hand, the NDP shows the ability to recover the original survival curves while keeping a reasonable credible interval width.

4 Conclusion

This paper compared three different BNP methods on a predictive task in a survival analysis context. First, they were compared on a simulated dataset with groups that came from three mixtures. Following, they were compared on a real world injury dataset from a Performance Art Company. For each of these analyses, the BNP models were a reasonable choice given that the groups could not be pooled directly, but were intuitively related. Using BNP methods, the clusters could be directly inferred from the data, and certain groups and observations could be pooled together to obtain better estimates of the survival curves.

It would be beneficial for the analysis of injury data, if BNP methods were used more often since they provide a good way to deal with uncertainty and allow for sharing of information across groups with high censoring. The next step would be to extend our model to handle recurrent events, as they are highly common in the analysis of injury data.
Acknowledgments

The work has been supported by CIHR and NSERC. The authors would like to thank James McVittie, Meng Zhao and all the members of professors Shrier and Steele’s group for their helpful comments.

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Appendix
Figure 4: Overview of the Performance Art Company dataset which was first grouped by show and then by role, whereby the white dots indicate censored observations and the black dots indicate time to first injury.