Bayesian Semiparametric Models for Survival Data with a Cure Fraction

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SUMMARY. We propose methods for Bayesian inference for a new class of semiparametric survival models with a cure fraction. Specifically, we propose a semiparametric cure rate model with a smoothing parameter that controls the degree of parametricity in the right tail of the survival distribution. We show that such a parameter is crucial for these kinds of models and can have an impact on the posterior estimates. Several novel properties of the proposed model are derived. In addition, we propose a class of improper noninformative priors based on this model and examine the properties of the implied posterior. Also, a class of informative priors based on historical data is proposed and its theoretical properties are investigated. A case study involving a melanoma clinical trial is discussed in detail to demonstrate the proposed methodology.

KEY WORDS: Cure rate model; Gibbs sampling; Historical data; Latent variables; Piecewise exponential; Posterior distribution; Semiparametric model; Smoothing parameter.

1. Introduction

A crucial issue with cure rate modeling and with semiparametric survival models in general is the behavior of the model in the right tail of the survival distribution. In these models, there are typically few subjects at risk in the tail of the survival curve after sufficient follow-up. Thus, estimation of the cure rate can be quite sensitive to the choice of the semiparametric model. Therefore, there is a need to carefully model the right tail of the survival curve and allow the model to be more parametric in the tail while also allowing the model to be nonparametric in other parts of the curve. In this article, we construct such a model by defining a smoothing parameter \( \kappa, 0 < \kappa < 1 \), that controls the degree of parametricity in the right tail of the survival curve. By an appropriate choice of \( \kappa \), we can choose a fully nonparametric model or a fully parametric model for the right tail of the survival distribution. Also, \( \kappa \) will allow us some control over the degree of parametricity in the beginning and middle part of the survival distribution. A more parametric shape of the model in the right tail facilitates more stable and precise estimate of the parameters and, as we show in Section 4, this results in an improved overall fit of the model.

To motivate our methodology, we consider two recent Eastern Cooperative Oncology Group (ECOG) phase III melanoma clinical trials, E1684 and E1690. The first trial, E1684, was a two-arm clinical trial comparing high-dose interferon (IFN) to observation (OBS). There were a total of \( n_0 = 286 \) patients enrolled in E1684. Here, relapse-free survival is defined as the time from randomization until progression of tumor or death, whichever comes first. E1690 was a subsequent phase III clinical trial involving identical treatments and patient populations as E1684. E1690 was intended as a confirmatory trial to E1684. The sample size for the E1690 trial was \( n = 427 \) patients on the combined IFN and OBS arms. E1690 serves as the current study and E1684 serves as the historical data for our example here. A Kaplan–Meier relapse-free survival (RFS) plot for E1690 shows a plateau, i.e., a cure fraction, in the survival curve after sufficient follow-up. Thus, a cure rate model appears appropriate for these data. We discuss the E1684 and E1690 trials in more detail in Section 4.

2. The Semiparametric Cure Rate Model

The cure rate model discussed in Yakovlev and Tsodikov (1996) and Chen, Ibrahim, and Sinha (1999) can be stated as follows. Suppose we have \( n \) subjects and, for the \( i \)th subject, let \( y_i \) denote the observed survival time, let \( \nu_i \) be the censoring indicator that equals one if \( y_i \) is a failure time and zero if it is right censored, and also let \( N_i \) denote the number of metastatic-competent tumor cells. Further, we assume that the \( N_i \)'s are i.i.d. Poisson random variables with mean \( \theta_i \), which is related to the covariates by \( \theta_i \equiv \theta(x'_i \beta) = \exp(x'_i \beta) \), where \( x'_i = (x'_{i1}, \ldots, x'_{ip}) \) denotes the \( p \times 1 \) vector of covariates for the \( i \)th subject and \( \beta = (\beta_1, \ldots, \beta_p)' \) is the corre-
sponding vector of regression coefficients, $i = 1, \ldots, n$. Further, let $Z_i$ denote the random vector for the $i$th metastatic-competent tumor cell to produce detectable metastatic disease. Let $S(t \mid \lambda)$ denote the survival function of the $Z_i$’s, which depends on the parameter $\lambda$, $F(t \mid \lambda) = 1 - S(t \mid \lambda)$, and $f(t \mid \lambda) = dF(t \mid \lambda)/dt$. Letting $N = (N_1, N_2, \ldots, N_n)$, the complete data is given by $D_c = (n, y, X, \nu, N)$, where $y = (y_1, \ldots, y_n)'$, $\nu = (\nu_1, \ldots, \nu_n)'$, and $X$ is the $n \times p$ matrix of covariates with ith row $x_i'$. Following Chen et al. (1999), we can write the complete data likelihood of $(\beta, \lambda)$ for the cure rate model as

$$L(\beta, \lambda \mid D_c) = \left( \prod_{i=1}^{n} \prod_{j=1}^{J} \exp \left\{ - (N_i - \nu_i) \delta_{ij} \right\} \right) \times \exp \left\{ \sum_{i=1}^{n} \left[ N_i x_i' \beta - \log(N_i!) - \exp(x_i' \beta) \right] \right\},$$

where $\delta_{ij} = 1$ if the $i$th subject failed or was censored in the $j$th interval and is zero otherwise.

We introduce a smoothing parameter in the prior for $\lambda_j$, denoted $\kappa$, such that the model converges to a parametric model in the right tail of the survival curve as $j \to \infty$. This smoothing parameter does not depend on the data. Since there are very few patients at risk in the right tail, estimation of $\kappa$ would be very unstable. Our approach is fundamentally very different from previous approaches for semiparametric Bayesian survival analysis, which primarily focus on specifying a prior process with a mean function and possibly a smoothing parameter, in which posterior properties of both of them depend on the data.

Let $F_0(t \mid \lambda_0)$ denote the parametric survival model we wish to choose for the right tail of the survival curve and let $H_0(t)$ denote the corresponding cumulative baseline hazard function. Now we take the $\lambda_j$’s to be independent $\text{a priori}$, each having a gamma prior distribution with mean

$$\mu_j = E(\lambda_j \mid \lambda_0) = \frac{H_0(s_j) - H_0(s_{j-1})}{s_j - s_{j-1}}$$

and variance

$$\sigma_j^2 = \text{var}(\lambda_j \mid \lambda_0, \kappa) = \mu_j \kappa^2,$$

where $0 < \kappa < 1$ is a smoothing parameter that controls the degree of parametricity in the right tail. We see that, as $\kappa \to 0$, $\sigma_j^2 \to 0$, so that small values of $\kappa$ imply a more parametric model in the right tail. In addition, we observe that, as $j \to \infty$, $\sigma_j^2 \to 0$, implying that the degree of parametricity is increased at a rate governed by $\kappa$ as the number of intervals increases. This property also implies that, as $j \to \infty$, the survival distribution in the right tail becomes more parametric regardless of any fixed value of $\kappa$. This is a novel construction of the semiparametric model that forces a high degree of parametricity with large $j$ and/or small $\kappa$ at a rate controlled by $\kappa$. The incorporation of $\kappa$ into the model makes the posterior estimation of the $\lambda_j$’s much more stable for large $j$, in which there are fewer subjects at risk. The properties of this model are attractive. For example, if $F_0(t \mid \lambda_0)$ is an exponential distribution, then $F_0(t \mid \lambda_0) = 1 - \exp(-\lambda_0 t)$, so that $\mu_j = \lambda_0$ and $\sigma_j^2 = \lambda_0 \kappa^2$. If $F_0(t \mid \lambda_0)$ is a Weibull distribution, then $F_0(t \mid \lambda_0) = 1 - \exp(-\gamma_0 \delta_0 t)$, $\lambda_0 = (\gamma_0, \delta_0)$, so that $\mu_j = \gamma_0(s_j^{\delta_0} - s_{j-1}^{\delta_0})/(s_j - s_{j-1})$ and $\sigma_j^2 = \gamma_0(s_j^{\delta_0} - s_{j-1}^{\delta_0})/(s_j - s_{j-1}) \kappa^2$. We also note that $J$ controls the overall parametricity of the model. The larger the number of intervals $J$, the more nonparametric the model is for $F(\cdot)$.

We are now formally state several properties for this new model. The proofs are given in the Appendix.

**PROPERTY 2.1:** Assume that $(s_j + s_{j-1})/2 \to t$ as $s_j - s_{j-1} \to 0$. Then, for any $j$, according to this prior process, $E(\lambda_j \mid \lambda_0) \to h_0(t)$ as $s_j - s_{j-1} \to 0$, where $h_0(t) = (d/dt) \times H_0(t)$.

For example, when $F_0(t \mid \lambda_0) = 1 - \exp(-\lambda_0 t)$, $E(\lambda_j \mid \lambda_0) = \lambda_0$ regardless of our choices of $s_1, \ldots, sJ$. When $F_0(t \mid \lambda_0) =$
gamma densities with mean nonparametric nature of exponential distribution, then of distribution, a gamma prior for it, i.e., the semiparametric cure doing analyses for several values of degree of parametricity in distribution of theorem establishes the propriety of the joint posterior where

\[ h_{\lambda}(t | \lambda) = \frac{1}{\lambda} \exp(-\lambda t) \]

This assures that, as \( j \) becomes large and \( s_j - s_{j-1} \to 0 \), this prior process approximates any prior process with prior mean \( h_0(t) \) defined on the hazard \( h^*(t | \lambda) \) corresponding to (2.2).

PROPERTY 2.2: Let \( S_p^*(t | \lambda) = \exp(-\theta F^*(t | \lambda)) \), where \( F^*(t | \lambda) \) is given by (2.2). Then \( S_p^*(t | \lambda) \to S_p(t | \lambda) \) as \( \kappa \to 0 \), where \( S_p(t | \lambda_0) = \exp(-\theta F_0(t | \lambda_0)) \).

PROPERTY 2.3: Let \( f^*(t | \lambda) = dF^*(t | \lambda)/dt \) and let \( h_{p}^*(t | \lambda) = \theta f^*_0(t | \lambda) \) denote the corresponding hazard function. Then \( h_{p}^*(t | \lambda) \to \theta f_0(t | \lambda_0) \) as \( \kappa \to 0 \), where \( f_0(t | \lambda_0) = dF_0(t | \lambda_0)/dt \).

Properties 2.1–2.3 are important since the estimation of the cure rate parameter, \( \theta \), could be highly affected by the nonparametric nature of \( F^*(t | \lambda) \). In practice, we recommend doing analyses for several values of \( \kappa \), and \( F_0(\cdot | \lambda_0) \) to examine the sensitivity of the posterior estimates to various choices of these parameters. Thus, the semiparametric cure rate model (2.3) is quite flexible since it allows us to model general shapes of the hazard function as well as to choose the degree of parametricity in \( F^*(t | \lambda) \) through suitable choices of \( \kappa \) and \( J \).

3. Prior Distributions

3.1 Noninformative Priors

We specify a hierarchical model and first consider a joint (improper) noninformative prior distribution for \((\beta, \lambda, \lambda_0)\). We specify the joint prior of these parameters as

\[
\pi(\beta, \lambda, \lambda_0) = \pi(\beta) \pi(\lambda | \lambda_0) \pi(\lambda_0) 
\approx \pi(\beta) \prod_{j=1}^{J} \pi(\lambda_j | \lambda_0) \frac{\lambda_0}{\lambda_0} \exp(-\tau_0 \lambda_0),
\]

(3.1)

As noted earlier, we take each \( \pi(\lambda_j | \lambda_0) \) to be independent gamma densities with mean \( \mu_j \) and variance \( \sigma_j^2 \). If \( F_0(\cdot) \) is an exponential distribution, then \( \lambda_0 \) is a scalar, and we specify a gamma prior for it, i.e., \( \pi(\lambda_0) \propto \lambda_0^{\zeta - 1} \exp(-\tau_0 \lambda_0) \), where \( \zeta_0 \) and \( \tau_0 \) are specified hyperparameters. If \( F_0(\cdot) \) is a Weibull distribution, \( \lambda_0 = (\gamma_0, \alpha_0) \). In this case, we take a prior of the form

\[
\pi(\lambda_0) = \pi(\alpha_0, \gamma_0) 
\propto \alpha_0^{\zeta - 1} \exp(-\tau_0 \alpha_0) \gamma_0^{\zeta - 1} \exp(-\tau_0 \gamma_0),
\]

(3.2)

where \( \zeta_0, \tau_0, \zeta_0, \tau_0 \) are specified hyperparameters. For \( \beta \), we consider a uniform improper prior. The next theorem establishes the propriety of the joint posterior distribution of \((\beta, \lambda, \lambda_0)\) when using an exponential distribution or a Weibull distribution for \( F_0(\cdot) \).

**Theorem 3.1:** Suppose, (i) when \( \nu_i = 1, \psi_{i0} > 0 \), (ii) there exists \( i_1, i_2, \ldots, i_J \) such that \( \nu_j = 1 \) and \( s_{j-1} < y_{ij} \leq s_j, j = 1, \ldots, J \) (iii) the design matrix \( X^* \) has ith row equal to \( \nu_i x_i^* \) is of full rank, (iv) if \( F_0(\cdot | \lambda_0) \) is an exponential distribution, \( \zeta_0 > 0, \tau_0 > 0 \), and \( \gamma_0 > 0 \), (v) if \( F_0(\cdot | \lambda_0) \) is a Weibull distribution, \( \zeta_0 > 0, \tau_0 > 0, \gamma_0 > 0 \), and \( \alpha_0 > 0, \gamma_0 > -\gamma_0 \log(1/s) \).

Then the posterior distribution of \((\beta, \lambda, \lambda_0)\) is proper, i.e., \( \int L(\beta, \lambda | D) \pi(\beta, \lambda, \lambda_0) d\beta d\lambda d\lambda_0 \) is the likelihood function based on the observed data \( D \).

A proof of Theorem 3.1 is given in the technical report by Ibrahim, Chen, and Sinha (1999). Theorem 3.1 provides a very general class of improper noninformative priors for \((\beta, \lambda, \lambda_0)\). First, we mention that, in condition (iv) of Theorem 3.1, \( \gamma_0 \) can be negative, thus resulting in an improper prior for \( \lambda_0 \) when \( F_0(\cdot | \lambda_0) \) is exponential. Second, \( \tau_0 \) is also allowed to be negative, resulting in a joint improper prior for \((\gamma_0, \alpha_0)\) when \( F_0(\cdot | \lambda_0) \) is Weibull.

3.2 Informative Priors from Historical Data

Prior elicitation using historical data has been discussed by the authors in Ibrahim and Chen (2000). The informative prior construction for the proposed semiparametric cure rate model proceeds as follows. Let \( n_0 \) denote the sample size for the historical data, \( y_0 = (y_{01}, y_{02}, \ldots, y_{0n_0})' \) be an \( n_0 \times 1 \) vector of right-censored failure times for the historical data with censoring indicators \( v_0 = (v_{01}, v_{02}, \ldots, v_{0n_0})' \), and \( X_0 \) is an \( n_0 \times k \) matrix of covariates with ith row \( x_{0i} \). Let \( D_0 = (n_0, y_0, X_0, v_0) \) denote the observed historical data. Our informative prior takes the form

\[
\pi(\beta, \lambda, \lambda_0, \alpha_0 | D_0) 
\propto L(\beta, \lambda | D_0)^{\alpha_0} \pi_0(\beta, \lambda | \lambda_0)^{\alpha_0 - 1} (1 - \alpha_0)^{\psi_0 - 1},
\]

(3.3)

where \( L(\beta, \lambda | D_0) \) is the likelihood function based on the observed historical data and \( \xi_0 \) and \( \psi_0 \) are prespecified hyperparameters. The quantity \( \pi_0(\beta, \lambda | \lambda_0) \) is the initial prior for \((\beta, \lambda, \lambda_0)\), which is (3.1) with \( \pi_0(\lambda_0) \) taking the form given by \( \pi_0(\lambda_0) \propto \lambda_0^{\zeta - 1} \exp(-\tau_0 \lambda_0) \) or by (3.2), depending on the form of \( F_0(\cdot | \lambda) \). The parameter \( \alpha_0 \) controls the influence of the historical data on the current data. Following the proofs of Theorem 3.1 and Theorem 3 of Chen et al. (1999), it can be shown that the prior distribution \( \pi(\beta, \lambda, \lambda_0, \alpha_0 | D_0) \) given by (3.3) is proper under some very general conditions.

4. Melanoma Data

We revisit the E1684 and E1690 trials discussed in Section 1. Our main purpose in this example is to examine the tail behavior of our proposed model as \( \kappa, \alpha_0, F_0, \) and \( J \) are varied. Of particular interest is the sensitivity of the posterior estimates of \( \beta, \lambda, \) and \( S^*(t | \lambda) = 1 - F^*(t | \lambda) \) as these parameters are varied, where \( F^*(t | \lambda) \) is defined in (2.2).

The E1690 study is quite suitable for our purposes here since the median follow-up for E1690 (4.3 years) is considerably smaller than for E1684 (6.9 years). Thus, cure rate estimation based on the E1690 study alone, i.e., \( \alpha_0 = 0 \), may be more sensitive than that of an analysis that incorporates the historical data E1684. In our example, three covariates were used and an intercept was included in the model. The three covariates are treatment (IFN, OBS), age, which is continuous, and gender (male, female). Let \( \beta = (\beta_1, \beta_2, \beta_3, \beta_4) \) be the regression coefficient vector corresponding to an intercept and the three covariates, respectively.

To assess the goodness of fit of the models for different choices of \( \kappa, \alpha_0, F_0(\cdot | \lambda_0), \) and \( J \), we use the conditional predictive ordinate (CPO) statistic. Let \( \text{CPO}_i \) denote the CPO statistic for the ith subject.

Our main purpose in this example is to examine the tail behavior of our proposed model as \( \kappa, \alpha_0, F_0, \) and \( J \) are varied. Of particular interest is the sensitivity of the posterior estimates of \( \beta, \lambda, \) and \( S^*(t | \lambda) = 1 - F^*(t | \lambda) \) as these parameters are varied, where \( F^*(t | \lambda) \) is defined in (2.2).
defined as $B = \Sigma_{i=1}^{n} \log(CPi)$. The larger the $B$, the better the fit of a given model.

Table 1 gives posterior means, standard deviations (SD), and 95% highest posterior density (HPD) intervals of $\beta$ for several values of $\kappa$ using the exponential and Weibull models for $F_0$ with $\beta = 10$ intervals and when $E(a_0 \mid D, D_0) = 0.33$. As $\kappa$ is varied for a given $a_0$ using an exponential or Weibull $F_0$, we see small to moderate changes in the posterior estimates of $\beta$. We also note from Table 1 that, the $B$ statistic is always largest for the smallest value of $\kappa$. This indicates that, when the model is more parametric in the right tail of the survival curve, the better the fit. As $a_0$ is varied, more substantial changes occur in the posterior estimates of $\beta$ across values of $\kappa$. For example, using an exponential $F_0$ and $\kappa = 0.05$, the posterior means, standard deviations, and 95% HPD intervals for the treatment coefficient, i.e., $\beta_2$, are $-0.209$, $0.130$, and $(-0.461, 0.050)$ when $a_0 = 0$ with probability one; $-0.242$, $0.115$, and $(-0.469, -0.018)$ when $E(a_0 \mid D, D_0) = 0.33$; and $-0.277$, $0.079$, and $(-0.462, -0.087)$ when $a_0 = 1$ with probability one. In general, the posterior standard deviations for $E(a_0 \mid D, D_0) > 0$ are smaller than those for $a_0 = 0$, therefore resulting in narrower 95% HPD intervals. A partial explanation of this is that, by incorporating the historical data, more precise estimates of the regression coefficients and right tail of the survival curve are obtained. Overall, for given $a_0$, we conclude that the estimates of $\beta$ are reasonably robust as $\kappa$ is varied but change substantially as $a_0$ is varied. We also observe that, for fixed $\kappa$, $B$ is a concave function of $a_0$. As an example, for $\kappa = 0.05$ and an exponential $F_0$, the $B$ statistics are $-518.87$ for $a_0 = 0$, $-518.07$ when $E(a_0 \mid D, D_0) = 0.33$, and $-518.21$ for $a_0 = 1$.

Table 2 shows posterior summaries of the cure rates and survival function $S^*(t)$ for varying $\kappa$ and $F_0$ when $E(a_0 \mid D, D_0) = 0.33$. For a given $F_0$, we see moderate changes in the cure rates as $\kappa$ is varied. When $a_0$ and $\kappa$ remain fixed and $F_0$ is changed, we see that the estimates are quite robust. Also from Table 2, we can see that a monotonic increase in the mean of the cure rate estimates occurs as $\kappa$ is increased. A similar phenomenon occurs with other values of $a_0$. In summary, Table 2 shows that small to moderate changes can occur in the cure rates as the degree of parametricity in the right tail of the survival curve, $\kappa$, is changed. We also computed estimates of $\lambda$ for several values of $\kappa$ and $a_0$ assuming that $F_0$ is exponential. We observe that, for a given $a_0$, the posterior estimates of $\lambda$ can change moderately to considerably as $\kappa$ varies. For example, with $a_0 = 0$, the posterior mean of $\lambda_{10}$ is 0.617 for $\kappa = 0.05$ and 0.788 when $\kappa = 0.95$. A similar phenomenon occurs when $a_0 = 1$. These changes in $\lambda$ can be summarized better by examining the estimated survival function $S^*(t \mid \lambda)$.

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Résumé

Nous proposons des méthodes d’inference bayésienne pour une nouvelle classe de modèles de survie avec une fraction de guérison. Précisément, nous proposons un modèle semi-paramétrique de taux de guérison avec un paramètre de lissage qui contrôle le degré de paramétrisation dans la queue droite de la distribution de survie. Nous montrons qu’un tel paramètre est crucial dans ce type de modèles, et peut avoir une influence sur les estimations a posteriori. Plusieurs propriétés nouvelles du modèle proposé sont déduites. De plus, nous proposons une classe d’a priori non informatifs impropre basés sur ce modèle, et examinons les propriétés impliquées a posteriori. Une classe d’a priori informatifs basés sur des données historiques est également proposée, et ses propriétés sont investiguées. Une étude de cas concernant un essai clinique sur le mélanome est discutée en détail pour expliciter la méthodologie proposée.

References


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APPENDIX

Proofs of Properties

Proof of Property 2.1
From the definition of \( E(A_j | \lambda_0) \) in (2.4), we have

\[
E(\lambda_j | \lambda_0) = \frac{H_0(s_j) - H_0(s_{j-1})}{s_j - s_{j-1}} - \frac{H_0(s_{j+1} - s_{j-1})}{s_j - s_{j-1}}.
\]

Now using the definition of a derivative of the function \( H_0(\cdot) \) and the assumption that \( \lambda \to 0 \), we have

\[
\lim_{s_j - s_{j-1} \to 0} E(\lambda_j | \lambda_0) = \frac{d}{dt} H_0(t) = h_0(t).
\]

Proof of Property 2.2
Note that, for \( t \in (s_j, s_{j-1}) \),

\[
E[H^*(t) | \lambda_0] = \mu_j(t) - \frac{s_j + s_{j-1}}{2} + \sum_{g=1}^{j-1} \mu_g(s_g - s_{g-1})
\]

\[
= \left( \frac{t - s_{j-1}}{s_j - s_{j-1}} \right) [H_0(s_j) - H_0(s_{j-1})] + H_0(s_{j-1}).
\]

Note that the right-hand side of (A.1) equals \( H_0(t) \) when \( t \in \{s_1, \ldots, s_J\} \). For other values of \( t \), it is only approximately equal in the sense that, as \( s_j - s_{j-1} \to 0 \), the right-hand side of (A.1) approaches \( H_0(t) \). Again, \[ \text{var}[H^*(t | \lambda) | \lambda_0] = (t - s_{j-1})^2 \mu_j + \sum_{g=1}^{j-1} \mu_g \rho^2(s_g - s_{g-1}) \to 0 \text{ as } \kappa \to 0. \]

This shows that \( H^*(t | \lambda) \to H_0(t) \) in probability for \( t \in \{s_1, \ldots, s_J\} \), and this implies \( F^*(t | \lambda) = 1 - \exp(-H^*(t | \lambda)) \to F_0(t | \lambda_0) \) in probability. So, given \( \theta \), the random survival function \( S^*_0(t | \lambda) = \exp[-\theta F^*(t | \lambda)] \) converges to \( \exp[-\theta F_0(t | \lambda_0)] \) in probability as \( \kappa \to 0 \). This convergence is exact for \( t \in \{s_1, \ldots, s_J\} \) and approximate for other values of \( t \). \qed

Proof of Property 2.3
From Chen et al. (1999), it is known that \( h^*_p(t | \lambda) = \theta f^*(t | \lambda) = \theta \lambda_j \exp(-\lambda_j t) \), where

\[
H^*_p(t | \lambda) = \lim_{\delta \to 0} \frac{P(T \in (t, t+\delta) | T > t, \theta, F^*)}{\delta},
\]

with the probability evaluated under the model in (3.2). For \( t \in (s_{j-1}, s_j) \), the moment generating function \( m_j(t) \) of \( \lambda_j \), under the prior process on \( F^* \) given \( (\lambda_0, \kappa) \), is given by

\[
m_j(t) = E[\exp(-\lambda_j t) | \mu_j, \kappa] = \left( \frac{\mu_j}{\mu_j + \mu_j \kappa^t} \right)^{\mu_j / \mu_j}. \quad (A.3)
\]

Using (A.3), we can show that \( E[\lambda_j \exp(-\lambda_j t) | \mu_j, \kappa] = -m_j'(t) \) approaches \( \mu_j \exp(-\mu_j t) \) as \( \kappa \to 0 \) and \( \text{var}[\lambda_j \times \exp(-\lambda_j t) | \mu_j, \kappa] = 0 \). Then it follows that \( h^*_p(t | \lambda) = \theta f^*(t | \lambda) \approx \theta \lambda_j \exp(-\lambda_j t) \) approaches \( \theta \mu_j \exp(-\mu_j t) \approx \theta f_0(t | \lambda_0) \) in probability as \( \kappa \to 0 \). \qed
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