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POSTERIOR COMPUTATION OF SURVIVAL MODEL WITH DISCRETE APPROXIMATION†

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ABSTRACT

In the proportional hazard model with the beta process prior, the posterior computation with the discrete approximation is considered. The time period of interest is partitioned by small intervals. On each partitioning interval, the likelihood is approximated by that of a binomial experiment and the beta process prior is by a beta distribution. Consequently, the posterior is approximated by that of many independent binomial model with beta priors. The analysis of the leukemia remission data is given as an example. It is illustrated that the length of the partitioning interval affects the posterior and one needs to be careful in choosing it.

AMS 2000 subject classifications. Primary 62N01; Secondary 62C10.
Keywords. Beta process, discrete approximation, Markov chain Monte Carlo, proportional hazard model.

1. INTRODUCTION

The beta process, proposed by Hjort (1990), is a popular nonparametric prior process used in survival models. The class of beta processes is a subclass of neutral to the right (NTR) processes (Doksum, 1974; Kalbfleisch, 1978; Ferguson and Phadia, 1979) and contains the celebrated Dirichlet processes (Ferguson, 1973).

Since the posterior distribution involving the beta process is not analytically available except the right censored data without covariate case, Markov chain Monte Carlo (MCMC) is used as the default computational tool for the posterior

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computation. The posterior computation methods involving the beta process or more generally the NTR process can be divided into two categories – process sampling methods and discrete approximation methods. The process sampling methods are those in which the sample path of the NTR process is generated in the course of MCMC iterations. These methods include the ϵ-approximation method (Lee and Kim, 2004), inverse Lévy measure (ILM) algorithm (Wolpert and Ickstadt, 1998), Poisson weighting algorithm (Lee, 2007) and acceptance-rejection method (Lee, 2007). All of NTR process sampling methods are based on the fact that the cumulative hazard function (*c.h.f.*) of the NTR process can be represented as an integral of the Poisson random measure (Kim and Lee, 2001, 2003). Since the Poisson random measure corresponding to the most NTR processes have infinitely many jumps, these methods approximate the sample path with finitely many jumps. When these methods are employed in the posterior computation of survival models, there is usually no need to further approximate the likelihood (Lee and Kim, 2004). The process sampling methods are satisfactory in that once the sample path is generated it can be plugged in the posterior and likelihood formulas to run the MCMC. But, coding the posterior simulation is quite involved and is a strenuous work for practitioners. On the other hand, the discrete approximation algorithm involves approximation of both the likelihood and the prior, but the standard MCMC program WinBUGS can be used for the posterior simulation and thus the practitioner can code it relatively easily.

In implementing the discrete approximation algorithm, the time period of interest is partitioned into small intervals, on which the likelihood and the prior process are approximated. Laud *et al.* (1998) proposed a kind of discrete approximation method where the increment of the beta process is approximated by Poisson weighted sums of random variables. Poisson weighting algorithm (Lee, 2007) is a continuous version of their discrete approximation algorithm. Ibrahim *et al.* (2001) presented a discrete approximation of the posterior and gave an MCMC algorithms to generate random sample from the approximated posterior when the prior process is the gamma or beta process.

In this paper, we investigate the discrete approximation algorithm. In particular, we take the discrete approximation of the posterior from the proportional hazard model with the beta process prior on the baseline *c.h.f.* and study the implementation of the algorithm and its behavior when the length of the partitioning interval tends to 0. Ibrahim *et al.* (2001) seem to be satisfied with coarse partitions – the length of the partitioning intervals is relatively large – for the approximation and in fact their algorithm can not be run when the length of the partitioning interval is too small. Our investigation shows that the length of the partitioning interval has nonnegligible effect on the posterior and smaller partitioning intervals are preferred to larger ones. But unfortunately, if the length of the partitioning interval is too close to 0, the likelihood can not be computed numerically. Thus, one needs to balance between the accuracy of the approximation and the numerical accuracy.

The paper is organized as follows. In Section 2, we discuss the discrete approximation of the prior and likelihood. The details of the posterior computation is discussed in Section 3. An example is given in Section 4.

2. DISCRETE APPROXIMATION

2.1. *Binomial likelihood approximation*

Let $X_1, \ldots, X_n$ be survival times with covariates $Z_1, \ldots, Z_n \in \mathcal{R}^p$ and follow the proportional hazard model. In particular, suppose the distribution F_i of X_i with covariate $Z_i \in \mathcal{R}^p$ is given by

$$1 - F_i(t) = (1 - F(t))^{\exp(\beta^T Z_i)},$$

where $\beta \in \mathcal{R}^p$ is the regression coefficient and F is the baseline distribution. The *c.h.f.* A of the distribution F is defined by $dA(t) = dF(t)/(1-F(t-))$. The *c.h.f.* A_i of F_i is defined similarly and can also be expressed in terms of A:

$$dA_i(t) = 1 - (1 - dA(t))^{\exp(\beta^T Z_i)}. \tag{2.1}$$

If A is absolutely continuous with respect to the Lebesgue measure, there exists a hazard function a such that $A(t) = \int_0^t a(s)ds$. In this case, the hazard function $a_i(t)$ of A_i exists and $a_i(t) = a(t)e^{\beta^T Z_i}$.

In most applications, the survival times are subject to right censoring, and only $D = \{(T_1, \delta_1, Z_1), \ldots, (T_n, \delta_n, Z_n)\}$ are observed, where $T_i = \min(C_i, X_i)$, $\delta_i = I(X_i \le C_i)$ and $C_1, \ldots, C_n$ are independent right censoring variables. For $i = 1, 2, \ldots, n$, define counting processes $N_i(t) = I(T_i \le t, \delta_i = 1)$ and $Y_i(t) = I(T_i \ge t)$. Let $N(t) = \sum_{i=1}^n N_i(t)$, $\Delta N(t) = N(t) - N(t-)$ and $Y(t) = \sum_{i=1}^n Y_i(t)$. Let $t_1 < t_2 < \cdots < t_{q_n}$ be the distinct ordered uncensored observations where q_n is the number of them. Define

$$\begin{aligned} D_n(t) &= \{i : T_i = t, \ \ \delta_i = 1, \ \ i = 1, \ldots, n\}, \\ R_n(t) &= \{i : t \le T_i, \ \ i = 1, \ldots, n\}, \\ R_n^+(t) &= R_n(t) - D_n(t). \end{aligned}$$

Let $[0, \tau]$ be the time period of interest and $\Pi_n = \{0 = s_0 < s_1 < s_2 < \cdots < s_k = \tau\}$ be a partition of $[0, \tau]$. The likelihood approximation will be based on the partition Π_n. Given the observation D, the likelihood function is given as follows:

$$
\begin{aligned}
L(\beta, A) &= \prod_{i=1}^{n} \prod_{t \in [0,\tau]} dA_i(t)^{dN_i(t)} (1 - dA_i(t))^{Y_i(t) - dN_i(t)} \\
&= \prod_{i=1}^{n} \prod_{t \in [0,\tau]} \left(1 - (1 - dA(t))^{e^{\beta^T z_i}}\right)^{dN_i(t)} (1 - dA(t))^{e^{\beta^T z_i}(Y_i(t) - dN_i(t))} \\
&= \prod_{i=1}^{n} \prod_{j=1}^{k} \prod_{t \in (s_{j-1}, s_j]} \left(1 - (1 - dA(t))^{e^{\beta^T z_i}}\right)^{dN_i(t)} (1 - dA(t))^{e^{\beta^T z_i}(Y_i(t) - dN_i(t))},
\end{aligned}
$$

where $R_n^+(t, \beta) = \sum_{j \in R_n^+(t)} \exp(\beta^T Z_j)$. Based on the partition Π_n, the product-integration is approximated by a finite product, *i.e.*,

$$
L_n(\beta, A) = \prod_{i=1}^{n} \prod_{j=1}^{k} \left(1 - (1 - \Delta A_j)^{e^{\beta^T z_i}}\right)^{\Delta N_{ij}} (1 - \Delta A_j)^{e^{\beta^T z_i}(Y_{ij} - \Delta N_{ij})},
$$

where $\Delta A_j = A(s_j) - A(s_{j-1})$, $\Delta N_{ij} = N_i(s_j) - N_i(s_{j-1})$ and $Y_{ij} = Y_i(s_{j-1}+)$.

Interestingly, the above likelihood is the same as that of the following model:

$$
\Delta N_{ij} | \beta, \Delta A_j \overset{\text{indep.}}{\sim} Binomial\left(Y_{ij}, p_{ij}\right), \tag{2.2}
$$

$$
p_{ij} = 1 - (1 - \Delta A_j)^{e^{\beta^T z_i}},
$$

for $i = 1, \ldots, n$ and $j = 1, \ldots, k$. Since

$$
\text{cloglog}(p_{ij}) = \log(-\log(1 - p_{ij})) = \beta^T z_i + \log(-\log(1 - \Delta A_j)),
$$

model (2.2) is none other than the binomial regression model with the complementary log-log link. The difference from the ordinary binomial regression model is the part $v_j = \log(-\log(1 - \Delta A_j))$, $j = 1, \ldots, k$. In the next section, we will derive the distribution of ΔA_j, thus, model (2.2) requires a nonstandard prior for v_j derived from that of ΔA_j.

2.2. Beta process approximation

The proportional hazard model has two parameters, the regression coefficient β and *c.h.f.* A. We adopt a probability measure on $\mathcal{R}^p$ with a density $\pi(\beta)$ –

usually a multivariate normal distribution – as the prior for β and the beta process prior for A. The prior on β can be used as the prior of β in the binomial model (2.2) without any change. The beta process prior of A, however, needs a modification to be used as the prior of model (2.2).

The beta process $\mathrm{BP}(c(t), A_0(t))$ is an nondecreasing independent increment process with Lévy measure

$$\nu(dt, dx) = \frac{c(t)}{x}(1-x)^{c(t)-1}\, dx\, dA_0(t)\,, \quad 0 < x < 1,\ t \geq 0.$$

From the beta process prior of A, the distribution of ΔA_j for the prior of the binomial model (2.2) needs to be derived. Unfortunately, the distribution of A_j is nonstandard and difficult to be used as the prior. For this problem, the original construction of the beta process given by Hjort (1990) is convenient. As in the likelihood approximation, let $\Pi_n = \{0 = s_0 < s_1 < s_2 < \cdots < s_k = \tau\}$ be a partition of $[0, \tau]$. For $j = 1, \ldots, k$, let

$$\begin{aligned} c_{1j} &= c(s_j)(A_0(s_j) - A_0(s_{j-1})), \\ c_{2j} &= c(s_j)(1 - (A_0(s_j) - A_0(s_{j-1}))), \\ \Delta A_j &\overset{\text{indep.}}{\sim} \mathrm{Beta}(c_{1j}, c_{2j}). \end{aligned} \tag{2.3}$$

From the independent beta random variables ΔA_j, define

$$A_n(t) = \sum_{s_j \leq t} \Delta A(s_j).$$

Then, $A_n(t)$ converges in distribution to the beta process, *i.e.*,

$$A_n(t) \xrightarrow{d} A(t) \text{ on } D[0, \tau],$$

where $A(t) \sim \mathrm{BP}(c(t), A_0(t))$. Thus, it is natural to use $\Delta A_j \overset{\text{indep.}}{\sim} \mathrm{Beta}(c_{1j}, c_{2j})$ as the prior of the binomial model (2.2).

3. POSTERIOR COMPUTATION

In this section, we fix a partition $\Pi_n = \{0 = s_0 < s_1 < s_2 < \cdots < s_k = \tau\}$ of the time period of interest $[0, \tau]$. We construct the posterior from the approximated likelihood and prior derived in Section 2. For the simplicity of notation, let $u_j = \Delta A_j$ for $j = 1, \ldots, k$ and $u = (u_1, \ldots, u_k)$ and c_{1j} and c_{2j} are defined as in (2.3).

By multiplying the binomial likelihood and prior, we get the discrete approximation of the posterior of u, β.

$$\pi(\beta, u|D)\, d\beta \prod_{j=1}^{k} du_j \propto \pi(\beta)\, d\beta \prod_{j=1}^{k} u_j^{c_{1j}-1}(1-u_j)^{c_{2j}-1} du_j$$
$$\times \prod_{j=1}^{k}\prod_{i=1}^{n}\left(1-(1-u_j)^{e^{\beta^T z_i}}\right)^{\Delta N_{ij}} (1-u_j)^{e^{\beta^T z_i}(Y_{ij}-\Delta N_{ij})}.$$

By setting $v_j = \log(-\log(1-u_j))$ for $j = 1, \ldots, k$, $d_{ij} = \Delta N_{ij}$, $D_j = \{i : d_{ij} = 1\}$ and $R_{+j}(\beta) = \sum_{i=1}^{n} e^{\beta^T z_i}(Y_{ij} - \Delta N_{ij})$, the posterior density is proportional to

$$\pi(\beta)\, d\beta \prod_{j=1}^{k}\left(1-e^{-\exp(v_j)}\right)^{c_{1j}-1} e^{-\exp(v_j)(c_{2j}-1)} e^{(v_j-\exp(v_j))} v_j\, dv_j$$
$$\times \prod_{j=1}^{k}\prod_{i=1}^{n}\left(1-e^{-\exp(v_j)e^{\beta^T z_i}}\right)^{d_{ij}} e^{-\exp(v_j)(e^{\beta^T z_i}(Y_{ij}-\Delta N_{ij}))}$$
$$= \pi(\beta)\, d\beta \prod_{j=1}^{k}\left[\left\{\prod_{i\in D_j}\left(1-e^{-\exp(v_j)e^{\beta^T z_i}}\right)^{d_{ij}}\right\}\right.$$
$$\left.\times e^{-\exp(v_j)(c_{2j}+R_{+j}(\beta))}\left(1-e^{-\exp(v_j)}\right)^{(c_{1j}-1)} v_j\, dv_j\right]. \quad (3.1)$$

In summary, the posterior distribution of the proportional hazard model with right censored data $D = \{(T_1, \delta_1, z_1), \ldots, (T_n, \delta_1, z_n)\}$ with the prior

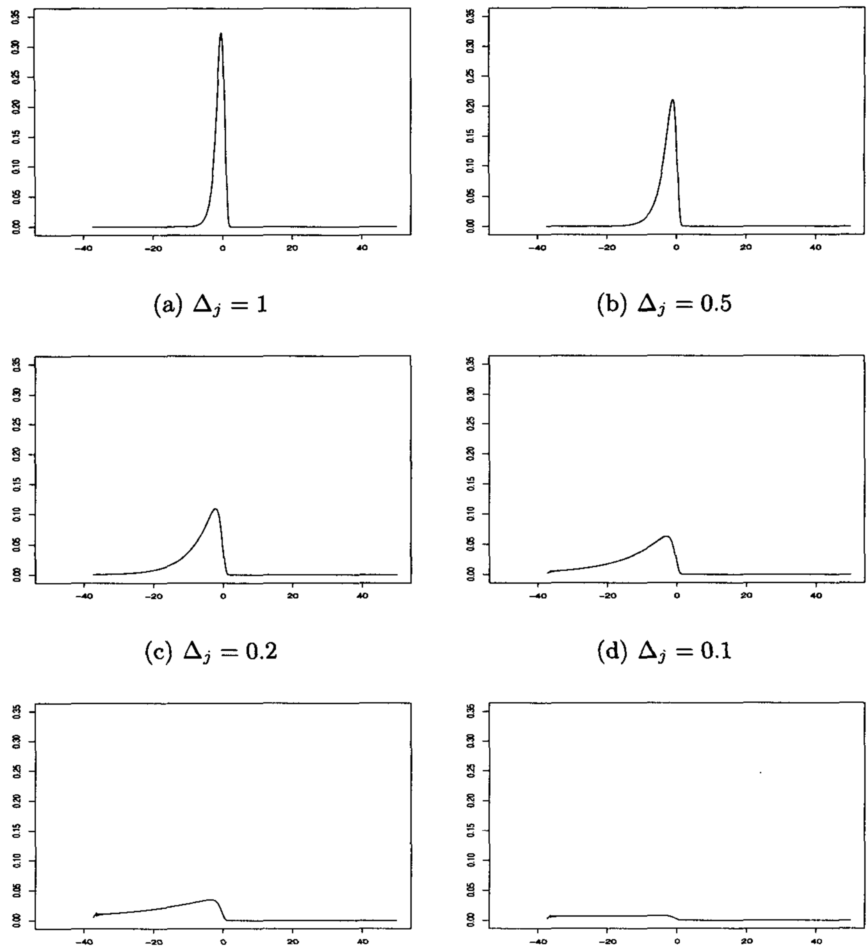
$$A(t) \sim \mathrm{BP}(c(t), A_0(t)),$$
$$\beta \sim \pi(\beta)$$

can be approximated by the posterior of the model (2.2) with the prior

$$\Delta A_j \sim \mathrm{Beta}(c_{1j}, c_{2j}), \quad j = 1, \ldots, k,$$
$$\beta \sim \pi(\beta),$$

where c_{1j} and c_{2j} are defined as in (2.3).

Because of a numerical reason, some care must be given to the posterior computation of the approximate binomial model. For the simplicity of the discussion, let $A(t) \sim \mathrm{BP}(c(t) = c, A_0(t) = t)$ and let $\Delta_j = s_j - s_{j-1}$ be the length



(a) $\Delta_j = 1$ (b) $\Delta_j = 0.5$

(c) $\Delta_j = 0.2$ (d) $\Delta_j = 0.1$

(e) $\Delta_j = 0.05$ (f) $\Delta_j = 0.01$

FIGURE 3.1 *Density plot of v_j for different Δ_j.*

of partitioning interval. For the interval $(s_{j-1}, s_j]$, the approximating beta random variable ΔA_j follows Beta$(c\Delta_j, c(1-\Delta_j))$. Theoretically, as $\Delta_j \to 0$, the approximated binomial posterior gets closer to the posterior. Thus, one wish to have finer partition with small Δ_j to get a close approximation. But, as $\Delta_j \to 0$, $\Delta A_j \to \delta_0$ in distribution, where δ_0 is the degenerate probability measure at 0. Consequently, as Δ_j is pushed to 0, most mass of ΔA_j get extremely close to 0, which generates an overflow in computing the likelihood. To give a clearer picture of the problem, for different Δ_j's in Figure 3.1, we draw the density of

TABLE 3.1 $Pr(v \leq -37)$ *for* Δ_j

Δ_j	1	0.5	0.2	0.1	0.05	0.01
$Pr(v_j \leq -37)$	$2.02E-13$	$5.24E-07$	0.0032	0.0569	0.2390	0.7513

$v_j = \log(-\log(1 - \Delta A_j))$ whose density is given by

$$f(v_j | c_{1j}, c_{2j}) = \frac{\Gamma(c_{1j} + c_{2j})}{\Gamma(c_{1j})\Gamma(c_{2j})} \left(1 - e^{-\exp(v_j)}\right)^{(c_{1j}-1)} e^{-c_{2j}\exp(v_j)} e^{v_j} \, dv_j.$$

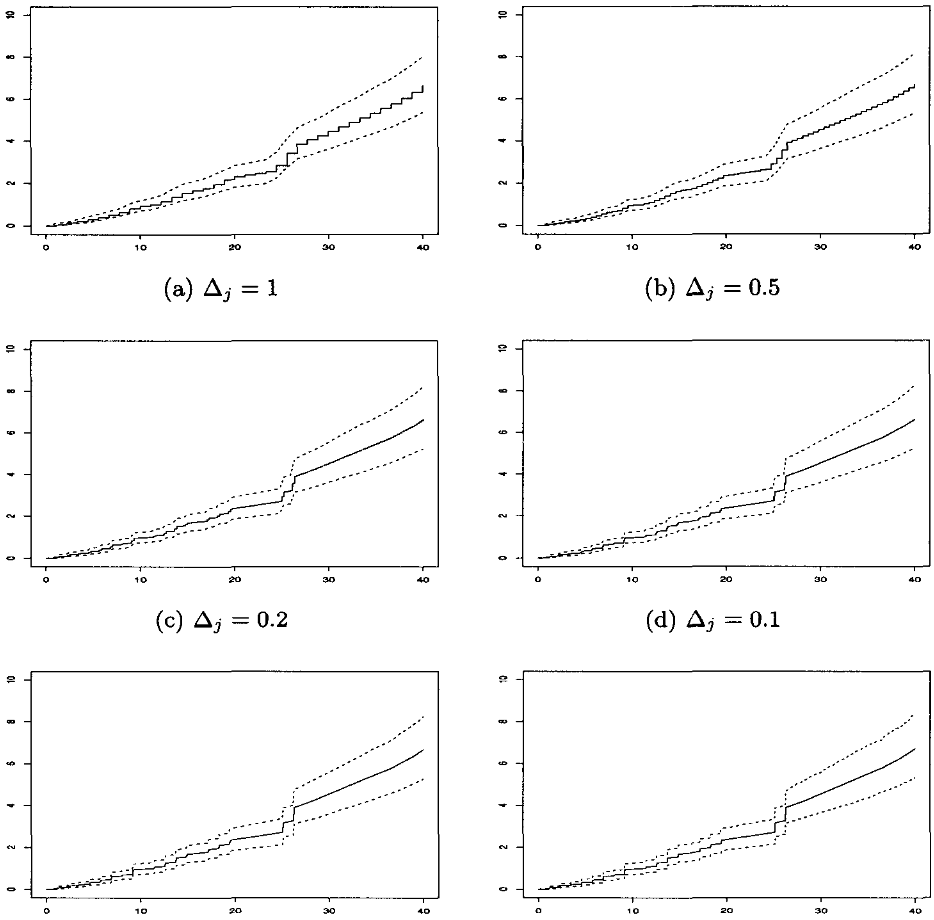
When Δ_j is relatively large, most mass of v_j is near 0, while as Δ_j gets smaller, the mass escapes to $-\infty$. If v_j is too small (for instance, $v_j < -37$), the likelihood can not be computed numerically. To be more specific, if $v_j = -37$, $\Delta A_j = 1 - e^{\exp(v_j)} \approx 1.1102E - 16$, thus, numerically $\Delta A_j = 1, (1 - \Delta A_j) = 0$ and the likelihood cannot be computed. Table 3.1 shows $P(v_j \leq -37)$. When $\Delta_j = 0.01$, most mass of v_j is below -37 where the likelihood cannot be computed numerically. Thus, the unfortunate fact is that one cannot use too small partitioning interval to get a good approximation of the posterior.

4. EXAMPLE

In this section we analyze the leukemia remission data, which was analyzed by many researchers including Cox (1972) and Laud *et al.* (1998). Total 42 leukemia patients are divided into two groups – control and treatment groups. Placebo and 6-mercaptopurine (6-MP) are given to the control and the treatment groups, respectively. The goal of the analysis is to see the effect of 6-MP to the remission time of leukemia patients. The proportional hazard model is assumed

TABLE 4.1 *Posterior mean and 90% credible sets for* β

Δ_j	c_{1j}	c_{2j}	$\hat{\beta}$	90% $C.I$
1	0.8	1.2	1.699	(1.27 , 2.14)
0.5	0.4	1.6	1.668	(1.28 , 2.09)
0.2	0.16	1.84	1.651	(1.23 , 2.10)
0.1	0.08	1.92	1.638	(1.20 , 2.07)
0.05	0.04	1.96	1.642	(1.22 , 2.07)
0.01	0.008	1.992	1.643	(1.22 , 2.09)



(a) $\Delta_j = 1$ (b) $\Delta_j = 0.5$

(c) $\Delta_j = 0.2$ (d) $\Delta_j = 0.1$

(e) $\Delta_j = 0.05$ (f) $\Delta_j = 0.01$

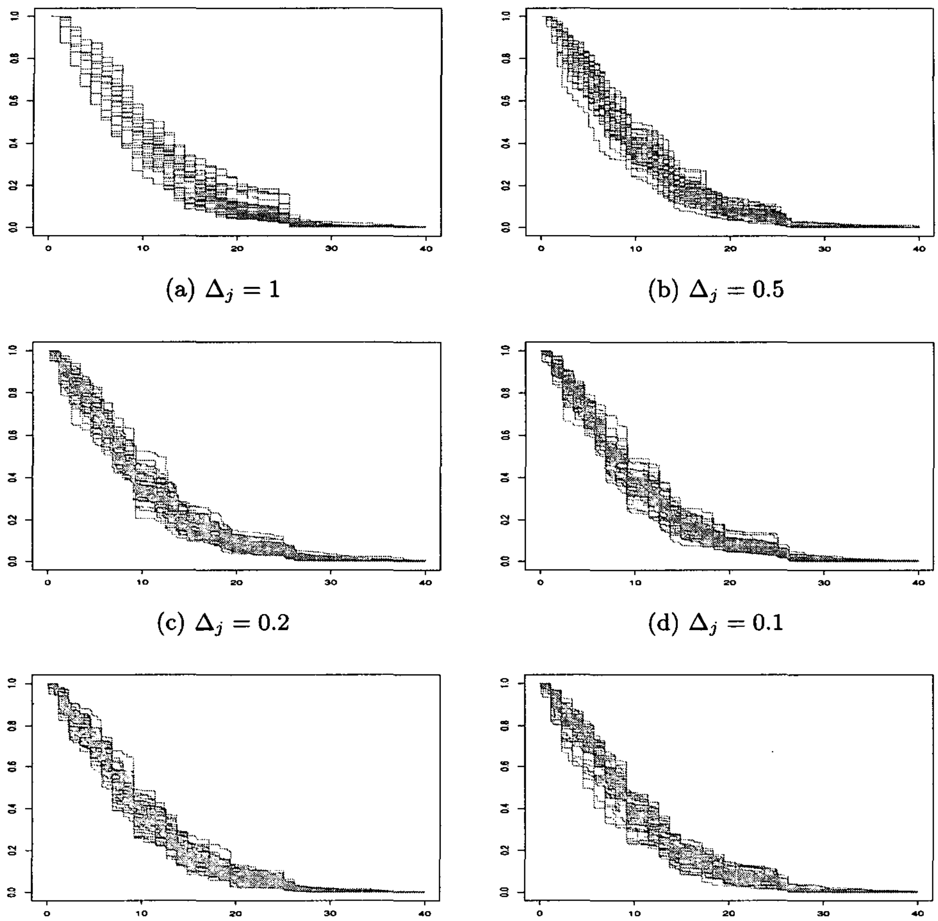
FIGURE 4.1 *Pointwise 90% credible sets of the cumulative hazard function A for different values of* Δ_j.

and we choose the prior

$$\begin{aligned} A(t) &\sim \mathrm{BP}(c(t) = 2, A_0(t) = 0.4t), \\ \beta &\sim N(0, \sigma^2 = 10^4). \end{aligned}$$

The prior for the approximated binomial model is thus

$$\begin{aligned} \Delta A_j &\sim \mathrm{Beta}(c_{1j} = 0.8\Delta A_j,\ \ c_{2j} = 2(1 - 0.4\Delta A_j)),\ \ j = 1, \ldots, k, \\ \beta &\sim N(0, \sigma^2 = 10^4). \end{aligned}$$



(a) $\Delta_j = 1$ (b) $\Delta_j = 0.5$

(c) $\Delta_j = 0.2$ (d) $\Delta_j = 0.1$

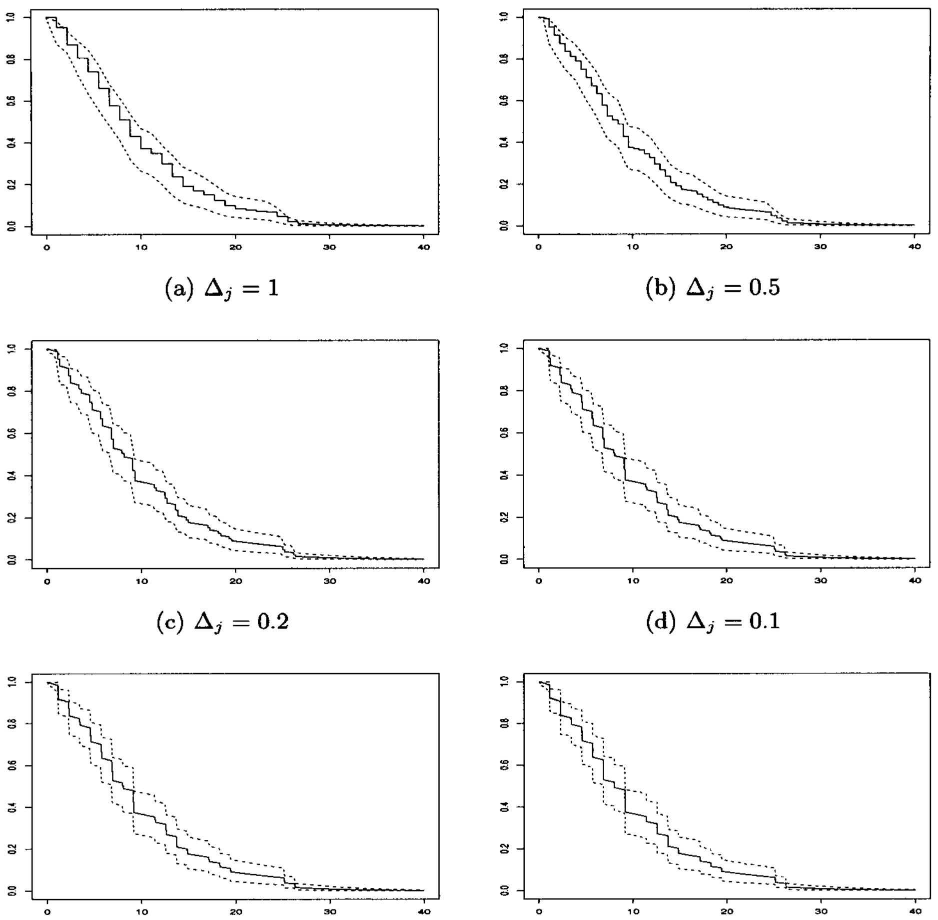
(e) $\Delta_j = 0.05$ (f) $\Delta_j = 0.01$

FIGURE 4.2 *Posterior samples of the survival function $S(t)$ for different values of Δ_j.*

We compute the posterior for different values of $\Delta_j = s_j - s_{j-1} = 1$, 0.5, 0.2, 0.1, 0.05 and 0.01. In actual implementation of the posterior computation, we used WinBUGS, which is the strong merit of this approximation. Generally there is no problem fitting the model (2.2), except the fact that the distribution of v_j is nonstandard. This problem can be overcome by approximating the distribution of v_j over the range $[-37, 50]$ with a discrete distribution.

The model specification procedure in WinBUGS for the proportional hazard model can be summarized as follows

- Specify approximate likelihood



(a) $\Delta_j = 1$ (b) $\Delta_j = 0.5$

(c) $\Delta_j = 0.2$ (d) $\Delta_j = 0.1$

(e) $\Delta_j = 0.05$ (f) $\Delta_j = 0.01$

FIGURE 4.3 *Pointwise 90% credible sets of the survival function $S(t)$ for different values of Δ_j.*

1. $\Delta N_{ij} \overset{\text{indep.}}{\sim} Binomial(Y_{ij}, p_{ij})$ for $j = 1, \ldots, k$, $i = 1, \ldots, n$,
2. $\log(-\log(1 - p_{ij})) = \beta^T z_i + v_j$.

- Specify prior for ΔA_j by approximate v_j for $j = 1, \ldots, k$

  1. Choose v_j from $\{a_0, a_1, \ldots, a_m\}$ with probability,

  $$Pr(v_j = a_l) = \int_{a_{l-1}}^{a_l} f(v_j | c_{1j}, c_{2j})\, dv_j,$$

  2. Set $\Delta A_j = 1 - e^{-\exp(v_j)}$.

- Specify prior for $\beta \sim \pi(\beta)$.

We calculated v and $Pr(v_j = v)$ for each Δ_j and employed $\pi(\beta)$ as the normal prior with mean 0 and standard deviation 100. The MCMC was run in WinBUGS for a total of 6000 iterations, the first 1000 iterations are discarded as burn-in, the 5000 samples are used for the analysis. Table 4.1 shows the posterior mean and 90% credible sets for the coefficient β for each Δ_j. Overall the posteriors of β are similar to those obtained by the ϵ-approximation method in Lee and Kim (2004). But as we expected, as the length of the partitioning interval Δ_j gets smaller, the posterior mean of β tends closer to 1.63, the posterior mean obtained from the ϵ-approximation method. Although it is subjective to say how close is good enough, we feel that the relative error of 4.2%, when $\Delta_j = 1$, can be considered large and we recommend to use smaller Δ_j. But, as we discussed in the previous section, too smaller value of Δ_j causes a numerical problem in calculating the likelihood. Thus, in practice, one needs to be careful to balance between the accuracy of the approximation and the numerical accuracy. Figure 4.1–4.3 show the plots of the credible sets and posterior sample of the *c.h.f.* and survival function. For a large value of Δ_j, the plots show the effect of discrete approximation which disappears as Δ_j gets smaller.

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