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■ ABSTRACT: In this paper, we present a Bayesian analysis of mixture models for survival data in the presence of one covariate, and type II censoring data. Considering Gibbs with Metropolis-Hastings algorithms, we get Monte Carlo estimates for the posterior quantities of interest, assuming different choices for the densities in the mixture model. We also present some considerations on model selection and we introduce a numerical example, to illustrate the proposed methodology.

■ KEYWORDS: Mixture models, regression analysis, Bayesian analysis, Gibbs samples, Metropolis-Hastings algorithm.

1. Introduction

The use of mixture models has been considered in the literature as an alternative to nonparametric methods to analyse survival data, since in many applications, the usual parametrical models (see for example, Cox and Oakes, 1984) could not be appropriate for the data set. These data could be observed when a group of subjects may not react to treatments (see for example, Farewell, 1982; or Kuo and Peng, 1995).

Considering the introduction of a covariate vector $\underset{\sim}{x}$ which may influence both the incidence probabilities and the conditional latency distributions, the mixture model (see for example, Kuo and Peng, 1995) assumes the density.

$$f(t \mid \underset{\sim}{x}, \underset{\sim}{\theta}) = \sum_{j=1}^{J} P(Y = j \mid \underset{\sim}{x}, \underset{\sim}{\gamma})\; f_j(t \mid Y = j, \underset{\sim}{x}, \underset{\sim}{\beta_j}) \tag{1}$$

where T is the lifetime of an individual and $\underset{\sim}{\theta} = (\underset{\sim}{\beta_1}, \underset{\sim}{\beta_2}, \ldots, \underset{\sim}{\beta_J}, \underset{\sim}{\gamma})$ is the vector of all unknown parameters.

The probabilities $P(Y = j \mid \underset{\sim}{x}, \underset{\sim}{\gamma})$, assumes that $\sum_{j=1}^{J} P(j \mid \underset{\sim}{x}, \underset{\sim}{\gamma}) = 1$, where $\underset{\sim}{\gamma}$ is the vector of parameters in the incidence probabilities.

Logistic regression links could be considered for the incidence probabilities, that is,

$$P(j \mid \underset{\sim}{x}, \underset{\sim}{\gamma}) = \frac{e^{\underset{\sim}{x}'\underset{\sim}{\gamma}_j}}{\sum_{j=1}^{J} e^{\underset{\sim}{x}'\underset{\sim}{\gamma}_j}} \tag{2}$$

The cumulative distribution function for T, derived from (1), is given by

$$F(t \mid \underset{\sim}{x}, \underset{\sim}{\theta}) = \sum_{j=1}^{J} P(Y = j \mid \underset{\sim}{x}, \underset{\sim}{\gamma}) \; F_j(t \mid \underset{\sim}{x}, \underset{\sim}{\beta}_j) \tag{3}$$

where F_j is the distribution function for f_j.

Classical inference methods for mixture models based on the maximum likelihood estimators could be difficult to obtain, even for simple cases considering $J = 2$ mixture distributions (see for example, Titterington et al, 1985).

A suitable way to analyse survival data with mixture models, is to consider Bayesian methods based on Gibbs sampling with Metropolis-Hastings algorithms (see for example, Smith and Roberts, 1993; or Robert, 1996). These Markov Chain Monte Carlo (MCMC) methods has been explored in the literature considering censored or uncensored observations (see for example, Diebolt and Robert, 1994; or Kuo and Peng, 1995).

In this paper, considering type II censored survival data, we develop a Bayesian analysis for mixture distributions considering some special choices for f_j, $j =$ 1,2 in (1).

We illustrate the proposed methodology and discuss some computational aspects of the implementation of the MCMC algorithms considering one simulated data set. We also consider the discrimination of the best model for a data set using Monte Carlo estimates for the predictive densities.

2. A Bayesian analysis for the model

Let us consider a type II censoring mechanism, that is, the experiment terminates when we observe r_i failures for each level of a covariate x_i, $i = 1, 2, ..., k$. Thus, with n_i units at the beginning of each test with covariate level x_i, we have the ordered uncensored observations given by t_{1i}, t_{2i},..., $t_{r_i i}$ and $n_i - r_i$ censored observations equal to $t_{r_i i}$, $i = 1, 2, ..., k$. Observe that $r_i = n_i$ when there is not censored observations.

The likelihood function for $\underset{\sim}{\theta}$ considering the data under covariate level x_i, is given by,

$$L(\underset{\sim}{\theta} \mid \underset{\sim}{t}, \underset{\sim}{x}) = \prod_{l=1}^{r_i} f(t_{li} \mid \underset{\sim}{x}, \underset{\sim}{\theta}) \; S^{n_i - r_i}(t_{r_i i} \mid \underset{\sim}{x}, \underset{\sim}{\theta}) \tag{4}$$

where $S(t_{r_i i} \mid \underset{\sim}{x}, \underset{\sim}{\theta}) = 1 - F(t_{r_i i} \mid \underset{\sim}{x}, \underset{\sim}{\theta})$ is the survival function at time $t_{r_i i}$.

Considering the data of k covariate levels x_1, x_2,...,x_k taken at random, the likelihood function for $\underset{\sim}{\theta}$ is given by

$$L(\underset{\sim}{\theta} \mid \underset{\sim}{t}, \underset{\sim}{x}) = \prod_{i=1}^{k} \prod_{l=1}^{r_i} f(t_{li} \mid \underset{\sim}{x}, \underset{\sim}{\theta}) \, S^{n_i - r_i}(t_{r_i i} \mid \underset{\sim}{x}, \underset{\sim}{\theta}) \tag{5}$$

where $f(t_{li} \mid \underset{\sim}{x}, \underset{\sim}{\theta})$ is the mixture distribution (1).

Considering the special case $J = 2$ and assuming a prior density $\pi(\underset{\sim}{\theta})$, the joint posterior density for $\underset{\sim}{\theta}$ is given by,

$$\pi(\underset{\sim}{\theta} \mid \underset{\sim}{t}, \underset{\sim}{x}) \propto \pi(\underset{\sim}{\theta}) \left\{ \prod_{i=1}^{k} \prod_{l=1}^{r_i} f(t_{li} \mid \underset{\sim}{x}, \underset{\sim}{\theta}) \, S^{n_i - r_i}(t_{r_i i} \mid \underset{\sim}{x}, \underset{\sim}{\theta}) \right\} \tag{6}$$

where $f(t_{li} \mid \underset{\sim}{x}, \underset{\sim}{\theta}) = \sum_{j=1}^{2} P(Y = j \mid \underset{\sim}{x}, \underset{\sim}{\gamma}) \, f_j(t_{li} \mid Y = j, \underset{\sim}{x}, \underset{\sim}{\beta_j})$,

and $S(t_{r_i i} \mid \underset{\sim}{x}, \underset{\sim}{\theta}) = 1 - \sum_{j=1}^{2} P(Y = j \mid \underset{\sim}{x}, \underset{\sim}{\gamma}) \, F_j(t_{r_i i} \mid \underset{\sim}{x}, \underset{\sim}{\beta_j})$.

To get better performance for the Gibbs sampling algorithm (see for example, Gelfand and Smith, 1990) and to simplify the conditional distributions needed for the Gibbs sampling algorithm, we introduce latent variables (data augmentation technique; see for example, Tanner and Wong, 1987) and the use of the EM algorithm (see Dempster, Laird and Rubin, 1977) that allow us to consider a likelihood of a product of components model for *i.i.d.* observations as opposed to the mixture likelihood and censored observations. This is given by augmenting the original data with two classes of latent variables: one is the truncated random variable W and other is the index variable denoted by Z that covert the mixture model to a model of independent components (see for example, Kuo and Peng, 1995).

For each right censored observation at time $t_{r_i i}$, $i = 1, 2, \ldots, k$, generate a latent variable w_i from the truncated density

$$f(w_i) / \left[1 - F(t_{r_i i})\right], \; w_i > t_{r_i i} \text{ by setting,}$$

$$w_i = F^{-1}\{F(t_{r_i i} \mid x_i, \underset{\sim}{\theta}) + U\left[1 - F(t_{r_i i} \mid x_i, \underset{\sim}{\theta})\right]\} \tag{7}$$

where $U \sim U(0, 1)$ (a uniform distribution) and F^{-1} is the inverse function of F. Therefore, for each fixed level x_i, $i = 1, 2, \ldots, k$, we have a random sample $w_{l1}, w_{l2}, \ldots, w_{ln_i}$, where $w_{li} = t_{li}$ if the l^{th} observation is uncensored.

In this case, the likelihood function for $\underset{\sim}{\theta}$ is given by

$$L(\underset{\sim}{\theta} \mid \underset{\sim}{t}, \underset{\sim}{x}) = \prod_{i=1}^{k} \prod_{l=1}^{r_i} f(w_{li} \mid \underset{\sim}{x}, \underset{\sim}{\theta}) \tag{8}$$

where $f(w_{li} \mid \underset{\sim}{x}, \underset{\sim}{\theta}) = \sum_{j=1}^{2} P(Y = j \mid \underset{\sim}{x}, \underset{\sim}{\gamma}) \, f_j(w_{li} \mid Y = j, \underset{\sim}{x}, \underset{\sim}{\beta_j})$.

The other class of latent variable is given by $\underset{\sim}{z_{li}} = (z_{li1}, z_{li2})$, i = 1,2,...,$k$; $l = 1, 2, ... n_i$, where $z_{li1} \mid \underset{\sim}{\theta}, w_{li}, x_i \sim b(1, h_{li1})$ (a Bernoulli distribution) with h_{li1} given by

$$h_{li1} = \frac{P(1 \mid x_i, \underset{\sim}{\gamma})\ f_1(w_{li} \mid x_i, \underset{\sim}{\beta_1})}{\sum_{j=1}^{2} P(j \mid x_i, \underset{\sim}{\gamma})\ f_j(w_{li} \mid x_i, \underset{\sim}{\beta_j})} \tag{9}$$

That is,

$$\pi(\underset{\sim}{z_i}) \propto h_{l,1}^{z_{li1}} (1 - h_{li1})^{z_{li2}} \tag{10}$$

where $z_{li1} = 1$ with probability h_{li1} ($z_{li1} = 0$ with probability 1-h_{li1}). Observe that $z_{li1}+z_{li2}=1$.

Thus,

$$\pi(\underset{\sim}{z_{l1}}, \ldots, \underset{\sim}{z_{lk}}) \propto \frac{\prod_{i=1}^{k} \prod_{l=1}^{n_i} \prod_{j=1}^{2} \left\{P(j \mid x_i, \underset{\sim}{\gamma})\ f_j(w_{li} \mid x_i, \underset{\sim}{\beta_j})\right\}^{z_{lij}}}{\prod_{i=1}^{k} \prod_{l=1}^{n_i} \left\{\sum_{j=1}^{2} P(j \mid x_i, \underset{\sim}{\gamma})\ f_j(w_{li} \mid x_i, \underset{\sim}{\beta_j})\right\}} \tag{11}$$

Combining (11) with (8), and considering a prior density $\pi(\underset{\sim}{\theta})$, the joint posterior density for $\underset{\sim}{\theta}$ is given by

$$\pi(\underset{\sim}{\theta} \mid \underset{\sim}{w}, \underset{\sim}{z}, \underset{\sim}{x}) \propto \pi(\underset{\sim}{\theta}) \left\{ \prod_{i=1}^{k} \prod_{l=1}^{n_i} \prod_{j=1}^{2} \left\{P(j \mid x_i, \underset{\sim}{\gamma})\ f_j(w_{li} \mid x_i, \underset{\sim}{\beta_j})\right\}^{z_{lij}} \right\} \tag{12}$$

To generate samples of the joint posterior distribution (12), we use the Gibbs sampling algorithm. Starting with initial values $\underset{\sim}{\theta}^{(0)} = (\theta_1^{(0)}, \ldots, \theta_p^{(0)})$, follow the steps:

(i) Generate samples $\underset{\sim}{w_i}^{(1)} = (\underset{\sim}{w_{l1}}^{(1)}, \underset{\sim}{w_{l2}}^{(1)}, \ldots, \underset{\sim}{w_{ln_i}}^{(1)})$, $i = 1, 2, \ldots, k$ from (7).
(i) Generate samples $\underset{\sim}{z_i}^{(1)} = (\underset{\sim}{z}_{l1}^{(1)}, \underset{\sim}{z}_{l2}^{(1)}, \ldots, \underset{\sim}{z}_{ln_i}^{(1)})$, $i = 1, 2, \ldots, k$ from (10).
(ii) Generate a sample of $\underset{\sim}{\theta}$, from the conditional distributions
$\pi(\theta_1 \mid \theta_2^{(0)}, \ldots, \theta_p^{(0)}, \underset{\sim}{z}^{(1)}, \underset{\sim}{w}^{(1)}, \underset{\sim}{x}), \pi(\theta_2 \mid \theta_1^{(1)}, \theta_3^{(0)} \ldots, \theta_p^{(0)}, \underset{\sim}{z}^{(1)}, \underset{\sim}{w}^{(1)}, \underset{\sim}{x}), \ldots,$
$\pi(\theta_p \mid \theta_1^{(1)}, \ldots, \theta_{p-1}^{(1)}, \underset{\sim}{z}^{(1)}, \underset{\sim}{w}^{(1)}, \underset{\sim}{x})$.

Then, continue iteration by repeating steps (i), (ii) and (iii).

3. A normal - exponential mixture model

Let us assume a mixture of normal- exponential distributions in (1) , one covariate x and the logistic regression link (2) ; that is,

$$f_1\left(t_i \mid x_i, \underset{\sim}{\beta_1}\right) = \frac{1}{\sqrt{2\pi}\,\sigma}\, exp\{ -\frac{1}{2\sigma^2}\left(t_i - \alpha_1 - \beta_1 x_i\right)^2 \},$$
$$\underset{\sim}{\beta_1} = (\alpha_1, \beta_1, \sigma),\ f_2\left(t_i \mid x_i, \underset{\sim}{\beta_2}\right) = \lambda_i\, exp\{ -\lambda_i t_i\}, \tag{14}$$

where $\lambda_i = (\alpha_2 + \beta_2 x_i)^{-1}$, $\underset{\sim}{\beta_2} = (\alpha_2, \beta_2)$,

$$P\left(1 \mid x_i, \underset{\sim}{\gamma}\right) = \frac{e^{\gamma + \tau x_i}}{1 + e^{\gamma + \tau x_i}} \quad , \underset{\sim}{\gamma} = (\gamma, \tau) \text{ and}$$
$$P\left(2 \mid x_i, \underset{\sim}{\gamma}\right) = 1 - P\left(1 \setminus x_i, \underset{\sim}{\gamma}\right) = \frac{1}{1 + e^{\gamma + \tau x_i}} \quad , i = 1, 2, \ldots, n.$$

Assuming prior independence among the parameters, consider the following prior densities for $\alpha_1, \beta_1, \sigma, \alpha_2, \beta_2, \gamma, \tau$:

(i) $\alpha_1, \beta_1, \sigma, \alpha_2, \beta_2$ locally uniform,

(ii) $\gamma \sim N(\gamma_0,\ s_1^2)$, $\gamma_0,\ s_1^2$ known, (15)

(iii) $\tau \sim N(\tau_0,\ s_2^2)$, $\tau_0,\ s_2^2$ known

where $N(a,b)$ denotes a normal distribution with mean a and variance b.

The joint posterior density (12) for $\underset{\sim}{\theta} = (\alpha_1, \beta_1, \sigma, \alpha_2, \beta_2, \gamma, \tau)$ is given by,

$$\pi(\underset{\sim}{\theta} \mid \underset{\sim}{w}, \underset{\sim}{z}, \underset{\sim}{x}) \propto \frac{\left\{\prod_{i=1}^{k} \prod_{l=1}^{n_i} (\alpha_2 + \beta_2 x_i)^{-z_{li2}}\right\}}{\left\{\prod_{i=1}^{k} \prod_{l=1}^{n_i} (1 + e^{\gamma + \tau x_i})\right\}} \frac{e^{\gamma r + \tau a_1}}{\sigma^r}$$
$$exp\left\{-\frac{1}{2\, s_1^2}(\gamma - \gamma_0)^2 - \frac{1}{2\, s_2^2}(\tau - \tau_0)^2\right\}$$
$$\left\{exp\left\{ -\frac{1}{2\sigma^2}\sum_{i=1}^{k}\sum_{l=1}^{n_i} z_{li1}\left(w_{li} - \alpha_1 - \beta_1 x_i\right)^2 - \sum_{i=1}^{k}\sum_{l=1}^{n_i} z_{li2} w_{li}\left(\alpha_2 + \beta_2 x_i\right)^{-1}\right\}\right\} \tag{16}$$

where $r = \sum_{i=1}^{k}\sum_{l=1}^{n_i} z_{li1}$, $n - r = \sum_{i=1}^{k}\sum_{l=1}^{n_i} z_{li2}$ and $a_1 = \sum_{i=1}^{k}\sum_{l=1}^{n_i} x_i z_{li1}$.

To generate samples of the joint posterior distribution (16), we use steps (i), (ii) and (iii) of the Gibbs algorithm (13), where the conditional distributions for the parameters are given by,

$$\text{(i)}\ \pi(v \mid \alpha_1, \beta_1, \alpha_2, \beta_2, \gamma, \tau, \underset{\sim}{z}, \underset{\sim}{w}, \underset{\sim}{x}) \sim \Gamma\left(\frac{r}{2}+1, \frac{\sum_{i=1}^{k}\sum_{l=1}^{n_i} z_{li1}(w_{li}-\alpha_1-\beta_1 x_i)^2}{2}\right)$$

where $v = \sigma^{-2}$

$$\text{(ii)}\ \pi(\alpha_1 \mid \beta_1, \sigma, \alpha_2, \beta_2, \gamma, \tau, \underset{\sim}{z}, \underset{\sim}{w}, \underset{\sim}{x}) \sim N\left(\frac{\sum_{i=1}^{k}\sum_{l=1}^{n_i} z_{li1}(w_{li}-\beta_1 x_i)}{r}, \frac{\sigma^2}{r}\right)$$

$$\text{(iii)}\ \pi(\beta_1 \mid \alpha_1, \sigma, \alpha_2, \beta_2, \gamma, \tau, \underset{\sim}{z}, \underset{\sim}{w}, \underset{\sim}{x}) \sim N\left(\frac{\sum_{i=1}^{k}\sum_{l=1}^{n_i} z_{li1} x_i(w_{li}-\alpha_1)}{\sum_{i=1}^{k}\sum_{l=1}^{n_i} z_{li1} x_i^2}, \frac{\sigma^2}{\sum_{i=1}^{k}\sum_{l=1}^{n_i} z_{li1} x_i^2}\right) \quad (17)$$

$$\text{(iv)}\ \pi(\alpha_2 \mid \alpha_1, \beta_1, \sigma, \beta_2, \gamma, \tau, \underset{\sim}{z}, \underset{\sim}{w}, \underset{\sim}{x}) \propto \alpha_2^{-(n-r)} exp\left\{-\frac{1}{\alpha_2}\sum_{i=1}^{k}\sum_{l=1}^{n_i} z_{li2} w_{li}\left(1+\frac{\beta_2}{\alpha_2}x_i\right)^{-1}\right\}\Psi_1(\underset{\sim}{\theta}),$$

$$\text{where } \Psi_1(\underset{\sim}{\theta}) = \prod_{i=1}^{k}\prod_{l=1}^{n_i}\left(1+\frac{\beta_2}{\alpha_2}x_i\right)^{-z_{li2}},$$

$$\text{(v)}\ \pi(\beta_2 \mid \alpha_1, \beta_1, \sigma, \alpha_2, \gamma, \tau, \underset{\sim}{z}, \underset{\sim}{w}, \underset{\sim}{x}) \propto \beta_2^{-(n-r)} exp\left\{-\frac{1}{\beta_2}\sum_{i=1}^{k}\sum_{l=1}^{n_i} z_{li2} w_{li}\left(\frac{\alpha_2}{\beta_2}+x_i\right)^{-1}\right\}\Psi_2(\underset{\sim}{\theta}),$$

$$\text{where } \Psi_2(\underset{\sim}{\theta}) = \prod_{i=1}^{k}\prod_{l=1}^{n_i}\left(\frac{\alpha_2}{\beta_2}+x_i\right)^{-z_{li2}}$$

$$\text{(vi)}\ \pi(\gamma \mid \alpha_1, \beta_1, \sigma, \alpha_2, \beta_2, \tau, \underset{\sim}{z}, \underset{\sim}{w}, \underset{\sim}{x}) \propto exp\left\{-\frac{1}{2\,s_1^2}(\gamma-\gamma_0)^2\right\}\Psi_3(\underset{\sim}{\theta}),$$

$$\text{where } \Psi_3(\underset{\sim}{\theta}) = exp\left\{\gamma r - \sum_{i=1}^{k}\sum_{l=1}^{n_i} ln(1+e^{\gamma+\tau x_i})\right\}$$

$$\text{(vii)}\ \pi(\tau \mid \alpha_1, \beta_1, \sigma, \alpha_2, \beta_2, \gamma, \underset{\sim}{z}, \underset{\sim}{w}, \underset{\sim}{x}) \propto exp\left\{-\frac{1}{2\,s_2^2}(\tau-\tau_0)^2\right\}\Psi_4(\underset{\sim}{\theta}),$$

$$\text{where } \Psi_4(\underset{\sim}{\theta}) = exp\left\{\tau a_1 - \sum_{i=1}^{k}\sum_{l=1} ln(1+e^{\gamma+\tau x_i})\right\}.$$

Here, $\Gamma(a,b)$ denotes a gamma distribution with mean $\frac{a}{b}$ and variance $\frac{a}{b^2}$.

Observe that, we need to use the Metropolis-Hastings algorithm to generate the variables α_2, β_2, γ and τ. In this way, we could generate candidates for the variables α_2 and β_2 from inverse gamma distributions and candidates for the variables γ and τ from the normal distributions $N(\gamma_i, s_1^2)$ and $N(\tau_i, s_2^2)$, respectively.

4. A normal-normal mixture model

Considering now, the normal- normal mixture in (1), with densities,

$$f_1(t_i \mid x_i, \underset{\sim}{\beta_1}) = \frac{1}{\sqrt{2\pi}\,\sigma_1} exp\left\{-\frac{1}{2\sigma_1^2}(t_i - \alpha_1 - \beta_1 x_i)^2\right\},$$

$\underset{\sim}{\beta_1} = (\alpha_1, \beta_1, \sigma_1)$, and

$$f_2(t_i \mid x_i, \underset{\sim}{\beta_2}) = \frac{1}{\sqrt{2\pi}\,\sigma_2} exp\left\{-\frac{1}{2\sigma_2^2}(t_i - \alpha_2 - \beta_2 x_i)^2\right\},$$

$\underset{\sim}{\beta_2} = (\alpha_2, \beta_2, \sigma_2)$ and the same logistic regression links given in (14), assume the following prior densities for $\alpha_1, \beta_1, \sigma_1, \alpha_2, \beta_2, \sigma_2, \gamma$ and τ:

(i) $\alpha_1, \beta_1, \sigma_1, \alpha_2, \beta_2, \sigma_2$ locally uniform,

(ii) $\gamma \sim N(\gamma_0, s_1^2)$, γ_0, s_1^2 known, (18)

(iii) $\tau \sim N(\tau_0, s_2^2)$, τ_0, s_2^2 known

We also assume independence among the parameters.

From (12), we obtain the joint posterior density for $\underset{\sim}{\theta} = (\alpha_1, \beta_1, \sigma_1, \alpha_2, \beta_2, \sigma_2, \gamma, \tau)$,

$$\pi(\underset{\sim}{\theta} \mid \underset{\sim}{w}, \underset{\sim}{z}, \underset{\sim}{x}) \propto \frac{\sigma_1^{-r}\,\sigma_2^{-(n-r)}}{\left\{\prod_{i=1}^{k}\prod_{l=1}^{n_i}(1+e^{\gamma+\tau x_i})\right\}}$$

$$exp\left\{-\frac{1}{2 s_1^2}(\gamma - \gamma_0)^2 + \gamma r - \frac{1}{2 s_2^2}(\tau - \tau_0)^2 + \tau a_1\right\} \tag{19}$$

$$\left\{exp\left\{-\frac{1}{2\sigma_1^2}\sum_{i=1}^{k}\sum_{l=1}^{n_i} z_{li1}(w_{li} - \alpha_1 - \beta_1 x_i)^2 - \frac{1}{2\sigma_2^2}\sum_{i=1}^{k}\sum_{l=1}^{n_i} z_{li2}(w_{li} - \alpha_2 - \beta_2 x_i)^2\right\}\right\}$$

where r, $n - r$ and a_1 are defined in (16).

The conditional distributions for the Gibbs sampling algorithm are given by,

(i) $\pi(v \mid \alpha_1, \beta_1, \alpha_2, \beta_2, \sigma_2, \gamma, \tau, \underset{\sim}{z}, \underset{\sim}{w}, \underset{\sim}{x}) \sim \Gamma\left(\frac{r}{2} + 1, \frac{\sum_{i=1}^{k}\sum_{l=1}^{n_i} z_{li1}(w_{li} - \alpha_1 - \beta_1 x_i)^2}{2}\right)$.

where $v = \sigma_1^{-2}$

(ii) $\pi(\alpha_1 \mid \beta_1, \sigma_1, \alpha_2, \beta_2, \sigma_2, \gamma, \tau, \underset{\sim}{z}, \underset{\sim}{w}, \underset{\sim}{x}) \sim N\left(\frac{\sum_{i=1}^{k}\sum_{l=1}^{n_i} z_{li1}(w_{li} - \beta_1 x_i)}{r}, \frac{\sigma_1^2}{r}\right)$

$$\text{(iii)}\ \pi(\beta_1 \mid \alpha_1, \sigma_1, \alpha_2, \beta_2, \sigma_2, \gamma, \tau, \underset{\sim}{z}, \underset{\sim}{w}, \underset{\sim}{x}) \sim N\left(\frac{\sum_{i=1}^{k}\sum_{l=1}^{n_i} z_{li1} x_i (w_{li}-\alpha_1)}{\sum_{i=1}^{k}\sum_{l=1}^{n_i} z_{li1} x_i^2}, \frac{\sigma_1^2}{\sum_{i=1}^{k}\sum_{l=1}^{n_i} z_{li1} x_i^2} \right) \qquad (20)$$

$$\text{(iv)}\ \pi(u \mid \alpha_1, \beta_1, \sigma_1, \alpha_2, \beta_2, \gamma, \tau, \underset{\sim}{z}, \underset{\sim}{w}, \underset{\sim}{x}) \sim \Gamma\left(\frac{(n-r)}{2} + 1, \frac{\sum_{i=1}^{k}\sum_{l=1}^{n_i} z_{li2} (w_{li}-\alpha_2-\beta_2 x_i)^2}{2} \right)$$

where $u = \sigma_2^{-2}$

$$\text{(v)}\ \pi(\alpha_2 \mid \alpha_1, \beta_1, \sigma_1, \beta_2, \sigma_2, \gamma, \tau, \underset{\sim}{z}, \underset{\sim}{w}, \underset{\sim}{x}) \sim N\left(\frac{\sum_{i=1}^{k}\sum_{l=1}^{n_i} z_{li2} (w_{li}-\beta_2 x_i)}{(n-r)}, \frac{\sigma_2^2}{(n-r)} \right)$$

$$\text{(v)}\ \pi(\beta_2 \mid \alpha_1, \beta_1, \sigma_1, \alpha_2, \sigma_2, \gamma, \tau, \underset{\sim}{z}, \underset{\sim}{w}, \underset{\sim}{x}) \sim N\left(\frac{\sum_{i=1}^{k}\sum_{l=1}^{n_i} z_{li2} x_i (w_{li}-\alpha_2)}{\sum_{i=1}^{k}\sum_{l=1}^{n_i} z_{li2} x_i^2}, \frac{\sigma_2^2}{\sum_{i=1}^{k}\sum_{l=1}^{n_i} z_{li2} x_i^2} \right)$$

$$\text{(vi)}\ \pi(\gamma \mid \alpha_1, \beta_1, \sigma_1, \alpha_2, \beta_2, \sigma_2, \tau, \underset{\sim}{z}, \underset{\sim}{w}, \underset{\sim}{x}) \propto exp\left\{ -\frac{1}{2 s_1^2}(\gamma - \gamma_0)^2 \right\} \Psi_1(\underset{\sim}{\theta}),$$

where $\Psi_1(\underset{\sim}{\theta}) = exp\left\{ \gamma r - \sum_{i=1}^{k}\sum_{l=1}^{n_i} ln(1 + e^{\gamma+\tau x_i}) \right\}$

$$\text{(vii)}\ \pi(\tau \mid \alpha_1, \beta_1, \sigma_1, \alpha_2, \beta_2, \sigma_2, \gamma, \underset{\sim}{z}, \underset{\sim}{w}, \underset{\sim}{x}) \propto exp\left\{ -\frac{1}{2 s_2^2}(\tau - \tau_0)^2 \right\} \Psi_2(\underset{\sim}{\theta}),$$

where $\Psi_2(\underset{\sim}{\theta}) = exp\left\{ \tau a_1 - \sum_{i=1}^{k}\sum_{l=1}^{n_i} ln(1 + e^{\gamma+\tau x_i}) \right\}$.

Observe that the variables γ and τ should be generated using the Metropolis-Hastings algorithm.

5. A gamma-normal mixture model

Consider the gamma-normal mixture in (1), with densities,

$f_1(t_i \mid x_i, \underset{\sim}{\beta_1}) = \frac{1}{\Gamma(\alpha_0)} (\alpha_1+\beta_1 x_i)^{\alpha_0} t_i^{\alpha_0 - 1} exp\{-(\alpha_1 + \beta_1 x_i) t_i\}$,
$\underset{\sim}{\beta_1} = (\alpha_0, \alpha_1, \beta_1)$, and
$f_2(t_i \mid x_i, \underset{\sim}{\beta_2}) = \frac{1}{\sqrt{2\pi}\,\sigma} exp\{-\frac{1}{2\sigma^2}(t_i - \alpha_2 - \beta_2 x_i)^2\}$,

$\underset{\sim}{\beta_2}=(\alpha_2,\ \beta_2,\ \sigma)$ and the same logistic regression links given in (11). Also, assume the following prior densities for α_0, α_1, β_1, α_2, β_2, σ, γ and τ,

(i) α_0, α_1, β_1, α_2, β_2, σ locally uniform,

(ii) $\gamma \sim N(\gamma_0,\ s_1^2)$, γ_0, s_1^2 known, (21)

(iii) $\tau \sim N(\tau_0,\ s_2^2)$, τ_0, s_2^2 known

We further assume independence among the parameters.

From (12), we obtain the joint posterior distribution for $\underset{\sim}{\theta}=(\alpha_0, \alpha_1, \beta_1, \alpha_2, \beta_2, \sigma, \gamma, \tau)$:

$$\pi(\underset{\sim}{\theta} \mid \underset{\sim}{w}, \underset{\sim}{z}, \underset{\sim}{x}) \propto \frac{e^{\gamma r+\tau a_1}}{\sigma^{(n-r)}\{\Gamma(\alpha_0)\}^r\left\{\prod_{i=1}^{k}\prod_{l=1}^{n_i}(1+e^{\gamma+\tau x_i})\right\}}$$
$$exp\left\{-\frac{1}{2\,s_1^2}(\gamma-\gamma_0)^2-\frac{1}{2\,s_2^2}(\tau-\tau_0)^2\right\}$$
$$\left\{\prod_{i=1}^{k}\prod_{l=1}^{n_i}(\alpha_1+\beta_1 x_i)^{\alpha_0 z_{li1}}\right\}\left\{\prod_{i=1}^{k}\prod_{l=1}^{n_i}w_{li}^{z_{li1}(\alpha_0-1)}\right\} \tag{22}$$
$$exp\left\{-\sum_{i=1}^{k}\sum_{l=1}^{n_i}z_{li1}w_{li}(\alpha_1+\beta_1 x_i)^2\right\}exp\left\{-\sum_{i=1}^{k}\sum_{l=1}^{n_i}z_{li2}(w_{li}-\alpha_2-\beta_2 x_i)^2\right\}$$

where r, a_1 and $n-r_i$ are given in (16).

The conditional distributions for the Gibbs sampling algorithm are given by

(i) $\pi(\alpha_0 \mid \alpha_1, \beta_1, \alpha_2, \beta_2, \sigma, \gamma, \tau, \underset{\sim}{z}, \underset{\sim}{w}, \underset{\sim}{x}) \propto \alpha_0^{\sum_{i=1}^{k}\sum_{l=1}^{n_i}z_{li1}}\ exp\left\{-\alpha_0\sum_{i=1}^{k}\sum_{l=1}^{n_i}z_{li1}x_i\right\}\Psi_1(\underset{\sim}{\theta})$,

where $\Psi_1(\underset{\sim}{\theta}) = \dfrac{\left\{\prod_{i=1}^{k}\prod_{l=1}^{n_i}(\alpha_1+\beta_1 x_i)^{\alpha_0 z_{li1}}\right\}\left\{\prod_{i=1}^{k}\prod_{l=1}^{n_i}w_i^{z_{li1}(\alpha_0-1)}\right\}}{\alpha_0^{\sum_{i=1}^{k}\sum_{l=1}^{n_i}z_{li1}}\ exp\left\{-\alpha_0\sum_{i=1}^{k}\sum_{l=1}^{n_i}z_{li1}x_i\right\}\{\Gamma(\alpha_0)\}^r}$

(ii) $\pi(\alpha_1 \mid \alpha_0, \beta_1, \alpha_2, \beta_2, \sigma, \gamma, \tau, \underset{\sim}{z}, \underset{\sim}{w}, \underset{\sim}{x}) \propto \alpha_1^{\alpha_0\sum_{i=1}^{k}\sum_{l=1}^{n_i}z_{li1}}$
$exp\left\{-\alpha_1\sum_{i=1}^{k}\sum_{l=1}^{n_i}z_{li1}w_{li}(1+\frac{\beta_1}{\alpha_1}x_i)\right\}\Psi_2(\underset{\sim}{\theta})$,

where $\Psi_2(\underset{\sim}{\theta}) = \prod_{i=1}^{k}\prod_{l=1}^{n_i}\left(1+\frac{\beta_1}{\alpha_1}x_i\right)^{\alpha_0 z_{li1}}$

(iii) $\pi(\beta_1 \mid \alpha_0, \alpha_1, \alpha_2, \beta_2, \sigma, \gamma, \tau, \underset{\sim}{z}, \underset{\sim}{w}, \underset{\sim}{x}) \propto \beta_1^{\alpha_0\sum_{i=1}^{k}\sum_{l=1}^{n_i}z_{li1}}$
$exp\left\{-\beta_1\sum_{i=1}^{k}\sum_{l=1}^{n_i}z_{li1}w_{li}(\frac{\alpha_1}{\beta_1}+x_i)\right\}\Psi_3(\underset{\sim}{\theta})$,

$$\text{where } \Psi_3(\underset{\sim}{\theta}) = \prod_{i=1}^{k} \prod_{l=1}^{n_i} \left(\frac{\alpha_1}{\beta_1} + x_i \right)^{\alpha_0 z_{li1}} \tag{23}$$

$$\text{(iv) } \pi(v \,|\, \alpha_0,\ \alpha_1, \beta_1,\ \alpha_2, \beta_2,\ \gamma, \tau, \underset{\sim}{z}, \underset{\sim}{w}, \underset{\sim}{x}) \sim \Gamma\left(\frac{(n-r)}{2} + 1,\ \frac{\sum_{i=1}^{k}\sum_{l=1}^{n_i} z_{li2}\,(w_{li} - \alpha_2 - \beta_2 x_i)^2}{2} \right)$$

where $v = \sigma^{-2}$

$$\text{(v) } \pi(\alpha_2 \,|\, \alpha_0,\ \alpha_1, \beta_1, \beta_2,\ \sigma, \gamma, \tau, \underset{\sim}{z}, \underset{\sim}{w}, \underset{\sim}{x}) \sim N\left(\frac{\sum_{i=1}^{k}\sum_{l=1}^{n_i} z_{li2}(w_{li} - \beta_2 x_i)}{(n-r)},\ \frac{\sigma^2}{(n-r)} \right)$$

$$\text{(vi) } \pi(\beta_2 \,|\, \alpha_0, \alpha_1, \beta_1,\ \alpha_2,\ \sigma, \gamma, \tau, \underset{\sim}{z}, \underset{\sim}{w}, \underset{\sim}{x}) \sim N\left(\frac{\sum_{i=1}^{k}\sum_{l=1}^{n_i} z_{li2} x_i (w_{li} - \alpha_2)}{\sum_{i=1}^{k}\sum_{l=1}^{n_i} z_{li2} x_i^2},\ \frac{\sigma^2}{\sum_{i=1}^{k}\sum_{l=1}^{n_i} z_{li2} x_i^2} \right)$$

$$\text{(vii) } \pi(\gamma \,|\, \alpha_0, \alpha_1, \beta_1, \sigma_1, \alpha_2, \beta_2, \sigma, \tau, \underset{\sim}{z}, \underset{\sim}{w}, \underset{\sim}{x}) \propto exp\left\{ -\frac{1}{2\,s_1^2}(\gamma - \gamma_0)^2 \right\} \Psi_4(\underset{\sim}{\theta}),$$

$$\text{where } \Psi_4(\underset{\sim}{\theta}) = \left\{ \gamma r - \sum_{i=1}^{k}\sum_{l=1}^{n_i} ln(\, 1 + e^{\gamma + \tau x_i}) \right\}$$

$$\text{(vii) } \pi(\tau \,|\, \alpha_0, \alpha_1, \beta_1, \sigma_1, \alpha_2, \beta_2, \sigma_2, \gamma, \underset{\sim}{z}, \underset{\sim}{w}, \underset{\sim}{x}) \propto exp\left\{ -\frac{1}{2\,s_2^2}(\tau - \tau_0)^2 \right\} \Psi_5(\underset{\sim}{\theta}),$$

$$\text{where } \Psi_5(\underset{\sim}{\theta}) = exp\left\{ \tau a_1 - \sum_{i=1}^{k}\sum_{l=1}^{n_i} ln(\, 1 + e^{\gamma + \tau x_i}) \right\}.$$

Observe that the variables $\alpha_0, \alpha_1,\ \beta_1, \gamma$ and τ should be generated using the Metropolis-Hastings algorithm.

6. Some considerations on model selection

For model selection, we could use the predictive density for t_i, $i = 1, 2, ..., n$, given $\underset{\sim}{t}_{(i)} = \{t_1, ..., t_{i-1}, t_{i+1}, ..., t_n\}$.

The predictive density for t_i given $\underset{\sim}{t}_{(i)}$ is given by

$$c_i = f(t_i \,|\, t_{(i)}, x_i) = \int f(t_i |\ \underset{\sim}{\theta}, x_i)\, \pi\left(\underset{\sim}{\theta} \,|\, t_{(i)}, x_{(i)} \right) d\underset{\sim}{\theta}\,, \tag{24}$$

where $\pi\left(\underset{\sim}{\theta} \,|\, t_{(i)}, x_{(i)} \right)$ is the posterior density for $\underset{\sim}{\theta}$ given $\underset{\sim}{t}_{(i)}$.

Using the Gibbs samples, (24) can be approximated by its Monte Carlo estimate,

$$\hat{f}\left(t_i \mid t_{(i)}, x_i\right) = \frac{2}{RS} \sum_{r=1}^{R} \sum_{s=\frac{S}{2}+1}^{S} f\left(t_i \mid x_i, \underset{\sim}{\theta}^{(r,s)}\right) \tag{25}$$

where $\underset{\sim}{\theta}^{(r,s)}$ are generated for S iterations in each of R chains considering different initial values for $\underset{\sim}{\theta}$.

We can use $c_i = f\left(t_i \mid t_{(i)}, x_i\right)$ in model selection. In this way, we consider plots of c_i versus $i\,(i = 1, 2, ..., n)$ for different models, large values of c_i (in average) indicates the better model. We also could choose the model such that $c(l) = \prod_{i=1}^{n} c_i(l)$ is maximum (l indexes models).

7. An example

Consider the survival data given in table 1, where we have the lifetimes of $n = 317$ insects receiving four dosages of a toxity. Among the 317 insects, 144, 69, 54 and 50 were sprayed with a insecticide at concentrations of 0.20, 0.32, 0.50 and 0.80 mg/cm^2, respectively. The log-doses (denoted by x) are -1.61, -1.14, -0.69 and -0.22, respectively. For each level of the covariate x_i, $i = 1, ..., 4$, the experiment terminates when we observe $r_1 = 38$, $r_2 = 33$, $r_3 = 34$, $r_4 = 35$ deaths, respectively.

Table 1. Survival times (in hours) of $n = 317$ insects exposed to 4 dosages of a insecticide.

Log-Dosage (x)	Survival Times (t)
x_1=-1.61 $n_1 = 144, r_1 = 38$	12,2(16),5(30),4(36),2(40),3(52),2(60),4(65),70,2(76), 2(80),3(90),2(100),2(110),130,2(140),106(140+)
x_2=-1.14 $n_2 = 69, r_2 = 33$	3(10),2(16),2(20),3(30),3(35),2(40),2(45),4(50),3(56), 2(60),2(65),5(80), 36(80+)
x_3=-0.69 $n_3 = 54, r_3 = 34$	2(10),2(18),20,3(30),2(32),2(40),45,4(50),3(60),2(65), 2(68),5(80),5(85), 20(85+)
x_4=-0.22 $n_4 = 50, r_4 = 35$	2(10),2(18),3(30),3(38),2(40),2(45),2(50),2(60),3(68), 70,4(80),5(86),4(88),15(88+)

(observation with + is censored)

In figure 1, we have the histograms for the uncensored data of table 1. In this figure, we clearly observe a bimodal frequency distribution, indicating the need of mixture distributions of the form (1).

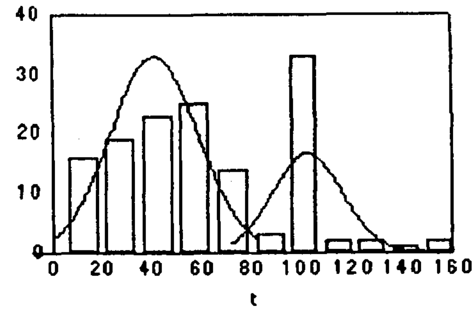


Figure 1. Histograms of Survival Data of Table 1 (140 uncensored observations).

To analyse the survival data of table 1, we assume some mixture distributions (1), with a ligistic regression link: a exponential-normal model, a normal-normal distribution and a normal-gamma distribution.

Considering the exponential-normal mixture model (14), and the prior distributions (15) with $\gamma_0 = 4.04$, $s_1^2 = 0.7$, $\tau_0 = 3.6$, $s_2^2 = 1.1$, we generated 3 separate Gibbs chains each of wich ran for 7000 iterations, and we monitored the convergence of the Gibbs samples using the Gelman and Rubin (1992) method that uses the analysis of variance technique to determine if further iterations are needed. For each parameter we considered the 10^{th}, 20^{th}, 30^{th}, ...iterations, which required a computational time of 37 hours working with the software SAS in a Pentium 166 MHZ. In table 2, we have the obtained posterior summaries for the parameters, and in figure 2 we have the approximate marginal posterior densities considering the $S = 2100$ Gibbs samples. We also have in table 2, the estimated potential scale reductions $\hat{R}$ (see Gelman and Rubin, 1992) for all the parameters. In this case, the considered number of iterations were sufficient for approximate convergence ($\sqrt{\hat{R}} < 1.1$ for all parameters).

Table 2. Posterior Summaries (Exponential-Normal Distribution)

Parameter	Mean	95% Credible Interval	$\hat{R}$
α_1	62.66000	(51.658; 73.514)	1.00049530
β_1	- 5.56100	(-17.838; -0.216)	1.00005074
σ	37.77800	(29.321; 50.367)	1.00132800
α_2	0.00460	(0.0033; 0.0057)	1.00168700
β_2	0.00041	(0.00027; 0.00053)	1.00000000
γ	3.96400	(2.4550; 5.537)	1.00482200
τ	3.64500	(1.665; 5.679)	1.00079900

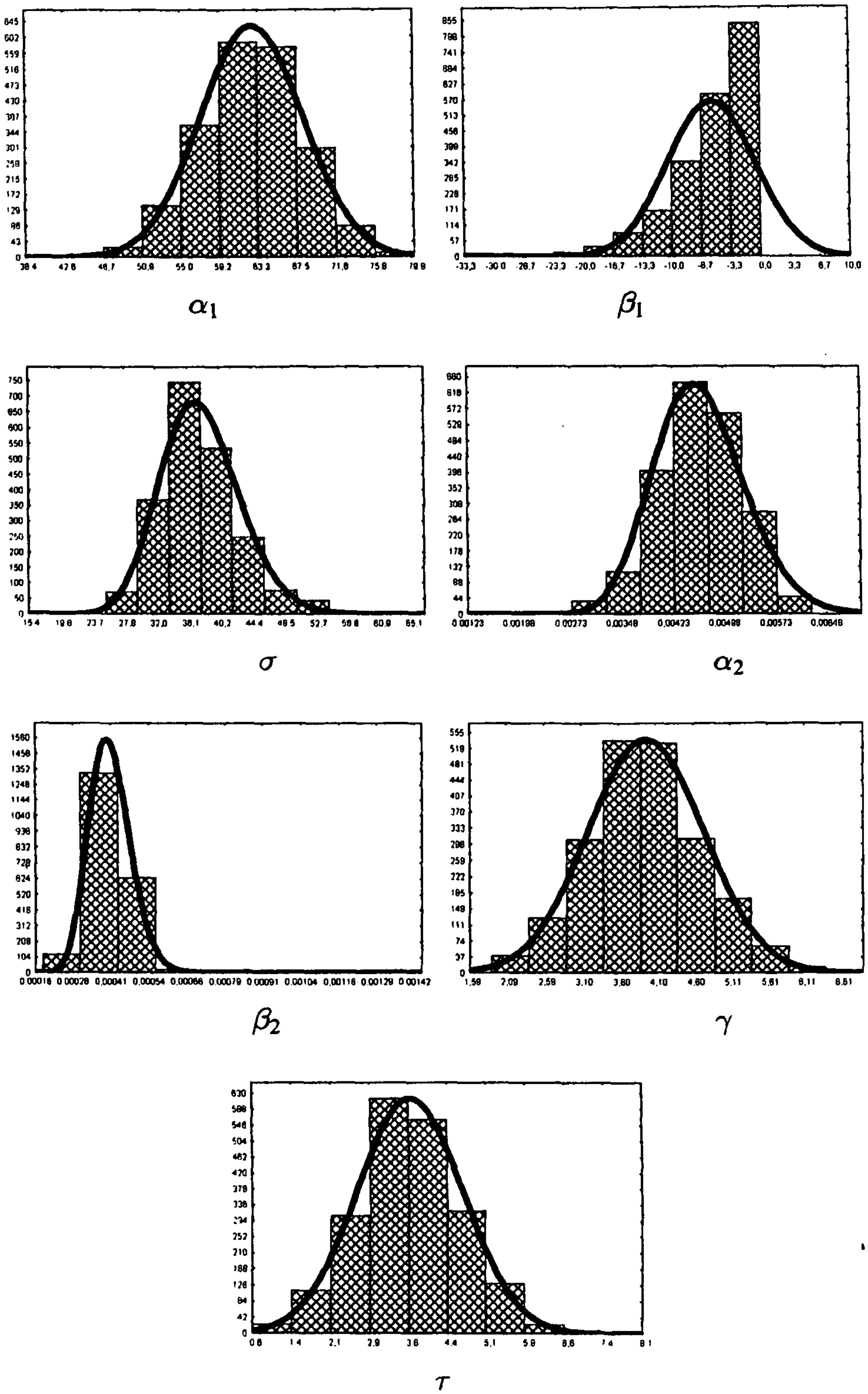
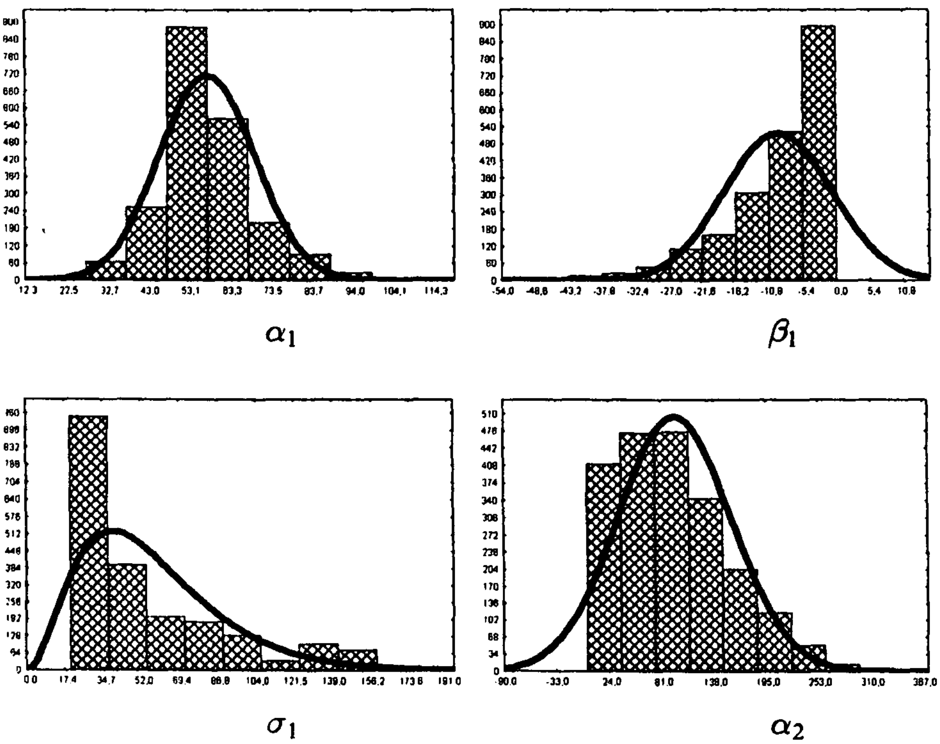


Figure 2. Approximate marginal posterior densities (exponential-normal distribution).

Considering the normal-normal mixture model (see section 4), and the prior densities (18) with $\gamma_0 = 4.0$, $s_1^2 = 0.70$, $\tau_0 = 3.6$, $s_2^2 = 1.1$, we also generated 3 separate Gibbs chains each of which ran for 7000 iterations, considering the 10^{th}, 20^{th}, 30^{th}, ...iterations, which required a computational time of 35 hours working with the software SAS in a Pentium 166 MHZ. In table 3, we have the obtained posterior summaries for the parameters, and in figure 3, we have the approximate marginal posterior densities considering the $S = 2100$ Gibbs samples. We also observe approximate convergence, since the estimated potential scale reductions introduced by Gelman and Rubin (1992) are close to one for all parameters.

Table 3. Posterior Summaries (Normal-Normal Distribution).

Parameter	Mean	95% Credible Interval	$\hat{R}$
α_1	57.849	(35.481; 85.786)	1.00096750
β_1	- 9.426	(-32.184; -0.265)	1.00512800
σ_1	57.440	(25.610; 152.020)	1.00057800
α_2	95.774	(5.756; 231.567)	1.00293320
β_2	- 414.919	(– 479.140; – 339.250)	1.00080900
σ_2	215.961	(154.395; 312.234)	1.00232900
γ	3.836	(2.538; 5.223)	1.00071700
τ	3.270	(2.097; 4.742)	1.00152600



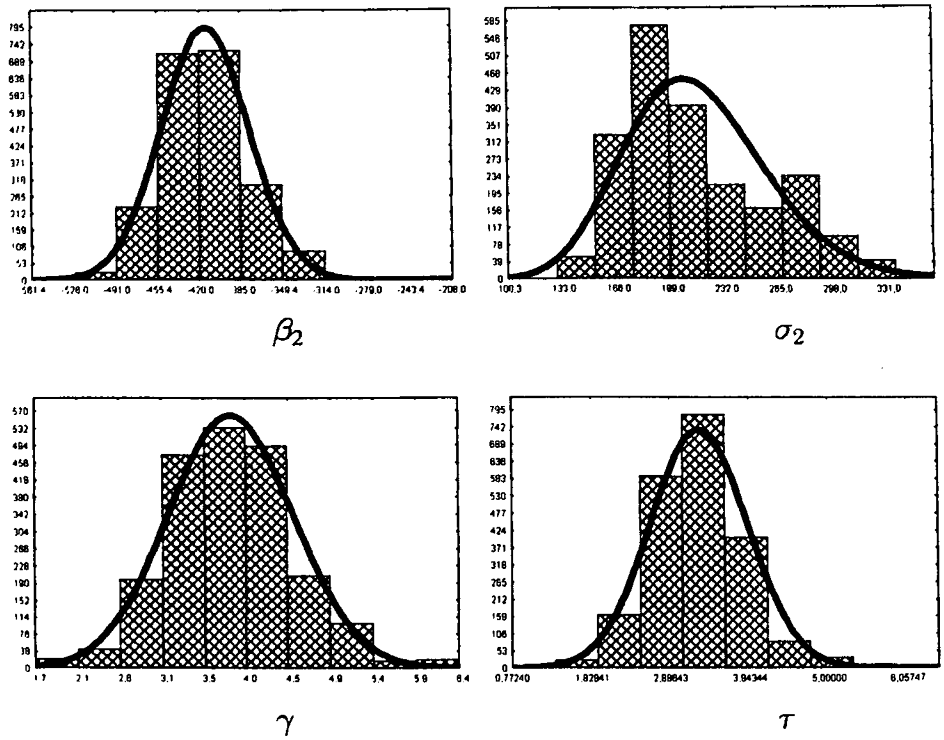


Figure 3. Approximate marginal posterior densities (normal-normal distribution).

Considering now, the gamma-normal mixture model (see section 5), and the prior densities (21) with $\gamma_0 = 4.04$, $s_1^2 = 0.7$, $\tau_0 = 3.6$, $s_2^2 = 1.1$, we generated 3 separate Gibbs chains each of wich ran for 7000 iterations, considering the 10^{th}, 20^{th}, 30^{th}, ...iterations, which required a computational time of 40 hours working with the software SAS in a Pentium 166 MHZ. In table 4, we have the obtained posterior summaries, and in figure 4, we have the approximate marginal posterior densities considering the $S = 2100$ Gibbs samples. For all parameters, we observe (see table 4), $\sqrt{\hat{R}} < 1.1$, indicating approximate convergence.

Table 4. Posterior Summaries (Gamma-Normal Distribution).

Parameter	Mean	95% Credible Interval	$\hat{R}$
α_0	0.967	(0.834; 1.194)	1.01019800
α_1	0.017	(0.013; 0.026)	1.01630900
β_1	0.003	(0.0007; 0.0042)	1.02498200
α_2	31.128	(1.363; 97.343)	1.00276200
β_2	- 315.213	(- 362.928; − 214.515)	1.00386600
σ	147.071	(94.676; 234.364)	1.00465200
γ	4.048	(2.494; 5.706)	1.00575100
τ	3.300	(1.568; 5.546)	1.00582800

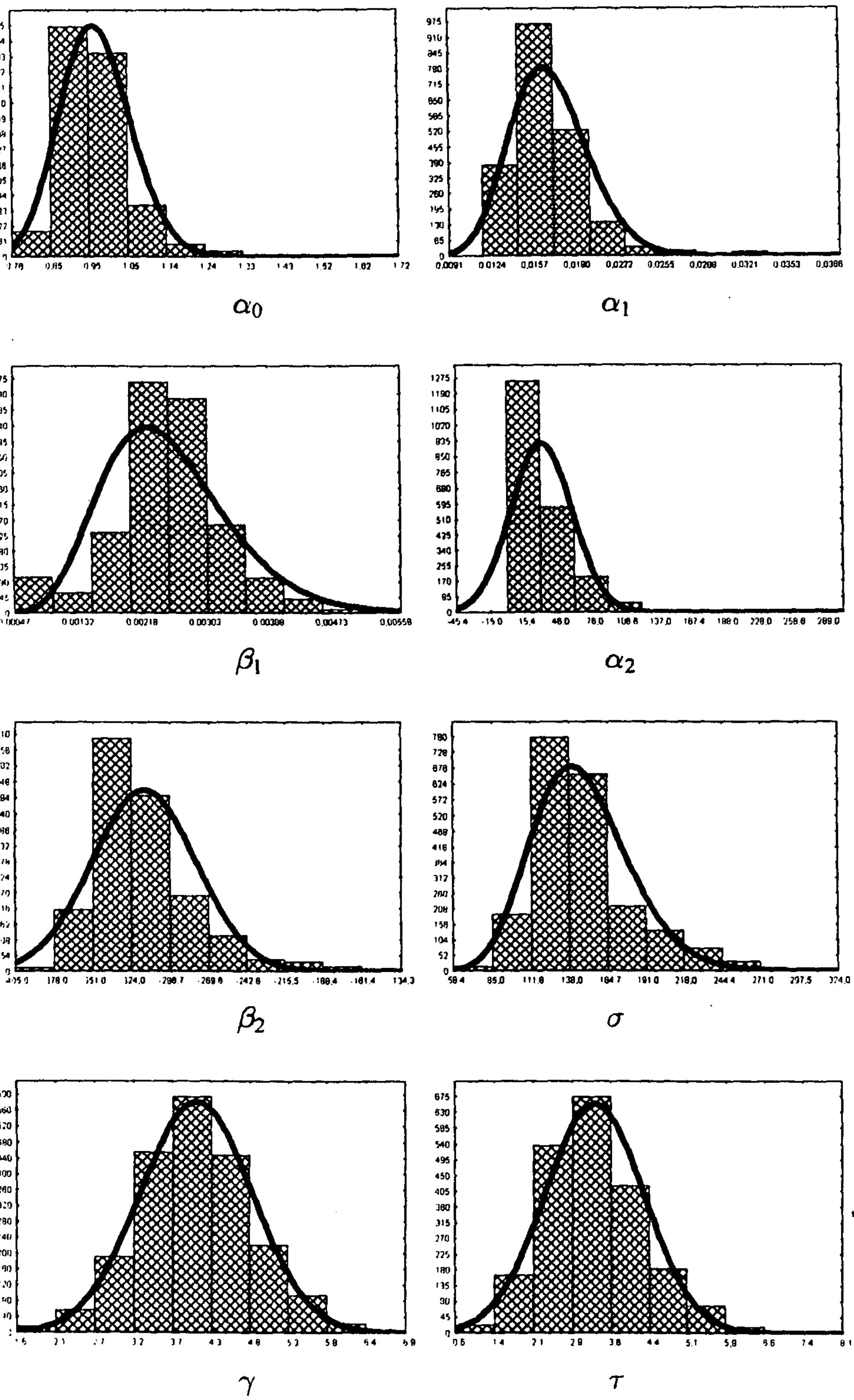


Figure 4. Approximate marginal posterior densities (gamma-normal distribution).

From the generated Gibbs samples, we also could get Monte Carlo estimates for the predictive densities $c_i = f(t_i \setminus t_{(i)}, x_i)$ (see section 6) to be considered in the selection of the best model for the survival data of table 1.

The values of $c(l) = \prod_{i=1}^{n} c_i(l)$, where l indexes models, considering the values of the predictive densities evaluated at the observed values t_i and x_i, are given by $c(1) = 2.01\text{x}100^{-550}$, (exponential-normal distribution), $c(2) = 2.22\text{x}100^{-459}$, (normal-normal distribution) and $c(3) = 2.62\text{x}100^{-489}$, (gamma-normal distribution), which indicates that the normal-normal mixture model has better fit for the survival data of table 1.

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