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ABSTRACT

Gibbs sampling with Metropolis-Hastings algorithms are proposed to perform a Bayesian analysis for a Weibull hazard function model with a change-point. We assume noninformative prior densities for the parameters. We also present some Bayesian criteria to discriminate different models proposed for medical data with a change-point. The methodology is illustrated with a data set introduced by Matthews and Farewell, 1982.

Key words: Weibull hazard model, change-point, Gibbs sampling, Metropolis algorithm.

1. Introduction

A common question posed by medical researchers concerns the inferences for a change in the failure rate for patients receiving a given treatment. Depending on the specified parametrical model for the random variable T denoting the lifetime of the patients, this inference problem could be very difficult to solve considering standard classical approach. Usually, with this type of experiment, the end of study is fixed by the research and the patients could not enter in study at the beginning time t_0 (Type I censoring data).

Associated with the true survival time, we assume a Weibull hazard function with a change-point τ, that is,

$$h_T(t) = \begin{cases} \lambda\gamma t^{\gamma-1} & , t < \tau \\ \lambda\alpha\gamma t^{\alpha\gamma-1} & , t \geq \tau \end{cases} \tag{1}$$

where $\lambda > 0$, $\gamma > 0$, $\alpha > 0$ and $\tau > 0$.

The density and survival function are, respectively,

$$f_T(t) = \begin{cases} \lambda\gamma t^{\gamma-1} exp\{-\lambda t^{\gamma}\} & , t < \tau \\ \lambda\alpha\gamma t^{\alpha\gamma-1} exp\{-\lambda[\tau^{\gamma} + t^{\alpha\gamma} - \tau^{\alpha\gamma}]\} & , t \geq \tau \end{cases} \tag{2}$$

and

$$S_T(t) = \begin{cases} exp\{-\lambda t^{\gamma}\} & , t < \tau \\ exp\{-\lambda[\tau^{\gamma} + t^{\alpha\gamma} - \tau^{\alpha\gamma}]\} & , t \geq \tau \end{cases} \quad (3)$$

Inferences based on standard asymptotic likelihood results are not possible with this model even for the simple case of constant hazard function with a change-point τ (see for example, Matthews and Farewell, 1982; or Matthews, Farewell and Pyke, 1985).

A suitable way to get inferences for change-point problems is the use of Bayesian methods (see for example Achcar and Bolfarine, 1989; or Ghosh, Joshi and Mukhopadhyay, 1993).

In this paper, we present a Bayesian analysis for the model (1) considering a noninformative prior density for the parameters and Markov Chain Monte Carlo (MCMC) methods with a combination of Gibbs sampling algorithms (see for example, Gelfand and Smith, 1990) and Metropolis-Hastings algorithms (see for example, Chib and Greenberg, 1995; or Smith and Roberts, 1993).

In section 2, we introduce the likelihood function assuming type I censoring data; in section 3 we introduce a Bayesian analysis for model (1); in section 4 we introduce the proposed methodology considering a data set introduced by Matthews and Farewell (1982); finally, in section 5, we present some discrimination Bayesian criteria considering Monte Carlo estimates for the predictive densities.

2. The likelihood function

Let $T_1^0, T_2^0, ..., T_n^0$ be the true survival times of n individuals considered as a random sample of size n and let $C_1, C_2, ..., C_n$ be the fixed censoring times associated to each individual (type I censoring). The observed data are given by $T_i = min(T_i^0, C_i)$. We define an indication variable δ_i such that $\delta_i = 1$ if $T_i = T_i^0$ (failure) and $\delta_i = 0$ if $T_i < T_i^0$ (censoring). Associated with the true survival times, we consider a Weibull hazard function (1) with a change-point τ.

Considering $\epsilon_i = 1$ if $T_i < \tau$ and $\epsilon_i = 0$ if $T_i \geq \tau$, the likelihood function is,

$$L(\lambda, \gamma, \alpha, \tau) =$$

$$\prod_{i=1}^{n} \left\{ \left[\lambda\gamma t_i^{\gamma-1} exp\{-\lambda t_i^{\gamma}\}\right]^{\epsilon_i} \left[\lambda\alpha\gamma t_i^{\alpha\gamma-1} exp\{-\lambda[\tau^{\gamma} + t_i^{\alpha\gamma} - \tau^{\alpha\gamma}]\}\right]^{1-\epsilon_i} \right\}^{\delta_i}$$

$$\prod_{i=1}^{n} \left\{ \left[exp\{-\lambda t_i^{\gamma}\}\right]^{\epsilon_i} \left[exp\{-\lambda[\tau^{\gamma} + t_i^{\alpha\gamma} - \tau^{\alpha\gamma}]\}\right]^{1-\epsilon_i} \right\}^{1-\delta_i} \quad (4)$$

with, $d_1(\tau) = \sum_{i=1}^{n} \epsilon_i \delta_i$, $\quad d_2(\tau) = \sum_{i=1}^{n} \epsilon_i$, $\quad d_3 = \sum_{i=1}^{n} \delta_i$, we have,

$$L(\lambda, \gamma, \alpha, \tau) = (\lambda\gamma)^{d_3} \alpha^{d_3 - d_1(\tau)} \prod_{i=1}^{n} \left[t_i^{\gamma-1}\right]^{\epsilon_i\delta_i} \prod_{i=1}^{n} \left[t_i^{\alpha\gamma-1}\right]^{(1-\epsilon_i)\delta_i}$$
$$exp\left\{ -\lambda \left[\sum_{i=1}^{n} \epsilon_i t_i^{\gamma} + \sum_{i=1}^{n} (1-\epsilon_i) t_i^{\alpha\gamma} + [n - d_2(\tau)][\tau^{\gamma} - \tau^{\alpha\gamma}] \right] \right\} \quad (5)$$

Given τ, we find $\widehat{\lambda}_\tau$, $\widehat{\gamma}_\tau$ and $\widehat{\alpha}_\tau$ that maximize $L(\lambda, \gamma, \alpha, \tau)$ by deriving the log-likelihood $l(\lambda, \gamma, \alpha \backslash \tau)$ with respect to λ,γ and α,

$$\frac{\partial l}{\partial \lambda} = \frac{d_3}{\lambda} - \sum_{i=1}^{n} \epsilon_i t_i^{\gamma} - \sum_{i=1}^{n} (1-\epsilon_i) t_i^{\alpha\gamma} - [n - d_2(\tau)][\tau^{\gamma} - \tau^{\alpha\gamma}]$$

$$\frac{\partial l}{\partial \gamma} = \frac{d_3}{\gamma} + \sum_{i=1}^{n} \epsilon_i \delta_i ln(t_i) + \alpha \sum_{i=1}^{n} (1-\epsilon_i)\delta_i ln(t_i) - \lambda \sum_{i=1}^{n} \epsilon_i t_i^{\gamma} ln(t_i) - \\ - \lambda\alpha \sum_{i=1}^{n} (1-\epsilon_i) t_i^{\alpha\gamma} ln(t_i) - \lambda[n - d_2(\tau)] ln(\tau)[\tau^{\gamma} - \alpha\tau^{\alpha\gamma}] \quad (6)$$

$$\frac{\partial l}{\partial \alpha} = \frac{d_3 - d_1(\tau)}{\alpha} + \gamma \sum_{i=1}^{n} (1-\epsilon_i)\delta_i ln(t_i) - \lambda\gamma \sum_{i=1}^{n} (1-\epsilon_i) t_i^{\alpha\gamma} ln(t_i) - \lambda\gamma[n - d_2(\tau)] ln(\tau)\tau^{\alpha\gamma}$$

From $\frac{\partial l}{\partial \lambda} = 0$, $\frac{\partial l}{\partial \gamma} = 0$ and $\frac{\partial l}{\partial \alpha} = 0$ we obtain $\widehat{\lambda}_\tau, \widehat{\gamma}_\tau$ and $\widehat{\alpha}_\tau$ with the maximum likelihood estimates for λ, γ , α and τ computed by maximizing $L(\widehat{\lambda}_\tau, \widehat{\gamma}_\tau, \widehat{\alpha}_\tau, \tau)$.

Let us define $S_i(.)$, $i = 1, ..., 8$; $r_j(.)$, $j = 1, ..., 4$, by

$$\begin{aligned}
S_1(\gamma,\tau) &= \sum_{i=1}^{n} \epsilon_i t_i^{\gamma} \\
S_2(\alpha,\gamma,\tau) &= \sum_{i=1}^{n} (1-\epsilon_i) t_i^{\alpha\gamma} \\
S_3(\tau) &= \sum_{i=1}^{n} \epsilon_i \delta_i ln(t_i) \\
S_4(\tau) &= \sum_{i=1}^{n} (1-\epsilon_i)\delta_i ln(t_i) \\
S_5(\gamma,\tau) &= \sum_{i=1}^{n} \epsilon_i t_i^{\gamma} ln(t_i) \\
S_6(\alpha,\gamma,\tau) &= \sum_{i=1}^{n} (1-\epsilon_i) t_i^{\alpha\gamma} ln(t_i) \qquad (7) \\
S_7(\gamma,\tau) &= \sum_{i=1}^{n} \epsilon_i t_i^{\gamma} [ln(t_i)]^2 \\
S_8(\alpha,\gamma,\tau) &= \sum_{i=1}^{n} (1-\epsilon_i) t_i^{\alpha\gamma} [ln(t_i)]^2
\end{aligned}$$

$$r_1(\alpha,\gamma,\tau) = \tau^{\gamma} - \tau^{\alpha\gamma}$$

$$r_2(\alpha,\gamma,\tau) = ln(\tau)[\tau^{\gamma} - \alpha\tau^{\alpha\gamma}]$$

$$r_3(\alpha,\gamma,\tau) = [ln(\tau)]^2[\tau^{\gamma} - \alpha^2\tau^{\alpha\gamma}]$$

$$r_4(\alpha,\gamma,\tau) = \tau^{\alpha\gamma} ln(\tau)[1 + \alpha\gamma\, ln(\tau)]$$

From $\frac{\partial l}{\partial \lambda} = 0$ (see (6)), we get

$$\widehat{\lambda_\tau} = \frac{d_3}{S_1(\gamma)+S_2(\alpha,\gamma)+[n-d_2(\tau)]r_1(\tau,\alpha,\gamma)} \tag{8}$$

Substituting (8) for λ in $\frac{\partial l}{\partial \gamma} = 0$ and $\frac{\partial l}{\partial \alpha} = 0$, we have two equations in γ and α given by

$$g_1(\alpha,\gamma) = \frac{\partial l}{\partial \gamma} = \frac{S_3(\tau)+\alpha S_4(\tau)+d_3\{\frac{1}{\gamma}-S_5(\gamma,\tau)-\alpha S_6(\alpha,\gamma,\tau)-[n-d_2(\tau)]r_2(\alpha,\gamma,\tau)\}}{D}$$

$$(9)$$

$$g_2(\alpha,\gamma) = \frac{\partial l}{\partial \alpha} = \frac{d_3-d_1(\tau)}{\alpha} + \gamma S_4(\tau) - \frac{d_3\gamma\{S_6(\alpha,\gamma,\tau)-[n-d_2(\tau)]ln(\tau)\tau^{\alpha\gamma}\}}{D}$$

where $D = D(\alpha,\gamma,\tau) = S_1 + S_2 + [n - d_2(\tau)][\tau^\gamma + \tau^{\alpha\gamma}]$

To find $\widehat{\alpha}_\tau$ and $\widehat{\gamma}_\tau$ from the non-linear equations (9), we could use the Newton-Raphson method (see for example, Bickel and Doksun, 1977).

3. A Bayesian analysis

Assuming τ known and prior independence among λ, γ and α, consider a noninformative prior density based on Jeffreys rule (see for example, Box and Tiao, 1973) given by

$$\pi_0(\lambda,\gamma,\alpha) \propto \frac{1}{\lambda\gamma\,\alpha} \tag{10}$$

The joint posterior density for λ, γ and α is given by

$$\pi(\lambda,\gamma,\alpha\backslash\tau,\mathcal{D}) \propto (\lambda\,\gamma)^{d_3-1}\alpha^{d_3-d_1(\tau)}\prod_{i=1}^{n}\left[t_i^{\gamma-1}\right]^{\epsilon_i\delta_i}\prod_{i=1}^{n}\left[t_i^{\alpha\gamma-1}\right]^{(1-\epsilon_i)\delta_i}$$
$$exp\left\{-\lambda\left[\sum_{i=1}^{n}\epsilon_i t_i^\gamma + \sum_{i=1}^{n}(1-\epsilon_i)t_i^{\alpha\gamma} + [n-d_2(\tau)][\tau^\gamma - \tau^{\alpha\gamma}]\right]\right\} \tag{11}$$

The conditional posterior densities for the Gibbs sampling algorithm are given by

$i)\ \lambda\backslash\alpha,\gamma,\tau,\mathcal{D} \sim \Gamma\left[d_3,\ S_1 + S_2 + [n-d_2(\tau)]r_1\right]$

$$ii)\ f(\alpha\backslash\lambda,\gamma,\tau,\mathcal{D}) \propto \alpha^{d_3-d_1(\tau)-1}exp\left\{\alpha\gamma S_4 - \lambda\left[S_2 - [n-d_2(\tau)]\tau^{\alpha\gamma}\right]\right\} \tag{12}$$

iii) $f(\gamma\backslash\lambda,\alpha,\tau,\mathcal{D}) \propto \gamma^{d_3-1} exp\Big\{\gamma\Big[S_3+\alpha S_4-\lambda\Big[S_1+S_2+[n-d_2(\tau)]r_1\Big]\Big\}$

where $\Gamma(a,b)$ denotes a Gamma distribution with mean a/b and variance a/b^2; S_i and r_j are defined in (7).

Observe that we should use the Metropolis-Hastings algorithm to generate the variables α and γ. We could monitor 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.

Now, let us assume τ unknown and taking discrete values $\tau_i = t_i$, with prior probabilities $\pi_0(\tau_i = t_i)$, $i = 1, 2, ..., n$. The prior density for λ, γ, α and τ_i is given by,

$$\pi(\lambda,\gamma,\alpha,\tau_i) = \pi_0(\lambda,\gamma,\alpha\backslash\tau_i)\pi_0(\tau_i = t_i) \tag{13}$$

Given $\tau_i = t_i$, we assume the noninformative prior for λ, γ and α given in (10), and a uniform prior density for τ_i proportional to $\frac{1}{n}$.

In this case, the conditional posterior densities for the Gibbs sampling algorithm are given by (12) for λ,γ and α, and by

$$\pi(\tau\backslash\gamma,\lambda,\alpha) \propto \alpha^{-d_1(\tau)} exp\Big\{\gamma\Big[S_3+\alpha S_4\Big] - \lambda\Big[S_1+S_2+[n-d_2(\tau)]r_1(\tau)\Big]\Big\} \tag{14}$$

We also need to use the Metropolis-Hastings algorithm to generate the variable τ.

4. An example

In table I, we have the remission times of 84 patients with acute nonlymphoblastic leukemia (data introduced by Matthews and Farewell, 1982). we have $n = 84$ and $d_3 = 51$ (the number of uncensored observations).

Non-censored observations (51 patients)

24	82	111	152	197	249	270	304	487	534	1160
46	89	117	166	209	254	273	332	510	608	
57	90	128	171	223	258	284	341	516	642	
64	90	143	186	230	264	294	393	518	697	
65	90	148	191	247	269	304	395	518	955	

Censored observations (33 patients)

68	182	182	182	182	182	182	182	182	1310	1908
119	182	182	182	182	182	182	182	182	1538	1966
182	182	182	182	182	182	182	182	583	1634	2057

Table I - Remission times in days.

Assuming $\tau = 697$ known (from a preliminary data analysis based on the product-limit estimator of Kaplan and Meier (1958) for the survival function), the maximum likelihood estimates for λ, γ and α are given by $\widehat{\lambda}_\tau = 0.000655$, $\widehat{\gamma}_\tau = 1.19159$, $\widehat{\alpha}_\tau = 0.80482$.

Considering the noninformative prior density (10) for λ, γ and α with $\tau = 697$ known, we generate 5 separate Gibbs chains each of which ran for 2000 iterations, and we monitored the convergence of the Gibbs samples using the Gelman and Rubin (1992) method. For each parameter, we considered the $515^{th}, 530^{th}, ..., 2000^{th}$ iterations, which for 5 chains yields a sample of size 500.

In table II, we have the obtained posterior summaries for the parameters λ, γ and α, and in figure 1, we have the approximate marginal posterior densities considering the 500 Gibbs samples. We also have in table II, the estimated potential scale reductions $\widehat{R}$ (see Gelman and Rubin, 1992) for all the parameters. In this case, the considered number of iterations were sufficient for approximate convergence ($\sqrt{\widehat{R}} < 1.1$ for all parameters).

In figure 2, we have plots showing the convergence of the algorithm with different initial values for all parameters and in figure 3 we have plots indicating that the generated samples have small autocorrelation.

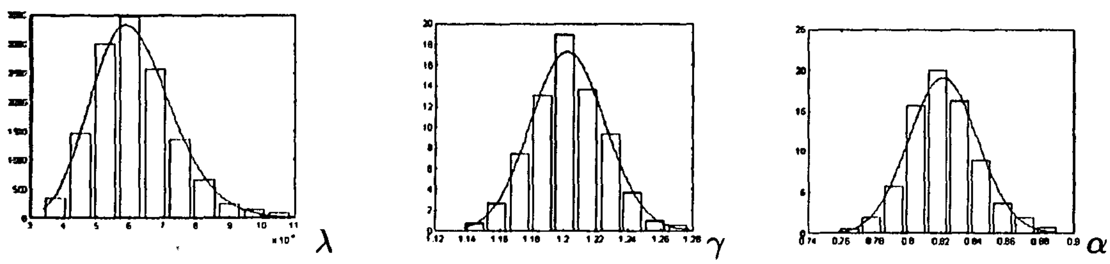

Figure 1 - Marginal posterior densities for λ, γ and α.

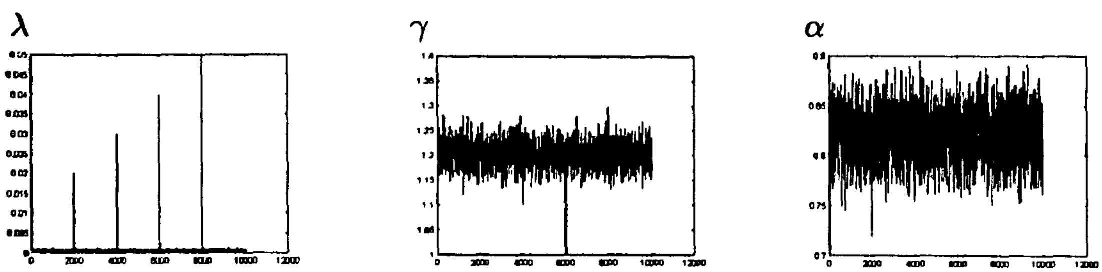

Figure 2 - Convergence for λ, γ e α.

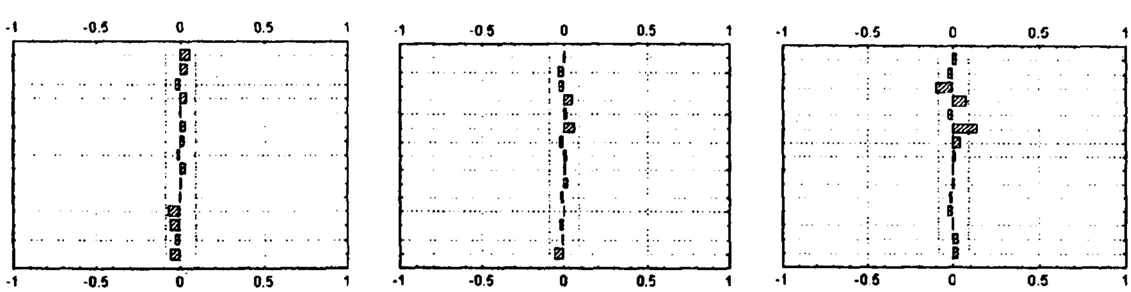

Figure 3 - Autocorrelation function for λ, γ e α, respectively.

	Mean	Mode	95% credible interval	$\widehat{R}$
λ	0.0006127	0.0006005	(0.00040129 ; 0.0008723)	0.9988
γ	1.2027	1.2000	(1.15841 ; 1.24711)	1.0024
α	0.8215	0.8179	(0.77188 ; 0.86635)	1.0082

Table II - Posterior summaries ($\tau = 697$ known)

Considering τ unknown, and the noninformative prior density $\pi_0(\lambda,\gamma,\alpha,\tau) \propto \frac{1}{\lambda\gamma\alpha}$, $\lambda > 0, \gamma > 0, \alpha > 0$ and $\tau > 0$, we generated 5 separate Gibbs chains each of which ran for 2000 iterations. For each parameter, we considered the $515^{th}, 530^{th}, \ldots, 2000^{th}$ iterations, which for 5 chains yields a sample of size 500.

In table III, we have the obtained posterior summaries for the parameters λ, γ, α and τ, and in figure 4, we have the approximate marginal posterior densities considering the 500 Gibbs samples. In this case, we also have approximate convergence ($\sqrt{\widehat{R}} < 1.1$ for all the parameters).

	Mean	Mode	95% credible interval	$\widehat{R}$
λ	0.00027	0.00024	(0.00017 ; 0.00039)	1.0179
γ	1.2296	1.2287	(1.1995 ; 1.2534)	1.0052
α	0.8469	0.8460	(0.8066 ; 0.8923)	1.0192
τ	723.627	780.1813	(537.2944 ; 797.7528)	1.0097

Table III - Posterior summaries (τ unknown)

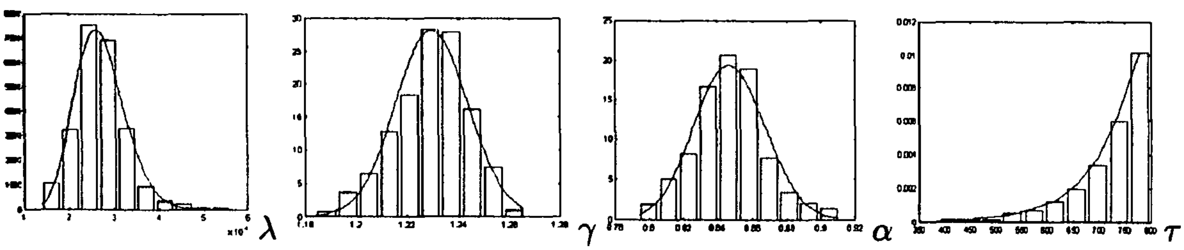

Figure 4 - Posterior summaries (τ unknown)

5. Some considerations on model selection

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

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

$$c_i = f(t_i \backslash \underset{\sim}{t}_{(i)}) = \int f(t_i \backslash \underset{\sim}{\theta}) \pi(\underset{\sim}{\theta} \backslash \underset{\sim}{t}_{(i)}) d\underset{\sim}{\theta} \qquad (15)$$

where $\pi(\underset{\sim}{\theta} \backslash \underset{\sim}{t}_{(i)})$ is the posterior density for a vector of parameters $\underset{\sim}{\theta}$, given the data $\underset{\sim}{t}_{(i)}$.

Using the Gibbs samples, (15) can be approximated by its Monte Carlo estimates,

$$\widehat{f}(t_i \backslash \underset{\sim}{t}_{(i)}) = \frac{1}{N}\sum_{j=1}^{N} f(t_i \backslash \underset{\sim}{\theta}^{(j)}) \tag{16}$$

where $\underset{\sim}{\theta}^{(j)}$ are the generated Gibbs samples, $j = 1, ..., N$.

We can use $c_i = \widehat{f}(t_i \backslash \underset{\sim}{t}_{(i)})$ in model selection. In this way, we consider plots of c_i versus i $(i = 1, .., n)$ 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).

Considering the Weibull hazard function with a change point τ (1) and the joint posterior density (11) for λ, γ and α with τ known, we have (from (16)),

$$\widehat{c}_{1i} = \frac{1}{N}\sum_{j=1}^{N} f_1(t_i \backslash \lambda^{(j)}, \gamma^{(j)}, \alpha^{(j)}) \tag{17}$$

where

$$f_1(t_i \backslash \lambda^{(j)}, \gamma^{(j)}, \alpha^{(j)}) = \begin{cases} \lambda^{(j)}\gamma^{(j)}\, t_i^{\gamma^{(j)}-1} e^{-\lambda^{(j)} t_i^{\gamma^{(j)}}} & \text{if } \ t_i < \tau \\ \lambda^{(j)}\alpha^{(j)}\gamma^{(j)}\, t_i^{\alpha^{(j)}\gamma^{(j)}-1} e^{-\lambda^{(j)}(\tau^{\gamma^{(j)}} + t_i^{\alpha^{(j)}\gamma^{(j)}} - \tau^{\alpha^{(j)}\gamma^{(j)}})} & \text{if } \ t_i \geq \tau \end{cases}$$

$i = 1, ..., n;\ j = 1, ..., N.$

Usually, for change-point problem in medical research, it is assumed an exponential hazard function model with a change-point τ (see for example, Matthews and Farewell, 1982) given by

$$h_2(t) = \begin{cases} \lambda & \text{if } \ t < \tau \\ \rho\lambda & \text{if } \ t \geq \tau \end{cases} \tag{18}$$

with density

$$f_2(t) = \begin{cases} \lambda e^{-\lambda t} & \text{if } \ t < \tau \\ \rho\lambda e^{-\lambda\tau - \rho\lambda(t-\tau)} & \text{if } \ t \geq \tau \end{cases} \tag{19}$$

In this case, assuming a noninformative prior density $\pi_0(\lambda, \rho) \propto \frac{1}{\lambda\rho}$ with τ known, we have (from (16)),

$$\widehat{c}_{2i} = \frac{1}{N}\sum_{j=1}^{N} f_2(t_i \backslash \lambda^{(j)}, \rho^{(j)}) \tag{20}$$

where

$$f_2(t_i \backslash \lambda^{(j)}, \rho^{(j)}) = \begin{cases} \lambda^{(j)} e^{-\lambda^{(j)} t_i} & \text{if } t_i < \tau \\ \rho^{(j)} \lambda^{(j)} e^{-\lambda^{(j)} \tau^* - \rho^{(j)} \lambda^{(j)} (t_i - \tau^*)} & \text{if } t_i \geq \tau \end{cases}$$

$i = 1, ..., n;\ j = 1, ..., N.$

In figure 5, we have plots of c_{ij} versus i; $j = 1, 2$; $i = 1, 2, .., n$ for the data set of table I. We observe better fit for the Weibull hazard function model (1) with a change-point τ. We also observe that for the Weibull hazard function model with a change-point τ, we have $c(1) = \prod_{i=1}^{n} \hat{c}_{1i} = 6.3338 \times 10^{-253}$ and for the exponential hazard function model (18) with a change-point τ we have $c(2) = \prod_{i=1}^{n} \hat{c}_{2i} = 2.7229 \times 10^{-255}$. That is, $\frac{c(1)}{c(2)} = 2.3261 \times 10^2$, indicating that model (1) is better fitted for the data set of table I.

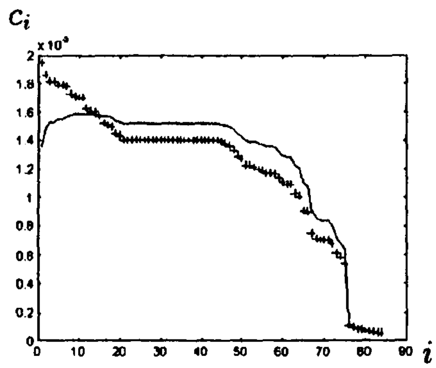

Figure 5 - Plot of c_i versus i, $j = 1, 2$
($j = 1$ (Weibull ----); $j = 2$ (Exponential +++))

6. Concluding remarks

The use of a Weibull hazard function model with a change-point τ could be of great interest for survival data, since in many applications the hazard function could be increasing for $T < \tau$. With the use of Gibbs sampling with Metropolis-Hastings algorithms we can get Monte Carlo estimates for the parameters of the model with great accuracy.

We also could use the Monte Carlo estimates of the predictive densities based on the Gibbs samples to get a simple criterium to discriminate different models for the survival data with a change-point.

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