

*Semiparametric inference for survival time models  
using hierarchical mixture modeling  
with generalized gamma processes*

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## Aim of the paper

Survival times data (censored or not)

MODEL: Accelerated failure time (AFT) model (**regression model on the log scale**) from a Bayesian semiparametric point of view; the error is distributed nonparametrically as a **species sampling mixture model** (of densities on the **positive reals**) where the mixing measure  $P$  is a (normalized) **generalized gamma measure**

AIM: for simulated and real datasets we compute **posterior inferences on the regression parameters** and the **survival times** via MCMC (incorporating censoring)

**Remark:** Density estimation can be performed

## The AFT model

### Accelerated failure time model

$$\log T = -x'\beta + W$$

$T$ : univariate survival time

$x = (x_1, \dots, x_p)'$ : fixed  $p$ -vector of covariates

$\beta = (\beta_1, \dots, \beta_p)'$ :  $p$ -vector of regression parameters

$W, V$  errors

Equivalently, if  $V := e^W$ :

$$T = e^{-x'\beta} \cdot V$$

## Bayesian semiparametric AFT models

$$\log T = -x'\beta + W \quad \text{or} \quad T = e^{-x'\beta} \cdot V$$

Christensen & Johnson ('88):  $V \sim$  Dirichlet process prior

Walker & Mallick ('99):  $W \sim$  0-median PT prior

Hanson & Johnson ('02):  $W \sim$  mixture of 0-median PT

Kottas & Gelfand ('01), Gelfand & Kottas ('03):  $W \sim$  semiparametric 0-median family of distributions (*scale mixture of split normals, skewness handled parametrically*)

Kuo & Mallick ('97):  $V \sim$  DPM prior (*location mixture of normal kernels*)

Ghosh & Ghoshal ('06):  $V \sim$  DPM prior (*scale mixture of Weibull kernels*)

Hanson ('06):  $V \sim$  DPM prior (*gamma densities, mixed both over the scale and the shape*)

Argiento, Guglielmi, Pievatolo ('07):  $V \sim$  DPM or NIG-mixture prior (*gamma densities, mixed over the scale and the shape*)

## Our model

$T_1, \dots, T_n$  survival times,  $x_i = (x_{i1}, \dots, x_{ip})'$  covariate vector

$$T_i = e^{-x_i' \beta} \cdot V_i, \quad i = 1, \dots, n,$$

$V_i | \theta_i \stackrel{ind}{\sim} k(\cdot; \theta_i)$  family of densities on  $\mathbb{R}^+$        $\Theta \subset \mathbb{R}^s$  parametric space

$$\theta_i | G \stackrel{iid}{\sim} G,$$

$G \sim q$ ,     $G$  is a (normalized) generalized gamma measure on  $\Theta$

$$\beta \perp G, \quad \beta \sim \pi(\beta)$$

### **Remark**

$$V_1, \dots, V_n | G \stackrel{iid}{\sim} f(v; G) = \int_{\Theta} k(v; \theta) G(d\theta)$$

## Generalized gamma measures (Brix, 1999)

$\mu$  random measure on  $(\Theta, \mathcal{B}(\Theta))$ ,  $\Theta \subset \mathbb{R}^s$

$\sigma \in (0, 1]$ ,  $\tau \geq 0$

$\kappa(\cdot)$  non-negative diffuse (**finite**) measure on  $\Theta$  ( $\Theta$  any Polish space),

$\mu$  is a *generalized gamma measure* if

- $\mu$  is *completely random* (Kingman, 1993), i.e.  $\mu(B_1), \dots, \mu(B_k)$  are mutually independent if  $B_1, \dots, B_k$  are disjoint
- for any  $B \in \mathcal{B}(\Theta)$ ,  $\mu(B)$  has mgf

$$\mathbb{E}(e^{-s\mu(B)}) = \exp\left(-\frac{\kappa(B)}{\sigma}[(\tau + s)^\sigma - \tau^\sigma]\right), \quad s \geq 0$$
$$(\mu(B) \sim G(\sigma, \kappa(B), \tau))$$

$0 < \sigma < 1$ :  $G(\sigma, \kappa(B), \tau)$  is the natural exponential family generated by the positive stable law ( $\tau = 0$ ), and  $\mu$  is the  $\sigma$ -stable process for  $\tau = 0$

$\sigma = 1$ :  $\mu$  degenerates on  $\kappa(\cdot)$

$\sigma \rightarrow 0$ :  $\mathbb{E}(e^{-s\mu(B)}) = \left(\frac{\tau}{\tau + s}\right)^{\kappa(B)}$  and  $\mu$  is the gamma random measure

## Generalized gamma measures

Theorem (Brix, 1999)

1.  $\mu(B) = \int_{[0,+\infty)} yN(dy, B),$

$N$  a Poisson random measure on  $[0, +\infty) \times \Theta$

$\nu$  intensity measure:

$$\nu(A \times B) = \frac{\kappa(B)}{\Gamma(1-\sigma)} \int_A s^{-\sigma-1} e^{-\tau s} ds = \kappa(B) \int_A \rho(ds),$$

$$A \in \mathcal{B}([0, +\infty)), B \in \mathcal{B}(\Theta)$$

2.  $\mu$  has no fixed atoms (since  $\kappa$  is diffuse), *i.e.*  $\mathbb{P}(\mu(\{x\}) > 0) = 0 \forall x$

3.  $\mu$  is almost surely purely atomic

## Generalized gamma random probability measures

$G$  random probability (distribution) built from a generalized gamma random measure  $\mu$  with parameters  $(\sigma, \kappa(\cdot), \tau)$  according to a **standard construction via normalization of completely random measures**

Kingman (1993), Pitman (2003), James (2005), Antonio Lijoi's talk

Since  $\int_{[0, +\infty) \times B} \min(s, 1) \nu(ds, dy) = \kappa(B) \int_{[0, +\infty)} \min(s, 1) \rho(ds) < +\infty$ ,

$$\mathbb{P}(\mu(\Theta) =: T < +\infty) = 1,$$

so that

$$G(\cdot) := \frac{\mu(\cdot)}{T} \text{ is a random probability measure on } \Theta$$

$G \sim GG(\sigma, \kappa(\Theta)G_0(\cdot), \tau)$  **generalized gamma rpm**,  $G_0(\cdot) := \kappa(\cdot)/\kappa(\Theta)$

**Remark:** this parameterization is not unique, *i.e.*

$(\sigma, \kappa(\Theta)G_0(\cdot), \tau)$  and  $(\sigma, s^\sigma \kappa(\Theta)G_0(\cdot), \tau/s)$  (for any  $s > 0$ ) yield the same distribution for  $G$  (see Pitman, 2003, “scaling property”)



## Generalized gamma rpm

Pitman (1996, 2003)

$$G \sim GG(\sigma, \kappa(\Theta)G_0(\cdot), \tau), \quad 0 \leq \sigma \leq 1, \kappa(\Theta) > 0, \tau \geq 0$$

$$G = \sum_{i=1}^{+\infty} P_i \delta_{X_i}, \quad (P_i) \perp (X_i), \quad (X_i) \stackrel{iid}{\sim} G_0,$$

$P_i := \frac{J_i}{T}$ ,  $(J_i)$  jump times of a Poisson process on  $[0, +\infty)$  with Levy density

$$\rho(ds) = \frac{1}{\Gamma(1-\sigma)} s^{-\sigma-1} e^{-\tau s} ds, \quad T = \sum_i J_i$$

$(\tilde{P}_i)$  (ranked) has the Poisson-Kingman distribution with Levy density  $\rho(ds)$

- $G$  is a **homogeneous Poisson-Kingman rpm with Levy density**  $\rho(ds)$
- $G$  is a **species sampling model**  $P(\cdot) = \sum_k p_k \delta_{Z_k} + (1 - \sum_k p_k)H(\cdot)$   
(( $p_k$ ) are positive random weights,  $\sum p_k \leq 1$ , ( $p_k$ ) and ( $Z_k$ ) independent,  
 $Z_k \stackrel{iid}{\sim} H(\cdot)$  non-atomic)

## Generalized gamma rpm

Pitman (2003)

Sampling from  $G$  induces a random partition  $\Pi$  on the positive integers  $\mathbb{N}$

$\theta_1, \dots, \theta_n | G \stackrel{iid}{\sim} G$  a.s. discrete: ties among  $(\theta_i)$

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If  $\Pi_n$  is the restriction of  $\Pi$  to  $\{1, \dots, n\}$ :

$$\mathcal{L}(\theta_1, \dots, \theta_n) \leftrightarrow \mathcal{L}(\Pi_n, \theta_1^*, \dots, \theta_{k(n)}^*)$$

$\theta_1^*, \dots, \theta_{k(n)}^*$  distinct values in  $(\theta_1, \dots, \theta_n)$

$\pi_n = \{C_1, \dots, C_k\}$ ,  $C_j = \{i : \theta_i = \theta_j^*\}$ ,  $n_j := \#C_j \geq 1$ ,  $\sum_1^{k(n)} n_j = n$ ,

$$\mathbb{P}(\Pi_n = \pi_n, \theta_1^* \in B_1, \dots, \theta_{k(n)}^* \in B_{k(n)}) = \mathcal{L}(\Pi_n = \pi_n) \cdot \prod_{j=1}^{k(n)} G_0(B_j)$$

$$(p \text{ symmetric non-negative}) = p(n_1, \dots, n_k) \prod_{j=1}^{k(n)} G_0(B_j),$$

$p$  *exchangeable partition probability function* (EPPF) determined by  $\Pi$

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Moreover:

$$\mathbb{P}(\theta_{n+1} \in B | \theta_1, \dots, \theta_n) = w_{0,n} G_0(B) + \sum_1^k w_{j,n} \delta_{\theta_j^*}(B)$$

$$w_{0,n} = \frac{p(n_1, \dots, n_k, 1)}{p(n_1, \dots, n_k)}, \quad w_{j,n} = \frac{p(n_1, \dots, n_{j+1}, \dots, n_k)}{p(n_1, \dots, n_k)}.$$

## Generalized gamma rpm

$$G \sim GG(\sigma, \kappa(\Theta)G_0, \tau) \quad 0 < \sigma \leq 1, \kappa(\Theta) > 0, \tau \geq 0$$

$\sigma \rightarrow 0$ :  $G$  Dirichlet process with parameter  $\kappa(\Theta)G_0$

$\sigma = 1/2$ :  $G$  normalized inverse-gaussian (NIG) process (Lijoi *et al.*, 2005)

$\sigma = 1$ :  $G$  is degenerate on  $G_0$

$\tau = 0$ : if  $0 < \sigma < 1$ ,  $G$  Poisson-Dirichlet process with two parameters  $(\sigma, 0)$

Generally  $\mathcal{L}(G(B_1), \dots, G(B_k))$  is not available in closed analytic form

## Properties of generalized gamma rpms

$$\mathbb{E}(G(B)) = G_0(B) \quad \text{Var}(G(B)) = G_0(B)(1 - G_0(B))\mathcal{I}(\sigma, \kappa(\Theta), \tau)$$

$$\text{Cov}(G(B_1), G(B_2)) = \left( G_0(B_1 \cap B_2) - G_0(B_1)G_0(B_2) \right) \mathcal{I}(\sigma, \kappa(\Theta), \tau)$$

$$\mathcal{I}(\sigma, \kappa(\Theta), \tau) := (1 - \sigma) \left( 1 - \left( \frac{\kappa(\Theta)\tau^\sigma}{\sigma} \right)^{1/\sigma} \exp\left( \frac{\kappa(\Theta)\tau^\sigma}{\sigma} \right) \right) \Gamma \left( -\frac{1}{\sigma} + 1, \frac{\kappa(\Theta)\tau^\sigma}{\sigma} \right),$$

where  $\Gamma(\alpha, x) := \int_x^{+\infty} e^{-t} t^{\alpha-1} dt$ . If  $\eta := \frac{\kappa(\Theta)\tau^\sigma}{\sigma}$ , then

$$\mathcal{I} = \mathcal{I}(\sigma, \eta) = \left( \frac{1}{\sigma} - 1 \right) \eta^{1/\sigma} e^\eta \Gamma \left( -\frac{1}{\sigma}, \eta \right)$$

$\forall 0 \leq \sigma < 1$   $\mathcal{I}(\sigma, \eta) \downarrow$  as  $\eta$  increases and  $\forall \eta > 0$   $\mathcal{I}(\sigma, \eta) \downarrow$  as  $\sigma$  increases

**Re-parameterization:**  $G \sim GG(\sigma, \eta, G_0)$ ,  $0 < \sigma \leq 1$ ,  $\eta \geq 0$

## Properties of generalized gamma rpms

**Remark:**

$$\theta_1, \dots, \theta_n | G \stackrel{iid}{\sim} G, \quad G \sim GG(\sigma, \eta, G_0)$$

$\Rightarrow \mathcal{L}(G | \theta_1, \dots, \theta_n)$  is NOT a  $GG$  rpm

Description of the posterior: James (2002, 2005)

## Predictive distributions

$\theta_1, \dots, \theta_n | G \stackrel{iid}{\sim} G$  and  $G \sim GG(\sigma, \eta, G_0)$ ,  $0 < \sigma \leq 1$ ,  $\eta \geq 0$

$\theta_1^*, \dots, \theta_k^*$  distinct observations,  $(n_1, \dots, n_k)$  multiplicities ( $\sum_j n_j = n$ ),

$$P(\theta_{n+1} \in B | \theta_1, \dots, \theta_n) = w_0(n, k; \sigma, \eta)G_0(B) + w_1(n, k; \sigma, \eta) \sum_{j=1}^k (n_j - \sigma) \delta_{\theta_j^*}(B)$$



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$$w_0(n, k; \sigma, \eta) = \frac{2}{n} \sigma \eta \frac{\epsilon_{n+1, k+1}}{\epsilon_{n, k}} = \frac{\sigma}{n} \frac{\sum_{i=0}^n \binom{n}{i} (-1)^i \eta^{i/\sigma} \Gamma(k+1 - i/\sigma; \eta)}{\sum_{i=0}^{n-1} \binom{n-1}{i} (-1)^i \eta^{i/\sigma} \Gamma(k - i/\sigma; \eta)}$$

$$w_1(n, k; \sigma, \eta) = \frac{2}{n} \frac{\epsilon_{n+1, k}}{\epsilon_{n, k}} = \frac{1}{n} \frac{\sum_{i=0}^n \binom{n}{i} (-1)^i \eta^{i/\sigma} \Gamma(k - i/\sigma; \eta)}{\sum_{i=0}^{n-1} \binom{n-1}{i} (-1)^i \eta^{i/\sigma} \Gamma(k - i/\sigma; \eta)}$$

Cerquetti (2007)

Lijoi et al. (2007)

$$\epsilon_{n, k} := \int_0^{+\infty} \frac{x^{n-1} e^{-\eta(1+2x)^\sigma}}{(1+2x)^{n-k\sigma}} dx$$

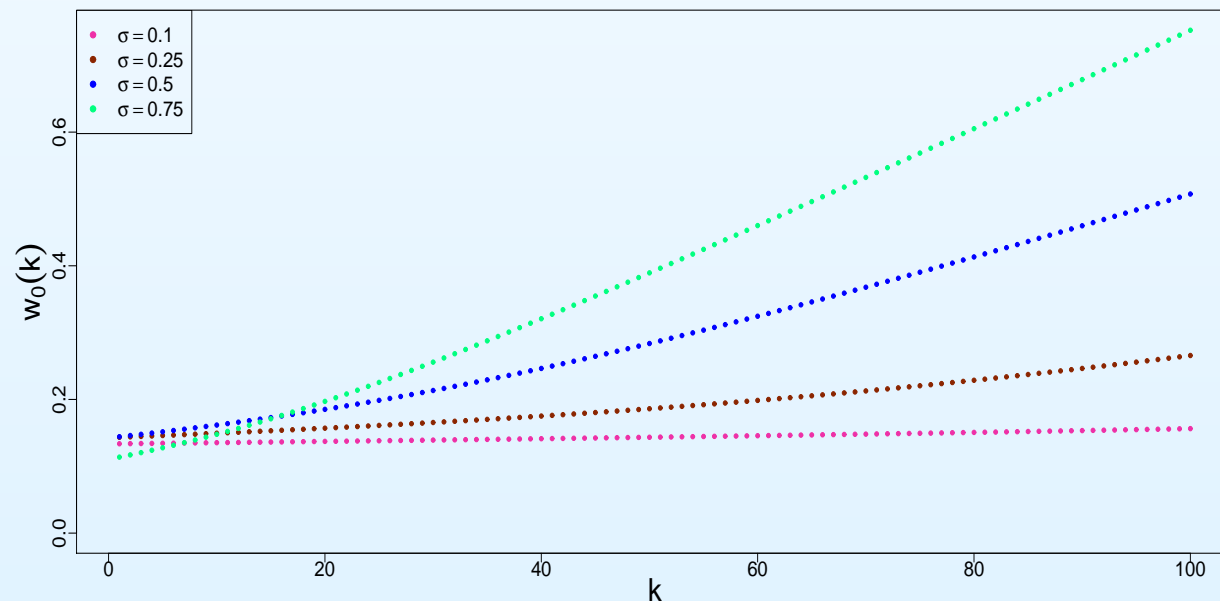
## Predictive distributions

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**Plot of  $w_0(100, k; \sigma, \eta)$  for some values of  $\sigma$**



## Prior distributions for the # of distinct observations

$K_n$  number of distinct observations in the sample  $(\theta_1, \dots, \theta_n)$  from  
 $G \sim GG(\sigma, \eta, G_0)$

$$\mathbb{P}(K_n = k) = \mathbf{S}(n, k; \sigma) \frac{2^n e^\eta \eta^k}{\Gamma(n)} \epsilon_{n,k} = \mathbf{S}(n, k; \sigma) \frac{e^\eta}{\sigma \Gamma(n)} \sum_{i=0}^{n-1} \binom{n-1}{i} (-1)^i \eta^{\frac{i}{\sigma}} \Gamma(k - \frac{i}{\sigma}; \sigma)$$

$\mathbf{S}(n, k; \sigma)$  generalized Stirling numbers of the first kind

## The model

$$T_i = e^{-x_i' \beta} \cdot V_i, \quad i = 1, \dots, n,$$

$$V_i | \theta_i \stackrel{ind}{\sim} k(\cdot; \theta_i) \quad \Theta \subset \mathbb{R}^2 \text{ parametric space}$$

$$\theta_i | G \stackrel{iid}{\sim} G,$$

$$G \sim GG(\sigma, \eta, G_0), \quad G_0(\cdot) := \mathbb{E}(G(\cdot)), \quad G_0 \text{ diffuse}$$

$$\beta \perp G, \quad \beta \sim \pi(\beta)$$

$$(\sigma, \eta) \sim \pi(\sigma, \eta)$$

$k(\cdot; \vartheta_1, \vartheta_2)$  gamma density with mean  $\vartheta_1/\vartheta_2$

$G_0$   $\text{gamma}(\omega_1, \gamma_1) \times \text{gamma}(\omega_2, \gamma_2)$

## Univariate marginal distribution of the error $V$

If  $\omega_1 = \omega_2 = 1$ :  $f_V(v) = \frac{\gamma_1 \gamma_2}{v(v + \gamma_2)(\gamma_1 + \log(\frac{v+\gamma_2}{v}))^2}$  ( $v > 0$ ), but

$$EV = +\infty$$

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**median regression model**

Prior information: median and IQR as functions of hyperparameters  $(\gamma_1, \gamma_2)$

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Prior information: median and IQR as functions of hyperparameters  $(\gamma_1, \gamma_2)$

If  $\omega_2 > j$ :  $\mathbb{E}(V^j) < +\infty$ ; in particular

$$\mathbb{E}(V) = \frac{\omega_1 \gamma_2}{(\omega_2 - 1) \gamma_1}, \quad \omega_2 > 1$$

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$$\mathbb{E}(V) = \frac{\omega_1 \gamma_2}{(\omega_2 - 1) \gamma_1}, \quad \omega_2 > 1$$

**mean regression model**

Prior information: first  $j$  moments as functions of hyperparameters  $(\gamma_1, \gamma_2)$



## Posterior estimates

Since  $T_i = e^{-x_i' \beta} \cdot V_i, i = 1, \dots, n$

$$\hat{f}_{T_{n+1}}(t|T_1, \dots, T_n) \longleftrightarrow \hat{f}_{V_{n+1}}(v|V_1, \dots, V_n, \underline{\beta})$$
$$\hat{\underline{\beta}} = \mathbb{E}(\underline{\beta}|T_1, \dots, T_n) \longleftrightarrow \mathbb{E}(\underline{\beta}|V_1, \dots, V_n)$$

Moreover

$$\hat{f}_{V_{n+1}}(v|V_1, \dots, V_n, \underline{\beta}) = \int \left( \int_{\Theta} k(v; \theta) G(d\theta) \right) \mathcal{L}(dG|\theta_1, \dots, \theta_n, \underline{\beta}) \mathcal{L}(d\underline{\theta}|V_1, \dots, V_n, \underline{\beta})$$

integrating out  $G = \int f_{V_{n+1}}(v|\underline{\theta}, \underline{\beta}) \mathcal{L}(d\underline{\theta}|\underline{V}, \underline{\beta})$  (1)

$\mathcal{L}(d\underline{\theta}|\underline{V})$  and  $\mathcal{L}(d\underline{\beta}|\underline{V})$  in (1): via a **Polya urn Gibbs sampler**

$$f_{V_{n+1}}(v|\underline{\theta}, \underline{\beta}) = w_0(n, k; \sigma, \eta) f_V(v) + w_1(n, k; \sigma, \eta) \sum_{j=1}^k (n_j - \sigma) k(v; \theta_j^*)$$

prior marginal distribution of  $V$  :  $f_V(v) = \int_{\mathbb{R}^+ \times \mathbb{R}^+} k(v; \vartheta_1, \vartheta_2) G_0(d\vartheta_1, d\vartheta_2)$

## Algorithms for posterior estimates

$$\hat{f}_{V_{n+1}}(v|V_1, \dots, V_n, \underline{\beta}) = \int \left( \int_{\Theta} k(v; \theta) G(d\theta) \right) \mathcal{L}(dG|\underline{\theta}, \underline{\beta}) \mathcal{L}(d\underline{\theta}|\underline{V}, \underline{\beta}) \quad (2)$$

(2) is fundamental in the GWCR algorithm (Ishwaran-James, 2003), when independent draws from  $\mathcal{L}(dG|\underline{\theta})$  are available: **Importance sampler algorithm** (iid draws from the importance distribution)

**Polya urn sequential importance sampler**: sequential draw for  $(\theta_1, \dots, \theta_n)$

$$\theta_1 \sim \mathcal{L}(d\theta_1|V_1)$$

$$\theta_{r+1} \sim w_0^*(r, k(r); \sigma, \eta) \mathcal{L}(d\theta_{r+1}|V_{r+1}) + \sum_{j=1}^{k(r)} w_1^*(r, k(r); \sigma, \eta) \delta_{\theta_{j,r}^*}, r = 2, \dots, n$$

Many  $w_0$  and  $w_1$  must be computed: Polya urn SIS is very *expensive*

**Accelerated Polya urn Gibbs sampler**: (i) integrating out  $G$  (ii) the update rule for  $\underline{\beta}$  is simple

## Prior for the regression parameters

Reparameterization:  $\alpha_j = e^{\beta_j}, j = 1, \dots, p$

$\alpha_j \stackrel{ind}{\sim} \text{gamma}(\alpha_{1j}^*, \alpha_{2j}^*), j = 1, \dots, p$

the full conditional posterior distributions of the  $\alpha_j$ 's associated to a binary covariate are still gamma

# Polya urn Gibbs sampler

Posterior estimates:

$$\hat{f}_{V_{n+1}|\underline{V}}(v | data) = \frac{1}{J} \sum_{j=1}^J f_{V_{n+1}}(v | data, \underline{\theta}^{(j)})$$

$$\hat{S}_{T_{n+1}|\underline{x}, \underline{T}}(t | x, data) = \frac{1}{J} \sum_{j=1}^J S_{V_{n+1}}\left(\prod_{i=1}^p (\alpha_i^{(j)})^{x_i} t \mid data, \underline{\theta}^{(j)}\right)$$

STEP 1 : draw  $\underline{\theta}^{(j+1)}$  from  $\mathcal{L}(d\underline{\theta}|\underline{\alpha}^{(j)}, data)$  via a

**Polya urn scheme with an *acceleration step*:**

state space:  $(\underline{c}, \underline{\theta})$  where  $\underline{\theta} = (\theta_1, \dots, \theta_n)$  and  $\underline{c} = (c_1, \dots, c_n)$  labels from 1 to  $k(n)$  ( $\neq$  distinct value in  $\underline{\theta}$ ) such that  $c_i = c_j \Leftrightarrow \theta_i = \theta_j$

$\underline{c} \xleftrightarrow{\text{bijection}} \Pi_n = \{C_1, \dots, C_{k(n)}\}, C_j := \{i : \theta_i = \theta_j^*\} = \{i : c_i = j\}$

## MCMC algorithm

### Completely observed data

STEP 1 (a): update pairs  $(c_i, \theta_i)$ , for  $i = 1, \dots, n$  from  $[(c_i, \theta_i) \mid c_{-i}, \underline{\theta}_{-i}, data]$

$$= [\theta_i \mid c_i, c_{-i}, \underline{\theta}_{-i}, data] \times [c_i \mid c_{-i}, \underline{\theta}_{-i}, data]$$

generalized Polya urn scheme

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generalized Polya urn scheme

STEP 1 (b): block update the sub-vectors of  $\underline{\theta}$  formed by elements with the same value (equivalent to updating the  $\theta_j^*$  values): **acceleration step**

**Remark:** in (a), when  $\omega_1 = \omega_2 = 1$ ,  $f_V$  is easy to evaluate (**conjugate prior**); otherwise: substitute  $G_0$  in  $f_V$  with the empirical distribution of a random sample of size  $m$  from  $G_0$  (**augmentation step**)

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STEP 2: generate  $\underline{\alpha}^{(j+1)}$  from  $\mathcal{L}(d\underline{\alpha} \mid \underline{\theta}^{(j+1)}, data)$ : for the  $\alpha_j$ 's not corresponding to binary covariates a Metropolis step is required

similar to Neal (2000)

## MCMC algorithm

STEP 1 (a): update pairs  $(c_i, \theta_i)$ , for  $i = 1, \dots, n$  from  $[(c_i, \theta_i) \mid c_{-i}, \underline{\theta}_{-i}, data]$

$$= [\theta_i \mid c_i, c_{-i}, \underline{\theta}_{-i}, data] \times [c_i \mid c_{-i}, \underline{\theta}_{-i}, data]$$

generalized Polya urn scheme

STEP 1 (b): block update the sub-vectors of  $\underline{\theta}$  formed by elements with the same value (equivalent to updating the  $\theta_j^*$  values): **acceleration step**

**Remark:** in (a), when  $\omega_1 = \omega_2 = 1$ ,  $f_V$  is easy to evaluate (**conjugate prior**); otherwise: substitute  $G_0$  in  $f_V$  with the empirical distribution of a random sample of size  $m$  from  $G_0$  (**augmentation step**)

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similar to Neal (2000)

STEP 3: augmentation step for **censored data** - unobserved survival times are sampled one at a time from their full conditional distribution truncated at their censoring points



## Choice of $(\sigma, \eta)$

Simulated dataset for density estimation

$$V_i | \theta_i \stackrel{iid}{\sim} k(\cdot; \theta_i), \quad i = 1, \dots, n$$

$$\theta_i | G \stackrel{iid}{\sim} G,$$

$$G \sim GG(\sigma, \eta, G_0), \quad G_0(\cdot) := \mathbb{E}(G(\cdot)), \quad G_0 \text{ diffuse} \quad (3)$$

$$(\sigma, \eta) \sim \pi(\sigma, \eta) \quad (\sigma, \eta) \text{ control the variance of } G \text{ from the mean } G_0$$

$(\sigma, \eta)$  fixed or random ?

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$(\sigma, \eta)$  **fixed or random ?**

test the fit of the  $GG(\sigma, \eta, G_0)$ -mixture w.r.t.  $(\sigma, \eta)$ : comparison between

$$\mathcal{M}_0 : V_1, \dots, V_n \stackrel{iid}{\sim} f_V(\cdot) = \int k(\cdot; \theta) G_0(d\theta) \quad \mathcal{M}_1 : GG(\sigma, \eta, G_0) - \text{mixture} \quad (3)$$

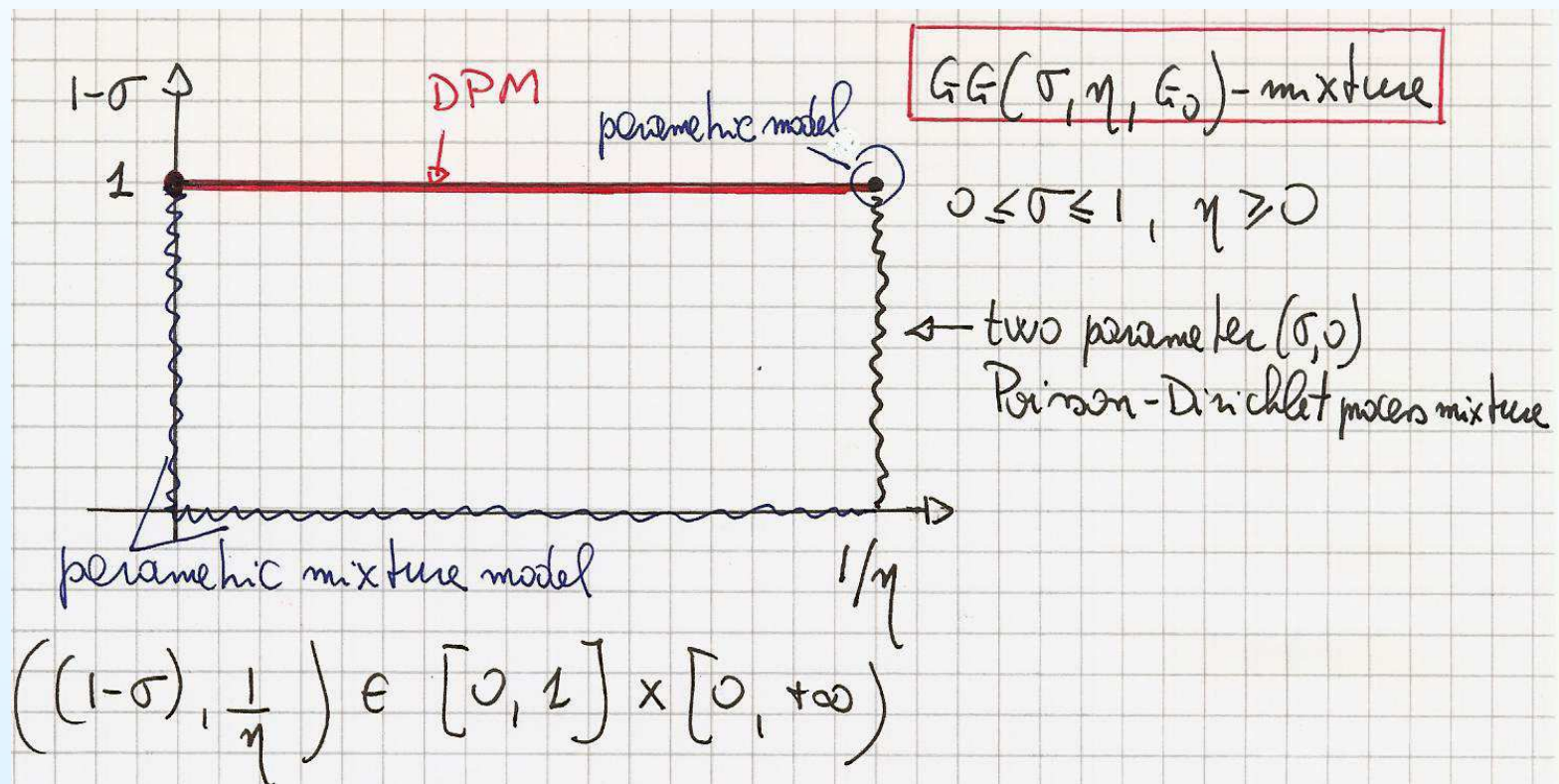
((3) when  $\sigma = 1$ ; **parametric mixture**)

$\mathcal{M}_1$  is *centered* on  $\mathcal{M}_0$ , *enlarging* it by adding extra parameters  $(\sigma, \eta)$  which control the variance from the centering distribution  $G_0$

# Bayes factors for $GG(\sigma, \eta, G_0)$ -mixtures

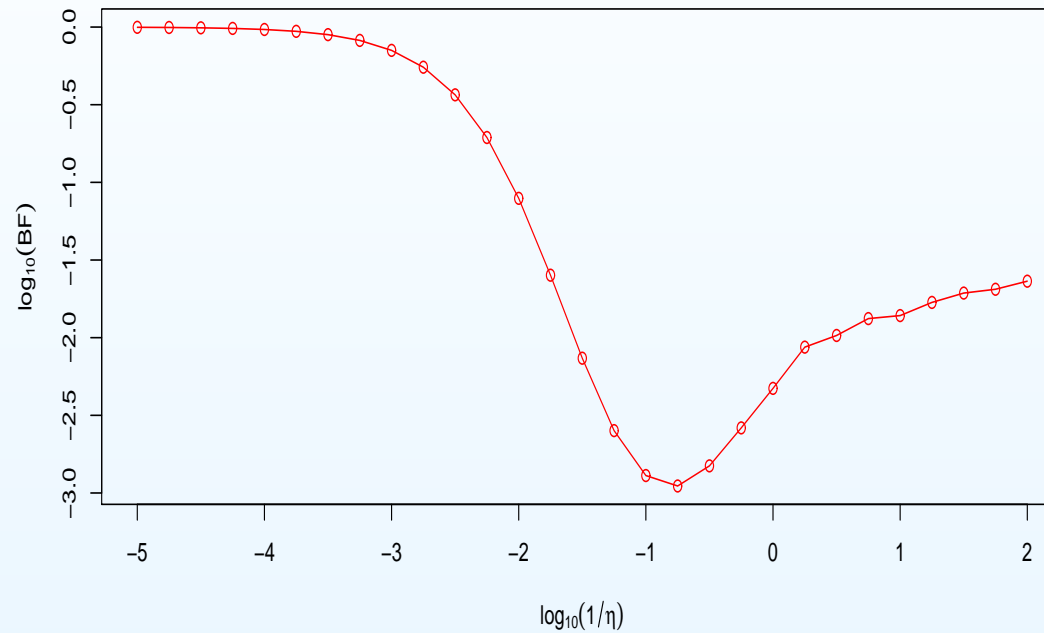
$$BF(\underline{v}; \sigma, \eta) := \frac{m_0(\underline{v})}{m_1(\underline{v}; \sigma, \eta)}$$

$\min_{(\sigma, \eta)} BF(\underline{v}; \sigma, \eta) =: BF(\underline{v}; \hat{\sigma}, \hat{\eta})$  indicates the parameters  $(\sigma, \eta)$  most favorable to the alternative, a smaller minimum indicating a better fit for the corresponding nonparametric mixture



## Bayes factors for $GG(\sigma, \eta, G_0)$ -mixtures

**Plot of  $\log_{10}(BF(\underline{v}; 0, \eta))$  as a function of  $\log_{10}(\frac{1}{\eta})$**



For any  $0 \leq \sigma < 1$ :

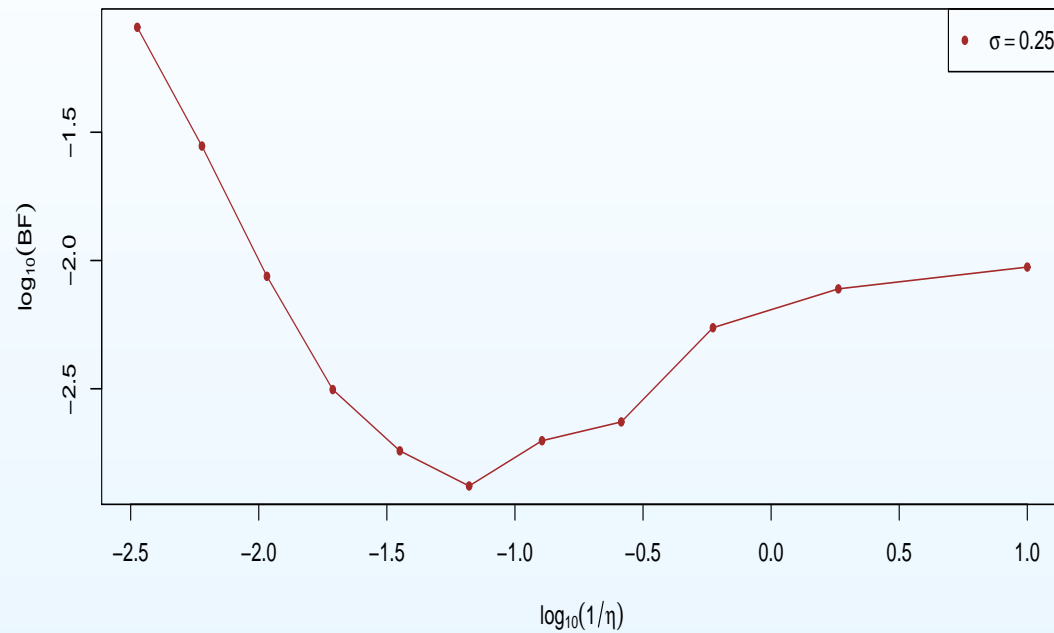
$\frac{1}{\eta} \rightarrow 0$  :  $\text{Var}(G(B)) \rightarrow 0$  and  $G \rightarrow G_0 \Rightarrow m_1(\underline{v}) \simeq m_0(\underline{v})$  and  $BF(\underline{v}) \simeq 1$

$\frac{1}{\eta} \rightarrow +\infty$  :  $(\tau \rightarrow 0)$   $G \rightarrow$  Pois-Dir process 2 parameters  $(\sigma, 0)$ ,  $BF(\underline{v}) \rightarrow h(\sigma)$

$BF$ s between these extremes: (i) increasing functions of  $\frac{1}{\eta}$  or (ii) first decreasing and then increasing

## Bayes factors for $GG(\sigma, \eta, G_0)$ -mixtures

Plot of  $\log_{10}(BF(\underline{v}; 0.25, \eta))$  as a function of  $\log_{10}(\frac{1}{\eta})$



For any  $0 \leq \sigma < 1$ :

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## Bayes factors for $GG(\sigma, \eta, G_0)$ -mixtures

Computation of  $BF$ s: via a SIS algorithm (Basu-Chib 2003, for DPM)

Computation of **many** weights  $(w_0(r, k(r); \sigma, \eta), w_1(r, k(r); \sigma, \eta))$ ,  
 $k(r) = 1, \dots, r, r = 2, \dots, n$  via **multiple precision arithmetics** (sums of  
several incomplete gamma functions)

Computations and MCMC simulations via R calling PARI/C library (as  
suggested by R. Mena)

When  $\eta$  is *small*, computation of  $BF$ s via SIS algorithm is tremendously slow

As an *exploratory* example we consider a simulated sample of size  $n = 25$

$\sigma$	0	0.1	0.25	0.5	0.75
$\min_{\eta} \log_{10}(BF(\underline{v}; \sigma, \eta))$	<b>-2.955</b>	<b>-2.943</b>	-2.879	-2.618	-2.159
$\hat{\eta}$	$\widehat{\kappa(\Theta)} = 5.623$	48.790	15.101	3.991	0.550

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$(\sigma, \eta) \sim \pi?$

$\eta$  fixed (not too small) and  $\sigma \sim \text{Beta}(a_0, b_0)$  (discretization on  
 $\{0.01, 0.02, \dots, 0.99\}$  is computationally convenient) such that  $\mathbb{E}(K_n)$   
reflects prior opinions

## Example 1 - Density estimation

- $n = 100$  data simulated from

$$0.2 \cdot \text{gamma}(40, 20) + 0.6 \cdot \text{gamma}(6, 1) + 0.2 \cdot \text{gamma}(200, 20)$$

- focus on *density estimation* and *detection of the number of cluster* when  $V \sim GG(\sigma, \eta, G_0)$ -mixtures
- $\omega_1 \in \{1, 3, 10\}$ ,  $\omega_2 = 2$ ,  $\gamma_2 \in \{0.01, 0.1, 1, 10\}$ , assigning **prior mean**  $\mathbb{E}(V) = 6$

$$\sigma \sim \text{discretized Beta}(1, 1) \quad \eta = 1.5 : \quad \mathbb{E}(K_n) = 30$$

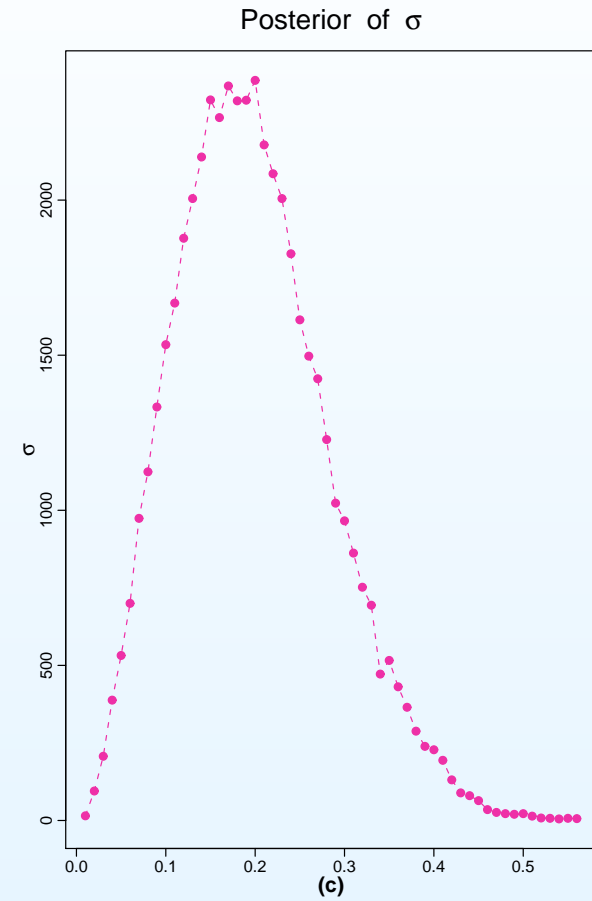
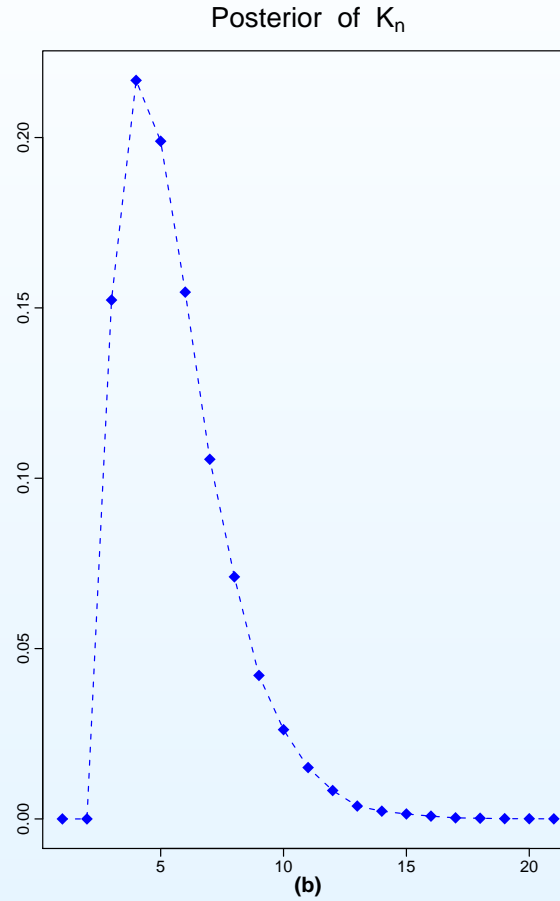
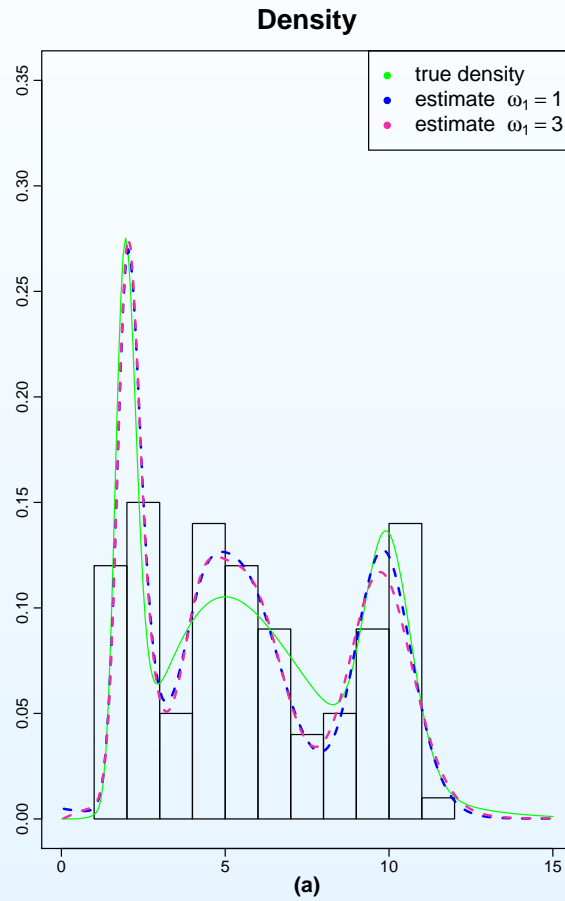
$$\sigma \sim \text{discretized Beta}(1, 7) \quad \eta = 4.5 : \quad \mathbb{E}(K_n) = 6$$

- $\omega_1 = \omega_2 = 1$  (**conjugate prior**),  $\gamma_2 \in \{0.01, 0.1, 1, 10\}$ , assigning **prior median**  $\text{med}(V) = 5.67$

$(\sigma, \eta)$  as before

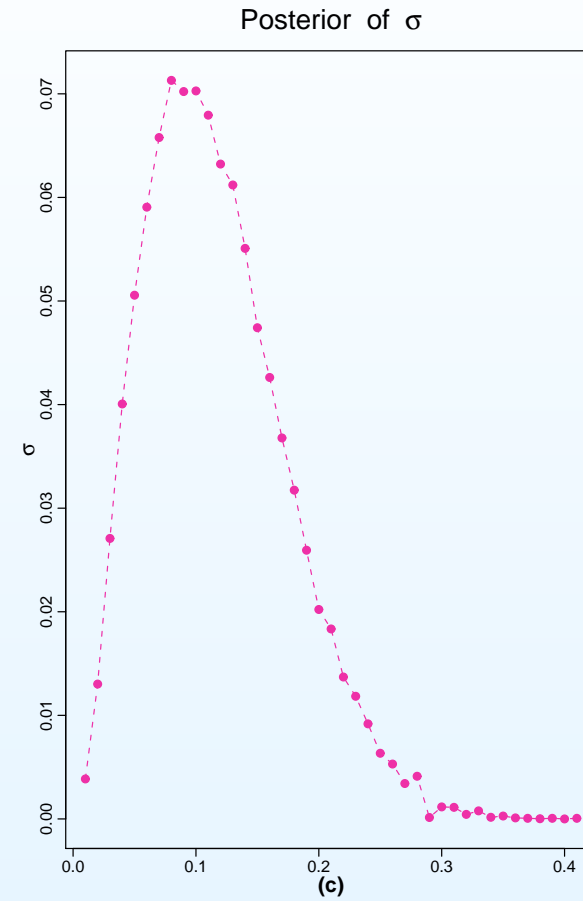
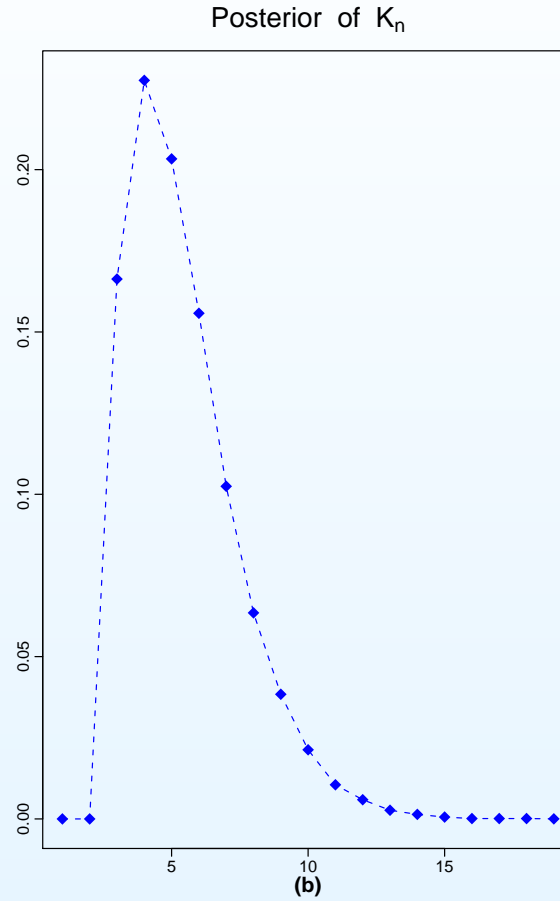
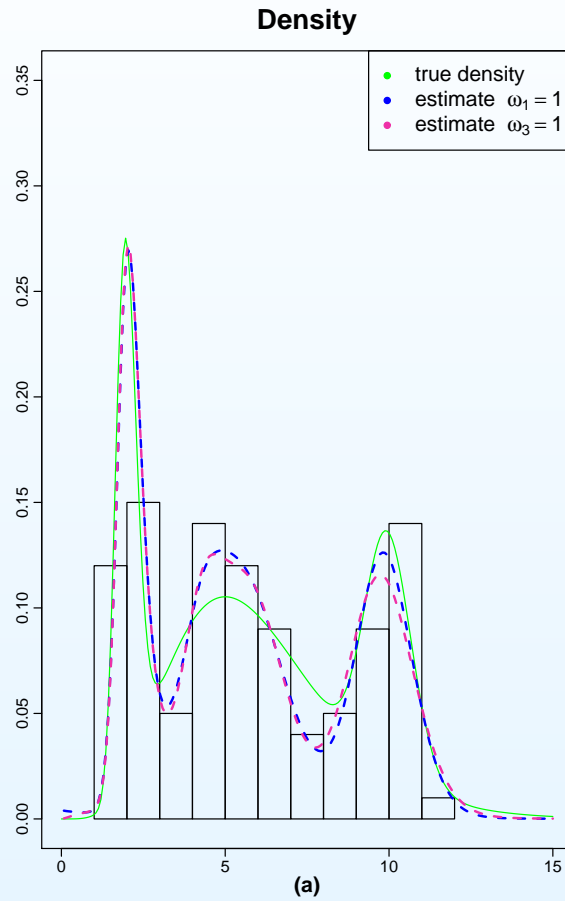


# Example 1 - Density Estimation



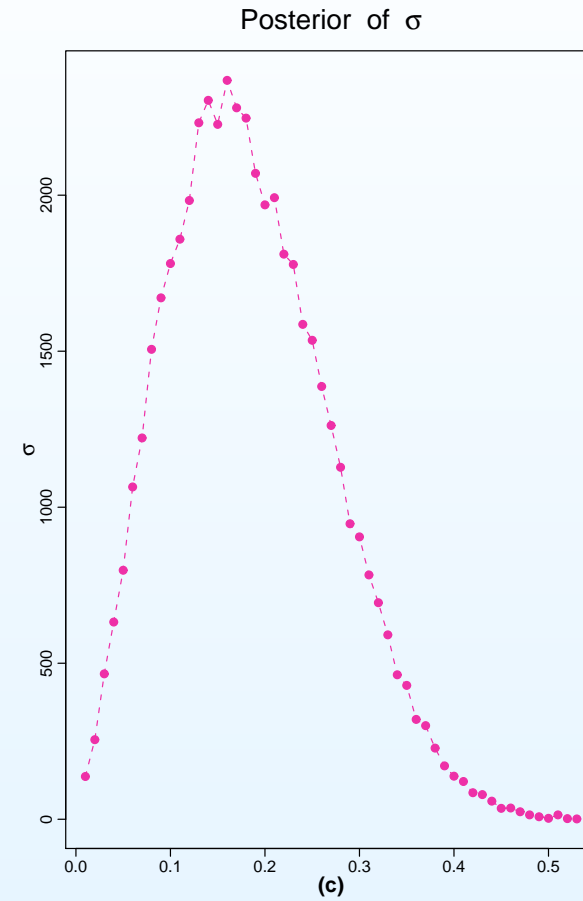
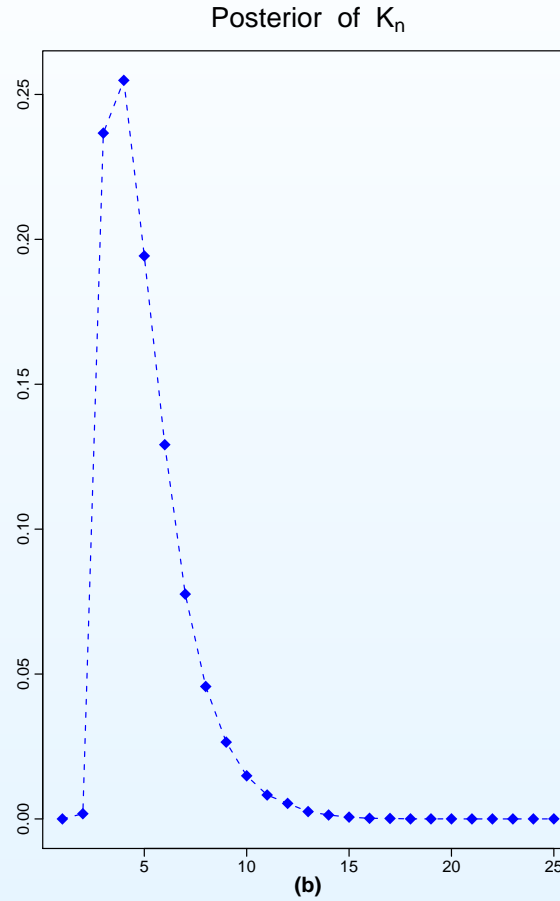
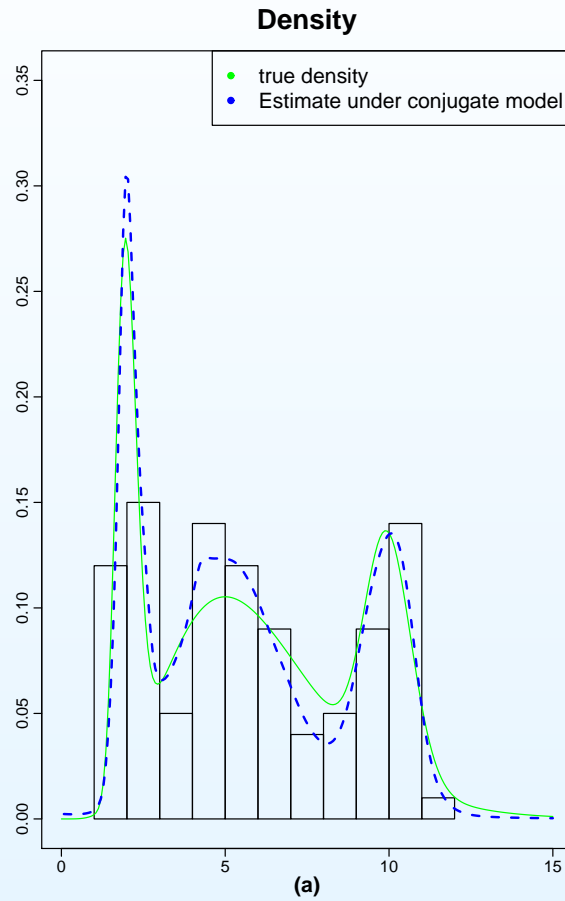
$\omega_2 = 2$  ( $G_0$  non-conjugate),  $\gamma_2 = 0.1$ ,  $\sigma \sim \text{Beta}(1,1)$  and  $\mathbb{E}(K_n) = 30$

# Example 1 - Density Estimation



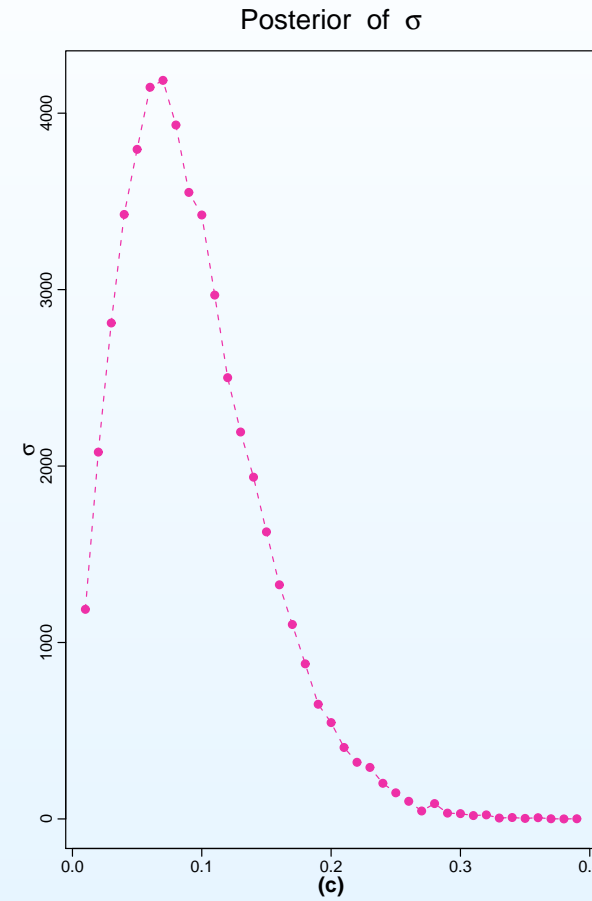
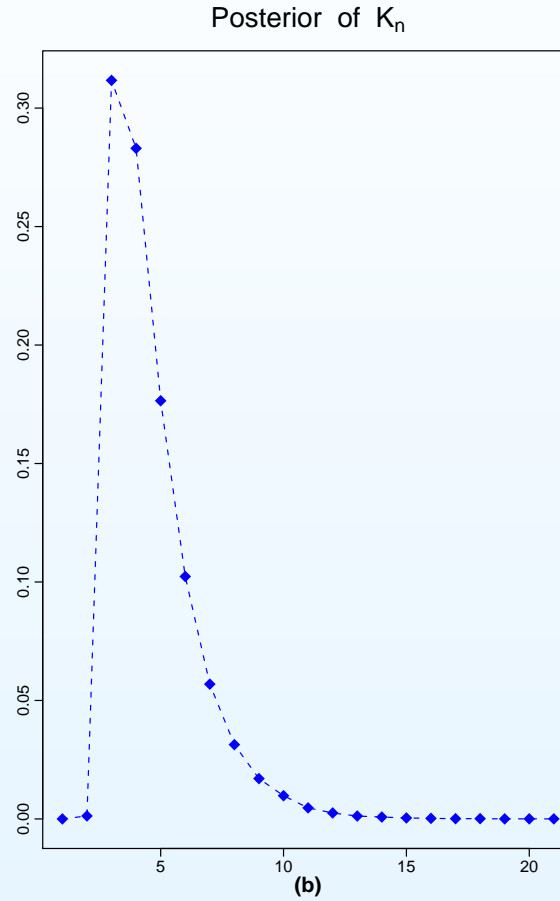
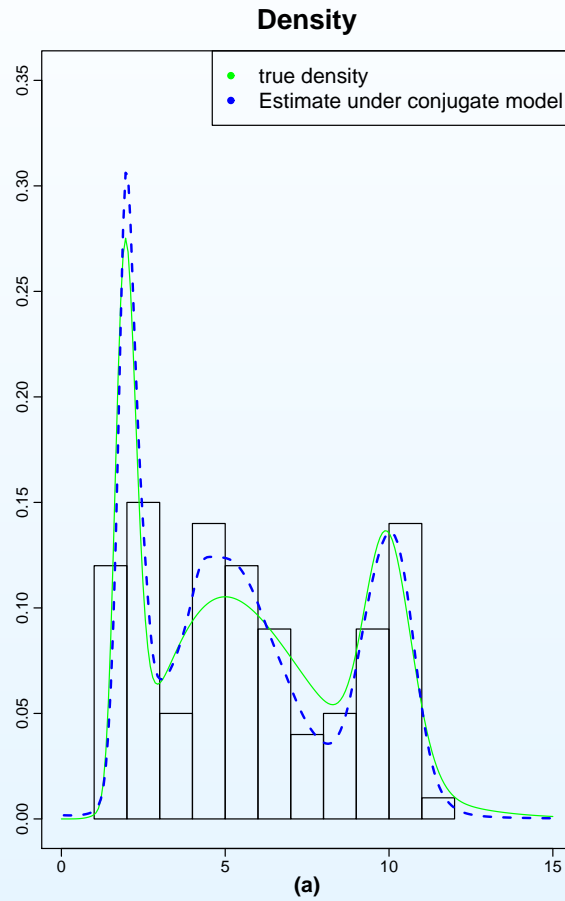
$\omega_2 = 2$  ( $G_0$  non-conjugate),  $\gamma_2 = 0.1$ ,  $\sigma \sim \text{Beta}(1,7)$  and  $\mathbb{E}(K_n) = 6$

# Example 1 - Density Estimation



$\omega_1 = \omega_2 = 1$  ( $G_0$  conjugate),  $\gamma_2 = 0.01$ ,  $\sigma \sim \text{Beta}(1,1)$  and  $\mathbb{E}(K_n) = 30$

# Example 1 - Density Estimation

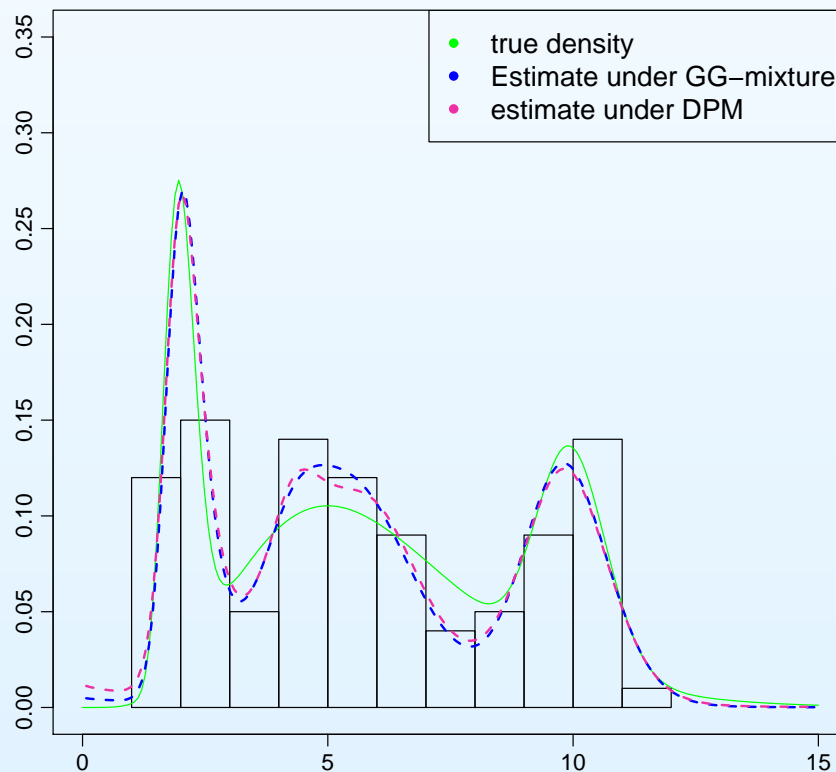


$\omega_1 = \omega_2 = 1$  ( $G_0$  conjugate),  $\gamma_2 = 0.01$ ,  $\sigma \sim \text{Beta}(1,7)$  and  $\mathbb{E}(K_n) = 6$

## Example 1 - Comparison with DPM - random total mass

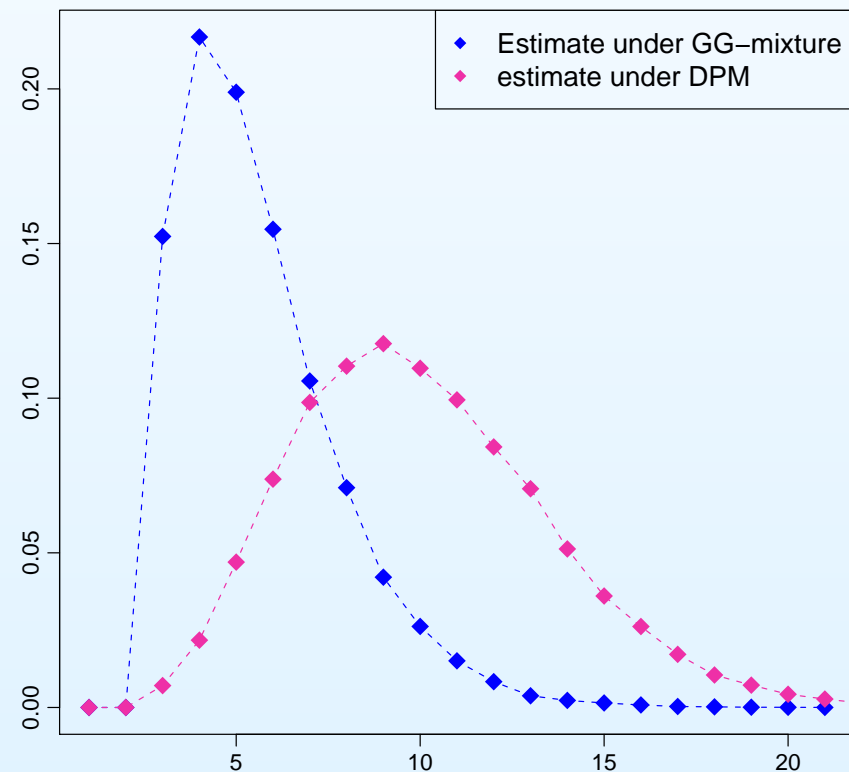
- $V \sim GG(\sigma, \eta, G_0): \omega_1 = 1, \omega_2 = 2, \gamma_2 = 0.1, \mathbb{E}(V) = 6$   
 $\sigma \sim \text{discretized Beta}(1, 1), \mathbb{E}(K_n) = 30$
- $V \sim GG(0, \eta, G_0) = DPM(aG_0)$ , same  $G_0$  and  $a \sim \text{gamma}(3.1, 0.2)$ ,  
 $\mathbb{E}(K_n) = 30$

Density



(a)

Posterior of  $K_n$



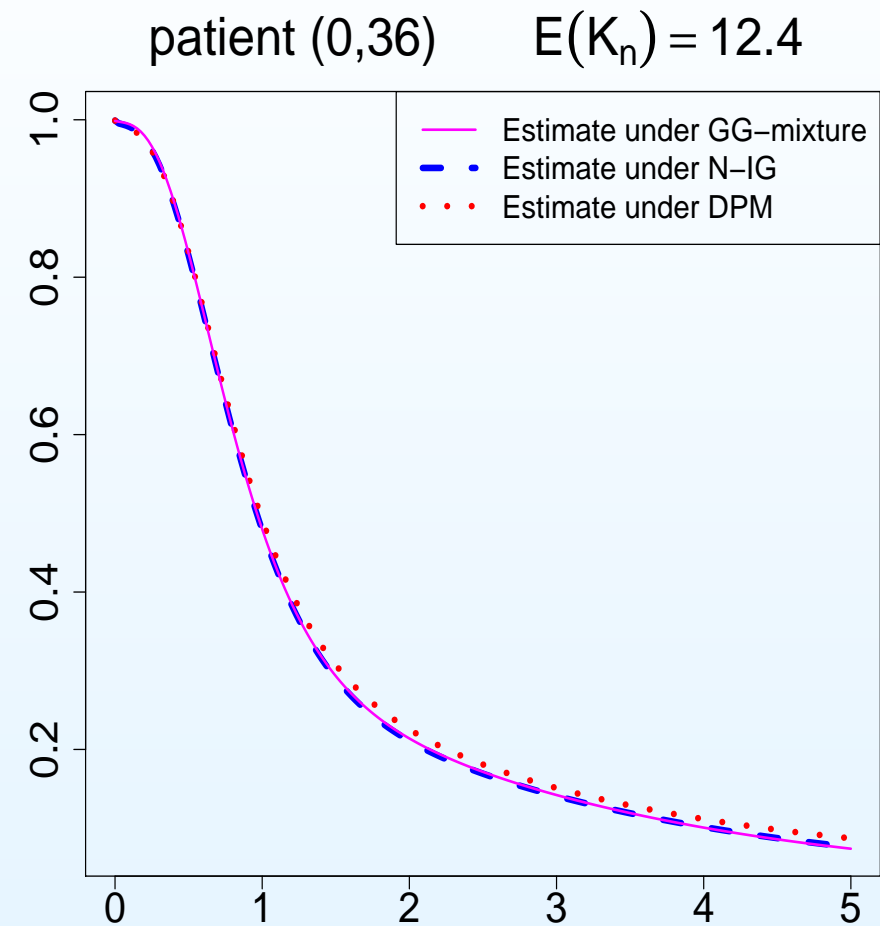
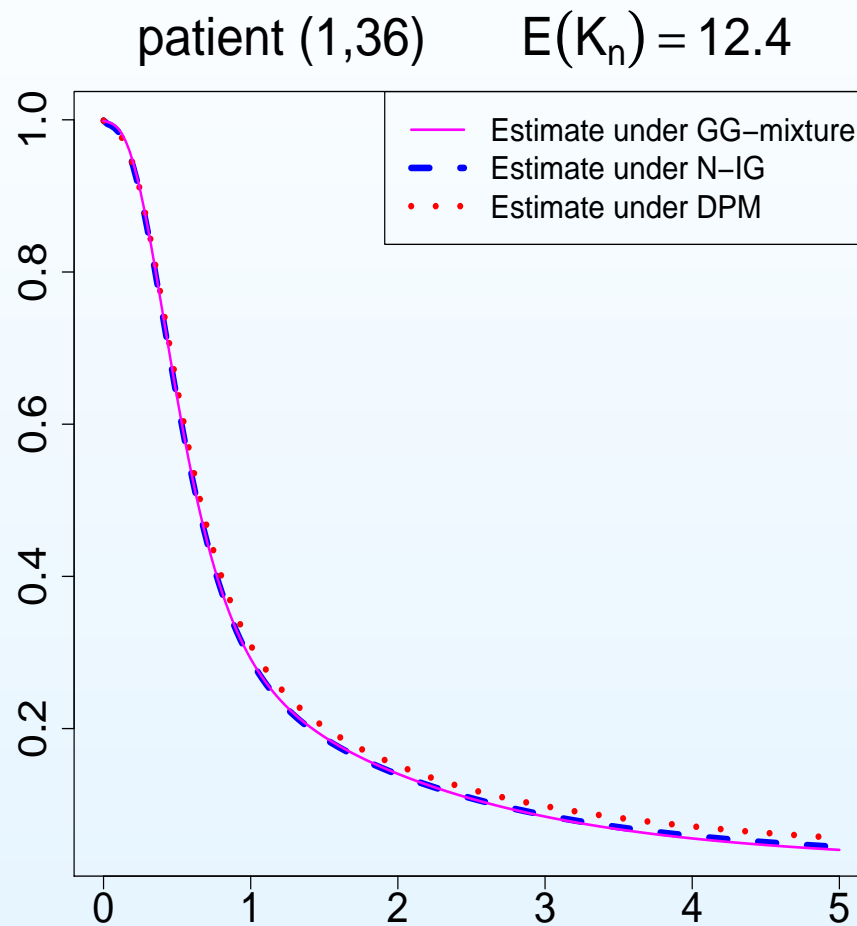
(b)

## Example 2 - Dataset with censoring

- $n = 121$  survival times (in thousands of days) of patients suffering from small-cell lung cancer; Walker & Mallick ('99), Kottas & Gelfand ('01), Hanson ('06)
- 2 treatments: A (62 patients) and B (59 patients)
- 23 patients right-censored
- **2 covariates**: treatment ( $x_1 = 0$  corresponds to A) and entry age; 2 regression parameters  $(\alpha_1, \alpha_2)$ , no intercept
- estimates (posterior mean) of  $(\alpha_1, \alpha_2)$ , 90% credible intervals, and estimates of the survival functions
- $\omega_1 = \omega_2 = 1$ ,  $\gamma_2 \in \{0.01, 0.1, 1, 10\}$ ,  $median(V) = 2.44$

$\sigma \sim \text{discretized Beta}(1, 4)$     $\eta = 5.77$  :    $\mathbb{E}(K_n) = 12.41$  (see EX 3 in Argiento et al., 2007)

## Example 2 - Survival functions



Estimated survival functions under the  $GG(\sigma, \eta, G_0)$ -mixture prior for 2 patients for small-cell lung cancer dataset when  $m = 2.44$  and  $\gamma_2 = 1$ .

## Example 2 - Estimates of regression parameters

estimates (posterior mean) of  $(\alpha_1, \alpha_2)$  and 90% credible interval for hyperparameters as specified before

$$1.529(1.229, 1.850); 1.015(1.006, 1.024)$$

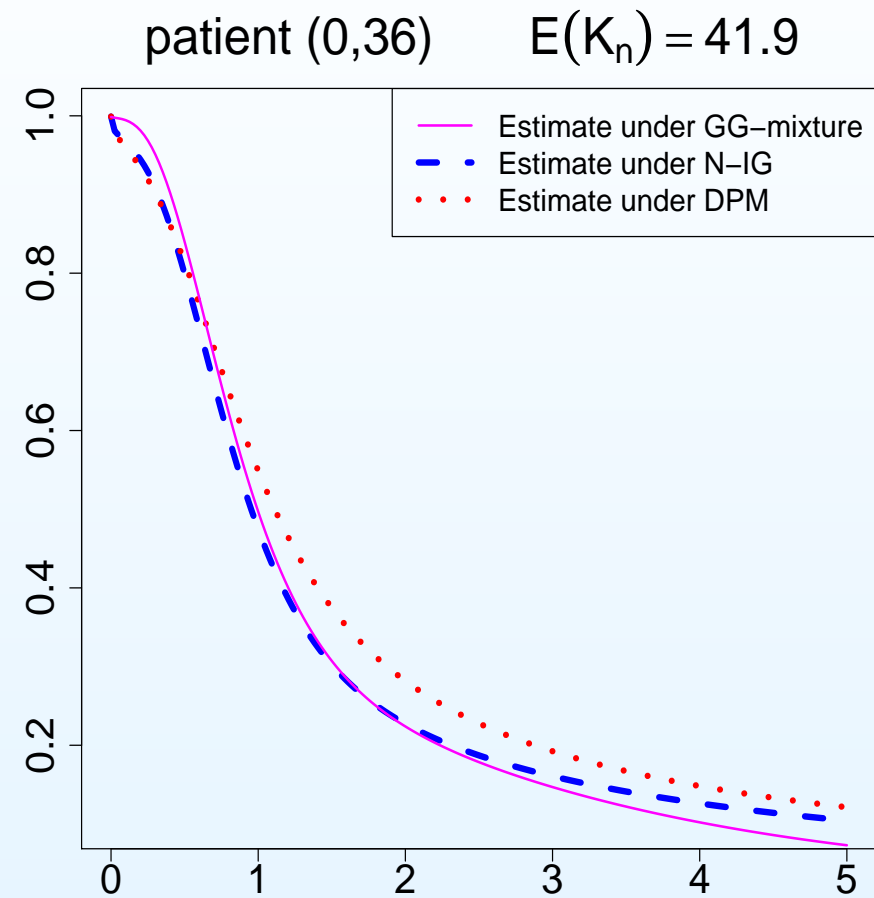
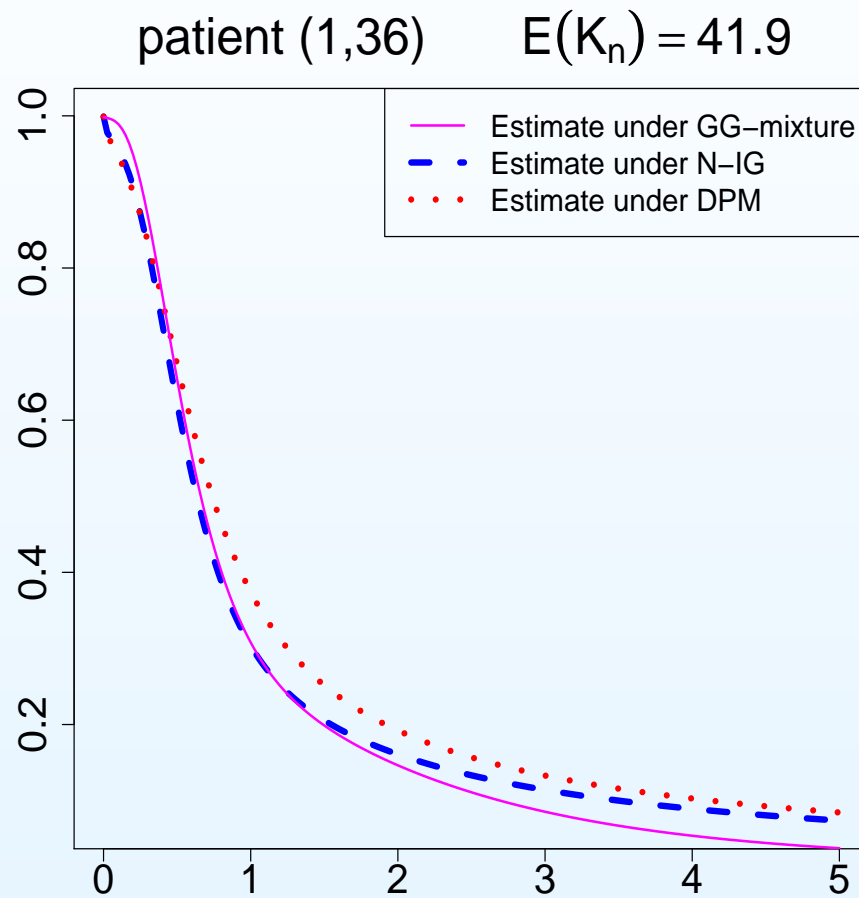
$$\mathbb{E}(\sigma|data) = 0.093$$

**Robustness analysis** with respect to  $\gamma_2$  (“bandwidth” parameter) and  $\sigma$

$(\hat{\alpha}_1, \hat{\alpha}_2)$	GG ( $\sigma$ random)	N-IG( $\sigma = 1/2$ )	DPM( $\sigma = 0$ )
$\gamma_2 = 0.1$	(1.488,1.010)	(1.149,1.011)	(1.437,1.772)
$\gamma_2 = 1$	(1.529,1.015)	(1.533,1.015)	(1.515,1.016)



## Example 2 - Survival functions



Estimated survival functions under the  $GG(\sigma, \eta, G_0)$ -mixture prior for 2 patients for small-cell lung cancer dataset when  $m = 2.44$  and  $\gamma_2 = 1$ ,  $E(K_n) = 41.93$ ,  $\sigma \sim \text{discretized } Beta(1, 1)$ .

## Comparison between two $GG(\sigma, \eta, G_0)$ -mixture

Predictive fit measure via a cross-validation approach “in the spirit” of Gelfand, Dey, Chang ('92) under the **median regression model**

$(t_1, \dots, t_n)$  survival times

$T_j \mid \underline{T}^{(-j)}, j \in S^* =$  index set of non-censored data

$\tilde{y}_j, j \in S^*$ , estimated median from the predictive distribution  $T_j \mid \underline{T}^{(-j)}$

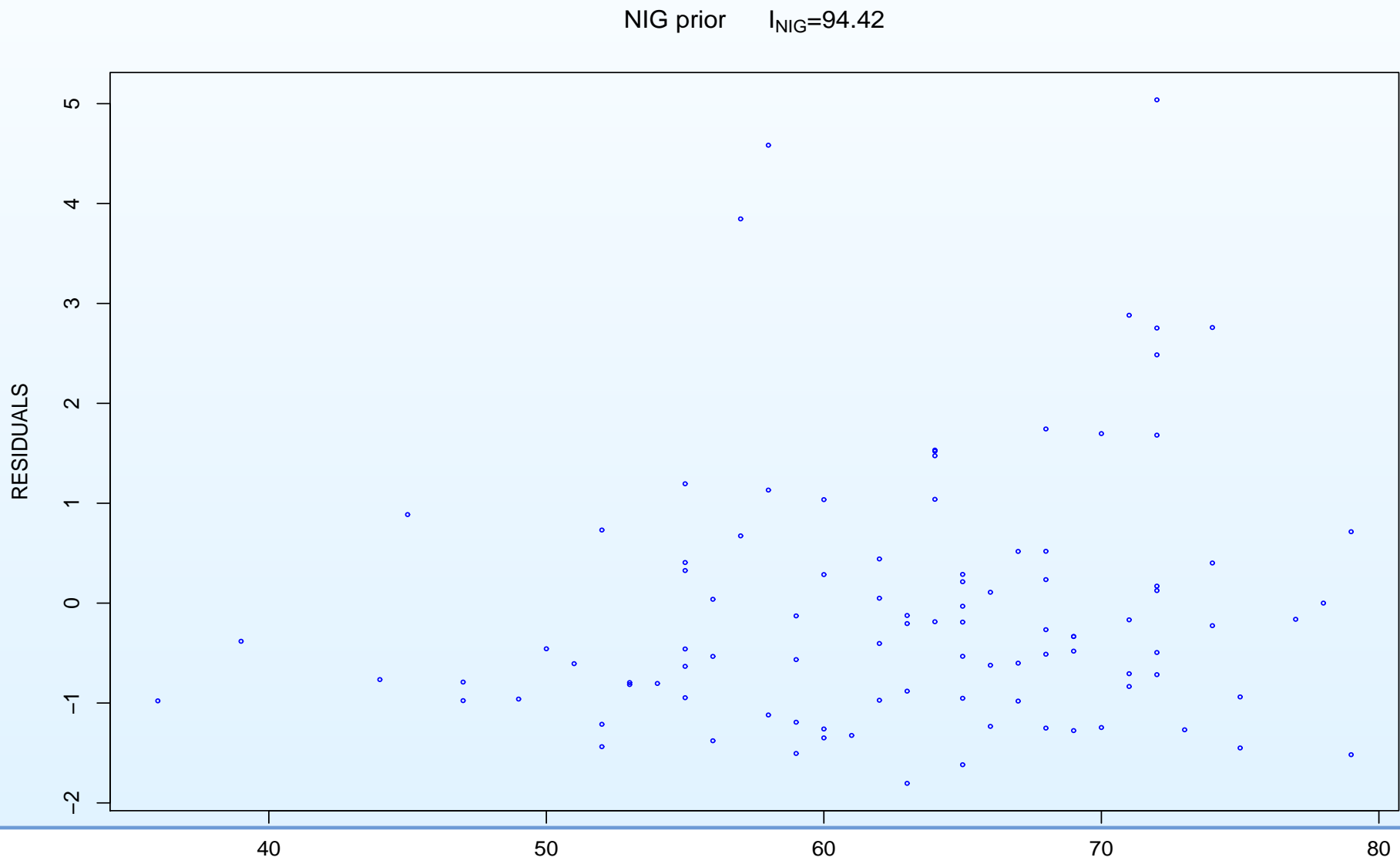
$t_j - \tilde{y}_j$ : **residual**

$\frac{t_j - \tilde{y}_j}{\text{med}_{T_j \mid \underline{T}^{(-j)}} |Y_j - \tilde{y}_j|}$ : **standardized residual**

$I := \sum_j \frac{|t_j - \tilde{y}_j|}{\text{med}_{T_j \mid \underline{T}^{(-j)}} |Y_j - \tilde{y}_j|}$ : **predictive fit index**

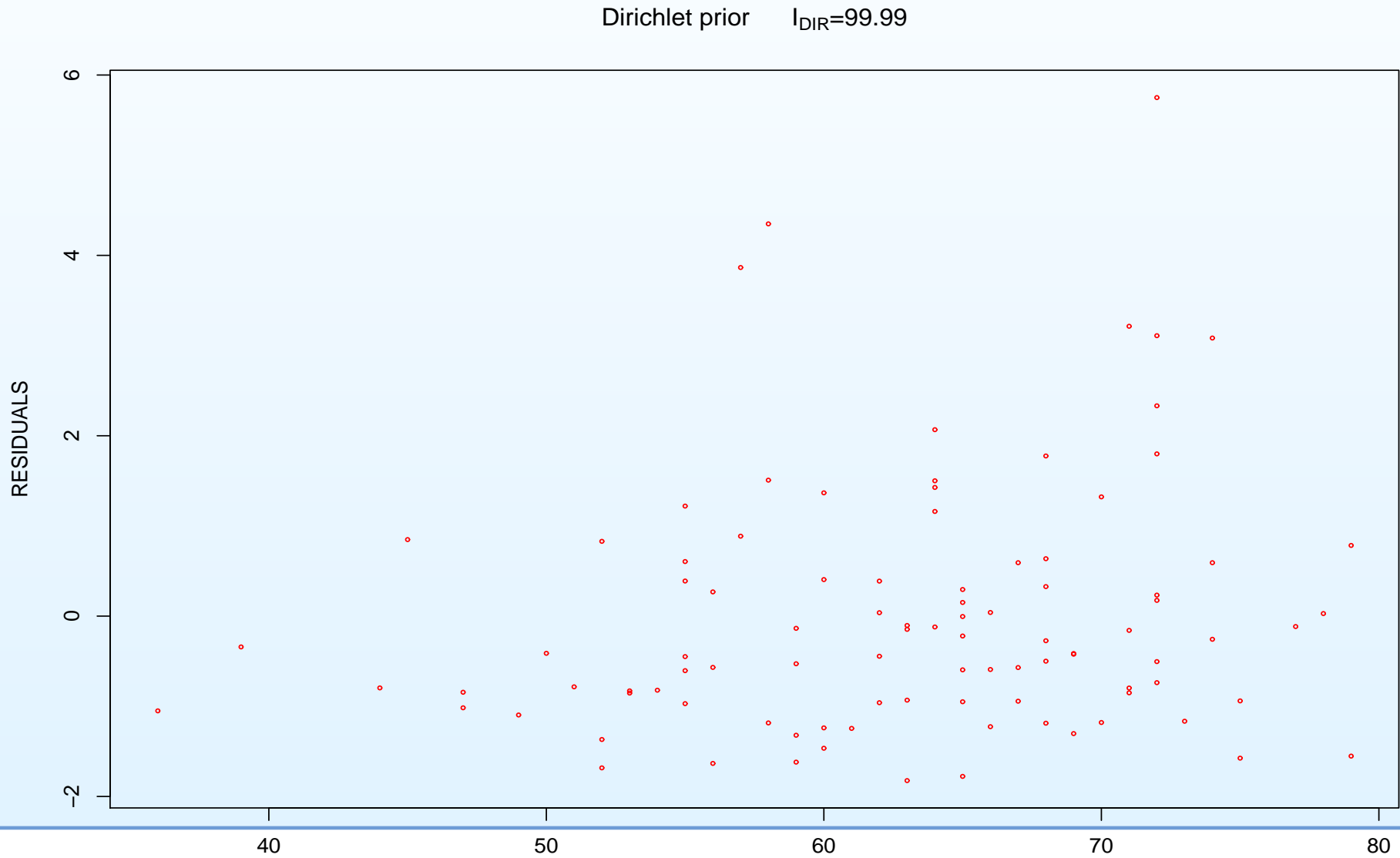
## Example 2 - Standardized Residuals

$\sigma = 1/2$ : AFT when the error  $V \sim \text{NIG-mixture}$

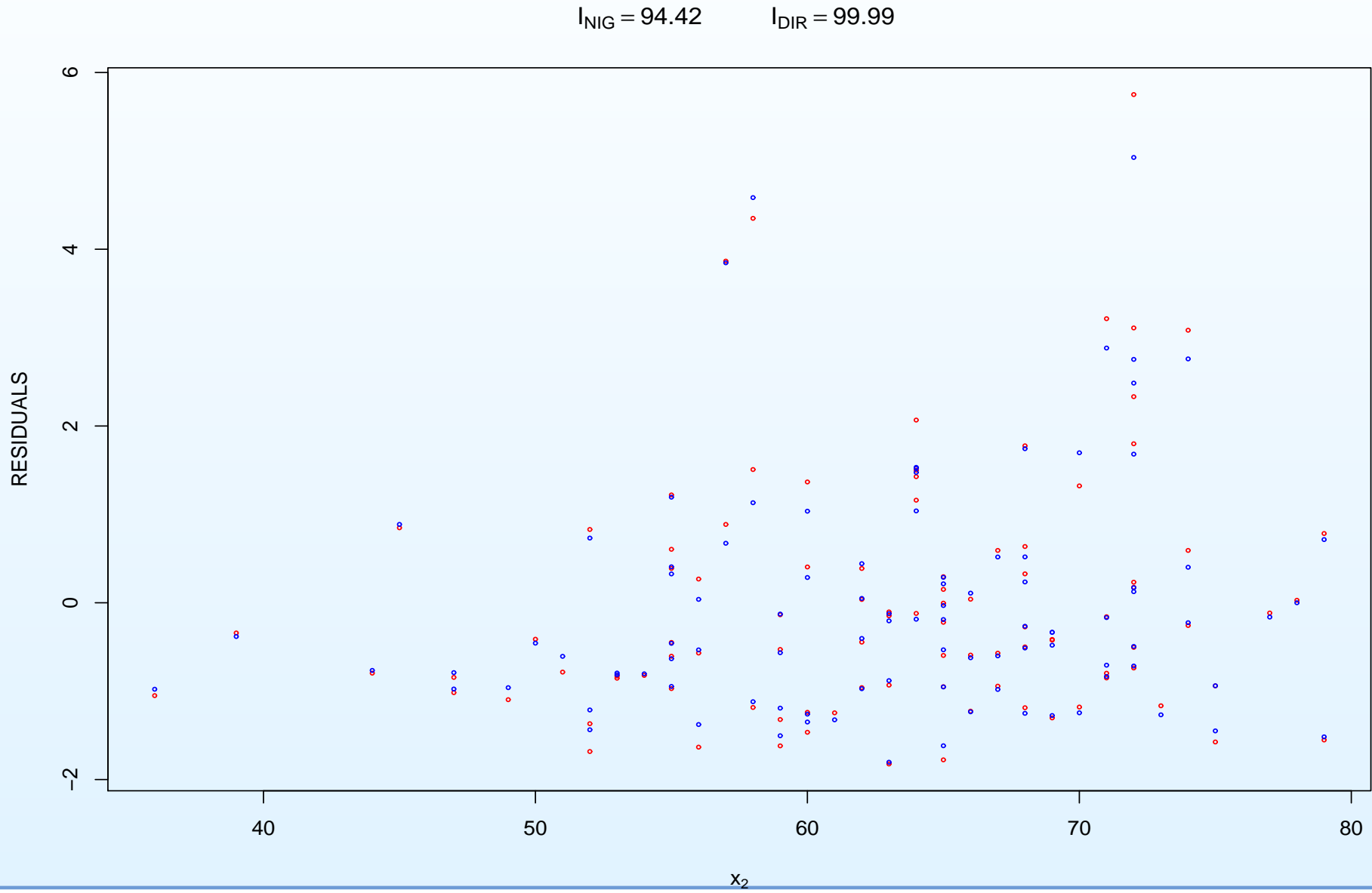


## Example 2 - Standardized Residuals

$\sigma \rightarrow 0$ : AFT when the error  $V \sim \text{DPM}$



## Example 2 - Standardized Residuals



## Comments and future work

- the density estimates (for densities on the positive reals) under the  $GG(\sigma, \eta, G_0)$ -mixture model with  $\sigma \sim \pi(\sigma)$  fundamentally agree with estimates under *similar* nonparametric models ( $GG(\sigma, \eta, G_0)$ -mixture with  $\sigma$  fixed) but seem more robust with respect to the choice of hyperparameters in  $G_0$
- $GG(\sigma, \eta, G_0)$ -mixture model with a random  $\sigma$  seems more effective in detecting the number of clusters in density estimation (as concluded in Lijoi *et al.* 2007 for mixtures of normals)
- $GG(\sigma, \eta, G_0)$ -mixture model with  $\sigma \sim \pi(\sigma)$  in the AFT setting seems more flexible than  $GG(\sigma, \eta, G_0)$ -mixture model with  $\sigma$  fixed
- the flexibility of the  $GG(\sigma, \eta, G_0)$ -mixture models is provided at higher computational cost
- $k(\cdot; \vartheta_1, \vartheta_2)$ =Weibull as already suggested in the literature
- simulation of prior/posterior trajectories of  $G$  in order to
  - efficiently compute Bayes factors for  $GG(\sigma, \eta, G_0)$ -mixtures
  - simulate functionals of  $G$

Thanks to Fabrizio Ruggeri

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