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A Bayesian sensitivity analysis of the effect of different random effects distributions on growth curve models

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Abstract. Growth curve data consist of repeated measurements of a continuous growth process of human, animal, plant, microbial or bacterial genetic data over time in a population of individuals. A classical approach for analyzing such data is the use of non-linear mixed effects models under normality assumption for the responses. But, sometimes the underlying population that the sample is extracted from is an abnormal population or includes some homogeneous sub-samples. So, detection of original properties of the population is an important scientific question of interest. (To be continued on page 2388).

Key words: Bayesian paradigm; Dirichlet process; growth curve models; mixed effects model; repeated measurements data; sensitivity analysis.
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Full Abstract Growth curve data consist of repeated measurements of a continuous growth process of human, animal, plant, microbial or bacterial genetic data over time in a population of individuals. A classical approach for analyzing such data is the use of non-linear mixed effects models under normality assumption for the responses. But, sometimes the underlying population that the sample is extracted from is an abnormal population or includes some homogeneous sub-samples. So, detection of original properties of the population is an important scientific question of interest. In this paper, a sensitivity analysis of using different parametric and non-parametric distributions for the random effects on the results of applying non-linear mixed models is proposed for emphasizing the possible heterogeneity in the population. A Bayesian MCMC procedure is developed for parameter estimation and inference is performed via a hierarchical Bayesian framework. The methodology is illustrated using a real data set on study of influence of menarche on changes in body fat accretion.

Résumé. (Abstract in French) Les courbes de croissance de données sont constituées de mesures repétées d'une progression continue sur des données portant sur des humains, animaux, plantes, de données génétiques microbiennes ou bactérielles sur une durée. Une approche classique pour analyser ces données est l'utilisation de modèles non-lineaires à effets mixtes sous l'hypothèse de normalité des réponses. Mais, parfois, la population sous-jacente dont l'échantillon est extrait est une population anormale ou une populqtion aui comprend des sous-échantillons homogènes. Ainsi, la détection des propriétés originales de la population est une importante question scientifique. Dans cet article, une analyse de sensibilité relative à l'utilisation de différentes distributions paramétriques et non paramétriques pour les effets aléatoires sur les résultats de l'application de modèles mixtes non linéaires est proposée pour mettre en exergue l'hétérogénéité possible de la population. Une procédure bayésienne MCMC est développée pour l'estimation des paramètres et l'inférence est effectuée dans un adre bayésien hiérarchique. La méthodologie est illustrée à l'aide d'un ensemble de données réelles sur l'étude de l'influence de la ménarche sur les changements d'accrétion de graisse corporelle.

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1. Introduction

Growth curve modeling includes a non-linear model for evaluating the growth trajectory of the repeated measurements. These kinds of models are broadly used for studying of growth behaviour of a quantity over time in medical, biology, forestry, agriculture, engineering, population ecology and economics Panik (2014). For a historical review of growth curve, one can refer to Bollen and Curran (2006).

A popular approach for analysing growth curve data is the use of some famous non-linear regression models for population average, for examples see Xie *et al.* (2009), Cancho *et al.* (2010), Cysneiros *et al.* (2010) and Cysneiros *et al.* (2008). Some of these nonlinear models, well-known as sigmoidal growth models, are Logistic models Verhulst (1838), Richards *et al.* (1959), Von Bertalanffy (1957), Gompertz (1825) and Janoschek (1957).

Usually a marginal model is used for analysing growth curve repeated measurements. In this framework, a normality assumption is considered for within-subject errors, but some studies such as Louzada *et al.* (2014) and Son *et al.* (2019) are considered assumption of abnormality for the response variable. Another popular approach for analysing growth curve repeated measurements data is a non-linear mixed effects model.

This non-linear model may be considered by some sigmoidal or spline models. The same as those discussed in traditional longitudinal models in this approach, the random effects are used for estimating inter-individual variability in intra-individual pattern Curran *et al.* (2010). A normal distributional assumption is often used for both inter-individual errors and the random effects (See Giolo *et al.* (2009), Chirwa *et al.* (2014) and Ghisletta *et al.* (2015)).

In this paper, mixed effects growth curve models under different parametric and non-parametric distributional assumptions for random effects are discussed. For this purpose, normal/independent distributional assumption, skew-normal/independent distributional assumption and Dirichlet process are considered for distribution of random effects. Statistical inferences are performed via a Bayesian paradigm. A real data set is also analysed for illustrating the approach.

The rest of the paper is organized as follows. In Section 2, formulation of the model is discussed. It also includes tools for a sensitivity analysis of the results on using different distributions for random effects and also discusses the Bayesian implementation of the proposed method. Section 3 includes our application where the proposed model is considered for analyzing a real data set. Some conclusions are given in the last section.

2. Model and parametric and non-parametric distributions for random effects

In this section model will be defined, parametric distribution for random effects will be discussed, Bayesian approach for using them will be mentioned and non-parametric Bayesian approach will be considered using Dirichlet process.

2.1. Model specification

Let Y_{it}, $i = 1, 2, ..., n$ and $t = 1, 2, ..., T_i$ be the repeated measurements for the i^{th} subject at time t. We consider the following mixed effect model for analyzing growth curve data:

$$Y_{it} = h(t, \boldsymbol{\theta}) + b_{i0} + b_{i1}t + \varepsilon_{it}, \tag{1}$$

where $h(t; \boldsymbol{\theta})$ is a non-linear function of t for considering the overall mean which will be considered in this paper in different forms as follows:

1. Logistic function Verhulst (1838) $h(t; \boldsymbol{\theta}) = \frac{\alpha}{1+\beta \exp(-\gamma t)}$, where $\boldsymbol{\theta} = (\alpha, \beta, \gamma)'$ and $\alpha, \beta, \gamma \in \Re$.
2. Richards function Richards *et al.* (1959))
$$h(t; \boldsymbol{\theta}) = \alpha(1 - \beta \exp(-\gamma t))^{-1/\delta},$$
where $\boldsymbol{\theta} = (\alpha, \beta, \gamma, \delta)'$ and $\alpha, \beta, \gamma, \delta \in \Re$.
3. Von Bertalanffy function Von Bertalanffy (1957)
$$h(t; \boldsymbol{\theta}) = \alpha(1 - \beta \exp(-\gamma t))^3,$$
where $\boldsymbol{\theta} = (\alpha, \beta, \gamma)'$ and $\alpha, \beta, \gamma \in \Re$. Note that Von Bertalanffy function is a special form of Richards function with $\delta = -\frac{1}{3}$.
4. Gompertz function Gompertz (1825)
$$h(t; \boldsymbol{\theta}) = \alpha \exp(-\exp(\beta - \gamma t)),$$
where $\boldsymbol{\theta} = (\alpha, \beta, \gamma)'$ and $\alpha, \beta, \gamma \in \Re$.
5. Janoschek function Janoschek (1957)
$$h(t; \boldsymbol{\theta}) = \alpha(1 - \beta \exp(-\gamma t)),$$
where $\boldsymbol{\theta} = (\alpha, \beta, \gamma)'$ and $\alpha, \beta, \gamma \in \Re$.

Figure 1 shows different forms of growth curve models.
Also, $\boldsymbol{b}_i = (b_{i0}, b_{i1})$ in equation (1) is the random effects term, where we assume that $\boldsymbol{b}_i \sim g(\boldsymbol{b}_i)$. In this paper we consider both models with only random intercept, $\boldsymbol{b}_i = b_{i0}$ and models with random intercept and random slope, $\boldsymbol{b}_i = (b_{i0}, b_{i1})$.

The purpose of this paper is a sensitivity analysis of the results with respect to different distributional assumptions for $\boldsymbol{b}_i$. These different distribution assumptions for b_i will be described in the next subsection.

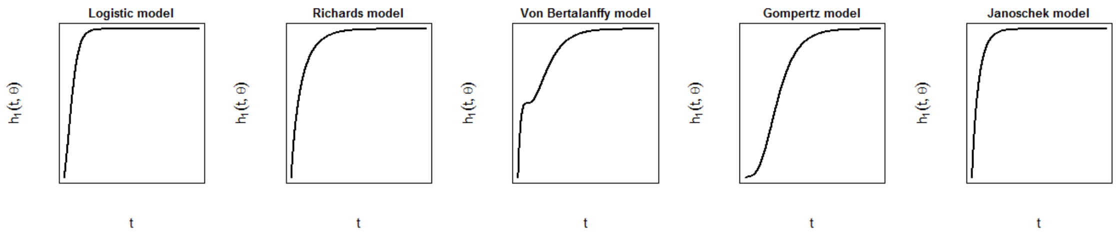

Fig. 1. Different forms of growth curve models.

2.2. Chosen parametric random effects distributions

In this paper, different parametric distributional assumptions are considered for $\boldsymbol{b}_i$. We use normal, class of normal/indepedent distributions including (t, slash and contaminated normal) and skew-normal/independent distributions including (skew-t, skew-slash and skew-contaminated normal). In the following these distributions are described and Bayesian approach for using them is given.

2.2.1. Normal/independent distributions

Based on Lange and Sinsheimer (1993) and Rosa *et al.* (2003), the vector $\boldsymbol{Y} = \boldsymbol{\mu} + \boldsymbol{\epsilon}/\sqrt{U}$ has distributed as normal/independent (N/I) distribution, when $\boldsymbol{\mu}$ is a location vector, U is a positive random variable, with density $g(u; \boldsymbol{\nu})$, where $\boldsymbol{\nu}$ is a scalar or random vector of parameters, and $\boldsymbol{U}$ is a normally distributed random vector with mean $\mathbf{0}$ and covariance matrix $\boldsymbol{\Sigma}$. In other words, given U, $\boldsymbol{Y}$ follows a normal distribution with location vector $\boldsymbol{\mu}$ and the scale matrix $U^{-1}\boldsymbol{\Sigma}$.

The class of N/I distributions includes the t, the slash, and the contaminated normal distributions. All these distributions, with mean $\boldsymbol{\mu}$, have heavier tails than the normal distribution, and can be used for robust inference. Some of these distributions are described in the following.

t distribution: The Student's t distribution with $\nu > 0$ degrees of freedom Kotz *et al.* (2000), $\boldsymbol{Y} \sim t(\boldsymbol{\mu}, \boldsymbol{\Sigma}, \nu)$, is an alternative to the normal distribution (See Little (1988), Lange *et al.* (1989), Geweke (1993) and Pinheiro *et al.* (2001)). In the N/I structure, if $U \sim \Gamma(\nu/2, \nu/2)$ which is a gamma distribution with mean 1, then $\boldsymbol{Y} \sim t(\boldsymbol{\mu}, \boldsymbol{\Sigma}, \nu)$.

Slash distribution: The slash distribution (see Wang *et al.* (2006)) is another normal/independent distribution. For a slash distribution, we shall use the notation $\boldsymbol{Y} \sim SL(\boldsymbol{\mu}, \boldsymbol{\Sigma}, \nu)$. If $G(u, \nu)$ is a beta distribution with parameter $(\nu, 1)$, then $\boldsymbol{Y} \sim SL(\boldsymbol{\mu}, \boldsymbol{\Sigma}, \nu)$.

Contaminated normal distribution: The *pdf* of a contaminated normal distribution (See Tukey (1960)) is a mixture of normal distributions. The notation $\boldsymbol{Y} \sim CN(\boldsymbol{\mu}, \boldsymbol{\Sigma}, \boldsymbol{\nu})$ will be used for this distribution. If the probability density of U, given the two-component parameter vector $\boldsymbol{\nu} = (w, \pi)'$, is:

$$g(u;\nu) = \begin{cases} \pi, & u = w \\ 1-\pi, & u = 1 \end{cases}$$

where, $0 < w < 1$ and $0 \leq \pi < 1$, then we have $Y \sim CN(\boldsymbol{\mu}, \boldsymbol{\Sigma}, \boldsymbol{\nu})$.

2.2.2. Skew-normal/independent distributions

A skew-normal/independent (SN/I) distribution is a stochastic representation of the vector $\boldsymbol{Y} = \boldsymbol{\mu} + \boldsymbol{\epsilon}/\sqrt{U}$, where $\boldsymbol{\mu}$ is a location vector, U is a positive random variable, with density $g(u;\boldsymbol{\nu})$, where $\boldsymbol{\nu}$ is a scalar or random vector of parameters, and $\boldsymbol{\epsilon}$ is a skew-normally distributed random vector with location vector $\mathbf{0}$, scale matrix $\boldsymbol{\Sigma}$ and vector of skewness parameter $\boldsymbol{\lambda}$.

The skew-normal distribution Arellano-Valle *et al.* (2007) with mean $\boldsymbol{\mu}$, scale matrix $\boldsymbol{\Sigma}$ and skewness matrix $\boldsymbol{\Lambda}$ such that $\boldsymbol{\Lambda} = diag(\boldsymbol{\lambda})$ $(SN(\boldsymbol{\mu}, \boldsymbol{\Sigma}, \boldsymbol{\Lambda}))$ is given as follows:

$$\begin{aligned} f(\boldsymbol{y}|\boldsymbol{\mu}, \boldsymbol{\Sigma}, \boldsymbol{\Lambda}) &= 2^k \phi(\boldsymbol{y}|\boldsymbol{\mu}, \boldsymbol{\Sigma} + \boldsymbol{\Lambda}\boldsymbol{\Lambda}') \\ &\times \Phi(\boldsymbol{\Lambda}'(\boldsymbol{\Sigma} + \boldsymbol{\Lambda}\boldsymbol{\Lambda}')^{-1}(\boldsymbol{y} - \boldsymbol{\mu})|0, (I + \boldsymbol{\Lambda}'\boldsymbol{\Sigma}\boldsymbol{\Lambda})^{-1}). \end{aligned} \tag{2}$$

The skew-t $(ST(\boldsymbol{\mu}, \boldsymbol{\Sigma}, \boldsymbol{\Lambda}, \nu))$, skew-slash $(SSL(\boldsymbol{\mu}, \boldsymbol{\Sigma}, \boldsymbol{\Lambda}, \nu))$ and skew-contaminated normal distribution $(SCN(\boldsymbol{\mu}, \boldsymbol{\Sigma}, \boldsymbol{\Lambda}, \boldsymbol{\nu}))$ are defined in the same manner as the previous subsection by replacing the normal distribution by the skew-normal one.

In the following, the means of univariate skew-normal and skew-normal/independent distributions are given.

If $Y \sim SN(\mu, \sigma, \lambda)$, then $E[Y] = \mu + \sigma\delta\sqrt{\frac{2}{\pi}}$, where $\delta = \frac{\lambda}{\sqrt{1+\lambda^2}}$ (See Azzalini (1985)).

If $Y \sim ST(\mu, \sigma, \lambda, \nu)$, then

$$\begin{aligned} E[Y] &= \mu + \sigma\delta\sqrt{\frac{2}{\pi}} \int_0^\infty \frac{1}{\sqrt{u}} g(u;\nu) du \\ &= \mu + \sigma\delta\sqrt{\frac{2}{\pi}} \frac{\Gamma((\nu-1)/2)}{\Gamma(\nu/2)} (\nu/2)^{1/2}. \end{aligned} \tag{3}$$

If $Y \sim SSL(\mu, \sigma, \lambda, \nu)$, then

$$E[Y] = \mu + \sigma\delta\sqrt{\frac{2}{\pi}} \frac{\Gamma(\nu+1)\Gamma(\nu - \frac{1}{2})}{\Gamma(\nu)\Gamma(\nu + \frac{1}{2})}. \tag{4}$$

If $Y \sim SCN(\mu, \sigma, \lambda, \nu)$, then

$$E[Y] = \mu + \sigma\delta\sqrt{\frac{2}{\pi}} \{(1-\pi) + \frac{1}{\sqrt{\omega}}\pi\}. \tag{5}$$

The means of multivariate skew-normal and skew-normal/independent distributions are given in the following.

If $\boldsymbol{Y} \sim SN(\boldsymbol{\mu}, \boldsymbol{\Sigma}, \boldsymbol{\Delta})$, then $E[\boldsymbol{Y}] = \boldsymbol{\mu} + \boldsymbol{\delta}\sqrt{\frac{2}{\pi}}$, where $\boldsymbol{\Delta} = diag(\boldsymbol{\delta})$ (Arellano-Valle et al., 2007).

If $\boldsymbol{Y} \sim ST(\boldsymbol{\mu}, \boldsymbol{\Sigma}, \boldsymbol{\Delta}, \nu)$, then

$$E[\boldsymbol{Y}] = \boldsymbol{\mu} + \boldsymbol{\delta}\sqrt{\frac{2}{\pi}}\frac{\Gamma((\nu-1)/2)}{\Gamma(\nu/2)}(\nu/2)^{1/2}. \tag{6}$$

If $\boldsymbol{Y} \sim SSL(\boldsymbol{\mu}, \boldsymbol{\Sigma}, \boldsymbol{\Delta}, \nu)$, then

$$E[\boldsymbol{Y}] = \boldsymbol{\mu} + \boldsymbol{\delta}\sqrt{\frac{2}{\pi}}\frac{\Gamma(\nu+1)\Gamma(\nu-\frac{1}{2})}{\Gamma(\nu)\Gamma(\nu+\frac{1}{2})}. \tag{7}$$

If $\boldsymbol{Y} \sim SCN(\boldsymbol{\mu}, \boldsymbol{\Sigma}, \boldsymbol{\Delta}, \nu)$, then

$$E[\boldsymbol{Y}] = \boldsymbol{\mu} + \boldsymbol{\delta}\sqrt{\frac{2}{\pi}}\{(1-\pi) + \frac{1}{\sqrt{\omega}}\pi\}. \tag{8}$$

2.2.3. Sensitivity analysis

In this section different distributional assumptions for the random effects are given. We considered two different structures for $\boldsymbol{b}_i$, the univariate with only random intercept and the bivariate with random intercept and random slope, the same as what is given in model (1). Also, we consider the following zero-mean distributional assumptions for $\boldsymbol{b}_i$:

1. $b_i \sim N(0, \sigma_b)$.
2. $b_i \sim T(0, \sigma_b, v)$.
3. $b_i \sim SL(0, \sigma_b, v)$.
4. $b_i \sim CN(0, \sigma_b, w, \pi)$.
5. $b_i \sim SN(-\sigma_b\delta_b\sqrt{\frac{2}{\pi}}, \sigma_b, \lambda_b)$, $\delta_b = \frac{\lambda_b}{\sqrt{1+\lambda_b^2}}$.
6. $b_i \sim ST(-\sigma_b\delta_b\sqrt{\frac{2}{\pi}}\sqrt{\frac{2}{\pi}}\frac{\Gamma((\nu-1)/2)}{\Gamma(\nu/2)}(\nu/2)^{1/2}, \sigma_b, \lambda_b, v)$.
7. $b_i \sim SSL(-\sigma_b\delta_b\sqrt{\frac{2}{\pi}}\frac{\Gamma(\nu+1)\Gamma(\nu-\frac{1}{2})}{\Gamma(\nu)\Gamma(\nu+\frac{1}{2})}, \sigma_b, \lambda_b, v)$.
8. $b_i \sim SCN(-\sigma_b\delta_b\sqrt{\frac{2}{\pi}}\sqrt{\frac{2}{\pi}}\{(1-\pi) + \frac{1}{\sqrt{\omega}}\pi\}, \sigma_b, \lambda_b, \omega, \pi)$.

Also, for a vector of two variables (underlined by subscript 2 in the following):

1. $\boldsymbol{b}_i \sim N_2(\boldsymbol{0}, \boldsymbol{D})$.
2. $\boldsymbol{b}_i \sim T_2(\boldsymbol{0}, \boldsymbol{D}, v)$.
3. $\boldsymbol{b}_i \sim SL_2(\boldsymbol{0}, \boldsymbol{D}, v)$.
4. $\boldsymbol{b}_i \sim CN_2(\boldsymbol{0}, \boldsymbol{D}, w, \pi)$.
5. $\boldsymbol{b}_i \sim SN_2(-\boldsymbol{\lambda}_b\sqrt{\frac{2}{\pi}}, \boldsymbol{D}, \boldsymbol{\lambda}_b)$.

6. $\boldsymbol{b}_i \sim ST_2(-\boldsymbol{\lambda}_b\sqrt{\frac{2}{\pi}}\frac{\Gamma((\nu-1)/2)}{\Gamma(\nu/2)}(\nu/2)^{1/2}, \boldsymbol{D}, \boldsymbol{\lambda}_b, v)$.
7. $\boldsymbol{b}_i \sim SSL_2(-\boldsymbol{\lambda}_b\sqrt{\frac{2}{\pi}}\frac{\Gamma(\nu+1)\Gamma(\nu-\frac{1}{2})}{\Gamma(\nu)\Gamma(\nu+\frac{1}{2})}, \boldsymbol{D}, \boldsymbol{\lambda}_b, v)$.
8. $\boldsymbol{b}_i \sim SCN_2(-\boldsymbol{\lambda}_b\sqrt{\frac{2}{\pi}}\sqrt{\frac{2}{\pi}}\{(1-\pi)+\frac{1}{\sqrt{\omega}}\pi\}, \boldsymbol{D}, \boldsymbol{\lambda}_b, w, \pi)$.

In all cases, we assume that the mean vector of skew-normal/independent distributions are equal to zero.

2.2.4. Bayesian implementation of parametric distributions

In this paper, a Bayesian paradigm by using Markov chain Monte Carlo (MCMC) is presented for statistical inference and parameter estimation. For this purpose, specifying prior distributions for the unknown parameters is necessary. We have no expert information, so we prefer to assign low-informative prior distributions to the parameters. Assume that the elements of the vector of parameters of the model are independent. The prior distributions for the parameters of non-linear overall mean $h(.;.)$ are given by:

$$\begin{aligned}\alpha &\sim N(\mu_\alpha, \sigma^2_\alpha),\\ \beta &\sim N(\mu_\beta, \sigma^2_\beta),\\ \gamma &\sim N(\mu_\gamma, \sigma^2_\gamma),\\ \delta &\sim N(\mu_\delta, \sigma^2_\delta),\end{aligned}$$

also, $\sigma^2 \sim \mathrm{I\Gamma}(\mathrm{a}_{\sigma^2}, \mathrm{b}_{\sigma^2})$, where $\mathrm{I\Gamma}(\mathrm{a}, \mathrm{b})$ denote the inverse gamma distribution with parameters a and b.

As mentioned in the previous subsection, two different structure for $\boldsymbol{b}_i$, the univariate with only random intercept and the bivariate with random intercept and random slope, the same as what is given in model (1), are considered. In all univariate cases $\sigma_b \sim \mathrm{I\Gamma}(\mathrm{a}_{\sigma_b}, \mathrm{b}_{\sigma_b})$ and in multivariate cases $\boldsymbol{D} \sim \mathrm{IWishart}(\Psi, \zeta)$. Also, in t and skew-t distributions $v \sim Uniform(a_v, b_v)$, in slash and skew-slash distributions $v \sim \Gamma(a_v, b_v)$, in contaminated-normal and skew contaminated-normal distributions $w \sim Beta(a_w, b_w)$ and $\pi \sim Beta(a_\pi, b_\pi)$, in univariate skewed distributions $\lambda_b \sim N(\mu_{\lambda_b}, \sigma_{\lambda_b})$ and in multivariate skewed distributions $\lambda_{b_k} \sim N(\mu_{\lambda_{b_k}}, \sigma_{\lambda_{b_k}}),\ k = 1, 2$ where $\boldsymbol{\lambda}_b = (\lambda_{b_1}, \lambda_{b_2})'$.

Let $\boldsymbol{\theta}$ be the vector of unknown parameters, the joint posterior distribution of the unknown parameters, $\boldsymbol{\theta}$, and the random effects, $\boldsymbol{b}_i$, is given by

$$\pi(\boldsymbol{\theta}, \boldsymbol{b}_i|\boldsymbol{y}_i, \boldsymbol{t}_i) \propto f(\boldsymbol{y}_i|\boldsymbol{t}_i, \boldsymbol{b}_i, \boldsymbol{\theta}_y)g(\boldsymbol{b}_i|\boldsymbol{\theta}_b)\pi(\boldsymbol{\theta}), \tag{9}$$

where $\boldsymbol{\theta}_y$ and $\boldsymbol{\theta}_b$ are the vector of parameters of the response and random effects distributions, respectively and $\boldsymbol{\theta} = (\boldsymbol{\theta}_y, \boldsymbol{\theta}_b)$. The posterior distributions of the unknown parameters can not be computed easily. Therefore, the MCMC procedure can be used to sample from the joint posterior distribution (9) using Gibbs sampler along with the Metropolis-Hastings algorithm. The Gibbs sampler works by drawing samples iteratively from conditional posterior distribution derived from (9). The Bayesian implementation of all models in this paper is performed by *OpenBUGS* package (See Spiegelhalter *et al.* (2002)).

2.3. Non-parametric Bayesian approach using Dirichlet process mixtures

In some practical studies, clustering of individuals is the main purpose of the study. A usual approach, via the model-based clustering, is based on considering a normal mixture model for the random effects and some criteria such as AIC, BIC or in Bayesian paradigm LPML (the logarithm of the pseudo-marginal likelihood) criterion for determining the best number of mixture components. Dirichlet process mixtures is applied in many applications to deal with this issue (See Ishwaran and James (2002) and Ishwaran and Zarepour (2000)).

In this structure instead of considering a distribution G on random effects b_i, a Dirichlet process (DP) is considered. The DP considers a distribution on G for accounting uncertainty about its form (See Gill and Casella (2009)). It involves a base distribution G_0, the expectation of G, and a precision parameter $\varpi > 0$ which control the concentration of G about its mean G_0. The sample distributions from a DP are discrete with probability one. As $\varpi \to 0$ G concentrates its mass on a single random point, whereas as $\varpi \to \infty$, G concentrates its mass on G_0 (See Murugiah *et al.* (2012)).

Based on Ferguson *et al.* (1973), for any partition B_1, B_2,...,B_P on the support G_0, the vector of probabilities $(G(B_1), G(B_2), ..., G(B_P))$ contain in the set $\{B_1, B_2, ..., B_P\}$ follows a Dirichlet distribution as follows:

$$(G(B_1), G(B_2), ..., G(B_P)) \sim Dir(\varpi G(B_1), \varpi G(B_2), ..., \varpi G(B_P)),$$

where Dir denotes the Dirichlet distribution. We use the notation $G \sim DP(\varpi, G_0)$ for distribution of G_0. The original form of DP assumes that G_0 is known (See Hanson *et al.* (2005)). The other form assumes that the parameters of G_0 are unknown and a set of parametric distributions based on a mixture of DP (See Walker *et al.* (1999), Jara (2007) Ohlssen *et al.* (2007)) may be used. Implementation of the latter form is simpler. The basic function of this form is to regard the density of b_i as an infinite mixture of mass or density functions (See Ohlssen *et al.* (2007)), such that

$$b_i \sim \sum_{k=1}^{\infty} \pi_k \kappa(b_i|\boldsymbol{\psi}_k).$$

This is well-known as *DP* mixtures Hanson *et al.* (2005). In practical applications, the infinite representation can be approximated by a truncation at $P \leq n$ components (See Ishwaran and James (2002) and Ishwaran and Zarepour (2000)) as follows

$$g(b_i) = \sum_{k=1}^{P} \pi_k \kappa(b_i|\boldsymbol{\psi}_k),$$

where $\pi_k,\ k = 1, 2, ..., P$ are generated from a method which is well-known as stick-breaking method (See Sethuraman *et al.* (1994) and Ishwaran and James (2002)). In this approach, π_ks are sampled by introducing $P - 1$ random variables which distributed as $V_k \sim Beta(c_k, d_k)$, and $V_P = 1$ to ensure the sum of the probabilities are one. Then $\pi_1 = V_1$ and

$$\pi_k = (1 - V_1)(1 - V_2)...(1 - V_{k-1})V_k;\ k > 1.$$

For an infinite dimension mixture, the DP is obtained by $c_k = 1$ and $d_k = \varpi$, that is $V_k \sim Beta(1, \varpi)$. In this status, using a large P is equivalent to the infinite DP for practical purpose (See Ishwaran and James (2002) and Ishwaran and Zarepour (2000)). Usually a Gamma distribution is used as prior distribution for ϖ. The Bayesian implementation of this model may performed by *OpenBUGS* package (Spiegelhalter *et al.* (2002)).

3. Applied example: Study of Influence of Menarche on Changes in Body Fat Accretion

The data are from a prospective study on body fat accretion in a cohort of 162 girls from the MIT Growth and Development Study, which can be found in Phillips *et al.* (2003) and Fitzmaurice *et al.* (2012). The study examined changes in percent body fat before and after menarche. The data represent a subset of the study materials and should not be used to draw substantive conclusions.

At the start of the study, all of the girls were pre-menarcheal and non-obese, as determined by a triceps skin-fold thickness less than the 85th percentile. All girls were followed over time according to a schedule of annual measurements until four years after menarche. The final measurement was scheduled on the fourth anniversary of their reported date of menarche. At each examination, a measure of body fatness was obtained based on bioelectric impedance analysis and a measure of percent body fat (PBF) was derived. In this data set there are a total of 1049 individuals percent body fat measurements, with an average of 6.4

measurements per subject. The numbers of measurements per subject pre- and post-menarche are approximately equal.

Also, time is coded as time since menarche and can be positive or negative. Although the measurement protocol is the same for all girls and the study design is balanced if the timing of measurement is defined as the time since the baseline measurement, it is inherently unbalanced when the timing of measurements is defined as the time since a girl experienced menarche.

Figure 2 shows individual profiles for a random sample from Menarche data which show a non-linear trend of individuals over time. Also, Figure 3 presents histograms and q-q plots of the response variables for all time points in this data set. Some of these q-q plots show that a robust distribution for some responses may be preferred to be used.

Table 1 shows Bayesian parameter estimates, posterior standard deviation and 95% credible interval for different trend functions h under normality assumption for the random effects. In this Table DIC and LPML are reported for model comparison. Based on these criteria Von Bertalanffy model is the best fitting model. All the parameters are significant by Von Bertalanffy model (the best fitting model). As β and γ are estimated negative with passage by time, PBF increases exponentially by time. The σ_b^2 is estimated positive and so there is heterogeneity among individuals. Figure 4 (a) shows individual profiles along with the fitted curves under different trend functions h. In general, based on the results, although the selection of different models with normal random effects lead to different estimated parameters for β, α and γ, they lead to similar curve fit on individual profiles, thus, in the following we consider one of them (Von Bertalanffy model) for sensitivity analysis on results with respect to different distributional assumptions for random effects.

In the following, different distributional assumptions are considered for the random effects, under Von Bertalanffy model. The results are reported in Table 2 for univariate random effects (intercept) and in Table 3 for bivariate random effects (intercept and time) and the fitted curves are drawn in Figure 4 (b) and (c), respectively.

Based on the results the skew-slash distribution assumption for random intercept is the best fitting model among the random intercept models. Also, the bivariate skew-normal distributional assumption is the best fitting among all the bivariate distributional assumptions.

For random intercept models, as the skew-slash model is the best fitting model and parameters β and γ are estimated negative, the interpretation is the same as before, but α is estimated smaller than before, so the intensity of exponentially by time is less.

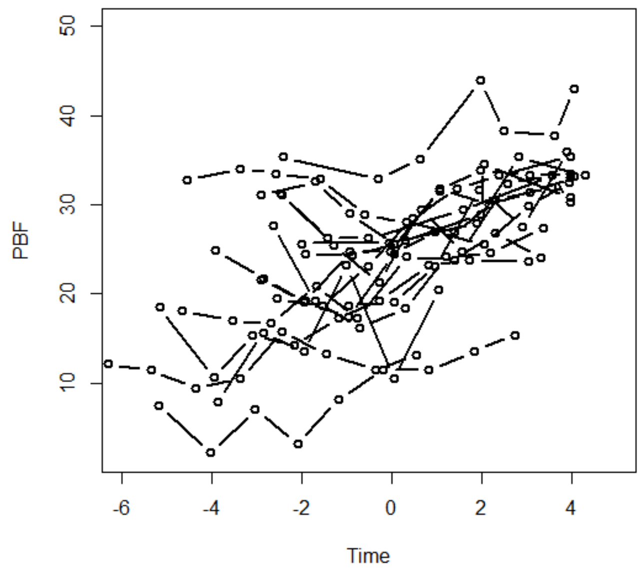

Fig. 2. Individual profiles for a randomly selected sample from Menarche data.

As the final analysis of this data with Von Bertalanffy model, we assume univariate and bivariate random effects using DP model with $P = 10$. The results are reported in Tables 4 and 5 for random intercept and bivariate random effects, respectively. For comparison of these two models LPML criterion is computed and this is -2370.405 for the univariate DP and is -2305.699 for bivariate DP. Therefore, the bivariate DP is more appropriate than univariate case. Also, individual profiles obtained by the fitted curves are given in Figure 5 (a) for univariate and bivariate DP models. Panels b and d; and panels c and f of figure 5 show the four clusters which are obtained by considering univariate distribution and the five clusters which are obtained by considering bivariate distribution, respectively. The panels of this figure show the lack of tendency toward larger number of clusters and satisfy good approximation of DP by stick-breaking representation.

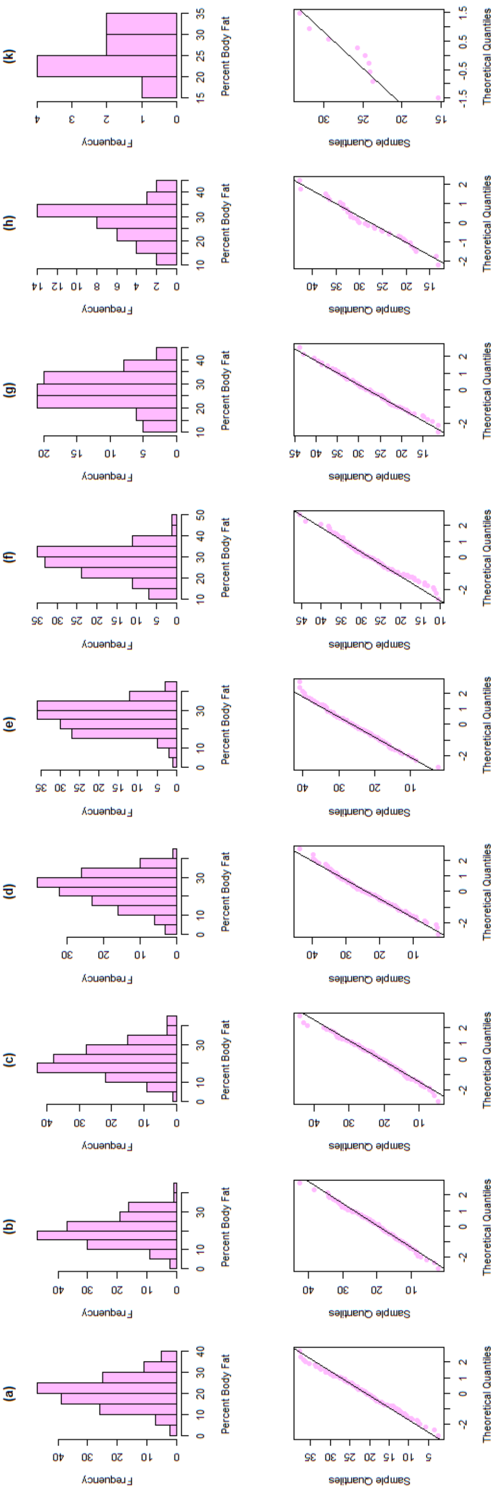

Fig. 3. Histograms and q-q plots of PBF in Menarche data set for 9 time points.

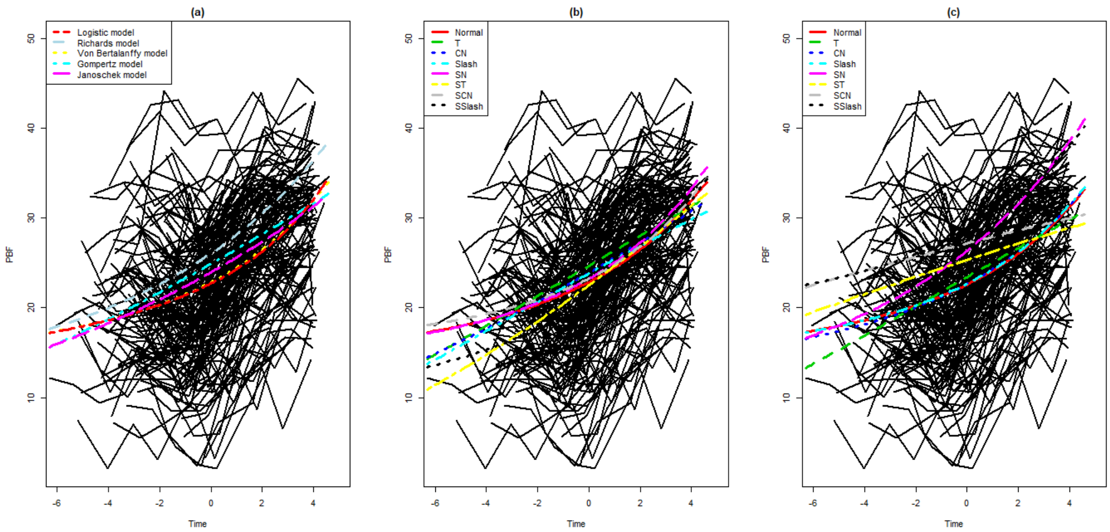

Fig. 4. (a): individual profiles along with the fitted curves under different trend functions h, (b): under different distributional assumptions for univariate random effects using Von Bertalanffy model and (c): under different distributional assumptions for bivariate random effects using Von Bertalanffy model.

Table 1. Bayesian parameter estimates, posterior means (standard deviations), and 95% credible intervals for the Menarche data under normality assumption for random effects and different trend functions h.

Par.	Est.	S.D.	2.5%	97.5%	Est.	S.D.	2.5%	97.5%	Est.	S.D.	2.5%	97.5%
	Von Bertalanffy model				Gompertz model				Logistic model			
β	-0.174	0.050	-0.279	-0.105	-0.461	0.129	-0.638	-0.266	-0.465	0.097	-0.560	-0.267
α	14.120	1.765	10.670	16.880	121.500	23.120	88.190	155.500	12.140	2.227	9.885	16.850
γ	-0.146	0.029	-0.200	-0.099	0.041	0.005	0.034	0.050	-0.072	0.029	-0.141	-0.046
σ^2	14.040	0.670	12.790	15.420	14.820	0.706	13.530	16.270	14.130	0.673	12.870	15.500
σ_b^2	36.970	4.388	29.210	46.380	36.900	4.421	29.190	46.640	36.930	4.419	29.150	46.460
DIC	5889				5909				5907			
LPML	-2359.871				-2389.944				-2362.671			
	Richards model				Janoschek model							
β	-0.047	0.023	-0.127	-0.033	49.240	12.880	32.200	76.590				
α	7.734	0.290	7.165	8.272	-0.497	0.122	-0.727	-0.308				
γ	-0.063	0.003	-0.067	-0.058	-0.066	0.003	-0.072	-0.060				
σ^2	14.170	0.675	12.910	15.550	14.520	0.683	13.240	15.950				
σ_b^2	37.070	4.464	29.230	46.770	36.990	4.410	29.250	46.550				
δ	0.043	0.020	0.031	0.112								
DIC	5655				5990							
LPML	-2364.024				-2398.721							

Table 2. Bayesian parameter estimates, posterior means (standard deviations), and 95% credible intervals for the Menarche data under different distribution assumptions for random intercept for Von Bertalanffy model.

Par.	Est.	S.D.	2.5%	97.5%	Est.	S.D.	2.5%	97.5%	Est.	S.D.	2.5%	97.5%
	T model				CN model				Slash model			
β	0.325	0.065	0.165	0.395	0.539	0.037	0.465	0.606	0.323	0.047	0.198	0.376
α	80.140	17.020	43.130	105.300	243.200	60.400	149.000	375.600	77.060	13.910	46.220	95.190
γ	0.047	0.015	0.033	0.096	0.020	0.008	0.014	0.026	0.047	0.012	0.035	0.083
σ^2	15.060	0.717	13.710	16.520	14.850	0.712	13.520	16.310	15.170	0.734	13.800	16.680
σ_b^2	32.940	4.677	24.380	42.780	26.280	21.530	3.861	42.080	27.580	6.170	15.690	39.410
ν	11.620	4.907	3.293	19.600					5.873	4.922	1.461	19.170
π					0.460	0.289	0.024	0.975				
w					0.548	0.254	0.089	0.976				
DIC	5973				5896				5976			
LPML	-2395.511				-2388.642				-2396.64			
	ST model				SCN model				SSlash model			
β	0.535	0.047	0.443	0.614	-0.142	0.032	-0.198	-0.088	-0.366	0.195	-0.801	-0.138
α	194.600	58.210	106.200	320.300	15.600	3.147	10.950	21.720	8.559	3.898	2.995	17.500
γ	0.025	0.008	0.017	0.036	-0.164	0.021	-0.207	-0.124	-0.112	0.034	-0.178	-0.059
σ^2	14.780	0.712	13.450	16.240	14.030	0.666	12.780	15.410	14.070	0.672	12.820	15.450
σ_b^2	23.070	6.727	11.430	36.890	21.730	9.887	2.512	39.250	21.360	7.052	8.727	35.730
Δ_b	5.582	2.773	-1.919	9.268	-0.473	3.901	-7.702	5.942	4.231	3.215	-5.158	8.506
ν	12.200	4.540	4.505	19.610					6.995	7.013	1.378	27.430
π					0.485	0.280	0.028	0.963				
w					0.540	0.265	0.068	0.976				
DIC	5950				5896				5056			
LPML	-2387.651				-2359.304				-2349.695			
	SN											
β	-0.189	0.09466	-0.498	-0.09159								
α	13.83	4.06	5.385	21.06								
γ	-0.1471	0.02945	-0.2018	-0.08096								
σ^2	14.04	0.67	12.79	15.41								
σ_b^2	31.03	6.784	17.39	43.59								
Δ_b	0.5528	4.183	-6.939	7.364								
DIC	5793											
LPML	-2359.92											

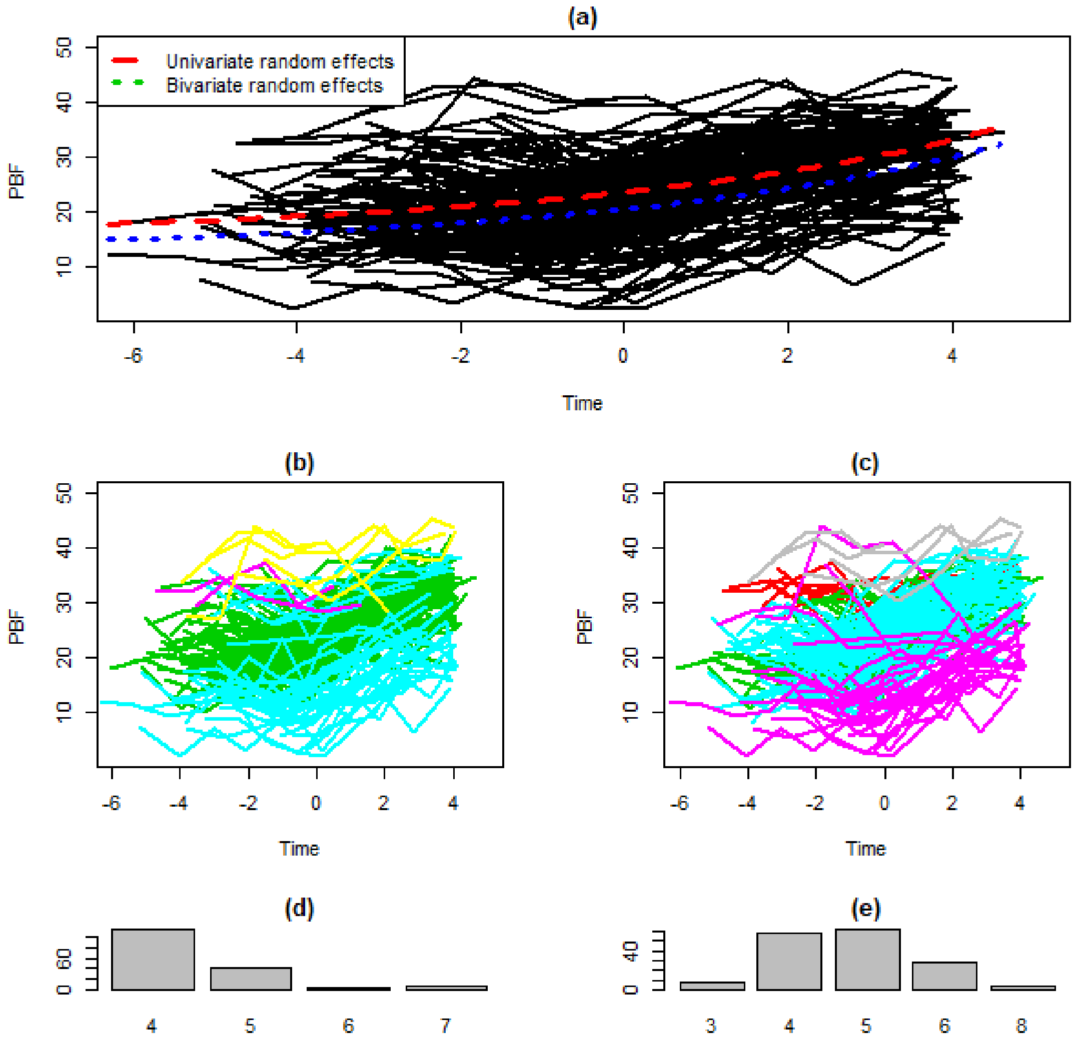

Fig. 5. Individual profiles along with the fitted curves under different number of clusters for Dirichlet process for random effects models using Von Bertalanffy model. (a): for univariate and bivariate random effects, (b): clusters of univariate random effects, (c): clusters of bivariate random effects, (d): barplot of the number of clusters for univariate random effects, (e): barplot of the number of clusters for bivariate random effects.

Table 3. Bayesian parameter estimates, posterior means (standard deviations), and 95% credible intervals for the Menarche data under different distribution assumptions for bivariate random effects using Von Bertalanffy model.

Par.	Est.	S.D.	2.5%	97.5%	Est.	S.D.	2.5%	97.5%	Est.	S.D.	2.5%	97.5%	Est.	S.D.	2.5%	97.5%
	Normal model				T model				Slash model				CN model			
β	-0.162	0.027	-0.226	-0.116	0.314	0.034	0.251	0.356	-0.169	0.031	-0.240	-0.113	-0.230	0.042	-0.336	-0.171
α	14.400	1.079	12.110	16.430	72.510	10.070	54.760	86.440	14.210	1.170	11.850	16.500	12.170	1.221	9.414	14.220
γ	-0.149	0.018	-0.188	-0.117	0.051	0.009	0.039	0.069	-0.147	0.019	-0.190	-0.113	-0.119	0.015	-0.147	-0.089
σ^2	11.260	0.595	10.150	12.470	11.700	0.625	10.550	12.990	11.220	0.594	10.120	12.440	11.170	0.589	10.070	12.380
d_{11}	37.860	4.484	30.060	47.630	33.380	4.973	24.040	43.610	26.290	6.321	15.480	39.530	20.970	9.612	6.297	40.230
d_{12}	-1.152	0.522	-2.227	-0.174	-1.060	0.519	-2.134	-0.091	-0.806	0.413	-1.719	-0.099	-0.647	0.434	-1.684	-0.050
d_{22}	0.544	0.113	0.348	0.791	0.600	0.130	0.371	0.881	0.374	0.114	0.188	0.628	0.315	0.145	0.104	0.638
ν					5.009	2.486	1.305	9.676	4.765	5.251	1.379	20.480				
π													0.416	0.250	0.036	0.944
w													0.415	0.214	0.134	0.933
DIC	5747				5800				5752				5751			
LPML	-2233.49				-2253.869				-2231.54				-2229.699			
	SN model				ST model				SSlash model				SCN model			
β	-0.460	0.014	-0.487	-0.435	0.230	0.021	0.177	0.267	-0.147	0.028	-0.205	-0.101	0.182	0.040	0.075	0.249
α	8.732	0.615	6.981	9.612	55.440	10.670	36.160	71.160	18.990	1.451	16.070	21.600	49.570	10.860	24.860	68.600
γ	-0.085	0.006	-0.100	-0.075	0.041	0.013	0.020	0.074	-0.144	0.018	-0.181	-0.111	0.040	0.013	0.021	0.073
σ^2	11.070	0.574	10.010	12.260	11.730	0.624	10.570	13.000	11.210	0.592	10.130	12.440	11.710	0.617	10.560	12.990
d_{11}	24.390	7.484	12.570	40.870	22.710	8.708	7.126	38.960	10.620	4.689	3.439	21.210	17.280	8.322	4.263	35.650
d_{12}	-1.136	0.510	-2.194	-0.182	-1.109	0.538	-2.232	-0.131	-0.714	0.390	-1.644	-0.107	-0.851	0.509	-1.994	-0.062
d_{22}	0.253	0.096	0.108	0.478	0.436	0.147	0.193	0.764	0.296	0.107	0.131	0.554	0.301	0.130	0.108	0.607
ν					5.112	2.647	0.984	9.747	3.122	3.710	1.069	16.630				
π													0.491	0.263	0.040	0.948
w													0.507	0.240	0.133	0.964
Δ_{b_1}	-5.896	2.242	-8.870	0.377	-2.605	5.449	-9.652	6.725	-7.184	1.325	-9.580	-4.569	-4.315	4.212	-9.259	6.101
Δ_{b_2}	-0.976	0.145	-1.253	-0.681	0.823	0.264	0.277	1.282	0.013	0.235	-0.414	0.517	1.029	0.245	0.554	1.508
DIC	5743				5806				5781				5751			
LPML	-2224.624				-2255.034				-2253.857				-2230.799			

Note: d_{ij}, $i, j = 1, 2$ are distinct components of the matrix $\boldsymbol{D}$.

Table 4. Bayesian parameter estimates, posterior means (standard deviations), and 95% credible intervals for the Menarche data under DP for random intercept.

Parameters	Est.	S.D.	CI 2.5%	CI 97.5%
β	-0.177	0.064	-0.323	-0.091
α	14.420	3.916	7.623	22.730
γ	-0.147	0.028	-0.201	-0.098
σ^2	14.330	0.691	13.030	15.740
ϖ	8.878	7.202	1.758	28.780

Table 5. Bayesian parameter estimates, posterior means (standard deviations), and 95% credible intervals for the Menarche data under DP for bivariate random effects.

Parameters	Est.	S.D.	CI 2.5%	CI 97.5%
β	-0.203	0.054	-0.294	-0.091
α	11.720	2.491	7.413	17.210
γ	-0.148	0.027	-0.213	-0.111
ϖ	5.585	1.974	2.225	9.511
d_{11}	162.300	130.400	41.460	530.900
d_{12}	-14.090	10.050	-40.110	-2.068
d_{22}	3.009	1.852	0.956	8.550

Note: $d_{ij},\ i,j = 1,2$ are distinct components of the matrix $\boldsymbol{D}$.

4. Conclusions

In this paper, a sensitivity analysis was performed on the results using different distributional assumptions of random effects in growth curve model. For this purpose, some parametric distributional assumptions (normal, normal/independent, skew-normal and skew-normal/independent) in a Bayesian paradigm and a Bayesian non-parametric approach by considering a Dirichlet process for the random effects were considered. The results under a famous sigmoidal growth model which has a better fitting versus usual normal model (Von Bertalanffy model) are reported. Also, the fitted curve for each model is superimposed on individual profiles. These fitted curves show similar behaviour of the random effects distributional assumptions. Also, the goodness of fit of different distributional assumptions are compared using some Bayesian criteria. In comparison with the Bayesian non-parametric approach, an interesting result was that one may find at least a nonparametric model which performs as similar as the parametric models via the Bayesian model comparison criterion LPML.

For future work, one may use other non-linear forms for the functions h in model (1). Also, in this paper, we considered the use of random intercept and bivariate random effects. One may also consider the effects of other covariates on the responses and also may consider higher order of random effects.

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