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ANALYZING THE EMERGENCE TIMES OF PERMANENT TEETH: AN EXAMPLE OF MODELING THE COVARIANCE MATRIX WITH INTERVAL-CENSORED DATA

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Analyzing the Emergence Times of Permanent Teeth: An Example of Modeling the Covariance Matrix with Interval-Censored Data

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Abstract

Adequate knowledge of timing and pattern of permanent tooth emergence is useful for diagnosis and treatment planning in paediatric dentistry and orthodontics and is essential in forensic dentistry. Based on a data set obtained in a large dental longitudinal study, conducted in Flanders (Belgium), the joint emergence distribution of seven teeth was modeled as a function of gender and caries experience on primary teeth. Besides establishing the marginal dependence of emergence on the covariates, there was also interest in examining the impact of the covariates on the association among emergence times. This allows to establish the preferred rankings of emergence and their dependence on covariates, but it necessitates to model the covariance matrix (of a multivariate normal distribution) as a function of covariates. Modeling the covariance matrix has received recently quite some attention in the literature. Indeed, in a variety of statistical models allowing the covariance matrix to depend on covariates can improve the fit of the model to the data considerably and can imply a dramatic change in the conclusion, especially for non-linear models. However, modeling must to be done with care since the positive definiteness of the covariance matrix needs to be assured. Further, it is preferable that all regression parameters of the model are interpretable. The modified Cholesky representation of the covariance matrix, as suggested by Pourahmadi (1999), splits up the covariance matrix into two parts where the parameters can be interpreted given a natural ranking of the responses. This approach was used to model

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tooth emergence data. However, the emergence times were recorded in an interval-censored manner. Hence, we opted for a Bayesian implementation of the Data Augmentation algorithm.

Key words: Bivariate survival; covariance matrix; data augmentation; emergence times; interval-censored; multivariate Normality.

1 INTRODUCTION

In this paper a Bayesian approach is applied to model multivariate normal interval censored data, whereby, besides the marginal distributions, also the covariance matrix is allowed to depend on covariates. Modeling a covariance matrix as a function of covariates is complex due to the requirement that it should be positive-definite (pd). A variety of approaches have been suggested to deal with the pd-condition. Further, in statistical modeling an important aspect is the interpretability of the model parameters. The approach suggested by Pourahmadi (1999) offers a trade-off between computational complexity and interpretability of the regression coefficients of the covariates. More specifically, he suggested to break up the covariance matrix into a unit lower triangular matrix T and a diagonal matrix D, by making use of the modified Cholesky decomposition of the inverse of the covariance matrix. One advantage of this parametrization is that the covariance matrix automatically satisfies the pd-condition. In addition, the elements of T can be interpreted as regression coefficients of conditional regression models, while the diagonal elements of D represent conditional variances.

The motivating example is taken from dentistry. More specifically, we have looked at the emergence times of permanent teeth. The emergence time of a tooth is the chronological age of the child when that tooth appears in the mouth. Adequate knowledge of timing and pattern of permanent tooth emergence is useful for diagnosis and treatment planning in paediatric dentistry and orthodontics and is essential in forensic dentistry. Further, according to Demirjian (1978) (and others) emergence standards should be derived from the relevant population. However, an extra complication is that it is impossible in practice to know the emergence time precisely. Indeed, the emergence time is always recorded in an interval-censored manner. That is, either the tooth has emerged before the first examination (left-censored), emerged in-between two examinations (interval-censored), or emerges after the last examination (right-censored). Consequently, we applied Pourahmadi 's (1999) approach on the true, but unobserved, emergence times which were supposed to follow a multivariate normal distribution. For this reason, we invoked the Data Augmentation algorithm and opted for a Bayesian approach. In three previous publications (Bogaerts et al., 2002; Leroy et al., 2003a,b) our group examined the emergence distribution of all permanent teeth (excluding the wisdom teeth) of Flemish children. For this we have used data from the Signal Tandmobiel®project, a 6-year prospective longitudinal study, which collected annually dental and oral behavior data from a representative sample of Flemish children. In our previous work we focussed at the marginal emergence distributions. Here we explored also whether the association between the emergence times depends on gender and caries experience on deciduous teeth. Modeling jointly the marginal and the association structure allowed us to establish the most preferred emergence rankings and to see how much the ranking depends on the covariates. Indeed, for a long time dental researchers were interested in the mean emergence ranking (obtained from the mean/median emergence times) but also in establishing the prevalence of the most preferred emergence rankings, see e.g.Adler (1963) and Savara and Steen (1973). However, establishing the prevalence of each emergence ranking is not trivial due to the large number of possible rankings. In this paper we explored the seven permanent teeth of the right maxilla quadrant. Hence, there were $7! = 5040$ possible rankings to consider.

In Section 2 we describe the Signal Tandmobiel® study, introduce the specific research questions and briefly overview the literature in this respect. In Section 3, we introduce the multivariate model and discuss approaches to model the covariance matrix as a function of covariates. We focus in this section on the modified Cholesky decomposition of the covariance matrix, the interpretation of the parameters and its use in modeling the covariance matrix. Bayesian modeling of multivariate interval censored normal data will be treated in Section 4. The application of this approach to the Signal Tandmobiel® data is described in Section 5. Some concluding remarks are given in Section 6.

2 The Dental Example

2.1 A brief overview of the research on emergence times

The interest for the timing and sequence of permanent teeth dates back to the 19th century, see e.g. Adler (1963). Since then, numerous publications have appeared on this topic, see e.g. Leroy et al. (2003a) and references therein. One reason for this interest is that emergence standards should be derived from the relevant population, as factors related to emergence may vary considerably geographically as well as over time, see e.g. Demirjian (1978). Virtanen et al. (1994) found several factors which have a relationship with the emergence time of permanent teeth in a Finnish population, namely: gender, ethnicity, environmental, socio-economic and secular factors. To establish the emergence distributions, two study types are in use: cross-sectional studies and cohort studies. In the cross-sectional study (e.g. Eskeli et al., 1999; Mungonzibwa et al., 2002) the eruption stage of each tooth is established at one time point. However, in this type of study the estimate of the distribution of the emergence times is confounded with secular trends. In a cohort study (e.g. Virtanen et al., 1994; Parner et al., 2001, 2002), the eruption stage is repeatedly measured in time. It is important to note that the emergence of a tooth can never be determined precisely in practice leading to interval-censored observations. Indeed, the only information available is that the tooth emerged between two study visits. In the past, one often replaced the interval wherein the tooth emerged by its mid-point thereby allowing to use classical survival methods to estimate the distribution of the emergence times, e.g. Savara and Steen (1973). However, it is known that this procedure yields biased parameter estimates of the emergence distribution, see e.g. Bogaerts and Lesaffre (2006). Recently, our group (Bogaerts et al., 2002; Leroy et al., 2003a) explored the marginal distribution of the emergence time of the 28 permanent teeth of children from Flanders (Belgium) using the Signal-Tandmobiel®data taking into account the interval-censored nature of emergence times. More specifically, we fitted a log-logistic survival model to each tooth separately and found that the emergence of permanent teeth differs by gender (inter-subject comparison), i.e. teeth of girls emerge earlier than those of boys. We also verified whether there are differences in the emergence distribution of contralateral (left-right) or opposing (upper-lower) teeth (intra-subject comparisons). In order to answer these questions, a log-logistic multivariate survival GEE model was fitted to take into account the dependency between teeth in the same mouth thereby treating the association of emergence times as nuisance. A significant difference in emergence ages for opposing teeth was found, both for girls and boys. Finally, Leroy et al. (2003b) found that caries experience on a deciduous molar has an impact on the emergence of the permanent successor. In general, caries on the deciduous molar accelerated the emergence of the successor. However, this was not seen for all molars and others reported that the effect depends on whether (and when) the deciduous molar was extracted or not, (see Kochhar and Richardson, 1998). Summarized, caries on the deciduous teeth distort the emergence process.

A number of papers looked at the association between emergence times. For instance, Parner et al. (2001) and Parner et al. (2002) studied the association between the emergence times of permanent teeth in a Danish population.They obtained maximum likelihood estimates for the correlation coefficients under the assumption of a bivariate normal distribution for a pair of emergence times. Bogaerts and Lesaffre (2006) proposed to calculate Kendall's τ for the association of interval-censored survival times based on a smooth estimate of the bivariate survival distribution. This technique was applied to the emergence times of the seven permanent teeth of the upper right quadrant of the mouth from children of the Signal Tandmobiel®study. The association pattern of boys was compared to that of girls, but no significant different patterns were found. Parner et al. (2002) estimated the correlation coefficients of the emergence times in their bivariate normal model, separately for boys and girls, but did not compare them statistically.

Finally, besides the mean ranking of emergence determined by the mean/median emergence time, there is also interest in knowing the prevalence of the emergence rankings. Adler (1963) argues that too often the impression is given that the emergence sequence of the teeth follows a definite and regular pattern and points out that this concern was already pointed out in the 19th century. Savara and Steen (1973) explored the sequences of tooth emergence for children from Oregon. However, their sample size was too small to make any inferences.

2.2 The Signal-Tandmobiel®study and the main goals of this study

The Signal-Tandmobiel®study is a prospective longitudinal survey, which was set up in 1996 to collect dental and oral health behavior data on a representative sample of Flemish children born in 1989. The sample represents about 7 per cent of the child population of the same age and comprises 4468 children with 2153 (48.2 %) girls and 2315 (51.8 %) boys. Among other things, the project provides data on permanent tooth emergence for Flemish children from 7 to 12 years of age. They were examined annually on pre-scheduled visits by sixteen trained dental examiners in a mobile dental clinic.

Tooth emergence was recorded at each examination by direct inspection (at least one cusp visible). Each permanent tooth was scored according to its clinical eruption stage (adapted from Carvalho et al., 1989). However, for this study the emergence status of a tooth was dichotomized: not emerged versus emerged. We refer to Vanobbergen et al. (2000) for a comprehensive description of the project. As the children were examined annually, the emergence data are interval censored. This means that the time of emergence of a tooth, Y, is only known to lie in an interval $[t_l, t_r]$, but for some children and teeth the emergence was left- or right-censored. Left- and right- censored data are special cases of interval-censored data, with $t_l = 0$ for left-censored observations and $t_r = \infty$ for right-censored observations.

As seen above, previous analyses of our group showed a dependence of the marginal distribution on gender and caries experience of the primary teeth, see e.g., Bogaerts et al. (2002), Leroy et al. (2003a) and Leroy et al. (2003b). In this paper, we treat the dependence of the association on the same covariates. In fact, we have modeled both the marginal as well as the association structure as a function of the covariates. This enabled us to estimate the prevalence of all emergence rankings and to evaluate how the prevalence changes with the values of the covariates.

In this paper, we study the emergence times of permanent teeth of the upper left quadrant of the mouth. In the European notation, these are the teeth denoted as 1x, where $x = 1, \ldots, 7$. The incisors are denoted as 11 and 12, the canine as 13, the pre-molars as 14 and 15, the molars as 16 and 17. Examining all 28 permanent teeth (excluding the wisdom teeth) jointly would be computationally too demanding, since it implies estimating e.g. 378 correlation coefficients. Since the emergence times are interval-censored and to avoid the calculation of complicated derivatives, an MCMC approach was preferred making use of the Data Augmentation algorithm (Tanner and Wong, 1987).

3 Modeling the covariance matrix of a multivariate normal distribution

To allow the association to depend on covariates implies that we need to model the covariance matrix of the multivariate normal model as a function of covariates. A brief overview of what has been proposed in the literature is given below.

3.1 Some parameterizations of the multivariate normal model

Assume that the response vector (of true emergences) for the *i-th* subject follows a multivariate normal distribution, i.e.

$$\boldsymbol{Y}_i \sim N_p(\boldsymbol{X}_i\boldsymbol{\beta}, \Sigma_i), \qquad (i = 1, \dots, n) \tag{1}$$

where $\boldsymbol{Y}_i$ is a $p \times 1$ vector of responses, $\boldsymbol{\beta} = (\boldsymbol{\beta}_1^T, \dots, \boldsymbol{\beta}_p^T)^T$, with $\boldsymbol{\beta}_s$ a $q \times 1$ vector of regression coefficients corresponding to the sth response, and $\boldsymbol{X}_i$ is a $p \times (q \times p)$ design matrix given by

$$\boldsymbol{X}_i = I_{pp} \otimes \boldsymbol{x}_i^T,$$

where I_{pp} is the $p \times p$ identity matrix, $\otimes$ the Kronecker product and $\boldsymbol{x}_i^T = (1, x_{1i}, \dots, x_{q-1,i})$. Further, Σ_i is the covariance matrix of the ith subject.

A natural parametrization of the covariance matrix, discussed by Barnard et al. (2000), is to use the variance-correlation decomposition. More specifically, this decomposition implies that $\Sigma_i = \Gamma_i R_i \Gamma_i$, where Γ_i is the diagonal matrix of the standard deviations and R_i the correlation matrix. If Σ_i depends on the subject, some statistical modeling is necessary to reduce the number of parameters. This can be achieved by expressing the (components of the) covariance matrix as a function of covariates. For the diagonal elements of Γ_i, σ_{si}, it is common to use the log link, i.e. $log(\sigma_{si}^2) = \boldsymbol{x}_i^T\boldsymbol{\lambda}_s$. For the elements of the correlation matrix, various authors (Song et al., 2004; Yan and Fine, 2004) suggested that Fisher's (or an analogous) transformation of the correlation coefficient be linearly related to covariates. That is, if $\rho_{st,i}$ is the (s,t)th entry of R_i then $\rho_{st,i} = \tanh(\boldsymbol{x}_i^T\boldsymbol{\psi}_{(s,t)})$. Fisher's transform removes the implied range constraints (due to the restrictions on correlations) on the covariates. This is useful, but is not sufficient to ensure positive definiteness of R_i when $p > 2$. In Figure 1 we display the smallest eigenvalue of a 3×3 correlation matrix where the Fisher's transform of the correlations depends linearly on a continuous covariate x. Clearly, positive definiteness is violated in some regions of the support of the covariate. But, even if R_i were positive definite in the range of the observed x-values of the sample, there is no guarantee that the correlation matrix remains positive definite for future values of x. This problem can also occur in the method proposed by Browne et al. (2002). Thus, while the approach yields interpretable parameters, this decomposition of the covariance matrix has undesirable computational properties.

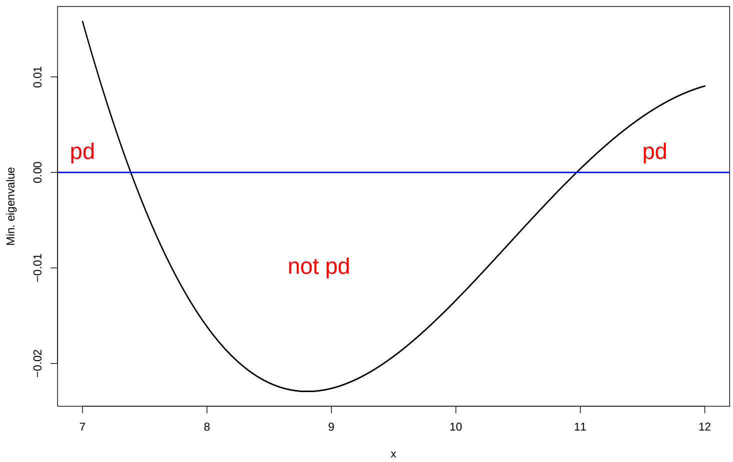

Figure 1: Positive definiteness of correlation matrix: minimum eigenvalue versus continuous covariate.

3.2 The modified Cholesky decomposition of the covariance matrix

Pinheiro and Bates (1996) described five different parameterizations for covariance matrices that ensure positive definiteness and leave the estimation process unconstrained. In particular, they considered two types of decompositions of the covariance matrix: the Cholesky and the spectral decomposition. In the Cholesky decomposition $\Sigma_i = L_i L_i^T$, where L_i is a lower triangular matrix. Further, they considered two related parameterizations. Two variations of the classical spectral decomposition were considered, both allowing unconstrained calculations. The classical spectral decomposition implies that $\Sigma_i = U_i \Lambda_i U_i^T$, where U_i is the orthogonal matrix of orthonormal eigenvectors of Σ_i and Λ_i the diagonal matrix of eigenvalues. Using a simulation study, they compared the performance of the five methods. It was found that computing time was less for the Cholesky decompositions. However, all of the decompositions lack good parameter interpretability.

Pourahmadi (1999) used the modified Cholesky decomposition of Σ_i^{-1} to propose a statistically unconstrained parametrization of the covariance matrix. The modified Cholesky decomposition is given by

$$T_i \Sigma_i T_i^T = D_i, \tag{2}$$

where T_i is a unique lower triangular matrix with 1's as diagonal entries and D_i a unique diagonal matrix with positive diagonal entries. In the next step the elements of T_i and D_i are expressed as functions of covariates. The elements of the decomposition enjoy a better interpretation than in the other decompositions, as we will show below.

Suppose $\boldsymbol{\beta}$ is given and $\Sigma_i \equiv \Sigma$. For simplicity reasons, we temporarily omit the dependence on the subject. Let $\hat{Y}_s$ be the linear least-squares predictor of Y_s, the sth component of $\boldsymbol{Y}$, on its predecessors $Y_{(s-1)}, \ldots, Y_1$ and $\epsilon_s = \hat{Y}_s - Y_s$ be its prediction error with variance $\tau_s^2 = var(\epsilon_s)$. Thus,

$$Y_s = \hat{Y}_s + \epsilon_s = \boldsymbol{x}^T \boldsymbol{\beta}_s + \sum_{j=1}^{s-1} \phi_{sj}(Y_j - \boldsymbol{x}^T \boldsymbol{\beta}_j) + \epsilon_s, \tag{3}$$

which is obtained by standard regression arguments. The components of this regression model are related to the elements of T and D. More specifically, $D = diag(\tau_1^2, \ldots, \tau_p^2)$ and $-\phi_{st}$ is the (s,t) entry of the matrix T. This decomposition allows to introduce covariates very easily through the unconstraint entries of the T matrix and the logarithm of the diagonal entries of the D matrix without any concern for the pd-condition.

Following Pourahmadi (1999), it is proposed here to model the dependence of the association structure on covariates as follows:

$$\log(\tau_{s,i}^2) = \boldsymbol{x}_i^T \boldsymbol{\lambda}_s, \tag{4}$$

$$\phi_{st,i} = \boldsymbol{x}_i^T \boldsymbol{\gamma}_{st}, \tag{5}$$

where $\boldsymbol{\lambda}_s$ $(s = 1, \ldots, p)$ and $\boldsymbol{\gamma}_{st}$ $(s = 2, \ldots, p; t = 1, \ldots, (p-1))$ are vectors of regression coefficients for the log-transformed conditional variances and the dependence parameters, respectively. Expressions (4) and (5) can be generalized by allowing different covariates for the conditional variances and dependence parameters.

Summarized, the parameters to be estimated in model (1) are:

- The regression parameters of the marginal distribution: $\boldsymbol{\beta} = (\boldsymbol{\beta}_1^T, \ldots, \boldsymbol{\beta}_p^T)^T$;
- The regression parameters of the conditional variances: $\boldsymbol{\lambda} = (\boldsymbol{\lambda}_1^T, \ldots, \boldsymbol{\lambda}_p^T)^T$;
- The regression parameters of the dependence parameters: $\boldsymbol{\gamma} = (\boldsymbol{\gamma}_{21}^T, \ldots, \boldsymbol{\gamma}_{p,(p-1)}^T)^T$.

For the interpretability of the parameters, the approach of Pourahmadi is based on the assumption that there is some logical ranking of the components of $\boldsymbol{Y}$. Such a natural ranking is present in longitudinal studies or time series. However, in our dental example, we cannot claim that there is a unique ranking of the emergence times in each subject. In fact, one of our goals is to look for the preferred rankings. Therefore, we have ranked the components of $\boldsymbol{Y}$ according to the estimated mean emergence time. While the statistical interpretation of the regression parameters remains the same their practical interpretability is less straightforward. An excellent overview of modeling covariance matrices can be found at the Website http://www.math.niu.edu/ pourahm/.

4 Modeling multivariate interval censored normal data

For the estimation of the regression parameters, we have followed the approach of Daniels and Pourahmadi (2002). Hence, we refer to that paper for more technical details. Briefly, the prior distributions for the parameter vectors $\boldsymbol{\beta}$, $\boldsymbol{\lambda}$ and $\boldsymbol{\gamma}$ are

$$\boldsymbol{\beta} \sim N(\boldsymbol{\beta}^*, \Sigma_\beta), \;\; \boldsymbol{\lambda} \sim N(\boldsymbol{\lambda}^*, \Sigma_\lambda), \;\; \boldsymbol{\gamma} \sim N(\boldsymbol{\gamma}^*, \Sigma_\gamma).$$

The normal priors for $\boldsymbol{\beta}$ and $\boldsymbol{\gamma}$ are conditionally conjugate to the full conditionals of the respective parameter vectors. Indeed, the full conditionals for $\boldsymbol{\beta}$ and $\boldsymbol{\gamma}$ are normals, which allows straightforward Gibbs sampling. The parameter vector $\boldsymbol{\lambda}$ can be sampled using a Random Walk Metropolis with a normal proposal. The covariance matrix of the normal proposal was chosen as a multiple of $(\boldsymbol{X}^T\boldsymbol{X})^{-1}$, where the scale factor was tuned to achieve an acceptance rate of about 26%.

Up to now, we have modeled the true, but *unobserved*, emergence times $\boldsymbol{Y}_i$. However, in our study we only have the interval censored emergence time, $\tilde{\boldsymbol{Y}}_i$. An extra Gibbs step using the Data Augmentation algorithm allows to generate easily the latent emergence times, given the interval censored observed emergence times. Basically, at each iteration of the MCMC chain, all 'true' observations are imputed from their full conditional distribution and then the parameter vector is updated based on the complete imputed sample. Under the assumption that the true emergence times $\boldsymbol{Y}_i$ follow a multivariate normal distribution, the full conditional distribution of $\boldsymbol{Y}_i$, given the remaining parameters and the observed data $\tilde{\boldsymbol{Y}}_i$, is multivariate normal truncated to the region determined by the Cartesian product of the intervals where each Y_{si}, $(s = 1, \ldots, p)$ lies. Let $C_i = [l_{1,i}, r_{1,i}] \times \ldots \times [l_{p,i}, r_{p,i}]$ be the region where $\boldsymbol{Y}_i$ $(i = 1, 2, \ldots, n)$ lies and let $\mathcal{D} = \{C_i\}_{1 \leq i \leq n}$ be the observed n hyper-cubes. Since the observations are independent given $\boldsymbol{\beta}$, $\boldsymbol{\gamma}$ and $\boldsymbol{\lambda}$ and assuming that censoring occurs non-informatively (as in the Signal Tandmobiel®study), it follows that

$$\boldsymbol{Y}_i \sim N(\boldsymbol{X}_\mathbf{i}\boldsymbol{\beta}, \Sigma_i) \times I_{C_i}, \tag{6}$$

where I_{C_i} is the characteristic function of the hyper-cube C_i, and $\Sigma_i = \Sigma_i(\boldsymbol{X}_i\boldsymbol{\lambda}, \boldsymbol{X}_i\boldsymbol{\gamma})$.

In order to sample from distribution (6), at each iteration of the Gibbs sampler, we sampled iteratively the components of $\boldsymbol{Y}_i$ which have truncated univariate normal distributions using the inverse function method (Ripley, 1987).

5 Application of the Bayesian approach to the Signal Tandmobiel®study

5.1 Details on the implemented Bayesian modeling procedure

Since many authors have found that the normal distribution fits the emergence times quite well, see e.g. Parner et al. (2001) and Parner et al. (2002), we assumed here that the true emergence times follows a multivariate normal distribution.

The Bayesian approach was programmed in C using the Scythe library (Quinn and Martin, 2002). One chain was run for $25,000$ iterations as burn-in. The convergence of the Gibbs sampler was monitored by examining trace plots of the parameters and using the convergence diagnostics of Heidelberger and Welch and of Raftery and Lewis, implemented in the R Coda package (Plummer et al., 2005). Since a large number of parameters needed to be sampled, a 1:5 thinning was applied for reasons of computer storage. For the estimation of the parameters, a further $25,000$ iterations were run, yielding $25,000/5 = 5,000$ samples from which the estimates were obtained. 95% highest posterior density (HPD) intervals were determined using the approach of Chen and Shao (1999) implemented in the R BOA package (Smith, 2005). As mentioned in Section 3.2, there is no unique ranking of the components of the response vector. Based on the mean ranking of the emergence times, we have taken the following ranking for the teeth: 16-11-12-14-13-15-17. This ranking defines the components of the vector $\boldsymbol{Y}$. The prevalence of all possible sequences of emergence was calculated for each gender$\times dmft$ combination separately. Let a sequence of emergence times be denoted as $i_1i_2i_3i_4i_5i_6i_7$, then the prevalence of this sequence was determined by

$$P(Y_{i_1} < Y_{i_2} < Y_{i_3} < Y_{i_4} < Y_{i_5} < Y_{i_6} < Y_{i_7}) = \int_S \phi(\mathbf{x}|\boldsymbol{\mu}, \Sigma)d\mathbf{x},$$

where $\phi(\mathbf{x}|\boldsymbol{\mu}, \Sigma)$ represents the multivariate normal density with mean vector $\boldsymbol{\mu}$ and covariance matrix Σ; and $S = \{(y_{i_1}, y_{i_2}, y_{i_3}, y_{i_4}, y_{i_5}, y_{i_6}, y_{i_7}) \in R^7 |\, y_{i_1} < y_{i_2} < y_{i_3} < y_{i_4} < y_{i_5} < y_{i_6} < y_{i_7}\}$. This integral was numerically calculated using Quasi-Monte Carlo Integration techniques. In contrast to the Monte Carlo Integration, the technique of Quasi Monte Carlo relies on point sets in which the points are not chosen i.i.d from the uniform distribution but rather interdependently using pseudo-random sequences (see e.g. Hickernell and Owen, 2005). In order to implement the Quasi Monte Carlo Integration, we slightly modified the *rmvnorm* function of Genz et al. (2005) changing the random generation from a normal distribution by the *rnorm.halton* function implemented in Wuertz (2005). This function calculates a matrix of normal distributed pseudo random numbers.

5.2 Results

We considered two determinants for emergence: (1) gender (0=boy, 1=girl) and (2) caries experience on the deciduous teeth at the age of seven. As indicated in Section 2, a gender effect on emergence has been established by several researchers. Namely, teeth emerge earlier in girls than in boys. Further, in Leroy et al. (2003b) the effect of caries experience in a deciduous molar on its successor has been examined for each premolar separately. Here, we have taken as covariate the $dmft$-index at the age of seven. The $dmft$-index is a popular measure for caries experience and is the sum of the deciduous teeth which are either decayed, or missing due to extraction because of caries, or filled. Thus, the $dmft$-index in our study is a surrogate marker for the brushing- and dietary behavior of the child in its first seven years. In Figure 2 the histogram of the $dmft$-index for the seven-year old children from the Signal Tandmobiel ®Study is shown. About 44% of the children were caries-free at the level of cavitation, but the very skewed distribution of the $dmft$-index shows that there are subgroups of children with quite some caries experience, already in their early childhood. Summarized, we fitted model (1) to the above defined seven permanent teeth and modeled Σ_i according to expressions (2), (4) and (5). The $dmft$-index was included linearly in the model for all components as a result of some exploratory parametric analyses using PROC LIFEREG (SAS Version 9.1) on the marginal distributions of the teeth emergences.

Marginal emergence distributions

The posterior means and the 95% HPD intervals of the regression parameters of the mean structure ($\boldsymbol{\beta}$) are shown in Table 1. Table 1 shows that the permanent teeth emerge earlier in girls than in boys, corroborating the findings of others. This also confirms the findings of an earlier analysis (not involving $dmft$-index) yielding as estimates (based on the median posterior summary statistic) for the mean emergence times (mean (tooth number)) in years for girls: 6.30 (16), 6.86 (11), 7.89 (12), 10.34 (14), 10.95 (13), 11.31 (15) and 12.02 (17). For boys the same ranking was found with values: 6.44 (16), 7.11 (11), 8.29 (12), 10.76 (14), 11.59 (13), 11.71 (15) and 12.35 (17). The present analysis shows that the emergence of all teeth is accelerated when there is (more) caries on the deciduous teeth, because of a negative regression coefficient for $dmft$. But only for teeth 13 (canine), 14 and 15 (pre-molars) the 95% HPD-interval does not encompass 0. These results confirm what has been reported by Leroy et al. (2003b).

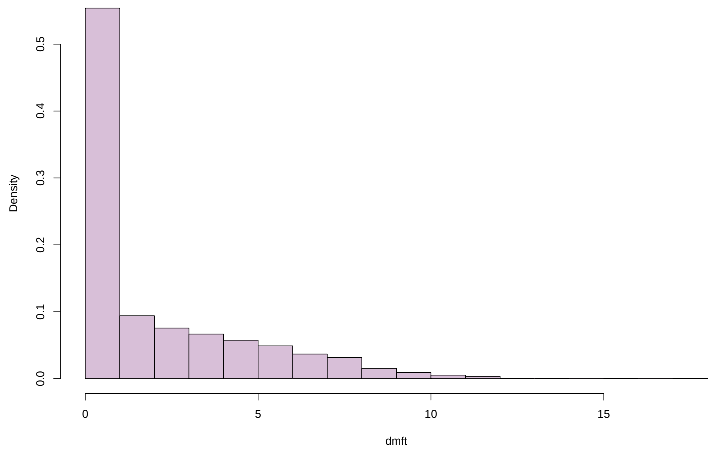

Figure 2: Signal Tandmobiel ®Study: distribution of $dmft$-index at the age of seven.

Table 1: Posterior means (95 % HPD) of regression coefficients ($\boldsymbol{\beta}$) for the marginal part of the multivariate normal model.

	Tooth	Intercept	Gender (1=Girls)	$dmft$ ($\times 100$)
Y_1	16	6.44	-0.13	-0.45
		(6.40,6.49)	(-0.19,-0.07)	(-1.48,0.55)
Y_2	11	7.11	-0.24	-0.07
		(7.07,7.16)	(-0.30,-0.19)	(-1.00,0.84)
Y_3	12	8.30	-0.39	-0.48
		(8.25,8.35)	(-0.45,-0.33)	(-1.56,0.54)
Y_4	14	11.03	-0.41	-12.63
		(10.96,11.10)	(-0.49,-0.33)	(-14.16,-11.11)
Y_5	13	11.64	-0.63	-2.39
		(11.55,11.71)	(-0.73,-0.54)	(-3.87,-0.79)
Y_6	15	11.89	-0.37	-10.46
		(11.80,11.99)	(-0.49,-0.27)	(-12.47,-8.39)
Y_7	17	12.38	-0.32	-0.98
		(12.28,12.49)	(-0.45,-0.19)	(-3.35,1.01)

Table 2 expresses the dependence of the (log)-conditional variance on the covariates. Again, there is a (significant) effect of the covariates for some of the teeth. The problem, however, is that it is not immediately clear what the impact is of these covariates on the marginal variances. For instance, it can be read off from this table is that, given teeth 16 and 11 have emerged, the variability of emergence of tooth 12 is higher for girls than for boys ($\lambda_{31} = 0.24$). On the whole it seems that the variability is less for girls than for boys. Further, a higher $dmft$-index implies overall a higher conditional variance. Since the effect of the $dmft$-index is quite consistent over teeth (except for tooth 16 where there seems to be a slight negative effect), we speculated that the marginal variance of emergence is higher in children with an inadequate diet- and/or brushing behavior in the first six years of their life.

Table 2: Posterior means (95 % HPD) of regression coefficients ($\boldsymbol{\lambda}$) for the log of conditional variances of the multivariate normal model.

	Tooth	Intercept	Gender (1 = Girls)	$dmft$ (×100)
Y_1	16	−0.94	−0.21	−0.10
		(−1.05,−0.85)	(−0.36,−0.07)	(−2.04,1.79)
Y_2	11	−0.91	−0.04	0.24
		(−1.01,−0.81)	(−0.17,0.11)	(−1.97,2.09)
Y_3	12	−0.88	0.24	0.51
		(−0.99,−0.77)	(0.10,0.34)	(−1.97,3.11)
Y_4	14	−0.05	−0.32	8.05
		(−0.16,0.06)	(−0.47,−0.16)	(5.89,10.13)
Y_5	13	−0.37	−0.21	3.74
		(−0.50,−0.23)	(−0.33,−0.06)	(0.57,6.65)
Y_6	15	−0.59	0.04	11.85
		(−0.78,−0.44)	(−0.17,0.21)	(9.15,14.52)
Y_7	17	−1.04	0.18	6.54
		(−1.31,−0.80)	(−0.16,0.61)	(2.28,12.59)

The marginal variance is a highly non-linear function of the covariates. A simple way to obtain an estimate of the marginal variances is to sample the posterior predictive distributions of the marginal emergences given a priori chosen gender× $dmft$-combinations. As an illustration, Table 3 shows the marginal variances of tooth 14 for boys and girls separately and for the subgroups $dmft = 0, 1, 5, 10$, and 15. It is clear that the above speculations based on the conditional variances were correct. In Table 4 we show the marginal variances for all teeth split up according to gender and $dmft$-index. Further, in Table 5 we compare the marginal variances of boys with girls at the average $dmft$-index. For all teeth except 12, the marginal variance of girls is lower than that of boys, but only for teeth 16 (molar) and 14 (pre-molar) the 95% HPD interval does not include 0. Table 6 shows the significant differences in marginal variances by gender at the average $dmft$.

Table 3: Posterior mean of marginal variances for tooth 14 as a function of $dmft$.

$dmft$	Girls	Boys
0	1.25	1.53
1	1.27	1.57
5	1.40	1.82
10	1.80	2.43
15	2.52	3.49

Table 4: Posterior mean of marginal variances by gender$\times dmft$.

		Girls					Boys				
		$dmft$					$dmft$				
Tooth	Node	0	1	5	10	15	0	1	5	10	15
16	σ^2_{11}	0.32	0.32	0.32	0.32	0.32	0.39	0.39	0.39	0.39	0.39
11	σ^2_{22}	0.53	0.53	0.51	0.5	0.49	0.56	0.55	0.54	0.52	0.52
12	σ^2_{33}	0.91	0.9	0.9	0.91	0.92	0.82	0.81	0.81	0.81	0.82
14	σ^2_{44}	1.25	1.27	1.4	1.8	2.52	1.53	1.57	1.82	2.43	3.49
13	σ^2_{55}	1.48	1.45	1.39	1.43	1.6	1.61	1.59	1.56	1.62	1.85
15	σ^2_{66}	1.66	1.71	2.08	3.04	4.87	1.82	1.87	2.22	3.13	4.87
17	σ^2_{77}	1.2	1.19	1.21	1.43	1.94	1.23	1.21	1.18	1.33	1.77

Dependence of association structure of emergence times on gender and $dmft$-index

The estimated $\boldsymbol{\gamma}$ regression coefficients, which determine the elements $\phi_{st,i}$ ($s = 2, \ldots, 7; t = 1, \ldots, 6$) of the lower unit triangular matrix T are shown in Table 7. While, some of the regression coefficients γ_{st} are significantly different from zero it is difficult, if not impossible, to get a clear picture of the impact of gender and $dmft$-index on the correlation coefficients. Therefore, we have shown in Table 8 the posterior mean of the correlations as a function of gender and the five $dmft$-subgroups. We see that for all teeth the correlation coefficient decreases with

Table 5: Posterior mean of marginal variances (95% HPD) at mean $dmft$ by gender.

Tooth		Girls	Boys
16	σ_{11}^2	0.32	0.39
		(0.29,0.34)	(0.36,0.42)
11	σ_{22}^2	0.52	0.55
		(0.48,0.57	(0.51,0.59)
12	σ_{33}^2	0.90	0.81
		(0.84,0.97)	(0.76,0.87)
14	σ_{44}^2	1.29	1.63
		(1.19,1.39)	(1.50,1.79)
13	σ_{55}^2	1.42	1.57
		(1.31,1.56)	(1.41,1.73)
15	σ_{66}^2	1.80	1.95
		(1.63,1.96)	(1.74,2.18)
17	σ_{77}^2	1.18	1.19
		(1.03,1.33)	(1.01,1.38)

Table 6: Posterior mean of differences in marginal variances by gender at mean $dmft$.

Tooth	Node	Mean (95% HPD)
16	$\sigma_{11}^{2g} - \sigma_{11}^{2b}$	-0.07
		$(-0.13,-0.03)$
14	$\sigma_{44}^{2g} - \sigma_{44}^{2b}$	-0.33
		$(-0.53,-0.16)$

increasing $dmft$-index. The explanation of this phenomenon is found in the fact that the impact of decayed deciduous teeth is complex and thereby increases the variability of the emergence process. Overall, caries on primary teeth distorts the emergence process and this has been indicated in several publications, see e.g. Leroy et al. (2003b) and Kochhar and Richardson (1998). Therefore, the distortion is more important for large values of $dmft$ and hence the association of the emergence times must be lower for higher $dmft$-values. In Table 9, we present the posterior correlation matrix by gender at the mean of $dmft$. Overall the correlations are quite similar, but some significant differences (in a Bayesian sense) are found, e.g. the correlation between emergence times of teeth 12 and 17 is lower for girls than for boys (Table 10).

Prevalence emergence times rankings

Above we have seen that for boys and girls the ranking obtained from the mean emergence times is: 16-11-12-14-13-15-17. Our analyses showed that this is also the most prevalent ranking for almost all gender$\times dmft$-combinations with prevalence varying between 10% and 18%. Further, the mean emergence times confirm what is known, namely that there are two phases of emergence. In the upper part of the mouth the first phase occurs between the ages of six and eight and involves teeth 16, 11 and 12 whereas the second phase occurs between the ages of 10 and 12. Thus, it did not come as a surprise that the next prevalent rankings differ from the most prevalent only by permutations within the phase. For example, the second most prevalent is often (but not always) the ranking: 16-11-12-14-15-13-17. We could have used this fact already from the start, which would have reduced the computations. However, we found it more elegant to analyze in this paper a whole quadrant of the mouth at once.

An important finding of our model is that caries distorts the ranking of emergence. This has been already indicated by others, see e.g. Adler (1963) and Savara and Steen (1973) but here this conclusion is based on a large number of children from a well controlled longitudinal dental study. The proof of this distortion is seen in Table 11. Firstly, we reported the number of rankings needed to cover 90% of the probabilities of the 7! possible rankings. For this, we first ranked the rankings in decreasing prevalence. It is seen in Table 11, that with increasing $dmft$-index the necessary number of rankings increases. A second measure is given by Shannon's entropy coefficient (see e.g., Shannon and Weaver, 1963). The higher the entropy the more dispersed the multinomial probabilities (of the 7! possible rankings) are. Clearly, the entropy coefficient increases with $dmft$-index indicating the ranking probabilities tend to show a more uniform profile when there is more caries in the deciduous teeth. In Tables 12-21 we show the estimated probabilities for the different rankings (up to cover 90% of the

Table 7: Posterior mean (95 %HPD) of the regression coefficients ($\boldsymbol{\gamma}$) of the entries of the T-matrix.

Tooth		Intercept	Gender (1=Girls)	$dmft$ ×100
11	ϕ_{12}	0.63	0.04	−1.02
		(0.54,0.71)	(−0.07,0.15)	(−2.88,0.87)
12	ϕ_{13}	0.11	0.09	−0.78
		(−0.01,0.23)	(−0.09,0.25)	(−3.27,1.77)
	ϕ_{23}	0.80	−0.04	0.27
		(0.72,0.88)	(−0.16,0.06)	(−1.48,1.97)
14	ϕ_{14}	0.28	0.29	−3.37
		(0.09,0.47)	(0.05,0.53)	(−7.61,0.69)
	ϕ_{24}	0.66	−0.32	0.66
		(0.50,0.83)	(−0.51,−0.11)	(−2.89,4.46)
	ϕ_{34}	0.22	0.13	−2.02
		(0.10,0.32)	(−0.01,0.25)	(−4.43,0.38)
13	ϕ_{15}	0.06	0.01	−0.58
		(−0.13,0.26)	(−0.21,0.25)	(−4.58,3.52)
	ϕ_{25}	0.27	−0.07	3.63
		(0.10,0.45)	(−0.27,0.12)	(0.42,7.17)
	ϕ_{35}	0.26	0.03	−0.11
		(0.15,0.37)	(−0.10,0.15)	(−2.18,2.10)
	ϕ_{45}	0.52	0.06	−3.40
		(0.45,0.58)	(−0.02,0.14)	(−4.67,−2.04)
15	ϕ_{16}	0.19	0.06	−0.28
		(−0.01,0.39)	(−0.20,0.31)	(−5.12,3.99)
	ϕ_{26}	0.23	−0.17	−0.44
		(0.06,0.41)	(−0.38,0.05)	(−4.72,3.66)
	ϕ_{36}	0.01	0.05	0.69
		(−0.11,0.11)	(−0.08,0.19)	(−1.77,3.27)
	ϕ_{46}	0.62	0.11	−0.37
		(0.54,0.70)	(0.00,0.20)	(−2.11,1.32)
	ϕ_{56}	0.18	−0.09	−0.12
		(0.09,0.26)	(−0.19,0.02)	(−2.10,1.85)
17	ϕ_{17}	0.95	−0.20	−5.80
		(0.69,1.18)	(−0.62,0.27)	(−10.98,−0.61)
	ϕ_{27}	0.10	−0.06	5.04
		(−0.13,0.33)	(−0.34,0.20)	(0.64,9.76)
	ϕ_{37}	0.07	−0.001	−0.68
		(−0.06,0.20)	(−0.15,0.15)	(−3.07,1.87)
	ϕ_{47}	0.11	−0.04	−0.22
		(−0.01,0.22)	(−0.17,0.09)	(−2.43,1.99)
	ϕ_{57}	0.03	0.05	0.41
		(−0.08,0.14)	(−0.07,0.16)	(−1.83,2.47)
	ϕ_{67}	0.17	0.12	−1.03
		(0.07,0.28)	(0.01,0.23)	(−2.69,0.77)

Table 8: Posterior mean of correlation coefficients by gender × $dmft$

	Girls					Boys				
	$dmft$					$dmft$				
Node	0	1	5	10	15	0	1	5	10	15
ρ_{12}	0.52	0.51	0.48	0.45	0.41	0.52	0.52	0.49	0.45	0.41
ρ_{13}	0.42	0.41	0.37	0.33	0.29	0.42	0.41	0.37	0.32	0.27
ρ_{14}	0.53	0.5	0.38	0.23	0.11	0.42	0.39	0.27	0.13	0.03
ρ_{15}	0.47	0.45	0.37	0.29	0.23	0.4	0.38	0.31	0.25	0.21
ρ_{16}	0.51	0.48	0.36	0.23	0.13	0.46	0.44	0.32	0.2	0.11
ρ_{17}	0.67	0.64	0.51	0.33	0.16	0.75	0.73	0.61	0.43	0.25
ρ_{23}	0.64	0.63	0.62	0.61	0.6	0.7	0.7	0.69	0.67	0.66
ρ_{24}	0.56	0.54	0.44	0.32	0.22	0.58	0.56	0.46	0.33	0.23
ρ_{25}	0.58	0.58	0.57	0.56	0.55	0.6	0.59	0.57	0.55	0.53
ρ_{26}	0.52	0.49	0.4	0.28	0.19	0.61	0.59	0.49	0.36	0.26
ρ_{27}	0.53	0.53	0.53	0.52	0.49	0.61	0.61	0.61	0.59	0.55
ρ_{34}	0.56	0.53	0.41	0.27	0.15	0.5	0.47	0.36	0.23	0.13
ρ_{35}	0.61	0.6	0.55	0.5	0.47	0.56	0.55	0.51	0.47	0.45
ρ_{36}	0.51	0.49	0.38	0.26	0.17	0.51	0.48	0.39	0.28	0.2
ρ_{37}	0.5	0.49	0.44	0.37	0.31	0.51	0.51	0.47	0.42	0.36
ρ_{45}	0.74	0.72	0.61	0.43	0.2	0.7	0.68	0.56	0.38	0.13
ρ_{46}	0.79	0.77	0.69	0.59	0.5	0.8	0.78	0.7	0.6	0.51
ρ_{47}	0.65	0.63	0.53	0.39	0.26	0.6	0.58	0.49	0.36	0.24
ρ_{56}	0.65	0.62	0.5	0.34	0.18	0.68	0.66	0.54	0.39	0.22
ρ_{57}	0.59	0.58	0.51	0.44	0.38	0.55	0.54	0.49	0.43	0.36
ρ_{67}	0.69	0.67	0.58	0.45	0.32	0.65	0.63	0.53	0.39	0.23

Table 9: Posterior correlation matrix at *mean* $dmft$ by gender (Girls/Boys, below/above diagonal).

Tooth	16	11	12	14	13	15	17
16	1	0.53	0.46	0.45	0.43	0.47	0.66
11	0.5	1	0.69	0.49	0.56	0.47	0.58
12	0.4	0.63	1	0.47	0.56	0.46	0.53
14	0.46	0.51	0.5	1	0.68	0.78	0.64
15	0.42	0.57	0.58	0.69	1	0.61	0.6
16	0.45	0.47	0.45	0.75	0.58	1	0.69
17	0.6	0.53	0.48	0.6	0.56	0.64	1

Table 10: Significant differences in correlation coefficients by gender at mean $dmft$.

Teeth pair	Node	
16-12	$\rho^g_{13} - \rho^b_{13}$	-0.06
		$(-0.09,-0.03)$
11-12	$\rho^g_{23} - \rho^b_{23}$	-0.06
		$(-0.1,-0.03)$
11-17	$\rho^g_{27} - \rho^b_{27}$	-0.04
		$(-0.09,-0.01)$
12-17	$\rho^g_{37} - \rho^b_{37}$	-0.05
		$(-0.09,-0.01)$
14-15	$\rho^g_{45} - \rho^b_{45}$	-0.04
		$(-0.07,-0.01)$

probabilities of the total rankings).

Table 11: Number of rankings to cover 90% of the total probability of rankings and Shannon's entropy coefficient for each gender$\times dmft$-index combination.

	Girls		Boys	
dmft	N	Entropy	N	Entropy
0	27	3.226	24	3.205
1	27	3.229	25	3.189
5	32	3.303	30	3.315
10	51	3.720	47	3.700
15	96	4.352	83	4.281

Table 12: Estimated probabilities (up to 90% of the total probability of rankings) for Boys $\times$ $dmft = 0$.

Teeth sequence							$\hat{\pi}$
6	1	2	4	3	5	7	0.152
6	1	2	4	5	3	7	0.121
6	1	2	3	4	5	7	0.079
6	1	2	4	3	7	5	0.075

Continued ...

Table 12 – Continued

Teeth sequence							$\hat{\pi}$
6	1	2	4	5	7	3	0.062
6	1	2	3	4	7	5	0.049
6	1	2	4	7	3	5	0.043
6	1	2	4	7	5	3	0.041
1	6	2	4	3	5	7	0.041
6	1	2	5	4	3	7	0.034
1	6	2	4	5	3	7	0.032
1	6	2	3	4	5	7	0.024
6	1	2	3	5	4	7	0.021
6	1	2	5	4	7	3	0.019
6	1	2	7	4	3	5	0.019
6	1	2	7	4	5	3	0.015
6	1	2	3	7	4	5	0.015
6	1	2	5	3	4	7	0.013
6	1	2	7	3	4	5	0.011
1	6	2	5	4	3	7	0.009
1	6	2	4	3	7	5	0.008
6	1	2	7	5	4	3	0.006
1	6	2	4	5	7	3	0.006
1	6	2	3	5	4	7	0.006

Table 13: Estimated probabilities (up to 90% of the total probability of rankings) for Girls $\times$ $dmft = 0$.

Teeth sequence							$\hat{\pi}$
6	1	2	4	3	5	7	0.171
6	1	2	3	4	5	7	0.104
6	1	2	4	5	3	7	0.103
6	1	2	4	3	7	5	0.077
6	1	2	3	4	7	5	0.061
1	6	2	4	3	5	7	0.049
6	1	2	4	5	7	3	0.039
1	6	2	3	4	5	7	0.037
6	1	2	5	4	3	7	0.032
6	1	2	4	7	3	5	0.026
1	6	2	4	5	3	7	0.024
6	1	2	4	7	5	3	0.020
6	1	2	3	5	4	7	0.017

Continued ...

Table 13 – Continued

Teeth sequence							$\hat{\pi}$
6	2	1	4	3	5	7	0.015
6	1	2	5	4	7	3	0.015
1	6	2	3	4	7	5	0.015
1	6	2	4	3	7	5	0.014
6	2	1	3	4	5	7	0.012
6	1	2	5	3	4	7	0.011
6	1	2	3	7	4	5	0.011
6	2	1	4	5	3	7	0.008
6	1	2	7	4	3	5	0.008
1	6	2	5	4	3	7	0.008
6	2	1	4	3	7	5	0.006
6	1	2	7	4	5	3	0.006
6	2	1	3	4	7	5	0.006
1	6	2	3	5	4	7	0.005

Table 14: Estimated probabilities (up to 90% of the total probability of rankings) for Boys $\times$ $dmft = 1$.

Teeth sequence							$\hat{\pi}$
6	1	2	4	3	5	7	0.15
6	1	2	4	5	3	7	0.13
6	1	2	4	3	7	5	0.07
6	1	2	3	4	5	7	0.07
6	1	2	4	5	7	3	0.07
6	1	2	3	4	7	5	0.04
6	1	2	4	7	5	3	0.04
6	1	2	4	7	3	5	0.04
6	1	2	5	4	3	7	0.04
1	6	2	4	3	5	7	0.04
1	6	2	4	5	3	7	0.03
6	1	2	5	4	7	3	0.02
1	6	2	3	4	5	7	0.02
6	1	2	3	5	4	7	0.02
6	1	2	7	4	3	5	0.01
6	1	2	5	3	4	7	0.01
6	1	2	3	7	4	5	0.01
6	1	2	7	4	5	3	0.01
1	6	2	5	4	3	7	0.01

Continued ...

Table 14 – Continued

Teeth sequence							$\hat{\pi}$
6	1	2	7	3	4	5	0.01
1	6	2	4	3	7	5	0.01
1	6	2	4	5	7	3	0.01
6	2	1	4	3	5	7	0.01
6	1	2	7	5	4	3	0.01
1	6	2	3	5	4	7	0.01

Table 15: Estimated probabilities (up to 90% of the total probability of rankings) for Girls $\times$ $dmft = 1$.

Teeth sequence							$\hat{\pi}$
6	1	2	4	3	5	7	0.18
6	1	2	4	5	3	7	0.12
6	1	2	3	4	5	7	0.09
6	1	2	4	3	7	5	0.07
6	1	2	3	4	7	5	0.05
1	6	2	4	3	5	7	0.05
6	1	2	4	5	7	3	0.04
6	1	2	5	4	3	7	0.04
1	6	2	3	4	5	7	0.03
1	6	2	4	5	3	7	0.03
6	1	2	4	7	3	5	0.03
6	1	2	4	7	5	3	0.02
6	1	2	5	4	7	3	0.02
6	2	1	4	3	5	7	0.02
6	1	2	3	5	4	7	0.02
1	6	2	4	3	7	5	0.01
1	6	2	3	4	7	5	0.01
6	1	2	5	3	4	7	0.01
6	2	1	3	4	5	7	0.01
6	2	1	4	5	3	7	0.01
1	6	2	5	4	3	7	0.01
6	1	2	3	7	4	5	0.01
6	1	2	7	4	3	5	0.01
6	2	1	4	3	7	5	0.01
1	6	2	3	5	4	7	0.01
6	1	2	7	4	5	3	0.01

Table 16: Estimated probabilities (up to 90% of the total probability of rankings) for Boys × $dmft = 5$.

Teeth sequence							$\hat{\pi}$
6	1	2	4	3	5	7	0.168
6	1	2	4	5	3	7	0.133
6	1	2	4	3	7	5	0.077
6	1	2	4	5	7	3	0.062
6	1	2	3	4	5	7	0.059
6	1	2	5	4	3	7	0.047
1	6	2	4	3	5	7	0.036
6	1	2	4	7	3	5	0.033
6	1	2	4	7	5	3	0.032
1	6	2	4	5	3	7	0.031
6	1	2	3	4	7	5	0.029
6	1	2	5	4	7	3	0.027
6	1	4	2	3	5	7	0.018
6	1	2	5	3	4	7	0.017
6	1	2	3	5	4	7	0.017
1	6	2	5	4	3	7	0.013
1	6	2	3	4	5	7	0.012
6	1	2	5	7	4	3	0.009
1	6	2	4	3	7	5	0.009
1	6	2	4	5	7	3	0.008
6	1	4	2	5	3	7	0.008
6	1	2	7	4	5	3	0.008
6	2	1	4	3	5	7	0.007
6	1	4	2	3	7	5	0.007
6	1	2	7	4	3	5	0.007
6	2	1	4	5	3	7	0.007
6	1	2	3	7	4	5	0.006
6	1	2	7	5	4	3	0.005
1	6	2	5	4	7	3	0.004
6	1	2	5	3	7	4	0.004

Table 17: Estimated probabilities (up to 90% of the total probability of rankings) for Girls $\times$ $dmft = 5$.

Teeth sequence							$\hat{\pi}$
6	1	2	4	3	5	7	0.168
6	1	2	4	5	3	7	0.158
6	1	2	4	3	7	5	0.065
6	1	2	3	4	5	7	0.058
6	1	2	5	4	3	7	0.056
6	1	2	4	5	7	3	0.049
1	6	2	4	3	5	7	0.042
1	6	2	4	5	3	7	0.033
6	1	2	3	4	7	5	0.032
6	1	2	5	4	7	3	0.023
1	6	2	3	4	5	7	0.020
6	1	2	4	7	3	5	0.019
6	2	1	4	3	5	7	0.016
6	1	2	4	7	5	3	0.015
6	2	1	4	5	3	7	0.015
1	6	2	4	3	7	5	0.015
6	1	2	5	3	4	7	0.013
1	6	2	5	4	3	7	0.013
6	1	2	3	5	4	7	0.012
6	1	4	2	5	3	7	0.011
1	6	2	3	4	7	5	0.010
6	2	1	3	4	5	7	0.007
6	1	4	2	3	5	7	0.007
1	6	2	4	5	7	3	0.007
6	2	1	5	4	3	7	0.006
6	2	1	4	3	7	5	0.005
6	1	2	3	7	4	5	0.005
1	2	6	4	3	5	7	0.005
1	6	2	3	5	4	7	0.004
6	1	2	5	7	4	3	0.004
6	1	2	7	4	3	5	0.004
1	6	2	5	3	4	7	0.004

Table 18: Estimated probabilities (up to 90% of the total probability of rankings) for Boys $\times$ $dmft = 10$.

Teeth sequence							$\hat{\pi}$
6	1	2	4	5	3	7	0.148
6	1	2	4	3	5	7	0.097
6	1	2	5	4	3	7	0.068
6	1	2	4	5	7	3	0.065
6	1	2	4	3	7	5	0.052
6	1	4	2	5	3	7	0.048
6	1	2	3	4	5	7	0.031
6	1	2	5	4	7	3	0.029
1	6	2	4	5	3	7	0.027
6	1	2	4	7	3	5	0.026
6	1	2	4	7	5	3	0.022
6	1	2	3	4	7	5	0.022
1	6	2	4	3	5	7	0.020
6	1	4	2	5	7	3	0.020
6	1	2	5	3	4	7	0.019
6	1	4	2	3	5	7	0.015
6	1	2	3	5	4	7	0.015
1	6	2	5	4	3	7	0.013
6	1	5	2	4	3	7	0.012
6	4	1	2	5	3	7	0.010
6	2	1	4	5	3	7	0.009
6	1	4	5	2	3	7	0.009
1	6	4	2	5	3	7	0.009
1	6	2	4	5	7	3	0.009
1	6	2	4	3	7	5	0.008
6	1	2	3	7	4	5	0.008
1	6	2	3	4	5	7	0.007
6	1	5	4	2	3	7	0.007
6	2	1	4	3	5	7	0.005
6	1	2	7	4	3	5	0.005
6	1	4	2	3	7	5	0.005
1	6	2	3	4	7	5	0.005
6	1	5	2	4	7	3	0.005
6	1	2	5	7	4	3	0.005
6	2	1	5	4	3	7	0.005
6	1	2	7	3	4	5	0.004
6	1	2	3	5	7	4	0.004
6	1	2	5	3	7	4	0.004
1	6	2	5	4	7	3	0.004

Continued ...

Table 18 – Continued

Teeth sequence							$\hat{\pi}$
1	6	2	5	3	4	7	0.004
1	6	2	4	7	3	5	0.004
6	4	1	5	2	3	7	0.004
1	6	4	2	3	5	7	0.004
6	1	2	3	7	5	4	0.003
1	6	2	3	5	4	7	0.003
1	2	6	4	5	3	7	0.003
6	1	4	5	2	7	3	0.003

Table 19: Estimated probabilities (up to 90% of the total probability of rankings) for Girls × $dmft = 10$.

Teeth sequence							$\hat{\pi}$
6	1	2	4	5	3	7	0.148
6	1	2	4	3	5	7	0.124
6	1	2	5	4	3	7	0.064
6	1	2	4	3	7	5	0.056
6	1	4	2	5	3	7	0.042
6	1	2	4	5	7	3	0.042
6	1	2	3	4	5	7	0.035
1	6	2	4	3	5	7	0.029
1	6	2	4	5	3	7	0.029
6	1	2	3	4	7	5	0.023
6	1	2	5	4	7	3	0.022
6	1	4	2	3	5	7	0.018
6	2	1	4	5	3	7	0.018
6	1	2	4	7	3	5	0.016
1	6	2	4	3	7	5	0.014
6	2	1	4	3	5	7	0.013
6	1	2	5	3	4	7	0.013
1	6	2	5	4	3	7	0.013
6	1	5	2	4	3	7	0.013
1	6	2	3	4	5	7	0.012
6	1	2	4	7	5	3	0.012
6	1	4	2	5	7	3	0.011
6	1	2	3	5	4	7	0.010
6	2	1	5	4	3	7	0.009
1	6	2	3	4	7	5	0.008

Continued ...

Table 19 – Continued

Teeth sequence							$\hat{\pi}$
6	1	4	5	2	3	7	0.008
6	4	1	2	5	3	7	0.007
1	6	2	4	5	7	3	0.007
1	6	4	2	5	3	7	0.006
6	1	5	4	2	3	7	0.006
6	1	5	2	4	7	3	0.005
6	1	4	2	3	7	5	0.005
6	2	1	3	4	5	7	0.005
1	6	2	5	4	7	3	0.005
6	2	1	4	3	7	5	0.005
6	1	2	3	7	4	5	0.004
1	6	4	2	3	5	7	0.004
6	2	1	4	5	7	3	0.004
1	6	2	4	7	3	5	0.004
1	2	6	4	3	5	7	0.003
1	6	2	5	3	4	7	0.003
6	1	2	5	7	4	3	0.003
2	6	1	4	5	3	7	0.003
1	6	2	3	5	4	7	0.003
2	6	1	4	3	5	7	0.003
1	2	6	4	5	3	7	0.003
6	1	4	5	2	7	3	0.003
6	1	5	4	2	7	3	0.003
6	2	1	5	4	7	3	0.003
6	4	1	5	2	3	7	0.002
2	1	6	4	5	3	7	0.002

Table 20: Estimated probabilities (up to 90% of the total probability of rankings) for Boys $\times$ $dmft = 15$.

Teeth sequence							$\hat{\pi}$
6	1	2	4	5	3	7	0.097
6	1	2	4	3	5	7	0.064
6	1	2	5	4	3	7	0.056
6	1	4	2	5	3	7	0.050
6	1	2	4	3	7	5	0.045
6	1	2	4	5	7	3	0.040
6	1	4	2	5	7	3	0.024

Continued . . .

Table 20 – Continued

Teeth sequence							$\hat{\pi}$
6	1	2	3	4	5	7	0.024
6	1	2	3	4	7	5	0.022
6	1	2	4	7	3	5	0.021
6	1	2	5	3	4	7	0.020
6	1	5	2	4	3	7	0.020
6	1	2	5	4	7	3	0.020
6	4	1	2	5	3	7	0.020
6	1	4	2	3	5	7	0.018
1	6	2	4	5	3	7	0.015
6	1	2	3	5	4	7	0.014
4	6	1	2	5	3	7	0.014
6	1	2	4	7	5	3	0.014
6	1	4	5	2	3	7	0.013
1	6	2	4	3	5	7	0.011
6	1	5	4	2	3	7	0.010
6	4	1	2	5	7	3	0.010
6	1	4	2	3	7	5	0.010
6	1	2	3	7	4	5	0.009
1	6	2	5	4	3	7	0.009
6	4	1	5	2	3	7	0.009
6	2	1	4	5	3	7	0.008
1	6	4	2	5	3	7	0.008
1	6	2	4	3	7	5	0.008
4	6	1	5	2	3	7	0.007
6	5	1	2	4	3	7	0.007
6	1	5	2	4	7	3	0.007
4	6	1	2	5	7	3	0.007
6	1	2	3	5	7	4	0.006
1	6	2	4	5	7	3	0.006
4	1	6	2	5	3	7	0.006
6	1	4	5	2	7	3	0.005
6	5	1	4	2	3	7	0.005
6	1	2	5	3	7	4	0.005
6	1	4	2	7	3	5	0.005
1	6	2	3	4	5	7	0.005
1	6	2	4	7	3	5	0.005
6	1	2	3	7	5	4	0.005
6	1	4	2	7	5	3	0.005
6	4	1	2	3	5	7	0.004
6	1	5	4	2	7	3	0.004
6	2	1	4	3	5	7	0.004
6	2	1	5	4	3	7	0.004

Continued . . .

Table 20 – Continued

Teeth sequence							$\hat{\pi}$
5	6	1	4	2	3	7	0.004
1	6	2	3	4	7	5	0.004
5	6	1	2	4	3	7	0.004
6	1	2	7	4	3	5	0.004
6	4	1	5	2	7	3	0.004
6	1	2	7	3	4	5	0.004
1	6	2	5	3	4	7	0.004
4	6	1	5	2	7	3	0.004
1	6	4	2	3	5	7	0.003
4	6	5	1	2	3	7	0.003
1	6	2	5	4	7	3	0.003
6	1	2	5	7	4	3	0.003
1	6	4	2	5	7	3	0.003
6	1	5	2	3	4	7	0.003
4	5	6	1	2	3	7	0.003
5	6	4	1	2	3	7	0.003
1	6	5	2	4	3	7	0.003
1	6	2	3	5	4	7	0.003
4	6	1	2	3	5	7	0.003
4	1	6	2	5	7	3	0.003
6	4	5	1	2	3	7	0.003
1	6	2	4	7	5	3	0.002
6	2	1	4	5	7	3	0.002
5	4	6	1	2	3	7	0.002
6	5	4	1	2	3	7	0.002
1	4	6	2	5	3	7	0.002
1	2	6	4	5	3	7	0.002
6	5	1	2	4	7	3	0.002
6	2	1	3	4	5	7	0.002
6	2	1	4	3	7	5	0.002
6	5	1	4	2	7	3	0.002
6	1	2	7	4	5	3	0.002
6	1	2	5	7	3	4	0.002
1	6	2	3	7	4	5	0.002

Table 21: Estimated probabilities (up to 90% of the total probability of rankings) for Girls × $dmft = 15$.

Teeth sequence							$\hat{\pi}$
6	1	2	4	5	3	7	0.098
6	1	2	4	3	5	7	0.082
6	1	4	2	5	3	7	0.050
6	1	2	5	4	3	7	0.049
6	1	2	4	3	7	5	0.048
6	1	2	4	5	7	3	0.026
6	1	2	3	4	5	7	0.025
6	1	4	2	3	5	7	0.023
6	1	2	3	4	7	5	0.022
6	4	1	2	5	3	7	0.019
6	1	5	2	4	3	7	0.018
1	6	2	4	5	3	7	0.017
1	6	2	4	3	5	7	0.017
6	2	1	4	5	3	7	0.016
6	1	2	5	4	7	3	0.015
6	1	4	2	5	7	3	0.014
6	1	2	5	3	4	7	0.014
6	1	2	4	7	3	5	0.014
6	1	4	5	2	3	7	0.013
1	6	2	4	3	7	5	0.012
6	2	1	4	3	5	7	0.011
6	1	4	2	3	7	5	0.010
6	1	2	3	5	4	7	0.010
6	1	5	4	2	3	7	0.010
4	6	1	2	5	3	7	0.010
1	6	2	5	4	3	7	0.009
6	2	1	5	4	3	7	0.009
1	6	4	2	5	3	7	0.008
6	5	1	2	4	3	7	0.008
6	4	1	5	2	3	7	0.008
6	1	2	4	7	5	3	0.007
1	6	2	3	4	5	7	0.007
1	6	2	3	4	7	5	0.007
6	1	5	2	4	7	3	0.007
6	4	1	2	3	5	7	0.006
1	6	2	4	5	7	3	0.006
6	5	1	4	2	3	7	0.006
6	4	1	2	5	7	3	0.006
6	1	2	3	7	4	5	0.005

Continued ...

Table 21 – Continued

Teeth sequence							$\hat{\pi}$
4	6	1	5	2	3	7	0.005
5	6	1	2	4	3	7	0.005
1	6	4	2	3	5	7	0.005
5	6	1	4	2	3	7	0.005
6	1	4	5	2	7	3	0.005
6	2	1	4	3	7	5	0.005
1	6	2	4	7	3	5	0.004
6	1	5	4	2	7	3	0.004
4	1	6	2	5	3	7	0.004
5	6	4	1	2	3	7	0.004
1	6	2	5	3	4	7	0.004
6	2	1	3	4	5	7	0.004
6	1	4	2	7	3	5	0.003
1	6	2	5	4	7	3	0.003
1	6	5	2	4	3	7	0.003
6	4	5	1	2	3	7	0.003
6	2	1	4	5	7	3	0.003
5	4	6	1	2	3	7	0.003
4	6	1	2	3	5	7	0.003
1	6	4	2	3	7	5	0.003
2	6	1	4	5	3	7	0.003
6	4	1	5	2	7	3	0.003
1	6	2	3	5	4	7	0.003
6	2	1	5	3	4	7	0.003
1	2	6	4	5	3	7	0.003
4	5	6	1	2	3	7	0.003
1	2	6	4	3	5	7	0.003
1	6	4	2	5	7	3	0.003
6	5	4	1	2	3	7	0.003
4	6	1	2	5	7	3	0.003
1	6	4	5	2	3	7	0.003
6	1	4	2	7	5	3	0.003
6	5	1	2	4	7	3	0.002
2	1	6	4	5	3	7	0.002
2	6	1	4	3	5	7	0.002
6	5	1	4	2	7	3	0.002
6	2	1	3	4	7	5	0.002
6	1	5	2	3	4	7	0.002
1	2	6	4	3	7	5	0.002
1	6	2	4	7	5	3	0.002
1	2	6	5	4	3	7	0.002
4	6	5	1	2	3	7	0.002

Continued . . .

Table 21 – Continued

Teeth sequence							$\hat{\pi}$
6	1	2	7	4	3	5	0.002
6	1	2	5	7	4	3	0.002
6	1	2	5	3	7	4	0.002
6	1	2	3	5	7	4	0.002
5	6	1	4	2	7	3	0.002
5	6	1	2	4	7	3	0.002
4	6	1	5	2	7	3	0.002
6	4	2	1	5	3	7	0.002
6	2	1	5	4	7	3	0.002
5	6	4	1	2	7	3	0.002
2	6	1	5	4	3	7	0.002
5	1	6	2	4	3	7	0.002
6	1	2	3	7	5	4	0.002
1	6	2	3	7	4	5	0.002
6	2	1	3	5	4	7	0.002
2	1	6	4	3	5	7	0.002

6 Concluding remarks

In this paper we have illustrated that the approach of Pourahmadi (1999) is useful for modeling the covariance matrix, but this could be inferred also from his original publication. However, here we have exemplified this approach for a relatively high dimension and in a completely different application area. The approach proved to be quite useful for taking care of the pd-condition. Further, the interpretability of the marginal and conditional variance parameters is satisfactory. But the parameters associated with the matrix T were too difficult to interpret, and this is not only due to the fact that there is no logical ranking of the responses in this example. Thus to a certain extent we could have used also one of the other deconstraining approaches discussed in Pinheiro and Bates (1996). However, the approach of Pourahmadi (1999) offers good interpretability of part of the parameters and the approach implies a relatively simple MCMC sampling approach due to the conditional conjugacy of part of the prior distributions.

Our approach of determining the most prevalent rankings in tooth emergence differs from all previous approaches. Indeed, we calculated the prevalence of the rankings using the multivariate normal probabilities of the latent true emergences. This avoids the inevitable problem of ties in the observed interval-censored emergence times.

Although the Signal Tandmobiel ®Study is a unique longitudinal study (large sample size and collection of detailed dental information), it falls short with respect to the age period that the children have been examined. Indeed, only the period that the children were in primary school was examined. This implies that for many children and teeth the permanent tooth had already emerged before the start of the study and did not emerge during the study period. Consequently, if the study period had been broader an even clearer picture of the multivariate emergence distribution could have been obtained. Nevertheless, our analysis is one of the very few that examined the ranking of emergence times on such a large and detailed dental data set and with well justified statistical technique avoiding as much as possible ad hoc procedures (like the mid-point approach).

Finally, our analysis shows that to know whether there are physiological trends in the emergence distribution of permanent teeth either geographically or temporally, it is inappropriate to look at the overall emergence distribution of the population as this distribution is too much affected by the caries process of the deciduous teeth. It seems, therefore, more logical to compare the emergence distributions of the children not demonstrating a high caries profile on their deciduous teeth, thereby hoping that they do constitute a biologically selected subpopulation.

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