State Space Representation of an Autoregressive Linear Mixed Effects Model for the Analysis of Longitudinal Data

Ikuko Funatogawa[1], Takashi Funatogawa [2]

[1]Department of Hygiene and Public Health, Teikyo University School of Medicine, 2-11-1 Kaga, Itabashi-ku, Tokyo 173-8605, Japan
[2]Clinical Planning Dept., Chugai Pharmaceutical Co., Ltd., 1-1, Nihonbashi Muromachi 2-Chome, Chuo-ku Tokyo, 103-8324, Japan

Abstract
Recently, we proposed an autoregressive linear mixed effects model for the analysis of longitudinal data in which the current response is regressed on the previous response, fixed effects, and random effects (Funatogawa et al., *Statist. Med.* 2007; 26:2113-2130). The model represents profiles approaching random equilibriums. Because intermittent missing is an inherent problem of the autoregressive (conditional) model, we provided the marginal (unconditional) representation of the model and the likelihood. In this study, we further provide a state space form of the model for calculating the likelihood without using large matrices. The proposed state space form corresponds to the marginal form of the likelihood instead of the conditional one. We modified the method proposed by Jones (1993) for a state space form of a usual linear mixed effects model. Following Jones (1993), the regression coefficients of the fixed effects are concentrated out of the likelihood.

Key Words: Autoregressive model, Equilibrium, Kalman filter, Linear Mixed Effects Model, Longitudinal data, State Space

1. Introduction

Recently, we proposed an autoregressive linear mixed effects model for the analysis of longitudinal data in which the current response is regressed on the previous response, fixed effects, and random effects (Funatogawa et al., 2007). The model represents profiles approaching random equilibriums. In biostatistical fields, the unconditional profile is usually more interested than the profile conditional on the previous response. Therefore we provided the unconditional (marginal) representation of this model. When there are intermittent missing values on responses, it means the missing values on previous responses as covariates in the conditional representation and we can not calculate the likelihood directly. To avoid this problem, we provided the unconditional (marginal) form of the likelihood (Funatogawa et al., 2007). The model was extended to the bivariate longitudinal data, where repeated assessments of two response variables are performed and the response profiles approaching random equilibriums (Funatogawa et al., 2008a). When the dropout process is missing at random (MAR), we can obtain consistent maximum likelihood estimators as long as both the mean and covariance structures are correctly specified. We have shown that the model provide a new parsimonious covariance structure for the profiles approaching random equilibriums (asymptotes), and the estimate of the asymptote is unbiased in MAR dropouts (Funatogawa et al., 2008b).

For a linear mixed effects model of longitudinal data, Jones (1993) showed a state space form and used the Kalman filter (Kalman, 1960) for calculating the likelihood without using large matrices. Jones (1993) described the merit of the state space form in the linear mixed effects model as follows. The calculation of likelihood usually requires matrices whose sizes depend on the number of observations on a subject. In the case of multivariate longitudinal data, it may become large. However, this method does not depend on the observation number and not use large matrices. We adopt this approach for the autoregressive linear mixed effects model. We provide a state space form of this model and use the Kalman filter to calculate the likelihood without using large matrices. The proposed state space form corresponds to the unconditional (marginal) form of the likelihood instead of the conditional form. We show the case of univariate and bivariate longitudinal data.

2. Autoregressive Linear Mixed Effects Model for Longitudinal Data

2.1 Autoregressive Linear Mixed Effects Model

Let $\mathbf{Y}_i = (Y_i(0), Y_i(1), Y_i(2), \cdots, Y_i(T_i))^T$ be the vector of responses corresponding to the i th $(i = 1, \cdots, N)$ subject measured from 0 to T_i. $Y_i(0)$ is a baseline measurement, and $Y_i(t)$ is the t th measurement after the baseline measurement. Note that t is not an actual time. A^T denotes the transpose of A. We define an autoregressive linear mixed effects model by the following model,

$$\mathbf{Y}_i = \rho \mathbf{F}_i \mathbf{Y}_i + \mathbf{X}_i \boldsymbol{\beta} + \mathbf{Z}_i \mathbf{b}_i + \boldsymbol{\varepsilon}_i, \quad (1)$$

where $\boldsymbol{\beta}$ is a $p \times 1$ vector of unknown fixed effects parameters, $\mathbf{X}_i$ is a known $(T_i + 1) \times p$ design matrix for fixed effects, $\mathbf{b}_i$ is a $q \times 1$ vector of unknown random effects parameters, $\mathbf{Z}_i$ is a known $(T_i + 1) \times q$ design matrix for random effects, and $\boldsymbol{\varepsilon}_i$ is a $(T_i + 1) \times 1$ vector of random errors. It is assumed that $\mathbf{b}_i$ and $\boldsymbol{\varepsilon}_i$ are both independent across subjects and independently normally distributed with mean zero and covariance matrices $\mathbf{G}$ and $\mathbf{R}_i$, respectively. $\mathbf{F}_i$ is a $(T_i + 1) \times (T_i + 1)$ matrix whose elements just below diagonal are 1 and the other elements are 0. $\mathbf{F}_i \mathbf{Y}_i = (0, Y_i(0), Y_i(1), \cdots, Y_i(T_i - 1))^T$ is the vector of previous responses. ρ is an unknown regression coefficient for previous responses. We show $\rho \mathbf{F}_i$ in the case of four measurement points,

$$\rho \mathbf{F}_i = \begin{pmatrix} 0 & 0 & 0 & 0 \\ \rho & 0 & 0 & 0 \\ 0 & \rho & 0 & 0 \\ 0 & 0 & \rho & 0 \end{pmatrix}.$$

Assuming $\rho \neq 1$, the equation (1) is transformed to

$$\mathbf{Y}_i = \mathbf{F}_i \mathbf{Y}_i + (1-\rho) \left\{ \frac{1}{(1-\rho)} \left(\mathbf{X}_i \boldsymbol{\beta} + \mathbf{Z}_i \mathbf{b}_i \right) - \mathbf{F}_i \mathbf{Y}_i \right\} + \boldsymbol{\varepsilon}_i .$$

Assuming $0 < \rho < 1$, the elements of $\left(\mathbf{X}_i \boldsymbol{\beta} + \mathbf{Z}_i \mathbf{b}_i \right) / (1-\rho)$ in the parenthesis can be interpreted as the asymptotes of i th subject. These are normally distributed with means $\mathbf{X}_i \boldsymbol{\beta} / (1-\rho)$ and a covariance matrix $\mathbf{Z}_i \mathbf{G} \mathbf{Z}_i^T / (1-\rho)^2$.

2.2 Covariance Structure

Let $\mathbf{V}_i$ be the covariance matrix of the response vector $\mathbf{Y}_i$ conditional on the previous response values, that is $\mathbf{V}_i = \mathbf{Z}_i \mathbf{G} \mathbf{Z}_i^T + \mathbf{R}_i$. We proposed the following error structure that is useful in practice (Funatoagawa et al., 2007).

$$\mathbf{R}_i = \begin{pmatrix} \sigma_{ME}^2 & -\rho\sigma_{ME}^2 & 0 & 0 \\ -\rho\sigma_{ME}^2 & \sigma_{AR}^2 + (1+\rho^2)\sigma_{ME}^2 & -\rho\sigma_{ME}^2 & 0 \\ 0 & -\rho\sigma_{ME}^2 & \sigma_{AR}^2 + (1+\rho^2)\sigma_{ME}^2 & -\rho\sigma_{ME}^2 \\ 0 & 0 & -\rho\sigma_{ME}^2 & \sigma_{AR}^2 + (1+\rho^2)\sigma_{ME}^2 \end{pmatrix}.$$

This structure is the sum of a serially correlated error and an additional independent error when the model is transformed to the marginal model.

3. Calculation of Likelihood

3.1 Conditional Model

We can obtain the maximum likelihood estimates (MLEs) of (1) by some maximization methods. We can consider the autoregressive linear mixed effects model as a linear mixed effects model by treating the previous responses as a fixed effect as $\mathbf{X}_i^* = (\mathbf{X}_i, \mathbf{F}_i\mathbf{Y}_i)$. Therefore, as long as there is no intermittent missing, we can use the estimation method of the linear mixed effects model. The calculation of Mixed procedure of SAS are given in Funatogawa et al. (2008b).

3.2 Marginal Model

The marginal (unconditional) representation of the response vector of (1) is written as

$$\mathbf{Y}_i = (\mathbf{I}_{T_i} - \rho\mathbf{F}_i)^{-1}\left(\mathbf{X}_i\boldsymbol{\beta} + \mathbf{Z}_i\mathbf{b}_i + \boldsymbol{\varepsilon}_i\right).$$

Here $\mathbf{I_a}$ means the $a \times a$ identity matrix. The corresponding unconditional covariance matrix is $\boldsymbol{\Sigma}_i = (\mathbf{I}_{T_i} - \rho\mathbf{F}_i)^{-1}\mathbf{V}_i\{(\mathbf{I}_{T_i} - \rho\mathbf{F}_i)^{-1}\}^T$.

-2 log likelihood ($-2ll$) of the autoregressive linear mixed effects model is given by

$$-2ll = \sum_i \{n_i \ln(2\pi) + \ln|\mathbf{V}_i| + (\mathbf{Y}_i - \rho\mathbf{F}_i\mathbf{Y}_i - \mathbf{X}_i\boldsymbol{\beta})^T \mathbf{V}_i^{-1}(\mathbf{Y}_i - \rho\mathbf{F}_i\mathbf{Y}_i - \mathbf{X}_i\boldsymbol{\beta})\}.$$

This is transformed to the marginal (unconditional) form as

$$-2ll = \sum_i [n_i \ln(2\pi) + \ln|\boldsymbol{\Sigma}_i| + \{\mathbf{Y}_i - (\mathbf{I}_{T_i} - \rho\mathbf{F}_i)^{-1}\mathbf{X}_i\boldsymbol{\beta}\}^T \boldsymbol{\Sigma}_i^{-1}\{\mathbf{Y}_i - (\mathbf{I}_{T_i} - \rho\mathbf{F}_i)^{-1}\mathbf{X}_i\boldsymbol{\beta}\}],$$

where $\ln|\boldsymbol{\Sigma}_i|$ is equal to $\ln|\mathbf{V}_i|$. We can get the MLEs based on either equation. When some elements of $\mathbf{Y}_i$ are intermittently missing but the corresponding elements of $\mathbf{X}_i$ are known, we can use only the marginal form with deleting the missing part of $\mathbf{Y}_i$ and the corresponding parts of $\left(\mathbf{I}_{T_i} - \rho\mathbf{F}_i\right)^{-1}\mathbf{X}_i$ and $\boldsymbol{\Sigma}_i$.

3.3 State Space Form

3.3.1 State Space Form

For a linear mixed effects model, Jones (1993) showed a state space form of the model and used the Kalman filter (Kalman, 1960) for calculating the likelihood without using large matrices. He also used this method for multivariate longitudinal data. We adopt this approach for the autoregressive linear mixed effects model. We provide a state space form of the model. The model (1) with the covariance matrix of error in 2.2 can be written with the state equation

$$\mathbf{s}_{i(t)} = \boldsymbol{\Phi}_{i(t;t-1)}\mathbf{s}_{i(t-1)} + \mathbf{X}_{i,t}\boldsymbol{\beta} + \boldsymbol{\upsilon}_{i,t}, \qquad (2)$$

and the observation equation

$$\mathbf{Y}_{i,t} = \mathbf{H}_{i,t}\mathbf{s}_{i(t)} + \boldsymbol{\xi}_{i,t}, \qquad (3)$$

where $\mathbf{s}_{i(t)} = (\mu_{i,t}, \mathbf{b}_i^T)^T$, $\boldsymbol{\upsilon}_{i,t} = (\varepsilon_{(AR)i,t}{}^T, \mathbf{0})^T$, $Var(\boldsymbol{\upsilon}_{i,t}) \equiv \mathbf{Q}_{i,t}$, $\mathbf{Y}_{i,t} = Y_i(t)$, $\mathbf{H}_{i,t} = \begin{pmatrix}1 & \mathbf{0}_{1\times q}\end{pmatrix}$, $\boldsymbol{\xi}_{i,t} = \varepsilon_{(ME)i,t}$, $Var(\varepsilon_{(ME)i,t}) = \sigma_{ME}^2$,

$$\boldsymbol{\Phi}_{i(t;t-1)} = \begin{pmatrix}\rho & \mathbf{Z}_{i,t} \\ \mathbf{0} & \mathbf{I}_q\end{pmatrix}, \text{ and } \mathbf{Q}_{i,t} = \begin{pmatrix}\sigma_{AR}^2 & \mathbf{0} \\ \mathbf{0} & \mathbf{0}\end{pmatrix}.$$

When $t = 0$, σ_{AR}^2 in $\mathbf{Q}_{i,t}$ is replaced by σ_{AR0}^2, which is 0 in 2.2. In these equations, $\mathbf{s}_{i(t)}$ is the state vector at time t, $\boldsymbol{\Phi}_{i(t;t-1)}$ is the state transition matrix from time $t-1$ to time t, $\mathbf{H}_{i,t}$ shows which elements of the state vector are observed. The notation $\mathbf{s}_{i(t|t-1)}$ and $\mathbf{s}_{i(t|t)}$ is used for the estimate of the state at time t given observations up to time

$t-1$ and t, respectively. The covariance matrices of these two state vector estimates are $\mathbf{P}_{i(t|t-1)}$ and $\mathbf{P}_{i(t|t)}$. The initial state and its variance are set to be $\mathbf{s}_{i(-1|-1)} = \mathbf{0}$ and

$$\mathbf{P}_{i(-1|-1)} = \begin{pmatrix} \mathbf{0} & \mathbf{0} \\ \mathbf{0} & \mathbf{G} \end{pmatrix}.$$

This state space form with the Kalman filter provides us the marginal (unconditional) form of the likelihood, so that this approach can be used even if there are intermittent missing responses.

3.3.2 Kalman Filter

In the case of a linear mixed effects model, the regression coefficients of the fixed effects can be concentrated out of the likelihood, by applying the Kalman filter not only to the observation vector, $\mathbf{Y}_i$, but also to each column of the fixed effects design matrices, $\mathbf{X}_i$, so that only variance parameters need to be estimated (Jones, 1993). In the case of an autoregressive linear mixed effects model, we apply the Kalman filter to $\mathbf{Y}_i$ and $\rho\mathbf{F}_i\mathbf{X}_i$, so that only ρ and variance parameters need to be estimated. $\boldsymbol{\beta}$ is concentrated out of the likelihood. For this purpose, we use a state matrix $\mathbf{S}_{i(t)}$ the size of which is $(1+q)\times(p+1)$, instead of the state vector $\mathbf{s}_{i(t)}$ the size of which is $(1+q)\times 1$. The values of $\rho\mathbf{F}_i\mathbf{X}_i$ at time t are recursively calculated in the following steps. The Kalman filter starts with the initial state matrix, $\mathbf{S}_{i(-1|-1)}$, and covariance matrix, $\mathbf{P}_{i(-1|-1)}$. We set $\mathbf{S}_{i(-1|-1)} = \mathbf{0}$. In the Kalman theory, the parameters of the model are assumed known, here, the unknown parameters are varied by a nonlinear optimization routine until MLEs are obtained.

The steps in the Kalman filter are as follows:

1. Calculate a one step prediction and the covariance matrix of this prediction,

$$\mathbf{S}_{i(t|t-1)} = \boldsymbol{\Phi}_{(t;t-1)}\mathbf{S}_{i(t-1|t-1)},$$
$$\mathbf{P}_{i(t|t-1)} = \boldsymbol{\Phi}_{(t;t-1)}\mathbf{P}_{i(t-1|t-1)}\boldsymbol{\Phi}'_{(t;t-1)} + \mathbf{Q}_{i,t}.$$

2. Calculate the covariate matrix of the fixed effect,

$$\mathbf{X}^*_{i,t} = \rho\mathbf{X}^*_{i,t-1} + \mathbf{X}_{i,t},$$

where $\mathbf{X}^*_{i,-1} = \mathbf{0}$.

3. Calculate the prediction of the next observation matrix,

$$[\mathbf{X}^*_{i,(t|t-1)} \quad \mathbf{Y}_{i,(t|t-1)}] = \mathbf{H}_{i,t}\mathbf{S}_{i(t|t-1)}.$$

The notation $[\mathbf{A} \quad \mathbf{B}]$ means the matrix $\mathbf{A}$ augmented by the matrix $\mathbf{B}$.

4. Calculate the innovation matrix and the covariance matrix of this innovation,

$$\mathbf{I}_{i,t} = [\mathbf{X}^*_{i,t} \quad \mathbf{Y}_{i,t}] - [\mathbf{X}^*_{i,(t|t-1)} \quad \mathbf{Y}_{i,(t|t-1)}],$$
$$\mathbf{V}_{i,t} = \mathbf{H}_{i,t}\mathbf{P}_{i(t|t-1)}\mathbf{H}'_{i,t} + \mathbf{r}_{(ME)}.$$

5. Accumulate the quantities needed to calculate $-2ll$ at the end of the recursion,

$$\mathbf{M} \leftarrow \mathbf{M} + \mathbf{I}'_{i,t}\mathbf{V}^{-1}_{i,t}\mathbf{I}_{i,t},$$
$$\Delta \leftarrow \Delta + \ln|\mathbf{V}_{i,t}|.$$

6. Update the estimate of the state vector and the covariance matrix of the state vector,

$$\mathbf{S}_{i(t|t)} = \mathbf{S}_{i(t|t-1)} + \mathbf{P}_{i(t|t-1)}\mathbf{H}'_{i,t}\mathbf{V}^{-1}_{i,t}\mathbf{I}_{i,t},$$
$$\mathbf{P}_{i(t|t)} = \mathbf{P}_{i(t|t-1)} - \mathbf{P}_{i(t|t-1)}\mathbf{H}'_{i,t}\mathbf{V}^{-1}_{i,t}\mathbf{H}_{i,t}\mathbf{P}_{i(t|t-1)}.$$

If there is a missing observation in $\mathbf{Y}_{i,t}$, the corresponding parts of $\mathbf{H}_{i,t}$ and $\mathbf{r}_{(ME)}$ are removed. If both observations are missing, the steps 3, 4 and 5 are skipped and the step 6 is $\mathbf{S}_{i(t|t)} = \mathbf{S}_{i(t|t-1)}$ and $\mathbf{P}_{i(t|t)} = \mathbf{P}_{i(t|t-1)}$. Now return to step 1 until the end of the data is reached. The matrix $\mathbf{M}$ now contains

$$\begin{bmatrix} \tilde{\mathbf{X}}'\tilde{\mathbf{X}} & \tilde{\mathbf{X}}'\tilde{\mathbf{Y}} \\ & \tilde{\mathbf{Y}}'\tilde{\mathbf{Y}} \end{bmatrix}.$$

The residual sum of squares is given by $RSS = \tilde{\mathbf{Y}}'\tilde{\mathbf{Y}} - \tilde{\mathbf{Y}}'\tilde{\mathbf{X}}\left(\tilde{\mathbf{X}}'\tilde{\mathbf{X}}\right)^{-1}\tilde{\mathbf{X}}'\tilde{\mathbf{Y}}$. $-2ll$ is given by $-2ll = \sum n_i \ln(2\pi) + \Delta + RSS$. The MLEs of the fixed effects are given by $\hat{\beta} = \left(\tilde{\mathbf{X}}'\tilde{\mathbf{X}}\right)^{-1}\tilde{\mathbf{X}}'\tilde{\mathbf{Y}}$.

3.3.3 Bivariate Longitudinal Data

The autoregressive linear mixed effects model for bivariate longitudinal model was proposed in Funatogawa et al. (2008a). Let $Y_{r,i,t}$ be the observed response of the r th (r =1,2) variable for subject i at time t ($t = 0, \cdots, T_i$). Consider the following model

$$\mathbf{Y}_{i,t} = \boldsymbol{\rho}\mathbf{Y}_{i,t-1} + \mathbf{X}_{i,t}\boldsymbol{\beta} + \mathbf{Z}_{i,t}\mathbf{b}_i + \boldsymbol{\varepsilon}_{i,t}, \qquad (4)$$

where $\mathbf{Y}_{i,t} = (Y_{1,i,t}, Y_{2,i,t})^T$, $\boldsymbol{\beta} = (\boldsymbol{\beta}_1^T, \boldsymbol{\beta}_2^T)^T$, $\mathbf{b}_i = (\mathbf{b}_{1,i}^T, \mathbf{b}_{2,i}^T)^T$, $\boldsymbol{\varepsilon}_{i,t} = (\varepsilon_{1,i,t}, \varepsilon_{2,i,t})^T$,

$$\boldsymbol{\rho} = \begin{pmatrix} \rho_{11} & \rho_{12} \\ \rho_{21} & \rho_{22} \end{pmatrix}, \ \mathbf{X}_{i,t} = \begin{pmatrix} \mathbf{X}_{1,i,t}^T & \mathbf{0} \\ \mathbf{0} & \mathbf{X}_{2,i,t}^T \end{pmatrix}^T, \text{ and } \mathbf{Z}_{i,t} = \begin{pmatrix} \mathbf{Z}_{1,i,t}^T & \mathbf{0} \\ \mathbf{0} & \mathbf{Z}_{2,i,t}^T \end{pmatrix}^T.$$

$\mathbf{X}_{r,i,t}$ is a known $1 \times p_r$ design matrix for fixed effects, $\mathbf{Z}_{r,i,t}$ is a known $1 \times q_r$ design matrix for random effects. With $\mathbf{Y}_i = (\mathbf{Y}_{i,0}^T, \mathbf{Y}_{i,1}^T, \cdots, \mathbf{Y}_{i,T_i}^T)^T$, $(\mathbf{F}_i \otimes \mathbf{I}_2)\mathbf{Y}_i = (0, 0, \mathbf{Y}_{i,0}^T, \mathbf{Y}_{i,1}^T, \cdots, \mathbf{Y}_{i,T_i-1}^T)^T$ is the vector of previous response values, where $\otimes$ means direct product. Then the model (4) can be written as

$$\mathbf{Y}_i = (\mathbf{F}_i \otimes \boldsymbol{\rho})\mathbf{Y}_i + \mathbf{X}_i\boldsymbol{\beta} + \mathbf{Z}_i\mathbf{b}_i + \boldsymbol{\varepsilon}_i,$$

where $\mathbf{X}_i = (\mathbf{X}_{i,0}^T, \cdots, \mathbf{X}_{i,T_i}^T)^T$, $\mathbf{Z}_i = (\mathbf{Z}_{i,0}^T, \cdots, \mathbf{Z}_{i,T_i}^T)^T$, $\boldsymbol{\varepsilon}_i = (\boldsymbol{\varepsilon}_{i,0}^T, \cdots, \boldsymbol{\varepsilon}_{i,T_i}^T)^T$. We define the errors as $\boldsymbol{\varepsilon}_{i,0} = \boldsymbol{\varepsilon}_{(AR)i,0} + \boldsymbol{\varepsilon}_{(ME)i,0}$ $\boldsymbol{\varepsilon}_{i,t} = \boldsymbol{\varepsilon}_{(AR)i,t} + \boldsymbol{\varepsilon}_{(ME)i,t} - \boldsymbol{\rho}\boldsymbol{\varepsilon}_{(ME)i,t-1}$ $(t > 0)$.

The state space form for the model (4) is defined by equations (2) and (3) with the following parameters, $\mathbf{s}_{i(t)} = (\boldsymbol{\mu}_{i,t}^T, \mathbf{b}_i^T)^T$ with $\boldsymbol{\mu}_{i,t} = (\mu_{1,i,t}, \mu_{2,i,t})^T$, $\boldsymbol{\upsilon}_{i,t} = (\boldsymbol{\varepsilon}_{(AR)i,t}{}^T, \mathbf{0})^T$, $Var(\boldsymbol{\upsilon}_{i,t}) \equiv \mathbf{Q}_{i,t}$, $\mathbf{H}_{i,t} = \begin{pmatrix}\mathbf{I}_2 & \mathbf{0}_{2\times(q_1+q_2)}\end{pmatrix}$, $\boldsymbol{\xi}_{i,t} = \boldsymbol{\varepsilon}_{(ME)i,t}$, $Var(\boldsymbol{\varepsilon}_{(ME)i,t}) = \mathbf{r}_{(ME)}$,

$$\boldsymbol{\Phi}_{i(t;t-1)} = \begin{pmatrix} \boldsymbol{\rho} & \mathbf{Z}_{i,t} \\ \mathbf{0} & \mathbf{I}_{q_1+q_2} \end{pmatrix}, \text{ and } \mathbf{Q}_{i,t} = \begin{pmatrix} \mathbf{r}_{(AR)} & \mathbf{0} \\ \mathbf{0} & \mathbf{0} \end{pmatrix}.$$

We apply the Kalman filter to $\mathbf{Y}_i$ and $(\mathbf{F}_i \otimes \boldsymbol{\rho})\mathbf{X}_i$, so that only $\boldsymbol{\rho}$ and variance parameters need to be estimated. $\boldsymbol{\beta}$ is concentrated out of the likelihood. For this purpose, we use a state matrix $\mathbf{S}_{i(t)}$ the size of which is $(2 + q_1 + q_2) \times (p_1 + p_2 + 1)$, instead of the state vector $\mathbf{s}_{i(t)}$ the size of which is $(2 + q_1 + q_2) \times 1$. The values of $(\mathbf{F}_i \otimes \boldsymbol{\rho})\mathbf{X}_i$ at time t are recursively calculated in the steps in 3.3.2.

4. Discussion

In this paper, we provide a state space form of autoregressive linear mixed effects model for calculating the marginal likelihood without using large matrices. The calculation of likelihood usually requires matrices whose sizes depend on the number of observations on a subject. In the case of multivariate longitudinal data, it may become large. However, this method does not depend on the observation number and not use large matrices as described in Jones (1993). In the case of the autoregressive linear mixed effects model, it is also important to calculate the marginal likelihood instead of the conditional likelihood. We used the latent variable, $\mu_{i,t}$, in the state vector, $\mathbf{s}_{i(t)} = (\mu_{i,t}, \mathbf{b}_i^T)^T$ in 3.3, so that we can get the marginal likelihood. If we define the state vector as $\mathbf{s}_{i(t)}^* = (y_{i,t}, \mathbf{b}_i^T)^T$ with the observed response, then it will provide the conditional likelihood and we can not use it when there are intermittent missing.

In the previous study, we have shown that there are several representations of the autoregressive linear model; representations in conditional and unconditional form, representation by each observation time for each subject, a vector representation for whole observation for each subject (Funatogawa et al., 2007). Furthermore, the autoregressive model corresponds to the monomolecular (the Mitcherlich) growth curve in continuous time (Funatogawa et al., 2007). In this paper, we further provided a representation as a state space form.

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