Generalized Linear Mixed Models for Longitudinal Data

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Abstract The study of longitudinal data plays a significant role in medicine, epidemiology and social sciences. Typically, the interest is in the dependence of an outcome variable on the covariates. The Generalized Linear Models (GLMs) were proposed to unify the regression approach for a wide variety of discrete and continuous longitudinal data. The responses (outcomes) in longitudinal data are usually correlated. Hence, we need to use an extension of the GLMs that account for such correlation. This can be done by inclusion of random effects in the linear predictor; that is the Generalized Linear Mixed Models (GLMMs) (also called random effects models). The maximum likelihood estimates (MLE) are obtained for the regression parameters of a logit model, when the traditional assumption of normal random effects is relaxed. In this case a more convenient distribution, such as the lognormal distribution, is used. However, adding non-normal random effects to the GLMM considerably complicates the likelihood estimation. So, the direct numerical evaluation techniques (such as Newton - Raphson) become analytically and computationally tedious. To overcome such problems, we propose and develop a Monte Carlo EM (MCEM) algorithm, to obtain the maximum likelihood estimates. The proposed method is illustrated using a simulated data.

Keywords Generalized Linear Mixed Models, Logistic Regression, Longitudinal Data, Monte Carlo EM Algorithm, Random Effects Model

1. Introduction

Longitudinal data consist of repeated observations, for the same subject, of an outcome variable. There may be a set of covariates for each subjects. Let $y_i = (y_{i1}, y_{i2}, \ldots, y_{im_i})^T$ be an $m_i \times 1$ vector representing the observed sequence of the outcome variable Y_{it} recorded at time $t = 1, 2, \ldots, m_i$, for the ith subject, $i = 1, 2, \ldots, n$. Also, assume that $\mathbf{x}_{ij} = (x_{it1}, x_{it2}, \ldots, x_{itp})$ is an $l \times p$ vector of p covariates observed at time t. Thus, X_i is an $m_i \times p$ matrix of covariates corresponding to the ith subject taking the form:

$$\begin{pmatrix} x_{i11} & \cdots & x_{i1p} \\ \vdots & \ddots & \vdots \\ x_{im_i1} & \cdots & x_{im_ip} \end{pmatrix}.$$

For simplicity we can assume that $m_i = m$.

The primary focus is on the dependence of the outcome on the covariates[3,5]. In other words, we are usually interested in the inference about the regression coefficients, in the usual linear models of the form

$$Y_i = X_i \beta + e_i,$$

where $\beta = (\beta_1, \ldots, \beta_p)^T$ is a $p \times 1$ vector of the regression coefficients. It is usually assumed that the errors, e_i, are independent and identically normally distributed. Therefore, these models are not used in situations when response variables have distributions other than the normal, or even when they are qualitative rather than quantitative. Examples include binary longitudinal data.

To solve this problem, Reference[18] introduce the generalized linear models (GLM) as a unified framework to model all types of longitudinal data[13, 15, 24]. These models assume that the distribution of Y_{it} ($i = 1, \ldots, n, t = 1, 2, \ldots, m$) belongs to the exponential family. The exponential family distributions can be written in the form:

$$f(y_{it}, \theta_{it}) = e^{\{(y_{it}\theta_{it} - a(\theta_{it}))/\phi + b(y_{it}, \phi)\}}, \qquad (1)$$

where $a(.)$ and $b(.)$ are specific functions defined according to the underlying distribution of the exponential family. Some examples of univariate distributions are given in Table (1). The parameters $\theta_{it} = h(\eta_{it})$ and $\eta_{it} = x_{it}\beta$. Also ϕ is the scale parameter and it is treated as a nuisance parameter when the main interest is in the regression coefficients[13]. The distribution in Equation (1) is the canonical form and θ_{it} is called the natural parameter of the distribution.

The first two moments of y_{it} in Equation (1) are given by

$$E(y_{it}) = \mu_{it} = a'(\theta_{it}) \text{ and } \text{Var}(y_{it}) = \frac{a''(\theta_{it})}{\phi} \qquad (2)$$

$$b1 = -\frac{1}{2}(y^2 + \sigma^{-2}\ln(2\pi\sigma^2))$$

For the GLM, the linear combination of the parameters of interest, $\beta_1, \beta_2, \ldots, \beta_p$, are equal to some function of the expected value of y_{it} (μ_{it}), i. e., $g(\mu_{it}) = \eta_{it}$ where g is a monotone and differentiable function called the link function. From Equation (1) and Equation (2), we can write the inverse of the link function as $g^{-1} = a' \circ h$. Note that a link function in which $\theta_{it} = \eta_{it}$ (e.g., h is the identity function)

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