Bayesian Semiparametric Estimation with Nonignorable Nonresponse

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Abstract

Statistical inference with nonresponse is quite challenging, especially when the response mechanism is nonignorable. Although existing methods often require correct model specifications for response models, the models cannot be verified based on the observed data and misspecification of the response models can lead to a seriously biased inference. To overcome this limitation, we develop an effective Bayesian semiparametric method for the response mechanism using logistic penalized spline methods. Using Polya-gamma data augmentation, we developed an efficient posterior computation algorithm via Markov Chain Monte Carlo. The performance of the proposed method is demonstrated in simulation studies and an application to a longitudinal data.

Key words: Longitudinal data; Markov Chain Monte Carlo; Multiple imputation; Polya-gamma distribution; Penalized spline
1 Introduction

Handling missing data in inappropriate ways may lead to crucial selection bias in data analysis. In particular, specification of the response mechanism is essential for analyzing such data. If the response mechanism is misspecified, the statistical inference on the parameter of interest would be seriously biased. Nevertheless, it is often assumed that the response mechanism is ignorable or missing at random (MAR) because the assumption does not require any specification for the response mechanism (Rubin, 1976). Moreover, there have been several useful methods for ignorable missing data enjoying nice properties such as the double robustness (Robins et al., 1994; Kang and Schafer, 2007) and the multiple robustness (Han, 2014). In real data analysis, however, there are many unacceptable situations to believe the ignorability. Therefore, it is requisite to develop a method for analyzing nonignorable or missing not at random (MNAR) data (Little and Rubin, 2002).

In order to analyze MNAR data, (i) a response model, which is a parametric model of the response mechanism, needs to be correctly specified as well as (ii) the outcome model (Greenlees et al., 1982; Diggle and Kenward, 1994). It has been criticized to analyze missing data under the MNAR assumption due to the strong assumption, and several types of semiparametric models have been considered. Tang et al. (2003) and Zhao and Shao (2015) proposed a semiparametric estimator for the outcome model without specifying any response model by using an instrumental variable. On the contrary, Qin et al. (2002), Chang and Kott (2008), and Kott and Chang (2010) proposed a semiparametric estimator for the response model without specifying any outcome model.

Recently, Kim and Yu (2011) and Shao and Wang (2016) proposed a semiparametric estimator for a semiparametric response model. In the semiparametric response model, terms on observed variables are modeled in a nonparametric way whereas the unobserved variable is still a simple linear function. However, we can not generally know or expect the effect of the unobserved variable. For example, if we are interested in a survey of income, and assume that lower-income earners tend
to refuse for the item of income, linear logistic model would be appropriate for the response model. However, if (super) higher-income earners also tend to refuse the item, quadratic or more complicated functions would be required. In this paper, we consider a semiparametric response model with a nonparametric unobserved part as considered in Sang and Morikawa (2018).

Multiple imputation (e.g. Rubin 1978, 1987) is nowadays a common method to analyze missing data. Galimard et al. (2014) considered a multiple imputation by chained equations via Heckman’s selection model. Instead of the classical multiple imputation method, multiple imputation with data augmentation (Tanner and Wong 1987) in terms of Bayesian perspectives have been proposed in several papers because the classical multiple imputation is essentially not “pure” Bayesian estimation. Durrant and Skinner (2006) proposed a Bayesian estimation for MNAR data by assuming parametric forms of both the response and the outcome models. In order to avoid specification of the outcome model, Im and Kim (2017) proposed a Bayesian approach using an outcome model for observed data, not for the whole data including missing responses, because it is more reasonable to assume a parametric model of the outcome model for observed data.

However, these existing Bayesian methods still suffer from misspecification of the response model, which could be essential to make statistical inference on parameters of interest. To overcome the difficulty, we propose a semiparametric selection model in which a functional form of nonresponse is not specified as considered in Sang and Morikawa (2018), and consider Bayesian estimation based on the model. We employ logistic-type selection models with penalized spline methods to estimate the unknown functional part, and develop an efficient Bayesian computation method using Markov Chain Monte Carlo methods and Polya-gamma data augmentation (Polson et al. 2013). We demonstrate that the proposed semiparametric method can flexibly capture the latent unknown missing-data mechanism and prevent bias caused by model misspecification of the response models through simulation studies. We also apply the proposed method to a longitudinal data from clinical trial regarding
drug therapies for Schizophrenia, which is available from R package “Surrogate”.

This paper is organized as follows. In Section 2, we provide details of the proposed methods as well as posterior computation. In Sections 3 and 4 we carry out simulation studies, and data analysis, respectively. Some discussions are given in Section 5.

2 Bayesian semiparametric estimation under nonignorable missing

2.1 Semiparametric selection models for missing-data mechanism

Suppose that we are interested in estimating the parametric conditional distribution $f(y|x; \theta)$, where $y$ is a response, $x$ is a vector of covariates, and $\theta$ is a vector of unknown parameters. For example, $f(y|x; \theta) = \phi(y; x^t \beta, \sigma^2)$ for a simple linear regression. We assume that $x$ is always observed whereas $y$ is subject to missingness.

Let $s$ be the missing indicator such that $s = 1$ if $y$ is observed and $s = 0$ otherwise. We assume that $s$’s independently follow a Bernoulli distribution with the success probability $\pi(x, y) = P(s = 1|x, y)$, which is referred to as the response mechanism.

In this article, we assume that the response mechanism is not missing at random or nonignorable, that is, the missing-data mechanism depends on unobserved response. Specifically, we consider the following missing-data mechanism (selection model):

$$
P(s = 1|y, x) = \psi(g^*(y) + z^t \delta),
$$

where $\psi(x) = \exp(x)/\{1 + \exp(x)\}$ is the logistic function, $g^*(\cdot)$ is an unknown function and $z$ is a sub-vector of $x$ known as the response instrumental variable [Wang et al. 2014]. Since $g^*(\cdot)$ is completely unspecified, the selection model (1) is semiparametric. For the estimation of $g^*(\cdot)$, we employ the P-spline of the form:

$$
g(y) = \phi_0 + \sum_{j=1}^q \phi_j y^j + \sum_{\ell=1}^K \gamma_{\ell}(y - \kappa_{\ell})_+^q.
$$
Here \( q \) is the degree of the spline, \( (x)^q \) denotes the function \( x^q I_{\{x > 0\}} \), \( \kappa_1 < \ldots < \kappa_K \) is a set of fixed knots (whose choice will be discussed later) and \( \phi = (\phi_0, \phi_1, \ldots, \phi_q)^t \) and \( \gamma = (\gamma_1, \ldots, \gamma_K)^t \) are the coefficient vectors for the parametric part and the spline part, respectively. If the knots are sufficiently spread over the range of \( x \) and the number of knots \( K \) is sufficiently large, then the class of functions \( g(\cdot) \) can precisely approximate the unknown function \( g^*(\cdot) \) even for small \( q \), e.g. 2 or 3. We here consider the case with fixed \( K \) and locations of knots, but sensitivity analysis could be done in practice. Since \( q + K + 1 \) parameters are used in \( g(y) \), we put a penalty on \( \gamma \) by treating \( \gamma \) as a random effect to avoid overfitting. Specifically, we assume \( \gamma \sim N(0, \lambda^{-1}I_K) \), where \( \lambda \) is an unknown precision parameter to be estimated from the data.

### 2.2 Bayesian estimation and posterior computation

We suppose the triplet \( \{(x_i, y_i, s_i)\} \) is available for \( i = 1, \ldots, n \), where \( n \) is the sample size. The unknown parameters are \( \theta \) in the outcome model, and \( \phi, \gamma, \delta \) and \( \lambda \) in the selection model. Let \( \Psi \) be the collection of these unknown parameters. The posterior distribution of \( \Psi \) as well as missing observation \( Y_{\text{mis}} = \{y_i \mid s_i = 0, i = 1, \ldots, n\} \) is given by

\[
\pi(\Psi, Y_{\text{mis}} \mid \text{Data}) \propto \pi(\Psi) \prod_{i=1}^{n} \{\exp\{g(y_i) + z^t_1 \delta\}\}^{s_i} \frac{1}{1 + \exp\{g(y_i) + z^t_1 \delta\}} f(y_i; x_i, \theta),
\]

\[
= \pi(\Psi) \prod_{i=1}^{n} \{\exp\{w^t_1 \phi + w^t_2 \gamma + z^t_1 \delta\}\}^{s_i} \frac{1 + \exp\{w^t_1 \phi + w^t_2 \gamma + z^t_1 \delta\}}{1 + \exp\{w^t_1 \phi + w^t_2 \gamma + z^t_1 \delta\}} f(y_i; x_i, \theta),
\]

where \( w_{1i} = (1, y_i, \ldots, y^q_i) \), \( w_{2i} = ((y_i - \kappa_1)^q_+, \ldots, (y_i - \kappa_K)^q_+) \). Using the Polya-gamma data augmentation [Polson et al., 2013], we obtain the following augmented posterior:

\[
\pi(\Psi, Y_{\text{mis}}, \omega \mid \text{Data}) \propto \pi(\Psi) \prod_{i=1}^{n} f(y_i; x_i, \theta) \exp\left\{ \left( s_i - \frac{1}{2}\right) u_i - \frac{\omega_i u_i^2}{2}\right\} p(\omega_i),
\]
where \( u_i \equiv u_i(y_i) = w_1^i\phi + w_2^i\gamma + z^i_1\delta \), and \( p(\cdot) \) is a density function of the Polya-gamma distribution \( \text{PG}(1,0) \). Note that the integral with respect to \( \omega_i \) reduces to the original posterior \( \Omega \). Under the expression, the conditional distribution of \( u_i \) is normal. For prior distributions on \( \Psi \), we use multivariate normal distributions for \( \phi \) and \( \delta \), that is, \( \phi \sim N(0, c^{-1}_\phi I_{q+1}) \), \( \delta \sim N(0, c^{-1}_\delta I_r) \), and a gamma distribution for \( \lambda \), that is, \( \lambda \sim \text{Ga}(c_\lambda, c_\lambda) \), where \( \text{Ga}(a,b) \) denotes a gamma distribution with shape parameter \( a \) and rate parameter \( b \). On the other hand, the specific choice of prior distributions for \( \theta \) would depend on the specific form of the outcome model \( f(y;x,\theta) \). To describe the sampling algorithm, we define \( W_1 = (w_{11},\ldots,w_{1n})^t \), \( W_2 = (w_{21},\ldots,w_{2n})^t \), \( Z = (z_1,\ldots,z_n)^t \), \( s_* = (s_1 - 1/2,\ldots,s_n - 1/2) \), and \( \Omega = \text{diag}(\omega_1,\ldots,\omega_n) \). The sampling algorithm is given as follows:

1. (Sampling \( \omega_i \)) The full conditional distribution of \( \omega_i \) is \( \text{PG}(1,u_i) \). Although its density have a complicated form, random samples can be efficiently generated from an algorithm given in Polson et al. (2013).

2. (Sampling \( \phi \)) The full conditional density of \( \phi \) is proportional to

\[
\pi(\phi) \prod_{i=1}^n \exp \left\{ \left( s_i - \frac{1}{2} \right) w_1^i\phi - \frac{\omega_i^2}{2} (w_1^i\phi + w_2^i\gamma + z^i_1\delta)^2 \right\},
\]

thereby the full conditional distribution of \( \phi \) is a multivariate normal distribution \( N(A_\phi m_\phi, A_\phi) \) with \( A_\phi = (W_1^t\Omega W_1 + c^{-1}_\phi I_{q+1})^{-1} \) and \( m_\phi = W_1^t\{s_* - \Omega(W_2\gamma + Z\delta)\} \).

3. (Sampling \( \gamma \)) Similarly to \( \phi \), the full conditional distribution of \( \gamma \) is a multivariate normal distribution \( N(A_\gamma m_\gamma, A_\gamma) \), where \( A_\gamma = (W_2^t\Omega W_2 + \lambda I_K)^{-1} \) and \( m_\gamma = W_2^t\{s_* - \Omega(W_1\phi + Z\delta)\} \).

4. (Sampling \( \delta \)) Similarly to \( \phi \), the full conditional distribution of \( \delta \) is a multivariate normal distribution \( N(A_\delta m_\delta, A_\delta) \), where \( A_\delta = (Z^t\Omega Z + c_\delta I_r)^{-1} \) and \( m_\delta = Z^t\{s_* - \Omega(W_1\phi + W_2\gamma)\} \).

5. (Sampling \( \lambda \)) Generate \( \lambda \) from its full conditional distribution given by...
Ga(c_\lambda + K, c_\lambda + \gamma^4 \gamma).

6. (Sampling y_i in Y_{mis}) The full conditional distribution of y_i is proportional to

\[ g(y_i) \equiv f(y_i; x_i, \theta) \exp \left\{ - \frac{u_i(y_i)}{2} - \frac{\omega_i u_i(y_i)^2}{2} \right\}, \]

which is an exponentially titled distribution, and is not a familiar form in general. We adopt the Metropolis-adjusted Langevin Monte Carlo algorithm to update current values of y_i’s. With the current value y_i, the proposal y^*_i is generated from the normal distribution \( N(y_i - hV(y_i), 2h) \), where h is a user-specified step-size and

\[ V(y_i) \equiv -\nabla \log g(y_i) \]

\[ = -\nabla \log f(y_i; x_i, \theta) + \left\{ \frac{1}{2} + \omega_i u_i(y_i) \right\} \left( \sum_{j=1}^q j \phi_j y_i^{-1} + q \sum_{\ell=1}^K \gamma_{i\ell} (y_i - \kappa_{i\ell}) \gamma_{i\ell}^{-1} \right). \]

Then, the proposal y^*_i is accepted with probability

\[ \min \left\{ 1, \frac{g(y_i)q_N(y_i; y^*_i - hV(y^*_i), 2h)}{g(y^*_i)q_N(y^*_i; y_i - hV(y_i), 2h)} \right\}, \]

where \( q_N(x; a, b) \) denotes the density function of \( N(a, b) \).

7. (Sampling \( \theta \)) Since the augmented complete data is available, the full conditional posterior distribution of \( \theta \) is proportional to \( \pi(\theta) \prod_{i=1}^n f(y_i; x_i, \theta) \), which is the standard posterior distribution of \( \theta \). Hence, we could employ existing sampling techniques to update \( \theta \) for the assumed outcome model \( f(y_i; x_i, \theta) \).

Owing to the Polya-gamma representation [3], sampling steps for unknown parameters in the spline selection model (11) are quite easy to carry out. The full conditional distribution of y_i in Y_{mis} is different from the assumed model \( f(y_i; x_i, \theta) \) by the exponential term, which comes from the non-ignorable missing-data mechanism. In fact, when the missing-data mechanism is missing at random, the selection model (11) is free from the unobserved value y_i and u_i does not depends on y_i, so that
the full conditional distribution is same as the assumed outcome model. In Sections 3 and 4, we use the standard linear regression model and linear mixed-effects model, respectively, for the outcome models, and we will provide some details regarding the step 7 in the corresponding part.

Finally, we address the way to select a suitable set of knots $\kappa_1 < \cdots < \kappa_K$. In order to make the spline method estimate the unknown missing-data mechanism flexibly even under small $q$, knots should be sufficiently spread over the space of the response variable. When the response variables are free from missing, it would suffice to set $\kappa_1$ and $\kappa_K$ to low and high (e.g., 10% and 90%) empirical quantiles of the observed responses, and set the other knots for equally spaced points between $\kappa_1$ and $\kappa_K$. However, such crude strategy might fail under nonignorable missing since the missing value may take values out of the range of the observed responses and the selection model depends on such missing values. To address this issue, we consider two methods. The first one is a similar adjustment to the crude method, that is, modify the crude values of $\kappa_1$ and $\kappa_K$ to $\kappa_1^* = \kappa_1 - a(\kappa_K - \kappa_1)/2$ and $\kappa_K^* = \kappa_K + a(\kappa_K - \kappa_1)/2$ for some positive constant $a$ specified by users. As the second method, we consider a more data-adaptive way to deal with the idea, that is, we treat the positive constant $a$ as an unknown parameter and assign prior distributions to make posterior inference. Since the knots are appeared in the posterior distributions through $u_i$’s, the full conditional posterior distribution of $a$ is proportional to

$$h(a) = \pi(a) \prod_{i=1}^n \exp \left\{ \left( s_i - \frac{1}{2} \right) u_i - \frac{\omega_i u_i^2}{2} \right\},$$

where $\pi(a)$ is the prior distribution on $a$. To generate posterior samples from the non-familiar distribution, we simply adopt a random-walk MH algorithm which generates the proposal $a^*$ from a bivariate normal distribution $N(a^\dagger, c)$ with current values $a^\dagger$ and a positive constant $c$, and accept the proposal with probability $\min\{1, h(a^*)/h(a^\dagger)\}$. 


3 Simulation study

We investigate the performance of the proposed method together with some existing methods. To this end, we consider a simple linear regression model:

\[ y_i = \beta_0 + \beta_1 x_{i1} + \beta_2 x_{i2} + \varepsilon_i, \quad \varepsilon_i \sim N(0, \sigma^2), \quad i = 1, \ldots, n, \]

where \( \beta \equiv (\beta_0, \beta_1, \beta_2) = (0.5, 0.7, 0.5) \) and \( \sigma^2 = 1 \). Here two covariates \( x_{i1} \) and \( x_{i2} \) were independently generated from \( N(0, 1) \), respectively. Based on the model, we generated the response value \( y_i \). For the response mechanism, we independently generated the missing indicator \( s_i \) from a Bernoulli distribution with the success probability \( \pi_i \), and \( y_i \) is observed/missing when \( s_i = 1 \) or 0. We considered the following five scenarios for \( \pi_i \):

(S1: Linear MNAR)

\[ \pi_i = \frac{\exp(\phi_0 + \phi_1 y_i + \delta x_{i1})}{1 + \exp(\phi_0 + \phi_1 y_i + \delta x_{i1})}, \]

where \( (\phi_0, \phi_1, \delta) = (1, 0.5, 0.2) \).

(S2: Quadratic MNAR-I)

\[ \pi_i = \frac{\exp(\phi_0 + \phi_1 y_i + \phi_2 y_i^2 + \delta x_{i1})}{1 + \exp(\phi_0 + \phi_1 y_i + \phi_2 y_i^2 + \delta x_{i1})}, \]

where \( (\phi_0, \phi_1, \phi_2, \delta) = (1.5, -0.5, -0.2, 0.2) \).

(S3: Quadratic MNAR-II)

\[ \pi_i = \frac{\exp(\phi_0 + \phi_1 y_i + \phi_2 y_i^2 + \delta x_{i2})}{1 + \exp(\phi_0 + \phi_1 y_i + \phi_2 y_i^2 + \delta x_{i2})}, \]

where \( (\phi_0, \phi_1, \phi_2, \delta) = (1.5, -0.5, -0.2, 0.2) \).

(S4: Complementary log-log MNAR)

\[ \pi_i = 1 - \exp\{-\exp(\phi_0 + \phi_1 y_i + \phi_2 y_i^2 + \delta x_{i1})\}, \]
where \( (\phi_0, \phi_1, \phi_2, \delta) = (1.3, -0.5, -0.2, 0.2) \).

(S5: Cubic MNAR)

\[
\pi_i = \frac{\exp(\phi_0 + \phi_1 y_i + \phi_2 y_i^2 + \phi_3 y_i^3 + \delta x_{i1})}{1 + \exp(\phi_0 + \phi_1 y_i + \phi_2 y_i^2 + \phi_3 y_i^3 + \delta x_{i1})},
\]

where \( (\phi_0, \phi_1, \phi_2, \phi_3, \delta) = (1.3, -0.2, -0.4, 0.1, -0.2) \).

For each response mechanism, the overall response rates were around 70%. We generated a random sample with \( n = 600 \) and \( n = 1,200 \), and applied the following three methods:

1. CC: Simply omit the samples with missing responses and apply the linear regression model to the data.

2. LS: Assume a parametric linear structure for the selection mechanism, that is, \( \pi_i = \psi(\phi_0 + \phi_1 y_i + \delta x_{i1}) \), where \( \psi(\cdot) \) is the logistic function, and estimate the linear regression.

3. BSS: Apply the proposed method with linear regression for the outcome model, using the semiparametric selection model (1) with \( z_i = x_{i1} \) and \( K = 10 \). We considered two cases for the setting of order \( q \): \( q = 2 \) and 3, which are denoted by BSS1 and BSS2, respectively.

It is noted that the selection model used in LS is correctly specified in scenario S1, whereas the linear structure is misspecified in the other scenarios. On the other hand, the proposed selection model covers the true selection model in scenarios S1, S2 and S5, while the model is slightly misspecified in scenarios S3 and S4. In the proposed method, we used a uniform prior on \((0, 1)\) for \( a \) that controls the amount of spread of knots. For two Bayesian methods, LS and BSS, we generated 3,000 posterior samples of \( \beta \) after discarding the first 2,000 samples as burn-in. We then computed the posterior means and 95% posterior credible intervals of each component in \( \beta \). In the CC method, estimators of regression coefficients \( \beta \) were obtained by the

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standard least squared estimator, and the Wald-type 95% confidence intervals of each component in \( \beta \) were computed.

For evaluating the performance of the point estimation, we calculated mean squared error (MSE) and bias, defined as

\[
\text{MSE} = \frac{1}{R} \sum_{r=1}^{R} (\hat{\beta}_k^{(r)} - \beta_k)^2, \quad \text{Bias} = \frac{1}{R} \sum_{r=1}^{R} \hat{\beta}_k^{(r)} - \beta_k,
\]

for \( k = 2 \) and \( 3 \), where \( \hat{\beta}_k^{(r)} \) is a point estimate of \( \beta_k \) in the \( r \)th replication. We set \( R = 500 \) in this study. Moreover, in order to evaluate the performance in terms of interval estimation (i.e. uncertainty quantification), we calculated coverage probability (CP) and average length (AL), defined as

\[
\text{CP} = \frac{1}{R} \sum_{r=1}^{R} I(\beta_k \in \text{CI}_k^{(r)}), \quad \text{AL} = \frac{1}{R} \sum_{r=1}^{R} |\text{CI}_k^{(r)}|,
\]

where \( \text{CI}_k^{(r)} \) is a credible interval in the \( r \)th replication and \( |\text{CI}_k^{(r)}| \) denotes the length of the interval. The results for the five scenarios are shown in Tables 1 and 2 in the case with \( n = 600 \) and \( n = 1,200 \), respectively. Overall, the CC method does not perform well as expected. Although the CC method produces reasonable point estimates compared with other methods in some cases such as scenarios 1 and 5, the interval estimation does not work well in terms of CP. In scenario 1, the LS model is the true model and it is natural that the LS achieves the best performance among the four methods while the proposed BSS methods works almost the same as the LS method. However, once the LS model is misspecified as in scenarios 2~5, it is observed that the posterior means tend to underestimate the true values and the CP is much smaller than the nominal level 95%. This shows that the misspecification of the selection model may lead to severely inappropriate statistical inference. On the other hand, the proposed BSS method produces almost unbiased posterior means and the CP is acceptably close to the nominal level in all the scenarios. Comparing the two choices of \( q \) in the proposed method, \( q = 2 \) seems slightly better than \( q = 3 \).
in this study. It should also be noted that the AL of the proposed method tends to be larger than that of the CC and LS methods in scenarios 2–5 since the proposed method can successfully capture the latent unknown missing-data mechanism and reflect its estimation error. Comparing Tables 1 and 2 it should be pointed out that the performance of the proposed BSS method has been reasonably improved by increasing the number of observations.

Finally, in Figure 1 we show point-wise posterior means and 95% credible intervals of the selection probability $\pi_i$ as a function of the response $y_i$, where the covariate $x_{i1}$ is fixed to 1, in the first replication in the simulation study with scenarios 3 and 4 and $n = 600$. It can be confirmed that the proposed semiparametric selection model successfully captures the true structure of missing-data mechanism in both scenarios while the standard linear selection model fails to detect the underlying missing-data mechanism especially around small values of the response variable. Such flexibility of the proposed method would lead to the superior performance in the estimation of parameters in the outcome model.

![Figure 1: Point-wise posterior means (solid lines) and 95% credible intervals (shaded parts) of selection probabilities in scenarios 3 and 4 in the simulation study.](image-url)
Table 1: Mean squared errors (MSE), bias of posterior means and coverage probabilities (CP) and average lengths (AL) of 95% credible/confidence intervals based on the complete-case (CC) analysis, simple linear selection (LS) model for missing-data mechanism, and the proposed Bayesian semiparametric selection model for missing-data mechanism with $q = 2$ (BSS1) and $q = 3$ (BSS2), in the case with $n = 600$.

| Scenario | CC  | LS  | BSS1 | BSS2 | CC  | LS  | BSS1 | BSS2 |
|----------|-----|-----|------|------|-----|-----|------|------|
| MSE      |     |     |      |      |     |     |      |      |
| 1        | 7.9 | 5.0 | 5.9  | 6.2  | 6.0 | 5.0 | 5.3  | 5.4  |
| 2        | 21.0| 19.6| 7.2  | 7.7  | 15.9| 14.0| 6.7  | 7.0  |
| 3        | 21.7| 18.6| 7.5  | 8.2  | 15.1| 13.6| 6.6  | 6.9  |
| 4        | 23.6| 23.4| 6.2  | 6.5  | 18.3| 14.1| 4.8  | 4.9  |
| 5        | 11.9| 14.0| 7.1  | 7.7  | 8.7 | 8.9 | 6.3  | 6.4  |
| Bias     |     |     |      |      |     |     |      |      |
| 1        | -6.3| 0.7 | -0.1 | -0.6 | -3.7| 0.5 | -0.2 | -0.8 |
| 2        | -20.6| -19.2| 1.7 | 0.7 | -15.2| -13.3| 0.9 | 0.3 |
| 3        | -21.2| -18.0| 0.5 | -0.5 | -14.5 | -12.9 | 0.6 | -0.1 |
| 4        | -23.2| -23.0| 0.3 | -0.1 | -17.9| -13.6| 0.7 | 0.5 |
| 5        | -11.0| -12.4| 0.0 | -1.7 | -7.3 | -7.3 | 0.5 | -0.5 |
| CP       |     |     |      |      |     |     |      |      |
| 1        | 74.2| 95.0| 93.8 | 92.2 | 88.8| 94.4| 95.8 | 95.4 |
| 2        | 0.0 | 0.6 | 94.4 | 92.6 | 6.6 | 17.6| 93.0 | 92.2 |
| 3        | 0.0 | 2.2 | 94.8 | 91.4 | 7.0 | 14.4| 96.0 | 93.8 |
| 4        | 0.0 | 0.0 | 92.6 | 91.2 | 0.0 | 7.6 | 97.4 | 96.0 |
| 5        | 36.2| 36.8| 93.6 | 91.0 | 68.4| 69.2| 95.4 | 93.8 |
| AL       |     |     |      |      |     |     |      |      |
| 1        | 18.5| 19.7| 22.7 | 22.5 | 19.2| 19.8| 21.0 | 20.7 |
| 2        | 17.3| 18.2| 26.4 | 26.5 | 17.5| 18.0| 24.7 | 24.8 |
| 3        | 18.0| 19.1| 28.0 | 28.4 | 16.6| 17.0| 24.0 | 24.2 |
| 4        | 15.9| 17.1| 22.7 | 22.9 | 15.2| 15.9| 20.4 | 20.4 |
| 5        | 18.6| 21.7| 26.4 | 26.3 | 19.2| 19.7| 24.3 | 24.2 |
Table 2: Mean squared errors (MSE), bias of posterior means and coverage probabilities (CP) and average lengths (AL) of 95% credible/confidence intervals based on the complete-case (CC) analysis, simple linear selection (LS) model for missing-data mechanism, and the proposed Bayesian semiparametric selection model for missing-data mechanism with $q = 2$ (BSS1) and $q = 3$ (BSS2), in the case with $n = 1,200$.

| Scenario | CC $\beta_2$ | LS $\beta_2$ | BSS1 $\beta_2$ | BSS2 $\beta_2$ | CC $\beta_3$ | LS $\beta_3$ | BSS1 $\beta_3$ | BSS2 $\beta_3$ |
|----------|---------------|---------------|----------------|----------------|---------------|---------------|----------------|----------------|
| 1        | 5.1           | 3.4           | 3.7            | 3.8            |               |               |                |                |
| 2        | 15.1          | 12.9          | 4.1            | 4.2            | 14.9          | 13.7          | 4.1            | 4.1            |
| 3        | 8.2           | 8.2           | 4.0            | 4.0            |               |               |                |                |
| 4        | 12.1          | 12.3          | 4.2            | 4.2            |               |               |                |                |
| 5        | 23.6          | 23.0          | 4.1            | 4.2            | 17.9          | 14.5          | 3.4            | 3.5            |

| Scenario | CC $\beta_2$ | LS $\beta_2$ | BSS1 $\beta_2$ | BSS2 $\beta_2$ | CC $\beta_3$ | LS $\beta_3$ | BSS1 $\beta_3$ | BSS2 $\beta_3$ |
|----------|---------------|---------------|----------------|----------------|---------------|---------------|----------------|----------------|
| 1        | 11.6          | 11.8          | 0.0            | -0.8           | -7.6          | -7.6          | 0.3            | -0.2           |
| 2        | 13.2          | 13.8          | 15.8           | 15.7           | 12.8          | 13.1          | 13.9           | 13.8           |
| 3        | 7.8           | 8.6           | 95.6           | 94.8           | 35.4          | 37.0          | 95.4           | 94.8           |
| 4        | 1.21          | 12.4          | 18.0           | 18.2           | 11.6          | 11.8          | 16.3           | 16.3           |
| 5        | 12.1          | 12.5          | 18.3           | 18.5           | 11.6          | 11.7          | 16.4           | 16.5           |

| Scenario | CC $\beta_2$ | LS $\beta_2$ | BSS1 $\beta_2$ | BSS2 $\beta_2$ | CC $\beta_3$ | LS $\beta_3$ | BSS1 $\beta_3$ | BSS2 $\beta_3$ |
|----------|---------------|---------------|----------------|----------------|---------------|---------------|----------------|----------------|
| 1        | 11.6          | 11.8          | 0.0            | -0.8           | -7.6          | -7.6          | 0.3            | -0.2           |
| 2        | 13.2          | 13.8          | 15.8           | 15.7           | 12.8          | 13.1          | 13.9           | 13.8           |
| 3        | 7.8           | 8.6           | 95.6           | 94.8           | 35.4          | 37.0          | 95.4           | 94.8           |
| 4        | 1.21          | 12.4          | 18.0           | 18.2           | 11.6          | 11.8          | 16.3           | 16.3           |
| 5        | 12.1          | 12.5          | 18.3           | 18.5           | 11.6          | 11.7          | 16.4           | 16.5           |
4 Example: Schizophrenia clinical trial

To illustrate the proposed method in practical situations, we applied the proposed method to a dataset of randomized clinical trial of drug therapies for Schizophrenia, which is available from R package “Surrogate”. In the trial, a placebo and a treatment groups were compared, and the response of interest is an integer showing severity of symptoms known as PANSS score, where high values indicate more severe symptoms. The patients were observed at weeks 1, 2, 4, 6 and 8 (t = 1, 2, 3, 4, 5) of the study. In the dataset, 2,151 patients are included and some patients have missing values. If patients did not feel good enough to see doctors, they would not be able to see doctors and the corresponding values would be missing, thereby the missing-data mechanism is considered as MNAR. The overall missing rate is about 20%. In this study, we are interested in the time-varying difference of PANSS scores between placebo and treatment groups. Let $y_{it}$ denote the PANSS score for the $i$th individual at $t$th time, and we modeled the individual PANSS score as

$$y_{it} = \sum_{k \in \{0, 1\}} R_{ik} (\beta_{0k} + \beta_{1k} T_t + \beta_{2k} T_t^2 + \beta_{3k} T_t^3) + v_i + \varepsilon_{ij},$$

(4)

where $R_{ik}$ is the indicator whether the $i$th patient is included in Placebo ($k = 0$) or Treatment ($k = 1$) groups, $T_t$ denotes the measurement time, $v_i$ is an individual effect and $\varepsilon_{ij}$ is an error term. We assume that $v_i$ and $\varepsilon_{ij}$ are mutually independent and distributed as $v_i \sim N(0, \tau^2)$ and $\varepsilon_{ij} \sim N(0, \sigma^2)$. Note that in the model (4), time change of the response variable $y_{it}$ is modeled by the measurement time separately for each group. We let $s_{it}$ be the missing indicator such that $s_{it} = 1$ if $y_{it}$ is observed, and $s_{it} = 0$ otherwise. For the missing-data mechanism, we employ the following model:

$$P(s_{it} = 1|y_{it}, s_{i,t-1}) = \psi\left(g(y_{it}) + \delta_1 T_t + \delta_2 R_{i1} + \delta_3 s_{i,t-1}\right),$$

(5)

where $\psi(\cdot)$ is the logistic function and $s_{i0} = 1$, and $g(\cdot)$ is a nonparametric function modeled by P-spline. Note that the inclusion of $s_{i,t-1}$ in the selection model ad-
addresses the time dependence of the missing indicator, and the joint distribution of 
\((s_{i1}, \ldots, s_{iT})\) given the other variables is expressed as the product of the probability 
given in (5), so that we can still apply the same algorithm for posterior computation 
given in Section 2.

For the unknown parameters in the model (4), we set independent normal priors 
\(N(0, 10^4)\) for the regression coefficients and inverse gamma priors \(IG(1, 1)\) for \(\tau^2\) and \(\sigma^2\). As noted in Section 2, the posterior sampling algorithm for unknown parameters 
in the outcome model is the same as one for complete data, thereby the posterior 
computation for the unknown parameters in (4) can be easily implemented by using 
existing Gibbs sampling algorithm for linear mixed models (e.g. Hobert and Casella, 1996).

We considered the proposed method with \(q = 2\) and \(K = 10\). For comparisons, 
we also applied the simple linear selection model that replaces a linear function of 
\(y_{it}\) with \(g(\cdot)\) in (5). We generated 40,000 posterior samples after discarding the first 
10,000 samples as burn-in. Based on the posterior samples, we computed the poste-
rior means and point-wise 95\% credible intervals of regression lines, which are shown 
in Figure 2. It is observed that the estimates of regression lines are different between 
the proposed method and linear selection model, and the credible intervals are over-
lapped at some measurement times in the linear selection method while the credible 
interval are clearly separated at all the measurement times. Based on the results of 
simulation study in Section 3, the result from the linear selection method is doubtful 
since it is subject to misspecification leading to serious bias in the estimation of pa-
rameters in outcome models. We also computed the posterior means and point-wise 
95\% credible intervals of the selection probability (5) as a function of PANSS score 
with \(T_t = 4\) and four combinations of \(R_{it} \in \{0, 1\}\) and \(s_{i,t-1}(= S) \in \{0, 1\}\), which 
are presented in Figure 3. It is revealed that the effect of treatment indicator on the 
missing probability is limited whereas the missing indicator of the previous time sig-
nificantly changes the missing probability. Also, the linear selection model produces 
a very simple structure (almost constant over PANSS score) for missing probability.
while the proposed method seems to capture the underlying missing-data mechanism flexibly as a complete function of PANSS score. Such difference of flexibility in the estimation of missing probability would lead to the difference of resulting regression lines as shows in Figure 2.

Finally, we considered sensitivity check of the selection model (5). To this end, we considered an alternative selection model adding $T^2_t$ to (5), and two choices of $K \in \{10, 20\}$. Based the same number of posterior samples, it has been revealed that the results have not been changed much, that is, the posterior means and credible intervals of PANSS score were quite similar to that given in Figure 2.

![Figure 2: Posterior means and point-wise 95% credible intervals of overall PANSS scores in two groups.](image)

5 Discussion

This paper developed an effective Bayesian approach to estimating missing mechanisms with an unspecified functional form for missing variables and a parametric form of observed covariates. Based on discussion given in Sang and Morikawa (2018),
Figure 3: Point-wise posterior means (solid lines) and 95% credible intervals (shaded parts) of selection probabilities based on the standard linear selection model and the proposed semiparametric for control and treatment group.

the flexible estimation of the functional form of missing variable could be more significant than that of observed covariates. However, the proposed method could be
extended to the case where the missing probability is an nonparametric function of both missing variable and covariates by using, for example, radial basis expansion.

For outcome models, we considered only a parametric model for simplicity, but we may employ semiparametric methods such as generalized method of moments (Yin 2009). It should be remarked that extension of the outcome modeling could be easily done since the posterior computation for outcome models is the same as that with complete data. Since the detailed investigation would extend the scope of this paper, we left it to an interesting future study.

Finally, although we employed the logistic function as a link function in the selection models due to its popularity in this context, we may use other link functions such as Probit link. In such cases, the posterior computation algorithm given in Section 2 should be changed in appropriate ways.

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