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Practical aspects of Bayesian multivariate meta-analysis

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Abstract

Multivariate meta-analysis is a mostly used approach when multivariate results of several studies are pooled together. The multivariate model of random effects provides a tool to perform the multivariate meta-analysis in practice. In this paper, we discuss Bayesian inference procedures derived for the multivariate model of random effects when the model parameters are endowed with two non-informative priors: the Berger-Bernardo reference prior and the Jeffreys prior. Moreover, two Metropolis-Hastings algorithms are presented, and their convergence properties are analysed via simulations.

Keywords: multivariate meta-analysis; multivariate model of random effects; Metropolis-Hastings algorithms; rank plot; split-hatR estimate.

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1. Introduction

Meta-analysis presents an important quantitative tool for combining measurement results obtained in different studies [1, 2]. It is widely used in several fields of science, like medical science, physical science and chemistry [1–4].

In many applications, each individual study performs measurements of a few features simultaneously, and, as such, the result of each individual study consists of a few measured values, which are reported together with the covariance matrix between the measured values. This covariance matrix provides information not only about the measurement uncertainties, but also presents the dependence structure of the calculated values. In such a situation, performing univariate meta-analysis for each measured feature separately would lead to the loss of information related to the dependence structure of measurement results. As a solution, the multivariate meta-analysis has been developed in [5–7].

Multivariate model of random effects is a multivariate extension of the univariate model of random effects, which is a widely spread statistical approach for performing meta-analysis [5–7]. Using the methods of frequentist statistics, the procedures for estimating the parameters of the multivariate model of random effects, i.e., the common mean vector and the heterogeneity matrix, were suggested in [5–7]. While the DerSimonian and Laird approach was generalized as the multivariate case in [5], the method based on the restricted maximum likelihood approach was discussed in [6]. Furthermore, the estimator derived by using the method of moments was presented in [7].

Another approach to estimate the parameters of the multivariate model of random effects utilizes Bayesian methods. Using the Laplace approximation, Bayesian estimators for the parameters of a two-dimensional model of random effects were given in [8]. Recently, Bayesian inference procedures for the parameters of the multivariate model of random effects were developed in [9] by using the Jeffreys prior and the Berger-Bernardo reference prior. The developed approaches were also implemented in the *R* package *BayesMultMeta* [10].

The rest of the paper is structured as follows. In Section 2, we present the objective Bayesian inference procedures derived for the parameters of the multivariate model of random effects together with two Metropolis-Hastings algorithms for generating samples from the posterior distribution. Section 3 provides the results of the simulation study where the convergence properties of the two suggested algorithms are studied, while concluding remarks are given in Section 4.

2. Bayesian inference procedures for the parameters of the multivariate model of random effects

Let $(x_i,\ U_i)$ be the reported results of the i-th individual study for $i=1,...,n,$ where $\boldsymbol{x}_i = \left(x_{i,1},...,x_{i,p}\right)^T$ is the vector consisting of the measurement results for p features and $\boldsymbol{U}_i = \left(u_{i,jk}\right)_{j,k=1,...,p}$ is the covariance matrix with the squared uncertainties on the diagonal and the covariance between the measurement results as non-diagonal elements. The multivariate model of random effects is defined by

$$\boldsymbol{x}_i = \boldsymbol{\mu} + \boldsymbol{\lambda}_i + \boldsymbol{\varepsilon}_i \text{ for } i=1,...n, \quad (1)$$

where $\boldsymbol{\lambda}_i$ and $\boldsymbol{\varepsilon}_i$ are independent, and p-dimensional multivariate is normally distributed for $i=1,...,n$ with $\boldsymbol{\lambda}_i \sim N_p(0,\Psi)$ and $\boldsymbol{\varepsilon}_i \sim N_p(0,\boldsymbol{U}_i)$. The vector $\boldsymbol{\mu}$ denotes the common mean vector, which is the main object of interest, while $\boldsymbol{\Psi}$ is the heterogeneity matrix, which determines the dark uncertainty and corresponds to the additional uncertainty, which appears when the results of several studies are pooled together.

Objective Bayesian inference procedures for the parameters ($\boldsymbol{\mu}$, $\boldsymbol{\Psi}$) of the multivariate model of random effects (1) were derived in [9]. They are established in the case of the model parameters endowed with the Berger-Bernardo reference prior and the Jeffreys prior, which were obtained in [9] and are given by

$$\pi_R(\boldsymbol{\mu},\boldsymbol{\Psi}) = \pi_R(\boldsymbol{\Psi}) \propto \sqrt{det\left(\boldsymbol{G}_p^T\left(\sum_{i=1}^{n}(\boldsymbol{\Psi}+\boldsymbol{U}_i)^{-1}\otimes(\boldsymbol{\Psi}+\boldsymbol{U}_i)^{-1}\right)\boldsymbol{G}_p\right)} \quad (2)$$

and

$$\pi_J(\boldsymbol{\mu},\boldsymbol{\Psi}) = \pi_J(\boldsymbol{\Psi}) \propto \pi_R(\boldsymbol{\Psi})\sqrt{det\left(\sum_{i=1}^{n}(\boldsymbol{\Psi}+\boldsymbol{U}_i)^{-1}\right)}, \quad (3)$$

respectively, where *det* (***A***) is the determinant of matrix ***A***, the symbol $\otimes$ denotes the Kronecker product, and $\boldsymbol{G}_p$ stands for the duplication matrix.

Let $\boldsymbol{X} = (\boldsymbol{x}_1,...,\boldsymbol{x}_n)$ be the observation matrix. Then, the conditional posterior for $\boldsymbol{\mu}$ is given by (see [9]),

$$\boldsymbol{\mu} \mid \boldsymbol{\Psi}, \boldsymbol{X} \sim N_p\left(\left(\sum_{i=1}^{n}(\boldsymbol{\Psi}+\boldsymbol{U}_i)^{-1}\right)^{-1}\sum_{i=1}^{n}(\boldsymbol{\Psi}+\boldsymbol{U}_i)^{-1}\boldsymbol{x}_i, \left(\sum_{i=1}^{n}(\boldsymbol{\Psi}+\boldsymbol{U}_i)^{-1}\right)^{-1}\right) \quad (4)$$

while the marginal posterior for $\boldsymbol{\Psi}$ is expressed as

$$\pi(\boldsymbol{\Psi} \mid \boldsymbol{X}) \propto \frac{\pi(\boldsymbol{\Psi})}{\sqrt{det\left(\sum_{i=1}^{n}(\boldsymbol{\Psi}+\boldsymbol{U}_i)^{-1}\right)}\prod_{i=1}^{n}\sqrt{det(\boldsymbol{\Psi}+\boldsymbol{U}_i)}} exp\left(-\frac{1}{2}\sum_{i=1}^{n}\left(\boldsymbol{x}_i - \tilde{\boldsymbol{x}}(\boldsymbol{\Psi})\right)^T(\boldsymbol{\Psi}+\boldsymbol{U}_i)^{-1}\left(\boldsymbol{x}_i - \tilde{\boldsymbol{x}}(\boldsymbol{\Psi})\right)\right) \quad (5)$$

where

$$\tilde{\boldsymbol{x}}(\boldsymbol{\Psi}) = \left(\sum_{i=1}^{n}(\boldsymbol{\Psi}+\boldsymbol{U}_i)^{-1}\right)^{-1}\sum_{i=1}^{n}(\boldsymbol{\Psi}+\boldsymbol{U}_i)^{-1}\boldsymbol{x}_i, \quad (6)$$

and $\pi(\boldsymbol{\Psi}) = \pi_R(\boldsymbol{\Psi})$ when the Berger-Bernardo reference prior is used, and $\pi(\boldsymbol{\Psi}) = \pi_J(\boldsymbol{\Psi})$ when the Jeffreys prior is used.

For practical implementations, two Metropolis-Hastings algorithms for generating samples from the posterior distribution (4)-(6) were suggested in [9]. Let

$$\bar{\boldsymbol{x}} = \sum_{i=1}^{n}\boldsymbol{x}_i \text{ and } \boldsymbol{S} = \frac{1}{\boldsymbol{n}-1}\sum_{i=1}^{n}(\boldsymbol{x}_i - \bar{\boldsymbol{x}})(\boldsymbol{x}_i - \bar{\boldsymbol{x}})^T \quad (7)$$

be the sample mean and the sample covariance matrix. In the case of the Berger and Bernardo reference prior, the two algorithms are given by (see [9]).

Algorithm A:

1. ***Initialization*:**

Choose the initial values $\boldsymbol{\mu}^{(0)}$ and $\boldsymbol{\Psi}^{(0)}$ for $\boldsymbol{\mu}$ and $\boldsymbol{\Psi}$ and set $b = 0$.

2. ***Generating new values of*** $\boldsymbol{\mu}^{(w)}$ and $\boldsymbol{\Psi}^{(w)}$:

a. For given data $\boldsymbol{X} = (\boldsymbol{x}_1,...,\boldsymbol{x}_n)$, generate $\boldsymbol{\mu}^{(w)}$ from

$$\boldsymbol{\mu} \mid \boldsymbol{X} \sim t_p\left(n-p, \bar{\boldsymbol{x}}, \frac{(n-1)}{n(n-p)}\boldsymbol{S}\right);$$

b. Using data $\boldsymbol{X}$ and $\boldsymbol{\mu}^{(w)}$ drawn in step (a), generate $\boldsymbol{\Psi}^{(w)}$ from

$$\boldsymbol{\Psi} \mid \boldsymbol{\mu}^{(w)}, \boldsymbol{X} \sim IW_p\left(n+p+1, \sum_{i=1}^{n}(\boldsymbol{x}_i - \boldsymbol{\mu}^{(w)})(\boldsymbol{x}_i - \boldsymbol{\mu}^{(w)})^T\right).$$

3. ***Calculation of the Metropolis-Hastings ratio:***

$$\boldsymbol{MH}^{(b)} = \frac{\pi\left(\boldsymbol{\mu}^{(w)}, \boldsymbol{\Psi}^{(w)} \mid \boldsymbol{X}\right)q\left(\boldsymbol{\mu}^{(b-1)}, \boldsymbol{\Psi}^{(b-1)} \mid \boldsymbol{X}\right)}{\pi\left(\boldsymbol{\mu}^{(b-1)}, \boldsymbol{\Psi}^{(b-1)} \mid \boldsymbol{X}\right)q\left(\boldsymbol{\mu}^{(w)}, \boldsymbol{\Psi}^{(w)} \mid \boldsymbol{X}\right)},$$

where $q(.,.|X)$ is the joint density calculated by using (a) and (b) of step 2.

4. ***Moving to the next state of Markov chain:***

a. Generate $U^{(b)}$ from the uniform distribution on [0,1];

b. If $U^{(b)} < min\left\{1, \mathrm{MH}^{(b)}\right\}$, then set $\boldsymbol{\mu}^{(b)} = \boldsymbol{\mu}^{(w)}$ and $\boldsymbol{\Psi}^{(b)} = \boldsymbol{\Psi}^{(w)}$ (Markov chain moves to the new state). Otherwise, set $\boldsymbol{\mu}^{(b)} = \boldsymbol{\mu}^{(b-1)}$ and $\boldsymbol{\Psi}^{(b)} = \boldsymbol{\Psi}^{(b-1)}$ (Markov chain remains in the previous state).

5. Return to step (2), increase b by 1, and repeat until the sample of size B is accumulated.

Algorithm B:

1. ***Initialization*:**

Choose the initial values $\boldsymbol{\mu}^{(0)}$ and $\boldsymbol{\Psi}^{(0)}$ for $\boldsymbol{\mu}$ and $\boldsymbol{\Psi}$ and set $b = 0$.

2. Generating new values of $\boldsymbol{\mu}^{(w)}$ and $\boldsymbol{\Psi}^{(w)}$:

a. For given data $\boldsymbol{X} = (\boldsymbol{x}_1,...,\boldsymbol{x}_n)$, generate $\boldsymbol{\Psi}^{(w)}$ from

$$\boldsymbol{\Psi} \mid \boldsymbol{X} \sim IW_p\left(n+p, (n-1)\boldsymbol{S}\right);$$

b. Using data $\boldsymbol{X}$ and $\boldsymbol{\Psi}^{(w)}$ drawn in step (a), generate $\boldsymbol{\mu}^{(w)}$ from

$$\boldsymbol{\mu} \mid \boldsymbol{\Psi}^{(w)}, \boldsymbol{X} \sim N_p\left(\bar{\boldsymbol{x}}, \frac{1}{\boldsymbol{n}}\boldsymbol{\Psi}^{(w)}\right).$$

3. ***Calculation of the Metropolis-Hastings ratio*:**

$$MH^{(b)} = \frac{\pi\left(\boldsymbol{\mu}^{(w)}, \boldsymbol{\Psi}^{(w)} \mid \boldsymbol{X}\right) q\left(\boldsymbol{\mu}^{(b-1)}, \boldsymbol{\Psi}^{(b-1)} \mid \boldsymbol{X}\right)}{\pi\left(\boldsymbol{\mu}^{(b-1)}, \boldsymbol{\Psi}^{(b-1)} \mid \boldsymbol{X}\right) q\left(\boldsymbol{\mu}^{(w)}, \boldsymbol{\Psi}^{(w)} \mid \boldsymbol{X}\right)},$$

where $q(.,.|\boldsymbol{X})$ is the joint density calculated by using (a) and (b) of step 2.

4. ***Moving to the next state of Markov chain*:**

a. Generate $U^{(b)}$ from the uniform distribution on [0,1];

b. If $U^{(b)} < min\left\{1, \mathrm{MH}^{(b)}\right\}$, then set $\boldsymbol{\mu}^{(b)} = \boldsymbol{\mu}^{(w)}$ and $\boldsymbol{\Psi}^{(b)} = \boldsymbol{\Psi}^{(w)}$ (Markov chain moves to the new state). Otherwise, set $\boldsymbol{\mu}^{(b)} = \boldsymbol{\mu}^{(b-1)}$ and $\boldsymbol{\Psi}^{(b)} = \boldsymbol{\Psi}^{(b-1)}$ (Markov chain remains in the previous state).

5. Return to step (2), increase b by 1, and repeat until the sample of size B is accumulated.

In Algorithms A and B, the symbol $t_p(d, \boldsymbol{a}, \boldsymbol{A})$ denotes the p-dimensional multivariate t-distribution with d degrees of freedom, location vector $\boldsymbol{a}$, and scale matrix $\boldsymbol{A}$, while $IW_p(d, \boldsymbol{A})$ stands for the p-dimensional inverse Wishart distribution with d degrees of freedom and parameter matrix $\boldsymbol{A}$. For the Jeffreys prior, changes in Algorithms A and B are present in step 2 only. In the case of Algorithm A, it is given by

2. ***Generating new values of*** $\boldsymbol{\mu}^{(w)}$ and $\boldsymbol{\Psi}^{(w)}$:

a. For given data $\boldsymbol{X} = (\boldsymbol{x}_1, ..., \boldsymbol{x}_n)$, generate $\boldsymbol{\mu}^{(w)}$ from

$$\boldsymbol{\mu} \mid \boldsymbol{X} \sim t_p\left(n - p + 1, \bar{\boldsymbol{x}}, \frac{(n-1)}{n(n-p)} \boldsymbol{S}\right);$$

b. Using data $\boldsymbol{X}$ and $\boldsymbol{\mu}^{(w)}$ drawn in step (a), generate $\boldsymbol{\Psi}^{(w)}$ from

$$\boldsymbol{\Psi} \mid \boldsymbol{\mu}^{(w)}, \boldsymbol{X} \sim IW_p\left(n + p + 2, \sum_{i=1}^{n} (\boldsymbol{x}_i - \boldsymbol{\mu}^{(w)})(\boldsymbol{x}_i - \boldsymbol{\mu}^{(w)})^T\right),$$

while for Algorithm B it becomes

2. ***Generating new values of*** $\boldsymbol{\mu}^{(w)}$ ***and*** $\boldsymbol{\Psi}^{(w)}$:

a. For given data $\boldsymbol{X} = (\boldsymbol{x}_1, ..., \boldsymbol{x}_n)$, generate $\boldsymbol{\Psi}^{(w)}$ from

$$\boldsymbol{\Psi} \mid \boldsymbol{X} \sim IW_p\left(n + p + 1, (n-1)\boldsymbol{S}\right);$$

b. Using data $\boldsymbol{X}$ and $\boldsymbol{\Psi}^{(w)}$ drawn in step (a), generate $\boldsymbol{\mu}^{(w)}$ from

$$\boldsymbol{\mu} \mid \boldsymbol{\Psi}^{(w)}, \boldsymbol{X} \sim N_p\left(\bar{\boldsymbol{x}}, \frac{1}{\boldsymbol{n}} \boldsymbol{\Psi}^{(w)}\right).$$

3. Convergence properties of the constructed Markov chains

In this section, we study the convergence properties of the constructed Markov chains using the two algorithms presented in the previous sections. In each case, four Markov chains of length 5000 observations are constructed with burn-in period of 1000. The data matrix $\boldsymbol{X}$ is drawn from (1) with the elements of $\boldsymbol{\mu}$ being generated from the uniform distribution on [1, 5]. The eigenvectors of $\boldsymbol{\Psi}$ and $\boldsymbol{U}_i$, $i = 1, ..., n$, are simulated from the Haar distribution. Finally, the eigenvalues of $\boldsymbol{\Psi}$ are drawn from the uniform distribution on [0.5, 2], while the eigenvalues of $\boldsymbol{U}_i$, $i = 1, ..., n$ are generated from the uniform distribution on [1, 4]. We set $p \in \{2, 4\}$ and $n = 10$.

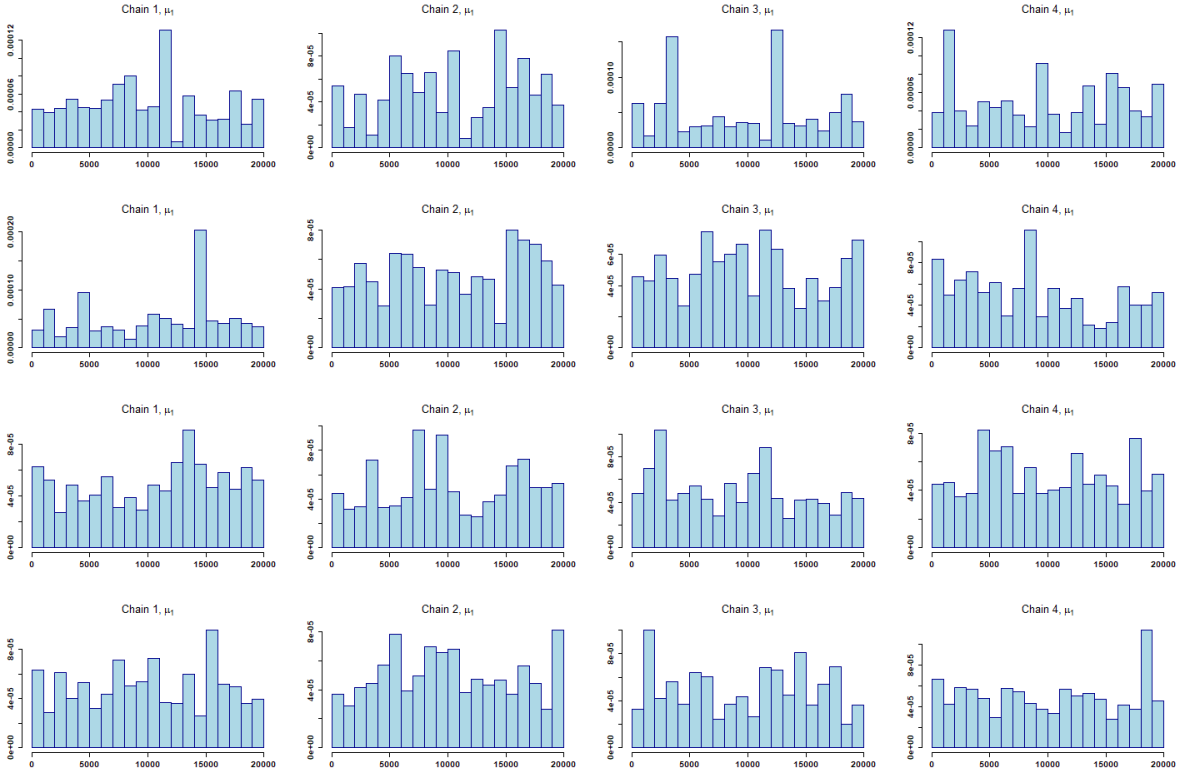

Fig. 1. Rank plots of posterior draws from four chains in the case of the parameter μ_1 for $p = 2$ and $n = 10$ under the Jeffreys prior (first and second rows) and the Berger-Bernardo reference prior (third and fourth rows). The samples from the posteriors are drawn by Algorithm A (first and third rows) and Algorithm B (second and fourth rows)

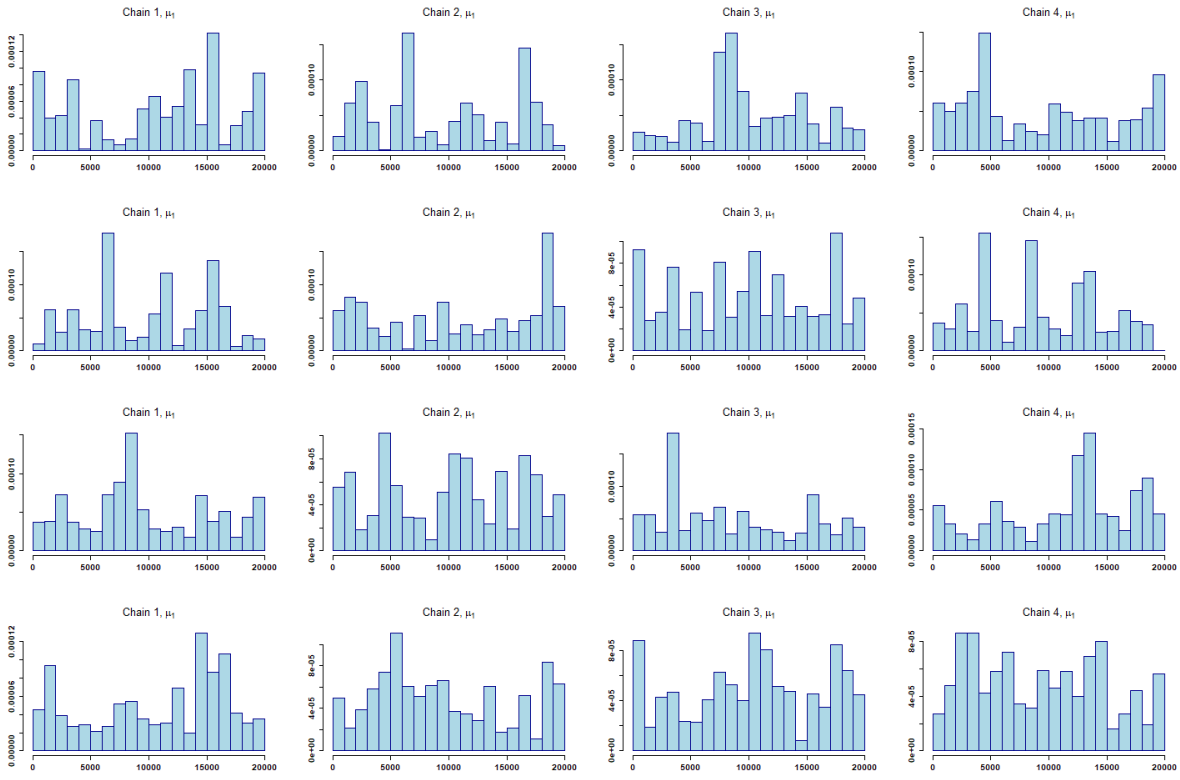

Fig. 2. Rank plots of posterior draws from four chains in the case of the parameter μ_1 for $p = 4$ and $n = 10$ under the Jeffreys prior (first and second rows) and the Berger-Bernardo reference prior (third and fourth rows). The samples from the posteriors are drawn by Algorithm A (first and third rows) and Algorithm B (second and fourth rows)

Table 1

Split-$\widehat{R}$ estimates based on the rank normalization

	Jeffreys, Algorithm A	Jeffreys, Algorithm B	Reference, Algorithm A	Reference, Algorithm B
$p = 2$	1.007623	1.007317	1.004983	1.002998
$p = 4$	1.015984	1.051825	1.017928	1.011817

The results of the simulation study are shown in Fig. 1 and 2, as well as in Table 1. To study the convergence properties of the constructed Markov chains, we analyse the rank plots of posterior draws from four chains in the case of the parameter μ_1 and the split-$\widehat{R}$ estimate based on the rank normalization following the recent results in [11]. If the constructed Markov chains possess good mixing properties, then the rank plots should approximately correspond to the histograms from the uniform distribution, while the split-$\widehat{R}$ estimate cannot be larger than 1.1.

As expected, better convergence properties of the constructed Markov chains are observed when $p = 2$. In this case, all calculated values of the split-$\widehat{R}$ estimate based on the rank normalization are below 1.01, and the recommended value is given in [11]. In addition, the plots in Fig. 1 can be better approximated by the uniform distribution in comparison to the plots in Fig. 2. Although the situation is a bit worse for $p = 4$, we still observe that all values of the split-$\widehat{R}$ estimates in Table 1 are below 1.1.

4. Conclusion

Multivariate meta-analysis is widely used in medicine, physics, and chemistry when the multivariate results of several studies should be pooled together. While the first approaches perform the multivariate meta-analysis by using the methods of the frequentist statistics, Bayesian multivariate meta-analysis has increased its popularity recently [8, 9]. In this paper, we review the procedure recently suggested in [9] and show how the samples from the posterior can be drawn using two Metropolis-Hastings algorithms. Finally, the convergence properties of the constructed Markov chains are studied via simulations following the recent approaches proposed in [11].

Практичні аспекти Байєсівського багатовимірного мета-аналізу

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Анотація

При обробці результатів фізичних, хімічних або медико-біологічних експериментів часто доводиться об'єднувати багатовимірні результати декількох досліджень. У цьому випадку кожне окреме дослідження виконує вимірювання кількох характеристик одночасно, і, таким чином, його результат складається з кількох виміряних значень, які повідомляються разом із коваріаційною матрицею між ними. Ця матриця надає інформацію не лише про невизначеності вимірювання, але й представляє структуру залежності між обчисленими значеннями. Тому застосування однофакторного мета-аналізу для кожної виміряної характеристики окремо призводить до втрати інформації, пов'язаної зі структурою залежності результатів вимірювання. Обґрунтовано можливість усунення цього недоліку на основі багатовимірного мета-аналізу, у рамках якого застосовується багатофакторна модель випадкових ефектів та Байєсівські методи. Обговорюються процедури Байєсівського аналізу, отримані для багатовимірної моделі випадкових ефектів, коли параметри моделі наділені двома неінформативними пріорами: пріором Бергера-Бернардо та пріором Джеффріса. Представлено два алгоритми Метрополіса-Гастінгса для генерації вибірок з апостеріорного розподілу та проаналізовано їхні властивості збіжності за допомогою нумеричних методів. Наведено висновки щодо властивостей конвергенції побудованих ланцюгів Маркова, які були досліджені за допомогою нумеричних методів.

Ключові слова: багатовимірний мета-аналіз; багатовимірна модель випадкових ефектів; алгоритм Метрополіса-Гастінгса; рангове зображення; оцінка split-hatR.

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