Vignette of Variance Components Model

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This package contains three approaches for estimating variance components of linear model [1]: the parameter expanded EM (PX-EM) algorithm [2, 3], Minorization-Maximization (MM) algorithm [4] and the Method of Moments (MoM) [5].

Variance components model

Suppose we have dataset $\{\mathbf{X}, \mathbf{Z}, \mathbf{y}\}$ where $\mathbf{X} \in \mathbb{R}^{n \times p}$ is the design matrix, $\mathbf{y} \in \mathbb{R}^n$ is the response vector and $\mathbf{Z} \in \mathbb{R}^{n \times c}$ is the covariate matrix of fixed effects. Here we first standardize the columns of \mathbf{X} so that they have mean 0 and variance 1/p (i.e., $\mathbf{x}_j \leftarrow (\mathbf{x}_j - \bar{\mathbf{x}}_j)/\mathbf{s}_j/\sqrt{p}$, where $\mathbf{x}_j \in \mathbb{R}^p$ is the j-th column of \mathbf{X} , $\bar{\mathbf{x}}_j$ and \mathbf{s}_j is the corresponding column mean and standard deviation). Hence the linear mixed model links \mathbf{y} with \mathbf{X} and \mathbf{Z} :

$$\mathbf{y} = \mathbf{Z}\boldsymbol{\omega} + \mathbf{X}\boldsymbol{\beta} + \mathbf{e}, \quad \boldsymbol{\beta} \sim \mathcal{N}(0, \sigma_{\beta}^2 \mathbf{I}_p), \quad \mathbf{e} \sim \mathcal{N}(0, \sigma_{\epsilon}^2 \mathbf{I}_n),$$
 (1)

where $\beta \in \mathbb{R}^p$ is the random effect, $\omega \in \mathbb{R}^c$ is the fixed effect and σ_{β}^2 and σ_e^2 are model parameters. This linear mixed model can also be re-written as a variance components model:

$$\mathbf{y} = \mathcal{N}(\mathbf{Z}\boldsymbol{\omega}, \sigma_{\beta}^2 \mathbf{K} + \sigma_e^2 \mathbf{I}_n), \tag{2}$$

where $\mathbf{K} = \mathbf{X}\mathbf{X}^T$. Since \mathbf{X} has been normalized with mean 0 and variance 1/p, $\mathrm{tr}(K) = \mathrm{tr}(\mathbf{I}_n) = n$. The goal is to estimate the variance components $\boldsymbol{\theta} = \{\sigma_{\beta}^2, \sigma_e^2\}$ [1]. This package provides three approaches to estimate the parameters: PX-EM algorithm, MM algorithm and the method of moments. The first two are based on maximum likelihood (MLE) approach and the third one adopts the moment matching approach.

PX-EM algorithm

The PX-EM algorithm is an extension of classical EM algorithm with faster speed [2, 3]. We first consider the parameter expanded version of (1):

$$\mathbf{v} = \mathbf{Z}\boldsymbol{\omega} + \delta \mathbf{X}\boldsymbol{\beta} + \mathbf{e}.$$

where $\delta \in \mathbb{R}^1$ is the expanded parameter. The complete-data log-likelihood is given as

$$\mathcal{L} = \log \Pr(\mathbf{y}, \boldsymbol{\beta} | \boldsymbol{\theta}; \mathbf{Z}, \mathbf{X})$$

$$= -\frac{n}{2} \log(2\pi\sigma_e^2) - \frac{1}{2\sigma_e^2} ||\mathbf{y} - \mathbf{Z}\boldsymbol{\omega} - \delta \mathbf{X}\boldsymbol{\beta}||^2$$

$$-\frac{p}{2} \log(2\pi\sigma_{\beta}^2) - \frac{1}{2\sigma_{\beta}^2} ||\boldsymbol{\beta}||^2,$$
(3)

from which we can easily recognize that the terms involving β are of a quadratic form:

$$\boldsymbol{\beta}^T (-\frac{\delta^2}{2\sigma_e^2} \mathbf{X}^T \mathbf{X} - \frac{1}{2\sigma_\beta^2} \mathbf{I}_p) \boldsymbol{\beta} + \frac{\delta}{\sigma_e^2} (\mathbf{y} - \mathbf{Z}\boldsymbol{\omega})^T \mathbf{X} \boldsymbol{\beta} + \text{Constant}.$$

Therefore, the posterior distribution of β is Gaussian $\mathcal{N}(\beta|\mu,\Sigma)$, where

$$\begin{split} \boldsymbol{\Sigma}^{-1} &= \frac{\delta^2}{\sigma_e^2} \mathbf{X}^T \mathbf{X} + \frac{1}{\sigma_\beta^2} \mathbf{I}_p, \\ \boldsymbol{\mu} &= (\frac{\delta^2}{\sigma_e^2} \mathbf{X}^T \mathbf{X} + \frac{1}{\sigma_\beta^2} \mathbf{I}_p)^{-1} \frac{\delta}{\sigma_e^2} \mathbf{X}^T (\mathbf{y} - \mathbf{Z} \boldsymbol{\omega}). \end{split}$$

Now in the E-step, we evaluate the Q-function by taking the expectation of the complete-data log-likelihood with respect to the posterior $\mathcal{N}(\beta|\mu,\Sigma)$. Specifically, the quadratic terms involving β are evaluated as following:

$$\mathbb{E}[||\tilde{\mathbf{y}} - \delta \mathbf{X}\boldsymbol{\beta}||^{2}] = \mathbb{E}[\tilde{\mathbf{y}}^{T}\tilde{\mathbf{y}} - 2\delta\tilde{\mathbf{y}}^{T}\mathbf{X}\boldsymbol{\beta} + \delta^{2}\boldsymbol{\beta}^{T}\mathbf{X}^{T}\mathbf{X}\boldsymbol{\beta}]$$

$$= \tilde{\mathbf{y}}^{T}\tilde{\mathbf{y}} - 2\delta\tilde{\mathbf{y}}^{T}\mathbf{X}\boldsymbol{\mu} + \delta^{2}\boldsymbol{\mu}^{T}\mathbf{X}^{T}\mathbf{X}\boldsymbol{\mu} + \delta^{2}\mathrm{tr}(\mathbf{X}^{T}\mathbf{X}\boldsymbol{\Sigma}),$$

$$\mathbb{E}[||\boldsymbol{\beta}||^{2}] = \boldsymbol{\mu}^{T}\boldsymbol{\mu} + \mathrm{tr}(\boldsymbol{\Sigma}),$$

where $\tilde{\mathbf{y}} = \mathbf{y} - \mathbf{Z}\boldsymbol{\omega}$. Then the \mathcal{Q} -function given the current parameter estimates $\boldsymbol{\theta}_{old}$ is obtained as:

$$Q(\boldsymbol{\theta}|\boldsymbol{\theta}_{old}) = -\frac{n}{2}\log(2\pi\sigma_e^2) - \frac{p}{2}\log(2\pi\sigma_\beta^2)$$

$$-\frac{1}{2\sigma_e^2}||\mathbf{y} - \mathbf{Z}\boldsymbol{\omega} - \delta\mathbf{X}\boldsymbol{\mu}||^2 - \frac{1}{2\sigma_\beta^2}\boldsymbol{\mu}^T\boldsymbol{\mu}$$

$$-\operatorname{tr}\left(\left(\frac{\delta^2}{2\sigma_e^2}\mathbf{X}^T\mathbf{X} + \frac{1}{2\sigma_\beta^2}\mathbf{I}_p\right)\boldsymbol{\Sigma}\right).$$
(4)

It the M-step, the new estimates of parameter θ is obtained by setting the derivative of Q-function to be zero. The resulting updates are given as follows:

$$\begin{split} \delta &= \frac{(\mathbf{y} - \mathbf{Z}\boldsymbol{\omega})^T \mathbf{X} \boldsymbol{\mu}}{\boldsymbol{\mu}^T \mathbf{X}^T \mathbf{X} \boldsymbol{\mu} + \operatorname{tr}(\mathbf{X}^T \mathbf{X} \boldsymbol{\Sigma})}, \\ \boldsymbol{\omega} &= (\mathbf{Z}^T \mathbf{Z})^{-1} \mathbf{Z}^T (\mathbf{y} - \delta \mathbf{X} \boldsymbol{\mu}), \\ \sigma_e^2 &= \frac{1}{n} [||\mathbf{y} - \mathbf{Z} \boldsymbol{\omega} - \delta \mathbf{X} \boldsymbol{\mu}||^2 + \delta^2 \operatorname{tr}(\mathbf{X}^T \mathbf{X} \boldsymbol{\Sigma})], \\ \sigma_\beta^2 &= \frac{1}{p} [\boldsymbol{\mu}^T \boldsymbol{\mu} + \operatorname{tr}(\boldsymbol{\Sigma})]. \end{split}$$

To check the convergence of PX-EM algorithm, we evaluate the lower bound after each E-step, when the incomplete-data log-likelihood is exactly equal to the lower bound (i.e. the bound is tight).

This PX-EM algorithm is summarized in Algorithm 1. After convergence, the posterior mean and variance of $\mathcal{N}(\boldsymbol{\beta}|\boldsymbol{\mu},\boldsymbol{\Sigma})$ can be evaluated given the obtained parameter estimates $\hat{\boldsymbol{\theta}} = \{\hat{\sigma}_e^2, \hat{\sigma}_\beta^2\}$ and $\hat{\boldsymbol{\omega}}$:

$$\Sigma^{-1} = \frac{1}{\hat{\sigma}_e^2} \mathbf{X}^T \mathbf{X} + \frac{1}{\hat{\sigma}_\beta^2} \mathbf{I}_p,$$

$$\mu = \left(\frac{1}{\hat{\sigma}_e^2} \mathbf{X}^T \mathbf{X} + \frac{1}{\hat{\sigma}_\beta^2} \mathbf{I}_p\right)^{-1} \frac{1}{\hat{\sigma}_e^2} \mathbf{X}^T (\mathbf{y} - \mathbf{Z}\hat{\boldsymbol{\omega}}).$$
(5)

Algorithm 1 PX-EM algorithm for model (1)

Initialization: Parameters are initialized by setting $\boldsymbol{\omega} = (\mathbf{Z}^T \mathbf{Z})^{-1} \mathbf{Z}^T \mathbf{y}$, $\sigma_e^2 = \sigma_\beta^2 = \text{Var}(y - \mathbf{Z}\boldsymbol{\omega})/2$. repeat

E-step: At the t-th iteration, evaluate the posterior $\mathcal{N}(\beta|\boldsymbol{\mu},\boldsymbol{\Sigma})$ given the current parameter estimates $\boldsymbol{\theta}^{(t)} = \{(\sigma_e^{(t)})^2, (\sigma_\beta^{(t)})^2\}, \, \boldsymbol{\omega}^{(t)} \text{ and set } \delta^{(t)} = 1$:

$$\begin{split} \boldsymbol{\Sigma}^{-1} &= \frac{(\delta^{(t)})^2}{(\sigma_e^{(t)})^2} \mathbf{X}^T \mathbf{X} + \frac{1}{(\sigma_{\beta}^{(t)})^2} \mathbf{I}_p, \\ \boldsymbol{\mu} &= \left(\frac{(\delta^{(t)})^2}{(\sigma_e^{(t)})^2} \mathbf{X}^T \mathbf{X} + \frac{1}{(\sigma_{\beta}^{(t)})^2} \mathbf{I}_p \right)^{-1} \frac{(\delta^{(t)})^2}{(\sigma_e^{(t)})^2} \mathbf{X}^T (\mathbf{y} - \mathbf{Z} \boldsymbol{\omega}^{(t)}), \\ ELBO^{(t)} &= \mathcal{Q}(\boldsymbol{\theta}^{(t)}) + \frac{1}{2} \log |2\pi \boldsymbol{\Sigma}|, \text{ where } \mathcal{Q} \text{ is defined in Equation(4)}. \end{split}$$

M-step: Update the model parameters by

$$\begin{split} \delta^{(t+1)} &= \frac{(\mathbf{y} - \mathbf{Z}\boldsymbol{\omega}^{(t)})^T \mathbf{X}\boldsymbol{\mu}}{\boldsymbol{\mu}^T \mathbf{X}^T \mathbf{X} \boldsymbol{\mu} + \operatorname{tr}(\mathbf{X}^T \mathbf{X} \boldsymbol{\Sigma})}, \\ \boldsymbol{\omega}^{(t+1)} &= (\mathbf{Z}^T \mathbf{Z})^{-1} \mathbf{Z}^T (\mathbf{y} - \delta \mathbf{X} \boldsymbol{\mu}), \\ (\sigma_e^{(t+1)})^2 &= \frac{1}{n_r} [||\mathbf{y} - \mathbf{Z}\boldsymbol{\omega}^{(t)} - \delta \mathbf{X} \boldsymbol{\mu}||^2 + \delta^2 \operatorname{tr}(\mathbf{X}^T \mathbf{X} \boldsymbol{\Sigma})], \\ (\sigma_{\beta}^{(t+1)})^2 &= \frac{1}{p} [\boldsymbol{\mu}^T \boldsymbol{\mu} + \operatorname{tr}(\boldsymbol{\Sigma})]. \end{split}$$

Reduction-step: Rescale $(\sigma_{\beta}^{(t+1)})^2 = (\delta^{(t+1)})^2 (\sigma_{\beta}^{(t+1)})^2$ and reset $\delta^{(t+1)} = 1$. **until** the incomplete-data log-likelihood $(ELBO^{(t)})$ stop increasing or maximum iteration reached

In practice. We can avoid frequently inverting the $p \times p$ matrix Σ by conducting a single eigen-dedomposition on $\mathbf{X}\mathbf{X}^T$ or $\mathbf{X}^T\mathbf{X}$, depending on the relative sizes of p and n. If $n \geq p$, we conduct the eigen-decomposition $\mathbf{X}^T\mathbf{X} = \mathbf{V}\mathbf{Q}\mathbf{V}^T$ before the iteration, where $\mathbf{Q} \in \mathbb{R}^{p \times p}$ is a diagonal matrix of eigenvalues q_j and $\mathbf{V} \in \mathbb{R}^{p \times p}$ is a matrix whose columns are corresponding eigenvectors of q_j . The resulting algorithm is shown in Algorithm 2.

Algorithm 2 PX-EM algorithm for model (1) when $n \ge p$

Initialization: $\boldsymbol{\omega} = (\mathbf{Z}^T \mathbf{Z})^{-1} \mathbf{Z}^T \mathbf{y}, \ \sigma_e^2 = \sigma_\beta^2 = \text{Var}(y - \mathbf{Z}\boldsymbol{\omega})/2$; conduct eigen-deomposition $\mathbf{X}^T \mathbf{X} = \mathbf{V} \mathbf{Q} \mathbf{V}^T$.

repeat

E-step: At the *t*-th iteration, evaluate the posterior $\mathcal{N}(\beta|\mu, \Sigma)$ given the current parameter estimates $\boldsymbol{\theta}^{(t)} = \{(\sigma_e^{(t)})^2, (\sigma_\beta^{(t)})^2\}, \boldsymbol{\omega}^{(t)} \text{ and set } \delta^{(t)} = 1$:

$$\begin{split} \tilde{q}_j &= q_j/(\sigma_e^{(t)})^2 + 1/(\sigma_\beta^{(t)})^2, \ \operatorname{diag}(\tilde{\mathbf{Q}}) = \tilde{q} = [\tilde{q}_1, ... \tilde{q}_p] \\ \boldsymbol{\mu} &= \frac{1}{(\sigma_e^{(t)})^2} \mathbf{V} [\mathbf{V}^T \mathbf{X}^T (\mathbf{y} - \mathbf{Z} \boldsymbol{\omega}^{(t)}) \odot 1/\tilde{q}] \\ ELBO^{(t)} &= -\frac{n}{2} \log(2\pi (\sigma_e^{(t)})^2) - \frac{p}{2} \log(2\pi (\sigma_\beta^{(t)})^2) - \frac{1}{2(\sigma_e^{(t)})^2} ||\mathbf{y} - \mathbf{Z} \boldsymbol{\omega}^{(t)} - \delta \mathbf{X} \boldsymbol{\mu}||^2 \\ &- \frac{1}{2(\sigma_\beta^{(t)})^2} \boldsymbol{\mu}^T \boldsymbol{\mu} - \frac{1}{2} \sum_j^p \log \tilde{q}_j. \end{split}$$

M-step: Update the model parameters by

$$\begin{split} \delta^{(t+1)} &= \frac{(\mathbf{y} - \mathbf{Z}\boldsymbol{\omega}^{(t)})^T \mathbf{X}\boldsymbol{\mu}}{\boldsymbol{\mu}^T \mathbf{X}^T \mathbf{X} \boldsymbol{\mu} + \sum_j^p q_j / \tilde{q}_j}, \\ \boldsymbol{\omega}^{(t+1)} &= (\mathbf{Z}^T \mathbf{Z})^{-1} \mathbf{Z}^T (\mathbf{y} - \delta \mathbf{X} \boldsymbol{\mu}), \\ (\sigma_e^{(t+1)})^2 &= \frac{1}{n_r} [||\mathbf{y} - \mathbf{Z}\boldsymbol{\omega}^{(t)} - \delta \mathbf{X} \boldsymbol{\mu}||^2 + \delta^2 \sum_j^p q_j / \tilde{q}_j], \\ (\sigma_\beta^{(t+1)})^2 &= \frac{1}{p} [\boldsymbol{\mu}^T \boldsymbol{\mu} + \sum_j^p 1 / \tilde{q}_j]. \end{split}$$

Reduction-step: Rescale $(\sigma_{\beta}^{(t+1)})^2 = (\delta^{(t+1)})^2 (\sigma_{\beta}^{(t+1)})^2$ and reset $\delta^{(t+1)} = 1$. **until** the incomplete-data log-likelihood $(ELBO^{(t)})$ stop increasing or maximum iteration reached

If p > n, we conduct the eigen-decomposition $\mathbf{X}\mathbf{X}^T = \mathbf{U}\mathbf{D}\mathbf{U}^T$ before the iteration, where $\mathbf{D} \in \mathbb{R}^{n \times n}$ is a diagonal matrix of eigenvalues d_i and $\mathbf{U} \in \mathbb{R}^{n \times n}$ is a matrix whose columns are corresponding eigenvectors of d_i . The resulting algorithm is shown in Algorithm 3.

MM algorithm

Unlike the PX-EM algorithm, the MM algorithm maximize the incomplete-data log-likelihood by considering the variance components model (2) [4]. The incomplete-data log-likelihood is given as

$$\log \Pr(\mathbf{y}|\boldsymbol{\theta}; \mathbf{Z}, \mathbf{K}) = -\frac{1}{2} \log |\mathbf{\Omega}| - \frac{1}{2} (\mathbf{y} - \mathbf{Z}\boldsymbol{\omega})^T \mathbf{\Omega} (\mathbf{y} - \mathbf{Z}\boldsymbol{\omega}), \tag{6}$$

where $\Omega = \sigma_{\beta}^2 \mathbf{K} + \sigma_e^2 \mathbf{I}_n$. The MM algorithm updates ω and $\boldsymbol{\theta}$ alternatively by iteratively maximizing the

Algorithm 3 PX-EM algorithm for model (1) when p > n

Initialization: $\boldsymbol{\omega} = (\mathbf{Z}^T \mathbf{Z})^{-1} \mathbf{Z}^T \mathbf{y}, \ \sigma_e^2 = \sigma_\beta^2 = \text{Var}(y - \mathbf{Z}\boldsymbol{\omega})/2$; conduct eigen-deomposition $\mathbf{X}\mathbf{X}^T = \mathbf{U}\mathbf{D}\mathbf{U}^T$.

repeat

E-step: At the *t*-th iteration, evaluate the posterior $\mathcal{N}(\beta|\boldsymbol{\mu}, \boldsymbol{\Sigma})$ given the current parameter estimates $\boldsymbol{\theta}^{(t)} = \{(\sigma_e^{(t)})^2, (\sigma_\beta^{(t)})^2\}, \, \boldsymbol{\omega}^{(t)} \text{ and set } \delta^{(t)} = 1$:

$$\begin{split} \tilde{d}_{i} &= d_{i}/(\sigma_{e}^{(t)})^{2} + 1/(\sigma_{\beta}^{(t)})^{2}, \ \operatorname{diag}(\tilde{\mathbf{D}}) = \tilde{d} = [\tilde{d}_{i}, ... \tilde{d}_{n}] \\ \boldsymbol{\mu} &= \frac{1}{(\sigma_{e}^{(t)})^{2}} \mathbf{X}^{T} \mathbf{U}[\mathbf{U}^{T}(\mathbf{y} - \mathbf{Z}\boldsymbol{\omega}^{(t)}) \odot 1/\tilde{d}] \\ ELBO^{(t)} &= -\frac{n}{2} \log(2\pi(\sigma_{e}^{(t)})^{2}) - \frac{p}{2} \log(2\pi(\sigma_{\beta}^{(t)})^{2}) - \frac{1}{2(\sigma_{e}^{(t)})^{2}} ||\mathbf{y} - \mathbf{Z}\boldsymbol{\omega}^{(t)} - \delta \mathbf{X}\boldsymbol{\mu}||^{2} \\ &- \frac{1}{2(\sigma_{\beta}^{(t)})^{2}} \boldsymbol{\mu}^{T} \boldsymbol{\mu} - \frac{1}{2} \sum_{i}^{n} \log \tilde{d}_{i} + \frac{p - n}{2} \log(\sigma_{\beta}^{(t)})^{2}. \end{split}$$

M-step: Update the model parameters by

$$\begin{split} \delta^{(t+1)} &= \frac{(\mathbf{y} - \mathbf{Z}\boldsymbol{\omega}^{(t)})^T \mathbf{X}\boldsymbol{\mu}}{\boldsymbol{\mu}^T \mathbf{X}^T \mathbf{X}\boldsymbol{\mu} + \sum_i^n d_i / \tilde{d}_i}, \\ \boldsymbol{\omega}^{(t+1)} &= (\mathbf{Z}^T \mathbf{Z})^{-1} \mathbf{Z}^T (\mathbf{y} - \delta \mathbf{X}\boldsymbol{\mu}), \\ (\sigma_e^{(t+1)})^2 &= \frac{1}{n_r} [||\mathbf{y} - \mathbf{Z}\boldsymbol{\omega}^{(t)} - \delta \mathbf{X}\boldsymbol{\mu}||^2 + \delta^2 \sum_i^n d_i / \tilde{d}_i], \\ (\sigma_\beta^{(t+1)})^2 &= \frac{1}{p} [\boldsymbol{\mu}^T \boldsymbol{\mu} + \sum_i^n 1 / \tilde{d}_i + (n-p)(\sigma_\beta^{(t)})^2]. \end{split}$$

Reduction-step: Rescale $(\sigma_{\beta}^{(t+1)})^2 = (\delta^{(t+1)})^2 (\sigma_{\beta}^{(t+1)})^2$ and reset $\delta^{(t+1)} = 1$. **until** the incomplete-data log-likelihood $(ELBO^{(t)})$ stop increasing or maximum iteration reached

lower bound of incomplete-data log-likelihood. Given $\boldsymbol{\theta}^{(t)}$, the updata of $\boldsymbol{\omega}$ is simply a weighted least square problem

$$\boldsymbol{\omega}^{(t)} = (\mathbf{Z}^T (\boldsymbol{\Omega}^{(t)})^{-1} \mathbf{Z})^{-1} \mathbf{Z}^T (\boldsymbol{\Omega}^{(t)})^{-1} \mathbf{y}. \tag{7}$$

The update of θ given ω depends on two minorizations. First,

$$-(\mathbf{y} - \mathbf{Z}\boldsymbol{\omega})^{T}(\boldsymbol{\Omega}^{(t)})^{-1}(\frac{(\sigma_{\beta}^{(t)})^{4}}{\sigma_{\beta}^{2}}\mathbf{K} + \frac{(\sigma_{e}^{(t)})^{4}}{\sigma_{e}^{2}})(\boldsymbol{\Omega}^{(t)})^{-1}(\mathbf{y} - \mathbf{Z}\boldsymbol{\omega}) \leq -\frac{1}{2}(\mathbf{y} - \mathbf{Z}\boldsymbol{\omega})^{T}\boldsymbol{\Omega}(\mathbf{y} - \mathbf{Z}\boldsymbol{\omega}), \tag{8}$$

which separates the variance components in the quadratic term of the likelihood (6). Second, the convexity of function $-\log |\Omega|$ implies that

$$-\log |\mathbf{\Omega}^{(t)}| - \operatorname{tr}((\mathbf{\Omega}^{(t)})^{-1}(\mathbf{\Omega} - \mathbf{\Omega}^{(t)})) \le -\frac{1}{2}\log |\mathbf{\Omega}|, \tag{9}$$

which separates the variance components in the log determinant of the likelihood (6). Combining (8) and (9), the overall minorization if given as

$$\mathcal{G}(m{ heta}|m{ heta}_{old})$$

$$= -\log |\mathbf{\Omega}^{(t)}| - \frac{1}{2} \operatorname{tr}((\mathbf{\Omega}^{(t)})^{-1}\mathbf{\Omega}) - \frac{1}{2} (\mathbf{y} - \mathbf{Z}\boldsymbol{\omega}^{(t)})^{T} (\mathbf{\Omega}^{(t)})^{-1} (\frac{(\sigma_{\beta}^{(t)})^{4}}{\sigma_{\beta}^{2}} \mathbf{K} + \frac{(\sigma_{e}^{(t)})^{4}}{\sigma_{e}^{2}}) (\mathbf{\Omega}^{(t)})^{-1} (\mathbf{y} - \mathbf{Z}\boldsymbol{\omega}^{(t)})$$

$$= -\log |\mathbf{\Omega}^{(t)}| - \frac{\sigma_{\beta}^{2}}{2} \operatorname{tr}((\mathbf{\Omega}^{(t)})^{-1}\mathbf{K}) - \frac{1}{2} \frac{(\sigma_{\beta}^{(t)})^{4}}{\sigma_{\beta}^{2}} (\mathbf{y} - \mathbf{Z}\boldsymbol{\omega}^{(t)})^{T} (\mathbf{\Omega}^{(t)})^{-1} \mathbf{K} (\mathbf{\Omega}^{(t)})^{-1} (\mathbf{y} - \mathbf{Z}\boldsymbol{\omega}^{(t)})$$

$$- \frac{\sigma_{e}^{2}}{2} \operatorname{tr}((\mathbf{\Omega}^{(t)})^{-1}) - \frac{1}{2} \frac{(\sigma_{e}^{(t)})^{4}}{\sigma^{2}} (\mathbf{y} - \mathbf{Z}\boldsymbol{\omega}^{(t)})^{T} (\mathbf{\Omega}^{(t)})^{-2} (\mathbf{y} - \mathbf{Z}\boldsymbol{\omega}^{(t)}).$$
(10)

By setting the derivative of \mathcal{G} -function to be zero, the resulting updates are given as follows:

$$\begin{split} &(\sigma_{\beta}^{(t+1)})^2 = (\sigma_{\beta}^{(t)})^2 \sqrt{\frac{(\mathbf{y} - \mathbf{Z}\boldsymbol{\omega}^{(t)})^T (\boldsymbol{\Omega}^{(t)})^{-1} \mathbf{K} (\boldsymbol{\Omega}^{(t)})^{-1} (\mathbf{y} - \mathbf{Z}\boldsymbol{\omega}^{(t)})}{\operatorname{tr}((\boldsymbol{\Omega}^{(t)})^{-1} \mathbf{K})}} \\ &(\sigma_e^{(t+1)})^2 = (\sigma_e^{(t)})^2 \sqrt{\frac{(\mathbf{y} - \mathbf{Z}\boldsymbol{\omega}^{(t)})^T (\boldsymbol{\Omega}^{(t)})^{-2} (\mathbf{y} - \mathbf{Z}\boldsymbol{\omega}^{(t)})}{\operatorname{tr}((\boldsymbol{\Omega}^{(t)})^{-1})}}. \end{split}$$

The convergence of MM algorithm is checked by evaluating the log-likelihood at each iteration. The resulting algorithm is summarized in Algorithm 4.

To avoid frequently inverting Ω in the iterations, we can conduct eigen-decomposition on $\mathbf{K} = \mathbf{U}\mathbf{D}\mathbf{U}^T$ before the algorithm, where $\mathbf{D} \in \mathbb{R}^{n \times n}$ is a diagonal matrix of eigenvalues d_i and $\mathbf{U} \in \mathbb{R}^{n \times n}$ is a matrix whose columns are corresponding eigenvectors of d_i . The resulting procedure is summarized in Algorithm 5.

Once the parameter estimates $\hat{\sigma}_{\beta}^2$, $\hat{\sigma}_{e}^2$ and $\hat{\boldsymbol{\omega}}$ are obtained, we can recover the posterior mean by

$$\boldsymbol{\mu} = \left(\mathbf{X}^T\mathbf{X} + \frac{\hat{\sigma}_e^2}{\hat{\sigma}_\beta^2}\mathbf{I}_p\right)^{-1}\mathbf{X}^T(\mathbf{y} - \mathbf{Z}\hat{\boldsymbol{\omega}}) = \mathbf{X}^T\left(\mathbf{X}\mathbf{X}^T + \frac{\hat{\sigma}_e^2}{\hat{\sigma}_\beta^2}\mathbf{I}_{n_1}\right)^{-1}(\mathbf{y} - \mathbf{Z}\hat{\boldsymbol{\omega}})$$

. Note that because **X** has been standardized, we need to re-scale the posterior mean by $\mu \leftarrow \mu/s/\sqrt{p}$ and then the intercept by $\hat{\omega}_0 \leftarrow \hat{\omega}_0 - \sum_j \bar{\mathbf{x}}_j \cdot \mu_j$.

Algorithm 4 MM algorithm for model (2)

Initialization: Parameters are initialized by setting $\boldsymbol{\omega} = (\mathbf{Z}^T \mathbf{Z})^{-1} \mathbf{Z}^T \mathbf{y}, \ \sigma_e^2 = \sigma_\beta^2 = \text{Var}(y - \mathbf{Z}\boldsymbol{\omega})/2.$ repeat

$$\begin{split} & \boldsymbol{\Omega}^{(t)} = (\sigma_{\beta}^{(t)})^{2} \mathbf{K} + (\sigma_{e}^{(t+1)})^{2} \mathbf{I}_{n}, \\ & \boldsymbol{\omega}^{(t)} = (\mathbf{Z}^{T} (\boldsymbol{\Omega}^{(t)})^{-1} \mathbf{Z})^{-1} \mathbf{Z}^{T} (\boldsymbol{\Omega}^{(t)})^{-1} \mathbf{y}, \\ & \text{evaluate } \mathcal{L}^{(t)} (\boldsymbol{\Omega}^{(t)}, \boldsymbol{\omega}^{(t)}) \text{ from Equation (6),} \\ & (\sigma_{\beta}^{(t+1)})^{2} = (\sigma_{\beta}^{(t)})^{2} \sqrt{\frac{(\mathbf{y} - \mathbf{Z}\boldsymbol{\omega}^{(t)})^{T} (\boldsymbol{\Omega}^{(t)})^{-1} \mathbf{K} (\boldsymbol{\Omega}^{(t)})^{-1} (\mathbf{y} - \mathbf{Z}\boldsymbol{\omega}^{(t)})}{\text{tr}((\boldsymbol{\Omega}^{(t)})^{-1} \mathbf{K})}, \\ & (\sigma_{e}^{(t+1)})^{2} = (\sigma_{e}^{(t)})^{2} \sqrt{\frac{(\mathbf{y} - \mathbf{Z}\boldsymbol{\omega}^{(t)})^{T} (\boldsymbol{\Omega}^{(t)})^{-2} (\mathbf{y} - \mathbf{Z}\boldsymbol{\omega}^{(t)})}{\text{tr}((\boldsymbol{\Omega}^{(t)})^{-1})}}. \end{split}$$

until the incomplete-data log-likelihood $(\mathcal{L}^{(t)})$ stop increasing or maximum iteration reached

Algorithm 5 Efficient MM algorithm for model (2)

Initialization: $\mathbf{K} = \mathbf{U}\mathbf{D}\mathbf{U}^T$, $\bar{\mathbf{Z}} = \mathbf{U}^T\mathbf{Z}$, $\bar{\mathbf{y}} = \mathbf{U}^T\mathbf{y}$, $\boldsymbol{\omega} = (\bar{\mathbf{Z}}^T\bar{\mathbf{Z}})^{-1}\bar{\mathbf{Z}}^T\bar{\mathbf{y}}$, $\sigma_e^2 = \sigma_\beta^2 = \mathrm{Var}(y - \mathbf{Z}\boldsymbol{\omega})/2$. repeat

$$\begin{split} \tilde{d}_i &= d_i/(\sigma_e^{(t)})^2 + 1/(\sigma_\beta^{(t)})^2, \ \operatorname{diag}(\tilde{\mathbf{D}}) = \tilde{d} = [\tilde{d}_i, ... \tilde{d}_n] \\ \boldsymbol{\omega}^{(t)} &= (\bar{\mathbf{Z}}^T \tilde{\mathbf{D}} \bar{\mathbf{Z}})^{-1} \bar{\mathbf{Z}}^T (\bar{\mathbf{y}} \odot \tilde{d}), \\ \mathcal{L}^{(t)}(\boldsymbol{\Omega}^{(t)}, \boldsymbol{\omega}^{(t)}) &= -\frac{1}{2} \sum_{i}^{n} \log \tilde{d}_i - \frac{n}{2} \log \sigma_\beta^2 - \frac{n}{2} \log \sigma_e^2 - \frac{n}{2} \log 2\pi - \frac{1}{2} \sum_{i}^{n} [(\bar{\mathbf{y}}_i - \bar{\mathbf{Z}}_i^T \boldsymbol{\omega}^{(t)})^2 / \tilde{d}_i] \\ (\sigma_\beta^{(t+1)})^2 &= \frac{\sigma_\beta^{(t)}}{\sigma_e^{(t)}} \sqrt{\frac{\sum_{i}^{n} [(\bar{\mathbf{y}}_i - \bar{\mathbf{Z}}_i^T \boldsymbol{\omega}^{(t)})^2 d_i / \tilde{d}_i^2]}{\sum_{i}^{n} d_i / \tilde{d}_i}}, \\ (\sigma_e^{(t+1)})^2 &= \frac{\sigma_e^{(t)}}{\sigma_\beta^{(t)}} \sqrt{\frac{\sum_{i}^{n} [(\bar{\mathbf{y}}_i - \bar{\mathbf{Z}}_i^T \boldsymbol{\omega}^{(t)})^2 / \tilde{d}_i^2]}{\sum_{i}^{n} 1 / \tilde{d}_i}}. \end{split}$$

until the incomplete-data log-likelihood $(\mathcal{L}^{(t)})$ stop increasing or maximum iteration reached

Standard errors of variance components for MLE methods

For MLE methods including MM and PX-EM, the covariance matrix of variance components estimates are calculated from inverse of Fisher Information Matrix (FIM). $FIM = -\mathbb{E}\left[\frac{\partial^2 \mathcal{L}}{\partial \theta^2}\right] = -\mathbb{E}\left[\frac{\partial^2}{\partial \theta^2} - \frac{1}{2}\log|\Omega| - \frac{1}{2}(\mathbf{y} - \mathbf{Z}\omega)^T\Omega^{-1}(\mathbf{y} - \mathbf{Z}\omega)\right]$. The first derivatives are:

$$\frac{\partial \mathcal{L}}{\partial \sigma_g^2} = \frac{1}{2} \text{tr} \left[-\mathbf{\Omega}^{-1} \mathbf{K} + (\mathbf{y} - \mathbf{Z} \boldsymbol{\omega})^T \mathbf{\Omega}^{-1} \mathbf{K} \mathbf{\Omega}^{-1} (\mathbf{y} - \mathbf{Z} \boldsymbol{\omega}) \right],
\frac{\partial \mathcal{L}}{\partial \sigma_e^2} = \frac{1}{2} \text{tr} \left[-\mathbf{\Omega}^{-1} + (\mathbf{y} - \mathbf{Z} \boldsymbol{\omega})^T \mathbf{\Omega}^{-2} (\mathbf{y} - \mathbf{Z} \boldsymbol{\omega}) \right];$$

and the second derivatives are given as

$$\begin{split} &\frac{\partial^2 \mathcal{L}}{\partial (\sigma_g^2)^2} = \frac{1}{2} \mathrm{tr} \left[(\mathbf{\Omega}^{-1} \mathbf{K})^2 - 2(\mathbf{\Omega}^{-1} \mathbf{K})^2 \mathbf{\Omega}^{-1} (\mathbf{y} - \mathbf{Z} \boldsymbol{\omega}) (\mathbf{y} - \mathbf{Z} \boldsymbol{\omega})^T \right], \\ &\frac{\partial^2 \mathcal{L}}{\partial (\sigma_e^2)^2} = \frac{1}{2} \mathrm{tr} \left[\mathbf{\Omega}^{-2} - 2\mathbf{\Omega}^{-3} (\mathbf{y} - \mathbf{Z} \boldsymbol{\omega}) (\mathbf{y} - \mathbf{Z} \boldsymbol{\omega})^T \right], \\ &\frac{\partial^2 \mathcal{L}}{\partial \sigma_g^2 \partial \sigma_e^2} = \frac{1}{2} \mathrm{tr} \left[\mathbf{\Omega}^{-1} \mathbf{K} \mathbf{\Omega}^{-1} - (\mathbf{\Omega}^{-1} \mathbf{K} \mathbf{\Omega}^{-2} + \mathbf{\Omega}^{-2} \mathbf{K} \mathbf{\Omega}^{-1}) (\mathbf{y} - \mathbf{Z} \boldsymbol{\omega}) (\mathbf{y} - \mathbf{Z} \boldsymbol{\omega})^T \right]. \end{split}$$

Since the only random variable is \mathbf{y} , and $\mathbb{E}[(\mathbf{y} - \mathbf{Z}\boldsymbol{\omega})(\mathbf{y} - \mathbf{Z}\boldsymbol{\omega})^T] = \mathbf{\Omega}$, the FIM is

$$FIM = -\frac{1}{2} \begin{bmatrix} \operatorname{tr}[(\mathbf{\Omega}^{-1}\mathbf{K})^2] - 2\operatorname{tr}[(\mathbf{\Omega}^{-1}\mathbf{K})^2] & \operatorname{tr}(\mathbf{\Omega}^{-1}\mathbf{K}\mathbf{\Omega}^{-1}) - 2\operatorname{tr}(\mathbf{\Omega}^{-1}\mathbf{K}\mathbf{\Omega}^{-1}) \\ & \operatorname{tr}[\mathbf{\Omega}^{-2}] - 2\operatorname{tr}[\mathbf{\Omega}^{-2}] \end{bmatrix}$$
$$= \frac{1}{2} \begin{bmatrix} \operatorname{tr}[(\mathbf{\Omega}^{-1}\mathbf{K})^2] & \operatorname{tr}(\mathbf{\Omega}^{-1}\mathbf{K}\mathbf{\Omega}^{-1}) \\ & \operatorname{tr}[\mathbf{\Omega}^{-2}] \end{bmatrix}.$$

Inverting the FIM leads to the covariance matrix of $\hat{\theta}$.

When handling the FIM, we can again make use of the pre-calculated eigenvectors and eigenvalues to avoid inverting Ω . For MM algorithm and PX-EM algorithm with $p \geq n$ case, we can evaluate Ω^{-1} using the identity $\Omega^{-1} = \mathbf{U}\tilde{\mathbf{D}}\mathbf{U}^T$ with \mathbf{U} , $\tilde{\mathbf{D}}$ from Algorithm 3 and 5. For PX-EM algorithm with n > p, we first define $\mathbf{\Lambda}^{-1} = (\sigma_e^2 \mathbf{I}_p + \sigma_\beta^2 \mathbf{X}^T \mathbf{X})^{-1}$. Then using the matrix inverse lemma, we have $\mathbf{X}^T \Omega^{-1} = \mathbf{\Lambda}^{-1} \mathbf{X}^T$. Therefore, we can express the FIM using the dual form:

$$\begin{split} \operatorname{tr}[(\boldsymbol{\Omega}^{-1}\mathbf{K})^2] = & \operatorname{tr}(\boldsymbol{\Omega}^{-1}\mathbf{X}\mathbf{X}^T\boldsymbol{\Omega}^{-1}\mathbf{X}\mathbf{X}^T) = \operatorname{tr}(\boldsymbol{\Lambda}^{-1}\mathbf{X}^T\mathbf{X}\boldsymbol{\Lambda}^{-1}\mathbf{X}^T\mathbf{X}) \\ \operatorname{tr}[\boldsymbol{\Omega}^{-1}\mathbf{K}\boldsymbol{\Omega}^{-1}] = & \operatorname{tr}[\boldsymbol{\Omega}^{-1}\mathbf{X}\mathbf{X}^T\boldsymbol{\Omega}^{-1}] = \operatorname{tr}(\boldsymbol{\Lambda}^{-2}\mathbf{X}^T\mathbf{X}) \\ \operatorname{tr}[\boldsymbol{\Omega}^{-2}] = & n(\frac{1}{\sigma_e^2})^2 - 2\frac{\sigma_\beta^2}{(\sigma_e^2)^2}\operatorname{tr}[\boldsymbol{\Lambda}^{-1}\mathbf{X}^T\mathbf{X}] + (\frac{\sigma_\beta^2}{\sigma_e^2})^2\operatorname{tr}[\boldsymbol{\Lambda}^{-1}\mathbf{X}^T\mathbf{X}\boldsymbol{\Lambda}^{-1}\mathbf{X}^T\mathbf{X}], \end{split}$$

where $\mathbf{\Lambda}^{-1} = \mathbf{V}\tilde{\mathbf{Q}}\mathbf{V}^T$ with \mathbf{V} and $\tilde{\mathbf{Q}}$ from Algorithm 2.

Method of Moments

While the MM algorithm and PX-EM algorithm adopts the MLE, MoM estimator is obtained by first multiplying Equation (2) by the projection matrix $\mathbf{M} = \mathbf{I}_n - \mathbf{Z}(\mathbf{Z}^T\mathbf{Z})^{-1}\mathbf{Z}^T$ and then solving the following ordinary least squares (OLS) problem [5]:

$$argmin_{\sigma_{\beta}^{2}, \sigma_{e}^{2}} ||(\mathbf{M}\mathbf{y})(\mathbf{M}\mathbf{y})^{T} - (\sigma_{\beta}^{2}\mathbf{M}\mathbf{K}\mathbf{M} + \sigma_{e}^{2}\mathbf{M})||_{F}^{2}.$$
(11)

Using the fact that $||\mathbf{A}||_F = \sqrt{\text{tr}(\mathbf{A}\mathbf{A}^T)}$, the OLS problem in (11) can be re-written as

$$argmin_{\sigma_e^2,\sigma_e^2} \text{tr}[((\mathbf{M}\mathbf{y})(\mathbf{M}\mathbf{y})^T - (\sigma_{\beta}^2 \mathbf{M}\mathbf{K}\mathbf{M} + \sigma_e^2 \mathbf{M}))((\mathbf{M}\mathbf{y})(\mathbf{M}\mathbf{y})^T - (\sigma_{\beta}^2 \mathbf{M}\mathbf{K}\mathbf{M} + \sigma_e^2 \mathbf{M}))^T],$$

which leads to the normal equation

$$\mathbf{S}\boldsymbol{\theta} = \mathbf{q},$$
with $\mathbf{S} = \begin{bmatrix} \operatorname{tr}(\mathbf{M}\mathbf{K}\mathbf{M}\mathbf{K}) & \operatorname{tr}(\mathbf{M}\mathbf{K}) \\ \operatorname{tr}(\mathbf{M}\mathbf{K}) & n - c \end{bmatrix}, \ \boldsymbol{\theta} = \begin{bmatrix} \sigma_{\beta}^{2} \\ \sigma_{e}^{2} \end{bmatrix}, \ \mathbf{q} = \begin{bmatrix} \mathbf{y}^{T}\mathbf{M}\mathbf{K}\mathbf{M}\mathbf{y} \\ \mathbf{y}^{T}\mathbf{M}\mathbf{y} \end{bmatrix}.$

$$(12)$$

The MoM estimates of $\boldsymbol{\theta}$ is then given by $\hat{\boldsymbol{\theta}} = \mathbf{S}^{-1}\mathbf{q}$. Once we have $\hat{\sigma}_{\beta}^2$ and $\hat{\sigma}_{e}^2$, the estimate of fixed effects can be obtained by

$$\hat{\boldsymbol{\omega}} = (\mathbf{Z}^T \hat{\boldsymbol{\Omega}}^{-1} \mathbf{Z})^{-1} \mathbf{Z}^T (\hat{\boldsymbol{\Omega}})^{-1} \mathbf{y},$$

where $\hat{\Omega} = \hat{\sigma}_{\beta}^2 \mathbf{X} \mathbf{X}^T + \hat{\sigma}_{e}^2 \mathbf{I}_{n_1}$. And again the posterior mean is given as

$$oldsymbol{\mu} = \left(\mathbf{X}^T\mathbf{X} + rac{\hat{\sigma}_e^2}{\hat{\sigma}_eta^2}\mathbf{I}_p
ight)^{-1}\mathbf{X}^T(\mathbf{y} - \mathbf{Z}\hat{oldsymbol{\omega}})$$

if n > p, or

$$\mathbf{X}^T \left(\mathbf{X} \mathbf{X}^T + rac{\hat{\sigma}_e^2}{\hat{\sigma}_eta^2} \mathbf{I}_{n_1}
ight)^{-1} \left(\mathbf{y} - \mathbf{Z} \hat{oldsymbol{\omega}}
ight)$$

if n < p. Note that because **X** has been standardized, we need to re-scale the posterior mean by $\boldsymbol{\mu} \leftarrow \boldsymbol{\mu}/\mathbf{s}/\sqrt{p}$ and then the intercept by $\hat{\boldsymbol{\omega}}_0 \leftarrow \hat{\boldsymbol{\omega}}_0 - \sum_j \boldsymbol{\mu}_j \cdot \bar{\mathbf{x}}_j$. The covariance matrix of MoM estimators are given by the sanwich estimator: $\boldsymbol{\Sigma}_{\boldsymbol{\theta}} = \mathbb{E} \begin{bmatrix} \frac{\partial B}{\partial \boldsymbol{\theta}} \end{bmatrix}^{-1} \operatorname{Cov}(B) \mathbb{E} \begin{bmatrix} \frac{\partial B}{\partial \boldsymbol{\theta}} \end{bmatrix}^{-1}$, where B is the normal equation $\mathbf{q} - \mathbf{S}\boldsymbol{\theta}$. Specifically,

$$\mathbb{E}\left[\frac{\partial B}{\partial \theta}\right]^{-1} = \mathbf{S}^{-1},\tag{13}$$

and

$$Cov(B) = Cov(\begin{bmatrix} \mathbf{y}^T \mathbf{M} \mathbf{K} \mathbf{M} \mathbf{y} \\ \mathbf{y}^T \mathbf{M} \mathbf{y} \end{bmatrix}) = \begin{bmatrix} Var(\mathbf{y}^T \mathbf{M} \mathbf{K} \mathbf{M} \mathbf{y}) & Cov(\mathbf{y}^T \mathbf{M} \mathbf{K} \mathbf{M} \mathbf{y}, \mathbf{y}^T \mathbf{M} \mathbf{y}) \\ Cov(\mathbf{y}^T \mathbf{M} \mathbf{K} \mathbf{M} \mathbf{y}, \mathbf{y}^T \mathbf{M} \mathbf{K} \mathbf{M} \mathbf{y}) & Var(\mathbf{y}^T \mathbf{M} \mathbf{y}) \end{bmatrix},$$
(14)

where the elements are calculated by $Var(\mathbf{y}^T \mathbf{M} \mathbf{K} \mathbf{M} \mathbf{y}) = 2tr([\mathbf{M} \mathbf{K} \mathbf{M} \mathbf{\Omega}]^2)$, $Var(\mathbf{y}^T \mathbf{M} \mathbf{y}) = 2tr([\mathbf{M} \mathbf{\Omega}]^2)$, $Cov(\mathbf{y}^T \mathbf{M} \mathbf{K} \mathbf{M} \mathbf{y}, \mathbf{y}^T \mathbf{M} \mathbf{y}) = 2tr(\mathbf{M} \mathbf{K} \mathbf{M} \mathbf{\Omega} \mathbf{M} \mathbf{\Omega})$.

Example

```
library(VCM)
n <- 1000
d <- 1000
sb2 <- 0.1
se2 <- 1
X <- matrix(rnorm(n*d),n,d)</pre>
X <- scale(X)/sqrt(d)</pre>
w <- c(rnorm(d,0,sqrt(sb2)))
y0 <- X%*%w
y \leftarrow y0 + sqrt(se2)*rnorm(n)
fit_PXEM <- linRegPXEM(X=X,y=y,tol = 1e-6,maxIter =500,verbose=F)</pre>
fit_MM <- linRegMM(X=X,y=y,tol=1e-6,maxIter = 500,verbose=F)</pre>
fit MoM <- linReg MoM(X=X,y=y)</pre>
c(fit_PXEM$se2,fit_PXEM$sb2)
## [1] 0.9808868 0.0305816
c(fit_MM$se2,fit_MM$sb2)
## [1] 0.98072286 0.03075612
c(fit_MoM$se2,fit_MoM$sb2)
## [1] 0.98216558 0.03029853
```

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