

Web Supplement for “A Bayesian Approach for Individual-Level Drug Benefit-Risk Assessment”

1 Full Conditionals

For illustration purpose, we assume that there are one binary outcome (denoted by y_{i1}) and one continuous outcome (denoted by y_{i2} , while models are formulated as Model ?? and Model ??, respectively. Assuming non-informative prior distribution for the parameter vector Φ is denoted by $f(\Phi)$, the joint likelihood is

$$\begin{aligned} L(\Phi; \cdot) &= p(\mathbf{y}|\boldsymbol{\theta})p(\boldsymbol{\theta})f(\Phi) \\ &\propto \prod_{i=1}^I \{p[Y_{i1} = y_{i1}]p[Y_{i2} = y_{i2}]\}p(\boldsymbol{\theta}_i) \\ &= \prod_{i=1}^I L_{y1}L_{y2} \cdot p(\boldsymbol{\theta}_i), \end{aligned}$$

where

$$\begin{aligned} L_{y1} &= p[y_{i1} = 1]^{y_{i1}}(1 - p[y_{i1} = 1])^{1-y_{i1}} \\ &= \{\text{expit}[\mathbf{x}_i^\top \boldsymbol{\beta}_1 + T_{ik}^\top \boldsymbol{\beta}_{tr1} + \boldsymbol{\theta}_i^\top \boldsymbol{\lambda}_1]\}^{y_{i1}} \{1 - \text{expit}[\mathbf{x}_i^\top \boldsymbol{\beta}_1 + T_{ik}^\top \boldsymbol{\beta}_{tr1} + \boldsymbol{\theta}_i^\top \boldsymbol{\lambda}_1]\}^{1-y_{i1}}, \\ L_{y2} &= \frac{1}{\sqrt{2\pi\sigma_{\varepsilon_2}^2}} \exp\left\{-\frac{[y_{i2} - \mathbf{x}_i^\top \boldsymbol{\beta}_2 - T_{ik}^\top \boldsymbol{\beta}_{tr2} - \boldsymbol{\theta}_i^\top \boldsymbol{\lambda}_2]^2}{2\sigma_{\varepsilon_2}^2}\right\}, \\ p(\boldsymbol{\theta}_i) &= \frac{1}{\sqrt{(2\pi)^J |\boldsymbol{\Sigma}|}} \exp\left[-\frac{1}{2}\boldsymbol{\theta}_i^\top \boldsymbol{\Sigma}^{-1}\boldsymbol{\theta}_i\right], \\ \text{expit}(\cdot) &= \frac{\exp(\cdot)}{1 + \exp(\cdot)}. \end{aligned}$$

The full conditionals of all parameters are

1. $f(\beta_{2p}|\text{others}) \propto N\left(\frac{\sum_{i=1}^I [y_{i2} - \mathbf{x}_{i,-p}^\top \boldsymbol{\beta}_{-p} - T_{ik}^\top \boldsymbol{\beta}_{tr2} - \boldsymbol{\theta}_i^\top \boldsymbol{\lambda}_2]}{I}, \frac{\sigma_{\varepsilon_2}^2}{I}\right);$
2. $f(\lambda_{2q}|\text{others}) \propto N\left(\frac{\sum_{i=1}^I [y_{i2} - \mathbf{x}_i^\top \boldsymbol{\beta}_2 - T_{ik}^\top \boldsymbol{\beta}_{tr2} - \boldsymbol{\theta}_{i,-q}^\top \boldsymbol{\lambda}_{2,-q}]}{\sum_{i=1}^I \theta_{iq}^2} \theta_{iq}, \frac{\sigma_{\varepsilon_2}^2}{\sum_{i=1}^I \theta_{iq}^2}\right);$
3. $f(\frac{1}{\sigma_{\varepsilon_2}^2}|\text{others}) \propto \text{Gamma}\left(\frac{I}{2} + 1, \frac{\sum_{i=1}^I [y_{i2} - \mathbf{x}_i^\top \boldsymbol{\beta}_2 - T_{ik}^\top \boldsymbol{\beta}_{tr2} - \boldsymbol{\theta}_i^\top \boldsymbol{\lambda}_2]^2}{2}\right);$
4. $[\boldsymbol{\beta}_1, \boldsymbol{\lambda}_1|\text{others}] \propto \prod_{i=1}^I L_{y_1};$
5. $[\boldsymbol{\theta}_i|\text{others}] \propto \{p[Y_{i1} = y_{i1}]p[Y_{i2} = y_{i2}]\} \cdot p(\boldsymbol{\theta}_i);$
6. $[\boldsymbol{\Sigma}|\text{others}] \propto \prod_{i=1}^I p(\boldsymbol{\theta}_i),$

where subscript $-p$ means without p -th elements.

2 Stan code

```
//Stan code for 'Bayesian Personalized Multi-Criteria Benefit-Risk
//Assessment of Medicines'

// define the data
data {
  int<lower=1> I; // number of subjects
  int<lower=1> p; // number of latent variable
  int<lower=1> k; // number of responds
  int<lower=1> q; // number of covariances
  real Y_c[I]; // continuous respond
  int<lower=0> Y_b[I]; // binary respond
  int<lower=0> Y_p[I]; // Poisson respond
  vector[q] X[I]; // covariates matrix
  vector[p] zero; // a zero vector
}

// define the parameters
parameters {
  matrix<lower=-10, upper=10>[k, q] betas;
  vector[p] U[I]; // latent variables
  real<lower=0> var_c_e;
  real<lower=0> var_u[p];
  real<lower=-1, upper=1> rho;
  matrix[k,p] b_random;
}

// define the intermediate parameters
transformed parameters {
  cov_matrix[p] Sigma_U; // variance covariance matrix of latent variables
  vector[k] thetas[I]; // subject criteria
  matrix[k,p] b; // latent variable loadings
  real<lower=0> sig_u[p];
  real<lower=0> sig_c_e;

  b <- b_random;
  b[2,1] <- 1; // constrain
  b[2,2] <- 0;
  b[3,2] <- 1;

  for(i in 1:I){
    for(j in 1:k){
      thetas[i,j] <- betas[j,]*X[i] + b[j,] * U[i]; // latent process
    }
  }

  // construct variance covariance matrix
  for(j in 1:p){
    sig_u[j] <- sqrt(var_u[j]);
    Sigma_U[j,j] <- var_u[j];
  }
}
```

```

Sigma_U[1,2] <- rho*sig_u[1]*sig_u[2];
Sigma_U[2,1] <- Sigma_U[1,2];
sig_c_e <- sqrt(var_c_e);
}
model {
  U ~ multi_normal(zero, Sigma_U); // sample latent variables

  // sample observations
  for(i in 1:I){
    Y_c[i] ~ normal(thetas[i,1], sig_c_e);
    Y_b[i] ~ bernoulli_logit(thetas[i,2]);
    Y_p[i] ~ poisson_log(thetas[i,3]);
  }

  // prior for parameters
  to_vector(betas) ~ normal(0,100);
  to_vector(b_random) ~ normal(0,100);
  var_u ~ inv_gamma(0.01,0.01);
  var_c_e ~ inv_gamma(0.01,0.01);
  rho ~ uniform(-1,1);
}

```