Web-based Supplementary Materials for "Modeling and Analysis of Multi-library, Multi-group SAGE Data with Application to a Study of Mouse Cerebellum" by Zailong Wang, Shili Lin, Magdalena Popesco, and Andrej Rotter

Web Appendix A

In this appendix, we provide technical details of our MCMC sampling algorithms, including the posterior distributions for each of the parameters, and the M-H algorithms for updating these parameters under a specified model, M. Specifically, the univariate full conditional distribution for each parameter associated with tags in either the DE set or the SE set is given in A.1. The M-H algorithms for updating the two types of parameters (priors or hyperpriors) are provided in A.2. Finally, in A.3, we supply the details of the reversible jump MCMC algorithm for updating the model M, including the acceptance probabilities for adding/deleting.

A.1. Conditional distributions of parameters for a given M

Since conditional on the model M, the tags within a library are assumed to be independently distributed, we can consider updating the parameters associated with each tag separately. For $g \in S_1$, denote $\theta_g = \{p_{1g}, \cdots, p_{Kg}\}$ for the associated parameters and $\delta_g = \{\alpha_{1g}, \cdots, \alpha_{Kg}\}$ for the hyperparameters. Using the priors and hyperpriors as specified in the main text, we can easily derive the full conditional distributions (up to a normalizing constant) for these parameters. For $k = 1, \cdots, K$,

$$\begin{aligned}
\alpha_{kg}|\delta_{-kg}, \theta_g, M &\sim \frac{\alpha_{kg}^{a_{kg}-1} e^{-b_k \alpha_{kg}}}{\Gamma(\alpha_{kg})\Gamma(\bar{N}_k - \alpha_{kg})} p_{kg}^{(\alpha_{kg}-1)} (1-p_{kg})^{(\bar{N}_k - \alpha_{kg}-1)} := f(\alpha_{kg}); \\
p_{kg}|\theta_{-kg}, \delta_g, M &\sim p_{kg}^{\alpha_{kg} + \sum_{i=1}^{n_k} X_{kig} - 1} (1-p_{kg})^{\bar{N}_k - \alpha_{kg} - 1} e^{-(\sum_{i=1}^{n_k} N_{ki}) p_{kg}} := f(p_{kg});
\end{aligned}$$

where δ_{-kg}, and θ_{-kg} are the parameter vectors δ_g and θ_g without the element δ_{kg} or θ_{kg} respectively.

Similar to that given above, we can derive the conditional distributions for the parameter and hyperparameter for each gene g in S_2, which are (again up to a constant):

$$\begin{aligned}
\alpha_g|p_g, M &\sim \frac{\alpha_g^{a_g-1}e^{-b\alpha_g}}{\Gamma(\alpha_g)\Gamma(\bar{N}-\alpha_g)}p_g^{(\alpha_g-1)}(1-p_g)^{(\bar{N}-\alpha_g-1)} := f(\alpha_g);\\
p_g|\alpha_g, M &\sim p_g^{\alpha_g+\sum_{i=1}^n X_{ig}-1}(1-p_g)^{\bar{N}-\alpha_g-1}e^{-(\sum_{i=1}^n N_i)p_g} := f(p_g).
\end{aligned}$$

Since these distributions are not from any well known families of distributions and are only known up to a constant, we use M-H algorithms to sample from them as detailed next.

A.2. M-H Algorithms for updating parameters

Updating the α hyperparameters: $\{\alpha_{1g}, \cdots, \alpha_{Kg}, \alpha_g\}$.

The following scheme works for any α parameter in the set. Suppose that the current value for α is $\alpha^{(n)}$. Set the proposal distribution as $\alpha^*|\alpha^{(n)} \sim$ Unif $(\alpha^{(n)}/d\alpha, \min\{\tilde{N}, \alpha^{(n)} \cdot d\alpha\})$, where $d\alpha > 1$ is a pre-specified constant (say $d\alpha = 2$). Also, $\tilde{N} = \bar{N}$ for $\alpha = \alpha_g$ and $\tilde{N} = \bar{N}_k$ for $\alpha = \alpha_{kg}$. Using this proposal distribution, the importance ratio is

$$\begin{aligned}
r &= \frac{f(\alpha^*)}{f(\alpha^{(n)})}\frac{q(\alpha^{(n)}|\alpha^*)}{q(\alpha^*|\alpha^{(n)})}\\
&= \frac{\Gamma(\alpha^{(n)})}{\Gamma(\alpha^*)}\frac{\Gamma(\bar{N}-\alpha^{(n)})}{\Gamma(\bar{N}-\alpha^*)}\left(\frac{\alpha^*}{\alpha^{(n)}}\right)^{a-1}\left(\frac{p\ e^{-b}}{1-p}\right)^{\alpha^*-\alpha^{(n)}}\frac{d\alpha\min\{\tilde{N},\alpha^{(n)}d\alpha\}-\alpha^{(n)}}{d\alpha\min\{\tilde{N},\alpha^*d\alpha\}-\alpha^*}.
\end{aligned}$$

Hence, with probability $\min\{1, r\}, \alpha^{(n+1)} = \alpha^*$. Otherwise $\alpha^{(n+1)} = \alpha^{(n)}$.

Updating the p parameters: $\{p_{1g}, p_{Kg}, p_g\}$.

The following algorithm applies to each of the p parameters in the list. Let $p^*|p^{(n)} \sim$ beta $(2, \frac{2}{p^{(n)}} - 2)$ where $p^{(n)}$ is the current value for the p parameter. The importance ratio is

$$
\begin{aligned}
r &= \frac{f(p^*)}{f(p^{(n)})}\frac{q(p^{(n)}|p^*)}{q(p^*|p^{(n)})} \\
&= \frac{(2-p^*)}{(2-p^{(n)})}\frac{p^{*(\alpha+\sum X_i-4)}(1-p^*)^{(\bar{N}-\alpha+3-2/p^{(n)})}}{p^{(n)(\alpha+\sum X_i-4)}(1-p^{(n)})^{(\bar{N}-\alpha+3-2/p^*)}}e^{-\sum N_i(p^*-p^{(n)})}.
\end{aligned}
$$

We set $p^{(n+1)} = p^*$ with probability $\min\{1, r\}$. Otherwise $p^{(n+1)} = p^{(n)}$.

A.3. Reversible jump MCMC

Suppose tag g is being considered for deletion from the DE set S_1. The new parameters associated with this tag, p_g and α_g, can be obtained from the following two equations, based on the values of the current parameters, as follows:

$$
\textstyle\sum_{k=1}^K p_{kg} = Kp_g, \qquad \displaystyle\sum_{k=1}^K \frac{\alpha_{kg}}{\bar{N}_k} = K\frac{\alpha_g}{\bar{N}}.
$$

In addition, we need to generate $2(K-1)$ new parameters for matching the dimensions (Green 1995). Specifically, we set $\lambda_{kg} = a_{kg}/b_k$, where a_{kg} and b_k are as defined in the main text, and generate these parameters using the following schemes:

$$
\begin{aligned}
u_{kg} &\sim \text{Beta}\left(\lambda_{kg}, \bar{N}_k - \lambda_{kg}\right)\mathbf{1}_{\{\max\{0,\,(Kp_g-1)/(K-1)\},\,\min\{1,\,Kp_g/(K-1)\}\}}, \\
v_{kg} &\sim \text{Gamma}\ (a_{kg}, b_k)\mathbf{1}_{\{\max\{0,\,\bar{N}_k(K\alpha_g/\bar{N}-1)/(K-1)\},\,\min\{\bar{N}_k,\bar{N}_kK\alpha_g/((K-1)\bar{N})\}\}}, \qquad (1) \\
&\qquad k = 1, \cdots, K-1.
\end{aligned}
$$

The proposal of adding a tag g to the DE set, the counterpart of deleting a tag from the set as defined above, can be achieved by setting the new parameters associated with the tag g being considered for membership in S_1 as follows:

$$
\begin{aligned}
p_{kg} &= u_{kg},\ k = 1, \cdots, K-1, \quad p_{Kg} = Kp_g - \sum_{k=1}^{K-1} u_{kg}, \\
\alpha_{kg} &= v_{kg},\ k = 1, \cdots, K-1, \quad \alpha_{Kg} = \bar{N}_K\Big(\frac{K\alpha_g}{\bar{N}} - \sum_{k=1}^{K-1}\frac{v_{kg}}{\bar{N}_k}\Big),
\end{aligned}
$$

where the values for $u_{kg}, v_{kg}, k = 1, \cdots, K-1$ are from the sampling values from the corresponding deleting move, as specified in (1).

The acceptance probability for adding is $\min\{1, A\}$, where

$$
\begin{aligned}
A \;=\;& \\
& P_\lambda \cdot K^2 \bigg(\prod_{k=1}^{K} p_{kg}^{\sum_{i=1}^{n_k} X_{kig}} \bigg) p_g^{-\sum_{i=1}^{n} X_{ig}} \exp\bigg(\sum_{i=1}^{n} N_i p_g - \sum_{k=1}^{K} \sum_{i=1}^{n_k} N_{ki} p_{kg} \bigg) \\
\times\;& \frac{\Gamma(\bar{N}_K + 1)\Gamma(a_g)\Gamma(\alpha_g)\Gamma(\bar{N} - \alpha_g) I\Gamma(b\bar{N}, a_g) \prod_{k=1}^{K-1} \Gamma(\lambda_{kg})\Gamma(\bar{N}_k - \lambda_{kg})}{\Gamma(\bar{N} + 1)\Gamma(a_{Kg}) \prod_{k=1}^{K} \Gamma(\alpha_{kg})\Gamma(\bar{N}_k - \alpha_{kg}) I\Gamma(b_k \bar{N}_k, a_{kg})} \\
\times\;& \frac{b_K^{a_{Kg}} \prod_{k=1}^{K} \alpha_{kg}^{a_{kg}-1} p_{kg}^{\alpha_{kg}-1} (1 - p_{kg})^{\bar{N}_k - \alpha_{kg} - 1}}{b^{a_g} \alpha_g^{a_g - 1} p_g^{\alpha_g - 1} (1 - p_g)^{\bar{N} - \alpha_g - 1} \prod_{k=1}^{K-1} u_{kg}^{\lambda_{kg}-1} (1 - u_{kg})^{\bar{N}_k - \lambda_{kg} - 1} v_{kg}^{a_{kg}-1}} \\
\times\;& \prod_{k=1}^{K-1} \Big\{ I\beta\big(\min\{1,\ Kp_g/(K-1)\}; k\big) - I\beta\big(\max\{0,\ (Kp_g - 1)/(K-1)\}; k\big) \Big\} \\
& \quad \times \Big\{ I\Gamma\big(b_k \cdot \min\{\bar{N}_k, \bar{N}_k K \alpha_g/((K-1)\bar{N})\}; a_{kg}\big) \\
& \qquad - I\Gamma\big(b_k \cdot \max\{0,\ \bar{N}_k (K\alpha_g/\bar{N} - 1)/(K-1)\}; a_{kg}\big) \Big\} \\
\times\;& \exp\big(b\alpha_g + \sum_{k=1}^{K-1} b_k v_{kg} - \sum_{k=1}^{K} b_k \alpha_{kg} \big).
\end{aligned}
$$

For the corresponding deleting proposal, the acceptance probability is $\min\{1, A^{-1}\}$ with the same expression for A as above. Here $P_\lambda = \frac{P(M \| \|M\| = s)}{P(M \| \|M\| = s-1)} = \frac{\lambda}{1-\lambda}$ is the prior ratio for model M (see equation (2) in the main document); $I\beta(x, k) = \int_0^x t^{\lambda_{kg}-1}(1-t)^{\bar{N}_k - \lambda_{kg} - 1} \mathrm{d}t / B(\lambda_{kg}, \bar{N}_k - \lambda_{kg})$ is an incomplete beta function; and $I\Gamma(x, a) = \int_0^x t^{a-1} e^{-t} \mathrm{d}t / \Gamma(a)$ is an incomplete gamma function.