Bivariate meta-analysis of sensitivity and specificity

The bivariate model is a model for meta-analysing diagnostic studies reporting pairs of sensitivity and specificity (Reitsma *and others* (2005)). Preserving the bivariate structure of the data, pairs of sensitivity (Se) and specificity (Sp) are jointly analysed. Any existing correlation between these two measures is taken into account via random effects. Covariates can be added to the bivariate model and have a separate effect on sensitivity and specificity.
Data are taken from a meta-analysis conducted by Scheidler *and others* (1997) to compare the utility of three types of diagnostic imaging - lymphangiography (LAG), computed tomography (CT) and magnetic resonance (MR) - to detect lymph node metastases in patients with cervical cancer. The dataset consists of a total of 46 studies: the first 17 for LAG, the following 19 for CT and the last 10 for *MR*. We analyse this data set using a generalised linear mixed model approach (Chu and Cole (2006)):

$$\mathrm{TN}^i|\mu_i \sim \mathrm{Bin}(\mathrm{TN}^i + \mathrm{FP}^i, \mathrm{Sp}^i), \qquad \mathrm{logit}(\mathrm{Sp}^i) = \boldsymbol{X}_i\boldsymbol{\alpha} + \mu_i, \tag{1}$$

$$\mathrm{TP}^i|\nu_i \sim \mathrm{Bin}(\mathrm{TP}^i + \mathrm{FN}^i, \mathrm{Se}^i), \qquad \mathrm{logit}(\mathrm{Se}^i) = \boldsymbol{Z}_i\boldsymbol{\beta} + \nu_i, \tag{2}$$

$$\begin{pmatrix}\mu_i\\ \nu_i\end{pmatrix} \sim \mathcal{N}\left[\begin{pmatrix}0\\0\end{pmatrix}, \mathbf{W}^{-1}\right], \tag{3}$$

where

$$\mathbf{W}^{-1} = \begin{pmatrix}1/\tau_\mu & \rho/\sqrt{\tau_\mu\tau_\nu}\\ \rho/\sqrt{\tau_\mu\tau_\nu} & 1/\tau_\nu\end{pmatrix},$$

and TN, FP, TP and FN represent the number of true negatives, false positives, true positives, and false negatives, respectively and $\boldsymbol{X}_i, \boldsymbol{Z}_i$ are (possibly overlapping) vectors of covariates related to $\mathrm{Sp} = \frac{\mathrm{TN}}{\mathrm{TN+FP}}$ and $\mathrm{Se} = \frac{\mathrm{TP}}{\mathrm{TP+FN}}$. The index i represents study i in the meta-analysis. Here, $\boldsymbol{X}_i\boldsymbol{\alpha} = \alpha_{\mathrm{LAG}} \cdot \mathrm{LAG}_i + \alpha_{\mathrm{CT}} \cdot \mathrm{CT}_i + \alpha_{\mathrm{MR}} \cdot \mathrm{MR}_i$ and $\boldsymbol{Z}_i\boldsymbol{\beta} = \beta_{\mathrm{LAG}} \cdot \mathrm{LAG}_i + \beta_{\mathrm{CT}} \cdot \mathrm{CT}_i + \beta_{\mathrm{MR}} \cdot \mathrm{MR}_i$ whereby

$$\mathrm{LAG}_i = \begin{cases}1 & \text{if} \quad i = 0, \ldots, 16\\ 0 & \text{else}\end{cases} \quad \mathrm{CT}_i \quad = \begin{cases}1 & \text{if} \quad i = 17, \ldots, 35\\ 0 & \text{else}\end{cases} \quad \mathrm{MR}_i = \begin{cases}1 & \text{if} \quad i = 36, \ldots, 45\\ 0 & \text{else}\end{cases}$$

The model has three hyperparameters $\boldsymbol{\theta} = (\log\tau_\mu, \log\tau_\nu, \rho)$. The correlation parameter is constrained to $[-1, 1]$. We reparameterise the correlation parameter ρ using Fisher's z-transformation as

$$\rho^\star = \mathrm{logit}\left(\frac{\rho+1}{2}\right)$$

which assumes values over the whole real line and assign the following prior distribution to $\rho^\star$

$$\rho^\star \sim \mathcal{N}(0, 1/0.4)$$

The prior precision of 0.4 corresponds, roughly, to a uniform prior on $[-1, 1]$ for ρ. For the other hyperparameters we assign the following prior distributions

$$\log\tau_\mu \sim \mathrm{LogGamma}(0.25, 0.025)$$
$$\log\tau_\nu \sim \mathrm{LogGamma}(0.25, 0.025)$$

The data file is structured, so that one study is represented by consecutive rows. The first row contains the number of diseased persons $\mathrm{TP}^i + \mathrm{FN}^i$, true positives TP^i, an index, followed by the covariates columns. Accordingly, the second row contains the number of non-diseased persons $\mathrm{TN}^i + \mathrm{FP}^i$, true negatives TN^i, an index, followed by the covariate columns.

Instead of specifying separate prior distributions for the hyperparameters we could also assume that the precision matrix

$$\mathbf{W} \sim \text{Wishart}_p(r, \boldsymbol{R}^{-1}), \quad p = 2,$$

where the Wishart distribution has density

$$\pi(\mathbf{W}) = c^{-1}|\mathbf{W}|^{(r-(p+1))/2} \exp\left\{-\frac{1}{2}\text{Trace}(\mathbf{WR})\right\}, \quad r > p+1$$

and

$$c = 2^{(rp)/2}|\mathbf{R}|^{-r/2}\pi^{(p(p-1))/4}\prod_{j=1}^{p}\Gamma((r+1-j)/2).$$

Then,

$$\text{E}(\mathbf{W}) = r\mathbf{R}^{-1}, \quad \text{and} \quad \text{E}(\mathbf{W}^{-1}) = \mathbf{R}/(r-(p+1)).$$

The parameters are r, R_{11}, R_{22} and R_{12}, where

$$\boldsymbol{R} = \begin{pmatrix} R_{11} & R_{12} \\ R_{21} & R_{22} \end{pmatrix}$$

and $R_{12} = R_{21}$ due to symmetry. The `inla` function reports the posterior distribution for the hyperparameters $\log\tau_\mu, \log\tau_\nu$ and $\rho^\star$ as for the other prior given above.
For this model the data need to be represented in a different format. Instead of an alternating structure (as before) a block structure is required. The first block contains the number of diseased persons $\text{TP}^i + \text{FN}^i$, true positives TP^i, an index, followed by the covariates columns for all $i = 1$ (LAG, CT, MR), while the second block contains the number of non-diseased persons $\text{TN}^i + \text{FP}^i$, true negatives TN^i, an index, followed by the covariate columns for all $i = 1$ (LAG, CT, MR). That means values for TP and TN do not alternate for each study, but are structured block-wise. (The provided example code should clarify the formatting issue.)

References

Chu, H. and Cole, S. R. (2006). Bivariate meta-analysis of sensitivity and specificity with sparse data: a generalized linear mixed model approach., *Journal of Clinical Epidemiology* **59**(12): 1331–1333.

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Scheidler, J., Hricak, H., Yu, K. K., Subak, L. and Segal, M. R. (1997). Radiological evaluation of lymph node metastases in patients with cervical cancer: a meta-analysis, *Journal of the American Medical Association* **278**(13): 1096–1101.