Appendix

Appendix: The procedure of parameter estimation

Denote $\theta^*=(\beta^T, \alpha, \omega, u^T,\sigma_0^2)$, and $a(x) = a(x;\beta^T,\alpha,\omega|V_F,V_B)$ since $a(x)$ is a functional vector of β^T, α, ω for given V_F and V_B. The log-likelihood function of θ^* with observations Y_{ij} at replication j of dose-level x_i (j =1,2,…, k_i; i = 1,2,…,n) for given all of V_F and V_B is

$$l\left(\theta^* \mid x,y;V_F,V_B\right)=-\frac{N}{2}log\left(2\pi\sigma_0^2\right)-\frac{1}{2\pi\sigma_0^2}\sum_{i=1}^{n}\sum_{j=1}^{k_i}\left(y_{ij}-100u^Ta\left(x_i;\beta^T,\alpha,\omega|V_F,V_B\right)\right)^2 \tag{A1}$$

where $N=k_1\ldots+k_n$. Then, the maximum likelihood estimates (MLEs) of u and σ_0^2 are given by

$$\begin{aligned} u &= \left(\sum_{i=1}^{n}k_ia^T\left(x_i\right)a\left(x_i\right)\right)^{-1}\sum_{i=1}^{n}\sum_{j=1}^{k_i}\left(100-y_{ij}\right)a\left(x_i\right) \\ \sigma_0^2 &= \frac{1}{N}\sum_{i=1}^{n}\sum_{j=1}^{k_i}\left(y_{ij}-100-u^Ta\left(x_i\right)\right)^2 \end{aligned} \tag{A2}$$

and the MLEs of β^T,α,ω are determined by

$$\min_{\beta^T,\alpha,\omega}\sum_{i=1}^{n}\sum_{j=1}^{k_i}\left(y_{ij}-100-u^Ta\left(x_i;\beta^T,\alpha,\omega|V_F,V_B\right)\right)^2 \tag{A3}$$

The iteration algorithm of parameter estimation:

Step 1. For given $\mu_1^{(t)}$ and $\sigma_0^{2(t)}$ we take iid samples $\left\{V_{F_i}^{(t)},\ V_{B_i}^{(t)};i=1,2,\ldots.\right\}$ from the normal distribution $N(\mu_1^{(t)}, \sigma_0^{2(t)})$, an ECM algorithm is employed to get the MLEs of parameters $\theta^{*(t)} = (\beta^{T(t)}, \alpha^{(t)}, \omega^{(t)}, u^{T(t)}, \sigma_0^{2(t)})$, based on (A2) and (A3).

Step 2. Using equation (3), we have that for given dose-level x_i

$$\begin{aligned} EY\left(x_i\right) &= \frac{1}{k_i}\sum_{j=1}^{k_i}y_{ij} = 100+u^{T(t)}E\left(a\left(x_i;\beta^{T(t)},\alpha^{(t)},\omega^{(t)},|V_F,V_B\right)\right) \\ &= 100+u^{T(t)}a\left(x_i;\beta^{T(t)},\alpha^{(t)},\omega^{(t)}\,|E\left(V_F\right)=E\left(V_B\right)=\psi\right) \end{aligned} \tag{A4}$$

for i =1, 2, …, n. Solve equation (A4) with respect to ψ. Denote the solutions by $\psi_1,\psi_2,\ldots,\psi_n$, we obtain the estimates of μ_1 and σ_1^2 as

$$\mu_1^{(t+1)}=\frac{1}{n}\sum_{i=1}^{n}\psi_i \text{ and } \sigma_1^{2(t+1)}=\frac{1}{n-1}\sum_{i=1}^{n}\left(\psi_i-\left(\mu_1^{(t+1)}\right)\right)^2$$

The algorithm is iterated until $\left\|\theta^{(t+1)}-\theta^{(t)}\right\|$ is sufficiently small. Assume that the algorithm converged at the $(t + 1)^{th}$ iteration, then the MLE $\hat{\theta}=\theta^{(t+1)}$.