

Our model:

$$\mathbf{y}_{ki} = \mathbf{X}_i(\boldsymbol{\beta}_k + \mathbf{b}_{ki} + \boldsymbol{\Gamma}_k(\boldsymbol{\alpha}'\mathbf{x}_i)) + \boldsymbol{\epsilon}_{ki} \quad (1)$$

where

- $\mathbf{X}_i$  is the  $n_t \times t$  dimension design matrix for subject  $i$ ;
- $\mathbf{x}_i = (x_{i1} \dots x_{ip})'$  is the  $p \times 1$  vector of predictors for subject  $i$ ;  $x_{ij}$  presents the  $j$ th predictor for the  $i$ th subject;  $\mathbf{x}_i \sim MVN(\mathbf{0}, \boldsymbol{\Sigma}_x)$
- $\boldsymbol{\beta}_k$  is the fixed effect coefficient with dimension  $t \times 1$ ;
- $\boldsymbol{\Gamma}_{kj}$  is the fixed effect coefficient with dimension  $t \times 1$ ;
- $\boldsymbol{\alpha}$  is a  $p \times 1$  vector.
- $\mathbf{b}_{ki} \sim N(0, \mathbf{D}_k)$ ,  $\mathbf{D}_k$  is a  $t \times t$  matrix, with  $\frac{t(t+1)}{2}$  parameters.
- $\boldsymbol{\epsilon}_{ki} \sim N(0, \sigma_k^2 \mathbf{I})$

Therefore, the expectation and variance of outcome  $Y_k$  given the predictors is

$$E(\mathbf{Y}_k|\mathbf{x}) = \mathbf{X}\boldsymbol{\beta}_k + \mathbf{X}\boldsymbol{\Gamma}_k\boldsymbol{\alpha}'\mathbf{x} \quad (2)$$

$$Var(\mathbf{Y}_k|\mathbf{x}) = \mathbf{X}\mathbf{D}_k\mathbf{X}' + \sigma_k^2\mathbf{I} \quad (3)$$

Therefore, the conditional distribution of outcome  $\mathbf{Y}_k|\mathbf{x}$  is

$$\mathbf{Y}_k|\mathbf{x} \sim MVN(\mathbf{X}\boldsymbol{\beta}_k + \mathbf{X}\boldsymbol{\Gamma}_k\boldsymbol{\alpha}'\mathbf{x}, \mathbf{X}\mathbf{D}_k\mathbf{X}' + \sigma_k^2\mathbf{I}) \quad (4)$$

Besides, the expectation of variance of the outcome is

$$E(\mathbf{Y}_k) = E(E(\mathbf{Y}_k|\mathbf{x})) = \mathbf{X}\boldsymbol{\beta}_k \quad (5)$$

since  $E(\mathbf{x}) = \mathbf{0}$ .

$$\begin{aligned} Var(Y_k) &= E(Var(\mathbf{Y}_k|\mathbf{x})) + Var(E(\mathbf{Y}_k|\mathbf{x})) \\ &= E(\mathbf{X}\mathbf{D}_k\mathbf{X}' + \sigma_k^2\mathbf{I}) + Var(\mathbf{X}\boldsymbol{\beta}_k + \mathbf{X}\boldsymbol{\Gamma}_k\boldsymbol{\alpha}'\mathbf{x}) \\ &= \mathbf{X}\mathbf{D}_k\mathbf{X}' + \sigma_k^2\mathbf{I} + \mathbf{X}\boldsymbol{\Gamma}_k\boldsymbol{\alpha}'\boldsymbol{\Sigma}_x(\mathbf{X}\boldsymbol{\Gamma}_k\boldsymbol{\alpha}')' \\ &= \mathbf{X}(\mathbf{D}_k + \boldsymbol{\Gamma}_k\boldsymbol{\alpha}'\boldsymbol{\Sigma}_x\boldsymbol{\alpha}\boldsymbol{\Gamma}_k')\mathbf{X}' + \sigma_k^2\mathbf{I} \end{aligned} \quad (6)$$

Therefore, the distribution of  $\mathbf{Y}_k$  is

$$\mathbf{Y}_k \sim MVN(\mathbf{X}\boldsymbol{\beta}_k, \mathbf{X}(\mathbf{D}_k + \boldsymbol{\Gamma}_k\boldsymbol{\alpha}'\boldsymbol{\Sigma}_x\boldsymbol{\alpha}\boldsymbol{\Gamma}_k')\mathbf{X}' + \sigma_k^2\mathbf{I}) \quad (7)$$

The joint distributions between  $\mathbf{Y}_k$  and  $\mathbf{x}$  is

$$\begin{aligned} f(\mathbf{y}_k, \mathbf{x}) &= f(\mathbf{Y}_k|\mathbf{x})f(\mathbf{x}) \\ &= \frac{1}{\sqrt{(2\pi)^{n_t}|\boldsymbol{\Sigma}_k|}} \exp\left(-\frac{1}{2}(\mathbf{y}_k - \boldsymbol{\mu}_k)'\boldsymbol{\Sigma}_k^{-1}(\mathbf{y}_k - \boldsymbol{\mu}_k)\right) \times \frac{1}{\sqrt{(2\pi)^p|\boldsymbol{\Sigma}_x|}} \exp\left(-\frac{1}{2}\mathbf{x}'\boldsymbol{\Sigma}_x^{-1}\mathbf{x}\right) \end{aligned} \quad (8)$$

where  $\boldsymbol{\Sigma}_k = \mathbf{X}\mathbf{D}_k\mathbf{X}' + \sigma_k^2\mathbf{I}$ ,  $\boldsymbol{\mu}_k = \mathbf{X}(\boldsymbol{\beta}_k + \boldsymbol{\Gamma}_k(\boldsymbol{\alpha}'\mathbf{x}))$

The covariance matrix between  $\mathbf{Y}_k$  and  $\mathbf{x}$  is

$$\begin{aligned} Cov(\mathbf{Y}_k, \mathbf{x}) &= Cov(\mathbf{X}(\boldsymbol{\beta}_k + \mathbf{b}_{ki} + \boldsymbol{\Gamma}_k(\boldsymbol{\alpha}'\mathbf{x})) + \boldsymbol{\epsilon}_k, \mathbf{x}) \\ &= Cov(\mathbf{X}\boldsymbol{\Gamma}_k\boldsymbol{\alpha}'\mathbf{x}, \mathbf{x}) \\ &= \mathbf{X}\boldsymbol{\Gamma}_k\boldsymbol{\alpha}'Cov(\mathbf{x}, \mathbf{x}) \\ &= \mathbf{X}\boldsymbol{\Gamma}_k\boldsymbol{\alpha}'\boldsymbol{\Sigma}_x \quad (n \times p) \\ Cov(\mathbf{x}, \mathbf{Y}_k) &= \boldsymbol{\Sigma}_x\boldsymbol{\alpha}\boldsymbol{\Gamma}_k'\mathbf{X}' \end{aligned} \quad (9)$$

$$\begin{pmatrix} \mathbf{x} \\ \mathbf{y}_k \end{pmatrix} \sim MVN\left(\begin{pmatrix} \mathbf{0} \\ \mathbf{X}\boldsymbol{\beta}_k \end{pmatrix}, \begin{pmatrix} \boldsymbol{\Sigma}_x & \boldsymbol{\Sigma}_x\boldsymbol{\alpha}\boldsymbol{\Gamma}_k'\mathbf{X}' \\ \mathbf{X}\boldsymbol{\Gamma}_k\boldsymbol{\alpha}'\boldsymbol{\Sigma}_x & \mathbf{X}(\mathbf{D}_k + \boldsymbol{\Gamma}_k\boldsymbol{\alpha}'\boldsymbol{\Sigma}_x\boldsymbol{\alpha}\boldsymbol{\Gamma}_k')\mathbf{X}' + \sigma_k^2\mathbf{I} \end{pmatrix}\right) \quad (10)$$

### Likelihood optimization

1. Optimize the conditional log-likelihood function  $\log(f(\mathbf{y}|\mathbf{x}))$

$$\begin{aligned}
l(\boldsymbol{\theta}|\mathbf{x}) = & -n \cdot n_t \log(2\pi) - \frac{n}{2} \log(|\boldsymbol{\Sigma}_1|) - \frac{n}{2} \log(|\boldsymbol{\Sigma}_2|) \\
& - \sum_{i=1}^n \frac{1}{2} (\mathbf{y}_i - \boldsymbol{\mu}_{1i})' \boldsymbol{\Sigma}_1^{-1} (\mathbf{y}_i - \boldsymbol{\mu}_{1i}) \\
& - \sum_{i=n+1}^{2n} \frac{1}{2} (\mathbf{y}_i - \boldsymbol{\mu}_{2i})' \boldsymbol{\Sigma}_2^{-1} (\mathbf{y}_i - \boldsymbol{\mu}_{2i})
\end{aligned} \tag{11}$$

where  $\boldsymbol{\Sigma}_k = \mathbf{X} \mathbf{D}_k \mathbf{X}' + \sigma_k^2 \mathbf{I}$ ,  $\boldsymbol{\mu}_k = \mathbf{X}(\boldsymbol{\beta}_k + \boldsymbol{\Gamma}_k(\boldsymbol{\alpha}'\mathbf{x}))$

2. Optimize the log-likelihood function  $\log(f(\mathbf{y}))$ .

$$\begin{aligned}
l(\boldsymbol{\theta}) = & -n \cdot n_t \log(2\pi) - \frac{n}{2} \log(|\boldsymbol{\Sigma}_{y1}|) - \frac{n}{2} \log(|\boldsymbol{\Sigma}_{y2}|) \\
& - \sum_{i=1}^n \frac{1}{2} (\mathbf{y}_i - \boldsymbol{\mu}_{y1i})' \boldsymbol{\Sigma}_{y1}^{-1} (\mathbf{y}_i - \boldsymbol{\mu}_{y1i}) \\
& - \sum_{i=n+1}^{2n} \frac{1}{2} (\mathbf{y}_i - \boldsymbol{\mu}_{y2i})' \boldsymbol{\Sigma}_{y2}^{-1} (\mathbf{y}_i - \boldsymbol{\mu}_{y2i})
\end{aligned} \tag{12}$$

where  $\boldsymbol{\mu}_{yki} = \mathbf{X}_i \boldsymbol{\beta}_k$ ,  $\boldsymbol{\Sigma}_{yk} = \mathbf{X}_i(\mathbf{D}_k + \boldsymbol{\Gamma}_k \boldsymbol{\alpha}' \boldsymbol{\Sigma}_x \boldsymbol{\alpha} \boldsymbol{\Gamma}_k') \mathbf{X}_i' + \sigma_k^2 \mathbf{I}$

3. Optimize the mean value of expectation of conditional log-likelihood function.

$$\begin{aligned}
E(l(\boldsymbol{\theta})) = & E(E(l(\boldsymbol{\theta}|\mathbf{x}))) \propto -\frac{n}{2} \log(|\boldsymbol{\Sigma}_1|) - \frac{n}{2} \log(|\boldsymbol{\Sigma}_2|) - \frac{n}{4} \text{tr}(\boldsymbol{\Sigma}_2^{-1} \boldsymbol{\Sigma}_1) - \frac{n}{4} \text{tr}(\boldsymbol{\Sigma}_1^{-1} \boldsymbol{\Sigma}_2) \\
& - \frac{n}{4} \{ (\mathbf{X}\boldsymbol{\beta}_1 - \mathbf{X}\boldsymbol{\beta}_2)' (\boldsymbol{\Sigma}_1^{-1} + \boldsymbol{\Sigma}_2^{-1}) (\mathbf{X}\boldsymbol{\beta}_1 - \mathbf{X}\boldsymbol{\beta}_2) \\
& + 2 [ (\mathbf{X}\boldsymbol{\beta}_1 - \mathbf{X}\boldsymbol{\beta}_2)' (\boldsymbol{\Sigma}_1^{-1} + \boldsymbol{\Sigma}_2^{-1}) (\mathbf{X}\boldsymbol{\Gamma}_1 - \mathbf{X}\boldsymbol{\Gamma}_2) \boldsymbol{\mu}_x' \boldsymbol{\alpha} \\
& + \boldsymbol{\alpha}' (\boldsymbol{\mu}_x \boldsymbol{\mu}_x' + \boldsymbol{\Sigma}_x) \boldsymbol{\alpha} ((\mathbf{X}\boldsymbol{\Gamma}_1 - \mathbf{X}\boldsymbol{\Gamma}_2))' (\boldsymbol{\Sigma}_1^{-1} + \boldsymbol{\Sigma}_2^{-1}) ((\mathbf{X}\boldsymbol{\Gamma}_1 - \mathbf{X}\boldsymbol{\Gamma}_2)) \}
\end{aligned} \tag{13}$$