

Derivation of The Fisher's Information for Slope of Regression

1. Derivation of the Fisher's Information for the Slope Estimate (Equation 2)

As defined previously, the covariance matrix of \mathbf{y}_i is

$$\mathbf{V}_i = \sigma^2 \mathbf{I}_{m_i} + \sigma_s^2 \mathbf{J}_{m_i}$$

where \mathbf{I}_{m_i} is the identity matrix with dimension m_i and \mathbf{J}_{m_i} is the matrix of 1's with dimension m_i . Therefore the inverse of \mathbf{V}_i is

$$\mathbf{V}_i^{-1} = \frac{1}{\sigma^2} \left[\mathbf{I}_{m_i} - \frac{\sigma_s^2}{\sigma^2 + m_i \sigma_s^2} \mathbf{J}_{m_i} \right].$$

The covariance matrix and the corresponding inverse for all response \mathbf{y} become

$$\mathbf{V} = \text{diag}\{\mathbf{V}_1, \mathbf{V}_2, \dots, \mathbf{V}_n\},$$

$$\mathbf{V}^{-1} = \text{diag}\{\mathbf{V}_1^{-1}, \mathbf{V}_2^{-1}, \dots, \mathbf{V}_n^{-1}\}.$$

Let $\mathbf{x}'_i = (x_{i1}, x_{i2}, \dots, x_{im_i})$ be the visit time vector for subject i and $\mathbf{x}'_{\mathbf{v}} = (\mathbf{x}'_1, \mathbf{x}'_2, \dots, \mathbf{x}'_n)$ be the visit time vector from all subjects. The design matrix (fixed effects) is a matrix with two columns as $\mathbf{x} = [\mathbf{1}, \mathbf{x}_{\mathbf{v}}]$ where $\mathbf{1}$ is a vector with all values as 1. Therefore the generalized least squares estimate of $\boldsymbol{\beta}$ becomes

$$\begin{aligned} \hat{\boldsymbol{\beta}} &= (\mathbf{x}'\mathbf{V}^{-1}\mathbf{x})^{-1} \mathbf{x}'\mathbf{V}^{-1}\mathbf{y} \\ \mathbf{V}(\hat{\boldsymbol{\beta}}) &= (\mathbf{x}'\mathbf{V}^{-1}\mathbf{x})^{-1} \end{aligned} \quad (1)$$

Plug in \mathbf{x} and \mathbf{V}^{-1} , we have

$$\begin{aligned} \mathbf{x}'\mathbf{V}^{-1}\mathbf{x} &= \begin{bmatrix} \sum_i \frac{m_i}{\sigma^2 + m_i \sigma_s^2} & \sum_j \frac{x_{ij}}{\sigma^2 + m_i \sigma_s^2} \\ \sum_i \frac{\sum_j x_{ij}}{\sigma^2 + m_i \sigma_s^2} & \frac{1}{\sigma^2} \sum_i \left[\sum_j x_{ij}^2 - \frac{\sigma_s^2}{\sigma^2 + m_i \sigma_s^2} \left(\sum_j x_{ij} \right)^2 \right] \end{bmatrix} \\ &= \begin{bmatrix} \sum_i \frac{m_i}{\sigma^2 + m_i \sigma_s^2} & \sum_i \frac{m_i \bar{x}_i}{\sigma^2 + m_i \sigma_s^2} \\ \sum_i \frac{m_i \bar{x}_i}{\sigma^2 + m_i \sigma_s^2} & \frac{1}{\sigma^2} \sum_i \frac{\sum_j x_{ij}^2 \sigma^2 + m_i \sigma_s^2 \sum_j x_{ij}^2 - \sigma_s^2 \left(\sum_j x_{ij} \right)^2}{\sigma^2 + m_i \sigma_s^2} \end{bmatrix} \\ &= \begin{bmatrix} A & B \\ B & C \end{bmatrix} \end{aligned} \quad (2)$$

Therefore the variance-covariance matrix $\mathbf{V}(\boldsymbol{\beta})$ becomes

$$(\mathbf{x}'\mathbf{V}^{-1}\mathbf{x})^{-1} = \frac{1}{A \cdot C - B^2} \begin{bmatrix} C & -B \\ -B & A \end{bmatrix}, \quad (3)$$

and the variance of the slope estimate $V(\beta) = A/(A \cdot C - B^2)$.

The item C can be further simplified as

$$\begin{aligned}
C &= \frac{1}{\sigma^2} \sum_i \frac{\sum_j x_{ij}^2 \sigma^2 + \sigma_s^2 \left[m_i \sum_j x_{ij}^2 - \left(\sum_j x_{ij} \right)^2 \right]}{\sigma^2 + m_i \sigma_s^2} \\
&= \frac{1}{\sigma^2} \sum_i \frac{\sum_j x_{ij}^2 \sigma^2 + \sigma_s^2 \left[m_i \sum_j \left(x_{ij} - \frac{\sum_j x_{ij}}{m_i} \right)^2 \right]}{\sigma^2 + m_i \sigma_s^2} \\
&= \frac{1}{\sigma^2} \sum_i \frac{(\sigma^2 + m_i \sigma_s^2) \sum_j \left(x_{ij} - \frac{\sum_j x_{ij}}{m_i} \right)^2 + \sum_j x_{ij}^2 \sigma^2 - \sigma^2 \sum_j \left(x_{ij} - \frac{\sum_j x_{ij}}{m_i} \right)^2}{\sigma^2 + m_i \sigma_s^2} \quad (4) \\
&= \frac{1}{\sigma^2} \sum_i \left[\sum_j (x_{ij} - \bar{x}_i)^2 + \frac{\sigma^2}{\sigma^2 + m_i \sigma_s^2} \left[\sum_j x_{ij}^2 - \sum_j (x_{ij} - \bar{x}_i)^2 \right] \right] \\
&= \frac{1}{\sigma^2} \sum_i \left[\sum_j (x_{ij} - \bar{x}_i)^2 + \frac{\sigma^2}{\sigma^2 + m_i \sigma_s^2} m_i \bar{x}_i^2 \right] \\
&= \sum_i \sum_j \frac{(x_{ij} - \bar{x}_i)^2}{\sigma^2} + \sum_i \frac{m_i \bar{x}_i^2}{\sigma^2 + m_i \sigma_s^2} \\
&= \frac{1}{V(\beta_w)} + \sum_i \frac{m_i \bar{x}_i^2}{\sigma^2 + m_i \sigma_s^2}
\end{aligned}$$

The Fisher's information (reciprocal of the variance) of the slope is therefore

$$\begin{aligned}
\frac{1}{V(\beta)} &= C - \frac{B^2}{A} \\
&= \sum_i \sum_j \frac{(x_{ij} - \bar{x}_i)^2}{\sigma^2} + \sum_i \frac{m_i \bar{x}_i^2}{\sigma^2 + m_i \sigma_s^2} - \frac{\left(\sum_i \frac{m_i \bar{x}_i}{\sigma^2 + m_i \sigma_s^2} \right)^2}{\sum_i \frac{m_i}{\sigma^2 + m_i \sigma_s^2}} \\
&= \frac{1}{V(\beta_w)} + \frac{1}{\sum_i \frac{m_i}{\sigma^2 + m_i \sigma_s^2}} \left[\sum_i \frac{m_i \bar{x}_i^2}{\sigma^2 + m_i \sigma_s^2} \sum_i \frac{m_i}{\sigma^2 + m_i \sigma_s^2} - \left(\sum_i \frac{m_i \bar{x}_i}{\sigma^2 + m_i \sigma_s^2} \right)^2 \right] \\
&= \frac{1}{V(\beta_w)} + \frac{1}{\sum_i \frac{m_i}{\sigma^2 + m_i \sigma_s^2}} \left[\sum_{i \neq k} \frac{m_i m_k \bar{x}_i^2}{(\sigma^2 + m_i \sigma_s^2)(\sigma^2 + m_k \sigma_s^2)} - \sum_{i \neq k} \frac{m_i m_k \bar{x}_i \bar{x}_k}{(\sigma^2 + m_i \sigma_s^2)(\sigma^2 + m_k \sigma_s^2)} \right] \\
&= \frac{1}{V(\beta_w)} + \frac{1}{\sum_i \frac{m_i}{\sigma^2 + m_i \sigma_s^2}} \left[\sum_{i < k} \frac{m_i m_k (\bar{x}_i - \bar{x}_k)^2}{(\sigma^2 + m_i \sigma_s^2)(\sigma^2 + m_k \sigma_s^2)} \right] \\
&= \frac{\sum_i \sum_j (x_{ij} - \bar{x}_i)^2}{\sigma^2} + \frac{\sum_{i < k} \frac{(\bar{x}_i - \bar{x}_k)^2}{\left(\frac{1}{m_i} + \gamma\right)\left(\frac{1}{m_k} + \gamma\right)}}{\sigma^2 \sum_i \frac{1}{\frac{1}{m_i} + \gamma}}
\end{aligned} \tag{5}$$

2. Derivation of the Fisher's Information for the Slope with Mean Data at Subject Level β_b (Equation 4)

With the subject level mean data \bar{x}_i and \bar{y}_i , the between-subject component of the slope, β_b , can be estimated by fitting a linear regression. To simplify the notation, let

$$\bar{V}_i = V(\bar{y}_i) = \frac{\sigma^2}{m_i} + \sigma_s^2,$$

and therefore

$$\bar{V}_i^{-1} = \frac{m_i}{\sigma^2 + m_i \sigma_s^2}.$$

So for $\bar{\mathbf{y}}' = (\bar{y}_1, \dots, \bar{y}_n)$, the covariance matrix is

$$\bar{\mathbf{V}} = \text{diag}\{\bar{V}_1, \bar{V}_2, \dots, \bar{V}_n\},$$

and its inverse is

$$\bar{\mathbf{V}}^{-1} = \text{diag}\{\bar{V}_1^{-1}, \bar{V}_2^{-1}, \dots, \bar{V}_n^{-1}\}.$$

Let $\bar{\mathbf{x}}'_v = (\bar{x}_1, \bar{x}_2, \dots, \bar{x}_n)$ be the mean visit time vector. The design matrix in this case is a matrix with two columns as $\bar{\mathbf{x}} = [\mathbf{1}, \bar{\mathbf{x}}_v]$ where $\mathbf{1}$ is a vector with all values as 1. Therefore the generalized least squares estimate of β_b becomes

$$\hat{\beta}_b = (\bar{\mathbf{x}}' \bar{\mathbf{V}}^{-1} \bar{\mathbf{x}})^{-1} \bar{\mathbf{x}}' \bar{\mathbf{V}}^{-1} \bar{\mathbf{y}}$$

$$\mathbf{V}(\hat{\beta}_b) = (\bar{\mathbf{x}}' \bar{\mathbf{V}}^{-1} \bar{\mathbf{x}})^{-1}$$

Plug in $\bar{\mathbf{x}}$ and $\bar{\mathbf{V}}^{-1}$, we have

$$\bar{\mathbf{x}}' \bar{\mathbf{V}}^{-1} \bar{\mathbf{x}} = \begin{bmatrix} \sum_i \frac{1}{\bar{V}_i} & \sum_i \frac{\bar{x}_i}{\bar{V}_i} \\ \sum_i \frac{\bar{x}_i}{\bar{V}_i} & \sum_i \frac{\bar{x}_i^2}{\bar{V}_i} \end{bmatrix} = \begin{bmatrix} a & b \\ b & c \end{bmatrix} \quad (6)$$

Therefore the Fisher's Information for the slope from such regression is

$$\begin{aligned} \frac{1}{V(\beta_b)} &= c - b^2/a \\ &= \sum_i \frac{\bar{x}_i^2}{\bar{V}_i} - \frac{\left(\sum_i \frac{\bar{x}_i}{\bar{V}_i}\right)^2}{\sum_i \frac{1}{\bar{V}_i}} \\ &= \frac{1}{\sum_i \frac{1}{\bar{V}_i}} \left[\sum_i \frac{\bar{x}_i^2}{\bar{V}_i} \sum_i \frac{1}{\bar{V}_i} - \left(\sum_i \frac{\bar{x}_i}{\bar{V}_i}\right)^2 \right] \\ &= \frac{1}{\sum_i \frac{1}{\bar{V}_i}} \left[\sum_{i \neq k} \frac{\bar{x}_i^2}{\bar{V}_i} \frac{1}{\bar{V}_k} - \sum_{i \neq k} \frac{\bar{x}_i \bar{x}_k}{\bar{V}_i \bar{V}_k} \right] \\ &= \frac{\sum_{i < k} \frac{(\bar{x}_i - \bar{x}_k)^2}{V(\bar{y}_i) V(\bar{y}_k)}}{\sum_i \frac{1}{V(\bar{y}_i)}} = \frac{\sum_{i < k} \frac{(\bar{x}_i - \bar{x}_k)^2}{\left(\frac{1}{m_i} + \gamma\right) \left(\frac{1}{m_k} + \gamma\right)}}{\sigma^2 \sum_i \frac{1}{\frac{1}{m_i} + \gamma}} \end{aligned} \quad (7)$$