# Lab 3.3 - ARMD Trial

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January 24, 2023

$$\text{VISUAL}_{it} = \beta_{0t} + \beta_1 \cdot \text{VISUAL0}_i + \beta_{2t} \cdot \text{TREAT}_i + \epsilon_{it}$$

for patient $i$ $(i = 1, ..., 234)$
at time $t$ with $t = 1\,(4 \text{ weeks}),\ 2\,(12 \text{ weeks}),\ 3\,(24 \text{ weeks}),\ 4\,(52 \text{ weeks})$
**Lab2 notation**: $\epsilon_{it} \sim \mathcal{N}(0, \sigma^2_{it})$
**Lab3 notation**: $\underline{\epsilon_i} \sim \mathcal{N}(\underline{0}, \sigma^2 \boldsymbol{\mathcal{R}}_i)$ where $\boldsymbol{\mathcal{R}}_i = \boldsymbol{\Lambda}_i \boldsymbol{\mathcal{C}}_i \boldsymbol{\Lambda}_i$

```
library(nlme)
lm1.form <- visual ~ -1 + visual0 + time.f + treat.f:time.f
```

## Model 9.2 - varPower($\cdot$) time ($< \delta >$-group)

$\underline{\delta} = \delta$ (scalar) since we do not include any stratification in the model
**Lab2 notation**: $\epsilon_{it} \sim \mathcal{N}(0, \sigma^2_{it})$ where

$$\begin{aligned} \sigma_{it} &= \sigma \cdot \lambda_{it} \\ &= \sigma \cdot \lambda(\ \delta,\ \text{TIME}_{it}\ ) \\ &= \sigma \cdot |\text{TIME}_{it}|^{\delta} \quad \text{since } \lambda \text{ is varPower}(\cdot) \end{aligned}$$

**Lab3 notation**: $\underline{\epsilon_i} \sim \mathcal{N}(\underline{0}, \sigma^2(\boldsymbol{\Lambda}_i \boldsymbol{\mathcal{C}}_i \boldsymbol{\Lambda}_i))$ where

$$\boldsymbol{\Lambda}_i = \begin{bmatrix} |\text{TIME}_{i1}|^{\delta} & 0 & 0 & 0 \\ 0 & |\text{TIME}_{i2}|^{\delta} & 0 & 0 \\ 0 & 0 & |\text{TIME}_{i3}|^{\delta} & 0 \\ 0 & 0 & 0 & |\text{TIME}_{i4}|^{\delta} \end{bmatrix}$$

and

$$\boldsymbol{\mathcal{C}}_i = \begin{bmatrix} 1 & 0 & 0 & 0 \\ 0 & 1 & 0 & 0 \\ 0 & 0 & 1 & 0 \\ 0 & 0 & 0 & 1 \end{bmatrix}$$

```
weights = varPower(form = ~time)
fm9.2 <- gls(lm1.form, weights = weights, data = armd)
```

We want to modify $\boldsymbol{\mathcal{C}}_i$, allowing the visual acuity measurements for the same individual to be correlated, while keeping the same $\boldsymbol{\Lambda}_i$. We make use of the empirical Semivariogram for choosing the appropriate correlation structure.

# Model 12.1 - corCompSymm($\cdot$)

*Compound Symmetry Correlation Structure*
$\underline{\epsilon_i} \sim \mathcal{N}(\underline{0}, \sigma^2(\boldsymbol{\Lambda}_i \boldsymbol{\mathcal{C}}_i \boldsymbol{\Lambda}_i))$ where

$$\boldsymbol{\Lambda}_i = \begin{bmatrix} |\text{TIME}_{i1}|^\delta & 0 & 0 & 0 \\ 0 & |\text{TIME}_{i2}|^\delta & 0 & 0 \\ 0 & 0 & |\text{TIME}_{i3}|^\delta & 0 \\ 0 & 0 & 0 & |\text{TIME}_{i4}|^\delta \end{bmatrix}$$

and

$$\boldsymbol{\mathcal{C}}_i = \begin{bmatrix} 1 & \rho & \rho & \rho \\ \rho & 1 & \rho & \rho \\ \rho & \rho & 1 & \rho \\ \rho & \rho & \rho & 1 \end{bmatrix}$$

```
weights = varPower(form = ~time)
correlation = corCompSymm(form = ~1|subject)
fm12.1 <- gls(lm1.form,
              weights = weights,
              correlation = correlation,
              data = armd)
```

# Model 12.2 - corAR1($\cdot$)

*Heteroscedastic Autoregressive Residual Errors*
$\underline{\epsilon_i} \sim \mathcal{N}(\underline{0}, \sigma^2(\boldsymbol{\Lambda}_i \boldsymbol{\mathcal{C}}_i \boldsymbol{\Lambda}_i))$ where

$$\boldsymbol{\Lambda}_i = \begin{bmatrix} |\text{TIME}_{i1}|^\delta & 0 & 0 & 0 \\ 0 & |\text{TIME}_{i2}|^\delta & 0 & 0 \\ 0 & 0 & |\text{TIME}_{i3}|^\delta & 0 \\ 0 & 0 & 0 & |\text{TIME}_{i4}|^\delta \end{bmatrix}$$

and

$$\boldsymbol{\mathcal{C}}_i = \begin{bmatrix} 1 & \rho & \rho^2 & \rho^3 \\ \rho & 1 & \rho & \rho^2 \\ \rho^2 & \rho & 1 & \rho \\ \rho^3 & \rho^2 & \rho & 1 \end{bmatrix}$$

```
weights = varPower(form = ~time)
correlation = corAR1(form = ~tp|subject)
fm12.2 <- gls(lm1.form,
              weights = weights,
              correlation = correlation,
              data = armd)
```

## Model 12.3 - corSymm($\cdot$)

*General correlation matrix for Residual Errors*
$\underline{\epsilon_i} \sim \mathcal{N}(\underline{0}, \sigma^2(\mathbf{\Lambda}_i \boldsymbol{\mathcal{C}}_i \mathbf{\Lambda}_i))$ where

$$\mathbf{\Lambda}_i = \begin{bmatrix} |\mathrm{TIME}_{i1}|^\delta & 0 & 0 & 0 \\ 0 & |\mathrm{TIME}_{i2}|^\delta & 0 & 0 \\ 0 & 0 & |\mathrm{TIME}_{i3}|^\delta & 0 \\ 0 & 0 & 0 & |\mathrm{TIME}_{i4}|^\delta \end{bmatrix}$$

and

$$\boldsymbol{\mathcal{C}}_i = \begin{bmatrix} 1 & \rho_{12} & \rho_{13} & \rho_{14} \\ \rho_{12} & 1 & \rho_{23} & \rho_{24} \\ \rho_{13} & \rho_{23} & 1 & \rho_{34} \\ \rho_{14} & \rho_{24} & \rho_{34} & 1 \end{bmatrix}$$

```
weights = varPower(form = ~time)
correlation = corSymm(form = ~tp|subject)
fm12.3 <- gls(lm1.form,
              weights = weights,
              correlation = correlation,
              data = armd)
```

## Model 12.3.b - corSymm($\cdot$) and varIdent($\cdot$)

We now re-fit the model 12.3 with the most general variance function (varIdent) which allows arbitrary (positive) variances of the visual acuity measurements made at different timepoints.
$\underline{\epsilon_i} \sim \mathcal{N}(\underline{0}, \sigma^2(\mathbf{\Lambda}_i \boldsymbol{\mathcal{C}}_i \mathbf{\Lambda}_i))$ where

$$\mathbf{\Lambda}_i = \begin{bmatrix} 1 & 0 & 0 & 0 \\ 0 & \delta_2 & 0 & 0 \\ 0 & 0 & \delta_3 & 0 \\ 0 & 0 & 0 & \delta_4 \end{bmatrix}$$

and

$$\mathcal{C}_i = \begin{bmatrix} 1 & \rho_{12} & \rho_{13} & \rho_{14} \\ \rho_{12} & 1 & \rho_{23} & \rho_{24} \\ \rho_{13} & \rho_{23} & 1 & \rho_{34} \\ \rho_{14} & \rho_{24} & \rho_{34} & 1 \end{bmatrix}$$

```
weights = varIdent(form = ~1|time.f)
correlation = corSymm(form = ~tp|subject)
fm12.3.b <- gls(lm1.form,
                weights = weights,
                correlation = correlation,
                data = armd)
```