Une étude de cas en biomécanique avec la fonction `lme` de R pour modéliser des structures complexes d'effets aléatoires et de matrice de variance-covariance des erreurs

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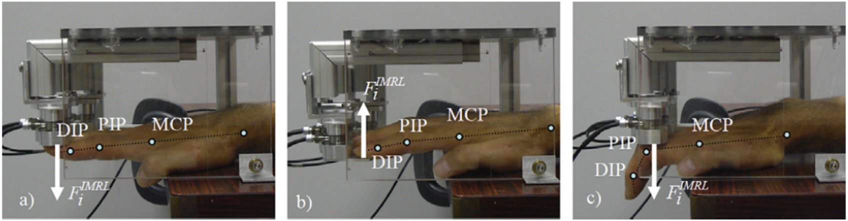
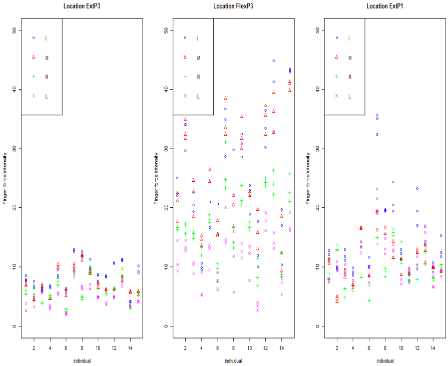
Biomechanical study (1/2)



Experimental setup, from Quaine et al. (2012).

- Aim : understand the coordination patterns of finger forces produced from different tasks
- 15 individuals
- simultaneous fingers force intensity measurements : I, M, R, L
- 3 tasks (locations) : ExtP3, FlexP3, ExtP1
- 3 repeated measures by individual and by location

Biomechanical study (2/2)

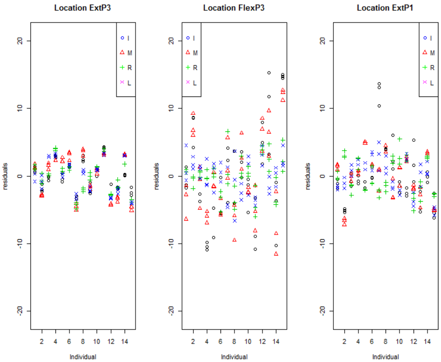


Finger force intensity by location, subject and finger.

- different intensity measures from a location to another and from a finger to another
- variability between locations
- variability between individuals

Two-factor ANOVA with repetitions (1/2)

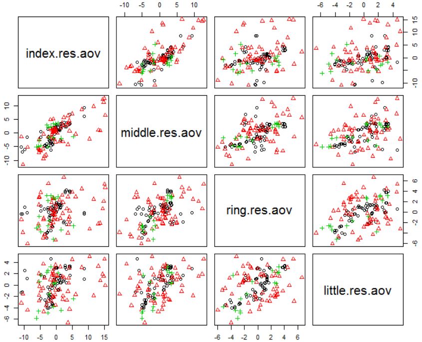
$$ANOVA : F_{lfik} = \mu + \alpha_l + \beta_f + \gamma_{lf} + \delta_i + \varepsilon_{lfik}, \qquad \varepsilon_{lfik} \sim \mathcal{N}(0, \sigma^2).$$



Residuals by location, subject and finger.

- different scattering from one location to another ⇒ need to allow a different variance per location
- different residuals from one individual to another ⇒ need a subject effect modelling

Two-factor ANOVA with repetitions (2/2)



Pairwise scatter plots of the ANOVA residuals for each pair of fingers.

- Residuals very correlated from one finger to another
- Empirical correlations :
  - 0.717 between index and middle,
  - 0.297 between index and ring,
  - 0.330 between index and little,
  - 0.510 between middle and ring,
  - 0.446 between middle and little,
  - 0.440 between ring and little

lme or lmer R library ?

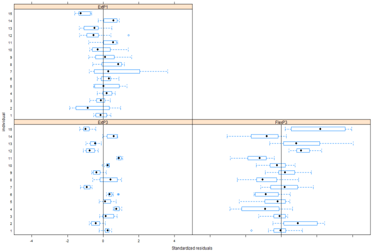
library function	nlme lme	lme4 lmer
Random effects Variance-covariance matrix	nested diagonal or blocked structure (flexible)	nested and crossed diagonal or block diagonal (simple only)
Residual variance-covariance matrix	within-group heteroscedasticity structure (VarFunc class) and within-group correlation structure (corStruct class)	

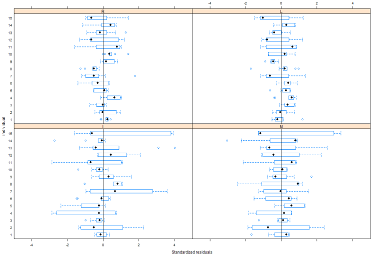
See Bates et al. (2013) for details
$\Rightarrow$ introduction of the random effects using lme

Modelling the random effect structure (1/3)

$$M_0 : F_{lfik} = \mu + \alpha_l + \beta_f + \gamma_{l,f} + \xi_i + \varepsilon_{lfik} \qquad \xi_i \sim \mathcal{N}(0, \tau_1^2), \varepsilon_{lfik} \sim \mathcal{N}(0, \sigma^2).$$

```
> fitM0 <- lme(F ~ finger*location, random=~1|individual, method="ML")
```





Individual boxplots of the standardized residuals by location and by finger

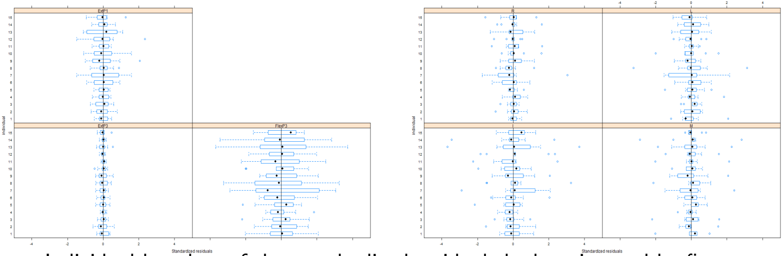
Boxplots by individuals are not centered ⇒ different individual effects from one location to another and from one finger to another.

Modelling the random effect structure (2/3)

$$M_1 : F_{lfik} = \mu+\alpha_l+\beta_f+\gamma_{l,f}+\xi_i+\xi_{il} + \xi_{if} + \xi_{ilf}+\varepsilon_{lfik}, \varepsilon_{lfik} \sim \mathcal{N}(0,\sigma^2)$$

$$\xi_i \sim \mathcal{N}(0,\tau_1^2), \xi_{il} \sim \mathcal{N}(0,\tau_2^2), \xi_{if} \sim \mathcal{N}(0,\tau_3^2), \xi_{ilf} \sim \mathcal{N}(0,\tau_4^2).$$

```
> fitM1 <- lme(F ~ finger*location, random=list(individual=
pdBlocked(list(pdIdent(~1), pdIdent(~location-1), pdIdent(~finger-1),
pdIdent(~location:finger-1)))), method="ML")
```



Individual boxplots of the standardized residuals by location and by finger

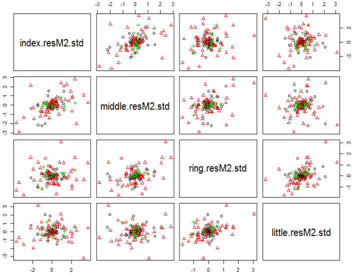
Different residual variability from one location to another ⇒ different variance per location for ξ_{il}.

Modelling the random effect structure (3/3)

$$M_2 : F_{lfik} = \mu+\alpha_l+\beta_f+\gamma_{l,f}+\xi_i+\xi_{il}+\xi_{if}+\xi_{ilf}+\varepsilon_{lfik}, \varepsilon_{lfik} \sim \mathcal{N}(0,\sigma^2)$$
$$\xi_i \sim \mathcal{N}(0,\tau_1^2), \xi_{il} \sim \mathcal{N}(0,\tau_l^2), \xi_{if} \sim \mathcal{N}(0,\tau_3^2), \xi_{ilf} \sim \mathcal{N}(0,\tau_4^2).$$

```
> fitM2 <- lme(F ~ finger*location,
random=list(individual=pdBlocked(list(pdIdent(~1), pdDiag(~location-1),
pdIdent(~finger-1), pdIdent(~location:finger-1)))), method="ML")
```

- The p-value of the likelihood ratio statistic show that M_2 gives a better fit.
- Introducing random effect terms did reduce correlation between fingers : 0.482 I/M, 0.187 I/R, 0.005 I/L, 0.370 M/R, -0.026 M/L, 0.405 R/L.
- M_2 does not improve the residual graphs : different residual variability remains.



Pairwise scatter plots of residuals for each pair of fingers

$\Rightarrow$ need to model the residual variance-covariance structure.

Modelling the residual variance-covariance structure

$$
\begin{aligned}
M_2: \begin{bmatrix} F_{IIik} \\ F_{IMik} \\ F_{IRik} \\ F_{ILik} \end{bmatrix} &= \mu \begin{bmatrix} 1 \\ 1 \\ 1 \\ 1 \end{bmatrix} + \alpha_I \begin{bmatrix} 1 \\ 1 \\ 1 \\ 1 \end{bmatrix} + \begin{bmatrix} \beta_I \\ \beta_M \\ \beta_R \\ \beta_L \end{bmatrix} + \begin{bmatrix} \gamma_{II} \\ \gamma_{IM} \\ \gamma_{IR} \\ \gamma_L \end{bmatrix} \\
&+\xi_i \begin{bmatrix} 1 \\ 1 \\ 1 \\ 1 \end{bmatrix} + \xi_{iI} \begin{bmatrix} 1 \\ 1 \\ 1 \\ 1 \end{bmatrix} + \begin{bmatrix} \xi_{iI} \\ \xi_{iM} \\ \xi_{iR} \\ \xi_{iL} \end{bmatrix} + \begin{bmatrix} \xi_{iII} \\ \xi_{iIM} \\ \xi_{iIR} \\ \xi_{iIL} \end{bmatrix} + \begin{bmatrix} \varepsilon_{IIik} \\ \varepsilon_{IMik} \\ \varepsilon_{IRik} \\ \varepsilon_{ILik} \end{bmatrix} \\
\begin{bmatrix} \varepsilon_{IIik} \\ \varepsilon_{IMik} \\ \varepsilon_{IRik} \\ \varepsilon_{ILik} \end{bmatrix} &\sim \mathcal{N}_4\left(0_4, \sigma^2 VCV\right), \; V = I_4, \; C = I_4
\end{aligned}
$$

Modelling the residual variance-covariance structure

$$M_{2.?}: \begin{bmatrix} F_{IIik} \\ F_{IMik} \\ F_{IRik} \\ F_{ILik} \end{bmatrix} = \mu \begin{bmatrix} 1 \\ 1 \\ 1 \\ 1 \end{bmatrix} + \alpha_I \begin{bmatrix} 1 \\ 1 \\ 1 \\ 1 \end{bmatrix} + \begin{bmatrix} \beta_I \\ \beta_M \\ \beta_R \\ \beta_L \end{bmatrix} + \begin{bmatrix} \gamma_{II} \\ \gamma_{IM} \\ \gamma_{IR} \\ \gamma_L \end{bmatrix}$$

$$+\xi_i \begin{bmatrix} 1 \\ 1 \\ 1 \\ 1 \end{bmatrix} + \xi_{il} \begin{bmatrix} 1 \\ 1 \\ 1 \\ 1 \end{bmatrix} + \begin{bmatrix} \xi_{iI} \\ \xi_{iM} \\ \xi_{iR} \\ \xi_{iL} \end{bmatrix} + \begin{bmatrix} \xi_{iII} \\ \xi_{iIM} \\ \xi_{iIR} \\ \xi_{iIL} \end{bmatrix} + \begin{bmatrix} \varepsilon_{IIik} \\ \varepsilon_{IMik} \\ \varepsilon_{IRik} \\ \varepsilon_{ILik} \end{bmatrix}$$

$$\begin{bmatrix} \varepsilon_{IIik} \\ \varepsilon_{IMik} \\ \varepsilon_{IRik} \\ \varepsilon_{ILik} \end{bmatrix} \sim \mathcal{N}_4 \left(0_4, \sigma^2 V_l C_l V_l \right)$$

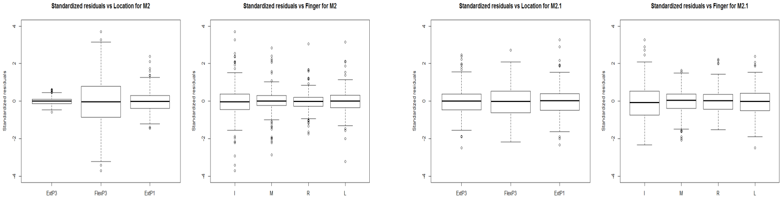
V_l diagonal matrix with standard deviation for each finger in location $l \Rightarrow$ allows heteroscedastic errors

C_l correlation matrix between fingers in location $l \Rightarrow$ allows correlated errors.

Modelling the residual variance matrix V_l (1/2)

$$M_{2.1}: V_l = \begin{bmatrix} \sigma_l & 0 & 0 & 0 \\ 0 & \sigma_l & 0 & 0 \\ 0 & 0 & \sigma_l & 0 \\ 0 & 0 & 0 & \sigma_l \end{bmatrix}, C = \begin{bmatrix} 1 & 0 & 0 & 0 \\ 0 & 1 & 0 & 0 \\ 0 & 0 & 1 & 0 \\ 0 & 0 & 0 & 1 \end{bmatrix}.$$

```
> fitM2.1 <- update(fitM2, weights=varIdent(form=~1|location),
control=lmeControl(msMaxIter=1000))
```



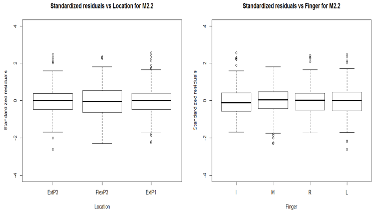
Boxplots of the standardized residuals by location and by finger for model M_2 (left) and model $M_{2.1}$ (right).

Similar residual scattering from one location to another
Different residual scaterring for the index finger w.r.t. the other fingers

Modelling the residual variance matrix V_l (2/2)

$$M_{2.2} : V_l = \begin{bmatrix} \sigma_{II} & 0 & 0 & 0 \\ 0 & \sigma_{Io} & 0 & 0 \\ 0 & 0 & \sigma_{Io} & 0 \\ 0 & 0 & 0 & \sigma_{Io} \end{bmatrix}, C = \begin{bmatrix} 1 & 0 & 0 & 0 \\ 0 & 1 & 0 & 0 \\ 0 & 0 & 1 & 0 \\ 0 & 0 & 0 & 1 \end{bmatrix}.$$

```
> fitM2.2 <-
update(fitM2.1,weights=varIdent(form=~1|location*Index))
```



Boxplots of the standardized residuals by location and by finger for model $M_{2.2}$.

Empirical correlations : 0.450 I/M, 0.053 I/R, 0.003 I/L, 0.198 M/R, -0.054 M/L, 0.330 R/L.

Lower correlations but still non negligeable $\Rightarrow$ need to model correlation between fingers

Modelling the residual correlation matrix C_l

$$M_{2.3} : V_l = \begin{bmatrix} \sigma_{ll} & 0 & 0 & 0 \\ 0 & \sigma_{lo} & 0 & 0 \\ 0 & 0 & \sigma_{lo} & 0 \\ 0 & 0 & 0 & \sigma_{lo} \end{bmatrix}, C = \begin{bmatrix} 1 & \sigma_{MI} & \sigma_{RI} & \sigma_{LI} \\ \sigma_{MI} & 1 & \sigma_{RM} & \sigma_{LM} \\ \sigma_{RI} & \sigma_{RM} & 1 & \sigma_{LR} \\ \sigma_{LI} & \sigma_{LM} & \sigma_{LR} & 1 \end{bmatrix}.$$

```
> fitM2.3 <-
update(fitM2.2,correlation=corSymm(form=~1|individual/trial))
```

- Empirical correlations : 0.435 I/M, 0.077 I/R, -0.001 I/L, 0.187 M/R, -0.100 M/L, 0.316 R/L.
- $\Rightarrow$ need to model different correlation matrix per location :

$$M_{2.4} : V_l = \begin{bmatrix} \sigma_{ll} & 0 & 0 & 0 \\ 0 & \sigma_{lo} & 0 & 0 \\ 0 & 0 & \sigma_{lo} & 0 \\ 0 & 0 & 0 & \sigma_{lo} \end{bmatrix}, C_l = \begin{bmatrix} 1 & \sigma_{MIl} & \sigma_{RIl} & \sigma_{LIl} \\ \sigma_{MIl} & 1 & \sigma_{RMl} & \sigma_{LMl} \\ \sigma_{RIl} & \sigma_{RMl} & 1 & \sigma_{LRl} \\ \sigma_{LIl} & \sigma_{LMl} & \sigma_{LRl} & 1 \end{bmatrix}.$$

```
> fitM2.4 <- update(fitM2.2,correlation=???) ☹
```

Results (1/2)

Final model $M_{2.3}$ fitted with REML for better variances estimates. Confirmed by :

- classical diagnostics plots : residuals fit the normal distribution, except for the extreme tails.
- higher variance components for the random effects than the residual ones

Estimated mean levels of the location-finger crossing groups

Location / finger	Index	Middle	Ring	Little
ExtP3	8.64	7.25	5.90	4.97
FlexP3	25.28	25.47	17.24	11.47
ExtP 1	14.73	11.16	9.83	10.94

Which differences are significant ? : contrasts tests.

Results (2/2)

Location / finger	Index	Middle	Ring	Little
ExtP3	8.64	7.25	5.90	4.97
FlexP3	25.28	25.47	17.24	11.47
ExtP1	14.73	11.16	9.83	10.94

- For one given finger, force intensity measures are significantly different
- For one given location,
  - No significant differences between two consecutive fingers in ExtP3
  - Significant differences between M/R and R/L in FlexP3
  - Significant differences between I/M in ExtP1

Conclusion and perpective

- Managed to model biomechanical data using linear mixed models with complex random effects structures and non-diagonal residual variance-covariance matrices.
- Failed at getting independant normalized residuals.
- Need to develop a new `corStruct` class integrating a more complex correlation matrix in the `nlme` library.

Bates, D. and Maechler, M. and Bolke, B. (2013) lme4 : Linear mixed-effects models using S4 classes, *R package version 0.999999-2*, `http://CRAN.R-project.org/package=lme4`.

Bazzoli, C. and Letué, F. and Martinez, M.J. (2015) Modelling finger force produced from different tasks using linear mixed models with `lme` R function, *CSBIGS*, **6(1)**, 16–36.

Quaine, F. and Paclet, F. and Letué, F. and Moutet, F. (2012) Force sharing and neutral line during finger extension tasks, *Human Movement Science*, **31**, 749–757.