

Mixed models with correlated measurement errors

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Example from Department of Health Technology

25 subjects were exposed to electric pulses of 11 different durations using two different electrodes (pin or patch).

Dependent variable: electric perception

The durations were applied in random order.

In total 550 measurements of response to pulse exposure.

Fixed effects in the model: electrode, Pulseform (duration), order of 22 measurements for each subject.

Order: to take into account habituation effect

Random effects: one random effect for each subject-electrode combination (50 random effects).

Mixed model with random intercepts

Model:

$$y_{ijk} = \mu_{ij} + U_{ij} + \epsilon_{ijk}$$

where $i = 1, \dots, 25$ (subject), $j = \text{pin, patch}$ (electrode), and $k = 1, \dots, 11$ measurement within subject-electrode combination.

U_{ij} 's and ϵ_{ijk} 's independent random variables.

μ_{ij} fixed effect part of the model depending on electrode, Pulseform and order of measurement. In R-code:

```
y~electrode*Pulseform+electrode*Order
```

Note electrode, Pulseform categorical, Order nominal (numerical)

Using lmer

```
fit=lmer(transfPT~electrode*Pulseform+  
         electrode*Order+(1|electrsubId),data=perception)
```

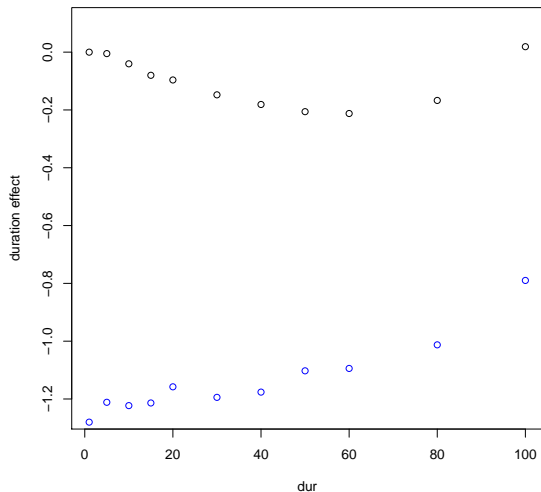
Random effects:

Groups	Name	Variance	Std.Dev.
electrsubId	(Intercept)	0.03479	0.1865
	Residual	0.01317	0.1148

Number of obs: 550, groups: electrsubId, 50

Large subject-electrode variance 0.03479. Noise variance 0.01317

Effect of Pulseform (duration)

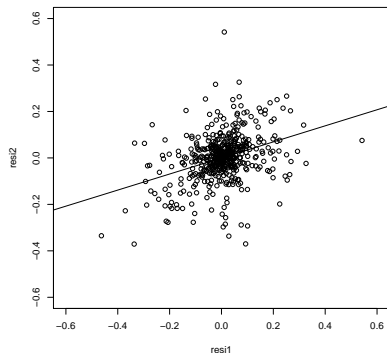


Blue: pin electrode. Black: patch electrode.

Serial correlation in measurement error ?

Maybe error ϵ_{ijk} not independent of previous error $\epsilon_{ij(k-1)}$ since measurements carried out in a sequence for each subject ?

For each subject-electrode combination ij plot residual r_{ijk} (`resid(fit)`) against previous residual $r_{ij(k-1)}$ for $k = 2, \dots, 11$.



Correlation

```
cor.test(resi1,resi2)
```

Pearson's product-moment correlation

```
data:  resi1 and resi2
```

```
t = 8.5284, df = 498, p-value < 2.2e-16
```

```
alternative hypothesis: true correlation is not equal to 0
```

```
95 percent confidence interval:
```

```
 0.2779966 0.4311777
```

```
sample estimates:
```

```
      cor
```

```
0.3569848
```

Mixed model with correlated errors

Analysis of residuals r_{ijk} (which are estimates of errors ϵ_{ijk}) suggests that ϵ_{ijk} are correlated (not independent).

Recall general mixed model formulation:

$$Y = X\beta + ZU + \epsilon$$

where ϵ normal with mean zero and covariance Σ .

So far $\Sigma = \sigma^2 I$ meaning noise terms uncorrelated and all with same variance σ^2

Extension: Σ not diagonal meaning $\text{Cov}[\epsilon_i, \epsilon_{i'}] \neq 0$.

Many possibilities for Σ - we will focus on autoregressive covariance structure that is useful for serially correlated error terms.

Basic model for serial correlation: autoregressive

Consider sequence of noise terms: $\epsilon_{ij1}, \epsilon_{ij2}, \dots, \epsilon_{ij11}$.

Model for variance/covariance:

$$\text{Cov}(\epsilon_{ijk}, \epsilon_{ijk'}) = \sigma^2 \rho^{|k-k'|} \quad \text{Corr}(\epsilon_{ijk}, \epsilon_{ijk'}) = \rho^{|k-k'|} \quad |\rho| < 1$$

Thus

$$\text{Var}\epsilon_i = \sigma^2$$

and ρ is correlation between two consecutive noise terms,

$$\rho = \text{Corr}(\epsilon_{ijk}, \epsilon_{ij(k+1)})$$

Interpretation of autoregressive model

Covariance structure arises from following autoregressive model:

$$\epsilon_{ij(k+1)} = \rho\epsilon_{ijk} + \nu_{ij(k+1)} \quad (1)$$

where $\epsilon_{ij1} \sim N(0, \sigma^2)$, and

$$\nu_{ijl} \sim N(0, \omega) \quad \omega = \sigma^2(1 - \rho^2) \quad l = 2, \dots, 11$$

$\epsilon_{ij1}, \nu_{ij2}, \dots, \nu_{ij11}$ assumed to be independent.

Yet another example of building correlation using independent building blocks !

Implementation

Not possible in lmer :(

However lme (from package nlme) can do the trick:

```
fit=lme(transfPT~electrode*Pulseform+electrode*Order,  
        random=~1|electrsubId,correlation=corAR1())
```

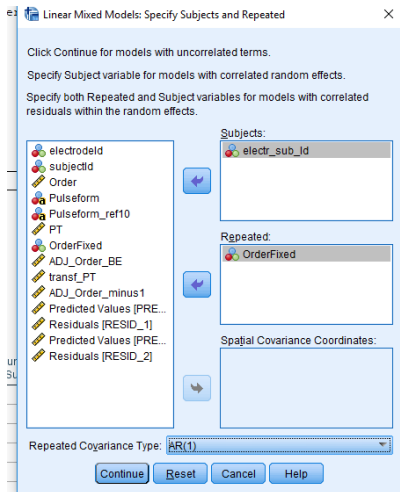
lme predecessor of lmer - both have pros and cons - but here lme has the upper hand.

SPSS: specification using Repeated. Here we can select

- ▶ repeated variable: order of observations within subject
- ▶ subject variable: noise terms for different “subjects” assumed to independent
- ▶ covariance structure for noise terms within subject

E.g. for perception data we may have 11 serially correlated errors for each subject-electrode combination but errors are uncorrelated between different subject-electrode combinations.

Repeated in SPSS



OrderFixed: from 1-11 within each electrode-subject combination

Covariance structure: AR(1)

Estimates of variance parameters

With uncorrelated errors: $\tau^2 = 0.035$ $\sigma^2 = 0.013$ BIC -511

With autoregressive errors: $\tau^2 = 0.030$ $\sigma^2 = 0.018$ BIC -646
 $\rho = 0.626$

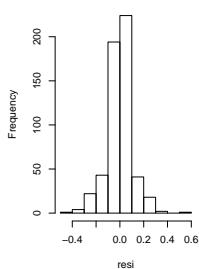
Variance parameters not so different but quite big estimated correlation for errors. BIC clearly favors model with autoregressive errors.

Quite similar (with/without autoregressive errors) fixed effects estimates.

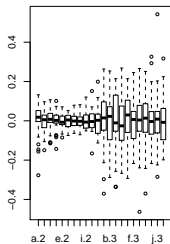
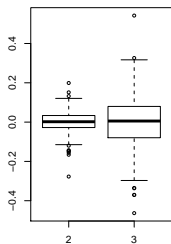
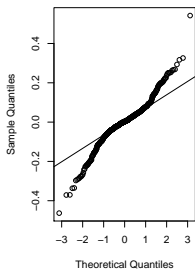
No clear pattern regarding sizes of standard errors of parameter estimates.

Model assessment - residuals

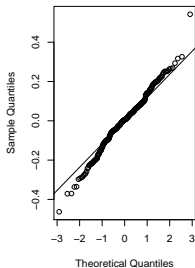
Histogram of resi



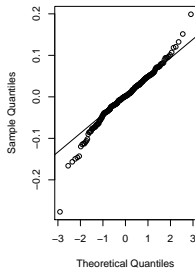
Normal Q-Q Plot



pin



patch



Much larger residual variance for pin electrode than for patch electrode.

Still room for improvement of model !

Can add `weights=varIdent(form=~1|factor(electrode))` in `lme`. Seems not available in SPSS or `lmer`.

Separate analyses for two electrodes ?

Software summary:

	F-test	correlated residuals	variance heterogeneity
<code>lmer</code>	yes	no	no
<code>lme</code>	no	yes	yes
SPSS	yes	yes	no

NB: package `lmerTest` adds fixed effects standard errors for `lmer`

Much larger residual variance for pin electrode than for patch electrode.

Fit model with variance heterogeneity:

```
fithetcorr=lme(transfPT~electrode*Pulseform+electrode*Order,
random=~1|electrsubId,data=perception,
weights=varIdent(form=~1|electrode),correlation=corAR1())
```

Random effects:

```
Formula: ~1 | electrsubId #correlation within electrode-subject
(Intercept) Residual
StdDev:    0.1732323 0.1691177
```

Correlation Structure: AR(1)

```
Formula: ~1 | electrsubId
```

Parameter estimate(s):

```
Phi
0.578185
```

Variance function:

Structure: Different standard deviations per stratum

Formula: ~1 | electrode

Parameter estimates:

pin	patch
1.0000000	0.4122666

BIC -814

Subject variance $0.1732^2 = 0.029$

Variance for pin electrode: $0.1691^2 = 0.028$

Variance for patch electrode: $0.1691^2 \cdot 0.4122^2 = 0.0049$

Exercises

1. Fit model with autoregressive errors to the Orthodont dataset.
2. Given the model (1) verify that $\epsilon_{ij(k+1)} \sim N(0, \sigma^2)$ and $\text{Corr}(\epsilon_{ijk}, \epsilon_{ij(k+1)}) = \rho$.