Mixed models with correlated measurement errors

Rasmus Waagepetersen

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Example from Department of Health Technology

25 subjects where exposed to electric pulses of 11 different durations using two different electrodes (3=pin, 2=patch).

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.

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 $i = 1, \ldots, 25$ (subject), $j = 2, 3$ (electrode), and $k = 1, \ldots, 11$ measurement within subject-electrode combination.

μ_{ij} fixed effect part of the model depending on electrode, Pulseform and order of measurement.

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

Using lmer

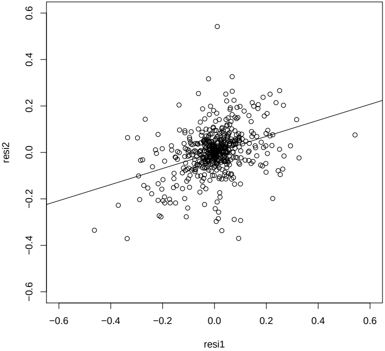
```
fit=lmer(transfPT~electrodeId*Pulseform+
     electrodeId*OrderFixed+(1|electrsubId),data=perceptio

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

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 $k = 2, \ldots, 11$.



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 $\mathbb{C}\mathrm{ov}[\epsilon_{ijk}, \epsilon_{ijk'}] \neq 0$.

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

Σ will be block-diagonal since we assume errors uncorrelated between subject-electrode combinations.

Basic model for serial correlation: autoregressive

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

Model for variance/covariance:

$$\mathbb{C}\mathrm{ov}(\epsilon_{ijk}, \epsilon_{ijk'}) = \sigma^2 \rho^{|k-k'|} \quad \mathbb{C}\mathrm{orr}(\epsilon_{ijk}, \epsilon_{ijk'}) = \rho^{|k-k'|}$$

Thus

$$\mathbb{V}\mathrm{ar}\epsilon_i = \sigma^2$$

and ρ is correlation between two consecutive noise terms,

$$\rho = \mathbb{C}\mathrm{orr}(\epsilon_{ijk}, \epsilon_{ij(k+1)})$$

AR(1) model:

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

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

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

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

Implementation

Not possible in `lmer` :(

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

```
fit=lme(transfPT~factor(electrodeId)*Pulseform+factor(electrodeId)*OrderFixed,
                         random=~1|electrsubId,data=perception,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.

Estimates of variance parameters

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

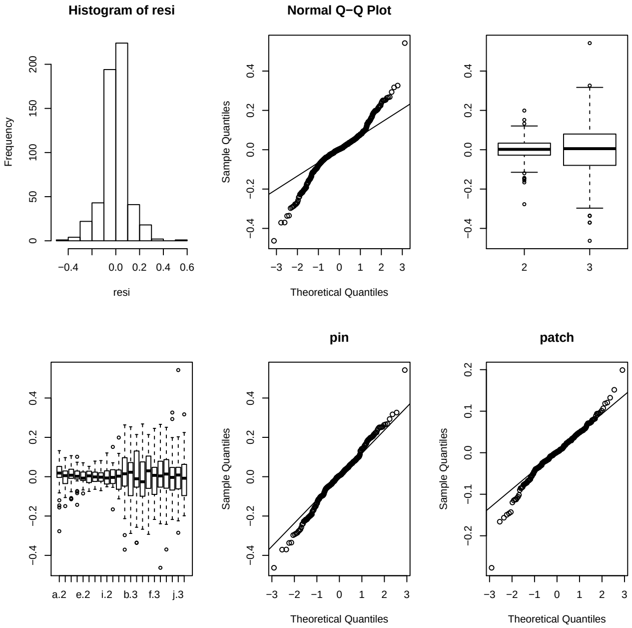
With autoregressive errors: $\tau^2 = 0.030$ $\sigma^2 = 0.018$ BIC -646
$\rho = 0.626$

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

Qualitatively same conclusions regarding significance of fixed effects (F-tests).

Not clear pattern regarding magnitudes of standard errors of parameter estimates (with or without correlated residuals)

Model assessment - residuals



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
        (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 electrode 3: $0.1691^2 = 0.028$
Variance for electrode 2: $0.1691^2 \cdot 0.4122^2 = 0.0049$

Alternative: separate analyses for two electrodes ?