Mixed Model (Analysis) Procedures

Overview

Linear Models
- Fixed effects
- Assumes errors NID
- Least squares (ANOVA, GLM)

Generalized Linear Models
- Fixed effects
- Non-normal (binomial, multinomial, Poisson)
- Iterative techniques (ML, REML implemented in SAS GLIMMIX)

Linear Mixed Models
- Fixed and random effects
- Normal data, can deal with heterogeneity and correlated errors
- Iterative techniques (ML, REML implemented in SAS MIXED)

Generalized Linear Mixed Models
- Fixed and random effects
- Non-normal (binomial, multinomial, Poisson)
- Iterative techniques (ML, REML implemented in SAS GLIMMIX)

Mixed Model Procedures

Model

$$y = X\beta + Zu + e$$

where:

y = a vector of observations
X = design matrix for fixed effects
β = a vector of fixed effects parameters
Z = design matrix for random effects
u = a vector of random effects parameters
e = a vector of residuals

Mixed Model Procedures

Random Effects

$$E\begin{bmatrix} u \\ e \end{bmatrix} = \begin{bmatrix} 0 \\ 0 \end{bmatrix}$$

$$Var\begin{bmatrix} u \\ e \end{bmatrix} = \begin{bmatrix} G & 0 \\ 0 & R \end{bmatrix}$$

$$Var(y) = ZGZ' + R$$

Mixed Model Procedures

Example

<u>Treatments</u>:

Blocks – 2

Treatments – 2

Samples - 2 (repeated on ij)

<u>Model</u>:

$Y_{ijk} = \mu + B_i + T_j + \varepsilon_{ij} + S_k + TS_{ik} + \varepsilon_{ijk}$

Mixed Model Procedures

Example - Observations

$$y = \begin{bmatrix} Y_{111} \\ Y_{112} \\ Y_{121} \\ Y_{122} \\ Y_{211} \\ Y_{212} \\ Y_{221} \\ Y_{222} \end{bmatrix}$$

→ Observation from the i^{th} block, j^{th} treatment, and k^{th} sample.

Mixed Model Procedures

Example – Fixed Effects

$$X = \begin{bmatrix} 1 & 1 & 0 & 1 & 0 & 1 & 0 & 1 & 0 & 0 & 0 \\ 1 & 1 & 0 & 1 & 0 & 0 & 1 & 0 & 1 & 0 & 0 \\ 1 & 0 & 1 & 1 & 0 & 1 & 0 & 1 & 0 & 0 & 0 \\ 1 & 0 & 1 & 1 & 0 & 0 & 1 & 0 & 1 & 0 & 0 \\ 1 & 1 & 0 & 0 & 1 & 1 & 0 & 0 & 0 & 1 & 0 \\ 1 & 1 & 0 & 0 & 1 & 0 & 1 & 0 & 0 & 0 & 1 \\ 1 & 0 & 1 & 0 & 1 & 1 & 0 & 0 & 0 & 1 & 0 \\ 1 & 0 & 1 & 0 & 1 & 0 & 1 & 0 & 0 & 0 & 1 \end{bmatrix}$$

Design Matrix

$$\beta = \begin{bmatrix} \mu \\ B_1 \\ B_2 \\ T_1 \\ T_2 \\ S_1 \\ S_2 \\ TS_{11} \\ TS_{12} \\ TS_{21} \\ TS_{22} \end{bmatrix}$$

Parameters

Mixed Model Procedures

Example – Random Effects

$$Z = \begin{bmatrix} 1 & 0 & 0 & 0 \\ 1 & 0 & 0 & 0 \\ 0 & 1 & 0 & 0 \\ 0 & 1 & 0 & 0 \\ 0 & 0 & 1 & 0 \\ 0 & 0 & 1 & 0 \\ 0 & 0 & 0 & 1 \\ 0 & 0 & 0 & 1 \end{bmatrix}$$

Design Matrix

$$u = \begin{bmatrix} e_{11} \\ e_{12} \\ e_{21} \\ e_{22} \end{bmatrix}$$

Parameters

Mixed Model Procedures

Example - Residuals

$$e = \begin{bmatrix} e_{111} \\ e_{112} \\ e_{121} \\ e_{122} \\ e_{211} \\ e_{212} \\ e_{221} \\ e_{222} \end{bmatrix}$$

→ Residual from the i^{th} block, j^{th} treatment, and k^{th} sample.

Repeated Measures

Standard Error of a Mean Difference
Correlated Measures

$$S_{\bar{x}_1-\bar{x}_2} = \sqrt{(s_p^2 - \sigma_{12})\left(\frac{1}{n_1}+\frac{1}{n_2}\right)}$$

Mixed Model Procedures

Simple Covariance Structure

Repeated measure	Repeated measure			
	time 1	time 2	time 3	time 4
time 1	s^2	0	0	0
time 2	0	s^2	0	0
time 3	0	0	s^2	0
time 4	0	0	0	s^2

Number of parameters = 1

Mixed Model Procedures

Unstructured Covariance Structure

Repeated measure	Repeated measure			
	time 1	time 2	time 3	time 4
time 1	s^2_1	s_{21}	s_{31}	s_{41}
time 2	s_{12}	s^2_2	s_{32}	s_{42}
time 3	s_{13}	s_{23}	s^2_3	s_{43}
time 4	s_{14}	s_{24}	s_{34}	s^2_4

Number of parameters = t(t-1)/2 + t

Mixed Model Procedures

Compound Symmetry Covariance Structure

Repeated measure	Repeated measure			
	time 1	time 2	time 3	time 4
time 1	$s^2 + s_1$	s_1	s_1	s_1
time 2	s_1	$s^2 + s_1$	s_1	s_1
time 3	s_1	s_1	$s^2 + s_1$	s_1
time 4	s_1	s_1	s_1	$s^2 + s_1$

Number of parameters = 2

Mixed Model Procedures
Toeplitz Covariance Structure

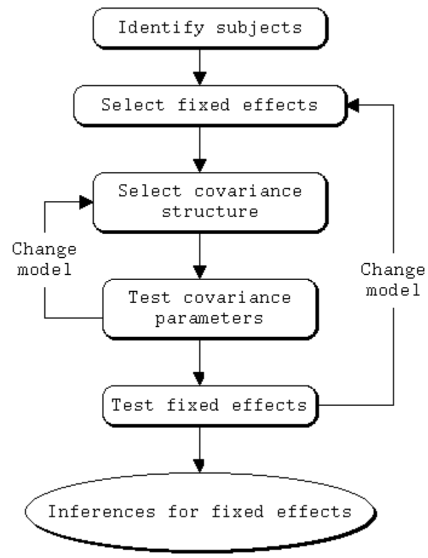
Repeated measure	Repeated measure			
	time 1	time 2	time 3	time 4
time 1	s^2	s_1	s_2	s_3
time 2	s_1	s^2	s_1	s_2
time 3	s_2	s_1	s^2	s_1
time 4	s_3	s_2	s_1	s^2

Number of parameters = t

Mixed Model Procedures
Repeated Measures Approach

- First run the analysis using the UN (unstructured) covariance structure.
- Next run the analysis using the compound symmetry (CS) structure.
- Run the analysis with any other covariance structures that seem reasonable.
- Use the model fitting criteria to compare how well the various structures fit the data.
- Select the model that describes the structure with the least number of parameters.

Mixed Model Repeated Measures



Source: Russ Wolfinger and Ming Chang, SAS Institute Inc., Cary, NC

Mixed Model Procedures

Covariance Structures

Structure	Number Parameters	Equal Spacing	Random Subject*	Equal Variance	Equal Covariance	Equal Correlation
CS	2	No	No	Yes	Yes	Yes
AR(1)	2	Yes	Yes	Yes	No	No
TOEP	t	Yes	No	Yes	No	No
CSH	t+1	No	No	No	No	Yes
ARH(1)	t+1	Yes	Yes	No	No	No
HF	t+1	No	No	No	No	No
TOEPH	2t-1	Yes	No	No	No	No
ANTE(1)	2t-1	No	No	No	No	No
UN	t(t+1)/2	No	No	No	No	No

* Requires Subject = source of variation to be included in the RANDOM statement in PROC MIXED.

Mixed Model Procedures

PROC MIXED Syntax

RCBD Repeated Measures

```
proc mixed;
  class blk trt date;
  model yield = blk trt date
     trt*date /ddfm=satterth;
  <random trt*blk;>
  repeated date / subject=trt*blk
     type=<structure> r rcorr;
run;
```

* Random statement required only for autoregressive structures, AR(1) and ARH(1).

Mixed Model Procedures

Model Fitting Criteria

- Residual Log Likelihood (-2RLL)
- Akaike's Information Criterion (AIC)
- Schwartz'z Bayesian Criterion (BIC)

Mixed Model Procedures

Model Fitting Criteria

Residual Log Likelihood Ratio Test

$$\chi^2 = \Delta\left[-2RLL\right]$$

$$df = \Delta\left[\#\, parameters\right]$$

Mixed Model Procedures

Model Fitting Criteria Example

Model	-2*l*	Parms
un	432.2605	10
cs	572.6072	2

χ^2 = 576.3460 - 432.2605 = 144.09**

9 df

χ^2 = 576.3460 - 572.6072 = 3.74

1 df

Null model -2RLL= 576.3460

1 Variance component – residual error

Mixed Model Procedures
Model Fitting Criteria

- Akaike's Information Criterion (AIC)
  $-2l + 2d$

- Schwartz'z Bayesian Criterion
  $-2l + d \ln(n)$

  d = # parameters
  n = # observations (subjects)

Mixed Model Procedures
Model Fitting Criteria

Model	$-2l$	Parms
un	432.2605	10
cs	572.6072	2

Unstructured
AIC = $-2l + 2d = 432.2605 + 2(10) = 452.3$
BIC = $-2l + d \ln(n) = 432.2605 + 10 \ln(27) = 465.2$

Compound Symmetry
AIC = $-2l + 2d = 572.6072 + 2(2) = 576.7$
BIC = $-2l + d \ln(n) = 572.6072 + 2 \ln(27)= 579.2$

Repeated Measures

Common Agronomic Examples

Experiment Type:

- Perennial crops
  Forages, Horticultural crops
- Crop rotations
  Cumulative effects of crop sequences
- Long-term experiments
  Experiments repeated over many years at same sites

In each of these cases, observations are made over time from the same experimental unit (plot).

The fixed year effect of the treatment is confounded with random growing season effects (weather, pests) and may not be independent from the plot effect.