**Section 2 Notation**

*y =X\beta +Zu + e*

*y \sim \mathcal{N}(X\beta,V)*

*u \sim \mathcal{N}(0,G)*

*e \sim \mathcal{N}(0,R)*

\mbox{V}  = \mbox{Var(y)} = \mbox{ZGZ}^T + R

**Section 3 Roy’s four tests**

**Test 1** Difference between the means of two methods. This test gives the bias and corresponding test statistic and p- value in the “solution for fixed effects” output.

**Test 2** Difference of “between subject” variability of the two methods.

**Test 3** Within subject variability of the two methods ( repeated measures)

**Test 4** Overall variability of the two methods.

\mbox{Block } \Omega_{i} = \mbox{Between Subj. Var. } + \mbox{Within Subj. Var. }

**Section 5 Variance Covariance Decomposition**

PB 5.1.3 Decomposing the Within Group VC structure.

Decompose WGVC into a variance structure component and a correlation structure component.

WGVC = V_{i}C_{i}V_{i}

(In PB, WGVC is denoted as \Lambda_{i})

V_{i} describes the variance of the within-group errors

C_{i} describes the correlation of the within-group errors

**5.1 nlme commands**

Varfunc function is used to specify WG variance models. The two main arguments are ‘value’ and ‘form’.

Corstruct function is used to specify WG correlation models.

corCompSymm implements the CS correlation structure.

**Section 6 - A Roy 2009**

This is the SAS code for fitting the linear mixed effects model to the data of Bland and Altman (1999, Table 1) under the null hypothesis that the two methods, the observer J and the blood pressure monitor S, **do not** have the same within-subject variabilities.

proc mixed data=BloodPressure1 method=ml covtest;

classes subj m\_var rep;

model y=m\_var /**s ddfm=kr**;

random m\_var /**type=un subject=subj** **v vcorr g**;

repeated m\_var/**type= un subject=rep(subj)** **r**;

Here we give the SAS code for fitting the linear mixed effects model to the same data under the alternative hypothesis that the two methods **have** the same within-subject variabilities.\*/

proc mixed data=BloodPressure1 method=ml covtest;

classes subj m\_var rep;

model y=m\_var /**s ddfm=kr**;

random m\_var /**type= un subject=subj** **v vcorr g**;

repeated m\_var/**type= cs subject=rep(subj)** **r**;

run;

The difference is in the arguments to the “repeated” parameter.

**Discussion of the code**

The **proc mixed** statement invokes the procedure, here using the dataset named “**BloodPressure1**.”

The **method = ml** option tells SAS to use full maximum likelihood estimation. [If you omit this option, by default SAS uses restricted maximum likelihood - REML.]

The **covtest** option tells SAS to display tests for the variance components. By default, SAS omits these tests.

The **/s** option [formally **/solution**] on the model statement tells SAS to display the estimated fixed effects (as well as the associated standard errors and hypothesis tests). [Random]

The **/r** option tells SAS to display the blocks of the estimated matrix . [Repeated]

**MAIN COMMANDS**

GROUP: varies covariance parameters by groups (BXC)

SUBJECT: identifies the subjects in the model (ARoy)

TYPE: specifies the covariance structure (Aroy)

**Section 7 - RANDOM STATEMENT**

The RANDOM statement specifies the random effect terms that are to be included in the model, along with a

covariance structure (TYPE= option) to specify how the random effects are related to each other.

More than one RANDOM statement can be used to define a PROC MIXED model.

This is useful when you have some random effects that are correlated, while there are others that need to be independent of those, as in hierarchical models. The SUBJECT= option can be used to specify different hierarchies.

The RANDOM statement defines the random effects constituting the http://support.sas.com/documentation/cdl/en/statug/63033/HTML/default/images/statug_mixed0009.png vector in the mixed model.

It can be used to specify traditional variance component models (as in the VARCOMP procedure) and to specify random coefficients.

Using [Mixed Models notation](http://support.sas.com/documentation/cdl/en/statug/63033/HTML/default/statug_mixed_sect022.htm) , the purpose of the RANDOM statement is to define the http://support.sas.com/documentation/cdl/en/statug/63033/HTML/default/images/statug_mixed0010.png matrix of the mixed model, the random effects in the http://support.sas.com/documentation/cdl/en/statug/63033/HTML/default/images/statug_mixed0009.pngvector, and the structure of http://support.sas.com/documentation/cdl/en/statug/63033/HTML/default/images/statug_mixed0012.png.

The http://support.sas.com/documentation/cdl/en/statug/63033/HTML/default/images/statug_mixed0010.pngmatrix is constructed exactly as the http://support.sas.com/documentation/cdl/en/statug/63033/HTML/default/images/statug_mixed0004.pngmatrix for the fixed effects, and the http://support.sas.com/documentation/cdl/en/statug/63033/HTML/default/images/statug_mixed0012.pngmatrix is constructed to correspond with the effects constituting http://support.sas.com/documentation/cdl/en/statug/63033/HTML/default/images/statug_mixed0010.png.

The structure of http://support.sas.com/documentation/cdl/en/statug/63033/HTML/default/images/statug_mixed0012.pngis defined by using the “[TYPE=](http://support.sas.com/documentation/cdl/en/statug/63033/HTML/default/statug_mixed_sect018.htm#statug.mixed.mixedrandomtype)” option.

..

random m\_var /**type=un subject=subj** **v vcorr g**;

..

“ random m\_var” identifies “m\_var” as the random effect.

“ TYPE=UN “ specifies the covariance structure of http://support.sas.com/documentation/cdl/en/statug/63033/HTML/default/images/statug_mixed0012.png as unstructured.

“subject=subj” identifies the subjects in the mixed model.

**“SUBJECT=effect” [or SUB=effect ]**

This option identifies the subjects in your mixed model. Complete independence is assumed across subjects; thus, for the RANDOM statement, the SUBJECT= option produces a block-diagonal structure in G with identical blocks.

The Z matrix is modified to accommodate this block diagonality.

In fact, specifying a subject effect is equivalent to nesting all other effects in the RANDOM statement within the subject effect.

**Section 8 - REPEATED STATEMENT**

The REPEATED statement controls the covariance structure imposed upon the residuals or errors.

In repeated measures models the SUBJECT= optional statement parameter is used to define which observations belong to the same subject, and which belong to different subjects, where different subjects are independent.

The TYPE= optional statement parameter specifies the model for the covariance structure of the errors.

The GROUP= optional statement parameter permits different levels of the GROUP effect to have different structure parameters, though the structure TYPE remains the same.

Only one REPEATED statement is permitted in a PROC MIXED model.

The REPEATED statement is used to specify the http://support.sas.com/documentation/cdl/en/statug/63033/HTML/default/images/statug_mixed0013.png matrix in the mixed model.

If no REPEATED statement is specified, http://support.sas.com/documentation/cdl/en/statug/63033/HTML/default/images/statug_mixed0013.pngis assumed to be equal to http://support.sas.com/documentation/cdl/en/statug/63033/HTML/default/images/statug_mixed0192.png.

For many repeated measures models, no repeated effect is required in the REPEATED statement. Simply use the “[SUBJECT=](http://support.sas.com/documentation/cdl/en/statug/63033/HTML/default/statug_mixed_sect019.htm#statug.mixed.mixedrepeatedsubject)” option to define the blocks of http://support.sas.com/documentation/cdl/en/statug/63033/HTML/default/images/statug_mixed0013.png and the “[TYPE=](http://support.sas.com/documentation/cdl/en/statug/63033/HTML/default/statug_mixed_sect019.htm#statug.mixed.mixedrepeatedtype)” option to define their covariance structure.

Model 1

….

repeated m\_var/**type= un subject=rep(subj)** **r**;

….

Model 2

….

repeated m\_var/**type= cs subject=rep(subj)** **r**;

….

“ TYPE=UN “ specifies the covariance structure of ***R*** as unstructured.

“ TYPE=CS “ specifies the covariance structure of ***R*** as compound symmetry structure.

**Section 9 - The lme4 and nlme packages**

One of the big differences between the lme4 package and the nlme package, or other software for fitting linear mixed models, is that lme4 is designed to handle models with non-nested random effects.

**Section 9.1 :** The optimization in lmer is done with respect to the elements of the variance-covariance matrix of the random effects relative to σ2. Given these values the conditional estimates of the fixed-effects parameters and of σ2 can be evaluated directly with some linear algebra. In the summary or show output of an lmer model there are two quantities called the MLdeviance and the REMLdeviance.

Those are based on the same relative variances but different conditional estimates of σ2 (and hence different estimates of the elements of the variance-covariance of the random effects). It turns out that there is very little difference in the value of the profiled log-likelihood at the ML estimates and at the REML estimates.

This is not to say that the log-likelihood is similar at the two (complete) sets of estimates - it is the profiled log-likelihoods that are similar and these are what are used to create the likelihood ratio test statistic, even when the models have been fit by REML.

**Section 10 - Other Commands used in Roy’s code**

G requests that the estimated G matrix be displayed. PROC MIXED displays blanks for values that are 0.

If you specify the SUBJECT= option, then the block of the G matrix corresponding to the first subject is displayed.

V requests that blocks of the estimated V matrix be displayed. The first block determined by the SUBJECT= effect is the default displayed block. PROC MIXED displays entries that are 0 as blanks in the table.

VCORR displays the correlation matrix corresponding to the blocks of the estimated matrix.

The value-list specification is the same as in the V= option.

**Section 11 Bland Altmans Data**

Roy includes a table from Bland and Altman’s 1999 paper which shows a set of systolic blood pressure data from a study in which **simultaneous** measurements were made by each of two experienced observers (denoted J and R) using a sphygmomanometer and by a semi-automatic blood pressure monitor (denoted S).

Three sets of readings were made in quick succession.

**SUBJECT=effect [or “SUB=effect” ]**

This option identifies the subjects in your mixed model.

Complete independence is assumed across subjects; therefore, the SUBJECT= option produces a block-diagonal structure in **R** with identical blocks.

When the SUBJECT= effect consists entirely of classification variables, the blocks of **R** correspond to observations sharing the same level of that effect.

These blocks are sorted according to this effect as well.

Bendix Carstensen et al 2008

***R implementation***

> lme( y ˜ meth + item,

+ random = list( item = pdIdent( ˜ meth-1 ) ),

+ weights = varIdent( form = ˜1 | meth ),

+ data=fat

+ )

***SAS implementation***

proc mixed data = rdata ;

class meth item ;

model y = meth item / s;

random meth \* item ;

repeated item / group = meth ;

run ;

**GROUP=effect [ “GRP=effect” ]**

defines an effect specifying heterogeneity in the covariance structure of R.

All observations having the same level of the GROUP effect have the same covariance parameters.

Each new level of the GROUP effect produces a new set of covariance parameters with the same structure as the original group.

You should exercise caution in properly defining the GROUP effect, because strange covariance patterns can result with its misuse. Also, the GROUP effect can greatly increase the number of estimated covariance parameters, which can adversely affect the optimization process.

**Summary**

1. Specify Maximum likelihood.
2. Display the estimated fixed effects, with associated inference values.
3. Call tests for the variance components.

getVarCov(..., type = random.effects) - extracts the covariance matrix of the random effects

lme for SAS PROC MIXED Users - Douglas Bates

The VarCorr function returns a table of variance estimates, the

corresponding standard deviations, and the estimated correlations.

The value of VarCorr is a character matrix, not a numeric matrix.

In general the random statement in PROC MIXED is

easy to translate into nlme. The repeated statement isn't.

The basic approach in lme is to define one or more factors that represent the grouping of the observations. In the example above the data contain the information that the grouping is by the "Subject"

factor

> formula(Oxboys)

height ~ age | Subject

A full specification of the model in fm1 is

> fm2 <- lme(fixed = height ~ age, data = Oxboys, random = ~ age | Subject)

> VarCorr(fm2)

Subject = pdLogChol(age)

Variance StdDev Corr

(Intercept) 65.3038159 8.081078 (Intr)

age 2.8248081 1.680717 0.641

Residual 0.4354534 0.659889