M. Two-way Random Effects ANOVA

The factors in higher-way ANOVAs can again be considered fixed or random, depending on the context of the study. For each factor:

- Are the levels of that factor of direct interest? Or do they just represent some larger “population” of levels that could have been included?
- If the study were to be conducted again, would the exact same levels of that factor be used again? Or would other levels be used?
Example Potassium measurements across labs

Ten commercial laboratories across the UK were chosen by administrators of the National Quality Control Scheme are interested in the differences across labs in measuring potassium in serum samples. Ten serum samples are created, each of which contains a pre-determined quantity of potassium. Each specimen is divided into ten equal portions. One portion from each specimen is sent to each lab in a completely randomized design.
Outcome =

Predictors =

Predictors should be fixed or random?
When would labs be considered a fixed factor?

When would labs be considered a random factor?
Example Inter-rater reliability

Studies of HIV+ patients on anti-retroviral treatments are interested in how the treatments may contribute to changes in metabolism, which can lead to changes in body shape. Changes which seem obvious to the eye can be difficult, however, to measure consistently (e.g., increased surface body fat).
Design a: Research nursing staff need to be trained to measure sub-scapular skin fold with calipers for an ongoing single-center clinical trial. $a$ patients are randomly chosen; the $b$ nurses measure each patient $r$ times in a randomized order (often $r = 1$ or $r = 2$).

Fixed or random:

Patients?

Nurses?
Design b: To assist in planning a clinical trial, researchers need to understand how consistently nursing staff can measure sub-scapular skin fold, since there will be several clinical sites once the trial begins. *a* patients are randomly chosen from the Principle Investigator’s clinic and the *b* nurses on staff there measure each patient *r* times in a randomized order (again, often *r* = 1 or *r* = 2).

Fixed or random:

Patients?

Nurses?
Two-way Random Effects Model

\[ Y_{ijk} = \mu + a_i + b_j + (ab)_{ij} + \epsilon_{ijk} \]

\[ a_i \sim iid \ N(0, \sigma_a^2) \]
\[ b_j \sim iid \ N(0, \sigma_b^2) \]
\[ (ab)_{ij} \sim iid \ N(0, \sigma_{ab}^2) \]
\[ \epsilon_{ijk} \sim iid \ N(0, \sigma_e^2) \]

where \( i = 1, \ldots, a \), \( j = 1, \ldots, b \), and \( k = 1, \ldots, r \) and \( a_i \), \( b_j \), \( (ab)_{ij} \), and \( \epsilon_{ijk} \) are all independent of each other.
\[ E[Y_{ijk}] = \]

\[ \text{Var}[Y_{ijk}] = \]

Note that this is still a model which assumes homoscedasticity across all observations.
$\text{Cov}[Y_{ijk}, Y_{ij'k'}] = \text{310}$
\text{Cov}[Y_{i,j,k}, Y'_{i',j',k'}] =
$\text{Cov}[Y_{ijk}, Y_{ijk'}] =$
Based on this model,

\[
\text{inter-rater reliability} = \frac{\sigma_a^2}{\sigma_a^2 + \sigma_b^2 + \sigma_{ab}^2 + \sigma_e^2}
\]

\[
\text{intra-rater reliability} = \frac{\sigma_b^2}{\sigma_a^2 + \sigma_b^2 + \sigma_{ab}^2 + \sigma_e^2}
\]

But watch out – interpretation is suspect if \(\sigma_{ab}^2 \neq 0!!\)

When \(a\) and \(b\) are small, we will not be able to estimate the variance components very well.
Estimation in PROC GLM

Using PROC GLM, mean estimation and sums of squares computation proceed exactly as they did for the fixed effects two-way ANOVA. With random effects, however, expected mean squares will change, and hence F-tests may change as well.

\[ \hat{\mu}_{..} = \bar{Y}_{..} \]

\[ \text{Var}[\hat{\mu}_{..}] = \frac{\hat{\sigma}^2_a}{a} + \frac{\hat{\sigma}^2_b}{b} + \frac{\hat{\sigma}^2_{ab}}{ab} + \frac{\hat{\sigma}^2_e}{rab} \]

Tests and confidence intervals can be constructed as usual.
### Testing

<table>
<thead>
<tr>
<th>Source</th>
<th>df</th>
<th>SS</th>
</tr>
</thead>
<tbody>
<tr>
<td>A</td>
<td>$a - 1$</td>
<td>$rb \sum_i (\bar{Y}<em>{i..} - \bar{Y}</em>{...})^2$</td>
</tr>
<tr>
<td>B</td>
<td>$b - 1$</td>
<td>$ra \sum_j (\bar{Y}<em>{.j} - \bar{Y}</em>{...})^2$</td>
</tr>
<tr>
<td>$AB$</td>
<td>$(a - 1)(b - 1)$</td>
<td>$r \sum_i \sum_j (\bar{Y}<em>{i.j} - \bar{Y}</em>{i..} - \bar{Y}<em>{.j} + \bar{Y}</em>{...})^2$</td>
</tr>
<tr>
<td>Error</td>
<td>$(r - 1)ab$</td>
<td>$\sum_i \sum_j (\bar{Y}<em>{ijk} - \bar{Y}</em>{ij.})^2$</td>
</tr>
<tr>
<td>Total</td>
<td>$rab - 1$</td>
<td>$\sum_i \sum_j (\bar{Y}<em>{ijk} - \bar{Y}</em>{...})^2$</td>
</tr>
<tr>
<td>Source</td>
<td>E[MS]</td>
<td>$F^*$</td>
</tr>
<tr>
<td>--------</td>
<td>-------</td>
<td>------</td>
</tr>
<tr>
<td>$A$</td>
<td>$\sigma_e^2 + rb\sigma_a^2 + r\sigma_{ab}^2$</td>
<td></td>
</tr>
<tr>
<td>$B$</td>
<td>$\sigma_e^2 + ra\sigma_b^2 + r\sigma_{ab}^2$</td>
<td></td>
</tr>
<tr>
<td>$AB$</td>
<td>$\sigma_e^2 + r\sigma_{ab}^2$</td>
<td></td>
</tr>
<tr>
<td>Error</td>
<td>$\sigma_e^2$</td>
<td></td>
</tr>
<tr>
<td>Total</td>
<td></td>
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</tr>
</tbody>
</table>
To test $H_0 : \sigma_{ab}^2 = 0$, reject $H_0$ at level $\alpha$ if $F_{AB}^* =$

To test $H_0 : \sigma_b^2 = 0$, reject $H_0$ at level $\alpha$ if $F_B^* =$

To test $H_0 : \sigma_a^2 = 0$, reject $H_0$ at level $\alpha$ if $F_A^* =$
Point estimates for the variance components are found by setting the observed mean squares equal to the expected mean squares and solving.

\[ MSA = \sigma^2 + rb\sigma_a^2 + r\sigma_{ab}^2 = MSE + rb\sigma_a^2 + r\sigma_{ab}^2 \]

\[ MSB = \sigma^2 + ra\sigma_b^2 + r\sigma_{ab}^2 = MSE + ra\sigma_b^2 + r\sigma_{ab}^2 \]

\[ MSA = \sigma^2 + r\sigma_{ab}^2 = MSE + r\sigma_{ab}^2 \]

\[ \Rightarrow \sigma_{ab}^2 = \frac{MSAB - MSE}{r} \]

\[ \sigma_b^2 = \frac{MSB - MSE - r\left(\frac{MSAB - MSE}{r}\right)}{ra} = \frac{MSB - MSAB}{ra} \]

\[ \sigma_a^2 = \frac{MSA - MSE - r\left(\frac{MSAB - MSE}{r}\right)}{rb} = \frac{MSA - MSAB}{rb} \]
\[
\rho = \frac{\sigma_b^2}{\sigma_a^2 + \sigma_b^2 + \sigma_{ab}^2 + \sigma_e^2}
\]

For all of these parameters, only approximate interval estimates exist, as for the one-way ANOVA. See Neter, Kutner, Nachtsheim, and Wasserman (1996), Chapter 24.
Estimation in PROC MIXED

As for the one-way random effects ANOVA, PROC GLM doesn’t actually fit a two-way random effects ANOVA. It fits a fixed effects ANOVA and then modifies the F-tests shown in the output to correspond to the appropriate expected mean squares.

We can use PROC MIXED instead.
PROC MIXED DATA=data;
CLASS a b;
MODEL y = / SOLUTION;
RANDOM INT / SUBJ=a SOLUTION;
RANDOM INT / SUBJ=b SOLUTION;
RANDOM INT / SUBJ=a*b SOLUTION;

Estimation is done via REML and testing is done with likelihood ratio tests or Z tests.
Using a likelihood ratio test, we can compare, for example,

Full model: $Y_{ijk} = \mu + a_i + b_j + (ab)_{ij} + \epsilon_{ijk}$

Reduced model: $Y_{ij} = \mu + a_i + b_j + \epsilon_{ij}$

We reject $H_0 : \sigma_{ab}^2 = 0$ at level $\alpha$ if

$$T^* = -2(\ell_{\text{Reduced}} - \ell_{\text{Full}}) > q_\alpha$$

where $\ell$ is the log likelihood and $q_\alpha$ is ???
There is no theory derived for this case. A conservative approach would be to compare $T^*$ to the $\alpha$-quantile of a $\chi^2_1$. 
SAS does offer a Z-test alternative in PROC MIXED by specifying

```
PROC MIXED DATA=dat COVTEST;
```

A z-test is constructed for each variance component:

\[
Z^* = \frac{\hat{\sigma}^2}{\sqrt{\text{Var}[\hat{\sigma}^2]}}
\]

and we reject \(H_0 : \sigma^2 = 0\) if \(z^* > z_\alpha\) (one-sided test).

What is the downside to this test?
Diagnostics

Diagnostics are carried out as for the one-way random effects ANOVA.
Higher-way Random ANOVAs

For some higher-way random ANOVAs such as a three-way model, the ANOVA table from PROC GLM shows that some factors cannot be tested. For example, with three factors $A$, $B$, and $C$,

$$E[MSA] = \sigma_e^2 + r\sigma_{abc}^2 + rc\sigma_{ab}^2 + rb\sigma_{ac}^2 + rbc\sigma_a^2$$

but no term in the model has expected mean square

$$\sigma_e^2 + r\sigma_{abc}^2 + rc\sigma_{ab}^2 + rb\sigma_{ac}^2$$

which we would need to write down an F-test for the main effect of $A$. 

Thus when using PROC GLM, one or more interactions must be dropped from the model to get a test for $A$, or the General Linear F-test approach can be used. It is preferable to just use PROC MIXED.

Otherwise, all procedures for higher way random ANOVAs are similar to those for the two-way model.