Chapter 571

Mixed Models (Simulation)

Introduction

This procedure power analyzes random effects designs in which the outcome (response) is continuous. Thus, as with the analysis of variance (ANOVA), the procedure is used to test hypotheses comparing various group means. Unlike ANOVA, this procedure relaxes the strict assumptions regarding the variances of the groups. Random effects models are commonly used to analyze longitudinal (repeated measures) data.

This procedure extends many of the classical statistical techniques to the case when the variances are not equal, such as

- Two-sample designs (extending the t-test)
- One-way layout designs (extending one-way ANOVA)
- Factorial designs (extending factorial GLM)
- Split-plot designs (extending split-plot GLM)
- Repeated-measures designs (extending repeated-measures GLM)
- Cross-over designs (extending GLM)

Types of Linear Mixed Models

Several linear mixed model subtypes exist that are characterized by the random effects, fixed effects, and covariance structure they involve. These include fixed effects models, random effects models, and covariance pattern models.

Fixed Effects Models

A fixed effects model is a model where only fixed effects are included in the model. An effect (or factor) is fixed if the levels in the study represent all levels of interest of the factor, or at least all levels that are important for inference (e.g., treatment, dose, etc.). No random components are present. The general linear model is a fixed effects model. Fixed effects models can include interactions. The fixed effects can be estimated and tested using the F-test.

The fixed effects in the model include those factors for which means, standard errors, and confidence intervals will be estimated and tests of hypotheses will be performed. Other variables for which the model is to be adjusted (that are not important for estimation or hypothesis testing) can also be included in the model as fixed factors.

Random Effects Models

A random effects model includes both fixed and random terms in the model. An effect (or factor) is random if the levels of the factor represent a random subset of a larger group of levels (e.g., patients). The random effects are not tested, but are included to make the model more realistic.
**Longitudinal Data Models**

Longitudinal data arises when more than one response is measured on each subject in the study. Responses are often measured over time at fixed time points. A time point is fixed if it is pre-specified. Various variance-matrix structures can be employed to model the variance and correlation among repeated measurements.

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**Types of Factors**

**Between-Subject Factors**

Between-subject factors are those that separate the experimental subjects into groups. If twelve subjects are randomly assigned to three treatment groups (four subjects per group), treatment is a between-subject factor.

**Within-Subject Factors**

Within-subject factors are those in which the response is measured on the same subject at several time points. Within-subject factors are those factors for which multiple levels of the factor are measured on the same subject. If each subject is measured at the low, medium, and high level of the treatment, treatment is a within-subject factor.

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**Technical Details**

**What is a Mixed Model?**

In a general linear model (GLM), a random sample of the individuals in is drawn. Treatments are applied to each individual and an outcome is measured. The data so obtained are analyzed using an analysis of variance table that includes an F-test.

A mathematical model may be formulated that underlies each analysis of variance. This model expresses the response variable as the sum of population parameters and a residual. For example, a common linear model for a two-factor experiment is

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

where \(i = 1, 2, \ldots, I\) (the number of levels of factor 1), \(j = 1, 2, \ldots, J\) (the number of levels of factor 2), and \(k = 1, 2, \ldots, K\) (the number of subjects in the study). This model expresses the value of the response variable, \(Y\), as the sum of five components:

- \(\mu\) the mean.
- \(a_i\) the contribution of the \(i^{th}\) level of a factor A.
- \(b_j\) the contribution of the \(j^{th}\) level of a factor B.
- \((ab)_{ij}\) the combined contribution (or interaction) of the \(i^{th}\) level of a factor A and the \(j^{th}\) level of a factor B.
- \(e_{ijk}\) the contribution of the \(k^{th}\) individual. This is often called the residual.

In this example, the linear model is made up of *fixed effects* only. An effect is fixed if the levels in the study represent all levels of the factor that are of interest, or at least all levels that are important for inference (e.g., treatment, dose, etc.).
The following assumptions are made when using the F-test in a general linear model.

1. The response variable is continuous.
2. The individuals are independent.
3. The $e_{ijk}$ follow the normal probability distribution with mean equal to zero.
4. The variances of the $e_{ijk}$ are equal for all values of $i$, $j$, and $k$.

The Linear Mixed Model (LMM)

The linear mixed model (LMM) is a natural extension of the general linear model. Mixed models extend linear models by allowing for the addition of random effects, where the levels of the factor represent a random subset of a larger group of all possible levels (e.g., time of administration, clinic, etc.). For example, the two-factor linear model above could be augmented to include random effects such as an adjustment for each patient, since a patient may be assumed to be a random realization from a distribution of patients. The general form of the mixed model in matrix notation is

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

where

- $y$ vector of responses
- $X$ known design matrix of the fixed effects
- $\beta$ unknown vector of fixed effects parameters to be estimated
- $Z$ known design matrix of the random effects
- $u$ unknown vector of random effects
- $\varepsilon$ unobserved vector of random errors

We assume

$$ u \sim N(0,G) $$
$$ \varepsilon \sim N(0,R) $$
$$ \text{Cov}[u, \varepsilon] = 0 $$

where

- $G$ variance-covariance matrix of $u$
- $R$ variance-covariance matrix of the errors $\varepsilon$

The variance-covariance matrix of $y$, denoted $V$, is

$$ V = \text{Var}[y] $$
$$ = \text{Var}[X\beta + Zu + \varepsilon] $$
$$ = 0 + \text{Var}[Zu + \varepsilon] $$
$$ = ZGZ' + R $$
Individual Subject Formulation

Because of the size of the matrices that are involved in mixed model analysis, it is useful for computational purposes to reduce the dimensionality of the problem by analyzing the data one subject at a time. Because the data from different subjects are statistically independent, the log-likelihood of the data can be summed over the subjects, according to the formulas below. Before we look at the likelihood functions, we examine the linear mixed model for a particular subject:

$$y_i = X_i \beta + Z_i u_i + \varepsilon_i, \quad i = 1, \ldots, N$$

where

- $y_i$ is an $n_i \times 1$ vector of responses for subject $i$.
- $X_i$ is an $n_i \times p$ design matrix of fixed effects for subject $i$ ($p$ is the number of columns in $X$).
- $\beta$ is a $p \times 1$ vector of regression parameters.
- $Z_i$ is an $n_i \times q$ design matrix of the random effects for subject $i$.
- $u_i$ is a $q \times 1$ vector of random effects for subject $i$ which has means of zero and covariance matrix $G_{sub}$.
- $\varepsilon_i$ is an $n_i \times 1$ vector of errors for subject $i$ with zero mean and covariance $R_i$.
- $n_i$ is the number of repeated measurements on subject $i$.
- $N$ is the number of subjects.

The following definitions will also be useful.

- $e_i$ is a vector of residuals for subject $i$ ($e_i = y_i - X_i \beta$).
- $V_i = \text{Var}[y_i] = Z_i G_{sub} Z_i' + R_i$.

To see how the individual subject mixed model formulation relates to the general form, we have

$$y = \begin{pmatrix} y_1 \\ y_2 \\ \vdots \\ y_N \end{pmatrix}, \quad X = \begin{pmatrix} X_1 \\ X_2 \\ \vdots \\ X_N \end{pmatrix}, \quad Z = \begin{pmatrix} Z_1 & 0 & 0 \\ 0 & \ddots & 0 \\ 0 & 0 & Z_N \end{pmatrix}, \quad u = \begin{pmatrix} u_1 \\ u_2 \\ \vdots \\ u_N \end{pmatrix}, \quad \varepsilon = \begin{pmatrix} \varepsilon_1 \\ \varepsilon_2 \\ \vdots \\ \varepsilon_N \end{pmatrix}$$

In order to test the parameters in $\beta$, which is typically the goal in LMM analysis, the unknown parameters ($\beta, G,$ and $R$) must be estimated. Estimates for $\beta$ require estimates of $G$ and $R$. In order to estimate $G$ and $R$, the structure of $G$ and $R$ must be specified. Details of the specific structures for $G$ and $R$ are discussed later.

The following assumptions are made when using the F-test in a LMM.

1. The response variable is continuous.
2. The individuals are independent.
3. The responses follow the normal probability distribution with mean equal to zero and variance structure given by $V$.

A distinct (and arguably the most important) advantage of LMM over the GLM is flexibility in random error and random effect variance component modeling (note that the equal-variance assumption of GLM is not necessary for LMM). LMM allows you to model both heterogeneous variances and correlations among observations through the specification of the covariance matrix structures for $u$ and $\varepsilon$. The variance matrix estimates are obtained using maximum likelihood (ML) or, more commonly, restricted maximum likelihood (REML). The fixed effects in the mixed model are tested using F-tests.
Structure of the Variance-Covariance Matrix

**The G Matrix**

The \( G \) matrix is the variance-covariance matrix for the random effects \( u \). Typically, when the \( G \) matrix is used to specify the variance-covariance structure of \( y \), the structure for \( R \) is simply \( \sigma^2 I \). Caution should be used when both \( G \) and \( R \) are specified as complex structures, since large numbers of sometimes redundant covariance elements can result.

The \( G \) matrix is made up of \( N \) symmetric \( G_{sub} \) matrices,

\[
G = \begin{pmatrix}
G_{sub} & 0 & 0 & \cdots & 0 \\
0 & G_{sub} & 0 & \cdots & 0 \\
0 & 0 & G_{sub} & \cdots & 0 \\
\vdots & \vdots & \vdots & \ddots & \vdots \\
0 & 0 & 0 & \cdots & G_{sub}
\end{pmatrix}
\]

The dimension of \( G_{sub} \) is \( q \times q \), where \( q \) is the number of random effects for each subject.

**Structures of \( G_{sub} \)**

The structure of the \( G_{sub} \) matrix in this procedure is diagonal.

\[
G_{sub} = \begin{pmatrix}
\sigma_1^2 \\
\sigma_2^2 \\
\sigma_3^2 \\
\sigma_4^2 
\end{pmatrix}
\]

**The R Matrix**

The \( R \) matrix is the variance-covariance matrix for errors, \( \varepsilon \). When the \( R \) matrix is used to specify the variance-covariance structure of \( y \), the \( G_{sub} \) matrix is not used.

The full \( R \) matrix is made up of \( N \) symmetric \( R \) sub-matrices,

\[
R = \begin{pmatrix}
R_1 & 0 & 0 & \cdots & 0 \\
0 & R_2 & 0 & \cdots & 0 \\
0 & 0 & R_3 & \cdots & 0 \\
\vdots & \vdots & \vdots & \ddots & \vdots \\
0 & 0 & 0 & \cdots & R_N
\end{pmatrix}
\]

where \( R_1, R_2, R_3, \cdots, R_N \) are all of the same structure.
## Structures of R

There are many possible structures for the sub-matrices that make up the \( R \) matrix. The \( R_{\text{Sub}} \) structures that can be specified in \textsc{PASS} are shown below.

### Diagonal

<table>
<thead>
<tr>
<th>Homogeneous</th>
<th>Heterogeneous</th>
<th>Correlation</th>
</tr>
</thead>
</table>
| \[
\begin{pmatrix}
\sigma^2 \\
\sigma^2 \\
\sigma^2 \\
\end{pmatrix}
\]  
| \[
\begin{pmatrix}
\sigma_1^2 \\
\sigma_2^2 \\
\sigma_3^2 \\
\end{pmatrix}
\]  
| \[
\begin{pmatrix}
1 \\
1 \\
1 \\
\end{pmatrix}
\]  |

### Compound Symmetry

<table>
<thead>
<tr>
<th>Homogeneous</th>
<th>Heterogeneous</th>
<th>Correlation</th>
</tr>
</thead>
</table>
| \[
\begin{pmatrix}
\sigma^2 & \rho \sigma^2 & \rho \sigma^2 \\
\rho \sigma^2 & \sigma^2 & \rho \sigma^2 \\
\rho \sigma^2 & \rho \sigma^2 & \sigma^2 \\
\end{pmatrix}
\]  
| \[
\begin{pmatrix}
\sigma_1^2 & \rho \sigma_1 \sigma_2 & \rho \sigma_1 \sigma_3 \\
\rho \sigma_2 \sigma_1 & \sigma_2^2 & \rho \sigma_2 \sigma_3 \\
\rho \sigma_3 \sigma_1 & \rho \sigma_3 \sigma_2 & \sigma_3^2 \\
\end{pmatrix}
\]  
| \[
\begin{pmatrix}
1 & \rho & \rho & \rho \\
\rho & 1 & \rho & \rho \\
\rho & \rho & 1 & \rho \\
\rho & \rho & \rho & 1 \\
\end{pmatrix}
\]  |

### AR(1)

<table>
<thead>
<tr>
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<th>Heterogeneous</th>
</tr>
</thead>
</table>
| \[
\begin{pmatrix}
\sigma^2 & \rho \sigma^2 & \rho^2 \sigma^2 & \rho^3 \sigma^2 \\
\rho \sigma^2 & \sigma^2 & \rho^2 \sigma^2 & \rho^3 \sigma^2 \\
\rho^2 \sigma^2 & \rho \sigma^2 & \sigma^2 & \rho^2 \sigma^2 \\
\rho^3 \sigma^2 & \rho^2 \sigma^2 & \rho \sigma^2 & \sigma^2 \\
\end{pmatrix}
\]  
| \[
\begin{pmatrix}
\sigma_1^2 & \rho \sigma_1 \sigma_2 & \rho^2 \sigma_1 \sigma_3 & \rho^3 \sigma_1 \sigma_4 \\
\rho \sigma_2 \sigma_1 & \sigma_2^2 & \rho \sigma_2 \sigma_3 & \rho^2 \sigma_2 \sigma_4 \\
\rho \sigma_3 \sigma_1 & \rho \sigma_3 \sigma_2 & \sigma_3^2 & \rho \sigma_3 \sigma_4 \\
\rho \sigma_4 \sigma_1 & \rho \sigma_4 \sigma_2 & \rho \sigma_4 \sigma_3 & \sigma_4^2 \\
\end{pmatrix}
\]  |

### Toeplitz

<table>
<thead>
<tr>
<th>Homogeneous</th>
<th>Heterogeneous</th>
</tr>
</thead>
</table>
| \[
\begin{pmatrix}
\sigma^2 & \rho_1 \sigma^2 & \rho_2 \sigma^2 & \rho_3 \sigma^2 \\
\rho_1 \sigma^2 & \sigma^2 & \rho_2 \sigma^2 & \rho_3 \sigma^2 \\
\rho_2 \sigma^2 & \rho_1 \sigma^2 & \sigma^2 & \rho_3 \sigma^2 \\
\rho_3 \sigma^2 & \rho_2 \sigma^2 & \rho_1 \sigma^2 & \sigma^2 \\
\end{pmatrix}
\]  
| \[
\begin{pmatrix}
\sigma_1^2 & \rho_1 \sigma_1 \sigma_2 & \rho_2 \sigma_1 \sigma_3 & \rho_3 \sigma_1 \sigma_4 \\
\rho_1 \sigma_2 \sigma_1 & \sigma_2^2 & \rho_1 \sigma_2 \sigma_3 & \rho_2 \sigma_2 \sigma_4 \\
\rho_2 \sigma_3 \sigma_1 & \rho_2 \sigma_3 \sigma_2 & \sigma_3^2 & \rho_3 \sigma_3 \sigma_4 \\
\rho_3 \sigma_4 \sigma_1 & \rho_3 \sigma_4 \sigma_2 & \rho_4 \sigma_4 \sigma_3 & \sigma_4^2 \\
\end{pmatrix}
\]  |
Correlation
\[
\begin{pmatrix}
1 & \rho_1 & \rho_2 & \rho_3 \\
\rho_1 & 1 & \rho_2 & \rho_3 \\
\rho_2 & \rho_1 & 1 & \rho_3 \\
\rho_3 & \rho_2 & \rho_1 & 1
\end{pmatrix}
\]

**Toeplitz(2)**

Homogeneous
\[
\begin{pmatrix}
\sigma^2 & \rho_1 \sigma^2 \\
\rho_1 \sigma^2 & \sigma^2 \\
\rho_1 \sigma^2 & \sigma^2 \\
\rho_1 \sigma^2 & \sigma^2
\end{pmatrix}
\]

Heterogeneous
\[
\begin{pmatrix}
\sigma_1^2 & \rho_1 \sigma_1 \sigma_2 \\
\rho_1 \sigma_1 \sigma_2 & \sigma_2^2 \\
\rho_1 \sigma_1 \sigma_2 & \sigma_2^2 \\
\rho_1 \sigma_1 \sigma_2 & \sigma_2^2
\end{pmatrix}
\]

**Banded(2)**

Homogeneous
\[
\begin{pmatrix}
\sigma^2 & \rho \sigma^2 \\
\rho \sigma^2 & \sigma^2 \\
\rho \sigma^2 & \sigma^2 \\
\rho \sigma^2 & \sigma^2
\end{pmatrix}
\]

Heterogeneous
\[
\begin{pmatrix}
\sigma_1^2 & \rho \sigma_1 \sigma_2 \\
\rho \sigma_1 \sigma_2 & \sigma_2^2 \\
\rho \sigma_1 \sigma_2 & \sigma_2^2 \\
\rho \sigma_1 \sigma_2 & \sigma_2^2
\end{pmatrix}
\]

Correlation
\[
\begin{pmatrix}
1 & \rho \\
\rho & 1 \\
\rho & 1 \\
\rho & 1
\end{pmatrix}
\]

Note: This is the same as Toeplitz(1).

**Banded(3)**

Homogeneous
\[
\begin{pmatrix}
\sigma^2 & \rho \sigma^2 & \rho \sigma^2 \\
\rho \sigma^2 & \sigma^2 & \rho \sigma^2 \\
\rho \sigma^2 & \rho \sigma^2 & \sigma^2 \\
\rho \sigma^2 & \rho \sigma^2 & \sigma^2
\end{pmatrix}
\]

Heterogeneous
\[
\begin{pmatrix}
\sigma_1^2 & \rho \sigma_1 \sigma_2 & \rho \sigma_1 \sigma_3 \\
\rho \sigma_1 \sigma_2 & \sigma_2^2 & \rho \sigma_2 \sigma_3 \\
\rho \sigma_1 \sigma_3 & \rho \sigma_2 \sigma_3 & \sigma_3^2 & \rho \sigma_3 \sigma_4 \\
\rho \sigma_1 \sigma_3 & \rho \sigma_2 \sigma_3 & \rho \sigma_3 \sigma_4 & \sigma_4^2
\end{pmatrix}
\]

Correlation
\[
\begin{pmatrix}
1 & \rho & \rho \\
\rho & 1 & \rho \\
\rho & 1 & \rho \\
\rho & 1 & \rho
\end{pmatrix}
\]
### Likelihood Formulas

There are two types of likelihood estimation methods that are generally considered in mixed model estimation: maximum likelihood (ML) and restricted maximum likelihood (REML). REML is generally favored over ML because the variance estimates using REML are unbiased for small sample sizes, whereas ML estimates are unbiased only asymptotically (see Littell et al., 2006 or Demidenko, 2004). Both estimation methods are available in PASS.

#### Maximum Likelihood

The general form -2 log-likelihood ML function is

\[-2L_{ML}(\beta, G, R) = \ln|V| + e'Ve + N_T \ln(2\pi)\]

The equivalent individual subject form is

\[-2L_{ML}(\beta, G, R) = \sum_{i=1}^{N} (\ln|V_i| + e_i'Ve_i'e_i) + N_T \ln(2\pi)\]

where \(N_T\) is the total number of observations, or

\[N_T = \sum_{i=1}^{N} n_i\]
Restricted Maximum Likelihood

The general form -2 log-likelihood REML function is

\[-2L_{\text{REML}}(\beta, G, R) = \ln|V| + e'e^{-1}e + \ln|X'V^{-1}X| + (N_T - p)\ln(2\pi)\]

The equivalent individual subject form is

\[-2L_{\text{REML}}(\beta, G, R) = \sum_{i=1}^{N} \left[ \ln|V_i| + e_i'e_i^{-1}e_i \right] + \ln\left| \sum_{i=1}^{N} X'V_i^{-1}X_i \right| + (N_T - p)\ln(2\pi)\]

where, again, \(N_T\) is the total number of observations, or

\[N_T = \sum_{i=1}^{N} n_i\]

and \(p\) is the number of columns in \(X\) or \(X_i\).

Estimating and Testing Fixed Effects Parameters

The estimation phase in the analysis of a mixed model produces variance and covariance parameter estimates of the elements of \(G\) and \(R\), giving \(\hat{R}\) and \(\hat{G}\), and hence, \(\hat{V}\). The REML and ML solutions for \(\hat{\beta}\) are given by

\[\hat{\beta} = \left(X\hat{V}^{-1}X\right)^{-1}X\hat{V}^{-1}y\]

with estimated variance-covariance

\[\hat{\Sigma} = \text{var}(\hat{\beta}) = \left(X\hat{V}^{-1}X\right)^{-1}\]

See, for example, Brown and Prescott (2006), Muller and Stewart (2006), or Demidenko (2004) for more details of the estimating equations.

Hypothesis tests and confidence intervals for \(\beta\) are formed using a linear combination matrix (or vector) \(L\). Although you don’t have to specify \(L\), it is important that you understand how its function.

L Matrix Details

\(L\) matrices specify linear combinations of \(\beta\) corresponding to means or hypothesis tests of interest. Essentially, the \(L\) matrix defines the mean or test. The number of columns in each \(L\) matrix is the same as the number of elements of \(\beta\). For estimating a particular mean, the \(L\) matrix consists of a single row. For hypothesis tests, the number of rows of \(L\) varies according to the test. Below are some examples of \(L\) matrices that arise in common analyses:

<table>
<thead>
<tr>
<th>No.</th>
<th>Effect</th>
<th>Food</th>
<th>L1</th>
<th>L2</th>
<th>L3</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>Intercept</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>2</td>
<td>Food</td>
<td>HighIron</td>
<td>1.0000</td>
<td>1.0000</td>
<td>1.0000</td>
</tr>
<tr>
<td>3</td>
<td>Food</td>
<td>LowIron</td>
<td>-1.0000</td>
<td>1.0000</td>
<td>1.0000</td>
</tr>
<tr>
<td>4</td>
<td>Food</td>
<td>None</td>
<td></td>
<td>-1.0000</td>
<td></td>
</tr>
<tr>
<td>5</td>
<td>Food</td>
<td>Salicyl</td>
<td></td>
<td></td>
<td>-1.0000</td>
</tr>
</tbody>
</table>
Mixed Models (Simulation)

L Matrix for a Single Mean (LowIron) of a Single Factor (4 levels) in a Single-Factor Model

<table>
<thead>
<tr>
<th>No.</th>
<th>Effect</th>
<th>Food</th>
<th>L1</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>Intercept</td>
<td>1.0000</td>
<td></td>
</tr>
<tr>
<td>2</td>
<td>Food</td>
<td>HighIron</td>
<td></td>
</tr>
<tr>
<td>3</td>
<td>Food</td>
<td>LowIron</td>
<td>1.0000</td>
</tr>
<tr>
<td>4</td>
<td>Food</td>
<td>None</td>
<td></td>
</tr>
<tr>
<td>5</td>
<td>Food</td>
<td>Salicyl</td>
<td></td>
</tr>
</tbody>
</table>

L Matrix for Testing a Single Factor (Drug – 3 levels) in a Two-Factor Model with Interaction

<table>
<thead>
<tr>
<th>No.</th>
<th>Effect</th>
<th>Drug</th>
<th>Time</th>
<th>L1</th>
<th>L2</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>Intercept</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>2</td>
<td>Drug</td>
<td>Kerlosin</td>
<td>0.5</td>
<td>0.1667</td>
<td>0.1667</td>
</tr>
<tr>
<td>3</td>
<td>Drug</td>
<td>Laposec</td>
<td>1</td>
<td>0.1667</td>
<td>0.1667</td>
</tr>
<tr>
<td>4</td>
<td>Drug</td>
<td>Kerlosin</td>
<td>1.5</td>
<td>0.1667</td>
<td>0.1667</td>
</tr>
<tr>
<td>5</td>
<td>Drug</td>
<td>Kerlosin</td>
<td>2</td>
<td>0.1667</td>
<td>0.1667</td>
</tr>
<tr>
<td>6</td>
<td>Drug</td>
<td>Kerlosin</td>
<td>2.5</td>
<td>0.1667</td>
<td>0.1667</td>
</tr>
<tr>
<td>7</td>
<td>Drug</td>
<td>Kerlosin</td>
<td>3</td>
<td>0.1667</td>
<td>0.1667</td>
</tr>
<tr>
<td>8</td>
<td>Drug</td>
<td>Kerlosin</td>
<td>0.5</td>
<td>-0.1667</td>
<td></td>
</tr>
<tr>
<td>9</td>
<td>Drug</td>
<td>Kerlosin</td>
<td>1</td>
<td>-0.1667</td>
<td></td>
</tr>
<tr>
<td>10</td>
<td>Drug</td>
<td>Kerlosin</td>
<td>1.5</td>
<td>-0.1667</td>
<td></td>
</tr>
<tr>
<td>11</td>
<td>Drug</td>
<td>Kerlosin</td>
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<td>-0.1667</td>
<td></td>
</tr>
<tr>
<td>12</td>
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<td>Kerlosin</td>
<td>2.5</td>
<td>-0.1667</td>
<td></td>
</tr>
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<td>Kerlosin</td>
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<td>-0.1667</td>
<td></td>
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<tr>
<td>14</td>
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<td>Laposec</td>
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<td>-0.1667</td>
<td></td>
</tr>
<tr>
<td>15</td>
<td>Drug</td>
<td>Laposec</td>
<td>1</td>
<td>-0.1667</td>
<td></td>
</tr>
<tr>
<td>16</td>
<td>Drug</td>
<td>Laposec</td>
<td>1.5</td>
<td>-0.1667</td>
<td></td>
</tr>
<tr>
<td>17</td>
<td>Drug</td>
<td>Laposec</td>
<td>2</td>
<td>-0.1667</td>
<td></td>
</tr>
<tr>
<td>18</td>
<td>Drug</td>
<td>Laposec</td>
<td>2.5</td>
<td>-0.1667</td>
<td></td>
</tr>
<tr>
<td>19</td>
<td>Drug</td>
<td>Laposec</td>
<td>3</td>
<td>-0.1667</td>
<td></td>
</tr>
<tr>
<td>20</td>
<td>Drug</td>
<td>Placebo</td>
<td>0.5</td>
<td>-0.1667</td>
<td></td>
</tr>
<tr>
<td>21</td>
<td>Drug</td>
<td>Placebo</td>
<td>1</td>
<td>-0.1667</td>
<td></td>
</tr>
<tr>
<td>22</td>
<td>Drug</td>
<td>Placebo</td>
<td>1.5</td>
<td>-0.1667</td>
<td></td>
</tr>
<tr>
<td>23</td>
<td>Drug</td>
<td>Placebo</td>
<td>2</td>
<td>-0.1667</td>
<td></td>
</tr>
<tr>
<td>24</td>
<td>Drug</td>
<td>Placebo</td>
<td>2.5</td>
<td>-0.1667</td>
<td></td>
</tr>
<tr>
<td>25</td>
<td>Drug</td>
<td>Placebo</td>
<td>3</td>
<td>-0.1667</td>
<td></td>
</tr>
</tbody>
</table>

Kenward and Roger Fixed Effects Hypothesis Tests

Hypothesis tests have the general form

\[ H_0: L \beta = 0 \]

where \( L \) is a linear contrast matrix of rank \( h \) corresponding to the desired comparisons to be made in the hypothesis test. Let \( d \) be the denominator degrees of freedom and \( q \) be the number of variance-covariance parameters, which is the dimension of \( W \) (defined below).

The Kenward and Roger (1997) test statistic for testing \( H_0 \) is currently the most recommended method of specifying the F-ratio and its degrees of freedom. The F-ratio is

\[
F_{h,d} = \frac{\hat{\lambda}}{h} \hat{\beta}' L (L'C L')^{-1} L \hat{\beta}
\]
where

\[ C^* = C + 2C \left\{ \sum_{r=1}^{q} \sum_{s=1}^{q} W_{rs} \left( Q_{rs} - P_r C P_s - \frac{1}{4} S_{rs} \right) \right\} C \]

\[ C = (X' V^{-1} X)^{-1} \]

\[ Q_{rs} = X' V^{-1} \hat{V}_r V^{-1} \hat{V}_s V^{-1} X = \sum_{i=1}^{N} X_i' V_i^{-1} \hat{V}_r V_i V_i^{-1} \hat{V}_s V_i^{-1} X_i \]

\[ P_r = -X' V^{-1} \hat{V}_r V^{-1} X = -\sum_{i=1}^{N} X_i' V_i^{-1} \hat{V}_r V_i V_i^{-1} X_i \]

\[ S_{rs} = X' V^{-1} \hat{V}_r V^{-1} X = \sum_{i=1}^{N} X_i' V_i^{-1} \hat{V}_{rs} V_i V_i^{-1} X_i \]

\[ W = H^{-1} \]

\[ \{H\}_{rs} = \{\text{Hessian}\}_{rs} \]

\[ \hat{V}_r = \frac{\partial V}{\partial \sigma_r} \]

\[ \hat{V}_{rs} = \frac{\partial^2 V}{\partial \sigma_r \partial \sigma_s} \]

\[ T = L'(LCL')^{-1} L \]

\[ a_i = \sum_{r=1}^{q} \sum_{s=1}^{q} W_{rs} \text{tr}(TCP_r C) \text{tr}(TCP_s C) \]

\[ a_2 = \sum_{r=1}^{q} \sum_{s=1}^{q} W_{rs} \text{tr}(TCP_r CTCP_s C) \]

\[ a_3 = \frac{a_1 + 6a_2}{2h}, \quad e = \left( 1 - \frac{a_2}{h} \right)^{-1}, \quad \nu = \frac{2}{h} \left\{ \frac{1 + c_4 a_3}{(1 - c_2 a_3)^2(1 - c_3 a_3)} \right\} \]

\[ c_1 = \frac{g}{3h + 2(1 - g)}, \quad c_2 = \frac{h - g}{3h + 2(1 - g)}, \quad c_3 = \frac{h + 2 - g}{3h + 2(1 - g)}, \quad c_4 = \frac{\nu}{2e^2} \]

\[ g = \frac{(h + 1)a_1 - (h + 4)a_2}{(h + 2)a_2} \]

\[ d = 4 + \frac{h + 2}{c_4 h - 1}, \quad \lambda = \frac{d}{e(d-2)} \]
Solution Algorithms


There are four techniques in the Mixed Models procedure for determining the maximum likelihood or restricted maximum likelihood solution (optimum): Newton-Raphson, Fisher Scoring, MIVQUE, and Differential Evolution.

The general steps for the Newton-Raphson, Fisher Scoring, and Differential Evolution techniques are (let \( \mathbf{\theta} \) be the overall covariance parameter vector):

1. Roughly estimate \( \mathbf{\theta} \) according to the specified structure for each.
2. Evaluate the likelihood of the model given the data and the estimates of \( \mathbf{\theta} \).
3. Improve upon the estimates of \( \mathbf{\theta} \) using a search algorithm. (Improvement is defined as an increase in likelihood.)
4. Iterate until maximum likelihood is reached, according to some convergence criterion.
5. Use the final \( \mathbf{\theta} \) estimates to estimate \( \mathbf{\beta} \).

Newton-Raphson and Fisher Scoring

The differences in the techniques revolve around the initial estimates in Step 1, and the improvements in estimates made in Step 3. For the Newton-Raphson and Fisher Scoring techniques, Step 3 occurs as follows:

3a. With the estimated \( \mathbf{\theta} \), compute the gradient vector \( \mathbf{g} \), and the Hessian matrix \( \mathbf{H} \).
3b. Compute \( \mathbf{d} = -\mathbf{H}^{-1}\mathbf{g} \).
3c. Let \( \lambda = 1 \).
3d. Compute new estimates for \( \mathbf{\theta} \), iteratively, using \( \mathbf{\theta}_{i+1} = \mathbf{\theta}_i + \lambda \mathbf{d} \).
3e. If \( \mathbf{\theta}_i \) is a valid set of covariance parameters and improves the likelihood, continue to 3f. Otherwise, reduce \( \lambda \) by half and return to Step 3d.
3f. Check for convergence. If the convergence criteria (small change in -2log-likelihood) are met, stop. If the convergence criteria are not met, go back to Step 3a.

The gradient vector \( \mathbf{g} \), and the Hessian matrix \( \mathbf{H} \), used for the Newton-Raphson and Fisher Scoring techniques for solving the REML equations are shown in the following table:

<table>
<thead>
<tr>
<th>Technique</th>
<th>Gradient (( \mathbf{g} ))</th>
<th>Hessian (( \mathbf{H} ))</th>
</tr>
</thead>
<tbody>
<tr>
<td>Newton-Raphson</td>
<td>( g_1 + g_2 + g_3 )</td>
<td>( H_1 + H_2 + H_3 )</td>
</tr>
<tr>
<td>Fisher Scoring</td>
<td>( g_1 + g_2 + g_3 )</td>
<td>( -H_1 + H_3 )</td>
</tr>
</tbody>
</table>

The gradient vector \( \mathbf{g} \), and the Hessian matrix \( \mathbf{H} \), used for the Newton-Raphson and Fisher Scoring techniques for solving the ML equations are shown in the following table:

<table>
<thead>
<tr>
<th>Technique</th>
<th>Gradient (( \mathbf{g} ))</th>
<th>Hessian (( \mathbf{H} ))</th>
</tr>
</thead>
<tbody>
<tr>
<td>Newton-Raphson</td>
<td>( g_1 + g_2 )</td>
<td>( H_1 + H_2 )</td>
</tr>
<tr>
<td>Fisher Scoring</td>
<td>( g_1 + g_2 )</td>
<td>( -H_1 )</td>
</tr>
</tbody>
</table>

where \( g_1, g_2, H_1, H_2, \) and \( H_3 \) are defined as in Wolfinger, Tobias, and Sall (1994).
Definitions

\[
\hat{V}_i = \frac{\partial V_i}{\partial \sigma_r}, \quad \hat{V}_ri = \frac{\partial^2 V_i}{\partial \sigma_r \partial \sigma_s}, \quad e_i = y_i - X_i \beta, \quad A_i = X'_i V_i^{-1} X_i, \quad A = \sum_{i=1}^{N} A_i, \quad C = A^{-1},
\]

\[
\hat{A}_r = \sum X'_i \left( \frac{\partial V_i^{-1}}{\partial \sigma_r} \right) X_i = -\sum X'_i (V_i^{-1} \hat{V}_ri V_i^{-1}) X_i = -P_r
\]

\[
X^* = XK, \quad KK' = (X'VX)^{-1}
\]

Likelihoods

\[
I_1 = \frac{1}{2} \sum_{i=1}^{N} \ln |V_i|, \quad I_2 = \frac{1}{2} \sum_{i=1}^{N} e'_i V_i^{-1} e_i, \quad I_3 = \frac{1}{2} \ln \left( \sum_{i=1}^{N} X'_i V_i^{-1} X_i \right) = \frac{1}{2} \ln \left( \sum_{i=1}^{N} A_i \right) = \frac{1}{2} \ln |A|
\]

First Derivatives

\[
g_{1r} = \frac{\partial I_1}{\partial \sigma_r} = \frac{1}{2} \sum_{i=1}^{N} \text{tr}(V_i^{-1} \hat{V}_ri)
\]

\[
g_{2r} = \frac{\partial I_2}{\partial \sigma_r} = -\frac{1}{2} \sum_{i=1}^{N} e'_i V_i^{-1} \hat{V}_ri V_i^{-1} e_i
\]

\[
g_{3r} = \frac{\partial I_3}{\partial \sigma_r} = -\frac{1}{2} \text{tr}[H'_3]
\]

Second Derivatives

\[
H_{1rs} = \frac{\partial^2 I_1}{\partial \sigma_r \partial \sigma_s} = -\frac{1}{2} \sum_{i=1}^{N} \left( \text{tr}(V_i^{-1} \hat{V}_ri) - \text{tr}(V_i^{-1} \hat{V}_ri V_i^{-1} \hat{V}_si) \right)
\]

\[
H_{2rs} = \frac{\partial^2 I_2}{\partial \sigma_r \partial \sigma_s} = \frac{1}{2} \left( H'^{rs}_2 - 2 H'^{rs}_2 H'^{rs}_2 \right)
\]

\[
H_{3rs} = \frac{\partial^2 I_3}{\partial \sigma_r \partial \sigma_s} = \frac{1}{2} \text{tr}(H'^{rs}_3 - H'^{rs}_3 H'^{rs}_3)
\]

See Wolfinger, Tobias, and Sall (1994), page 1299, for details.

**MIVQUE**

The MIVQUE estimates of \( \theta \) in REML estimation are found by solving

\[
-(H_i + H_3) \theta = -g_2.
\]

The MIVQUE estimates of \( \theta \) in ML estimation are found by solving

\[
-H_1 \theta = -g_2.
\]

See Wolfinger, Tobias, and Sall (1994), page 1306, for details.
**Differential Evolution**

The differential evolution techniques used in this procedure for the ML and REML optimization are described in Price, Storn, and Lampinen (2005). This algorithm is very slow, but it is also very robust. As it stands now, it is too slow to be used. However, as computers become faster, this algorithm will become more viable.

---

**Specifying the Minimum Detectable Difference**

The four main parameters of a power analysis are the sample size, the effect size, the significance level, and the power level. Other extraneous parameters, such as the variance, must also be specified. This section describes the specification of the effect size, or minimum detectable difference (MDD) as we choose to call it in this chapter.

Power is defined as the probability of rejecting the null hypothesis of zero difference when the actual difference is a given amount. As the size of the actual difference increases, so does the power. The MDD (or minimum effect size) is the smallest difference among the population means that will be detected by an experiment at the specified settings of the other parameters.

Typically, a longitudinal design includes a between-subjects factor, a within-subject factor, and their interaction. A MDD must be specified for each. As the number of factors grows, the number of interactions grows, and the number of MDD’s that must be specified also grows. It becomes crucial that you specify these values in a meaningful and accurate way.

In the Repeated Measures module, PASS only requires the standard deviation of the group means. Unfortunately, this is a quantity that researchers have very little experience with. It seldom appears on any of the standard reports that are produced by commercial software. It is seldom present in the written reports of analyses. A different method is used to specify the MDD in PASS.

In this routine, the MDD is specified as the difference between the smallest and largest effects. For example, suppose that a factor has three levels with means 10, 15, 18. The detectable difference is 18 – 10 = 8. This is a simply quantity that is easy to interpret.

**The Effect Pattern for Factors**

When there are more than two means, the minimum detectable difference does not uniquely define a set of means that can be simulated. For example the following sets of means all have identical MDD’s, but the means themselves are quite different: (10, 12, 18), (10, 14, 18), and (10, 18, 18). The following method for defining the pattern is quite informative:

1. Set the first (low) value to -0.5.
2. Set the last (high) value to 0.5.
3. Set each value in between to (Mean – Min) / MDD – 0.5.

Using these steps, the three sets of means may be reduced to MDD and a pattern as follows:

<table>
<thead>
<tr>
<th>Original</th>
<th>MDD</th>
<th>Pattern</th>
<th>MDD x Pattern</th>
</tr>
</thead>
<tbody>
<tr>
<td>10, 12, 18</td>
<td>8</td>
<td>-0.5, -0.25, 0.5</td>
<td>-4, -2, 4</td>
</tr>
<tr>
<td>10, 14, 18</td>
<td>8</td>
<td>-0.5, 0.0, 0.5</td>
<td>-4, 0, 4</td>
</tr>
<tr>
<td>10, 18, 18</td>
<td>8</td>
<td>-0.5, 0.5, 0.5</td>
<td>-4, 4, 4</td>
</tr>
</tbody>
</table>

Thus, each set of means can be easily reduced to two components: the MDD and a pattern. This is the method that PASS uses to supply the sets of means. Using this method, it is easy to compare various sizes of means. You simply enter different values for the MDD, keeping the pattern the same.
The Effect Pattern for Interactions

Specifying the structure of the interactions is a little more problematic. Often, you are not interested in the interaction. When the interaction is of interest, you may have only a vague idea of its structure. Part of your analysis will be to investigate the effect of the interaction, with little or no knowledge of its pattern beforehand.

Specifying the MDD for the interaction is somewhat intuitive. The MDD defines the largest difference among the interaction effects. A difficulty still arises in that there is a very large number of possible patterns, many of which are useful. For planning purposes, we have decided to use a standard pattern in PASS. The interaction pattern used in PASS is defined as the Kronecker product of the factor patterns that make up the interaction, scaled so that the largest value is 0.5 and the smallest value is -0.5.

Example

Suppose that a two-factor interaction is made up of a three-level factor A with a pattern of -0.5, 0, 0.5 and a two-level factor B with a pattern of -0.5, 0.5. The interaction pattern would be found as follows. The Kronecker product of these two patterns is 0.25, -0.25, 0.0, 0.0, -0.25, 0.25. Rescaling so that the minimum is -0.5 and the maximum is 0.5 is achieved by doubling the values. The final interaction pattern is 0.5, -0.5, 0.0, 0.0, -0.5, 0.5. This pattern compares the difference due to factor B across the levels of factor A.

Suppose the MDD for A is set to 8, the MDD for B is set to 15, and the MDD for AB is set to 10. Suppose the overall mean is 12. The six cell means would be found by adding the individual effects as follows

<table>
<thead>
<tr>
<th></th>
<th></th>
<th></th>
<th></th>
<th></th>
<th></th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td>A</td>
<td>-4.0</td>
<td>-4.0</td>
<td>0.0</td>
<td>0.0</td>
<td>4.0</td>
<td>4.0</td>
</tr>
<tr>
<td>B</td>
<td>-7.5</td>
<td>7.5</td>
<td>-7.5</td>
<td>7.5</td>
<td>-7.5</td>
<td>7.5</td>
</tr>
<tr>
<td>AB</td>
<td>5.0</td>
<td>-5.0</td>
<td>0.0</td>
<td>0.0</td>
<td>-5.0</td>
<td>5.0</td>
</tr>
<tr>
<td>Total</td>
<td>-6.5</td>
<td>-1.5</td>
<td>-7.5</td>
<td>7.5</td>
<td>-8.5</td>
<td>16.5</td>
</tr>
<tr>
<td>Overall</td>
<td>12.0</td>
<td>12.0</td>
<td>12.0</td>
<td>12.0</td>
<td>12.0</td>
<td>12.0</td>
</tr>
<tr>
<td>Cell Mean</td>
<td>5.5</td>
<td>10.5</td>
<td>4.5</td>
<td>19.5</td>
<td>3.5</td>
<td>28.5</td>
</tr>
</tbody>
</table>

The cell means are then used to simulate the data for power and sample size calculation. This set of cell means has the MDD’s and patterns specified.

Specifying the Simulated Variance-Covariance Matrix

As stated above, the variance of y is \( V = ZGZ' + R \). In this PASS Mixed Models module, \( ZGZ' \) is called the random component and R is called the residual component. Since V is block-diagonal (with one block for each subject), it is specified by specifying the random and residual components for one subject and repeating those components for each subject.

\( ZGZ' \)

When the random component is included, the model is called a random effects model. For a design with four time points, the structure of \( ZGZ' \) is

\[
\begin{pmatrix}
g & g & g & g \\
g & g & g & g \\
g & g & g & g \\
g & g & g & g \\
\end{pmatrix} = g[J_4]
\]

This structure only requires a single value: g.
The structure of $R$ is quite flexible. Since it is a variance-covariance matrix, the only stipulation is that it must be non-negative definite. Possible choices for $R$ when the variance is constant are

**Diagonal**

$$
\begin{pmatrix}
\sigma^2 \\
\sigma^2 \\
\sigma^2 \\
\sigma^2 \\
\end{pmatrix}
$$

**Constant (Compound Symmetric)**

$$
\begin{pmatrix}
\sigma^2 & \rho \sigma^2 & \rho \sigma^2 & \rho \sigma^2 \\
\rho \sigma^2 & \sigma^2 & \rho \sigma^2 & \rho \sigma^2 \\
\rho \sigma^2 & \rho \sigma^2 & \sigma^2 & \rho \sigma^2 \\
\rho \sigma^2 & \rho \sigma^2 & \rho \sigma^2 & \sigma^2 \\
\end{pmatrix}
$$

**AR(1) List**

$$
\begin{pmatrix}
\sigma^2 & \rho^2 \sigma^2 & \rho^3 \sigma^2 \\
\rho \sigma^2 & \sigma^2 & \rho \sigma^2 \\
\rho \sigma^2 & \rho \sigma^2 & \sigma^2 \\
\rho \sigma^2 & \rho \sigma^2 & \rho \sigma^2 \\
\end{pmatrix}
$$

**Diagonal**

$$
\begin{pmatrix}
\sigma_1^2 \\
\sigma_2^2 \\
\sigma_3^2 \\
\sigma_4^2 \\
\end{pmatrix}
$$

**Constant**

$$
\begin{pmatrix}
\sigma_1^2 & \rho \sigma_1 \sigma_2 & \rho \sigma_1 \sigma_3 & \rho \sigma_1 \sigma_4 \\
\rho \sigma_1 \sigma_2 & \sigma_2^2 & \rho \sigma_2 \sigma_3 & \rho \sigma_2 \sigma_4 \\
\rho \sigma_1 \sigma_3 & \rho \sigma_2 \sigma_3 & \sigma_3^2 & \rho \sigma_3 \sigma_4 \\
\rho \sigma_1 \sigma_4 & \rho \sigma_2 \sigma_4 & \rho \sigma_3 \sigma_4 & \sigma_4^2 \\
\end{pmatrix}
$$

**AR(1) List**

$$
\begin{pmatrix}
\sigma_1^2 & \rho \sigma_1 \sigma_2 & \rho \sigma_1 \sigma_3 & \rho \sigma_1 \sigma_4 \\
\rho \sigma_1 \sigma_2 & \sigma_2^2 & \rho \sigma_2 \sigma_3 & \rho \sigma_2 \sigma_4 \\
\rho \sigma_1 \sigma_3 & \rho \sigma_2 \sigma_3 & \sigma_3^2 & \rho \sigma_3 \sigma_4 \\
\rho \sigma_1 \sigma_4 & \rho \sigma_2 \sigma_4 & \rho \sigma_3 \sigma_4 & \sigma_4^2 \\
\end{pmatrix}
$$

**ZGZ' + R**

When $ZGZ'$ is included and $R$ is set to diagonal as recommended, the value of $V$ becomes

$$
\begin{pmatrix}
\sigma^2 + g & g & g & g \\
g & \sigma^2 + g & g & g \\
g & g & \sigma^2 + g & g \\
g & g & g & \sigma^2 + g \\
\end{pmatrix}
$$

This is the compound symmetric pattern that is assumed in the repeated measures analysis of variance (RMANOVA). This model is often used to compare LMM with RMANOVA.
Power Calculations using Computer Simulation

Computer simulation allows us to estimate the power that is actually achieved by a test procedure in situations such as LMM that are not mathematically tractable. Computer simulation was once limited to mainframe computers. But, in recent years, as computer speeds have increased, simulation studies can be completed on desktop and laptop computers in a reasonable period of time. The simulations can still be time consuming, so we have proposed some steps below that will significantly shortened the time needed to obtain answers.

The Simulation

It is important that you understand how the simulation is setup. There are three main tabs (panels or windows) that contain parameters that you will need to set. These are the Data tab, the Covariance tab, and the Fitted Model tab.

Data Tab

The Data tab contains all the parameters associated with the sample size, the effect size, and the significance level (alpha). The effect size parameters define the experimental design.

Covariance Tab

The Covariance tab specifies the parameters used to define the covariance of the data that is generated. Note that the covariance of the data you generate does not have to match the covariance model that you use to fit the data. In fact, since you seldom know even the structure of the true covariance matrix, it is more realistic to generate data using one type of covariance matrix and then fit the generated data with a different covariance structure.

Fitted Model Tab

The Fitted Model tab specifies the covariance matrix that is actually fit to your data. As stated above, the model does not need to coincide with the model used to generate the data. It may be more realistic if it does not.

Steps in Conducting a Simulation Analysis

Simulation Steps

The steps to a simulation study are

1. Specify the design that will be studied. Enter the sample size, MDD’s, and variance covariance matrix. Specify the covariance matrix of the model that is fitted to the data.

2. Generate random samples from the design specified. Calculate the F-tests from the simulated data and determine if the null hypothesis is accepted or rejected. Tabulate the number of rejections and use this to calculate the test’s power.

3. Repeat step 2 several hundred or more times, tabulating the number of times the simulated data leads to a rejection of the null hypothesis. The power is the proportion of simulated samples in step 2 that lead to rejection.

4. Additionally, you can run a separate simulation to determine if the significance level (alpha) of the F-test matches the significance level you have selected. This is done by setting the MDD’s to zero.
Saving Simulation Time

Simulations for large models or large sample sizes take several hours to run. The simulation time can be reduced by running the simulation in two steps.

1. Specify a reasonable range for the group sample sizes. For example, you may want to try group sample sizes of 5, 10, 30, 80, and 120. Set the number of simulations to 300 or 500. Although these is not a large enough simulation size to give you definitive results, you can study the confidence intervals for power provided in the reports and plots to determine a reduced range of sample sizes.

2. Reduce the range of the sample size values, increase the number of simulations to 1000 or 2000, and rerun the simulations. These simulations may run for a while, so be prepared for running times of several minutes or hours. The power values that come from these simulations should be very precise.

Generating the Random Numbers

The simulation proceeds by generating the normal random deviates in groups that are the size of the number of time points. That is, a set of normals are generated for a single subject. This set of normals is transformed into a set of normals having the desired covariance structure using the commonly know technique of multiplying the generated unit normals by the square root of the variance-covariance matrix. The square root is taken using the Choleski decompositions. The resulting response vector matrix has the desired covariance matrix.

Symbolically, suppose there are t time points and further suppose that the desired variance-covariance matrix of the data to be simulated is given by V. Find a matrix W such that V = WW'. Note that, by construction, W is lower triangular. If we generate t unit random normal deviates and place them in a vector z, the vector y = Wz has variance-covariance matrix WW' = V. Finally, the appropriate cell mean (based on the minimum detectable differences) is added to the y to obtain the simulation data with the desired properties. Once all of the data required for a complete experiment is generated, the mixed model is solved using the mixed model algorithm coded for NCSS’s mixed model procedure.

Procedure Options

This section describes the options that are specific to this procedure. These are located on the first three tabs. To find out more about using the Reports and Plot tabs go to the Procedure Window chapter.

Design: Effect Size Tab

This tab contains most of the parameters and options necessary to define the sample size, significance level, effect size, and simulation size.

Solve For

Solve For

This procedure always solves for the power, so there is no specific Solve For option.

Sample Size

n (Subjects Per Group)

Specify one or more values for the number of subjects per group. The total sample size is the sum of the individual group sizes across all groups.

You can specify a list such as 2 4 6. The items in the list may be separated with commas or blanks. The interpretation of the list depends on the =n's check box. When the =n's box is checked, a separate analysis is calculated for each value of n. When the =n's box is not checked, PASS uses the n's as the actual group sizes. In
this case, the number of items entered must match the number of groups in the design, which is equal to the product of the number of levels of A and B.

You can also enter the sample sizes in columns of the spreadsheet. The column contains the group sample sizes, one per row. Columns are indicated by adding an equals sign to the left of the first entry. For example, if you have entered a set of unequal group sample sizes in column 2, you would enter ‘=C2’ here. Multiple columns, such as columns 2 through 4, are specified as ‘=C2 C3 C4’.

= n’s
This option controls whether or not the number of subjects per group is to be equal for all groups. When checked, the number of subjects per group is equal for all groups. A list of values such as ‘5 10 15’ represents three designs: one with five per group, one with ten per group, and one with fifteen per group. A simulation is conducted for each value.

When this option is not checked, the n’s are assumed to be unequal. A list of values represents the size of the individual groups. For example, ‘5 10 15’ represents a single, three-group design with five in the first group, ten in the second group, and fifteen in the third group. If four values are needed, but only two are entered, the last value is carried forward.

### Alpha

This option specifies the probability of a type-I error (alpha) for each factor and interaction. A type-I error occurs when you reject the null hypothesis of zero effects when in fact they are zero. Since they are probabilities, alpha values must be between zero and one. Routinely, the value of 0.05 is used for alpha. This value may be interpreted as meaning that about one F-test in twenty will falsely reject the null hypothesis.

### Simulations

This option specifies the number of iterations, M, used in each simulation. Larger numbers of iterations result in longer run times but more accurate results.

The precision of the simulated power estimates can be determined by recognizing that they follow the binomial distribution. Thus, confidence intervals may be constructed for power estimates. The following table gives an estimate of the precision that is achieved for various simulation sizes when the power is either 0.50 or 0.95. The table values are interpreted as follows: a 95% confidence interval of the true power is given by the power reported by the simulation plus and minus the ‘Precision’ amount given in the table.

<table>
<thead>
<tr>
<th>Simulation Size M</th>
<th>Precision when Power = 0.50</th>
<th>Precision when Power = 0.95</th>
</tr>
</thead>
<tbody>
<tr>
<td>100</td>
<td>0.100</td>
<td>0.044</td>
</tr>
<tr>
<td>500</td>
<td>0.045</td>
<td>0.019</td>
</tr>
<tr>
<td>1000</td>
<td>0.032</td>
<td>0.014</td>
</tr>
<tr>
<td>2000</td>
<td>0.022</td>
<td>0.010</td>
</tr>
<tr>
<td>5000</td>
<td>0.014</td>
<td>0.006</td>
</tr>
<tr>
<td>10000</td>
<td>0.010</td>
<td>0.004</td>
</tr>
<tr>
<td>50000</td>
<td>0.004</td>
<td>0.002</td>
</tr>
<tr>
<td>100000</td>
<td>0.003</td>
<td>0.001</td>
</tr>
</tbody>
</table>

Notice that a simulation size of 1000 gives a precision of plus or minus 0.014 when the true power is 0.95. Also note that as the simulation size is increased beyond 5000, there is only a small amount of additional precision achieved.
Because of the long run time needed to obtain an estimate of power, it is crucial that you set this parameter carefully. We suggest the following two-step procedure.

Step 1
Set the number of simulations to 200, 300, or 500 and run examples for a realistic range of sample sizes. Study the results (especially the confidence intervals) to determine a range of sample sizes you want to investigate more carefully.

Step 2
Reduce the range of N to just one or two values and set the number of simulations to a large amount.

Step 3 (Optional)
Take the rest of the day off—the simulation may take awhile!

Random Seed
Specify a numeric seed for random number generation. This value must be between 0 and 2147483647 and may be a decimal number.

Obtaining a Computer-Generated Random Seed
Enter Random, 0, or leave this option blank for a randomly generated seed based on the computer’s internal clock. If a randomly generated seed is used, it’s value will be displayed in the output.

Using a Non-Zero Random Seed
If you enter a non-zero random seed, the same random sequence will be generated with each run and the output will not change. This is often used to replicate previous results.

Effect Size
Specify Effects Using
Indicate which options are used to specify the Effect Size. The possible choices are Means in Spreadsheet Columns or the reset of the options on this panel.

Means in Spreadsheet Columns
Specify spreadsheet columns containing a hypothesized means matrix that represents the minimum detectable differences among the means. Under the null hypothesis, this matrix is all zeros.

The between-subject factors (A & B) are represented across the columns of the spreadsheet and the within-subject factors (C & D) are represented down the rows. The number of columns specified must equal the number of groups, which is equal to the number of levels in A times the number of levels in B. The number of rows must equal the number of time points, which is equal to the number of levels in C multiplied by the number of levels in D.

For example, suppose you are designing an experiment that is to have two between factors (A & B) and two within factors (C & D). Suppose each of the four factors has two levels. The columns of the spreadsheet would represent


The rows of the spreadsheet would represent

C1D1
C1D2
C2D1
C2D2
Example
To see how this option works, consider the following table of hypothesized means for an experiment with one between factor (A) having two groups and one within factor (C) having three time periods. The values in columns C1 and C2 of the spreadsheet are

<table>
<thead>
<tr>
<th>C1</th>
<th>C2</th>
</tr>
</thead>
<tbody>
<tr>
<td>2.0</td>
<td>4.0</td>
</tr>
<tr>
<td>4.0</td>
<td>6.0</td>
</tr>
<tr>
<td>6.0</td>
<td>11.0</td>
</tr>
</tbody>
</table>

By subtracting the appropriate means, the following table of effects results

<table>
<thead>
<tr>
<th>C1</th>
<th>C2</th>
<th>Means</th>
<th>Effects</th>
</tr>
</thead>
<tbody>
<tr>
<td>0.5</td>
<td>-0.5</td>
<td>3.0</td>
<td>-2.5</td>
</tr>
<tr>
<td>0.5</td>
<td>-0.5</td>
<td>5.0</td>
<td>-0.5</td>
</tr>
<tr>
<td>-1.0</td>
<td>1.0</td>
<td>8.5</td>
<td>3.0</td>
</tr>
</tbody>
</table>

---

Effect Size – Factors Separating Subjects into Groups (Between)

These options specify the effect sizes of the between-subjects factors (A and B).

Levels
Specify the number of levels (categories) in this factor. Typical values are from 2 to 8. Set this to a blank (or 0) to ignore the factor in the design.

Effects Pattern
This option specifies the pattern of the means for this factor. This pattern is multiplied by the Detectable Difference to form the factor means used in the simulation. For example, suppose that the pattern of a five-category factor is -.50 -.25 0.0 .25 0.5 and the detectable difference is 10. The resulting effects are -5.0 -2.5 0.0 2.5 5.0. The power reported by the simulation is the value to detect a difference of 10 (5 – (– 5)) when the pattern of means is a linear growth pattern. Note that the power depends on both the pattern and the detectable difference.

Possible choices are displayed next using examples that assume that the factor has five categories.

- **List of Means**
  Enter a list of means directly into the List of Means box to the right.

- **Linear Up or Down**
  Up: -.50 -.25 0.0 .25 0.5. Down: .50 .25 0.0 -.25 -.50.

- **First Effect High or Low**
  High: .5 -.5 -.5 -.5 -.5. Low: -.5 .5 .5 .5 .5.

- **Last Effect High or Low**
  High: -.5 -.5 -.5 -.5 .5. Low: .5 .5 .5 .5 -.5.

- **First Half High or Low**
  High: .5 .5 .5 -.5 .5. Low: -.5 -.5 -.5 .5 .5.

- **Zig Zag High or Low**
  High: .5 -.5 .5 -.5 .5. Low: -.5 .5 -.5 .5 -.5.
Interaction Effect Patterns
The effect patterns of interactions are formed as the Kronecker product of the individual factor patterns.

Detectable Difference
This is the difference between the largest and smallest effects associated with this factor or interaction. This represents the minimum detectable difference between any two levels (or factor-level combinations). The actual means used in the simulation are found by multiplying the Effects Pattern by this value.

Each value specified here results in a separate simulation. Note that, because of report and plot labeling, it is best if you only put multiple values in one of these boxes at a time. Otherwise, the plots will be labeled using the less-informative term 'Combination'.

Example
Suppose that you selected Linear Up as the Effects Pattern of a five-level factor and set the detectable difference to 8. Further suppose that the Baseline Mean (below) is set to 20. The resulting means for this factor would be: 16 18 20 22 24.

Note that the maximum difference between any two of these means is 8.

List of Means
You can specify a list of means directly instead of specifying the pattern and detectable difference. When you do so, the effects pattern and detectable difference are calculated from the means you specify.

When you specify too many values for the number of levels in the factor, the extra values are ignored. When you specify too few values, the last value you specify is copied forward.

Using Columns in the Spreadsheet
You can specify the list of means in columns of the spreadsheet. When you do this, you enter the column(s) name(s) here using the equal sign.

For example, if you stored two sets of means, one in C5 and the other in C6, you would enter ‘=C5 C6’ here (or you could select the columns by pressing the button to the right). Once you have entered values into a spreadsheet, it is up to you to load that spreadsheet each time you run the simulation.

Note that a separate simulation is run for each column you specify.

Effect Size – Factors with Multiple Levels Within a Subject (Within)
These options specify the effect sizes of the within-subject factors (C and D).

Levels
Specify the number of levels (categories) in this factor. Typical values are from 2 to 8. Set this to a blank (or 0) to ignore the factor in the design.

Note that the number of time points is calculated as the product of the number of levels factors C and D.
The rest of these options behave as described in the Between-Subject section above.
Possible choices are displayed next using examples that assume that the factor has five categories.
**Effect Size – Interactions**
These options specify the effect sizes of any interactions that are specified.

**Interaction Check Box**
Check this box to include the corresponding interaction in the model. In most situations, you should include all appropriate interactions since these have an impact on the degrees of freedom of the F-tests. You can set their Detectable Difference near zero if you want to ignore them.

Occasionally, you will want to limit the number of interactions that you include in the model.

Note that the model is forced to be hierarchical. This means that if you include the three-way interaction ABC in the model, you must also include A, B, C, AB, AC, and BC.

**Detectable Difference**
This is the difference between the largest and smallest effects associated with this term. This represents the minimum detectable difference between any two factor-level combinations. The actual means used in the simulation are found by multiplying the effects pattern by this value. The effect pattern is created by forming the Kronecker product of the effect patterns of each factor in the interaction. The result is standardized so that the maximum difference in the pattern is 1.0. Each item in the pattern is multiplied by the Detectable Difference. The cell means are found by adding the appropriate effects for the main effects, interaction effects, and baseline mean.

Each value specified here results in a separate simulation. Note that, because of report and plot labeling, it is best if you only put multiple values in one of these boxes at a time. Otherwise, the plots will be labeled using the less-informative term ‘Combination’.

**Design: Covariance Tab**
This tab specifies \( V(Y) = ZGZ' + R \) which is used to form the simulated data. Note that the covariance matrix specified here does not have to match the covariance of the fitted model. This allows you to study the robustness of the fitted model to errors in the covariance specification.

There are two matrices that can be specified: the random effects (G) and the residual structure R.

**Group Option**

**Grouping Factor**
Specify a grouping factor--either Factor A or B. This causes a unique covariance matrix to be generated for each level of the selected factor.

- **None**
  No group extension of the covariance matrix is done. Grouping is ignored in the formation of G and R.

- **A (or B)**
  The structures of G and R are extended to include separate matrices for each level of factor A (or B). The number of groups is equal to the number of levels of A (or B). Individual values for each group are entered for \( g, \sigma^2 \) for R, and \( \rho \). These individual group values can be entered as a list in the box or in a column of the spreadsheet.
G (Covariance of Random Effects)

Include G
Specify whether to include G (the variance of the random effects term u) in the covariance model.

- **Not Checked**
  Do not include G in the model, that is, all elements of G are zero. Hence, V(Y) is specified using only R.

- **Checked**
  Include the diagonal matrix G, and hence ZGZ', in the model. The diagonal elements of G are all set to g.

Variances (Diagonal Elements of G)

g (Subject $\sigma^2$)
This is used to generate the diagonal elements of G (all off-diagonal elements are zero). It is the variance of a subject (random effect). Since the value is a variance, it must be positive. It is usually obtained from a previous run of similar data through a mixed model.

When a **Grouping Factor** (A or B) is used, a separate value must be entered for each level of the group factor. This can be done by entering a list or by entering the values in a column of the spreadsheet and specifying that column here using the “=C1” type syntax.

For example, if there were 4 categories in factor A and factor A was selected as the **Grouping Factor**, you might enter “2 3 4 5” in this box or you could enter “=C2” here and make a similar entry in column C2 of the spreadsheet. Assuming that there are 3 time points, the G matrix would be

\[
\begin{bmatrix}
2 & 0 & 0 \\
0 & 2 & 0 \\
0 & 0 & 2 \\
3 & 0 & 0 \\
0 & 3 & 0 \\
0 & 0 & 3 \\
4 & 0 & 0 \\
0 & 4 & 0 \\
0 & 0 & 4 \\
5 & 0 & 0 \\
0 & 5 & 0 \\
0 & 0 & 5 \\
\end{bmatrix}
\]
**R (Covariance of Residuals)**

**Specify R Using**

Specify how you want to specify R. Three choices are available:

- **Variance Only**
  This option indicates that R includes only diagonal elements (no autocorrelations).

- **Variances and Autocorrelations**
  This option indicates that R includes both diagonal (variance) and off-diagonal (autocorrelation) parameters.

- **R in Spreadsheet**
  R is to be read in from the spreadsheet.

**Times**

This option specifies the time points at which measurements of the subjects are made. Often, measurements are made at equi-distant points through time. But this is not always the case. The number of time points is the product of the number of levels of all within factors. The time metric influences the values of the variances as well as the correlations between two measurements on the same individual.

The autocorrelations are based on the formula: Corr(Yi,Yj) = $\rho ^ {(|ti-tj|)}$, where $\rho$ is the base autocorrelation and $ti$ and $tj$ are two points in the time metric list. This formula allows you to easily specify many different types of autocorrelation structures.

The syntax for entering the time metric is given next:

- **STEP START INC**
  Measurements are made at time intervals of length INC, beginning at START. For example, "STEP 0 2" would generate the time series: 0, 2, 4, 6, etc.

- **RANGE MIN MAX**
  A set of equal-spaced time points is generated from the MIN value to the MAX value. This setting is very useful when you want to investigate the impact of increasing/decreasing the number of measurements per subject during the same period of time. For example, you might want to determine if the study will last five weeks, will the power of the statistical tests increase if you take 10 measurements rather than 5?

- **LIST**
  You may enter a list of values separated by blanks or commas. For example, you could enter 0 0.143 1 2 3 if times were 0 weeks, 1/7 week (day 1), 1 week, 2 weeks, 3 weeks.

**Variances (Diagonal Elements of R)**

**Pattern**

This option specifies how the diagonal (variance) elements of R are specified. Possible choices are

- **Constant in $\sigma^2$ for R**
  All variances are set to the value of $\sigma^2$ for R.

  When a *Grouping Factor* is used, a list of group variances can be entered in the box or read in from the spreadsheet using the “="C1" syntax to designate which column. In this case, each row of the spreadsheet provides the variance for the corresponding group.
Set of $\sigma^2$ for R values proportional to Times

The values of $\sigma^2$ to $R$ range from the first value below to the second value. The values between these two endpoints are constructed so that they have the same relative magnitude as the Times entry.

For example, suppose there are four levels of factor C (the within factor) and the Times values are 1, 2, 9, 10. Further suppose that the two values of $\sigma^2$ for R are 10 and 100. The diagonal elements of R will be 10, 20, 90, and 100.

When a Grouping Factor is used, lists of the first and last values of $\sigma^2$ for R can be entered in the box or read in from the spreadsheet using the same syntax described above. For example, suppose there are 4 levels in factor C and two in factor A. If the Grouping Factor is set to A, the entries in the first box $\sigma^2$ for R is “4 5” and the second is “7 8,” the resulting value of R would be

```
4 0 0 0
0 5 0 0
0 0 6 0
0 0 0 7
5 0 0 0
0 6 0 0
0 0 7 0
0 0 0 8
```

$\sigma^2$ List

A list of variances, one per time point, is specified. The list can be entered in the box or specified as rows of the spreadsheet using the equals sign, e.g. “=C3.”

$\sigma^2$ for R (first)
The (first) value of $\sigma^2$ for R is specified here.

When a Grouping Factor is used, a list of variances can be entered in the box or read in from the spreadsheet. The column containing the group variance entries is specified with an equals sign, e.g. “=C1.” When this option is used, each row of the spreadsheet provides $\sigma^2$ for R for the corresponding group.

$\sigma^2$ for R (last)

This is the final value in the specification of the set of variances. It is used to specify the final diagonal element in the linear sequence. The intermediate values of $\sigma^2$ for R are calculated so that their order and magnitude are proportional to the Time values.

When a Grouping Factor is used, a list of variances can be read in from the spreadsheet. A column containing the group variances is specified with an equals sign, e.g. “=C2.” When this option is used, each row of the spreadsheet provides the final diagonal element of the corresponding group. An example is given in the discussion of Pattern above.

$\sigma^2$ List

A list of $\sigma^2$ values, one per time point, is specified here. The number of items in the list must match max(1,levels of C) x max(1,levels of D).

The list can also be specified as a column of the spreadsheet using the equals sign, e.g. “=C3.”
Autocorrelations (Off-Diagonal Elements of R)

Pattern
This option specifies the pattern of the autocorrelations R. The three options are

- **Constant in ρ**
  All autocorrelations are the same and equal to the value of ρ.

- **1st Order: ρ, ρ², ρ³, ...**
  The value of ρ is used to generate a first order autocorrelation series. This pattern reduces the magnitude of the autocorrelation at each successive step by multiplying the value at the previous step by ρ. Thus the pattern is ρ, ρ², ρ³, etc.

  Note that the exponent in this series is equal to the difference between the corresponding time points. For example, if the time points are 1, 3, 9, 10 the successive exponents of ρ are 2, 6, and 1.

- **ρ List**
  A list of ρ values, separated by blanks or commas, is used to specify the autocorrelation pattern across the time points within a subject.

ρ (Autocorrelation)
This is the value of ρ between two measurements made on a subject at two time points that differ by one time unit. A value near 0 indicates low correlation. A value near 1 indicates high correlation. Its use depends on the selection in the Pattern option.

The possible values range from -1 to 1. However, in this situation, a positive value is usually assumed, so the more realistic range is 0 to 1.

If Time >
This is the maximum time difference between two measurement points before the autocorrelation is set to the value in the box to the left.

For example, you might wish to specify a constant ρ of 0.4 for the first two time periods, and then, for any two measures that are greater than two time values apart, switch ρ to zero. If you have specified a Constant autocorrelation pattern, and set this value to ‘2’, the resulting autocorrelation pattern of R would be

```
1.0  0.4  0.4  0.0  0.0
0.4  1.0  0.4  0.4  0.0
0.4  0.4  1.0  0.4  0.4
0.0  0.4  0.4  1.0  0.4
0.0  0.0  0.4  0.4  1.0
```

When you want to ignore this value, set it to a large number such as 100.

Then ρ =
This is the second ρ value. It is used when the time difference between two measurement points is larger than the value to the left.

ρ List
This is a list of autocorrelations, one for each time point. The number of autocorrelations must match the number of time values which is equal to the product of the number of levels for factors C and D.

Since this is a type of correlation, possible values range from -1 to 1. However, positive values are usually assumed, so the realistic range is 0 to 1. A value near 0 indicates low correlation. A value near 1 indicates high correlation.
You can alternatively enter the list of autocorrelations in a column of the spreadsheet and specify that column here. When the program finds an equals sign in this box, it reads in the values of the designated column. Blanks are converted to zeros. For example, if you have entered the autocorrelation list in column one, you would enter “=C1” here.

If there are not enough values entered, the last value is copied forward.

---

**R in Spreadsheet**

**Columns**

This option designates which columns on the spreadsheet hold R. The number of columns and number of rows with entries must match the number of time periods at which the subjects are measured. The matrix must be positive definite.

Press the button at the right to select the columns from the spreadsheet.

---

**Fitted Model Tab**

This tab controls the variance-covariance model that is actual fit during the solution of each simulation sample.

---

**G (Random Effects Component)**

Specify whether to include G (the random effects component in) the fitted model. Possible choices are

- **None**
  - Do not include G in the fitted model.

- **G (Random Effects for Subjects)**
  - Include G in the fitted model. In this case, the R should be set to *Diagonal* (which does not include autocorrelations).

**Groups**

Specify a grouping factor: either factor A or B.

When selected, a set of variance and autocorrelation parameters are fit for each level of this factor.
**R (Residual Component)**

**Pattern**
Specify the type of R matrix (Residual Component Pattern) to be generated. The default type is the Diagonal matrix. When terms are specified in the Random Model, this option should be set to Diagonal. A brief summary of the various structures follows.

\( \rho = \text{Autocorrelation} \)

\( \rho_i = \text{ith autocorrelation} \)

\( \rho_{ij} = \text{autocorrelation between ith and jth time points} \)

\( \sigma_i^2 = \sigma^2 \text{ for ith time point} \)

- **Diagonal**
  \[
  \begin{pmatrix}
  \sigma^2 & 0 & 0 & 0 \\
  0 & \sigma^2 & 0 & 0 \\
  0 & 0 & \sigma^2 & 0 \\
  0 & 0 & 0 & \sigma^2 \\
  \end{pmatrix}
  \]

- **Compound Symmetry**
  \[
  \begin{pmatrix}
  \sigma^2 & \rho \sigma^2 & \rho \sigma^2 & \rho \sigma^2 \\
  \rho \sigma^2 & \sigma^2 & \rho \sigma^2 & \rho \sigma^2 \\
  \rho \sigma^2 & \rho \sigma^2 & \sigma^2 & \rho \sigma^2 \\
  \rho \sigma^2 & \rho \sigma^2 & \rho \sigma^2 & \sigma^2 \\
  \end{pmatrix}
  \]

- **AR(1)**
  \[
  \begin{pmatrix}
  \sigma^2 & \rho \sigma^2 & \rho^2 \sigma^2 & \rho^3 \sigma^2 \\
  \rho \sigma^2 & \sigma^2 & \rho \sigma^2 & \rho^2 \sigma^2 \\
  \rho^2 \sigma^2 & \rho \sigma^2 & \sigma^2 & \rho \sigma^2 \\
  \rho^3 \sigma^2 & \rho^2 \sigma^2 & \rho \sigma^2 & \sigma^2 \\
  \end{pmatrix}
  \]

- **Toeplitz(i)**
  e.g. Toeplitz(3) =
  \[
  \begin{pmatrix}
  \sigma^2 & \rho_1 \sigma^2 & \rho_2 \sigma^2 & 0 \\
  \rho_1 \sigma^2 & \sigma^2 & \rho_1 \sigma^2 & \rho_2 \sigma^2 \\
  \rho_2 \sigma^2 & \rho_1 \sigma^2 & \sigma^2 & \rho_1 \sigma^2 \\
  0 & \rho_2 \sigma^2 & \rho_1 \sigma^2 & \sigma^2 \\
  \end{pmatrix}
  \]

\( \sigma \) represents the residual variance.
• Banded(i)
  e.g. Banded(2) =
  \[
  \begin{pmatrix}
  \sigma^2 & \rho \sigma^2 & 0 & 0 \\
  \rho \sigma^2 & \sigma^2 & \rho \sigma^2 & 0 \\
  0 & \rho \sigma^2 & \sigma^2 & \rho \sigma^2 \\
  0 & 0 & \rho \sigma^2 & \sigma^2 
  \end{pmatrix}
  \]

• Unstructured
  \[
  \begin{pmatrix}
  \sigma^2 & \rho_{12} \sigma^2 & \rho_{13} \sigma^2 & \rho_{14} \sigma^2 \\
  \rho_{12} \sigma^2 & \sigma^2 & \rho_{23} \sigma^2 & \rho_{24} \sigma^2 \\
  \rho_{13} \sigma^2 & \rho_{23} \sigma^2 & \sigma^2 & \rho_{34} \sigma^2 \\
  \rho_{14} \sigma^2 & \rho_{24} \sigma^2 & \rho_{34} \sigma^2 & \sigma^2 
  \end{pmatrix}
  \]

• Heterogeneous covariance structures allow for nonconstant values for $\sigma^2$.
  e.g. Diagonal - Heterogeneous =
  \[
  \begin{pmatrix}
  \sigma_1^2 \\
  \sigma_2^2 \\
  \sigma_3^2 \\
  \sigma_4^2 
  \end{pmatrix}
  \]

Force Positive Covariances
When checked, this option forces all values in the R and G matrices to be non-negative. When this option is not checked, covariances can be negative.

Usually, negative covariances are okay and should be allowed. However, some Residual Component patterns such as ‘Compound Symmetry’ assume that covariances (autocorrelations) are positive.

Solution Options

Likelihood Type
Specify the type of likelihood equation to be solved. The options are:

• MLE
  The Maximum Likelihood solution has become less popular.

• REML (recommended)
  The Restricted Maximum Likelihood solution is recommended. It is the default in other software programs (such as SAS).
Solution Method
Specify the method to be used to solve the likelihood equations. The options are:

- **Newton-Raphson**
  This is an implementation of the popular 'gradient search' procedure for maximizing the likelihood equations. Whenever possible, we recommend that you use this method.

- **Fisher-Scoring**
  This is an intermediate step in the Newton-Raphson procedure. However, when the Newton-Raphson fails to converge, you may want to stop with this procedure.

- **MIVQUE**
  This non-iterative method is used to provide starting values for the Newton-Raphson method. For large problems, you may want to investigate the model using this method since it is much faster.

- **Differential Evolution**
  This grid search technique will often find a solution when the other methods fail to converge. However, it is painfully slow—often requiring hours to converge—and so should only be used as a last resort.

---

Solution Options – Newton-Raphson / Fisher Scoring Options

**Fisher Scoring Iter's**
This is the maximum number of Fisher Scoring iterations that occur in the maximum likelihood finding process. When Solution Method is set to Newton-Raphson, up to this number of Fisher Scoring iterations occur before beginning Newton-Raphson iterations. We recommend setting this to ‘1’.

**Newton-Raphson Iter's**
This is the maximum number of Newton-Raphson iterations that occur in the maximum likelihood finding process. When Solution Method is set to Newton-Raphson, Fisher-scoring iterations occur before beginning Newton-Raphson iterations. We recommend setting this to ‘5’.

**Lambda**
Each parameter’s change is multiplied by this value at each iteration. Usually, this value can be set to one. However, it may be necessary to set this value to 0.5 to implement step-halving: a process that is necessary when the Newton-Raphson diverges.

Note: this parameter only used by the Fisher-Scoring and Newton-Raphson methods.

**Convergence Criterion**
This procedure uses relative Hessian convergence (or the Relative Offset Orthogonality Convergence Criterion) as described by Bates and Watts (1981).

Recommended: The default value, 1E-8, will be adequate for many problems. When the routine fails to converge, try increasing the value to 1E-6.

**Zero (Rounding)**
This cutoff value is used by the least-squares algorithm to lessen the influence of rounding error. Values lower than this are reset to zero. If unexpected results are obtained, try using a smaller value, such as 1E-32. Note that 1E-5 is an abbreviation for the number 0.00001.

Recommended: 1E-10 or 1E-12.
Range: 1E-3 to 1E-40.
Variance Zero
When an estimated variance component (diagonal element) is less than this value, the variance is assumed to be zero and all reporting is terminated since the algorithm has not converged properly.

To correct this problem, remove the corresponding term from the Random Factors Model or simplify the Repeated Variance Pattern. Since the parameter is zero, why would you want to keep it?
Recommended: 1E-6 or 1E-8.
Range: 1E-3 to 1E-40.

Correlation Zero
When an estimated correlation (off-diagonal element) is less than this value, the correlation is assumed to be zero and all reporting is terminated since the algorithm has not converged properly.

To correct this problem, remove the corresponding term from the Random Factors Model or simplify the Repeated Variance Pattern. Since the parameter is zero, why would you want to keep it?
Recommended: 1E-6 or 1E-8.
Range: 1E-3 to 1E-40.

Max Retries
Specify the maximum number of retries to occur. During the maximum likelihood search process, the search may lead to an impossible combination of variance-covariance parameters (as defined by a matrix of variance-covariance parameters that is not positive definite). When such a combination arises, the search algorithm will begin again. Max Retries is the maximum number of times the process will re-start to avoid such combinations.
We recommend setting this to ‘1’.

Solution Options – Differential Evolution Options

Crossover Rate
This value controls the amount of movement of the differential evolution algorithm toward the current best. Larger values accelerate movement toward the current best, but reduce the chance of locating the global maximum. Smaller values improve the chances of finding the global, rather than a local, solution, but increase the number of iterations until convergence.
RANGE: Usually, a value between .5 and 1.0 is used.
RECOMMENDED: 0.9.

Mutation Rate
This value sets the mutation rate of the search algorithm. This is the probability that a parameter is set to a random value within the parameter space. It keeps the algorithm from stalling on a local maximum.
RANGE: Values between 0 and 1 are allowed.
RECOMMENDED: 0.9 for random coefficients (complex) models or 0.5 for random effects (simple) models.

Max Iter’s
Specify the maximum number of differential evolution iterations used by the differential evolution algorithm. A value between 100 and 200 is usually adequate. For large datasets, i.e., number of rows greater than 1000, you may want to reduce this number.
Min Relative Change

This parameter controls the convergence of the likelihood maximizer. When the relative change in the likelihoods from one generation to the next is less than this amount, the algorithm concludes that it has converged. The relative change is $|L(g+1) - L(g)| / L(g)$ where $L(g)$ is absolute value of the likelihood at generation 'g'. Note that the algorithm also terminates if the Maximum Generations are reached or if the number of individuals that are replaced in a generation is zero. The value 0.00000000001 (ten zeros) seems to work well in practice. Set this value to zero to ignore this convergence criterion.

Solutions/Iter'n

This is the number of trial points (solution sets) that are used by the differential evolution algorithm during each iteration. In the terminology of differential evolution, this is the population size.

RECOMMENDED: A value between 15 and 25 is recommended. More points may dramatically increase the running time. Fewer points may not allow the algorithm to converge.
Example 1 – Power of a Two Factor Repeated Measures Design

Researchers are planning a study of the impact of a drug on heart rate. They want to evaluate the differences in heart rate among two age groups: 20-55 and over 55. Their experimental protocol calls for a baseline heart rate measurement, followed by administration of a certain level of the drug, followed by an additional measurement 30 minutes later. They want to be able to detect a 10% difference in heart rate among the age groups. They want to detect 5% difference in heart rate within an individual across time. They decide the experiment should detect interaction effects of the same magnitude as the within-subject factor. From a heart rate of 93, a 10% reduction gives 84, a difference of 9. Similarly, a 5% reduction within a subject would result in a heart rate of 88, a difference of 5.

They plan to analyze the data using a random effects model, setting the significance level at 0.05. Similar studies have found an average heart rate of 93, a subject variance of 11, and a residual variance of 11.

They want to look at the power for group sizes of 3, 5, 7, and 9.

Setup

This section presents the values of each of the parameters needed to run this example. First, from the PASS Home window, load the procedure window. You may then make the appropriate entries as listed below, or open Example 1 by going to the File menu and choosing Open Example Template.

<table>
<thead>
<tr>
<th>Option</th>
<th>Value</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Design: Effect Size Tab</strong></td>
<td></td>
</tr>
<tr>
<td><strong>Sample Size</strong></td>
<td></td>
</tr>
<tr>
<td>n (Subjects Per Group)</td>
<td>3 5 7 9</td>
</tr>
<tr>
<td>= n’s</td>
<td>Checked</td>
</tr>
<tr>
<td>Alpha</td>
<td>0.05</td>
</tr>
<tr>
<td>Simulations</td>
<td>100</td>
</tr>
<tr>
<td>Random Seed</td>
<td>Blank or Random</td>
</tr>
<tr>
<td><strong>Effect Size</strong></td>
<td></td>
</tr>
<tr>
<td>Specify Effects Using</td>
<td>Effects Patterns, etc.</td>
</tr>
<tr>
<td><strong>Factors Separating Subjects into Groups (Between)</strong></td>
<td></td>
</tr>
<tr>
<td>Levels (A)</td>
<td>2</td>
</tr>
<tr>
<td>Effects Pattern (A)</td>
<td>Linear Up</td>
</tr>
<tr>
<td>Detectable Difference (A)</td>
<td>9</td>
</tr>
<tr>
<td><strong>Factors with Multiple Levels Within a Subject (Within)</strong></td>
<td></td>
</tr>
<tr>
<td>Levels (C)</td>
<td>2</td>
</tr>
<tr>
<td>Effects Pattern (C)</td>
<td>Linear Up</td>
</tr>
<tr>
<td>Detectable Difference (C)</td>
<td>5</td>
</tr>
<tr>
<td><strong>Interactions</strong></td>
<td></td>
</tr>
<tr>
<td>AC</td>
<td>Checked</td>
</tr>
<tr>
<td>Baseline Mean</td>
<td>93</td>
</tr>
<tr>
<td><strong>Design: Covariance Tab</strong></td>
<td></td>
</tr>
<tr>
<td>G (Covariance of Random Effects)</td>
<td></td>
</tr>
<tr>
<td>Include G</td>
<td>Checked</td>
</tr>
<tr>
<td>g (Subject σ²)</td>
<td>11</td>
</tr>
</tbody>
</table>
**R (Covariance of Residuals)**
Specify R Using: Variances Only
Times: STEP 0 1
Variance Pattern: Constant in $\sigma^2$ for R
$\sigma^2$ for R: 11

**Fitted Model Tab**

**Fitted V(Y) Model**
G Estimation: None
Groups: None
R Estimation: Diagonal
Groups: None

**Solution Options**
Likelihood Type: REML
Solution Method: Newton-Raphson

**Reports Tab**
Simulation Alpha: 0.05

---

### Annotated Output

Click the Calculate button to perform the calculations and generate the following output.

#### Power Report for Each Design

<table>
<thead>
<tr>
<th>Model Term</th>
<th>Power</th>
<th>Lower 95% C.L. of Power</th>
<th>Upper 95% C.L. of Power</th>
<th>N(1)</th>
<th>N</th>
<th>Minimum Detectable Difference</th>
<th>Alpha</th>
<th>Number of Simulation Samples</th>
<th>Factor Pattern</th>
</tr>
</thead>
<tbody>
<tr>
<td>A (2)</td>
<td>0.4300</td>
<td>0.3314</td>
<td>0.5329</td>
<td>3</td>
<td>6</td>
<td>9.00</td>
<td>0.0500</td>
<td>100</td>
<td>Linear Up</td>
</tr>
<tr>
<td>C (2)</td>
<td>0.4800</td>
<td>0.3790</td>
<td>0.5822</td>
<td>3</td>
<td>6</td>
<td>5.00</td>
<td>0.0500</td>
<td>100</td>
<td>Linear Up</td>
</tr>
<tr>
<td>AC</td>
<td>0.4900</td>
<td>0.3886</td>
<td>0.5920</td>
<td>3</td>
<td>6</td>
<td>5.00</td>
<td>0.0500</td>
<td>100</td>
<td></td>
</tr>
<tr>
<td>A (2)</td>
<td>0.8200</td>
<td>0.7305</td>
<td>0.8897</td>
<td>5</td>
<td>10</td>
<td>9.00</td>
<td>0.0500</td>
<td>100</td>
<td>Linear Up</td>
</tr>
<tr>
<td>C (2)</td>
<td>0.7900</td>
<td>0.6971</td>
<td>0.8651</td>
<td>5</td>
<td>10</td>
<td>5.00</td>
<td>0.0500</td>
<td>100</td>
<td>Linear Up</td>
</tr>
<tr>
<td>AC</td>
<td>0.9000</td>
<td>0.8238</td>
<td>0.9510</td>
<td>5</td>
<td>10</td>
<td>5.00</td>
<td>0.0500</td>
<td>100</td>
<td></td>
</tr>
<tr>
<td>A (2)</td>
<td>0.9600</td>
<td>0.9007</td>
<td>0.9890</td>
<td>7</td>
<td>14</td>
<td>9.00</td>
<td>0.0500</td>
<td>100</td>
<td>Linear Up</td>
</tr>
<tr>
<td>C (2)</td>
<td>0.8700</td>
<td>0.7880</td>
<td>0.9289</td>
<td>7</td>
<td>14</td>
<td>5.00</td>
<td>0.0500</td>
<td>100</td>
<td>Linear Up</td>
</tr>
<tr>
<td>AC</td>
<td>0.9500</td>
<td>0.8872</td>
<td>0.9836</td>
<td>7</td>
<td>14</td>
<td>5.00</td>
<td>0.0500</td>
<td>100</td>
<td></td>
</tr>
<tr>
<td>A (2)</td>
<td>0.9900</td>
<td>0.9455</td>
<td>0.9997</td>
<td>9</td>
<td>18</td>
<td>9.00</td>
<td>0.0500</td>
<td>100</td>
<td>Linear Up</td>
</tr>
<tr>
<td>C (2)</td>
<td>1.0000</td>
<td>0.9638</td>
<td>1.0000</td>
<td>9</td>
<td>18</td>
<td>5.00</td>
<td>0.0500</td>
<td>100</td>
<td>Linear Up</td>
</tr>
<tr>
<td>AC</td>
<td>0.9900</td>
<td>0.9455</td>
<td>0.9997</td>
<td>9</td>
<td>18</td>
<td>5.00</td>
<td>0.0500</td>
<td>100</td>
<td></td>
</tr>
</tbody>
</table>

Simulation Time: 65.78 seconds.

This report gives the simulated power for each term in the design for each value of N, one design at a time. It is useful when you want to compare the powers of the terms in the design at a specific sample size.

The definitions of each of the columns of the report are as follows.

**Model Term**
This column contains the identifying label of the term. The number of levels for a factor is given in parentheses.

**Power**
This is the simulated power for the term.
Lower and Upper 95% C.L. of Power
These are the lower and upper confidence limits of a 95% confidence interval for the simulated power. These are exact, distribution-free, confidence limits based on the binomial distribution.

N(1)
The value of the number of subjects per group.

N
The value of N is the total number of subjects in the study.

Minimum Detectable Difference
This is the value of the minimum detectable difference that was entered (or calculated) for this term. This is a measure of the magnitude of the effect size.

Alpha
Alpha is the significance level of the F-test for this term.

Number of Simulation Samples
This is the number of simulation samples for which the mixed model algorithm converged.

Factor Pattern
This is the type of factor pattern that was used with the detectable difference to form the group means.

Term Reports

<table>
<thead>
<tr>
<th>Model Term</th>
<th>Power</th>
<th>Lower 95% C.L. of Power</th>
<th>Upper 95% C.L. of Power</th>
<th>N(1)</th>
<th>N</th>
<th>Minimum Detectable Difference</th>
<th>Alpha</th>
<th>Number of Simulation Samples</th>
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<td>Linear Up</td>
</tr>
<tr>
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<td>0.8200</td>
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<td>0.8897</td>
<td>5</td>
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<td>7</td>
<td>14</td>
<td>9.00</td>
<td>0.0500</td>
<td>100</td>
<td>Linear Up</td>
</tr>
<tr>
<td>A (2)</td>
<td>0.9900</td>
<td>0.9455</td>
<td>0.9997</td>
<td>9</td>
<td>18</td>
<td>9.00</td>
<td>0.0500</td>
<td>100</td>
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</tr>
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<td>3</td>
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<td>5.00</td>
<td>0.0500</td>
<td>100</td>
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<td>0.9289</td>
<td>7</td>
<td>14</td>
<td>5.00</td>
<td>0.0500</td>
<td>100</td>
<td>Linear Up</td>
</tr>
<tr>
<td>C (2)</td>
<td>1.0000</td>
<td>0.9638</td>
<td>1.0000</td>
<td>9</td>
<td>18</td>
<td>5.00</td>
<td>0.0500</td>
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<td>Linear Up</td>
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<td>AC</td>
<td>0.4900</td>
<td>0.3886</td>
<td>0.5920</td>
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<td>5.00</td>
<td>0.0500</td>
<td>100</td>
<td></td>
</tr>
<tr>
<td>AC</td>
<td>0.9000</td>
<td>0.8238</td>
<td>0.9510</td>
<td>5</td>
<td>10</td>
<td>5.00</td>
<td>0.0500</td>
<td>100</td>
<td></td>
</tr>
<tr>
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<td>0.8872</td>
<td>0.9836</td>
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<td>0.9997</td>
<td>9</td>
<td>18</td>
<td>5.00</td>
<td>0.0500</td>
<td>100</td>
<td></td>
</tr>
</tbody>
</table>

This report provides the same information as the previous Design report, so the item definitions are the same. It is sorted by term, to make comparison of powers across various sample sizes easier.
Whole Design Power Plots

This plot shows the power values on the vertical axis and the sample sizes across the horizontal axis. The plot symbols represent different model terms.

Confidence Interval Power Plots

These plots show the confidence limits for the power for each term across the various sample sizes. Using these plots, you can quickly see for which sample sizes you might want to run a more precise (larger) simulation.
### Individual Term Power Plots

These plots show the power for each term across the various sample sizes without including the confidence limits.

### Detectable Differences for Each Term

<table>
<thead>
<tr>
<th>Combination No.</th>
<th>A</th>
<th>C</th>
<th>AC</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>9.00</td>
<td>5.00</td>
<td>5.00</td>
</tr>
</tbody>
</table>

This report shows the values of the Minimum Detectable Differences for each term. It is particularly useful to identify each combination when you enter several different values for various terms, so that there are several combinations.

### Effect Pattern Section

<table>
<thead>
<tr>
<th>Levels</th>
<th>Value</th>
<th>Levels</th>
<th>Value</th>
<th>Levels</th>
<th>Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>-0.50</td>
<td>1</td>
<td>-0.50</td>
<td>1.1</td>
<td>0.50</td>
</tr>
<tr>
<td>2</td>
<td>0.50</td>
<td>2</td>
<td>0.50</td>
<td>1.2</td>
<td>-0.50</td>
</tr>
<tr>
<td></td>
<td></td>
<td>2,1</td>
<td>-0.50</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td>2,2</td>
<td>0.50</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

This report shows the patterns of each of the active terms in the model. These values are multiplied by the corresponding minimum detectable differences to form the effects associated with each term.
Expanded Effect Pattern Section

<table>
<thead>
<tr>
<th>Levels</th>
<th>Value</th>
<th>Levels</th>
<th>Value</th>
<th>Levels</th>
<th>Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>1,1</td>
<td>-0.50</td>
<td>1,1</td>
<td>-0.50</td>
<td>1,1</td>
<td>0.50</td>
</tr>
<tr>
<td>1,2</td>
<td>-0.50</td>
<td>1,2</td>
<td>0.50</td>
<td>1,2</td>
<td>-0.50</td>
</tr>
<tr>
<td>2,1</td>
<td>0.50</td>
<td>2,1</td>
<td>-0.50</td>
<td>2,1</td>
<td>-0.50</td>
</tr>
<tr>
<td>2,2</td>
<td>0.50</td>
<td>2,2</td>
<td>0.50</td>
<td>2,2</td>
<td>0.50</td>
</tr>
</tbody>
</table>

This report shows the effect patterns of each of the cells in the model. These values are multiplied by the corresponding minimum detectable difference and summed to form the cell means for each group in the design.

Hypothesized Means Matrix for Detectable Differences Combination 1

<table>
<thead>
<tr>
<th>Factors</th>
<th>A1</th>
<th>A2</th>
</tr>
</thead>
<tbody>
<tr>
<td>C1</td>
<td>88.50</td>
<td>92.50</td>
</tr>
<tr>
<td>C2</td>
<td>88.50</td>
<td>102.50</td>
</tr>
</tbody>
</table>

This report shows hypothesized means matrix for each combination of detectable differences. Note that the between factors are represented across the columns of the report and the within factors are represented down its rows.

Variance-Covariance Matrix

<table>
<thead>
<tr>
<th>Factors</th>
<th>C1</th>
<th>C2</th>
</tr>
</thead>
<tbody>
<tr>
<td>C1</td>
<td>22.00</td>
<td>11.00</td>
</tr>
<tr>
<td>C2</td>
<td>11.00</td>
<td>22.00</td>
</tr>
</tbody>
</table>

This report shows the variance-covariance matrix used to generate the data. You should check that they are correct.

Variance and Autocorrelations

<table>
<thead>
<tr>
<th>Factors</th>
<th>C1</th>
<th>C2</th>
</tr>
</thead>
<tbody>
<tr>
<td>C1</td>
<td>22.00</td>
<td>0.50</td>
</tr>
<tr>
<td>C2</td>
<td>0.50</td>
<td>22.00</td>
</tr>
</tbody>
</table>

This report shows the variances on the diagonal and the autocorrelations on the off-diagonal. You should check that they are correct.

Brown and Prescott (2006) pages 268-269 present the following example of determining a sample size for a repeated measures design that is analyzed using a linear mixed model. Note that this analytic procedure is provided in PASS as the procedure entitled *Inequality Test for Two Means in a Repeated Measures Design*. That procedure is sometimes called the *time-averaged difference*.

In this example, a group size of 31 is found to achieve 80% power when the residual variance is 76, the autocorrelation is 0.53, the minimum detectable difference of a single between-subject factor is 5, the number of repeated measurements is 4, and the significance level is 0.05.

In this example, because of the long running time, the number of simulation samples will be set to 100. You can increase this to 500 or 1000 to obtain greater precision.

For reproducibility, we’ll use a random seed of 5326608.

---

### Setup

This section presents the values of each of the parameters needed to run this example. First, from the PASS Home window, load the procedure window. You may then make the appropriate entries as listed below, or open Example 2 by going to the **File** menu and choosing **Open Example Template**.

<table>
<thead>
<tr>
<th>Option</th>
<th>Value</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Design: Effect Size Tab</strong></td>
<td></td>
</tr>
<tr>
<td><strong>Sample Size</strong></td>
<td></td>
</tr>
<tr>
<td>n (Subjects Per Group)</td>
<td>31</td>
</tr>
<tr>
<td>= n’s</td>
<td>Checked</td>
</tr>
<tr>
<td>Alpha</td>
<td>0.05</td>
</tr>
<tr>
<td>Simulations</td>
<td>100</td>
</tr>
<tr>
<td>Random Seed</td>
<td>5326608</td>
</tr>
<tr>
<td><strong>Effect Size</strong></td>
<td></td>
</tr>
<tr>
<td>Specify Effects Using</td>
<td>Effects Patterns, etc.</td>
</tr>
<tr>
<td><strong>Factors Separating Subjects into Groups (Between)</strong></td>
<td></td>
</tr>
<tr>
<td>Levels (A)</td>
<td>2</td>
</tr>
<tr>
<td>Effects Pattern (A)</td>
<td>Linear Up</td>
</tr>
<tr>
<td>Detectable Difference (A)</td>
<td>5</td>
</tr>
<tr>
<td><strong>Factors with Multiple Levels Within a Subject (Within)</strong></td>
<td></td>
</tr>
<tr>
<td>Levels (C)</td>
<td>4</td>
</tr>
<tr>
<td>Effects Pattern (C)</td>
<td>Linear Up</td>
</tr>
<tr>
<td>Detectable Difference (C)</td>
<td>5</td>
</tr>
<tr>
<td><strong>Interactions</strong></td>
<td></td>
</tr>
<tr>
<td>AC</td>
<td>Not Checked</td>
</tr>
<tr>
<td>Baseline Mean</td>
<td>93</td>
</tr>
<tr>
<td><strong>Design: Covariance Tab</strong></td>
<td></td>
</tr>
<tr>
<td>G (Covariance of Random Effects)</td>
<td>Not Checked</td>
</tr>
<tr>
<td>Include G</td>
<td>Not Checked</td>
</tr>
</tbody>
</table>
R (Covariance of Residuals)
Specify R Using ................................ Variances and Autocorrelations
Times .................................................. STEP 0 1
Variance Pattern .................................. Constant in $\sigma^2$ for R
$\sigma^2$ for R ........................................ 76
Autocorrelation Pattern .................. Constant in $\rho$
$\rho$ ................................................ 0.53
If Time > ............................................ 100
Then $\rho =$ ........................................ 0

Fitted Model Tab

Fitted V(Y) Model
G Estimation ................................ G (Random Effects for Subjects)
Groups .............................................. None
R Estimation .................................... Diagonal
Groups .............................................. None

Solution Options
Likelihood Type ............................ REML
Solution Method .............................. Newton-Raphson

Reports Tab
Simulation Alpha ................................... 0.05

Output
Click the Calculate button to perform the calculations and generate the following output.

Power Report for Each Design

<table>
<thead>
<tr>
<th>Model Term</th>
<th>Power</th>
<th>Lower 95% C.L. of Power</th>
<th>Upper 95% C.L. of Power</th>
<th>Minimum Detectable Difference</th>
<th>Number of Simulation Samples</th>
<th>Factor Pattern</th>
</tr>
</thead>
<tbody>
<tr>
<td>A (2)</td>
<td>0.8000</td>
<td>0.7082</td>
<td>0.8733</td>
<td>5.00</td>
<td>0.0500</td>
<td>Linear Up</td>
</tr>
<tr>
<td>C (4)</td>
<td>1.0000</td>
<td>0.9638</td>
<td>1.0000</td>
<td>5.00</td>
<td>0.0500</td>
<td>Linear Up</td>
</tr>
</tbody>
</table>

Note that for just a 100 simulations, the power 0.79 has come out remarkably close to the actual value of 0.80 given by Brown and Prescott. The confidence interval, 0.7082 to 0.8733, is wide and could be run with a larger number of simulations to obtain a more precise answer.
Example 3 – Validation using Repeated Measures ANOVA

For balanced designs, LMM and Repeated Measures ANOVA can be used to analyze the same data. Although they both produce F-tests, the values of the F-test are different for the two tests. It is instructive to compare the power of these competing procedures.

In this example, we will determine the power for group sizes of 3, 9, and 15 when the random effects (subject) variance is 2, the residual variance is 2, the minimum detectable differences of all three terms is 1.0, the number of repeated measurements is 2, and the significance level is 0.05. A random effects model will be fit. The number of simulation samples will be set to 500.

For reproducibility, we’ll use a random seed of 5338912.

Setup

This section presents the values of each of the parameters needed to run this example. First, from the PASS Home window, load the procedure window. You may then make the appropriate entries as listed below, or open Example 3 by going to the File menu and choosing Open Example Template.

<table>
<thead>
<tr>
<th>Option</th>
<th>Value</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Design: Effect Size Tab</strong></td>
<td></td>
</tr>
<tr>
<td><strong>Sample Size</strong></td>
<td></td>
</tr>
<tr>
<td>n (Subjects Per Group)</td>
<td>3 9 15</td>
</tr>
<tr>
<td>= n’s</td>
<td>Checked</td>
</tr>
<tr>
<td>Alpha</td>
<td>0.05</td>
</tr>
<tr>
<td>Simulations</td>
<td>500</td>
</tr>
<tr>
<td>Random Seed</td>
<td>5338912</td>
</tr>
<tr>
<td><strong>Effect Size</strong></td>
<td></td>
</tr>
<tr>
<td>Specify Effects Using</td>
<td>Effects Patterns, etc.</td>
</tr>
<tr>
<td><strong>Factors Separating Subjects into Groups (Between)</strong></td>
<td></td>
</tr>
<tr>
<td>Levels (A)</td>
<td>2</td>
</tr>
<tr>
<td>Effects Pattern (A)</td>
<td>Linear Up</td>
</tr>
<tr>
<td>Detectable Difference (A)</td>
<td>1</td>
</tr>
<tr>
<td><strong>Factors with Multiple Levels Within a Subject (Within)</strong></td>
<td></td>
</tr>
<tr>
<td>Levels (C)</td>
<td>2</td>
</tr>
<tr>
<td>Effects Pattern (C)</td>
<td>Linear Up</td>
</tr>
<tr>
<td>Detectable Difference (C)</td>
<td>1</td>
</tr>
<tr>
<td><strong>Interactions</strong></td>
<td></td>
</tr>
<tr>
<td>AC</td>
<td>Checked</td>
</tr>
<tr>
<td>Detectable Difference (AC)</td>
<td>1</td>
</tr>
<tr>
<td>Baseline Mean</td>
<td>0</td>
</tr>
<tr>
<td><strong>Design: Covariance Tab</strong></td>
<td></td>
</tr>
<tr>
<td>G (Covariance of Random Effects)</td>
<td></td>
</tr>
<tr>
<td>Include G</td>
<td>Checked</td>
</tr>
<tr>
<td>g (Subject σ²)</td>
<td>2</td>
</tr>
</tbody>
</table>
R (Covariance of Residuals)
Specify R Using ...................................... Variances Only
Times ...................................................... STEP 0 1
Variance Pattern ...................................... Constant in $\sigma^2$ for R
$\sigma^2$ for R ........................................... 2

Fitted Model Tab

Fitted V(Y) Model
G Estimation ...................................... G (Random Effects for Subjects)
Groups .................................................. None
R Estimation ........................................... Diagonal
Groups .................................................. None

Solution Options
Likelihood Type ...................................... REML
Solution Method ..................................... Newton-Raphson

Reports Tab
Simulation Alpha ..................................... 0.05

Output
Click the Calculate button to perform the calculations and generate the following output.

Power Report for Each Design

<table>
<thead>
<tr>
<th>Model Term</th>
<th>Power</th>
<th>Lower 95% C.L. of Power</th>
<th>Upper 95% C.L. of Power</th>
<th>N(1)</th>
<th>N</th>
<th>Minimum Detectable Difference</th>
<th>Alpha</th>
<th>Number of Simulation Samples</th>
<th>Factor Pattern</th>
</tr>
</thead>
<tbody>
<tr>
<td>A</td>
<td>0.0380</td>
<td>0.0230</td>
<td>0.0587</td>
<td>3</td>
<td>6</td>
<td>1.00</td>
<td>0.0500</td>
<td>500</td>
<td>Linear Up</td>
</tr>
<tr>
<td>C</td>
<td>0.1760</td>
<td>0.1436</td>
<td>0.2123</td>
<td>3</td>
<td>6</td>
<td>1.00</td>
<td>0.0500</td>
<td>500</td>
<td>Linear Up</td>
</tr>
<tr>
<td>AC</td>
<td>0.2140</td>
<td>0.1788</td>
<td>0.2526</td>
<td>3</td>
<td>6</td>
<td>1.00</td>
<td>0.0500</td>
<td>500</td>
<td></td>
</tr>
<tr>
<td>A</td>
<td>0.2240</td>
<td>0.1862</td>
<td>0.2631</td>
<td>9</td>
<td>18</td>
<td>1.00</td>
<td>0.0500</td>
<td>500</td>
<td>Linear Up</td>
</tr>
<tr>
<td>C</td>
<td>0.4820</td>
<td>0.4374</td>
<td>0.5268</td>
<td>9</td>
<td>18</td>
<td>1.00</td>
<td>0.0500</td>
<td>500</td>
<td>Linear Up</td>
</tr>
<tr>
<td>AC</td>
<td>0.5520</td>
<td>0.5072</td>
<td>0.5962</td>
<td>9</td>
<td>18</td>
<td>1.00</td>
<td>0.0500</td>
<td>500</td>
<td></td>
</tr>
<tr>
<td>A</td>
<td>0.3580</td>
<td>0.3159</td>
<td>0.4018</td>
<td>15</td>
<td>30</td>
<td>1.00</td>
<td>0.0500</td>
<td>500</td>
<td>Linear Up</td>
</tr>
<tr>
<td>C</td>
<td>0.7520</td>
<td>0.7117</td>
<td>0.7893</td>
<td>15</td>
<td>30</td>
<td>1.00</td>
<td>0.0500</td>
<td>500</td>
<td>Linear Up</td>
</tr>
<tr>
<td>AC</td>
<td>0.7280</td>
<td>0.6867</td>
<td>0.7666</td>
<td>15</td>
<td>30</td>
<td>1.00</td>
<td>0.0500</td>
<td>500</td>
<td></td>
</tr>
</tbody>
</table>

Next, we will run this same design through the Repeated Measures ANOVA procedure. To make it comparable, set both the between and within factors (B and W) to have two levels each with Sm set to 0.5. The covariance is set with SD1 equal to 2 and R1 equal to 0.5.

The results of this run are presented next.
### Power Report for RMANOVA

<table>
<thead>
<tr>
<th>Term</th>
<th>Test</th>
<th>Power</th>
<th>n</th>
<th>N</th>
<th>Multiply Means By (Sm)</th>
<th>SD of Effects (Sigma)</th>
<th>Standard Deviation of Effects (Sigma)</th>
<th>Effect Size</th>
<th>Alpha</th>
<th>Beta</th>
</tr>
</thead>
<tbody>
<tr>
<td>B(2)</td>
<td>F</td>
<td>0.0859</td>
<td>3</td>
<td>6</td>
<td>1.00</td>
<td>0.50</td>
<td>1.73</td>
<td>0.29</td>
<td>0.0500</td>
<td>0.9141</td>
</tr>
<tr>
<td>W(2)</td>
<td>F</td>
<td>0.1588</td>
<td>3</td>
<td>6</td>
<td>1.00</td>
<td>0.50</td>
<td>1.00</td>
<td>0.50</td>
<td>0.0500</td>
<td>0.8412</td>
</tr>
<tr>
<td>BW</td>
<td>F</td>
<td>0.1588</td>
<td>3</td>
<td>6</td>
<td>1.00</td>
<td>0.50</td>
<td>1.00</td>
<td>0.50</td>
<td>0.0500</td>
<td>0.8412</td>
</tr>
</tbody>
</table>

The above results are summarized in the following table.

### Comparing LMM and RMANOVA Power

<table>
<thead>
<tr>
<th>Model Term</th>
<th>Power</th>
<th>Lower 95% C.L. of Power</th>
<th>Upper 95% C.L. of Power</th>
<th>RMANOVA Power N(1)</th>
</tr>
</thead>
<tbody>
<tr>
<td>A (2)</td>
<td>0.0380</td>
<td>0.0230</td>
<td>0.0587</td>
<td>0.0859</td>
</tr>
<tr>
<td>C (2)</td>
<td>0.1760</td>
<td>0.1436</td>
<td>0.2123</td>
<td>0.1588</td>
</tr>
<tr>
<td>AC</td>
<td>0.2140</td>
<td>0.1788</td>
<td>0.2526</td>
<td>0.1588</td>
</tr>
</tbody>
</table>

By studying the values in this table, we see that two procedures agree very well for group sample sizes of 9 and 15. However, when the group sample size is 3, the power of RMANOVA is higher.
Example 4 – Repeated Measures with Heterogeneous Variances

One of the features offered by LMM is the ability to specify unequal group variances. This example will look at how to do this.

In this example, we will determine the power for group sizes of 6 when the random effects (subject) variance is 2 when A = 1 and 4 with A = 2, the residual variance is 2 when A = 1 and 4 when A = 2, the minimum detectable differences of all three terms is 1.0, the number of repeated measurements is 2, and the significance level is 0.05. A random effects model will be fit. The number of simulation samples will be set to 100.

Setup

This section presents the values of each of the parameters needed to run this example. First, from the PASS Home window, load the procedure window. You may then make the appropriate entries as listed below, or open Example 4 by going to the File menu and choosing Open Example Template.

<table>
<thead>
<tr>
<th>Option</th>
<th>Value</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Sample Size</strong></td>
<td></td>
</tr>
<tr>
<td>n (Subjects Per Group) ...............</td>
<td>6</td>
</tr>
<tr>
<td>= n’s ........................................</td>
<td>Checked</td>
</tr>
<tr>
<td>Alpha ........................................</td>
<td>0.05</td>
</tr>
<tr>
<td>Simulations ................................</td>
<td>100</td>
</tr>
<tr>
<td>Random Seed ................................</td>
<td>Blank or Random</td>
</tr>
<tr>
<td><strong>Effect Size</strong></td>
<td></td>
</tr>
<tr>
<td>Specify Effects Using ..................</td>
<td>Effects Patterns, etc.</td>
</tr>
<tr>
<td><strong>Factors Separating Subjects into Groups (Between)</strong></td>
<td></td>
</tr>
<tr>
<td>Levels (A) ...............................</td>
<td>2</td>
</tr>
<tr>
<td>Effects Pattern (A) ....................</td>
<td>Linear Up</td>
</tr>
<tr>
<td>Detectable Difference (A) ............</td>
<td>1</td>
</tr>
<tr>
<td><strong>Factors with Multiple Levels Within a Subject (Within)</strong></td>
<td></td>
</tr>
<tr>
<td>Levels (C) ...............................</td>
<td>2</td>
</tr>
<tr>
<td>Effects Pattern (C) ....................</td>
<td>Linear Up</td>
</tr>
<tr>
<td>Detectable Difference (C) ............</td>
<td>1</td>
</tr>
<tr>
<td><strong>Interactions</strong></td>
<td></td>
</tr>
<tr>
<td>AC .............................................</td>
<td>checked</td>
</tr>
<tr>
<td>Detectable Difference (AC) ...........</td>
<td>1</td>
</tr>
<tr>
<td>Baseline Mean ............................</td>
<td>0</td>
</tr>
<tr>
<td><strong>Design: Covariance Tab</strong></td>
<td></td>
</tr>
<tr>
<td><strong>Group Option</strong></td>
<td></td>
</tr>
<tr>
<td>Grouping Factor ..........................</td>
<td>A</td>
</tr>
<tr>
<td><strong>G (Covariance of Random Effects)</strong></td>
<td></td>
</tr>
<tr>
<td>Include G ...................................</td>
<td>Checked</td>
</tr>
<tr>
<td>g (Subject σ²) ............................</td>
<td>2 4</td>
</tr>
</tbody>
</table>
### R (Covariance of Residuals)

Specify R Using ........................................... Variances Only
Times .............................................................. STEP 0 1
Variance Pattern ................................................... Constant in $\sigma^2$ for R
$\sigma^2$ for R ........................................................... 2 4

### Fitted Model Tab

**Fitted V(Y) Model**

G Estimation .................................................. G (Random Effects for Subjects)
Groups ............................................................... A
R Estimation ................................................... Diagonal
Groups ............................................................... A

### Solution Options

Likelihood Type ............................................... REML
Solution Method ................................................ Newton-Raphson

### Reports Tab

Simulation Alpha ............................................... 0.05

---

### Output

Click the Calculate button to perform the calculations and generate the following output.

#### Power Report for Each Design

<table>
<thead>
<tr>
<th>Model Term</th>
<th>Power</th>
<th>Lower 95% C.L. of Power</th>
<th>Upper 95% C.L. of Power</th>
<th>Minimum Detectable Difference</th>
<th>Alpha N(1)</th>
<th>Number of Simulation Samples</th>
<th>Factor Pattern</th>
</tr>
</thead>
<tbody>
<tr>
<td>A (2)</td>
<td>0.1500</td>
<td>0.0865</td>
<td>0.2353</td>
<td>6 12</td>
<td>0.0500</td>
<td>100</td>
<td>Linear Up</td>
</tr>
<tr>
<td>C (2)</td>
<td>0.2200</td>
<td>0.1433</td>
<td>0.3139</td>
<td>6 12</td>
<td>0.0500</td>
<td>100</td>
<td>Linear Up</td>
</tr>
<tr>
<td>AC</td>
<td>0.2800</td>
<td>0.1948</td>
<td>0.3787</td>
<td>6 12</td>
<td>0.0500</td>
<td>100</td>
<td></td>
</tr>
</tbody>
</table>

#### Variance-Covariance Matrix

<table>
<thead>
<tr>
<th>Factors</th>
<th>C1</th>
<th>C2</th>
</tr>
</thead>
<tbody>
<tr>
<td>A1C1</td>
<td>4.00</td>
<td>2.00</td>
</tr>
<tr>
<td>A1C2</td>
<td>2.00</td>
<td>4.00</td>
</tr>
<tr>
<td>A2C1</td>
<td>8.00</td>
<td>4.00</td>
</tr>
<tr>
<td>A2C2</td>
<td>4.00</td>
<td>8.00</td>
</tr>
</tbody>
</table>

Note that now there are two variance-covariance matrices displayed.

#### Variances and Autocorrelations

<table>
<thead>
<tr>
<th>Factors</th>
<th>C1</th>
<th>C2</th>
</tr>
</thead>
<tbody>
<tr>
<td>A1C1</td>
<td>4.00</td>
<td>0.50</td>
</tr>
<tr>
<td>A1C2</td>
<td>0.50</td>
<td>4.00</td>
</tr>
<tr>
<td>A2C1</td>
<td>8.00</td>
<td>0.50</td>
</tr>
<tr>
<td>A2C2</td>
<td>0.50</td>
<td>8.00</td>
</tr>
</tbody>
</table>

Notice how easy it is to obtain a power analysis for the case of unequal variances.
Example 5 – T-Test with Heterogeneous Variances (Searching for \( n \))

This example will show how to determine the power of a design that is usually analyzed with a t-test. However, in this example, the variances of the two groups are known to be very different.

In this example, the variance of the first group is 4, the variance of the second group is 9, the minimum detectable difference is set to 1.0, the significance level is 0.05, and the number of simulation samples is 100. There are no repeated measurements. Since a sample size search capability is not available in this routine, we will conduct a manual search by calculating the power for group sample sizes of 10, 20, 30, 40, 50, 60, 70, 80, 90, and 100.

**Setup**

This section presents the values of each of the parameters needed to run this example. First, from the PASS Home window, load the procedure window. You may then make the appropriate entries as listed below, or open Example 5 by going to the File menu and choosing Open Example Template.

<table>
<thead>
<tr>
<th>Option</th>
<th>Value</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Design: Effect Size Tab</strong></td>
<td></td>
</tr>
<tr>
<td>Sample Size</td>
<td></td>
</tr>
<tr>
<td>( n ) (Subjects Per Group)</td>
<td>10 20 30 40 50 60 70 80 90 100</td>
</tr>
<tr>
<td>( = n's )</td>
<td>Checked</td>
</tr>
<tr>
<td>Alpha</td>
<td>0.05</td>
</tr>
<tr>
<td>Simulations</td>
<td>100</td>
</tr>
<tr>
<td>Random Seed</td>
<td>Blank or Random</td>
</tr>
<tr>
<td>Effect Size</td>
<td></td>
</tr>
<tr>
<td>Specify Effects Using</td>
<td>Effects Patterns, etc.</td>
</tr>
<tr>
<td>Factors Separating Subjects into Groups (Between)</td>
<td></td>
</tr>
<tr>
<td>Levels (A)</td>
<td>2</td>
</tr>
<tr>
<td>Effects Pattern (A)</td>
<td>Linear Up</td>
</tr>
<tr>
<td>Detectable Difference (A)</td>
<td>1</td>
</tr>
<tr>
<td>Factors with Multiple Levels Within a Subject (Within)</td>
<td></td>
</tr>
<tr>
<td>Levels (C)</td>
<td>0</td>
</tr>
<tr>
<td>Interactions</td>
<td>0</td>
</tr>
<tr>
<td>Design: Covariance Tab</td>
<td></td>
</tr>
<tr>
<td>Group Option</td>
<td></td>
</tr>
<tr>
<td>Grouping Factor</td>
<td>A</td>
</tr>
<tr>
<td><strong>G (Covariance of Random Effects)</strong></td>
<td></td>
</tr>
<tr>
<td>Include G</td>
<td>Not Checked</td>
</tr>
<tr>
<td><strong>R (Covariance of Residuals)</strong></td>
<td></td>
</tr>
<tr>
<td>Specify R Using</td>
<td>Variances Only</td>
</tr>
<tr>
<td>Times</td>
<td>STEP 0 1</td>
</tr>
<tr>
<td>Variance Pattern</td>
<td>Constant in ( \sigma^2 ) for R</td>
</tr>
<tr>
<td>( \sigma^2 ) for R</td>
<td>4 9</td>
</tr>
</tbody>
</table>
Fitted Model Tab

**Fitted V(Y) Model**
- G Estimation: None
- R Estimation: Diagonal
- Groups: A

**Solution Options**
- Likelihood Type: REML
- Solution Method: Newton-Raphson

Reports Tab
- Simulation Alpha: 0.05

### Output

Click the Calculate button to perform the calculations and generate the following output.

#### Power Report for 10, 20, 30, 40, 50, 60, 70, 80, 90, 100 – Simulations = 100

<table>
<thead>
<tr>
<th>Model Term</th>
<th>Power</th>
<th>Lower 95% C.L. of Power</th>
<th>Upper 95% C.L. of Power</th>
<th>Minimum Detectable Difference</th>
<th>Alpha</th>
<th>Number of Simulation Samples</th>
<th>Factor Pattern</th>
</tr>
</thead>
<tbody>
<tr>
<td>A (2)</td>
<td>0.2200</td>
<td>0.1433</td>
<td>0.3139</td>
<td>10</td>
<td>20</td>
<td>1.00</td>
<td>0.0500 100 Linear Up</td>
</tr>
<tr>
<td>A (2)</td>
<td>0.4000</td>
<td>0.3033</td>
<td>0.5028</td>
<td>20</td>
<td>40</td>
<td>1.00</td>
<td>0.0500 100 Linear Up</td>
</tr>
<tr>
<td>A (2)</td>
<td>0.4500</td>
<td>0.3503</td>
<td>0.5527</td>
<td>30</td>
<td>60</td>
<td>1.00</td>
<td>0.0500 100 Linear Up</td>
</tr>
<tr>
<td>A (2)</td>
<td>0.6200</td>
<td>0.5175</td>
<td>0.7152</td>
<td>40</td>
<td>80</td>
<td>1.00</td>
<td>0.0500 100 Linear Up</td>
</tr>
<tr>
<td>A (2)</td>
<td>0.6500</td>
<td>0.5482</td>
<td>0.7427</td>
<td>50</td>
<td>100</td>
<td>1.00</td>
<td>0.0500 100 Linear Up</td>
</tr>
<tr>
<td>A (2)</td>
<td>0.7500</td>
<td>0.6534</td>
<td>0.8312</td>
<td>60</td>
<td>120</td>
<td>1.00</td>
<td>0.0500 100 Linear Up</td>
</tr>
<tr>
<td>A (2)</td>
<td>0.8600</td>
<td>0.7763</td>
<td>0.9213</td>
<td>70</td>
<td>140</td>
<td>1.00</td>
<td>0.0500 100 Linear Up</td>
</tr>
<tr>
<td>A (2)</td>
<td>0.8500</td>
<td>0.7647</td>
<td>0.9135</td>
<td>80</td>
<td>160</td>
<td>1.00</td>
<td>0.0500 100 Linear Up</td>
</tr>
<tr>
<td>A (2)</td>
<td>0.9000</td>
<td>0.8238</td>
<td>0.9510</td>
<td>90</td>
<td>180</td>
<td>1.00</td>
<td>0.0500 100 Linear Up</td>
</tr>
<tr>
<td>A (2)</td>
<td>0.9800</td>
<td>0.9296</td>
<td>0.9976</td>
<td>100</td>
<td>200</td>
<td>1.00</td>
<td>0.0500 100 Linear Up</td>
</tr>
</tbody>
</table>

If our goal is to achieve 90% power, it appears that we should investigate group sample sizes of 70, 75, 80, 85, and 90 using a larger simulation size, say 500. Putting these values in for \( n \) and running gives the following results.

#### Power Report for 70, 75, 80, 85, 90 – Simulations = 500

<table>
<thead>
<tr>
<th>Model Term</th>
<th>Power</th>
<th>Lower 95% C.L. of Power</th>
<th>Upper 95% C.L. of Power</th>
<th>Minimum Detectable Difference</th>
<th>Alpha</th>
<th>Number of Simulation Samples</th>
<th>Factor Pattern</th>
</tr>
</thead>
<tbody>
<tr>
<td>A (2)</td>
<td>0.8680</td>
<td>0.8351</td>
<td>0.8964</td>
<td>70</td>
<td>140</td>
<td>1.00</td>
<td>0.0500 500 Linear Up</td>
</tr>
<tr>
<td>A (2)</td>
<td>0.8640</td>
<td>0.8308</td>
<td>0.8928</td>
<td>75</td>
<td>150</td>
<td>1.00</td>
<td>0.0500 500 Linear Up</td>
</tr>
<tr>
<td>A (2)</td>
<td>0.8840</td>
<td>0.8526</td>
<td>0.9107</td>
<td>80</td>
<td>160</td>
<td>1.00</td>
<td>0.0500 500 Linear Up</td>
</tr>
<tr>
<td>A (2)</td>
<td>0.9040</td>
<td>0.8747</td>
<td>0.9284</td>
<td>85</td>
<td>170</td>
<td>1.00</td>
<td>0.0500 500 Linear Up</td>
</tr>
<tr>
<td>A (2)</td>
<td>0.9240</td>
<td>0.8972</td>
<td>0.9457</td>
<td>90</td>
<td>180</td>
<td>1.00</td>
<td>0.0500 500 Linear Up</td>
</tr>
</tbody>
</table>

It appears that a group sample size of 90 will give us a power of 90%.
It appears that a group sample size of 90 will give us a power of 90%.

<table>
<thead>
<tr>
<th>Model Term</th>
<th>Power</th>
<th>Lower 95% C. L. of Power</th>
<th>Upper 95% C. L. of Power</th>
<th>Minimum Detectable Difference</th>
<th>Number of Simulation Samples</th>
<th>Factor Pattern</th>
</tr>
</thead>
<tbody>
<tr>
<td>A (2)</td>
<td>0.9185</td>
<td>0.9056</td>
<td>0.9301</td>
<td>90</td>
<td>180</td>
<td>Linear Up</td>
</tr>
</tbody>
</table>