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curve fitting, statistical analysis, and plotting.

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Repeat measures ANOVA is a special type of 2-way ANOVA where the rows in the data matrix are subjects but the columns are now repeated observations of the same variable in some sequence, for instance at fixed intervals of time. It is usual to investigate the data for sphericity, which is when the covariance matrix of orthonormal contrasts is a multiple of the identity matrix, as this is required before the repeat measures ANOVA procedure is valid. Note that SIMFIT also provides the options for Hotelling T^2 and Friedman nonparametric ANOVA tests at the same time, in case the hypothesis of sphericity is not supported but the indication of a column effect is still of interest.

Open the main SIMFIT menu, choose [Statistics], [ANOVA], then repeat measures, and analyze the default data set contained in test file `anova6.tf1`, which has four measurements of the same variable for each of five subjects arranged as follows.

Subject	Measurement 1	Measurement 2	Measurement 3	Measurement 4
A	30	28	16	34
B	14	18	10	22
C	24	20	18	30
D	38	34	20	44
E	26	28	14	30

Now choose to analyze without a data transformation which leads to the following result where a likelihood ratio test statistic ($LRTS$) is calculated to test for sphericity.

Repeat-Measures Analysis of Variance

Data file: `anova6.tf1`

Sphericity test on CV of Helmert orthonormal contrasts

H_0 : Covariance matrix = k *Identity (for some $k > 0$)

Number of small eigenvalues	0	i.e. $< 1.00E - 07$
Number of variables (m)	4	
Sample size (n)	5	
Determinant of CV	154.9	
Trace of CV	28.20	
Mauchly W statistic	0.1865	
$LRTS(-2 \log(\lambda))$	4.572	
Degrees of Freedom	5	
$P(\chi^2 \geq LRTS)$	0.4704	
e (Geisser-Greenhouse)	0.6049	
e (Huynh-Feldt)	1.0000	
e (lower bound)	0.3333	

Clearly the hypothesis of sphericity cannot be rejected for these data.

The next table displays the ANOVA results with, in this example, the optional Friedman nonparametric test, and Hotelling T^2 test also included.

Results for repeat-measures ANOVA: Grand mean 24.90

Source	SSQ	NDOF	MSSQ	F	p
Subjects	6.808E+02	4			
Treatments	6.982E+02	3	232.7	24.76	0.0000
					0.0006 Greenhouse-Geisser
					0.0000 Huyhn-Feldt
					0.0076 Lower-bound
Remainder	112.8	12	9.400		
Total	1492	19			

Results for Friedman Nonparametric Two-Way Analysis of Variance

Test Statistic	13.56
Number of degrees of freedom	3
Significance	0.0036

Results for the Hotelling one sample T^2 test

H_0 : Column means are all equal

Number of rows	5
Number of columns	4
Hotelling T^2	170.5
F Statistic (FTS)	28.41
Degrees of Freedom ($d1, d2$)	3, 2
$P(F(d1, d2) \geq FTS)$	0.0342 <i>Reject H_0 at 5% significance level</i>

Note that, for these data, all three tests reject the null hypothesis of the absence of a column effect.

Theoretical details

The repeat measures procedure is used when you have paired measurements, and wish to test for absence of treatment effects. With two samples it is equivalent to the two-sample paired t test, so it can be regarded as an extension of this test to cases with more than two columns. If the rows of a data matrix represent the effects of different column-wise treatments on the same subjects, so that the values are serially correlated, and it is wished to test for significant treatment effects irrespective of differences between subjects, then repeated-measurements design is appropriate. The simplest, model-free, approach is to treat this as a special case of 2-way ANOVA where only between-column effects are considered and between-row effects, i.e., between subject variances, are expected to be appreciable, but are not considered. Many further specialized techniques are also possible, when it is reasonable to attempt to model the treatment effects, e.g., when the columns represent observations in sequence of, say, time or drug concentration, but often such effects are best fitted by nonlinear rather than linear models. A useful way to visualize repeated-measurements ANOVA data with small samples (≤ 12 subjects) is to input the matrix into the exhaustive analysis of a matrix procedure and plot the matrix with rows identified by different symbols.

The previous tables show the results from analyzing data in the test file `anova6.tf1` in three sections, a Mauchly sphericity test, an ANOVA table, and a Hotelling T^2 test, all of which will now be discussed.

In order for the normal two-way univariate ANOVA to be appropriate, sphericity of the covariance matrix of orthonormal contrasts is required. The test is based on a orthonormal contrast matrix, for example a Helmert matrix of the form

$$C = \begin{pmatrix} 1/\sqrt{2} & -1/\sqrt{2} & 0 & 0 & 0 & \dots \\ 1/\sqrt{6} & 1/\sqrt{6} & -2/\sqrt{6} & 0 & 0 & \dots \\ 1/\sqrt{12} & 1/\sqrt{12} & 1/\sqrt{12} & -3/\sqrt{12} & 0 & \dots \\ \dots & \dots & \dots & \dots & \dots & \dots \end{pmatrix}$$

which, for m columns, has dimensions $m - 1$ by m , and where every row sum is zero, every row has length unity, and all the rows are orthogonal. Such Helmert contrasts compare each successive column mean with the average of the preceding (or following) column means but, in the subsequent discussion, any orthonormal contrast matrix leads to the same end result, namely, when the covariance matrix of orthonormal contrasts satisfies the sphericity condition, then the sums of squares used to construct the F test statistics will be independent chi-square variables and the two-way univariate ANOVA technique will be the most powerful technique to test for equality of column means.

The sphericity test uses the sample covariance matrix S to construct the Mauchly W statistic given by

$$W = \frac{|CSC^T|}{[Tr(CSC^T)/(m-1)]^{m-1}}.$$

If S is estimated with ν degrees of freedom then

$$\chi^2 = - \left[\nu - \frac{2m^2 - 3m + 3}{6(m-1)} \right] \log W$$

is approximately distributed as chi-square with $m(m-1)/2 - 1$ degrees of freedom. Clearly, the results in the previous tables show that the hypothesis of sphericity cannot be rejected, and the results from two-way ANOVA can be tentatively accepted. However, in some instances, it may be necessary to alter the degrees of freedom for the F statistics as discussed next.

The model for univariate repeated measures with m treatments used once on each of n subjects is a mixed model of the form

$$y_{ij} = \mu + \tau_i + \beta_j + e_{ij},$$

where τ_i is the fixed effect of treatment i so that $\sum_{i=1}^m \tau_i = 0$, and β_j is the random effect of subject j with mean zero, and $\sum_{j=1}^n \beta_j = 0$. Hence the decomposition of the sum of squares is

$$\sum_{i=1}^m \sum_{j=1}^n (y_{ij} - \bar{y}_{.j})^2 = n \sum_{i=1}^m (\bar{y}_{i.} - \bar{y}_{..})^2 + \sum_{i=1}^m \sum_{j=1}^n (y_{ij} - \bar{y}_{i.} - \bar{y}_{.j} + \bar{y}_{..})^2,$$

that is

$$SSQ_{\text{Within subjects}} = SSQ_{\text{treatments}} + SSQ_{\text{Error}}$$

with degrees of freedom

$$n(m-1) = (m-1) + (m-1)(n-1).$$

To test the hypothesis of no treatment effect, that is

$$H_0 : \tau_i = 0 \text{ for } i = 1, 2, \dots, m,$$

the appropriate test statistic would be

$$F = \frac{SSQ_{\text{treatment}}/(m-1)}{SSQ_{\text{Error}}/[(m-1)(n-1)]}$$

but, to make this test more robust, it may be necessary to adjust the degrees of freedom when calculating critical levels. In fact the degrees of freedom should be taken as

$$\begin{aligned} \text{Numerator degrees of freedom} &= \epsilon(m-1) \\ \text{Denominator degrees of freedom} &= \epsilon(m-1)(n-1) \end{aligned}$$

where there are four possibilities for the correction factor ϵ , all with $0 \leq \epsilon \leq 1$.

1. The default epsilon.

This is $\epsilon = 1$, which is the correct choice if the sphericity criterion is met.

2. The Greenhouse-Geisser epsilon.

This is

$$\epsilon = \frac{(\sum_{i=1}^{m-1} \lambda_i)^2}{(m-1) \sum_{i=1}^{m-1} \lambda_i^2}$$

where λ_i are the eigenvalues of the covariance matrix of orthonormal contrasts, and it could be used if the sphericity criterion is not met, although some argue that it is an ultraconservative estimate.

3. The Huyhn-Feldt epsilon.

This can also be used when the sphericity criterion is not met, and it is constructed from the Greenhouse-Geisser estimate $\hat{\epsilon}$ as follows

$$\begin{aligned} a &= n(m-1)\hat{\epsilon} - 2 \\ b &= (m-1)(n-G - (m-1)\hat{\epsilon}) \\ \epsilon &= \min(1, a/b), \end{aligned}$$

where G is the number of groups. It is generally recommended to use this estimate if the ANOVA probabilities given by the various adjustments differ appreciably.

4. The lower bound epsilon.

This is defined as

$$\epsilon = 1/(m-1)$$

which is the smallest value and results in using the F statistic with 1 and $n-1$ degrees of freedom.

If the sphericity criterion is not met, then it is possible to use multivariate techniques such as MANOVA as long as $n > m$, as these do not require sphericity, but these will always be less powerful than the univariate ANOVA just discussed.

One possibility is to use the Hotelling T^2 test to see if the column means differ significantly, and the results displayed in the previous tables were obtained in this way. Again a matrix C of orthonormal contrasts is used together with the vector of column means

$$\bar{y} = (\bar{y}_1, \bar{y}_2, \dots, \bar{y}_m)^T$$

to construct the statistic

$$T^2 = n(C\bar{y})^T (CSC^T)^{-1} (C\bar{y})$$

since

$$\frac{(n-m+1)T^2}{(n-1)(m-1)} \sim F(m-1, n-m+1)$$

if all column means are equal.