Repeated Measures ANOVA

- The unstructured multivariate approach makes no assumptions concerning the covariance structure

- While this is robust, it can result in low power

- For normally-distributed responses, it would be natural to use ANOVA methods if the repeated measurements were independent

- A traditional approach to repeated measures is to:

  - perform a standard ANOVA
    (as if the observations were independent)

  - determine if additional assumptions or modifications are required to make the analysis valid

Repeated Measures ANOVA
The Fundamental Model

- Let y_{ij} denote the response from subject i at time j, for $i = 1, \ldots, n$, $j = 1, \ldots, t$

- The general basis for repeated measures ANOVA is the model

$$y_{ij} = \mu_{ij} + \pi_{ij} + e_{ij}$$

- μ_{ij} is the mean at time j for individuals randomly selected from the same population as individual i

- π_{ij} is the consistent departure of y_{ij} from μ_{ij} for the ith individual

- e_{ij} is the departure of y_{ij} from $\mu_{ij} + \pi_{ij}$ for individual i at time j

Types of Effects in the Model

- The μ_{ij} parameters are called *fixed* effects

  μ_{ij} has a fixed value irrespective of the particular individual

  "an immutable constant of the universe"

- The π_{ij} parameters are called *random* effects

  π_{ij} varies randomly over the population of individuals

  "a lasting characteristic of the individual"

- The e_{ij} parameters are random error terms

  "a fleeting aberration of the moment"

- Since the fundamental model contains both fixed and random effects, it is often called the mixed model

Assumptions of the Fundamental Model

Means and Variances:

- For given j, $\mathrm{E}(\pi_{ij}) = 0$ and $\mathrm{Var}(\pi_{ij}) = \sigma^2_{\pi j}$

  The variance is constant over individuals

  Any nonzero mean is absorbed in μ_{ij}

- For given j, $\mathrm{E}(e_{ij}) = 0$ and $\mathrm{Var}(e_{ij}) = \sigma^2_j$

  The error variance is constant over individuals

Correlation Structure:

- $\mathrm{Cov}(\pi_{ij}, \pi_{i'j}) = \mathrm{Cov}(\pi_{ij}, \pi_{i'j'}) = 0$

  The random effects for different subjects are uncorrelated

- $\mathrm{Cov}(\pi_{ij}, \pi_{ij'}) = \sigma_{\pi jj'}$

  Within-subject covariances of random effects are the same across subjects

Assumptions of the Fundamental Model

<u>Correlation Structure</u>:

- $\mathrm{Cov}(e_{ij}, e_{i'j'}) = 0$ if $i \neq i'$ or $j \neq j'$

  the error terms are all uncorrelated

- $\mathrm{Cov}(\pi_{ij}, e_{i'j'}) = 0$ for all i, j, i', j'

  The random effects and the error terms are uncorrelated

<u>Distributional Assumptions</u>:

- The random effects π_{ij} and the error terms e_{ij} are normally distributed

<u>Some Common Simplifications</u>:

- $\sigma^2_{\pi j} = \sigma^2_\pi$ is constant across time points
- $\sigma_{\pi jj'}$ is constant for all j, j'
- $\sigma^2_j = \sigma^2$ is constant across time points

Consequences of the Assumptions

- $\mathrm{E}(y_{ij}) = \mu_{ij} \quad$ (since $\mathrm{E}(\pi_{ij}) = \mathrm{E}(e_{ij}) = 0$)

- $$\begin{aligned}\mathrm{Cov}(y_{ij}, y_{i'j'}) &= \mathrm{E}[(y_{ij} - \mu_{ij})(y_{i'j'} - \mu_{i'j'})] \\ &= \mathrm{E}[(\pi_{ij} + e_{ij})(\pi_{i'j'} + e_{i'j'})] \\ &= \mathrm{E}[\pi_{ij}\pi_{i'j'} + \pi_{ij}e_{i'j'} + \pi_{i'j'}e_{ij} \\ &\qquad + e_{ij}e_{i'j'}]\end{aligned}$$

- $\mathrm{E}(\pi_{ij}\pi_{i'j'}) = \begin{cases} \mathrm{Var}(\pi_{ij}) & \text{if } i = i',\, j = j' \\ \mathrm{Cov}(\pi_{ij}, \pi_{i'j'}) & \text{otherwise} \end{cases}$

- $\mathrm{E}(\pi_{ij}\pi_{i'j'}) = \begin{cases} \sigma^2_{\pi j} & \text{if } i = i',\, j = j' \\ \sigma_{\pi jj'} & \text{if } i = i',\, j \neq j' \\ 0 & \text{if } i \neq i' \end{cases}$

- Thus, $\mathrm{E}(\pi_{ij}\pi_{i'j'}) = \delta_{ii'}\sigma_{\pi jj'}$, where

$$\delta_{ii'} = \begin{cases} 1 & \text{if } i = i' \\ 0 & \text{otherwise} \end{cases}$$

and $\sigma_{\pi jj} = \sigma^2_{\pi j}$

Consequences of the Assumptions

- $\mathrm{Cov}(y_{ij}, y_{i'j'}) = \mathrm{E}[\pi_{ij}\pi_{i'j'} + \pi_{ij}e_{i'j'} + \pi_{i'j'}e_{ij}$
$$+e_{ij}e_{i'j'}]$$

- $\mathrm{E}(\pi_{ij}e_{i'j'}) = 0, \quad \mathrm{E}(\pi_{i'j'}e_{ij}) = 0$

- $\mathrm{E}(e_{ij}e_{i'j'}) = \begin{cases} \mathrm{Var}(e_{ij}) & \text{if } i = i',\ j = j' \\ \mathrm{Cov}(e_{ij}, e_{i'j'}) & \text{otherwise} \end{cases}$

- $\mathrm{E}(e_{ij}e_{i'j'}) = \begin{cases} \sigma_j^2 & \text{if } i = i',\ j = j' \\ 0 & \text{otherwise} \end{cases}$

  or $\mathrm{E}(e_{ij}e_{i'j'}) = \delta_{ii'}\delta_{jj'}\sigma_j^2$

- Thus, the model specification for the first two moments of y_{ij} is

$$\mathrm{E}(y_{ij}) = \mu_{ij}$$

$$\begin{aligned} \mathrm{Cov}(y_{ij}, y_{i'j'}) &= \delta_{ii'}\sigma_{\pi jj'} + \delta_{ii'}\delta_{jj'}\sigma_j^2 \\ &= \delta_{ii'}(\sigma_{\pi jj'} + \delta_{jj'}\sigma_j^2) \end{aligned}$$

Correlation Structure

- Observations from different individuals ($i \neq i'$) are uncorrelated

- The correlation between measurements on the same individual is called an *intraclass correlation* and is given by

$$\mathrm{Corr}(y_{ij}, y_{ij'}) = \frac{\sigma_{\pi jj'}}{[(\sigma_{\pi jj} + \sigma_j^2)(\sigma_{\pi j'j'} + \sigma_{j'}^2)]^{1/2}}$$

- In the special case where $\sigma_j^2 = \sigma^2$ and $\sigma_{\pi jj'} = \sigma_\pi^2$,

$$\rho = \mathrm{Corr}(y_{ij}, y_{ij'}) = \frac{\sigma_\pi^2}{\sigma_\pi^2 + \sigma^2}$$

- ρ ranges from 0 to 1 as σ_π^2/σ^2 ranges from 0 to ∞ and measures the strength of the "personal touch"

One-Sample Repeated Measures ANOVA

The model is: $y_{ij} = \mu + \pi_i + \tau_j + e_{ij}$

- y_{ij} is the response from subject i at time j
- μ is the (fixed) overall mean
- π_i is a random effect for subject i which is constant over all occasions
  - π_i are independent $N(0, \sigma_\pi^2)$ random variables
- τ_j is the fixed effect of time j ($\sum_{j=1}^{t} \tau_j = 0$)
- e_{ij} is a random error component specific to subject i at time j
  - e_{ij} are independent $N(0, \sigma_e^2)$ random variables
  - e_{ij} and π_i are independent

One-Sample Repeated Measures ANOVA

- In terms of the general model

$$y_{ij} = \mu_{ij} + \pi_{ij} + e_{ij}:$$

- $\mu_{ij} = \mu + \tau_j$

  (Note that the subscript i is unnecessary)

- $\pi_{ij} = \pi_i$ (constant across time points)

- $\sigma^2_{\pi j} = \sigma^2_\pi$ (constant across time points)

- $\sigma^2_{\pi jj'} = \sigma^2_\pi$ (constant across time points)

- $\sigma^2_j = \sigma^2_e$ (constant across time points)

- $\text{Corr}(y_{ij}, y_{ij'}) = \dfrac{\sigma^2_\pi}{\sigma^2_\pi + \sigma^2_e}$

Covariance Structure

- $\text{Var}(y_{ij}) = \text{Var}(\mu + \pi_i + \tau_j + e_{ij}) = \sigma_\pi^2 + \sigma_e^2$

- $\text{Cov}(y_{ij}, y_{i'j}) = 0$, for $i \neq i'$

- $\text{Cov}(y_{ij}, y_{ij'}) = \sigma_\pi^2$, for $j \neq j'$

- Thus, the covariance matrix of the vector $y_i = (y_{i1}, \ldots, y_{it})'$ is given by

$$\Sigma = \begin{pmatrix} \sigma_\pi^2 + \sigma_e^2 & & \sigma_\pi^2 \\ & \ddots & \\ \sigma_\pi^2 & & \sigma_\pi^2 + \sigma_e^2 \end{pmatrix}$$

$$= (\sigma_\pi^2 + \sigma_e^2) \begin{pmatrix} 1 & & \rho \\ & \ddots & \\ \rho & & 1 \end{pmatrix},$$

where $\rho = \dfrac{\sigma_\pi^2}{\sigma_\pi^2 + \sigma_e^2} = \text{Corr}(y_{ij}, y_{ij'})$

Compound Symmetry

- Although all random variables in the model are independent, the repeated observations from a subject are correlated

- The resulting covariance matrix with equal diagonal elements and equal off-diagonal elements is said to have compound symmetry

- This covariance structure implies that the correlation between any pair of repeated observations is the same, regardless of the "spacing" between observations

- This assumption is highly restrictive and often unrealistic, especially when the repeated measures factor is time

Analysis of Variance Table

- The ANOVA table is the same as that of the two-way mixed model with one observation per cell and no subject $\times$ time interaction

Source	SS	df	MS	E(MS)
Time	SS_T	$t-1$	MS_T	$\sigma_e^2 + n\sigma_\tau^2$
Subjects	SS_S	$n-1$	MS_S	$\sigma_e^2 + t\sigma_\pi^2$
Residual	SS_R	$(n-1)(t-1)$	MS_R	σ_e^2

where σ_τ^2 is a function of the τ_j fixed effects

$$\mathrm{SS_T} = \sum_{i=1}^{n}\sum_{j=1}^{t}(\overline{y}_{.j} - \overline{y}_{..})^2 = n\sum_{j=1}^{t}(\overline{y}_{.j} - \overline{y}_{..})^2$$

$$\mathrm{SS_S} = \sum_{i=1}^{n}\sum_{j=1}^{t}(\overline{y}_{i.} - \overline{y}_{..})^2 = t\sum_{i=1}^{n}(\overline{y}_{i.} - \overline{y}_{..})^2$$

$$\mathrm{SS_R} = \sum_{i=1}^{n}\sum_{j=1}^{t}(y_{ij} - \overline{y}_{i.} - \overline{y}_{.j} + \overline{y}_{..})^2$$

Computational Procedures and Hypothesis Tests

- $\mathrm{SS_T}$, $\mathrm{SS_S}$, and $\mathrm{SS_R}$ can be computed using a standard ANOVA program for a two-way main-effects model with one observation per cell

- The null hypothesis that there are no differences among time periods can be tested using the statistic $F = \mathrm{MS_T}/\mathrm{MS_R}$

- This test statistic has the $F_{t-1,(n-1)(t-1)}$ distribution if the null hypothesis is true *and* if the compound symmetry assumption holds

- Linear contrasts of the time period means can also be tested

Comments

- If compound symmetry holds, the F test is more powerful than T^2

- However, since the F test is anti-conservative in the absence of compound symmetry, rejection decisions cannot be trusted

- Compound symmetry can be tested

  Rouanet and Lepine (1970, *Br. J. Math. Statist. Psych.*)

- Although this condition is sufficient for the F statistic to have a null $F_{t-1,(n-1)(t-1)}$ distribution, it is not necessary

Scheffé's Mixed Model

Scheffés' (1959) model is: $y_{ij} = \mu + \pi_i + \tau_j + e_{ij}$

- y_{ij}, μ, and τ_j are defined as before
- The error components e_{ij} now include subject $\times$ time interaction, as well as measurement error
  - The π_i and e_{ij} components are jointly normal
  - $\mathrm{Cov}(e_{ij}, e_{ij'}) \neq 0$, $\mathrm{Cov}(\pi_i, e_{ij}) \neq 0$
- Many texts do not make a distinction between the two models
- Provided that certain assumptions are satisfied, the analysis is the same for both models

ANOVA for Scheffé's Mixed Model

Source	SS	df	E(MS)
Time	$\mathrm{SS_T}$	$t-1$	$\sigma_e^2 + \sigma_{\mathrm{T\times S}}^2 + n\sigma_\tau^2$
Subjects	$\mathrm{SS_S}$	$n-1$	$\sigma_e^2 + t\sigma_\pi^2$
T×S Inter.	$\mathrm{SS_{TS}}$	$(n-1)(t-1)$	$\sigma_e^2 + \sigma_{\mathrm{T\times S}}^2$

where σ_τ^2 is a function of the τ_j fixed effects

$$\mathrm{SS_T} = \sum_{i=1}^{n}\sum_{j=1}^{t}(\overline{y}_{.j} - \overline{y}_{..})^2 = n\sum_{j=1}^{t}(\overline{y}_{.j} - \overline{y}_{..})^2$$

$$\mathrm{SS_S} = \sum_{i=1}^{n}\sum_{j=1}^{t}(\overline{y}_{i.} - \overline{y}_{..})^2 = t\sum_{i=1}^{n}(\overline{y}_{i.} - \overline{y}_{..})^2$$

$$\mathrm{SS_{TS}} = \sum_{i=1}^{n}\sum_{j=1}^{t}(y_{ij} - \overline{y}_{i.} - \overline{y}_{.j} + \overline{y}_{..})^2$$

- The statistic $F = \mathrm{MS_T}/\mathrm{MS_{TS}}$ tests

  H_0: no differences among time periods

Sphericity Condition

- Compound symmetry is a special case of a more general situation under which the F test is valid
- The sphericity condition can be expressed in a number of alternative ways:

  a. The variances of all pairwise differences between variables are equal

     $\text{Var}(y_{ij} - y_{ij'})$ is constant

  b. $\epsilon = 1$, where

$$\epsilon = \frac{t^2(\overline{\sigma}_{ii} - \overline{\sigma}_{..})^2}{(t-1)(s - 2t\sum \overline{\sigma}_{i.}^2 + t^2\overline{\sigma}_{..}^2)}$$

  $\overline{\sigma}_{ii}$ = mean of entries on main diagonal of Σ

  $\overline{\sigma}_{..}$ = mean of all elements of Σ

  $\overline{\sigma}_{i.}$ = mean of entries in row i of Σ

  s = sum of the squares of the elements of Σ

Test of the Sphericity Condition

- Mauchly (1940, *Ann. Math. Statist.*)

- Has low power for small sample sizes

- For large sample sizes, the test is likely to show significance even though the effect on the F-test may be negligible

- Sensitive to departures from normality

  conservative for light-tailed distributions

  anti-conservative for heavy-tailed distributions

- Very sensitive to outliers

- Not of great practical use

What if the Sphericity Assumption is Unreasonable?

1. Use the unstructured multivariate approach

2. Modify the univariate approach

   When sphericity doesn't hold, the F-statistic has an approximate $F_{\epsilon(t-1),\epsilon(t-1)(n-1)}$ distribution, where ϵ is a function of the actual covariance matrix

$$\epsilon = \frac{t^2(\overline{\sigma}_{ii} - \overline{\sigma}_{..})^2}{(t-1)(s - 2t\sum \overline{\sigma}_{i.}^2 + t^2\overline{\sigma}_{..}^2)}$$

   $\overline{\sigma}_{ii}$ = mean of entries on main diagonal of Σ

   $\overline{\sigma}_{..}$ = mean of all elements of Σ

   $\overline{\sigma}_{i.}$ = mean of entries in row i of Σ

   s = sum of the squares of the elements of Σ

   It can be shown that $1/(t-1) \leq \epsilon \leq 1$

Modified Univariate ANOVA Tests

1. Use the lower bound for ϵ

   - With $\epsilon = 1/(t-1)$, the $F_{\epsilon(t-1),\epsilon(t-1)(n-1)}$ distribution is replaced by $F_{1,n-1}$

   - This test is very conservative

2. Use $\widehat{\epsilon} = \epsilon(S)$ computed from the sample covariance matrix S

   - Greenhouse & Geisser (1959, *Psychometrika*)

   - The maximum likelihood estimate of ϵ

   - Seriously biased for $\epsilon > .75$ and $n < 2t$

   - Tends to overcorrect the degrees of freedom and produce a conservative test

Modified Univariate ANOVA Tests

3. Use

$$\widetilde{\epsilon} = \min\Big(1, \frac{n(t-1)\widehat{\epsilon} - 2}{(t-1)(n-1-(t-1)\widehat{\epsilon})}\Big)$$

- Hunyh and Feldt (1976, *J. Educ. Statist.*)
- Based on unbiased estimators of the numerator and denominator of ϵ
- Less biased than $\widehat{\epsilon}$
- $\widetilde{\epsilon} \geq \widehat{\epsilon}$
- $\widehat{\epsilon}$ better for $\epsilon \leq .5$, but $\widetilde{\epsilon}$ better for $\epsilon \geq .75$

  However, ϵ is unknown in practice

Greenhouse-Geisser Approach

1. Conduct the univariate F-test

2. If not significant, then stop

3. If significant, conduct the conservative test

   Use $\epsilon = 1/(t-1)$, which leads to the $F_{1,n-1}$ distribution

   a. If significant, then stop

   b. If not significant, estimate ϵ and conduct an approximate test

      $\widehat{\epsilon}$ is more conservative than $\widetilde{\epsilon}$

Reference

Greenhouse, S.W. and Geisser, S. (1959). On methods in the analysis of profile data. *Psychometrika* **24**, 95–112.

Example

- Deal et al. (1979) measured ventilation volumes (l/min) of eight subjects under six different temperatures of inspired dry air

	Temperature (°C)					
Subject	−10	25	37	50	65	80
1	74.5	81.5	83.6	68.6	73.1	79.4
2	75.5	84.6	70.6	87.3	73.0	75.0
3	68.9	71.6	55.9	61.9	60.5	61.8
4	57.0	61.3	54.1	59.2	56.6	58.8
5	78.3	84.9	64.0	62.2	60.1	78.7
6	54.0	62.8	63.0	58.0	56.0	51.5
7	72.5	68.3	67.8	71.5	65.0	67.7
8	80.8	89.9	83.2	83.0	85.7	79.6

- Is ventilation volume affected by temperature?

Reference

Deal, E. C., McFadden, E. R., Ingram, R. H. et al. (1979). Role of respiratory heat exchange in production of exercise-induced asthma. *J Appl Physiol* **46**, 467–475.

SAS Statements for Example

```
 data a;
   input subject vv1-vv6;
   cards;
1 74.5 81.5 83.6 68.6 73.1 79.4
           ...
8 80.8 89.9 83.2 83.0 85.7 79.6
 ;
 proc glm data=a;
   model vv1-vv6= / nouni;
   repeated ventvol / nom printe;
```

- The `nouni` option omits separate analyses for each dependent variable
- The `nom` option omits the unstructured multivariate analysis
- The `printe` option provides Mauchly's (1940) sphericity test

Comments

- The unadjusted and conservative analyses can be carried out even if specialized repeated measures capabilities are not available

- With some effort, the values of $\widehat{\epsilon}$ and $\widetilde{\epsilon}$ could also be calculated

- The analysis using a standard ANOVA program requires that the data be restructured

  (Instead of one observation per subject, t observations are required)

- For large problems, the computational technique of *absorption* may be required

  (provides a large reduction in time and memory requirements for certain types of models)

SAS Statements for Example
(Classical ANOVA Approach)

```
data b; set a;
temp=-10; ventvol=vv1;  output;
temp= 25; ventvol=vv2;  output;
temp= 37; ventvol=vv3;  output;
temp= 50; ventvol=vv4;  output;
temp= 65; ventvol=vv5;  output;
temp= 80; ventvol=vv6;  output;

proc glm data=b;
class subject temp;
model ventvol=temp subject;
title1 'Usual ANOVA';

proc sort data=b; by subject;
proc glm data=b;
absorb subject;
class temp;
model ventvol=temp;
title1 'Usual ANOVA with Absorption';
```

Comments on Absorption

- Classic use is when the model contains a blocking factor with a large number of levels

- A main effect variable that does not participate in interactions can be absorbed

- Thus, the effect can be "adjusted out" before construction and solution of the rest of the model

- The size of the $X'X$ matrix is then a function only of the effects in the MODEL statement

- Several variables can be specified; each is assumed to be nested in the preceding one

- In SAS, the data set must be sorted by the variables in the `ABSORB` statement

Repeated Measures ANOVA for Multiple Samples

- Suppose that repeated measurements at t time points have been obtained from s groups of subjects

- Let n_h denote the number of subjects in group h ($n = \sum_{h=1}^{s} n_h$)

- Let y_{hij} denote the response at time j from the ith subject in group h, for $h = 1, \ldots, s$, $i = 1, \ldots, n_h$, and $j = 1, \ldots, t$

- There are at least three models for this situation, all resulting in the same ANOVA table

- The simplest is

$$y_{hij} = \mu + \gamma_h + \tau_j + (\gamma\tau)_{hj} + \pi_{i(h)} + e_{hij}$$

Interpretation of Parameters

- μ is the overall mean
- γ_h is the fixed effect of group h: $\sum_{h=1}^{s} \gamma_h = 0$
- τ_j is the fixed effect of time j: $\sum_{j=1}^{t} \tau_j = 0$
- $(\gamma\tau)_{hj}$ is the fixed effect for the interaction of the hth group with the jth time: $\sum_{h=1}^{s}(\gamma\tau)_{hj} = \sum_{j=1}^{t}(\gamma\tau)_{hj} = 0$
- $\pi_{i(h)}$ are random effects for the ith subject in the hth group: $\pi_{i(h)} \sim N(0, \sigma_\pi^2)$
- e_{hij} are random error terms: $e_{hij} \sim N(0, \sigma_e^2)$
- In terms of the general model:
  - $\mu_{ij} = \mu + \gamma_h + \tau_j + (\gamma\tau)_{hj}$
  - $\pi_{ij} = \pi_{i(h)}$
  - $e_{ij} = e_{hij}$

Analysis of Variance Table

- The sources of variation, degrees of freedom, and expected mean squares are given below:

Source	df	E(MS)
Groups	$s-1$	$\sigma_e^2 + t\sigma_\pi^2 + D_G$
Subjects(Groups)	$n-s$	$\sigma_e^2 + t\sigma_\pi^2$
Time	$t-1$	$\sigma_e^2 + D_T$
Groups $\times$ Time	$(s-1)(t-1)$	$\sigma_e^2 + D_{GT}$
Residual	$(n-s)(t-1)$	σ_e^2

- The residual sum of squares is due to Subjects(Groups $\times$ Time)

- The quantities labelled D_G, D_T, and D_{GT} measure differences among groups, time points, and the group $\times$ time interaction, respectively

Comments

1. An alternative model includes an additional random effect for the subjects × time interaction

   - This effect is usually assumed to be uncorrelated with the random subject effect

   - Although the expected mean squares differ, the sums of squares and test statistics are identical

2. The F-test for differences among groups requires the assumption that the within-group covariance matrices are equal

3. The F-tests for the "time" and "groups × time" effects require equality of covariance matrices *and* the sphericity condition

Example

- A seven-week study of the effect of a vitamin E diet supplement on the growth of 15 guinea pigs
- In addition to a control group, low and high doses of vitamin E were studied (with five animals assigned to each of the three groups)
- All animals were given a growth-inhibiting substance during week 1 and treatment was initiated at the beginning of week 5
- The body weight, in grams, of each animal was recorded at the end of weeks 1, 3, 4, 5, 6, and 7
- Do the growth profiles of the three groups differ?

Reference

Crowder, M. J. and Hand, D. J. (1990). *Analysis of Repeated Measures*. London: Chapman and Hall, p. 27.

Guinea Pig Body Weights

		Week					
Group	ID	1	3	4	5	6	7
Control	1	455	460	510	504	436	466
	2	467	565	610	596	542	587
	3	445	530	580	597	582	619
	4	485	542	594	583	611	612
	5	480	500	550	528	562	576
	Mean	466.4	519.4	568.8	561.6	546.6	572.0
Low	6	514	560	565	524	552	597
Dose	7	440	480	536	484	567	569
	8	495	570	569	585	576	677
	9	520	590	610	637	671	702
	10	503	555	591	605	649	675
	Mean	494.4	551.0	574.2	567.0	603.0	644.0
High	11	496	560	622	622	632	670
Dose	12	498	540	589	557	568	609
	13	478	510	568	555	576	605
	14	545	565	580	601	633	649
	15	472	498	540	524	532	583
	Mean	497.8	534.6	579.8	571.8	588.2	623.2

SAS Statements
(Multivariate Data Structure)

```
data a;
* 1=control, 2=low dose, 3=high dose;
input group animal w1 w3-w7;
cards;
1  1 455 460 510 504 436 466
            ...
3 15 472 498 540 524 532 583
;
proc glm; class group;
model w1 w3-w7=group / nouni;
repeated week / printe nom;
```

- The `nouni` option omits separate analyses for each dependent variable
- The `nom` option omits the unstructured multivariate analysis
- The `printe` option provides Mauchly's (1940) sphericity test

SAS Statements

(Univariate Data Structure)

```
data b; set a; drop w1 w3-w7;
week=1;  weight=w1;  output;
week=3;  weight=w3;  output;
week=4;  weight=w4;  output;
week=5;  weight=w5;  output;
week=6;  weight=w6;  output;
week=7;  weight=w7;  output;

proc glm;
class group animal week;
model weight=group animal(group)
      week group*week;
test h=group e=animal(group);

proc glm;
class group animal week;
model weight=group animal(group)
      week group*week;
random animal(group) / test;
```