Applying the appropriate computation formulas, the following sums of squares are obtained:

ROWS

$$\frac{1}{C}\sum_{r=1}^{R} T_{r.}^2 - \frac{T^2}{N} = \frac{394{,}350}{4} - \frac{(1{,}970)^2}{40} = 1{,}565.00$$

COLUMNS

$$\frac{1}{R}\sum_{c=1}^{C} T_{.c}^2 - \frac{T^2}{N} = \frac{1{,}045{,}756}{10} - \frac{(1{,}970)^2}{40} = 7{,}553.10$$

INTERACTION

$$\sum_{r=1}^{R}\sum_{c=1}^{C} X_{rc}^2 - \frac{1}{C}\sum_{r=1}^{R} T_{r.}^2 - \frac{1}{R}\sum_{c=1}^{C} T_{.c}^2 + \frac{T^2}{N}$$

$$= 122{,}984 - \frac{394{,}350}{4} - \frac{1{,}045{,}756}{10} + \frac{(1{,}970)^2}{40}$$

$$= 16{,}843.40$$

TOTAL

$$\sum_{r=1}^{R}\sum_{c=1}^{C} X_{rc}^2 - \frac{T^2}{N} = 122{,}984 - \frac{(1{,}970)^2}{40} = 25{,}961.50$$

Table 19.2 summarizes the analysis-of-variance data for this example. Because this is a mixed model with $n = 1$ and $F_r = s_r^2/s_{rc}^2 = .279$, no meaningful test of row effects is possible. The proper error term for column effects is s_{rc}^2. The F ratio for column effects is found to be 4.04. The F ratios required for significance with 3 and 27 degrees of freedom associated with the numerator and denominator, respectively, are 2.96 at the 5 percent and 4.60 at the 1 percent levels. Thus the column differences

Table 19.2

Analysis of variance for data of Table 19.1

Source of variation	Sum of squares	Degrees of freedom	Variance estimate
Rows	1,565.00	9	$173.89 = s_r^2$
Columns	7,553.10	3	$2{,}517.70 = s_c^2$
Interaction	16,843.40	27	$623.83 = s_{rc}^2$
Total	25,961.50		

$F_c = \frac{s_c^2}{s_{rc}^2} = 4.04 \qquad F_r = \frac{s_r^2}{s_{rc}^2} = .279$

FERGUSSON

19

REPEATED-MEASUREMENT AND OTHER EXPERIMENTAL DESIGNS

19.1 INTRODUCTION

In previous chapters the basic ideas involved in the design, analysis, and interpretation of one-way classification experiments, and factorial experiments, were discussed in considerable detail. In psychology and education considerable use is made, both through choice and necessity, of other experimental designs. The purpose of this chapter is to introduce the reader in an elementary way to a number of other experimental designs in common use. Some of these designs involve assumptions, and present problems, that are not involved in designs previously discussed. Some awareness and understanding of these assumptions and problems are essential to the proper use of these designs.

Research workers in psychology and education make frequent use of experimental designs in which measurements are repeated a number of times on the same subjects. These designs, and the assumptions underlying their use, are described in some detail in this chapter. Randomized block designs, designs with nested factors, and Latin square designs are also described.

The treatment of these designs in this chapter must of necessity be elementary. Some of these designs can be combined and extended in a variety of ways leading to experiments of much complexity. Because of the ready availability of computers for data analysis, the current trend in psychology and education is toward more complex designs. Questions can be raised regarding the merits of this trend toward complexity. A much more advanced treatment of the topics discussed in this chapter will be found in books by Winer (1971), Myers (1972), and other authors.

19.2 EXPERIMENTS WITH REPEATED MEASUREMENTS

Many experiments in psychology and education require the repeated measurement of the same subjects under a number of different conditions or treatments. Such experiments may be single-factor experiments in which each subject is tested or measured under a number of different experimental conditions. The simplest experiment of this kind would be one in which the same subjects are tested under two experimental conditions. Sometimes, when the same subjects are tested under a number of different treatments, the order of the presentation of treatments to subjects is randomized independently for each subject or a systematic plan for the ordering of the presentation of treatments to subjects is adopted. The purpose of either randomization, or the use of a systematic plan for the ordering of treatments, is to eliminate effects which might result from the order of the treatments. In some situations randomization is not appropriate because the different levels of the treatment variable have a natural order. This is the case where performance is measured at different time intervals, as, for example, in the study of changes in dark adaptation with time, or for different numbers of trials in a simple learning experiment.

Experiments of the type described above are called *one-factor experiments with repeated measurements*. In such experiments N subjects are measured under k conditions or treatments. The matrix of data thus obtained is a table of numbers containing N rows and k columns.

Repeated measurements may, however, be used in two-way classification or higher-order factorial experiments. For example, in a 2×2 factorial experiment four treatment combinations exist, four groups of experimental subjects are used, and each combination is applied to a different group of subjects. Experiments may be designed in which each of the N subjects receives all four treatment combinations. The matrix of data is a block of numbers containing two rows, two columns, and N layers, each layer corresponding to a subject. In general, for an $R \times C$ factorial experiment with repeated measurements the matrix of data is an $R \times C \times N$ block of numbers. The idea involved here can be extended to higher-order factorial experiments.

Two-way classification experiments may also be conducted with repeated measurements over one factor but not over the other factor. Consider an experiment involving two factors with three levels of one factor and two levels of the other. If this were an independent-groups factorial experiment, six treatment combinations and six groups of subjects would be used. The investigator may, however, decide to use two groups of subjects, with each of the two groups receiving only one level of one factor but all three levels of the other. Thus the experiment has repeated measurements over the factor with three levels, but not over the factor with two levels.

Experiments with repeated measurements have advantages and disadvantages. One advantage is that the measurements obtained under the different treatment conditions will in many experiments be highly correlated since they are made on the same subjects. The presence of these correlations will reduce the error term. Another advantage resides in the number of subjects. It may be more economical in terms of time and effort to test the same subjects under each treatment. A further point here is that the nature of certain experimental problems demands the use of repeated-measurement designs. One disadvantage of experiments with repeated measurements is that performance under prior treatments may affect performance under subsequent treatments due to either fatigue, practice, boredom, or some other circumstance. Effects resulting from such circumstances are sometimes called carry-over effects. An investigator may not be able to clearly decide whether the results observed under the different treatments are due to those treatments or are due to the carry-over effects. A further problem associated with repeated measurement designs in the assumption made in the analysis of data. Not only is the usual assumption of homogeneity of variances made but also an assumption is made regarding the homogeneity of covariances. This matter is discussed in some detail in Section 19.9.

19.3 ONE-FACTOR EXPERIMENTS WITH REPEATED MEASUREMENTS: COMPUTATION AND EXPECTATION OF MEAN SQUARES

As indicated above, the data resulting from a one-factor experiment with repeated measurements may be represented as a table of numbers in which rows represent experimental subjects and columns represent treatments; that is, the representation of the data is the same as that for the two-way classification with one observation per cell. The analysis of such data involves nothing new. The data are analyzed as in the two-way classification case with one observation per cell. The required computation formulas are given in Section 16.9. Three sums of squares result: sums of squares for subjects (rows), treatments (columns), and interaction.

For a one-factor experiment with repeated measurements, subjects constitute a random variable and treatments are usually viewed as fixed. The model is the mixed model for $n = 1$. The expectations of the mean squares are as follows:

Mean squares	Expectation of mean squares
Subjects, s_r^2	$\sigma_e^2 + C\sigma_a^2$
Treatments, s_c^2	$\sigma_e^2 + \sigma_{ab}^2 + R\sigma_b^2$
Interaction, s_{rc}^2	$\sigma_e^2 + \sigma_{ab}^2$

The proper error term for testing differences between treatments is s_{rc}^2; that is, $F_c = s_c^2/s_{rc}^2$. No unbiased test of individual differences between subjects is possible, unless it is assumed that the interaction term is 0. With nearly all sets of data this assumption is not warranted, because the performance of subjects under different pairs of treatments is correlated. Ordinarily in most experiments of this type individual differences between subjects are of limited interest anyway, because with most variables that are the object of study the investigator expects a priori substantial differences between subjects.

19.4 ILLUSTRATIVE EXAMPLE OF ONE-FACTOR EXPERIMENT WITH REPEATED MEASUREMENTS

Table 19.1 shows hypothetical data for a one-factor experiment with repeated measurements. Rows are individuals, and columns are treatments. The data are presumed to relate to a random sample of individuals tested under different treatment conditions. This is a mixed model. One basis of classification, the columns, is fixed. The other basis of classification, the rows, is random.

Table 19.1

Data for the analysis of variance with two-way classification: $n = 1$, scores for a sample of subjects tested under four different conditions

	Conditions					
Subject	A	B	C	D	$T_{r.}$	$\bar{X}_{r.}$
1	31	42	14	80	167	41.75
2	42	26	25	106	199	49.75
3	84	21	19	83	207	51.75
4	26	60	36	69	191	47.75
5	14	35	44	48	141	35.25
6	16	80	28	76	200	50.00
7	29	49	80	39	197	49.25
8	32	38	76	84	230	57.50
9	45	65	15	91	216	54.00
10	30	71	82	39	222	55.50
$T_{.c}$	349	487	419	715		$T = 1{,}970$
$\bar{X}_{.c}$	34.90	48.70	41.90	71.50		$\bar{X}_{..} = 49.25$

$\sum_{r=1}^{R} T_{r.}^2 = 394{,}350$ $\quad \sum_{c=1}^{C} T_{.c}^2 = 1{,}045{,}756$ $\quad \sum_{r=1}^{R}\sum_{c=1}^{C} X_{rc}^2 = 122{,}984$

Applying the appropriate computation formulas, the following sums of squares are obtained:

ROWS

$$\frac{1}{C}\sum_{r=1}^{R} T_{r.}^2 - \frac{T^2}{N} = \frac{394{,}350}{4} - \frac{(1{,}970)^2}{40} = 1{,}565.00$$

COLUMNS

$$\frac{1}{R}\sum_{c=1}^{C} T_{.c}^2 - \frac{T^2}{N} = \frac{1{,}045{,}756}{10} - \frac{(1{,}970)^2}{40} = 7{,}553.10$$

INTERACTION

$$\sum_{r=1}^{R}\sum_{c=1}^{C} X_{rc}^2 - \frac{1}{C}\sum_{r=1}^{R} T_{r.}^2 - \frac{1}{R}\sum_{c=1}^{C} T_{.c}^2 + \frac{T^2}{N}$$

$$= 122{,}984 - \frac{394{,}350}{4} - \frac{1{,}045{,}756}{10} + \frac{(1{,}970)^2}{40}$$

$$= 16{,}843.40$$

TOTAL

$$\sum_{r=1}^{R}\sum_{c=1}^{C} X_{rc}^2 - \frac{T^2}{N} = 122{,}984 - \frac{(1{,}970)^2}{40} = 25{,}961.50$$

Table 19.2 summarizes the analysis-of-variance data for this example. Because this is a mixed model with $n = 1$ and $F_r = s_r^2/s_{rc}^2 = .279$, no meaningful test of row effects is possible. The proper error term for column effects is s_{rc}^2. The F ratio for column effects is found to be 4.04. The F ratios required for significance with 3 and 27 degrees of freedom associated with the numerator and denominator, respectively, are 2.96 at the 5 percent and 4.60 at the 1 percent levels. Thus the column differences

Table 19.2

Analysis of variance for data of Table 19.1

Source of variation	Sum of squares	Degrees of freedom	Variance estimate
Rows	1,565.00	9	$173.89 = s_r^2$
Columns	7,553.10	3	$2{,}517.70 = s_c^2$
Interaction	16,843.40	27	$623.83 = s_{rc}^2$
Total	25,961.50		

$F_c = \frac{s_c^2}{s_{rc}^2} = 4.04 \qquad F_r = \frac{s_r^2}{s_{rc}^2} = .279$

ie following sums of

,565.00

7,553.10

$\frac{045{,}756}{10} + \frac{(1{,}970)^2}{40}$

5,961.50

ta for this example.
$= s_r^2/s_{rc}^2 = .279$, no
error term for col-
s found to be 4.04.
grees of freedom as-
vely, are 2.96 at the
column differences

are significant at the 5 percent level but fall short of significance at the 1 percent level.

19.5 TWO-FACTOR EXPERIMENTS WITH REPEATED MEASUREMENTS

In Sections 19.3 and 19.4 one-factor experiments with repeated measurements were considered. On occasion experiments are encountered that involve two factors with repeated measurements. Given R levels of one treatment and C levels of another, each subject may be tested under each of the RC treatments. If $R = 2$ and $C = 2$, the levels of R being R_1 and R_2 and of C being C_1 and C_2, there are four treatment combinations, R_1C_1, R_1C_2, R_2C_1, and R_2C_2. Each of N subjects might receive all the four treatments, the presentations being possibly, although not necessarily, arranged in random order for each subject.

Such data constitute an RCN block of numbers. Rows and columns are treatments, and layers are experimental subjects. These data are analyzed as in the triple-classification case with one observation in each cell. Use the computation formulas given in Section 17.8, writing $n = 1$. Seven sums of squares result: rows, columns, subjects, $R \times C$, $R \times S$, $C \times S$, and $R \times C \times S$. There is, of course, no within-cells sum of squares.

The model here is a mixed model with $n = 1$. Rows and columns will ordinarily be fixed variables. Layers, or subjects, is a random variable. For this model the expectation of the sums of squares and the degrees of freedom are as follows:

Mean square	Expectation of mean square	*df*
Rows, s_r^2	$\sigma_e^2 + C\sigma_{ac}^2 + NC\sigma_a^2$	$R - 1$
Columns, s_c^2	$\sigma_e^2 + R\sigma_{bc}^2 + NR\sigma_b^2$	$C - 1$
Subjects, s_s^2	$\sigma_e^2 + RC\sigma_c^2$	$N - 1$
$R \times C$, s_{rc}^2	$\sigma_e^2 + \sigma_{abc}^2 + N\sigma_{ab}^2$	$(R - 1)(C - 1)$
$R \times S$, s_{rs}^2	$\sigma_e^2 + C\sigma_{ac}^2$	$(R - 1)(N - 1)$
$C \times S$, s_{cs}^2	$\sigma_e^2 + R\sigma_{bc}^2$	$(C - 1)(N - 1)$
$R \times C \times S$, s_{rcs}^2	$\sigma_e^2 + \sigma_{abc}^2$	$(R - 1)(C - 1)(N - 1)$

Inspection of these expectations indicates that the appropriate error term for testing row effects is the $R \times S$ mean square, $F_r = s_r^2/s_{rs}^2$. The appropriate error term for testing column effects is the $C \times S$ mean square, $F_c = s_c^2/s_{cs}^2$. The appropriate error term for testing $R \times C$ interaction is the $R \times C \times S$ mean square, $F_{rc} = s_{rc}^2/s_{rcs}^2$. Unless the $R \times S$, $C \times S$, and $R \times C \times S$ interactions are assumed to be 0, which with most sets of data will not be the case, no unbiased test of differences between subjects, or $R \times S$ or $C \times S$ interactions, can be made. These are ordinarily not of interest.

19.6 ILLUSTRATIVE EXAMPLE OF TWO-FACTOR EXPERIMENT WITH REPEATED MEASUREMENTS

The following are fictitious illustrative data for a repeated-measurement experiment with six experimental subjects tested under $2 \times 3 = 6$ treatment combinations.

Subject 1

	C_1	C_2	C_3	
R_1	4	5	7	16
R_2	1	4	2	7
	5	9	9	

Subject 2

	C_1	C_2	C_3	
R_1	6	8	10	24
R_2	3	6	6	15
	9	14	16	

Subject 3

	C_1	C_2	C_3	
R_1	1	6	5	12
R_2	3	5	4	12
	4	11	9	

Subject 4

	C_1	C_2	C_3	
R_1	2	10	12	24
R_2	1	4	7	12
	3	14	19	

Subject 5

	C_1	C_2	C_3	
R_1	5	10	10	25
R_2	5	6	5	16
	10	16	15	

Subject 6

	C_1	C_2	C_3	
R_1	1	7	8	16
R_2	2	8	7	17
	3	15	15	

For computational purposes it is necessary to write down the totals for rows by columns summed over subjects, rows by subjects summed over columns, and subjects by columns summed over rows. Viewing the data as a cube of numbers, these are the numbers on the surface of the cube. The totals for rows by columns summed over subjects, $T_{rc.}$, are as follows:

$T_{rc.}$

	Columns			$T_{r..}$
Rows	19	46	52	117
	15	33	31	79
$T_{.c.}$	34	79	83	$196 = T_{...}$

The totals above are obtained by adding the cell totals over subjects. Thus $4 + 6 + 1 + 2 + 5 + 1 = 19$, and so on. Totals for rows $T_{r..}$, for columns $T_{.c.}$, and the grand total are shown. The totals for rows by subjects summed over columns are as follows:

$T_{r.s}$ Subjects

							$T_{r..}$
Rows	16	24	12	24	25	16	117
	7	15	12	12	16	17	79
$T_{..s}$	23	39	24	36	41	33	$196 = T_{...}$

Here the number 16 in the top left cell is obtained by summing the cells for the first subject over columns; thus $4 + 5 + 7 = 16$. Likewise $1 + 4 + 2 = 7$, and so on. The totals for columns by subjects summed over rows, $T_{.cs}$, are as follows:

$T_{.cs}$ Subjects

							$T_{.c.}$
Columns	5	9	4	3	10	3	34
	9	14	11	14	16	15	79
	9	16	9	19	15	15	83
$T_{..s}$	23	39	24	36	41	33	$196 = T_{...}$

Here the values in the left-hand column in the above table are obtained by summing the cells for the first subject over rows; thus $4 + 1 = 5$, $5 + 4 = 9$, $7 + 2 = 9$, and so on.

Use is now made of the computational formulas given in Section 17.8. In the present example $n = 1$. Also a slight notational change has been made. In this example layers are subjects and the symbol S is used instead of L. In the formulas to follow S is the same as L in the formulas of Section 17.8. The factor S has N levels, where N is the number of subjects.

First we calculate *eight* quantities which are used in the computation formulas. For this illustrative example these are as follows:

$$\frac{1}{CN}\sum^{R} T_{r..}^2 = \frac{1}{3\times 6}\times 19{,}930 = 1{,}107.22$$

$$\frac{1}{RN}\sum^{C} T_{.c.}^2 = \frac{1}{2\times 6}\times 14{,}286 = 1{,}190.50$$

$$\frac{1}{RC}\sum^{N} T_{..s}^2 = \frac{1}{2\times 3}\times 6{,}692 = 1{,}115.33$$

$$\frac{1}{N}\sum^{R}\sum^{C} T_{rc.}^2 = \frac{1}{6}\times 7{,}456 = 1{,}242.67$$

$$\frac{1}{C}\sum^{R}\sum^{N} T^2_{r.s} = \frac{1}{3} \times 3{,}540 = 1{,}180.00$$

$$\frac{1}{R}\sum^{C}\sum^{N} T^2_{.cs} = \frac{1}{2} \times 2{,}544 = 1{,}272.00$$

$$\sum^{R}\sum^{C}\sum^{N} X^2_{rcs} = 1{,}360.00$$

$$\frac{T^2}{RCN} = \frac{1}{36} \times 38{,}416 = 1{,}067.11$$

In the above computation the quantity $\sum^{R} T^2_{r..} = (117)^2 + (79)^2 = 19{,}930$; $\sum^{C} T^2_{.c.} = (34)^2 + (79)^2 + (83)^2 = 14{,}286$; and so on. Applying the computation formulas of Section 17.8, and remembering that $L = S$, the required sums of squares are as follows:

ROWS

$$\frac{1}{CN}\sum^{R} T^2_{r..} - \frac{T^2}{RCN} = 1{,}107.22 - 1{,}067.11 = 40.11$$

COLUMNS

$$\frac{1}{RN}\sum^{C} T^2_{.c.} - \frac{T^2}{RCN} = 1{,}190.50 - 1{,}067.11 = 123.39$$

SUBJECTS

$$\frac{1}{RC}\sum^{N} T^2_{..s} - \frac{T^2}{RCN} = 1{,}115.33 - 1{,}067.11 = 48.22$$

$R \times C$ INTERACTION

$$\frac{1}{N}\sum^{R}\sum^{C} T^2_{rc.} - \frac{1}{CN}\sum^{R} T^2_{r..} - \frac{1}{RN}\sum^{C} T^2_{.c.} + \frac{T^2}{RCN}$$
$$= 1{,}242.67 - 1{,}107.22 - 1{,}190.50 + 1{,}067.11 = 12.06$$

$R \times S$ INTERACTION

$$\frac{1}{C}\sum^{R}\sum^{N} T^2_{r.s} - \frac{1}{CN}\sum^{R} T^2_{r..} - \frac{1}{RC}\sum^{N} T^2_{..s} + \frac{T^2}{RCN}$$
$$= 1{,}180.00 - 1{,}107.22 - 1{,}115.33 + 1{,}067.11 = 24.56$$

$C \times S$ INTERACTION

$$\frac{1}{R}\sum^{C}\sum^{N} T^2_{.cs} - \frac{1}{SR}\sum^{C} T^2_{.c.} - \frac{1}{RC}\sum^{N} T^2_{..s} + \frac{T^2}{RCN}$$
$$= 1{,}272.00 - 1{,}190.50 - 1{,}115.33 + 1{,}067.11 = 33.28$$

$R \times C \times S$ INTERACTION

$$\sum^{R}\sum^{C}\sum^{N} X_{rcs}^2 - \frac{1}{N}\sum^{R}\sum^{C} T_{rc.}^2 - \frac{1}{C}\sum^{R}\sum^{N} T_{r.s}^2 - \frac{1}{R}\sum^{C}\sum^{N} T_{.cs}^2 + \frac{1}{CN}\sum^{R} T_{r..}^2$$

$$+ \frac{1}{RN}\sum^{C} T_{.c.}^2 + \frac{1}{RC}\sum^{N} T_{..s}^2 - \frac{T^2}{RCN} = 1{,}360.00 - 1{,}242.67$$

$$- 1{,}180.00 - 1{,}272.00 + 1{,}107.22 + 1{,}190.50$$

$$+ 1{,}115.33 - 1{,}067.11 = 11.27$$

TOTAL

$$\sum^{R}\sum^{C}\sum^{N} X_{rcs}^2 - \frac{T^2}{RCN} = 1{,}360.00 - 1{,}067.11 = 292.89$$

The analysis-of-variance table for these data is given in Table 19.3. As indicated in Section 19.5 the appropriate error term for testing row effects is s_{rs}^2, for column effects s_{cs}^2, and for $R \times C$ interaction s_{rcs}^2. The F ratios are as follows:

$$F_r = \frac{s_r^2}{s_{rs}^2} = \frac{40.11}{4.91} = 8.17 \qquad p < .05$$

$$F_c = \frac{s_c^2}{s_{cs}^2} = \frac{61.70}{3.33} = 18.53 \qquad p < .01$$

$$F_{rc} = \frac{s_{rc}^2}{s_{rcs}^2} = \frac{6.03}{1.13} = 5.34 \qquad p < .05$$

In this illustrative example the column effects are significant at better than the .01 level, whereas row effects and $R \times C$ interaction fall between the .05 and .01 levels of significance.

Table 19.3

Analysis-of-variance table for illustrative examples of two-factor experiment with repeated measures

Source of variation	Sum of squares	Degrees of freedom	Variance estimate
Rows	40.11	1	$40.11 = s_r^2$
Columns	123.39	2	$61.70 = s_c^2$
Subjects	48.22	5	$9.64 = s_s^2$
$R \times C$	12.06	2	$6.03 = s_{rc}^2$
$R \times S$	24.56	5	$4.91 = s_{rs}^2$
$C \times S$	33.28	10	$3.33 = s_{cs}^2$
$R \times C \times S$	11.27	10	$1.13 = s_{rcs}^2$
Total	292.89	35	

19.7 TWO-FACTOR EXPERIMENTS WITH REPEATED MEASUREMENTS ON ONE FACTOR

A not uncommon type of experiment in psychological and educational research is a two-factor experiment with repeated measurements over one factor only. To illustrate, consider an experiment involving four different learning trials under two drug treatments. Two groups of n subjects each may be used. The first group may be tested on the four learning trials under the first drug treatment. The second group may be tested on the four learning trials under the second drug treatment. Designs of this type are sometimes called mixed designs, but this term should not be confused with mixed models, where the mixing is with respect to fixed and random factors rather than repeated- and nonrepeated-measurement factors.

The notation for such an experiment may be illustrated in the particular case where two experimental groups of three subjects are used with each subject measured under four experimental conditions. The data may be represented as follows:

		Subjects	C_1	C_2	C_3	C_4	Means
Group 1	R_1	1	X_{111}	X_{121}	X_{131}	X_{141}	$\bar{X}_{1.1}$
		2	X_{112}	X_{122}	X_{132}	X_{142}	$\bar{X}_{1.2}$
		3	X_{113}	X_{123}	X_{133}	X_{143}	$\bar{X}_{1.3}$
		Means	$\bar{X}_{11.}$	$\bar{X}_{12.}$	$\bar{X}_{13.}$	$\bar{X}_{14.}$	$\bar{X}_{1..}$
Group 2	R_2	4	X_{214}	X_{224}	X_{234}	X_{244}	$\bar{X}_{2.4}$
		5	X_{215}	X_{225}	X_{235}	X_{245}	$\bar{X}_{2.5}$
		6	X_{216}	X_{226}	X_{236}	X_{246}	$\bar{X}_{2.6}$
		Means	$\bar{X}_{21.}$	$\bar{X}_{22.}$	$\bar{X}_{23.}$	$\bar{X}_{24.}$	$\bar{X}_{2..}$
		Means	$\bar{X}_{.1.}$	$\bar{X}_{.2.}$	$\bar{X}_{.3.}$	$\bar{X}_{.4.}$	$\bar{X}_{...}$

Here triple subscripts are used. The first subscript identifies the row or group to which the subject belongs, the second subscript identifies the column or the level of the repeated measurement, the third subscript identifies the subject. For example, X_{214} is a measurement for the fourth subject in the second group at the first level of the repeated measurement.

For this type of experimental design the total sum of squares may be partitioned into two parts, a between-subjects and a within-subjects sum of squares. The between-subjects sum of squares can be further partitioned into two parts, a row sum of squares and a subjects-within-groups sum of squares. Denote this latter term by S/R. The within-subjects sum of squares can be further partitioned into three parts, a column sum of squares, a row-by-column interaction, and a third part which is a column-by-subject interaction pooled over groups or rows. Denote this latter term by $(S \times C)/R$. Thus, in effect, the total sum of squares is partitioned into five separate sums of squares. These sums of squares with the associated number of degrees of freedom and variance estimates are shown in Table 19.4.

Some comment on the sums of squares in Table 19.4 is appropriate. The meaning of the row, column, and interaction sums of squares is obvious. These are concerned with variability due to the main effects and the interaction between the main effects. The subjects-within-groups sum of squares, S/R, is simply the variability among subjects for the first group, added to the variability among subjects for the second group, and so on for all levels of R. It may be viewed as the variability among subjects with the variability due to row treatment effects, as it were, removed. The $(C \times S)/R$ term is a column-by-subject interaction for the first group, added to the column-by-subject interaction for the second group, and so on for all levels of R.

The numbers of degrees of freedom associated with row, column, and $R \times C$ interaction sums of squares are $R-1$, $C-1$, and $(R-1)(C-1)$, respectively. The S/R term has associated with it $n-1$ degrees of freedom for each group, and for R groups the number of degrees of freedom is $R(n-1)$. The $(C \times S)/R$ term involves the summing of the $C \times S$ interaction over R groups or levels. The number of degrees of freedom associated with each level is $(n-1)(C-1)$; consequently the total number of degrees of freedom associated with this term is $R(n-1)(C-1)$.

Table 19.4

Analysis of variance for two-factor experiments with repeated measurements on one factor

Source of variation	Sum of squares	df	Variance estimate
Between subjects	$C\sum^{R}\sum^{n}(\bar{X}_{r.s}-\bar{X}_{...})^2$	$Rn-1$	s_b^2
Rows	$nC\sum^{R}(\bar{X}_{r..}-\bar{X}_{...})^2$	$R-1$	s_r^2
S/R	$C\sum^{R}\sum^{n}(\bar{X}_{r.s}-\bar{X}_{r..})^2$	$R(n-1)$	$s^2_{s/r}$
Within subjects	$\sum^{C}\sum^{R}\sum^{n}(X_{rci}-\bar{X}_{r.s})^2$	$Rn(C-1)$	s_w^2
Columns	$nR\sum^{C}(\bar{X}_{.c.}-\bar{X}_{...})^2$	$C-1$	s_c^2
$R \times C$	$n\sum^{R}\sum^{C}(\bar{X}_{rc.}-\bar{X}_{r..}-\bar{X}_{.c.}+\bar{X}_{...})^2$	$(R-1)(C-1)$	s_{rc}^2
$(C \times S)/R$	$\sum^{C}\sum^{R}\sum^{n}(X_{rci}-\bar{X}_{r.s}-\bar{X}_{rc.}+\bar{X}_{r..})^2$	$R(n-1)(C-1)$	$s^2_{cs/r}$
Total	$\sum^{R}\sum^{C}\sum^{n}(X_{rci}-\bar{X}_{...})^2$	$RCn-1$	

The expectations of the variance estimates or mean squares for a two-factor experiment with repeated measurements on one factor, and assuming the row and column treatment variables to be fixed, are as follows:

ROWS, s_r^2	$\sigma_e^2 + C\sigma_s^2 + nC\sigma_a^2$
S/R, $s_{s/r}^2$	$\sigma_e^2 + C\sigma_s^2$
COLUMNS, s_c^2	$\sigma_e^2 + \sigma_{bs}^2 + nR\sigma_b^2$
$R \times C$, s_{rc}^2	$\sigma_e^2 + \sigma_{bs}^2 + n\sigma_{ab}^2$
$(C \times S)/R$, $s_{cs/r}^2$	$\sigma_e^2 + \sigma_{bs}^2$

The quantities σ_a^2, σ_b^2, σ_{ab}^2, and σ_e^2 are variance components as described in Section 16.6. The quantity σ_s^2 is a variance component which is due to the variation of subjects within groups.

Examination of the above expectations indicates that the correct error term for testing row effects is the S/R variance estimate. The correct error term for testing column and $R \times C$ interaction effects is the $(C \times S)/R$ variance estimate.

19.8 COMPUTATION FORMULAS FOR TWO-FACTOR EXPERIMENTS WITH REPEATED MEASUREMENTS ON ONE FACTOR

Computation formulas may readily be obtained to compute the required sums of squares. As previously the sum of all nRC observations will be denoted by T. We denote the row and column totals by $T_{r..}$ and $T_{.c.}$, respectively. The total for the rth row and cth column summed over subjects is $T_{rc.}$. The total for any subject in any row summed over columns is $T_{r.s}$. The total for n subjects for any group summed over columns is $T_{rc.}$. Given this notation, the computation formulas are as follows:

BETWEEN SUBJECTS

[19.1] $$\frac{1}{C}\sum^{R}\sum^{n} T_{r.s}^2 - \frac{T^2}{nRC}$$

ROWS

$$\frac{1}{nC}\sum^{R} T_{r..}^2 - \frac{T^2}{nRC} \tag{19.2}$$

S/R

$$\frac{1}{C}\sum^{R}\sum^{n} T_{r.s}^2 - \frac{1}{nC}\sum^{R} T_{r..}^2 \tag{19.3}$$

WITHIN SUBJECTS

$$\sum^{R}\sum^{C}\sum^{n} X_{rci}^2 - \frac{1}{C}\sum^{R}\sum^{n} T_{r.s}^2 \tag{19.4}$$

COLUMNS

$$\frac{1}{nR}\sum^{C} T_{.c.}^2 - \frac{T^2}{nRC} \tag{19.5}$$

$R \times C$

$$\frac{1}{n}\sum^{R}\sum^{C} T_{rc.}^2 - \frac{1}{nC}\sum^{R} T_{r..}^2 - \frac{1}{nR}\sum^{C} T_{.c.}^2 + \frac{T^2}{nRC} \tag{19.6}$$

SC/R

$$\sum^{R}\sum^{C}\sum^{n} X_{rci}^2 - \frac{1}{C}\sum^{R}\sum^{n} T_{r.s}^2 - \frac{1}{n}\sum^{R}\sum^{C} T_{rc.}^2 + \frac{1}{nC}\sum^{R} T_{r..}^2 \tag{19.7}$$

TOTAL

$$\sum^{R}\sum^{C}\sum^{n} X_{rci}^2 - \frac{T^2}{nRC} \tag{19.8}$$

In practical computation a number of these terms can be obtained by simple subtraction.

19.9 ILLUSTRATIVE EXAMPLE OF A TWO-FACTOR EXPERIMENT WITH REPEATED MEASUREMENTS ON ONE FACTOR

Table 19.5 shows illustrative data for a two-factor experiment with repeated measurements on one factor. Two groups of four subjects were used. Each subject was measured under five experimental conditions. The totals required for computational purposes are also shown in this table.

Table 19.5

Illustrative data for a two-factor experiment with repeated measurements on one factor

		Subjects	C_1	C_2	C_3	C_4	C_5	$T_{r.s}$
Group 1	R_1	1	2	7	6	7	9	31
		2	4	3	7	12	14	40
		3	7	6	4	12	10	39
		4	1	3	3	6	6	19
		$T_{rc.}$	14	19	20	37	39	$T_{1..} = 129$
Group 2	R_2	1	4	4	7	9	1	25
		2	10	12	12	12	16	62
		3	8	7	8	12	10	45
		4	5	7	6	7	8	33
		$T_{rc.}$	27	30	33	40	35	$T_{2..} = 165$
		$T_{.c.}$	41	49	53	77	74	$T = 294$

From this table *six* quantities can be readily calculated as follows:

$$\frac{1}{C}\sum^{R}\sum^{n} T^2_{r.s} = \tfrac{1}{5}[(31)^2 + (40)^2 + \cdots + (33)^2] = 2{,}405.20$$

$$\frac{1}{nC}\sum^{R} T^2_{r..} = \frac{1}{4 \times 5}[(129)^2 + (165)^2] = 2{,}193.30$$

$$\frac{1}{nR}\sum^{C} T^2_{.c.} = \frac{1}{4 \times 2}[(41)^2 + (49)^2 + \cdots + (74)^2] = 2{,}287.00$$

$$\frac{1}{n}\sum^{R}\sum^{C} T^2_{rc.} = \tfrac{1}{4}[(14)^2 + (19)^2 + \cdots + (35)^2] = 2{,}347.50$$

$$\sum^{R}\sum^{C}\sum^{n} X^2_{rci} = (2)^2 + (7)^2 + \cdots + (8)^2 = 2{,}664.00$$

$$\frac{T^2}{nRC} = \frac{(294)^2}{4 \times 2 \times 5} = 2{,}160.90$$

Applying the computation formulas given in Sec. 19.8, the required sums of squares are as follows:

BETWEEN SUBJECTS

$$\frac{1}{C}\sum^{R}\sum^{n} T^2_{r.s} - \frac{T^2}{nRC} = 2{,}405.20 - 2{,}160.90 = 244.30$$

ROWS

$$\frac{1}{nC}\sum^{R} T^2_{r..} - \frac{T^2}{nRC} = 2{,}193.30 - 2{,}160.90 = 32.40$$

S/R

$$\frac{1}{C}\sum^{R}\sum^{n} T^2_{r.s} - \frac{1}{nC}\sum^{R} T^2_{r..} = 2{,}405.20 - 2{,}193.30 = 211.90$$

WITHIN SUBJECTS

$$\sum^{R}\sum^{C}\sum^{n} X^2_{rci} - \frac{1}{C}\sum^{R}\sum^{n} T^2_{r.s} = 2{,}664.00 - 2{,}405.20 = 258.80$$

COLUMNS

$$\frac{1}{nR}\sum^{C} T^2_{.c.} - \frac{T^2}{nRC} = 2{,}287.00 - 2{,}160.90 = 126.10$$

R × *C*

$$\frac{1}{n}\sum^{R}\sum^{C} T^2_{rc.} - \frac{1}{nC}\sum^{R} T^2_{r..} - \frac{1}{nR}\sum^{C} T^2_{.c.} + \frac{T^2}{nRC}$$
$$= 2{,}347.50 - 2{,}193.30 - 2{,}287.00 + 2{,}160.90 = 28.10$$

SC/R

$$\sum^{R}\sum^{C}\sum^{n} X^2_{rci} - \frac{1}{C}\sum^{R}\sum^{n} T^2_{r.s} - \frac{1}{n}\sum^{R}\sum^{C} T^2_{rc.} + \frac{1}{nC}\sum^{R} T^2_{r..}$$
$$= 2{,}664.00 - 2{,}405.20 - 2{,}347.50 + 2{,}193.30 = 104.60$$

TOTAL

$$\sum^{R}\sum^{C}\sum^{n} X^2_{rci} - \frac{T^2}{nRC} = 2{,}664.00 - 2{,}160.90 = 503.10$$

The analysis-of-variance table for these data is shown in Table 19.6. The degrees of freedom for rows are $R - 1 = 2 - 1 = 1$; for columns are, $C - 1 = 5 - 1 = 4$; and for $R \times C$ interaction are, $(R - 1)(C - 1) =$

Table 19.6

Analysis of variance for the data of Table 19.5

Source	Sum of squares	Degrees of freedom	Variance estimate
Between subjects	244.30		
Rows	32.40	1	$32.40 = s_r^2$
S/R	211.90	6	$35.32 = s^2_{s/r}$
Within subjects	258.80		
Columns	126.10	4	$31.53 = s_c^2$
R × *C*	28.10	4	$7.03 = s_{rc}^2$
SC/R	104.60	24	$4.36 = s^2_{sc/r}$
Total	503.10	39	

$(2-1)(5-1) = 4$. The S/R term is the variation within subjects summed over groups, and the degrees of freedom are $R(n-1) = 2(4-1) = 6$. The SC/R term is the subject-by-column interactions summed over rows, and the degrees of freedom are $R(n-1)(C-1) = 2(4-1)(5-1) = 24$.

The appropriate error term for testing row effects is the S/R variance estimate. The appropriate error term for testing column effects and $R \times C$ interaction is the SC/R variance estimate. The F ratios are as follows:

$$F_r = \frac{s_r^2}{s_{s/r}^2} = \frac{32.40}{35.32} = .92 \qquad p > .05$$

$$F_c = \frac{s_c^2}{s_{sc/r}^2} = \frac{31.53}{4.36} = 7.23 \qquad p < .01$$

$$F_{rc} = \frac{s_{rc}^2}{s_{sc/r}^2} = \frac{28.10}{4.36} = 6.44 \qquad p < .01$$

In this illustrative example the row effects are not significant, whereas the column effects, row-by-column effects, and row-by-column interaction are significant at better than the .01 level.

19.10 ASSUMPTIONS UNDERLYING REPEATED-MEASUREMENT DESIGNS

A basic assumption in the analysis of variance is the homogeneity of variance assumption. In, for example, a simple analysis of variance involving k independent groups this assumption may be stated in the form $\sigma_1^2 = \sigma_2^2 = \cdots = \sigma_k^2 = \sigma^2$. It has been shown that reasonable violations of this assumption will not seriously bias the F test. The analysis-of-variance procedures are said to be robust with respect to violations of the homogeneity of variance assumption. In the analysis of variance involving repeated measurements, assumptions are made not only regarding the homogeneity of variance but also regarding the homogeneity of covariance. To illustrate, in a one-factor experiment with repeated measurements N subjects are measured under C treatments. All the covariances, $r_{ij}s_is_j$, between pairs of treatments may be calculated. The homogeneity of covariance assumption is that all $r_{ij}s_is_j$ are estimates of the same population covariance. If, for example, repeated measurements were made for N subjects on four conditions, the following covariance table, or matrix, might be calculated.

	1	2	3	4
1	s_1^2	$r_{12}s_1s_2$	$r_{13}s_1s_3$	$r_{14}s_1s_4$
2	$r_{12}s_1s_2$	s_2^2	$r_{23}s_2s_3$	$r_{24}s_2s_4$
3	$r_{13}s_1s_3$	$r_{23}s_2s_3$	s_3^2	$r_{34}s_3s_4$
4	$r_{14}s_1s_4$	$r_{24}s_2s_4$	$r_{34}s_3s_4$	s_4^2

In this table variances appear along the main diagonal, and covariances appear on either side of the main diagonal. The homogeneity of variance-covariance assumption means that the variances and covariances in the population sampled are as follows:

	1	2	3	4
1	σ^2	$\rho\sigma^2$	$\rho\sigma^2$	$\rho\sigma^2$
2	$\rho\sigma^2$	σ^2	$\rho\sigma^2$	$\rho\sigma^2$
3	$\rho\sigma^2$	$\rho\sigma^2$	σ^2	$\rho\sigma^2$
4	$\rho\sigma^2$	$\rho\sigma^2$	$\rho\sigma^2$	σ^2

Here ρ is the value of the population correlation coefficient, and $\rho\sigma^2$ is the population covariance. If the homogeneity of variance-covariance assumption is not satisfied in repeated measurement designs, the F test is positively biased. This means that more significant differences will be found, and more null hypotheses rejected, than would have been the case had the F test not been biased.

A method exists for testing the homogeneity of variance-covariance assumption. This method is due to Box (1953), and a description of it is found in more advanced texts such as Winer (1971). Application of the procedure involves considerable arithmetical labor, and the computation required is best done on a computer.

If the homogeneity of variance-covariance assumption is not satisfied, Box (1954) has suggested a procedure which for a one-factor experiment with repeated measurements uses the same F ratio, $F_c = s_c^2/s_{rc}^2$, that would be appropriate if the assumption had been satisfied. Different degrees of freedom are, however, used on entering the F table. Instead of $(C - 1)$ and $(R - 1)(C - 1)$, the Box procedure uses 1 and $(R - 1)$. Since in this design R is the number of subjects, $(R - 1) = (N - 1)$. This is a conservative procedure and is based on a maximal departure of the observed covariance matrix from the homogeneity assumption. This procedure in most situations will be negatively biased and will lead to too few significant differences. Since the investigator will usually wish to proceed without applying a proper test of the homogeneity of the variance-covariance assumption, the following has been suggested. Test for column effects by using the F test with 1 degree of freedom associated with the numerator and $(R - 1)$ with the denominator. If the result is significant at the desired level, no further test is required, because this is a conservative test that works against obtaining a significant difference. If the result is not significant, test the F ratio by using $(C - 1)$ and $(R - 1)(C - 1)$ degrees of freedom. If this is not significant, no further test is required, because this is a liberal procedure that works in the direction of too many significant differences. If the conservative procedure indicates that the F ratio is not significant, and the liberal procedure indicates that it is significant, then a test of the homogeneity of variance-covariance assumption is required.

When the Box procedure as described above is applied to tests used in a two-factor experiment with repeated measurements, row, column, and interaction effects are tested by using an F ratio with 1 degree of freedom associated with the numerator and $N - 1$ degrees of freedom associated with the denominator. In a two-factor experiment with repeated measurements on one factor only, no adjustment is made in the number of degrees of freedom used in the F ratio for testing row effects, because repeated measurements are not involved in the row factor. Thus the row effect is tested with $R - 1$ and $R(n - 1)$ degrees of freedom associated with the numerator and denominator, respectively, of the F ratio. Adjustments should, however, be made in the degrees of freedom used in the F ratios for column and $R \times C$ interaction effects. Here, using the Box procedure, the column effect is tested with 1 and $R(n - 1)$ degrees of freedom associated, respectively, with the numerator and denominator of the F ratio. The $R \times C$ interaction is tested by using $(R - 1)$ and $R(n - 1)$ degrees of freedom. Here again, because of the conservative nature of these tests, if a significant result is found by using the F test with adjusted degrees of freedom, the result is significant *a fortiori*, regardless of the homogeneity of variance-covariance assumption.

19.11 RANDOMIZED BLOCK DESIGNS

Consider a one-way classification experiment of the type described in Chapter 15, where N subjects are assigned at random to k treatment groups. Assume that the groups are of equal size with n subjects in each of the k groups. Between-groups and within-groups sums of squares are obtained with $k - 1$ and $N - k$ degrees of freedom, respectively. The precision of such experiments can be increased, sometimes substantially, by grouping the subjects into a number of blocks, using a variable that is known to be correlated with the dependent variable. For example, assume that four different methods of learning an artificial language are under investigation and 40 subjects are available. In the usual one-way classification experiment these 40 subjects would be allocated to the four methods at random resulting in 4 groups of 10 subjects each. Measures of scholastic achievement may, however, be available, and this variable may be thought to be correlated with the performance of subjects in learning the artificial language. Subjects may be divided into two groups, or blocks, of 20 subjects each. One group may be a high, the other a low, scholastic achievement group. The 20 subjects in each block may then be assigned at random to the four methods, resulting in eight groups of five subjects. Such an experiment is called a randomized block experiment. The essence of the idea of a randomized block experiment is that subjects can be grouped into blocks according to a known classification variable, which is correlated with the dependent variable. Subjects within blocks are then assigned at random to the k treatments. The analysis of data for such an experiment presents no problems. In the example above the analysis of data is the same as for a double-classification factorial experiment as described in Chapter 16. Four sums of squares are obtained. Given k treatments and B blocks the degrees of freedom associated with treatments, blocks, interaction, and within-cells sums of squares are $k-1$, $B-1$, $(k-1)(B-1)$, and $N-Bk$, respectively.

What is the purpose of a randomized block experiment? The primary purpose is to reduce the size of the error term used in the denominator of the F ratio, which for the fixed model is the within-cells mean square. The relative efficiency of the experiment is thereby increased in relation to the one-way classification experiment. If the blocking variable has a substantial correlation with the dependent variable, the sums of squares associated with blocks may prove to be of some appreciable size; also an interaction term of some magnitude may be found. The effect of this will be to reduce the size of the within-group sum of squares and the within-group mean square and, thereby, increase the likelihood of obtaining a significant difference for the main effect.

The reader should note that in the one-way classification experiment the number of degrees of freedom associated with the error term, the within-groups mean square, is $N-k$, whereas in the randomized block experiment the number of degrees of freedom associated with the error term is $N-Bk$. Thus in the randomized block experiment a loss in degrees of freedom associated with the error term occurs, which must be compensated for by the sum of squares associated with blocks and interaction. An informative discussion of this point will be found in Myers (1972). Myers' treatment of the subject shows that the relative efficiency of the randomized block experiment in relation to the usual one-way classification experiment will be greater than 1 whenever the F test of the combined block and interaction effects exceeds 1. The relative efficiency will increase as the sum of squares associated with blocks and interaction effects increases.

Because the degrees of freedom associated with the error term in a randomized block design are $N-Bk$, the power of the F test will decrease as the number of blocks increases. Also, as the number of blocks increase the within-cells sum of squares decreases. These are opposing effects which suggest that in a randomized block experiment some optimum number of blocks exists. This topic has been investigated by Feldt and Mahmoud (1958). The reader will find Myers' (1972) discussion of this topic helpful. The gist of the matter is that the optimum number of blocks is related to the correlation between the blocking variable and the dependent variable, sample size N, and the number of treatment levels k. The optimum number of blocks increases with increase in the correlation and sample size N and decreases with increase in the number of treatment levels. In the design of a randomized block experiment investigators should inform themselves of these matters and keep them in mind.

The blocking variable is usually a classification variable which is characteristic of the subjects and is in no way under the control of the investigator. Examples are sex, socioeconomic level, scholastic achievement, IQ, litter membership, strain, and so on. A blocking variable may be of the nominal, ordinal, or interval-ratio type. With ordinal or interval-ratio variables arbitrary groupings (such as high, medium, and low) are used as blocks.

In some experiments the blocking variable is of no interest to the investigator and is used purely for the purpose of error reduction. In other experiments the blocking variable may be of considerable intrinsic interest in itself and may be an integral part of the experiment. In such experiments error reduction may not be a matter of concern. Such experiments are in effect ordinary factorial experiments, where one or more of the variables are classification rather than treatment variables.

Randomized block experiments are on occasion conducted with one observation per cell. To illustrate, let the treatment variable be four different dosages of a drug intended to alleviate depression and let the blocking variable be a score on a depression scale administered prior to the administration of any drug. Let the dependent variable be a measure of motor performance, such as reaction time. If 20 subjects were available, these subjects could be divided into 5 blocks of 4 subjects each. The four subjects with the highest scores on the depression scale would constitute the first block, the next highest subjects the second block, and so on. Within each block subjects are assigned to treatments at random. The result is a 5×4 table of numbers with one observation per cell. Such data are analyzed using the two-way classification analysis with one observation per cell. The total sum of squares is partitioned into treatment, block, and interaction sums of squares. Care must be exercised in the choice of error term in applying the F ratio. Frequently, as in the illustrative example above, the blocking variable may be viewed as a random variable and the treatment variable as a fixed variable; that is, the model is mixed. The proper error term for testing treatment effects is the interaction mean square. No test of the effects due to blocks can be made. In general in randomized block designs investigators must concern themselves with whether the blocking variable may be viewed as fixed or random, and govern themselves accordingly in the choice of the appropriate error term.

19.12 EXPERIMENTS WITH NESTED FACTORS

Consider an experiment which is intended to investigate two different drugs, A and B, in the treatment of depressed patients. The dependent variable is a measure of improvement under the drug. Assume that the patients are under treatment by three different therapists. Such an experiment might be conducted as a 2×3 factorial experiment with six groups of n experimental subjects. All six treatment combinations are present in the experiment. In such a factorial experiment both factors are said to be crossed. In the example above each of the two drugs crosses, as it were,