Table 9.3 *Design 2*

Sequence	Period		
	1	2	3
1	A	B	B
2	B	A	A

Table 9.4 *Design 3*

Sequence	Period		
	1	2	3
1	A	B	B
2	B	A	A
3	A	A	B
4	B	B	A

can be written in the form

$$y_{ijk} = \mu + \psi_i + s_{(i)k} + \pi_j + \tau_{d(i,j)} + \lambda_{d(i,j-1)} + \epsilon_{ijk} \tag{9.3}$$

where y_{ijk} is the response of the kth subject in the ith group and jth period. ψ_i is the sequence group effect. $s_{(i)k}$ is the subject within group or block effect, which can be treated as a fixed or random factor. π_j is the period effect, $d(i,j)$ is the treatment assigned to period j for sequence group i, τ_l is the effect of the lth treatment, and λ_l is the first-order carryover effect of the lth treatment.

As an example of the use of this model, consider the data in Table 9.5 that comes from a bioequivalence study presented by Chi (1994), where half of the 36 subjects were randomly assigned to the ABB sequence and the other half to the BAA sequence in design 2.

The data in Table 9.5 is available in the data frame `bioequiv` in the R package `daewr`. The variables in this data frame are coded in a way that model 9.3 can be fit. The treatment, $d(i,j)$, given in the jth period and the ith treatment group, is the variable `Treat` in the data frame. The carryover, $d(i,j-1)$ in the jth period and the ith treatment group, is the variable `Carry` in the data frame, and its value is the treatment given in the $j-1$st period (if one was given) or none. The remaining variables in the data frame are the group indicator `Group`, the subject indicator `Subject`, and the period indicator `Period`.

The first twelve lines of the data frame `bioequiv` is shown on page 360, and there it can see the carryover indicator is always labeled `none` in the first period. In the second period the carryover indicator is the treatment given in the first period, and in the third period the carryover indicator is the treatment given in the second period.

Table 9.5 *Data from Bioequivalence Study Where Subjects in Sequence Group 1 Were Given ABB and Subjects in Sequence Group 2 Were Given BAA*

Group	Subject	Period 1	Period 2	Period 3
1	2	112.25	106.36	88.59
1	3	153.71	150.13	151.31
1	6	278.65	293.27	295.35
1	8	30.25	35.81	34.66
1	10	65.51	52.48	47.48
1	12	35.68	41.79	42.79
1	13	96.03	75.87	82.81
1	14	111.57	115.92	118.14
1	18	72.98	70.69	74.20
1	19	148.98	157.70	178.62
1	21	140.22	119.83	139.48
1	23	60.44	44.09	35.53
1	26	136.10	161.76	163.57
1	28	111.19	101.83	101.70
1	31	85.87	99.60	107.48
1	34	111.25	114.90	135.94
1	36	58.79	96.42	122.60
1	129	299.50	303.45	385.34
2	1	52.66	47.65	13.91
2	4	128.44	173.22	140.44
2	5	233.18	88.18	31.93
2	7	53.87	89.18	70.08
2	9	62.07	54.99	73.39
2	11	183.30	153.88	122.41
2	15	51.91	73.01	23.10
2	16	90.75	89.70	111.94
2	17	59.51	56.26	48.87
2	24	83.01	73.85	71.30
2	25	85.37	86.67	92.06
2	27	84.85	75.41	79.45
2	30	70.33	40.80	46.91
2	32	110.04	102.61	113.18
2	33	93.58	87.31	87.58
2	35	66.54	43.29	84.07
2	120	59.67	56.86	69.49
2	122	49.02	50.29	51.71

```
> library(daewr)
> data(bioequiv)
> head(bioequiv,12)
   Group Subject Period Treat Carry      y
1      1       2      1     A  none 112.25
2      1       2      2     B     A 106.36
3      1       2      3     B     B  88.59
4      1       3      1     A  none 153.71
5      1       3      2     B     A 150.13
6      1       3      3     B     B 151.31
7      1       6      1     A  none 278.65
8      1       6      2     B     A 293.27
9      1       6      3     B     B 295.35
10     1       8      1     A  none  30.25
11     1       8      2     B     A  35.81
12     1       8      3     B     B  34.66
```

Once the data frame is available, model 9.3 can be fit using the code below. Since the subject indicators within each group are unique, the `Group` term can be left out of the model and the sum of squares for subjects will represent both the random group and subject effects.

```
> modc<-lm(y~Subject+Period+Treat+Carry,data=bioequiv)
> anova(modc)
Analysis of Variance Table

Response: y
          Df Sum Sq Mean Sq F value Pr(>F)
Subject   35 414306 11837.3 22.5016 <2e-16 ***
Period     2    287   143.3  0.2723 0.7624
Treat      1   2209  2209.1  4.1993 0.0443 *
Carry      1   1051  1050.6  1.9970 0.1622
Residuals 68  35772   526.1
---
Signif. codes:  0 ‘***’ 0.001 ‘**’ 0.01 ‘*’ 0.05 ‘.’ 0.1 ‘ ’ 1
```

The results show that the treatments are not equivalent (since there is a significant treatment effect at the $\alpha = 0.05$ significance level), and that the carryover effects are nonsignificant. The `lsmeans` package can be used to get the adjusted means for each treatment level as shown on the next page. The results show that treatment B has a higher average response.