Blood Flow Within-cases

bloodflow.data

ROW	Increase	Patient	Drug A	Drug B
1	2	1	0	0
2	10	1	0	1
3	9	1	1	0
4	25	1	1	1
5	-1	2	0	0
6	8	2	0	1
7	6	2	1	0
8	21	2	1	1

. . .

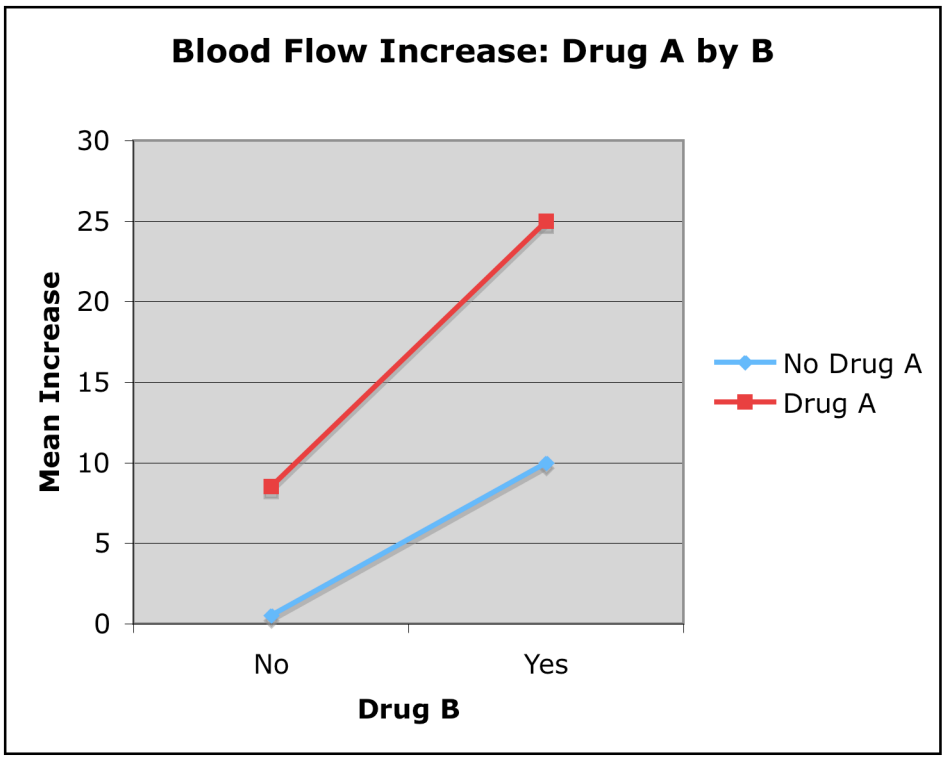
```
/* bloodflow3.sas */
options linesize=79 pagesize=100 noovp formdlim='_';
title 'Two within-subjects factors: Blood flow data (NWK p. 1181)';
proc format;
     value ynfmt  0 = 'No'  1 = 'Yes';

data blood;
     infile 'bloodflow.data' firstobs=2; /* Skip the first line */
     input row1 iflow1 patient1 DrugA1 DrugB1
           row2 iflow2 patient2 DrugA2 DrugB2
           row3 iflow3 patient3 DrugA3 DrugB3
           row4 iflow4 patient4 DrugA4 DrugB4 ;
     format druga1-druga4 drugb1-drugb4 ynfmt.;

proc means n mean stddev;
     var iflow1-iflow4;

proc glm;
     title2 'Multivariate Approach';
     model iflow1-iflow4 = ;                /* No IV (just intercepts) */
     repeated Drug_A 2, Drug_B 2 / short summary;
             /* Variable on the right changes fastest */

data uvblood;
     infile 'bloodflow.data' firstobs=2; /* Skip the first line */
     input row iflow patient DrugA DrugB;
     label iflow = 'Increase in Blood Flow';
     format DrugA DrugB ynfmt.;

proc glm;
     title2 'Univariate approach: Subject is a random effect';
     class DrugA DrugB patient;
     model iflow = DrugA|DrugB patient;
           /* Note no interactions with patient -> compound symmetry */
     random patient / test;

proc mixed;
     title2 'Covariance Structure Approach: Unknown Covariances';
     class DrugA DrugB;
     model iflow = DrugA|DrugB;
     repeated / type=un subject=patient r;
```

```
proc mixed;
     title2 'Covariance Structure Approach: Compound Symmetry';
     class DrugA DrugB;
     model iflow = DrugA|DrugB;
     repeated / type=cs subject=patient r;
```

Two within-subjects factors: Blood flow data (NWK p. 1181) 1

The MEANS Procedure

Variable	N	Mean	Std Dev
iflow1	12	0.5000000	2.1105794
iflow2	12	10.0000000	3.1908961
iflow3	12	8.5000000	2.0225996
iflow4	12	25.0000000	3.4377583



As usual, we skip the univariate tests on the untransformed dependent variables.

Repeated Measures Analysis of Variance

Repeated Measures Level Information

Dependent Variable	iflow1	iflow2	iflow3	iflow4
Level of Drug_A	1	1	2	2
Level of Drug_B	1	2	1	2

MANOVA Test Criteria and Exact F Statistics
for the Hypothesis of no Drug_A Effect
H = Type III SSCP Matrix for Drug_A
E = Error SSCP Matrix

S=1 M=-0.5 N=4.5

Statistic	Value	F Value	Num DF	Den DF	Pr > F
Wilks' Lambda	0.01397950	775.87	1	11	<.0001
Pillai's Trace	0.98602050	775.87	1	11	<.0001
Hotelling-Lawley Trace	70.53333333	775.87	1	11	<.0001
Roy's Greatest Root	70.53333333	775.87	1	11	<.0001

MANOVA Test Criteria and Exact F Statistics
for the Hypothesis of no Drug_B Effect
H = Type III SSCP Matrix for Drug_B
E = Error SSCP Matrix

S=1 M=-0.5 N=4.5

Statistic	Value	F Value	Num DF	Den DF	Pr > F
Wilks' Lambda	0.02052644	524.89	1	11	<.0001
Pillai's Trace	0.97947356	524.89	1	11	<.0001
Hotelling-Lawley Trace	47.71764706	524.89	1	11	<.0001
Roy's Greatest Root	47.71764706	524.89	1	11	<.0001

MANOVA Test Criteria and Exact F Statistics for
the Hypothesis of no Drug_A*Drug_B Effect
H = Type III SSCP Matrix for Drug_A*Drug_B
E = Error SSCP Matrix

S=1 M=-0.5 N=4.5

Statistic	Value	F Value	Num DF	Den DF	Pr > F
Wilks' Lambda	0.07836991	129.36	1	11	<.0001
Pillai's Trace	0.92163009	129.36	1	11	<.0001
Hotelling-Lawley Trace	11.76000000	129.36	1	11	<.0001
Roy's Greatest Root	11.76000000	129.36	1	11	<.0001

Multivariate Approach

The GLM Procedure
Repeated Measures Analysis of Variance
Univariate Tests of Hypotheses for Within Subject Effects

Source	DF	Type III SS	Mean Square	F Value	Pr > F
Drug_A	1	1587.000000	1587.000000	775.87	<.0001
Error(Drug_A)	11	22.500000	2.045455		

Source	DF	Type III SS	Mean Square	F Value	Pr > F
Drug_B	1	2028.000000	2028.000000	524.89	<.0001
Error(Drug_B)	11	42.500000	3.863636		

Source	DF	Type III SS	Mean Square	F Value	Pr > F
Drug_A*Drug_B	1	147.0000000	147.0000000	129.36	<.0001
Error(Drug_A*Drug_B)	11	12.5000000	1.1363636		

These univariate tests are based on a mixed model in which Drug A and Drug B are fixed, and subjects (patients) is random. The model does include interactions between subjects and the other factors. This is a bit non-standard, but the virtue is that when the within-subjects factors have only two levels, the univariate and multivariate test statistics are identical. The more standard approach is to have subjects not interact with any other factors; this yields the classical compound symmetry pattern in the within-subjects covariance matrix.

Note that we are skipping the output from the mixed-model approach to repeated measures with proc glm; it's easier and better to get the analysis from proc mixed with the `type=cs` option.

The Mixed Procedure

Model Information

Data Set	WORK.UVBLOOD
Dependent Variable	iflow
Covariance Structure	Unstructured
Subject Effect	patient
Estimation Method	REML
Residual Variance Method	None
Fixed Effects SE Method	Model-Based
Degrees of Freedom Method	Between-Within

Class Level Information

Class	Levels	Values
DrugA	2	No Yes
DrugB	2	No Yes

Dimensions

Covariance Parameters	10
Columns in X	9
Columns in Z	0
Subjects	12
Max Obs Per Subject	4

Number of Observations

Number of Observations Read	48
Number of Observations Used	48
Number of Observations Not Used	0

Iteration History

Iteration	Evaluations	-2 Res Log Like	Criterion
0	1	224.25476467	
1	1	179.84564795	0.00000000

Convergence criteria met.

Estimated R Matrix for Subject 1

Row	Col1	Col2	Col3	Col4
1	4.4545	4.0000	2.7273	4.0909
2	4.0000	10.1818	5.2727	9.3636
3	2.7273	5.2727	4.0909	6.2727
4	4.0909	9.3636	6.2727	11.8182

Covariance Parameter Estimates

Cov Parm	Subject	Estimate
UN(1,1)	patient	4.4545
UN(2,1)	patient	4.0000
UN(2,2)	patient	10.1818
UN(3,1)	patient	2.7273
UN(3,2)	patient	5.2727
UN(3,3)	patient	4.0909
UN(4,1)	patient	4.0909
UN(4,2)	patient	9.3636
UN(4,3)	patient	6.2727
UN(4,4)	patient	11.8182

Fit Statistics

-2 Res Log Likelihood	179.8
AIC (smaller is better)	199.8
AICC (smaller is better)	206.5
BIC (smaller is better)	204.7

Null Model Likelihood Ratio Test

DF	Chi-Square	Pr > ChiSq
9	44.41	<.0001

Type 3 Tests of Fixed Effects

Effect	Num DF	Den DF	F Value	Pr > F
DrugA	1	11	775.87	<.0001
DrugB	1	11	524.89	<.0001
DrugA*DrugB	1	11	129.36	<.0001

The Mixed Procedure

Model Information

Data Set	WORK.UVBLOOD
Dependent Variable	iflow
Covariance Structure	Compound Symmetry
Subject Effect	patient
Estimation Method	REML
Residual Variance Method	Profile
Fixed Effects SE Method	Model-Based
Degrees of Freedom Method	Between-Within

Class Level Information

Class	Levels	Values
DrugA	2	No Yes
DrugB	2	No Yes

Dimensions

Covariance Parameters	2
Columns in X	9
Columns in Z	0
Subjects	12
Max Obs Per Subject	4

Number of Observations

Number of Observations Read	48
Number of Observations Used	48
Number of Observations Not Used	0

Iteration History

Iteration	Evaluations	-2 Res Log Like	Criterion
0	1	224.25476467	
1	1	197.70764453	0.00000000

Convergence criteria met.

Estimated R Matrix for Subject 1

Row	Col1	Col2	Col3	Col4
1	7.6364	5.2879	5.2879	5.2879
2	5.2879	7.6364	5.2879	5.2879
3	5.2879	5.2879	7.6364	5.2879
4	5.2879	5.2879	5.2879	7.6364

Covariance Parameter Estimates

Cov Parm	Subject	Estimate
CS	patient	5.2879
Residual		2.3485

Fit Statistics

-2 Res Log Likelihood	197.7
AIC (smaller is better)	201.7
AICC (smaller is better)	202.0
BIC (smaller is better)	202.7

Null Model Likelihood Ratio Test

DF	Chi-Square	Pr > ChiSq
1	26.55	<.0001

Type 3 Tests of Fixed Effects

Effect	Num DF	Den DF	F Value	Pr > F
DrugA	1	11	675.75	<.0001
DrugB	1	11	863.54	<.0001
DrugA*DrugB	1	11	62.59	<.0001

%