BLOOD-BRAIN BARRIER EXPERIMENT

8. Alternative Regression Models

The regression model discussed in the previous section is based on the assumption of a linear relationship between the log-transformed responses and the log-transformed sacrifice times. However, a scatterplot displayed in Section 4.4 exhibited a slight curvature indicating that a straight-line regression model may be not adequate.

One model for incorporating curvature includes squared log of sacrifice time denoted as *SQLNTIME* as an additional explanatory variable:

$$LNRATIO = \beta_0 + \beta_1 * LNTIME + \beta_2 * SQLNTIME + \beta_3 * TREAT + \beta_4 * LNTIMTRE + \beta_5 * DAYS + \beta_6 * SEX + \beta_7 * WEIGHT + \beta_8 * LOSS + \beta_9 * TUMOR + ERROR.$$

If we run regression in SPSS for the blood-brain barrier data, we will obtain the following output:

ANOVA[b]

Model		Sum of Squares	df	Mean Square	F	Sig.
1	Regression	158.121	8	19.765	56.897	.000[a]
	Residual	8.685	25	.347		
	Total	166.806	33			

a. Predictors: (Constant), LNTIMESQ, TREAT, LOSS, WEIGHT, TUMOR, DAYS, SEX, LNTIME

b. Dependent Variable: LNRATIO

Coefficients[a]

Model		Unstandardized Coefficients		Standardized Coefficients	t	Sig.
		B	Std. Error	Beta		
1	(Constant)	-6.931	3.135		-2.211	.036
	LNTIME	.781	.164	.675	4.750	.000
	TREAT	.854	.213	.193	4.016	.000
	DAYS	.281	.276	.058	1.018	.318
	SEX	.247	.361	.047	.686	.499
	WEIGHT	6.012E-04	.005	.007	.118	.907
	LOSS	-4.91E-02	.030	-.093	-1.648	.112
	TUMOR	1.677E-03	.001	.077	1.351	.189
	LNTIMESQ	7.122E-02	.046	.233	1.544	.135

a. Dependent Variable: LNRATIO

The p-value of 0.135 for the squared log sacrifice time coefficient indicates that the squared term can be removed from the model. The model considered in Section 7 appears

still to be more adequate. The output confirms again that the final model used to estimate the treatment effect has only two terms: *LNTIME* and *TREAT*.

It is also possible to develop an alternative regression model by treating sacrifice time as a factor with four levels corresponding to the four sacrifice time values: 0.5, 3, 24, and 72. As there are 4 levels, then 4-1=3 indicator variables are needed as explanatory variables. Selecting the first level, 0.5 hours, as the reference level, the multiple linear regression model is

$$LNRATIO = \beta_0 + \beta_1 * D3 + \beta_2 * D24 + \beta_3 * D72 + \beta_4 * TREAT + ERROR.$$

The dummy variables D3, D24, and D72 are defined as follows:

TIME	D3	D24	D72
0.5	0	0	0
3	1	0	0
24	0	1	0
72	0	0	1

The dummy variables can be incorporated into the SPSS data file, by using the *Recode into Different Variables* feature in the *Transform* menu. The SPSS output for the regression model is displayed below:

Model Summary[b]

Model	R	R Square	Adjusted R Square	Std. Error of the Estimate
1	.975[a]	.951	.944	.5328

a. Predictors: (Constant), TREAT, D72, D24, D3

b. Dependent Variable: LNRATIO

ANOVA[b]

Model		Sum of Squares	df	Mean Square	F	Sig.
1	Regression	158.573	4	39.643	139.646	.000[a]
	Residual	8.233	29	.284		
	Total	166.806	33			

a. Predictors: (Constant), TREAT, D72, D24, D3

b. Dependent Variable: LNRATIO

The value of the F statistic is equal to 139.646 with the corresponding p-value of 0 provides very strong evidence of the utility of the model.

The estimates and standard errors are displayed in the next table:

Coefficients[a]

Model		Unstandardized Coefficients		Standardized Coefficients	t	Sig.	95% Confidence Interval for B		Collinearity Statistics	
		B	Std. Error	Beta			Lower Bound	Upper Bound	Tolerance	VIF
1	(Constant)	-4.302	.205		-21.010	.000	-4.720	-3.883		
	D3	1.134	.252	.226	4.501	.000	.619	1.650	.676	1.480
	D24	4.257	.259	.815	16.431	.000	3.727	4.787	.691	1.447
	D72	5.154	.259	.987	19.892	.000	4.624	5.684	.691	1.447
	TREAT	.797	.183	.180	4.346	.000	.422	1.172	.993	1.007

a. Dependent Variable: LNRATIO

In particular, the coefficient of the indicator variable for the blood-brain barrier disruption treatment is 0.797. So, expressed in accordance with the interpretation for log-transformed responses, the median ratio of antibody concentration in the brain tumor to antibody concentration in the liver is estimated to be exp(0.797) = 2.22 times greater for the blood-brain diffusion treatment than for the saline control. The estimate is a little bit smaller than the estimate of 2.33 obtained for the model discussed in Section 7.

Moreover, according to the above table, the 95% confidence interval for the ratio is from exp(.422) = 1.56 to exp(1.172) = 3.15.

As the values of tolerance are not very small and VIF not very large, there is no evidence any problem with collinearity in this case. The regression diagnostics for the model is discussed in detail in the next section.