

In a follow-up study, we took 20 mice with tumor (10 from strain B6 and 10 from Cast) and 20 mice without tumor (10 B6 + 10 Cast), and measure the expression of a gene that is important in tumor progression at three tissues of each mouse: left forebrain, left hind-brain, and right whole brain. We have altogether $(20+20)*3 = 120$ measurements of gene expression.

(c) (2pts) Please describe the structure of the $120*120$ covariance matrix of these 120 observations. How many elements of this matrix are expected to be 0?

(d) (2pts) Here are the results of one mixed effect model, what kind of covariance structure are assumed for three expression measurements per mouse?

Estimated R Matrix for mouseID 1				
Row	Col1	Col2	Col3	
1	2.1015	0.6881	0.6881	
2	0.6881	2.1015	0.6881	
3	0.6881	0.6881	2.1015	
Fit Statistics				
-2 Res Log Likelihood	417.4			
AIC (smaller is better)	421.4			
AICC (smaller is better)	421.5			
BIC (smaller is better)	424.8			
Null Model Likelihood Ratio Test				
DF	Chi-Square	Pr > ChiSq		
1	11.11	0.0009		
Type 3 Tests of Fixed Effects				
Effect	Num Den	DF	F Value	Pr > F
tumor	1	37	4.43	0.0421
strain	1	37	22.02	<.0001

symmetry
compound

- unstructured*
- (e) (3pts) Here are the results of the other mixed effect model, what kind of covariance structure are assumed for the three expression measurements per mouse in this model? Compare this model with previous one by a Likelihood Ratio test, write down test statistic, degree of freedom and the distribution of the test statistic when Null hypothesis is correct.

The Mixed Procedure				
Estimated R Matrix for mouseID 1				
Row	Col1	Col2	Col3	
1	2.4998	1.3469	0.1251	
2	1.3469	1.9588	0.5887	
3	0.1251	0.5887	1.8423	
Fit Statistics				
-2 Res Log Likelihood				404.3
AIC (smaller is better)				416.3
AICC (smaller is better)				417.1
BIC (smaller is better)				426.5
Null Model Likelihood Ratio Test				
DF	Chi-Square	Pr > ChiSq		
5	24.21	0.0002		
Type 3 Tests of Fixed Effects				
Effect	Num DF	Den DF	F Value	Pr > F
tumor	1	37	4.22	0.0471
strain	1	37	23.26	<.0001

$$\begin{aligned}
 LRT &= 417.4 - 404.3 \\
 &= 13.1 \sim \chi^2_4
 \end{aligned}$$

- (f) (3pts) Someone ignored the fact that these mouse are not independent and did a fixed effect linear regression. Compared the following results with the results from question (e), explain (i) which assumption of general linear regression is violated, (ii) why we see smaller p-values in the fixed effect linear model? (iii) Give a reasonable guess