

POWER CALCULATIONS

I was given control data from 11 different experiments. Within each experiment, there were four animals and three replicates per animal. For each animal, I averaged the three replicates, and then averaged the four individual animal means to obtain overall control means and SD's for that experiment. I also averaged the log transformed data. The summary statistics are given below.

Summary of the Control Absorbance Data for the LLNA: BrdU-ELISA

Experiment	Original Scale		Log Scale	
	Mean	SD	Mean	SD
1	0.0676	0.0051	-2.70	0.077
2	0.1197	0.024	-2.14	0.221
3	0.1068	0.0425	-2.29	0.367
4	0.0982	0.0216	-2.34	0.212
5	0.0695	0.0275	-2.73	0.410
6	0.0766	0.0329	-2.64	0.457
7	0.0687	0.0062	-2.68	0.092
8	0.4833	0.0681	-0.74	0.151
9	0.4516	0.110	-0.82	0.249
10	0.2479	0.1425	-1.52	0.590
11	0.2252	0.1044	-1.58	0.491

Several comments on the data:

Note that there is considerable study-to-study variability. For example, note that if Experiments 8 and 9 were actually a "treatment", then it would be declared active relative to most if not all of the first 7 control groups (treated/control ratio >3).

There is much less within-study variability. Note also that on the original scale, the SD tends to increase with increasing means. This suggests that a log transformation will help to stabilize the variability, which in fact was the case.

Another important advantage of taking logs is that the apparent variable of interest is the ratio of the treated to control response. Testing the null hypothesis that this ratio is one is equivalent to testing the null hypothesis that the difference in the logs is zero, which is the test that I chose to focus on for the power calculations.

The first step in the power calculation was to use the data from the 11 experiments to derive a representative mean and SD for the control response. Although alternative approaches are certainly possible, I elected to simply take the mean mean and mean SD (on the log scale). These were mean=-2.02 and SD=0.302. The corresponding control mean on the original scale is 0.133.

I then looked at the three hypothetical changes that were of interest: a tripling of the

control response (on the original scale, obviously), a doubling of the control response, and a 1.3-fold increase in the control response. Although more elegant tests may be possible, I chose to base my power calculations on a simple one-sided Student's t test applied to the log-transformed data. The calculations that are given below assume the same design that was used in the 11 experiments (i.e., three replicates per animal). I focused on an N of 4, but also looked at other sample sizes as well.

The results are summarized below assuming a control response of -2.02 (log scale) and an SD of 0.302.

Treatment Group (Rx) Response Relative to Controls

Parameter	3-fold Increase	2-fold Increase	1.3-fold Increase
Mean Rx response	0.399	0.266	0.173
Log (mean Rx response)	-0.92	-1.32	-1.75
Difference from control (log scale)	1.10	0.70	0.27
SD of the difference from control	3.64	2.32	0.89
Power for N=4	99%	80-90%	<50%
Other power	95% (N=3)	95% (N=5)	50% (N=8)
Other power		50-80% (N=3)	80% (N=16)
Other power			90% (N=22)

I conclude that four animals per group with three replicates per animal is sufficient to detect a three-fold increase in the control response and would likely (with reasonable power) detect a two-fold increase (an additional animal would give 95% power; N=3 would be more problematic). However, it would not be realistic to expect to detect a 1.3 fold increase in the control response without a significant addition of animals.

Slight changes in the underlying assumptions would not change the results of these power calculations in any meaningful way.