Assignment #13

Due on Wednesday, November 28, 2007

Read Chapter 6 on *Modeling Bacterial Resistance* in the class lecture notes, starting on page 55, at `http://pages.pomona.edu/~ajr04747/`

Read on *Probability Distributions in Genetics* in Allman and Rhodes (pp. 228–237).

Background Information. Luria and Delbrück[1] devised the following procedure (known as the *fluctuation test*) to estimate the *mutation rate, a*, for certain bacteria:

Imagine that you start with a single normal bacterium (with no mutations) and allow it to grow to produce several bacteria. Place each of these bacteria in test–tubes each with media conducive to growth. Suppose the bacteria in the test–tubes are allowed to reproduce for n division cycles. After the n^{th} division cycle, the content of each test–tube is placed onto a agar plate containing a virus population which is lethal to the bacteria which have not developed resistance. Those bacteria which have mutated into resistant strains will continue to replicate, while those that are sensitive to the virus will die. After certain time, the resistant bacteria will develop visible colonies on the plates. The number of these colonies will then correspond to the number of resistant cells in each test tube at the time they were exposed to the virus.

Do the following problems

1. If p_o denotes the fraction of the plates that show no colonies of resistant bacteria, give a formula for estimating the average number of mutations in the n division cycles.

2. If p_o denotes the fraction of the plates that show no colonies of resistant bacteria, give a formula for estimating the mutation rate, a, in terms of n and p_o.

3. The data in Table 1 were taken from page 504 of the Luria and Delbrück 1943 paper.

   (a) Estimate the average number of mutations that occured before the bacteria were plated with the virus.

   (b) Given that the number of bacteria in each culture was about 5×10^8, estimate the mutation rate a.

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[1](1943) *Mutations of bacteria from virus sensitivity to virus resistance. Genetics*, **28**, 491–511

Table 1: Number of resistant bacteria in a series of similar cultures

Test–tube #	1	2	3	4	5	6	7	8	9	10	11	12
# of Mutants	1	0	0	7	0	303	0	0	3	48	1	4

4. For the data in Table 1:

   (a) Estimate the average number of resistant bacteria right before the plating was made.

   (b) Use the *sample–variance* formula

   $$s^2 = \frac{\displaystyle\sum_{i=1}^{n}(r_i - \overline{r})^2}{n-1},$$

   where r_i denotes the number of resistant cells in test–tube i and $\overline{r}$ is the average number of resistant bacteria, to estimate the variance of the distribution.

   (c) Based on your results in the previous part and what you know about the Poisson process, would you say that the number of resistant bacteria follows a Poisson process? Justify your answer.

5. Problem 6.2.5 on page 238 in Allman and Rhodes.