

2. In class we derived that the burst size distribution for an ion channel follows a geometric distribution

$$P(n = k) = \frac{\beta \gamma^{k-1}}{(\gamma + \beta)^k}$$

given that at least one opening was observed.

Explicitly calculate the average and CV of the burst size distribution to check the claims I made in class.

$$\begin{aligned} \langle n \rangle &= \sum_{n=0}^{\infty} n \frac{\beta \gamma^{n-1}}{(\gamma + \beta)^n} \\ &= \frac{\beta}{\gamma} \sum_{n=0}^{\infty} n \left(\frac{\gamma}{\gamma + \beta}\right)^n e^{\mu n} \Big|_{\mu=0} \\ &= \frac{\beta}{\gamma} \sum_{n=0}^{\infty} \frac{\partial}{\partial \mu} \left(\frac{\gamma}{\gamma + \beta}\right)^n e^{\mu n} \Big|_{\mu=0} \\ &= \frac{\beta}{\gamma} \frac{\partial}{\partial \mu} \sum_{n=0}^{\infty} \left(\frac{\gamma e^{\mu}}{\gamma + \beta}\right)^n \Big|_{\mu=0} \\ &= \frac{\beta}{\gamma} \frac{\partial}{\partial \mu} \frac{1}{1 - \frac{\gamma e^{\mu}}{\gamma + \beta}} \Big|_{\mu=0} \\ &= \frac{\beta}{\gamma} \frac{\partial}{\partial \mu} \frac{\gamma + \beta}{\gamma + \beta - \gamma e^{\mu}} \Big|_{\mu=0} \\ &= \frac{\beta}{\gamma} \gamma (r + \beta) \frac{e^{\mu}}{(\gamma + \beta - \gamma e^{\mu})^2} \Big|_{\mu=0} \\ &= \frac{\gamma + \beta}{\beta} \end{aligned}$$

$$\begin{aligned} \langle n^2 \rangle &= \sum_{n=0}^{\infty} n^2 \frac{\beta \gamma^{n-1}}{(\gamma + \beta)^n} \\ &= \frac{\beta}{\gamma} \sum_{n=0}^{\infty} n^2 \left(\frac{\gamma}{\gamma + \beta}\right)^n e^{\mu n} \Big|_{\mu=0} \\ &= \frac{\beta}{\gamma} \sum_{n=0}^{\infty} \frac{\partial^2}{\partial \mu^2} \left(\frac{\gamma}{\gamma + \beta}\right)^n e^{\mu n} \Big|_{\mu=0} \\ &= \frac{\beta}{\gamma} \frac{\partial^2}{\partial \mu^2} \sum_{n=0}^{\infty} \left(\frac{\gamma e^{\mu}}{\gamma + \beta}\right)^n \Big|_{\mu=0} \\ &= \frac{\beta}{\gamma} \frac{\partial^2}{\partial \mu^2} \frac{1}{1 - \frac{\gamma e^{\mu}}{\gamma + \beta}} \Big|_{\mu=0} \\ &= \frac{\beta}{\gamma} \frac{\partial^2}{\partial \mu^2} \frac{\gamma + \beta}{\gamma + \beta - \gamma e^{\mu}} \Big|_{\mu=0} \\ &= \frac{\beta}{\gamma} (r + \beta) \gamma e^{\mu} \frac{2\gamma e^{\mu} + \gamma + \beta - \gamma e^{\mu}}{(\gamma + \beta - \gamma e^{\mu})^3} \Big|_{\mu=0} \\ &= \frac{\beta}{\gamma} (r + \beta) \gamma \frac{2\gamma + \beta}{\beta^3} \\ &= \frac{(r + \beta)(2\gamma + \beta)}{\beta^2} \end{aligned}$$

$$\begin{aligned} \text{var}(n) &= \langle n^2 \rangle - \langle n \rangle^2 \\ &= \frac{(r + \beta)(2\gamma + \beta)}{\beta^2} - \left(\frac{\gamma + \beta}{\beta}\right)^2 \\ &= \frac{\gamma(r + \beta)}{\beta^2} \\ \text{CV}_n &= \frac{\sqrt{\text{var}(n)}}{\langle n \rangle} \\ &= \sqrt{\frac{\gamma}{\gamma + \beta}} \end{aligned}$$

Checked by Wiki

3. You are growing a population of bacteria starting from a single cell that divides every 20 min. After 10 h you have around  $10^9$  cells at which point you add a toxin that kills bacteria after 19 min and 59 s just before the next round of cell division.

(a) Imagine the following scenario: in response to the toxic environment, bacteria switch on a mutational response mechanism that gives each cell a probability of  $10^{-8}$  of acquiring a protective mutation before the next cell division.

- What is the probability distribution for the number of cells that you will find alive 19 min and 59 s after adding the toxin? (Feel free to make use of any approximations for a binomial distribution in the appropriate regime.)
- How does the variance relate to the mean? Does this relation depend on the mean?
- What is the probability that all  $10^9$  cells will be found alive? Comment on your answer.

(Assume that none of the bacteria had the protective mutation at the time you added the toxin.)

just for clarifying

It is assumed that

if a cell mutates before dividing, both of its offsprings are resistant to toxin.

This argument makes sense since genes in bac are usually multi-copied (?? I not sure).

If not, more complexity ... (for DNA is double-strand)

(a) assume during this round,  $n$  will alive (among  $N = 10^9$ ,  $p = 10^{-8}$ )

distribution:  $B(n; N, p) = \frac{N!}{(N-n)! n!} p^n (1-p)^{N-n}$

not that  $N \gg 1$ ,  $p \ll 1$ ,  $Np = 10 \Rightarrow N!$  too large

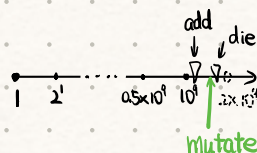
Approximation: set  $\gamma = Np$

$$\begin{aligned} &\lim_{N \rightarrow \infty} \frac{N!}{(N-n)! n!} \left(\frac{\gamma}{N}\right)^n \left(1 - \frac{\gamma}{N}\right)^{N-n} \\ &= \lim_{N \rightarrow \infty} \frac{1}{n!} \frac{N!}{(N-n)!} \left(\frac{\gamma}{N}\right)^n \left(1 - \frac{\gamma}{N}\right)^{-n} \left(1 - \frac{\gamma}{N}\right)^{N-n} \\ &= \lim_{N \rightarrow \infty} \frac{1}{n!} N^n \left(\frac{\gamma}{N}\right)^n \left[\left(1 - \frac{\gamma}{N}\right)^{-\frac{N}{\gamma}}\right]^{-\gamma} \end{aligned}$$

$$= \frac{1}{n!} N^n \frac{1}{N^n} \gamma^n e^{-\gamma} = \frac{\gamma^n e^{-\gamma}}{n!} = P(n; \gamma)$$

$$B(n; N, p) \xrightarrow[p \ll 1]{N \gg 1} P(n; \gamma)$$

$$P(n; 10) = \frac{10^n e^{-10}}{n!} \text{ where } \gamma = Np = 10$$



$$\begin{aligned} \langle n \rangle &= \sum_{n=0}^{\infty} n \frac{\gamma^n e^{-\gamma}}{n!} \\ &= \frac{\partial}{\partial \mu} \sum_{n=0}^{\infty} \frac{\gamma^n}{n!} e^{\mu n} e^{-\gamma} \Big|_{\mu=0} \\ &= \frac{\partial}{\partial \mu} \sum_{n=0}^{\infty} \frac{(\gamma e^{\mu})^n}{n!} e^{-\gamma} \Big|_{\mu=0} \\ &= \frac{\partial}{\partial \mu} e^{\gamma e^{\mu}} e^{-\gamma} \Big|_{\mu=0} \\ &= \gamma e^{\gamma} e^{\gamma e^{\mu}} e^{-\gamma} \Big|_{\mu=0} \\ &= \gamma \end{aligned}$$

$$\begin{aligned} \text{var}(n) &= \langle n^2 \rangle - \langle n \rangle^2 \\ &= \gamma^2 + \gamma - \gamma^2 \\ &= \gamma \end{aligned}$$

$$\begin{aligned} \langle n^2 \rangle &= \sum_{n=0}^{\infty} n^2 \frac{\gamma^n e^{-\gamma}}{n!} \\ &= \frac{\partial^2}{\partial \mu^2} \sum_{n=0}^{\infty} \frac{\gamma^n}{n!} e^{\mu n} e^{-\gamma} \Big|_{\mu=0} \\ &= \frac{\partial^2}{\partial \mu^2} e^{\gamma e^{\mu}} e^{-\gamma} \Big|_{\mu=0} \\ &= \frac{\partial}{\partial \mu} \gamma e^{\mu} e^{\gamma e^{\mu}} e^{-\gamma} \Big|_{\mu=0} \\ &= \gamma e^{\gamma} (\gamma e^{\gamma} e^{\gamma e^{\mu}} + e^{\gamma} e^{\gamma e^{\mu}}) \Big|_{\mu=0} \\ &= \gamma^2 + \gamma \end{aligned}$$

$$\frac{\text{var}(n)}{\langle n \rangle} = 1, \text{ not dependent on parameter}$$