1. When an influenza virus binds to the surface of a cell, it must diffuse laterally in the plane of the membrane until it encounters a small specialized circular region of the membrane, a "coated pit", where it is efficiently trapped and transported into the cell. In one particular cell type, the cell is ~80 µm in diameter and the coated pits are ~1 µm. Dr. Zell Biologist discovers that a mutation in one of the constituent proteins doubles the diameter of the coated pits. By what factor will this mutation accelerate or slow diffusion of membrane-bound virus to the pit? (For simplicity, you can assume there is only one pit per cell.)

![Diagram of cell and coated pit](image)

\[<\omega>_{2D} = \frac{L^2}{2D} \cdot \ln \left(\frac{L}{b}\right)\]

\[<\omega>_{\text{mut}} = \frac{\ln (40/1)}{\ln (40/0.5)} = 0.84 \Rightarrow \text{time to capture shorter by 0.84 - fold, capture faster by } 1/0.84\]

This is only approximate; the cell is a sphere, not a circle.

2. The nuclear envelope (the membrane that surrounds the nucleus in a eukaryotic cell) contains pores which allow the free diffusion of small proteins between the nucleus and the cytoplasm. This means that there is zero net movement of such a protein through the pore if its nuclear and cytoplasmic concentrations are equal. One such protein, GFP (diffusion coefficient = $10^{-7}$ cm$^2$ s$^{-1}$), is so highly fluorescent that the diffusion of single molecules of GFP can be followed using fluorescence microscopy.

A cell biologist, Dr. Coulter Counter, focuses his microscope on a single pore in a cell in which the free GFP concentrations in the nucleus and the cytoplasm are maintained at $[\text{GFP}]_{\text{nuc}} = 1$ nM and $[\text{GFP}]_{\text{cyto}} = 10$ nM, respectively. These concentrations are sufficiently low to ensure that no more than one GFP molecule will be in the pore at a time.

a. Dr. Counter finds that during 1 minute of observation, 120 GFP molecules travel completely through the pore from cytoplasm to nucleus, while only 15 go all the
way through the pore from the nucleus to the cytoplasm, giving a net rate of transport equal to 105 molecules per minute. Predict how both the two unidirectional rates and the net rate will change if the concentration of GFP in the cytoplasm is doubled while the nuclear concentration is left unchanged. Explain your reasoning.

c → n will \[\text{double}\] to \(240\ \text{min}^{-1}\)

n → c will \[\text{not change}\]; \(15\ \text{min}^{-1}\)

\[\text{so net increases from } 105 \text{ to } 225 \text{ min}^{-1}\]

Doubling \([\text{GFP}]_{\text{cyto}}\) can only affect the rate of entry at the cyto side. Double conc ⇒ double the number of entries, because the rate of protein collision with the pore entry doubles.

You could also make an argument based on concentration gradients & Fick’s equation, but this would only tell you the net flux.

cytoplasm is doubled while the nuclear concentration is left unchanged. Explain your reasoning.

b. Dr. Counter also decides to tabulate the fate of each molecule that reaches the middle of the pore. For each molecule that comes to the point halfway across the nuclear envelope, Dr. Counter follows it to see whether it exits the pore by going into the cytoplasm or by going into the nucleus. What is the predicted difference between the number per minute of these molecules exiting into the nucleus and into the cytoplasm? Explain your reasoning.
The difference must be zero, as there is no net force to bias diffusion through the pore. (If this were not true, the pore would do no transport when
\[[\text{GFP}]_{\text{nuc}} = [\text{GFP}]_{\text{cyto}}\] without energy input, which would violate the 2nd law of Thd.)
*or the random walk, if you prefer.

3. a. Using the \(n\)-trial binomial distribution

\[P(r) = \binom{n}{r} p^r (1-p)^{n-r}\]

derive an equation for the mean value of \(r\), \(<r>\), in terms of \(n\) and \(p\). (Hint: use the binomial theorem.)

Intuitively, if \(p = \frac{1}{2}\), then \(\frac{1}{n}\) of the coin tosses will be heads, so we expect \(<r> = np\). Let's prove it:

\[
<r> = \sum_{r=0}^{n} r P(r)
= \sum_{r=0}^{n} \left[ r \frac{n!}{r! \cdot (n-r)!} p^r (1-p)^{n-r} \right]
\]

given that 1. The first term of the above series is zero, and
2. \(r/r! = 1/(r-1)!\)
we have:

\[ \langle r \rangle = \sum_{r=1}^{n} \left[ \frac{n!}{(r-1)! (n-r)!} \cdot \rho^r (1-\rho)^{n-r} \right] \]

factoring out \( n \) and \( \rho \)

\[ \Rightarrow \langle r \rangle = n \rho \sum_{r=1}^{n} \left[ \frac{(n-1)!}{(r-1)! (n-r)!} \cdot \rho^{r-1} (1-\rho)^{n-r} \right] \]

let \( s = n-1 \), \( t = r-1 \) \( \Rightarrow s-t = n-r - 1 \)

\[ \Rightarrow \langle r \rangle = n \rho \sum_{t=0}^{s} \left[ \frac{s!}{t! (s-t)!} \cdot \rho^t (1-\rho)^{s-t} \right] \]

The binomial theorem says this is just

\[ [\rho + (1-\rho)]^s = 1^s = 1 \]

\[ \Rightarrow \langle r \rangle = n \rho \]

b. For any quantity \( r \), prove that its standard deviation, \( \sigma_r \), is equal to

\[ \sqrt{\langle r^2 \rangle - \langle r \rangle^2} \]

\( \sigma_r \) is the root-mean-square deviation of \( r \) from its mean, hence:

\[ \sigma_r^2 = \frac{1}{N} \sum_{i=1}^{N} \left( r_i - \langle r \rangle \right)^2 \]

\[ = \frac{1}{N} \sum_{i=1}^{N} \left( r_i^2 - 2 r_i \langle r \rangle + \langle r \rangle^2 \right) \]
c. Using the binomial distribution derive an equation for \( \sigma_r \) in terms of \( n \) and \( p \).

First, let's figure out what \( \langle r^2 \rangle \) is...

\[
\langle r^2 \rangle = \sum_{r=0}^{n} r^2 P(r)
\]

\[
= \sum_{r=0}^{n} \left[ \frac{n!}{r! (n-r)!} \cdot p^r (1-p)^{n-r} \right]
\]

As in the term is zero

\[ = np \sum_{r=1}^{n} \left[ \frac{(n-1)!}{(r-1)! (n-r)!} \cdot p^r (1-p)^{n-r} \right] \]

Let \( s = n - 1 \), \( \ell = r - 1 \) \( \implies s - \ell = n - r \)

\[
= np \sum_{\ell=0}^{S} \left[ (\ell+1) \cdot \frac{s!}{\ell! (s-\ell)!} \cdot p^{\ell} (1-p)^{s-\ell} \right]
\]
\[ A = \sum_{t=0}^{s} \left[ \frac{s!}{t!(s-t)!} \cdot p^t (1-p)^{s-t} \right] \quad \Rightarrow \quad s \cdot p = (n-1) \cdot p \]

\[ B = \sum_{t=0}^{s} \left[ \frac{s!}{t!(s-t)!} \cdot p^t (1-p)^{s-t} \right] \quad \Rightarrow \quad 1 \]

\[ \langle r^2 \rangle = np (np - np + 1) = np^2 + np(1-p) \]

\[ \sigma_r = \sqrt{\langle r^2 \rangle - \langle r \rangle^2} = \sqrt{(np)^2 + np(1-p) - (np)^2} \]

\[ = \sqrt{np(1-p)} \]