Notes for Translation simulation

RNA size

I’ll assume a protein of 400 amino acids, which is the “typical” protein size for eukaryotes (http://book.bionumbers.org/how-big-is-the-average-protein/). This corresponds to 400 codons, or 1200 base pairs.

One base pair is about 0.34 nm (https://en.wikipedia.org/wiki/Base\_pair). This means that a “typical” mRNA coding region is about 1200\*.34 = 408 nm long. Also, it shows that a codon is very close to 1 nm.

System size

I’m going to define the system to be 500 nm by 200 nm. This has an area of 100,000 nm2.

Ribosome translation speed

Ribosomes move 3-20 codons per second (Ferrin\_Subramanian\_2017). Using the values from above that a base pair is 0.34 nm long and there are 3 base pairs per codon means that ribosome speed is 3 to 20 nm per second.

I’ll choose 10 nm/s.

Ribosome diffusion coefficient

Note that 1 um2/s = 106 nm2/s.

Ribosomes are 4.5 MDa. From Andrews\_2012 diffusion equation, this implies a diffusion coefficient of 15.8 um2/s in water and 4.0 um2/s in eukaryotic cytoplasm. This is 4,000,000 nm2/s.

Another value is 0.04 um2/s. This is the experimental value for a polysome, which is multiple ribosomes bound to a single mRNA, all diffusing together. This diffusion coefficient is 40,000 nm2/s. (https://bionumbers.hms.harvard.edu/bionumber.aspx?id=108596&ver=0)

I’ll choose the latter value.

Ribosome concentration

The number of ribosomes in a cell varies strongly with the cell growth rate. However, a rough estimate is 50,000 um-3. (http://book.bionumbers.org/how-many-ribosomes-are-in-a-cell/).

I’m using a 2D simulation with area 100,000 nm2 = 0.1 um2. Assume my slice is 10 nm thick. In that case, there should be 0.1\*0.01\*50,000 = 50 ribosomes.

Translation initiation rate

Assume about 1 s-1 on average (Ferrin\_Subramanian\_2017).

I’m running the simulation in 2D, and I’m going to assume an activation-limited mechanism because diffusion is very fast relative to reactions. So, suppose the concentration of ribosomes is *Crib*, in ribosomes per square nm. The binding radius is *rbind*, meaning that the binding area is π*rbind*2. Multiply by *Crib* to get the probability that a ribosome is within the binding radius at any particular moment, which is *Crib*π*rbind*2. Divide this by the time step to get the ribosomes binding per second, as

*kon* = *Crib*π*rbind*2/∆*t*

If I want *kon* to be about 1 s-1, and *rbind* to be about 1 nm, then *Crib* = 0.3 ∆*t*. If ∆*t* = 1 ms and the area is 100,000 nm2, then this implies that there are 30 ribosomes in the system. In practice, this isn’t working out, since I’m getting about 1/3 of the desired binding rate. I’m not sure what’s wrong.

I ended up using 50 ribosomes, as discussed above.

Stall duration

I didn’t read the Ferrin\_Subramanian\_2017 paper closely enough to be certain of their stall duration, but their figure 7 suggests that they explored off-rates between 2-6 and 22 s-1.

In my brief exploration, I used 0.5 s-1.

Next steps

I should probably change to a 3D simulation because it would be interesting to have an actual binding reaction rate constant rather than some 2D equivalent. However, I’m not pursuing this project more at the moment anyhow because I ran a few tests and it looks like the number of proteins produced increases linearly with the binding rate for small binding rates (as it should) but then levels off at some constant value for high binding rates. I had hoped that it might reach a maximum and then decrease again, but this doesn’t seem to be the case. As a result, the problem doesn’t suit my current needs, which is a system that I can optimize.