CS904 Computational Biology – Second Assignment Modelling Single Cell dynamics

DUE DATE: 19th February at noon

If tasks refer to problems from labs, please see for more details there.

TASK 1 [15 points]

Provide your code and results for Problem 1 (Channel gating) of Lab 4. Use $k^+ = 0.1/\text{ms}$ and $k^- = 0.3/\text{ms}$.

a) Use a reasonably long enough time interval T to capture enough events, and state the value of T in your write-up. Find a suitable way of plotting the opening/closing of the channel, for the purpose of visualisation perhaps for a shorter time interval.

b) State the average open and closed time from your simulation experiment and compare them to the expected values ($\langle \tau_O \rangle = \frac{1}{k^-}; \langle \tau_C \rangle = \frac{1}{k^+}$).

c) Plot the distribution of open and closed times from your simulation experiment and compare them to their theoretically expected distributions (see section on Dwell times from script).

Hint: If creating the distribution of closed times, for example, note that a channel that has been closed for a total duration of 1 sec, also contributes to the counts of channels that have been closed for 0.1 , 0.2 , ... , 0.9 seconds, if you were to sample at an interval of 0.1 seconds (width of your histogram bins). Choose a reasonable sampling interval and normalise the histogram so that you can plot it together with the theoretical distribution. The latter can be plotted as a line.

Task 2 [15 points]

Provide your code and results for Problem 2 from Lab 4 (Modelling Calcium entry).

a) Produce simulation runs (until M reaches $M_{max} = 1000$, or a sensible value which makes plotting not too difficult!) and plots which demonstrate when the channel is open or closed and how the number of intracellular ions, M, increases.

Hint: You can either use different sets of propensity function depending on whether your channel is open or closed, or you can use the following, where propensities automatically evaluate to 0 if a transition cannot take place (the lab script uses a mixture of both, which is lacking in rigour; thanks to Scott for pointing this out).

$\alpha_1 = k^+ C$; $\alpha_2 = k^- O$; $\alpha_3 = k^m [M_{extra}] O$;

Task 3 [40 points]

Provide your code and results for Problem 3 from Lab 4 (Simulating intracellular diffusion of Calcium ions)

Note: Scaling space and time in b) to reasonable dimensions is not easy, and it looks that the values given in the lab script do not allow to show the effect of subdiffusion. The effective diffusion constant ($D = 5 \times 10^{-6} \frac{cm^2}{sec}$, units correct as stated) was determined experimentally, so should not be changed. Instead, change the size of the bounding box determined by y_t, x_l and x_r ($y_b = 0$). Determine the maximum distance x_{max} travelled by the ions in a) and try for example $y_t = \frac{1}{4}x_{max}$, $x_l = -\frac{1}{8}x_{max}$ and $x_r = +\frac{1}{8}x_{max}$. If you have already come up with a different approach to demonstrate subdiffusion due to spatial hindrance, then keep that (even if it is based on scaling D), stating what exactly you did.

Task 4 [20 points]

Provide your code and results for Problem 1a from Lab 5 (Simulation model of the Kai cyanobacterial clock)

Plot timecourses of the variables T, S, D, U, and A. Confirm that the period of your clock is approximately 24 hours.

Task 5 [10 points]

This task is related to the Hungarian algorithm from lecture 12.

a) Try to devise a mathematical formula for a suitable cost function to solve the assignment problem of matching corresponding cells in subsequent time frames of a 2D image time series. The parameters to consider are vector $\mathbf{x}$, the position of cell centres, and I the average intensity of each cell. The assumption is that for a corresponding pair of cells $\mathbf{x}$ and I will not change drastically. Hint: The distance function used to define similarity between data points in the previous diffusion mapping might come in handy.

b) The Hungarian algorithm requires a square cost matrix. What would you do if you deal with images where cells are entering or leaving the field? In words, describe a strategy (no more than 4-5 sentences).