Reaction-Diffusion Exercises

Exercise 1:

Consider the signaling molecule IP3, which in Wagner et al 2004 was modeled as having a diffusion coefficient in the cytosol of 0.283 µm^2/ms. (Our units here are not those usually used by cell biologists, but they are the ones used by NEURON's reaction-diffusion module as they are reasonable for neuronal electrophysiology.)

Consider a 101-micron long section of dendrite discretized into 101 compartments. Set IP3 at an initial concentration of 1 µM for 0.4 ≤ `seg.x` ≤ 0.6 and 0 elsewhere. (Be careful about units.) How long does it take the concentration at `seg.x` = 0.7 to rise to a concentration of 100 nM? What is the peak concentration obtained at this point over all time? What is the limiting value as $t \rightarrow \infty$?

In 25 °C water, calcium has a diffusion coefficient of 1.97×10^{-5} cm^2/s according to [1]. What is this in NEURON's units of µm^2/ms? (Note: calcium will have a different effective diffusion constant in a cell than in water due to buffering molecules, etc.) Answer the question about time for a concentration increase at seg.x = 0.7 for calcium in water. Do the same for glucose which has a diffusion coefficient of 6×10^{-6} cm^2/s according to the same source. How does varying the diffusion coefficient affect the time it takes to raise concentration at a given distance by a given amount?

Exercise 2:

Construct a simple Hodgkin-Huxley model that given constant current injection fires periodically. What happens to intracellular sodium and potassium in this model?

Use rxd.Species to declare Na+ and K+. How does this change the answer to the previous part? What happens as $t \rightarrow \infty$?

Add a simple homeostatic phenomenological model to partly restore the initial behavior.

Exercise 3:

Import a CA1 pyramidal cell into NEURON from NeuroMorpho.Org. Declare chemical species X to diffuse across the entire cell at D=1 µm^2/ms with initial concentration of 1 mM in the soma and 0 elsewhere. View the distribution of X at 5 and 25ms on both a ShapePlot and along the

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[1] http://www.physiologyweb.com/calculators/diffusion_time_calculator.html

apical as a function of distance from the soma. Plot a time series of the concentration of X at the center of the soma.

Exercise 4:

Neurons are well-known for their propagating action potentials, but electrical signaling is not their only form of regenerative signaling. Berridge 1998 described neuronal calcium dynamics as functioning as a "neuron-within-a-neuron."

Why is pure diffusion insufficient? What is the expected time for a molecule of IP3 to travel a distance of 50 microns? 100 microns? 1 meter (the approximate length of the longest axon in a human)?

Hint: $E[t] = \frac{x^2}{2D}$

The actual dynamics underlying these calcium wave dynamics is complicated, so let's start with the simplest reaction-diffusion model of a propagating wave:

On a 500 micron long piece of dendrite add a species Y with diffusion constant 1 changing by an `rxd.Rate` of `scale * (0 - y) * (alpha - y) * (1 - y)`. For a first test take `scale = 1` and `alpha = 0.3`. Set initial conditions such that Y is 1 where `seg.x < 0.2` and 0 elsewhere. Plot the concentration of Y vs position at several time points to show the development of a traveling wave front.

Run the same simulation with `alpha = 0.7`. What changes? More generally, how does alpha affect the wave?

Calculate the speed of propagation of the wave front at `alpha = 0.3`. How can you change `scale` and the diffusion coefficient to get a wave of the same shape that travels at 50 microns per second? What happens to the shape of the wave front if the diffusion coefficient is increased but the other parameters stay the same?

Things to consider:

How do you know if you are using an appropriate value of `nseg` or `dt`?

Exercise 5.

Suppose a spine head with volume 0.5 μm^3 had a calcium concentration of 100 nM, a plausible biological value. What percentage difference would one single calcium ion diffusing away have on the calcium concentration in the spine head? Hint: one cubic micron at 1 mM concentration has about 602,000 molecules.

References

Berridge, M. J. (1998). Neuronal calcium signaling. Neuron, 21(1), 13-26.

Wagner, J., el al. (2004). A wave of IP 3 production accompanies the fertilization Ca 2+ wave in the egg of the frog, Xenopus laevis: theoretical and experimental support. Cell Calcium, 35(5), 433-447.