Problem Set 2:
Two-State Ionic Channels in Python

Week 5, SoSe 2022 — Benoit Scholtes
Computational Neuroscience — & Stefan Rotter

The currents flowing through the neuron membrane – responsible for changes in the membrane potential and action potentials – flow through channels in the membrane which stochastically open and close. At the level of the whole neuron or patches of the membrane which include many channels, the law of large numbers however dictates that the total current flowing through these channels add up to appear deterministic rather than stochastic in nature. A result of this is the relative accuracy of the *deterministic* differential equations of the Hodgkin-Huxley model in describing membrane dynamics for large enough patches of the membrane. In this sheet, we will work on the level of a single two-state channel to appreciate the stochastic nature of the channel dynamics.

The experiment

We will base this sheet on a hypothetical voltage clamp experiment. In this experiment, you observe a patch of membrane with identical channels which stochastically open and close, though you only ever observe channels being either open or closed. You observe many such identical channels over a period of time, from which you determine that the rate of closed channels opening is $\alpha' = 1$ Hz (per channel), while that of open channels closing is $\beta' = 2$ Hz. You observe that these transition rates are independent of time (stationary process) and independent of the history of the state dynamics apart from the current state (Markov process).

Problem 1: Probability of transition — 4 points

Given that you only observe channels being either open or closed, and never transitions between, you would like to model the channel dynamics as a *discrete-time* Markov processes, such that at each time step t_i, a channel is either open $X_i = 1$ or closed $X_i = 0$.

What are the probabilities of the individual transition of a single such channel occurring over a *small* period of time Δt – i.e. closed to closed, closed to open, open to closed, and open to open? Let the time-step Δt be small enough such that you can assume that no *multiple* transitions can occur.

Define the probability vector as $x_i = \big(\mathbb{P}(X_i = 0),\, \mathbb{P}(X_i = 1)\big)^T$, such that the channel being open is given by $x_i = \big(0,\, 1\big)^T$. What then is the left-stochastic matrix A of the Markov chain for time steps $\Delta t = 0.1$ s?

Problem 2: Simulation of a single channel — 4 points

Simulate the stochastic dynamics of a single channel opening and closing in python using the discrete-time Markov chain you obtained in Problem 1. Use time-step $\Delta t = 0.1$ s, total time of the simulation $T = 500$ s, and initial state as open $X = 1$. Plot the state X_i over time. What is the mean state $\bar{X}$ over the whole simulation?

Problem 3: Channel dwell times 4 points

Calculate the time periods elapsed in closed states and open states separately from the simulation performed for Problem 2. Plot histogram for these dwell times for both states. You may need to simulate the dynamics for longer (e.g. $T = 5000$ s) to obtain representative distributions.

What are your theoretical expectations for these distributions? Do they agree with those you obtained from your simulation? Calculate the mean open and closed times of your simulation, do they agree with your theoretical calculations?

Problem 4: Propagation of state probabilities 4 points

Determine the propagation of the state probabilities x_i of any such channel over the same period of time ($dt = 0.1$ s and $T = 500$ s) as the original simulation. Do the asymptotic ($t \to \infty$) probabilities agree with the mean you calculated in your simulation in Problem 1? Do they agree with your theoretical expectations obtained from the eigenvectors of the stochastic matrix A and the equilibrium state x_∞ in the differential equation $\tau \dot{x} = x_\infty - x$ defining the dynamics of the probability x? What about the time-constant τ?