Nonequilibrium Statistical Mechanics (Honours)
Assignment 4

1. **Epileptic seizures and the stability of the human brain.** The human cerebral cortex contains $\sim 10^{10}$ neurons packed into a sheet which, when unfolded, measures $0.6\,\mathrm{m} \times 0.6\,\mathrm{m}$. Electroencephalograms (EEGs), which record and map the spatiotemporal pattern of electrical activity in the brain, can resolve a surface area of a few cm^2 at best. Consequently, in order to interpret the rich dynamics observed in EEG traces (e.g. alpha rhythms at 8–13 Hz), it is wise to construct a continuum model of the cortex, in which the electrical response is smoothed over patches of a few cm^2, which contain huge numbers of neurons.

   Neurons fire at a rate $Q(\mathbf{x}, t)$. When a neuron fires, it emits a pulsed electrical signal, which travels along a fibre called an axon until it reaches a synaptic junction, where it is communicated to many other neurons via fibres called dendrites. (This picture is oversimplified but adequate for a continuum model.) The firing rate is related to the mean dendritic potential $V(\mathbf{x}, t)$ at that neuron, relative to the threshold potential V_0, by the empirical law

   $$Q(\mathbf{x}, t) = \frac{1}{1 + e^{-C[V(\mathbf{x},t) - V_0]}} \ . \tag{1}$$

   Note that Q is normalised to the saturation firing rate ($\sim 10^3\,\mathrm{Hz\,neuron}^{-1}$) and V is normalised to the standard deviation of the underlying threshold potential distribution, with $C \approx 1.8$ and $V_0 \approx 3.0$ in these units.

   The mean dendritic potential $V(\mathbf{x}, t)$ responds to the arrival rate of incoming pulses, $Q_a(\mathbf{x}, t)$, with a characteristic time lag $\alpha^{-1} \approx 5\,\mathrm{ms}$, i.e.

   $$\frac{\partial V(\mathbf{x}, t)}{\partial t} = g\alpha Q_a(\mathbf{x}, t) - \alpha V(\mathbf{x}, t) \ . \tag{2}$$

   Typically, humans are found to have $g \approx 36$. To be precise, $Q_a(\mathbf{x}, t)$ is an average rate measured at the synaptic junctions leading to the dendrites in the $\sim$ cm^2 patch centred at position $\mathbf{x}$. The time lag α^{-1} arises because the dendrites form an RC network, which connects a synaptic junction to a neuron.

   Two kinds of neurons populate the human cerebral cortex: pyramidal ones, which are *excitatory* (subscript e), and nonpyramidal ones, which are *inhibitory* (subscript i), with numbers in the ratio 85% : 15%. The pyramidal (nonpyramidal) neurons emit pulses which act to accelerate (decelerate) the firing rate of other neurons.

   The arrival rate of incoming pulses at an excitatory neuron is the sum of three terms:

   $$Q_{ae}(\mathbf{x}, t) = \mu_e Q_{ns} + a_{ee}\Phi_e(\mathbf{x}, t) - a_{ei}\Phi_i(\mathbf{x}, t) \ . \tag{3}$$

   The first term is a uniform, static contribution from the sea of "uncoordinated" electrical activity generated at the neuron by parts of the brain outside the cortex. The second term is proportional to the arrival rate of excitatory pulses at the synaptic junction, $\Phi_e(\mathbf{x}, t)$. The third term is proportional to the arrival rate of inhibitory pulses at the synaptic junction, $\Phi_i(\mathbf{x}, t)$. Likewise, the arrival rate of incoming pulses at an inhibitory neuron is given by

   $$Q_{ai}(\mathbf{x}, t) = \mu_i Q_{ns} + a_{ie}\Phi_e(\mathbf{x}, t) - a_{ii}\Phi_i(\mathbf{x}, t) \ . \tag{4}$$

Physiologists measure $a_{ee} \approx 0.85$, $a_{ei} \approx 0.011$, $a_{ie} \approx 0.13$, and $a_{ii} \approx 0.0020$ in humans.

Once emitted by neurons at a rate $Q(\mathbf{x}, t)$, the pulses propagate collectively as a "wave" of electrical activity along axons, $\Phi(\mathbf{x}, t)$, travelling with phase speed v. The wave decays in amplitude over a length scale r, corresponding to the average length of an axon, because the axon network thins out as it spreads. Hence the arrival rate of excitatory pulses satisfies a damped wave equation

$$\left(\frac{\partial^2}{\partial t^2} + 2\gamma_e \frac{\partial}{\partial t} + \gamma_e^2 - v^2 \nabla^2\right) \Phi_e(\mathbf{x}, t) = \gamma_e^2 Q_e(\mathbf{x}, t) \ , \tag{5}$$

with $\gamma_e = v/r_e$. Similarly, $\Phi_i(\mathbf{x}, t)$ satisfies a wave equation like (5), with γ_e and Q_e replaced by γ_i and Q_i, but v remaining the same.

Our model of the cerebral cortex therefore involves eight functions of space and time: Q_e, Q_i, V_e, V_i, Q_{ae}, Q_{ai}, Φ_e, and Φ_i. These functions obey the following eight equations: (1) (for e and i), (2) (for e and i), (3), (4), and (5) (for e and i).

(a) Solve (2) explicitly for $V(\mathbf{x}, t)$. By choosing a specific test function Q_a, show that (2) indeed describes a lagged response. As mentioned above, the lag arises from the capacitance and resistance of the dendritic fibres.

(b) Physiologists measure $r_e \approx 0.084\,\mathrm{m}$, $r_i \approx 10^{-4}\,\mathrm{m}$, and $v \approx 9\,\mathrm{m\,s^{-1}}$ in humans. Explain why this implies $\Phi_i \approx Q_i$.

(c) Show that the cortex supports three uniform equilibria if

$$Q_{ns} < \frac{CV_0 - 1 - \ln(Cga_{ee})}{Cg\mu_e} \ , \tag{6}$$

in the regime $a_{ee} \ll a_{ei}$ and $a_{ie} \ll a_{ii}$; otherwise, it supports one equilibrium.

(d) Now perturb the uniform equilibria in part (c) assuming an infinitely extended cortex, such that the perturbations are proportional to $\exp(-i\omega t + i\mathbf{k} \cdot \mathbf{x})$.

i. Derive the dispersion relation

$$(\alpha - i\omega)[(\gamma_e - i\omega)^2 + k^2 v^2] - \alpha \gamma_e^2 G = 0 \ , \tag{7}$$

where $G = ga_{ee}(dQ_e/dV_e)_{\mathrm{eq}}$ is evaluated in the equilibrium state.

ii. G is called the *gain*. What does it signify physically?

(e) i. Show, analytically or numerically, that the cortex is unstable for

$$G > 1 + k^2 r_e^2 \ . \tag{8}$$

ii. Hence show that two of the equilibria in part (c) are stable, while the third is not.

iii. Describe in words the pattern of neuronal activity corresponding to the two stable equilbria. Which one corresponds to a grand mal epileptic seizure?

(f) Now consider a more realistic, finite topology where the cortex has periodic boundary conditions.

i. Briefly explain how the instability threshold changes, and what effect this has on brain activity.

ii. Calculate the lowest few oscillation frequencies of the finite system, and compare with EEG measurements of the alpha rhythm and other features. Choose sensible dimensions for your model cortex.

(g) Explore the spatial patterns that develop on your model cortex near equilibrium states and at the instability threshold. By choosing parameters wisely, e.g. near points of instability, you should see some cool stuff.

A web-based solver of nonlinear reaction-diffusion equations is available at `http://seth.ph.unimelb.edu.au` to help you with this task. Please consult the file `readme.pdf` for instructions and examples.