MA4G4

THE UNIVERSITY OF WARWICK

FOURTH YEAR EXAMINATION: SUMMER 2015

INTRODUCTION TO THEORETICAL NEUROSCIENCE

Time Allowed: **3 hours**

Read carefully the instructions on the answer book and make sure that the particulars required are entered on each answer book.

Calculators are not needed and are not permitted in this examination.

ANSWER 4 QUESTIONS.

If you have answered more than the required 4 questions in this examination, you will only be given credit for your 4 best answers.

The numbers in the margin indicate approximately how many marks are available for each part of a question.

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1. Cable theory

The axial-current equation and cable equation for a cylindrical dendrite with characteristic length constant λ and resistance constant R_λ can be written

$$I_a(x) = -\frac{\lambda}{R_\lambda}\frac{dV}{dx} \quad \text{and} \qquad (1)$$

$$\tau\frac{dV}{dt} = E - V + \lambda^2\frac{d^2V}{dx^2}. \qquad (2)$$

The dendritic radius is a and its axial resistivity is r_a (units of resistance×length). The capacitance and conductance per unit area of dendritic surface are C and g respectively, E is the resting potential and τ is the membrane time constant.

a) Derive the axial current equation (1) in terms of r_a and a by considering a short length of dendrite. By comparing your form to that of equation (1) relate λ/R_λ to a and r_a and show that R_λ is the axial resistance for a length λ of dendrite. **[4]**

b) Derive the cable equation (2) by considering the currents entering and leaving a short section of dendrite. By comparing your solution to equation (2) give forms for τ and λ^2 in terms of the constants C, g, a and r_a. **[5]**

c) Here and in part (d) it is convenient to measure voltage from rest $v = V - E$. A dendrite of length L with parameters λ and R_λ receives a current I_L entering at $x = L$. It also receives a current I_0 entering at $x = 0$ such that the voltage is at rest ($v = 0$) at $x = 0$. Solve the cable equation (2) in the steady state in terms of I_L. Show that for $v = 0$ at $x = 0$ requires that $I_0 = -I_L/\cosh(L/\lambda)$. **[6]**

d) We now consider a neuron in the shape of a letter Y that has three dendrites with the same properties (λ, R_λ) except that two each have an excitatory synapse at the end (conductance G_e) and the third has an inhibitory synapse (conductance G_i) at the end. The synaptic reversal potentials measured from rest are $\mathcal{E}_e$ and $\mathcal{E}_i$. The synaptic strengths are such that at the vertex $v = 0$. Show that

$$-\frac{\mathcal{E}_i}{\mathcal{E}_e} = \frac{2G_e}{G_i}\frac{1 + G_i R_\lambda \tanh(L/\lambda)}{1 + G_e R_\lambda \tanh(L/\lambda)}. \qquad (3)$$

[10]

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2. Type I and II spiking-neuron models

The type I model considered in parts (a-b) is described by the following equation

$$\frac{dV}{dt} = V^2 + I. \tag{4}$$

If the voltage reaches a value $\theta > 0$ then a spike is registered and the voltage is reset to $-\theta$. The type II model considered in parts (c-d) is described by two equations

$$\frac{dV}{dt} = F(V) - W \tag{5}$$

$$\frac{dW}{dt} = \epsilon(2V - W) \tag{6}$$

where $\epsilon \ll 1$ so that the dynamics of the W variable is much slower than the voltage variable. The function $F(V)$ is piecewise-linear such that: $F = V$ for $-1 < V < 1$; $F = 2 - V$ for $V > 1$; and $F = -2 - V$ for $V < -1$.

a) Give formulas for the fixed points for the type I model when $I < 0$. By linearising equation (4) identify which of the fixed points is stable. **[3]**

b) For the type I model with $I > 0$ and with $I/\theta^2 \ll 1$ show that

$$r \simeq \frac{\sqrt{I}}{\pi}\left(1 + \frac{2\sqrt{I}}{\pi\theta} + \text{higher-order corrections}\right) \tag{7}$$

approximates the firing rate. The integral $\int_{-\infty}^{\infty} dx/(1+x^2) = \pi$ will be of use. **[8]**

c) For the type II model given by equations (5,6) provide formulas for the V and W nullclines. Sketch the nullclines on the $V-W$ phase plane and draw arrows of flow on the nullclines in the distinct regions (this requires four arrows) with their relative lengths reflecting the magnitude of the rate of change. **[5]**

d) Sketch an example trajectory on the phase plane from part (c) taking note of the fact that the dynamics of W are slower than that of V. By considering which parts of the trajectory dominate the time taken to traverse the whole limit cycle, derive a formula for the firing rate to first order in the small quantity ϵ. **[9]**

3. Mean, variance and skew of a fluctuating synaptic conductance

The synaptic conductance a neuron receives obeys the stochastic differential equation

$$\tau \frac{dg}{dt} = \tau\gamma \sum_{\{t_k\}} \delta(t - t_k) - g \tag{8}$$

where $\{t_k\}$ are the uncorrelated, Poissonian arrival times of synaptic impulses occuring at rate R. The probability $P(N)$ that N impulses arrive during a time Δ

$$P(N) = e^{-\lambda} \frac{\lambda^N}{N!} \tag{9}$$

will be of use, where $\lambda = R\Delta = \langle N \rangle$ is the mean number of impulses in a time Δ.

a) Confirm using Eq. (9) that $\langle N \rangle = \lambda$, and derive $\langle N^2 \rangle$ and $\langle N^3 \rangle$ in terms of $\lambda = R\Delta$. Show that $\langle (N-\lambda)^2 \rangle = R\Delta$ and that $\langle (N-\lambda)^3 \rangle$ is also equal to $R\Delta$. (NB: Considering the quantity $e^{-\lambda}(\lambda \frac{d}{d\lambda})^m e^{\lambda}$, where $m = 1, 2, 3$, may help.) **[6]**

b) We now coarse-grain the impulse sum in equation (8) by averaging it over time segments Δ and introduce a new quantity ξ_j that satisfies

$$\frac{1}{\Delta} \int_{j\Delta}^{(j+1)\Delta} dt \sum_{\{t_k\}} \delta(t - t_k) = R + \sqrt{R}\,\xi_j. \tag{10}$$

Use part (a) to show $\langle \xi_j \rangle = 0$ and $\langle \xi_i \xi_j \rangle = 1/\Delta$ if $i = j$, but is zero otherwise. **[4]**

c) In the continuum limit the mean of $\xi(t)$ is zero and the autocorrelation becomes $\langle \xi(t)\xi(t') \rangle = \delta(t - t')$. Use these results and the solution to the equation

$$\tau \frac{dh}{dt} = \tau\gamma\sqrt{R}\,\xi(t) - h, \tag{11}$$

where $h(t) = g(t) - \langle g \rangle$, to show that the autocorrelation of the conductance is

$$\langle h(t)h(t') \rangle = \sigma^2 e^{-|T|/\tau}. \tag{12}$$

Give the conductance mean $\langle g \rangle$ and variance σ^2 in terms of γ, R and τ. **[8]**

d) We now go beyond a Gaussian approximation of the impulse sum. Use the result $\langle (N-\lambda)^3 \rangle$ from part (a) and equation (10) from part (b) to argue that

$$\langle \xi(t)\xi(t')\xi(t'') \rangle = \delta(t - t')\delta(t - t'')/\sqrt{R}. \tag{13}$$

Use this result to calculate the autocorrelation $\langle h(t)h(t')h(t'') \rangle$ where $t < t' < t''$. **[7]**

4. Firing rate of a non-leaky IF neuron with inhibitory boundary

The non-leaky integrate-and-fire neuron has a probability density P(V) that obeys

$$\tau \frac{\partial P}{\partial t} = \sigma^2 \frac{\partial^2 P}{\partial V^2} - E\frac{\partial P}{\partial V}. \quad (14)$$

This model has no resting potential and so E should be interpreted as being proportional to a steady current flowing into the cell. These dynamics are supplemented by a spike threshold at V_{th} and a reset to V_{re}. There is also a lower boundary $E_i < V_{re}$ below which the voltage may not pass - the probability flux on this boundary is zero. The membrane time constant τ and the noise strength σ are both positive quantities.

a) Write down the continuity equation relating probability density P to flux J. Compare it to equation (14) to extract the P-dependent form of the flux. Give an explanation of why the steady-state flux is also equal to $J = r\theta(V - V_{re})$ where r is the firing rate and $\theta(y) = 1$ when $y > 0$ and is zero otherwise. **[5]**

b) It is convenient to rescale the voltage variables in the steady-state flux equation before solving it by introducing the quantity $x = V/\sigma$, with x_{th} and x_{re} defined analogously. The notation $x_i = E_i/\sigma$ and $\mu = E/\sigma$ can also be used. Write down the rescaled flux equation relating r to a differential equation for the probability density $p(x)$. **[3]**

c) Integrate the rescaled flux equation to give $p(x)$ as a function of the unknown firing rate r, for the two voltage ranges $x_{th} > x > x_{re}$ and $x_{re} > x > x_i$. (HINTS: $p(x_{th}) = 0$ and no additional steps are needed to account for the lower boundary E_i because $J = 0$ for $V < V_{re}$ in any case). **[7]**

d) The firing rate r is found using $\int p(x)dx = 1$ where the integration range is x_i to x_{th} (this is where the effect of the lower boundary is apparent). Substitute in the form for $p(x)$ calculated in (c) and show that the firing rate can be written

$$r = \frac{\mu^2}{\tau} \frac{1}{(\mu(x_{th} - x_{re}) + \exp(-\mu(x_{th} - x_i)) - \exp(-\mu(x_{re} - x_i)))}. \quad (15)$$

Demonstrate that for $\mu > 0$ the firing rate becomes independent of noise when the inhibitory boundary is removed (i.e. when $x_i \to -\infty$). **[10]**

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5. Excitatory network with synaptic depression

An excitatory network with synaptic depression obeys the following equations

$$\tau_R \frac{dR}{dt} = \Phi(I + qRXp) - R \quad (16)$$

$$\frac{dX}{dt} = (1 - X)/\tau_D - RXp \quad (17)$$

where $R(t)$ is the neuronal firing rate and $X(t)$ is the fraction of available synaptic vesicles. The quantities τ_R, τ_D, q and p are positive parameters. The function $\Phi(I)$ is the firing rate of an uncoupled population when each neuron receives a current I from outside the network.

a) To find the fixed point (R^*, X^*) equations (16) and (17) must be solved simultaneously with $\dot{R} = \dot{X} = 0$. The first equation gives $R_1 = \Phi(\tilde{I})$ where $\tilde{I} = I + qRXp$ is the total current each neuron receives in the network. Show

$$R_2 = \frac{\tilde{I} - I}{p(q - \tau_D(\tilde{I} - I))} \quad (18)$$

provides the second simultaneous equation. **[4]**

b) Sketch curves R_1 and R_2 ($\tilde{I}$ on the x-axis). Assume the rate function $\Phi(\tilde{I})$ is monatonically increasing and R_1 and R_2 intersect once. Where does R_2 cross the $\tilde{I}$ axis and at what $\tilde{I}$ does it diverge? Explain using the sketch why the uncoupled population rate $\Phi(I)$ is recovered if the synaptic strength $q \to 0$. **[4]**

c) Linearise equations (16) and (17) around the fixed points R^* and X^* by introducing the small parameters $r = R - R^*$ and $x = X - X^*$ to give the

$$\frac{dr}{dt} = -\alpha r + \beta x \quad \text{and} \quad \frac{dx}{dt} = -\gamma r - \delta x \quad (19)$$

and give α, β, γ and δ in terms of model parameters evaluated at the fixed point. Verify that β, γ and δ are postive whereas α can be either sign. **[7]**

d) Now rescale time by introducing $t = s/\delta$ and rescale x by introducing $x = z\gamma/\delta$. Show that the rescaled equations from part (c) can be written

$$\frac{dr}{ds} = -ar + bz \quad \text{and} \quad \frac{dz}{ds} = -r - z. \quad (20)$$

Give a and b in terms of α, β, γ δ (do not substitute for underlying model parameters). Find the eigenvalues of equation set (20). Noting that a is positive or negative but b is positive, sketch on the a–b plane (a on x-axis) regions where the system has a stable fixed point and also where damped oscillations occur. **[10]**
