EGT2
ENGINEERING TRIPOS PART IIA

Tuesday 23 April 2019   2:00 to 3:40

Module 3G3

INTRODUCTION TO NEUROSCIENCE

Answer not more than ***three*** *questions.*

All questions carry the same number of marks.

The ***approximate*** *percentage of marks allocated to each part of a question is indicated in the right margin.*

Write your candidate number ***not*** *your name on the cover sheet.*

STATIONERY REQUIREMENTS
Single-sided script paper

SPECIAL REQUIREMENTS TO BE SUPPLIED FOR THIS EXAM
CUED approved calculator allowed
Engineering Data Book

10 minutes reading time is allowed for this paper at the start of the exam.

You may not start to read the questions printed on the subsequent pages of this question paper until instructed to do so.

1 (a) In a few sentences, explain what a spike train is, and describe the classical problem of "elucidating the neural code for sensation". [20%]

(b) Consider a cylindrical neurite of radius R, with axial resistivity r_a (in $\Omega \cdot$ mm), unit membrane resistance r_m (in $\Omega \cdot \text{mm}^2$), and unit membrane capacitance c_m (in nF/mm^2).

(i) Explain, with reason, whether the following statement is true or false: "A neurite of radius $2R$ has the same membrane time constant as a similar neurite of radius R". [15%]

(ii) Explain, with reason, whether the following statement is true or false: "The total axial resistance to current flow is the same for a portion of neurite of length L and radius $2R$ as it is for a portion of length $L/2$ and radius R (of an otherwise similar neurite)". [15%]

(iii) Write down a formula for the *length constant* of the neurite. How does it depend on the ion channel density in the membrane? [20%]

(iv) Consider a brief current pulse injected somewhere along the neurite. Explain, with the aid of a sketch, how the propagation of this input signal along the neurite depends on the length constant. You may assume the neurite has infinite length. [20%]

(v) Describe three ways that signal propagation can be improved in a neurite, along with any disadvantages or biologically relevant constraints for each. [10%]

2 (a) Write short notes on the following:

(i) The physical and biological features from which uncertainty in sensory perception arises; [15%]

(ii) The properties of mechanoreceptors that determine the spatial resolution of stimulus encoding. [15%]

(b) A subject engages in an auditory detection task. Brief flashes of light mark the beginning and end of each trial. In each trial, a pure-frequency tone with intensity $I > 0$ is presented with 50% probability; this divides trials into "ON trials" (sound) and "OFF trials" (no sound).

The subject's brain gathers noisy sensory evidence summarized by a number s (arbitrary units), assumed to be drawn in each trial from a normal distribution. This distribution has a fixed unit variance $\sigma^2 = 1$, and a mean μ directly proportional to I in ON trials and equal to zero in OFF trials. The subject then reports hearing a sound if s is greater than the subject's "internal decision threshold" θ, and not hearing a sound otherwise.

(i) Give expressions for the hit rate (the probability to report hearing a sound in an ON trial) and false alarm rate (the probability to report hearing a sound in an OFF trial), as functions of μ and θ. You may use the standard normal cumulative density function defined as

$$\Phi(y) = \frac{1}{\sqrt{2\pi}} \int_{-\infty}^{y} e^{-x^2/2} dx.$$

[15%]

(ii) Sketch the corresponding Receiver Operating Characteristic (ROC) curve *qualitatively*, for $\mu = 1$ and for $\mu = 2$, and provide a brief interpretation. [20%]

(iii) The experimenter now pays the subject one pound for each hit, but deducts from their payment L pounds for each false alarm. In order to maximize their expected payment, where should the subject place their internal decision threshold θ? Derive an expression as a function of μ and L. [20%]

(iv) How would you build on the above experiment to investigate whether humans make optimal decisions? [15%]

3 This question is about evidence accumulation. A monkey performs a classical random dot motion discrimination task. In each trial, a random dot field moves with some coherence level c on a display, in direction $m \in \{L;R\}$ (Left or Right) chosen randomly with equal probability. The monkey must infer m and report its choice as soon as possible by making a saccade in the corresponding direction, thereby ending the trial, collecting a reward (if correct), and proceeding to the next trial.

During the experiment, a scientist records the firing activity of a single neuron in area MT of this monkey. Time in each trial is discretized in successive, adjacent bins of 50 ms duration indexed by an integer variable t ($t = 1,2,\ldots$). The response x_t of this neuron in each time bin is binarized such that $x_t = 0$ if the neuron is silent in that bin, and $x_t = 1$ if at least one action potential is produced. The recorded neuron is found to fire stochastically, such that for a trial with direction m, its response x_t appears to be drawn independently in each time bin from a Bernoulli distribution with mean α_m.

(a) What recording technique is this scientist most likely to be using, and why? [10%]

(b) Another area of the monkey's brain observes the responses of the recorded neuron as they unfold during each trial, and represents the cumulated log-likelihood ratio

$$D_t = \log \frac{p(x_1, x_2, \ldots, x_t | m = R)}{p(x_1, x_2, \ldots, x_t | m = L)}$$

in each time bin of each trial. Derive a simple update rule for D_t as a function of D_{t-1}, x_t, α_L and α_R. [Hint: the probability mass function for a Bernoulli variable x of mean α can be conveniently written as $p(x) = \alpha^x (1-\alpha)^{1-x}$.] [30%]

(c) The monkey reports rightward motion as soon as D_t exceeds some threshold θ, and leftward motion as soon as D_t falls below $-\theta$. Assume $\alpha_L = 0.2$ and $\theta = 3$. Sketch the timecourse of D_t for two example correct "right trials" ($m = R$), one with $\alpha_R = 0.4$ and the other with $\alpha_R = 0.8$. Explain the differences between the two. [20%]

(d) The scientist now changes the frequency of occurence of left and right trials, such that $p(m = R) = 0.6$ (and therefore $p(m = L) = 0.4$). How would you alter the sequential update rule for D_t to take into account this information? [20%]

(e) Finally, the scientist searches for neurons that encode the decision variable D_t. Suggest one brain area where such neurons are likely to be found, and give two properties of firing responses that you would expect from such "decision neurons" but *not* from sensory neurons such as the one recorded by the scientist in area MT. [20%]

4 (a) Describe the evolutionary advantage of learning. Include the following in your answer:

- The relationship between genotype and phenotype, and how learning can affect this relationship.
- The circumstances under which learning can be beneficial, and the way in which learning can increase fitness under these circumstances.

You may illustrate your answer with simple diagrams. [40%]

(b) Imagine that we engineer a new receptor channel that has a reversal potential which is equal to the resting potential of the cell. Sketch the postsynaptic potential trace when this receptor is activated at a time when the postsynaptic cell is at rest. In addition, explain the effect of receptor activation on the postsynaptic cell's behaviour, with special regard to whether this effect is excitatory, inhibitory, or neither. [30%]

(c) In contrast to the interpretation of dopamine signals based on prediction errors discussed during lectures, another theory posits that dopamine signals are related to 'surprise'. According to this theory, dopaminergic cells increase their firing rates whenever something salient but unexpected happens. In this context, a stimulus is said to be salient if it is rewarding itself, or if the animal has associated it with reward.

(i) Explain how this alternative theory would account for the pattern of dopamine signals before and after training in a classical conditioning paradigm. [15%]

(ii) Devise an experimental paradigm that can adjudicate between the surprise- and prediction error-based accounts of the dopamine response. Explain, with reasons, which theory is favoured by the available experimental data discussed during lectures. [15%]

END OF PAPER

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