EGT2
ENGINEERING TRIPOS PART IIA

Tuesday 9 May 2023   9:30 to 11:10

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.

You may not remove any stationery from the Examination Room.

1 A neuroscientist trained a macaque monkey to perform centre-out reaching movements of length d with its right hand in a vertical plane, starting at a 'centre' position and ending on a 'target' location that could be placed at any angle θ from the horizontal (Fig. 1). During the task, the scientist simultaneously recorded the spiking activity of $N > 50$ neurons in the monkey's primary motor cortex (left hemisphere). Let r_i be the random variable that describes the observed number of action potentials emitted by neuron i per unit time during the course of a reach. The scientist performed basic statistical analysis of these noisy neural responses $\{r_1, r_2, \dots, r_N\}$ and found them to be well modelled by a factorized Gaussian conditional density

$$p(\{r_1, \dots, r_N\}|\theta) = \prod_{i=1}^{N} \mathcal{N}(r_i; f_i(\theta), \sigma^2). \tag{1}$$

The conditional mean $f_i(\theta)$ was found to be modulated by the reach angle θ according to $f_i(\theta) = \alpha + \beta \cos(\theta - \theta_i)$, where $0 < \beta < \alpha$ are two constants and θ_i is the 'preferred direction' of neuron i.

(a) What recording technique is likely to have been used in this experiment, and why? [10%]

(b) Explain why r_i is best modelled as a random variable, and why θ_i is called the 'preferred direction' of neuron i. [10%]

(c) Express $f_i(\theta)$ as a function of $\vec{v}(\theta)$ and $\vec{v}(\theta_i)$, where $v(\theta) = \begin{pmatrix} \cos\theta \\ \sin\theta \end{pmatrix}$. [10%]

(d) In order to decode the reach angle θ that underlies a set of responses $\{r_1, \dots, r_N\}$, the scientist proposes to use the 'population vector' defined as

$$\vec{x}(\{r_1, \dots, r_N\}) = \frac{1}{N} \sum_{i=1}^{N} (r_i - \alpha)\, \vec{v}(\theta_i) \tag{2}$$

with $v(\cdot)$ defined as in part (c). Assume that the neurons' preferred directions $\{\theta_1, \dots, \theta_N\}$ are approximately uniformly distributed between 0 and 2π. Show that, on average over repeated reaches and in the limit of large N, $\vec{x}(\{r_1, \dots, r_N\})$ is proportional to $\vec{v}(\theta)$. Briefly discuss the implications for decoding. [30%]

(e) Prove that, in the limit of large N, the population vector $\vec{x}(\{r_1, \dots, r_N\})$ is in fact proportional to $\vec{v}(\theta)$ for *any single reach* at angle θ (as opposed to being proportional to $\vec{v}(\theta)$ *only on average* over repeated reaches, as already shown in part (d)). [30%]

(f) Now consider the more realistic scenario in which the constants α and β are different for each neuron, and are therefore denoted by α_i and β_i. Modify the definition of $\vec{x}(\{r_1, \ldots, r_N\})$ such that the property shown in part (d) continues to hold. [10%]

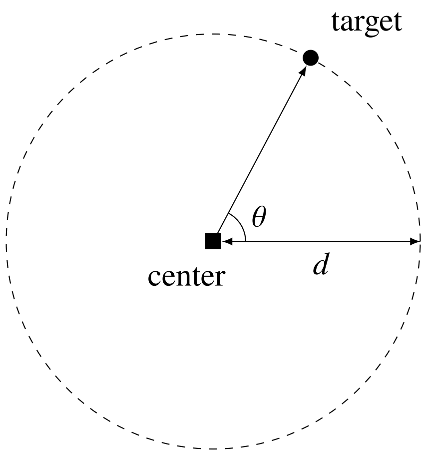

Fig. 1

2 (a) A scientist is studying a neuron *in vitro*. The membrane potential of this neuron is at rest (−70 mV).

(i) What is the net current flowing through the membrane, and why? [5%]

(ii) A scientist wonders how the membrane current would behave if, somehow, the cell's membrane potential was suddenly brought to 0 mV and kept constant at that value. How could their curiosity be satisfied experimentally? Explain the principle underlying your proposed solution. [20%]

(iii) The scientist performs the experiment in part (a)(ii) under a pharmacological manipulation that allows them to isolate the sodium current. Sketch the timecourse of this sodium current and explain the mechanism underlying its shape. [20%]

(b) A monkey wears a custom headset allowing a pure tone to be played simultaneously to the left and right ears with different intensities A_L and A_R, respectively. During the presentation of such an auditory stimulus, noisy aggregate neural activity, x_L and x_R, can be measured in the primary auditory cortices of the left and right hemispheres, respectively. The neural responses x_R and x_L are positive scalar quantities that depend on the contralateral intensities A_L and A_R, respectively, and vary independently across repeated stimulus presentations following exponential distributions

$$p(x_R|A_L) = \frac{1}{cA_L}\exp\left(-\frac{x_R}{cA_L}\right) \quad \text{and} \quad p(x_L|A_R) = \frac{1}{cA_R}\exp\left(-\frac{x_L}{cA_R}\right) \tag{3}$$

where $c > 0$ is a constant gain factor.

(i) For $\beta > 0$, derive an expression for the probability that x_R exceeds βx_L. Give your answer in terms of $\log(A_L/A_R)$ and $\log\beta$ (where log denotes the natural logarithm). [30%]

(ii) Sketch this relationship for $\beta = 0.5$, $\beta = 1.0$ and $\beta = 2$. [10%]

(iii) A scientist hypothesises that the monkey perceives a sound source to be located in the left (respectively right) hemifield when the corresponding responses in primary auditory cortex obey $x_R/x_L > \beta$ (respectively $x_R/x_L < \beta$). Based on your answers to parts (b)(i) and (b)(ii), describe a behavioural task for the monkey to perform, based on which the scientist could corroborate their hypothesis and estimate the value of β.

[15%]

3 (a) This question is about synaptic transmission.

(i) What are the main events following the generation of a presynaptic action potential that lead to the generation of an excitatory postsynaptic potential at a glutamatergic synapse with AMPA receptors? [10%]

(ii) Explain with reasons which of the events that you described in your answer to part (a)(i) directly require the cell to use energy? [30%]

(iii) Neuronal membranes contain selective molecular pumps that expend energy to maintain differences in the concentrations of ions inside and outside the cell. (Indeed, the energy used by these pumps constitutes a major part of energy used for signalling in the brain.) Based on this, explain with reasons which of the events you described in your answer to part (a)(i) will lead (albeit indirectly) to energy expenditure by these pumps. [30%]

(b) This question is about the *Aplysia* gill withdrawal reflex.

(i) What neurotransmitter receptor(s) do the sensory neurons have, and are they ionotropic, or metabotropic? [5%]

(ii) What neurotransmitter receptor(s) do the motor neurons have, and are they ionotropic, or metabotropic? [5%]

(iii) What secondary messengers in the sensory neurons play a role in the reflex and the forms of learning associated with it that we covered during lectures? [10%]

(iv) What secondary messengers in the motor neurons play a role in the reflex and the forms of learning associated with it that we covered during lectures? [10%]

(TURN OVER

4 (a) This question is about the hippocampus.

(i) Where in the human brain is the hippocampus? [10%]

(ii) What distinguishes it from most other parts of the cortex? [10%]

(iii) What are the main regions of the hippocampus? [10%]

(iv) Describe the 'trisynaptic loop', the main route of information flow through the hippocampus. In your answer, include the names of relevant brain areas, their respective principal cell types, and the pathways connecting them. [20%]

(v) Explain with reasons what anatomical, physiological, and functional features make the hippocampus an ideal brain area to study learning and memory. [20%]

(b) Explain with reasons whether it is true that, according to the Rescorla-Wagner rule, the strength of association between a CS and a US only depends on the number of trials in which they co-occurred. Support your answer by describing suitable experimental paradigms that could be used to demonstrate the correctness of your answer. [30%]

END OF PAPER