Imperial College London

BSc/MSci EXAMINATION May 2012

BIOPHYSICS OF NERVE CELLS

For Third-Year and Fourth-Year Physics Students

Wednesday 30th May, 14:00 – 16:00

Answer THREE out of FIVE questions

Marks shown on this paper are indicative of those the Examiners anticipate assigning.

General Instructions

Write your CANDIDATE NUMBER clearly on each of the THREE answer books provided.

If an electronic calculator is used, write its serial number in the box at the top right hand corner of the front cover of each answer book.

USE ONE ANSWER BOOK FOR EACH QUESTION

Enter the number of each question attempted in the horizontal box on the front cover of its corresponding answer book.

Hand in THREE answer books even if they have not all been used.

You are reminded that the Examiners attach great importance to legibility, accuracy and clarity of expression.

Please go to the next page

Copyright Imperial College London 2012

$T = 310$ K, $R = 8.314$ J K^{-1} mol^{-1}, $F = 96{,}500$ C mol^{-1}

The distributions of sodium, potassium and chloride ions across the membrane of a nerve cell can be taken to be:

Ion	*Inside*	*Outside*
Sodium	14 mM	125 mM
Potassium	124 mM	5 mM
Chloride	6 mM	77 mM

Please go to the next page

Copyright Imperial College London 2012

1) a) Show that the current i_m that flows per unit area across the membrane of an unmyelinated nerve axon is given by:

$$i_m = \frac{a}{2\rho_i \theta^2} \frac{d^2 V_m}{dt^2}$$

where ρ_i is the resistivity of the cytoplasmic space, a is the axon radius, θ is the velocity of the action potential and V_m is the membrane potential. [6 Marks]

b) What can be inferred about how the velocity of the action potential in an unmyelinated nerve varies with the axon diameter? [3 Marks]

c) Explain from first principles why the velocity of the action potential in a myelinated nerve should increase in proportion to the diameter of the axon. [4 Marks]

d) Show that, to give the most rapid propagation of an action potential for a given diameter nerve, the optimum ratio between the internal and external radii of nerve myelin is given by:

$$\ln\left\{\frac{a}{b}\right\} = -\frac{1}{2}$$

where a is the internal radius and b is the external radius. [The capacitance per unit length of a coaxial cable with internal radius a and external radius b is given by:

$$C = \frac{2\pi\varepsilon_r\varepsilon_o}{\ln\left(\frac{b}{a}\right)}$$

where ε_o is the permittivity of free space and ε_r is the relative dielectric constant.] [7 Marks]

Total Marks 20

Please go to the next page

Copyright Imperial College London 2012

2) a) Draw the total membrane current as a function of time, following a voltage step (from -80 mV to 0 mV) in a voltage-clamped squid giant axon and describe the principal features. [3 Marks]

b) What would the current look like if the sodium channels were blocked by tetrodotoxin (TTX) or the potassium channels blocked by tetraethylammonium (TEA)? [2 Marks]

c) How does this voltage-clamp data explain the observed changes in membrane potential during an action potential? [5 Marks]

d) Hodgkin & Huxley described the current through the sodium channels by the equation:

$$I_{Na} = m^3 h \, \bar{g}_{Na} (V_m - V_{Na})$$

What do the parameters *m* and *h* mean and draw sketches for how they change with time. [2 Marks]

e) If *m* and *h* are assumed to change with first order kinetics characterized by time constants τ_h and τ_m, write the equations which govern their changes with time. Why are they written as m^3h in the equation? [3 Marks]

f) Suppose that *mh* was the appropriate form, derive an expression giving the time to the peak sodium current (you may assume that the initial values of *m* and *h* are 0 and 1 respectively and their final values are 1 and 0 respectively)? Would this be sooner or later than the m^3h channel? [5 Marks]

Total Marks 20

Please go to the next page

Copyright Imperial College London 2012

3) a) Describe the basic principles that enable an EEG signal to be recorded from surface electrodes on the scalp.

[5 marks]

b) Discuss how the characteristics of the EEG signal differ between the sleeping and the awake brain in relation to neuronal activity recorded within the thalamocortical projection.

[10 marks]

c) What are the advantages/disadvantages of the EEG signal compared to the BOLD signal obtained during an fMRI experiment?

[5 marks]

Total Marks 20

Copyright Imperial College London 2012

4) The interaction between neurotransmitters and ligand-gated ion channels can be described using the Hill-Langmuir equation of the form:

$$P_{AR} = \frac{[A]^n}{[A]^n + K_d}$$

a) What does each of the parameters represent?

[5 marks]

b) Starting from the Law of Mass Action, show how the Hill-Langmuir equation is derived.

[10 marks]

c) Discuss the limitations of this simple relationship when considering the behaviour of ligand-gated ion channels, paying particular attention to the distinction between binding and gating.

[5 marks]

Total Marks 20

Please go to the next page

Copyright Imperial College London 2012

5) Are the following statements true or false? Explain your reasoning (N.B. no reasoning, no marks).

a) Neurons are in a state of equilibrium with their environment.

[2 marks]

b) The internal chloride ion concentration determines whether the action of the neurotransmitter GABA on $GABA_A$ receptors is excitatory or inhibitory.

[2 marks]

c) In the Hodgkin and Huxley model, the kinetics of the sodium conductance are dictated by the state of a single gating particle.

[2 marks]

d) The negative resting membrane potential of a neuron is correlated with the relative permeability of the cell membrane to sodium ions.

[2 marks]

e) The subunit composition of a ligand-gated ion channel can influence the duration a postsynaptic conductance change.

[2 marks]

f) The probability of neurotransmitter release occurring at a central synapse is linearly related to external calcium ion concentration.

[2 marks]

g) The time-course of an excitatory postsynaptic potential is different to that of the underlying conductance change.

[2 marks]

h) Local anaesthetics act faster when the external pH is high.

[2 marks]

i) The electroencephalogram reflects extracellular current flow in populations of neurons.

[2 marks]

j) REM sleep occurs when you are dreaming, which is why you are paralysed.

[2 marks]

Total Marks 20

End of examination

Copyright Imperial College London 2012