EGT2 ENGINEERING TRIPOS PART IIA

Tuesday 9 May 2023 14.00 to 15.40

Module 3G2

MATHEMATICAL PHYSIOLOGY

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 <u>not</u> 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) Trimix is a breathing gas made of a mixture of oxygen, nitrogen and helium. It is used for diving applications to limit the narcotic effect of nitrogen. For a 100 m deep dive, the following proportions are recommended: 10% oxygen, 70% helium, and 20% nitrogen. What would be the partial pressures of oxygen and nitrogen in the Trimix mixture at a depth of 100 m? How would they compare with the partial pressures of oxygen and nitrogen in the air at surface level, and how would you justify any differences? [30%]

(b) Consider a volume of pure water placed at room temperature in contact with a gas of constant partial pressure of CO₂, $P_c = 40$ Pa. The solubility of CO₂ in water is $\sigma = 3.3 \cdot 10^{-5}$ Molar/mm Hg. (1 mm Hg = 133 Pa.) Using the set of reactions listed below, calculate the pH of the water solution at equilibrium. You may ignore here the contribution of the second reaction. [40%]

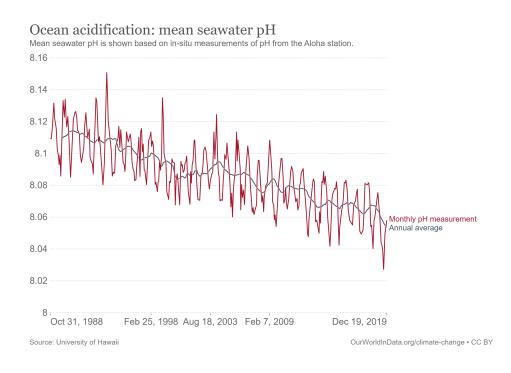
$$CO_{2} + H_{2}O \xrightarrow{K_{1}} H^{+} + HCO_{3}^{-} \text{ with } K_{1} = \frac{[H^{+}][HCO_{3}^{-}]}{[CO_{2}]} = 4.30 \cdot 10^{-7} \text{ mol } L^{-1}$$

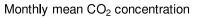
$$HCO_{3}^{-} \xrightarrow{K_{2}} H^{+} + CO_{3}^{2-} \text{ with } K_{2} = \frac{[H^{+}][CO_{3}^{2-}]}{[HCO_{3}^{-}]} = 5.61 \cdot 10^{-11} \text{ mol } L^{-1}$$

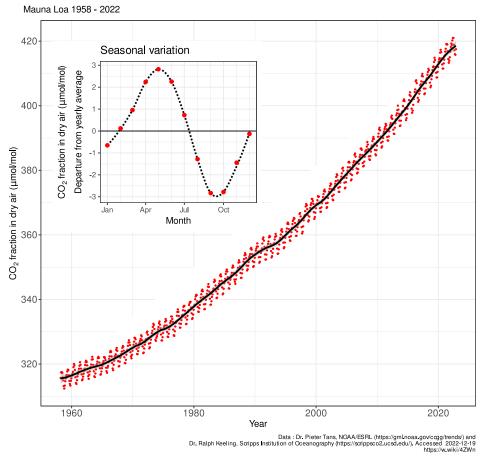
$$H_{2}O \xrightarrow{K_{d}} H^{+} + OH^{-} \text{ with } K_{d} = [H^{+}][OH^{-}] = 10^{-14} \text{ mol}^{2}L^{-2}$$

(c) Figure 1 shows the evolution of the pH of the oceans over the last 30 years, as well as the evolution of CO_2 amounts in the atmosphere over the last 60 years. Explain what may cause the pH of the oceans to change over time. [15%]

(d) The shells of many sea creatures are made of calcium carbonate, (Ca^{2+}, CO_3^{2-}) . (Note that carbonate is one of the species involved in the reactions above.) How would these organisms be affected by an increased level of CO₂ in the atmosphere? Justify your answer. [15%]







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2 (a) This question is about the movement of an ionic species through an ion channel. The diffusion coefficient of the ion at body temperature $(T = 37 \text{ C}^{\circ})$ is $D = 1.8 \cdot 10^{-3} \text{ mm}^2 \text{s}^{-1}$, and its electrovalence is z = 2. The length of the ion channel is L = 12 nm.

(i) The concentration of the ion everywhere in and around the channel (including at both ends) is constant and fixed over time. The electric potential everywhere in the channel (including at both ends) is V = 0 mV. Consider an ion that is placed at one end of the channel (x = 0) at time t = 0.

A. Provide the formula describing the probability density with which this ion will be at some other position x at time t > 0 (for these purposes, you can assume the channel is infinitely long). [20%]

B. Calculate the effective velocity of the ion based on the time it takes for the ion to have maximal probability to appear at the other end of the channel. [20%]

(ii) The concentration of the ion at the external and internal ends of the channel is $c_e = 150 \text{ mM}$ and $c_i = 50 \text{ mM}$, respectively, and it changes linearly with distance inside the channel (but is kept fixed with respect to time). The electric potential everywhere in the channel (including at both ends) is V = 0 mV. Explain with reasons if the effective velocity of the ion has changed from what you were asked to calculate in part (a) (i), and if so, how. [10%]

(iii) The concentration of the ion everywhere in the channel (including at both ends) is c = 50 mM (and is kept fixed over time). The electric potential at the external and internal ends of the channel is $V_e = 0 \text{ mV}$ and $V_i = 120 \text{ mV}$, respectively, and it changes linearly with distance inside the channel (but it is also kept fixed with respect to time). Calculate the 'drift' velocity of ions due to electric flux. For your calculations, you can approximate all relevant physical constants to the first three significant digits.

Hint: The electric flux generated by moving particles can be treated as being proportional to the number of particles in a volume defined by a unit cross-sectional area and the distance travelled by these particles over unit time, given their concentration and 'drift' velocity. [30%]

(b) Sort from smallest to largest each of the following sets of constants of the Hodgkin-Huxley model:

(i) $h_{\infty}, m_{\infty}, n_{\infty} \text{ at } V = 100 \text{ mV};$ [10%]

(ii)
$$\tau_{\rm h}, \tau_{\rm m}, \tau_{\rm n} \text{ at } V = 0 \,{\rm mV};$$
 [10%]

where the resting membrane potential is defined to be at 0 mV.

Version AJK/2

3 (a) The following reaction is used to model the binding of oxygen to haemoglobin.

$$4O_2 + Hb \xleftarrow{k_+}{k_-} Hb(O_2)_4$$

What are the limitations of this model? Find an expression for the proportion of boundhaemoglobin as a function of oxygen concentration.[20%]

(b) To study the effect of pH on the binding of oxygen to haemoglobin, we consider the following set of reactions where o represents the concentration of oxygen, and h the concentration of H⁺ ions.

$$\begin{array}{ccc} \text{Hb} & \stackrel{k_1o^4}{\longleftarrow} & \text{Hb}(O_2)_4 \\ k_2h & \stackrel{\uparrow}{\longleftarrow} k_{-2} & \stackrel{\bar{k_1}o^4}{\longleftarrow} & \frac{\bar{k_2}h}{\downarrow} & \stackrel{\uparrow}{\downarrow} \bar{k_{-2}} \\ \text{HbH}^+ & \stackrel{\bar{k_1}o^4}{\longleftarrow} & \text{Hb}(O_2)_4\text{H}^+ \end{array}$$

Show that the proportion *Y* of oxygen-bound haemoglobin takes the following form:

$$Y = \frac{o^4}{o^4 + K(h)}$$

Find an expression for the function K(h).

[50%]

(c) What condition on the rate constants must be satisfied for H⁺ to inhibit the binding of oxygen to haemoglobin? [15%]

(d) Why is it physiologically useful for H^+ to have such an inhibitory role? [15%]

4 (a) A fluid flows inside a rigid cylindrical vessel of constant radius R and length L. Using cylindrical polar coordinates, the pressure p(r, x) and shear stress $\tau(r)$ along the vessel direction (x) satisfy the following equations for a steady flow:

$$\frac{1}{r}\frac{\partial(r\tau)}{\partial r} = \frac{\partial p}{\partial x}$$
$$\frac{\partial p}{\partial r} = 0$$

Assuming that the fluid is Newtonian with viscosity μ , find a mathematical expression for the velocity profile u(r) in the vessel as a function of the pressure drop across the ends of the vessel. [35%]

(b) When the flow is not steady, the velocity profile is now controlled by the following equation:

$$\rho \frac{\partial u}{\partial t} = -\frac{\partial p}{\partial x} + \frac{\mu}{r} \frac{\partial}{\partial r} \left(r \frac{\partial u}{\partial r} \right)$$

Assuming that the pressure gradient is oscillating in the complex plane, $\frac{\partial p}{\partial x} = Ae^{i\omega t}$, and looking for solutions with separated variables, $u(r,t) = v(r)e^{i\omega t}$, show that v(r) satisfies the following equation:

$$R^2 \frac{d^2 v}{dr^2} + \frac{R^2}{r} \frac{dv}{dr} - i\alpha^2 v = \frac{R^2 A}{\mu}$$

Explain the significance of the variable α and write its expression as a function of the other parameters of the problem. [35%]

(c) Find an approximate expression for u(r, t) when α is large and sketch it as a function of *r* for different times. [15%]

(d) Find an approximate expression for u(r, t) when α is small and sketch it as a function of *r* for different times. [15%]

END OF PAPER