

EGT2  
ENGINEERING TRIPOS PART IIA

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Tuesday 9 May 2023 14.00 to 15.40

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**Module 3G2**

**MATHEMATICAL PHYSIOLOGY**

**ANSWER:**

*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.**

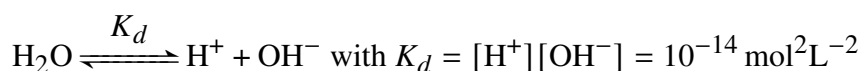
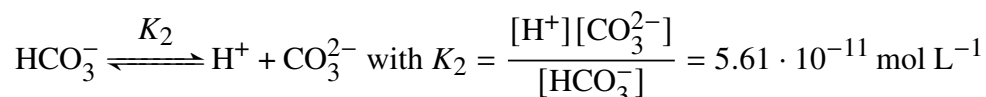
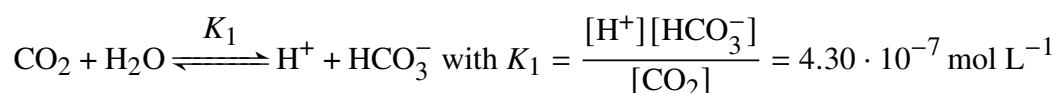
**You may not start to read the questions printed on the subsequent pages of this question paper until instructed to do so.**

**You may not remove any stationery from the Examination Room.**

1 (a) 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%]

Answer: The overall pressure at 100 meter depth is approximately 11 atm. 10% oxygen would provide 1.1 atm of oxygen, which is 5.5 times higher than at the surface. We would have 2.2 atm of nitrogen, which is about 2.5 times higher than at the surface. It may be surprising that these values are so much bigger than those at the surface, especially for oxygen. However, these would enable the divers to experience suitable levels of oxygen whilst going down or up (improving safety), and acceptable level of nitrogen.

(b) Consider a volume of pure water placed at room temperature in contact with a gas of constant partial pressure of  $\text{CO}_2$ ,  $P_c = 40 \text{ Pa}$ . The solubility of  $\text{CO}_2$  in water is  $\sigma = 3.3 \cdot 10^{-5} \text{ Molar/mm Hg}$ . (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%]



Answer: The partial pressure needs to be converted from Pa to mmHg, and the multiplied by the solubility. The concentration of dissolved  $\text{CO}_2$  is approximately  $9.9 \text{ E-6 Molar}$ .

This is quite low, so depending on how carefully one wants to be, we may or may not neglect the production of  $\text{H}^+$  from the dissociation of water. Whichever is the approach chosen, the approximations need to be explained. Here, we do it without assuming the solution is very acidic. Using electroneutrality, or the fact that  $\text{H}^+$  is produced either from the first or last equation, we have:

$[\text{HCO}_3^-] + [\text{OH}^-] = [\text{H}^+]$  Using the equilibrium constants to eliminate the negative ion concentrations, and multiplying by  $[\text{H}^+]$ , we get:

$$[\text{H}^+]^2 = K_1 [\text{CO}_2] + K_d$$

This leads to  $[\text{H}^+] = 2.07 \text{ E-6 Molar}$ , or equivalently  $\text{pH} = 5.7$ .

(c) Figure 1 shows the evolution of the pH of the oceans over the last 30 years, as well as the evolution of CO<sub>2</sub> amounts in the atmosphere over the last 60 years. Explain what may cause the pH of the oceans to change over time. [15%]

Answer: We have established in the first section that the amount of CO<sub>2</sub> makes water more acidic. Before suggesting a cause, it is important to assess how much CO<sub>2</sub> is actually present in the atmosphere, and determine if it is likely to impact oceans.

The fraction of CO<sub>2</sub> in the atmosphere is of the order of 400 μmol/mol or 400 ppm. The partial pressure is 400 E-6 x 1 atm = 40 Pa. This is the value used in the previous section. So this amount of CO<sub>2</sub> could change the pH of neutral water. In the case of sea water, the baseline is slightly alkaline, but close enough to neutral that small variations of CO<sub>2</sub> level will affect the pH.

(d) The shells of many sea creatures are made of calcium carbonate, (Ca<sup>2+</sup>, CO<sub>3</sub><sup>2-</sup>). (Note that carbonate is one of the species involved in the reactions above.) How would these organisms be affected by an increased level of CO<sub>2</sub> in the atmosphere? Justify your answer. [15%]

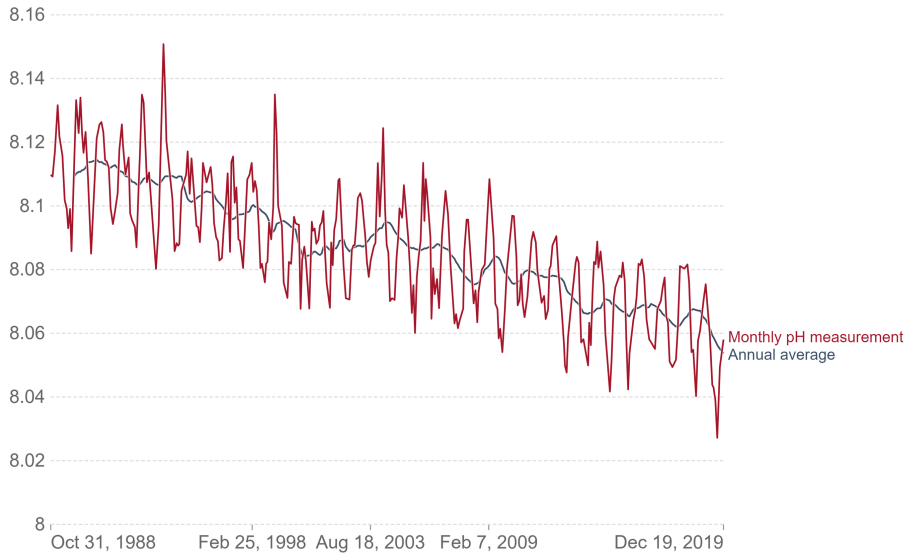
Answer: On one hand, more CO<sub>2</sub> may lead to more carbonate in water which is good. On the other hand, however, the acidification also leads to the formation of bi-carbonate from carbonate, according to the second reaction, from right to left. The net effect is therefore difficult to predict without the knowledge of the role of the other chemicals in water.

By combining K<sub>2</sub> and K<sub>1</sub> to eliminate HCO<sub>3</sub><sup>-</sup>, we get:  $K_1 K_2 [\text{CO}_2] / [\text{H}^+]^2 = [\text{CO}_3^{2-}]$

[CO<sub>2</sub>] increased by 20% based on the graphs over the last 30 years. The pH changed from 8.12 to 8.06, so [H<sup>+</sup>] increased by 15%, and therefore [H<sup>+</sup>]<sup>2</sup> by roughly 30%. So the net effect is a decrease in the amount of carbonate, which is very bad news for organisms that rely on it.

### Ocean acidification: mean seawater pH

Mean seawater pH is shown based on in-situ measurements of pH from the Aloha station.

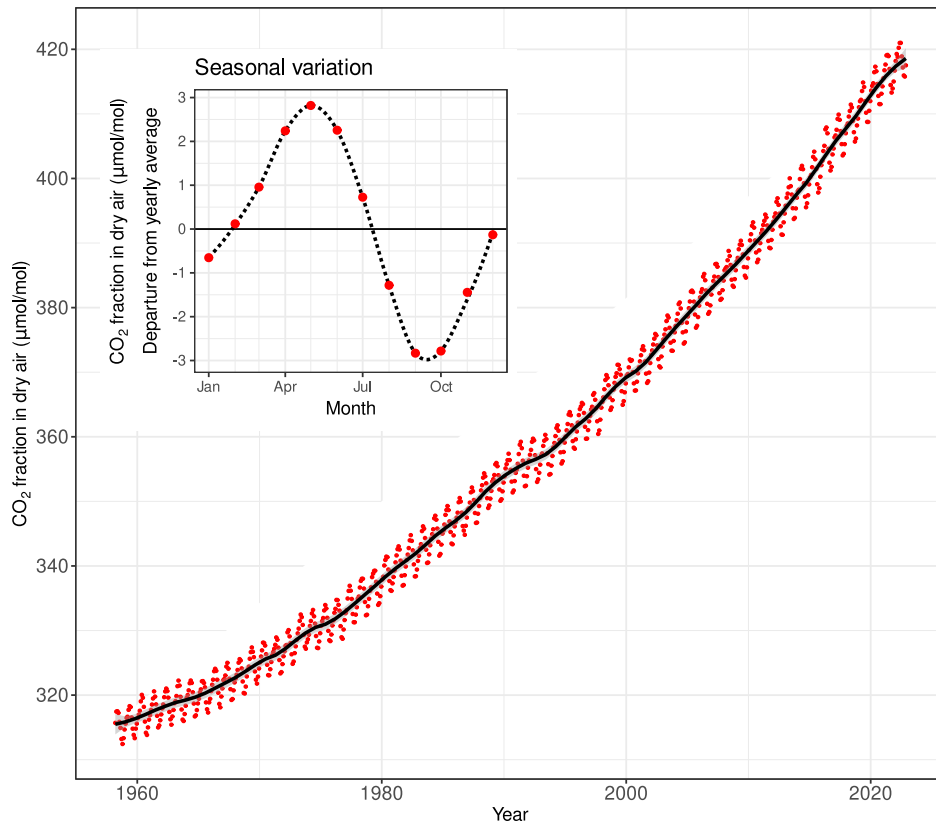


Source: University of Hawaii

OurWorldInData.org/climate-change • CC BY

### Monthly mean CO<sub>2</sub> concentration

Mauna Loa 1958 - 2022



Data : Dr. Pieter Tans, NOAA/ESRL (<https://gml.noaa.gov/ccgg/trends/>) and Dr. Ralph Keeling, Scripps Institution of Oceanography (<https://scrippsco2.ucsd.edu/>), Accessed 2022-12-19 <https://www.wiki/4ZWN>

Fig. 1

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  $L = 12 \text{ nm}$ .

(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  $V = 0 \text{ mV}$ . 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%]

Answer: In this case, as there is no electric field, only pure diffusion acts on the ion. This means that the spatial probability density of the ion (undergoing Brownian motion) at time  $t$  will be a Gaussian with a variance that is  $D t$ :

$$p(x; t) = \frac{1}{\sqrt{2\pi D t}} e^{-\frac{1}{2} \frac{x^2}{D t}}$$

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%]

Answer: This requires us to find the maximum of the probability density as a function of  $t$  at  $x = L$ . For this, to make the calculation easier, we find the  $t$  that maximises the log probability:

$$\ln p(L; t) = -\frac{1}{2} \left[ \ln(2\pi D t) + \frac{L^2}{D t} \right]$$

Taking the derivative w.r.t.  $t$ , setting it to zero, and solving for  $t$ , we obtain:

$$t = \frac{L^2}{D}$$

And so the effective speed of the ion is

$$v = \frac{L}{t} = \frac{D}{L} = 0.15 \frac{\text{m}}{\text{s}}$$

(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  $V = 0 \text{ mV}$ . 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%]

Answer: In this case, it is still only diffusion that acts on the ion, as there is still no electric field.

Although there is a concentration gradient, this does not change the nature of diffusion (including the diffusion coefficient itself) as such, and therefore the effective velocity of the ion remains the same as before:

$$v = \frac{D}{L} = 0.15 \frac{\text{m}}{\text{s}}$$

(iii) The concentration of the ion everywhere in the channel (including at both ends) is  $c = 50 \text{ mM}$  (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%]

Answer: Given Planck’s equation, the (magnitude of the) electric flux is:

$$J = D \frac{zF}{RT} c \frac{\Delta V}{L} \approx 67.5 \frac{\text{mol}}{\text{m}^2 \text{ s}}$$

where  $F = 96500 \frac{\text{C}}{\text{mol}}$ ,  $R = 8.31 \frac{\text{J}}{\text{mol K}}$ , and  $T = 310 \text{ K}$ , are the Faraday and universal gas constants, and body temperature, as usual (up to the first three significant digits), and  $\Delta V = |V_e - V_i| = |120 - 0| \text{ mV} = 120 \text{ mV}$  is the electric potential difference between the two ends. Based on the hint, we can write down the following equation between ‘drift’ velocity,  $v$ , and flux:

$$J = \frac{v \tau A c}{\tau A}$$

where,  $\tau$  and  $A$  are unit time and area. This gives us:

$$v = \frac{J}{c} = D \frac{zF}{RT} \frac{\Delta V}{L} \approx 1.35 \frac{\text{m}}{\text{s}}$$

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

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

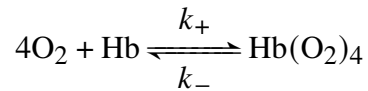
Answer:  $h_\infty, n_\infty, m_\infty$

(ii)  $\tau_h, \tau_m, \tau_n$  at  $V = 0 \text{ mV}$ ; [10%]

Answer:  $\tau_m, \tau_n, \tau_h$

where the resting membrane potential is defined to be at  $0 \text{ mV}$ .

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



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

Answer: This model neglects the intermediate steps and assumes that all oxygen molecules bind at the same time as a single elementary reaction (as indicated by the rate constants at the top of the arrows).

$$\frac{d[\text{Hb}(\text{O}_2)_4]}{dt} = k_+[\text{Hb}][\text{O}_2]^4 - k_-[\text{Hb}(\text{O}_2)_4]$$

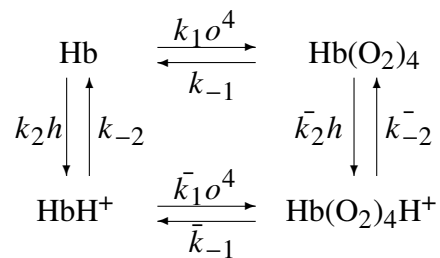
At the equilibrium, we can define the constant  $K_1$  such that:

$$\frac{[\text{Hb}(\text{O}_2)_4]}{[\text{Hb}][\text{O}_2]^4} = \frac{k_+}{k_-} = K_1(T)$$

The percentage of bound haemoglobin is therefore:

$$Y = \frac{[\text{Hb}(\text{O}_2)_4]}{[\text{Hb}] + [\text{Hb}(\text{O}_2)_4]} = \frac{[\text{O}_2]^4}{K_1^{-1} + [\text{O}_2]^4}$$

- (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  $\text{H}^+$  ions.



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%]

Answer: We use the following notations:  $C_b = [\text{Hb}]$ ,  $C_{bh} = [\text{Hb}(\text{H}^+)]$ ,  $C_{bo} = [\text{Hb}(\text{O}_2)_4]$ ,  $C_{bho} =$

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$[\text{Hb}(\text{H}^+)(\text{O}_2)_4]$ ,  $C = C_b + C_{bh} + C_{bo} + C_{bho}$ ,  $h = [\text{H}^+]$  and  $o = [\text{O}_2]$ .

Assuming the equilibrium (with equilibrium constants defined as the ratio of the corresponding rate constants), we find that:

$$C_{bo} = K_1 o^4 C_b$$

$$C_{bh} = K_2 h C_b$$

$$C_{bho} = \bar{K}_1 o^4 C_{bh} = \bar{K}_1 K_2 o^4 h C_b$$

$$C = \left(1 + K_2 h + (K_1 + \bar{K}_1 K_2 h) o^4\right) C_b$$

The resulting saturation curve is :

$$Y = \frac{C_{bo} + C_{bho}}{C} = \frac{o^4}{o^4 + K(h)}, \text{ with } K(h) = K_1^{-1} \frac{(1 + K_2 h)}{1 + \frac{\bar{K}_1}{K_1} K_2 h} \quad (1)$$

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

Answer: Inhibition implies that there should be less binding (lower Y) when  $h$  increases. We therefore need  $K(h)$  to increase with  $h$ . This is satisfied when  $\frac{\bar{K}_1}{K_1} < 1$ . This is sensible as this means the Hb is less likely to bind to oxygen if there is already on  $\text{H}^+$  attached to it.

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

Answer: This is very useful because tissues naturally produce  $\text{CO}_2$  as they burn oxygen, making the pH more acidic as a result. This favours the release of oxygen when it is most needed. Conversely, in the lungs, when  $\text{CO}_2$  is released, Hb is more likely to capture oxygen.



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  $\mu$ , 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%]

Answer: Since  $\frac{\partial p}{\partial r} = 0$ , the pressure depends on  $x$  only and we can separate variables. Using  $\tau = \mu \frac{du}{dr}$ :

$$\mu \frac{1}{r} \frac{d}{dr} \left( r \frac{du}{dr} \right) = \frac{dp}{dx} = \text{constant}$$

The pressure varies linearly along the pipe. Treating  $\frac{dp}{dx} = \Delta p/L$  as a constant (negative if flow towards positive  $x$ ), we can integrate:

$$\frac{d}{dr} \left( r \frac{du}{dr} \right) = \frac{1}{\mu} \frac{dp}{dx} r$$

with a no slip boundary condition at the surface of the pipe/vessel,  $u(R) = 0$ .

The resulting velocity profile is:

$$u(r) = \frac{r^2 - R^2}{4\mu} \frac{dp}{dx}$$

(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,  $\frac{\partial p}{\partial x} = A e^{i\omega t}$ , 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  $\alpha$  and write its expression as a function of the other parameters of the problem. [35%]

Answer: By substituting  $u$  with its expression in terms of  $v$  and the time dependent factor, we get:

$$i\omega\rho v e^{i\omega t} = -A e^{i\omega t} + \frac{\mu}{r} \frac{\partial}{\partial r} \left( r \frac{\partial v}{\partial r} \right) e^{i\omega t}$$

Rearranging the terms:

$$\frac{d^2 v}{dr^2} + \frac{1}{r} \frac{dv}{dr} - \frac{i\omega\rho}{\mu} v = \frac{A}{\mu}$$

Multiplying by  $R^2$  makes the equation dimensionally similar to the target expression.

$$R^2 \frac{d^2 v}{dr^2} + \frac{R^2}{r} \frac{dv}{dr} - i \frac{R^2 \omega \rho}{\mu} v = \frac{AR^2}{\mu}$$

We therefore find that  $\frac{R^2 \omega \rho}{\mu} = \alpha^2$  is a dimensionless number. It characterises the importance of inertial forces relative to viscous forces for harmonic pulsations at the frequency  $\omega$ . Large values of  $\alpha^2$  indicate that the inertial forces dominate over the viscous forces. The higher the frequency, and the larger the vessel, the more important inertial terms are. On the opposite end, viscous terms dominate and the flow can be considered quasi-steady.

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

Answer: When  $\alpha$  is large, we can neglect some terms in the equation to get:

$$\begin{aligned} i \frac{R^2 \omega \rho}{\mu} v &= \frac{AR^2}{\mu} \\ v &= -i \frac{A}{\omega \rho} \\ u &= \frac{A}{\omega \rho} e^{i(\omega t - \pi/2)} \end{aligned}$$

Here, the velocity  $v$  is constant, so the profile is a plug flow. It varies in time with a  $\pi/2$  phase difference with the pressure.

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

Answer: In this case, we can neglect the time derivative:

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

This leads to the same equation as in part (a), i.e. a parabolic flow profile, but which is now modulated over time.

$$u(r) = \frac{r^2 - R^2}{4\mu} A e^{i\omega t}$$

**END OF PAPER**