CBE 40445
Fall 2020
Test #2
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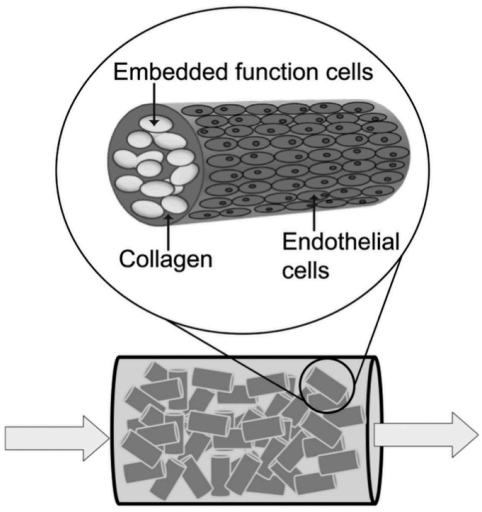
1. Tissue engineering (60 points)

In the 1990's, Professor Robert Langer and colleagues were culturing (rat) heart cells in laboratory dishes and creating thin cellular layers that would "beat" when electrically stimulated. It seemed that "tissue engineering" would soon allow the synthesis of pieces of heart, liver or other tissue (*ex vivo* — outside the living creature) in a laboratory setting. This tissue could then be transplanted into people to repair, say a portion of a damaged heart.

Soon, reality struck! The thickness of the sheets was ultimately limited by diffusion of nutrients and perhaps most significantly by oxygen levels. Of course this is why blood vessels infiltrate all tissue and no active cells are more than ~20 μm away from a capillary (less for heart tissue).

Even 25+ years later this limitation is a "show-stopper" despite various microfabrication techniques being applied to create artificial "pores" and specific efforts at synthesizing blood vessels.

A work around, but not at the level of functioning heart tissue is shown in figure 1.



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Effectiveness factor and diffusion limitations in collagen gel modules containing HepG2 cells

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Figure 1.
Modular tissue engineering. Small collagen rods containing embedded functional cells and coated with endothelial cells are randomly packed to form a "packed bed" construct. Interstitial spaces between modules allow the construct to be perfused.

In this paper they note that it had previously been assumed that cells cultured inside the collagen rods would be healthy because there would be no internal diffusion resistance. However, above a certain diameter, the cultured cells die. They use a Thiele modulus and effectiveness factor analysis to quantify this problem. Note that the normal assumption for oxygen as a nutrient for living cells is that the reaction is 0 order.

The authors define a Thiele modulus as

$$\phi^2 \equiv \frac{\rho_{cell}\ (OUR)\ L_p^2}{C^*\ D_{eff}}$$

where ρ_{cell} is the cell density (cells/m^3), *OUR* is the oxygen uptake rate per cell (mole O_2/cell-s), L_p is the characteristic length of the cylindrical modules (m), C* is the molar concentration of O_2 in the bulk fluid (mol O_2/m^3) and D_{eff} is the effective diffusivity of oxygen in the modules (m^2/s).

The effectiveness factor can be defined as

$$\eta \equiv \frac{\text{average volumetric reaction rate}}{\text{reaction rate with } C = C^* \text{ in entire volume}}$$

And we know that η can be calculated using

$$\eta = \frac{\tanh(\phi)}{\phi}$$

For this problem we would like to be able to support a cell density of 1 X10^9 cells/m^3, healthy cells have an *OUR* of 5X10^{-15} mol/cell-s, D_{eff} for this material is 1 X10^{-9} m^2/s and C* = 0.001 mol/m^3.

a. What is the physical meaning of the Thiele modulus?
b. Explain how the definition here is consistent with 0 order kinetics.
c. What is the value of the Thiele modulus for a 2 mm diameter module (L_p = 5 X10^{-4} m)[1] ?
d. What are the values of the concentration in a 2 mm diameter module (L_p = 5 X10^{-4} m) at the center and 1/2 of the distance from the center to the surface of a module?
e. What is the effectiveness factor for this diameter?
f. If you want the effectiveness factor to be > 0.85, what is the largest diameter module that could be used?

The reaction is supposed to be 0 order so we can try a different approach to the analysis. Let's choose a differential equation that describes 0 order kinetics in a slab.

g. What differential equation would describe diffusion with 0 order kinetics in a slab (rectangular) geometry?
h. Use a solution for this 0-order rectangular geometry case to find the concentration within a rectangular slab that matches the 2mm particle (so the slab needs to be 5 X10^{-4} m) that you solved for in part d. Do these match?
i. Is there a range of ϕ where the match should be best? Why?

Extra credit: What would you have to know to verify that there is no external resistance in this configuration?

[1] The author's didn't consider finite length

TEST 2

#1) a) $\frac{\text{REACTION RATE}}{\text{DIFFUSION RATE}}$

b)

b

$$\phi^2 = \frac{g_{CELL}\,(OUR)\left(\frac{d_m}{4}\right)^2}{C^* \; D_{eff}}$$

TOGETHER THIS IS 0 ORDER RATE CONSTANT WITH THE CONCENTRATION IN DENOMINATOR TO GET CORRECT UNITS

$$\frac{\left(\frac{CELLS}{m^2}\right)\left(\frac{MOLE\ O_2}{CELL \cdot S}\right)\left(\frac{dm}{4}\right)^2 \quad (L^2)}{\left(\frac{mol\ O_2}{m^3}\right) \qquad D_{eff} \quad \left(L^2/_{TIME}\right)}$$

$\frac{1}{TIME}$

c)

$$\phi^2 = \frac{(10^9)(5\times10^{-15})\left(5.4\times10^{-4}\right)^2}{(.001)(1\times10^{-9})}$$

$$= 11.25$$

d) $\eta(w) = \dfrac{\cosh \phi w}{\cosh \phi}$

$\eta(0) = \dfrac{\cosh(0)}{\cosh(\sqrt{1.25})} =$

$\eta(0) \doteq .591$

$\eta(.5) = .685$

e) $\eta = \dfrac{\tanh \phi}{\phi} \doteq .685$

f) $\phi = .55$

$d_p = .33 \text{ mm}$

g) $\frac{d^2\psi}{d\omega^2} - \phi^2 = 0$ $\quad \psi(1) = 1$ $\quad \psi'(0) = 0$

$$\frac{d}{d\omega}\frac{d\psi}{d\omega} = \phi^2$$

$$\int d\left(\frac{d\psi}{d\omega}\right) = \int \phi^2 \, d\omega$$

$$\frac{d\psi}{d\omega} = \phi^2 \omega + C_1$$

$\psi'(0) = 0 \quad \therefore C_1 = 0$

$$\int d\psi = \int \phi^2 \omega \, d\omega$$

$$\psi = \frac{\phi^2 \omega^2}{2} + C_2$$

$$1 = \frac{\phi^2}{2} + C_2 \quad 2 = 1 - \frac{\phi^2}{2}$$

$$\eta = \frac{\omega^2}{2}\phi^2 - \frac{\phi^2}{2} + 1$$

$$\phi^2 = 1.25$$

$\eta(0) = .373$ | $.59$

(10) $\eta(.5) = .53$ | $.69$

DON'T MATCH

(5) i) $\phi < 1$ $C \sim$ CONST

(5) h) EITHER $Bi >> 1$

OR O_2 CONCENTRATION

RIGHT AT SURFACE

2. Analysis of a sequential reaction (30 points)

Consider a reaction scheme we have seen before for A-> M using a catalyst on a surface.

$$A + * \underset{k_{des}}{\overset{k_{ads}}{\longleftrightarrow}} A* \xrightarrow{k_2} M + *$$

It is not too hard to show that the rate of this reaction sequence is

$$r = \frac{k_2 K_{ads} [A] [*]_0}{1 + \frac{k_2}{k_{des}} + K_{ads}[A]},$$

where $K_{ads} \equiv \frac{k_{ads}}{k_{des}}$

A. For which values of which parameters could the initial adsorption step be close to equilibrium?
B. If this is not the case, could the A* concentration be approximated as being at a steady state concentration? Explain.
C. Adsorption experiments have provided a value of 10 l/mol for K_{ads}, also k_{des} =0.1/s. Use these rate data to "estimate" k_2 and $[*]_0$.

[A] (mol/l)	r mol/(l-s)
2	2
1	1.9
0.01	0.1

D. Suppose that an inert, *B*, is present that can also reversibly adsorb on the surface as

$$B + * \underset{k_{Bdes}}{\overset{k_{Bads}}{\longleftrightarrow}} B*, \qquad K_{Bads} \equiv \frac{k_{Bads}}{k_{Bdes}}$$

Explain why this inert will affect the observed reaction rate of A->M.

E. What you would have to know to quantify this effect?

#2 a) $k_2 << k_{des}$

b) YES, IT IS AN INTERMEDIATE COMPLEX

#2 c

$$2 = \frac{k_2 K_{ads} [A][\ast]_0}{1 + \frac{k_2}{k_{des}} + K_{ads}[A]}$$

ASSUME $K_{ads}[A] >> 1, \frac{k_2}{k_{des}}$

$$2 = k_2[\ast]_0$$

THEN

$$.01 = \frac{k_2 K_{ads}[A][\ast]_0}{1 + \frac{k_2}{k_{des}} + K_{ads}[A]}$$

(-1)

$$.01 = \frac{2(10)(.01)}{1 + \frac{20}{\gamma}}$$

$$.5 = \frac{2}{1 + \frac{20}{\gamma}}$$

$$= 1 + \frac{20}{\gamma}$$

$\gamma = 20$

$k_2 = .1$

!!

D) IT WILL OCCUPY ACTIVE SITES FOR REACTION

E) EQUILIBRIUM CONSTANT OF K_S COMPARED TO $K_A + \frac{k_2}{k_{des}}$

3. A->M reaction as function of temperature. (10 points)

For the above reaction, the follow data as function of temperature are available.

T (K)	[A] (mol/l)	r mol/(l-s)
300	2	2
320	2	3.5

a. What is the apparent activation energy for this reaction?
b. Under what conditions would you expect that this activation energy could be used to get an accurate prediction of the rate at 340 K?

(5) ASSUME $k = A \exp\left(-\frac{E_a}{RT}\right)$

rate $\sim k$ [C] ...

$$\ln\left(\frac{3.5}{2}\right) = -\frac{E_a}{R}\left(\frac{1}{320} - \frac{1}{300}\right)$$

(5) $E_a = 2684\ R = 22.3\ kJ$

BUT TO GENERALIZE

NEED $[A] \Rightarrow$ SAME

OR 1ST ORDER

KINETICS

NOT DIFFUSION

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