SUBSTRATE CONCENTRATIONS IN A KROGH’S TISSUE CYLINDER EXHIBITING FIRST ORDER KINETICS

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The mathematical analysis of a model for substrate concentration in tissue is presented for the case of first order consumption by the tissue. The model consists of a single capillary from which substrate diffuses into a surrounding cylinder of tissue. Blum’s equations describing the model are used and results are obtained numerically for capillary and tissue concentrations. Capillary permeability, which has no influence on the amount of substrate consumed in the tissue in a zeroth order rate of tissue consumption, is found to alter it in the present study.

INTRODUCTION

A quantitative treatment of the problem of substrate concentrations in tissue surrounding a capillary was considered first by Krogh (1936) with several idealizing assumptions. His model consisted of a single capillary from which substrate diffused into surrounding cylinder of tissue. It attracted considerable attention in view of its significance in micro-circulatory physiology (Middleman 1972, Lih 1975). Blum (1960) studied the same problem for various modes of tissue consumption and his results reigned supreme in this area for a considerable length of time until recently, when they were proved to be incorrect by Salathe and Wang (1980). Their analysis pertained to the case of a zeroth order rate of tissue consumption.

It is to be noted that the usual Michaelis-Menten rate-law which has been established as a satisfactory description of the relation between steady state reaction rate and the concentration of the substrate in general, is known to degenerate into either zeroth order or first order kinetics, depending on whether the concentration in the system is high or low (Blum and Jenden 1957). The present study aims at solving the above problem for the second case, viz., for a first order rate of tissue consumption.

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ANALYSIS

This model (cf. Fig. 1) has been discussed in detail by Blum (1960). This consists of a single capillary of radius $R_c$ and length $L$ surrounded by a concentric cylinder of tissue of radius $R_t$. Blood containing the substrate at concentration $C_A$ enters the arterial end of the capillary with flow velocity $\bar{v}$. Assuming a thorough radial mixing, the substrate concentration inside the capillary surrounded by the tissue cylinder, $C_b$, is taken to be a function of the axial distance $z$. The concentration of the substrate that diffuses into the tissue cylinder, and the radial and axial diffusion coefficients are denoted by $c(r, z)$, $D_r$ and $D_z$, respectively. The permeability of the membrane to the substrate is denoted by $H$.

In terms of the non-dimensional variables $C = C_b/C_A$, $c = c_l/C_A$, $r = r/R_t$ and $Z = \bar{z}/L$, the governing equations and boundary conditions are

\[
\frac{1}{r} \frac{\partial}{\partial r} \left( r \frac{\partial c}{\partial r} \right) + \epsilon^2 \frac{\partial^2 c}{\partial z^2} - M_0 c = 0, \quad 0 \leq z \leq 1, \quad R \leq r \leq 1 \quad \ldots (1)
\]

\[
\frac{\partial c}{\partial r} = 0, \quad r = 1, \quad 0 \leq z \leq 1 \quad \ldots (2)
\]

\[
\frac{\partial c}{\partial z} = 0, \quad z = 0, 1, \quad R \leq r \leq 1 \quad \ldots (3)
\]

\[
\left. \frac{\partial c}{\partial r} \right|_{r=R} = - h \left[ C(z) - c(R, z) \right], \quad 0 \leq z \leq 1 \quad \ldots (4)
\]

\[
\beta \frac{dc}{dz} = \left. \frac{\partial c}{\partial r} \right|_{r=R}, \quad 0 \leq z \leq 1 \quad \ldots (5)
\]

where

\[
R = R_c/R_t, \quad \epsilon = \sqrt{D_z/D_r} \left( R_t/L \right)
\]

\[
M_0 = MR_t^3/D_r \quad (M - \text{absorption rate constant}), \quad h = HR_t/D_r, \quad \text{and}
\]

\[
\beta = \bar{v}R_tR_c/2D_zL.
\]
Solutions

As the method of solution is almost the same as that given by Salathe and Wang (1980) for a zeroth order consumption rate, the solutions are recorded briefly.

An eigen function expansion satisfying eqns. (1)–(3) is given by

\[ c(r, z) = \alpha \left\{ I_0(\sqrt{M_0}r) K_1(\sqrt{M_0}) + K_0(\sqrt{M_0}) I_1(\sqrt{M_0}) \right\} + \sum_{n=1}^{\infty} B_n \left\{ I_0(\rho_n r) K_1(\rho_n) + I_1(\rho_n) K_0(\rho_n) \right\} \cos n\pi z \quad \ldots(6) \]

where \( I_n, K_n \) are modified Bessel functions of order \( n \), \( \alpha \) and \( B_n \) are constants to be determined using the boundary conditions, and

\[ \rho_n^2 = M_0 + \epsilon^2 n^2 \pi^2. \]

Using the following notations

\[ u_n = \rho_n K_1(\rho_n) I_1(\rho_n R) - I_1(\rho_n) K_1(\rho_n R) \]
\[ v_n = I_0(\rho_n R) K_1(\rho_n) + I_1(\rho_n) K_0(\rho_n R) \]
\[ p = I_0(\sqrt{M_0} R) K_1(\sqrt{M_0}) + K_0(\sqrt{M_0}) I_1(\sqrt{M_0}) \]
\[ q = M_0 I_1(\sqrt{M_0} R) K_1(\sqrt{M_0}) - K_1(\sqrt{M_0} R) I_1(\sqrt{M_0}) \quad \ldots(7) \]

and the orthogonal properties of \( \cos n\pi z \) and the condition \( C(0) = 1 \), the capillary substrate concentration can be written as

\[ C(z) = 1 + \frac{\alpha q}{\beta} z + \sum_{n=1}^{\infty} \frac{B_n u_n}{\beta n \pi} \sin n\pi z. \quad \ldots(8) \]

The constant \( \alpha \) involved in the above equation can be seen to be given by the expression

\[ \alpha = \{ p - q(1/h + 1/2\beta) \}^{-1} \left[ 1 + \sum_{n=1}^{\infty} \frac{2a_n \sin \{1 - (-1)^n\}}{\beta n^2 \pi^2 (v_n - u_n/h)} \right] \quad \ldots(9) \]

where the unknowns \( a_n \) are defined as

\[ a_n = \int_0^1 C(z) \cos n\pi z \, dz. \]

Multiplying eqn. (8) by \( \cos n\pi z \) and integrating between 0 to 1, one gets an infinite set of algebraic equations in the infinite set of unknowns as
\[ a_m - \sum_{n=1}^{\infty} e_{mn} a_n = 0 \]  \hspace{1cm} (for even values of \( m \))

\[ a_m = \left\{ \begin{array}{l}
(p - q (1/h + 1/2\beta))^{-1} \sum_{n=1}^{\infty} a_n \left[ e_{mn} - \frac{4q u_n (1 - (-1)^n)}{\beta n^2 m^2 n^4 (v_n - u_n/h)} \right] \\
- \frac{2q}{\beta n^2 m^2} \{ p - q (1/h + 1/2\beta) \}^{-1} \hspace{1cm} (for odd values of \( m \))
\end{array} \right. \]

where

\[ e_{mn} = \left\{ \begin{array}{l}
0 \hspace{1cm} \text{if } m = n \text{ or } m + n \text{ is even} \\
\frac{4u_n}{\beta (v_n - u_n/h) (n^2 - m^2) \pi^2} \hspace{1cm} \text{if } m + n \text{ is odd.}
\end{array} \right. \]

The above system of equations has been solved by the method of truncation outlined by Salathe and Wang (1980).

**Numerical Results and Discussion**

Substrate concentration profiles are presented for a Krogh cylinder of diameter 110 \( \mu m \) surrounding a capillary of length 1000 \( \mu m \) and diameter 10 \( \mu m \) similar to the calculation of Salathe and Wang (1980). The axial and radial diffusion coefficients are taken to be the same.

Figure 2 shows substrate concentration profiles in the capillary for various values of the diffusion coefficient. They are quite different in nature from the ones

**Fig. 2.** Concentration profiles in the capillary for various values of \( D_r \).

**Fig. 3.** Concentration profiles in the capillary for various values of \( H \).
obtained earlier for a constant rate of consumption by Salathe and Wang (1980) (shown in broken lines). It is to be noted that this should not be mistaken for comparison of data obtained from Salathe and Wang (1980) with the present results as the non-dimensional scheme for obtaining $M_0$ in these procedures are different. For a fixed proportional constant of absorption $M_0$, the capillary diffusivity has been noted to have limitations in altering the amount of substrate absorbed, i.e., variations in concentrations profiles becomes less with the increase of the diffusion coefficient.

Since the capillary permeability is almost infinite for a substrate like oxygen, substrate distributions in tissue and capillary are analysed for high values of $H$. A linear oxygen dissociation relationship mentioned in (Salathe et al. 1980) is incorporated with $\beta$ (which simply increases its value), throughout our study with a view to generalizing the analysis so as to include oxygen in the class of substrates.

It has been found that for fixed values of $M$, $D_\tau$, and $\bar{V}$, the permeability $H$ influences the solution exactly in a similar way as $D_\tau$ does, when all other parameters are kept fixed (cf. Figures 2 and 3). The curves for high permeability coefficients can also be seen to correspond qualitatively to the case of $H \rightarrow \infty$ (cf. Figure 3).

Figures 4 and 5 show tissue concentration as a function of axial positions at the capillary wall and at the outer edge of the Krogh cylinder respectively. The

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**Fig. 4.** Concentration profiles in the tissue for various values of $H$.

**Fig. 5.** Concentration profiles in the tissue for various values of $H$. 
tissue concentration can be seen to decrease with $H$. The same effect has been observed on decreasing the values of $M$ and $D_r$. For all values of $H$ above zero, substrate concentration remains positive, though less, in contrast to the phenomenon noted in the zeroth order kinetics by Salathe and Wang (1980) where a decrease in $H$ below 2 $\mu$m/sec resulted in meaningless negative concentration profiles. It is important to note that for a fixed $\bar{u}$, an increase in $M$ gives rise to negative concentrations suggesting that an increase in the absorption rate cannot increase the amount of substrate consumed in tissue space.

Figure 6 shows a decrease in the amount of substrate loss in the capillary with increasing values of $\bar{u}$. We note that at high altitudes the concentration of oxygen in the environment will be less and in such cases, as mentioned earlier, a first order kinetics may be assumed to take place in utilizing this essential substrate at tissue level, by birds in flight. This enables us to remark on the inability of the Krogh model to explain the results obtained for blood flow and oxygen consumption in avian skeletal muscle during hypoxia (Grubb 1981). In view of the role played by $\bar{v}$, the present model fails to account for the observations on the existence of a possible luxuriant resting blood flow rate to supply the skeletal muscles of birds with adequate oxygen.
Figures 7–9 show the concentration profiles as a function of radial position at $z = 0, 0.3$ and 1.0. These profiles show steep concentration gradients at the arterial end for moderately high diffusivities ($D_r > 300 \, \mu m/sec$) for all $H \geq 10 \, \mu m/sec$.

The numerical values of the solutions are computed in double precision in DEC 1090 computer with 120 terms in the infinite series. A further increase in the number of terms has been observed to alter the results in the 6th decimal place only.

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REFERENCES

