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Research Article

Unsteady Diffusive Mass Transfer in a Follicle Modelled as an Annular Region

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Abstract. Oxygen supply in a follicle is modelled using the species transport equation. The follicle is modelled as an annular region formed by concentric circles where the inner circle represents the granulosa layer fluid and cells. Concentration is obtained analytically and graphically depicted. Oxygen transport in the outer follicle region remains constant with time and increases in the antrum layer from a very low value and reaches a constant value close to that of the outer region.

Keywords. Species transport equation, Mass transfer, Follicle, Annular region, Diffusivity

Mathematics Subject Classification (2020). 76Rxx

1. Introduction

Oxygen and nutrients are very important factors in the growth of any human being. The ovarian follicle is also not an exception. The growth of ovarian follicles is an interesting phenomenon to observe. It needs nutrients as well as oxygen supply in order to grow. Understanding this phenomenon need knowledge of ovarian follicle structure, granulosa layer, and vascular thickening. There is a lack of information about this in the literature.

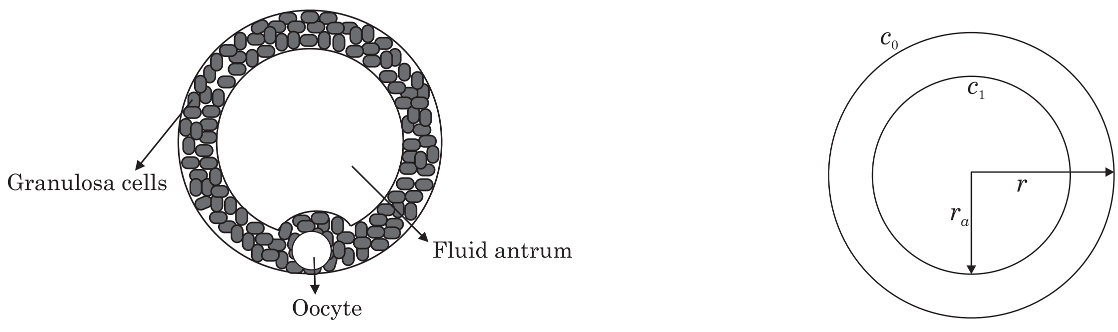
Hirshfield [7] has suggested to us, the thickening of the granulosa layer results in reduced oxygen supply and results in follicle atresia. Gosden and Byatt-Smith [6] have speculated that overcoming a lack of oxygen supply can be possible by antrum formation. Van Blerkom [3] depicts that to overcome this oxygen level inside the follicle might rise. Many researchers in their studies have tried to understand the importance of oxygen and tried to measure dissolved oxygen (see Bhal *et al*. [2], Chui *et al*. [4], and Kim *et al*. [8]).

These difficulties have proved the importance of mathematical modelling of unsteady diffusive mass transfer (oxygen transport). A study conducted by Clark *et al*. [5] on oxygen transport has revealed that the cells consume a small amount of oxygen. Morimoto *et al*. [9] have studied the impact of oxygen supply by supplying high concentrations and found that the development is accelerated. Rodgers and Rodgers [11] have studied the process of antrum formation. Redding *et al*. [10] have developed a mathematical model to study oxygen transport in order to predict whether oxygen reaches oocytes using the same assumption as that of Gosden and Byatt-Smith [6]. The effect of low oxygen levels on granulosa cells has been studied by Baddela *et al*. [1].

In the present study based on Redding *et al*. [10], a mathematical model to study mass transfer with reference to follicle modelled as the annular region is considered by assuming unsteady diffusive mass transfer. Closed-form solutions are obtained analytically and graphically depicted.

2. Mathematical Formulation

The physical configuration is shown in Figure 1. An analogy of a follicle is considered as an annular region where the inner circle represents a fluid-filled antrum and the outer circle represents a granulosa cell-filled layer. Oxygen has to diffuse from the outer layer into the oocyte situated inside in a radial direction.



(a) Actual follicle **(b)** Geometry considered

Figure 1. Physical configuration

The governing equations which describes the oxygen transport in the follicle are:

$$\frac{\partial c_1}{\partial t} = \frac{D_1}{r^2}\frac{d}{dr}\left(r^2\frac{dc_1}{dr}\right) - \alpha_1 c_1 \tag{1}$$

and

$$\frac{\partial c_2}{\partial t} = \frac{D_2}{r^2}\frac{d}{dr}\left(r^2\frac{dc_2}{dr}\right) - \alpha_2 c_2\,, \tag{2}$$

where D_1 and D_2, α_1 and α_2 are the oxygen diffusivity, reaction rate respectively of the follicle. The appropriate boundary conditions for the problem are:

$$\begin{aligned} &c_1 = c_2,\ \ D_1\frac{\partial c_1}{\partial r} = D_2\frac{\partial c_2}{\partial r} \ \text{ at } r = r_f,\\ &c_2 = c_0 \quad \text{at } r = r_a,\\ &c_1 = c_{in} \ \text{ at } r = r_e, \end{aligned} \tag{3}$$

where r_f and r_a are the radius of the follicle and radius of the assumed inner circle, respectively. Using the following dimensionless parameters,

$$c_1^* = \frac{c_1}{c_0},\ \ r^* = \frac{r}{r_a},\ \ t^* = \frac{tD_1}{r_a^2}\,, \tag{4}$$

where the asterisks $(*)$ denote dimensionless quantities.

The equations (1) and (2), after non-dimensionalisation become (after neglecting the asterisks for simplicity),

$$\frac{\partial c_1}{\partial t} = \frac{1}{r^2}\frac{d}{dr}\left(r^2\frac{dc_1}{dr}\right) - \frac{\alpha_1 r_a^2}{D_1}c_1 \tag{5}$$

and

$$\frac{\partial c_2}{\partial t} = \frac{1}{r^2}\frac{d}{dr}\left(r^2\frac{dc_2}{dr}\right) - \frac{\alpha_2 r_a^2}{D_2}c_2\,. \tag{6}$$

Similarly, the boundary conditions become

$$\begin{aligned} &c_1 = c_2,\ \ D_1\frac{\partial c_1}{\partial r} = D_2\frac{\partial c_2}{\partial r} \ \text{ at } r = r_f,\\ &c_2 = 1 \quad \text{at } r = 1,\\ &c_1 = c_0 \ \text{ at } r = r_e\,. \end{aligned} \tag{7}$$

The above equations are reduced using the transformation,

$$c_i = \theta_i(r)e^{-\omega^2 t}, \tag{8}$$

where ω is the frequency.
In view of equation (8), the equations (5) and (6) reduces to,

$$\frac{d^2\theta_i}{dr^2} + \frac{2}{r}\frac{d\theta_i}{dr} - \delta_i^2\theta_i = 0\,, \tag{9}$$

where $\delta_i^2 = \left(\frac{\alpha_i r_a^2}{D_i} - \omega^2\right)\frac{1}{\lambda_i}$ and $\lambda_i = 1$, $i = 1(1)2$.
Similarly, the boundary conditions given in equation (7) reduces to

$$\theta_1 = \theta_2,\ \ \frac{\partial\theta_1}{\partial r} = \lambda\frac{\partial\theta_2}{\partial r} \ \text{ at } r = r_f,$$

$$\theta_2 = 1 \quad \text{at } r = 1,$$
$$\theta_1 = \theta_0 \ \text{ at } r = r_e. \tag{10}$$

The governing equations obtained from equation (9) for $i = 1$ and $i = 2$ can be solved using series solution method and solution is obtained as

$$\theta_1(r) = b_{11}\frac{e^{-\delta_1 r}}{r} + b_{21}\frac{e^{\delta_1 r}}{\delta_1 r} \tag{11}$$

and

$$\theta_2(r) = b_{12}\frac{e^{-\delta_2 r}}{r} + b_{22}\frac{e^{\delta_2 r}}{\delta_2 r}. \tag{12}$$

Using the boundary conditions given in equation (10), we can obtain the following simulataneous equations

$$\begin{aligned} l_{11}a_{31} + l_{21}a_{32} + l_{12}a_{33} + l_{22}a_{34} &= 0,\\ l_{11}a_{41} + l_{21}a_{42} + l_{12}a_{43} + l_{22}a_{44} &= 0,\\ l_{12}a_{23} + l_{22}a_{24} &= 1,\\ l_{11}a_{11} + l_{21}a_{12} &= \theta_0, \end{aligned} \tag{13}$$

where $a_{31} = \frac{e^{-\delta_1 r_f}}{r_f}$, $a_{32} = \frac{e^{-\delta_1 r_f}}{\delta_1 r_f}$, $a_{33} = -\frac{e^{-\delta_2 r_f}}{r_f}$, $a_{34} = -\frac{e^{-\delta_2 r_f}}{\delta_2 r_f}$, $a_{41} = -\left[\frac{1+\delta_1 r_f}{r_f^2}\right] e^{-\delta_1 r_f}$, $a_{42} = -\left[\frac{-1+\delta_1 r_f}{\delta_1 r_f^2}\right] e^{\delta_1 r_f}$, $a_{43} = \lambda\left[\frac{1+\delta_2 r_f}{r_f^2}\right] e^{-\delta_2 r_f}$, $a_{44} = -\lambda\left[\frac{-1+\delta_2 r_f}{\delta_2 r_f^2}\right] e^{\delta_2 r_f}$, $a_{23} = e^{-\delta_2}$, $a_{24} = \frac{e^{\delta_2}}{\delta_2}$, $a_{11} = \frac{e^{-\delta_1 r_e}}{r_e}$, $a_{12} = \frac{e^{\delta_1 r_e}}{\delta_1 r_e}$.

Solving the above system of equations, we get the following solution,

$$\begin{aligned} l_{22} &= \frac{f_4}{d_{44}},\\ l_{12} &= \frac{1}{a_{23}}\left[1 - \frac{a_{24}f_4}{d_{44}}\right],\\ l_{21} &= \frac{1}{b_{22}}\left[f_1 - \frac{b_{24}f_4}{d_{44}} - \frac{b_{23}}{a_{23}}\left(1 - \frac{a_{24}f_4}{d_{44}}\right)\right],\\ l_{11} &= \frac{1}{a_{11}}\left[\theta_0 - \frac{a_{12}}{b_{22}}\left\{f_1 - \frac{b_{24}f_4}{d_{44}}\frac{b_{23}}{a_{23}}\left(1 - \frac{a_{24}f_4}{d_{44}}\right)\right\}\right], \end{aligned} \tag{14}$$

where $d_{44} = l_{43}a_{24} - a_{23}l_{44}$, $f_4 = a_{43} - a_{23}f_3$, t $e_{43} = b_{42}b_{23} - b_{22}b_{43}$, $e_{44} = b_{42}b_{24} - b_{22}b_{44}$, $f_3 = b_{42}f_1 - b_{22}f_2$, $b_{22} = a_{31}a_{12} - a_{11}a_{32}$, $b_{23} = -a_{11}a_{33}$, $b_{33} = -a_{11}a_{34}$, $f_1 = a_{31}\theta_0$, $b_{42} = a_{41}a_{12} - a_{11}a_{42}$, $b_{43} = -a_{11}a_{43}$, $b_{44} = -a_{11}a_{44}$, $f_2 = a_{41}\theta_0$.

3. Results and Discussion

The follicle is idealised into an annular region between two circles of radius r_a and r_f. Concentration diffusion in radial direction is obtained analytically and plotted for non-dimensional parameter like diffusivity ratio λ, non-dimensional follicle radius r_f and frequency ω.

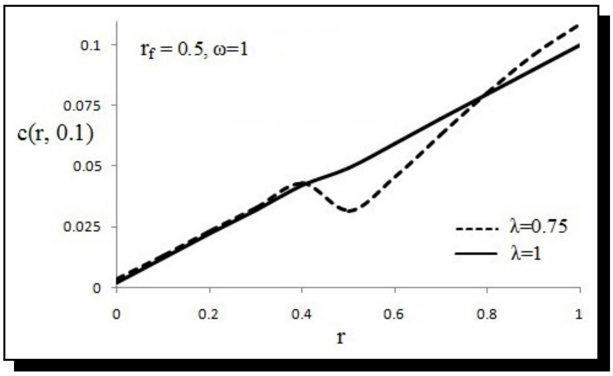


Figure 2. Radial concentration profile for different values of λ

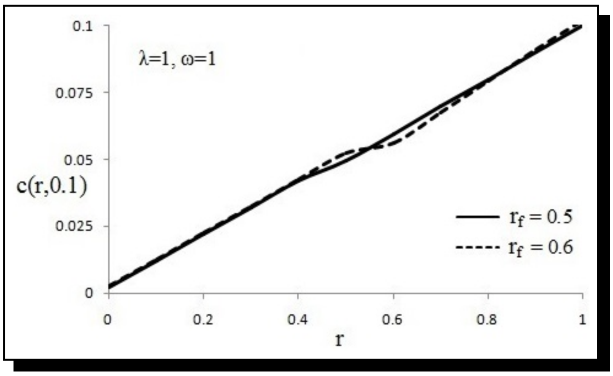


Figure 3. Radial concentration profile for different values of follicle radius r_f

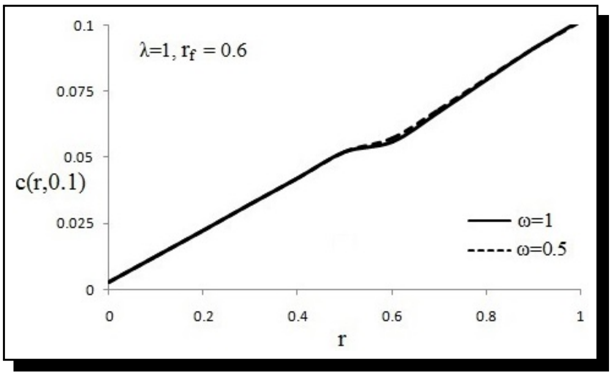


Figure 4. Radial concentration profile for different values of reaction rate ω

Figures 2, 3 and 4 depict the radial concentration profile for different values of λ, r_f and ω, respectively. If diffusivity is considered same in both granulosa as well as surrounding layer, we see that concentration profile increases uniformly from the centre to the outer membrane and at the centre oxygen concentration is higher than zero as predicted by Redding *et al.* [10]. If granulosa layer has lesser diffusivity then we see that concentration decreases a little at the interface and then increases due to higher diffusion rate at surrounding layer. If the radius of antrum is higher, then the same feature of slight decrease at the interface is seen. This is due to more consumption of oxygen by surround cells of the granulosa. ω does not show much effect in the oxygen supply.

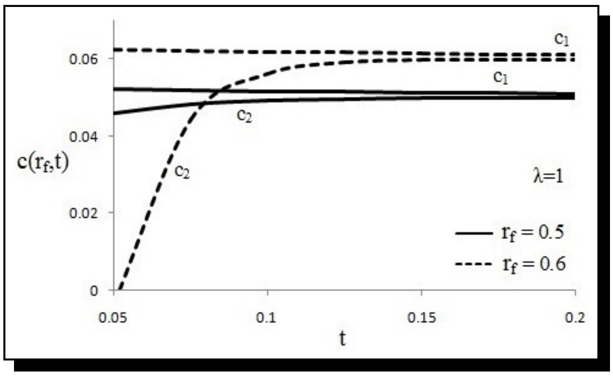


Figure 5. Plot of concentration vs time for different values of reaction rate ω

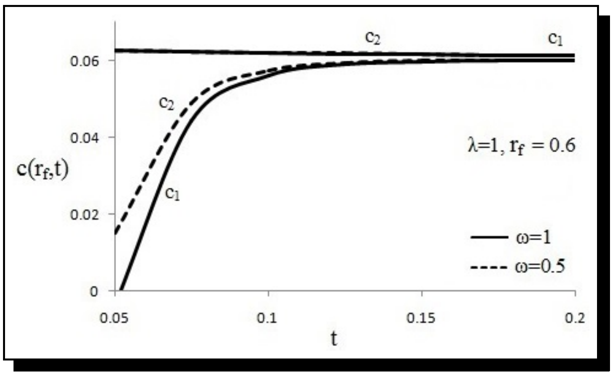


Figure 6. Plot of concentration vs time for different values of reaction rate ω

Figures 5 and 6 shows the plot of concentration vs. time for different radius and frequency (ω). We see that c_1 remains almost constant where as c_2 increases from close to zero to a constant value almost equal to c_1. As time progresses both concentration reach a constant level, where c_2 is slightly less than c_1. This shows that some amount of oxygen gets stored in the granulosa region from consumption of growing antrum.

4. Conclusions

The follicle is initiated inside the cellular domain of the oocyte. The region actually behaves like a packed, porous medium. As the follicle grows, the liquid-filled central area starts decreasing, and the cellular outer covering expands. This situation is represented as a concentric annular region with an increasing follicle radius and decreasing inner radius. Since a simple model is adopted here, the time dependency of the radius is not considered since the study focused on the supply of oxygen to the follicle. The concentration in inner and outer regions is plotted. In the inner region, which is a fluid region, due to the lack of cells, oxygen is constant, while in the outer region, it increases with time and reaches a constant over time. The advantage of the present model is that fewer parameters are required for the study. This can be improved by considering moving the inner boundary with a decreasing time dependent radius. The diffusivity of oxygen is the main contributor for the transport in the region around follicles.

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Competing Interests

The authors declare that they have no competing interests.

Authors' Contributions

All the authors contributed significantly in writing this article. The authors read and approved the final manuscript.

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