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A NUMERICAL MODEL TO STUDY THE ROLE OF ADVECTION DIFFUSION OF Ca^{2+} IN MONITORING FREE Ca^{2+} CONCENTRATION IN PRESENCE OF BUFFER

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Abstract: Astrocytes are directly involved in synaptic processes, and may more actively contribute to the information processing in the brain than previously thought. Ca^{2+} signalling appears to provide the most versatile and crucial mechanisms for such a glial contribution. Intracellular calcium distribution is responsible to maintaining the cellular metabolic functions. Many factors that affect the cytosolic calcium concentration in Astrocytes. The main objective of this paper to study the effect of advection diffusion of cytosolic calcium concentration in Astrocytes in presence of buffers. A mathematical model is developed in the form of advection diffusion equation. Interdependence of all the important parameters like immobile buffer, diffusion coefficient and influx over $[Ca^{2+}]$ profile has been studied. it is found that advection has significant effect in the presence of low affinity buffer but in the presence of high affinity buffer advection term does not show much effect on calcium concentration in

nerve cells like astrocytes.

AMS Subject Classification: 92C20
Key Words: advection diffusion, buffer, FVM, astrocytes

1. Introduction

Calcium is an important second messenger, found in almost all types of cell. The dynamics of calcium Ca^{2+} is very important in cellular physiology because Ca^{2+} binds to many proteins and regulates their activity and interactions. The precise mechanism governing the initiation and propagation of astrocytic Ca^{2+} waves are not completely understood. Ca^{2+} waves are dependent on the diffusion of Ca^{2+} ions both within and possibly between the cells; modulating Ca^{2+} ion diffusion may predictably alter the spatial and temporal character of the Ca^{2+} wave. The astrocytic Ca^{2+} signalling depend of Ca^{2+} buffering. This effect is a function of both the Ca^{2+} affinity and the quantity of the exogenous buffer. Experimentally Wang et al (1997) first reported and illustrate directly that cytoplasmic calcium buffering constitutes an important and powerful mechanism for modulating astrocytic Ca^{2+} waves [11]. Most of this work has been done on neuron cell [2,5,6,7].

From the above literature survey, it is clear that almost all the models have been developed incorporating diffusion of calcium [1, 2, 6, 7, 9, 10]. Actually when calcium molecules enters into the cytosol it moves randomly. Due to random movement we have considered lateral diffusion of calcium molecules also. This has not been taken so far by research workers as evident from the literature survey. In view of above, Jha, Adlakha and Mehta have developed a model to study advection diffusion of calcium in astrocytes [3, 4]. Now the combined effect of buffer and advection diffusion is studied with flux across the plasma membrane. Finite volume method is applied to solve the problem [2, 4, 8].

2. Mathematical Formulation

Calcium kinetics in astrocytes is governed by a set of reaction-diffusion equations which can be framed assuming the following bimolecular reaction between Ca^{2+} and buffer species:

$$\left[Ca^{2+}\right] + [B_j] \underset{k^-}{\overset{k_j^+}{\leftrightarrow}} [CaB_j] \tag{1}$$

where $[B_j]$ and $[CaB_j]$ are free and bound buffer respectively , and j is an index over buffer species. where k_j^+ andk_j^- are association and dissociation rate constants for buffer j respectively. The resulting partial differential equation for equation (1) using fickian diffusion can be stated as [5].

$$D_{Ca}\frac{d^2\left[Ca^{2+}\right]}{dx^2} - v\frac{d\left[Ca^{2+}\right]}{dx} - R_j + f(Ca^{2+}) = 0 \tag{2}$$

where

$$R_j = -k_j^+\left[B_j\right]\left[Ca^{2+}\right] + k_j^-\left[CaB_j\right] \tag{3}$$

$$f(C) = J_{in} - J_{out} \tag{4}$$

D_{Ca} is diffusion coefficients of free calcium. $[Ca^{2+}]_\infty$is background calcium concentration. where J_{in} and J_{out} are Ca^{2+} influx across the plasma membrane, and Ca^{2+} extrusion. Along with the boundary conditions

$$\lim_{x\to 0}(-D_{Ca}\frac{\partial\left[Ca^{2+}\right]}{\partial x}) = \sigma_{Ca} \tag{5}$$

$$\lim_{x\to 0}\left[Ca^{2+}\right] = 0.1\mu M \tag{6}$$

The finite volume scheme is employed to solve equation (2) together with (5) and (6). In order to apply the finite volume method the domain is divided into discrete control volumes. taking 30 nodal points in the space between A and B. Each node is surrounded by a control volume or cell. A general nodal point is identified by P and its neighbours in a one-dimensional geometry, the nodes to the west and east, are identified by W and E respectively. The west sides face of the control volume is referred by w and the east side control volume face by e. The distances between the nodes W and P, and between nodes P and E, are identified by . Similarly the distance between face w and point P and between P and face e are denoted by $\delta x/2$. Nodal values to the east and west are available at nodal values 2, 3, 4.....29.

The biophysical parameters used in the model are as stated in the table below unless stated along with figures. A MATLAB program has been developed using finite volume method for the entire problem and simulated on an AMD-Turion 32-bit machine to compute the numerical results.

Figure 1 (a) shows the variation of calcium with the space for different values of speed of advective flux u and BAPTA. Since BAPTA has high affinity for calcium concentration so calcium concentration decreases rapidly from to $x = 0$ to $x = 5\mu m$ and then after become constant . Thus the effect of BAPTA shows more significant than the EGTA.

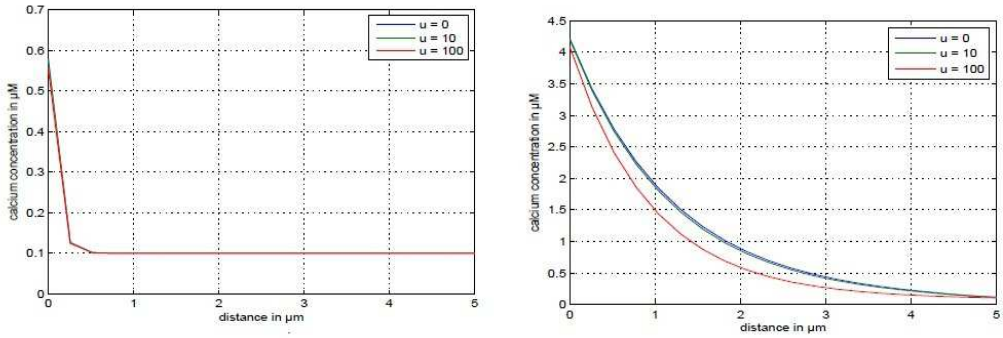

Figure 1: Spatial variation of calcium for different values of u for EGTA

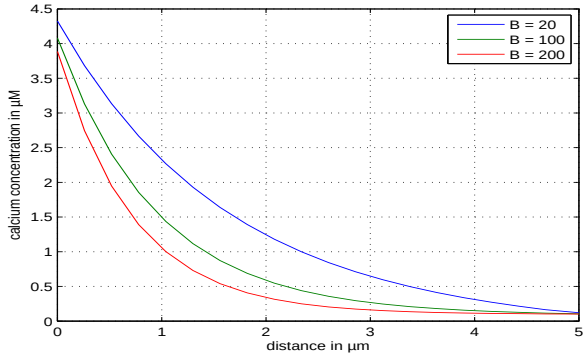

Figure 2: Spatial variation of calcium for different values of buffer B

Figure 1 (b) shows the variation of calcium with the space for different values of speed of advective flux u and EGTA. It is observed that calcium concentration is higher at lower speed throughout from to and there after converges to at i.e. near the source this difference in calcium concentration is quite significant and decreases gradually as we move away from the source. Figure 2 shows the variation of calcium with the space for different values of buffer concentration. It is observed that calcium concentration decrease more rapidly as buffer concentration increased and finally become constant as we moves away from the source i.e. near the source this difference in calcium concentration is quite significant and decreases gradually as we move away from the source.

3. Conclusion

It is observed that calcium buffering activity has significant effect. Calcium concentration gives better central regions little away from the source. Advection of calcium molecule has significant effect for low affinity buffer but in the case of high affinity buffer it show less change in calcium profile. The FVM developed here gives us quite interesting results, as such models can be developed to generate information about relationship among physical and physiological parameter in word in the problem and give us better insights and understanding of the chemical signaling phenomena in Astrocytes.

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