World Academy of Science, Engineering and Technology
International Journal of Mathematical and Computational Sciences
Vol:5, No:8, 2011

Closed Form Solution to problem of Calcium Diffusion in Cylindrical Shaped Neuron Cell

Amrita Tripathi and Neeru Adlakha

Abstract—Calcium $[Ca^{2+}]$ dynamics is studied as a potential form of neuron excitability that can control many irregular processes like metabolism, secretion etc. Ca^{2+} ion enters presynaptic terminal and increases the synaptic strength and thus triggers the neurotransmitter release. The modeling and analysis of calcium dynamics in neuron cell becomes necessary for deeper understanding of the processes involved. A mathematical model has been developed for cylindrical shaped neuron cell by incorporating physiological parameters like buffer, diffusion coefficient, and association rate. Appropriate initial and boundary conditions have been framed. The closed form solution has been developed in terms of modified Bessel function. A computer program has been developed in MATLAB 7.11 for the whole approach.

Keywords—Laplace Transform, Modified Bessel function, reaction diffusion equation, diffusion coefficient, excess buffer, calcium influx .

I. Introduction

CALCIUM $[Ca^{2+}]$ domains are of importance for understanding fast $[Ca^{2+}]$ entry through the synaptic transmission. Synaptic transmission is the process that regulates the information from one part of the body to other part through the chemical molecules. Calcium dynamics provides the better understanding of chemical signaling in neuron cell.
Mathematical modelling has played the crucial role in solving many real life problems. The development of digital computers and computational sciences has increased the scope of application of mathematics, in solving problems of science, technology and biology etc. The problem of biology is more challenging for mathematics in comparison to the problem of science and technology. The analytical and numerical techniques have been widely used by the research workers in biology science and technology etc. However it is preferable to obtain analytical solution than a numerical solution to any problem. But when we include more-more details of parameters and the problem becomes more complicated and analytical methods fails in giving solution of such problems. Thus one has to switch over to numerical techniques for solution. Here an attempt has been made to use analytical method in solving one dimensional problem of calcium diffusion in neuron cell. The analytical description of mathematical model is given by [5, 8, 14].

$$\frac{\partial\left[Ca^{2+}\right]}{\partial t}=D_{Ca}\bigtriangledown^{2}\left[Ca^{2+}\right]-k_{m}^{+}\left[B\right]_{\infty}\left(\left[Ca^{2+}\right]-\left[Ca^{2+}\right]_{\infty}\right) \tag{1}$$

The calcium kinetics in neuron is governed by a set of reaction-diffusion equation given by [7, 13, 1]:

$$\left[Ca^{2+}\right]+\left[B_{j}\right]\underset{k^{-}}{\overset{k^{+}}{\leftrightarrow}}\left[CaB_{j}\right] \tag{2}$$

$$\frac{\partial\left[Ca^{2+}\right]}{\partial t}=D_{Ca}\left(\frac{1}{r}\frac{\partial}{\partial r}\left(r\frac{\partial\left[Ca^{2+}\right]}{\partial r}\right)\right)+\Sigma_{j}R_{j}+\delta\left(r\right) \tag{3}$$

$$\frac{\partial\left[B_{j}\right]}{\partial t}=D_{B_{j}}\left(\frac{1}{r}\frac{\partial}{\partial r}\left(r\frac{\partial\left[B_{j}\right]}{\partial r}\right)\right)+R_{j} \tag{4}$$

$$\frac{\partial\left[CaB_{j}\right]}{\partial t}=D_{CaB_{j}}\left(\frac{1}{r}\frac{\partial}{\partial r}\left(r\frac{\partial\left[CaB_{j}\right]}{\partial r}\right)\right)-R_{j} \tag{5}$$

Where

$$R_{j}=-k_{j}^{+}\left[B_{j}\right]\left[Ca^{2+}\right]+k_{j}^{-}\left[CaB_{j}\right] \tag{6}$$

where $[B_j]$ and $[CaB_j]$ are free and bound buffer respectively. j is an index over buffer species. The resulting partial differential equations for equation (1) using Fickian diffusion can be stated as [8]. $D_{Ca}, D_{B_j}, D_{CaB_j}$ are diffusion coefficients of free calcium, free buffer and Ca^{2+} bound buffer respectively. k_j^+ andk_j^- are association and dissociation rate constants for buffer j respectively. $[Ca^{2+}]_\infty$ is background calcium concentration. For stationary immobile buffers or fixed buffers.

Initial studies were the experimental investigations made with fruitful results by T. Meyer and L. Stryer [18], obtained the results using the molecular modelling for receptor of Calcium profile. E. Neher [5], they performed analysis on the linearized buffered $[Ca^{2+}]$ diffusion in micro domains; Smith and Keizer [12] modeled the above-mentioned phenomenon for a spherically symmetric region to estimate rapid buffering approximation near an open $[Ca^{2+}]$ channel. Some theoretical investigations have also been carried out during the last few decades. K. R. Pardasani and N. Adlakha [15] give the exact solution of to a Heat Flow Problem in Peripheral Tissue Layers with a Solid Tumor in the Dermis. S. Tewari and K. R. Pardasani [16] studied the finite element model to study the cytosolic $[Ca^{2+}]$ concentration with one and two dimensions. S. Tewari and K. R. Pardasani [17] obtained the solution of existing mathematical model of system of reaction-diffusion equations of cytosolic $[Ca^{2+}]$ concentration for excess buffer

A. Tripathi is Research Scholar with the Department of Applied Mathematics S. V. National Institute of Technology, Surat, INDIA, (phone-919662932581,e-mail:t.amrita@ashd.svnit.ac.in ,tripathi.amrita28@gmail.com)
N. Adlakha is Associate Professor with the Department of Applied Mathematics S. V. National Institute of Technology, Surat India,(e-mail: nad@ashd.svnit.ac.in)

approximation (EBA) and other is rapid buffer approximation (RBA). B. Jha et al.[4] studied the Finite Volume Model to Study the Effect of Buffer on Cytosolic Ca^{2+} Advection Diffusion in astrocyte cell. A. Tripathi and N. Adlakha [1] obtained the finite volume model to study calcium diffusion in spherical shaped neuron cell. A. Tripathi and N. Adlakha N [2, 3] have also obtained the calcium distribution in neuron cell using finite element method for one and two dimensions in polar coordinates. Here an attempt has been made to study $[Ca^{2+}]$ dynamics in neuron cell by using modified Bessel function for one dimensional unsteady state case in polar cylindrical coordinates. A computer program has been developed in MATLAB 7.11 for the entire problem and simulated on Core i3 processor with 2.13 GHz processing speed, 64-bit machine with 320 GB memory. Numerical values of physiological parameters have been used to study the calcium concentration.

II. Mathematical Formulation

The model given by equation (1) has been developed in polar cylindrical coordinates for a one-dimensional unsteady state case as:

$$\begin{aligned}\frac{\partial\left[Ca^{2+}\right]}{\partial t} &= D_{Ca}\left(\frac{\partial^2}{\partial r^2}+\frac{1}{r}\frac{\partial}{\partial r}\right)\left[Ca^{2+}\right] \\ &- k_m^+\left[B\right]_\infty\left(\left[Ca^{2+}\right]-\left[Ca^{2+}\right]_\infty\right) \quad (7)\end{aligned}$$

Where $[B]_\infty$ and $[Ca^{2+}]_\infty$are the buffer concentration and calcium concentration respectively. It is assumed that neuron is of cylindrical shape and radius r=5μm [19].

The initial and boundary conditions governing the calcium diffusion are given by:
Initial Condition

$$\left[Ca^{2+}\right]_{t=0}=0.1\mu M \quad (8)$$

Boundary Conditions
At r=0, assuming the point source of calcium concentration. Thus boundary condition can be given as [6, 19]:

$$\lim_{r\to 0}(-2\pi r D_{Ca}\frac{\partial\left[Ca^{2+}\right]}{\partial r})=\sigma_{Ca} \quad (9)$$

It is also assumed that background concentration of $[Ca^{2+}]$ is 0.1 μ M and as it goes far away from the source boundary condition:

$$\lim_{r\to 5}\left[Ca^{2+}\right]=0.1\mu M \quad (10)$$

Using suitable transformation, the problem is transformed into simpler form without making any further simplifying any assumptions and retaining the realistic properties of parameters:
Substituting $\overline{[Ca^{2+}]}$=$[Ca^{2+}]$-$[Ca^{2+}]_\infty$ in equation (7-10), the following partial differential equation is obtained:

$$\frac{1}{D_{Ca}}\frac{\partial\overline{[Ca^{2+}]}}{\partial t}=\left(\frac{\partial^2}{\partial r^2}+\frac{1}{r}\frac{\partial}{\partial r}\right)\overline{[Ca^{2+}]}-\frac{\lambda}{D_{Ca}}\overline{[Ca^{2+}]} \quad (11)$$

The transformed initial and boundary conditions are given by:

$$\overline{[Ca^{2+}]}_{t=0}=0 \quad (12)$$

$$\lim_{r\to 0}(-2\pi r D_{Ca}\frac{\partial\overline{[Ca^{2+}]}}{\partial r})=\sigma_{Ca} \quad (13)$$

$$\lim_{r\to 5}\overline{[Ca^{2+}]}=0 \quad (14)$$

Applying Laplace transform [11] on both sides of the equation (11-14) we get the following solution,

$$\left(\frac{d^2[\widehat{Ca^{2+}}]}{dr^2}+\frac{1}{r}\frac{d[\widehat{Ca^{2+}}]}{dr}\right)-\left(\frac{s+\lambda}{D_{Ca}}\right)[\widehat{Ca^{2+}}]=0 \quad (15)$$

Where $[\widehat{Ca^{2+}}]$ is the Laplace transforms of $\overline{[Ca^{2+}]}$ and transformed initial and boundary conditions are:

$$[\widehat{Ca^{2+}}]_{t=0}=0 \quad (16)$$

$$\lim_{r\to 0}(-2\pi r D_{Ca}\frac{d[\widehat{Ca^{2+}}]}{dr})=\frac{\sigma_{Ca}}{s} \quad (17)$$

$$\lim_{r\to 5}[\widehat{Ca^{2+}}]=0 \quad (18)$$

$$r^2[\widehat{Ca^{2+}}]+r[\widehat{Ca^{2+}}]-r^2\left(\frac{s+\lambda}{D_{Ca}}\right)[\widehat{Ca^{2+}}] \quad (19)$$

After using the transformations, the realistic properties of parameters, such that analytical solution is obtained in terms of modified Bessel function. The solution of Bessel equation (19) is,

$$[\widehat{Ca^{2+}}](r,s)=C_1 I_0\left(\sqrt{\frac{s+\lambda}{D_{Ca}}}\right)r+C_2 K_0\left(\sqrt{\frac{s+\lambda}{D_{Ca}}}\right)r \quad (20)$$

At the solution r $\to\infty$ is not finite, it becomes:

$$[\widehat{Ca^{2+}}](r,s)=C_2 K_0\left(\sqrt{\frac{s+\lambda}{D_{Ca}}}\right)r \quad (21)$$

$$C_2=-\frac{\sigma_{Ca}}{2\pi r D_{Ca}s}$$

Finally taking inverse Laplace transform of equation (21) we get the following solutions,

$$\left[Ca^{2+}\right]=\frac{\sigma_{Ca}}{4\pi r D_{Ca}}\exp\left(\frac{-r^2\lambda}{4D_{Ca}t}\right)+\left[Ca^{2+}\right]_\infty \quad (22)$$

where

$$\lambda=k_m^+\left[B\right]_\infty$$

TABLE I
LIST OF PHYSIOLOGICAL PARAMETERS USED IN NUMERICAL RESULTS

Symbol	Parameter	Values
D_{Ca}	diffusion coefficient	250 $\mu m^2/s$
k_j^+ EGTA	buffer association rate	1.5 $\mu M^{-1}s^{-1}$
k_j^+ BAPTA	buffer association rate	600 $\mu M^{-1}s^{-1}$
k_j^+ Troponine	buffer association rate	90 $\mu M^{-1}s^{-1}$
k_j^+ Calmodulin	buffer association rate	250 $\mu M^{-1}s^{-1}$
$[B]_\infty$	total buffer concentration	$50\mu M$
$[Ca^{2+}]_\infty$	background Calcium concentration	$0.1\mu M$
σ	flux	$1pA$
r	radius	$5\mu m$

III. RESULTS AND DISCUSSION

The numerical values of physical and physiological parameters used for computation of numerical results are given:
m=meter, s= second, M= Mole

Fig. 1 shows the radial distribution of calcium concentration in neuron cell for exogenous buffer EGTA and BAPTA at buffer concentration taken to be 50 μM. The Ca^{2+} concentration is maximum near the source along radial direction. The Ca^{2+} concentration near the source for EGTA is very significantly high than that for BAPTA. For EGTA is Ca^{2+} concentration false down sharply between r=0 μm to r=0.5 μm, and then falls down gradually between from r=0.5 μm to r=1.5 μm and finally converges its minimum value of Ca^{2+} profile 0.1 μM. For BAPTA the maximum Ca^{2+} concentration near the source is 0.4 μM and falls down gradually between r=0 μm to r=0.5 μm and again its minimum value of Ca^{2+} its 0.1 μM beyond r=5 μ m. The difference in EGTA and BAPTA is due to the fact that EGTA is slow buffer and BAPTA is fast chelator.

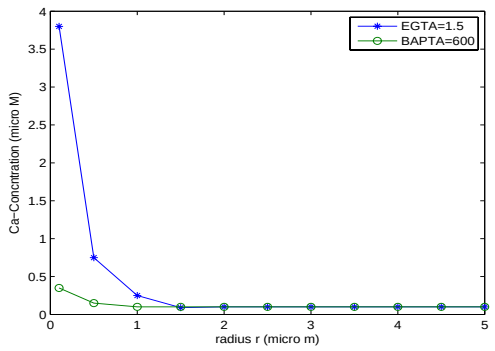

Fig. 1. Radial distribution of calcium concentration for the exogenous buffers EGTA and BAPTA

Fig. 2 shows the radial distribution of calcium concentration in neuron cell for endogenous buffer the $\wedge$ curve represents Troponine-c and ':' curve represents Calmoduline-D28k.at buffer concentration taken to be 50 μM. The Ca^{2+} concentration is maximum near the source along radial direction. The Ca^{2+} concentration near the source for Troponine is very significantly high than that for Colmoduline. For Troponine is Ca^{2+} concentration false down sharply between r=0 μm to r=0.5 μm, and then becomes constant between r=0.5 μm to r=5 μm and finally approaches its minimum value of Ca^{2+} profile 0.1 μM. For Colmoduline the maximum Ca^{2+} concentration near the source is 1.2 μM and falls down sharply between r=0 μm to r=0.5 μm and again its minimum value of Ca^{2+} its 0.1 μM beyond r=5 μm. The difference in Troponine and Colmoduline is due to the fact that Troponine is slow chelator and Colmoduline is fast chelator.

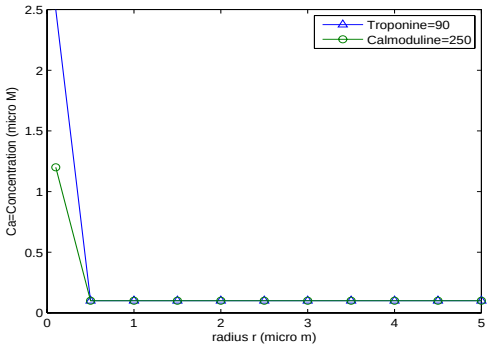

Fig. 2. Radial distribution of calcium concentration for the endogenous buffers Troponine and colmoduline

Fig. 3 shows the radial distribution on Ca^{2+} concentration profiles for EGTA buffer with buffer concentration 50 μM and different values of flux. It is observed that the calcium concentration is higher for higher values of flux sigma= 4 pA this profile near the source and they converge to Ca^{2+} concentration is 0.1 μM after r=1.5 μm. This implies that the flux is significant effect on Ca^{2+} concentration near the source.

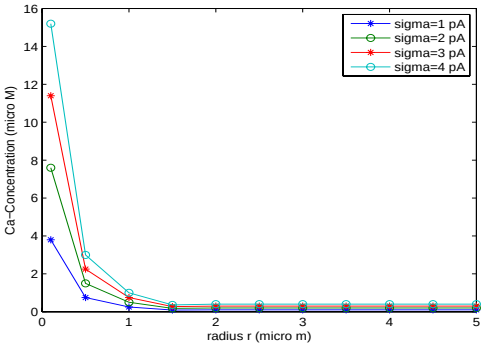

Fig. 3. Radial distribution of calcium concentration with different values of flux

Fig. 4 shows the temporal variation on calcium concentration profiles, at radial points (r = 1 μm, 2.5 μm, 5 μm) for diffusion cofficient 250. The Ca^{2+} concentration rises sharply at the free radial points between t=0 ms to t=10 ms, and there after achieve the steady states. The rising concentration profiles much higher at radial point 1 μm that is near the

source as compared to that at other radial points away from the source.

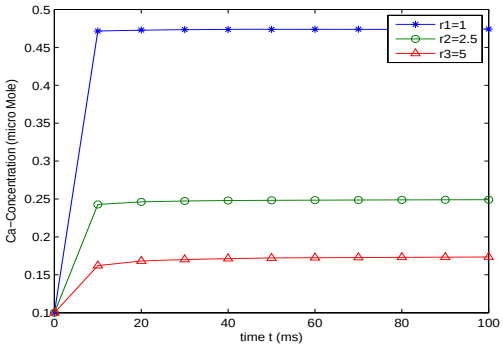

Fig. 4. Temporal distribution of calcium concentration with different values of radius at diffusion coefficient 250

Fig. 5 also shows temporal variation on Ca^{2+} concentration diffusion cofficient 10 at different radial points. The rise in Ca^{2+} concentration is significantly high at radial point r= 1 μm between t=0 ms to 100 ms in comparison to that at other radial points away from the source. On comparing figure 4 and 5 that rise in Ca^{2+} concentration for diffusion cofficient 10 is high value in comparison for longer period of time in that for diffusion cofficient 250 that where the rise in Ca^{2+} profile is very sharp for a small period of time. This is because, the diffusion cofficient is directly prapotional to Ca^{2+} concentration.

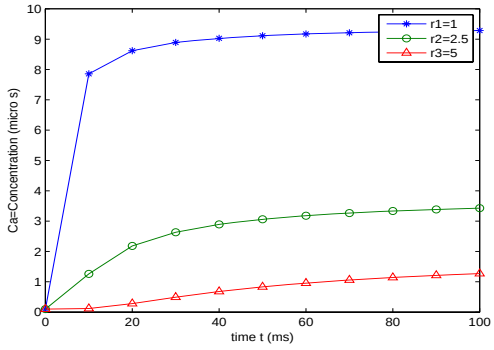

Fig. 5. Temporal distribution of calcium concentration with different values of radius at diffusion coefficient 10

IV. Conclusion

The mathematical models developed give us interesting results regarding relationships among various parameters like Ca-concentration, diffusion coefficients, radius, buffer etc. such models can be developed to generate information for better insights and understanding of the problem.

References

[1] A. Tripathi and N. Adlakha Finite Volume Model to Study Calcium Diffusion in Neuron Cell under Excess Buffer Approximation International J. of Math. Sci. and Engg. Appls. (2011), vol. 5 No III, 437-447

[2] A. Tripathi and N. Adlakha Finite Element Model to Study Calcium Diffusion in Neuron Cell in Presence of Excess Buffer for One Dimensional Steady State Global Journal of Computational Science and Mathematics (2011), vol I No. I 21-30

[3] A. Tripathi and N. Adlakha Two Dimensional Coaxial Circular Elements in FEM to Study Calcium Diffusion in Neuron Cells Applied Mathematical Sciences paper accepted

[4] B. Jha N. Adlakha and M. N. Mehta Finite Volume Model to Study the Effect of Buffer on Cytosolic Ca^{2+} Advection Diffusion World Academy of Science, Engineering and Technology (2011) 75, 983-986

[5] E. Neher, Concentration profiles of intracellular Ca^{2+} in the presence of diffusible chelator. Exp. Brain Res. Ser, 14 (1986) 80-96

[6] G.D. Smith, L. Dai, R. M. Miura, and A. Sherman, Asymptotic analysis of buffered calcium diffusion near a point source, SIAM J. of Applied of Math (2001), vol.61 1816-1838.

[7] G. D. Smith Modeling Intracellular Calcium diffusion, dynamics and domains (2004) 339-371 No(10)

[8] G. D. Smith Analytical Steady-State Solution to the Rapid Buffering Approximation near an open $Ca^{2+}|$ Channel Biophys J (1996), 71 (6), 30643072

[9] G. D. Smith and J. Keizer Spark- to-wave transition: salutatory transmission of $Ca^{2+}|$ waves in cadiac mayocytes Biophys Chem (1998), 72 (1-2), 87-100

[10] J. Crank The mathematics of diffusion (1975), Oxford, U.K.: Clarendon Press

[11] J. L. Schiff The Laplace Transform and its Applications Springer-verleg New York Berlin Heidelberg(1988) , ISBN-0-387-98698-7 1-2

[12] L. Fain Gordon Molecular and Cellular Physiology of Neuron (2005), Prentice- Hall of India;

[13] J Means, Smith, shephered, F. shaded. D. Smith, Wilson and M Wojcikiewicz, Reaction Diffusion Modeling of Calcium Dynamics with Realistic ER Geometry (2006), Biophys J, vol (91), 537-557

[14] J. Wanger and J. Keizer Effect of rapid buffers on $Ca^{2+}|$ diffusion and $Ca^{2+}|$ Oscillations (1994) Biophys. J. 447- 456

[15] K. R. Pardasani and N. Adlakha Exact Solution to a Heat Flow Problem in Peripheral Tissue Layers with a Solid Tumor in the Dermis Indian J. of Pure and Applied Mathematics(1991) 22(8), 679-687

[16] S. Tewari and K. R. Pardasani Finite Element Model to Study Two Dimensional Unsteady State Cytosolic Calcium Diffusion in Presence of Excess Buffers, IAENG International Journal of Applied Mathematics (2010), 40:3, IJAM-40-3-01

[17] S. Tewari and K. R. Pardasani Finite Difference Model to Study the effects of $Na^{+}|$ Influx on Cytosolic $Ca^{2+}|$ Diffusion International journal of Biological and Medical Sciences (2009) 205-209

[18] T. Meyer and L. Stryer Molecular Model for Receptor- Stimulated Calcium 5. Spiking (1988), PNAS, vol. 85 no. 14 5051-5055

[19] Y. Tang T. Schlumpberger T. Kim, M. Lueker and R.S. Zucker Effects of Mobile Buffers on Facilitation: Experimental and Computational Studies (2000), Biophys. J., 78, 27352751