BULLETIN OF BIOMATHEMATICS

Bulletin of Biomathematics, 2023, 1(1), 24–39

https://bulletinbiomath.org
ISSN Online: 2980-1869 / Open Access
https://doi.org/10.59292/bulletinbiomath.2023002

RESEARCH PAPER

Analysis of the disturbance effect in intracellular calcium dynamic on fibroblast cells with an exponential kernel law

Hardik Joshi [1,*,‡], **Mehmet Yavuz** [2,‡] **and Ivanka Stamova** [3,‡]

[1]Department of Mathematics, LJ Institute of Engineering and Technology, LJ University, Ahmedabad-382210, India, [2]Department of Mathematics and Computer Sciences, Necmettin Erbakan University, 42090 Konya, Türkiye, [3]Department of Mathematics, The University of Texas at San Antonio, San Antonio, TX 78249, USA

*Corresponding Author
‡ hardik.joshi8185@gmail.com (Hardik Joshi); mehmetyavuz@erbakan.edu.tr (Mehmet Yavuz); Ivanka.Stamova@utsa.edu (Ivanka Stamova)

Abstract

The maintenance of free calcium in the cytoplasm is requisite for cell integrity and the regime of the multi-cellular process. Overproduction and degradation to manage this cellular entity produce offensive changes in tissue performance and as a result, commence fibrotic diseases. Thus, there is a necessity to know the cellular process for the inclusion and extrusion of free calcium. Here, a mathematical model is framed to investigate the role of buffer and calcium concentration on fibroblast cells. In this context, the Caputo-Fabrizio advection reaction-diffusion model along with apposite biophysical initial and boundary conditions is considered. The analytical solution is obtained and used to analyze the diverse mechanisms of calcium on fibroblast cells. The obtained results reveal that when the fractional order goes to one, the Caputo–Fabrizio fractional derivative provides a concise calcium profile and well-managed cellular entity due to the exponential kernel law.

Keywords: Calcium concentration; buffer; fibroblast cells; fractional advection reaction-diffusion equation; Caputo-Fabrizio fractional derivative

AMS 2020 Classification: 26A33, 35Q92, 35R11, 92B05, 97M10

1 Introduction

Fibroblast is non-excitable and heterogeneous structural cells whose primary function is the production of extracellular matrix for tissue maintenance and repair. It plays a pivotal role in maintaining tissue integrity, and in healing processes. They participate in fibrotic disorders in the lung, skin, and other tissues. All these events are closely related to another mechanism in cells, particularly with the signals from the local environment or extracellular medium and the

➤ **Received:** 18.03.2023 ➤ **Revised:** 18.04.2023 ➤ **Accepted:** 23.04.2023 ➤ **Published:** 30.04.2023

calcium diffusion mechanisms [1]. Calcium ion acts as a messenger to perform all these functions in fibroblasts cell. Fibroblast cell regulates calcium concentration at different levels in response to the requirements for activation and performance of various physiological processes like wound healing, tissue remodeling, and tissue growth. This calcium regulation mechanism and the calcium concentration levels are required for cellular activities and their maintenance [2]. Therefore, it is necessary to understand calcium regulation processes in fibroblast cells. This calcium regulation mechanism involves processes like diffusion, advection, flux, and buffering phenomena.

Buffer binds the excess calcium present in the cell to form bound buffers and lower the calcium concentration in the cell [3]. The calcium in excess of a limit for a longer span will be toxic and can cause cell death [4]. On the requirement for a higher concentration of calcium for any physiological process in fibroblast cells, these bound buffers release it to fulfill the requirement. Thus, the buffers act as stores of calcium concentration and also perform functions like source and sinks to regulate the concentration levels.

Experimental studies have shown that fibroblast shows excitability in particular growth stages. The excitability of a cell is an important mechanism in calcium signaling since a strong interplay exists between the membrane potential and the internal calcium concentration. The increase in intracellular calcium associated with action potentials provides a mechanism for long-range and fast-coordinated calcium signaling in excitable cells. Although in-excitable cells it has been reported that fibroblast functions are unclear. Thus to fully understand the calcium regulation mechanisms in fibroblast cells, it will be important to understand the local changes in calcium levels.

Several theoretical investigations are reported in the literature to study calcium dynamics in fibroblast cells [5, 6]. Also, some mathematical model has been developed in the literature to study calcium dynamics in astrocyte [7–9], neuron [10–18], myocytes [19], oocyte [20, 21], T lymphocyte [22, 23], cholangiocyte [24] and another cell. But, no attempt is reported in the literature to study the effect of disturbances in intracellular calcium dynamic on fibroblast cells with an exponential kernel law. In the view of above, here an attempt has been made to develop a mathematical model to investigate the role of buffer and calcium concentration on fibroblast cells with the Caputo-Fabrizio fractional operator. To the best of the author's knowledge, no attempts are registered to investigate the effect of calcium dynamics on fibroblast cells by using fractional calculus approaches. Fractional derivative is a natural extension of classical derivative to study differential equations with a memory-dependent derivative [25–30]. Fractional derivative provides great freedom for the choice of order of derivative and thus illustrates the reality of complex phenomena in a more understanding and expressive way [31–37]. In this attempt, we use the Caputo-Fabrizio derivative due to its non-singular exponential kernel.

The structure of the paper is as follows: In Section 2, we introduce some mathematical preliminaries. In Section 3, we developed the Caputo-Fabrizio advection reaction-diffusion model for calcium dynamics in fibroblast cells. In Section 4, we present numerical simulations for various physiological conditions of the calcium model. Finally, the conclusion is provided in section 5.

2 Mathematical preliminaries

In this section, some preliminaries are provided about the Caputo-Fabrizio fractional derivative with a nonsingular kernel. According to [26], the formal definition of Caputo-Fabrizio fractional derivatives is defined as follows:

Definition 1 *Let $f \in H^1(x, y)$, with $y > x$, then the Caputo-Fabrizio derivative of function $f(t)$ of order*

$\alpha \in [0,1]$ *is defined as*

$$ {}^{CF}D_t^{\alpha} f(t) = \frac{M(\alpha)}{1-\alpha} \int_x^t f'(w) \exp\left[-\alpha \frac{t-w}{1-\alpha}\right] dw, \tag{1} $$

where $M(\alpha)$ *is a normalization function and satisfies* $M(0) = M(1) = 1$.

If $f \notin H^1(x,y)$, *then the derivative of function* $f(t)$ *is defined as*

$$ {}^{CF}D_t^{\alpha} f(t) = \frac{\alpha M(\alpha)}{1-\alpha} \int_x^t (f(t) - f(w)) \exp\left[-\alpha \frac{t-w}{1-\alpha}\right] dw. \tag{2} $$

Remark 1 *If* $\beta = \frac{1-\alpha}{\alpha} \in [0,\infty), \alpha = \frac{1}{1+\beta}$, *then the equation (2) can be modified as*

$$ {}^{CF}D_t^{\alpha} f(t) = \frac{N(\alpha)}{\alpha} \int_x^t f'(t) \exp\left[-\frac{t-w}{\beta}\right] dw, \tag{3} $$

where $N(0) = N(\infty) = 1$. *Moreover,*

$$ \lim_{\beta \to 0} \left(\frac{1}{\alpha} \exp\left(-\frac{t-w}{\beta}\right) \right) = \delta(w-t). \tag{4} $$

According to [38], the Caputo-Fabrizio integral is defined as follows:

Definition 2 *The Caputo-Fabrizio integral of function* $f(t)$ *of order* $\alpha \in [0,1]$ *and* $t \geq 0$ *is defined as*

$$ {}^{CF}I_t^{\alpha} f(t) = \frac{2(1-\alpha)}{(2-\alpha)M(\alpha)} f(t) + \frac{2\alpha}{(2-\alpha)M(\alpha)} \int_0^t f(s) ds. \tag{5} $$

Further simplification gives us as

$$ \frac{2(1-\alpha)}{(2-\alpha)M(\alpha)} + \frac{2\alpha}{(2-\alpha)M(\alpha)} = 1. \tag{6} $$

3 Mathematical model and solution

The mathematical model includes diffusion of calcium and buffer in calcium signaling phenomena. The process occurs inside the plasma membrane of the cells. The calcium kinetics in fibroblast cells is governed by a set of advection reaction-diffusion equations in the form of a bimolecular reaction between Ca^{2+} and buffer [3, 39, 40].

$$ \left[Ca^{2+}\right] + [B] \underset{k^-}{\overset{k^+}{\Leftrightarrow}} [CaB]. \tag{7} $$

The remaining reaction-diffusion equations can be derived using Fickian diffusion as [39, 40]

$$\frac{\partial \left[Ca^{2+}\right]}{\partial t} = D_C \cdot \nabla^2 \left[Ca^{2+}\right] + \sum_k R_k, \tag{8}$$

$$\frac{\partial \left[B\right]}{\partial t} = D_B \cdot \nabla^2 \left[B\right] + R_k, \tag{9}$$

$$\frac{\partial \left[CaB\right]}{\partial t} = D_{CB} \cdot \nabla^2 \left[CaB\right] - R_k, \tag{10}$$

where $R_k = -k^+ \left[B\right] \left[Ca^{2+}\right] + k^- \left[CaB\right]$, known as the reaction term and D_K is the diffusion coefficient for the respective entity. Although, the buffer do not capable to diffuse with other entity is considered a stationary buffer and mathematically described by setting $D_B = D_{CB} = 0$. Now, including equations (7-10) the mathematical model is become as

$$\frac{\partial u}{\partial t} = D_c \frac{\partial^2 u}{\partial x^2} - v \frac{\partial u}{\partial x} - k^+ \cdot \left[B\right]_\infty \left(u - u_\infty\right), \tag{11}$$

where $u = [Ca^{2+}]$.

The apposite biophysical initial condition is defined as

$$u(x, 0) = u_\infty, x > 0, \tag{12}$$

and the boundary conditions are

$$u(0, t) = u_0, \quad t > 0, \quad \frac{\partial u}{\partial x} = 0, \quad x \to \infty, \quad t > 0. \tag{13}$$

For simplicity, we replaced $u - u_\infty = u$ and $k^+ \cdot [B]_\infty = f$ then the mathematical model is rearranged as

$$\frac{\partial u}{\partial t} = D_c \frac{\partial^2 u}{\partial x^2} - v \frac{\partial u}{\partial x} - fu. \tag{14}$$

The apposite biophysical initial and boundary conditions are modified as

$$\begin{aligned} &u(x, 0) = 0, x > 0, \\ &u(0, t) = u_\infty - u_0, \quad t > 0, \quad \tfrac{\partial u}{\partial x} = 0, \quad x \to \infty, \quad t > 0. \end{aligned} \tag{15}$$

The non-dimensional calcium model is formulated by introducing the dimensionless variables

$$x^* = x\sqrt{\frac{f}{D_C}}, \quad t^* = ft, \quad u^* = \frac{u}{u_0}, \quad k = \frac{v}{\sqrt{fD_C}}.$$

Hence, equation (14) turns out to be the following equation as

$$\frac{\partial u}{\partial t} = \frac{\partial^2 u}{\partial x^2} - k\frac{\partial u}{\partial x} - u, \tag{16}$$

and the corresponding conditions are

$$\begin{aligned} &u(x,0) = 0, \quad x > 0, \\ &u(0,t) = u_\infty - u_0, \quad t > 0, \quad \tfrac{\partial u}{\partial x} = 0, \quad x \to \infty, \quad t > 0. \end{aligned} \tag{17}$$

Next, we defined a new solute concentration $u(x,t) = \exp\left(\frac{kx}{2}\right)\gamma(x,t)$ and it is easy to verify that $\gamma(x,t)$ satisfies the following non-dimensional calcium problem.

$$\frac{\partial \gamma}{\partial t} = \frac{\partial^2 \gamma}{\partial x^2} - \left(\frac{k^2}{2} + 1\right)\gamma. \tag{18}$$

For simplicity, we replaced $\left(\frac{k^2}{2} + 1\right) = \xi^2$. Finally, the calcium model is formulated as follows

$$\frac{\partial \gamma}{\partial t} = \frac{\partial^2 \gamma}{\partial x^2} - \xi^2\gamma, \tag{19}$$

and the corresponding conditions are

$$\begin{aligned} &\gamma(x,0) = 0, \quad x > 0, \\ &\gamma(0,t) = u_0 - u_\infty, \quad t > 0, \quad \gamma(x,t) = 0, \quad x \to \infty, \quad t > 0. \end{aligned} \tag{20}$$

Now we convert the calcium model into the Caputo-Fabrizio sense to improve the accuracy and introduce a memory and hereditary behavior of cells. Thus the Caputo-Fabrizio calcium model for fibroblast cells is represented as follows:

$${}^{CF}D_t^\alpha \gamma(x,t) = \frac{\partial^2 \gamma}{\partial x^2} - \xi^2\gamma. \tag{21}$$

Applying the Laplace transform on equation (21), we obtain the following transformed problem as

$$\frac{s\bar{\gamma}(x,s) - \gamma(x,0)}{(1-\alpha)s + \alpha} = \frac{\partial^2 \bar{\gamma}(x,s)}{\partial x^2} - \xi^2\bar{\gamma}(x,s), \tag{22}$$

where $\bar{\gamma}(x,s)$ is the Laplace transformation of $\gamma(x,t)$.

Next, applying the Fourier sine transform on equation (22), the transformed problem is recast as

$$\frac{\hat{s}\hat{\gamma}(w,s)}{(1-\alpha)s + \alpha} = -w^2\hat{\gamma}(w,s) + w\bar{\gamma}(0,s) - \xi^2\hat{\gamma}(w,s), \tag{23}$$

where $\hat{\gamma}(w,s)$ is the Fourier sine transform of $\bar{\gamma}(x,s)$. By using equation (20) we obtain as

$$\frac{\hat{s}\hat{\gamma}(w,s)}{(1-\alpha)s + \alpha} = -w^2\hat{\gamma}(w,s) + w(u_0 - u_\infty) - \xi^2\hat{\gamma}(w,s). \tag{24}$$

By simple rearrangement give us the following expression

$$\hat{\gamma}(w,s) = \frac{w(u_0-u_\infty)}{w^2+m+\xi^2} + \frac{\alpha m^2 w(u_0-u_\infty)}{(w^2+m+\xi^2)^2}\frac{1}{s+\frac{\alpha m(w^2+\xi^2)}{w^2+m+\xi^2}}, \tag{25}$$

where $m = 1/(1-\alpha)$. Next, by inverting the Laplace and Fourier transform of equation (25), we have

$$\begin{aligned}\gamma(x,t) &= \tfrac{2(u_0-u_\infty)\delta(t)}{\pi}\int_0^\infty \tfrac{w\sin(wx)}{w^2+m+\xi^2}dw \\ &+ \tfrac{2(u_0-u_\infty)}{\pi}\int_0^\infty \tfrac{\alpha m^2 w\sin(wx)}{(w^2+m+\xi^2)^2}\exp\left(\tfrac{\alpha m(w^2+\xi^2)t}{w^2+m+\xi^2}\right)dw.\end{aligned} \tag{26}$$

By using the relation

$$\int_0^\infty \frac{w\sin(wx)}{w^2+b^2}dw = \frac{\pi}{2}e^{-bx}. \tag{27}$$

Equation (26) turns out to be

$$\begin{aligned}\gamma(x,t) &= (u_0-u_\infty)\delta(t)\exp\left(-x\sqrt{m+\xi^2}\right) \\ &+ \tfrac{2(u_0-u_\infty)}{\pi}\int_0^\infty \tfrac{\alpha m^2 w\sin(wx)}{(w^2+m+\xi^2)^2}\exp\left(\tfrac{\alpha m(w^2+\xi^2)t}{w^2+m+\xi^2}\right)dw.\end{aligned} \tag{28}$$

Then by transforming equation (28) to the original coordinate system, we get the calcium concentration in fibroblast cells at any instant as

$$\begin{aligned}u(x,t) &= (u_0-u_\infty)\delta(t)\exp\left(-x\sqrt{m+\xi^2}+\tfrac{kx}{2}\right) \\ &+ \tfrac{2(u_0-u_\infty)}{\pi}\exp\left(\tfrac{kx}{2}\right)\int_0^\infty \tfrac{\alpha m^2 w\sin(wx)}{(w^2+m+\xi^2)^2}\exp\left(-\tfrac{\alpha m(w^2+\xi^2)t}{w^2+m+\xi^2}\right)dw.\end{aligned} \tag{29}$$

Limiting case of the model (Caputo-Fabrizio order $\alpha \to 1$)

The classical solution of the calcium model is obtained here as a special case or limiting case of the Caputo-Fabrizio calcium model by approaching $\alpha \to 1$.

When $\alpha \to 1$ we have,

$$\begin{aligned}\gamma(x,t) &= \lim_{\alpha\to 1}\tfrac{2(u_0-u_\infty)}{\pi}\int_0^\infty \tfrac{\alpha m^2 w\sin(wx)}{(w^2+m+\xi^2)^2}\exp\left(-\tfrac{\alpha m(w^2+\xi^2)t}{w^2+m+\xi^2}\right)dw \\ &= \frac{2(u_0-u_\infty)}{\pi}\int_0^\infty w\sin(wx)\exp\left(-(w^2+\xi^2)t\right)dw.\end{aligned} \tag{30}$$

Then by using equation (30), equation (29) rearrange as follows

$$\gamma(x,t) = \frac{(u_0-u_\infty)}{2\sqrt{\pi}}\frac{x}{t\sqrt{t}}\exp\left(-\xi^2 t - \frac{x^2}{4t}\right), \tag{31}$$

and again by transforming equation (31) to the original coordinate system, we get the calcium concentration in fibroblast cells for the classical case as

$$u(x,t) = \frac{(u_0 - u_\infty)}{2\sqrt{\pi}} \frac{x}{t\sqrt{t}} \exp\left(-\xi^2 t - \frac{x^2}{4t} + \frac{kx}{2}\right). \tag{32}$$

4 Numerical results and discussion

In this section, we portrayed the spatial and temporal calcium concentration in fibroblast cells for various amounts of buffer, diffusion coefficient, advection flux, and Caputo-Fabrizio derivative. The numerical values of a bio-physiological parameter used to simulate the result are provided in Table 1.

Table 1. Values of bio-physiological parameters [3, 5, 40]

Symbol	Parameter	Value
D_C	Diffusion coefficient	260-400 $\mu m^2/s$
$[B_m]$	Buffer concentration	60-200 μM
k^+ (EGTA)	Buffer association rate	1.6-30 $\mu M^{-1}s^{-1}$
k^+ (BAPTA)	Buffer association rate	600-900 $\mu M^{-1}s^{-1}$
$[Ca^{2+}]_\infty$	Background Ca^{2+} concentration	0.1 μM
v	Advection flux	0-30 $\mu m/s$

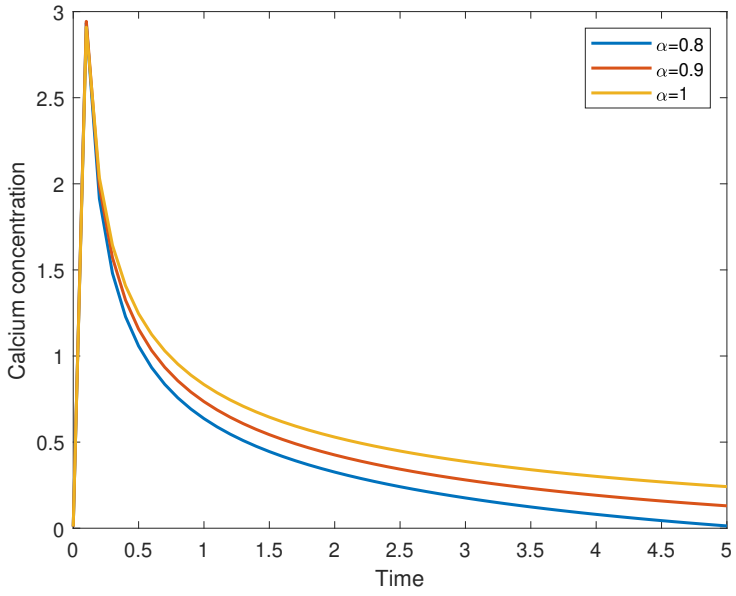

Figure 1. Calcium concentration against time for various orders of Caputo-Fabrizio derivative

Figure 1 shows the calcium concentration in a fibroblast cell against time for diffusion coefficient 290 $\mu m^2/s$, advection flux 10 $\mu m/s$, and EGTA buffer 1.6 μM. The highest concentration is observed near the source then it decreases to reach its equilibrium conditions. This happened near the source as free calcium reacted with the buffer and made a calcium-bound buffer. As a result, the sharp fall is observed after 0.5 seconds and it shows the notable role of a buffer up to 0.5 seconds. Also, the kernel of the Caputo-Fabrizio derivative plays a significant role due to the exponential kernel law and forces the calcium profile to early achieved stable conditions.

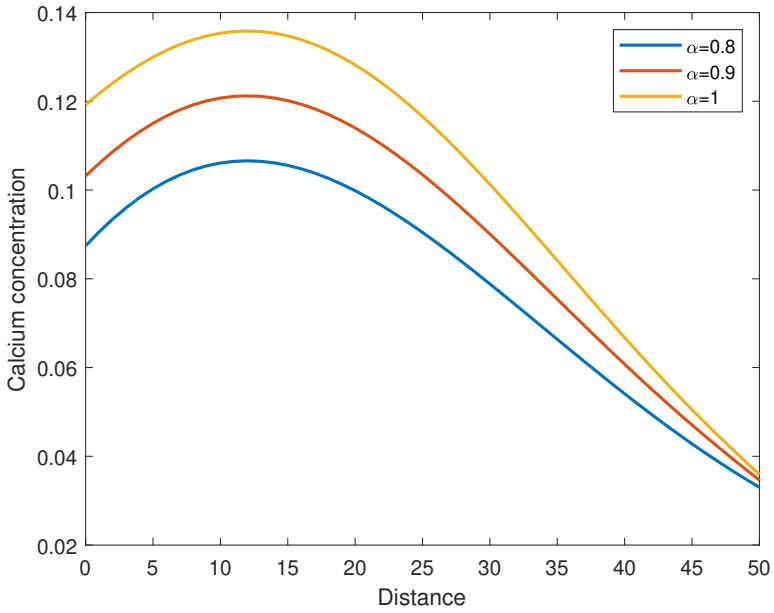

Figure 2. Calcium concentration against distance for various orders of Caputo-Fabrizio derivative

Figure 2 shows the calcium concentration in a fibroblast cell against distance for diffusion coefficient 290 $\mu m^2/s$, advection flux 10 $\mu m/s$, and EGTA buffer 1.6 μM. The highest concentration is observed near the source then subtle rises due to the entry of buffer affinity and then decreases gradually to reach its equilibrium conditions. The sharp fall is observed after 20 μm, and it shows the notable role of buffer in the initial stage of cellular activities. As Caputo-Fabrizio derivative moves to integer order, the calcium concentration is increasing then finally achieved stable conditions. Figures 1 and 2 show the significant role of the Caputo-Fabrizio derivative due to the exponential kernel law and hence Figures 3-10 are produced only for Caputo-Fabrizio fractional order $\alpha = 0.9$.

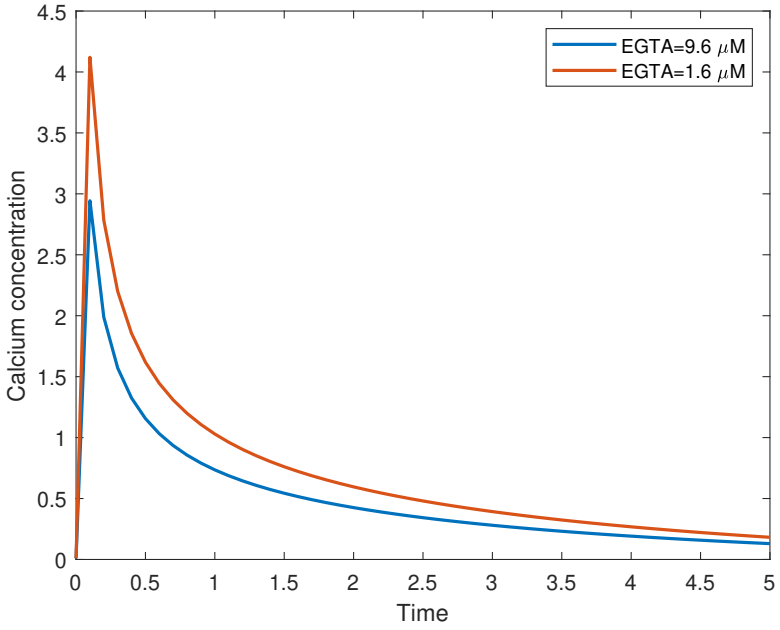

Figure 3. Calcium concentration against time for various amounts of EGTA buffer

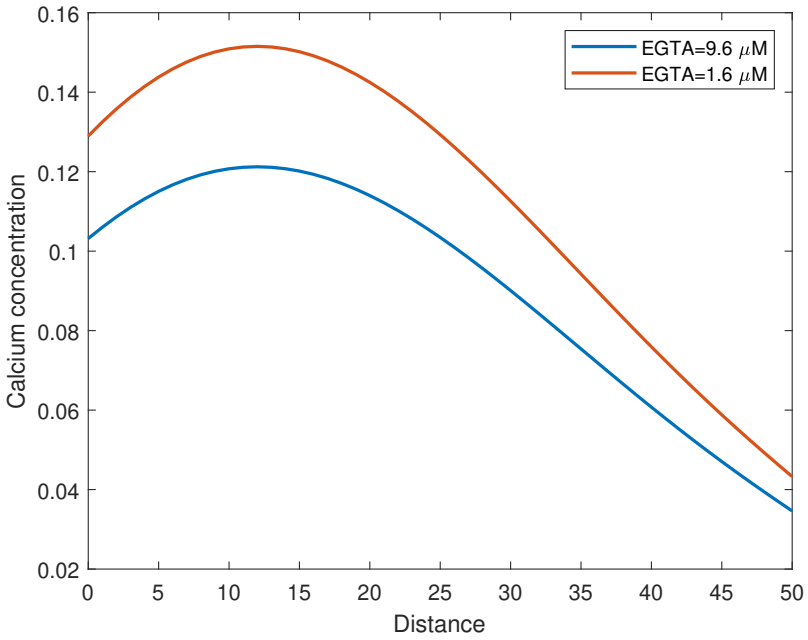

Figure 4. Calcium concentration against distance for various amounts of EGTA buffer

Figures 3 and 4 show the calcium concentration in a fibroblast cell against time and space respectively. The bio-physiological parameters used to simulate the result are the same as listed above. Here, we examine the effect of EGTA buffer over time and space. From the figures, we confirmed that as the value of buffer increases calcium concentration initiates to decrease due to the free buffer binds with free calcium.

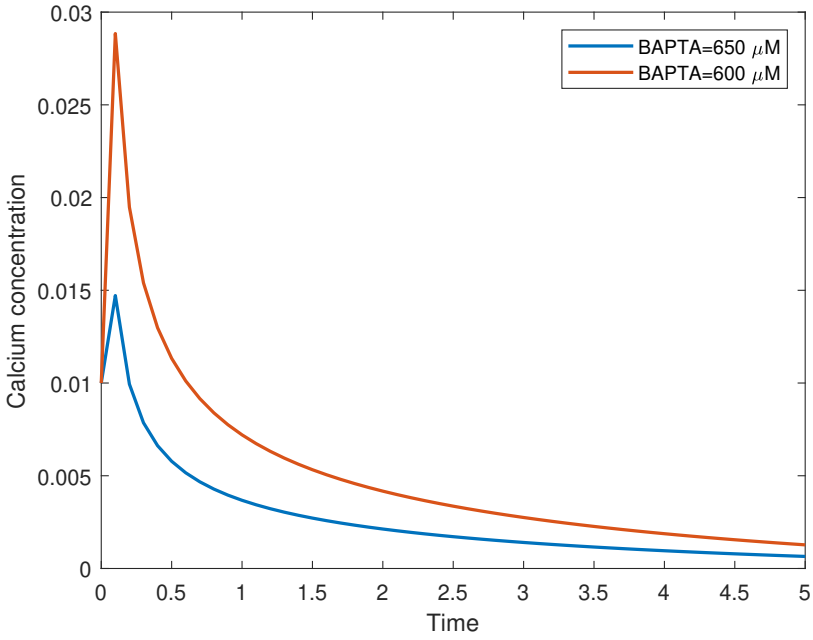

Figure 5. Calcium concentration against time for various amounts of BAPTA buffer

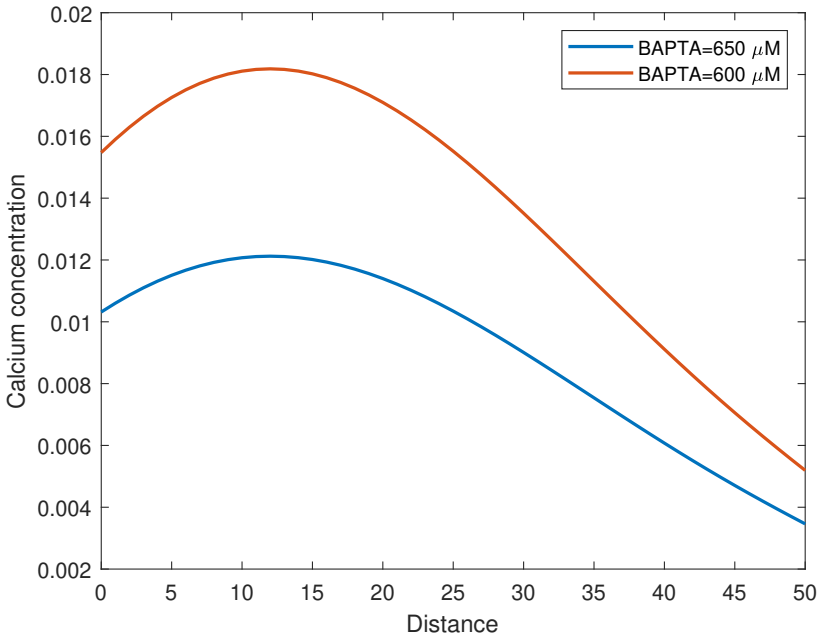

Figure 6. Calcium concentration against distance for various amounts of BAPTA buffer

Figures 5 and 6 show the calcium concentration in a fibroblast cell against time and space respectively. Here, we examine the effect of BAPTA buffer over time and space. From the figures, we confirmed that as the value of the buffer increases calcium concentration decrease. Also, it is observed that calcium concentration is dramatically reduced as compared to EGTA buffer due to the association rate of BAPTA buffer.

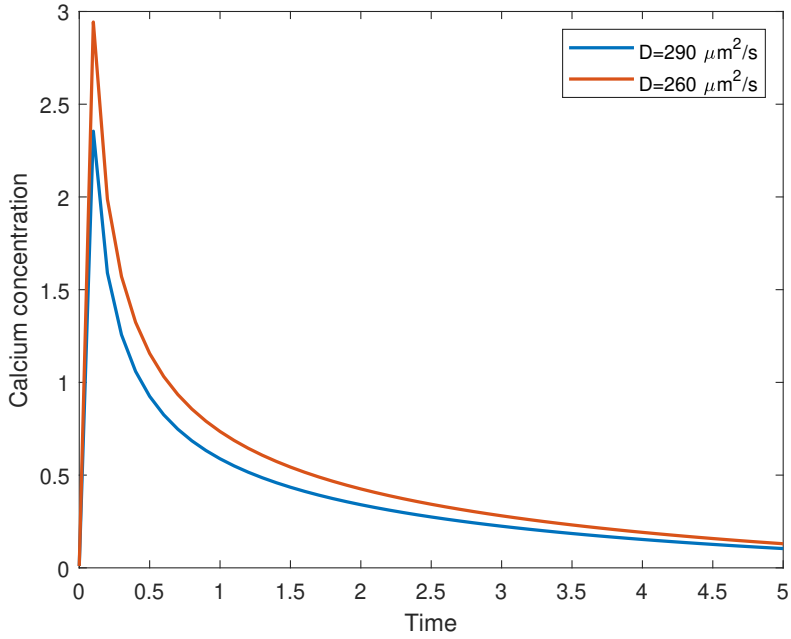

Figure 7. Calcium concentration against time for various diffusion coefficient

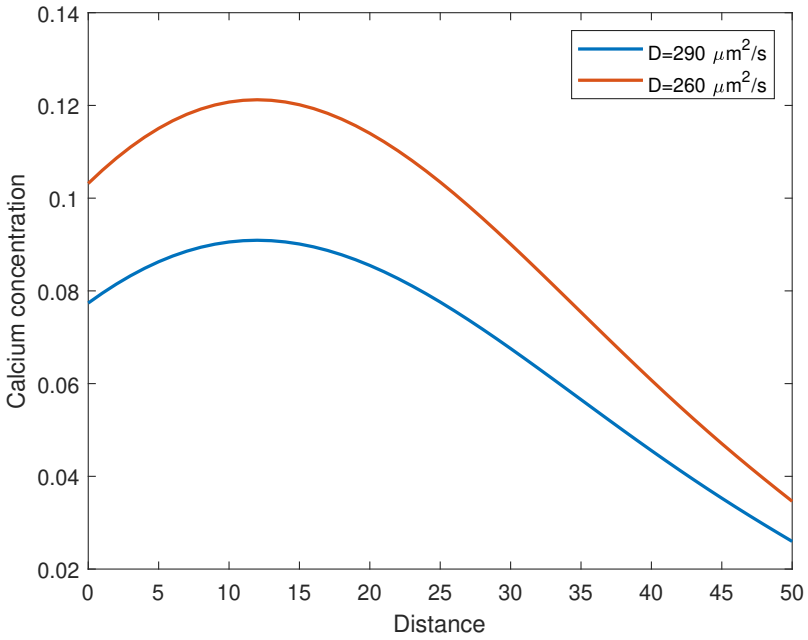

Figure 8. Calcium concentration against distance for various diffusion coefficient

Figures 7 and 8 show the calcium concentration in a fibroblast cell against time and space for various diffusion coefficients. From the figures, we confirmed that as the value of diffusion coefficients increases calcium concentration decreases and hence it plays a dual role in the absence of buffer and contributes to managing cellular activities.

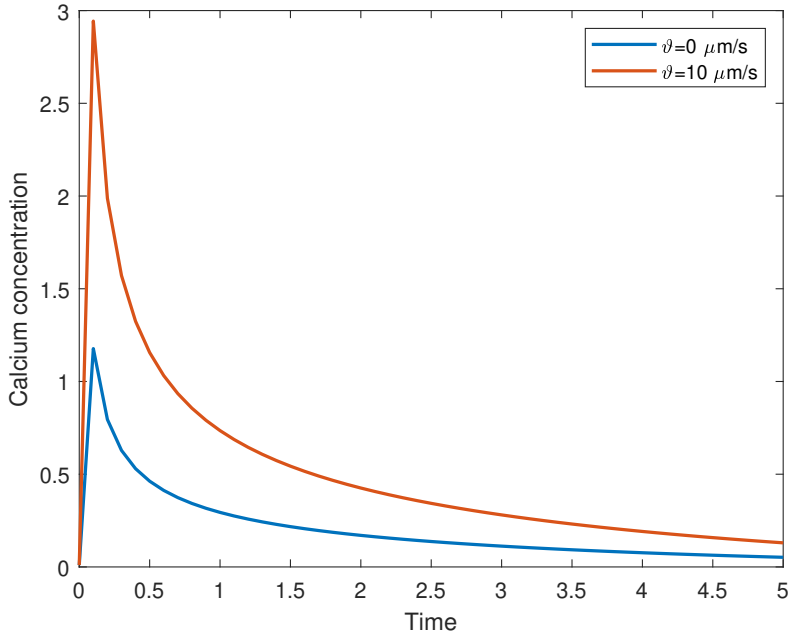

Figure 9. Calcium concentration against time for presence and absence of advection flux

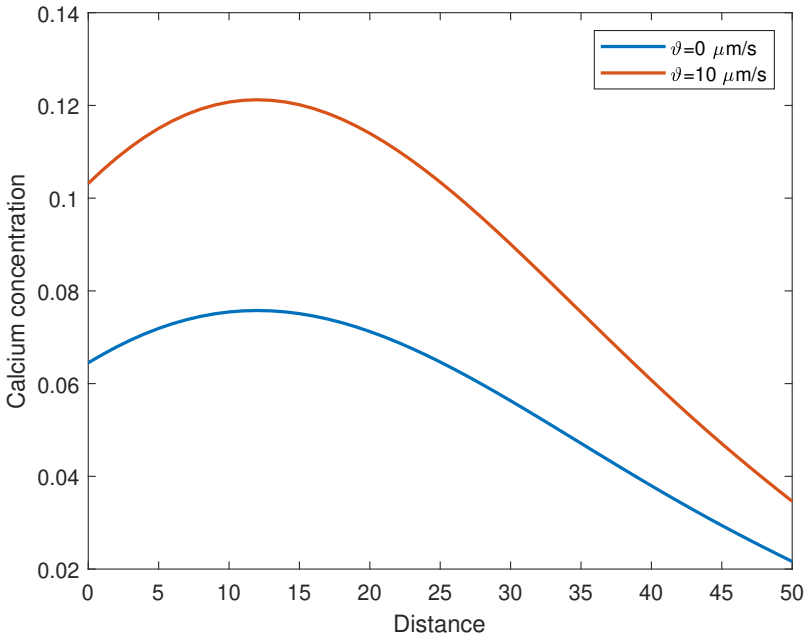

Figure 10. Calcium concentration against distance for presence and absence of advection flux

Figures 9 and 10 show the calcium concentration in a fibroblast cell against time and space for the presence and absence of advection flux. From the figures, we confirmed that the presence of flux significantly rise the calcium concentration and is thus involved in cellular activities such as secretion, cell integrity, and so on.

5 Conclusion

We analyzed the effect of disturbances in intracellular calcium dynamic on fibroblast cells with the Caputo-Fabrizio advection reaction-diffusion equation. The analytical solution is derived by use of Laplace and Fourier transform techniques. Also, the limiting case of the model is obtained by setting the Caputo-Fabrizio fractional operator to unity. Numerical simulation is presented for various physiological conditions to study calcium diffusion in a fibroblast cell. This approach provides us with a comparably good approximation of the complex geometry of the cell including various biophysical parameters like buffer, diffusion coefficient, and advection flux. The results imply that buffer concentration, the binding affinity of EGTA and BAPTA, the presence and absence of advection flux, and the Caputo-Fabrizio fractional operator has a significant effect on calcium concentration in fibroblast cells. Moreover, the results shown here are in agreement with the physiological facts and hence they play an important role in generating specific calcium concentration patterns necessary for activation, continuation, and termination of fibroblast during wound healing, fibrotic diseases, and cardiovascular disease. Recently, there are many new fractional derivatives introduced such as the generalized fractional derivative known as the Abu-Shady-Kaabar fractional derivative. This fractional derivative can work and obtain the same results as other well-known fractional derivatives in a very simple way. Therefore, it is a good direction for future research works to study the present problem in the sense of the Abu-Shady Kaabar fractional derivative.

Declarations

Consent for publication

Not applicable

Conflicts of interest

The authors declare that they have no conflict of interest.

Funding

None. No funding to declare.

Author's contributions

H.J.: Methodology, Writing-Original draft preparation, Software. M.Y.: Investigation, Writing-Reviewing and Editing. I.S.: Visualization, Supervision, Validation. All authors discussed the results and contributed to the final manuscript.

Acknowledgements

The authors are thankful to the associate editor and referees for their valuable time and suggestions that improved the quality of this manuscript.

References

[1] Camelliti, P., Borg, T.K. and Kohl P. Structural and functional characterisation of cardiac fibroblasts. *Cardiovascular Research*, 65(1), 40-51, (2005). [CrossRef]

[2] Michailova, A., DelPrincipe, F., Egger, M. and Niggli, E. Spatiotemporal features of Ca^{2+} buffering and diffusion in atrial cardiac myocytes with inhibited sarcoplasmic reticulum. *Biophysical Journal*, 83(6), 3134–3151, (2002). [CrossRef]

[3] Schwaller, B. Cytosolic Ca^{2+} buffers. *Cold Spring Harbor Perspectives in Biology*, 2(11), a004051, (2010). [CrossRef]

[4] Clapham, D.E. Calcium signaling. *Cell*, 131(6), 1047-1058, (2007). [CrossRef]

[5] Kotwani, M., Adlakha, N. and Mehta, M.N. Numerical model to study calcium diffusion in fibroblasts cell for one dimensional unsteady state case. *Applied Mathematical Sciences*, 6(102), 5063-5072, (2012).

[6] Kothiya, A.B. and Adlakha, N. Cellular nitric oxide synthesis is affected by disorders in the interdependent Ca^{2+} and IP_3 dynamics during cystic fibrosis disease. *Journal of Biological Physics*, (2023). [CrossRef]

[7] Joshi, H. and Jha, B.K. Advection diffusion model to study the astrocyte calcium regulation in neurodegenerative disease. *Mathematics in Engineering, Science & Aerospace (MESA)*, 13(2), (2022).

[8] Jha, B.K., Adlakha, N. and Mehta, M.N. Two-dimensional finite element model to study calcium distribution in astrocytes in presence of excess buffer. *International Journal of Biomathematics*, 7(03), 1450031, (2014). [CrossRef]

[9] Jha, B.K., Adlakha, N. and Mehta, M.N. Two-dimensional finite element model to study calcium distribution in astrocytes in presence of VGCC and excess buffer. *International Journal of Modeling, Simulation, and Scientific Computing*, 4(02), 1250030, (2013). [CrossRef]

[10] Joshi, H. and Jha, B.K. Modeling the spatiotemporal intracellular calcium dynamics in nerve

cell with strong memory effects. *International Journal of Nonlinear Sciences and Numerical Simulation*, (2021). [CrossRef]

[11] Dave, D.D. and Jha, B.K. Mathematical modeling of calcium oscillatory patterns in a neuron. *Interdisciplinary Sciences: Computational Life Sciences*, 13, 12-24, (2021). [CrossRef]

[12] Jha, A. and Adlakha, N. Two-dimensional finite element model to study unsteady state Ca^{2+} diffusion in neuron involving ER LEAK and SERCA. *International Journal of Biomathematics*, 8(01), 1550002, (2015). [CrossRef]

[13] Joshi, H. and Jha, B.K. Generalized diffusion characteristics of calcium model with concentration and memory of cells: A spatiotemporal approach. *Iranian Journal of Science and Technology, Transactions A: Science*, 46, 309-322, (2022). [CrossRef]

[14] Jha, A., Adlakha, N. and Jha, B.K. Finite element model to study effect of $Na^+ - Ca^{2+}$ exchangers and source geometry on calcium dynamics in a neuron cell. *Journal of Mechanics in Medicine and Biology*, 16(02), 1650018, (2016). [CrossRef]

[15] Joshi, H. and Jha, B.K. 2D dynamic analysis of the disturbances in the calcium neuronal model and its implications in neurodegenerative disease. *Cognitive Neurodynamics*, (2022). [CrossRef]

[16] Joshi, H. and Jha, B.K. 2D memory-based mathematical analysis for the combined impact of calcium influx and efflux on nerve cells. *Computers & Mathematics with Applications*, 134, 33-44, (2023). [CrossRef]

[17] Joshi, H. and Jha, B.K. Chaos of calcium diffusion in Parkinson's infectious disease model and treatment mechanism via Hilfer fractional derivative. *Mathematical Modelling and Numerical Simulation with Applications*, 1(2), 84-94, (2021). [CrossRef]

[18] Pawar, A. and Pardasani, K.R. Effects of disorders in interdependent calcium and IP_3 dynamics on nitric oxide production in a neuron cell. *The European Physical Journal Plus*, 137(5), 543, (2022). [CrossRef]

[19] Pathak, K. and Adlakha, N. Finite element model to study two dimensional unsteady state calcium distribution in cardiac myocytes. *Alexandria Journal of Medicine*, 52(3), 261-268, (2016). [CrossRef]

[20] Naik, P.A. and Pardasani, K.R. Finite element model to study calcium signalling in oocyte cell. *International Journal of Modern Mathematical Sciences*, 15(01), 58-71, (2017).

[21] Naik, P.A. and Pardasani, K.R. Finite element model to study effect of Na^+/K^+ pump and Na^+/Ca^{2+} exchanger on calcium distribution in oocytes in presence of buffers. *Asian Journal of Mathematics and Statistics*, 7(01),21-28, (2014).

[22] Naik, P.A. and Zu, J. Modeling and simulation of spatial-temporal calcium distribution in T lymphocyte cell by using a reaction-diffusion equation. *Journal of Bioinformatics and Computational Biology*, 18(02), 2050013, (2020). [CrossRef]

[23] Naik, P.A. Modeling the mechanics of calcium regulation in T lymphocyte: a finite element method approach. *International Journal of Biomathematics*, 13(05), 2050038, (2020). [CrossRef]

[24] Nakul, N., Mishra, V. and Adlakha, N. Finite volume simulation of calcium distribution in a cholangiocyte cell. *Mathematical Modelling and Numerical Simulation with Applications*, 3(1), 17-32, (2023). [CrossRef]

[25] Kilbas, A.A., Marichev, O.I. and Samko, S.G. *Fractional Integrals and Derivatives (Theory and Applications)*, (1993).

[26] Caputo, M., and Fabrizio, M. A new definition of fractional derivative without singular kernel.

Progress in Fractional Differentiation and Applications, 1(2), 73-85, (2015).

[27] Podlubny I. *Fractional Differential Equations: An Introduction to Fractional Derivatives, Fractional Differential Equations, to Methods of Their Solution and Some of Their Applications* (Vol. 1). Academic Press, Elsevier, (1998).

[28] Kilbas, A.A., Srivastava, H.M. and Trujillo, J.J. *Theory and Applications of Fractional Differential Equations* (Vol. 204). Elsevier, (2006).

[29] Atangana, A. and Baleanu, D. New fractional derivatives with nonlocal and non-singular kernel: Theory and application to heat transfer model. *Thermal Science*, 20(2), 763-769, (2016). [CrossRef]

[30] Abu-Shady, M. and Kaabar, M.K. A generalized definition of the fractional derivative with applications. *Mathematical Problems in Engineering*, 2021, 9444803, (2021). [CrossRef]

[31] Din, A. and Abidin, M.Z. Analysis of fractional-order vaccinated Hepatitis-B epidemic model with Mittag-Leffler kernels. *Mathematical Modelling and Numerical Simulation with Applications*, 2(2), 59-72, (2022). [CrossRef]

[32] Ahmad, S., Qiu, D. and ur Rahman, M. Dynamics of a fractional-order COVID-19 model under the nonsingular kernel of Caputo-Fabrizio operator. *Mathematical Modelling and Numerical Simulation with Applications*, 2(4), 228-243, (2022). [CrossRef]

[33] Yavuz, M. and Ozdemir, N. Analysis of an epidemic spreading model with exponential decay law. *Mathematical Sciences and Applications E-Notes*, 8(1), 142-154, (2020). [CrossRef]

[34] Avci, D., Yavuz, M. and Ozdemir, N. Fundamental solutions to the Cauchy and Dirichlet problems for a heat conduction equation equipped with the Caputo-Fabrizio differentiation. In *Heat Conduction: Methods, Applications and Research* (pp. 95-107). Hauppauge, New York, USA: Nova Science Publishers, (2019).

[35] Premakumari, R.N., Baishya, C. and Kaabar, M.K. Dynamics of a fractional plankton–fish model under the influence of toxicity, refuge, and combine-harvesting efforts. *Journal of Inequalities and Applications*, 2022, 137, (2022). [CrossRef]

[36] Achar, S.J., Baishya, C. and Kaabar, M.K. Dynamics of the worm transmission in wireless sensor network in the framework of fractional derivatives. *Mathematical Methods in the Applied Sciences*, 45(8), 4278-4294, (2022). [CrossRef]

[37] Martínez, F. and Kaabar, M.K. A Novel theoretical investigation of the Abu-Shady–Kaabar fractional derivative as a modeling tool for science and engineering. *Computational and Mathematical Methods in Medicine*, 2022, 4119082, (2022). [CrossRef]

[38] Losada, J. and Nieto, J.J. Properties of a new fractional derivative without singular kernel. *Progress in Fractional Differentiation and Applications*, 1(2), 87-92, (2015).

[39] Crank, J. *The Mathematics of Diffusion*. Oxford university press, (1979).

[40] Smith, G.D. Analytical steady-state solution to the rapid buffering approximation near an open Ca^2+ channel. *Biophysical Journal*, 71(6), 3064-3072, (1996).

How to cite this article: Joshi, H., Yavuz, M. & Stamova, I. (2023). Analysis of the disturbance effect in intracellular calcium dynamic on fibroblast cells with an exponential kernel law. *Bulletin of Biomathematics*, 1(1), 24-39. https://doi.org/10.59292/bulletinbiomath.2023002