

Optimal Levels of Ions Concentration and Cell Sizes in Animal Cells

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ORIGINAL RESEARCH

Abstract— The rapid growth of the world population has intensified the need for increased food production, leading to scientific efforts aimed at accelerating the growth of plants and animals. However, these efforts have sometimes resulted in undesirable outcomes, such as uncontrolled cell growth that can lead to conditions like cancer. Proper regulation of cell size is essential for maintaining healthy organisms. This study focuses on the relationship between ion concentrations and cell size in animal cells. A mathematical model was developed to simulate ion transport optimization and analyze its effects on cellular size using MATLAB SIMULINK. The study reveals that precise modulation of specific ion levels is key to controlling cell size, with potential implications for treating conditions related to abnormal cell growth. This research enhances our understanding of the relationship between ion concentration and cell size, providing insights for future applications in bioengineering and medical treatments.

Keywords—Homeostasis, mathematical modeling, simulation, membrane potential, optimal ion concentration.

1 INTRODUCTION

1.1 Background of the Study

Cellular homeostasis is essential for all living organisms, and a critical mechanism for maintaining this balance is the regulation of ion concentrations within cells. Key ions such as sodium (Na^+), potassium (K^+), and calcium (Ca^{2+}) play vital roles in numerous biological processes, including sustaining the membrane potential and cell volume regulation (Alberts et al., 2002). Precise control of these ion levels is essential for proper cell functioning and growth.

The study of ion dynamics in cells has a rich history, beginning with early work in the 20th century that laid the foundation for our understanding of the electrical properties of cells (Hodgin & Katz, 1949). Notable discoveries include the sodium-potassium pump (Na^+/K^+ ATPase) by Jens Christian Skou in 1957, which highlighted the critical role of this pump in maintaining low intracellular Na^+ and high intracellular K^+ concentrations in animal cells (Skou, 1957). The quantitative explanations of ion mobility during action potentials provided by Hodgkin and Huxley (1952) further advanced this field.

To regulate ion concentrations, cells use various strategies such as active transport via ATP-powered pumps, secondary active transport coupled to other ions, and passive diffusion through highly selective ion channels (Allman & Rhodes, 2013 and Hille, 2001). These channels

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Section A- AGRICULTURAL ENGINEERING AND RELATED SCIENCES

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open or close in response to stimuli, such as voltage changes or ligand binding, ensuring selective permeability of the membrane to different ions. Maintaining proper ion concentration gradients is crucial not only for membrane potential but also for regulating cell size and preventing pathological conditions.

Ion concentration imbalances are linked to a range of cellular abnormalities, including cancer, where uncontrolled cell growth is a key issue (Blaustein & Hamlyn, 2016, Vishnu & Harald, 2011 and Petterson & Hoffman, 2023). Understanding the relationship between ion levels and cell size is critical for both fundamental biology and applied bioengineering. Recent advances in computational modeling, particularly through mathematical models, have provided significant insights into how ion concentrations affect cellular behavior. These models allow researchers to simulate ion transport dynamics and predict cellular responses under various conditions.

Building on this body of knowledge, this study aims to explore the relationship between optimal ion concentrations and cell size in animal cells. Using mathematical modeling and numerical simulation techniques in MATLAB SIMULINK, this research compares different ion concentration levels to identify those that promote healthy cell growth. The findings will contribute to a deeper understanding of ion regulation and its potential applications in bioengineering, particularly in developing strategies for managing conditions associated with abnormal cell size.

1.2 Literature Review

Overview

Animal cells depend on the control of ion concentrations to sustain their size, functions, and general homeostasis. Ion transport mechanisms affect signaling pathways,

electrical excitability, and cell size regulation, among other functions. To sustain optimal cellular function, a precise balance of ions such as calcium (Ca^{2+}), potassium (K^+), and sodium (Na^+) must be maintained across cell membranes (Keener & Sneyd, 2009). Cell viability may be impacted by disruptions in these concentrations that result in pathological situations such as cell enlargement or shrinking (Stein, 2012). This review of the literature looks at the most recent findings about ideal ion concentrations, how they affect cell growth regulation, and mathematical models designed to maximize ion transport in animal cells.

Transport of Ions and Stability of Cells

In order to keep cells in a homeostasis, ion transport is essential. Ion channels, pumps, and exchangers control the concentration of ions across the cell membrane. One of the primary processes in charge of preserving low intracellular Na concentrations and high intracellular K concentrations is the sodium-potassium pump, also known as Na^+/K^+ ATPase (Blaustein & Hamlyn, 2016). These ions are essential for controlling cell volume and setting the membrane potential. Research conducted in 2012 by Kandel et al. highlights the role ion channels play in preserving cell size (Kandel et al., 2012). Cells may inflate or shrink as a result of an imbalance in ion transport. While a decrease in intracellular K^+ produces cell shrinking, which is frequently associated with apoptosis, an increase in intracellular Na^+ concentrations results in cell proliferation.

Calcium Ions' (Ca^{2+}) Function

Calcium ions (Ca^{2+}) are essential in modulation of cellular processes. Low Ca^{2+} concentrations are maintained, with brief spikes employed for signaling. These spikes start a number of biological reactions, such as the release of neurotransmitters, the contraction of muscles, and the division of cells. Dysregulated Ca^{2+} signaling, as observed in malignant cells, can cause cell death or unchecked proliferation, according to Hille (2001). Ca^{2+} ions regulate actin and micro-tubule dynamics, which are critical for preserving the structural integrity of the cytoskeleton, in terms of cell size. The cytoskeleton is a complex network of protein fibers within the cytoplasm of cells, providing structural support and enabling various cellular functions. It plays a critical role in maintaining cell size, enabling movement, facilitating intracellular transport, and organizing organelles within the cell. Excessive intracellular Ca^{2+} has been demonstrated in studies to cause cytoskeleton disintegration and loss of cell size control, both of which are harmful to the health of cells (Lang, 2007, Peter & Julio, 2014 and Yang & Hinner, 2015).

Ion Concentration and Membrane Potential

The membrane potential is essential for cellular excitability and ion transport, and it is mainly controlled by Na^+ and K^+ ions (Stein, 2012). The resting membrane potential of animal cells is normally maintained between -60mV and -70 mV (Hille, 2001). The selective permeability of ion channels and the differential distribution of ions establish this potential.

The electrical properties of cells, which are primarily controlled by ion concentrations and the membrane potential, have been greatly described by mathematical models, such as those developed by Hodgkin and Huxley in 1952.

The equilibrium potential for individual ions and the total membrane potential are frequently described by the Nernst equation and the Goldman-Hodgkin-Katz (GHK) equation, respectively (Goldman, 1943, Hodgkin & Katz, 1949 and Murase & Kitano, 2011). These models shed light on how variations in ion concentrations impact membrane potential and, in turn, the operations of cells.

Mathematical Models for Optimizing Ion Transport

The optimum balance of Na^+ , K^+ , and Ca^{2+} ions is crucial in order to maintain the membrane potential in animal cells within the ideal range, which is normally about -70 mV (Goldman, 1943 and Hille, 2001). According to research, departures from this potential may result in pathological circumstances, such as changed cell sizes and abnormal cellular processes (Hoffman & Dunham, 1995, Lang, 2007 and Vishnu & Harald, 2011). It has been claimed that models that combine dynamics of membrane potentials with ion flux rates can mimic how cells react to different ionic conditions (Rob & Maria, 2005, Smith et al., 2017 and Yang & Hinner, 2015). Models that use differential equations to describe ion transport in excitable cells, capturing the interaction between ion concentrations and membrane potential have been studied (Hodgkin & Huxley, 1952 and Keener & Sneyd, 2009). These models are crucial for comprehending how alterations in ion transport impact the regulation of cell growth and general cellular behaviour.

Ion Concentration and Cell Size Regulation

The equilibrium of sodium (Na^+), potassium (K^+), and calcium (Ca^{2+}) ions, which are essential for preserving osmotic balance and membrane potential, closely controls cell growth (Lang, 2007). Studies conducted by Blaustein et al. (2016) revealed that substantial alterations in cell volume result from disturbances in the Na^+/K^+ ion gradient caused by malfunctioning Na^+/K^+ ATPase pumps. When Na^+ is not properly extruded, it accumulates in the cell along with Ca^{2+} , which leads to enlarged cell size. According to the study, high intracellular Ca^{2+} further destabilizes the cytoskeleton, impairing cell integrity and changing volume control systems. Since maintaining ion homeostasis is essential for maintaining correct cell physiology, this imbalance can potentially harm cellular processes in addition to affecting cell size (Gadsby & Nakao, 2003 and Jeremy et al., 2002). Additionally, by influencing the channels and transporters that regulate other ions, the dysregulation of calcium ion concentration contributes to changes in cell volume. Research has indicated that increased amounts of Ca^{2+} can block K^+ channels, aggravating the imbalance and causing additional modifications to cell size (Hoffman & Dunham, 1995, George et al., 2011 and Remignate et al.,

2022). This highlights the relationship between Na^+ , K^+ , and Ca^{2+} ions in controlling cell volume as well as the possible effects of their dysregulation on the well-being of cells.

1.3 Objective

The objective of this study is to investigate the relationship between ion concentrations and cell size in animal cells.

1.4 Significance of the Study

The comparison of optimal ion concentrations and cell sizes in animal cells is a critical area of research with broad implications for both fundamental science and practical applications in biotechnology and medicine.

First, this study enhances our understanding of how specific ion concentrations regulate cell size, which is essential for maintaining cellular homeostasis and proper function. Disruptions in ion levels are linked to a variety of diseases, including cancer, where abnormal cell growth is a key feature. By identifying optimal ion levels that promote healthy cell growth, this research offers valuable insights into the mechanisms that control cell size and how they can be manipulated to prevent or correct pathological conditions.

Second, the findings contribute to medical science by providing a foundation for developing targeted therapies. Ion channels and transporters, which play a central role in regulating ion concentrations, could serve as potential drug targets for conditions related to cell size abnormalities, offering new avenues for personalized medicine and treatments.

Additionally, this study has significant implications for bioengineering. By applying ion optimization principles, it may be possible to improve the design and function of engineered cells for use in pharmaceuticals, tissue engineering, and other biotechnological applications. The ability to regulate cell size precisely can also contribute to the development of more robust synthetic cells capable of adapting to various environments.

The use of computational models in this research, particularly through MATLAB SIMULINK, enhances the accuracy and efficiency of simulating ion transport and its effects on cell size. This not only advances interdisciplinary research but also reduces the reliance on extensive in vivo testing, making the research process more efficient and ethically sound.

Lastly, this study offers educational value by deepening our understanding of cellular physiology and the relationship between ion dynamics and cell size regulation. It provides a foundation for future research in fields such as biophysics, physiology, and medical sciences.

Overall, this research addresses significant challenges in health and biotechnology, offering insights that could lead to advancements in disease treatment, synthetic biology, and bioengineering.

2.0 MATERIALS AND METHODS

2.1 Numerical Solution-Finite difference method(FDM)

This numerical approach is appropriate for partial differential equations (PDEs) that take into account spatial fluctuations in ion concentration (Allman & Rhodes, 2013, Morton & Mayer 2005 and Smith & Brown 2020). Time and space must be discretized.

In this study we encounter inhomogeneous PDEs governing the flow of ions across cell membrane with spatial fluctuations in ion concentrations on the inside and outside of the cell. The particular method for this problem is the central finite difference method, with a uniform time step (n) and spatial step (m). The following partial derivatives are expressed as follows

$$\frac{\partial^2 u}{\partial y^2} = u_{yy} = \frac{u_{i,j+1} - 2u_{i,j} + u_{i,j-1}}{m^2} \quad (1)$$

$$\frac{\partial u}{\partial y} = u_y = \frac{u_{i,j+1} - u_{i,j-1}}{2m} \quad (2)$$

Let the mesh point at time t be denoted by n . Then the forward difference for the first order derivative with respect to time t will be

$$\frac{\partial u}{\partial t} = u_t = \frac{u_{i+1,j} - u_{i,j}}{n} \quad (3)$$

2.2 Mathematical Model for Ion Optimization in Animal Cells

The mathematical model for ion optimization in animal cells involves differential equations that describe the movement of ions across the cell membrane and their interactions with various cellular processes (Allman & Rhodes, 2013 and Bartlomiej, 2019).

Goldman-Hodgkin-Katz equation (GHK)

$$V_m = \frac{RT}{F} \ln \left(\frac{P_{Na}[Na^+]_o + P_K[K^+]_o + P_{Ca}[Ca^{2+}]_o}{P_{Na}[Na^+]_i + P_K[K^+]_i + P_{Ca}[Ca^{2+}]_i} \right) \quad (4)$$

This formula calculates the resting membrane potential by putting into consideration the permeabilities and concentrations of various ions (Keener & Sneyd, 2009 and Murase & Kitano 2011). Where V_m is membrane potential, P is permeability of the membrane to the ion, and subscripts o and i denote the extra cellular and intracellular concentrations of the ion respectively.

Poisson equation

This formula determines the electric potential $\psi(x, t)$ that helps us to calculate the ions flux using the Nernst-Planck equation. The electrochemical potential ψ for a given charge distribution can be solved using the Poisson equation, which is stated as follows (Bartlomiej, 2019):

$$-\epsilon \nabla^2 \psi = \sum_i z_i e C_i \quad (5)$$

where i is the i^{th} species, z is the ion valence, e is the elementary charge, C is the ion concentration, and ϵ is the electrolyte permittivity. To discretize this equation the second spatial derivative for the electric potential is expressed using central difference formula as follows

$$-\epsilon \frac{\psi^n(j+1) - 2\psi^n(j) + \psi^n(j-1)}{\Delta x^2} = \sum_i z_i e C_i^n(j) \quad (6)$$

Nernst-Planck equation: The Nernst-Planck equation for the ion concentration $C_i(x,t)$ of ion species i in differential form is given by (Murase & Kitano, 2011 and Rob & Maria, 2005);

$$\frac{\partial C_i}{\partial t} = \nabla \cdot (D_i \nabla C_i - \frac{D_i z_i e}{k_B T} C_i \nabla \psi) \quad (7)$$

Where D_i is the diffusion coefficient of ion i , z_i is the valence of ion i , e is the elementary charge, k_B is the Boltzmann constant, T is the temperature and $\psi(x,t)$ is the electric potential.

Discretizing this equation using a time step Δt and a one-dimensional grid with spacing Δx , the spatial derivatives are expressed by use of the central difference formula while temporal derivatives uses the forward difference formula (Morton & Mayer, 2005, Murase & Kitano, 2011 and Wang et al., 2022).

$$\frac{C_i^{n+1}(j) - C_i^n(j)}{\Delta t} = \frac{D_i}{\Delta x^2} (C_i^n(j+1) - 2C_i^n(j) + C_i^n(j-1)) - \dots - \frac{D_i z_i e}{k_B T \Delta x} \left(\frac{C_i^n(j+1)\psi^n(j+1) - C_i^n(j-1)\psi^n(j-1)}{2} \right)_t \quad (8)$$

Where $C_i^n(j)$ is the concentration of ion i at grid point j and time step n and $\psi^n(j)$ is the electric potential at grid point j and time step n .

2.3 Numerical Simulation and Optimization

Here we formulate the algorithm that finds the minimum of constrained nonlinear multivariable function using MATLAB `fmincon` (Cuevas et al., 2024 and Paluszek & Thomas, 2023). This is a nonlinear programming algorithm that finds the minimum of a problem specified by

$$\min f(x) \text{ such that } \begin{cases} c(x) \leq 0 \\ ceq(x) = 0 \\ A b \leq b \\ Aeq.x = beq \\ lb \leq x \leq ub \end{cases} \quad (9)$$

Where, b and beq are vectors, A and Aeq are matrices, $c(x)$ and $ceq(x)$ are functions that return vectors, and $f(x)$ is a function that returns a scalar. $f(x)$, $c(x)$, and $ceq(x)$ can be nonlinear functions. x , lb , and ub can be passed as vectors or matrices.

We then construct this problem in MATLAB as follows;

$$x = \text{fmincon}(\text{problem}) \text{ or } x = \text{fmincon}(\text{fun}, x0, A, b, Aeq, beq, lb, ub, \text{nonlcon}, \text{options}) \quad (10)$$

This algorithm minimizes the objective function fun subject to the following constraints;

Homeostasis constraint: To ensure stable internal conditions in an animal cell, the appropriate ions concentration ranges are maintained by employing the following constraint;

$$[ion]_{\min} \leq [ion]_{actual} \leq [ion]_{\max} \quad (11)$$

Membrane potential constraint: To ensure that the voltage difference across a cell membrane is maintained within physiologically healthy ranges the conditions prescribed by the GHK equation are observed.

$$V_m = (R * T / F) * \log((P_K * K_out + P_Na * N_out + P_Ca * Ca_out) / \dots (P_K * K_in + P_Na * N_in + P_Ca * Ca_in))$$

$$ceq = V_m + 70; \quad (12)$$

We now formulate the objective function by considering the minimum sum of the squared differences between actual and observed ion concentrations, subject to homeostasis and membrane potential constraints. The objective is to minimize the deviation of actual ion concentrations from their observed values. The square is to make the differences positive. We thus write:

$$\text{fun} = \text{minimize} \sum_{ion} ([ion]_{actual} - [ion]_{observed})^2 \quad (13)$$

The summation is taken over all ions under consideration, with $[ion]_{actual}$ being the actual concentration of a given ion and $[ion]_{observed}$ the observed concentration of that ion.

In this problem we start with an initial guess or set of actual concentrations ($x0$). The optimization algorithm then adjusts x iteratively to minimize the objective function, thereby making x converge toward the optimal concentrations. In this problem we determine observed values based on theoretical models and previous

experiments that are known to be beneficial for cell function.

2.4 Solve the Optimization Problem

To solve the optimization problem a MATLAB code is developed. An initial guess for the ions concentrations is made, computation is done by adjusting the ions concentrations in the direction that reduces the objective function while convergence is achieved by looping the code for sufficient iterations.

3.0 Results

3.1 Findings and Discussion

The optimal levels of ions concentrations in a cell and the size of a normal and abnormal cell are presented.

3.1.1 Optimal Levels of Concentration of Ions in a cell.

The bar plot in figure 1 shows the optimal and exceeded ion concentrations of a cell.

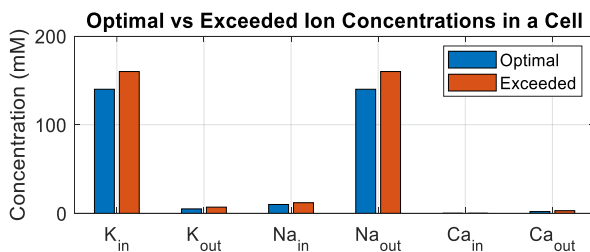


Figure 1 optimal and exceeded ion concentrations

The bar graph displays the optimal ions concentration levels both on the outside and on the inside of a cell. These ion levels ensure that a cell remains physiologically healthy. The figures for the optimal ion concentration levels are as listed below.

The optimal ions concentration levels ;

$$k_{in} : 140.1236mM$$

$$k_{out} : 3.5mM$$

$$Na_{in} : 10.0054mM$$

$$Na_{out} : 139.8965mM$$

$$Ca_{in} : 1e-04mM$$

$$Ca_{out} : 2mM$$

These results from the mathematical model on optimal ion concentrations are compared with experimental data for validation. According to Alberts et al. (2014) experimental results for sodium, potassium, and calcium ion concentrations in an animal cell which are also corroborated by Gadsby & Nakao (2003) are in agreement with the optimal ion concentrations from this study. However, the experimental data available from the relevant literature expresses the ion concentrations as a range of values while the data from our model computes an optimal value. Furthermore, more researchers are in

agreement with outcome from this study (Cohen,2023 and Hu & Huang, 2020).

3.1.2 Normal cell size against an Abnormal size

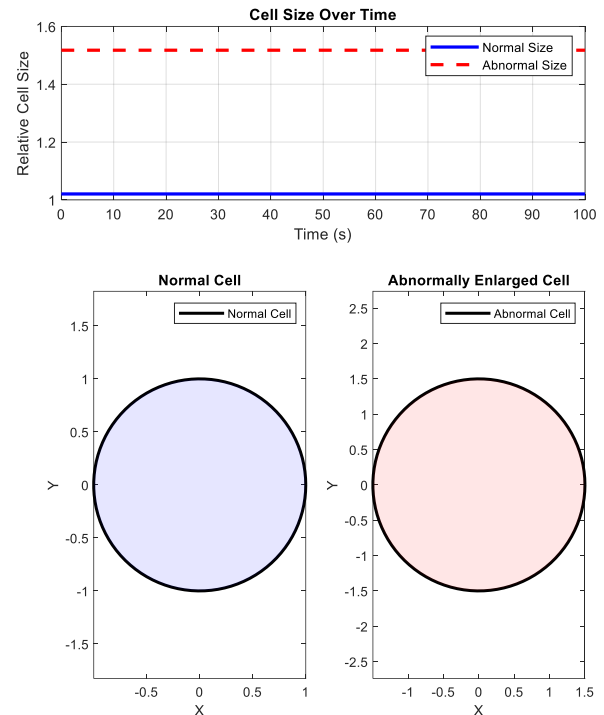


Figure 2 The normal and abnormal cell sizes

Figure 2 displays two graphs

This graph shows the Normal size of a cell as a result of optimal ions concentration levels against an Abnormal cell size where these levels are exceeded.

Normal size=1.06165: This is as a result of the optimal ions concentration

Abnormal size=1.51765: This is due to the exceeded ions concentration

This shows that exceeding optimal ion levels leads to an abnormal cell size, which potentially contributes to cellular dysfunction and development of cancerous behavior.

The optimal ion levels are used as the bases for the normal size of a cell. The abnormal size is computed relative to the normal size, if the actual normal size of a cell is known then this model can be used to compute the size of the cell at any time when the ions concentration starts to deviate from the optimal levels. This could be used as an early detection of a cell malfunction and a possible pointer to cancer development. In a normal physiological process a cell undergoes self destruction(apoptosis) to eliminate damaged or unwanted cells which if hindered results in uncontrolled cell growth. This uncontrolled cell growth is predominantly due to cell channel inability to observe optimal cell concentrations over time. The results have shown that exceeding optimal ion levels leads to cellular dysfunction which could potentially contribute to

development of cancer due to the uncontrolled cell size (Gerisch & Chaplain, 2014).

3.1.3 Effect of each ion

Calcium: Elevated intracellular calcium (levels above $1e-04mM$) can lead to uncontrolled cell growth and reduced apoptosis, contributing to cancer progression (Peter & Julio, 2014).

Potassium: Abnormal potassium levels (levels above $140.1236mM$) can disrupt cell cycle regulation and promote survival in environments where cells would normally undergo apoptosis (Hillesdon et al., 1995).

Sodium: Elevated sodium levels (levels above $10.0054mM$) can lead to increased cellular volume and changes in cell shape, contributing to a pro-cancerous environment (House et al., 2010)

3.2 Limitations

It is crucial to acknowledge the restrictions of this research. To begin with, there was no experimental research conducted; instead, the results are entirely theoretical and based on models and simulations. Furthermore, it's possible that the study's consideration of cells particular to animals limited the applicability of its findings to other biological systems. Finally, the analysis only took into account sodium, calcium, and potassium ions, leaving out other ions that could be potentially relevant for cellular processes. These limitations suggest that further experimental validation and a larger ion inclusion are needed for a deeper comprehension.

3.3 Conclusion

In this research an investigation of the optimal levels of ions concentration in relation to the electrochemical gradient in a cell using a numerical computational technique was undertaken. A determination of a normal cell size against an abnormal cell size in relation to the optimal levels of ions concentration has also been done.

Ions transport governing equations were used to create a suitable model for this problem and finite difference numerical method used to solve the problem. MATLAB software was used to simulate the model and visualize the results.

The mathematically determined optimal levels of ion concentrations were used to determine healthy cell size. The model simulates the effects of both intracellular and extracellular ion concentrations on cell size, offering insights into normal and abnormal cellular growth. A line plot was used to visualize the change in cell size over time, providing a comparative view of normal versus abnormal sizes.

The model's applications extend to the medical field, where the size of the cell can be computed at any time when the ions concentration starts to deviate from the optimal levels. This could be used as an early detection of a cell malfunction and a possible pointer to cancer development. Further, this model can be used to develop treatments for conditions

related to ion imbalances, offering a strategic approach to restoring or maintaining healthy ion levels in cells. Furthermore, this model can be improved to accurately simulate various conditions in bioengineering, enhancing its relevance and applicability in optimizing cell-based biotechnological processes.

It is however important for more studies to be carried out to improve this mathematical model by adding more biological components in order to improve the model's precision and suitability for use in a variety of biological systems.

3.4 RECOMMENDATIONS

1. Doctors and stake holders in the health sector can adopt this model as a diagnostic tool to identify early signs of cellular malfunction, such as abnormal cell size, which could be a pointer to underlying health problems, thereby enabling timely intervention.
2. We recommend more studies to improve this mathematical model by adding biological components like genetic regulation and environmental effects. This may improve the model's precision and suitability for use in a variety of biological systems.
3. An experimental verification process on the model is recommended to establish the model as a dependable tool in professional fields.

REFERENCES

- Alberts, B., Johnson, A., Lewis, J., Raff, M., Roberts, K., & Walter, P. (2002). *Molecular Biology of the Cell* (4th ed.). Garland Science.
- Allman, E. S., & Rhodes, J. A. (2013). *Mathematical models in biology: An introduction*. Cambridge University Press.
- Bartłomiej Matejczyk (2019). *Mathematical modelling and simulations of the ion transport through confined geometries*. Mathematics Institute, The University of Warwick 2019; warwick.ac.uk/lib-publications
- Blaustein, M. P., & Hamlyn, J. M. (2016). Sodium transport and hypertension. *Current Opinion in Nephrology and Hypertension*, 25(6), 513-521.
- Cohen, B. (2023). What are the concentrations of different ions in cells? Bionumbers. Retrieved from <https://bionumbers.hms.harvard.edu/bionumber.aspx?id=104390>
- Cuevas, E., Luque, A., & Escobar, H. (2024). *Computational Methods with MATLAB*. Springer Cham.
- Gadsby, D. C., & Nakao, M. (2003). Ionic composition in mammalian organisms. *The Journal of Physiology*, 541(3), 635-645. <https://doi.org/10.1113/jphysiol.2003.045674>.
- Gerisch, A., & Chaplain, M. A. (2014). Mathematical modelling of cancer cell invasion of tissue: Local and non-local models and the effect of adhesion. *Mathematical Biosciences*, 264, 232-248. DOI: 10.1016/j.mbs.2014.10.001
- Goldman, D. E. (1943). Potential, impedance, and rectification in membranes. *The Journal of General Physiology*, 27(1), 37-60.
- Hille, B. (2001). *Ionic Channels of Excitable Membranes* (3rd ed.). Sunderland, MA: Sinauer Associates.
- Hillesdon, A.J.; Pedley, T.J.; Kessler, J.O. (1995). The development of concentration gradients in a suspension of chemotactic bacteria. *Bull. Math. Biol.* 1995, 57, 299–344. [Google Scholar] [CrossRef] [PubMed]
- Hodgkin, A. L., & Huxley, A. F. (1952). A quantitative description

- of membrane current and its application to conduction and excitation in nerve. *The Journal of Physiology*, 117(4), 500-544.
- Hodgkin, A. L., & Katz, B. (1949). The effect of sodium ions on the electrical activity of the giant axon of the squid. *The Journal of Physiology*, 108(1), 37-77.
- Hoffmann, E. K., & Dunham, P. B. (1995). Membrane mechanisms and intracellular signalling in cell volume regulation. *International Review of Cytology*, 161, 173-262.
- House CD, Vaske CJ, Schwartz AM, Obias V, Frank B, Luu T, Sarvazyan N, Irby R, Strausberg RL, Hales TG, Stuart JM, Lee NH.(2010). Voltage-gated Na⁺ channel SCN5A is a key regulator of a gene transcriptional network that controls colon cancer invasion. *Cancer Res* 70: 6957–6967, 2010 [PMC free article] [PubMed] [Google Scholar]
- Hu J. and Huang X., (2020). A fully discrete positivity-preserving and energy-dissipative finite difference scheme for Poisson–Nernst–Planck equations. *Numer. Math.* 145, 77–135.1.4 . <https://doi.org/10.1007/s00211-020-01109-z>
- Ieee transactions on Nano bioscience, vol. 4, no. 1, march 2005
- Jeremy M B., John L.T., and Lubert S. (2002). *Biochemistry*, 5th edition. New York: W H Freeman; 2002. ISBN-10: 0-7167-3051-0. <https://www.ncbi.nlm.nih.gov/books/NBK22454/>.
- Kandel, E. R., Schwartz, J. H., & Jessell, T. M. (2012). *Principles of Neural Science* (5th ed.). McGraw-Hill.
- Keener, J., & Sneyd, J. (2009). *Mathematical Physiology* (2nd ed.). Springer.
- Lang, F. (2007). Mechanisms and significance of cell volume regulation. *Journal of the American College of Nutrition*, 26(5), 613S-623S.
- Morton,K.W.,Mayer, D.F.,(2005). *Numerical Solution of Partial Differential Equations; An introduction*; Cambridge University Press; Cambridge, MA, USA,2005. [Google Scholar]
- Murase, H., & Kitano, H. (Eds.). (2011). *Mathematical modeling in systems biology: Methods and protocols*. Humana Press.
- Paluszek, M., & Thomas, S. (2023). *Practical MATLAB deep learning: A project- based approach* (2nd ed.). Apress
- Peter William Atkins and Julio de Paula (2014). *Physical chemistry* (10th ed). Oxford: Oxford University Press.
- Rob D. Coalson and Maria G. Kournikova, (2005). Poisson–Nernst–Planck Theory Approach to the Calculation of Current Through Biological Ion Channels.
- Skou, J. C. (1957). The influence of some cations on an adenosine triphosphatase from peripheral nerves. *Biochimica et Biophysica Acta*, 23, 394-401.
- Smith, J., & Brown, R. (2020). A high-order finite difference method for solving the compressible Euler equations: consistency, convergence, and stability analysis. *Journal of Computational Physics*, 402, 109014. DOI: 10.1016/j.jcp.2019.109014
- Smith, N. P., Crampin, E. J., & Niederer, S. A. (2017). Computational modelling of the heart: from cell to organ. *Philosophical Transactions of the Royal Society A: Mathematical, Physical and Engineering Sciences*, 375(2102), 20160017.
- Stein Wilfred (2012). Transport and diffusion across cell membranes.
- Vishnu AC and Harald S (2011) Ion channels and tranporters in cancer: *Am J Physiol Cell Physiol.* : C541–C549. doi: 10.1351.42/ajpcell.00102.2011.
- V'yacheslav L., George S., Roman S., and Natalia P. (2011): Ion channels and transporters in cancer. 5. Ion channels in control of cancer and cell apoptosis: *American Journal of Physiology-Cell Physiology*. doi.org/10.1152/ajpcell.00249.2011
- Wang, C.X.; Chertock, A.; Cui, S.M.; Kurganov, A.; Zhang, Z.(2022). A diffuse-domain based numerical method for a Chemotaxis-Fluid model. *Numer. Anal.* 2022, 33, 341–375. [Google Scholar] [CrossRef]
- Yang, N. J., & Hinner, M. J. (2015). Getting across the cell membrane: An overview for small molecules, peptides, and proteins. In A. Gautier & M. J. Hinner (Eds.), *Site-Specific Protein Labeling: Methods and Protocols* (Vol. 1266, pp. 29–53). Humana Press. https://doi.org/10.1007/978-1-4939-2272-7_3
- Pedersen, S. F., & Hoffmann, E. K. (2023). Ion channels and transporters in cell volume regulation: Recent advances and new challenges. *American Journal of Physiology-Cell Physiology*, 324(5), C939–C963. <https://doi.org/10.1152/ajpcell.00210.2022>
- Remigante, A., Gavazzo, P., Morabito, R., & Dossena, S. (2022). Editorial: Ion transporters and channels in cellular pathophysiology. *Frontiers in Cell and Developmental Biology*, 10. <https://doi.org/10.3389/FCELL.2022.1049433>