“Skin-like” Layer Formation around Cytoskeleton Filaments and their Exceptional Biophysical Properties

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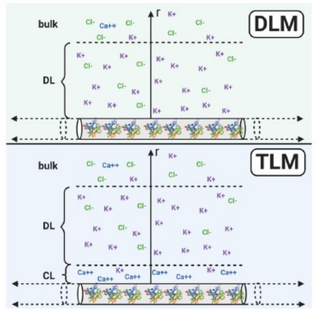
Abstract

A compact and stable ionic aqueous layer is formed between the surrounding fluid and the filament surface due to the strong interactions between them. This tiny “skin-like” layer provides cytoskeleton filaments with the extraordinary ability to change structures dynamically in response to alterations in the intracellular biological environment, which vary depending on the cell compartment and type. This property is crucial for eukaryotic cells to achieve key biological functions. Additionally, this “skin-like” layer is able to transmit electrical signals in the form of ionic wave packets along its conducting surface in response to changes in the cellular electric potential and cell membrane ionic currents. This recently discovered property may be crucial for understanding neuronal information processing (learning and memory). In this presentation, we introduce a multi-scale Actin filament model capable of accounting for the atomistic details of a protein molecular structure and its biological environment to characterize the thickness and the ionic electrical conductivity, current, and capacitance properties of this “skin-like” layer in physiological and pathological conditions. Temperature changes and pH differences, which are known to occur in unhealthy muscle and non-muscle cells, were shown to result in different ion accumulations at the surface of the filament, ionic conductivities, and ionic wave packet velocities. Additionally, G-actin proteins in the excited neuron state displayed higher nonlinear accumulation of charge and conductivity when compared with the resting state due in part to a larger fraction of condensed calcium ions and an increase in width of the condensed layer thickness when increasing the calcium concentrations. Our findings are expected to advance our understanding of molecular principles governing the biological functions of cytoskeleton filaments as well as the prevention and treatment of their associated diseases.

Cytoskeleton “skin” formations



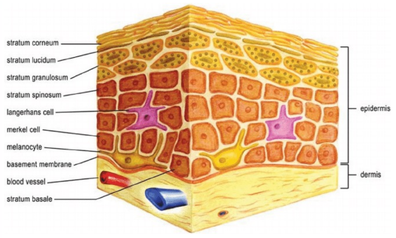


Figure: ion distribution in the radial direction of the cylindrical actin filament [1].

Double layer: Bulk layer and diffuse layer (DL).
Triple layer: (In addition to bulk and DL) Condensed layer(CL).

Multiscale theory for cytoskeleton “skin” in physiological conditions

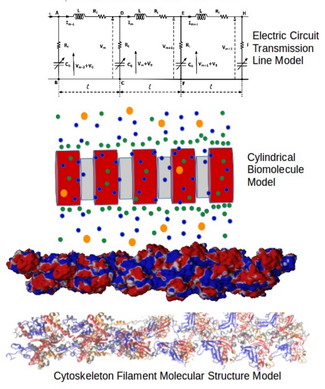


Figure: Actin; molecular structure model to cylindrical model [2].

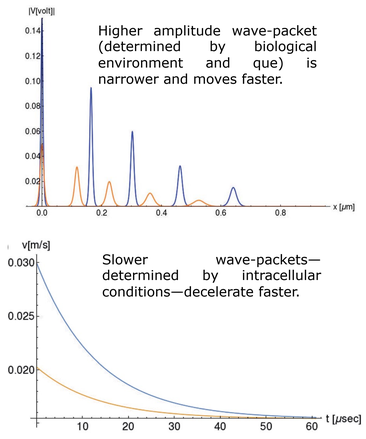


Figure: (top) Transmission line model—one cell of the transmission line represents an actin monomer; (bottom) soliton solution.

Physiological conditions (continued …)

Results for actin filaments in physiological conditions:

- In intracellular conditions, we find that electrical impulses along Actin filaments are sharper and travel faster due to the strong ion condensation and higher nonlinear behavior of the ionic capacitance [2].
- In in-vitro conditions, the electrical impulses are wider and run slower, and the peak attenuation is higher. In both conditions, our results reveal that an increase in the voltage stimulus increases the propagation velocity and peak height [2].
- Ionic waves are able to travel distances ~ microns—cell sizes [2].
- G-actin proteins in the excited neuron state displayed higher nonlinear accumulation of charge and conductivity when compared with the resting state. This is due in part to a larger fraction of condensed calcium ions and an increase in the width of the condensed layer thickness when increasing the calcium concentrations. Additionally, our results revealed a less dispersed wave packet of calcium ions, as well as a faster propagating soliton for larger calcium concentrations and input voltages [1].

Multiscale theory extended to study biophysical properties of cytoskeleton ”skin” in pathological conditions

We extended the multiscale approach for developing a Mathematica application to study soliton properties in physiological and pathological conditions [3].

- 298K to 320K
- $\log \mu = A + \frac{B}{C-T}$, μ is the viscosity (Kg/m.s) ; A, B, and C are constants
- Relative permittivity—intracellular condition, $80\epsilon_0$; in-vitro condition, $78.358\epsilon_0$.
- pH—from 6 to 8.
- Ion mobility, $u(T) = u_0 Exp[-U_0/K_b T]$, u_0 and U_0 are determined by fitting experimental data

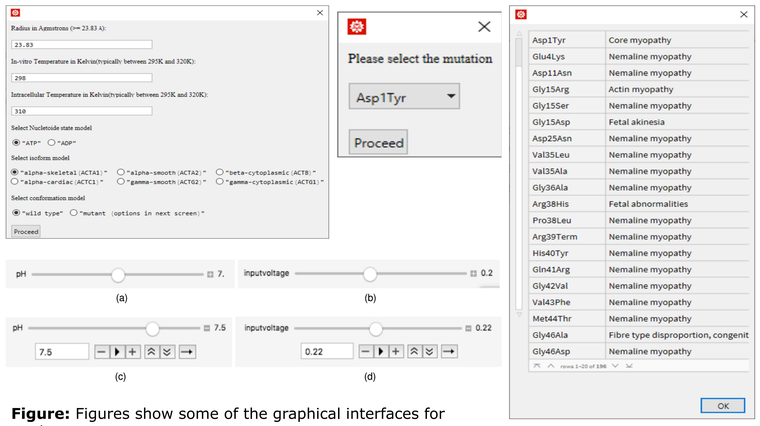


Figure: Figures show some of the graphical interfaces for study.

Effects of mutation on wave-packet propagation

- A mutation that results in a higher negative charge shows a faster traveling wave.

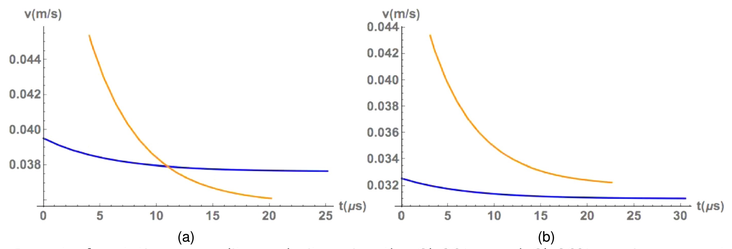


Figure. Impact of mutations on soliton velocity using the Gly36Arg and Glu362Lys missense mutations in subfigures (a) and (b), respectively. (*T* = 298.15K and *T* = 310K for invitro (blue) and intracellular (orange) electrolyte conditions.)

Pathological conditions (continued …)

Effects of pH change

- Changes in the pH of the surrounding solution affect the current density profiles of actin filament and show a more drastic impact on the intracellular condition.

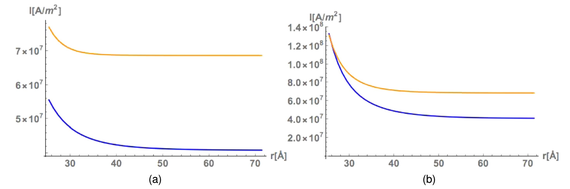
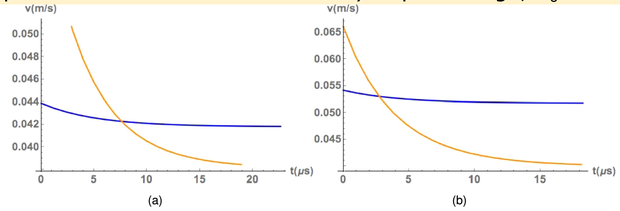


Figure: Current density profiles in the axial direction for pH 6 (subfigure a) and pH 7 (subfigure b). [R = 23.83Å]. The blue curves are for invitro conditions with *T* = 298.15K; the orange curves are for intracellular conditions with *T* = 310K.

Effects of temperature change

- A temperature increase results in a wave packet with faster velocity, also the packet decay more rapidly. Thus, solitons travel approximately the same distance. (The effects are more pronounced in invitro conditions as we considered a more significant amount of temperature change in this condition.)

Temperature effects on soliton velocity. Input voltage, $V_0 = 0.15V$.



Temperature effects on the soliton peak attenuation.

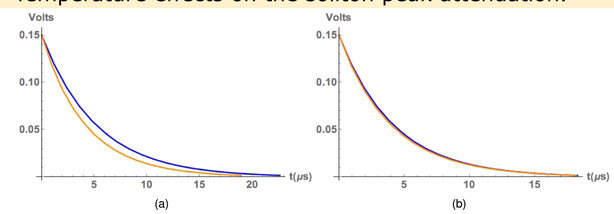


Figure: The radius, *R* = 23.83Å; the blue curves represent invitro conditions, and the orange curves represent intracellular conditions. The temperature is *T*=298.15 (invitro) and *T* = 310K (intracellular) for subfigures (a), and *T*=310K (invitro) and *T* = 313K (intracellular) for subfigures (b).

Ongoing research and future direction

- ❑ Two connected “skins”: A novel coupled transmission line circuit model for microtubule. Expect to get oscillatory wave-packets.
- ❑ We want to adopt machine learning models to analyze more complex systems (bundles and other higher order structures) which are otherwise not possible to study using the analytical approach above.

References

[1] Hunley, Christian, and Marcelo Marucho. “Electrical Propagation of Condensed and Diffuse Ions Along Actin Filaments.” *Journal of Computational Neuroscience*, vol. 50, no. 1, Feb. 2022, pp. 91–107.

[2] Hunley, Christian, et al. “A Multi-Scale Approach to Describe Electrical Impulses Propagating along Actin Filaments in Both Intracellular and in Vitro Conditions.” *RSC Advances*, vol. 8, no. 22, Mar. 2018, pp. 12017–28.

[3] Hunley, Christian, et al. “Electrical Impulse Characterization along Actin Filaments in Pathological Conditions.” *Computer Physics Communications*, vol. 275, June 2022, p. 108317.