Poster

Category: Modeling at nanoscale

MATHEMATICAL SIMULATION OF AN ENGINEERED NANOSCALE EXCITABLE VESICLE

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Overview:

Recent advances in protein research and laboratory protocols have ushered in a new era where engineered devices can be constructed in the nanometer scale. A proposed idea by our group incorporates basic components required to generate a neuronal action potential (AP) into a spherical polymer vesicle about 200nm in diameter.

Membrane-bound ion channels, which are selective to specific ions, regulate the flow of ions into and out of cells. The flow of certain ions across the cell membrane, mainly sodium and potassium, results in the APs seen in neurons. We propose the possibility of creating an artificial "excitable vesicle" (EV) by purifying these ion channels from cell membranes and inserting them into the polymer membrane organized into a vesicle structure. A schematic for the EV system is shown in Figure 1. Potential uses for EVs range from investigating the ionic current dynamics in a single vesicle that characterize the AP, to studying complex systems by linking the EVs to form a network. Developing computer modeling techniques to simulate the operation of EVs can predict whether particular ion channel combinations will be compatible. A computer program of this nature not only saves time and cost by taking the guesswork out of constructing the actual device, but can be used as a tool to study the underlying mechanism of the AP.

Description of Model:

The model shall be tentatively developed according to the plan shown in Figure 2. Currently, two basic models are nearing initial stage of completion: a deterministic model based on Hodgkin-Huxley kinetics,[1] and a stochastic channel gating model that is based on the traditional Hodgkin-Huxley structure.[2]

Current Work:

An initial area of interest is the effect of a smaller volume during an AP. For instance, during an AP in a typical neuron, the intracellular changes in concentrations of sodium and potassium ions are negligible. As volume decreases, these concentration changes become significant and the mechanics of the action potential begin to be affected. Initial data from the deterministic model is shown in Figure 3. This is an "AP-like" contour that was obtained by drastically increasing the number of sodium pumps in the membrane. Figure 4 shows the same situation without the action of the pump. We believe this occurs due to the limited amount of ions available in a vesicle of this size. The results were obtained using parameters for the sodium channel (NaChBac) obtained by Ren et al.[3] and potassium channel (KvAP) from Ruta at al.[4] Also, the analysis was performed with the realization that channel behavior may differ from the performance values published in literature due to differing environments and large swings in ionic concentration.

Another area of interest is investigating the situation where there are small numbers of ion channels in the system. The stochastic behavior of individual ion channels will appear as noise in the action potential contour. The stochastic model is the precursor to the 3-D spatial model which will take into effect the local effects of a concentration gradient on a single ion channel.

Future Work:

Once the 3D stochastic model for a single vesicle has been established, we plan to link the vesicles to form a network of vesicles for studies in the areas of neural networks and emergent behavior in complex systems.

FIGURES:

Figure 1:
System schematic of excitable vesicle

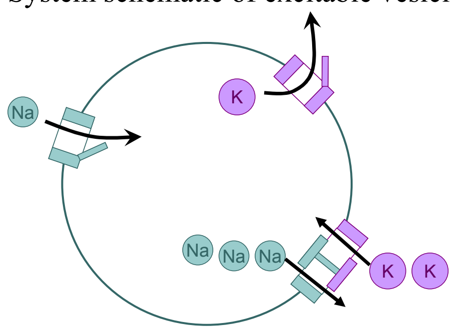


Figure 2:

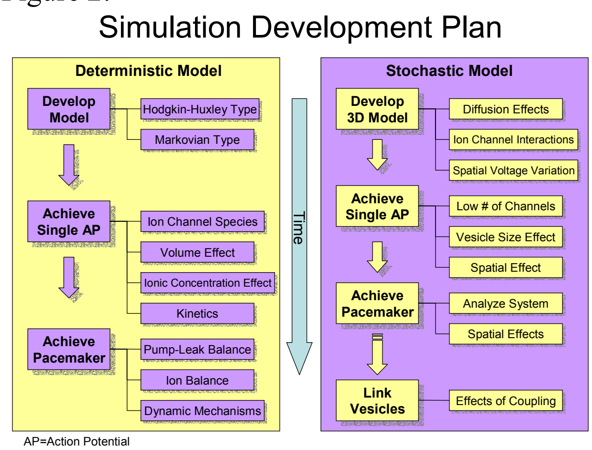


Figure 3:
Action potential from deterministic model with strong sodium pump

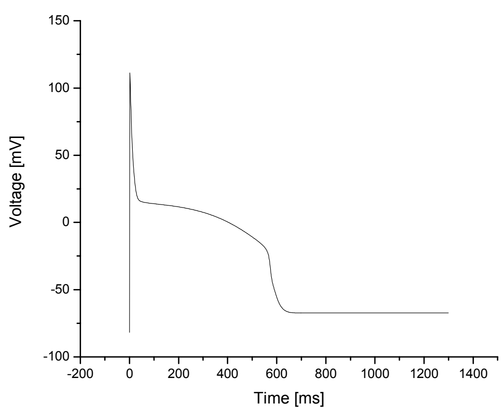
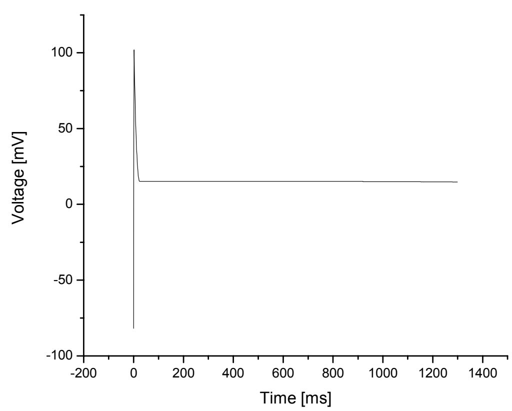


Figure 4:
Action potential from deterministic model without sodium pump



REFERENCES:

1. Luo, C.H. & Rudy, Y. A dynamic model of the cardiac ventricular action potential. I. Simulations of ionic currents and concentration changes. *Circ Res* **74**, 1071-1096 (1994).

2. Clay, J.R. & DeFelice, L.J. Relationship between membrane excitability and single channel open-close kinetics. *Biophys J* **42**, 151-157 (1983).

3. Ren, D. et al. A prokaryotic voltage-gated sodium channel. *Science* **294**, 2372-2375 (2001).

4. Ruta, V., Jiang, Y., Lee, A., Chen, J. & MacKinnon, R. Functional analysis of an archaebacterial voltage-dependent K+ channel. *Nature* **422**, 180-185 (2003).