

A Simulation-Based Teaching and Learning Resource for Electrophysiology: iCell

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Abstract— An interactive web resource, iCell (<http://ssd1.bme.memphis.edu/icell/>), was developed as a simulation-based teaching and learning tool for electrophysiology. The web site integrates education and research, and provides JAVA applets that represent models of various cardiac cells and neurons, and simulation data of their bioelectric activities at cellular level. Each JAVA-based model allows the user to go through menu options to change model parameters, run and view simulation results. The site also hosts a glossary section for the scientific terms. iCell has been used as a teaching and learning tool for five graduate courses at the Joint Biomedical Engineering Program of University of Memphis and University of Tennessee. This modeling tool has been also used as a collaboration site among our colleagues interested in simulations of cell membrane activities. Scientists from the fields of biosciences, engineering, life sciences and medical sciences in Argentina, Belgium, Brazil, Canada, China, England, Germany, Greece, Ireland, the Netherlands, New Zealand, Republic of Korea, Spain, Turkey and USA have tested and utilized iCell as a simulation-based teaching, learning and collaboration environment. The cellular modeling resource, iCell, provides us with a platform-independent, interactive and user-friendly teaching and learning tool, and also a collaboration environment for electrophysiology to be shared over the Internet.

Keywords: computational tool for electrophysiology; single cell models; simulation data, computational JAVA models; internet application.

Introduction

The interactive cell modeling internet resource, iCell, integrates research and education for electrophysiology. The site is located at <http://ssd1.bme.memphis.edu/icell/>. iCell consists of JAVA applets representing models of various cardiac cells and neurons, and provides simulation data of their bioelectric activities at single cell level. Each JAVA-based cell model gives an overview of the cell, demonstrates the cell membrane with an electrical equivalent circuit and cites the published modeling paper for further information (as seen in Figure1). The cell models in iCell are grouped into versions, and cardiac or neuron "modelboxes".

The Cardiac Modelbox has the applets for cardiac electrophysiology and these applets are for

- (1) a rabbit sinoatrial node cell model (Demir *et al*, 1994) (as seen in Figure 1),
- (2) a guinea pig ventricular cell model (Luo and Rudy, 1991),
- (3) a rabbit atrial cell model (Lindblad *et al*, 1997),
- (4) a human atrial cell model (Nygren *et al*, 1998),
- (5) a dog ventricular cell model (Winslow *et al* 1999),
- (6) a bullfrog atrial cell model (Rasmusson *et al* 1990),
- (7) a frog ventricular cell model (Riemer *et al* 1999), and
- (8) a rat ventricular cell model (Pandit *et al*, 2001).

Currently, the applets in the Neuron Modelbox are for

- (1) a squid axon model (Hodgkin and Huxley, 1952) and
- (2) an Aplysia R15 bursting neuron model (Demir *et al*, 1997) (Figure 1).

The iCell models were presented as JAVA applets in HTML pages and can be executed in any JAVA-enabled browser. All of these JAVA applets were developed under JDK1.2 (Java Development Kit) of Sun Microsystems Inc. Each applet has a user-friendly interface and allows the user to go through menus to choose simulation protocols, change model parameters, run simulations, select and view the simulation data. iCell also has a glossary section for the scientific terms to overcome the language problem among the scientists from different disciplines.

Teaching and Learning by iCell

I have used iCell as a teaching and learning tool for five graduate courses; Life Sciences I for Biomedical Engineers, Medical Physics, Bioelectricity, Computational Modeling of Cellular Systems and Advanced Cardiac Electrophysiology, at the Joint Biomedical Engineering Program of University of Memphis and University of Tennessee.

Simulation-Based Teaching: I have used iCell as a teaching tool when the course material covered the dynamics of cell membranes (e.g. action potential and the underlying ionic concentrations of calcium, potassium, sodium and chloride, and the ionic currents; ion channels, membrane pumps and exchangers). During the lectures, I run simulations with iCell to demonstrate the electrical behavior of the cell membrane and the interactions between the ionic currents. I display the simulations with different conditions to show the changes in the nonlinear behaviors of the cells. These simulations demonstrate the significance of computational models to the students and how the models can investigate more conditions than the experiments can since we can change the parameters and conditions numerically, and how the models can be used as predictive tools.

Simulation-Based Learning: The students in the courses used iCell as a self-learning tool while they were assigned to do homework with it. The assigned homework had certain simulation protocols to run. The students were asked to prepare reports and tables of their simulation results for the changes they observed for the assigned simulation protocols.

Simulation-Based Teaching, Learning and Collaboration Environment

This modeling tool iCell was also used as a collaboration site among our colleagues interested in simulations of cell membrane activities. The iCell site has been used by many scientists and students from the fields of biosciences, engineering, life sciences and medical sciences (<http://ssd1.bme.memphis.edu/icell/people.htm>) in Argentina, Belgium, Brazil, Canada, China, England, Germany, Greece, Ireland, the Netherlands, New Zealand, Republic of Korea, Spain, Turkey and USA as a simulation-based teaching, learning and collaboration environment. Some professors from the following universities and disciplines requested permission to use iCell in their courses: Johns Hopkins University (Biomedical Engineering, Medical School), University of Utah (Bioengineering, Medical School), Texas A & M University (Bioengineering, Physiology and Pharmacology), California State Univ. Fullerton (Biological Sciences), Hope College (Biology), Kansas University Medical Center (Molecular and Integrative Physiology), Georgia University (Anatomy and Physiology, Nursing Anesthesia), University of Amsterdam (Cardiology, Physiology), University Hospital Groningen (Cardiology), University of Utrecht (Physiology), and Universitat de les Illes Balears (Animal Physiology).

Conclusions

We are enhancing iCell by developing more applets for the Cardiac and Neuron Modelboxes. We are also adding more features to analyze and to display the simulation results. One of the future goals is to use iCell for distance teaching. The platform-independent software, iCell, provides us with an interactive and user-friendly teaching, learning and collaboration environment for electrophysiology to be shared over the Internet. iCell continues to motivate the development the students and scientists in the cross-disciplinary fields of engineering and life sciences in different parts of the world.

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Model of the Rabbit Sinoatrial Node Cell - Microsoft Internet Explorer

Address: http://ssdl.lbne.memphis.edu/cell/Satrial.htm

Model of a Rabbit Sinoatrial Node Cell in iCell

S.S. Demir, J.W. Clark, C.R. Murphey, and W.R. Giles, 1994

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The screenshot shows a graph of membrane voltage (mV) versus time (ms). The voltage starts at approximately -80 mV, rises to a peak of about 40 mV at 100 ms, falls to a trough of about -60 mV at 200 ms, rises to another peak of about 40 mV at 300 ms, and then falls to about -80 mV at 400 ms. The status bar at the bottom of the graph shows $\Delta V = 78.75$ mV and $\Delta t = 24.0$ ms.

PARAMETER	VALUE
final time	500.0000 ms
start time	0.0000 ms
P_Na	0.0034 (mm ³ /s)
G_CaL	21.1594 nS
G_CaT	25.2175 nS
G_K	18.7599 nS
G_I	13.6375 nS
G_BNa	0.1603 nS
G_BCa	0.0365 nS
G_BK	0.0694 nS
K_NaCa	0.0125 pA/(mM ⁴)
I_NaK_ss	219.2457 pA
I_CaP_ss	28.6302 pA

CHOOSE FIGURES: membrane voltage, final time: 500.0, SET VALUE, Save all?, Draw during calc?, RESET VALUES, CALCULATE, STOP, [DONE] 100.00 %

This is a JAVA-based simulation of the electrical activity in a rabbit sinoatrial node cell model. The model was developed by the equations presented in *A Mathematical Model of a Rabbit Sinoatrial Node Cell* (S.S. Demir, J.W. Clark, C.R. Murphey, and W.R. Giles, *American Journal of Physiology* 266: C832-C852, 1994).

Electrical Equivalent Circuit of the Membrane

The diagram shows an electrical equivalent circuit of the membrane. It consists of a capacitor C_m connected to a bath (top) and cytoplasm (bottom). Several current sources are connected between the bath and cytoplasm: I_{Na} , I_{CaL} , I_{CaT} , I_K , I_f , I_B , I_{NaK} , I_{NaCa} , and I_{CaP} . Each current source is associated with a reversal potential: E_{Na} , E_{Ca} , E_{Ca} , E_K , E_f , E_B , E_{NaK} , E_{NaCa} , and E_{CaP} .

Instructions

- Click on "CALCULATE" to calculate and draw the graph.
- Click "STOP" to abort the calculation before it has finished.
- Select "Draw during calc?" to draw the graph as it calculates. (NOTE: Having this option selected will slow the calculation)
- Select a parameter, type a new value in the VALUE text-field, and click on "SET VALUE" to change the value of the parameters.
- A definition of the selected parameter is given in the status line.
- The current values of all parameters are displayed to the right of the graphing area.
- All parameters will default to their control values if certain limits are exceeded.
- Click "RESET VALUES" to set all parameters except for final time and start time to their default (control) values.
- Click within the graphing area to find the millisecond and millivolt values at that point.
- Select from "CHOOSE FIGURES" to display the membrane voltage, the ionic currents, or the calcium concentration.
- Select "Save all?" to save all figures. (NOTE: Having this option selected will slow the calculation)

NOTE: This simulation looks and functions best when run in Netscape Navigator 4.05+

Model Development by Semahat S. Demir and JAVA(tm) "Satrial" Applet by Joe McManis and Yiming Liu

Cell model equations and parameters taken from the C source codes of Semahat S. Demir

Last updated Sept. 29, 1999 by Yiming Liu

Web development and design by Semahat S. Demir

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Figure 1: A sample JAVA applet from iCell. A JAVA applet in the Cardiac Modelbox: Demir, S.S., Clark, J.W., Murphey, C.R. and Giles, W.R. A mathematical model of a rabbit sinoatrial node cell. *American Journal of Physiology* 266: C832-C852, 1994.