An Electrophysiological Simulation Model of the Myocardial Cell Using E-Cell System

Motohiro Yoneda[1,2] moto@sfc.keio.ac.jp
Yasuhiro Naito[1,3] ynaito@sfc.keio.ac.jp
Shoko Miyamoto[1,4] s99869sm@sfc.keio.ac.jp
Sayaka Ishinabe[1,3] t99068si@sfc.keio.ac.jp
Shinobu Kuratomi[5] kuratomi@card.med.kyoto-u.ac.jp
Nobuaki Sarai[5] sarai@card.med.kyoto-u.ac.jp
Satoshi Matsuoka[5] natsuoka@card.med.kyoto-u.ac.jp
Akinori Noma[5] noma@card.med.kyoto-u.ac.jp
Masaru Tomita[1,3] mt@sfc.keio.ac.jp

[1] Institute for Advanced Biosciences, Keio University, Tsuruoka 997-0035, Japan
[2] Graduate School of Media and Governance, Keio University, Fujisawa 252-8520, Japan
[3] Department of Environmental Information, Keio University, Fujisawa 252-8520, Japan
[4] Department of Policy Management, Keio University, Fujisawa 252-8520, Japan
[5] Department of Physiology and Biophysics, Graduate School of Medicine, Kyoto University, Yoshida-Konoe, Sakyo-Ku, 606-8501 Kyoto, Japan

Keywords: electrophysiology, simulation, myocardial cell, E-CELL

1 Introduction

We are constructing a model for electrophysiological simulation of the myocardial cell using E-CELL System. The E-CELL System is a modeling and simulation environment for biochemical and genetic processes [1]. We need to integrate various types of cellular functions such as membrane potential, ionic current, intracellular metabolism, signal transduction, and muscle contraction system to represent behavior of myocardial cell. E-CELL System, which can integrate multiple mathematical models, is therefore fit for our purpose.

Our eventual goal is to construct a simulation model of the whole myocardial cell. We intend to integrate the physiological model with biochemical pathways such as energy metabolism and signal transduction like phosphorylation by protein kinase.

In this poster, we present a model of electrophysiological myocardial cell that works with E-CELL System.

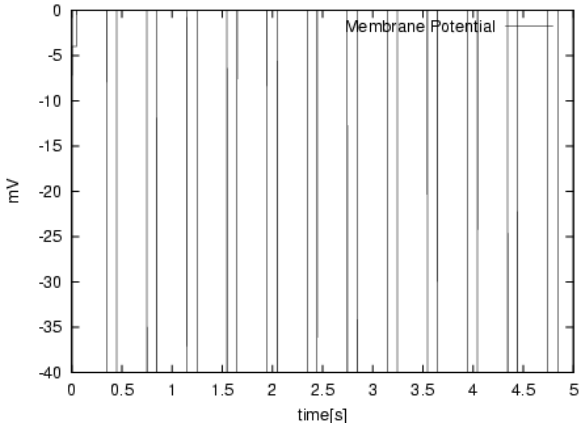
2 Method

Here we introduce a simulation of action potential in myocardial cell by calculating behavior of ion channels using the E-CELL System. E-CELL System had not been able to represent electrophysiological phenomena. So we extended the E-CELL System to handle electrophysiological parameters e.g. membrane potential.

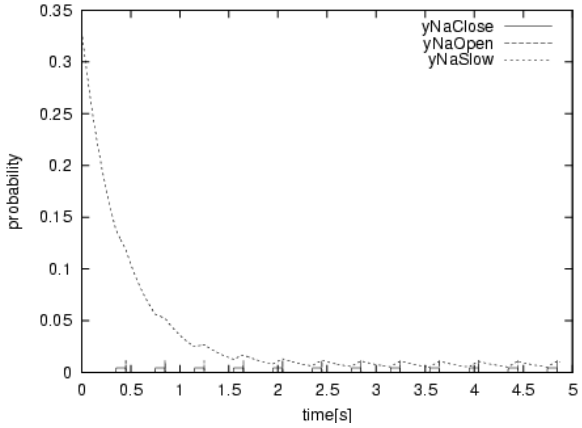
Then a model was constructed using the extended version of E-CELL. The model contains all 14 ion channels in myocardial cell. Empirical formula and parameters that represent actions of ion channels derived from work by Noma *et al.* [2].

3 Result

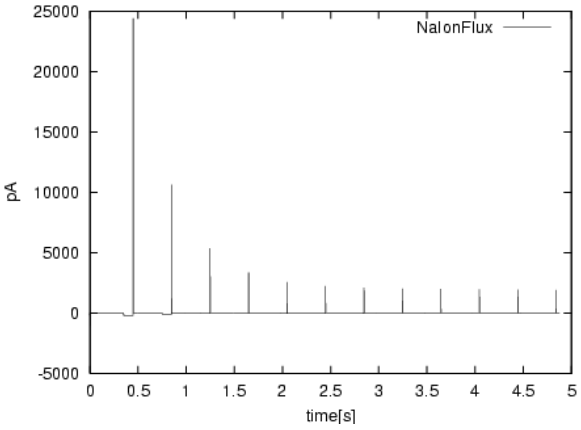
Figure 1 shows a results of simulation. These results are consistent with experimental data and existing models.



1-(a) Membrane Potential (mV).



1-(b) Fraction of opened Na^+ Channel.



1-(c) Ion flux thorough Na^+ channel(pA).

Figure 1. The simulation results of voltage clamp experiment. (a) Membrane potential. The potential goes up and down in each fixed time. According to the change of the membrane potential,gate open probability of ion channels and ionic currents were calculated. (b) Distribution of Na^+ ion channel that open or close, which affected by membrane potential change. 'yNaClose', 'yNaOpen' and 'yNaSlow' indicates fraction of closed gates, opened gates and slowly opened gates, respectively. (c) Inward Na^+ current. If membrane potential changes from -40mV to 0mV, fraction of opened Na^+ ion channel gets higher and inward Na current goes up.

4 Future Works

Electrophysiological model of myocardial cell has now been constructed. Next, we should integrate energy metabolism pathways and signal transduction pathways to approve the myocardial cell model. In E-CELL project, there are several groups modeling biochemical pathways. We will modify and implement these models to extend our model effectively.

Acknowledgement

This work was supported in part by Japan Science and Technology Corporation.

References

[1] Tomita, M., Hashimoto, K., Takahashi, K., Shimizu, T.S., Matsuzaki, Y., Miyoshi, F., Saito, K., Tanida, S., Yugi, K., Venter, J.C., and Hutchison, C.A. 3rd, E-CELL: software environment for whole-cell simulation, *Bioinformatics*, 15(1):72–84, 1999.

[2] http://www.card.med.kyoto-u.ac.jp/