In Silico Simulation Represents Adenoviral Gene Knockdown of Myocardial Ventricular Cell

Yasuhiro Naito[1,2]
ynaito@sfc.keio.ac.jp

Motohiro Yoneda[1,3]
moto@sfc.keio.ac.jp

Sayaka Ishinabe[1,3]
sayakai@sfc.keio.ac.jp

Shoko Miyamoto[1,3]
shikosan@sfc.keio.ac.jp

Nobuaki Sarai[4]
sarai@card.med.kyoto-u.ac.jp

Satoshi Matsuoka[4]
matsuoka@card.med.kyoto-u.ac.jp

Akinori Noma[4]
noma@card.med.kyoto-u.ac.jp

Masaru Tomita[1,2]
mt@sfc.keio.ac.jp

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

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1 Introduction

The Kyoto model, which is one of the most precise cell models, includes ion fluxes through all known myocardial ion channels, membrane potential, mitochondrial Ca^{2+} handling, and contraction, and represent the dynamics of ventricular cell and sinoatrial node cell of the guinea pig [1, 3]. We have ported the Kyoto model to the E-Cell simulation environment for *in silico* investigations [4]. Last year, Miake and his colleagues showed that adenoviral gene transfer of mutant *Kir2.1* transformed guinea pig's ventricular cells into pacemakers [2]. Their experiments were modeled and are implemented to the Kyoto model, then *in silico* experiments were executed using the E-Cell system. *in silico* results resembled Miake's results closely.

2 Model

The ventricular cell model of the Kyoto model was adopted as foundation of the model. Effects of adenoviral gene transfer were modeled as reduction of relative ion channel's conductance in which intact value was one. The conductance of the ion channel Kir2.1 (G_{Kir}) was decreased to values between 1 to 0.1.

3 Results and Discussion

Figure 1 shows the results of simulation with 0.22 of G_{Kir} value. The upper part shows membrane potential, and the lower part shows the total ionic current passing through the cell membrane. On this condition, *in silico* results resembled in vitro results most closely. The *in vitro* condition, which created the pacemaker successfully, was approximately 80% suppression of Kir2.1. It is strongly consistent with our *in silico* results. Further and detailed analyses of the *in silico* results should make elucidate the mechanisms underlying the remarkable change of phenotype, creation of the pacemaker.

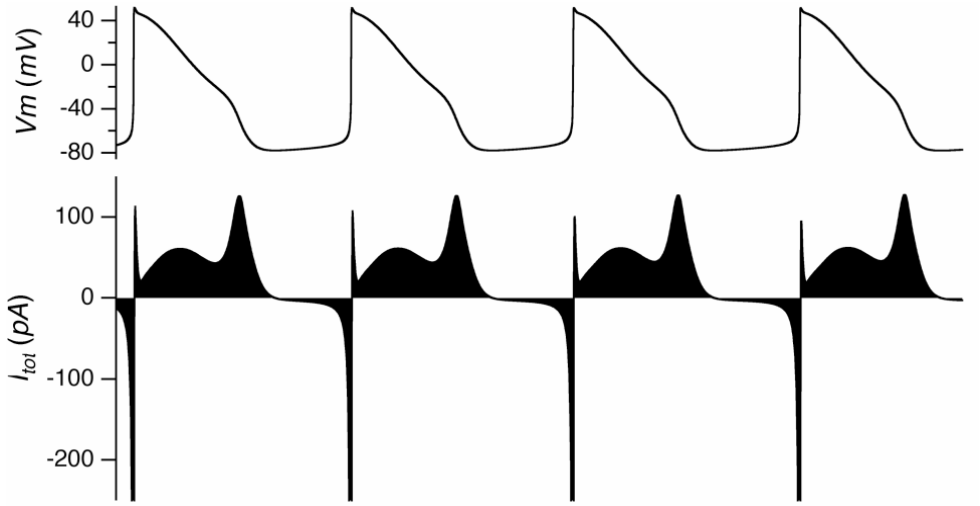

Figure 1: Simulation results.(See text for details.)

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