PL-1

Simulation of ATP Metabolism in Cardiac Excitation – Contraction Coupling

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We have developed a cardiac cell model (Kyoto Model) for the sinoatrial node and ventricle, which is composed of a common set of kinetic equations of membrane ionic currents, Ca^{2+} dynamics of sarcoplasmic reticulum and contractile protein[1,2]. To expand this model by including metabolic pathways, the intracellular ATP metabolism, which is pivotal in cardiac excitation – contraction coupling, was incorporated.

ATP consumption by the sarcolemmal Na^+ pump and the Ca pump in the sarcoplasmic reticulum were calculated with stoichiometry of 3Na:2K:1ATP and 2Ca:1ATP, respectively. ATP consumption by contraction was estimated according to experimental data[3]. Dependence of contraction on ATP and inorganic phosphate was modeled, based on data of skinned cardiac fiber[4]. ATP production by mitochondrial oxidative phosphorylation was modified from Korzeniewski & Zoladz (2001)[5], and creatine kinase and adenylate kinase reactions were incorporated. ATP dependence of ATP-sensitive K channel and L type Ca channel were also included.

In this model, steady state concentrations of most of metabolites were within the experimental range. The time course of change in metabolites under anoxic condition was in agreement with P-31 NMR study [6]. When inhibition of contraction by FCCP, a mitochondrial uncoupler, was simulated, the time course was similar to those observed in single cell experiments.

We concluded that this model well reproduces major systems of ATP metabolism in cardiac myocytes. This model will be further improved to establish a comprehensive cardiac cell model.

References

1. Matsuoka, Sarai, Kuratomi, Ono, & Noma. 2003. Role of individual ionic current systems in ventricular cells hypothesized by a model study. *Jpn. J. Physiol. in press.*
2. Sarai, Matsuoka, Kuratomi, Ono, & Noma. 2003. Role of individual ionic current systems in the SA node hypothesized by a model study. *Jpn. J. Physiol. in press.*
3. Farmer et al. *Life Sci* 1983. 33:1-18.
4. Mekhfi & Ventura-Clapier. Pflügers Arch. 1988. 411:378-385.
5. Korzeniewski & Zoladz, *Biophys Chem.* 2001 92:17-34.
6. Kay, Saks & Rossi. *J Mol Cell Cardiol.* 1997. 29:3399-411.