Mathematical Model of the Calcium-Dependent Chloride Current in a Smooth Muscle Cell

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Employing the Hodgkin-Huxley formalism, we have developed a mathematical model of the calcium-dependent chloride current on the basis of published experimental data concerning the kinetics of such current in cells of different types. The obtained results are destined for further use in a currently developed model of a smooth muscle cell of the bladder detrusor. A feature of the simulated current is the presence of two components with common kinetics of calcium-dependent activation and different (fast and slow) kinetics of voltage-dependent activation. In computational experiments performed with the use of a protocol of stepwise clamp of the membrane potential or the intracellular calcium concentration ($[Ca^{2+}]_i$), static and dynamic dependences of the current on the membrane potential and $[Ca^{2+}]_i$ (the current-voltage and current-concentration relations, IVs and ICs, respectively) were obtained; analogous dependences of the kinetic variables of calcium- and voltage-dependent activation of the current were also plotted. The obtained characteristics of the simulated current were close to those of the prototype currents. The following properties were typical of the current: (i) the outward rectification, (ii) enhancement of the rectification effect with increase in the $[Ca^{2+}]_i$, and (iii) a higher sensitivity to $[Ca^{2+}]_i$ deviations from the basal level (manifested in greater ratios of the current/concentration increments) within the range <1 µM, as compared to that within the range of higher concentrations.

INTRODUCTION

Calcium-dependent chloride currents first found in *Xenopus* oocytes [1, 2] have been recorded in cells of many types, particularly in smooth muscle cells (SMCs) of the airways [3], stomach [4], blood vessels [5], urethra [6], and bladder [7], and also in cells of the secretory glands [4] and in hepatocytes [8]. As was suggested, these currents play an important role in cellular electrical processes. In particular, due to its equilibrium potential, which is less negative compared to the resting potential (from –32 to about +2.2 mV, according to different publications, [7] and [5], respectively), this inward current can significantly shift the membrane potential (MP) toward depolarization and thus promote the development of electrical excitation [7, 9], muscle contraction [3], and other functionally important processes inherent to cells of one type or another. However, many aspects of biophysics and molecular physiology concerning these functionally important currents remain unexplored. It is not completely known what membrane proteins can play the role of channels for this current; specific roles of this current in the formation of the set of cellular electrical and biochemical processes are even less explored. Mathematical modeling, more and more widely used as a complementary technique in the respective studies, can help in resolving the listed problems, but models of the mentioned type remain rare so far. Recently, such models have been created just for endothelial cells [10] and pulmonary artery SMCs [11]. For SMCs of the urinary bladder detrusor (the object of our special interest), such models are absent. This motivated our work described below. The aim was to develop and explore a model of the calcium-dependent chloride current, which could be further used in building a biologically realistic model of SMC of the urinary bladder detrusor.

MODEL DESCRIPTION

The model of calcium-dependent chloride current was described using equations of the Hodgkin-Huxley type [12]. The current density (per unit

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