Competitive Permeation of Calcium Ion with other cation ions through the Calcium Release Channel (Ryanodine Receptor) of Cardiac Muscle: an Application of Coupled Poisson-Nernst-Planck System of Equations

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Abstract

The coupled set of Poisson-Nernst-Planck (PNP) equations is extended to include the local chemical interaction of mobile charged ions with the ion channel — a porous protein facilitating electrical signal transduction in biology. This set of coupled equations is then solved numerically to calculate the ion fluxes. The numerical result is then compared directly with single channel current-voltage (IV) relations measured from the calcium release channel of cardiac sarcoplasmic reticulum (RyR2) in twenty-one mixed solutions of 250mM alkali metal ions (Na^+, K^+, and Cs^+) with sarcoplasmic reticulum lumenal Ca^{++} ranging from 5mM to 50mM, and Mg^{++} from 1mM to 50mM. The measured IV relations were analyzed by the extended Poisson-Nernst-Planck (PNP) formulation to reveal the competitive permeating of Ca^{++} and other cations, in particular Mg^{++}. The results indicate that applying PNP theory, two adjustable parameters (diffusion coefficient (D) and "excess" chemical potentials ($\overline{\mu}$)) suffice to predict the flow of Ca^{++} from the sarcoplasmic reticulum in cardiac muscle. The data are used to predict the calcium ion activity profiles in the RyR2 pore, the calcium ion fluxes in solutions of physiological interest, and the competitive permeation of Ca^{++} and Mg^{++}. The coupling of ion permeation is through purely electrostatic interaction, promoted by the local chemical interaction of ion specific interaction with the pore of ion channel proteins. The analogy to the charge coupling phenomena found in the semiconductor devices is discussed.

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