

MAR14-2013-000468

Abstract for an Invited Paper
for the MAR14 Meeting of
the American Physical Society

Single-Molecule Ion Channel Conformational Dynamics in Living Cells

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Stochastic and inhomogeneous conformational changes regulate the function and dynamics of ion channels that are crucial for cell functions, neuronal signaling, and brain functions. Such complexity makes it difficult, if not impossible, to characterize ion channel dynamics using conventional electrical recording alone since that the measurement does not specifically interrogate the associated conformational changes but rather the consequences of the conformational changes. Recently, new technology developments on single-molecule spectroscopy, and especially, the combined approaches of using single ion channel patch-clamp electrical recording and single-molecule fluorescence imaging have provided us the capability of probing ion channel conformational changes simultaneously with the electrical single channel recording. By combining real-time single-molecule fluorescence imaging measurements with real-time single-channel electric current measurements in artificial lipid bilayers and in living cell membranes, we were able to probe single ion-channel-protein conformational changes simultaneously, and thus providing an understanding the dynamics and mechanism of ion-channel proteins at the molecular level. The function-regulating and site-specific conformational changes of ion channels are now measurable under physiological conditions in real-time, one molecule at a time. We will focus our discussion on the new development and results of real-time imaging of the dynamics of gramicidin, colicin, and NMDA receptor ion channels in lipid bilayers and living cells. Our results shed light on new perspectives of the intrinsic interplay of lipid membrane dynamics, solvation dynamics, and the ion channel functions.