数学与系统科学研究院

计算数学所学术报告

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报告题目：

Exploring the ion selectivity in voltage-gated sodium channels using molecular dynamics simulation

邀请人：　　卢本卓 研究员

报告时间：**2013** 年 **12** 月 **2** 日（周一）

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报告地点：　　科技综合楼三层 **311**

计算数学所报告厅

Abstract:

In this work, we first studied the Na^+/Ca^{2+} selection in voltage-gated sodium (Na_v) channels by simulating the structure of a recently determined structure of Na_vRh, a marine bacterial NaChBac ortholog. According to the thermodynamic calculation at the two ion binding sites within the selectivity filter of this prokaryotic protein, we found that Ca^{2+} ions are prone to be trapped at the extracellular binding sites due to the strongly favorable electrostatic interactions there, which then blocks the entrance of both Na^+ and Ca^{2+} to the vestibule of the SF. This observation provided insights into the mechanism of ion selectivity on Na^+ over Ca^{2+} in mammalian Na_v channels. In the next step, we continued to explore mechanism of Na_v channels in discriminating Na^+ and K^+, two ions which are highly similar in chemistry. Different from the homo-tetrameric structure of the prokaryotic Na_v channels, the mammalian channels are composed of four non-identical domains, each of which donates a specific residue at the constriction site within the selectivity filter. In order to analyze the role of these key residues, we modeled the mammalian Na_v channel by mutating the residues at the constriction site in the prokaryotic Na_vRh structure to its mammalian counterpart. By simulating the mutant structure, we finally proposed a model to explain the Na^+/K^+ selectivity in mammalian Na_v channels: Lys screens most weakly Na^+-selective locations within the constriction site through electrostatic repulsion and repels the cation to pass through a highly Na^+-selective location formed by the clustered carboxylate groups of Asp and Glu.

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