

Seminar

Mechanisms of voltage- and ligand-dependent activation of pacemaker ion channels

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Pacemaker ion channels are an unusual class of voltage-gated ion channels that are involved in pacemaking activity in rhythmic circuits found in the human brain and heart. Unlike most voltage-dependent ion channels, these channels become active upon membrane hyperpolarization rather than depolarization. The activity of these channels is also directly regulated by second messengers such as cAMP which bind to the cyclic nucleotide-binding domain in the C-terminus. In the first part of the presentation, I will discuss the molecular and structural mechanisms that underlie reversed voltage-dependent gating of these ion channels. cAMP binding to pacemaker ion channels is allosterically regulated but the proposed mechanism is controversial. In the second half, I will describe recent advances in using single molecule methods to study energetics of long-range coupling. We are able to obtain a direct estimate of the various equilibrium constants associated with each of the ligation states and probe the mechanism of allostery in these ion channels at an unprecedented detail.

Thursday, July 13th 2023

4:00 PM (Tea / Coffee 3.45 PM)

Auditorium, TIFR-H