Ciclo di incontri – Tavolo di discussione

Collective phenomena in neuron membranes: are critical fluctuations responsible for ion channel clustering and cooperativity?

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The activation of voltage gated ion channels has been intensely investigated for decades and it is now so well characterized that we have an atomically-detailed description of the major conformational changes taking place at the level of the single molecule. However, this accurate picture cannot accommodate recent experimental observations that highlight a dramatic and so far unsuspected collective behavior: voltage gated ion channels in physiological membranes form clusters and gate cooperatively. I will present a quantitative theory that bridges these two vastly different length scales and reconciles these seemingly conflicting views. This novel conceptual framework, which is rooted in the statistical physics of immiscible fluids, accounts for the formation of lipid rafts and for the bias they entail on the conformation of the residing ion channels. First, I will discuss long time-scale MARTINI simulations showing that annular lipids have a distinct compositional bias, which is different in the resting and the activated states. These simulations will be then used to estimate channel-lipid interactions and thus parametrize a mesoscopic model to explore the spatial organization of ion channels and their response (in the time domain) to changes in the transmembrane potential. I will show that channels embedded in membranes close to a miscibility transition develop attractive long-range interactions that give rise to clustering effects. Strikingly, the lipid phase behavior is itself affected by the activation state of the ion channels. Finally, the strong activation cooperativity and long time-scales hysteresis effects can potentially explain the modal gating phenomena observed in many single channel recordings.

Mercoledì 26 Ottobre 2022 - Ore 15.00
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