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Hydrophobic Gating in nanochannels: understanding single channel mechanisms for designing better nanoscale sensors

HyGate

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Hydrophobic gating is the phenomenon by which the flux of ions or other molecules through biological ion channels or synthetic nanopores is hindered by the formation of nanoscale bubbles. Recent studies suggest that this is a generic mechanism for the inactivation of a plethora of ion channels, which are all characterized by a strongly hydrophobic interior. The conformation, compliance, and hydrophobicity of the nanochannels – in addition to external parameters such as electric potential, pressure, presence of gases – have a dramatic influence on the probability of opening and closing of the gate. This largely unexplored confined phase transition is known to cause low frequency noise in solid-state nanopores used for DNA sequencing and sensing, limiting their applicability. In biological channels, hydrophobic gating might conspire in determining the high selectivity towards a specific ions or molecules, a characteristic which is sought for in biosensors.

The objective of HyGate is to unravel the fundamental mechanisms of hydrophobic gating in model nanopores and biological ion channels and exploit their understanding in order to design biosensors with lower noise and higher selectivity. In order to achieve this ambitious goal, I will deploy the one-of-a-kind simulation and theoretical tools I developed to study vapor nucleation in extreme confinement, which comprises rare-event molecular dynamics and confined nucleation theory. These quantitative tools will be instrumental in designing better biosensors and nanodevices which avoid the formation of nanobubbles or exploit them to achieve exquisite species selectivity. The novel physical insights into the behavior of water in complex nanoconfined environments are expected to inspire radically innovative strategies for nanopore sensing and nanofluidic circuits and to promote a stepwise advancement in the fundamental understanding of hydrophobic gating mechanisms and their influence on bio-electrical cell response.