Molecular dynamics simulations of gating in model hydrophobic nanopores

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Keywords: ion channels, molecular dynamics, hydrophobic gating,

Biological ion channels are the gates of cells which allow the exchange of ions and molecules across cellular membranes. The typical size of the interior of biological channels is of the nanometer or below, often characterized by hydrophobic residues. Molecular dynamics simulations have reported [1] that, in some ion channels, such confined conditions promote the formation of a nanoscale vapor cavity which is capable of blocking the flux of ions – giving rise to the so-called hydrophobic gating mechanism [2]. While molecular dynamics has proven an invaluable tool to connect the structure of such channels with their function, an open challenge for simulations concerns the timescales that can be afforded on current architectures, still far from the biologically relevant ones, typically in the millisecond range.

In this work, molecular dynamics is combined with specialized rare-event methods in order to access the long timescales of the thermally-activated formation of vapor cavities (Figure 1) in hydrophobic nanopores immersed in water [3]. The mechanism and the kinetics of bubble formation are investigated in simple pore geometries, reproducing some salient features of biological ion channels (Figure 2). The effect of extreme confinement on the phase behavior of water is assessed, revealing that nanoscale effects, such as line tension and enhanced hydrophobicity, play a major role in accelerating the formation of nanoscale bubbles. The relevance of these preliminary results for hydrophobic gating in biological ion channels is discussed together with more technology-oriented applications to porous materials with controlled wetting properties [4] (Figure 3). Although several simplifications are adopted in modelling the pore, the presented methods are able to disclose the timescales of gating, opening the way to a direct comparison of simulations with electrophysiology experiments.

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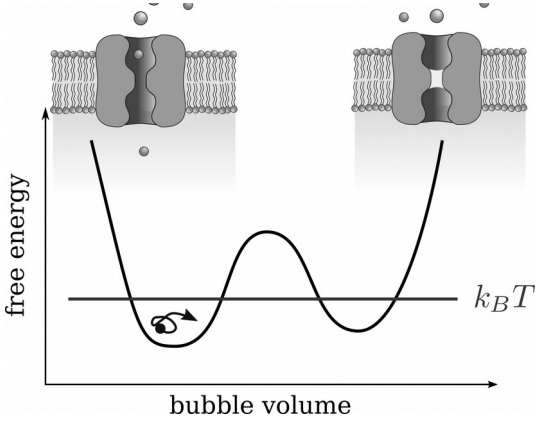

Figure 1. Illustration of the thermally-activated formation of a nanoscale vapor cavity within a generic ion channel, giving rise to hydrophobic gating, in which the vapor cavity blocks ion currents. The free-energy profile shows that the bubble formation is a "rare event", i.e., it happens on timescales which are not amenable of brute force simulation, but require specialized sampling methods.

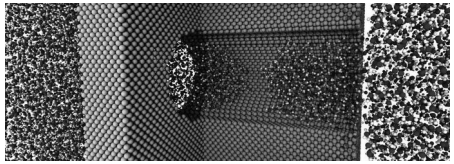

Figure 2. Model system – a hydrophobic cylindrical pore – used to investigate bubble formation within a hydrophobic nanopore via rare-event molecular dynamics simulations [3].

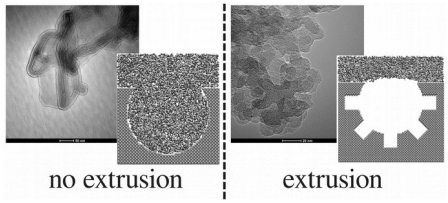

Figure 3. Experiments and simulations show that the geometry and surface roughness of nanoporous materials are critical to determine whether bubbles will form within the pores [4]