Free energy surfaces of the ion conduction through the small viral potassium channel Kcv_{PBCV-1}

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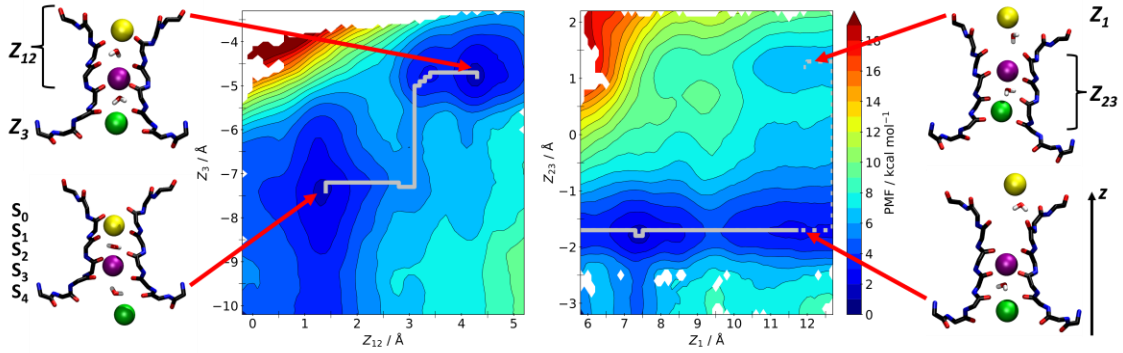
Potassium channels are transmembrane proteins that facilitate the selective transport of K^+ through the cell membrane. Therefore, they play a crucial role in numerous physiological processes and can be found in almost all organisms. Although a large number of studies of the conduction mechanisms through the selectivity filter have been carried out, it has not yet been possible to identify the dominating scheme, let alone the potential transferability of mechanistic features from one K^+ channel to another. Here we focus on the small tetrameric viral potassium channel Kcv_{PBCV-1} as a minimal model system. The tetrameric channel is composed of only 94 amino acids per monomer. [1,2] Despite its small size, the channel shares the same core pore module conserved in all K^+ channels.



Molecular dynamics (MD) simulations are a commonly used method for investigating ion channels in solution and embedded within a membrane environment. To facilitate sampling in high-barrier regions like the selectivity filter and hence enable the calculation of a free energy surface, enhanced sampling methods such as umbrella sampling (US) are applied. [3] Suitable structures for the US are obtained from an MD simulation at +425 mV, starting with a homology model based on the NaK2K ion channel. [4] Snapshots were chosen to ensure that the selectivity filter is occupied by three potassium ions with a water molecule between each ion. For the definition of collective coordinates governing transport, we refer to previous publications on KcsA. [5,6] Analogously, we split the conduction pathway into two 2D topographic maps where two ions are represented by their centre of gravity. Unbiasing of the data and calculation of the potential of mean force (PMF) were done by using the multistate Bennett acceptance ratio (MBAR). [7] The results obtained reveal the relevance of concerted ion motion along the transition pathway formed by selectivity filter binding sites, in agreement with findings obtained for KcsA. This therefore demonstrates that the specific transport mechanism investigated here is a common feature of K^+ channels with similar filter structure, despite otherwise strong structural differences.

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