Mechanisms of sodium selectivity in membrane ion transport

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Ion channels are membrane proteins that catalyse rapid and selective transport of ions across cell membranes, and are essential for the generation of nerve impulses that control crucial functions in the body. We have carried out extensive atomic-level molecular dynamics simulations of different ion channels to uncover common features of selective ion transport. Voltage-gated sodium channels are responsible for the generation of action potentials, yet the mechanisms by which they select for sodium over other abundant ions remain elusive. Our simulations have demonstrated efficient multi-ion conduction, where protein carboxylate groups play intimate and dynamic roles in the transport process. We have observed ion-carboxylate complexes that are unique to sodium, and which are responsible for creating a high field strength site that preferentially selects for sodium. Shared features of conduction are seen in both bacterial and model mammalian channels, despite distinct EEEE and DEKA signature sequences. Moreover, free energy simulations reveal analogous ion-protein complex involvement in ASIC channels, which mediate sodium currents in response to increased extracellular proton concentrations. These results are leading towards a general understanding of the principles governing sodium-selective protein binding and transport.