Free Energies of Ion Binding and Selectivity in the Bacterial CLC-ec1 Chloride Membrane Transporter

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The chloride channel/transporter family of proteins facilitates anion transport across biological membranes. There is extensive physiological and bioinformatic evidence that the channels and transporters are closely related. Each monomer of a homodimeric CLC transport protein contains a narrow selectivity filter. Investigating the ion binding properties inside the filter is crucial for understanding key mechanistic states during ion transit. Here computer simulations are used to explore the free energies of Cl − ions in the binding sites of the wild-type CLC-ec1 transporter and its mutant E148A. The calculations indicate a close synergy between anion binding and protonation of the external glutamate gate. In addition, quantum chemical calculations on the F − , Cl − , and Br − ions in the central binding site are used to examine ion selectivity. The calculations show a significant extent of charge transfer from the ion to the nearby residues. The computed free energies, in conjunction with experimental measurements, place constraints on proposed mechanisms for the transport cycle.