Mapping the importance of 4 factors in creating monovalent ion selectivity in biological molecules

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The ability of macrocycles, enzymes, ion channels, transporters and DNA to differentiate between ion types is often crucial to their function. Using molecular dynamics simulations on both detailed systems and simple models we quantify the importance of four factors which affect the ion selectivity of such molecules, including the number of coordinating ligands (Thomas, Jayatilaka & Corry, 2007), their dipole moment (Noskov, Berneche & Roux, 2004), the cavity size (Doyle *et al.*, 1998) and their vibrational motion. The information resulting from our model systems is distilled into a series of 'selectivity maps' that can be used to 'read off' the relative free energy associated with binding of different ions, and to provide an estimate of the importance of the various factors. While our maps cannot capture all elements of real systems, it is remarkable that our simple model produces differential site binding energies in line with experiment and more detailed simulations for a variety of systems. This makes our maps a very useful tool for assisting in understanding the origins of selective binding and transport. Our studies show that the various suggested mechanisms of ion selectivity can be important in various situations. The chemical nature of the coordinating ligands is essential for creating thermodynamic ion selectivity in flexible molecules (such as 18-crown-6), but as the binding site becomes more rigid the number of ligands (as in ion channels) and the reduction of thermal fluctuations (as in amino acid transporters) can become important. In the future, our maps could aid in the determination of the local structure from binding energies and assist in the design of novel ion selective molecules.

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