On resolution of the selectivity/conductivity paradox for the potassium ion channel

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The ability of the potassium channel to conduct K^+ at almost the rate of free diffusion, while discriminating strongly against the (smaller) Na^+ ion, is of enormous biological importance [1]. Yet its function remains at the center of a "many-voiced debate" [2,3]. In this presentation, a first-principles explanation is provided for the seemingly paradoxical coexistence of high conductivity with high selectivity between monovalent ions within the channel. It is shown that the conductivity of the selectivity filter is described by the generalized Einstein relation. A novel analytic approach to the analysis of the conductivity is proposed, based on the derivation of an effective grand canonical ensemble for ions within the filter. The conditions for barrier-less diffusion-limited conduction through the KcsA filter are introduced, and the relationships between system parameters required to satisfy these conditions are derived. It is shown that the Eisenman selectivity equation is one of these, and that it follows directly from the condition for barrier-less conduction. The proposed theory provides analytical insight into the "knock-on" [1] and Coulomb blockade [4] mechanisms of K^+ conduction through the KcsA filter. It confirms and illuminates an earlier argument [3] that the "snug-fit" model cannot describe the fast diffusion-limited conduction seen in experiments. Numerical examples are provided illustrating agreement of the theory with experimentally-measured I-V curves. The results are not restricted to biological systems, but also carry implications for the design of artificial nanopores.

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