How nature discriminates between sodium and potassium ions

ab initio molecular simulations successfully answer long-standing puzzle of critical membrane function

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Natural systems excel at being able to discriminate between molecules on the basis of subtle structural differences. Membrane-spanning protein channels, for example, are exquisitely designed to differentiate between Na^+ (sodium) and K^+ (potassium) ions despite the identical charges and sub-Angstrom differences in size. Consequently, nearly all cells can selectively transport these ions across their membranes, a process that underlies such diverse physiological tasks as cell volume control, nerve cell signaling, heart rhythm control, vision, and kidney function.

Because of their charges, ions are "solvated" or surrounded by ligands to shield the charge. While scientists have long known that ion selectivity often lies in the ability of ion channel proteins to satisfy or frustrate ion solvation requirements, the persistent question revolves around how channel structures give rise to such a subtle effect between Na^+ and K^+. Recent work at Sandia provides a novel explanation. Using quantum chemical methods in a statistical mechanical framework for analysis, we analyzed ion binding to clusters of water and other ligands embedded in various environments. We found that in addition to the specific number and chemistry of ligands coordinating with the ions, the hydrogen-bonding proclivity of the surrounding environment created by the channel protein also plays a crucial role in ion selectivity. Interestingly, octa-coordinated channel binding sites (Figure 1) over-coordinate K^+ to achieve selectivity. Loss in the numbers of coordinating ligands can lead to lost selectivity or transient channel blockage.

These new ideas imply that ion discrimination could be incorporated into synthetic channel design. If we can understand these transport processes at the most fundamental level of ion discrimination by membrane proteins, we can potentially impact the development of drugs designed to counter malfunctions. Furthermore, by understanding how protein structure leads to such a remarkable level of discrimination, we can also aim to harness nature's design principles in nano-scale devices that mimic biological function. For example, Sandia researchers are exploring ways to perform ion discrimination for implantable electric energy sources to power artificial retinas (Figure 2).

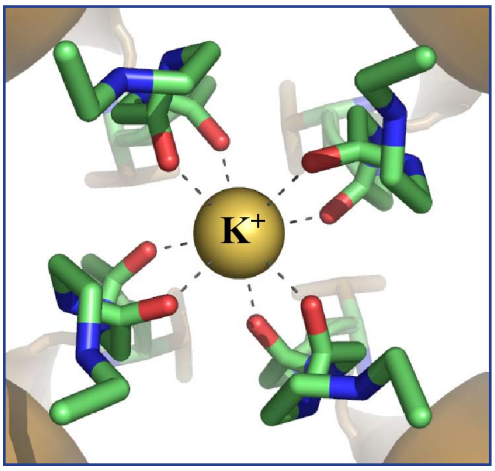

Figure 1: Octa-coordinated channel binding sites achieve K^+ selectivity.

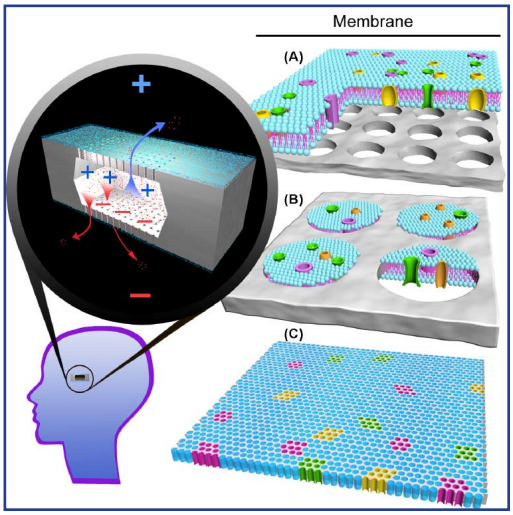

Figure 2. Biomimetic membranes could form components of useful new nanodevices, such as implantable electrical power sources to drive artificial retina.

Publications

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