Ion Discrimination in Proteins and DNA

D. A. Doyle et al. describe the crystal structure of a potassium (K⁺) channel, which provides critical insight into the mechanism of ion movement across membranes (1). They describe some features of the metal coordination by the protein that are similar to the ion binding we have observed in the high-resolution crystal structure of a DNA tetraplex (2). In this DNA molecule, the structure is stabilized by a chain of alkali ions that line a central core (Fig. 1). Although the DNA tetraplex represents a stable equilibrium structure, details of the ion coordination in this core appear to support the proposals of Doyle et al. (1) with regard to the K⁺ channels’ remarkable selectivity for K⁺ and discrimination against sodium (Na⁺) ions. The distribution of counter ions along the DNA axis (2) may also shed light on the mechanism of ion flux in the ion channel (1).

The DNA structure (Fig. 1) shows that each Na⁺ ion is coordinated by the carbonyl oxygens of guanine bases, and that each ion is free of any hydration shell. The hydration shell is replaced by the coordinating O atoms provided by up to eight guanine bases. This observation agrees with the suggestion (1) that, in the K⁺ channel, dehydrated K⁺ ions are similarly coordinated by eight peptide backbone carbonyl O atoms.

The dimensions of a bound ion are complemented in the cases of both the DNA (2) and the protein (1) by the arrangement of the coordinating O atoms, which in turn give rise to size-selective cavities that define the coordination geometry for the recognized ion. Failure to satisfy the coordination and size criteria would result in a poor stereochemical match between the ligand and acceptor. For example, in the central position of the DNA tetraplex, the hole is far too small to accept a K⁺ ion, but ideally proportioned to receive a Na⁺ ion. Alternatively, in the case of the K⁺ channel, a bound Na⁺ counter ion would fit the available cavity, but its radius would be less than that required for ion coordination, thus Na⁺ would be rejected in favor of K⁺.

Doyle et al. note (1) that metal coordinating oxygens line the narrow selectivity filter in the channel and define successive binding sites for K⁺. Similarly, we observe (2) successive coordination tiers in the DNA, where each available binding site is fully occupied by Na⁺. At the center of the DNA structure, Na⁺ is symmetrically coordinated, as is the ion at the outer extremity of the selectivity filter in the K⁺ channel. Doyle et al. propose (1) that K⁺ ions flow freely through this channel by binding to each site in turn, while mutual electrostatic repulsion between adjacent ions forces them through successive binding tiers. In the DNA tetraplex (2), away from the central ion position, each ion becomes increasingly displaced from the center of the binding site in successive coordination tiers, in the direction of the DNA poles. This displacement is probably a result of mutual electrostatic repulsion, and it shifts the Na⁺ away from positions of, presumably, optimal coordination geometry. The chain of Na⁺ counter ions, in the context of the relatively inflexible DNA structure, may thus represent a snapshot of the dynamic process of ion flux proposed (1) for the K⁺ channel.

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References

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Fig. 1. Stereoscopic view of three central ion coordination tiers of the DNA tetraplex (2) with five Na⁺ counter ions. One DNA strand has been removed for clarity. Each Na⁺ ion is coordinated by eight O atoms (only six shown per ion). Central ion is bipyramidally coordinated by the upper and lower planes of guanine bases, but each successive ion shows a slight displacement from this ideal site, toward the poles of the DNA.
Editor's Summary