Reply to: Remarks on the nature of ion-ion interactions in channels

It is well documented from theory that the Maxwellian distribution and the average speed $(8kT/\pi m)^{1/2}$ are valid in both the gas and the condensed state (3). Recently, this law was tested in the condensed state through molecular dynamics simulations. The resulting velocity distributions are Maxwellian (6). Thus, for a substance at a given temperature, the average speed is a constant regardless of phase. This speed should not be mistaken for the macroscopic speed (mobility) which is much lower in liquids. The use of the Maxwellian distribution to calculate the fraction of molecules passing a energy barrier is not restricted to the gas state. It has been applied to the evaporation of molecules from condensed state (1) and the liberation of electrons from an incandescent source (5).

The applicability of this theory to the selectivity filter of a pore depends on whether the mean free path (MFP) of an ion is comparable to the distance for an ion to pass a barrier. The former = $1/(2^{1/2}\pi n d^2)$ introduced by Maxwell, where n is the number of molecules per volume and d is the diameter of the molecules (2). The latter distance is 1–2.5 Å in the selectivity filter in my model (10, 11). Among known channels, the dimensions of gramicidin A (25 Å long and 4 Å in diameter) are best resolved. There are several independent methods to determine the number of water molecules in the channel. The results from water permeability coefficient measurements suggest that there are 5 water molecules in a gramicidin A channel (8). The number obtained from streaming potentials is 6–7 (7). Provided the diameter of a water molecules ~ 2.9 Å, the MFP is estimated to be 1.12–1.40 Å. This number has been revised by molecular dynamics simulations in recent years. The computations suggest that there are 8 water molecules or 7 water molecules plus one ion in a gramicidin A channel (4, 9). The MFP in this situation is 1.05 Å. These estimated MFP's are very close to the distance to cross the barrier. Further, thermal fluctuations around the MFP provide opportunities that allow the transitions to be accommodated beyond the MFP (vacancies). Therefore, the transitions over 1–2.5 Å distance in my work are feasible. If the distance to cross the barrier is much larger than the MFP, the probability of such a vacancy occurring could drop markedly. A correction factor that describes this probability is then needed.

Using the discrete rate process and knock-on theme, Miller provided an alternative formulation to interpret "multi-ion" behavior. However, the molecular bases of these rate constants were not specified and the high affinity of Tl^+ over K^+ remains unexplained. The water-ion interactions are not included.

The involvement of mass in ion-ion and water-ion interactions is a direct outcome of my dynamic approach (11). It interprets "multi-ion" phenomena at the molecular level without imposing ion species dependent presumptions. I am aware that this may not be the sole determinant, and other atomic parameters, e.g., ionic polarizability could well be important, as suggested by Miller. I would be glad to see results that can specify the contribution of this property to "multi-ion" behavior.

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