

# Ions in Channels, Natural Nanovalves

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**Abstract:** Ion channels are proteins with a hole down their middle, that act as natural nanovalves that allow a handful of atoms to control macroscopic flows.

Classical statistical mechanics was not designed with interacting systems in mind, let alone systems in which atoms controlled machines. A different form of mechanics is needed when nanovalves are engineered. In my view, one needs the recently developed variational mechanics of complex fluids, like liquid crystals.

‘All sphere’ models of ions in channels and solutions are surprisingly successful in dealing with two very different (and important) channels over a large range of conditions. Amazingly, the same model **with the same two parameters accounts quantitatively for the selectivity of very different calcium  $\text{Ca}_v$  and sodium  $\text{Na}_v$  channels**. Binding free energy is an output of the calculation, produced by the crowding of charged spheres in a very small space. The model does not involve any traditional chemical ‘quantum’ binding energies at all.

How can such a simple model give such specific results when crystallographic wisdom and chemical intuition says that selectivity depends on the precise structural relation of ions and side chains? The answer is that **structure is a computed consequence of forces** in this model and is very important, but as an output of the model, not as an input. **Binding is a consequence of the ‘induced fit’ of side chains to ions and ions to side chains. Binding sites are self-organized and at their free energy minimum, forming different structures in different conditions.**

The effective structure of an ion channel depends on interactions of ions with each other and the channel protein. The theory of complex fluids uses variational methods to deal with such interacting systems. Variational theory allows the engineering of interacting molecules in liquid crystals. Variational methods are just now be applied to ions in channels and solution.

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