Cyclodextrin ion channels

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Although a cyclodextrin derivative was the first synthetic ion channel reported (Tabushi et al, *Tetrahedron Lett.*, **1982**, *23*, 4601-4604), there have been only sporadic reports of cyclodextrin-derived channels in the intervening three decades. Nonetheless, a channel constructed with a cyclodextrin "mouth" and a "throat" consisting of 6-8 identical units appended to the cyclodextrin in a single step is a very appealing concept that deserves further development.

We have prepared a large suite of cyclodextrin derivatives via a "click' reaction of terminal acetylenes to per¬-6'-azido- α- and β-cyclodextrins. These compounds are generally less than a full bilayer thickness in overall length with a majority expected to act as "half" channels in a gramicidin-like fashion in which end-to-end dimerization would produce the membrane-spanning channel.

The channel-forming activity of this series of compounds has been extensively explored using the voltage-clamp technique to apply a potential and record the ionic currents as a function of time. Although gramicidin-like on-off step behaviours in the conductance-time traces are evident for many of the compounds, they are a minority observation. More commonly observed are a number of other recognizable types of behaviour: "flickers" between a few different open states; transitions within an ensemble of open states; short duration spikes of high conductance. There are also some apparently completely erratic behaviours. We have been able to show that some of these of erratic behaviours appear to be governed by a power-law dependence of the lifetimes of events above a threshold (*Chem. Comm*, **2010**, *46*, 4169-4171).

We have developed tools for the systematic analysis of conductance behaviours in a way allows the set of behaviours of a single compound, or a group of compounds to be presented and analysed.From this dataset we derive: 1) an apparent underlying structure of the conductance records that we regard as the "normal" behaviours of these compounds (and indeed of all reported synthetic ion channels); and 2) criteria to assess unusual or anomalous behaviours; that 3) we can relate to the probable channel structures. The methodology also leads to a multidimensional appreciation of structure-activity relationships that will be useful as we develop persistent open channels for sensor applications.