Membrane ion channels singled out

This year’s Nobel prize for physiology or medicine celebrates a technique that allows detailed study of membrane function.

The study of ion transport across biological membranes is a paradoxically old field: Nasse described the exchange of anions across red blood cell membranes a decade before Arrhenius proposed his ionic theory. Nasse actually talked of the acids rather than anions per se. The area has remained quirky ever since, with the study of ion channels proceeding full steam ahead at a time when the existence of the biological membrane itself was under debate. It has had its share of luminaries, such as Luigi Galvani who demonstrated that electrical stimulation could mimic nervous excitation for muscle contraction, Hodgkin and Huxley who dissected the ionic components of the action potentials of nerve, and, more recently, Neher and Sakmann who devised techniques to study the movement of ions through individual channels in biological membranes.

A biological membrane is oil-like (philic) in composition and presents a formidable barrier to passage of charged species like sodium or calcium ions. Most membranes have structures that form molecular conduits through the membrane, filled with water, which permit easy passage of ions. The channels responsible for the action potential in nerve are capable of passing many millions of ions per second while retaining the ability to distinguish between species as similar as sodium and potassium ions. The traditional method of studying these molecules was to insert electrodes into cells and monitor the passage of ions through the entire ensemble of channels in the membrane as an electrical signal that could be detected with appropriate electronics (currents of the order of nanoamperes to microamperes were seen).

A very few channels could be purified to homogeneity and incorporated into artificial bilayer lipid membranes (BLMs). Electrodes could then be placed in the aqueous compartments on either side of the BLM and currents measured. This limited study to a few well-characterized membrane channel proteins and was carried out in an artificial setting. However, by playing around with the concentration of the channels in the BLM, it was sometimes possible to observe transport through a single open channel at a time (single-channel currents). This provided a wealth of information that forms the basis of our current thinking about the molecules that make up such channels. Neher and Sakmann pioneered a method (the patch clamp) for study, at a similar resolution, of channels in their native setting.

The patch-clamp technique involves pressing a pipette against a cell membrane and generating a seal that is tight enough to prevent the passage of ions between the pipette and the membrane. If an electrode is introduced into the pipette, the only current that can be detected will be that passing through