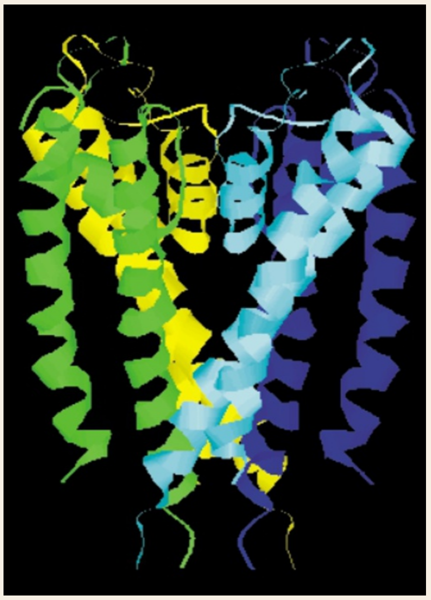
ION CHANNELS

Potassium ions shed their skin



The structure of the potassium channel KcsA, determined by X-ray crystallography, is regarded as a milestone in the study of ion channel function. But the original description of this structure was only the beginning. Two papers from the group of Rod MacKinnon are the latest contributions to a story that continues to amaze us with unimaginable insights into the workings of channel proteins.

In the first study, Zhou *et al.* asked a fundamental question about the interactions between the permeant ions and the channel: how do K^+ ions shed their hydration shells as they pass through the selectivity filter? The authors solved the structure of KcsA in complex with a Fab antibody fragment that recognized the tetrameric, but not the monomeric, form of the channel. They found that the central cavity of KcsA holds a K^+ ion surrounded by eight water molecules. As K^+ enters the selectivity filter, oxygen atoms from different amino-acid carbonyl groups surround the ion and stabilize it in four precise positions as it flows through. As K^+ channels normally face two very different ionic concentrations (high inside the cell and low outside), the authors found that the selectivity filter adopts two distinct conformations that depend on K^+ concentration.

In the second study, Morais-Cabral *et al.* set out to discover how KcsA achieves nearly diffusion-limited rates of ion flow by analysing its structure in the presence of K^+ or of slightly larger, but permeant, Rb^+ ions. As the distribution of ions inside the selectivity filter differed depending on the ion, the authors showed that, although the filter can hold ions in four different positions, it usually contains only two ions separated by a water molecule. The ions move in a concerted manner between positions 1,3 and 2,4 such that, when an ion enters the filter on one side, a second one is expelled on the other. This arrangement minimizes the energy difference between the different states, while maximizing the rate of conduction.

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References and links

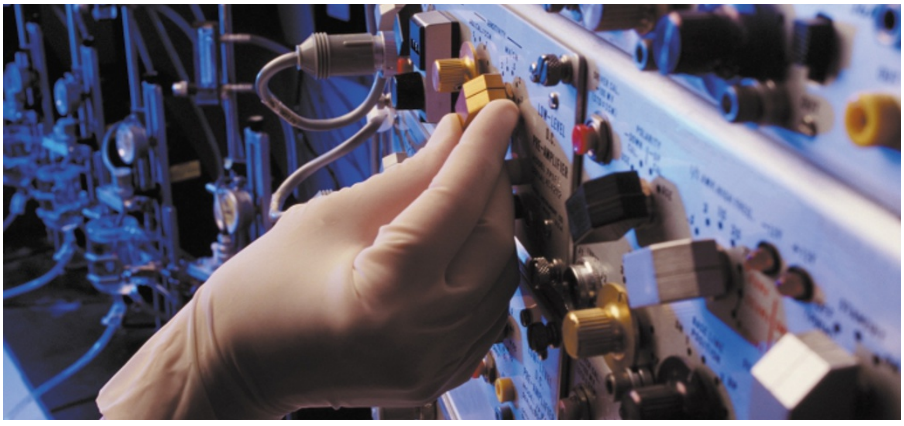
ORIGINAL RESEARCH PAPER Zhou, Y. *et al*. Chemistry of ion hydration and coordination revealed by a K^+ channel–Fab complex at 2.0 Å resolution. *Nature* (1 November 2001) | Morais-Cabral, J. H. *et al*. Energetic optimization of ion conduction rate by a K^+ selectivity filter. *Nature* (1 November 2001)

NEUROPHYSIOLOGY

Noises on

The idea that noise has a detrimental effect on signal detection is a commonly held view; as noise increases, the signal-to-noise ratio (SNR) is expected to decrease. But in some systems, noise can actually enhance signal detection, an effect known as stochastic resonance. In these systems, SNR is not a linear function of noise; instead, gradual increases in noise are initially associated with a steep and coincident increase in SNR, before signal detection begins to degrade. Do neurons show stochastic resonance? In other words, can increases in noise lead to an enhanced detection of synaptic inputs? Stacey and Durand have recently provided evidence in support of this intriguing idea.

Using a computer model of hippocampal neurons, the authors have previously shown that the external introduction of physiological levels of noise improve signal detection. They have now gone on to show, in hippocampal slices, that endogenous noise can have a similar effect. Stacey and Durand applied subthreshold currents to the CA3 hippocampal region, a manipulation that enhanced random synaptic activity and increased noise levels recorded from individual CA1 neurons. The authors simultaneously delivered test pulses on an independent pathway to evoke subthreshold synaptic potentials in CA1 neurons, and observed that the triggering of action potentials by the test pulses significantly increased when the noise source was on. So, SNR increased steeply as a function of noise, roughly following the predictions of the stochastic-resonance model — an initial increase and a subsequent reduction of SNR. However, levels of noise high enough to start degrading the signal could not be induced because of experimental constraints, and the predicted decrease in SNR was only observed in a computer simulation. But despite this limitation, the observations of Stacey and Durand indicate that noise can enhance the detection of synaptic activity in the hippocampus. As the random activity used by the authors as the source of noise falls within physiological levels, stochastic resonance might indeed favour the detection of weak or distal synaptic inputs.



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ORIGINAL RESEARCH PAPER Stacey, W. C. & Durand, D. M. Synaptic noise improves detection of subthreshold signals in hippocampal CA1 neurons. *J. Neurophysiol.* **86**, 1104–1112 (2001)

FURTHER READING Stacey, W. C. & Durand, D. M. Stochastic resonance in hippocampal CA1 neurons. *J. Neurophysiol.* **83**, 1394–1402 (2000)