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Press Release

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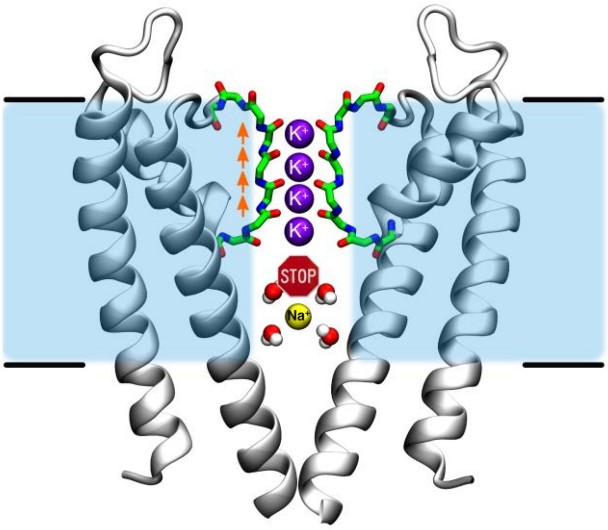
Size does matter

Scientists reveal how ion channels strictly select between different types of ions

Ion channels play a crucial role in important processes in our body such as nerve cell communication and muscle contraction. They form pores in the cell membrane and allow charged particles (ions) to flow into and out of cells at high speed. Many ion channels are specific for a certain type of ion. A team of scientists at the Max Planck Institute (MPI) for Biophysical Chemistry as well as the Universities of Dundee (UK) and Groningen (Netherlands) has now clarified how potassium ions slip through potassium channels so efficiently and exclusively: They pass through the channels "naked". *(Nature Chemistry, July 20, 2018)*

Potassium channels represent the largest family of ion channels. Among others, they control the duration of cardiac contraction, are involved in regulating blood flow, and terminate individual nerve impulses. For all these processes to function smoothly, it is essential that potassium channels only let potassium ions pass through, while other ions are prevented from entering.

The narrowest part of the channel serves as a filter for the ions: This ensures that only ions of the appropriate size and electrical charge flow through. But why do potassium channels allow the rapid flow of potassium ions while the smaller sodium ions are reliably excluded? It cannot be due to the charge, because it is the same for both of them. A team of scientists at the MPI of Biophysical Chemistry as well as the Universities of Dundee and Groningen have now succeeded in answering this question: Only potassium ions can strip off their water shell to get through the narrow channel.



Potassium (K^+) channels let potassium ions pass through, while efficiently preventing sodium ions (Na^+) from entering. *(Image: Wojciech Kopec / Max Planck Institute for Biophysical Chemistry)*

Researchers have long suspected that the channel does not only contain ions but also water molecules that surround and separate the ions. “This assumption was always taken into account in computational experiments simulating currents through ion channels in order to investigate the mechanism in greater detail. However, the currents in the simulations have never been as high as in direct measurements in living cells,” says Bert de Groot, research group leader at the MPI for Biophysical Chemistry in Göttingen.

A few years ago, new analyses by de Groot and other researchers revealed that potassium ions line up in the filter just like a string of pearls and sit very closely together – without water molecules to shield the charged particles from each other. This spatial proximity causes the charges to repel each other like identical magnetic poles and thus accelerates the flow through the channel. Finally, the results of simulations and cell experiments were matching.

In their latest publication, the scientists have used elaborate computer simulations to reconstruct why the channel selects potassium ions so well and why sodium ions cannot easily pass through the potassium channel. Wojciech Kopec, a postdoctoral fellow in de Groot's research group and first author of the work now published in the journal Nature Chemistry, reports on the latest results: “Potassium ions completely remove their water shell to get through the narrow pore. Sodium ions, in contrast, retain theirs. As a result, they are ultimately larger than 'naked' potassium ions – and too large for the narrow potassium filter. Thus, their size efficiently prevents them from flowing through the channel.”

But why do sodium ions not do the same as potassium ions and also get rid of their water shell? The smaller sodium ions retain their water covering more firmly: They interact more strongly with the water molecules of the environment as their charge is more compact. Therefore, more energy is needed to free them from their water shell. “In fact, sodium ions usually pass through the cell membrane along with water molecules. That is why sodium channels have pores almost three times as wide as potassium channels,” explains Ulrich Zachariae of the University of Dundee, who led the scientific work together with de Groot. Since ion channels are important targets of many drugs, for example those against cardiac arrhythmia, a detailed understanding of the functioning of ion channels is fundamental. (ad)

<u>Original publication</u>

Wojciech Kopec, David A. Köpfer, Owen N. Vickery, Anna S. Bondarenko, Thomas L.C. Jansen, Bert L. de Groot, Ulrich Zachariae: A single principle governs high conductance as well as strict ion selectivity in K+ channels. *Nature Chemistry* **10**, 813–820 (2018).

<u>Further information</u>

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