IMP Press Release

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Studying dynamics of ion channels

Scientists from the Vaziri lab at the Vienna Biocenter (Austria), together with colleagues at the Institute for Biophysical Dynamics at the University of Chicago, have developed a method using infrared spectroscopy and atomistic modeling that would allow to better understand the mechanism behind the extreme ion selectivity and transport properties in ion channels. Their findings have recently been published in The Journal of Physical Chemistry B.

Ion channels are essential structures of life.

Ion channels are specialized pores in the cell membrane and move charged atoms known as ions in and out of cells, thereby controlling a wide variety of biological processes including brain function and heartbeat. Ion channels are generally selective for certain ions, allowing specific types of ions to flow through at very high rates, while hindering the flow of others. On the basis of this selective permeability, ion channels are classified as potassium channels, sodium channels, etc.

The cell's most ubiquitous gateways are potassium ion channels – the importance of this type of ion channels was underpinned in 2003 when Roderick MacKinnon received the Nobel Prize in Chemistry for resolving the first atomic structure of the bacterial KcsA potassium channel.

Despite a large body of work, the exact molecular details underlying ion selectivity and transport of the potassium channel remain unclear. "Since conventional methods, such as X-ray crystallography, capture only averaged frozen structures, it is not possible to investigate how the dynamic of the protein could be involved in key aspects of their function", explains physicist Alipasha Vaziri, a joint group leader at the Max F. Perutz Laboratories (MFPL) and the Institute of Molecular Pathology (IMP) and head of the research platform „Quantum Phenomena & Nanoscale Biological Systems" (QuNaBioS) of the University of Vienna.

New method to unravel the secret of ion channel selectivity

Vaziri's team, together with researchers at the Institute for Biophysical Dynamics (University of Chicago), have now used infrared (IR) spectroscopy coupled with molecular dynamic-based simulations of the obtained spectra to investigate the subtlest changes in the shape of the KcsA potassium channel that are induced by binding either potassium or the only 0.04 nanometers smaller sodium ion. This combination proved to be a powerful tool to disentangle convoluted IR spectra – which contain contributions from the whole protein – by assigning each part of the spectrum to the amino acids that contribute to it.

"This new approach allows us to probe these mechanisms in a non perturbative way, meaning without tedious and expensive isotope labeling strategies. Moreover, it opens the way to study the structure and dynamics of ion channels on

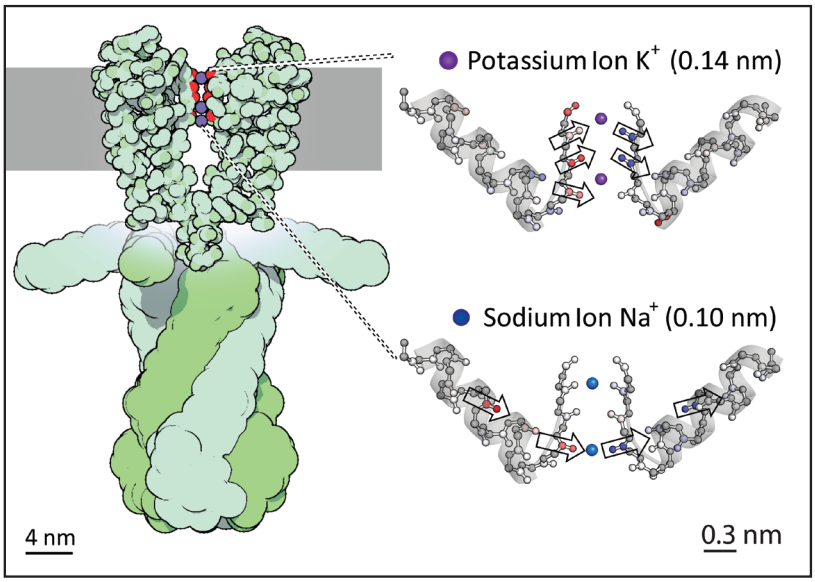

Image Caption
The potassium channel KcsA in the bacterial cell membrane.
Right: changes in strength and direction of vibrational coupling inside the filter depending on the ion species, as found by the study.
Illustration: David S. Goodsell & RCSB Protein Data Bank

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their biologically relevant timescales by extending it to two-dimensional infrared spectroscopy", says Christoph Götz, PhD student in the Vaziri lab and co-author of the paper.

The study shows for the first time that the combination of the two methods can be used to detect subtle conformational changes in large membrane proteins, such as the KcsA potassium channel. Furthermore, it opens the way to capture the dynamics of proteins in real time at atomic resolution, which has been impossible with standard techniques until now.

Publication in The Journal of Physical Chemistry B:
Paul Stevenson, Christoph Götz, Carlos R. Baiz, Jasper Akerboom, Andrei Tokmakoff and Alipasha Vaziri: Visualizing KcsA Conformational Changes upon Ion Binding by Infrared Spectroscopy and Atomistic Modeling. In: The Journal of Physical Chemistry B (April 2015). DOI: http://dx.doi.org/10.1021/acs.jpcb.5b02223

About the Vienna Biocenter
The Vienna Biocenter (VBC) is Vienna's largest life science hub and a center of molecular biological research excellence. In addition to six institutions that are dedicated to basic research, 14 companies are currently on location in New Marx. More than 1,400 employees and 700 students make the VBC a hotspot of innovative approaches in the life sciences. In the academic field, the Research Institute of Molecular Pathology (IMP), the Institute of Molecular Biotechnology (IMBA), the Gregor Mendel Institute (GMI) and the Max F. Perutz Laboratories (MFPL) are the flagships of the Vienna Biocenter. The Campus Science Support Facilities (CSF) provide state-of-the-art scientific services.

About the Max F. Perutz Laboratories
The Max F. Perutz Laboratories (MFPL) are a center established by the University of Vienna and the Medical University of Vienna to provide an environment for excellent, internationally recognized research and education in the field of Molecular Biology. On average, the MFPL host 60 independent research groups, involving more than 500 people from 40 nations.

About the IMP
The Research Institute of Molecular Pathology (IMP) in Vienna is a basic biomedical research institute largely sponsored by Boehringer Ingelheim. With over 200 scientists from 35 nations, the IMP is committed to scientific discovery of fundamental molecular and cellular mechanisms underlying complex biological phenomena. Research areas include cell and molecular biology, neurobiology,disease mechanisms and computational biology. The IMP is located at the Vienna Biocenter.

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