Researchers advance knowledge of little 'nano-machines' in our body

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A discovery by Canada-U.S. biophysicists will improve the understanding of ion channels, akin to little 'nano-machines' or 'nano-valves' in our body, which when they malfunction can cause genetic illnesses that attack muscles, the central nervous system and the heart.

As reported in the current issue of the *Proceedings of the National Academy of Sciences* (*PNAS*), researchers from the Université de Montréal and the University of Chicago have developed a novel method to detect the movement of single proteins that control the ion exchange between the cells and their environment.

Much like an iris in a camera, these proteins open and close and thereby control the movement of ions between the cells and their environment, which allows the transmission of electrical signals along our nerve cells. The size of these small valves is about a million times smaller than the pupil of a human eye. The new technique will allow scientist to measure one single ion channel at the time and investigate how different parts inside the ion channels communicate.

The research team was led by Rikard Blunck, a professor from the Université de Montréal's Department of Physics, M.Sc. student Hugo McGuire and their collaborators at the University of Chicago, Francisco Bezanilla and H. Clark Hyde.

"Our discovery will help advance the basic understanding of ion channels. These membrane proteins mark a major drug target, since they play a central role in the entire body and mutations in their genes cause many severe genetic illnesses," says Dr. Blunck, who was recruited to the Université de Montréal from UCLA to become the Canada Research Chair on Molecular Mechanisms of Membrane Proteins and member of the Groupe d'étude des protéines membranaires, a multidisciplinary research group that studies protein functions and their involvement in physiological systems.

The *PNAS* study is important, as biophysics researchers seek to better understand the structure and movement of ion channels because the malfunctioning of these channels is implicated in a number of diseases.

For this study, the research team investigated potassium channels built out of four identical subunits, which form a pore through the membrane that can open and close in order to allow or block ion conduction.

They solved a long debate in the field: Do the four subunits of a K+ channel function independently or in a concerted action?

To answer this question, the physicists developed a fluorescence spectroscopy technique that allows distinguishing between the subunits so that one can follow, for the first time, the movement of each of the four subunits, information that was lost in previous measurements. They found that the four molecules act together, which explains why no intermediate steps are found in the electrical current measured in electrophysiological experiments.

Paper: "Fluorescence detection of the movement of single KcsA subunits reveals cooperativity," was authored by Blunck R., McGuire H., Hyde H.C., Bezanilla F., and published in the *Proceedings of the National Academy of Sciences*: www.pnas.org/content/early/200 … /0807056106.abstract .

Source: University of Montreal