

# Revolution in understanding of ion channel regulation

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A study at Rush University Medical Center in Chicago published this week in the online version of *Biophysical Journal* proposes that bubbles may control the opening and closing of ion channels. This new understanding of the channels that control much of life in health and disease provides a vital piece of the molecular puzzle.

The work of experts in mathematics, physics and molecular biology at Rush has produced a new explanation for how ion channels open and close. This discovery provides a springboard to a better understanding of many diseases and their treatment.

The body, like so many other mechanical and computing systems, is controlled by the on and off response of its smallest components. “Life is controlled by switches and valves, in the same way that computers and cars are, but life’s valves are proteins that open and close, providing gates for pathways for ions to enter cells,” says Robert S. Eisenberg, PhD, professor and chairman of molecular biophysics and physiology at Rush University. “The problem is, if anything goes wrong with these ion channel gates, disease results or, worse death.”

For years, researchers have been searching for the mechanism that opens and closes the pore-like ion channels that are an integral part of each cell membrane. These atomic-size channels control the movement of ions, or charged electrical particles, across the cell membrane. This, in turn, controls the function of the cell. An enormous range of biological functions are controlled by these channels, and failures in these channels

produce many of the diseases that plague mankind.

“Through rigorous analysis, we propose that bubbles form and break inside the tiny pores of the channel and that these bubbles are the gates that have been long sought by so many scientists,” says Eisenberg. “The bubbles create a vacuum that cannot conduct electricity as the surrounding water does; therefore, the channel is effectively in the ‘off’ position. When the bubble breaks, the channel is in the ‘on’ position. It’s a rather effective, efficient and elegant design.”

The understanding of the link between ion channels and disease is a relatively recent development. Researchers have found that many diseases — for example, cystic fibrosis, or even such complex and systemic diseases as type 2 diabetes — involve malfunctions of ion channels. When the valves in a car or in plumbing get stuck, the car can stop or the sink can overflow. In the same way, when gates in the ion channels of your cells get stuck, there can be serious health consequences.

“An amazing number of diseases have been found to be related to ion channels,” says Eisenberg. “Heart disease is an excellent example. Channels control the flow of electricity in the heart. If we could simply fix what’s happening electrically in the heart, we could change the course of the disease and its impact on our society.”

The proposal that bubbles are indeed the gates of ion channels needs further study. The Rush group and its collaborators are proposing a sophisticated and plausible guess. Testing that guess will be most informative.

“This type of paradigm shift is fantastically important, because we can save researchers from wasting valuable time and energy heading in the wrong direction,” says Eisenberg. “This new insight will really change

the way people are doing their work and could bring us amazing new leaps in our understanding of certain disease processes and how to manage and ultimately cure them.”

Source: Rush University Medical Center

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