# Realistic simulation of ion flux through membrane sheds light on antibiotic resistance

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As the gatekeepers of ion flow through cell membranes, ion channels are of key interest in numerous cellular processes. Now, a new study describes an innovative new computational model that realistically simulates the complex conditions found in biological systems and allows for a more accurate look at ion channel function at the level of individual atoms. The research, published by Cell Press in the August 17th issue of the *Biophysical Journal*, provides a remarkably detailed look at the function of a bacterial channel that kills brain cells in people with bacterial meningitis and provides insight into mechanisms that underlie deadly antibiotic resistance.

"Ion channels play an essential role in cellular homeostasis and signaling," says senior study author, Dr. Ulrich Zachariae, from the Max Planck Institute for Biophysical Chemistry. "The study of their function is crucial both for an understanding of intercellular communication and to develop drugs against a plethora of channel-induced diseases." By developing a new computational model, Dr. Zachariae and colleagues were able to directly simulate ion flux through membrane channels under conditions that closely resembled those experienced by living cells.

The researchers used their new method to study PorB, a bacterial channel that is formed by pathogenic Neisseria meningitidis. PorB inserts into the membranes of key intracellular structures in the infected host brain cells and causes them to die. The new approach enabled Dr. Zachariae's group to study detailed molecular mechanisms of ion flux through PorB and to explore the effects of specific mutations on ion

passage through the channel. This is medically relevant because these deadly bacteria are quick to develop antibiotic resistance by mutating the PorB channel, which is also the main entrance gate into the bacteria, so that common antibiotics no longer fit through the channel. "A major goal of our research is to determine how common antibiotics should be modified to again pass through bacterial channels," explains Dr. Zachariae.

In summary, the new approach allowed for an extraordinarily meticulous look at ion channel function. "We showed that our method accurately predicted ion conductance and selectivity and elucidated ion conduction mechanisms in great detail," concludes Dr. Zachariae. "Thus we expect it to be useful for studies of the molecular mechanisms of ion passage, such as for the improvement of drug design against ion channel targets like PorB. Results from such studies may prove to be crucial for a large group of dangerous bacterial infections which develop more and more resistance against antibiotics."

Provided by Cell Press