# Researchers solve complex problem in membrane biochemistry through study of amino acids

January 24 2013

(Phys.org)—After years of experimentation, researchers at the University of Arkansas have solved a complex, decades-old problem in membrane biochemistry. The consequence of their work will give scientists more information about the function and structure of proteins, the workhorses within the cells of the human body.

"Historically, lysine and arginine, both basic amino acids, were considered to have very similar properties and therefore to be essentially interchangeable," said Denise Greathouse, a research associate professor in the department of chemistry and biochemistry. "Our results demonstrate that despite their similarities, the differences in their behavior in membrane environments provide important clues for understanding membrane protein function."

The findings, which appear in the January issue of the journal Proceedings of the National Academy of Sciences, address long-standing questions in the study of protein structure and function and help explain how charged amino acids are able to modulate the behavior of proteins in cellular membranes.

Greathouse, former doctoral students Nicholas Gleason and Vitaly Vostrikov, and Roger Koeppe II, Distinguished Professor of chemistry and biochemistry, wrote the article, "Buried lysine, but not arginine, titrates and alters transmembrane helix tilt."

Proteins do nearly all the work in the cells of our bodies, ranging from brain function and nerve transmission to metabolic energy production and muscular contraction. Moreover, many diseases are associated with defects in protein function. Future advances in the diagnosis and treatment of human disease will depend upon better understanding of the thousands of proteins that are encoded within the genomes of humans and human pathogens.

The structure and function of membrane proteins both play a crucial role in cell signaling and the regulation of biological function. The authors developed experimental methods that determine how lysine and arginine interact in the lipid bilayer membrane environment. In the last 10 years there have been computational predictions of the behavior of lysine and arginine in the membrane but not methods to test those predictions.

"It is the first measurement of its type, its complexity makes it an elegant method, and it opens the door for other people to apply these methods on biologically important problems," Koeppe said. "There is a lot of interest in trying to understand what's going on in these membranes, especially with protein molecules that carry particular electric charges. Unless we can understand it at the fundamental level, then we can't extrapolate it to the nervous system. We're trying to develop foundational knowledge that is needed to understand the nervous system.

"We're excited about this study because it makes available knowledge that other researchers can use," he said. "Those making the computer predictions can refine their methods and make better predictions because they know that they were able to reproduce some of our results."

Lysine and arginine are ionizable, which means they can have a positive electric charge. The research team created a framework for experimentation that uses magnetic resonance imaging to measure whether the groups remain charged or become uncharged as the acidity

or the pH of the environment is changed. To make their procedure work, the scientists synthesized peptides, which are chemical compounds consisting of several or more linked amino acids. To enable the magnetic resonance experiments, some of the hydrogen atoms in the peptides were replaced with deuterium, a heavy isotope of hydrogen.

"We've spent about 15 years doing this," Koeppe said. "We developed first- and second-generation families of model peptides, and we examine them in model lipid membranes in order to understand the properties of real cell membranes and real cell proteins. This is at a molecular level. We are not even up to the cell yet."

Vostrikov and Gleason earned their doctorates in 2011 and 2012, respectively. Vostrikov is a postdoctoral fellow at the University of Minnesota and Gleason teaches chemistry at Shiloh Christian School in Springdale.

The National Science Foundation provided the grant for the experiments described in the *Proceedings of the National Academy of Sciences*. The National Institutes of Health provided the financial support for the early stages of development of the peptide framework and for the facilities.

**More information:** www.pnas.org/content/early/201 … /1215400110.abstract

Provided by University of Arkansas