

o n t h e f r o n t i e r s o f s c i e n c e

# Pitt Shares \$5 Million U.S. Defense Department Biotechnology Grant

*Transport protein study could aid drug development, antibiotefforts*

By John Fedele

Researchers at the University of Pittsburgh and the University of Cincinnati have been awarded a \$5 million grant from the U.S. Department of Defense's Multidisciplinary University Research Initiative program to study ion transport through proteins in synthetic membranes, a process that could assist fields as diverse as developing sensors to detect dangerous chemicals, fuel cell technology, drug discovery, and drug delivery.

Rob Coalson, professor of chemistry and physics in Pitt's Faculty of Arts and Sciences, is working with a team at the University of Cincinnati led by

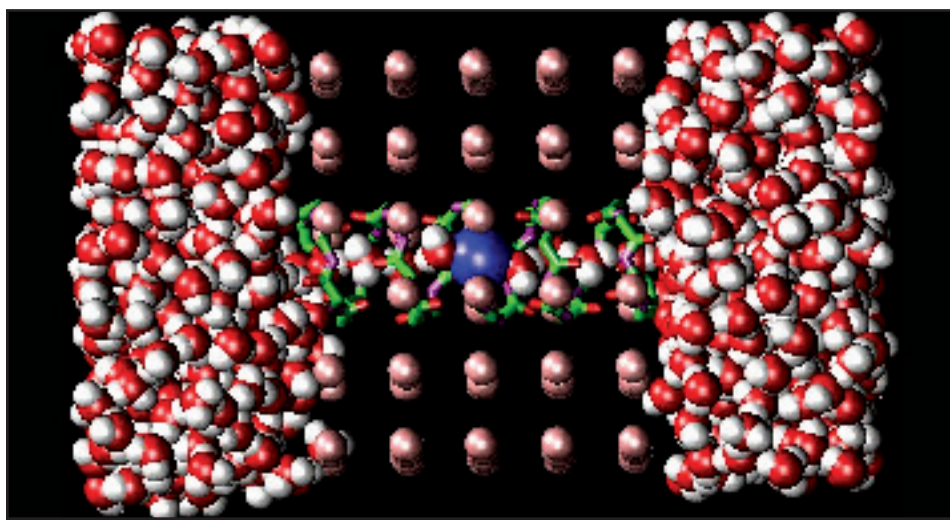
John Cuppoletti, a professor of molecular and cell physiology.

"The potential impact of this work is significant and varied," said Coalson. "It has ramifications in biotechnology, for example, in creating molecular-level chemical sensors, which could be used to fight bioterrorism or monitor blood glucose levels. If we could harness the extraordinary efficiency of ion channels—carriers and ion pumps that transport substances across cell membranes—they can be used to develop these new devices.

"A wide range of applications to medical science also can be envisaged," Coalson



**Rob Coalson**



*Snapshot from a molecular dynamics simulation of a potassium ion (blue) permeating through the Gramicidin protein channel. The protein channel spans a lipid bilayer membrane, which is represented by violet spheres. The remaining red and white entities are water molecules.*

continued. "Half of all drugs on the market work on transport proteins, or 'protein channels', as they are called. Protein channels play an essential role in many physiological processes. These channels are defective, corrupted by neurotoxins in diseases such as cystic fibrosis, and their function is altered by drug molecules, which bind to them. Understanding the structure and function of transport proteins will have implications for drug design, the treatment of serious diseases, the development of better anesthetics, and other biomedical ramifications."

The research will:

- explore how native and engineered

channel proteins pass such substances as ions like sodium and chloride through cell membranes;

- create proteins that will transport new substances, such as polypeptides; and
- develop new materials and devices containing biological proteins.

Coalson's expertise in chemical dynamics theory—particularly in molecular-level modeling of the transport of ions and biopolymers like polypeptides and DNA through protein channels—will help the team. With team member Thomas Beck, professor of chemistry at Cincinnati, Coalson's group will use supercomputers and mathematical

modeling to understand transport and structural changes in the protein that occur over short and long time intervals.

As Cuppoletti explained, "Once we know how the structure of the transporters changes during the transport process and how each amino acid within the protein interacts with the transported substances, we can use computational chemistry to predict how the transported substances will interact with native proteins, and how to change the protein to transport new substances. Thus, we will attempt to use computational chemistry to change and improve upon nature."

The five-year grant will help pay for several postdoctoral fellows or graduate student researchers, and Coalson believes the impact could spur growth in the field at Pitt and in the region.

"There is considerable expertise in biophysics and, especially, computational biology at the University of Pittsburgh and neighboring institutions," Coalson says. "We already interact strongly with the Center for Computational Biology and Bioinformatics, directed by Professor Iveta Bahar at Pitt Medical School, and Pitt's Center for Molecular and Materials Simulation, directed by Pitt Chemistry Professor Kenneth Jordan. If we can expand and fully harness these connections, we are confident that exciting new research directions will emerge at Pitt and that this research can help drive the budding biotech industry in Pittsburgh."

The other coprincipal investigators, all from the University of Cincinnati, include professors Beck; F. James Boerio, professor of materials science and engineering; Jerry Y.S. Lin, professor of chemical engineering; and Paul Rosevear, professor of molecular genetics.

MAMONOV, COALSON, NITZAN, AND KURNIKOVA