



TEXAS ADVANCED COMPUTING CENTER

THE UNIVERSITY OF TEXAS AT AUSTIN

General Info

- Home Page
- TACC Overview
- Staff
- New Users
- Press & Events
- Affiliations
- Contact Info
- Visitor Info
- Employment

Resources

- HPC Systems
- Visualization
- Data Storage
- Networking
- Software & Tools
- Allocations
- Usage Policies

Services

- User Portal
- User Guides
- User News
- Consulting
- Training
- Cluster Support
- EOT

Research/Development

- TACC Projects
- TACC Publications
- ▶ User Research
- SciVis Gallery
- Industrial Partners
- Petascale Lecture Series
- International Partners

Focus Areas

- HPC
- SciVis
- DIS
- Dist./Grid Computing

Search

The Flu and the Mystery of Proton Transport

TACC's Lonestar and other TeraGrid HPC resources enable new insight into proton movement and anti-flu drugs

The symptoms appear suddenly and often—a continuous fever, shaking chills, body aches, muscle pain, fatigue, loss of appetite, and nausea. Most of us have suffered from the viral illness influenza, commonly known as the flu. In most cases, home treatment is all that is needed for recovery, but sometimes the flu can lead to life-threatening complications, such as bacterial pneumonia.

Chemistry professor Gregory Voth (University of Utah) and his research team recently published a study on the uniqueness of the influenza A M2 channel and its effect on proton transport in the virus. The M2 channel is a trans-membrane, four-helix channel believed to play a key role in the viral life cycle by allowing protons to flow through it. This transport of protons facilitates the viral replication process in a host cell.

In terms of basic research, the M2 channel is of considerable relevance to drug design and virology, the study of biological viruses and virus-like agents. In biology, many such channels with different roles exist, but the M2 channel exhibits unique pH-gated behavior as opposed to the voltage-gated behavior of many other proton channels.

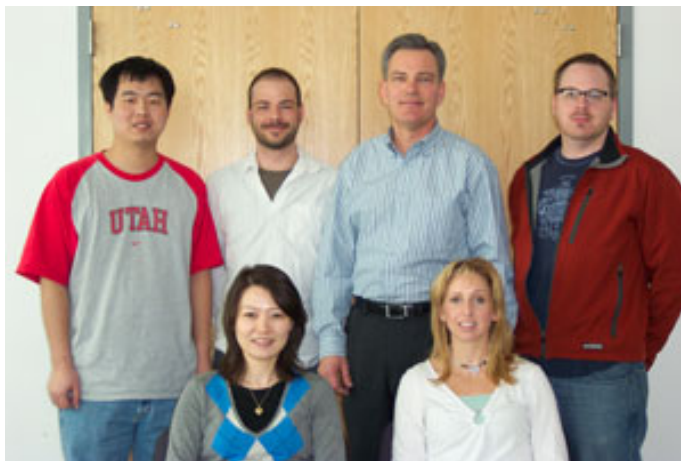
Voth and his research team used TACC's Dell cluster, [Lonestar](#), and the Big Red HPC system at Indiana University to carry out this research. They also used systems at NCSA to develop a multi-state empirical valence bond approach (MS-EVB), which allows explicit proton transport to be simulated using molecular dynamics simulations.

According to Voth, the challenge of understanding proton transport requires computational simulations benchmarked against experimental results. "I'm a huge fan of the TeraGrid," said Voth, who is the second-largest TeraGrid user. "The TeraGrid cluster systems are phenomenally useful. There isn't any doubt that these resources have enabled our research."



Proton transport is one of the most challenging molecular processes to study through computer simulation. This project required approximately 768,000 CPU hours on TACC's Lonestar supercomputer (pictured above)!

[Feedback](#)
[Site Map](#)



*The M2 channel research team. Top row, left to right: Hanning Chen, Matt K. Petersen, Gregory A. Voth, C. Mark Maupin. Bottom row, left to right: Jiancong Xu, Jessica M. J. Swanson. Image courtesy of the Center for Biophysical Modeling and Simulation, University of Utah. **Click image for more details and a larger view.***

The calculation of proton transport pathways requires a novel computational methodology combined with extensive simulation over many fast processors to achieve meaningful statistical convergence. This makes proton transport one of the most challenging molecular processes to study through computer simulation for two reasons: 1) it involves a chemical bonding topology that is continuously formed and broken because of the ability of protons to shuttle through water molecules and certain amino acids, and 2) the excess proton charge is delocalized and constantly changing its location.

Despite these challenges, Voth believes that the computer simulations made possible by the TeraGrid play a critical role in determining the mechanism of proton transport. "One of the hallmarks of our research is that we avoid cutting

corners on the accurate modeling to the extent possible," Voth said. "We set very high standards and constantly refine and validate the model. We also keep pushing the frontiers of what we're doing in terms of its complexity and challenge."

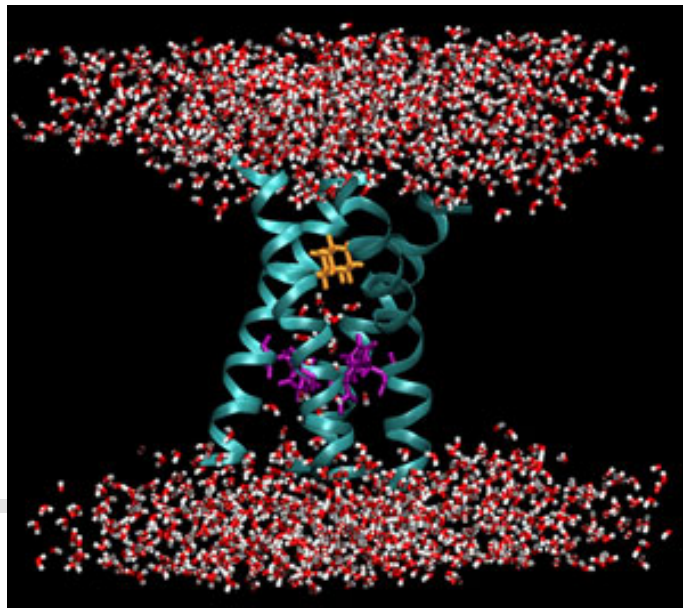
Using Lonestar and Big Red, Voth and his research group have solved part of the proton transport mystery. Their study explains how the M2 channel operates as a proton conductor in responding to the acidic conditions on either side of the cell membrane. The study also explains how the anti-flu drug amantadine blocks the channel and causes it to shut down.

As new experimental measurements of proton conductance and the structure of the full M2 protein (not just the trans-membrane channel) become available, Voth's next step is to study the strains of M2 that do not bind amantadine to see if other compounds might be effective anti-flu drugs. Voth said he looks forward to using TeraGrid's next-generation computational resources, such as TACC's forthcoming [Ranger](#) system, to simulate the proton transport behavior of the full protein.

More information:

<http://www.cbms.utah.edu/>

The M2 channel with the proton-conducting water wire disrupted by the presence of the anti-flu drug amantadine. The helices of the M2 channel (blue), the proton-gating His37 residues (mauve), and the proton-blocking amantadine molecule (orange) are



depicted. The lipid bi-layer membrane is not shown so that the channel can be seen more clearly. Image courtesy of Hanning Chen.

by Faith Singer-Villalobos
Texas Advanced Computing Center
October 2007

[Feedback](#)

[Office of the Vice President for Research](#)
© Copyright 2006 [The University of Texas at Austin](#)