Interacting protein theory awaits test from new neutron analysis tools

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An international collaboration directed by an Oak Ridge National Laboratory researcher has performed the first-ever atomic-detail computer simulation of how proteins vibrate in a crystal.

Jeremy Smith, who leads ORNL's Center for Molecular Biophysics, said experimental testing of the theoretical work will require the capabilities of the Office of Science's recently completed Spallation Neutron Source at ORNL.

The study is a collaboration between Smith, who also holds a University of Tennessee-ORNL Governor's Chair, and researchers from the California Institute of Technology and the National Institute of Chemistry, Ljubljana, Slovenia. The work is published in the current issue of *Physical Review Letters*.

Understanding how proteins--life's worker molecules--interact with each other is a major goal of biological sciences. The simulation, which was made possible by recent advances in scientific computing, describes the forces and vibrations involved in protein crystals, which provide an environment in which the proteins are ordered and thus lend themselves to detailed study.

According to Smith, lattice dynamics describe how the repeating units of a crystal vibrate relative to each other. The resulting "phonon dispersion relations" relate the frequencies to the wavelengths of the oscillations.

Phonon dispersion relations provide information on how proteins interact with each other that could be useful for understanding protein-protein interactions in the living cell. Until now, researchers have lacked the computing power to allow atomic-detail lattice dynamical calculations.

Smith said the PRL paper predicts the existence and forms of the protein crystal lattice modes.

"In doing so it throws out a challenge to next-generation neutron science to finally make the breakthrough and determine the forms and frequencies of the vibrations experimentally," he said.

In other words, having overcome their computational hurdle, the lattice dynamics team is now ready for the SNS to test the simulation work and see if what is predicted is really there.

"Atomic-detail crystal dynamics calculations have not been possible before, and now we also have an experimental tool--the SNS--that will have the capability to test our simulations. We are looking forward to seeing the next generation of instruments at SNS demonstrate their talents." Smith said, humbly adding, "Hopefully, the calculations won't be too painfully off the mark."

Smith believes the SNS and its arsenal of specialized analytical instruments will be able to confirm--or contradict--what the simulations indicate.

"We appreciate that examining complicated proteins in this way will not be easy, even for SNS. However, with SNS instruments expected to be in some cases hundreds of times improved over currently existing facilities, we are confident that the neutron breakthrough is within reach," Smith said.

Source: Oak Ridge National Laboratory