Mathematical model gives clearer picture of physics of cells, organelles

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(PhysOrg.com) -- Cells are filled with membrane-bound organelles like the nucleus, mitochondria and endoplasmic reticula. Over the years, scientists have made much progress in understanding the biomolecular details of how these organelles function within cells, but understanding the actual physical forces that maintain the structures of these organelles' membranes continues to be a challenge.

Now, UCLA Henry Samueli School of Engineering and Applied Science researcher William Klug and colleagues from the California Institute of Technology and the Whitehead Institute for Biomedical Research in Massachusetts have devised a mathematical procedure for accurately predicting the three-dimensional forces involved in creating and maintaining certain organelle membranes.

Their study, which appears Dec. 8 in *Proceedings of the National Academy of Sciences* and is currently available online, could potentially shed light on the life cycles of membrane-bound viruses such as HIV.

"The study is exciting because it provides a roadmap for ways we can do predictive computational science," said Klug, an assistant professor of mechanical and aerospace engineering. "The mathematical model is able to provide us with a quantitative understanding of the physics of cells that is essentially impossible to obtain directly by experiment."

To understand the researchers' mathematical description of how forces can lead to deformations in a membrane, one can consider the simple

concept of a bathroom scale.

"When you step on a scale, a small spring in the scale defines how heavy you are or what force is being applied to the scale," said study co-author Paul Wiggins, a fellow at the Whitehead Institute. "Similarly, with membranes, springs or forces cause them to bend. In a sense, we wanted to see if we could play the same game with the organelles of a cell — to take the observed structure and see if we can predict what forces are applied to give rise to the structure and essentially hold the structure together."

The team used an artificial biomembrane to investigate the dynamic forces that act on a cell's membrane and organelles. With optical tweezers — a scientific instrument that uses a focused laser beam to provide an attractive or repulsive force — they were able to trap and move parts of the cell. This enabled the researchers to exert known forces in different ways, giving them an opportunity to analyze both the response of the membranes when their structures were changed dramatically and to validate their mathematical procedure for predicting forces based on the deformed shapes of the membranes.

"We have this geometry, so what are the forces?" said Klug. "It seems straightforward if you write it out mathematically but in practice, actually measuring the forces reliably where you can quantify the error is really tricky."

The researchers believe that understanding the forces and mechanisms that are responsible for maintaining the geometries of the organelles will help them uncover the crucial factors that lead to changes or malfunctions in organelles.

"When cells undergo oxygen damage, that usually leads to a change in the structure of the mitochondria — the specialized organelles often

referred to as the powerhouses of cells," Wiggins said. "There is a close link between the ability of the mitochondria to function and its structure. By relating structure to force, we can uncover the crucial factors that lead to the change in the structure of the mitochondria and other organelles as well."

Membrane-bound viruses like HIV infect cells and then replicate and break from the cells by budding. This budding process eventually uses up the cell membrane and kills it.

"The forces that lead to the process of budding are essentially unknown," Klug said. "Researchers have looked at the image data of HIV in different stages of budding to try to understand the forces that lead up to it. If we can eventually understand what those forces are, we might be able to come up with a way to disrupt the viral assembly process. And that's a different strategy than what is being done today to treat retroviruses and HIV in particular."

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