

MU researchers develop advanced 3-D 'force microscope'

December 17 2013

Membrane proteins are the "gatekeepers" that allow information and molecules to pass into and out of a cell. Until recently, the microscopic study of these complex proteins has been restricted due to limitations of "force microscopes" that are available to researchers and the one-dimensional results these microscopes reveal. Now, researchers at the University of Missouri have developed a three-dimensional microscope that will yield unparalleled study of membrane proteins and how they interact on the cellular level. These microscopes could help pharmaceutical companies bring drugs to market faster.

"Force microscopes are very different from the microscopes we used in [biology class](#)," said Gavin King, assistant professor of physics and astronomy in the College of Arts & Science at MU, and joint assistant professor of biochemistry. "Instead of using optics, force microscopes incorporate a tiny needle that gets dragged across the surface of the slide or specimen, similar to how a blind person reads Braille or comparable to the needle of an old record player. However, the one-dimensional, traditional method of studying [membrane proteins](#) through a force microscope—while good—only yields limited results," King said.

Normally, force microscopes measure the compression of the needle against the specimen by bouncing a single laser off the cantilever, or arm, that holds the microscopic needle in place. As the cantilever moves, it deflects light that is sent back to a highly advanced computer. There, the results are interpreted, giving researchers an idea of how the membrane proteins are interacting with the cell.

Usually, to determine membrane protein structure in detail, specimens must be crystallized, or frozen; therefore, the specimen cannot be studied as it would behave in the primarily liquid environment found in the body.

King and his fellow researcher, Krishna Sigdel, a postdoctoral fellow in the Department of Physics, solved the problem by building their own force microscope that is able to study membrane proteins in conditions similar to those found in the body. Using a traditional one-dimensional force microscope as a guide, the team added an additional laser that measures the second and third dimensions of tip movement, giving researchers "real-time" access to the measurement of peaks and valleys in the membrane protein and dynamic changes in those structures.

"By adding a new laser that is focused from below, we essentially gave the force microscope two additional dimensions," King said. "Using this new laser, we collect the back-scattered light from not only the cantilever holding the needle, but also the tip of the needle that gives additional measurements. This added flexibility allows us to collect information faster and allows our microscope to work in near-native conditions in fluid like those found in the cell, yielding more realistic results."

King suggested that an advantage of three-dimensional force microscopy is that it allows for better interpretation of how a protein's dynamic shape also dictates its function. King said that by studying how the shape of proteins change, researchers can determine how drugs bind and interact with cells. Using membrane protein information, [pharmaceutical companies](#) can determine which [molecules](#) to pursue.

More information: King's work, "Three-dimensional atomic force microscopy: interaction force vector by direct observation of tip trajectory," was published in *Nano Letters*.

Provided by University of Missouri-Columbia

Citation: MU researchers develop advanced 3-D 'force microscope' (2013, December 17)
retrieved 24 April 2024 from <https://phys.org/news/2013-12-mu-advanced-d-microscope.html>

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