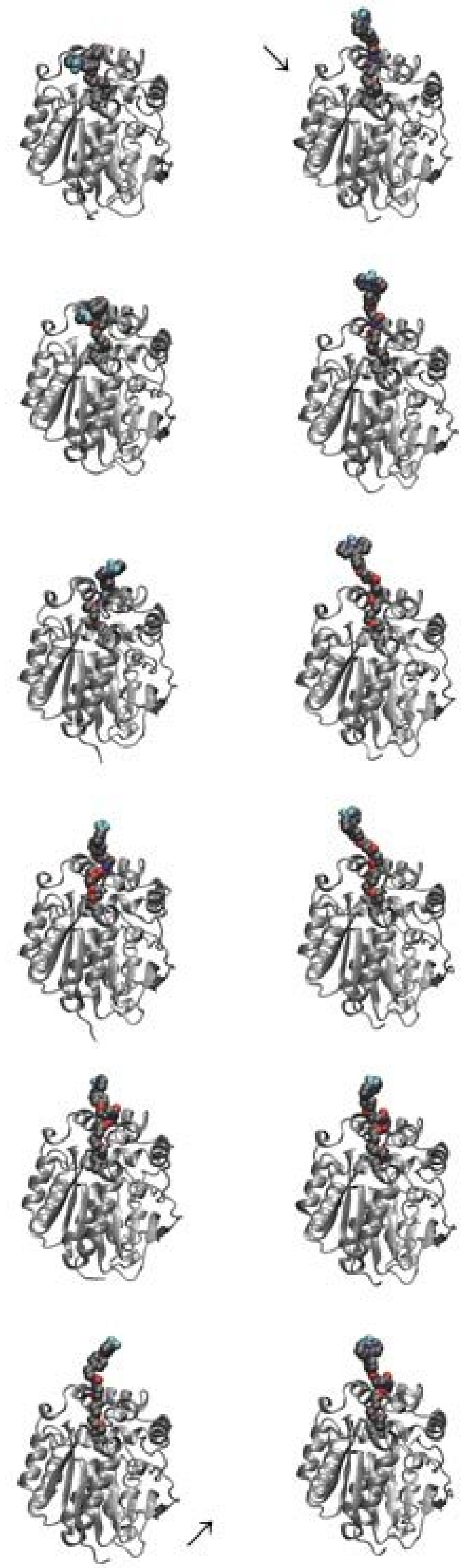
Fluorescent molecule could shed light on the inner workings of the cellular environment

October 4 2018



Snapshots of the rotating fluorescent molecule at gradually increasing microviscosity show how the probe becomes more and more extended and exposed. Credit: A*STAR Bioinformatics Institute

A fluorescent molecule whose luminosity depends upon how fast it can rotate is helping researchers measure how viscous the fluid is inside different parts of a cell.

"There's a lot of interest in the biophysical field in developing chemical probes that can be used to characterize the environment inside a cell or any kind of biological compartment," says Peter Bond, from A*STAR's Bioinformatics Institute.

Researchers from the United Kingdom and Singapore—including A*STAR scientists such as Bond's team who led the computational arm of the project—have modeled, developed and tested a molecule comprising two parts; a genetic probe designed to home in on particular proteins, so it can be directed to wherever in a cell that protein is found; and a molecular rotor—a fluorescent molecule whose fluorescence lasts longer, the slower it spins. A*STAR researchers simulated how this molecule would perform in different microenvironments at scales of millionths or even billionths of a meter.

Microviscosity refers to how viscous, or thick, the fluid is in particular parts of a cell. Since cell contents are mobile in a liquid environment, microviscosity can have a major impact on how proteins and biological molecules interact and communicate with each other. "These proteins are affected by interactions with each other, and by local differences in osmolytes and other small molecules, such as nutrients," Bond says.

To measure the microviscosity inside a cell, the researchers first needed to understand the dynamics of how this probe might behave in environments of different viscosities. Using computer simulations of liquids, they were able to show that as the viscosity of the solution increased, the rate of rotation of the probe decreased and its fluorescence changed in a measurable way.

Meanwhile their colleagues in the United Kingdom were conducting experiments in cells and found very similar results. Using the newly-developed microviscosity probe, the researchers were able to study how mitochondria, the powerhouses of the cell, react to environmental changes. They found that the interior of mitochondria maintained stable viscosity conditions even in the face of large changes in external electrolyte concentrations and viscosity.

Microviscosity is believed to play an important role in diseases such as Alzheimer's disease, with evidence suggesting microviscosity inside the brain cells may change as the disease progresses.

"If we could understand factors such as microviscosity, as well as understand basic biological mechanisms, we can develop new approaches to treating diseases," Bond says.

More information: Joseph E. Chambers et al. An Optical Technique for Mapping Microviscosity Dynamics in Cellular Organelles, *ACS Nano* (2018). DOI: 10.1021/acsnano.8b00177

Provided by Agency for Science, Technology and Research (A*STAR), Singapore

molecule-cellular-environment.html