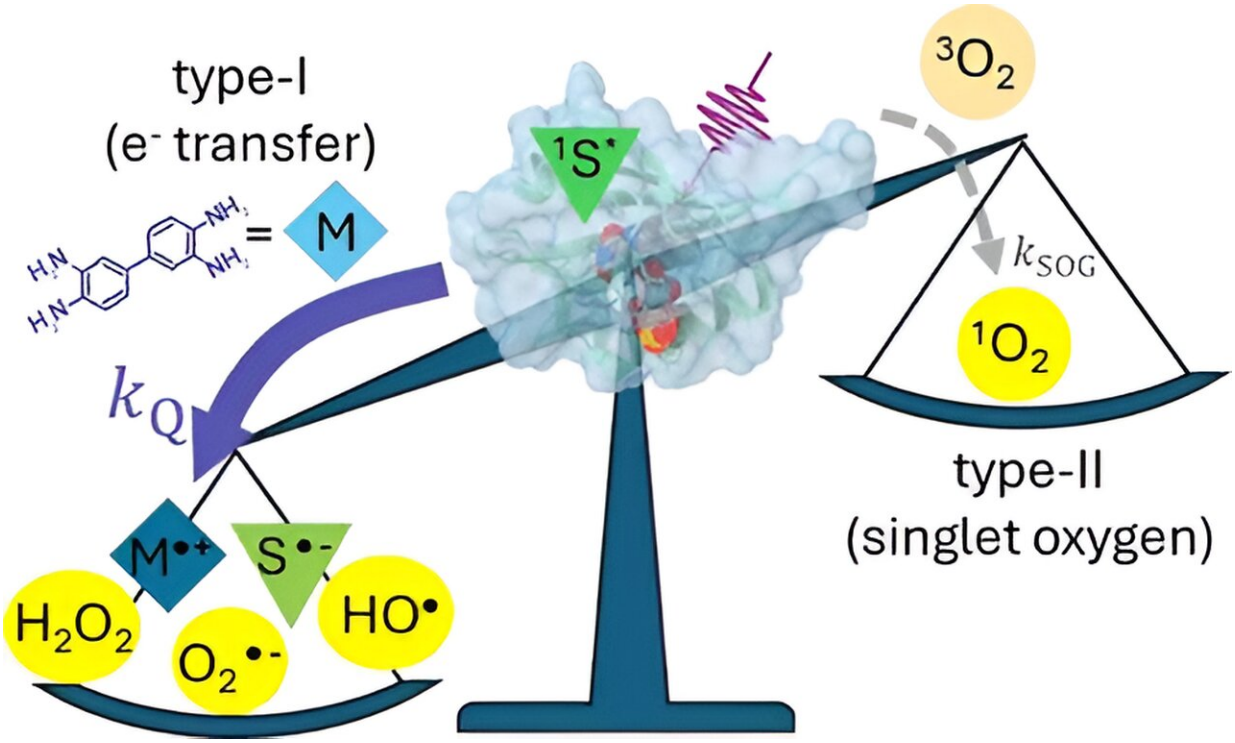
Labs collaborate to enhance imaging tools for cell observation

September 5 2024, by Brian Maffly



Credit: *Journal of the American Chemical Society* (2024). DOI: 10.1021/jacs.4c05397

Two labs at the University of Utah's Department of Chemistry joined forces to improve imaging tools that may soon enable scientists to better observe signaling in functioning cells and other molecular-scale processes central to life.

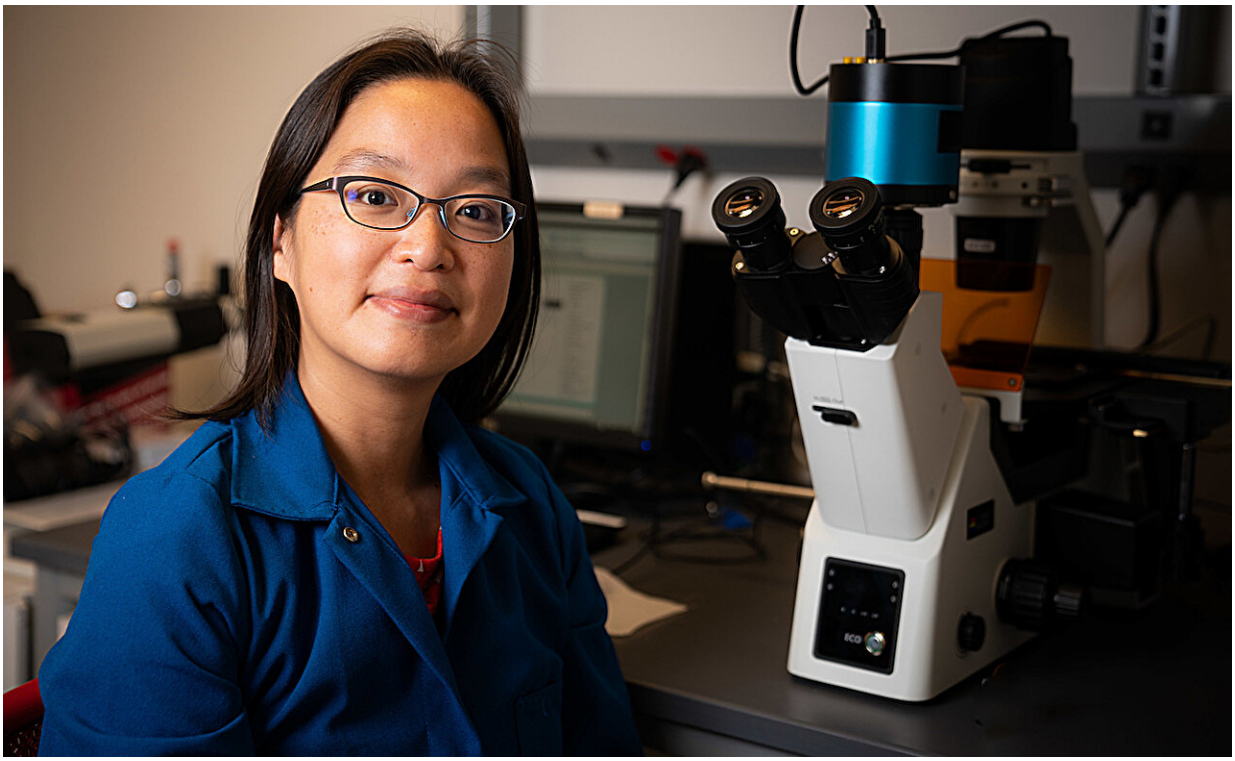
The Noriega and Hammond labs, with complementary expertise in materials chemistry and chemical biology, made critical discoveries announced this month in the *Journal of the American Chemical Society* that could advance this goal.

"We're trying to develop a new kind of imaging method, a way to look into cells and be able to see both their structural features, which are really intricate, while also capturing information about their activity," co-author Ming Hammond said.

"Current methods provide high-resolution details on cellular structure but have a challenging 'blind spot' when it comes to function. In this paper, we study a tool that might be applied in electron microscopy to report on structure and function at the same time."

Biological samples often need "markers," or molecules that are the source of detectable signals, explained co-author Rodrigo Noriega. A widely used type of markers are flavoproteins which, when photoexcited, trigger a chemical reaction that yields metal-absorbing polymer particles whose high contrast in electron microscopy is easily seen.

"Previous work focused on the markers without the materials they generate, but our study incorporates the materials chemistry steps in the model," said Noriega, who was named a Sloan Research Fellow this year under a program that recognizes early-career scientists whose research has the potential to revolutionize their fields.



Ming Hammond, associate professor of chemistry. Banner photo, courtesy of Unsplash, shows a CDC scientist using an electron microscope studying the virus that causes smallpox. Credit: Dave Titensor, University of Utah

Scientists had long assumed that a mechanism involving singlet oxygen generation, a special kind of reactive oxygen species, was at play. However, the U team found that electron transfer between the photoexcited marker and the polymer building blocks is the main contributor to the process.

"We're studying a tool that other people have used a lot as the basis for this new kind of imaging, and everyone thought that it worked a certain way," Hammond said, "but our photophysical studies revealed a surprising mechanism." This previously overlooked electron transfer pathway generates reactive species that yield the desired source of

contrast for electron microscopy, without the need for singlet oxygen.

This new information could help scientists improve the design of these markers, according to Noriega and Hammond. The U's collaborative team, for example, has built upon these results to expand the number and types of polymer building blocks employed, as well as using markers that are poor singlet oxygen sources but are excellent electron transfer partners, and growing contrast agents in environments that were not feasible before.

"Beyond their use in electron microscopy, what these markers allow you to do is obtain two images from the same sample, one using light microscopy and another one with electron microscopy, and this sort of multilayer image contains much more information than either of them alone," Noriega said. This method, called correlative microscopy, is like the different layers in Google Maps, Noriega explained.

These advances may enable scientists to better understand cell signaling, one of the fundamental processes of life, and not just within individual cells, but among communities of cells.

"Cells use chemicals to communicate with each other. That's their language, how they know whether their neighbors are friendly or antagonistic. It's how they work together, compete, and even disguise themselves within a community," Hammond said.

Mapping these chemical signals between groups of cells in a complex spatial arrangement requires them to detect activity levels within the context of the sample structure. "We would love to be able to see their communication, but we also want to see their neighborhood."

More information: Mohd Sajid Lone et al, Electron Transfer Drives the Photosensitized Polymerization of Contrast Agents by Flavoprotein

Tags for Correlative Microscopy, *Journal of the American Chemical Society* (2024). DOI: 10.1021/jacs.4c05397