

## Fluorescent nanoparticles serve as flashlights in living cells

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Scientists from the University of Twente, The Netherlands, have successfully exploited the optical properties of fluorescent nanoparticles to broaden the scope of single-cell microscopy. By using nanoparticles, they succeeded in combining two different optical microscopy techniques on the same cell. This opens exciting new possibilities for cellular imaging. Henk-Jan van Manen and Cees Otto from the Biophysical Engineering Group of the MESA+ Institute for Nanotechnology describe their results in *Nano Letters*.

The 'quantum dot' nanoparticles used by Van Manen and Otto replace existing fluorescent labels that are employed to enable the cell's biomolecules to light up under the microscope. While fluorescence microscopy continues to be instrumental in unraveling the intricate biological processes that take place inside living cells, it would be even more informative to combine it with the intracellular chemical analysis capabilities of vibrational spectroscopy techniques such as Raman microscopy.

Common fluorescent labels are not suitable for this combination, however, because the much stronger fluorescence overshadows the intrinsic weak Raman signals coming from cells. By taking fluorescent quantum dots that emit light in a wavelength region that is well-separated from Raman signals, the Dutch researchers now show that fluorescence microscopy can indeed be combined with Raman microscopy on the same cell.



## Vibrations inside cells

Techniques based on vibrational spectroscopy are able to detect the specific vibrations that occur inside the cell's biomolecules (such as DNA, proteins, and lipids), making them very powerful tools for 'chemical fingerprinting' of cells. In contrast to fluorescence microscopy, vibrational spectroscopy does not require the biomolecules of interest to be labeled, which is a great advantage. The Biophysical Engineering Group at the University of Twente, headed by prof. Vinod Subramaniam, has pioneered the application of Raman spectroscopy to investigate the chemical make-up of single cells, and this group is now worldwide at the front of high-resolution chemical mapping of cells by Raman microscopy.

In their Nano Letters article, the researchers demonstrate two applications of the hybrid fluorescence Raman technique. By illuminating white blood cells with UV light at a wavelength of 413 nm, the Raman signal from an enzyme that is critical in the innate immune response can be detected and visualized across the cell. The fluorescence signal of quantum dot nanoparticles that have been ingested by the cells can be visualized separately. The second application employs light at a wavelength of 647 nm, which results in the separate detection of Raman signals from cellular proteins and lipids and the fluorescence signal from the nanoparticles.

Van Manen and Otto expect that the fluorescence Raman microscopy combination will provide exciting new possibilities: the nanoparticles might be coated on their surface with antibodies against, for example, marker proteins for cancer cells. In this way the quantum dots will serve as a torch for specific cells, which can subsequently be subjected to a detailed chemical analysis by using Raman microscopy.

Source: University of Twente



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