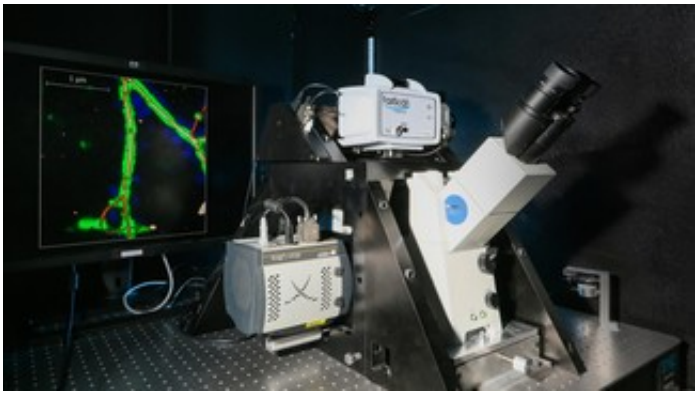
A look at living cells down to individual molecules

August 3 2015



Credit: EPFL / Alain Herzog

EPFL scientists have been able to produce footage of the evolution of living cells at a nanoscale resolution by combining atomic force microscopy and an a super resolution optical imaging system that follows molecules that have been made to blink.

By combining two cutting edge microscopy techniques into one instrument, researchers at EPFL's bioengineering institute have captured images of living cells with unprecedented resolution and have even been able to observe the evolution of their structure and molecular characteristics. Their work is being published in the journal *ACS Nano* Letters.

The secret is in combining the images produced by two very high level technologies. The device the researchers developed is composed of a high-speed atomic force microscope (AFM)—an instrument that "feels" the surface being observed using a tiny force sensitive needle—and a single molecule localization microscope, a technique whose inventors have been awarded the Nobel Prize last year. The first is installed above the sample, and the second, mounted "upside-down," observes the sample from below. The scientists developed special software that assembles the images from the two instruments and gives a precise, 3D visualization of the observed sample.

Two viewpoints, one image

"The AFM makes it possible to see the 3D structure of the cell in nanoscale resolution," explains Pascal Odermatt, a PhD student in EPFL's Laboratory of Bio- and Nano-instrumentation, directed by Georg Fantner. "On the other hand, it can not see the nature of the molecules inside the cell."

The second technology they used, known as PALM (photo-activated light microscopy), uses of contrasts to make certain selected molecules blink, and then follows their path in the interior of a cell.

By uniting the best of these two worlds, the scientists can put super-resolution images of specific proteins into the structural context of the cells – even living ones.

By taking successive images of the same living cell, the scientists were, for the first time ever, able to follow the behavior of protein clusters in relation to the 3D structure of the cell. "That could, for example, allow us to observe the inner workings of cell division, or unravel how stem cells react to mechanical forces" says Henrik Deschout, post doctoral researcher in EPFL's Laboratory of Nanometer-Scale Biology directed by Aleksandra Radenovic.

The EPFL-built setup, which is still in the prototype stage, has already attracted the interest of many other researchers as well as leading microscope manufacturer. The microscope could be of great interest to researchers in cellular-, micro- and mechanobiology, allowing scientists to shed new light on the intricate mechanisms occurring in living cells.

Provided by Ecole Polytechnique Federale de Lausanne