Scientists increase imaging efficiency in cell structure studies

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Scientists in the National Institute of Biomedical Imaging and Bioengineering (NIBIB) Laboratory of Bioengineering and Physical Science have developed a new technique that allows researchers to visualize fine details of cell structure three-dimensionally in thick sections, thus providing greater insight into how cells are organized and how they function. The work is described in a report published online this week in *Nature Methods*.

The new electron tomography method, referred to as BF STEM tomography, lets researchers image samples that are more than three times the thickness of typical samples.

Electron tomography is carried out at the nanoscale on individual cells. Conventionally, high-resolution imaging of biological specimens has been accomplished by cutting cells into thin sections (300 nanometers or less) and imaging each section separately. Although reconstructing an entire structure from thin sections is laborious, thin sections are used because images of thicker sections typically are blurred. Serial BF STEM tomography accomplishes the same work using fewer yet thicker specimen sections, leading to faster reconstruction of intact organelles, intracellular pathogens, and even entire mammalian cells.

Drs. Alioscka Sousa, Martin Hohmann-Marriott, Richard Leapman and colleagues in NIBIB, in collaboration with Dr. Joshua Zimmerberg and colleagues in the Eunice Kennedy Shriver National Institute of Child Health and Human Development (NICHD), demonstrated feasibility and advantages of BF-STEM tomography in a study of red blood cells infected with Plasmodium falciparum, a parasite that causes malaria. High-resolution 3D reconstructions of entire cells were generated by serially imaging just a few thick sections. The intricate system of red blood cell and parasite membranes, as well as several organelles, can be seen in detail.

"We believe that the new technique, which was conceived by Dr. Sousa on the project team, will lead to improved 3D visualization of larger internal structures in mammalian cells at a nanoscale. And it will complement cryo electron tomography and super-resolution optical imaging approaches," according to Dr. Leapman.

Most high-performance electron microscopes can readily be equipped to utilize the BF STEM tomography approach. "This exciting new method, with its ability to provide nanoscale structural details over three dimensions, has the potential for broad application in cell biology," says NIBIB Director Roderic Pettigrew. "This should open new vistas in the understanding of the interplay between cellular structure and function, and is a great example of NIBIB-supported research that moves medical science forward through technological innovation."

Source: NIH/National Institute of Biomedical Imaging & Bioengineering

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