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Technion improves microscope resolution 10-fold

By JUDY SIEGEL-ITZKOVICH
22/05/2012

"Breakthrough" uses computational method to improve resolution of microscopes and imaging systems.

Haifa's Technion-Israel Institute of Technology has registered a patent for a new technique that improves tenfold the performance of any type of sophisticated microscope and imaging system without making hardware changes.

The discovery, which has just been published in the *Nature Materials* journal, has aroused great interest in the scientific world and industry, being described as a "breakthrough with the potential to change" these fields.

Their innovative method substantially improves the resolution – the ability to distinguish between details – of images seen through microscopes.

"When you look through an optical microscope at an object with features [optical information] smaller than one-half the wavelength of light, you necessarily see a blurred image," explained Prof. Moti Segev of the Technion's physics department. "The reason for this is that the information about the structure of very small features does not propagate through space and thus does not reach the eye or the microscope camera."

Methods exist to achieve a resolution under one-half of the wavelength of light, he said, but they all require point-by-point scanning of the object, meaning that these approaches may be used only for a static object, which does not change during the scan.

Scientists have tried for many years to find algorithms to reconstruct the subwavelength information lost between the object and the microscope camera. But until now, all such attempts were largely unsuccessful. The main reason is that "noise" – random scattering of light, which is inevitable in optical systems – has thus far prevented algorithmic reconstruction of features smaller than one-half the wavelength of light from measurements of the blurred image.

Now the Technion team has presented a breakthrough algorithmic method for improving the resolution of microscopes to considerably under one-half the wavelength of light.

The project was successful due to interdisciplinary collaboration between several research groups from four different Technion faculties: those of Segev and Dr. Oren Cohen of the physics department; Prof. Yonina Eldar of the electrical engineering department; Prof. Irad Yavneh and Dr. Michael Zibulevsky of the computer science department; and Prof. Shy Shoham of the biomedical engineering department.

“The algorithmic method relies on finding the most suitable reconstruction that meets two criteria – the reconstructed high-resolution image must conform to the blurred image, and it must minimize the number of the degrees of freedom,” Segev explained.

“The second has to do with understanding compact [sparse] representation of information and with the effect caused by noise in the measurement system. Random ‘noise’ occupies all ‘degrees of freedom,’ whereas information has some structure, hence it occupies a given number of ‘degrees of freedom’ and never all of them.”

He continued: “In many cases, there is some sort of a priori knowledge about the information. In principle, in such a case the information may be presented compactly, such that mathematically it is represented by a small number of projections onto basis functions that cover all the possibilities of spatial information. It is then said that the information is sparsely represented, and the number of degrees of freedom it occupies is small.”

About two years ago, Cohen proposed adding an important layer to the algorithm, which in effect replaces the need for phase measurement, and to thus obtain image reconstruction at a higher resolution than one-half the wavelength of light, using a regular camera.

In fact, Cohen proposed that two research directions be combined – Segev and Eldar’s idea of sub-wavelength imaging and “lensless imaging,” in which images are algorithmically reconstructed from measurements of the intensity of the light at a very far distance from the image.

This area of lensless imaging has recently become a central field in science. When the construction of three short pulse X-ray lasers in the US, Germany and Japan are completed at a cost of \$1 billion dollars per laser, researchers intend to use lensless imaging to measure the structure of hundreds of thousands of single molecules that cannot be assembled into a crystallized structure. Understanding the structure of these molecules will pave the way for chemists, biologists and doctors to understand many biological processes at the molecular level.

Until now, the resolution of all “lensless imaging” methods has been limited to features bigger than a wavelength. However, the methods the Technion researchers have developed could bring about a revolutionary improvement in the entire lensless imaging field, and allow measurement of dynamically changing molecules, Segev said.

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