Scientists 'fingerprint' nanoscale objects and viruses

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Spanish scientists at the University of Barcelona have found a way of effectively identifying nanoscale objects and viruses that could offer a breakthrough for biomedical diagnostics, environmental protection and nano-electronics

Scientists have made amazing progress in the last two decades in seeing and manipulating materials at the nanoscale. New generation microscopes enable researchers to explore the morphology of nanoscale objects, such as nanoparticles, single molecules and atoms, in their natural environment.

Despite the technological advances, however, there are still major hurdles to overcome in measuring the mechanical, chemical, electrical and thermal properties that make each object unique. This is crucial, because only by understanding these properties can we distinguish and monitor nano-objects of similar shapes but different chemical species and, when it comes to biological complexes, study how they function and discover the crucial roles they play in the body.

Scientists working at the nanoscale have long had to rely on chemical labeling – incorporating a visible substance, such as fluorescent dye, into the target object – to detect its presence and physical distribution. But labeling molecules can give misleading results about their properties. For this reason, a pressing need in materials science and biology is to identify the composition of nano-objects in situ – where they manifest their functions – without resorting to labeling.

Now, scientists at the University of Barcelona (UB) and the Institute for Bioengineering of Catalonia (IBEC), in collaboration with the Centro National de Biotecnologia (CNB-CSIC) in Madrid, have perfected a new technique that uses an electrostatic force microscope (EFM), a type of atomic force microscope, to unambiguously identify nano-objects with no need for labels.

In atomic force microscopy, a nano-sized tip on the end of a micro-lever is dragged across a nanoscale object. This senses its shape, much as a person moves their fingers over Braille to read. The movement of the lever is electronically monitored to reconstruct the image in a computer. “However, this image remains limited to the surface structure, which is not much use if our target object lies among others of similar shape and we don’t know exactly where,” explains Laura Fumagalli, lead author on the study that appears in *Nature Materials* yesterday. “In this situation, humans would use one of their other senses, such as smell or taste, to recognize what exactly a substance is – so we used a similar approach.”

All objects exhibit a characteristic ‘dielectric constant’, or permittivity, which gives an indication of how the material they are made of reacts to an applied electric field. By using EFM, the researchers applied the electric field to the nano-objects using the nano-tip, and sensed the tiny movement of the lever induced by the dielectric responses of the objects.

“When we had quantified their dielectric constants precisely, we were then able to use these as a ‘fingerprint’ to discriminate objects of identical shape but different composition, which would otherwise be impossible to recognize without labeling,” explains Fumagalli. “Previously, EFM had only been able to distinguish between metallic and non-metallic nano-objects in black-and-white experiments. Now we have quantitatively recognized those made of very similar materials and with low dielectric constants, as is the case with many biological complexes.”

The key developments the researchers made to achieve this were to increase the electrical resolution of the microscope by almost two orders of magnitude, so they were able to detect ultra-weak forces. They also used geometrically stable nano-tips, as well as a precise method of modeling their results that takes into account the physics of a system and all its geometrical artifacts.

"Our method, an non-invasive way of determining the internal state of objects and correlate these with their functions without slicing or labeling, will be an invaluable tool for diverse areas of scientific research," says Gabriel Gomila, co-author of the study and group leader at IBEC. "It is particularly important in nanomedicine for biomedical diagnostics, opening the door to quantitative label-free detection of biological macromolecules such as viruses based on their dielectric properties. Similarly, it can be applied to detect nanoparticles for environmental monitoring and protection."

The researchers have applied their technique to important biological complexes, such as viruses. By unraveling for the first time the dielectric properties of such nano-objects, which have up until now remained inaccessible, they may be able to uncover important aspects of a virus's functionality. With their technique, they discriminated between empty and DNA-containing viruses, for example, which are the ones that can insert their genetic material into a host cell's DNA.

"These results are also a breakthrough in the fundamental study of nanoscale dielectrics, which are the building blocks that determine the performance of the new generation of nano-electronic devices around today," adds Fumagalli, who is also a lecturer at the Electronics Department of the University of Barcelona, as is Gomila. "Our new technique promises to shed light on questions about the dielectric properties of newly developed nanocomposites and hybrid nanodevices, and can tell us at how small a scale a dielectric object can retain its properties – in other words, how small we can go."

Provided by University of Barcelona