Device For Weighing Individual Molecules

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Physicists at the California Institute of Technology have created the first nanodevices capable of weighing individual biological molecules. This technology may lead to new forms of molecular identification that are cheaper and faster than existing methods, as well as revolutionary new instruments for proteomics.

According to Michael Roukes, professor of physics, applied physics, and bioengineering at Caltech and the founding director of Caltech's Kavli Nanoscience Institute, the technology his group has announced this week shows the immense potential of nanotechnology for creating transformational new instrumentation for the medical and life sciences. The new devices are at the nanoscale, he explains, since their principal component is significantly less than a millionth of a meter in width.

The Caltech devices are "nanoelectromechanical resonators"--essentially tiny tuning forks about a micron in length and a hundred or so nanometers wide that have a very specific frequency at which they vibrate when excited. Just as a bronze bell rings at a certain frequency based on its size, shape, and composition, these tiny tuning forks ring at their own fundamental frequency of mechanical vibration, although at such a high pitch that the "notes" are nearly as high in frequency as microwaves.

The researchers set up electronic circuitry to continually excite and monitor the frequency of the vibrating bar. Intermittently, a shutter is opened to expose the nanodevice to an atomic or molecular beam, in this case a very fine "spray" of xenon atoms or nitrogen molecules. Because the nanodevice is cooled, the molecules condense on the bar and add their mass to it, thereby lowering its frequency. In other words, the mechanical vibrations of the now slightly-more-massive nanodevice become slightly lower in frequency--just as thicker, heavier strings on an instrument sound notes that are lower than lighter ones.

Because frequency can be measured so precisely in physics labs, the researchers are then able to evaluate extremely subtle changes in mass of the nanodevice, and therefore, the weight of the added atoms or molecules.

Roukes says that their current generation of devices is sensitive to added mass at the level of a few zeptograms, which is few billionths of a trillionth of a gram. In their experiments this represents about thirty xenon atoms-- and it is the typical mass of an individual protein molecule.

"We hope to transform this chip-based technology into systems that are useful for picking out and identifying specific molecules, one-by-one--for example certain types of proteins secreted in the very early stages of cancer," Roukes says.

"The fundamental problem with identifying these proteins is that one must sort through millions of molecules to make the measurement. You need to be able to pick out the 'needle' from the 'haystack,' and that's hard to do, among other reasons because 95 percent of the proteins in the blood have nothing to do with cancer."

The new method might ultimately permit the creation of microchips, each possessing arrays of miniature mass spectrometers, which are devices for identifying molecules based on their weight. Today, high-throughput proteomics searches are often done at facilities possessing arrays of conventional mass spectrometers that fill an entire laboratory and can cost upwards of a million dollars each, Roukes adds. By contrast, future nanodevice-based systems should cost a small fraction of today's technology, and an entire massively-parallel nanodevice system will probably ultimately fit on a desktop.

Roukes says his group has technology in hand to push mass-sensing technology to even more sensitive levels, probably to the point that individual hydrogen atoms can be weighed. Such an intricately accurate method of determining atomic-scale masses would be quite useful in areas such as quantum optics, in which individual atoms are manipulated.

The next step for Roukes' team at Caltech is to engineer the interfaces so that individual biological molecules can be weighed. For this, the team will likely collaborate with various proteomics labs for side-by-side comparisons of already known information on the mass of biological molecules with results obtained with the new method.

Roukes announced the technology in Los Angeles on Wednesday, March 24, at a news conference during the annual American Physical Society convention. Further results will be published in the near future.

The Caltech team behind the zepto result included Dr. Ya-Tang Yang, former graduate student in applied physics, now at Applied Materials; Dr. Carlo Callegari, former postdoctoral associate, now a professor at the University of Graz, Austria; Xiaoli Feng, current graduate student in electrical engineering; and Dr. Kamil Ekinci former postdoctoral associate, now a professor at Boston University.

Source: California Institute of Technology