Oscillating Microscopic Beads Could be Key to Biolab on a Chip

If you throw a ball underwater, you'll find that the smaller it is, the faster it moves: A larger cross-section greatly increases the water's resistance. Now, a team of MIT researchers has figured out a way to use this basic principle, on a microscopic scale, to carry out biomedical tests that could eventually lead to fast, compact and versatile medical-testing devices.

The results, based on work by graduate student Elizabeth Rapoport and assistant professor Geoffrey Beach, of MIT's Department of Materials Science and Engineering (DMSE), are described in a paper published in the journal *Lab on a Chip*. MIT graduate student Daniel Montana '11 also contributed to the research as an undergraduate.

The balls used here are microscopic magnetic beads that can be "decorated" with biomolecules such as antibodies that cause them to bind to specific proteins or cells; such beads are widely used in biomedical research. The key to this new work was finding a way to capture individual beads and set them oscillating by applying a variable magnetic field. The rate of their oscillation can then be measured to assess the size of the beads.

When these beads are placed in a biological sample, biomolecules attach to their surfaces, making the beads larger — a change that can then be detected through the biomolecules effect on the beads' oscillation. This would provide a way to detect exactly how much of a target biomolecule is present in a sample, and provide a way to give a virtually instantaneous electronic readout of that information.

This new technique, for the first time, allows these beads — each about one micrometer, or millionth of a meter, in diameter — to be used for precise measurements of tiny quantities of materials. This could, for example, lead to tests for disease agents that would need just a tiny droplet of blood and could deliver results instantly, instead of requiring laboratory analysis.

In a paper published earlier this year in the journal Applied Physics Letters, the same MIT researchers described their development of a technique for creating magnetic tracks on a microchip surface, and rapidly transporting beads along those tracks. (The technology required is similar to that used to read and write magnetic data on a computer's hard disk.) An operational device using this new approach would consist of a small reservoir above the tracks, where the liquid containing the magnetic beads and the biological sample would be placed.

Rather than pumping the fluid and the particles through channels, as in today's microfluidic devices, the particles would be controlled entirely through changes in

applied magnetic fields. By controlling the directions of magnetic fields in closely spaced adjacent regions, the researchers create tiny areas with extremely strong magnetic fields, called magnetic domain walls, whose position can be shifted along the track. "We can use the magnetic domain walls to capture and transport the beads along the tracks," Beach says.

In the researchers' most recent paper, Rapoport explains, they have now shown that once a bead is captured, a magnetic field can be used to shake it back and forth. Then, the researchers measure how fast the bead moves as they change the frequency of the oscillation. "The resonant frequency is a function of the bead size," she says — and could be used to reveal whether the bead has grown in size through attachment to a target biomolecule.

Besides being potentially quicker and requiring a far smaller biological sample to produce a result, such a device would be more flexible than existing chip-based biomedical tests, the researchers say. While most such devices are specifically designed to detect one particular kind of protein or disease agent, this new device could be used for a wide variety of different tests, simply by inserting a fresh batch of fluid containing beads coated with the appropriate reactant. After the test, the material could be flushed out, and the same chip used for a completely different test by inserting a different type of magnetic beads. "You'd just use it, wash it off, and use it again," Rapoport says.

There are dozens of types of magnetic beads commercially available now, which can be coated to react with many different biological materials, Beach explains, so such a test device could have enormous flexibility.

The MIT team has not yet used the system to detect biological molecules. Rather, they used magnetic beads of different sizes to demonstrate that their system is capable of detecting size differences corresponding to those between particles that are bound to biological molecules and those that are not. Having succeeded in this proof of concept, the researchers' next step will be to repeat the experiment using biological samples.

"We now have all the elements required to make a sensing device," Beach says. The next step is to combine the pieces in an operational device and demonstrate its performance.

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