Sculpted 3-D particles could aid diagnostics, tissue engineering

Anne Trafton

MIT engineers have used ultraviolet light to sculpt three-dimensional microparticles that could have many applications in medical diagnostics and tissue engineering. For example, the particles could be designed to act as probes to detect certain molecules, such as DNA, or to release drugs or nutrients.

The new technique offers unprecedented control over the size, shape, and texture of the particles. It also allows researchers to design particles with specific chemical properties, such as porosity (a measure of the void space in a material that can affect how fast different molecules can diffuse through the particles).

With this method, you can rationalize design particles and precisely place chemical properties,” said Patrick Doyle, associate professor of chemical engineering. Doyle is one of the authors of a paper on the work that appeared in the Dec. 3 issue of the journal Angewandte Chemie, published by the German Chemical Society.

The research team started with a method that Doyle and his students reported in a 2006 issue of Nature Materials to create two-dimensional particles. Called continuous flow lithography, this approach allows shapes to be imprinted onto flowing streams of liquid polymers. Wherever pulses of ultraviolet light strike the flowing stream of small monomeric building blocks, a reaction in set off that forms a solid polymeric particle. They have since modified the method to add three-dimensionality.

This process can create particles very rapidly: Speeds range from 1,000 to 10,000 particles per second, depending on the size and shape of the particles. The particles range in size from about a milliliter of a meter to a millimeter.

The team’s new process works by shining ultraviolet light through two transparen cellular masks, which define and focus the light before it reaches the flowing monomers. The first mask, which controls the size and shape of the particles, is part of the technique reported last year by Doyle and his students. The second mask, which is based on MIT professor Edwin Thomas’ work in multibeam lithography, adds three-dimensional texture and other physical traits, such as porosity.

The collaboration sprang from a conversation between Ji-Hyun Jang, a postdoctoral associate in Thomas’ lab, and Dhananjay Dedukuri, a recent Ph.D. recipient in Doyle’s lab, who are also authors on the paper. “It’s very easy to integrate the second phase mask into the microfluidic apparatus,” said Thomas, Morris Cohen Professor of Materials Science and Engineering and head of the Department of Materials Science and Engineering. “Professor Doyle was controlling the overall phase shape, and now what we’re doing is controlling these inner labyrinth networks.”

Adding inner texture is desirable because it increases the particles’ surface-to-volume ratio, which means if the payload is loaded with probes, there are more potential binding sites for target molecules.

In a paper published in Science earlier this year, Doyle and MIT graduate student Daniel Freginon showed that the particles can be used as probes to identify DNA and other molecules.

Other applications for the particles include tissue engineering. For example, they could form a scaffold that would both provide structural support for growing cells and release growth factors and other nutrients. The particles can be designed so diffusion occurs in a particular direction, allowing researchers to control the direction of nutrient flow.

Alan Hatton, the Ralph Landau Professor of Chemical Engineering Practice, is also an author on the paper. This research was funded by the U.S. Army Research Office through the MIT Institute for Soldier Nanotechnologies.

Remote-control nanoparticles deliver drugs directly into tumors

Elisabeth Dougherty

MIT scientists have devised remotely controlled nanoparticles that, when pulsed with an electromagnetic field, release drugs to attack tumors. The innovation, reported in the Nov. 15 online issue of Advanced Materials, could lead to the improved diagnosis and targeted treatment of cancer.

In earlier work, the team, led by Sangeeta Bhatia, an associate professor in the Harvard-MIT Division of Health Sciences and Technology (HST) and in MIT’s Department of Electrical Engineering and Computer Science, developed functional nanoparticles designed to flow through the bloodstream, home to tumors and clamp together. Clumped particles help clinicians visualize tumors through magnetic resonance imaging.

With the ability to see the clumped particles, Geoff von Maltzahn, Bhatia’s co-author in the current work, asked the next question: “Can we talk back to them?”

The answer, the team found, is yes. The system makes it possible for a single DNA tether to simultaneously control the size, shape and texture of microparticles.

To test the particles, the researchers implanted mice with a tumor-like gel saturated with nanoparticles. They placed the implanted mouse into the well of a cup-shaped electrical coil and activated the magnetic pulse. The results confirm that without the pulse, the tethers remain unbroken. With the pulse, the tethers break and release the drugs into the surrounding tissue.

The experiment is a proof of principle demonstrating a safe and effective means of tunable remote activation. However, work remains to be done before such therapies become viable in the clinic.

To heat the region, for example, a critical mass of injected particles must clamp together inside the tumor. The team is still working to make intravenously injected particles clamp effectively enough to achieve this critical mass.

“Our overall goal is to create multifunctional nanoparticles that home to a tumor, accumulate and provide custom-tunable, remotely activated drug delivery right at the site of the disease,” said Bhatia.

Co-authors on the paper are Austin M. Derfus, a graduate student at the University of California, San Diego; Todd Harris, an HST graduate student; Erdki Rosalbaht and Dania Duza of the Burnham Institute for Medical Research in La Jolla, Calif.; and Kenneth S. Vecchio of the University of San Diego.

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