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Shape Matters for Nanoparticles

Particles the size and shape of bacteria could more effectively deliver medicine to cells.

By Kevin Bullis

Nanoparticles shaped to resemble certain bacteria can more easily infiltrate human cells, according to a new study. The results suggest that altering the shape of nanoparticles can make them more effective at treating disease.

[Joseph DeSimone](#), a professor of chemistry and chemical engineering at the University of North Carolina at Chapel Hill and at North Carolina State University, tested how nano- and microparticles shaped like cubes, squat cylinders, and long rods were taken up into human cells in culture. He found that long, rod-shaped particles slipped into cells at four times the rate of short, cylindrical shapes with similar volumes.

DeSimone, who reported the findings this week in the *Proceedings of the National Academy of Sciences*, notes that the faster nanoparticles resemble certain types of bacteria that are good at infecting cells. "A lot of rodlike bacteria get into cells quickly," he says. "Using the same size and shape, our particles get in very quickly too."

Researchers have long suspected that mimicking the distinctive shapes of bacteria, fungi, [blood cells](#)--even pollen--could improve the ability of nanoparticles to [deliver drugs to diseased cells](#) in the body. But it has been difficult to test this suspicion. What's needed is a way to quickly make billions of particles of identical size, chemistry, and shape, and then systematically vary these parameters to learn what effect they have.

DeSimone [developed a way](#) to easily design and test a wide variety of particle shapes, while at the same time controlling for size and chemical composition. For example, he can make particles of various shapes--boomerangs, donuts, hex nuts, cylinders, cubes--while keeping the size constant. He can also make boomerang-shaped particles of various sizes, or keep size and shape constant and vary only the chemical composition of the particles. The process gives researchers an unprecedented level of control, he says, which makes it easy to quickly test how changing various parameters of the

nanoparticles, including shape, affect how they behave in tissues.

"Historically, most of the work with particles has been with spherical particles because making particles of different shapes has been very challenging," says [Samir Mitragotri](#), a professor of chemical engineering at the University of California, Santa Barbara. DeSimone "demonstrates a very powerful technology that shows [that] particles of different shapes and materials can be prepared," Mitragotri says. "It goes well beyond current tools." He adds that the paper shows that "shape makes a big difference in biological response."

DeSimone also identified the precise mechanisms by which cells take in particles of different shapes. These mechanisms determine where the particles end up inside the cell. This new data could help researchers design particles that reach particular compartments within a cell that have a known level of acidity. The researchers could then fine-tune the particles so that they break down and release their cargo only once they reach the desired compartment. That way, the particles will only release drugs inside targeted cells, leaving healthy cells unharmed.

DeSimone is using his manufacturing technique to produce nanoparticles that deliver drugs to cancer cells. He's starting trials in mice for a number of cancer types--breast, ovarian, cervical, lung, prostate--and lymphoma. He's able to conduct so many trials because it's easy to add different treatment molecules to his particles. Particles developed for targeting breast cancer can easily be changed to target lung cancer, for example. During the tests, DeSimone will systematically vary doses, sizes, and so on to determine the least toxic, most effective combinations. "You can now barrage a lot of different cancers and look at what's the most efficacious design parameters you can put in the system," he says.

DeSimone has developed particles that resemble red blood cells in size, shape, and flexibility to help them circulate in the bloodstream without being removed by biological barriers. (He's testing these in animals as a potential basis for artificial blood.) He is also testing long, wormlike particles that can't easily be consumed by macrophages. "The particle has to overcome so many hurdles before it reaches its destination," Mitragotri says. Previously, researchers have been limited to changing the size and chemistry of particles. Adding the ability to control shape provides a "big boost in overcoming these hurdles," Mitragotri says.