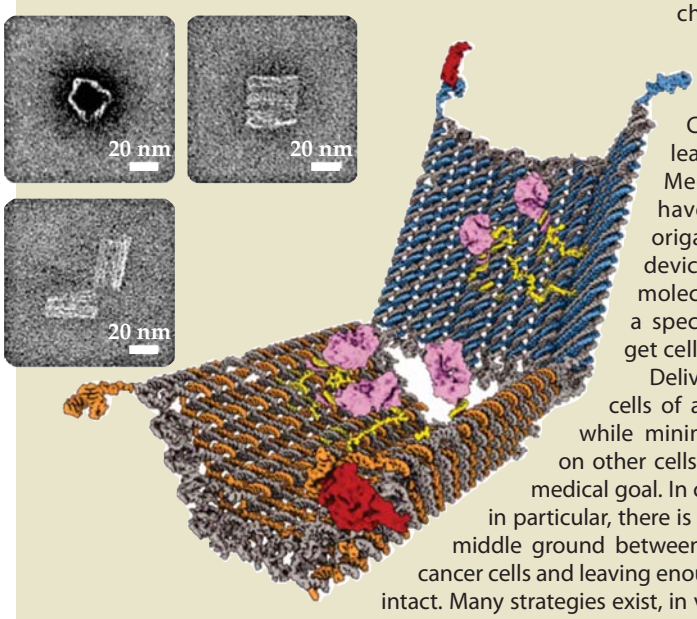
DNA nanobarrel delivers the goods

DNA origami is the folding of a single, long DNA strand into any desired rigid shape, which is held in place by many short strands. In his original 2006 demonstration, Caltech's Paul Rothemund used the technique to make smiley faces and other whimsical shapes.[1] Since then, researchers have developed more functional structures, such as boxes that can be locked and unlocked with DNA keys[2] and nanomachines that pick up nanoparticle cargo in response to chemical cues in the machines' environment.[3] Now, George Church and colleagues at Harvard Medical School have applied DNA origami to create a device that delivers a molecular payload to a specific class of target cells.[4]



Delivering a drug to cells of a particular type while minimizing its effect on other cells is an important medical goal. In cancer medicine, in particular, there is often little or no middle ground between killing enough cancer cells and leaving enough healthy cells intact. Many strategies exist, in various stages of development, for overcoming that challenge by using nanomaterials and other technologies. Church and colleagues' work may represent another possible approach.

The Harvard researchers' device is a barrel-shaped container, as shown in the schematic and transmission electron microscopy (TEM) images in the figure. The barrel's two halves are hinged together and can be fastened at the unhinged end by a pair of DNA locks. Each of those locks consists of two partially complementary single DNA strands (one orange and one blue in the figure), which bind together and hold the barrel closed. Each lock is designed to open when it encounters a particular antigen (red) that populates the surface of the target cells. Inside the barrel are antibodies (pink) held in place by chemically modified DNA strands (yellow). When both locks are opened, the antibodies are exposed and can disrupt or neutralize the target cells. The top two TEM images show barrels in the locked conformation from two different angles; the bottom image shows an unlocked barrel.

The use of two locks is important: There may be no single antigen that uniquely characterizes the target cells, but a combination of two antigens may do the trick. It's thanks to the DNA origami's rigidity, unusual among nanomaterials, that the antibodies are not exposed when just one of the locks is opened. Church and colleagues designed six different nanobarrels, each with a different combination of locks, and tested them on six lines of cancer cells, each with a different combination of antigens. Only when the cells had the right antigens to open both locks did the barrels open.

Treating cancer in a living human or animal is a lot more complicated than attacking cancer cells in a petri dish. The DNA nanobarrels have to avoid being cleared from the body by the liver and the spleen for long enough to make it to the site of the tumor. And in the case of a solid tumor, they need to reach the cells deep inside, not just the ones on the surface. "If these sorts of problems can be solved," says Rothemund, then the nanobarrels "have a chance at becoming real therapeutics."

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References

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2. E. S. Andersen et al., *Nature* **459**, 73 (2009).
3. H. Gu et al., *Nature* **465**, 202 (2010).
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pulse, SL shows up as a bright region in the bubble's center. About 60 ns after the arrival of a laser pulse, a new bright spot is apparent at the bubble's right edge near the pulse's point of entry. Already, the implication is that the pulse is absorbed and reemitted before it can penetrate through to the bubble's left side. Roughly 300 ns later, the bright spot at right remains. "Basically," says Putterman of the bubbles, "you can't see through them."

Although the UCLA researchers weren't able to pin down the precise mean free path of photons in the bubble, they could assume it was less than the bubble's radius of about 85 μm. Given that the bubble absorbs light primarily via electron–ion interactions—the inverse of bremsstrahlung—the researchers concluded that at the moment of SL, the unbound charge density must have been at least 10^{20} cm^{-3}. In other words, nearly 20% of the bubble's Xe atoms were ionized.

No shock wave

The results are consistent with measurements made in 2010 by Kenneth Suslick (University of Illinois at Urbana-Champaign) and his graduate student David Flannigan (now at Caltech). By analyzing spectral-line broadening in a sonoluminescing argon bubble, the two were able to infer that the bubble's unbound charge density ranged from 10^{17} cm^{-3} to 10^{21} cm^{-3}, depending on the acoustic pressure and frequency.[5] At the highest driving pressures, virtually all of a bubble's Ar atoms ionized, some doubly or triply. The same bubble's surface temperature, however, was estimated to be about 16 000 K, or 1.5 eV. That's a mere 1/10 the ionization energy of Ar and less than 1/30 the double ionization energy. How could so many ions abound in so seemingly cool a system?

One possible explanation is the theory, proposed nearly two decades ago, that shock waves in a supersonically imploding bubble converge to generate an energetic, highly ionized core. The core might be orders of magnitude hotter than the surface. Indeed, hydrodynamic models suggest Suslick and Flannigan's system was almost certainly in the shock-wave regime.

What's surprising about the ionization fractions measured in Putterman and company's experiment is that they were achieved with relatively weak acoustic forcing. "The implosions were at one-tenth the speed of sound," says Putterman. "I would say our system doesn't have a hot inner core." If that's true, then the standard statistical mechanical model—embodied in what's known as