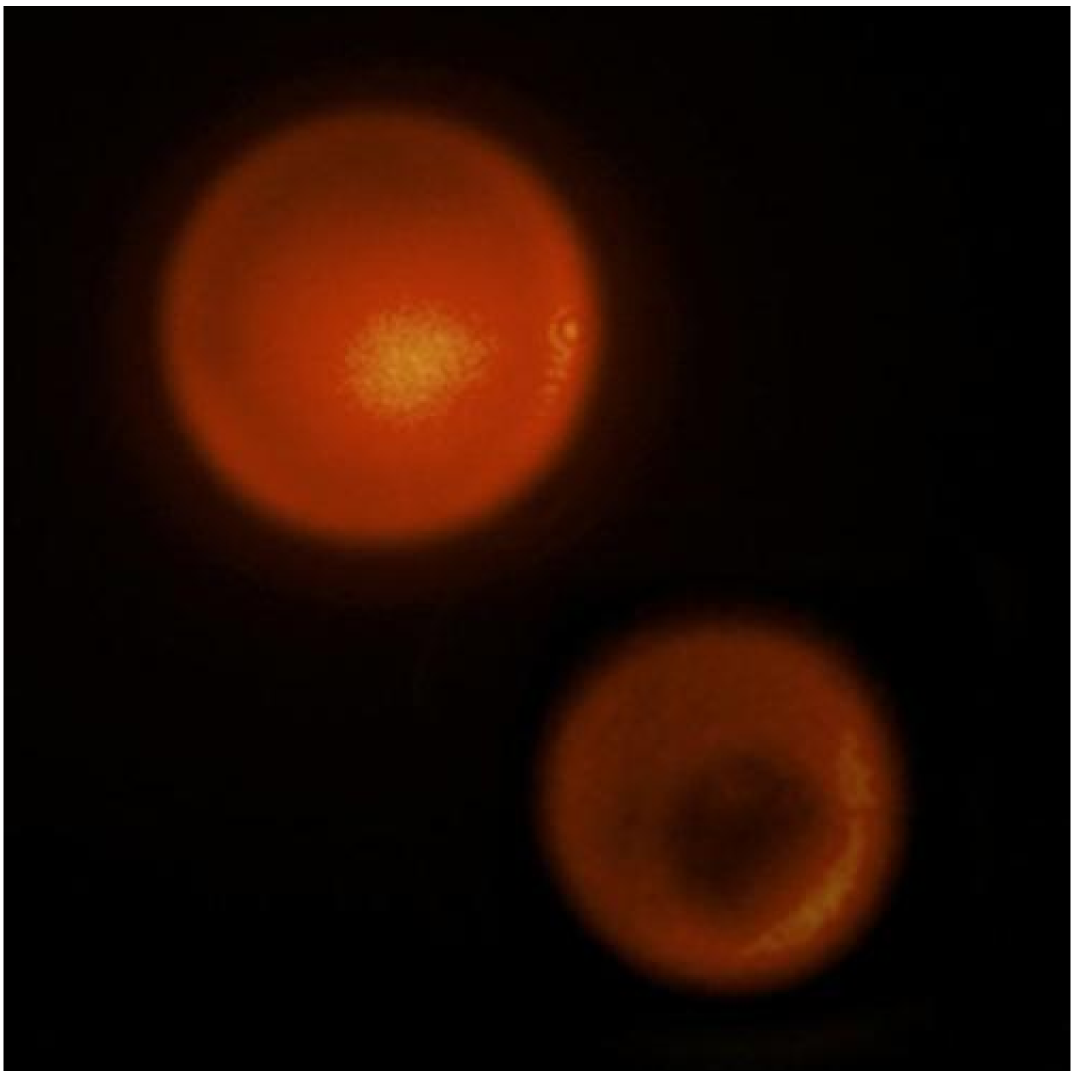
Controlled laser cavitation creates new possibilities for local drug delivery

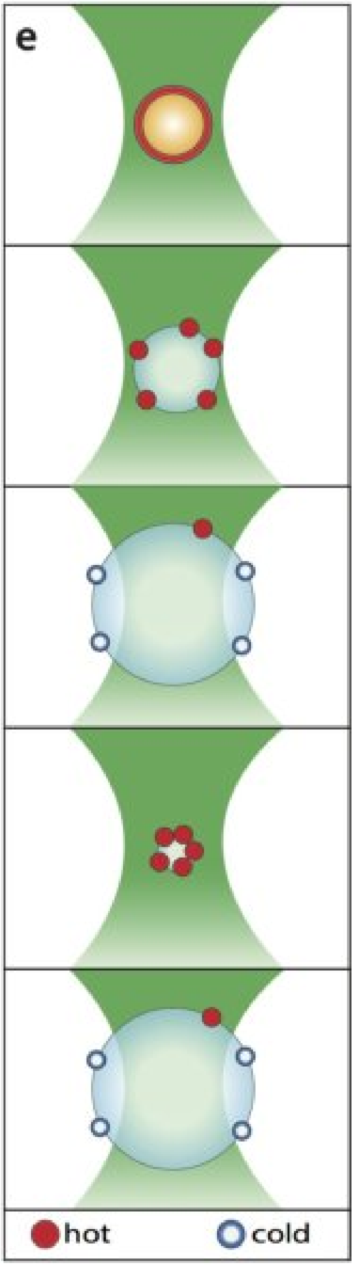
May 2 2014, by Jochem Vreeman



Researchers from the MESA+ and MIRA research institutes of the University of Twente, The Netherlands, have developed a technology for the generation of imploding microbubbles (cavitation) with precise control, both in place and in time, as well as for the understanding of the physical mechanisms underlying the vaporization process. Upon heating with a laser the polymeric microcapsules are activated and release the oil core. Furthermore, the microcapsules can also be used as a novel contrast agent for photoacoustics, a diagnostic imaging modality where a laser beam is sent through tissue and the sound produced by absorbing particles is picked up for the quantification of increased blood flow or the localization of tumors. This work has been published in the prominent scientific magazine *Nature Communications*.

Cavitation is the formation of vapour bubbles by either decreasing the pressure or raising the temperature in a liquid. In the latter case, we generally speak of boiling. Usually, cavitation is a chaotic and destructive process. For instance, marine propellers and pumps may be corroded by cavitation. If cavitation can be controlled, this might clear the way for a whole range of new applications, e.g. precise ultrasonic cleaning and chemistry at micro scale. In medical applications, kidney stones are pulverized in a controlled manner by means of cavitation. With the aid of cavitation bubbles, researchers seek to dissolve blood clots in order to restore the blood flow.

The physical phenomena of vaporization at micro scale are not well understood, owing to the ultra short nanosecond time scales in which these processes occur. From now on, this will change. "We have managed to measure the vaporization process at the relevant time scale, both optically and acoustically," says Michel Versluis, professor in physical and medical acoustics at the University of Twente. "What we observed is that a polymeric microcapsule of 3 micrometres is heated up and starts to melt in a microsecond. In that short span of time, the oil in the microcapsule is heated up to 250 degrees and the water around the microcapsule is just above its boiling point. As soon as the microcapsule's polymeric shell is fully melted, the hot oil will flow into the superheated water. This will result in a instant vaporization of the water and the formation of a vapour bubble, which subsequently implodes. We have developed a model to accurately measure the thermal management in and around the microcapsule, and we have observed a excellent correspondence between the model and experiment. The imploding, microscopically small bubble produces a short snap and we are now able to measure (and model) that sound. This way, we can also use these microcapsules as contrast agents for photoacoustics. To this end, a laser beam is sent through tissue and the sound that is produced by these microcapsules, is picked up in the far field for sensitive and specific diagnosis."



More discoveries

During their research activities, the researchers made some other discoveries as well.

- Microcapsules that were only filled with gas, worked just as well as microcapsules filled with oil. In this case, the released gas acts as a nucleation site for boiling at the moment the polymer shell is fully melted. The function of the oil is that it enables us to dissolve drugs in it. The researchers have also looked at polymers with a much lower melting point and a liquid core with a very low boiling point. Versluis: "In this way, we can activate the system at a much lower laser intensity and at a lower temperature. This will enable us to release a wider range of drugs.".
- When the microcapsule was not illuminated with a short laser pulse, but with continuous wave laser light (with a much lower intensity), it became clear that the microcapsule was continuously giving off acoustic signals. "It appeared that the polymeric microcapsule initially bursts open and that during the formation of the vapour bubble, polymer fragments were pushed out of the laser beam, as a result of which they cooled off again. As a consequence of this cooling off, the vapour bubble recondensed (shrinks/implodes) and this created the effect that the fragments were drawn back into the laser, resulting in a rapid heating and the formation of a new vapour bubble. This process continues as long as the laser is on. These surprising discoveries open the way to novel applications in the field of medical imaging, which are more economic and, furthermore, which are safer and thus more broadly applicable."

More information: "Ultrafast vapourization dynamics of laser-activated polymeric microcapsules." Guillaume Lajoinie, et al. *Nature Communications* 5, Article number: 3671 DOI: 10.1038/ncomms4671. Received 30 May 2013 Accepted 17 March 2014 Published 22 April 2014