Improved ultrasound capabilities with nanoscale imaging agents made by microbes

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Dr. Mikhail Shapiro was interested in developing nanoscale imaging agents for ultrasound to enable non-invasive imaging of a much broader range of biological and biomedical events in the body. Turning to nature for inspiration, he and his colleagues at Caltech and UC Berkeley, successfully created the first ultrasound imaging agent based on genetically encoded gas-containing structures.

Shapiro's team utilized photosynthetic micro-organisms that form gas nanostructures called "gas vesicles," that the researchers discovered were excellent imaging agents for ultrasound, with several unique properties making them especially useful in biomedical applications.

This new nanotechnology method opens the door to a broad variety of potential imaging applications where the nanometer size is advantageous, (e.g., in labeling targets outside the bloodstream), and could have a significant impact on ultrasounds - one of the most widely used imaging modalities in biomedicine.

Previously, most ultrasound imaging agents were based on small gas bubbles, which ultrasound can detect because they have a different density than their surroundings and can resonate with sound waves. Unfortunately, these "microbubbles" could only be synthesized at sizes of several microns (or larger) because of their fundamental physics: the smaller you tried to make them, the less stable they became. As a result, they were always confined to the bloodstream and could only image a limited number of biological targets.

The researchers wanted to find another way of making gas-filled structures that could be nanoscale. In particular, certain photosynthetic micro-organisms regulate their buoyancy by forming protein-shelled gas nanostructures called "gas vesicles" inside the cell body. These structures interact with gas in a way that is fundamentally different from microbubbles, allowing them to have nanometer size. In this study, they discovered that gas vesicles are excellent imaging agents for ultrasound.

The researchers showed that they were able to easily attach biomolecules to the gas vesicle surface to enable targeting. In addition, because these structures are encoded as genes, they now have a chance to modify these genes to optimize gas vesicles' ultrasound properties. Already the team has shown that gas vesicles from different species, which vary in genetic sequence, exhibit different properties that can be used to, for example, distinguish them from each other in an ultrasound image.

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