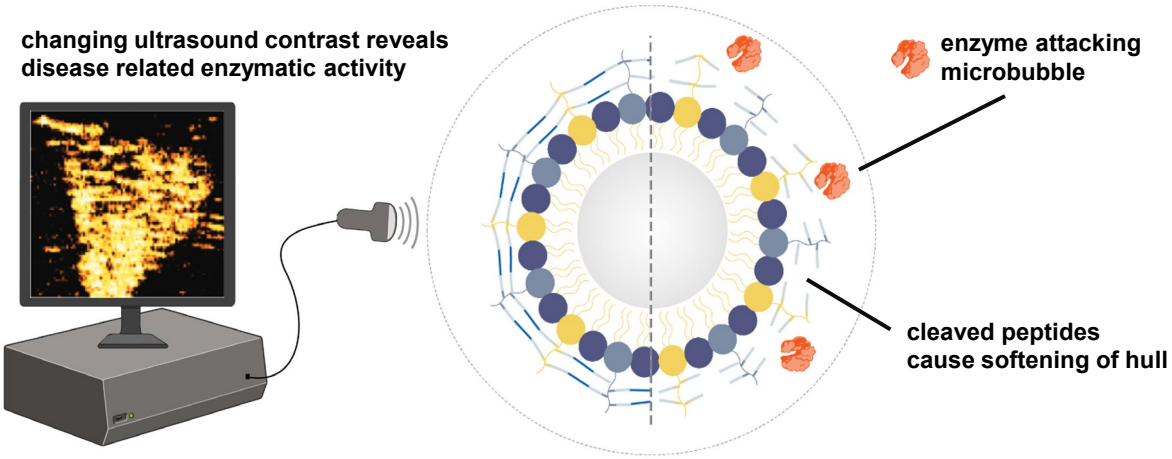
ETH zürich

Licensing Opportunity

Measurement of enzymatic activity at the disease site for advanced diagnostics and therapy monitoring



Application

Ultrasound imaging assesses in vivo and in situ the activity of enzymes with diagnostic relevance. Changes in i.e. the activity of proteases, a class of enyzmes, indicate diseases such as inflammatory bowel disease, arthritis, autoimmune diseases, bacterial or viral infections, cancer and metastasis, impaired blood coagulation, cardiovascular diseases, COPD or asthma and metabolic diseases.

Features & Benefits

- local, non-invasive read-out at target site
- specificity for the protease of interest
- customizable towards the protease of interest
- read-out equipment is readily available in clinics

Publications

- D. Dubey, M. G. Christiansen, M. Vizovisek, S. Gebhardt, J. Feike, S. Schuerle, “Engineering Responsive Ultrasound Contrast Agents through Crosslinked Networks on Lipid-Shelled Microbubbles”, Small (2022), https://doi.org/10.1002/smll.202107143
- Patent pending in EP, WO/2021/069732

transfer

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Reference 2019-036

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Technology Readiness Level

1 2 **3** 4 5 6 7 8 9

Background

Abnormal protease activity is associated with many diseases and serves as a powerful diagnostic biomarker. Ideally, the activity is monitored in vivo at the site of disease in a non- or minimally invasive and cost-effective manner.

Invention

Gas-filled microbubbles are commonly used as contrast agents in ultrasound imaging because they scatter sound waves effectively, making images brighter. A new type of microbubble allows to image enzymatic activity, such as of proteases, through a change in ultrasound contrast. The bubbles have an outer shell made of lipopolymers, connected by peptides (small aminoacid sequences) that certain enzymes, like proteases, selectively cut. This dense network suppresses volumetric oscillations of the bubbles, and thus, the image remains darker. When the targeted enzyme breaks these connections, the bubble’s shell becomes softer, causing the bubble to expand more easily when hit by ultrasound waves, which in turn yields in strong scattering and brightening of the image.

The microbubbles are biocompatible as they degrade over time and immune cells remove lipid residues. Selectivity for a specific protease can be enhanced by combining relevant peptides which lead to multiple cleavage events. Peptide sequences are readily changeable to customize the probe towards the protease of interest. Since ultrasound imaging is affordable and widely available, this approach provides an inexpensive, easy-to-use diagnostic tool suitable for point-of-care testing.

Laboratory based tests successfully monitored cleavage kinetics of recombinant proteases at varying concentrations down to nanomolar levels.