Rapid, Multiscale Sensing Using Acoustic Detection Mechanisms

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The overall goal of this work is to design a new class of in vitro and in vivo acoustic biosensors based on the interactions of biomolecules with the surfaces of soft colloidal particles. A technology that can provide a convenient, inexpensive, and portable method for detecting biomolecules without sample manipulation would provide new avenues for measuring both systemic and localized biomolecular concentrations in many different environments and media. For in vitro detection, an in-solution acoustic sensor would obviate the need for sample processing and washing steps, be scalable from microfluidics to batch process, and possess almost no background. For in vivo imaging, development of a contrast agent that can respond to levels of specific soluble biomarkers in a localized environment would provide considerable power to a ubiquitous imaging modality.

The work presented here focuses on two avenues of exploration. First, we have designed microbubbles that are able to change their response to incident ultrasound waves based on specially tuned interactions of biomolecules with their environment. Microbubbles were prepared with DNA oligonucleotides placed as crosslinkers on their surface. Through an aptamer-target interaction, the biomarker thrombin was found to displace the crosslinking strands on the bubble, restoring the bubble's ability to generate highly specific nonlinear echoes. This process resulted in 20 dB (100-fold) activation ratios and was validated in a rabbit thrombosis model, representing the first ultrasound contrast agent that could sense soluble biomarkers in vivo.

In the second approach, we are focusing on the vaporization of superheated liquid droplets specifically in response to interactions with biomolecules. Perfluorocarbon droplets are relatively stable and can be prepared ~ 200 nm in diameter for preferential extravasation into tumor tissue. While by themselves the droplets are poor ultrasound contrast agents, they can be subjected to high intensity pulses that vaporize them in situ into high contrast microbubbles, producing a very large change in ultrasound contrast. Thus a mechanism that could specifically prime the droplets for vaporization into bubbles would represent a mechanism for inducing signal in response to biomolecular challenge. Studies showing the effect of droplet aggregation on ultrasound vaporization will be presented along with future research directions.