The study of biological function in intact organisms and the development of targeted cellular therapeutics necessitate methods to image and control cellular function in vivo. Technologies such as fluorescent proteins and optogenetics serve this purpose in small, translucent specimens, but are limited by the poor penetration of light into deeper tissues. In contrast, most non-invasive techniques such as ultrasound and magnetic resonance imaging — while based on energy forms that penetrate tissue effectively — are not effectively coupled to cellular function. Our work attempts to bridge this gap by engineering biomolecules with the appropriate physical properties to interact with magnetic fields and sound waves. In this talk, I will describe our recent development of biomolecular reporters and actuators for ultrasound. The reporters are based on gas vesicles — a unique class of gas-filled protein nanostructures from buoyant photosynthetic microbes. These proteins produce nonlinear scattering of sound waves, enabling their detection with ultrasound. I will describe our recent progress in understanding the biophysical and acoustic properties of these biomolecules, engineering their mechanics and targeting at the genetic level, developing methods to enhance their detection in vivo, expressing them heterologously as reporter genes, and turning them into dynamic sensors of enzyme activity. In addition to their applications in imaging, gas vesicles can be used to control cellular location and function by serving as receivers of acoustic radiation force or seeding localized bubble cavitation. Additional remote control is provided by thermal bioswitches — biomolecules that provide switch-like control of gene expression in response to small changes in temperature. This allows us to use focused ultrasound to remote-control engineered cells in vivo.

Mikhail Shapiro is a Professor of Chemical Engineering at Caltech and an Investigator of the Howard Hughes Medical Institute. The Shapiro laboratory develops biomolecular technologies allowing cells to be imaged and controlled inside the body using sound waves and magnetic fields to enable the study of biological function in vivo and the development of cell-based diagnostic and therapeutic agents. Mikhail received his PhD in Biological Engineering from MIT and his BSc in Neuroscience from Brown, and conducted post-doctoral research at the University of Chicago and the University of California, Berkeley, where he was a Miller Fellow. Mikhail’s awards include the NIH Pioneer Award, the Packard Fellowship, the Pew Scholarship, the Camille Dreyfus Teacher-Scholar Award and the Roger Tsien Award for Excellence in Chemical Biology. More information about the Shapiro Lab can be found online at shapirolab.caltech.edu.