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Nanoscale probing of coherent phonons in single cells

During several fundamental biological transitions, notably differentiation and tissue morphogenesis, cells can regulate and adapt their mechanical properties. Similarly, many diseased conditions of the cell are correlated with altered cell mechanics, as in the case of cancer progression. The precise mechanisms that underlie these behaviors remain largely undetermined, primarily due to the lack of a clear description of the mechanical properties of the cell. Cells have a complex composition that yields an intricate rheological behavior, appealing for measurements over a wide frequency range. However the existing techniques cannot exceed the kHz range, and rely for most on injected or contacting functionalized microprobes. Here, we use coherent phonons to probe the mechanical properties of single cells.

We culture animal cells on top of a biocompatible Ti metal film. Low-energy femtosecond laser pulses are focused at the bottom of the film to a micron spot to allow single-cell investigation. The subsequent ultrafast thermal expansion launches a longitudinal acoustic pulse in Ti, with a broad spectrum extending up to 200 GHz. The acoustic pulse is transmitted to the cell owing to the cell-Ti intimate contact.

The phonon propagation in the cell is measured remotely with an ultrafast laser probe through Brillouin light scattering. This yields a direct measurement of the local stiffness and viscosity of cells. Simultaneously, the acoustic reflection coefficient at the Ti-cell interface is measured through the transient optical reflectance changes. Time-frequency analysis of the reflected acoustic pulses with a wavelet transform reveals an anomalous frequency dispersion of the acoustic reflection coefficient. This innovative technique offers a unique mean to investigate quantitatively cellbiomaterial interactions without fluorescent labels or mechanical contact to the cell.

As an alternative to one-dimensional metal films, a promising way to probe cell mechanics at a nanoscale is to use single nanoparticles as opto-acoustic nanotransducers. For illustration, we use a standard picosecond ultrasonics setup to detect the breathing mode of a single gold nanoparticle embedded in a transparent PMMA film. We demonstrate that the Brillouin scattering magnitude in PMMA can be enhanced by adjusting the size of the nanoparticle so that the breathing mode frequency matches the Brillouin frequency. With breathing frequencies reaching tens of GHz and a resolution of a few tens of nanometers, this result suggests strong potential to perform 3D local elastic probing at a submicron scale of single cells.