

# Microcavity Vibrational Spectroscopy for Single-Cell Fingerprinting

In addition to forming the basis of our tone system, Pythagoras' observation of natural vibrations in strings has had profound impacts on modern science. Such natural vibrations are ubiquitous in objects of all sizes and are widely utilized to derive an object's species, constituents and morphology. For example, molecular vibrations at terahertz rates have become the most common fingerprints for the identification of chemicals and structural analysis of large biomolecules.

Recently, natural vibrations of particles at the mesoscopic scale—ranging from 100 nm to 100  $\mu\text{m}$  in size—have seen growing interest, since this category includes a wide range of functional particles as well as most biological cells and viruses.<sup>1</sup> These natural vibrations, however, have remained hidden from existing technologies.<sup>2</sup> Mesoscopic-scale particles are expected to exhibit faint vibrations in the megahertz to gigahertz range. This frequency regime cannot be resolved by current Raman and Brillouin spectroscopies due to strong Rayleigh-wing scattering, while the performance of piezoelectric techniques commonly used in macroscopic systems degrades significantly at frequencies beyond a few megahertz.<sup>3</sup>

We recently demonstrated real-time measurement of natural vibrations of individual mesoscopic particles using an optical microresonator, extending the reach of vibrational spectroscopy to the megahertz-to-gigahertz frequency window.<sup>4</sup> In our work, the vibrational modes of the particles are stimulated photoacoustically by laser pulse absorption and coupled to optical resonances by stimulating acoustic waves within the microresonator. As a result of the formation of whispering galleries through total internal reflection, the microresonator offers high-Q optical resonances that respond to acoustic waves in real time.<sup>5</sup> We verified this concept of microcavity vibrational spectroscopy (MVS) by measuring mesoscopic

particles with different constituents, sizes and internal structures, showing an unprecedented signal-to-noise ratio of 50 dB and a detection bandwidth of more than 1 GHz.

Using this new technology, we have further demonstrated biomechanical fingerprinting of the species and living states of microorganisms at the single-cell level. Specifically, we used MVS to measure three types of microorganisms—cyanobacteria, *Aspergillus sydowii* and *Aspergillus niger*—in the atmospheric environment. We observed that microorganisms of the same species exhibited bunched natural frequencies, forming unique fingerprints due to the highly defined and stable morphology of certain biological species. Additionally, the spectral information, including natural frequencies and mechanical quality factors, provides a measure of the viscoelastic properties of cells.

The spectroscopic technology we demonstrated possesses a detection bandwidth exceeding 1 GHz, making it suitable for a wide range of mesoscopic particles and offering invaluable opportunities for investigating biomechanics and nanomechanics at the single-particle level. **OPN**

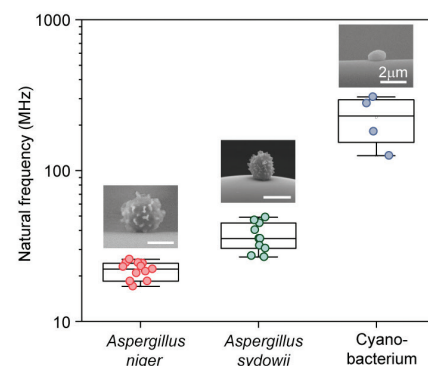
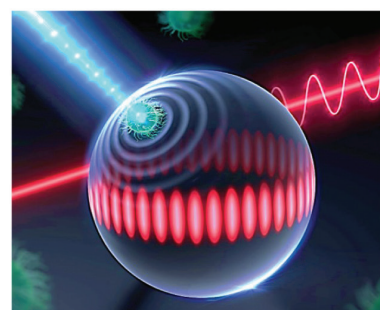
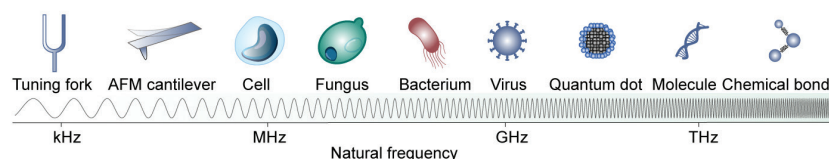
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## REFERENCES

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Top: Natural frequencies of representative objects across different scales. Bottom left: Artist's view of microcavity vibrational spectroscopy. Bottom right: Measured natural frequencies of three types of microbial cells.