Emerging nanophotonic platforms for infectious disease diagnostics: Re-imagining the conventional microbiology toolkit

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Abstract

We present our research controlling light at the nanoscale for infectious disease diagnostics, including detecting bacteria at low concentration, sensing COVID gene sequences, and visualizing in-vivo inter-cellular forces. First, we combine Raman spectroscopy and deep learning to accurately classify bacteria by both species and antibiotic resistance in a single step. We design a convolutional neural network (CNN) for spectral data and train it to identify 30 of the most common bacterial strains from single-cell Raman spectra, achieving antibiotic treatment identification accuracies exceeding 99% and species identification accuracies similar to leading mass spectrometry identification techniques. Our combined Raman-CNN system represents a proof-of-concept for rapid, culture-free identification of bacterial isolates and antibiotic resistance. Second, we describe resonant nanophotonic surfaces, known as "metasurfaces" that enable multiplexed detection of SARS-CoV-2 gene sequences. Our metasurfaces utilize guided mode resonances excited in high refractive index nanostructures. The high quality factor modes produce a large amplification of the electromagnetic field near the nanostructures that increase the response to targeted binding of nucleic acids; simultaneously, the optical signal is beam-steered for multiplexed detection. We describe how this platform can be manufactured at scale for portable, low-cost assays. Finally, we introduce a new class of *in vivo* optical probes to monitor biological forces with high spatial resolution. Our design is based on upconverting nanoparticles that, when excited in the near-infrared, emit light of a different color and intensity in response to nano-to-microNewton forces. The nanoparticles are sub-30nm in size, do not bleach or photoblink, and can enable deep tissue imaging with minimal tissue autofluorescence. We present the design, synthesis, and characterization of these nanoparticles both in vitro and in vivo, focusing on the forces generated by the roundworm *C. elegans* as it feeds and digests its bacterial food.