Label-free Ultra-sensitive Biomolecular Detection for Basic Science and Translational Medicine

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Abstract: Label-free single molecule detection has been a long-standing goal of bioengineers and physicists. The main obstacle in the detection of single molecules, however, is to sufficiently decrease the noise level of the measurements such that a single molecule can be distinguished from background fluctuations. We have used laser frequency locking in combination with balanced detection and data processing techniques to improve the signal-to-noise ratio of microtoroid optical resonators and report the detection of a wide range of nanoscale objects including nanoparticles with radii from 100 to 2.5 nm, exosomes, ribosomes, and single protein molecules (mouse immunoglobulin G and human interleukin-2). We further extend the exosome results toward the creation of a minimally-invasive tumor biopsy assay. Our results agree with established model predictions for the frequency shift of the resonator upon particle binding across several orders of magnitude of particle radius (100 nm to 2 nm). We anticipate that our results will enable many applications, including more sensitive medical diagnostics and fundamental studies of single receptor-ligand and protein-protein interactions in real time. Future research thrusts will also be discussed.

Dr. Judith Su (https://wp.optics.arizona.edu/jsu/) is an Assistant Professor in Biomedical Engineering and an Assistant Professor of Optical Sciences at the University of Arizona. She is also an Associate Member of the University of Arizona Cancer Center and a Visiting Associate in the Division of Biology and Biological Engineering at Caltech. Judith received her B.S. and M.S. from MIT in Mechanical Engineering and her Ph.D. from Caltech in Biochemistry & Molecular Biophysics. Her background is in imaging, microfabrication, and optical instrument building for biological and medical applications. In general, her research interests are to develop new imaging, sensing, and rheological techniques to reveal basic biological functions at the molecular, cellular, and tissue levels. Recently her work has centered on label-free single molecule detection using microtoroid optical resonators with a focus on basic research, and translational medicine through the development of miniature field portable devices.
3D Nanophotonic Systems For Environmental and Biological Sensing

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Abstract: The fabrication of nanophotonic elements out of soft materials provides new frontiers for the integration of photonics with biosystems, and provides ways to realize microscopic devices that could not be made otherwise. Here we present one example: a nanoparticle and virus imaging platform enabled by nanoscale lenses that are self-assembled out of polyethylene glycol. Currently, nanoparticle sizing and imaging are typically performed using sophisticated laboratory-based electron microscopes or optical systems, even though such analyses can be time-intensive, costly, and/or not readily available in areas such as developing or rural regions. Rapid and inexpensive nanoparticle imaging and sizing is important in medical, environmental, and basic research, and could enable, for example, point-of-care quantification of viral load in HIV patients, multiplexed biochemical assays, or widespread air quality and water quality environmental monitoring. Here we perform accurate nanoparticle imaging and sizing using the combination of nanolenses and on-chip, in-line holography. This combined approach simultaneously provides high resolution, large field of view, and a cost-effective and field-portable hardware system. We can size particles of diameter 40 - 100 nm, where the accuracy is ±11 nm for the 40 - 500 nm range. Our approach can size more than $10^5$ particles simultaneously, can detect particles of various shapes, and can recover multi-modal distributions of sizes, all within a compact and inexpensive prototype device.

Dr. Euan McLeod has been an assistant professor at the College of Optical Sciences in the University of Arizona since 2015. He was previously a postdoc in Electrical Engineering and Bioengineering at UCLA, as well as a postdoc in Applied Physics at Caltech. He received his Ph.D. from Princeton University in 2009, and his B.S. from Caltech in 2004. Euan’s background and interests lie at the intersection of optics, nanoscience, and soft bio-materials science. He has published more than 20 papers on these topics in peer-reviewed journals, with major contributions in the areas of high-speed varifocal lenses based on acoustic modulation, optical trap-assisted nanopatterning, and lensfree holographic imaging of nanoparticles and viruses.