Optical Interference for multiplexed, label-free, and dynamic biosensing: protein, DNA and single virus detection

M. Selim Ünlü

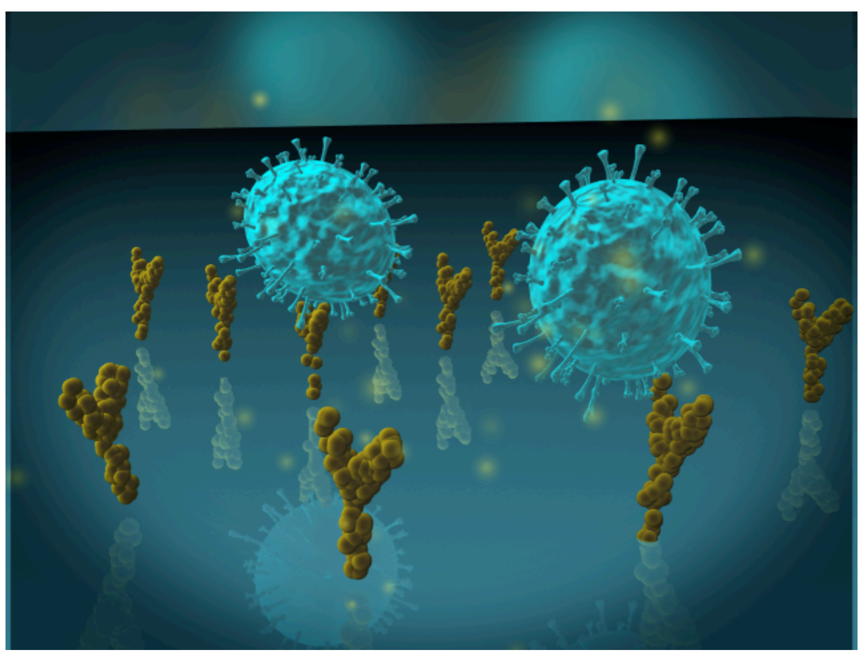
Boston University

Electrical and Computer Engineering and Biomedical Engineering

Center for Nanoscience and Nanobiotechnology and Photonics Center

Direct monitoring of primary molecular binding interactions without the need for secondary reactants would markedly simplify and expand applications of high-throughput label-free detection methods. We have developed the Interferometric Reflectance Imaging Sensor (IRIS) for label-free, high throughput, high sensitivity and dynamic detection of molecular binding on a solid surface. IRIS has demonstrated protein-protein binding and DNA-protein binding in real time, label-free, and in a high-throughput format with exquisite sensitivity (~10 pg/mm^2) and reproducibility [1,2] as well as label-free measurements of DNA hybridization kinetics [3] and viral detection [4].

Recently, we have significantly advanced IRIS beyond the original tunable-laser configuration [1] and implemented a multi-LED discrete wavelength system that allows for high spatial resolution imaging with the demonstrated ability to detect single nanoscale particles [5]. To detect and size pathogens, IRIS shines light from multi-color LED sources sequentially on nanoparticles bound to the sensor surface, which consists of a silicon dioxide layer on top of a silicon substrate. Interference of light reflected from the sensor surface is modified by the presence of particles producing a distinct signal that reveals the size of the particle. We have successfully detected 35 nm and 50 nm radius particles and H1N1 viruses (illustrated in the conceptual picture) with accurate size discrimination [3]. The device has a very large surface area and can capture the telltale interferometric responses, in parallel, of up to a million nanoparticles. Size discrimination allows for reducing the noise resulting from many smaller particles that may be present in the target solution that may bind to the sensor indiscriminately. IRIS has a great advantage in that we can employ both polarization and pupil function engineering to characterize the shape, size and orientation of particles with resolution beyond the classical diffraction limit.



References

1. Ozkumur E., J. W. Needham, D. A. Bergstein, R. Gonzalez, M. Cabodi, J. M. Gershoni, B. B. Goldberg, and M. S. Ünlü. "Label-free and Dynamic Detection of Biomolecular Interactions for High-throughput Microarray Applications." *Proceedings of the National Academy of Sciences*, Vol. 105, No. 23, Pages: 7988-7992, (2008).

2. Özkumur E., A. Yalçın, M. Cretich, C. A. Lopez, D. A. Bergstein, B. B. Goldberg, M. Chiari, and M. S. Ünlü. "Quantification of DNA and Protein Adsorption by Optical Phase Shift." *Biosensors and Bioelectronics*, Vol. 25, No. 1, 167-172, (2009).

3. E. Ozkumur, S. Ahn, A. Yalcin, C. Lopez, E. Cevik, R. Irani, C. DeLisi, M. Chiari, and M. S. Ünlü, "Label-free microarray imaging for direct detection of DNA hybridization and single-nucleotide mismatches," *Biosensors and Bioelectronics*, Vol. 25, No. 7, 15, pp. 1789-1795, (2010).

4. C. Lopez, G. G. Daaboul, R. S. Vedula, E. Ozkumur, D. A. Bergstein, T. W. Geisbert, H. Fawcett, B. B. Goldberg, J. H. Connor, and M. S. Ünlü, "Label-free multiplexed virus detection using spectral reflectance imaging," *Biosensors and Bioelectronics*, doi:10.1016/j.bios.2011.01.019, (2011).

5. G. G. Daaboul, A. Yurt, X. Zhang, G. M. Hwang, B. B. Goldberg, and M. S. Ünlü, "High-Throughput Detection and Sizing of Individual Low-Index Nanoparticles and Viruses for Pathogen Identification," *Nano Letters*, Vol. 10, No. 11, pp. 4727-4731 (2010).