Invited Paper

# Applications of Optical Resonance to Biological Sensing and Imaging

**M. Selim Ünlü and Bennett B Goldberg**
*Boston University Department of Electrical and Computer Engineering, Department of Physics, Photonics Center and Center for Nanoscience and Nanobiotechnology, Boston, MA 02215, USA*
*Author e-mail address:* selim@bu.edu, goldberg@bu.edu

**Abstract:** Optical resonators designed for biological sensing and imaging are demonstrated to yield sub-nanometer position accuracy in DNA conformation, high-sensitivity in ring-resonators for biosensing, and massively parallel, non-labeled detection in a Resonant Cavity Imaging Biosensor.

Resonance is an enabling property of a myriad of optical devices such as interference filters and lasers and here we present applications of optical resonance and micro-resonators to biological sensing and imaging techniques. The importance of optical resonance has long been recognized and the interference due to multiple reflections had in fact been analyzed theoretically by George Airy nearly two centuries ago. The optical resonator has become a household name since Fabry and Perot and has been used for numerous sensing applications to improve sensitivity. Over the past 20 years we have been involved in the development of optoelectronic devices whose performance is enhanced by placing the active device structure inside a resonant microcavity [1].

A novel application of resonance to fluorescence microscopy promises nanometer resolution in biological imaging. We have developed a new technique – spectral self-interference fluorescent microscopy (SSFM) – that transforms the variation in emission intensity for different path lengths used in fluorescence interferometry to a variation in the intensity for different wavelengths in emission, thus encoding the high-resolution information in the emission spectrum [2]. Using monolayers of proteins as well as single and double stranded DNA we have demonstrated sub-nanometer axial height determination for thin layers of fluorophores. Using SSFM, we have estimated the shape of coiled single-stranded DNA, the average tilt of double-stranded DNA of different lengths, and the amount of hybridization [3]. The data provide important proofs of concept for the capabilities of novel optical surface analytical methods of the molecular disposition of DNA on surfaces. Additionally, the determination of DNA conformations on surfaces and hybridization behavior provide information required to move DNA interfacial applications forward and thus impact emerging clinical and biotechnological fields.

We have recently developed a new label-free microarray technique, Resonant Cavity Imaging Biosensor (RCIB), that sensitively detects surface binding and is designed for parallel sensing on very large arrays[4]. The resonant cavity is formed between two facing planar Bragg reflectors which have been developed for Si resonant cavity enhanced photodetectors [5]. The wavelength illumination is swept in time using a wavelength tunable laser source. When the wavelength satisfies the resonant condition of the cavity for a particular location, or pixel, the cavity builds up local energy that couples through and is recorded by the camera pixel corresponding to that location, or alternatively a photodiode in a photodiode array.

Finally, we have also demonstrated application of vertically coupled glass microring resonators to biomolecular sensing. Using balanced photodetection, very high signal to noise ratios, and thus high sensitivity to refractive index changes (limit of detection of $1.8 \times 10^{-5}$ refractive index units), are achieved. Experimental data obtained separately for a bulk change of refractive index of the medium and for avidin-biotin binding on the ring surface demonstrated repeatability and close-to-complete surface regeneration after binding.

## 4. References

[1] M. S. Ünlü, and S. C. Strite, "Resonant Cavity Enhanced Photonic Devices," *J. Appl. Phys.*, Vol. 78, No. 2, , pp.607 – 639, (1995)

[2] A. K. Swan, L. Moiseev, C. R. Cantor, B. J. Davis, S. B. Ippolito, W. C. Karl, B. B. Goldberg, and M. S. Ünlü, "Towards nanoscale optical resolution in fluorescence microscopy," *IEEE J. Select. Topics Quantum Electron.*, Vol. 9, No. 2, pp. 294-300, (2003)

[3] L. Moiseev, M. S. Ünlü, A. K. Swan, B. B. Goldberg, and C. R. Cantor, "DNA Conformation on Surfaces Measured by Fluorescence Self-Interference," *Proceedings of the National Academy of Science*, Vol. 103, pp. 2623-2628, (2006)

[4] D. Bergstein, M. F. Ruane, and M. S. Ünlü, "Silicon Substrates with Buried Distributed Bragg Reflectors for Biosensing," *Int'l.Semiconductor Dev.Res. Symp.* 2005, 7-9 December 2005.

[5] M. K. Emsley, O. I. Dosunmu, and M. S. Ünlü, "Silicon Substrates with Buried Distributed Bragg Reflectors for Resonant Cavity-Enhanced Optoelectronics," *IEEE J. Select. Topics Quantum Electron.,* Vol. 8, pp. 948-955, (2002)

[6] A. Yalcin, K. C. Popat, J. C. Aldridge, T. A. Desai, J. Hryniewicz, N. Chbouki, B. E. Little, O. King, V. Van, S. Chu, D. Gill, M. F. Anthes-Washburn, M. S. Ünlü, and B. B. Goldberg, "Optical Sensing of Biomolecules Using Microring Resonators," *IEEE J. Select. Topics Quantum Electron.*, Vol. 12, No. 1, pp. 148-155, (2006)