MAR09-2008-020137

Abstract for an Invited Paper
for the MAR09 Meeting of
the American Physical Society

Single Molecule Detection in Living Biological Cells using Carbon Nanotube Optical Probes

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Nanoscale sensing elements offer promise for single molecule analyte detection in physically or biologically constrained environments. Molecular adsorption can be amplified via modulation of sharp singularities in the electronic density of states that arise from 1D quantum confinement [1]. Single-walled carbon nanotubes (SWNT), as single molecule optical sensors [2-3], offer unique advantages such as photostable near-infrared (n-IR) emission for prolonged detection through biological media, single-molecule sensitivity and, nearly orthogonal optical modes for signal transduction that can be used to identify distinct classes of analytes. Selective binding to the SWNT surface is difficult to engineer [4]. In this lecture, we will briefly review the immerging field of fluorescent diagnostics using band gap emission from SWNT. In recent work, we demonstrate that even a single pair of SWNT provides at least four optical modes that can be modulated to uniquely fingerprint chemical agents by the degree to which they alter either the emission band intensity or wavelength. We validate this identification method in vitro by demonstrating detection and identification of six genotoxic analytes, including chemotherapeutic drugs and reactive oxygen species (ROS), which are spectroscopically differentiated into four distinct classes. We also demonstrate single-molecule sensitivity in detecting hydrogen peroxide, one of the most common genotoxins and an important cellular signal. Finally, we employ our sensing and fingerprinting method of these analytes in real time within live 3T3 cells, demonstrating the first multiplexed optical detection from a nanoscale biosensor and the first label-free tool to optically discriminate between genotoxins. We will also discuss our recent efforts to fabricate biomedical sensors for real time detection of glucose and other important physiologically relevant analytes in-vivo. The response of embedded SWNT in a swellable hydrogel construct to osmotic pressure gradients will be discussed, as well as its potential as a unique transduction mechanism for a new class of implantable sensors.

[1] Saito, R., Dresselhaus, G. & Dresselhaus, M. S. *Physical Properties of Carbon Nanotubes* (Imperial College Press, London, 1998).

[2] Barone, P. W., Baik, S., Heller, D. A. & Strano, M. S. Near-Infrared Optical Sensors Based on Single-Walled Carbon Nanotubes. *Nature Materials* **4**, 86-92 (2005).

[3] Jeng, E. S., Moll, A. E., Roy, A. C., Gastala, J. B. & Strano, M. S. Detection of DNA hybridization using the near infrared band-gap fluorescence of single-walled carbon nanotubes. *Nano Letters* **6**, 371-375 (2006).

[4] Heller, D. A. et al. Optical detection of DNA conformational polymorphism on single-walled carbon nanotubes. *Science* **311**, 508-511 (2006).