11th International Conference
on Advanced Materials

Rio de Janeiro Brazil
September 20 - 25

ICAM2009

Single molecule biodetection and multi-modality in single walled carbon nanotube optical sensors

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Carbon nanotubes, like inorganic nanowires, are materials were electrons are confined to a single physical dimension, resulting in new and unusual properties. Our laboratory has been focused on understanding their chemistry and on engineering 1D materials for applications specifically in biodetection. Nanoscale sensing elements offer promise for single-molecule analyte detection in physically or biologically constrained environments. Single-walled carbon nanotubes (SWNT), as optical sensors, offer unique advantages such as photostable near-infrared (n-IR) emission for prolonged detection through biological media and single-molecule sensitivity. Two systems will be discussed in this presentation. In the first, we demonstrate detection of single molecule H_2O_2 signaling from Epidermal Growth Factor Receptor using fluorescent single-walled carbon nanotubes. An emerging concept in cell signaling is the natural role of reactive oxygen species, such as hydrogen peroxide (H_2O_2), as beneficial messengers in redox signaling pathways. Despite growing evidence, the nature of H_2O_2 signaling is confounded by the difficulty in tracking it in living systems both spatially and temporally at sub-nanomolar concentrations. In this work, we demonstrate a platform for selectively measuring the H_2O_2 efflux from living cells at the single molecule level. An array of near infrared fluorescent single walled carbon nanotubes is capable of recording the discrete, stochastic quenching events that occur as H2O2 molecules are emitted from individual A431 human epidermal carcinoma cells in response to epidermal growth factor (EGF). We show mathematically that such detection arrays have the unique property of distinguishing between molecules originating near the membrane from those with no memory of origination, or background. We find that EGF induces on average 0.04 nmol H_2O_2/min/active receptor over a period of 50 min after exposure to EGF. This platform promises a new approach to understanding reactive oxygen signaling at the cellular level. In the second system, we have recently documented that SWNT possess 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, but we have shown that even a pair of single-walled carbon nanotubes 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 of six genotoxic analytes and their chemical kinetics in NIH-3T3 cells, 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. An array of such sensors has allowed us to study a new signaling pathway of the Epidermal Growth Factor Receptor (EGFR) involving biocatalyzed H_2O_2 production on the membrane protein receptor itself in response to ligand binding. We show the detection of single molecule H2O2 at the membrane surface for the first time, and map the kinetics of the receptor in the bound and unbound state while on the live cell surface. The platform is promising for extending single molecule kinetic analysis to traditionally difficult biological systems.