Designing Electrochemical Sensors based on Ultrathin Biomolecular Films and Nano-materials

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Films of nanometer thickness combining DNA, enzymes, inactive polyions "glue", and catalytic redox polyions can provide active elements for a wide variety of electrochemical sensors. Such films can be prepared by layer-by-layer electrostatic assembly of alternately charged polyion materials on conventional electrodes such as carbon or gold. Miniaturization of sensors and arrays can be pursued by using easily processable nano-materials such as single walled carbon nanotubes (SWNT). In this paper, procedures for film assembly and attachment of biomolecular detection elements on conventional electrodes and on *SWNT forests* will be addressed. While these approaches are general for many sensing applications, examples of sensing chemical toxicity, oxidative stress, and chemical antigens will be presented.

Films designed to detect DNA damage can be used as the basis of promising sensors to screen the toxicity of chemicals and their metabolites, and to monitor oxidative stress. Films containing DNA and enzymes enable detection of structural damage to DNA from toxic chemicals as a basis for toxicity screening. These films bioactivate chemicals to their metabolites, which can then react with DNA, mimicking toxicity pathways in the human liver. Metallopolyions that catalyze DNA oxidation can be incorporated into DNA/enzyme films leading to "reagentless" sensors.

Sensors featuring the polymer $[Os(bpy)_2(PVP)_{10}Cl]^+$ [PVP=poly(vinylpyridine)] have been developed to selectively monitor DNA oxidation, and measure mainly 8-oxoguanosine. Such films may be applicable to determination of oxidized DNA as a clinical biomarker for oxidative stress. Detection limits of 3 oxidized guanines per 10,000 guanines in calf thymus DNA have been achieved. Inclusion of the analogous ruthenium metallopolymer in the sensor provides a monitor for oxidation of other nucleobases.

Single-walled carbon nanotubes (SWNTs) with ~1.4 nm diameters have the world's highest known specific conductivity per unit mass. We employ carbon nanotubes with functionalized ends standing on electrical contacts in 20-200 nm diameter bundles called *SWNT forests* prepared by room temperature solution processing. Our goal is to combine nanotube electrical transduction with specific molecular recognition of antibodies for proteins and bacteria. We currently focus on peroxidase-linked amperometric immunoassays, in which enzyme-catalyzed reduction of hydrogen peroxide provides electrical signals transmitted via the SWNT forests. In preliminary work, we bound anti-biotin antibodies to SWNT forests and achieved detection of biotin in the picomolar range. SWNTs sensors arranged in arrays should be applicable to detection of multiple antigens including proteins and pathogenic bacteria.