# Nanotubes and Nanowires as Chemical and Biological Sensors: Approaching the Single-molecule Limit

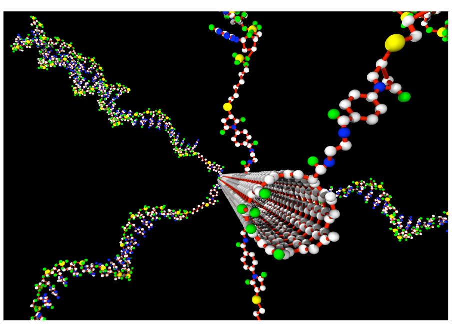
*NSF NIRT Grant* ***DMR-0210806***

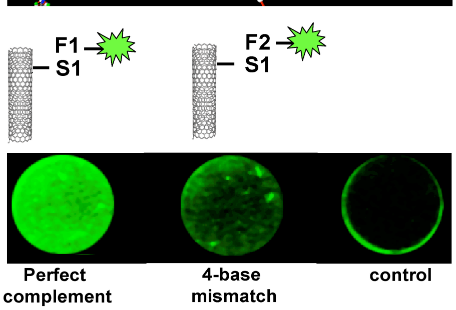
**PIs: Robert J. Hamers, Lloyd M. Smith, and Daniel van der Weide**
University of Wisconsin-Madison

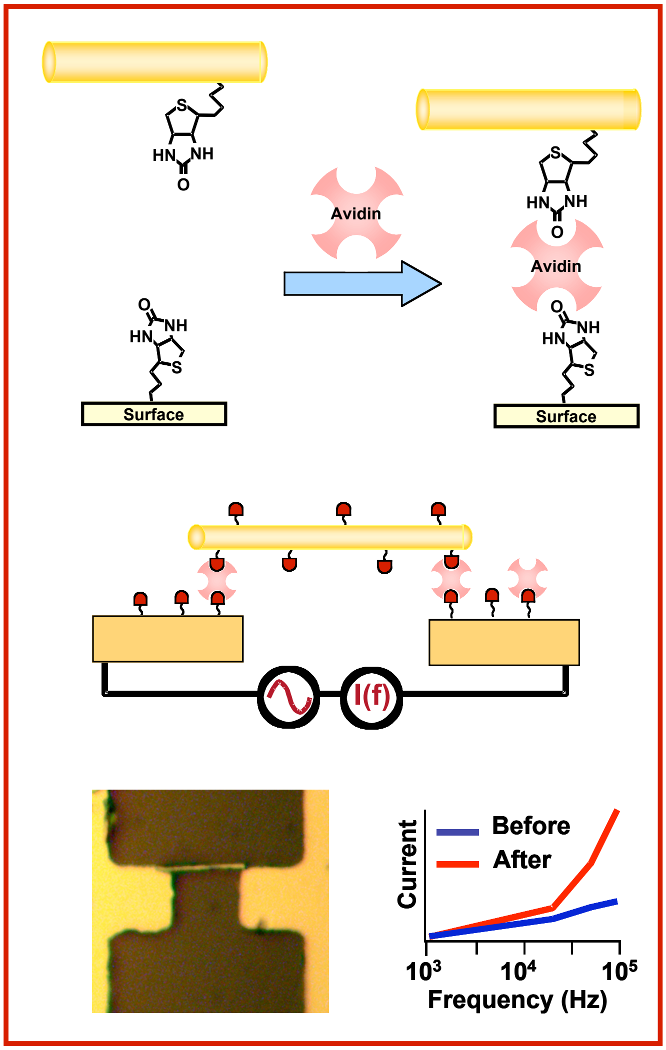
Nanotubes and nanowires have great potential as the basis for a new generation of chemical and biological sensors. Recent work from our group has shown the ability to directly detect biological binding processes (DNA hybridization and antibody-antigen interactions) via changes in the electrical impedance across biologically-modified interfaces.[2-4] Our NIRT grant is aimed at using these ideas and scaling them to nanometer dimensions to provide biological sensors that have the potential to detect biomolecules at the single-molecule level.

The use of nanowires/nanotubes as the basis for biosensors has three major elements: (1) Chemistry for biologically-modified nanostructures, (2) Assembly, and (3) Electrical characterization. Each of these elements is being addressed in our NIRT project. There are two fundamentally different approaches for fabrication of nanoscale sensors in a array geometry. In one approach, individual nanoscale elements are functionalized with biomolecules of interest, and then are assembled into a more complex structure. In a second approach, nanostructured objects are fabricated on a surface and are then individually functionalized. The first approach has the advantage that the individual sensing elements can be fabricated, purified, and tested before the assembly process; this convergent assembly process may be more reliable by distributing the complexity among several steps. The latter approach may provide more reproducible elecrical structures because the growth process can, in some cases (such as metal nanowires), be controlled quite precisely.

Practical sensors must be stable in a variety of environments. Because related work from our groups showed that carbon-based materials such as diamond are extremely stable in aqueous environments,[2-4] our initial work focused on leveraging these ideas to the fabrication and characterization of biologically-modified single-wall carbon nanotubes (BMSWNTs).[5-6] Our measurements show that BMSWNTs retain their biological selectivity, as evidenced by their ability to recognize and bind to complementary vs. non-complementary sequences. Additionally, the hybridization could be repeated many times, demonstrating that the covalent linkages retain the chemical stability needed for processing the nanowires into more comlex structures. These result is important because they demonstrate that the nanotubes have the two most important properties (1) A high degree of biological selectivity, and (2) A high degree of chemical stability, that are needed for incorporation as integral element of nanoscale sensing systems. Additionally, the biomolecular recognition capability can be used to guide the assembly of nanotubes/nanowires and can lead to new bioelectronic sensors.







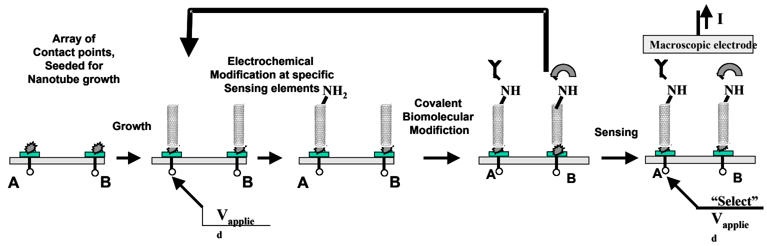

While there are many approaches to nanoscale sensing, one approach is to use biomolecular interactions to induce nanotubes/nanowires to link across a set of electrical contacts. For example, the protein avidin has four binding sites that can link to biotin. By creating biotin-modified surfaces and using biotin-modified nanowires, it is possible to use the biomolecule avidin as a kind of "molecular glue" to induce selective binding of nanowires to the surface. As an example, we have fabricated nanowires and modified them with biotin, producing a dilute solution of biotin-modified nanowires. Similarly, two gold contact pads separated by a distance of approximately 5 microns were modified with biotin. The biotin-modified wires have no significant affinity for the biotin-modified surface. However, if avidin is present, it acts as a molecular glue and links the nanowires *irreversibly* to the surface, while nanowires that are not bound via biomolecular interactions will easily wash away. The net consequence is that the biotin-avidin biological interaction causes the nanowires to form an electrically conductive bridge across the gap between the contact pads. The briding causes the AC conductance across the gap to increase significantly, as shown in the above graph.

This essentially represents a nanoscale bio-electronic switch in a which a small number of molecules create a large change in electrical properties. This is just one example of how nanoscale materials can be combined with electrical measurements and biological systems to yield new types of bioelectronic devices.

At the nanoscale, detection of electrical properties can easily become plagued by stray capacitance and leakage resistance. One method for avoiding this problem is to take advantage of the fact that interfaces often exhibit highly non-linear electrical properties. These non-linear properties can be used to perform novel types of frequency mixing and/or frequency doubling experiments.[7,8] For example, if sinusoidal modulations at two different frequencies $f_1$ and $f_2$ are applied to a non-linear element, then the current will contain components at $f_1$, $f_2$, $f_1 + f_2$, and $f_1 - f_2$

The new signals at $f_1+f_2$ and $f_1+f_2$, are produced only by the *non-linear* electrical components, and thereby localize the electrical response measurement to the interface of interest.[8]

Yet another appoach to the fabrication of nanoscale sensing systems is the use of electrically-addressable chemical modification. Since nanotubes and nanowires can be grown in specific locations using a combination of lithgraphic and growth processes, it is rather straightforward to produce an array of electrically-addressable nanoscale elements (nanotubes, nanowires). Electrochemical modification processes can then be used to selectively modify specific elements. This process can be repeatedto create a high-density array of distinct biomolecular recognition elements, each of which is electrically addressable.




The research carried out under this grant is highly interdisciplinary and benefits greatly from the cooperative interactions of students, postdocs, and faculty with strong backgrounds in surface chemistry, biochemisty, physics, and electrical engineering.

The use of biomolecular recognition, in combination with nanoscale elements and electrical detection, provides a a set of tools for the fabrication of a new generation of bioelectronic sensors that have the potential to achieve extremely high sensitivity. Many of the key factors controlling the assembly process are becoming controllable, suggesting that in the not-to-distant future it should be possible to achieve high-density biomolecular detection and perhaps even to use electrical signals to probe the response of individual molecules.

**References:**

[1] For further information about this project link to http://hamers.chem.wisc.edu/ or email **rjhamers@facstaff.wisc.edu**

[2] Wensha Yang, James E. Butler, Wei Cai, John Carlisle, Dieter Gruen, Tanya Knickerbocker, John N. Russell, Jr., Lloyd M. Smith, and Robert J. Hamers, "DNA-modified nanocrystalline diamond films as stable, biologically active substrates", Nature Materials, **1**, 253-257 (2002).

[3] Wei Cai, John Peck, Daniel van der Weide, and Robert J. Hamers, "Direct electrical detection of DNA Hybridization at DNA-modified silicon surfaces", Biosensors & Bioelectronics, in press (published on-line 12/03).

[4] Tami L. Lasseter, Wei Cai, and Robert J. Hamers, "Frequency-dependent Electrical Detection of Protein Binding Events", The Analyst, in press (published on-line 12/03).

[5] Sarah Baker, Wei Cai, Tami Lasseter, Kevin Weidkamp, and Robert J. Hamers, "Covalently-bonded adducts of DNA with single-walled carbon nanotubes: Synthesis and hybridization", Nano Letters, **2**, 1413-1417 (2002).

[6] Sarah E. Baker, Tami L. Lasseter, Lloyd M. Smith, and Robert J. Hamers, "Covalently-linked Adducts of Single-walled Nanotubes with Biomolecules: Synthesis, Hybridization, and Biologically-Directed Surface Assembly", Mat. Res. Soc. Sym. Proc., **737**, F4.6.1 (2003).

[7] J.R. Peck, R.J. Hamers, and D. Van der Weide, "Linear and Non-linear Measurements of Surface Protonation", Langmuir, submitted 12/03.

[8] Extending the Range for Electrochemical Impedance Spectroscopy Measurements using Radiofrequency Reflectometry", Review of Scientific Instruments, in preparation