Development, Functionalization and Assembly of Nanoscale Biological Sensors

NSF NIRT Grant ECS-0210332

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Detection of biomolecular substances is of critical importance in modern biological and medical sciences. Although the sensitivity and selectivity of modern detection methods have improved dramatically in recent years, the detection speed remains slow and the equipment cumbersome, limiting applications mostly to laboratory environments. There is an urgent need for biological sensors which are not only sensitive and selective but also fast and portable, suitable for in-field applications such as quick diagnostics in medical emergencies, ultra-light health and environmental monitoring, and bio-chemical sensing in battle fields. We are developing and optimizing two types of solid-state sensor units that may fulfill such functions: 1) Ultra-sensitive Hall gradiometers for magnetic detection; and 2) Nanobelt field effect transistors (FET) for electrochemical detection.

Hall gradiometers, based on the two-dimensional electron gas in semiconductor heterostructures, are a class of magnetic sensors with sensitivity approaching that of a micro-SQUID but with operational temperature and magnetic field range rivaling that of giant magnetoresistive devices. Recently, through systematic miniaturization and noise minimization, we have improved the sensitivity of GaAs/AlGaAs Hall gradiometers to the point of being able to measure the magnetic signal of a *single* 6-nm diameter Fe nanoparticle [1] at low temperatures. A representative measurement is shown in Figure 1. InAs Hall gradiometers promise similar sensitivity and room temperature operation, and are currently under active development. The surface of Hall gradiometers will be functionalized with specific biomolecules (e.g. ligand, single strand DNA etc.) for selective detection. The specific assembly of complementary biological molecules tagged with magnetic particles will be detected by measuring the dipole field from attached magnetic nanoparticles. Considering the sensitivity of our current Hall sensors, single molecule detection might be possible.

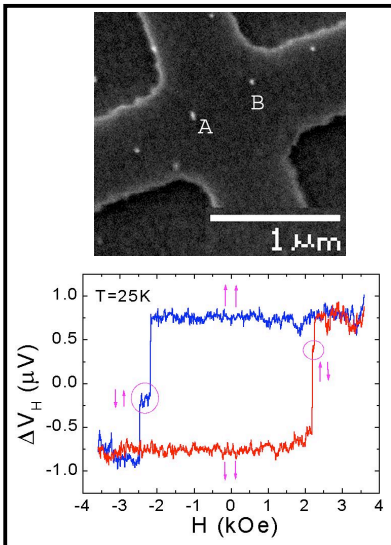

Figure 1 SEM micrograph of a Hall cross and iron nanoparticles grown on top; Hall signal clearly resolving the hysteresis of two individual iron nanoparticles.

The second sensor unit is a nanoscale FET. The FETs are based on a group of nanostructured semiconducting oxide materials including SnO_2, ZnO, In_2O_3, and CdO [2]. These nanoscale ribbon-like structures have widths of 30 - 300 nm, thicknesses of 10-30 nm, and lengths as long as millimeters, and they are termed "nanobelt" because of their unique geometry (Figure 2). Bulk materials of many of these oxides have shown good electrical sensitivity to the type and concentration of molecules adsorbed on their surface. The large surface to volume ratio of the nanobelts makes them ideal choices as nanoscale sensors with extraordinarily high sensitivity.

We have built FETs with nanobelt units and functionalized the nanobelts with specific receptor molecules. Biomarkers of interest (e.g., antibodies associated with cardiac arrest) have been attached to the complimentary ligand molecules. The functionalization of both the nanobelts and the biomarkers has been systematically verified with fluorescent observations. Electrical characterizations of the FETs are ongoing, and subsequently the detection of the assembly of functionalized biomarkers will be pursued via measurement of the change in the FET conductance.

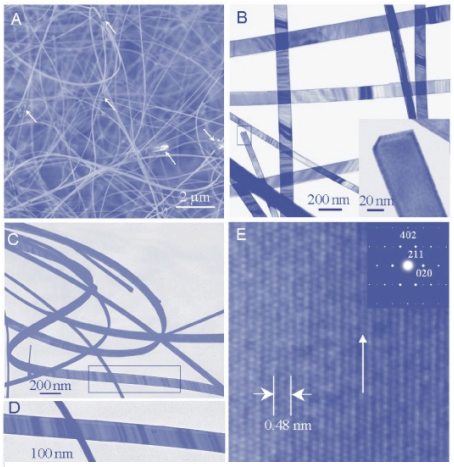

Figure 2 (A) SEM image of as-synthesized SnO_2 nanobelt; (B)-(D) TEM images; (E) high resolution TEM image of nanobelts

The small size of both of these sensors promises unprecedented sensitivity and portability for bio-detection. It also creates numerous exciting possibilities for integrated biosensing applications and sophisticated nano-assembly schemes. For example, each device in an array of Hall gradiometers and nanobelt FETs on the same chip can be decorated with different biomolecular units, which allows the integration of multiple biosensors on a single chip (integrated biochip), and multiple nano-FET's can be assembled onto specific locations on a substrate or in a circuit via surface-templated nano-assembly [3]. A major challenge in achieving these goals is controlled functionalization of the sensors down to nanoscale with biological substances. The main technique we use for such nanoscale functionalization is dip pen nanolithography (DPN) [4]. DPN is capable of general molecular patterning down to 15nm. More importantly, DPN is a direct deposition method with high spatial registry precision. It can : 1) directly functionalize solid device surfaces without any complicated processing steps; 2) selectively functionalize devices with high spatial resolution (as illustrated in Figure 3).

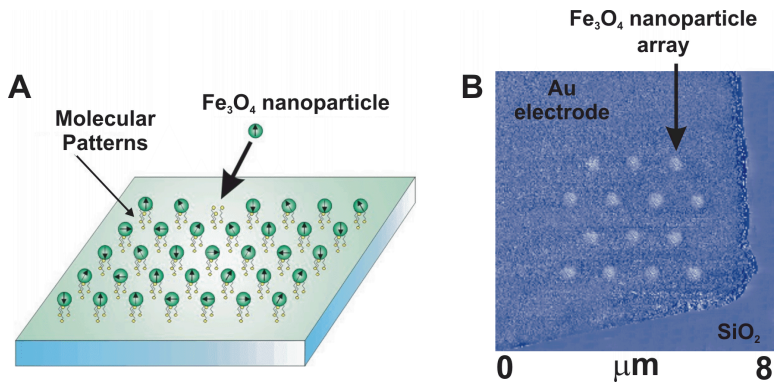

Figure 3 (A) Schematic diagram depicting nanoparticle assembly process on molecular patterns on solid surface; (B) Fe_3O_4 magnetic nanoparticle assembly onto DPN-generated molecular patterns on microfabricated electrode surfaces.

References:

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