Nanowire Nanoelectronics: Building Interfaces with Tissue and Cells at the Natural Scale of Biology

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Central to the bottom-up assembly of functional devices is the tailoring of the optical, electrical, geometrical and chemical composition properties of the assembled nanomaterials, such as nanocrystals and nanowires. A new class of molecular-scale electronic interfaces can be formed with cells and tissue using chemically-synthesized semiconductor nanowires (NWs) as functional elements. These NWs have received intense interest in recent years, leading to the development of structures with rationally controlled geometry, composition, and electronic properties (1-3). These characteristics have enabled semiconductor NWs to emerge as powerful building blocks for the bottom-up assembly of functional devices with applications areas from nanoelectronics, (4-7) to the biosciences (8-11). Most importantly, the interface between nanoscale electronic devices and biological systems enables interactions at length-scales natural to biology, and thus should maximize communication between these two diverse yet complementary systems. Moreover, nanostructures and nanostructured substrates show enhanced coupling to artificial membranes, cells, and tissue. Such nano-bio interfaces offer better sensitivity and spatial resolution as compared to conventional planar structures.

In the last few years I have pioneered a flexible approach to synthesize and interface highly-sensitive NW field-effect transistors (NWFETs) with tissue and cells, and demonstrated this approach for silicon NWFET arrays coupled to (a) embryonic chicken hearts and (b) cardiomyocytes. First, I developed a new flexible device layout by incorporating the SiNWs on a thin plastic substrates and fabricating arrays of devices to monitor signal propagation on the surface of embryonic chicken heart (12). Second, I developed an entirely novel technique that involved culturing cells on thin polymer sheets such as polydimethylsiloxane (PDMS) that can easily be interfaced with the device arrays (13, 14). Third, I developed a new synthetic method that combines the vapor-liquid-solid (VLS) and vapor-solid-solid (VSS) NW growth mechanisms to produce synthetically-encoded NW devices with ultrasharp (<5 nm) highly doped n-type (n⁺⁺)/intrinsic dopant transitions along the NW growth direction. Using this method, I synthesized short-channel n⁺⁺/intrinsic/n⁺⁺ NW FET devices with independently controllable diameters and channel lengths and further demonstrated the smallest device ever to be interfaced with electroactive cells, a device as small as a few protein molecules across (15). Taken together, these techniques have enabled investigation of cell-device interfaces at multiple length scales, from whole embryonic heart down to the subcellular regime, and open up unique and complementary measurements.

Initially, I explored the millimeter length scale regime (12), using whole embryonic heart. In this project, I characterized the electrical properties of NWFET arrays interfaced with spontaneously-beating embryonic chicken hearts. I was able to facilitate for the first time electrical recordings from NWFET devices synchronized with the beating heart with NW signal amplitude directly related to the device transconductance. Multiplexed measurements made from NWFET arrays show that signal propagation across the myocardium can be mapped, with a potential resolution significantly better than microelectrode techniques. Most importantly, I exploited the unique capability of the bottom-up approach to fabricate NWFET arrays on flexible and transparent plastic substrates, and demonstrated that these novel device arrays enable multiplexed signal recording in a number of 3D conformations as well as registration of the devices to the heart surface by back-side viewing using an optical microscope.
Furthermore, I have taken this work to a new level of complexity by interfacing nanodevices with cells (13, 14). Culturing cells directly on the devices substrate hinders manipulation of the cells, hence significantly limiting the investigation of their electrical activity. I developed a novel and flexible approach to interface NWFETs with cells. Embryonic chicken cardiomyocytes were cultured on thin, optically-transparent PDMS sheets and then brought into contact with Silicon NWFET arrays fabricated on standard substrates under precise three-dimensional control within an optical microscope with manipulator. NWFET conductance signals recorded from cardiomyocytes exhibited excellent signal-to-noise (as high as 25), with signal amplitudes that can be tuned by varying device sensitivity. Significantly, I showed that signals recorded as a function of increasing/decreasing pressure, by displacing the PDMS/cell support, exhibited a reversible >2x increase in signal. I demonstrated that multiplexed recording of signals from registered device elements within NWFET arrays interfaced to cardiomyocyte monolayers enabled temporal shifts and signal propagation that could be determined with excellent spatial and temporal resolution, allowing me to illuminate ‘resistive’ vs. ‘conductive’ junctions to signal propagation between cells. Our modular approach simplifies the process of interfacing cardiomyocytes and other cells to high-performance NWFETs, thus increasing the experimental versatility of NWFET arrays and enabling device registration at the subcellular level.
Next, I performed the first electrical measurements in the subcellular regime with “point-like” synthetically-encoded SiNW devices (15). I developed a new synthetic method that combines the vapor-liquid-solid (VLS) and vapor-solid-solid (VSS) NW growth mechanisms to produce synthetically-encoded ultrasharp short channel devices. When interfaced with spontaneously beating cardiomyocytes, devices with channel lengths of 50, 80, and 130 nm exhibit well-defined extracellular signals with excellent signal-to-noise. Significantly, these “point-like” devices yield signals on a time scale of ~500 μs, comparable to the reported time constant for sodium ion channels. We synthesized multiple FET devices on a single SiNW, allowing a device separation smaller than 2 μm and measured time lag of 2.5-7.5 μs. These short-channel NW FET devices provide a new opportunity to create nanoscale biomolecular sensors that operate on length and time scales previously inaccessible by any...
other techniques but necessary to investigate fundamental, sub-cellular biological processes, and will create powerful new tools for fundamental studies of cardiac biophysics, real-time drug assays, and development of novel applications such as prosthetic interfaces.

Figure 3. Synthetically-encoded short-channel nanowire transistors for fast point-like cellular signal detection. A. (A) Illustration of Au nanoparticle catalyzed Si nanowires with well controlled axial dopant profiles using a VSS growth mechanism. Initial step is synthesis of a highly doped n-type source (S) electrode (n++) via the VLS method. Subsequently, either lightly doped (n) or intrinsic (i) active device regions are encoded by VSS mechanism. The last step is another VLS synthesized highly doped (n++) drain electrode (D). (B) Short-channel n++/i/n++ SiNWs with channel lengths of 150 nm (I), 80 nm (II), and 50 nm (III) using growth times of 160 min, 80 min, and 40 min, respectively, at a VSS growth temperature of 340 °C. Scale bars are 150 nm. Note that the Au catalysts were ~80 nm in diameter and NWs were selectively etched to reveal the active channel. (C) Conductance of NW devices as a function of water-gate potential for channel lengths of 150 nm (I; blue), 80 nm (II; green), and 50 nm (III; red). Black trace is a control device fabricated on an n++ segment without an active channel. (D) Typical recorded signals from cardiomyocytes for devices presented in panel A. The n++ control (Black trace) was recorded simultaneously with II. Note that for case III, a 40 nm diameter NW was used whereas all other devices were 80 nm in diameter. For cases I and II, devices were interfaced with cells at \( V_g = 0 \) V, and sensitivities were 13.5 nS/mV and 21 nS/mV respectively. For case III, the device was interfaced with cells at \( V_g = +0.3 \) V, and its sensitivity was 6.4 nS/mV. The control device was interfaced at \( V_g = 0.3 \) V with sensitivity of 0.3 nS/mV.

Last, my results have been recognized by other scientists both within my research group and in the broader scientific community. For example, I used my acquired experience and hands-on expertise to collaborate with other researchers in the group to design and explore novel interfaces between cells and nanostructures (16-18). This work has also been recognized by a Materials Research Society (MRS) Gold Graduate Student Award and the third place award in the prestigious Collegiate Inventors Competition.
References


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