# Digital Biosensing of Influenza Virus with Single Serpentine Si Nanowire Field Effect Transistor

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Nanowire field effect transistor (NW FET) biosensors have shown strong potential for sensitive detection of biomolecules. However, its accuracy is limited by the non-specific analog signals from non-specific binding, variation of ionic strength and pH of sample solutions, *etc*. The down-scaling of nanowire size also leads to higher noise level. To overcome these limitations, here we show a digital detection methodology based on single molecule counting, i.e. electronically detecting/counting individual binding events of a single analyte over time. In this way, the target binding frequency instead of NW signal magnitude is used to determine analyte concentrations.

Previously, single virus detection has been demonstrated with CVD SiNW [1], but the straight NW requires high probe density ($>10^{12}/cm^2$) that is difficult to achieve. In addition, the CVD NWs are incompatible with CMOS processes for system integration. Straight NW also suffers from the higher noise level with the downscaling of NW size. In our digital virus biosensing process, we use a NW with a novel serpentine shape in a configuration of Si on insulator FETs, leading to better binding dynamics, lower noise, as well as maintaining single virus sensitivity. The SiNW was defined by e-beam lithography followed by plasma etch. We "folded" a 2 μm long 16 nm wide nanowire similar to [1] into the 5-fold serpentine morphology (Figure 1a) with 50 nm pitch in a small footprint (0.6 × 0.2 μm) enabling high device density. Figure 1b shows a straight NW with 200 nm in length for comparison. 10 nm gate dielectric was formed via atomic layer deposition of $Al_2O_3$. Figure 2a shows the characteristics of both types of NWFETs. The longer serpentine NW exhibited 0.4V increase of threshold voltage from the straight, but benefited from lower noise shown in Figure 2b. The device surface was modified with anti-influenza A hemagglutinin antibody, utilizing monolayer of trimethoxysilyl alkyl aldehyde as the linker, and followed by passivation with bovine serum albumin. With the antibody density of $0.6\sim1\times10^{11}/cm^2$, it is estimated that straight NW had only few antibodies on the surface to bind the virus. Also due to the binding signal similar to the noise level, we did not observe any binding events for the straight NW devices. For the serpentine NW, the antibody count increased by one order (>50 per NW), and since a virus of 80-120 nm might bind to multiple segments of the NW, the binding affinity was greatly enhanced. In Figure 3a, the serpentine sensor shows negative pulses of 10~15 mV, expected from the binding of negatively charged virus molecules in a solution of 10 μM KOH with pH 8.2. Increasing pulse frequency and width was observed for higher viral concentrations. Figure 3b summarizes the monotonic correlation between binding frequency and viral concentration, demonstrating the concept of digital biosensing that is immune to signal baseline shifts and noise due to non-specific solution interference.

[1] F. Patolsky et al., PNAS **101** (2004).

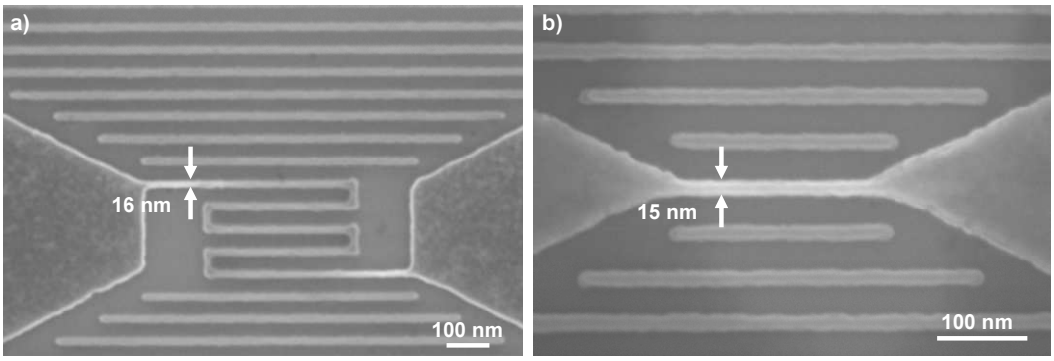


*Figure 1: Electron Micrographs of Serpentine (a) and Straight (b) Si Nanowire:* The linewidths of both nanowires are around 15 nm, and the length is 200 nm for the straight nanowire and 1.96 μm for the 5-fold serpentine nanowire.

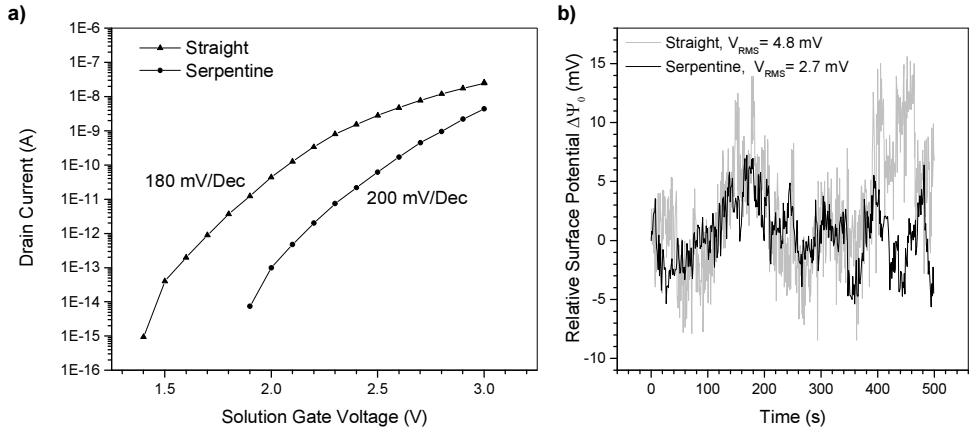


*Figure 2: Transfer Characteristics (a) and RMS Noise (b) of Serpentine and Straight Si NWFETs.* The devices were biased by a Ag/AgCl electrode in DI water saturated with air.

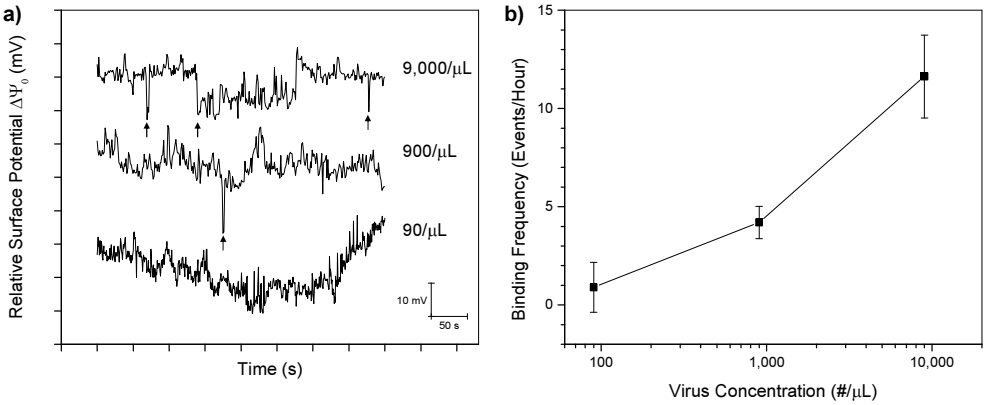


*Figure 3: Influenza Virus Sensing Results of the Serpentine Nanowire FET Modified with Anti-Influenza A Hemagglutinin Antibody:* (a) Exemplary raw sensor output at three different viral concentrations; (b) Plot of the binding frequency vs the viral concentration, showing a monotonic relationship.