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Real-time detection of biomolecules on surfaces

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MOTIVATION

Detection of biomolecules and real-time observation of binding kinetics are common issues of fundamental areas of health-care and life sciences, ranging from early detection of diseases, environmental monitoring, personalized medicine, and drug screening.
Kinetics and affinity information of a large number of biomolecular interactions can be achieved by real-time measurements of the binding processes performed on the basis of affinity based sensors.
Among other techniques, field-effect-based sensors such as Silicon Nanowires (SiNWs) are promising candidates to become general platforms for ultrasensitive label-free and real-time detection of biomolecular interactions on surface [1].

SiNWs SENSORS

A SiNW molecular sensor operates as a highly sensitive nanoscale field-effect transistor (FET) in which the gate terminal is removed and the channel exposed to the biochemical species. The nanometric size of the sensing area makes these sensors the ideal means to probe charged biomolecules that are comparable in size, such as proteins, nucleic acids, cells, viruses.
The SiNWs are fabricated on Silicon-On-Insulator (SOI) wafers and defined by means of standard top-down CMOS compatible processes, such as Deep Ultraviolet (DUV) photolithography, e-beam lithography and Reactive Ion Etching (RIE) [2].

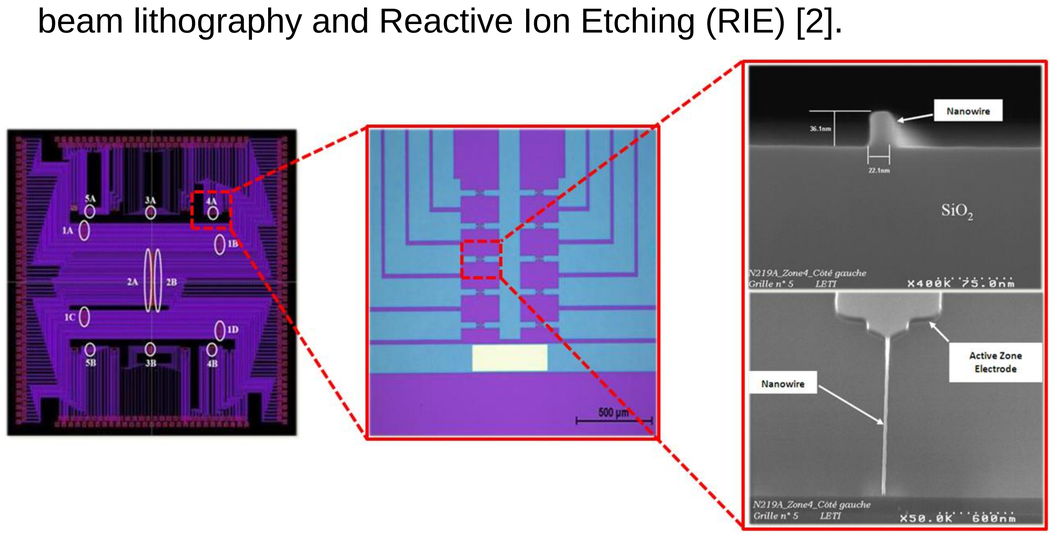
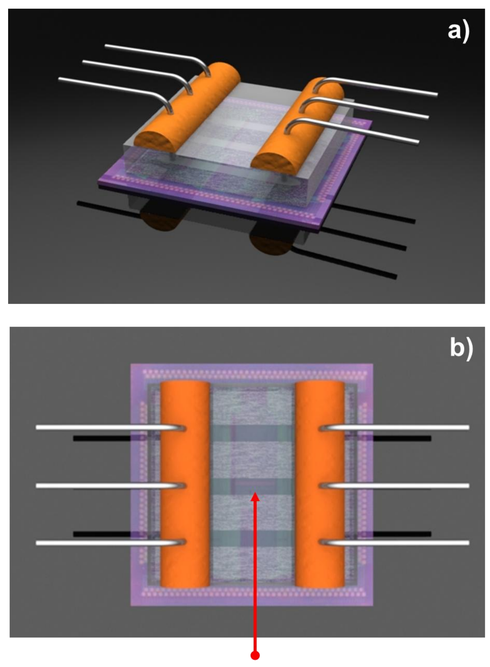


Fig. 1. Optical and SEM pictures of SiNW sensor devices. SEM pictures courtesy of CEA-LETI (Grenoble, France)

MICROFLUIDICS SETUP

The developed microfluidic setup allows reduced solvents and reagents consumption, portability and ease of integration with the SiNWs chip.
The microchannels are realized with a chemical resistant double-coated tape, patterned by laser micromachining. The height of the channels are defined by the thickness of the tape (190 µm). A PMMA cap is placed to seal the channels and the inlets and outlets tubes inserted. A sealing polymer is used to avoid fluid leakages from the inlets/outlets.



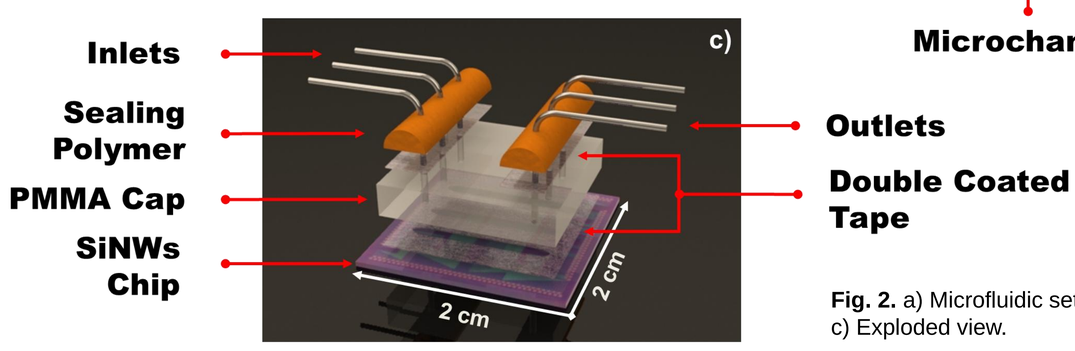
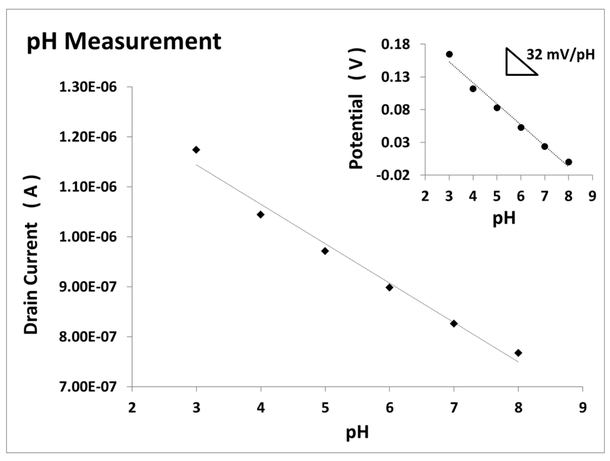


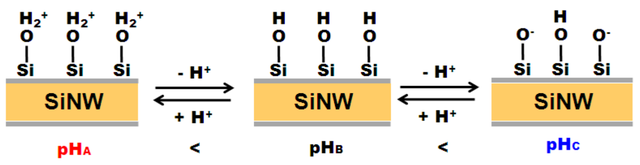
Fig. 2. a) Microfluidic setup. b) Top view; c) Exploded view.

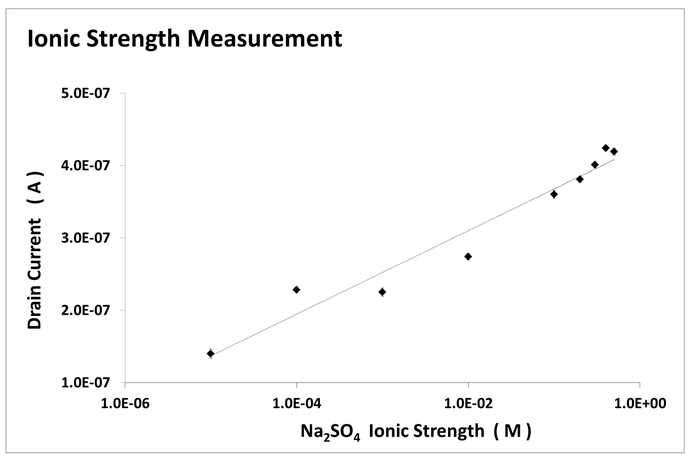
REAL-TIME MEASUREMENT

The SiNWs are sensitive to changes in the charge distribution in the nearby of the exposed channel, resulting in a modulation of its surface potential and conductivity, thus providing electrical transduction [3].

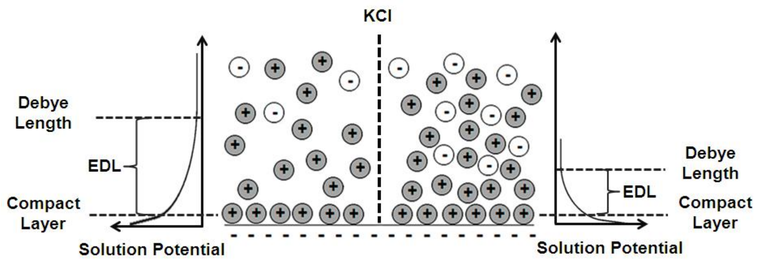


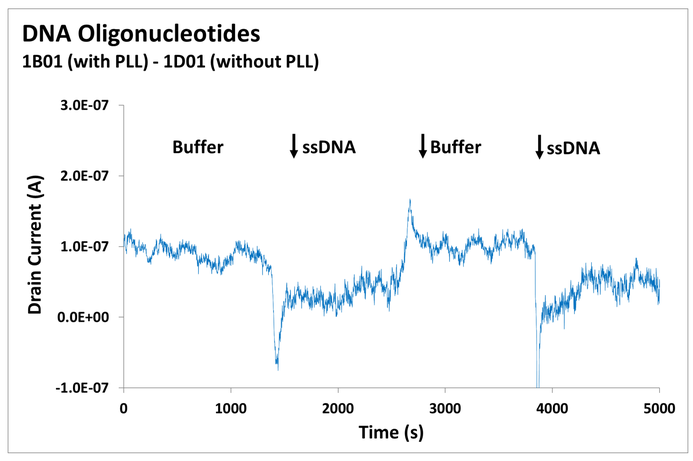
When the electrolyte solutions have pH values greater than the isoelectric point of the silica (pI~2-3), its surface becomes negatively charged due to the deprotonation of the silanol groups.
Keeping fixed the ionic strength of the solution, the increase of the pH leads to a decrease in the conductance of an n-type SiNW.
The different pH solutions were made from 10 mM phosphate buffers with 100 mM KCl.



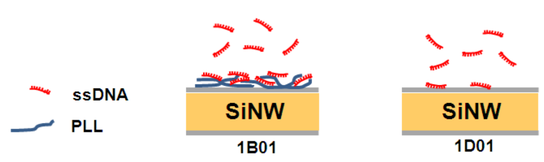


The charged surface attracts a layer of counter-ions next to the silica surface to maintain the overall charge neutrality, forming an Electrical Double Layer (EDL).
Keeping constant the pH, the ionic strength of the solution affects the distribution of ions close to the SiNWs channel, thus affecting its surface potential.





Differential response obtained by subtracting the signals of two SiNWs (1B01 and 1D01) with identical nominal dimensions. Positively charged Poly-L-Lysine (PLL) was spotted and adsorbed on 1B01.
A buffer solution (10 µM KCl) and a solution of negatively charged ssDNA (1 µM in 10 µM KCl) were alternatively injected into the microchannel.
The PLL electrostatically attracts the ssDNA, leading to an accumulation of negative charges close to the 1B01 exposed surface and to a decrease of the drain current.



References

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