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Sensors and Actuators B: Chemical

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Highly sensitive pH measurements using a transistor composed of a large array of parallel silicon nanowires

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ARTICLE INFO

Article history:

Received 28 November 2011

Received in revised form 19 January 2012

Accepted 20 January 2012

Available online xxx

Keywords:

Silicon nanowire

FET

Nanosensors

Biosensing

ABSTRACT

Silicon nanowire field-effect transistors (SiNW FETs) have emerged as good candidates for ultra-sensitive electrical detection of biological species, presenting a label-free alternative to colorimetry and fluorescence techniques. Here, a top-down approach has been used to fabricate the SiNW FETs using silicon-on-insulator (SOI) substrates. As in previous work, a change of the transistor conductance according to the pH of the solution is observed on a large pH interval [3–10.5], even for small variations of 0.1 pH units. The influence of several physico-chemical parameters such as gate voltage and buffer salinity, usually not adequately taken into account in previous papers, is discussed to achieve a better understanding of the detection phenomena.

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1. Introduction

The interest for nanosystems resulting from the combination of solid-state nanotechnology and biology has been rapidly increasing in recent years. This alliance opens new perspectives, particularly in the field of chemical and biological sensing. Some interesting devices for this application are transistors based on one-dimensional nanostructures such as silicon nanowires (SiNWs). In contrast with standard fluorescence techniques, field-effect devices can achieve direct and label-free electrical readout of the presence or absence of a molecule. They also have a high potential for integration into miniaturized systems. Moreover, the use of nanowires instead of planar channels in field-effect devices is expected to enhance sensitivity, due to their high surface/volume ratio [1].

A standard field-effect transistor (FET) consists of three terminals: the source, drain, and gate. The current flow between the source and drain is controlled by the voltage applied to the gate electrode. In 1972, Bergveld introduced the first **ion sensitive field-effect transistor** and showed that the FET channel conductance can be modulated by the change of charge at the silicon-solution interface, in the case of a pH detection [2]. In continuity with this work, several groups reported the monitoring of biological

reactions by modifying the gate terminal with molecular receptors or ion-selective membranes for the analyte of interest (e.g. penicillin [3], DNA [4]).

More recently similar experiments with devices based on SiNWs were reported. After demonstrating a pH detection [5], a wide range of biological entities (proteins [6], virus [7], nucleic acids [8]) were monitored with extremely low detection limits. The transistors in these articles were based on one single silicon nanowire, fabricated by a “bottom-up” approach [9]. Indeed, the device fabrication consisted of a sequence of steps that began with nanowire synthesis by **chemical vapour deposition** (CVD) growth. The nanowires were then harvested and dispersed in ethanol. A drop of this nanowire solution was further deposited on the substrate, followed by the definition of metallic contacts by optical or e-beam lithography. Due to the use of randomly positioned nanowires, this process leads to the fabrication of a limited number of functional devices. This highlights the severe integration issues which hinder widespread application in commercial products. To overcome this problem, an alternative way has been proposed, called the “top-down” approach [10], which consists in patterning and etching nanowires in a silicon layer, using micro and nanolithography techniques, the latter benefiting from the batch manufacturing capabilities of planar microelectronics. Indeed, this approach allows the fabrication of SiNWs on a large area with high density and uniformity. Therefore, we have focused our efforts on the **realization** and characterization of SiNW-based transistors using this approach

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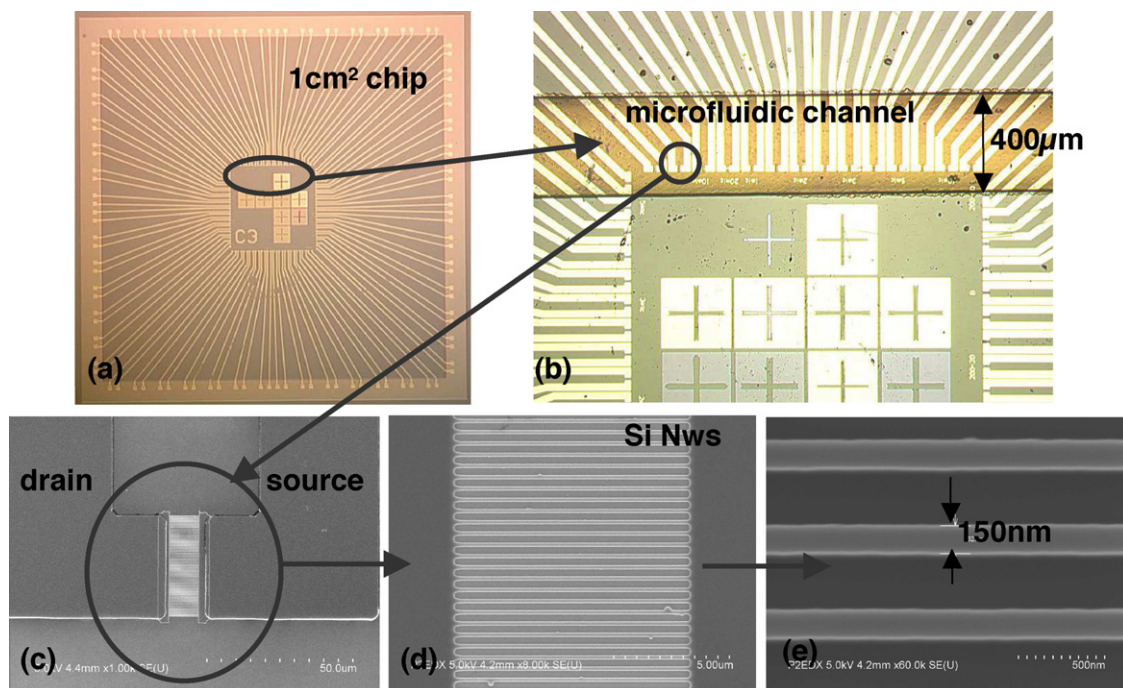


Fig. 1. Overall and detailed views of the top-down fabricated device, with microfluidics and close-ups of the SiNWs. (a) Overall view of the fabricated chip containing 56 transistors. The transistor position is highlighted by the circle. The drain and sources electrode leads spread to the borders of the chip in order to contact the transistors in an easier way. (b) Microfluidic channel integrated on the chip. The PDMS channel is positioned on a series of 14 transistors and has been fixed after exposition to an O₂ plasma. (c) SiNW-based transistor. As shown by this enlarged view, the transistors are composed of quite a few SiNWs. (d) SiNWs fabricated in parallel (transistor channel). (e) detail of SiNWs section. The SiNWs width is 150 nm.

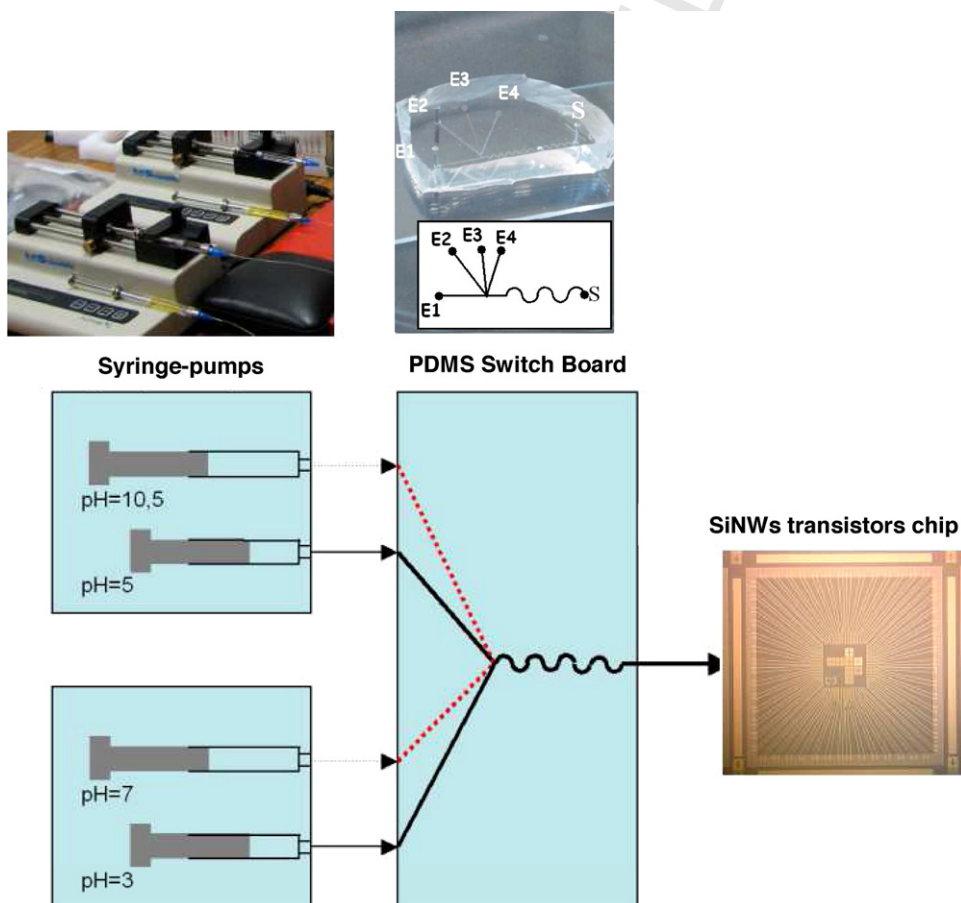


Fig. 2. The experimental set-up for pH testings, using four different pH values. The PDMS switch board with its four entries (E1, E2, E3 and E4) allows a 4-way selection of different chemical solutions at a constant flow rate and solution mixing.

which appears to be more suitable for an industrial application. We have chosen to fabricate a large number of parallel nanowires in order to improve the potential for sensing a larger part of all the bio-molecules in the solutions (by enhancing the sensitive surfaces). Moreover, if a defect appears during fabrication in one or a few nanowires, this will have a small impact on the transistor response.

Although the monitoring of several biological interactions has been previously reported [5–8], the optimal working conditions of the sensor are far from being clearly identified. In this paper, we present an in-depth study of the main parameters which have to be taken into account and to be tested before monitoring a biological reaction, in order to achieve suitable results. We consider the case of a pH level detection and study the performance of SiNW-based sensors, particularly the stability and reproducibility of the measurements over a large pH interval. Moreover, the influence of the choice of the gate voltage and of the ionic strength of the solution are investigated.

2. Sample preparation and experimental set-up

2.1. Sample preparation

The SiNW-based sensors were fabricated using silicon-on-insulator (SOI) substrates (6 μ m purchased from SOITEC, France). The SOI wafers had a 100 nm-thick silicon layer on a 200 nm-thick buried oxide layer. They were uniformly doped by ion implantation with boron, to a concentration of 10^{18} cm $^{-3}$. Ion implantation was followed by activation at 900 °C in a N $_2$ atmosphere for 1 h. The SiNWs were defined using e-beam lithography and reactive ion etching (RIE). Next the source and drain electrodes were patterned using optical lithography. A 150 nm-thick layer of aluminium was then deposited by electron gun evaporation before the photoresist lift-off. Finally, to eliminate any possible interference from the electronic leads during sensor tests, the areas outside the SiNWs regions were covered with a 30 nm-thick SiO $_2$ layer. For this purpose, a photoresist mask was defined over the nanowire regions and lifted-off after the deposition of silicon oxide.

We have designed and fabricated 1 cm 2 chips containing 56 transistors (Fig. 1). The transistor channel was composed of 70 parallel nanowires, 150 nm wide, 100 nm high and 10 μ m long. This top-down nanofabrication process allowed us to fabricate an array of perfectly aligned nanowires, through a reproducible process, which is completely suitable for industrial applications.

2.2. Experimental set-up

Electrical device characterizations were performed using two Keithley 2636 source meters. All the measurements were done at room temperature. A 400 μ m-wide microfluidic channel was fabricated using PDMS on an SU8 mold and bonded on the chip (Fig. 1). A microfluidic switch board, also made of PDMS was placed upstream, allowing a 4-way selection of different chemical solutions at a constant flow rate (Fig. 2).

The flow in the fluidic system could be controlled using peristaltic pumps or syringe-pumps. Indeed, we have performed measurements using successively each of these devices (Fig. 3). We observe that the flow fluctuation strongly affects the transistor conductance in the case of the peristaltic pump (Fig. 3a). A few works have quantified the impact of fluidic and ionic transport on the conductance level of silicon nanowire sensors configured as field effect transistors. Considering the work of Kim et al. [11], we suggest that the flow velocity sensing is a consequence of the variation of the streaming potential as

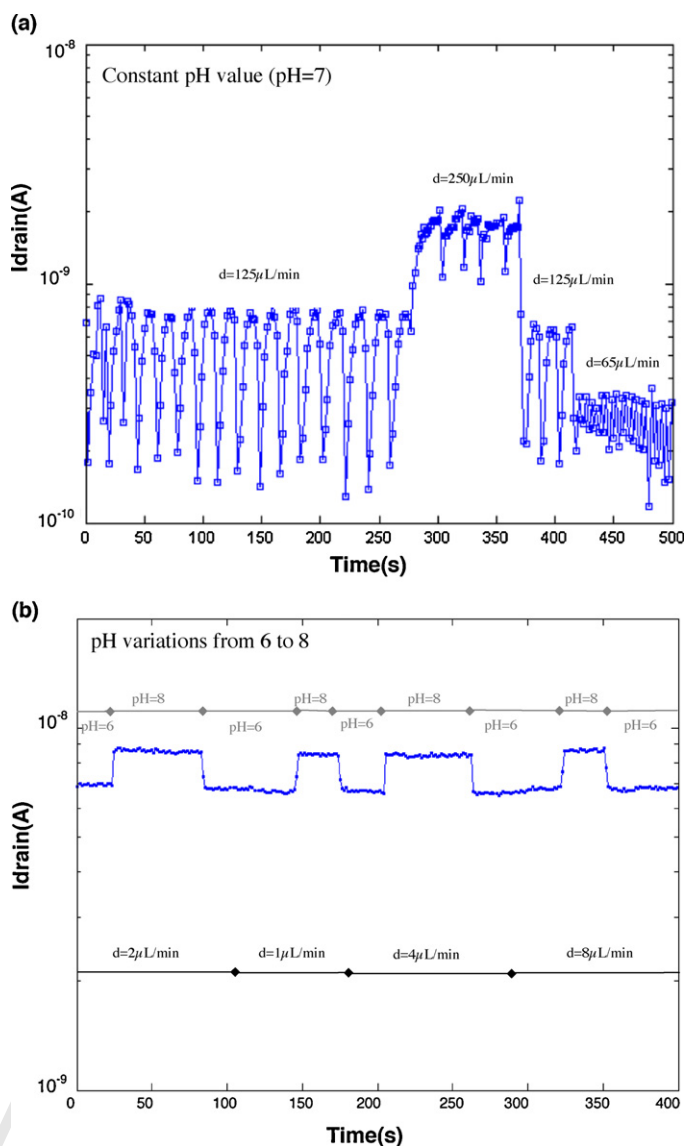


Fig. 3. Comparison of the stability of pH measurements using two different flow injection systems: (a) Using peristaltic pumps, drain current I_d varies with the flow rate at a constant pH value (pH 7). (b) Using syringe-pumps, the flow has no effect on the drain current level, even after pH variations from 6 to 8 and 8 to 6.

a function of the flow velocity. This streaming potential [12] is generated by the movement of counterions inside the electrical double layer (EDL) of the silica substrate. By changing the surface potential, the streaming potential acts in the same way as the charged analytes and affects the conductance of the transistor.

To minimize this effect, we have used syringe pumps. These latter have the advantage of providing lower flow rates and because of their working principle they generate less flow fluctuations than peristaltic pumps. Indeed the results obtained with the syringe pumps (Fig. 3b) exhibit a very stable signal for a constant pH. This figure also demonstrates that the level of current remains the same for different flow velocities, even after a pH variation from 6 to 8, and then from 8 to 6.

Considering these results, we have decided to use syringe pumps in our following experiments in order to sidestep the effect of the flow on the SiNWs response.

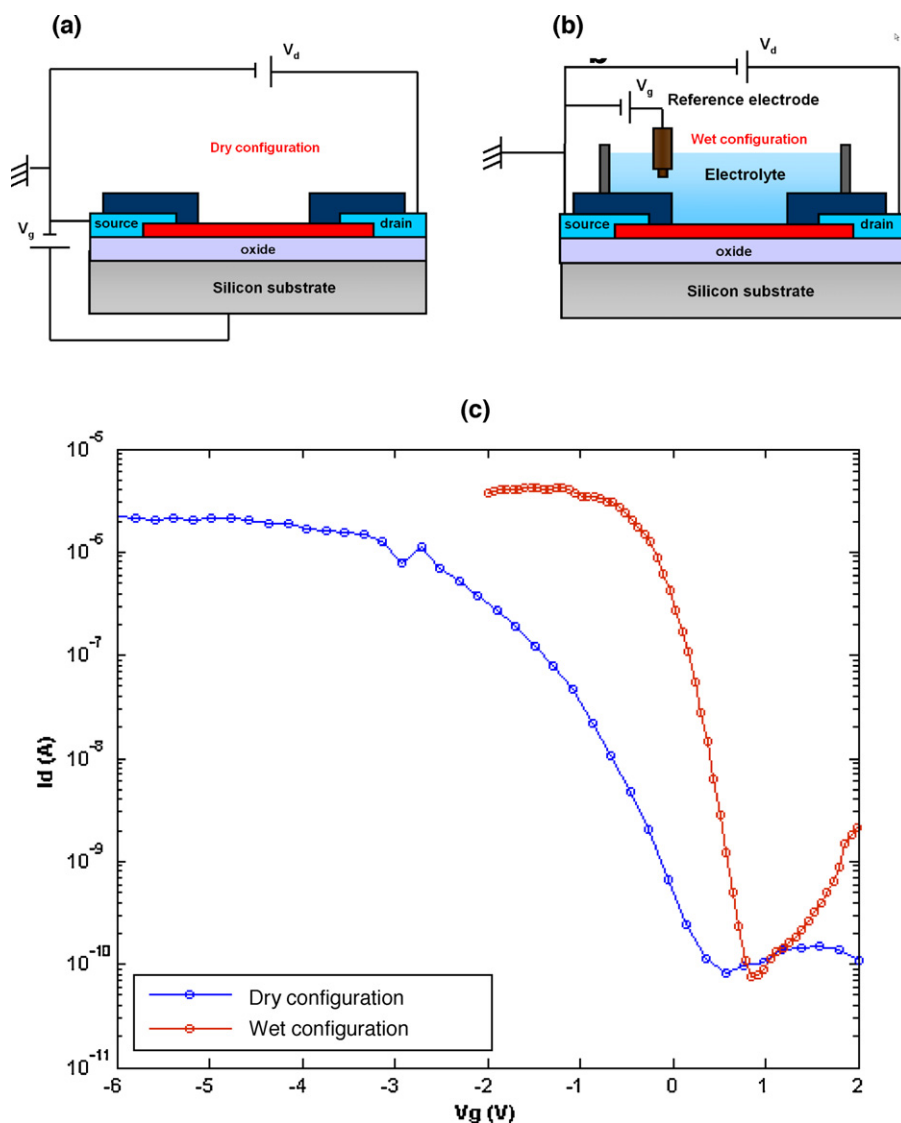


Fig. 4. Comparison of the transistor transfer characteristics for two different gate configurations (the characterized transistor has 70, 150 nm-wide, SiNWs). (a) SiNW-based transistor in the “dry configuration”. In this case the gate is the substrate (back-gate). (b) SiNW-based transistor in the “wet configuration”. In this case the gate voltage is applied to the electrolyte through a reference electrode. This configuration can be assimilated to a top-gate configuration. (c) Transistor characterizations $I_d(V_g)$ using the two configurations, for $V_d = 1$ V.

3. Results and discussion

3.1. pH measurements

Preliminary measurements were performed using an Ag/AgCl reference electrode with a 20 mM phosphate buffer solution (pH 7.4) as the electrolyte. The first characteristic that we evaluated was the change of the transistor sub-threshold slope using a SiNW-based transistor before (“dry configuration”) and after soaking it into water (“wet configuration”), using respectively the back-gate configuration (the substrate as the gate) or the reference electrode (see Fig. 4). The results show that the sub-threshold slope is around 4 times larger in the wet configuration compared with the dry configuration. The expression of the sub-threshold slope for the dry configuration is:

$$S = \frac{kT}{q} \ln(10) \left(1 + \frac{C_d + C_{it}}{C_{ox}} \right)$$

where C_d is the capacitance associated to the depletion zone of the semiconductor, C_{ox} the gate oxide capacitance, C_{it} the capacitance

associated to interface states, q the elementary charge, T the temperature and k the Boltzmann constant [13]. In the wet configuration we have to take into account the double layer capacitance C_{dl} . Hence the term C_{ox} at the denominator is replaced by a combination of C_{dl} and C_{ox} , which gives a higher term than C_{ox} [14]. Therefore the sub-threshold slope obtained for dry configuration is higher than the slope obtained for wet configuration.

Transistors are preferentially operated in the sub-threshold regime. Devices with steeper sub-threshold slopes exhibit large signal variations for small gates changes and therefore for small pH variations (molecular gating effect).

The next measurements have consisted of exposing the SiNW-based transistors to solutions with different pH values. Four different pH buffer solutions (3, 5, 7, 10.5) were prepared from a 5 mM acetate phosphate buffer solution and were put in contact successively with the nanowire device. The conductance was measured versus time and the values are reported in Fig. 5. The conductance increases stepwise with discrete changes in pH and is steady for a given pH value. The SiNW sensors showed a large operation range for pH detection (pH 3–10.5) with an average sensitivity

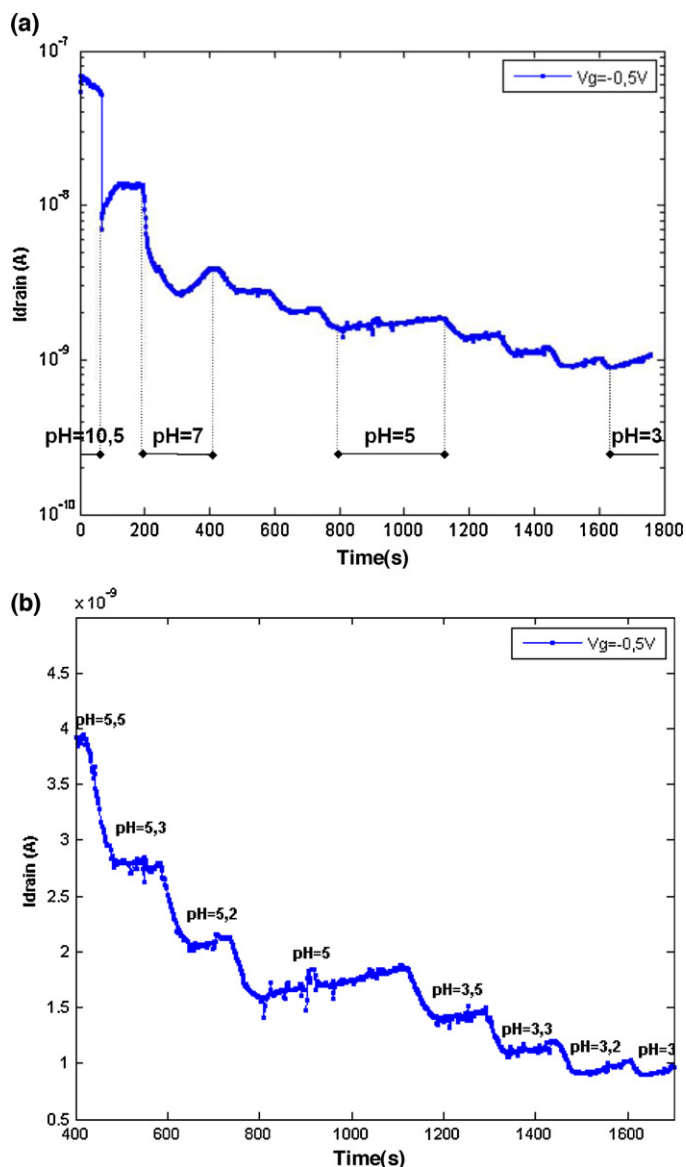


Fig. 5. (a) Transistor current variation as a function of the pH variation in time (between 10.5 and 3). (b) Detail of the top picture: pH monitoring for small variations of pH values between 5.5 and 3 with increments smaller than 0.2 unit.

of 5nS/pH unit (Fig. 5a). As expected, the conductance decreases when the pH decreases. Indeed we use p-doped nanowires and we operate the transistor in accumulation mode. When the pH decreases, silanol groups are protonated [15] and the positive surface charge increase tends to deplete the channel and decreases the conductance.

To realize solutions with intermediate values of pH, we mixed the starting solutions with pH value of 3/5, 5/7, 7/10.5 using the PDMS switch board, while keeping the proportions respectively at 2:1, 1:1, and 1:2. This method allowed us to achieve steps of 0.1 unit for the pH value. In Fig. 5b, we can clearly observe that our device is able to detect a variation of 0.1 units of pH. This result demonstrates the high sensitivity of our device.

Some other very important parameters are the measurement reversibility and the signal stability. In order to investigate these two points, we have performed measurements changing the value of pH from 10.5 to 3 and from 3 to 10.5 without stopping the session (Fig. 6). We have observed that our device response is stable over a long time interval (~200 s), after each pH step. Even if it is difficult

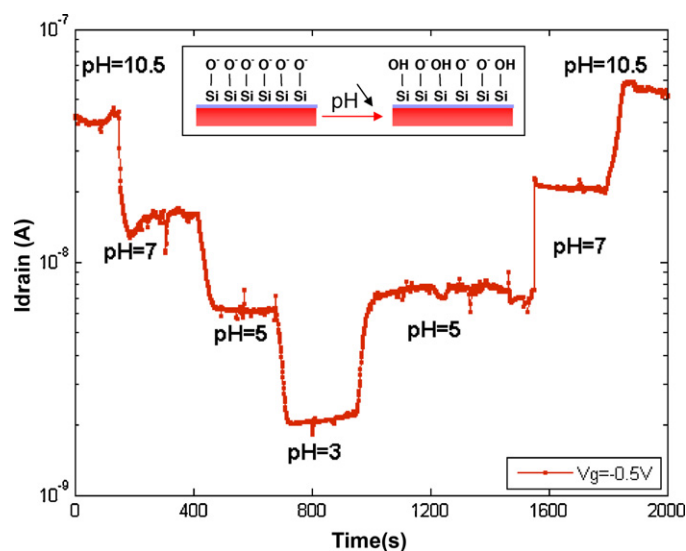


Fig. 6. Reversible pH monitoring on a large range of pH values: I_d recorded versus time for pH values from 10.5 to 3 (5 mM acetate phosphate buffer solutions). The inset shows the protonation mechanism of the silanol groups which is at the base of the change of the detected signal.

to compare rigorously our signal stability to others works considering the numerous parameters that have to be taken into account (time interval after each pH change, level of current, method of electrical measurements, ...), the signal can be favourably compared, qualitatively, to state-of-the-art works [16].

Moreover, after reaching 3 pH units, increasing the pH we obtain reproducible results: the current value steps are nearly the same for the same values of pH in the two directions (the relative change of the current for each step in the second ramp, compared to the first one, is around 15% which is comparable to the results obtained by Stern et al. [16]).

3.2. Sensitivity as a function of back-gate voltage

In this section we want to highlight the importance of the choice of the gate voltage value. The p-doped Si substrate was used as the gate. Conductance was recorded versus time, for a succession of pH changes from 6 to 8, and the results are reported in Fig. 7(a-c). The sensitivity S is defined as the ratio of variation of conductance from pH 6 to 8 to the conductance for pH 6. Beyond the subthreshold regime ($V_g < -1.25$ V), the sensitivity is low. In the subthreshold regime, sensitivity increases with V_g , reaching a maximum around $V_g \approx -0.5$ V. As it has been previously reported with a "bottom-up" NW-based device [17], this maximum corresponds mathematically to the maximal slope of the $I_d(V_g)$ characteristic and physically to the strongest gate coupling.

To go further and to clearly demonstrate the influence of the gate voltage on sensitivity, we have performed similar measurements for $V_g = +0.5$ V (Fig. 7b). Considering its slightly ambipolar behavior, our transistor was in the inversion mode regime for this gate value. As expected, the pH variations became opposite to those in previous measurements. This shows that gate tuning allows us to choose the optimal working point of the sensor, providing significant enhancement of the sensitivity.

3.3. Influence of buffer salt concentration

Electrolyte solutions with ionic compounds such as sodium chloride (NaCl) are commonly used for biochemical sensing. The concentration of these buffer salts determines the ionic strength, which is a critical parameter for molecular binding and

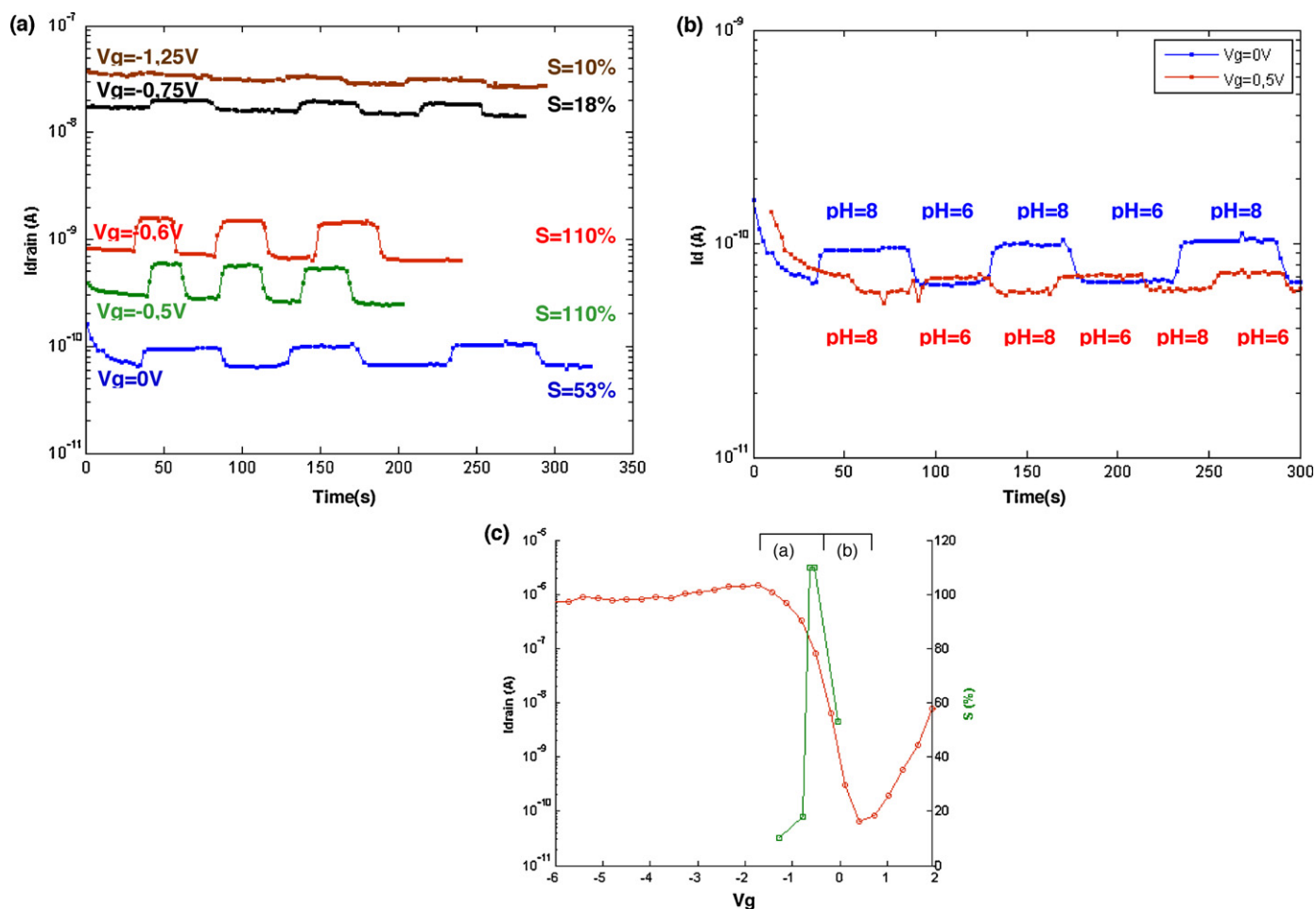


Fig. 7. Influence of the gate voltage on the sensitivity of the SiNW sensor. The characterized transistor has seventy 150 nm-wide nanowires. 20 mM phosphate buffer solutions (pH 6 or 8) flow into the microfluidic system at a 8 $\mu\text{L}/\text{min}$ flow rate thanks to syringe pumps. (a) Conductance variations for different gate voltages, (b) behaviour in the inversion regime, (c) $I_d = f(V_g)$ curve for $V_d = 1\text{V}$ and transistor sensitivity versus gate voltage.

detection/monitoring. Indeed, for DNA detection, a minimum salt concentration is required for hybridization [18]. However, because of Debye screening considerations, it is often necessary to decrease the salt concentration. Consequently one may use a sequential protocol: hybridization at high ionic strength, followed by detection

at lower ionic strength. This method imposes to change buffer salts concentrations during the measurements, motivating us to study the impact of a variation of salt concentration on the conductance.

In our experiments, solutions were prepared from 20 mM phosphate buffer solution (pH 7). NaCl was added with different

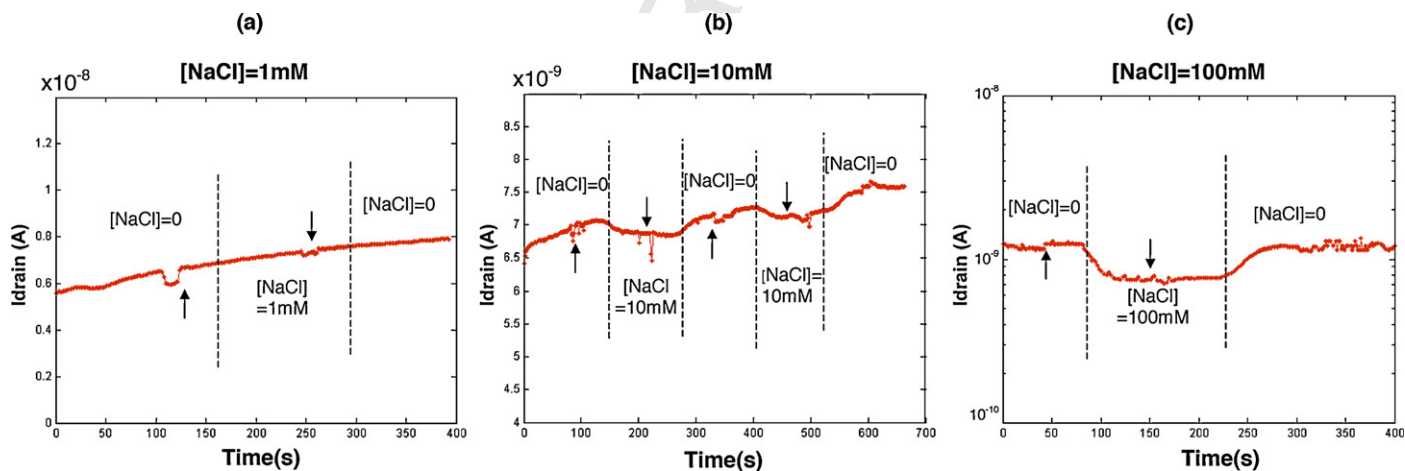


Fig. 8. Influence of the ionic strength on the sensitivity of the SiNW sensor. The characterized transistor has seventy 150 nm-wide nanowires. 20 mM phosphate buffer solutions with different NaCl concentrations are used. The black arrows correspond to the activation of the syringe pumps for solution change (8 $\mu\text{L}/\text{min}$ flow rate). (a) $[\text{NaCl}] = 1\text{mM}$, (b) $[\text{NaCl}] = 10\text{mM}$, (c) $[\text{NaCl}] = 100\text{mM}$.

concentrations (1 mM, 10 mM and 100 mM). The conductance was recorded versus time while the sensor was successively exposed to a salt-free solution and to a salted solution. Results are reported in Fig. 8, where the arrows correspond to the activation of the syringe pumps for solution change.

For a 1 mM NaCl concentration, the conductance does not increase after salt injection. Conversely, for 10 mM and 100 mM NaCl solutions, the conductance decreases respectively of about tens of nS and about hundreds of nS after the solution change. These results are in good agreement with previous reports [19]. The sensitivity of SiNWs to Na⁺ ions can be explained by their selective adsorption on the surface of the SiNWs. Considering the point of zero charge of SiO₂, the surface charge on the SiNW is negative for pH 7. In the electrolyte, positive counterions such as Na⁺ are electrostatically attracted by this negatively charged silicon surface and form Si–O–Na groups [20]. This positive surface charge variation tends to deplete p-doped nanowires FET thus decreasing the conductance. As a result, we can conclude that a variation of the buffer salt concentrations affects significantly the conductance of the sensor. Indeed, this parameter, often disregarded in scientific works on biosensing, has to be taken into account carefully in order to obtain valuable results.

4. Conclusion

In conclusion, the operation of a SiNW-based transistor is demonstrated for pH monitoring and the influence of several key experimental parameters has been analyzed. We used a “top-down” approach to fabricate our SiNW-based transistors. They display a stable and reversible variation of the conductance for a large pH range, with a lowest detection limit of 5 nS/pH unit. A minimal detection threshold of 0.1 unit of pH is achieved.

The influence of several parameters is evaluated. We highlighted the importance of the choice of the gate voltage, which allowed us to tune the sensitivity of the sensor. The ionic strength of the solution was also investigated and we have found that the presence of Na⁺ ions can affect the sensitivity of the measurements when concentration is above 10 mM. These effects have to be taken into account so that a biological reaction can be correctly monitored.

Acknowledgment

This work was supported by the French National Research Agency (ANR) in the framework of the Nanobiosensor project and by the French Delegation for Armament (DGA).

DP would like to acknowledge partial funding from the WCU (World Class University) program through the National Research

Foundation of Korea funded by the Ministry of Education, Science and Technology (R31-2008-10029).

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