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# Contents

Volume 90  
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## Special Issue on Modern Sensing Technologies

### Editorial

#### Modern Sensing Technologies

*Subhas Chandra Mukhopadhyay and Gourab Sen Gupta* ..... 1

### Sensors for Medical/Biological Applications

#### Characteristics and Application of CMC Sensors in Robotic Medical and Autonomous Systems

*X. Chen, S. Yang, H. Natuhara K. Kawabe, T. Takemitsu and S. Motojima* ..... 1

#### SGFET as Charge Sensor: Application to Chemical and Biological Species Detection

*T. Mohammed-Brahim, A.-C. Salaün, F. Le Bihan* ..... 11

#### Estimation of Low Concentration Magnetic Fluid Weight Density and Detection inside an Artificial Medium Using a Novel GMR Sensor

*Chinthaka Gooneratne, Agnieszka Łekawa, Masayoshi Iwahara, Makiko Kakikawa and Sotoshi Yamada* ..... 27

#### Design of an Enhanced Electric Field Sensor Circuit in 0.18 $\mu\text{m}$ CMOS for a Lab-on-a-Chip Bio-cell Detection Micro-Array

*S. M. Rezaul Hasan and Siti Noorjannah Ibrahim* ..... 39

### Wireless Sensors

#### Coexistence of Wireless Sensor Networks in Factory Automation Scenarios

*Paolo Ferrari, Alessandra Flammini, Daniele Marioli, Emiliano Sisinni, Andrea Taroni* ..... 48

#### Wireless Passive Strain Sensor Based on Surface Acoustic Wave Devices

*T. Nomura, K. Kawasaki and A. Saitoh* ..... 61

#### Environmental Measurement OS for a Tiny CRF-STACK Used in Wireless Network

*Vasanth Iyer, G. Rammurthy, M. B. Srinivas* ..... 72

#### Ubiquitous Healthcare Data Analysis And Monitoring Using Multiple Wireless Sensors for Elderly Person

*Sachin Bhardwaj, Dae-Seok Lee, S.C. Mukhopadhyay and Wan-Young Chung* ..... 87

### Capacitive Sensors

#### Resistive and Capacitive Based Sensing Technologies

*Winncy Y. Du and Scott W. Yelich* ..... 100

<b>A Versatile Prototyping System for Capacitive Sensing</b> <i>Daniel Hrach, Hubert Zangl, Anton Fuchs and Thomas Bretterklieber</i> .....	117
<b>The Physical Basis of Dielectric Moisture Sensing</b> <i>J. H. Christie and I. M. Woodhead</i> .....	128
<b>Sensors Signal Processing</b>	
<b>Kalman Filter for Indirect Measurement of Electrolytic Bath State Variables: Tuning Design and Practical Aspects</b> <i>Carlos A. Braga, João V. da Fonseca Neto, Nilton F. Nagem, Jorge A. Farid and Fábio Nogueira da Silva</i> .....	139
<b>Signal Processing for the Impedance Measurement on an Electrochemical Generator</b> <i>El-Hassane Aglzim, Amar Rouane, Mustapha Nadi and Djilali Kourtiche</i> .....	150
<b>Gas Sensors</b>	
<b>Gas Sensing Performance of Pure and Modified BST Thick Film Resistor</b> <i>G. H. Jain, V. B. Gaikwad, D. D. Kajale, R. M. Chaudhari, R. L. Patil, N. K. Pawar, M. K. Deore, S. D. Shinde and L. A. Patil</i> .....	160
<b>Zirconia Oxygen Sensor for the Process Application: State-of-the-Art</b> <i>Pavel Shuk, Ed Bailey, Ulrich Guth</i> .....	174
<b>Image Sensors</b>	
<b>Measurement of Digital Camera Image Noise for Imaging Applications</b> <i>Kenji Irie, Alan E. McKinnon, Keith Unsworth, Ian M. Woodhead</i> .....	185
<b>Calibration-free Image Sensor Modelling Using Mechanistic Deconvolution</b> <i>Shen Hin Lim, Tomonari Furukawa</i> .....	195
<b>Miscellaneous</b>	
<b>Functional Link Neural Network-based Intelligent Sensors for Harsh Environments</b> <i>Jagdish C. Patra, Goutam Chakraborty and Subhas Mukhopadhyay</i> .....	209
<b>MEMS Based Pressure Sensors – Linearity and Sensitivity Issues</b> <i>Jaspreet Singh, K. Nagachenchaiah, M. M. Nayak</i> .....	221
<b>Slip Validation and Prediction for Mars Exploration Rovers</b> <i>Jeng Yen</i> .....	233
<b>Actual Excitation-Based Rotor Position Sensing in Switched Reluctance Drives</b> <i>Ibrahim Al-Bahadly</i> .....	243
<b>A Portable Nuclear Magnetic Resonance Sensor System</b> <i>R. Dykstra, M. Adams, P. T. Callaghan, A. Coy, C. D. Eccles, M. W. Hunter, T. Southern, R. L. Ward</i> .....	255
<b>A Special Vibration Gyroscope</b> <i>Wang Hong-wei, Chee Chen-jie, Teng Gong-qing, Jiang Shi-yu</i> .....	267
<b>An Improved CMOS Sensor Circuit Using Parasitic Bipolar Junction Transistors for Monitoring the Freshness of Perishables</b> <i>S. M. Rezaul Hasan and Siti Noorjannah Ibrahim</i> .....	276

<b>Sensing Technique Using Laser-induced Breakdown Spectroscopy Integrated with Micro-droplet Ejection System</b> <i>Satoshi Ikezawa, Muneaki Wakamatsu, Joanna Pawlat and Toshitsugu Ueda .....</i>	284
<b>A Forward Solution for RF Impedance Tomography in Wood</b> <i>Ian Woodhead, Nobuo Sobue, Ian Platt, John Christie.....</i>	294
<b>A Micromachined Infrared Sensor for an Infrared Focal Plane Array</b> <i>Seong M. Cho, Woo Seok Yang, Ho Jun Ryu, Sang Hoon Cheon, Byoung-Gon Yu, Chang Auck Choi.....</i>	302
<b>Slip Prediction through Tactile Sensing</b> <i>Somrak Petchartee and Gareth Monkman.....</i>	310
<b>Broadband and Improved Radiation Characteristics of Aperture-Coupled Stacked Microstrip Antenna for Mobile Communications</b> <i>Sajal Kumar Palit.....</i>	325
<b>The Use of Bragg Gratings in the Core and Cladding of Optical Fibres for Accurate Strain Sensing</b> <i>Ian G. Platt and Ian M. Woodhead.....</i>	333

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## SGFET as Charge Sensor: Application to Chemical and Biological Species Detection

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**Abstract:** A review of the large possibilities of sub-micron gap Suspended-Gate FETs, namely SGFET, to detect chemical and biologic species with high sensitivity, is presented. Examples of detection of humidity, gas, pH of liquid solutions, DNA (through one mutation of BRCA1 gene that is the main indication of the possibility for a woman to have breast cancer) and proteins (through the transferrin that is the only carrier of iron in blood) are presented to highlight these possibilities. The high sensitivity is explained from the charge distribution inside the sub-micron gap due to the high field effect. *Copyright © 2008 IFSA.*

**Keywords:** Electronic detection, Suspended-gate FET, Sensitivity, Chemical detection, Biologic detection

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### 1. Introduction

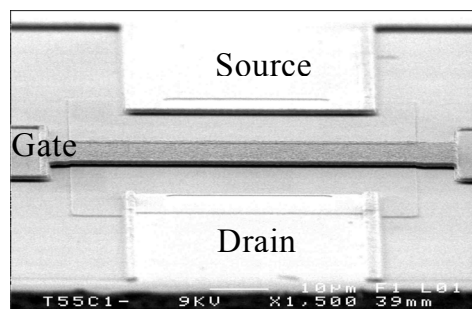
The need of rapid and precise detection of early disease symptom, as well as the need of safe environment, becomes now the main leitmotiv of the societal development. Following these needs, there is a great demand for easy to use and low cost systems that can detect rapidly different chemical and biologic species with high sensitivity and specificity. The systems have to integrate sensing functions and conditioning electronics to increase the reliability. Electrical detection will participate to this integration. Moreover, electrical signal measurement is much easy and cheap. Finally, the electrical detection offers the capability of supplying a quick result with a competitive cost-in-use. Here, generic structure, namely Suspended-gate-field-effect-transistor with submicron gap, is presented and used in different applications (humidity, gas, pH of liquid solutions, DNA and proteins

detection) to show its high sensitivity in the detection of electrical charges. The high sensitivity is explained from the charge distribution induced by the high applied field under the gate-bridge that is suspended at sub-micron distance.

SGFET based sensors are extensively investigated since ever the work of Janata [1]. Different variations of the structure (Hybrid SGFET [2], Floating Gate FET [3]) were introduced to improve the performance. All these structures use the work function variation as sensitive parameter. Then, their sensitivity is limited to the Nernstian response. Using recent surface microtechnology techniques, the present SGFET structure uses gate-bridge that is suspended at submicron distance. In this way, it is possible to increase highly the sensitivity by introducing the field effect as additional parameter.

## 2. Technological Aspects

SGFET structure (Fig. 1) is based on MOSFET device for which the gate insulator is composed of classical isolation with an additional free zone between the gate insulator and the suspended bridge.



**Fig. 1.** SEM image of a suspended gate field effect transistor (SGFET).

This suspended bridge is achieved by considering two goals: the production of a flat and homogeneous suspended gate-bridge with good electrical and mechanical characteristics and the use of a sacrificial layer easy to deposit and to etch. The gate-bridge has to be electrically insulated from the ambience. Moreover, it has to stay horizontal (constant distance between the gate insulator and the bridge so that the transistor characteristics will be reproduced) when the gate bias is applied and when the structure is dipped into liquid and then dried a lot of times [4]. Such conditions on the mechanical behaviour can appear particularly hard to meet.

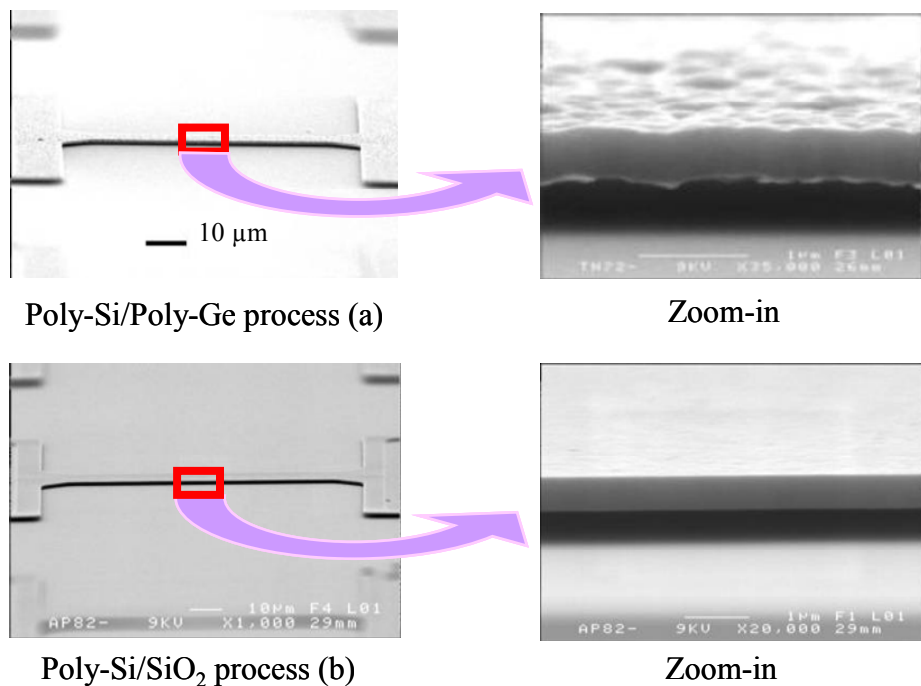
### 2.1. Suspended Gate Fabrication

To reach the goaled mechanical behaviour, micro-bridges were fabricated using different materials to estimate the effect of the stress on their mechanical properties. The main process steps of surface micromachining to fabricate suspended bridge are basics: first, the sacrificial layer is deposited and then patterned using standard photolithography techniques [5]. Then, the anchor windows are opened. Finally, the structural films are deposited and patterned to form the micro-bridges.

The electrical conductive structural layer is a 500nm polysilicon doped layer amorphously deposited at 550°C and crystallized during 12h at 600°C. Two sacrificial materials have been investigated: APCVD silicon oxide and LPCVD germanium. Silicon oxide is deposited in a conventional APCVD reactor at 400°C. The deposition conditions have been optimized to obtain a high etch rate in hydrofluoric acid

(HF). The etch rate in HF 49% is measured to be around 700 nm/min. Germanium is deposited in a LPCVD reactor at 500°C with 50 sccm GeH<sub>4</sub>. Then, the germanium sacrificial layer is easily etched using hydrogen peroxide (H<sub>2</sub>O<sub>2</sub>) warmed at 90°C and then rinsed in DI water. Both sacrificial layers were 500 nm thick.

Fig. 2 shows an example of these free standing micro-bridges using germanium (Fig. 2(a)) or SiO<sub>2</sub> (Fig. 2(b)) as sacrificial layer. The down face of polysilicon bridge is very rough when using germanium and smooth with SiO<sub>2</sub>. The roughness of polysilicon deposited on germanium is attributed to the rough surface of the sacrificial germanium that is polycrystalline as-deposited. The mechanical behaviour of the bridge is highly improved when using germanium. This improvement can be explained from the surface roughness as asperities significantly reduce the area over which the adhesion is active. In other words, smooth surfaces are more highly prone to collapse with another smooth surface [6].



**Fig. 2.** SEM image of micro-bridges realized using Ge sacrificial layer (a) or SiO<sub>2</sub> sacrificial layer (b) and zoomed-in view of the central zone. Ge has roughened the down face of polysilicon in touch.

Moreover the beneficial effect of the use of germanium on the mechanical properties, the etching step of the sacrificial layer is much easy as the etching selectivity of Ge versus all other materials used in the process is very high. H<sub>2</sub>O<sub>2</sub> does not etch any more silicon, SiO<sub>2</sub>, and Si<sub>3</sub>N<sub>4</sub>. The etching rate of Ge by H<sub>2</sub>O<sub>2</sub> is very high. Its value is 100 nm/min at ambient temperature, but can be as high as 1100 nm/min at 90°C [7]. These important properties lead to an easier integration of MEMS devices with their electronics.

The mechanical behaviour of the bridge improves more, when conductive doped polysilicon is embedded between 2 layers of Silicon Nitride (Si<sub>3</sub>N<sub>4</sub>) to ensure its electrical insulating. Indeed, it has been shown [8] that boron doped polysilicon micro-cantilever has a high positive mechanical stress gradient which can lead to out-of-plane deflection of the cantilever. On the other hand, Si<sub>3</sub>N<sub>4</sub> layers present a negative stress. The negative stress of Si<sub>3</sub>N<sub>4</sub> layers balances the positive stress of doped polysilicon layer and the mechanical behaviour of the embedded bridge is improved.

## 2.2. SGFET Process

Eight masks were designed for the fabrication of the sensor based on classical MOS technology. This sensor has also been developed in low temperature technology (>600°C) on glass by using undoped polysilicon for the channel and highly doped polysilicon for drain and source regions [9]. Both technologies can be developed for N-type or P-type field effect transistors.

Fig. 3 presents a scheme of P-type SGFET just before removing the sacrificial layer that is the germanium film. It is nearly a usual MOSFET where the silicon dioxide insulator is replaced by the Ge film. Wafers used are <100> oriented and low-doped N type. The drain and source wells come from nitride boron diffusion at 1100°C with a 650 nm SiO<sub>2</sub> as protect layer. The channel is oxidized at 1100°C on 70nm. Then, the channel oxide is protected by a 50nm Si<sub>3</sub>N<sub>4</sub> LPCVD (Low Pressure Chemical Vapor Deposition) layer performed at 600°C. On the nitride layer, a 500nm Ge sacrificial layer is deposited by LPCVD at 550°C, following by a 50 nm silicon nitride layer, which acts as isolation layer for the bottom of the gate. Gate and drain source contacts are silicon thin films amorphyously deposited at a temperature of 550°C and a pressure of 90 Pa in a Low Pressure Chemical Vapor Deposition (LPCVD) reactor and are *in-situ* solid phase crystallized at 600°C. This technology allows depositing boron *in situ* doped silicon films using a mixture of either silane or disilane, and diborane as doping gas. Previous study [10] showed that a boron doped polysilicon layers deposited from disilane gas that is temperature compatible with diborane gas have good electrical characteristics, with the advantage of a high deposition rate. A last 50 nm silicon nitride layer protects the top of the gate. Vias are opened in the nitride layer for the contact with Aluminium path. Due to the use of liquid ambience, all metal layers are insulated with a last photoresist coat. The last step of the process is the releasing of the gate-bridge by wet etching of the Ge sacrificial layer using hydrogen peroxide (H<sub>2</sub>O<sub>2</sub>).

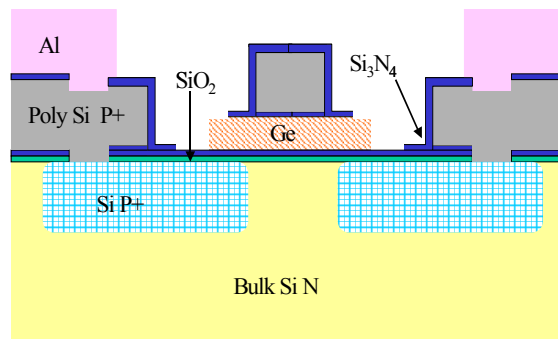


Fig. 3. Process of the P type SGFET before the releasing of the Ge sacrificial layer.

## 3. Modeling of Charge Detection

Intrinsically, SGFET structure is a sensor of electrical charge that can be present between the bridge and the channel. Indeed, the threshold voltage  $V_{TH}$  of MOSFET can be expressed by:

$$V_{TH} = \Phi_{MS} + 2\phi_F + \frac{Q_{SC}}{C} - \frac{1}{C e_{ox}} \int_0^{e_{ox}} x \rho(x) dx, \quad (1)$$

where  $\Phi_{MS}$  is the difference between the work function of the gate material and the semiconductor,  $\phi_F$  is the Fermi level position in the semiconductor versus the mid-gap,  $Q_{SC}$  is the space charge in the semiconductor,  $C$  is the total capacitance between the gate material and the semiconductor,  $e_{ox}$  is the

thickness of the insulator (air-gap, Si<sub>3</sub>N<sub>4</sub> and SiO<sub>2</sub>),  $\rho(x)$  is the charge in the insulator, located at a distance  $x$  from the gate.

$V_{TH}$  value depends on the charge and on its distribution inside the insulator. In the present SGFET, the gate insulator is a sandwich of 4 layers SiO<sub>2</sub>, Si<sub>3</sub>N<sub>4</sub>, air-gap, Si<sub>3</sub>N<sub>4</sub>. For fixed charges in the SiO<sub>2</sub> film and both Si<sub>3</sub>N<sub>4</sub> layers,  $V_{TH}$  depends on the variation of the charges and their distribution in the air-gap.

Moreover this dependence,  $V_{TH}$  can change when  $\Phi_{MS}$  varies due to some chemical reactions at the inner surface of the gate material and at surface of the insulator channel film. Commonly, only this last dependence is considered in historic SGFET. Indeed, when the air-gap is thick, the field effect has a small influence over charges and the distribution of the electrical charge is uniform inside the air-gap.

However, the present SGFET shows a very low air-gap, 500 nm, between active layer and gate, implying an important field effect inside the thin air-gap. In this case, the distribution of the electrical charge becomes non-uniform due to high field, leading to a variation of  $\rho(x)$ . Moreover, the high field can influence the adsorption by shifting the charges on the surface. All these effects lead to a variation of  $\Phi_{MS}$  but, also, of the last term in the  $V_{TH}$  expression. Then,  $V_{TH}$  variation can be very large if the effect of high field are considering. However, this effect can occur only with very high fields: we observed a high decrease of the sensibility when the air-gap increases from 500 to 800 nm. The charges sensitivity becomes high due to an increase of charges content accumulated on the surface channel. This accumulation becomes more and more important when the gate-source voltage increases.

The modeling is based on the determination of interface charges concentration  $Q_{SS}$ , depending of the gate voltage [11]. It is the original part of this modeling, this effect being not taken into account in the classical MOS theory. The insulator is supposed to contain constant positive charges concentration,  $N_{TOT}$ . These charges are moving under electrical field, due to positive gate  $V_G$ , and accumulated to the channel surface where there are fixed. The positive charges concentration by surface unit on channel surface  $Q_{SS}$ , is took proportionally to  $V_G$ . The variation rate of  $Q_{SS}$  with  $V_G$  is proportional to the positive charges concentration  $N_{TOT}$  present in the air between gate and channel.

We take into account that it needs  $N_{LIM} = 10^{14}$  charges by surface unit to cover completely silicon surface (by taken the silicon atomic density to  $5.10^{22}$  atom/cm<sup>3</sup>). In this case, the variation rate of  $Q_{SS}$  with  $V_G$  is also proportional to the number of empty places at the silicon surface ( $qN_{LIM} - Q_{SS}$ ) as:

$$\frac{dQ_{SS}}{dV_G} = \alpha q N_{TOT} (q N_{LIM} - Q_{SS}), \quad (2)$$

where  $\alpha$  is an experimental factor.

From this model, the concentration of accumulated charges in the channel by surface unity,  $Q_n$  has been calculated and has been drawn in Fig. 4. For few positive charges  $N_{TOT}$  in the air between gate and channel, the quantity of accumulated charges in the channel increases slowly versus gate voltage. When the density of positive charges increases, the subthreshold slope decreases, leading a strong increasing of drain current. Finally, when  $N_{TOT} > 10^{13}$  cm<sup>-3</sup>, there is a value of gate voltage  $V_g$  for which the current  $I_{ds}$  saturates.

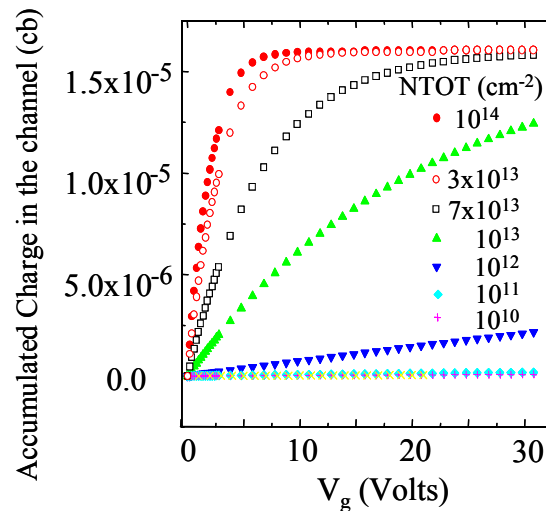


Fig. 4. Accumulated charges in the channel  $Q_n$  vs. gate voltage for different concentration of positive charges in insulator.

Effect of charges on the air-gap transistor characteristics depends on the density and on the type (positive or negative) of charges  $Q_{ss}$ . We have summarized the evolution of transfer characteristic for p-type and n-type SGFET in Fig. 5. After introduction of positive  $Q_{ss}$ , the  $I_{DS}$  ( $V_{GS}$ ) curve of n-type SGFET shifts towards lower voltages (negative shift of the threshold voltage). On the other hand, the presence of negative charges has the contrary effect on the air-gap transistor characteristics: transfer characteristic shifts towards higher voltages (positive shift of the threshold voltage).

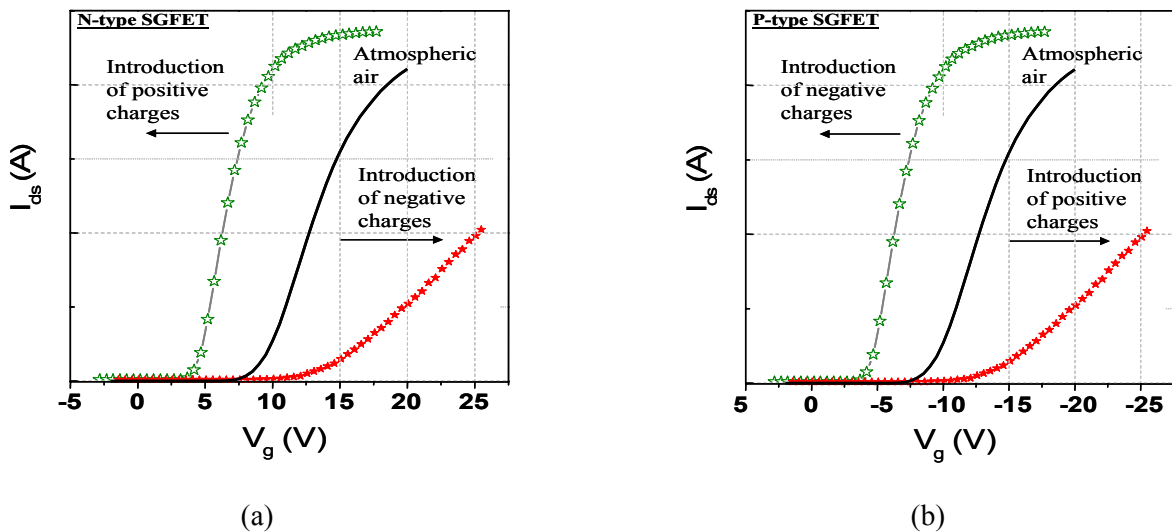
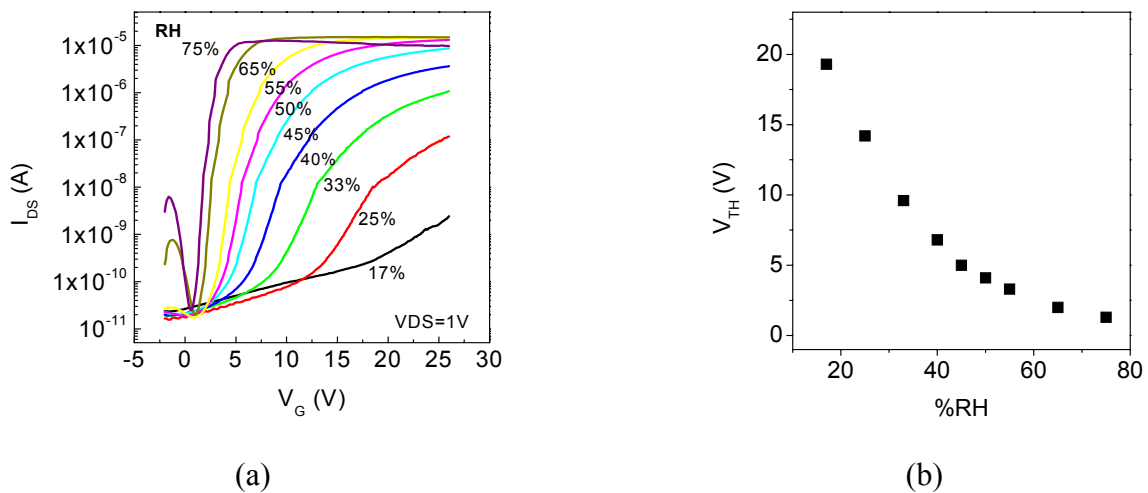


Fig. 5. Evolution of transfer characteristic of (a) P-type and (b) N-type SGFET after introduction of positive or negative charges.

#### 4. Humidity

To check the charge sensitivity of the present SGFET and its modeling, the device is characterized in the air-water mixture with different relative humidity (RH). It is known that the content of negative charges decreases when RH increases.

SGFET is placed in a moisture chamber where humidity and temperature are controlled. Transfer characteristics, drain-source current  $I_{DS}$  – gate-source voltage  $V_{GS}$  of an N-type SGFET, at fixed RH, are plotted in Fig. 6(a). The threshold voltage (Fig. 6(b)) and the subthreshold slope highly decrease and in the same time,  $I_{DS}$  saturates at lower gate-source voltage when humidity increases. The threshold voltage shift is more than 18V when the humidity ratio varies from 17 to 70%. The variation is particularly important for low humidity rates. It highlights the high sensitivity of the present sub-micron SGFET. The decrease of  $V_{TH}$  is well compatible with the use of N-Type SGFET and the decrease of negative charges when RH increases [12].



**Fig. 6.** (a) Transfer characteristic drain-source current  $I_{DS}$  – gate-source voltage  $V_{GS}$  of a N-type SGFET for different humidity ratio and (b) threshold voltage versus relative humidity RH.

## 5. Gas Sensor

The detection of humidity confirmed the possibility to use SGFET in charges sensing with high sensitivity. Next step consists to check the SGFET possibility in gas sensing. N-type SGFETs are placed in a stainless steel test chamber (200 ml) where a controlled atmosphere was provided by means of mass flow controllers connected to a computer [13]. The transfer characteristic, drain current versus gate voltage  $I_{ds}$  ( $V_g$ ) at constant drain-source voltage  $V_{ds}$ , is measured at room temperature under a flow of synthetic humid air at a flow of  $200 \text{ ml min}^{-1}$ . Therefore, the gas is introduced at the same flow rate, keeping constant the level of relative humidity. Then the transistor is characterized another time.

The SGTFT sensor shows its ability to detect specific gas with a very high sensibility through the examples of the detection of  $\text{NO}_2$  and  $\text{NH}_3$ . These two gases were chosen for their contrary effect on the threshold voltage shift. Indeed, whereas introducing  $\text{NH}_3$ , the current curve shifted towards lower voltages, i.e. negative shift of the threshold voltage. Introducing  $\text{NO}_2$  had the reverse effect.

Fig. 7(a) shows the variation of transfer characteristics under different  $\text{NO}_2$  concentrations. The detection is based only on the reaction of  $\text{NO}_2$  with silicon surface. The molecules of  $\text{NO}_2$  act as acceptor centres [14]. Once they have been adsorbed on silicon surface, the acceptor-like character would lead to an increase of free carrier (holes) concentration in silicon: negative ions  $\text{NO}_2^-$  act as negative charges  $-Q_{SS}$  in gate insulator thus explaining threshold voltage increasing. This negative charges support the known oxidizing character of  $\text{NO}_2$  [15-16].

Fig. 7(b) shows the variation of transfer characteristics under different  $\text{NH}_3$  concentrations. The negative shift of the threshold voltage confirms its reducing character [17-18]. The molecules of

ammoniac are dipolar and act as donor centres. Once they have been adsorbed on silicon surface, positive ions  $\text{NH}_3^+$  act as positive charges  $Q_{SS}$  in air thus explaining threshold voltage decreasing.

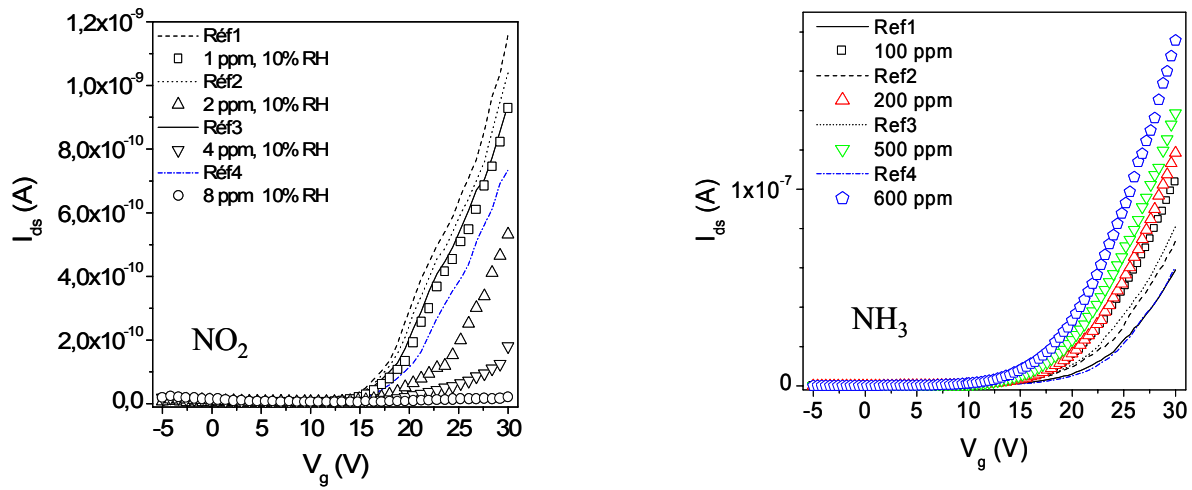


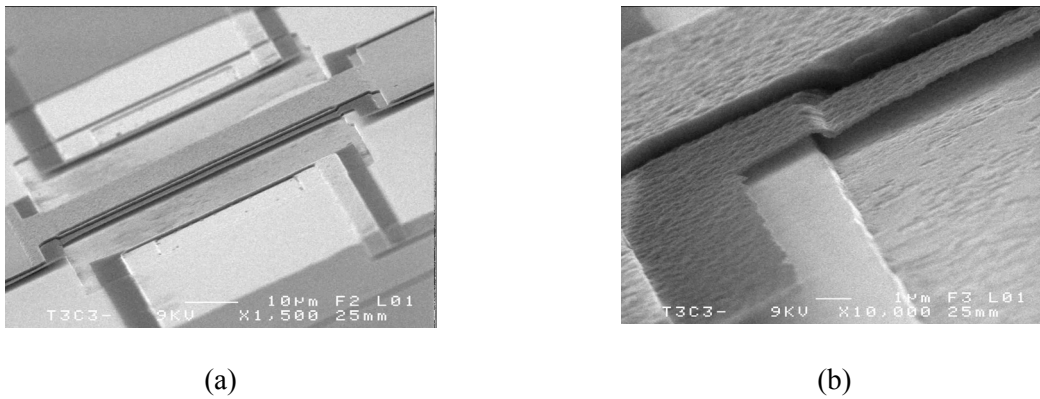
Fig. 7. Transfer characteristics of SGTFT under different  $\text{NO}_2$  (a) and  $\text{NH}_3$  (b) concentrations. The reference is synthetic humid air.

## 6. pH of Liquid Solutions

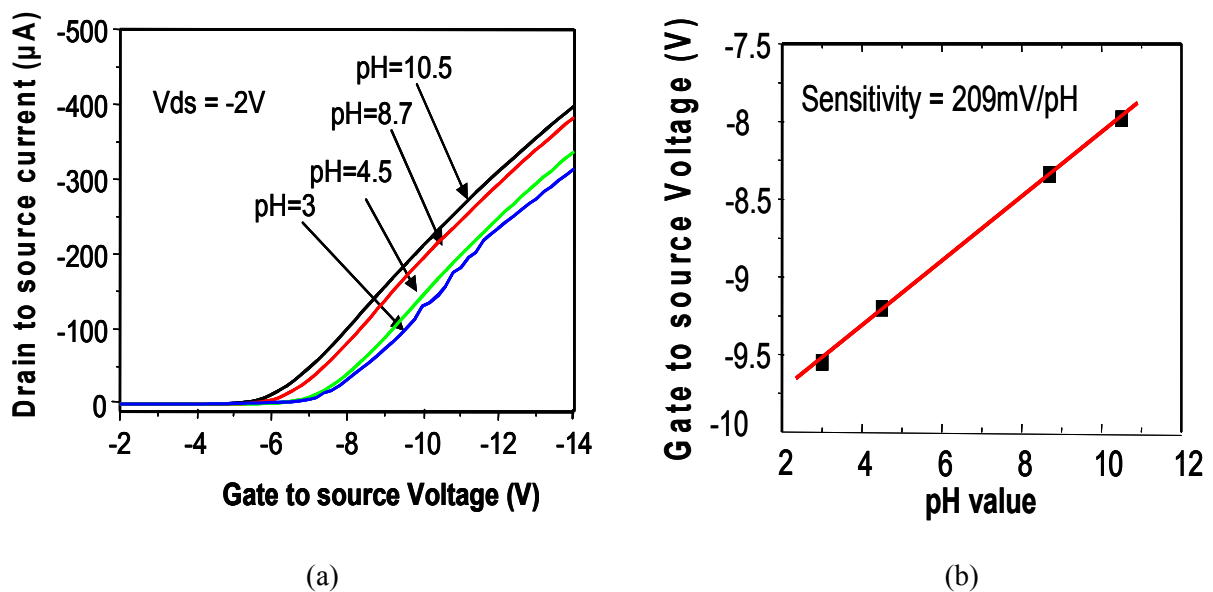
One of the main problems when using suspended microstructures in liquid solutions is their mechanical behaviour when they are submitted to multiple diving and drying. Indeed, the effect of sticking forces can be important particularly when the distance between the suspended structure and the substrate is submicron as here. So, it is important to check the behaviour of the present gate-bridge before using SGFET as sensor in liquid solutions. Fig. 8 shows Scanning Electron Microscope image of SGFET after several diving in different solutions. The bridge stays horizontal as shown in Fig. 8(a) and confirmed in the zoom-in view (Fig. 8(b)).

Then, SGFET can be used in liquid ambience to sense charges. Obvious application is solution pH sensing. The experimental procedure follows the next steps. The SGFET is dived into a buffer solution for which the pH was fixed before. Then, the transfer characteristics drain-source current  $I_{DS}$  versus the gate voltage  $V_{GS}$  is measured. The drain-source voltage  $V_{DS}$  is kept constant at  $-2$  V during this measurement. The SGFET under testing is rinsed using de-ionized water between 2 measurements in buffer solution with different pH values. The pH value is varied between 3 and 10. Fig. 9(a) shows the transfer characteristics  $I_{DS}$ - $V_{GS}$  of the same P-type SGFET dived in buffer solution with different pH values at ambient temperature. The threshold voltage decreases for higher pH values and then for lower  $\text{H}^+$  concentration. To check the sensitivity of SGFET to solution pH, the  $V_{GS}$  value at  $I_{DS} = -100 \mu\text{A}$  is plotted as a function of the pH in Fig. 9(b). The variation of  $V_{GS}$  with pH is perfectly linear. The slope of the straight line gives a sensitivity of 209 mV/pH [19].

The present SGFET is sensitive to solution pH. However, the more important is the very high value of this sensitivity. It is much higher than the usual value given by the commercially available ISFETs. In the classical ISFET theory [20, 21], the concentration of  $\text{H}^+$  ions that is adsorbed at the surface of silicon nitride, is in equilibrium with the  $\text{H}^+$  concentration in the solution. Then, the concentration of adsorbed  $\text{H}^+$  ions varies with pH value that leads to a variation of the threshold voltage. ISFET Nernstian response gives a pH sensitivity limited to 59 mV/pH at ambient temperature [22, 23].



**Fig. 8.** SEM image of the gate-bridge after several diving in different solutions and drying (a). The zoom-in view (b) highlights the good mechanical behaviour of the bridge.



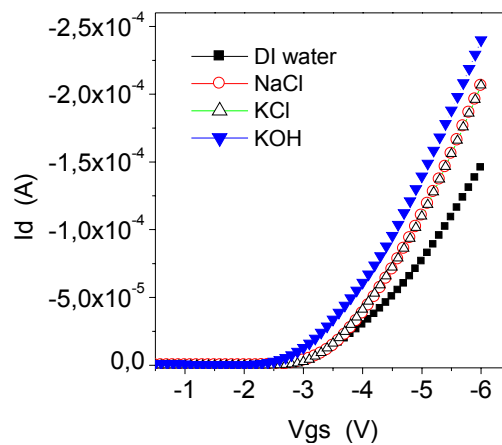
**Fig. 9.** (a) Transfer characteristics of the same SGFET dived into solutions with different increasing pH values at ambient temperature. (b) Plot of the  $V_{GS}$  values versus pH for a drain-source current fixed to  $-100 \mu\text{A}$  at ambient temperature.

The high SGFET sensitivity can be explained by the submicron gap where a high field effect appears when the gate voltage is applied. The  $\text{H}^+$  concentration becomes then non-uniform in the gap. The  $\text{OH}^-$  ions contained in the solution are shifted near the channel and the  $\text{H}^+$  near the gate. This effect leads to an increase of the device sensitivity. The effect of the low gap height is highlighted by the lower sensitivity obtained when the gap is larger. Indeed, when using an  $800 \text{ nm}$  gap instead of the usual  $500 \text{ nm}$  value, the sensitivity decreases from  $209 \text{ mV/pH}$  to  $90 \text{ mV/pH}$ . This high decrease of the sensitivity highlights also the non-linear effect of the field.

In fact, it seems that both the adsorption as in usual ISFET and the effect of the new charge distribution induced by the high field, participate to the SGFET answer. It is possible to separate experimentally these both effects by using salt solutions that do not change the pH and do not introduce an adsorption at the surface. Salt solutions of KCl and NaCl and basic solution KOH are prepared with exactly the same concentration. pH does not change when using salt solutions as KCl and NaCl. When plotting transfer characteristics of SGFET that is dipped in these salt solutions, only effect of the field on the charge distribution will be observed. In the presence of KOH, pH change and

then both effects of the new distribution of charges inside the gap and of the adsorption will be observed. Fig. 10 shows the transfer characteristics of SGFET dipped in DI water and in solutions of KCl, NaCl and KOH with the same concentration. Similar shift of the characteristics is shown in presence of KCl or NaCl with the same concentration. This shift is only due to the distribution of charges induced by the field inside the gap.  $V_{TH}$  shift is induced by the variation of the last term of equation (1). Same charge content gives same shift. With same concentration KOH solution, extra shift is observed. It can be due to the pH of KOH and then to the charges that adsorb at the surface of silicon nitride (first term in equation (1)). Then in presence of KOH the shift is due to both the charge distribution and the adsorbed charge. Both origins contribute to the high pH sensitivity of the present device.

Another advantage of the present SGFET consists on the extreme small volume needed to measure the pH. The commercially available ISFETs require a small probe but in combination with a rather large reference electrode. The use of a REFET (identical FET that does not react with the ion concentration, and so covered with insensitive membrane) needs a differential amplifier system [24].



**Fig. 10.** Transfer characteristics when SGFET is dipped in DI water, and in solutions of NaCl, KCl or KOH. These 3 solutions have the same concentration.

## 7. Biologic Species Detection

The high sensitivity of the submicron SGFET to electrical charges that can be present in liquid solutions opens the way to biologic species detection. Indeed, DNA or proteins electrical sensing consists on the detection of the variation of charges induced by linking between complementary strands of DNA or antigens-antibodies for proteins. These links insure the specificity of the detection in the same time.

### 7.1. DNA Detection

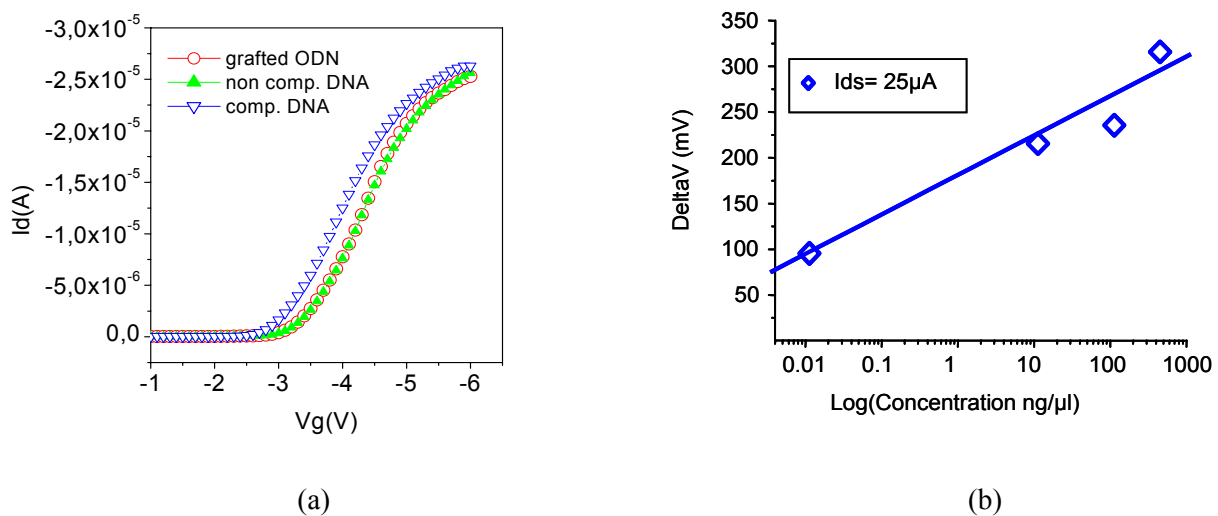
DNA detection systems have opened the field for several years to a very important technological step in the field of knowledge of the genome. The detection system uses the concept of DNA hybridization, where known single strand DNA sequences (probe) are immobilized onto a surface and the complementary DNA strand (target) is recognized by its specific binding affinity.

SGFET sensors detection consists to immobilize under the gate well-defined sequences of DNA single strands and to put the device in contact with solution containing the target to be detected. When probes

and targets are complementary, the molecular hybridization occurs and the adjunction of negatives charges (brings by phosphate groups) under the gate involves a shift of the threshold voltage  $V_{TH}$  of the transistor.

Before and after each step of the procedure of the DNA immobilization, SGFET is characterized by plotting its transfer characteristics, Drain-Source current  $I_d$  as a function of the Gate-Source bias  $V_g$  with fixed Drain-Source voltage. This characterization is systematically done with SGFET dipped in the same ambience. Indeed, the transistor characteristic depends on any electrical charge that comes in the space under the bridge. So, it is important to produce a constant ambience that does not change between 2 steps of the procedure. Any variation of the transistor characteristics has to be attributed only to the extra charge coming from the attachment of the DNA. Neutral solution of Phosphate Buffer Saline (PBS) was chosen as constant ambience during the electrical measurements.

Fig. 11(a) shows the transfer characteristics when P-type SGFET is dipped in PBS after grafting of 25-mer ODN, after hybridization trying of non-complementary and complementary DNA. A displacement of the characteristic in the direction of the lower negative voltages is observed after hybridization with complementary DNA. It corresponds to the detection of negative charges due to the phosphates groups of the complementary DNA which was grafted (the direction of this displacement is in conformity with the addition of a negative charge for a P-type MOSFET). The shift for a fixed current of  $-1 \times 10^{-5}$  A is of 0.35V. We also observed that there is a relation between the value of the voltage shift and the concentration of the biological liquid.

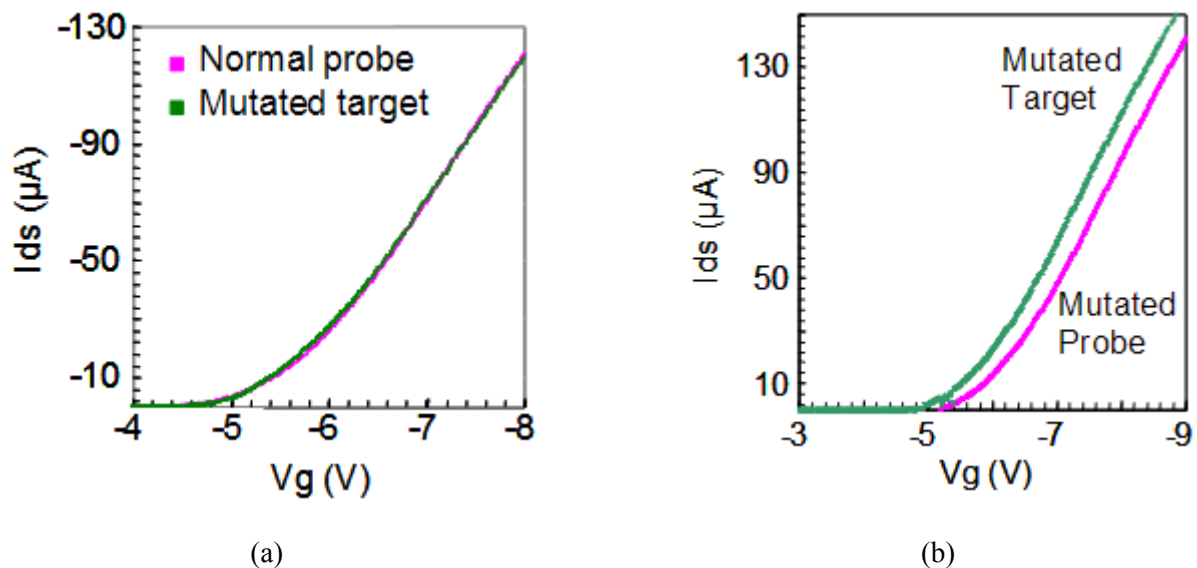


**Fig. 11.** (a) Transfer characteristics when SGTFT is dipped in PBS after grafting of ODN, after hybridization trying of non-complementary and complementary DNA. Positive shift shows the presence of negative charge. (b) Shift of the SGFET characteristic at constant drain current ( $25 \mu\text{A}$ ) as a function of the target concentration.

Fig. 11(b) shows the increase of the voltage shift of the electrical characteristic taken at fixed drain current ( $-25 \mu\text{A}$ ) when the concentration of the sequence targets increases. As expected, the curve of the shift as a function of the logarithm of the concentration is perfectly linear (Fig. 11(b)). Remarkably, the sensitivity is constant over 5 decades of concentration. Such large range is unusual with biosensors. Moreover concentration, as weak as  $10 \text{pg}/\mu\text{l}$ , is detected. Such high sensitivity can open the way for detection without biologic amplification (PCR).

The high sensitivity of the present sensor for DNA detection [25] led us to check the possibility to detect one particular mutation of BRCA1 gene that is known to be difficult to sense by usual techniques. This variant, known as (c.2731 C>T, p.Pro871Leu), consists in the substitution of only one base. One C base is replaced by one base T in the mutated gene. Mutations of BRCA1 and BRCA2 are the main indication of the possibility for a woman to have breast cancer [26]. Indeed, in case of these mutations, the risk of breast cancer is multiplied by 8. Success in such detection is vital as breast cancer is the first cause of women mortality between forty and forty-five years.

For the detection of (c.2731 C>T, p.Pro871Leu) mutation, two 25-bases sequences are used as probes. One is healthy (with C base) and the other is mutated (with T base). The healthy and the mutated targets had 240 bases and were furnished by the Nantes Hospital (France). Moreover to the possibility to detect the mutation, it can be possible to know if the subject is homozygote or heterozygote. As a consequence 6 tests must be done (Table 1). For example, if DNA of the subject (target) doesn't hybridize with healthy probe and hybridize with mutate probe (Fig. 12), we can conclude that the subject is mutated homozygote.



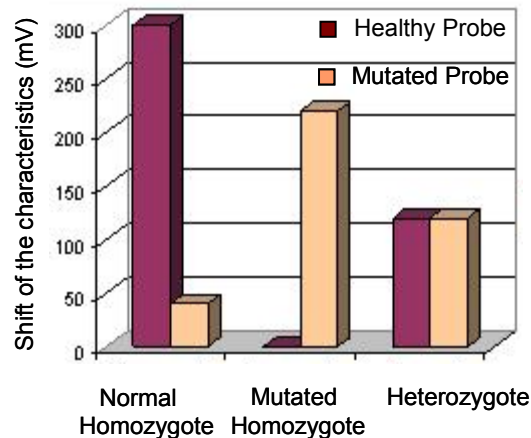
**Fig. 12.** (a) Characteristics before and after hybridization test of a mutated homozygote target with a normal probe. These characteristics are confounded because of the absence of hybridization (b) Characteristics before and after hybridization test of a mutated homozygote target with a mutated probe. Shift of the characteristic is due to hybridization.

Fig. 13 summarizes the results of the 6 possibilities given in Table 1. It gives the shift of the transfer characteristics of the transistor for these 6 possibilities. When the subject is homozygote, the difference between hybridization and no hybridization is well highlighted. When the subject is heterozygote, both hybridizations with healthy and mutated probes occur. However, the shift is smaller than its value in the case of the homozygote. Moreover both shifts are similar. Then the heterozygote subject can be also well identified.

Then the present example of the breast cancer highlights well the powerful use of the SGFET sensor [27]. Indeed, the detection was faced to only one base that is substituted in a very long sequence (240 bases).

**Table 1.** Prediction of results.

Probe Target	Healthy probe	Mutated probe
Healthy homozygote	Hybridization	No Hybridization
Mutated homozygote	No Hybridization	Hybridization
Heterozygote	Hybridization	Hybridization

**Fig. 13.** Shift of the transfer characteristics of the SGFET for the 6 possibilities given in Table 1.

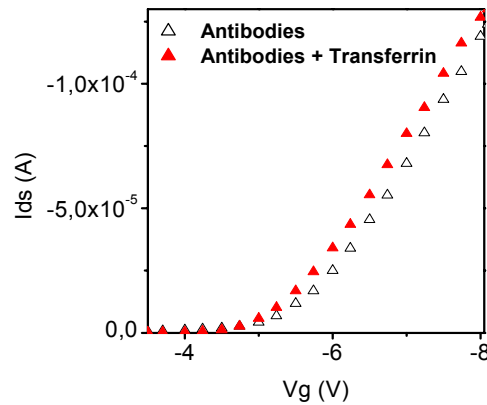
## 7.2. Proteins Detection

As for DNA detection field, there is high demand in a rapid, low cost and quantitative detection of proteins that can be targeted for diagnosis or prognosis. Indeed, the high cost of the present techniques limits their expanded use into the healthcare system. Here, the selectivity is insured through specific antibodies covalently bound to the surface of SGFET [28].

The example of the detection of transferrin is given here to show the powerful of SGFET in the detection and quantification of proteins. Transferrin is iron-binding glycoprotein. It is the only carrier of iron. It circulates in blood plasma and is produced by the liver. Its level in blood is important to detect iron diseases in the iron metabolism: overload or anemia. Fig. 14 shows the transfer characteristics when SGFET is dipped in PBS after linking antibodies and after specifically linking transferrin to antibodies. Obvious shift of the characteristics is related to the specific attachment and then to the detection of transferrin.

## 8. Conclusion

Submicron Suspended Gate Field Effect Transistor showed its possibility to detect any charge variation under the bridge with very high sensitivity. This sensitivity level was explained and experimentally demonstrated from the effect of the large electrical field that induces new distribution of the charges under the bridge.



**Fig. 14.** Transfer characteristics after linking of antibodies (anti-transferrin) to SGFET surface and after specific linking of transferrin on its antibody. Shift of the characteristic is due to specific detection of transferrin.

Examples of the use of SGFET to detect humidity, gas, pH of liquid solutions, DNA and proteins were shown to highlight the large range of possibilities offered by this structure. It can work in gaseous or liquid ambience. The example of pH detection is particularly telltale of the high possible sensitivity, 209 mV/pH, as the usual pH sensitivity of usual sensors is known to be theoretically limited to the Nernstian response, 59mV/pH at ambient temperature.

The use of submicron SGFET in liquid solutions assumes tacitly that the gate-bridge stays horizontal when the gate bias is applied and when the structure is dipped into liquid and then dried a lot of times. It means that all the technological difficulties were surmounted as shown in this paper.

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