The surface of TiO$_2$ gate of 2DEG-FET in contact with electrolytes for bio sensing use

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Abstract

In order to apply two-dimensional electron-gas-field-effect-transistors (2DEG-FETs) for cell-viability sensors, we investigated the chemical/electrical properties of TiO$_2$ thin films (13–17 nm) prepared with the sol–gel technique on the gate surface of AlGaAs/GaAs 2DEG-FETs. Photochemical/electrochemical reactions on GaAs surface in electrolytes, which induce the degradation of 2DEG-FET performance, are effectively suppressed by introducing a TiO$_2$ thin film on the gate area of 2DEG-FETs. Compared to conventional ion-selective FETs (ISFETs), the TiO$_2$/2DEG-FETs in this study exhibit a high sensitivity (410 mV/mM) for H$_2$O$_2$ detection. TiO$_2$ surfaces show better biocompatibility than GaAs surfaces as demonstrated by direct cell culture on these surfaces.

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1. Introduction

Surface physics of semiconductors or oxides in electrolytes are of great importance especially for bio sensing devices. In the conventional Si-based FETs used in electrolytes, the gate area of FETs is protected by a capping layer of insulators, typically thicker SiO$_2$ or SiN layers (50–200 nm). The surfaces of SiO$_2$ or SiN have proton or OH$^-$ sensitivity, so that they are widely utilized for pH sensors, known as ISFETs [1–8]. In order to develop AlGaAs/GaAs 2DEG-FET bio sensors, expecting better S/N ratios and higher sensitivities for cell activities compared with the conventional Si-based ISFETs, we have investigated in our previous work [9] the oxidation behaviors and biocompatibility of GaAs surfaces. In the investigation, direct cell culture on the uncovered gate surface (GaAs) of the 2DEG-FETs was intended for a high sensitivity for cell activities. The surface of GaAs has no toxicity against cells cultured directly on the surfaces, but the FET performance of AlGaAs/GaAs 2DEG-FETs is degraded by surface oxidation/etching in cell culture medium especially when the surface is exposed to visible light [9]. For the protection of FET gate surfaces against oxidation/etching, thin films of TiO$_2$ are more attractive than thicker SiO$_2$ or SiN layers when the bio sensors are concerned, since higher biocompatibilities are expected for TiO$_2$ surfaces [10]. However, there are few reports on TiO$_2$ thin films employed as a gate insulator of FETs operated in electrolytes.

Our long-term aims are to develop and demonstrate the bio sensors based on AlGaAs/GaAs 2DEG-FETs that enable us the long-term, quantitative, and highly sensitive measurement of the activities of cells cultured directly on the gate TiO$_2$ surface. In this report, we describe the chemical/electrical properties of TiO$_2$ thin films prepared with the sol–gel technique [11,12] on the gate surface of 2DEG-FETs. The TiO$_2$/2DEG-FETs exhibit better sensitivities for H$_2$O$_2$ than the commercially available ISFETs, which will be advantageous to realize bio sensors using enzymes with H$_2$O$_2$ production abilities. A better
biocompatibility for TiO₂ surfaces than that for GaAs surfaces is demonstrated by direct cell culture on these surfaces.

2. Experiments

AlGaAs/GaAs 2DEG-FETs used in this study were fabricated from 2DEG wafers (Sumitomo Electric Industries Ltd.). The top layer of the wafer was Si-doped GaAs (Si = 2.0 × 10¹⁸ cm⁻³), and the 2DEG layer was formed 65 nm beneath the top surface. The sheet carrier density and electron mobility measured at room temperature were 6.9 × 10¹⁵ cm⁻² and 6400 cm²/V s, respectively. The conventional photolithographic techniques and wet etching were employed to form a gate channel of 460 μm in width. A maskless-exposure system (Sanyo Electric Co. Ltd., MMP-100S) [13] was used instead of conventional contact-mask-exposure system in the photolithography, from the viewpoint of flexible gate-pattern design. Then TiO₂ thin film was prepared on the entire surface of the 2DEG-FET. The sol–gel TiO₂ film was spin coated (3 wt.% of titanium tetra-isopropoxide Ti[O(CH₂)₃CH₃]₄ in ethanol, 5000 rpm × 20 s), followed by thermal treatment (450 °C for 30 s in air). The thermal treatment reduces the thickness of as-prepared TiO₂ film approximately to the half of it. The crystallinity of the TiO₂ films should be anatase or amorphous, since the temperature in our thermal treatment is too low to generate rutiles (more than 800 °C required [14]). The typical thickness of TiO₂ was 13–17 nm (measured with a spectroscopic ellipsometer, J. A. Woollam Co. Inc., M-2000 U1). Finally, the entire surface was covered with a resist film (8.8 μm in thickness), and a gate area with 260 μm in gate length was opened by photolithography. The opened gate area contacts to electrolytes.

The electrical characteristics of TiO₂/2DEG-FETs were measured in phosphate equimolal solution (0.25 mM-KH₂PO₄ + 0.25 mM-Na₂HPO₄, pH 6.9), whereas long-term sustainability was examined in the cell culture medium (Dulbecco’s modified Eagle’s medium, DMEM [15–17]). The drain voltage (Vₘₐₜ), gate voltage (V₉₉), drain current (Iₘₐₜ), and gate current (I₉₉) of the TiO₂/2DEG-FET circuit were independently regulated (or measured) by two source meters (Keithley, 2400) and a data acquisition computer (NEC, PC-9821NF). A reference electrode (Ag/AgCl(KCl), BAS Inc., RE-1C) was placed in the solution to apply the gate voltage V₉₉. The outputs of source meters were directly connected to the TiO₂/2DEG-FET terminals without any source/load resistances.

3. Results and discussion

The 2DEG-FETs fabricated were depletion type, having the threshold gate voltage in the range of −2.0 V to −3.0 V. Gradual threshold shift to the negative side of V₉₉ was observed when the 2DEG-FET was operated in electrolytes under light with depletion region (Iₘₐₜ close to zero). The negative threshold shift was attributed to the accumulation of photoexcited holes at the interface of TiO₂/2DEG-FET, which will be reported separately. Typical transconductance (gₙ₉₉ = ΔIₘₐₜ/ΔV₉₉) measured in electrolytes was approximately 0.20 mA/V with I₉₉ less than 50 nA in the dark.

The long-term sustainability of TiO₂/2DEG-FET operation was examined in DMEM solution at room temperature under light (white room light, approximately 60 μW/cm²). Constant voltages of Vₘₐₜ = 1.0 V and V₉₉ = 0.5 V were applied to TiO₂/2DEG-FET, and current Iₘₐₜ was monitored. The same experiment was performed for bare-gate/2DEG-FET for comparison. As shown in Fig. 1, the Iₘₐₜ of the bare-gate/2DEG-FET decreased quickly after 30 min operation and fell down to zero within 3 h. This is because the bare-gate surface of 2DEG-FET was damaged by photoinduced oxidation and by etching by H₃PO₄ ions in DMEM solution as we previously reported [9]. When the channel size of 2DEG-FET was increased to 3 mm in width and 1.5 mm in gate length, the Iₘₐₜ decrease started after 3 h operation and fell down to zero within 10 h. On the contrary, the Iₘₐₜ of the TiO₂/2DEG-FET was reduced only 2.0% for 72 h, showing that the electrochemical oxidation/etching is effectively suppressed by thin film of TiO₂ covering the gate. The gate current I₉₉ was less than 250 nA, indicating that the electrochemical oxidation or etching is not significant on the TiO₂ surfaces. The TiO₂ thickness required to suppress the oxidation/etching of 2DEG-FET in DMEM under light was estimated to be approximately 8–10 nm. When TiO₂ with 8.5 nm in thickness was used to cover the gate area, the Iₘₐₜ in the similar experiment started to decrease after 1 h and fell to the half of the initial within 4 h. The TiO₂ films prepared in this study have a surface roughness of height root mean square (RMS) of 1.5 nm as described later. For the TiO₂ thickness less than 8–10 nm, the surface coverage by TiO₂ is not sufficient (probably due to pinholes in the TiO₂ films) to prevent the photochemical/electrochemical oxidation/etching of 2DEG-FET surfaces.

The TiO₂/2DEG-FET showed a good pH sensitivity (71 mV/pH), comparable or better than that of the conventional ISFETs. It indicates that there is Ti–OH bonding at the TiO₂ surfaces, which acts as a proton receptor, as many as Si–OH at SiO₂ surfaces. The TiO₂/2DEG-FET has also sensitivity for H₂O₂. The examination of H₂O₂ sensitivity was performed in the test solution of 14 ml phosphate equimolal solution (0.25 mM-KH₂PO₄ + 0.25 mM-Na₂HPO₄, pH 6.9). One hundred micro-litre solution of 0.3% H₂O₂ (diluted in 0.25/0.25 mM phosphate equimolal buffer) was injected into the 14 ml test solution five
times. The final concentration of H$_2$O$_2$ after the five injections was approximately 3.0 mM. The $V_{gs}$ was adjusted to maintain $I_{ds} = 100$ μA with $V_{ds} = 1.0$ V, and the temporal change of $V_{gs}$ was recorded. The examination was carried out in the dark in order to avoid photochemical effects. The resulted change of $V_{gs}$ is shown in Fig. 2, together with a result obtained with a conventional ISFET (BAS, ISFET, No. 001314). By the H$_2$O$_2$ injection indicated by arrows in Fig. 2, the $V_{gs}$ of TiO$_2$/2DEG-FET was increased stepwise, although the step fluctuated after the fourth injection. From the first step height, the H$_2$O$_2$ sensitivity of 410 mV/mM was estimated. A slower decrease (18 mV/min) followed the first and second step increase (270 mV/min) by H$_2$O$_2$ injection, to approximately 80% of the step increase. The step increase and slower decrease followed suggest that two distinct chemical reactions take place on TiO$_2$ surface with different time constants, although both remain unidentified so far. On the contrary, the $V_{gs}$ of the conventional ISFET decreased with a very slow rate (0.66 mV/min) without any clear steps corresponding to the H$_2$O$_2$ injection. The topmost layer of the ISFET used was Ta$_2$O$_5$ (not SiO$_2$ or SiN), which may lead to insensitiveness against H$_2$O$_2$. The pH measured separately before/after the five H$_2$O$_2$ injections was approximately pH 7.07/6.96. The pH-change was only 0.11, which should increase the $V_{gs}$ 7.8 mV by the five H$_2$O$_2$ injections (far below the $V_{gs}$ increase observed for TiO$_2$/2DEG-FET).

The surface of TiO$_2$ prepared on GaAs (0 0 1) substrates was smooth but porous as seen in Fig. 3, the surface image after thermal treatment observed with an atomic force microscope (AFM, PNI Corp., Nano-I2). Nanometer scale porous structures (30–60 nm in width and 5–10 nm in height) were observed with RMS 1.5 nm. The height thickness of this TiO$_2$ film was 16.7 nm. The water contact angle for the as-prepared TiO$_2$ surface was approximately 21°, while that of thermally treated TiO$_2$ surface was approximately 8.3°. In general, a porous surface exhibits a larger hydrophobicity than a smooth surface. The small contact angle obtained for the thermally treated TiO$_2$ surfaces suggests that the surface is terminated mainly by hydrophilic functional groups. The effective surface area of the TiO$_2$ gate is increased by the nanometer-scale porosity of TiO$_2$ surfaces, which may result in the higher H$_2$O$_2$ sensitivity observed in this study.
The biocompatibility of the TiO₂ surface was examined by direct cell culture on the surfaces without fibronectin (FN) or collagen coating. Alveolar type-2 epithelial cells of rats immortalized by SV40-large T antigen (T2 cells) [9,18,19] were seeded on four individual 10 mm × 7 mm TiO₂ surfaces (and on four individual as-cut GaAs (0 0 1) surfaces for control) with a density of 1.9 × 10⁵ cm⁻². The cells were incubated for 1 day in 625 μl DMEM solution without serum, in a CO₂ incubator at 37 °C. The surfaces were then observed with an optical phase-contrast microscope (Olympus, IX71) without further surface treatment (Fig. 4). As clearly seen in Fig. 4, a better cell adhesion was resulted on TiO₂/GaAs surfaces than on as-cut GaAs surfaces. The averaged density of living cells on the surfaces was 22,000 cells/cm² for TiO₂/GaAs surfaces, and 4300 cells/cm² for as-cut GaAs surfaces. We have observed no improvement of the cell adhesion for slightly etched GaAs with higher hydrophilicities (water contact angle 55°) than for the as-cut GaAs with less hydrophilicities (water contact angle 86°), suggesting that the hydrophilicity has little affect on cell adhesion. Therefore, we consider that the porosity in Fig. 3 contributes to the better cell adhesion, rather than the high hydrophilicity of the TiO₂ surfaces. Further investigation on this point is now under going and will be reported elsewhere.

4. Conclusion

The chemical/electrical properties of the surfaces of TiO₂ thin films prepared with the sol–gel technique were examined in order to develop TiO₂/2DEG-FETs for bio-sensing use. Thin TiO₂ film of 13–17 nm in thickness was effective to prevent the photochemical/electrochemical degradation of 2DEG-FET gate surfaces. The TiO₂/2DEG-FET showed the better H₂O₂ sensitivity of 410 mV/mM than the conventional ISFET. The surface of thermally treated TiO₂ was porous with nanometer scale roughness, and exhibits a high hydrophilicity. The direct T2 cell culture on the TiO₂ surfaces without pretreatment by FN or collagen was demonstrated.

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