

Quasi-Two-Dimensional Metal Oxide Semiconductors Based Ultrasensitive Potentiometric Biosensors

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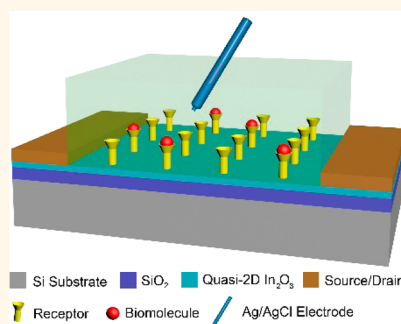
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Supporting Information

ABSTRACT: Ultrasensitive field-effect transistor-based biosensors using quasi-two-dimensional metal oxide semiconductors were demonstrated. Quasi-two-dimensional low-dimensional metal oxide semiconductors were highly sensitive to electrical perturbations at the semiconductor–bio interface and showed competitive sensitivity compared with other nanomaterial-based biosensors. Also, the solution process made our platform simple and highly reproducible, which was favorable compared with other nanobioelectronics. A quasi-two-dimensional In_2O_3 -based pH sensor showed a small detection limit of 0.0005 pH and detected the glucose concentration at femtomolar levels. Detailed electrical characterization unveiled how the device's parameters affect the biosensor sensitivity, and lowest detectable charge was extrapolated, which was consistent with the experimental data.

KEYWORDS: field-effect transistor, oxide semiconductor, quasi-two-dimensional, pH sensors, glucose sensors



Biosensors are of paramount importance in the field of medical diagnostics,¹ agriculture,² the food industries,³ environmental monitoring,^{4,5} and national security.⁶ Particularly, as we prepare for an aging society in the coming years, there are emerging demands for a new paradigm of medical services that can provide point-of-care testing with high accuracy and low cost, among which biosensors are a possible application.⁷ To this end, new technologies for the development of wearable medical devices that can assist in the management of chronic disease and the monitoring of vital signs are in high demand.^{8–12} Thus, the ubiquitous field-effect transistors (FETs) have been proposed as one of the most promising biomedical technologies and devices as they can be used as core sensing components.¹³ This is, due to their intrinsic amplification, rapid label-free detection and amenability for scale-up and integration with signal processing electronics.^{14–16}

Transistor-based biosensors (Bio-FETs) are a kind of FET in which the traditional gate and dielectric structure is replaced by a reference electrode, specific biomolecule receptors on the sensing surface, and an electrolyte between the electrode and the surface.^{17,18} Although the operation of the biological element can vary, as a potentiometric device, the performance of Bio-FETs normally relies on the effective charge of a binding biological analyte over the channel surface, which induces a change in the effective gate potential as well as the carrier

concentration in the transistor channel through capacitive coupling.^{19,20} Then, the variations are transduced into readable signals through changes in the electrical characteristics of the Bio-FETs.

Due to the intrinsic properties of Bio-FETs, shrinking the dimension of the channel material is an effective way to make them highly sensitive. Recent work has reported Bio-FETs based on one-dimensional (1D) and two-dimensional (2D) nanostructures such as nanowires,^{21–23} nanotubes,²⁴ nanobelts,²⁵ and nanosheets.^{26–29} Although those nanostructure Bio-FETs possess high sensitivity, both production and application pose major challenges due to significant device-to-device variation and complicated process integration.^{30–32}

Oxide semiconductors are leading candidates for n-type transistors and microelectronics with high yield and uniformity.^{33–36} The high electron mobilities ($>10 \text{ cm}^2 \text{ V}^{-1} \text{ s}^{-1}$) of oxide FETs guarantee high sensitivity and high signal-to-noise ratio in biosensing.^{37,38} Also, the high tolerance of structural defects and the minimized band tail trapping³⁹ of oxide semiconductors allow oxide FETs to be processed at low temperature ($<350^\circ\text{C}$), and solution processing is a convenient and feasible approach to deposit high-performance oxide

Received: January 27, 2017

Accepted: April 21, 2017

Published: April 21, 2017



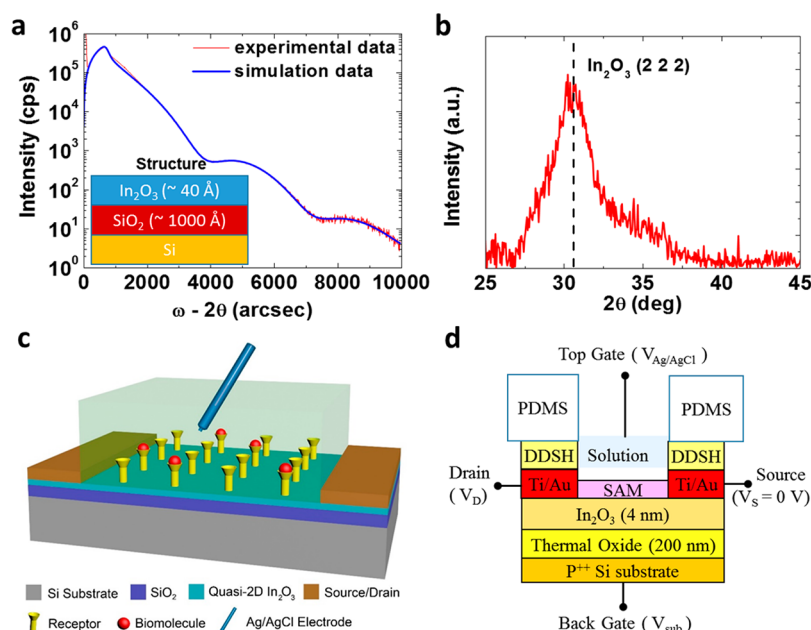


Figure 1. Quasi-2D In_2O_3 thin films and Bio-FETs. (a) X-ray reflectivity measurement and simulation result of quasi-2D In_2O_3 thin film. (b) Grazing incidence X-ray diffraction pattern of quasi-2D In_2O_3 thin film, indicating that it is crystallized. (c) Schematic representation of the Bio-FET and sensing scheme. (d) Device structure and measurement configuration.

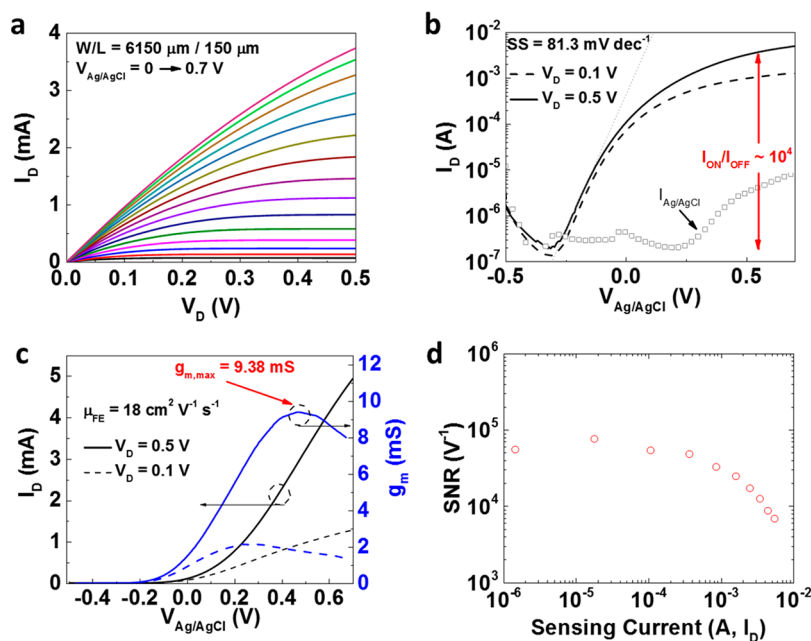


Figure 2. Quasi-2D In_2O_3 thin film transistors operated using aqueous salt gate. (a) Output characteristics. (b) Transfer characteristics in semilogarithmic scale under different drain bias. (c) Transfer characteristics and transconductance plot in linear scale. (d) Signal-to-noise ratio of the device as a function of the drain current.

semiconductors on a large scale at low cost.^{40–45} Previously, aqueous metal oxide precursor solutions^{46–52} were used successfully to fabricate high-quality oxide semiconductors with field-effect mobility as high as $36.31 \text{ cm}^2 \text{ V}^{-1} \text{ s}^{-1}$,⁴⁶ to fabricate conformal bioelectronics for wearable health-monitoring platforms⁵³ and for sub-nanomolar neurotransmitter detection.⁵⁴ Yet, to date, there have been limited systematic studies of oxide semiconductor-based Bio-FETs that addressed the fundamental factors of how the devices' parameters affect their sensitivity or any detailed electrical characterization to estimate the lowest detectable charge.

Herein, we present a quasi-2D oxide semiconductor-based Bio-FET and establish a proper characterization protocol to examine various performance metrics and identify high sensitivity. Oxide semiconductors with ultrathin thicknesses of 4 nm, high uniformity, and smooth surfaces with roughness averaging only 0.4 nm were demonstrated. These low-dimensional oxide semiconductors can be designated as a quasi-2D material because the thickness is even smaller than many of the nanostructures mentioned previously. For Bio-FETs made with quasi-2D oxide semiconductors, the ultrathin channels have a higher surface-to-volume ratio, which allows for

better electrostatic control of the devices' channels and their turn-on characteristics than a thicker channel would.^{55,56} Since the carriers in the quasi-2D semiconductors are confined within the channel in the surface normal direction, electronic perturbation at the semiconductor surface can induce a remarkable effect on the transistors' conductance, so the quasi-2D Bio-FETs are more sensitive to analytes. We successfully demonstrated pH sensors with detection limits as low as 0.0005 and glucose sensors with <7 fM detection limits. Detailed electrical characterization of transconductance and low-frequency noise established the correlation between intrinsic transistor performance and biosensor benchmarks, and comparisons conducted between various nanostructures for the Bio-FETs showed that the quasi-2D Bio-FETs yielded superior performances while requiring only simple processing. By understanding the correlation between the properties of the channel material and the devices' performance metrics, we were able to provide performance benchmarks and guidelines for the design of stable and sensitive Bio-FETs for various sensing applications.

RESULTS AND DISCUSSION

The quasi-2D In₂O₃ thin films used in the Bio-FETs were fabricated following our previous reports,⁴⁶ and X-ray reflectivity (XRR) measurements and simulations verified that a representative film was obtained that had a thickness of 4 nm, a surface roughness of 0.4 nm, and an average density of 5.3 g cm⁻³ (Figure 1a). A representative grazing incidence X-ray diffraction (GIXRD) plot of the film is shown in Figure 1b; the plot showed a weak peak of (222)-In₂O₃ preferred orientation, which indicated that the film had a nanocrystalline structure. Controlling the crystalline structure of the film is crucial in determining the electrical properties of the quasi-2D In₂O₃ thin film, and we will discuss how it affects the performance of the biosensor later. The schematic of the device's structure and the measurement configuration of the quasi-2D In₂O₃ Bio-FET are shown in Figures 1c,d, respectively. The device's detailed fabrication and decoration are shown in the Methods section.

To evaluate the performance of the quasi-2D Bio-FET, first, it was important to understand the general principles associated with the operation of a Bio-FET in an aqueous salt environment (pH 4, 0.1 M buffer solution). Figure 2a shows that, in the "on" state, the output curves demonstrated clear ohmic behavior with a well-defined linear regime at low bias, and the drain current became saturated when the bias voltage increased further. The saturation behavior was similar to the pinch-off effect in conventional silicon FETs, which was caused by a local accumulation of carriers around the drain electrode. All current–voltage (*I*–*V*) curves passing through the origin point indicate the minimal contribution of the gate leakage current (*I*_{Ag/AgCl}) to the drain current (*I*_D). Also, the linear region showed no rectifying behavior, even when the gate bias (*V*_{Ag/AgCl}) was 0.7 V. The transfer curve in semilogarithmic scale at a constant *V*_D = 0.1 V (in the linear region) and *V*_D = 0.5 V (saturation region) showed clearly a turn-on voltage of −0.316 V and on/off ratio greater than 10⁴. The typical *I*_{Ag/AgCl} was measured to be at least 2 orders of magnitude smaller than *I*_D, and it can be reduced further by patterning the channel region. The subthreshold swing (SS) was determined empirically from the transfer curve shown in Figure 2b, using the following equation:

$$SS = \frac{dV_{Ag/AgCl}}{d(\log I_D)} \quad (1)$$

The quasi-2D In₂O₃ Bio-FET had an SS value of 81.3 mV dec⁻¹ and showed an excellent aqueous electrolyte dielectric property. Although the thermodynamic limit for a conventional FET is 60 mV dec⁻¹, the SS in our devices can be improved further by suppressing the surface defects in the metal oxide and optimizing the surface decoration process. For the evaluation of transistor's performance, the transconductance (*g*_m) of the quasi-2D Bio-FET was calculated from an *I*_D–*V*_{Ag/AgCl} curve using the following equation:

$$g_m = \frac{dI_D}{dV_{Ag/AgCl}} = \frac{W}{L} C_{DL} \mu_{FE} V_D \quad (2)$$

where *W* is the channel width, *L* is the channel length, and *C*_{DL} is the electrical double layer capacitance per unit area in 0.1 M ionic strength aqueous solution reported previously (25.52 μF cm⁻²).⁵⁷ Figure 2c shows that *I*_D and *g*_m increased with increasing *V*_{Ag/AgCl}, and the maximum *g*_m value of 9.38 mS was obtained at a drain voltage bias of 0.5 V at *V*_{Ag/AgCl} = 0.472 V. We extracted a *μ*_{FE} of 18 cm² V⁻¹ s⁻¹ from electrolyte-gated driving, which was impressive, considering its simple process and superiority to other electrolyte-gated oxide FETs that have been reported.^{57–64}

Quasi-2D metal oxide FETs have several properties and advantages. First, due to the nature of solution processing regarding solvent evaporation and precursor decomposition, nanopores are left behind in the film during deposition, typically.⁶⁵ An ultrathin film minimizes the formation of nanopores and yields high film density.³⁶ Second, reducing the oxide semiconductor dimension, especially below 20 nm, also widens the energy band gap due to energy quantization phenomena,⁶⁶ and a wider band gap can suppress off-current more effectively.²⁷ Third, there are reduced shallow trap densities per unit area in the ultrathin semiconductor channel due to its reduced thickness. As a result, SS improves, which leads to fast filling-up of states as the Fermi level moves toward the conduction band when the FET switches from the off-state to the on-state.^{67,68} Because channel thickness is much smaller than the Debye length of the metal oxide,^{69,70} bulk accumulation is possible, and it contributes to better gate control. The *μ*_{FE} extracted from electrolyte-gated driving was very similar to that extracted from SiO₂ gate-dielectric driving (19 cm² V⁻¹ s⁻¹, Figure S1). This result indicates that different dielectric–semiconductor interfaces have little influence on the field-effect mobility,⁵⁷ which is likely due to bulk conduction in ultrathin semiconductor films and can lead to improved *μ*_{FE} and device-to-device uniformity (Figure S2).⁵⁵ However, further study, including simulation of the device, will be needed to verify the last argument.

As described in eq 1, transconductance indicates how sensitive the sensing signal is in response to a gating effect. However, the noise associated with the signal also increases as the sensing current increases (Figure S3a), and a trade-off exists between maximizing *g*_m and minimizing current noise power density (*S*_I). Therefore, the signal-to-noise ratio (SNR) was proposed as an important performance metric for sensor devices to determine their limit of detection (LOD)^{37,71,72} by taking into account signal transduction as well as noise limitation, and this can be written as

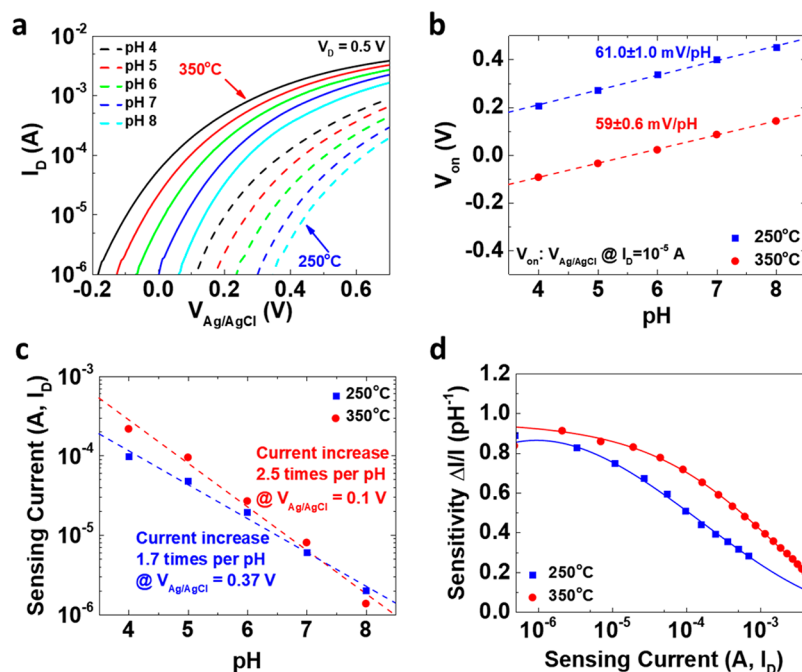


Figure 3. Quasi-2D In₂O₃ Bio-FETs as pH sensors using indium oxide semiconductors with different structures. (a) Transfer characteristics after exposure to varying pH. (b) Turn-on voltage and (c) sensing current versus pH. (d) Sensitivity versus sensing current.

$$SNR = \frac{\Delta\Phi_s \times g_m}{\sqrt{BW \times S_I (f = 1 \text{ Hz})}} \quad (3)$$

where S_I ($f = 1$ Hz) is the drain current noise power density at 1 Hz (Figure S3b), and BW is the measurement bandwidth. In the rest of the discussion, we will refer to SNR for BW = 1 and $\Delta\Phi_s = 1$ V for fair comparison with the literature.³⁸ Figure 2d shows that SNR was high in the subthreshold region and decreased as the sensing current increased. This is crucial information because it determines the proper gate bias to use in a real-time sensing scheme. A peak SNR of $\sim 10^5$ V⁻¹ translated into a minimum detectable voltage of 30 μ V (SNR = 3), and assuming a quasi-2D Bio-FET top-gate capacitance of 2.35×10^{-5} F, we obtained the minimum detectable charge to be around 7.06×10^{-10} C. Assuming that each analyte molecule carries one charge, the platform theoretically is capable of sensing analytes with concentrations as low as 7 fM. With an ideal pH sensitivity of 60 mV/pH for the quasi-2D Bio-FET, we obtained an LOD in terms of pH of 0.0005.

It is well-known that processing temperature greatly affects the structure of the thin film and the performance of the device. We examined the electrical performance of quasi-2D Bio-FETs annealed at 250 °C (Figure S4) and 350 °C. Comparison with 350 °C annealed In₂O₃ Bio-FETs and a turn-on voltage (V_{on}) of 250 °C annealed devices had a positively shifted and much lower g_m (0.9 mS) as shown. The average μ_{FE} values extracted from the electrolyte-gated and SiO₂ dielectric-gated devices were around 2 cm² V⁻¹ s⁻¹. To understand the difference in electrical performance, GIXRD (Figure S5) and X-ray photoelectron spectroscopy (XPS, Figure S6) were performed. Whereas In₂O₃ films showed nanocrystalline structures, regardless of annealing temperatures, 350 °C annealed In₂O₃ films had a higher proportion of oxide lattices and oxygen deficiencies than the 250 °C annealed film. The higher annealing temperature (350 °C) promotes the dehydroxylation and conversion of the indium hydroxide into the In₂O₃

crystalline lattice, and it also increases the oxygen vacancies and electron concentration in the thin film.

To acquire an intuitive understanding of the importance of μ_{FE} and V_{on} on biosensing, pH sensing was conducted using Bio-FETs annealed at 250 and 350 °C, respectively. The pH sensing is based on the protonation/deprotonation of the channel surface terminating groups depending on the pH value of the electrolyte, thereby changing the channel surface potential. When the channel surfaces of Bio-FETs are functionalized with (3-aminopropyl)triethoxysilane (APTES), a linear dependence of the surface potential on the electrolyte pH is expected.⁷³ The channel sensing surfaces were exposed to 100 mM buffer solution with various pH values, and the resulting transfer curves were analyzed. The measurements showed that I_D increased with $V_{Ag/AgCl}$ with the same SS, irrespective of the pH value (Figure 3a), which consequently produced a linear shift of the turn-on voltage V_{on} (Figure 3b) and an exponential dependence of I_D in the subthreshold region (Figure 3c). The role of APTES is to protect quasi-2D oxide films and to provide a sensing surface with pH sensitivity reaching the Nernst limit (60 mV pH⁻¹, Figure S7) irrespective of oxide surface properties. However, quasi-2D Bio-FETs annealed at 250 °C showed a μ_{FE} almost 10 times smaller than those annealed at 350 °C. Similarly, the sensing signal (I_D) was smaller for quasi-2D Bio-FETs annealed at 250 °C, and it only increased 1.7 times when the pH value increased by 1 (pH⁻¹) in the subthreshold regime, whereas the quasi-2D Bio-FETs annealed at 350 °C increased 2.5 times.

Sensitivity, as another important performance metric, is defined as the relative change in the sensing signal corresponding to a unit change in the pH value. Figure 3d shows the comparison of sensitivities between Bio-FETs annealed at different temperatures. From these comparisons, we found that the devices annealed at 350 °C showed a larger sensitivity in the entire operation regime, reaching peak sensitivity of ~ 1 in the subthreshold region. A comparison of

the sensitivities of Bio-FETs made with various materials is summarized in Table 1, which shows that, for oxide

Table 1. Comparison of Quasi-2D In_2O_3 with Other Nanoscale Semiconductors for Bio-FET Application

nanoscale semiconductors	dimension (nm)	maximum sensitivity ($\Delta I/I$) [pH^{-1}]	comments	ref
graphene	7	0.02	no band gap	87
silicon nanowire	30	1.3	batch-to-batch variation and	75
MoS_2 nanosheet	5	1.9	challenging process	27
SnO_2 nanobelt	150	0.57	integration	25
In_2O_3 nanoribbon	20	0.66	lower uniformity of sputtered thin film	70
quasi-2D In_2O_3	4	~ 1	simple process and high reproducibility	this work

semiconductors, thinner channels result in higher sensitivity, which is consistent with the findings of a previous report.⁷⁰ This result provided guidance to boost the sensitivity of the Bio-FETs.

Devices annealed at 250 °C showed a positively shifted V_{on} . To achieve optimal SNR and sensitivity, it was found that the devices had to be gate-biased at $V_{\text{Ag/AgCl}} = 0.37$ V in the sensing scheme. In contrast, the devices annealed at 350 °C could be gate-biased close to 0 V. This is an important note because higher gate bias induces charge injection and ion migration at the semiconductor/liquid interface (in addition to possible signal drifting),⁷⁴ and it also increases power consumption. So, in the latter part of the discussion, we selected 350 °C annealed Bio-FET decorated with APTES and measured it in the subthreshold regime to obtain high sensitivity for biosensing.⁷⁵

Next, the specific sensing of biomolecules using the quasi-2D Bio-FET was investigated through the boronic acid–glucose

interaction in which the boronic acid and glucose act as models for receptor and target molecules, respectively. Figure 4a shows the operation principle of glucose detection. A quasi-2D oxide surface functionalized with boronic acid was exposed to a glucose environment, and the bound glucose molecules created boronate anions to modulate the electronic transport properties of the Bio-FET in a concentration-dependent manner. The detailed surface functionalization process is described in the Methods section, and it was confirmed by XPS analysis (Figures S8 and S9). The functionalization process has been reported and characterized by other researchers,^{76–78} so we focused on the electrical properties of the functionalized Bio-FETs. Figure 4b shows that a device functionalized with boronic acid exhibited a significant decrease (18%) in sensing current upon the addition of a 3 pM glucose solution (in 0.1× phosphate-buffered saline, PBS). This agrees with the effect of boronate anion–glucose electrostatic gating, which depletes electron carriers at the semiconductor/liquid interface in the n-type In_2O_3 film. The whole process is reversible, and the device can return to the baseline after being immersed in DI water for a while.

To quantify the sensor's response to glucose, we plotted the continuous monitoring of sensing signal response as a function of glucose concentration (Figure 4c). By adding glucose solution with increasing concentration into the 0.1× PBS solution, we observed that the device had a wide sensing range from 10^{-13} to 10^{-3} M. In the optimal sensing range (10^{-11} to 10^{-5} M), the sensing current increased an average of 22% when the glucose concentration reduced by a factor of 10 in each step. This result was consistent with the V_{on} shift of 8.1 mV dec^{-1} , which was extracted from transfer curves (Figure 4d). The plot of V_{on} versus glucose concentration agreed with the

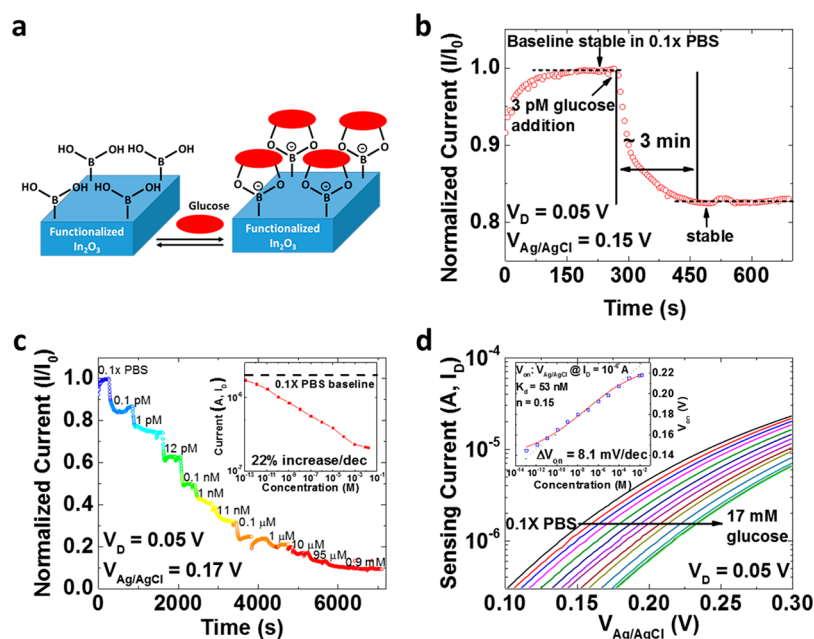


Figure 4. Quasi-2D In_2O_3 Bio-FETs as glucose sensors. (a) Illustration of the principle of glucose sensing on boronic acid functionalized In_2O_3 sensing surface. Bound glucose forms a boronate anion complex that has electrostatic effects on the quasi-2D In_2O_3 . (b) Normalized electrical output (I/I_0) versus time showing clear plateau and transition region before and after glucose addition. (c) Response for a functionalized device to various concentration of glucose. The inset is a stabilized sensing current versus concentration in logarithmic scale. (d) Transfer curves for a functionalized device responding to various concentration of glucose. The inset is threshold voltage versus glucose concentration in semilogarithmic scale.

Table 2. Comparison of Analytical Performance of Glucose Sensors with Direct Electrostatic Sensing

device platform	sensitivity ($\Delta I/I$) [%/dec]	optimum sensing range (M)	detection limit (M)	K_d (M)	ref
carbon nanotube	5.5	10^{-5} – 10^{-4}	3×10^{-7}	7.6×10^{-5}	82
reduced graphene oxide	9.1	10^{-9} – 10^{-2}	2×10^{-9}	1.5×10^{-8}	85
graphene	13	10^{-6} – 10^{-3}	5×10^{-7}	3.9×10^{-5}	83
quasi-2D In_2O_3	22	10^{-11} – 10^{-5}	10^{-13}	5.3×10^{-8}	this work

Hill–Langmuir equation⁷⁹ for equilibrium ligand–receptor binding:

$$V_{\text{on}} = \Delta V_{\text{on,max}} \frac{(c/K_d)^n}{1 + (c/K_d)^n} + V_{\text{on,pristine}} \quad (4)$$

where c is the glucose concentration, K_d is the dissociation constant of boronic acid–glucose interaction, n is the Hill coefficient describing the cooperativity of the binding, $\Delta V_{\text{on,max}}$ is the V_{on} shift when the boronic acid molecules are bound to glucose, and $\Delta V_{\text{on,pristine}}$ is the V_{on} in the PBS solution. The best fit to the glucose data indicated that $\Delta V_{\text{on,max}} = 93$ mV, $\Delta V_{\text{on,pristine}} = 137$ mV, $K_d = 53$ nM, and $n = 0.15$. The extracted cooperative parameter, n , was smaller than 1, consistent with a previous report in which it was indicated that the boronic acid–glucose interaction is a negative cooperative binding.⁸⁰ Also, the extracted dissociation constant was much lower than various non-enzymatic glucose sensors reported previously,^{80–83} which is highly desirable for the detection of low concentrations of glucose. With a LOD below 7 fM (Figure S10) and a wide optimum sensing range from 10^{-11} to 10^{-5} M, this device has performance metrics superior to those of the various glucose sensors that use direct electrostatic sensing (Table 2).^{84,85}

We used PBS solutions for sensing because they can regulate the pH when hydrogen ions are generated during the boronic acid–glucose interaction, ensuring that changes in the sensing signal can be attributed solely to the generation of boronate anions. However, the PBS concentration cannot be too high because the sensitivity of the device to glucose was degraded critically due to Debye screening when the experiment was conducted in $1\times$ PBS (Supporting Information S1). To rule out the possibility of nonspecific interactions and false signals, a control experiment was conducted using an unfunctionalized device in which the surface terminating group was APTES (Supporting Information S2). The small increase in the sensing current ($\sim 5\%$) likely was observed due to nonspecific binding and was not correlated with glucose concentration.

CONCLUSIONS

In summary, we demonstrated a Bio-FET based on the quasi-2D In_2O_3 that has high field-effect mobility and an ultrathin structure, which make it highly advantageous for biosensing compared with other nanostructure semiconductors. Not only can quasi-2D In_2O_3 provide excellent electrostatics and sensitivity due to its atomically thin nature, it also provides a scalable platform that facilitates mass fabrication at low cost, which is an imperative requirement for practical applications. A pH sensor with ultrahigh sensitivity (1 pH^{-1}) as well as small LOD (0.0005 pH) was demonstrated. Specific detection of glucose also was demonstrated, and an extremely low LOD (<7 fM) was achieved in $0.1\times$ PBS solution. Measurement in the subthreshold region resulted in high sensitivity as well as a high signal-to-noise ratio. In addition, it was shown ultrasensitive surfaces of the quasi-2D In_2O_3 could be greatly affected by the interaction interface between boronic acid molecules and

glucose. Given the simplicity and sensitivity of the demonstrated biosensor platform, we expect that quasi-2D oxide Bio-FETs will provide great opportunities in the healthcare and food industry applications.

METHODS

Precursor Preparation. The 0.1 M quasi-2D In_2O_3 precursor was prepared by dissolving 0.3 g of indium nitrate hydrate ($\text{In}(\text{NO}_3)_3 \cdot x\text{H}_2\text{O}$, Aldrich, 99.999%) in 10.0 mL of deionized (DI) water (Sigma).

Device Fabrication. The transistor has a bottom-gate, top-contact structure. P^{++} highly doped silicon wafers with 200 nm thermal oxide were used and cut into pieces as substrates. The substrates were sonicated in acetone and isopropyl alcohol to remove grease and dust. Afterward, the substrates were treated with ultraviolet irradiation for 10 min to remove organic residues and to improve wettability. The In_2O_3 precursor was spin-coated on substrates at 3000 rpm for 30 s. As-spun films were prebaked at 100°C for 1 min followed by thermal annealing at the desired temperature for 3 h. Titanium (Ti) and gold (Au) of 10 and 30 nm thicknesses were deposited sequentially using an e-beam evaporator through the shadow mask to form interdigitated source and drain electrodes. The length and width of the transistor channel were estimated to be 6150 and 150 μm , respectively.

Surface Functionalization and Immobilization. Electrodes were protected from the electrolyte environment by anchoring 1-dodecanethiol (DDSH) molecules on the gold surface through the sulfur that terminated the alkyl thiol chains. The electrodes behaved as ideal polarized electrodes and suppressed charge transfer across the metal–solution interface.⁸⁶ The substrates were incubated in a 1 mM ethanolic solution of DDSH ($\text{CH}_3(\text{CH}_2)_{11}\text{SH}$) for 1 h and rinsed with ethanol. Thereafter, the substrates were silanized in a 1% ethanolic solution of (3-aminopropyl)triethoxysilane ($\text{H}_2\text{N}(\text{CH}_2)_3\text{Si}(\text{OC}_2\text{H}_5)_3$) for 24 h, rinsed with ethanol, and then dried with flowing nitrogen to form an amine-terminated sensing surface. For glucose sensing, two steps were followed to form a boronic acid terminated group.^{77,78} First, the substrates were immersed in 20 mM glutaraldehyde (GA, $\text{CH}_2(\text{CH}_2\text{CHO})_2$) in a PBS ($1\times$) solution for 24 h and rinsed with DI water. Then, the substrates were immersed in 10 mL of $1\times$ PBS solution containing 0.1 g of 3-aminophenylboronic acid (APBA, $\text{H}_2\text{NC}_6\text{H}_4\text{B}(\text{OH})_2$) and 0.4 g of sodium cyanoborohydride (NaBH_3CN) for 24 h.

Film and Device Characterization. XRR and GIXRD measurements were performed on a Jordan Valley D1 diffractometer using $\text{Cu K}\alpha_1$ radiation. Both the XRR and the GIXRD used double axis diffraction. The incident angle in GIXRD was kept at 0.5° , and the count time and step size for GIXRD were 5 s and 0.05° , respectively. Jordan Valley REFS 4.5 software was utilized to fit the XRR experimental data to determine the density, thickness, and roughness of the film (the grading characteristics). The chemical properties of the films were examined using X-ray photoelectron spectroscopy (Kratos XPS Axis Ultra DLD). The device measurements were performed using an Agilent 4155C semiconductor parameter analyzer. For the top-gate measurement, a silver chloride electrode (World Precision Instruments, Super Dri-Ref Reference Electrode) was used as the gate to guarantee the stable operation of a biosensor. A polydimethylsiloxane (PDMS) solution reservoir chamber was used to define the contact area of the analyte solution. When conducting pH sensing, solutions for each pH buffer (100 μL , 100 mM) were introduced into the PDMS chamber using a syringe. The solution to be analyzed was used to flush the PDMS chamber between measurements. When conducting glucose sensing, first 50 μL of PBS solution was added into

the PDMS chamber, and the baseline was recorded. Glucose solutions (2 μ L) of increasing concentration were added into the PDMS chamber, subsequently.

ASSOCIATED CONTENT

Supporting Information

The Supporting Information is available free of charge on the ACS Publications website at DOI: 10.1021/acsnano.7b00628.

Back-gate measurement of the Bio-FET, device uniformity, signal-to-noise analysis, device performance with 250 °C annealing temperature, indium oxide surface property with different annealing temperatures, pH sensitivity with and without surface decoration, surface decoration process, dependence of glucose sensor sensitivity on Debye length, response of unfunctionalized devices to glucose (PDF)

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Notes

The authors declare no competing financial interest.

ACKNOWLEDGMENTS

We would like to thank Dr. Yufei Mao, Dr. Andrew Pan, and Hongxiang Zhao for valuable discussions on device physics, noise analysis, and organic chemistry, respectively. This work was financially supported by grants from the National Science Foundation (Grant No. ECCS-1202231, Program Director Dr. Paul Werbos; ECCS is a program under Engineering Division), National Science Foundation (Grant No. CHE-1230598, Program Manager Linda S. Sapochak), and was supported by the MISP (Ministry of Science, ICT & Future Planning), Korea, under National program for Excellence in Software program (the SW oriented college support program) (R7718-16-1005) supervised by the IITP (Institute for Information & Communications Technology Promotion).

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