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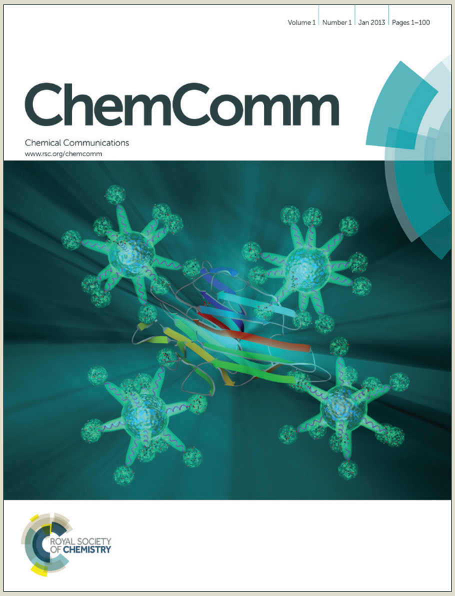
Volume 1 | Number 1 | Jan 2013 | Pages 1–100

ChemComm

Chemical Communications

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Cite this: DOI: 10.1039/c0xx00000x

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ARTICLE TYPE

An extended-gate type organic field effect transistor functionalised by phenylboronic acid for saccharide detection in water

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Received (in XXX, XXX) Xth XXXXXXXXX 20XX, Accepted Xth XXXXXXXXX 20XX
DOI: 10.1039/b000000x

Saccharides in water are detected electrically using an extended-gate type organic field effect transistor (OFET) functionalised by a phenylboronic acid monolayer. The response patterns for the monosaccharides are significantly different, suggesting that OFET devices can successfully read out the saccharide recognition behaviour of boronic acids and be potentially applied to healthcare devices modified with supramolecular receptors.

Playing a fundamental role in metabolism, saccharides are one of the most important biomolecules.[1] For example, glucose is the primary source of metabolic energy in cells. A decline in glucose transport is associated with serious health issues.[2] For example, diabetes mellitus has now spread globally and causes complications such as blindness, heart disease, apoplectic stroke and kidney failure.[3] Therefore, a significant amount of attention is being devoted to the development of saccharide sensors for use in healthcare applications. To date, one of the most popular glucose sensors has been based on an enzymatic reaction between glucose oxidase and glucose.[4] The disadvantages of enzyme-based sensors is their stability, which is insufficient for long-term use and storage. In addition, they are influenced by dissolved oxygen in biological fluids.

Saccharide sensors based on artificial receptors are being researched extensively. Although smart artificial receptors can bind saccharides noncovalently,[5] the noncovalent recognition of heavily solvated saccharides in water is generally difficult. In this context, our focus has been on the utilisation of phenylboronic acid (PBA) for saccharide detection. PBA derivatives not only serve as a Lewis acid metal centre,[6] but also form cyclic boronate esters with *cis*-diol moieties of saccharides in aqueous media.[7] Accordingly, colourimetric,[8] fluorometric,[9] electrochemical,[10] and surface plasmon resonance[11] detection of saccharides based on boronate esterification have been reported. Recently, inorganic or carbon nanotube transistors modified with PBAs have also been developed as saccharide sensor devices.[12] We are proposing new saccharide sensor devices based on organic field effect transistors (OFETs) that are modified with PBA receptors. OFETs can be applied to wearable and disposable sensors because of their mechanical flexibility and low manufacturing costs.[13] For these reasons, we believe that the OFET sensors are one of the more promising candidates for use in healthcare devices. Although enzyme-based OFET saccharide sensors have been thoroughly investigated,[14] the research of non-enzyme-based OFETs is still in its early stages. We herein report for the first time on an enzyme-free detection of saccharides in water using an extended-gate type OFET device.

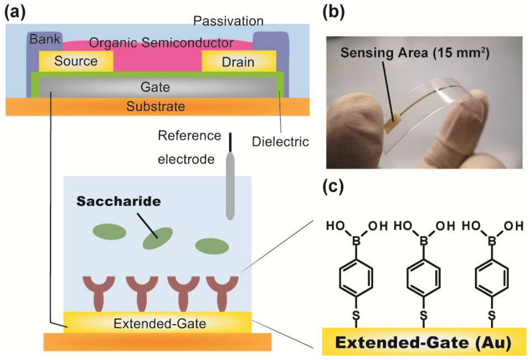

Fig. 1 (a) Schematic structure of the extended-gate type OFET designed for saccharides detection. (b) A photograph of the detection portion (*i.e.* the extended-gate electrode). (c) The extended-gate electrode functionalized by PBA.

We designed an extended-gate type OFET saccharide sensor, based on research work that assumes saccharide detection is performed in water using OFETs. In the designed device, the transistor device portion is separated from the saccharide sensing site, hence degradation of the organic transistor in water can be prevented. A gold (Au) thin-film on a thin plastic film was used as the extended-gate electrode, allowing us to functionalise its surface with PBA derivatives. The device structure for the extended-gate type OFET is shown in Fig. 1 (a). The transistor was specifically designed to achieve low-voltage operation. To fabribate the device, an Aluminum (Al) gate electrode was deposited onto a glass substrate using thermal evaporation (30 nm in thickness). A gate dielectric was then created consisting of an aluminum-oxide layer (5 nm) and a tetradecylphosphonic acid self-assembled monolayer (SAM).[15] The aluminum oxide layer was formed by treating the Al gate electrode, with an oxygen plasma. The SAM layer was prepared by immersing the substrate in a 2-propanol solution of tetradecylphosphonic acid at room temperature. Au source-drain electrodes (30 nm)

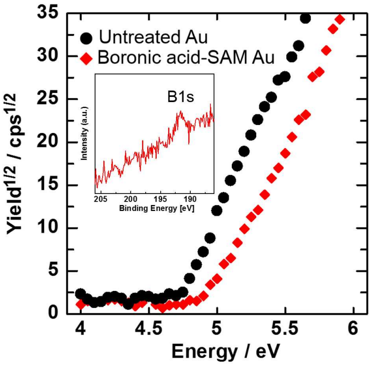

Fig. 2 Photoelectron yield spectroscopy measurements of the gold (Au) gate electrodes in air. Untreated Au (black circle), 4-mercaptophenyboronic acid-treated Au (red diamond). Inset shows a XPS spectrum of B 1s region of the PBA-SAM Au.

were deposited on the gate dielectric layer using thermal evaporation and patterned using a shadow-mask, such that the resultung channel width and length of the OFET were 1000 and 50 µm, respectively. For preparation of the bank layers, an amorphous fluoropolymer (Teflon® AF1600) in fluorinert™ (FC-43) was applied using a dispensing equipment. Then, a semiconductive polymer, poly(2,5-bis(3-hexadecylthiophene-2-yl)thieno[3,2-*b*]thiophene[16] in 1,2-dichlorobenzene was drop-casted, and then annealed at 175 °C in N_2 atmosphere. For passivation of the device, Cytop® was spin-coated onto the device (100 nm) and baked at 100 °C. Finally, an extended-gate electrode consisiting of Au was prepared on a polyethylene naphthalate film substrate (125 µm) using thermal evaporation, such that the sensing area for the extended-gate electrode was 15 mm^2 (Fig. 1 (b)). The extended-gate Au electrode was immersed in a methanol solution containing 10 mM of 4-mercaptophenylboronic acid for 1 h at room temperature to form a SAM layer (Fig. 1(c)). The treated electrode was rinsed using ethanol and water and used for the saccharide dectection in an aqueous solution.

First, we proceeded to inspect the PBA-SAM layer on the Au electrode surface with photoelectron yield spectroscopy measurements in air, which showed a higher ionisation potential on the SAM-treated Au electrode (5.00±0.06 eV) than an untreated Au electrode (4.79±0.05 eV) (Fig. 2), which indicated that the electron-withdrawing functional group (*i.e.* PBA) covered the Au surface.[17] Additionally, X-ray photoelectron spectroscopy (XPS) revealed the presence of carbon, oxygen, sulfur, and boron with their expected binding energies (see Fig. 2 (inset) and the SI).[18] Furthermore, we measured a water contact angle on the SAM-treated Au electrode using a contact angle goniometer. The water contact angle of the SAM-treated Au electrode (50.9±2.3°) was higher than that on the untreated Au electrode (40.5±1.3°) (see the SI), which was presumed to be due to the hydrophobicity of the phenyl moiety. The thickness of the PBA layer was estimated to be 0.8 nm (an assuming refractive index = 1.72) by using variable angle spectroscopic ellipsometry measurements at seven incident angles from 45 ° to 75 ° in steps of 5 °. Overall, characterisation results of the Au surface supported that the functionalisation of PBA on the Au was successfully accomplished.

The electrical characteristics of the OFET were measured. As anticipated, the fabricated OFET device functioned reproducibly at below 3 V, confirming that the device could be applied to sacchride detection in water. We next investigated the ability of the extended-gate type OFET to detect saccharides. Fig. 3 shows the transfer characteristics of the OFET upon titration with phosphate buffer solutions[19] of saccharides. Fig. 3 inset exhibits no significant changes in the gate-source current (I_{GS}-V_{GS}), meaning that electrochemical reaction did not occur at the gate.[20] We observed distinct positive shifts of the transfer curves with increasing the saccharide concentrations, although the changes in the field effect mobility for the OFET devices were very small. These observed positive shifts are attributed carrier concentration changes in the OFET channel by the negatively charged boronate esters on the extended-gate electrode, because the operation mechanism of extended-gate type FET sensors can be explained by an interfacial potential shift at the gate/solution interface.[21] These results suggest that the OFET device could read out the molecular recognition behaviour of PBAs.

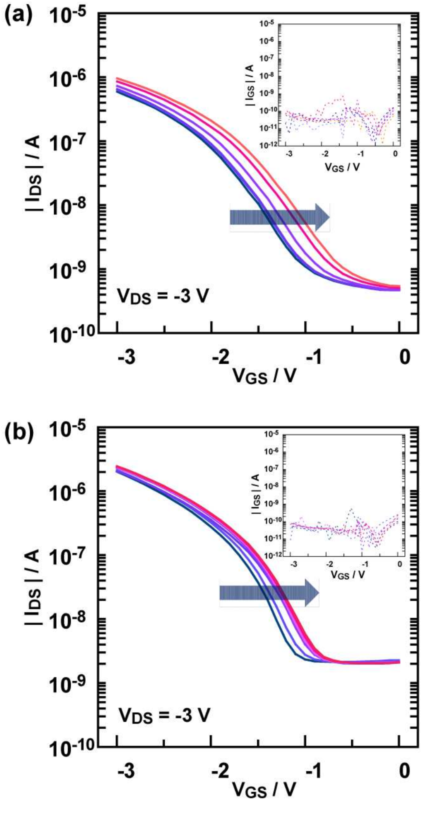

Fig. 3 Transfer characteristics (I_{DS}-V_{GS}) of the OFET device upon titration with saccharides, (a) glucose and (b) fructose, in a phosphate buffer solution (100 mM) at pH 7.4 at r.t. [Saccharide] = 0-20 mM. Inset shows the gate-source current (I_{GS}-V_{GS}).

Fig. 4 shows the relationship between the saccharide concentration and change in threshold voltage, as calculated from the transfer characteristics. While the titration profile of glucose showed a sigmoidal response,[12c] significant responses to 20 mM saccharides were unpredictably found to be in following order: glucose > galactose ≥ fructose > mannose.

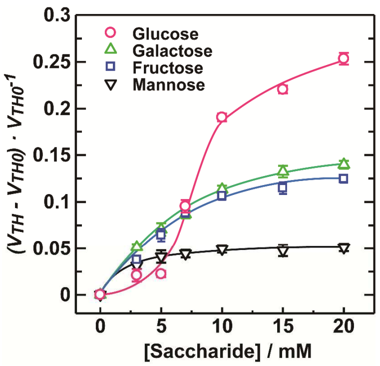

Fig. 4 Changes in threshold voltage for the OFET devices by the saccharides at various concentrations in a phosphate buffer solution (100 mM) with pH 7.4 at r.t. [Saccharide] = 0-20 mM.

The value of (V_{TH}-V_{TH0}) / V_{TH0} for glucose is larger than with the values for other saccharides under similar conditions by a factor of 2.1 for galactose, 2.3 for fructose, and 5.6 for mannose. James et al. reported similar selectivity of saccharides using diboronic acid fluorescent photo-induced electron transfer sensors,[3] implying that the SAM layer formed from PBAs on the extended-gate might bind glucose with bis(boronate complex).[22] The response pattern of glucose is different among saccharides, which could suggest different of the binding modes.[23] To promote a greater understanding of the detection mechanism of glucose, we attempted to detect glucose using the fabricated OFET device with an extended Au electrode functionalised by a SAM of a benzenethiol/4-mercaptophenylboronic acid mixture (1:1 molar ratio). Mixing with benzenethiol results in reducing the density of PBA on the Au electrode. As a result, we observed no sigmoidal response, although the response pattern to glucose was similar to those to other saccharides (see the SI). This supports that the main binding mode between glucose and PBA-SAM on the Au electrode is not 1:1 molar ratio. Various response patterns are very important to achieving multi-analyte sensing using sensor arrays.[24] OFET devices can readily be integrated into an array, hence the OFET sensor device fabricated here would be suitable for simultaneous sensing of saccharides.

In summary, we have successfully demonstrated a reliable supramolecular sensor device utilising an OFET to detect saccharides in water. The titration results showed that the OFET device can read out electrically the saccharide-recognition behaviour of the PBA-SAM. The OFET device can detect glucose concentrations higher than 5 mM, a sensitivity which covers the threshold for the diabetes diagnosis (a fasting plasma glucose level is 7 mM, a nominal plasma glucose level is 11 mM).[25] To the best of our knowledge, this is the first report of a saccharide sensor employing an extended-gate type OFET with an artificial receptor. We believe that these results widen the avenues for the potential development for future OFET-based supramolecular sensors used for saccharide detection in healthcare applications.

We gratefully acknowledge the financial support from JST and JSPS (Grant-in-Aid for Research Activity Start-up, No.26888002). We also thank Dr. M. Mamada of Yamagata University for his helpful discussions.

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† Electronic Supplementary Information (ESI) available: General information of experiments, water contact angle measurements, XPS and transfer characteristics of the OFET. See DOI: 10.1039/b000000x/

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