



Short communication

Effect of passivation on the sensitivity and stability of pentacene transistor sensors in aqueous media

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ARTICLE INFO

Article history:

Received 29 December 2010

Received in revised form 4 March 2011

Accepted 27 March 2011

Available online 2 April 2011

Keywords:

OTFT sensors

Encapsulation effect

pH sensor

AntiBSA detection

Bioelectronics

ABSTRACT

Charge-detecting biosensors have recently become the focal point of biosensor research, especially research onto organic thin-film transistors (OTFTs), which combine compactness, a low cost, and fast and label-free detection to realize simple and stable in vivo diagnostic systems. We fabricated organic pentacene-based bottom-contact thin-film transistors with an ultra-thin insulating layer of a cyclized perfluoro polymer called CYTOP (Asahi Glass Co., Tokyo, Japan) on SiO₂ for operation in aqueous media. The stability and sensitivity of these transistor sensors were examined in aqueous buffer media with solutions of variable pH levels after the passivation of perfluoro polymers with thicknesses ranging from 50 to 300 nm. These transistor sensors were further modified with an ultra-thin film (5 nm) functional layer for selective BSA/antiBSA detection in aqueous buffer media, demonstrating a detection capability as low as 500 nM of concentrated antiBSA. The dissociation constant from the antiBSA detection results was 2.1×10^{-6} M. Thus, this study represents a significant step forward in the development of organic electronics for a disposable and versatile chemical and bio-sensing platform.

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1. Introduction

As the demand for diagnostic laboratories continues to increase with increased health care costs, the necessity for rapid and inexpensive medical analyses has become increasingly apparent. The use of optical measurements is predominant, but this method has several limitations due to the required fluorescent dyes and expensive detectors (Neumann et al., 2002). In addition, because optical equipment is not portable, in vivo and in situ measurements are also very difficult. Recent advances in bio-chemical detection research, in part benefiting from the overwhelming progress made in organic electronics, have shown great promise for a viable, low-cost alternative to current optical detection systems (Khan et al., 2010; Roberts et al., 2008).

To date, progress in organic materials has shown a great deal of promise due to the utilization of thin-film and multilayer devices, especially for organic light-emitting diodes (OLEDs) (Friend et al.,

1999; Bhansali et al., 2009) and organic solar cells (Wohrle and Meissner, 1991). The rapid progress in this field has been, in part, due to improvements in fabrication processes and the design of new materials, with remarkable upgrading in the electronic properties of semiconducting (Murphy and Fréchet, 2007) and insulating (Klauk et al., 2007; Roberts et al., 2009) materials.

Additionally, micro-biosensors based on OTFTs have recently attracted a considerable amount of attention owing to their potential for miniaturization, standardization, mass-production and a suitable configuration for smart sensor (Khan et al., 2010; Torsi et al., 2008). However, the development of devices based on an air/aqueous stable organic semiconductor still faces many challenges. The open morphology with large clefts between the grains of polycrystalline organic molecules limits the charge transport, which shortens the life of the devices due to degradation of the materials (Dimitrakopoulos and Mascaró, 2001; Zhu et al., 2002; Andraz and Gvido, 2009). Another relevant issue is the method of encapsulation or surface modification, which are both considered to be unfavorable due to solution processing issues (Khan et al., 2010; Sreenivasan and Gleason, 2009).

In this work, we evaluate bottom-contact pentacene transistors as bio-chemical sensors in aqueous media with two different types of top passivation with variable thicknesses, i.e., perfluoro-1-3-dimethylcyclohexam (PFDMCH) and/or a cyclized perfluoro polymer called CYTOP by plasma-enhanced chemical vapor depo-

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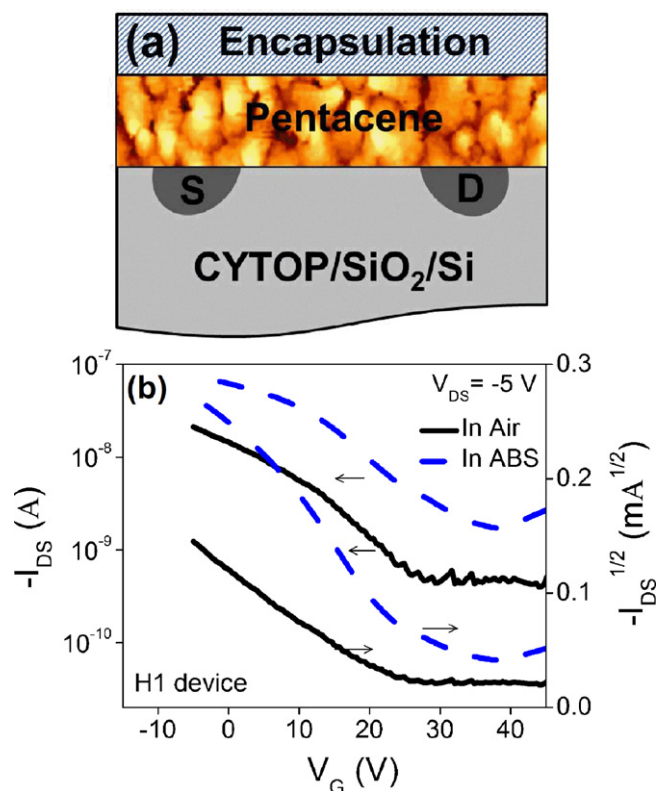


Fig. 1. (a) Schematic representation of the OTFT as a bio-chemical sensor investigated in this study. Fabrication procedure for a bottom contact OTFT with 30 nm pentacene on 15 nm CYTOP/200 nm SiO₂ and source-drain electrodes with a channel *W/L* of 10. The entire device was passivated with PE-CVD based ppPDMCH layer and/or spin coated CYTOP layer with variable thickness. (b) [H1-sensor] transfer characteristics (I_{DS} vs. V_G) at V_{DS} of -5 V in ambient (solid curves) and in PBS (blue dashed curves). (For interpretation of the references to color in this figure legend, the reader is referred to the web version of the article.)

sition (PE-CVD) and/or spin-coating. Since medical analyses are conducted by monitoring the pH variations that occur during various bio-chemical reactions, therefore, we underscore the effect of variable pH levels on these transistor sensors. Additionally, the transistor sensor surfaces were modified with functional layer of maleic anhydride (MA) using PE-CVD and were used to detect BSA/antiBSA immunoassay formation as a model system to demonstrate the resulting detection possibilities.

2. Experimental

All materials were purchased from Aldrich and were used as received without further purification unless otherwise stated. *N*-ethyl-*N'*-(3-dimethylaminopropyl)-carbodiimide hydrochloride (EDC) and *N*-hydroxysuccinimide (NHS) were purchased from Fluka and rabbit monoclonal antiBSA was obtained from Millipore.

The fabrication of the bottom-contact pentacene transistor is schematically illustrated in Fig. 1a. Additional details pertaining to the fabrication procedure are given in supporting information (SI) section (Khan et al., 2011). The polymerization of perfluor-1-3-dimethylcyclohexam and maleic anhydride was carried out in a custom-built PE-CVD reactor following a well-established procedure in our laboratory (Khan et al., 2010, 2011). Three different thicknesses were used on top of the transistor devices: H1 consisting of 50 nm PE-CVD of PFDMDCH polymer, H2 consisting of 300 nm of spin-coated CYTOP polymer, and H3 consisting of 600 nm of spin-coated CYTOP polymer.

For operation in aqueous media for bio-chemical sensing experiments, all bio-chemical molecules were diluted in 10 mM of a

freshly prepared concentrated phosphate buffered saline (PBS) solution at pH 7.4. For the pH detection experiments, solutions with different pH levels were prepared using a specific amount of HCl and NaOH depending on the required pH. A custom-built flow cell constructed with Plexiglas was used to confine the buffer and analyte solution to the OTFT channel region, as shown in online SI section, Fig. S1. The contact area was sealed with a Viton O-ring and the flow channel was connected to a peristaltic pump (NovoChem). The peristaltic pump delivered the solution from the solution reservoirs to the sample at a constant rate of 300 μ L/min to minimize mass transfer limitations of the analyte to the sensor surface, which has been shown to occur below 20–30 μ L/min (Mabeck and Malliaras, 2006).

All electrical and biosensing measurements were performed with a Keithley 4200 semiconductor characterization system in ambient air and in aqueous buffer media.

3. Result and discussion

Details of the device fabrication, functionalization, and experimental conditions used here are described in detail elsewhere and can be found in SI section (Khan et al., 2010, 2011). Briefly, we fabricated a bottom-contact OTFT with 30 nm of pentacene as the active layer on a polymer dielectric with a width (*W*) of 500 μ m and length (*L*) of 50 μ m (Fig. 1a). The transfer and output characteristic in ambient air at drain-source voltage (V_{DS}) = -10 V are featured in online SI, Fig. S2. These devices exhibited an average field-effect mobility of 0.0054 cm²/V s with an on-off ratio of 7×10^4 and a threshold voltage (V_{th}) of -2 V at V_{DS} = -10 V. Moreover, these devices showed no hysteresis due to the CYTOP thin insulation layer on SiO₂ (Jang et al., 2008).

OTFTs with a top passivation layer were further characterized in air and PBS at a low V_{DS} of -5 V, which is necessary for stable operation in aqueous media. The transfer characteristics at V_{DS} = -5 V are shown in Fig. 1b, and Fig. S3 represents the typical behavior of the p-type OTFTs under ambient conditions (greater detail regarding these results are summarized in Table S1). The flow cell was laminated on to the transistor surface with an inlet and outlet opening. After injecting PBS solution, we observed an increase in both the on- and off-current with a small/negligible shift in V_{th} , as illustrated by the blue dashed curve (H1 device, Fig. 1b). The H2 and H3 devices showed an increase in both the on- and off-current with a rather high shift in V_{th} , as shown in SI section, Fig. S3a and b, respectively. The exact mechanisms are still not fully understood at this point, but it is clear that water and (deprotonated) surface hydroxyl groups play a central role by acting as charge carrier traps in polaronic states at the water-semiconductor interface. However, strong dipole fluctuations in the PBS lead to a change in the mobility via thermally activated hopping in the direction parallel to the interface (Tobias et al., 2009; Kumaki et al., 2008; Chua et al., 2005). Nevertheless, these influences were small. Remarkably, the transistors still functioned well in PBS. The output plots are shown in SI, Fig. S4.

To evaluate the implementation of the label-free detection method for monitoring bio-chemical species electronically based on micro-fabricated OTFTs, we used constant bias conditions in which V_G and I_{DS} were set to facilitate the current flow within the channel. The occurrence of a chemical or physical absorption is subsequently converted to the ΔI_{DS} response as a function of time, which ultimately depends on the analyte composition, concentration, and the OTFT bias conditions.

Biosensing experiments, particularly antibody-antigen interactions, depend mainly on the pH of the working solution due to the different isoelectric point (pI) of proteins (Lahiri et al., 1999; Carvalho and Carmona-Ribeiro, 1998). Thus, the sensitivity and

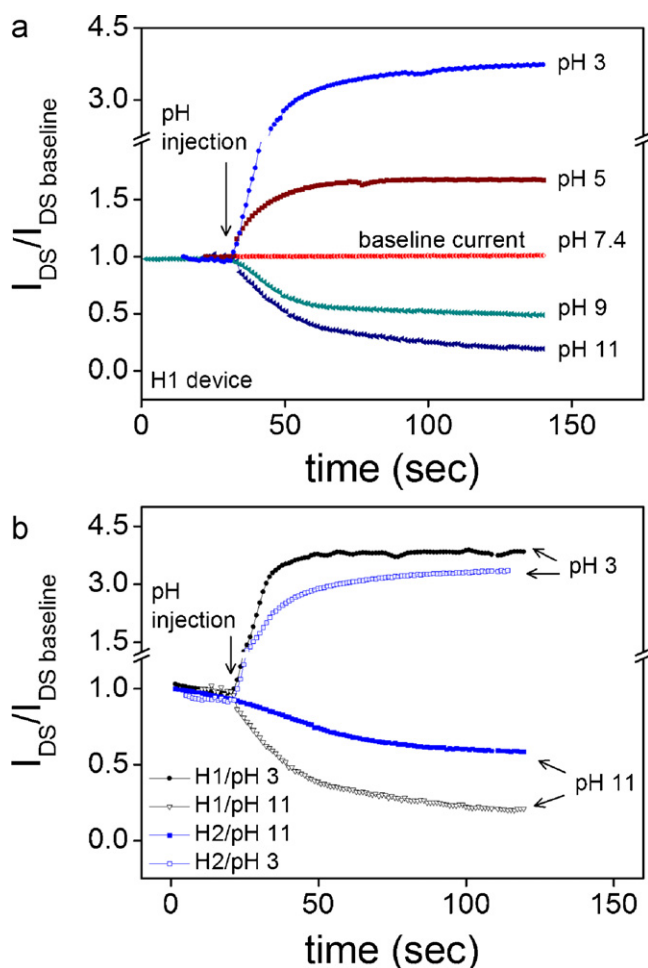


Fig. 2. pH detection in PBS of a representative OTFT with 30 nm pentacene on 15 nm CYTOP/200 nm SiO_2 and W/L of 10 measured at constant bias ($V_G = -2$ V and $V_{DS} = -5$ V) with a flow rate of 300 $\mu\text{L}/\text{min}$. (a) [H1-device] current response ($I_{DS}/I_{DS\text{ baseline}}$) with time upon exposure to the solutions of four different pH (3, 5, 9 and 11) and (b) current response ($I_{DS}/I_{DS\text{ baseline}}$) with time upon exposure to solution of pH 3 and pH 11 to H1 (black curves) and H2 (blue curves) devices. (For interpretation of the references to color in this figure legend, the reader is referred to the web version of the article.)

long-term stability of all three devices were initially examined in parallel by exposing the unfunctionalized OTFT channel to different pH solutions. In PBS, the baseline I_{DS} was recorded after 60 s of constant bias (a drain-source bias $V_{DS} = -2$ V and a gate bias $V_G = -5$ V) prior to the injection of the pH solution. Next, four solutions with pH 11, 9, 5 and 3 at a concentration of 10 mM were injected sequentially onto the H1 device. The recorded value of ΔI_{DS} against time is shown in Fig. 2a. Between each trial, the device was rinsed extensively with PBS to restore the baseline I_{DS} . We observed an increase in I_{DS} with the acidity (pH 3, 5) and a decrease with the basicity (pH 9, 11) of the solution (Roberts et al., 2008). Further experiments were performed to endorse the role of passivation on the sensitivity by injecting identical pH solutions onto the H2 and H3 devices, as shown in Fig. 2b. Remarkably, we observed a response of the H2 device to the pH 3 and pH 11 solutions, whereas the H3 device showed no response at all. Further chemical detection using ethanol on the H1 device is shown in SI section, Fig. S5.

More detailed studies on these transistors were carried out using the protein as a detecting species. The search for methods and a format for the sensitive detection of immunoassay reaction is currently attracting considerable attention due to wide application of the findings in gene therapy (Agrawal and Lyer, 1995), single-molecule enzymology, microarrays and microchip-

based capillary electrophoresis (Chiem and Harrison, 1998). The covalent attachment of an antigen is only possible when there is surface functionality (Khan et al., 2010). To accomplish this requirement, maleic anhydride (MA) monomer was polymerized within a plasma chamber during the PE-CVD process to achieve an ultra-thin film (5 nm) of poly maleic anhydride (pMA) on all three devices. The functionality originating from the monomer is retained in the polymer film as a consequence of the low average power obtained by pulsing the input power (Schiller et al., 2002). In the presence of PBS, the anhydride groups on the pMA surface are activated using a standard EDC/NHS activation step (Khan et al., 2010, 2011). Proteins consist of amino-acids; thus, the amine terminations of BSA are expected to attach to the pMA layer by means of amide bond formation, as schematically exposed in the inset of Fig. 3a. Moreover, BSA has been shown to be effective for the detection of antibodies (Chiem and Harrison, 1998). Intuitively, it is clear that the protein shows polarity, which is a function of the aqueous phase, pH and ionic strength, among other properties. This polarity normally defined by the isoelectric point of a respective analyte. The pI of bovine serum is pH 5.4; thus, above this pH, the amino-acids of BSA show average negative charges, and vice versa. Thus, we anticipate a decrease in the current upon immuno formation on the sensor surface (Carvalho and Carmona-Ribeiro, 1998; Park and Salleo, 2009).

Next, we injected the BSA with an identical concentration at 0.5 μM onto all three devices and monitored the change in I_{DS} over-time, as shown in Fig. 3a. The I_{DS} value of the H1 device (blue curve) started to decrease with time until equilibrium between the bulk concentrations (C_0) and the corresponding surface coverage was reached. In contrast, the H2 (black curve) and H3 devices (pink curve) showed no change in their I_{DS} values. We also applied a highly concentrated solution of BSA ~ 50 μM to the surface of the H2 and H3 devices only and measured the ΔI_{DS} . The I_{DS} value started to decrease (the black curve of the H2 device) while the H3 device current remained steady (pink curve), as shown in Fig. 3b. The sensing behavior was consistent with the pH detection on all three devices. From these results, we presume that the back-gate effect became no more effective when the passivation thickness reached some threshold limit.

We further demonstrated the efficiency of the H1 series of OTFTs using an antibody for concentration-dependent sensing applications. In this experiment, the antigen was chemically attached to a transistor sensor surface (cf. Fig. 3a) that would eventually detect the antibody selectively from the solution, as schematically shown in the inset of Fig. 3c. In PBS, the baseline I_{DS} was recorded after 30 s of constant bias followed by an injection of a 0.5 μM solution of monoclonal antiBSA, and decrease in the I_{DS} was measured as a function of time until equilibrium between the bulk concentration and the corresponding surface coverage was reached. We repeated the immunodetection process with 1 μM , 5 μM and 10 μM concentrated solutions of antiBSA (Fig. 3c), which provides excellent discrimination at different concentrations of antiBSA within the initial 20 s.

These findings were consistent with our initial hypothesis that BSA/antiBSA possesses negative charges above the pI, resulting in a decrease in the value of I_{DS} . It was previously reported that in the case of bovine serum, a larger change in the electric flux occurs at pH values above the pI (Chun and Stroeve, 2002), which results in a high density of carboxylate ions (COO^-) in the BSA/antiBSA complex. We can presume that these COO^- ions will draw the holes from the transistor channel region and increase the overall channel resistance, leading to a decrease in I_{DS} . Additionally, the use of 10 mM PBS ensures the detection of BSA/antiBSA within the Debye length (λ_D) ~ 7 nm (Ishikawa et al., 2009a).

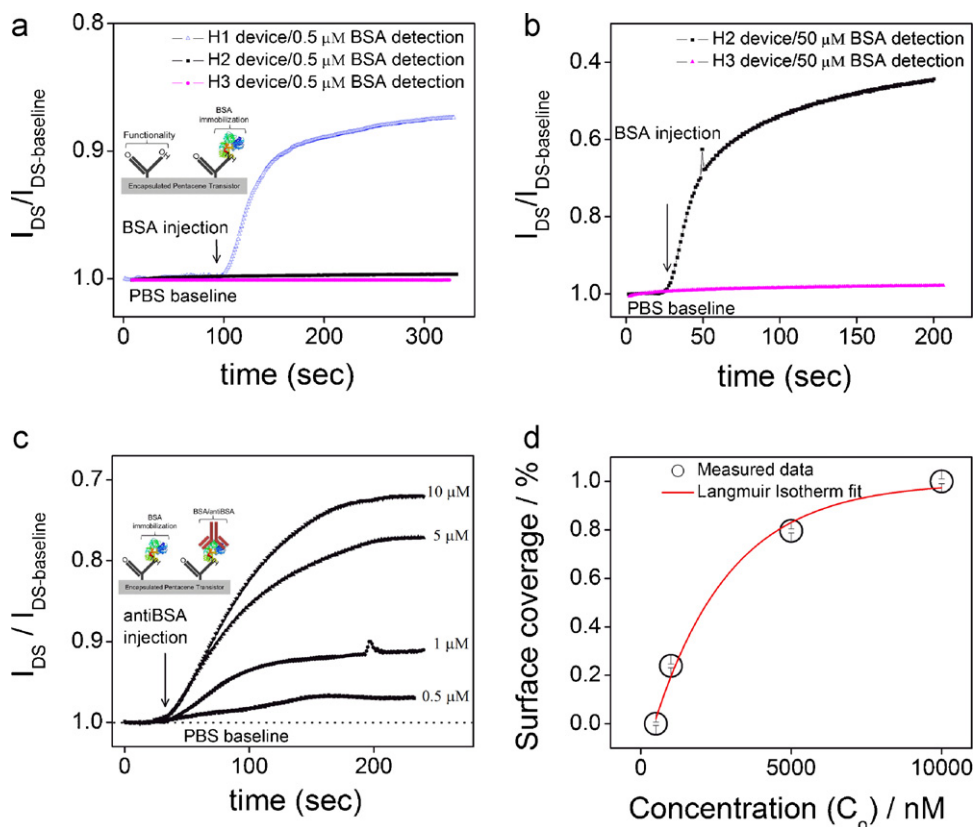


Fig. 3. Kinetic measurement showing the normalized I_{DS} vs. time using pentacene transistors at a constant bias ($V_G = -2$ V and $V_{DS} = -5$ V) with a flow rate of 300 $\mu\text{L}/\text{min}$. (a) OTFT current response ($I_{DS}/I_{DS\text{-baseline}}$) with time upon exposure to the BSA (0.5 μM) blue curve (H1), black curve (H2) and pink curve (H3). Inset; the schematic representation of in situ immobilization of the BSA protein. (b) OTFT current response ($I_{DS}/I_{DS\text{-baseline}}$) with time upon exposure to the BSA (50 μM) black curve (H2-device) and pink curve (H3-device). (c) [H1-device] current response ($I_{DS}/I_{DS\text{-baseline}}$) with time upon exposure to the antiBSA at different concentration. Inset; the schematic representation of in situ BSA/antiBSA immunodetection and (d) the Langmuir isotherm plot between the surface coverage and the antiBSA concentration for the data points taken from part "c". Red curve shows the Langmuir fit. (For interpretation of the references to color in this figure legend, the reader is referred to the web version of the article.)

A plot of the sensor response vs. the antiBSA concentration (dots) was fitted using a conventional Langmuir isotherm model (solid curve) is shown in Fig. 3d (Langmuir, 1916; Ishikawa et al., 2009b). Application of this analytical model yields a dissociation constant (K_D) of 2.1×10^{-6} M, which is three orders of magnitude smaller than that of N-protein using In_2O_3 nanowire transistor-based sensors (Ishikawa et al., 2009a). Regardless, many advantages exist when using organic devices created through a simple, low-cost processing method.

4. Conclusion

We demonstrated a thin-film transistor sensor based on a multilayer structure that is stable in aqueous media, thus facilitating a significant step forward in the development of a label-free and versatile real-time sensing platform. The sensitivity of the OTFT sensors was tailored by the passivation layer thickness; however, highest sensitivity was achieved using a PE-CVD-based 50 nm PFDMCH passivation layer. A Langmuir isotherm model was used to fit the data, resulting in a dissociation constant (K_D) of 2.1×10^{-6} M. Most importantly, our approach allows for the incorporation of water-unstable organic semiconductors as the active transport layer rather than restricting the selection to highly stable materials.

Acknowledgments

H.U.K. acknowledges the financial support from IRTG/1404 (funded by the DFG) and the Max-Planck Society (Germany). J.-

J.K. acknowledges the WCU (R31-2008-000-10075-0) and BSR (R15-2008-006-01001-0) support through the NRF funded by the Ministry of Education, Science and Technology of Korea.

Appendix A. Supplementary data

Supplementary data associated with this article can be found, in the online version, at doi:10.1016/j.bios.2011.03.031.

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