Accurate Cortisol Detection in Human Saliva by an Extended-Gate-Type Organic Transistor Functionalized with a Molecularly Imprinted Polymer

Y. Zhang[1)], Y. Sasaki[1)], H. Fan[1)], K. Ohshiro[1)], Q. Zhou[1)], W. Tang[1)], X. Lyu[1)], and T. Minami*[,1)]
[1)] Institute of Industrial Science, The University of Tokyo, 4-6-1 Komaba, Meguro-ku, Tokyo 153–8505, Japan

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Corresponding author*: tminami@iis.u-tokyo.ac.jp

Abstract
We herein report an extended-gate-type organic field-effect transistor functionalized with a molecularly imprinted polymer (MIP-OFET) for sensitive and selective detection of salivary cortisol as a reliable biomarker for psychological disorders. The fabricated MIP-OFET sensor has successfully detected salivary cortisol at a low limit of detection value (i.e., 0.72 μg/L) owing to the synergy effect of the optimized MIP design and the inherent amplification ability of the OFET device. In addition, the highest sensor response to cortisol over similarly structured steroids and interferents contained in human saliva indicated favorable selectivity. Furthermore, the applicability of the sensor device for real-sample analysis has been evaluated by a spike-and-recovery test. The accurate recovery rates (102-110%) suggested that the MIP-OFET sensor can be used for a diagnosis of salivary cortisol levels.

1. Introduction
Salivary cortisol is a reliable parameter for the evaluation of states of psychological disorders, and thus the development of easy-to-use chemical sensors for cortisol is required. For this purpose, we decided to employ a solution-processable organic field-effect transistor (OFET) device as an extended-gate-type chemical sensor platform for sensitive detection owing to its inherent amplification ability. A molecularly imprinted polymer (MIP), which provides three-dimensional recognition networks with appropriate geometric configurations, is a promising artificial molecular recognition material for selective cortisol detection. In this study, the OFET-based chemical sensor functionalized with the MIP layer was developed for salivary analysis (Figure 1(a)).

2. Experiment
In the OFET device fabrication, vacuum thermal deposition was performed to form a gate electrode made of aluminum and source/drain electrodes made of gold (Au). An organic semiconductor material, poly{2,5-bis(3-tetradecylthiophen-2-yl)thieno[3,2-*b*]thiophene} (PBTTT-C14) was drop-casted onto the channel region (width:50 μm, length:1000 μm). The surface of OFET was entirely covered with a hydrophobic polymer for passivation. Next, the extended-gate electrode was fabricated on a polyethylene naphthalate (PEN) film, which consisted of a thermally deposited Au layer and an Au nanostructure layer for enhancement of the adhesion by physisorption between the MIP layer and the Au electrode surface. Density functional theory calculations were performed for the optimization of a preorganized structure of cortisol (as a template) and 1,2-diaminobenzene (as a monomer for MIP), which

determined 1:5 molar ratio (= cortisol:1,2-diaminobenzene) as appropriate conditions. The polymerization of 1,2-diaminobenzene was performed by electrochemical deposition in the presence of cortisol, followed by the extraction of the template cortisol from the polymer layer in a NaOH solution. The surface morphology of the polymer layer was characterized by using various surface analysis methods, which indicated the successful formation of the MIP layer. In the sensing mechanism using the extended-gate structure, the gate voltage of OFET was applied through an Ag/AgCl reference electrode, and the detectability of the MIP-OFET sensor was evaluated at low operation voltages (<|3| V).

3. Results and discussion

Figure 1(b) shows the change in the transfer characteristics of the OFET device with an increase in cortisol concentrations. A sensitive response to cortisol with a limit of detection of 0.72 µg/L indicated the applicability of the MIP-OFET sensor to the quantification of salivary cortisol. Moreover, the MIP-OFET sensor exhibited a highly selective response to cortisol over similar structural steroids and interferents contained in human saliva. Notably, the spike-and-recovery test results for cortisol in non-diluted human saliva (Ethics Authorization Code: 22–312) showed accurate recovery rates (102-110%), which suggested the potential of MIP-OFET as a diagnostic tool for salivary cortisol levels (Figure 1(c)).

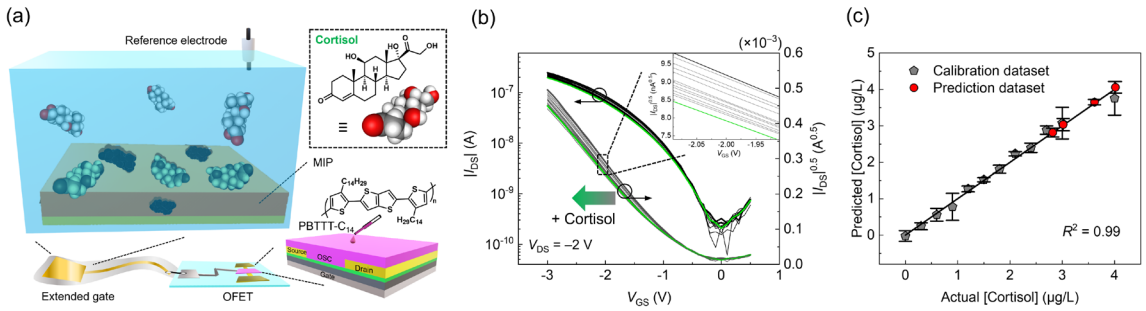

Figure 1 (a) Conceptual illustration of the extended-gate-type OFET functionalized with the MIP layer for cortisol sensing. (b) Transfer characteristics of the MIP-OFET sensor upon the addition of cortisol in Dulbecco's phosphate-buffered saline. (c) Spike-and-recovery test for cortisol in human saliva.

4. Conclusions

We developed a MIP-OFET sensor for accurate analysis of salivary cortisol. The low limit of detection value (0.72 µg/L) and the high selectivity in salivary cortisol sensing suggested the synergy effect of the optimized MIP design and the inherent amplification ability of the OFET device. We believe that the combination of MIPs and OFETs will burden the potential of organic electronics as point-of-care diagnostic devices.

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Reference

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