Functionalized Organic Thin Film Transistors for Biosensing

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Conspectus

The rising of organic bioelectronics efficiently bridges the gap between semiconductor devices and biological systems, leading to flexible, light-weight and low-cost organic bioelectronic devices suitable for health or body signal monitoring. The introduction of organic semiconductors in the devices can soften the boundaries between microelectronic systems and dynamically active cells and tissues. Therefore, organic bioelectronics has attracted much attention recently due to the unique properties and promising applications. Organic thin film transistors (OTFTs), owing to their inherent capability of amplifying received signals, have emerged as one of the state-of-the-art biosensing platforms. The advantages of organic semiconductors in terms of synthetic freedom, low temperature solution processing, biocompatibility and mechanical flexibility, render OTFTs ideal transducers for wearable electronics, e-skin and implantable devices.

How to realize highly sensitive, selective, rapid and efficient signal capture and extraction of biological recognition events is the major challenge in the design of biosensors. OTFTs are prone to converting the presence or change of target analytes into specific electrical signals even in

complex biological systems. More importantly, OTFT sensors can be conveniently functionalized with chemical or biological modifications and exhibit substantially improved device sensitivity and selectivity as well as other analytical figure of merits, including calibration range, linearity and accuracy. However, the stability and reproducibility of the organic devices need to be further improved.

In this account, we first introduce the unique features of OTFTs for bioelectronic applications. Two typical OTFT configurations, including organic electrochemical transistor (OECT) and electrolyte gated organic field effect transistor (EGOFET), are highlighted in their sensing applications mainly due to the operation of the devices in electrolytes and the combination of ionic and electronic charge transports in the devices. These devices are potentiometric transducers with low working voltages (<1V) and high sensitivity, and are thus suitable for wearable applications with low power consumption.

Secondly, the functionalization strategies on channel materials, electrolytes and gate electrodes based on various modification methods and sensing mechanisms are discussed in sequence. In an OECT or EGOFET -based biosensor, the device performance is particularly sensitive to the physical properties of the two interfaces, including channel/electrolyte and gate/electrolyte interfaces. Any change in the potential drop or capacitance of either interface can influence the channel current substantially. Therefore, the functionalization of the interfaces is critical to the sensing performance. In particular, when an electrochemically active material is modified on the interfaces, the reaction of the analyte catalyzed by the modified material can influence the interface potential and lead to a channel current response much stronger than that of a conventional electrochemical measurement. So the biosensors are much more sensitive than typical analytical methods due to the signal amplification of the transistors.

Thirdly, the processing techniques including screen printing and inkjet printing and the possibility for mass production are discussed. The applications of organic transistors in wearable electronics and healthcare monitoring systems especially the fabric OECT-based biosensors for noninvasive detections are presented. It is expected that the versatile organic transistors will enable various compact, flexible and disposable biosensors compatible with wearable electronics.

1. Introduction

Since the first discovery of animal electricity in the experiment carried out by Luigi Galvani in the 18th century, the world of bioelectronics has experienced numerous changes and leap-forward developments. Extensive research works have been carried out, aiming to achieve efficient communications between biological systems and electrical circuity. The bioelectronic communications have been systematically investigated along two directions, one is for electrical sensing and detection of biological substances and signals, while the other focuses on mimicking biofunctionalities with artificial devices. A typical bioelectronic device is composed of several essential components, including active interface materials to transduce biological signals to electrical ones, circuitry for signal transformation and recording, and a power source. Undoubtedly, the devices especially the interface materials should have good biocompatibility, stability and conformability with biological systems.

Organic semiconductors have been extensively studied for bioelectronic applications, thanks to their similar chemical structures with various biological molecules and their intrinsic biocompatibility.[1] Some organic semiconductors possess several key features in terms of synthesis freedom, mechanical flexibility and solution processability, making it possible to integrate multi-functional organic devices on low-cost flexible substrates.[2] More importantly, the swelling

characteristic of organic materials can lead to soft interfaces and good compatibility with biological tissues. In electrolyte solutions, hydrated ions can be easily injected into the bulk of the organic materials for efficient ion-electron exchange and transfer, which is also a critical feature of organic biosensors.[3]

Among all sorts of organic bioelectronic devices, organic thin film transistor (OTFT)- based sensors have received much attention for their promising applications on monitoring neural signals and cell activities, and sensitive detections of biological analytes, due to their inherent amplification function.[4] Typically, two major categories of OTFTs are employed in biosensing applications. One is organic electrochemical transistor (OECT), which is based on electrochemical doping/dedoping processes upon the bulk injection of ionic species to the active channel materials, and the other is electrolyte-gated organic-field-effect transistor (EGOFET) with the channel current modulated by the gate voltage via a capacitive field-effect mechanism at the channel/electrolyte interface.[5,6] For detailed device physics of OECTs and EGOFETs, interested readers can refer to previous reviews.[4,5,7] Both of the transistors are promising for biological sensing due to their operation in electrolyte solutions with reliable performance. Furthermore, to meet the demand for specific detections of biological analytes, OTFTs need to be functionalized with the consideration of the following aspects: the sites of modification (channel, gate or incorporation into the electrolytes), modification methods (physical absorption, electrostatic interaction, or chemical bonding) and working mechanisms (changes in surface potential, electrochemical reactions induced charge redistribution or capacitance change due to biorecognition). In this account, we detail these critical issues in functionalizing OTFT biosensors based on three categories, including the channel, electrolyte and gate functionalization. Subsequently, the strategies and recent advances on printing techniques of electronic materials

and biological elements for the fabrication of flexible OTFT biosensors are reviewed. Fabric OTFT-biosensors are then introduced in the last section, demonstrating the promising future for integrating the flexible organic biosensors into the demand scenarios of wearable electronics.

2. Channel Functionalization

A typical OECT or EGOFET consists of three components, including channel, electrolyte and gate. Although it cannot be directly used as a biosensor, functionalization on the channel surface would lead to a device response to specific analytes when an interaction between the analyte and the channel occurs. Various strategies on channel/electrolyte interface engineering are discussed as follows.

2.1 Grafting biomolecules for biorecognition

From a synthetic point of view, the introduction of bioactive groups or biorecognition sites on the backbones of organic semiconductors would make the synthesis routes more complex and critical. Therefore, chemical immobilization on the surface of a semiconducting layer has been demonstrated as a facile strategy widely adopted for channel functionalization in an OTFT. In 2012, we first reported the application of OECTs based on poly(3,4-ethylenedioxy thiophene):poly(styrenesulfonate) (PEDOT:PSS) for the capture and detection of *E. coli* O157:H7 bacteria (Figure 1a).[8] The PEDOT:PSS channel was chemically modified with amino end groups for further covalent bonding with anti-*E. coli* antibodies which are biorecognition elements for specific capture of this bacteria. The electrostatic interactions between the negatively charged bacteria and PEDOT:PSS change the potential drop at the channel/electrolyte interface (Figure 1b), resulting in a quantitative detection of the bacteria down to 10^3 cfu·mL^{-1}. Similar approaches employing high-affinity binding interactions between antibody and antigen were extensively

investigated for OTFT-based immunosensors due to their high sensitivity and selectivity.[9] Nanomaterials such as gold nanoparticles were integrated in the modification processes to improve the sensitivity and dynamic range of the sensors (Figure 1c).[10]

Besides, enzymes were frequently employed for the detection of biological molecules because they can specifically accelerate analyte reactions. For example, penicillinase was immobilized on the surfaces of α-sexithiophene channel of EGOFETs by chemical bonding and used for a specific detection of penicillin.[11] (Figure 1d) Molecular antenna was also introduced for the detection of adenosine triphosphate through a plasma-assisted interfacial grafting method.[12] In this approach, both high carrier mobility (~0.4 $cm^2V^{-1}s^{-1}$) and high grafting efficiency of the channel could be maintained after the plasma treatment, which is critical to the device performance.

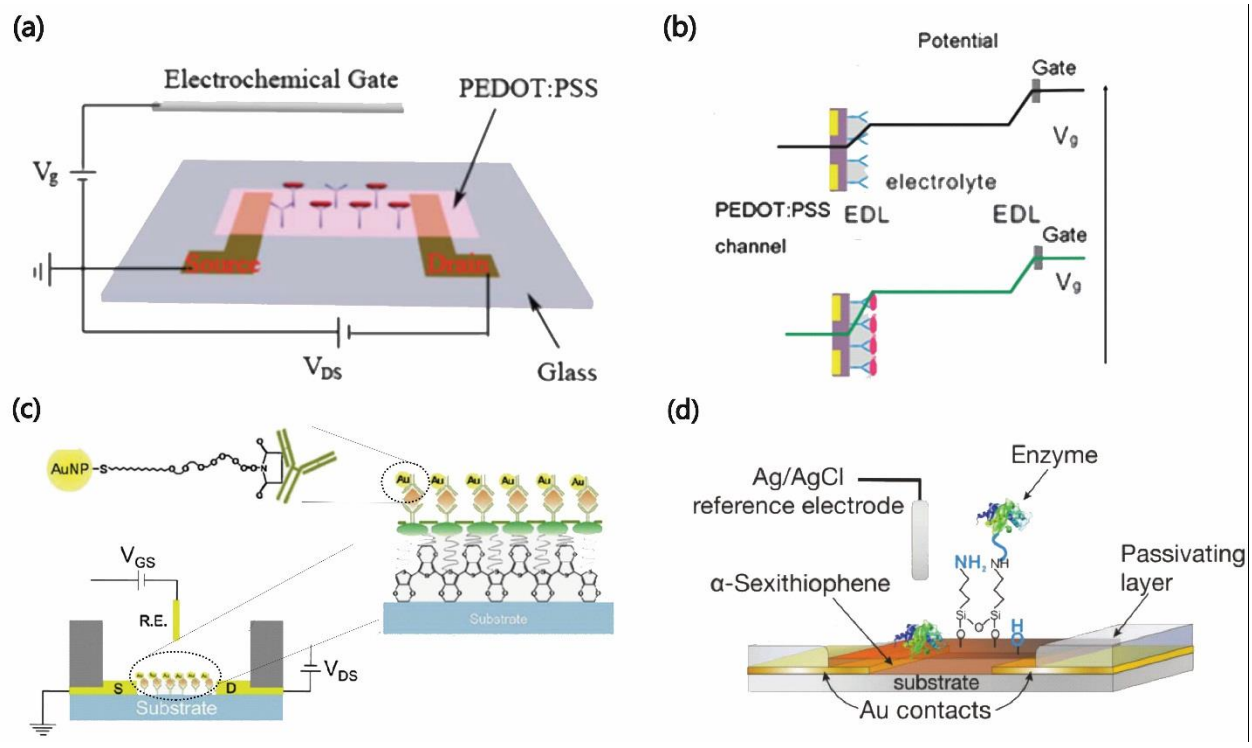

Figure 1. (a) Device structure of an OECT sensor for capture of E. coli. bacteria; (b) potential drop profile before and after the capture of bacteria on the PEDOT:PSS surface.[8] Reproduced with

permission from ref. 8. Copyright 2012 Royal Society of Chemistry. (c) OECT based immunosensor with the signal amplified by linked gold nanoparticles.[10] Reproduced with permission from ref. 10. Copyright 2010 Elsevier. (d) Structure of a biofunctional EGOFET with covalently bonded enzymes on the surface of α-sexithiophene thin film.[11] Reproduced with permission from ref. 11. Copyright 2012 Wiley.

To avoid possible damages induced by certain immobilization processes (plasma treatment, thermal annealing or solvent erosion), organic channels can be functionalized with materials based on weak interactions, such as electrostatic force or amphiphilic self-assembly. This mild modification at the interface can modulate charge injection into the channel and provide an efficient strategy for biosensing, such as RNA detection in physiologically relevant electrolytes.[13] Lactate oxidase was immobilized on the channels of OECTs based on a n-type-conjugated polymer by simply physical absorption, which was then employed for the direct detection of lactate.[14] Phospholipid bilayers (PL) were also chosen for channel modification since they are versatile bio-systems.[15] One remarkable advantage is that the biotinylated PLs can provide binding sites for streptavidin labeled analytes, demonstrating the possibility for immobilizing antibodies and proteins indirectly immobilized on channel areas without any side effect. For example, a PL-modified EGOFET was successfully adopted for monitoring protein binding events beyond the Debye's length.[15]

2.2 Surface treatments for cell detections

The applications of OTFTs in cell-based sensors have attracted great interests recently. Because some organic semiconductors are biocompatible, cells or tissues could be in-situ cultivated and monitored on device surfaces. In 2010, our group reported cell-based OECT biosensors for the

first time (Figure 2a).[16] The activities of human cancer cell lines cultivated on an OECT were monitored by measuring the device performance. As shown in Figure 2b, the transfer curve of the OECT was shifted horizontally for ~150 mV when cells were detached or removed from the channel, indicating an electrostatic interaction between the cells and the organic channel. Because the culture condition for cancer cell line is not critical, the device was treated by ultraviolet radiation for sterilization in our experiments. However, some cells with specific functions may need critical cultivation conditions and the pre-treatment process becomes complicated. Effective strategies should be adopted for enhancing the biocompatibility, reducing the chances of infection and promoting cell culture on the surface, without the degradation of device performance. For example, the recording and mapping of cardiac action potential generated from cardiomyocytes were demonstrated by a 16-channel OECT array,[17] in which the cardiomyocytes were directly cultured on the OECT channels (Figure 2c). The devices were sterilized by UV exposure and ethanol immersion, followed by surface coating with a protein fibronectin that can enhance the adhesion of various types of cells on the channel surfaces. So protein coating pretreatment is an effective method to enhance the biocompatibility of devices and guide cell adhesion processes. Another example was demonstrated by chemically coating a layer of polypeptide poly-$_L$-lysine on PEDOT:PSS.[18] Figure 2d shows that neuron cell line PC12 are perfectly confined to grow and differentiate only on top of the protein coated PEDOT:PSS regions. The feasibility of controlling cell adhesion and migration through surface coating processes indicates a great potential for tight integration of living cells with OTFTs in further applications, such as stimulation and monitoring of specific cell functions, growth of designed neuron patterns for the investigation of artificial neuronal networks.

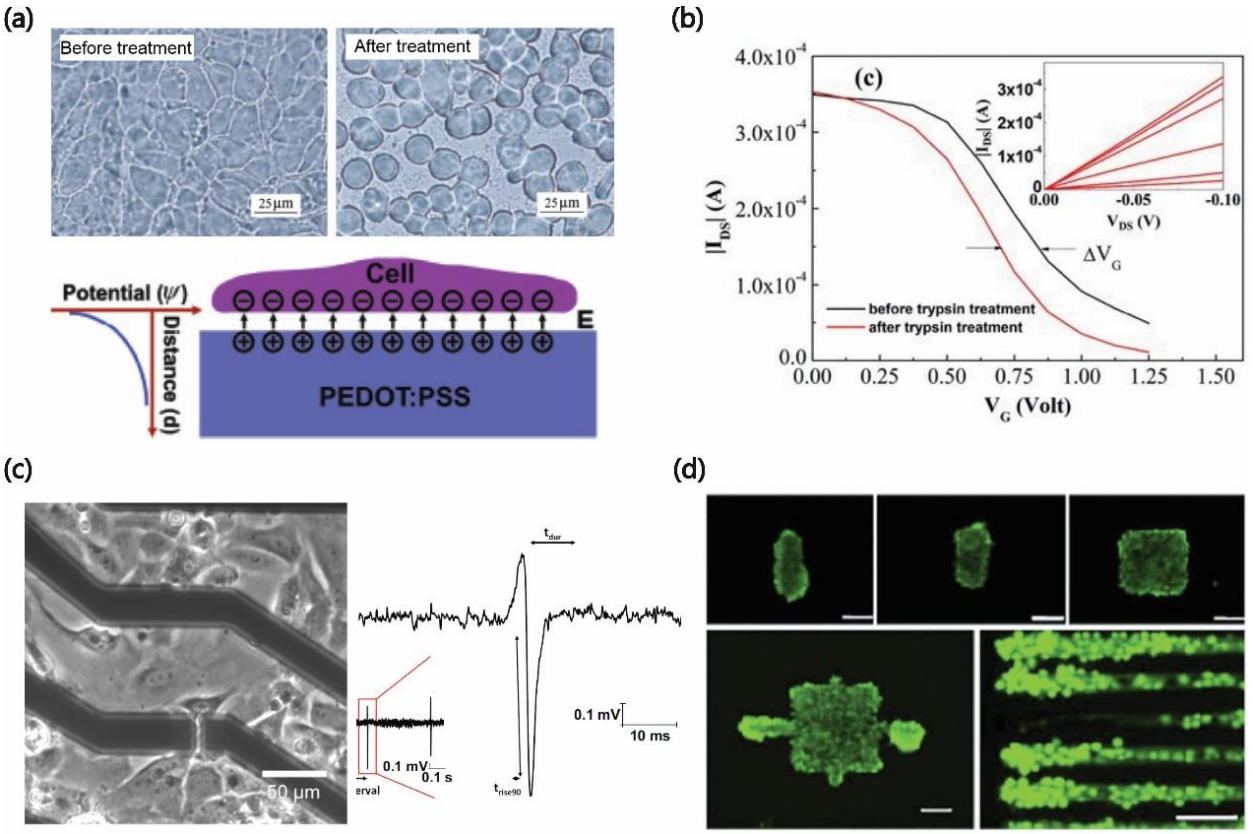

Figure 2. (a) Optical images of cancer cells cultured on the channel of an OECT and its interaction with channel material; (b) transfer characteristics of the OECT before and after trypsin treatment.[16] Reproduced with permission from ref. 16. Copyright 2010 Wiley. (c) Optical images of cardiomyocyte cells cultured on OECT arrays, and a single action potential recorded.[17] Reproduced with permission from ref. 17. Copyright 2016 Wiley. (d) Fluorescence images of live (green) and dead (red) neuron cells cultured on a functionalized PEDOT:PSS pattern.[18] Reproduced with permission from ref. 18. Copyright 2014 Royal Society of Chemistry.

3. Electrolyte functionalization

Due to continuously growing demands for disposable and wearable electronics, OTFTs with solid-state electrolytes have been developed for biological applications without the involvement of complex liquid handling. Bioactive mediators could be incorporated into the electrolytes to

enhance the capability for specific detections. A flexible OECT-based lactate sensor was first realized by incorporating a lactate oxidase enzyme into solid-state electrolytes (Figure 3a).[19] Several unique properties, such as wide electrochemical window, high stability and ionic conductivity, make this kind of solid electrolytes suitable for OECT operation. The device was integrated in a bandage-type sensor, which could detect lactate levels in sweats when they diffused into the solid electrolyte, demonstrating its potential application for health monitoring. Screen-printed OECTs were used for similar detections, as shown in Figure 3b.[20] Several metabolites were detected in real human sweat samples, with optimized detection limits suitable for epidermal applications. Solid-state OECTs can also be used as gas sensors for health monitoring. A disposal breathalyzer for alcohol sensing was realized by using a paper-based OECT that has a collagen-based gel electrolyte embedded with alcohol dehydrogenase and its cofactor (Figure 3c).[21] The OECT breathalyzer demonstrated advantages over commercialized products in terms of low cost, disposability and environmental friendly nature.

Besides various attempts to employ solid electrolytes into OTFT sensors, there are some efforts focusing on the functionalization of aqueous electrolytes. As shown in Figure 3d, an ion selective membrane was inserted into a liquid electrolyte, to separate it into an analyte region and inner filling solution.[22] The integration of this functional membrane provides the capability for selective and reversible ion detections. Since no direct modification or binding occurred on the semiconducting layer, the device demonstrated excellent stability. Reversible detections could be realized by a simply flushing process. Furthermore, the detection of different ions by the same device could be achieved by choosing specific ion-selective membranes, which significantly expands its applications.

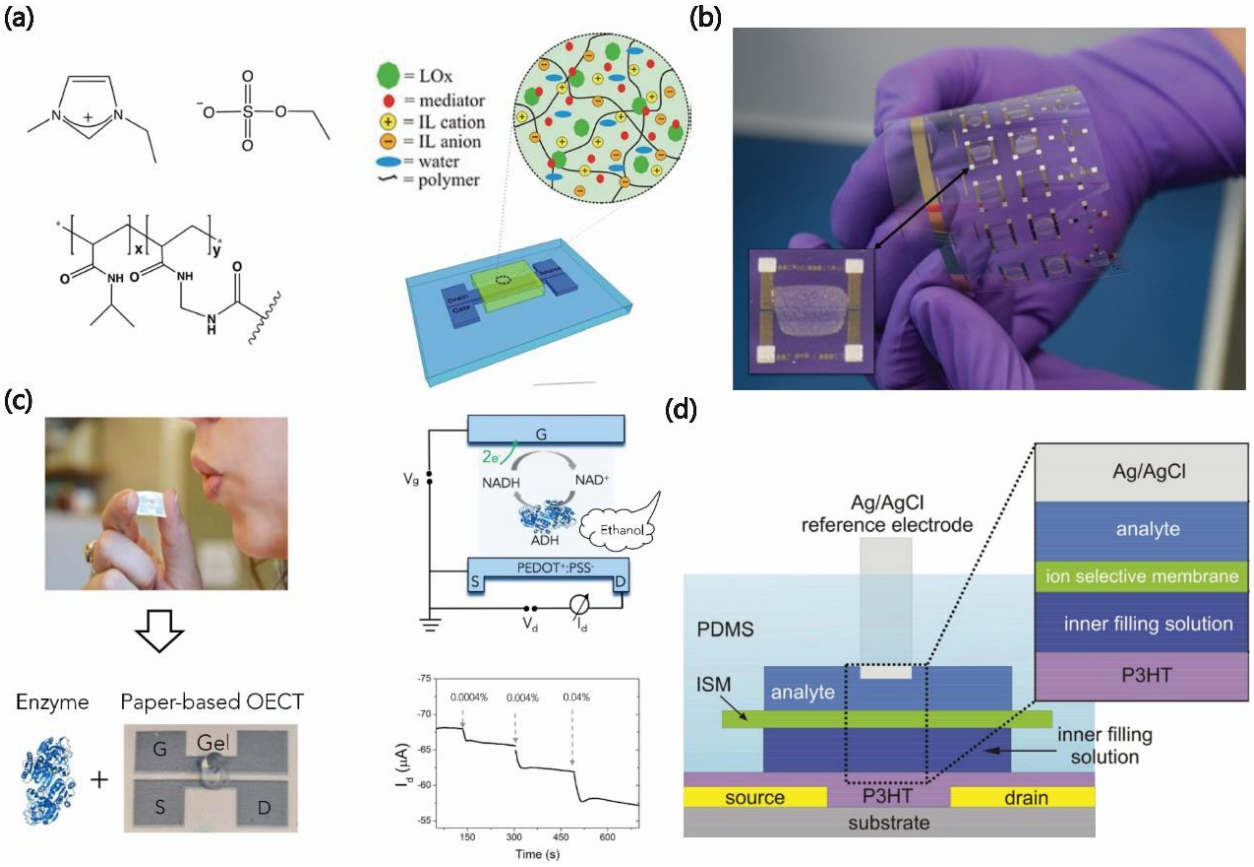

Figure 3. (a) The chemical structure and schematic description of components in ionic-gel electrolytes.[19] Reproduced with permission from ref. 19. Copyright 2012 Royal Society of Chemistry. (b) Photograph of the screen-printed all-solid-state OECT on flexible substrates.[20] Reproduced with permission from ref. 20. Copyright 2015 Materials Research Society. (c) Breathing on the enzyme-embedded OECT on paper, associated with the mechanism and the drain current response of the device towards exposure to ethanol.[21] Reproduced with permission from ref. 21. Copyright 2016 Springer Nature. (d) Schematic structure of the EGOFET integrated with an ion selective membrane.[22] Reproduced with permission from ref. 22. Copyright 2013 Wiley.

4. Gate Functionalization

The major research interests and efforts of some research groups have been concentrated on gate functionalization of OTFTs to enhance the device performance. Because gates are normally isolated from the channel regions in OECTs and EGOFETs, the surface modification on the gates will not influence channel properties. According to the working principle of a transistor that the channel current (output) between source and drain electrodes is modulated by the gate voltage (input), a small change in the gate property can result in a pronounced response of the channel current. Several strategies for gate functionalization, such as the modifications for capturing charged molecules and the immobilization of electrochemically active biomolecules, nanomaterial and biorecognition elements, have been developed recently.

4.1 Surface modification for the capture of charged biomolecules

The detection of intrinsic charges from biological molecules is a convenient approach for direct, label-free and non-destructive sensing. The capture of these charged biomolecules on a gate would influence the electrostatic potential on the gate surface, which can be classified as surface potential modulation. We reported an OECT-based flexible microfluidic system employed for label-free detections of DNA with a detection limit down to 10 pM.[23] The whole microfluidic device was deposited on a flexible substrate with a thiolated probe DNA immobilized on the gold gate electrode. Then a target DNA was injected in the channel to have DNA hybridization with the probe (Figure 4a, 4b). The DNA hybridization could decrease the surface potential of the gate electrode because DNA molecules have negative charges in physiological environment due to their low isoelectric point (Figure 4c). Consequently, a higher gate voltage was needed to offset the effect induced by the DNA hybridization, resulting in a horizontal shift of the transfer curve to a

positive voltage (Figure 4d), and the concentration of the target DNA could be differentiated according to the gate voltage shift.

Similarly, a floating gate OTFT for DNA sensing was reported by Bonfiglio's group, which was also based on the detection of the negative charge of DNA showing a detection limit of 0.1 nM.[24] A similar functionalization strategy was also adopted in a poly(3-hexylthiophene)-based EGOFET by Frisbie's group for DNA detection.[25]

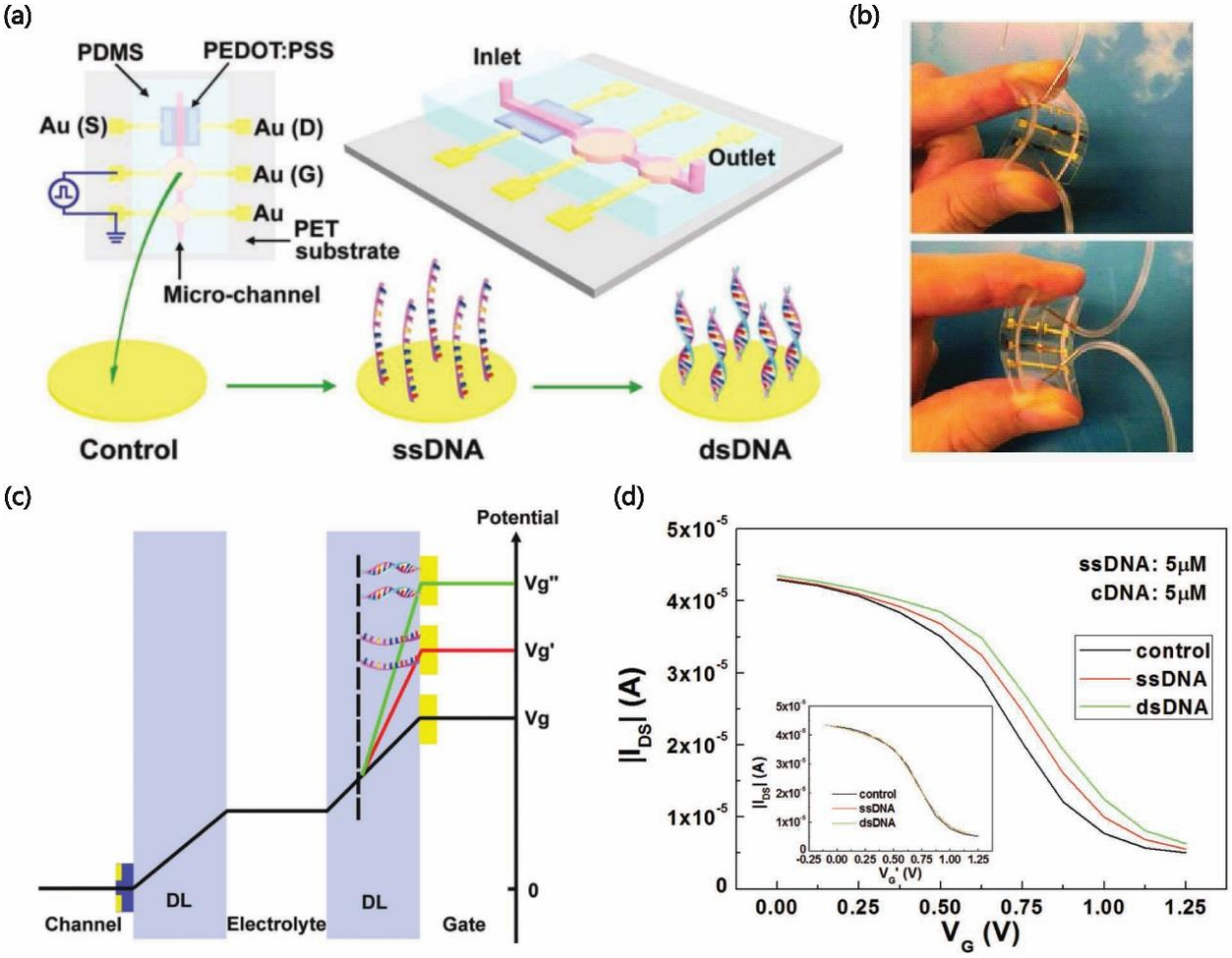

Figure 4. (a) Schematic of an OECT integrated in a microfluidic system, with DNA molecules on gate electrodes. (b) Photograph of a flexible device bent to different directions. (c) Potential drop profiles with the immobilization of probe (red line, Vg') and target (green line, Vg'') DNA

molecules. (d) Transfer characteristics of the OECT before and after the modification and hybridization of DNA on gold electrode.[23] Reproduced with permission from ref. 23. Copyright 2011 Wiley.

4.2 Modification with electrochemically active components

The modification of gate electrodes with electrochemically active components is a promising strategy to further improve the sensitivity and selectivity of OTFT-based biosensors. Recently, our group developed protein biomarker sensors based on the modification of Horseradish peroxidase (HRP) -labeled nanoprobes on OECTs.[26] HRP is an electrochemically active enzyme that can efficiently catalyze the reduction of H_2O_2. The surface of gate electrode was first modified with a layer of specific antibody to selectively capture target protein biomarkers. (Figure 5a) Then the captured proteins were further functionalized with catalytic nanoprobes which were Au nanoparticles linked with both the protein detection antibody and HRP. Quantitative characterization of the HRP molecules by an electrochemical reaction of H_2O_2 was utilized to determine the concentration of target proteins or cells. The OECTs could specifically detect cancer biomarkers down to 10^{-14} g/mL, which is 6 orders of magnitude lower than the detection limit of a conventional cyclic voltammetry measurement. (Figure 5b, 5c) The functionalization strategy establishes a versatile platform for highly sensitive detections of various protein biomarkers in future applications.

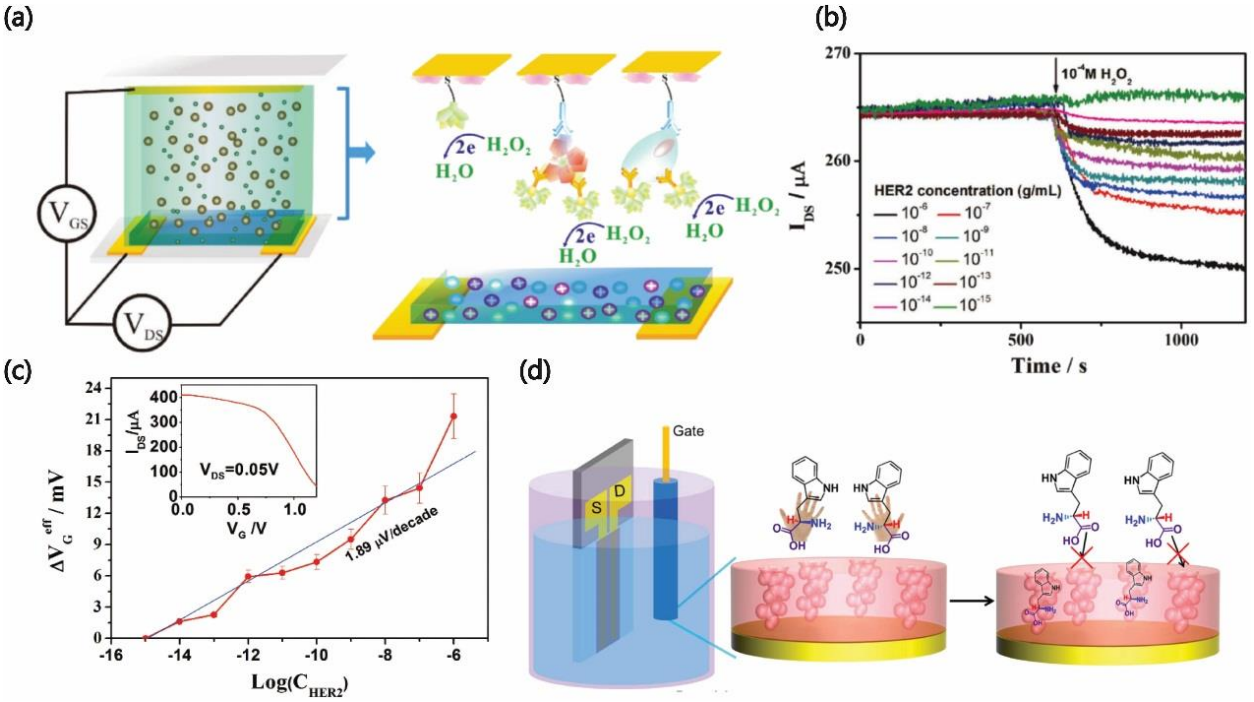

Figure 5. (a) Gate electrode modification of OECTs for proteins or cells detection. (b) Channel current responses and (c) effective gate voltage changes of OECTs exposed to cancer cell biomarker with different concentrations.[26] Reproduced with permission from ref. 26. Copyright 2017 Wiley. (d) Chirality detection of amino acid enantiomers by OECTs modified with molecularly imprinted polymer films.[27] Reproduced with permission from ref. 27. Copyright 2018 Elsevier.

Other enzymes, such as glucose oxidase,[28] lactate oxidase,[29] cholesterol oxidase[30] and nitrate reductase[31], were also integrated in OTFTs for electrochemical sensing. Besides, molecularly imprinted polymer (MIP) films were introduced in OECTs for the specific chiral recognition of D/L-tryptophan, and D/L-tyrosine (Figure 5d).[27] The MIP films catalyzed the oxidation of the two amino acids and generated different electrochemical signals amplified by the transistors, leading to a relatively low detection limit of 2 nM.

4.3 Modification of functional materials for enhanced sensitivity and selectivity

Functional materials especially nanomaterials have been introduced in the modification of gate electrodes to further improve the device performance, which is similar to many approaches for conventional electrochemical biosensors. For example, graphene and other carbon-based nanomaterials can improve the electrochemical activity of gates owing to their unique properties including high carrier mobilities and large specific surface areas.[32,33] Functional polymers modified on gate surfaces can improve the device selectivity due to electrostatic interactions.[34]

Our group reported a versatile OECT sensing platform for highly selective detection of uric acid, cholesterol and glucose based on the gate modification of polyaniline/nafion-graphene bilayer films.[34] (Figure 6a) As polyaniline and nafion contain positive and negative charges in neutral solutions, respectively, the bilayer films can strongly repel both positively and negatively charged biomolecules, like uric acid and dopamine. In addition, the diffusion of large molecules such as glucose across the polymer film is prohibited. So many interferences were effectively blocked by the bilayer films, and consequently, the OECTs demonstrated a high sensitivity and selectivity to H_2O_2 (Figure 6b), as evidenced by the selective responses to additions of H_2O_2 and major interferences (Figure 6c). Then the devices were further developed as high-performance sensors for glucose, uric acid and cholesterol by modifying suitable enzymes on the gates. The enzymes can catalyze the reaction of analytes and generate H_2O_2 that is detectable to the devices. Thanks to the high sensitivity and selectivity of the biosensors, we have successfully utilized the devices in saliva analysis and obtained the concentrations of glucose and uric acid in human saliva, which may provide a viable way for the non-invasive detections of these molecules in human body.

We also demonstrated the modification of gates with graphene flakes for dopamine sensing (Figure 6d).[32] The device sensitivity was improved for one order of magnitude and the detection limit was extended to 5 nM (Figure 6e) because the graphene flakes can enhance charge transfer during electrochemical reactions. The device selectivity was also improved by the co-modification of nafion or chitosan due to their electrostatic interaction with interferences (Figure 6f). Besides, other carbon-based nanomaterials such as single wall or multiwall carbon nanotubes were also successfully utilized for enhancing the device sensitivity to epinephrine[33] and gallic acid.[35]

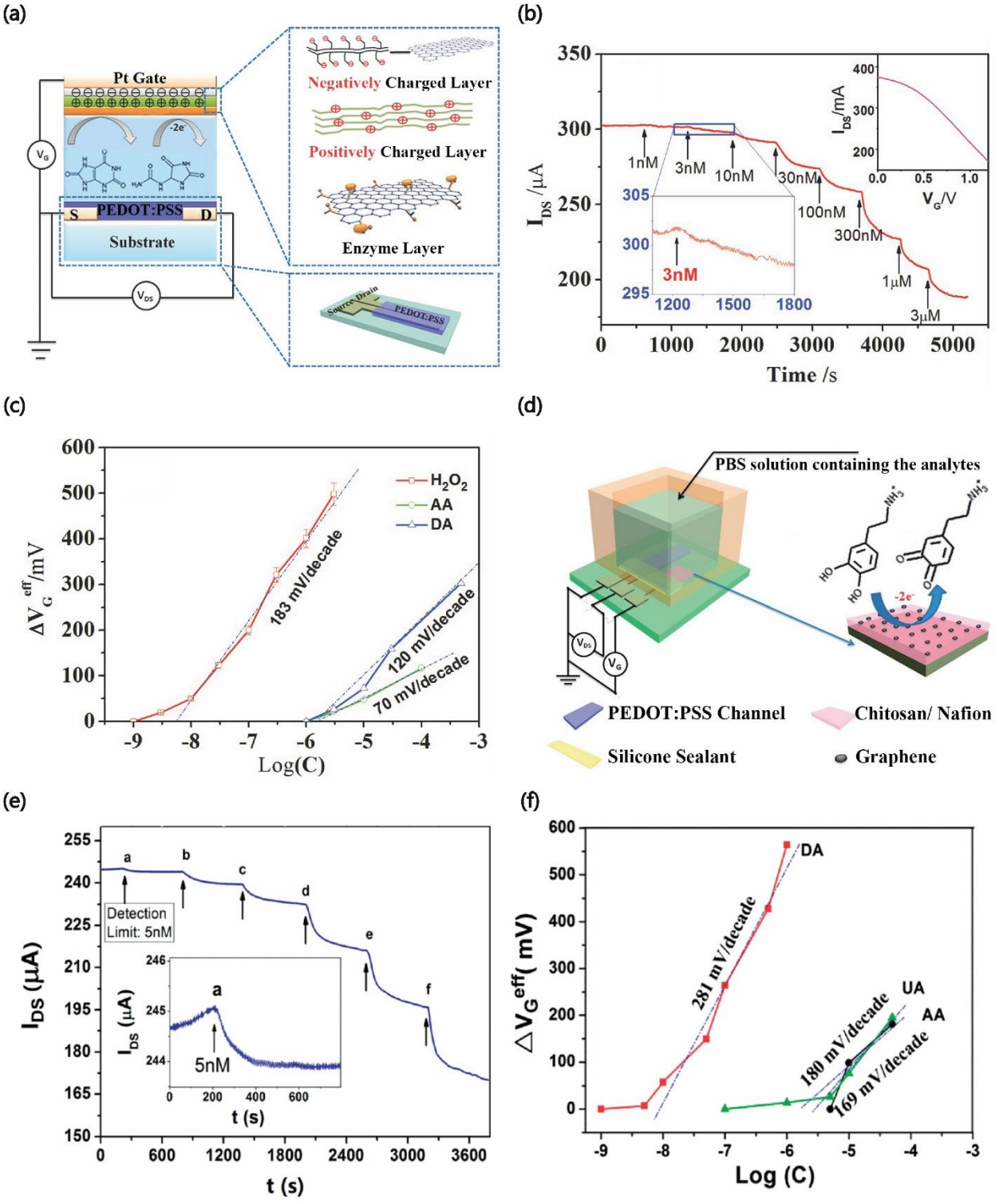

Figure 6. (a) Schematic diagram of an OECT with an enzyme/polyaniline/nafion-graphene modified gate. (b) Channel current responses to additions of H_2O_2 with various concentrations. (c)

Variation of effective gate voltage versus concentrations of H_2O_2, ascorbic acid (AA), and dopamine(DA).[34] Reproduced with permission from ref. 34. Copyright 2014 Wiley. (d) Chitosan and graphene modified gate for selective dopamine sensing. (e) Channel current responses to dopamine additions with various concentrations. (f) Change of effective gate voltage versus concentrations of DA, uric acid (UA) and AA.[32] Reproduced with permission from ref. 32. Copyright 2014 Royal Society of Chemistry.

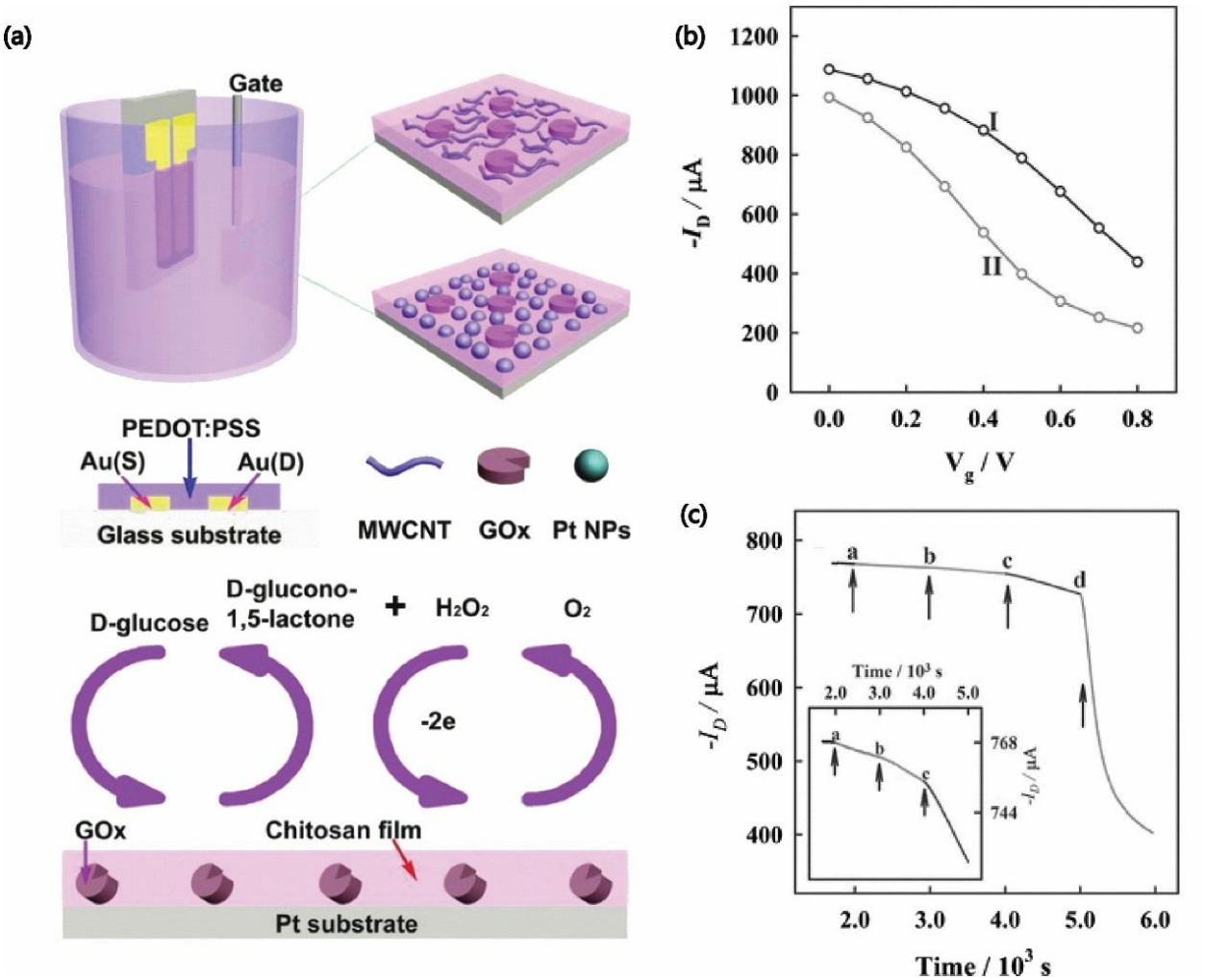

Figure 7. (a) OECT-based glucose sensor modified with multiwall carbon nanotube (MWCNT) or Pt nanoparticles. (b) Transfer characteristics of a Pt nanoparticle functionalized OECT in (I) blank and (II) 100 μM glucose PBS solutions. (c) Channel current responses to glucose additions

with concentrations of a-d, 0.005, 0.05, 0.5 and 5 μM. [36] Reproduced with permission from ref. 36. Copyright 2011 Wiley.

Platinum nanoparticles (Pt NPs) have been widely used in the functionalization of gate electrodes because of their excellent electrocatalytic activity and large specific surface area for enzyme immobilization. In 2011, we reported the immobilization of Pt NPs on the gate electrodes of OECTs.[36] (Figure 7a) The device was particularly sensitive to glucose and demonstrated a significant horizontal shift of the transfer curve after adding 100 μM glucose in the electrolyte. (Figure 7b) The detection limit of the glucose sensor is down to 5 nM (Figure 7c), which is three orders of magnitude better than that of a control device without any nanomaterial modification.

4.4 Modification with biorecognition elements

Recently, biorecognition elements have been introduced in the gate modification of OTFT-based sensors due to their high coupling affinity and specificity. For example, ultra-sensitive detection of chiral differential interaction in odorant binding proteins (OBP) was demonstrated by employing an EGOFET based on a ligand-induced capacitance change.[37] Another example is to modify OECTs with phenylboronic acid for label-free detection of sialic acid, due to the specific interaction between sialic acid and phenylboronic acid.[38] Not only the free molecules, but also the cells with glycan terminal sialic acid presented on the membrane surface could be directly captured by the modified gate electrodes. These biosensors presented the capacity to distinguish cancer cells from normal ones, without the need of labeling or enzyme modification. Recently our group successfully demonstrated the detection of cell surface glycans based on a gate modification of con-canavalin A, a specific active binding site for mannose.[39] The devices exhibited a sensitivity

down to 10 cells/μL and could selectively monitor the mannose expression activity on cancer cell surfaces.

5. Printing technologies for OTFT biosensors

Printing technologies have been utilized in the fabrication of OTFT-based biosensors.[40] Their capability of depositing and patterning each layer simultaneously simplifies the fabrication process and significantly lowers the cost. Meanwhile, printing approaches enable the integration of OTFT sensors both on rigid and flexible substrates, which paves the avenue for the mass production of flexible and disposable bioelectronic strips.

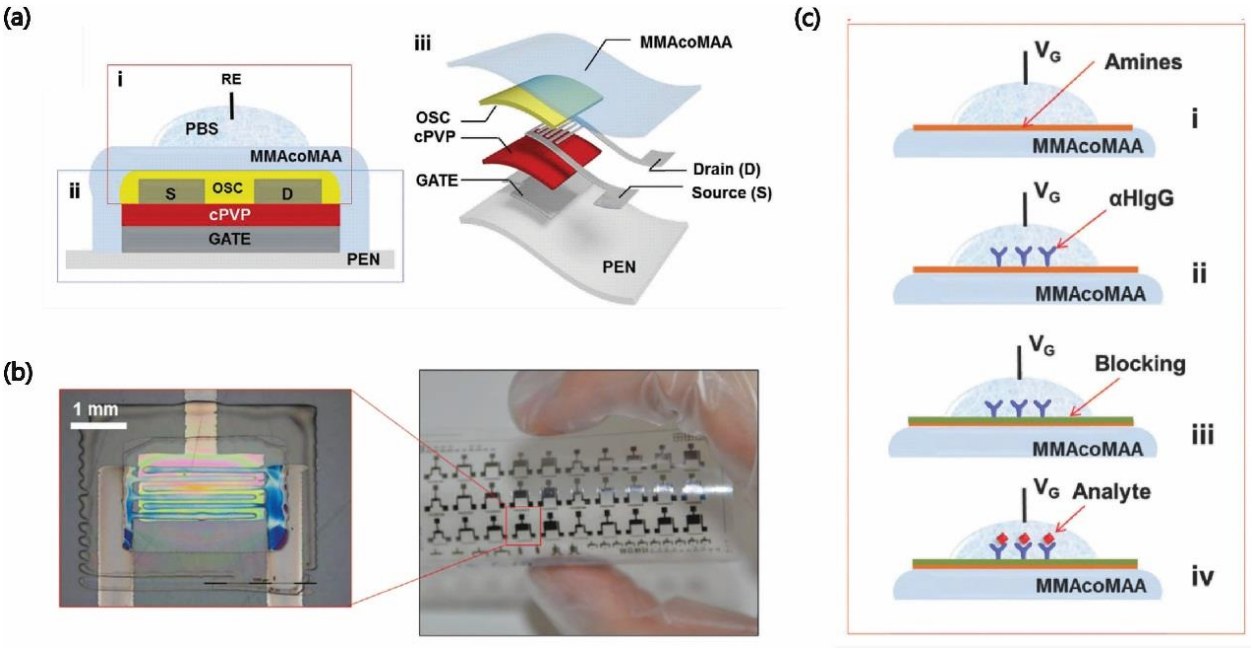

Figure 8. (a) Design of a flexible OTFT biosensor. (b) Photograph of printed OTFT arrays. (c) Functionalization processes at the insulator/electrolyte interface.[41] Reproduced with permission from ref. 41. Copyright 2014 Wiley.

Two representative printing methods including screen-printing and inkjet-printing are suitable for OTFT fabrications. The resolution of screen-printing is usually limited when it comes to smaller-sized features (< 100 μm). Besides, it cannot achieve a layer thinner than the screen mask considering viscosity issues. Therefore, screen-printing is mainly utilized for printing electrodes or dielectric layers, while it is not recommended for the deposition of the active layers of OTFTs. Inkjet-printing demonstrates advantages of low cost, high throughput and remarkable self-improvement in high resolution.[42] More importantly, drop-on-demand mode for inkjet-printing may need only a small volume of ink, which is an advantage for biosensing applications especially when the biological species are expensive and available in limited amounts. Medina-Sanchez et al.[41] reported an OTFT biosensor array with source, drain and gate electrodes inkjet-printed with silver nanoparticle solution and printed organic semiconductor channels (Figure 8a). The device array (Figure 8b) was then functionalized with antibodies separately for label-free detection of proteins (Figure 8c). Human immunoglobulin G (HIgG) at the concentration of 100 $ng \cdot mL^{-1}$ was successfully detected with the printed sensors.

Inkjet-printing can also be utilized for enzyme modification. Elkington et al. fabricated an EGOFET-based glucose sensor with a linear response in the range of 0.1-100 mM.[43] Conventional drop-cast modification was replaced with screen-printed nafion followed by inkjet-printed glucose oxidase. In addition to lowering the fabrication cost, the introduction of inkjet-printing also avoids variations in layer thickness and the aggregation of enzymes, resulting in improved device-to-device consistency for mass production.

6. Organic transistors for wearable electronics

Wearable electronics has been an emerging field due to a huge potential market.[44] Currently, wearable electronics relies mostly on physical sensors, which record signals such as movement, heat or electrocardiograph changes. However, the integration of chemical or biological sensors into textile substrates is still challenging. Recently, a robust and flexible fabric OECT biosensor was reported by our group, which is promising for non-invasive detection of biomolecules in wearable applications.[45] In the fiber-based OECTs, electrodes with a metal/PEDOT:PSS core-shell structure was designed to enhance the bending stability. As shown in Figure 9a, the highly conductive PEDOT:PSS layer coated on the metal surface can connect the separated metal fraction and maintain a stable conductivity of the electrode. Consequently, the devices showed stable performance even after 5000 times bending tests.

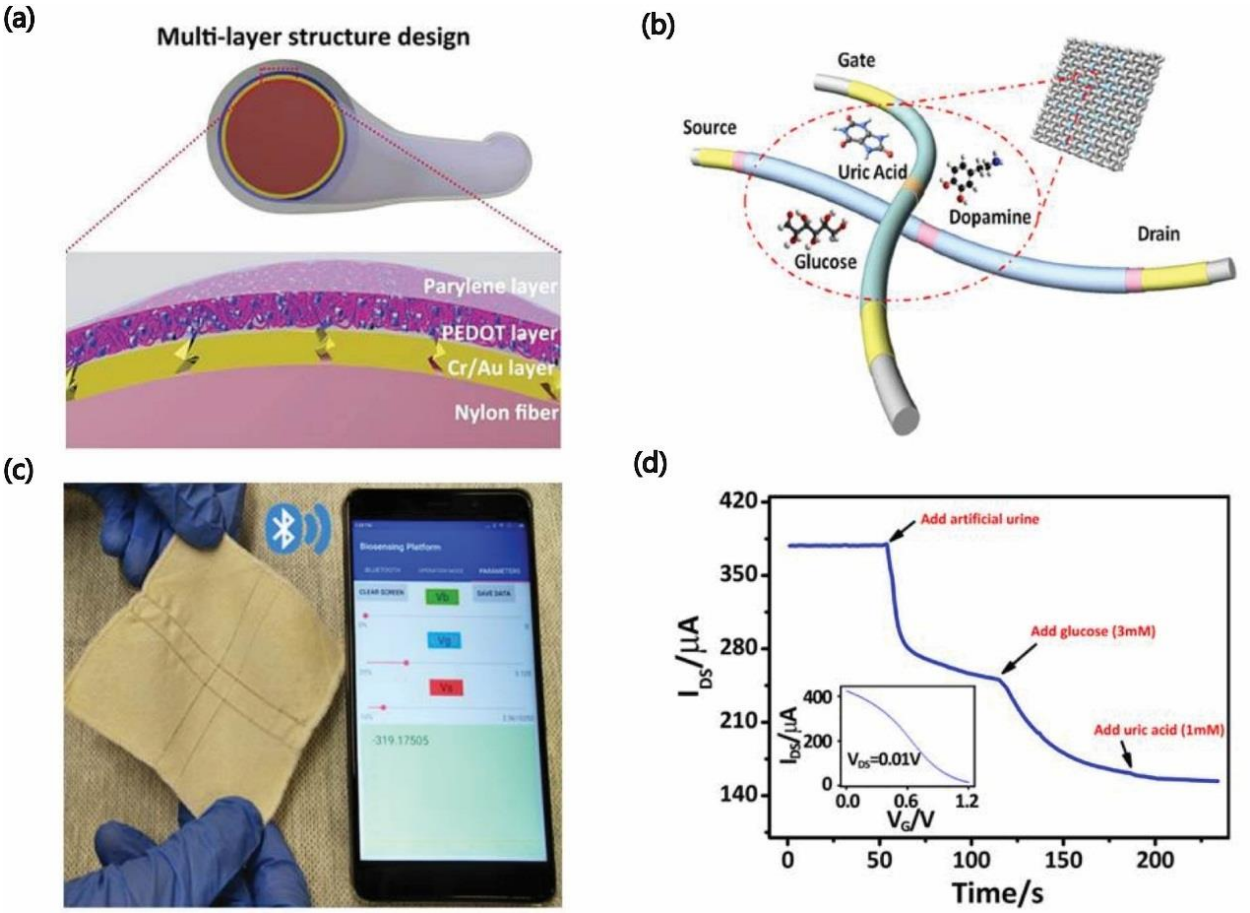

Figure 9. (a) The design of multilayer electrodes in OECTs prepared on nylon fibers. (b) Illustration of OECT integrated into textiles as fabric sensor for different sensing scenarios. (c) Photograph of fabric OECTs controlled by a mobile phone through Bluetooth. (d) Channel current responses of an fabric OECT integrated in a diaper to artificial urines with the additions of glucose and uric acid (interference), respectively.[45] Reproduced with permission from ref. 45. Copyright 2018 Wiley.

Fabric biosensors were then fabricated by weaving the fiber-based sensors together with cotton yarns (Figure 9b). The sensing signals were collected by a readout circuit and transmitted to a mobile phone for real time visualization through Bluetooth (Figure 9c). The device embedded into a diaper was successfully used for monitoring the glucose level in artificial urine (Figure 9d). The highly sensitive and stretchable fabric biosensors are light weight, portable and low cost and can be conveniently integrated into wearable electronic systems, such as skin adhesive patch, epidermal electronics and smart e-textiles.

7. Conclusion and Outlook

In this account, recent efforts in functionalizing both OECT and EGOFET devices for biological sensing applications are reviewed. A series of modification strategies have been developed based on various operating mechanisms with a view to meeting the demands for specific healthcare and diagnosis applications. Notably, the realization of novel biosensors with improved figure of merits and unique features relies on a better understanding of the device design, functionalization and operation principles. Essential printing techniques for preparing flexible/stretchable devices should be further investigated to enable the practical applications of organic biosensors in wearable electronic scenarios. Moreover, the stability and reproducibility of the organic bioelectronic

devices should be further improved. With the enormous efforts from the fundamental device physics to the mass production and commercialization of the devices, organic bioelectronics is expected to play an important role in the emerging wearable electronic era.

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The authors declare no competing financial interest.

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