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Topical Review

Expanding the potential of biosensors: a review on organic field effect transistor (OFET) and organic electrochemical transistor (OECT) biosensors

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Abstract

Organic electronics have gained significant attention in the field of biosensors owing to their immense potential for economical, lightweight, and adaptable sensing devices. This review explores the potential of organic electronics-based biosensors as a revolutionary technology for biosensing applications. The focus is on two types of organic biosensors: organic field effect transistor (OFET) and organic electrochemical transistor (OECT) biosensors. OFET biosensors have found extensive application in glucose, DNA, enzyme, ion, and gas sensing applications, but suffer from limitations related to low sensitivity and selectivity. On the other hand, OECT biosensors have shown superior performance in sensitivity, selectivity, and signal-to-noise ratio, owing to their unique mechanism of operation, which involves the modulation of electrolyte concentration to regulate the conductivity of the active layer. Recent advancements in OECT biosensors have demonstrated their potential for biomedical and environmental sensing, including the detection of neurotransmitters, bacteria, and heavy metals. Overall, the future directions of OFET and OECT biosensors involve overcoming these challenges and developing advanced devices with improved sensitivity, selectivity, reproducibility, and stability. The potential applications span diverse fields including human health, food analysis, and environment monitoring. Continued research and development in organic biosensors hold great promise for significant advancements in sensing technology, opening up new possibilities for biomedical and environmental applications.

Keywords: biosensor, OFET, OECT

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1. Introduction

Organic electronics has emerged as a burgeoning field with enormous potential in biosensor applications. Biosensors are devices that detect and analyze biological or biochemical substances, and their applications span across a variety of fields, including medicine, food safety, and environmental monitoring [1–3]. Two types of organic biosensors that have gained significant attention in recent years are organic field effect transistors (OFETs) and organic electrochemical transistors (OECTs) [4].

The foundation of OFETs lies in a three-terminal device structure and operate by controlling the flow of charge carriers through a semiconducting organic material using an applied electric field [5]. The fundamental principle of OFET biosensors is based on modulating of the electrical characteristics of the semiconductors in response to the attachment of biological analytes onto the surface of the transistor. This modulation results in alterations in the electrical output of the transistor, enabling measurement and correlation with the concentration of the biological analyte present in the sample [6]. OFET biosensors have been employed in detecting various biological analytes including proteins, DNA, and cells [7].

OECTs, on the other hand, are based on a similar three-terminal device structure but operate by controlling the doping level of a conducting polymer using an electrolyte solution [8]. Like OFETs, OECT biosensors also operate by modulating the electrical properties of organic materials, responding to the biological analytes. However, in this case, the modulation occurs through changes in the doping level of the material, controlling by the concentration of the electrolyte solution. OECT biosensors have been employed in detecting of a diverse range of biological analytes including neurotransmitters, bacteria, and viruses [9].

Based on the length constraints, here we will only present a brief overview of the fundamental principles behind OFET and OECT biosensors. Additionally, we will showcase a few representative examples to demonstrate the immense potential of these sensors. Please note that there have been many advancements in this field [8, 10–19], which we will not be able to cover comprehensively in this review.

2. OFET biosensors

2.1. The working principle of OFET biosensors

In OFETs, charge carriers gather at the junction of the organic semiconductor (OSC) and dielectric layer through the application of a bias voltage connecting the gate and source electrodes. Additionally, the movement of these charge carriers along the active layer and the insulated dielectric interface is aided by a bias voltage connecting the drain and source electrodes [1, 20].

There are four main architectures of OFETs (figure 1(a)): BGTC, TGBC, BGBC and TGTC (B: bottom, G: gate, T: top, C: contact). The main differences between the four OFET architectures are the location of the gate and contact electrodes in relation to the active layer. The choice of OFET architecture relies on the specific requirements, such as the desired performance, fabrication complexity, and cost [21].

For p-type OFETs [22, 23], a negative V_g accumulates holes at the OSC/dielectric interface, while hole transport is facilitated by a negative V_{ds} ($V_{ds} > V_T$). For n-type OFETs [24–26], positive V_g and V_{ds} accumulate and transport electrons, respectively. Ambipolar OFETs can accumulate holes/electrons and transport both as well at the OSC/dielectric interface (figure 1(b)).

The transport of charge carriers in OFETs is driven by the combined effect of V_g and V_{ds}, ideally, a small V_g is necessary to store up charges (figure 1(c)). However, trapped charges at the OSC/dielectric interface can affect the turn-on of the transistor. In such cases, a specific V_g is necessary to counteract the electric potential, which was produced by those charges trapped prior to the involvement of additional carriers, contributing to I_{ds} ($V_g > V_T$).

Transistors demonstrate two distinct operation modes: the linear regime and the saturation regime (depicted in figure 1(c)). When no driving voltage is applied ($V_{ds} = 0$), charge carriers consistently accumulate at the interface between the active layer and the dielectric insulated layer, leading to $I_{ds} = 0$. Within the linear range, characterized by a small V_{ds} (specifically $V_{ds} \ll V_g - V_T$), a linear charge density gradient is established between the two electrodes (source and drain), and Ids exhibits a proportional relationship with V_{ds}. As V_{ds} increases, a pinch-off region forms near the drain electrode when $V_{ds} = V_g - V_T$, depleting the charge carriers. Further increases in V_{ds} do not enhance I_{ds}, indicating entry into the saturation regime. In the saturation regime, carriers are propelled from the pinch-off point to the drain by a higher electric field in the depletion region. As V_{ds} continues to rise (specifically when $V_{ds} \gg V_g - V_T$), the pinch-off point shifts further away from the drain, while the channel length (L) experiences minimal shortening. Once reaches the pinch-off condition, I_{ds} saturates at $V_{ds} = V_g - V_T$.

The working principle of OFET biosensors involves the detection of alterations in the electrical properties of the semiconductor channel, which was induced by the presence of an analyte of interest. In biosensing applications, a dedicated ligand or receptor is utilized to functionalize the OSC channel, allowing for the specific identification of target analytes (e.g. enzymes, antibodies, aptamers) that can selectively bind to the analyte of interest. The interaction between the analyte and the functionalized channel leads to alterations in the electrical properties of the channel, such as the threshold voltage or the mobility of charge carriers. This change in electrical properties is detected as an electrical signal, which directly correlates with the concentration of the analyte.

It is common to utilize extended gate-OFETs in biosensor applications [27, 28]. An extended gate-OFET is a type of transistor that has an extended gate, which is a separate electrode that is in contact with the solution being sensed. This extended gate allows the OFET to be used as a chemical

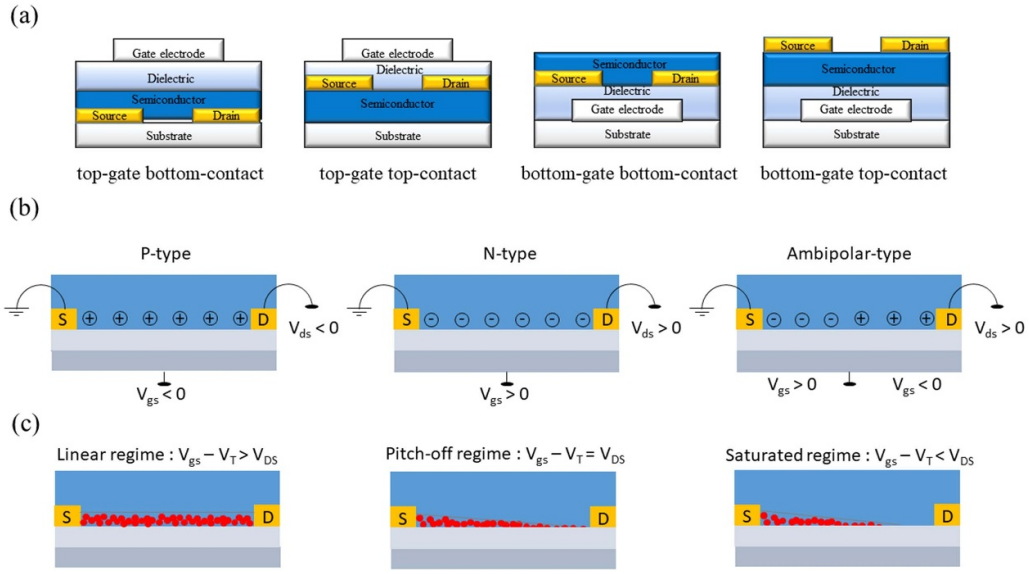

Figure 1. Basic working principles of OFETs: (a) four device architectures; (b) different charge carrier types. (c) Mechanism for the generation of linear and saturation regime.

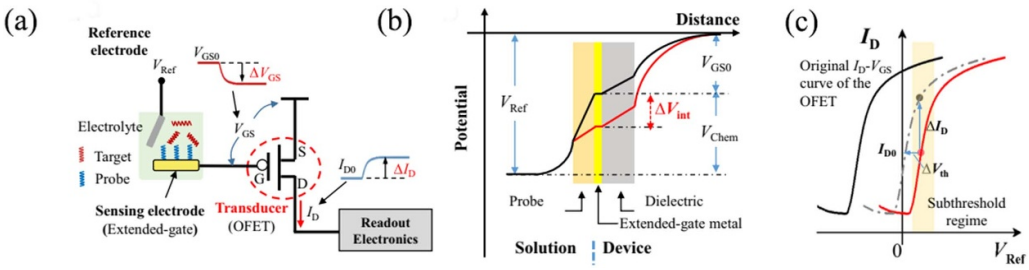

Figure 2. (a) A diagrammatic depiction of an OFET-based biochemical sensor; (b) a schematic representation illustrates the potential variation across a simplified cell model; (c) the shift in the transfer curve of the OFET. Reproduced from [29]. CC BY 4.0.

or biological sensor. By interacting with the extended gate, the analyte induces changes in the electrical properties of the transistor, enabling the measurement of such modifications. This detection approach can effectively identify the presence as well as determine the concentration of the analyte. Extended gate-OFETs offer multiple advantages compared to traditional sensors, including their ability to operate at low voltages, their cost-effectiveness, and their ease of miniaturization. They are also highly sensitive, selective, and can operate in aqueous environments. In addition, the extended gate can be easily modified to detect specific analytes, making these sensors highly customizable and versatile.

Figure 2(a) depicts the fundamental configuration of an OFET biosensor. It consists of an OFET biosensor integrated with two components: the extended-gate electrode (SE) and the reference electrode (RE). Those two electrodes establish the necessary measurement configuration [29]. Notably, the SE is functionalized with a probe that specifically captures target analytes from the surrounding solution. Throughout the measurement process, initially, a voltage bias (V_{Ref}) is continuously employed to the RE. Concurrently, the OFET gate (V_{GS0}) initiates a potential that propagates through the solution, thereby eliciting the current.

Figure 2(b) demonstrates the relationship between V_{GS0} and the voltages V_{Ref} and V_{Chem} in the OFET-based biochemical sensor. V_{GS0} can be represented as a function of V_{Ref} and V_{Chem}. V_{Chem}, defined as the voltage between the RE and the SE, can be divided into two components: an interfacial potential drop (V_{int0}) and the sum of a constant V_{Chem0}. V_{int0} is affected by the dipole formed at the interface between the electrode and electrolyte, and it can be adjusted by the presence of captured charged biomolecules. The open circuit potential method can be employed to measure and quantify this modulation.

When the SE captures negatively or positively charged analyte targets, it initiates a modification in the interfacial potential drop (ΔV_{int}) and hence ΔV_{GS}. This change in V_{GS} causes a corresponding change in output current (Δ_{ID}) that can be detected and measured by the readout circuit, facilitating digitalization of the signal, as exemplified in figure 2(c).

A notable advantage of OFET biosensors lies in the simplicity and ease of fabrication, which enables the creation of

cost-effective and disposable biosensors. Additionally, OFET biosensors can operate in ambient conditions and do not require complex readout equipment, making them well-suited for applications at field-based scenarios and point-of-care settings. The focus of this review will be on the diverse range of applications of OFET biosensors, which is successfully utilized for the detecting of diverse analytes, including but not limited to glucose, DNA, enzymes, ions, gases and more.

2.2. OFET-based glucose sensors

OFET biosensors have been shown to be effective for detecting glucose, a biomolecule commonly used as a marker for diabetes. It is essential for managing various health conditions such as diabetes, hypoglycemia, and hyperglycemia. It allows individuals to monitor their blood glucose levels and adjust their diet, exercise, and medication accordingly. In glucose detection, OFET biosensors work based on the change in the electrical conductance of the OSC channel upon interaction with glucose or glucose oxidase (GOx).

In 2008, Liu *et al* [30] developed an a glucose sensor based on OFETs that uses a conducting polymer film known as poly(3,4-ethylenedioxythiophene–poly(styrene-sulfonate)) (PEDOT–PSS) as the channel, which was functionalized with immobilized GOx enzyme. The immobilization of GOx on PEDOT–PSS is achieved through a straightforward process involving spin-coating method and electrochemical polymerization. The resulting glucose sensor exhibits a linear response to variations in glucose concentration. The glucose sensor shows a sensitivity of 1.65 μA per 1 mM of glucose concentration, providing a linear range of response spanning from 1.1 to 16.5 mM of glucose. Additionally, the sensor exhibits a response time of 10–20 s. By encapsulation the sensor within a membrane (cellulose acetate), the dissolution of GOx and PEDOT–PSS matrix in glucose solution is effectively prevented. The OFET-based glucose sensor retains the bioactivity of the enzyme and has potential application for glucose sensing applications.

Based on the work above, Elkington *et al* [31] demonstrates that GOX can be incorporated into OFET devices without requiring modification the structure of the enzyme or polymer matrix, and without loss of enzyme activity. Poly(3-hexylthiophene) (P_3HT) was used as the semiconductor in this case. A new model for OFET glucose sensing devices was depicted in the current generation, as illustrated in figure 3(a). They suggest that the diffusion of glucose through the PEDOT gate and Nafion, potentially acts as the rate-limiting step. However, glucose undergoes rapid oxidation at the GOX enzyme, leading to the formation of gluconolactone and H_2O_2. Subsequently, H_2O_2 is swiftly oxidized to protons at the built-in potential of the device (around 0.7 V). Additionally, due to the high hydration nature of the PVP sol–gel material, any protons generated enzymatically can efficiently migrate to the PVP/P_3HT interface through the Grotthuss mechanism [32]. The protons then dope the active layer (P_3HT), leading to the observed changes in I_D. This work represented a practical strategy for a printable glucose sensor based on OFETs and demonstrated high sensitivity within the range of glucose concentrations commonly found in saliva.

2.3. OFET-based DNA sensors

The conventional methods for DNA detection, such as microarrays and real-time PCR, often require the use of costly fluorescent dyes and optical sources/detectors, which can impose limitations in some applications. In contrast, OFET technology provides a straightforward platform for creating cost-effective, scalable, and flexible devices that offer advantages such as air stability, low power consumption, biocompatibility, and easy surface modification. These features make OFET-based sensors suitable for detecting various analyte species across different fields of application [33].

Khan *et al* [34] introduced a novel detection scheme using OFETs as the electrical read-out platform for *in situ* and real-time detection of DNA targets with short chains selectively (figure 3(b)). In order to modify the surfaces of the OFETs, they employed a technique named plasma-enhanced chemical vapor deposition to introduce a thin maleic anhydride polymer layer. This modification enabled the attachment of peptide nucleic acid (PNA) strands covalently. These PNA strands were utilized as superior candidates for detecting the target DNA, benefiting from their enhanced affinity, selectivity and stability in comparison to the DNA counterparts. The experimental findings demonstrated that the OFET sensor achieved comparable affinity constants to those observed with a highly sensitive surface plasmon fluorescence spectroscopy detection system when detecting *in situ* hybridization. Moreover, the OFET devices exhibited excellent discrimination between single-base and double-base mismatches within the target DNA sequence. This study represents the first documented instance of label-free *in situ* detection of target DNA sequences using OFET sensors, offering promising prospects for future advancements in the field of DNA sensing.

Most of these sensors cannot be operated in liquids due to the sensitivity of OSCs to oxygen and humidity. Lai *et al* [35] developed a DNA-hybridization sensor, operating in aqueous environments at low voltages with high sensitivity and selectivity, as illustrated in figure 3(c). The sensor relies on the change in the threshold voltage of the OFET for detection. However, it is important to note that the sensing layer is separate from the OSC, indicating that the sensing mechanism is independent of the characteristics of the OSC, which is particularly important since the stability of the semiconductor limits the operability of many devices. The proposed structure, called organic charge-modulated FET, introduces a control electrode integrated on the substrate, fully exploiting the advantages of organic technology while avoiding its drawbacks. The results highlight a remarkable limit of detection (LOD) in DNA hybridization and enhanced sensitivity in detecting single nucleotide polymorphisms for organic devices, surpassing previous research in this field. Additionally, the

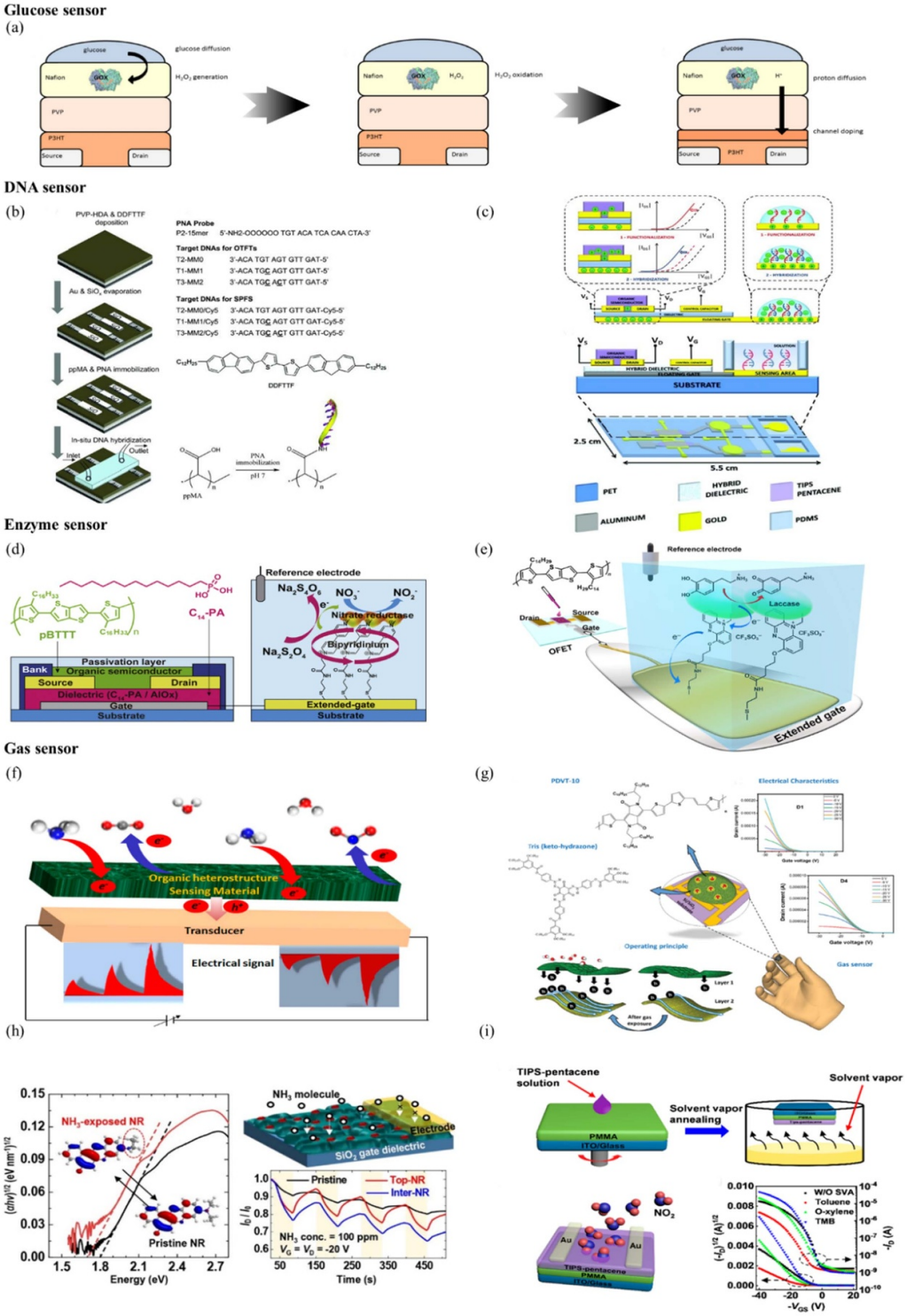

Figure 3. Glucose sensor: (a) using OFET to detect saliva-range glucose concentrations. Reprinted from [31], with the permission of AIP Publishing. DNA sensor: (b) utilizing OFETs for label-free, *in situ* detection of DNA. [34] John Wiley & Sons. [Copyright © 2010 WILEY-VCH Verlag GmbH & Co. KGaA, Weinheim]. (c) Development of an ultralow voltage sensor based on OTFTs for the label-free detection of DNA. [35] John Wiley & Sons. [Copyright © 2013 WILEY-VCH Verlag GmbH & Co. KGaA, Weinheim]. Enzyme sensor: (d) enzymatic sensor based on an extended-gate OFET for selective nitrate detection. Reprinted from [36], Copyright (2016), with permission from Elsevier. (e) An enzymatic sensor utilizing an extended-gate-type organic transistor for the detection of dopamine in human urine. Reproduced from [37]. CC BY 4.0. Gas sensor: (f) a novel approach utilizing organic heterojunction devices based on phthalocyanines. Reproduced from [38]. CC BY 4.0. (g) A highly selective sensor for facilitated detection of H_2S based on electron affinity. Reproduced from [39]. CC BY 3.0. (h) Utilizing a solvatochromic medium with twisted intramolecular charge-transfer behavior for the detection of ammonia gas. Reprinted with permission from [40]. Copyright (2021) American Chemical Society. (i) Achieving the sensitivity of NO_2 detection by controlling the grain boundaries of organic semiconductors through the application of solvent vapor annealing. Reproduced from [41]. CC BY 4.0.

results are comparable to the FET-based DNA sensors with inorganic materials as the active layers. These outcomes are due to the utilization of gate dielectric with high capacitance, obtained by combining materials and optimizing the interface of the device.

2.4. OFET-based enzyme sensors

OFET based enzyme sensors are biosensors that utilize the OFET technology to detect and measure various biomolecules. The OFETs are constructed using organic materials as semiconductors and can detect the change in the conductance of the active layer caused by the interaction between the enzyme and the substrate.

The first selective nitrate biosensor device was reported by Minami *et al* [36] in 2016. The device utilized an extended-gate type OFET functionalized with a mediator (specifically, a ¼a bipyridinium derivative) and a nitrate reductase enzyme, along with an OFET-based transducer. Poly{2,5-bis(3-hexadecylthiophene-2-yl)thieno[3,2-b]thiophene (pBTTT) (with C_{16} chains) was used as the semiconductor layer (figure 3(d)). The mechanism of nitrate detection involves an electron-relay effect on the gate electrode (extended), leading to changes in the electric properties of the OFET. The nitrate biosensor was found to have a detection limit of 45 parts per billion (ppb) in water, demonstrating sensitivity comparable to conventional detection methods. Additionally, the OFET biosensor was used to successfully detect nitrate in diluted human saliva, with results consistent with those obtained using conventional colorimetric measurement.

Dopamine, a neurotransmitter, serves an important role in regulating several physiological functions in the human body, such as mood, attention, movement, and the reward system. Ohshiro *et al* [37] introduced a highly selective dopamine biosensor in human urine using an extended-gate-type OFET-based approach, employing a laccase-linked mediator. PBTTT (with C_{14} chains) was used in this case (figure 3(e)). The detection mechanism of this biosensor relies on the oxidation of dopamine through the enzymatic action of laccase in the presence of a mediator. This oxidation process induces an electronic relay on the gate electrode (extended), leading to a measurable quantitative change in the transistor characteristics. By incorporating an enzyme-linked self-assembled monolayer (SAM) on the extended-gate electrode, the OFET demonstrates selective detection of dopamine while minimizing interference from other substances. The detection limit of the OFET-based sensor is determined to be approximately 0.029 ppm (0.19 μM) using the 3σ method, making it well-suited for the detection of dopamine levels in human urine, considering the typical concentration range of urinary dopamine (<0.39 ppm, 2.5 μM). Furthermore, the viability of this biosensor for urinalysis is demonstrated through successful spike-and-recovery tests performed on non-diluted human urine samples without any prior treatment, revealing a high degree of accuracy with recovery rates ranging from 97% to 104%.

2.5. OFET-based gas sensors

OFET gas sensors have emerged as a promising platform for high sensitivity, efficiency, low cost, and mechanical flexibility [42]. OFET gas sensors have diverse applications in healthcare, food quality control, and air pollution monitoring [42]. OFET-based gas sensors have been extensively studied, and various protocols have been developed for high-performance gas sensing [43]. The sensing mechanism of OFET gas sensors relies on the ability of OSCs to undergo noncovalent π-interactions with analyte molecules, which trap charge carriers and result in a change in the electrical properties of the semiconductor [11]. Additionally, OFET gas sensors can be repeatedly used, as the trapped charge carriers can be detrapped by applying an opposite voltage [11]. The development of nanostructured receptors and ultrathin OSC films has further enhanced the sensitivity and selectivity of OFET gas sensors [10, 44].

Figure 3(f) illustrates a simplified depiction of the sensing mechanism employed by gas sensors that utilize organic heterostructures to leverage their electrical properties [38]. In this mechanism, redox gases interact with the sensing layer of the heterostructure, either donating or withdrawing electrons based on their oxidizing or reducing characteristics. This interaction induces chemical doping within the sensing layer, leading to alterations in the electrical output of the transducer. These alterations manifest as an increase or decrease in current, depending on the concentration of the gas. It is important to acknowledge that the specific sensing mechanism may vary dependent on the arrangement of the heterostructure and its incorporation into the transducer circuit. The incorporation of organic heterostructures in gas sensors has exhibited advancements in multiple metrological and analytical parameters. Establishing uniform definitions for these parameters across all sensor types can be challenging. However, in the context of gas sensors, sensitivity pertains to the relative variation in response per unit alteration exposed to the sensor. Selectivity denotes the sensor's ability to generate an output signal specific to a particular analyte in the existence of gas mixtures. The operational range of a gas sensor, along with the LOD representing the minimum accurately measurable concentration of the target analyte, are crucial factors to consider. The kinetics of the sensor's response, which encompass response and recovery times, also hold significant importance in assessing the metrological performance of gas sensors.

Yuvaraja *et al* [39] introduced a novel hybrid heterostructure comprising a polymer-monomer heterostructure derived from CP (PDVT-10) and a recently reported monomer [tris(keto-hydrazone)] in an OFET platform (figure 3(g)). This hybrid structure exhibits remarkable sensitivity (525% ppm^{-1}) and selectivity to H_2S gas, accompanied by a low LOD (1 ppb), excellent ambient stability (approximately 5% current degradation over 150 d), and favorable response-recovery characteristics. Additionally, the PDVT-10/tris(keto-hydrazone) OFET sensor demonstrates outstanding electrical behavior and reproducibility in gas

response. These significant findings pave the way for the integration of advanced gas sensors into a diverse range of applications.

Oh *et al* [40] developed an OFET gas sensor by integrating Nile red (NR), a solvatochromic dye with twisted intramolecular charge-transfer (TICT) behavior, as an auxiliary sensing medium (aNR-SM) in their design (figure 3(h)). When a polar molecule like ammonia (NH_3) approaches, NR experiences intra-charge transfers, causing the donor functional group to twist and increasing the dipole moment. The Top-NR configuration, with the aNR-SM covering only the top of the OSC layer, demonstrated superior gas sensing performance. Compared to the pristine case, this configuration showed enhanced response and recovery rates, measuring 46% and 94%, respectively, compared to the pristine case. They also observed a sensitivity of 0.87 ± 0.045 $ppm^{-1}\%$ with excellent linearity (0.999) across the measured NH_3 concentrations, resolving the saturation problem in the OFET-based gas sensor. These findings not only enhanced the performance of the OFET biosensor but also provided a reliable sensing performance by utilizing the solvatochromic and TICT behaviors of the auxiliary sensing medium.

Enhancing the performance of gas sensors relies significantly on the microstructure of the OSC. Junsheng Hou *et al* [41] introduced a solvent vapor annealing (SVA) process in order to control the morphology of the active layer (6,13-bis(triisopropylsilylethynyl)-pentacene, TIPS-pentacene), resulting in highly sensitive nitrogen dioxide (NO_2) sensors based on OFETs (figure 3(i)). Comparative analysis with pristine devices showed that toluene SVA-treated devices exhibited a ten-fold increase in responsivity when exposed to 10 ppm NO_2, achieving a detection limit as low as 148 ppb. In-depth analysis demonstrated that the SVA process led to the development of compact grain boundaries within the TIPS-pentacene films, amplifying the adsorption capacity for gas molecules and leading to heightened sensitivity towards NO_2. This uncomplicated SVA technique presents a proficient and dependable approach for attaining NO_2 sensors based on OFETs with remarkable sensitivity.

3. OECT biosensors

3.1. The working principle of OECT biosensors

Figure 4 illustrates the distinctions between OFET, EGOFET, and OECT. Typically, OFETs consist of a channel OSC layer and a gate electrode that are detached by a dielectric insulated layer. Applying a voltage to the gate electrode generates electrostatic charges at the interface, specifically the gate, altering the conductance of the channel [24] (figure 4(a)). Replacing the conventional solid gate dielectric with an electrolyte brings about the generation of an electrical double layer (EDL) at the boundary connecting the organic semiconducting layer and electrolyte. This modification gives rise to a distinct type of OFET called an EGOFET. Compared to OFETs, EGOFETs have a significantly higher capacitance, allowing them to operate at reduced gate voltages, commonly below 2 V [46, 47] (figure 4(b)). When the channel material permits ion permeability, it allows for the accumulation of charges throughout the entirety of the channel material's volume, leading to the formation of an OECT [48] (figure 4(c)). In OECTs, nano-crystallites or singular polymer chains create a capacitive interface, leading to a volumetric capacitance that can be orders of magnitude larger than the EDL capacitance. It is worth noting that OECTs typically exhibit slow operating speeds since they rely on the migration of ions through a solid medium. Typical OECTs are limited to operating below the kHz frequency range, which is considerably lower compared to the MHz range achieved by OFETs [49–51].

The operating mode (depletion mode or accumulation mode) of the OECT is determined by the inherent conductivity of the channel material in its initial, pristine state, i.e. without a gate voltage [45]. When a channel material with a high conductivity and an abundance of free charge carriers, for instance, poly(3,4-ethylenedioxythiophene) doped with PEDOT:PSS, is utilized in an OECT, the device operates in the depletion mode. PEDOT:PSS is a widely recognized example of a mixed ionic-electronic conductor that enables efficient charge transport in both ionic and electronic forms, making it suitable for depletion-mode OECT operation. In the case of depletion-mode OECTs, when no gate voltage is applied, the transistor is 'on', due to the compensating effect of the sulfonate groups in poly(styrene sulfonate) (PSS) on the mobile holes in the PEDOT channel. However, when applying a positive gate voltage, the transistor switches off. This occurs because injected cations replace the holes, leading to a reduction in conductivity and turning off the device. On the other hand, accumulation mode OECTs employ undoped organic semiconducting materials as the channel in their pristine state when no gate voltage is applied, the device is off. However, when applying a gate voltage, ions are flowing into the channel, doping it and increasing its conductivity. This allows mobile carriers to accumulate in the channel, resulting in the activation of the transistor and turning the device on.

The transconductance (g_m) is a critical performance metric for OECT device, which measures the device's ability to amplify an input signal by correlating the alteration of the drain current (I_D) with the variation of the gate voltage (V_G). To calculate the transconductance, one must take the first derivative of the transfer curve, which is influenced by biasing conditions and the channel geometry. Therefore, it is crucial to account for device geometries, such as the channel width (W), channel length (L) and film thickness (d), when evaluating and comparing the performance of various OECT channel materials. A widely used model for depletion mode OECT, proposed by Bernards *et al* [52], expresses the transconductance in the saturation regime as

$$g_m = \frac{\partial I_D}{\partial V_G} = \frac{Wd}{L}\mu_n C^* \left(V_{th} - V_G\right).$$

The transconductance is calculated by factors such as the charge-carrier mobility (μ), the volumetric capacitance (C^*),

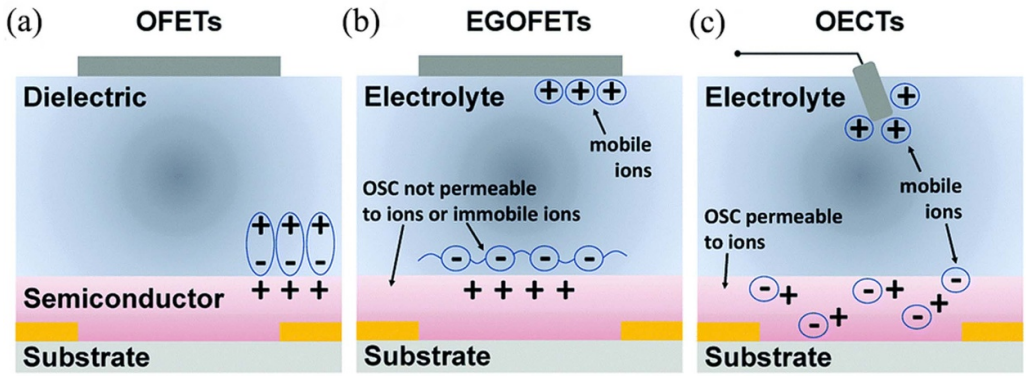

Figure 4. Basic working principles of OECT. Reproduced from [45]. CC BY 3.0.

and the threshold voltage (V_{th}). While μ is commonly used in OFET and EGOFET literature for assessing semiconductor performance, in the context of OECT materials, there is a notable shift in using the μC^* product as a benchmark for defining semiconductor performance. OECTs exhibit significantly higher channel capacitance compared to OFETs, leading to the ability to achieve larger drain currents under equal geometries and biasing conditions. This increased channel capacitance directly contributes to larger transconductance values in OECTs. The enhanced capacitance allows for more efficient modulation of the drain current, resulting in improved signal amplification capabilities of OECT devices. OECTs demonstrate a remarkable increase in channel capacitance, enabling them to achieve substantially higher drain currents compared to OFETs under similar biasing conditions and geometries. This enhanced channel capacitance empowers OECTs to facilitate a more efficient modulation of the drain current, resulting in significantly larger current outputs. Consequently, OECTs are expected to have much larger g_m values. Typically, OECTs demonstrate g_m values in the mS range, whereas OFETs and EGOFETs have reported values in the μS range [49]. A noteworthy characteristic of OECTs, which distinguishes them from other types of OFETs, is their inherent capability to operate at low working voltages, typically below 1 V. This feature is particularly significant as it renders OECTs highly suitable for applications in biological systems. The low operating voltages minimize the risk of electrochemical reactions or damage to delicate biological samples, making OECTs well-suited for interfacing with biological materials, such as cells or tissues. This exceptional property underscores the potential of OECTs in a wide range of bioelectronic applications where low-voltage operation is essential for maintaining the integrity and functionality of biological systems.

OECT biosensors are a type of biosensor that utilize conducting materials as the active material in their sensing mechanism. The pliability of its mechanical properties, adaptability to various fabrication techniques, and capacity to assume distinctive form factors have made bioelectronic integration feasible for capturing electrophysiological signals (such as neural and cardiac signals) as well as physical and chemical signal transduction, both *in vitro* and *in vivo* [19, 49]. As an amplifying transducer, an OECT can function as a sensor and can be easily incorporated into uncomplicated amplifying circuits [53]. The uncomplicated nature of OECTs arises from their simplified design, ease of fabrication, and compatibility with organic and flexible substrates. These characteristics make it easier to incorporate OECTs into amplifying circuits without requiring extensive modifications or complex circuitry. Based on those merits mentioned, OECT-based architectures are highly suitable for use as biological sensors. In this section, we primarily discussed the operational mechanisms and explored the latest applications of biological sensors based on OECT technology.

Over the last two decades, OECTs have been extensively studied for their distinctive properties and applications in diverse fields, such as neural interfaces, printed circuits, neuromorphic devices, clinical and biomedical research, and chemical and biological sensors [9]. OECTs have been utilized as both recording and stimulation devices in electrophysiological signals and can measure cell coverage, barrier tissue organization, and cellular microenvironment (figure 5). Compared to impedance sensing, OECTs have superior performance and can operate in complex environments like blood and milk, facilitating multi-analyte assays in complex environments. OECT-based biosensors can detect metabolites in electrolytes or body fluids, enabling early detection of human diseases. OECTs can be easily integrated with various fabrication techniques, resulting in flexible and wearable applications. They possess ultra-high transconductance, stability in electrolytes, cytocompatibility, and can be biofunctionally modified, making them suitable for bioelectronics fabrication. Conducting polymers were used to prepare OECTs, facilitating the modulation of the biochemical, mechanical, and electrochemical microenvironment of cells and enabling the monitoring of cell behavior.

3.2. OECT-based enzyme sensors

The OECT biosensors most frequently utilized are typically associated with enzymes [9]. Enzymatic OECT sensors operate based on the following sensing mechanism: Immobilized enzymes on the gate electrode of OECTs catalyze substrates to enzymatic products, causing electron gain or loss on the electrode. This leads to concurrent changes in the channel

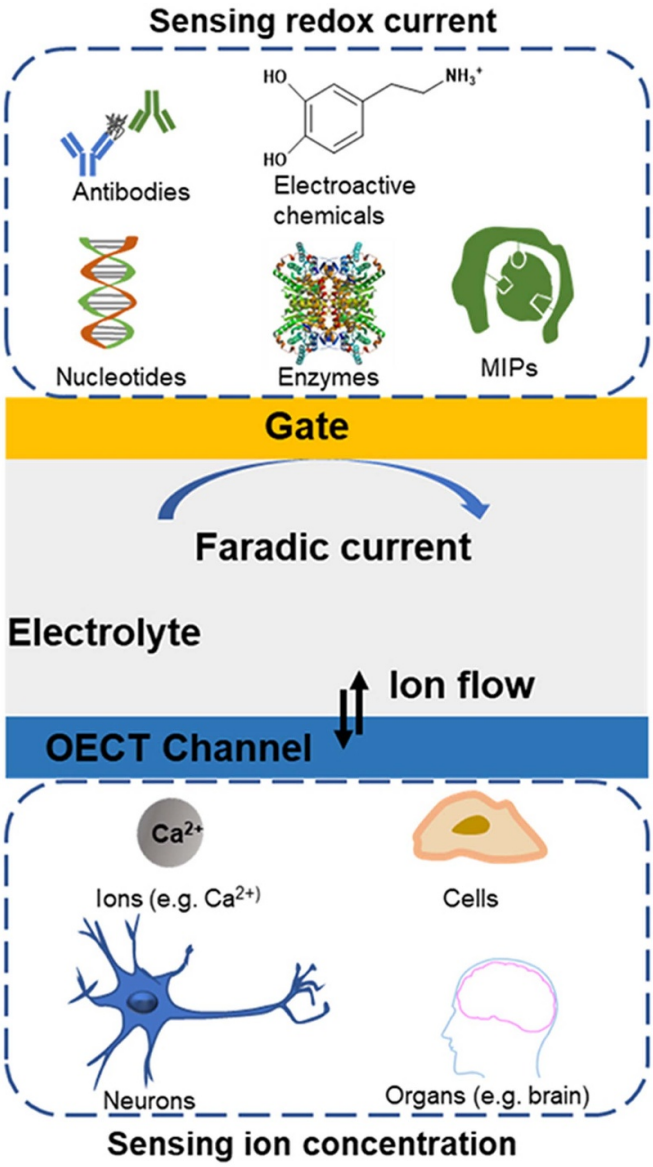

Figure 5. Exploration of applications in biological systems using OECTs. Reproduced from [9]. CC BY 4.0.

current, transmitting electrical signals to the gate electrode. To maintain charge neutrality in both the ionic and electronic circuits, the conducting polymer film was permeated by a cation, compensating for the anionic polymer (e.g. PSS^-) and replacing the cationic polymer (e.g. $PEDOT^+$). As a result, V_g^{eff} is altered, resulting in a logarithmic reduction in channel current proportional to the concentration of enzymatic substrates.

The first application was pioneered by Nishizawa *et al* [54], who utilized the penicillinase enzyme to establish a relationship between the conductivity of the polypyrrole material and the pH changes. However, the pH-dependent nature of the polypyrrole film constrained its linearity range, and it was unable to regulate neural pH environments effectively. Later, PEDOT:PSS has emerged as a powerful material for OECT sensors owing to the stability across a wide pH range, making it suitable for enzymatic sensing in neutral environments [55]. The small bias potentials between gate and channel prevent electrolyte hydrolysis, and the transistor's initial properties are sufficient for detecting various analytes. PEDOT:PSS has since played a significant role in OECT enzymic sensors.

Braendlein *et al* [56] developed an electronic platform for accurately sensing metabolites in highly interfering samples, such as cell culture media. The active layer in this electronic platform was composed of PEDOT:PSS. The platform employs a sensor circuit with a reference, which integrates included two OECTs with different functionalization in a Wheatstone bridge layout, as shown in figure 6(a). In the biofunctionalization scheme utilized for the sensing OECT, the gate of the device was biofunctionalized by immobilizing an oxidase-type enzyme, specifically lactate oxidase, along with an electrochemical mediator. This biofunctionalization strategy made the sensor highly specific to detecting lactate, enabling accurate and targeted measurements. In a similar manner, the gate electrode of the reference OECT was subjected to biofunctionalization. However, instead of using lactate oxidase, a nonspecific protein (bovine serum albumin) was immobilized on the gate electrode. This ensured a comparable surface environment and response time between the sensing and reference OECTs. To establish a calibration curve for lactate detection, the researchers measured the chronopotentiometric response of the Wheatstone bridge sensor in both OECTs after adding increasing concentrations of lactate into the wells. The obtained calibration curve was generated using lactate solutions in buffer (1 $\times$ phosphate-buffered saline (PBS)). To assess the sensitivity of their device, the researchers performed a titration curve to assess the response of their lactate sensor when exposed to increasing levels of lactate in cell media. The cell media was incubated with peripheral blood mononuclear cells to simulate a realistic physiological environment. The results of their study demonstrated that their device exhibited high sensitivity, capable of detecting lactate produced by a limited number of cells (approximately tens). Moreover, the device showed the ability to distinguish samples with elevated lactate concentrations compared to control samples. This indicates the device's potential for precise and reliable detection of lactate levels, even in scenarios where lactate production is relatively low or when higher lactate concentrations are present. In the calibration curve conducted in PBS, the obtained signal showed saturation and some noise. However, when the calibration curve was performed using cells, the signal remained linear up to an NR (normalized response) value of 0.1. This indicates that the device's response to lactate concentration in the presence of cells exhibits a linear relationship over a wider range, providing more accurate and reliable measurements within that range compared to the calibration in PBS.

The distinctive biological behavior and pharmacological activity demonstrated by different enantiomeric α-amino acids have attracted considerable interest. In a notable study conducted by Zhang *et al* [57] in 2020, an OECT-based biosensor was developed for the selective identification of various α-amino acids. The biosensor utilized PEDOT:PSS as a key component and showed promise for potential applications

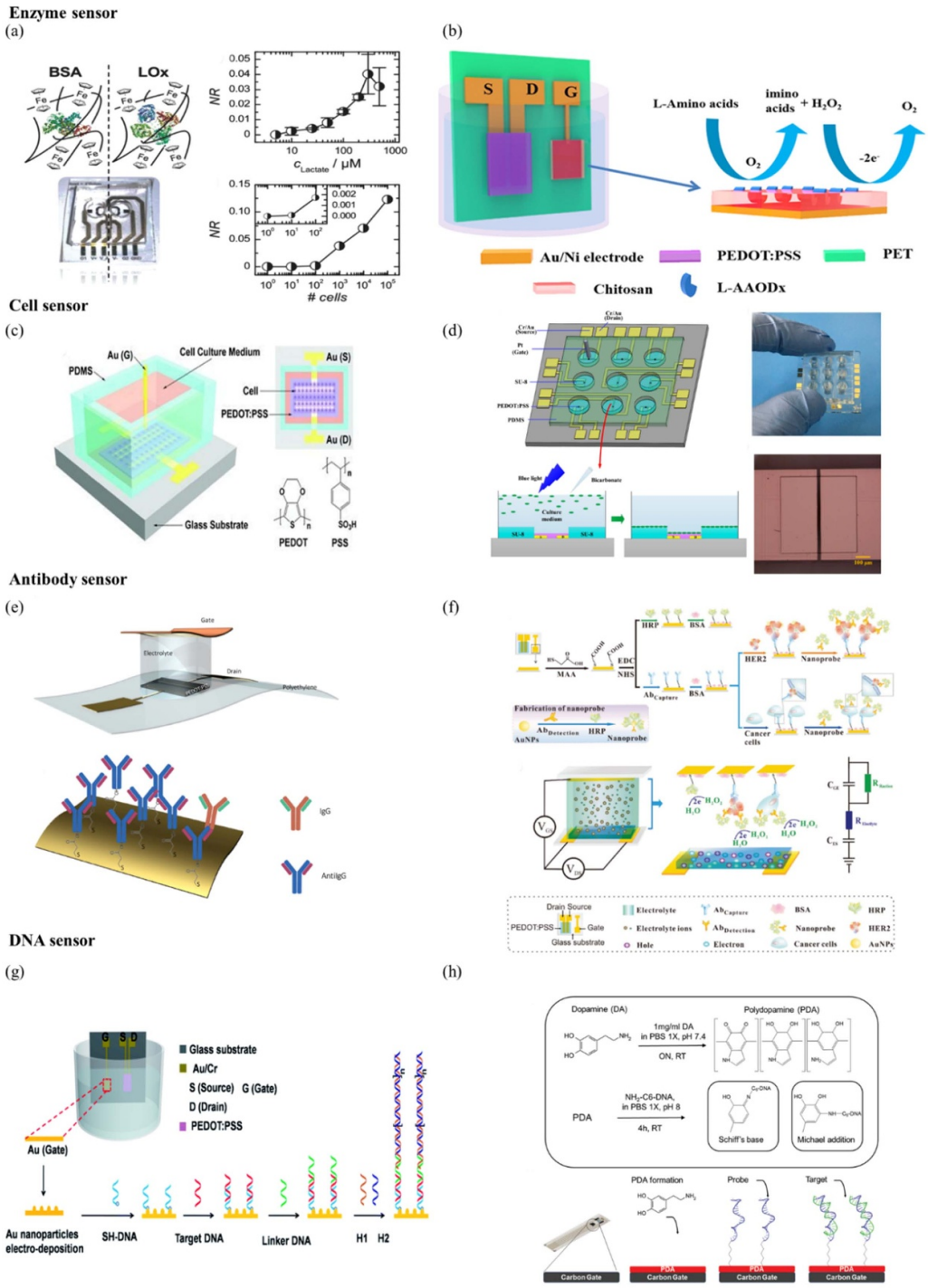

Figure 6. Enzyme sensor: (a) detection of lactate in tumor cell cultures utilizing OECTs. [56] John Wiley & Sons. [© 2017 WILEY-VCH Verlag GmbH & Co. KGaA, Weinheim]. (b) An enzyme-based sensor platform for the detection of α-amino acid enantiomers employing PEDOT-PSS. Reproduced from [57]. © 2020 The Electrochemical Society ('ECS'). Published on behalf of ECS by IOP Publishing Limited. All rights reserved. Cell sensor: (c) the application of OECTs in the development of cell-based biosensors. [58] John Wiley & Sons. [Copyright © 2010 WILEY-VCH Verlag GmbH & Co. KGaA, Weinheim]. (d) Advancement of an innovative OECT-based platform to monitor the green vegetative phase in previously senescent *Haematococcus pluvialis* cells. Reproduced from [59]. CC BY 4.0. Antibody sensor: (e) ultra-sensitive protein detection using OECTs fabricated on plastic substrates. Reproduced from [60]. © IOP Publishing Ltd. All rights reserved. (f) Achieving highly sensitive detection of protein biomarkers using OECTs. [61] John Wiley & Sons. [© 2017 WILEY-VCH Verlag GmbH & Co. KGaA, Weinheim]. DNA sensor: (g) utilizing OECTs and nucleic acid self-assembly signal amplification for a sensitive DNA detection platform. Reproduced from [62] with permission from the Royal Society of Chemistry. (h) Polydopamine-functionalized OECTs for monitoring DNA hybridization. Reproduced from [63]. CC BY 4.0.

in chiral recognition of enantiomers (figure 6(b)). In addition to PEDOT:PSS, several other conjugated semiconductor materials have been specifically engineered to cater to the needs of OECT-based sensors. Pappa *et al* [64] developed a transistor platform at micrometer-scale for detecting lactate, a crucial metabolite involved in cellular metabolic pathways linked to essential health status. P-90 is a conjugated polymer with an n-type character that serves as the active material in our device. It is based on an NDI-T2 copolymer, which combines an electron-rich unit (T2) and an electron-poor unit (NDI). The approach utilizes an electron-transporting OSC with hydrophilic side chains to improve ion transport and facilitate enzyme conjugation. The device integrates redox enzymes and functions as a network with the ability to switch between the reduced and neutral states. This design enables rapid, selective, and sensitive detection of metabolites. This technology can potentially harness the power of enzymes to drive efficient energy generation and storage, making it a promising avenue for biosensor and energy research.

3.3. OECT-based cell sensors

Researchers have developed a technique that involves coupling OECTs with live mammalian cells to monitor their responses and properties, such as toxicity and diagnostics. Bolin *et al* [65] were the first to successfully couple OECTs with cells and detect cell gradients on the OECT channel. They achieved this by seeding Madin Darby canine kidney (MDCK) epithelial cells for OECTs and creating a potential gradient using a channel bias. By controlling the gate and source voltages, they could modulate the potential gradient of the channel, which in turn affected the MDCK cell and resulted in a gradient of cell quantity.

In 2010, Peng Lin and colleagues [58] published a study in which they developed sensors that combined OECTs with fibroblasts and cancer cells to sense cell activities in an *in vitro* environment (figure 6(c)). These sensors operate based on the electrostatic interactions occurring at the interfaces between the cells and the reactive layer of the OECT. Due to its high sensitivity to surface charge changes caused by cell adhesion, the device is well-suited for solution processing, enabling the creation of miniature and integrated cell-based sensors. This feature holds great potential for enhancing cell-based testing, including drug screening and toxicity testing. *Haematococcus pluvialis* (*H. pluvialis*), a freshwater unicellular microalga, is highly valued for its astaxanthin metabolite, a potent antioxidant. To induce maximum astaxanthin production, precisely distinguishing the senescent green vegetative phase of *H. pluvialis* cells is crucial for the targeted utilization of growth promoters. However, conventional methods for determining this phase are labor-intensive and time-consuming. To address this, a new platform was developed by Zhang *et al* [59] using OECTs. The OECTs detected significant changes in channel current when *H. pluvialis* cells settled on the PEDOT:PSS layer. The senescent green vegetative phase was determined through blue light irradiation and sodium bicarbonate additives, reaching a stationary stage at approximately 120 min post-treatment. Consequently, the optimal timing for applying astaxanthin production inducers was established as 120 min after sample loading, utilizing the OECTs in their original configuration. This research holds promise for the development of a real-time biosensor capable of indicating the precise moment to administer inducers for maximal astaxanthin yield in *H. pluvialis* cells. Figure 6(d) presents a measurement setup utilizing an OECT array for detecting the initiation of the senescent green vegetative phase in *H. pluvialis* cells [59]. The platform incorporates a PEDOT:PSS film, a conducting polymer, as the functional layer of the OECT. The source and drain electrodes are fabricated with a patterned film of Cr/Au. The growth medium, enclosed within PDMS, acts as the electrolyte, while a Pt wire submerged in the electrolyte and acted as the gate electrode. Following treatment involving sodium bicarbonate solution additives and blue light irradiation, the channel current of the OECT undergoes changes when *H. pluvialis* cells settle onto the device, signifying the initiation of the vegetative phase in previously senescent cells.

3.4. OECT-based antibody sensors

The early detection of severe diseases relies heavily on identifying protein biomarkers. While there have been numerous advances in achieving highly sensitive protein detection over the last decade, most of these methods involve complex assay setups that make them unsuitable for on-the-spot diagnosis and point-of-care applications. Luisa Torsi and colleagues [60] have presented a biosensor employing a printed OECT on plastic substrates for the highly selective detection of Immunoglobulin G (IgG). The obtained results exhibit concentrations significantly lower than the detectable thresholds of conventional clinical diagnostic enzyme-linked immunosorbent assays, comparable to those achieved using label-dependent single molecule arrays. This study highlights the versatility and effectiveness of plastic OECT-based biosensors in immunoassay technology, providing advantages such as simplicity, affordability, non-invasiveness, and remarkable sensitivity. Figure 6(e) depicts the schematic structure of the OECT [60]. The PEDOT:PSS device channel is located on a plastic substrate and connected by gold electrodes serving as the source and drain. The gate electrode is constructed using a gold-plated Kapton foil and modified with a condensed SAM containing immobilized anti-IgGs. The channel region is enclosed within a polydimethylsiloxane well, which contains 300 μl of 10 mM PBS, creating an electrochemical linkage between the gate electrode and the PEDOT:PSS channel.

Feng Yan and colleagues [61] have introduced a novel biosensor utilizing an OECT to achieve ultrahigh sensitivity in detecting cancer protein biomarkers. Existing low-cost electrochemical approaches often lack the necessary sensitivity for detecting low-concentration protein biomarkers in physiological environments. In this investigation, the biosensors detect variations in electrochemical activity on gate electrodes, correlating with the concentration of proteins

labeled with catalytic nanoprobes. Notably, the biosensors demonstrate the capability to detect the cancer biomarker human epidermal growth factor receptor 2 (HER2) at concentrations as low as 10^{-14} g ml^{-1}, surpassing the sensitivity limits of previously reported electrochemical methods by several orders of magnitude. Additionally, the devices exhibit the capacity to discriminate between breast cancer cells and normal cells at different concentrations. The remarkable sensitivity of the protein sensors arises from the inherent amplification function of the OECTs. This investigation showcases a promising avenue in the advancement of cost-effective and highly sensitive biosensors for the detection of diverse protein biomarkers in clinical analysis. Figure 6(F) depicts the configuration of an OECT-based biosensor employed in the detection of the cancer cell protein biomarker HER2 [61]. Initially, the biosensor undergoes a gate modification process, enabling it to identify the presence of HER2 protein biomarker and cancer cells. The subsequent steps involve the fabrication of a multifunctional nanoprobe with exceptional electrochemical activity, as portrayed in the diagram below. Following this, OECTs featuring functionalized gates are evaluated in liquid electrolytes to assess their performance. The middle section of the figure showcases three variations of gates, each modified with HRP, HER2 protein, or cancer cells, to enable specific detection capabilities in the OECTs. Finally, the right side of the figure demonstrates an equivalent circuit representing the interconnection between the gate and the channel of an OECT immersed in an electrolyte.

3.5. OECT-based DNA sensors

Detecting DNA with high sensitivity is crucial for identifying genetic damage, errors, and diagnosing diseases. However, current methods for highly sensitive OECT-based DNA detection rely on the use of materials with good conductivity, which can be can sometimes be challenging due to the complexity of their synthesis and modification processes. Chen *et al* [62] proposes a DNA biosensor that combines OECT with signal amplification through hybridization chain reaction (HCR). To enhance the surface area, the biosensor employs electrochemically deposited Au nanoparticles on the Au gate electrode. The HCR process generates long double-stranded DNA products with a negative charge that can connect to the target DNA through hybridization. This connection results in an increased effective gate voltage offset in the OECT. The experimental findings highlight the high sensitivity of this approach, capable of detecting target DNA as low as 0.1 pM, accompanied by a significant voltage shift. Moreover, the biosensor exhibits good selectivity in distinguishing target DNA from mismatched DNA. By efficiently amplifying the signal in the OECT, the proposed HCR-based DNA detection method opens up new possibilities for achieving highly sensitive and selective DNA detection (figure 6(g)).

Sensi *et al* [63] introduced a rapid and convenient method to modify the carbon gate of fully screen-printed OECTs for biosensing applications (figure 6(h)). OECTs are extensively employed in biosensing due to their exceptional sensitivity, wide dynamic range, and low LOD. Conventionally, the immobilization of a biorecognition probe on the gate or channel of an OECT involves multiple time-consuming chemical procedures. In their study, they employed a polydopamine (PDA) film to functionalize the carbon gate of an OECT. They chemically immobilized a single-stranded oligonucleotide, terminated by an amine and contained the HSP70 promoter CCAAT sequence. The CCAAT sequence was layered on the PDA film, enabling the detection of the compatible DNA strand. The specificity of the genosensor was assessed by comparing its response to fully complementary, partially complementary, and noncomplementary oligonucleotides. The sensor demonstrated a theoretical LOD of 100×10^{-15} M and a dynamic range spanning four orders of magnitude.

4. Conclusion

Organic electronics-based biosensors offer significant advantages over conventional biosensors, including low-cost, lightweight, and flexible sensing devices. This review focused on two types of organic biosensors, OFETs and OECTs, and highlighted their fundamental operating principles and recent advancements. While OFET biosensors have been widely used for biological sensing applications, they suffer from limitations such as low sensitivity and selectivity. In contrast, OECT biosensors have shown superior performance due to their unique mechanism of operation, which involves the modulation of electrolyte concentration to control the conductivity of the conducting polymer. Recent advancements in OECT biosensors have demonstrated their potential for biomedical and environmental sensing, including the detection of neurotransmitters, bacteria, and heavy metals. As the science of organic electronics advances, these biosensors have the potential to revolutionize the field of biosensing by playing an increasingly significant role in fields as diverse as healthcare, food safety, and environmental monitoring.

5. Future perspectives

Biosensors have revolutionized various industries by enabling rapid and accurate detection of biological and chemical substances. However, despite significant progress, there are still unresolved challenges that require attention in the field of biosensor development.

In terms of OFET biosensors, the main disadvantage is their limited sensitivity and selectivity, which can lead to false positive or false negative results. To enhance the sensitivity and selectivity of OFET biosensors, researchers can explore the development of new OSCs. These semiconducting materials can be carefully selected and optimized to possess improved charge transport properties and higher sensitivity towards target analytes. By utilizing these advanced

materials, the detection limits of OFET biosensors can be significantly improved, enabling more reliable and accurate results. Device design plays a vital role in the performance of OFET biosensors. By optimizing the architecture and configuration of the device, researchers can enhance sensitivity and selectivity. Additionally, integrating OFET biosensors with other technologies, such as microfluidics, holds great promise. Microfluidic systems allow for precise control over sample delivery, efficient mixing, and multiplexed analysis. The integration of microfluidics with OFET biosensors can lead to improved performance, expanded applications, and increased versatility in biomedical diagnostics, environmental monitoring, and other fields.

For OECT biosensors, the main challenge is achieving reproducibility and stability of the device performance. This is due to the complex interplay between the conducting polymer, electrolyte solution, and biological analytes. To address the challenge of reproducibility and stability, future research efforts should focus on developing more stable and reproducible OECT biosensors. This can be achieved through optimization of device fabrication processes and materials. Researchers can explore new conducting polymers and electrolyte formulations that offer improved stability and compatibility with biological analytes. By enhancing the stability and reproducibility of OECT biosensors, their reliability can be significantly improved, making them more suitable for practical applications. Furthermore, exploring new device architectures can enhance the performance of OECT biosensors. Novel electrode configurations, such as patterned electrodes or three-dimensional structures, can increase the surface area for analyte interaction and enhance charge transport. These advancements can lead to improved sensitivity, selectivity, and overall performance of OECT biosensors.

The future directions of OFET and OECT biosensors involve addressing the limitations mentioned above and developing more advanced devices with enhanced sensitivity, selectivity, reproducibility, and stability. By focusing research and development efforts on these aspects, significant improvements can be achieved in the field of biosensing technology. In a comprehensive perspective, the advancements in OFET and OECT biosensors hold great potential for a wide range of biomedical and environmental applications. These technologies have the power to revolutionize fields such as medical diagnostics, environmental monitoring, food safety, and more, ultimately leading to major improvements in sensing technology and positively impacting various industries and sectors.

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References

[1] Chen H *et al* 2017 Dithiopheneindenofluorene (TIF) semiconducting polymers with very high mobility in field-effect transistors *Adv. Mater.* **29** 1702523
[2] Zhang T, Ren W, Xiao F, Li J, Zu B and Dou X 2022 Engineered olfactory system for *in vitro* artificial nose *Eng. Regen.* **3** 427–39
[3] Tian L, Jackson K, Chan M, Saif A, He L, Didar T F and Hosseinidoust Z 2022 Phage display for the detection, analysis, disinfection, and prevention of Staphylococcus aureus *Smart Med.* **1** e20220015
[4] Katz E and Willner I 2004 Biomolecule-functionalized carbon nanotubes: applications in nanobioelectronics *ChemPhysChem* **5** 1084–104
[5] Luo L and Liu Z 2022 Recent progress in organic field-effect transistor-based chem/bio-sensors *View* **3** 20200115
[6] Basiricò L, Mattana G and Mas-Torrent M 2022 Editorial: organic electronics: future trends in materials, fabrication techniques and applications *Front. Phys.* **10** 307
[7] Forrest S R 2004 The path to ubiquitous and low-cost organic electronic appliances on plastic *Nature* **428** 911–8
[8] Marks A, Griggs S, Gasparini N and Moser M 2022 Organic electrochemical transistors: an emerging technology for biosensing *Adv. Mater. Interfaces* **9** 2102039
[9] Bai L, Elósegui C G, Li W, Yu P, Fei J and Mao L 2019 Biological applications of organic electrochemical transistors: electrochemical biosensors and electrophysiology recording *Front. Chem.* **7** 313
[10] Surya S G, Raval H N, Ahmad R, Sonar P, Salama K N and Rao V R 2019 Organic field effect transistors (OFETs) in environmental sensing and health monitoring: a review *TrAC, Trends Anal. Chem.* **111** 27–36
[11] Yuvaraja S, Nawaz A, Liu Q, Dubal D, Surya S G, Salama K N and Sonar P 2020 Organic field-effect transistor-based flexible sensors *Chem. Soc. Rev.* **49** 3423–60
[12] Dimov I B, Moser M, Malliaras G G and McCulloch I 2022 Semiconducting polymers for neural applications *Chem. Rev.* **122** 4356–96
[13] Feng K *et al* 2021 Fused bithiophene imide dimer-based n-type polymers for high-performance organic electrochemical transistors *Angew. Chem., Int. Ed.* **60** 24198–205
[14] Wu R, Matta M, Paulsen B D and Rivnay J 2022 Operando characterization of organic mixed ionic/electronic conducting materials *Chem. Rev.* **122** 4493–551
[15] Koklu A, Ohayon D, Wustoni S, Druet V, Saleh A and Inal S 2022 Organic bioelectronic devices for metabolite sensing *Chem. Rev.* **122** 4581–635
[16] Mariano A, Lubrano C, Bruno U, Ausilio C, Dinger N B and Santoro F 2022 Advances in cell-conductive polymer biointerfaces and role of the plasma membrane *Chem. Rev.* **122** 4552–80

[17] Kukhta N A, Marks A and Luscombe C K 2022 Molecular design strategies toward improvement of charge injection and ionic conduction in organic mixed ionic–electronic conductors for organic electrochemical transistors *Chem. Rev.* **122** 4325–55

[18] Zhu M, Li P, Li J-L and Lei T 2022 Molecular packing and film morphology control in organic electrochemical transistors *Mol. Syst. Des. Eng.* **7** 6–20

[19] Rivnay J, Inal S, Salleo A, Owens R M, Berggren M and Malliaras G G 2018 Organic electrochemical transistors *Nat. Rev. Mater.* **3** 17086

[20] Feng K, Guo H, Sun H and Guo X 2021 N-type organic and polymeric semiconductors based on bithiophene imide derivatives *Acc. Chem. Res.* **54** 3804–17

[21] Blom P W M 2020 Polymer electronics: to be or not to be? *Adv. Mater. Technol.* **5** 2000144

[22] Wadsworth A *et al* 2020 Modification of indacenodithiophene-based polymers and its impact on charge carrier mobility in organic thin-film transistors *J. Am. Chem. Soc.* **142** 652–64

[23] Chen H *et al* 2019 The effect of ring expansion in thienobenzo[b]indacenodithiophene polymers for organic field-effect transistors *J. Am. Chem. Soc.* **141** 18806–13

[24] Chen H *et al* 2021 Acene ring size optimization in fused lactam polymers enabling high n-type organic thermoelectric performance *J. Am. Chem. Soc.* **143** 260–8

[25] Xiao M *et al* 2021 Charge transport physics of a unique class of rigid-rod conjugated polymers with fused-ring conjugated units linked by double carbon-carbon bonds *Sci. Adv.* **7** eabe5280

[26] Feng K *et al* 2019 Fluorine-substituted dithienylbenzodiimide-based n-type polymer semiconductors for organic thin-film transistors *ACS Appl. Mater. Interfaces* **11** 35924–34

[27] Zhou Q, Wang M, Yagi S and Minami T 2021 Extended gate-type organic transistor functionalized by molecularly imprinted polymer for taurine detection *Nanoscale* **13** 100–7

[28] Didier P, Lobato-Dauzier N, Clément N, Genot A J, Sasaki Y, Leclerc É, Minamiki T, Sakai Y, Fujii T and Minami T 2020 Microfluidic system with extended-gate-type organic transistor for real-time glucose monitoring *ChemElectroChem* **7** 1332–6

[29] Tang W, Fu Y, Huang Y, Li Y, Song Y, Xi X, Yu Y, Su Y, Yan F and Guo X 2022 Solution processed low power organic field-effect transistor bio-chemical sensor of high transconductance efficiency *npj Flex. Electron.* **6** 18

[30] Liu J, Agarwal M and Varahramyan K 2008 Glucose sensor based on organic thin film transistor using glucose oxidase and conducting polymer *Sens. Actuators* B **135** 195–9

[31] Elkington D, Belcher W J, Dastoor P C and Zhou X J 2014 Detection of saliva-range glucose concentrations using organic thin-film transistors *Appl. Phys. Lett.* **105** 043303

[32] Li T, Zhong G, Fu R and Yang Y 2010 Synthesis and characterization of Nafion/cross-linked PVP semi-interpenetrating polymer network membrane for direct methanol fuel cell *J. Membr. Sci.* **354** 189–97

[33] Sun C, Wang X, Auwalu M A, Cheng S and Hu W 2021 Organic thin film transistors-based biosensors *EcoMat* **3** e12094

[34] Khan H U, Roberts M E, Johnson O, Förch R, Knoll W and Bao Z 2010 *In situ*, label-free DNA detection using organic transistor sensors *Adv. Mater.* **22** 4452–6

[35] Lai S, Demelas M, Casula G, Cosseddu P, Barbaro M and Bonfiglio A 2013 Ultralow voltage, OTFT-based sensor for label-free DNA detection *Adv. Mater.* **25** 103–7

[36] Minami T, Sasaki Y, Minamiki T, Wakida S-I, Kurita R, Niwa O and Tokito S 2016 Selective nitrate detection by an enzymatic sensor based on an extended-gate type organic field-effect transistor *Biosens. Bioelectron.* **81** 87–91

[37] Ohshiro K, Sasaki Y and Minami T 2023 An extended-gate-type organic transistor-based enzymatic sensor for dopamine detection in human urine *Talanta Open* **7** 100190

[38] Kumar A, Meunier-Prest R and Bouvet M 2020 Organic heterojunction devices based on phthalocyanines: a new approach to gas chemosensing *Sensors* **20** 4700

[39] Yuvaraja S, Bhyranalyar V N, Bhat S A, Surya S G, Yelamaggad C V and Salama K N 2021 A highly selective electron affinity facilitated H2S sensor: the marriage of tris(keto-hydrazone) and an organic field-effect transistor *Mater. Horiz.* **8** 525–37

[40] Oh S, Khan M R R, Choi G, Seo J, Park E, An T K, Park Y D and Lee H S 2021 Advanced organic transistor-based sensors utilizing a solvatochromic medium with twisted intramolecular charge-transfer behavior and its application to ammonia gas detection *ACS Appl. Mater. Interfaces* **13** 56385–93

[41] Hou S, Zhuang X, Fan H and Yu J 2021 Grain boundary control of organic semiconductors via solvent vapor annealing for high-sensitivity NO_2 detection *Sensors* **21** 226

[42] Sagdullina D, Lukashkin N, Parfenov A, Lyssenko K and Troshin P 2020 Highly sensitive OFET-based gas sensors using fluorinated naphthalenediimide semiconductor films *Synth. Met.* **260** 116289

[43] Zhang C, Chen P and Hu W 2015 Organic field-effect transistor-based gas sensors *Chem. Soc. Rev.* **44** 2087–107

[44] Zhang S, Zhao Y, Du X, Chu Y, Zhang S and Huang J 2019 Gas sensors based on nano/microstructured organic field-effect transistors *Small* **15** 1805196

[45] Sun H, Gerasimov J, Berggren M and Fabiano S 2018 N-type organic electrochemical transistors: materials and challenges *J. Mater. Chem.* C **6** 11778–84

[46] Zhao D *et al* 2019 Polymer gels with tunable ionic Seebeck coefficient for ultra-sensitive printed thermopiles *Nat. Commun.* **10** 1093

[47] Xia Y, Zhang W, Ha M, Cho J H, Renn M J, Kim C H and Frisbie C D 2010 Printed sub-2 V gel-electrolyte-gated polymer transistors and circuits *Adv. Funct. Mater.* **20** 587–94

[48] Rivnay J *et al* 2015 High-performance transistors for bioelectronics through tuning of channel thickness *Sci. Adv.* **1** e1400251

[49] Khodagholy D *et al* 2013 High transconductance organic electrochemical transistors *Nat. Commun.* **4** 2133

[50] Giovannitti A, Sbircea D-T, Inal S, Nielsen C B, Bandiello E, Hanifi D A, Sessolo M, Malliaras G G, McCulloch I and Rivnay J 2016 Controlling the mode of operation of organic transistors through side-chain engineering *Proc. Natl Acad. Sci.* **113** 12017–22

[51] Bucella S G, Luzio A, Gann E, Thomsen L, McNeill C R, Pace G, Perinot A, Chen Z, Facchetti A and Caironi M 2015 Macroscopic and high-throughput printing of aligned nanostructured polymer semiconductors for MHz large-area electronics *Nat. Commun.* **6** 8394

[52] Bernards D A and Malliaras G G 2007 Steady-state and transient behavior of organic electrochemical transistors *Adv. Funct. Mater.* **17** 3538–44

[53] Braendlein M, Lonjaret T, Leleux P, Badier J-M and Malliaras G G 2017 Voltage amplifier based on organic electrochemical transistor *Adv. Sci.* **4** 1600247

[54] Nishizawa M, Matsue T and Uchida I 1992 Penicillin sensor based on a microarray electrode coated with pH-responsive polypyrrole *Anal. Chem.* **64** 2642–4

[55] Gao N, Yu J, Tian Q, Shi J, Zhang M, Chen S and Zang L 2021 Application of PEDOT:PSS and its composites in

electrochemical and electronic chemosensors *Chemosensors* **9** 79
[56] Braendlein M, Pappa A-M, Ferro M, Lopresti A, Acquaviva C, Mamessier E, Malliaras G G and Owens R M 2017 Lactate detection in tumor cell cultures using organic transistor circuits *Adv. Mater.* **29** 1605744
[57] Zhang L, Li Q, Li Z, Du Z, Hong X and Qiu L 2020 An enzyme biosensor based on organic transistors for recognizing α-amino acid enantiomers *J. Electrochem. Soc.* **167** 067517
[58] Lin P, Yan F, Yu J, Chan H L W and Yang M 2010 The application of organic electrochemical transistors in cell-based biosensors *Adv. Mater.* **22** 3655–60
[59] Wei W, Xiao K, Tao M, Nie L, Liu D, Ke S, Zeng X, Hu Z, Lin P and Zhang Y 2017 A novel organic electrochemical transistor-based platform for monitoring the senescent green vegetative phase of Haematococcus pluvialis cells *Sensors* **17** 1997
[60] Macchia E, Romele P, Manoli K, Ghittorelli M, Magliulo M, Kovács-Vajna Z M, Torricelli F and Torsi L 2018 Ultra-sensitive protein detection with organic electrochemical transistors printed on plastic substrates *Flex. Print. Electron.* **3** 034002
[61] Fu Y, Wang N, Yang A, Law H K-W, Li L and Yan F 2017 Highly sensitive detection of protein biomarkers with organic electrochemical transistors *Adv. Mater.* **29** 1703787
[62] Chen C, Song Q, Lu W, Zhang Z, Yu Y, Liu X and He R 2021 A sensitive platform for DNA detection based on organic electrochemical transistor and nucleic acid self-assembly signal amplification *RSC Adv.* **11** 37917–22
[63] Sensi M, Migatti G, Beni V, D'Alvise T M, Weil T, Berto M, Greco P, Imbriano C, Biscarini F and Bortolotti C A 2022 Monitoring DNA hybridization with organic electrochemical transistors functionalized with polydopamine *Macromol. Mater. Eng.* **307** 2100880
[64] Pappa A M, Ohayon D, Giovannitti A, Maria I P, Savva A, Uguz I, Rivnay J, McCulloch I, Owens R M and Inal S 2018 Direct metabolite detection with an n-type accumulation mode organic electrochemical transistor *Sci. Adv.* **4** eaat0911
[65] Bolin M H, Svennersten K, Nilsson D, Sawatdee A, Jager E W H, Richter-Dahlfors A and Berggren M 2009 Active control of epithelial cell-density gradients grown along the channel of an organic electrochemical transistor *Adv. Mater.* **21** 4379–82