Solution processed low power organic field-effect transistor bio-chemical sensor of high transconductance efficiency

Wei Tang1, Ying Fu2, Yukun Huang1, Yuanzhe Li2, Yawen Song1, Xin Xi1, Yude Yu3, Yuezeng Su1, Feng Yan2, and Xiaojun Guo3

INTRODUCTION
There are rapidly growing demands for ubiquitous perception of various biomarkers (ions or biomolecules) in blood, body fluids, secretions, excretion, and tissue cells of human for personalized medical diagnosis and healthcare1,2. To realize that, the biosensing devices need to be highly customizable to meet diverse system requirements in terms of biocompatibility, cost, and form factor (compact, thin, flexible, or comfortable), while producing output signal of high-enough signal-to-noise ratio (SNR) under strict power constraint. The most affordable and convenient way would be based on electrical measurements, which avoid using additional bulky, power-hungry, and expensive optical components. Transducers made by integration of the sensor interface with a field-effect transistor (FET) have been widely studied, since the FET can convert the sensed signal into an amplified output signal for potentially large SNR. In addition, with FET switches, multiplexed detection in a single reaction is convenient to be implemented for high-throughput and multi-analyte analysis. The organic FET (OFET), composed of organic semiconductors (OSCs) and polymer dielectric layers, shows several competitive advantages over inorganic counterparts for such biosensing applications4,5. The use of solution-printing processes and versatile structures might facilitate integration of various sensing interfaces or probes at the device level in great freedom6. With low processing temperature and superior intrinsic mechanical flexibility of the full organic stacks, truly flexible sensor electronics can be fabricated using common low Young’s modulus thin plastic foils with much less stress-management efforts7. In the past, OFETs have been studied for detecting various biomolecules, including enzyme, DNA, and protein8-11. As a popularly used approach, probes are immobilized on the gate or its extended part to capture the target molecules. Once the molecules are being captured, the resulted potential change at the gate is recorded or converted to output-current change through the OFET for further processing. These work well proved that the capability of OFETs to be designed for various biosensing functions through material- and device-structure engineering. However, many of the devices required vacuum processes and inorganic dielectric layers, which would sacrifice the technical competence of the OFET.

Although solution-based processes at low temperature might offer attractive features for high customizability at low cost, they suffer difficulties in fine control of layer thickness, especially for very-thin films, and formation of high-quality semiconductor/dielectric films and interfaces. With such constraints, the achievable device performance is severely limited. In the past, there have been significant efforts on improving the carrier mobility in the OSC channels through material molecule design and crystallization-controlled processing methods12,13. However, for biochemical sensors to detect very low concentration of analyte in various portable, wearable, or implantable scenarios, large SNR with low operating voltage and power would be a prerequisite14,15. However, there is lack of studies on optimal design of the OFET for such figure of merits considering the interplay between device structures and material stacks under processing constraints.

This work derives the OFET-design principles for biochemical sensor transducers of large transconductance efficiency ($g_m/\lambda_0$) for large SNR with low operation voltage. Steep subthreshold swing (SS), proper threshold voltage ($V_{th}$), and operational stability are shown to be the key parameters to determine the optimal performance. Based on the design principles, low-voltage OFETs are then fabricated on plastic substrate in low-temperature solution processes to obtain the required performance, through formation of a low trap-state density channel interface on high-k/low-k bilayer-structure gate insulator. To verify its transduction performance, a plastic sensor tag is implemented through encapsulating the OFET with a sensing electrode and a reference electrode for miRNA detection. miRNAs are key biomarkers for many diseases, and label-free miRNA detection in electrochemical ways would provide low-cost and convenient tools for both biological fundamental studies and clinical diagnosis15-17. However, miRNAs are of low charge level due to their short intrinsic molecule length, and thus challenging to be detected at very low
where \( I \) is the operation current, \( K \) is a process-dependent coefficient, \( f \) is the frequency, and \( \alpha \) and \( \beta \) are noise parameters (with \( \alpha = 1 \) and \( \beta = 2 \) in theory in subthreshold regime). Correspondingly, the SNR for an OFET transducer operating in subthreshold regime at low frequency is deduced to be:

\[
\text{SNR} = 10 \log \left( \frac{P_{\text{signal}}}{P_{\text{noise}}} \right) = 10 \log \left( \frac{\Delta I}{\delta I} \right) \approx 10 \log \left( \frac{\Delta I}{\delta I} \right) = 10 \log \left( \frac{f}{K} \right)
\]

According to (4), the SNR depends on the relative current-output signal change over the background level \( (\Delta I/\delta I) \). As a result, to improve the detection limit, it would be important to maximize \( \Delta I/\delta I \) of the OFET transducer for a certain concentration of analytes. \( \Delta I/\delta I \) can be described as

\[
\Delta I = \frac{g_m \Delta V_G}{\delta I} = -\frac{g_m}{\delta I} \Delta V_{\text{int}} = -\left( \frac{\text{ln} 10}{SS} \right) \Delta V_{\text{int}}
\]

where \( g_m \) is transconductance and \( SS \) is the subthreshold swing. Therefore, to maximize \( \Delta I/\delta I \) enlarging the transconductance efficiency \( (g_m/\delta I) \) is as important as achieving effective immobilization of specific targets on the gate electrode (increasing \( \Delta V_{\text{int}} \)). In other words, \( g_m/\delta I \) is an important figure-of-merit to benchmark the sensing capability of extended-gate OFET sensors. Since the maximum of \( g_m/\delta I \) occurs in the subthreshold regime, and is proportional to the inverse of \( SS \), steep SS would thus be required to design OFET transducers of large \( g_m/\delta I \) for large SNR.

As illustrated in Fig. 1c, when the OFET is operated in the sensor system, the obtained transfer curve by sweeping \( V_{\text{ref}} \) would have a shift compared with the original \( I_D-V_{\text{GS}} \) curve of the OFET. Such a shift is due to the presence of an interfacial potential between the surface of the gate electrode and the aqueous solution. To enable operation of the OFET in the subthreshold regime with a small \( V_{\text{ref}} \), a proper near-zero threshold voltage \( (V_{\text{th}}) \) is also required. Operational stability is another concern to be considered, since a certain waiting time (i.e., tens of minutes) is often required for interaction between the probes and the target biomolecules. As illustrated in Fig. 1c, when the OFET is biased in the subthreshold regime, even a slight \( V_{\text{th}} \) shift would induce significant output-current change \( (\Delta I) \), causing false-positive or false-negative results. Similar to the electrical bias stress, since the flexible device is inevitably subject to some bending state, attention should also be paid to the mechanical durability during bending stress.

According to the above analysis, it is concluded that steep SS, proper threshold voltage, and operational stability under electrical bias and mechanical stress are key prerequisites for designing low-power OFET biochemical sensor transducers of large SNR.

### RESULTS AND DISCUSSION

#### Design principles

Figure 1a illustrates the structure of an OFET-based biochemical sensor, consisting of an OFET transducer with an extended-gate sensing electrode (SE) and a reference electrode (RE). The probe-immobilized SE is to capture analyte targets in solution through immobilized SE is to capture analyte targets in solution through immobilized antibodies or other probe molecules that are able to recognize the specific analyte. The OFET transducer with an extended-gate structure can enhance the sensitivity and selectivity of the detection process.

The OFET sensor is tested in solution by sweeping \( V_{\text{ref}} \) and the induced significant output-current change from the background level \( (\Delta I_{\text{DO}}) \) in the subthreshold regime even at a small threshold-voltage shift \( (\Delta V_G) \). The output current \( (I_D) \) can be measured at the OFET gate \( (V_{\text{GS}}) \) seen from the OFET.

\[
V_{\text{GS}} = V_{\text{GS0}} + \Delta V_G
\]

where \( V_{\text{GS0}} \) is the initial potential drop over a simplified electrochemical cell model with an extended-gate metal as the interfacial material for sensing. The charged molecules captured onto this surface create a potential shift \( (\Delta V_G) \) at the OFET gate \( (V_{\text{GS}}) \).

### Illustration of an OFET-based biochemical sensor

- **a**: Schematic of the biosensor design for analyte detection in electrolyte solution. The biosensor consists of an OFET transducer and an extended-gate sensing electrode immobilized with probes. \( V_{\text{ref}} \) is the bias voltage at the reference electrode (Ag/AgCl). \( V_{\text{GS}} \) is the resulted gate-to-source voltage on the OFET. \( I_D \) is the drain current to be measured by the subsequent readout electronic system.

- **b**: Diagram for potential over a simplified electrochemical cell model with an extended-gate metal as the interfacial material for sensing. The charged molecules captured onto this surface create a potential shift \( (\Delta V_G) \) at the OFET gate \( (V_{\text{GS}}) \).

- **c**: Illustration of the transfer-curve shift from the \( I_D-V_{\text{GS}} \) curve of the OFET to the \( I_D-V_{\text{ref}} \) curve when the OFET sensor is tested in solution by sweeping \( V_{\text{ref}} \) and the induced significant output-current change from the background level \( (\Delta I_{\text{DO}}) \) in the subthreshold regime even at a small threshold-voltage shift \( (\Delta V_G) \).
Device fabrication and characterizations

To meet the requirements as discussed above, an OFET design combining a low trap-state density channel and a high-k/low-k gate dielectric layer is implemented, to achieve steep transistor behaviors and a steep subthreshold swing of about 80 mV·dec$^{-1}$, with low threshold voltage for 3000 s, there is negligible change ($\Delta V_{th}$) exceeding those of previously reported extended-gate OFET biosensors (Supplementary Table 1). The measured high operational stability make the device a promising transducer for biomolecule detection. The operational stabilities under continuous switching and constant bias stress were characterized and shown in Fig. 2f. The device exhibits nearly identical transfer characteristics after sweeping between OFF and ON for 120 times. With a bias stress at a $V_{GS}$ near threshold voltage for 3000 s, there is negligible $V_{th}$ shift (less than 0.01 V). The relative current change ($\Delta I(D)/I(D=0)$) is less than 15% after constant bias stress for more than 4 hours. Such a device design owns low trap density-of-state (DOS) channel and high-k gate dielectric layer, proper $V_{th}$, and high operational stability make the device a promising transducer for biomolecule detection.

Evaluation of mechanical stability

The mechanical stability of the flexible OFET device encapsulated by CYTOP was evaluated by measuring its electrical characteristics with changing bending angles. Figure 3a shows the measurement system for assessing the stability of the OFET device under bending states. The investigated bending angle ($\theta$) is estimated to be $4.3 \times 10^{10}$ eV$^{-1}$ cm$^{-2}$, similar to previous work using a single low-k gate dielectric layer and also superior to those used in extended-gate OFET biosensors (Supplementary Table 1).

The maximum processing flexibility of the CYTOP passivation layer was shown in Fig. 2c to obtain a low-trap OSC/dielectric interface for temperature is kept below 100 °C. The surfaces of the source/drain electrodes were treated by biomolecule detection of high sensitivity and low detection limit at low $V_{GS}$ (<1 V).
and radius (R) for the OFET under bending test are illustrated in Supplementary Fig. 1. Figure 3b shows the transfer characteristics of the OFET device before and after undergoing bending at various angles, presenting negligible degradation in the subthreshold characteristics even at a large bending angle of about 73°. The corresponding output characteristics (Supplementary Fig. 2) also show no apparent change after bending by about 51°, while only a slight degradation of on-current was observed after a large bending angle of about 73°. In this regard, the contact resistance (R_C) during the bending test was further estimated by using a transmission-line method (TLM). It is realized by taking the total normalized on-resistance (R_{ON}/W) from the output characteristics of OFET devices with various channel lengths in the linear regime and then extrapolating the linear fit to a channel length of zero to obtain R_C. As shown in Supplementary Fig. 3, the bent OFETs with channel length ranging from 50 to 110 μm present well-behaved output performance with a clear saturation of the drain current beyond the pinch-off. Accordingly, the corresponding width-normalized R_{ON}/W can be calculated and plotted as a function of channel length for OFET under different bending conditions (Supplementary Fig. 4). As shown in Fig. 3c, the R_C extracted by TLM at the most significant bending angle of 73° is approximately 0.3 – 0.38 MΩ·cm. Although such R_C is slightly dependent on the gate bias voltage, it remains nearly unchanged during the measured bending states (Fig. 3d). Electrical measurements of the flexible device were further performed under bending stress. For this purpose, a stressing cycle was applied to the device by repeatedly bending it to radius = 10 mm and immediately releasing it to its initial state at a rate of 12 times per minute. Figure 3e shows that the flexible OFET device maintained well-functional transfer characteristics during the bending stress. Even after 3500 complete cycles, the change in subthreshold swing was not exceeding 5 mV/dec⁻¹, while threshold voltage shift was less than 0.03 V (Fig. 3f), revealing negligible change in subthreshold performance during the performed bending stress. These results illustrate that the developed low-voltage OFET can sustain the inevitable bending during usage and maintain its electrical performance for proper signal transduction.

**Probe immobilization and hybridization**

To verify the device concept of the designed OFET transducer for biosensing, this work takes miR-21 detection as an example, which is one of the potential candidate biomarkers for primary breast cancer [27,28]. The scheme for immobilizing probes on the extended-gate SE is depicted in Fig. 4a. A thiolated single-stranded DNA (ssDNA) probe was designed to match the miR-21 for specific detection. Based on the well-established thiol-gold chemistry, the ssDNA probes and the 6-mercapto-1-hexanol (MCH) were able to self-assemble onto the gold electrode surface efficiently via a strong SH-gold binding. The ssDNA probes work as the receptor for capturing miRNA targets, while the MCH, as a blocking layer, reduces miRNA hybridization reaction between the miR-21 targets and the ssDNA probes.

To verify the hybridization-reaction procedure, miR-21 was labeled with fluorescent dyes (FAM) for fluorescence measurement. As shown in Fig. 4b, the ssDNA-immobilized gold incubated to the 1X phosphate-buffered saline (PBS 1X) solution shows no fluorescence. After incubation of the electrode surface to the FAM-labeled miR-21 solution, there is weak fluorescence occurring at a concentration of 1 nM. With increase of the concentration to 100 µM, the signal becomes strong. The results prove the hybridization reaction between the miR-21 targets and the ssDNA probes.
Implementation of miRNA sensor

The individual OFET was cut from the fabricated large area sample, and then encapsulated onto a carrier PEN substrate with the extended-gate SE and the Ag/AgCl RE to complete a sensor tag for use as shown in Fig. 5a. The encapsulation processes are described in details in "METHODS". After the extended-gate SE and the RE being placed in the PBS 1X solution, the $I_{DS}$–$V_{GS}$ curve was measured by sweeping $V_{GS}$ at a $V_{DS} = -0.5$ V, presenting an obvious shift to the negative direction compared with the $I_{DS}$–$V_{GS}$ curve of the pristine OFET, as seen in Fig. 5b. After immobilization of ssDNA probes onto the extended-gate SE, there is a small shift backward due to the negatively charged probes. As a result, with a proper $V_{th}$, the OFET transducer was able to be biased in the subthreshold regime for large $g_{m0}/I_D$, at a low $V_{th}$ (~0.1 V). Figure 5c shows the measured $I_{DS}$–$V_{GS}$ curve using the same sensor when the concentration of miR-21 targets varies from 0 to 10 µM. $V_{th}$ values were extracted from the $I_{DS}$–$V_{GS}$ curves at a drain current of 1 nA. The measured $V_{th}$ shift ($\Delta V_{th}$) at various concentrations of miR-21, calculated by using the $V_{th}$ value at 0 M of miR-21 as blank ($\Delta V_{th} = V_{th}(\text{miRNA}) - V_{th}(\text{Blank})$), is shown in Fig. 5d. The solution containing a 3-base mismatch miRNA of a much higher concentration (100 µM) was also tested for comparison. The results show that $\Delta V_{th}$ for the lowest measured miR-21 concentration (10 pM) is 16.9 ± 5 mV, much higher than the value (0.2 ± 5 mV) for 3-base mismatch miRNAs of high concentration (100 µM), indicating high selectivity. Moreover, the limit of detection (LOD) was used to interpret the detectability of the sensor. It is defined as the concentration that leads to a sensor response equal to three times the standard deviation of the negative control sample ($\Delta V_{th}$ mean ± 3σ), where $\Delta V_{th}$ mean is the average response, and σ is the relative standard deviation. (100) According to this definition, the LOD was estimated to be 4.5 pM by taking the response of 3-base mismatch miRNA as the negative control sample. Note that the response at 10 pM is beyond the LOD (Fig. 5d), verifying the OFET biosensor’s high sensitivity capability at such a low concentration. The measured relative current change ($\Delta I_D/I_D$) at $V_{th}$ = 0.1 V for various miR-21 concentrations is shown in Fig. 5e. For a low concentration of 10 pM, $\Delta I_D/I_D$ of 20% is able to be obtained for large-enough SNR to be processed by the subsequent readout electronics for digitalization. Therefore, the sensor is able to achieve a detection limit below 10 pM to the target miRNAs with good selectivity at a low operation voltage (<1 V). The overall performance shows competence over that of the previous work based on a Si-FET in Table 1, in terms of the detection limit, the operation voltage, and the static power.

In summary, the derived design principles of the OFET transducer for biosensors build relationships between the SNR and the key OFET-performance parameters, including $g_{m0}/I_D$, $V_{th}$, and bias-stress stability. Combining a low trap-state density channel and high-k/low-k structure gate dielectric, OFETs fabricated on PEN substrate with low temperature solution-based processes can meet the optimal design requirements, exhibiting steep $SS$, near-zero $V_{th}$, and good-enough bias-stress stability and mechanical durability. Extended-gate structure OFET biosensors were further constructed for label-free detection of miR-21, a potential biomarker for primary breast cancer. The results demonstrate that the sensor can achieve a detection limit below 10 pM to the target miRNAs with good selectivity at a low operation voltage (<1 V). The overall performance is competitive over that of the previous work based on the Si-FET, in terms of the detection limit, the operation voltage and the static power. This work would pave the way to developing low-cost and convenient biosensors based on OFETs to have large SNR for customizable detection of disease biomarkers in both biological studies and clinical diagnosis.

METHODS

Materials and reagents

In all, 125-µm-thick polyethylene naphthalate (PEN) plastic films (Teonex Q65HA) were purchased from DuPont Teijin Films. Poly(vinyl cinnamate) (PVCN, $M_w = 40$ kDa), polystyrene ($PS, M_w = 524$ kDa), perfluorobenzonethiol (PFBT), and 6-mercaptop-1-hexanol (MCH) were purchased from Sigma-Aldrich. Poly(vinylidene fluoride–trifluoroethylene–chlorotrifluoroethylene) (56/36/5.7 mol%) terpolymer (P(VDF-TrFE-CFE)) was synthesized by the suspension-polymerization process (12). 1,13-bis(trisopropylsilyl)hexyl) perfluoroctane (TIPS-pentacene) (FN4023) was provided by Merck Chemicals Ltd. CYTOP (C7000) was obtained from Asahi Glass. Silver (Ag) pastes were obtained from Hisense Electronics, Kunshan, China. Silicone sealant was purchased from Shanghai Qianru Building Materials. Phosphate-buffered saline (PBS 1X, pH = 7.2) solution was obtained from Thermo Fisher Scientific. The sequences of probe single-stranded DNA (5’SH-CCCCTCCAAACATCGTCTGAATGC-3’),

![Fluorescence image of extended-gate sensing electrode. a Illustration of the scheme for immobilizing the designed ssDNA probes on the extended-gate sensitive electrode for specific detection of miR-21 through DNA/miRNA hybridization. b Fluorescence images for ssDNA-immobilized gold incubated to the PBS 1X solution, and the solutions containing fluorescent dyes labeled miR-21 of different concentrations: 10 pM, 1 nM and 100 µM, respectively.](npj Flexible Electronics (2022) 18 Published in partnership with Nanjing Tech University)
Device fabrication

OFET devices in a bottom-gate bottom-contact structure were fabricated on a plastic PEN foil laminated on a glass carrier. PVCN was dissolved in chlorobenzene with a concentration of 10 mg/ml and spin-coated at 3000 rpm onto the substrate as a planarization layer, followed by UV cross-linking (UV Curer KW-4AC, CHEMAT) for 20 min and then heating at 100 °C for 1 h. Next, 40 nm-thick silver (Ag) gate electrodes were deposited by thermal evaporation using a stainless-steel mask. Then, a high-k P(VDF-TrFE-CFE) (dissolved in methyl ethyl ketone, 40 mg/ml) and a low-k PVCN (dissolved in chlorobenzene, 10 mg/ml) were subsequently spin-coated to form a thick bilayer-gate dielectric. Ag source/drain (S/D) electrodes were obtained using the same processes as that for formation of the gate electrodes, defining a channel width of 2000 µm and a channel length of 70 µm, respectively. Devices with the same channel width (1500 µm) and a series of channel lengths (50, 70, 90, and 110 µm) were also used to evaluate the mechanical stability. Before the deposition of the semiconductor layer, the sample was immersed into a PFBT solution (5 mM in isopropanol) for 15 min to form self-assembled monolayers on the S/D electrodes. After this treatment, it was carefully rinsed with isopropanol and blown by dry N2 gas, followed by annealing at 100 °C on a hot plate for 1 min. The semiconductor/polymer-blended solution was prepared by mixing TIPS-pentacene and PS solutions (dissolved in chlorobenzene, 10 mg·mL⁻¹) in 3:1 ratio by volume. The semiconducting film was formed using a soft-contact coating approach with a rotatable steel sheet as the meniscus guide at coating speed of 20 mm/s, followed by annealing at 100 °C for 30 min. Finally, CYTOP solution (10 µL) was drop-cast to passivate the channel and annealed at 80 °C for 30 min.

Sensor-tag encapsulation

After completing the preparation of OFET device, its supporting PEN foil was carefully peeled off from the glass carrier. Subsequently, individual CYTOP-passivated OFET was cut from it to mount onto another holding PEN substrate with prefabricated screen-printed silver interconnects and pads. A bonding process was developed by flipping over the OFET device and attaching to the substrate using silver paste, followed by annealing at 80 °C for 10 min. Finally, a silicone sealant was dispensed with a dispenser robot to seal the device.

Sensing-electrode preparation

Extended-gate sensing electrode consisting of chromium (10 nm) and gold (100 nm) was deposited using magnetron sputtering, which was further encapsulated with silicone sealant to define a sensing area of 9 mm². Prior to immobilization of probes, the electrode surface was cleaned by O₂ plasma.
plasma for 10 min. Then, 10 μL of 5'-SH–modified capture ssDNA solution (10−4 M, dissolved in PBS 1X) was added onto the gold electrode and incubated at 4 °C in humid condition overnight, followed by rinsing thoroughly with PBS 1X solution. After immobilization of probes, the electrode was posttreated with 10 μL of MCH aqueous solution (1 mM) for 1 h to remove nonspecifically bound oligonucleotides and block extracellular gold surface, followed by rinsing with PBS 1X solution. The obtained sensing electrodes were used immediately to subject to 10 μL of fully complementary targets (miR-21 or FAM-dyed miR-21) and noncomplementary targets (3-base mismatch miRNA) diluted to desired concentration in PBS 1X solutions for hybridization, respectively, followed by rinsing with PBS 1X solution carefully.

**Characterization and measurement**

The polarized optical micrograph for TIPS-pentacene crystalline was taken with a microscope (XPF-300C, Caikon). The fluorescence images were obtained from inverted fluorescence microscopy (IX71, Olympus Life Science). The cross-sectional scanning electron microscopy (SEM) image was obtained on a Zeiss Ultra Plus Field Emission Scanning Electron Microscope at an electric voltage of 5 kV. The cyclic bending test of the flexible OFET was performed on a stretching machine at bending radius of 10 mm with a speed of 5 s/cycle. The sensor tag was connected to the extended-gate sensing electrodes and reference electrode (Ag/AgCl) via copper wires. The electrical characterizations of the OFETs and biosensors were performed using a semiconductor parameter analyzer (Keithley 4200 system). All measurements were carried out at room temperature in ambient air.

**DATA AVAILABILITY**

The data that support the findings of this study are available from the corresponding author upon reasonable request.

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**REFERENCES**

1. Sakata, T. Biologically coupled gate field-effect transistors meet in vitro diagnostics. ACS Omega 4, 11852–11862 (2019).
2. Lee, M. Y., Lee, H. R., Park, C. H., Han, S. G. & Oh, J. H. Organic transistor-based chemical sensors for wearable bioelectronics. Acc. Chem. Res. 51, 2825–2838 (2018).
3. Syu, Y.-C., Hsu, W.-E. & Lin, C.-T. Review-field-effect transistor biosensing: devices and clinical applications. ECS J. Solid State Sci. Technol. 7, Q3196–Q3207 (2018).
4. Zang, Y., Huang, D., Di, C. A. & Zhu, D. Device engineered organic transistors for flexible sensing applications. Adv. Mater. 28, 4549–4555 (2016).
5. Magliulo, M., Manoli, K., Macchia, E., Palazzo, G. & Torsi, L. Tailoring functional interlayers in organic field-effect transistor biosensors. Adv. Mater. 27, 7528–7551 (2015).
6. Khan, H. U. et al. In situ, label-free DNA detection using organic transistor sensors. Adv. Mater. 22, 4452–4456 (2010).
7. Jiang, C., Cheng, X. & Nathan, A. Flexible ultralow-power sensor interfaces for E-skin. Proc. IEEE 107, 2084–2105 (2019).
8. Lai, S., Barbaro, M. & Bonfiglio, A. Tailoring the sensing performances of an OFET-based biosensor. Sens. Actuators B Chem. 233, 314–319 (2016).
9. Song, J. et al. Influence of bioreceptor layer structure on myelin basic protein detection using organic field effect transistor-based biosensors. Adv. Funct. Mater. 28, 1802605 (2018).
10. Minamikawa, T. et al. Accurate and reproducible detection of proteins in water using an extended-gate type organic transistor biosensor. Appl. Phys. Lett. 104, 243703 (2014).
11. Minami, T. et al. Selective nitrate detection by an enzymatic sensor based on an extended-gate type organic field-effect transistor. Biosens. Bioelectron. 81, 87–91 (2016).
12. Wang, C., Deng, H., Jiang, L. & Hu, W. Organic semiconductor crystals. Chem. Soc. Rev. 47, 422–500 (2018).
13. Gu, X., Shaw, L., Gu, K., Toney, M. F. & Bao, Z. The meniscus-guided deposition of semiconducting polymers. Nat. Commun. 9, 534 (2018).
14. Moser, N., Rodriguez-Manzano, J., Lande, T. S. & Georgiou, P. A scalable ISFET sensing and memory array with sensor auto-calibration for on-chip real-time DNA detection. IEEE Trans. Biomed. Circuits Syst. 12, 390–401 (2018).
15. Douthwaite, M., Koutsos, E., Yates, D. C., Mitcheson, P. D. & Georgiou, P. A thermally powered ISFET array for on-body pH measurement. IEEE Trans. Biomed. Circuits Syst. 11, 1324–1334 (2017).
16. Rajan, N. K., Brower, K., Duan, X. & Reed, M. A. Limit of detection of field effect transistor biosensors: effects of surface modification and size dependence. Appl. Phys. Lett. 104, 084106 (2014).
17. Kilic, T., Erdem, A., Oztu, M. & Carrara, S. microRNA biosensors: Opportunities and challenges among conventional and commercially available techniques. Biosens. Bioelectron. 99, 525–546 (2018).
18. Kaist, M. et al. Real-time wash-free detection of unlabeled DNA-DNA hybridization using discrete fet sensor. Sci. Rep. 7, 15734 (2017).
19. Thompson, M. et al. Label-free detection of nucleic acid and protein microarrays by scanning Kelvin nanosensor. Biosens. Bioelectron. 20, 1471–1481 (2005).
20. Liu, W. et al. pH sensing and low-frequency noise characteristics of low temperature (400 °C) p-channel SOI schottky ISFETs. IEEE Electron Device Lett. 38, 1146–1149 (2017).
21. Ishige, Y., Shimoda, M. & Kamahori, M. Immobilization of DNA probes onto gold surface and its application to fully electric detection of DNA hybridization using field-effect transistor sensor. Jpn. J. Appl. Phys. 45, 3776–3783 (2006).
22. Xu, S. et al. Real-time reliable determination of binding kinetics of DNA hybridization using a multi-channel graphene biosensor. Nat. Commun. 8, 14902 (2017).
23. Huang, Y. et al. Scalable processing of low voltage organic field effect transistors with a facile soft-contact coating approach. IEEE Electron Device Lett. 40, 1945–1948 (2019).
24. Tang, W., Feng, L., Yu, P., Zhao, J. & Guo, X. Highly efficient all-solution-processed low-voltage organic transistor with a micrometer-thick low-k polymer gate dielectric layer. Adv. Electron. Mater. 2, 1500454 (2016).
25. Lee, W. H., Choi, H. H., Kim, D. H. & Cho, K. 25th anniversary article: microstructure dependent bias stability of organic transistors. Adv. Mater. 26, 1660–1680 (2014).
26. Mittal, S., Kaur, H., Gautam, N. & Martha, A. K. Biosensors for breast cancer diagnostic: a review of bioreceptors, biotransducers and signal amplification strategies. Biosens. Bioelectron. 88, 217–231 (2017).
27. Qian, S. et al. Boronic acid functionalized Au nanoparticles for selective microRNA signal amplification in fiber-optic surface plasmon resonance sensing system. ACS Sens 3, 929–935 (2018).
28. Yang, C.-T., Pourhassan-Moghaddam, M., Wu, L., Bai, P. & Thierry, B. Ultrasensitive detection of cancer prognostic microRNA biomarkers based on surface plasmon enhanced light scattering. ACS Sens. 2, 635–640 (2017).
29. Dorvel, B. R. et al. Silicon nanowires with high-k hafnium oxide dielectrics for sensitive detection of small nucleic acid oligomers. ACS Nano 6, 6150–6164 (2012).
30. Lu, N. et al. CMOS-compatible silicon nanowire field-effect transistors for ultrasound and label-free microRNA sensing. Small 10, 2022–2028 (2014).
31. Ganguli, A., Watanabe, Y., Hwang, M. T., Huang, J.-C. & Bashir, R. Robust label-free detection of cancer prognostic miRNA biomarkers based on surface plasmon resonance based on fused silica. Adv. Mater. 30, 4549–4560 (2018).
32. Li, J., Sun, Z. & Yan, F. Solution processable low-voltage organic thin film transistors with high-k relaxor ferroelectric polymer as gate insulator. Adv. Mater. 24, 88–93 (2012).
ADDITIONAL INFORMATION

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Correspondence and requests for materials should be addressed to Feng Yan or Xiaojun Guo.

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