Chemical and Biomolecule Sensing with Organic Field-effect Transistors

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Abstract

The strong and controllable chemical sensitivity of organic semiconductors (OSCs) and the amplification capability of transistors in circuits make the use of OSC-based field-effect transistors compelling for chemical sensors. Analytes detected and assayed range from few-atom gas-phase molecules that may have adverse health and security implications to biomacromolecules (proteins, nucleic acids) that may be markers for physiological processes and medical conditions. This review highlights recent progress in organic field-effect transistor (OFET) chemical sensors, emphasizing advances from the past five years and including aspects of OSC morphology and the role of adjacent dielectrics. Design elements of the OSCs and various formats for the devices are illustrated and evaluated. Challenges associated with the present state of the art and future opportunities are also discussed.

1. Introduction

1.1 Field-effect transistors

The attraction of field-effect transistors (FETs) for chemical sensing is manifold. Their electronic conductance is dominated by materials (semiconductors) whose conductivities vary over many orders of magnitude, and are perturbable via multiple mechanisms involving surfaces, chemistry in the bulk, and local electric fields. These conductivity variations can be readily induced by analytes. The local electric fields near the semiconductors are imparted by adjacent dielectric materials whose polarities and polarizabilities can also be modulated by analytes. The FETs as circuit elements can be used to amplify signals or be cascaded in logical sequences for multianalyte detection or computational decision-making.

A field-effect transistor (FET) essentially consists of source and drain electrode, each in contact with a semiconductor layer whose charge density is modulated by an electric field applied between the semiconductor and a gate electrode (Figure 1, device schematic and references therein). This field is exerted in the direction perpendicular to the plane of an insulator, or "dielectric" layer placed between the semiconductor and gate electrode. The dielectric covers one interface of the semiconductor, and the gate electrode is placed at the interface of the insulator away from the semiconductor.[1-2] Different configurations are possible for the source-drain electrodes relative to the dielectric, either at the interface between the semiconductor and the dielectric or on the semiconductor interface that does not contact the dielectric. The gate electrode may either be placed as the top layer of the device, where it may interact with chemical species in the environment, or at the bottom of a device mounted on a substrate, where it would be isolated from the environment. Thus, the electric field may be applied entirely across the dielectric or may drop across both the dielectric and semiconductor in series, though in the latter case the generally higher resistivity of the dielectric should ensure that the field still drops primarily across the dielectric. The essential function of a FET is to translate input voltage signals from the gate electrodes into output signals delivered from drain electrodes to other elements in a circuit. The output signals can be currents, or they can be read as voltages by having the currents be directed through other resistive elements in series. Logic function can be enhanced by having the drain electrodes electrically coupled to additional FETs, and by having source-drain voltages greatly exceed gate voltages so that amplification results.

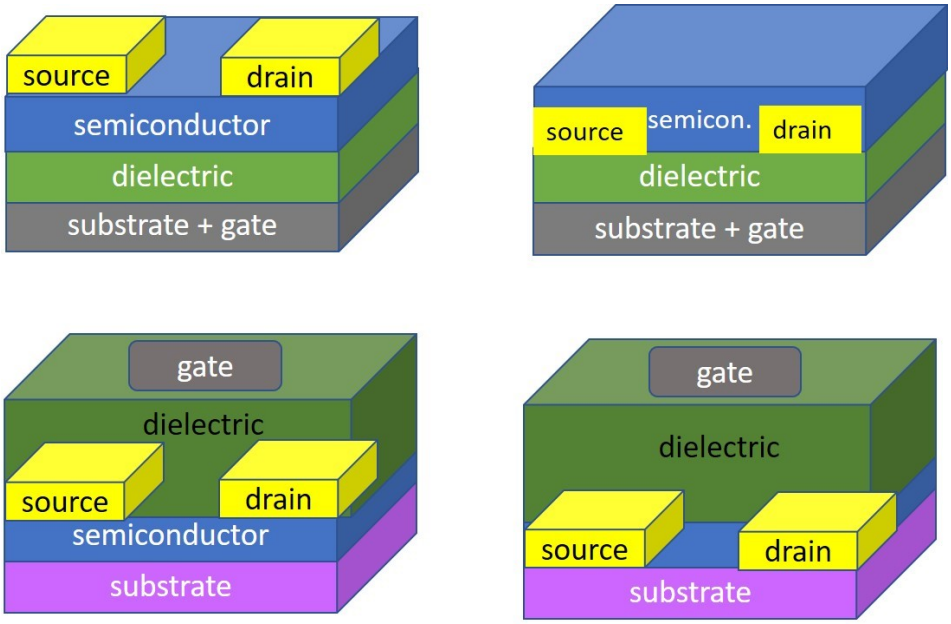


Figure 1. Four configurations of FETs. Features include electronic contacts in correct positions, but are not to scale. Analyte molecules are assumed to be in contact with the uppermost layers of devices as they are oriented in this figure. For general FET operational principles and the incorporation of contact resistance, field-dependent mobility, and gate leakage current, see: [3-8]

The voltage on the gate controls the charge density in the semiconductor by serving as one plate of a capacitor, with the semiconductor acting as the other plate. Charging this capacitor changes the charge density in a region of the semiconductor near the dielectric, called the channel, along which current flows between the source and the drain if charge density is high enough and sufficient voltage is applied (Figure 2). This situation is called the "on" state, while the converse low-charge-density condition is called the "off" state. The ratio of currents at the two states is called the "on/off ratio".

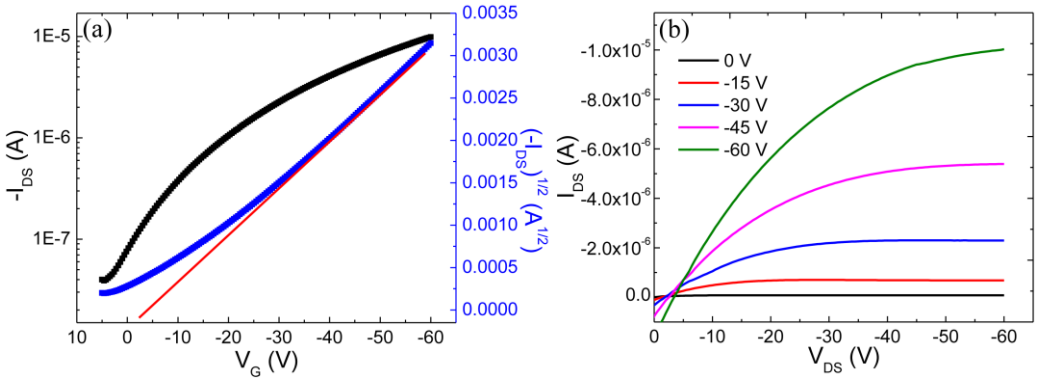


Figure 2. I vs V_G (transfer) curve (log and sqrt) (a) and I vs V_D (output) curve (b) for poly(bisdodecylquaterthiophene). V_G are indicated in the legends. Voltages are negative because holes are induced in the OSCs.

The magnitude of the current depends on the electrode voltages, the dimensions of the channel, the capacitance of the dielectric, and the avoidance of hindrances to current flow such as traps, scattering sites, and barriers to charge transport. The presence of traps and dopants determines the gate voltage at which the device becomes decidedly "on", called the "threshold voltage" (V_T), above which additional induced charge carriers are considered mobile. Traps are sites in or adjacent to the semiconductor where charges are at lower energy levels than in the bulk of the semiconductor, so that they require thermal activation or high drain-source voltages to become mobile. Dopants are chemical species that introduce relatively mobile charge carriers into the semiconductor, increasing its conductivity at all applicable source-drain voltages, often including the case where no source-drain voltage is applied. Scattering sites and barriers decrease the speed at which charge can be induced to move by an applied voltage per unit device length (the source-drain field); this speed per field is called the "mobility" (μ). For a given gate voltage (V_G) in a well-behaved FET, there is a maximum drain-source voltage (V_D), known as the threshold voltage (V_T) beyond which the depletion of carrier density near the drain electrode cancels the increased force exerted by the voltage on the carriers, so the current no longer increases; this phenomenon is called "saturation". Accordingly, there are separate equations relating current to voltages in the low-V_D regime (the "linear" region, where a form of Ohm's

Law applies) and the saturation region, where current is independent of V_D. The latter equation balances increased current driving force and greater depletion of carrier density near the drain electrode as V_G increases (expressed in the former equation by the $V_D^2/2$ term), and is also consistent with the requirement that I be a continuous function of V_D. Mobility and V_T are extracted by fitting data such as what is shown in Figure 2 to the equations given below:

$$I_D = \frac{WC\mu}{L}\left[\left(V_G - V_T\right)V_D - \frac{V_D^{\,2}}{2}\right]$$

$$I_{D,sat} \cong \frac{WC\mu_{sat}}{2L}\left(V_G - V_T\right)^2$$

where I_D is the drain current, C is the capacitance per unit area of the gate dielectric layer, W and L are the channel width and length, respectively. The data can be fit directly to the linear regime equation. Alternatively, square roots of values for saturation current, at the rightmost ends of the data curves, are plotted against V_G to obtain lines with slope = sqrt(WCμ/2L) and x-intercept = V_T, as apparent from the equations above.

The mobility is ideally a solid-state property of the semiconductor, but an empirical mobility often includes extrinsic factors such as semiconductor-electrode contact resistance and electronic states conferred by the dielectric and/or by impurities and imperfections in the semiconductor. The contact resistance can be V_G-dependent, in which case the OFET may be appropriately modeled by a pair of FETs in series, each with a different μ and V_T, or by a charge injection barrier in series with the semiconductor, modulated by V_G. The empirical μ can also be V_G-dependent, as it indicates ease of charge carrier transport averaged among carriers at all energy levels filled when V_G is applied. Carriers induced by lower V_G typically have lower μ because they are more susceptible to being trapped. These extrinsic factors can complicate the treatment of μ and V_T as independent variables, since the designation of the minimum current to be considered “on” may become somewhat arbitrary and the sqrt(I) plots from saturation data may be nonlinear. These extrinsic factors are also

likely to lead to disagreement between values of μ determined from linear regime or saturation regime data. Finally, the currents utilized in determination of OFET parameters need to be corrected for any leakage currents that arrive at the drain electrodes through the gate dielectrics.

Organic materials are being considered for FETs where mechanical flexibility, low processing temperatures, and print-deposition are needed, or additional chemical functionality to create chemical specificity needed for functioning chemical sensors, is desired.[9-12] Such devices are commonly designated as "organic FETs" or "OFETs" Organic semiconductors (OSCs) may be molecular or polymeric. Because OSCs generally have lower mobilities than inorganic semiconductors, they require higher drain and gate voltages to generate useful currents. These voltages and the various chemical reactivity modes of OSCs lead to lower reliability than the inorganic materials. Therefore the sensor responses and easier fabrication processes of OSCs must outweigh these drawbacks.

OSCs contain conjugated subunits of various lengths to stabilize charge density and enable charge transport mechanisms. Charge transport is usually dominated by a thermally activated hopping mechanism, either among the molecules themselves or among trapping sites, leading to lower mobility than what is observed in covalent inorganic solids (see references to Figure 3). The molecules interact more weakly than is typical for atoms in inorganic semiconductors. Figure 3 shows a small but representative sample of recent OSC molecular structures;[13] others are mentioned in the sensor examples below. For the highest mobility and on/off ratio, these subunits need to be crystallized or packed in arrangements that minimize hindrances to charge transport, and must be purified and ideally be structurally homogeneous over the device length scale so that extrinsic trapping and doping do not decrease mobility and on/off ratio. It is interesting that a search of the review literature on FET topics from the decade preceding 2018 yields a majority of references related to organic material-based devices and technologies.

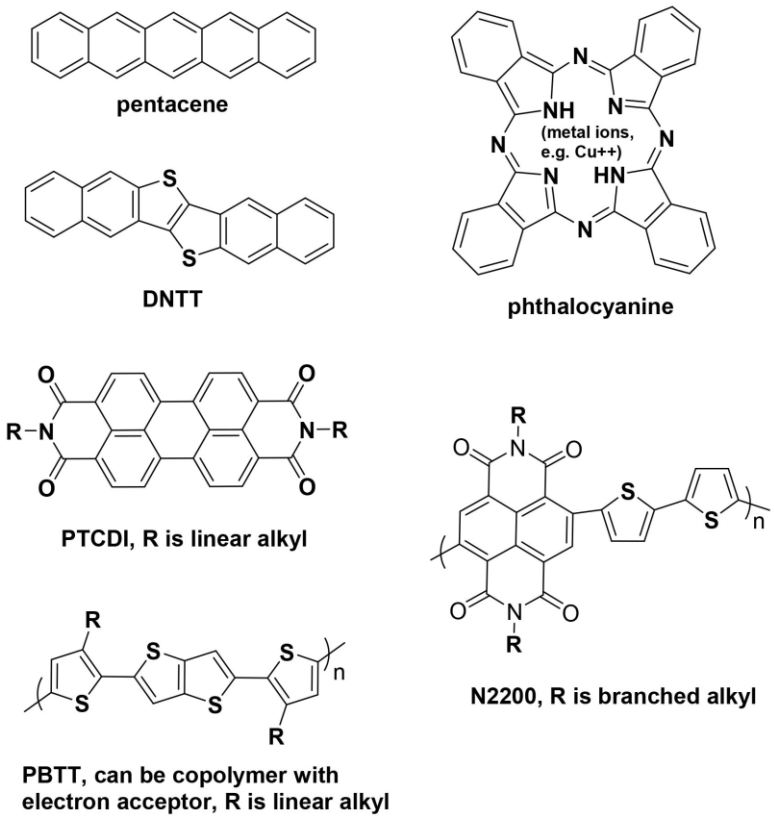


Figure 3. Structures used in recent high-performance OSC materials. Reviews of molecular and polymeric semiconductors, including the above structures, are: [14-19]

1.2 Organic field-effect Transistors (OFETs) in sensors

Because of the capability of environmental chemical species to interact with OSC molecules and the morphological features in OSC solids, their presence at an exposed OFET interface can alter the current-voltage relationships in OFETs and thus be signaled. When OSCs are positioned between a pair of electrodes and their intrinsic resistivities are modulated by chemical (analyte) exposure, the device is termed a chemiresistor. When a gate electrode is used to preset the conductivity or provide a V_G sweep, the device becomes an OFET sensor. The analyte may exert an electronic effect via several possible mechanisms, such as by creating traps, acting as a dopant, imposing resistive interfacial barriers, changing the existing intermolecular interactions between molecular subunits in OSCs and dielectrics, and inducing an electric field that perturbs the effective V_G. The analyte becomes an extrinsic influence on the parameters μ and V_T discussed in the previous section. However, unlike in the case of

OFETs intended for purely circuit functions, it is desirable for the analyte-induced influence to be as high (and selective) as possible. Thus, an analyte affecting μ would ideally exert this effect throughout the applicable V_G range, including the highest accessible V_G, so large current modulations can be obtained as a result of analyte interactions. On the other hand, an analyte affecting V_T would preferably be sensed at a V_G nearly equal to V_T, so that the turn-on regime, whccich has a higher (exponential) dependence of I on V_G than do the linear or saturation regimes, is modulated by the analyte.

A schematic of an OFET sensor integrated with a gaseous analyte delivery system and one in contact with a condensed phase analyte mixture, are shown in Figure 4. The use of OSCs in vapor sensing has been covered in numerous prior reviews.[20-24] OFETs are also an emerging, real-time biomolecule sensor platform with the ability to detect a variety of biomolecules, including DNA, glucose, and various proteins and enzymes.[25-36]

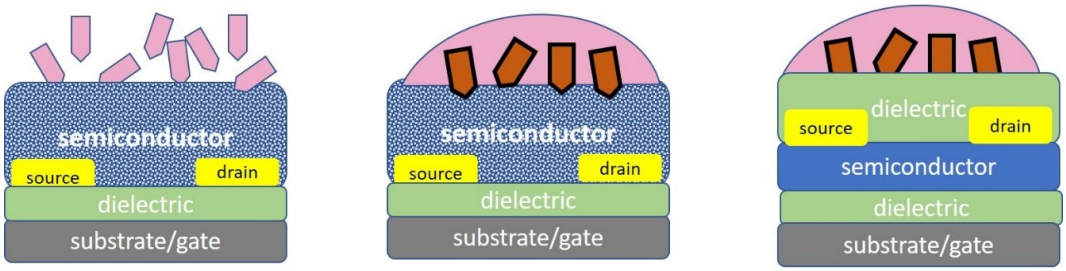


Figure 4. Three ways in which analytes can interact with OFETs, from left to right: gas interacting with polycrystalline semiconductor, solute interacting with a polycrystalline semiconductor, and solute interacting with a dielectric overlying a semiconductor.

Scope of the review. This review explores the use of OFETs in both vapor and condensed-phase chemical sensors. The emphasis is on broad coverage of advances from the past five years, where designed and well-explained interactions between analytes and device materials (OSCs, gate dielectrics) are utilized. Earlier references are provided to put the more recent advances in context. Analytes in vapor and solution phases, ranging in size from few-atom molecules to biomacromolecules, are

considered. The progression of the review is from device fundamentals to materials, material modifications, and applications.

While carbon nanotubes and graphene are arguably "organic" semiconductors as well, they are largely outside the scope of this review. However, for completeness, we provide a brief summary of their status as field-effect sensor materials, taken from recent review literature.[37-43] Carbon nanotubes and graphene can have surface areas of >1000 m^2/g, so the density of adsorbed molecules and thus the electronic response per weight of active material can be very high. The fact that nanoscale domains of these materials, including a single nanotube, are sufficient as active regions of devices opens special miniaturization opportunities. Their high charge carrier mobilities decrease power requirements. Because both of these materials present similar and relatively unreactive graphitic carbon functionality to the environment, they are not inherently selective for most analytes of interest. However, receptor functionalization procedures that are compatible with many desirable functional groups have been developed for graphitic carbon materials, so selectivity to a wide range of analytes can be obtained via these processes. OSCs, on the other hand, are themselves more broadly functional, so they contribute receptor chemistry themselves, and the receptor interactions are then intimately influential on the conductive paths through the OSCs. For example, many OSC subunits include mildly basic nitrogen atoms in rings or hydrogen-bondable carbonyl groups, and side chains can include ion-complexing poly(ethylene glycol) chains.

Accommodation of environmentally-induced signal drift is needed for both carbon and OSC sensor materials, though both of these materials can also be more water-stable than some inorganic semiconductors. Both graphitic carbons and OSCs can be used in arrays. For the purpose of diversifying the array elements, the CNTs and graphene would be functionalized with various receptors, while OSC chemical composition and morphology can be varied in addition to added covalent functionality. While OSCs may be more convenient to prepare in printable form, graphitic carbons bring high

mechanical strength. Both CNTs and polymeric OSCs possess a certain fundamental heterogeneity; CNTs have varied topology (including some that are metallic and some that are semiconducting) and catalyst particle residues while polymer OSCs have variations in molecular lengths, end group functionality, chemical impurities, and processing-induced morphology. Molecular solid OSCs and pristine have the greatest chance of being free of such variation, though the latter can be elusive to prepare. Graphene is generally conductive and thus shows low on/off ratios in FETs, but its highly conductive forms are subject to strong electronic perturbation by defects that can be introduced by analytes, above and beyond any changes brought about by receptor functionalization.

2. Organic semiconductors (OSCs) for active sensor layers

Numerous OSCs for OFETs have been developed over the past few decades, aiming primarily for high charge carrier mobility, and more recently, environmental stability. Some of the higher performance OSCs, characterized by dense packing of charge-carrying conjugated subunits and well-organized side chains, may be less appropriate for sensor applications, because what is most important for sensors is the sensitivity of parameters, such as μ, V_T, I_d, and on/off ratio to the presence of analytes. Maximization of these changes is in some sense contrary to the goal of stability. These changes are strongly dependent of the morphologies and redox properties of semiconductor and the interaction between semiconductors and analytes. A somewhat porous, high-free-volume morphology enables analytes to penetrate the OFET materials in large numbers and with greater coupling to the charge transport pathways. OSC oxidation requiring slightly stronger oxidants than oxygen itself, or reduction requiring a slightly stronger reductant than water, optimizes selectivity and sensitivity to analytes. Functional groups that promote hydrogen bonding or dipolar interactions between semiconductors and analytes increases the number of analyte molecules captured by semiconductors as well as the electronic signaling of the analyte molecules.

2.1 Small molecule semiconductors as active layers

Organic small molecule semiconductors are widely used in sensors because of their purity and controllable crystalline form. Structures of compounds mentioned in the references below are shown in Figure 5.

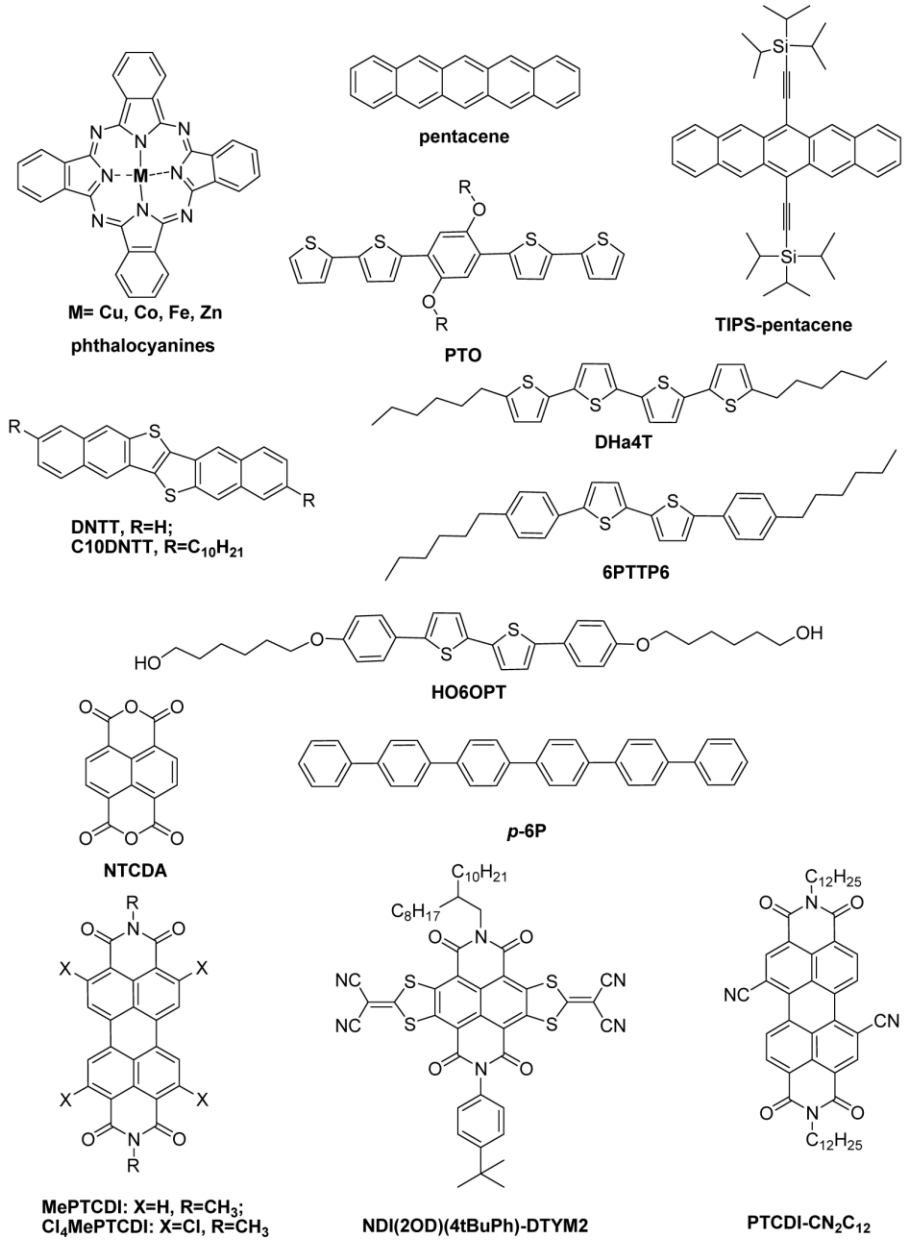


Figure 5. The small molecule semiconductors mentioned in this section. General references to these types of compounds were listed for Figure 3. Individual references appear in the text below.

Among these semiconductors, phthalocyanines (Pcs) are well known for their thermal and chemical stability and good OFET performance. Laurs and Heiland fabricated devices based on various phthalocyanines to study their responses to oxidizing gases. Although the term "transistor" was not mentioned at that time, field effect is used to explain the drift mobility. The changes in source-drain currents are dominated by trap density upon doping with oxygen, iodine, and bromine.[44] For example, surface conductivity increased five orders of magnitude on exposure to iodine vapor.

Adding a strong Lewis acid, tris-(pentafluorophenyl)borane (TPFB), into CuPc or CoPc semiconductor layer can reduce the mobility of transistor by altering the morphology and/or creating charge trapping sites in the channel. TPFB also acts as an NH_3 receptor. Exposed to NH_3, the drain current significantly decreased because strong B-N interaction and hydrogen bonds formed between H and F atoms result in strong NH_3 binding to TPFB. High NH_3 sensitivity was achieved even under very low concentration (20% conductance change on exposure to 0.45 ppm).[45]

An efficient way to improve the sensitivity of phthalocyanine layers is to increase surface-area-to-volume ratio by reducing the thickness of the semiconductor layer, depositing it using the Langmuir-Blodgett (LB) technique[46-48] or preparing a nanostructured semiconductor.[49-50] CuPc nanowires were used in a gas-dielectric FET sensor to detect SO_2 molecules (Figure 6a).[51] On one hand, all the surface area of a CuPc nanowire can be exposed to SO_2 molecules, increasing the probability of SO_2-nanowire interactions. The interactions diminish the effect of shallow traps in the nanowire, inducing significantly increased I_{on} and mobility (Figure 6b). The dramatic change of mobility (from 0.005 $cm^2\ V^{-1}\ s^{-1}$ to 0.05 $cm^2\ V^{-1}\ s^{-1}$ in 20 ppm) is different from the most frequently reported types of OFET sensors in which the change of the V_T is the basis of the gas sensing mechanism.

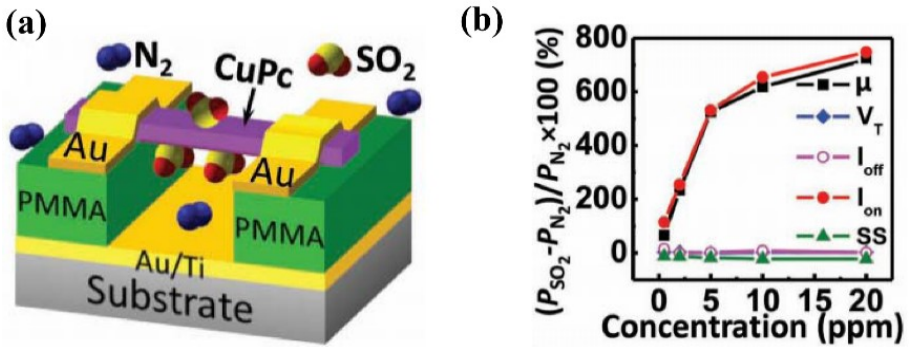


Figure 6. (a) The scheme of the gas dielectric OFET sensor based on CuPc single crystalline nanowires. (b) OFET parameters (listed on the right of the plot) changeing with increasing SO_2 concentration, extracted from transfer curves. Reprinted with permission from Ref. 51. Copyright 2013 Wiley.

Dielectric surface treatment can change the interfacial trap density of transistors.[52] A nitrogen dioxide (NO_2) gas sensor was recently reported based on a CuPc transistor with UV-ozone (UVO)-treated polymeric gate dielectric.[53] NO_2 can diffuse through the grain boundaries of CuPc and be absorbed by oxygenated polar functionalities at the surface of UVO-treated polystyrene (PS). The mobility of devices increases more in response to NO_2 in devices with greater duration of UVO treatment. For example, the mobility has negligible increase over its original value under 30 ppm NO_2 exposure without UVO treatment, while it becomes two times higher with 300 s UVO-treatment under the same NO_2 exposure, indicating that shallow traps, or a decreased carrier energy level relative to the transport level, are created by the UVO processing. An advantage of dielectric modifications for sensor improvement is that chemical interaction with analytes is decoupled from functionality and morphology that define OSC electronic properties. On the other hand, access of the analyte to the modified dielectric interface cannot be guaranteed, and the mechanism by which the dielectric modification changes OSC properties is less direct than for functionalization of the OSC itself.

Transistors based on polycrystalline pentacene can be optimized by fabrication processes that control grain size and grain surface area.[54] Zhu et al. grew pentacene film

on a room temperature substrate. The film shows field-effect hole mobility of 0.03 $cm^2\ V^{-1}\ s^{-1}$ and on/off ratio of 10^4.[55] Note that this is well below the state of the art for a device functioning purely as a transistor. However, the saturation current decreased with the increase of humidity, making for an effective means of monitoring relative humidity (RH) changes in the atmosphere. For example, the mobility drops to 9×10^{-4} $cm^2\ V^{-1}\ s^{-1}$ after a 30 min exposure to 72% RH. The grain size of pentacene is strongly dependent of the dielectric layer, thus resulting in different charge carrier trap density at the semiconductor-dielectric interface.[54, 56-57]

A low polarity of dielectric layers contributes to the relatively smaller grain size of pentacene and low surface trap density, both of which proved beneficial to realizing high performance NH_3 sensors. Furthermore, introducing ZnO particles into polymer dielectric layers can decrease the grain size of pentacene and promote contact between NH_3 and ZnO or pentacene, which significantly improves the response to NH_3.

Using an ultrathin film transistor with a multilayer of pentacene, Mizra et al. increased the sensing response to NO_2 by three orders of magnitude compared with a thick layer sensor device.[58] NO_2 molecules can interact directly with the grain boundaries and positively charge sites that would otherwise trap mobile holes. Thus, the average hole energy reaches the transport level, and the mobility of gate-induced holes increases. The mobility changes from 0.038 $cm^2\ V^{-1}\ s^{-1}$ to 0.045 $cm^2\ V^{-1}\ s^{-1}$ with 10 ppm NO_2, which can be attributed to the filling of traps by the NO_2. While ultrathin OSC layers increase electronic coupling between analytes and OFET channels, such layers are less environmentally stable in general than thick layers, providing an inferior margin for degradation over time. Perhaps the use of thicker, porous layers would be more effective in providing stability of electronic properties against degradation while promoting access and binding of analytes to electronically impactful sites in the OFET. In addition, pentacene-based OFETs can be operated in water and still maintain moderate mobility and on/off ratio,[59] which allows this material to detect analytes like

DNA, proteins or neurotransmitters. This aspect will be discussed in the following sections.

Pentacene derivatives and analogs, such as 6,13-bis(triisopropylsilylethynyl)-pentacene (TIPS-pentacene), provide relatively high-mobility films via various processing methods because of well-organized molecular arrangements conferred by the substituents. An OFET was fabricated to detect NH_3 by spray-coating TIPS-pentacene on a PMMA dielectric layer.[60] The adsorption of polar NH_3 molecules decreases the saturation current. The average mobility of original devices falls from 0.068 $cm^2 V^{-1} s^{-1}$ to 0.05 $cm^2 V^{-1} s^{-1}$ with increasing NH_3 gas concentration to 100 ppm. The on/off ratio also falls from 10^4 to 10^3. Dinaphtho[2,3-b:2',3'-f]thieno[3,2-b]thiophene (DNTT) can be regarded as an analog of pentacene in which one benzene is substituted by the thieno[3,2-b]thiophene group. Lu et al. prepared a porous DNTT film by a simple vacuum freeze-drying template method.[61] Despite the output current of a porous OFET being 5 times lower than that of an OFET with fully dense DNTT, the porous structure adds adsorption sites and provides direct pathways for NH_3 to interact directly with charge carriers in the conductive channel, as suggested above in the discussion of ultrathin layers. Modification of the DNTT structure makes this compound solution-processable.[62] Peng et al. reported the monolayer crystals of 2,9-didecyl-dinaphtho[2,3-b:2',3'-f]thieno[3,2-b]thiophene (C10-DNTT) with an exemplary carrier mobility of up to 10.4 $cm^2 V^{-1} s^{-1}$ by using a new dual solution-shearing method.[63] High mobility is beneficial for maximizing the current sensitivity caused by small amounts of NH_3. For this case, the "ultrathin" active layer approach was used to can shorten the diffusion time for NH_3 to reach the conductive channel, so the monolayer crystal based OFETs can sense ammonia concentrations as low as 10 ppb, and current changes two orders of magnitude on exposure to 100 ppb.

Oligothiophene materials show wide tunability in their electrical properties from varying conjugation length as well as grain size and shape.[64-66] A series of

oligothiophenes were compared in sensing devices, showing that the magnitude of response to vapors increases with increasing the number of CH_2 groups in n-alkyl side chains. Due to different semiconductor-analyte interactions, it is possible to construct combinatorial arrays of sensors to recognize a range of gaseous analytes, which is a prerequisite for an electronic nose.[67] The response to analyte of oligothiophenes is sensitive to the number of grains within the active channel, as was the case for pentacene discussed above. By changing the channel length of α,ω-dihexylquarterthiophene (DHα4T)-based OFET on the same film, Someya et al. adjusted the number of grain boundaries per device systematically and found that the vapor sensing occurs mainly at grain boundaries because the response increases with more grain boundaries in channel.[68]

An early ambient-stable n-type semiconducting naphthalene diimide (NDI) was reported by Katz et al. in 2000 with the derivative H,H-NDI-CH2C7F15 (μ = 0.1 cm^2 V^{-1} s^{-1}; on/off = 10^5).[69] The mobility can be enhanced to 0.7 cm^2 V^{-1} s^{-1} with an on/off ratio of 10^7 via additional surface modification.[70] Torsi gave evidence that an OFET based on the NDI precursor, 1,4,5,8-naphthalene tetracarboxylic dianhydride (NTCDA), can be used as a novel O_2 and H_2O sensor. This n-type material shows stable mobility of 1×10^{-4} cm^2 V^{-1} s^{-1} with on/off ratio of 10^4. The on- and off-current values of transistors decrease on exposure to oxygen because chemisorbed oxygen acts as a deep trap for electrons.[71] Furthermore, when H_2O molecules interact with an NTCDA thin film, I_{on} and μ decrease and exhibit reversibility while I_{off} responds with hysteresis and slightly increases with the humidity increases due to an ionic conductivity characteristic of protons dissociated from generated COOH groups. Zang et al. reported devices with NH_3 adsorbed on NDI derivatives (NDI(2OD)(4tBuPh)-DTYM2) showing unexpected sensitivity to HCl because of the combination of chemical adsorption and chemical reaction occurring on organic transistors (Figure 7a).[72] Because HCl has a relatively weak doping ability, exposure to 1000 ppm HCl induces negligible current changes for NDI(2OD)(4tBuPh)-DTYM2-based OFETs, but NH_3-adsorbed NDI(2OD)(4tBuPh)-DTYM2 devices show unexpected reversible

sensitivity to HCl (30-90% current decrease) and the response rate is comparable with that of commercial HCl sensors. Via thickness modulation, receptor implantation and device geometry optimization, flexible OFET sensors can be also achieved.[73] Perylene tetracarboxylic diimides (PDI) are another promising class of n-type semiconductor since its performance under ambient conditions is comparable with that of p-type semiconductors.[74]

Huang et al. reported a series of perylenediimide derivatives and found the electron affinities, as indicated by reduction potentials of micro/nanostructures based on these compounds, are independent of the surface area and morphology of those structures. However, the lowered *molecular* reduction potential that results from affixing the electron-withdrawing group, CN, to a PTCDI ring system allows PTCDI-CN_2C_{12} to be highly sensitive to NH_3 molecules (tens of times less resistance from 1% exposure) and maintain a stable sensitivity after exposure to air for 14 days.[75] A decrease of electrical conductivity, associated with the change in either charge carrier mobility μ *or* the charge carrier concentration *n*, was observed when O_2, ethanol, acetone, or n-butane was adsorbed by films of perylene tetracarboxylic diimide derivatives, MePTCDI or Cl_4MePTCDI.[76] The diffusion of gas molecules into the bulk increases the distance between hopping centers on pairs of grains, and thus increases the energy barriers and finally, leads to a decrease of μ. Therefore, gas molecules significantly affect the effective charge carrier mobility distinctly from the charge carrier concentration *n* because of the weak interactions within Cl_4MePTCDI film, while the effect from μ is less than n because acetone and ethanol molecules are restricted to an adsorption at the surface of crystalline MePTCDI.

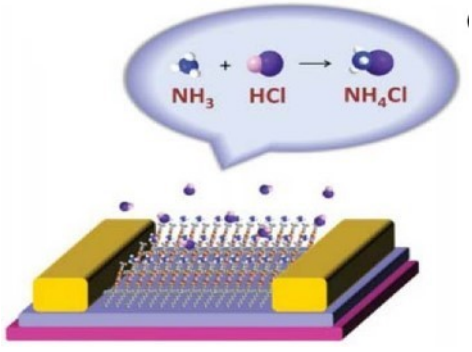


Figure 7. The device structure and sensing mechanism. Reprinted with permission from Ref. 72. Copyright 2014 Wiley.

Huang et al. used a sensor array combing the CuPc transistor with two other organic transistors to recognize eight analytes, by analyzing the direction and different responses of current, mobility and threshold voltage changes.[77] Thus, we see a set of responses from n-channel OSCs to analytes that are distinct from responses of p-channel OSCs, useful in creating patterns of responses that increase selectivity of analyte reporting. A challenge associated with the n-channel materials, however, is their increased electronic property instability because of interactions with the ambient environment. While barrier functionality such as fluoroalkyl chains helps stabilize n-channel materials in ordinary organic electronic circuits, this runs counter to the goal of promoting interactions with environmental analytes.

Combining different materials together in a single OSC film is an additional way to improve sensitivity. This strategy allows channel formation in a highly organized molecular layer with separate incorporation of selective binding functionality close enough to the channel to result in electronic responses to analyte binding.

Dimethyl methylphosphonate (DMMP) is a nerve gas stimulant. OFETs with two hydroxy-functionalized semiconductors, 5,5′-bis(4-n-hexyl-phenyl)-2,2′-bithiophene (6PTTP6) and 5,5′-bis(4-hydroxyhexyloxyphenyl)-2,2′-bithiophene (HO6OPT), were fabricated by Huang et al. group to selectively detect as low as tens of ppm level

DMMP, as shown in Figure 8.[78]

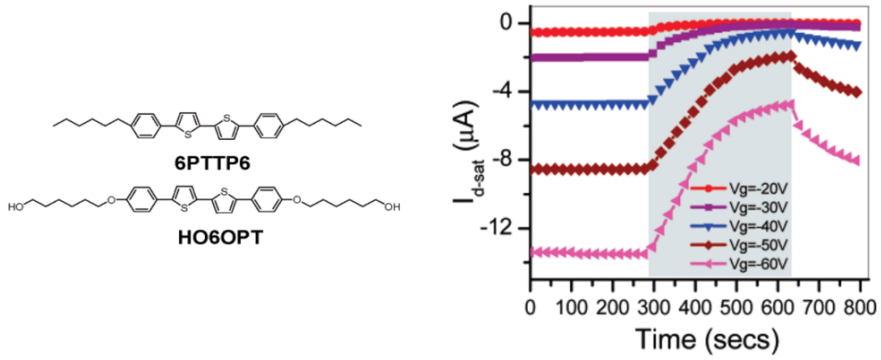


Figure 8. Molecular structure illustration of 6PTTP6 and HO6OPT and reversible responses of OFET integrating two-layer blend films upon exposure to 150 ppm DMMP vapor. Reprinted with permission from Ref. 78. Copyright 2007 ACS Publishing.

The hydroxy group is the simplest receptor that could be utilized for enhancing this interaction. Large and reproducible source-drain current changes were observed upon exposure to DMMP vapor. The enhanced performance of the mixture was due to the strong electric fields in the immediate vicinity of the molecules induced by DMMP. A monolayer-dimensional 6PTTP6 and HO6OPT blend based OFET was used to enhance the detect limit of DMMP down to 5 ppm.[65] They also fabricated a transistor with a two-layer blend as active layer (Figure 9), in which a blend layer included hydroxylated and nonhydroxylated semiconductor as upper layer on 5,5'-bis(4-n-hexyl-phenyl)-2,2'-bithiophene (6PTTP6) layer.[78]

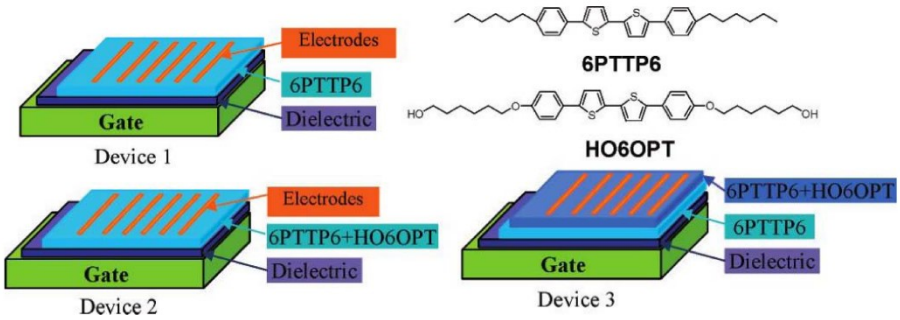


Figure 9. The device structures and semiconductor molecular structures. Single 6PTTP6 (device 1), single blend (device 2), and two-layer blend (device 3). Reprinted with permission from Ref. 78. Copyright 2007 ACS Publishing.

Compared with the device with single 6PTTP6 or single blend as active layer, this heterostructure shows higher sensitivity to the analyte dimethyl methylphosphonate (DMMP). Rather than a microstructural effect, the trapping charge carriers diffusing from the top layer probably penetrate to the conductive channel between grains, where DMMP adsorbs, which enhances the sensing performance. Furthermore, the response times of these sensors were dramatically shortened by reducing the film thickness.[65]

Torsi et al. reported that a bilayered OFET,[79] including an achiral phenylene-thiophene oligomer (PTO) as inner layer and a chiral molecule bearing *L*-phenylalanine amino acid groups or *β*-D-glucosidic units as outer layer, is capable of differentially detecting optical isomers. The achiral PTO inner layer acted as a charge transport layer, while the chiral outer layer worked for enantioselective recognition. A double heterojunction was achieved by Ji et al..[80] Vanadyl phthalocyanine (VOPc) was grown on the ultra-thin heterojunction surface of *N*,*N*'-diphenyl perylene tetracarboxylic diimide (PTCDI-Ph) and para-hexaphenyl (*ρ*-6P). On one hand, the highly ordered conductive heterojuction layer of PTCDI-Ph/*ρ*-6P improves the charge-carrier transport; on the other hand, VOPc is a very sensitive p-type material to NO_2. These combinations make the relative-response five times larger than that of the single-heterojunction device. Very recently, Huang et al. fabricated an organic p-n junction structure and achieved direct detection of solid chemical analytes by OFETs for the first time.[81] With this horizontal side-by-side diode structure, chemical solids can directly interact with charge carriers near the surface of the OSC layer.

2.2 Polymer semiconductors as active layer for sensors

Polymer semiconductors show good solution processability, film-forming properties, and high flexibility in thin-film devices relative to many low molecular weight compounds. With a view to p-type polymer semiconductors, polythiophenes are among the most investigated conjugated polymer types for OFET devices due to the efficiency with which they can be synthesized. Structures of polymers discussed in this section are shown in Figure 10.

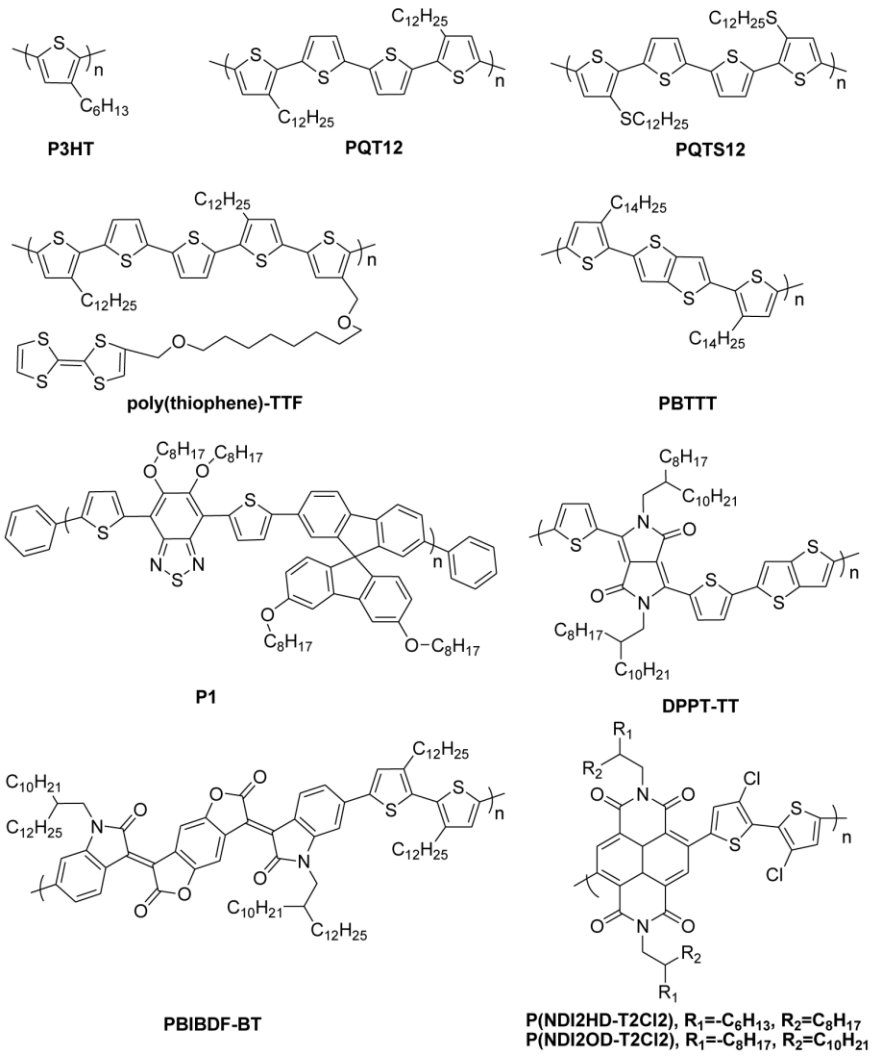


Figure 10. The polymer semiconductors mentioned in this section. General references to semiconducting polymers were listed for Figure 3. Individual references appear in the text below.

Poly(3-hexylthiophene) (P3HT) has been extensively studied for use in chemical sensors based on thin-film or nanostructured OFETs. Functional groups were incorporated along the P3HT backbone or as the end-capping groups.[82] Functionalized P3HT can be applied to gas sensor arrays that demonstrate a ‘‘finger-print’’ response to volatile organic solvents, including alcohols, organic acids, and amines, with a sensitivity at the low ppm level. Li and Lambeth reported a nanostructured regioregular P3HT and proposed the sensing mechanisms are mainly intragrain effect and a grain

boundary effect existing at the same time, which show contrary responses.[83] Additives, such as polystyrene[84] and nanostructured inorganic oxides,[85-86] make the blend active layers more sensitive to the analytes. The addition of palladium particles into P3HT film induce additional pores to increase overall sensing area.[87] Furthermore, these particles act as ethylene receptor sites where ethylene has an affinity to bind with transition metals, and thus result in an increased sensing response of 30% current decrease from 5 ppm exposure over 5 minutes.

Because of their deeper HOMO levels, poly(quaterthiophene)s (PQTs) (5.2 eV) are less sensitive to air and humidity compared to P3HT (4.9-5.0 eV) and show good OFET performance with mobilities of 0.07-0.12 cm^2 V^{-1} s^{-1} and on/off ratio of 10^6-10^7.[88] These polymers contain roughly the same number of CH_2 groups in side chains as to the poly(alkylthiophenes) such as P3HT, but only half of the thiophene rings are alkylated, decreasing the electron-donating character of the conjugated systems. Kong et al. investigated pure PQT12 film and PQT12/TPT-TTF blend film as active layers to detect 2,4,6-trinitrotoluene (TNT).[89] A "turn-on" current response from blend OFETs was observed when the devices were exposed to dilute TNT analyte solutions. This can be attributed to the electron donating-electron accepting pairing of TPT-TTF and TNT which increasing the concentration of mobile holes, or inhibit hole trapping. They also copolymerized PQTs with tetrathiafulvalene (TTF)-functionalized thiophene.[90] The introduction of the TTF group induced the loss of hole mobility and a negative Seebeck coefficient due to the strong hole trapping activity of the TTF additive, but enabled a current-increase response to TNT. A flexible ammonia sensor platform based on polydidodecylquaterthiophene (PQT12) with a sensitivity of 0.5 ppm and a limit of detection of 0.1 ppm was achieved by Besar et al.,[91] which is well suited for large area (or roll-to-roll) and cost-efficient processes. Li et al. modified the structure of PQT12 by inserting sulfur atoms into the side chains which increase trap density in film and promotes redox interactions between the polymer and NO_2 molecules (Figure 11).[92] The increased trap density and decreased domain sizes in polybisdodecylthioquaterthiophene (PQTS12) film are responsible for the higher

sensitivity of PQTS12 to NO_2 gas compared with PQT12. Notably, the ratio of response from these two polymers can distinguish low concentrations for extended times from exposures to high concentrations from shorter times and can be used as a marker for ratiometric sensing.

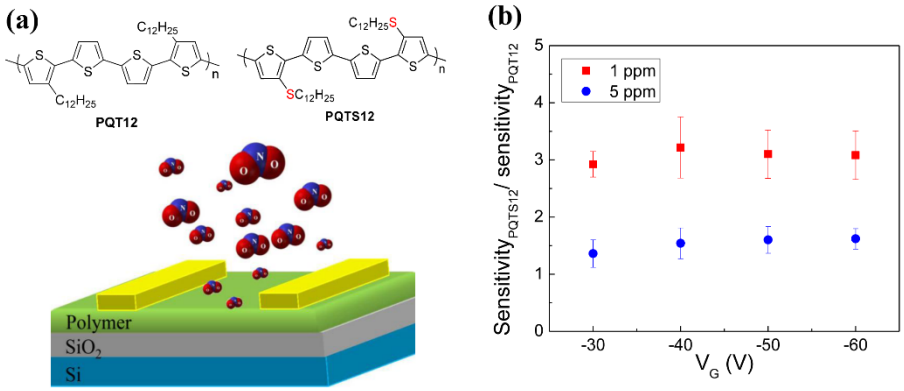


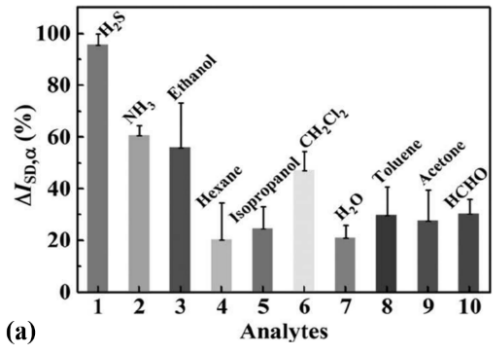
Figure 11. (a) The molecular structure of PQT12 and PQTS12 and device structure based on these polymers. (b) Sensitivity ratio of PQT12 and PQTS12 varies with different NO_2 concentration. Reprinted with permission from Ref. 92. Copyright 2017 ACS Publishing.

PBTTT is also more stable in air and has higher mobilities relative to P3HT.[93] The responses of PBTTT to alcohols and acetone are larger than those to P3HT due to large crystalline domains in PBTTT film where larger numbers of analyte molecules can be adsorbed between the grains.[94] In addition, top-contact/bottom gate structures of OFETs based on PBTTT show an enhancement of response compared with bottom-contact/bottom gate structure. One reason is the possible change of the metal work function after the adsorption of the polar analyte molecules on the bare electrode surface. Another reason is that the bulk conductivity changes when carriers inject from the metal to the bulk of semiconductor and reach the channel.

Donor-acceptor alternative polymers are attractive semiconductors for sensor application because of their structural tunability and high charge mobility. Sensitivity to NH_3 and humidity was improved by introduction of microporous structures in D-A polymer layers by washing away one additive[95-96] or removing specific groups of polymers.[97] Lv et al. reported a spirobifluorene-based OFET sensor for H_2S and

achieved detection limitation as low as 1 ppb.[98] According to the different and changing rates of absorption and desorption of H_2S molecules in the sensor, they propose that thinning the active layer does not simply favor an improved sensitivity. Based on the optimized thickness of the polymer, they obtained the detection limit of as low as 1 ppb, which was to date the most sensitive H_2S sensor. Further, the OFET showed excellent selectivity as shown in Figure 12a. Khim et al. reported the precise control of thickness of DPPT-TT where mobility decreased with the thinner film.[99] For instance, the mobility is 1.78 (±0.39) $cm^2 V^{-1} s^{-1}$ for 12.8 (±1.0) nm thick film, while 1.1 (± 0.26) for a 2.2 (±0.3) nm ultrathin film. The gas sensitivity to 10 ppm NH_3 is as high as 82% for 2 nm thick film and decreases with the thicker film. Even ethylene detection was achieved (a few % current decrease from 1000 ppm) without any additives based on this ultra-film OFET. Other p-type polymers for chemical sensing can be found in this review.[100]

N-type polymers are not widely applied into chemical sensor limited by the air/water degradation and low mobility compared with small molecules and p-type polymers. Nevertheless, the porous film based on n-type polymer PBIBDF-BT can be obtained by mixing poly(1,4-butylene adipate) (PBA) into polymer semiconductor followed by washing with acetone (Figure 12b).[101] A higher sensitivity can be obtained as the PBIBDF-BT contents in the blend films decreased because of larger pores formed in the film. The sensing mechanism is mainly attributed to the change of carrier mobility since the mobility gradually decreased with increasing humidity.



(b)

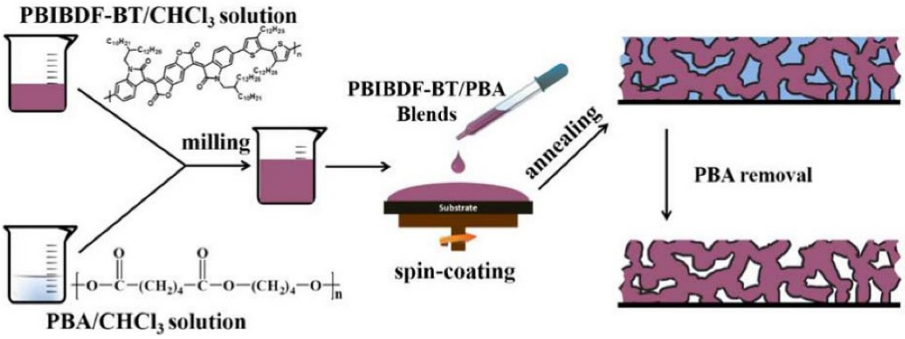


Figure 12. (a) Selectivity test of the OFET under 30 s exposure, the concentrations were 1ppm for H_2S, 50 ppm for NH_3, 470 ppm for HCHO and more than10 000 ppm for other solvent analytes. Reprinted with permission from Ref. 98. Copyright 2016 Wiley. (b) The preparation of porous film based on n-type polymer PBIBDF-BT. Reprinted with permission from Ref. 101. Copyright 2017 ACS Publishing.

There have been very few reported works about n-type polymers in OFET sensors. The challenges for using n-polymers in sensors encompasses material properties and device configurations. The design of air-stable solution processable n-channel polymers is constrained because unusually deep lowest unoccupied molecular orbital (LUMO) energy levels are needed to make the polymers sufficiently stable in air or high humidity. Gi-Seong et al. reported two derivatives of N2200 [102] with chlorination on the π-backbone, P(NDI2HD-T2Cl2) and P(NDI2OD-T2Cl2). The polymers can be operated in water while keeping good transport properties. The results make these polymers promising for application in chemical and biological sensor in aqueous

media.[103] Although the influence of humidity and oxygen on electron mobility is negative, n-type polymers still have potential applications in sensors if the interaction mechanisms between the polymers and analytes can be better understood.

Thus, many of the strategies that were discussed for small molecules apply to polymers as well. The electronic energy levels are similar, and film deposition can be more facile, especially as printing methods become more refined. An additional issue for polymers is the greater difficulty of preventing any analyte binding functionality from adversely impacting the molecular-scale organization of the charge-carrying channel, increasing the device resistance and power requirements.

3. Physical enhancements for sensing amplification

While there are only a few distinct field-effect transistor configurations applicable for sensing applications (bottom, top, side, or electrochemical gates), to date there have been dozens of reported chemical and material modifications of transistor components that result in amplified responses. A variety of steric, chemical, or biological mechanisms can lead to increased electronic signals. Alterations to the device layers can include addition of particles or formation of pores. Secondary labelling enhancements include particles and probes that are added to the device after the initial sensing binding event has occurred.

3.1 Embedded pores and metal particles

The addition of pores to an otherwise flat sensing layer offers two primary benefits. Firstly, pores can drastically increase the overall free surface area for analyte interaction while maintaining the same dimensions. Assuming correlation of electrical response with quantity of bound analyte, this corresponds to a greater signal change per concentration than a standard flat surface. As an additional benefit, sufficient pores of suitable size can act as a protective screening layer to prevent larger objects such as dust particles from overwhelming the sensing platform.

Pores in polymers may be created in a variety of ways. Al-Hardan et al crafted a highly sensitive pH sensor using porous silicon in the gate geometry, thereby achieving a "super Nernstian" value and overcoming a frequent drawback found in this orientation.[104] Wu et al. achieved similarly increased response in a humidity sensor by using a phase-separation phenomenon to create a macroscopic porous structure.[101] An enhanced ammonia sensor had a similarly improved gas response, and created a porous structure through use of a simple vacuum freeze-drying template method, as shown in Figure 13(a), (b), (c), and (d).[61]

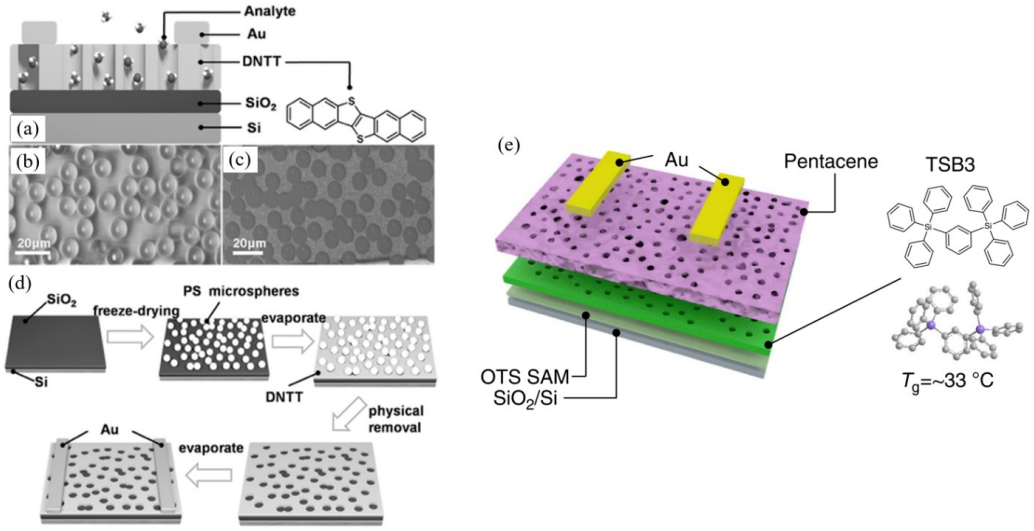


Figure 13. OFET-based sensors. (a) The device structure of the porous OFET-based sensors and the molecular structure of DNTT. Optical images of a porous DNTT film (b) with polystyrene microspheres and (c) after removing polystyrene microspheres. (d) The fabrication procedure of the porous OFET-based sensors. Reprinted with permission from Ref. 61. Copyright 2017 Wiley. (e) Device schematic and the molecular structure of TSB3. Reprinted with permission from Ref. 105. Copyright 2014 Nature Publishing Group.

In 2014, Kang *et al*. developed an approach of evaporating pentacene on top of m-bis(triphenylsilyl)benzene (TSB3), resulting in extraordinary morphology with far fewer grain boundaries and myriad nanometre-sized pores in pentacene, as shown in Figure 12e.[105] These peculiar structures were formed by differences in molecular interactions between the organic layers and the substrate surface. The pore-rich structure improved the sensitivity of the OFET to methanol gas. While not precisely

'pores', Yu et al. clearly demonstrated the positive sensing impact of increase surface area by altering the morphological characteristics of the ammonia sensing semiconductors.[106]

The addition of specific metallic particles or nanowires to semiconducting layers has shown similar promise in increasing electronic response, though for very different mechanistic reasons. Surya et al. developed a hydrogen sulfide detection system by incorporating tin oxide nanoparticles into the sensing area.[107] Zheng et al. used ultrafine platinum nanoparticles to obtain a marked response increase to dinitrotoluene (DNT) vapor, as illustrated in Figure 14.[108] This improvement was attributed to the particles' charge transfer interactions with the vapor, compared to a film with no particles. A different enhancement mechanism was demonstrated by Han et al. when they incorporated zinc oxide particles into a pentacene layer, thereby decreasing the average grain size. This promoted diffusion of CuPc molecules to the interface.[109] The effects of pores and particles can also act in synergy, as demonstrated by Besar et al. in development of an ethylene vapor sensor, which, as already mentioned, used both palladium particles and chemically-induced porosity to achieve a substantially higher specific sensing response.[87] While porosity has the advantage of being applicable without changing the OSC electronic energy levels, metal particles introduce new electronic states and even conducting pathways. On the other hand, metal surfaces provide distinct sites for analyte binding that can alter charge transport in both OSC and metal states.

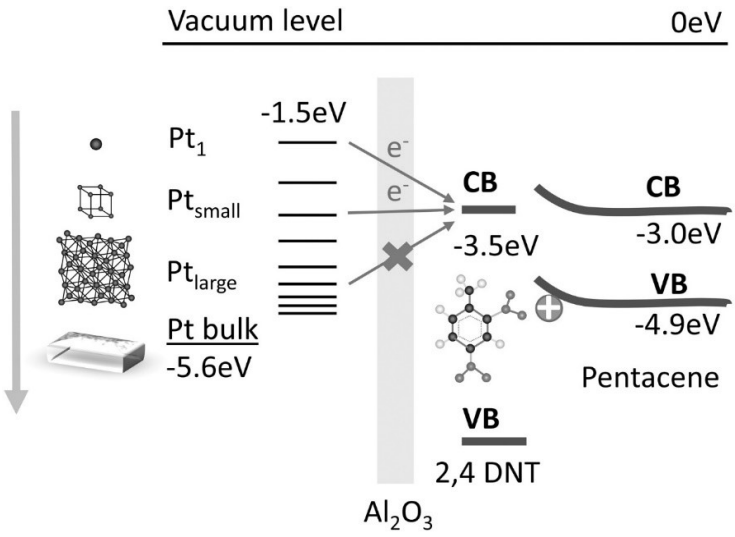


Figure 14. Schematics of energy band diagram of device with different sizes of Pt NPs under zero gate bias. Reprinted with permission from Ref. 108. Copyright 2013 AIP Publishing.

3.2 Secondary signal amplification techniques

Some chemical approaches to increasing electronic effects of analyte binding are somewhat analogous to the enzyme-linked immunosorbent assay (ELISA) well developed for diagnostic testing. Very generally, this type of system involves an analyte-binding entity bound to a substrate, the addition of the analyte of interest, many washing steps, followed by any of several potential amplifiers that would bind to the opposite end of the analyte and produce a more drastic signal. While highly sensitive and effective, this system can take many hours, use expensive reagents, and require trained technicians in a professional lab setting to successfully complete and read the outcome.[110] However, similar secondary binding and amplification techniques are being used in electronic testing with promising results. Jang et al. combined the ELISA system with the typical ion-selective field-effect transistor (ISFET), resulting in increased sensitivity.[111] This method of adding functionalized particles is of great interest in a variety of bioelectronic sensing situations, for example in the case of electrochemical impedance spectroscopy where Zhu et al. used the sandwich approach to specifically bind a secondary gold nanoparticle to the surface, significantly altering the impedance more than the original analyte of interest, Clostridium difficile toxin, as presented in Figure 15.[112]

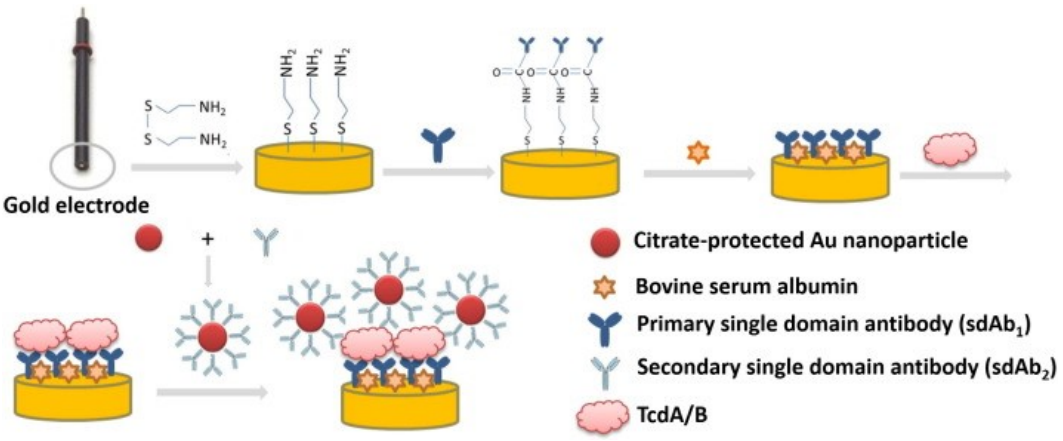


Figure 15. Illustration of the immobilization process of the sandwich-type electrochemical impedance immunosensor. Reprinted with permission from Ref. 112. Copyright 2015 Elsevier.

3.3 Dielectric and receptor layers

Non-conducting portions of FET sensors usually serve one of two purposes. All FETs require a so-called "dielectric" layer between the source/drain and gate electrodes capable of sufficiently high charge polarization to produce mobile charge carriers, above the trap energy levels, that can carry current along the channel when practical voltages are applied to drain and gate electrodes. While this may simply be the oxide layer on silicon or layer of a simple polymer such as PMMA, in many cases the dielectric layer is specially fabricated for the sensor. In some architectures, this layer or the semiconductor itself may also serve as the analyte receptor area, though frequently a second specialized receptor layer is needed to complete the sensor.

A useful metric for characterizing dielectric layers is their complex impedance, which is determined over a broad range of frequencies and consists of a real part (comprised of the resistance of the system) and the imaginary or "out of phase" portion (linked to the capacitance, or rarely, inductance, of the system). A variety of mechanisms may result in a measurable shift of either part of the complex impedance. Gradual water infiltration of the layer will typically lead to a much higher capacitance, and electrolyte infiltration will lead to lower resistance. Binding events on the surface of the film can

similarly change these qualities based on specific analyte interactions, typically leading to a decrease in capacitance if significant height is added onto the layer, as expected in a double plate capacitor system.[113] Measuring the change in complex impedance of a system can be used as a sensing tool itself, or it can be used to elucidate the underlying mechanisms taking place in the layers comprising an FET.

Choosing an appropriate dielectric layer is of utmost importance in device design, since it will partially determine device stability, sensitivity, and power consumption. A study of the ability of the choice of dielectric material to change the threshold voltage of an OFET was completed by Martinez Hardigree et al.[114] Being able to tune the threshold voltage can significantly reduce required gate voltage, increasing the range of use of the device. In a similar vein, Alley et al examined various substituted polystyrene layers and their effects on a pentacene transistor. By altering the dielectric layers, Alley was able to explore the interface effects of charging in the device and also reduce bias stress.[115]

Huang et al attributes a very high sensitivity ammonia sensor to the qualities of the polystyrene dielectric layer, concluding that the sensing mechanism lies in the interface between dielectric and semiconductor, making choice of dielectric material extremely important. Besides altering the chemical composition of the dielectric polymer, it is also possible to use additives to create a desired effect.[116] Han et al added ZnO particles to a standard PMMA dielectric film, which resulted in decreased grain size in the pentacene layered on top. The increased length of grain boundary of pentacene resulted in many more sensing opportunities for the analyte of interest, NO_2.[109]

Dielectric receptor layers are usually chosen based on having the chemical attributes to attract and hold the analyte of interest, whether through charged group interactions or through a more specific biological attachment such as an antibody binding to a protein. Ideally this layer should be as thin as possible while maintaining integrity, such that the largest possible event signal will be measured by the system.[117] Additional

consideration should be given to bind any potentially reactive sites in the receptor layer to prevent false signal from occurring. Physical alterations of dielectric layers such as added film porosity have been shown to have a potential positive effect on sensitivity a receptor layer by increasing surface area available for analyte binding as shown in Figure 16.[118] However, in this case it is often necessary to ensure that the dielectric layer retains enough structural integrity to not allow excessive leakage current and thereby ruin the functionality of the transistor, depending on exact device geometry.

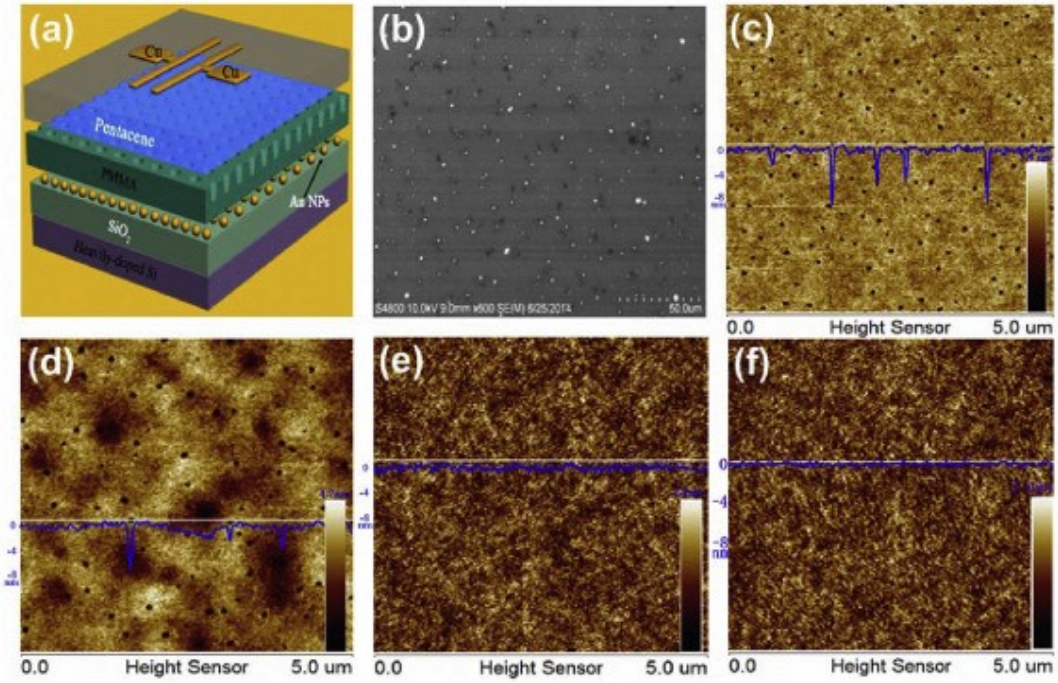


Figure 16. (a) The schematic illustration of the floating-gate OFET memory devices with the porous structure of PMMA tunneling layer. (b) The SEM images of Au-NPs floating layer. The AFM images of (c) high density and (d) low density porous and (e) thick nonporous and (f) thin nonporous structure of PMMA film. Reprinted with permission from Ref. 118. Copyright 2016 Elsevier.

Dielectric layers not only serve an important function in the formation of FETs, but are also vital to the functioning of the sampling impedimetric sensor. Impedance characterization incorporates the resistance, capacitance, and inductance across a system. Due to the nature of adding capacitors in series, in impedance-based

biosensors it is frequently ideal to begin with a dielectric/binding layer that has a very high capacitance, since any antibody of protein binding on top of the layer will generally have a lower capacitance. Since the inverse of the resulting capacitance is equal to the sum of the inverse of these two values, a much larger shift will be seen if the base layer as a high capacitance, due to either its dielectric constant or its thinness. While impedance sensing is largely outside the scope of this present review, the authors recommend a thorough review by Sapountzi et al. for further discussion of this topic.[117]

4. Biomaterials added to organic field-effect transistors

To minimize long term plastic waste products[119] from electronic technologies, biocompatible and biodegradable materials are increasingly sought for these applications. Most biomaterials are organic materials which possesses the merits of abundance, environmental friendliness, low toxicity, and low cost.[120-123] Industrial interest for the fabrication of such biomaterial-engaged electronics will only be raised with the availability and amenability of large-scale roll-to-roll production processes. Key to a high-performance biomaterial in OFETs is compatibility between the biomaterial and the other organic materials being used. The utilization of biomaterials in OFETs can be for the tuning of electronic device properties or for recognition/transduction functionalities in sensors.

In the 1990s, enzyme-related materials were the first biomaterials to be introduced into electronic devices.[124-125] Since then, biomaterials have been adopted as substrate, dielectric, and even semiconductor in organic electronic devices. For OFETs specifically, caramelized glucose, edible hard gelatin, and commercially available plastics made of potato or corn starch can be fabricated as the metabolizable or biodegradable substrates.[126] DNA, naturally occurring small organic molecule nucleobases, as well as various sugars could serve as the dielectric.[127-128] DNA has also worked as the electron blocking layer in organic light-emitting devices (OLEDs) to improve the light emission efficiency.[127, 129] The most exciting attempt is the

development of biomaterials to work as the semiconductor. Typical examples are small organic molecules of beta-carotene and indigo, which are p-type and n-type (indigo is also reported to work as a bipolar material) semiconductors respectively, yielding a charge mobility of ~10^{-4} cm^2/Vs.[130-131] A summary of the biomaterials which have been used in OFETs is shown in Figure 17.

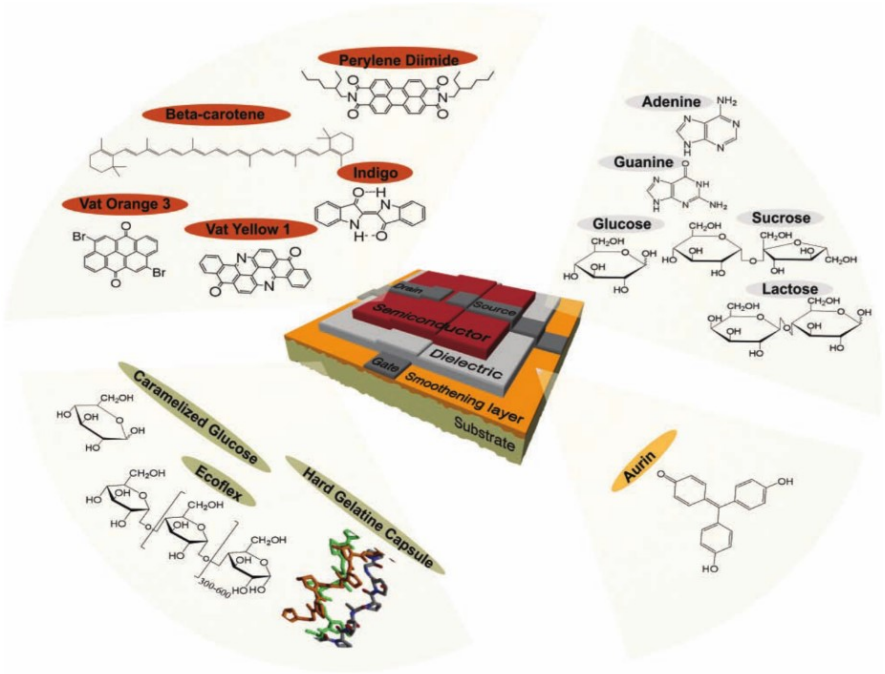


Figure 17. Utilization of natural materials or materials inspired by nature in OFETs. Reprinted with permission from Ref. 126. Copyright 2010 Wiley.

4.1 Biomaterials as interface modification layers in organic field-effect transistors

Since biomaterials have versatile functional groups, they are suitable to serve as interface modification layers (or buffers) in OFETs. As known, the efficient charge carrier channel lies in the first few molecular layers of the semiconductor resting on the dielectric in OFETs.[7, 132-134] Therefore, the modification of the interface between the semiconductor and the dielectric is an effective way to enhance the performance of OFETs. The adoption of a modification layer upon or in the dielectric or semiconductor is a common way to optimize this interface. The small organic molecule guanine is a good bio-candidate to serve as the modification layer, owing to its highest melting point of 360 degrees C among the four kinds of DNA bases, and high density of 2.2 g/cm^3,

which increase the stability of the guanine molecule.[126, 135] Moreover, guanine is an excellent dielectric with low dielectric losses of 10^{-2} at 10 mHz and high breakdown strength between 1.5 and 3.5 MV cm^{-1}.[126]

In 2014, Lee et al. reported the application of guanine embedded into aluminum oxide (Al_2O_3), which much improved the gate stability.[135] This was due to the hydrogen ion gettering activity of guanine in the gate dielectric and the charge trapping ability of guanine to which the voltage pulse-driven charges might be injected from channel. Further, in 2016, Shi et al. employed guanine on top of silicon dioxide to enhance the performance of pentacene OFETs, as illustrated in Figure 18a and b.[136] The higher ionization energy of guanine molecule indicated that it will not trap the mobile holes in the pentacene film as shown in Figure 18d. A tripling of the field-effect mobility, from 0.13 cm^2/V s to 0.42 cm^2/V s, was achieved by introducing a 2 nm guanine layer as presented in Figure 18e. They demonstrated the increased field-effect mobility was mainly attributed to the hydrogen bonding capacity of otherwise unassociated guanine molecules, which enabled them to neutralize trapping sites on the silicon dioxide surface.

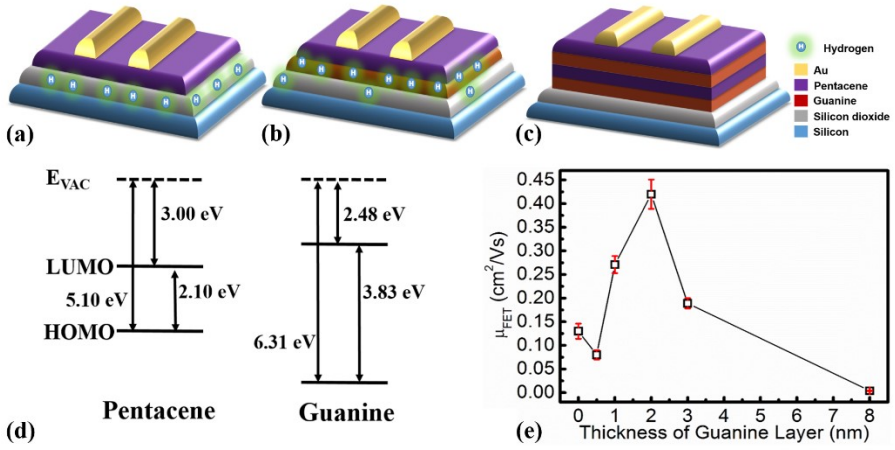


Figure 18. Device architecture of the OFET and representation of the location of hydrogen atoms in (a) OFET without guanine layer. (b) OFET with guanine layer. Reprinted with permission from Ref. 136. Copyright 2016 AIP Publishing. (c) OFET with guanine/pentacene/guanine/pentacene structure. Reprinted with permission from Ref. 57. Copyright 2017 AIP Publishing. (d) Schematic energy-level diagrams of pentacene and

guanine base pair with vacuum-level (E_{VAC}) alignment. (e) Field-effect mobilities of OFETs with different thicknesses of guanine layer. Reprinted with permission from Ref. 136. Copyright 2016 AIP Publishing.

Shi et al. also inserted one more guanine layer into pentacene layers as shown in Figure 18c.[57] Through adjusting the layer thickness ratio of guanine and pentacene, the tradeoff of charge carrier mobility and current on/off ratio was controlled. They illustrated that the charge mobility was enhanced by increasing the proportion of pentacene in the layer-by-layer system, while the current on/off ratio was increased via the decreased off current induced by the guanine layers. They also elucidated that the tunable device performance was also ascribed to the trap and dopant neutralizing properties of the guanine layers. Furthermore, the cost of the device could be reduced remarkably via replacing some of the pentacene with low-cost guanine.

4.2 Biomaterials as functional layers in organic field-effect transistor-based gas sensors

Indigo is a small organic dye produced from plants that which has been cultivated for at least 4000 years in China, India, and Egypt for coloring textiles. Indigo has an extremely low solubility and a high melting point (390-392 °C), explained by stabilization from inter- and intra-molecular hydrogen bonding. Intermolecular interactions of π-domains also strongly influence the electronic and vibrational spectra of indigo in solutions and dispersions.[137] The first investigated biomaterial serving as a functional sensing layer can be dated back to 1981, when indigo was employed to determine the ozone in water.[138] The precision of the analysis was 2% or 3 μg/L for low concentrations if a spectrophotometer or a good filter instrument was used. The research on integrating indigo in OFETs has been continuous over the past decades. In 2013, Dubois et al. made indigo adsorbed on carbonaceous nanomaterials as chemical filter for the selective detection of nitrogen dioxide (NO_2) in the environment.[139] The surface of multi-walled carbon nanotubes (MWCNTs) was coated by π-stacking with adsorbed indigo molecules. An excess of indigo has resulted in a biphasic sample

where nanotubes covered with indigo coexist with free indigo particles. They successfully realized similar average filtering yields toward ozone (O_3) (close to 100%) and NO_2 (around 0%) of four kinds of structures: indigo, MWCNTs, MWCNTs covered with indigo (hybrid), and biphasic as shown in Figure 19a.

Guanine can also play a role in OFET-based sensors. Shi et al. fabricated a guanine and pentacene OFET pair, which were sensitive and selective to NO_2 and five other vapor analytes (including acetone, IPA, ethyl acetate, water, and acetic acid).[140] OFETs with two configurations were fabricated, one of which used thermally deposited guanine and pentacene layer-by-layer as shown in Figure 18c, which was more sensitive to NO_2. The other one only adopted pentacene as the sensing element. These two kinds of OFETs showed opposite responses and/or different response magnitudes to the other five vapor analytes as shown in Figure 19b and c. Therefore, the sensing responses of the two OFETs presented distinct patterns and thus could distinguish individual analytes including nitrogen dioxide.

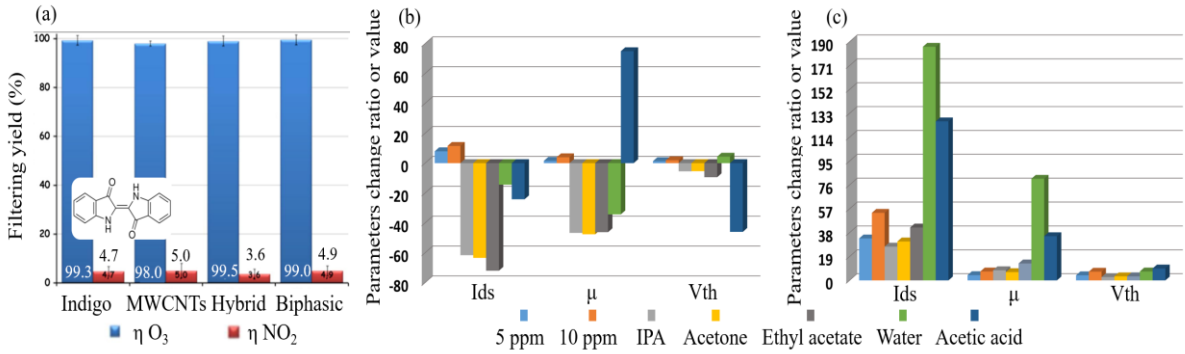


Figure 19. (a) Filtering yields toward O_3 and NO_2 for the indigo and MWCNTs as well as their associations, the inset shows the molecular structure of indigo. Reprinted with permission from Ref. 139. Copyright 2013 Elsevier. Drain current and mobility change ratio, and threshold voltage change value of (b) pentacene, and (c) guanine-pentacene OFETs to 5 ppm NO_2, 10 ppm NO_2, IPA, acetone, ethyl acetate, water, and acetic acid under 5 min exposure. Reprinted with permission from Ref. 57. Copyright 2017 Elsevier.

Polymeric biomaterials can also contribute to OFET based sensors. In 2013, Daniela et al. fabricated an OFET integrating polymeric phospholipid (PL) membranes between the dielectric and P3HT semiconductor to detect the volatile general anesthetic molecules such as diethyl ether and halothane, as shown in Figure 20a and b.[141] This technology allows the direct interface of a PL layer to an electronic transistor channel, and direct probing of subtle changes occurring in the bio-layer. Silk fibroin (SF) is another polymeric material employed in the OFET-based sensor; its molecular structure is shown in Figure 19c. Li et al. fabricated SF on top of PMMA dielectric to improve the NO_2 detection as shown in Figure 20d.[142] The enhancement of the sensing property was owing to the interaction between the hydroxyl and the amidogen of the SF biomaterial and NO_2 molecules at the interface of dielectric/organic layer.

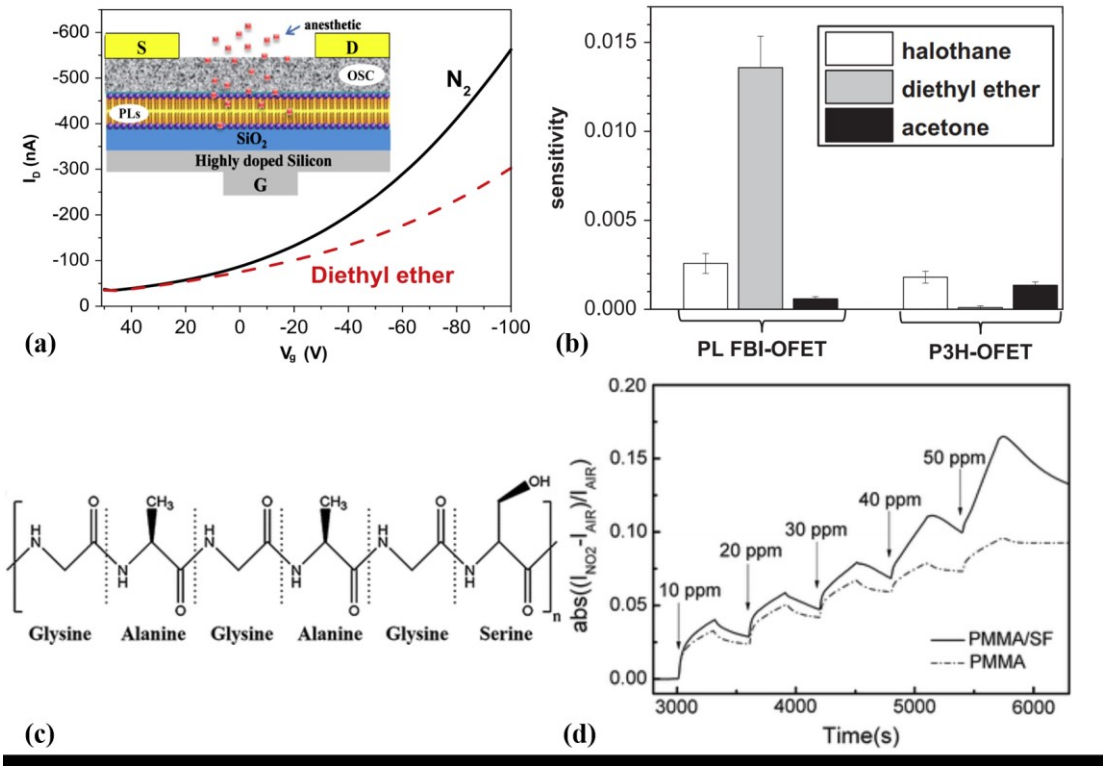


Figure 20. (a) Transfer characteristics for a PL OFET measured in N_2 and in a controlled atmosphere of diethyl ether at a concentration of 3.0 wt% in N_2 atmosphere, the inset is the side view of the PL OFET device. (b) Differential analytical sensitivities (ΔI×[saturated vapor fraction]-1) of PL-OFET and P3HT OFET sensors exposed to diethyl ether, halothane and acetone. For all the compounds the maximum concentration tested was half the saturated vapor. Reprinted with permission from Ref. 141. Copyright 2013 Elsevier. (c) Molecular structure of

SF. (d) Real-time response curves of devices exposed to NO_2 in the concentrations ranging from 10 to 50 ppm. Reprinted with permission from Ref. 142. Copyright 2015 Springer-Verlag.

The biomaterials that have been integrated as OFET components are summarized in Table 1.

Table 1. Biomaterials integrated into electronic devices.

Device	Biomaterial	Function	Result and product	Ref
OFET	Poly(L-lactide-co-glycolide)	Substrate		[143]
OFET	Shellac	Substrate and dielectric		[144]
OFET	Guanine	Hydrogen getter and charge-trapping layer	*Boolean* logic	[135]
OFET	Guanine	Trap neutralizing layer	3 times enhancement of mobility	[136]
OFET	Guanine	Trap neutralizing layer	Controlled mobility and on/off ratio	[57]
OFET	Guanine	Trap neutralizing layer	NO_2 sensor	[140]
OFET	DNA	Gate dielectric	Memory element	[128]
OFET	Silk fibroin	Gate dielectric	High mobility and low operating voltage	[145-146]
OFET	Polymeric phospholipid	Gate dielectric	Vapor sensor	[141]
OFET	Indigo	Semiconductor	Invertor	[131]
OLED	DNA	Electron blocking layer	10 times more efficient	[129]

OLED = organic light-emitting diode

It has thus been demonstrated that biomaterials can make constructive contributions to OFET biosensors. Biopolymers in particular possess functional group arrangements that are unlikely to be obtainable, or even envisioned, in synthetic materials. Some

biomaterials confer recognition capabilities for other molecules, whilc others bring unique physical property enhancements. While biological origin or biodegradability are sometimes viewed as values in their own right, these must be weighed against their importance to the utility of the application at hand.

5. Health-related vapor sensors using organic semiconductors

OFETs show promising applications with many of the required features (sensitivity, reliability, reproducibility, and room temperature operation compatibility) in the health-related sensing field, which is compatible with cloud technology and massive networking related to healthcare data management and analytics.[147]

Vapors are among the analytes that can be related to health effects or conditions. Alcohols are the most common health-related vapors needing to be monitored. Methanol, excessive ethanol, and a wide variety of alcohols are harmful to our health.[148] Polymers with thiophene repeat units are widely adopted in the detection of alcohols. Crone et al. reported a set of oligothiophenes used in OFET sensors responding to a series of primary alcohols.[67] All the devices show obvious response to alcohols, while the response magnitude increases as the length of the semiconductor hydrocarbon end group increases, as mentioned earlier in the Section 2.1. Such effect of the side chain of the polymers on the response to alcohols was also observed by Torsi et al. They reported that ether functional subunits on semiconducting polymer side chains altered the response of the polymer to alcohol vapors.[149] As a result, polythiophene OFETs were sensitive to ethanol, while related poly(alkylthiophene) OFETs were not. Small organic molecules also play an important role in alcohol detection, where a pore-rich structure (discussed in Section 3.1) improved the sensitivity of the OFET to methanol gas.[105]

Phosphonates, used commonly in pesticides, also have deleterious nervous system effects. Thus, phosphonate analogs are used to develop sensors for this class of vapors. Besides the thiophene oligomer heterostructure example described earlier in Section 2.1, See et al. developed the n-type material of *N*,*N*′-bis(1H,1H-per-fluorooctyl)naphthalene-1,4,5,8-tetracarboxylic diimide (F15-NTCDI) to enhance the sensitivity of the OFET to DMMP,[150] a simulant for hazardous phosphonate compounds.

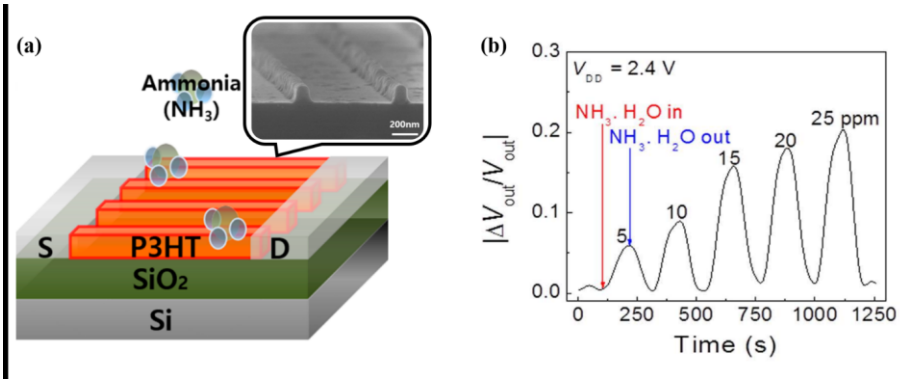


Figure 21. (a) Schematic illustration of a P3HT single-crystal nanowire OFET and its interaction with ammonia, the inset is the SEM perspective image of the P3HT nanowires. Reprinted with permission from Ref. 152. Copyright 2017 ACS publications. (b) The measured relative change of V_{out} over time upon NH_3 exposure of different estimated concentrations from 5 ppm to 25 ppm. Reprinted with permission from Ref. 153. Copyright 2016 Nature Publishing Group.

Ammonia (NH_3), NO_2 and sulfurous gases are typical health-related gases which could be monitored by OFETs. Ammonia possesses potential association with chronic diseases like asthma, severe respiratory inflammations, and lung diseases arising from its presence as an environmental pollutant.[151] Besar et al. recently fabricated a printable OFET using poly (3, 3‴-didodecylquaterthiophene) (PQT-12) as active layer to detect ammonia gas with the concentration of as low as 0.5 ppm.[91] Mun et al. further decreased the detection limit of NH_3 to 0.01 ppm by employing an array of single-crystal poly(3-hexylthiophene) (P3HT) nanowires as shown in Figure 21a.[152] This strategy of increasing the interaction area to enhance the sensitivity was used by

Lyu et al. to demonstrate an OFET with porous dinaphtho [2,3-b:2′,3′-f] thieno [3,2-b] thiophene (DNTT) films, as discussed in the physical modification section, by a simple vacuum freeze-drying template method (as shown in Figure 12b) to achieve a sensitivity of as high as 3.4% upon exposure to 10 ppb NH_3.[61] Figure 12c and d illustrate optical images of the porous DNTT films with polystyrene microspheres and after removing polystyrene microspheres, respectively. On the other hand, decreasing the power consumption is a research concern to make the OFETs compatible with the future targeted portable devices. Operational stability under electrical bias storage and lifetime are also prerequisites for practical use. Feng et al. used bis(triisopropylsilylethynyl)-pentacene (TIPS-pentacene) and polystyrene (PS) blend to fabricate flexible OFETs with a steep subthreshold swing less than 100 mV/decade, and an on/off ratio of 10^6 at a voltage swing of 3 V.[153] The low voltage and stable operation allowed the sensor to be incorporated into a battery-powered electronic system for continuously reliable sensing of ammonia vapor down to 5 ppm (as shown in Figure 21b) in ambient air with very small power consumption of ~50 nW.

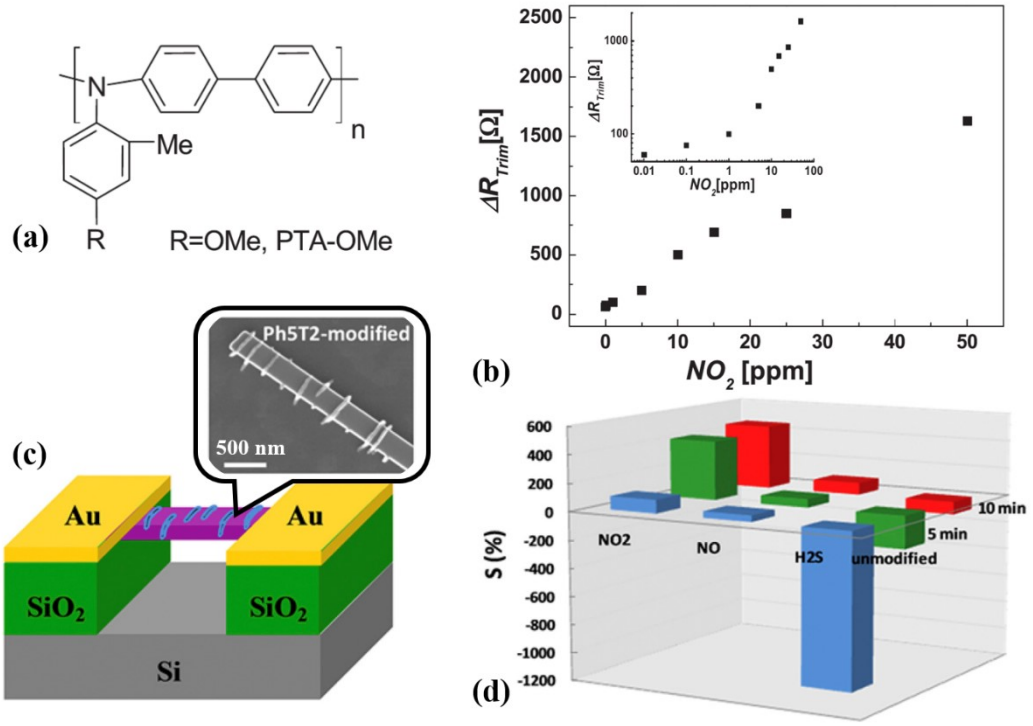


Figure 22. (a) Molecular structures of the PTA-OMe. (b) The required resistance change in the gain trim potentiometer (ΔR_{trim}) response of PTA-OMe based OFETs to NO_2, the inset shows the same data on a log-log scale. Reprinted with permission from Ref. 155. Copyright 2010

Wiley. (c) Schematic diagram of the OFET with Ph5T2 on the CuPc nanowire, the inset presents the typical SEM image of one CuPc nanowire under 10 min Ph5T2 modification by vacuum evaporation deposition process. (d) Effect of Ph5T2 deposition time on the response of 10 ppm NO_2, NO and H_2S. Reprinted with permission from Ref. 156. Copyright 2017 Elsevier.

NO_2 is one of the most common and detrimental air pollutant oxidizing, which is produced and released into atmosphere from combustion and automotive emission. It is linked with a number of adverse effects on the respiratory system such as chronic bronchitis, emphysema, and respiratory irritation at low concentrations.[154] Das et al. detected NO_2 using amorphous semiconducting polymers with methoxy-substituted poly(triarylamine) (PTA-OMe) as shown in Figure 22a.[155] The PTA-OMe based OFET was able to respond to 10 ppb NO_2, as presented in Figure 22b. Ji et al. adopted a highly ordered organic ultra-thin film heterojunction consisting N,N′-diphenyl perylene tetracarboxylic diimide (PTCDI-Ph) and para-hexaphenyl (p-6P) ultra-thin film to achieve impressive room-temperature detection of NO_2.[80] They further introduced a double-heterojunction sensor by depositing vanadyl phthalocyanine (VOPc) on top of the PTCDI-Ph layer, which obtained a 90% relative response to 5 ppm NO_2 during the room-temperature testing process. Song et al. used a dinaphtho[3,4-d:3′,4′-d′]benzo[1,2-b:4,5-b′]dithiophene (Ph5T2)-modified copper phthalocyanine (CuPc) single crystal nanowire with gas dielectric, a configuration related to the one discussed in Figure 5, to selectively detect NO_2, NO, and H_2S down to sub-ppm level as depicted in Figure 22c.[156] This OFET exhibited high response and excellent controllable selectivity at room temperature as shown in Figure 22d. Use of a hybrid semiconductor is another strategy to achieve high sensitivity.[84] Yang investigated the NO_2 sensing properties of the hybrid P3HT and zinc oxide -graphene oxide shell-core nanoparticles.[86] The hybrid semiconductor could obtain a 210% sensing response to 5 ppm NO_2 gas exposure for 5 min at room temperature. Introducing a pre-reaction to enhance the interaction between the sensor and the vapor is also effective. Zang et al. reported that reversible and effective detection of NO_2 could be achieved when assisted by the chemical adsorbed NH_3 in the organic layer, as

was discussed above for detecting HCl. Reversible detection of 10 ppm NO_2 was achieved by using NH_3 (1000 ppm) exposed OFETs, with the sensitivity of 50%.[72]

Sulfurous gases include sulfur dioxide (SO_2) and hydrogen sulfide (H_2S). SO_2 is released during the burning of fossil fuels and plays a major role in the formation of acid rain. However, until now, only a few efforts have been made to develop semiconductor-based SO_2 sensors and almost all of them are resistor-type. The most typical OFET based SO_2 fabricated by Shaymurat et al. also adopted the single crystal and gas dielectric strategy to improve the sensing performance.[51] They employed CuPc nanowire as the active layer, and for the first time, introduced gas as the dielectric to obtain complete recovery and room-temperature detection of SO_2. The detect limitation was down to sub-ppm levels (0.5 ppm) with high sensitivity (119%) and high resolution (100 ppb).

H_2S is a toxic and flammable pollutant gas with a characteristic odor of rotten egg. Industrial activities, such as coke production, petroleum/natural gas drilling and refining, and wastewater treatment, generate a large quantity of H_2S. The optimization of the thickness of the active film is crucial to the H_2S detection. The synthesis of the new material is still the most straightforward way to obtain high sensing performance. Luo et al. developed a new cruciform donor-acceptor p-type molecule, *viz.* 2,2′-((5,5′-(3,7-dicyano-2,6-bis (dihexylamino)benzo[1,2-b:4,5-b′]difuran-4,8-diyl)bis (thiophene-5,2-diyl))bis (methanylylidene)) dimalononitrile (BDFTM), which showed highly sensitive and selective detection of H_2S gas (down to 10 ppb levels) in OFET based sensors as shown in Figure 23.[157]

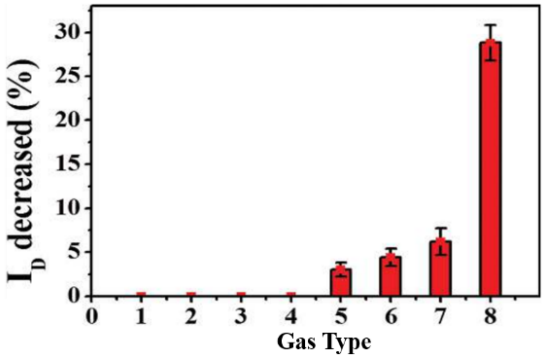


Figure 23. Variation of the drain current after exposed to different gas vapors: 1. H_2 (pure); 2. CO_2 (pure); 3. hexane (52000

ppm); 4. CH_2Cl_2 (301000 ppm); 5. CH_3OH (6500 ppm); 6. acetone (1000 ppm); 7. NH_3 (150 ppb); 8. H_2S (100 ppb). Reprinted with permission from Ref. 157. Copyright 2014 Wiley. Cover (b) in picture

Health-related vapor monitoring can be divided into two time scales. Diagnosis of health disorders by assessing breath components or volatiles over biological tissues only requires sampling over a time of minutes. Many organic active sensing materials are already well suited for such short-time use, though further selectivity improvements would be welcome. On the other hand, monitoring of environmental pollutants may need to be done by a single sensor on days-to-months time scales, for which substantial stability improvements are still needed.

The health-related vapor sensors using organic semiconductors base OFETs are summarized in Table 2.

Table 2. Health-related vapor sensors using organic semiconductors base OFETs. LOD: limit of detection.

Material	Analyte	LOD	Ref
Pentacene	Methanol	-	[103]
6PTTP6 and HO6OPT	DMMP	5 ppm	[65, 78]
F15-NTCDI	DMMP	-	[150]
PQT-12	NH_3	0.5 ppm	[91]
Single-crystal P3HT	NH_3	0.01 ppm	[152]
DNTT	NH_3	10 ppb	[61]
TIPS-pentacene and polystyrene blend	NH_3	5 ppm	[153]
PTA-OMe	NO_2	10 ppb	[155]
PTCDI-Ph and para-hexaphenyl	NO_2	5 ppm	[80]

Single-crystal CuPc	NO_2	sub-ppm	[156]
P3HT and zinc oxide -graphene oxide shell-core nanoparticles	NO_2	5 ppm	[86]
NH_3 treated semiconductor	NO_2	10 ppm	[72]

6. OFET-based large molecular weight biomaterial detection

A biosensor is "a device that uses specific biochemical reactions mediated by isolated enzymes, immuno systems, tissues, organelles or whole cells to detect chemical compounds, usually by electrical, thermal or optical signals" (defined by the International Union of Pure and Applied Chemistry). Since the first study of FET-based biosensor was reported by Janata in 1976,[158] there has been worldwide research focus on using different kinds of FETs as biosensors detecting a wide range of biomolecules, already summarized in some comprehensive reviews.[22, 159-160] Particularly, the research about OFET-based biosensors has been studied for the potential of fast and sensitive clinical diagnostics.[161-168] Also, the structure of an OFET-based biosensor can be adjusted according to the need, which is a significant advantage in this area.[104, 169-179] In this section, we will briefly cover detection of large molecular weight biomacromolecules, such as DNA, peptides and proteins, using OFETs. Different device structures, including bottom gate, electrolyte gate, extended gate and floating gate structure devices are also described.

6.1 OFET-based sensors for DNA detection

So far, different possible mechanisms have been used for realizing an OFET-based DNA sensor.[31, 162-163, 180-188] This kind of device was firstly proposed by Zhang and Subramanian.[188] In this case, DNA molecules are immobilized directly on a thin pentacene layer by physical adsorption, and can produce an unambiguous

doping-induced threshold voltage shift upon hybridization. The device distinguishes both single-stranded DNA and double-stranded DNA, which induce substantially differing threshold voltage shifts due to their different net doping and immobilization efficiencies. A similar method was also reported by Kim et al. by using a top-contact OFET with glass substrate.[183] They realized that negatively charged DNA molecules can attract holes from the channel causing a decrease in the transistor current. The device was further tested for detection of λ-phage genomic DNA using probe hybridization. Based on these works, we can say that the "label-free" detection technique for DNA hybridization is possible through direct measurement of electrical properties of DNA-immobilized OFETs.

However, these detectors all require dry environments. To perform measurements in liquids, different device structures have been realized. Khan et al. reported a real-time, in situ selective detection scheme for short-chain DNA targets by employing organic transistors as the electrical read-out platform.[31] The surfaces of the OFETs were modified with a thin maleic anhydride polymer layer using plasma-enhanced chemical vapor deposition to allow the covalent attachment of the peptide nucleic acid strands, which were then used to selectively detect the target DNA. This is the first demonstration of high sensitivity *in situ* label-free detection of DNA using OFETs. Kergoat et al. reported a DNA sensor based on a water-gated organic field-effect transistor in which the dielectric is constituted by a simple droplet of aqueous PBS or even pure water.[182] The advantage of this device is that the solution gate can effectively overcome the Debye screening length. Also, a very high electric field is generated at the electrolyte/channel interface due to the formation of an electric double layer, so that the device can be operated below 1 V.

OSCs are generally sensitive to oxygen and humidity. To solve this problem, Demelas et al. realized a novel DNA sensor which can detect the DNA hybridization in liquids using a floating gate structure.[180] Compared to other examples of OFET-based DNA sensors, this device has two noticeable features: the probe area is completely separated

from the transistor area and the sensing mechanism is not reliant on the choice of the device materials. Moreover, the device architecture has been designed to avoid any damaging treatment that may reduce the stability of the organic semiconductor. Then, Lai et al. reported an ultra-low-voltage OFET-based sensor for DNA detection; the structure is shown in Figure 24.[184] The detection mechanism is based on the shift of the threshold voltage of the OFET, as in the previously presented examples, but the sensing layer is distinct from the OSC; as a consequence, the sensing mechanism of the device is not reliant on the properties of the organic semiconductor.

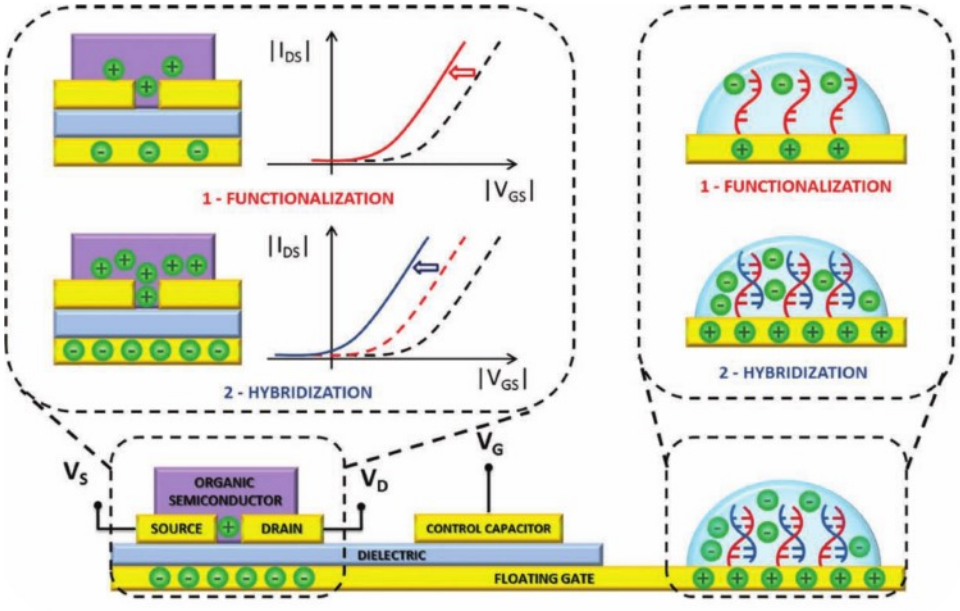


Figure 24. Structure and detection mechanism of the organic charge-modulated field effect transistor. Reprinted with permission from Ref. 184. Copyright 2013 Wiley.

6.2 OFET-based sensors for protein and peptide detection

OFET based sensors have been used in detecting a wide range of proteins.[25, 27, 165-167, 172, 189-193] Hammock et al. presented an OFET based biosensor with gold nanoparticle binding sites for thrombin protein detection.[25] The effect of different parameters, like the spacing between receptors, pH of the buffer, and ionic strength of the buffer, were thoroughly studied. They demonstrate a detection limit of 100 pM for this protein with high selectivity over other proteases in situ. Magliulo et al. described a label-free C-reactive protein (CRP) OFET-based sensor.[172] The device is fabricated by physical adsorption of the anti-CRP monoclonal antibody onto a poly-3-hexyl thiophene

(P3HT) organic semiconductor surface. The linear range of this device is from 4 pM to 2 μM with a detection limit of 2 pM. The device also shows very good selectivity, which is compatible with the development of label-free electronic arrays where multiple target analytes can be measured simultaneously in clinical relevant fluids such as serum, saliva, or tear fluid. Huang et al fabricated a sensitive, large-area OFET based sensor for real time quantification of glial fibrillary acidic protein in solution;[189] the scheme is shown in Figure 25. They used pentacene and naphthalenetetracarboxylic diimide OSCs as semiconductors, which were combined with a receptor–antibody-functionalized top dielectric layer. This structure can provide maximum capacitive coupling and minimal interference from the aqueous analyte solution, and allowed convenient solvent processing of the antibody coupling layer. Furthermore, they have described a new antibody immobilization method, which can yield high surface coverage. This was an early demonstration of the expected opposite current responses by p- and n-channel semiconductors to the same protein.

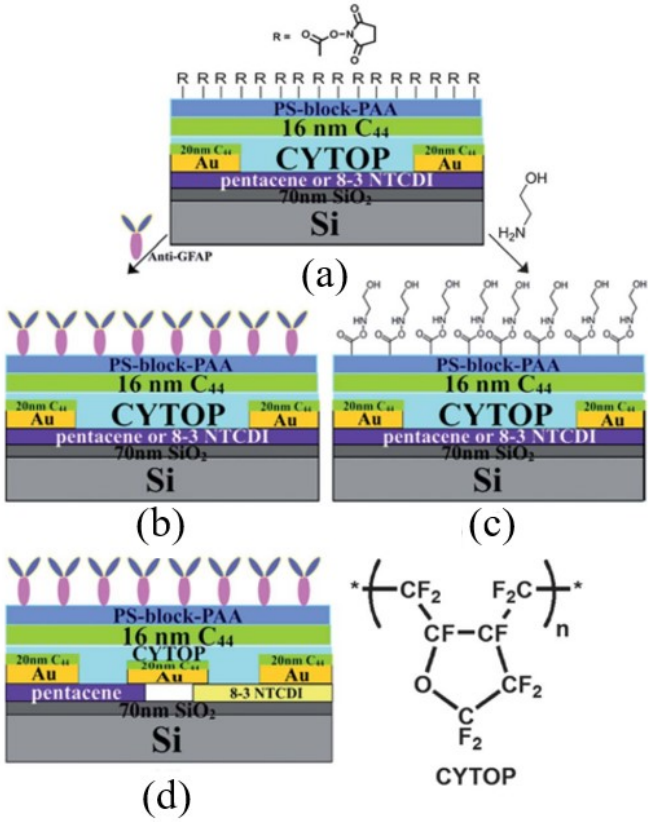


Figure 25. Device architecture of GFAP sensor: (a) activated carboxylate surface (b) anti-GFAP modified device; (c) hydroxyethylamide control device; (d) anti-GFAP modified

inverter based on pentacene and 8-3 NTCDI. The CYTOP structure is also shown at the bottom right. Reprinted with permission from Ref. 189. Copyright 2014 RSC Publishing.

In order to achieve a more stable protein sensor, Minamiki et al demonstrated a OFET based biosensor with an extended gate for immunoglobulin G (IgG) detection.[191] The anti-IgG was modified on the extended gate which can move the sensing area away from the organic semiconductor layer and provide a dry environment for OFET devices. The titration results from the target IgG in the presence of a bovine serum albumin interfere, clearly exhibiting a negative shift in the OFET transfer curve with increasing IgG concentration which is due to the specific interaction between target IgG and the immobilized anti-IgG antibody. Then, they reported a high sensitive histidine-rich protein detector without any labeling by use an OFET based sensor.[166] They choose Ni^{II}-nitrilotriacetic acid complex as the protein receptor and modified it on the extended gate electrode to detect the target analyte in solution. The device exhibited a sensitively responded to the histidine-rich protein (LOD=6×10^{-13} M). These results demonstrate that the combination of the OFET with the artificial receptor is an ideal approach for label-free and immune-free protein detection.

The Debye screening length, beyond which voltage changes are not sensed in a solution, is a great challenge for FET based biosensors. Palazzo et al. successfully overcame more than 20 nm Debye length by using an electrolyte-gated OFET based biosensor.[193] Song et al also reported an extended solution gate structure where the sensing area and the organic semiconductor are separated, and a reference electrode is not needed.[167] Different molecular weight polyethylene glycols are mixed into the bio-receptor layer to help extend the Debye screening length. They also found that the sensitivity increased after V_G was decreased because the lower V_G is much closer to V_T and the influence of attached negatively charged proteins becomes more apparent.

Cytokines are peptides that play fundamental roles in inflammatory processes in the human body. In particular, interleukin (IL)-6 is a multifunctional cytokine, which is

closely associated with infection, cancer and inflammation. The detection of IL-6 concentration is very important in early stages of inflammation and in chronic diseases. Diacci et al. reported two solution gate OFET based biosensors for IL-6 detection, featuring monoclonal antibodies and peptide aptamers adsorbed at the gate.[165] The current I_{DS} changed upon exposure of the gate electrode to different concentration IL-6. The sensor can work on a wide range of IL-6 concentrations and exhibit a detection limit of 1 pM. All the references are summarized and listed in Table 3.

It is clear that great progress has been made using OFET architectures for detection of biomacromolecules. There has also been recent attention paid to a fundamental limitation of OFET sensitivity, namely the Debye screening of electronic signals from biomacromolecule binding.

Table 3 Summary of OFET based protein and peptide sensors (from 2011 to 2017)

Authors	**Years**	**Analyte**	**Detection limit**	**Device structure**	**Ref.**
Khan et al.	2011	BSA/anti-BSA	500 nM	Bottom gate	[190]
Hammock et al.	2013	Thrombin protein	100 pM	Bottom gate	[25]
Magliulo et al.	2013	Streptavidin BSA	10 nM	Electrolyte gate	[27]
Huang et al.	2014	GFAP	20 pM	Bottom gate	[189]
Minamiki et al.	2014	IgG	4 nM	Extended gate	[191]
Minamiki et al.	2015	IgA	2.1 μg/mL	Extended gate	[192]
Palazzo et al.	2015	C-reactive protein	Overcome 20 nm Debye's Length	Electrolyte gate	[193]
Magliulo et al.	2016	C-reactive	2 pM	Electrolyte	[172]

		protein		gate	
Minamiki et al.	2017	Histidine-Rich Protein	40 pg/mL	Extended gate	[166]
Diacci et al.	2017	Interleukin-6	1 pM	Electrolyte gate	[165]
Song et al.	2017	GFAP	1 ng/mL	Extended electrolyte gate	[167]

It is not yet established whether this limitation will inevitably restrict the use of OFETs for macromolecules known to be at high concentration (>1 nM) in biological fluids of interest, or whether further material and device improvements will allow picomolar detection, and thus a wider range of medically relevant assays.

6.3 Different configurations of the OFET based biosensors

Various configurational improvements over the simple OFET structure described at the start of this review have been proposed for OFET-based biosensors. Magliulo et al. have introduced some of them.[27] One common architecture is the "bottom gate" sensor which puts the solution sensing area over the OSC and can exhibit relatively high sensitivities; the typical scheme is shown in Figure 26.

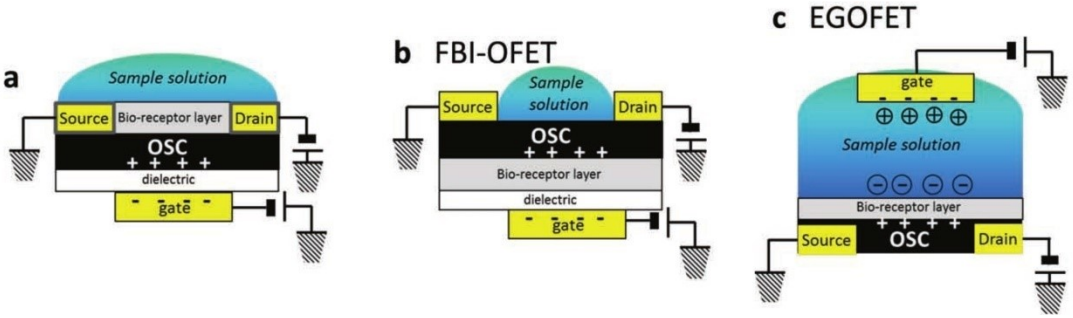


Figure 26. Schemes of the architectures of OFET biosensors proposed to date: (a) bi-layer OFET; (b) functional biological interlayer (FBI) OFET; (c) electrolyte-gated OFET (EGOFET). Reprinted with permission from Ref. 27. Copyright 2013 Wiley.

ultrathin bio-receptor layer was designed so the analyte will indirectly modulate charge carrier density in OSCs.[25, 189-190] In some architectures, the bio-receptor layer is placed between the semiconductor layer and the gate dielectric for low molecular weight analyte detection.[194]

The electrolyte gate configuration is a new approach for large molecular weight biomaterial detection. The proper functionalization of semiconductor layer or receptor layer can lead to stable and reliable label-free electronic sensing toward certain analytes.[27, 165, 172, 193] For large biomolecule detection, PBS is a good choice for gating medium because of its good biocompatibility. This architecture was also applied in electro-chemical OFET sensors, which was limited to the detection of electrochemically active species, like glucose and certain amino acids.[195-196] The gating media for these latter devices were ionic liquids, which can provide good electron transfer environments.

The extended gate structure, which moved the sensing area away from the organic semiconductor layer, can provide a dry environment for the OFET devices that make up parts of the sensors. The receptor layer is a modification on the extended gate, and the gating media can also be PBS for large biomolecule detection. Particularly, researchers from Bonfiglio's group described the floating gate device, the architecture of which is was shown in Figure 25. This device has two noticeable features: the probe area is completely separated from the transistor area and the sensing mechanism is not reliant on the choice of the device materials. Moreover, the device architecture has been designed to avoid any damaging treatment that may reduce the stability of the organic semiconductor.

7. Small biomolecule detection

Small molecules such as neurotransmitters, amino acids, vitamins, and organic compounds (< 900 daltons or 1 nm) found in body fluids are important biomarkers to potentially monitor an individual’s state of health. Non-invasive wearable sensor

platforms for those small molecules have been achieved utilizing key features of organic materials such as flexibility, transparency, and molecular diversity while OFET electronics can be embedded into clothing or other everyday items. Early research demonstrates that intrinsic OSCs possess sensitivity for small molecules or ions in sub-millimolar levels.[197] Non-covalent interactions exist between the grain boundaries in OSCs and small molecules diffused into the grain boundaries. Since then, selectivity/sensitivity for targeting molecules has been reinforced by employing receptors or enzymes.[198]

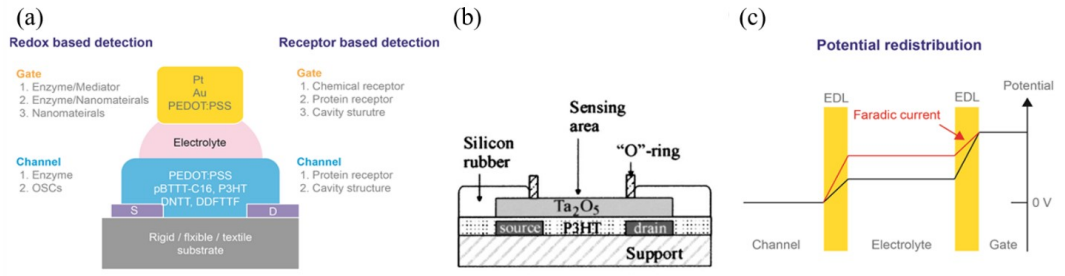


Figure 27. (a) A brief schematic diagram of general device structure, materials, and strategies for small molecules detections. (b) Schematic representation of the device structure employing pH sensitive membrane to detect gluconic acid produced from glucose catalyzed by GOx. Reprinted with permission from Ref. 202. Copyright 2003 AIP Publishing. (c) Schematic illustration of the potential redistribution (red line) in the interfaces by Faradic current which contributes to drain current change. Reprinted with permission from Ref. 204. Copyright 2013 RSC Publishing

In this section, we categorize recent research progress in OFET-based small molecule liquid-phase sensors by two detection mechanisms: 1) redox-, and 2) receptor-based detection (Figure 27a). The organic electrochemical transistor (OECT) structure is driving progress in small molecule solution sensors. Electrolyte is used as an insulator between the channel and the gate electrode as depicted in Figure 27a. Any electrical and chemical changes in the interfaces between gate/electrolyte and electrolyte/channel are measured as electrical signal for the targeted analyte. In this type of device, PEDOT:PSS has been widely used because of its water stability in a doped state and a unique sensing reaction.[199] PEDOT becomes positively charged as it is doped by

poly(styrenesulfonic acid) with "PSS" serving as the counterions, imposing sensitivity for cations when they act as counterions to sulfonate groups as doped PEDOT becomes re-reduced, and conductivity decreases.

7.1 Enzymatic redox-based detection

Enzymatic sensors have had a major role in recent research progress, falling into a category of redox-based detection (Table 1). Oxidase enzymes functionalized on either channel[200] or gate electrode[201] catalyze reactions generating products such as hydrogen peroxide (H_2O_2) and changing pH value. A sensing layer then responds to these chemical changes. Some glucose sensors, for example, have employed a pH sensitive layer in the device to detect gluconic acid, produced from glucose catalyzed by glucose oxidase (GOx) (Figure 27b).[202] Similarly, an ammonia sensor quantified urea from a pH change caused by OH^- produced from urea catalyzed by urease (UOx).[164] DNTT used for the channel has been one of the pH sensitive OSCs.[203]

A more common approach in enzymatic sensors is to measure H_2O_2 levels generated by detection chemistry. H_2O_2 is oxidized at the gate electrode, consequently transferring electrons to the gate electrode.[204] This Faradic current leads to the redistribution of potential at both gate/electrolyte and electrolyte/channel interfaces, leading to a change in drain current (I_D) (Figure 27c). Naturally, the enzymatic layer has been often immobilized on the gate electrode where the oxidation of H_2O_2 directly takes place.

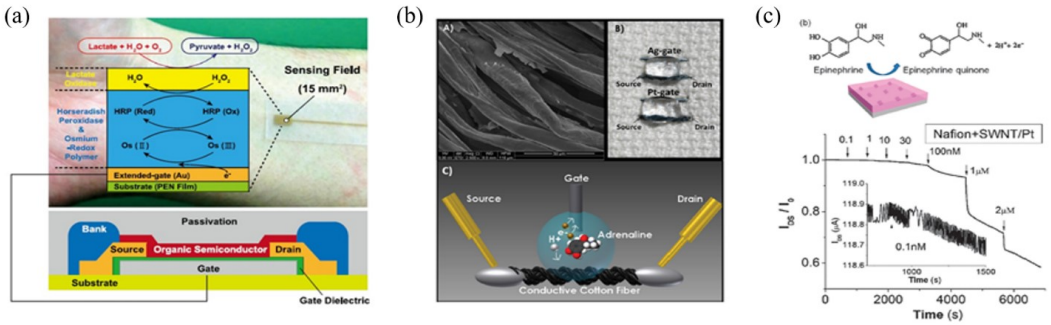


Figure 28. Redox-based detection. (a) Schematic illustration of device operating mechanism based on the extended-gate OFET with HRP osmium-redox polymer on the top of extended

Au gate electrode as a mediator. Reprinted with permission from Ref. 206. Copyright 2015 Elsevier. (b) SEM image of the cotton wire functionalized with PEDOT:PSS on the left above and a picture of the cotton-OECT integrated on clothing with Pt gate on the right above. Schematic illustration of sensing process for AD. Reprinted with permission from Ref. 210. Copyright 2014 RSC Publishing. (c) The normalized current responses of OECTs with Nafion and SWNT films modified on Pt gate to the increasing epinephrine concentration in PBS solution. Reprinted with permission from Ref. 215. Copyright 2015 RSC Publishing.

To obtain a higher sensitivity, an electrochemical mediator has been often mixed with an enzymatic layer on the gate, which shuttles electrons to the gate electrode and prevents the loss of electrons from electroactive compounds in the media. Braendlein et al. investigated the detection of lactate directly secreted by cancer cells using lactate oxidase (LOx) and mediator, chitosan-ferrocene, immobilized at the gate.[205] 1 mM lactate was recorded from tumor cells with the detection of limit (LOD) of 10 μM in pure PBS. Another type of mediator, horseradish peroxidase (HRP) osmium-redox polymer coated onto the extended Au gate electrode, achieved a low LOD of 66 nM for lactate (Figure 28a).[206] The mediator has increased sensitivity for targeting analyte though it may degrade the applicability of the electrode design. Battista et al. reported a wearable tyrosine sensor on a single cotton yarn without using any mediator.[207] Fungal laccase, employed as the enzyme, has a higher oxidizing capability of phenolic compounds in tyrosine than the conventional enzyme used, tyrosinases. Therefore, 10 nM LOD for tyrosine was gained with no mediator.

In other mediator-less enzymatic sensors, nanomaterials and nanostructures such as graphene, graphene oxide, nanoparticles (NPs), and nanotubes (NTs) have been exploited to improve electrocatalytic activity of the gate electrode[21, 25-26] (Table 2). A larger surface to volume ratio from nanoscale morphology and the higher conductivity of nanomaterials have increased the number of electrons transfers to the gate electrode. In this tactic, biocompatible polymers such as chitosan and Nafion have been often

used as a support for enzyme immobilization. Glucose and urea in sub-millimolar levels have been detected in saliva sample using the modified gate.[208]

Utilizing enzymes for the sensors has conferred enhanced specificity and selectivity for targeting molecules. Several drawbacks, however, exist such as the limited categories of enzymes usable, resultant limited targeting analyte, degradation of enzyme/mediator, and unsatisfactory sensitivity in physiological conditions.

7.2 Electrochemical detection of small molecules by device materials

Enzyme/mediator-free sensor platforms are available for electroactive small molecules such as dopamine (DA),[209] ascorbic acid (AA),[199] adrenaline (AD),[210] and tyrosine,[211] all of which are easily oxidized on the gate electrode (Table 3). In a basic operation mechanism, the electro-oxidation of small molecules at the gate releases H^+ ions into a medium that then move toward a PEDOT:PSS surface. De-doping of PEDOT:PSS by H^+ injection decreases drain current in turn. This implies that the material of a gate electrode has a significant influence on the response of the sensor. Pt has been considered as the standard gate electrode material to show satisfactory dynamic range of analyte observed under physiological conditions.[209-210] Coppede et al. have investigated a stress OECT sensor to monitor AD level on cotton-fiber functionalized with PEDOT:PSS and Pt gate (Figure 28b).[210] The dynamic range of this sensor is from 10 μM to 1 mM in NaCl solution. 1 mM AD was monitored in a human sweat sample.

Recently, the Pt electrode has been replaced by PEDOT:PSS in a device termed an all-PEDOT:PSS sensor, since it makes a device fabrication easier while maintaining sensitivity and selectivity shown with the Pt electrode.[199, 212-214] Gualandi et al. reported an all-PEDOT:PSS sensor on textile for multiple small molecules such as AA, DA, AD in sweat. LOD of 0.5 mM, 10 μM, and 10 μM were shown for AA, DA, and AD in artificial sweat samples, respectively.[213]

By a similar rationale mentioned in the previous section, the modification of the gate with nanomaterials has increased sensitivity of electroactive molecules.[211, 215-217] Mak et al. lowered LOD of AD down to 100 pM using a Pt gate electrode modified by Nafion and carbon-based nanomaterials, including single walled carbon nanotubes (SWNTs), graphene, and graphene oxide (Figure 28c).[215] Carbon-based nanomaterials have promoted electron transfer reactions and enhanced the electrocatalytic activity of the gate electrode. Furthermore, Nafion that was employed in the gate has enhanced the selectivity of DA against the other electro-active substances, like AA and UA, because of the negatively charge of Nafion in a PBS solution that could effectively impede the diffusion of the anions through it by electrostatic interactions.

Detection of many electroactive small molecules has been broadly reported based on a similar operating mechanism. A main challenge is multiplexed detections for those molecules in body fluids that there are many factors to interfere the signals because electroactive molecules have been simply discriminated by differences in redox potentials, many of which are similar.

7.3 Receptor-based detection

There are several types of receptors depending on the detection mechanism: chemical reaction or physical absorption. Picomolar sensitivity to DA was achieved by an OECT sensor using a chemical receptor, 4-formylphenyl boronic acid, functionalized on the gate electrode. 4-formylphenyl boronic acid, the formyl group on which serves as a covalent anchor to the gate electrode surface, enables covalent binding of DA.[218] A phenylboronic acid receptor showed sensitivity/selectivity between boronic acid and saccharides including glucose, galactose, fructose, and mannose. Higher sensitivity was shown for glucose (5 mM).[219] Guo et al. reported 8 μM LOD for sialic acid with a phenylboronic acid receptor.[220]

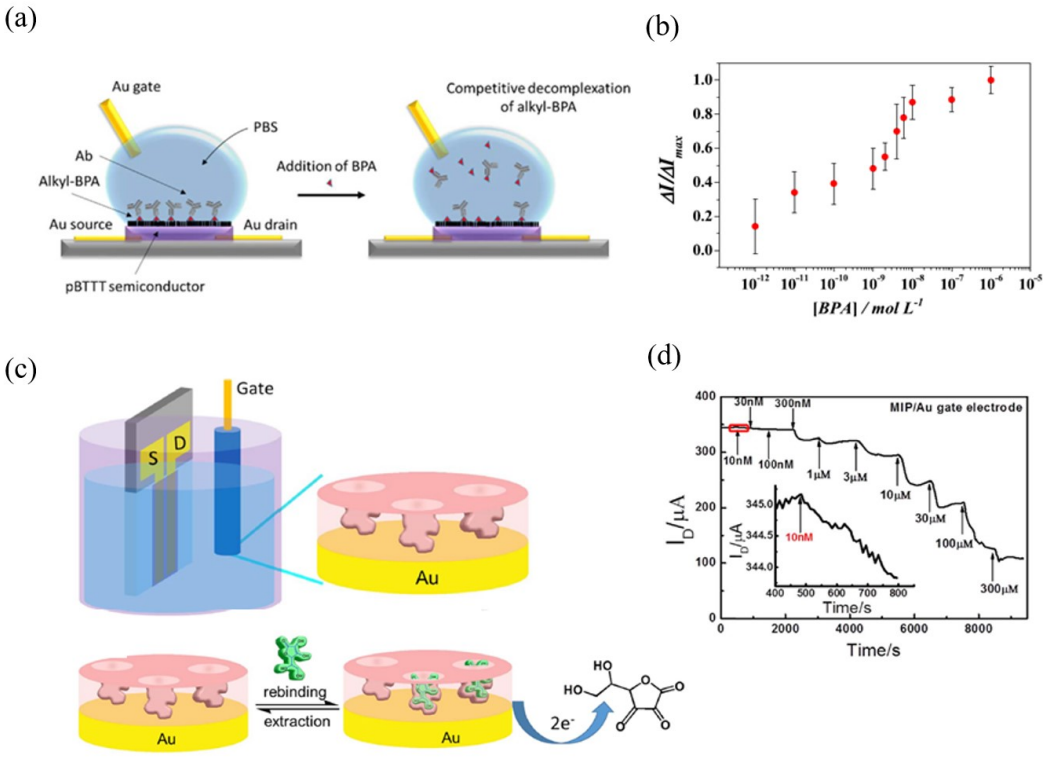


Figure 29. Receptor-based detection. (a) Schematic image of detection mechanism by the competitive chemical reaction at the semiconductor/electrolyte interface. (b) $\Delta I/\Delta I_{max}$ as a function of BPA concentration, for V_D: - 0.45 V and V_G: - 0.6 V. Reprinted with permission from Ref. 221. Copyright 2017 Elsevier. (c) Schematic of an OECT-based AA sensor modified with the MIP film. AA captured by the MIP film surface is oxidized on the gate electrode. (d) Typical I_D vs. time curves for AA detection using MIP film. Reprinted with permission from Ref. 223. Copyright 2018 Elsevier.

Piro et al proposed a different strategy to detect small molecules such as bisphenol A.[221] The basic idea was to use a competitive chemical reaction between analyte (bisphenol A) and a target mime immobilized on the sensing surface (Figure 29a and 29b). The target mime here consisted of antibody (charged molecule), hapten anchoring antibody, and alkyl-BPA-holding hapten. Competitive exchange occurred between diffused analyte (bisphenol A) and hapten. The electrical signal was changed with a detachment of antibody from the surface that contributed to a change in the gate capacitance. This approach resembles the label-based immunoassay. Recently, Mulla et al. has employed odorant binding protein immobilized on the gate of OECT as a receptor for neutral

carvone enantiomers.[169] The sensing mechanism is based on the subtle change in the gate capacitance as binding of carvone enantiomer to odorant binding proteins occurs. Park et al. has demonstrated nanovesicle dopamine receptors constructed from HEK-293 cells. Structure of nanovesicles immobilized on PEDOT nanotubes provided the enlarged active sites for DA binding. Signal induced by the binding events activated Ca^{2+} channels in the nanovesicle that are analogous to cell membranes.[222]

Recently, Zhang et al. reported a molecularly imprinted polymer (MIP) for AA detection on the gate of OECT.[223] The MIP created cavities that selectively exhibited affinity for AA in a polymer matrix (Figure 29c and 29d). AA captured by the cavities was oxidized on the gate electrode, producing Faradic current. From this strategy, selectivity for AA could be reinforced because of the specific size of cavities corresponding to the physical size of AA. LOD remained at a similar level to the other work (10 nM).

Another synthetic receptor for acetylcholine, cucurbit[6]uril derivative, was reported by Jang et al.[224] The synthetic receptor immobilized on the channel provides two critical features: 1) a small size of cavity (5.5 Å diameter) which can encapsulate small organic molecules and 2) selectivity for acetylcholine, in keeping with its capability to form complexes with cationic functional groups appended to hydrocarbon or otherwise nonpolar segments. This receptor showed low LOD down to 1 pM in OFET-based sensors thanks to advantages of the receptor to enhance both physical absorption and chemical reaction.

Table 4. Recent research progress (from 2013 to 2018) based on the enzymatic detection of small molecules. Enzyme is immobilized on either gate or channel in OFETs. COx: cholesterol oxidase.

Device structure (Gate/semiconductor)	Analyte (Enzyme)	Mediator	LOD	Ref
Pt+Ir/DNTT	Ammonia (UOx)	N.A.	750 μM	[164]
Pt/PEDOT:PSS	Glucose (GOx)	N.A.	950 nM	[200]
All PEDOT:PSS	Lactate (LOx)	Chitosan-ferrocene	10 μM 1 mM (from tumor cell)	[205]
All PEDOT:PSS	Lactate (LOx) Cholesterol (COx) Glucose (GOx)	Chitosan-ferrocene	50 μM 10 μM 10 μM	[201]
Extended Au /pBTTT-C_{16}	Lactate (LOx)	HRP/Osmium-redox polymer	66 nM	[206]
Extended Au /pBTTT-C_{16}	Histamine (Diamine oxidase)	HRP/Osmium-redox polymer	1.2 μM	[225]
Pt/PEDOT:PSS on cotton	Tyrosine (Laccse)	N.A.	10 nM	[217]

Table 5. Recent research progress (from 2013 to 2018) based on enzymatic detection of small molecule using the gate electrode decorated by nanomaterials. PBS: phosphate buffered saline, PANI: polyaniline.

Device materials (Gate/semiconductor)	Analyte (Enzyme)	Gate materials	LOD	Media	Ref
Ti/PEDOT:PSS	Glucose (GOx)	Nafion/PtNPs/TiO_2 NTs	100 nM	PBS	[226]
Pt+Ti/PEDOT:PSS	Glucose (GOx)	Graphene	10 nM	PBS	[204]
Pt/PEDOT:PSS	Cholesterol (COx) Glucose (GOx) Urea (UOx)	PANI/Nafion/graphene	100 nM 103 μM 173 μM	PBS Saliva Saliva	[208]

Table 6. Progress (from 2013 to 2018) for electroactive small molecule detection by OECTs. PDDA: poly(diallyldimethylammonium chloride), MWCNT: multiwall carbon nanotubes.

Device materials (Gate/semiconductor)	Analyte	Sensing part	LOD	Media	Ref
Pt/PEDOT:PSS on textile	Adrenaline	Pt gate	10 μM	NaCl	[210]
Pt/PEDOT:PSS	Eumelanin	Pt gate	10 μM	PBS	[227]
All PEDOT:PSS	Ascorbic acid	Channel and gate	10 nM	PBS	[212]
All PEDOT:PSS	Ascorbic acid	Channel and gate	13 nM	PBS	[199]
All PEDOT:PSS	Dopamine	Channel and gate	6 μM	PBS	[214]
All PEDOT:PSS on textile	Ascorbic acid Dopamine Adrenaline	Channel and gate	0.5 mM 10 μM 10 μM	Sweat	[213]

Au/PEDOT:PSS	Tyrosine	PDDA/MWCNT/AuNPs /Au gate	10 nM	PBS	[211]
Au/PEDOT:PSS	Gallic acid	PDDA/MWCNT/Au gate	10 nM	PBS	[216]
Pt/PEDOT:PSS	Adrenaline	Nafion/SWNT/Pt gate	100 pM	PBS	[215]
Pt/PEDOT PSS	Dopamine	Graphene/Pt gate	5 nM	PBS	[217]

Table 7. Progress (from 2013 to 2018) in small molecule sensing by various receptors functionalized on either gate or channel. GC: glass carbon, RE: reference electrode

Device materials (Gate/semiconductor)	Analytes	Receptor (sensing mechanism)	LOD	Media	Ref
Pt/DNTT	Ammonia	DNTT (pH detection)	1 mM	PBS	[203]
Au/P3HT	Dopamine	4-formylphenyl boronic acid on gate (esterification)	1 pM	PBS	[218]
Extended Au /pBTTT	Glucose	Phenylboronic acid on extended gate (esterification)	5 mM	PBS	[219]
GC/PEDOT:PSS	Sialic acid	Poly (3-aminophenylboronic acid) on gate (esterification)	8 μM	PBS	[220]
Au/pBTTT	Bisphenol A	Alky-bisphenol A/ haptens (capacitance change)	1 pg/ml	PBS	[221]
Au/ PBTTT-C_{14}	Carvone enantiomers	Odorant binding proteins on gate (capacitance change)	10 pM	Water	[169]
RE /PEDOT NT	Dopamine	Dopamine receptor nanovesicles on channel (Ca^{2+} pump)	10 pM	Serum	[222]
Au/ PEDOT:PSS	Ascorbic acid	Molecularly imprinted polymer on Au gate (physical absorption/chemical reaction)	10 nM	PBS	[223]
Bottom gate /DDFTTF	Acetylcholine	Cucurbituril on channel (physical absorption)	1 pM	PBS	[224]

8. Conclusions and future outlook

The remarkable progress in developing high performance OFETs based on molecular design and process engineering has created a platform for low-cost, light and flexible chemical sensors. High sensitivity and selectivity have been achieved and some of the achievements can be applied to more complex circuits for gas detection or compound identification based on multiplexed devices and comparisons with training samples.

The choice of using OSCs in general as active materials in devices instead of many other possible classes of materials, such as inorganic semiconductors, carbon nanomaterials, organometallic framework solids, and metal nanoparticles, depends on the degree to which the analyte binding and charge transport mechanisms associated with polymers and molecular solids enhance the electronic responses. For example, functional groups and even structural subunits of OSCs can serve as a more diverse set of binding sites for analytes than can the interiors or native surfaces of most inorganic or carbon nanomaterial solids. Grain boundaries within polycrystalline OSCs, while limiting mobility for switching applications, are sites at which chemical binding can modulate current more strongly than in more continuous materials. The ability to introduce porosity while maintaining charge transport capability is more generally available in OSCs than in other classes of materials. For example, while porosity is generally intrinsic to framework solids, charge transport needs to be carefully imparted by employing conjugated linker segments with electron donating or accepting capability, designing bonds between linkers and nodes to promote conjugation across nodes, allowing linkers to approach each other closely enough to allow hopping, or including conductive guest material so that charge transport is not interrupted. Doping, as is frequently done with conjugated polymers, is also effective for framework materials to increase conductivity. Considerable progress toward increasing conductivity and mobility of framework solids has been reported in the last five years, including the first demonstrations of chemical sensing capability.[228-234]

Inorganic films and nanowires[235-241] and carbon materials (the latter also discussed in Section 1.2) are readily surface-functionalized with receptors for analytes, so as long as the receptor-analyte interaction occurs with sufficient electronic coupling to the charge transport pathway, useful sensing can be accomplished. The surface-functionalization approach is often more compatible with aqueous and biological analyte solutions when used with carbon and inorganic materials compared to OSCs.

OSCs are more likely to be printable or deposited at low enough temperatures to allow the use of dielectrics and contact materials with melting and softening temperatures within 100-200 °C of ambient. OSCs are among the most mechanically flexible of semiconductor alternatives, though admittedly there are thin film forms of inorganic and carbon materials that are also considerably flexible. Finally, because of their relative convenience in handling and fabrication, OSCs can be useful platforms for prototyping FET sensing architectures even if a different material would be used in the ultimate application.

Multiple challenges remain for the application of OFETs in chemical sensors. Regarding materials, 1) Molecular design of π-conjugated semiconductors with simultaneous high mobility and high sensitivity remains difficult; 2) Material stability and response reproducibility, speed, and reversibility still lag behind their inorganic counterparts, especially for some solution-processed polymers. Materials with high sensitivity, high stability, and good reproducibility are especially required by liquid-phase sensors, biosensors and sensors used in extreme environments. On the other hand, device physics, including morphology of active layers, device configurations, and properties of dielectric layers and electrode materials, need to be taken into account for performance improvement. The introduction of porous structures or additives to device materials (receptors and/or nanomaterials) offer the potential to improve the performance of vapor sensors and biosensors, but we still do not have a complete understanding of the mechanism of charge transport through

semiconductor layers and the detailed interaction after the analytes contact with it. Also, there is still space and opportunity to modify and optimize the device structures to meet the demand for commercial applications. The use of environmentally friendly biomaterials as dielectric layers or functional layers promotes device biocompatibility, for monitoring of the health-related issues, though the use of such biomaterials is in its infancy and their purely electronic performance is generally inferior to that of synthesized polymers.

Many small molecules have been detected by OECT structures and PEDOT:PSS. It is sometimes helpful, but not required, to use enzymes/mediators in detecting many electroactive small molecules that are discriminated by differences in redox potential at the gate electrode, but selectivity of those sensors needs to be enhanced for practical and clinical applications. Meanwhile, there are many attempts to increase sensitivity and selectivity for small molecules employing many types of receptors and nanomaterials, with stability greater than that of enzymes, embedded in OECT sensors.

OFET based biosensors bring great opportunity for sensing biomacromolecules because of advantages including being label free, sensitive, low-cost and selective. Flexible device structures which can be adjusted using simple printing codes also show good promise for further application and commercial development. The OFET device architecture is particularly well suited for logic and amplification circuitry, and OSCs contribute functionality of their own to increase analyte recognition capabilities.

We hope this review will give some inspiration for better understanding of the requirements for new materials, not only including π-conjugated semiconductors as sensing layer but also focusing on non-conjugated biomaterials or receptors as additives that contribute to the physical processes of electronic sensing.

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Biographies

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Wei Shi received her B.A. degree from Veterinary Medicine, Huazhong Agricultural University in 2011. She received her second B.A. degree from the School of Optical and Electronic Information, Huazhong University of Science and Technology in 2010. She received her Ph.D degree from the School of Optoelectronic Information of Electronic Science and Technology of China (UESTC) in 2017. She joined Howard E Katz' group and worked as a visiting scholar at the Department of Materials Science and Engineering, Johns Hopkins University from 2015-2017. Her main research interests are biomaterial integrated OFETs, the development of the application of biomaterials in the OFETs, OFETs based chemical sensor applications, and the biomaterials compatible fabrication process of spray coating. Her most recent

publications focused on the selective sensing to NO_2 based on the guanine-integrated OFET sensor, and fabrication of performance enhanced OFET by introducing guanine or DNA modification layer. Her research goal is to realize the bio-compatible organic electronic devices which could serve well in human health monitoring and therapy fields.

Jian Song received his BS degree in Electronic Information Science and Technology at Jilin University, China in 2011 and received his PhD degree in Microelectronics and Solid State Electronics in 2016 from the same university. Then he joined the research group of Prof. Howard E Katz in the department of materials science and engineering as a postdoctoral fellow at the Johns Hopkins University. His research is mainly focus on the structure development of OFET-based biosensors and the detection of brain injury biomarkers like GFAP and MBP. So far, he has more than 20 scientific publications in high-impact-factor journals.

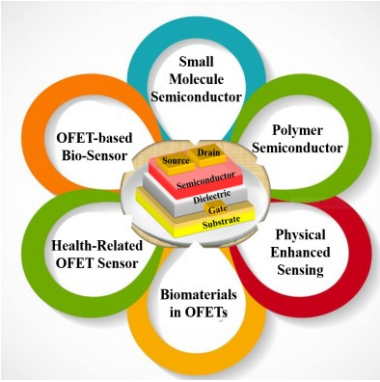
Hyun-June Jang received the B.E. and M.E. degrees in electronic materials engineering from Kwangwoon University, Seoul, Korea, in 2011 and in 2013, respectively. He worked as a research scientist at Korea Institute of Science and Technology in 2014 and Korea Research Institute of Bioscience & Biotechnology in 2015. Since 2015, he has been carrying out graduate research in Materials Science and Engineering at the Johns Hopkins University. He is studying diverse types of inorganic- and organic-based electronics for biosensors and thermoelectric applications. He authored/coauthored about 21 SCI papers (h-index: 12 in Google scholar).

Jennifer Dailey is an NSF graduate research program fellow at Johns Hopkins University in the department of materials science and engineering. She has a BA in Physics from the University of Pennsylvania and a Master's degree in Materials Science from Johns Hopkins University. Her research interests include nanoelectronic

devices, synthesis of biofunctional dielectric films, sensing and tracking the spread of antimicrobial resistance, and materials science education at the undergraduate level. She has numerous publications on the topic of carbon nanotube-based field effect transistor biosensors, including for prostate specific antigen and Lyme disease. More recently, she is focused on flexible substrate vapor sensors and chemically embedded amplification schemes for creation of point-of-care protein sensors in health care or agricultural settings. She is serving as an American Physical Society Congressional Fellow for the 2018-2019 academic year.

Junsheng Yu received his Ph.D. degree from the Graduate School of Bio-Applications & System Engineering at Tokyo University of Agriculture and Technology in 2001. He has studied as a Post-doc at Osaka University from 2001 to 2003, and at Georgia Institute of Technology from 2003 to 2005. He is presently a Professor at the State Key Laboratory of Electronic Thin Film & Integrated Devices at UESTC majoring in organic photoelectronic and electronic materials and devices, mainly includes the OLED, OFET, and OPV devices and their applications.

Howard Katz is Professor and Immediate Past Chair of Materials Science and Engineering at Johns Hopkins University. His research interests are organic, hybrid, and interfacial electronics, applied to chemical and biomolecule sensors, dielectric heterostructures, compound semiconductor-organic hybrid structures, self-assembled nanostructures, and thermoelectric energy conversion. He has published over 280 papers and obtained over 50 patents, with an H-index above 70. He is a Fellow of four professional societies and the National Academy of Inventors Hall of Fame, and has two R&D100 Awards. He earned degrees from MIT (Sc.B., Chemistry, and Humanities and Science, 1978) and UCLA (Ph.D., Organic Chemistry, 1982), was Distinguished Member of Technical Staff at Bell Laboratories (to 2004), and the 2004 President of the Materials Research Society. He served as DOE Materials Chemistry meeting chair and NIH panel member in 2014, was on multiple journal and company advisory boards, and was elected to the JHU Academic Council.



TOC Graphic

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