Material and circuit design for organic electronic vapor sensors and biosensors

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ABSTRACT

We summarize our recent results on material, device, and circuit structures for detection of volatile analytes in the atmosphere and proteins in aqueous solution. Common to both types of sensing goals is the design of materials that respond more strongly to analytes of interest than to likely interferents, and the use of chemical and electronic amplification methods to increase the ratio of the desired responses to the drift (signal/noise ratio). Printable materials, especially polymers, are emphasized. Furthermore, the use of multiple sensing elements, typically field-effect transistors, increases the selectivity of the information, either by narrowing the classes of compounds providing the responses, distinguishing time-dependent from dose-dependent responses, and increasing the ratio of analyte responses to environmental drifts. To increase the stability of systems used to detect analytes in solution, we sometimes separate the sensing surface from the output device in an arrangement known as a remote gate. We show that the output device may be an organic-based or a silicon-based transistor, and can respond to electrochemical potential changes at the sensing surface arising from a variety of chemical interactions.

KEYWORDS

vapor sensing, thiophene polymers, biosensing, protein detection, field effect transistor, remote gate, inverter circuit, dielectric, dopant

INTRODUCTION

The ability to control the carrier energy levels, functional group polarity, and film morphology make organic and polymeric semiconductors (OSCs) especially attractive for chemical sensing.[1] Their mechanical flexibility, low temperature processing, potential printability, capability of blending to form composites, and predictable activity in various electronic circuit configurations are additional attractive features. For biosensing, the most important electronic perturbations occur as an analyte interacts with a receptor functional group bound to either a conductive or capacitively coupled interfacial material layer. For the case of capacitive coupling, a means of transferring a change in interfacial potential or capacitive impedance to a change in charge density in a semiconductor material is desired. The overarching theme of this manuscript is the design of polymer semiconducting and dielectric materials that maximize the primary electronic changes that result from analyte binding thereto, and that provide convenient means of converting those local changes in material electronic properties to readable output signals selective for analytes of interest.

RESULTS

In our recent work on vapor sensors, we demonstrated the selective and quantitative detection of nitrogen dioxide (NO_2), an important component of polluted air, using dosimetric polymer-based organic field-effect transistor (OFET) sensing elements.[2] Two thiophene polymers, poly(bisdodecylquaterthiophene) and poly(bisdodecylthioquaterthiophene) (PQT12 and PQTS12, respectively), were used as active layers in bottom gate, gold top contact devices constructed on Si/SiO_2 substrates. The device schematics and chemical structures are shown in Figure 1. Responses of several hundreds of percent current increases were obtained, among the highest sensitivities reported for an NO_2-responsive device based on an organic semiconducting film.

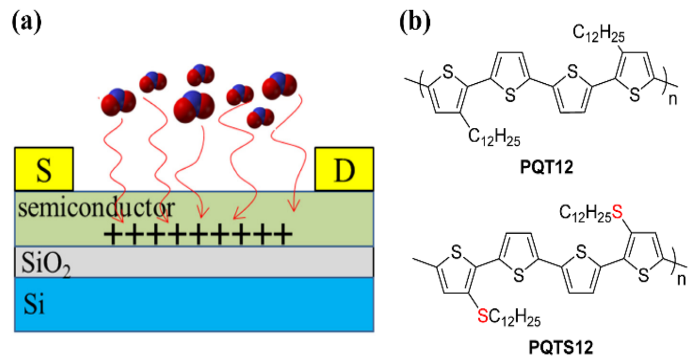

Figure 1. (a) Schematic diagram of device structure. (b) Chemical structures of polymer semiconductors. © Reference 2.

With gate voltage of -30 V, the sensors based on PQTS12 films exhibit remarkably high sensitivity to NO_2, up to 360% and 410% under 1 ppm for 60 min and 5 ppm for 15 min, respectively. PQT12 films were somewhat less sensitive to under the same exposure conditions. Of importance for distinguishing dose and exposure time contributions to response, we observed that the average *ratio* between the sensitivities of PQTS12 and PQT12 (R = $\text{sensitivity}_{(PQTS12)}$/ $\text{sensitivity}_{(PQT12)}$) shows a particular correlation with the concentration of NO_2, with a higher ratio associated with a smaller concentration. Thus, the concentration of gas could be detected by the ratio of sensitivity used in conjunction with the proportional current changes, even if one of the measured current changes was the same for different combinations of concentration and exposure time.

From measurements of cyclic voltammetry and the electronic characteristics, we found that the introduction of sulfurs into the side chains induces traps in films of the PQTS12 and decreases domain sizes, both of which could contribute to the higher sensitivity of PQTS12 to NO_2 gas. The ratio of responses of PQTS12 and PQT12 is higher for exposures to lower concentrations, allowing us to distinguish responses to low concentrations for extended times from exposures to high concentrations from shorter times, important for monitoring of indoor air quality, and contributing to the selectivity of the detection over likely interferent vapors. Introduction of new circuit designs and material combinations enables greater output selectivity and signal digitization. Sensitivities using different NO_2 concentrations, exposure times, and gate voltages are shown in Figure 2.

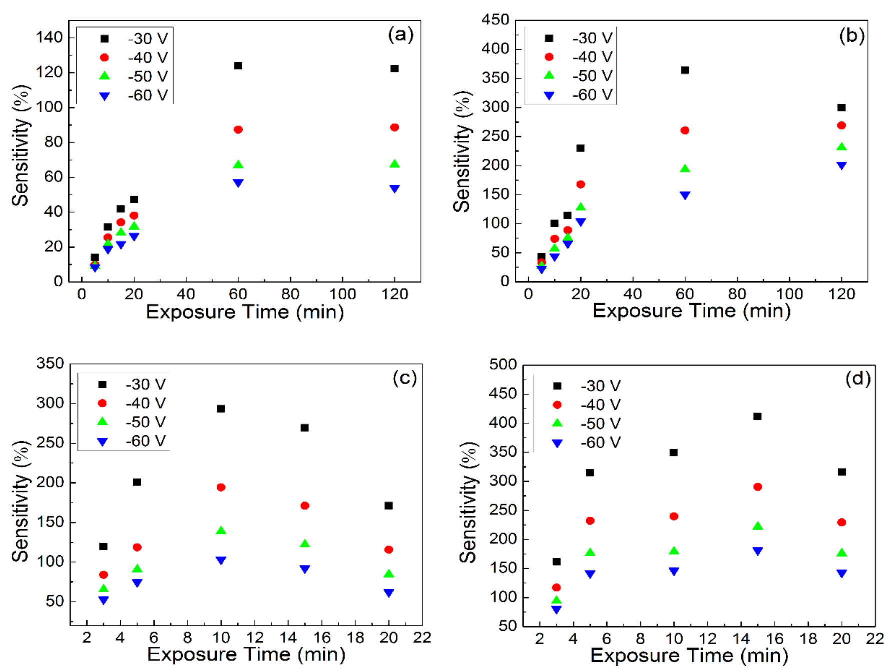

Figure 2. The current changes measured under different exposure time with different gate voltages with NO_2 concentration being 1 ppm (a, b) and 5 ppm (c, d). PQT12: a, c; PQTS12: b, d. © Reference 2.

The results so far are among our latest examples using individual OFETs to obtain responses to analytes. There are further advantages that can be exploited using combinations of OFETs in circuits. For example, the coupling of two OFETs in series with a common gate enables the acquisition of a response signal by measuring the voltage at the conductive link between the two OFETs. Because of the possible nonlinearity of the voltage change as a function of analyte concentration, the output becomes a digital indication of whether the concentration is above or below a certain threshold.[3] More recently, we showed that this kind of configuration can be obtained from printable semiconductors and dielectrics on a plastic poly(ethylene terephthalate) substrate that was flexible enough that devices thereon were shown to be wearable while retaining their sensing functionality.[4]

We used DPPCN, an n-type quinoidal molecular solid with two dicyanovinyl terminal groups, and poly(3-hexylthiophene) (P3HT), the well-known p-type polymer. These showed comparable responses, but of opposite sign, to the presence of ammonia, because ammonia can transfer electrons to the DPPCN and quench holes in the P3HT. The dielectric was a dual polymer layer, with polystyrene PS) on the bottom and poly(N-2-hydroxypropyl methacrylamide) (PHMPA) on top acting as a dissolution inhibitor for the polystyrene while preserving the charge transport properties of the semiconductors. Figure 3 shows the device layout and the inverter characteristics shifted by the exposure of the circuit to 5 ppm ammonia vapor for five minutes. By monitoring the output voltage while the input voltage was held constant near 0 V, the exposure to a dosage at or exceeding this level would be signaled.

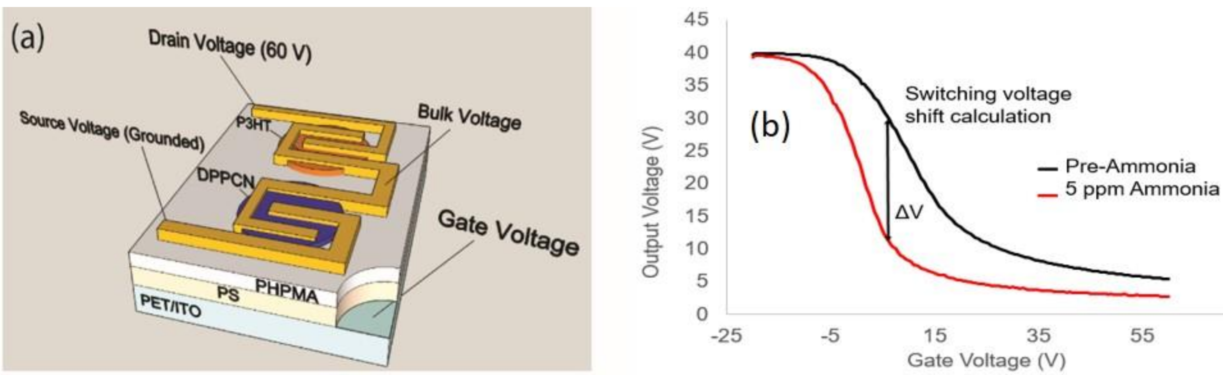

Figure 3. Inverter schematic and inverter characteristic switching (change in "bulk voltage") in response to 5 ppm ammonia. © Reference 4.

One final implementation of a two-transistor device is where both transistors are p-channel and have drifts of similar magnitude but opposite sign, so if both are placed in series or parallel circuits, the net drift is decreased. If the responses of these transistors to an analyte of interest are of the same sign, then the ratio of the response of the circuit to the drift of the circuit is higher than for the individual devices.[5] Figure 4 shows schematics of the devices used for this demonstration. One transistor in each circuit, parallel or series, is made from PQT12 and the other is made from PQTS12. While p-channel polymer transistors in general, and these in particular, show decreased conductances as they are stored in ordinary air, we achieved the opposite drift sign by keeping the PQT12 transistor in the dark while exposing the PQTS12 transistor to moderate intensity light from a light-emitting diode. With appropriately adjusted light intensity, the drifts nearly cancel, as shown in Figure 4, while the responses to analytes remain strong.

Figure 5 shows responses to NO_2 vapor as a function of exposure time, gate voltage used, and NO_2 mass fraction in carrier air. Sensitivity is highest at low gate voltages, where the transistors are not yet fully "on" but the NO_2 moves the transistors more fully into the accumulation regime. Response increases with both exposure time and mass fraction. Most importantly, the ratio of responses to NO_2 by the circuits to responses to the ordinary air (colored bars, figures 5e and 5f) are higher than the corresponding ratios for individual devices. This demonstrates the principle of drift compensation in polymer transistor-based sensor circuits.

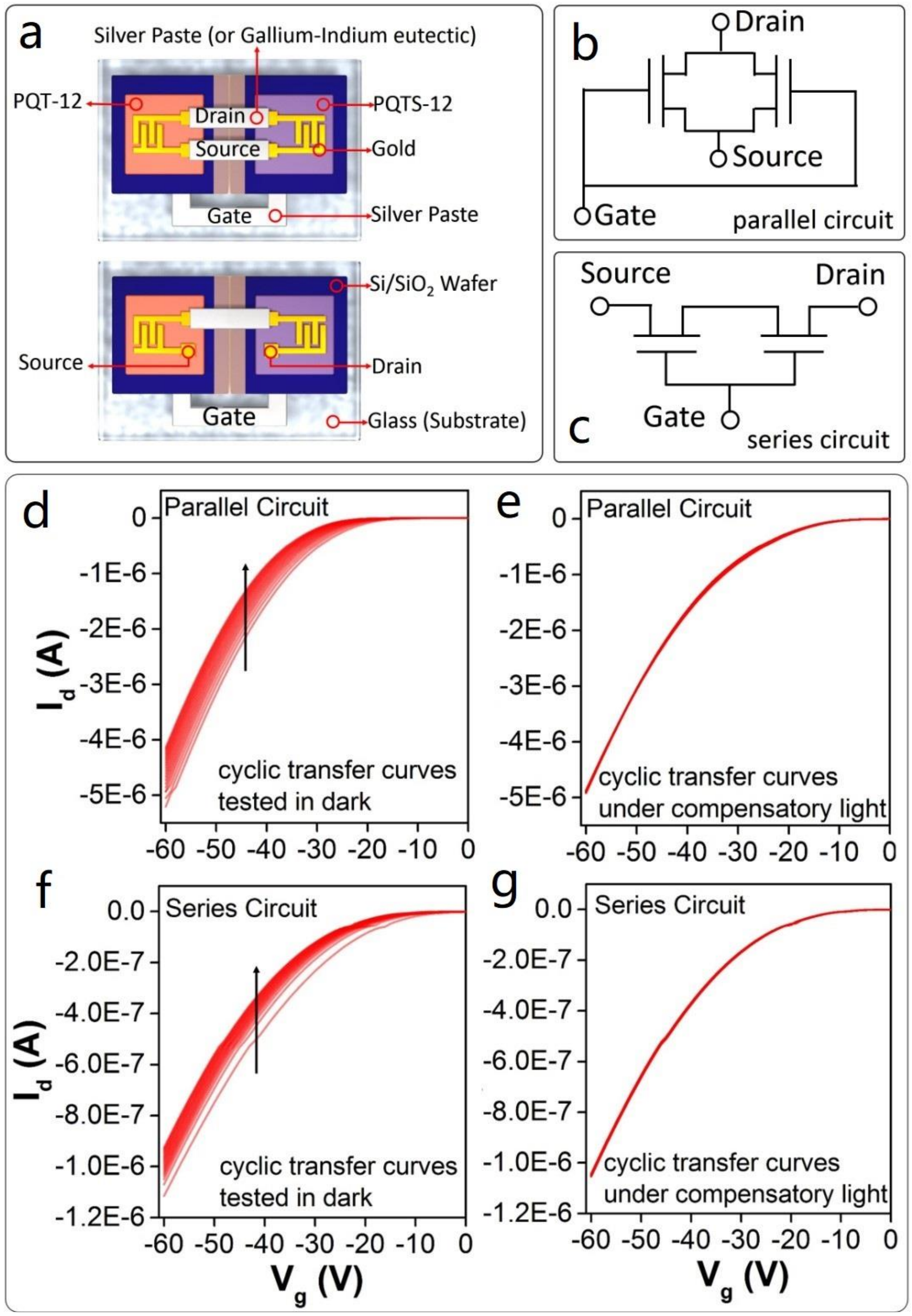

Figure 4. (a) Schematic diagram of parallel circuit (above) and series circuit (below). Circuit diagrams of (b) parallel circuit and (c) series circuit. Twenty cyclic transfer curves of (d) parallel circuit tested in dark and (e) under compensatory light (f) series circuit tested in dark and (g) under compensatory light. Drain voltage is -60 V. © Reference 5.

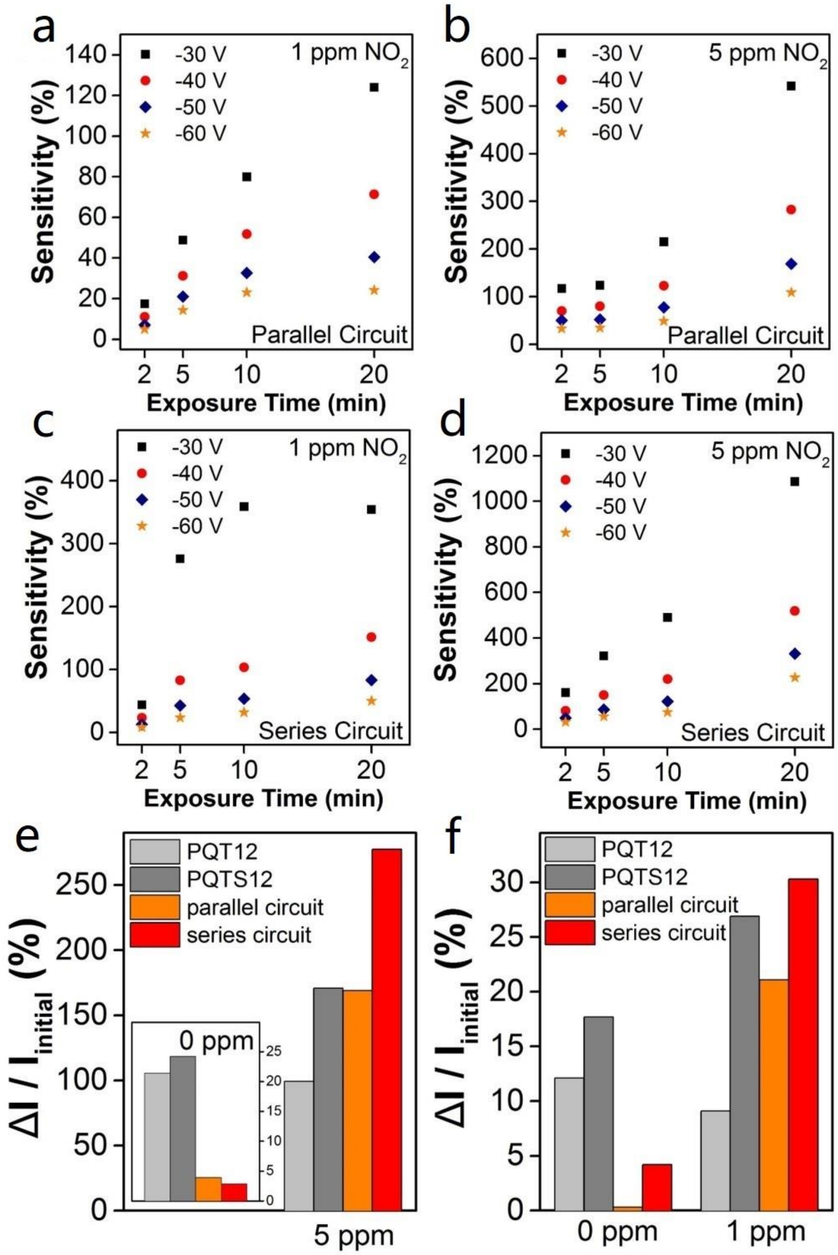

Figure 5. Current change with exposure time of (a) parallel circuit for 1 ppm NO_2 detection and (b) 5 ppm NO_2 detection (c) series circuit for 1 ppm NO_2 detection and (d) 5 ppm NO_2 detection. Uncertainties are listed in Table 1. Comparison of response performance between four kinds of NO_2 sensors: (e) Response to 0 ppm (control device) and 5 ppm NO_2 for exposure time of 20 min (Vg = -50 V). (f) Response to 0 ppm (control device) and 1 ppm NO_2 for exposure time of 5 min (Vg = -50 V). © Reference 5.

After having considered very small vapor-phase molecules as analytes, we now turn our attention to very large biomacromolecules in solution. While a very broad range of substrate materials can generate an electronic signal from the adsorption of bioanalytes, receptors are required to add selectivity to the binding and signaling of the molecules of interest. Antibodies are used in our work and that of many other researchers as selective receptors of protein analytes. The electronic signal that arises from protein-antibody interactions can arise from a change in potential difference across a material layer containing the antibodies as receptors and/or a change in impedance across that layer. Coupling these changes to the gate of a transistor allows them to be read as changes in currents flowing through the transistor or as changes in voltage dropping between the source and drain of the transistor in series with other resistive elements. These changes are amplified by optimal adjustment of voltages applied to the transistors and receptor layers, and the dimensions of transistor materials and receptor layers. Maximizing the area or volume density of receptor subunits in the receptor layer materials increasing the likelihood of binding events in a given solution concentration of analyte and is thus another way of increasing the signal from a dissolved analyte.

Polymer receptor layers rich in carboxylic acid (COOH) groups are effective choices for receptor attachment because of the availability of coupling chemistry for those groups, where NH_2 residues on proteins are peptide-coupled to the COOH groups either throughout the polymers before deposition or on the polymer surfaces after deposition. On the other hand, having hydrophobic monomer residues on the polymer is helpful in stabilizing receptor polymers to exposures to aqueous solutions, making the receptor layers less likely to dissolve or delaminate in the presence of analyte solutions.[6] The structures of the OFET sensor devices and materials used therein are shown in Figure 6.

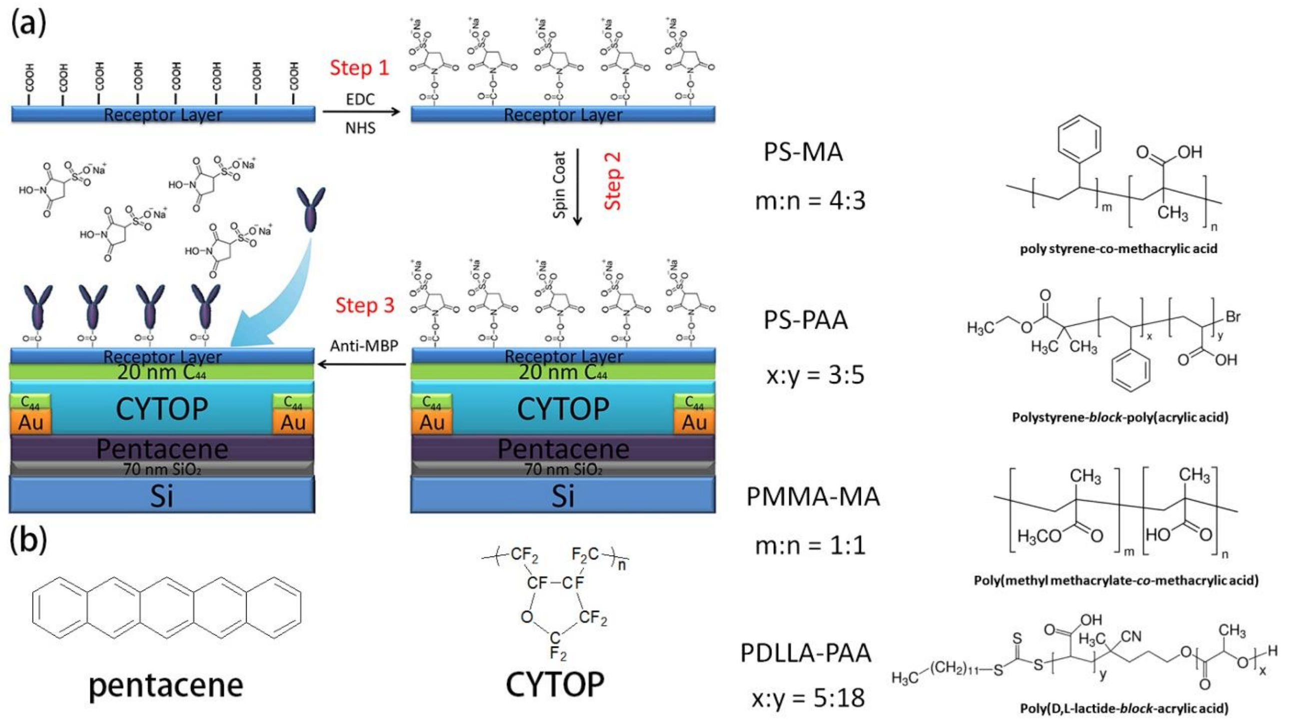

Figure 6. Device structures and polymer receptor materials used for protein sensing. © Reference 6.

We compared the retention of immobilized biomolecules on various acrylic copolymers shown in Figure 6 after multiple washing steps. Four different copolymers that combine hydrophobicity and high COOH concentrations (polystyrene-co-methacrylic acid (PS-MA), polystyrene-co-acrylic acid (PS-PAA) poly(methyl methacrylate-co-methacrylic acid) (PMMAMA) and poly(d,l-lactide-block-acrylic acid) (PDLLA-PAA)) were chosen for bioreceptor layers. Fluorescein isothiocyanate-labeled antibody was used to assess the retention of the antibody during aqueous rinsing. The retention was in the order PS-MA > PMMA-MA >> PA-PAA > PDLLA-PAA.

We utilized the neurologically important myelin basic protein (MBP), with isoelectric point of 12, and its corresponding antibody, as a representative antibody– antigen pair. We compared the sensing responses the four receptor layer materials by measuring drain current changes upon exposure to 100 ng mL−1 of MBP. For PS-MA, the best-performing polymer, sensitivity in the 1-10 ng/mL range was achieved. The order of the sensitivities was PS-MA > PMMA-MA ~ PS-PAA > PDLLA-PAA. While the sequences for retention and sensitivity were roughly the same, PS-PAA had a surprisingly high sensitivity considering its relatively poor antibody retention, perhaps indicating that the configuration or electronic environment of the retained antibody in that polymer was especially effective for generating a binding-induced electronic property change.

Selectivity experiments were also performed by using PS-MA as the receptor layer. Glial fibrillar acidic protein, GFAP, a known brain injury biomarker with isoelectric point of 5.4, was chosen as an interference protein. MBP is positively charged in pH 7.4 phosphate-buffered saline (PBS) while GFAP is negatively charged in pH = 7.4 PBS. While the mechanism of binding-induced signal generation is not definitely known and is the subject of ongoing research, it would be reasonable to expect that proteins with opposite net charges would give the opposite signs of current changes. This was indeed found to be the case. Besides the anti-MBP device being selective for MBP over GFAP, it gave the opposite polarity responses to what we had previously reported for GFAP. Transfer curves showing typical responses are illustrated in Figure 7.

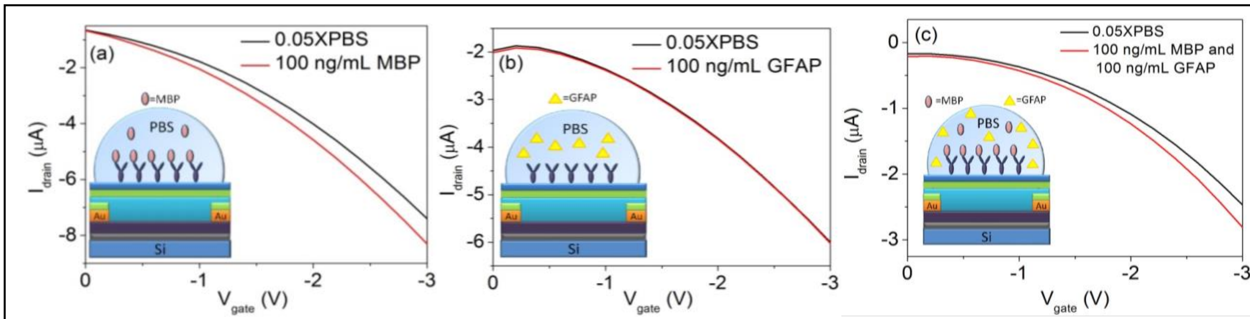

Figure 7. Transfer characteristics of OFET based anti-MBP-functionalized sensor exposed to (a) 100 ng/mL MBP, (b) 100 ng/mL GFAP and (c)100 ng/mL MBP and GFAP. Note the lack of response in the mismatched system b, and the consistent response to MBP even in the presence of interfering GFAP. © Reference 6.

To increase the stability of transistors in the presence of analyte solutions, we adopted an extended gate architecture in which capacitive coupling of the receptor interface to a transistor semiconductor is maintained, but where the solution and the semiconductor are macroscopically separated.[7] We used this architecture to show that the addition of poly(ethylene glycol) (PEG) to an anti-GFAP-functionalized receptor layer increases sensitivity of a pentacene OFET to GFAP binding to the receptor layer.[8] We hypothesize that this increase is because of the longer Debye length that results when PEG replaces or interacts with some of the water near the binding site, so that the electronic effects of the binding are less screened. The configuration is shown in Figure 8, along with proportional current sensitivities as a function of the molecular

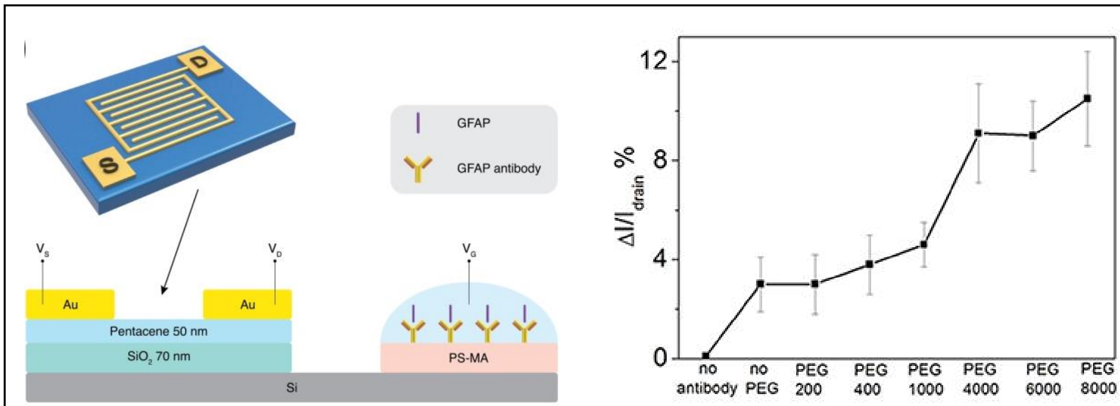

Figure 8. Extended gate OFET biosensor configuration and sensitivities of the device to 100 ng/mL GFAP in 0.05X PBS. Gate voltage (V_g) and drain voltage (V_d) were set to -2 V relative to the source voltage(V_s). © Reference 8.

weight of added PEG. We observe that there is a threshold molecular weight, on the order of a few thousand, above which the PEG is effective at increasing the sensitivity. Because of the possibility of the PEG promoting the penetration of analyte solutions into the pentacene semiconductor, the extended gate configuration was essential to this experiment.

We have also begun using a "remote" rather than extended gate for coupling interfacial electronic signals to transistors. In this case, the transistor need not be an OFET or even a thin film transistor that we make; a commercial and addressable n-type silicon transistor is sufficient for our purposes. This avoids the need for fabricating the transistors in the laboratory and removes one source of device-to-device variability. We have used the remote gate to probe interactions between cortisol and its antibody,[9] as well as conductive polymers with dopants in solution.[10]

Development of the remote gate configuration was supported by the National Science Foundation, Division of Materials Research, grant number 1807292. Investigation of compensating senor circuits was supported by the National Science Foundation, Division of Electrical, Communications, and Cyber Systems grant number 1807293. Figures are used with permission of copyright holders.

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