Ion-Selective Organic Electrochemical Transistors

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The selective detection and quantification of ionic species in aqueous media is of importance for several applications such as health monitoring, environment, water and food analysis. In particular, the monitoring of biologically relevant ions (K^+, Na^+, Ca^{2+}, Cl^-, etc.), which is widely used around the world for diagnosis purpose, relies almost entirely on the use of carrier- based ion-selective electrodes (ISEs).[1] Thanks to the extensive and systematic research carried out over the last 50 years, ISEs are now firmly established, with commercial electrodes avail- able for a wide variety of cationic and anionic species.[2] The working principle of an ISE is rather complex, with the main constituent being an ion-selective membrane (ISM) able to selectively exchange ions with the analyte thus establishing a measurable interface potential. In biomedical applications, the needs for miniaturization and multi-modal sensing has driven the field toward the development of more sophisticated ion-sensors based on inorganic field-effect transistors (FETs). Besides working on the same sensing principle of ISEs, ion-selective FETs (ISFETs) have the advantage of being solid-state, micro-scale devices with characteristic short response time and produced through established electronics manufacturing.[3,4] Moreover, transistors can be directly integrated into signal processing electronic boards leading to monolithic sensing systems. Organic FETs (OFETs) potentially represent a step beyond this technology, because they bring together the advantages of inorganic FETs with the possibility of inexpen- sive manufacturing, mechanical flexibility and ease of functionalization through synthetic chemical modification.[5,6] The latter property is unique among electronic materials and allows, for example, the direct incorporation of the ionophore into a conducting polymer.[7,8] While the use of conducting polymers as solid contact in ISEs has been the focus of a large number of studies,[9–12] their application in transistors for ion-sensing remains rather unexplored. OFETs have been used to prepare simple pH sensors,[13–15] and to detect K^+, Na^+ and Ca^{2+} in water,[16,17] but these examples lack the selectivity and sensitivity necessary for practical application. These properties can be attained only through the use of the specific ionophores and device structures that are widely and successfully employed in ISEs. Recently, Schmoltner et al.[18] adapted the classical structure of an ISE to that of an electrolyte-gated

OFET:[19] the channel of the polymer transistor was put in contact with an inner reference electrolyte, separated from the analyte by a polyvinylchloride (PVC) based Na^+-selective membrane. Changes in Na^+ concentration in the analyte cause variation of the potential at the membrane interface, which then modulates the drain current Id of the transistor. While the device design leads to performances similar to those of ISEs employing the same ISM and inner solution (detection limit of about 10^{-6} M, Nernstian sensitivity and reversible response), the average cur- rent modulation was small, in the range of 250–500 nA dec^{-1}. As a matter of fact, besides high performance OFETs have been reported using polymer/gel electrolytes,[20,21] their current density is considerably lower when operating in aqueous electrolytes. A device type which is especially suited for applications in aqueous media is the organic electrochemical tran- sistor (OECT).[22] OECTs make use of hydrated, ion-permeable conducting polymers, such as poly(3,4-ethylenedioxythiophene) poly(styrenesulfonate) (PEDOT:PSS), which are able to change their conductivity by reversibly exchanging ions with an elec- trolyte. In particular, by application of a positive gate bias V_g, cations penetrate the polymer diminishing the hole density and thus lowering the drain current.[23] In contrast to electrolyte- gated OFETs, in OECTs doping and de-doping processes take place through the bulk of the conducting polymer at very low gate bias, and the current modulation is proportional to the amount of charge injected into the channel. This means that the corresponding transconductance ($g_m = \partial I_d / \partial V_g$) is extremely large (typically > 1 mS for micro-scale devices), making the OECTs ideal ion-to-electron transducers.[24] Thanks to these merits, OECTs have been successfully used as biosensors,[25] interfaced with living cells[26,27] and even used for in vivo monitoring of brain activity.[28] In this work, we integrate a K^+-selective membrane with an OECT and employ a hydrogel as the internal electrolyte in contact with the PEDOT:PSS channel. We demonstrate how an all-solid-state ion-selective OECT (IS-OECT) is capable of monitoring K^+ with a low detection limit and in a reversible manner. More importantly, we show that the sensitivity approaches 50 µA dec^{-1} in the 10^{-4} – 10^{-1} M K^+ con- centration (c_{K^+}) range, which paves the way for integrated applications of organic transistors in ionsensing.

The device structure is reported in Figure 1. Transistors with channel width/length of 25/25 µm were fabricated on microscope glass slides. Gold source/drain electrodes and interconnects were patterned by photolithography and lift-off and isolated from the electrolyte with 2 µm thick Parylene C (PaC). A second, sacrificial layer of PaC was used to define the PEDOT:PSS channel, which was deposited by spin casting of commercial high conducting grade suspension. After annealing of the conducting polymer, a glass ring was fixed around the OECT array and the chamber was filled with a hot water solu- tion containing agarose (1 wt.%), KCl (10^{-3} M), and disodium ethylenediamine tetraacetic acid (Na_2EDTA, $5 \cdot 10^{-2}$ M). This composition should allow for an increased response at the membrane maintaining its selectivity.[29] After gelation of the electrolyte at room temperature, the chamber was sealed by placing a standard PVC-based K^+-selective membrane on top of the hydrogel. Finally, a top rubber chamber (2 mL volume) was used for containing the analyte solution and the gate electrode (Ag/AgCl). Despite the rather complex stack, the IS-OECT shows typical low-voltage operation and high current modulation (Figure 1b), indicating proper gating through the PVC membrane and the gel electrolyte. Calibration of the IS- OECTs was performed by adding stock solutions of know K^+ concentration (c_{K^+}) into the top chamber while monitoring the variation of the drain current Id at fixed gate and drain voltages ($V_g = 0$ V, $V_D = -0.7$ V). As shown in Figure 2a, I_d consistently follows the stepwise increase and decrease of the ionic concentration, varying approximately 200 µA over the whole range (10−7 M – 10−1

M). The calibration was sequentially repeated 4 times in order to ensure significance of the response. The drain current values at equilibrium were plotted against the correspondent c_{K^+} to extract the sensor parameters (Figure 2b). The IS-OECT shows a linear response for $\log(c_{K^+})$ in the range of 10^{-4} – 10^{-1} M, with a sensitivity of 46 µA dec^{-1} (current per order of magnitude change in c_{K^+}) when increasing the concentration, and of 47 µA dec^{-1} when decreasing it. The obtained sensitivity is considerably larger than any previous report of ion-sensing organic transistors, which is attributed to the high transconductance of OECTs. In this case, the ISM potential drops entirely on the channel, forcing K^+ ions into the bulk of PEDOT:PSS and drastically changing its conductivity. The device response is reversible both in time and as a function of concentration. We observed only a small fluctuation of the current when starting the measurement from very dilute solutions (c_{K^+} <10^{-6} M), an effect which is not observed when the experiment is started from high concentrations (Figure 2b). The systematic shifts introduce a small hysteresis in the diretion of the concentration of the solution in which the ISM was previously immersed. This is related to the small volume of the top chamber (<2 mL) and to the absence of agitation or flux in the analyte.[30] Nevertheless, the hysteresis itself was small and highly reproducible, and can be avoided if sufficient time is allowed for the system to equilibrate. To improve the accuracy of the analysis, a common practice is to average the measured values and to plot them against ion concentration.[31] Figure 3a reports the average calibration curve for the potassium selective OECT, characterized by a sensitivity of 47 µA dec^{-1} in the concentration range $10^{-4} \leq c_{K^+} \leq 10^{-1}$ M and a detection limit of $1.5 \cdot 10^{-5}$ M. The detection limit was estimated as the cross point between the slope of the dataset and a line passing through the current response obtained at low K+ concentration. Since the gate biased is maintained at 0 V, it is possible to directly calculate the membrane potential ($V_{g,m}$) from the transfer curve of the IS-OECT (3b). The extracted sensitivity in the linear regime is 48 mV dec^{-1}, which is somewhat lower if compared to the theoretical Nernstian response of 59.16 mV dec^{-1}. Eventually, current leakage between the inner and outer electrolytes could lead to a reduced sensitivity due to a compensation of the potential drop at the membrane. This phenomena seems to not be an issue in our device, since in the working regime of the membrane (0 – 200 mV), the measured gate current is very small (1–2 nA, Figure 3b), several orders of magnitude lower compared to the drain current. The sensitivity is likely to be improved by optimization of the ISM, for example by tuning the content and ratio of the potassium ionophore and the anionic exchanger potassium tetrakis(4-chlorophenyl)- borate in the PVC matrix.[32] The detection limit of the sensor can also be calculated from the transfer characteristic of the device, and it was found to be $8 \cdot 10^{-6}$ M (note that this value is somehow lower compared to the one extracted from current response, $1.5 \cdot 10^{-5}$ M, due to the non-linearity of the transfer curve). These values are sufficient in view of applications for in vivo monitoring of K^+ activity, where it is of particular interest to record fluctuations primarily in the 10^{-3} – 10^{-2} M concentration range.[33] With this perspective, the IS-OECTs performs remarkably well in terms of both reversibility and sensitivity. The selectivity of the IS-OECTs to potassium with sodium as primary interfering ion has also been evaluated by comparing the sensitivity to pure potassium or sodium stock solutions (Figure 4a). It has to be noted that an accurate determination of selectivity coefficients through standard techniques requires the response to be Nernstian.[34] The matched potential method is, however, totally independent of the ISM model and overcomes the difficulty in obtaining accurate selectivity coefficients in non-ideal situations.[35] In this method, the selectivity coefficient is defined as the activity (concentration) ratio of the primary ion and the interfering ion which gives the same potential change in a reference solution. The selectivity coefficient was calculated to be $-\log K_{K^+,Na^+} =$

2.7, comparable to what is obtained (3.3) for the correspondent ISE employing the same membrane composition.[36]

When continuous monitoring of ions in a living tissue is of interest, the response time of the sensor needs to be adjusted to the time scale of ionic fluxes of the physiological system. The current response of the IS-OECT for a step increase in potassium concentration from 10^{-4} M to 10^{-3} M, was measured as a function of time and applied gate bias (Figure 4b). Note that the output of the transistor at 10^{-4} M has been set to zero in order to facilitate the comparison. We observed an interesting trend with the equilibration time of the device varying with the applied gate bias. By fitting the step response of the drain cur- rent with a single exponential (Figure S2), we observed how the IS-OECT biased at $V_g = 0.2$ V has a time constant of only 36 s compared to 77 and 74 s for $V_g = 0$ and $V_g = 0.4$, respectively. On the other side, the current modulation is also dependent on the gate voltages, since the transistor response is dictated by the transconductance. At this range of concentration, the membrane responds with a potential ranging from 100 to 200 mV, which correspond to the maximum device transconductance ($g_m = 1.2$ mS, Figure 4b), meaning that the signal transduction is also maximized. As a matter of fact, the current modulation of the sensor biased at $V_g = 0.2$ is considerably higher compared to the other gate voltages. In Figure 4b, the direct correlation between the drain current modulation (response to a K^+ concentration change from 10^{-4} M to 10^{-3} M, at $V_g = 0$, 0.2, 0.4 V) and the trend of the g_m versus the gate voltage is highlighted. These findings represents an important guideline for future applications of IS-OECTs since, from geometrical considerations, it is possible to tune the sensors working regime towards the maximum transconductance, where the current modulation is increased and, at the same time, the time response is faster.[37]

In summary, we demonstrate that OECTs are promising candidates for solid-state organic-based ion-selective sensors. Thanks to the high transconductance of this devices, very high sensitivity can be obtained without sacrificing reversibility and selectivity. The proposed device structure is very versatile, allowing for independent tuning of i) the ion selective membrane, ii) the inner gel composition and iii) the transistor geometry in order to meet the needs of virtually any ion-sensing applications.

Experimental section

Transistor Fabrication: when not specified, all chemicals were purchased from Sigma-Aldrich. Devices were prepared as recently reported.[38] Briefly, glass slides were cleaned using chemical and plasma methods. Shipley 1813 photoresist was spin coated and exposed to UV light using a SUSS MBJ4 contact aligner, and then developed using MF-26 developer. After a brief O_2 plasma cleaning, a thin film composed by 5 nm of chromium and 100 nm of gold was thermally evaporated. Lift-off was performed by immersion of the samples in acetone mixture for 2 hours. 2 µm thick PaC layers were deposited using a SCS Labcoater 2. 3-(Trimethoxysilyl)propyl methacrylate was added into the chamber and used as an adhesion promoter for the first PaC coating. A dilute solution of industrial cleaner (Micro-90) was spin coated onto the first PaC layer, acting as an anti-adhesive for the second PaC film. Substrates were subsequently patterned with AZ9260 photoresist and AZ developer (AZ Electronic Materials), while openings were obtained by reactive ion

etching with an O2 plasma using an Oxford 80 Plasmalab plus. For the preparation of the PEDOT:PSS films, 20 mL of aqueous dispersion (CleviosTM PH 1000 from Heraeus Holding GmbH) were mixed with 1 mL of ethylene glycol, 50 μL of dodecyl benzene sulfonic acid, and 200 μL of (3-glycidyloxypropyl)- trimethoxysilane, and the resulting dispersion was spin-coated on the substrate. Finally, the sacrificial PaC layer was peeled-off leaving behind the OECT array structure. Devices were subsequently annealed at 140 °C for 1 h and then immersed in deionized water to remove any excess of low molecular weight compounds.

Preparation of the ISM: the membranes were prepared by drop-casting a THF mixture containing high molecular weight PVC (36.5 wt.%), diisodecyl adipate (60.5 wt.%), potassium tetrakis(4-chlorophenyl)-borate (0.5 wt.%) and potassium ionophore III (2.5 wt.%) onto a glass slide. The size of the membrane was defined by confining the liquid with a rubber ring. The mixture was allowed to dry at ambient conditions and peeled-off with the rubber ring.

Assembly of the IS-OECTs: A glass ring was attached by means of a thin layer of polydimethylsiloxane on the transistor array. An aqueous solution containing agar (1 wt.%), KCl (10–3 M) and Na2EDTA (10−2 M) was obtained by microwave heating all species in DI water. The glass chamber was filled with the warm mixture and the device was cool down in a fridge. The ISM was placed onto the hydrogel, and a small chamber with a bottom hole was pressed on top, completing the device stack.

Device Characterization: A reference Ag/AgCl device stack. Device Characterization: A reference Ag/AgCl electrode was used as the top electrode and the analyte was directly added into the chamber. Calibration was performed by exchanging stock solution of KNO3 in the analyte chamber. When decreasing the concentration, the chamber was rinsed with DI water before every measurement to avoid cross-contamination. For the time response experiment, an amount of solution concentrated enough to lead to an overall concentration of 10−3 M in potassium was added to the 10^{-4} M solution. All recording were performed with Keithley 2612 SourceMeter and customized Labview software.

Supporting Information

Supporting Information is available from the Wiley Online Library or from the author.

Acknowledgements

This work has been supported by the European Union (HYSENS, Grant STRP 263091), the Spanish Ministry of Economy and Competitiveness (MINECO) (MAT2011–24594), and the Generalitat Valenciana (Prometeo/2012/053). J.R. was supported by a Marie Curie Post-doctoral Fellowship, E.B. acknowledges MINECO for an FPI grant.

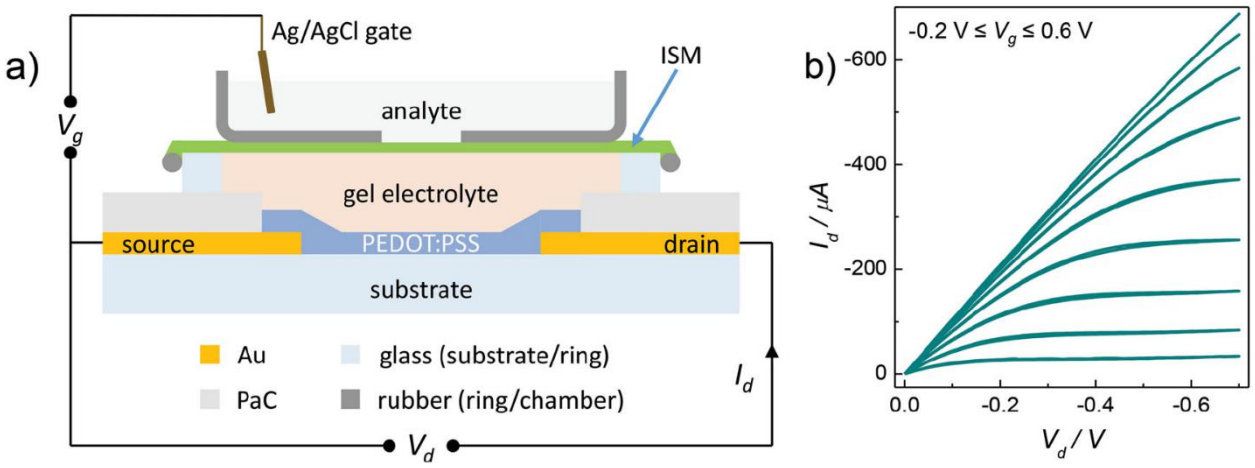

Figure 1. (a) Cross section schematic and wiring of the IS-OECT and (b) output curve of the device from $V_g = -0.2$ V (top) to 0.6 V, recorded with aqueous 10^{-3} M KCl.

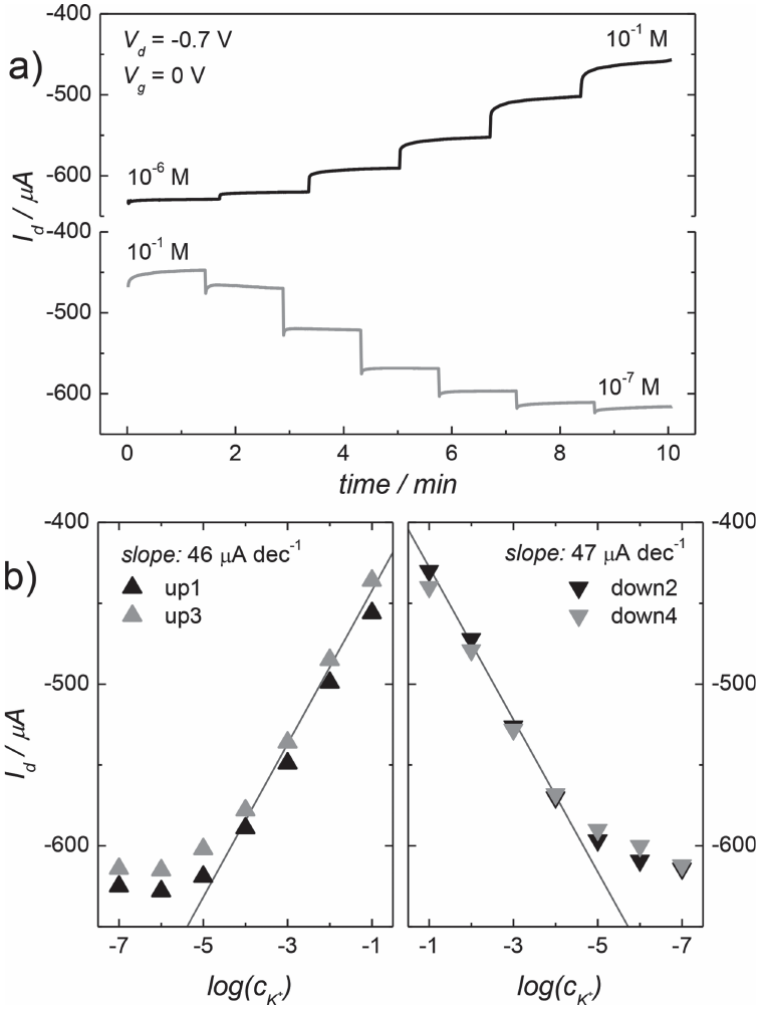

Figure 2. (a) Monitoring of the drain current Id for increasing (black) and decreasing (gray) concentration of K+ (the graph is a sum of the single concentration measurements) and (b) correspondent transistor calibration curves (repeated twice in both directions). The sensitivity (slope) of the data is obtained by fitting the linear region of the response.

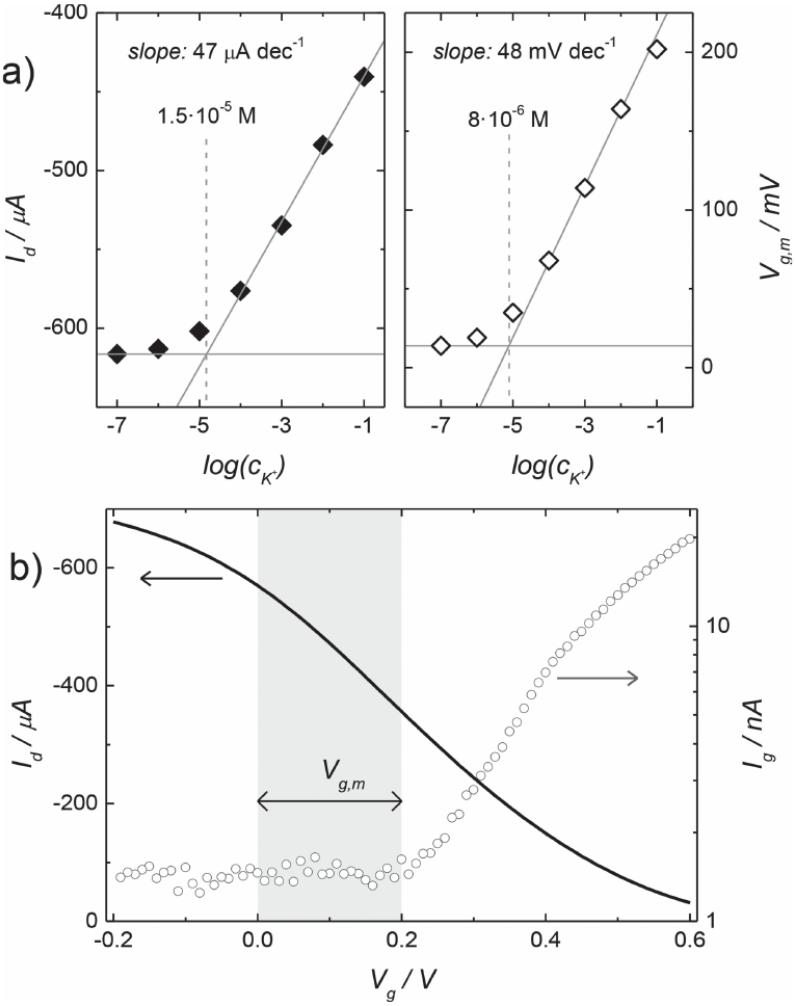

Figure 3. (a) Sensor parameters resulting from the average of four sub- sequent calibration of the current response (full symbols), and calculated average potentiometric response (empty symbols). The latter data were calculated from the transfer characteristic of the device. (b) Transfer curve and correspondent gate current Ig of the IS-OECT, measured withaqueous 10^{-3} M KCl.

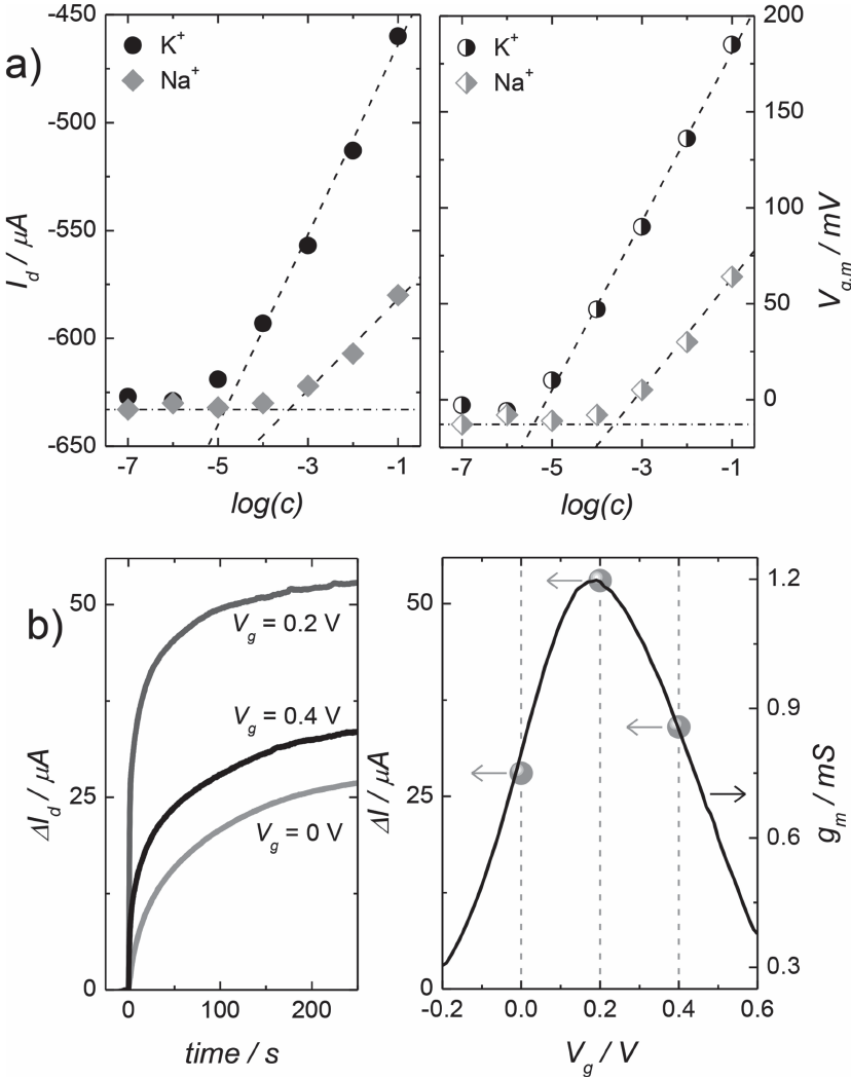

Figure 4. (a) Calibration of the IS-OECTs to potassium and to pure sodium solutions. Both the measured current response (left) and the calculated membrane voltage (right) are shown. (b) Drain current modulation to a sudden change in potassium concentration from 10^{-4} M to 10^{-3} M, for increasing applied gate voltages. On the right, the current modulation at different gate voltages (right axis) is superposed to the transconductance curve (left axis) of the device measured at $C_{\mathrm{K}^+} = 10^{-3}$ M.

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ADVANCED MATERIALS

Supporting Information

for *Adv. Mater.,* DOI: 10.1002/adma.201400731

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Supplementary Information on

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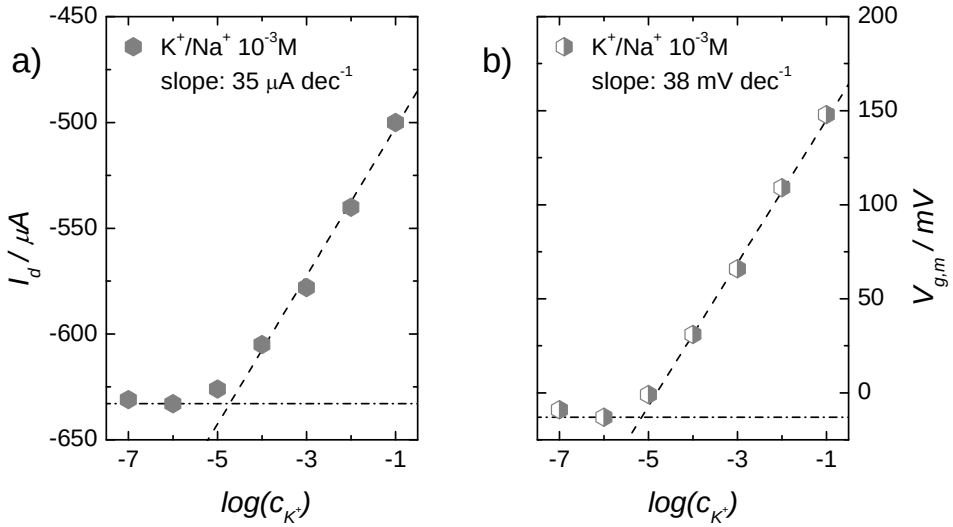

Figure S1. (a) Current response (sensitivity) of the IS-OECT to increasing potassium concentration and with a fixed interfering concentration of sodium (10^{-3} M). (b) Correspondent voltage response calculated from the transfer curve of the device.

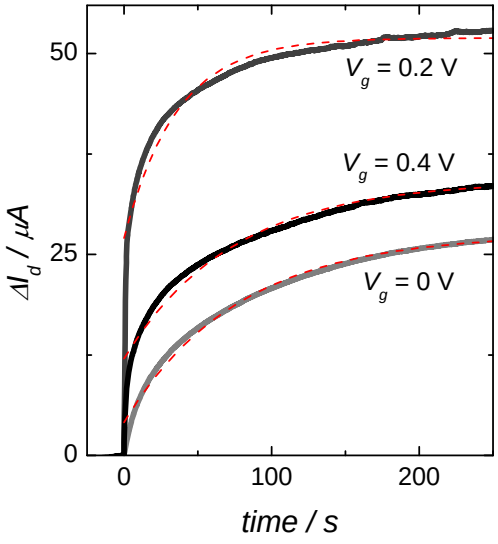

Figure S2. Drain current modulation to a sudden change in K^+ concentration from 10-4 M to 10-3 M, for increasing applied gate voltages. The red line is a fit of the curve performed using a simple exponential function, used to extrapolate the time constant τ: $I_d = I_d^0 + ae^{-\tau/t}$