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Nicola Coppedè*, [a][1], Marco Giannetto, [b][1], Marco Villani, [a], Valeria Lucchini, [a, b], Edmondo Battista [c], Maria Careri, [b], Andrea Zappettini [a]

* Corresponding author.

E-mail address: nicola.coppede@imem.cnr.it (N. Coppedè).

[1] Authors equally contributed to the work.

[a]-IMEM-CNR Institute of Materials for Electronics and Magnetism, Italian National Research Council, Parco Area delle Scienze, 37/A, 43124, Parma, Italy

[b]-Department of Chemistry, Life Sciences and Environmental Sustainability, University of Parma, Parco Area delle Scienze 17/A, 43124 Parma, Italy

[c]-CRIB (Centro di Ricerca Interdipartimentale sui Biomateriali) Università degli Studi di Napoli, Federico II, p.le Tecchio, 80, Napoli, Italy

Abstract:

Textile organic electrochemical transistors (txOECTs) are a new class of wearable biosensors used to monitor physiological parameters in bio fluids of clinical interest. Herein the selectivity of a textile biosensor was improved directly functionalizing the textile device with ion selective membranes. The device was prepared by a series of consecutive functionalization of the textile fiber, first by applying the conductive polymer poly(3,4-ethylenedioxythiophene):poly(styrene sulfonate) (PEDOT:PSS) and subsequently the ion selective membrane based on different ionophores with the aim of measuring electrolytes in sweat. The ion selective membranes were previously tested and optimized by potentiometric measurements. The biosensor devices were studied with different concentration of electrolytes. Membrane selectivity was tested comparing transistor response with interfering ions, proving successfully the selective response to sodium, potassium and calcium ions. The ability of the textile biosensors to discriminate among the cations was demonstrated over the 10^{-5} - 1 M concentration range, a concentration range found in sweat. The electronic parameters of the txOECTs show differences not only in modulation response but also in time constants of kinetic behavior. The selective determination of potassium and calcium in sweat has a great importance in different applications, for example, in human sweat monitoring, to understand physiological conditions, like dehydration, cardiac bioactivity and hypokalemia.

1. Introduction

The request for wearable sensors, specifically designed for medical and sports medicine applications, is driving an increasing interest in research focused on innovative devices able to monitor biometric data that, at this moment, are still inaccessible. The approach consists in the combination of new organic electronic materials for the realization of easy-to-use devices with a simple architecture and effective applications for measurements in non-conventional conditions providing unique advantages in terms of high stability, simple realization and industrial scalability [1]. In particular, industrial textile materials have being re-engineered and designed to give new functionalities, such as sensitivity and functional response to specific substances in biometric wearable analysis [2]. Recently, biosensors able to monitor physiological fluids have been realized and investigated from different research groups in order to perform easy control of physiological parameters through the detection of ions and molecular species of biological concern [3]. In this context, the applications of textile substrates for sweat analysis are of great interest, since the direct interaction of these materials with the real sample allows non-invasive monitoring of this physiological fluid. [4]. There have been different attempts to use textile materials for sensing devices, offering high performance in terms of comfort, cost reduction, and sensitivity [5]. Among the materials used as smart textile substrates to promote sensing functions, conducting polymers are mostly used with successful applications. In particular, poly(3,4-ethylenedioxythiophene):poly(styrene sulfonate) (PEDOT:PSS) has been successfully used as active layer in Organic Electrochemical Transistors (OECTs) devices consisting of PEDOT-functionalized textile thread, showing excellent results because of PEDOT:PSS good conductivity, high stability and biocompatibility [6]. Consequently, OECTs are particularly suitable for biosensing in liquid samples because they can be operated at low voltage and PEDOT:PSS is biocompatible. In addition, electrochemical transistors present the highest value of trans-conductance among transistor sensing devices [7]. In recent years, OECTs appeared as an enabling technology for the development of a variety of applications ranging from sensors for simple molecules such as hydrogen peroxide [8] to more complex bio-structures such

as liposomes, [9] micelles [10], DNA [11] and pigments [12]. The different applications of OECT have been extensively reviewed concerning biosensing and bio-integration approaches [13], with innovative applications that involves also precision agriculture and plant monitoring [14]. Generally, OECTs present high sensitivity and low selectivity (below one order of magnitude, if we consider frequency measurements [15]), being sensitive to all cationic species, allowing the de-doping of transistor channel. To overcome these limitations different approaches have been tested. In particular, biochemical functionalization through lipid membranes have been used to discriminate between monovalent and divalent ions in an OECT sensor [16], whereas the analysis of diffusion coefficients in OECT kinetic models enabled to discriminate among different ions [17]. Then ion selective membranes have been applied on OECT devices realized on rigid silicon substrates [18,19,20,21]. Moreover, one of the most common approaches to induce selectivity of sensing devices involves the use of enzymes, which catalyze specific reactions. Hence, immobilization of glucose oxidase in the polymer matrix is a feasible approach for glucose detection or lactate oxidase for lactate detection in OECT devices [22, 23]. The direct functionalization of textile fibers as active channel has wide application in the analysis of liquid samples, such as sweat, aimed at monitoring patients and athletes' physiological conditions [24, 25]. The aforementioned approach consists in using the textile substrate to simplify the absorption of the sweat sample and to exploit the wearable properties of the device, realized using the common textile materials used for everyday clothes. After the realization of OECT on textile substrates, the specific objective of this work was to make key improvements to enhance selectivity in such a way to develop devices able to respond to specific ions.

In fact, great importance in the knowledge of physiological condition is related to the ability of the sensor to detect specific ion species such as potassium, which is an ionic metabolite playing an important role for the correct physiological equilibrium. In this work we address the lack of selectivity of conventional OECTs realizing a novel functionalization of textile OECTs, based on the use of ion selective membranes. We prepared different ion selective membranes based on polyvinylchloride as polymer matrix to be applied on conducting polymer channel [26]. This approach preserves the flexibility and the hydrophilicity properties of the textile OECT device.

The ion selective polymeric membrane was deposited on textile fibers, previously functionalized with active film of PEDOT:PSS as conducting polymer. Textile ion selective devices were realized and characterized using potassium- and calcium-selective membranes. The device response has been analyzed, using sodium ions as interfering specie. Such ions are the most representative for human sweat, in terms of occurrence, and because of their role in physiological metabolism. Sodium is taken here as a standard because it is the most abundant cations in human sweat, and the main challenge is to selectively detect the other species respect to sodium, which present the higher interference signal. The measurements show the feasibility of this approach, while the selectivity with other species is not considered. The ionic selectivity of the membranes was first tested by potentiometric measurements carried out with the different interfering ions, then the response of the OECT devices, with ion selective membrane, was tested in different operative conditions in order to investigate the kinetic behavior of ionic de-doping.

Experimental

Device fabrication

A detailed sketch of the selective textile OECT architecture is shown in Figure 1a. A plastic box vessel is used as test vial hosting the OECT device. On top view, the black central line represents the conductive polymer (i.e. the transistor channel (Source - Drain), whereas the membrane is designed as a double thin line around the channel. The grey square represents the gate electrode made of a silver wire. In Fig1.b, a real picture of the device. The textile OECT device was fabricated by a soaking an acrylic textile thread with PEDOT:PSS, as previously reported [1]. Briefly, the PEDOT:PSS solution was modified in order to increase electrical conductivity and decrease solubility in water [27,28]. The yarn was immersed into an aqueous solution of PEDOT:PSS (CleviosPH1000), ethylene glycol (10%) and dodecyl benzene sulfonic acid (DBSA) surfactant (3%) for 30 min. Then a baking process in oven at constant temperature of 130° C was carried out for 3 hours. The flexibility of acrylic yarns was not

significantly modified and the resulting electrical resistivity was 120 Ohm/cm. Then, in order to deposit the ion-selective membrane, the textile was soaked in the potassium selective membrane solution with the following W/W composition, already optimized in our previous studies [29]: 64,70% bis(2-ethylhexyl)sebacate, 32,80% high molecular weight poly-vinyl chloride, 2% valynomicine (potassium ionophore), 0,5% potassium tetrakis (4-chlorophenyl)borate (ionic exchanger). Tetrahydrofuran (THF) was used as volatile solvent mediator allowing the proper solubilization and homogenization of the membrane components. The ion selective membrane was then dried at room temperature for 24 h in order to allow complete evaporation of THF. The same approach was used to synthesize the calcium-selective membrane, with the following w/w composition: 65,60% bis(2-ethylhexyl)sebacate, 32,80% high molecular weight poly-vinyl chloride, 1% N,N,N',N'-tetracyclohexyl-3-oxapentanediamide (calcium ionophore), 0,6% potassium tetrakis (4-chlorophenyl)borate (ion exchanger) [30]. The result is a still flexible channel presenting a double functionalization on its surface. The textile electrode functionalized with PEDOT:PSS and ion selective membrane was tested by potentiometry to evaluate the selectivity of the membrane. The potentiometric measurements were carried out using the doubly functionalized textile fiber as indicator electrode and an Ag/AgCl wire as pseudoreference electrode. The potential variation of the pseudo-reference Ag/AgCl electrode was taken into account calculating it on the basis of chloride concentration, according to Nernst's equation applied to the reduction of AgCl to Ag°. The calculated value was then added to the measured EMF in order to obtain the corrected potential ascribable to indicator electrode (Platinum or textile fiber coated with ion-selective membranes). The potentiometric selectivity of functionalized textile electrodes was evaluated according to the fixed interference method [31]: for this purpose, KCl ranging from 10^{-5} to 1 M with or without interfering ions (Na^+ or Ca^{2+} at a fixed concentration of 10^{-3} M) was used in order to assess the selectivity. The results of potentiometric characterization are reported in Supporting information (Figure S1). To evaluate the textile OECT device performance, 500 μL of electrolyte solution was placed in the plastic box in such a way to completely cover all the electrodes. In this respect, it is important to note that the output characteristics are not altered by bending the textile electrode.

Device characterization

The main physical quantities measured on OECT device are two currents, the drain current (Id) and the gate - source current (Ig), respectively flowing through the channel and through the liquid. The currents are generated by two applied voltages, the drain source voltage (Vds) applied on the channel, and the gate-source voltage (Vgs) applied on the gate. OECT performance is evaluated by measuring Id vs time, for a fixed Vds = -0.05 V and setting Vgs in the 0 and 1 V range using 0.2 V steps. Transfer characteristics are expressed as current modulation (or Response) $(Id\text{-}Id_0)/Id_0$ vs $Vgs.$ Current values are determined as the steady state values of the time-varying current. The application of Vds induces a drift of the holes along the PEDOT:PSS backbone, generating a Id. Upon application of a positive Vgs, the cations (Y^+) from the electrolyte enter the PEDOT:PSS channel causing its de-doping according to equation (1) [32]:

$$PEDOT^+ : PSS^- + Y^+ + e^- \rightarrow PEDOT^0 + Y^+ : PSS^- \qquad (1)$$

In the "de-doping process" [33] a decrease of the module of drain current |Id| (i.e. reduction of holes available for conduction) is induced as a consequence of positive ions incorporation into the PEDOT:PSS structure and reduction of the oxidized PEDOT$^+$ to PEDOT^0. Finally, the overall process is reversible, so when Vgs is switched off (Vgs= 0 V), ions diffuse back from PEDOT:PSS to the electrolyte, increasing the number of conducting holes and, consequently |Id|. Such a process is commonly defined as "doping" [34].

Potassium-selective OECTs were tested comparing the response at different K^+ and Na^+ concentrations. The devices were measured testing different gate voltages as a function of ion concentration. The results were reported as a function of time for different gate voltages. Analogous measurements were performed using calcium-selective OECTs and the responses at different concentration for both ion species were reported to compare selectivity.

Results and discussion

In order to characterize the realized potassium-selective txOECTs, as first approach, we analyzed the channel current as a function of time at different gate voltages for different ion concentrations. *Id* vs time plots are reported in Figure 2a for increasing Na^+ concentrations. The response does not change significantly in the range from 10^{-5} to 10^{-3} M, whereas a significant modulation increase was observed for higher concentration up to 1 M. The kinetic of the *Id* modulation (evaluated when the *Vgs* is non-zero) presents a non-complete saturation with a relatively higher time constant in the exponential behavior. This performance is related to the dynamic of inlet of the sodium ions in the PEDOT:PSS backbone [35]. Analogous measurements carried out with primary ions (K^+), reported in Figure 2b, showed a quite different behavior. In fact, the changes in the *Id* current absolute value resulted higher and increase with potassium concentration. The range of *Id* values already begins from 10^{-4} M and the variation in *Id* module increases for every concentration value up to 1 M. All *Id* modifications resulted to be reversible and the *Id* current value was restored when the *Vgs* was switched off to 0. This behavior suggests that the presence of the ion selective membrane does not hamper the diffusion of potassium ions during the doping phase when the *Vgs* is turned to 0. From a kinetic point of view, the change of *Id* current over time is faster when a gate voltage is applied and presents a faster time constant. Moreover, the time constants of the exponential change of *Id* associated to the response to K^+ resulted lower with respect to sodium. This can be explained taking into account the active role played by the ion selective membrane, allowing a diffusion of potassium ions in the PEDOT:PSS backbone faster with respect to Na^+, so determining a consequently faster de-doping process. A membrane potential develops at the ion selective membrane/electrolyte interface, and this membrane potential reduces the gate voltage, leading to an offset in threshold/pinch-off voltage; at the same time ion-transport through the ion selective membrane, results different for different ions, leading to different on/off time-constants. The selectivity in the devices measurements is related to these effects at the membrane interfaces. Figure 3a shows the values of *Id* current modulation (I_{max}-I_0/I_0), which is the response of the OECT transistor used as ion sensor. Modulation is proportional to the concentration of the cation species in solution

and is in agreement with literature data [5]. The *Id* current modulation values were plotted for different *Vgs* ranging from 0.2 to 1 V, for both sodium and potassium, at different concentrations. When exposed to sodium solutions ranging from 10^{-5} to 10^{-3}M, the txOECT current did not show significant change by varying gate voltages. Only for Na^+ concentration higher than 10^{-2} M and Vgs above 0.4V, a significant Id variation is measured but lower than that measured with potassium ions. In fact, Figure 2 also reports the data obtained with K^+ ions, showing higher modulation values in the time-depending curves, from concentration values starting from 10^{-5} M, and proportionally increasing with the ion concentration and with the gate voltage. The amplitude of the signal changes over ion concentration is significantly higher for K^+ with respect to Na^+, with a trend proportional to the potassium concentration, as reported in Figure 3a. The txOECT response reflects the selectivity induced by the membrane (figure 3b). Response was significantly higher for K^+ ions than Na^+ ions and showed a wider response range, for ion concentration higher than 10^{-4} M up to 1 M, whereas the txOECT detects Na^+ ions for concentration higher than 10^{-2} M only. Sensitivity values (*S*) of 3.49 M^{-1} and 0.71 M^{-1} were assessed with K^+ and Na^+, respectively, obtaining a selectivity factor of S_{Na}/S_K*100= 20.34 %, showing the effectiveness of the integration of the ion selective membrane in txOECTs for realization of a potassium-selective sensor. The reversibility of the sensing device is still maintained since the ion selective membrane allows the ion diffusion upon switching off the gate voltage. As an application example, if we consider the real case of monitoring different cations concentration in human sweat, we have a range of sodium concentration going from 10^{-1} to 10^{-2} M, which present a response range from 0.02 to 0.065. The range of potassium in human sweat instead is around 10^{-3} to 10^{-4} M, but has a range in the response from 0.1 to 0.3, giving a margin to detect separately the two species, in the practical application of a wearable textile device. So, even if the selectivity is limited (<10), the improvement in selectivity is relevant in practical cases, as showed here for the wearable detection in human sweat.

An analogous approach was followed for the preparation of a series of devices based on the calcium-selective membrane. The devices were realized as described in the experimental section and their responses as a function

of Vg are reported in figure 4. The Ca^{2+} ion selective membrane produced a lower response to Na^+ interfering ions with respect to Ca^{2+} primary ions for all the tested concentrations. The response to Na^+ was measured in the 0.1 range, whereas Ca^{2+} generated higher signals at all the Vg values, significantly increasing with ion concentration from 10^{-4} M up to 10^{-1} M and reaching a maximum value of 0.8 V for Vg=1V. The 0.6 value obtained with potassium-selective txOECTs under analogous conditions is probably ascribable to the different charge of ions. The correlation between the outputs from Ca-selective txOECTs and calcium concentration resulted less linear if compared with response to potassium exhibited by K-selective txOECTs; however, a remarkable increase for each concentration step was observed. Sensitivity values S_{Ca}=6.64 M^{-1} and S_{Na} = 0.81M^{-1} were assessed for calcium and sodium, respectively, giving rise to a selectivity factor S_{Na}/S_{Ca}*100=12.19 %, obtained from the combination of kinetic and response data. Hence the steady response of PEDOT:PSS is cation-specific with moderate selectivity factors (around 10). Finally, the maximum response of the OECT to potassium/calcium present values up to 0.6 and 0.9 respectively, which are around one order of magnitude higher respect to sodium response. The correlated applied Vgs voltage at which the response is higher, as expected, are 0.8 V and 1 V, which are a compatible range for OECT measurements and present the most important de-doping effect. This work has been specifically performed to build a device on textile substrate, to exploit its specific industrial and technical advantages. The selectivity factor improves with membranes, and even if for OECT on silicon substrate it is possible a selectivity factor of around 3 times for potassium, here we have a factor 5 for potassium and a factor of 10 for calcium. Even if the improvement is limited, the textile fiber device with a ion selective membrane demonstrate to improve OECT selectivity, in such a way to be to be applied in real cases (human sweat).

To improve the information on the de-doping process and obtain supplementary data to increase selectivity, a detailed analysis of the kinetic processes in the modulation of the device was performed (Figura 5). Thus, by fitting the Id current over time with an exponential curve upon application of a Vg ranging from 0.2 V to 1 V when the de-doping process takes place, a characteristic time constant τ is calculated for each curve representing the de-doping kinetic occurring at the OECT channel, as reported in [36]. More details of the fitting process and τ

calculation are described in supplementary data (Figure S2). Figure 5b shows response values as a function of the calculated τ for each applied gate voltage; five different Vg values were considered for different concentrations of NaCl and KCl, ranging from 10^{-5} M to 1 M. The collocation of data points in the Response/τ plot is different for each salt, the overall range of τ value is comparable with what is reported in literature [16]. NaCl present long τ and low response values, whereas KCl data lie in short τ and high response area. Moreover, in each area, the position is also dependent on the concentration value, moving from long τ and low response to short τ and high response over ion concentration increase. These findings demonstrate that the ion selective membrane induces a distinction not only in the intensity of response but also in the kinetic of ion diffusion, so allowing to improve the discrimination between different salts. This specific property of the de-doping process increases not only selectivity but also quantitative sensitivity for different concentration values, associated to different τ and similar response values. As shown in figure 5b, the bi-dimensional representation of response and τ constant allows to discriminate different ion concentrations, making the txOECTs sensors suitable for quantitative purposes and increasing their ability to accurately measure the chemical properties of the solution investigated. Respect to other OECT measurement at different frequencies [15], here we exploit all the potential information in steady state (or very low frequency) condition. Moreover, these results confirm the ability of OECT to work on textile substrate as cloth integrated wearable sensors for real-time monitoring of liquid samples, especially sweat, with improved selectivity and sensitivity. In fact, experimental data shows that textile OECT is able to selectively monitor potassium and calcium in a concentration range compatible with biological levels of these electrolytes in human sweat, with features of greatest importance in medical and sport application, like easy sample absorption and extreme comfort of the wearable device. In particular, the application to human sweat allows the determination of the hydration level and the amount of salt loss in patients and athletes. The access to this data could give crucial information on personal medicine, improving athletes' performances and patients' safety.

Conclusions:

A new class of textile organic electrochemical transistor based on ion selective membrane have been realized. The approach of functionalization of textile thread has been followed, maintaining the flexibility and the hydrophilicity properties of the device. The result is to simplify the sample acquisition process and contemporary to obtain a selective detection on specific ions. The device has been tested in saline solutions with different concentration over static and dynamic regimes and as a function of different gate voltages. The selectivity of txOECT sensing devices towards specific ion concentration was verified for potassium and calcium. The introduction of an ion selective membrane, combined with the dynamic analysis of the time constants, allowed to improve significantly the selectivity of the developed devices, giving additional information on the specific kinetic of different ions. The reversible process, based on polymer channel de-doping, combined with improved selectivity allows to monitor each electrolyte in real time, by noninvasive way, directly from liquid samples. In particular, the application to sweat monitoring, could give access to physiological data currently not accessible, dramatically improving the monitoring of patients' health. The perspectives of noninvasive and wearable textile ion selective devices for sweat analysis could provide a paramount contribution in health and sports application, giving solution for big data approach.
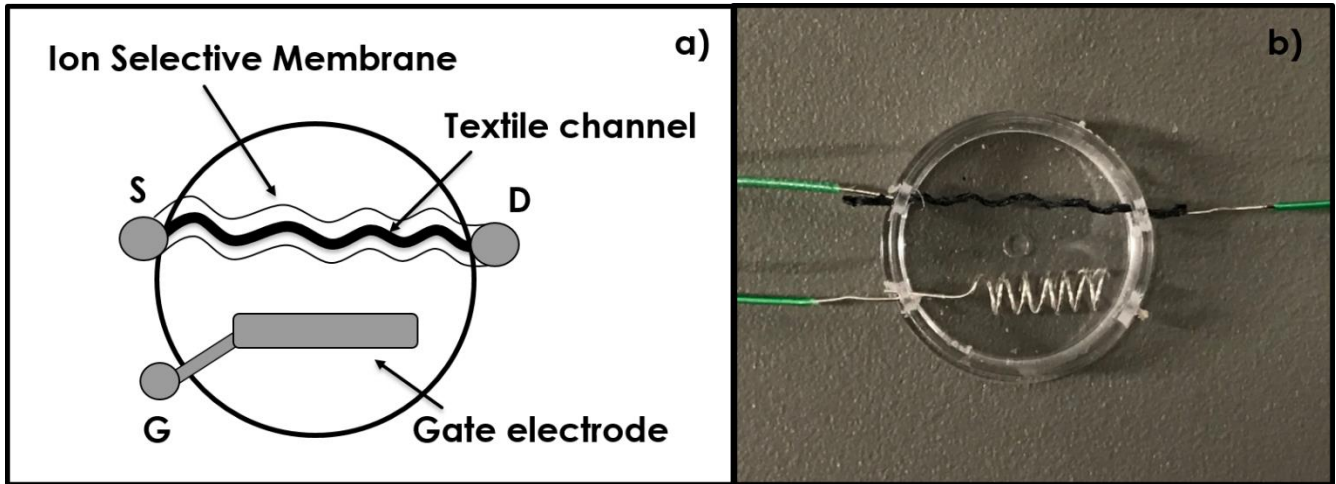
Figure1: a) Textile ion selective organic electrochemical transistor sketch, ion selective membrane deposited around textile channel is indicated in figure a, gate electrode is an Ag wire; b) real device picture, the space between the electrodes is filled with sample solutions
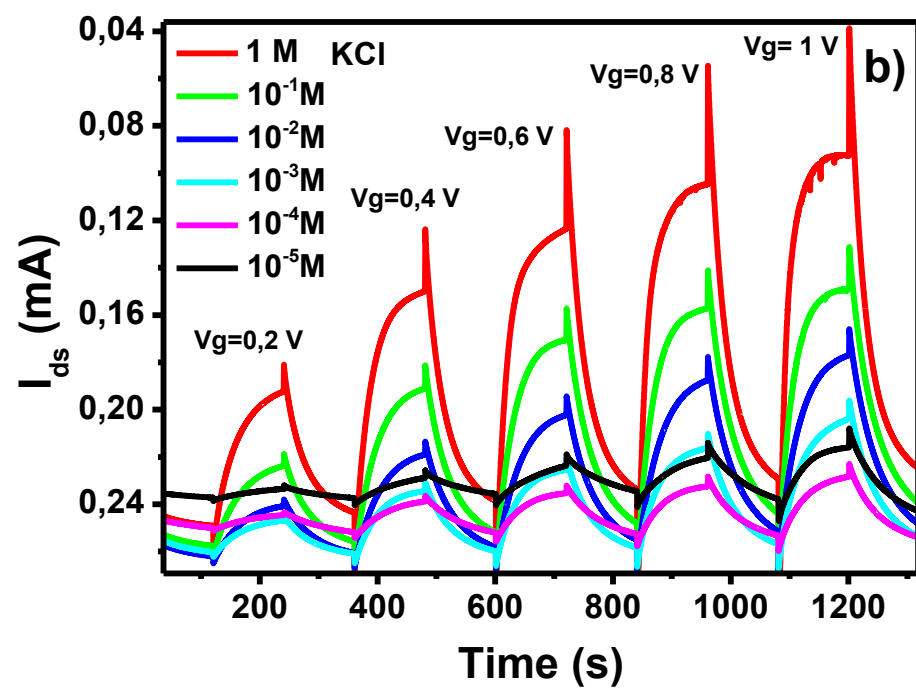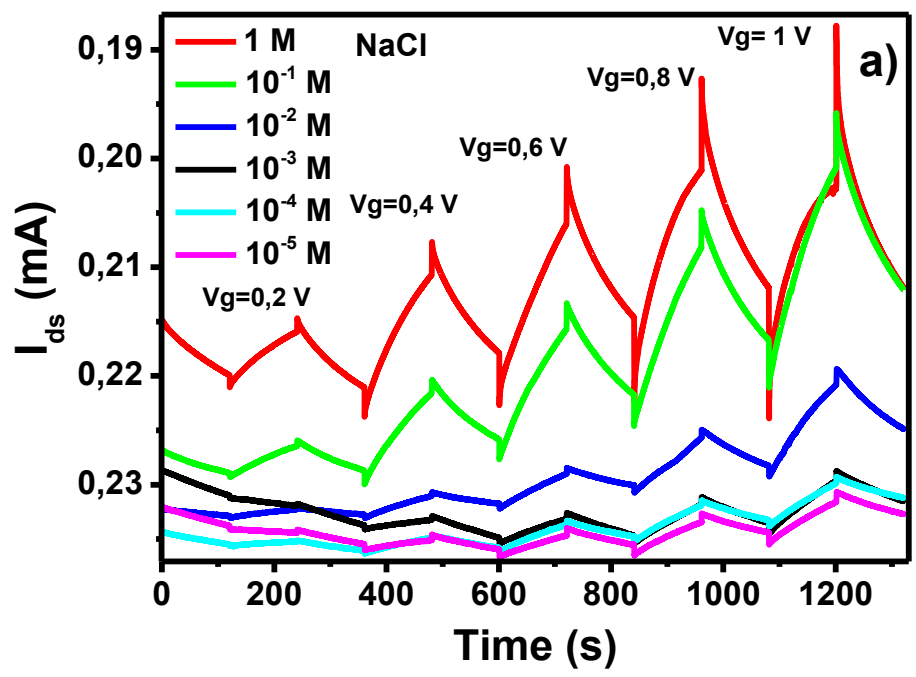
Figure 2 Responses of Textile OECT device functionalized with potassium-selective membrane. a) Channel current Id *vs* time for different gate voltage, ranging from 0.2 to 1 V with steps of 0.2 V alternate with 0 V, for NaCl concentration ranging from 10^{-5}M to 1M. b) Channel current *vs* time for different gate voltage, ranging from 0.2 to 1 V with steps of 0.2 V alternate with 0 V, for KCl concentration ranging from 10^{-5}M to 1M.
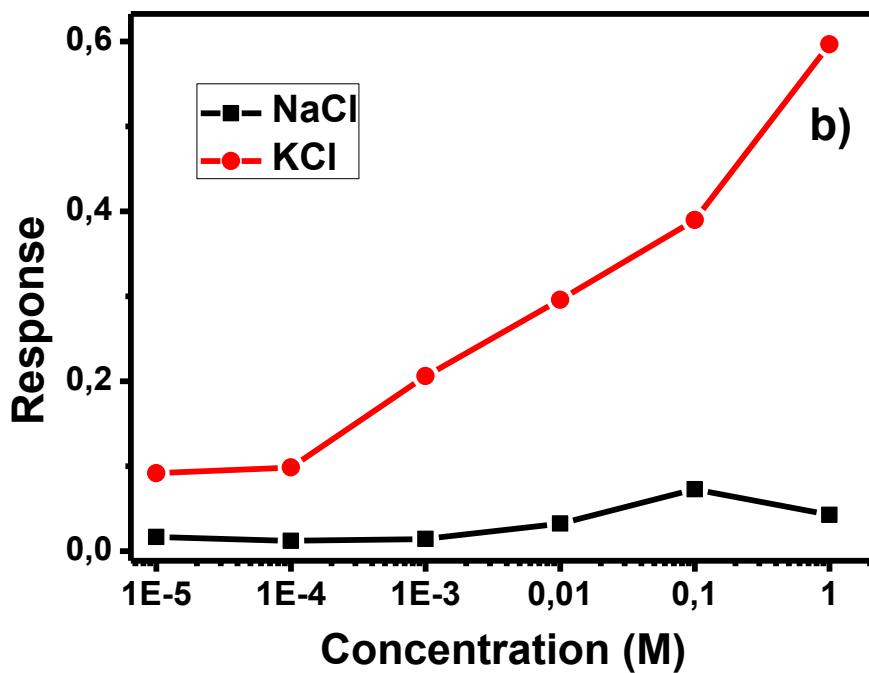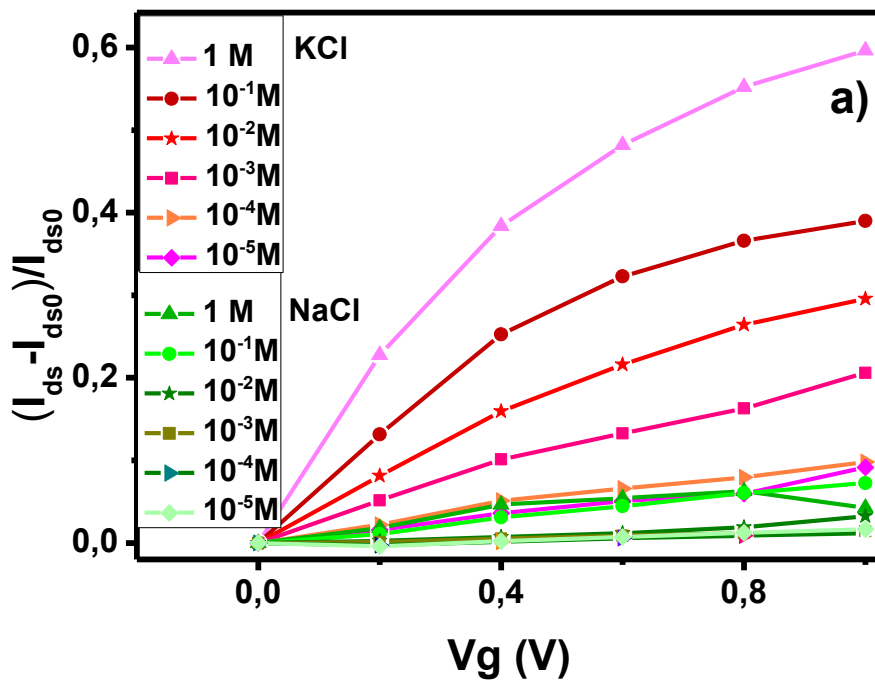
Figure 3: Comparison between responses obtained with NaCl and KCl solutions on potassium-selective textile OECT; a) Response as a function of gate voltage from 0.2 to 1 V with 0.2 V step for different concentrations of NaCl (green tones) and KCl (red tones) from 10^{-5}M to 1M. b) Responses at 1 V Vg as a function of NaCl and KCl concentrations
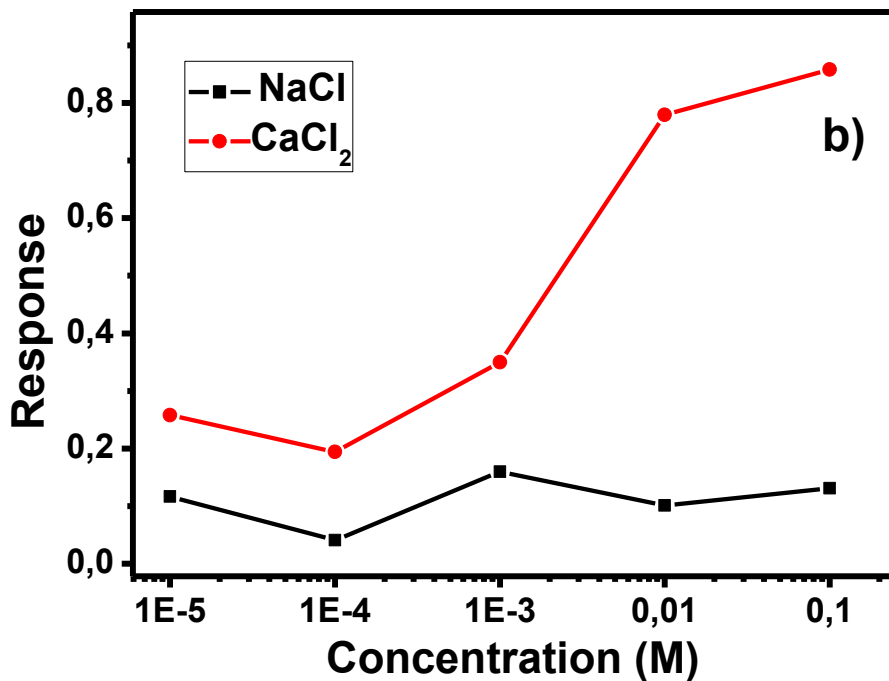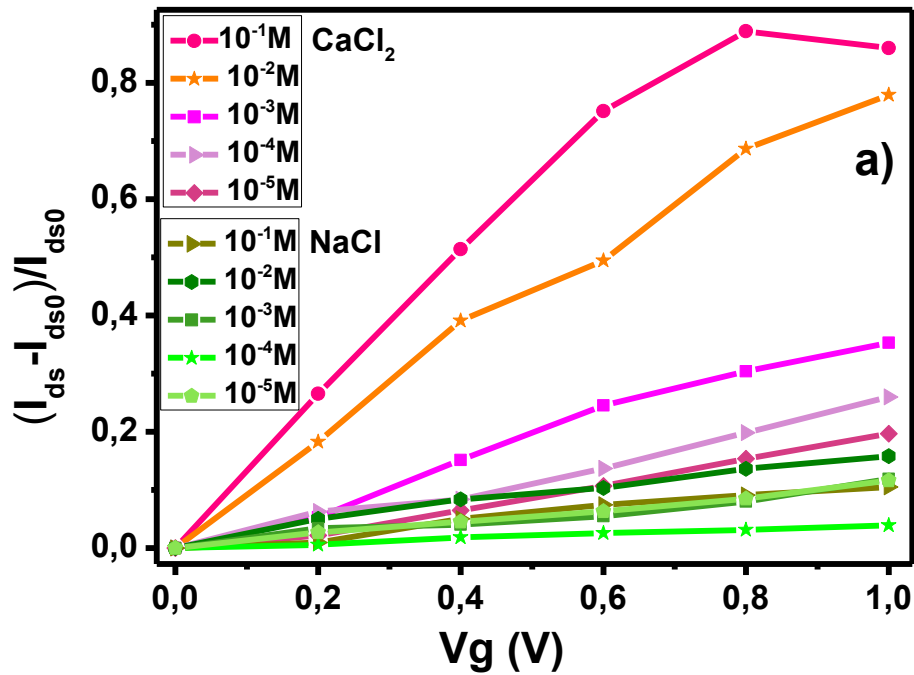
Figure 4: Comparison between responses obtained with $CaCl_2$ and NaCl solutions on calcium-selective textile OECT ;a) Response as a function of gate voltage from 0.2 to 1 V with 0.2 V step for different concentration of NaCl (green tones) and $CaCl_2$ (red tones) from 10^{-5}M to 10^{-1}M; b) Responses at 1 V *Vg* as a function of NaCl and $CaCl_2$ concentrations
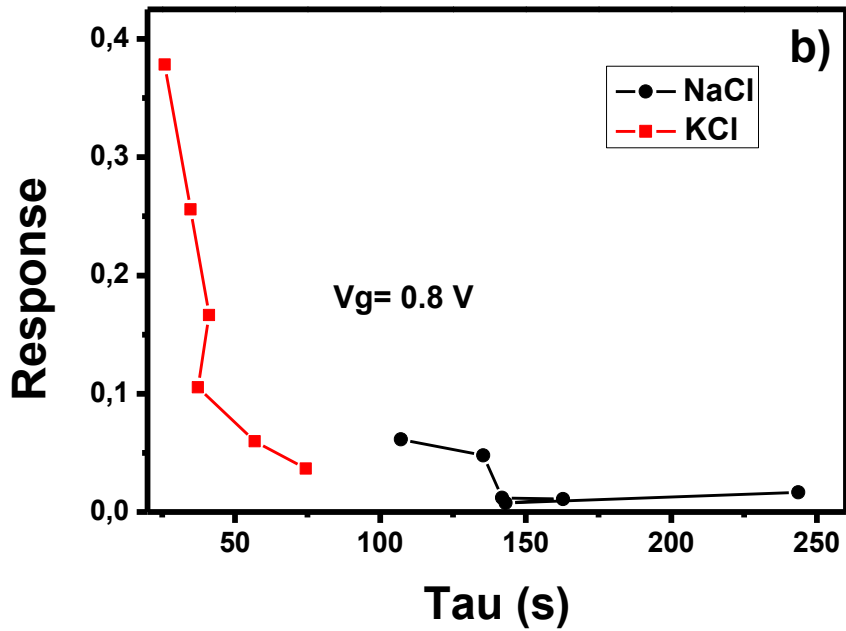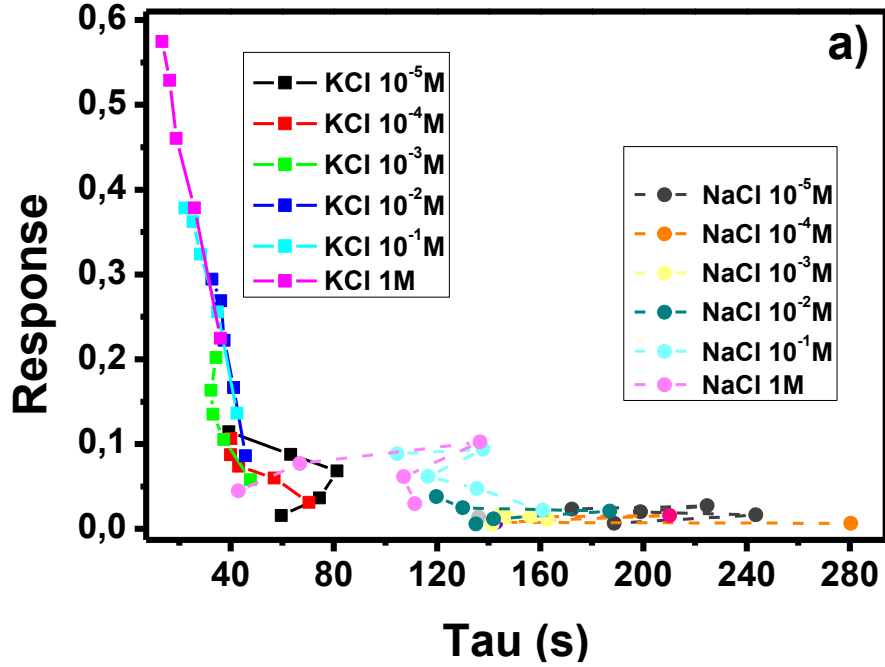
Figure 5: a) Response in terms of τ constant for NaCl and KCl solutions, obtained with potassium-selective textile OECT, for ion concentrations ranging from 10^{-5} to 1M and gate voltages from 0.2 to 1 V; b) Response in terms of τ constant for NaCl and KCl concentrations ranging from 10^{-5} to 1M and gate voltage fixed at 0.8 V.

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