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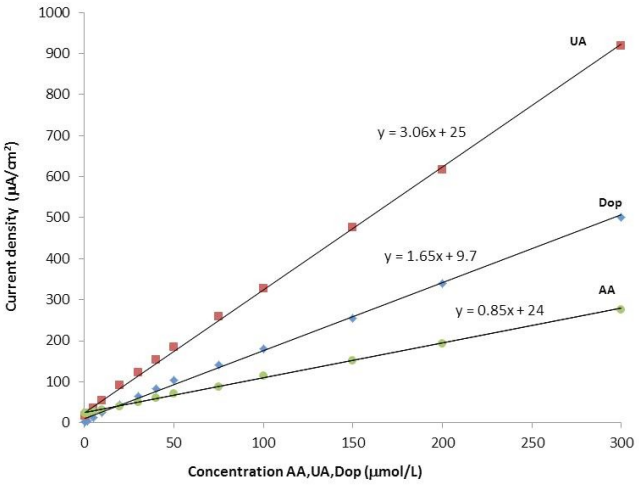

PEDOT-MODIFIED INTEGRATED MICROELECTRODES FOR THE DETECTION OF ASCORBIC ACID, DOPAMINE AND URIC ACID

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Abstract:

Integrated (Pt/PEDOT – Pt – Ag/AgCl) and (Au/PEDOT – Pt – Ag/AgCl) electrochemical microcells (ElecCell) were elaborated for the detection of ascorbic acid, dopamine and uric acid by differential pulse voltammetry. Specific attention was brought to the integration of poly(3,4-ethylenedioxythiophene) (PEDOT) film by electropolymerization. Gold and platinum working microelectrodes were investigated while using ethylenedioxythiophene (EDOT) electrodeposition processes in water or acetonitrile solvents. For the three antioxidant species, best (multi-)detection properties were obtained for acetonitrile-based PEDOT films deposited on gold working electrode. Thus, using integrated (Au/PEDOT – Pt – Ag/AgCl) ElecCell microdevices, analytical performances were determined for ascorbic acid, dopamine and uric acid, exhibiting high selectivity (oxidation potential: -40, 150 and 280 mV respectively), linear concentration range from 0.1 to 300 µM, high sensitivities (0.85, 1.65 and 3.06 µA/µM.cm^2 respectively) and low detection limit (0.2

μM, 0.1 μM and 0.05 μM respectively).

Keywords: integrated microelectrode, electrochemical microcell, PEDOT, ascorbic acid, dopamine, uric acid

1. Introduction

During the last two decades, the area of sensors has greatly benefited from the development of micro/nanotechnologies in term of design, fabrication and detection performances. This was also true for chemical microsensors and electrochemical analysis for biosensing applications. Consequently, integrated microelectrodes have become well-accepted tools for clinical, environmental, chemical and pharmaceutical applications with high spatial and temporal resolution [1,2]. Indeed, they present many advantages: specificity, high sensitivity, fast response time, small capacitive currents, enhanced mass transport, low ohmic drop allowing their use in low conducting and highly viscous media, as well as versatility. Moreover, compared to ultra-microelectrodes (UME) sealed into glass-capillaries [3-6], they take advantage of mass fabrication at low cost thanks to the use of silicon-based microtechnologies [7-9], addressing many bioanalytical applications [10-14]. Nevertheless, to realize a simple and functional electrochemical sensor, microfabrication strategies have to address the problems related to the analysis of real samples, emphasizing on sensitivity, selectivity, stability, reproducibility and reliability. We have selected this approach to develop an integrated electrochemical microsensor for the simultaneous detection of ascorbic acid (AA), dopamine (Dop) and uric acid (UA) in the frame of antioxidant species analysis.

The detection of these three analytes is of particular interest in clinical, chemical, pathology, food analysis and many other fields [15-17]. AA is a vital vitamin popularly known for its antioxidant properties and is present in mammalian brain along with several neurotransmitter amines such as dopamine. Ascorbic acid has been used for prevention and treatment of common cold, mental illness, infertility and cancer [18]. Dopamine is an important neurotransmitter for message transfer in central nervous system [19]. Abnormal levels of Dop lead to neurological disorders such as Parkinsonism and Schizophrenia [20]. Meanwhile, uric acid is the primary final product of purine metabolism. The extreme abnormalities of UA levels lead to some diseases, such as hypertension, hyperuricaemia, gout and Lesch-Nyan diseases [21].

In real biological samples, AA, Dop and UA usually coexist, so the development of accurate, selective and simultaneous determination methods for these three analytes is highly desired especially in biomedical chemistry and medical diagnostics. AA, Dop and UA are electroactive compounds and can be detected using electroanalytical techniques. Unfortunately, with bare unmodified metallic electrodes, they are oxidized at nearly same potentials and their voltammetric responses overlap makes their discrimination in real samples very difficult [22,23]. Besides, bare electrodes often suffer from a pronounced fouling affect due to the accumulation of oxidized products on electrode surface. Furthermore, the modified electrode must be insensitive to interfering chemicals present in biological media. To overcome this problem, many modification strategies have been adopted to lower the overpotential, to increase detection sensitivity and to improve selectivity. In the frame of antioxidant detection, they have led to the realisation of various modified (micro)electrodes based on quantum dots [24], nanoparticles [25-27], carbon nanotubes [28-30], graphene [25-27,29,31-33] and conductive polymers [28,34-36]. Among them, poly(3,4-ethylenedioxythiophene) (PEDOT) was one of the widely used conducting polymers for the detection of AA, Dop and UA [37-42]. It has a low oxidation potential and moderate band gap with good stability and transparency in the oxidized state, high electrical conductivity [43], excellent thermal stability, intrinsically low thermal conductivity and low price [44,45]. In parallel, electropolymerization is one of the methods used for the preparation of polymer film with good quality. It allows the reproducible formation of organic polymer films with precise spatial resolution. Moreover, film thicknesses are easily controlled by the deposition charge and the polymer is directly obtained in his conducting state [46]. Thus, electrodeposition protocol of PEDOT is easier compared to others strategies of electrode modifications. Finally, ethylenedioxythiophene (EDOT) is a commercially available monomer that eliminates synthesis steps.

In the frame of the detection of antioxidant species, PEDOT acts as a redox mediator responsible for oxidation catalysis. Since ascorbic and uric acids are in their anionic form (HA^-) at physiological pH, the occurring catalytic mechanism is globally given by [47]:

$$PEDOT_{ox} + HA^- \text{ -----> } PEDOT_{red}^- + A$$

$$PEDOT_{red}^- \text{ -----> } PEDOT_{ox} + H^+ + 2e^-$$

In the case of dopamin known to be in its cationic form at physiological pH, the global catalytic mechanism is [37]:

$$PEDOT_{ox} + Dop \text{ -----> } PEDOT_{red} + DoQ$$

$$PEDOT_{red} \text{ -----> } PEDOT_{ox} + 2H^+ + 2e^-$$

Our previous works illustrated that PEDOT deposited on hand-made microelectrodes has good catalytic properties for the electrochemical oxidation of ascorbic and uric acids and can be used for their simultaneous detection [39]. This work goes further towards technological integration and mass fabrication of PEDOT-based microelectrodes, focusing on three main goals: (i) to study the electropolymerization of PEDOT on thin-film-based microelectrodes, (ii) to integrate fully PEDOT-based electrochemical microcells (ElecCell), and (iii) to analyse PEDOT-based ElecCell performances for the selective detection of antioxidant species. Thus, combining the advantageous features of silicon-based microtechnologies [23,48] and catalytic properties of PEDOT [46], we presented here the analytic performances of integrated electrochemical microdevices modified with PEDOT electrodeposited in different conditions of polymerization for a simultaneous assay of AA, Dop, and UA.

2. Experimental

2.1 Chemicals

3,4-ethylenedioxythiophene (EDOT) monomer, poly(sodium 4-styrenesulfonate) (NaPSS), ascorbic acid (AA), dopamine (Dop) and uric acid (UA) were purchased from Sigma Aldrich. Tetrabutylammonium perchlorate (TBAPC), potassium dihydrogenophosphate KH_2PO_4, di-potassium hydrogenophosphate K_2PHO_4, sodium chloride NaCl and acetonitrile CH_3CN were purchased from Acros. All reagents were of analytical grade and used as received. The aqueous solutions were prepared with high-quality water (MilliQ gradient A10 system, Millipore, Bedford, MA). High pure nitrogen was used for deaeration.

2.2 Materials

Electrochemical Impedance Spectroscopy (EIS) measurements were made in 0.1 M NaCl solution by applying a 5 mV RMS sine wave with frequencies ranging from 10 Hz to 10 kHz. Scanning electron microscopy (SEM) studies were carried out using a focused ion beam (FIB) HELIOS 600i equipment operating at 3 kV. Samples were mounted on a double-sided adhesive carbon and optical microscope images were then made using a Hirox Microscope (HI-SCOPE advanced KH-3000). PEDOT electropolymerization and electrochemical experiments were performed using a VMP3 potentiostat (Biologic) interfaced to a microcomputer and using the EC-Lab software.

2.3 Electrochemical microcell (ElecCell) fabrication

Integrated (Pt – Pt – Ag/AgCl) and (Au – Pt – Ag/AgCl) electrochemical microcells (ElecCell) were fabricated on silicon chip using silicon-based microtechnologies (figure 1a) [23]. Oxidized silicon wafers were used in order to ensure electrical insulation between the different microelectrodes (oxide thickness: ~ 1 μm). Then, the different thin metallic layers were deposited by evaporation in conventional physical vapour deposition (PVD) equipment, and patterned using a bilayer lift-off process in order to improve fabrication reproducibility. Three PVD processes were

performed in a row: firstly, a 200 nm platinum layer was deposited on a 20 nm titanium underlayer in order to ensure platinum adhesion on silicon oxide, followed by a 800 nm gold and a 400 nm silver layers. Finally, a biocompatible Si_3N_4 passivation layer (thickness: 100 nm) was deposited at the wafer level and patterned using photolithography techniques [48]. According to this final wafer-level passivation process, the different metallic layers were insulated electrically and their active surfaces were defined precisely. The gold and platinum working microelectrodes were defined as disks and their electroactive area was approximately 4.9×10^{-4} mm^2 (diameter: 25 µm). In contrast, very large silver/silver chloride reference microelectrode (0.02 mm^2) and platinum counter microelectrode (1 mm^2) were fabricated. After the silicon wafer dicing, (Pt – Pt – Ag) and (Au – Pt – Ag) electrochemical microcells were manufactured on silicon chip (figure 1a). The whole chip was then placed and glued by an epoxy insulating glue on a specifically coated printed circuit, wire bonded and packaged at the system level using a silicone glop-top in order to be fully compatible with liquid phase measurement.

For each microdevice, the silver/silver chloride Ag/AgCl pseudo-reference was finally obtained by oxidizing the silver-based microelectrode in a 0.01 M KCl solution. This was performed by linear voltammetry (potential scan rate: 1 mV/s between 0.1 and 0.25 V/SCE) using a standard saturated calomel electrode (SCE) $Hg/Hg_2Cl_2/KCl_{sat}$ as reference. Thus, (Pt – Pt – Ag/AgCl) and (Au – Pt – Ag/AgCl) ElecCell microdevices were finally realized.

2.4 Preparation and characterization of PEDOT modified electrode

PEDOT electropolymerization processes were carried out in organic, i.e. acetonitrile-based, or inorganic, i.e. water-based, solutions.

For the organic acetonitrile-based process, the integrated working microelectrode surface was modified in a deaerated acetonitrile solution containing 2.5 mM EDOT monomer and 0.1 M TBAPC as supporting electrolyte [39]. Then, polymerization was performed by cyclic voltammetry at a scan rate of 250 mV/s between -0.88 and 1.5 V.

For the inorganic water-based process, electropolymerization experiment was performed from EDOT (0.1% W/V, 0.01 M) and NaPSS (0.7% W/V) in aqueous deaerated solutions. Such concentration was lower than EDOT solubility in water (estimated around 15 mM at 25°C) to ensure its complete dissolving. Then, cyclic voltammetry was carried between -0.9 and 1.2 V at a scan rate of 25 mV/s [49].

In both cases, i.e. acetonitrile or water solvents, the amount of PEDOT synthesized corresponded to the same anodic charge of 12 mC/cm^2. After the electropolymerization, the modified electrodes were rinsed with acetonitrile and/or deionized water in a row to remove any physically adsorbed monomer (Fig 1b).

2.5 Electrochemical experiments of PEDOT-based ElecCell integrated microdevice

For the quantitative determination of AA, Dop and UA, differential pulse voltammetry (DPV) was investigated since it is more sensitive than cyclic voltammetry. Differential pulse voltammograms were collected in the potential range between 0.2 and 0.4 V, with a 50mV amplitude, a 6 mV potential step, a 119ms pulse time, a 1s interval time and a 6 mV/s potential scan rate. Integrated (Au/PEDOT – Pt - Ag/AgCl) and (Pt/PEDOT - Pt – Ag/AgCl) electrochemical microcells were used for these DPV experiments. For each of them, gold or platinum PEDOT-modified microelectrodes were used as working electrodes whereas the platinum and silver/silver chloride microelectrodes were used as counter and pseudo-reference electrodes respectively. All electrochemical experiments were performed in a glass cell containing 100 mL of 0.1 M deaerated phosphate buffer solution (PBS, pH=7.0) with different concentrations of AA, Dop, and UA. The standard addition method was applied for drawing the calibration curves for each specie. Freshly concentrated solutions of AA, Dop, and UA were prepared and stored at 4°C. Then a small known concentration of desired element is increasingly added to PBS solutions. Currents were then plotted against the added concentrations. The limit of detection was estimated for a signal-to noise-ratio equal to three.

3. Results and discussion

3.1 Effect of EDOT solvent

The solvent used during the electropolymerisation step has a key influence on the conducting polymers ultimate properties. It should lead to a high electrical conductivity and good electrochemical stability against decomposition at high potentials required to oxidize the monomer. Thus, electrosynthesis of PEDOT is often performed in organic solvent [37,39]. Nevertheless, even if water has some drawbacks such as high nucleophilicity, narrow potential window for electrochemical stability and high EDOT oxidation potential (higher than the acetonitrile one), it was also used as solvent for PEDOT electrodeposition even if the EDOT monomer is slightly soluble in aqueous solution [49,50]. Above all these problems, the selection of water as the synthesis medium would be self-evident merely from environmental, economic and biocompatibility reasons.

Figures 2a and 2b show the cyclic voltammograms recorded during PEDOT electrogeneration on a gold integrated microelectrode, in water-based or in acetonitrile-based solutions respectively. Similar electrochemical behaviours were observed for both solvents. In water (figure 2a), the EDOT monomer oxidation starts at 0.6 V and the anodic current increases from cycle to cycle indicating the polymer growth. Then, the PEDOT redox properties are evidenced at -0.1 V. The electropolymerization potential decrease was attributed to the strong electrostatic interactions between $EDOT^{+\cdot}$ cation radicals and PSS^- species, facilitating the polymerization process [51].

In acetonitrile (figure 2b), it is clearly visible that the EDOT monomer oxidation stars at 1.2 V whereas the redox potential of PEDOT is obtained around –0.25 V. It is known that peaks position of the polymer redox activity is relative to p-doping process, leads to differences in conductivity properties [52], and might indicate that a higher molecular mass polymer is obtained when electrosynthesis is performed in organic medium. Thus, even if a similar anodic charge of 12

mC/cm^2 was chosen for the PEDOT synthesis, this should also be responsible for some thickness and morphology discrepancies for the different PEDOT layers.

To have further information on PEDOT depositions, they were characterized by impedancemetry and scanning electron microscopy (SEM). Compared to water solvent, acetonitrile leads to lower impedance modulus and therefore to higher electrical conductivity (data not shown). Such difference in term of electrical conductivity might be explained by the doping level of each PEDOT film. Indeed, the use of TBAPC, and especially the perchlorate ion ClO_4^-, as charge compensation was shown to give PEDOT films with higher doping level and better stability [53].

Nevertheless, more significant results were obtained by SEM. Figures 3a and 3b present the different surface morphologies of PEDOT layers electrodeposited on gold microelectrode while using water and acetonitrile solvents. In contrast to water-based PEDOT that forms a cauliflower-type, compact structure, acetonitrile-based ones show a porous complex structure. To the best of our knowledge, the effects of solvent on morphological features, and the correlation between the morphology of electropolymerized films and their catalytic properties were never systematically investigated. To explain the significant differences between the morphological properties of PEDOT films prepared in water or in acetonitrile, we can speculate that these changes are attributed to the different intrinsic properties of each solvent that contribute to different solute-solvent and/or polymer-solvent interactions. The best solvents were found to have high dipole moments, low polarizability and high capacity to donate electrons [54]. Furthermore, higher dielectric constants (~80 for water compared to ~36 for acetonitrile) lead to lower electropolymerization rate and to more compact films [55]. Meanwhile, we cannot exclude the factor that the solubility of EDOT oligomers produced at initial stages of electropolymerization in both solvents might be responsible of such morphological structures [56]. Certainly, in the very beginning stage of polymerization, oxidation of monomers and coupling of radical cations take place. When the chain length of oligomers is high enough, they precipitate onto the electrode, generating the first polymer nuclei. At this point, the PEDOT deposition on the electrode starts, i.e. nucleation begins, and subsequently

the propagation of polymer chains and polymer precipitation are the main processes. In water, the presence of poly-styrenesulphonate (PSS), which is a good solubilizing agent for both EDOT monomer and PEDOT polymer, facilitates the formation of relatively long polymeric chains on solution and consequently smoother films are observed. In acetonitrile, short oligomers are deposited on the electrode, leading to a high number of nucleation centres, which yield to more heterogeneous and very rough films as observed in SEM. Finally, since it was shown that the surface morphology is influenced by the polymerisation potential [57], electropolymerization at higher oxidation potential (1.2-1.5 V) in acetonitrile should produces rougher PEDOT films.

The modified microdevices were therefore tested in an equimolar solution of AA, Dop and UA 1 mmol/L pH 7.0. Results are shown in Figure 4. It is clear that the PEDOT grown in acetonitrile has much better performances than the PEDOT grown in water. For acetonitrile-based PEDOT layers, the oxidation peaks of AA, Dop and UA appear at -0.04, 0.15 and 0.28 V respectively, and higher sensitivities are evidenced. For water-based ones, oxidation of AA, Dop and UA occurs at more positive potentials, i.e. 0.125, 0.335 and 0.45 V, inducing lower sensitivities. Such results should be associated to the differences between PEDOT films in terms of structure, morphology and electrical conductivity (as shown by SEM and impedancemetric characterizations, see below). In the case of acetonitrile, rougher and more porous morphologies as well as higher electrical conductivity provide larger electroactive surface, faster diffusion phenomena in and out the polymer network, and better access to electroactive sites, enhancing PEDOT films electrocatalytic properties and improving further antioxidant detection properties [47].

Finally, even if water was successfully developed and gave acceptable results, acetonitrile appears to be the best solvent for integrating PEDOT-modified electrochemical microsensors and improving PEDOT-based detection performances of antioxidant species in terms of sensitivity and selectivity.

3.2 Effect of working electrode nature

As described previously in section 2.3, the integrated working microelectrode can be made from platinum or gold. Previous works showed that the physico-chemical properties of the anode metallic material could determine the nature and the strength of the bond between the electropolymerized polymer and the electrode, impacting its resulting properties [46]. So, we studied the influence of the metal nature on the PEDOT-based detection properties. In this view, acetonitrile solvent was used for the electrodeposition of PEDOT films on gold and platinum working surfaces (see section 3.1). Then, the electrochemical performances of the PEDOT-modified working microelectrodes were evaluated in an equimolar solution of AA, Dop and UA 1 mmol/L pH 7.0. For comparison, bare gold and platinum integrated microelectrodes were also studied in the same way. Results are shown in figures 5 and 6.

For bare gold and platinum microelectrodes, a badly defined peak and low current values are observed (figure 5). Such amperometric responses were related to competitive oxidation phenomena between AA, Dop and UA. Indeed, by studying separately each analyte (result not shown), their respective oxidation potentials appear at 0.26, 0.42 and 0.47 V on gold microelectrode, and at 0.32, 0.28 and 0.52 V on platinum microelectrode, in agreement with previous results [22,23].

On PEDOT-based microelectrodes made from gold or platinum, three well-defined oxidation peaks are observed corresponding to the oxidation of AA, Dop and UA respectively (figure 6). Compared to the broad and overlapped amperometric responses obtained with bare electrodes, all above results clearly validate the catalytic activity of PEDOT for the electrochemical oxidation of AA, Dop and UA by lowering the oxidation potential and increasing the current [37,38,47]. Nevertheless, electrochemical performances are still slightly lower on platinum PEDOT modified microelectrode: the peak potentials are shifted to more positive values, and more precisely at 0.01, 0.215 and 0.34 V respectively (compared to -0.04, 0.15 and 0.28 V, see section 3.1), and with lower sensitivities. Earlier, by studying the experimental conditions of polymerization, we have observed that the morphological properties of PEDOT films determine to a large extent the catalytic behaviour for the assay of AA and UA [39]. So, this electrochemical performances discrepancy could be also due to

the electrical, morphological and structural properties of the resulting polymers. Indeed, through impedancemetric characterization, PEDOT synthesized on gold is confirmed to have the higher electrical conductivity compared to platinum one. These differences can be due either to the intrinsic conductivities or to the roughness of PEDOT films [49]. Furthermore, SEM characterizations show that acetonitrile-based PEDOT films deposited on platinum surface show less porous structure than those deposited on gold surface (figures 3b and 3c). On the other hand, PEDOT adhesion is best on gold surface due to the strong interactions between gold and sulphur atoms [58,59]. Thus, compared to platinum-based ones, (Au/PEDOT – Pt – Ag/AgCl) ElecCell integrated microdevices are more suitable for the simultaneous electrochemical determination of antioxidant species at millimolar concentration levels.

3.3 Analytical performances

According to our previous results and optimizations (see sections 3.1 and 3.2), acetonitrile-based PEDOT electrodeposition was performed on gold microelectrode. Since silicon-based integration enables mass fabrication, these investigations were performed for five different (Au/PEDOT – Pt – Ag/AgCl) electrochemical microcells. Figures 7a, 7b and 7c represent the DPV responses of the PEDOT-modified microelectrodes to various concentrations of AA, Dop and UA respectively. Calibration plots indicate an excellent linearity of the amperometric responses with AA, Dop and UA concentrations at -0.04, 0.15 and 0.28 V respectively (Figure 8). For AA, an excellent linear relationship (sensitivity: 0.85 $\mu A/\mu M.cm^2$) was obtained in the concentration range from 0.5 to 300 µM, with a limit of detection estimated at 0.2 µM for a signal to noise ratio of 3. Then, the calibration for dopamin was also found to be linear in the range of 0.2 to 300 µM. In this case, a higher slope (1.65 $\mu A/\mu M.cm^2$) value and a limit of detection of 0.1 µM were evidenced. Finally, in the case of UA, a linear relationship was found again in the range of 0.1 to 300 µM with a still higher sensitivity (3.06 $\mu A/\mu M.cm^2$) and a limit of detection of 0.05 µM. All these analytical responses can be resumed as following ($R^2 > 0.998$):

- Ascorbic acid detection (oxidation potential: -0.04 V): $j\ (\mu A/cm^2) = 24 + 0.85C_{AA}\ (\mu M)$

- Dopamine detection (oxidation potential: 0.15 V): $j\ (\mu A/cm^2) = 9.7 + 1.65C_{Dop}\ (\mu M)$

- Uric acid detection (oxidation potential: 0.28 V): $j\ (\mu A/cm^2) = 25 + 3.06C_{UA}\ (\mu M)$

In term of concentration ranges, these results were well suited to the assay of these analytes in medical fields [60,61]. Compared to works reported in literature for the simultaneous determination of AA, Dop, and UA on PEDOT-modified electrodes, it is worth to note that our results were better or comparable to most of these electrodes (table 1), although analytes were used in excess for most of them. Finally, with the integrated electrochemical microdevice, it appears that a significant improvement in limits of detection was obtained compared to our previous results [39], making it more suitable for biological analysis.

3.4 Reproducibility and stability

The reproducibility and stability of the sensor were investigated by sensing studies. Ternary mixture of an equimolar solution of AA, Dop and UA 100 µM was used for the reproducible examinations of five different (Au/PEDOT – Pt – Ag/AgCl) ElecCell. The relative standard deviation (RSD) was found to be lower than 4.2% for AA, 4.5% for Dop and 3.2% for UA, suggesting that the ElecCell technology reproducibility was sufficiently good to deal with calibration. The stability of our sensors was examined in ternary mixture after being stored two weeks in air or in phosphate buffer solution (PBS). Thus, PEDOT modified microdevices retained 90% of their initial sensitivities to the different antioxidant species studies (data not shown).

4. Conclusion

We have developed fully integrated, PEDOT-based, electrochemical microcells (ElecCell) allowing the selective detection of ascorbic acid, dopamine and uric acid in aqueous media. PEDOT has been successfully synthesized on integrated gold and platinum microelectrodes while using water and acetonitrile as solvent. According to DPV characterization, results show improved detection performances in term of sensitivity and selectivity for electrodeposited PEDOT layers, emphasizing good results using water as solvent, better results using acetonitrile as solvent and best results on gold surfaces compared to platinum ones. For this last and best case, detection properties of ascorbic acid, dopamine and uric acid were studied, exhibiting well-separated oxidation phenomena (oxidation potential: -0.04, 0.15 and 0.28 V respectively), linear current variations, high sensitivities (0.85, 1.65 and 3.06 $\mu A/\mu M.cm^2$ respectively) and low detection limit (0.2 µM, 0.1 µM and 0.05 µM respectively). As a result, the ElecCell technological platform is adapted to the mass fabrication of PEDOT-modified electrochemical devices for the analysis of antioxidant species. It was applied to model solutions up to now, but should be extended to real samples of blood sera and/or urines in the frame of clinical diagnosis and/or environmental applications.

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Figures captions

Table 1. Comparison of the analytical performances of different electrochemical, PEDOT-modified, electrodes for the simultaneous detection of AA, Dop, and UA

Figure 1. Optical microscope images of
(a) the integrated (Au-Pt-Ag/AgCl) electrochemical microcell (ElecCell) device and
(b) the electrodeposited PEDOT film on the gold working electrode (solvent: acetonitrile)

Figure 2. Cyclic voltammogramms of electropolymerization at gold working microelectrode in deaerated 0.1 mol/L TBAPC and 2.5 mmol/L EDOT
(a) water-based (potential scan rate: 25 mV/s) and
(b) acetonitrile-based solutions (potential scan rate: 250 mV/s)

Figure 3. Scanning electron microscopy (SEM) pictures of PEDOT films deposited on (a) on gold surface using water as solvent, (b) on gold surface using acetonitrile as solvent and (c) on platinum surface while using acetonitrile as solvent

Figure 4. Differential pulse voltammograms (DPV) of (Au/PEDOT – Pt - Ag/AgCl) ElecCell in 0.1 M PBS pH 7.0 solution containing an equimolar AA/Dop/UA (1 mmol/L): PEDOT electrodeposited in acetonitrile solution (plain line) or in aqueous solution (dashed line)

Figure 5. Differential pulse voltammograms (DPV) of (Au – Pt - Ag/AgCl) (plain line) and (Pt – Pt - Ag/AgCl) (dashed line) ElecCell in 0.1 M PBS pH 7.0 solution containing an equimolar AA/Dop/UA mixture (1 mmol/L)

Figure 6. Differential pulse voltammograms (DPV) of (Au/PEDOT – Pt - Ag/AgCl) (plain line) and (Pt/PEDOT – Pt - Ag/AgCl) (dashed line) ElecCell in 0.1 M PBS pH 7.0 solution containing an equimolar AA/Dop/UA mixture (1 mmol/L)

Figure 7. Differential pulse voltammograms of (Au/PEDOT-Pt-Ag/AgCl) elecCell in 0.1 M PBS (pH 7.0) containing different concentrations of (a) ascorbic acid, (b) dopamine and (c) uric acid

Figure 8. Calibration curves for the three analytes: ascorbic acid, dopamine and uric acid.

ref.	E_p vs SCE (mV)			limit of detection (μM)			linear range (μM)	
	AA	Dop	UA	AA	Dop	UA	AA	Dop
[37]	-50	150	365	-	1	1	-	1-30
[38]	-80	120	275	7.4	-	-	500-3500	20-80
[39]	-94	-	308	2.5	-	1.5	5-300	-
[40]	100	250	320	-	-	-	100-500	100-500
[41]	3	210	360	10	1.5	2.7	20-1400	12-48
[42]	69	232	364	400	6	2	400-8000	6-75
this work	-40	150	280	0.2	0.1	0.05	0.5-300	0.2-300

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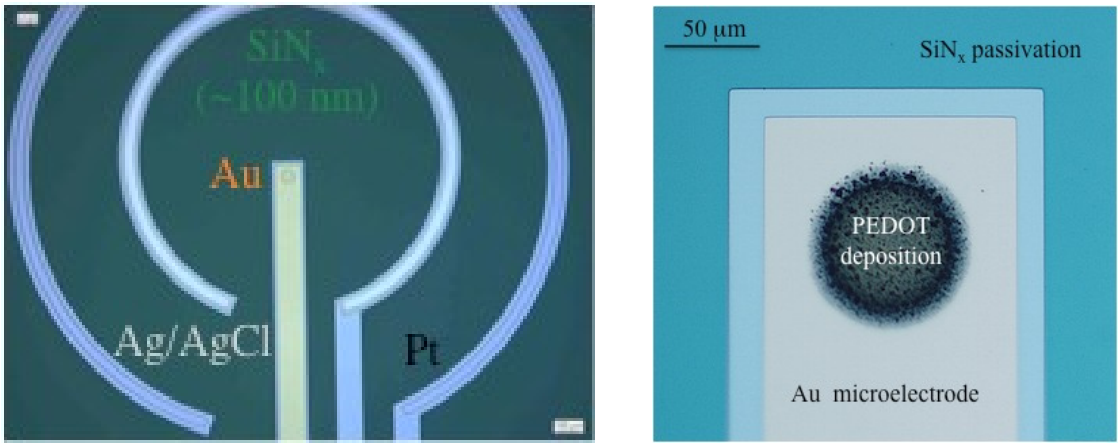

a) b)

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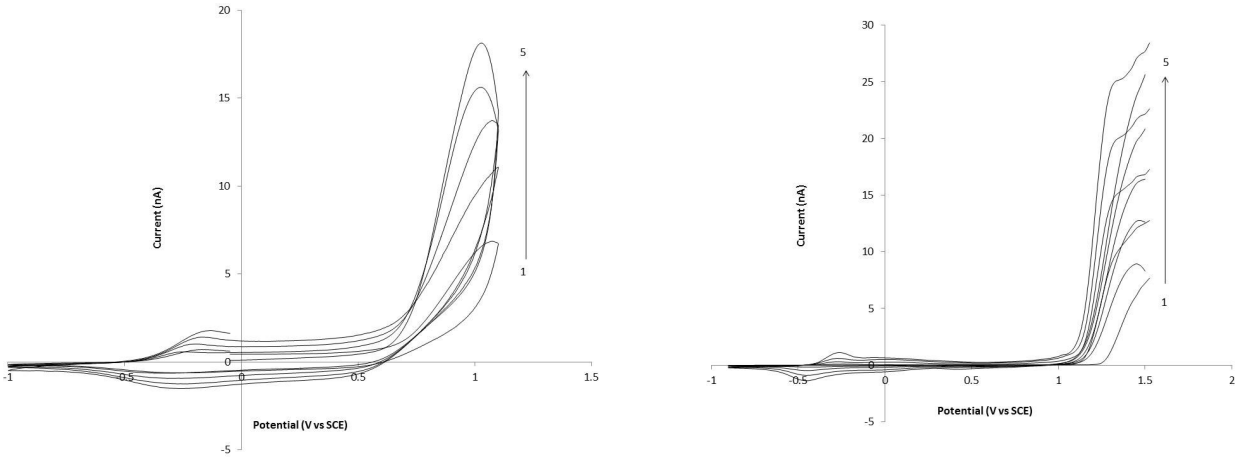

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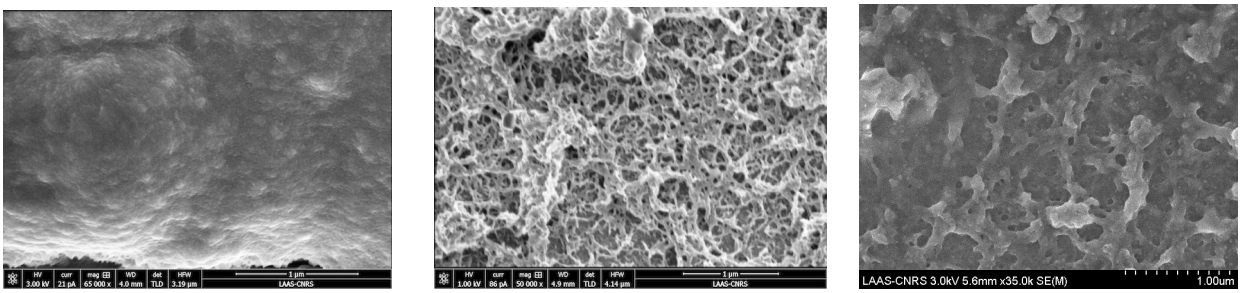

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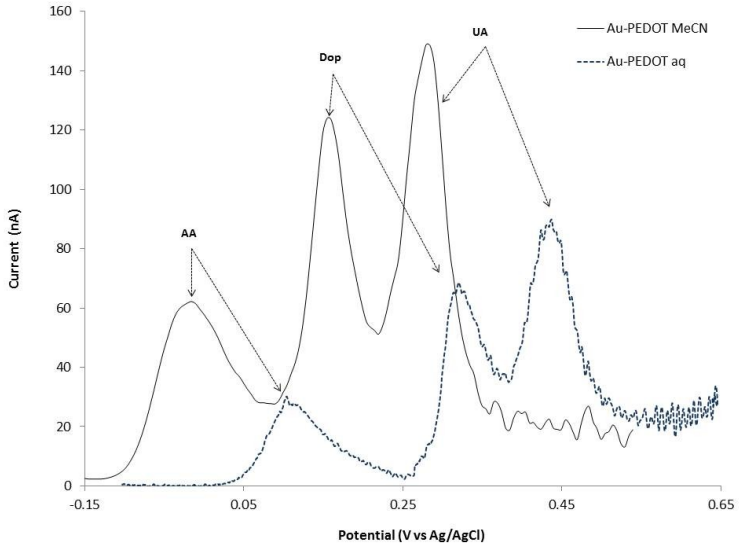

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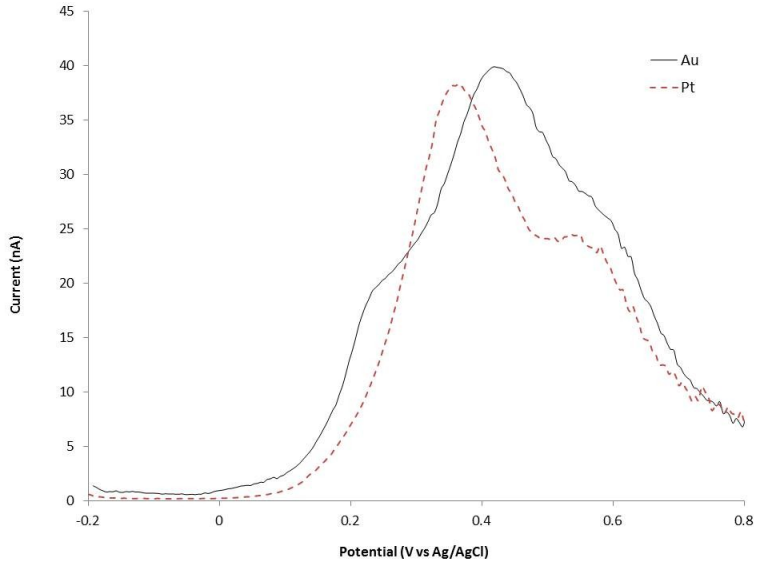

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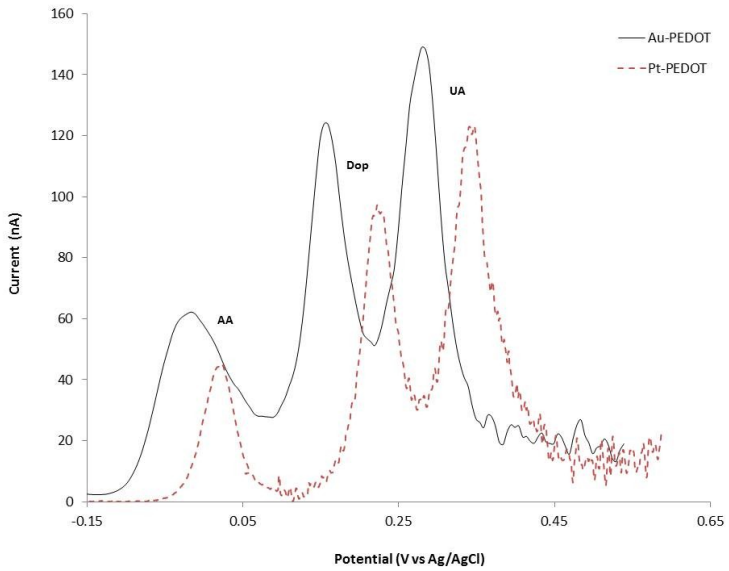

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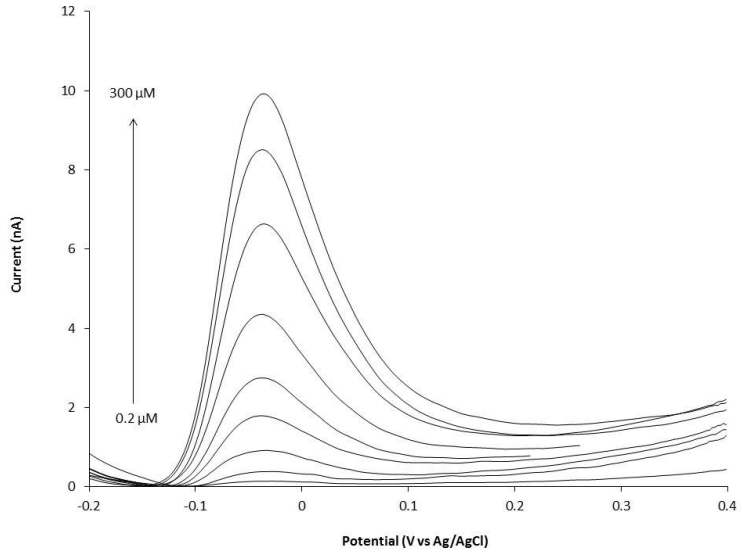
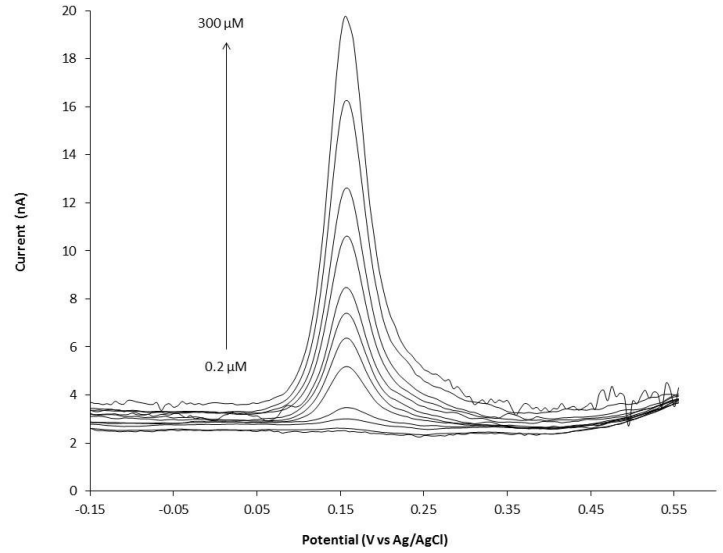
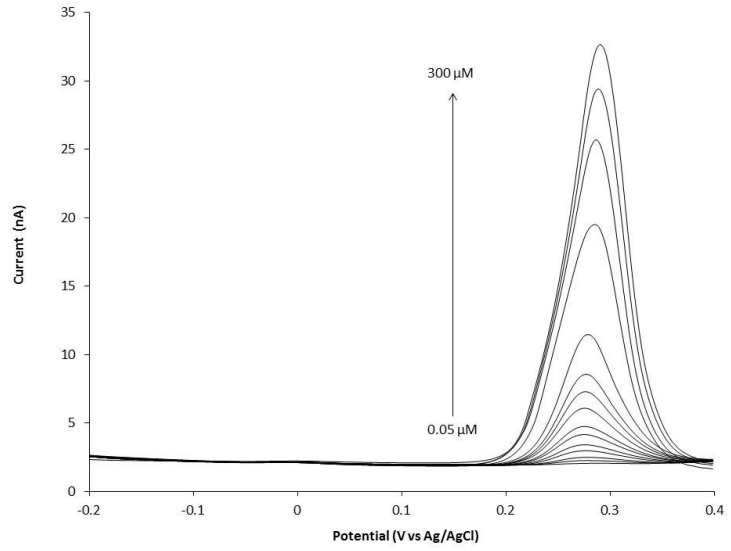

300 µM
0.2 µM
Current (nA)
Potential (V vs Ag/AgCl)

a)


300 µM
0.2 µM
Current (nA)
Potential (V vs Ag/AgCl)

b)


300 µM
0.05 µM
Current (nA)
Potential (V vs Ag/AgCl)

c)

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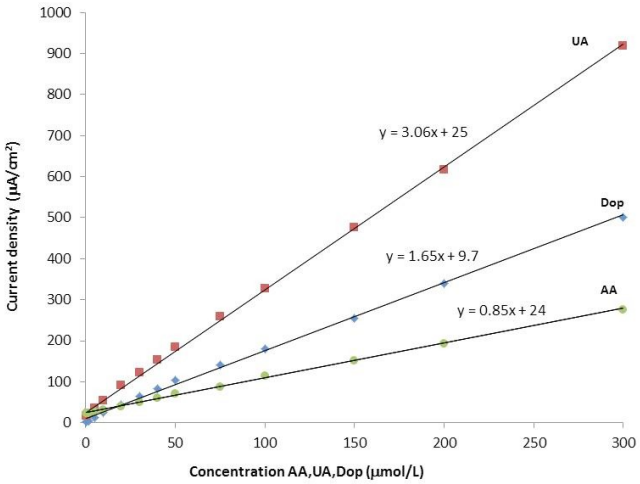

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