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HYBRID CARBON-POLYMER COMPOSITES FOR MEDICAL APPLICATIONS

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ABSTRACT
A new concept of hybrid bio-sensors are proposed for collecting microfluidic probes, in order to study and treat e.g. neurological disorders. The micro-electrode features at nanoscale are based on incorporating via electropolymerization of oxidized conjugated polymer - as charge-balancing - with dopants (e.g. Pyrrole derivatives, PEDOT, ProDOT, ProDOP and their copolymers), at the surface of carbon structures with nanopores of predefined architectures. The mechanical, fatigue and adhesion properties of the experimental coatings were assessed by using nanoindentation, high frequency impact and scratch specific tests. The electrochemical characterization (Potentiostat/Galvanostat method) was performed by using reference redox molecules such as ferricyanide, p-aminophenol, hydroquinone etc. Some applications were emphasized by testing the sensors sensitivity and reproducibility at different concentrations of dopamine, epinephrine and norepinephrine in acid medium (0.1 M HCl). In order to tailor the hybrid bio-sensors for medical applications, the potential interferences within biological samples of ascorbic acid, uric acid etc. were also taken into account. Finally, a functional on-chip model was developed, by integrating: interaction area (microelectrode exposure array), detection area (detection circuits) and processing and transmission area (signal processing and communication features).

Keywords: conductive polymers, carbon nanostructures, neurotransmitters detection

INTRODUCTION
The medical market is interested in promoting new concepts of nano-bio-sensors specialised mainly in the detection of biologically important neurotransmitters/markers. Catecholamines are a set of molecules called neurotransmitters that are released into the bloodstream. In this set of molecules are included dopamine, adrenaline (or epinephrine) and noradrenaline (or norepinephrine). All have an amino group which confers electroactivity, so that the most common analytical methods for monitoring and quantification are based on detection of electrochemical base. The neurotransmitters are involved in the functioning of renal, cardiovascular, hormonal and nervous systems, but were also related to neurological diseases such as Parkinson's, Alzheimer's and schizophrenia, were found relevant in neurodegeneration, neuroblastomas and adrenal gland cancer, and are supposed to play a role in drug addiction and some manifestations of HIV. The related microelectrodes should allow subsecond measurements during neurotransmission with minimal tissue damage.
Such biosensors must be related to the biological redox processes at the cellular and subcellular level - intended to be put in evidence. If made available, hybrid carbon/polymer micro-sensors and related lab-on-chip systems have clear advantages as regards measurements sensitivity and reliability, comparing to conventional metallic / Pt + Au

electrodes, and represent a consistent step forward. Carbon nano-structures can be formed with unique structures, architecture and dimensions, which together with chemical, electronic and mechanical properties make them interesting for development of new micro-electrodes (P. Salazar, I. Ojeda 2012). On the other hand, conductive polymers provide a high electrocatalytic capacity, by reducing the necessary potential for oxidation or reduction of numerous molecules (I. Ojeda, 2012). Accordingly, the incorporation via electropolymerization of such polymers - as charge-balancing (e.g. Pyrrole derivatives, PEDOT, ProDOT, ProDOP and their copolymers), at surface of carbon nano-structures represents an important breakthrough (S. Cetiner, 2010).

MICROELECTRODES DESIGN AND PREPARATION

Carbon nanostructures have unique architecture and dimensions, which together with chemical, electronic and mechanical properties make them interesting for the development of new sensors and electrochemical assays. Carbon nanostructures: carbon nano-fibers, multiwall nanotubes and single wall nanotubes can be used as electrode material, facilitating the transfer of electrons between the electroactive species and the electrode. Having high electrocatalytic capacity, they can reduce the necessary potential for oxidation or reduction of numerous molecules. On the other hand, conducting polymers are very interesting as electrode materials by having a conductivity type, which depends on the charge and the environment in which they are located. One of the most interesting conductive polymers is PEDOT - poly (3,4-ethylenedioxythiophene) poly(styrenesulfonate) - a polymer mixture of two ionomers. In order to better understand the electrochemical activity of micro-electrodes, in Figure 1 the activity of PEDOT and carbon electrodes is comparatively presented. By using PEDOT working electrodes, a considerable increase in oxidation and reduction current of the reference species is achieved. In hydrochloric acid medium a redox process (approximately 350 mV) is observed, due to polymer electrochemical characteristic.

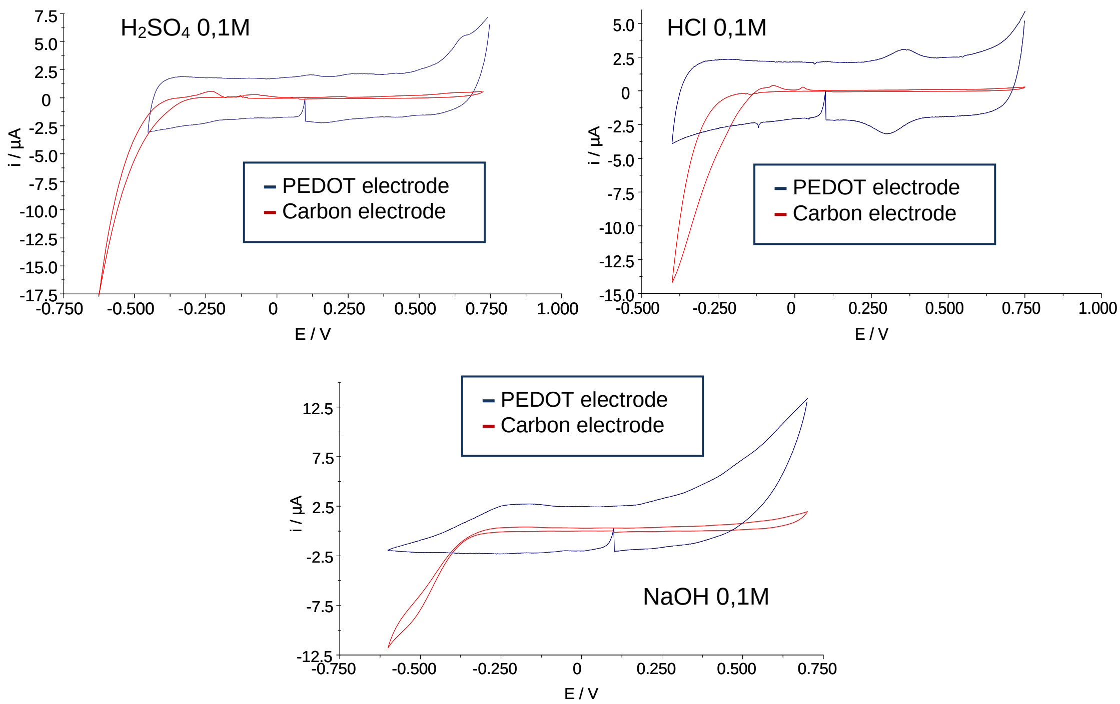

Fig. 1. Electrochemical behavior of PEDOT (blue line) and carbon electrode (red line) in different experimental electrolytes.

But these materials considered alone may offer only a partial view, comparing to their synergetic potential when associated in a new concept of hybrid electrode. Among the various methods of synthesis of such hybrid carbon-polymer electrodes, two methods are generally considered: electropolymerization on the carbon electrode surface and chemical polymerization in the vicinity of carbon material support. The first type of synthesis is based on electrochemical oxidation of the monomer by applying an oxidation potential or current, resulting free-radical cations that are coupled together and give rise to polymer repetition. Finally, a polymeric film is directly chemically bonded to the electrode surface. Chemical polymerization is based on adding an oxidizing agent to a monomer solution. This agent chemically oxidizes the monomers, generating new free-radical cations which initiate polymerization and coupling between them, forming the polymer. Finally the polymer attaches to the carbon support. The electropolymerization is obviously a simpler process (may be done at room temperature) and more reproducible ar regards micro-electrode architecture, having a higher control on the layout and thickness of the polymer film (by controlling the application time of the current or potential). However the process may be associated with the chemical one, involving individual modifications of each micro-electrode. An example of typical architecture of hybrid microelectrode is shown in Figure 2.

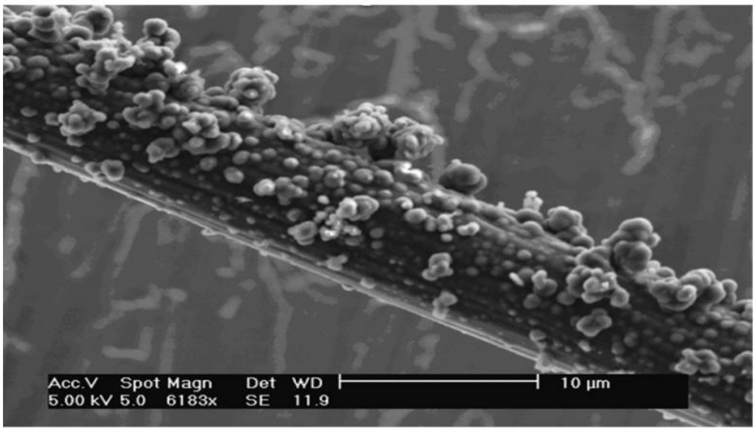

Fig. 2. Nano-active surfaces generation, by polymer electrocoating on carbon microelectrode

Such an example is given for a hybrid polyaniline – carbon micro-electrode. Polyaniline has unique properties, being one of the few conductive polymers which are stable in air, with high conductivity when it is protonated and able to easily bind many proteins. An aqueous solutions of 1M of H_2SO_4 and 0.1 M of aniline were prepared with triply distilled water. Prior to use, aniline was distilled to remove all oxidizing impurities and stored in a dark place. The suspension of dopamine was prepared in1M of H_2SO_4 by mixing for 1 hour. The final solution with 1M of H_2SO_4, 0.1M of aniline and buffers was ultrasonically treated prior to measurements. In this case, the tests involved the working polymer – carbon fiber micro-electrode, a silver wire as reference electrode and a platinum wire as counter electrode. The reference electrode was externally calibrated using 5mM ferrocene electrolyte solution. The electrochemical oxidation of dopamine on hybrid microelectrode was recorded in 0.1M phosphate buffer solution, pH = 7, using cyclic voltammetry by 2 scans.
In Figure 3, the electrochemical responses of normal and hybrid carbon microelectrodes in buffer, and respectively buffer with dopamine solution, in the potential range between -1V and 1V, are comparatively analysed. The preliminary results were very spectacular, i.e. the hybrid electrode is sensitive at dopamine, unlike original normal carbon microelectrode which is completely insensitive.

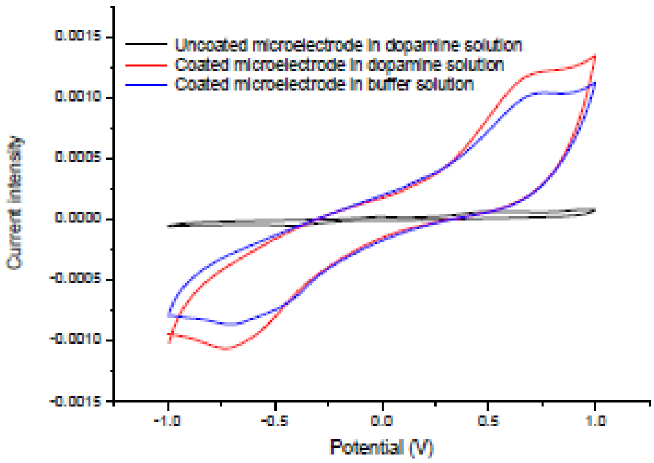

Fig. 3. Cyclic voltammograms for: uncoated carbon microelectrode in dopamine solution (black line); hybrid microelectrode in dopamine solution (red line) and hybrid microelectrode in buffer solution (blue line).

By the electrocoating process of electrochemically active polymers on carbon fiber microelectrodes, very sensitive electrodes can be obtained, for the detection of low/very low neurotransmitters content. When e.g. dopamine is oxidized on micro-electrodes, some polymeric oxidation products are formed, and are irreversibly bounded to the electrode surface during the analysis. As a result, the regeneration of electrode surface may be a crucial problem. But the new technology offers the possibility of producing large mass of disposable electrodes to overcome this drawback, and can lead to new concepts of lab-on-chip systems.

DEVELOPMENT OF FUNCTIONAL SENSORS

The development of functional sensors presumes the analysis of hybridisation of different carbon nanostructures: carbon nano-fibers, multiwall nanotubes MWCNT and single wall nanotubes SWCNT. The mechanical, fatigue and adhesion properties of the experimental coatings were assessed by using nanoindentation, high frequency impact and scratch specific tests. The electrochemical characterization (Potentiostat/Galvanostat cyclic voltammetry method) was performed by using reference redox molecules such as ferricyanide, p-aminophenol, hydroquinone etc. Comparing to metal or common carbon electrodes, an improved detection limits was noticed with respect to hybrid carbon electrodes, as presented in Figure 4 for carbon fiber, SWCNT and MWCNT / polyaniline hybrid electrodes. It was noticed that, even if in relation to hydroquinone all carbon types used for hybrid electrodes seemed to offer homologue information, in relation with neurotransmitters the carbon nanotubes are obviously more efficient, especially single wall nanotubes. More than this, extended tests on different types of hybrid electrodes based on carbon nanotubes emphasized a high sensitivity and reproducibility at different concentrations of dopamine, epinephrine and norepinephrine in acid medium (0.1 M HCl), but provided also selectivity to each molecule studied. In order to tailor the hybrid bio-sensors for medical applications, the potential interferences within biological samples of ascorbic acid, uric acid etc. were also taken into account, and the results emphasized once again the superiority of hybrid carbon-nanotubes electrodes. The results obtained have shown a high electrocatalytic capacity, higher signal intensities and improved analytical electron transfer of hybrid carbon nanotubes electrodes in comparation with conventional carbon electrodes and therefore they can be used in the detection of catecholamine too, especially the SWCNT-based electrodes (P. Fanjul-Bolado and Dropsens – Spain team, 2009-2012).

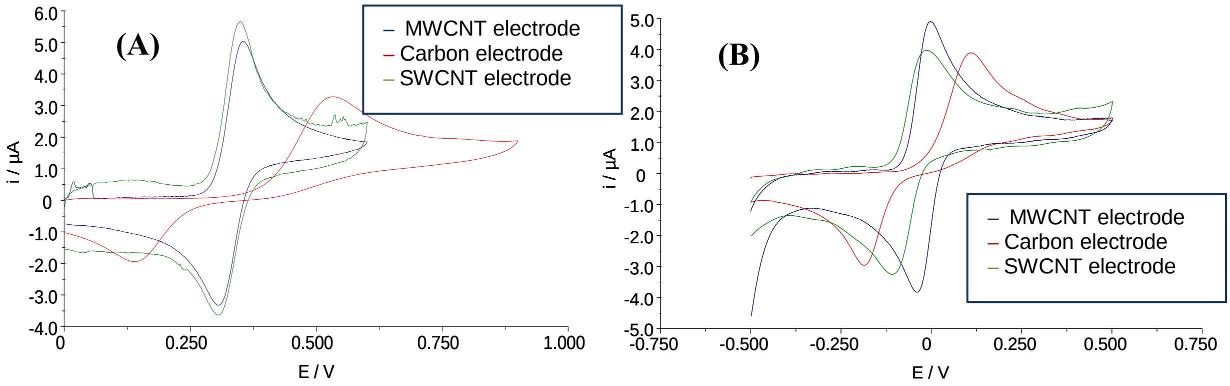

Fig. 4. Electrochemical behavior of hybrid polyaniline / carbon fiber electrodes (red line), / multiwall nanotube electrode - MWCNT (blue line) and / nanotube monopared electrode - SWCNT (green line), both functionalized in the presence of dopamine (A), and hydroquinone (B).

A functional on-chip model is under development, by integrating: microelectrode exposure array, detection circuits and signal processing and communication features (M. Neves, 2012).

CONCLUSION

A new concept of hybrid bio-sensors are proposed with a large domain of medical applications. By the electrocoating process of electrochemically active polymers on carbon nano-structures, very sensitive electrodes can be obtained, for the detection of very low neurotransmitters content. The results obtained have shown a high electrocatalytic capacity, higher signal intensities and improved analytical electron transfer of hybrid carbon nanotubes electrodes comparing to conventional carbon or metal electrodes. The new technology offers the possibility of producing large mass of disposable electrodes to overcome the drawbacks of active surface regeneration and reversibility, lading to new concepts of lab-on-chip systems.

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