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Molecularly Imprinted Polypyrrole Based Impedimentric Sensor for Theophylline Determination

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ABSTRACT

In this study development of impedimetric sensor based on oxygen terminated boron-doped nanocrystalline diamond (B:NCD:O) modified with theophylline imprinted polypyrrole is described. Hydrogen peroxide induced chemical formation of polypyrrole molecularly imprinted by theophylline was applied for the modification of conducting silicon substrate covered by B:NCD:O film. Non-imprinted polypyrrole layer was formed on similar substrate in order to prove efficiency of imprinted polypyrrole. Electrochemical impedance spectroscopy was applied for the evaluation of analyte-induced changes in electrochemical capacitance/resistance. The impact of polymerization duration on the capacitance of impedimetric sensor was estimated. A different impedance behavior was observed at different ratio of polymerized monomer and template molecule in the polymerization media. The influence of ethanol as additive to polymerization media on registered changes in capacitance/resistance was evaluated. Degradation of sensor stored in buffer solution was evaluated.

1. Introduction

Interest to various forms of diamond films and particles is growing up due to their unique properties such as biocompatibility, hardness, chemical inertness, stability of electrical properties and many others. Nanocrystalline diamond (NCD) films are used in biomedicine as a scaffolds for cell growth [1], in electrochemistry as substrates for functionalization [2] and deposition of MIPs [3]. Various technological applications of NCD are well summarized in reviewing source [4]. Undoped diamond is an insulator and it cannot be used as electrode material. It was demonstrated, that natural or undoped diamond has bandgap of 5.45 eV and resistivity in range of 10^{20} $\Omega\times$cm [5]. Doping is applied in order to gain additional conductivity and other advanced properties of NCD that could be adjusted for different purposes. Chemical vapor deposition (CVD) is the main method to regulate properties of NCD by doping with B, N, P, S, O, etc.[5–7]. Boron-doped nanocrystalline diamond films (B:NCD) are semiconductors and their properties depend on boron content. Typically this boron content is in the range of 10^{18} and 10^{21} atom $\times$ cm^{-3} and the resistance of such film is in the range of 10^4 and 10^{-2} Ω, respectively [5]. Homogeneous distribution of boron in the diamond lattice also highly affect the quality of B:NCD electrodes. Characterization of boron-doped diamond electrodes by electrochemical impedance spectroscopy (EIS) showed that low "electrochemical activity" of boron-doped diamond electrodes can be influenced by partial blocking of the diamond electrode surface [8]. This partial blocking is mainly based on non-homogeneous distribution of the boron dopant in the diamond lattice, formation of structural defects and influence of the surface [9] etc. Additional regulation of B:NCD surface properties could be performed by mean of hydrogen or oxygen termination. Both hydrogen and oxygen termination are usually applied in order to change hydrophobicity of NCD or B:NCD surface. Thermal oxidation in air at high temperature

Abbreviations: B:NCD, boron-doped nanocrystalline diamond; B:NCD:O, oxygen terminated boron-doped nanocrystalline diamond; C_d, capacitance of diamond; C_{dl}, double-layer capacitance; CVD, chemical vapor deposition; MIP, theophylline imprinted polypyrrole; NCD, nanocrystalline diamond; NIP, not imprinted polypyrrole; PBS, phosphate buffered saline solution; PPy, polypyrrole; R_d, is the resistance; R_{lm}, capacity of PPy film on the B:NCD:O; R_s, is resistance of solution; R_t, resistance of polarization.

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[10], electrochemical oxygen termination [2,5], UV induced ozone oxidation [11,12], oxidation with O_2 plasma [13] are applied in order to perform termination by oxygen. Electrochemical hydrogen termination [14] and H_2 microwave plasma [15] are mostly used methods for termination by hydrogen. In some particular cases mixed termination of diamond by both hydrogen and oxygen is performed [16]. For electrochemical purposes the most important is that the presence of oxygen on the diamond surface significantly affects their electrical conductivity, chemical reactivity and other properties independently on the activation method applied [2,9]. It was demonstrated, that the oxidation of NCD film reduces their conductivity, increases surface roughness and lowers the sp^3/sp^2 ratio in comparison to hydrogenated film [15]. The same above mentioned study indicated that oxidation of NCD forms a 'wide electrochemical window' and increases film resistance, capacitance and polarization resistance.

Electrochemical evaluation of some xanthine derivatives such as caffeine, were performed on blank B:NCD electrodes [17–20]. Cyclic voltammetry was used to analyze mixture of xanthine and 3 its derivatives: theophylline, theobromine and caffeine and it was demonstrated that electrochemical oxidation of xanthine derivatives occurs according to a mechanism similar to that of purine derivative oxidation at the pyrolytic graphite based electrode [17]. The main limitation of applied method was based on the fact that the mixture of all these xanthine derivatives could not be evaluated due to the very similar oxidation peak potentials in analyzed pH range. Other mentioned studies describe electrochemical evaluation methods of caffeine in pharmaceutical formulations [18–20].

Among many other polymers polypyrrole (PPy) has number of unique properties that can be exploited in order to increase the sensitivity of electrochemical detection based analytical systems [21]. However, the combination of PPy and the NCD were investigated just for few times [22–25]. Electrochemically and chemically stable conjugated chains are formed during the polymerization of PPy [23,26]. The other very important feature of PPy and diamond system is that PPy potentially could form a covalent bond with diamond [22,24,27,28]. PPy-based systems also were applied in optical systems. For these applications the most important features are a broad-range absorption of visible light and fluorescence quenching [25,29]. The theoretical [24] and experimental [28] studies demonstrated formation of the covalent bond between the molecular chain of PPy and the NCD, which enhances both mechanical stability of system and the electron transfer to/from the contact. But in other study it was suggested that the polypyrrole is covalently attached to the diamond surface via carbon–carbon bond while replacing terminating hydrogen atom [27]. This study showed that surface conductivity of diamond decreases after deposition of PPy. But in other study it was demonstrated that PPy can form one- or two-bond interface with diamond surface [24]. Moreover, this study demonstrated that interfaces of one- or two-bond with NCD has semiconducting properties with a significant gap decrease from 2.08 eV for an infinite PPy to about 1.3 eV. It was suspected that this effect is based on changes of PPy conductance. One research demonstrates the suitability of highly boron-doped diamond microfiber electrodes modified by overoxidized polypyrrole in combination with amperometric detection for dopamine determination with high sensitivity and advanced selectivity, which excluded interference of ascorbic acid [30]. In other study the application of modified B:NCD for the selective detection of dopamine was applied. For this purpose the B:NCD electrode was modified in several steps: (i) the B:NCD was modified with sulfobutylether-β-cyclodextrin-doped poly(N-acetyltyramine) and (ii) after that on top of this film the PPy was electrodeposited. However to our best knowledge until recent time no researches on the application of diamond electrode for the electrochemical detection in combination with molecularly imprinted polypyrrole were published. But it is well known that molecularly imprinted polymers in analytical systems provide such advantages as advanced specificity. It is mainly based on two factors: (i) optimal shape of cavities formed in imprinted polymer, (ii) chemical functionalities spatially positioned around the cavity in a pattern, which is complementary to the chemical structure of the imprinted molecule [31–34].

Table 1
The CVD parameters of the B:NCD film on p-type boron-doped silicon (resistivity 10 kΩ×cm).

Deposition parameters	Values
Substrate temperature	700 °C
Microwave power	3500 W
Vacuum	5333 Pa
Methane/hydrogen	3% CH_4/97% H_2
trimethyl boron/methane	5000 ppm

The aim of this study was to construct impedimetric sensor based on nanocrystalline oxygen terminated boron-doped diamond deposited on boron-doped silicon with molecularly imprinted polypyrrole suitable for selective theophylline detection. The impact of some chemical polymerization parameters including the duration of polymerization, the ratio of monomer and template molecules and ethanol as additive in the polymerization bulk solution on impedimetric properties of obtained sensors was evaluated.

2. Experimental setup

2.1. Materials and reagents

All chemical were of analytical grade if it is not stated otherwise. 30% H_2O_2, 37% HCl, 25% NH_4OH and absolute ethanol were purchased from VWR (Fontenay-Sous-Bois, France), pyrrole - from Fluka (Buchs, USA), ultra pure H_2O was prepared with Sartorius Stedim biotech (Goettingen, Germany) system and was 0.055 μS/cm × C, theophylline was from Sigma (Steinheim, Germany). Phosphate buffered saline solution (PBS) was prepared using 1.29 M NaCl from Sigma-Aldrich (Steinheim, Germany), 54.5 mM $Na_2HPO_4 \times 2H_2O$ from Fluka (Buchs, Germany), 15.4 mM KH_2PO_4 from Sigma (Steinheim, Germany) and pH 7.0 was adjusted with NaOH from Merck (Darmstadt, Germany) using Metler Toledo (Schwerzenbach, Switzerland) pH meter. All solutions for electrochemical impedance spectroscopy were prepared in PBS.

Boron-doped nanocrystalline diamond was grown on boron-doped silicon wafer. Chemical vapor deposition method was applied and B:NCD films were grown in an ASTEX 6500 microwave plasma reactor after a pre-treatment step with a colloidal solution of ultra dispersed (5–10 nm) nanodiamond [35,36]. During B:NCD growth the temperature was monitored by a Williamson Pro92 dual-wavelength pyrometer. The detailed deposition parameters are listed in Table 1.

The growth was stopped when the B:NCD layers reached a thickness of ≈200 nm and cooling down was performed under hydrogen flow. Hydrogen-termination of B:NCD was performed by hydrogen plasma cooled down from 700 °C to 100 °C. Silicon slices of 1 cm ×1 cm were covered with B:NCD and were used as substrates for further modifications.

2.2. Boron-doped nanocrystalline diamond surface preparation

Before deposition of polypyrrole by chemical polymerization the boron-doped nanocrystalline diamond (B:NCD) was cleaned in few steps: first with 37% HCl + 30% H_2O_2 + H_2O at ratio 1:1:6 for 10 min at 70 °C temperature and following this it was cleaned with 27% NH_4OH + 30% H_2O_2 + H_2O at ratio 1:1:5 for next 10 min at 70 °C temperature. The cleaned B:NCD was oxidized by UV induced ozone