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Full Length Article

Microfabrication atomic layer deposited Pt NPs/TiN thin film on silicon as a nanostructure signal Transducer: Electrochemical characterization toward neurotransmitter sensing

Yalda Shoja^{a,*}, Noora Isoaho^b, Ville Jokinen^a, Sami Franssila^{a,*}

^a Department of Chemistry and Materials Science, Aalto University, Tietotie 3, Micronova, 02150 Espoo, Finland

^b Division of Micro and Nanosystems, KTH Royal Institute of Technology, Stockholm, Sweden

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ABSTRACT

Titanium nitride (TiN) is widely utilized in microelectrode array fabrication for electrophysiological recordings due to its relatively low noise levels, long term stability, and exceptional biocompatibility. Atomic layer deposition (ALD) is a well-established approach for the fabrication of TiN thin films, offering great control over the thickness and properties of the films. Although, advanced procedures have been reported to develop micro and nanostructured electrodes, TiN thin film has yet not been widely applied as electrode material for electrochemical sensing, and characterization of these ALD fabricated TiN films is lacking. Here, we study the use of TiN thin films as electrochemical signal transducer for neurotransmitter dopamine (DA) detection with emphasis on investigation the effect of oxygen functionalities on the electrochemical performance of the films. We find that in order to have high enough sensitivity and selectivity the electrode material used to realize the measurements must be modified. In this work, we described TiN thin film surface modification through hybridization of microfabrication and nanocomposite approaches. Because of its good adhesion, TiN is considered as a high interesting support for Pt catalyst. Therefore, ALD was used to deposit TiN thin films and to design Pt nanoparticles (Pt NPs) on highly conductive boron-doped silicon. Further modification was done through multiwalled carbon nanotubes (MWCNTs), which were immobilized on Pt NPs/ TiN hybrid electrode by Nafion film. Synergistic effect of Pt NPs, MWCNTs, and Nafion film caused significant increase in the electrocatalytic activity towards DA electrooxidation. The proposed sensor material was characterized by focused ion beam milling combined with scanning electron microscopy (FIB-SEM), X-ray photoelectron spectroscopy (XPS), transmission electron microscopy (TEM), spectroscopic ellipsometry, contact angle measurement and its electrochemical behavior was studied by cyclic voltammetry (CV). CV technique was applied for sensing DA in the range of 0.05–35 μM ($R^2 = 0.990$) with a good sensitivity (16.31 $\mu\text{A}/\mu\text{M}$) and a low detection limit of 40 nM (for $S/N = 3$). The developed sensor exhibited reasonable response time and good stability.

1. Introduction

Parkinson's disease (PD) is the second most common chronic progressive neurodegenerative disorder, with distinct motor and non-motor symptoms stemming from pathology in both the central and peripheral nervous systems [1]. The early diagnosis of PD remains limited since the understanding of the mechanism of the loss of dopaminergic (DA) neurons is incomplete. The main clinical symptoms of PD occur when approximately 70% of DA neurons in the region of substantia nigra (SN) have been lost [2]. Currently available PD diagnostics are based on clinical symptoms that can find other types of neurodegenerative

disorders [3]. To tackle these challenges, identification of biomarkers associated with PD to improve early diagnosis, to monitor disease progression and to discriminate PD from the other diseases with extrapyramidal symptoms, are needed [4–6].

Oxidative stress, which results in imbalance between reactive oxygen species (ROS) production and cellular antioxidant activity, is considered as a major factor with fundamental mechanism at the cellular level [7–10]. According to literature there are many sources of oxidative stress produced by ROS in which ROS derived by DA auto-oxidation itself can be the main oxidative stress generator [11,12]. Finally, selective loss of the DA neurons in the SN lead to dopamine depletion in

* Corresponding authors.

E-mail addresses: yalda.shoja@aalto.fi, yalda.shoja.iut@gmail.com (Y. Shoja), sami.franssila@aalto.fi (S. Franssila).

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different striatal sub-regions, and decrease DA clinical concentration to nanomolar range in PD. Consequently, it is of utmost importance to be able to do ultra-sensitive monitoring of DA. Moreover, its metabolites have been considered as a potential biomarker for the early diagnosis of PD [13,14].

Electrochemical techniques have revealed their great advantages in the fast, sensitive, and selective sensing of different neurotransmitter as PD biomarkers [15,16]. Several electrochemical approaches have been reported for DA detection based on various electrode materials, including solid-state devices and metal electrodes [17,18]. Despite the research efforts, these state-of-the-art materials are still incapable of measuring DA in a sensitive and selective manner with the demanded biocompatibility, spatial resolution, and response time.

In a recent study, high-surface-area nanostructured titanium nitride (TiN) electrode was utilized for electrophysiological recordings in neuronal cell culture [19]. This was enabled by the special combination of chemical, electrical, and physical properties including biocompatibility, hardness, inertness, thermal and oxidative stability, low cost, immunity to corrosion, and relatively low impedance and noise levels arising from the porous or columnar structure. Such nanostructured TiN thinfilm electrodes can be fabricated by sputtering, chemical vapor deposition (CVD) and atomic layer deposition (ALD) [20–22]. Controllable ultra-thin conformal and multilayer film deposition is the main advantage of ALD, stemming from the self-limiting surface reactions and separation of precursor pulses [23–26].

Electrochemical dopamine sensing suffers from interference from ascorbic acid which typically has the same oxidation potential as DA and is also present at higher concentrations in real sample. Therefore, modification of electrode surfaces by means of advanced nanomaterials and microfabrication techniques for enhanced selectivity is needed. Metal-coated TiN thin films have been presented for the development of biopotential electrodes and as the catalyst and electrocatalyst supports for the oxidation reaction and electrochemical process [13,27]. Noble metal nanoparticles such as Pt nanoparticles (Pt NPs) have attracted much attention due to their unique electrochemical catalytic activity and controllable effective surface area [28,29]. In this regard, ALD is a novel well-established technique for the direct growth of metallic catalyst nanoparticles with controllable dimensions at the nanometer scale [30,31].

It has revealed the direct electron transfer (DET) process for biomolecules that directly adsorbed on the electrode surface, can be affected by orientation of adsorbed molecules (biological incompatibility) and large oxidation potential of DET [32,33]. Appropriate biological microenvironment can be obtained by employing carbon-based nanomaterials as an interface between metal electrode and biomolecules. Carbon nanotube, (CNT)-based nanocomposites can act not only as anti-fouling agents but also as promoters of electron transfer due to their unique electronic structure. CNTs, including multi-walled carbon nanotube (MWCNT), can also prevent the slightly irreversible TiN electrochemical oxidation in aqueous electrolyte solution [23].

In this work, our aim was to i) conduct in-depth electrochemical characterization of ALD TiN thinfilms, which is currently lacking in the literature, and ii) utilize these films for DA detection. In order to improve selectivity and sensitivity of TiN electrodes over both ascorbic acid (AA) and uric acid (UA), the two main interfering species in the central nervous system, we propose here a Nafion/MWCNTs/Pt NPs nanocomposite designed to modify the TiN electrode. Nafion is a cation exchange polymer that has significant role in DA sensing because it can eliminate interference from uric acid- [34,35]. ALD was applied to fabricate TiN-based electrodes and to deposit the Pt NPs. Chemical composition and physical properties of the developed sensor was characterized by, photoelectron spectroscopy (XPS), four-point probe, spectroscopic ellipsometry, focused ion beam milling combined with scanning electron microscopy (FIB-SEM), and transmission electron microscopy (TEM). Structural data is correlated to electrochemical

cyclic voltammetry (CV) measurements. With the modified electrodes, we could detect clinically relevant dopamine levels in the range of 50 nM–35 μ M.

2. Experimental

2.1. Apparatus

Picosun R-200 advanced remote plasma-enhanced ALD tool was applied to deposit TiN and Pt NPs on highly boron-doped p-type silicon wafers (resistivity 0.001 Ohm-cm). Thickness of TiN was measured by spectroscopic ellipsometer SE-2000 (Semilab). Resistivity was measured by four-point probe Loresta. Contact angles were measured with a contact angle meter THETA (Biolin Scientific). FIB-SEM and TEM images were obtained using JEOL JIB-4700F – NMC and JEOL-2200FS FEG respectively. GMS 3 analysis software was used to process images and calculate particle sizes. XPS surface analyses were carried out using the Kratos Axis Ultra ESCA - NMC. The TiN and Pt NPs/TiN samples were diced with Disco DAD3220 dicing saw.

2.2. Materials and reagents

All chemicals, including dopamine hydrochloride (CAS Number: 62-31-7, purity > 98.0 %), hexaammineruthenium(III) chloride, (Ru(NH₃)₆^{2+/3+}), (CAS Number:14282-91-8, purity 98.0 %), ascorbic acid, AA, (CAS Number: 50-81-7, purity > 99.0 %), uric acid, UA, (CAS Number: 69-93-2, purity:>99%), potassium hydrogen phosphate (K₂HPO₄) (CAS Number: 7758-11-4, purity 98.0 %), potassium dihydrogen phosphate (KH₂PO₄) (CAS Number :7778-77-0, purity 99.0 %), were purchased from Sigma-Aldrich Chemical Co. Trimethyl-(methylcyclopentadienyl)-platinum (IV) (MeCpPtMe₃) (CAS Number: 94442-22-5, purity > 99 %) was prepared from Strem Chemicals. Titanium tetrachloride, (TiCl₄) (CAS Number: 7550-45-0, purity: >99.0%) was purchased from Fluka Analytical. Prior to electrochemical measurements, the solutions were purged with N₂ for 15 min and during measurements the electrochemical cell was retained under a N₂ atmosphere. All the electrochemical experiments were performed at room temperature. To prevent spontaneous oxidation of the analytes, (Ru(NH₃)₆^{2+/3+}), DA, AA, and UA solutions were prepared on the day of the experiments.

2.3. TiN thin film and Pt NP deposition by ALD

The TiN films were deposited on highly boron-doped p-type silicon wafers by ALD. 25 nm thick TiN took 1344 cycles. Deposition temperature was 450 °C, and precursors used were TiCl₄ and NH₃ as precursor, N₂ as carrier gas for both precursor transportation and the purging of the reaction chamber after each precursor pulse. The precursor and purge pulses were 0.1–6–0.1–2 s for TiCl₄—N₂—NH₃—N₂ respectively. Both precursors were kept at room temperature (20 °C) with Peltier cooling elements and vapor drawn from the precursor bottles. After deposition, samples designated as “TiN/N₂” had a cooldown period of 20 min in N₂ atmosphere in the loadlock. The other sample type, designated as “TiN/Air”, was cooled down in air, allowing the surface to oxidize. Pt was deposited by ALD using MeCpPtMe₃ and O₂-plasma under the optimized parameters reported previously [36]. MeCpPtMe₃ was heated to 55 °C to achieve enough vapor pressure. MeCpPtMe₃ pulse length was 1.0 s followed by a 4.0 s purge. O₂-pulse was 10.5 s consisting of 2 s flow stabilization prior to initiation of 2000 W RF power for 8 s followed by 0.5 s post plasma stabilization time. After the oxygen pulse, the reactor was purged for 10 s. Carrier gas through the plasma unit was argon whereas nitrogen was used as carrier gas for other precursors. For Pt particle size analysis 60 ALD cycles of Pt was deposited on the TiN thin film (thickness 25 nm) which was on top of 50 nm thick silicon nitride (Si₃N₄) TEM windows (Ted Pella, Inc.).

2.4. Fabrication of Nafion/MWCNTs/Pt NPs/TiN sensor

All three sample types (TiN/N₂, TiN/Air and Pt NPs/TiN) were diced into 7 mm × 7 mm pieces with Disco DAD3220 dicing saw. Nafion/MWCNTs/Pt NPs/TiN sample was developed based on modification Pt NPs/TiN/Air sample as substrate in this way that the Nafion/MWCNT composite was immobilized by dropping 10 µl solution containing 5 mg of MWCNTs dispersed in 1 ml of 0.05 wt% Nafion in ethanol [37]. The Nafion/MWCNTs/Pt NPs/TiN electrode was allowed to dry in room temperature for 20 min. Then, the backside of the diced modified TiN-based samples was placed in contact with a copper sheet. Both the copper sheet and the sample were covered with Teflon tape in a manner that the solution could be in contact with the sample surface only through a 3 mm hole cut in the tape. All mentioned development steps of fabricated sensor are shown in Scheme 1a and b.

2.5. Electrochemical experiments

Cyclic voltammetry experiments were done with a Gamry Reference 600 or 600 + potentiostat in a three-electrode setup with an Ag/AgCl reference electrode (Radiometer Analytical) and a Pt wire as counter

electrode driven with Gamry Echem Software. Solutions of 1 mM Ru (NH₃)₆^{2+/3+} in 1 M KCl, 50 nM-500 µM DA in phosphate buffered saline (PBS), (pH 7.4), 100 mM UA in PBS and 1 mM AA in PBS were prepared to probe the electrochemical properties of developed TiN-based sensors. All electrochemical measurements were carried out inside a Faraday's cage at room temperature.

3. Results and discussion

3.1. Characterization of Nafion/MWCNTs/Pt NPs/TiN sensor

The ALD TiN thin film can provide extremely conformal layer [38]. In ALD process, film thickness is directly a function of the number of ALD cycles. The growth rate per cycle (GPC), in our ALD process was ~ 0.185 Å per cycle which was used to deposit TiN films with various thicknesses. The cross-section of ALD TiN on silicon was made using focused ion beam (FIB) and was analyzed using SEM, (Fig. 1), to approve GPC. Fig. 1a and b confirmed the uniformly formation of a conformal ~ 100 nm TiN thick layer on Si substrate after 15,376 ALD cycles. Entire FIB cross section-cutting is depicted in Fig. 1c. The Carbon layer acts as a protection layer in order to protect the surface from incurring FIB

Scheme 1. (a) fabrication process of Nafion/MWCNTs/Pt NPs/TiN microelectrode, (b) preparation of microelectrode on copper sheet.

Fig. 1. FIB-SEM images of ALD TiN thin film deposited on Si wafer: (a) cross-sectional image of TiN thin film, (b) complete FIB-SEM thickness map: 100 nm TiN by 5376 ALD cycles, and (c) top view of the cross-sectional cutting with undercut layers, (d) ellipsometry map thickness of ALD TiN on Si wafer.

induced damage. Therefore, 1344 ALD cycles were conducted to reach ~ 25 nm TiN thin film. Spectroscopic ellipsometry was used to check film thickness. For thickness measurement and its uniformity investigation, Si wafer coated with 25 ± 3 nm TiN thin film was mapped with spectroscopic ellipsometer (Fig. 1d) and thickness variation was observed to be under 2.7 nm with $\sim 5.4\%$ uniformity (Table. S1).

Resistivity, sheet resistance and film thickness are related by Eqs. (1) and (2).

$$\rho = RWt/L \quad (1)$$

where, ρ is resistivity, R = resistance, t is the thin film thickness and W/L is the width divided by length constant which for round silicon wafer equals to 4.532. Resistivity (ρ) was obtained via Eq. (2):

$$\rho = R_s * t \quad (2)$$

in which R_s is sheet resistance. It was observed that for both TiN/N₂ and TiN/Air samples resistivity decreases as thickness increases from 3 nm to 25 nm and then stabilizes until the thickest film inspected here (100 nm) (Figure S1), which is a general trend: charge carrier mobility increases with increased grain size [39]. Also, both samples showed roughly the identical values in resistivity. Therefore 25 nm was chosen as optimum thickness for sensor fabrication not only due to its minimum resistivity but also since it has been reported that 25 nm thick TiN electrode showed transparency in both fluorescence imaging and bright field [22].

Wettability and surface properties of TiN/Air, Pt NPs/TiN, MWCNTs/Pt NPs/TiN, and Nafion/MWCNTs/Pt NPs/TiN samples were further characterized by water contact angle measurements. Low contact angle implies high surface energy and high wettability and vice versa [40]. The changes in the TiN/Air surface composition after the deposition of Pt NPs affected the wettability and the surface energy

(Figure S2a and b) higher contact angle values were found for Pt NPs/TiN ($\sim 76^\circ \pm 2^\circ$) than TiN/Air ($\sim 51^\circ \pm 3^\circ$) due to the lower surface energy for Pt NPs [41]. Nafion/MWCNTs/Pt NPs modification changed the surface properties of TiN/Air sample to more hydrophobic. MWCNTs/Pt NPs/TiN sample exhibited superhydrophobic behavior (contact angle $> 150^\circ \pm 1^\circ$) due to the hydrophobic nature of MWCNTs and nanotube geometry, while the Nafion caused the surface to become less hydrophobic (contact angle $\sim 82^\circ \pm 2^\circ$) which indicates that Nafion thin film is covering almost the whole electrode surface (Figure S2c and d) [42].

Pt NPs were deposited by plasma enhanced ALD (PEALD) at 300°C on ALD TiN/Air surface. The Pt NPs loading was controlled with number of ALD cycles. TEM images of Pt NPs on ALD TiN/Air are shown in Fig. 2a and b. As can be seen in these figures, Pt NPs deposition by 60 ALD cycles showed a good uniformity with narrow size distribution in the range $4-5 \pm 1.2$ nm. Fig. 2c and d display the TEM images of MWCNTs and MWCNTs immobilized on TiN/Air by Nafion film respectively. According to the TEM images there is no difference between MWCNTs and Nafion/MWCNT, which implies the coating of MWCNTs with Nafion film has not changed the tube shape and nano-structure of MWCNTs.

The surface concentrations of the titanium, oxygen, platinum, and nitrogen elements were determined with XPS characterization of TiN/Air and Pt NPs/TiN samples with the aim to approve the existence of oxynitride functional group and Pt NPs on the TiN/Air surface. Table 1 presents the elemental composition of TiN/Air and Pt NPs/TiN obtained by their broad XPS spectrum (shown in Fig. 3a). The N 1s and Ti 2p spectra are a very characteristic spectra for nitride (N³⁻) and TiO₂ in the TiN compound respectively (Fig. 3b and c). The peak at 397.0 eV corresponds to the nitride, while in the oxidized TiN, the oxidized

Fig. 2. (a) and (b): TEM images of Pt NPs on top of 25 nm oxidized TiN thin film sample (TiN/Air). The number of Pt NPs deposition cycles: 60, (c): TEM image of MWCNTs, and (d) TEM image of Nafion/MWCNTs immobilized on TiN/Air.

Table 1

XPS results showing the elemental composition of TiN/Air and Pt NPs/TiN. The rest of at% for both samples is related to Si wafer and its chemical components which are not necessary to mention.

At%	Ti 2p	N 1s	O 1s	Pt 4f
TiN/Air	8.8	8.4	33.6	0.0
Pt NPs/TiN	4.6	5.2	19.7	6.1

nitride state in the N1s region is observed at lower binding energy (396.0 eV) compared to the pure nitride state [43]. Pt NPs formation was confirmed on the TiN/Air sample surface by the occurrence of the corresponding Pt peaks in the Pt 4f spectrum binding energies of 72 and 75 eV which are attributed to the Pt 4f 7/2 and 4f 5/2 orbitals, respectively (Fig. 3d) [44].

3.2. Kinetic and electrochemical characterization

Fig. 4a demonstrates the water windows for TiN/N₂ and TiN/Air electrodes in KCl. Both electrodes showed similar broad safe potential window and low background current.

One of the main electrochemical properties of an electrode is electron transfer rate at the electrode surface which is associated to peak

separation (ΔE_p). The electron transfer rate of TiN-based electrodes was investigated with outer sphere redox reactions using CVs of 0.1 M KCl containing 1 mM Ru (NH₃)₆^{2+/3+}.

Fig. 4b shows the CVs for TiN/N₂, TiN/Air, Pt NPs/TiN, MWCNTs/Pt NPs/TiN, and Nafion/MWCNTs/Pt NPs/TiN electrodes in 0.1 M KCl solution containing 1 mM Ru (NH₃)₆^{2+/3+}. As can be seen from Fig. 4b ΔE_p is 137.0 ± 4.8 mV, 71.9 ± 2.1 mV, 162.0 ± 3.7 mV, 87.0 ± 5.6 mV, and 335.0 ± 8.1 mV for those electrodes, respectively. Therefore, the outer sphere redox reactions of (NH₃)₆^{2+/3+} is more reversible on TiN/Air electrode than the other electrodes. As mentioned in 2.3. section, TiN/Air sample was let to cooldown in air that has likely resulted in formation of oxygen functionalities oxynitrides (TiO_yN_x) on its surface which clearly affect the electrochemical properties. It can be deduced that the outer sphere redox reactions are more reversible on TiN/Air surface in comparison with TiN/N₂ sample, owing to oxygen functionalities of TiN/Air electrodes surface [45]. The outer sphere redox reactions showed less reversibility on Nafion/MWCNTs/Pt NPs/TiN electrode surface, than the other electrodes, suggesting that can be due to the enhancement in electron transport resistance through Nafion film [46].

Also, as is clear from Fig. 4b that the corresponding peak current for MWCNTs/Pt NP/TiN is higher than in the other samples. This indicates a larger effective surface area for this electrode.

Fig. 3. Broad spectrum XPS (a) TiN/Air and Pt NPs/TiN, high-resolution XPS spectra of (b) N 1s, (c) Ti 2p, and (d) Pt 4f.

Fig. 4. (a) Water windows for TiN/N₂ and TiN/Air electrodes. (b) CV voltammograms obtained with TiN/N₂, TiN/Air, Pt NPs/TiN, MWCNTs/Pt NPs/TiN, Nafion/MWCNTs/Pt NPs/TiN electrodes. All in 0.1 M KCl solution containing 1 mM Ru (NH₃)₆^{2+/3+} at a scan rate of 50 mV/s.

The Randles–Sevcik equation gives peak current for a reversible process at 25 °C.

$$i_p = (2.69 \times 10^5) n^{3/2} A C D^{1/2} \nu^{1/2} \quad (3)$$

where A is the effective surface area (in cm²), n is the number of electrons transferred, D is the diffusion coefficient (that for Ru (NH₃)₆^{2+/3+} 7.7 × 10^{−6} cm²s^{−1}), n is the number of electrons in the electron-transfer

process, ν is the scan rate (in V/s) and C is the bulk concentration (in mol cm^{−3}). To determine the effective surface area, as a microscopic characteristic of the modified electrodes, we did CV measurements with varying scan rates ranging from 10 mV/s to 400 mV/s in 0.1 M KCl solution, containing 1 mM Ru (NH₃)₆^{2+/3+}. The results are shown in Figure S3.

As stated by Eq. (3) anodic peak current is directly proportional with square root of potential scan rate (Fig. 5a), thus, from the slope of anodic

Fig. 5. (a) The fitted I_{pa} versus the square root of the scan rates, (b) The cathodic and anodic peak potentials versus the scan rates. All in 0.1 M KCl solution containing 1 mM $Ru(NH_3)_6^{2+/3+}$.

peak current (I_{pa}) versus square root of scan rates, the effective surface areas (A) were calculated to be 0.09 ± 0.05 , 0.05 ± 0.02 , 0.13 ± 0.02 and 1.7 ± 0.06 cm² for TiN/N₂, TiN/Air, Pt NP/TiN, and MWCNTs/Pt NP/TiN electrodes respectively while the geometric (nominal) surface area for all samples is the same (0.07 cm²).

The largest effective surface areas which are found for MWCNTs/Pt NP/TiN and Pt NP/TiN electrodes are related to the synergistic effect between MWCNTs, Pt NPs and TiN nanostructure film for MWCNTs/Pt NPs/TiN electrode and the synergistic effect between Pt NPs and TiN nanostructure film for NPs/TiN electrodes [47,48].

Furthermore, it was observed from Fig. 5a that anodic current varied linearly with the square root of the potential scan rate which indicates mass transfer-controlled process for all electrodes.

Fig. 5b shows the anodic and cathodic peak potentials plotted vs. potential scan rates. As can be seen from Fig. 5b, TiN/Air electrode showed almost constant peak separation with increasing of potential scan rate. This demonstrates the highest electron transfer rate for outer sphere redox reactions on surface this electrode which is accordance the most reversibility of outer sphere reaction on this electrode surface. The peak separation increased markedly with increasing of the scan rate for all the other samples, which implies the restriction in the electrochemical reaction between the active redox sites of the electrode surface and $Ru(NH_3)_6^{2+/3+}$ due to low electron transfer rate of outer sphere redox reactions.

Thus, it can be concluded TiN/Air electrode exhibited the fast electron transfer rate toward outer sphere redox probe. Surface oxidation of TiN and formation TiO_yN_x on its surface causes an enhancement of the TiN isoelectric point pH (pH_{IEP}) from the pH range 3–5 toward the less acidic TiO_2 ($pH_{IEP} \sim 6.3$) [49,50]. Considering the pH_{IEP} of TiN/N₂, TiN/Air (TiO_yN_x), Pt NPs/TiN ($pH_{IEP, Pt NPs} \sim 3.5$) [51], MWCNTs/Pt NPs/TiN ($pH_{IEP, MWCNT} \sim 5-8$) [52], and environment pH (0.1 mM KCl, pH ~ 7), it can be inferred that all the electrode samples have approximately similar condition in terms of electrostatic interaction between electrode surface charged and positively charged $Ru(NH_3)_6^{2+/3+}$ probe. Therefore, $Ru(NH_3)_6^{2+/3+}$ is heavily affected by TiO_yN_x oxygen functional content for TiN/Air sample and oxygen functional content and sp^3/sp^2 ratio for MWCNTs/Pt NPs/TiN sample which lead to change electronic structure of these electrodes surface. Such a behavior, role of sp^3/sp^2 ratio on the electrocatalytic properties of various carbon-based materials has been reported [45,53,54].

The total surface coverage of the electrode can be roughly calculated according to the following Eq. (3):

$$\Gamma = Q/nFA \quad (4)$$

where Γ (mol cm⁻²) is the surface coverage, Q is the charge obtained by integrating the anodic peak at a low scan rate of 10 mVs⁻¹, A is the electrode surface geometrical area (0.07 cm²), n is the number of electrons transferred and F is Faraday's constant (96 485C/mol) [55]. The surface coverage for Pt NPs depositing on TiN/Air (Figure S4) was estimated to be about $7.40 \times 10^{-8} \pm 0.06$ mol cm⁻² that prove the more efficient formation of Pt NPs on oxide surface [56,57].

3.3. Electrocatalytic dopamine sensing

Electrochemical behavior of the TiN-based electrodes in 50 mM PBS (pH = 7.4) with scan rate of 50 mV/s was investigated by CV and the results are illustrated in Fig. 6.

Fig. 6 shows that there are no obvious redox peaks for TiN/N₂, TiN/Air, and MWCNTs/TiN electrodes in the absence of analyte molecules in 50 mM PBS, which can indicate that both TiN samples and MWCNT/TiN are stable under potential region between -0.7 to 1.2 V. An anodic peak around -0.58 V and a small broad peak at -0.032 V for cathodic peak were observed at the Pt NP/TiN electrode surface [58,59]. Similar behavior occurred for MWCNTs/Pt NP/TiN electrode. One can conclude this redox peak is related to Pt NPs electrooxidation. Nafion film can act as a protective layer that causes to cover of the Pt NPs activity [60,61]. It can also be observed from Fig. 6 that the background current is lower for TiN/N₂, TiN/Air, and Pt NP/TiN electrodes. In contrast, MWCNTs/Pt NP/TiN, MWCNTs/TiN, and Nafion/MWCNTs/Pt NP/TiN electrodes showed the largest capacitance current respectively. It has been reported one of the substantial aspects on capacitive current is the double-layer capacitance at the electrode-electrolyte interface, which is directly proportional to the effective surface area [62,63]. Thus, the highest capacitive current is in accordance with the largest effective surface area for MWCNT/Pt NP/TiN electrode.

Electrocatalytic response of TiN sensor was evaluated by characterization TiN/N₂ and TiN/Air sensors CV behavior in PBS in presence of DA. Fig. 7a shows the CVs of TiN/N₂ and TiN/Air electrodes in 50 mM PBS (pH = 7.4) containing 100 μ M of DA. It can be observed that TiN/Air sample is more sensitive toward the oxidation of DA in compared with TiN/N₂ electrode. We suggest that this arises from the formation of titanium oxynitrides on the TiN/Air sample during the cooldown period. Furthermore, there is a synergistic effect between titanium oxynitride functional groups as active sites and titanium nitride functional groups as nucleophile center that cause intense interaction between DA and TiN/Air surface (Fig. 7b) [64,65]. Considering the substantial sensitivity of TiN/Air electrode toward DA sensing, development of Nafion/MWCNTs/Pt NPs/TiN sensor was conducted based on TiN/Air sample.

Fig. 6. CV voltammograms of inset: both TiN/Air and TiN/N₂ electrode, (a) Pt NPs/TiN electrode, (b) MWCNTs/TiN electrode, (c) MWCNTs/Pt NPs/TiN electrode, and (d) Nafion/MWCNTs/Pt NPs/TiN electrode in 50 mM PBS (pH = 7.4) in absence of dopamine.

Fig. 7. (a) CVs of TiN/N₂ and TiN/Air electrodes in PBS solution (50 mM, pH = 7.4) containing 100 μM DA at scan rate of 50 mV/s. (b) supposable scheme of DA electrooxidation mechanism at TiN/Air electrode surface.

Next, we investigated the electrochemical response of TiN/Air electrode modified by Nafion/MWCNTs/Pt NP nanocomposite towards DA. Fig. 8a presents the voltammograms of different TiN modified electrodes in 50 mM PBS (pH = 7.4) at presence of 100 μM DA. Electrooxidation of DA at the Pt NPs/TiN and MWCNTs/TiN electrode surfaces replicated the behavior of TiN/Air electrode but with a higher anodic current. Two well-defined redox pair peaks, in the range of 0.3–0.75 V, were observed at Nafion/MWCNTs/Pt NPs/TiN electrode surface for DA electrooxidation. The anodic peak at 0.75 V can be considered oxidation of dopamine to dopaminoquinone and the other one at 0.31 V can be associated with oxidation leucodopaminochrome to dopaminochrome (Fig. 8b) [66].

The modified Nafion/MWCNTs/Pt NP/TiN electrode revealed the

most electrocatalytic activity toward DA oxidation that can be attributed to the synergistic effect between Nafion, MWCNTs, and Pt NPs as following. MWCNTs/Pt NP nanocomposite brings about the enhancement in the sensitivity by improvement of the mass transfer rate owing to its largest effective surface area. Stability immobilization of MWCNTs on Pt NPs/TiN surface by Nafion, caused to produce a rich and dense π -electron network of the MWCNTs that can decrease an activation potential for DA oxidative reaction [67]. In addition to the desirable electrochemical performance of developed modified sensor in this work, loading the used amount of MWCNTs in 0.05 wt% Nafion solution, was found to be still optimized concentration [37].

Fig. 8. (a) CVs of Pt NPs/TiN electrode (curve a), MWCNT/TiN electrode (curve b), MWCNTs/Pt NPs/TiN electrode, and Nafion/MWCNTs/Pt NPs/TiN electrode in PBS solution (50 mM, pH = 7.4) containing 100 μM DA at scan rate of 50 mV/s. (b) supposed scheme of DA electrooxidation mechanism at Nafion/MWCNTs/Pt NPs/TiN electrodes surface.

3.4. Analytical performance of TiN-based sensor

High temporal resolution technique is necessitated for monitoring chemical dynamics in the synaptic cleft including the evaluation of rapid DA transients. [68]. It has been reported CV technique can provide the higher temporal resolution than the other electrochemical techniques such as square-wave voltammetry (SWV) and differential pulse voltammetry (DPV) [69]. Hence, for reaching the results which are more reliable for in vivo application, CV was applied to DA measurement.

Voltammograms for different concentration of DA in the range of 100 nM–500 μM for TiN/N₂ and TiN/Air electrodes in 50 mM PBS (pH = 7.4) are demonstrated in Figure S5a and b.

The wide linear range suggested that TiN electrodes can be considered as a capable candidate for practical applications. However, the relevant physiological concentration range of DA is 50 nM–1 μM [68]. Therefore, determination of DA at Nafion/MWCNTs/Pt NPs/TiN surface as developed work electrode was obtained in the range of 50 nM–35 μM in PBS (pH = 7.4) which is included the physiological range (Fig. 9a). The associated calibration curves for DA, in accordance with changes in electrochemical response of DA, are presented in Figure S5c and Fig. 9b.

All three electrodes, TiN/N₂, TiN/Air and Nafion/MWCNTs/Pt NPs/TiN showed a linear response toward DA concentration. Sensitivity was found 0.005, 0.012, and 16.301 μAμM⁻¹ for TiN/N₂, TiN/Air, and Nafion/MWCNT/Pt NPs/TiN sensors, respectively. According to these results, it is clearly obvious the Nafion/MWCNTs/Pt NPs/ composite-modified TiN sensor has the most sensitivity toward DA oxidation. The calculated limits of detection were calculated about 100 nM for TiN/N₂ and TiN/Air, and was found 40 ± 1.6 nM for Nafion/MWCNTs/Pt NPs/TiN electrode all at S/N of 3. Nafion membrane can reduce electrode surface passivation but generally it increases the response time. Reaching about 90% of the maximum output signal, the modified TiN sensor showed reasonable response time of 5 s. In comparison with some various electrochemical methods published previously on DA measurement and the proposed TiN based sensors in this work in Table 2, our sensors compare favorably from the analytic point of view.

3.5. Effect of the potential scan rate on sensor performance

For kinetic evaluation of DA electrochemical oxidation at the surface of the Nafion/MWCNTs/Pt NPs/TiN electrode, the effect of the potential

Fig. 9. CVs of (a) Nafion/MWCNTs/Pt NPs/TiN electrode upon increasing the concentration of DA in PBS (50 mM, pH = 7.4) at scan rate of 50 mV/s. (b) Calibration curve obtained from CV voltammogram data for Nafion/MWCNTs/Pt NPs/TiN electrode in the range 50 nM–35 μM of DA.

Table 2

Comparison between of our developed TiN based sensors performance for determination of DA with some various methods and electrodes previously reported.

Material	Linear range (μM)	Detection limit (nM)	Method	Ref.
15 nm ta-C + CNT	0.01–5	30.6	CV	[70]
50 nm ta-C + CNT	0.05–10	35.9	CV	[70]
SU-8 PyC	0.05–1	40	CV	[71]
SU-8 PyC-O ₂	0.05–1	20	CV	[71]
OMC/Nafion/GCE	1–90	500	DPV	[72]
DAAO-Hb/MnO ₂	0.01– 2.25	41	DPV	[73]
NPs/PTth/GCE				
TiN/N ₂	0.1– 500	100	CV	this work
TiN/Air	0.1– 500	100	CV	this work
Nafion/MWCNT/Pt NPs/TiN	0.05– 35	40	CV	this work

scan rate on sensor response was investigated. Fig. 10a shows CV voltammograms of Nafion/MWCNTs/Pt NPs/TiN electrode for DA (20 μM) in PBS solution (pH = 7.4, 50 mM) at different potential scan rates (10, 20, 30, 40, 50, 70, 80 and 100 mV/s). DA oxidation and reduction peak currents vs. square root of scan rate are exhibited in Fig. 10b. The results show that with increasing of potential scan rate, anodic and cathodic peak currents also increase and that there is a linear relation between them in 10 mV/s–100 mV/s range. This indicates that the electrochemical oxidation of dopamine at Nafion/MWCNTs/Pt NPs/TiN surface is a diffusion-controlled quasi-reversible reaction. The logarithmic curve of oxidation current ($\log i_p$) versus scan rate ($\log v$) is presented in Figure S6. According to the Randles–Sevcik (equation (1)) logarithmic the plot's slope should be equal to 0.5 for solely diffusion-controlled and the greater slope indicates a weak effective adsorption-controlled process [74]. It seems, from Fig. 10b and Figure S6, the DA oxidation involved both diffusion and weak adsorption processes which is in accordance with the large effective surface area and fast electron transfer kinetics observed for MWCNTs/Pt NPs/TiN electrode.

3.6. Selectivity and interference study of TiN based electrodes

In order to study the interference effect on the response of modified TiN based sensor toward DA, we have evaluated the selectivity of as prepared TiN/N₂ and TiN/Air sensors in presence of ascorbic acid (AA) and uric acid (UA). AA and UA are the main interfering species in vivo applications. It is important to be able to measure DA without getting

any additional signal from their oxidation. The electrochemical selectivity tests were carried out in solutions containing 1 mM AA or 100 μM UA and varying amounts of DA. These concentrations of AA and UA are in accordance with their average neurophysiological concentration found in glia and human brain system [75,76]. There were no oxidation peak of AA and UA on either TiN/N₂ or TiN/Air electrodes. (Fig. 11). These results indicate that the influence of AA and UA on the DA detection are negligible on both TiN sensor surfaces. In the next step, the selectivity of modified Nafion/MWCNTs/Pt NPs/TiN electrode was inspected in a ternary PBS solution containing 1 mM ascorbic acid, 100 μM uric acid and diversified DA concentration. Modified TiN sensor seems to be selective to DA over both AA and UA (Fig. 12). Combination of selectivity of TiN/Air as base electrode, electrochemical catalytic activity of the MWCNTs/Pt NPs composite, and the permselectivity of Nafion as cation-exchange polymer film [77], caucused selective detection of DA at modified Nafion/MWCNTs/Pt NPs/TiN electrode

3.7. Fouling and passivation of TiN electrodes

Fouling is a considerable threat on the sensor's analytical performance in real biological samples [78]. The fouling of TiN sensors was investigated in presence of DA as inner sphere redox (ISR). During continuous potential cycling (10 cycles) in 50 mM PBS (pH = 7.4) containing 1 mM DA, there is some slight passivation for the TiN/N₂ samples, both in presence and absence of 1 mM AA. When there is 100 μM UA in the solution containing 1 mM DA, the passivation is more pronounced (Figure S7).

As it can be seen from the DA oxidation mechanism in Fig. 8, the polymerization process is being by further oxidation of 5,6-Dihydroxyindole to indole quinone at the last step [67]. The CV voltammograms of DA fouling at TiN/Air electrode confirmed the polymerization of DA at its surface both in presence and absence of 1 mM AA and 100 μM UA. It is obvious from the Figure S8, that the DA oxidation peak current intensity decreased substantially over consecutive scans during DA fouling. Therefore, the oxygen functionalities seem to make TiN/Air sample more prone to fouling by dopamine. It is possible that the hydrophilic oxynitride functional groups on TiN/Air surface cause increased absorption of the polar oxidized dopamine products such as dopaminochrome molecules [33]. Similar behavior was reported in electrochemical study of theophylline and norepinephrine on reduced graphene oxide and graphene oxide modified glassy carbon surfaces [79,80].

Fig. 10. CVs of (a) Nafion/MWCNTs/Pt NPs/TiN electrode in PBS (50 mM, pH = 7.4) containing dopamine (100 μM) at different scan rates (10, 20, 30, 40, 50, 70, 80 and 100 mV/s), (b) dependence of anodic currents vs. square root of scan rate.

Fig. 11. CV voltammograms of both TiN/N₂ and TiN/Air electrodes in PBS solution (50 mM, pH = 7.4) containing various dopamine concentration in the presence of 1 mM ascorbic acid (a, b) and 100 μM uric acid (c, d) at scan rate of 50 mV/s.

Fig. 12. CVs of Nafion/MWCNTs/Pt NPs/TiN electrode in PBS solution (50 mM, pH = 7.4) containing various dopamine concentration in the presence of 1 mM ascorbic acid and 100 μM uric acid at scan rate of 50 mV/s.

3.8. Stability and reproducibility of sensors

The long-term stability of developed MWCNTs/Pt NPs/TiN and Nafion/MWCNTs/Pt NPs/TiN sensors was assessed by monitoring their response over a period of 30 days without surface polishing. After each

measurement, the sensors were rinsed with phosphate buffer at pH 7.4 and then the electrodes were stored in PBS solution, pH 7.4 at room temperature. After 2 days, the response current of Nafion/MWCNTs/Pt NPs/TiN was approximately at the same level of its initial value, but a sharp fall-off was found for MWCNTs/Pt NPs/TiN electrode, with response falling to 65% of its maximum initial value. The instability in MWCNTs immobilization on Pt NPs/TiN/Air surface caused this initial decrease. Afterwards, the response of Nafion/MWCNTs/Pt NPs/TiN continued to decrease slowly. Finally, the sensor maintained 70% of its maximum original response after 30 days which could be resulted from the fouling or passivation surface of sensor. The reasonable stability of Nafion/MWCNTs modified sensor could be attributed to the protective performance of the Nafion immobilization matrix [81,82]. Reproducibility of the measured data was evaluated by three successive measurements of constant concentration of DA (100 μM) by three different Nafion/MWCNTs/Pt NPs/TiN sensors from the same fabrication process lot. Relative standard deviations of DA electrooxidation responses were 4.83%.

4. Conclusions

In this work, we have demonstrated ALD TiN-based sensors for dopamine electrochemical detection and covered their characterization, modification, and electrochemical applications. First, two types of TiN electrodes, TiN/N₂ and TiN/Air, were deposited on silicon by thermal ALD process. Both TiN/N₂ and TiN/Air samples represent a wide potential water window, good linear relationship for DA measurement in concentration range of 100 nM–500 μM and, good selectivity toward DA

against AA and UA. TiN/Air oxidized surface sensor showed more sensitive electrochemical response and more pronounced tendency to fouling toward DA electrooxidation compared to the TiN/N₂ electrode. This was suggested to arise from the formation of surface oxygen functionalities during the cooldown step of the ALD process. Thus, TiN/Air sample was selected for further development through the use of both MWCNTs/ Pt NPs nanocomposite-modified sensor. Plasma-enhanced ALD process was used to deposit Pt NPs on TiN/Air thin film and MWCNTs/Nafion composite was immobilized on Pt NPs/TiN/Air sensor to improve electron transfer rate, electrochemical effective surface area, selectivity, and stability. In addition, possessing suitable reproducibility and stability, the prepared nanostructure electrochemical sensor showed good sensitivity to DA oxidation (16.31 $\mu\text{A}/\mu\text{M}$) with reasonable linear response ($R^2 = 0.990$) in physiologically relevant concentration range (50 nM–35 μM), and low detection limit (40 nM). We conclude that based on the combination of physical, chemical, and electrochemical properties, the ALD TiN films can be offered as high capability material for biomedical application such as electrochemical immunoassay biosensors or electrochemical neurochemical sensor. Modification of TiN microelectrode with Nafion/MWCNTs/Pt NPs nanocomposite confirmed the unique electrocatalytic properties of carbon-based material toward neurotransmitter electrooxidation sensing such as DA.

CRedit authorship contribution statement

Yalda Shoja: Investigation, Methodology, Visualization, Writing - original draft, Writing - review & editing, Data curation, Formal analysis, Software. **Noora Isoaho:** Investigation, Visualization, Methodology, Data curation, Software, Writing - original draft & editing. **Ville Jokinen:** Conceptualization, Visualization, Investigation, Writing - review & editing. **Sami Franssila:** Project administration, Conceptualization, Supervision, Funding acquisition, Writing - review & editing, Resource, Validation.

Declaration of Competing Interest

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

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Appendix A. Supplementary material

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