Electrochemistry Communications 79 (2017) 33–36

Contents lists available at ScienceDirect

Electrochemistry Communications

journal homepage: www.elsevier.com/locate/elecom

The interplay of electrode- and bio-materials in a redox-cycling-based clozapine sensor

Thomas E. Winkler[a,b,1,2], Robert Dietrich[a,b,2], Eunkyoung Kim[c], Hadar Ben-Yoav[a,3], Deanna L. Kelly[d], Gregory F. Payne[b,c], Reza Ghodssi[a,b,*]

[a] MEMS Sensors and Actuators Laboratory (MSAL), Department of Electrical and Computer Engineering, Institute for Systems Research, University of Maryland, College Park, MD 20742, United States
[b] Fischell Department of Bioengineering, University of Maryland, College Park, MD 20742, United States
[c] Institute for Bioscience and Biotechnology Research, University of Maryland, College Park, MD 20742, United States
[d] Maryland Psychiatric Research Center, University of Maryland School of Medicine, Baltimore, MD 21228, United States

ARTICLE INFO

Keywords:
Therapeutic drug monitoring
Clozapine
Redox cycling
Titanium nitride
Platinum black

ABSTRACT

We investigate gold, TiN, and platinum in combination with a chitosan–catechol-based redox-cycling system (RCS) for electrochemical detection of the antipsychotic clozapine. We have previously demonstrated the RCS for detection of clozapine in serum, but challenges remain regarding low signal-to-noise ratios. This can be mitigated by selection of electrode materials with beneficial surface morphologies and/or compositions. We employ cyclic voltammetry to assess the redox current generated by clozapine, and differentiate solely surface-area-based effects from clozapine-specific ones using a standard redox couple. We find that nano- and microstructured platinum greatly amplifies the clozapine signal compared to gold (up to 1490-fold for platinum black). However, the material performs poorly in the presence of chloride ions, and RCS modification provides no further amplification. The RCS combined with atomic-layer-deposited (ALD) TiN, on the other hand, increases the signal by 7.54 times, versus 2.86 times for RCS on gold, with a 9.2-fold lower variability, indicating that the homogenous and chemically inert properties of ALD-TiN may make it an ideal electrode material.

1. Introduction

Electrochemical sensors are appealing due to their ability to directly translate chemical events into electronic signals, which are easily read out [1]. This makes them uniquely versatile and well-suited for miniaturization. A major challenge, especially in clinical samples like blood, is interference from multitudes of other chemical species, many of them redox active [2]. Typical applications, therefore, utilize highly specific recognition elements (e.g. antibodies) or target high-concentration analytes (e.g. glucose) [3,4]. To open up a wider range of targets, however, different electrode modification strategies to confer selectivity are required and have been pursued [5,6]. Particularly when applying biomaterial-based modifications on top of solid-state electrodes, one point of great interest (yet often neglected) is the choice of the underlying electrode material, which fundamentally affects the ability of the sensor to interact with the analyte to produce a signal. Surface morphology, physicochemical interaction with the target analyte, and propensity for fouling or oxidation are all material characteristics that affect sensor performance. Optimization of these systems requires careful investigation into the physicochemical properties of the electrode and its interactions with the analyte and interferents.

In the present work, we specifically consider a biomaterial-based redox-cycling system (RCS) for amplification of electrochemical signals from small molecule analytes [7]. Our RCS comprises an electrodeposited chitosan matrix that facilitates grafting of catechol near the electrode surface. This yields a redox capacitor, allowing for repeated analyte oxidation at the electrode following reduction by catechol, leading to signal amplification. We have previously applied the RCS toward sensing pyocyanin and, more recently, clozapine [8,9]. Clozapine is an antipsychotic drug, the most effective one available for managing treatment-resistant schizophrenia [10–12]. Electrochemical sensing has the potential to greatly decrease the burden associated with

* Corresponding author at: MEMS Sensors and Actuators Laboratory (MSAL), Department of Electrical and Computer Engineering, Institute for Systems Research, University of Maryland, College Park, MD 20742, United States.
E-mail address: ghodssi@umd.edu (R. Ghodssi).
[1] Present address: Department of Micro- and Nanosystems, KTH Royal Institute of Technology, Stockholm, 100 44, Sweden.
[2] Thomas E. Winkler and Robert Dietrich contributed equally to this paper.
[3] Present address: Department of Biomedical Engineering, Ben-Gurion University of the Negev, Beer Sheva, 8410501, Israel.

http://dx.doi.org/10.1016/j.elecom.2017.04.009
Received 20 February 2017; Received in revised form 2 April 2017; Accepted 11 April 2017
Available online 13 April 2017
1388-2481/

Table 1
Electrochemical characterization results for the electrode materials studied in this work. The model redox couple ferri/ferrocyanide gives an indication of the effective electrochemical surface area. Toward therapeutic drug monitoring of clozapine, materials were tested with (RCS) and without (bare) further redox-cycling system modification in either PB or PBS. For each group, the relevant gold reference is in *italics*, and relative amplification by more than a factor of five is in bold.

Material	Electrochemical peak current (normalized to bare gold electrode)				
	Ferri/ferrocyanide	Clozapine in PB		Clozapine in PBS	
	Bare	Bare	RCS	Bare	RCS
Au	*1.00 ± 0.02*	*1.00 ± 0.05*	3.04 ± 0.59	*1.00 ± 0.25*	2.86 ± 1.25
TiN	1.05 ± 0.01	0.88 ± 0.07	**6.14 ± 0.86**	1.10 ± 0.15	**7.54 ± 0.36**
Pt-ref	1.40 ± 0.04	**250 ± 56**	**125 ± 19**	**32 ± 11**	–
Pt-black	2.70 ± 0.18	**1490 ± 150**	–	**193 ± 20**	–

required safety and efficacy monitoring (therapeutic range: 1–3 μM) by reducing sample volumes and bringing testing closer to the patient [13]. Like many electrochemical sensors, the use of our RCS has so far been limited to gold electrodes, achieving a detection limit of below 1 μM in human serum [14]. Gold is easily microfabricated and well-characterized; however, it is not as inert as many studies assume, and may not be an optimal choice for a given sensor [15]. Different surface chemistry could specifically reduce the free energy associated with clozapine oxidation ($E \approx +0.38$ V vs. Ag/AgCl 1 M KCl) and different surface morphologies could increase the area for interaction.

In this work, we evaluate gold, TiN, and platinum in combination with the RCS for detection of clozapine. TiN is a conductive ceramic with excellent inertness and stability [16]. In the context of analytical electrochemistry this material has to date only been utilized in the form of thicker and more porous physical or chemical vapor deposition films; we instead utilize atomic layer deposition (ALD) to create a low-defect, homogenous film that allows us to further emphasize its inherent inert properties. By contrast, platinum is a noble metal with well-established catalytic properties. Electroplating allows us to further focus on this aspect by comparing reflective (Pt-ref) and highly textured (Pt-black) surface morphologies [17]. Although this is a relatively common electroanalytical electrode material, it has not been considered as a substrate for further modification, or in the context of clozapine sensing. In our study, we visualize the morphologies of the electrodes using electron microscopy. We employ cyclic voltammetry for the electrochemical characterization, initially with a standard redox couple to assess surface area enhancement. Finally, we quantify the specific clozapine sensing performance of the electrode materials with and without the RCS relative to bare gold electrodes.

2. Materials and methods

2.1. Electrochemical setup

VSP-300 potentiostat (Bio-logic); platinum counter electrode; Ag/AgCl reference electrode (1 M KCl electrolyte; CH Instruments; all potentials are denoted vs. this reference).

2.2. Working electrode fabrication

We fabricated thin-film gold electrodes (5 × 5 mm^2; 200 nm gold on 20 nm chrome adhesion layer) by sputter deposition, photolithography (Shipley 1813), and wet etching on SiO_2. After dicing, the electrodes were cleaned by successive rinsing with acetone, isopropanol, and methanol, 1 min immersion in Piranha solution(1:3 hydrogen peroxide:sulfuric acid), and finally rinsing with deionized water. Pt-ref was subsequently electroplated in 1% chloroplatinic acid, 0.0025% hydrochloric acid solution by applying − 2.500 mA for 5 min. Pt-black was fabricated similarly, with addition of 0.05% lead acetate as a catalyst and a higher current of − 7.500 mA [17]. TiN was coated with ALD (Beneq TFS 500; 400 cycles ≈ 30 nm). RCS films were applied following published procedures after another Piranha cleaning step [9].

2.3. Surface characterization

The effective electrochemical surface area was characterized by cyclic voltammetry (± 0.25 V around open circuit potential, scan speed 100 mV/s) in 10 mM sodium phosphate buffer (PB; pH 7) containing 5 mM ferricyanide, 5 mM ferrocyanide, 100 mM NaCl. Scanning electron microscopy (SEM) relied on a Hitachi SU-70 and a Tescan XEIA.

2.4. Sample solutions

We purchased all chemicals from Sigma-Aldrich, and prepared solutions with deionized water (> 16 MΩ cm). Solutions were based on either 0.1 M PB (pH 7) or 1 × phosphate-buffered saline (PBS; 10 mM PB, 2.7 mM KCl, 137 mM NaCl; pH 7.4). Samples contained either 50 μM hexaammineruthenium(III) chloride alone (reducing mediator required for RCS; negative control), or had an additional 50 μM clozapine.

2.5. Electrochemical testing

We performed cyclic voltammetry (potential range − 0.4 V to + 0.7 V, scan speed 10 mV/s), recording negative controls followed by clozapine samples for each electrode. We present the averages ($N = 3$) of the background-subtracted recordings.

3. Results and discussion

We summarize our results in Table 1, where we report electrochemical signals in terms of the normalized peak current (with bare gold defined as 1.00) and the associated standard deviation (referred to subsequently as variability, and discussed in the text as a percentage of the associated mean) for each solution and all materials investigated. We discuss these results in depth in the following sections.

3.1. Surface area characterization

Initially, we consider the effective electrochemical surface area as determined with the model ferri/ferrocyanide redox couple. This should allow for de-coupling of specific clozapine signal enhancement from pure increases in surface area. TiN shows a minimal 1.05-fold increase, with the effective surface area still defined by the underlying gold due to negligible lateral conductivity in the thin unpatterned TiN film. With Pt-ref, we observe a 1.40-fold gain, indicating that the electroplating process introduces non-negligible surface roughness, in spite of appearing gray and reflective under visual inspection. As expected, Pt-black exhibits the most robust surface area enhancement of 2.70 ×, matched by a deep black color of the film. It also became apparent that manufacturing variability increases disproportionately

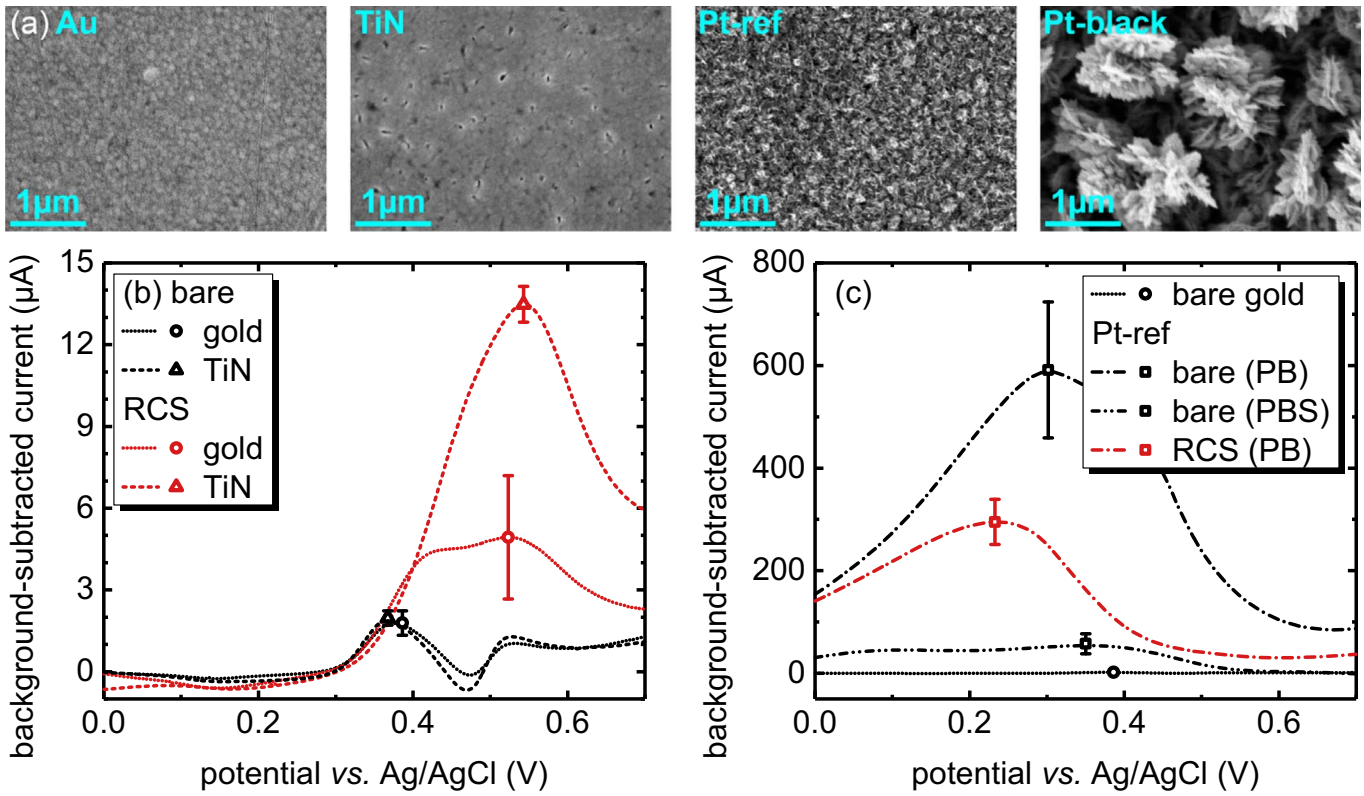

Fig. 1. (a) SEM images of gold, TiN, platinum, and Pt-black electrodes. (b–c) Cyclic voltammograms (oxidative section of third cycle) of clozapine solutions (b) in PBS utilizing gold and TiN electrodes, without or with further RCS modification; (c) in PB or PBS utilizing gold (same as in b) and Pt-ref electrodes, without or with further RCS modification. Peak potentials are marked by symbols on the curves together with peak current standard deviations.

for this material, exceeding 5%.

We visualize the surface morphology of the materials through SEM in Fig. 1a, supporting the electrochemical results. Gold and TiN appear very similar – flat surfaces with only nanoscale defects – as is expected from the thin, conformal nature of the ALD TiN coating. Pt-ref exhibits structure at the sub-micron level, explaining its effective surface area increase while remaining highly reflective in the visual spectrum. Pt-black stands out with well-defined fractal micro/nano surface morphology. We verified the material compositions with simultaneous energy-dispersive X-ray spectroscopy (EDS; not shown).

3.2. Titanium nitride

In Fig. 1b, we show the electrochemical oxidation of clozapine in PBS with bare (black) and RCS-modified (red) TiN electrodes (dashed lines) in comparison to gold ones (dotted lines). As expected from the initial characterization in the previous section, the bare electrode signals are nearly identical between these two materials, with a pronounced clozapine signal around 0.38 V. In the PBS solution used here, the secondary peak around 0.5 V is attributed to a reaction between chloride and the ruthenium-based reducing mediator [14]. As with gold, TiN also shows significant clozapine signal amplification with RCS modification, accompanied by a peak shift from 0.38 V to 0.54 V due to the slower overall kinetics from multiple reactions in redox cycling. However, the increase in current with RCS-TiN is much more pronounced at 7.54 × compared to 2.86 × for RCS-gold in PBS (the latter in line with previous data [9,18]). At the same time, while variability increases to 44% for RCS-gold, it reduces to 5% for RCS-TiN, reflecting an improvement in the signal-to-noise ratio by a factor of 9.2. The use of TiN thus allows us to overcome one of the main challenges of the RCS, namely a low reproducibility on gold electrodes. We hypothesize that this is related to nanoscopic defects in the gold translating into much larger inhomogeneities in the RCS film, as well as due to oxidative surface fouling during chitosan electrodeposition wherein cell potentials exceed + 1.5 V. Both of these factors are eliminated with TiN, due to the high homogeneity of an ALD film and reduced oxidative fouling of the electrode during RCS modification consistent with e.g. Avasarala's work [19]. The same trends are also observed in PB, although they are somewhat less pronounced due to the absence of the aforementioned chloride reaction.

3.3. Platinum

In Fig. 1c, we present the electrochemical oxidation of clozapine in PB with bare (black) and RCS-modified (red) Pt-ref electrodes (dash-dotted lines), as well as data from PBS with bare Pt-ref (dash-dot-dotted line), compared to bare gold (dotted line). An orders-of-magnitude increase in signals with Pt-ref over gold becomes immediately apparent. Interestingly, the highest performance is achieved with bare platinum in PB, with an amplification factor of 250 for Pt-ref. As seen in Table 1, Pt-black extends this even further to 1490. To rule out experimental artifacts, we confirmed the concentration-dependent nature of the peak (not shown). Combined with the negative shift in peak potentials, the signal amplification appears to confirm the catalytic nature of the material. We hypothesize, however, that purely surface morphology-based factors are also at play. Discussion of this needs to consider the much less pronounced 1.40 × (2.70 ×) enhancement for Pt-ref (Pt-black) with the standard redox couple in Section 3.1, as well as the morphologies observed in SEM. A key difference between the ferri/ferrocyanide reaction and clozapine oxidation is that the former is diffusion limited, while the latter is kinetics limited [20]. With a diffusion-limited reaction, the electrochemical depletion layer thickness is on the order of tens of microns; any surface morphologies at lower size scales will not contribute to the electrochemical signal. Ferri/ferrocyanide thus only shows a modest signal increase with the nanostructured Pt-ref, and a somewhat more robust one in the addi-

tional presence of the Pt-black microstructures. The kinetics-limited clozapine, on the other hand, yields a much more surface-conformal depletion layer. Its oxidation is thus selectively amplified by the nano-scale pores and roughness that our electroplated platinum exhibits, functionally similar to certain non-enzymatic sensors for glucose (another kinetics-limited analyte) [21,22].

Upon further modification of Pt-ref with the RCS, we observe the signal to decrease two-fold, disproving our initial hypothesis of synergistic effects between redox catalysis and cycling. It is consistent, however, with part of the signal amplification with Pt-ref arising from its surface morphology combined with the kinetics-limited clozapine. In combination, the RCS film slows down diffusion, shifting the limitation from kinetics toward diffusion [18]. The depletion layer is thereby extended, which reduces the benefits of the nano-structured surface and outweighs that gained from the catalytic electrode surface.

While these findings make bare platinum seem a good candidate for a stand-alone clozapine sensor, it suffers from three major limitations. First, we observe high variability, which we attribute to a lack of process reproducibility akin to formation of the RCS on gold, i.e. defects in the gold potentiating during electroplating. We note that this variability appears to affect mostly the nano-scale structure, since it is not apparent with the model redox couple on Pt-ref (3%, vs. 22% for clozapine), but is comparable for both redox species on Pt-black (7% vs. 10%). Second, PBS – where the major difference compared to PB is the presence of a near-physiological 140 mM chloride ions – depresses the signal a practically identical 7.8- and 7.7-fold for Pt-ref and Pt-black, respectively. This is in stark contrast to bare gold or TiN, where chloride only resulted in a minor increase in variability due to the additional signal from its purported reaction with the reducing mediator. The signal degradation observed with platinum is believed to be the result of the formation of a Pt—Cl complex at the electrode surfaces [23]. The presence of chloride ions, however, cannot easily be avoided in biological samples. Third, without the RCS to confer additional specificity for clozapine, interference from other kinetics-dominated redox species such as uric and ascorbic acid would likely pose a challenge [21,24]. Additionally, Pt-black electrodes were found to degrade rapidly with use and storage, no longer yielding a viable signal after just a few days (not shown), likely due to high levels of surface oxygen interaction [25].

4. Conclusions

The use of alternate electrode materials produced drastically different electrochemical data and highlights the importance of material consideration during sensor design. Our study for the first time considered atomic-layer-deposited TiN and electroplated platinum not only as electrode materials in their own right, but as substrates for additional biomaterial-based sensor modifications. Electroplated platinum electrodes inherently produced a very high clozapine signal, but actually performed worse in combination with the redox-cycling system. Moreover, the negative interactions in solutions containing chloride ions make it a poor choice of material for use in a clinical sensor platform. TiN, on the other hand, performed similar to gold on its own, but showed a significantly improved signal-to-noise ratio after modification with the RCS. This is largely attributed to the homogenous nature of the ALD film increasing process reproducibility, while inert material properties also confer the advantage of better electrode stability, including for storage. In the future, we plan on combining the morphological advantages of platinum-based electrodes with the material ones of TiN. Meanwhile, due to the combination of inherently beneficial material properties with ALD coating, TiN may be viewed as a highly desirable electrode candidate for biomaterial-based electrochemical sensors.

Acknowledgements

The authors are grateful to Sheryl E. Chocron for useful discussions. We further thank the National Institutes of Health (Grant R56-MH105571), the Robert W. Deutsch Foundation, and the Maryland Innovation Initiative (MII; Grant STMD0613008) for financial support. The authors also appreciate the support of the Maryland NanoCenter, its FabLab, and its AIMLab.

References

[1] J. Wang, Analytical Electrochemistry, John Wiley & Sons, 2006.
[2] N. Psychogios, D.D. Hau, J. Peng, A.C. Guo, R. Mandal, S. Bouatra, I. Sinelnikov, R. Krishnamurthy, R. Eisner, B. Gautam, N. Young, J. Xia, C. Knox, E. Dong, P. Huang, Z. Hollander, T.L. Pedersen, S.R. Smith, F. Bamforth, R. Greiner, B. McManus, J.W. Newman, T. Goodfriend, D.S. Wishart, The human serum metabolome, PLoS ONE 6 (2011) e16957, http://dx.doi.org/10.1371/journal.pone.0016957.
[3] D. Grieshaber, R. MacKenzie, J. Vörös, E. Reimhult, Electrochemical biosensors - sensor principles and architectures, Sensors 8 (2008) 1400–1458, http://dx.doi.org/10.3390/s8031400.
[4] Y. Wang, H. Xu, J. Zhang, G. Li, Electrochemical sensors for clinic analysis, Sensors 8 (2008) 2043–2081, http://dx.doi.org/10.3390/s8042043.
[5] D.W. Kimmel, G. LeBlanc, M.E. Meschievitz, D.E. Cliffel, Electrochemical sensors and biosensors, Anal. Chem. 84 (2012) 685–707, http://dx.doi.org/10.1021/ac202878q.
[6] C. Zhu, G. Yang, H. Li, D. Du, Y. Lin, Electrochemical sensors and biosensors based on nanomaterials and nanostructures, Anal. Chem. 87 (2015) 230–249, http://dx.doi.org/10.1021/ac5039863.
[7] E. Kim, Y. Liu, X.-W. Shi, X. Yang, W.E. Bentley, G.F. Payne, Biomimetic approach to confer redox activity to thin chitosan films, Adv. Funct. Mater. 20 (2010) 2683–2694, http://dx.doi.org/10.1002/adfm.200902428.
[8] E. Kim, T. Gordonov, W.E. Bentley, G.F. Payne, Amplified and in situ detection of redox-active metabolite using a biobased redox capacitor, Anal. Chem. 85 (2013) 2102–2108, http://dx.doi.org/10.1021/ac302703y.
[9] H. Ben-Yoav, T.E. Winkler, E. Kim, S.E. Chocron, D.L. Kelly, G.F. Payne, R. Ghodssi, Redox cycling-based amplifying electrochemical sensor for in situ clozapine antipsychotic treatment monitoring, Electrochim. Acta 130 (2014) 497–503, http://dx.doi.org/10.1016/j.electacta.2014.03.045.
[10] R.W. Buchanan, J. Kreyenbuhl, D.L. Kelly, J.M. Noel, D.L. Boggs, B.A. Fischer, S. Himelhoch, B. Fang, E. Peterson, P.R. Aquino, W. Keller, The 2009 schizophrenia PORT psychopharmacological treatment recommendations and summary statements, Schizophr. Bull. 36 (2010) 71–93, http://dx.doi.org/10.1093/schbul/sbp116.
[11] R.R. Conley, C.A. Tamminga, D.L. Kelly, C.M. Richardson, Treatment-resistant schizophrenic patients respond to clozapine after olanzapine non-response, Biol. Psychiatry 46 (1999) 73–77, http://dx.doi.org/10.1016/S0006-3223(99)00029-3.
[12] J. Kane, G. Honigfeld, J. Singer, H. Meltzer, Clozapine for the treatment-resistant schizophrenic. A double-blind comparison with chlorpromazine, Arch. Gen. Psychiatry 45 (1988) 789–796.
[13] D.L. Kelly, H. Ben-Yoav, G.F. Payne, T.E. Winkler, S.E. Chocron, E. Kim, V. Stock, G. Vyas, R.C. Love, H.J. Wehring, K.M. Sullivan, S. Feldman, F. Liu, R.P. McMahon, R. Ghodssi, Blood draw barriers for treatment with clozapine and development of point-of-care monitoring device, Clin. Schizophr. Relat. Psychoses (2015), http://dx.doi.org/10.3371/CSRP.KEBE.070415 in press.
[14] H. Ben-Yoav, S.E. Chocron, T.E. Winkler, E. Kim, D.L. Kelly, G.F. Payne, R. Ghodssi, An electrochemical micro-system for clozapine antipsychotic treatment monitoring, Electrochim. Acta 163 (2015) 260–270, http://dx.doi.org/10.1016/j.electacta.2015.02.112.
[15] L.D. Burke, P.F. Nugent, The electrochemistry of gold: II the electrocatalytic behaviour of the metal in aqueous media, Gold Bull. 31 (1998) 39–50, http://dx.doi.org/10.1007/BF03214760.
[16] C. Nunes Kirchner, K.H. Hallmeier, R. Szargan, T. Raschke, C. Radehaus, G. Wittstock, Evaluation of thin film titanium nitride electrodes for electroanalytical applications, Electroanalysis 19 (2007) 1023–1031, http://dx.doi.org/10.1002/elan.200703832.
[17] A.M. Feltham, M. Spiro, Platinized platinum electrodes, Chem. Rev. 71 (1971) 177–193, http://dx.doi.org/10.1021/cr60270a002.
[18] T.E. Winkler, S.L. Lederer, E. Kim, H. Ben-Yoav, D.L. Kelly, G.F. Payne, R. Ghodssi, Molecular Processes in an Electrochemical Clozapine Sensor, Biointerphases (2017) in press.
[19] B. Avasarala, P. Haldar, Electrochemical oxidation behavior of titanium nitride based electrocatalysts under PEM fuel cell conditions, Electrochim. Acta 55 (2010) 9024–9034, http://dx.doi.org/10.1016/j.electacta.2010.08.035.
[20] J.-M. Kauffmann, G.J. Patriarche, G.D. Christian, Electrochemical oxidation of derivatives of dibenzodiazepin. Dibenzothiazepin and dibenzoxazepin, Anal. Lett. 12 (1979) 1217–1234, http://dx.doi.org/10.1080/00032717908067911.
[21] K.E. Toghill, R.G. Compton, Electrochemical non-enzymatic glucose sensors: a perspective and an evaluation, Int. J. Electrochem. Sci. 5 (2010) 1246–1301.
[22] S. Park, H. Boo, T.D. Chung, Electrochemical non-enzymatic glucose sensors, Anal. Chim. Acta 556 (2006) 46–57, http://dx.doi.org/10.1016/j.aca.2005.05.080.
[23] N. Priyantha, S. Malavipathirana, Effect of chloride ions on the electrochemical behaviour of platinum surfaces, J. Natl. Sci. Counc. Sri Lanka 24 (1996) 237–246, http://dx.doi.org/10.4038/jnsfsr.v24i3.5556.
[24] S.E. Chocron, B.M. Weisberger, H. Ben-Yoav, T.E. Winkler, E. Kim, D.L. Kelly, G.F. Payne, R. Ghodssi, Multidimensional mapping method using an arrayed sensing system for cross-reactivity screening, PLoS ONE 10 (2015) e0116310, http://dx.doi.org/10.1371/journal.pone.0116310.
[25] J.S. Mayell, S.H. Longer, A study of surface oxides on platinum electrodes, J. Electrochem. Soc. 111 (1964) 438–446, http://dx.doi.org/10.1149/1.2426148.