

Article

Electrochemical Evaluation of Polymer-Based Microelectrode Arrays: Analytical Performance on Oxygen and Hydrogen Peroxide

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Abstract

This study investigates the electrochemical properties of polymer-based microelectrode arrays (pMEAs) and their performance in measuring oxygen (O₂) and hydrogen peroxide (H₂O₂). Morphological characterization by scanning electron microscopy (SEM), energy-dispersive X-ray spectroscopy (EDS) and X-ray diffraction (XRD) revealed a uniform, fine-grained platinum surface with nanoscale roughness, consistent with the Ti/Pt/Au/Pt multilayer stack architecture. The electrochemical behavior of the pMEAs was assessed using cyclic voltammetry (CV) and electrochemical impedance spectroscopy (EIS), which demonstrated favorable responses for both O₂ reduction and H₂O₂ oxidation, together with low impedance (41.1 kΩ at 1 kHz). For O₂ detection, amperometric measurements at −0.6 V vs. Ag/AgCl indicated a sensitivity of -0.25 ± 0.04 nA μM^{−1} and a detection limit of 5.4 ± 1.4 nM. For H₂O₂ detection, application of +0.7 V vs. Ag/AgCl resulted in a sensitivity of 88.13 ± 7.61 nA mM^{−1} and a detection limit of 41.9 ± 5.6 nM. Selectivity evaluation showed effective interferent exclusion following *m*-phenylenediamine electrodeposition, without compromising analytical performance. Overall, these findings indicate the suitability of pMEAs for real-time, in vivo monitoring of O₂ and H₂O₂ in brain tissue with high spatial and temporal resolution, supporting applications in oxidative stress research and neurometabolic sensing.

Keywords: polymer microelectrode arrays; electrochemical characterization; oxygen reduction; hydrogen peroxide detection

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1. Introduction

Understanding the intricate relationship between brain chemistry and electrophysiology is fundamental in deciphering how the brain functions, communicates,

and maintains homeostasis. This interplay governs how chemical signals, such as neurotransmitters, modulate electrical activity, including action potentials, thereby ensuring efficient neural communication [1,2]. Advancements in electrophysiological and electrochemical sensors and biosensors now enable simultaneous recording of electrochemical and electrophysiological signals, offering a more comprehensive view of neuronal activity and chemical signaling [3–7]. These neural tools are essential for capturing the dynamic interactions between neurotransmitter release, neurometabolic processes, and electrical activity, providing critical insights into both normal brain function and neurological disorders [6–9].

Microelectrode arrays (MEAs) can be fabricated from diverse substrates, including silicon, ceramics and polymers, and have gained significant relevance in neurobiology both as recording and stimulation probes [10–12]. Ceramic-based microelectrodes are widely valued for their mechanical stability, biocompatibility, and excellent electrical properties [11,13,14]. Their robustness allows them to withstand mechanical stresses associated with *in vivo* applications, while their chemical inertness and established biocompatibility support their use in chronic neural interfacing applications [13,15]. Additionally, these electrodes can be engineered to exhibit favorable electrical characteristics, such as low impedance and high charge injection capacity, which are essential for long-term neural interfacing [16,17]. Further surface modifications using conducting polymers, nanotubes, or nanoparticles can significantly enhance their electrochemical performance, which can improve sensitivity for neurotransmitter detection [18,19].

Polymer-based microelectrodes offer distinct advantages in terms of flexibility, ease of fabrication, and adaptability [20,21]. Their compliant mechanical properties tend to reduce tissue damage during implantation, while their customizable designs allow for tailored electrode configurations [22]. Those fabricated from Parylene C have gained prominence due to their biocompatibility, flexibility and chemical inertness, making them well-suited substrates for long-term neural recording and stimulation [23–27]. The unique properties of Parylene C ensure that the electrodes maintain their electrical characteristics even under bending or other mechanical stress, thereby preserving stability and reliability during *in vivo* recordings [28].

Despite the growing interest in pMEAs for neural interfacing, the electrochemical properties of Parylene C-based devices featuring multilayer metal stacks have not been systematically characterized to the depth required for their reliable deployment as neurochemical biosensors. In this study, we address this gap by providing a comprehensive electrochemical characterization of a Parylene C-based pMEA (Polymer Implantable Electrode (PIE) Foundry, University of Southern California, CA, USA) with a Ti/Pt/Au/Pt multilayer active surface [26], encompassing surface morphology, electrochemical active surface area determination, impedance spectroscopy, and amperometric detection of O₂ and H₂O₂. We further demonstrate the platform's compatibility with permselective surface modifications strategies and establish key structure–performance relationships governing electrode sensitivity and selectivity. These results provide the electrochemical foundation necessary for the translation of this flexible polymer platform into functional biosensors for real-time, multimodal neurochemical and electrochemical monitoring in biological systems.

2. Materials and Methods

2.1. Chemicals and Solutions

All reagents used were of analytical grade and obtained from Sigma-Aldrich, Lisbon, Portugal. *In vitro* electrode evaluations were conducted in either phosphate-buffered saline (PBS Lite) 0.05 M (pH 7.4), composed of 100 mM NaCl, 10 mM NaH₂PO₄ and 40

mM Na₂HPO₄, or in an acidic electrolyte medium of 0.1 M H₂SO₄. For operational stability assessments in a more biologically representative matrix, artificial cerebrospinal fluid (aCSF) was prepared, composed of 147.6 mM NaCl, 3 mM KCl, 1.4 mM CaCl₂, 0.8 mM MgCl₂, and 1 mM NaH₂PO₄, supplemented with 10 mM glucose and 0.5 mg mL⁻¹ bovine serum albumin (BSA). Unless stated otherwise, all solutions were prepared using bi-deionized water with a resistivity of ≥ 18 M Ω cm (Millipore Corporation, Burlington, MA, USA). When needed, solutions were deoxygenated by purging with nitrogen gas (Air Liquide, Lisbon, Portugal) for a minimum of 15 min. For electrode calibration, oxygen-saturated solutions were prepared by bubbling PBS Lite with 100% O₂ (Air Liquide, Lisbon, Portugal) for 15 min, achieving an O₂ concentration of approximately 1.4 mM concentration at 20 °C [29]. The H₂O₂ (9.8 mM), ascorbic acid (20 mM) and dopamine (20 mM) stock solutions were prepared freshly each day.

2.2. Polymer Microelectrode Arrays

In this study, we used a 64-site Parylene C (poly-monochloro (*p*-xylylene))-based polymer microelectrode array, ganged into 8 independent recording zones (8 pads per zone). This array features a multilayered stacked active surface composed of Ti/Pt/Au/Pt layers with thickness of 20/25/155/25 nm, respectively. Each recorded signal captures the aggregate response of up to eight active sites on the electrode by shorting groups of electrodes together. The electrodes in Figure 1 were provided by the PIE Foundry at the University of Southern California, Los Angeles, CA, USA and were previously described in [26]. These pMEAs comprise three key structural components: a base layer of Parylene C, a metal layer containing the electrodes, traces and contact pads, and an insulating top layer of Parylene C. The insulating layer was selectively etched to expose the electrodes and contacts. The fabrication of these pMEAs involves photolithography, chemical vapor and electron beam deposition, and plasma etching, all conducted in a class 1000 (ISO 6) cleanroom environment [26]. Briefly, the fabrication process began with 100 mm diameter silicon carrier wafers, which were vapor-coated in approximately 10 μ m of Parylene C (Specialty Coating Systems, Indianapolis, IN, USA) to form the base layer. The wafers were then baked at 150 °C for 4 h under vacuum or a nitrogen atmosphere to increase the crystallinity of the Parylene C, reducing its thermal expansion and preparing it for the subsequent metal deposition.

A thin-film metal layer containing all traces, contact pads, electrodes, and labels was then fabricated using image-reversal photolithography, metal evaporation, and solvent-assisted metal lift-off. The wafers were coated with AZ 5214E-IR photoresist (Integrated Micro Materials, Denton, TX, USA) at a thickness of 1.1 μ m and patterned in image-reversal mode. To enhance adhesion, the Parylene C surface was treated with mild O₂ plasma prior to metal deposition. A Ti/Pt/Au/Pt metal stack (20/25/155/25 nm, respectively) was deposited by e-beam evaporation, and the patterned metal layer was defined via solvent lift-off. Residual unpatterned photoresist was removed in a bath of N-methyl-2-pyrrolidone (NMP) (Integrated Micro Materials, Denton, TX, USA) at 60 °C, followed by ultrasonic treatment.

The wafers were subsequently treated with A174 silane (Specialty Coating Systems, Indianapolis, IN, USA), an adhesion promoter, and coated with a second 10 μ m thick Parylene C layer to serve as the insulating top surface of the pMEA, bringing the total multilayer thickness to approximately 20 μ m. The electrodes and contact pads were exposed, and the pMEA shape was defined by etching the wafers with O₂ plasma through two separate photoresist masks. For the first etch, wafers were treated with 15 μ m thick AZ 12XT-20PL-15 photoresist (Integrated Micro Materials, Denton, TX, USA), patterned by contact UV lithography and etched to a depth of 10 μ m using reactive ion etching. After initial etching step, the photoresist mask was stripped, a second mask was applied, and

the etching process was repeated to complete the design. Following the second etch, the mask was stripped and the devices were released by submerging the wafer in deionized water, where individual devices were carefully peeled off using tweezers.

To enhance adhesion between the Parylene C layers and improve barrier properties, the pMEAs were annealed under vacuum at 200 °C for 48 h, sandwiched between ceramic alumina plates (0.635 mm thick), and subsequently at 275 °C for 5 h [26]. Finally, the electrodes were cleaned with a brief O₂ plasma exposure prior to use.

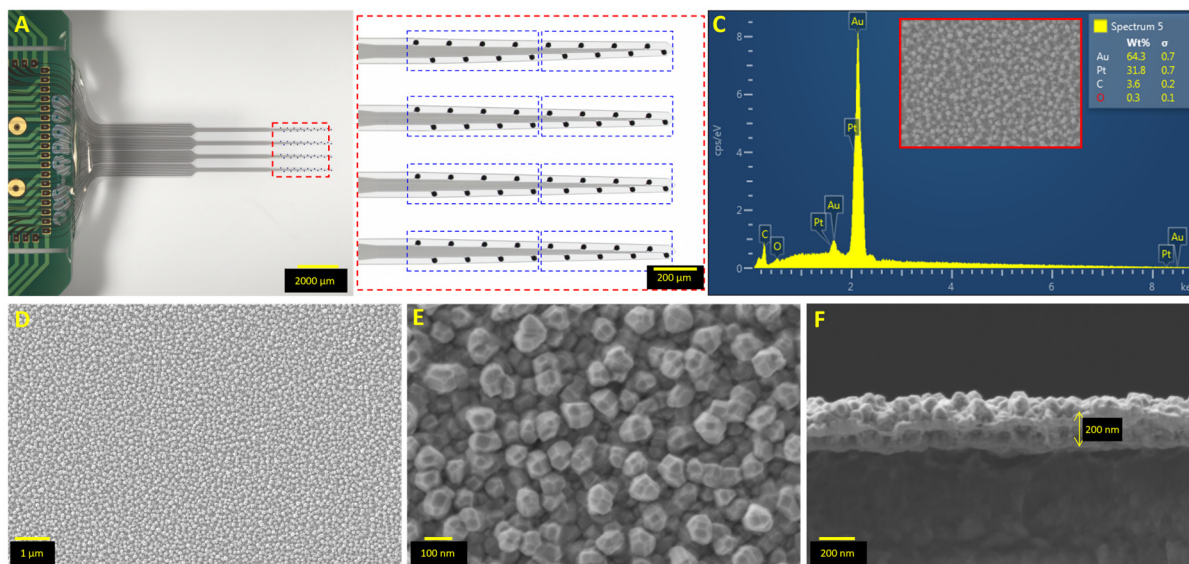


Figure 1. Morphological and chemical analysis of the pMEA Ti/Pt/Au/Pt stack surface. (A) Brightfield microscopic image of the MEA and (B) high-magnification view of the active surface with the eight zones distinguished by the dashed blue rectangles (region of interest indicated with dashed red square in (A)). (C) Elemental composition of the Ti/Pt/Au/Pt stack active surface layer of the pMEA obtained by SEM/EDS elemental analysis at 10 keV. (D) High-resolution SEM micrograph image of the planar active surface and (E) high-magnification view of the Pt layer. (F) Cross-sectional SEM micrograph of the stacked metal layer on the silicon carrier wafer, revealing nanoscale elevations on the Pt surface.

2.3. Scanning Electron Microscopy and Elemental Composition Characterization

High-resolution scanning electron microscopy (SEM) was performed using a Zeiss Merlin scanning electron microscope (Oberkochen, Germany) equipped with a GEMINI II column, offering advanced imaging capabilities with exceptional resolution and contrast. The instrument was coupled with energy-dispersive X-ray spectroscopy (EDS) for elemental analysis, enabling qualitative and quantitative identification of the sample's composition. EDS analysis was conducted at an accelerating voltage of 10 keV using an X-Max detector (Oxford Instruments, High Wycombe, UK).

2.4. X-Ray Diffraction Characterization

The electrode structure was analyzed by X-ray diffraction (XRD) using a Rigaku MiniFlex 600 diffractometer (Rigaku, Tokyo, Japan). Test coupons (approx. 2 × 2 cm²) consisting of the stacked metal on a silicon substrate were used. The diffractometer was operated at 40 kV and 15 mA using CuK α radiation (λ = 1.5406 Å), which is well-suited for studying crystalline materials due to its high energy that ensures effective penetration and scattering, and its wavelength, which is ideal for resolving atomic-scale features.

2.5. Electrochemical Instrumentation

Electrochemical characterization and amperometric calibrations were performed using a MultiPalmSens4 potentiostat (PalmSens BV, Houten, The Netherlands), controlled by MultiTrace v. 4.2 software. A three-electrode electrochemical cell configuration was employed, with the pMEA as the working electrode, an Ag/AgCl reference electrode (3 M KCl; RE-5B, BASi Research Products Inc., West Lafayette, IN, USA), and a platinum wire as the auxiliary electrode.

2.6. Microelectrode Calibration

The pMEAs were evaluated for their response to O₂ and H₂O₂. Amperometric calibrations were conducted in 40 mL of 0.05 M PBS Lite (pH 7.4) at room temperature (20 °C) with continuous stirring at 240 rpm. To remove dissolved O₂, the calibration solution was purged with N₂ for a minimum period of 15 min. After purging, the N₂ delivery needle was repositioned above the solution surface to minimize O₂ back-diffusion into the calibration medium. Before calibration, the background current was allowed to stabilize under constant polarization for approximately 20 min. Then, 10 µM aliquots of O₂-saturated solution were sequentially added to obtain a final concentration range of 0–50 µM. To assess the upper limit of the linear range, the O₂ calibration protocol was extended to a concentration range of 0–150 µM. For the H₂O₂ calibrations, once a stable baseline was established, 9.8 µM aliquots of the H₂O₂ stock solution were sequentially added to obtain a final concentration range of 0–39.2 µM. To establish the upper limit of the linear range, the H₂O₂ calibration protocol described above was extended to a concentration range of 0–2 mM on a subset of electrodes ($n = 4$, same devices/sites as the original calibration). Unless otherwise stated, reported sensitivity, LOD, and calibration parameters ($n = 8$) were obtained from 4 ganged recording sites on each of 2 independently fabricated pMEA devices, capturing both inter-device and inter-site variability.

2.7. Electrochemical Impedance Spectroscopy Measurements

Electrochemical impedance spectroscopy (EIS) measurements were performed over a frequency range of 100 kHz to 0.1 Hz (10 frequencies per decade) at the open-circuit potential (OCP = +0.03 V vs. Ag/AgCl). Measurements were carried out in N₂-saturated 0.05 M PBS Lite (pH 7.4) using a three-electrode configuration. Impedance spectra were fitted to an equivalent circuit comprising the solution resistance (R_s) in series with a parallel combination of a constant phase element (CPE) and a leakage resistance (R_e), using complex nonlinear least squares minimization.

2.8. Selectivity Measurements

For permselective membrane deposition, *m*-phenylenediamine (*m*-PD) was electropolymerized onto the Pt surface by cyclic voltammetry in deoxygenated PBS Lite (pH 7.4) containing 5 mM *m*-PD monomer, by cycling the potential between +0.25 and +0.75 V vs. Ag/AgCl at a scan rate of 50 mV s^{−1} for 50 cycles.

The selectivity of the pMEA towards O₂ and H₂O₂ was evaluated by amperometry in the presence of ascorbic acid (AA) and dopamine (DA). Selectivity tests were performed in 40 mL of 0.05 M PBS Lite (pH 7.4) at room temperature (20 °C) with continuous stirring at 240 rpm, at both detection potentials (−0.6 V and +0.7 V vs. Ag/AgCl, respectively). Once a stable baseline was established, the target analyte (O₂ or H₂O₂) were sequentially added to a known concentration of AA (100 µM) and DA (5 µM), and the current response was recorded. Selectivity evaluation ($n = 4$) was performed on 4 ganged recording sites of a single pMEA device. The selectivity ratio was calculated as the ratio of the sensitivity to the target analyte over the sensitivity to each interferent species.

2.9. Operational Stability and Biofouling Assessment

To evaluate electrode operational stability and anti-fouling performance under a more biologically representative matrix, a single pMEA device ($n = 4$ ganged recording sites) was initially calibrated for O_2 and H_2O_2 and then continuously polarized at the respective working potentials in an aCSF + glucose + BSA solution for 4 h at room temperature, after which a second calibration was performed under identical conditions. Baseline drift was calculated as the difference between mean baseline currents recorded immediately before the initial (T_0) and final (T_i) calibrations, divided by the elapsed time.

2.10. Data Analysis

Data analysis was conducted using MultiTrace v. 4.2, OriginPro 2016 (OriginLab, Northampton, MA, USA) and GraphPad Prism 8 (GraphPad Software, San Diego, CA, USA). The sensitivity of the pMEA to O_2 and H_2O_2 was determined by linear regression analysis over the ranges of 0–50 μM and 0–39.2 μM , respectively. The limit of detection (LOD) was defined as the concentration corresponding to a signal-to-noise ratio of 3. Response times ($t_{90}-t_{10\%}$) were determined by fitting the amperometric current traces to a Boltzmann sigmoid function by calculating the time to reach 10% and 90% of the steady-state response. Values are given as the mean $\pm$ standard deviation (SD).

3. Results and Discussion

3.1. Morphology and Chemical Analysis

All pMEAs used in this work were ganged 64-channel arrays with eight recording sites, including two recording-site regions on each electrode shank, which were designed for (sub)cortical recording, as highlighted in the dashed blue rectangles in Figure 1B. The 64 channels were evenly distributed across 4 shanks each approximately 5.4 mm long, in a boot-lace layout (Figure 1A,B). Each active site had an estimated geometric area of $7.06 \times 10^{-6} \text{ cm}^2$ (30 μm diameter).

To characterize the elemental composition of the pMEA active surface, EDS was employed. Since each element has distinct energy levels, the emitted X-rays can be used to identify the elements present in the sample. As shown in Figure 1C, the active surface primarily consists of Au and Pt (approximately 64.3% and 31.8% respectively), with smaller amounts of C and O. The high Au content observed in the EDS spectrum can be attributed to the penetration depth of the electron beam at 10 keV, which extends beyond the thin outermost Pt layer (25 nm), resulting in a high Au signal relative to the true composition of the outermost surface composition. Because EDS is not intrinsically surface-sensitive, the Au/Pt proportions measured at 10 keV reflect the elemental composition of the multilayer stack within the electron beam interaction volume rather than exclusively the outermost surface. The characteristic hydrogen adsorption/desorption and Pt oxide formation/reduction features observed by cyclic voltammetry (Section 3.2) indicate that the electrochemically accessible surface is predominantly Pt. Moreover, no resolvable Au oxide reduction peak was detected. Nevertheless, trace or highly localized Au exposure cannot be completely excluded. The outermost Pt layer constitutes the electrochemically accessible surface, as confirmed by the characteristic Pt behavior observed in cyclic voltammetry in both acidic and neutral media (Section 3.2) [13,30].

To further examine the surface morphology, SEM micrographs were acquired. As shown in Figure 1D, the planar surface of the multilayer pMEA displays a uniform surface, with no visible micro-cracks or defects, suggesting a high degree of precision in the fabrication. Higher-magnification images (Figure 1E) revealed well-defined, fine-grained structures characteristic of the e-beam evaporation process used to deposit the

stack metal layer. This uniformly distributed nanoscale roughness, arising from the deposition process, is expected to support excellent electrical conductivity and mechanical stability, both of which are critical for the pMEA performance [31]. Figure 1F shows a cross-sectional SEM micrograph revealing a deposited metal layer approximately 200 nm thick, in agreement with the manufacturing specifications of the pMEA [32].

To further characterize the pMEA, XRD was used to investigate the atomic and molecular structure of the silicon carrier wafer with the Ti/Pt/Au/Pt metal stack [33]. As illustrated in Figure 2, the positions and intensities of the diffraction peaks in the XRD spectra reveal the presence of multiple crystalline phases, consistent with a layered material structure. Each diffraction peak corresponds to a specific set of lattice planes in the crystal structure. The peak at approximately $2\theta \approx 13^\circ$ is a low-angle feature likely associated with an organic or polymeric structure, such as Parylene C [34]. Sharp and intense peaks at $2\theta \approx 28^\circ$ and 69° are attributed to crystalline silicon phases (Si (111) and Si (400), respectively) [33]. Peaks at $2\theta \approx 40^\circ$, 47° , 68° , and 82° correspond to Pt (111), Pt (200), Pt (220), and Pt (222), confirming a Pt face-centred cubic (FCC) structure [35,36]. Similarly, peaks at $2\theta \approx 38^\circ$, 44° , and 64° are assigned to Au (111), Au (200), and Au (220), characteristic of Au's FCC structure [35,37].

The Si (400) peak exhibits the highest intensity, reflecting the dominance of the crystalline silicon in carrier wafer. The Au and Pt peaks are moderately intense, consistent with the thin-film nature of these layers and their expected quantities in the pMEA stack.

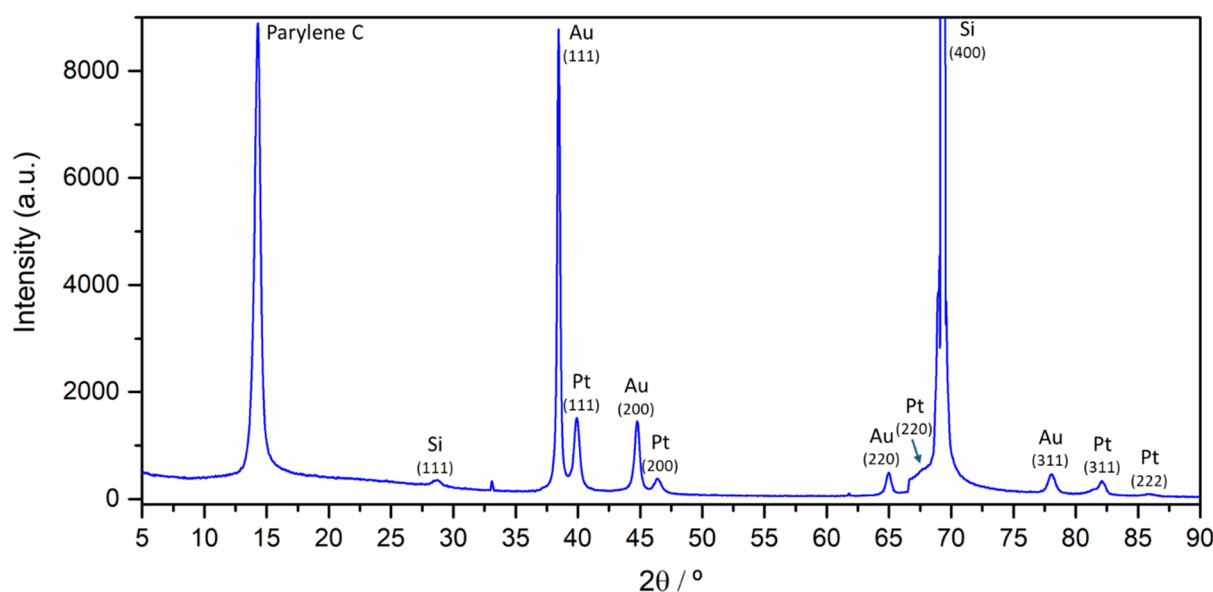


Figure 2. X-ray diffraction spectrum of the pMEA Ti/Pt/Au/Pt metal stack deposited on a silicon carrier wafer, with identification of the principal diffraction peaks corresponding to Parylene C, platinum (Pt), gold (Au), and silicon (Si). Spectra were acquired at 40 kV and 15 mA using CuK α radiation.

3.2. Electrochemical Behavior in Acidic Electrolyte and in Neutral PBS

Characterization of the electrochemical behavior of Pt pMEAs in acidic media is important for understanding their catalytic properties, particularly in reactions such as the hydrogen evolution reaction (HER) and oxygen reduction reaction (ORR). Acidic solutions significantly enhance the kinetics, leading to more efficient electron transfer processes [30,38].

Figure 3A shows cyclic voltammograms recorded for a single ganged site of the pMEA between -0.3 and $+1.2$ V vs. Ag/AgCl at scan rates ranging from 50 to 1000 mV s $^{-1}$. The voltammograms exhibit the characteristic features of a Pt surface, including hydrogen

adsorption peaks at -0.05 and -0.19 V vs. Ag/AgCl during the cathodic sweep and three hydrogen desorption peaks at -0.26 , -0.15 and -0.09 V vs. Ag/AgCl during the anodic sweep [30,39]. The presence of multiple desorption peaks suggests surface roughness or the presence of different adsorption sites, reflecting the interactions between hydrogen and the Pt surface that underpin various electrochemical processes [30]. Distinct anodic and cathodic peaks corresponding to the formation and reduction of Pt oxides are also observed, namely an oxidation wave at $E > 0.5$ V corresponding to the formation of Pt-O and Pt-OH oxide species and a reduction peak at $E \approx -0.5$ V corresponding to their reduction. These redox features provide important insights into the surface chemistry and catalytic properties of the electrode [40].

Figure 3B compares voltammograms recorded in neutral media between -0.7 and $+1.1$ V vs. Ag/AgCl and in acidic media between -0.3 and $+1.2$ V vs. Ag/AgCl. In acidic electrolyte, the higher proton availability leads to more pronounced hydrogen adsorption and desorption peaks reflecting enhanced electrocatalytic activity. By contrast, in neutral media, the lower proton concentration suppresses these hydrogen adsorption features, resulting in less distinct peaks and potentially lower overall catalytic activity compared to the acidic conditions [30]. As shown in Figure 3B, the potential window in neutral media spans approximately 1.5 V compared to approximately 1.0 V in acidic media, consistent with the reduced occurrence of side reactions at neutral pH [30,41].

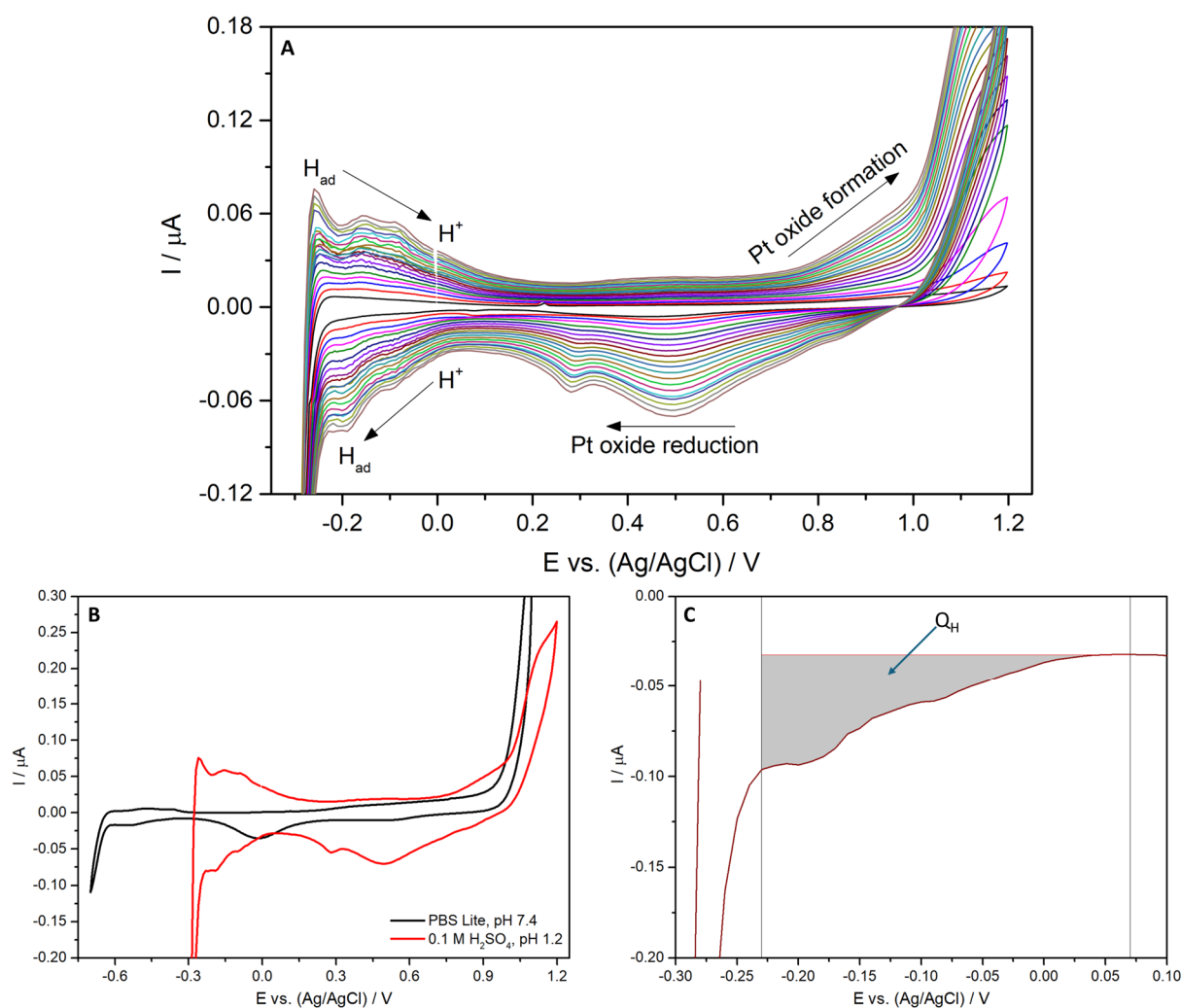


Figure 3. Electrochemical behavior in acidic and neutral electrolyte media. (A) Successive cyclic voltammograms (10th scan) recorded at increasing scan rates (50 – 1000 mV s^{-1}) in N_2 -saturated 0.1 M H_2SO_4 , illustrating typical Pt oxide formation and reduction, hydrogen adsorption (two peaks)

and desorption (three peaks), as well as double-layer regions. (B) Cyclic voltammograms (200 mV s⁻¹) recorded in N₂-saturated 0.05 M PBS Lite (pH 7.4, black line) and N₂-saturated 0.1 M H₂SO₄ (pH 1.2, red line), demonstrating the positive shift in hydrogen evolution potential and increased currents for Pt oxide formation and reduction at lower pH on the Pt surface of the pMEAs. (C) Representative cyclic voltammogram recorded in N₂-saturated 0.1 M H₂SO₄ for the determination of the ECSA of the Pt ganged sites on the pMEA. The shaded area (Q_H) corresponds to the charge associated with hydrogen adsorption, integrated between E₁ = -0.23 V and E₂ = +0.07 V vs. Ag/AgCl (vertical lines), which was used to calculate the ECSA.

3.3. Electrochemical Active Surface Area

Cyclic voltammetry in acidic media can also provide important information regarding the electrochemical active surface area (ECSA) of the Pt electrode. The hydrogen adsorption peaks observed at negative potentials are indicative of hydrogen underpotential deposition (H_{UPD}) on the Pt surface [13], and the area under these peaks is proportional to the number of active sites available [30,42]. Because ECSA is closely related to catalytic performance, it represents a key parameter for evaluating Pt electrodes in electrochemical applications [43].

As shown in Figure 3C, the hydrogen adsorption charge (Q_H) was determined by integrating the current in the hydrogen adsorption region of the negative-going sweep of the CV recorded in 0.1 M H₂SO₄, after correction for the double-layer pseudocapacitance. The integration was performed between E₁ = -0.23 V and E₂ = +0.07 V, corresponding to the onset and end of the hydrogen adsorption region, respectively, as defined by the voltammogram (Figure 3C). Q_H was calculated according to Equation (1):

$$Q_H = \int_{E_1}^{E_2} \frac{I(E)}{v} dE \quad (1)$$

which expresses the relationship between electric current and charge in an electrochemical system, where (Q_H) is the total electric charge that is passed through the system during a specific process, E₁ and E₂ are the integration limits of the hydrogen adsorption region, and *v* is the scan rate. The ECSA was then calculated by dividing the integrated charge by the established hydrogen charge density for Pt of 210 μC cm⁻² [30,39,44], leading to Equation (2):

$$ECSA = \frac{Q_H}{210 \mu C cm^{-2}} \quad (2)$$

The ganged active site of the pMEA exhibited an ECSA of $3.52 \times 10^{-5} \pm 0.58 \times 10^{-5}$ cm².

3.4. Electrochemical Impedance Spectroscopy

Electrochemical impedance spectroscopy (EIS) was used to investigate the interfacial and electrical properties of the Pt pMEA, providing insight into the electrode–electrolyte interface. The resulting Bode and Nyquist plots are shown in Figure 4A,B, respectively. The impedance data was fitted to the equivalent circuit described in Section 2.7 (inset, Figure 4B), comprising an R_s in series with a parallel CPE and R_e. This circuit topology captures the essential features of an electrode interface, where double-layer charging dominates the response across the entire frequency window and no significant faradaic process is present [45].

The fitted parameters are listed in Table 1. The R_s value of 2.48 kΩ reflects the ohmic resistance of the PBS electrolyte. The CPE describes the non-ideal double-layer capacitance of the Pt surface, with an exponent value of *n* = 0.84. The deviation of *n* from unity reflects the distributed capacitive response arising from nanoscale surface roughness introduced during e-beam evaporation of the Pt layer, consistent with the surface morphology observed by SEM [46]. The leakage resistance R_e converged to a value of 1.3 GΩ, several orders of magnitude larger than the maximum measured impedance,

confirming that the electrode behaves as a near-ideal blocking interface in PBS at OCP with no redox-active species present.

In EIS studies, the impedance at 1 kHz is commonly used as a standard reference frequency in neural electrode characterisation, as it aligns with the characteristic range of bioelectrical signals and the impedance of biological tissues [47,48]. At this frequency, the impedance is governed primarily by the double-layer capacitance rather than by charge transfer resistance [45]. The ganged site of the pMEA exhibited a total impedance of 41.1 k Ω (1.17 Ω cm²) at 1 kHz, a value which falls within the range considered suitable for in vivo neural recording and is directly associated with an improved signal-to-noise ratio [39,47]. These low impedance values, combined with the favourable surface characteristics revealed by CV, further support the use of pMEAs for concurrent electrophysiological and neurochemical monitoring [7].

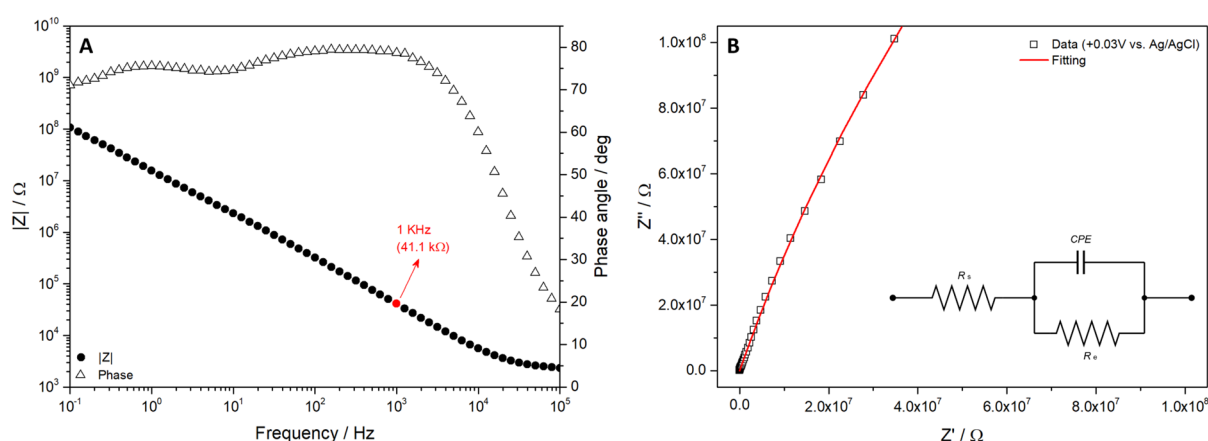


Figure 4. EIS analysis. (A) Bode plot showing the impedance magnitude $|Z|$ (filled circles, left axis) and phase angle (open triangles, right axis) as a function of frequency for a Pt ganged site of the pMEA, recorded at OCP (+0.03 V vs. Ag/AgCl). The red-filled circle highlights the $|Z|$ value at 1 kHz (41.1 k Ω). (B) Nyquist plot of the experimental EIS data (open squares) for the Pt ganged site. The red line represents the fitted model using the equivalent circuit shown in the inset, comprising R_s (solution resistance) in series with a parallel combination of CPE (constant phase element) and R_e (leakage resistance).

Table 1. Summary of fitted parameters results for impedance spectroscopy measurements for the Pt pMEAs.

R_s (k Ω)	R_e	CPE	n
2.48	1.3 G Ω	13.0 nF s ^{$n-1$}	0.84
	45.76 ^[a] k Ω cm ²	369.3 ^[a] μ F cm ⁻² s ^{$n-1$}	

^[a] Values normalized by ECSA.

3.5. Oxygen Reduction Reaction at the Pt Surface

Pt is a well-established electrocatalyst for the oxygen reduction reaction (ORR), producing a faradaic reduction current proportional to O₂ concentration that forms the basis of amperometric O₂ sensing [39,49,50]. Figure 5A shows representative cyclic voltammograms recorded in PBS (pH 7.4) under N₂-saturated and air-saturated (0.27 mM O₂) conditions. In the presence of O₂ (blue curve), the reduction current begins to increase at approximately −0.2 V, indicating the onset of the ORR, and reaches a plateau ca. −0.4 V, suggesting that this potential is favourable for detecting O₂ with minimal interference. By contrast, the O₂-free CV (black curve) exhibits minimal current between −0.2 V and −0.6 V, indicating low background interference in this region. At more negative potentials (ca. −0.6 V vs. Ag/AgCl), the onset of HER is evident from the sharp increase in current

observed in both curves. Based on these observations, the optimal working potential for O₂ monitoring lies between −0.4 V and −0.6 V, where the ORR plateau region is established and interference from HER and capacitive currents remains limited.

Figure 5B shows a representative calibration of a ganged site of the pMEA at −0.4 V and −0.6 V vs. Ag/AgCl, with the corresponding calibration curves (inset). At −0.4 V, the ganged Pt site exhibited an O₂ sensitivity of $-0.13 \pm 0.01 \text{ nA } \mu\text{M}^{-1}$ ($n = 8$; $R^2 = 0.995 \pm 0.003$), corresponding to an area-normalised sensitivity of $-6.51 \pm 2.47 \text{ mA mM}^{-1} \text{ cm}^{-2}$ and an LOD of $5.5 \pm 2.1 \text{ nM}$. At −0.6 V, the sensitivity increased to $-0.25 \pm 0.04 \text{ nA } \mu\text{M}^{-1}$ ($n = 8$; $R^2 = 0.996 \pm 0.002$), with a normalised sensitivity of $-11.54 \pm 4.75 \text{ mA mM}^{-1} \text{ cm}^{-2}$ and an LOD of $5.4 \pm 1.4 \text{ nM}$. A rapid response is observed for each O₂ addition, with a response time ($t_{90}-t_{10\%}$) of $5.7 \pm 0.6 \text{ s}$ ($n = 8$, $R^2 = 0.981 \pm 0.009$). The amperometric response remained linear up to $150 \mu\text{M}$ ($R^2 = 0.993 \pm 0.002$). Further extension of the linear range was constrained by back-diffusion of O₂ into the deoxygenated calibration solution and by the increasing dilution effect of the injected calibration volumes at higher analyte concentrations. However, this concentration range is higher than the O₂ concentration levels expected to be found in vivo in tissues [51]. At more negative potentials, the greater overpotential for the ORR enhances the reduction kinetics, resulting in a higher faradaic current. This relationship provides a practical means of tuning the electrode response to the concentration range of relevant species for a given application. In view of the higher sensitivity achieved at −0.6 V together with a comparable LOD and a rapid response time, this potential was selected as the optimal working potential for O₂ monitoring in agreement with previous reports [13,52].

The sensitivity and LOD values for O₂ detection using microelectrodes typically vary due to factors such as surface area, electrode geometry, and the electrochemical techniques employed. The sensitivity obtained in this study is consistent with that reported for other Pt and carbon-based microelectrodes [13,53–56]. Moreover, the LOD is lower than those reported for other microelectrode designs [13,53,56,57], underscoring the suitability of the present pMEA for monitoring O₂ fluctuations in brain tissue, where basal O₂ levels are approximately $30 \mu\text{M}$ [13,58]. Table 2 summarizes the key analytical performance metrics of the present pMEA alongside recently reported O₂-sensing microelectrodes, highlighting their favorable sensitivity, LOD, and response time relative to comparable devices.

Table 2. Analytical Performance Comparison of Microelectrode Arrays for Oxygen Detection ^a.

Microelectrode Type	Electrode Material (Dimensions, μm)	Sensitivity (nA μM^{-1})	Sensitivity/Unit Area (mA mM ^{−1} cm ^{−2})	LOD (nM)	Z at 1 kHz/Unit Area ($\Omega \text{ cm}^2$)	Response Time (s)	Ref.
Flexible (Parylene-C)	Pt (30 $\varnothing$)	-0.25 ± 0.04	-11.54 ± 4.75	5.4 ± 1.4	1.17	5.7 ± 0.6	This work
Flexible (SU-8)	Pt (20 $\times$ 20)	-0.00426^b	-1.065^b	nd	nd	<15	[59]
Ceramic	Pt (15 $\times$ 333)	-0.16 ± 0.02	-3.2 ± 0.5	330 ± 200	10.8	na	[13]
Silicon	Pt (30 $\varnothing$)	nd	nd	nd	nd	nd	[60]
Silicon	Pt (17.5 $\times$ 17.5)	-0.0082	-2.68	20,090	nd	nd	[52]

^a Data is presented as mean $\pm$ SD; ^b Calculated from data in publication; nd, not determined.

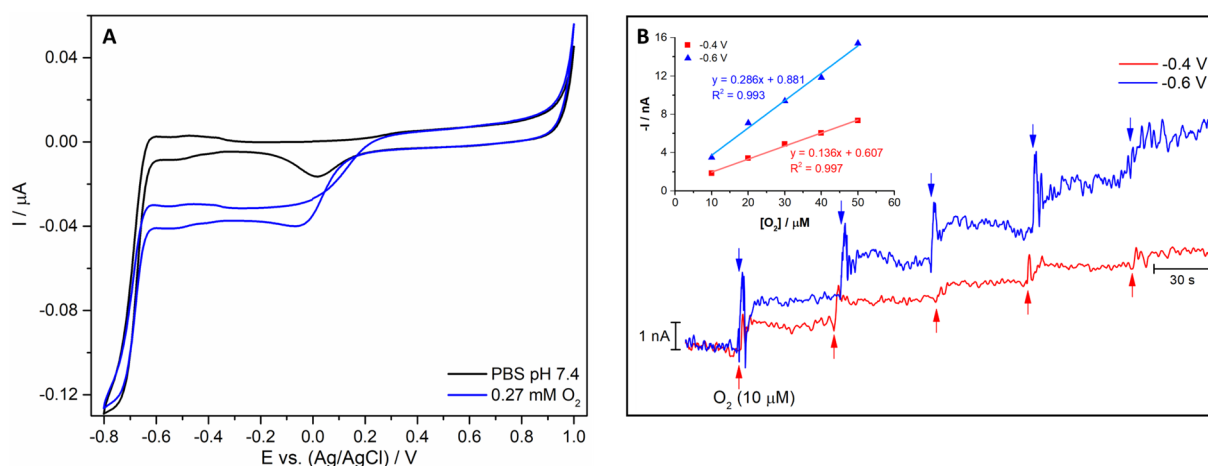
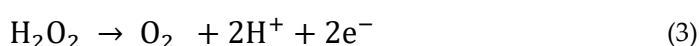


Figure 5. Electrochemical behavior of oxygen reduction on the ganged Pt site of the pMEA. **(A)** Cyclic voltammograms recorded at 100 mV s^{-1} in 0.05 M PBS Lite (pH 7.4), comparing the absence (N_2 -saturated, black line) and the presence (0.27 mM O_2 , blue line) of oxygen. **(B)** Representative amperometric calibration of a single ganged site at -0.4 V (red) and -0.6 V (blue) vs. Ag/AgCl , showing five sequential additions of O_2 (10 μM each; concentration range $0\text{--}50 \text{ μM}$). The corresponding calibration curves for each applied potential are shown in the inset. Arrows indicate the time points of each addition.

3.6. Hydrogen Peroxide Oxidation Reaction at the Pt Surface

The electrochemical oxidation of H_2O_2 on a Pt surface is of particular interest in oxidase-based biosensors (e.g., glucose or lactate biosensors) [5,61,62]. The reaction begins with the adsorption of H_2O_2 onto the Pt surface, which facilitates subsequent electrochemical oxidation. Upon application of a sufficiently positive potential, the Pt surface promotes the transfer of 2 electrons from the H_2O_2 to the electrode, resulting in the oxidation of H_2O_2 into O_2 and protons. During this process, intermediate species may form, contributing to the overall reaction mechanism. The oxidation products, O_2 and protons, are then released from the electrode surface, thereby generating active sites for further reactions. The overall reaction is described by reaction 3 [63]:



Several factors influence the efficiency of H_2O_2 oxidation on a Pt surface. Solution pH plays a role, as the reaction proceeds more efficiently in acidic or neutral conditions where protons are available to facilitate the desorption step. The electrode surface area and roughness are also important, since a larger electroactive surface area and a greater nanoscale roughness increase the number of available active sites for H_2O_2 adsorption and intermediate reactions. In contrast, contaminants or impurities present on the Pt surface may reduce the electrode performance by blocking active sites or modifying the surface properties [64].

Figure 6A shows representative cyclic voltammograms recorded in PBS (pH 7.4) in the absence and presence of 200 μM of H_2O_2 . In the presence of H_2O_2 (green curve), the oxidation current increases progressively from $+0.2 \text{ V}$, reaching a broad maximum around $+0.6\text{--}0.7 \text{ V}$, beyond which no further increase is observed. By contrast, the H_2O_2 -free scan (black curve) shows minimal current throughout this range, confirming low background interference. Based on these observations, $+0.7 \text{ V}$ vs. Ag/AgCl was selected as optimal working potential, as it provides a stable oxidation current, while minimizing noise.

Figure 6B shows a representative calibration of a ganged pMEA site at $+0.7 \text{ V}$ vs. Ag/AgCl , and the corresponding calibration curve (inset). A rapid response was observed for each H_2O_2 addition, with a response time ($t_{90\text{--}t_{10\%}}$) of $8.5 \pm 0.2 \text{ s}$ ($n = 8$, $R^2 = 0.994 \pm 0.001$).

The ganged Pt site exhibited a H_2O_2 sensitivity of $88.13 \pm 7.61 \text{ nA mM}^{-1}$ ($n = 8$, $R^2 = 0.996 \pm 0.002$), an area-normalised sensitivity of $2.56 \pm 0.48 \text{ mA mM}^{-1} \text{ cm}^{-2}$, and an LOD of $41.9 \pm 5.6 \text{ nM}$. The amperometric response remained linear up to 2 mM ($n = 4$, $R^2 = 0.998 \pm 0.002$), confirming that the linear dynamic range extends beyond the physiologically relevant concentrations.

As noted above, both sensitivity and LOD are highly influenced by multiple factors, including electrode geometry, surface properties, and experimental conditions. The sensitivity obtained is particularly higher than that reported for other Pt-based microelectrodes [61,65,66], and significantly higher than values reported for modified glassy carbon electrode [67–69], reflecting the favourable electrocatalytic properties of the pMEA Pt surface towards H_2O_2 oxidation. The LOD falls within the range reported for microelectrode-based H_2O_2 detection (10 nM to $10 \text{ }\mu\text{M}$) [70] and is well suited for monitoring H_2O_2 in biological media where concentrations are typically in the low micromolar range. A comparison with other Pt-based microelectrode arrays is presented in Table 3. These results support the suitability of these pMEAs for monitoring H_2O_2 in brain extracellular space, including studies of oxidative stress in neurological disorders [71,72].

Table 3. Analytical performance comparison of microelectrode arrays for hydrogen peroxide detection ^a.

Microelectrode Type	Electrode Material (Dimensions, μm)	Sensitivity ($\text{nA } \mu\text{M}^{-1}$)	Sensitivity/Unit Area ($\text{mA mM}^{-1} \text{ cm}^{-2}$)	LOD (nM)	$ Z $ at 1 kHz/Unit Area ($\Omega \text{ cm}^2$)	Response Time (s)	Ref.
Flexible (Parylene-C)	Pt (30 ϕ)	88.13 ± 7.61	2.56 ± 0.48	41.9 ± 5.6	1.17	8.5 ± 0.2	This work
Ceramic	Pt (50 $\times$ 50)	0.0122	0.488 ^b	133	nd	nd	[73]
Ceramic	Pt (100 $\times$ 50)	0.006743	0.135 ^b	nd	nd	nd	[74]
Silicon	Pt Black (20 ϕ)	nd	nd	10	nd	<1	[75]
Glass	Pt Black (20 ϕ)	0.0172 ^b	5.48	nd	nd	nd	[76]

^a Data is presented as mean $\pm$ SD; ^b Calculated from data in publication; nd, not determined.

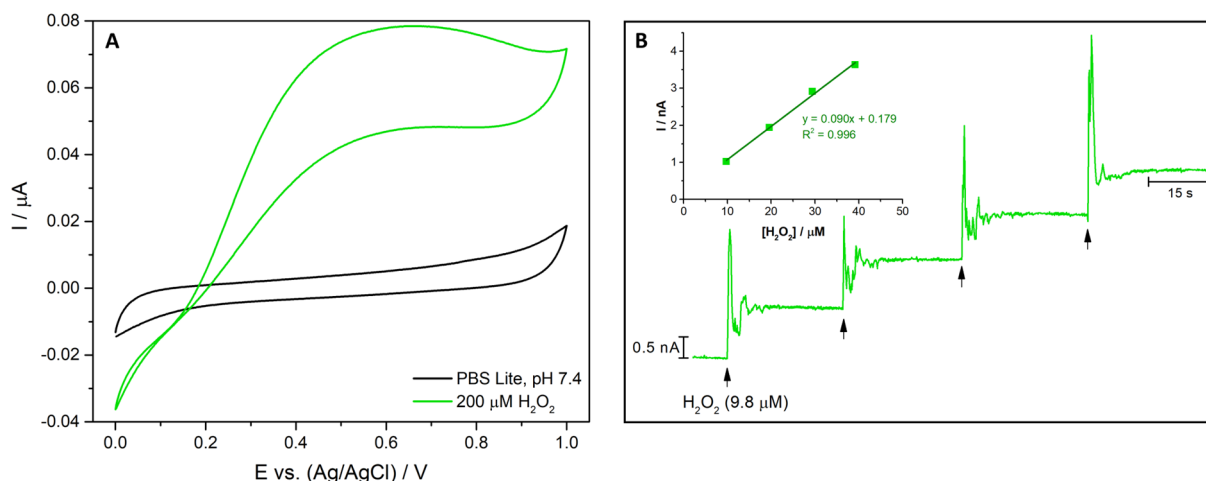


Figure 6. Electrochemical behavior of hydrogen peroxide oxidation on the ganged Pt site of the pMEA. (A) Cyclic voltammograms recorded at 100 mV s^{-1} in N_2 -saturated 0.05 M PBS Lite (pH 7.4), comparing the absence (black line) and the presence (green line) of $200 \text{ }\mu\text{M}$ H_2O_2 . (B) Representative amperometric calibration of a single ganged site at $+0.7 \text{ V}$ vs. Ag/AgCl showing four sequential additions of H_2O_2 ($9.8 \text{ }\mu\text{M}$ each; concentration range $0\text{--}39.2 \text{ }\mu\text{M}$), with the corresponding calibration curve shown in the inset. Arrows indicate the time points of each addition.

3.7. Selectivity Evaluation

To assess the selectivity of the pMEA against common electroactive interferents present in the brain extracellular environment, the responses of both bare Pt and *m*-PD-coated sites to AA and DA were evaluated by amperometry at both detection potentials. *m*-PD is a well-established permselective coating for Pt microelectrodes in neurochemical biosensing, acting as a size exclusion barrier that restricts the access of larger electroactive molecules to the electrode surface while allowing the smaller H₂O₂ molecule to diffuse through freely [65,77–79]. AA and DA were selected because of their electroactive nature and their presence in the brain extracellular space [71,80–82].

Selectivity at +0.7 V vs. Ag/AgCl was initially evaluated at the bare Pt electrode with sequential additions of AA (100 µM), DA (5 µM) and H₂O₂ (9.8 µM). This resulted in current changes corresponding to H₂O₂–interferent selectivity ratios, on a molar basis, of $1.2 \pm 0.06:1$ ($n = 4$) for AA and $0.85 \pm 0.35:1$ ($n = 4$) for DA. Following *m*-PD electrodeposition, selectivity towards AA and DA was increased to $20.3 \pm 0.63:1$ ($n = 4$) and $76.9 \pm 9.89:1$ ($n = 4$), respectively, as shown in Figure 7. The corresponding blocking efficiencies were 95% to AA and 99% to DA, demonstrating effective exclusion of both interferents by the permselective membrane. At −0.6 V vs. Ag/AgCl, the bare Pt electrode already exhibited negligible interference from AA and DA with selectivity ratios of $306.3 \pm 51.6:1$ ($n = 4$) and $63.6 \pm 4.60:1$ ($n = 4$), respectively. Following *m*-PD coating, selectivity values remained comparably high, reaching $532.8 \pm 23.4:1$ ($n = 4$) for AA and $88.0 \pm 7.39:1$ ($n = 4$) for DA. These values corresponded to blocking efficiencies of 99.8% to AA and 98.8% to DA.

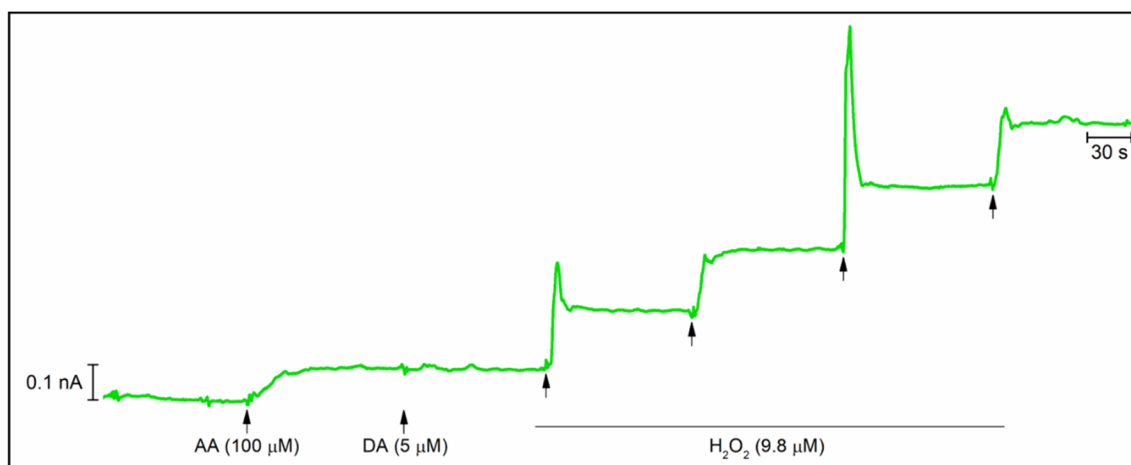


Figure 7. Representative recording of the *m*-PD-coated pMEA ganged site at +0.7 V vs. Ag/AgCl, showing the current response to sequential additions of ascorbic acid (AA, 100 µM), dopamine (DA, 5 µM) and H₂O₂ (9.8 µM) in 0.05 M PBS Lite (pH 7.4). Arrows indicate the time points of each addition.

Taken together, these results demonstrate that the pMEA Pt surface exhibits inherent selectivity for O₂ detection at cathodic potentials, and that *m*-PD electrodeposition effectively suppresses interferent signals at oxidative potentials without compromising analytical performance.

3.8. Operational Stability and Biofouling Effects

To assess the operational stability and biofouling performance of the pMEA under more physiologically challenging conditions, calibrations were performed before (T_0) and after (T_f) a 4 h continuous polarization period in artificial cerebrospinal fluid supplemented with glucose and BSA. For O₂, baseline current drifted at a rate of $-0.34 \pm$

0.10 nA h⁻¹ ($-1.8 \pm 0.5\%$ h⁻¹), with a sensitivity and LOD decrease of $9.6 \pm 0.4\%$ and a $22.7 \pm 5.5\%$ over the 4 h period, respectively. For H₂O₂, baseline current drifted at a rate of -0.005 ± 0.002 nA h⁻¹ ($-14.7 \pm 5.7\%$ h⁻¹), with a sensitivity and LOD decrease of approximately $36.2 \pm 1.3\%$ and $51.4 \pm 12.7\%$ respectively, over the 4 h period.

The observed decrease in sensitivity for both analytes is consistent with the formation of a diffusional fouling layer on the Pt surface, arising from the adsorption of proteinaceous components (BSA) present in the aCSF, consistent with fouling mechanisms broadly reported for carbon- and metal-based neurochemical microelectrodes [83,84]. Such a layer would increase the effective path length for H₂O₂ to reach the electroactive Pt surface, thereby slowing the amperometric response. The LOD improved for both analytes following the stabilization period, which can be attributed to a reduction in baseline noise observed in the T_f calibration relative to T₀.

These results indicate that, while decrease in sensitivity occurs over a 4 h exposure to a biologically representative matrix, the pMEA retains functional responsiveness to both O₂ and H₂O₂ throughout the tested period.

4. Conclusions

This work provides a comprehensive morphological and electrochemical characterization of a Parylene C-based pMEA featuring a Ti/Pt/Au/Pt multilayer active surface. The active sites exhibited a uniform, defect-free surface with nanoscale platinum structures while cyclic voltammetry confirmed typical bulk Pt behavior and diffusion-controlled kinetics for both O₂ reduction and H₂O₂ oxidation. The low impedance at 1 kHz further demonstrates the suitability of the platform for in vivo neural recording. The Pt-based pMEAs showed excellent electrocatalytic activity, high sensitivity and a low limit of detection, and rapid response times for both analytes with linear dynamic ranges extending to 150 μM for O₂ and 2 mM for H₂O₂, comparing favorably with recently reported Pt-based microelectrode arrays. For O₂ detection, -0.6 V vs. Ag/AgCl was selected as the optimal working potential, where a well-defined reduction plateau region is established. For H₂O₂ detection, $+0.7$ V vs. Ag/AgCl provided a stable oxidation current with minimal noise. The selectivity evaluation showed that O₂ detection at negative potentials is unaffected by interference from common electroactive species, whereas for H₂O₂ detection, the electropolymerized *m*-phenylenediamine membrane efficiently minimized ascorbic acid and dopamine interference. Operational stability assessments in a biologically representative matrix (aCSF supplemented with glucose and BSA) revealed a decrease in sensitivity for both analytes over 4 h, consistent with the formation of a diffusional fouling layer on the Pt surface, while the pMEA retained functional responsiveness to both O₂ and H₂O₂ throughout the tested period. Overall, these results establish this pMEA platform as a promising neural probe for in vivo multimodal monitoring, enabling the integration of neurochemical sensing with electrophysiological recording. In addition, they provide a robust electrochemical basis for the future development of enzyme-based and other advanced biosensors for real-time in vivo measurements in the brain.

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References

1. Kress, G.J.; Mennerick, S. Action Potential Initiation and Propagation: Upstream Influences on Neurotransmission. *Neuroscience* **2009**, *158*, 211–222. <https://doi.org/10.1016/j.neuroscience.2008.03.021>.
2. Wu, F.; Yu, P.; Mao, L. New Opportunities of Electrochemistry for Monitoring, Modulating, and Mimicking the Brain Signals. *JACS Au* **2023**, *3*, 2062–2072. <https://doi.org/10.1021/jacsau.3c00220>.
3. Liu, Y.; Liu, Z.; Tian, Y. Real-Time Tracking of Electrical Signals and an Accurate Quantification of Chemical Signals with Long-Term Stability in the Live Brain. *Acc. Chem. Res.* **2022**, *55*, 2821–2832. <https://doi.org/10.1021/acs.accounts.2c00333>.
4. Li, H.; Wang, J.; Fang, Y. Recent Developments in Multifunctional Neural Probes for Simultaneous Neural Recording and Modulation. *Microsyst. Nanoeng.* **2023**, *9*, 4. <https://doi.org/10.1038/s41378-022-00444-5>.
5. Fernandes, E.; Ledo, A.; Gerhardt, G.A.; Barbosa, R.M. Amperometric Bio-Sensing of Lactate and Oxygen Concurrently with Local Field Potentials during Status Epilepticus. *Talanta* **2024**, *268*, 125302. <https://doi.org/10.1016/j.talanta.2023.125302>.
6. Ledo, A.; Lourenço, C.F.; Laranjinha, J.; Gerhardt, G.A.; Barbosa, R.M. Concurrent Measurements of Neurochemical and Electrophysiological Activity with Microelectrode Arrays: New Perspectives for Constant Potential Amperometry. *Curr. Opin. Electrochem.* **2018**, *12*, 129–140. <https://doi.org/10.1016/j.coelec.2018.05.018>.
7. Siwakoti, U.; Jones, S.A.; Kumbhare, D.; Cui, X.T.; Castagnola, E. Recent Progress in Flexible Microelectrode Arrays for Combined Electrophysiological and Electrochemical Sensing. *Biosensors* **2025**, *15*, 100. <https://doi.org/10.3390/bios15020100>.
8. Ledo, A.; Lourenço, C.F.; Laranjinha, J.; Gerhardt, G.A.; Barbosa, R.M. Combined in Vivo Amperometric Oximetry and Electrophysiology in a Single Sensor: A Tool for Epilepsy Research. *Anal. Chem.* **2017**, *89*, 12383–12390. <https://doi.org/10.1021/acs.analchem.7b03452>.
9. Malekshoaraie, M.H.; Wu, B.; Krahe, D.D.; Ahmed, Z.; Pupa, S.; Jain, V.; Cui, X.T.; Chamanzar, M. Fully Flexible Implantable Neural Probes for Electrophysiology Recording and Controlled Neurochemical Modulation. *Microsyst. Nanoeng.* **2024**, *10*, 91. <https://doi.org/10.1038/s41378-024-00685-6>.
10. Vetter, R.J.; Williams, J.C.; Hetke, J.F.; Nunamaker, E.A.; Kipke, D.R. Chronic Neural Recording Using Silicon-Substrate Microelectrode Arrays Implanted in Cerebral Cortex. *IEEE Trans. Biomed. Eng.* **2004**, *51*, 896–904. <https://doi.org/10.1109/TBME.2004.826680>.
11. Burmeister, J.J.; Gerhardt, G.A. Self-Referencing Ceramic-Based Multisite Microelectrodes for the Detection and Elimination of Interferences from the Measurement of L-Glutamate and Other Analytes. *Anal. Chem.* **2001**, *73*, 1037–1042. <https://doi.org/10.1021/ac0010429>.
12. Yi, D.; Yao, Y.; Wang, Y.; Chen, L. Design, Fabrication, and Implantation of Invasive Microelectrode Arrays as in Vivo Brain Machine Interfaces: A Comprehensive Review. *J. Manuf. Process.* **2024**, *126*, 185–207. <https://doi.org/10.1016/j.jmapro.2024.07.100>.
13. Ledo, A.; Lourenço, C.F.; Laranjinha, J.; Brett, C.M.A.; Gerhardt, G.A.; Barbosa, R.M. Ceramic-Based Multisite Platinum Microelectrode Arrays: Morphological Characteristics and Electrochemical Performance for Extracellular Oxygen Measurements in Brain Tissue. *Anal. Chem.* **2017**, *89*, 1674–1683. <https://doi.org/10.1021/acs.analchem.6b03772>.
14. Xu, M.; Zhao, Y.; Xu, G.; Zhang, Y.; Sun, S.; Sun, Y.; Wang, J.; Pei, R. Recent Development of Neural Microelectrodes with Dual-Mode Detection. *Biosensors* **2023**, *13*, 59. <https://doi.org/10.3390/bios13010059>.

15. Choi, J.R.; Kim, S.M.; Ryu, R.H.; Kim, S.P.; Sohn, J.W. Implantable Neural Probes for Brain-Machine Interfaces-Current Developments and Future Prospects. *Exp. Neurobiol.* **2018**, *27*, 453–471. <https://doi.org/10.5607/en.2018.27.6.453>.
16. Lecomte, A.; Descamps, E.; Bergaud, C. A Review on Mechanical Considerations for Chronically-Implanted Neural Probes. *J. Neural Eng.* **2018**, *15*, 031001. <https://doi.org/10.1088/1741-2552/aa8b4f>.
17. Fu, T.M.; Hong, G.; Zhou, T.; Schuhmann, T.G.; Viveros, R.D.; Lieber, C.M. Stable Long-Term Chronic Brain Mapping at the Single-Neuron Level. *Nat. Methods* **2016**, *13*, 875–882. <https://doi.org/10.1038/nmeth.3969>.
18. Fuchsberger, K.; Goff, A.L.; Gambazzi, L.; Toma, F.M.; Goldoni, A.; Giugliano, M.; Stelzle, M.; Prato, M. Multiwalled Carbon-Nanotube-Functionalized Microelectrode Arrays Fabricated by Microcontact Printing: Platform for Studying Chemical and Electrical Neuronal Signaling. *Small* **2011**, *7*, 524–530. <https://doi.org/10.1002/sml.201001640>.
19. Xu, T.; Ji, W.; Wang, X.; Zhang, Y.; Zeng, H.; Mao, L.; Zhang, M. Support-Free PEDOT:PSS Fibers as Multifunctional Microelectrodes for In Vivo Neural Recording and Modulation. *Angew. Chem.-Int. Ed.* **2022**, *61*, e202115074. <https://doi.org/10.1002/anie.202115074>.
20. Steins, H.; Mierzejewski, M.; Brauns, L.; Stumpf, A.; Kohler, A.; Heusel, G.; Corna, A.; Herrmann, T.; Jones, P.D.; Zeck, G.; et al. A Flexible Protruding Microelectrode Array for Neural Interfacing in Bioelectronic Medicine. *Microsyst. Nanoeng.* **2022**, *8*, 131. <https://doi.org/10.1038/s41378-022-00466-z>.
21. Wang, X.; Xu, M.; Yang, H.; Jiang, W.; Jiang, J.; Zou, D.; Zhu, Z.; Tao, C.; Ni, S.; Zhou, Z.; et al. Ultraflexible Neural Electrodes Enabled Synchronized Long-Term Dopamine Detection and Wideband Chronic Recording Deep in Brain. *ACS Nano* **2024**, *18*, 34272–34287. <https://doi.org/10.1021/acsnano.4c12429>.
22. Zhao, H.; Liu, R.; Zhang, H.; Cao, P.; Liu, Z.; Li, Y. Research Progress on the Flexibility of an Implantable Neural Microelectrode. *Micromachines* **2022**, *13*, 386. <https://doi.org/10.3390/mi13030386>.
23. Metallo, C.; White, R.D.; Trimmer, B.A. Flexible Parylene-Based Microelectrode Arrays for High Resolution EMG Recordings in Freely Moving Small Animals. *J. Neurosci. Methods* **2011**, *195*, 176–184. <https://doi.org/10.1016/j.jneumeth.2010.12.005>.
24. De La Oliva, N.; Mueller, M.; Stieglitz, T.; Navarro, X.; Del Valle, J. On the Use of Parylene C Polymer as Substrate for Peripheral Nerve Electrodes. *Sci. Rep.* **2018**, *8*, 5965. <https://doi.org/10.1038/s41598-018-24502-z>.
25. Zhang, Y.; Zhang, J.; Le, S.; Niu, L.; Tao, J.; Liang, J.; Zhang, L.; Kang, X. Parylene C as an Insulating Polymer for Implantable Neural Interfaces: Acute Electrochemical Impedance Behaviors in Saline and Pig Brain In Vitro. *Polymers* **2022**, *14*, 3033. <https://doi.org/10.3390/polym14153033>.
26. Scholten, K.; Xu, H.; Lu, Z.; Jiang, W.; Jin, Z.; Ortigoza-Diaz, J.; Petrossians, A.; Orlor, S.; Gallonio, R.; Liu, X.; et al. A Comprehensive Research Dissemination Model for Polymer-Based Neural Interfaces. *IEEE Trans. Biomed. Eng.* **2026**, *73*, 934–944. <https://doi.org/10.1109/TBME.2025.3596222>.
27. Gatti, I.; Eisawi, K.; Siwakoti, U.; Jadwin, G.; Sigdel, A.; Chiappalone, M.; Kumbhare, D.; Naguib, M.; Castagnola, E. MXene/PEDOT Functional Coatings on Flexible Microelectrode Arrays for Multianalyte In Vivo Neurochemical Sensing and Electrophysiology. *Adv. Funct. Mater.* **2026**, *36*, e75402. <https://doi.org/10.1002/adfm.75402>.
28. Cortés-Salazar, F.; Deng, H.; Peljo, P.; Pereira, C.M.; Kontturi, K.; Girault, H.H. Parylene C Coated Microelectrodes for Scanning Electrochemical Microscopy. *Electrochim. Acta* **2013**, *110*, 22–29. <https://doi.org/10.1016/j.electacta.2013.03.158>.
29. Sander, R. Compilation of Henry's Law Constants (Version 4.0) for Water as Solvent. *Atmos. Chem. Phys.* **2015**, *15*, 4399–4981. <https://doi.org/10.5194/acp-15-4399-2015>.
30. Daubinger, P.; Kieninger, J.; Unmüssig, T.; Urban, G.A. Electrochemical Characteristics of Nanostructured Platinum Electrodes-A Cyclic Voltammetry Study. *Phys. Chem. Chem. Phys.* **2014**, *16*, 8392–8399. <https://doi.org/10.1039/c4cp00342j>.
31. Talauliker, P.M.; Price, D.A.; Burmeister, J.J.; Nagari, S.; Quintero, J.E.; Pomerleau, F.; Huettl, P.; Hastings, J.T.; Gerhardt, G.A. Ceramic-Based Microelectrode Arrays: Recording Surface Characteristics and Topographical Analysis. *J. Neurosci. Methods* **2011**, *198*, 222–229. <https://doi.org/10.1016/j.jneumeth.2011.04.004>.
32. Scholten, K.; Xu, H.; Song, D.; Meng, E. A shared resource for building polymer-based microelectrode arrays as neural interfaces. In *Proceedings of the 11th International IEEE/EMBS Conference on Neural Engineering (NER 2023)*, Baltimore, MD, USA, 24–27 April 2023; IEEE Computer Society: Washington, DC, USA, 2023. <https://doi.org/10.1109/NER52421.2023.10123883>.
33. Pandey, A.; Dalal, S.; Dutta, S.; Dixit, A. Structural Characterization of Polycrystalline Thin Films by X-Ray Diffraction Techniques. *J. Mater. Sci. Mater. Electron.* **2021**, *32*, 1341–1368. <https://doi.org/10.1007/s10854-020-04998-w>.
34. Marszalek, T.; Gazicki-Lipman, M.; Ulanski, J. Parylene C as a Versatile Dielectric Material for Organic Field-Effect Transistors. *Beilstein J. Nanotechnol.* **2017**, *8*, 1532–1545. <https://doi.org/10.3762/bjnano.8.155>.
35. Saksena, A.; Chien, Y.-C.; Chang, K.; Kümmerl, P.; Hans, M.; Völker, B.; Schneider, J.M. Metastable Phase Formation of Pt-X (X = Ir, Au) Thin Films. *Sci. Rep.* **2018**, *8*, 10198. <https://doi.org/10.1038/s41598-018-28452-4>.

36. Cozma, S.; Vlădoiu, R.; Mandes, A.; Dinca, V.; Prodan, G.; Buršíková, V. Characterization of Platinum-Based Thin Films Deposited by Thermionic Vacuum Arc (TVA) Method. *Materials* **2020**, *13*, 1796. <https://doi.org/10.3390/ma13071796>.
37. Bulowski, W.; Skibińska, K.; Żabiński, P.; Wojnicki, M. Optimization of Gold Thin Films by DC Magnetron Sputtering: Structure, Morphology, and Conductivity. *Coatings* **2025**, *15*, 1240. <https://doi.org/10.3390/coatings15111240>.
38. Sheng, W.; Gasteiger, H.A.; Shao-Horn, Y. Hydrogen Oxidation and Evolution Reaction Kinetics on Platinum: Acid vs Alkaline Electrolytes. *J. Electrochem. Soc.* **2010**, *157*, B1529. <https://doi.org/10.1149/1.3483106>.
39. Weltin, A.; Kieninger, J. Electrochemical Methods for Neural Interface Electrodes. *J. Neural Eng.* **2021**, *18*, 052001. <https://doi.org/10.1088/1741-2552/ac28d5>.
40. Rinaldo, S.G.; Lee, W.; Stumper, J.; Eikerling, M. Mechanistic Principles of Platinum Oxide Formation and Reduction. *Electrocatalysis* **2014**, *5*, 262–272. <https://doi.org/10.1007/s12678-014-0189-y>.
41. Lai, B.-C.; Wu, J.-G.; Luo, S.-C. Revisiting Background Signals and the Electrochemical Windows of Au, Pt, and GC Electrodes in Biological Buffers. *ACS Appl. Energy Mater.* **2019**, *2*, 6808–6816. <https://doi.org/10.1021/acsaem.9b01249>.
42. Ivanovskaya, A.N.; Belle, A.M.; Yorita, A.M.; Qian, F.; Chen, S.; Tooker, A.; Lozada, R.G.; Dahlquist, D.; Tolosa, V. Electrochemical Roughening of Thin-Film Platinum for Neural Probe Arrays and Biosensing Applications. *J. Electrochem. Soc.* **2018**, *165*, G3125–G3132. <https://doi.org/10.1149/2.0171812jes>.
43. Johnson, A. Electrochemical Surface Area (ECSA) Evaluation in Electrocatalysis: Principles, Measurement Techniques, and Future Perspectives. *J. Eng. Ind. Res.* **2025**, *6*, 212–222. <https://doi.org/10.48309/jeires.2025.513554.1182>.
44. Yohannes, W.; Belenov, S.V.; Guterman, V.E.; Skibina, L.M.; Volotchaev, V.A.; Lyanguzov, N.V. Effect of Ethylene Glycol on Electrochemical and Morphological Features of Platinum Electrodeposits from Chloroplatinic Acid. *J. Appl. Electrochem.* **2015**, *45*, 623–633. <https://doi.org/10.1007/s10800-015-0820-5>.
45. Barsoukov, E.; Macdonald, J.R. (Eds.) *Impedance Spectroscopy Theory, Experiment, and Applications*, 2nd ed.; Wiley-Interscience: Hoboken, NJ, USA, 2005.
46. Hirschorn, B.; Orazem, M.E.; Tribollet, B.; Vivier, V.; Frateur, I.; Musiani, M. Determination of Effective Capacitance and Film Thickness from Constant-Phase-Element Parameters. *Electrochim. Acta* **2010**, *55*, 6218–6227. <https://doi.org/10.1016/j.electacta.2009.10.065>.
47. Harris, A.R.; Molino, P.J.; Kapsa, R.M.I.; Clark, G.M.; Paolini, A.G.; Wallace, G.G. Correlation of the Impedance and Effective Electrode Area of Doped PEDOT Modified Electrodes for Brain-Machine Interfaces. *Analyst* **2015**, *140*, 3164–3174. <https://doi.org/10.1039/c4an02362e>.
48. Zeng, Q.; Xia, K.; Zhang, Y.; Wu, T. Well Controlled 3D Iridium Oxide/Platinum Nanocomposites with Greatly Enhanced Electrochemical Performances. *Adv. Mater. Interfaces* **2019**, *6*, 1900356. <https://doi.org/10.1002/admi.201900356>.
49. Huang, L.; Zaman, S.; Tian, X.; Wang, Z.; Fang, W.; Xia, B.Y. Advanced Platinum-Based Oxygen Reduction Electrocatalysts for Fuel Cells. *Acc. Chem. Res.* **2021**, *54*, 311–322. <https://doi.org/10.1021/acs.accounts.0c00488>.
50. Ahsan, M.A.; He, T.; Eid, K.; Abdullah, A.M.; Sanad, M.F.; Aldalbahi, A.; Alvarado-Tenorio, B.; Du, A.; Puente Santiago, A.R.; Noveron, J.C. Controlling the Interfacial Charge Polarization of MOF-Derived 0D–2D vdW Architectures as a Unique Strategy for Bifunctional Oxygen Electrocatalysis. *ACS Appl. Mater. Interfaces* **2022**, *14*, 3919–3929. <https://doi.org/10.1021/acsaami.1c17283>.
51. Keeley, T.P.; Mann, G.E. Defining Physiological Normoxia for Improved Translation of Cell Physiology to Animal Models and Humans. *Physiol. Rev.* **2019**, *99*, 161–234. <https://doi.org/10.1152/physrev.00041.2017>.
52. Tedjo, W.; Obeidat, Y.; Catandi, G.; Carnevale, E.; Chen, T. Real-Time Analysis of Oxygen Gradient in Oocyte Respiration Using a High-Density Microelectrode Array. *Biosensors* **2021**, *11*, 256. <https://doi.org/10.3390/bios11080256>.
53. Xiang, L.; Yu, P.; Zhang, M.; Hao, J.; Wang, Y.; Zhu, L.; Dai, L.; Mao, L. Platinized Aligned Carbon Nanotube-Sheathed Carbon Fiber Microelectrodes for in Vivo Amperometric Monitoring of Oxygen. *Anal. Chem.* **2014**, *86*, 5017–5023. <https://doi.org/10.1021/ac500622m>.
54. Bazzu, G.; Puggioni, G.G.M.; Dedola, S.; Calia, G.; Rocchitta, G.; Migheli, R.; Desole, M.S.; Lowry, J.P.; O'Neill, R.D.; Serra, P.A. Real-Time Monitoring of Brain Tissue Oxygen Using a Miniaturized Biotelemetric Device Implanted in Freely Moving Rats. *Anal. Chem.* **2009**, *81*, 2235–2241. <https://doi.org/10.1021/ac802390f>.
55. Bolger, F.B.; Bennett, R.; Lowry, J.P. An in Vitro Characterisation Comparing Carbon Paste and Pt Microelectrodes for Real-Time Detection of Brain Tissue Oxygen. *Analyst* **2011**, *136*, 4028–4035. <https://doi.org/10.1039/c1an15324b>.
56. Sosna, M.; Denuault, G.; Pascal, R.W.; Prien, R.D.; Mowlem, M. Development of a Reliable Microelectrode Dissolved Oxygen Sensor. *Sens. Actuators B Chem.* **2007**, *123*, 344–351. <https://doi.org/10.1016/j.snb.2006.08.033>.

57. Chen, Y.P.; Liu, S.Y.; Fang, F.; Li, S.H.; Liu, G.; Tian, Y.C.; Xiong, Y.; Yu, H.Q. Simultaneous Determination of Nitrate and Dissolved Oxygen under Neutral Conditions Using a Novel Silver-Deposited Gold Microelectrode. *Environ. Sci. Technol.* **2008**, *42*, 8465–8470. <https://doi.org/10.1021/es8010157>.
58. Pennings, F.A.; Schuurman, P.R.; Van Den Munckhof, P.; Bouma, G.J. Brain Tissue Oxygen Pressure Monitoring in Awake Patients during Functional Neurosurgery: The Assessment of Normal Values. *Proc. J. Neurotrauma* **2008**, *25*, 1173–1177.
59. Liu, S.-Y.; Chen, Y.-P.; Fang, F.; Xu, J.; Sheng, G.-P.; Yu, H.-Q.; Liu, G.; Tian, Y.-C. Measurement of Dissolved Oxygen and Its Diffusivity in Aerobic Granules Using a Lithographically-Fabricated Microelectrode Array. *Environ. Sci. Technol.* **2009**, *43*, 1160–1165. <https://doi.org/10.1021/es802662e>.
60. Xiao, T.; Li, X.; Wei, H.; Ji, W.; Yue, Q.; Yu, P.; Mao, L. In Vivo Monitoring of Oxygen Fluctuation Simultaneously at Multiple Sites of Rat Cortex during Spreading Depression. *Anal. Chem.* **2018**, *90*, 13783–13789. <https://doi.org/10.1021/acs.analchem.8b04348>.
61. Lourenço, C.F.; Caetano, M.; Ledo, A.; Barbosa, R.M. Platinized Carbon Fiber-Based Glucose Microbiosensor Designed for Metabolic Studies in Brain Slices. *Bioelectrochemistry* **2019**, *130*, 107325. <https://doi.org/10.1016/j.bioelechem.2019.06.010>.
62. Yu, H.; Yu, J.; Li, L.; Zhang, Y.; Xin, S.; Ni, X.; Sun, Y.; Song, K. Recent Progress of the Practical Applications of the Platinum Nanoparticle-Based Electrochemistry Biosensors. *Front. Chem.* **2021**, *9*, 677876. <https://doi.org/10.3389/fchem.2021.677876>.
63. Katsounaros, I.; Schneider, W.B.; Meier, J.C.; Benedikt, U.; Biedermann, P.U.; Auer, A.A.; Mayrhofer, K.J.J. Hydrogen Peroxide Electrochemistry on Platinum: Towards Understanding the Oxygen Reduction Reaction Mechanism. *Phys. Chem. Chem. Phys.* **2012**, *14*, 7384–7391. <https://doi.org/10.1039/c2cp40616k>.
64. Li, Y.; Sella, C.; Lemaître, F.; GuilleCollignon, M.; Thouin, L.; Amatore, C. Highly Sensitive Platinum-Black Coated Platinum Electrodes for Electrochemical Detection of Hydrogen Peroxide and Nitrite in Microchannel. *Electroanalysis* **2013**, *25*, 895–902. <https://doi.org/10.1002/elan.201200456>.
65. Chatard, C.; Sabac, A.; Moreno-Velasquez, L.; Meiller, A.; Marinesco, S. Minimally Invasive Microelectrode Biosensors Based on Platinized Carbon Fibers for in Vivo Brain Monitoring. *ACS Cent. Sci.* **2018**, *4*, 1751–1760. <https://doi.org/10.1021/acscentsci.8b00797>.
66. Wang, B.; Wen, X.; Chiou, P.Y.; Maidment, N.T. Pt Nanoparticle-Modified Carbon Fiber Microelectrode for Selective Electrochemical Sensing of Hydrogen Peroxide. *Electroanalysis* **2019**, *31*, 1641–1645. <https://doi.org/10.1002/elan.201900362>.
67. Yao, Y.; Bai, X.; Shiu, K.K. Spontaneous Deposition of Prussian Blue on Multi-Walled Carbon Nanotubes and the Application in an Amperometric Biosensor. *Nanomaterials* **2012**, *2*, 428–444. <https://doi.org/10.3390/nano2040428>.
68. Chang, S.H.; Yeh, M.H.; Rick, J.; Su, W.N.; Liu, D.G.; Lee, J.F.; Liu, C.C.; Hwang, B.J. Bimetallic Catalyst of PtIr Nanoparticles with High Electrocatalytic Ability for Hydrogen Peroxide Oxidation. *Sens. Actuators B Chem.* **2014**, *190*, 55–60. <https://doi.org/10.1016/j.snb.2013.08.022>.
69. Sellen, S.C.; Siwakoti, U.; Sigdel, A.; Jaiswal, B.; Zivanovic, S.; Castagnola, E. Advancing Glassy Carbon Microelectrode Arrays for Neurochemical Sensing: Impact of Double Pyrolysis on Structure and Function. *Front. Bioeng. Biotechnol.* **2025**, *13*, 1642063. <https://doi.org/10.3389/fbioe.2025.1642063>.
70. Giaretta, J.E.; Duan, H.; Oveissi, F.; Farajikhah, S.; Dehghani, F.; Naficy, S. Flexible Sensors for Hydrogen Peroxide Detection: A Critical Review. *ACS Appl. Mater. Interfaces* **2022**, *14*, 20491–20505. <https://doi.org/10.1021/acsaami.1c24727>.
71. Spanos, M.; Gras-Najjar, J.; Letchworth, J.M.; Sanford, A.L.; Toups, J.V.; Sombers, L.A. Quantitation of Hydrogen Peroxide Fluctuations and Their Modulation of Dopamine Dynamics in the Rat Dorsal Striatum Using Fast-Scan Cyclic Voltammetry. *ACS Chem. Neurosci.* **2013**, *4*, 782–789. <https://doi.org/10.1021/cn4000499>.
72. Wilson, L.R.; Panda, S.; Schmidt, A.C.; Sombers, L.A. Selective and Mechanically Robust Sensors for Electrochemical Measurements of Real-Time Hydrogen Peroxide Dynamics in Vivo. *Anal. Chem.* **2018**, *90*, 888–895. <https://doi.org/10.1021/acs.analchem.7b03770>.
73. Burmeister, J.J.; Moxon, K.; Gerhardt, G.A. Ceramic-Based Multisite Microelectrodes for Electrochemical Recordings. *Anal. Chem.* **2000**, *72*, 187–192. <https://doi.org/10.1021/ac9907991>.
74. Carriere, V.M.; Rodrigues, J.P.; Tan, C.; Arumugam, P.; Poh, S. In Vitro Electrochemical Detection of Hydrogen Peroxide in Activated Macrophages via a Platinum Microelectrode Array. *Sensors* **2021**, *21*, 5607. <https://doi.org/10.3390/s21165607>.
75. Ben-Amor, S.; Vanhove, E.; Sékli Belaïdi, F.; Charlot, S.; Colin, D.; Rigoulet, M.; Devin, A.; Sojic, N.; Launay, J.; Temple-Boyer, P.; et al. Enhanced Detection of Hydrogen Peroxide with Platinized Microelectrode Arrays for Analyses of Mitochondria Activities. *Electrochim. Acta* **2014**, *126*, 171–178. <https://doi.org/10.1016/j.electacta.2013.11.104>.
76. Pang, H.; Yin, B.; Liu, X.; Jiang, T.; Wu, S. Simultaneous Electrochemical Detection of Dopamine and Hydrogen Peroxide Based on Bifunctional Microelectrode Array. *J. Mater. Sci. Mater. Electron.* **2023**, *34*, 883. <https://doi.org/10.1007/s10854-023-10282-4>.

77. Killoran, S.J.; O'Neill, R.D. Characterization of Permselective Coatings Electrosynthesized on Pt-Ir from the Three Phenylenediamine Isomers for Biosensor Applications. *Electrochim. Acta* **2008**, *53*, 7303–7312. <https://doi.org/10.1016/j.electacta.2008.03.076>.
78. Soldatkina, O.V.; Kucherenko, I.S.; Pyeshkova, V.M.; Alekseev, S.A.; Soldatkin, O.O.; Dzyadevych, S.V. Improvement of Amperometric Transducer Selectivity Using Nanosized Phenylenediamine Films. *Nanoscale Res. Lett.* **2017**, *12*, 594. <https://doi.org/10.1186/s11671-017-2353-9>.
79. Adediji, M.Y.; Billa, S.; Siddiqui, S.; Arumugam, P.U. Enhancing the Sensitivity of Gamma-Aminobutyric Acid and Glutamate Biosensors by Electrochemically Roughening Platinum Microelectrodes. *Front. Neurosci.* **2025**, *19*, 1679591. <https://doi.org/10.3389/fnins.2025.1679591>.
80. Miele, M.; Fillenz, M. In Vivo Determination of Extracellular Brain Ascorbate. *J. Neurosci. Methods* **1996**, *70*, 15–19. [https://doi.org/10.1016/S0165-0270\(96\)00094-5](https://doi.org/10.1016/S0165-0270(96)00094-5).
81. Lakard, S.; Pavel, I.-A.; Lakard, B. Electrochemical Biosensing of Dopamine Neurotransmitter: A Review. *Biosensors* **2021**, *11*, 179. <https://doi.org/10.3390/bios11060179>.
82. Keteklahijani, Y.Z.; Sharif, F.; Roberts, E.P.L.; Sundararaj, U. Enhanced Sensitivity of Dopamine Biosensors: An Electrochemical Approach Based on Nanocomposite Electrodes Comprising Polyaniline, Nitrogen-Doped Graphene, and DNA-Functionalized Carbon Nanotubes. *J. Electrochem. Soc.* **2019**, *166*, B1415–B1425. <https://doi.org/10.1149/2.0361915jes>.
83. Castagnola, E.; Lee, K.H.; Ricci, D. Editorial: Carbon Microelectrodes for Neurochemical Sensing. *Front. Bioeng. Biotechnol.* **2026**, *14*, 1799334. <https://doi.org/10.3389/fbioe.2026.1799334>.
84. Liljeström, T.; Kontturi, K.S.; Durairaj, V.; Wester, N.; Tammelin, T.; Laurila, T.; Koskinen, J. Protein Adsorption and Its Effects on Electroanalytical Performance of Nanocellulose/Carbon Nanotube Composite Electrodes. *Biomacromolecules* **2023**, *24*, 3806–3818. <https://doi.org/10.1021/acs.biomac.3c00449>.

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