Electronic supplementary information

Well-modulated interfacial ion transport enables D-sorbitol/PEDOT:PSS fibers to sense brain electrophysiological signals in vivo

Tianci Xu*

School of Chemistry and Chemical Engineering, Liaoning Normal University, Dalian 116029, P.R. China

E-mail: xutianci@lnnu.edu.cn

1. Preparation of DS/PEDOT:PSS fibers, CPFEs, and Pt fiber microelectrodes

DS/PEDOT:PSS fibers were prepared by wet spinning. Firstly, DS (Sigma-Aldrich, USA) was added to PEDOT:PSS (Batch No. 9005534368, 1.0 wt%, 22 mPa·s, Clevios PH1000, Germany) to yield spinning formulation with DS/PEDOT:PSS weight ratio in the range of 1–10. After stirring vigorously for 60 min, the formulation was loaded into a 2-mL syringe mounted on a syringe pump and extruded into an isopropanol coagulation bath through a 23-gauge spinneret at flow rates of 0.9–1.8 mL h^{-1}. The fibers were collected by winding onto a spool, rinsed with water, and dried at 105 °C for 1 h. To prepare CPFEs, the middle part of the fiber was insulated with polydimethylsiloxane (Sylgard 184, Dow Corning, USA), the front end was exposed to a length of 200 μm, and by silver adhesive, the tail end was connected to a circuit board that was pre-soldered onto a metal pin connector. All conductive connections were sealed and stabilized with epoxy for 24 h. To fabricate a Pt fiber microelectrode, a single Pt fiber (25 μm in diameter, 99.95% in purity; Alfa Aesar, UK) was attached to a copper wire with silver adhesive and then inserted into a glass capillary (o.d. 1.5 mm) that was pulled on a microelectrode puller (WD-1, Chengdu Instrument Factory, China) with a sharp fine tip at 30−50 μm in diameter. With both ends sealed with epoxy, the capillary was dried at 100 °C for 2 h. Before use, the exposed Pt fiber was cut to an equivalent geometric surface area with CPFEs.

2. Characterization of DS/PEDOT:PSS and CPFEs

Surface morphology of the fibers was observed by a Model SU8010 scanning electron microscope (Hitachi, Japan). X-ray diffraction data were obtained under conditions of 2θ = 2.5−35°, Cu Kα radiation, 40.0 kV and 30.0 mA on an XRD-7000 X-ray diffractometer (Shimadzu, Japan). Pseudo-crystallinity was evaluated by the ratio of the integrated peak intensity of (100) to the total integrated intensity. Electrochemical measurements were carried out in 100 mM KCl at room temperature (≈25 °C) using a PARSTAT 4000 electrochemical workstation (Princeton Applied Research, USA) or an Autolab PGSTAT302N electrochemical workstation (Metrohm, Switzerland). A three-electrode electrolytic cell was used with CPFE as the working electrode, a Pt counter electrode, and a single-junction Ag/AgCl/KCl(sat.) reference electrode. EIS was measured by applying a 10 mV RMS AC sinusoidal excitation (1–10^5 Hz) at the open circuit potential. The prepared Pt fiber microelectrode was used as the working electrode when performing the EIS Nyquist plot measurement for it. For CPFEs, Current reversal chronopotentiometry was performed by applying a current of ± 1 nA, each for 60s.

3. In vivo electrophysiological sensing with $CPFE_{DPP6}$

All animal procedures were in accordance with the guide for the care and use of laboratory animals from Chinese Ministry of Health and approved by the Ethics Committee of Liaoning Normal University (LL2023040). Adult male Sprague-Dawley rats aged 5 weeks (Charles River Laboratories, China) were kept in a 12:12 h light/dark cycle environment at ≈25°C, with food and water provided *ad libitum*. Rats were anesthetized with isoflurane (4% induction, 2% maintenance) through a R520 gas pump. Body temperature was maintained at 37 °C with a

regulated heating blanket. A skin incision was made to expose the skull where craniotomies were done subsequently, and $CPFE_{DPP6}$ was implanted into the primary somatosensory cortex (S1; AP: +0.8 mm, ML: −3.8 mm, DV: −1.2 mm from dura)[1] with the assistance of a tungsten wire shuttle. Briefly, the CPFE was put together with a tungsten wire of 20 μm diameter, then dipped in a polyethylene oxide bath and air-dried, after which $CPFE_{DPP6}$ was mechanically pasted to the tungsten wires along the length. The $CPFE_{DPP6}$/tungsten complex was inserted into the craniotomy to reach the target region. After the implantation, the tungsten wires were retracted, leaving only $CPFE_{DPP6}$ inside the brain. The craniotomies were sealed with the silicone elastomer (Kwik-Sil, WPI), followed by dental acrylic. A stainless-steel screw was embedded in the skull to serve as a reference and ground electrode. Intracortical evoked potentials were recorded after applying stimulus (1.0 mA, 0.5 ms of pulse width, 0.2 Hz) to the rat wrist by a pulse stimulator (Master-9, AMPI, Israel). In the study of focal seizures, the following drugs were locally injected in S1: 4AP (15 mM; Sigma-Aldrich, USA), quinine sulfate (0.84 mM; Yuanye, China) or vehicle (0.9% saline; Solarbio, China). All electrophysiological sensing was conducted on an Omniplex acquisition system (Plexon, USA). Time-frequency analysis was carried out by a short-time Fourier transform using a Hanning window. To compare the in vivo sensing performance of the Pt fiber microelectrode and $CPFE_{DPP6}$, both electrodes were implanted in the primary somatosensory cortex (AP: −1.6 mm, ML: −5.0 mm, DV: −1.2 mm from dura) of the rat brain, and the LFPs were recorded simultaneously through dual channels, with the resulting data unfiltered.

4. Assessing the biocompatibility of $CPFE_{DPP6}$

After 4 weeks of intracortical implantation of $CPFE_{DPP6}$, rats were anesthetized and transcardially perfused with PBS followed by 4% paraformaldehyde. The brain was extracted, postfixed in 4% paraformaldehyde (24 h at 4 °C), and then successively soaked in 15% and 30% sucrose solution. The brain was dehydrated with alcohol, embedded in paraffin, and then cut as vertical slices by a rotary microtome (Leica RM2016, China). Tissue sections were then heated in 10 mM citrate buffer (pH 6.0) for antigen retrieval. Then slices were stained with established markers for astrocytes (glial fibrillary acidic protein, GFAP), microglia (ionized calcium-binding adapter molecule 1, Iba-1), and nuclei (4',6-Diamidino-2-phenylindole dihydrochloride, DAPI). Images were taken on a fluorescence microscope (Nikon Eclipse C1, Japan) with a Nikon DS-U3 digital camera (Nikon, Japan).

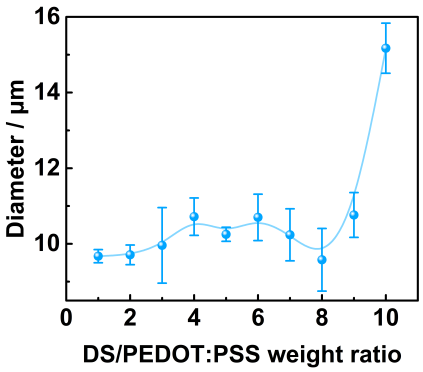

Fig. S1 Fiber diameter measurements at various DS/PEDOT:PSS weight ratios.

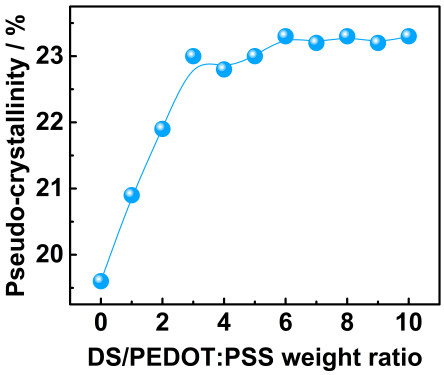

Fig. S2 Influence of DS/PEDOT:PSS weight ratio on the pseudo-crystallinity.

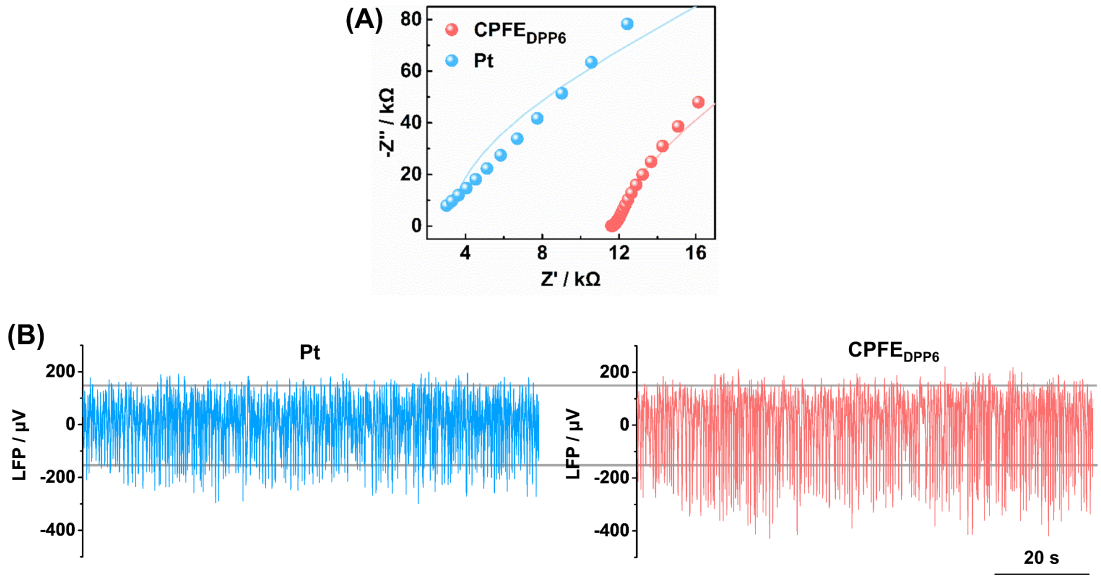

Fig. S3 (A) EIS Nyquist plots measured at the Pt electrode and CPFE$_{DPP6}$. (B) LFPs recorded at the Pt fiber electrode and CPFE$_{DPP6}$.

According to the EIS fitting in Fig. S3A, the diffusion resistance of the Pt fiber microelectrode is 3.16 MΩ, which is much larger than that of CPFE$_{DPP6}$ (179 kΩ,). Additionally, the EDL capacitance of the Pt fiber microelectrode is 3.10 nF, which is much smaller than that of CPFE$_{DPP6}$ (2.72 μF).

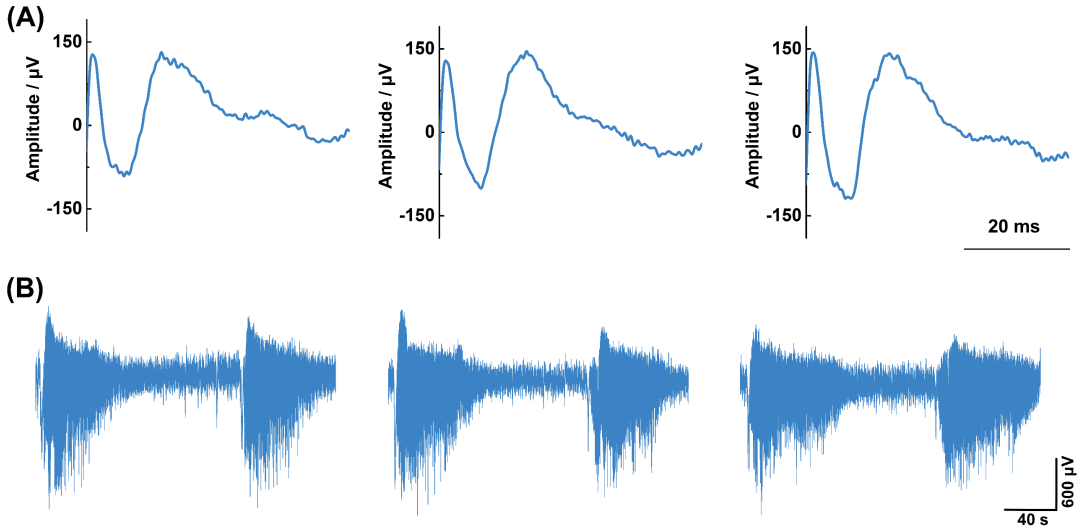

Fig. S4 Multiple measurements of SEPs (A) and 4AP-induced cortical focal seizures (B). *n* = 3.

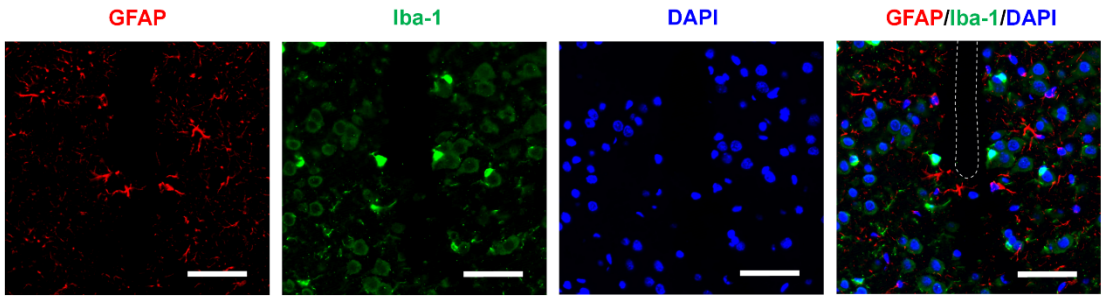

Fig. S5 Immunohistochemistry images showing tissue response to $CPFE_{DPP6}$ after 4 weeks of implantation (scale bars: 30 μm; white dashed line: implantation footprint).

Notes and references

1. G. Paxinos and C. Watson, *The rat brain in stereotaxic coordinates*, Elsevier, USA, 6th edn., 2007.