SELF-ASSEMBLED ULTRA-FLEXIBLE MESH PROBES FOR STABLE NEURAL RECORDINGS

Kejun Tu[1,2], Longchun Wang[1,2], Bin Yang[1] and Jingquan Liu[1]

[1] National Key Laboratory of Advanced Micro and Nano Manufacture Technology, Shanghai Jiao Tong University, Shanghai, 200240, CHINA and

[2] Department of Micro/Nano Electronics, School of Electronic Information and Electrical Engineering, Shanghai Jiao Tong University, Shanghai, 200240, CHINA

2025 IEEE 38th International Conference on Micro Electro Mechanical Systems (MEMS) | 979-8-3315-0889-0/25/$31.00 ©2025 IEEE | DOI: 10.1109/MEMS61431.2025.10917865

ABSTRACT

Neuronal activity monitoring is crucial for deciphering brain function, yet traditional neural interfaces face challenges due to immune responses and mechanical mismatches. Mesh probes, with the tissue-like structure and unique mechanical properties, are a new paradigm for brain probes, but facing challenges in their delivery. Here, we design a symmetric mesh structure and present a novel implantation method by utilizing a biodegradable polyethylene glycol (PEG) melt to facilitate the self-assembly of the mesh probe into a sharp-tipped, minimally invasive configuration, which could be directly implanted into the brain and unfolded after dissolving PEG. In vivo experiments demonstrated numerous single-neuron resolution signals over months, indicating the potential for stable neural recording. This study advances the field by simplifying probe delivery and enlarging the recording span, paving the way for chronic neural interface applications.

KEYWORDS

Neural Interfaces, Self-assembled Mesh Probes, Minimally Invasive Implantation, Stable Neural Recording, Single-neuron Resolution

INTRODUCTION

Tools that can record the activities of neurons are pivotal to understanding the functional mechanisms of the brain [1]. Consequently, a variety of neural interfaces, including metal wires [2], silicon arrays [3], and thick-film probes [4], have been engineered to facilitate this understanding. However, the mismatch in structure, mechanical properties, and topology between these devices and biological tissues often provoke immune responses [5]. Such reactions can result in disconnections at the brain-probe interface, potentially compromising the integrity and functionality of the nervous system.

Mesh electronics have emerged as a transformative paradigm for brain probes [6, 7]. They provide many benefits, including better compatibility with brain tissue, lower immune responses, and the ability to record single-neuron activity over a long time [8]. These benefits are attributed to their tissue-like structure and unique mechanical properties, which mimic the softness and flexibility of neural tissue. This similarity reduces invasiveness during implantation and helps decrease the subsequent immune responses [9, 10].

However, the precise delivery of mesh probes remains a significant challenge due to their softness, which makes it difficult to penetrate tissue without twisting or bending [11, 12]. Traditional syringe-injectable methods, which rely on semi-automated controlled injection machines [6-16], are complex and time-consuming, and the rigidity of the syringe can cause permanent neural damage along its path. An alternative approach involves using a polymer shuttle, a reinforced layer for the mesh probes [17]. While this method induces less damage, it is also complicated, necessitating two manipulators for probe insertion and shuttle extraction. Moreover, the wound's cross-section is

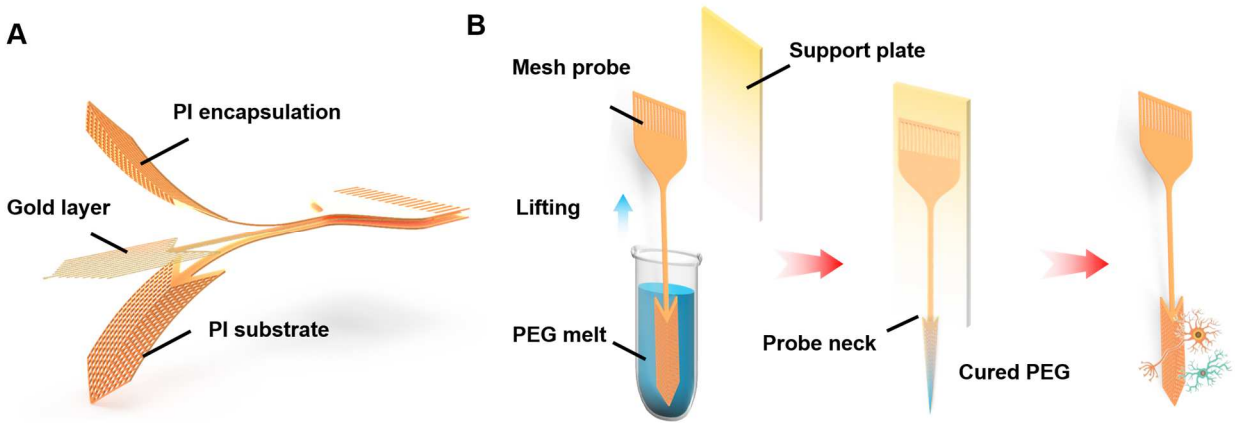

Figure 1: (A) Structural diagram of the mesh probe; (b) Scheme of the self-assembled process for mesh probe to direct implant and unfold afterwards.

broader than desired, as the mesh probe maintains an open and unfolded structure, which can lead to increased tissue disruption. Therefore, developing advanced delivery methods that are both minimally invasive and precise is crucial for the future of mesh electronics in brain probes.

Here, we developed a novel, simple method for direct implanting tissue-like mesh probes into the mouse brain. It is realized by slowly drifting the symmetric mesh probe from the biodegradable PEG melt, where the probe will be self-assembled to form a sharp tip at the end and fold its open structure for a minimal footprint during implantation. The self-assembled mesh probes can also deploy their structure post-implantation, resulting in an expansive electrode distribution that enhances recording coverage over a larger area. The further long-term implantation of the probe within the mouse hippocampus demonstrated its ability to consistently record neural activity with single-neuron precision for months, affirming the potential for stable, high-resolution neural monitoring in vivo.

DESIGN AND FABRICATION

As depicted in Figure 1A, the mesh probe mainly contains three layers, where gold traces are sandwiched between two ultrathin polyimide (PI) films. The distinctive mesh design boasts a two-dimensional (2D) open area that approximates 90%, offering a high degree of permeability, thereby minimizing the potential for neuronal damage.

In preparation for implantation, the probe undergoes a process where it is immersed in and subsequently lifted from a PEG melt at 80°C, as illustrated in Figure 1B. Due to its exceptional flexibility and symmetrical, arrow-like shape, the mesh probe readily self-assembles into a sharp-tipped configuration under interfacial tension and gravity. The probe's neck is then affixed to a support plate for reinforcement. Once the PEG has solidified, the probe acquires sufficient rigidity for brain implantation. After implantation, the residual PEG can be readily dissolved by saline solution, facilitating detachment from the support plate. This innovative approach ensures a minimally invasive procedure, optimizing the probe's integration with neural tissue.

The mesh probes were fabricated using standard flexible microelectromechanical systems (MEMS) techniques [18]. The process commenced with depositing a 200-nm-thick aluminum layer onto a pristine silicon wafer, serving as a sacrificial layer. Subsequently, a polyimide (PI) photoresist was applied via spin-coating and patterned to create a 1-μm-thick flexible substrate. Following a curing step at 350°C, a 20-nm-thick chromium layer and a 200-nm-thick gold layer were sequentially sputtered onto the PI substrate and subsequently patterned using ion-beam etching. An additional 1-μm-thick PI encapsulation layer was spun-coated and patterned, exposing pads and electrode sites. The final step involved the release of the ultra-flexible mesh probes in a diluted hydrochloric acid solution, which effectively removed the sacrificial layer and allowed the probes to be freed from the silicon wafer. The probes were connected to a flexible printed circuit using an anisotropic conductive film to facilitate electrical interfacing. This connection is crucial for subsequent electrochemical modifications and measurements, ensuring the probes' functionality in the recording.

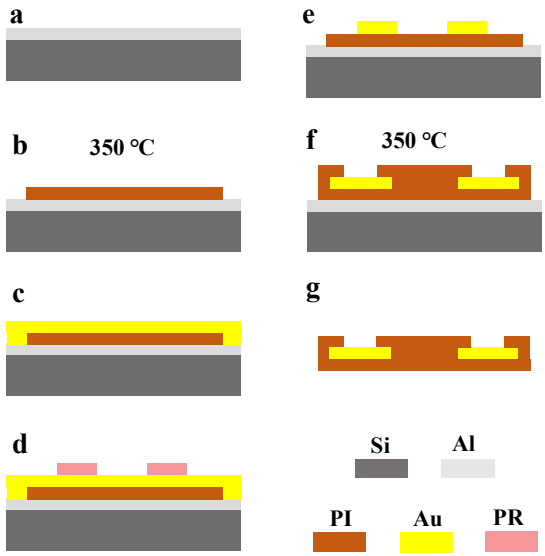

Figure 2: The microfabrication process of mesh probes.

RESULTS AND DISCUSSION

Figure 3 presents a detailed morphological characterization of the released mesh probes, elucidating the microelectrode dimensions, displacement, and the underlying microstructure. As depicted in Figure 3A, the probes exhibit exceptional flexibility, allowing them to curl effortlessly. This critical flexibility enables the probes to cause minimal invasiveness in the moving brain. The sixteen microelectrodes integrated into the mesh network are symmetrically and uniformly distributed, ensuring a consistent recording capacity across the probe's expanse. Each microelectrode has a diameter of 20 μm, as shown in Figure 3B, a dimension that is strategically chosen to optimize signal capture while minimizing tissue disruption. Upon electroplating with a Pt-black coating, the surfaces of the microelectrodes are significantly roughened, leading to a substantial increase in specific surface area (Figure 3C and 3D). The increased surface area can improve their performance in neural recording.

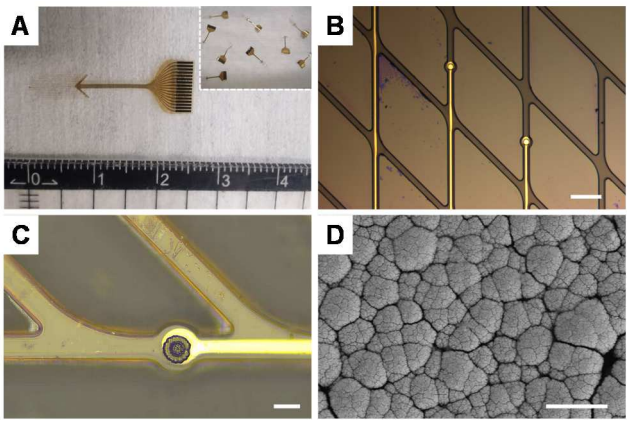

Figure 3: (A) Released ultra-flexible mesh probe; Optical photos of microelectrodes (B) with and (C) without Pt-black coating; (D) SEM of Pt-black coating. Scale bars in (B-D) are 100 μm, 20 μm and 2 μm, respectively.

The electrochemical properties of the microelectrodes were evaluated using Cyclic Voltammetry (CV) and Electrochemical Impedance Spectroscopy (EIS) techniques. The charge storage capacity (CSC) can be calculated through CV curves (Figure 4A). The results demonstrated a significant enhancement in CSC for the Pt-black modified electrodes, which exhibited 83.7 mC cm^{-2}, compared to the bare gold electrodes, which were 6.3 mC cm^{-2}. Moreover, the EIS measurements revealed a marked decrease in impedance at 1 kHz after Pt-black modification, from 917.2 kΩ for the bare gold electrodes to 29.8 kΩ for the modified electrodes (Figure 4B). This reduction in impedance indicates improved electrical communication between the electrode and the surrounding tissue. Additionally, the phase angle, another critical parameter in EIS, decreased after electroplating with Pt-black, suggesting a more favorable capacitive behavior (Figure 4C). In summary, the Pt-black modification of the microelectrodes resulted in superior electrochemical properties (Figure 4D), offering the potential for better performance in neural recording.

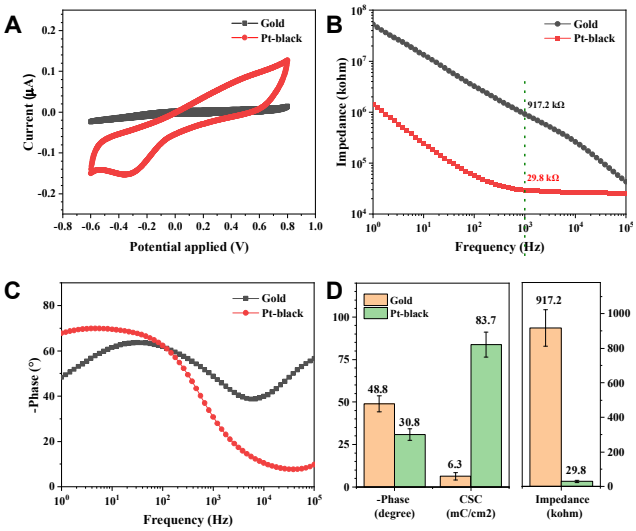

Figure 4: The electrochemical performance of microelectrodes before and after modification. (A) CV; (B, C) EIS and (D) Comparison of the phase, impedance and CSC.

Further, we accessed the implantation process within a transparent brain phantom composed of 0.6 wt% agarose gel, exhibiting mechanical properties analogous to cerebral tissue. The self-assembled mesh probe solidified tip with PEG was temporarily fixed on a glass plate (Figure 5A and 5B) and slowly invaded the model. As shown in Figure 5C, the probe could be easily inserted into the model without any buckling. After implantation, the residual PEG was dissolved in a saline solution. Notably, the immersed probe maintained its implantation depth and gradually opened its mesh structure (Figure 5D). This self-deployment is a significant advantage, as it enables the probe to extend its recording capabilities over a broader area, thereby enhancing the capture of neural signals.

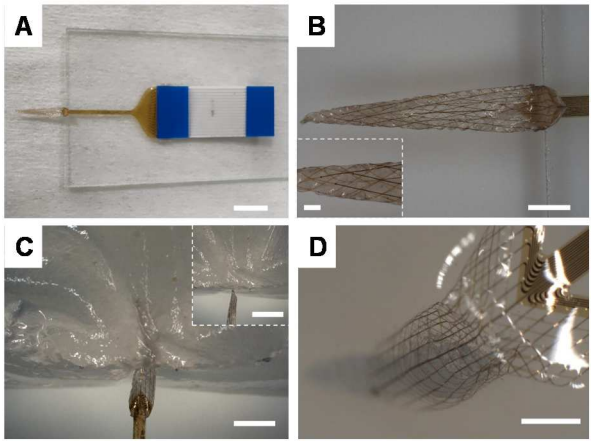

Figure 5: (A-B) Optical photos of Self-assembled ultra-flexible mesh probe; (C-D) in vitro implantation in agar model; Scale bars: 5mm in (A), 1mm and 200 μm in (B) and insert, 1mm in (C-D).

Lastly, we conducted a series of in vivo experiments to evaluate the potential of our self-assembled mesh probe for neural recording. Figure 6A presents a surgical image of our electrode being directly implanted into the hippocampal regions of mice. After several days of recovery, they were secured in cages designed for signal recording, as depicted in Figure 6B. This setup ensured the mice's comfort while enabling stable and uninterrupted signal acquisition. We observed continuous neural signals and sorted various spikes over the subsequent three months (Figure 6C and 6D), proving the effectiveness of our self-assembled mesh probe for stable neural recordings.

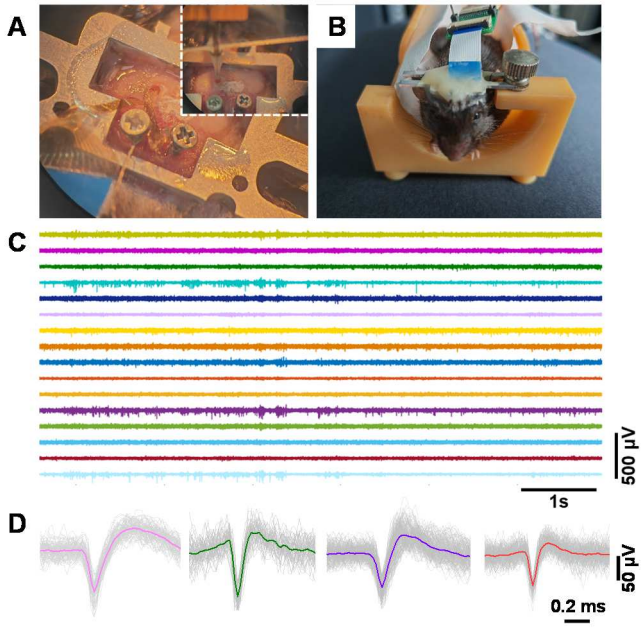

Figure 6: In vivo experiment. Photos of (A) animal surgery and (B) signal recording; (C) filtered continuous waveforms and (D) sorted spikes in 3 months.

CONCLUSION

This paper demonstrates an innovative, straightforward method for directly implanting tissue-like mesh probes into the brain. This method leverages the slow drift of a symmetric mesh probe from a biodegradable PEG melt, enabling the probe to self-assemble into a sharp-tipped configuration that minimizes tissue disruption during implantation. After implantation, the self-assembled mesh probes can expand their electrode distribution to cover a broader recording area. Long-term implantation studies within the mouse hippocampus have validated the probe's capacity for stable, single neural recording over several months, confirming its potential for reliable, high-fidelity neural monitoring in vivo.

This work can also be combined with optogenetics and drug delivery by self-assembling the probe with optical fiber and drugs in the future, leading to more effective treatments and a deeper understanding of the brain's complex neural circuits.

ACKNOWLEDGEMENTS

This work was partially supported by the STI 2030—Major Projects (2022ZD0208601, 2022ZD0208600), the National Key R&D Program of China under grant (2022YFF120301), the Fundamental Research Funds for the Central Universities, the Strategic Priority Research Program of Chinese Academy of Sciences (Grant No. XDA25040100, XDA25040200 and XDA25040300), Project supported by Shanghai Municipal Science and Technology Major Project (2021SHZDZX), Shanghai Pilot Program for Basic Research - Shanghai Jiao Tong University (No. 21TQ1400203), The authors are also grateful to the Center for Advanced Electronic Materials and Devices (AEMD) of Shanghai Jiao Tong University.

REFERENCES

[1] G. Hong, C.M. Lieber, "Novel electrode technologies for neural recordings", *Nat. Rev. Neurosci.*, vol. 20, pp. 330-345, 2019.

[2] D.H. Hubel, "Tungsten microelectrode for recording from single units", *Science*, vol. 125, pp. 549-550, 1957.

[3] N.A. Steinmetz, C. Aydin, A. Lebedeva, M. Okun, M. Pachitariu, M. Bauza, M. Beau, J. Bhagat, C. Böhm, M. Broux, S. Chen, J. Colonell, R.J. Gardner, B. Karsh, F. Kloosterman, D. Kostadinov, C. Mora-Lopez, J. O'Callaghan, J. Park, J. Putzeys, B. Sauerbrei, R.J.J. van Daal, A.Z. Vollan, S. Wang, M. Welkenhuysen, Z. Ye, J.T. Dudman, B. Dutta, A.W. Hantman, K.D. Harris, A.K. Lee, E.I. Moser, J. O'Keefe, A. Renart, K. Svoboda, M. Häusser, S. Haesler, M. Carandini, T.D. Harris, "Neuropixels 2.0: A miniaturized high-density probe for stable, long-term brain recordings", *Science*, vol. 372, pp. eabf4588, 2021.

[4] C.Y. Kim, M.J. Ku, R. Qazi, H.J. Nam, J.W. Park, K.S. Nam, S. Oh, I. Kang, J.-H. Jang, W.Y. Kim, J.-H. Kim, J.-W. Jeong, "Soft subdermal implant capable of wireless battery charging and programmable controls for applications in optogenetics", *Nat. Commun.*, vol. 12, pp. 535, 2021.

[5] J.W. Salatino, K.A. Ludwig, T.D.Y. Kozai, E.K. Purcell, "Glial responses to implanted electrodes in the brain", *Nat. Biomed. Eng.*, vol. 1, pp. 862-877, 2017.

[6] G. Hong, X. Yang, T. Zhou, C.M. Lieber, "Mesh electronics: a new paradigm for tissue-like brain probes", *Curr. Opin. Neurobiol.*, vol. 50, pp. 33-41, 2018.

[7] E. Gibney, "Injectable brain implant spies on individual neurons", *Nature*, vol. 522, pp. 137-138, 2015.

[8] T.-M. Fu, G. Hong, T. Zhou, T.G. Schuhmann, R.D. Viveros, C.M. Lieber, "Stable long-term chronic brain mapping at the single-neuron level", *Nat. Meth.*, vol. 13, pp. 875-882, 2016.

[9] G. Hong, R.D. Viveros, T.J. Zwang, X. Yang, C.M. Lieber, "Tissue-like Neural Probes for Understanding and Modulating the Brain", *Biochemistry*, vol. 57, pp. 3995-4004, 2018.

[10] X. Yang, T. Zhou, T.J. Zwang, G. Hong, Y. Zhao, R.D. Viveros, T.-M. Fu, T. Gao, C.M. Lieber, "Bioinspired neuron-like electronics", *Nat. Mater.*, vol. 18, pp. 510-517, 2019.

[11] G. Hong, T.-M. Fu, T. Zhou, T.G. Schuhmann, J. Huang, C.M. Lieber, "Syringe Injectable Electronics: Precise Targeted Delivery with Quantitative Input/Output Connectivity", *Nano Lett.*, vol. 15, pp. 6979-6984, 2015.

[12] B. Tian, J. Liu, T. Dvir, L. Jin, J.H. Tsui, Q. Qing, Z. Suo, R. Langer, D.S. Kohane, C.M. Lieber, "Macroporous nanowire nanoelectronic scaffolds for synthetic tissues", *Nat. Mater.*, vol. 11, pp. 986-994, 2012.

[13] J. Liu, T.-M. Fu, Z. Cheng, G. Hong, T. Zhou, L. Jin, M. Duvvuri, Z. Jiang, P. Kruskal, C. Xie, Z. Suo, Y. Fang, C.M. Lieber, "Syringe-injectable electronics", *Nat. Nanotechnol.*, vol. 10, pp. 629-636, 2015.

[14] C. Xie, J. Liu, T.-M. Fu, X. Dai, W. Zhou, C.M. Lieber, "Three-dimensional macroporous nanoelectronic networks as minimally invasive brain probes", *Nat. Mater.*, vol. 14, pp. 1286-1292, 2015.

[15] T.-M. Fu, G. Hong, R.D. Viveros, T. Zhou, C.M. Lieber, "Highly scalable multichannel mesh electronics for stable chronic brain electrophysiology", *Proceedings of the National Academy of Sciences*, vol. 114, pp. E10046-E10055, 2017.

[16] T. Zhou, G. Hong, T.-M. Fu, X. Yang, T.G. Schuhmann, R.D. Viveros, C.M. Lieber, "Syringe-injectable mesh electronics integrate seamlessly with minimal chronic immune response in the brain", *Proceedings of the National Academy of Sciences*, vol. 114, pp. 5894-5899, 2017.

[17] S. Zhao, X. Tang, W. Tian, S. Partarrieu, R. Liu, H. Shen, J. Lee, S. Guo, Z. Lin, J. Liu, "Tracking neural activity from the same cells during the entire adult life of mice", *Nat. Neurosci.*, vol. 26, pp. 696-710, 2023.

[18] Z. Guo, F. Wang, L. Wang, K. Tu, C. Jiang, Y. Xi, W. Hong, Q. Xu, X. Wang, B. Yang, B. Sun, Z. Lin, J. Liu, "A flexible neural implant with ultrathin substrate for low-invasive brain–computer interface applications", *Microsyst. Nanoeng.*, vol. 8, pp. 133, 2022.

CONTACT

*J.Q. Liu, tel: +86-21-34207209; jqliu@sjtu.edu.cn