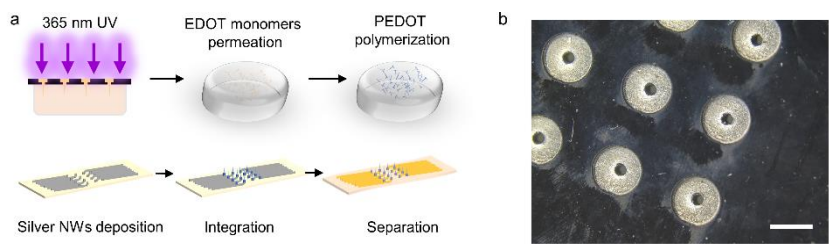


# Uniaxial extending neural probes for bleeding-absent implantation

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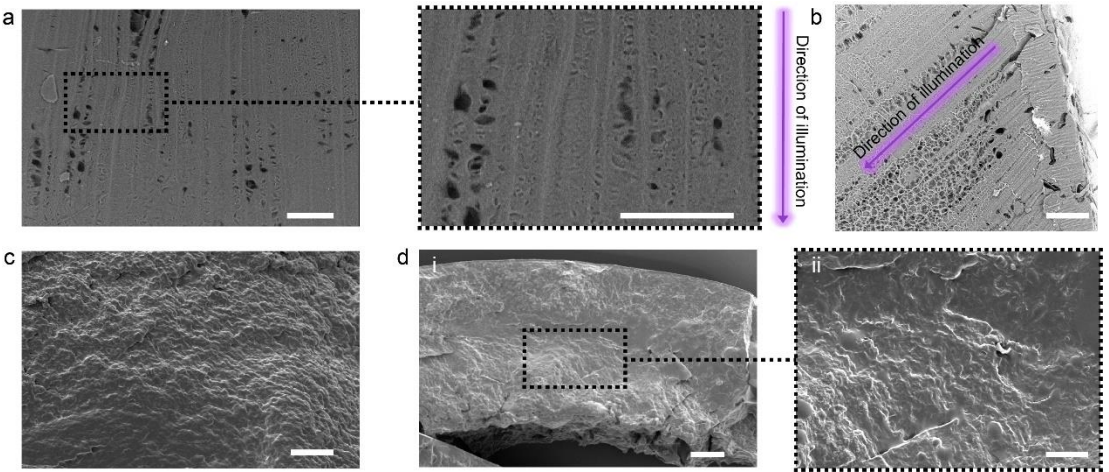
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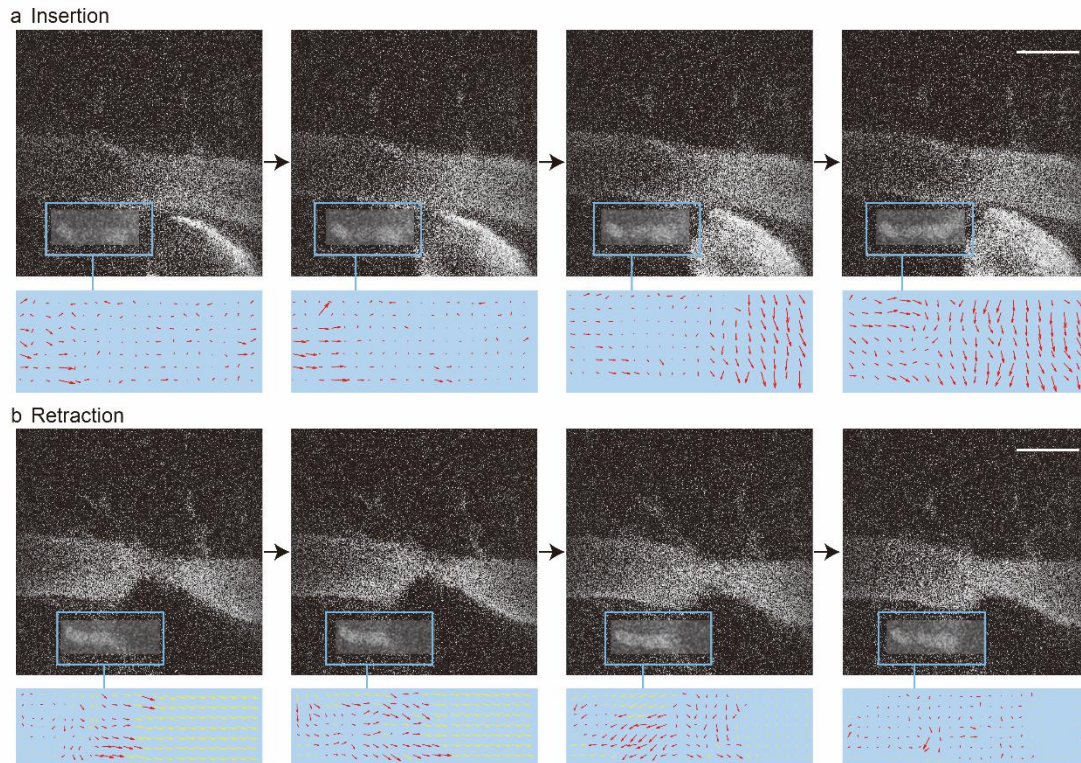
**Supplementary Fig. 1** a The fabrication process of UENPs. The mask plate blocks light in the micropores shown in (b), producing slender scaffolds. Scale bar, 1 mm.

**Supplementary Table 1** The element concentrations of UENP before and after in situ polymerization.

| Element name | Weight concentration percentage |                              |
|--------------|---------------------------------|------------------------------|
|              | Before in situ polymerization   | After in situ polymerization |
| Carbon       | 0.465                           | 0.423423                     |
| Oxygen       | 0.532                           | 0.557558                     |
| Sulfur       | 0.003                           | 0.019019                     |



**Supplementary Fig. 2** The SEM images of the PEG-DA/PSS scaffold fabricated by vertical (a) and inclined (b) illumination. c The SEM image of the thermo-cured hydrogel. d The SEM image of light-cured hydrogel with greatly reduced illumination intensity. Scale bars in a, b, c and d ii are 100 μm. Scale bar in d i is 300 μm.



**Supplementary Fig. 3** The local deformations of the postcapillary venule during insertion (a) and retraction (b) of UENP are analyzed by particle image velocimetry (PIV) analysis. The arrows in the lower blue boxes stand for the motion direction of the particles. Red arrows represent valid pixel points whose velocity is within the allowable range, and yellow arrows represent pixel points whose corresponding pixel points are moving at velocity out of threshold. Scale bar, 100  $\mu\text{m}$ .

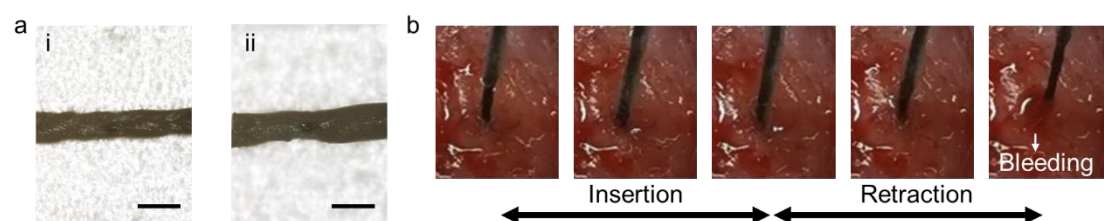
**Supplementary Table 2** The summary of mechanically transformable neural probes.

| Diameter/Width<br>( $\mu\text{m}$ ) | Bending stiffness<br>( $\text{N m}^{-1}$ ) | Soften<br>time | Stiffener                       | Ref.      |
|-------------------------------------|--------------------------------------------|----------------|---------------------------------|-----------|
| 237.22                              | 0.02                                       | 60 s           | PEG-DA                          | This work |
| 36                                  | 100                                        | 10 s           | $\text{Ca}^{2+}$ crosslinked SA | 1         |
| 200                                 | 0.014                                      | 20 min         | natural silk                    | 2         |
| ~300                                | 53                                         | 10 min         | PAAm-Alg                        | 3         |
| 150                                 | 9.7 GPa                                    | NG             | $\text{Ca}^{2+}$ crosslinked SA | 4         |
| 400                                 | 2.89                                       | 1 week         | silk                            | 5         |
| 180                                 | 0.012                                      | 240 min        | Tyrosine-derived polycarbonates | 6         |
| 200                                 | 8.4                                        | 27 days        | PLGA                            | 7         |
| 110                                 | 0.24 mN for 2.8 mm length                  | 20 min         | PEG                             | 8         |

SA: Sodium alginate; PAAm-Alg: poly (acrylamide)-alginate; PLGA: poly(DL-lactide-co-glycolide); PEG: Polyethylene glycol.

## Reference

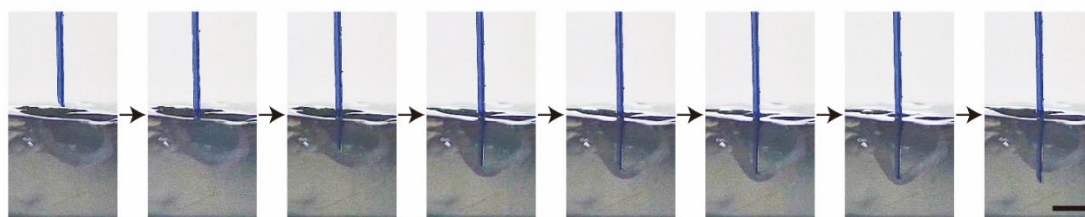
1. Tang, C. et al. A fiber-shaped neural probe with alterable elastic moduli for direct implantation and stable electronic–brain interfaces. *J. Mater. Chem. B* 8, 4387-4394 (2020).
2. Zhou, Y. et al. A silk-based self-adaptive flexible opto-electro neural probe. *Microsyst. Nanoeng.* 8, 1-12 (2022).
3. Park, S. et al. Adaptive and multifunctional hydrogel hybrid probes for long-term sensing and modulation of neural activity. *Nat. Commun.* 12, 3435 (2021).
4. Feng, J., Chen, C., Sun, X. & Peng, H. Implantable Fiber Biosensors Based on Carbon Nanotubes. *Acc. Mater. Res.* 2, 138-146 (2021).
5. Tien, L. W. et al. Silk as a Multifunctional Biomaterial Substrate for Reduced Glial Scarring around Brain-Penetrating Electrodes. *Adv. Funct. Mater.* 23, 3185-3193 (2013).
6. Lewitus, D., Smith, K. L., Shain, W. & Kohn, J. Ultrafast resorbing polymers for use as carriers for cortical neural probes. *Acta Biomater.* 7, 2483-2491 (2011).
7. Foley, C. P., Nishimura, N., Neeves, K. B., Schaffer, C. B. & Olbricht, W. L. Flexible microfluidic devices supported by biodegradable insertion scaffolds for convection-enhanced neural drug delivery. *Biomed. Microdevices* 11, 915-924 (2009).
8. Wang, X. et al. A Parylene Neural Probe Array for Multi-Region Deep Brain Recordings. *J. Microelectromechanical Syst. Jt. IEEE ASME Publ. Microstruct. Microactuators Microsens. Microsyst.* 29, 499-513 (2020).



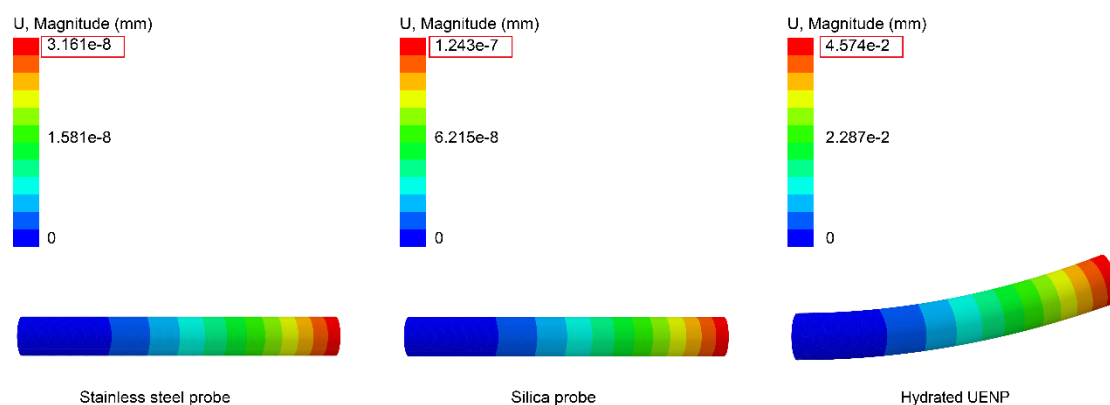
**Supplementary Fig. 4** **a** Unstiffened (i) and stiffened (ii) probe. Scale bar, 300 μm. **b** The insertion and retraction of the stiffened probe in a living rat's brain.



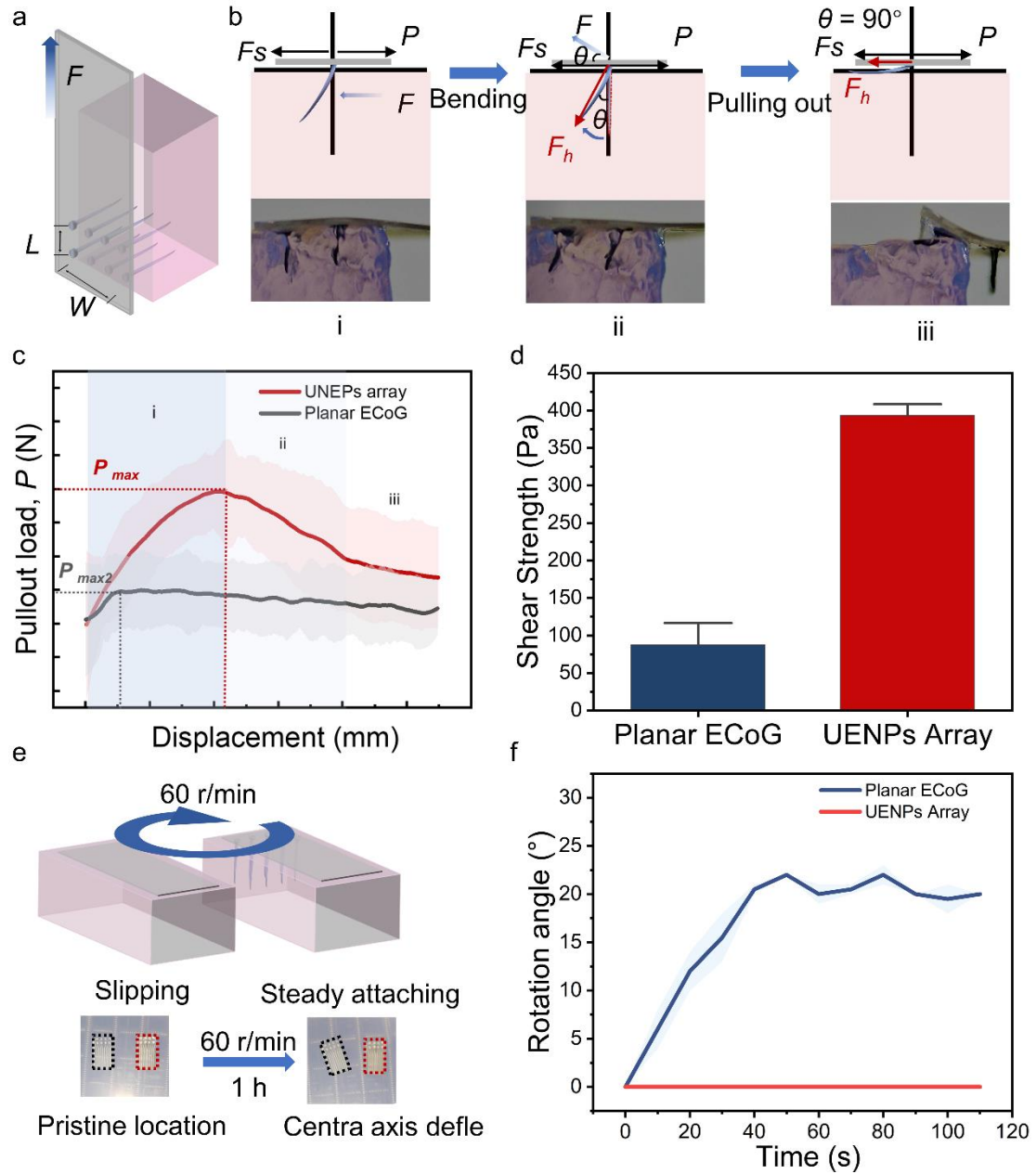
**Supplementary Fig. 5** The isolated microvessel in the phantom brain. Scale bar, 1 mm.



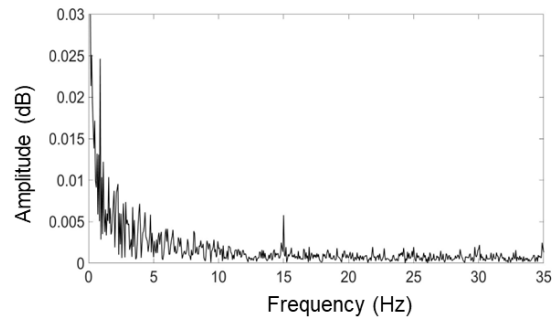
**Supplementary Fig. 6** The successive footage of the silica probe poking and pushing the microvessel in the phantom brain. Scale bar, 1mm.



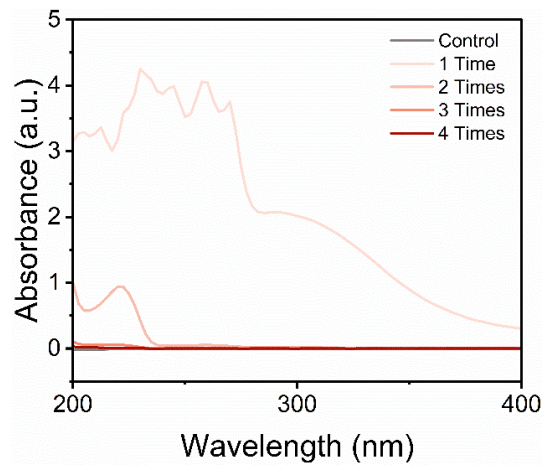
**Supplementary Fig. 7** The displacement ( $u$ ) of the free ends of the stainless steel probe ( $3.161 \times 10^{-8}$  mm), silica probe ( $1.243 \times 10^{-7}$  mm), and hydrated UENP ( $4.574 \times 10^{-2}$  mm) when applying  $10^{-6}$  N on the ends.



**Supplementary Fig. 8** **a** Schematic diagram of the UENPs array pull-out test. **b** The force on the UENPs arrays at **i** The initial state of pulling out; **ii** The state of UENPs are pulled out; **iii** The state that probes have all been pulled out. **c** The pullout curves of UENPs arrays and planar ECoGs.  $P_{max}$  is the maximum load the array can withstand, and the array starts to move after the load is greater than  $P_{max}$ . **d** The shear strength of UENPs arrays and planar ECoGs based on the equation of  $\text{Shear Strength} = \frac{P_{max}}{WL}$ . **e** The UENPs array demonstrates stable attachment on the wet and slippery phantom brain surface during rotation. In contrast, planar ECoG exhibits significant shifts and rotations. The rotation angles of UENPs arrays and ECoGs are shown in **f**. Data are given as the mean  $\pm$  SD.



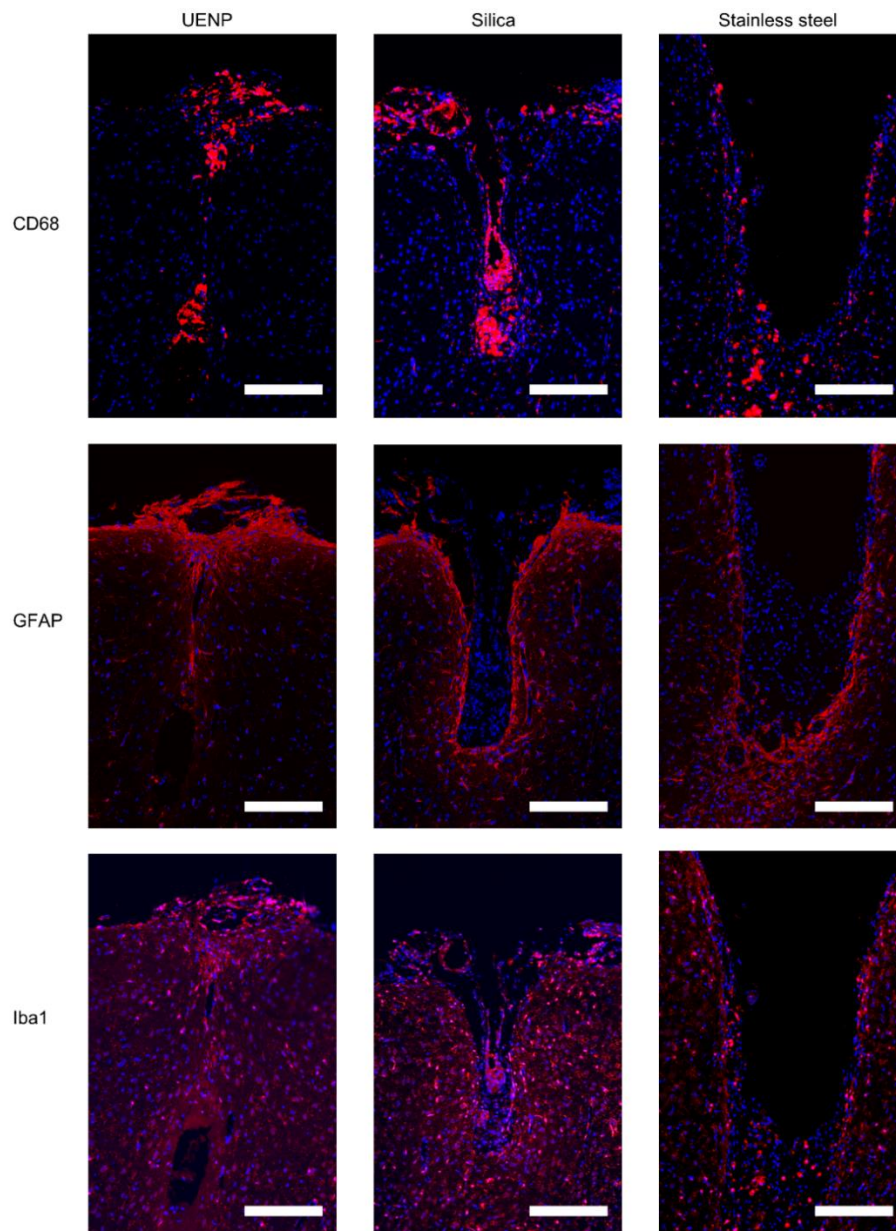
**Supplementary Fig. 9** The representative spectral analysis result of UENP-acquired potential signals.



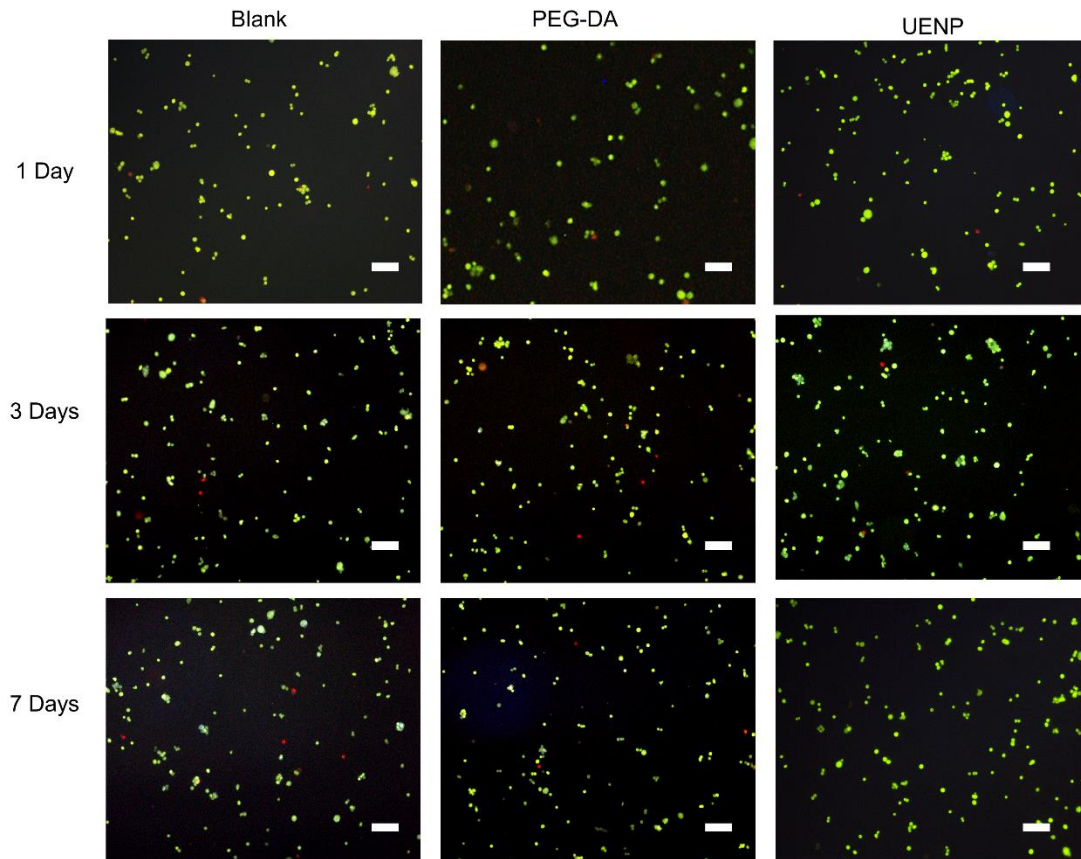
**Supplementary Fig. 10** The UV spectrum of the washing solution after multiple times washing of the UENPs.



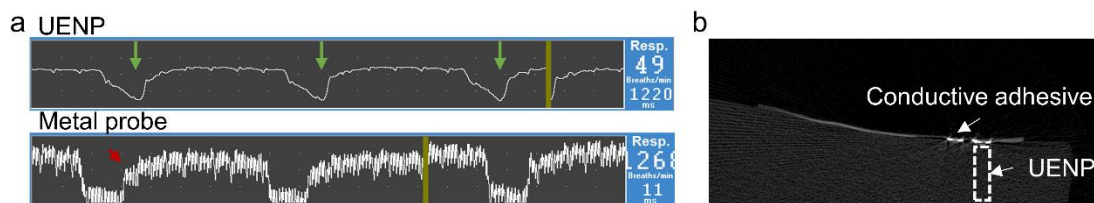
**Supplementary Fig. 11** The UENP was unscathedly retrieved after implantation for 14 days. Scale bar, 1.5 mm.



**Supplementary Fig. 12** Representative image of fluorescently labeled cells after implanting 2 months. Red indicates CD68, GFAP, and Iba1 positive cells, whereas blue indicates cell nucleus. Scale bar, 200  $\mu\text{m}$ .



**Supplementary Fig. 13** The Calcein-AM/PI stained cells after coculturing with PEG-DA scaffolds, the UENPs, and the blank group for 1 day, 3 days, and 7 days. Scale bar, 100  $\mu\text{m}$ .



**Supplementary Fig. 14 a** The real-time respiratory rate during MRI scanning of rat implanted UENP and metal probe. **b** The Micro-CT scan for the UENPs array. The UENPs are invisible and the conductive adhesive shows metallic artifacts.

**Supplementary Table 3** Mechanical properties for probe materials in FEA models.

| Materials       | Young's modulus | Poisson's ratio |
|-----------------|-----------------|-----------------|
| Stainless steel | 193 GPa         | 0.265           |
| Silica          | 50 GPa          | 0.17            |
| Hydrated UENP   | 135.26 kPa      | 0.3             |
| Brain           | 9 kPa           | 0.5             |