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*Published in:*
IEEE Sensors Journal

*DOI:*
10.1109/JSEN.2021.3078358

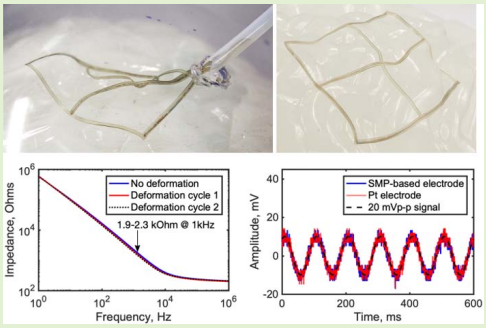
Published: 01/08/2021

*Document Version*
Publisher's PDF, also known as Version of record

# Shape Memory Polymer-Based Insertable Electrode Array Towards Minimally Invasive Subdural Implantation

Anastasiia Kravtcova, Antoniya Toncheva, Samuel Rantataro, Emilia Peltola, Jean-Marie Raquez, Pierre Lambert, and Quan Zhou, *Member, IEEE*

***Abstract*—Minimally invasive implantation of subdural electrodes can dramatically benefit the patients with various neurological diseases. In modern clinical practice, the implantation procedure of the electrode arrays remains traumatic for patients and increases postoperative infection risk. Here we report a design and insertion technique of thermally activated shape-memory polymer-based electrode array that can recover up to ten times length deformation. The compressed four-centimeter wide array can be easily packed into a three-millimeter diameter tube and subsequently deployed thought five-millimeter opening in a restricted space between a brain phantom and a simulated skull. The mechanical properties of the developed array are comparable to the materials traditionally employed for the purpose, and the electrical and signal recording properties are preserved after shape deformation and recovery. Additionally, the array is biocompatible and exhibits conformability to a curvy brain surface. The results demonstrate that insertion of the electrode array through a small hole into a restricted space similar to subdural cavity is possible, which may inspire future solution of minimal invasive implantation for patients suffering from epilepsy, amyotrophic lateral sclerosis or tetraplegia.**




***Index Terms*—Electrodes, minimally invasive implantation, poly(ε-caprolactone), shape memory polymer, smart materials.**

Manuscript received March 9, 2021; revised April 25, 2021; accepted April 25, 2021. Date of publication May 7, 2021; date of current version July 30, 2021. This work was supported in part by the Academy of Finland under Grant 296250, Grant 321996, and Grant 328854; in part by the Aalto University School of Electrical Engineering Doctoral School Funding; in part by the Jane and Aatos Erkko Foundation; in part by the European Union's Project H2020-FETPROACT-2018-01 under Grant 824070; in part by the Finnish Society of Automation, Kansallis-Osake-Pankki Fund; in part by the Orion Foundation; in part by the Finnish Society of Information Technology and Electronics (TiES), Sähköinsinööriliiton Säätiö, Finnish Foundation for Technology Promotion (TES), BEWARE under Project 410161; in part by the Fellowships Academia Program by the COFUND Program of the European Union (FP7-Marie Curie Actions); in part by the Belgian Federal Government Office of Science Policy under Grant SSTC-PAI 6/27; and in part by the LCFM-BIOMAT Project. The associate editor coordinating the review of this article and approving it for publication was Dr. Eduardo Garcia-Brejio. *(Corresponding author: Quan Zhou.)*

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This article has supplementary downloadable material available at https://doi.org/10.1109/JSEN.2021.3078358, provided by the authors.

Digital Object Identifier 10.1109/JSEN.2021.3078358

## I. Introduction

MINIMALLY invasive implantation of subdural electrodes can dramatically benefit the patients with wide classes neurological diseases such as epilepsy [1], amyotrophic lateral sclerosis [2] or tetraplegia [3]. Traditionally, a centimetre-scale electrode array is placed on the cortex of the brain under dura mater during the craniotomy procedure, which involves a large skull opening in the range of 25-65 $cm^2$. [4] Today the procedure remains traumatic for the patients [5], increasing infection risks [6] and expensive for the healthcare system [7]. The clinically approved subdural electrode arrays, fabricated from silicone sheet of millimetre thickness with metal electrodes and interconnections [8], have limited flexibility and conformability [9], and make the implantation through smaller skull opening challenging.

The problem of craniotomy size reduction has been approached by using active and passive materials in the electrode design. The electrodes fabricated from thin and flexible passive materials such as polydimethylsiloxane (PDMS), have potential to reduce the required craniotomy size from 3.2 mm to 3 mm [10], but do not provide centimetre-scale measurement area crucial for certain applications such as focal epilepsy diagnostics [4]. In contrast, integration of the stimuli-responsive active materials into the electrode structure

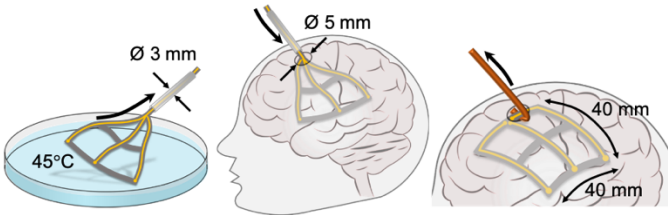


Fig. 1. Concept of the SMP-based electrode array insertion technique. The array is packed into the tube, released into simulated subdural space through a small opening, and then retrieved through the same opening.

can minimize craniotomy size up to several times by compacting electrode array before implantation and expanding it after insertion. Temperature triggered shape memory polymer (SMP) has been used in microelectrode array designs with applications in retina [11] and nerve [12], [13] stimulation as well as softening electrodes for improved tissue compatibility [14], [15]. Although these prototypes have the potential of minimally invasive implantation, none demonstrated the ability to recover the initial shape in a confined space such as subdural cavity. Implantation into subdural space through the opening two times smaller than the size of the array has been demonstrated by shape memory alloys (SMAs) [16] and electroactive polymers [17] -based electrode arrays. However, the rigid SMA wires have significant mechanical mismatch with the brain tissue while softer electroactive polymers require an external electric field for activation.

In the present study, we report a design and insertion technique of thermally activated SMP-based electrode array, that can be successfully deployed into a simulated subdural space between a brain phantom and a simulated skull, while preserving the electrical measurement capability. This is a feasibility study focusing on the insertion mechanism, where the main goal is to evaluate if an active material such as SMP can achieve insertion through a thin tube into a confined space where both the diameter of the tube and the thickness of the space are near an order of magnitude smaller than the electrode itself. The actual *in vivo* implantation is not in the scope of this study. Nevertheless, the electrical functionality of the device and biocompatibility with cell culture samples are demonstrated.

The concept of insertion technique into a simulated subdural space is illustrated in Fig. 1. The electrode array can be (*i*) easily packed into a 3 mm inner diameter delivery tube, then (*ii*) inserted through a 5 mm opening into a tight space of several millimetres, and (*iii*) subsequently unfolded into a 40 × 40 $mm^2$ mesh after being released from the tube. We selected a poly($\varepsilon$-caprolactone) ($PCL_{SMP}$), capable of thermo-reversible Diels-Alder (DA) reactions [18], as a substrate. The $PCL_{SMP}$ network exhibits melting temperature ($T_m$) transition starting at 45°C and good shape-memory properties with fixity and shape recovery ratio >98% [18] The $PCL_{SMP}$ has also high elastomeric properties, where the strain deformation before breaking is up to 600%. [19]

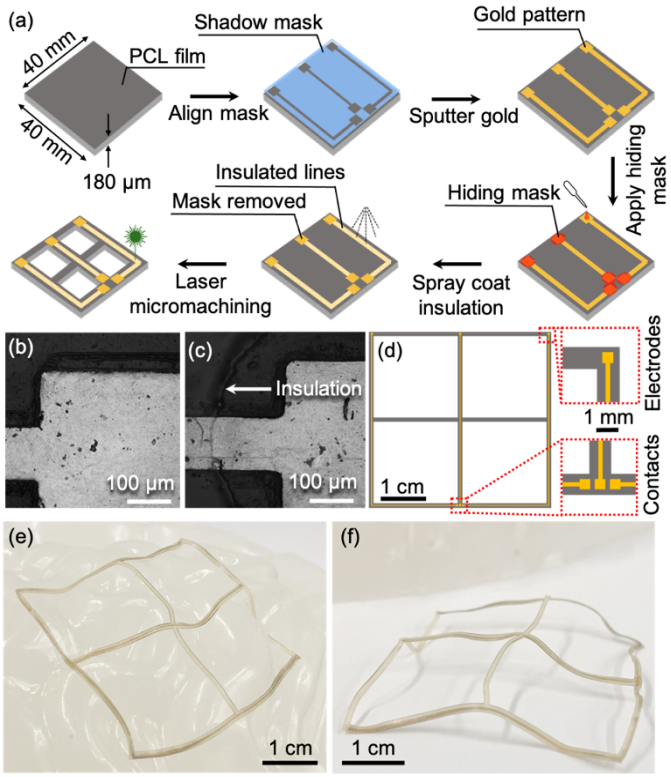


Fig. 2. (a) SMP-based electrode array fabrication process. (b) Optical micrograph of a gold electrode and the interconnection line. (c) Gold electrode with insulation around it. (d) Schematic presentation of the electrode array design. Photograph of the fabricated electrode array (e) placed on the curvy brain phantom surface after pre-heating to 45°C, and (f) removed from the brain phantom surface after cooling down to 22°C and fixing its conforming shape.

## II. Experiments and Results

### A. Fabrication of the SMP-Based Electrode Array

To fabricate the electrode array successfully, it is important to preserve the $PCL_{SMP}$ material integrity and physicochemical properties avoiding its melting and shape deformation. The defined maximum working temperature ($T_{max}$) at which the $PCL_{SMP}$ polymer melts by stimulating the retro-DA reactions and destructing the polymer network is 120°C. Based on $T_{max}$ limitation, the fabrication process using a combination of shadow and hiding masks, deposition techniques, and laser micromachining was developed (Fig. 2a). $PCL_{SMP}$ films with thickness of 180 $\mu$m were prepared by compression molding at 120°C. After that, the samples were gradually cooled down and kept at 60°C for 8 h ensuring the progressive occurrence of the DA reactions and the subsequent formation of the thermo-reversible network. A shadow mask, fabricated from 100 $\mu$m thick acetate sheet, was placed onto the surface of $PCL_{SMP}$ film and a 150 nm layer of Au was sputter deposited (BAL-TEC SCD 005). Further, the mask was removed, and the electrodes were covered with Ecoflex elastomer (00-20, Smooth-On) by drop casting method as a hiding mask in order to protect them from insulation. Acrylic resin spray (PLASTIK 70, KONTAKT CHEMIE) was applied to the exposed regions of the film at the working distance of 25 cm

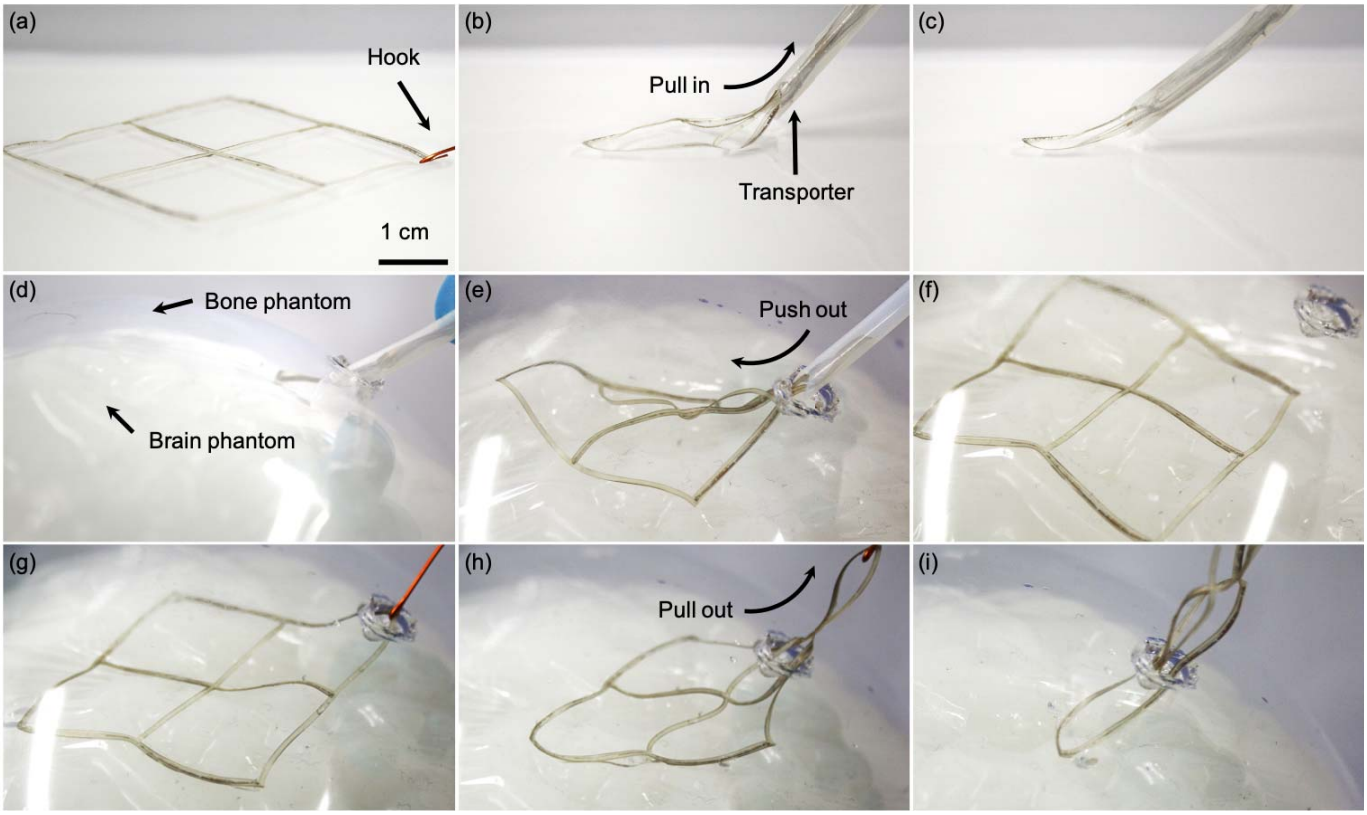


Fig. 3. Implantation procedure. (a-c) Loading the electrode array into a transporter of 3 mm inner diameter: the array floating on the surface of 45°C water is picked by a hook and pulled into the transporter. (d-f) Unloading into a simulated subdural space between bone and brain phantoms through 5 mm hole: a cylindrical releasing rod is inserted into the transporter and pushes the array out into a 5 mm thick simulated subdural space filled with 45°C water. The array unfolds during unloading. (g-i) Retrieving from the simulated subdural space: the array is pulled out using a hook.

for 2 s. Morphological structure of the deposited electrodes (Fig. 2b) and insulation (Fig. 2c) was examined by optical microscopy (OPTON, Zeiss), revealing uniform deposition of the layers and lack of macroscopic cracks. The thickness of the deposited layers was assessed with profilometry (Fig. S1, Appendix). Lastly, the $PCL_{SMP}$ film with exposed metal pattern and insulated conductive lines was micromachined into the final shape of electrode array (Fig. 2d) using custom 520 nm femtosecond laser system.

The synthesized $PCL_{SMP}$ polymer has $T_m$ (melt of the $PCL_{SMP}$ crystalline phase) of about 45°C that makes the electrode array to soften and conform curvy surfaces such as a brain phantom (Fig. 2e). The mechanical flexibility of such $PCL_{SMP}$ after actuation is similar to PDMS electrodes investigated elsewhere. [10] At a temperature below $T_m$, the electrode array hardens and preserves its temporary shape (Fig. 2f). The temperature difference between the $T_m$ and $T_{body}$ allows precise control of shape recovery at a desired moment, as well as a fixed shape of the electrode array at $T_{body}$ during the potential measurements.

### B. Insertion Into Simulated Subdural Space

The fabricated electrode array was experimentally tested for insertion in a subdural space phantom that comprised (i) a real sized human brain model fabricated from Ecoflex elastomer (00-20, Smooth-On), (ii) a transparent acrylic half sphere of 160 mm in diameter resembling skull bone and (iii) a polyethylene transparent thin film representing arachnoid mater that lines the brain cortex (Fig. 3). The water of 45°C was injected into simulated subdural space. A 5 mm hole was made in the skull bone simulation for electrode array insertion and removal.

A flexible tube (3 mm inner diameter and 4 mm outer diameter) was employed as an implantation transporter. Firstly, the electrode array was placed into 45°C warm water for softening. As the DA-based crosslinks maintained the integrity of the network, the corner of the electrode array was picked by a hook (0.5 mm diameter copper wire) inserted into the transporter (Fig. 3a-c). The array was then slowly pulled into the transporter at a speed of 2 mm/s until it was fully packed inside. The compacted electrode array was kept in the transporter at room temperature until the $PCL_{SMP}$ material cooled and fixed the temporary shape. To implant the electrode array, the transporter was placed through a 5 mm diameter hole in the bone phantom into a 5 mm thick simulated subdural space filled with 45°C water (Fig. 3d-f). A 2 mm thick cylindrical releasing rod was inserted into the tube pushing the electrode array out at a speed of 2 mm/s. The electrode array softened and unfolded in the simulated subdural space followed by cooling to $T_{body}$ that maintains the conforming shape. The unfolded array is then ready for attaching the connector and performing the measurements. Thereafter, the array can be

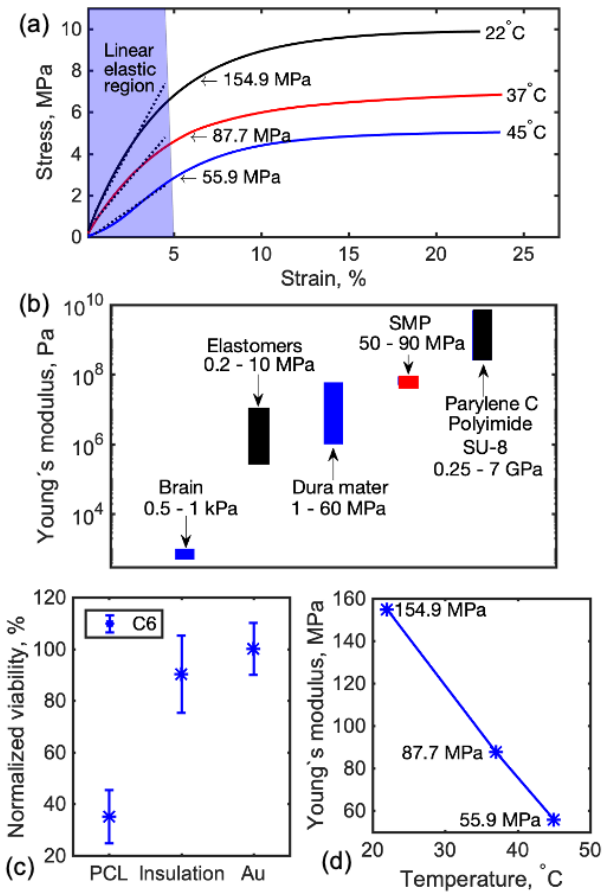


Fig. 4. (a) Tensile test of SMP-based electrode array at 22°C, 37°C, and 45°C. (b) Comparison of Young's modulus of SMP-based electrode array ("SMP") at 37°C and 45°C (red) with traditional materials used for subdural electrode arrays (black) and relevant biological tissues (blue). (c) Viability assay on $PCL_{SMP}$ polymer ("PCL"), SMP-based electrode array ("Insulation") and gold layer over $PCL_{SMP}$ ("Au"). (d) Young's modulus of SMP-based electrode array at 22°C, 37°C, and 45°C.

retrieved by pulling it out from the simulated subdural space using the hook (Fig. 3g-i). Retrieval can be performed at $T_{body}$ or $T_m$ due to mechanical flexibility of the structure at both temperatures. Detailed implantation procedure is provided in Movie S1, Supporting information.

### C. Thermomechanical Properties

To understand the thermomechanical properties of the SMP-based electrode array at room, body and shape recovery temperatures, the stress-strain relation was studied at three different temperatures by dynamic mechanical thermal analysis (DMTA, Q800, TA Instruments, USA) as shown in Fig. 4a. A force ramp (0.5 N/min) with maximal force of 18N was applied.

The Young's modulus of the samples was evaluated in the elastic region, resulting in stiffnesses of 154.9 MPa, 87.7 MPa and 55.9 MPa at 22°C, 37°C and 45°C respectively (Fig. 4d). It was found that the measured Young's modulus values were close to the ones of other materials commonly used for subdural electrodes fabrication (Fig. 4c). The SMP-based electrode array ("SMP") was one to two orders of magnitude softer than parylene C, PI and SU-8, and comparable to elastomers (∼50 MPa). [20] Even though the electrode array is much stiffer than the brain tissue (∼1 kPa) [21], its Young's modulus at biologically relevant temperatures is in the same range as of dura mater (1-60 MPa) [22] which envelops and protects the brain.

### D. Electrical Properties

The electrical properties of the electrode array were characterized using electrochemical impedance spectrum (EIS) measurement. The EIS was performed with a Gamry potentiostat (Reference 600 Plus, Gamry Instruments). Measurements adopted a three-electrode setup, which consisted of SMP-based electrode as a working electrode, an Ag/AgCl reference electrode, and a Pt wire as a counter electrode. The electrodes were immersed into 0.9% PBS at 22°C and 37°C. The PBS gas levels were ambient (no bubbling was done). The measurements were performed with scanning frequencies of 1 Hz – 1 MHz and 10 mV signal amplitude. Stabilization time of 5 min was taken before each measurement.

The results indicated that the electrodes have impedance values of 1.8 – 2.3 kΩ at a frequency of 1 kHz and temperature of 22°C, which is well below the required impedance of the *in vivo* recording electrodes (600 kΩ at 1kHz). [23] The increase of PBS temperature from 22°C to 37°C had no significant impact on the impedance at 1 kHz (Fig. 5a). The effect of mechanical deformation was assessed by performing two consequent deformation and shape recovery cycles in a manner similar to the implantation procedure. The experiment had little effect on the impedance confirming preservation of electrical properties after potential implantation (Fig. 5b). The same behaviour has been observed in phase measurements presented in Fig.S2 in Appendix. The results demonstrate that the developed electrode array is suitable for implantation and *in vivo* recording.

### E. Biocompatibility of SMP-Based Electrode Array

The XTT viability assay of C6 cells on SMP-based electrode array samples ("Insulation") and plain $PCL_{SMP}$ samples ("PCL") was compared to the samples where cells were in contact with the sputtered gold layer only ("Au"). Three replicas from each sample type were used. Gold was selected as a reference material due to its wide acceptance as a biocompatible material for neural interfacing, which has been proven by various separate studies including both cell viability [24] and neural activity [25]. For cell culturing experiments the samples were sterilized in 70% ethanol for 60 min, dried in air, washed with PBS (21-031-CV, Corning), and illuminated under UV light for 15 min. C6 (ATCC® CCL107™) rat glial cells were cultured in DMEM/F-12 (1X) medium without phenol red (Gibco), supplemented by 15% (v/v) heat-inactivated horse serum (Gibco), 2.5% (v/v) fetal bovine serum (FBS, Gibco), and 1.0% (v/v) Penicillin (10 000 U/mL)-Streptomycin(10 000 $\mu$g/mL) solution (Gibco). A cell culture (passage 3) was taken and cultured at 37 °C in a humidified incubator with 5% $CO_2$. When the culture had reached log-phase, subculturing was done by trypsinization (Trypsin-EDTA 1X, Biowest) and cells

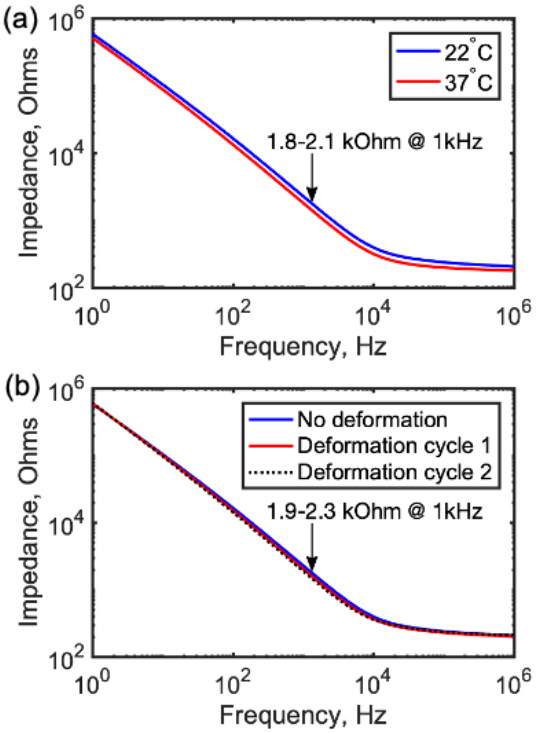


Fig. 5. (a) Comparison of the SMP-based electrode impedance before and after two consequent deformation cycles and (b) at 22°C and 37°C. (blue).

were seeded at 40 000 cells/cm$^2$ density into 12-well plate containing the samples (1 cm$^2$). The full XTT viability assay protocol is described in Appendix.

As presented in Fig. 4c, viability of the cells on "Insulation" samples corresponded closely to "Au" samples indicating that the insulation material did not impair cell metabolism: 90% dehydrogenase activity was shown to be retained. Cell viability on "PCL" samples was 35%, which we attribute to the impurity of the material since purified $PCL_{SMP}$ is biocompatible. [26] However, since $PCL_{SMP}$ is covered with biocompatible gold and insulation during fabrication process, SMP-based electrode array is considered biocompatible and suitable for implantation.

### F. Electrical Signal Recording

The electrical recording functionality of the designed SMP-based electrode was assessed *in vitro* in 0.9% PBS bath agitated by a function generator as shown in Fig. 6a to simulate the subdural conditions. Sine wave signal of 20 mVp-p at 10 Hz and 1 kHz frequency was supplied by the function generator (33210A, Keysight Technologies). (Pt) electrode from commercial subdural grid (Ad-Tech Medical Instrument) was used as a reference during the measurements. SMP-based electrode, Pt electrode, and a signal probe connected to the function generator, were immersed into 0.9% PBS bath. SMP-based and Pt electrodes were clamped into FFC connector (66226-003LF, Amphenol) and connected to the oscilloscope (DSO3102A, Agilent Technologies) for signal output and recording.

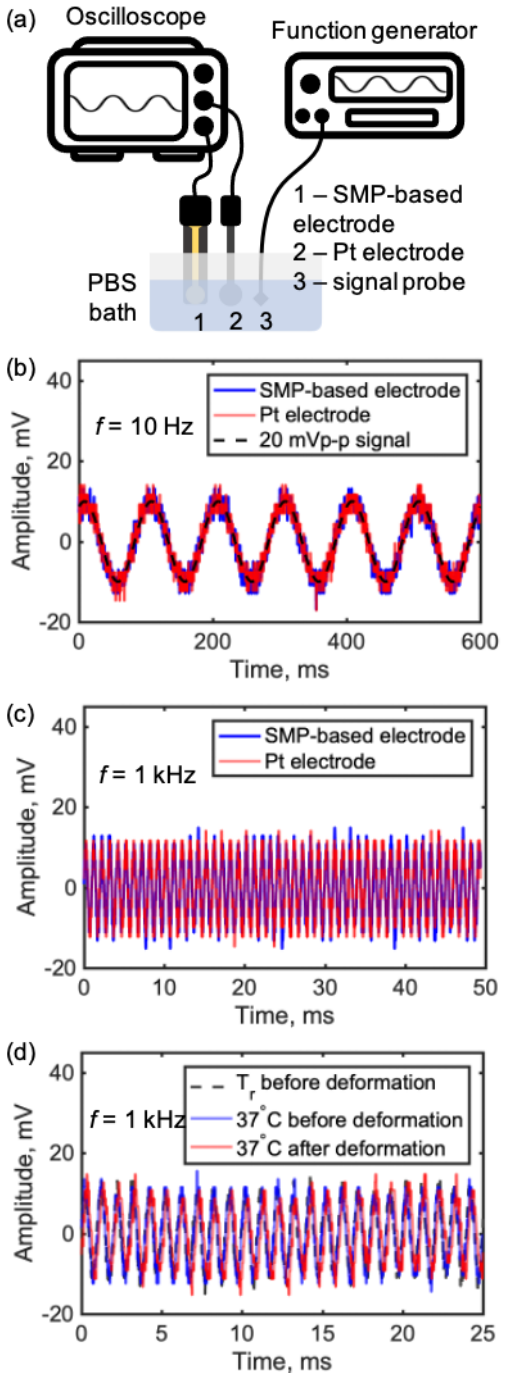


Fig. 6. (a) Schematic presentation of the *in vitro* measurement setup. Electrical signal by SMP-based electrode and Pt reference electrode at (b) 10 Hz and (c) 1 kHz. (d) Electrical signal by SMP-based electrode at room temperature ($T_r$, 22°C), and at 37°C before deformation and after shape recovery.

The designed SMP-based electrode could successfully record sine waveform signals of 20 mVp-p at both low 10 Hz and high 1 kHz frequencies at room temperature of 22°C (Fig. 6b-c). To evaluate the performance in simulated *in vivo* environment, the recording was also performed at physiological temperature of 37°C, and after shape deformation and recovery cycle required for potential implantation. It was found that independently of the working conditions, the recording performance of the SMP-based electrode was

preserved (Fig. 6d). Furthermore, the signal obtained with the developed electrode was comparable to commercial Pt one in all of the performed measurements with respective SNR of 12.7 dB and 12.1 dB. With this it was demonstrated that the SMP-based electrode can be considered promising for *in vivo* measurements.

## III. Discussion and Conclusion

In summary, we developed a stimuli-responsive biocompatible SMP-based electrode array that can be inserted into a restrict space through a small hole, where both the height of the space and the diameter of the hole is near an order of magnitude smaller than the electrodes. Specifically, a $40 \times 40$ mm$^2$ electrode array was successfully packed into a 3 mm inner dimeter transporter tube and inserted into a 5 mm thick simulated subdural space through a 5 mm diameter opening. Owning to the tuneable physicochemical properties of the synthetized $PCL_{SMP}$ polymer, the electrode array can recover over ten times of length deformation, significantly reducing the size of required craniotomy, while preserving the electrical properties and signal recording functionality of the electrodes.

The temperature-adaptive stiffness of the electrode array at both insertion and baseline body temperatures revealed great potential of mechanical compatibility with the biological tissues. The conformability of the array to the curvy brain surface can potentially improve the quality of signal recording. The $T_m$ of $PCL_{SMP}$ is 8°C higher than the baseline temperature of the human body ($T_{body}$), which is high but still below the previously reported 13°C increase of brain surface temperature over $T_{body}$ that does not cause permanent thermal damage to the brain tissue. [27] Other classes of SMP, for example, with shape recovery at lower temperature, IR or aqueous stimuli will be investigated in future to make the procedure closer to clinical requirements and allow performance at body temperature. Additionally, the developed fabrication process supported the production of electrode arrays of desired shapes and dimensions from wide variety of materials with low working temperature requirement. Altogether, we believe that the present concept will inspire the scientific community for new generation of implantable flexible electronics for minimally invasive medical applications.

## Appendix

### *Synthesis of $PCL_{SMP}$ Thermo-Reversible Network*

*Materials:* In the present study, shape-memory films were obtained from $\alpha$, $\omega$-dihydroxyl poly($\varepsilon$-caprolactone) (PCL-diol; CAPA2402, $M_n$ = 4000 g/mol with PDI = 1.48) and $\alpha$, $\alpha'$, $\omega$, $\omega'$-tetrahydroxyl poly($\varepsilon$-caprolactone) (PCL-tetraol; CAPA4801, $M_n$ = 8000 g/mol, PDI = 1.48). The commercially available PCL-based oligomers were end-functionalization using 1-(3-hydroxylpropyl)-1H-pyrrole-2,5-dione [MAL(OH), obtained from 3-aminopropan-1-ol (Acros), exo-3,6-epoxy-1,2,3,6-tetrahydrophtalic anhydride (Sigma Aldrich), ethanol 96% vol (VWR)] and furfuryl isocyanate (Sigma Aldrich). Dichloromethane, chloroform ($CHCl_3$) and ethanol (EtOH) were supplied by Merck.

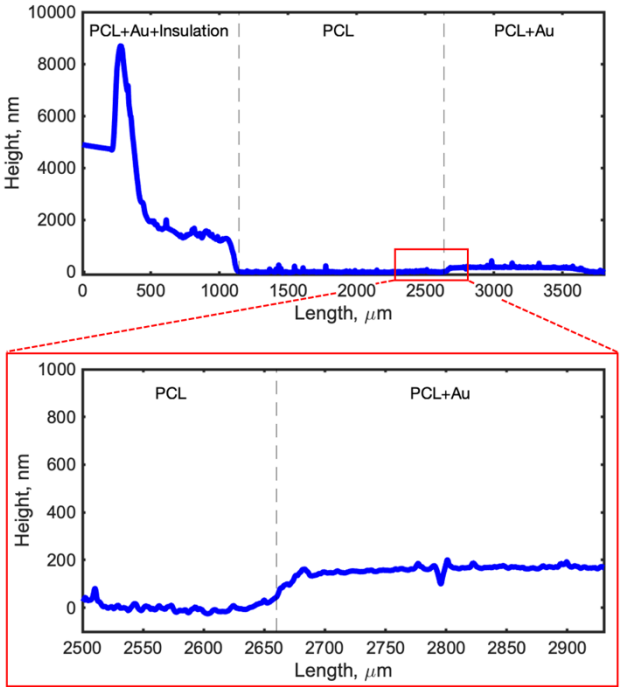


Fig. S1. 2D profile of SMP-based test sample obtained using stylus profiler (DektakXT, Bruker). The thickness of spray coated insulation and Au layer is 4.8 – 8.7 $\mu$m and 150 nm respectively.

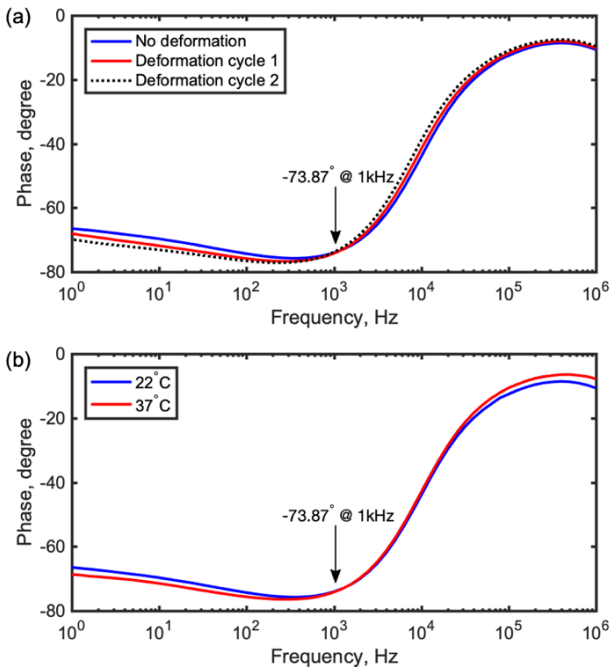


Fig. S2. (a) Phase profile before deformation and after two consecutive deformation cycles. (b) Phase profile at room temperature and at 37°C.

*Synthesis of Functionalized PCL:* For the synthesis of the thermo-reversible network, PCL-tetraol oligomers were end-functionalized with furfuryl moieties [$PCL(FUR)_4$] in bulk overnight in presence of furfuryl isocyanate (1.5 eq, excess) at 110°C. The reaction is taking place in pre-conditioned flask (250 ml) under inert atmosphere. During the purification step, the functionalized oligomers were dissolved in $CH_2Cl_2$ and poured in cold methanol

aiming the remove out of any excess of non-reacted furfuryl isocyanate. Maleimide functionalized PCL [PCL(MAL)$_2$] was obtained by reactive extrusion under nitrogen flow: PCL-diol, 1-(3-hydroxylpropyl)-1H-pyrrole-2,5-dione and methylene diphenyl diisocyanate were introduced into twin-screw DSM micro-compounder (15 cm$^3$) at temperature of 55°C and twin-screws rotation speed of 30 rpm. The reaction took place at temperature of 140°C and rotation speed of 70 rpm for 40 min. The residual protected maleimide chain end groups were deprotected by placing the polymer matrix in an oven under vacuum at 110°C overnight.

*Synthesis of Shape-Memory Network:* For the production of the thermo-reversible network, reactive extrusion procedure was applied as followed: appropriate amount of PCL(FUR)$_4$ was introduced in twin-screw DSM micro-compounder (15 cm$^3$ at 55°C) in presence of PCL(MAL)$_2$ (stoichiometric ratio between furfuryl and maleimide functions) with rotation speed of the twin-screws of 30 rpm and constant nitrogen flow. After 30 min, the reaction was completed, while the reaction temperature was of 80°C and rotation speed of 70 rpm. To complete the Diels-Alder coupling reactions, the synthesized product was placed in oven at 65°C.

### Viability assay

To evaluate biocompatibility, XTT cell viability assay was used on three replicas from each sample type. After culturing cells for 33 h, old media was discarded and changed to DMEM high-glucose medium without phenol red (D1145, Sigma) supplemented with 10% (v/v) FBS, 1% (v/v) 200 mM Glutamine (HyClone), and 1.0% (v/v) Penicillin-Streptomycin solution. Activated XTT solution (XTT cell viability assay kit, Biotium) was added to each well (volume ratio 1:2 with respect to the medium) and cells were incubated for 4 h before measuring the absorbance at 450 nm.

Blank-corrected optical density (OD) values were compared to the "Au" sample that acted as a negative control. The reported OD values correspond to mean average values from the three replica samples. Sample is considered to be cytotoxic if cell culture viability decreases below 70% compared to the negative control sample. The following equation was used to evaluate cell viability on "PCL" and "Insulation":

$$\%Viability = (100 \times OD_{450,sample})/OD_{450,Au}, \qquad (1)$$

where $OD_{450,sample}$ denotes the OD value of cell culture either on the "PCL" or "Insulation" sample, while $OD_{450,Au}$ denotes that on the negative control.

### Captions of Supporting Movie

Movie S1: A movie demonstrates (i) packing the SMP-based electrode array into the implantation transporter; (ii) insertion and unfolding of the SMP-based electrode array into simulated subdural space filled with 45°C water; (iii) retrieval from the simulated subdural space.

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