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Research Update: Platinum-elastomer mesocomposite as neural electrode coating

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Platinum is electrochemically stable and biocompatible,and remains the preferred material for the fabrication of implantable neural electrodes. In a foil or film format, platinum is mechanically stiff compared to interfaced biological tissue. We report a soft, highly stable platinum-elastomer composite that offers both mechanical compliance *and* the electrochemical properties of platinum. We demonstrate the high-performance of the novel mesocomposite printed on stretchable microelectrodes both *in vitro* and *in vivo*. The platinum-elastomer composite is a new promising coating for chronic neural interfaces. [http://dx.doi.org/10.1063/1.4906502]

The optimization of the electrochemical properties of implantable neural electrodes is a major focus in the fields of materials science, bioelectronics, and neural engineering.[1,2] The electrode is the electrical link between electrogenic neurons and electronic hardware, and transduces ionic into electronic currents, and vice versa. Scientists aim at developing coatings that reduce the electrode-electrolyte impedance and inject reversibly and safely charges into the biological tissue. Candidate materials include conducting polymers such as PEDOT and polypyrrole;[3] metal oxides, e.g., iridium oxide;[4] and nanocarbons such as nanotubes and graphene.[5] However, these materials are brittle and mechanically stiff compared to biological tissues. In this study, we describe a novel soft mesocomposite coating based on platinum that meets both electrical and mechanical demands of neural electrodes.

Platinum has good charge injection capability and is the material of choice for clinical electrodes.[6] Silicone rubber is a widely used elastomer for medical devices and implants. This prompted us to develop a composite material consisting of silicone filled with platinum particles. The composite combines the electrochemical properties of platinum with the mechanical compliance of silicone, and offers satisfactory options for micropatterning and integration with a range of implant substrates.

We describe the integration of the composite coating with elastomer-based microelectrode arrays (MEAs) to demonstrate its compatibility with highly deformable substrates. However, the coating is versatile and can be applied to MEAs prepared on glass, silicon, or plastic foil. The stretchable MEA technology used here has been described previously.[7,8] Briefly, the MEA interconnects are made of a patterned thin metal film (3 nm chromium/30 nm gold) sandwiched between two silicone membranes (polydimethylsiloxane (PDMS), Sylgard 184, Dow Corning). The lower membrane (100 μm thickness) supports the stretchable gold interconnects, and the upper one (20 μm thickness) serves as electrical passivation. A schematic cross-section of the MEA is

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presented in Fig. 1(a). Prior to the application of the composite coating, the active electrode site has a recessed bare gold surface. The electrode diameter is 300 μm.

The electrode coating is a blend of platinum particles and silicone. It is prepared by mixing platinum powder (100 mg) with solvent diluted PDMS (1:2 w:w PDMS:heptane, i.e., 5 mg PDMS and 15 μl heptane). This mixture is thoroughly stirred and put aside for evaporation of the heptane fraction. Addition of heptane diluted PDMS doses is repeated until the mixture becomes a paste. Paste formation occurs when the PDMS content is 15 – 20% by weight. The platinum particle diameter varies in the 0.5-1.2 μm range. The dimension of the metallic filler is selected to ensure electrical percolation of the mesocomposite and compatibility with sub-millimeter feature patterning. The surface of the metallic particles is not treated with an adhesive primer prior to compounding. The electrode coating is then patterned using a modified screen-printing process. A 20 μm thick PDMS "screen" is temporarily bonded to the encapsulated MEA. Openings in the screen match the position of the electrode sites. The conductive composite is spread across the MEA (Fig. 1(a) middle). The screen is subsequently peeled off the encapsulated array leaving bumps of the composite precisely at the electrode active sites. The array is then placed in a convection oven at 60 °C overnight to ensure complete cross-linking of the conductive paste.

A photograph of a soft MEA coated with the mesocomposite is shown in Fig. 1(b). The MEA is compliant, conforming easily to the curvilinear surface of a sphere. The surface of the coated electrode is rough. The mesoporous structure of the composite, shown in Fig. 1(b), is beneficial as it increases the electrochemical surface area of the electrode. The platinum particles are clearly visible on the scanning electron microscopy images and well distributed throughout the composite.

The electrode array is then connected to electronic hardware by "soldering" Teflon coated steel wires to matching gold pads on the silicone substrate with soft silver paste.[8] Using the assembled MEA, Electrochemical Impedance Spectroscopy (EIS) measurements were conducted in phosphate buffered saline (PBS, pH 7.4, Gibco) at room temperature using a three-electrode setup and a potentiostat equipped with a frequency response analyzer (Reference 600, Gamry Instruments).

The complex impedances (modulus and phase) of a bare gold and a composite-coated gold electrodes with identical geometric surface area are compared in Fig. 2(a). The spectra demonstrate that the composite coating lowers the impedance of the electrode by approximately one order of

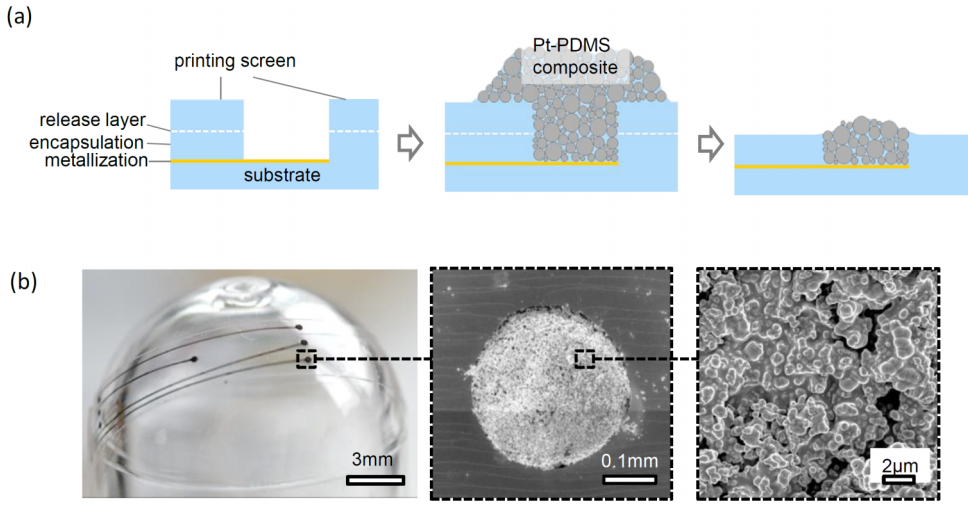

FIG. 1. Platinum-silicone composite electrode coating for MEAs. (a) Screen-printing through a stencil allows precise patterning of the composite on the active site of encapsulated MEAs. A 1H,1H,2H,2H-41 perfluorooctyltriethoxysilane (SigmaAldrich) release monolayer separates the PDMS encapsulation and screen layer. (b) Left panel: a PDMS-based stretchable MEA conforms the curvilinear surface of a sphere of 15 mm diameter. Middle panel: low magnification scanning electron micrograph (SEM) of the composite coating pasted on a 300 μm diameter electrode. Right panel: high magnification SEM of the porous micro-structure of the mesocomposite.

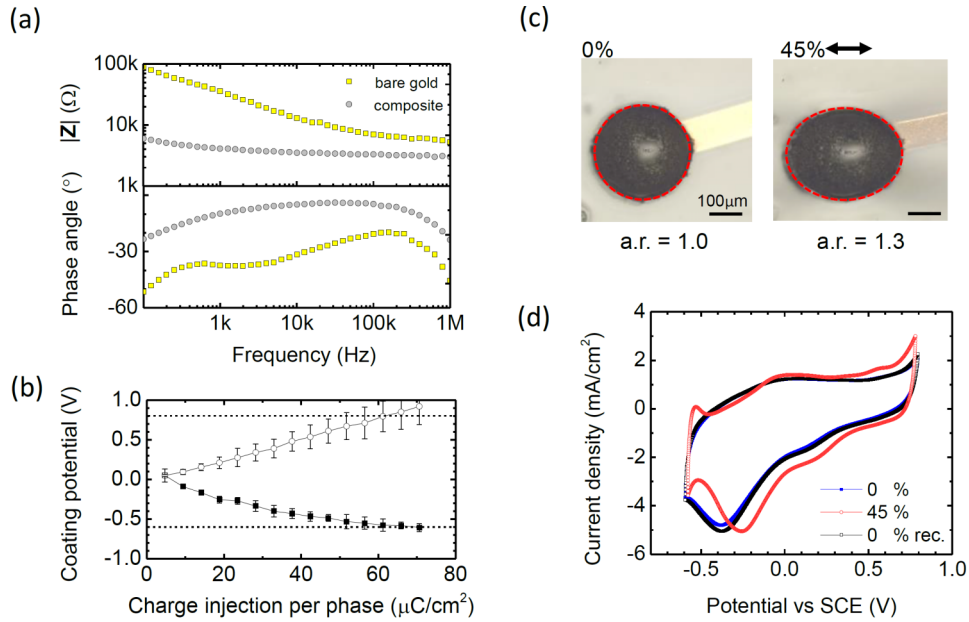

FIG. 2. Electrochemical and electromechanical characterisations of the soft composite coating. (a) Comparison of impedance spectra of bare gold and composite-coated gold electrodes, both 300 μm in diameter. A 5 cm long Pt wire served as counter electrode and a SCE as reference. Impedance spectra were recorded at the open circuit potential. The excitation voltage amplitude was 7 mV. (b) Polarization of the composite coating (vs SCE) in response to biphasic charge balanced current pulses (200 μs per phase). The polarization due to spreading resistance and interconnect resistance has been removed. The dotted lines at −0.6 V and 0.8 V indicate the limits of the water window. (c) Optical micrographs of a coated electrode (with stretchable gold film interconnect visible) at rest at 0% and at 45% uniaxial tensile strain. a.r. denotes aspect ratio. (d) Cyclic voltammograms (PBS pH 7.4) at rest (0%), at applied tensile strain (45%), and upon returning the MEA to its original length (0% recovery).

magnitude. The phase plot also indicates the pseudo-resistive behavior of the composite-electrolyte interface over the range of assessed frequencies.

Next, we applied biphasic charge balanced current pulses (200 μs per phase) to determine the charge injection limit of the soft composite. The limits are defined by the electrochemical potential window for reduction and oxidation of water, −0.6 V and 0.8 V versus Standard Calomel Electrode (SCE), respectively. Polarization outside of the water window leads to hydrolysis, pH changes, gas bubble formation, and electrode corrosion. The maximum cathodic and anodic electrochemical potential excursions of the coated electrode as a function of the charge density per pulse phase are plotted in Fig. 2(b). The maximal charge injection per phase was found to be 57 ± 9 μC/cm^2, which is comparable to the injection limit of platinum.[1]

To assess the mechanical integrity of the coating integrated with the soft MEA, we combined cyclic voltammetry (CV) with cyclic mechanical stretching. The platinum-silicone mesocomposite has a tensile modulus of ∼10 MPa, one order of magnitude higher than that of plain PDMS.[9] Stretching of the soft array is conducted in a LabView-controlled, custom-built uniaxial tensile stretcher, equipped with a reservoir where the MEA is immersed in saline solution (PBS, pH 7.4, Gibco). Upon uniaxial stretch to 45%, the composite electrode deforms from a circle (aspect ratio, a.r. ≈ 1.0) to an ellipse (a.r. ≈ 1.3) to accommodate the applied strain. This allows the composite coating to remain integrated in the stretchable MEA without delamination or electrical failure (Fig. 2(c)). Cyclic voltammograms are recorded when the electrode is held at 0%, 45%, and then at 0% strain (50 mV/s in pH = 7.4 PBS).[10] The high effective surface area of the platinum-silicone composite results in a large cathodal charge storage capacity of 47 ± 3 mC/cm^2, two orders of magnitude higher than those of smooth platinum film.[11] At 45% strain, the overall shape of the CV remains broadly unchanged (Fig. 2(d)). The soft composite electrodes are very robust and display stable electrochemical and electromechanical responses.

We applied the soft electrode technology to stimulate the spinal cord of rats and evaluate the ability of the composite coating to deliver functional electrical stimulation *in vivo*. All surgical procedures were performed in accordance with Swiss federal legislation and under the guidelines established at EPFL. A soft MEA (Fig. 1(b)) carrying seven composite-coated electrodes (300 μm diameter) distributed along a length of 3 cm was manufactured and sterilized in ethanol. The implant was surgically inserted over the epidural surface of the spinal cord in 3 rats, covering spinal segments S1 to L2. Epidural electrical stimulation applied over the dorsal aspect of the spinal cord recruits specific reflex circuits.[12] This paradigm is also capable of eliciting locomotor-like movement of the leg[12] (Figs. 3(a) and 3(b)). The rats were standing bipedally using a robotic interface that provided 80% of bodyweight support against the direction of gravity. Bipolar electrodes were chronically implanted into the tibialis anterior (TA) muscle to record electromyographic (EMG) activity, and thus monitor motor responses following electrical stimulation. EMG signals

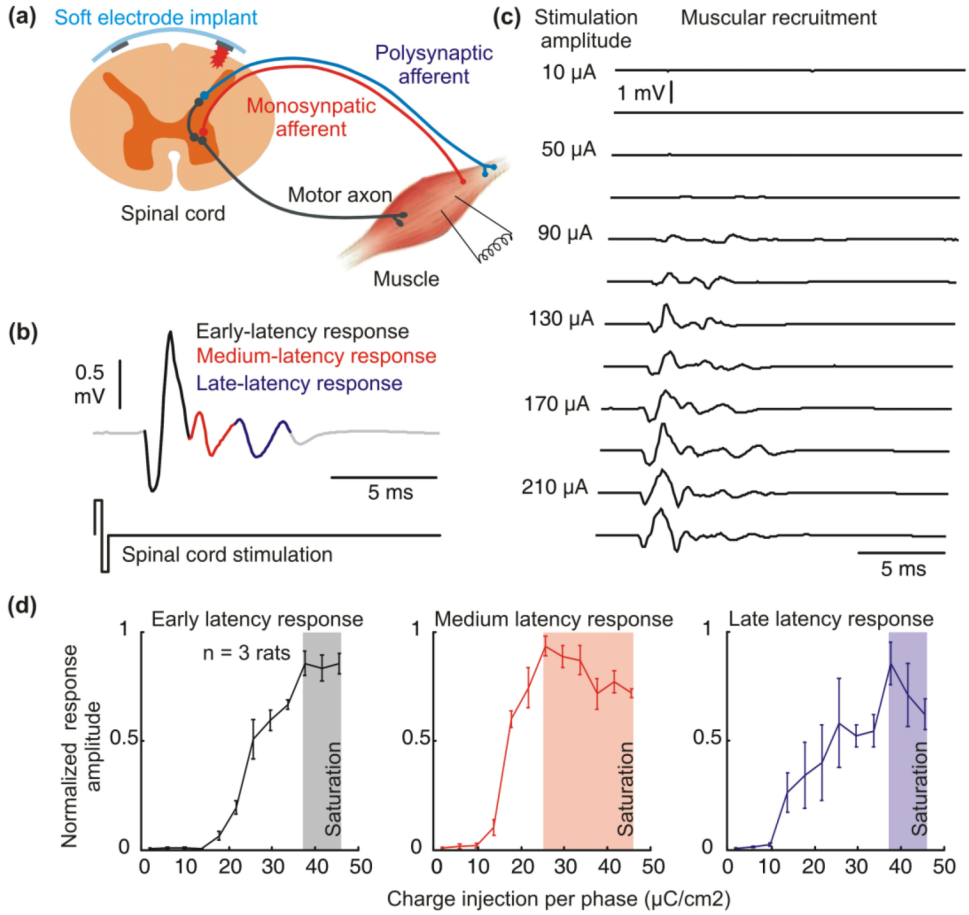

FIG. 3. Application of the soft composite coating for stimulation of neural tissue. (a) Cartoon illustrating the placement of the MEA over the dorsal aspect of the spinal cord, and a simplified representation of the neural circuits recruited with this stimulation. Electrostimulation through the composite coating elicits motor responses in the TA muscle, which are recorded through chronically implanted bipolar EMG electrodes. The recruitment of motor nerves and afferent pathways leads to motor responses with distinct latencies (early, medium, and late). (b) Typical EMG trace recorded in the TA muscle following a single pulse of stimulation delivered through the MEA. Early, medium, and late latency responses are indicated. (c) Gradual increase of the stimulation pulse amplitude leads to a progressive increase in the amplitude of the different components of the motor responses. (d) Recruitment curves of the different components of the motor responses recorded in the TA muscle following electrical stimulation through the more caudal electrode of the soft MEA at increasing intensities. The coating is able to deliver current density sufficient to activate efferent and afferent neural pathways over the entire range of possible muscle activation (n = 3 rats). Data reported as mean ± SEM.

(12.207 kHz) were amplified, filtered (1–5000 Hz bandpass), and stored for off-line analysis. Rectangular, biphasic current pulses (200 μs per phase) were delivered at a rate of 0.5 Hz through the soft implant. The intensity of the electrical stimulation was increased progressively from 10 μA to 250 μA (in steps of 20 μA) until the amplitude of motor responses saturated (Figs. 3(b) and 3(c)). The onset latency and peak amplitude of the different components recorded in motor responses[13,14] were determined through custom-made software in Matlab (MathWorks). Early latency, medium latency, and late latency responses were calculated using the following time windows: 2-4 ms, 4-7 ms, and 7-11 ms, with respect to the onset of electrical stimulation pulse (Figs. 3(b) and 3(c)). The resulting recruitment curves for each component of motor responses are displayed Fig. 3(d). The amplitude of motor responses saturated for injected charges below 40 $\mu C/cm^2$. The charge density required for maximal activation of all the muscle fibers is therefore within the charge injection limit supported by the platinum-silicone composite coating. We did not detect macroscopic damage of the electrode coating after explantation of the soft MEA one week post-surgery. The MEA survived both demanding surgical manipulation and the movement of a freely behaving rat.

We demonstrated that microelectrodes coated with platinum-silicone composite display suitable characteristics for chronic functional neural stimulation. Our results illustrate the integration of the soft coating with elastomeric microelectrode arrays for chronic applications *in vivo*. However, the screen-printing like patterning process is also suitable to MEMS-based *in vitro*. The platinum-silicone composite was designed after platinum black morphology but adds a dimension of mechanical robustness and compliance to the neurostimulation coatings.The soft composite exhibits unique concurrent electrochemical and mechanical performances, which provides a novel material for the design of a variety of long-term bioelectronic implants.

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