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# A novel neural probe for simultaneous electrical recording and local thermal control in sleep spindle oscillation studies

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## Abstract

Slow wave sleep may have a role in memory consolidation [1]. To understand better the temperature dependent changes of its parameters it is necessary to use invasive methods instead of common surface observation. In the following we introduce a novel single crystalline silicon-based, MEMS microelectrode – named thermoelectrode – which is able to record deep brain multiunit activity and local brain temperature simultaneously by 4- or 8-channel platinum recording sites and resistance thermometer respectively. These functionalities are located on the same electrode shaft within tens of µm-s, so the results are from a very close volume while minimizing brain tissue damage as well. Further advantage is the simple extension of the fabrication process as it does not need additional technological steps. After we present the technology we display fulfilled results made by our thermoelectrodes. Not only bench top calibration but in vivo validation as well.

*Keywords:* brain temperature; electrophysiology; resistance thermometer; silicon microelectrode; thermometer calibration

## 1. Motivation and specification

Sleep spindles (7-15 Hz, lasting 1-3 s) are generated in 3 mm depth in mice brain (ventral posteromedial nucleus). To record these signals one need a probe that has proper dimensions to reach that certain area with minimal tissue damage made of implantable, biocompatible material. Silicon based MEMS technology facilitates

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further improvement in combining temperature and electrical recording function on microelectrode shaft of limited dimensions [2].

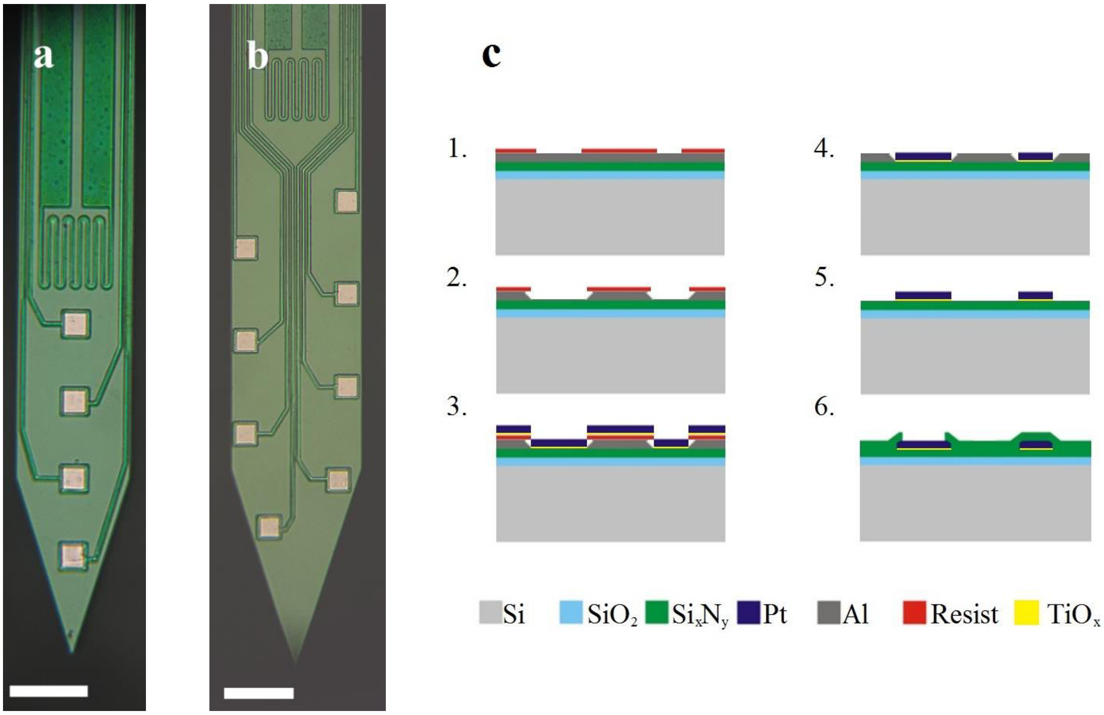

Fig. 1. Optical microscopic image of (a) 4- and (b) 8-channel thermoelectrode tips with the meander-shape resistance thermometer. Scale bars represent 100 µm. (c) Steps of the manufacturing technology of the thermoelectrode.

## 2. Design and technology

The fabrication of the thermoelectrode is based on standard silicon MEMS process described in this section and illustrated in Fig. 1 (c). The initial substrate is a 380 µm thick (100) single-crystalline silicon wafer. Silicon wafers were oxidized in wet atmosphere at 1100 °C in order to grow a 50 nm thick thermal $SiO_2$ layer on the substrate surface. To further isolate the recording sites from the bulk Si, a 300 nm thick low-stress silicon nitride ($SiN_x$) film was then deposited on top of the $SiO_2$ by low-pressure chemical vapour deposition (LPCVD) at 830 °C. A sacrificial Al layer was used to define the pattern of the $TiO_x$/Pt recording sites, temperature monitoring filament and conductor paths via a standard lift-off process. First, the 300 nm thick sacrificial Al layer was deposited by electron beam evaporation. This was followed by the first photolithography and etching steps defining the inverse pattern of the conductor path. The conductor layer consisted of a 15 nm thick adhesion layer of $TiO_x$ formed by reactive sputtering of Ti in an Ar/$O_2$ atmosphere. In the same vacuum cycle, 270 nm thick Pt was sputtered on top of $TiO_x$. The photoresist together with the overlying $TiO_x$/Pt layer was removed using acetone. The Al layer was etched away as before, to complete with the lift-off process. In the next step the upper passivation layer is formed, 300 nm thick $SiN_x$ layers were deposited using LPCVD at 830 °C, respectively. Contact and bonding sites were defined by additional photolithography step followed by selective $SiO_2$ and $SiN_x$ wet etching process in $NH_4F$ buffered HF and phosphorous acid until the total removal of the oxide and nitride layers. The probe shaft was micromachined by dry etching using Bosch recipe in an Oxford Plasmalab System 100 DRIE chamber (Oxford Instruments Plc, UK). Masking layer was standard photoresist on the front side, while the etch stop layers were electron beam evaporated Al film and subsequently spin-coated photoresist.

The desired thickness of the probe is 65 µm, so the depth of the DRIE pre-etch was 95 µm. After the photoresist mask is removed in acetone, the pre-etched microelectrodes are then ground by DISCO GmbH, Germany and finally released.

## 3. Results

### *3.1. Electrical characterization*

Potentiostatic electrochemical impedance spectroscopy (EIS) was used to validate the 30 × 30 µm rectangular platinum recording sites (Reference 600, Gamry Instruments, PA, USA). Fig. 2. shows a representative Bode-diagram of our measurements. The impedance of the recording sites at 1 kHz is |Z| = 769 ± 87 kΩ.

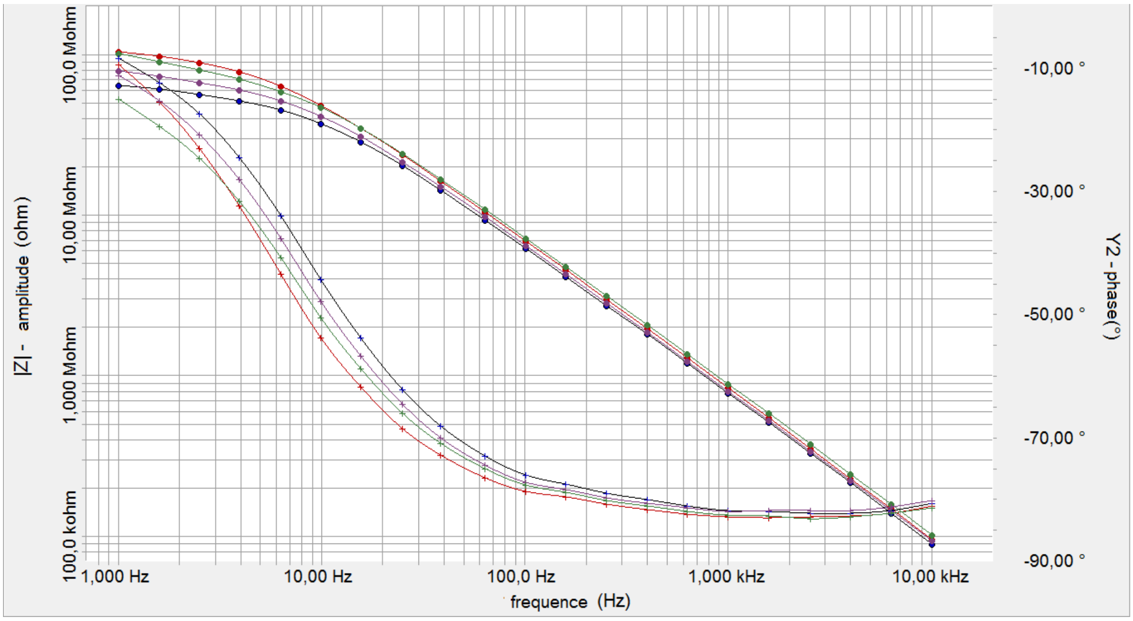

Fig. 2. Representative Bode-diagram of the platinum recording sites measured with electrochemical impedance spectroscopy. Each colour means different site of a 4-channel thermoelectrode. Primary and secondary ordinate represent the amplitude and phase values at various frequencies, respectively.

### *3.2. Thermal calibration*

Each thermoelectrode contains a meander-shape platinum resistance thermometer within a distance of 30 and 100 µm from the recording sites as Fig. 1 (a) and (b) show. They were calibrated with a negative temperature coefficient (NTC) thermistor ($\Delta T = \pm 0.14$ °C, Semitec 223Fµ5183-15U004, Mouser Electronics). At body temperature, the Callendar–Van Dusen equation is linear: $R_t = R_0 \cdot [1 + \alpha \cdot \Delta T]$. The two parameters are $R_0 = 333.15 \pm 14.84$ Ω and $\alpha = 1801 \pm 155$ ppm/K in our case. The resistance of the temperature sensing filament is measured by four-wire setup with 1 mA measuring current (Keithley 2000 multimeter and Keithley 6221 current source). Using higher driving current may cause considerable temperature rise in the close vicinity of the thermoelectrode in the brain tissue. This potential may be further used to control the local tissue temperature.

### *3.3. In vivo validation*

Fig. 3 presents in vivo results in urethane anesthetized mice with externally controlled temperature. Brain temperature follows body temperature between certain bounds, but is generally lower by ~2 °C. Multiunit activity shows an increase at higher body temperature. Core body temperature was measured by rectal temperature sensor. Red curves shows the smoothed multiunit activity (arbitrary units) recorded simultaneously by the thermoelectrode. According to the measurement data, our thermoelectrode is able to record local tissue temperature and unit activity simultaneously with a resolution of ca. 0.2 °C.

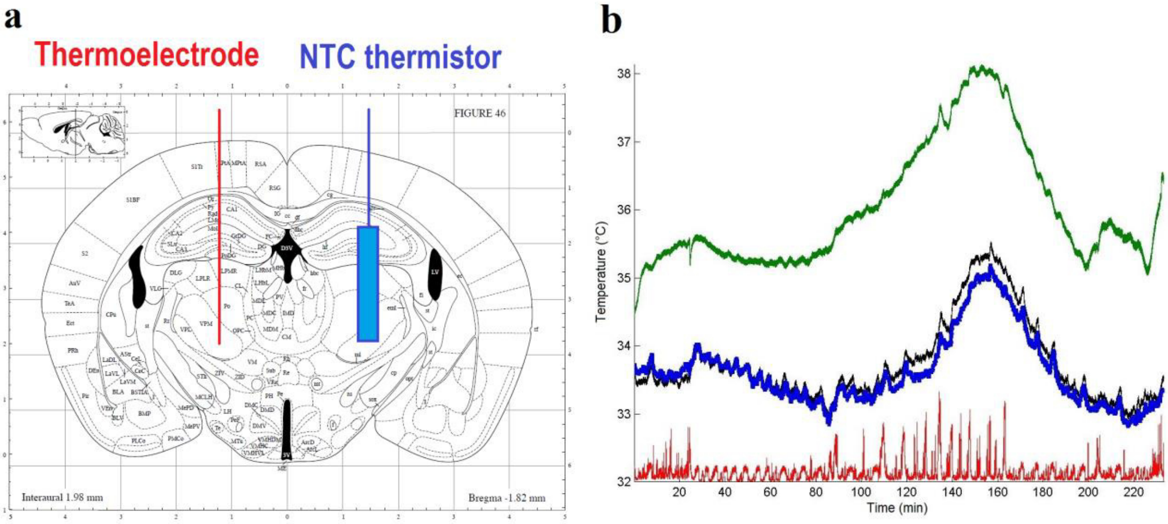

Fig. 3. (a) Schematic of the coronal section of a mouse representing the implanted thermoelectrode and NTC thermistor. The implantation depth was 3 mm; (b) In vivo validation of the thermoelectrode's simultaneous functionality in urethane anesthetized mouse with externally controlled temperature. Meaning of colors: green: core body temperature, black: brain temperature by NTC thermistor, blue: brain temperature recorded by thermoelectrode, red: multiunit activity (arbitrary unit).

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