In vitro and *in vivo* study of temperature increases in the brain due to a neural implant

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Abstract – A chronically implantable, wireless neural interface device requires integrating electronic circuitry with the interfacing microelectrodes in order to eliminate wired connections. Since the integrated circuit (IC) dissipates a certain amount of power, it will raise the temperature in surrounding tissues where it is implanted. In this paper, the thermal influence of the integrated 3-dimensional Utah Electrode Array (UEA) device implanted in the brain was investigated by experimental measurement *in vitro* as well as *in vivo*. The maximum temperature increase due to the integrated UEA system was measured to be 0.067 °C/mW for *in vitro* and 0.050 °C/mW for *in vivo* conditions. Lower temperature increases of *in vivo* measurement are due to convection through the blood perfusion presenting in the living tissues.

I. INTRODUCTION

Over the last decades, neural prosthetic devices have been used in various applications to restore and rehabilitate disabled sensory and motor functions. Still, issues of safety remain about the chronic use of these active implanted devices. One safety concern is the consequence of using such implants on the heating of implanted tissues as these devices become more intelligent with the help of integrated electronics and as the number of recording and/or stimulation channels increases. As is well known from hyperthermia therapies, temperature increases above a certain level can kill cells, change metabolism, or induce physiological abnormalities [1]-[4]. It has been reported that temperature increases greater than 1 °C can have long-term effects on the brain tissue [5]. To prevent any thermal consequences, the neural interface devices must be shown not to cause significant temperature increases in the implanted tissue.

A few studies have been reported on temperature increases in tissues due to neuroprosthetic implants. These studies mainly employed numerical methods to predict the temperature increase in implanted tissues [6]-[10]. In studies on temperature elevation of the eye due to a retinal stimulator [6]-[8], a finite-difference time-domain method (FDTD) was used to predict the thermal effects of the implant. Besides numerical investigation, they also presented measured results. But their study was limited to a measurement of the *in vivo* temperature only in the center of the dog's eyeball and did not show the spatial distribution of the temperature in the tissue near the implant. Also, the position of the measurement probe was not controlled precisely. According to their study, a 60-electrode retinal stimulator resulted in a maximum temperature rise of 0.8 °C on the surface of the chip as it dissipated a power of 12.4 mW. More recently, there has been a study reporting thermal effects of a single electrode used for deep brain stimulation (DBS) [9]. Their numerical study predicted that clinically used stimulation currents can induce temperature increases up to 1 °C near the DBS electrodes. However, there have been no studies addressing the thermal consequences induced by the use of active 3-dimensional microelectrode arrays implanted in the brain before the study by the authors [10]. In this previous study, we investigated the thermal impact of power dissipation by the 3-D Utah Electrode Array (UEA) integrated with electronic circuitry by using numerical analysis. A numerical model has been established taking into account the effects of conduction heat transfer, blood perfusion, and tissue metabolism. The present study reports the experimental measurements to validate the developed numerical model.

The UEA [11], [12] is a 3-dimensional silicon-based structure consisting of a 10×10 array of tapered silicon spikes, each with a base width of 80 µm and a length of 1.5 mm, as shown in Fig. 1(a). Currently, progress is underway to turn the conventional wired UEA into a fully implantable wireless device [13]-[16], in which all the necessary functional components such as power source and signal processing and telemetry electronics are densely integrated with the microelectrode array. The implantable electronic circuitry is embodied in a custom designed IC as shown in Fig. 1(b) [15], which amplifies detected neural signals, processes and transmits them to an extracorporeal receiver. Since the integrated UEA/IC system [14] dissipates a certain amount of power during operation, it will



Fig. 1: (a) SEM (scanning electron micrograph) of the Utah Electrode Array. (b) Photograph of the IC chip for 100-channel neural signal recording. The chip measures approximately $5 \times 6 \text{ mm}^2$ and dissipates a maximum power of 13 mW.

increase the temperature in surrounding tissues where it is implanted.

II. EXPERIMENTAL METHOD

To mimic the heat generation by the IC, a Ti/Pt micro heating element was deposited on the backside of the UEA as shown in Fig. 2, so that an amount of power can be supplied from an external power source and dissipated through the microelectrodes. The microheater element has a meander shape with a width/spacing of 70 µm and an effective area of $5 \times 6 \text{ mm}^2$, which is equivalent to the area of the IC. The thicknesses of the deposited metal films were 50 nm and 600 nm for Ti and Pt, respectively. The electrical resistance of the fabricated microheaters measured $788 \pm 3.1 \Omega$. which was comparable to the IC's load [15]. Agarose gel (1.5%) was used to simulate the brain tissue since it has a similar thermal conductivity to the brain [17]. It was contained in a petri dish with 10 cm diameter and 5 mm depth. The UEA was inserted into the agarose gel so that the heat was dissipated into the volume. An amount of power from an external source (SourceMeter 2400 from Keithley Instruments, Cleveland, OH) was supplied to the micro heating element through insulated Pt wires in a diameter of 125 µm. 3 µm of Parylene was deposited on the microheater in order to protect the deposited metal trace and electrical contacts between Pt wires and the heating element.

During measurements, the temperature of the dish containing agar gel and the UEA/heater system was maintained constant in a thermally regulated water bath (Endocal RTE-8DD from Neslab, Newington, NH). The temperature of the water bath was kept at 37 °C so that the temperature at the boundary of the volume of agar gel was also kept at 37 °C.



Fig. 2: Photograph of a UEA with a deposited Ti/Pt micro heating element on the backside to mimic the heat generation by an integrated IC.

To detect the spatial temperature distribution on the UEA and its surrounding medium, an infrared (IR) thermal camera (ThermaCAM PM390 from Inframetrics, currently FLIR Systems, Wilsonville, OR) was used. The technical specifications of the used camera are as following:

- detection range: -20 to 450 °C
- wavelength: 3.4 to 5 μm
- sensitivity: < 0.1° C
- spatial resolution: 170 μm

The IR camera was calibrated before each set of measurements. The calibration plot and equation used in this study are shown in Fig. 3. To eliminate the distortion of thermal images due to different emission properties of Pt heating element and Si substrate [18], [19], the surface of the heating element was coated with thin black paint by spraying, so that the surface emission was assumed to be close to the ideal black body. The thickness of the sprayed paint was measured to be 14.8 μ m. The *in vitro* experimental setup that was used is shown in Fig. 4. The temperature on the surface of the UEA and agar was measured after the system reached at steady state, since chronic temperature increases in the tissue was of our interest.



Fig. 3: Calibration of the IR thermal camera over the measurement range.



Fig. 4: *In vitro* experimental setup to measure the temperature increase on the UEA and surrounding medium. The dish containing agarose gel and the UEA system was contained in a 37 °C water bath.

Since the *in vitro* experiments employing agar gel cannot reflect the contribution of convection through blood perfusion, which in fact plays a significant role in thermal regulation of a living body, *in vivo* experiments were also performed. The UEA/heater system used for the *in vitro* measurement was implanted in the cerebral cortex of an anesthetized cat, as shown in Fig. 5. A small square opening in about 2×2 cm² was made in the skull, and the dura was removed. The cortex of the cat remained exposed during measurements. The temperature on the surface of the UEA and cortex was again measured in the steady state, using the IR thermal imaging camera.



Fig. 5: *In vivo* experiment using the UEA implanted in the cerebral cortex of an anesthetized cat. The cortex of the cat remained exposed during measurements.

III. RESULTS AND DISCUSSION

Examples of the thermal images of the surface of the UEA and the surrounding medium are shown in Fig. 6 for in vitro condition when the IC dissipates a power of 13 mW, the maximum power dissipation of the IC to be expected in full operation mode [15]. Fig. 7 shows the thermal images of the UEA and the surrounding brain tissue in in vivo condition according to different amounts of power dissipation through the UEA. It shows the spatial distribution of temperature over the surface, in which tissue heating next to the UEA is observable as the power dissipation through the UEA increases. Fig. 8 shows the maximum temperature rises in in vitro and in vivo conditions as a function of the amount of power dissipation by the integrated UEA system. We analyzed the temperature and temperature rise on the UEA since the temperature in the surrounding medium such as tissue or agar is no greater than the UEA temperature.



No power dissipation

13 mW power dissipation

Fig. 6: Thermal images of the surface of the UEA and surrounding medium in *in vitro* (agarose gel) condition.

Both *in vitro* and *in vivo* measurements show that the temperature increases linearly with power dissipation through the UEA, with an amount of 0.067 °C/mW for *in vitro* and 0.050 °C/mW for *in vivo* conditions. These results were well within the computationally predicted limits [20]; the minimum temperature increase when blood perfusion

was present and the maximum temperature increase when no perfusion was considered. The *in vivo* measurement showed a 22 % lower temperature increase than the *in vitro* measurement, reflecting the effect of the blood circulation in the brain removing heat away from the implanted tissue.



Fig. 7: Thermal images of the surface of the UEA and surrounding tissue in *in vivo* (cerebral cortex of a cat) condition. The red spot at the left lower corner of the opened brain represents blood accumulation.



Fig. 8: Temperature increase in the UEA obtained from *in vitro* and *in vivo* measurements as a function of power dissipation through the UEA.

IV. CONCLUSION

In this study, the thermal impact of a powered 3-D Utah Electrode Array, implanted in the brain for cortical neural signal recording, was investigated using experimental *in vitro* and *in vivo* measurements. The *in vitro* and *in vivo* experiments employed an IR thermal imaging camera for non-invasive temperature detection. The experimental results were used to validate the numerical model developed

by the authors, and the measurement and the numerical simulation were in good agreement. The integrated UEA system implanted in the brain of an anesthetized cat increased the temperature by 0.65 °C for a power dissipation of 13 mW through the UEA, which is the maximum power dissipation expected by the integrated IC for our application. This result implicates that the temperature increase due to power dissipated by a 3-D UEA implanted in the brain is in a safe range, i.e., lower than the 1 °C range that is stated as the allowable temperature increase in the literature.

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