Assessment of Subdural Insertion Force Of Single-Tine Microelectrodes in Rat Cerebral Cortex

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Abstract- **We investigated the implant mechanics of single tine silicon microelectrodes and conventional tungsten needle electrodes in rat cerebral cortex. Seven acute rat experiments were performed in which the force during a series of insertion/retraction into brain tissue (depth = 2 mm, velocity = 2 mm/s, 2 repetitions) were measured. We compared the single tine VSAMUEL microelectrode (opening angle = 4°, cross sectional area = 950 μm^2) with a group of five commonly used single tine microelectrodes (opening angle = 3°-10°, cross sectional area = 750-1962 μm^2). Initially, we observed dimpling of the brain surface before the first penetration (0.62±0.23 mN). The force maintained to increase after penetration until advancement had stopped (first penetration: 0.87±0.13 mN). A tension force was measured during the needle retraction phase (first retraction: 0.54±0.13 mN). The force was statistically significantly lower during the second insertion phase (Turkey-Kramer multiple comparison, alpha = 0.05). The insertion properties of the VSAMUEL probes were not significantly different from other commonly used microelectrodes. We showed that the microelectrodes had to survive a compression force of approximately 1 mN when inserted into rat cerebral cortex tissue and a tension force of 0.5 mN when retracted.**

Keywords— **VSAMUEL, microelectrode, insertion force, cortex, rat, in-vivo**

I. Introduction

Advancement in neural prosthetics systems go hand in hand with our ability to interface and interpret human neural systems at peripheral, spinal and supra-spinal level. Recording from individual nerve cells in the brain has been one of the main techniques to study how the brain processes information to control body functions [1]. Today, these recordings are routinely obtained using single-channel microelectrodes (e.g. metal- or glass electrodes or micro-pipettes). The future success of neuroscience research and clinical neuroprosthetic applications will depend on the availability of reliable and highly selective neural interfaces. The EU VSAMUEL consortium (www.vsamuel.de) has developed micro-fabricated silicon arrays that one day may provide such an interface [2]. The consortium is currently evaluating the electrical and mechanical properties of the electrodes [3;4;5;6], and the feasibility of using the electrodes in neuroscience research [6;5;11].

Within rehabilitation, recent studies indicate that a high number of channels may be necessary to study the temporal and spatial encoding of neural population encoding in the brain. For example, Wessberg et al. used up to 96 micro-wires implanted to estimate hand trajectory in monkeys from primary motor cortex cells in open-loop experiments, however their theoretical estimate showed that 150 to 600 cells would be necessary to obtain better results [7]. In another study, Schwartz et al. estimated 3D joint movement from up to 40 primary motor cortex cells in monkeys recorded with a micro-wire array [8]. A single VSAMUEL array may carry up to 128 channels distributed on 1-8 shafts and mounted on a flexible cable that are easy to handle [9;10].

We have previously studied the insertion mechanics of the VSAMUEL microelectrodes into peripheral nerve [3]. The objective of the present work was to investigate the insertion mechanics of a single tine VSAMUEL microelectrode into cerebral cortex tissue. We measured the tension and compression forces applied on the microelectrode by the brain tissue and compared the insertion force for the VSAMUEL microelectrode with a group of commonly used microelectrodes.

II. Methodology

A. Experimental Setup and Measurements

Approval for all experimental procedures was obtained from the Danish Committee for the Ethical Use of Animals in Research. Data were collected from 7 adult Wistar rats (M/F, approx. 400 g) in acute experiments. The rat was anaesthetized using an intramuscular injection of a Rompun cocktail (25mg/ml Ketamine, 1.25 mg/ml Xylazine HCL and 0.25 mg/ml Acepromaxine Maletate). The injections were administered approximately every hour to maintain the anaesthesia. We regulated the depth of the anaesthesia by continuously monitoring the heart rate and blood oxygen saturation. The rat's body temperature was maintained at 38ºC using a heating pad. At the end of the experiments euthanasia was induced by an overdose injection of pentobarbital.

TABLE 1. Data on the microelectrodes included in the study. * Tungsten Rod: A-M Systems, Inc. , **VSAMUEL, ACREO A/S Sweden, ***Caltech Microprobe. The Opening angle for T10 and T3 are estimated from pictures taken through a microscope.

Electrode ID	Opening Angle	Material	Coating	Provider	Shaft size	Cross Sectional Area	Shaft Shape	Number of insertions
T10	10°	Tungsten	None	Tungsten rod**	Ø = 50 µm	1962 µm^2	Round	20
T3	3°	Tungsten	None	Tungsten rod	Ø = 50 µm	1962 µm^2	Round	34
A4	4°	Silicon	Silicon Nitride	VSAMUEL**	20 x 38 µm	950 µm^2	Square	10
C12	12°	Silicon	Silicon Nitride	Caltech***	25 x 30 µm	750 µm^2	Square	34
C8	8°	Silicon	Silicon Nitride	Caltech	25 x 30 µm	750 µm^2	Square	4
C4	4°	Silicon	Silicon Nitride	Caltech	25 x 30µm	750 µm^2	Square	64

The rat's head was anchored in a stereotaxic frame using ear bars (Narishige Co., LTD, Japan). An incision was made down the midline of the cranium to expose the skull and the skin flaps were pulled back and attached to a small plastic ring to produce a watertight pool, see Figure 1B. A craniotomy was performed over the somatosensory cortex (2 to 4 mm lateral and 2 to 4 mm caudal relative to Bregma). The dura was carefully retracted. The exposed brain was continuously covered with artificial cerebral spinal fluid (130 mM NaCl, 26 mM $NaHCO_3$, 1.2 mM Na H_2PO_4, 5 mM KCL, 1.5 mM $CaCl_2$ and 2.2 mM $MgSO_4$) to prevent the surface from drying out.

The cerebral cortex area was chosen as implant site, since this is the area we aim to record from in the future. An insertion depth of 2 mm was chosen, since the main target of sensory information arriving from the thalamus is in layer 4 located at a depth of approximately 2-4 mm.

B. The Microelectrodes

Six single-tine microelectrodes were included in this study. Specific data on the individual microelectrodes are given in Table 1. We chose a group of commonly used microelectrodes of similar size of the VSAMUEL probes, i.e. 1) Electrosharpened tungsten rods and 2) Caltech microfabricated electrodes.

C. Data Analysis

Simultaneous recordings of the force and the distance traveled were made during insertion and retraction of the electrodes. The experimental setup is depicted in Figure 1. The microelectrode was attached to a load cell (Sensotec Inc., model 31/1435-02, resolution of 1.31 mV/g) using a self-locking system. The electrode was placed as close to the brain surface as possible under visual guidance and using a manually operated 3-axis micromanipulator (Fine Science Tools, MM-33). The microelectrodes were advanced according to a ramp and hold profile (velocity = 2 mm/s, excursion = 2 mm). The movement was controlled by a computer controlled micromanipulator (Narishige MMO-220 Unidimensional Oil Hydraulic Micromanipulator). The ramp-and-hold movements were repeated twice at the same position, before the electrode was moved to a new insertion point. We carefully avoided to penetrate the tissue more than twice at the same point.

The force and length signals were sampled at 2.5 kHz and stored for offline analysis. Data were then low pass filtered at 25Hz.

We selected four points for comparison during the ramp-and-hold movement, i.e. 1) the point of penetration, 2) the maximum force experienced by the needle during the insertion phase, 3) the minimum force experienced by the needle when it was fully advanced into the brain (also referred to as the *rest* force), and 4) the maximum force experienced by the needle during the retraction phase (also referred to as the *drag* force). We selected all data points manually by comparing the force and the stress/strain curve (see example in Figure 2). Statistical evaluation of the force at the selected points was performed (3-factor ANOVA analysis and Turkey-Kramer multiple comparison, alpha = 0.05).

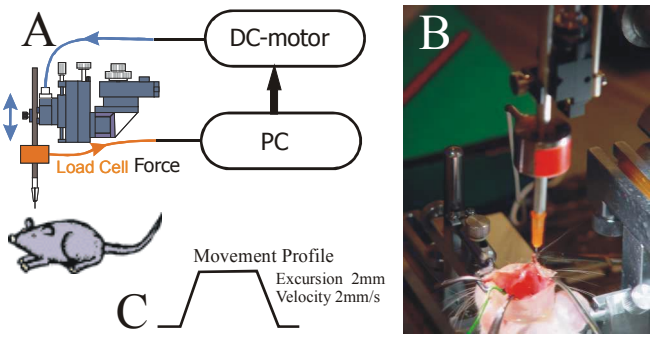

Fig. 1. Experimental setup. A) Schematic drawing of the setup including the rat, a motor-controlled micromanipulator and a PC, B) A picture of the experimental setup, and C) the movement profile used to advance and retract the microelectrodes into the cerebral cortex tissue.

III. RESULTS

The top panel in Figure 2 depicts an example of the measured force and distance traveled during a series of two consecutive insertions and retractions of a single tine VSAMUEL microelectrode into rat cerebral cortex tissue. The bottom panel of Figure 2 shows the corresponding stress/strain curve. The four data points selected for comparison are depicted in both panels.

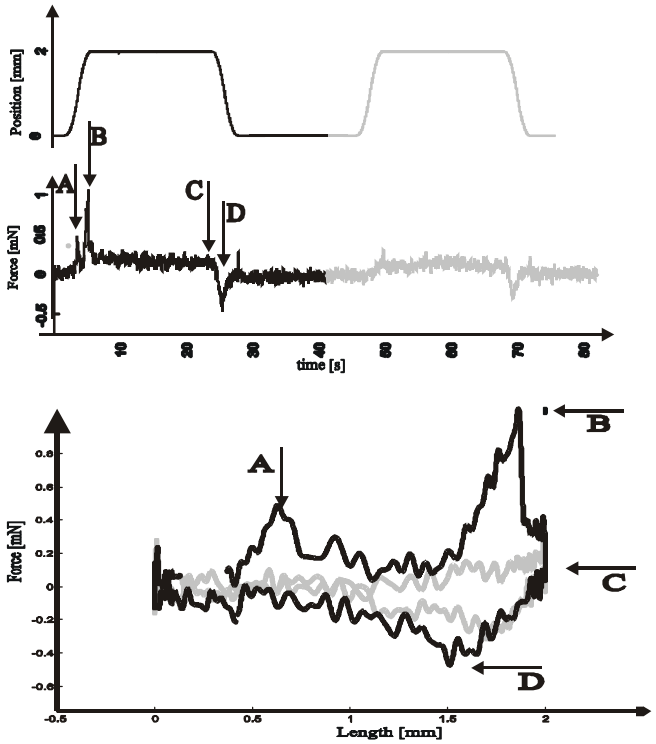

Fig. 2. Top panel depicts the force and length measured during insertion of a single tine VSAMUEL microelectrode (black trace= first insertion, grey trace = second insertion). The bottom panel shows the corresponding stress/strain curves. A: Force at the point of penetration, B: Maximal compression force measured at any point during insertion, C: Minimal compression force measured while the needle was fully advanced (2 mm), D: Maximal tension force measured during the retraction phase.

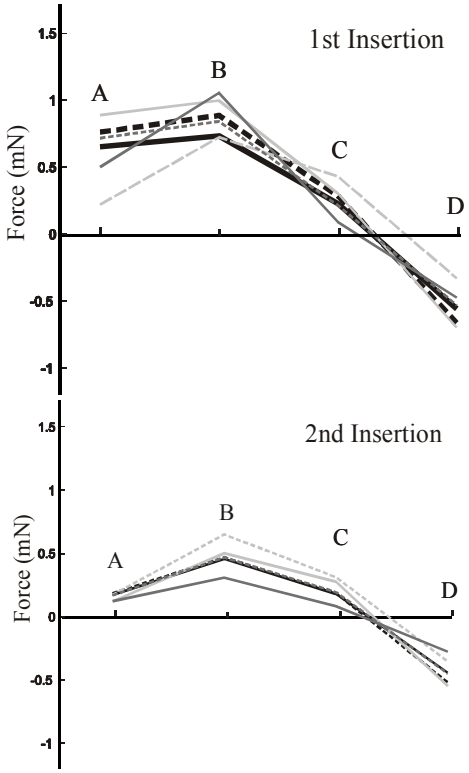

Fig. 3. Mean force at the two consecutive insertions with all six microelectrodes, A: Force at the point of penetration, B: Maximal compression force measured at any point during insertion, C: Minimal compression force measured while a microelectrode was fully advanced (2mm), D: Maximal tension force measured during the retraction phase. The individual microelctrodes are represented by: T3 (black) T10 (dashed black), A4 (dark grey), C4 (light grey), C8 (dashed light grey) and C12 (dashed dark grey).

Compression is defined as positive and tension defined as negative in Figure 2.

Until the first point of penetration (see mark A in Figure 2), there was a clear increase of the force, and we observed a clear dimpling of the brain surface. The point of penetration was dependent on the individual microelectrodes, however the variation among was not statistically significant. The mean force was 0.62±0.23 mN and 0.15±0.03 mN at the first and second penetration, respectively.

Once the microelectrode penetrated the pia layer the force decreased abruptly, and the force then maintained to increase until the advancement of the microelectrode stopped (mark B in Figure 2). The maximal compression force measured during the first insertion was 0.87±0.14 mN and 0.47±0.11 mN during the second insertion.

When the movement stopped, the force declined until a constant compression force level. We never observed that the force declined to zero when the needle was fully advanced in these studies even in selected trials, where we maintained the microelectrodes inserted for a period of 30 s (not included in the dataset of in the present study).

During the retraction phase a tension force (mark D in Figure 2) was observed in all cases.

The drag force was 0.54±0.13 mN and 0.44± 0.10 mN in the two insertion phases, respectively. The occurrence of a tension force during retraction was used as an indication of that the needle actually had penetrated. In comparison we attempted in several trials to insert electrodes with the dura maintained intact, where no penetration was possible, and in these cases no tension force was observed.

Figure 3 compares the mean forces at penetration, the maximum force, the rest force and the drag force for all six microelectrodes. The top panel in Figure 3 depicts data from the first insertion and the bottom panel depicts data from the second insertion. The variation among the data was largest at the point of the first penetration (see top panel in Figure 3), which could be explained by the difference in the texture of the underlying tissue (e.g. penetrating blood vessels). We observed no clear connection between the mean force and the differences in opening angle, shape or cross sectional area of the microelectrodes, i.e. there were no statistical significant difference among the data. However, a statistical significant difference was found between the mean force of the first and second insertion

IV. Discussion and conclusions

The penetration forces observed in this study are comparable with the measured penetration force of a tungsten needle in rat cerebral cortex by Hofmann et al. [12]. However, the force measurement device used in this study allowed us to measure both compression and tension applied to a microelectrode during insertion and retraction, which thereby provide us with new and unique information.

We observed a constant compression force when the microelectrodes were fully advanced into the brain. This indicates that chronically implanted electrodes experience a constant compression force while inserted in the brain, that may slowly pushed the electrode out of the brain with time.

We observed a tension force when the microelectrodes were retracted from the brain tissue, which indicates that brain tissue stick to the electrode within a short time period (<2s). Brain electrodes that are re-used in acute experiments must therefore not only be strong enough to survive a maximal force that exceeds the penetration force (approximately 1mN in these experiments), but it must also be able to withstand tension force during retraction (approximately 0.5mN in these experiments).

Future work will include modeling of the insertion mechanics of electrodes in brain and peripheral nervous tissue, with the aim to design more efficient electrodes and implant techniques.

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