FLEXIBLE MICROELECTRODE ARRAYS WITH INTEGRATED INSERTION DEVICES

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ABSTRACT

Flexible microelectrode arrays (FMAs) allow interfacing to delicate living tissues such as neural tissue with a minimum of physical disruption of that tissue during and after insertion. This physical disruption is minimized since the compliant FMAs can deform along with the tissue. However, a problem with these arrays is the insertion and subsequent precise positioning of the arrays in the tissue. Previous FMAs required hand assembly of the flexible array with another rigid structure. This may not be feasible if the dimensions of the flexible array are too small. In this work, FMAs with integrated rigid insertion devices were designed, fabricated, and assessed. Thin-film technology and electrodeposition were used to create flexible arrays with attached rigid insertion devices in a single sequence of fabrication steps. These arrays can be designed in two different configurations. The first type allows for flexible electrodes to be sewn through a nerve. The second allows for insertion into a surface such as the cerebral cortex or the spinal cord. After insertion, the rigid portion of the FMA is removed from the tissue with the flexible portion remaining behind. These two implantation schemes were tested on tissue models and found to be straightforward and reliable. In addition, comparisons of the potential to cause tissue damage between flexible and rigid arrays of similar dimensions were made under three different conditions of mechanical perturbation. In all cases, FMAs caused no damage to the tissue model above that caused by the original electrode insertion track while rigid arrays caused significant tearing. Finally, FMAs were shown to successfully stimulate neural tissue in an experimental setting.

INTRODUCTION

Micromachining has been used to create a variety of rigid microelectrode arrays that can record from or stimulate neural tissue [1-3]. FMAs have also been developed for the same purpose [4-10]. One shortcoming of flexible arrays is that they must rely on a rigid device to provide enough mechanical support in order to introduce them into tissue. For example, Mastrototaro et al. inserted their flexible array into a living heart by placing it in between two rigid pieces of metal using hand assembly [4]. As electrode dimensions decrease, however, this approach would be increasingly difficult to realize. One solution to this problem would be to incorporate photolithographically-defined electrodeposited rigid insertion devices that are attached to flexible electrodes during an integrated sequence of fabrication steps [6]. This would eliminate the need for hand assembly, allow for minimization of the rigid insertion device dimension, and allow the entire device to be batch fabricated. Furthermore, the use of photolithography allows for precise control over the region of attachment of the flexible and rigid structures. The rigid structures would serve to guide the flexible electrodes into the tissue. After a desired location is found, the rigid structures would be removed and the flexible electrodes would be left in the tissue. In this paper, thin-film technology and electrodeposition were used to create two types of FMAs with integrated rigid insertion devices in a single sequence of fabrication steps. The first type allows for flexible electrodes to be sewn through a nerve. The second allows for insertion into a surface such as the cerebral cortex or the spinal cord. The insertion protocols of each type of device were tested in tissue models, tissue damage comparisons with rigid arrays were made using a tissue model, and the array was used in-vivo in an experimental setting.

DESIGN AND FABRICATION

Compared to standard microelectrodes, flexible electrodes have a much smaller cross-sectional area. For example, a flexible electrode that is 3 μm thick and 10 μm wide has a cross-sectional area of 30 μm^2. A standard microelectrode made of wire with a diameter of 50 μm would have a cross-sectional area of approximately 2000 μm^2. Flexible electrodes would displace a very small volume of tissue and cause much less compression of the surrounding tissue than a standard microelectrode.

Rigid microelectrodes have a higher chance of causing mechanical damage to surrounding neural tissue than flexible electrodes. This is due to large differences in compliance between the two structures. Compliance is a property of object material as well as object geometry. The first property of interest is the mechanical stiffness of the materials used. The elastic modulus of brain tissue is many orders of magnitude lower than solid metals so it is obvious that small diameter (100μm) rigid metallic needles inserted into tissue will have a great potential to cause damage if they are displaced in directions that are perpendicular to the needle's long axis. It is therefore likely that using materials of lower mechanical stiffness, such as polymers, could minimize the risk of this type of injury. The elastic moduli of polymeric materials such as polyimide are roughly two orders of magnitude smaller than that of metals but still six orders of maginitude higher than that of brain tissue. Flexible electrodes, however, can have much smaller cross-sectional areas than metal electrodes. Even though both metals and polyimide have high moduli compared to brain tissue, in their final forms flexible electrodes offer much less elastic force under similar conditions of displacement.

As described above, two types of FMAs have been designed and fabricated. In the first type, each element of the FMA is integrated with a rigid needle, which can be grasped by a surgeon and sewn through neural tissue. After positioning of the FMA in the tissue, the rigid needle can be detached from the FMA, leaving behind only the flexible portion of the FMA embedded in the tissue. In the second type of FMA, each of the rigid tips is

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connected together, to allow insertion of the entire array beneath the surface in one step, followed by removal of the rigid portion of the array.

To further clarify these FMAs and their operation, figures 1 and 2 show the insertion and detachment processes in detail. Figure 1 depicts the basic steps of the implantation scheme for a single sew-through-type electrode. In step 1, the insertion needle has penetrated into the tissue. In step 2, the insertion needle protrudes from the opposite side of the tissue. The tip can now be grasped to pull the flexible electrode into the tissue. In step 3, the flexible electrode has been pulled through until the active site is placed at the desired location. In step 4, the insertion needle is removed from the flexible electrode. Subsequent electrodes of the array are implanted sequentially in the same manner. Figure 2 depicts the insertion procedure for implanting a single flexible electrode into a tissue surface. In step 1, the tip of the insertion needle is placed at the surface of the tissue with the attached flexible electrode lying on the surface. In step 2, the insertion needle is driven into the tissue and pulls the flexible electrode with it to a desired location. In step 3, the flexible electrode is fixed at the surface of the tissue while the insertion needle is driven downward by a distance equal to the region of attachment between the insertion needle and flexible electrode. This action causes the flexible electrode to lose adhesion and peel away from the insertion needle. In step 4, the insertion needle is removed leaving the flexible electrode in place.

Figure 3 shows a side view of the basic sequence of fabrication steps for FMAs that can be sewn through a nerve. (1) 10 μm x 10 mm long photolithographically-defined gold conducting lines (black) are encapsulated within two layers of polyimide cured at 300^{O} C for 1 hr. (2) A 20 μm x 11 mm titanium mask is patterned onto this surface. This mask will be used to define the flexible electrode's outline, bonding pad and recording/stimulation sites. Seed layers for electrodeposition (top layer in this step) are deposited onto the titanium mask. (3) Thick photoresist is patterned to create a mold into which the rigid insertion device (dark gray on topmost layer) is electroplated. (4) The mold is removed and seed layers are wet etched. (5) RIE is used to expose bonding pads, electrode sites and the flexible electrode's outline. (6) The substrate is immersed in 95^{O} C deionized water which causes lift-off of the FMAs. (7) Top view of the finished device.

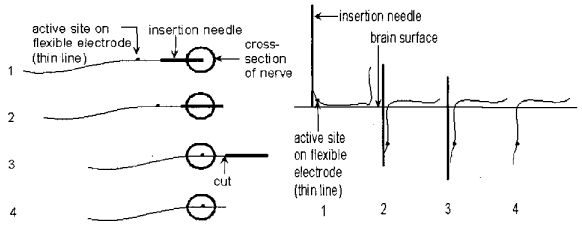

Figure 1: Insertion procedure

Figure 2: Insertion procedure

EXPERIMENTAL DETAILS AND RESULTS

Insertion Tests The two types of flexible arrays were tested on gelatin tissue models to see if the proposed implantation system could effectively and reproducibly implant flexible electrodes to a desired location. Figure 4 shows the results of an insertion test using a sew-through-type flexible electrode array. It is seen that all of the flexible electrodes of the array have been implanted to their desired locations. The insertion needles have been removed by cutting with fine point scissors. Figure 5 shows the results of an insertion test using an insertion type electrode array. This picture shows the four individual flexible electrodes descending into the gelatin surface after the insertion device was withdrawn.

Comparisons of the potential to cause tissue damage were made between FMAs and rigid arrays of similar design and dimension. The only difference in dimension between the two was the thickness. The FMA was 5μm thick and the rigid array was 30μm thick. All the tests used gelatin to simulate neural tissue. This is because gelatin is a soft material with an elastic modulus (15 kPa) that is on the same order of magnitude as brain tissue (46 kPa) [11]. Three types of tests were performed: a bending test, a mechanical shock (acceleration) test, and a lateral deflection test. In all cases, the resultant damage done to the gelatin by the FMAs and the conventional rigid microelectrode arrays was assessed and compared.

Bending Gelatin was cut into 6mm x 6mm x 2cm slabs. Rigid or pull-in type FMAs were inserted according to their respective previously described protocols. After implantation, pressure was applied on either end of the slab along its long axis. This pressure caused the slab to bend with a certain curvature. The gelatin was then allowed to relax to its original unstrained position. The penetration sites were photographed using a stereomicroscope. Rigid electrode arrays invariably damaged the gelatin material in these tests. Rigid arrays caused tearing of the gelatin close to the surface (figure 6). If adequate slack was allowed for between the gelatin surface and the beginning of the flexible electrode's base FMAs caused no damage to the gelatin with displacements up to 3 mm and never changed their positions in the gelatin (figure 5).

Mechanical Shock Shock tests were performed to compare the potential for tissue damage when an impulsive load is delivered to a tissue-electrode system. In this test, rigid or flexible electrode

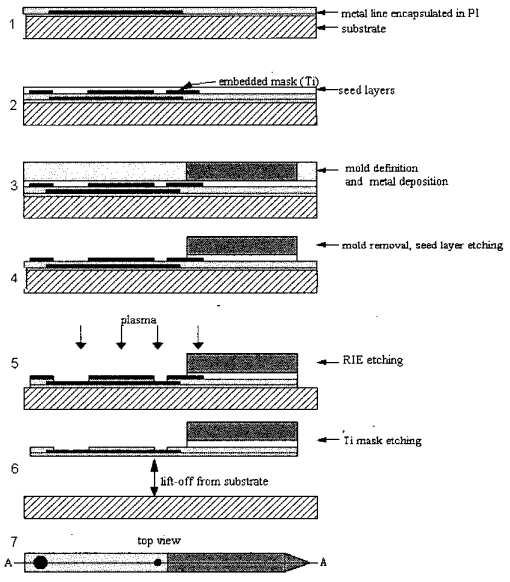

Figure 3: Fabrication sequence: The sequence for the two types of FMA differ only in the pattern of the mask which defines the rigid insertion device.

arrays were inserted so that the long axes of the electrodes were normal to the surface of the gelatin. After insertion, the electrode/petri dish system was then affixed to a flat object that was dropped from various heights. In order to determine the ranges of accelerations experienced by the test system, an accelerometer (Analog Devices ADXL150) was placed onto a flat object and dropped from a height of 10 cm. The accelerometer's output showed that its maximum value of 5 V was reached within 7 ms, which corresponded to an acceleration of 25 g. Shock tests with rigid electrodes invariably caused tissue damage in addition to that of the original electrode track. Surface tears and disruptions below the surface were always observed. Shock tests were performed with the same methods as above using flexible arrays in order to compare them with rigid arrays. Flexible arrays never exhibited any additional damage above that caused by the original implantation track.

Lateral Deflection It is known that the brain can shift its position within the cranium. In a chronic cortical electrode implantation, wires are used to connect the microelectrode to an electrical connector affixed to the skull. The stiffness of these wires can transmit forces as the brain shifts its position with respect to the cranium. It is proposed that under conditions where the brain shifts along a line parallel to the skull flexible electrodes would cause less damage to tissue than rigid probes that were attached to the skull. In order to test the hypothesis a test was designed which compared the tissue damage potential of rigid and flexible arrays that were displaced in a direction perpendicular to the axis of penetration. In this test a thin (2 cm x 3 cm x 2 mm high) slab of gelatin was placed onto a fixed platform on a horizontal surface. The rigid array was affixed to a moveable platform on the same horizontal surface in a manner that allowed it to be moved to stable positions in the horizontal plane. The moveable platform was then slowly until the tips of the electrodes had penetrated 2 mm within the gelatin surface. Displacements perpendicular to the axis of penetration then performed and any damage to the gelatin was noted and recorded. A deflection of 0.5mm caused the rigid arrays to impart sufficient force to cause fracture of the gelatin matrix (figure 7) while a corresponding deflection using the flexible arrays caused no damage (figure 8).

In-Vivo Demonstration The FMAs were tested in-vivo in an experimental setting. In this experiment a decerebrate cat preparation was used and the left hindlimb was rigidly fixed. The distal tendon of gastrocnemius muscle was dissected and attached to a force transducer and the nerve was stimulated with a Grass stimulator. A sew-through type FMA was implanted and used to stimulate a nerve which subsequently caused activation of the muscle (figure 9).

CONCLUSION

FMAs were successfully fabricated with integrated rigid insertion devices. Two insertion schemes were tested and found to be straightforward and reliable. In addition, it was found that FMAs have much less potential to cause tissue damage than rigid arrays of similar dimension. Because FMAs are more compliant than rigid arrays they are able to bend with a delicate material without causing damage. This was demonstrated in the bending and lateral displacement tests. Furthermore, their low mass prevents damage to fragile materials that undergo an impulsive mechanical perturbation. The FMAs were also able to elicit muscle activation via stimulation of nervous tissue.

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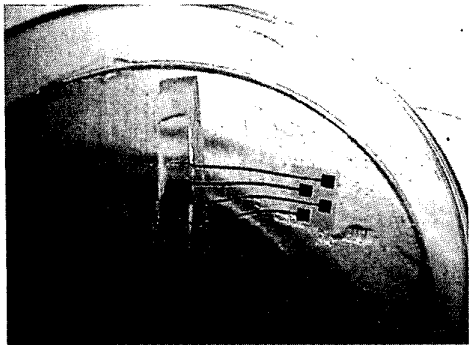

Figure 4: *Insertion test of sew-through-type flexible electrode array with electrodes in their final locations and insertion needles removed. Bonding pads on right are 1x1 mm.*

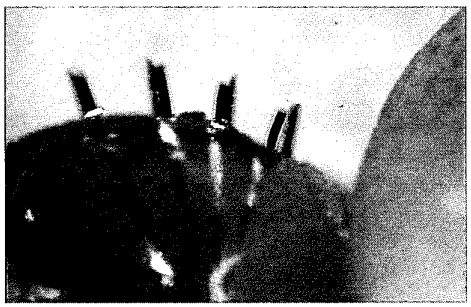

Figure 5: *Demonstration of successfully inserted FMAs. Flexible electrodes inserted into gelatin are able to bend during the deformation. No damage to the gelatin was observed.*

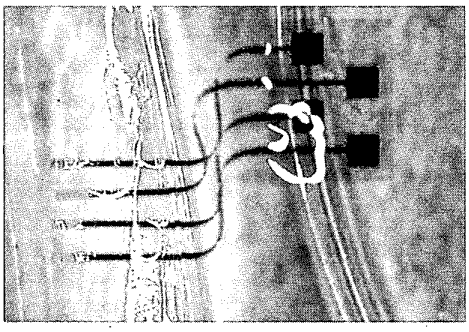

Figure 8: *Lateral displacement of 3 mm using FMA. Electrodes are spaced 1 mm apart.* ***No damage to the gelatin was observed.***

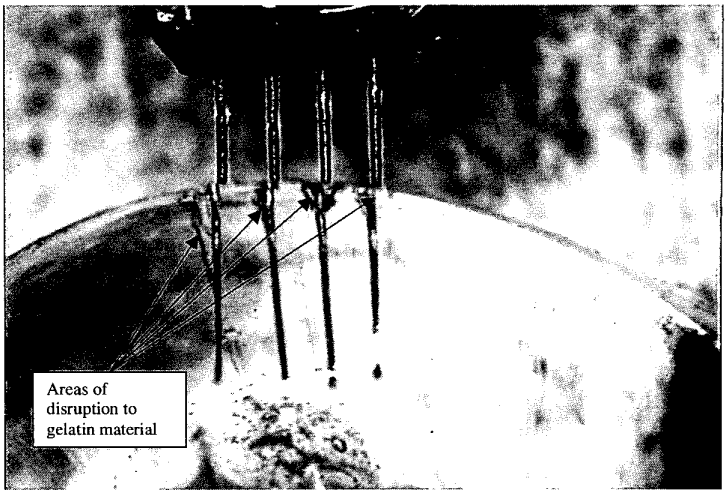

Figure 6: *Damage to gelatinby rigid arrays after bending. Rigid electrodes are spaced 1 mm apart.*

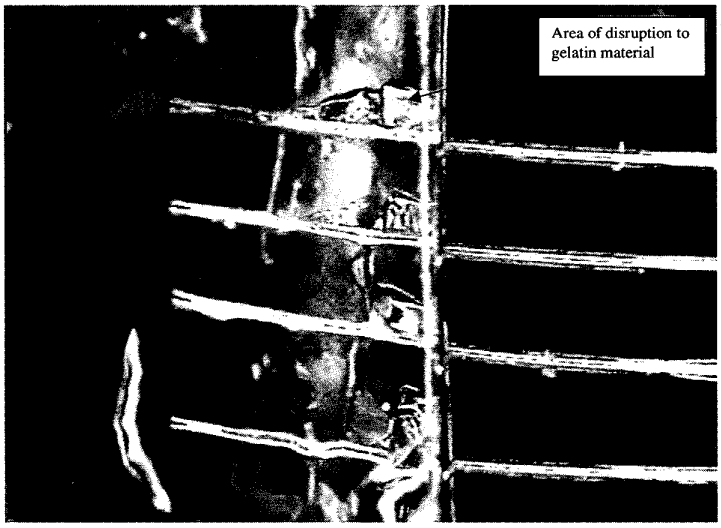

Figure 7: *Disruption to gelatin material after 0.5 mm lateral displacement using rigid arrays. Electrodes are spaced 1 mm apart.*

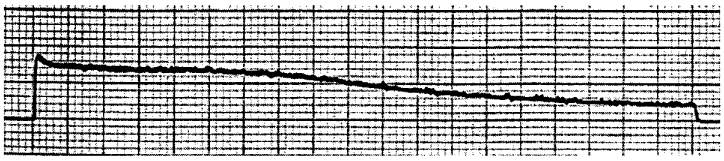

Figure 9: *Force output of cat gastrocnemious muscle during stimulation using a sew-through type FMA. Vertical scale: each major division is approximately 10 N. Horizontal scale: each major division is 5 s.*