Development of Three Dimensional Neural Sensing Device by Stacking Method

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***Abstract*—This study reports a stacking method for assembling a 3-D microprobe array. To date, various 3D array structures have been reported with complex assembly steps, vertical interconnection for 3-D signal transmission which may suffer from low structure strength and large implantable opening. By applying the proposed stacking method, the previous problems were no longer existed. Also, ASIC chips could be substituted for the spacers in the stacked arrays achieving system integration, design flexibility and volume usage efficiency. To avoid overflow of the adhesive fluid during assembly, an anti-overflow design which made use of capillary action force was applied in the stacking method as well. Presented stacking procedure consumes only 35 minutes in average for a 4 × 4 3D microprobe array without requiring specially made assembly tools. The advantages of the proposed stacking method for 3D array assembly include simplified assembly process, high structure strength, smaller opening area and integration ability with active circuits. This stacking assembly technique allows an alternative method to create 3-D structures from planar components.**

I. INTRODUCTION

In recent years, advance micromachined/assembled micro probe arrays with electrical stimulation/recording ability have come to play an essential role in exploring central neural systems. Simultaneous observation of a larger number of cell activities has become the general requirement to understand the nervous system [1]. Advances in neuroscience and neuroprosthetics now require microelectrode arrays that are able to access numerous neurons simultaneously with high spatial resolution [2]. Recording of the extracellular action potentials has been accomplished by surgically implanting neural probes into the target neurons of interest, which resulted from neural activities [3]. Probes that could insert a large number of recording sites into neural tissues with minimal tissue damage are therefore needed.

To access the full cell activity that originates in the target tissue, three dimensional microprobe arrays are strongly required with precisely controlled dimensions and front-end circuitry compatibility. In other words, to achieve detailed studies of neural networks and implementation of neural prostheses, we need to access three-dimensional volumes of tissue with three-dimensional distributed recording sites. In modern neural system researches, 3D microprobe array allows the recording and mapping of the neural signal network and interconnections among the 3D brain structure. The recording and mapping would be impossible to achieve by using 2-D planar arrays [4].

Currents methods of fabricating three-dimensional microprobe array structures include (1) Silicon bulk etched microprobe array (2) polymer-constructed array (3) Creating 3-D arrays by the assembling of 2-D parts. For the silicon bulk etched out-of-plane microprobe arrays, every probe shaft in the array only functions as a single recording site [5]. The total number of the recording sites was limited when high recording density and number are strongly required as in recent research. Moreover, when the silicon bulk etched array was integrated with active circuitries or interconnection boards [6], the minimal opening for implantation increased. Polymer-constructed arrays utilized various polymer materials to support the 3-D structure [7], but they suffered from process incompatibility with CMOS circuitry. Creating 3-D arrays by the assembly of 2-D parts is now the most popular method to construct a 3-D structure [2] [8-12]. The 2-D parts usually include 2-D arrays, vertical spacers and supporting platform. The supporting platform acts as a substrate, and the vertical spacers are erected on the supporting platform by tethers, joints and snap fasteners. The spacers fixed the 2-D arrays vertically on the supporting platform, and made the probe shafts pass through the holes of the supporting platform. However, the studies mentioned above neglect the importance of smaller opening for surgery implantation. Smaller opening of skull can reduce the implantation damage to the subject, prevent the rise of brain pressure, and decrease the infection probability of the wound.

Although previous work [2] [8-12] creating 3-D arrays by assembly of 2-D arrays successfully achieves high electrode density by packaging active probes onto the supporting platform with some micromechanical packaging technique, some problems still exist. Previous approaches that use 2-D silicon probes to form full 3-D arrays required complex schemes for assembling submillimeter parts including perpendicular connectors and interconnections between

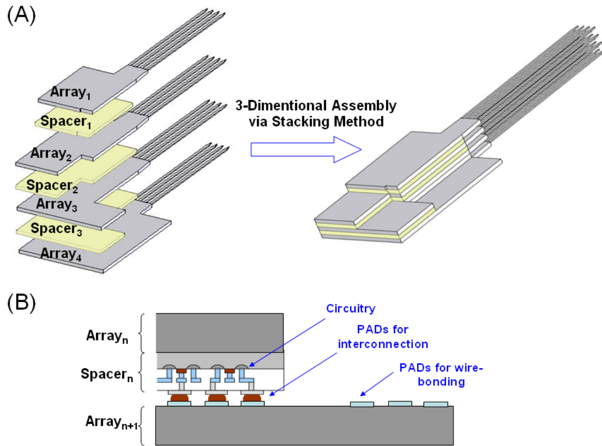

Fig. 1. (A) The schematic of stacking a 4 × 4 3D microprobe array. (B) Spacers are replaced by chips with signal processing circuitry

orthogonal planes for signal transmission. These arrays were fixed only by the perpendicular bonding pads and the tenons. Low structure strength can cause stability problem in implantation. Finally, the rooms between the spacers and the 2-D probes were wasted and the total volume of structure increases rapidly as the number of probes increased.

To improve the problems described above, this work reports a new stacking method for fabricating 3-D neural probe arrays. In this study, the 3-D orthogonal interconnection was replaced with 2-D wire bonding by the present stacking method, and the perpendicular bonding and snap fasteners which were used in previous work were no longer needed. This new stacking method can also provide reliable structure strength and probability toward system integration and volume usage efficiency as well.

II. Design and Method

The stacking method for three-dimensional neural probe arrays creates 3-D probe arrays by assembling 2-D arrays and spacers layer by layer, as shown in Fig. 1(A). For a 4 × 4 3-D array, four 2-D arrays (gray color) with four probes in each array and three spacers (yellow color) were required. The shapes of each 2-D arrays were carefully designed so they can be wire-bonded individually with different height levels. Spacers with an anti-overflow mechanism were also proposed in this paper. The present anti-overflow mechanism can also be realized on 2-D arrays if active circuit chips are used as spacers and therefore achieve integration. Each planar 2-D array, electrode sites, interconnect routing and bonding pads were located in the same plane. The bonding pads were arranged on the different sides of four 2-D probe arrays for wire bonding. Therefore, each 2-D array can be wire-bonded individually and the 3-D perpendicular bonding pads used in previous work are no longer needed.

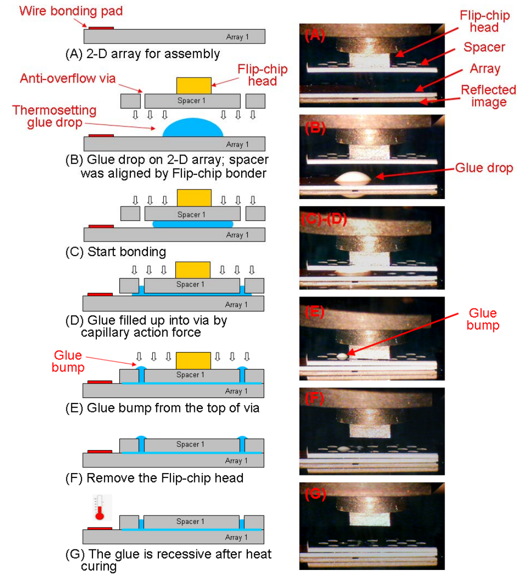

Fig. 2. The proposed assembly anti-flow mechanism process and related practical photographs.

III. Fabrication and Assembly with Anti-Overflow Mechanism

A. Fabrication of 2D parts

The fabrication steps of the 2-D array are briefly described as follows: (1) 250 µm-thick silicon with 3 µm-thick polyimide for isolation. (2) 1 µm-thick Cr/Au for wire interconnects. (3) 3 µm-thick layer polyimide for encapsulation. (4) Define electrode sites and bonding pads. (5) 3 µm-thick Au for electrode and bonding pad material. (6) The final shape was defined and released by DRIE.

B. 3D Probe Array Assembly

After the assembly parts were successfully fabricated, a flip-chip bonder and thermosetting polymer were used to complete the 3-D neural probe array assembly process. Convenient flip-chip technology was employed to accomplish alignment, pressurization and heating process, while the thermosetting polymer (glue) provided adhesive layer between two stacked components (array and spacer). The thermosetting glue was solidified at 185 °C in 180 s with an adhesive strength of 150–180 kg/cm^3.

The maximal placement accuracy of the flip-chip was 0.5 µm in a single bonding step. Thus, the total miss-alignment error can be neglected. Moreover, the average assembly time for a 4 × 4 3D microprobe array by manual alignment was approximately 35 minutes (including heat curing time). In the present study, we applied about 0.26 µL of gel between spacers and arrays. The appropriate amount of the adhesion get combined the stacking well without spilling to the proximate pads.

Fig. 2(A)–(G) illustrate how the anti-overflow mechanism functions in the practical assembly process. The details are displayed as follows: (A) the fabricated 2-D array (Array$_n$) was fixed on the flip-chip holder (not shown). (B) A drop of

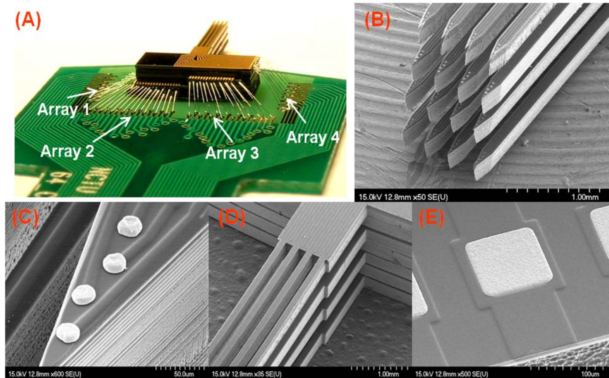

Fig. 3. The photographs of successfully assembled 3-D microprobe array. (A) The wire-bonded result of 3-D microprobe array. Four different bonding levels were marked. (B) Close view of 4 × 4 shafts. (C) The electrodes sites located at the shaft tip. (D) The cantilever shaft structure. (E) Pad for wire bonding.

thermosetting polymer was deposited onto the 2-D probe array and the spacer ($Spacer_n$) was picked by the flip-chip bonder head and aligned. (C) Start bonding – the aligned spacer was moved downward and controlled by the flip-chip bonder head. After the spacer came into contact with the glue drop, the drop spread in random directions because it was squeezed by the spacer. (D) The spacer was moved continuously downward, and the glue filled the via by capillary force when it flowed past the via. (E) The spacer came into contact with the 2-D array. The gel bump occurred on the top of the via because the pressure from bonding. (F) The flip-chip bonding head was removed. (G) The assembly process was completed following thermal solidification of the thermosetting glue. The gel bump over the via rapidly receded after heat curing.

After applying the steps described in Fig. 2, we successfully assembled 3-D microprobe arrays, as shown in Fig. 3. Fig. 3(A) displays stacked 3-D microprobe array was mounted and wire-boned onto a pre-designed PCB (~600 µm in thickness). Fig. 3(B) shows a close view of 4 × 4 shafts. Fig. 3(C) presents the electrodes sites at the shaft tip. Fig. 3(D) illustrates the cantilever shaft structure. Fig. 3(E) shows the pad for wire bonding (without wire-bonding). The electrode sites on the probe shafts were over-electroformed to ensure that the electrode can come into contact with neural tissue during implantation. Fig. 3(A) also shows that the 3-D signal transmission was achieved by 2-D wire-bonding with four level of bonding pads ($Array_1$, $Array_2$, $Array_3$ and $Array_4$) in a 4 × 4 3D array.

IV. Characterization and Neural Recording of 3D Probe Array

A. Impedance Test

Electrode impedance spectroscopy (EIS) was used to evaluate the fabricated stacked 3-D probe arrays. The impedance characterization of 3-D neural probe array in the electrode-electrolyte interface is of utmost importance in impedance-based biosensing and neuroprotheses. When the electrode sites come into contact with tissue, an electrode-tissue interface impedance was established. The electrode-tissue interface impedance and the amplifier input impedance act as a voltage divider when a neural signal passes through the electrode into the front-end amplifier. Hence, high electrode-tissue interface impedance will cause signal attenuation and induce considerable thermal noise in weak raw signal recording.

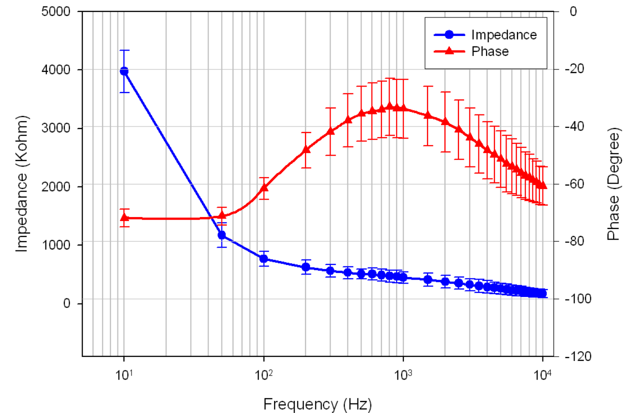

Fig. 4. The electrode impedance spectroscopy of fabricated microprobe array in physiologic saline solution. Means and standard deviations are given

The final assembled array was characterized in physiologic saline solution at room temperature using a multi-frequency LCR meter. Fig. 4 presents the measured impedance of the electrodes (n =16) on the microprobe. The in-vitro impedance was 463 ± 107 kΩ and the phase was -33 degree at 1 kHz.

B. Neural Recording

To demonstrate the practical function, the fabricated 3-D neural probe array was implanted into an anesthetized rat. Fig. 5(A) shows the photograph of a stacked 3-D microprobe array that was inserted into the brain of an anesthetized rat by a manual 3-axis moving stage (not shown in the Fig.). The screw on the skull was adopted as a reference for measurement. The opening in the skull was about 2 mm by 3 mm. Fig. 5(B) shows the photomicrograph of the implantation section. The Fig. was modified by superimposing a lesion marker, an implantation track, and overlaying a scaled image of the microprobe array. One lesion marker arrowhead (red) was used to identify the location of the outermost recording site, in relation to the field CA1 of the hippocampus. Fig. 5(C) presents neural signals from the 16-channel microprobe array, acquired with a Multi-Channel Acquisition Processor. During recordings, electrical signals were passed from the headstage to an amplifier through a band-passed filtered and sampled at 40 kHz per channel.

V. Discussion and Conclusion

The minimal opening is the area that must be resected, including skull and dura, to fully place an implantable device onto the brain. A smaller skull opening can reduce the implantation damage such as the rise of intracranial pressure, and the probability of wound infection. In previous work, the opening area was never less than the supporting platform [9] [10] to make sure all the probes were completely inserted into tissue. Therefore, the minimal surgical opening area was defined by the supporting platform in this case. Additionally, the supporting platform area was significantly increased when

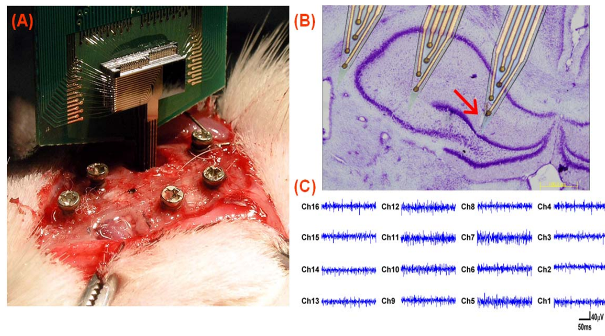

Fig. 5. (A) Photograph of a stacked 3-D microprobe array inserted into the brain of an anesthetized rat. (B) The in situ location of microprobe array was shown in the photomicrograph Nissl-stained coronal section. (C) The 16-channel neural activities simultaneously recorded from CA1 in of hippocampus.

ASIC chips were mounted onto the platform for system integration [2]. In the proposed stacking method, the system integration will not increase the opening area because it can be accomplished by replacing spacers with ASIC chips. The opening area of present 3-D probe array depends only on the probe array dimension. The minimum opening area of the stacked 3-D probe array is less than 1.75 mm × 1 mm, which can be readily shrunk by using thinner and narrow shafts.

Previous work may also induce additional tissue damage in the bottom of the platform as well. The interlocking structures, including tethers and joints, can cause the protrusion and damage to the tissue underneath [2]. For the stacked 3-D array, only probe array will be in contact with the target tissue.

The strength of the assembled structure is also an important issue in implantable device. Compared with the proposed 3D array, structures with tethers and joints used in previous work may not provide reliable strength to fix the probes on the platform during implantation [2] [9]. The thermosetting polymer in the stacked 3-D array provided an adhesive strength of 150–180 kg/cm3 after curing. Thus, sufficiently structural strength was guaranteed in the present design.

In summary, compared with previous 3-D array studies, the advantages of using the stacking method for constructing 3-D arrays include easier assembly processes, stronger structure strength, smaller opening area and less damage to the tissue surrounding the implanting region. ASIC chips can be substituted for spacers to achieve system integration without increasing device size as well. The stacking method can therefore increase the design flexibility and enhance the volume usage efficiency. The time for manually assembling a 4 × 4 3-D microprobe array was approximately 35 minutes. Compared with previous 3-D array studies, the advantages of using the stacking method for constructing 3-D arrays include easier assembly processes, stronger structure strength, smaller opening area and less damage to the tissue surrounding the implanting region. Practical in-vivo neural spike recordings also demonstrated the functionality of the proposed neural probe array.

ACKNOWLEDGMENT

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