MEMS Neural Probes by CMOS Technology and Micromachining

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Abstract

Intracerebral probes based on complementary metal-oxide-semiconductor and post-processing micromachining technologies are versatile tools for interfacing with the neuronal activity of the brain. With switching elements integrated on the shafts of the probes and assembled into three-dimensional systems, silicon probes allow neuronal activity to be monitored via a larger number of channels than ever before.

1. Introduction

Whether the brain is the last frontier of science, as has been surmised, may be questioned. However without any doubt, its about 10¹¹ neurons and their 10¹⁴ interconnections make the brain a multiscale system of awe-inspiring complexity leaving much to discover.

In order to interact with the brain with minimal invasivity when trying to fundamentally understand the dynamics of neuronal circuits or to practically realize brain-machine interfaces for patients with cerebral dysfunctions like Parkinson's disease and epilepsy or disabilities caused by stroke and paralysis, tools of highly delicate construction are needed. Indeed the typical neuron-to-neuron distance in the mammalian cortex is about $50 \ \mu m$; far from being void, the space in-between is filled with an intricate web of neuronal interconnection lines, i.e., axons and dendrites.

Neuroscientists have investigated neuronal circuits with a rapidly growing number of miniaturized electrodes inserted into the brain tissue. From a review of 56 papers, Stevenson et al. [1] concluded that the maximum number of recording channels in neuroscientific studies has kept doubling about every 7.4 years over the last five decades, bringing the current electrode count in individual experiments to several hundred. Often the employed electrodes have been thin, insulated wires, or silicon-based structures



Fig. 1: Selected intracerebral neural probes: (a) passive probes with up to 64 channels (ch) and (b) active EDC probes with on-shaft circuitry for selecting eight out of 188 channels per shaft.

fabricated using micro-electromechanical systems (MEMS) technologies. Well-known structures of the latter type are the so-called Utah [2] and Michigan [3] probes, whose technologies are being commercialized by *Blackrock Microsystems* and *NeuroNexus*, respectively.

At the University of Freiburg, MEMS-technologybased intracortical and deep brain probes have been under development since 2006 with the European projects *NEU-ROPROBES* [4] and *NEUROSEEKER* [5], and the cluster of excellence *BRAINLINKS-BRAINTOOLS* [6], funded by the German Science Foundation (DFG), among others. In these projects, intracortical probes relying on CMOS technology have been developed or are currently being brought to the next level. The more mature probes are being commercialized by the spin-off company *Atlas Neuroengineering* [7].

2. CMOS neural probes

Previous state of the art in MEMS neural probes

Fabrication of the Michigan probes [3] has traditionally made use of heavily boron-doped silicon shafts with thicknesses around 15 μ m fixed on a thicker base and connected to the external instrumentation by ribbon cables based on the same highly doped material. In the case of the Utah probes [2] the fabrication has proceeded by ion migration through thicker silicon substrates than standard wafers followed by trenching using dicing, and sharpening by isotropic etching.

University of Freiburg approach

A third approach benefiting of similar design freedom in view of the lateral shaft dimensions as the University of Michigan's, but at the same time offering additional design freedom regarding shaft thickness, has been proposed by the authors' team [8]. It is termed etch-before-grinding (EBG) technology. After completion of the thin film deposition and structuring processes necessary for the definition of the recording sites and interconnection leads as well as their passivation, the probe shape is defined by deep reactive ion etching (DRIE) of the wafer front; the intended probe thickness is obtained by rear wafer grinding. Electrode metalizations applying Pt or IrOx are combined with Ti/Au/Pt layer sandwiches used for interconnection leads along the slender probe shafts. Probes with shaft lengths between 1 and 40 mm, widths down to 30 µm, and thicknesses down to 25 μ m have been demonstrated. Impedances for electrodes sites with areas of 962 μ m² at 1 kHz are typically 1.2 M Ω and 140 k Ω for Pt and IrOx electrodes, respectively [9,10]. Examples of probes are shown in Fig. 1.

Similarly fabricated probes with integrated fluidic channels [11] and biosensors [12] have been realized by dual-side DRIE of Si combined with additional Si micromachining, bonding processes, and integration of dedicated sensing layers.

Electronic depth control probes

Using the above techniques it is straightforward to realize probes with integrated microelectronic circuitry as well. To this end, before the EBG process, the substrates are processed using commercial CMOS technology. The advantage is that a vastly larger number of electrode sites can be integrated along the shafts, each site switchable to a given number of output lines. In shafts with 4 mm lengths realized in a 0.6 µm CMOS technology by X-FAB, Erfurt, Germany, 188 sites can each be switched to two among eight output lines. Likewise combs with four shafts feature 752 electrode sites. The switches are transmission gates controlled by D-flip-flops linked as a shift register [10]. The switch arrangement allows any configuration of two tetrodes and a large number of configurations with eight sites scattered along the shaft to be selected. Since the microelectronic components are distributed along the shafts, the probe systems benefit of a relatively small base, which facilitates probe usage in sub-chronic experiments [13]. EDC probes are shown in Fig. 1(b).

In *BRAINLINKS-BRAINTOOLS* [6] this state of the art is being pushed further by the use of a 6-metal 0.18 μ m technology by X-FAB. This technology node enables significantly more smartness to be integrated into the probe shafts and bases.

3. Three-dimensional probes

In order to arrange stimulation and recording sites into even more powerful three-dimensional (3D) arrays we have explored successively refined assembly techniques. Probes of the planar type described above were inserted into dedicated platforms with micromachined bays for hosting probe bases. In a first generation, the challenge of the vertical-to-horizontal lead transfer from probe to base was addressed by electroplated Au contacts overhanging the bays



Fig. 2: 3D probe array based on stacking modules for probe alignment (adapted from [17]).

[14]. Relaxing the severe geometrical tolerances of this approach, the bays were later enhanced by thermomechanical actuators pressing the bases against the contacts on a platform/cable assembly [15]. A third design relied on bridging the gaps between the contacts on the platform and the basis by electroplating [16].

Most recently, we have explored the modular system shown in Fig. 2 with spacer modules separating probe levels with a high angular accuracy better than 1°, both in the plane of the probe and in the out-of-plane direction [17].

4. Conclusions

Probes of the above types serve as tools in acute and sub-chronic neuroscientific experiments in animal models by partners of the author's laboratory. Transferring the approach to human subjects will require a prolonged effort in order to ensure the minimal invasiveness and long-term reliability of the probes.

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