

# Acute Multisite Recording Probes for Neurons in Mice and Men

Ulrich G. Hofmann, Marion Bär, Peter Detemple, Maria Kindlundh and Peter Norlin

*Even though the microscopic biological interface between brain cells and microelectrodes is essentially the same in all higher animals, their differing macroanatomy requires varying solutions for different applications and settings. We show two types of multisite microelectrodes intended to be used in acute rodent and acute clinical procedures to record from as many neurons as possible of the minimally disturbed organ. The former setting is meant to shed light on basic information processing within the brain, whereas the latter aims to improve electrophysiological targeting procedures of deep brain structures in the Parkinsonian patient. Animal use probes are fabricated by a Silicon batch process, whereas the clinical use probes are manufactured mainly by precision mechanics showing the complementarity of both interdigitating technologies.*

## Applications of multisite neuronal recordings

Our brain features one of the most complex, yet coherently working, structures known to man in the universe. It consists of up to  $10^{10}$  electrically active cells and an uncoun-

number of support cells. However, there is a clear consensus among neuroscientists and neurologists that our brain features properties which are way superior than might be expected by just looking at the sum and functions of its singular constituents. Those are the results of the  $10^{13}$  connections made among these neurons [1].

In order to shed light on some of the most striking brain features and information processing schemes of its widely distributed activity, it is mandatory to synchronously tap as many neurons as possible by extra-

cellular recordings in vivo. This type of network analysis may in the long run even improve technological network developments and the ever-growing Internet.

Clinical neurology and neurosurgery are using with increasing frequency methods provided by electrophysio-

logy in order to precisely target deep brain structures for the treatment of Parkinson's disease.

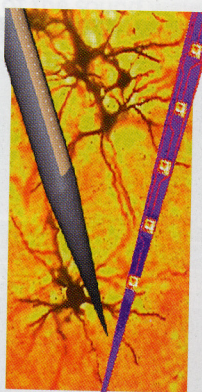
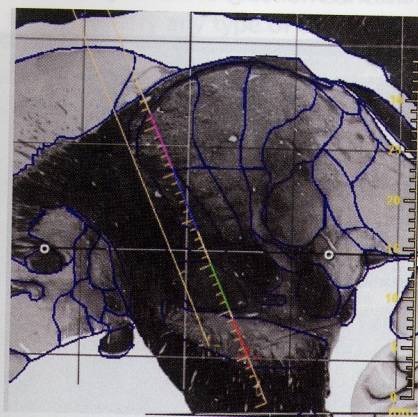
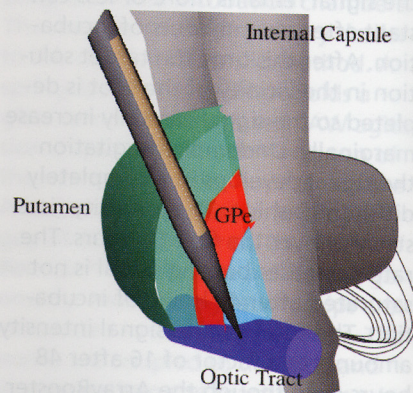


Figure 1: Illustrative sketch of micro-electrode arrays in close neighbourhood with stained neurons (not to scale).

Figure 2: Sketch (top) of the electrophysiological targeting procedure prior to Deep Brain Stimulation in the Globus Pallidus Internus (Gpi) of the human brain. (bottom) Projection of a stereotaxic trajectory on a brain atlas, depicting the estimated target area.



Clearly, to improve the precision achievable, the method of choice is to match the planned trajectory during a stereotaxic procedure to neuronal activity characteristically spread over a depth profile of brain tissue [2] (Fig. 2).

### **Microtechnology for the cellular brain-probe system**

Common specifications to be maintained across target organisms are e.g.

- low traumatisation of brain tissue upon insertion,
- similar electrode-tissue impedances due to comparable recording site sizes and electrode materials,
- anatomically adapted distribution of sites on the supporting carrier structure.

However, the medical use probes have to comply with drastically stricter requirements for mechanical integrity (unbreakable), length of implantable probes (250-350 mm compared to 15 mm in rats) and guaranteed biocompatibility of the materials used.

Consequently, both types of probes are not to be produced with the same MST procedures, leading to two branches of multisite recording probes.

The animal use type of probes may be based on standard lithographic processes, known from Silicon microtechnology, and thus leading to delicate and small, but batch fabricated Silicon devices (Fig. 3). While the other is to be made from a robust, yet very long fine-mechanical structure, since no known batch process covers the required length (Fig. 5). Both are intended to minimise brain tissue damage by a low volume displacement in the brain, while maximising the number of recording sites implanted into the neuropil. Due to their differing target species, they do differ in the distribution of electrodes as well: The animal-use probes spread a number of electrodes (up to 64) flat into a relatively large area of tissue (1,6 x 2 mm), while the clinical-use probes carry all their 32 electrodes on the very final 15 mm of a 350 mm long probe. This allows the positioning of recording sites in different layers of the target brain while only producing one single implantation track. We are thus



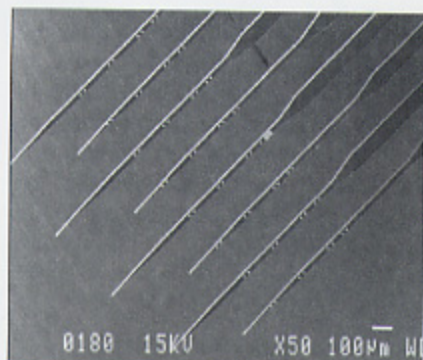


Figure 3: EM picture of 64 electrodes placed on a fork-like micro-probe array.

able to measure an electrical activity profile from the depth of the mid-brain [3], which is supposed to help the neurosurgeon to orient himself in an area he can't look into.

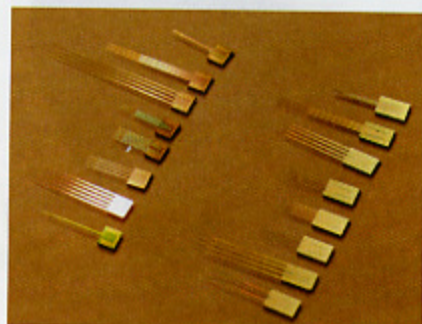


Figure 4: 32 (left) and 64 (right) site Silicon probes of different designs. Longest shafts span 15 mm, shortest 4 mm.

#### Animal use probes

Animal probes are manufactured by a 1 µm resolution, all dry etch process from Silicon-On-Insulator (SOI) wafers utilising front and rear deep reactive ion etching (DRIE). The process is described in detail elsewhere [4] and results in sixteen different probe designs, covering many possible experimental procedures with 25 µm thin tines (see Figures 3 and 4).

Our Silicon probes are used with neurophysiological experimentalists on a regular basis and have proven their usability and superior insertion features [5].

#### Clinical use probes

The manufacturing process for the medical use probes is determined by their required length (>300 mm) and thickness (<800 µm) to maintain compatibility with standard procedures and the target area in the mid-brain of a human patient. We choose precision-mechanical processes to overcome this hurdle: A stainless steel tube with an outer diameter of

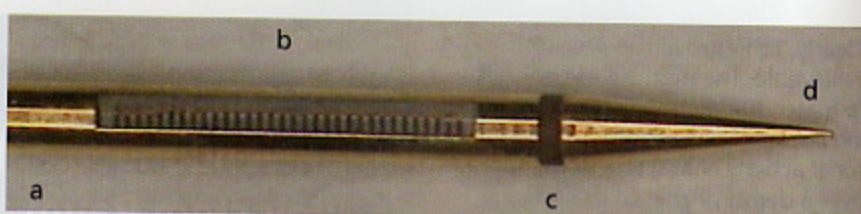


Figure 5: Micrograph of the working end of a clinical multisite neuro-probe with an 650 µm outer diameter. For description see text.

650 µm (Fig. 5a) is fitted in its working end with a "micro-comb" loaded with 31 insulated micro-wires (Fig. 5b). The micro-wires are threaded into the hollow inner core of the tube together with the one wire connecting the stainless steel tip (Fig. 5d). Tip and tube are mechanically connected by an insulating ring (Fig. 5c). All components are embedded and sealed by a thermally curable epoxy resin in order to assure a durable and reliable fixation of sufficient mechanical strength. The cross-sections of the microwires are opened by precision turning and the epoxy coating at the very end of the tip is removed by excimer laser ablation. Finally, the resulting electrode faces are covered with a thin electroplated gold layer. The resulting electrodes have an impedance roughly 2-4 times smaller than the Silicon probes, but are still well within the useful range.

Special care was taken to have all materials in this probe comply with biocompatibility guidelines and thus avoid unnecessary tissue damage. The materials used are furthermore intended to withstand clinical sterilisation procedures, thus making re-use of sophisticated probes possible. It must be emphasised that even though the diameter of 8/10 of a millimetre appears quite big for a surgical procedure on the brain, it is as small as a current standard single electrode recording device, while providing 32 times more information at a time. At the time of this writing we are performing implantation experiments in model substances and cadaver studies to prepare for pre-clinical testing of the new probes.

#### Conclusion and Outlook

Even though the biological application areas for multisite neuronal recordings differ in their specific requirements by several orders of magnitude, the basic idea is the same: Record from as many neurons as possible in the living brain without do-

ing to much damage to the organ. Silicon probes and their infrastructure (amplifier and data acquisition systems) have already proven to support this dogma and are commercially available [6], while clinical probes are in the prototypical test phase.

Although the progress made on these bio-microtechnological devices is impressive and was not foreseen a couple of years ago, both types of probes share one limitation: They are intended for short-term, acute procedures only.

However, the true challenge still lies ahead: a true chronic multisite implant to provide reliable signals from many neurons over a human's lifetime in order to control robotic helper devices for the severely handicapped - the Human-Computer Interface.

#### Acknowledgement

Funding by the EC, IST-1999-10073, and the BMBF 165V1433 is acknowledged. Fig. 2 bottom by Brainlab AG, München.

#### References

- [1] ER Kandel et al., Principles of neural science. 1991, London:Prentice-Hall.
- [2] M Zonenshayn et al. Neurosurgery, 2000. 47(2): p. 282-294, 3. UG Hofmann et al. Europ. J. Neurosci., 1998. 10(Suppl. 10): p. 431.
- [3] P Norlin et al. J. Micromechanics and Microengineering, 2002. 12(4): p. 414-419.
- [4] GR Biella et al., J. Neurophysiol, 2002. 88(3): p. 1159-1165.
- [5] UG Hofmann et al. Biomedizinische Technik, 2002. 47(E 1): p. 194-197.

#### Contact:

PD Dr. Hofmann  
University of Lübeck  
Institute for Signal Processing  
Phone: +49.451.3909552  
E-Mail: hofmann@isip.mu-luebeck.de