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Multi-microelectrode devices for intrafascicular use in peripheral nerve

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Abstract - This minisymposium paper gives an overview of experimental, modeling, design and microfabrication steps which lead towards the University of Twente threedimensional 128-fold silicon microelectrode device. The device is meant for implantation in peripheral nerve for neuromuscular control purposes and is estimated to be able to selectively control 10-20 motor fibres.
Also, the potentialities of an alternative LIGA microfabrication technology are considered.
A brief comparison is made with the twodimensional sieve and flexible foil types of neuro electronic interfaces, under development elsewhere.
Microfabrication technologies appear to be an important tool, but evidence is accumulating that for selective neuro-electronic interfacing the micro devices are not yet small/selective enough. More precison and selectivity is needed to contact individual axons intimately and selectively. Therefore, new lines of research develop towards in-vitro-neuron-cultured MEP's (Multi Electrode Plates) to be implanted in neural tissue.

THE UNIVERSITY OF TWENTE THREEDIMENSIONAL 128-MICROELECTRODE DEVICE

Experiments, modeling and design

If selective contact of one-electrode-one-fiber is to be obtained, one has to bring an electrode close to one of the nodes of Ranvier of a fibre. The only 'garantuee' for that in a 'random' population of fibers is the use of a redundant number of electrodes in the nerve. For example, the peroneal nerve of the rat controls four muscles. One of these is the Extensor Digitorum Longum (EDL) muscle, with 70 motor units. Assuming a random topology for the position of the EDL motor fibres in the fascicle, one calculates that for the control of 10-20 fibres a number of 128 electrodes will be sufficient. Control of all 70 fibres would imply a multiple of 128 electrodes, which is not possible on a microfabrication scale [4 - 13, 21].
Experiments with a linear 12-fold silicon electrode array and a twodimensional 24-fold wire-array (Figure 1, [9]) in the peroneal nerve of rat, and volume conduction modeling studies, lead to the optimal dimensions for a 3D multi micro electrode with 128 electrode sites (Figs. 2 and 3) [4,5,14, 15,16].

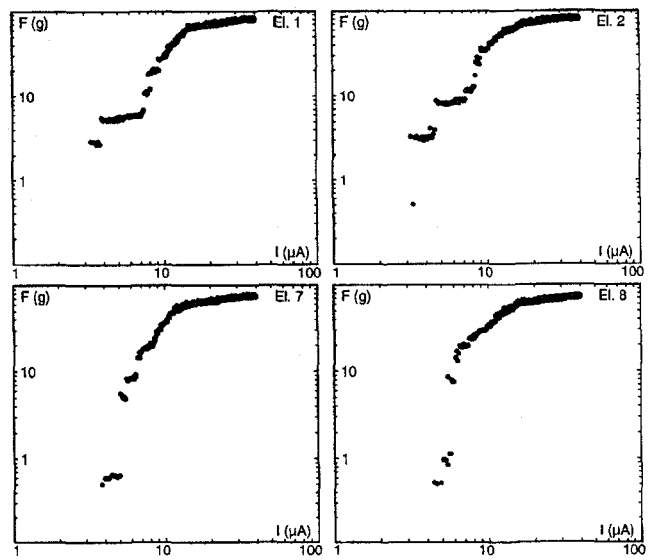

Figure 1. Twitch force recruitment curves of rat EDL muscle stimulated by a 24-fold 2D electrode array (see inset), electrode spacing is 120 μm. Scales are log-log. Vertical scale ranges from 0.1 to 100 grams, horizontal from 1 to 100 μA. Only 4 curves of the 24 are shown. See [9] for more detail.

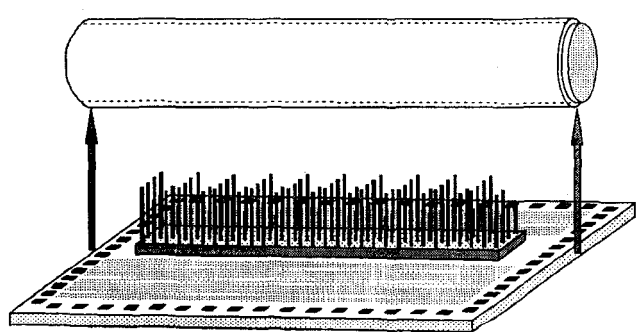

Figure 2. Schematic overview of a CMOS chip carrying a 3D array of 128 microelectrodes, to be inserted into a nerve. For dimensions, see Fig. 3.

Microfabrication

The fabrication of a 3D silicon based multi micro electrode involves a large number of challenging steps [14], not only for

the 'brush' itself, but also for the control electronics chip [15] and the contacting technology (between electrode-brush and control chip) [16].
The chip has been completed, the solder bump contacting technology (flip-chip technology) is ready, and nearly all fabrication steps of the brush are successful now.

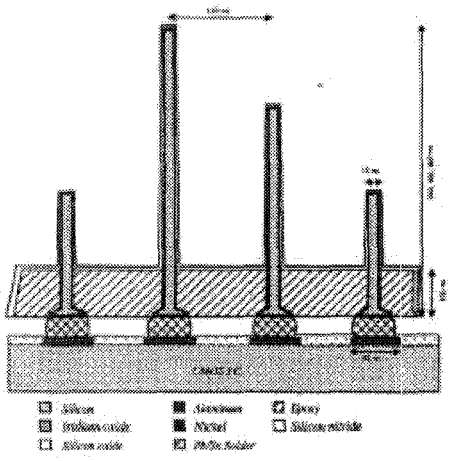

Figure 3. Dimensions of multi electrode array mounted on CMOS chip.

Insertion of a multi micro electrode

The insertion of a 128 fold 'brush' multi electrode into the peroneal nerve is not straightforward. The viscoelasticity of the nerve tissue does not allow penetration of the epineurium by simply pushing. Also, high speed pneumatic insertion methods fail.
By a modified electrosurgical high frequency cutting/vaporization method we were able to create microscopic holes in the epineural layer, allowing the electrodes to be forwarded in the fascicle easily [21]. This way of controlled 'hole-burning' results in some neural tissue damage (which may be temporary), reflecting itself in some reduction of maximum force and increased threshold.

Force control capabilities and closed loop control

A strategy for using the electrodes in the array to control the rat EDL muscle has been designed. The algorithm is based on force regulation in nature; its task is basically to find a combination of rate coding and recruitment to produce a required force, keeping fatigue minimized. From simulations it was found that approximately 20 electrodes could be identified as 'virtual motor units' (i.e. 20 out of the 128 electrodes are each controlling one, or a small group of, nearby fiber(s)). These 20 electrodes were able to control the force pattern satisfactorily, in a simulated environment [18].

Forward stimulation of muscle by intraneural electrodes would evolve into local closed loop control of muscle force if supplemented by feedback information, recorded from (small groups of) afferent fibers. The multi-microelectrode device might as well be used for recording (the chip has built-in amplifiers for this purpose). However, it is not well known whether introduction of micro-metal electrodes in nerve is allowed for recording. Action potential propagation may be blocked or, unintentionally, action potentials (ap's) may be evoked or distorted by fiber membrane irritation. Therefore, a comparison of ap model shapes with microelectrode recordings was done [19]. It seemed that blocking and irritation are indeed serious side-effects, possibly preventing closed loop control by a dual-function intraneural device.

LIGA fabrication

The silicon backbone structure of the multi electrode is obtained by sawing grooves into the silicon.
An alternative way would be to combine silicon technology with the socalled LIGA technique (Lithographie, Galvanoformung, Abformung) . Nickel needles are grown from a seed layer through narrow channels in 200 µm PMMA (polymethylmethacrylate) (Fig. 3). Although the nickel growth process is still delicate, and the yield low, this combination of techniques may be useful for fabrication of neuroprostheses. Also, the length of the needles must be increased to about 500 µm [20].
The advantage of the LIGA method may be that electrical isolation of the needles is easier, it will reduce the number of process steps.

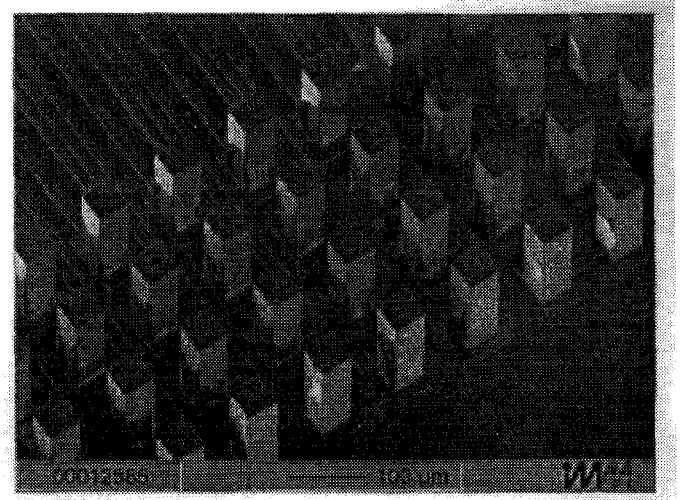

Figure 4 Array with 200 µm tall needles, realized with aligned x-ray lithography (LIGA) on silicon substrate with 8 µm Cu interconnection wiring.

BRIEF COMPARISON TO TWODIMENSIONAL SIEVE AND FLEXIBLE FOIL MULTIELECTRODE DEVICES

While a number of groups attempts 3D devices for intrafascicular [University of Twente] or cortical use [1] ,[2]

[University of Utah group], 2D devices offer a number of advantages.
Twodimensional 'sieve' devices permit nerve fibers to regenerate through the metalised via hole-electrodes of the sieve [3] [this conference: Univ. of Lund group, Fraunhofer Institute St Ingbert/Univ. of Barcelona group].
Main advantage of this method is that microfabrication of 'flat' devices is easier than 3D devices. Another advantage is that, once the nerve has been regenerated, the device is fixed firmly to the nerve. However, since the flats are typically only 10 µm thick, there is a limited chance that nodes of Ranvier will be close to an electrode (typical internode spacing of a 10 µm thick fiber is 1 mm), thereby limiting the selectivity of stimulation/recording.
Another class of 2D electrodes are the flexible foil multi electrodes, which are intended for flat or bended use in between or around fascicles [this conference: Univ. of Aalborg group, Case Western Reserve Univ. Cleveland group, Fraunhofer Institute St Ingbert group]. Main difference with brush and sieve type is that they do not penetrate fascicles. This will limit fiber selectivity [19], but may enhance gross fascicular selectivity. Main advantage is the easy way of fabrication, which is essentially two-dimensional. Fixation of the flat type will need special attention.

FUTURE DEVELOPMENTS: CULTURED MULTI ELECTRODE PLATES AS 'NEURAL PROBES'

Our multielectrode device with 128 electrodes on top of 15-40 µ m thick tapered needles is expected to have an "efficiency' of 10-20 motor fibres to be contacted selectively. The device is not yet small/selective enough. However, one reaches the limit of what 3D microfabrication can offer.
Increase of efficiency is possible by a different approach. Instead of 'putting in more and more electrodes', the process is reversed: nerve fibres are 'seduced' to grow to electrodes, with natural cells as intermediates. The electrodes are covered (in the lab) by cultured nerve cells, which are grown in a controlled way on a chemically/topologically/electrically patterned Multi Electrode Plates (MEP) [22]. The cultured MEP is inserted/inplanted in the nerve (see also Pine's contribution on 'cultured probe' to this minisymposium).

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