TOWARDS A VERSATILE SYSTEM FOR ADVANCED NEURONAL RECORDINGS USING SILICON MULTISITE MICROELECTRODES.

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INTRODUCTION

The current understanding of how the nervous system functions is based on numerous observations of the behaviour of single units or a small ensemble of units correlated to some external stimulation or behavioural event [1]. However, the processing power of the nervous system lies in its network and interconnections [2]. Thus, the key to understand the nervous system is to make simultaneous observations of the activity of numerous cells forming acting and responding networks [3-5]. The obviously resulting need for a high number of extracellular recording sites placed in close proximity to those cells within the brain is a well know fact [6]. However, even the most up-to-date techniques are still depending on the use of singular microelectrodes or micro-wires to be implanted into the brain area under observation [7]. The use of bundled (stereo- or tetrodes) or brush-like arranged microelectrode-arrays helps to increase the number of recording sites, however, long and tedious implantation surgeries are still mandatory [8]. It appears therefore highly desirable to increase the productivity of a single surgery by implanting a multitude of recording sites at once [9]. Our project VSAMUEL set out to bring current micro-machining technologies to work and to produce not only batch fabricated multi-site microelectrode arrays, but high quality data acquisition systems as well.

PROJECT OUTLINE

The EU funded project's objective is to develop multi-site microelectrode recording system based on silicon microelectrode arrays for acquiring signals from nervous tissue in vivo. The project VSAMUEL will utilize advanced micro-structuring to design and fabricate probes with an increasing number of recording sites: up to 128 sites placed on tiny fork shaped probes, arranged in a way as to satisfy the needs of experimental groups (Fig.1 #2).

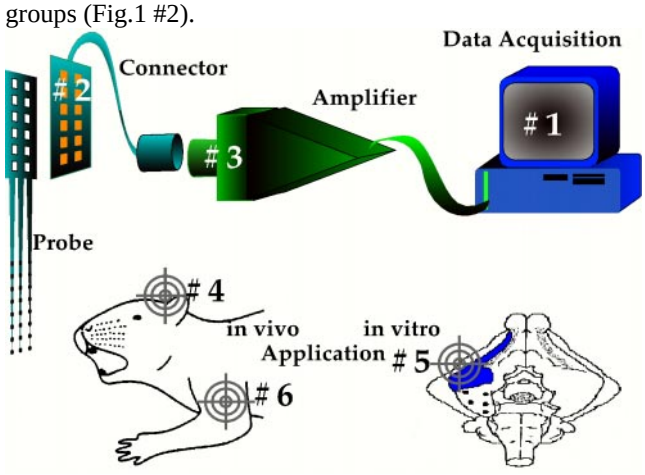

Fig.1: Overview on the whole VSAMUEL-project: The numbers of project parts correspond to it's authors affiliations

This will not only include development of easy-to-use connectors and suitable multi-channel signal amplifiers (Fig.1 #3), but also a novel high-quality, high-throughput data acquisition system (DAQ), based on commodity type PC-computers and signal processing boards (Fig.1 #1). Fig. 1 gives an overview over the whole project.

TECHNICAL SPECIFICATIONS

The silicon probes consist of one or more shafts with a minimal cross section of 20µm*20µm, a very small tip taper (<4°) and a full wafer thickness base section with pads on it suitable for ultrasonic bonding. Each of the shafts carries a number of Iridium microelectrodes (10µm*10µm) as recording sites on their side. Recording properties of electrodes are therefore expected to be sideways directed, perpendicular to the shaft direction. Because our utilized etching techniques allow for complete control over tip and shaft design, the shaft geometry may be chosen almost arbitrarily to account for experiment specifics (see below).

Finished silicon probes are wire-bonded to a flexible PC-board on a rigid carrier, suitable for mounting on a standard micro-drive. The macroscopic multi-channel connector on the flex-board itself connects to a multi-channel, modular preamplifier of gain 20, which itself connects via an electronically controlled amplifier to the DAQ. The DAQ is based on a standard, commodity PC, controlling up to 4 Digital Signal Processor Cards (each acquiring 32 channels with 50 kSamples per second at 16 bit resolution) which relieve the main CPU from most of the required computing for data storage, retrieval and analysis.

EXPERIMENTAL REQUIREMENTS

Due to a lack of space, we are only presenting one exemplary experiment and the requirements put forward to the design of silicon multisite probes: This investigation is an in vitro study and aims to record extracellular field responses during acute experiments. These are performed on the isolated guinea pig brain preparation (Fig. 2) maintained ***in vitro*** by arterial perfusion.

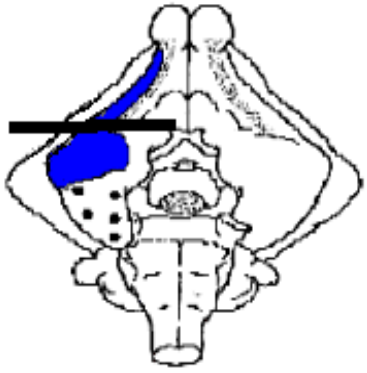

Fig.2: a) Schematics of a guinea pigs brain seen from below. The shaded and dotted areas are regions of interest: pirifrom and enthorhinal cortex resp. Bar shows cross section in Fig.3.

In one set of experiments, cortical oscillations at 25-40 Hz (*gamma* activity) caused by muscarinic cholinergic activation will be simultaneously studied with more than 32 sites at different cortical sites (entorhinal, perirhinal cortices) on both hemispheres. Electrode arrays will be designed to adapt to the slightly curved surface of the cortex. The changes in correlation of *gamma* activity across the entorhinal cortex in different experimental conditions (before and after different patterns of stimulation) will be verified. Fig.3 shows a sketch depicting the cross section of a guinea pigs cortex with an electrode array projected on it.

To satisfy the requirements, the probe is bearing 5 shafts 500µm center-to-center apart from each other with 6(7) electrode sites on each shaft. The center-to-center distance between the recording sites is 200µm with on site close to the central tip unusual big (25µm*40µm). This site will act as current source for electric lesions to verify probe locations in the brain [7].

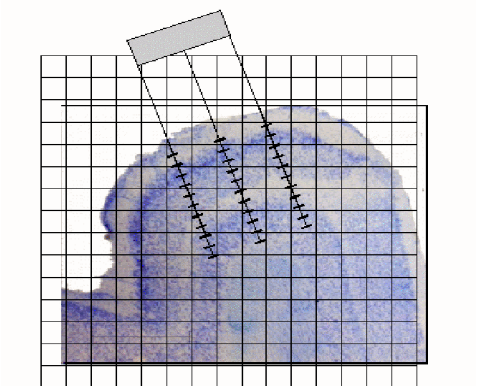

Fig. 3: Artistic sketch of a 32 site micro-array projected onto a cross section of piriform cortex with stereotaxic grid to it(bar in Fig.2).

STATE OF THE PROJECT

The following table 1 shows basic specs of the probes, in the fabrication process at time of this writing.

Table 1: Target areas in a guinea pig/rat and probe specs for 32 probes

Target area	**shaft -#**	**distance**	**Length**	**probes #**	**distance**
Piriform Cortex	1	-	5000µm	32	50
Piriform Cortex	5	300	4000µm	6(7)	200
Cerebellum	4	400	5000µm	8	100
Cerebellum	8	200	4000µm	4	~200
Deep Cereb Nuclei	4	200	5000µm	8	200
Peripheral Nerve	4	500	15000µm	8	100
Brainstem	4	250	10000µm	8	100
Triangulation	4	50	5000µm	8	50

DAQ and Amplification are in the design/ implementation process as well, ready to show by the time of the conference.

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