

Development of 3-dimensional multi electrode arrays for simultaneous stimulation and measurement of neuronal activity in the retina

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The objective of this project is the development of implantable multi electrode arrays for the simultaneous stimulation of retinal neurons and the measurement of the neuronal activity in the retina as well as the fluctuation of the local pH-value. These electrodes are supposed to allow new studies of the process of degeneration of retinal cells during retinitis pigmentosa.

Signal processing inside the retina

The retina of most species is about 200µm thick. It is a layered structure and consists of several different cell types. The outer retina, which points away from the incoming light, is formed by the photoreceptors, the rods and cones. The photoreceptors transmit their information via synapses on the bipolar cells. The soma of these cells together with the somas of horizontal cells and amacrine cells form the inner nuclear layer. The bipolar cells transmit their information further to the ganglion cells. The ganglion cells with their somas and axons make up the most inner layer of the retina (the ganglion cell layer and the nerve fibre layer). The inner layer faces the incoming light.

The electrical stimulation of ganglion cells by stimulation electrodes can be done in two ways:

1. By direct stimulation of a soma or an axon.
2. By electrically stimulating presynaptical cells, which then synaptically stimulate the following ganglion cells.

Electrical stimulation of neurons

Functional electrical stimulation is performed in a variety of applications to restore lost functionalities. One example is the cochlear implant. By proper stimulation of nerve cells of the cochlear deaf people are able to hear again [5]. By deep brain stimulation the tremor of Parkinson patients can be suppressed [2]. World wide different research teams are working on retina implants. By proper stimulation of nerve cells in the retina visual perceptions had been achieved.

Penetrating multielectrodes for stimulation and measurement

For studies of neuronal ensembles, like retinal ganglion cells, multi extracellular measurements of neuronal activity by penetrating electrode arrays were found to be the proper technique for experimental tests [3], [6], [8], [17]. They allow the measurement of the electrical activity of different neurons in an ensemble with a high temporal resolution.

Furthermore penetrating electrodes are used for the stimulation of neuronal tissue. The use of this type of electrodes, for example in the cochlea, has some advantages compared to the use of planar electrodes [9]. The use of these electrodes in the auditory brain stem has also been reported [21], [19]. As far as we know, penetrating multielectrodes have not yet been used for the stimulation and the study of the neuronal activity in the retina.

Production and structure of penetrating multielectrodes

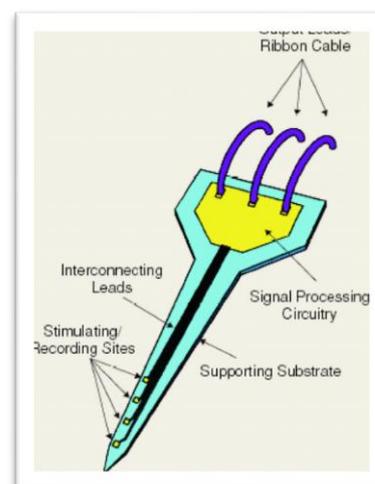


Fig.1: Structure of a penetrating silicon electrode with several stimulation electrodes [26].

The first studies on the use of silicon technology for the manufacturing of dense arrays of thin film electrodes for the measurement of neuronal signals, so called neuroprobes, were made in 1966 at the Stanford University [24], [25], [26], [13]. This technology allowed the simultaneous measurement of neuronal signals at different points of a probe. Fig.1 shows the structure of such a neuroprobe.

The active surfaces of the electrodes had a size in the range between $100 \mu\text{m}^2$ and $400 \mu\text{m}^2$, the distances between the electrodes ranged from $50 \mu\text{m}$ to $200 \mu\text{m}$ [15]. The materials used for the electrodes were polysilicon, tantalum, gold, platinum, titanium nitride, platinum iridium or iridium oxide [15], [22]. This technology allows the production of neuroprobes with several shanks [26]. The use of SOI-substrates (silicon on insulator) can simplify the manufacturing of such probes [18], [4], [11]. In this case the buried oxide serves as an etch-stop for anisotropic etching.

The first studies on the integration of CMOS-circuits on the shanks were presented in 1986 by the group of Kensall D. Wise [1], [14]. But only the monolithic integration of complex CMOS-circuits allowed the production of electrode arrays with a huge number of electrodes [14], [26].

Neuroprobes like the one shown in Fig.1 are not only used as a carrier for electrodes, but are equipped with additional features. Wise for example presented a neuroprobe, in which channels for the application of medication had been integrated [26], [20]. In addition neuroprobes were developed, which allow the detection of chemical values like pH [10], choline or L-glutamate [7].

Arrays of penetrating electrodes for the stimulation of an area in a certain depth were for example developed at the University of Utah [12] and at the University of Chicago [23]. These assemblies bear the disadvantages, that there is only one electrode on the tip of each shank and that each shank needs a separate electrical connection.

The measurement and stimulation in three dimensions is possible with an electrode array developed by the group of K. D. Wise [27]. In this approach neuroprobes with several shanks are arranged via micromechanic plug-in connectors to a three dimensional array with 256 electrodes on a silicon platform (Fig.2 and Fig.3). The platform contains the entire circuits for the control of the electrodes. In a European project a similar approach is being tested [16].

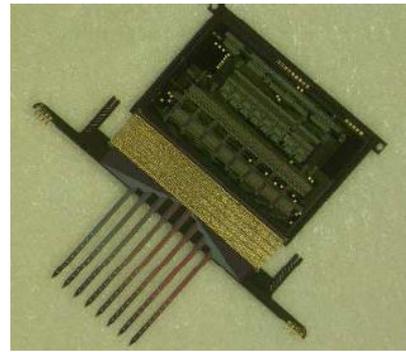


Fig.2: Three-dimensional microelectrode array [27]. Single element with eight shanks and 64 electrodes

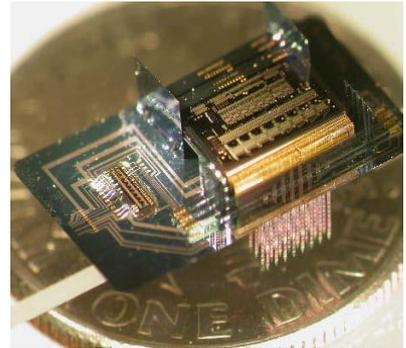


Fig.3: Three-dimensional microelectrode array [27]. 3D electrode array consisting of four separate elements.

In this project a three dimensional array is to be developed similar to the work of Wise [27]. While penetrating electrodes typically have shanks with a length of several mm, in this project we have to develop probes with a shank length of about $200 \mu\text{m}$. These probes will be optimized for the studies of degeneration processes in the Retina. The array will contain additional sensors for the detection of local pH-values.

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