Microelectrode Array for Neural Interface

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A microelectrode array (MEA) chip for in-vitro electrophysiology measurements was integrated in 0.35 u CMOS technology. The MEA features 4096 full-duplex electrodes for sensing and stimulation, and is embedded in a multi-well system. This enables to run in parallel multiple experiments for testing drugs on neurobiological models.

In vitro neurobiological models are the most valuable tools to validate brain drug efficacy and toxicity before clinical trials. Pharma companies have a great need to access new technologies to improve the read-outs from in vitro screenings. Conventional patch clamp or MEA MEMS-based technologies can simultaneously access signals, but from a few cells only. This significantly limits the understanding of the collective behavior of neuronal circuits. Conversely, CMOS-based electrical biosensors (also termed High Density MEA or HD-MEA) integrate thousands of electrical sensors on chip, which drastically increases the experimental capability of sensing large neuronal networks. It allows the simultaneous measurement of the signals generated by thousands of neuronal cells, which enables the study of the electrical activity of neuronal circuits at network level. As a result, it is possible to record the electrical signatures of a network of cells to assess functional (healthy) or dysfunctional (diseased) states, and most importantly, to track the pharmacological response to a drug.

A CMOS chip with a 64×64 pixel array has been developed. Each pixel of 60×60 um^2 features a flat electrode made in the top metal layer of the process, in-pixel voltage amplification and filtering to amplify with a gain of 100 the small biopotential signal present at the interface between the metal plate and the living tissue. In addition to sensing, each electrode can also be used individually for voltage stimulation, thus enabling to generate fine stimulation patterns and observe how the biological cell tissue reacts. Figure 1 shows a microphotograph of the chip encapsulated in the reservoir which holds the living tissue.

Figure 1: Microphotograph of the chip in its container.

Using through silicon via technology avoids bonding wires and enables a flat area extending on all sides of the chip to improve the quality of contact between the tissue and chip and therefore maximize tissue recording quality.

With 4096 electrodes able to both record and stimulate, it offers the highest number of stimulation sites available on the market, and also the largest active area. The characteristics of the microelectrode array chip are summarized in Table 1.

The device will be incorporated in a multi-well microtiter plates architecture for parallelized and semi-automated drug screening.

Table 1: Characteristics of the chip.

Parameter	**Value**
Resolution	64×64 pixels
Pixel pitch	60 um
Active area	3.9×3.9 mm^2
Gain	10 - 1600
Frame rate	18 kfps
Maximum stimulation voltage	5 V
Electrode input common mode	0 - 400 mV
Electrode input signal (high gain)	+/- 2 mV
Power consumption	350 mW

Figure 2 shows neuronal spike activity of hippocampal neuronal cells seeded on a microelectrode chip, recorded by a single channel. Neuronal spikes are clearly visible.

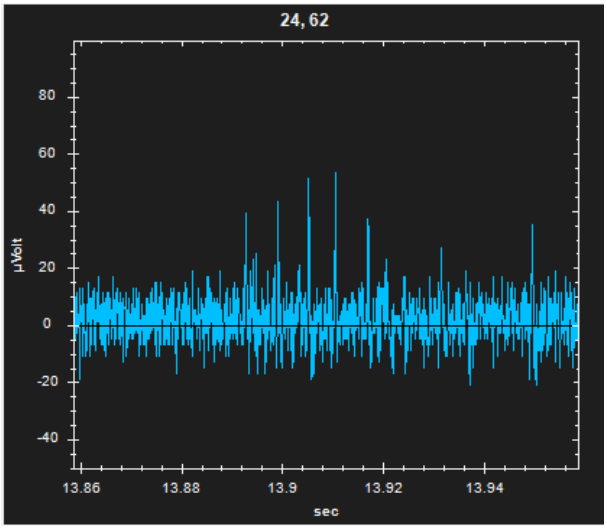

Figure 2: Output of a single channel.

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