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a division of Harvard Bioscience, Inc.

CMOS-MEA5000-System

Extracellular recordings and stimulation at the highest resolution

- Active microelectrode arrays for recording and stimulation
- 4,225 recording and 1,024 stimulation sites
- Outstanding signal quality
- Recordings at sub-cellular level
- Powerful recording and analysis software

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Highest resolution with active arrays

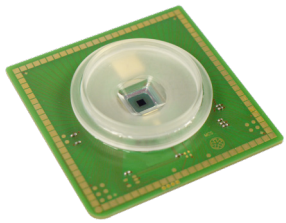
Based on the complementary metal-oxide semiconductor technology, the CMOS-MEA5000-System from Multi Channel Systems opens up new possibilities in electrophysiological research.

With more than 4,000 recording sites, each of them sampled at 25 kHz, the chip allows extracellular recordings at a very high spatio-temporal resolution. By including amplification on the chip itself, noise is minimized and a high signal quality is guaranteed.

As stimulation sites are included in the chip and a stimulus generator in the headstage, the system is ideal for closed-loop experiments.

Compact design, powerful components

The CMOS-MEA5000-System consists of three components, which are all designed to be efficient and powerful, while fitting ideally on the lab bench and microscopes.



CMOS-Chip

The chip is based on complementary metal oxide semiconductor (CMOS) technology, facilitating fast, high-resolution imaging of electrical activity. The chip is equipped with a culture chamber to house your sample, while allowing the use of a microscope. You can choose between culture chambers optimized for cell culture or for slice recordings.

Headstage

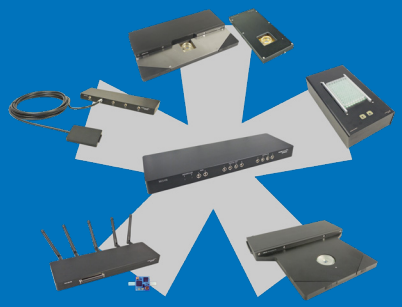
The core of the system is the headstage. It samples the data coming from the chip at 25 kHz per channel (all electrodes simultaneously). Besides A/D conversion and amplification, the headstage also houses a 3-channel stimulator. You can freely design the stimulation patterns via software and select each of the 1,024 stimulation sites.

Interface board

The interface board offers the USB 3.0 interface to transfer the recorded data to a computer. Moreover, it has analog and digital in- and outputs for synchronization with other instruments.

Computer with software

The system is operated by two powerful programs, CMOS-MEA-Control for recording and CMOS-MEA-Tools for off-line data analysis. It facilitates a real-time activity overview on the complete chip with the ability to zoom in and various tools to analyze the data.



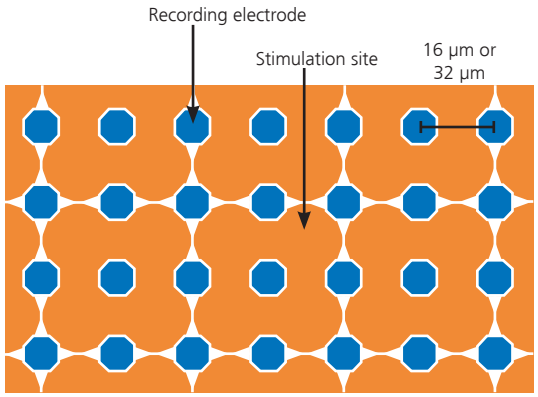
Interface board multiboot

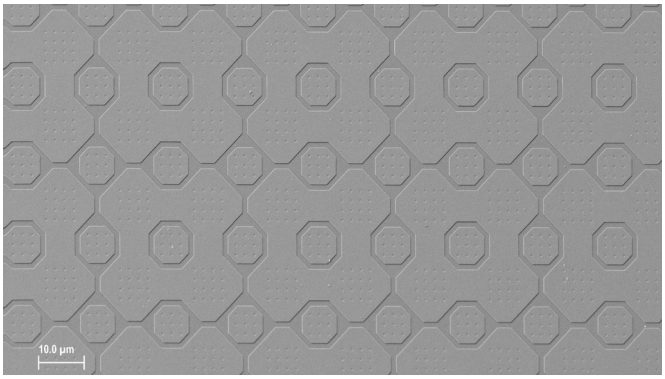
The MCS-IFB 3.0 multiboot is a new generation of interface boards, which enables you to operate a wide range of MCS *in vitro* and *in vivo* headstages: MEA2100-HS, MEA2100-Mini-HS, MEA2100-Beta-Screen-HS, Multiwell-MEA-HS, CMOS-MEA-HS, W2100-RE, and ME2100-HS. This allows cost-effective combinations with only one interface board and multiple recording systems.

Chip layouts

The CMOS-chip has a 65x65 layout and is available with 16 µm or 32 µm interelectrode distance (center to center). The electrode diameter always is 8 µm. Between the recording electrodes, there is a grid of 32x32 bigger stimulation sites. Summarizing, you can record from 4,225 electrodes and stimulate your sample at 1,024 sites.

The chip is coated with a planar oxide, similar to glass, enhancing the biocompatibility and biostability. Recording and stimulation works purely capacitively, removing any DC offsets by design.





Electron micrograph of the CMOS-chip surface (NMI Reutlingen, Germany)

Advantages of the CMOS-MEA5000-System

Highest resolution of chip

First, the 16 µm interelectrode distance chip offers the world-wide highest resolution. Second, with the high number of electrodes, you can record from a large surface (1 mm² @ 16 µm distance, 4 mm² @ 32 µm distance). Thereby, you can see the signals from every single cell and even the signal propagation along an axon, while still getting an overview on your complete sample, e.g. a cell culture, and see how the cells interact.

Highest data quality

Your data is sampled at 25 kHz per channel. Thus, no signal is lost - even axonal spikes are displayed and recorded thoroughly. Together with the A/D conversion at 14 bit, the system ensures accurate and precise data.

Integrated stimulation

The integrated stimulator facilitates arbitrary stimulation shapes on selected areas of the 1,024 stimulation sites. One big advantage is that you can record instantly after stimulation. Even on the electrode right next to the stimulation site, recording is possible <1ms after the stimulation pulse.

Ease-of-use

The CMOS-MEA5000-System is very easy to use. The headstage can be positioned on a microscope. After opening the lid, you just place the chip in the headstage. When the lid is closed, the contact pins are pressed on the pads on the chip and signals are transmitted. There is no need for many cables, the interface board and headstage only need one eSATA cable. Connection to the computer is done via USB 3.0, so again no complication here.

Technologically advanced interface board

The interface board offers various inputs and outputs for synchronization with other instruments. Apart from digital and analog in- and outputs, you can use the same interface board for a variety of *in vitro* and *in vivo* applications by connecting other MCS headstages.

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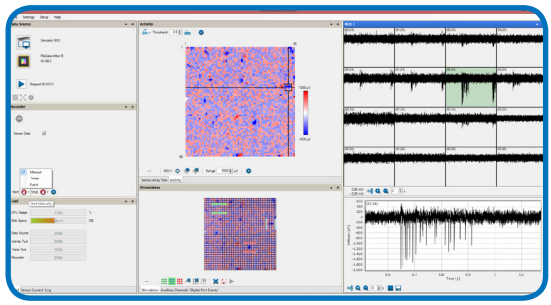
Versatile and high performance control software CMOS-MEA-Control

Data acquisition with the CMOS-MEA5000-System is controlled by CMOS-MEA-Control. The software gives an online, real-time activity overview on the complete chip. The intuitive false color plot allows easy identification of active areas on the chip. Regions of interest can be defined, so you can look at the raw data of any area in real time. Data is recorded directly in the open source HDF5 format, which is compatible with Matlab and Python.

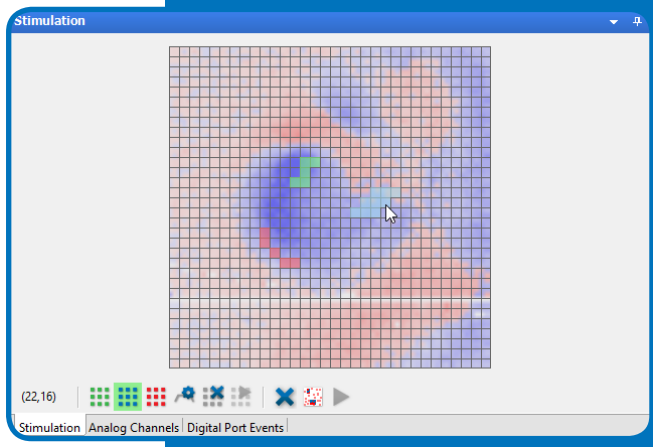


Adaptive filtering

High pass and low pass filter limits can be adjusted in the software at any time, from DC to 10 kHz. However, subsequent filtering is also possible during off-line analysis.

Flexible recording control

Recording can be controlled manually, but also by external TTL inputs and internal timers. Recording can be restricted to subareas of the chip.

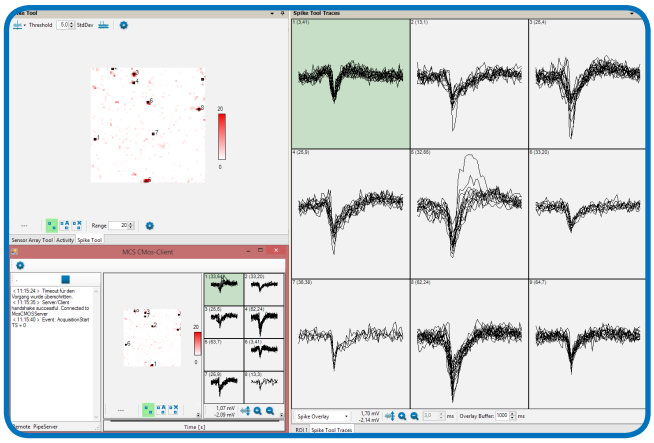


Stimulation with highest spatial resolution

You can freely define three independent stimulus patterns, using and adjusting the drag'n'drop modules. Each pattern can be assigned freely to any of the 1,024 stimulation sites covering the complete chip area. An overlay of the activity allows precise positioning of stimulation sites in active areas (see screenshot on the right hand side).

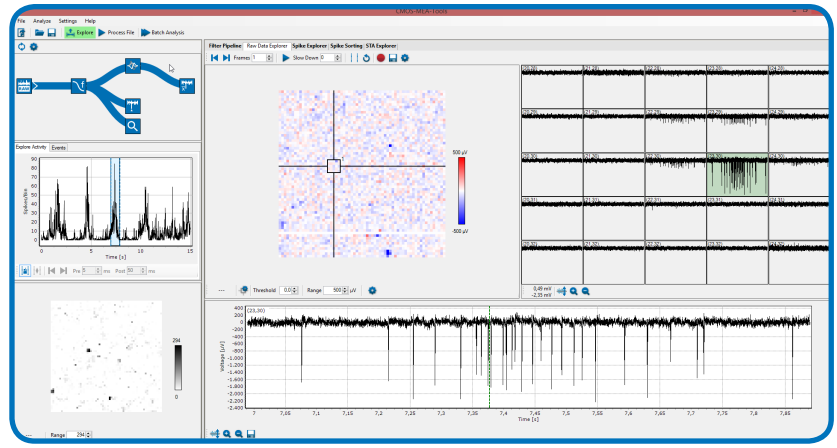
Online spike detection and streaming

Spikes can be detected online with a choice of adaptive detection algorithms. Detected events can be streamed live via a pipe connection to a second application on the same computer, or also to a second computer in the same network.



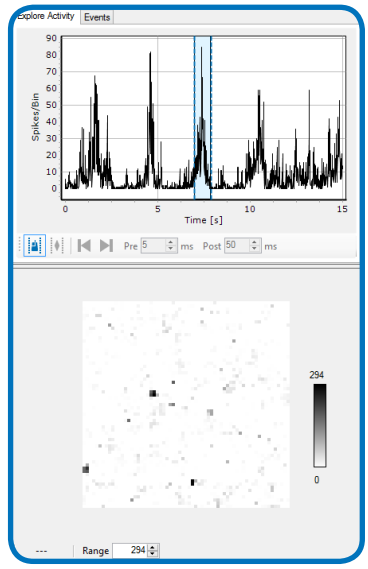
Powerful analysis software CMOS-MEA-Tools

Offline analysis of CMOS data can be done in the program CMOS-MEA-Tools. Results can be exported in ASCII or HDF5 format to other applications.
The software provides multiple filtering options, as well as spike detection, spike triggered average movies, and fully automated spike sorting.



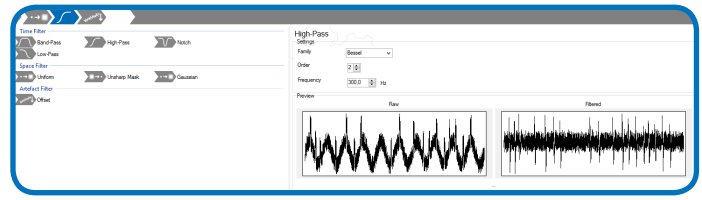
Activity summary

The one-click activity summary generates a temporal and spatial overview of the activity in the file and allows easy navigation to the interesting times and areas.



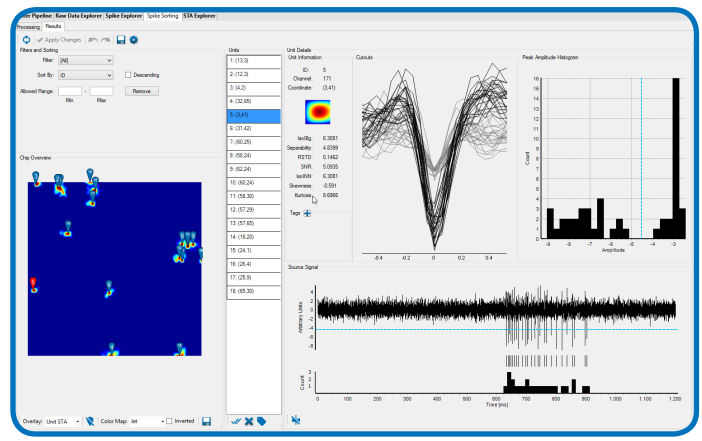
Filter pipeline

A filter pipeline can be assembled from a number of spatial and temporal filters to optimize signal quality before spike detection and sorting.



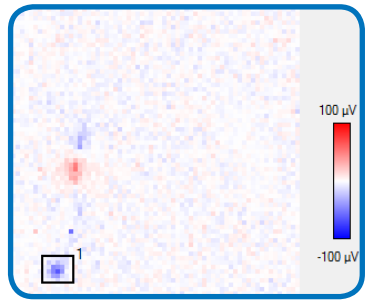
Spike detection and sorting

CMOS-MEA-Tools features a fully automated spike sorting. The spike sorting algorithm implemented in the software is based on the work published in Leibig et al., J.Neurosci. Meth., 2016. It allows unsupervised identification of neuronal units with a single mouse click. A client software allows to run performance intensive sorting tasks on several computers in a network simultaneously.



Spike triggered average movies

Spike triggered averages allow to detect repetitive events correlated to each spike on a specific electrode, like axonal signals, which are usually hidden in the noise. The travelling axonal signals can be visualized and exported as a movie.



CMOS-MEA5000-System: Technical specifications

General characteristics

Dimensions (W x D x H)	Headstage: 256 mm x 230 mm x 25 mm
	Interface board: 250 mm x 83 mm x 25 mm
Weight	Headstage: 1.4 kg
	Interface board: 0.3 kg

Amplifier

Data resolution	14 bit
Number of recording channels	4,225
Bandwidth	DC to 10 kHz

Stimulus generator

Number of stimulation patterns	3 independent patterns
Signal shapes	Freely programmable (monophasic, biphasic, bursts, sinusoidal) or Ground
Stimulation sites	1,024
Output voltage	3.4 V amplitude with 10 µs rise time for high capacitive currents

Data converter and USB interface

Control interface	USB 3.0
Sampling rate per channel	up to 25 kHz on all channels simultaneously

Heating element and temperature sensor

Heating element impedance	20 Ω
Temperature sensor type	PT 100 with 4 wire connection

Software

Operating system	Microsoft Windows® 10 and 8.1 (64 bit)
	English and German versions supported
CMOS-MEA-Control software	Version 2.2.0 and higher
CMOS-MEA-Tools software	Version 2.2.0 and higher
Data format	HDF5
Data acquisition	CMOS-MEA-Control or via C# DLL

For complete solutions for electrophysiology visit:
www.smart-ephys.com

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a division of Harvard Bioscience, Inc.

Made in Germany

Developed in cooperation with Prof. Roland Thewes, TU Berlin, and Dr. Günther Zeck, Natural and Medical Sciences Institute (NMI), Reutlingen, Germany

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Multi Channel Systems
MCS GmbH

Aspenhaustrasse 21
72770 Reutlingen
Germany

Phone +49-7121-9 09 25 25
Fax +49-7121-9 09 25 11

sales@multichannelsystems.com
www.multichannelsystems.com