Quickstart

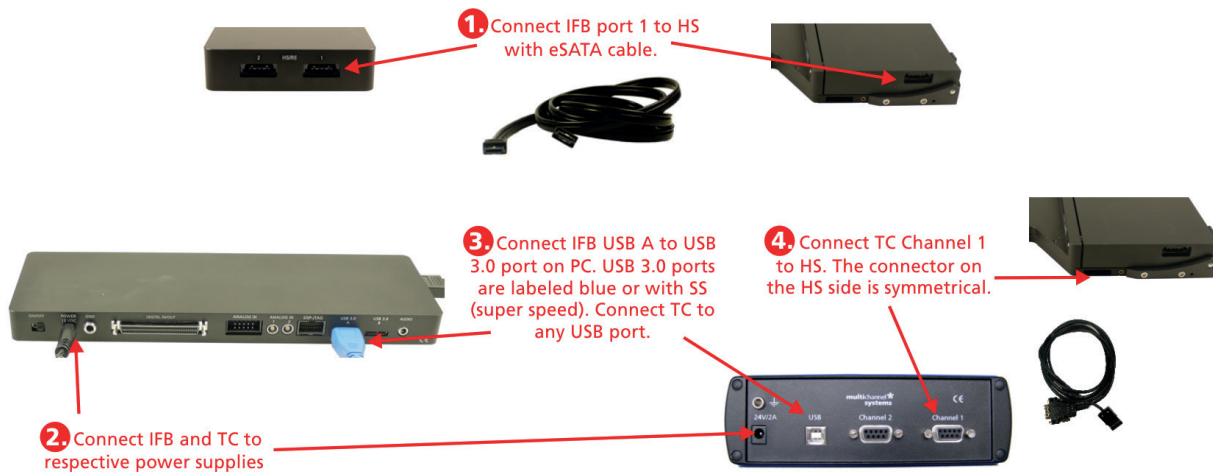## CMOS-MEA5000-System

This tech paper summarizes some general facts and guidelines concerning the CMOS-MEA5000-System from Multi Channel Systems. More detailed information on hard- and software can be found in the respective manual.

1. Setup

1. Connect IFB port 1 to HS with eSATA cable.

3. Connect IFB USB A to USB 3.0 port on PC. USB 3.0 ports are labeled blue or with SS (super speed). Connect TC to any USB port.

4. Connect TC Channel 1 to HS. The connector on the HS side is symmetrical.

**2.** Connect IFB and TC to respective power supplies

A **computer from MCS** with Intel® USB 3.0 ports and a SSD drive for data recording is mandatory. All live data must be recorded to the **SSD drive**, recording to a regular HDD is not possible for performance reasons.

2. Array Setup
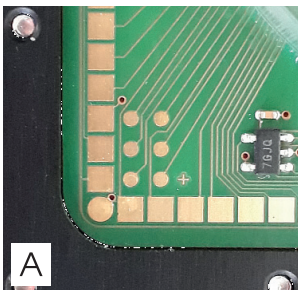
Mount the CMOS array in the amplifier. The array will only fit in one orientation, mind the **rounded corner** on the front left side of the system (A). The dark square in the center of the CMOS array is the actual sensor area, the size is either 1 or 4 mm^2 (B). The surface layer of the CMOS arrays consists of approx. 30 nm of Titanium Oxide and Zirconium Oxide. CMOS arrays are **reusable**, cleaning and sterilization procedures are provided here. Carefully wiping the sensor area with a cotton swab is possible. Use of regular coating procedures as well as slice grids is possible.
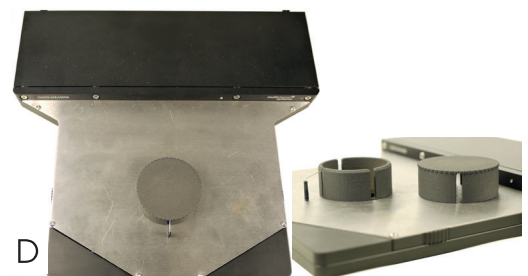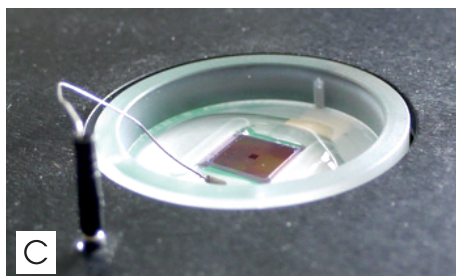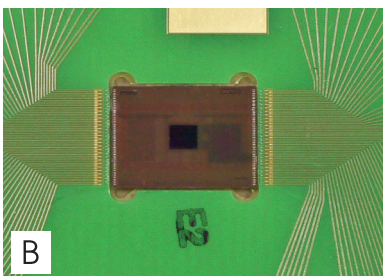

Pixel errors (not working sensor spots) are normal for all CMOS chips. White rows point to bad contact of one connection pin, as all sensors of one row are multiplexed on one contact pin. CMOS sensors are **light sensitive**, so recordings should be performed under **stable light conditions**. The sensor area must be completely covered with medium / PBS. An **Ag/AgCl reference electrode** connected to the system ground must be used (C). Only CMOS MEAs with a **culture chamber** (CMOS-MEA-16/32-CC) have an **integrated reference**. The easiest way to ensure stable light conditions is to cover the array area, and let the chip equilibrate for a few minutes before starting the calibration process in the software (D).

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3. Calibration

CMOS chips are active devices and must be **calibrated** before each use. The calibration runs automatically, and usually takes 2-3 minutes. Don't interrupt the calibration, even if it takes longer. The last step is applying a sine wave stimulation to the bath, which can be seen in the data display. If the sine wave doesn't show up, there was no calibration pulse, and the signals will be in the nV range.
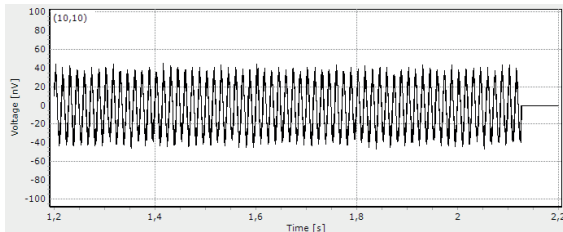
Most likely explanations are:

- For the Test-CMOS-MEA (black PCB chip), wrong connections on the chip, ODD must be connected to EVEN, and EVEN to BATH

- For a CMOS-MEA, the reference electrode might be missing

The final message after successful calibration is **"Finished automatic system calibration"**. After calibration, the **noise level** on the Test-CMOS-MEA should be 1.2 mV peak to peak, for a CMOS-MEA 300-400 µV are normal.

4. Recording

As the CMOS-MEAs contain active components, take care not to switch on and off the recording device with an array inside. Do not open the recording device while the array is powered, always **power down the chip** before opening the amplifier or switching off the device.

The CMOS System generates **large amounts of data**, please consider the file size when recording for longer periods of time. It's possible to start and stop the recording with an internal timer to generate segments of data. Spikes can be **detected on-line,** and recording can be restricted to spike cutouts only, to reduce data volume. Likewise, spike cutouts can be streamed on-line via a pipe connection to a different application for analysis, or even via network to a different PC, using the **Spike Server** function.

5. Stimulation
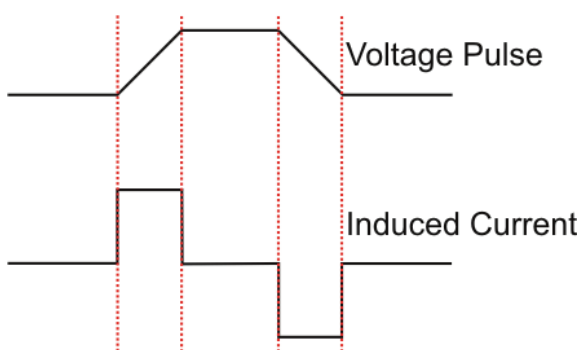
Due to the nature of CMOS sensors, only a changing voltage will induce a current flow, constant voltages have no effect. A **voltage ramp** will induce a constant current in the sample. Only **positive voltages**, up to 3.4 V amplitude can be used. Sine waves or custom waveforms must be shifted to the positive range. About 9 stimulation pads (3x3) minimum are needed for an effective stimulation (valid for retina). In contrast to regular MEAs, neighboring recording sensors will usually **not saturate** during stimulation, so recording in very close proximity to the stimulation site is possible.

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6. Signals

General noise level is much higher on CMOS-MEAs than on regular MEAs with passive metal electrodes. However, the signals are equally lager, so the **signal to noise ratio** is fairly identical. The images below show spikes recorded from primary neurons at DIV10 with a CMOS-MEA (A) and a regular passive MEA (B). For details, please see Zeck et al., 2017.
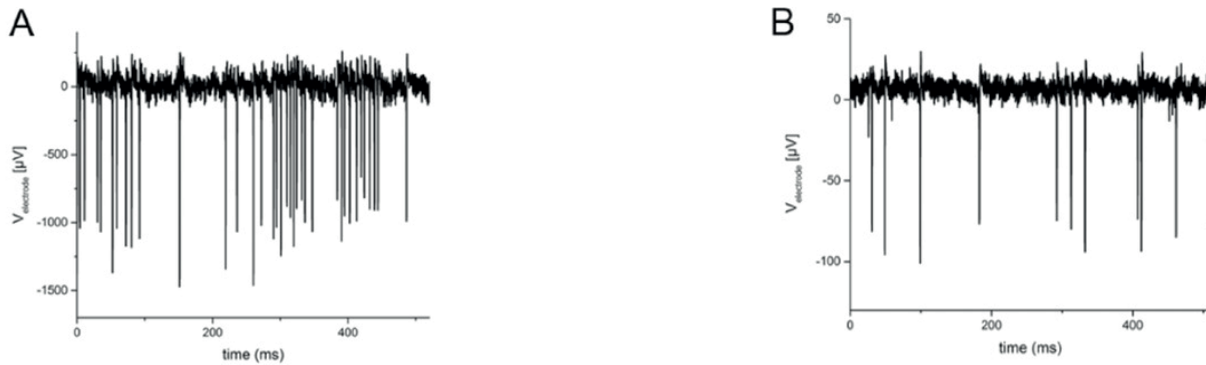
When comparing signals from the CMOS System to data from other application systems, also consider that the filter settings of the device have an significant influence on signal size and shape. See images below, provided by G. Zeck. See below, spikes filtered with different cut-off frequencies.
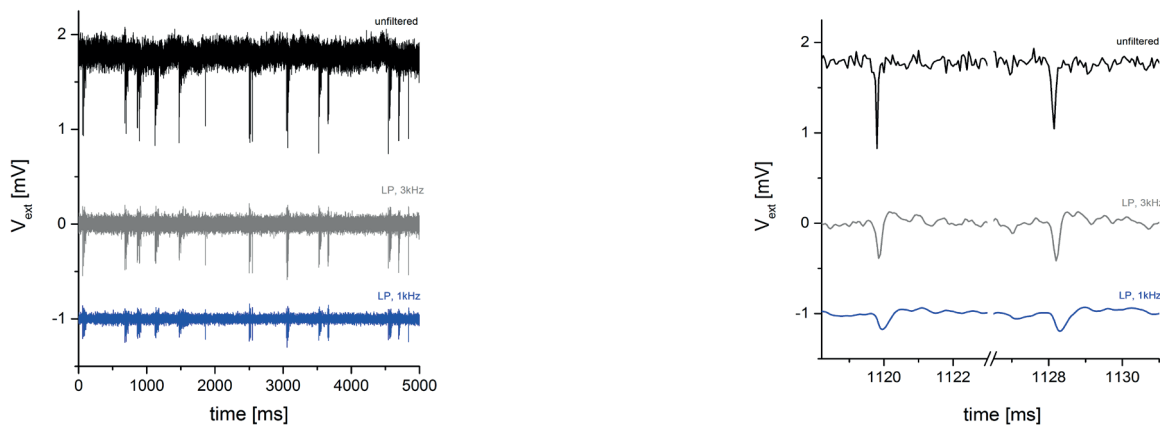
7. Analysis and Export

The CMOS-MEA-Tools provide multiple filtering and spike detection options, and a **fully automated, unsupervised spike sorting** tool. Raw data or sorted spikes can be readily exported, for continued analysis in 3rd party software or platforms like Matlab or Python.

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● in
● Germany