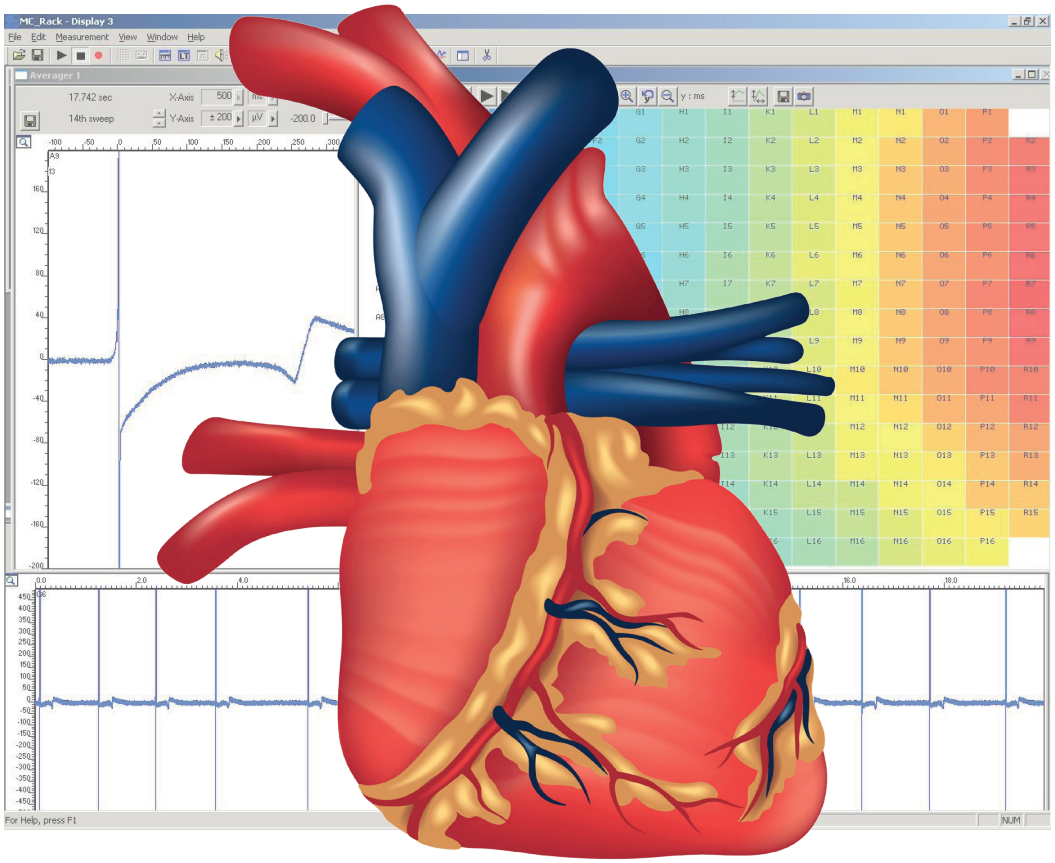
Smart Ephys

multichannel systems
a division of Harvard Bioscience, Inc.



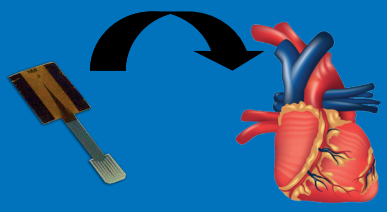
Cardiac applications

- Whole heart *in vitro* & *in vivo*
- Primary cardiomyocytes
- Stem cells and iPS cells
- Cardiac slice recordings

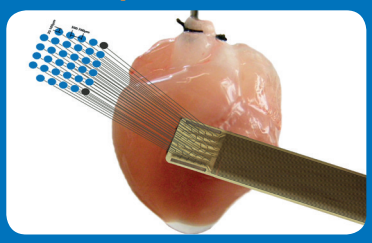
multichannel systems

Innovations in Electrophysiology

Chip on a heart



Chip on a heart

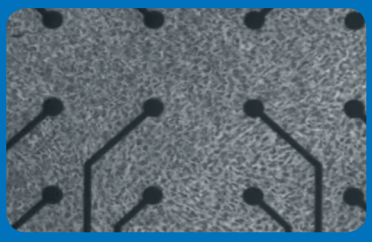


Whole heart *in vitro* & *in vivo*

With flexible microelectrode arrays (FlexMEAs) it is possible to sample electrical activity from every area of a Langendorff-heart or even record *in vivo* from beating hearts of anesthetized animals. Just position the array on your preparation.

- Discover supraventricular and ventricular arrhythmia
- Calculate conduction velocity
- Monitor frequency patterns

Heart on a chip

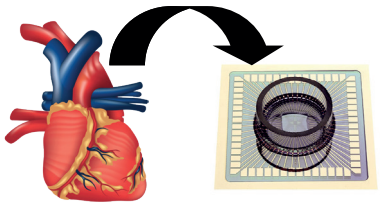


ES and iPS cells

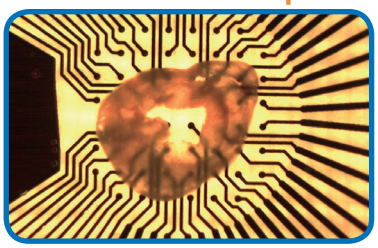
Stem cells are omnipotent or pluripotent cells, that can be differentiated into various subtypes of cardiomyocytes.

- Characterization of the cells
- Drug testing
- Model system for transplantation of the cells into native tissue
- Safety pharmacology

Heart on a chip



Heart on a chip

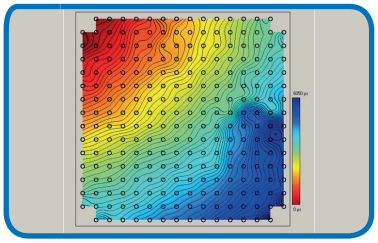


Cardiac slice recordings

After being used in brain research for a long time, slice technology is now used in cardiac research. Cardiac slices are placed on a MEA, from where you can record and analyze the signals from up to 252 electrodes.

- Map transmural signal propagation
- Investigate repolarization disturbances
- Bridge the gap between cells and organs

Heart on a chip



Primary cardiomyocytes

Primary cardiomyocytes can be isolated from neonatal rodents as well as embryonic chicken by simple enzyme digestion. These cells can be cultured and recorded on a variety of microelectrode arrays (MEA)s.

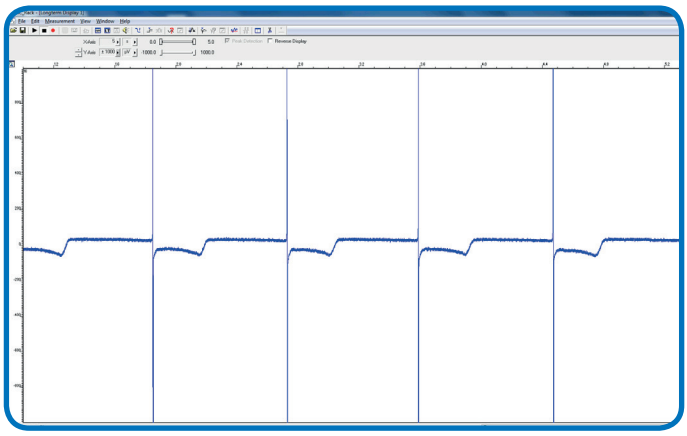
- Drug testing
- Excitation patterns
- Arrhythmia research
- Safety pharmacology

Cardiac field potentials

The recording electrodes are located in close proximity to the beating cardiac cells or tissue. The signal detected is an extracellular field potential. This signal consists of a rapid depolarization (sodium), a plateau phase (calcium), and a repolarization (potassium). Due to the similarity in shape with a ECG the depolarization is compared to QRS complex, whereas the repolarization is referred to as T wave. The field potential is the first negative derivative of the action potential.

The advantages of MEA technology in cardiac research are:

- High spatial resolution
- All components of action potential reflected
- Shape comparable to ECG



Cardiac field potential: The signal recorded by MEA reflects depolarization,plateau and repolarization. Recorded from Cor4U cells from Axiogenesis, Cologne.

In vitro recording systems for 60, 120 or 252 electrodes (A: MEA2100-System) or 288 electrodes in multiwell-format (B).
In vivo system for epicardial mapping (C) and stimulus generators (D).

Amplifiers, stimulators & data acquisition

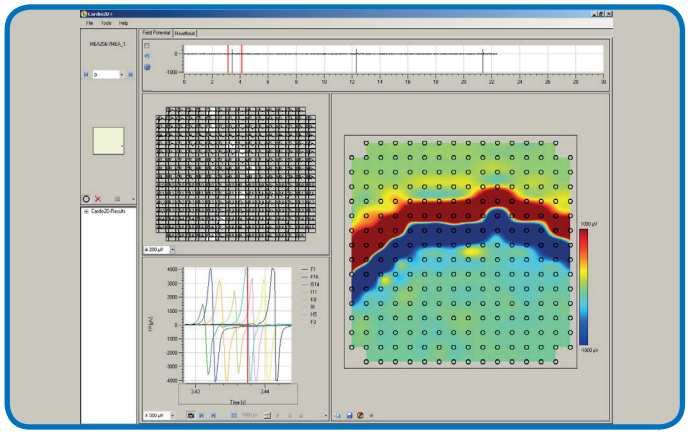
From cell cultures to whole heart preparations, from high throughput to high content, from single components to complete systems: Multi Channel Systems covers the full range of hardware products.

- MEA-System: complete system solutions for *in vitro* recordings from microelectrode arrays (MEAs), including perfusion and data acquisition. System for 60-,120- or 252-electrode MEAs with integrated stimulation (MEA2100-System).
- Multiwell-MEA-System: Solution for high throughput *in vitro* electrophysiology in 24- or 96-well format
- Epicardial mapping systems: flexible and scalable data acquisition systems with the matching electrodes, headstages, and filter amplifiers.
- STG: 2, 4 or 8 channel stimulus generator for current and voltage driven stimulation of cardiomyocytes.

Software

Multi Channel Systems offers various software programs combining complex tasks with a user-friendly interface.

- MC_Rack: The universal software solution for complex questions. Combine instruments into a virtual rack and analyze multiple parameters simultaneously. Analysis can be done online and offline.
- Multi Channel Suite: New software for data acquisition and analysis online and offline. Create your own plug-in for custom analysis.
- Cardio2D: The mapping tool. Measure from as many as 256 electrodes and get your local activation times, isochronous lines, and movies within seconds.
- Compatibility: Software from Multi Channel Systems is compatible with Matlab and Notocord-hem.



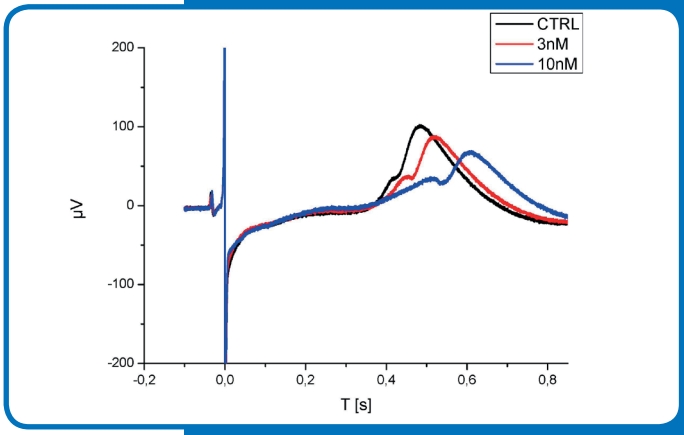
Screenshot of Cardio2D software: Easy wave propagation analysis, isochronous lines, and local activation times.

multichannel systems
Innovations in Electrophysiology

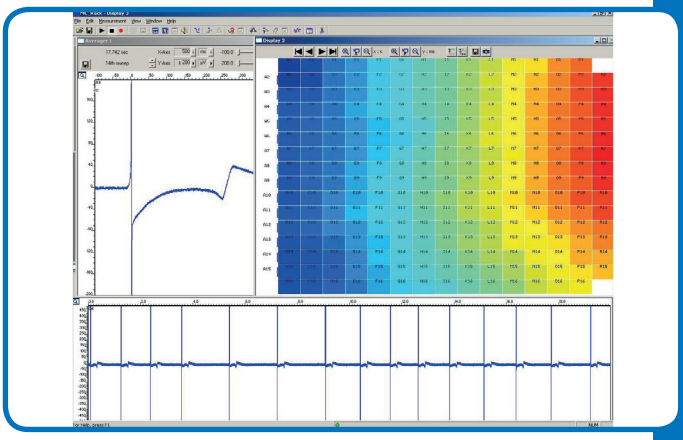
Field potential duration, slope, and amplitude

Drug screening and pharmacological research can be done using MEA technology and stem cell derived or primary cardiomyocytes – or even cardiac slices and whole hearts.

The graph on the left shows that a hERG blocker will prolong the duration of the field potential (E4031, Quinidine, Sotalol), whereas a L Type calcium channel blocker will shorten the field potential (Nifedipine). Sodium channel blockers will reduce slope and amplitude of the depolarisation peak. These effects can either be used to validate the cells on the MEA or to do drug testing with well-characterized cardiomyocytes.



E4031 on Cor4U cardiomyocytes from Axiogenesis, Cologne.



Integrated anlaysis by MC_Rack: Multiple instruments are customized to obtain a multiparameter analysis of cardiac activity.

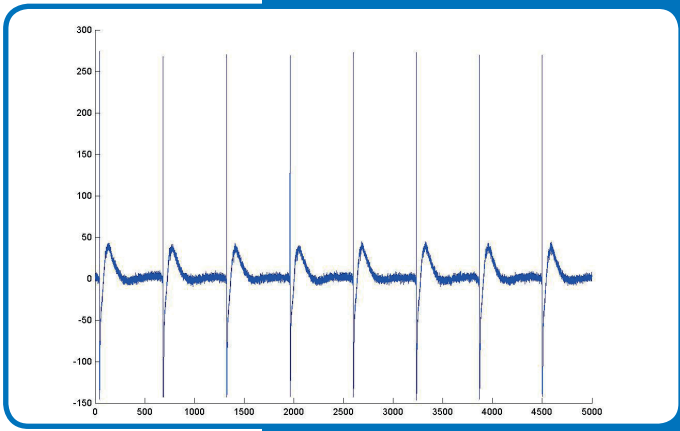
Excitation patterns

On the left-hand side a typical excitation pattern is displayed. It shows the local activation times in reference to a custom defined trigger point. The delays can be displayed as numbers or false color plots. This allows an easy detection of disturbances in the signal conduction pathway. Another parameter monitored is conduction velocity. Our MC_Rack and Cardio2D software will help you to get these results easy and fast and enable you to analyze additional parameters. These tools are especially useful to detect reentry, circling excitations or investigate inhomogenities in conduction velocity plots after lesions or in co-cultures.

Heart rate & proarrhythmic events

Spontaneously beating cardiac preparations can be monitored by viewing heart rate in real-time. The multitude of electrodes allows detecting multiple pacemakers and analyzing clusters separately. Depending on the arrhythmogenic mechanisms drug induced arrhythmia can be studied *in vitro*.

- Plot heart rate / RR interval vs. time
- Detect Early Afterdepolarizations
- Perform beat-beat variability analysis
- Detect tachycardia and bradycardia

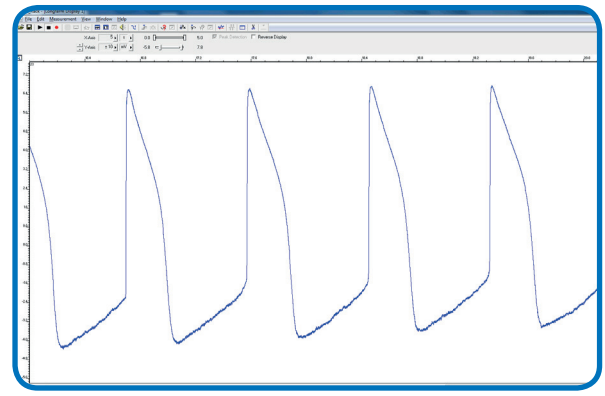


Trace of rhythmicly beating cardiomyocytes derived from stem cells recorded on a MEA.

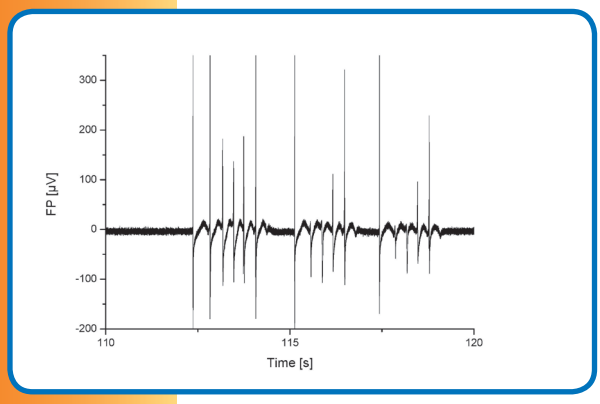
Whole heart *in vitro* & *in vivo*

The electrophysiological mapping of the cardiac surface is an important tool in understanding mechanisms of supraventricular and ventricular arrhythmia.

- FlexMEAs offer recording of electrical activity with highest spatial and temporal resolution.
- Record either field potentials or monophasic action potentials.
- Data acquisition handles up to 256 channels in real-time.



Monophasic action potentials recorded on iPS cardiomyocytes. Courtesy of Axiogenesis, Cologne, and NMI, Reutlingen.



Dofetilide evokes arrhythmia in vitro on cardiomyocytes cultured & recorded on a MEA.

Primary cardiomyocytes

Primary cardiomyocytes are a highly predictive high-content assay system for drug testing. Many drugs prolong the QT interval in the ECG. On a cellular level this corresponds to a prolonged ventricular action potential.

Usually, just one pacemaker triggers the syncytium of cardiomyocytes linked by gap junctions. The mapping allows monitoring important indicators of arrhythmogenic potential of a drug:

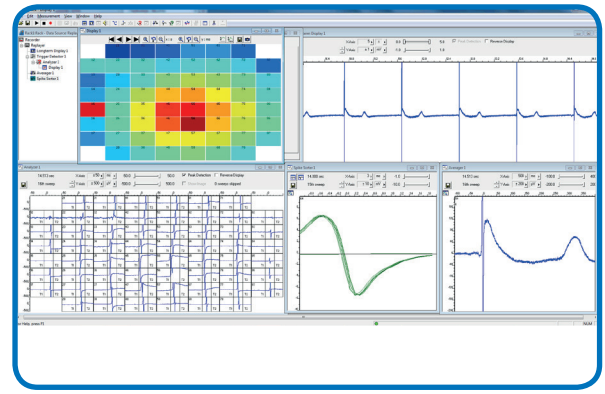
- Drawing isochronous lines
- Measuring conduction velocity

Stem cells and iPS cells

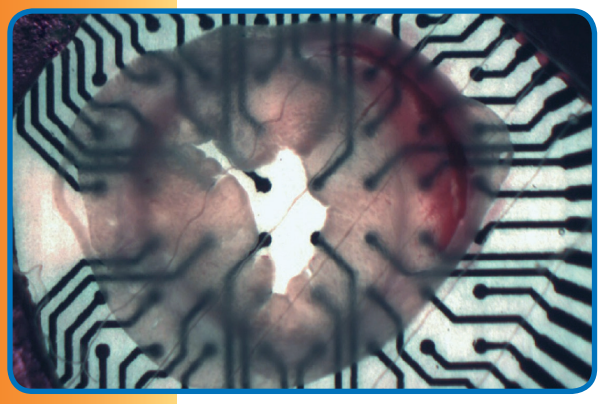
The electrodes of the MEA chip record the field potential of stem cell clusters. Electrophysiological characterization opens up various opportunities:

- Classification of cells as atrial or ventricular phenotype.
- Pharmacological characterization.
- Utilization of validated stem cell derived cardiomyocytes for drug screening.

Multi Channel Systems offers multiwell solutions for high throughput experiments with high impact cardiac data using 24- or 96-well plates with integrated electrodes.



Recording of cardiac field potentials on human iPS cell derived cardiomyocytes. Courtesy of Axiogenesis, Cologne, and NMI, Reutlingen.



Cardiac slice on a 60-electrode MEA. Picture courtesy of NMI Reutlingen.

Cardiac slice recordings

Due to the intact structure of the tissue it is possible to map the excitation from the point of stimulation.

- Obtain field potential parameters from multiple electrodes.
- Detect differences between epicardial, midmyocardial, and endocardial cells.
- Detect transmural dispersion of drug induced ventricular field potential prolongation early and *in vitro*.

Heart on a chip: Microelectrode Array (MEA)-Systems

- Complete, compact, and versatile system solution for *in vitro* recordings from MEAs
- Primary cardiomyocytes, stem cell and iPS cell derived cardiomyocytes, and cardiac slices
- Perfect for long-term recordings
- All systems can be connected to any computer (USB connection)
- One system for a variety of applications (MEA2100-System)
    - Can operate 1, 2 or 4 microelectrode arrays
    - Microelectrode arrays with 60, 120 or 252 electrodes (wide variety of layouts)
    - Integrated stimulator (blanking circuit for simultaneous stimulation and recording without stimulus artifacts)
- Multiwell-MEA-System for higher throughput (Multiwell-MEA-System)
    - Recording system for 24- or 96-well plates with 288 channels with up to 1152 electrodes
    - Integrated stimulator
    - Ambient controlled chamber: Temperature, humidity, and CO_2

Chip on a heart: Epicardial mapping systems

- Complete recording system for *in vivo* and *in vitro* applications
- Portable-ME-Systems: 16 or 32 channels available
    - Filter amplifier and data acquisition integrated in one device
- Stationary-ME-Systems: 64, 128 or 256 channels available
    - Separate devices for data acquisition, filter amplifier and signal collector
- Different adapters for multielectrode arrays and headstages are available.
- High spatial and temporal resolution
- Flexible electrode grids
- Customized arrays for large animals
- Easy handling with convenient analysis software

Distributed by:

Made in Germany

Multi Channel Systems
MCS GmbH

Aspenhaustrasse 21
72770 Reutlingen
Germany

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

sales@multichannelsystems.com
www.multichannelsystems.com