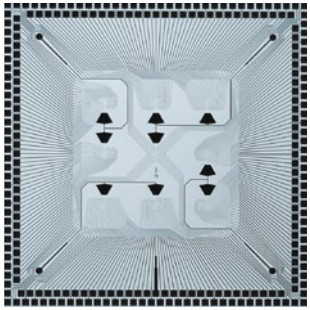
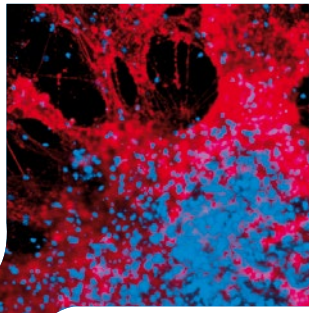
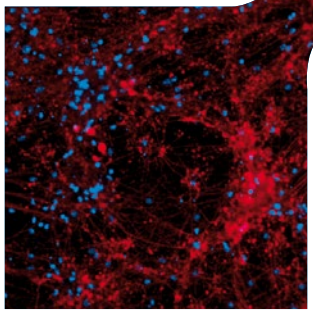
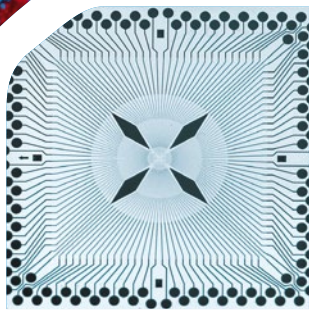
Microelectrode arrays for extracellular electrophysiology

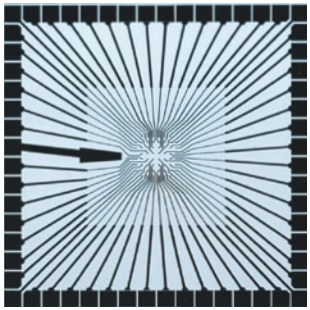
NMI
achieving results

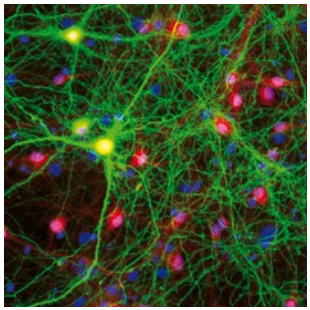


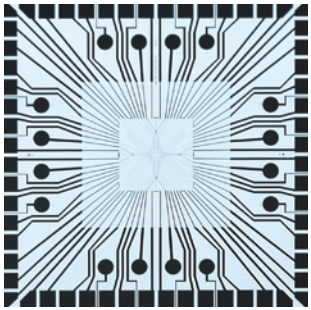


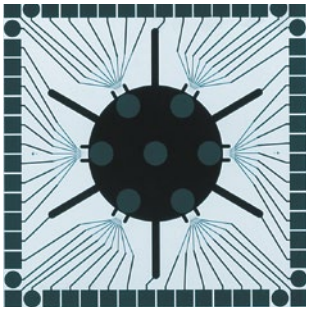












Innovating research
Improving health
Promoting safety

* We are the MEA Powerhouse >>

Microelectrode arrays (MEAs) were introduced in 1972 as a "convenient non-destructive method for maintaining electrical contact with an individual culture, at a large number of points, over periods of days or weeks."[1]

Since then, a broad spectrum of applications employing MEA systems has been established. They have helped to unravel the fundamental physiological functions of the brain, such as memory, learning, circadian rhythms, and neuronal development. Through MEAs, we are beginning to broaden our understanding of cognitive diseases, such as Alzheimer's disease and epilepsy. Advancements in MEA technology have given new momentum to cardiovascular, stem cell, and retina research.

The Natural and Medical Sciences Institute (NMI) operates at the interface between the life sciences and material sciences. Our broad, interdisciplinary expertise was invaluable in developing the potential of MEA technology and we produced our first MEA in the late 1980s. Today, our production line is standardized and the high quality of MEAs manufactured in state-of-the-art cleanrooms is guaranteed.

From the very beginning, we made a commitment to offer scientists the perfect tool, one which enabled them to find answers to questions – however extraordinary – concerning electrophysiology.

[1] Thomas, C. A. Jr. et al. A miniature micro-electrode array to monitor the bioelectric activity of cultured cells. Exp Cell Res. 1972 Sept;74(1):61-66.

Our partner, Multi Channel Systems MCS GmbH, serves as our link to customers and users of MEA technology. Diverse layouts and different types of electrodes are being delivered across the globe by MCS to more than 700 academic and industrial laboratories. Many publications thus refer to our MEAs as MCS-MEAs.

In this booklet we present our track record, which shows how excellent scientific results can be achieved by using our MEAs. We cite publications relating to basic research, therapeutic concepts, drug screening, and neurotechnology – as a whole, they bear witness to the wide range of questions that have been answered by means of MEAs in recent time. We also quote our industrial customers, as they testify to how MEAs have also found their way into the pharmaceutical sector where they excel in tests of efficacy and safety. Lastly, we present an overview showing how MEAs work and why they are so special. We also outline the MEA innovations we offer for innovating research, improving health and promoting safety.

We are the MEA powerhouse!

We are committed to providing the perfect tool to scientists.

NMI Natural and Medical Sciences Institute at the University of Tübingen

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Innovating research »

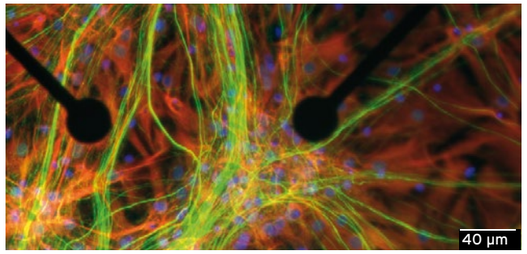
"The major benefit of the MEA system is that it can be used to do phenotypic drug screening from cultured neurons that form functional networks retaining physiological activity and plasticity. With it we study the maturation of neurons by means of their general electrophysiological properties and developmental changes in their activity patterns. A further outstanding feature of the system is the robust and easy recording of acute brain slices."

Dr. Frédéric Knoflach, Principal Scientist,
F. Hoffmann-La Roche Ltd, Switzerland.

10 µm

Picture: Primary rat cortical cultures characterized by immunostainings over time. Kindly provided by Helena Hogberg, PhD, Johns Hopkins Center for Alternatives to Animal Testing, United States.

The MEA system – answering fundamental questions about the brain, eye and heart



Established methods and technologically sophisticated measuring instruments are valuable tools in science. In recent years, the MEA system has proven to be a reliable workhorse and, as such, has played an important role in resolving important questions on the function of the brain, eye and heart – as documented in many excellent publications in these fields of research.

Picture: Primary rat cortical cultures characterized by immunostainings over time. Kindly provided by Helena Hogberg, PhD, Johns Hopkins Center for Alternatives to Animal Testing, United States.

Investigating brain functions
By combining extracellular stimulation and recording paradigms with MEAs, it has for many years been possible to carry out intensive investigations of information processing in networks [2]. MEAs are powerful tools for observing the dynamics of neuronal networks in both time and space [3], which is essential for any neurobiologist who monitors activity patterns in acute slices and dissociated neuronal networks over several hours or days. The results led, e.g., to the interesting hypothesis that neuronal avalanche activity is a signature of neuronal assemblies, which are strong candidates for the representation of information in neuronal networks [4].

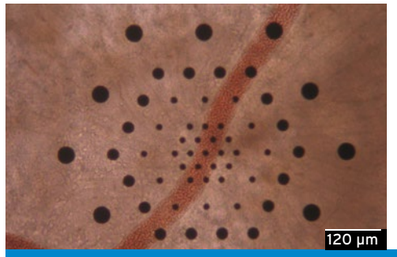
Searching for the master pacemaker
MEAs allow researchers interested in circadian rhythms to conduct for the first time – continuous, long-term measurements *in vitro*. A US-based research group used microelectrode recordings as a supplementary method to determine the role of neurotransmitter vasoactive intestinal polypeptide within the mammalian suprachiasmatic nucleus (SCN), a master circadian pacemaker. The MEA system enabled them to perform extracellular and non-invasive, long-term recordings of the firing rates of SCN neurons, for a minimum of five days, from 60 electrodes simultaneously [5].

Innovating research

Retina and the correct circuitry to the visual cortex
MEAs have been intensively used over many years for the study of activity in explanted retinas [6]. Developmental biologists from the University of San Francisco addressed the question about whether patterned, spontaneous retinal activity was required for the development of precise connections to the visual cortex during the first postnatal week. Besides other methods, they used MEAs to successfully record spikes from wild-type and pharmacologically manipulated retinal ganglion cells [7].

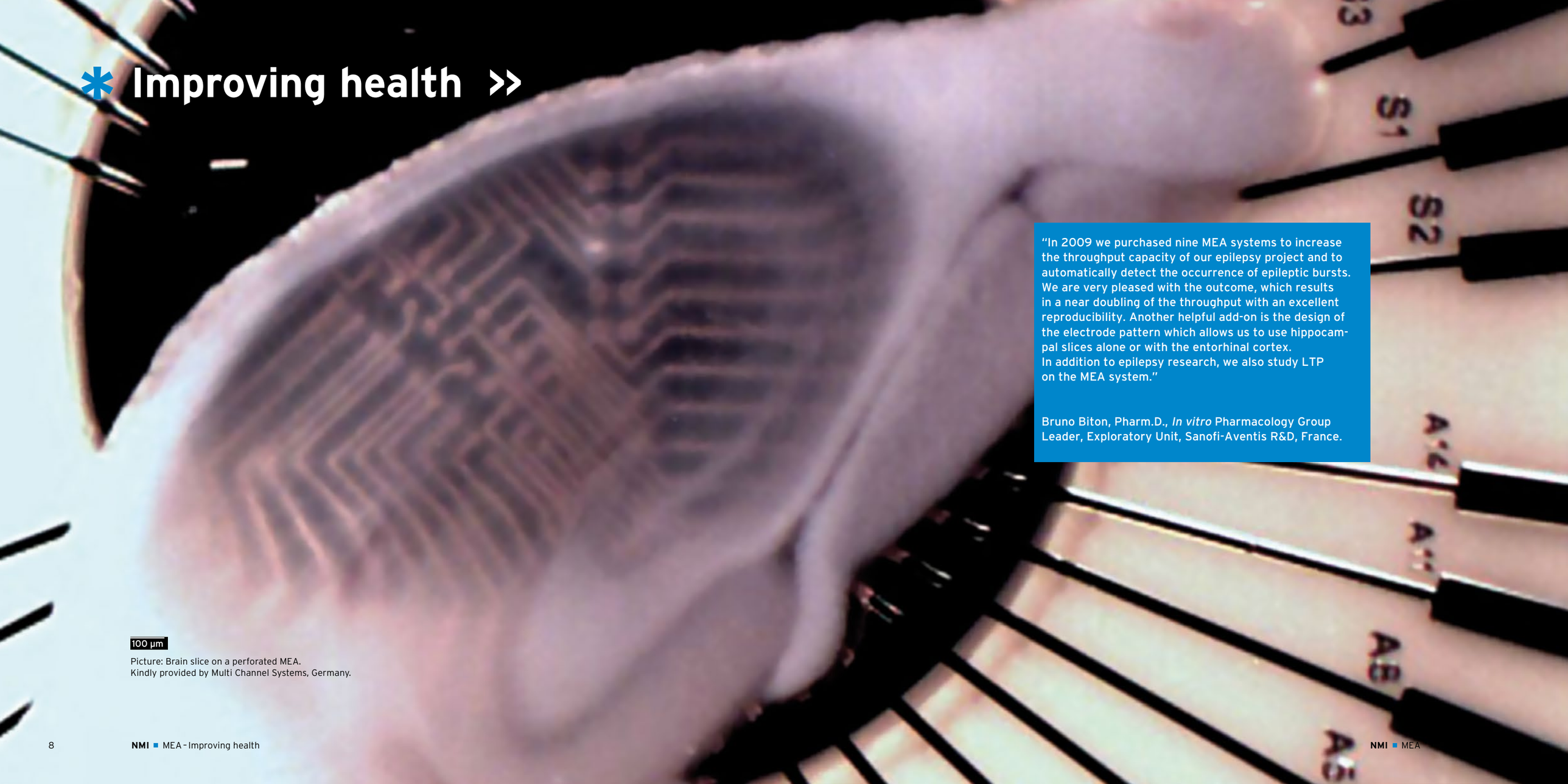
Cardiac cells on the advance
MEAs are also implemented in cardiac research: the system helped in characterizing one of the earliest human cardiovascular progenitor cells in the development of the human heart and revealed that these cells were electrically coupled to one another [8]. Other researchers used extracellular recordings to characterize the electrophysiological properties of human induced pluripotent [9] and embryonic stem cell-derived cardiomyocytes [10].

Picture: A rat retina with blood vessel, flat mounted on a MEA with a hexagonal electrode array.
Source: NMI, Germany.



[2] Marom, S. et al. Development, learning and memory in large random networks of cortical neurons: lessons beyond anatomy. Q Rev Biophys. 2002 Feb;35(1):63 – 87.
[3] Morin F.O. et al. Investigating neuronal activity with planar microelectrode arrays: achievements and new perspectives. J Biosci Bioeng. 2005 Aug;100(2):131 – 43.
[4] Plenz D. et al. The organizing principles of neuronal avalanches: cell assemblies in the cortex? Trends Neurosci. 2007 Mar;30(3):101 – 10.
[5] Aton S. J. et al. Vasoactive intestinal polypeptide mediates circadian rhythmicity and synchrony in mammalian clock neurons. Nat Neurosci. 2005 Apr;8(4):476 – 83.
[6] Meister M et al. Multi-neuronal signals from the retina: acquisition and analysis. J Neurosci Methods. 1994 Jan;51(1):95 – 106.
[7] Cang J. et al. Development of precise maps in visual cortex requires patterned spontaneous activity in the retina. Neuron. 2005 Dec 8;48(5):797 – 809.
[8] Yang L. et al. Human cardiovascular progenitor cells develop from a KDR+ embryonic-stem-cell-derived population. Nature. 2008 May 22;453(7194):524 – 8.
[9] Zwi L. et al. Cardiomyocyte differentiation of human induced pluripotent stem cells. Circulation. 2009 Oct 13;120(15):1513 – 23.
[10] Harding S. E. et al. The human embryonic stem cell-derived cardiomyocyte as a pharmacological model. Pharmacol Ther. 2007 Feb;113(2):341 – 53.

Improving health »



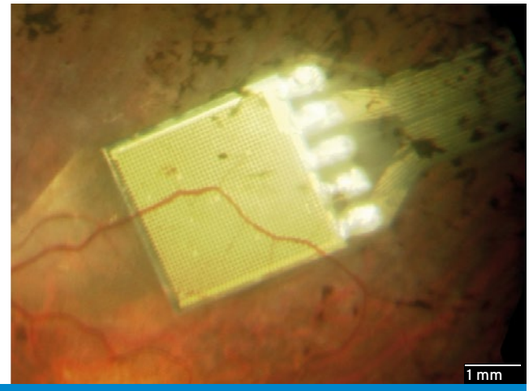
"In 2009 we purchased nine MEA systems to increase the throughput capacity of our epilepsy project and to automatically detect the occurrence of epileptic bursts. We are very pleased with the outcome, which results in a near doubling of the throughput with an excellent reproducibility. Another helpful add-on is the design of the electrode pattern which allows us to use hippocampal slices alone or with the entorhinal cortex.
In addition to epilepsy research, we also study LTP on the MEA system."

Bruno Biton, Pharm.D., *In vitro* Pharmacology Group Leader, Exploratory Unit, Sanofi-Aventis R&D, France.

100 µm

Picture: Brain slice on a perforated MEA.
Kindly provided by Multi Channel Systems, Germany.

The MEA system – a reliable partner in establishing new therapeutic concepts



Only a proportion of known diseases are curable today. The development of new treatments follows multiple strategies and extends from classical pharmaceutical drug development up to gene therapy and stem cell research. MEA recordings are often successfully used as an adjuvant method to conduct functional studies on different cells and tissues.

Picture: Fundus photography of a human eye showing a subretinal implant that converts incident light into an electrical signal which is then transmitted onto the bipolar cells. Kindly provided by Retina Implant AG, Germany.

New approaches against blindness
Retinitis pigmentosa is a congenital disease that leads to incurable blindness, and affects two million people world-wide. A joint project involving several international research groups was able to demonstrate that the expression of the archaebacterial vision pigment halorhodopsin in cones of blind mouse models successfully restored the light sensitivity. MEAs were used to record spike trains from control and halorhodopsin-injected mouse retinal ganglion cells [11]. MEAs also have been used as supportive technology to unravel the cellular basis of retinal hypovascularization diseases like the rare Norrie Syndrome, which is characterized by congenital blindness [12].

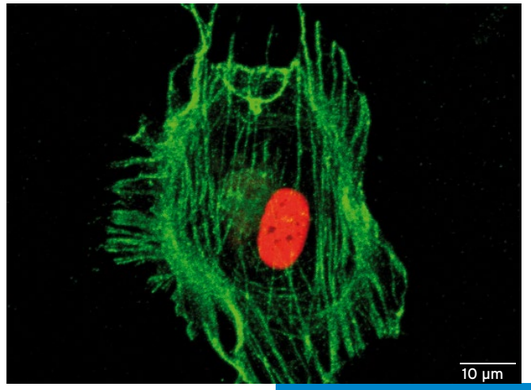
Restoring vision via electrical stimulation
Restoring vision in blind people, via retinal implants, is one of the hot topics in neurotechnology. Research on implants has benefited from the use of MEAs for multi-site electrical stimulation of retinas [13, 14] and key lessons on how to evoke spatio-temporal, well-ordered network activity in the diseased retina have been learned. As a result, in clinical trials, blind patients who received a subretinal implant were able to recognize faces, read words, and move around without assistance: the chip was basically designed according to parameters obtained from experiments in which chicken retinas were attached to MEAs [15].

Ultra-sensitive: Alzheimer mouse model on MEA
The microelectrode technology is also considered as a rapid and effective tool for analyzing transgenic mouse models with Alzheimer's disease pathology. Due to neuronal responses across 60 electrodes, Belgian researchers were able to detect hippocampal, sub-region specific synaptic changes even before the typical amyloid or tau pathology was evident [16].

Using induced pluripotent stem-cell derived cardiomyocytes against cardiac death
Medical research expects great potential from human induced pluripotent stem cells (iPSC).
An Israeli research group is examining whether this technology might one day help to discover new therapies against one of the inherited arrhythmogenic syndromes (LQTS), which can lead to sudden cardiac death. Field potential recordings with MEAs could confirm findings which showed that LQTS patient iPSC-derived cardiomyocytes exhibit the significant, pathologic prolongation of the action potential duration: MEAs are thus suitable for studying disease mechanisms and helpful in developing new therapies [17].

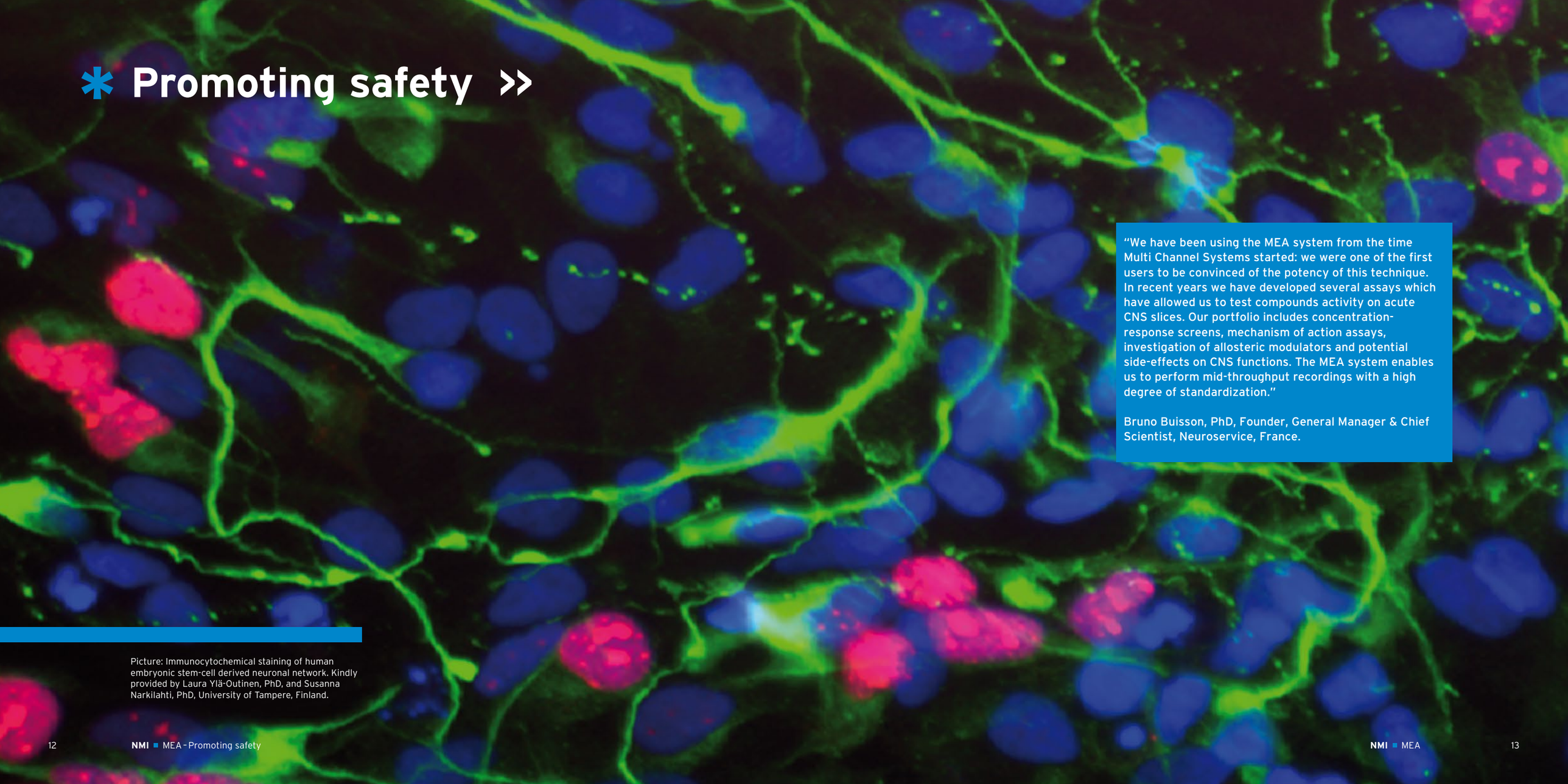
Picture: Human embryonic stem-cell derived cardiomyocyte. Kindly provided by Prof. Sian E. Harding and Dr. Nadire Ali, Imperial College, United Kingdom.

Improving health –
restoring function



[11] Busskamp V. et al. Genetic reactivation of cone photoreceptors restores visual responses in retinitis pigmentosa. Science. 2010 Jul 23;329(5990):413 – 7.
[12] Ye X. et al. Norrin, frizzled-4, and Lrp5 signaling in endothelial cells controls a genetic program for retinal vascularization. Cell. 2009 Oct 16;139(2):285 – 98.
[13] Stett A. et al. Electrical multisite stimulation of the isolated chicken retina. Vision Res. 2000;40(13):1785 – 95.
[14] Sekirnjak C. et al. High-resolution electrical stimulation of primate retina for epiretinal implant design. J Neurosci. 2008 Apr 23;28(17):4446 – 56.
[15] Zrenner E. et al. Subretinal electronic chips allow blind patients to read letters and combine them to words. Proc Biol Sci. 2011 May 22;278(1711):1489 – 97.
[16] Chong S. A. et al. Synaptic dysfunction in hippocampus of transgenic mouse models of Alzheimer's disease: a multi-electrode array study. Neurobiol Dis. 2011 Dec;44(3):284 – 91.
[17] Itzhaki I. et al. Modelling the long QT syndrome with induced pluripotent stem cells. Nature. 2011 Mar 10;471(7337):225 – 9.

Promoting safety »



"We have been using the MEA system from the time Multi Channel Systems started: we were one of the first users to be convinced of the potency of this technique. In recent years we have developed several assays which have allowed us to test compounds activity on acute CNS slices. Our portfolio includes concentration-response screens, mechanism of action assays, investigation of allosteric modulators and potential side-effects on CNS functions. The MEA system enables us to perform mid-throughput recordings with a high degree of standardization."

Bruno Buisson, PhD, Founder, General Manager & Chief Scientist, Neuroservice, France.

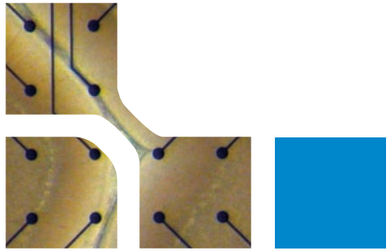
Picture: Immunocytochemical staining of human embryonic stem-cell derived neuronal network. Kindly provided by Laura Ylä-Outinen, PhD, and Susanna Narkilahti, PhD, University of Tampere, Finland.

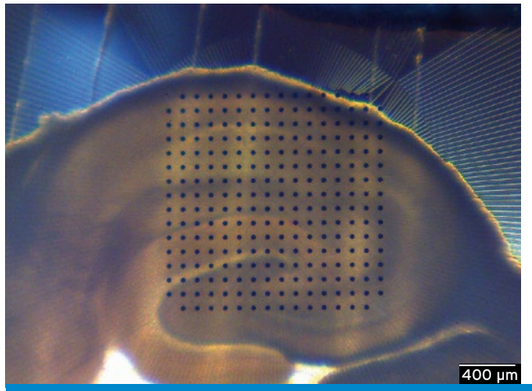
The MEA system – for meaningful, sensitive and reliable screening

Scientists are always searching for reliable and efficient *in vitro* screening methods to identify new drug candidates. Toxicologists require appropriate models to identify noxious environmental poisons. The MEA system is becoming increasingly popular in conducting many types of screening studies because it completely meets the individual needs of a broad spectrum of researchers.

Targeted drug development

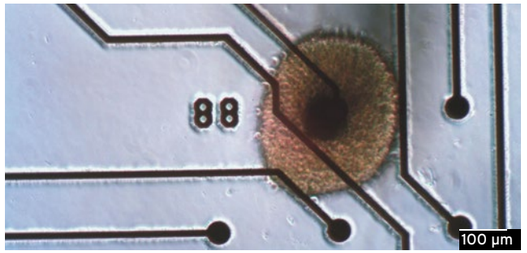
The hippocampus and MEA harmonize well with each other. A team of French scientists showed that acute hippocampal slices contain every important neuronal player necessary for conducting network studies with classic protocols such as paired-pulse, LTD or LTP. Pharmacological testing of compounds was done with significant throughput. Further benefits are the high sensitivity and region-specific resolution of compound effects through multi-sites recordings [18].





Picture: Hippocampal slice on a MEA with 256 electrodes.
Source: NMI, Germany.

[18] Steidl E. M. et al. The adult rat hippocampal slice revisited with multi-electrode arrays. Brain Res. 2006 Jun 22;1096(1):70 – 84
[19] Chong S. A. et al. Synaptic dysfunction in hippocampus of transgenic mouse models of Alzheimer's disease: a multi-electrode array study. Neurobiol Dis. 2011 Dec;44(3):284 – 91.
[20] Pfeiffer T. et al. Rapid functional evaluation of beta-cells by extracellular recording of membrane potential oscillations with microelectrode arrays. Pflugers Arch. 2011 Dec;462(6):835 – 40.
[21] Harding S. E. et al. The human embryonic stem cell-derived cardiomyocyte as a pharmacological model. Pharmacol Ther. 2007 Feb;113(2):341 – 53.
[22] Braam S. R. et al. Cardiomyocytes from human pluripotent stem cells in regenerative medicine and drug discovery. Trends Pharmacol Sci. 2009 Oct;30(10):536 – 45.
[23] Zwi L. et al. Cardiomyocyte differentiation of human induced pluripotent stem cells. Circulation. 2009 Oct 13;120(15):1513 – 23.



Picture: Single mouse islet of Langerhans.
Source: NMI, Germany.

[24] Camelliti P. et al. Adult human heart slices are a multicellular system suitable for electrophysiological and pharmacological studies. J Mol Cell Cardiol. 2011 Sep;51(3):390 – 8.
[25] Itzhaki I. et al. Modelling the long QT syndrome with induced pluripotent stem cells. Nature. 2011 Mar 10;471(7337):225 – 9.
[26] Shafer TJ (2011). Neurotoxicity Testing Using Microelectrode Arrays (MEAs): A Growing Trend. http://alttox.org/ttrc/toxicity-tests/neurotoxicity/way-forward/shafer/
[27] Novellino A. et al. Development of Micro-Electrode Array Based Tests for Neurotoxicity: Assessment of Interlaboratory Reproducibility with Neuroactive Chemicals. Front Neuroeng. 2011 Apr 27;4:4.
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[30] Ylä-Outinen L. et al. Human cell-based micro electrode array platform for studying neurotoxicity. Front Neuroeng. 2010 Sep 30;3. pii: 111.

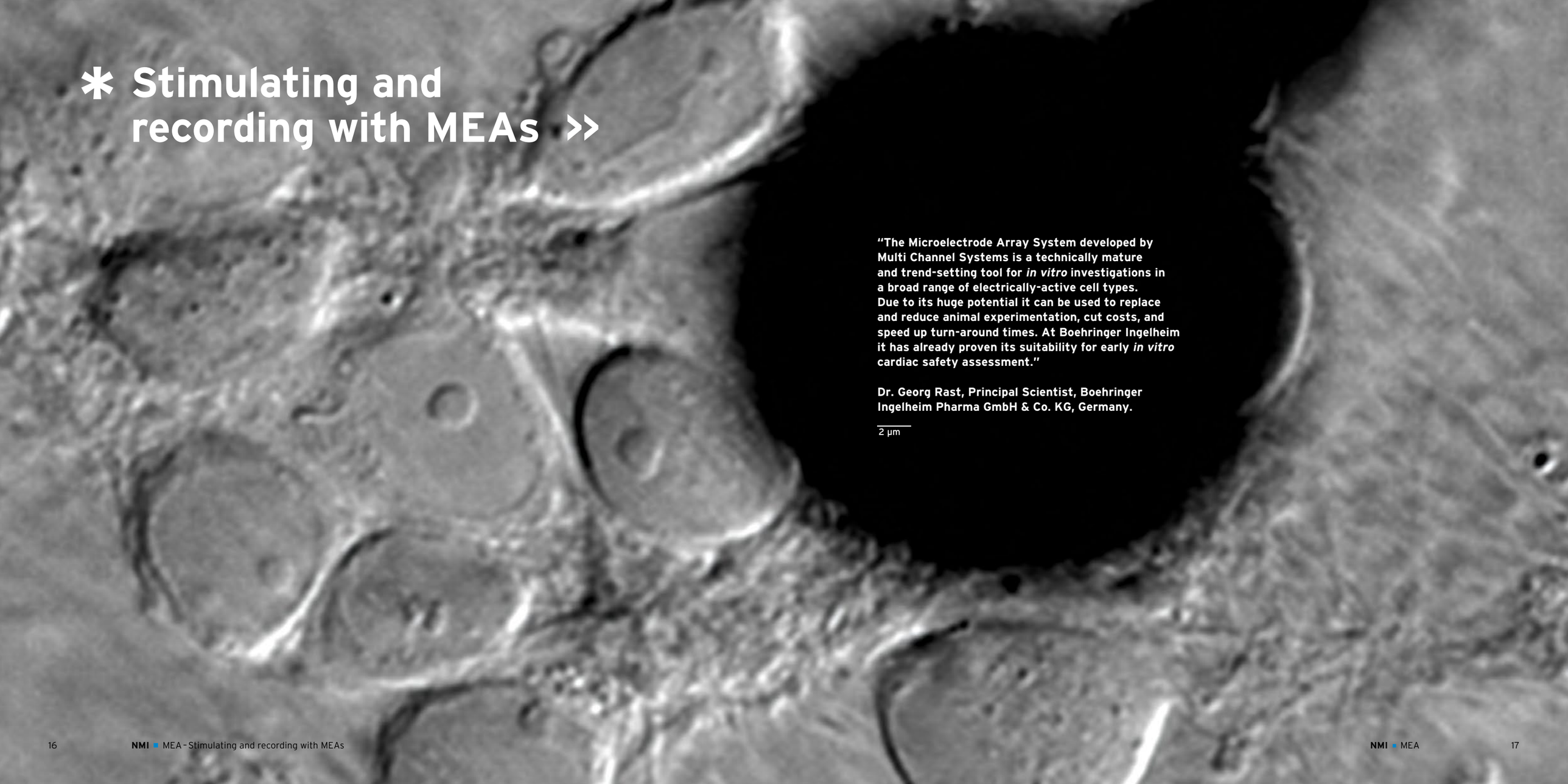
Screening goes personalized

A rapidly advancing field is the establishment of disease- and patient-specific screening methods. Studies have shown that Alzheimer mouse models can be employed with MEAs in identifying new therapeutic agents [19]. Another approach uses primary islets of Langerhans to test antidiabetic drugs in real-time. This method also has the potential to check the metabolic integrity of human donor islet cells prior to transplantation [20]. Human embryonic and human pluripotent stem cell-derived cardiomyocytes [21 – 23], myocardial slices from patients' heart biopsies [24], and patient-specific long-QT stem cell lines [25] in the MEA system are also suitable for investigations on the safety and efficacy of pharmacological agents. Moreover, these preparations hold great promise for the study of heart failure and cardiovascular regenerative medicine.

Meeting the goals of neurotoxicity testing

The assessment of neurotoxicity is a major challenge in the development and registration of new chemicals and drugs. Current guidelines recommend the use of *in vivo* tests for systemic toxicity evaluation. Recently, the U.S. Environmental Protection Agency focused on the fact that MEAs represent a useful system for *in vitro* toxicity testing, including developmental neurotoxicity testing [26].
Studies performed on neuronal cells have shown that MEAs provide an alternative method with respect to reproducibility, sensitivity, throughput, and long-term measurements [27 – 30].

* Stimulating and recording with MEAs »

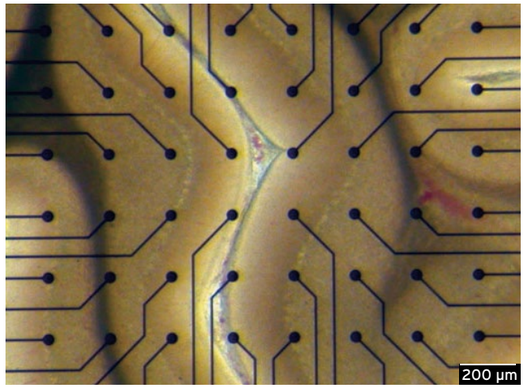


"The Microelectrode Array System developed by Multi Channel Systems is a technically mature and trend-setting tool for *in vitro* investigations in a broad range of electrically-active cell types. Due to its huge potential it can be used to replace and reduce animal experimentation, cut costs, and speed up turn-around times. At Boehringer Ingelheim it has already proven its suitability for early *in vitro* cardiac safety assessment."

Dr. Georg Rast, Principal Scientist, Boehringer Ingelheim Pharma GmbH & Co. KG, Germany.

2 µm

Principles of extracellular stimulation and recording with MEAs



Basically, a MEA is a two-dimensional arrangement of microelectrodes for the extracellular stimulation and monitoring of electrical activity in electrogenic cells, either isolated or in tissue samples.

A unique feature of MEAs is the opportunity for two-way interfacing of cells and tissue. While listening to the cellular network by recording at many sites, simultaneous stimulation can be done with the same array and even the same electrodes that were used for the recording [31].

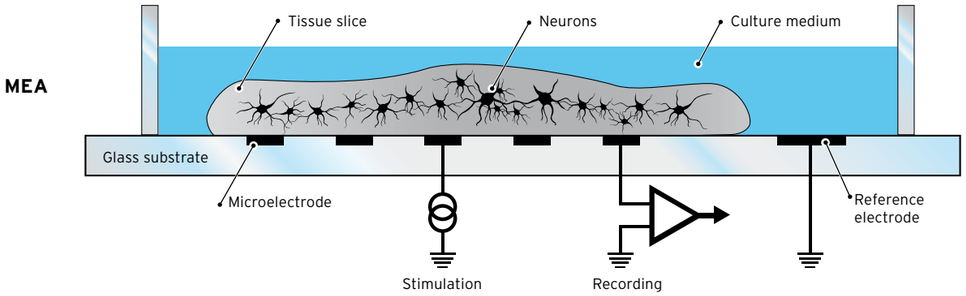
Picture: Cerebellar slice on MEA. Kindly provided by Prof. Dr. Ulrich Egert, Albert-Ludwigs University Freiburg, Germany.

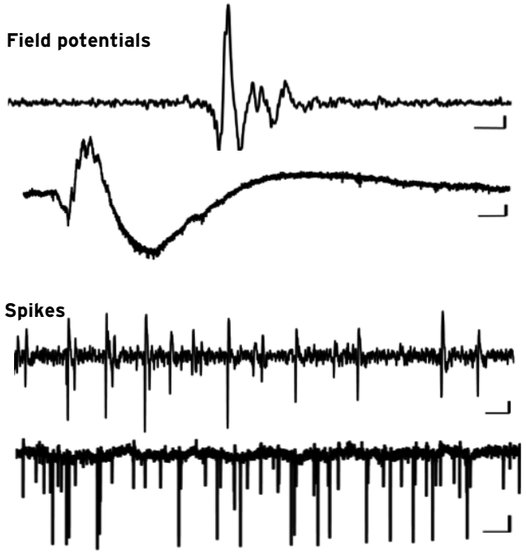
Recording with MEAs
The electrical activity of cells is always accompanied by the flow of current through the fluid surrounding the cells. Related to the current is an extracellular voltage profile that varies in time and space, according to the time course of the temporal activity as well as the spatial distribution and orientation of the cells. Through MEAs, this extracellular voltage profile can be sampled simultaneously from many recording sites. Typically, signals from sources within a radius of 30 µm around a microelectrode can be detected. Microelectrodes should offer low impedance to ensure low noise.

Electrical stimulation through MEAs
By applying voltage or current pulses to the microelectrodes, a current flow through the dish is produced. It generates a transient voltage gradient that polarises the membrane of cells and leads to excitation or inhibition of electrical activity of cells.

The voltage of the electrodes must always be as low as possible in order to avoid damage to the electrodes or cells. Thus, microelectrodes should offer a high charge-injection capacity, a parameter marking the limit of the electrode being charged, without leading to an irreversible electrochemical reaction at the electrode/electrolyte interface.

[31] Stett A. et al. Biological application of microelectrode arrays in drug discovery and basic research. Analytical and Bioanalytical Chemistry, 2003 Aug 16; 377, 486 – 495.



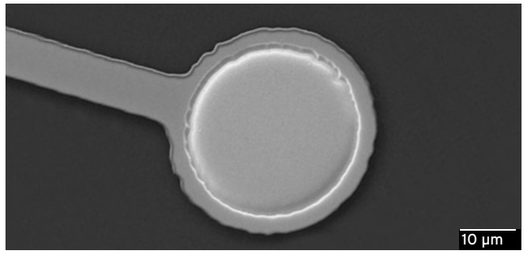


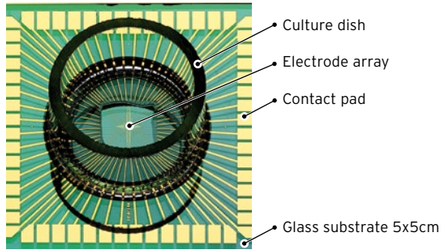
By means of MEAs, voltages above the electrodes are measured with respect to the reference electrode located in the bath solution. The recordings exhibit slow field potentials (overlapping potentials of larger populations of cells), as well as fast spikes, the extracellular correlate of action potentials generated by a single neuron. These components may occur as a mix that can be separated by appropriate filtering and digital processing of the raw voltage traces. The better the signal-to-noise ratio and resolution in space and time, the more accurate is the signal analysis.

Recordings (from above): Slow potential from cortex slice (scale bar 5 ms, 20 µV), light-evoked electroretinogramm from *ex vivo* retina (5 ms, 50 µV), spontaneous spikes from dissociated cortex neurons (10 ms, 10 µV), spiking retinal ganglion cells in *ex vivo* retina (50 ms, 50 µV). Source: NMI, Germany.

The MEA system – how it works

Principles of extracellular stimulation and recording with MEAs





Low noise – high signal – long life
As planar microelectrodes have high impedance, they are usually platinized, because this reduces the impedance and thus increases the signal-to-noise ratio. However, Pt-treated microelectrodes are not stable over prolonged periods and need to be re-platinized before they are re-used. Our standard MEA electrode is made either from stable nanocolumnar TiN or nanoporous IrOx, which reduces the noise level of the electrode and allows continuous and reliable electrical stimulation, even over a time period of several weeks. We routinely observe a noise level of less than +/- 10 µV, measured with a 30 µm MEA electrode at a frequency cut-off of 1 Hz to 3 kHz and a sampling rate of 25 kHz.

The electrodes are mechanically stable and withstand even repeated cleaning and sterilization procedures in autoclaves. This guarantees that the MEAs can be re-used many times.

Glass on top comes out on top
As the surface of the MEAs serves as the bottom of a culture dish, it must be carefully prepared. Our standard MEA is covered by a specifically processed glass layer (Si_3N_4) which has proved its merit in several challenging cell culture experiments. Glass is the ideal substrate for protein coatings such as poly-D-lysine, laminin, and fibronectin used for promoting cell adhesion and cell growth. MEAs only comprise glass, biocompatible metallic lanes and electrodes – there are no polymers or resist coating and no soldered connections.

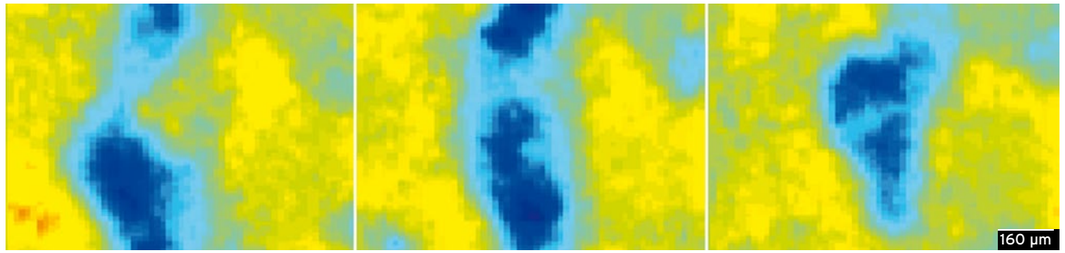
Picture (left): TiN microelectrode for electrical stimulation and recording. Source: NMI, Germany.

Picture (right): MEA with culture dish.
Source: Multi Channel Systems, Germany

Looking into the future

Neurochips – the next generation of electrode arrays

The very latest technology: Neurochips, the successors of the pioneering "Fromherz" chips, feature intermingled sensor and stimulation sites – perfectly designed for closed-loop experiments.



Hundreds are not enough: The next generation of electrode arrays features thousands of recording and stimulation sites that are only separated by a few microns. The first prototype of these neurochips, featuring 128 x 128 recording sites, was used to record electrical activity in snail neurons [32]. Applications were extended to neural cultures and tissues from hippocampus, cerebellum or retina. In many cases, the propagation of electrical activity could be imaged at sub-cellular resolution. In addition, capacitive stimulation with arbitrary stimulus shapes was observed [33]. It allowed for repetitive and long-term stimulation without any electrochemistry at the electrode/cell interface.

A neurochip resembles a digital camera. The two technologies share on-chip integrated electronics that allow fast read-outs from the densely packed electrodes/pixels and instant signal amplification [34]. The main conceptual difference is that one system images visual activity and the other (the much faster) electrical activity. Neurochips, which demand high computational power, will complement microelectrode applications wherever high resolution electrical imaging is desired.

Pictures: Propagating local field potentials (blue) recorded by a neurochip with 128 x 128 recording sites in a 1 mm^2 area of a blind mouse retina. Kindly provided by Dr. Günther Zeck, NMI, Germany. Published by [35].

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[33] Eickenscheidt, M. et al. Electrical stimulation of retinal neurons in epiretinal and subretinal configuration using a multicapacitor array, J. Neurophysiol. 2012 May;107(10):2742 – 5
[34] Hierlemann, A. Growing Cells Atop Microelectronic Chips: Interfacing Electrogenic Cells *In vitro* With CMOS-Based Microelectrode Arrays. Proc. IEEE. 2011 Feb;99(2):252 – 84
[35] Menzler, J. et al. Network Oscillations in Rod-Degenerated Mouse Retinas. J Neurosci. 2011 Feb;31(6):2280 – 91

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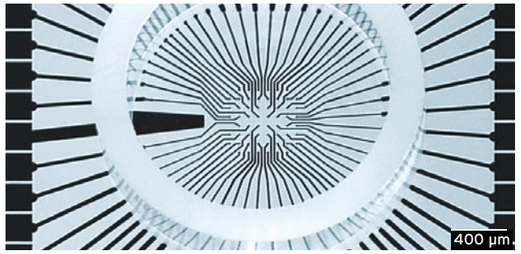
"We bought the MEA system, after careful study of all the technology available on the market at that time, to build up a system that helped in identifying drug potency in native brain tissue. The MEA system from Multi Channel Systems was the best choice in terms of technology and price at the time. With the system, we now mainly target identification and validation for drugs that target receptors important for synaptic transmission and improvement of brain function. For this purpose, we mainly use brain slice and neuronal cell cultures.

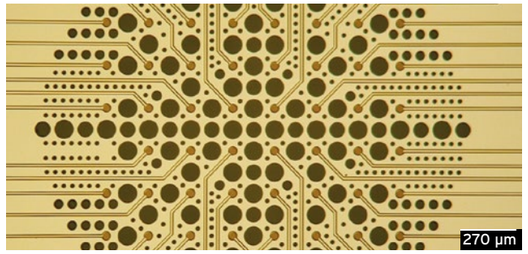
The great thing about the MEA system is that we get a quick and easy readout of brain function and synaptic physiology and plasticity. Moreover, the technology can be easily taught to other lab personnel without knowledge of electrophysiology. Additionally, the compact system does not take up much lab space and is easy to maintain."

Hamdy Shaban, PhD, Principal Scientist (Neuroscience),
Janssen Pharmaceutica NV, Belgium.

Mature tools for scientific excellence

>> Microelectrode arrays for extracellular electrophysiology





Custom-designed MEAs
Specific scientific questions and experimental designs require specific MEA layouts.
Many different layouts and types of electrodes, optimized for a wide range of *in vitro* and *in vivo* applications, are available.

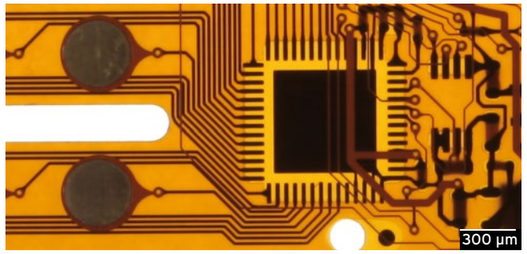
We are committed to providing the perfect tool to scientists, one which enables them to find answers to questions – however extraordinary – concerning electrophysiology.

Benefit from your own MEA layout
In meeting specific requirements, we are constantly developing application-specific MEAs with high-quality surfaces and electrodes and offer individualized manufacturing services. The routine production of small batches ensures short-time-to-application and consistently high quality.

The layout and performance are fully compatible with the Multi Channel Systems MCS hardware.

We are committed to providing the perfect tool to scientists.

Mature tools for scientific excellence



Flexible MEAs
MEAs based on polyimide technology for recording and microstimulation are widely used to assess the functioning of the central and peripheral nerve system.

We apply established thin-film technology, and the layout and size of our flexible MEAs can easily be adapted to specific anatomic structures and experimental requirements.

Our MEA technology serves as the basis for new concepts for active implants.

Active MEA boards
Miniaturized implants open up a whole new spectrum of neurotechnological possibilities. They facilitate more specific diagnosis, more effective therapies and aids used on a daily basis by patients undergoing rehabilitation for neurological disorders.

Our MEA technology serves as the basis for new concepts for active implants. A special challenge is posed by the demand for implants that function safely over the long term. We focus in particular on the development of microelectrodes, flexible circuit boards and biostable encapsulations.

Mature tools for scientific excellence

>> Microelectrode arrays for extracellular electrophysiology

■ **Dedicated to producing high-quality MEAs**
At the NMI we have over 20 years of experience in developing and producing microelectrode arrays and microsensor chips. Production of MEAs on glass and flexible polyimide substrates is carried out in cleanrooms conforming to strict quality assurance regulations, thus ensuring that our MEAs are always of excellent and consistent quality.

For the challenging applications in the life sciences, we only use biocompatible materials and apply the highest standards when it comes to the quality of surfaces.

Because MEAs matter to us!

■ **MEA community**
We organize a biennial conference for scientists, from both industry and academia, involved in developing and using MEAs. This MEA Meeting, including workshops, has become an internationally-renowned, information-packed scientific forum and the number of participants has grown steadily over the years.

www.nmi.de/meameeting

Picture (back side): Adult animal heart slice. Kindly provided by Dr. Patrizia Camelliti, National Heart & Lung Institute, United Kingdom.

Synergy effect: NMI and MCS
Our partner Multi Channel Systems MCS GmbH, serves as our link to the user: Our MEAs are sold exclusively by MCS to more than 700 academic and industrial laboratories worldwide.

Moreover, MCS is the specialist for high-end devices: they develop and market high-performance equipment and user-friendly software for MEA applications.

Customers appreciate their excellent support service operated by scientists with longstanding experience in the field of electrophysiology.

Contact
MEA development and custom-made MEAs:
mea@nmi.de

Standard MEAs and MEA systems:
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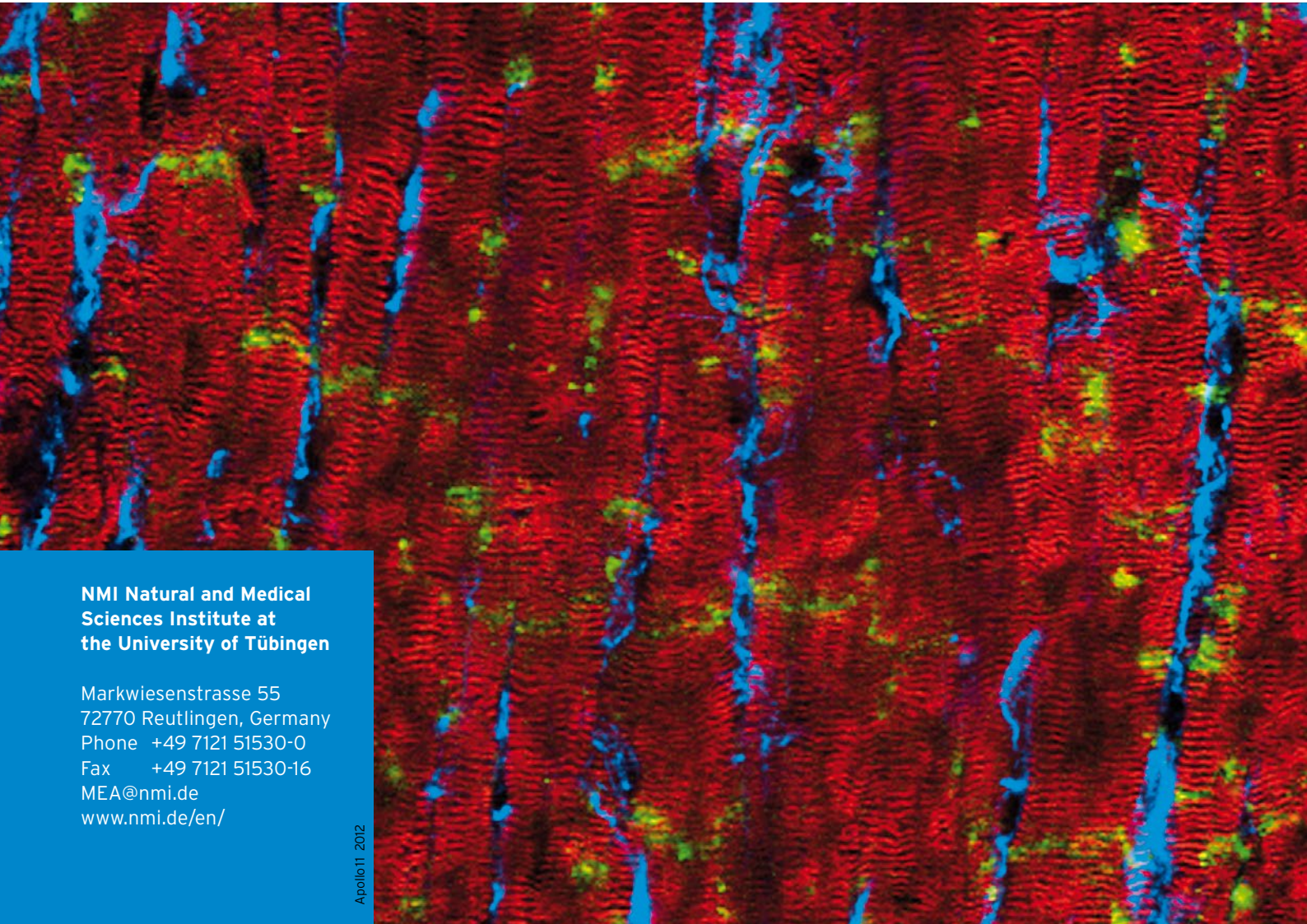

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