MED64

A low-noise multi-electrode array system for *in vitro* extracellular electrophysiology

IDEAL FOR STUDYING:

- Evoked and spontaneous activities (fEPSP, Spikes)
- Synaptic plasticity (LTP, LTD)
- Spontaneous rhythmic activities (oscillations)
- Pacing and propagation in myocytes
- Safety pharmacology (QT prolongation / CNS toxicology)
- Drug testing with acute tissue slices
- Chronic drug testing with cultures
- Stem cell research

ALPHA MED SCIENTIFIC

MED64 product information
www.med64.com

MED64

Record high-quality extracellular signals with the industry's lowest-noise system

MED64 is a user-friendly multi-electrode array (MEA) system for stimulation and recording of field potentials (extracellular signals) from multiple areas within a biological sample over hours, days, weeks and even months. The unique construction of the system eliminates the need for many cumbersome and expensive components of conventional electrophysiology rigs, including a faraday cage, an anti-vibration table, micromanipulators, glass microelectrodes, and an electrode puller.

Acute or cultured biological preparations are placed or grown directly on a grid of 64 planar microelectrodes, which serve a dual purpose of stimulus-delivery and signal recording. The MED64 system is a complete, fully-integrated solution for *in vitro* electrophysiology including six components: MED probe (multi-electrode array), MED connector, Head amplifier, Main amplifier, PC system, and Mobius software for data acquisition and analysis. The MED64 system features the industry's lowest-impedance planar microelectrode, which enables data acquisition with low-noise and superior signal-to-noise ratios. The MED64 system can be used for diverse research applications involving the central nervous system (CNS), the heart, or any other excitable tissue.

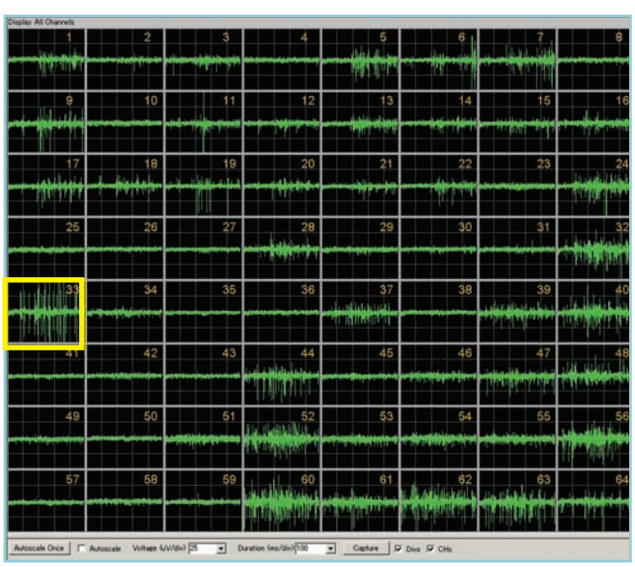
Features:

Simultaneous recording of extracellular signals across 64 channels without pulling glass electrodes

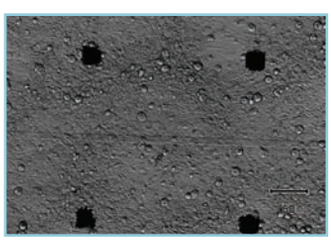
- Signals (evoked potentials or spontaneous activity) are acquired with 64 planar microelectrodes patterned on the MED probe (multi-electrode array).
- Any of the 64 electrodes can be used for stimulation (up to two simultaneously). Stimulus channels and waveforms are selectable by software.

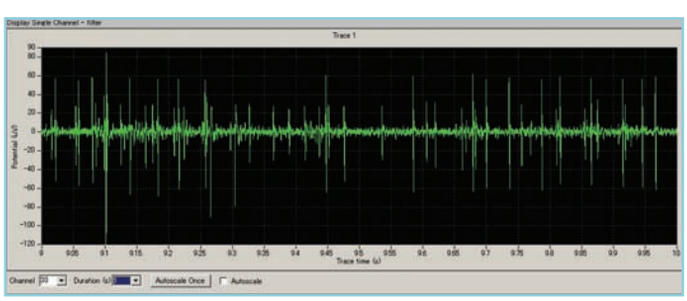
Stable, low-noise, high signal-to-noise ratio recording with 1 µV r.m.s noise level

- The MED64 system's low-noise level is achieved through the use of the industry's lowest-impedance electrodes (10 kΩ at 1 kHz, typically). The MED64 does not require a Faraday cage or vibration-isolation table, and can thus be installed on a common table or lab bench.
- The measured noise level is 1 µV r.m.s. – lower than any other commercial multi-electrode array system. The superior signal-to-noise ratio enables acquisition of particularly small signals such as single-unit activities from acute brain slices (even from SCN slices).



(25 µV, 100 ms / Div)

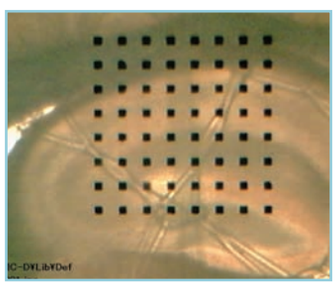


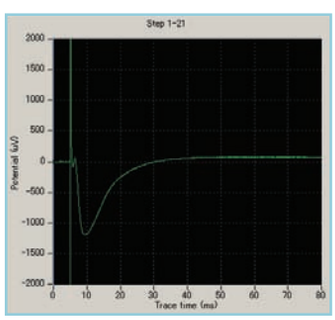


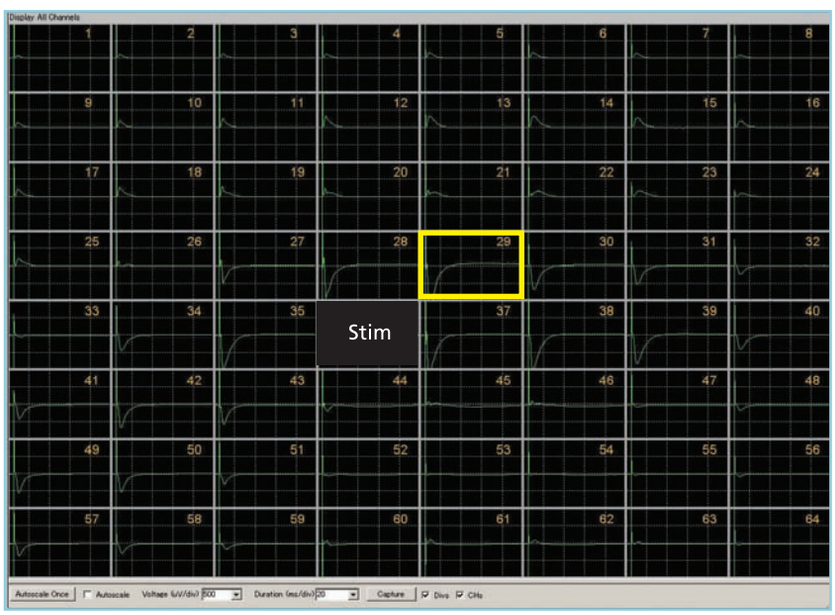
Micrograph of dissociated neurons cultured on MED probe. (top-right)
Spontaneous neuron spikes acquired from dissociated neuron cultures at all 64 channels (left) and magnification of the signal at ch 33 (bottom-right).

Effective stimulation and high-quality evoked signals

- Use of the MED64 system for recording electrically evoked signals has been demonstrated in many scientific publications. The planar platinum-black-coated microelectrodes have very high capacitance values (50,000 pF for 50 x 50 µm microelectrodes), enabling stimulation with high frequencies and large current amplitudes (up to 200 µA / 0.2 msec).
- Stimulus artifacts are very short in duration, returning to 0 µV within 0.5 ms at non-stimulated channels. Clean, high-quality electrically evoked signals can thus be recorded soon after stimulation without interference.





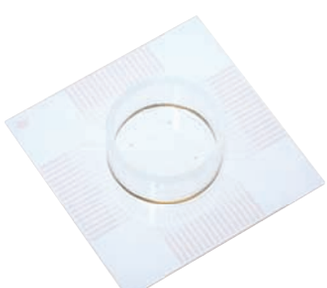


Mouse hippocampus slice on a MED probe (top-left), Acquired signals at all channels (right), and magnification of the signal at channel 29 (bottom left).

(500 µV, 20 ms / Div)

Long-term observation in a humidified incubator

- Dissociated cells and tissue (e.g. slices) can be cultured directly on the MED probe.
- Non-invasive planar microelectrodes are ideal for long-term recording.
- The MED probe and connector can be kept in an incubator with 100% humidity, allowing hands-free recordings to be made automatically over the course of days, weeks, and months while the sample sits undisturbed in the incubator.



MED Probe

Various applications

- The MED64 system is well-suited for acute tissue preparations, as well as cultured tissue or dissociated cells. Its low-noise and user-friendliness make it an extremely powerful tool for drug testing.
- The low-impedance microelectrodes and wide-bandwidth amplifier enable acquisition of widely varying signal types, including slow-wave signals such as fEPSPs, signals from smooth muscle tissue (~ 0.1 Hz), as well as high-frequency signals such as neuronal spikes.

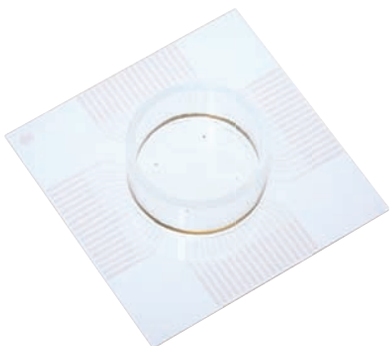
On-line analysis with powerful software

- MED64 Mobius software allows MED64 users to analyze signals both on-line (during acquisition) and off-line for all 64 channels .
- The broad set of analysis functions is useful for many different kinds of applications.

MED64 System

Multi-electrode array with the industry's lowest impedance electrodes

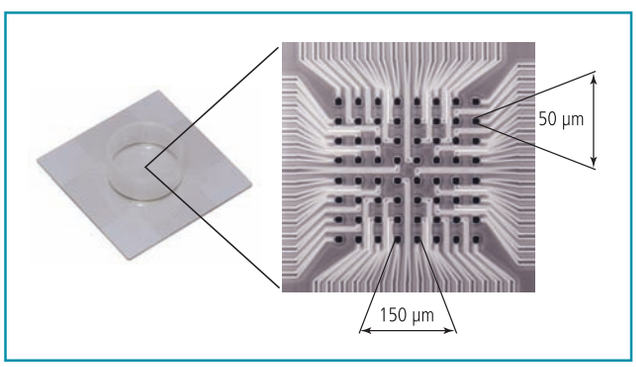
The standard MED probe has 64 planar microelectrodes arranged in an 8 x 8 grid embedded in the center of a transparent glass plate. The surrounding glass or plastic cylinder makes the MED probe a self-contained recording chamber. Four models with inter-electrode spacings of 100, 150, 300, and 450 µm enable measurements of fine detail from small regions of a sample to larger scale interactions across the sample. Each electrode is 50 µm x 50 µm in size for 150, 300, and 450 µm spacing configuration, or 20 µm x 20 µm for 100 µm spacing configuration.



Also available are probes featuring a hippocampus-specific electrode pattern, and a hexagonal pattern, as well as 2- and 4-well MED probes for increased sample throughput (e.g. for drug screening).

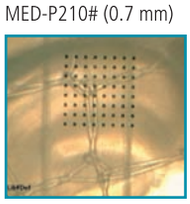
Standard 8x8 Arrays

Product Number	Chamber Depth	Electrode Size	Interpolar Distance of Electrodes	
			Recording/stimulating	Reference
MED-P2105	5 mm	20 x 20 µm	100 µm	8.5 mm
MED-P210A	10 mm	20 x 20 µm	100 µm	8.5 mm
MED-P5155	5 mm	50 x 50 µm	150 µm	8.5 mm
MED-P515A	10 mm	50 x 50 µm	150 µm	8.5 mm
MED-P5305	5 mm	50 x 50 µm	300 µm	9.2 mm
MED-P530A	10 mm	50 x 50 µm	300 µm	9.2 mm
MED-P5455	5 mm	50 x 50 µm	450 µm	10.2 mm
MED-P545A	10 mm	50 x 50 µm	450 µm	10.2 mm



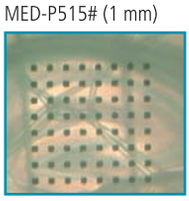
Close-up view of microelectrodes on MED-P515A

MED-P210# (0.7 mm)



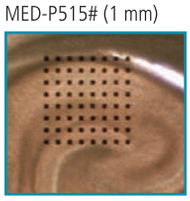
Mouse Hippocampus CA1

MED-P515# (1 mm)



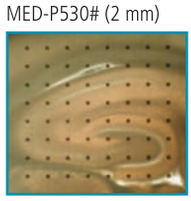
Mouse Hippocampus

MED-P515# (1 mm)



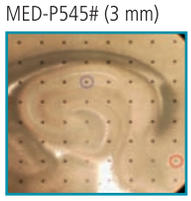
Rat Hippocampus CA1

MED-P530# (2 mm)



Rat Hippocampus

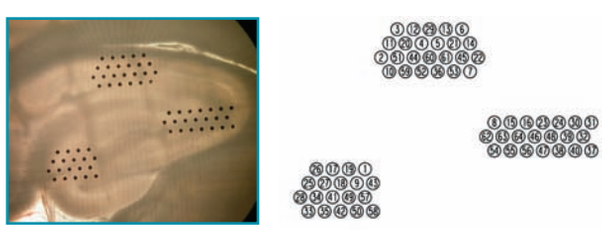
MED-P545# (3 mm)



Rat Hippocampus and Peripheral area

Hippocampal Pattern Arrays (CA1, CA3, & DG)

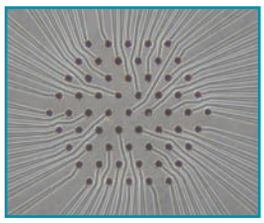
Product Number	Chamber Depth	Electrode Size	Interpolar Distance of Electrodes	
			Recording/stimulating	Reference
MED-P50015 For Rat	5 mm	ø50 µm	150 µm	8.5 mm
MED-P5001A For Rat	10 mm	ø50 µm	150 µm	8.5 mm
MED-P50025 For Mouse	5 mm	ø50 µm	150 µm	8.5 mm
MED-P5002A For Mouse	10 mm	ø50 µm	150 µm	8.5 mm



NED-P5001A
Micrograph of rat hippocampal slice and arrangement of microelectrodes

Hexagonal Arrays (61 electrodes)

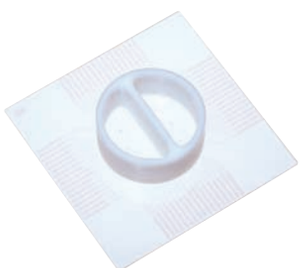
Product Number	Chamber Depth	Electrode Size	Interpolar Distance of Electrodes	
			Recording/stimulating	Reference
MED-P2H075	5 mm	ø20 µm	70 µm	8.5 mm
MED-P2H07A	10 mm	ø20 µm	70 µm	8.5 mm

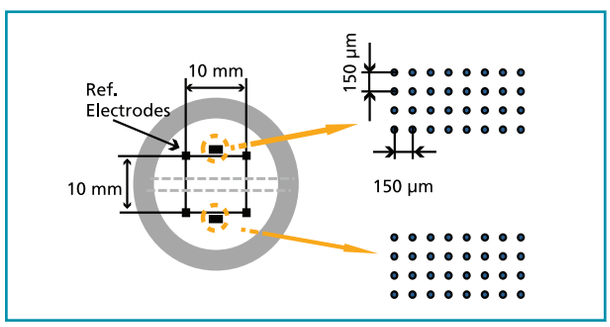


MED-P2H07A
Close up view and arrangement of microelectrodes

Probes for Parallel Sample Processing

2-Sample MED probe

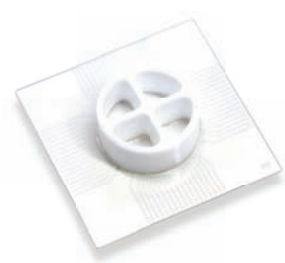


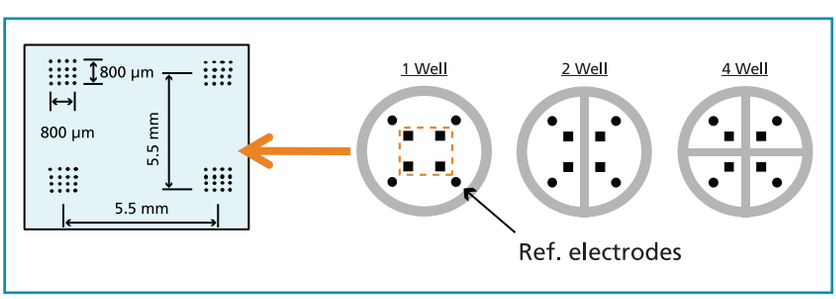


2-Sample MED Probe (2 Well type: MED-P5D15A) (left) and arrangement of microelectrodes (right)

Product Number	Number of wells	Electrode Size	Inter-polar distance (The smallest)	Distance between electrode blocks	Chamber Depth	Partition-height
MED-P50035	1	Ø 50 µm	150 µm	12 mm	5 mm	NA
MED-P5003A	1	Ø 50 µm	150 µm	12 mm	10 mm	NA
MED-P5D15A	2	Ø 50 µm	150 µm	NA	10 mm	10 mm
MED-P5D15B	2	Ø 50 µm	150 µm	NA	10 mm	5 mm

4-Sample MED probe





4-Sample MED Probe (4 Well type: MED-P5FF15) (left) and arrangement of microelectrodes (right)

Product Number	Number of wells	Electrode Size	Inter-polar distance (The smallest)	Distance between electrode blocks	Chamber Depth	Partition-height
MED-P50045	1	Ø 50 µm	150 µm	5.5 mm	5 mm	NA
MED-P5004A	1	Ø 50 µm	150 µm	5.5 mm	10 mm	NA
MED-P5DF15	2	Ø 50 µm	150 µm	NA	10 mm	10 mm
MED-P5FF15	4	Ø 50 µm	150 µm	NA	10 mm	10 mm

Specifications

Substrate

Glass substrate	50 x 50 x 0.7 mm
Glass cylindrical chamber	ID=22, OD=25 mm
Conducting layer	Indium tin oxide (ITO) (0.15 µm)
Insulation layer	Polyacrylamide (1.5 µm)

Recording / Stimulating electrodes

Material	ITO + Platinum Black
Impedance	< 22 kΩ (Typical:10 kΩ) for 50 µm electrodes < 40 kΩ (Typical : 30 kΩ) for 20 µm electrodes (1 kHz, 50 mV applied sinusoidal wave)

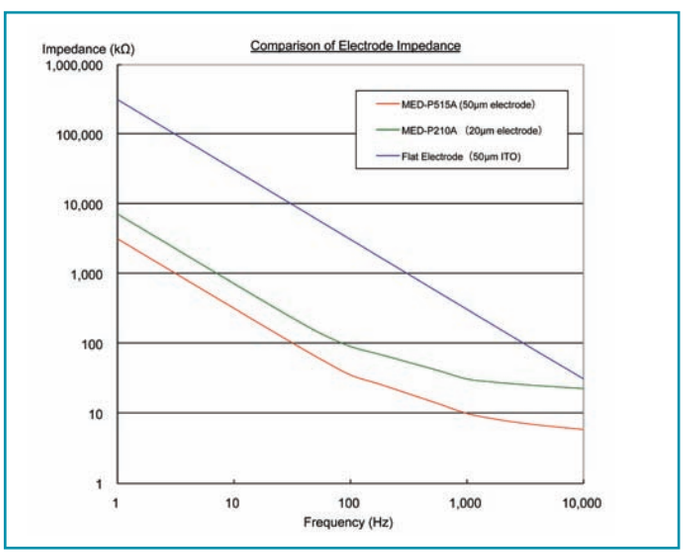
Reference electrodes

Material	ITO + Platinum Black
Size	200 x 200 µm Ø 100 µm x 4 (MED-P2H07#, MED-P500##, MED-P5D###, MED-P5F###)

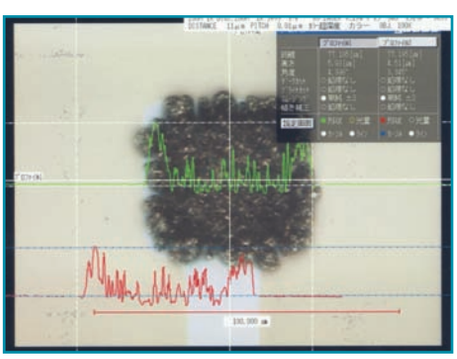
Technologies

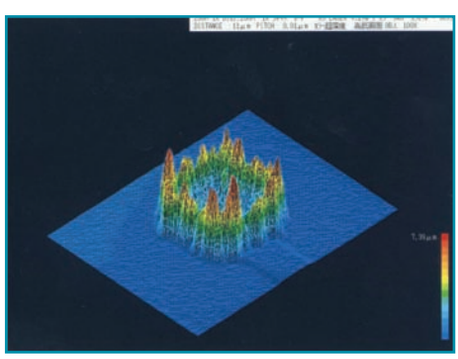
The microelectrodes on the MED probe are coated with platinum black using a proprietary method. This construction resolves a major issue with planar microelectrodes: electrode impedance (and noise) is inversely proportional to surface area, but the overall geometry of the electrode must be small for recording from cells. The platinum black coating increases the effective surface area 100-200 times (vs. the standard plating methods of competing systems) without increasing the diameter of the electrode. This reduces the electrode impedance to only 10 kΩ at 1 kHz (for 50 x 50 µm electrode, 30 kΩ for 20 x 20 µm electrode). Benefits include:

- Better signal to noise ratio (Lower intrinsic Johnson noise)
- Higher signal stability (lower sensitivity to exogenous noise)
- No need for head-stage amplifier near electrodes
- Delivery of larger stimulus current
- Smaller stimulus artifact



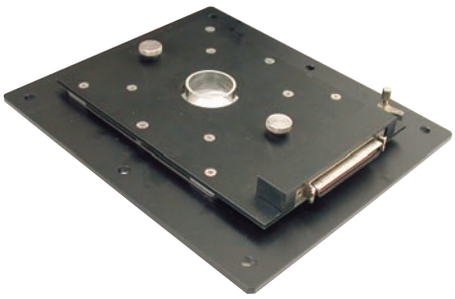
Impedance of platinum black microelectrodes on the MED probe (Red: 50 x 50 µm, Green: 20 x 20 µm) compared with completely flat ITO electrode (Blue: 50 x50 µm)





Close up view of microelectrode surface

HARDWARE / **MED Connector**



MED Connector

- Used for communication between the MED probe and amplifier.
- Provides a mechanically-stable platform for the MED probe.
- Multi-layer electrical shielding rejects hum noise and provides excellent signal-to-noise ratios.
- NO active on board electrical circuitry; Connectors can safely be placed in high-humidity environment (e.g. cell culture incubator).
- Provides clear optical path through probe for microscopy.

HARDWARE / **MED64 Head amplifier / Main amplifier**

MED64 Head amplifier (top) and Main amplifier (bottom)

- Wide bandwidth of 0.1-10 kH allows users to record several types of extracellular potentials.
- Low-cut filter (High pass filter) with 0.1, 1, 10, and 100 Hz cutoff.
- High cut filter (Low pass filter) with 1, 2.5, 5, 7.5, and 10 kHz cutoff.
- Built-in 2-channel stimulator allows users to program and deliver complex stimulation sequences independently through any 2 electrodes.
- USB connection to computer.

Specifications

MED64 Head Amplifier
(MED-A64HE1)

Amplifier	
Number of channels	64
Gain	x 10
Bandwidth	0.1 -100 kHz (+0dB to -3dB)
Input impedance	100 MΩ
Output impedance	10 kΩ
Stimulator	
Number of channels	2
Output format	Constant current
Maximum input voltage	+/- 4 V
Maximum output current	+/- 200 µA
General	
Power supply	DC +/- 12V
Weight	6.6 Kg
Dimensions	W430 x H74 x D437 mm
Power supply unit	
Input	AC 100-240V (50-60Hz)
Output	DC +/- 12 V

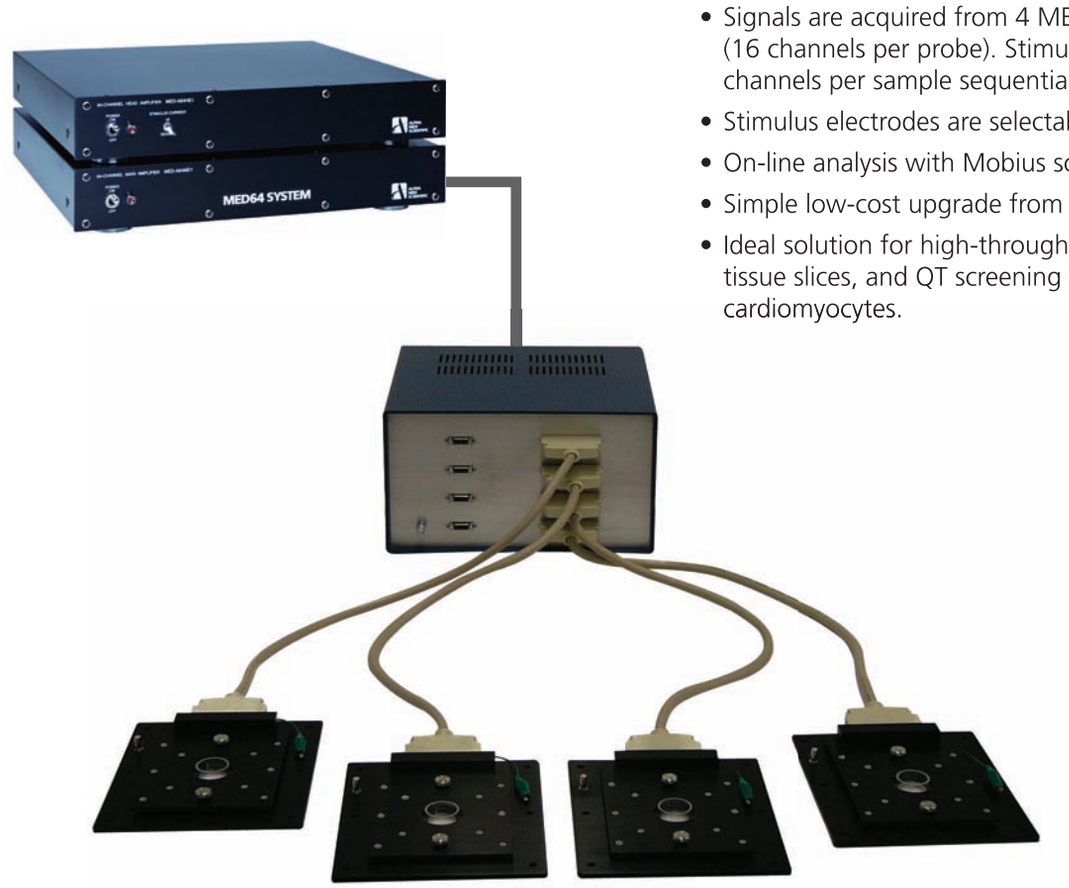
MED64 Main Amplifier
(MED-A64MD1)

Amplifier	
Number of channels	64
Gain	1-217
Bandwidth	0.1-10 kHz (+0dB to -3dB)
Analog high cut filter	1, 2.5, 5, 7.5, 10 kHz (-6dB/oct)
Analog low cut filter	0.1, 1, 10, 100 Hz (-12dB/oct)
Input impedance	100 MΩ
Digitizer	
Resolution	16 bit
Sampling rate	20 kHz
Output	USB
General	
Power supply	DC +/- 12V
Weight	5.9 Kg
Dimensions	W430 x H74 x D437 mm
Power supply unit	
Input	AC 100-240V (50-60Hz)
Output	DC +/- 12 V

MED Connector
(MED-C03)

MED probe securing mechanism	Screw down
Material	Aluminum
Contact resistance	<30 mΩ
Printed Wiring	4 layers (reject hum noise by a multi-shield structure)
Dimensions	W174 x H21 x D150 mm

UPGRADE / **MED64 4-sample system**



- Signals are acquired from 4 MED probes simultaneously (16 channels per probe). Stimulation is applied through 2 channels per sample sequentially.
- Stimulus electrodes are selectable for each probe.
- On-line analysis with Mobius software.
- Simple low-cost upgrade from a standard MED64 system.
- Ideal solution for high-throughput drug testing with acute tissue slices, and QT screening with iPS/ES cell-derived cardiomyocytes.

PERFUSION ACCESSORIES

The MED64 system can easily be configured for perfusion of your sample. Two types of perfusion accessories are available:

The Perfusion Cap fits neatly into the top of a MED probe, and features adjustable solution inflow and outflow pipes, a Pt ground wire, and a port for delivery of gas. It is easily removed and replaced for slice mounting. For applications requiring an open top, such as imaging or conventional microelectrode electrophysiology, a **Perfusion Pipe Holder Kit** is available.

Perfusion cap placed onto a MED probe

Perfusion pipe holder kit installed on a MED connector

Highly-sophisticated, user-friendly software

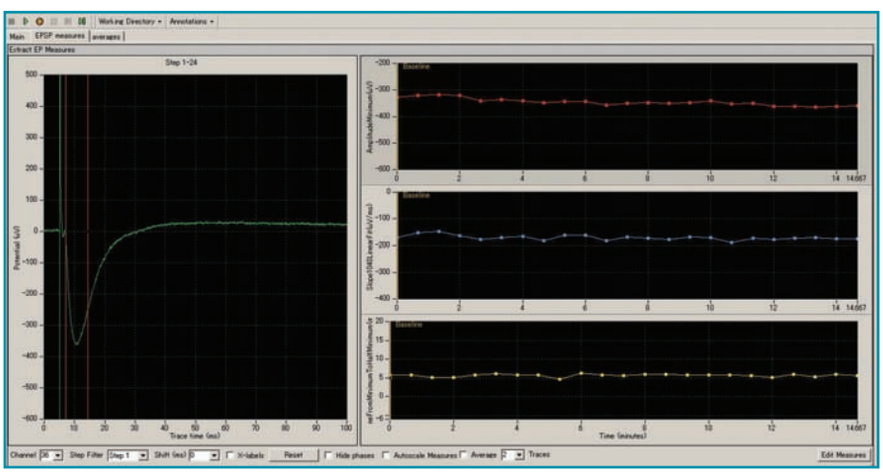
MED64 Mobius software is a data acquisition and analysis package for the MED64 system, featuring a broad set of analysis functions available both online (i.e. during acquisition) and offline (i.e. post-acquisition). It is designed to be easy for beginners and powerful enough for advanced users. Mobius comes in various application-specific packages including "Evoked Potential Measurements", "Spike Sorter", "QT", as well as combined packages for multi-application users.

The Mobius user interface consists of various task-specific control panels, which can be quickly combined using a simple workflow editor to create custom experimental protocols and workflows. However, convenient pre-defined "workflow templates" are available for users who want to quickly set-up and run standard types of experiments.

Evoked Potential Measurement Package

Recording and analysis of fEPSP / LTP/ LTD

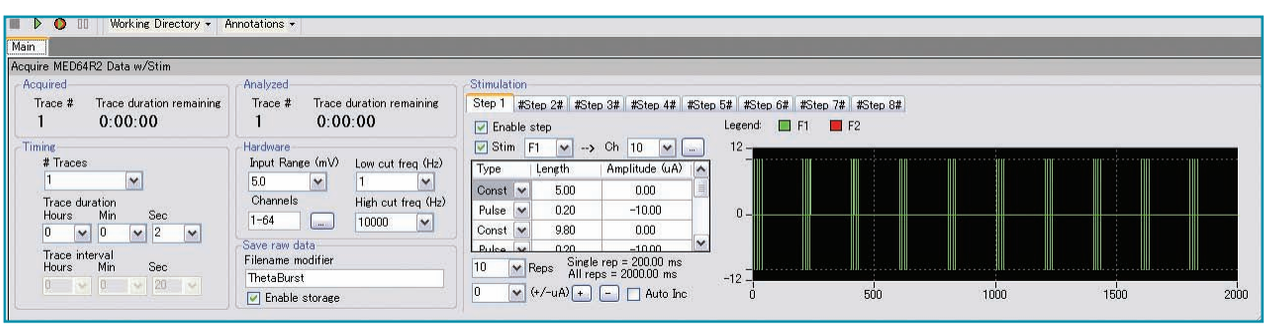
- Evoked local field potentials (e.g. fEPSP's) on all 64 channels can be recorded in response to highly configurable user-defined stimulation parameters. Templates are included for delivery of repetitive (e.g. theta) stimuli.
- Analysis of amplitude, slope and area parameters can be performed automatically during or after acquisition, and graphed independently for each channel. An arbitrary number of measures can be enabled, limited only by the processing power of your PC.
- Online and offline measures are also available for paired-pulse paradigms.
- Averages and standard deviations for measurements can be automatically computed for all channels and graphed for user-defined "phases" of an experiment. This allows for easy construction of dose-response curves.
- Users can design and apply complex stimulation sequences independently for each stimulator.
- Raw data can be exported in binary or ASCII text file (csv) format.
- Measurement graphs can be saved as "csv" formatted text files.



Available measurement protocol

- Amplitude (Minimum, Maximum, Peak to Peak)
- Slope (10-90%, 10-40%, Linear fit)
- Absolute Area
- Area Pop Spike
- Paired-pulse Ratio for above protocols
- Time of Amplitude Minimum (or Maximum)
- Time of Amplitude Minimum (or Max) to Minimum (or Max)
- Time from Minimum (Max) to Half-minimum (max)

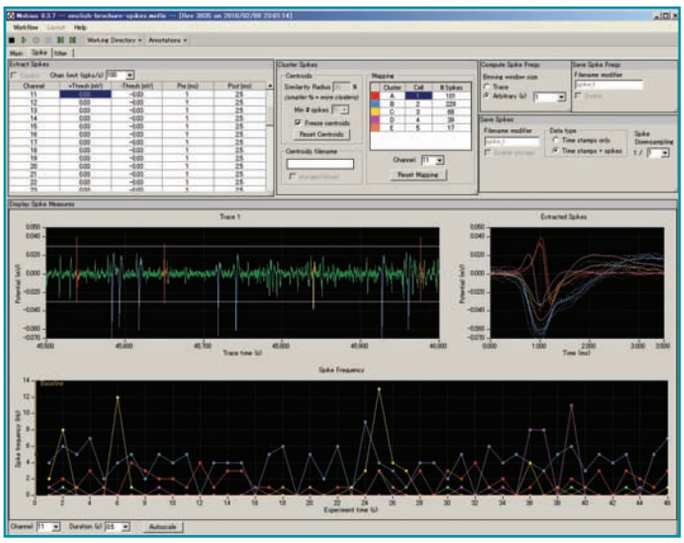
fEPSP analysis: [Left] extracted evoked signal [Right] Time course of measured 1) Amplitude Minimum (red), 2) Slope 10-40% (blue), and 3) Time from Minimum to Half-Minimum (yellow)



Control panel for acquisition/stimulation parameters

Spike Sorter

Recording and analysis of spikes from brain slices or neuronal cultures



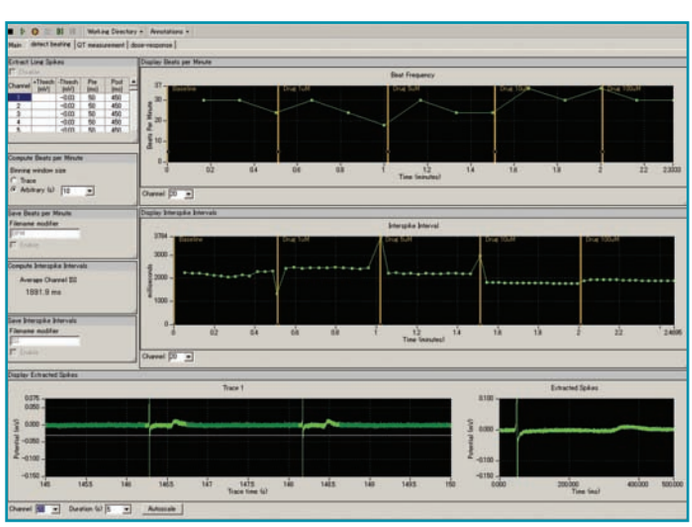
Spike Sorting: Thresholds are set in the left-top chart. Detected spikes (middle-left) are extracted and sorted (middle-right), and analyzed for frequency (bottom)

- Spontaneous signals are recorded at all 64 channels according to user-defined acquisition parameters.
- Spikes exceeding user-defined thresholds are automatically extracted and can be sorted based on waveform similarity.
- Spike frequency is computed and graphed for each channel.
- Averages and standard deviations for spike frequencies on all 64 channels can be automatically computed and graphed for each user-defined phase of an experiment. Easy for making multi-step dose-response curves.
- Spike time-stamps, waveforms of extracted spikes, and spike frequency charts can be saved in ASCII text file (csv) format, even WITHOUT saving raw data.
- Raw data can be exported to binary or ASCII text file (csv) formats.

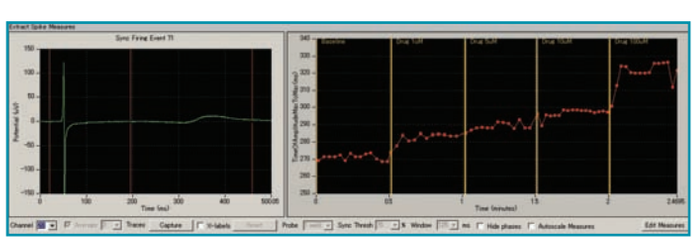
QT Package

Recording and analysis of myocardial signals / Evaluation of QT prolongation

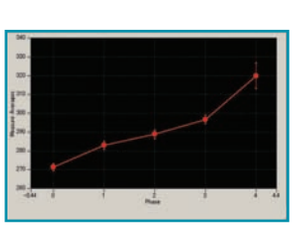
- Ideal for recording and analysis of cardiomyocyte preparations, including iPS/ES cell-derived cardiomyocytes, primary myocyte cultures, and acute heart tissue.
- Myocardial signals are automatically extracted according to user-defined thresholds and analyzed for beat frequencies and inter-spike intervals.
- Multiple types of slope, amplitude, time, and area measurements can be performed automatically on extracted signals. Field potential prolongation (indicating a prolonged QT interval) can also be measured from extracted waveforms with the "Time of Amplitude Minimum (or Max) to Minimum (or Max)" measure.
- Averages and standard deviations for the beat frequencies, inter-spike intervals, and waveform analysis on all 64 channels can be automatically computed and graphed for each user-defined phase of an experiment. Dose-response curves can thus be easily constructed.
- Raw data can be exported in binary or ASCII text file (csv) format.
- Extracted spikes and all measurement charts can be saved as "csv" formatted text files.



Detected myocardial signals [Bottom, highlighted in light green], beat frequency [Top], and inter-spike-interval calculated from extracted spikes [Middle].



[Left] Extracted myocardial signal. [Right] Time between peaks(Fileld potential duration) of the extracted waveforms is calculated using the "Time of Amplitude Max to Max" measure.

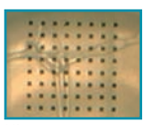
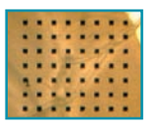
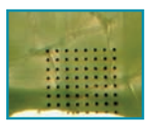
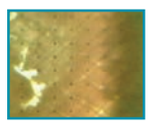
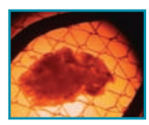
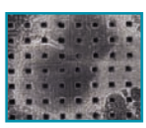
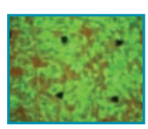
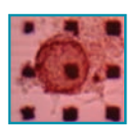


The average for each phase (defined by yellow bars on the top chart) is computed and graphed.

APPLICATIONS

The MED64 is widely used in studies of the central and peripheral nervous system, as well as myocardial and other muscle preparations. It is well-suited for experiments on acute tissue preparations or cultures, and provides an ideal solution for drug testing due to its ease-of use, high-throughput, and high-reproducibility.

Applications by preparation

	CNS	Myocardium and smooth muscle
Acute Slices	 Hippocampus  Cortex  Thalamus  SCN  Amygdala  Spinal cord  Retina Substantia nigra Superior colliculus Brain stem	 Ventricular Slice  Atrium  Smooth muscle
Slice Cultures	 Hippocampus  SCN  Cerebellum  Co-cultures	
Cell Cultures	Hippocampus Cerebellum Cortex SCN DRG cells	 Cardiomyocytes (CMs)  Stem cell (iPS/ES cell)-derived CMs and more

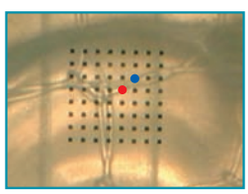
Applications by study / experiment

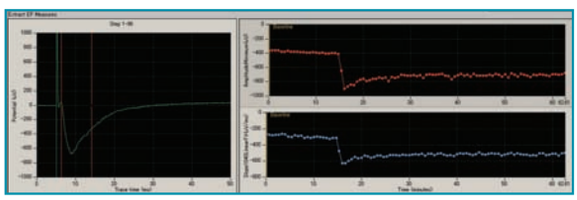
- Evoked activities (fEPSPs)
- Spontaneous activity (spiking)
- Rhythmic activity / oscillations
- Synaptic plasticity (LTP/LTD), learning, memory
- Pacing and propagation in myocytes
- Stem cell research
- Safety pharmacology (e.g. CNS toxicity and QT Prolongation)
- Drug testing on acute tissue preparations (epilepsy, Alzheimer, pain, obesity, anorexia, arrhythmias, etc.)
- Chronic drug testing with cultures
- QT prolongation screening with iPS/ES cell-derived myocytes
- and more

ACUTE SLICE APPLICATIONS

Spontaneous and evoked signals from acute brain slices are easy to record with the MED64 system. The MED64 system offers technical advantages over competing systems that make it particularly well-suited for acute slice recording. Its low-impedance electrodes make small single-unit activity easier to resolve, and the high capacitance of its electrodes make synaptic potentials easier to evoke using the highly-configurable built-in stimulators.

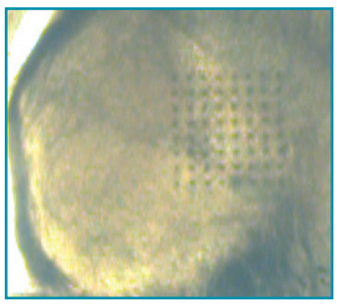
LTP FROM HIPPOCAMPAL SLICES





[Left] Micrograph of a C57BL6 mouse hippocampal slice placed on MED probe. fEPSP's were elicited with a single pulse stimulation to electrode 22 (marked in blue). Responses were recorded at the remaining 63 electrodes.[Right] The time course of the slope (10-40%) and minimum amplitude of the fEPSP recorded at electrode 29 (marked in red).

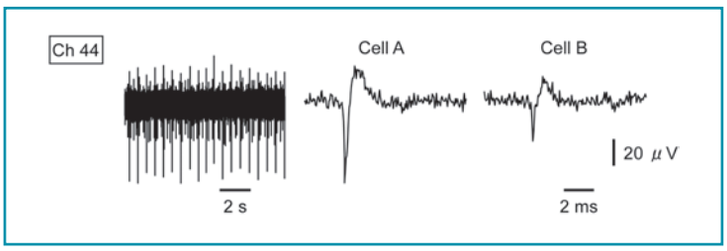
Single-unit activities in the substantia nigra



A

B

(20 µV, 500 ms / Div)



C

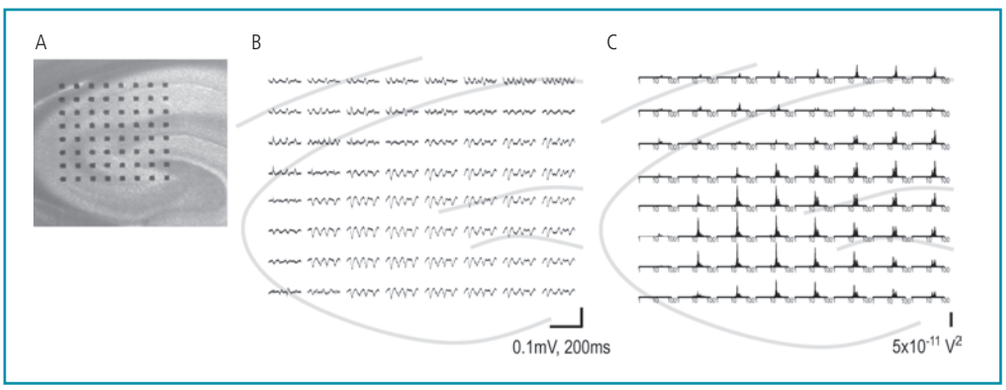
A: Photograph of a horizontal midbrain slice containing the substantia nigra, placed over the 8 x 8 array of electrodes on a MED probe.

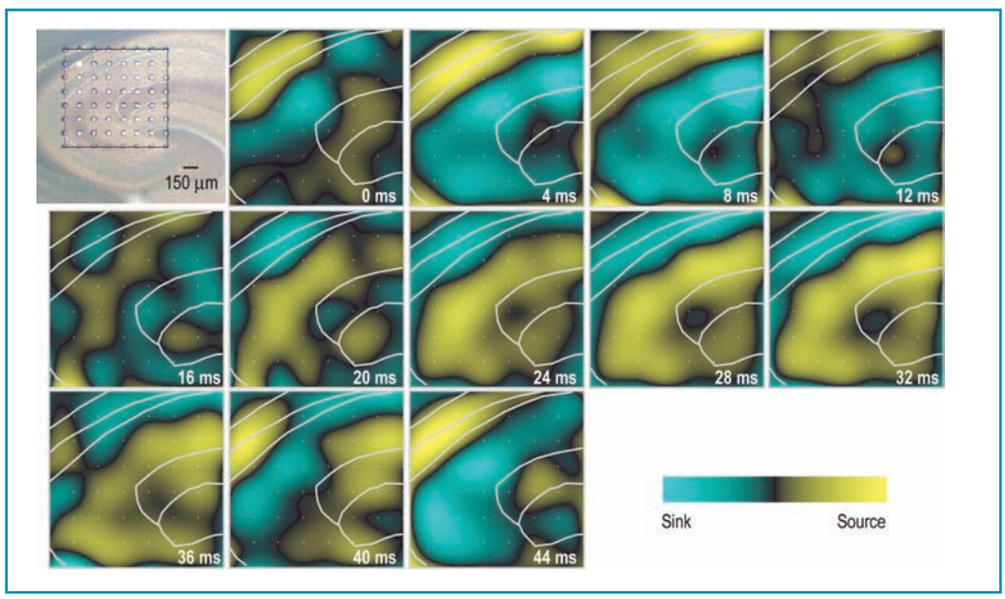
B: Spontaneous single unit activities acquired at all 64 channels

C: Spontaneous activity acquired at channel 44. The expanded traces show spikes corresponding to two different cells (A and B) recorded by the same channel.

Courtesy of Dr. Nicola Beretta, Fondazione Santa Lucia IRCCS Rome, Italy

Rhythmic Activity in the hippocampus





D

A. Micrograph of a hippocampal slice on a MED probe (MED-P515A: 150 µm inter-polar distance)

B. Spontaneous rhythmic activity in the presence of 50 µM carbachol

C. Fast Fourier transforms displaying the frequency (x-axis) and amplitude (y-axis) of rhythmic activity

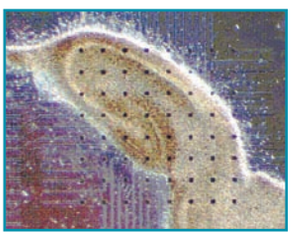
D. Current source density analyses of carbachol-induced activity. The pseudo-colored panels show the computed current source density in the region of the electrode array at several time points during a carbachol-induced oscillation. The outlines of the pyramidal and granule cell fields and their apical dendrites are overlayed. At 0 ms, a sink appears in the apical dendrites of the border between fields CA3 and CA1 with a corresponding source in the basal dendrites. The fields merge and intensify and then dissipate after ~12 ms. At ~20 ms, a source appears in the apical dendrites with a corresponding sink in the basal dendrites. Theseexpand and intensify before dissipating at ~40 ms, after which an apical sink reappears to reinitiate the cycle.

K. Shimono et al. Origin and distribution of cholinergically induced beta rhythms in hippocampal slices. J. Neurosci. 15, 8462-8473 (2000)

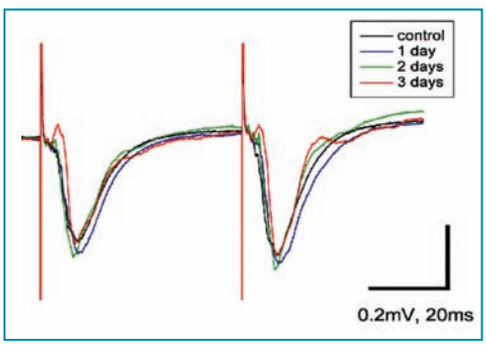
CULTURE APPLICATIONS

Cells or slices can be cultured directly on the MED probe and recorded continuously. Recording with non-invasive planar microelectrodes in a humidified incubator enable recording even over weeks and months.

Chronic drug effects on cultured hippocampal slices



A



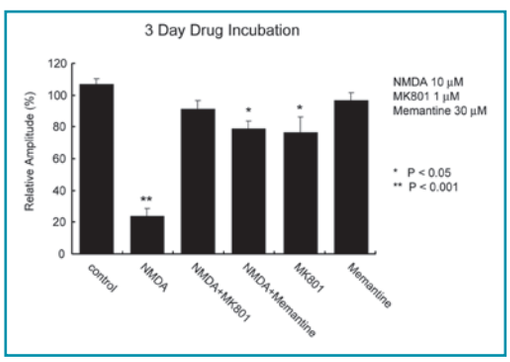
B

A: Rat Hippocampal slice cultured directly on a MED probe (MED-P530A; 300 µm inter-polar distance, 10 days in culture)

B: Extracellular field potentials in CA1 evoked by paired-pulse stimulation. Responses remained stable over days.

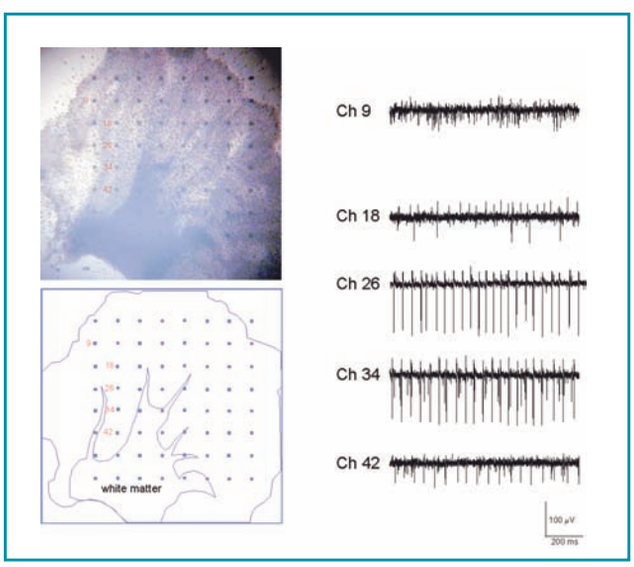
C: Comparison of the effects of various chronic treatments on synaptic responses. fEPSPs were measured in cultured hippocampal slices 3 days after treatment with drug(s). fEPSP amplitude was expressed as a percent of the pre-drug baseline response for each slice. Co-incubation with NMDA antagonists, such as 1 µM MK801 and 30 µM Memantine, blocked the excitotoxic action of NMDA (10 µM).

Shimono K et al. J Neurosci. Methods 2002, 120(2): 193-202



C

Recording from cultured cerebellar slice



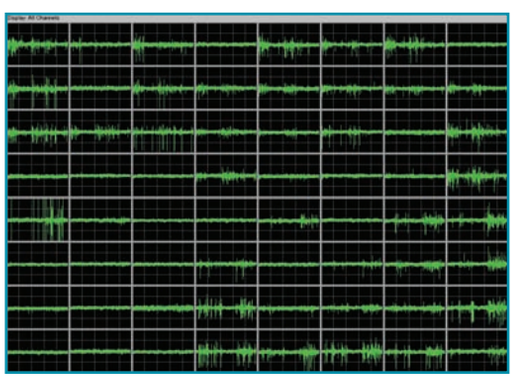
[Left] Cerebellar slice cultured on a MED probe. The slice was prepared from a 10-day old rat, grown in culture for 10 days on a methylcellulose membrane, and transferred to the MED probe. The scheme underneath shows the gross structure and electrode arrangement.

[Right] Spontaneous activity recorded from multiple channels. The recording sites and corresponding channels within the slice are indicated in the image on the left. The presence of spikes with large amplitude indicates that an active neuron resides nearby.

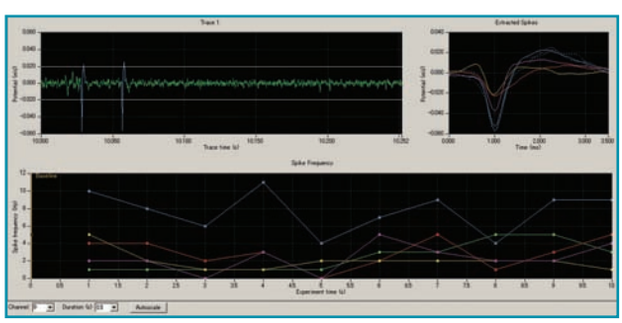
Single units can be followed for weeks, allowing long-term observation of the physiology and pharmacology of cerebellar synapses.

Courtesy of Dr. Amy Arai, Southern Illinois University

Recording from neuronal cultures



(25 µV, 100 ms / Div)



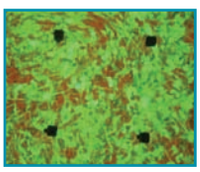
A: Spontaneous single-unit activities obtained from dissociated hippocampal neurons cultured for 30 days in a MED probe.

B: Spike sorting for a single channel (9) performed by Mobius software. Spikes were extracted based on a +/-20 µV threshold and clustered based on waveform similarity. 4 different spikes are detected in this channel and their individual frequencies are displayed on the bottom.

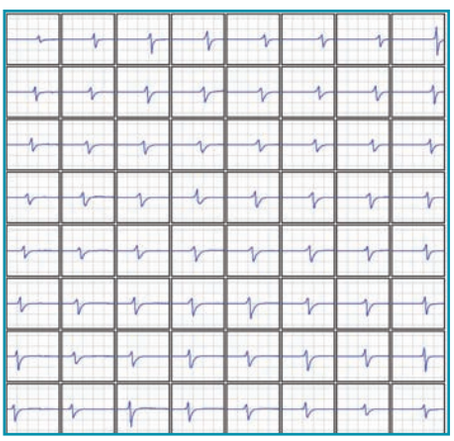
CARDIAC APPLICATIONS

MED probes are ideal for culture of primary cardiomyocytes and cardiac cell lines (e.g. HL-1), or for recording from acutely-prepared cardiac tissue. The MED probe's high-capacitance electrodes allow delivery of stimulus current as high as 200 µA through any of the 64 electrodes, enabling acquisition of "paced" or spontaneous signals. Simultaneous recording from the 64 electrodes allows 2-D propagation patterns and velocities to be observed.

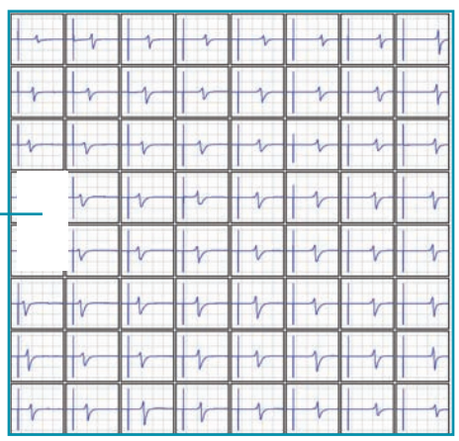
Spontaneous and paced signals in primary cardiomyocyte cultures



A

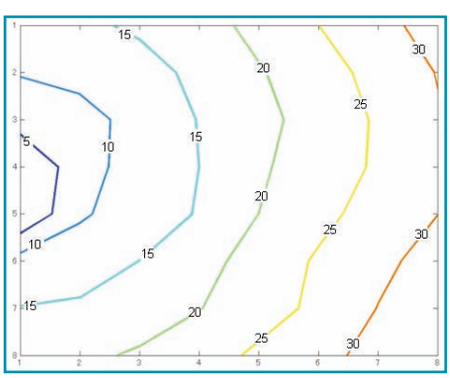


B (500 µV, 10 ms / Div)



C (500 µV, 10 ms / Div)

Stimulation

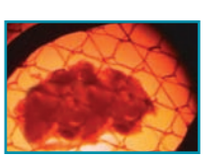


D

A. Fluorescence micrograph of cardiomyocyte cultures on MED probe (MED-P545A; 450 µm inter-polar distance)
B. Spontaneous responses obtained from 64 electrodes.
C. Signals evoked by stimulation at two adjacent electrodes.
D. Phase map of pacing activity. Each color shows the latency (ms) of the responses evoked by stimulation.

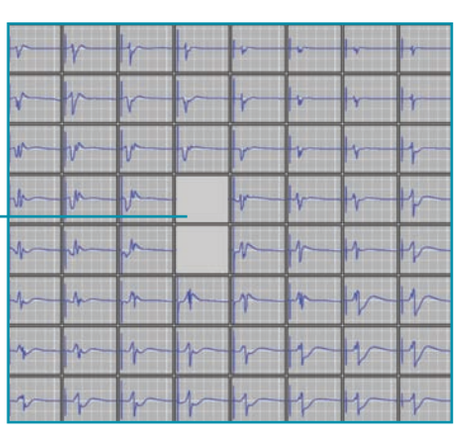
Courtesy of Dr.s. Lee and Kodama, Nagoya University, Japan

Response to pacing of left atrium

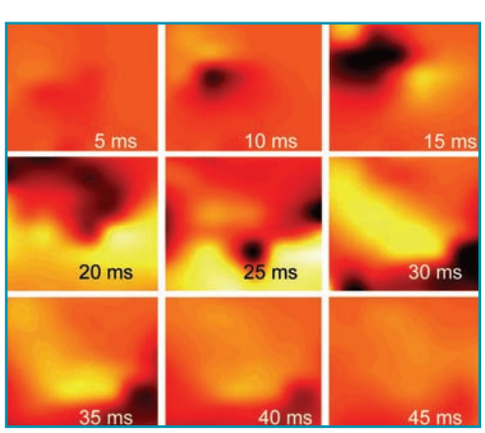


A

Stimulation



B (2.0 mV, 20 ms / Div)



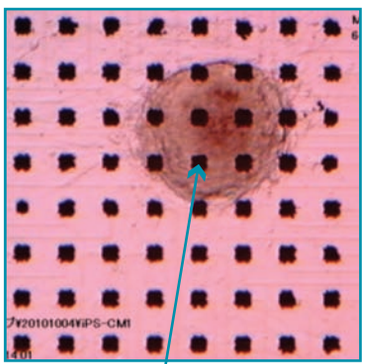
C

A: Micrograph of rat left atrium on MED probe (MED-P545A; 450 µm inter-polar distance).
B: Pacing responses evoked by stimulation at two electrodes (blank panels) on the MED probe.
C: Propagation of the pacing activity. Each time frame shows the computed two-dimensional field potential distribution over time. Positive potentials are white and negatives are black.

STEM CELL APPLICATIONS

ES or iPS cell-derived cardiomyocytes and neurons can be cultured directly in the MED probes and observed for long periods of time with the non-invasive planar microelectrodes. The MED64 system can be a powerful tool for studying formation of electrical connectivity in stem cell cultures, as well as drug screening with ES/iPS cell-derived cardiomyocytes and neurons.

Evaluation of drug-induced field potential prolongation with iPSC-derived cardiomyocytes



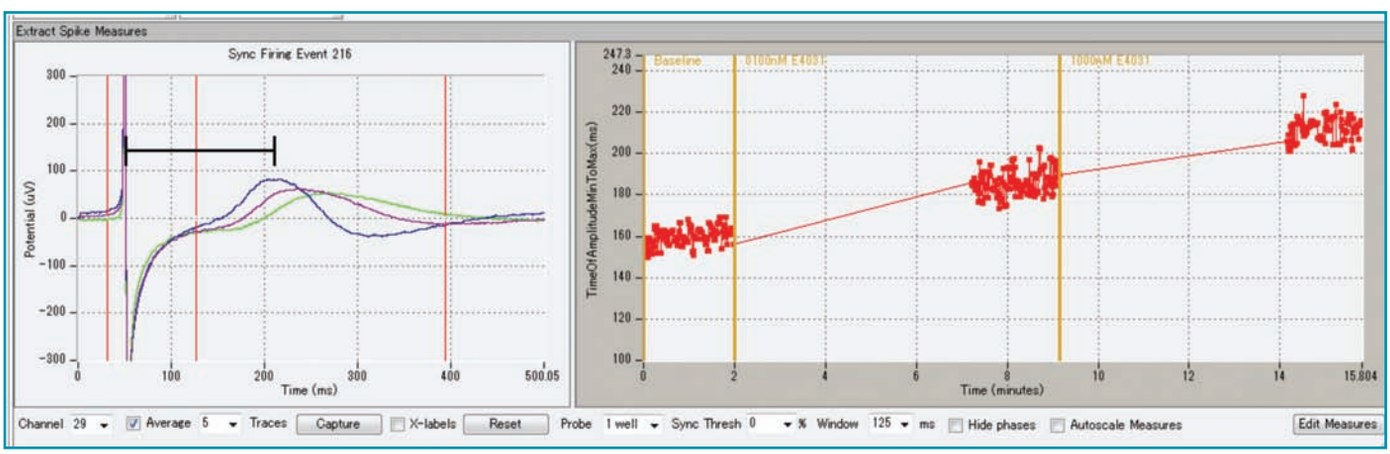
[Top] Human iPSC-derived cardiomyocytes on a MED probe. (MED-P515A: 150 µm inter-polar distance)

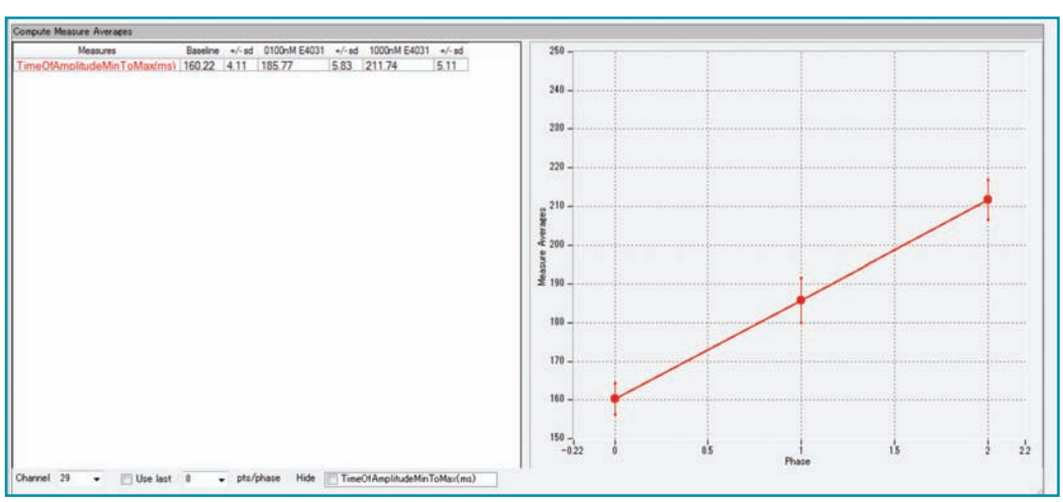
[Middle] The left chart shows signals acquired from electrode 29 in the absence (Blue) and presence of E4031 (Purple: 100 nM, Green: 1 µM). E4031 prolongs the waveform and decreases rising and descending slopes in a dose dependent manner.

The duration between peaks for depolarization and repolarization phases ("field potential duration"; black bar) of the waveform is automatically measured and graphed by Mobius software (right panel).

Yellow bars represent user-defined experimental phases used to delineate E4031 concentrations for computing average values below.

[Bottom] Average and SD of field potential duration computed automatically by Mobius software for above data.





MED64 product information
www.med64.com

Alpha MED Scientific Inc.

209 Saito-incubator
7-7-15, Saito-asagi, Ibaraki Osaka,
567-0085, Japan

Phone: +81-72-648-7973
FAX: +81-72-648-7974
E-mail: info@amedsci.com

Manufactured by Alpha MED Scientific Inc.

U.S.: RE38323: RE37977: 5,810,725: 6,151,519: 6,297,025: 6,511,817: 6,890,762: CA: 2316213
Europe: EP0689051B1
Japan: 2949845: 3101122: 3193471: 32204875: 3577459: 361972
Korea: 150390: 291052: 4933913
Taiwan: 128335: 243483
CN: 988133156.6