
MED64

The most sensitive microelectrode array system
for *in vitro* extracellular electrophysiology

Product Manual

MED64 Head Amplifier

P/N: MED-A64HE1S



ALPHA MED SCIENTIFIC

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Version: 1.10; January 1, 2017

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1. Safety precautions

Before using this unit please read these operating instructions carefully. Take special care to follow the warnings indicated on the unit itself as well as the safety suggestions listed below. Keep these precautions at hand for future reference.

1-1. Placement

- Avoid placing the unit in areas of:
 - direct sunlight.
 - high temperature.
 - high humidity.
 - excessive vibration.
 - uneven surfaces. (Place the unit on a flat level surface.)

Such conditions might damage the cabinet and/or other component parts and thereby shorten the unit's service life.

1-2. Stacking

- Never place heavy items on top of the unit, the DC power supply unit, or AC power cord.

1-3. Voltage

- A DC power source cannot be used. Be sure to check the power source carefully.

1-4. Power cord protection

- Avoid using AC power cords with cuts, scratches, or poor connectors, as this may result in fire or electric shock. Excessive bending, pulling or slicing of the cord should also be avoided.
- Do not pull on the cord when you are disconnecting the power. This could cause an electric shock. Grasp the plug firmly when you disconnect the power supply.
- Never touch the plug with wet hands as a serious electric shock could result.

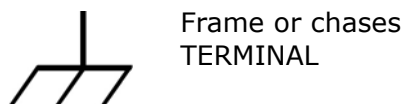
1-5. Foreign materials

- Ensure that no foreign objects (e.g. - needles, coins, screwdrivers), accidentally fall into the unit. Otherwise, a serious electric shock, short circuit, or other malfunction could occur.
- Be extremely careful about spilling water or liquid on or into the unit, as a fire, short circuit, or electric shock can also occur. Disconnect the power plug and contact your dealer immediately if this occurs.
- Avoid spraying volatile chemicals (e.g.- insecticides, alcohol, paint thinner) on or into the unit. They contain flammable gases which can be ignited.
- Insecticides, alcohol, paint thinner and similar chemicals should never be used to clean the unit. They can cause flaking or cloudiness to the cabinet finish.

1-6. Service

- Never attempt to repair, disassemble or modify the unit if there seems to be a problem. A serious electric shock could result if you ignore this precautionary measure.
- If a problem occurs during operation (smoke is detected, etc.) contact your dealer immediately.
- Disconnect the power supply if the unit will not be used for a long time. Otherwise the unit's lifetime could be shortened.

Safety-related symbols used on equipment and documentation:



1-7. Environmental conditions

- Indoor use.
- Altitude up to 2000 m.
- Temperature: 5 - 40 °C.
- Maximum relative humidity 80% for temperatures up to 31 °C decreasing linearly to 50% relative humidity at 40 °C.
- Main supply voltage fluctuations not to exceed +/- 10% of the nominal voltage.

1-8. Maintenance

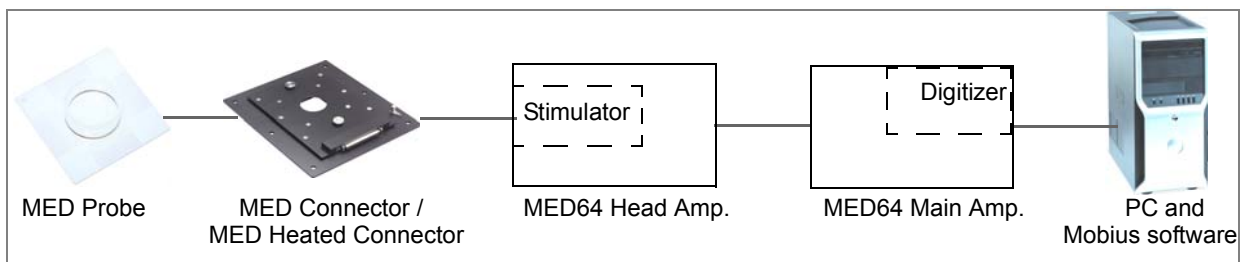
- Clean the cabinet, panel and controls with a soft cloth lightly moistened with mild detergent solution.
- Do not use any type of abrasive pad, scouring power or solvent such as alcohol or benzene.
- Supply voltage fluctuations must not to exceed +/- 10% of the nominal voltage.

2. MED64 Head Amplifier components and functions

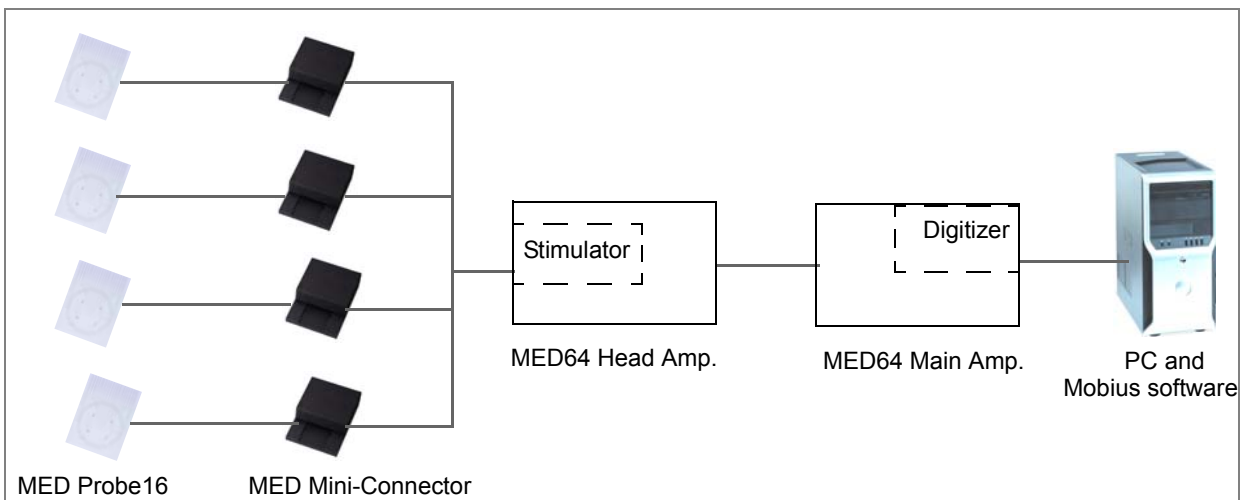
The MED64 Head Amplifier (MED-A64HE1S) is the head amplifier for the MED64-Basic, Quad II, and Allegro systems. Field potentials (extracellular signals) are acquired from the acute or cultured biological preparations that are placed onto the 64 planar microelectrodes in the MED Probe. The acquired raw signals are amplified by x10 with the MED64 Head Amplifier, then sent to the MED64 Main Amplifier (MED-A64MD1), where the input signals are amplified further and digitized. Stimulus current can be delivered via any of the 64 electrodes using the built-in stimulator in the MED64 Head Amplifier.

2-1. System configurations

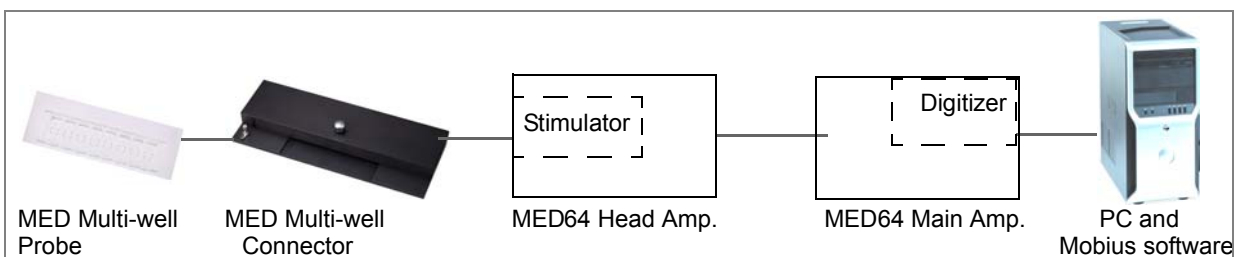
MED64-Basic



MED64-Quad II



MED64-Allegro



2-2. Components and their functions

Front panel



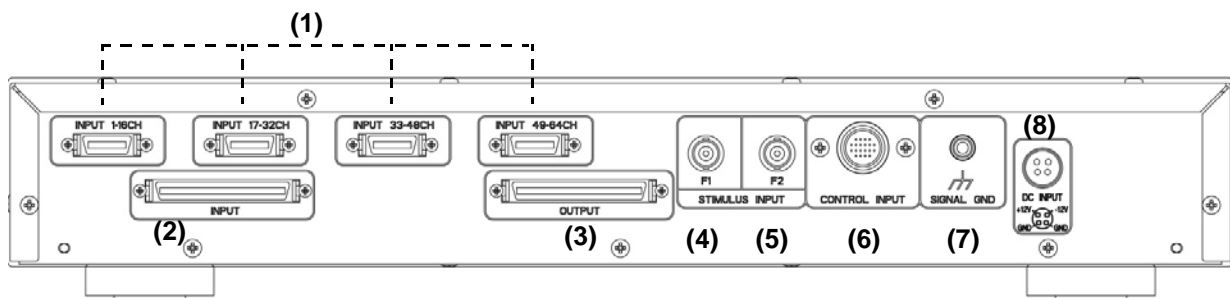
(1) POWER

Turns amplifier ON and OFF.

(2) STIMULUS CURRENT

Selection of x2 doubles the output stimulus current. Selecting NORMAL maintains the output stimulus current amplitude equal to the value set in the software. (e.g. when 10 μ A is set in the software with x2 selected, the output stimulus current amplitude is 20 μ A. When 10 μ A is set in the software with NORMAL selected, the output stimulus current amplitude is 10 μ A)

Back panel



(1) INPUT 1-16CH, 17-32CH, 33-48Ch, 49-64CH

Signal input for the MED Multi-well Connector (MED-C11), MED Mini-Connector (MED-C04). Connects to the 20 pin terminals of the either Connector(s). Leave these terminals OPEN when the 68 INPUT(2) is connected.

(2) INPUT

Signal input for the MED (Heated) Connector (MED-C03, MED-CP02H). Connect to the 68 pin terminals of the MED (Heated) Connector (MED-C03, MED-CP02H). Leave this terminal open when INPUTS 1-16CH, 17-32CH, 33-48CH, or 49-64CH are connected.

CAUTION:

Do NOT Connect (1) and (2) simultaneously.

(3) OUTPUT

Signal output. Connects to the [INPUT] terminal on the MED64 Main Amplifier (MED-A64MD1).

(4) F1 STIMULUS INPUT

Input for F1 stimulator. Connects to the [F1 STIMULUS OUTPUT] on the MED64 Main Amplifier (MED-A64MD1).

(5) F2 STIMULUS INPUT

Input for F2 stimulator. Connects to the [F2 STIMULUS OUTPUT] on the MED64 Main Amplifier (MED-A64MD1).

(6) CONTROL INPUT

Input for control of stimulus channels. Connects to the [CONTROL OUTPUT] on the MED64 Main Amplifier (MED-A64MD1).

(7) SIGNAL GND

Ground terminal for signals.

MED64-Basic (for MED-C03, MED-CP02H Connector)

Grounding here is not usually necessary.

- Connect the grounding wire onto the MED Connector cable here for the old-model cable wrapped around by gray conductive tape.

MED64-Quad II (for MED-C04 Connector):

Connect the grounding wire onto the MED connector cable here.

MED64-Allegro System (for MED-C11 Connector):

Connect the GND terminal of the MED-C11 Connector here with a grounding wire.

(7) DC INPUT

DC power supply cord inserts here.

Accessory



DC Power supply unit -1unit-

3. MED64 Head Amplifier set-up

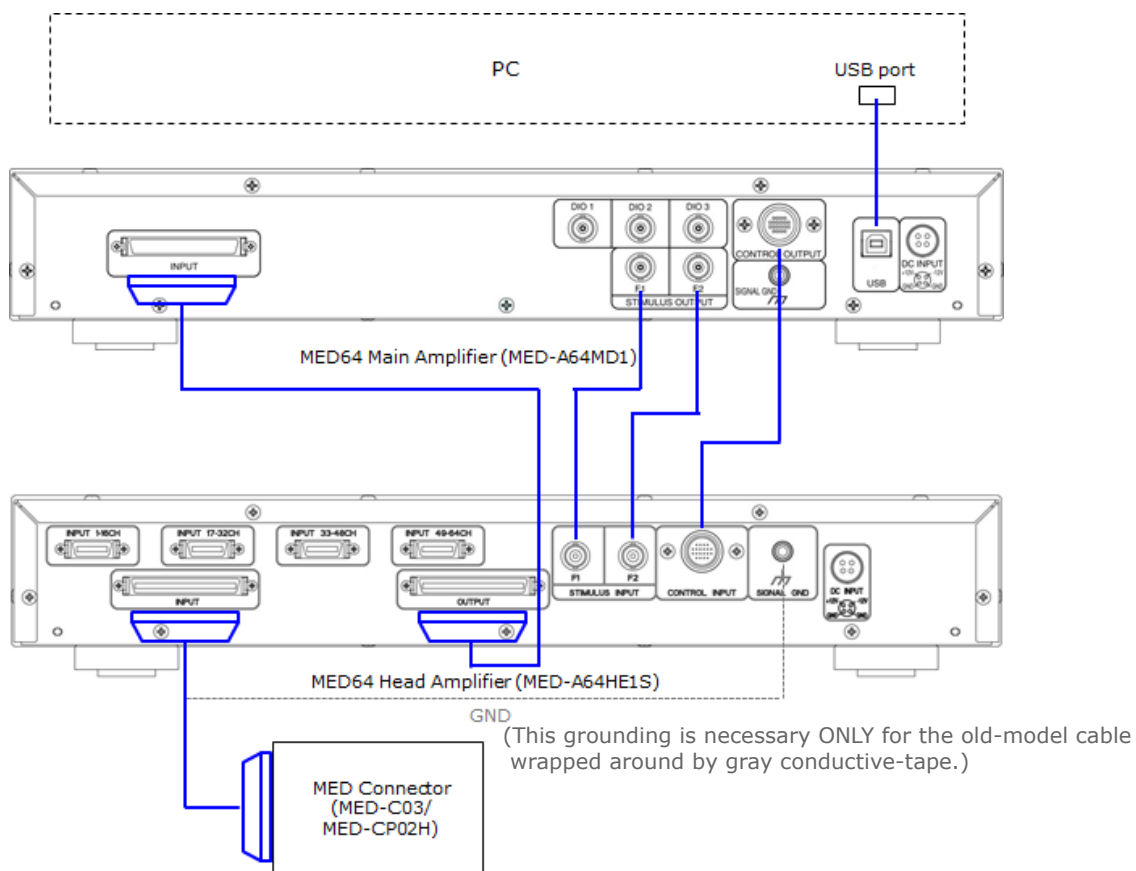
The MED64 systems have several technical advantages due to the low-impedance platinum-black microelectrodes on the MED Probe (typically 10 kΩ at 1kHz for 50 μm electrodes). These include:

1. The system is more resistant to exogenous noise (e.g. hum noise).
2. Very low Johnson noise (baseline noise) as low as a few microvolts can be achieved.
3. The MED Probe/Connector can be physically separate from the amplifier (such as during long-term recordings in a humidified incubator). It is connected with a cable as long as 2m without noise or signal attenuation.

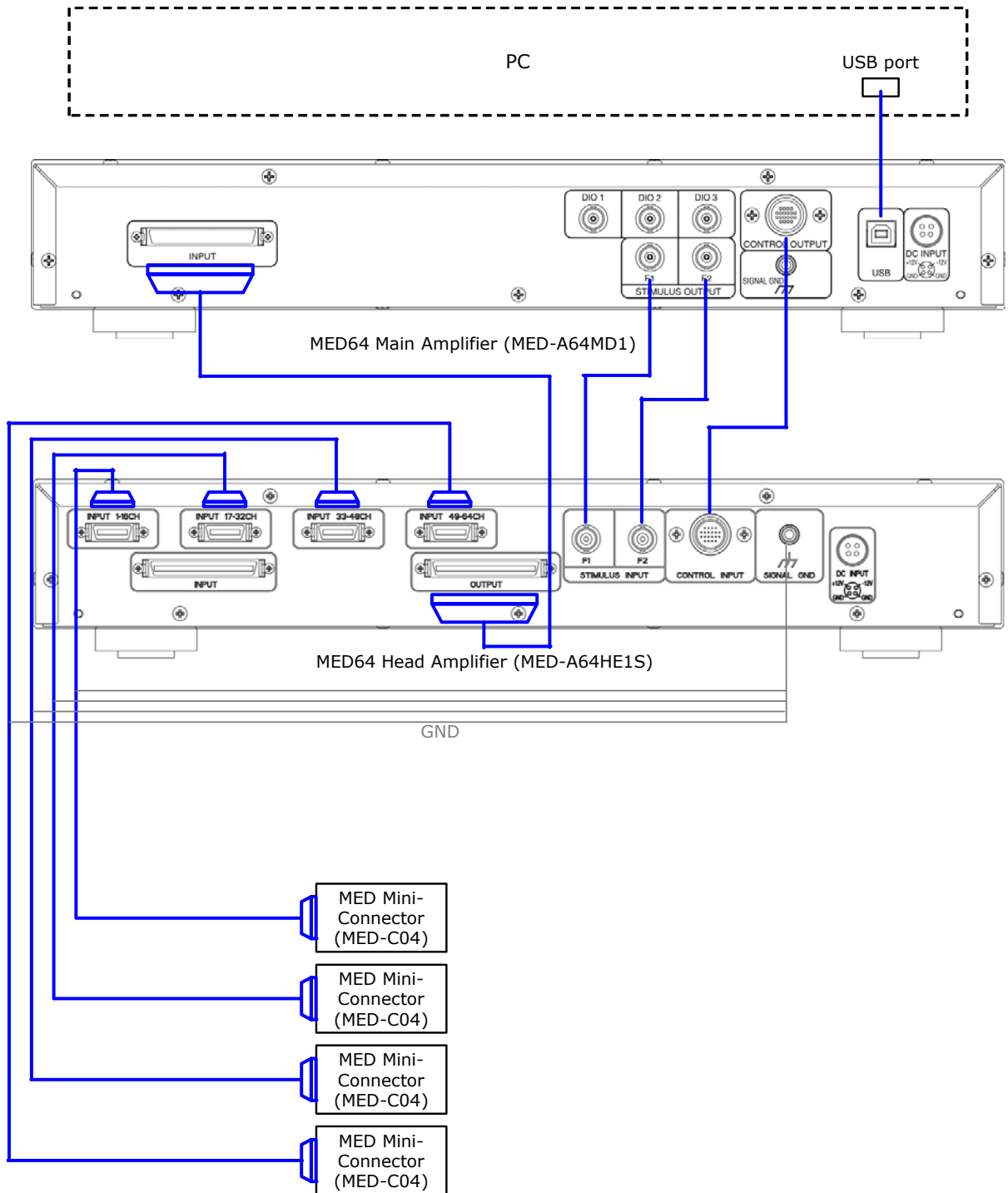
The MED64 Systems do NOT usually require a Faraday cages or vibration isolation tables necessary for conventional electrophysiology rigs. It is recommended that the MED64 system be **installed on a STABLE TABLE** such as lab bench using aluminium foil except when the system is used in conjunction with other equipment such as an incubator or microscope. Please refer to "MED64 Handbook Vol1 Hardware" for the installation and operation of the MED64 Systems.

3-1. Connecting the MED64 Head Amplifier to other components

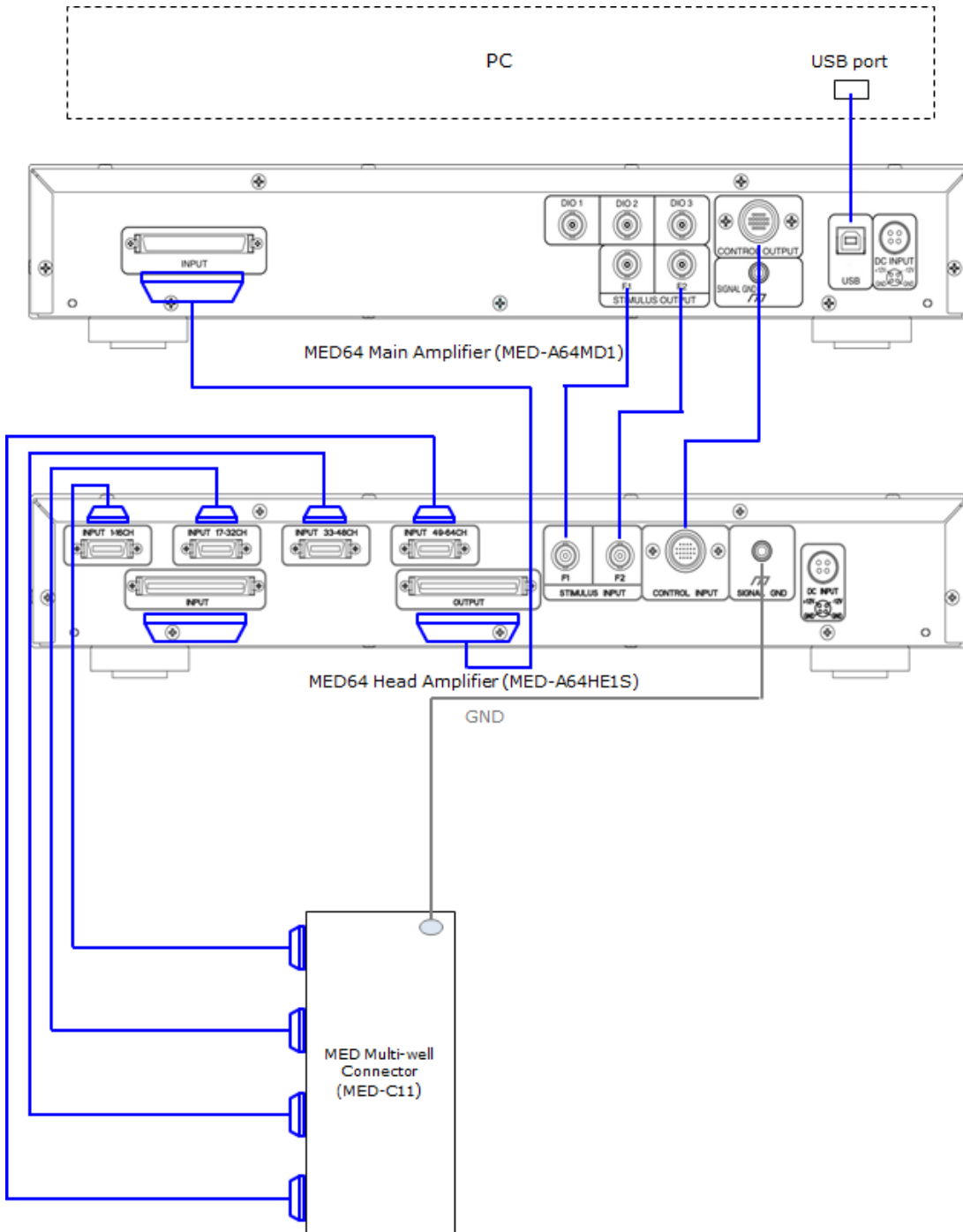
MED64-Basic (To MED-C03/MED-CP02H Connectors)



MED64-Quad II (To MED-C04 Connector)



MED64-Allegro (To MED-C11 Connector)



4. Signal acquisition with the MED64 Systems

The MED Probe has 64 recording electrodes and 4 (or 8, 16) reference electrodes. The difference between potentials at the recording electrodes and the reference electrodes are measured with the MED64 systems. Figure .1 shows a schematic diagram of the circuit between the recording and reference electrodes with the MED64 System.

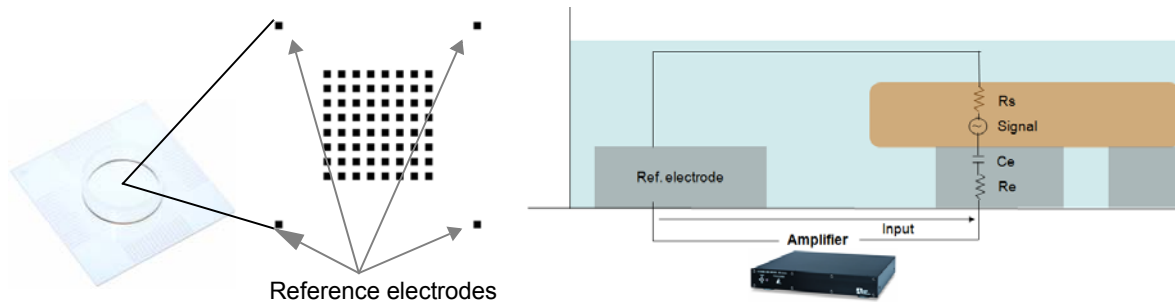


Figure 1. Electrodes embedded on the MED Probe (The Standard 8x8 array, left) and the mechanism of recording of field potentials using the MED64 Systems.

5. Amplifier input-impedance requirements for avoiding signal attenuation

One of the planar microelectrode's unique characteristics is that it forms an "electric double layer capacitor" between the electrode and solution. This "electric double layer capacitor" results in a rise in the electrode impedance at low frequencies. (See Figure 2) This detail should be noted because acquired signals are attenuated if the electrode impedance becomes higher than the input impedance of the amplifier.

The platinum-black microelectrodes on the MED Probe intrinsically have very low-impedances (10 k Ω for 50 μm electrodes, 15 k Ω for 20 μm electrodes, at 1 kHz). The impedances are small even at low frequencies (as seen in Figure 2). Thus, the input-impedance of 100 M Ω is high enough for the MED64 System. Low-frequency signals such as fEPSPs or even slower signals such as from smooth muscle (0.1 Hz) can be acquired without attenuation.

If 1Hz signal is acquired with flat ITO electrodes, signals are attenuated because the electrode impedances are larger than 100 M Ω (blue line in Figure 2.). However, when 1Hz signals are acquired with the platinum-black electrode on the MED Probe, signals are acquired without attenuation because the electrode impedances are smaller than 100 M Ω (green and red lines in the Figure 2).

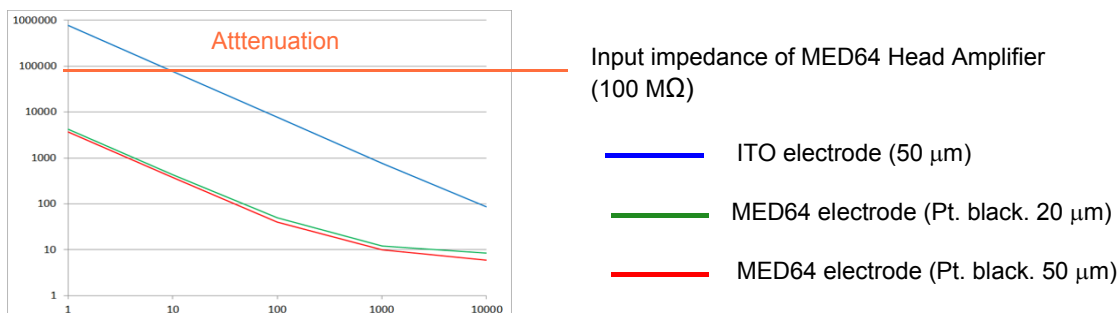


Figure 2. Electrode impedance and input impedance of the MED64 Head Amplifier.

6. Stimulation using planar microelectrodes

6-1. Stimulation using planar microelectrodes

The MED64 Head Amplifier has a built-in 2 channel current-driven stimulator that enables stimulation via any of the 64 electrodes. Figure 4 shows a schematic diagram of the extracellular electrical stimulation circuit for the MED64 Systems. The stimulus current flows from the selected electrode to reference electrodes. The applied stimulus current charges the “electrical double-layer capacitor” at the interface of electrode, subsequently changing the voltage of C_e (V_c). This voltage change modulates the field potential, which results in depolarization of cellular membranes. The field potentials (V_f) change according to the output current (I_s) as seen on the right in the Figure 3.

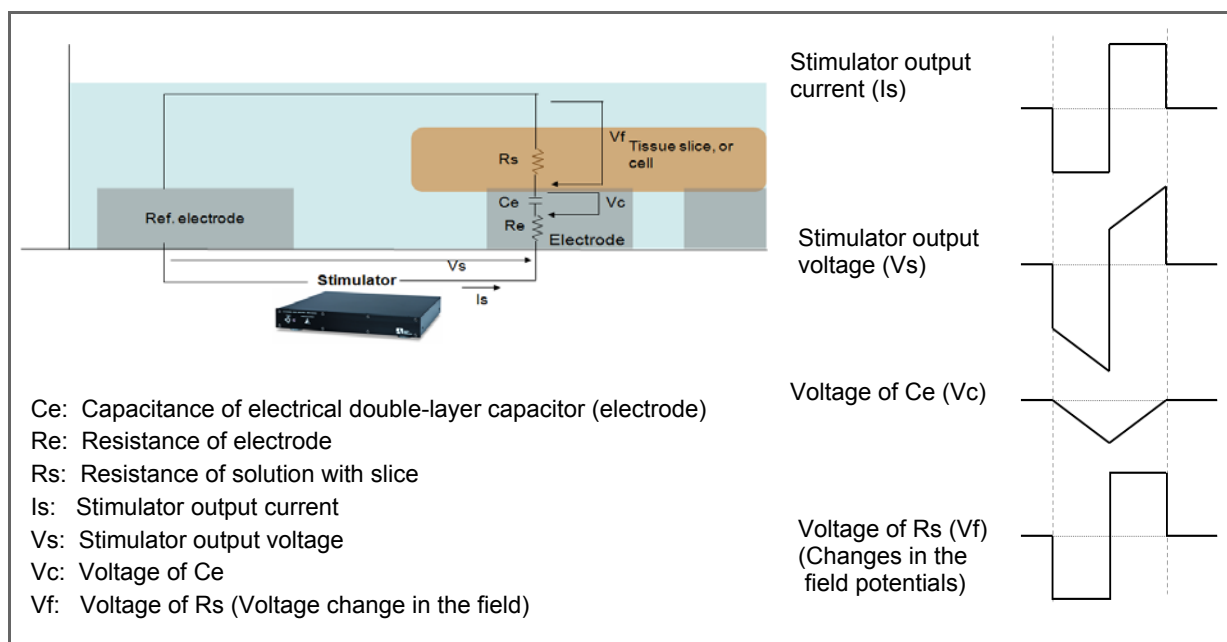


Figure 3. Stimulation using microelectrodes at the MED64 System.

6-2. Stimulus artifacts and biphasic stimulation

When stimulation is enabled, stimulus pulses are recorded at recording channels (non-stimulating channels) due to crosstalk, causing "stimulus artifacts". These stimulus artifacts can persist even after the stimulus pulse returns to zero and can interfere with the recording of real biological signals.

This is mainly due to following factors:

1. The incoming stimulus artifacts' amplitude often exceeds 5 mV, the maximum input voltage for the MED64 amplifier, causing a temporary saturation. The amplifier needs some time to recover. This delay becomes larger in proportion to the stimulation output voltage (V_s).
2. The electrode often needs longer time to discharge than to charge. This delay also becomes larger as the voltage of C_e (V_c) becomes larger.

The duration of the stimulus artifact using the MED64 microelectrodes and amplifiers should be minimal with proper operation because both (V_s) and (V_c) levels are low due to the electrodes' low-impedance and high-capacitance.

Please follow the directions described below in order to minimize the stimulus artifact duration.

1. Make sure to apply **current-driven biphasic stimulation with identical durations for the negative and positive components** as seen in the Figure 4.

When biphasic stimulation is applied, the electrode is charged and discharged quickly. However, when mono-phasic stimulation is applied the electrodes need longer time to discharge than to charge, which will dramatically prolong stimulus artifacts and damage electrodes. (Refer to Figure 4.)

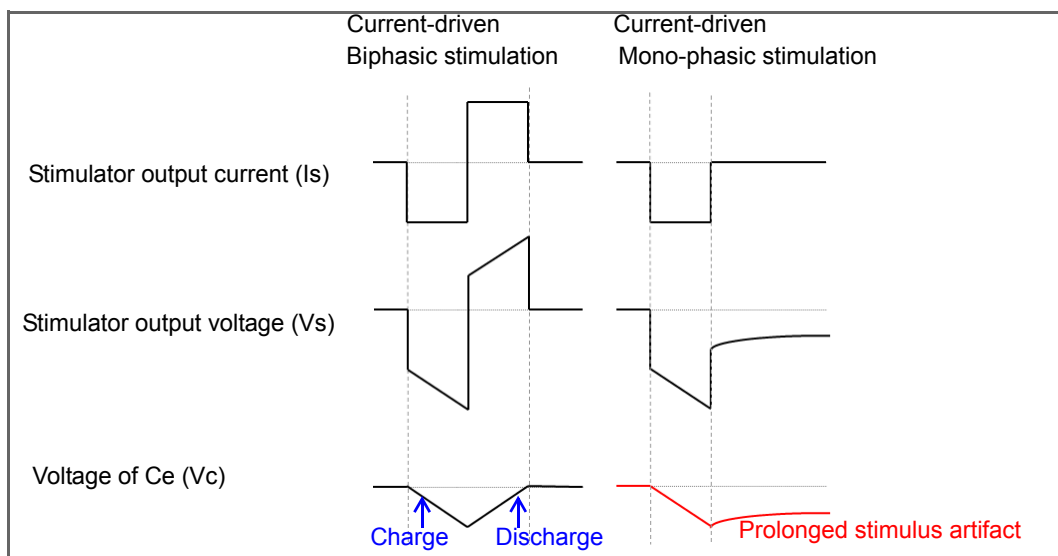


Figure 4. Biphasic stimulation and mono-phasic stimulation.

CAUTION:

- **ONLY** current-driven biphasic stimulation with identical durations for negative and positive pulses is recommended for the MED64 Systems.
- Do **NOT** apply mono-phasic stimulation, which will damage the electrode.

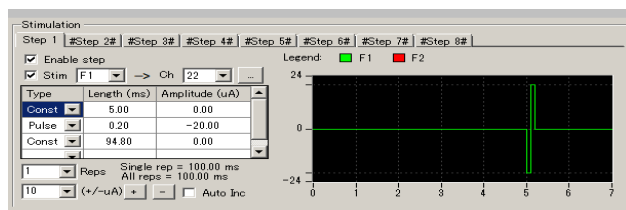


Figure 5. Biphasic stimulation with identical durations for the negative and positive pulses.

2. **Use the platinum-wire** as additional reference electrodes.
-Please refer to the "MED64 Handbook vol.1" for the use of platinum wire.

6-3. Stimulus Current to be applied to electrodes

As described in the previous section, the applied stimulus current charges the electrical double-layer capacitor and causes the voltage (V_c) to change (Figure 7). When the voltage (V_c) rises beyond 1V, the electrode will undergo electrolysis and release H₂ gas. This causes the stimulation efficiency to drop dramatically, introduces extremely large stimulus artifacts, harms cells, and damages the electrodes. Thus, the stimulus current (I_s) should not go beyond this level.

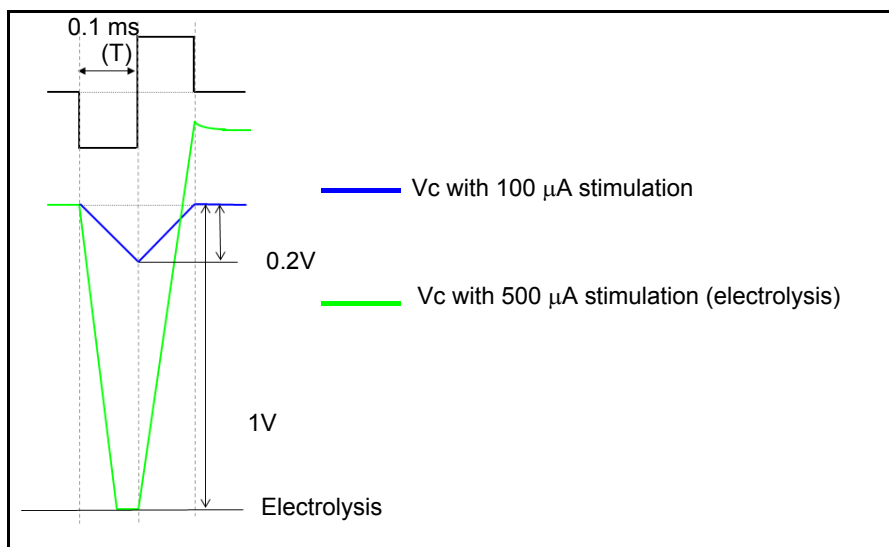


Figure 6. Changes for Voltage of Ce (V_c) with different stimulus current amplitude.

The (V_c) is defined by $V_c = I_s \times t / C_e$. (*1) The capacitance (C_e) of the MED64 microelectrode is as high as 50,000 pF for 50 x 50 μm electrodes (22,000 pF for 20 x 20 μm electrodes), allowing stimulation with current amplitudes up to 200 μA for 0.2 msec (duration for each phase is 0.1 msec). DO NOT use stimulus current/duration parameters outside the shaded area in the Figure 8.

(*1) V_c : Voltage of Ce
 I_s : Stimulator output current
 T : Pulse duration
 C_e : Electrode capacitance (electrical double layer capacitor's capacitance)

CAUTION:

- DO NOT use combinations of stimulus current & duration outside the shaded area in the Figure 7. Higher values might damage the electrodes.
- The numerical value of this graph is based on "Single pulse stimulation". If multi-paired stimulation with pulse interval shorter than 1 second is used, please decrease the stimulus current and duration values to 80% of the graph.

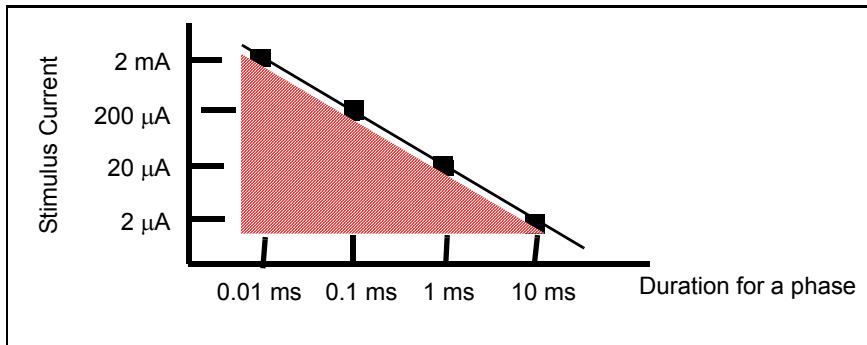


Figure 7. Suggested stimulation parameters.

6-4. Setting-up the stimulus protocols

The stimulus current amplitudes and channels are set in the [Acquire MED64R2 Data w/Stim] module in the MED64 Mobius software. Please refer to the Mobius Tutorial for setting up the stimulation parameters. Note that the amplifier requires 5 seconds to recover and be ready for acquisition at non-stimulated channels. **Set the Trace interval for longer than 5 msec when stimulation is applied.** (The stimulated channel requires 20 seconds for the recovery.)

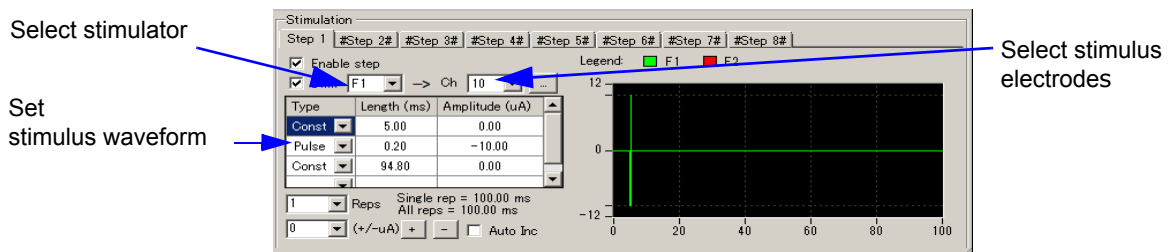


Figure 8. Mobius' control panel for setting stimulus parameters.

Stimulation for the MED64-Quad II , Allegro systems

For the MED64-Quad II and Allegro Systems, delay the stimulus timing per Probe (for Quad II) or well (for Allegro) using the Mobius’s different Steps. Set the delay for longer than 5 seconds. Avoid stimulating simultaneously over Probes (or wells) because the system could pick up the stimulus artifacts leaked from Probes (or wells) that stimulation is applied to.

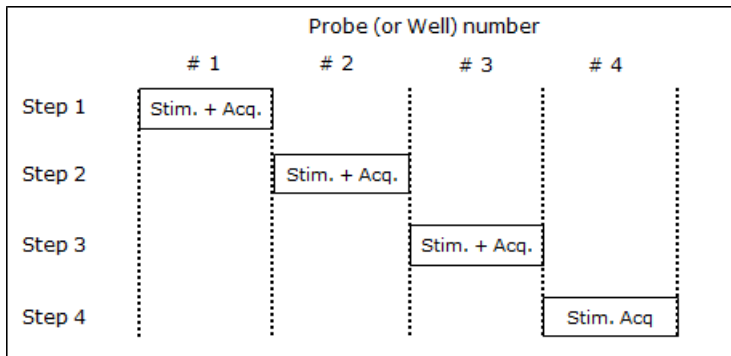


Figure 9. Stimulation and acquisition scheme for the MED64-Quad II and Allegro (4 well) System.

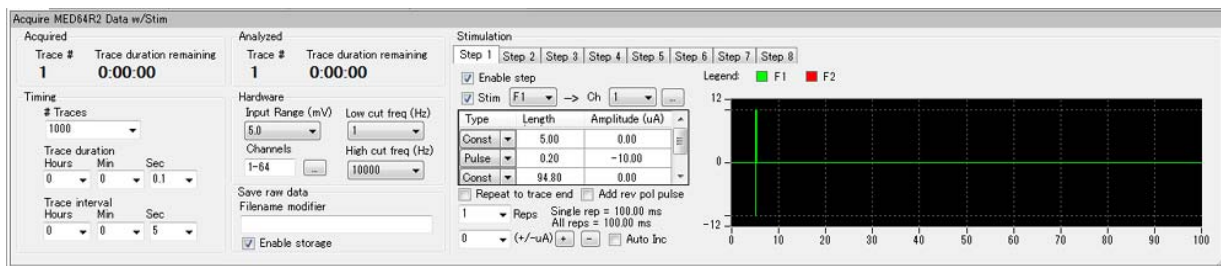


Figure 10. An example of stimulation and acquisition parameters for the MED64-Quad II/Allegro (4 well) System. The Steps 1-4 are activated to stimulate with a delay of 5 seconds.

7. Warranty

This product will be repaired with new or refurbished parts, free of charge, for one (1) year from the date of original purchase in the event of a defect in materials or workmanship.

The product warranty covers failures due to defects in materials or workmanship which occur during normal use. It does NOT cover damage incurred during shipment or problems which are caused by products not supplied by Alpha MED Scientific. In addition, this warranty does not cover problems resulting from alteration, accident, misuse, neglect, faulty installation, maladjustment of user controls, improper maintenance, modifications or service by anyone other than AMS or damage attributable to acts of God.

8. Specifications

Amplifier

Number of channels	64
Gain	x 10
Bandwidth	0.1Hz - 100 kHz (+0dB to -3dB)
Input impedance	100 M Ω
Output impedance	10 k Ω
Input terminal	68 pin x 1, 20 pin x 4
Output terminal	68 pin x 1
RMS noise (Typical)	
* Input short-circuited:	14 nV / $\sqrt{\text{Hz}}$
* MED-P515A:	0.8 μV (f < 3 kHz)
	1.2 μV (f < 5 kHz)
	1.8 μV (f < 10 kHz)

Stimulator

Number of channels	2
Output format	Current-driven
Maximum input voltage	+/- 4V
Maximum output current	+/- 200 μA

General

Power supply	DC +/- 12V
Weight	6.6 Kg (without power supply unit)
Dimensions	W430 x LD437 x H74mm (without power supply unit)

Power supply unit

Input	AC 100-240 V (50-60 Hz)
Output	DC +/-12 V

*Specifications may not be satisfied depending upon the type of computer or operating environments used.
Only for use in animal studies research.
Specifications and external appearance are subject to change without notice.*

January 1, 2017



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