OPERATING INSTRUCTIONS AND SYSTEM DESCRIPTION FOR THE

<u>MVCS Series</u>

IONTOPHORESIS SYSTEMS

With Fast Capacitance Compensation

Without Fast Capacitance Compensation

VERSION 4.0
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Table of Contents

About this Manual

This manual should help you setup and use the MVCS-02C system correctly and to perform accurate experiments.

Generally, two different versions of the MVCS-02C system are available:

- System **without** headstage, R_{EL} test and CAPACITY COMPENSATION (MVCS-02C versions)
- System **with** headstage, R_{EL} test and CAPACITY COMPENSATION (MVCS-**C**-02C versions)

Note: In this manual, the slow MVCS-02C version is referred as MVCS, whereas the fast MVCS-**C**-02C version is referred as MVCS-C.

If you are not familiar with the use of instruments for iontophoretic application of substances, please read the manual completely. The experienced user should read at least chapters 1, 4, and 5.

Important: Please read chapter 1 carefully! It contains general information about safety regulations and how to handle highly sensitive electronic instruments.

Signs and conventions

In this manual names of all elements of the front panel are written in capital letters as they appear on the front panel.
System components that are shipped in the standard configuration are marked with ✓, optional components with ➪. In some chapters the user is guided step by step through a certain procedure. These steps are marked with ❑.
Important information, hints and special precautions are highlighted in gray.

Abbreviations

I_{EL} current at electrode
R_{EL} electrode resistance
V_{EL} voltage at electrode

1. Safety Regulations

<u>VERY IMPORTANT</u>: **Instruments and components supplied by npi electronic are NOT intended for clinical use or medical purposes (e.g. for diagnosis or treatment of humans) or for any other life-supporting system. npi electronic disclaims any warranties for such purpose. Equipment supplied by npi electronic must be operated only by selected, trained and adequately instructed personnel. For details please consult the GENERAL TERMS OF DELIVERY AND CONDITIONS OF BUSINESS of npi electronic, D-71732 Tamm, Germany.**

1) GENERAL: This system is designed for use in scientific laboratories and must be operated by trained staff only. General safety regulations for operating electrical devices should be followed.

2) AC MAINS CONNECTION: While working with the npi systems, always adhere to the appropriate safety measures for handling electronic devices. Before using any device, please read manuals and instructions carefully.
   The device is to be operated only at 115/230 Volt 60/50 Hz AC. Please check for appropriate line voltage before connecting any system to mains.
   Always use a three-wire line cord and a mains power-plug with a protection contact connected to ground (protective earth).
   Before opening the cabinet, unplug the instrument.
   Unplug the instrument when replacing the fuse or changing line voltage. Replace fuse only with an appropriate specified type.

3) STATIC ELECTRICITY: Electronic equipment is sensitive to static discharges. Some devices such as sensor inputs are equipped with very sensitive FET amplifiers, which can be damaged by electrostatic charge and must therefore be handled with care. Electrostatic discharge can be avoided by touching a grounded metal surface when changing or adjusting sensors. **Always turn power off when adding or removing modules, connecting or disconnecting sensors, headstages or other components from the instrument or 19” cabinet.**

4) TEMPERATURE DRIFT / WARM-UP TIME: All analog electronic systems are sensitive to temperature changes. Therefore, all electronic instruments containing analog circuits should be used only in a warmed-up condition (i.e. after internal temperature has reached steady-state values). In most cases a warm-up period of 20-30 minutes is sufficient.

5) HANDLING: Please protect the device from moisture, heat, radiation and corrosive chemicals.

6) CURRENT INJECTION HIGH VOLTAGE HEADSTAGE: The current injection headstages have an output compliance of ±45 V up to ±225 V. In addition, some headstages are equipped with a driven shield electrode connector (marked "Driven Shield" on the headstage enclosure). After turning on the instrument do not touch the interior contact or the shield of the electrode plug or of the cable that is connected to this plug. **In addition, it is extremely important that the instrument is turned off when changing or adjusting the electrode.**

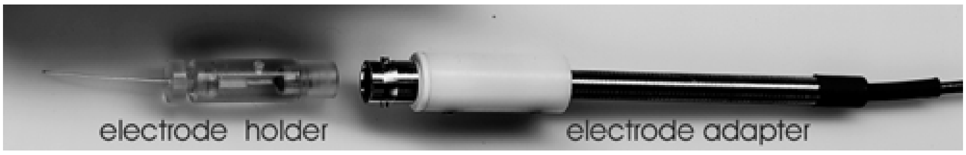
2. MVCS Components

The following items are shipped with a MVCS system:

- ✓ MVCS amplifier
- ✓ Headstage (MVCS-C systems only)
- ✓ GND connector for headstage (2.6 mm, MVCS-C systems only)
- ✓ Electrode cables (MVCS systems only)
- ✓ Power cord
- ✓ User manual

Optional accessories:

- ➪ Electrode holder
- ➪ Electrode adapter with BNC- and SMB connector



3. System Description

MVCS-02C systems are high-voltage current sources for iontophoresis or other applications, where constant currents in the nano- or microampere range are needed. Standard MVCS-02C systems have an output compliance of ±45 V and can generate currents up to 450 nA into 100 MΩ while high-voltage MVCS-02C systems work with up to ±225 V generating currents up to 2.25 µA into 100 MΩ.
Generally, two different versions of MVCS-02C system are available:

- System **without** headstage, R_{EL} test and CAPACITY COMPENSATION (MVCS-02C versions)
- Systems **with** headstage, R_{EL} test and CAPACITY COMPENSATION (MVCS-**C**-02C versions)

Note: In this manual the slow MVCS-02C version is referred as MVCS whereas the fast MVCS-**C**-02C version is referred as MVCS-C.

The operating and display elements of these instruments facilitate the application of drugs in physiological, pharmacological and biochemical studies. All systems allow very fast drug applications in the millisecond range, and even the sub-millisecond range, if equipped with the fast capacitance compensation option. Therefore, these systems can be used to simulate synaptic events (Renger et al., 2001; Cottrell et al., 2000; Liu et al., 1999).

The MVCS systems are available as 19” instruments or as modules for the EPMS-07 modular system. The standard system described here, is housed in a 19" rackmount cabinet. The MVCS-02C consists of two independent channels, one is for current injection and the other, COMPENSATION, is for balancing the applied current automatically. Each injection channel has digital ten-turn potentiometer for EJECT or RETAINING currents and CAPACITY COMPENSATION. Each injection channel also has a digital display, overrange LEDs and two switches for selection of the operating mode. The COMPENSATION channel has the same controls, but no potentiometer for adjusting current.

In fast systems with CAPACITY COMPENSATION (MVCS-C), the injecting electrodes are connected via small SUBCLIC or BNC shielded connectors that are mounted to a small headstage avoiding artifacts caused by long cables.
Systems for slow, long lasting applications, in the second or minute range (MVCS), need no headstages. In this case, the electrodes are connected by special connectors at the front panel with shielded cables.

For EJECT or RETAIN currents modes of operation include manual activation and automatic control by digital TTL signals (HI = EJECT, LO = RETAIN). An automated electrode resistance test mode (MVCS-C) is also available.

3.1. Compensation (Balance) Unit

To avoid artifacts caused by iontophoretic drug application, the MVCS-02C systems have the compensation unit built in. The compensation signal (inverted sum of current output signals divided by 10), generated internally, is applied to a separate compensation electrode, if the OPERATE mode is selected for the injection channel(s) and COMPENSATE mode is selected for the COMPENSATION channel.

3.2. Fast Capacitance Compensation (MVCS-C System)

The MVCS-C iontophoresis instruments have been designed for high-speed application of drugs in electrophysiological experiments. In addition to the standard features of the slow MVCS devices each channel has a capacity compensation circuit and an R_{EL} test unit (see chapter 3.3). The capacity compensation circuit is operated by the control marked CAPACITY COMPENSATION.

The correct tuning of the capacity compensation is very important if high speed operation in conjunction with high resistance microelectrodes is required. Uncompensated stray capacitances are charged from the iontophoretic current that is supplied by the instrument. Uncompensated stray capacitance therefore slows application. The tuning procedure is described in chapter 7.1.

The CAPACITY COMPENSATION control is based on the well-known conventional compensation: stray capacitances around the electrode are compensated by passing amounts of the electrode signal through a small capacitor. The circuit is set so that overshoots are avoided as far as possible.

Caution: Just like any feedback circuit, this circuit can cause overshoots or oscillations if it is overcompensated.

3.3. Electrode Resistance Test (MVCS-C System)

MVCS-C systems are equipped with an automatic electrode resistance test facility. By switching the V_{EL}, I_{EL}, R_{EL} switch to R_{EL}, the value of the electrode resistance is shown on the digital display in MΩ. The electrode resistance test uses current pulses of ±10 nA to measure the electrode resistance. These pulses are monitored at the CURRENT OUTPUT BNC and the voltage response can be seen on the V_{EL}/10 BNC. In this way, changes of electrode resistance can be recorded with a chart recorder or computer based data acquisition system. In addition, the electrode resistance test mode can be used to tune the fast capacity compensation (see chapter 7.1).

Electrode resistance test for EJECT channels

- ❑ In SET mode, the resistance inside the headstage (10 MΩ) is monitored.
- ❑ In OPERATE mode, the resistance of the electrode is displayed.

No square shaped signals should be applied to INPUT connector of the respective channel. For testing rectification, the EJECT potentiometer or a ramp signal at the INPUT connector should be used instead.
Testing of rectification of the electrode is done, e.g. by application of different current levels both, positive and negative to the electrode (using the EJECT potentiometer) and testing the resistance of the electrode. This resistance must not change over the range of current which is used during the experiment.

Electrode resistance test for COMPENSATE channel

- ❑ In COMPENSATE or EXTERN mode, the resistance of the electrode is displayed.
- ❑ In OFF mode, the resistance inside the headstage (10 MΩ) is monitored.

Important: The CAPACITY COMPENSATION unit must be tuned properly. Otherwise the electrode resistance display may be inaccurate.
Tuning capacity compensation can be done using the pulses of the electrode resistance test.

4. Description of the Front Panel

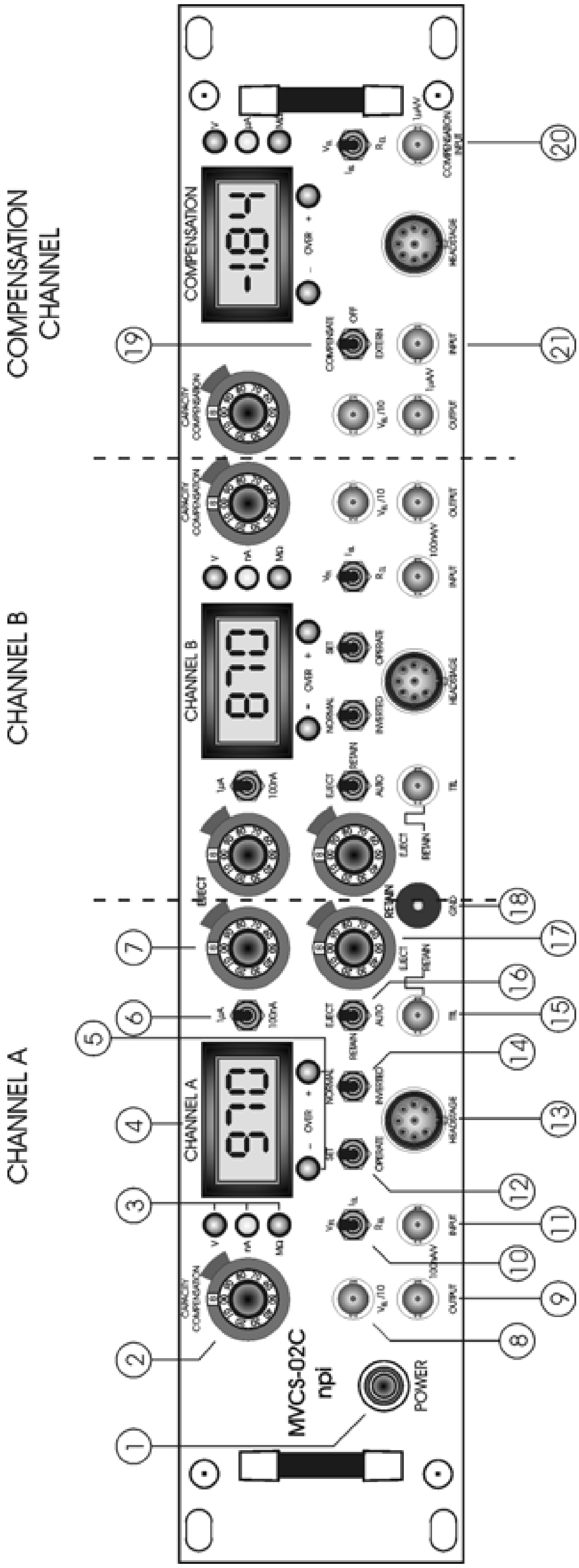


Figure 1: MVCS-C-02C front panel view (the numbers are related to those in the text below)

4.1. Front Panel Elements

In the following description of the front panel elements, each element has a number that is related to that in Figure 1. The number is followed by the name (in uppercase letters) written on the front panel and the type of the element (in lowercase letters). Then, a short description of the element is given.

The front panel can be divided into three functional units:

CHANNEL A, CHANNEL B and COMPENSATION CHANNEL

Most of the elements are identical for each unit (with identical functions and labels) and therefore, are numbered and described only once (e.g. #**12**, HEADSTAGE connector that is also present for CHANNEL B and the COMPENSATION CHANNEL).

Figure 1 shows the MCVS-C-02C (fast system) with capacity compensation and the automatic electrode resistance test facility. These two features are not present in the MVCS-02C (slow system). In the slow system the CAPACITY COMPENSATION potentiometer is not installed and the function of R_{EL} is somewhat different (see below).

(**1**) POWER switch

Switch to turn POWER on (switch pushed) or off (switch released).

(**2**) CAPACITY COMPENSATION potentiometer

Ten-turn control to set amount of compensation of electrode stray capacitance (see also chapter 7.1).

(**3**) V / nA / MΩ LEDs

LEDs indicating the unit of the reading of the DISPLAY (**4**).

(**4**) CHANNEL A display

3 1/2 digit display for the electrode potential in V (XXX.X V), the electrode current in nA (XXXX nA for channels A and B, XX.XX µA for COMPENSATION channel) or the electrode resistance in MΩ (XXXX MΩ, i.e. 0100 correspond to 100 MΩ), selected by toggle switch (**10**). For the correct value of the electrode resistance display it is necessary to adjust the capacity compensation accurately (see chapter 7.1).

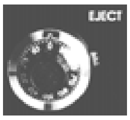
(**5**) – OVER + LEDS

LEDs indicating that the current source is out of linear range or that the electrode voltage / current is 10% below the maximum output voltage / current.

(**6**) 1 µA / 100 nA switch

Two position switch to select the range of the eject current (maximal 1 µA or maximal 100 nA).

(**7**) EJECT potentiometer



Ten-turn control to set the EJECT current. The maximal EJECT current is selected by switch (**6**).

(**8**) V_{EL}/10 connector

BNC connector monitoring the electrode potential divided by 10. Normally used to monitor the electrode resistance (scaling: 1 mV / MΩ, see also chapters 3.3 and 7.1).

(**9**) OUTPUT 100nA/V connector

BNC connector monitoring the EJECT or RETAIN current.
Calibration for channels A and B: 100 nA / V
Calibration for the COMPENSATION channel: 1 µA / V.
(The OUTPUT is not isolated from system ground.)

(**10**) V_{EL}, I_{EL}, R_{EL} switch

3 position toggle switch to set the mode of display CHANNEL A (**4**).
Position V_{EL}: the electrode potential is displayed. Position I_{EL}: the current flowing through the electrode is displayed. Position R_{EL}: the electrode resistance is displayed.

Important: The R_{EL} mode is an option that is only implemented in MVCS-C (fast) systems. In MVCS (slow) systems, the R_{EL} position of the switch has the same function as the I_{EL} position (middle position).

(**11**, **21**) INPUT connector

BNC connector for an auxiliary INPUT. This BNC is directly connected to the output current source and is not isolated from ground.

Calibration for channels A and B: 100 nA / V
Calibration for the COMPENSATION channel (**21**): 1 µA / V.

Note: The COMPENSATION channel can be used as an additional injection channel by linking an external waveform to this connector and setting switch (**19**) to EXTERN.

(**12**) SET / OPERATE switch

Two position switch to set the mode of operation. In SET position the electrode outputs are connected to an internally grounded load and no COMPENSATION signal is generated. Thus, the SET position is used to preset the desired values at the EJECT / RETAIN controls on a well defined basis. In the OPERATE position, the current preset at the EJECT / RETAIN controls will flow through the electrode.

(**13**) HEADSTAGE connector

8 pole connector for the HEADSTAGE (MVCS-C systems) or for the cable directly connected to the injecting electrode (MVCS systems).

Important: Always turn power off when connecting or disconnecting headstages from the 19" cabinet (see also chapter 1).

(**14**) NORMAL / INVERTED switch

Switch to set polarity of EJECT and RETAIN current: NORMAL = EJECT positive, RETAIN = negative.

(**15**) TTL connector

Optically isolated BNC connector for external control in the AUTO mode (see also **16**). LO = RETAIN, HI = EJECT.

(**16**) EJECT / RETAIN / AUTO switch

Switch to select the mode of operation. EJECT: the EJECT current set with (**7**) is applied to the electrode. RETAIN: the RETAIN current set with (**17**) is applied to the electrode. AUTO: Operation controlled by a TTL pulse at (**15**).

Remember: Current is applied to the electrode only if switch (**12**) is set to OPERATE.

(**17**) RETAIN potentiometer

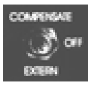
Ten-turn control to set the RETAIN current, range 0-100 nA.

(**18**) GROUND connector

Banana jack providing system ground (same as GND at the headstage, see chapter 5). This ground is isolated from power ground (PROTECTIVE EARTH, see chapter 4.2) and the TTL INPUT ground.

COMPENSATION Channel Only

(**19**) COMPENSATE / OFF / EXTERN switch



Switch to select the operation mode of the COMPENSATION channel.

COMPENSATE: The inverted sum of channels A and B is applied to the electrode.
OFF: No current is applied to the electrode.
EXTERN: The output current source is connected directly to INPUT BNC (**21**). In this mode the COMPENSATION channel can be used as an additional injection channel. If, for example, 1 V is connected at (**21**), an injection current of 1 µA is applied to the electrode connected to the COMPENSATION channel.

(**20**) COMPENSATION INPUT

BNC connector for an additional COMPENSATION current. This INPUT can be used to generate COMPENSATION current for two MVCS or MVCS-C systems using only one compensation electrode.

Suppose one has two MVCS or MVCS-C systems, system 1 and system 2. The COMPENSATION OUTPUT of the system 2 (without compensation electrode) can be fed into the COMPENSATION INPUT of system 1 (with compensation electrode). With switch (**19**) in COMPENSATE position (both systems) the current flowing through the compensation electrode connected to system 1 is then the sum of both COMPENSATION channels. Thus, the current of all injection electrodes are balanced with only one compensation electrode.

4.2. Rear Panel Elements

POWER / FUSE / LINE VOLTAGE SELECTOR

The power cord is connected by a standardized coupling which comprises also the fuse, voltage selector and a line filter. With 230V AC the fuse must be 0.4A (slow), with 115V AC it must be 0.8A (slow).

***Caution*:** Always use a three-wire line cord and a mains power-plug with a protection contact connected to ground. Before opening the cabinet unplug the instrument. Unplug the instrument also when replacing the fuse or changing line voltage. Replace fuse only by appropriate specified type (see also chapter 1).

GROUND / PROTECTIVE EARTH CONNECTORS

In order to avoid ground loops, the internal zero (ground) signal of the instrument is not connected to the mains ground and the cabinet. The cabinet and mains ground are connected to the green/yellow connector, the internal ground is connected to the yellow connector. See also GND connector (chapter 4.1 and chapter 5).

5. Headstage (MVCS-C System)

The headstage is housed in a small box that can be mounted directly onto a micromanipulator. It is connected to the main amplifier by means of a shielded flexible cable and a multi-pole connector.

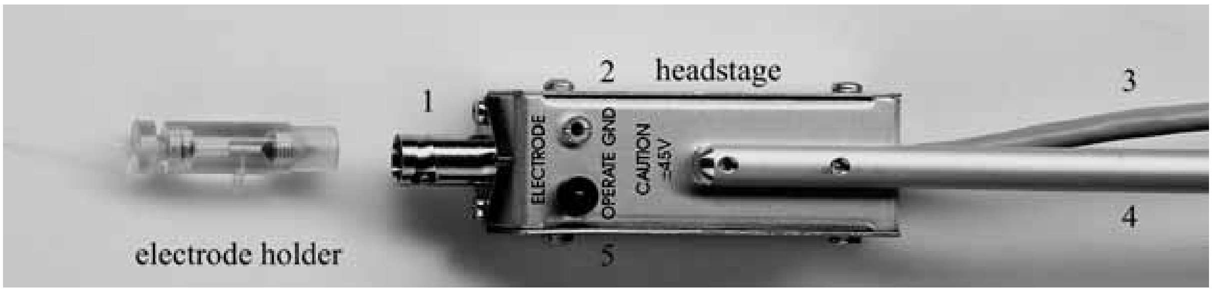


Figure 2: MVCS-C-02C headstage

1 ELECTRODE: BNC connector for the electrode holder, grounded shield
2 GND: ground
3 headstage cable to amplifier
4 holding bar
5 OPERATE LED: indicates that injection takes place

GND (GROUND) connector

The bath (or reference) of the recording chamber is connected to GND. This is the ”lowest” signal level in the recording system, i.e. all signals are related to this signal. This connector must be connected to the ground signal of the recording amplifier / chamber.

ELECTRODE INPUT

In order to avoid disturbances on the recording amplifier, the microelectrode holder is connected via a BNC connector with a grounded shield.

***Caution*:** The current injection headstages have an output compliance of ±45 V up to ±150 V. In addition, all headstages are equipped with very sensitive FET amplifiers that can be damaged with electrostatic charge and must therefore be handled with care (see also chapter 1.

Very Important: Always turn power off when connecting or disconnecting headstages from the 19" cabinet or when changing or adjusting the electrodes.

Also very important: Each headstage is adjusted for a specific channel and instrument. They are labeled A and B for the EJECT channels, and C for the COMPENSATION channel. Please **do not exchange headstages** for a respective instrument or between different MVCS instruments.

Systems for slow, long lasting applications (in the second or minute range) need no headstages (MVCS systems). In these systems the electrodes are connected from special connectors on the front panel with shielded cables:
Pin 2: white/blue wire = ground
Pin 5: yellow/red wire = electrode

6. Setting up the MVCS / MVCS-C System

The following steps should help you set up the MVCS / MVCS-C system correctly. Always adhere to the appropriate safety measures (see chapter 1).
After unpacking, the MVCS / MVCS-C system is attached to the setup by assembling the electrical connections.

Electrical connections

- ❑ Turn POWER off.
- ❑ Plug the instrument into a grounded outlet.
- ❑ MVCS: Connect your injection- and COMPENSATION electrodes to the special connectors with shielded cables at the front panel.
  Pin 2: white/blue wire = ground
  Pin 5: yellow/red wire = electrode
- ❑ MVCS-C: Connect the headstages to the HEADSTAGE connectors (#**13**, Figure 1) at the front panel.
- ❑ If the recording chamber is not grounded, connect GND of the headstage (MVCS-C) or GND (#**18**, Figure 1) to the chamber.

Note: System ground is isolated from mains ground. The 19" cabinet is connected to mains ground, headstage enclosures are connected to the internal system ground.

- ❑ MVCS-C: Connect the V_{EL}/10 connectors to an oscilloscope or to a data acquisition system.

- ❑ If you intend to control the MVCS/MVCS-C system externally (e.g. by a computer) connect the gating waveform to TTL (#**15**, Figure 1), the stimulus waveform to INPUT (#**11**, Figure 1) and the current OUTPUT (#**9**, Figure 1) to the analog input of the data acquisition system.

7. Operation

MVCS/MVCS-C systems are housed in standard 19" rackmount cabinets. Each system is composed of two independent channels marked A and B and a COMPENSATION CHANNEL.

Each channel has an auxiliary analog input and an output that monitors the current flowing through the electrode. Each channel is equipped with a digital display and two overload LEDs.

All numbered items refer to Figure 1, page 8, in the following discussion.

The Systems can be operated manually by means of a toggle switch on the front panel (#**16**) or by an external digital pulse (TTL) connected to #**15**.

- ❑ Turn CAPACITY COMPENSATION (#**2**) for all channels to less than 1 to avoid oscillations.
- ❑ Turn POWER on.
- ❑ Set the operation mode of all channels to SET using switch #**12** to disable current output.
- ❑ Set the EJECT and/or RETAIN current amplitude to the desired values using #**7** and #**17.**
- ❑ MVCS-C: First, compensate the stray capacitances of the electrodes (see chapter 7.1) and second, check the electrode resistances by switching #**10** to R_{EL}.

<u>Important</u>: The values of the ELECTRODE RESISTANCE are accurate only if the capacitances of the electrodes are compensated properly.

- ❑ Put the injection- and compensation electrodes to the desired position.
- ❑ Start iontophoresis either manually by setting switch #**16** to EJECT and switch #**12** to OPERATE or remotely by setting switch #**16** to AUTO and applying a TTL pulse to #**15**.

7.1. Capacity Compensation Tuning Procedure (MVCS-C System)

The tuning of the capacity compensation controls is performed with the help of the electrode potential monitor BNC marked V_{EL}/10 (#**8**) and square pulses applied to the electrode. This pulse can originate from the built-in ELECTRODE RESISTANCE TEST circuit or from an external signal source. The pulses generated internally by the ELECTRODE RESISTANCE test unit have an amplitude of ±10 nA.

The tuning must be performed with the electrode in the bath immersed to the maximal depth required during the experiment. Square pulses (positive and negative) of a few nA and 0.1-10 ms duration are applied to one of the INPUT BNCs (#**11**) or by activating the ELECTRODE RESISTANCE test unit (#**10**). The signals from the V_{EL}/10 and CURRENT OUTPUT BNCs (#**9**) are monitored on an oscilloscope.
The CAPACITY COMPENSATION control (#**2**) is turned on clockwise until the signal at the V_{el}/10 BNC is as square as possible (see Figure 3). The highest speed is obtained with a small overshoot (theoretically 4.3 %).

The CAPACITY COMPENSATION control is based on the well-known conventional compensation: stray capacitances around the electrode are compensated by passing amounts of the electrode signal through a small capacitor. The circuit is designed to minimize oscillations.

***Caution*:** Just as in any feedback circuit, this circuit can cause overshoots or oscillations, if it is overcompensated.

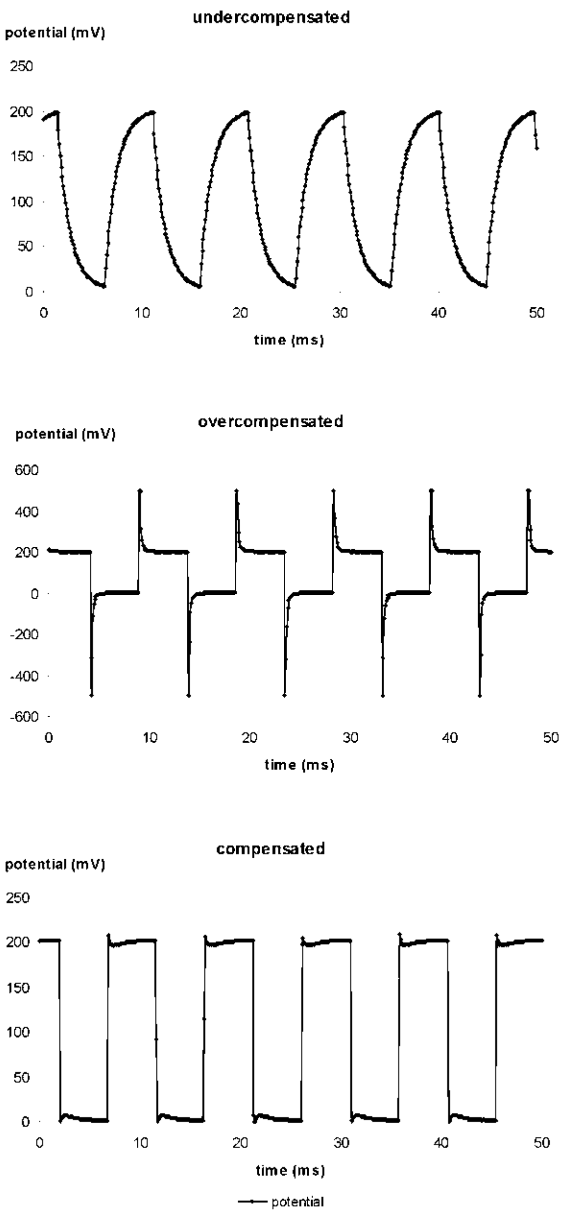


Figure 3: Capacity compensation of the electrode

8. Literature

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9. Technical Data

Electrode output:	floating current source, output impedance $>10^{12}\ \Omega$
Maximum current:	450 nA [1.5 µA] into 100 MΩ load
Display:	current: XXXX nA, balance: XX.XX µA, voltage: XXX.X V, R_{el}: XXXX MΩ, displayed value is set by a three position toggle switch, separate displays for each channel
Over LEDs:	activated 10% below maximum current / voltage
Eject:	ten-turn control, range: 100 nA or 1 µA, selected by switch
Minimum pulse duration:	50 µs
Retain:	ten-turn control, maximum 100 nA
Capacity compensation:	ten-turn control, range 0-30 pF
Output current polarity:	selected by INVERTED/NORMAL toggle switch
Modes of operation:	set by two toggle switches EJECT/RETAIN/AUTO switch enables manual or TTL controlled operation SET/OPERATE switch connects automatically electrode outputs to ground (SET position)
TTL input (AUTO mode):	LO = RETAIN, HI = EJECT, isolated, $R_{in} > 5$ kΩ
Analog input:	sensitivity 100 nA / V, $R_{in} > 100$ kΩ, range ±10 V
Current monitor:	sensitivity 100 nA / V, $R_{out} = 250\ \Omega$, not isolated
Voltage monitor:	V_{EL} / 10, $R_{out} = 250\ \Omega$, not isolated
Electrode resistance test:	1 mV / MΩ at voltage monitor V_{EL} / 10
Balance output:	inverted sum of all injection currents, sensitivity 1 µA / V
Power requirements:	230 V / 115 V, 50 Hz / 60 Hz AC, 50W, fuse 0.4 A / 0.8 A, slow

Output connector pins and cable colors: (for systems without headstage)	Pin 2: white/blue wire = ground Pin 5: yellow/red wire = electrode

Dimensions

Amplifier:	standard 19" rackmount cabinet 19” (483 mm), 10” (250 mm), 3.5” (88 mm)
Headstage:	65x25x25 mm [100x40x20 mm with heat sink]