Electronic Instruments for the Life Sciences

made to measure

OPERATING INSTRUCTIONS AND
SYSTEM DESCRIPTION FOR THE

ION-01X

IONSENSITIVE AMPLIFIER

VERSION 1.0
npi 2026

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Table of Contents

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.

2. ION-01X

2.1. *Components of the ION-01X*

The following items are shipped with the ION-01X system:

- Amplifier in 19” housing
- Differential headstage
- Ground connector (2 mm banana plug)
- Electrode connectors (1.0 mm banana plugs)
- Test adapter
- Manual

2.2. *System Description*

The ION-01X amplifier is designed for recording signals from ion-sensitive microelectrodes. The system consists of a main amplifier system and a small headstage with differential input. It can be used in all kinds of preparations e.g. single cells, slices or *in vivo* preparations. It has a low-noise high common mode rejection (CMR) differential input equipped with ultra-low bias amplifiers (fA range). The OUTPUT has two gains selectable by a toggle switch (x10 or x100). Both inputs (S: sample/sense or signal, R: reference) have a capacity and an OFFSET compensation. Both the reference input and the sense input can be filtered to improve AC CMR.

Warning: Both headstage inputs are very sensitive to static discharges and can be damaged by electrostatic charge and must therefore be handled with care. Touching a grounded metal surface when changing or adjusting electrodes can avoid electrostatic discharge. **Always turn power off when connecting or disconnecting the headstage from the instrument.**

2.3. *Description of the Front Panel and Operation*

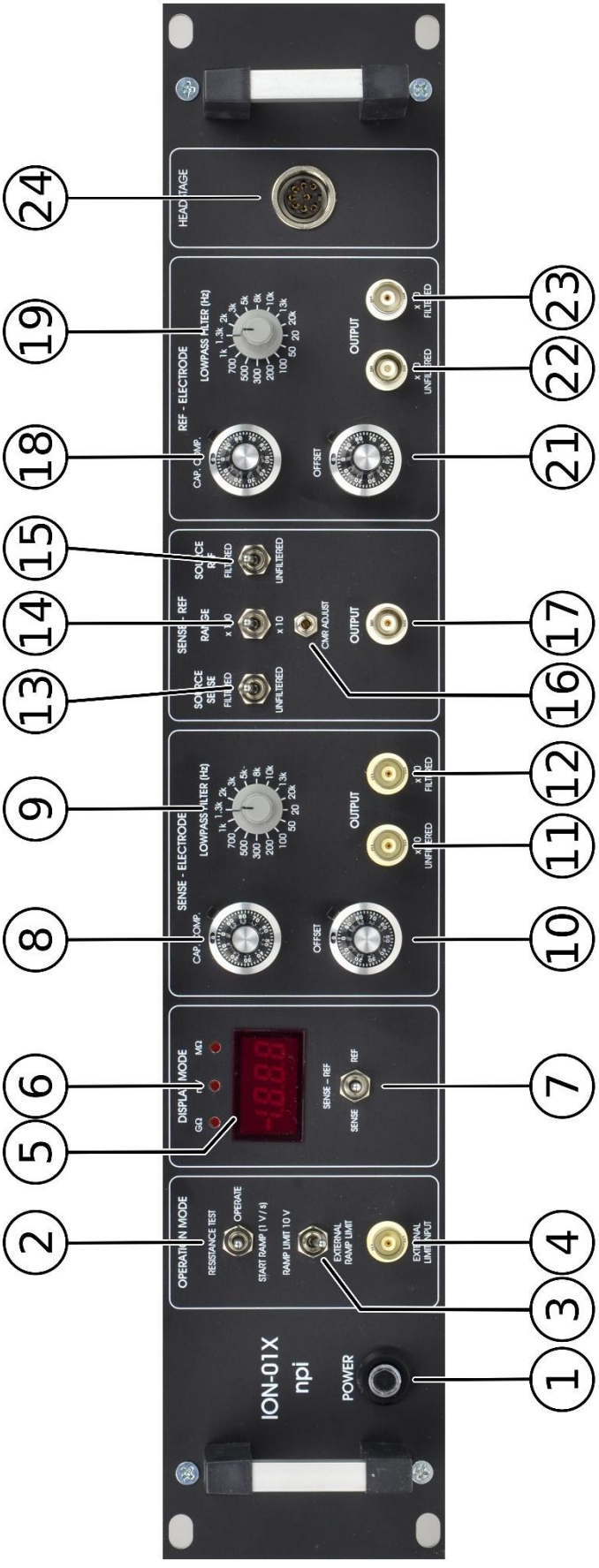

Figure 1: Front panel view of the ION-1X

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.

(1) POWER switch

Main switch to power the ION-01X ON or OFF.

OPERATION MODE section

(2) OPERATE switch

Switch for selecting an internal generated ramp (1 V/s) for electrode depolarization (see also **#9**) or for electrode resistance measurement using a periodic signal. The device shows the electrode resistance at display **#(5)**. The electrode to be tested is selected by switch **#(7)**. See also chapter 3.4 and 3.6 for further information.

(3) EXT. RAMP LIMIT connector

BNC connector for connecting an analog input signal (±10 V max.) which serves as the final voltage of the applied ramp, if switch **#(4)** is set to EXT. RAMP LIMIT and switch **#(2)** starts the ramp. The ramp signal is fed into a capacitor, differentiated and generates a rectangular signal at the electrode's resistance. This signal is provided at the OUTPUT SENSE or OUTPUT REF connectors respectively. Its amplitude is proportional to the electrode's resistance. See also chapter 3.6 for further information.

(4) RAMP LIMIT switch

Switch for selecting the limit of the internally generated ramp. In upper position, the ramp will run from 0 V to 10 V. In the lower position, the ramp will run from 0 V to the voltage given into the EXT. RAMP LIMIT connector **#(3)**. See also chapter 3.6 for further information.

DISPLAY MODE section

(5) Digital display

Display showing the voltage selected by switch **#(7)** or the resistance of the sense electrode or the resistance of the reference electrode. XXX.X mV or XX.XX GΩ (sense electrode) or XXX.X MΩ (reference electrode).

(6) GΩ / MΩ / mV LEDs

LEDs indicating the unit of display **#(5)**.

(7) DISPLAY MODE switch

Switch for selecting the electrode whose signal that is displayed at **#(5)** (voltage or resistance)
SENSE: Voltage at the sense electrode or resistance of the sense electrode
SENSE-REF: Signal at the sense electrode minus signal at the reference electrode
REF: Voltage at the reference electrode or resistance of the reference electrode.

Hint: If electrode resistance test is selected and the switch is in SENSE-REF position, the voltage difference SENSE-REF is shown anyway, and the GΩ / MΩ / mV LEDs are switched off!

SENSE – ELECTRODE section

(8) CAP. COMP. SENSE potentiometer

10-turn potentiometer for setting the capacity compensation for the sense electrode. See also chapter 3.3 for further information.

(9) LOWPASS FILTER (Hz) rotary switch

16 position rotary switch to select the corner frequency of the lowpass Bessel filter.

(10) OFFSET SENSE potentiometer

10-turn potentiometer for setting the OFFSET compensation for the sense electrode; range: ±100 mV.

(11) OUTPUT x10 UNFILTERED connector

BNC connector providing the voltage at the sense electrode amplified by 10.

(12) OUTPUT x10 FILTERED connector

BNC connector providing the lowpass-filtered voltage at the sense electrode amplified by 10. Corner frequency of the lowpass filter is selected by switch #**(9)**

SENSE – REF section

(13) SOURCE SENSE switch

(14) RANGE switch

Switch for setting the range (x10 or x100) of the OUTPUT of the SENSE-REF signal.

(15) SOURCE REF switch

(16) CMR ADJUST trimpot

Trimmer potentiometer for adjusting the CMR (common-mode rejection). CMR is adjusted by linking the same rectangular signal to both inputs S and R, looking at the OUTPUT SENSE-REF signal, and turning the trimpot with a small flat screwdriver until no signal can be seen at the oscilloscope. See also chapter 3.5 for further information.

(17) OUTPUT SENSE - REF connector

BNC connector providing the voltage at the sense electrode minus the signal at the reference electrode. The amplification factor is set by **#(14)**.

REF – ELECTRODE section

(18) CAP. COMP. REF potentiometer

10-turn potentiometer for setting the capacity compensation for the reference electrode. See also chapters 3.3 for further information.

(19) LOWPASS FILTER (Hz) rotary switch

16 position rotary switch to select the corner frequency of the lowpass Bessel filter for the REF signal.

(20) OFFSET REF potentiometer

10-turn potentiometer for setting the OFFSET compensation for the reference electrode; range: ±100 mV.

(21) FILTER REF potentiometer

Potentiometer for setting the low pass FILTER for the reference electrode. The low pass filter improves AC CMR; range: 20 Hz…10 kHz.

(22) OUTPUT x10 UNFILTERED connector

BNC connector providing the voltage at the reference electrode amplified by 10.

(23) OUTPUT x10 FILTERED connector

BNC connector providing the lowpass-filtered voltage at the reference electrode amplified by 10. Corner frequency of the lowpass filter is selected by switch #**(19)**

(24) HEADSTAGE connector

Connector for connecting the headstage.

2.1. *Description of the Rear Panel*

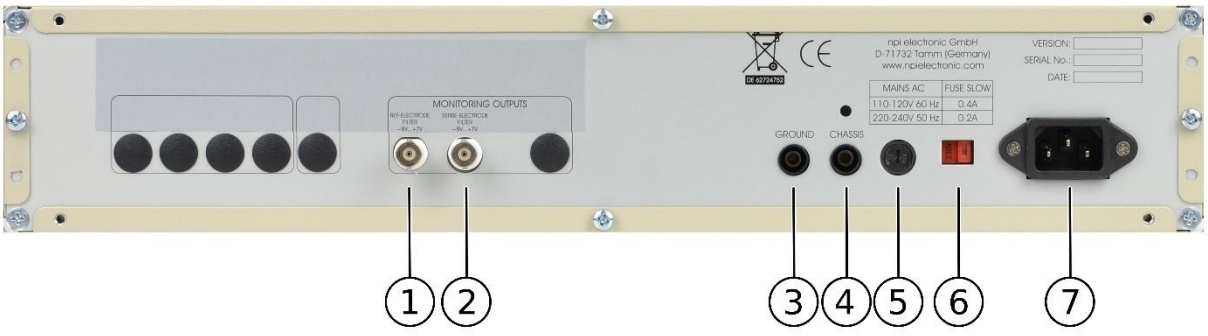

Figure 2: Rear panel view of ION-01X.

In the following description of the rear 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 rear panel and the type of the element (in lowercase letters). Then, a short description of the element is given.

MONITORIN OUTPUTS section

(1) REF-ELECTRODE FILTER connector

BNC connector providing a voltage monitoring the position of the LOWPASS FILTER switch of the REFERENCE electrode (-8 V to +7 V, 1 V/STEP).

(2) SENSE-ELECTRODE FILTER connector

BNC connector providing a voltage monitoring the position of the LOWPASS FILTER switch of the SENSE electrode (-8 V to +7 V, 1 V/STEP).

(3) GROUND connector

This connector is linked to the internal system ground which has no connection to the 19" cabinet (CHASSIS) and the mains ground to avoid ground loops.

(4) CHASSIS connector

This connector is linked to mains ground (green / yellow wire, protective earth).

(5) FUSE holder

Holder for the line fuse. Replaced fuse if necessary, using a flat screwdriver to open the fuse holder.

***Important*:** Unplug the instrument before replacing a fuse. Replace fuse only by appropriate specified type.

(6) VOLTAGE SELECTOR switch

Rotary switch for selecting the operating voltage (115 V / 230 V).

Caution: Always switch to the appropriate voltage before connecting the ION-01X to power.

(7) MAINS connector

Plug socket for the mains power-plug.

***Important*:** Check line voltage before connecting the ION-01X amplifier to power. Always use a three-wire line cord and a mains power-plug with a protection contact connected to ground. Disconnect mains power-plug when replacing the fuse or changing line voltage. Replace fuse only by appropriate specified type. Before opening the cabinet unplug the instrument.

2.2. *Headstage*

Figure 3: Headstage of ION-01X.

1: electrode mount with clamp screw and washer
2: connector for the sense (ionsensitive) electrode (1 mm jack), EL
3: connector for the reference electrode (1 mm jack), REF
4: connector for ground, GND

2.3. *Test adapter*

A test adapter is provided to test the amplifier. It connects the inputs to ground with 1 GΩ (EL) or 100 MΩ, respectively.

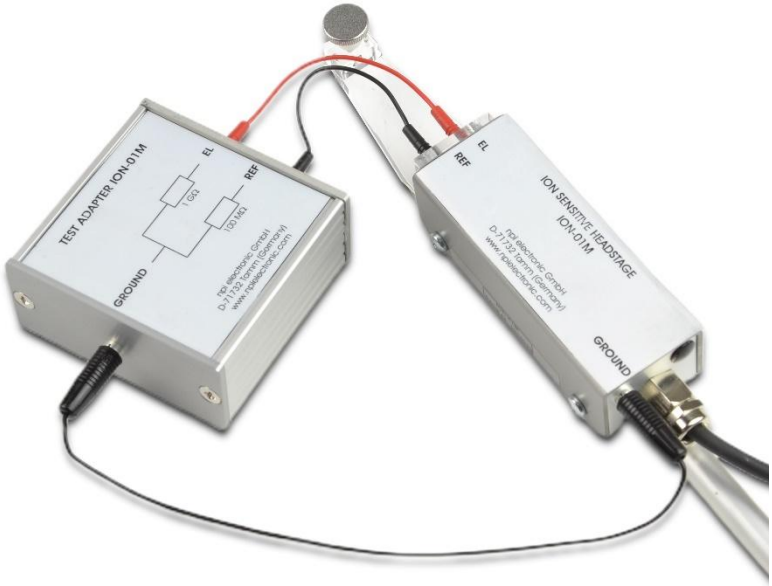

Figure 4: Headstage of ION-01X with connected test adapter.

Note: To avoid damage due to electrostatic discharge, connect the GROUND wire first, then the electrode wires. When unplugging, remove the electrode wires first and the GROUND wire last.

3. Operation

3.1. *Electrode connection and signal detection*

The ION-01X is a high-input impedance, low-noise differential amplifier optimized for recording small voltage differences generated by ion-selective electrodes (ISEs). It is ideally suited for precise measurement of ion concentrations in and around biological cells.

Electrode Configuration

- **Sensing Electrode (ISE):** A microelectrode with an ion-selective membrane or cocktail (e.g., for K^+, Na^+, H^+, or Cl^-), which generates a potential that depends on the activity of the target ion in the local environment.
- **Reference Electrode:** A stable, non-polarizable electrode, placed in a region of constant ionic composition. It provides a fixed potential against which the sensing electrode is compared.
- **Grounding Electrode:** A separate Ag/AgCl electrode (or similar) placed in the bath solution or sample chamber. It provides a **common ground** for the biological preparation and ensures that the amplifier operates with a defined electrical reference relative to the solution potential.

The **sensing** and **reference electrodes** are connected to the differential inputs of the ION-01X amplifier's headstage (see Figure 8). This is realized by clamping the glass micropipettes to the headstage's clamp screw (see Figure 3, **#1**) and connecting the wires directly to the 1 mm connectors (see Figure 3, **#2, #3**). The **grounding electrode** is connected to the headstage's ground input (see Figure 3, **#4**).

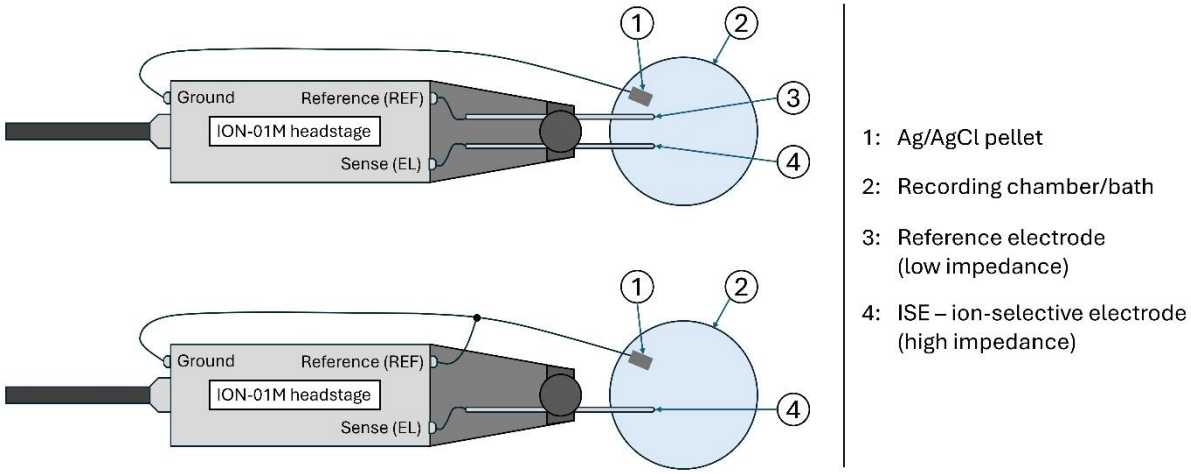

Figure 5: Schematic drawing of an ion-sensitive measurement with three electrodes (top) and two electrodes (bottom).

Important: We recommend clamping the electrodes for SENSE and REFERENCE directly into the headstage's electrode fixing clamp (see Figure 3, **#1**). It is not recommended to use any extension wires between the headstage and the electrodes. The additional capacitance in these wires might disturb proper signal detection.

Also Important: When working in single-ended configuration (only two electrodes) make sure the Reference input of the headstage is connected to ground (see Figure 8, bottom).

Output Signal

The amplifier outputs the voltage difference between the sensing and reference electrodes (OUTPUT SENSE-REF, **#17**). This differential voltage represents the **Nernst potential** for the target ion and is related to ion activity via the Nernst equation:

$$E = E_0 + \frac{RT}{zF} ln[a_{ion}]$$

Where:

- E is the measured potential (output of the amplifier),
- E_0 is a constant offset specific to the electrode system,
- R is the gas constant,
- T is temperature (in Kelvin),
- z is the valence of the ion,
- F is the Faraday constant,
- a_{ion} is the activity of the ion.

Calibration

To interpret the amplifier output in terms of absolute ion concentrations, **calibration is essential**. This involves recording the output voltage of the ISE (ion-sensitive electrode) in at least two standard solutions of known ion concentration. A calibration curve is then created, plotting output voltage against the logarithm of ion concentration. This allows conversion of recorded voltages to quantitative ion activity values.

Important: The headstage inputs are very sensitive and can be damaged by electrostatic charge. Therefore, be handled with great care. Touching a grounded metal surface when changing or adjusting electrodes can avoid electrostatic discharge.

3.2. *Offset compensation*

When the electrodes for GROUND, SENSE and REFERENCE are in the solution, a certain electrochemical potential is generated between GROUND on one side and SENSE or REFERENCE, respectively, on the other side. These potentials can be corrected using the OFFSET potentiometers for the respective electrodes (see chapter 2.3: **#21** for REFERENCE and **#10** for SENSE)

3.3. *Capacity compensation*

Since the impedances of ion-selective electrodes a quite high, it is important to compensate the electrodes' capacitances to avoid low-pass filtering effects in the recorded signal.
One easy way of doing this is using the built-in electrode resistance test (**#2**). This will create a square pulse which is fed to the connected electrode. The aim is to adjust the CAP. COMP potentiometers (**#8** or **#18**) so that the output signal of the respective electrode (**#11** or **#22**) is as square as possible (see Figure 6).

Important: When the capacity compensation is tuned to the maximum, the intrinsic noise will increase. Reducing the capacity compensation slightly will decrease the noise significantly.

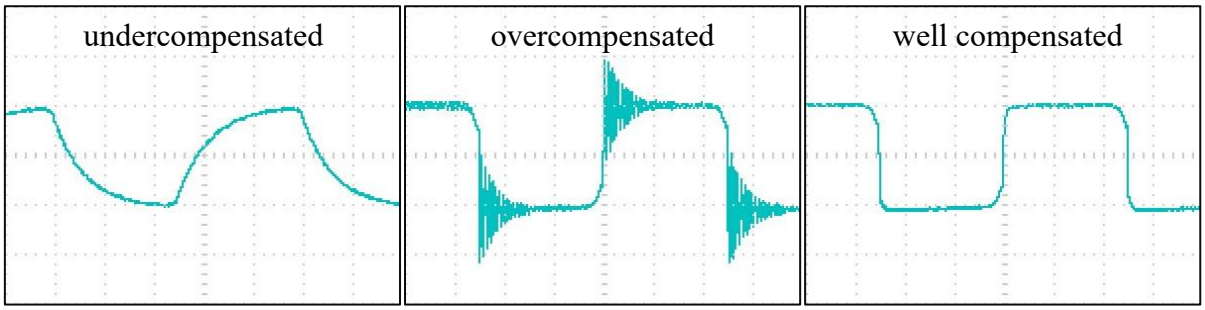

Figure 6: Signal traces during capacity compensation.

3.4. *Measuring the electrode resistances*

The resistance of both the SENSE and the REFERENCE electrode can be determined using the built-in electrode resistance test. It is activated by setting the OPERATE switch **#2** to RES.TEST. The electrode to be tested is selected by switch **#7**. The respective electrode's resistance is shown at display **#6**.

Important: The electrode resistance test only works correctly, if the capacity compensation has been properly adjusted.

3.5. *Adjusting CMR (common mode rejection)*

The aim of Common Mode Rejection (CMR) is to ensure that a differential amplifier responds only to the difference in voltage between its two inputs and rejects any voltage that is common to both. The ION-01X allows adjusting CMR with two parameters: the amplitude and speed of the signal.
To properly adjust the CMR, it is important that both inputs (REF and SENSE) are fed with the exact same input signal. When using the model cell/test adapter, this can be easily accomplished by feeding the signal into the GND connector of the test adapter. With real electrodes, this signal can be fed to the solution via the grounding pellet.
In this way, use a square wave as input signal. Then look at the output from SENSE-REF at an oscilloscope (see Figure 7, left).
Use the CMR trimpot (see **#16**, Figure 1) to adjust the difference in amplitude between the different pulses. The aim is to get a flat line with only capacitive artifacts remaining (see Figure 7, middle).
These capacitive artifacts originate from the difference in the electrodes' capacitance and impedance: the REF electrode has a lower resistance and therefore has a faster signal detection. To accommodate this, use REF-ELECTRODE LOWPASS FILTER (**#19**, Figure 1). This will deliberately make the REF input slower. The aim is to get rid of the capacitive artifacts from the SENSE-REF signal (see Figure 7, right).

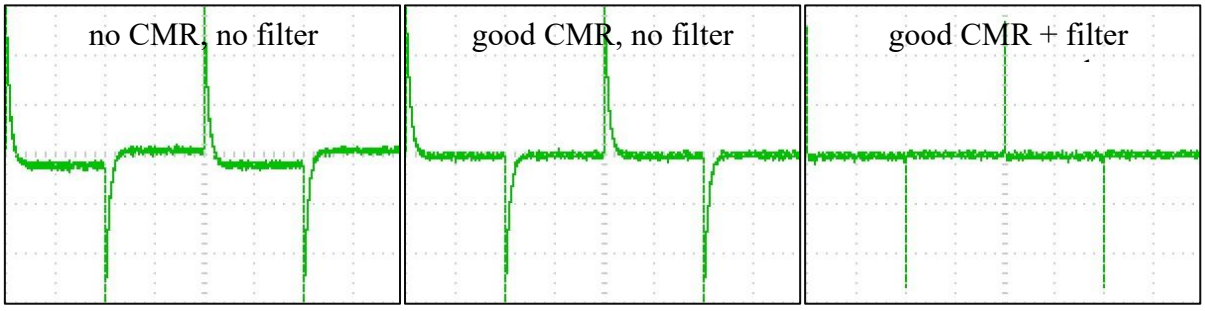

Figure 7: Signal traces during CMR adjustment

3.6. *Using the internal ramp*

The ION-01X can generate a ramp input signal with 1 V/s. This signal is fed to the capacity compensation circuit, resulting in a DC shift of -10 mV at the respective electrode connector. The ramp starts a 0 V and ends at 10 V – or at the voltage given by the input signal at #16: EXT. RAMP LIMIT. Since the slope of the ramp is always 1 V/s, the duration of the ramp and thus the DC shift in "s" is equivalent to the voltage given as limit: e.g. 10 V → 10 s, 5 V → 5 s, etc..

4. Literature

- Polder, H.R., M. Weskamp, K. Linz and R. Meyer **Voltage-Clamp and Patch-Clamp Techniques**, Chapter 3.4, pp. 272-323 in Dhein, St.; Mohr, F.W.; Delmar, M. (Eds.) **Practical Methods in Cardiovascular Research,** Springer Heidelberg 2004
- Schwarz, W. and J. Rettinger (2003) **Foundations of Electrophysiology** Second Edition, Shaker Verlag Aachen, 2003
- Voipio, J., M. Pasternack and K. Macleod (1996) **Ion-sensitive microelectrodes**, Chapter 11 in Ogden, D (ed.) (1996) **Microelectrode Techniques - The Plymouth Workshop Handbook**, Second Edition, The Company of Biologists Ltd., Cambridge.

5. Technical Data

Input range:	±1000 mV
Input impedance:	>10 TΩ, related to ground
Input bias:	<150 fA
Differential input:	CMR >120 dB @ gain 100
LOWPASS-FILTER	8-pole low-pass, corner frequencies: 20, 50, 100, 200, 300, 500, 700, 1k, 1.3k, 2k, 3k, 5k, 8k, 10k, 13k, 20k Hz
GAIN (SENSE-REF):	x10, x100, selected by toggle switch
OFFSET compensation:	range: ±100 mV
CAPACITANCE compensation:	range: 0-100 pF
Output:	range: ±12 V into 1 kΩ / ±1 V into 50 Ω
Electrode Resistance Test:	REFERENCE electrode: 10 MΩ - 200 MΩ measured with a square pulse @ 65 Hz SENSE electrode: 100 MΩ - 5 GΩ measured with a square pulse @ 20 Hz Accuracy: 0…1 GΩ: ±1% 1…5 GΩ: ±10% > 5 GΩ: ±25%
Digital display:	XXX.X mV or XX.XX GΩ (sense electrode) or XXX.X MΩ (reference electrode)
Dimensions:	19” rackmount cabinet, 19” x 10” x 3.5” (483 x 250 x 88 mm³)
Power requirements:	115/230 V AC, Fuse: 0.2 A / 230 V; 0.4 A / 115 V
Test adapter:	Resistor for EL: 1 GΩ Resistor for REF: 100 MΩ