

Model 260

Microiontophoresis Current Programmer

INSTRUCTION MANUAL

Serial No._____

041307

World Precision Instruments



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Introduction

The Model 260 Microiontophoresis Current Programmer is a floating, batteryoperated instrument designed for the electroiontophoresis of dyes, drugs and charged substances from micropipettes. Two identical battery operated current generators are available. In ordinary use, the two current generators are operated in parallel providing two distinct currents; one for preventing substances in the micropipette from outward diffusion (the retain or hold current) and the second for the active ejection of charged material. For pipettes with submicron tips, a hold current may not be necessary if there is little outward diffusion of pipette material.

Model 260 is powered by four standard 9 volt transistor batteries. Their life expectancy can be considerably improved if the user remembers to turn off the power switch when the instrument is not in use.





Controls (each channel)

POWER ON/OFF	Instrument power switch. To maximize battery life, turn power OFF when the channel is not in use.
CURRENT LEVEL	This control varies the current amplitude as indicated on the ammeter. To prevent accidental current flow via \he output terminals place the OUTPUT switch in the PRESET position while adjusting current amplitude.
CURRENT RANGE	Selects either 100 or 1000 nanoampere current range
MODE SELECT	MANUAL operation allows the user to apply a DC current when the OUTPUT switch is changed from PRESET to ENABLE. AUTO operation requires the user to apply a +5 volt command potential to initiate the flow of current.
OUTPUT POLARITY NORMAL	indicates that the red output connector is positive with respect to the black connector. INVERT reverses connector polarity.
AUTO INPUT	If the MODE SELECT switch is in the AUTO position the AUTO INPUT connector controls current turn-on. Five volts positive with respect to the outer connector shell will maintain current for as long as this voltage is applied. The CURRENT LEVEL control continues to dictate the actual current amplitude.
OUTPUT	In the PRESET position, the red and black current output terminals are disconnected from the current generating circuit. ENABLE connects the output terminals to the current source. If the OUTPUT switch is in the PRESET mode current cannot flow out of the instrument in either MANUAL or AUTO operating modes.
CHAS GND	This green binding post is connected to the chassis or metallic enclosure of the instrument. It should normally be connected by the user to the ground point of his recording system.



Operation

Preliminary Instrument Check

Switch the OUTPUT switch to PRESET on either channel. This disconnects the red and black output terminals and internally short circuits the output of the current generator. Switch the MODE SWITCH to MANUAL. Turn on the POWER switch located just below the current indicating ammeter. Notice that as the CURRENT LEVEL control is rotated, the ammeter reading will change accordingly. Switch current ranges and note the similar ammeter behavior. Note that one may easily reach and exceed the ammeter's maximum reading. If one cannot reach and exceed full scale on the ammeter, the transistor batteries may need replacement. If the OUTPUT switch is changed from PRESET to ENABLE at any current setting an audible alarm will sound and a red lamp on the front panel will light to indicate that the output current pathway is an open circuit. (At very low nanoampere current settings, the alarm may take several seconds to be activated.) Check the performance of both channels in the manner indicated above. Ground the CHAS GND green binding post to assure low noise. The instrument is now ready to use.

Single Channel Operation

Model 260 contains two completely independent floating, battery operated current generators which may be operated independently or in parallel connection. As an independent current generator the user need only connect his external electrode pair to the red and black output terminals of channel 1 (HOLD) or 2 (EJECT). While making these connections and any preliminary control adjustments, the OUTPUT switch should be in the PRESET position. This will prevent any accidental current flow. Proceed to set the CURRENT RANGE and CURRENT LEVEL controls. For currents below 100 nanoamperes the 100 nanoampere range is recommended because one may adjust these low current values with better resolution in the lower current range.

Adjust the CURRENT LEVEL control until the required DC current value is observed on the channel ammeter. Select the OUTPUT POLARITY desired. NORMAL yields a positive potential at the red output terminal. Switching the OUTPUT switch from PRESET to ENABLE releases the required current from the output terminals. To halt current flow, return to the PRESET mode.



Two Channel Operation, Hold-Eject

As will be described in the Application Notes the electrophoretic release of charged substances from micropipettes often requires the use of a second current to counter the outward diffusion of material from the delivery pipette. This current has been referred to in the literature as "backing, holding or retaining" current. One causes a small current to flow in a direction that will offset the spontaneous leakage of the active agent from the pipette until it is required.

Connect a shorting wire or jumper to tie the red OUTPUT terminals of the HOLD channel and the EJECT channel together. Connect an identical jumper wire between the black OUTPUT terminals. This effectively connects the two current generating channels in parallel. Current does not flow from one channel into the other but will sum algebraically in the common electrode pathway if both channels are operating simultaneously. Place both channels in the PRESET mode to prevent accidental current flow during set up. Set the polarity and current amplitude on the HOLD channel to retain the active agent in the electrode. Now set the polarity and amplitude of the current in the EJECT channel. Two operating procedures are possible:

- One may leave the hold current on at all times and effect ejection by superimposing the larger eject current by operating the PRESET/ENABLE switch on the EJECT channel. Thus the ejection current will swamp the smaller hold current. One must then algebraically add the hold current to the eject current to compute the actual ejection current. For example, if the hold\ current had been -5 nanoamperes and the eject current were +50 nanoamperes, the effective ejection current is +45 nanoamperes. This method has the advantage that one need only operate a single PRESET/ENABLE switch on the EJECT channel during the experiment.
- 2. Alternatively, one may simultaneously operate the PRESET/ENABLE switches on both channels so that the hold current is shut off at the moment the eject current is applied. In the above example the eject current would then be +50 nanoamperes.

AUTO Operation

The timing of current flow from each channel of the model 260 can be externally controlled by the use of a pulse generator or computer that can supply a logic level of at least +5 volts to the AUTO INPUT terminal. The outer shell of this connector should be connected to the user's generator ground. It is not connected to the 260



instrument case. To use the instrument in this way first place the channel in the AUTO mode. Place the OUTPUT switch in the ENABLE position. Current amplitude and polarity should be preset as described in "Single Channel Operation" (page 3). Upon application of the +5 volt command potential to the AUTO INPUT terminal, the preset current will flow from the output terminals for as long as the command potential is maintained. Note: If the instrument is in the MANUAL mode, the application of the AUTO INPUT signal will halt the current for as long as this command is maintained. This is the complement of normal AUTO operation.

Compliance Alarms

Each current generator channel contains an audible and visual alarm circuit that is activated when the current amplitude is large enough to cause the voltage compliance to be exceeded. In other words, the load resistance is too high for the amount of current flowing. The user is thus informed that the instrument cannot deliver the amount of current indicated on the panel ammeter. The alarm will also be triggered if the output path is open-circuited by a loose connection, air bubble or a blocked micropipette. The initial compliance voltage exceeds 100 volts but will decrease proportionately as the battery voltage falls with age.

Battery Replacement

Each channel contains two 9-volt transistor batteries. These should be replaced when the user can no longer get full scale deflection of the ammeter as described in "Preliminary Instrument Check" (page 3), although the instrument will continue to operate satisfactorily for some time after this condition is observed. Turn off the power switch for each channel and remove the cover of the instrument by unscrewing the four screws, two on each side, which secure the instrument cover. The batteries are mounted in pairs held to the printed circuit board by a spring clip assembly. Observe the male and female connectors on the battery mounts and insert the new batteries so that the connectors mate correctly. Any 9-volt battery will perform satisfactorily but WPI recommends Duracell 9 volt alkaline batteries or their equivalent because of their superior life expectancy and their resistance to leakage. Normal carbon-zinc cells should be replaced when needed or every six months. Alkaline cells should be replaced when needed or every twelve months. To avoid potential problems, replace all six batteries at the same time with batteries of the same brand and lot number.



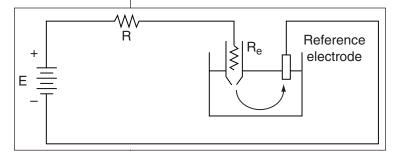
Application Notes

The following is a reprint of a note on microiontophoresis first published by WPI in 1976.

Current injection in Microiontophoresis

This applications note addresses itself primarily to electrical circuit considerations and is a brief introduction to the fundamentals of WPI's instrumentation for the injection of ions from glass micropipette electrodes.

Constant Current



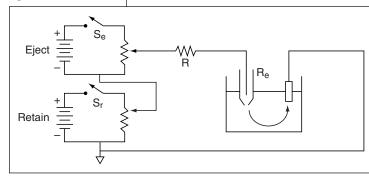
To pass ions through an electrolyte filled micropipette, a source of current is necessary. Since the currentvoltage characteristics of small tipped micropipette electrodes are generally not linear or constant with time and exhibit tip junction potentials, it is necessary to use a large DC potential in series with a

Fig. 1

very large resistor to generate a current as shown in Figure 1. The resulting current flow is $I = (E + junction P.D.) / (R + R_e)$. If E is large and $R > R_e$ then the current I = E/R is said to be constant (that is, independent of the electrode's resistance). The driving potential E is called the "compliance" voltage or the maximum voltage available to force current through the electrode-solution pathway. The compliance is the voltage to which the current generator's terminals will rise if the electrode is lifted form the solution or if the electrode resistance is very much larger than R.



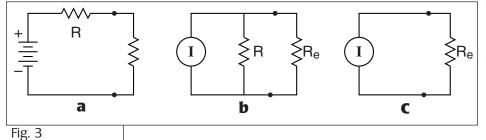
The basic circuit of Figure 1 can be elaborated, as shown in Figure 2, to yield a



practical working circuit for the phoresis, for example, of cations.

When the switch S_r is closed, a small "holding" or "braking" current flows through the electrode to prevent diffusion or hydrostatic pressure from allowing the cations to escape outside the microelectrode. (It should be noted





that an undesirable consequence of this procedure is that the tip of the micropipette does experience an inflow of some of the external electrolyte, thus diluting the contents of

the pipette near the tip opening.) When the switch $S_{\rm e}$ is closed, the net driving potential becomes positive, swamping the smaller retaining potential difference. A cation current will result.

It can be shown that the equivalent circuit of Figure 3a, which is a simple version of Figure 1, is shown in Figure 3b. An "ideal" current generator with infinite source resistance generates a current of E/R amperes.



 \mathbf{I}_{r}

Ie

 \uparrow

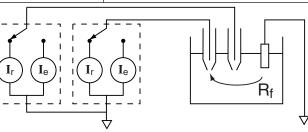
Further, if $R > R_{e}$, Figure 3b can be simply represented by Figure 3c.

The concept of an ideal current generator is useful. Practical electronic circuits have been constructed using photocells and transistors to achieve current sources which are virtually independent of electrode resistance. WPI has used its own field proven solid state constant current generators for several years. The actual circuit details are omitted here but the manner in which they are used is suggested by Figure 4 below. The current sources are arranged in a paired parallel combination. A switch changes the current from I_r (hold) to I_e (eject).

Current Return

Up to this point, we have assumed that the resistance to the ground terminal of the external solution is negligible. The current return path through the solution for one

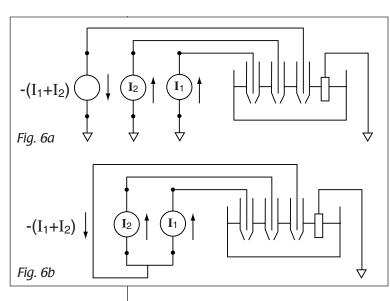




or more current passing electrodes includes the sum of all currents flowing from the electrodes to ground, as shown in Figure 5.

As shown, the current generators are "singleended", that is the current return path is via the ground pathway. Some applications cannot tolerate the resulting potential at the current





electrode site owing to the IR voltage drop across the fluid resistance Rf. This current flow to ground is found undesirable in some cases because: (1) The voltage of cells being measured near the current release site may include an error potential owing to the current induced local potential; or (2) The current may be large enough to cause local stimulation of excitable membrane.

To prevent the flow of current from the phoresing electrodes to ground, it is necessary to introduce a common or current return electrode which will "sink" or absorb all of the current locally

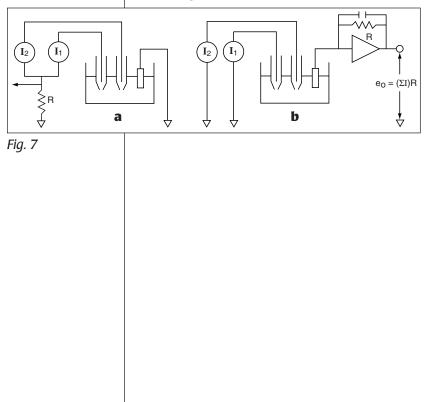
generated by ionophoresing electrodes. As shown in Figure 6a the effect will be to maintain the site of the multi-current electrodes a net zero potential with respect to the ground electrode.

WPI's floating current generators are differential as shown in Figure 6b. This means that if the common terminals of the current generators are all connected to the return electrode, the net ground current is zero. If the generation of local potentials is negligible, then one may connect WPI's floating current source as a ground referred current source. Thus these generators can be used as ground referred or floating current sources.



Measuring Current

WPI's floating battery operated current generator contains a built in ammeter. External electrodes may be disconnected by operating a PRESET switch. This allows the user to preset the desired levels of eject and retain currents while observing the ammeter. Current may also be measured by two other techniques as shown in Figure 7. As shown in 7a the normally grounded side of the current generator pair is connected to ground through a known resistance. A recorder or oscilloscope may then monitor the p.d. across this resistor as a measure of the current. An alternative method shown in 7b replaces the preparation ground return with a "current to voltage" converter. This instrument maintains the ground (zero) potential and simultaneously displays a voltage at its output proportional to current flow. Further information about **IVA** (WPI's current-to-voltage converter) can be obtained by contacting WPI.





References

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2. **Spencer, J.J.**, Programmable Nanoampere Constant Current Sources for Iontophoresis, *Pergamon Press*, 1971, pp 683

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Specifications (each channel)

Current Range 0 to 100 nanoamperes 0 to 1000 nanoamperes
Maximum Output Voltage (compliance) 100 volts
Operating Modes Manual or Auto (external control)
Auto Input (external control for current on/off)+5 volts
Auto Input Resistance 1.5 KOhms, approx.
Auto Input Delay < 100 microseconds
Output Polarity NORMAL red terminal, positive
Current Meter Error +/- 2% max.
Power Two 9-volt alkaline cells



Warranty

WPI (World Precision Instruments, Inc.) warrants to the original purchaser that this equipment, including its components and parts, shall be free from defects in material and workmanship for a period of one year* from the date of receipt. WPI's obligation under this warranty shall be limited to repair or replacement, at WPI's option, of the equipment or defective components or parts upon receipt thereof f.o.b. WPI, Sarasota, Florida U.S.A. Return of a repaired instrument shall be f.o.b. Sarasota.

The above warranty is contingent upon normal usage and does not cover products which have been modified without WPI's approval or which have been subjected to unusual physical or electrical stress or on which the original identification marks have been removed or altered. The above warranty will not apply if adjustment, repair or parts replacement is required because of accident, neglect, misuse, failure of electric power, air conditioning, humidity control, or causes other than normal and ordinary usage.

To the extent that any of its equipment is furnished by a manufacturer other than WPI, the foregoing warranty shall be applicable only to the extent of the warranty furnished by such other manufacturer. This warranty will not apply to appearance terms, such as knobs, handles, dials or the like.

WPI makes no warranty of any kind, express or implied or statutory, including without limitation any warranties of merchantability and/or fitness for a particular purpose. WPI shall not be liable for any damages, whether direct, indirect, special or consequential arising from a failure of this product to operate in the manner desired by the user. WPI shall not be liable for any damage to data or property that may be caused directly or indirectly by use of this product.

Claims and Returns

• Inspect all shipments upon receipt. Missing cartons or obvious damage to cartons should be noted on the delivery receipt before signing. Concealed loss or damage should be reported at once to the carrier and an inspection requested. All claims for shortage or damage must be made within 10 days after receipt of shipment. Claims for lost shipments must be made within 30 days of invoice or other notification of shipment. Please save damaged or pilfered cartons until claim settles. In some instances, photographic documentation may be required. Some items are time sensitive; WPI assumes no extended warranty or any liability for use beyond the date specified on the container.

• WPI cannot be held responsible for items damaged in shipment en route to us. Please enclose merchandise in its original shipping container to avoid damage from handling. We recommend that you insure merchandise when shipping. The customer is responsible for paying shipping expenses including adequate insurance on all items returned.

• Do not return any goods to WPI without obtaining prior approval and instructions (RMA#) from our returns department. Goods returned unauthorized or by collect freight may be refused. The RMA# must be clearly displayed on the outside of the box, or the package will not be accepted. Please contact the RMA department for a request form.

· Goods returned for repair must be reasonably clean and free of hazardous materials.

• A handling fee is charged for goods returned for exchange or credit. This fee may add up to 25% of the sale price depending on the condition of the item. Goods ordered in error are also subject to the handling fee.

- Equipment which was built as a special order cannot be returned.
- Always refer to the RMA# when contacting WPI to obtain a status of your returned item.
- · For any other issues regarding a claim or return, please contact the RMA department

Warning: This equipment is not designed or intended for use on humans.

World Precision Instruments, Inc.

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* Electrodes, batteries and other consumable parts are warranted for 30 days only from the date on which the customer receives these items. WORLD PRECISION INSTRUMENTS, INC.

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DECLARATION OF CONFORMITY

We:

World Precision Instruments, Inc. 175 Sarasota Center Boulevard Sarasota FL 34240-9258 USA

as the manufacturers of the apparatus listed, declare under sole responsibility that the product(s):

Title: 260

to which this declaration relates is/are in conformity with the following standards or other normative documents:

Safety:	EN 61010-1:1993 (IEC 1010-1:1990)
EMC:	EN 50081-1:1992 EN 50082-1:1992

and therefore conform(s) with the protection requirements of Council Directive 89/336/EEC relating to electromagnetic compatibility and Council Directive 73/23/EEC relating to safety requirements.

Issued on: 18 th February	2000
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