



Cell Simulator

2410

INSTRUCTION MANUAL FOR CELL SIMULATOR MODEL 2410

Version 4.0
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Disclaimer

THIS EQUIPMENT IS NOT INTENDED FOR USE WITH HUMAN SUBJECTS IN ANY WAY.

Document

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Safety

This instrument is provided with terminal for protective grounding. Before applying power, verify that the correct safety precautions are taken (see the following warnings). In addition, note the external markings on the instrument that are described under Safety Symbols. Do not operate the instrument with its cover removed. Replace fuse only with specified type.

Supply Voltage

This equipment comes with an external power supply that is customized at the factory for line voltages of the county of destination. The required line voltage is indicated on the supply.

WARNING

Do not attach a line voltage that does not match the line voltage specified on the power supply.

Before turning on the instrument, you must connect the protective earth terminal of the instrument to the protective earth conductor of the (mains) power cord. The mains plug must only be inserted in a socket outlet with a protective earth contact.

Service should be performed by trained personnel only. To avoid dangerous electric shock, do not perform any service unless qualified to do so.

Do not operate the instrument in the presence of flammable gases or fumes. Operation of any electrical instrument in such an environment constitutes a definite safety hazard.

Safety Symbols

The product is marked with this symbol when it is necessary for you to refer to the instruction manual in order to protect against damage to the product.

WARNING

The Warning symbol calls attention to a procedure or practice, which, if not correctly performed could result in injury. Do not proceed beyond a Warning symbol until the indicated conditions are fully understood and met.

CAUTION

The Caution symbol calls attention to a procedure or practice, which, if not correctly performed could result in damage to the product. Do not proceed beyond a caution until the indicated conditions are fully understood and met.



Overview

The Model 2410 is an electrical equivalent circuit of several cell recording scenarios that occur during voltage and current clamping. This model can be used to train students in patch clamp techniques. It is also useful to test patch clamp instrumentation without having to worry about connections and pipette problems.

About This Manual

This manual consists of two chapters. Chapter 1 gives a description of the circuitry used in the Model 2410. It will describe which parts of an experiment each part of the circuit is meant to represent, but it will not go into a mathematical derivation of why the circuit is equivalent, this information can be found by reading the references. Chapter 2 is a description of a recording scenario that substitutes the Model 2410 for a real cell and illustrates how the cell simulator might be used by a researcher.

Chapter 1

Controls and Connectors

PROBE

Three connectors under PROBE are used to connect a patch clamp amplifier's probe to the 2410. The BNC can be used with probes that have a BNC connectors. Note the outer conductor of this BNC is not ground, but is uses the patch clamps driven shield to reduce current leakage among the high value resistors in the model 2410. A ground connection must be placed between the patch clamp probe and the GND connection on the 2410. The other connector under PROBE is a 2mm socket, designed for mating with probes that terminate in a 2mm pin.

CHANNELS

CHANNELS switches are used to activate the equivalent circuit for their specific channel type. These circuit elements are only implemented in certain MODE positions:

CHANNEL	Active MODE positions
PATCH	PATCH SEAL
K+	PATCH SEAL, POOR WHOLE CELL, GOOD WHOLE CELL
Na+	PATCH SEAL, POOR WHOLE CELL, GOOD WHOLE CELL

Instead of using the switch to “open” or “close” the channel, a TTL level signal can be applied to the GATE input. Voltage levels above 3.0V will open the channel, voltage levels below 1V will close the channel.

POWER

Power is necessary for the CHANNELS and the OUTPUT portions of the Model 2410. However the Model 2410 can still be used as a non-active, non-monitoring model cell without these features turned on.

OUTPUT

The OUTPUT monitors the equivalent circuits membrane voltage with a gain of 10. This is useful, since patch clamping instruments assume that the clamping signal is the same as the membrane voltage. To set the membrane voltage close to the clamping voltage, the patch clamp amplifier must be tuned. By monitoring the output of the Model 2410 it is possibly to properly tune a patch clamp amplifier.

MODE

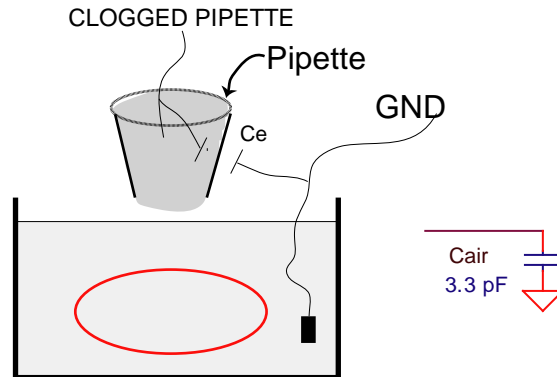
The MODE switches between the different equivalent circuits. The circuit descriptions are described in the next section, and illustrated in each figure.

NO CONNECTION

When the MODE switch is in the NO CONNECTION position, the PROBE input is not connected to any of the internal circuitry of the model 2410.

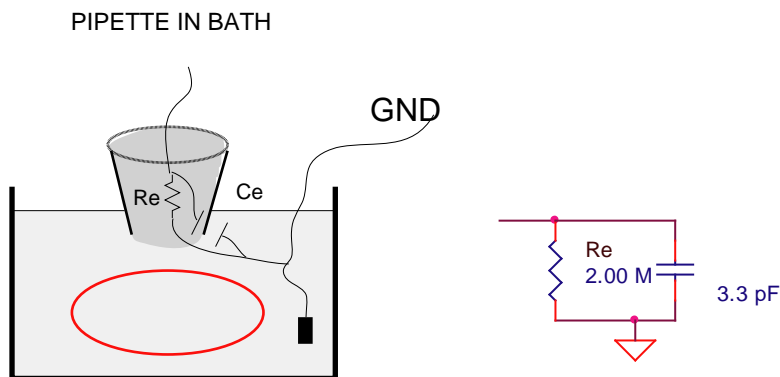
CLOGGED PIPETTE

A clogged pipette and a pipette out of the bath/animal will have a similar equivalent circuit because the only connection between the amplifier and ground will be the capacitance through the electrode (C_e). This means that only transient currents can flow through the amplifier.



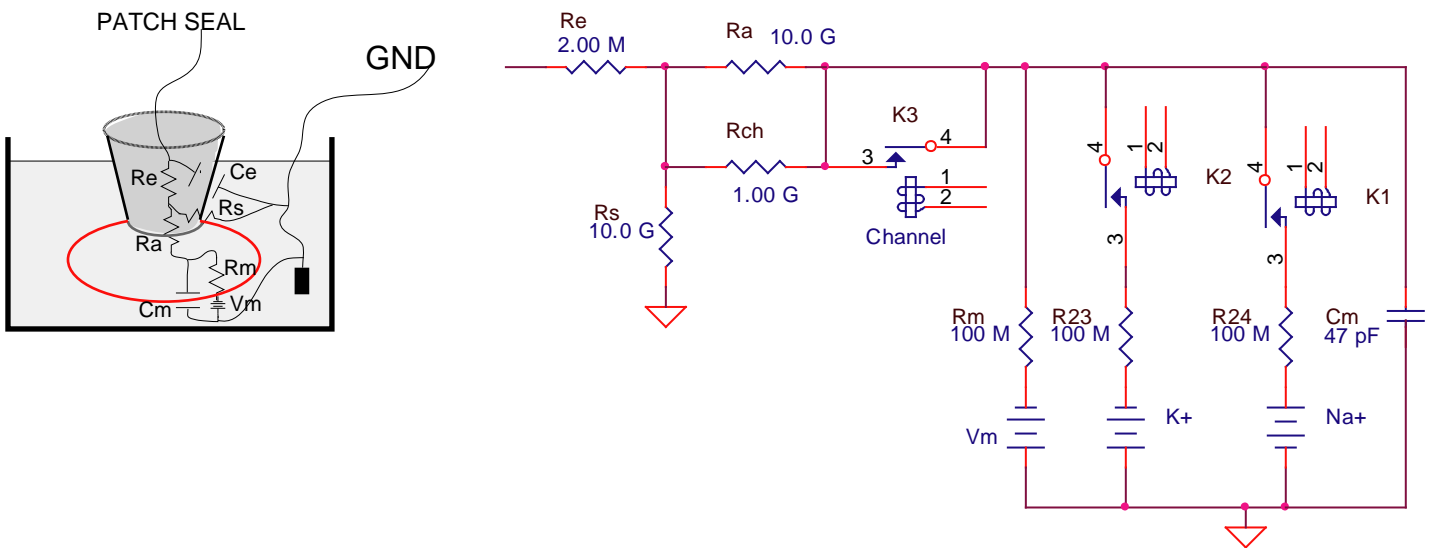
PIPETTE IN BATH

Once the pipette enters the bath, there is an added parallel resistance of the electrode's resistance (R_e), allowing constant currents to be observed.



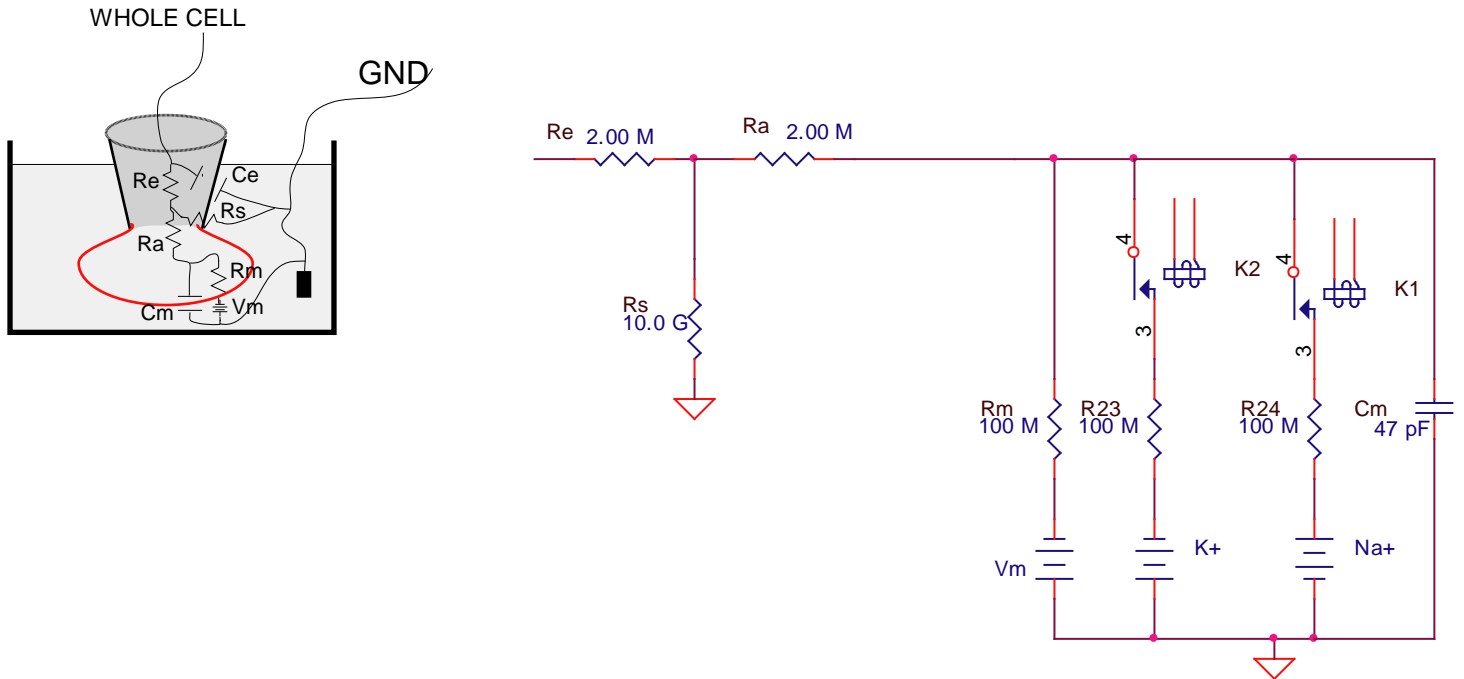
PATCH SEAL

A patch seal is modeled by adding a series access resistance (R_a) that provides access to the cell, and a seal resistance (R_s) that provides leakage of signal to ground. The passive components of the cell's membrane are modeled by a resistor (R_m) and a battery (V_m) in parallel with a capacitor (C_m). The active components are modeled by a switch in series with a resistance and a battery. The battery is set for the equilibrium potential of a particular ion and the resistance is set to give the conductance of the ion's channel. In a patch seal the access resistance is very large compared to the cell's membrane resistance; as such, the active channels of the cell do not contribute to the response unless the active component is located within the patch. This activity is modeled by a small decrease in the access resistance, controlled by the PATCH channel relay (operated by the front panel PATCH switch or TTL controlled front panel PATCH GATE).



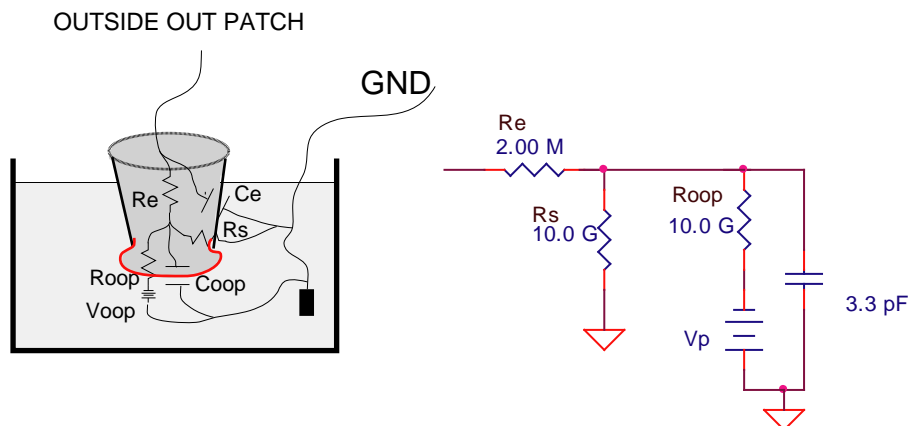
POOR WHOLE CELL/GOOD WHOLE CELL

Whole cell recording's equivalent circuit is essentially the same as patch recording except for the important thousand-fold decrease in access resistance. The POOR WHOLE CELL circuit's access resistance is 10M compared to the patch's access resistance of 10G. The GOOD WHOLE CELL circuit's access resistance is 2M.



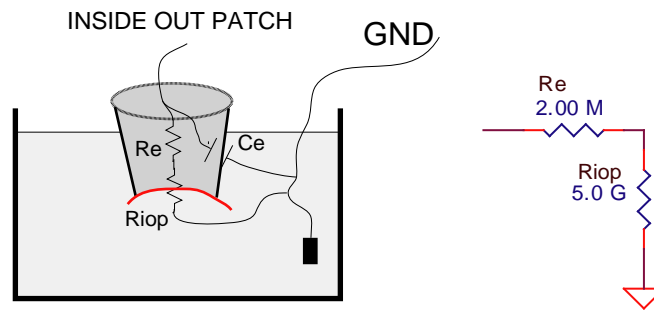
OUTSIDE OUT PATCH

An OUTSIDE OUT PATCH's equivalent circuit eliminates the active components from the patch. Active patch channels are not included because the purpose of this circuit is to differentiate from the whole cell circuit, since outside out patches are formed after a whole cell patch is formed.



INSIDE OUT PATCH

An INSIDE OUT PATCH is formed after a Patch seal by detaching a small section of the cell off of the whole cell. This results in an equivalent circuit that differs from the patch seal by a reduction in membrane capacitance (C_m) and usually a reduction in seal resistance (R_s). This results in an equivalent circuit with essentially no capacitance. The access resistance in an inside out patch seal is equal the electrical equivalent of two parallel resistors, the patch access resistance and the patch seal resistance, resulting in a value about half of the Patch's seal resistance.



Chapter 2

Sample experiment

The Model 2410 is designed to connect to a patch clamp amplifier's probe input. It will accept a BNC, or a 2mm pin input. If your amplifier has a different input connector then an adapter will need to be made. The center pin of the BNC, or 2mm socket should connect to the input of the patch clamp probe, and the GND connector should connect to your GND connector on your probe. Once the Model 2410 is connected to your amplifier, you can start simulated experiments. Make sure the patch clamp amplifier is properly connected to a clamping signal source and the output is connected to one channel of an oscilloscope. Connect the output of the Model 2410 to channel two on the oscilloscope.

Set the MODE switch to CLOGGED PIPETTE, this will simulate an electrode connected to your probe, but not inside the bath. Use the controls on the amplifier to apply a searching clamp signal to your simulated cell. The resulting waveform on the output should have transients at the frequency of your clamping signal.

When the MODE switch is set to PIPETTE IN BATH, a DC current should now be visible on the scope proportional to your clamping voltage. If your clamping signal is 10mV and your amplifier

gain is 1mV/pA then your output should be 5 volts. $\left(\frac{1 * 10^{-3} V}{2 * 10^6 \Omega} * 10^9 \frac{V}{A} \right)$.

By switching the MODE to PATCH SEAL, you can simulate the formation of a seal on a cell. The amplitude of the amplifier's output should suddenly drop leaving mostly transients. However there should be a voltage offset of the clamping signal proportional to the equivalent cell's membrane voltage. Transients can be canceled using capacity compensation on the patch clamp amplifier. At this point, it is useful to start watching the output of the 2410. This output give the true voltage that the model cell is clamped at, which can be vastly different then the desired clamping signal that the patch clamp amplifier is sending. Switching CHANNELS PATCH to OPEN, while the mode is in PATCH SEAL will simulate a channel opening in the patch.

To simulate going from a patch seal to whole cell is done by switching MODE to POOR WHOLE CELL or GOOD WHOLE CELL. When you switch to whole cell there will be a dramatic shift in the DC potential, and large capacitance transients will occur. Compensation for capacitance transients is accomplished by using the whole cell compensation controls on your patch clamp amplifier. Here is where the 2410 can be the most useful for training on how to properly use these controls. As the controls are adjusted, you can watch both the change in the output on your patch clamp amplifier and watch how the true membrane voltage output from the 2410 approaches the desired clamping signal from your patch clamp amplifier.

Pulling an OUTSIDE OUT PATCH is done from a whole cell electrode connection. The Model 2410 can be used to illustrate the difference in recording output by switching the MODE from GOOD WHOLE CELL to OUTSIDE OUT PATCH. You should now have large long duration transients from improperly tuned whole cell parameters. You will need to re-adjust, or turn off your patch clamps whole cell compensation.

Detaching a section of cell membrane from a patch seal recording forms an INSIDE OUT PATCH. The Model 2410 can be used to illustrate difference's observed when transitioning between these two conditions by switching the MODE switch from PATCH SEAL to INSIDE OUT PATCH. The main differences seen should be a small DC shift in the output of the patch clamp amplifier.

Specifications

OUTPUT gain	10.0 ±0.2
Giga-ohm resistor precision	<20%
Other component precision	1%
Minimum gate switching time	1ms

Warranty

What does this warranty cover?

A-M Systems, LLC (hereinafter, “A-M Systems”) warrants to the Purchaser that the Instruments manufactured by A-M Systems (hereinafter the “hardware”), and sold after January 1, 2020, is free from defects in workmanship or material under normal use and service for the lifetime of the hardware. Headstages manufactured by A-M Systems and sold after January 1, 2020, will be repaired under warranty only once per year. This warranty commences on the date of delivery of the hardware to the Purchaser. “Lifetime” is defined as the time all components in the instrument can still be purchased from mainstream, common, electronic component distributors such as Digi-Key Electronics, Newark, or Mouser Electronics.

For hardware sold prior to January 1, 2020, the warranty in effect at time of purchase applies, with the maximum warranty period of three (3) years for new purchases, and one (1) year for those that have been repaired by A-M Systems. For headstages manufactured by A-M Systems and sold prior to January 1, 2020, the maximum warranty period is one (1) year.

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What is not covered by this warranty?

This warranty is contingent upon proper use and maintenance of the hardware by the Purchaser and does not cover batteries. Neglect, misuse whether intentional or otherwise, tampering with or altering the hardware, damage caused by accident, damage caused by unusual physical, electrical, chemical, or electromechanical stress, damage caused by failure of electrical power, or damage caused during transportation are not covered by this warranty. Further, no guarantee is made regarding software compatibility with future updated operating systems. Products may not be returned to A-M Systems for service, whether under warranty or otherwise, which are contaminated by infectious agents, radioactive compounds or other materials constituting a health hazard to employees of A-M Systems

LIMITED WARRANTY, cont

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Revision History:

Rev	Date	Description
1	6/30/06	Initial document control release
2	4/28/10	DCR201200 Warranty and Company info
3	1/18/19	DCR202615. Update for drawing\warranty info.
4	3/19/20	DCR 203316. Update Warranty