

Myocyte Contractility Recording System

**Complete real-time, turnkey system for
contractility recording**

- 1000 cell and sarcomere length measurements/
second



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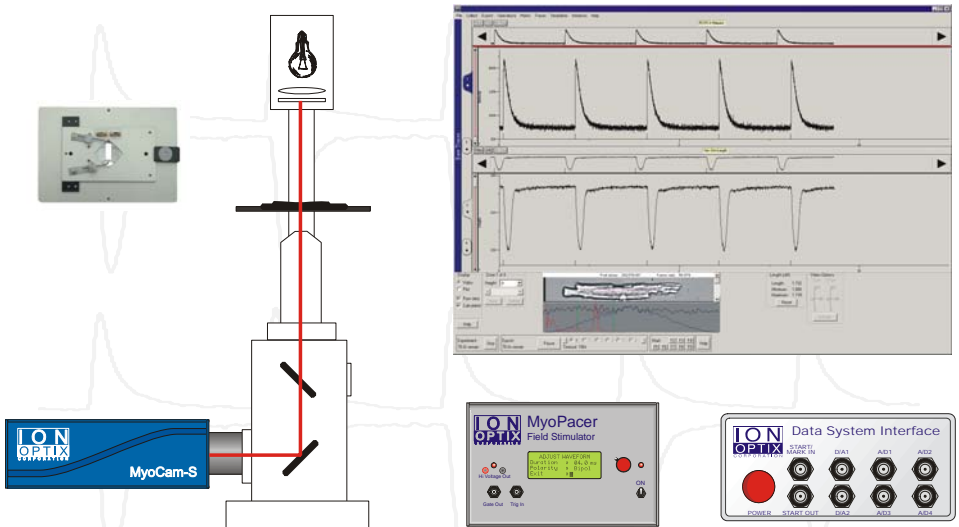
March 2010

Myocyte Contractility System Overview

Interest in the physiology and pathology of the heart has led to a substantial increase in the number of laboratories studying the myocardium at the cellular level using isolated cardiac muscle cells or myocytes. Although excitation-contraction (EC) coupling, the process by which electrical stimuli induce a mechanical response in myocytes, has been an area of intense investigation for over half a century, elucidation of the fundamental molecular and biophysical mechanisms remains at the forefront of cardiovascular research. Impairment to the regulatory machinery governing EC coupling correlates strongly with the onset and progression of many myopathies. Cellular dimensioning recordings offer an important measure of EC coupling in isolated myocytes and myofibers while also providing key insights into the processes that affect cardiovascular health.

IonOptix developed its **Myocyte Contractility Recording System (MCSYS)** over many years of collaboration with top cardiovascular researchers. We take pride in a line of precision products that are application driven and built to meet the needs of a demanding research environment. Since its inception in 1990 IonOptix has built and installed hundreds of high performance, turnkey systems in research laboratories worldwide.

A complete system includes everything necessary for simultaneously acquiring and analyzing calcium and cellular geometry data with our new IonWizard 6 software. MCSYS also includes an inverted dimensioning microscope with brilliant optics, a cell stimulator with a stimulation/superfusion chamber and temperature control, and a suite of A/D analog and digital connections for synchronous data collection.



IonWizard Software Suite

Acquisition of EC Coupling Data in Myocytes

Our complete systems are built from components designed to work seamlessly with one another and our IonWizard core software, providing completely synchronous and accurate data acquisition. IonWizard's core functions are expanded through the **SoftEdge** and **SarcLen** acquisition modules to record cell and sarcomere length data. Through these acquisition modules, IonWizard communicates directly with two root devices, the MyoCam-S video acquisition camera and our data system interface.

IW6 is capable of acquiring up to 4 channels of 1000 Hz analog data. It also supports analog data outputs and digital inputs. IW6 now features a signal generator function for programming voltages to drive and control external hardware.

EDQACQ provides the ability to detect the cell boundaries at separate lines for left and right edges. A threshold is then used to locate the edge within the detection window. This dynamic measurement allows up to 1000 length recordings per second when coupled to the MyoCam-S.

SARACQ performs an average of the lines within the area of interest to create a well resolved striation pattern. A fast Fourier transform (FFT) is then calculated and the peak within the power spectrum represents the average sarcomere spacing, measured in real time up to 1000 times per second.

Features

- Coupled with a Data System Interface, SoftEdge and SarcLen form a powerful integrated myocyte recording and analysis system.
- Cell length or sarcomere data are sampled at rates as high as 1000 Hz.
- Multiple 'epochs' define separate acquisition regimes. Within each epoch, independent sampling rates for sarcomere and cell length, and analog data are specified.
- Switches between different epochs occur automatically or via user intervention.
- SoftEdge & SarcLen work seamlessly with the IonOptix MyoCam-S™.
- Edge detection is based on either image intensity or the derivative of image intensity.
- Edges are detected from "outside in" on both cell edges.
- Independent left and right edge analysis on separate video lines improves the accuracy of length measurement.
- Cell length data is optionally output as an analog voltage in real-time.



IONWIZARD



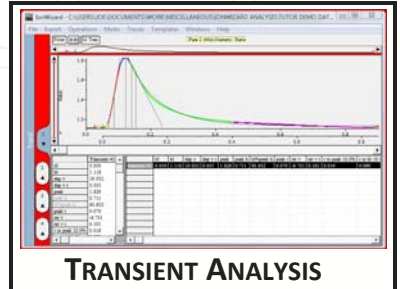
SARLEN

IonWizard Software Suite (cont.)

Analysis of EC Coupling Data in Myocytes

Transient Analysis

IonWizard has extensive transient fitting capacities. Each transient is marked for analysis either automatically or manually via IonWizard's transient mark facility. Subsequently, the transients are fit by a series of high order polynomials to arrive at a mathematical model of the curve. This model is used to determine a variety of characteristic transient parameters (over 30 in total). IonWizard automatically detects upward or downward going transients thus calculating and presenting the parameters appropriately. The user may peruse each transient to confirm the accuracy of the fits. A graphical feedback mechanism permits verification of each parameter. The transient parameters are exported to a file or copied directly into a spreadsheet using the clipboard.



Transient Parameters Found by IonWizard:

Time Zero. The beginning time of the transient. This can be found three ways: via a baseline finding algorithm, by user specification, or keyed off an external mark.

Baseline. The value of the transient at time zero.

Departure/Return Velocity (i.e. dc/dt , dL/dt). The maximum (minimum) velocity reached on the rising and falling phases of the transient. These values can also be presented as a percentage of the baseline value and as a percentage of the transient height. The time of the departure/return velocity is also given.

Peak/Peak Height. The peak is the highest/lowest value reached by the transient. This parameter is also used to calculate peak height. The height can be shown as a percentage of the baseline (i.e. percent shortening for length data). The time of the peak relative to time zero is also given.

Time to % Peak / Time to % Baseline. The user can configure IonWizard to find the time required for the transient to reach up to three different levels on the rising and falling phases. These times may be reported relative to either time zero or to the peak time.

Exponential Fit. A single exponential curve is fit to the trace starting at one of three places: the peak, the time of maximum return velocity, or some user defined % return to baseline. Three parameters are fit: amp, tau, and off. The equation fit is $y = amp * e^{-t/tau} + off$.

Bi-exponential Fit. A bi-exponential curve is fit to the trace starting at time zero. Four parameters are fit: amp, tau rise, tau fall, and off. the equation fit is $y = amp * (e^{-t/tau\ fall} - e^{-t/tau\ rise}) + off$.

Area. The area under the curve (i.e. from baseline to peak) is calculated for two time ranges: from time zero to peak and from the peak to the end of the transient. For upward going transients, the area from the baseline down to zero is also found for both time ranges.

MyoCam-S High Speed Digital Video

The IonOptix MCS100 represents the "next generation" of our popular MyoCam. It's an all-digital, variable field rate camera that utilizes the USB 2.0 standard to remove the restrictions of analog video formats and frame grabbers. Its maximum pixel clock rate is twice that of the MyoCam so that our "standard" 1/4 field rate jumps to 380Hz; sufficient to capture/characterize the fastest cardiac myocyte contractile transient. The MyoCam-S™ gives you complete control over all aspects of video acquisition to deliver the optimum combination of temporal and spatial resolution needed for your experimental requirements. All analog processing and digitization is done inside the camera to minimize analog noise. The digital data is then transferred to the computer using a standard high-speed USB 2.0 port eliminating the cost of a frame grabber.



Features

- **CCD sensor.** 774 pixels wide by 245 lines (progressive) or 490 lines (interlaced).
- **Frame rates (lines).** 97Hz (245 lines), 250Hz (87 lines), 500Hz (36 lines), 1000Hz (10 lines).
- Complete control of camera acquisition window (start pixel & width, start line & height).
- **Selectable pixel clocks.** Standard, 2x high-speed, and low-noise.
- 12-bit A/D converter with 8 or 12 bit read-out.
- Programmable CCD gain and offset.
- Programmable integration time to stop fast movement or increase camera sensitivity.
- Programmable frame interval and external trigger to synchronize with other recording devices.
- Multiple cameras can be exactly synchronized.
- Compatible driver for use with any standard Windows video application

Myocyte Contractility Microscope: Motic AE31

The IonOptix-configured Motic AE31 inverted microscope provides an ideal platform for dimensioning measurements. It features upscale research functions, such as halogen Koehler illumination and epifluorescence capacity. The AE31 also incorporates Motic's Color Corrected Infinity Optical System [CCIS®] to produce crisp, flat, high contrast images. We equip our microscope packages according to the specific demands of the proposed IonOptix system. Properly equipped, the Motic serves as an exceptional choice for researchers in search of reliable, high fidelity data acquisition at an affordable price.

Features

- **CCIS Optics.** Color corrected infinity optical system.
- **Brightfield Illumination.** Koehler illumination system w/ true DC 6V-30W output delivers bright, consistent illumination at all optical magnifications.
- **Mechanical Stage.** Precise control of sample position. Comfortable long wand allows user to rest forearm while manipulating stage.
- **Trinocular Head.** Easy access to auxiliary components. Efficient transmission of light for photometry and cellular dimensioning.



MOTIC AE31 MICROSCOPE

- **Microscope Base.** Wide base for strength and rigidity. Inverted "Y" support provides additional lateral support. Ergonomic design provides easy adjustment of focus and stage controls.

Data System Interface: System Integration

The IonOptix Data System Interface, model DSI300, provides all the standard non-video analog and digital input/ output hardware needed for your contractility system. The interface box is significant to contractility measurements in that it allows you to combine external stimuli (e.g. pacing pulses) with data traces. Synchronizing data points to the pacing stimulus allows full use of the powerful tools IonWizard provides for averaging contractility events.

The DSI300 may be connected to external devices using the four analog inputs, the two analog outputs or the digital start/ mark trigger input. IonWizard's flexible device configuration allows the experimenter to specify the name and unit scaling of each auxiliary signal for easy-to-read data files.

Features

Inputs

- **Start/ mark in.** This TTL signal allows external initiation of data sampling and/ or can be recorded during data acquisition to provide event synchronization information.
- **Analog to Digital.** Four channels of 16-bit A/D with input voltage range of $\pm 5V$.



DSI300

Outputs

- **Digital to Analog.** Two channels of $\pm 5V$. 12-bit D/A outputs can be configured as a variety of monitor or control signals.

Includes

- Includes half-length, full-height PCI computer interface card and six foot cable.
- IonWizard driver software for Windows 2000, XP.

Acute Cell Stimulators

MyoPacer

The IonOptix MyoPacer is a cell stimulator that has been designed specifically around the needs of the myocyte research community. The microcontroller driving the pacer allows for greater protocol versatility. Five frequencies can be pre-programmed to allow easy and rapid frequency changes. Its ability to emit bipolar stimuli or to alternate stimulus polarity greatly reduces problems with electrolysis at the electrodes. Output voltage (± 40 V), frequency (.010 to 99 Hz), and duration (.4 msec to 90 msec) can be easily adjusted from the front panel. All programmed features are saved in non-volatile memory for quick start-up.



Features

- **Digital adjustment of:**
 - frequency (0.010-99Hz)
 - pulse duration (0.4-90 msec)
 - voltage (up to ± 40 V)
- **Software sync.** TTL synchronization with Fluorescence or Data System Interface allows interpretation of stimulation events by IonWizard, enabling event averaging of selected transients.
- Pulses can be uni-polar, bi-polar, or alternate polarity between pulses.

Inputs / outputs

- **High Voltage Out.** ± 40 V.
- **Trigger In.** Trigger a stimulus with a TTL pulse.
- **Gate out.** TTL pulse concurrent with high voltage pulse.

Acute Cell Stimulators

MyoPacer EP

The IonOptix MyoPacer EP cell stimulator incorporates the functionality of our current MyoPacer plus many of the new features requested by users for electrophysiological studies. It was created to give researchers the capability of delivering pre-designed stimulation sequences for obtaining restitution curves and doing arrhythmia and defibrillation studies. It is based on the original MyoPacer and retains original functionality, but adds the ability to generate off beats, delays, and multiple frequency protocols. The MyoPacer EP is designed around the strategy of creating multi-phase protocols. Each protocol can have up to 5 phases. A phase can be defined either as a pulse train or a delay. If it is defined as a pulse train, a period or frequency is selected.

Phases end either after a programmed time/# of pulses, or when a manual or external TTL trigger is received. The end of a phase will immediately initiate the next phase or, if on the last phase, the return to the first phase. As traditional electrophysiological researchers have used the terminology S1, S2... to describe the various phases, the MyoPacer EP will automatically display the appropriate label when looking at a phase.



MYOPACER EP
(w/ FHD CHAMBER)

Unique EP Features

- **Restitution Protocols.** Deliver fixed number of pulses initiated by an external TTL pulse or manual start.
- **Arrhythmia Protocols.** Insert an offbeat pulse at a fixed interval.
- **Exercise Protocols.** Run multiple pulse trains with individually programmable frequency and duration.
- **Irregular Pacing.** Random variation of specified frequency within definable percentage window and guaranteed average effective rate.
- **External Triggering.** Change to next pulse train with TTL 'advance' input and/or trigger individual pulses with TTL 'pulse' input.
- **Programmable TTL Output.** Flexible output options for synchronizing your experiment.

Standard MyoPacer Features

- Maximum current: 240mA.
- Digital adjustment of frequency (0.010-99Hz), pulse duration (0.4-24 msec), and voltage (up to $\pm 40V$).
- Bipolar pulses reduce electrolysis byproducts.
- TTL Gate output is concurrent with high voltage pulse.

Microscope Chamber Systems

FHD

The FHD Microscope Chamber System is a newly designed chamber system to perfuse and stimulate cardiac myocytes on the microscope's stage. The silicone gasket seals disposable coverslips, preventing leakage without the use of sealing grease or vasoline. The FHD chamber system is ideal for use with either freshly isolated or cultured cells.

Features

- **Hinged lid.** Includes all the paraphernalia of solution line, solution height adjustment, ground wires, and platinum stimulation wires.
- **Molded silicone insert.** Forming the flow area of the chamber, the insert is available in a variety of designs and is easily replaced, exchanged, and cleaned.
- **Rapid exchange of cover slips.** Ideal for those researchers using cells cultured or plated on 25mm cover slips. The chamber offers effortless insertion of fresh slips with only a twist of the lid lock.



FHDRC1

- **Very low solution levels.** Rapid solution change with nearly laminar flow and minimal turbulence while separate aspiration port maintains stable solution level.
- **Thermistor.** Independent thermistor assembly with standard resistance for feedback temperature controller/ monitor. Can be used with our TEMPC2 package to monitor bath temperature.

C-Stim

The C-Stim is a new Cell MicroControls (CMC) superfusion chamber system for microscopy studies. The C-Stim utilizes a reusable, autoclavable chamber insert. Its coverslip bottom is glued in place, which nearly eliminates solution leakage into the scope. The chamber holder is designed for quick and easy removal of one chamber insert and replacement. The platinum wire stimulation assembly is also a "snap-in part" and is configured with a built in thermistor to sample bath temperature. The geometry of the inflow/outflow ports permits a stable solution level at low bath volume (<0.5ml) and achieves nearly laminar flow at a flow rate of up to 2ml/min.



CMC C-STIM

Features

- Reusable & autoclavable chamber inserts.
- Integral coverslip bottom prevents solution leakage.
- Low chamber volume and tapered inflow/outflow channels achieve laminar flow; separate aspiration port maintains stable solution level.
- Platinum wire field-stimulation electrode assembly is easy to insert/remove, connects easily to MyoPacer and other field stimulators.
- Stimulation assembly includes a built-in thermistor which works in conjunction with the CMC feedback temperature controller.

Temperature Control

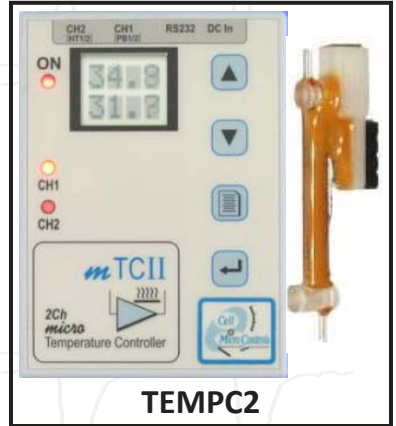
TEMPC2: CMC mTCII & HPRE2

The mTCII micro-Temperature Controller is a versatile 2 channel temperature controller powerful enough to heat small tissue baths, microscope stages, small animal heaters etc. but also able to control miniature heating devices like the included HPRE2. The mTCII uses state-of-the-art microcontrollers to provide a flexible, standalone instrument that allows control over the user interface and instrument function while maintaining temperature accurately. The mTCII has two ways of driving heaters, with a PWM (pulse width modulated 2.5-20kHz) or an analog output for lower noise. In the PWM mode it can control currents up to 1.5Amps provided by a Li-ion battery or 15V power supply. The HPRE2 Pre-heater is a 3 loop capillary heater for pre-heating solution.

Features

mTCII

- Sophisticated PID miniature controller accurately establishes and holds temperature.
- 2 independent channels.
- Compatible with many low voltage heater elements.
- RS232 port for control, logging.
- 2 heating modes, PWM [8W] or analog [2W].
- Maintains setpoint & parameters in non-volatile memory.
- Reprogrammable firmware.



TEMPC2

HPRE2

- Dimensions: 45x14x7mm (LxWxH)
- Heater resistance \approx 17 Ω
- Thermistor sensor: 10k Ω NTC
- Plugs into Heater Aux of mTCII

IonOptix Systems

Our goal is to support the scientific research community with an array of systems that meet experimental demands while adhering to our philosophy of designing and developing innovative high-performance products at fair prices. The following are some of the application-driven systems currently available. Visit us at www.IonOptix.com for more information.

Calcium and Contractility/ Diameter

- Myocyte Calcium and Contractility Recording Systems
 - HyperSwitch Configuration (HMSYS)
 - μ Step Configuration (MMSYS)
- Myocyte Contractility System (MCSYS)
- Vessel Calcium and Diameter Recording System (HVSYS)
- Vessel Diameter System (VDSYS)

General Photometry

- Fluorescence Photometry System (HPSYS & MPSYS)

Tissue Bath Fluorometry

- FluoroPlex

Cell Pacing

- Cell Culture Pacing

Myocyte Harvesting

- Myocyte Harvesting System

ION OPTIX



“The Barn” — IonOptix Headquarters in Milton, Massachusetts

Company History

IonOptix makes quality ratiometric fluorescence and cell dimensioning data acquisition systems. We have been making reasonably priced, high performance systems since 1990.

IonOptix prides itself on post-sale customer support. Telephone and email support is available on an unlimited basis. More importantly, every system sale includes a one to two day installation visit to set up the system and train the customer. We consider this training to be critical as it gets the customer up and running as quickly as possible. We run experiments with your preparations during the visit to be assured that all technical issues particular to the experimenter’s preparations have been covered.

Resellers

Our good friends at Cairn Research are currently our only resellers. They sell our components in conjunction with their fluorescence and electrophysiology systems.



Cairn Research

www.cairn-research.co.uk

Authorized Representatives

In efforts to afford this high level of service to all our customers, IonOptix has entered into agreements with local representatives in several countries. The representatives have been chosen based on their technical and biological expertise, familiarity with our products, and on their customer service skills.



Bioprobes Ltd.

China, Hong Kong

www.bioprobeshk.com

www.bioprobeschina.com



Primetech

Japan

www.primetech.co.jp



Scitech Korea Inc.

Korea

www.scitechkorea.co.kr



Kuo Yang Scientific Corp.

Taiwan, Republic of China

www.kuoyang.com.tw



Commat Ltd.

Turkey

www.commat.com.tr



SDR Clinical Technology

Australia, New Zealand

www.sdr.com.au