SI-CTS200 Cell Tester

Characterize and investigate functional physiological properties of single living cells

A revolutionary new kind of tool for cellular investigation

Overview

The **Cell Tester** is the product of three years of design and field testing. It represents a blending of state-of-the-art technologies, including electronics, mechanics and optics. The end result is a revolutionary new research tool for cellular investigation.

All living systems can be studied from several perspectives. We can examine the entire organism or a specific organ system. We can characterize a single organ in a system or a type of tissue in an organ or the cells that make up that tissue. To completely understand any system, all of these perspectives must be considered. Often, entirely different systems are needed in a parallel experimental paradigm. The **Cell Tester** accomplishes this on one platform.

*The **Cell Tester** can, without any changes, be used for one single living cell, for a small multi-cellular preparation and for single or larger skinned muscle strip preparations.* Translational experiments from the single living cells to the intact multi-cellular level can be accomplished. For example, using the **Cell Tester**, the influence of the connective tissue on muscle function can be distinguished from the clean muscle work for the first time. Conversely, skinning allows a direct comparison between the living cell response and a cell, whereby the subcellular contractile proteins are studied with full experimental access to cell signalling and cellular biochemistry.

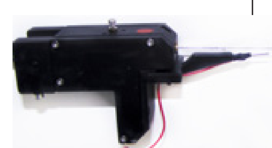
The **Cell Tester** provides researchers with the comprehensive ability to investigate and characterize the physiological, bio-mechanical and bio-physical properties of single isolated living cells and extend these findings to the sub- and multi-cellular level.

- Integral microtweezer apparatus facilitates cellular attachment
- Two integrated piezo manipulators are standard
- Bio-compatible adhesive included
- Unique rotational stage–easy cellular alignment, improved experimental throughput
- Ultra-quiet force transducer included
- Linear displacement motor stretches or compresses cells with 25nm precision
- Fits ANY inverted microscope
- Use native cuvette or ANY 35mm glass bottom dish

System Organization

The **Cell Tester** is designed to sit on top of the stage of any standard inverted research microscope. The optical path of the microscope is left intact for simultaneous fluorescence or confocal imaging.

Nanomotor



The heart of the system is a tuned and paired combination of a linear actuator offering nanometer (nm) precision and a force transducer with nano Newton nN) sensitivity. Each element (actuator and sensor) is equipped with a remote controlled micro grabber that allows tissues to be held firmly. In addition, a critically important, non-cytotoxic adhesive (MyoTak ™) facilitates the bonding of tissue to the measuring device where needed.

Force Transducer

KG-series force transducers measure a large range of detectable forces. The transducer with the highest sensitivity (20nN) is sufficient to measure the force of a single heart cell. Because all transducers are extraordinarily rugged, withstanding even overload forces, they come with a lifetime warranty on the optical transducer heads.

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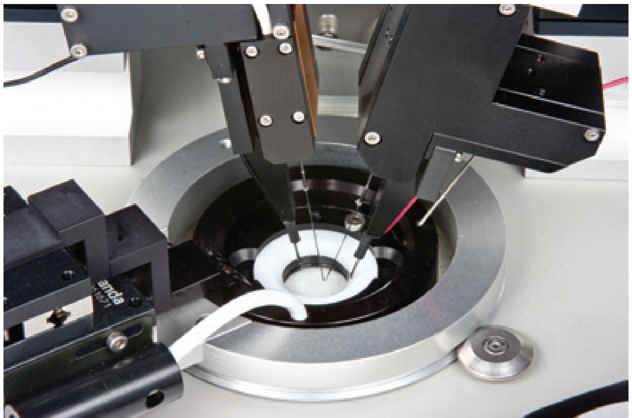
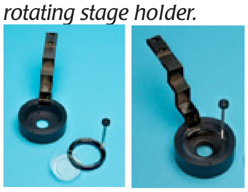


The cuvette rotates to allow for precise positioning of the cells to be mounted.

The two inserts fit into the rotating stage holder.



(Left) The 35mm glass bottom dish fits into the first insert. (Right) The insert and dish are placed in the rotating cuvette.

Rotating Cuvette

The complete system utilizes a unique rotating bath to dramatically improve experimental throughput. The rotating bath is designed to orient cells in the XY plane so that no physical manipulation of the position of the cell itself is required prior to capture by the grabbing devices attached to the force sensor and linear actuator.

This bath has two interchangeable inserts. The first holds any 35mm glass bottom dish (WPI #**FD35-100**). When coating tweezers or glass rods with MyoTak biocomaptible adhesive, insert a Fluorodish into the holder and place it in the rotating cuvette. When finished, remove the insert and dispose of the Fluorodish. Then, insert the native cuvette insert containing the live cells.

Electronics

WPI's **Signal Conditioning Amplifier System** is a customizable electronic platform. It consists of an 8-channel, rack-mountable frame with an ultra quiet, shielded power supply. For the **Cell Tester**, it includes the Nanomotor position controller, the **SI-BAM21LCB** amplifier, the **SI-AOSU** anti-oscillation unit and the **SI-STCM2** 2-channel temperature control module.

The Cell Tester nanomotor and force transducer are extremely sensitive. The position controller is used to open and close the micro grabbers on both devices, and to control the movement of the nanomotor used to stretch or release the cell or fiber held by the micro grabber.

The **SI-BAM21-LCB** KG Optical Force Transducer Amplifier powers the force transducer and outputs an analog voltage proportional to the force applied to the force transducer. The force feedback signal can be multiplied by a factor of 1, 2, 5 or 10 to provide better resolution for a minimal change in applied force.

The anti-oscillation option eliminates the native resonance frequency of the transducer and mounting support for unparalleled low noise recording and fidelity.

When temperature control is required, the **SI-TCM2** is used. One channel powers the cuvetter heater, and the other simultaneously powers an optional, inline solution heater. This module uses digital control to maintain a constant temperature. It has both high and low alarm warnings which can be user defined.

(Below) The Cell Tester electronics are configured in a single rack mountable frame with an ultra-quiet power supply.

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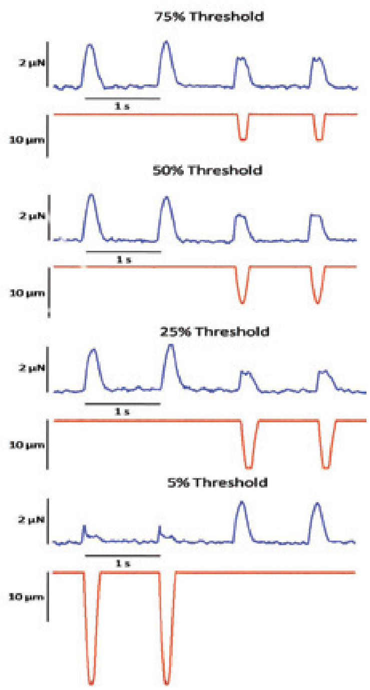
Research

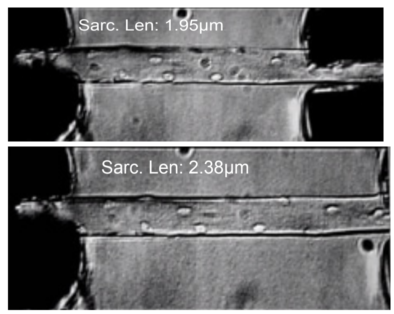
Classic Cross-Bridge Cycling Study in Heart



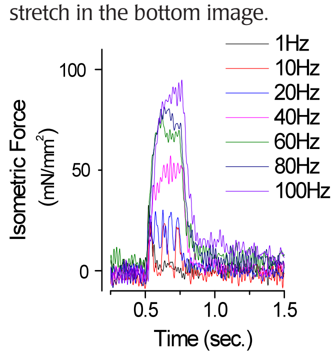
A cell was allowed to develop force after an electrical field stimulation. At 5%, 25%, 50% or 75% of maximal developed force (taken from the average of the previous 10 isometric twitches), the cell is actively shortened by the system so that force is held constant. At the moment the force transient would again reach that force level while relaxing, the actuator re-lengthens the cell to complete the transient. This simulates, at the cellular muscle level, the contraction of the ventricle, ejection phase, and finally, refilling and relaxation of the left ventricle at different levels of afterload. Plotting and analysis of length versus force allows analysis of work under the different levels of simulated afterload.

Prosser BL, Ward CW, Lederer WJ.: Preliminary unpublished results.

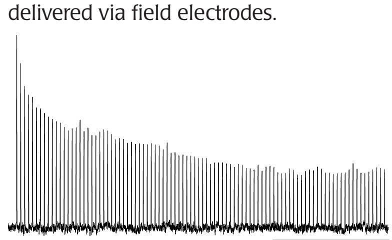
Skeletal Muscle Axial Stretch and Isometric Force



A single enzymatically isolated skeletal FDB is held with MyoTak coated micro-tweezers. The passive length of the FDB is shown in the top image, and unset stretch in the bottom image.



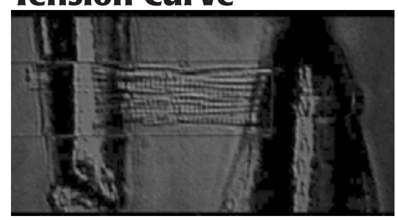
This graph shows the force-frequency relationship of a single FDB myofiber to which 250ms trains of pulses were delivered via field electrodes.



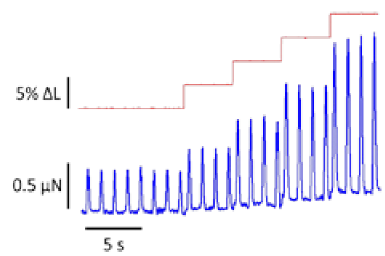
A single FDB was stimulated with a 200ms train of 100Hz pulses delivered at 0.2Hz. The FDB fatigues to approximately 30% of its initial force.

Ward CW, Khairallah, R.: Preliminary unpublished results.

Cardiomyocyte Axial Stretch and Length Tension Curve

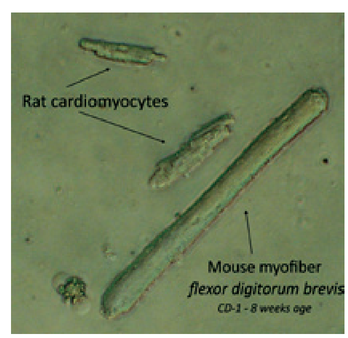


Cardiac myocyte is held by two glass rods using myotak on the cell tester.



Isometric force of a single paced ventricular myocyte is tracked during incremental length changes.

Modified from: **Prosser BL, Ward CW, Lederer WJ.** "X-ROS signaling: rapid mechano-chemo transduction in heart" (*Science*). 2011 Sep 9; 333(6048):1440-5. [PMID:21903813]



Cells used in the preliminary experiments include single rat cardiac myocytes next to a single mouse muscle cell from the FDB skeletal muscle.

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CELL TESTER SPECIFICATIONS

The manipulators tilt up and fold back to facilitate system setup and coating with MyoTak. There are two programmable memory positions (home and target) for easy exchange of the 35mm dishes, providing access to the bath so you can add the live cells. The combination of these features enables high experimental throughput.

Base Dimensions ... 8.25x9" (21x23cm)

Chassis

Maximum Power Consumption ... 1.3A at 115V 50/60Hz, 1.8A at 230V 50/60Hz

Position Controller Specifications

Power Requirements ... 12V DC provided by the chassis
Position In Range ... ±10V, IV = 104µ
Position Out Range ... ±10V, IV = 104µ

SI-BAM21LCB Optical Force Transducer Amplifier

Input Configuration ... Current to voltage converter
Gain ... 1X, 2X, 5X, 10X - Switch selectable*
Offset (with a 1X gain) ... 10mV
Output Impedance ... 470Ω
Power Requirements ... 12V DC at 3A provided by the chassis
Output Range ... ±10V DC

*An optional factory setting increases the multiplier by a factor of 10, allowing to signal to be multiplied by 10, 20, 50 and 100.

SI-AOSUB Specifications

Power ... 12V DC provided by the chassis
Input ... ±10V DC

SI-TCM2 2-Channel Temperature Controller

Input Configuration ... Current to voltage converter
Power Requirements ... 12V DC at 2.5A 50/60Hz provided by the chassis
Operating Temperature Range ... Room temperature
Display Precision ... 0.1ºC
Controller Resolution ... 0.1ºC

Cuvette Temperature Sensor ... 1000Ω RTD (1000Ω at 0ºC)

Nanomotor

Total Travel ... ±90µm
Resolution ... 20nm
Smallest Step ... 60nm
Input ... ±10V (calibrated at 10µm/V)

SI-KG7TWE Force Transducer

Range ... 0–5mN (0–0.5g)
Force Resolution ... 20nN at 10X gain
Compliance ... 10µm/mN
Noise ... 0.3µN
Resonance Frequency ... 250Hz
(This is eliminated from the measurement by the AOSU)
Time Resolution ... 7ms

Resolutions were determined while using the **SI-AOSUB** anti-oscillation filter.

97204 Pulser Specifications

Time Resolution ... 7ms
Pulser Output ... 0–10V DC adjustable
Damping Frequency Range ... 85Hz–1.0KHz
Output Range ... ±10V

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