

# Agilent Cardio and CardioECR Systems

A comprehensive solution for *in vitro* cardiac safety assessment and cardiovascular drug discovery

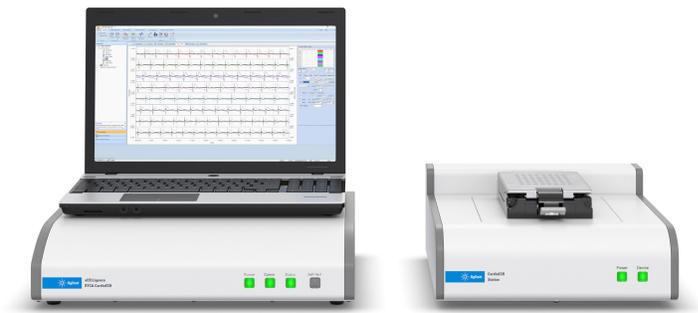




# Two Instruments for Your Cardiomyocyte Research

Agilent offers two instruments for assessment, drug discovery, screening, and the evaluation of cardiomyocyte models:

- The Agilent xCELLigence RTCA Cardio, which measures viability and contractility.
- The Agilent xCELLigence RTCA CardioECR, which measures viability and contractility, with the added benefit of ion channel activity and functional maturation of cardiomyocytes.



## The xCELLigence RTCA Cardio system

The xCELLigence real-time cell analysis (RTCA) Cardio instrument expands upon Agilent's proven microelectronic biosensor technology. Your laboratory can monitor the physical properties of beating cardiomyocytes, to assess cardiotoxicity and evaluate cell health viability.

- Exceptionally fast: The xCELLigence RTCA Cardio system employs a proprietary noninvasive electrical impedance technology to monitor contractility in milliseconds.
- Label free: No fluorescent dyes to interfere with the physical properties (contractility and viability) of the cardiomyocytes. Simply plate and go.
- Flexible time course studies: Monitor cell responses in milliseconds, or monitor temporal changes over days and weeks.
- High throughput: 96-well plate format enables rapid compound evaluation and screening of lead compounds.
- Compact design: Easily accommodated within a standard CO<sub>2</sub> incubator or hypoxia chamber.

# For an Easy Workflow, Simply Plate and Go

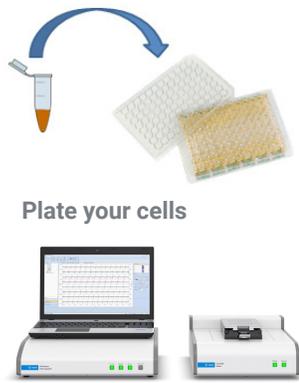
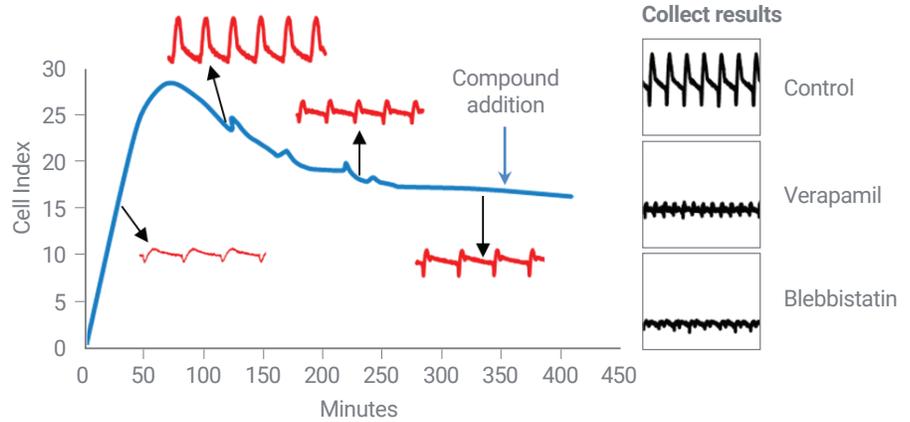
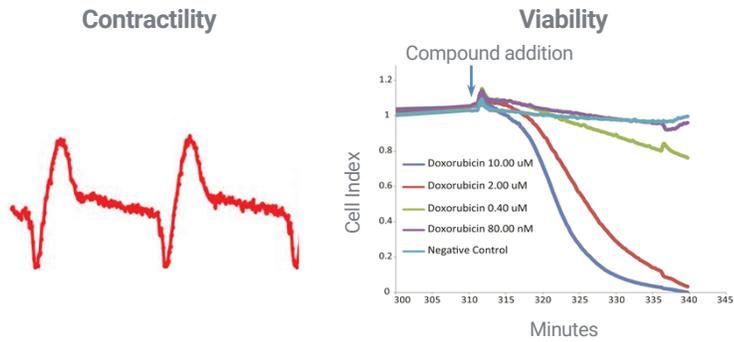


Plate your cells

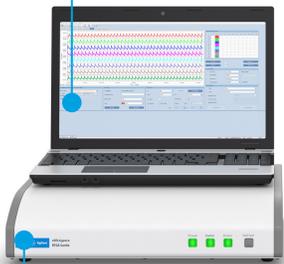
Acquire data



Simultaneous monitoring of contractility and viability



RTCA Cardio control unit with RTCA Cardio software



RTCA Cardio analyzer



E-Plate Cardio 96



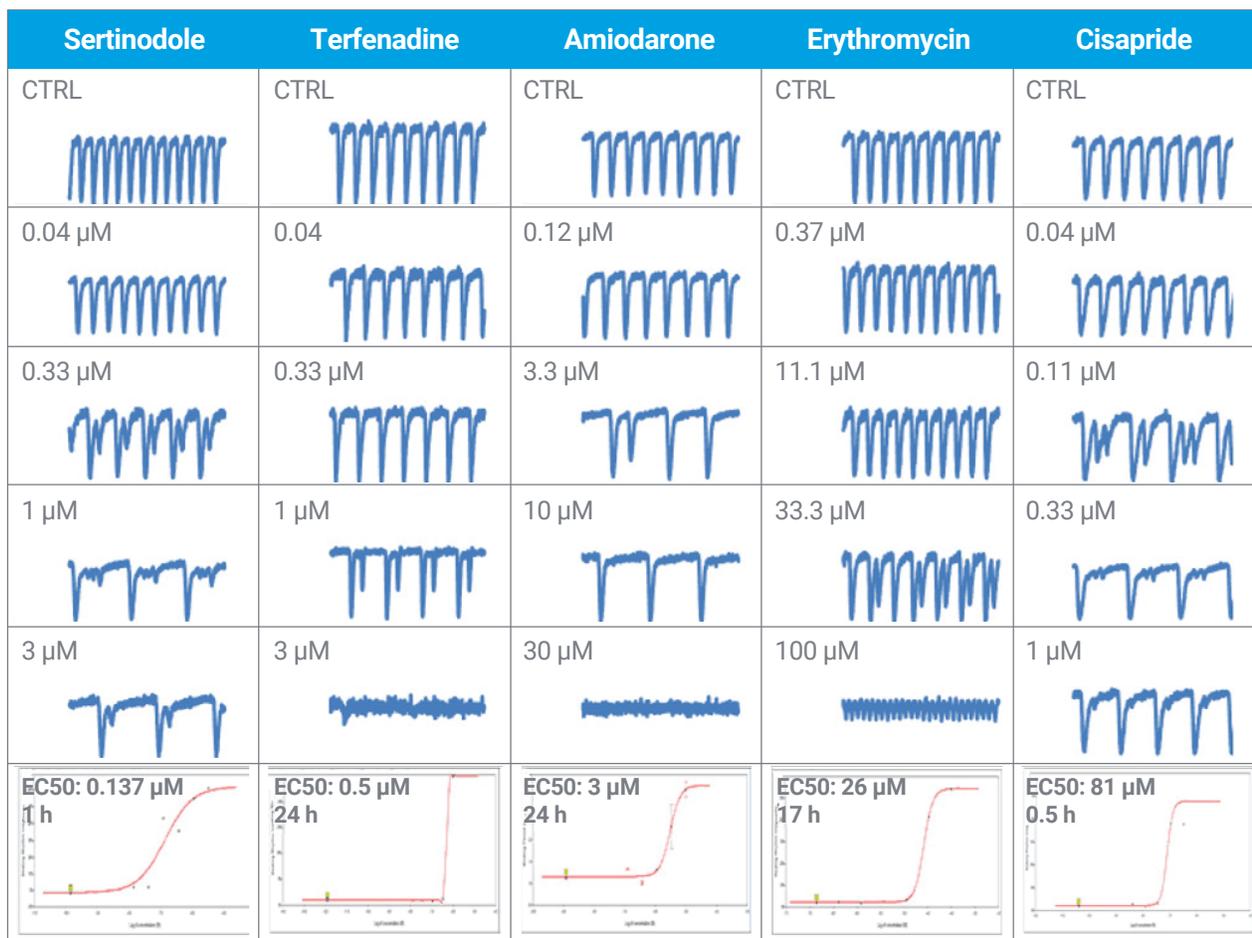
RTCA Cardio temperature tool

An accessory for the RTCA Cardio instrument, the RTCA Cardio temperature tool is designed to stabilize the temperature of the E-Plate Cardio 96 during experimental procedures outside the RTCA Cardio station.

RTCA Cardio station

# Is Your Current Technology Truly Predictive of Proarrhythmia

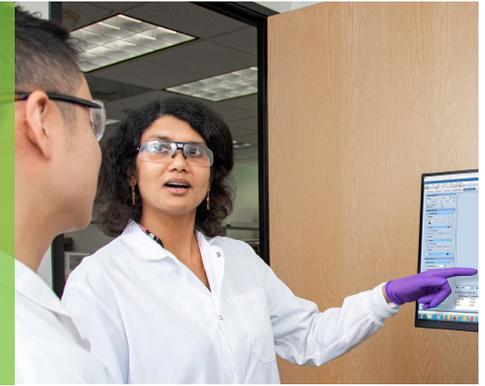
The xCELLigence RTCA Cardio system removes much of the guess work from the rapid screening of potentially toxic compounds. Proarrhythmia and cardiotoxicity screens can be conducted in a matter of minutes or hours after compound addition, providing actionable information on a new drug candidate.



## Pharmacological assessment of ion channel modulators using the xCELLigence RTCA Cardio system.

Induced Pluripotent Stem Cell (iPSC)-derived cardiomyocytes were treated with multiple concentrations of each compound. Representative time points shown are from 0.5 to 24 hours.

# Unlock the Full Potential of Cardiomyocyte Models with the xCELLigence RTCA CardioECR System



## Powerful multiplexing

Experience evolutionary technology that can simultaneously monitor ion channel activity, contractility, and viability.

## Captures the intricate excitation contraction coupling relationship

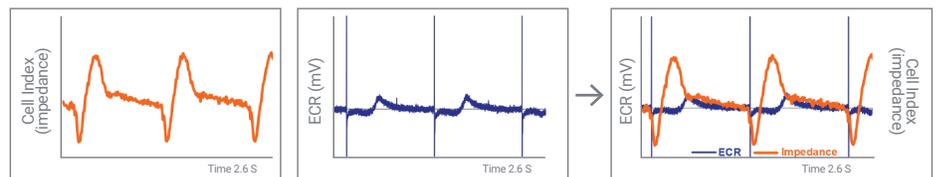
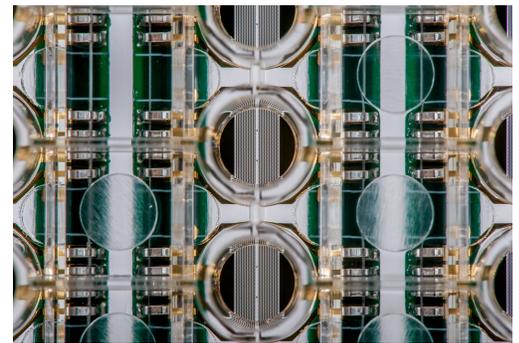
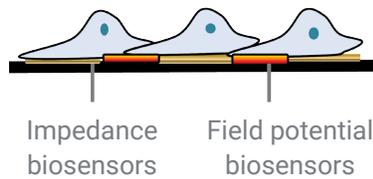
Monitor the impact of drugs on integrated ion channel activity and downstream contractility.

## Powerful pacing feature

Eliminate variability and increase confidence in your results.

## Technology

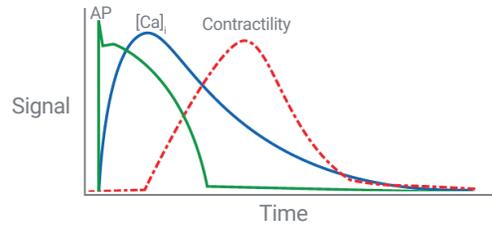
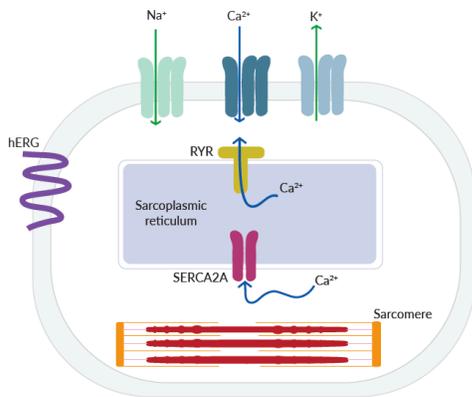
The principle of detection for the xCELLigence RTCA CardioECR system is based on impedance and field potential measurements. The interdigitated gold impedance biosensors are interspersed with two field potential (FP) biosensors. These biosensors are designed for simultaneous measurement of field potential and contractility within each well. This proprietary design allows for the identification and measurement of adverse compound action on integrated ion channel activity, contractility, and long-term viability. These measurements in turn provide a highly predictive assay system for cardiac risk assessment and cardiovascular drug discovery.



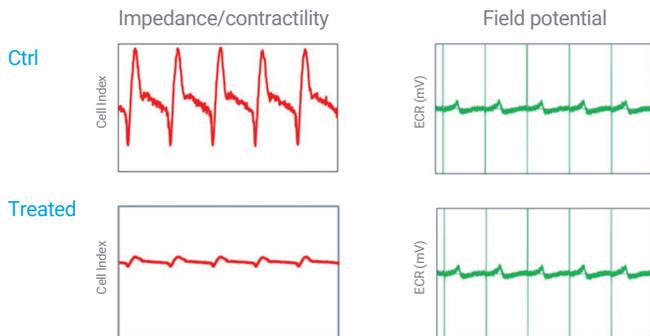
The xCELLigence RTCA CardioECR system simultaneously measures cardiomyocyte contraction and integrated ion channel activity at millisecond time resolution. The CardioECR software can display and overlay the data in real time.

# Simultaneously Monitor Contractility, Viability, and the Excitation Coupling Relationship

For rapid screening of potentially toxic compounds, the xCELLigence RTCA Cardio system removes much of the guess work. Proarrhythmia and cardiotoxicity screens can be conducted minutes or hours after compound addition, providing actionable information on a new drug candidate.



During cardiac action potential (AP), Ca<sup>2+</sup> entry into the cells triggers Ca<sup>2+</sup> release from the sarcoplasmic reticulum. The combination of Ca<sup>2+</sup> influx and release raises the free intracellular Ca<sup>2+</sup> concentration, leading to sarcomere shortening and contractility.



## Cardiac excitation-contraction coupling

The xCELLigence RTCA CardioECR instrument simultaneously measures electrophysiological signals and contractility. Blebbistatin, a myosin inhibitor, does not inhibit the ion channel signal of treated cells (green), but greatly impairs the mechanical contraction and beating (red). The ability to monitor this excitation-contraction coupling relationship provides a complete picture for assessment of compounds during drug development.

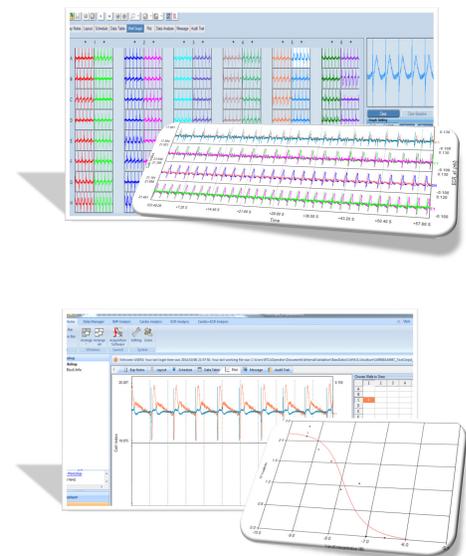
## Integrated software provides continuous monitoring and data analysis

Whether you are screening for toxicity, novel use, or familial disorders, the xCELLigence RTCA CardioECR software is the ideal tool for data analysis.

Fast turnaround: Automatically generates reports on beating rate, beating amplitude, firing rate, and field potential.

Powerful cell status assessment: Cell status quality control ensures compound addition is conducted when cells are fully ready.

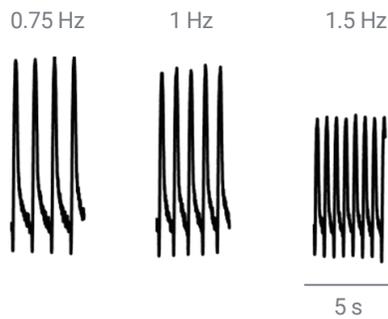
Intuitive data evaluation and comparison: Easily overlay beating rates, beating amplitudes, and field potential waveforms across different samples, time points, and experiments.



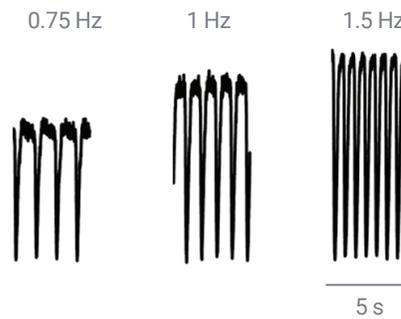
# Are Your iPSC Cardiomyocytes Mature?



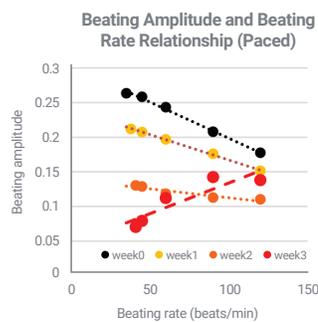
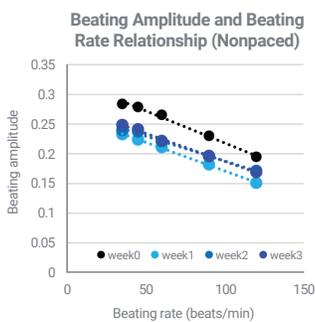
**Nonpaced iPSC cardiomyocytes**  
Negative force-frequency relationship



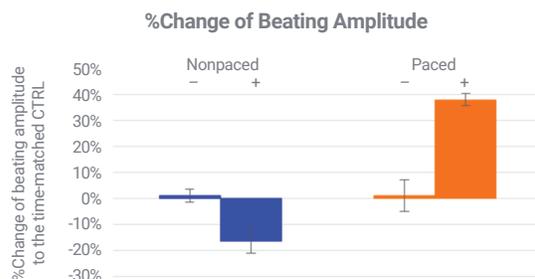
**Paced iPSC cardiomyocytes**  
Positive force-frequency relationship



- iPSC cardiomyocytes (iPSC-CMs) have an inherent neonatal phenotype, which is not an ideal model for testing drugs.
- iPSC-CMs display a negative force-frequency relationship due to a less well-developed cytoskeleton and calcium handling machinery (left panel).
- The xCELLigence RTCA CardioECR system performs chronic pacing of iPSC-CMs, enhances functionality, and leads to the positive force-frequency relationship that is expected of adult cardiomyocytes (right panel).



These graphs show the beating amplitude and beating rate relationship before (week 0) and during a three-week pacing process. iPSC cardiomyocytes were either submitted to directed electrical pacing (right) using the xCELLigence RTCA CardioECR system or cultured without electrical pacing (left).

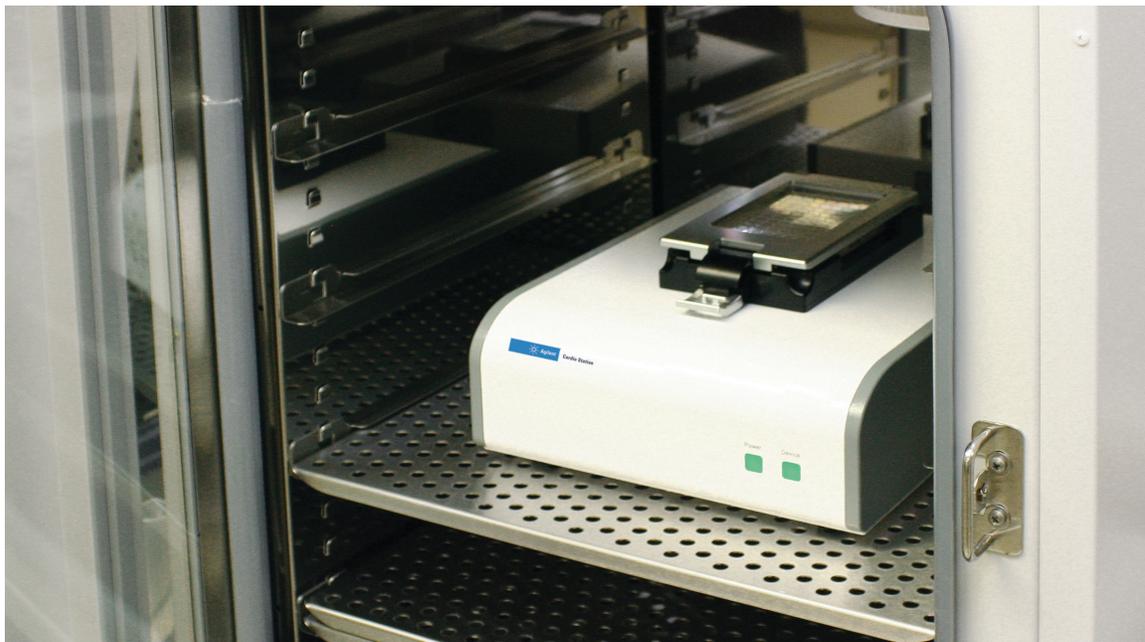


This shows the beating amplitude change after isoproterenol treatment in paced and nonpaced cells. (-): DMSO; (+): Isoproterenol. Paced cardiomyocytes display a positive increase in beating amplitude.

# Compare Cardio Versus CardioECR

	Cardio	CardioECR
Recording in incubator	✓	✓
<b>System</b>		
IMP electrodes	✓	✓
FP electrodes		✓
Electrical pacing function		✓
<b>Device</b>		
Plate	96-well E-Plate	48-well E-Plate
<b>Application</b>		
Cell attachment and viability	✓	✓
Contractility	✓	✓
FP (ion channels) assessment		✓
Acute assay (seconds to minutes)	✓	✓
Long-term assay (hours to days)	✓	✓

<b>Recording</b>	Recording in incubator	96 wells, 12.9 ms	Up to 24 wells -1ms; all 48 wells - 2ms
	Field potential sampling rate	N/A	10 kHz
	Sampling capability	Simultaneous recording of impedance in 96 wells	Simultaneous recording of impedance and field potential electrodes in all 48 wells
<b>Stimulation</b>	Stimulation voltage range	N/A	-2.5 V to +2.5 V
	Simultaneous stimulation	N/A	Up to 48 wells (across the entire plate)





# xCELLigence RTCA CardioECR System

Product	Part No.
xCELLigence RTCA CardioECR – Complete system bundle	00380601210
xCELLigence RTCA CardioECR – Analyzer	00380601180
xCELLigence RTCA CardioECR – Station	00380601190
xCELLigence RTCA CardioECR – Control unit (laptop with pre-installed software)	00380601200
E-Plate CardioECR 48 (6 plates)	00300600940
E-Plate CardioECR 48 (36 plates)	00300600950

# xCELLigence RTCA Cardio System

Product	Part No.
xCELLigence RTCA Cardio – Complete system bundle	00380601060
xCELLigence RTCA Cardio – Analyzer	06416993001
xCELLigence RTCA Cardio – Station	06417019001
xCELLigence RTCA Cardio – Control unit (laptop with pre-installed software)	06200184001
E-Plate Cardio 96 (6 plates)	06417051001
E-Plate Cardio 96 (36 plates)	06417035001

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