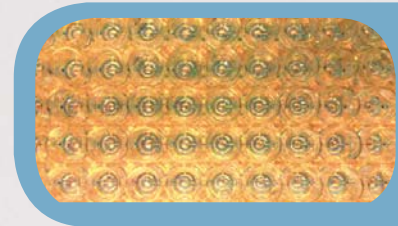


# The CardioExcyte 96.

Contractility. Electrophysiology. Viability.



Power tool for

**CIPA**

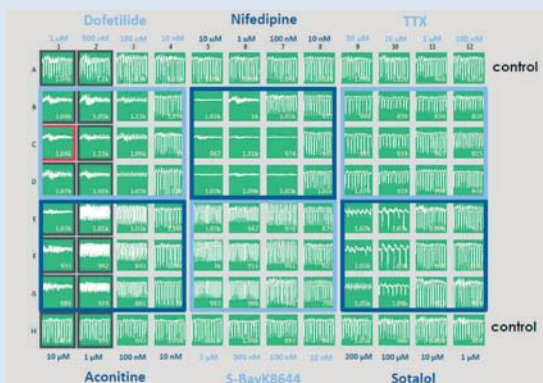
The CardioExcyte 96

**nanjion**

# CardioExcyte 96 Label-free cardiac safety screening

- 96 recording wells in parallel
- Contractility, viability & electrophysiology
- Non-invasive & label-free measurements
- Monitoring acute and chronic effects
- Electrical and optical pacing options
- Integrated liquid handling system
- Real-time access to beating parameters
- Incubation System
- Cost efficient consumables
- Leverage maturity of your cardiac cells with FLEXcyte 96 Add-On
- Ideal for cardio-oncology and cyto-tox

## Short term effects



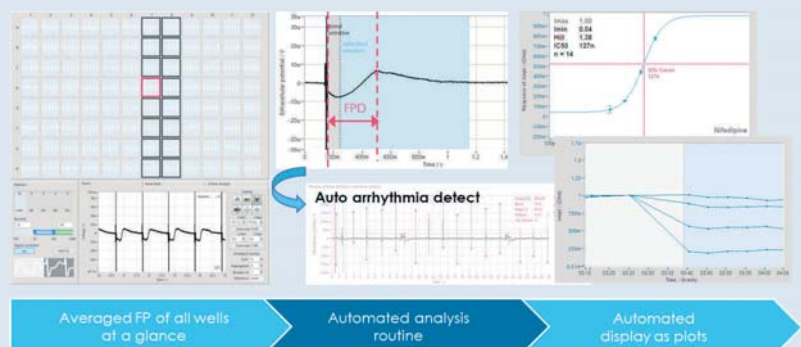
Different concentrations of compounds induced effects on beat rate, amplitude, beat irregularity in Cor.4U cells

## Cardiotoxicity screening on beating cellular networks

The CardioExcyte 96 is a hybrid device supporting highly resolved impedance-based contractility measurements, electric field potential recordings and cell viability monitoring. It has a small footprint and performs fully automated recordings from 96 wells in parallel. With embedded control electronics and sophisticated sensor technology, the CardioExcyte 96 is a turn-key system for efficient cardiac safety screening and long-term monitoring of cell viability. The CardioExcyte 96 has been validated with stem cell-derived cardiomyocytes from several providers (NCardia, Cellular Dynamics International, Takara Bio Europe AB and GE Healthcare) in addition to 3D-clusters (Takara Bio Europe AB).

## Experimental workflow on the CardioExcyte 96

Typical workflow on the CardioExcyte 96. An overview of all wells recorded is the first step in the analysis process. Parameters such as FPD are automatically calculated and arrhythmia events detected. Finally, average concentration response curves for all wells receiving a particular compound are pooled and displayed, along with timecourse plots for individual wells.



# DataControl 96 Software Package.

## Versatile data analysis & data handling.

The CardioExcyte 96 control software supports online analysis of beating parameters. The unique Mean Beat Function automatically visualizes the average of beat traces from one well, enveloped by the standard deviation, indicating the consistency of the beat pattern within the recording well, i.e. if the cellular network is synchronously beating or not.

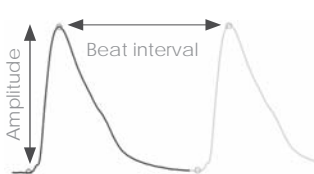
The control software is intuitive and easy-to-use, at the same time very powerful in terms of experimental set-up and online visualization of the recorded data.

The **DataControl 96** software package is an independent software package to load and analyze data recorded on the CardioExcyte 96 or FLEXcyte 96. Customized export formats of analysis results are integrated.

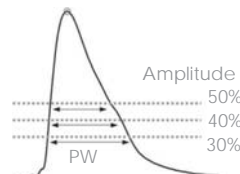
Supporting standardized processes, analysis templates can be saved and re-loaded. Normalization methods, for example, provide control group normalization or pooling of data across many wells. Compound effects of individual wells or the average concentration response curves of all wells can be easily inspected.

- Easy-to-use yet very powerful software
- *Ad* and *post hoc* data analysis possible
- Raw data traces, results and arrhythmia detection all on one single screen
- Mean beat analysis for improved data quality and consistency
- Instant recalculation of data upon parameter changes
- Highly customizable exporting to databases
- Broad range of QC options
- Templated data analysis allows for results within seconds
- Data can be analyzed on multiple computers making inter-department collaborations easy
- For CardioExcyte 96 and FLEXcyte 96

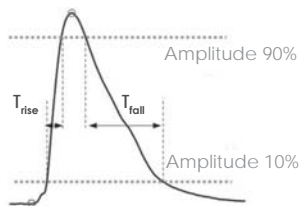
### Amplitude and Beat Rate



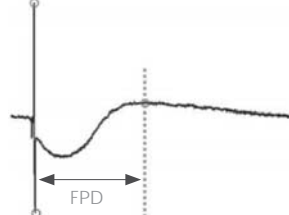
### Pulse width



### Rise & Fall Time



### Field Potential Duration

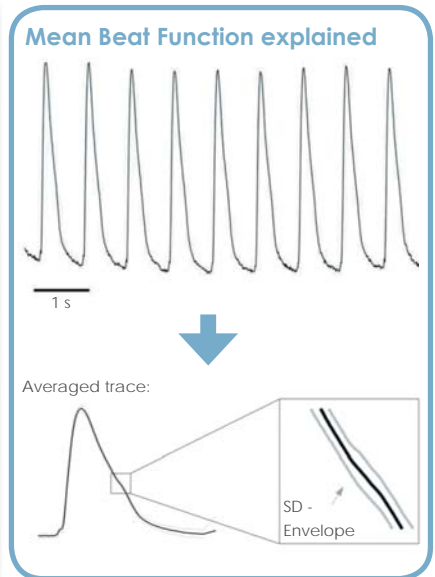
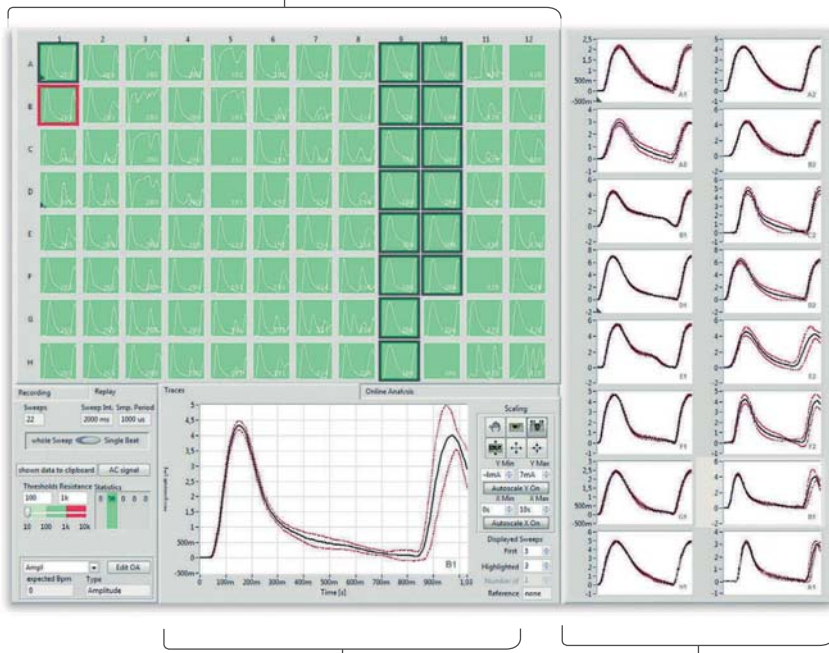


An adaptive peak detection algorithm extracts the positions and values of beating events within the EFP- and impedance recordings.

### CardioExcyte 96 Online Analysis

- Real-time geometric beat analysis
- Intelligent peak detection with primary and secondary (arrhythmia) beat distinction
- Signal read out: Beat rate/regularity, amplitude, FPD-max, FPD-zero, rise time, fall time, pulse width etc.
- Base impedance read out
- Sensor temperature read out
- Adaptive peak detector and trigger
- Compound Arrhythmia Factor analysis based on primary and secondary beats
- Multiple measurement types on one sensor
- *Ad & Post hoc* analysis of data

96-well live view showing dynamic impedance and impedance baseline.



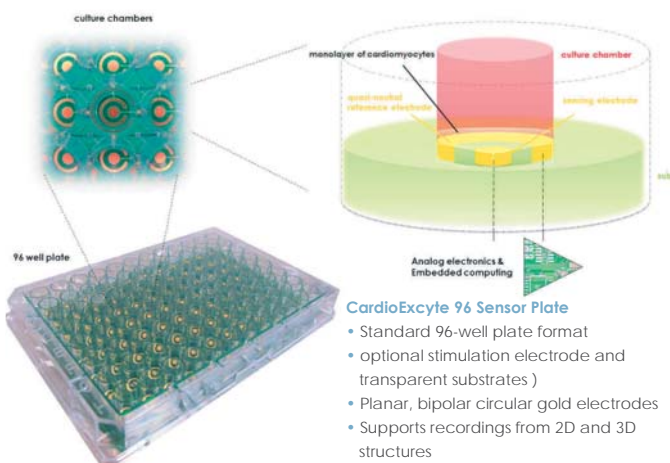
Single-well detailed view allowing zoom in and trace selection, here showing mean beat signals. Red traces show the standard deviation from the mean.

16-well group view: mean beat traces (and SD in red) from selected wells.

Power tool for



## CardioExcyte 96 Sensor Plate



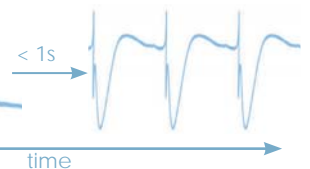
### CardioExcyte 96 Sensor Plate

- Standard 96-well plate format
- optional stimulation electrode and transparent substrates)
- Planar, bipolar circular gold electrodes
- Supports recordings from 2D and 3D structures
- Hybrid sensor design for both EFP and impedance recordings

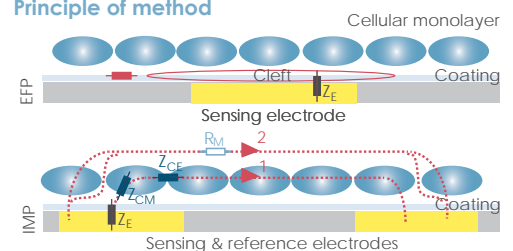
### Impedance Signal



### EFP Signal



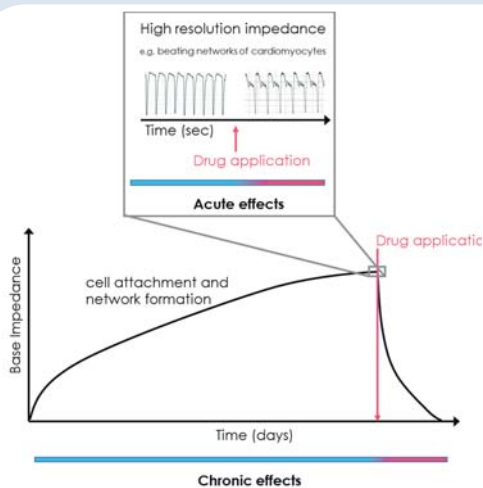
### Principle of method



## CardioExcyte 96 Specifications:

supported recording modes:	impedance-, electric field potential (MEA-like) recordings
impedance / EFP resolution & bandwidth:	Imp: 1-10 ms, 0-500 Hz / EFP: 0.1-1ms, 0.1Hz-5kHz
impedance spectral range:	0.1-100 kHz
temperature sensing:	multi-sensor temperature control
validated induced human pluripotent stem cells:	Cor.4U®, iCell®, Cellartis hiPS-CM™, ReproCardio™ 2, Pluricyte
validated embryonic stems cells:	hES-CMC™, Cytiva™, Cor.At®
parallel recording channels:	96
stand-alone system:	integrated Incubation System
automated liquid handling:	Integra Viaflow Assist
cardiac cell pacing:	electrical and optical (optional)
plates available:	standard plates; stimulation plates; transparent plates

Multi-parametric readout: cell attachment, contractility and viability



### Efficient and reliable cardiotoxicity profiling

The CardioExcyte 96 bridges the gap between *in vivo* cardiotoxicity testing and patch clamp-based compound screening by offering relevant means for *in vitro* recordings from intact, synchronously beating networks of cardiomyocytes. Altered beating patterns give an indication of what ion channel is affected upon the investigation of the extracellular field potentials. High-resolution impedance enables contractility investigations from a morphological view and long-term base impedance investigations allow for viability studies which are e.g. relevant in cardio-oncological assays.

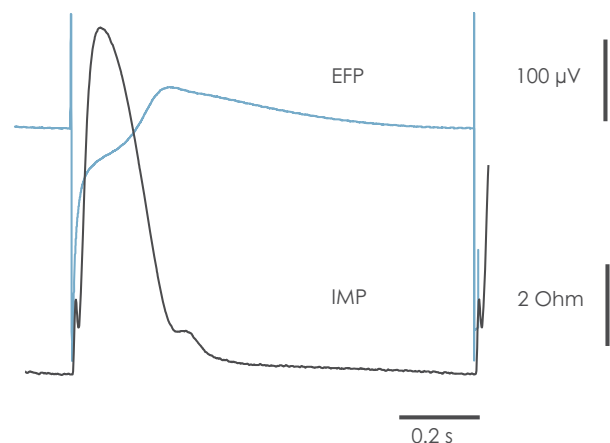
In this way, the CardioExcyte 96 is an excellent complementary device to automated patch clamp offering new strategies for efficient and reliable safety and cardiotoxicity screening.

### The hybrid approach:

#### Combining impedance and MEA-like recordings

The CardioExcyte 96 is the only system providing access to high resolution contractility and EFP data from the same cells. Analysis parameters such as field potential duration (FPD) and pulse width of beatings confer a correlation between the morphological and electrical activity of the cardiac cells, where the parameters display the same behavior, but different aspects of cardiac repolarization. The hybrid approach increases the significance and quality of *in vitro* cardiac safety assessment.

Ask us today how the CardioExcyte 96 can take your cardiotoxicity screening projects to the next level!



Overlay of EFP trace (blue) and impedance trace (black) recorded from a beating cardiac monolayer

*"We are happy to have acquired the CardioExcyte 96 from Nanion and look forward to publishing the first of many papers. We looked at several different devices on the market but were impressed by the resolution and ease-of-use of the CardioExcyte 96 and Nanion's enthusiasm and friendly customer support. I was particularly intrigued by the pacing feature, the single electrode design giving better signal to noise ratio, the dual EFP + impedance capability, and the environmental chamber so that you can run everything on the benchtop. The new optical pacing feature added in 2017 has further expanded the utility of the instrument for drug testing and disease modeling: For the first time, rate-dependent changes of cardiac electrophysiology and contractility can be easily quantified."*

*Prof. Bjorn C. Knollmann, Director of the Center for Arrhythmia Research and Therapeutics  
Vanderbilt University School of Medicine*

*"DataControl 96 allows us to analyze large amounts of data and represents a huge step towards standardized experiment analysis. All the well's individual raw data, analysis results, concentration response curves and also the averaged fits grouped by compound are displayed on a single screen, which means that all relevant information is right where we want to see it. Analysis templates can be used to re-do the same analysis procedures on a different compound, but same target, thus reducing the effort for data handling to just a couple of mouse clicks. Powerful averaging with standard deviation display and referencing methods provide great quality control. Furthermore, multiple export options are available to allow seamless integration into databases."*

*Hans-Peter Scholz, Biopharma, Global Early Non Clinical Safety  
Merck KGaA, Darmstadt, Germany*

*"CardioExcyte 96 is an easy-to-use system, providing impedance-based and MEA-like cardiac safety data from a diversity of stem cell-derived cardiomyocytes, and constitutes an excellent complement to automated patch clamp-based safety screening. Concentration- and time-dependence of a compound's potential cardiotoxicity can efficiently be obtained where the alteration of beating patterns can give a hint as to which cardiac ion channel is affected, at which point detailed electrophysiology investigations can take over. Cardiac network responses offer a comprehensive view of a compound's safety profile, without having to use in-vivo methods, which saves time, costs and suffering. Furthermore, the powerful software for recording and analysis, employs comprehensive beat investigation algorithms, displaying detailed beating kinetics in real-time. Data handling and export is straightforward, easy to grasp and yet very, very powerful."*

*Dr. Ralf Kettenhofen, Head of Laboratory  
NCardia, Cologne, Germany.*

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