Applied BioPhysics
Quantifying Cell Behavior

Dunn Labortechnik

Electric Cell-substrate Impedance Sensing (ECIS®), Analyser for non-invasive, label-free monitoring of cells

Index:

Applications:

- Attachment and Spreading
- Cell Proliferation
- Differentiation and Stem Cell Biology
- Barrier Function
- Signal Transduction
- Cell Invasion
- Cell Toxicity
- Cell Migration
- Inflammation
- TEER (Trans-epithelial/endothelial electrical resistance)

ECIS® Z-Theta

- **Complex impedance analyser**
  - ECIS® (Electric Cell-substrate Impedance Sensing) quantifies morphology changes in the sub-nanometer to micrometer ranges.
  - Small altering currents are applied across an electron pattern at the bottom of the array which results in a potential across the electrodes being measured by the system. Cells act as insulators increasing the impedance.
  - Stimulating cells to change their function alter the impedance which can be detected by the system.
  - The instrument can use a range of AC-frequencies from 100 to 100 kHz and complex impedance measurement to determine different cell morphology parameters including barrier function, close contacts, and membrane capacitance.
- **16- or 96-well station** for use with 8-well or 96-well arrays
  - Station is designed to put in an incubator for optimal cell growth → Incubators are also available from Dunn Labortechnik. Please enquire for further information.
- Optional 8-well transfilter array station available (see page 3)
- **Laptop (WIN 11)**
- **Software** for data acquisition and analysis

Dunn Labortechnik GmbH · Thelenberg 6 · 53567 Asbach Germany
Tel. +49 (0) 26 83 / 4 30 94 · e-mail: info@dunnlab.de · Internet: www.dunnlab.de

NEW!

ECIS® TEER Z

Continuous, Real-time TEER Measurement System:

- Experience seamless and repeatable label-free automated transepithelial electrical resistance (TEER) measurements, allowing you to electrically track cell layers in real-time.
- TEER in 24- or 96-well format
- TEER monitored under standard cell incubation
- Non-invasive measurement
- Read 96 wells in under 5 minutes
- Uses Millipore® or Corning® cell-culture insert plates

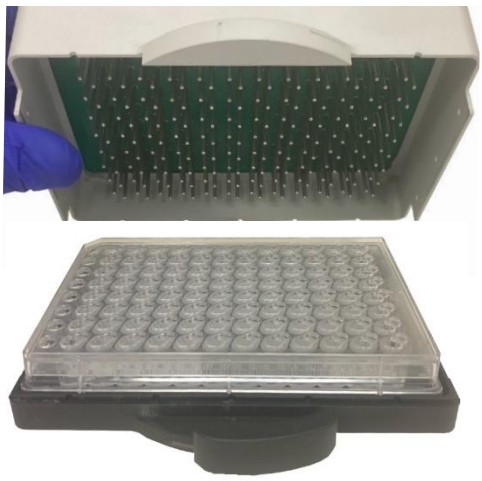
Specifications:

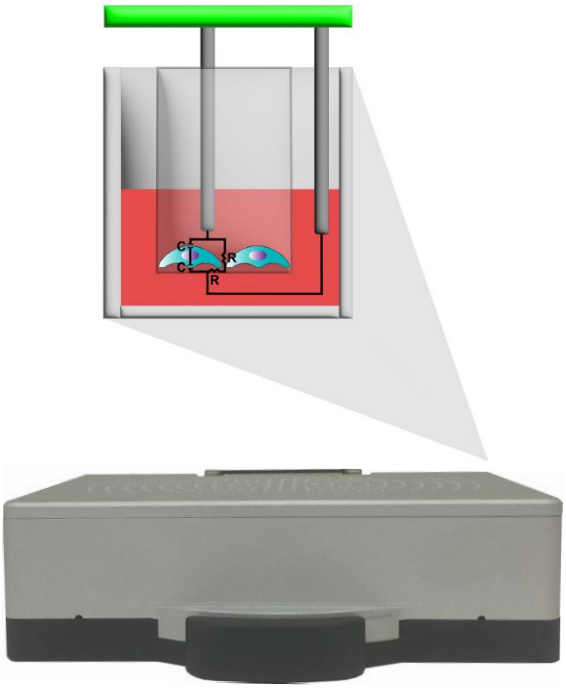
- Reads 24- or 96-well filter plates
- Medical-grade stainless steel electrode dipping pins
- 75 Hz sinusoidal excitation
- Power: < 2 watts, 12 V dc
- Station: 30 x 13 x 25 cm
- Controller: 48.3 x 43.2 x 21.6 cm
- Windows PC with ECIS® Software

User Friendly Software:

- TEER values vs. time graph
- Click-button initiation
- Colour-coded well mapping
- Stores values without cells (flat-fielding)
- Group average and compare data
- Statistical error bars
- Data output in CSV or graphical (JPEG, TIFF)

The ECIS® TEER Z Cartridge, seamlessly transitions your cell culture plate from the incubator to the cell culture hood while ensuring a sterile environment is maintained. The upper section of the plate features pairs of medical-grade stainless steel dipping pins for easy and precise insertion.





ECIS® 8-well Transfilter Array

Benefits:

- Automated TEER measurements under incubated conditions
- Continuous monitoring
- Uses standard 24-well cell culture inserts
- Non-invasive and label-free

The ECIS® 8-well Transfilter Array (8wTFA) allows researchers to measure transepithelial electrical resistance (TEER) on standard cell culture 24-well inserts using Electric Cell-substrate Impedance Sensing (ECIS®). The 8wTFA can be used with the ECIS® Z-Theta 16-well station (see page 1) and can monitor TEER continuously in real-time without having to remove the cells from the incubator.

CO_2 Incubators from ShelLab and N-Biotek

We also offer suitable CO_2 incubators, which can be purchased to dedicate a specific space for the Z-Theta and the TEER Z systems to run, as fluctuations in CO_2 and temperature can influence the measurement. All incubators are equipped with an access port.

Cat. No.	Manufacturer	Chamber capacity	Shelves	Dimensions exterior (w x d x h) [cm]	Dimensions chamber (w x d x h) [cm]
NB203	N-Biotek	42 l	2	40.8 x 48.2 x 55.0	32.0 x 35.0 x 37.0
NBT203	N-Biotek	42 l	2	40.8 x 48.2 x 55.0	32.0 x 35.0 x 37.0
SCO2W-2	ShelLab	42 l	3	53.4 x 57.2 x 68.6	40.0 x 40.0 x 26.0

N-BIOTEK
Leading Life science

NB203 NBT203

SHELLAB

SCO2W-2

Separate brochures for CO_2 incubators available. Please contact us for further information.

ECIS® Cultureware

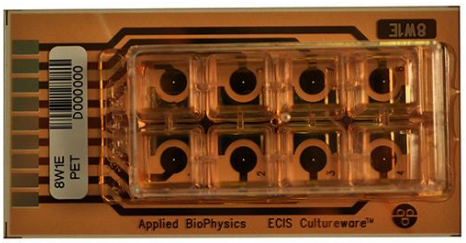
ECIS® Cultureware consists of sterile disposable electrode arrays containing gold film electrodes delineated with an insulating film. The well top assembly is made of polystyrene. The gold layer is thin enough to allow microscopic observation of the cells using a standard inverted tissue culture microscope. The ECIS® electrode array is placed in an array holder located in the incubator.

Standard 8-well Arrays

Array	Electrodes per Well	Electrode Area (mm^2)	Maximum Number of Cells Measured	Well Volume (µL)
8W1E PET or PC	1	0.049	50 - 100	600
8W10E PET or PC	10	0.49	500 - 1,000	600
8W10E+ PET or PC	40	1.96	2,000 - 4,000	600
8W20idf PET	idf	3.985	4,000 - 8,000	600

8W1E PET or PC

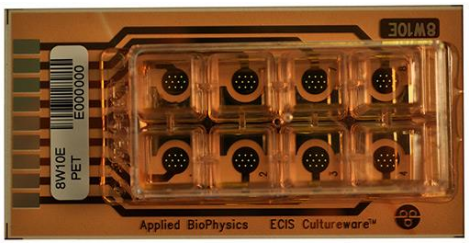
The 8 wells contain a single circular 250 µm diameter active electrode each. Every well has a substrate area of 0.8 cm^2 and a maximum volume of 600 µl. On average, with a confluent cell layer, approximately 50 to 100 cells will be measured by the electrode, but even a single cell can be observed.



Application: Barrier Function, Signal Transduction Assays, Cell Invasion, In situ Cell Electroporation and Monitoring, Cell Migration / Wound Healing, Correlated Microscopy and ECIS Experiments

8W10E PET or PC

The 8 wells contain ten circular 250 µm diameter active electrodes connected in parallel on a common gold pad each. Every well has a substrate area of 0.8 cm^2 and a maximum volume of 600 µl. On average, with a confluent cell layer, approximately 500 to 1,000 cells will be measured by the electrodes.

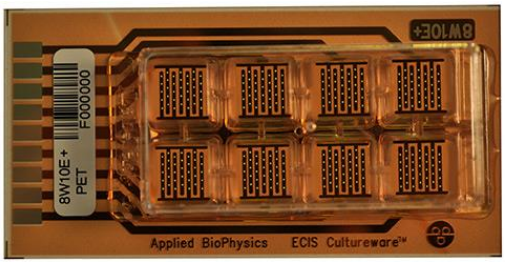


Application: Cell Attachment and Spreading, Cell Proliferation, Cell Differentiation, Barrier Function, Cell Invasion, Signal Transduction Assays, Cytotoxicity

8W10E+ PET or PC

The 8 wells have two sets of 20 circular 250 µm diameter active electrodes located on inter-digitated fingers each to provide measurements of cells upon a total of 40 electrodes. Every well has a substrate area of 0.8 cm^2 and a maximum volume of 600 µl. On average, with a confluent layer, approximately 2000 to 4000 cells will be measured by the electrodes.

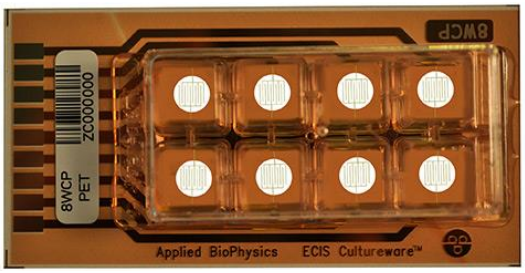
The 10E+ arrays are designed to monitor larger numbers of cells, sampling over the entire bottom of the well. Because of the relatively high number of cells, impedance fluctuations due to micromotion are smoothed out and do not obscure subtle changes in impedance due to the experimental conditions.



Application: Cell Attachment and Spreading, Cell Proliferation, Cell Differentiation, Barrier Function, Cell Invasion, Signal Transduction Assays, Cytotoxicity, Cell-ECM Protein Interactions

8W20idf PET

The 8 wells have a total electrode area of 3.985 mm^2 located on inter-digitated fingers (idf) each to provide measurements of cells. Every well has a substrate area of 0.8 cm^2 and a maximum volume of 600 µl. On average, with a confluent layer, approximately 4,000 to 8,000 cells will be measured by the electrodes.



The 8W20idf PET arrays are designed to monitor larger numbers of cells, sampling over the entire bottom of the well. Because of the relatively high number of cells, impedance fluctuations due to micromotion are smoothed out and do not obscure subtle changes in impedance due to the experimental conditions.

Application: Cell Attachment and Spreading, Cell Proliferation, Cytotoxicity

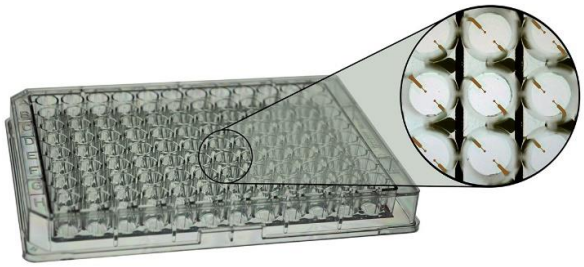
Standard 96-well Arrays

Array	Electrodes per Well	Electrode Area (mm^2)	Maximum Number of Cells Measured	Well Volume (µL)
96W1E+ PET	2	0.256	100 - 200	300
96W10idf PET	idf	2.09	2,000 - 4,000	300
96W20idf PET	idf	3.985	4,000 - 8,000	300

96W1E+ PET

The 96 wells are configured in a standard plate format and contain two circular 350 µm diameter active electrodes on a transparent PET substrate each (measuring from 100 - 200 cells). As with other 1E arrays, a major use of this array is for the ECIS® wound-healing assays where the small electrodes assure the high current pulse will result in complete cell killing.

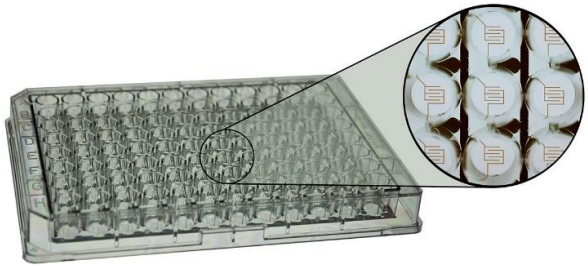
Only a small population of cells is monitored on the small electrodes resulting in a fluctuating impedance signal due to the random like movement of the cells (micromotion).



Application: Barrier Function, Signal Transduction Assays, Cell-ECM Protein Interactions, Cell Migration, Measurement of Micromotion, Detection of invasion of endothelial cell layers by metastatic cells, In situ Cell Electroporation and Monitoring

96W10idf PET

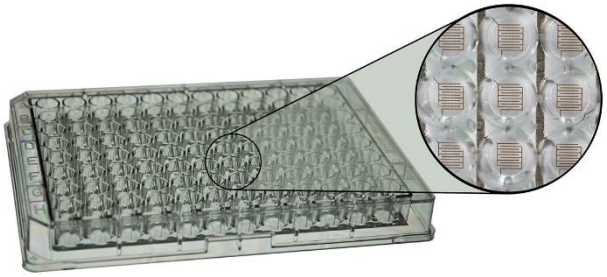
The 96 wells have an inter-digitated finger (idf) configuration each. The total electrode area is 2.09 mm^2 which measures a maximum of 2,000 – 4,000 cells.



Application: Barrier Function, Signal Transduction Assays, Cell-ECM Protein Interactions, Detection of invasion of endothelial cell layers by metastatic cells, Cell Proliferation

96W20idf PET

The 96 wells have an inter-digitated finger (idf) configuration each. The total electrode area is 3.985 mm^2 which measures a maximum of 4,000 – 8,000 cells.



Application: Barrier Function, Signal Transduction Assays, Cell-ECM Protein Interactions, Detection of invasion of endothelial cell layers by metastatic cells, Cell Proliferation

24-well Transfilter Array

The 24 wells in a standard plate configuration contain a gold electrode each covering the entire bottom of the wells on a transparent PET substrate. This plate is compatible with any commercially available 24-well sized filter. Filters are not included.

Application: TEER

Array	Electrodes per Well	Std. Filter Area (cm^2)	Maximum Number of Cells Measured	Well Volume (µL)
24WTEER PET	1	0.33	30,000 - 40,000	1,000, 200 (transfilter)

Speciality Arrays

Array	Electrodes per Well	Electrode Area (mm^2)	Maximum Number of Cells Measured	Well Volume (µL)
8W2x1E PET or PC	2 x 1	2 x 0.049	50 - 100	600
8W1CXE PET or PC	1	0.049	50 - 100	600
8W2LE PET or PC	2	0.20	200 - 400	600
2W4x10E PC	4 x 10	4 x 0.49	2,000 - 4,000	600

8W2x1E PET or PC or Medusa Array

This array is also called the Medusa Array. The wells in this array have two independent single 250 µm diameter active electrodes each. The Medusa Array is useful for duplicating readings in the same well or to wound/electroporate one electrode while leaving the other as a control within the same well.

When connected to the array holder only the upper four wells are measured. To use the other four wells, the array is turned around and the contact pads at the other end are connected.

Application: Barrier Function, Signal Transduction Assays, Cell Invasion, In situ Cell Electroporation and Monitoring, Cell Migration / Wound Healing, Correlated Microscopy and ECIS Experiments

8W1CXE PET or PC

This array is used to monitor the movement of cells in response to chemical gradients and is used in chemotaxis measurements first described by Hadjout, N. et al. (2001) Biotechniques 31 (5) 1130. The measuring electrode in this array is a thin gold line between two registry marks.

The wells have a substrate area of 0.8 cm^2 and a maximum volume of 600 µl. On average, with a confluent layer, approximately 50 to 100 cells will be monitored by the electrode.

Application: Cell Chemotaxis

8W2LE PET or PC

The 8 wells contain each a single linear electrode with dimensions of 667 µm x 150 µm and a measurement value equal to that of standard 250 µm circular electrodes. The wells have a substrate area of 0.8 cm^2 and a maximum volume of 600 µl. On average, with a confluent cell layer, approximately 200 to 400 cells will be measured by the electrode, but even a single cell can be observed.

Application: Cell Migration / Wound Healing, Correlated Microscopy and ECIS Experiments

2W4x10E PC

The 2 circular 25 mm diameter wells contain four independent sets of ten 250 µm diameter active electrodes each measuring from 2,000 – 4,000 cells. In addition, the 2W4x10E array is useful for duplicating readings in the same well or to wound/electroporate one electrode while leaving the other as a control within the same well.

Application: Barrier Function, Signal Transduction Assays, Cell Invasion, Cell Attachment and Spreading, Cell Proliferation, Cell Differentiation, Cytotoxicity, Correlated Microscopy and ECIS Experiments

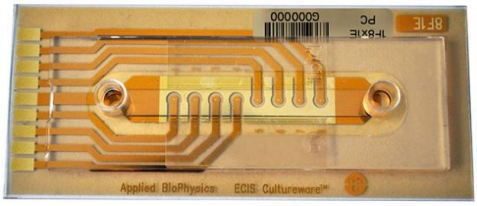
Flow Arrays

Flow Arrays are designed for ECIS® measurements of cells under perfused conditions or to mimic the shear stress endothelial cells experience in vivo.

Array	Electrodes per Well	Electrode Area (mm^2)	Maximum Number of Cells Measured	Well Volume (µL)	Channel Height x Width (mm)
1F8x1E PC	8 x 1 (1 channel)	0.049	50 - 100	90/60	0.36 x 5
1F8x10E PC	8 x 10 (1 channel)	0.49	500 - 1,000	90/60	0.36 x 5
6F1E PC	1 (6 channels)	0.049	50 - 100	45/60	0.66 x 5
6F10E PC	10 (6 channels)	0.49	500 - 1,000	45/60	0.66 x 5
1F2Y8x10E PC	8 x 4 x 2 (30 and 45 degree sides)	0.49	500 - 1,000	165/60	0.66 x 5

1F8x1E PC

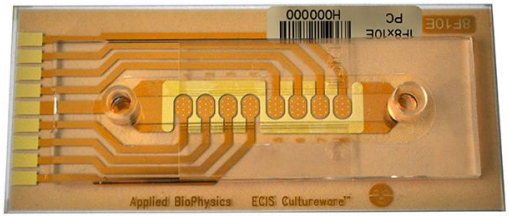
This is a specialized flow array having 8 active 250 µm diameter electrodes (each measuring from 50 - 100 cells) located in the central region at the base of a flow channel measuring 50 mm in length, 5 mm in width and 0.36 mm in height with a total channel volume of 90 µl.



Application: Barrier Function, Signal Transduction Assays, Cell Invasion, In situ Cell Electroporation and Monitoring, Cell Migration / Wound Healing, Cell Proliferation, Cell Differentiation, Cytotoxicity

1F8x10E PC

This is a specialized flow array having 8 sets of 10 active 250 µm diameter electrodes (each measuring from 500 - 1,000 cells) located in the central region at the base of a flow channel measuring 50 mm in length, 5 mm in width and 0.36 mm in height with a total channel volume of 90 µl.

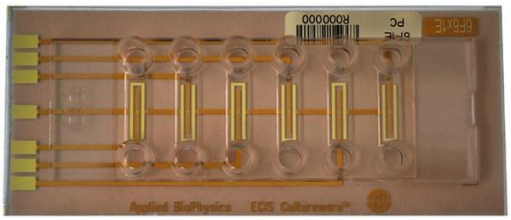


Application: Barrier Function, Signal Transduction Assays, Cell Invasion, In situ Cell Electroporation and Monitoring, Cell Migration / Wound Healing, Cell Proliferation, Cell Differentiation, Cytotoxicity

6F1E PC

This flow array allows 6 independent flow assays to be run simultaneously. The channels are 0.66 mm in height and 5 mm wide with 1 active 250 µm diameter electrode (measuring from 50 - 100 cells) per channel.

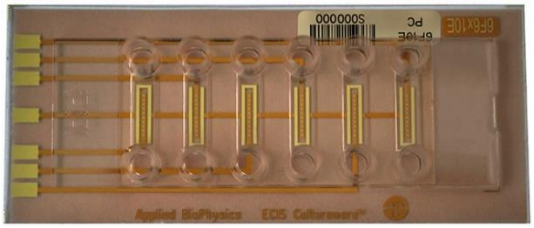
The channels have a volume of 45 µl with 60 µl reservoirs.



Application: Barrier Function, Signal Transduction Assays, Cell Invasion, In situ Cell Electroporation and Monitoring, Cell Migration / Wound Healing, Cell Proliferation, Cell Differentiation, Cytotoxicity

6F10E PC

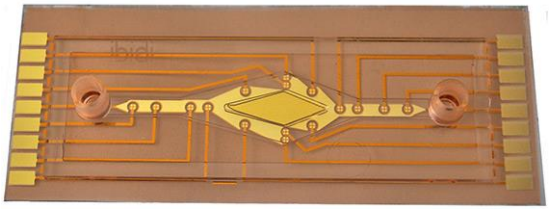
This flow array allows 6 independent flow assays to be run simultaneously. The channels are 0.66 mm in height and 5mm wide with 10 active 250 µm diameter electrodes (each measuring from 500 – 1,000 cells) per channel. The channels have a volume of 45 µl with 60 µl reservoirs.



Application: Barrier Function, Signal Transduction Assays, Cell Invasion, In situ Cell Electroporation and Monitoring, Cell Migration / Wound Healing, Cell Proliferation, Cell Differentiation, Cytotoxicity

1F2Y8x10E PC

This flow array is intended for bifurcation studies and blood vessel simulation. It splits into a 30-degree Y-channel in one direction and a 45-degree Y-channel in the other direction.



The array is double ended with 8 measurement channels available at each end. Eight measurement points, each with 4 circular active electrodes (with an area of 0.49 mm^2 measuring from 500 – 1,000 cells, the area is the same as a 10E electrode), are located along the channel and through the Y-portion of the channel. One end of the array is used to monitor the 30-degree Y-channel and the other end is used to monitor the 45-degree Y-channel. The electrodes are located close in the corners of the flow direction transition points. The channels have a volume of 165 µl with 60 µl of reservoirs. The flow is always laminar, i.e., turbulent flows are not possible. For simulation of turbulence flow we recommend oscillating the flow.

Recommended for the following applications under shear stress conditions:

- Simulation of the bifurcation of blood vessels for arteriosclerosis research
- Rolling and adhesion of leukocytes on endothelial cells cultured under flow
- Cell-cell interaction studies and cell-drug interaction screenings under flow conditions

Customized Arrays are also possible.
Please contact us for more information regarding this service.

.

Barcode

All arrays include a bar code (code 128) label and serial number. The ECIS® software embeds the type of array and serial number information in the ECIS® data file. The information can be scanned in via a bar code scanner or keyed in manually. Requires ECIS® software V 1.2.135 or later.

Nomenclature

The nomenclature for standard ECIS® Cultureware has two parts: The well number and the electrode type. 8W (Wells) 10E+ (Electrode) 96W (Wells) 20idf (Electrode). There are two categories of electrode geometries, small circular electrodes (1E, 1E+ 10E+, 10E) and interdigitated finger electrodes (10 idf, 20 idf and CP). Arrays come in 2-, 8- or 96-well formats (2W, 8W, 96W) along with single or 6-channel flow arrays (1F, 6F).

How ECIS® works

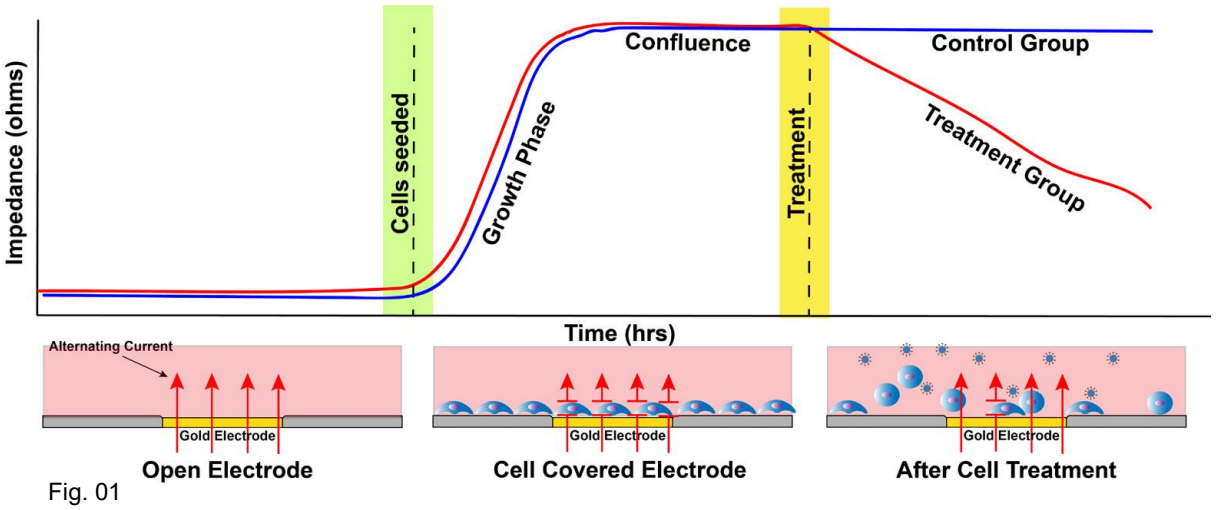


Fig. 01

Schematic representation of ECIS data with impedance vs time. As cells grow and cover electrodes, impedance data rises proportional to cell coverage of the gold electrodes.

Cell function modulates cell morphology. ECIS® is capable of detecting and quantifying morphology changes in the sub-nanometer to micrometer range. In ECIS® a small alternating current (I) is applied across the electrode pattern at the bottom of the ECIS® arrays (direct current cannot be used). This results in a potential (V) across the electrodes which is measured by the ECIS® instrument.

The impedance (Z) is determined by Ohm's law Z = V/I. When cells are added to the ECIS® Arrays and attach to the electrodes, they act as insulators increasing the impedance. As cells grow and cover the electrodes, the current is impeded related to the number of cells covering the electrode, the morphology of the cells and the nature of the cell attachment. When cells are stimulated to change their function, the accompanying changes in cell morphology alter the impedance. The data generated is impedance versus time (see figure above).

How Frequencies Reveal Cell Behaviour

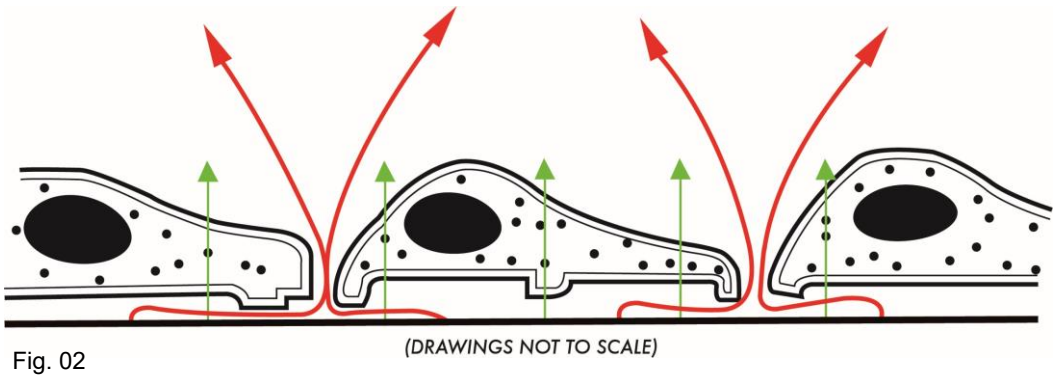


Fig. 02

To understand why AC frequency is important in ECIS® we have to consider how frequency affects the current paths of cell-covered electrodes. (Note: the total current is maintained constant and voltage changes are measured.) At relatively low frequencies (< 2,000Hz_see figure 2 above) most of the current flows in the solution channels under and between adjacent cells (red lines).

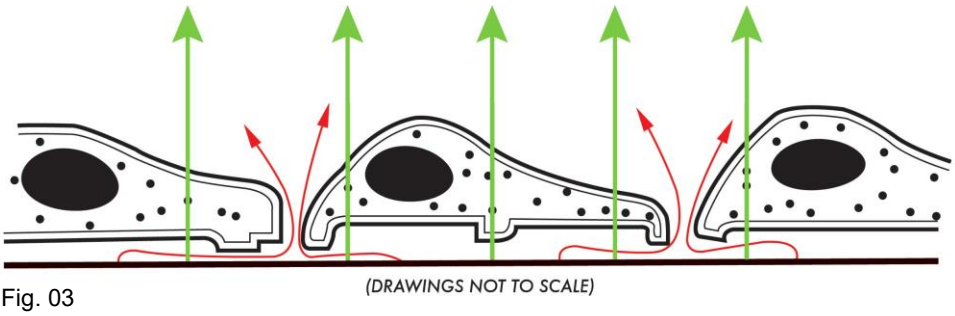


Fig. 03

At higher frequencies (> 40,000 Hz_see figure 03) more current now capacitively couples directly through the insulating cell membranes (green lines).

The high frequency impedance is more affected by cell-coverage, whereas the low frequency responds more strongly to changes in the spaces under and between the cells. With the more advanced Z instrument, where the impedance is broken down into its components (resistance and capacitance), quantitative information about the cells can be obtained by modeling (Giaever and Keese PNAS 1991).

Using impedance data at multiple AC frequencies the ECIS® model calculates time course changes in:

- The barrier function (permeability) of the cell layer
- The degree of constricted flow of current under the cells
- The cell membrane capacitance

How Electrode Designs Reveal Aspects of Cell Behaviour

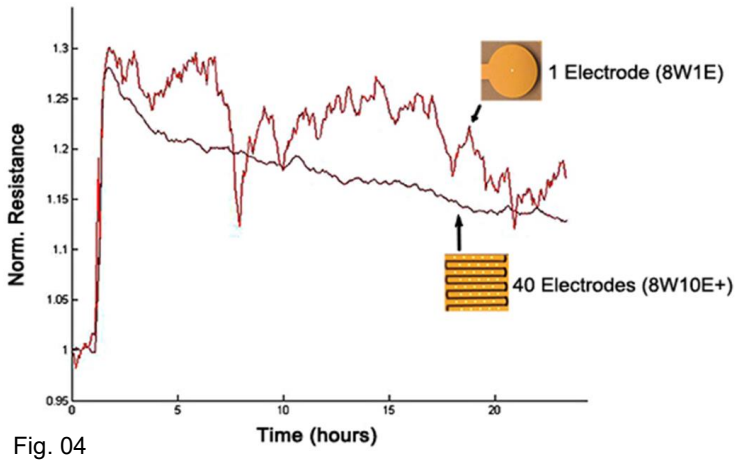
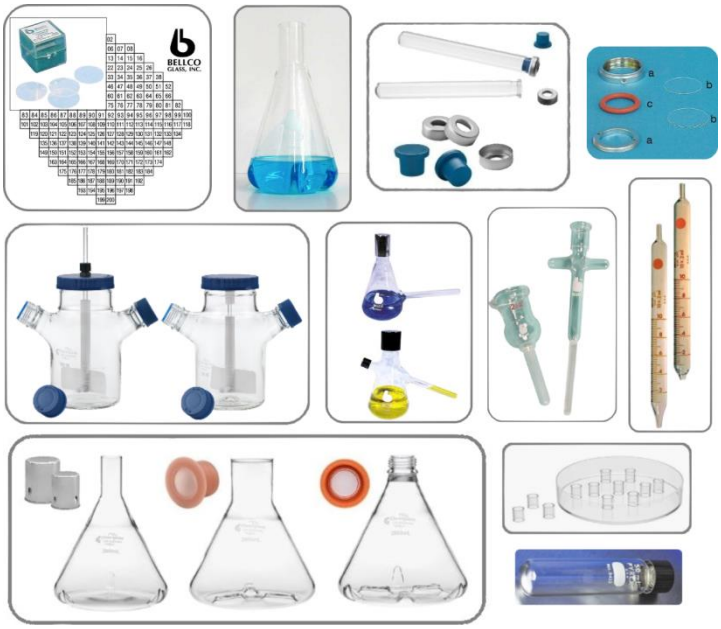


Fig. 04

Small Electrodes
Small electrodes (1E, 10E, 10E+ type arrays) and their layout within the wells ensure that all current passes through the cell monolayer (see also figure 04). This allows the ability to analyse data with the ECIS® modelling software to determine barrier function, cell membrane capacitance as well as the spacing between the cell basal membrane and electrode. Keeping the total surface area of the electrodes small also allows for a relatively low AC current to generate the large electric field necessary to either electroporate or kill the cells in migration experiments.
Small electrodes also provide the ability to monitor the uncorrelated nano-scale morphological changes of individual or small populations of cells (<100), while larger or multiple electrodes provide the averaged morphological response of many cells (1000+).

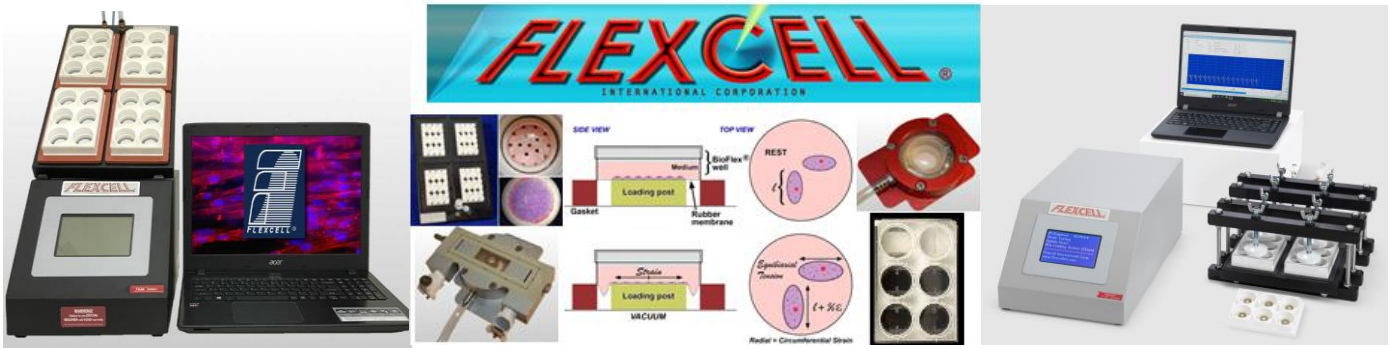
Large Electrodes
Some experimental protocols, such as cell proliferation, require sparse inoculations leading to a variance of cell density at the bottom of the well. Large electrodes (CP Array) or a large collection of small electrodes (10E+Array) increases the sampling size resulting in less variability (see also figure 04).

Glass Products for Cell Culture



- Anaerobic culture tubes and bottles
- Bioreactor vessels & accessories
- Cloning cylinders
- Coverslips/Slides: photo-etched, round, square
- Flasks: Erlenmeyer, Fernbach, Roux
- Homogenizer, Tissue Grinders
- Bottles: Roller, Spinner
- Shake flasks with / without baffles
- Tubes, Leighton, Centrifuge, Hungate

  and much more…



Cellular biomechanical systems from Flexcell® for simulation and investigation of cyclic or static tensile strains or compression as well as fluid shear stress to cells cultured *in vitro* (2D and/or 3D cell cultures).

- User-friendly systems that have been used so far worldwide for more than 4,000 publications in scientific journals such as „Journal of Cell Biology“, „Nature“, „PNAS“, and many more.
- The modular equipment allows the user to upgrade the Flexcell® systems to their individual requirements, such as the 24-well Baseplate Kit for high-throughput applications, the microscopy devices for real-time observation of cells, or additional controllers to perform different tests at the same time.