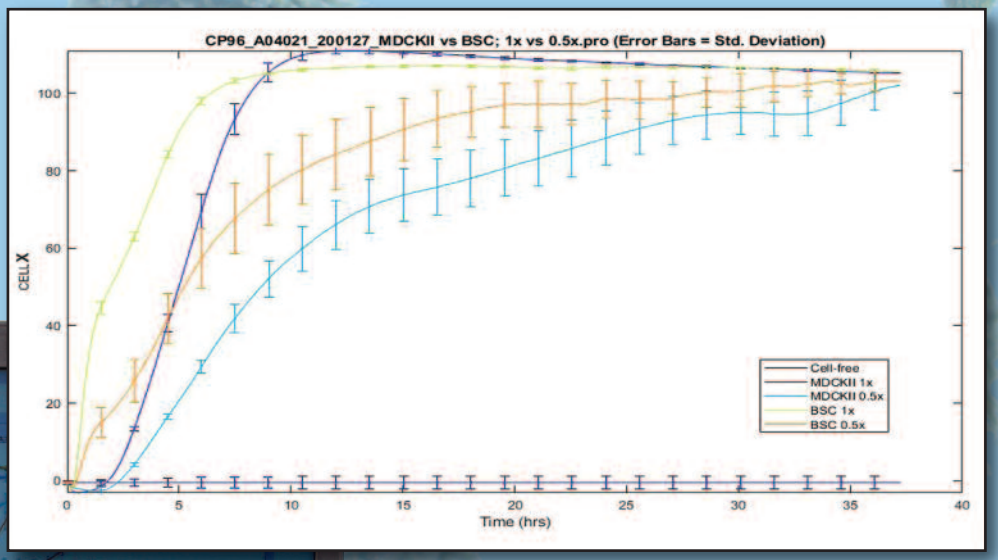
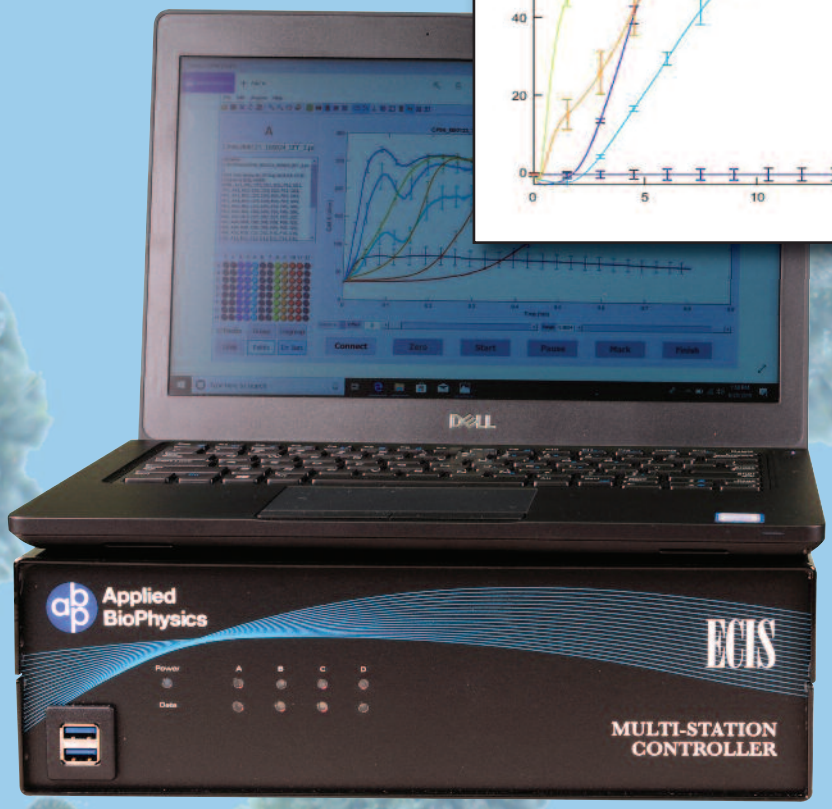
Cytopathic Effects: Virology with ECIS®





Applied BioPhysics

Quantifying Cell Behavior

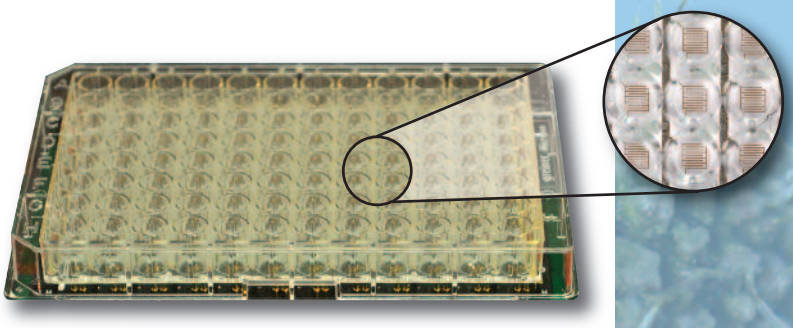
www.biophysics.com

Electric Cell-substrate Impedance Sensing

ECIS® (Electric Cell-substrate Impedance Sensing) is a real-time, impedance-based method to study many of the activities of cells when grown in tissue culture. ECIS instruments measure the impedance of a non-invasive AC current moving through cell-culture media in ECIS well-arrays with gold electrodes as cell substrates. As cells attach and grow over these electrodes, the AC current is impeded proportional to the number of cells and the intercellular barriers that are formed. The ECIS® impedance-based cell monitoring technology was invented and later commercialized by the founders of Applied BioPhysics, Inc.

The ECIS® approach has been applied to numerous investigations including measurements of the invasive nature of cancer cells, the barrier function of endothelial cells, signal transduction involving GPCR's for modern drug discovery, and in vitro toxicology and cytopathic effects as an alternative to animal testing.

ECIS® Measurements:



- **Applied AC current is non-invasive**

  As cells grow over gold electrodes on ECIS® array plates, an applied weak AC current is impeded and recorded with no effects to the cells.

- **Real-time Data**

  When electrical impedance is being measured, data is shown continuously in real-time and in graphical format.

- **Cellular Behavior Assays**

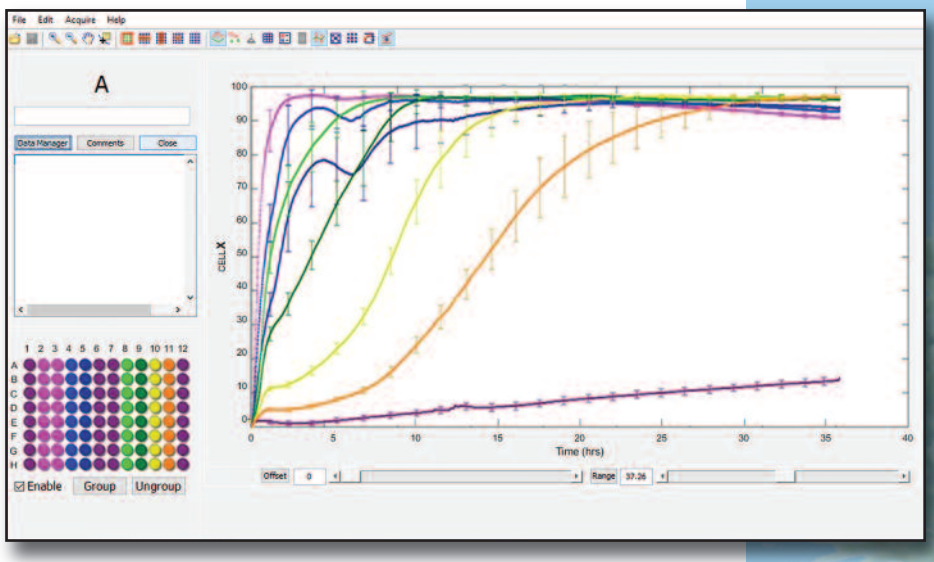
  ECIS® instruments measure multiple cellular behaviors including cell proliferation, cytotoxicity, barrier function, TEER, migration, and more.

- **Incubator Compatible**

  All data can be taken under incubated conditions for days and even weeks at a time.

- **User-friendly Software**

  ECIS® software is intuitive and displays data continuously. Data can be exported and used in statistical programs.



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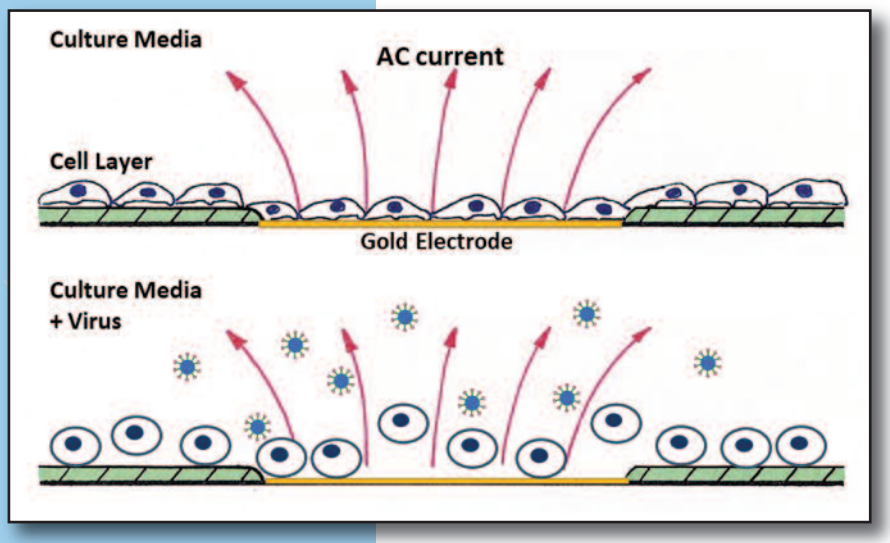
ECIS® and Virology

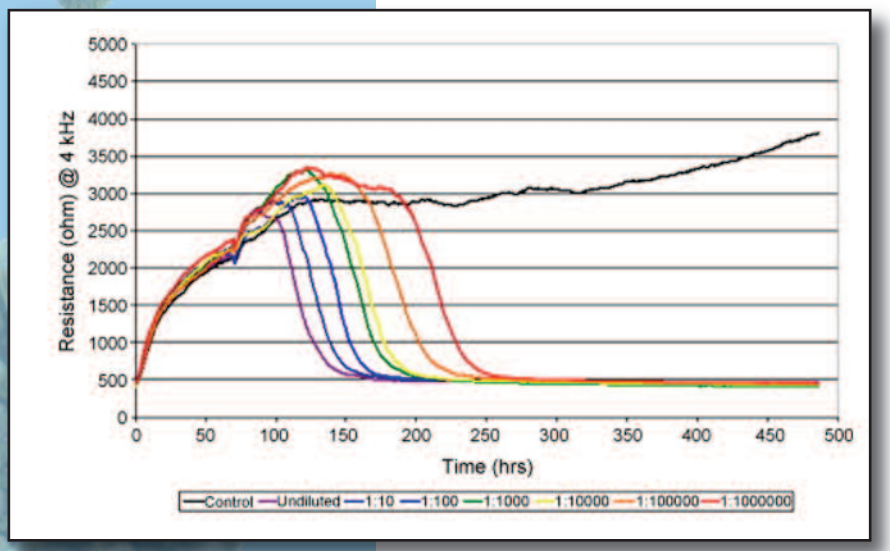
Cytopathic effects from viral infections of cells have long been difficult to quantify due to the subjective nature of monitoring cell viability. The advantage of ECIS® technology is the ability to monitor cell behavior (e.g. growth, toxicity, cytopathic effects) quantitatively and in real-time. When cells grown on the gold electrodes of ECIS® arrays show changes from viral infections in vitro, their morphology and viability will be detected from the change in impedance measured by the ECIS® instruments.

Detecting Cytopathic Effects



- Cells are seeded into ECIS® electrode arrays
- Cells are grown to confluency. This will be represented by a plateau in the ECIS® software graph.
- Cells are then treated with specified virus
- Cells will exhibit cytopathic effects by changes in morphology and viability as cells reduce their barrier function and detach from the gold electrodes
- These cytopathic effects can be viewed in real-time as changes in impedance on the ECIS® software graph

ECIS® Software and Cytopathic Effects



(Campbell, Laane, Haugarvoll, & Giaever, 2007).

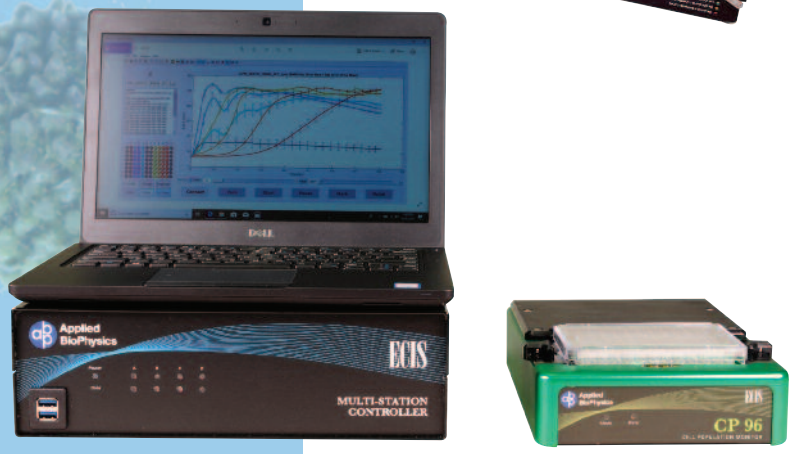
When cells are displaying cytopathic effects following their infection with viruses, the ECIS® instrumentation detects these changes in real time.

The graph on the left is an example of this, where endothelioma papulosum cyprini cells (EPC) were exposed to infectious hematopoietic necrosis virus (IHNV) in 10-fold dilutions. The graph represents resistance changes that are clearly dependent upon the titer of the virions applied to the cell layers. The black trace is resistance from an uninfected control.

ECIS® Instruments

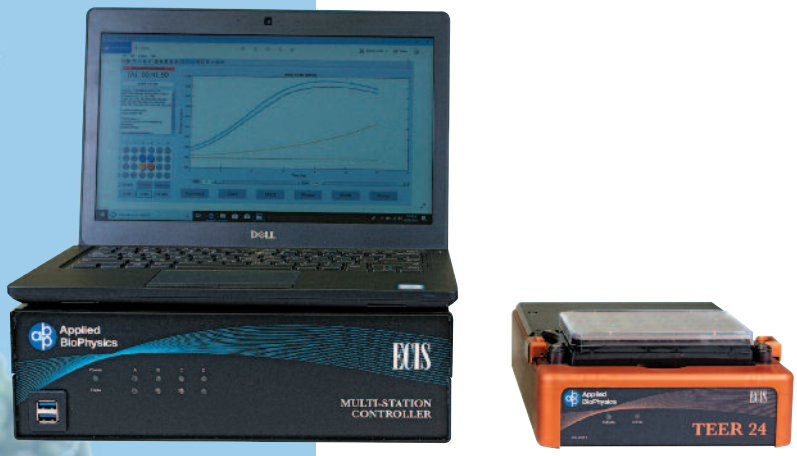
ECIS® Z-Theta:

The ECIS® Z-Theta is our most advanced all-in-one instrument with the ability to accurately measuring cellular behaviors including proliferation, migration, barrier function, attachment, and much more. Not only is the ECIS Z-Theta capable of a multitude of assays, it's all done in real time, giving it the edge in impedance-based assays.



ECIS® CP96:

The CP96 Cell Population Monitor is a single-purpose instrument is based upon the ECIS® technology where cells are grown upon gold electrodes carrying very weak AC signals. CP96 is focused on cell proliferation/toxicology with the capability to calculate and display EC50 values. This complete turn-key system provides a means to carry out reproducible, label-free, automated cell population measurements without damaging the cells.



ECIS® TEER24:

The ECIS® TEER24 is another single-purpose instrument designed to carry out traditional trans-epithelial/endothelial electrical resistance measurements using ECIS® technology to monitor the barrier function of cell layers grown on membrane insert filters. Data is collected continuously from up to 24 independent wells and reported as real-time barrier function changes in ohm-cm^2.

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