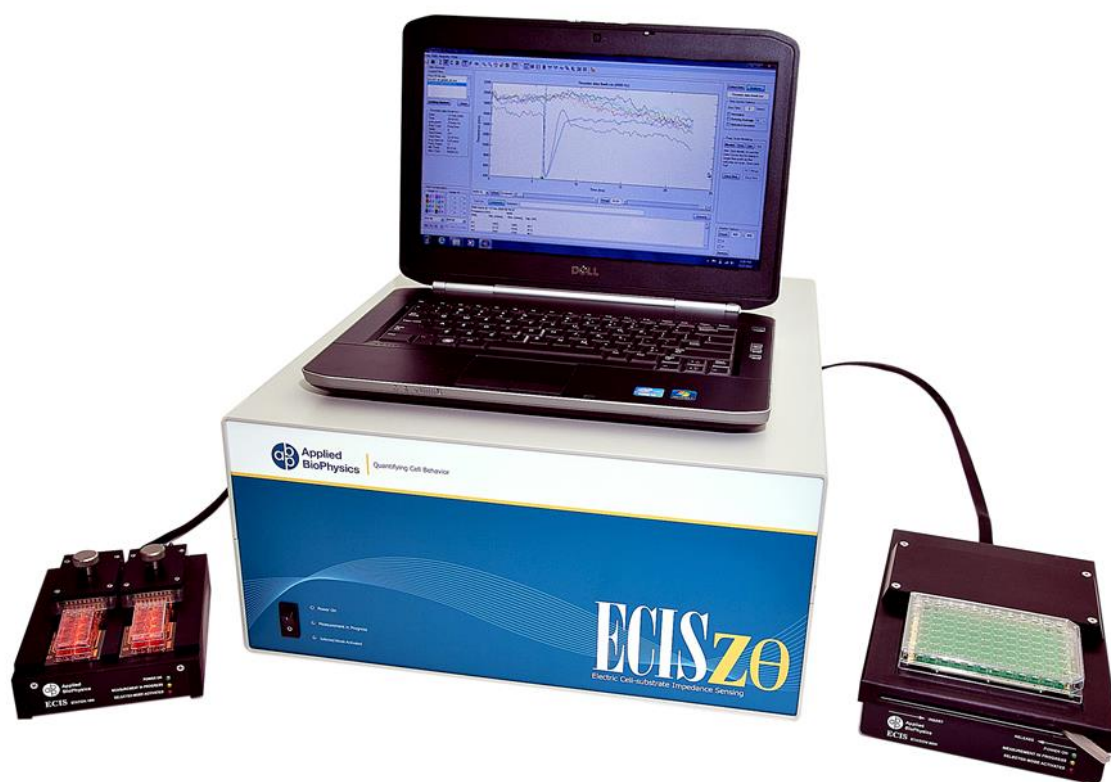


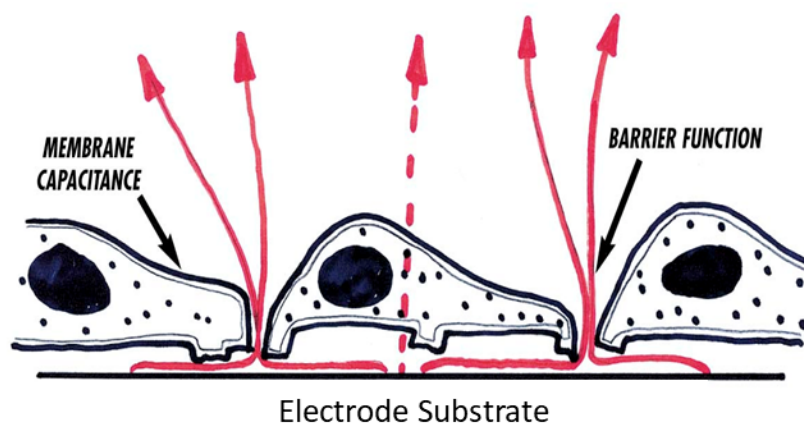
# ECIS®: A Real-time, Non-invasive System to Measure Cancerous Cell Behavior



# What is ECIS®?

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. These include morphological changes, cell locomotion, and other behaviors directed by the cell's cytoskeleton. Impedance-based cell monitoring technology was invented by the originators of Applied BioPhysics, Inc. to commercialize ECIS® and other biophysical technologies. The ECIS® approach has been applied to numerous investigations including measurements of the invasive nature of cancer cells, the barrier function of endothelial cells, in vitro toxicity testing as an alternative to animal testing, and signal transduction involving GPCR's for modern drug discovery.

## HOW TO QUANTIFY CELL BIOLOGY



Cell function modulates cell morphology. ECIS® is capable of detecting and quantifying morphology changes in the subnanometer to micrometer range. In ECIS® a small alternating current ( $I$ ) is applied across the electrode pattern at the bottom of the ECIS® arrays. This results in a potential ( $V$ ) across the electrodes which is measured by the ECIS® instrument and converted into impedance and its components.

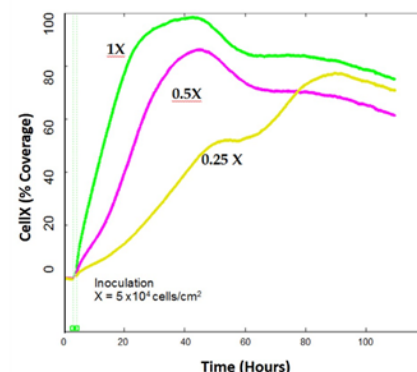
When cells are added to the ECIS® arrays and attach to the electrodes, they act as insulators increasing the impedance. As cells grow and cover the electrodes, the current is impeded in a manner related to the number of cells covering the electrode, the morphology of the cells and the nature of the cell 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.

# ECIS<sup>®</sup> & Cancer

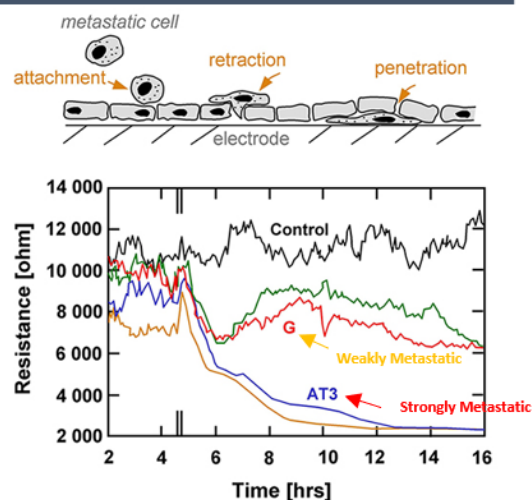
## Cell Proliferation

The hallmark of cancer is the proliferation of cells without control. As cells proliferate two factors act to change the impedance: cell number and cell morphology. In most instances the cells grow asynchronously and the impedance gradually increases until a maximum when cells become confluent. With ECIS<sup>®</sup>, these impedance changes are recorded over time allowing for accurate measurements of proliferation rates of cancerous cells.



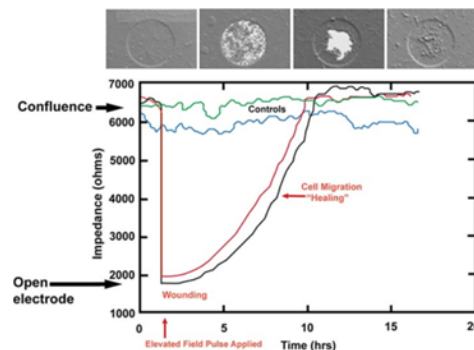
## Cancer Metastasis

We have used the ability of ECIS<sup>®</sup> to detect changes in cell morphology to design whole-cell assays related to the behavior of the cancer cell including metastatic potential. The drawing shows the type of activities expected to occur during the challenge of the normal endothelial cell layer with the metastatic cell lines. The data shows a control culture receiving only additional medium. The other traces are of duplicated cultures challenged with the weakly metastatic G subline or the metastatic AT3 subline of prostatic cancer cells.



## Automated Wound Healing

Wound healing assays allow researchers to observe cell migration. ECIS<sup>®</sup> instruments include an elevated field mode allowing for automated wounding. The ECIS<sup>®</sup> wound is precisely defined, as it includes only those cells on the electrode. Additionally, with ECIS<sup>®</sup> the ECM protein coating is not scraped off and is unaffected by the current.





# ECIS<sup>®</sup> Applications

## ATTACHMENT AND SPREADING

Traditional "counting attached cells assays" can only quantify the number of cells attached to any ECM coating. ECIS<sup>®</sup> assays give feedback on the strength of the attachment of the cells to the ECM.

## CELL PROLIFERATION

As cells proliferate two factors act to change the impedance: cell number and cell morphology. In most instances the cells grow asynchronously and the impedance gradually increases until a maximum when cells become confluent. The impedance change is approximately linear with cell number while the cells are sub-confluent.

## DIFFERENTIATION AND STEM CELL BIOLOGY

When cells differentiate they change their behavior allowing ECIS<sup>®</sup> to follow the events of cell differentiation. While most tools available to characterize stem cells preclude their further use, the label-free non-invasive nature of ECIS<sup>®</sup> allows for subsequent use of characterized stem cells.

## BARRIER FUNCTION

Epithelial cells and endothelial cells regulate the passage of molecules across cell layers. Diseases, especially vascular disease, occur when this function is impaired.

## SIGNAL TRANSDUCTION

ECIS<sup>®</sup> is especially useful to monitor the signal transduction pathways activated by G protein coupled receptors (GPCR). GPCR activation, regardless of the second messenger, results in alterations of the cell's cytoskeletal elements, causing morphological changes.

## CELL INVASION

ECIS<sup>®</sup> can distinguish between transmigration mechanisms that leave the monolayer intact from those that disrupt the cell layer. Published examples include metastatic cell and leukocyte trans-endothelial migration, as well as the migration of pathogens such as yeast, anthrax, streptococcus, plasmodium, trypanosomes, and spirochetes.

## CELL TOXICITY

The ECIS<sup>®</sup> system has been used specifically to assess the cytotoxicity of a variety of toxicants. ECIS-based toxicity tests are far superior to simple cell death assays, because cell function is also monitored.

## CELL MIGRATION

ECIS instruments include an elevated field mode allowing for electroporation and wounding. The ECIS<sup>®</sup> wound is precisely defined, as it includes only those cells on the electrode. Additionally, with ECIS<sup>®</sup> the ECM protein coating is not scraped off and is unaffected by the current.

## INFLAMMATION

ECIS recovery-after-wounding assays allow for the discovery of molecules which aid in the process of tissue repair. ECIS barrier function assays specifically measure the response of epithelial and endothelial cells to secreted cytokines and can give indirect information about the binding of immune cells to the epithelium or endothelium.

## TEER

Continuous long-term measurement of TEER under 10 to 1,000 ohm cm<sup>2</sup> in up to 24 wells using commercially available 6mm membrane inserts. Fast barrier function dynamics can be accurately monitored

\*To view ECIS<sup>®</sup> publications, visit [www.biophysics.com](http://www.biophysics.com)

Distributed by: