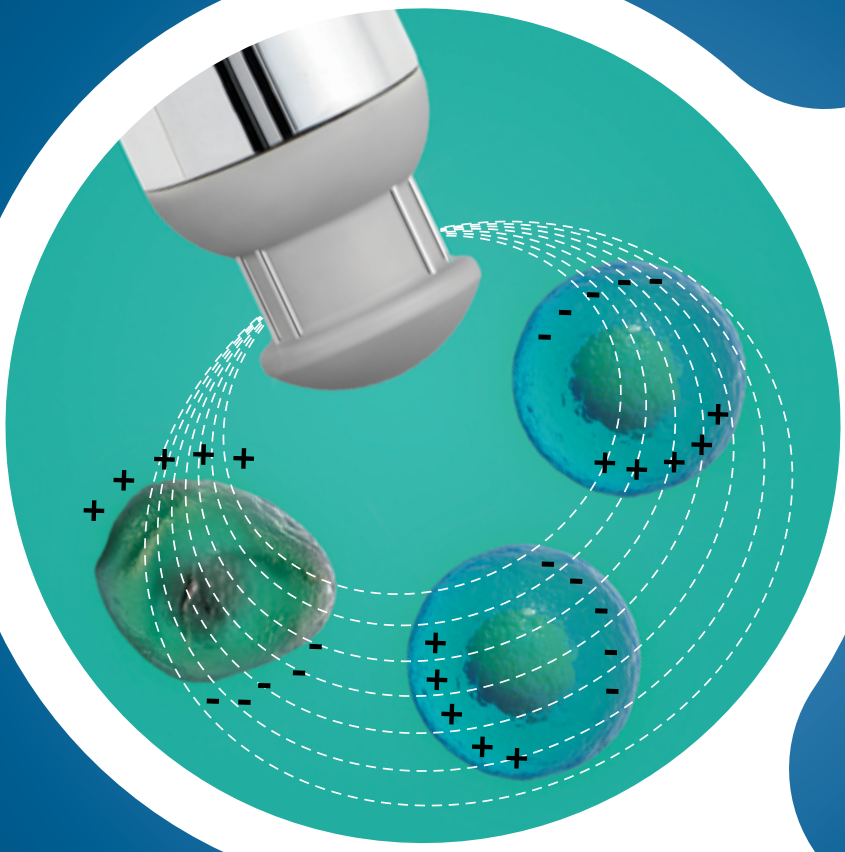
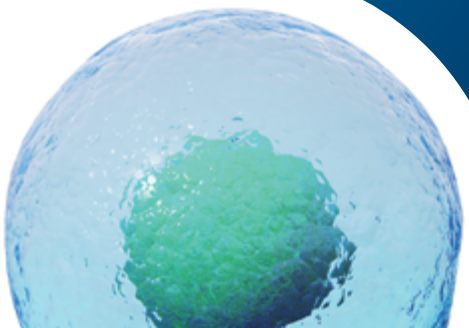
HAMILTON

INTTERTECH RIO
CONTROLE DE PROCESSOS E INSTRUMENTAÇÃO

Cell Density
Applications eBook

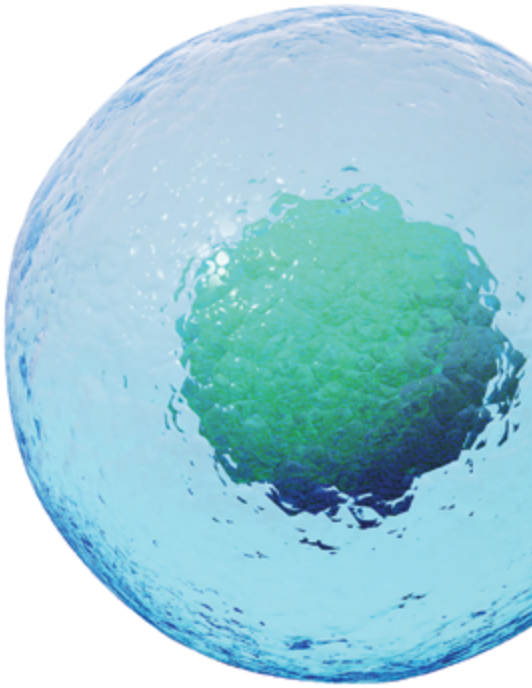




Publication Overview

Hamilton's on-line cell density sensors have been used by a variety of customers for applications ranging from feed control to continuous processing. This eBook provides a summary of relevant data and references to published research that employed those sensors.

Introduction



By Application

By Cell Line / Strain

Discover On-Line Cell Density

Innovative Methods that Improve and Streamline Cell Density Monitoring

Traditional cell density measurement and monitoring is time- and labor-intensive. It also lacks real-time, continuous data and makes assumptions based off of off-line sampling and manual cell counting.

Hamilton Process Analytics has revolutionized and modernized this process. Rather than counting the cells directly, Hamilton sensors use the principles of permittivity measurement (capacitance per area) and light absorbance which correlate to the cell count in solution at the production line. It's an improvement that saves time and allows for advanced process control.

The following pages detail real applications of these sensors and measurement principles to show the benefits and opportunities offered by this shift in technology.

About Incyte

Real-Time, On-Line Viable Cell Density Measurement by Permittivity

Incyte sensors measure permittivity in the on-line process to give a continuous, in-situ reading of viable cells in solution. This eliminates time-intensive manual cell counting.

Incyte Highlights:

- Not influenced by changes in the media, microcarriers, dead cells, or debris
- Can increase yield and lower production costs
- Can detect changes in cell physiology with frequency scanning
- Offers precise data to control harvesting in continuous culture
- Offers early detection of process deviations
- Available in optimized versions for multiple conductivity ranges

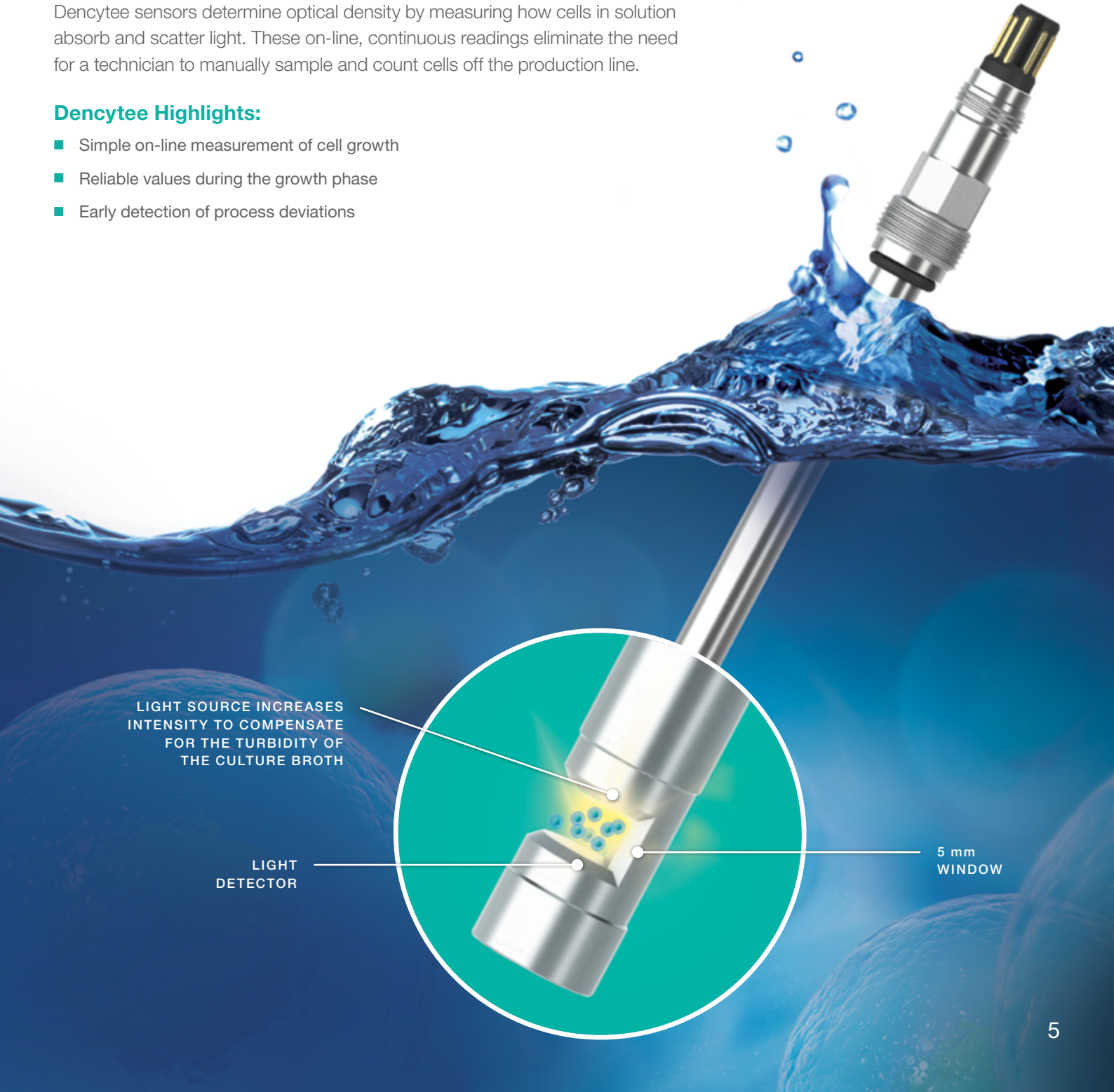
About Dencytee

Real-Time, On-Line Total Cell Density Measurement by Optical Density

Dencytee sensors determine optical density by measuring how cells in solution absorb and scatter light. These on-line, continuous readings eliminate the need for a technician to manually sample and count cells off the production line.

Dencytee Highlights:

- Simple on-line measurement of cell growth
- Reliable values during the growth phase
- Early detection of process deviations

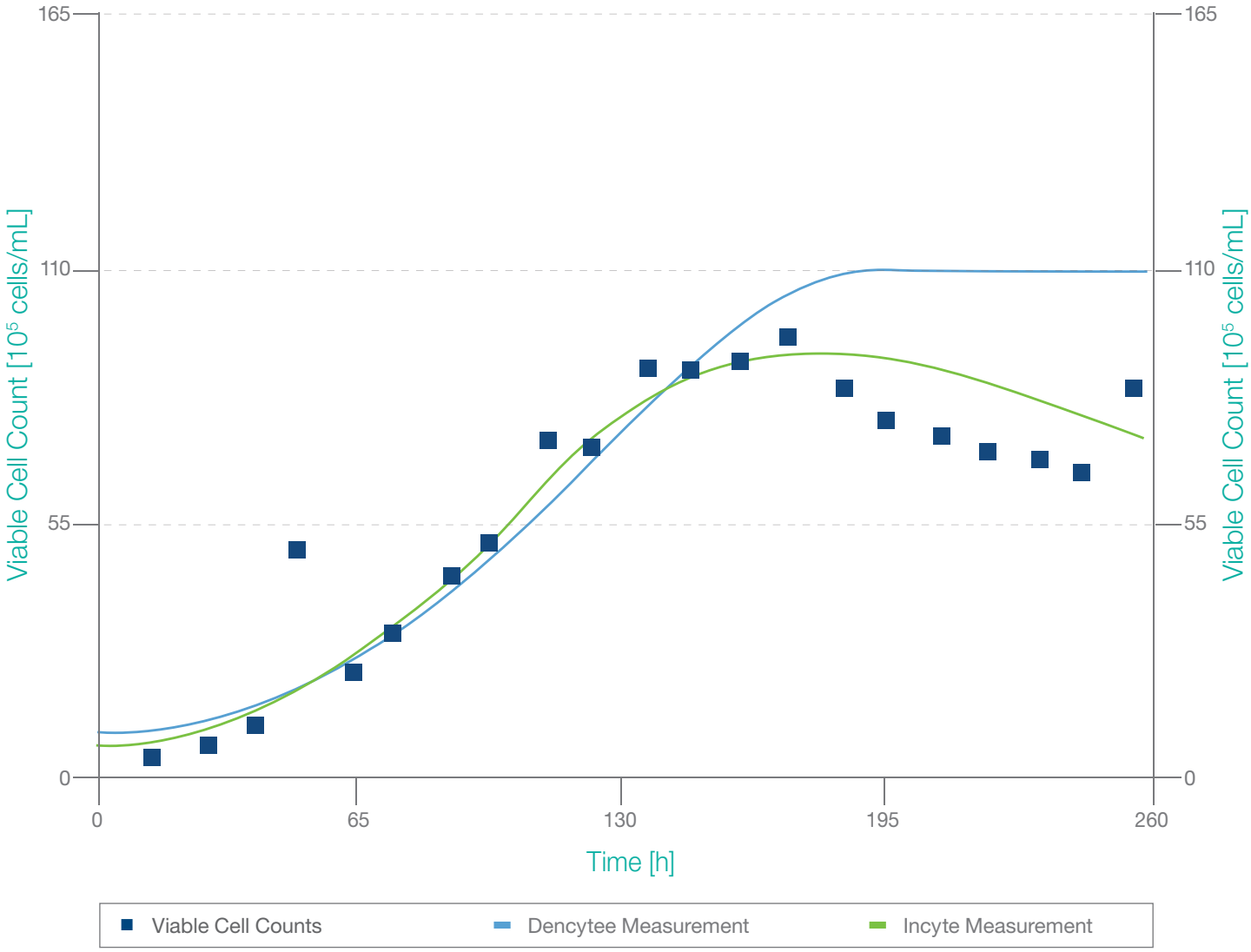


Viable and Total Cells

Mammalian Cells (CHO)

Obtaining relevant on-line data about viable and total cell density.

- Incyte correlates well with viable cell counts throughout process
- Incyte and Dencytee together can be used to estimate viability



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Kandra, Kulwant, et al. On-Line Monitoring of CHO Cell Culture. Hamilton Company, 2014.

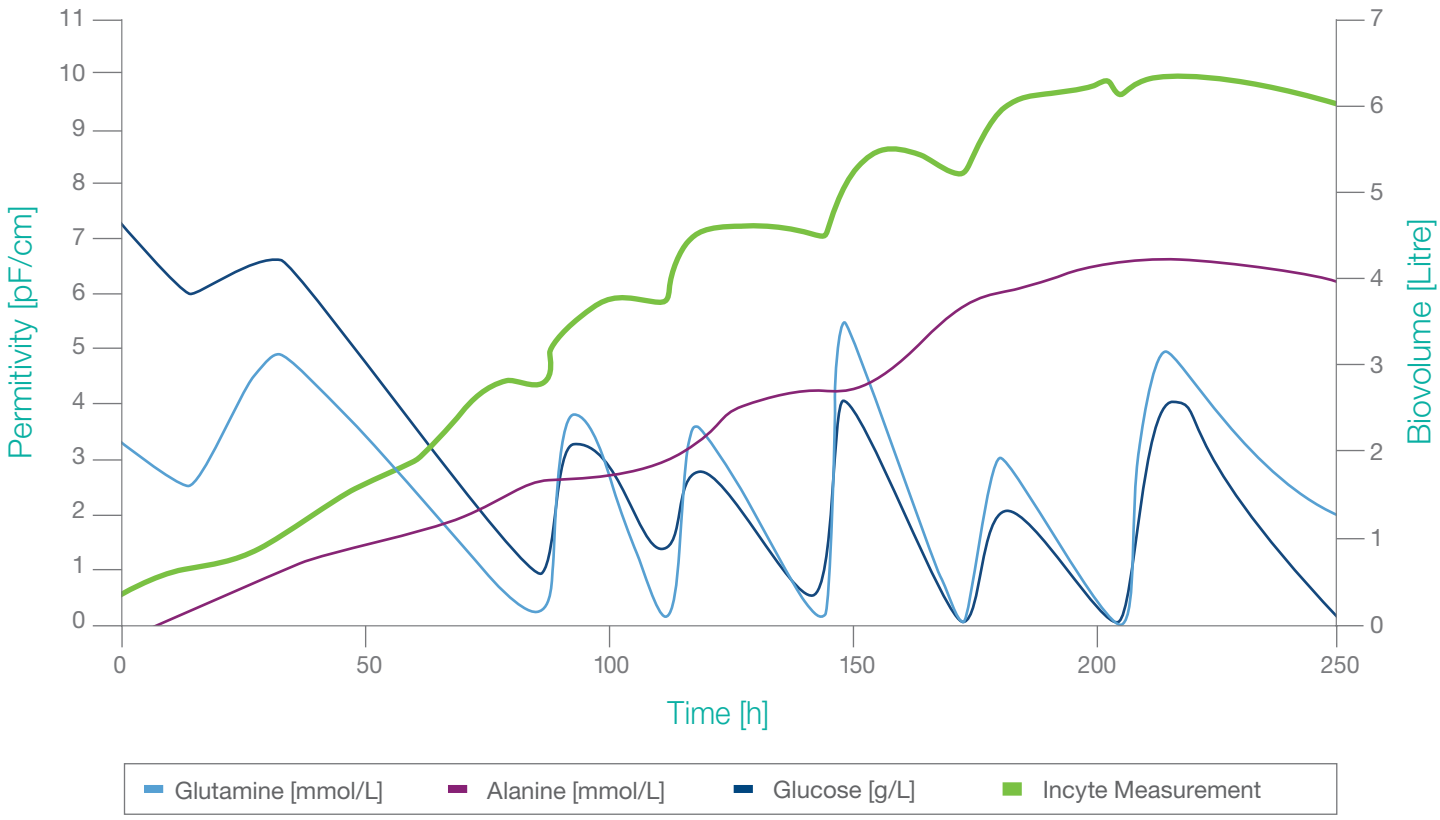
Optimize the Process

Mammalian Cells (CHO)

Monitoring permittivity provides the possibility to control feeding and enable optimal nutrition supply.

In this study, alanine is an indicator for the protein of interest. As glutamine nears depletion, the metabolism of the cells change and alanine is similarly depleted. At that point there is no productivity.

- Drop in permittivity, as measured by Incyte, triggered glucose and glutamine feeding
- Expanded alanine production phase of the protein of interest by three days as compared with a non feed-controlled process (greatly reducing workload of new batch startup)



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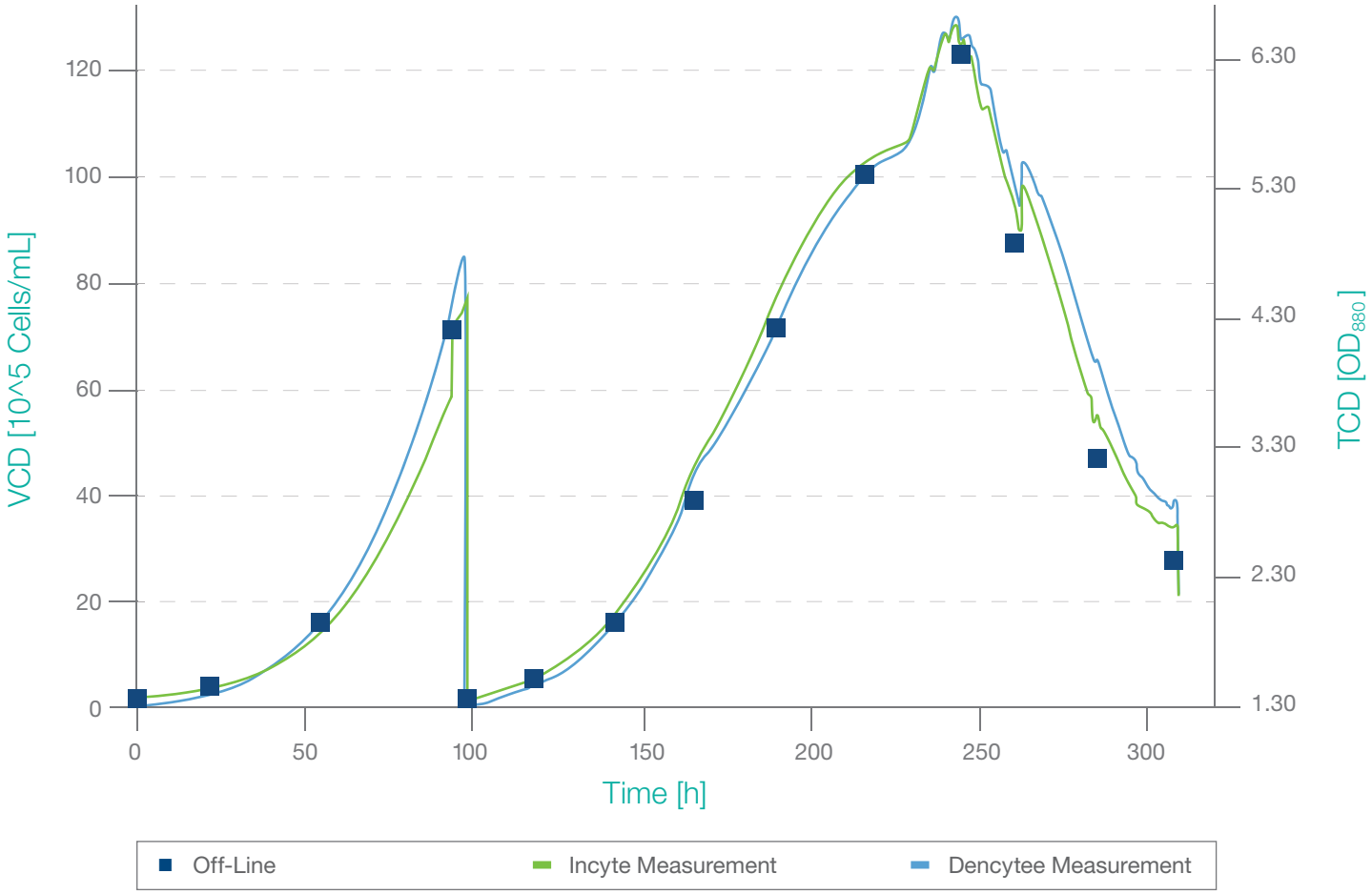
Roche (2005) CHO Biomass nutrients limit. Poster at ESACT19

Continuous Processing

Mammalian Cells (CHO)

Viable Cell Density monitoring correlates with the off-line Cedex counts.

- Incyte and Dencytee correlate throughout continuous (perfusion) process
- No sensor adjustment needed when harvesting



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Real-time Cell Density Measurement for PAT Applications,
Dr. Heino Büntemeyer, Anica Schmidt, Zellkulturtechnik, Technische Fakultät, Universität Bielefeld.

Cells on Microcarriers

Mammalian Cells (BHK)

The correlation of permittivity to viable cell count is not influenced by the presence of microcarriers.

- Incyte helps avoid misinformed decisions caused by outliers (marked with the red circle)
- Microcarriers have no impact on permittivity measurements

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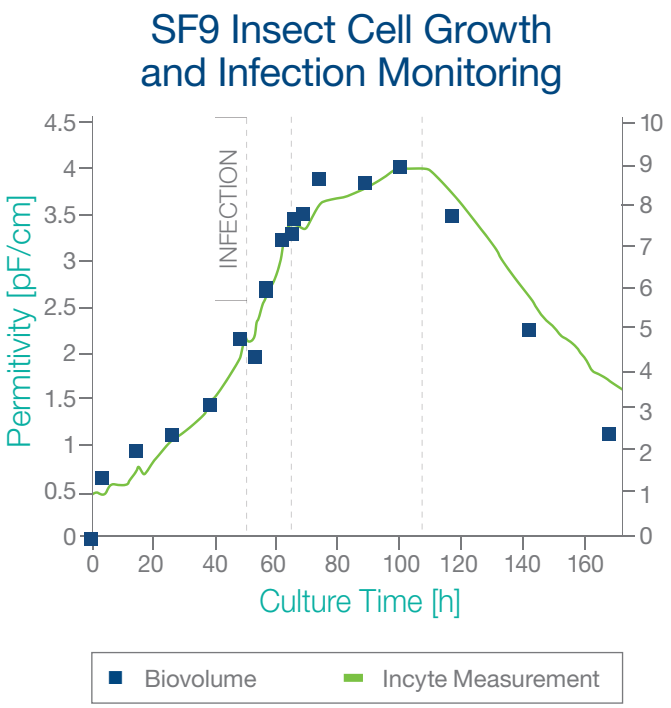
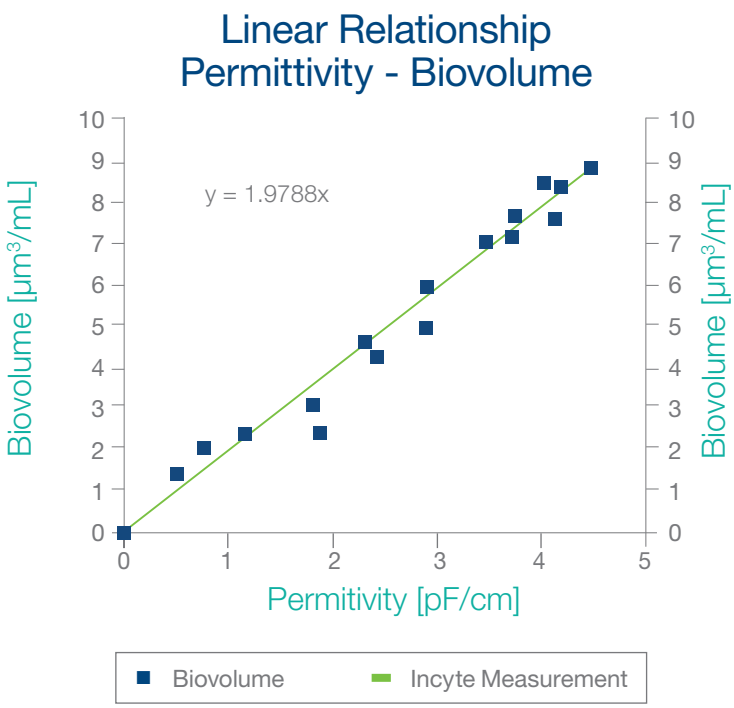
Biovolume to Permittivity

Insect Cells (SF9)

Permittivity shows a high correlation to off-line measurements of biovolume.

- Incyte correlates with biovolume throughout process





Esteban, G. (2006) On-Line Viable Cell Density and Physiological States Monitoring by Dielectric Spectroscopy sf9 Growth and Infection Process. Poster at Cell Culture Engineering X.

Related work: On-Line Monitoring of Infected Sf-9 Insect Cell Cultures by Scanning Permittivity Measurements and Comparison with Off-Line Biovolume Measurements. Sven Ansorge. Cytotechnology (2007) 55:115–124

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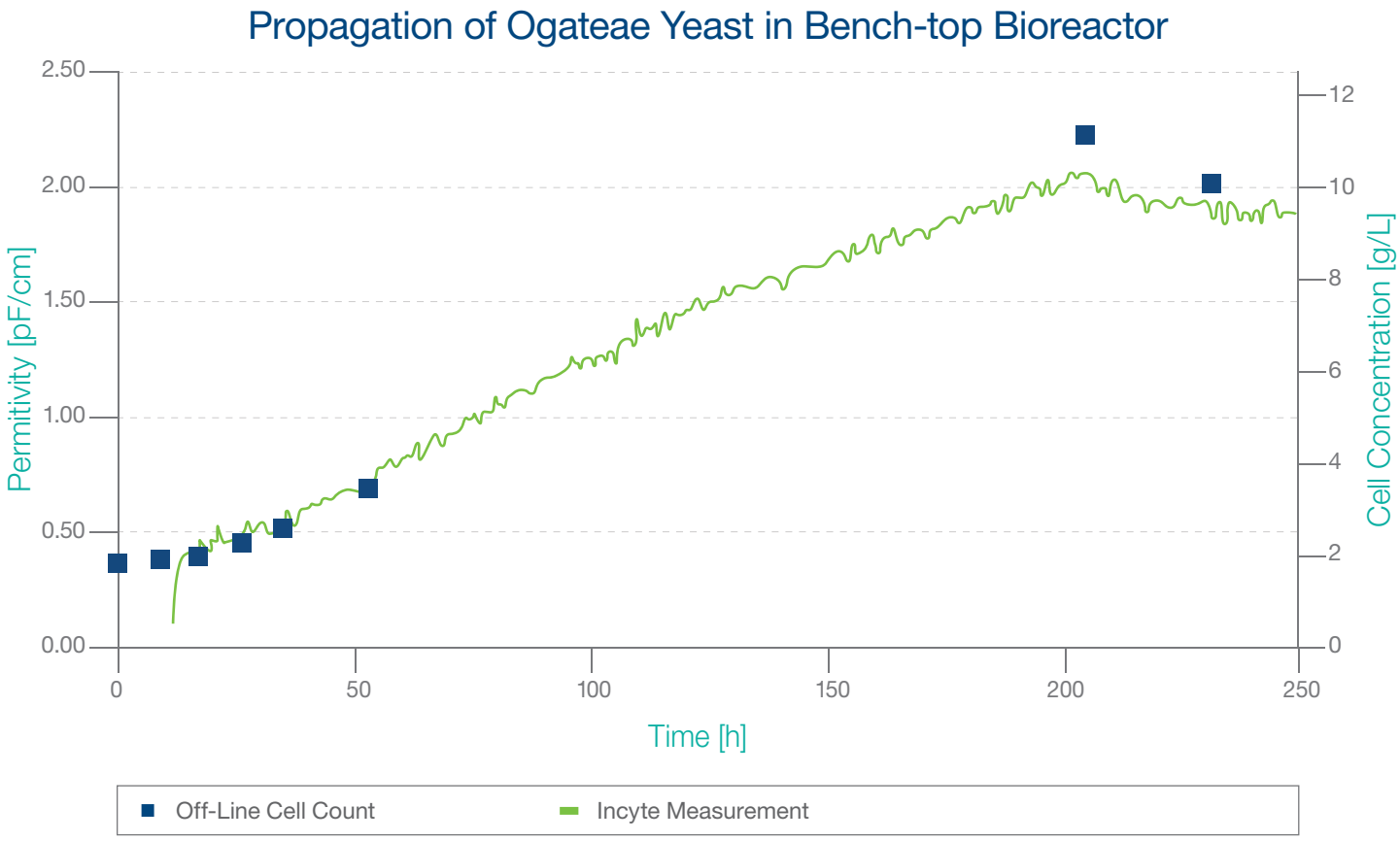
Concentration to Permittivity

Yeast (Orgatae)

Viable cell density monitoring correlates with the off-line measurement.

- Good correlation with dry weight throughout process
- On-line monitoring provides data 24 hours/day and 7 days/week, as compared with off-line sampling that is only done when technicians are on duty



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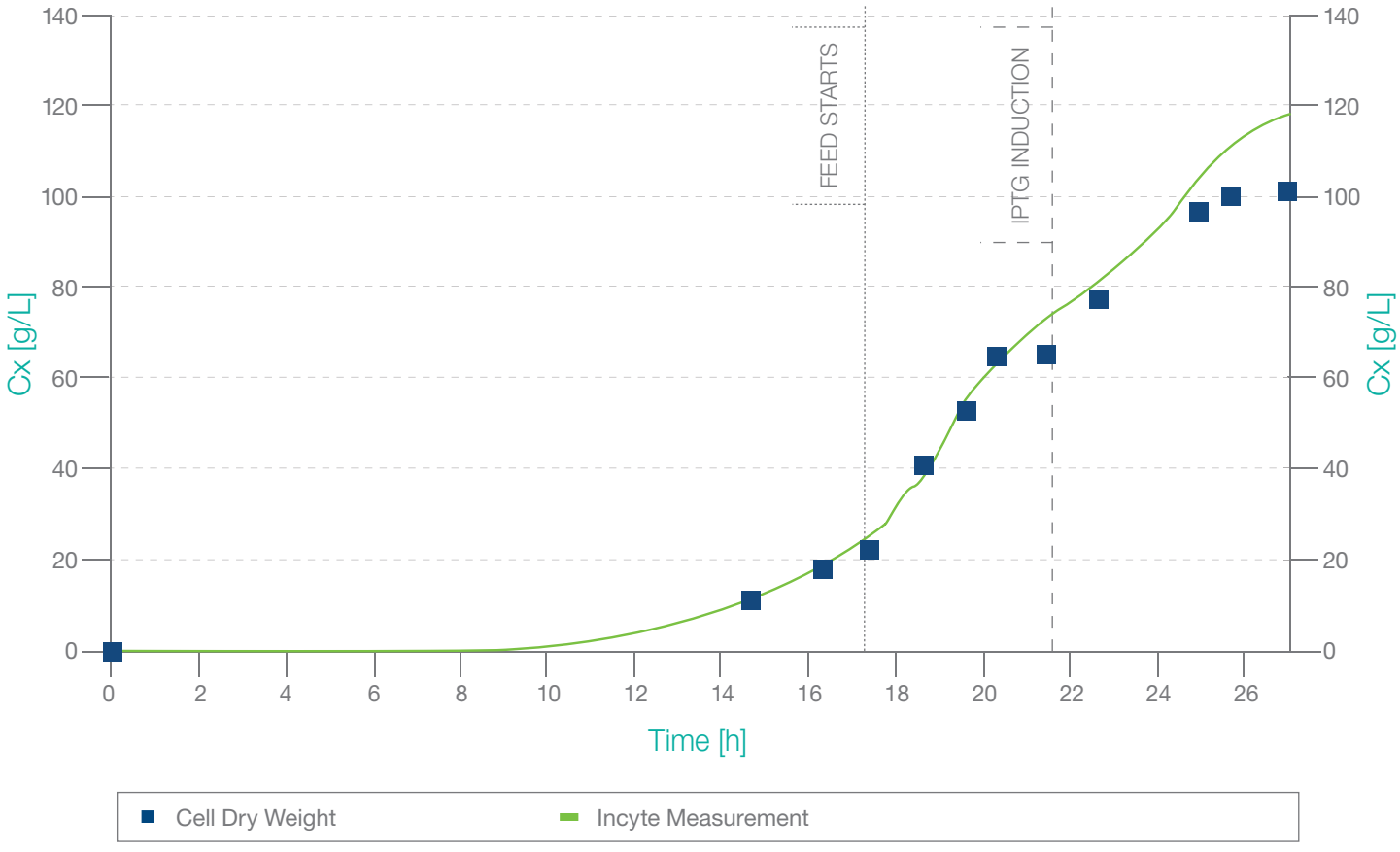
Dry Weight to Permittivity

Bacteria (E. coli)

Viable cell density monitoring correlates with the dry weight measurement.

- Incyte correlates to dry cell weight throughout feed and differs after induction, when production phase starts
- IPTG Induction starts the production phase and leads to increased bacterial size and permittivity



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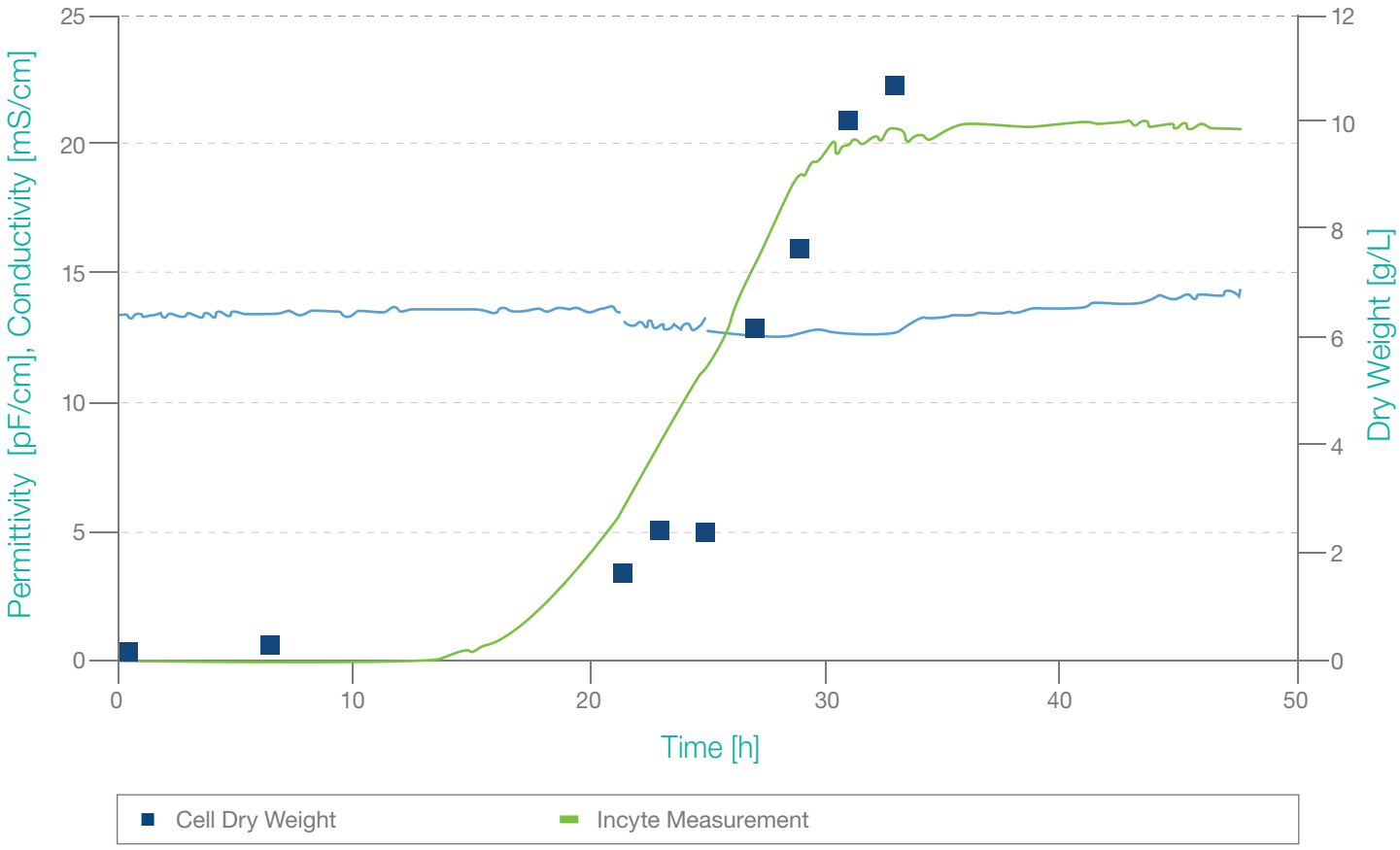
Dry Weight to Permittivity

Filamentous Fungi (Absidia)

Viable cell density monitoring correlates with the off-line method.

- Filamentous fungi show a high heterogeneity during cultivation, therefore reliable off-line sampling is very difficult
- Incyte can be used for on-line measurement of viable microorganisms – no sampling needed



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Talk to a Hamilton Expert About Your Cell Density Application

Now that you've seen Incyte and Dencytee in action, contact a Hamilton sales representative about how to apply this technology to your application and process.

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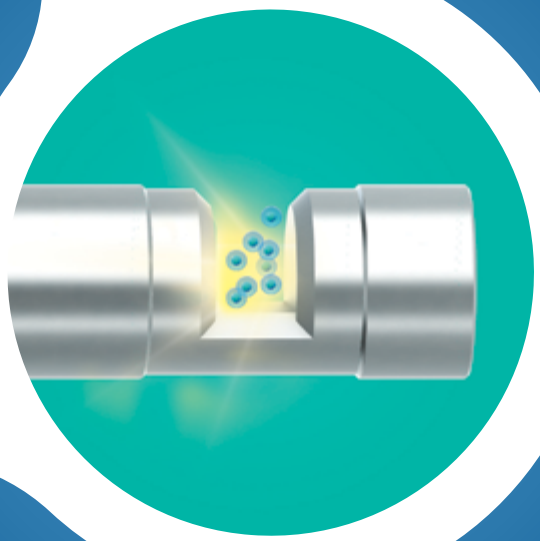
Europe: +41-58-610-10-10



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