HAMILT®N®

Online Data Real-Time Decisions Viable and Total Cell Density Sensors

Online Cell Density Monitoring

For the first time, you can monitor cells in real-time, obtain actionable data, and automate process adjustments

2

3

4

EASVFERNI PLUSARC 12

VISIFERIA DO ARC 120

Online measurement with methods such as control of pH and dissolved oxygen are common for most biological processes. In fact, many parameters can be monitored but those directly related to cell physiology are time consuming offline measurements that only provide a reactionary window into the past.

Incyte and Dencytee sensors provide a means for directly measuring viable and total cell density in real-time. Obtain advanced control with never-before instantly available data. With clear, up-to-date information, critical events that could have been missed between offline samples are now immediately recognizable. Automate production processes and strategize product development with new awareness in R&D.

1. TOTAL CELL DENSITY

Monitoring the total cell density is a reliable method for measuring cell growth. The most relevant information is obtained during the lag and growth phase before significant cell death occurs. With online measurements it is possible to detect process deviations and make the required adjustments.

2. VIABLE CELL DENSITY

Detecting when cells begin to die can be difficult when looking at the total cell density. Monitoring the viable cell density will show an immediate change and depending on the culture and timing will indicate next steps to take to maximize yield. In addition to cell death this measurement also provides information on changes in cell physiology.

3. pH

Precise control over pH is critical to generate the right product and maximize yield. Online pH control enables more frequent, small adjustments to pH that minimize stress and maintain a constant environment.

4. DISSOLVED OXYGEN

Oxygen is the most important gas for bioprocesses. Too little oxygen will result in apoptosis or anaerobic digestion, reducing the viability and yield significantly. Online monitoring and control of dissolved oxygen (DO) ensures the optimal amount of oxygen to maintain high quality products.

OFFLINE SAMPLING



ONLINE MONITORING

Obtain more data without manual intervention

- Early detection of process deviations
- Reduced labor and risk of contamination from grab sampling
- Increased product yield



Incyte

ONLINE MEASUREMENT OF VIABLE CELL DENSITY

The Incyte sensor enables real-time, online measurement of viable cells in solution. The measurement is not influenced by changes in the media, microcarriers, dead cells, or debris. Online measurement of viable cells makes it possible to detect events and respond in real time without sampling.

ELECTRIC

ELECTRODES

- Increase yield and lower production costs
- Detect changes in cell physiology with frequency scanning
- Precisely control harvesting for continuous culturing
- Early detection of process deviations
- Sensors optimized for multiple conductivity ranges

HOW IT WORKS

The Incyte measurement principle is based on capacitance. In an alternating electrical field, viable cells behave like small capacitors. The charge from these small capacitors is measured by the sensor and reported as permittivity (capacitance per area).

| | Conductivity Range (mS/cm) | Example Applications |
|--------------------|-------------------------------|---|
| Incyte Standard | 2 – 50 | General application (e.g. mammalian cell culture) |
| Incyte LC | 0.5 – 10 | Yeast propagation |
| Incyte HC | 5 – 100 | Bacterial fermentation with organic acid production (significant pH adjustmen |

DEAD CELLS HAVE DAMAGED MEMBRANES AND DO NOT POLARIZE

VIABLE CELLS POLARIZE

LC = Low Conductivity HC = High Conductivity





ONLINE MEASUREMENT OF TOTAL CELL DENSITY

The Dencytee sensor performs online measurement of total cell density in solution. The sensor is based on optical density, which measures the turbidity of the cell suspension. The measurement is made at NIR (near-infrared) wavelengths so it is insensitive to changes in media color. All particles and molecules that absorb or scatter light at 880 nm will be detected, including living and dead cells as well as cell debris. This measurement is effective after inoculation, when cells are expanding quickly but concentrations are low, making permittivity-based readings less reliable.

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

HOW IT WORKS

The Dencytee sensor emits light through a 5 mm window onto a light detector. Cells in suspension absorb and scatter light so less light is read by the detector. To compensate, the sensor increases the amount of light emitted by the light source to maintain a constant reading at the detector. By reading the amount of light that is increased at the light source, the Dencytee sensor can measure solutions with high cell densities. LIGHT SOURCE INCREASES INTENSITY TO COMPENSATE FOR THE TURBIDITY OF THE CELL SOLUTION

5 mm WINDOW

— LIGHT DETECTOR

Cell Density Measuri

INCYTE FOR VIABLE CELL DENSITY

A sensor unit consists of an Incyte sensor and a pre-amplifier, which converts the analog measurement to a stable digital signal. The digital signal is read by a Control Unit equipped with the Incyte License and optional Incyte Scan License.

| Ordering Information | | + Unit* | | | Replacement Sensors | | |
|----------------------|----------|----------|--------|--------|---------------------|--------|--------|
| | a-length | Standard | LC | HC | Standard | LC | HC |
| Incyte DN25 – SG | 70 | 243710 | _ | _ | 243730 | _ | _ |
| Incyte DN25 – DG | 46 | 243711 | _ | _ | 243731 | _ | _ |
| Incyte DN25 – DG BE | 54 | 243712 | _ | _ | 243736 | _ | _ |
| Incyte DN12 | 120 | 243700 | 243704 | 243762 | 243732 | 243716 | 243766 |
| Incyte DN12 | 220 | 243701 | 243705 | 243763 | 243733 | 243717 | 243767 |
| Incyte DN12 | 320 | 243702 | 243706 | 243764 | 243734 | 243718 | 243768 |
| Incyte DN12 | 420 | 243703 | 243707 | 243765 | 243735 | 243719 | 243769 |

SG = Single Gasket (Ingold) DG = Double Gasket (Sartorius / B.Braun) DG BE = Double Gasket Bioengineering LC = Low Conductivity HC = High Conductivity * When purchased as a unit, the sensor and pre-amp are factory calibrated.



Val/Cal Kit Incyte Ref. 243740 Solution A Ref. 238988 Solution B Ref. 243742
 Permittivity Simulator Ref. 243743

 Incyte Pre-Amp Ref. 243720

 5 m Cable M12/M12 Ref. 243870

10 m Cable M12/M12 Ref. 243871 20 m Cable M12/M12 Ref. 243872 40 m Cable M12/M12 Ref. 243873

DENCYTEE FOR TOTAL CELL DENSITY

A sensor unit consists of the Dencytee sensor and a pre-amplifier. It is connected to a Control Unit equipped with a required Dencytee License.

| Ordering Information | + | E Trans | |
|----------------------|----------|---------|---------------------|
| | a-length | Unit* | Replacement Sensors |
| Dencytee | 120 | 243755 | 243750 |
| Dencytee | 225 | 243756 | 243751 |
| Dencytee | 325 | 243757 | 243752 |
| Dencytee | 425 | 243758 | 243753 |

* When purchased as a unit, the sensor and pre-amp are factory calibrated.



Val/Cal Solution OD Ref. 243886 Dencytee Pre-Amp Ref. 243760 5 m Cable M12 Ref. 243870 10 m Cable M12 Ref. 243871 20 m Cable M12 Ref. 243872 40 m Cable M12 Ref. 243873



ng Loops



CONTROL UNIT

ARC VIEW CONTROLLER

Review all of your data at a glance. The Arc View Controller is used to collect and record data generated by the Incyte and Dencytee sensors. The Controller is a stand alone device designed for a production area with robust stainless steel housing. It can connect to either two (265) or four (465) sensors at the same time. The 265 and 465 Controllers have a 5.7" diagonal touch screen, while the 465XL has a larger 12" diagonal touchscreen for simplified viewing of multiple sensors. The Arc View Controller can wirelessly record Arc sensors, such as pH and dissolved oxygen, so all parameters can easily be viewed from a single screen.

- Record, display, and export measurement data
- Output measurement data as 4-20 mA*, OPC**, Profibus***, or Modbus
- Store calibration data for multiple sensors
- Wizards for calibration and troubleshooting
- Requires Ref. 243850, 4-20 mA Output Box with Cell Density and Conductivity outputs as well as four alarms ** Requires Ref. 243820, OPC License
- *** Requires Ref. 243889 Arc View Controller Profibus Converter

COMBOX

The ComBox is a compact alternative to the Arc View Controller 265 and is designed to easily fit minimal space requirements (19 x 8.5 x 5.6 cm). The ComBox is operated by a simple connection to an existing computer.

INTEGRATION KIT

Cell Density Integration Kit is designed to allow easy integration into skid fermenter controllers or production cabinets.

REQUIRED LICENSES

To properly run an Incyte or Dencytee sensor, the Control Unit must be equipped with the proper licenses. A license must be purchased for each Control Unit and is not transferable. An Incyte License is required to use Incyte sensors. An Incyte Scan License is optional for measurement at 17 additional frequencies to analyze the bioprocess in a more detailed manner. A Dencytee License is required to use Dencytee sensors. An OPC License is optional for connection to OPC network.

Ordering Information

| Choose Controller | | Choose License(s) - Mark Included (1) or Not Included (0) | | | | | |
|--|--|---|----------------|-------------------------------------|-----------------------|----------------------------|--|
| | Arc View 265 (2 – Sensor Inputs) 243800- | Code | Incyte License | | | | |
| | | 1 | Included | Included | | | |
| | | 0 | Not Incl | Not Included | | | |
| | Arc View 465 (4 – Sensor Inputs) 243801- | | Code | le Incyte Scan License ¹ | | | |
| | | | 1 | Included | Included | | |
| | | 0 Not Included | | ided | | | |
| | Arc View 465 XL (4 – Sensor Inputs) 243802- | | | Code | Code Dencytee License | | |
| | | | | 1 | Included | d | |
| | | | | 0 | Not Inclu | Not Included | |
| m | ComBox (2 – Sensor Inputs) 243810- | | | | Code | OPC License ^{2,3} | |
| | | | | | 1 | Included | |
| | | | | | 0 | Not Included | |
| | | Code | Code | Code | Code | Order Code | |
| Example of order code using the above table: | | ¹ Requires Incyte License | | ² Optional License for | | ³ OPC XML-DA | |

243800-1001 is an Arc View 265 with an Incyte and OPC License.

Dencytee or Incyte

ACCESSORIES

4-20 mA Output Box Ref. 243850 Dencytee License Ref. 243824 OPC License Ref. 243820

5 m Cable Output Box Ref. 243851 Incyte License Ref. 243822 Incyte Scan License Ref. 243823

Arc View Controller Profibus Converter Ref. 243889 10 m Cable Output Box Ref. 243852 Cell Density Integration Kit Ref. 243809

SPECIFICATIONS

Incyte

| | | a-length | 70 mm (SG), 46 mm (DG), or 54 mm (DG BE) | | |
|-----------------------------|--|------------------------------|---|--|--|
| | DN25 | O-ring Position (Gaskets) | 28 mm (SG), 28 mm and 52 mm (DG), or 28 mm and 44 mm (DG BE) | | |
| Dimensions | | Process Connection | G 1¼ (Ingold, Sartorius, or Bioengineering) | | |
| | DN12 | a-length | 120, 220, 320, 420 mm | | |
| | | Diameter | 12 mm | | |
| | | Process Connection | PG13.5 | | |
| Operating Temperature Range | 0 to 60 °C | | | | |
| Steam Sterilizable | Yes, maximum temperature 135 °C | | | | |
| Autoclavable | Yes | | | | |
| CIP | Yes | | | | |
| Measuring Range | 0 – 700 pF/cm, equivalent to viable cell density of: Mammalian cells in suspension 5·10 ⁵ cells/mL to 8·10 ⁹ cells/mL Fermentation 5 to 200 g/L dry weight | | | | |
| Conductivity Range | Standard: 2 – 50 mS/cm | LC: 0.5 – 10 mS/cm | HC: 5 – 100 mS/cm | | |

Dencytee

| a-length | 120, 225, 325, 425 mm |
|-----------------------------|---|
| Diameter | 12 mm |
| Optical Path Length | 5 mm |
| Process Connection | PG13.5 |
| Operating Temperature Range | 0 to 80 °C |
| Steam Sterilizable | Yes, maximum temperature 135 °C |
| Autoclavable | Yes |
| CIP | Yes |
| Optical Density 880 | 0 - 2500, equivalent to total cell density of: Mammalian cells in suspension 10^5 cells/mL to 7.10 ⁸ cells/mL Fermentation 0.5 to 100 g/L dry weight |
| Wavelength | 880 nm (NIR) |

©2017 Hamilton Company. All rights reserved. All other trademarks are owned and/or registered by Hamilton Company in the U.S. and/or other countries. Lit. No. 691141/06 — 11/2017

HAMILT®N

Web: www.hamiltoncompany.com USA: 800-648-5950 Europe: +41-58-610-10-10

Hamilton Americas & Pacific Rim

Hamilton Americas & Pac Hamilton Company Inc. 4970 Energy Way Reno, Nevada 89502 USA Tel: +1-775-858-3000 Fax: +1-775-856-7259 sales@hamiltoncompany.com Hamilton Europe, Asia & Africa Hamilton Bonaduz A.G. Via Crusch 8 CH-7402 Bonaduz, Switzerland Tel: +41-58-610-10-10 Fax: +41-58-610-00-10 contact.pa.ch@hamilton.ch

To find a representative in your area, please visit hamiltoncompany.com/contacts.