TELEDYNE ANALYTICAL INSTRUMENTS

Viable Cell Growth Monitor for the Bioprocessing Industry

Teledyne offers a low cost, fiber optic based, Fluorescence transmitter and in-situ probe for monitoring the growth rate of bacterial, yeast, or mammalian cells in a fermentation batch reactor via the fluorescence of NADH. The system incorporates state-of-the-art electronics connected to a fiber optic based in-situ probe. The probe is a patent pending, front surface fluorescence probe minimally affected by the inner-filter effect.

Defining the Problems

Product yields may be greatly increased if monitoring of cell growth is managed properly. There are many factors affecting the maximum growth of cells in a batch reactor such as; proper balance of dissolved nutrients, pH, temperature, pO2, pCO2, etc. Continuously monitoring the rate of growth can provide a record that the cells have reached their maximum density within a given time frame.

Monitoring cell growth traditionally has been done with scatter or turbidity type instruments that measure the optical density (OD630) in the NIR region. Although this approach is an indicator of cell density, it also measures the TOTAL amount of light scattered which is the sum of the living cells, dead cells, cell debris, and possible reabsorption by the growth media.

One very important parameter for the assessment of bioprocesses is the metabolic state of the organisms. This parameter yields information about the metabolic activity of the growing cells, the biomass development, and changes in the composition of the nutrition medium.

Endogenous fluorescence signals attributed to the amount of reduced nicotinamide adenine dinucleotide (NADH) in the cell have been correlated with viable cell growth. Additionally, possible consequences of increasing NADH content can indicate;

- Viable cell activity
- Nutritional media uptake
- Growth of specified organism
- Respiration
- Biosynthetic reduction

The Teledyne Solution

Numerous bioanalytical assays are based on the fact that the coenzyme NADH is fluorescent, while NAD+ is not. As a result, all enzymatic reactions based on NAD/NADH are amenable to fluorescence analysis. TAI's Viable Cell Growth Monitor delivers excitation energy from a pulsed UV lamp and monitors the amount of fluorescencent NADH in the cell. The system consists of a fiber optic based UV fluorescence transmitter and probe (patent pending) that can be permanently mounted into either a bench top or process batch reactor.

Photometric Transmitter

Teledyne's photometric transmitter displays and retransmits a 4-20 mA signal proportional to the amount of fluorescent energy captured in the fermentation reaction vessels. This reading is based on the amount of fluorescence from the viable cell suspension in the fermentor as compared to a reference signal.

A pulsed Xenon UV lamp delivers the excitation energy to the fiber optic probe and the emitted energy is measured with two solid state surface mounted photomultiplier tubes. A ratio of the fluorescence to baseline signals are scaled over a 4-20 mA output. This design makes monitoring in the kinetic mode (above the background) easy to set up. Monitoring the relative signal change and not total intensity can reduce background interferences.

Viable Cell Growth Monitor for the Bioprocessing Industry

Calibration

Calibration of the Viable Cell Monitor is performed by a span filter that is integral to the transmitter and allows the user to employ a calibration by standard addition technique without mixing solutions or running samples to a lab. All span/calibration filters are supplied with their respective fluorescence response. Introduction of the span filter can be performed either remotely, via contact closure, or at the front of the transmitter by pressing the span switch.

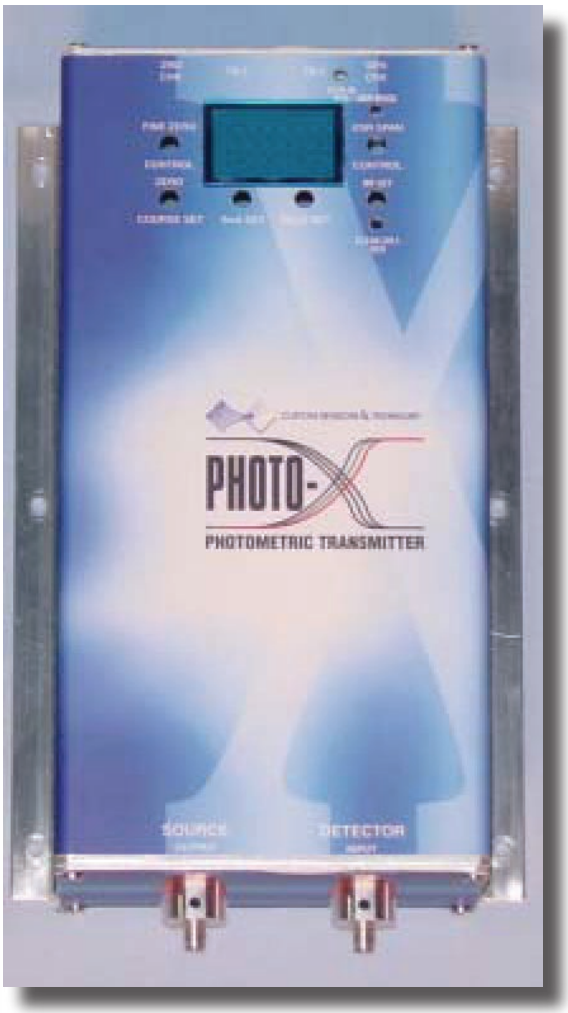
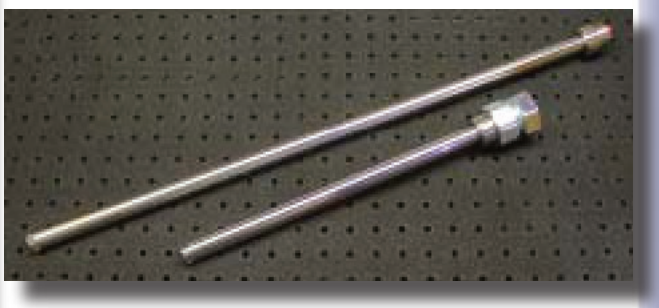


Photo-X Viable Cell Growth Transmitter

TAI's probes are designed to withstand CIP, SIP, and Autoclave conditions. The sample interface devices can be supplied with sanitary designs that fit the standard Ingold type fittings and 12 mm diameter bodies with PG 13.5 nuts.

Front surface probe tip showing central collection fiber surrounded by a ring of illuminating fibers. Geometry of the front surface design significantly reduces the inner-filter effect and greatly increases dynamic range.

Probe fibers are completely isolated from the process. A low surface energy optical window further reduces the amount of material that can stick to the front surface.



Two fiber optic probe body lengths, patents pending

Where can the unit be used?

- Fermentation
- Pharmaceutical plants
- Agricultural plants
- Yeast plants
- Mammalian cells
- Upstream processing

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SPECIFICATIONS

Transmitter

Measured parameter:	Viable cell density based on NADH fluorescence
Temperature range:	-40 to +125° F
Response time:	< 5 sec
Maximum Zero shift:	< 0.5% of full scale
Long term output drift:	< 2 % / month
Repeatability:	1% of range
Range:	0-20 g/l
Source:	Xenon Flash Lamp, typical life is 3 years

User Display & Control

Type of display:	LED display
Display:	Numerical format, 3-1/2 digits in user defined engineering units

Electrical

Power requirement:	24 VDC (9-32 VDC)
Power consumption:	0.48 Watts
Analog outputs:	4-20 mA isolated
Analog loop resistance:	500 Ohms, maximum @ 24V

Mechanical

Analyzer weight:	1.5 lbs
Enclosure:	Extruded aluminum, NEMA 4X optional 8” H x 3-7/8” W x 1.5” D

Front Surface Fluorescence Probe

Materials:	316SS, other material available, please consult factory
Temperature rating:	315.5° C (600° F)
Diameter:	12 mm with PG 13.5 nut
Length:	120, 200, 325 mm; please specify
Pressure rating:	Up to 5,000 psig

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Warranty

Instrument is warranted for 1 year against defects in material or workmanship. NOTE: Specifications and features will vary with application. The above are established and validated during design, but are not to be construed as test criteria for every product. All specifications and features are subject to change without notice.

CERTIFIED
ISO 9001 : 2000

Accredited by the Council for Accreditation (RvA)

National Accreditation Program

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