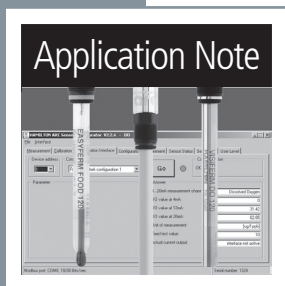


Oxygen Measurement in Fermentation with VISIFERM DO



Dissolved Oxygen Sensor in Microbial Fermentation: Lower maintenance costs, higher reliability, immediately ready to use

Industry: Pharmaceutical / R & D / Protein Synthesis

Application: Fermentation

HAMILTON Product: VISIFERM DO

Fermenters for Research and Development have to meet very high standards in regard to flexibility, so that they can be easily adapted to the requirements of a wide variety of micro-organisms and process conditions. For that purpose, modular fermentation systems were developed, consisting of single modules like drive, fermentation vessel, analytical instrumentation, stirrer, foam separator, ventilation and so on. This allows for individual assembly and upgrades.

In order to achieve good growth of the micro-organisms and high yields in protein expression the following factors in fermentation are important: medium, gas metabolism, temperature, pH, and pressure.

The concentration of dissolved oxygen in the medium (proportional to the pO_2^* value) is an important parameter of the gas metabolism. The HAMILTON VISIFERM DO sensor was tested for four months monitoring this parameter.

The measurement site

The rate of the stirring speed and air flow starts with a default value set by the process control system (PCS). During fermentation the oxygen concentration in the medium declines. The PCS adjusts stirring speed and air flow in order to keep the oxygen concentration at 50% saturation.

As shown in the graph, the entire fermentation process lasts only about five hours. At the end of fermentation the content of the fermenter is cooled and centrifuged. The empty fermenter with the VISIFERM DO still installed is filled with 0.1 M KOH and dead autoclaved (sterilized) at 121 °C for 25 minutes. Subsequently, it is flushed with deionized water. This procedure is very demanding on the DO sensor, due to the many cleaning and sterilization cycles per week.

* The partial oxygen pressure (pO_2) is determined as dissolved oxygen (DO).

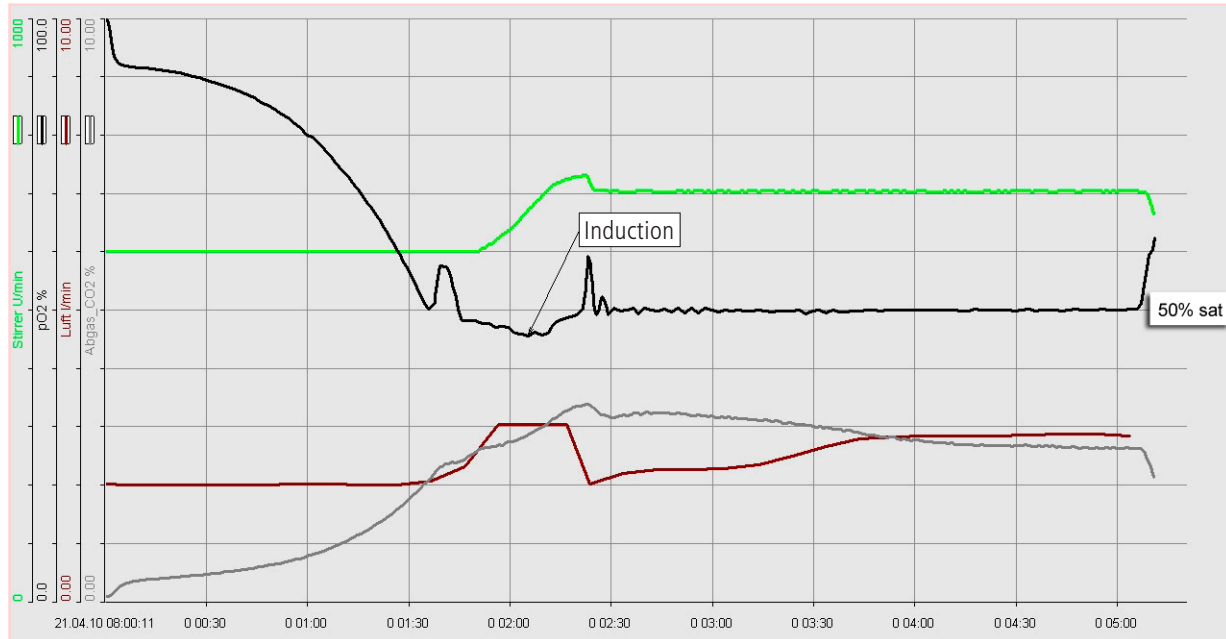


Figure 1: Measurement values from the process control system:

— Stirrer in RPM — Dissolved Oxygen measured with VISIFERM DO as %sat — Air in l/min
— Exhaust gas CO₂ in %



Improvements with VISIFERM DO

The user handling of VISIFERM DO is much easier than that of an electrochemical Clark sensor. The frequent exchange of electrolyte and membrane caps is unnecessary, and long wait times are eliminated because there is no polarization needed - the sensor is ready for use immediately.

Furthermore, the VISIFERM DO shows more stable readings after the frequent sterilization cycles shown in this application. With the help of the VISIFERM D4 power adapter, the VISIFERM DO sensor was run in ECS mode* without any technical changes to the existing PCS.

* In ECS mode, VISIFERM DO emulates the electrical behavior of an electrochemical DO sensor (ECS).

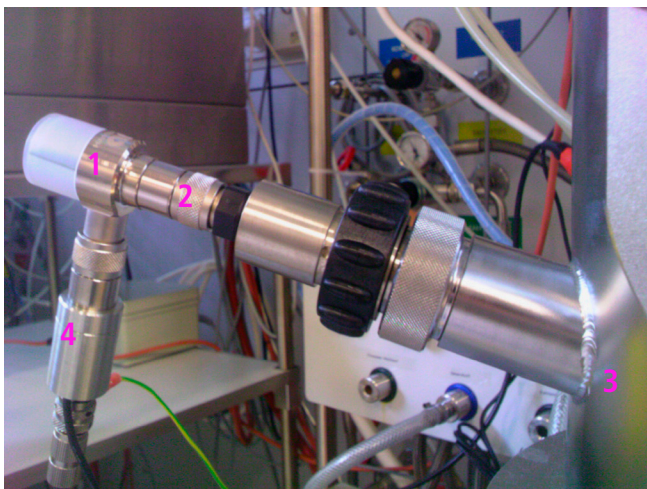


Figure 2:

- 1 ARC Wi Sensor Adapter
- 2 VISIFERM DO
- 3 Fermenter
- 4 VISIFERM D4 Power Adapter

Technical data Visiferm DO

Range of measurement:	0.05 to 300% air saturation
Detection limit:	0.01 %-vol
Response time t98%:	< 30 s at 25°C, from air to nitrogen
Oxygen consumption:	None
Required flow:	None
Operating temperature:	-10 to 130°C; the sensor provides no DO reading above 80°C
Pressure range:	0 - 12 bar; spikes up to 80 bar
Measurement principle:	Oxygen dependent luminescence
Medium contacted materials:	Stainless steel 316L/DIN 1.4435 FDA approved silicone and EPDM
Surface quality of steel:	Ra = 0.4 µm (N5)
Interface:	Configurable 4-20 mA interface (DO or Temperature), digital RS485 Modbus RTU interface

User benefits of VISIFERM DO:

- Long sensor life-time under frequent sterilizations
- Maintenance free: No exchange of electrolyte, robust sensor cap
- Ready to use: No waiting time for polarization
- Highly stable DO readings after sterilization

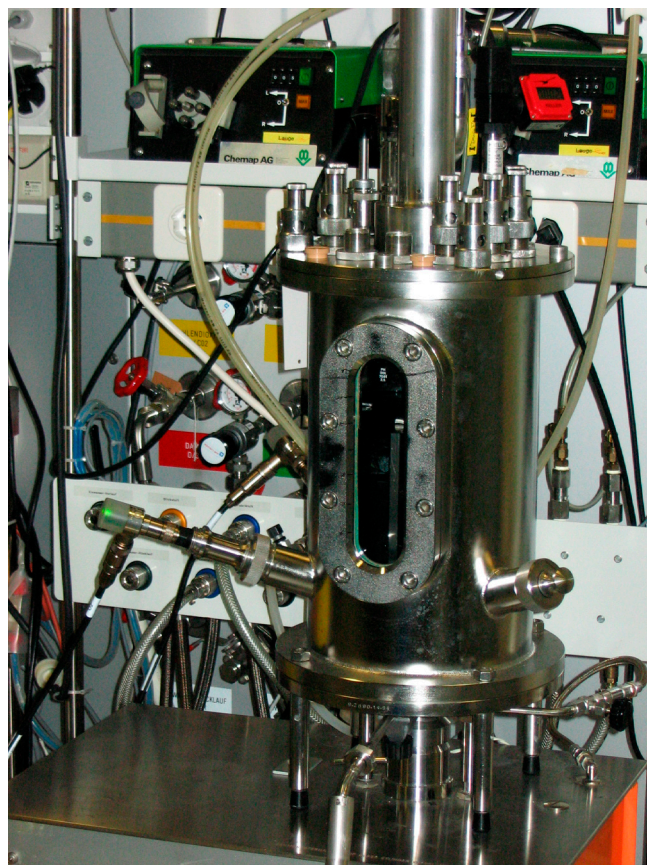


Figure 3: Fermenter with Visiferm DO and ARC Wi Sensor Adapter

Author:

Christian Miscenic
Technical Support & Fermentation
F. Hoffmann-La Roche Ltd
CH-4070 Basel
www.roche.com



www.hamiltoncompany.com

PN: 695098/00 10-2010

HAMILTON Bonaduz AG
Via Crusch 8
CH-7402 Bonaduz, Schweiz
Telephone: +41 81 660 60 60
Fax: +41 81 660 60 70
contact@hamilton.ch

HAMILTON Company
4970 Energy Way
Reno, Nevada 89520 USA
Telephone: +1 775 858 3000
Fax: +1 775 856 7259
sales@hamiltoncompany.com

HAMILTON Shanghai Rep.
German Centre, 88 Keyuan Road
201203 Shanghai, PRC
Telephone: +86 21 2898-6567
Fax: +86 21 2898-6275
hlu@hamilton.ch

Contact in Japan
Sibylle Ito
Mobile: +81 90 8032 2727
Email: sito@hamilton.ch