Bioreactor Design for Syngas Fermentations

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Agenda

Overview Bioreactor Design

Bioreactor Design for Syngas Bioprocesses

Suitable Software

Conclusions
Our company is true to its roots and to our traditional Swiss values. We combine perfection with passion. We work on each solution with scrupulous care and imaginative flair until everything fits like clockwork. We are instinctively quality-conscious and place a high value on top-quality materials and expertly trained employees. Our stable corporate culture ensures that we remain firmly grounded and determinedly independent. To us, our Swiss heritage means that we also act sustainably — in environmental, social and economic terms.
History

1965  Founding of Hawrylenko Technique by Alexander Hawrylenko, 1st patent

1967  First shaker for high-speed applications

1968  First 75 L bioreactor

Today  Complete solution portfolio for cultivations from 1 mL up to 1000 L paired with powerful software; Microbial, cell culture, biofuel 2nd and 3rd gen. and specialised bioprocess platforms
Strong Bioprocess Platforms Enhanced by Powerful Software
Overview Bioreactor Design
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- Motor
- Exit Gas Cooler
- Corrective Agents
- Culture Vessel
- Human Machine Interface (HMI)
- Sensors
- Pumps
- Gas Supply
- Base Unit w/ Controller
Bioreactors for Syngas Bioprocesses

- Provide syngas (& safety requirements)
- Understand and control process (sensors)
- Adapt to requirements of process
  - Slower growth
  - Low CO & H₂ solubility
Supply of Syngas

- Easy to set up, but composition of syngas cannot be adjusted easily.
• Gas mix station with 4 individual MFCs (CO, CO2, N2, H2)
• Can provide any syngas composition to bioreactor
• Ideal for process development
Safety Measures for Syngas

Explosive range

- $\text{H}_2$ 4-77 vol% (air, 1013 mbar, 20 °C)
- CO 10.9-76 vol% (air, 1013 mbar, 20 °C)

Toxicity

- CO Threshold limit value = 30 ppm
- CO$_2$ Threshold limit value = 5000 ppm (0.5 vol%)
Safety Measures for Syngas: Prevent Leakages

- Powerful addon to Labfors 5
- Small footprint (size of an DIN A4 paper)
- CIP and SIP with hot NaOH and strong energy input by stirring
- Developed in cooperation with Novartis, CH, and further optimised during SYNPOL project
- No need for error-prone dis- and reassembly of bioreactor for cleaning → Syngas lines stay connected safely
1. New fume hoods (Sysmex Digitana AG) and new ventilation system (GD Climat)

2. Gases stored outside the lab and brought to the fume hoods with newly installed pipes equipped with electrovalves (PanGas)

3. Emergency kill switch (for the manual switch-off of electrovalves)

4. Detectors of H₂ and CO (GFG AG) automatically switching off the electrovalves if triggered

5. Alarm panels + sound warnings (GFG AG) inside and outside the lab
Understanding and Controlling the Process: Sensors

- What happens inside the bioreactor?
- Which gas(es) are actually used?
The Redox Potential (Oxidation Reduction Potential, ORP)

- ORP = Measurement of the tendency of a solution to either acquire or lose electrons, influenced by:
  
  ✓ Temperature
  
  ✓ Dissolved oxygen
    main parameter for aerobic conditions: \( E_{O_2/H_2O}^0 = +820 \text{ mV} \)
  
  ✓ Gases
    \( O_2 \) increases the redox potential
    \( H_2 \) decreases the redox potential
    \( N_2 \) indirectly acts on the ORP by stripping off \( O_2 \) or \( H_2 \).
  
  ✓ Ratio oxidizing/reducing compounds
    nutrients, metabolites,…

- Extracellular ORP = indicator of the net outcome of intracellular metabolism (e.g. electron transfer and redox balance)

- Many biological functions are affected by the intracellular ORP (e.g. gene expression, enzyme synthesis)
Understanding the Process: Mass Spectrometer

- How much syngas is used? Is one of the gasses limiting?
- Other than for O\textsubscript{2}, no online sensors suitable for bioprocesses exist
- Exit gas is analysed using a mass spectrometer
- Multiplexing possible: 1 MS for multiple bioreactors
- All information is transmitted and stored with batch data from bioreactor
Adapting for Process: Precise & Slow Feeding of Substrates

- Slow growing process requires low feed volumes: 6.66 µL min\(^{-1}\) to 333 µL min\(^{-1}\)

- Use standard bioreactor pump with low diameter tubing for low flow rate

- Precise feeding thanks to closed loop control using coriolis flow sensor
Adapting for Process: Improving Gas Transfer

- Choosing the right sparger, impeller, and parameters
- Sinter sparger: more & smaller bubbles even at lower stirrer speeds & flow rates
Adapting for Process: Gas Recycling

- A variable portion of the exit gas can be re-circulated → Increase the aeration rate without wasting syngas

- Flow is generated by a pump and monitored with the MFM
Adapting for Process: Overpressure

- Direct effect on gas transfer & solubility → Availability can be greatly increased
- Difficult in glass bioreactor due to risk of rupture
- Consequently limited to 500 mbar overpressure
- Higher overpressure can be achieved in (usually larger) stainless steel vessels
- Also, hydrostatic pressure helps in large, production scale bioreactors
Summary Bioreactor Design: Features & Modifications

- LabCIP for safe and risk-free handling
- 5 Mass Flow Controllers (custom syngas & O2)
- Infrastructure for safe work with syngas
- Sensors & analysers (Redox, Mass-spec)
- Precise feeding w/ low flow rates
- Optimisation of gas transfer & usage:
  - Different sparger designs for better kLa
  - Gas-recycling loop (w/ pump and MFM)
  - Possibility for overpressure up to 0.5 bar
eve® - the platform from planning to project success

Plan | Prepare | Process | Analyze | Successful project

The bioprocess platform software that integrates:
- INFORS HT bioreactors and shakers
- 3rd party devices
- other software (Matlab…)
eve® is an excellent planning tool

Architecture for big projects

Helps organize strain information and media composition

Plan single & multi batches

Overview for planned batches

Share selected recipes & results with group and/or project partners
A revolutionary batch strategy tool

Intuitive horizontal batch strategy design:
- Made for “bioprocess minds”
- Preconfigured functions – no coding needed
- Time and event-based phases
Modern monitoring

State of the art charting technology:

- Up to 4 charts per window
- Charts highly customisable
- Dynamic or fixed range alarms
- Real-time comparison of running and completed batches (synchronization function)
eve® unifies bioprocesses. All of them.

All bioprocess information centralised
- NoSQL (not only SQL) Database: ElasticSearch
- Ready for big data
- Reliable and secure

Work where you are
- Web-based technology
- Unlimited user access from everywhere with authorization to access the network
- Only one central server needed, no installation on clients
Web-based technology:
• No installation is needed
• Platform independent (Mac, Windows, Linux…)

centralised server
stable & performant

Other data sources