THE IMPORTANCE OF THE OXYGEN TRANSFER RATE IN BIOREACTORS

- Cells in aerobic cell culture, but also bacteria and yeast, take up oxygen from the liquid phase. The rate of oxygen transfer from gas to liquid is of prime importance, where the demand for dissolved oxygen is high.
- To eliminate oxygen limitations and allow cell metabolisms to function at their best, the dissolved oxygen concentration has to be above a critical level at any point of the bioreactor.
- An increasing oxygen depletion (anaerobic environment) in a bioreactor causes both a lower productivity and undesired metabolites.
- The whole upstream process is impaired in terms of product quantity, quality, purity and safety.
- The scale-up and scale-down of the process has to be guaranteed.
- The bioreactor design and operation can highly affect the OTR.

INNOVATIVE SOLUTIONS FOR OUR CUSTOMERS

- FDA GENERAL GUIDANCE FOR PROCESS VALIDATION
  - Laboratory or pilot scale models to be representative of the industrial process
  - Laboratory or pilot scale assist in prediction of the industrial process
  - Laboratory and pilot scale provide additional assurance that the commercial manufacturing process performs
  - To understand the industrial process sufficiently, the manufacturer will consider the effects of scale

EVOLUTION OF TECHNOLOGY

- Why measuring kLa?
  - Ensure adequate supply of oxygen
  - Optimize control variables
  - For a better process understanding
  - Optimize scale-up and scale-down models
  - For an improved bioreactor design

- KEY VALUES OF kLa OPTIMIZATIONS:
  - Higher product yield and quality
  - Better product purity and safety
  - Optimized processing time
  - Lower power consumption

BIOREACTOR CHARACTERIZATION – FOCUS ON kLa MEASUREMENT

- The bioreactor should create a biosphere that provides the ideal environment for optimum growth conditions for microorganisms to meet the main target of production: maximum product formation.
- The design of a bioreactor for the optimal process is a challenge for bioengineers. In this context special focus is set on the oxygen transfer rate (OTR), and the kLa value in particular, which is among the most critical parameters for the design. In biotechnological processes, the kLa factor indicates the efficiency of oxygen supply. Possible measures taken to increase the kLa include: increased power input and gassing rate, optimization of fermenter design and agitator geometry and optimization of the media composition, thus overall improving the performance of the biological process. Since the kLa value depends on numerous hydrodynamic conditions, it cannot be precisely predicted. Therefore empirical investigation by means of kLa measurements is imperative to the success and stability of the process.

ZETA Business Activities

- Bioreactors & Fermentation Systems
- Downstream Systems
- Preparation Systems
- CIP/SIP Systems
- Magnetic Agitators
- Freeze & Thaw Systems
- Engineering
- Automation

Customer Benefits

- Deep process understanding
- GMP FDA Compliance
- Super-Skid Design
- Focus on sterility
- High process reliability
- Scale-up capabilities
- Experience in complex biologics
- Customized process systems

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Optimized reactor design & process scale-up

STARTING-POINT:
- The bioreactor design is not fixed
- Concept phase under development

STRATEGY:
- The services after testing of different design and sparger design combinations to find the most suitable system for the biotechnological process.
- They include test runs with DW water under defined process conditions.
- Performance indicators kLa, mixing time and shear stress are determined.

BENEFITS OF THE SERVICE:
- Optimized control variables on the basis of the characterization of the bioreactor system (kLa, mixing time, shear stress).
- Deep understanding of process conditions on bioreactor equipment or scale-up.
- Insights on process criteria as crucial adjustment parameters for various process conditions.

ADVANCED-SERVICE: BIOREACTOR CHARACTERIZATION

Knowledge based optimization on production scale bioreactors

STARTING-POINT:
The existing lab- or pilot production scale bioreactors are scaled-down under operation at customer's side.

STRATEGY:
- The services include test runs with DW water under defined process conditions.
- Performance indicators kLa and mixing time are determined.

BENEFITS OF THE SERVICE:
- Higher productivity and quality due to optimized process design.
- Faster optimization of bioreactor geometries, agitation design and process conditions.
- Insights on process criteria as crucial adjustment parameters for various process conditions.

MEASUREMENT METHOD
- Fast detection system using high speed oxygen probes
- Measurement points all over the bioreactor for a comprehensive vessel characterization
- No structural changes of the fermenter needed
- Bubble separator prior to measurement for optimization measurement results
- Accurate data analysis by using proven calculation models

SUBSTANTIAL ADVANTAGES
- Fast and efficient test runs with DW water under defined process conditions.
- Performance indicators kLa and mixing time are determined.

TYPICAL APPROACH OF MEASUREMENT

Modeling

Measurements and data analysis

Prior knowledge

Design of Experiments (DoE)

Results

Parameter optimization

Design optimization - bioreactor scaling

Design optimization - bioreactor scaling

Model validation for kLa prediction

Results

Parameter optimization for scale-up

Parameter optimization for scale-up

Model for scale-up for larger commercial scale

Model for scale-up for larger commercial scale

Modeling

Measurements and data analysis

Prior knowledge

Design of Experiments (DoE)