

# Innovative microbioreactor applications in bioprocess development

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## AIMS & OBJECTIVES

- **Novel design of micro-technologically manufactured cultivation systems**
  - Investigation of scale up/down effects
  - Restrictions in miniaturization
- **Primary focus on rapid generation of data for process development**
- **Implementation of online measurements and multiparametric online analysis** for automated cultivation system
  - Promoting parallelization
- **Open up new fields of application for microreactor systems with increased specialization**

Development of microbioreactor (MBR) systems with improved oxygen transfer and mixing characteristics

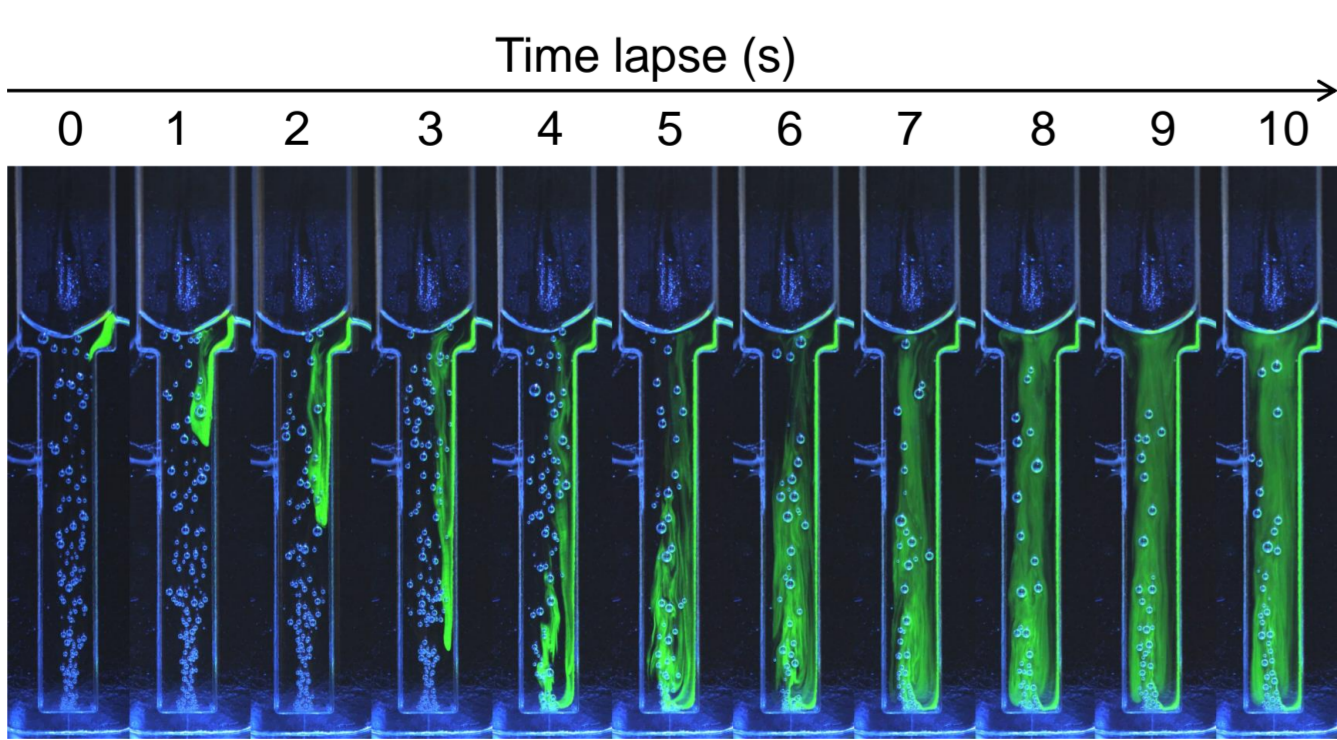
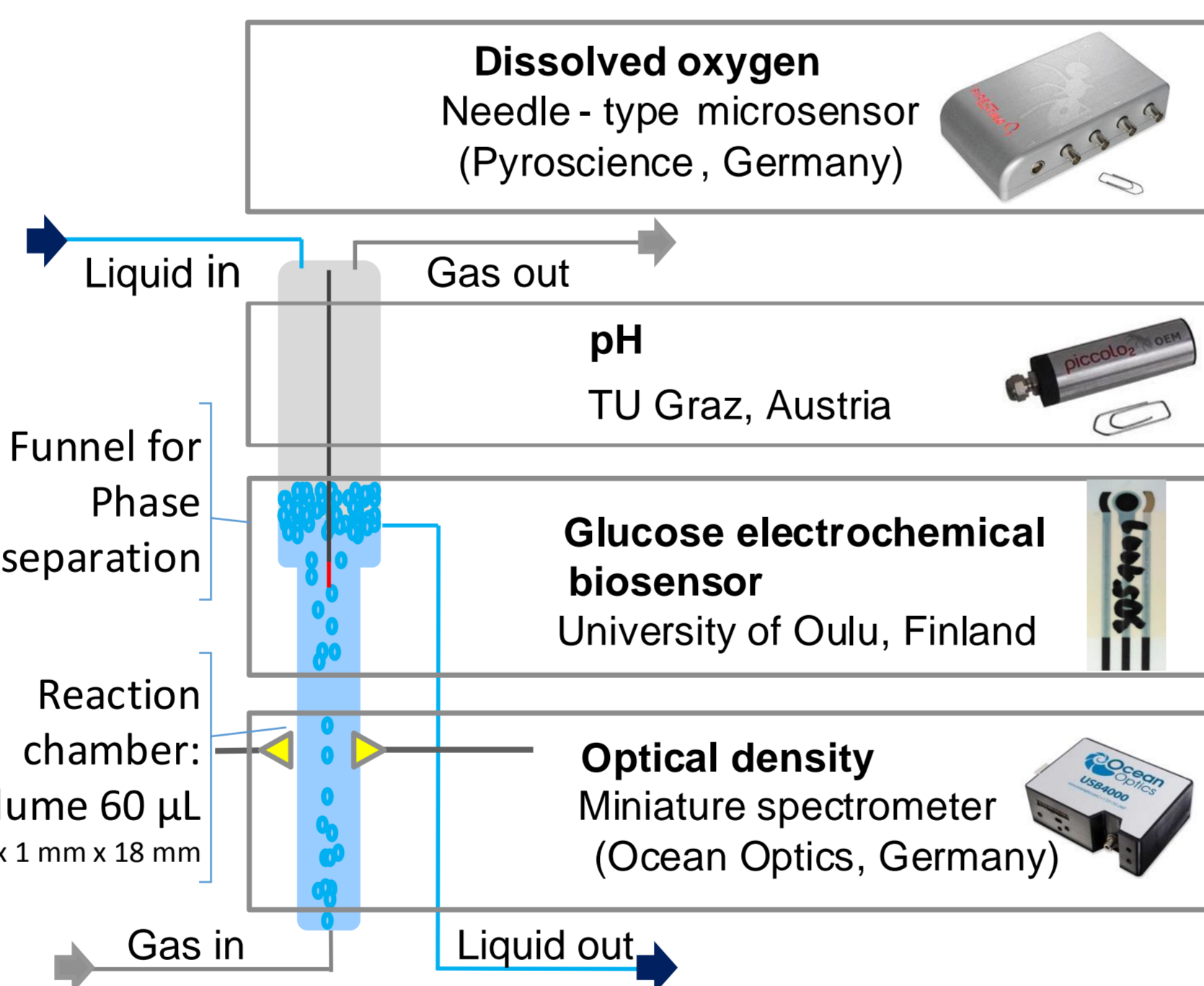
Improvement of sensor technology for precise measurement and analysis  
→ Increase in accuracy, robustness and validity

Application of MBR for optimization in biopharmaceutical research and process development

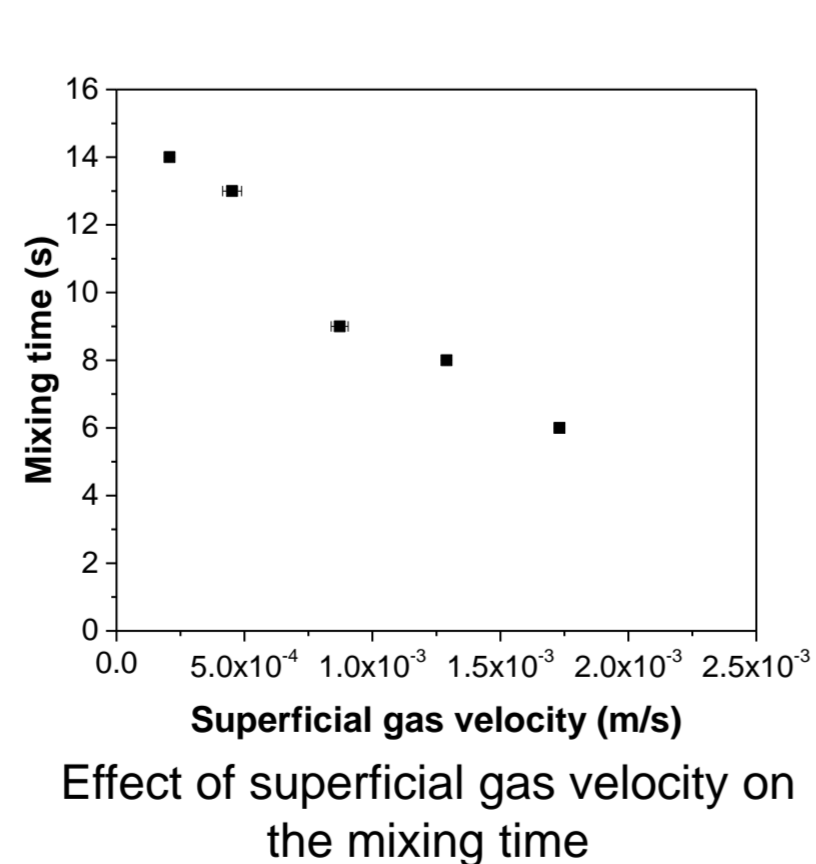
Long term goal: Lab-on-a-chip system  
→ Integration of all sensor equipment on single device for automated experiments

## MICROBUBBLE COLUMN-BIOREACTOR ( $\mu$ BC)

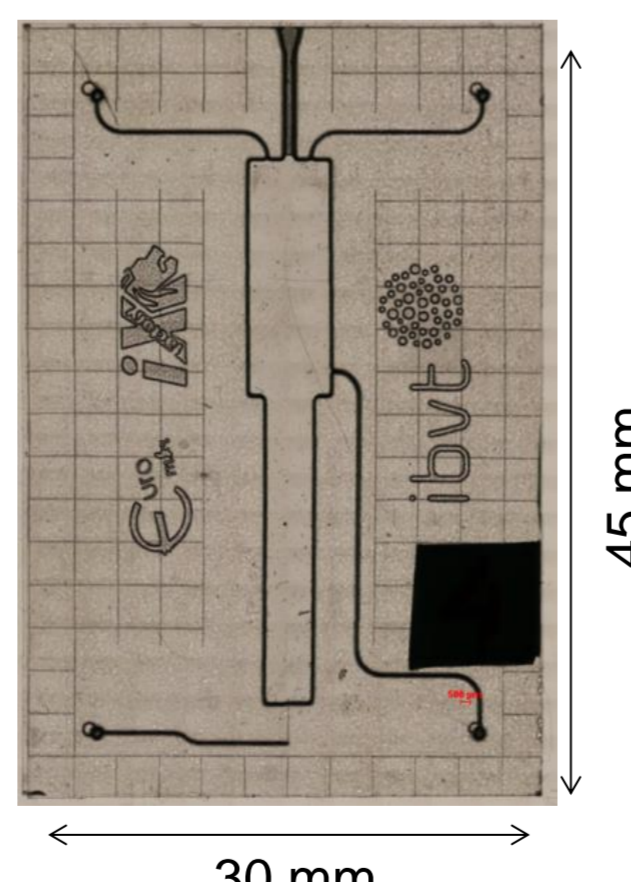
- Continuous stream of microbubbles that rises through the vertical device
- Homogenization and aeration through convective flow of bubbles induced into bottom  
→ Agitation of cultivation broth solely by insufflation of air
- No error prone movable parts for increased reliability
- Fabricated by wet etching and powder blasting technology in borosilicate glass (Micronit GmbH, Dortmund).
- Pressurized air is supplied through a nozzle ( $\phi = 26 \mu\text{m}$ ) at the base of the  $\mu$ BC
- Online measurement of optical density, pH, oxygen and glucose



A pulse of 2  $\mu\text{L}$  of fluorescent tracer is introduced while the air flow is set at 0.6  $\mu\text{L/s}$ .



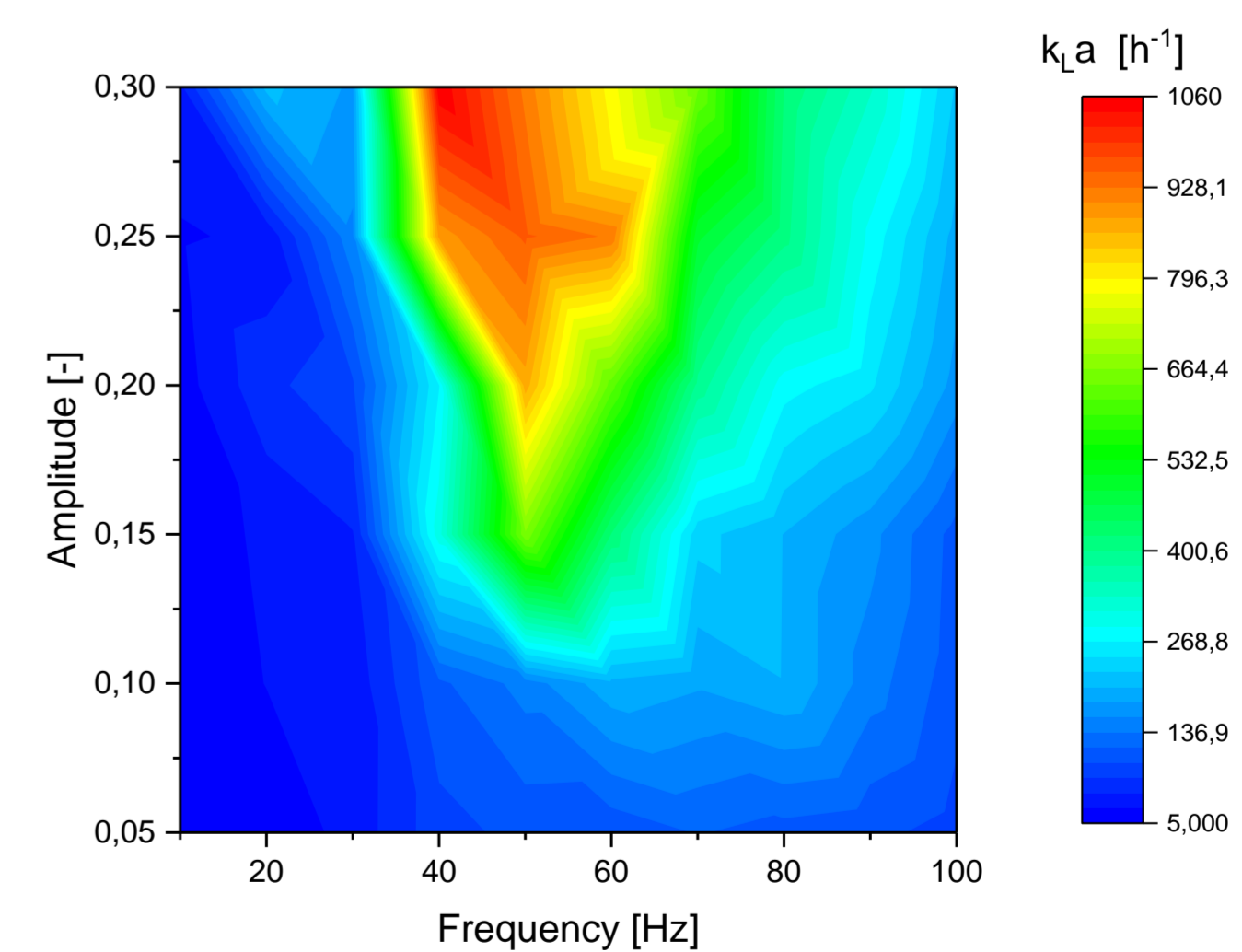
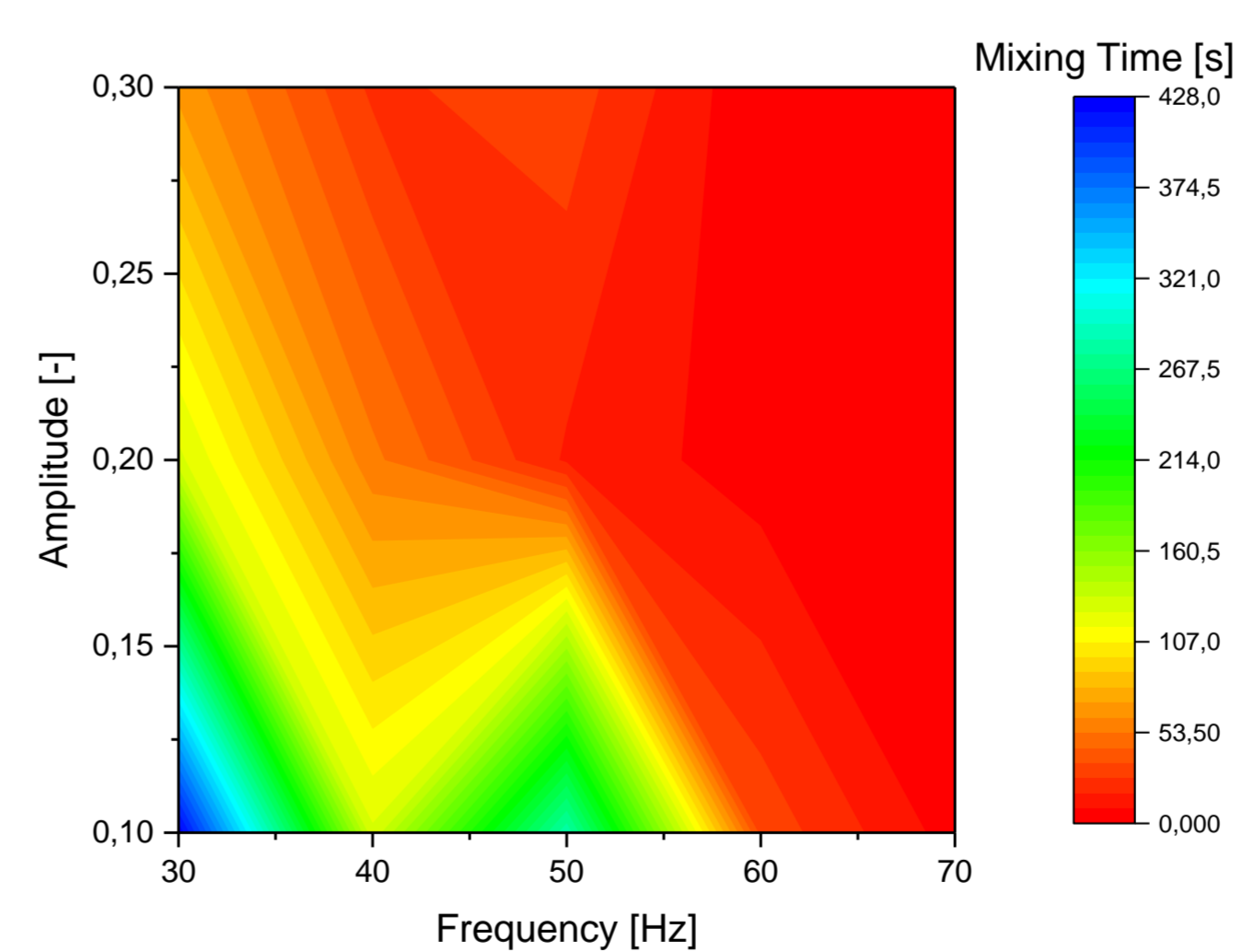
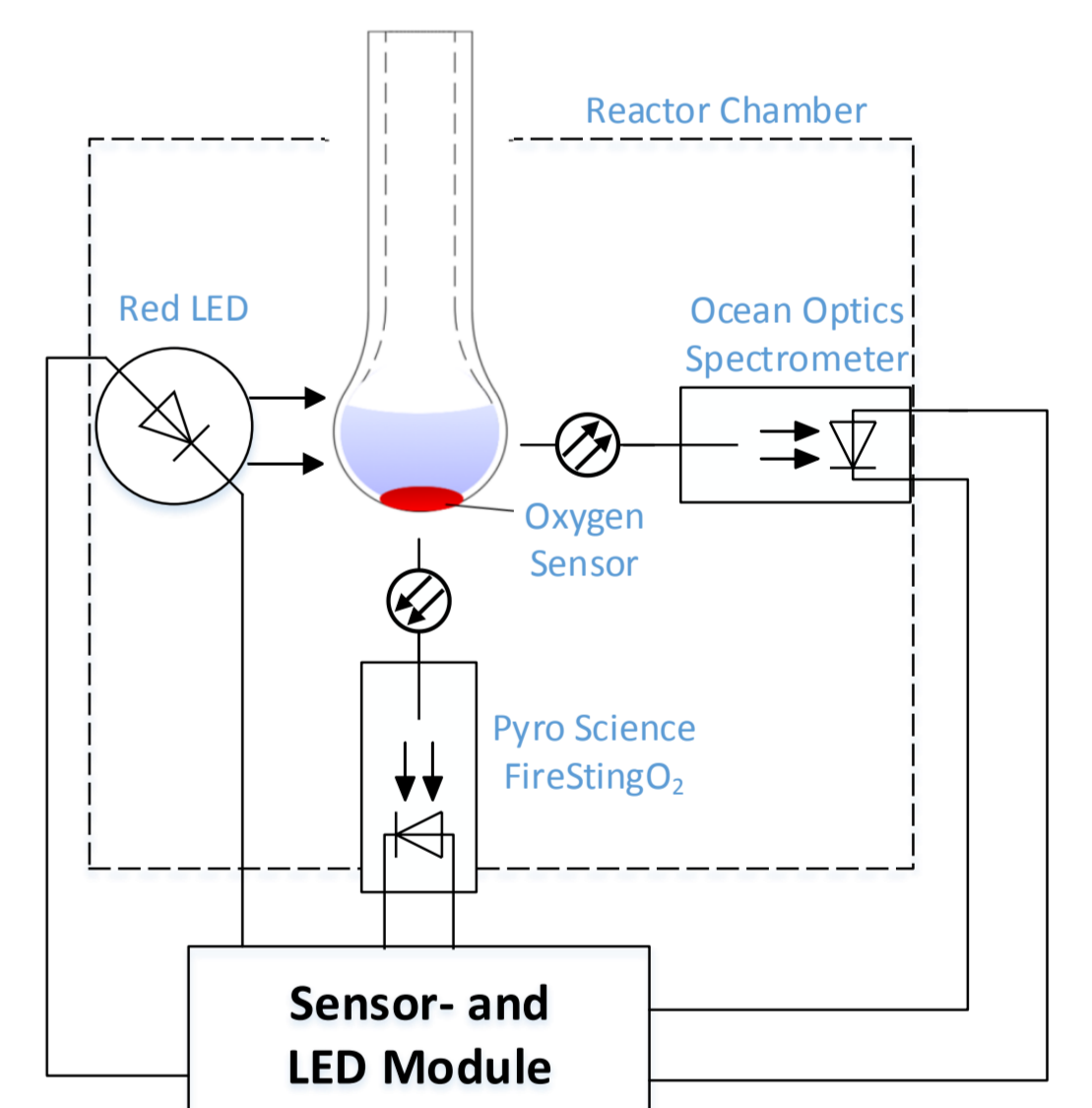
Effect of superficial gas velocity on the mixing time



➔ Fine dispersion of air results in large specific interface, improving oxygen mass transfer rate and ensuring sufficient homogenization

## MICRO FLASK REACTOR

- Micro Flask Reactor for biopharmaceutical screening applications
- Mixing via surface acoustic waves created by electrodynamic exciter  
→ Oscillation sets cultivation media into defined movement  
→ Liquid surface swings and works as pump
- Spherical reaction volume entirely made of Borosilicate glass ( $V_L = 20 \mu\text{L}$ )  
→ "Bottle neck" to prevent evaporation
- Online sensors: absorbance, scattered light, oxygen, fluorescence, image processing



➔ Rapid homogenization and sufficient oxygen supply caused by oscillation allows for great scope of pharmaceutical and biotechnological application

## References

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