DOTS

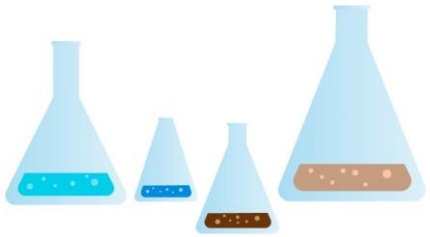
sbi SCIENTIFIC BIOPROCESSING

Liquid Injection System (LIS)

AUTOMATED FEEDING IN SHAKE FLASKS

Before, automated feeding experiments could not be performed in shake flasks, limiting their use for bioprocess development.

Problem: Lack of Feeding Technologies for Shake Flask Cultures

	Microtiter Plate	Shake Flask	Bioreactor
			
Automated Feeding Availibility	✓	✗	✓
Feeding Applications	Fed-batch, pH control, automated induction	✗	Fed-batch, pH control, addition of antifoam, automated induction

LIS is the first technology allowing for automated feeding of liquids into shake flask cultures.

Liquid Injection System (LIS)

The LIS Drive and the LIS Cartridge are the two key components that allow for feeding of liquids into shake flasks.

Components of the LIS System (1/2)

LIS Drive

- Programmable miniature pump
- Controls feeding of liquid from the LIS cartridge into the flask
- Controlled wirelessly with the DOTS Software

LIS Cartridge

- Sterile single use consumable with the shape of a shake flask lid
- Reservoir that can be filled with up to 25 mL of the desired feeding liquid
- Only compatible with 38 mm straight neck flasks

LIS Flask

- Shake flask for optimized oxygen supply through 2nd neck

Octagrab and Ring

- Connects the LIS Drive and LIS Cartridge
- Guarantees tight fit
- Easy to handle

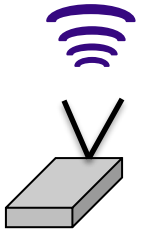
The DOTS Software and LIS hub enable you to set up, control and monitor LIS experiments wirelessly.

Components of the LIS System (2/2)

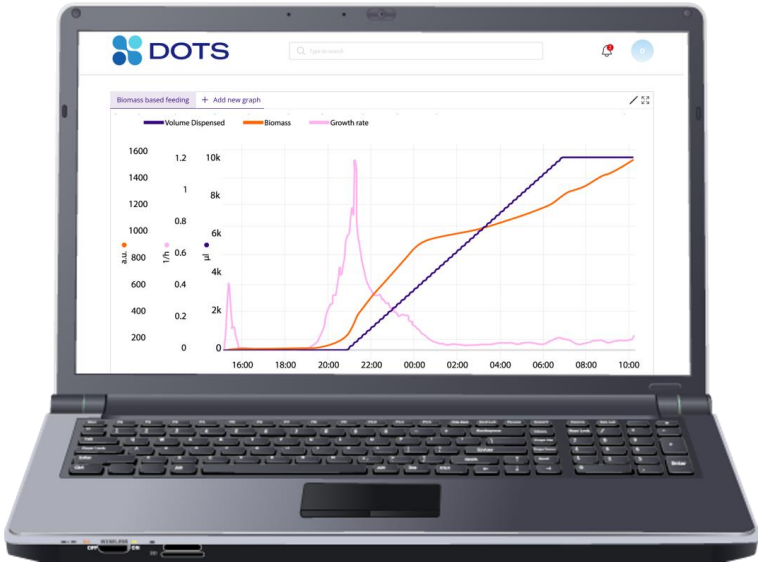
LIS Drive & Cartridge

Wireless Communication

DOTS Software & LIS Coordinator



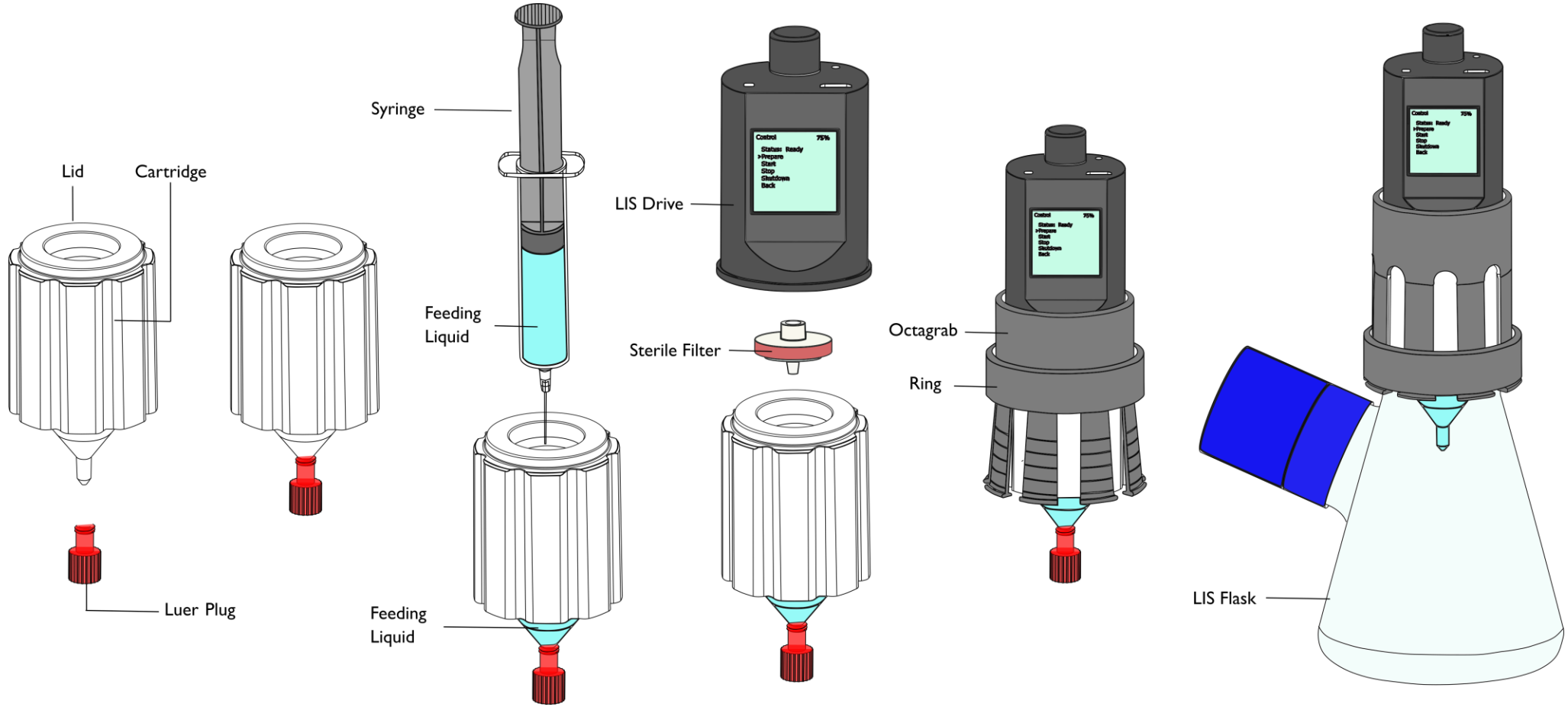
LIS Wireless Hub



DOTS Software

LIS is easy to assemble: Fill the cartridge with the feeding liquid, connect the LIS drive to the cartridge and start feeding.

LIS Assembly



LIS creates significant value enabling scientists to perform feeding experiments on a shake flask level.

LIS Key Facts

Key Facts

Wireless control and monitoring
Control and monitor your feeding experiments wirelessly with the DOTS Software

Compatible with various substances
Sugars (e.g., 40% glucose), alcohols (e.g., 50% methanol), glycerol, acids, bases,…

Create any feeding profile you want
Single or multi shot, delay, exponential or continuous feeding

Easy to install and use
Fill the sterile cartridge, program the LIS drive and start feeding your culture

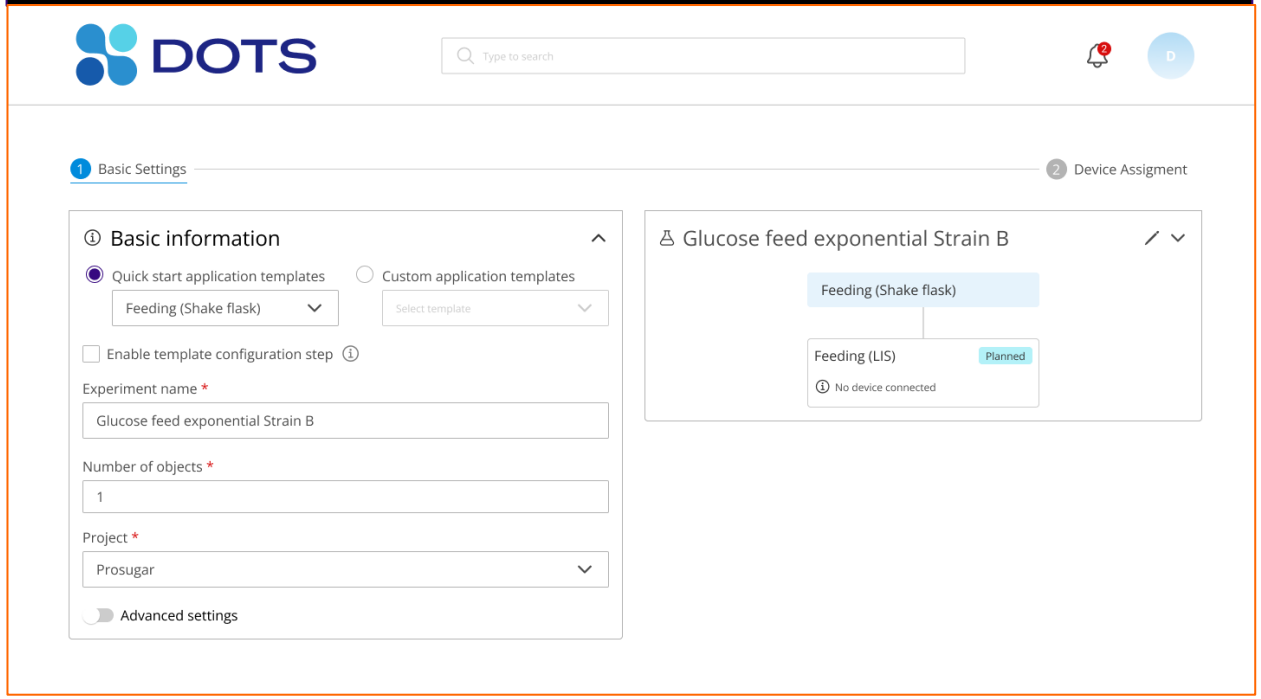
Flexible feeding rates
From 100 µl droplets to 1 mL/min feeding rate

For a broad range of applications
Fed-batch, gene induction, pH regulation, automated inoculation, toxicity assay,…

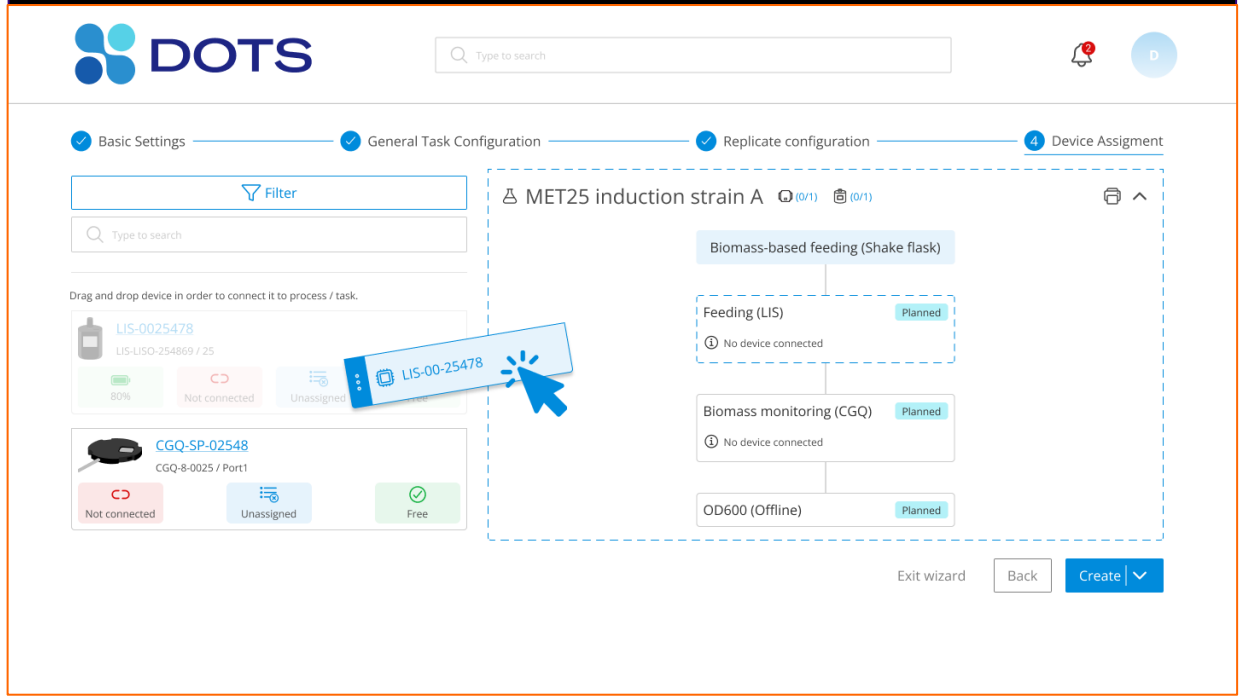
The DOTS Software enables easy sensor handling and experiment set up.

Exemplary Screenshots

Create an experiment with pre-defined application templates



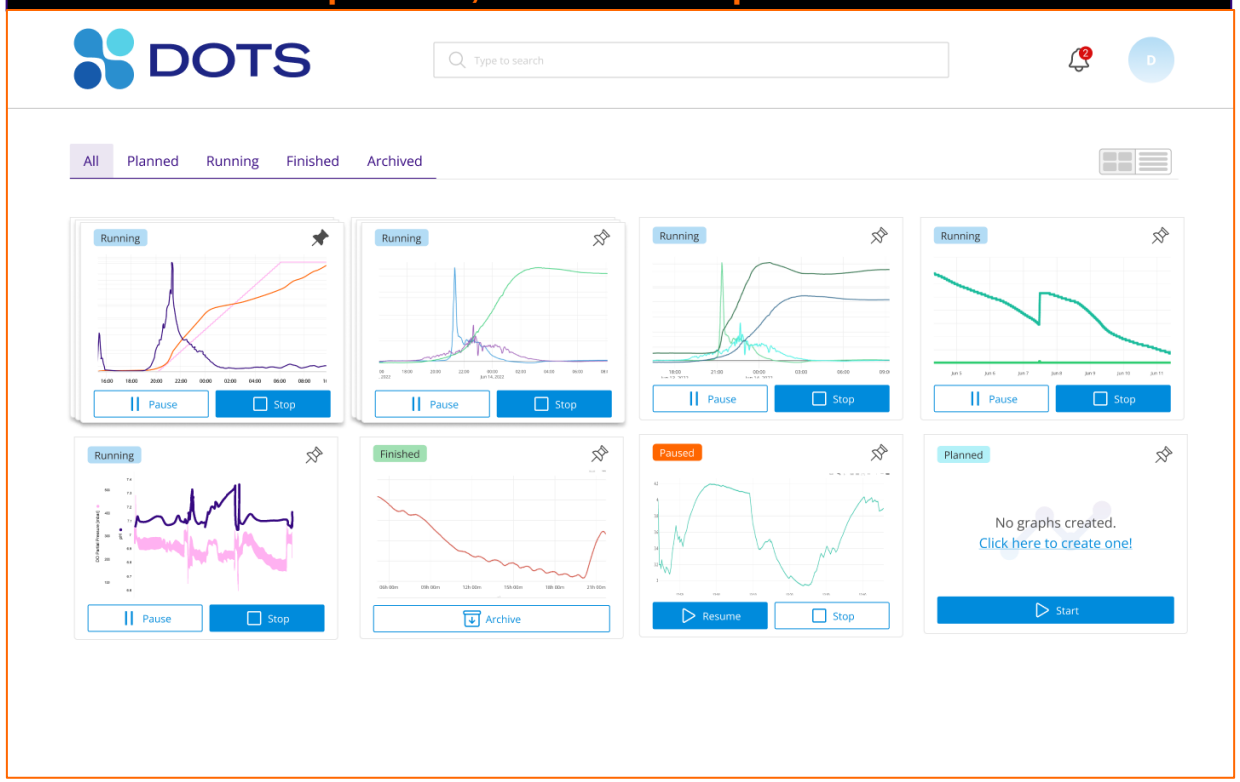
Assign sensors to planned experiments via drag and drop



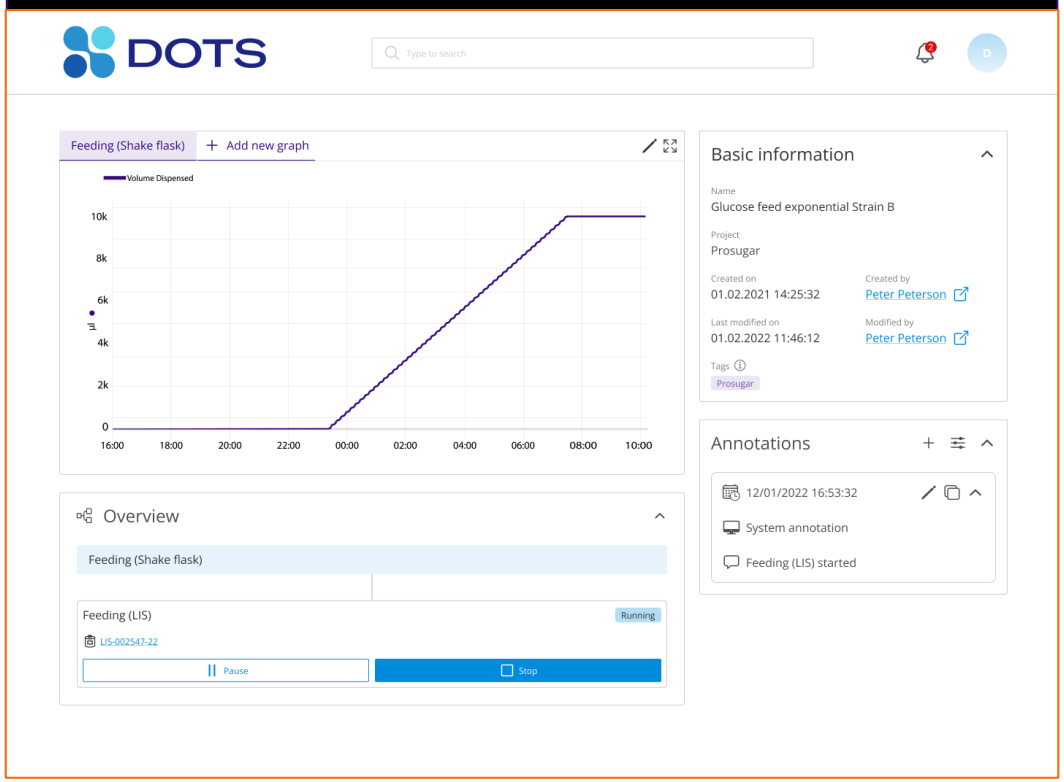
The DOTS Software provides a comprehensive overview of your experiments and visualizes your data in real-time.

DOTS Software Modules for Data Visualization

The dashboard schema provides an overview over all running, planned, or finished experiments

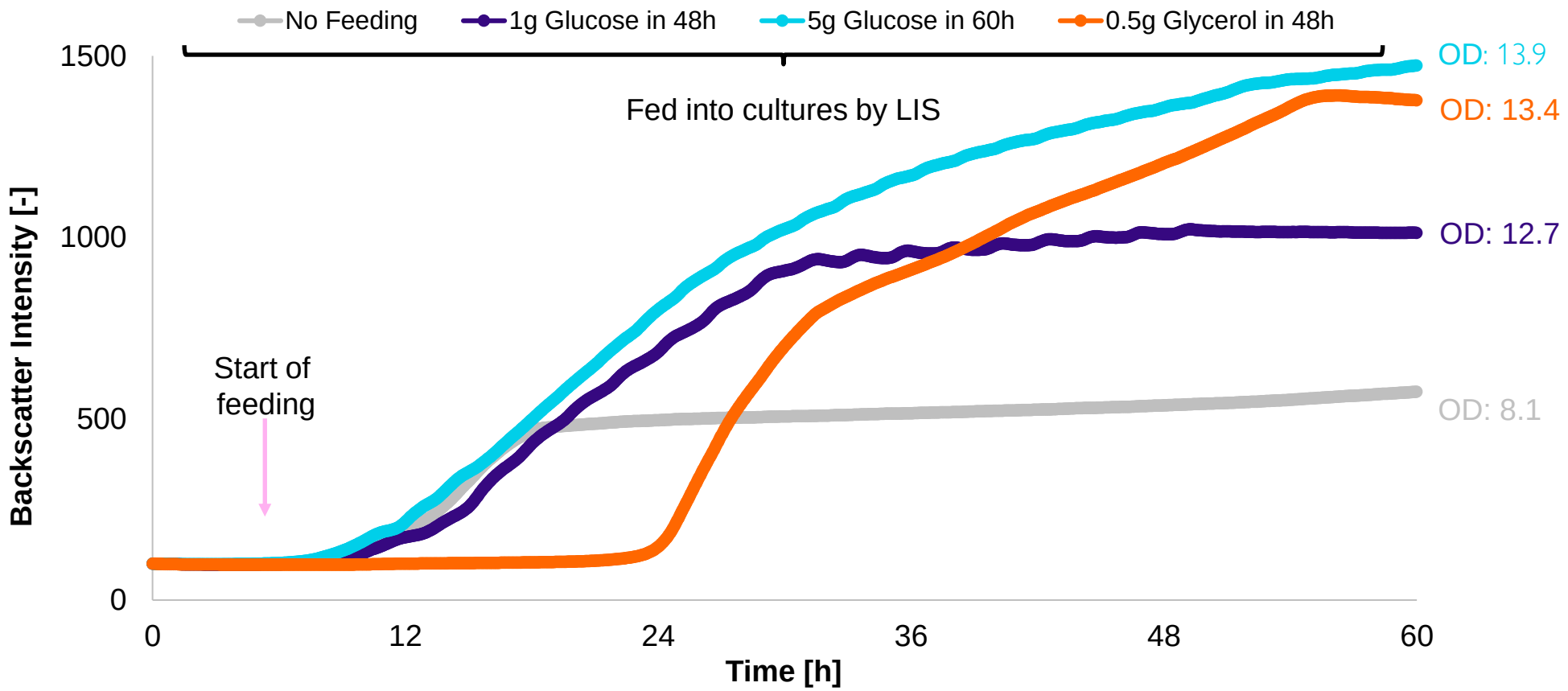


Data visualization tools enable a customized display of data in real-time



LIS can be used to create fed-batch conditions for microbial shake flask cultures and increase biomass and product titers.

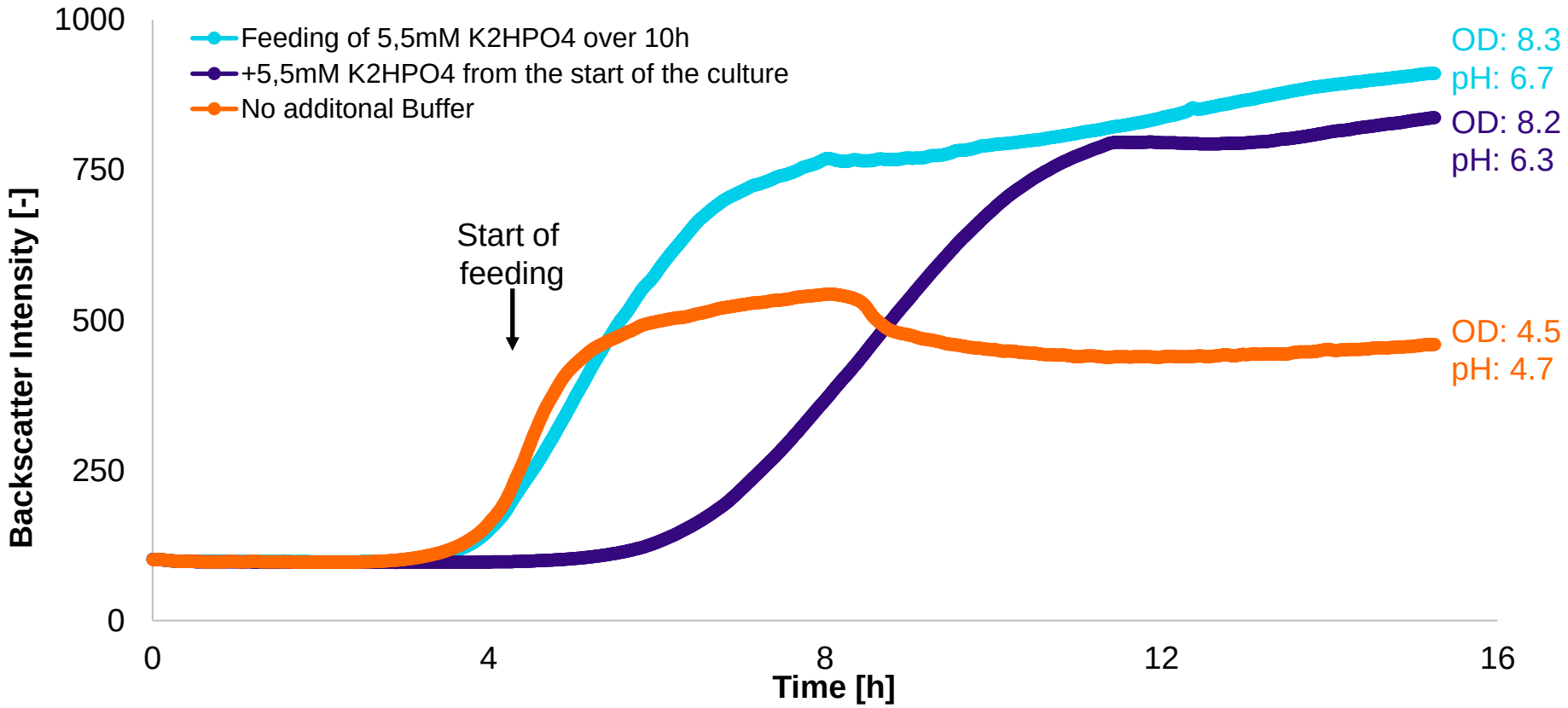
Example Use Case (1/2): Fed-Batch



Saccharomyces cerevisiae, 25 mL YPD Medium, 250 mL Shake Flasks, 30 °C, 250 rpm; growth curves monitored with the CGQ

LIS can be used to control pH drifts of *Escherichia coli* shake flask cultures by automatically feeding buffer to the culture.

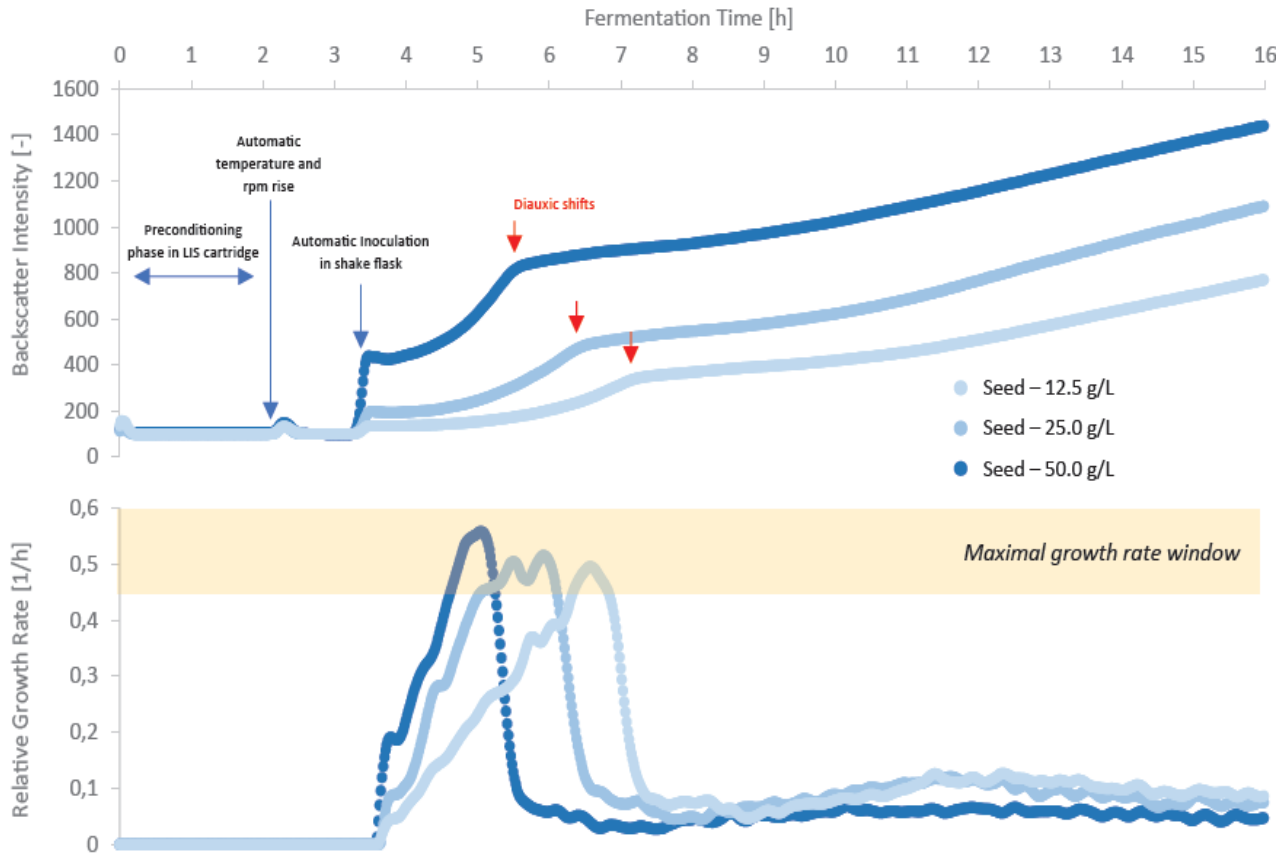
Example Use Case (2/2): pH Regulation



Escherichia coli, 25 mL LB Medium + 2% Glucose, 250 mL Shake Flask, 37°C, 250 rpm growth curves monitored with the CGQ

LIS and CGQ (biomass monitoring) allow for automated seed inoculation for the perfect bioreactor pre-culture in shake flasks.

CGQ and LIS for Seed Train Applications



Key Facts

- CGQ (biomass monitoring) and LIS (feeding) work together to prepare the perfect culture in the shortest time
- No interaction required
- No risk of contamination, no interruption of the process, better results

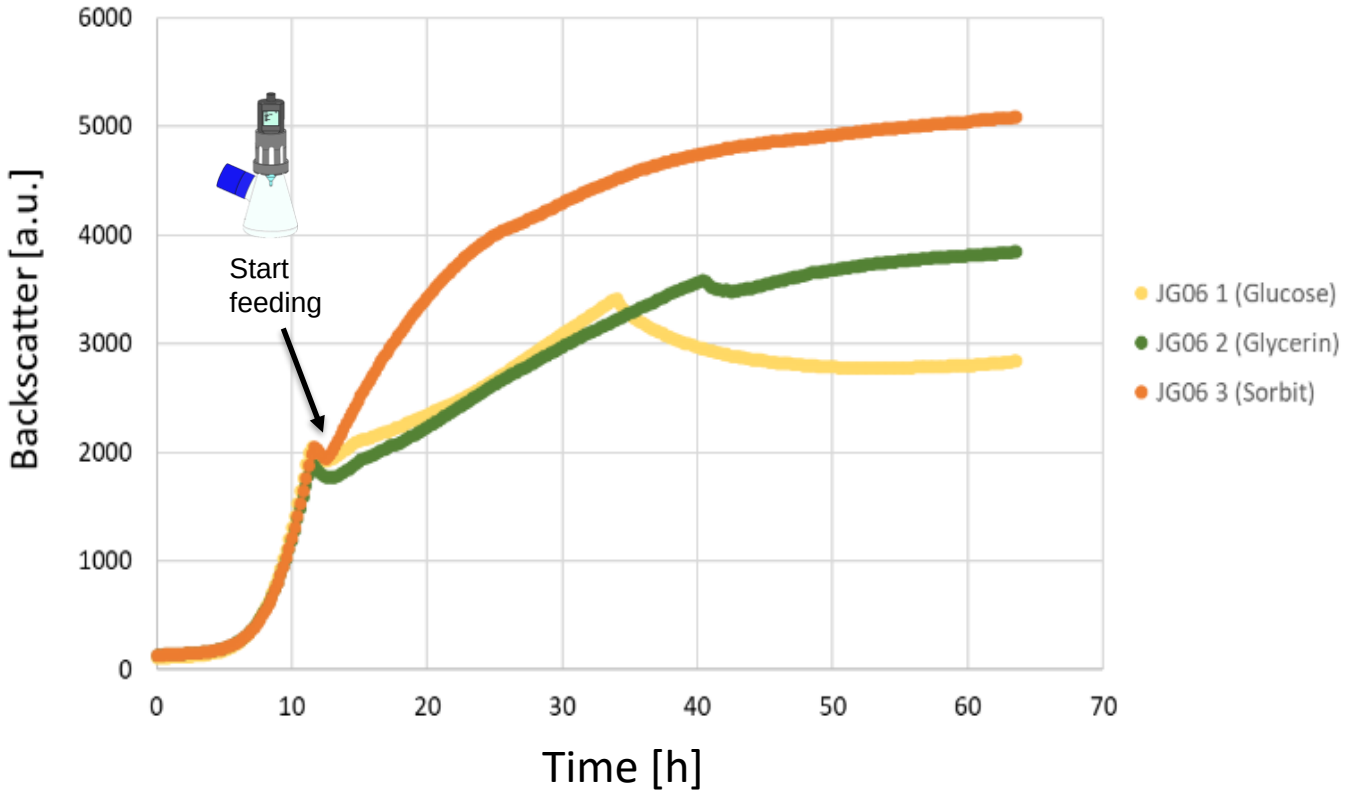
(Data from Eppendorf Application Note)

eppendorf

S. cerevisiae grown on YPD + 20 g/L Glc. Shaking speed: 100 – 210 rpm, 50 mm throw, temperature 10-30°C. Feeding: Yeast with 12.5 g/L – 50 g/L Glc

LIS and CGQ (biomass monitoring) enable bioreactor-like automated experiments in shake flasks.

Biomass-Based Automated Fed-Batch Feeding



H. polymorpha grown on mineral medium, 180 rpm, 30°C. Feeding rate: 2.5 g/L*h

Key Facts

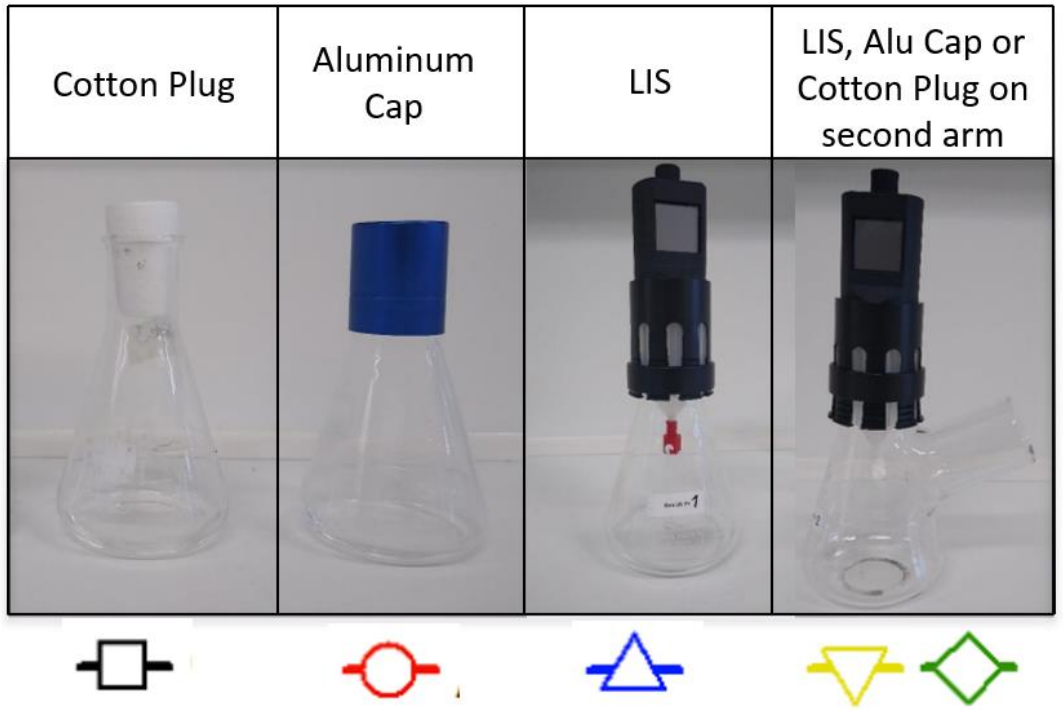
- LIS started feeding when the CGQ (biomass monitoring) detected the end of the batch phase
- Different sugars fed
- No risk of contamination, no interruption of the process, perfect time to feed without the need to be in the lab

(Preliminary data from Application Note)

Westfälische Hochschule
Gelsenkirchen Bocholt Recklinghausen
University of Applied Sciences

A technical review measured evaporation rates through different flask closure types to determine oxygen availability in LIS flasks.

Comparison of Mass Transfer Rates Through Different Flask Closures



250 mL flasks, 25 mL H_2O, 250 rpm, 37°C, 50 mm Shaking Diameter, 70% Humidity

The use of LIS does not lead to a stronger oxygen limitation compared to conventional flask closures.

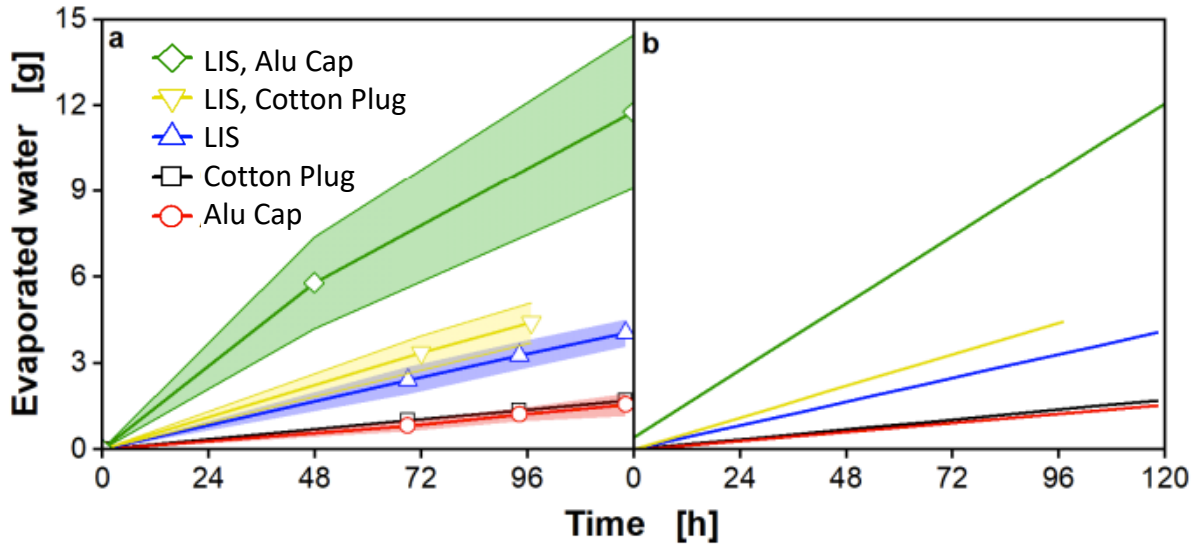
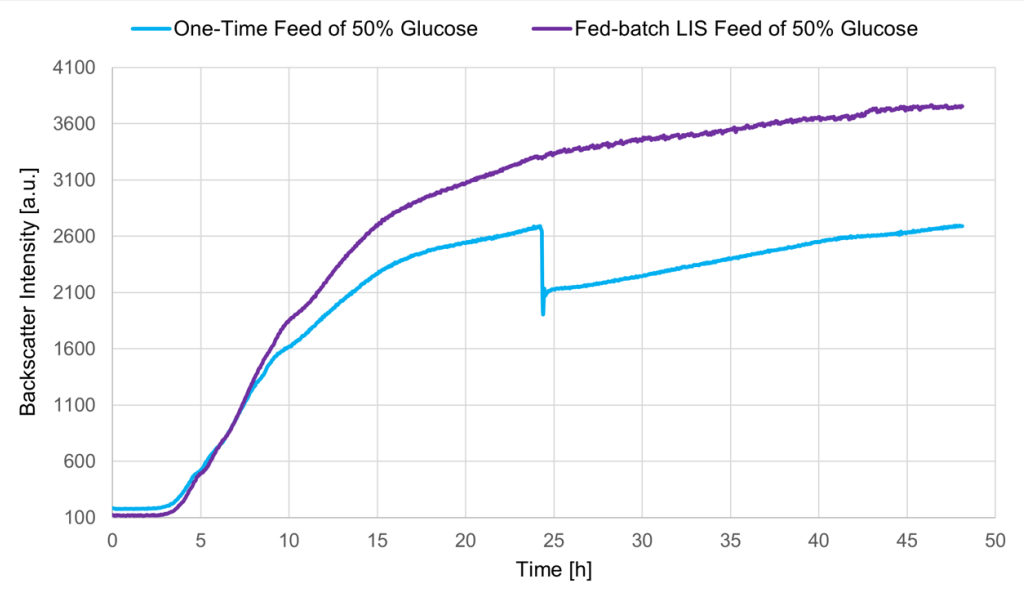


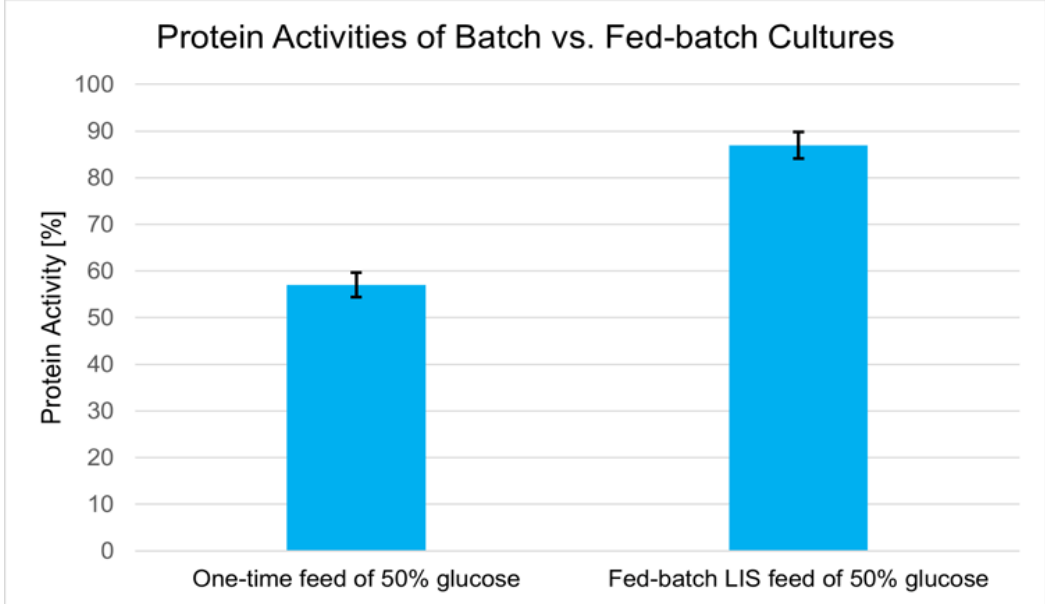
Figure: (a) Evaporation of water through various closures. (b) Linear fit, which was used to determine the evaporation rate.

Customer Success Story - Clariant

Clariant Uses the Liquid Injection System (LIS) to Improve Strain Development Experiments in Shake Flasks



Using the **LIS** on shake flasks enabled **fed-batch cultivations** in small scales, resulting in **improved strain development experiments** in shake flasks.

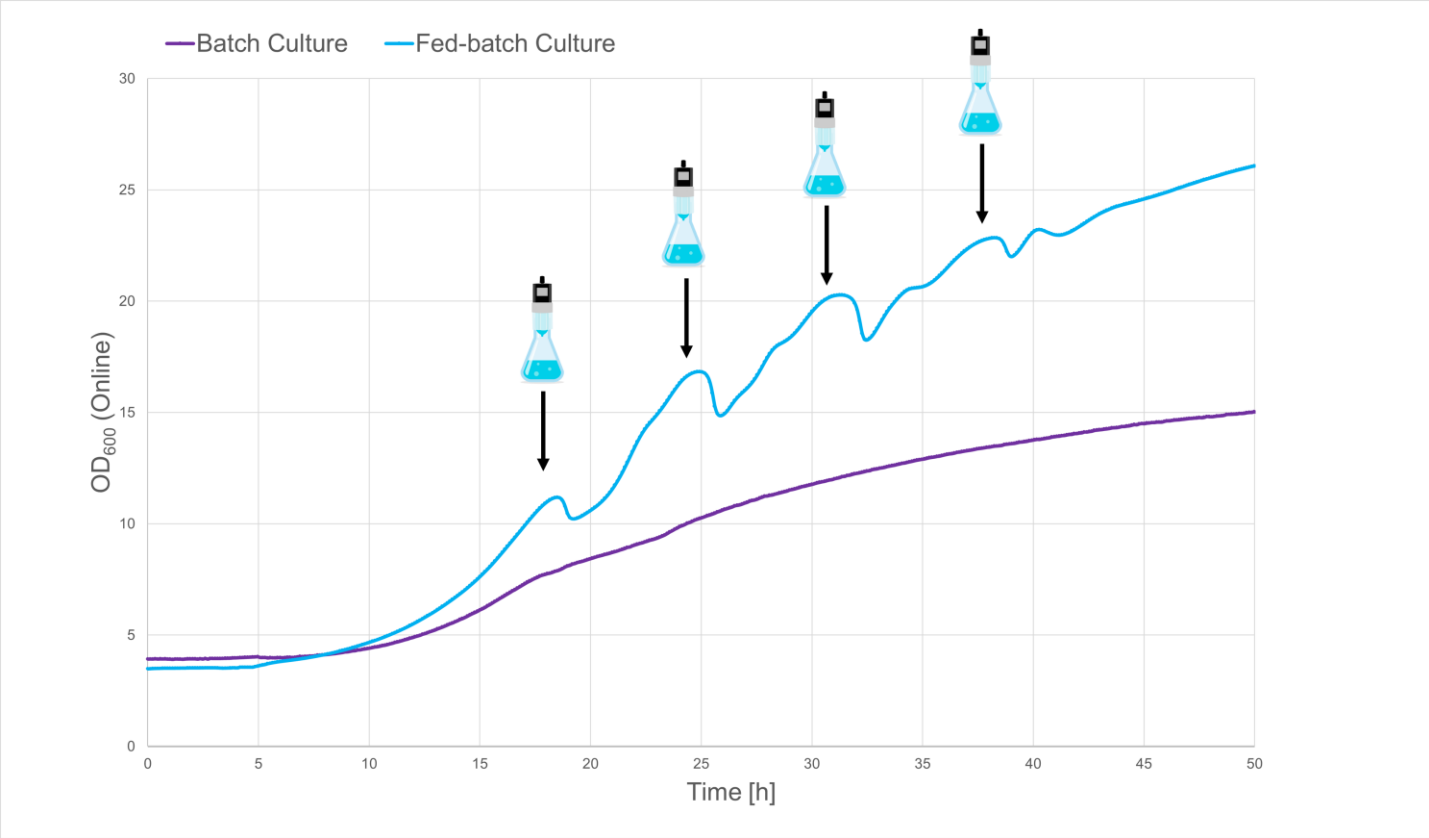


When compared with the culture with a one-time feed, the fed-batch feeding of glucose to the medium via LIS resulted in a nearly **30% increase in final protein yield**.

CLARIANT

Customer Success Story - CentraleSupélec

CentraleSupélec Uses LIS To Compare Fed-batch Processes With Conventional Batch Cultures, Modeling Bioreactor-like Runs In Shake Flasks



The Liquid Injection System (LIS), enables fed-batch process conditions in shake flasks. The controlled addition of substrate reduces the concentration of growth inhibitors in the medium, resulting in nearly 2x more ***Saccharomyces cerevisiae*** growth on potato waste.

Chaire de Biotechnologie CentraleSupélec

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