Kuhner shaker

Kuhner TOM
Off-gas analysis in shake flask

16.10.2022

What is TOM doing

TOM measures oxygen consumption and CO_2 production of microorganisms or cells in up to 16 shake flasks via non-invasive head space analysis

Why do we need TOM

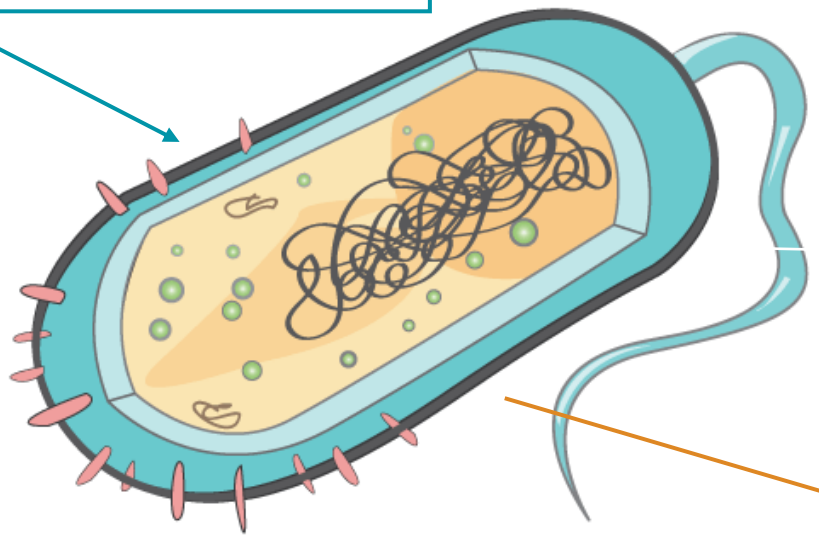
Oxygen uptake and CO_2 production are essential in cell metabolism

Oxygen

Oxygen uptake rate = OUR

Cell growth

Carbon source
(Sugar, Glycerol, Alcohol, Fats, Acids…)



Products
(Proteins, Polymers, Fuel, Acids)

Nitrogen source
(Proteins, Yeast extract, Urea, Ammonium…)

CO_2

Volume elements
(Phosphorus, Sulfur, Magnesium, Potassium, calcium…)

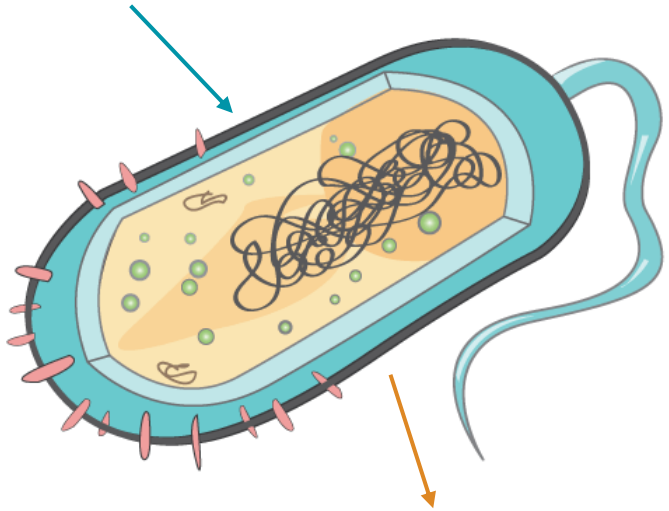
Carbon dioxide evolution rate = CER

Vitamins and trace elements

Why do we need TOM

TOM measures oxygen transter rate (OTR) and carbon dioxide transfer rate (CTR)

Oxygen uptake rate = OUR



Carbon dioxide evolution rate = CER

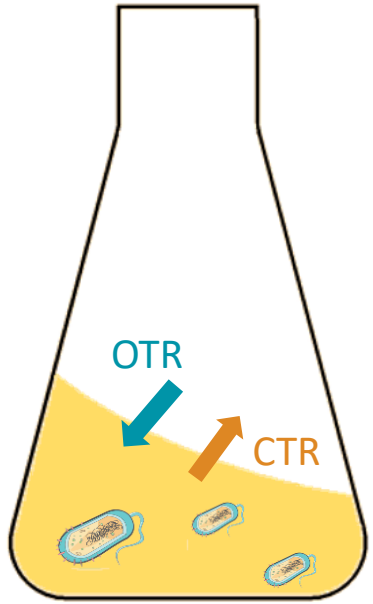
OTR = OUR
Solubility of oxygen in medium is low

CTR ≈ CER
Microbial process

CTR ≠ CER
In bicarbonate buffered medium, CTR is influenced by both, **cell metabolism and pH**

TQ = CTR/OTR
Transfer quotient (TQ) ≈ Respiration quotient (RQ) in microbial process

Transfer quotient (TQ) ≠ Respiration quotient (RQ) in bicarbonated buffered medium



Value of OTR and CTR measurement

Most quantities that are measured in biotechnological processes such as temperature, pH, DOT or other concentrations are the result of processes that happened in the past. They cannot directly be compared between different cultivation conditions and scales. E.g. the DOT (dissolved oxygen tension) is a result of shaking speed, fill volume etc. and consumption of oxygen in the past.

On the other side “Rates” like OTR and CTR give us the quantitative measure of what is happening in that moment. They tell us “how much” is consumed or produced “now”.

Therefore, OTR and CTR can be correlated to other important parameters like substrate consumption, viable cell density, product formation and are comparable through all scales and conditions. Comparison of OTR and CTR (respiration quotient) can even tell what is produced or consumed via stoichiometric correlations.

Wide range of applications

Preculture observation (also in production)

Reduced sampling at interesting timepoints

Easier scale up

- k_La determination
- Kown Aeration

Metabolic flux analysis (RQ, carbon balancing)

Measurement of μ, k_La, $Y_{X/S}$

Media development/optimization

Substrate inhibition/limitation, pH inhibition

Process monitoring and improved understanding for process development (PAT), for aerobic and anaerobic microbial cultures or cell cultures

Detection of unwanted cultivation conditions (limitations, out of phase operation)

Cell viability

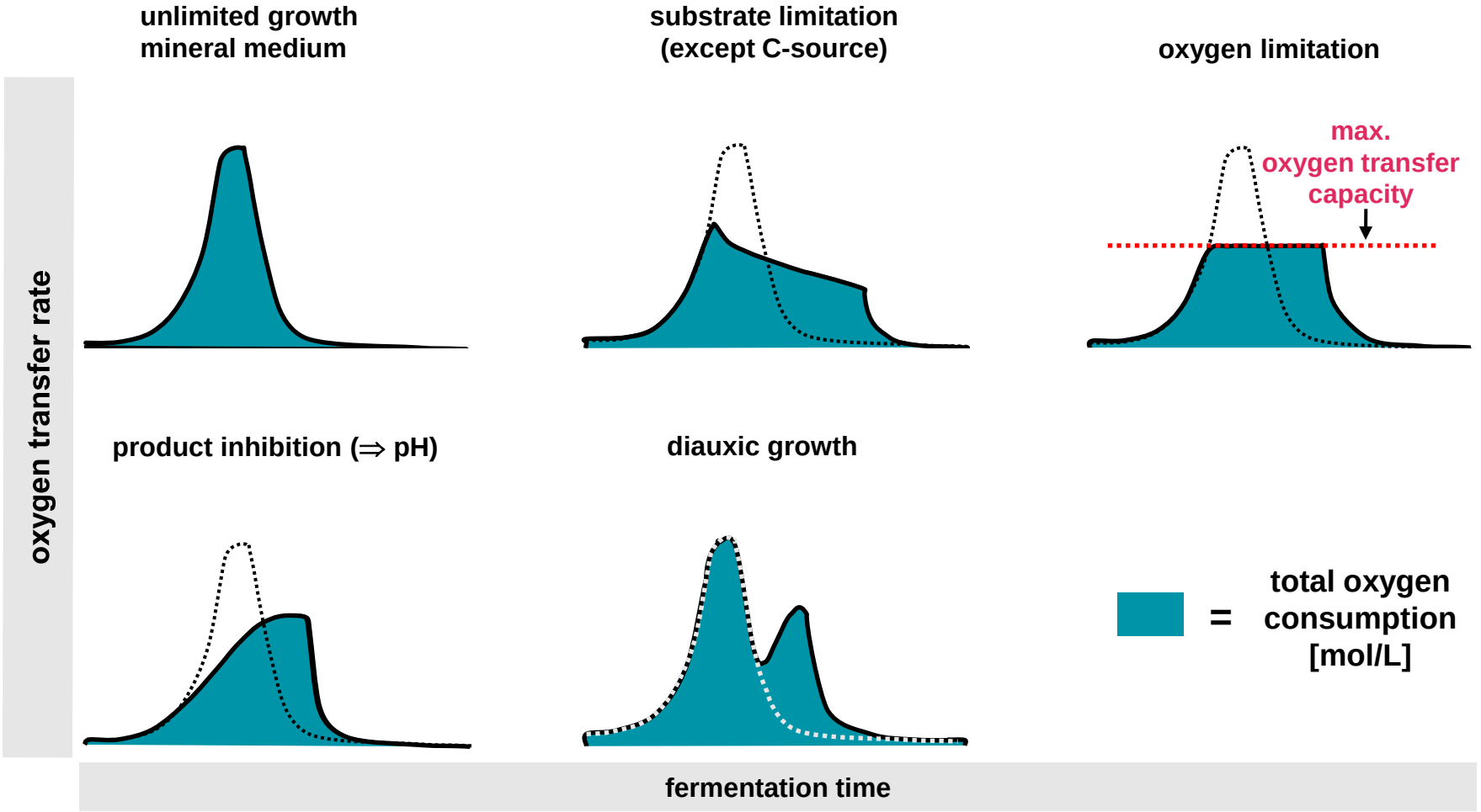
pH changes

OTR potentially related to glucose consumption

Non-invasive gas phase measurement

- Solid substrate
- Adherent cells
- Turbid medium
- Filamentous organisms

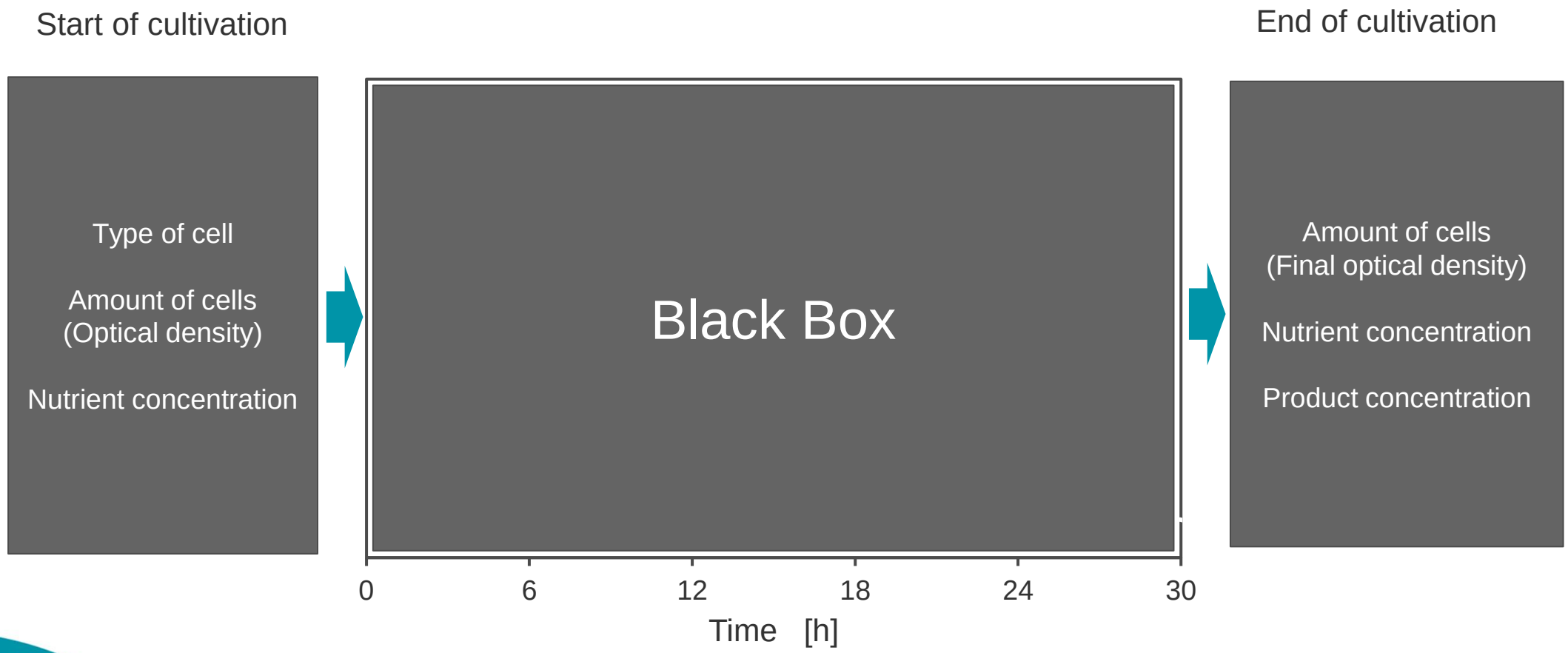
Interprete Oxygen transfer rate



Anderlei, Tibor & Büchs, Jochen. (2000). Device for sterile online measurement of the oxygen transfer rate in shaking flask. Biochemical Engineering Journal. 7.

Motivation

From blackbox cultivation to easy process understanding



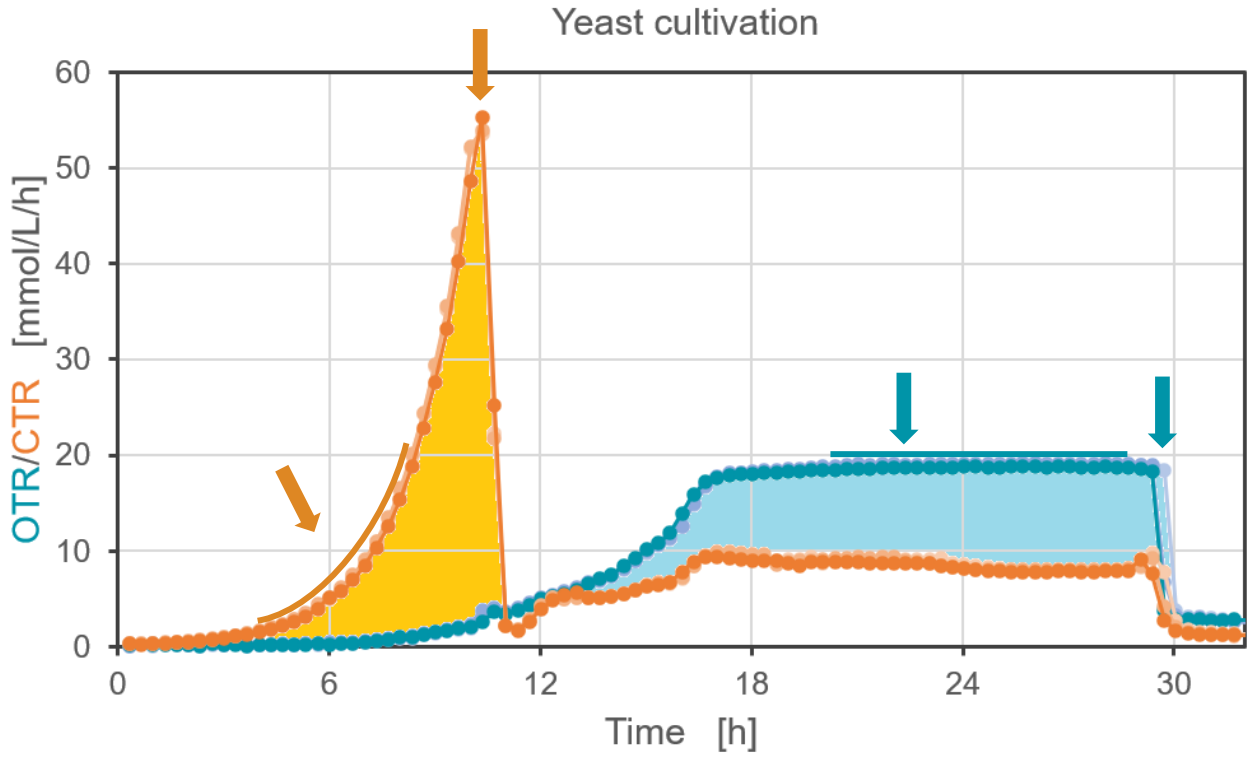
Motivation

Exemplary interpretation of a yeast cultivation

CTR
Growth rate
C-source depletion

OTR
Oxygen limitaton
End of process

Respiratory quotient
Ethanol formation
Ethanol consumption



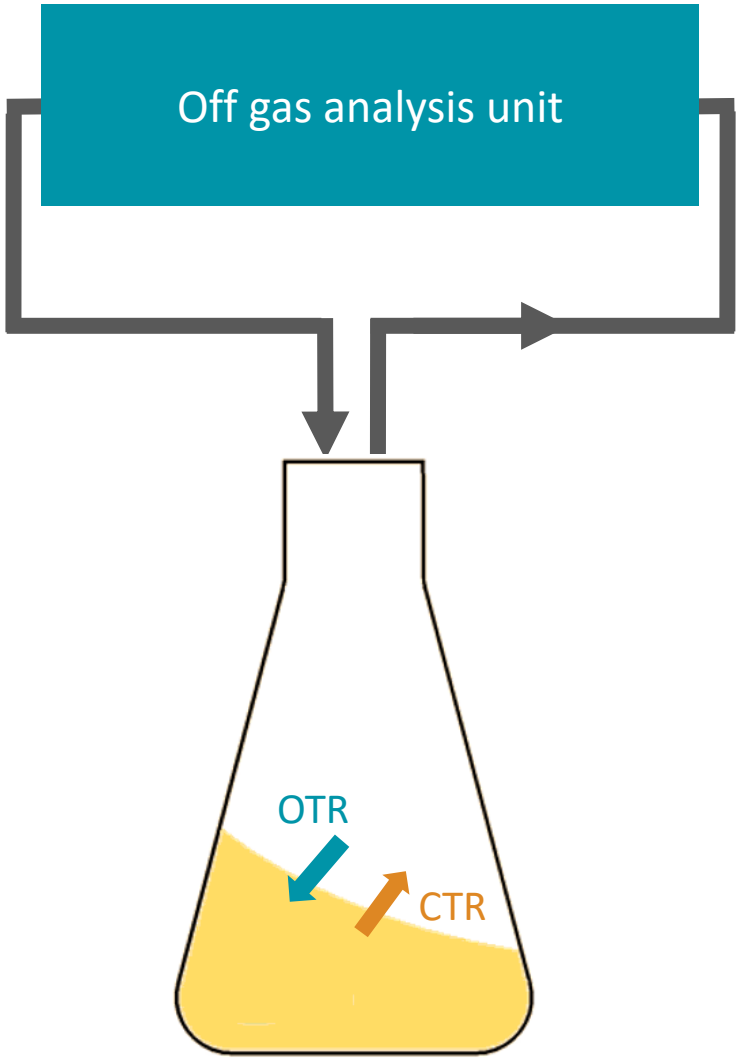
Oxygen and CO_2 is detected in an off-gas recycle

Robust to shaking movement

Sensitive electronics are not shaken

No footprint on shaker tray

Any flask could be fitted with an appropriate plug

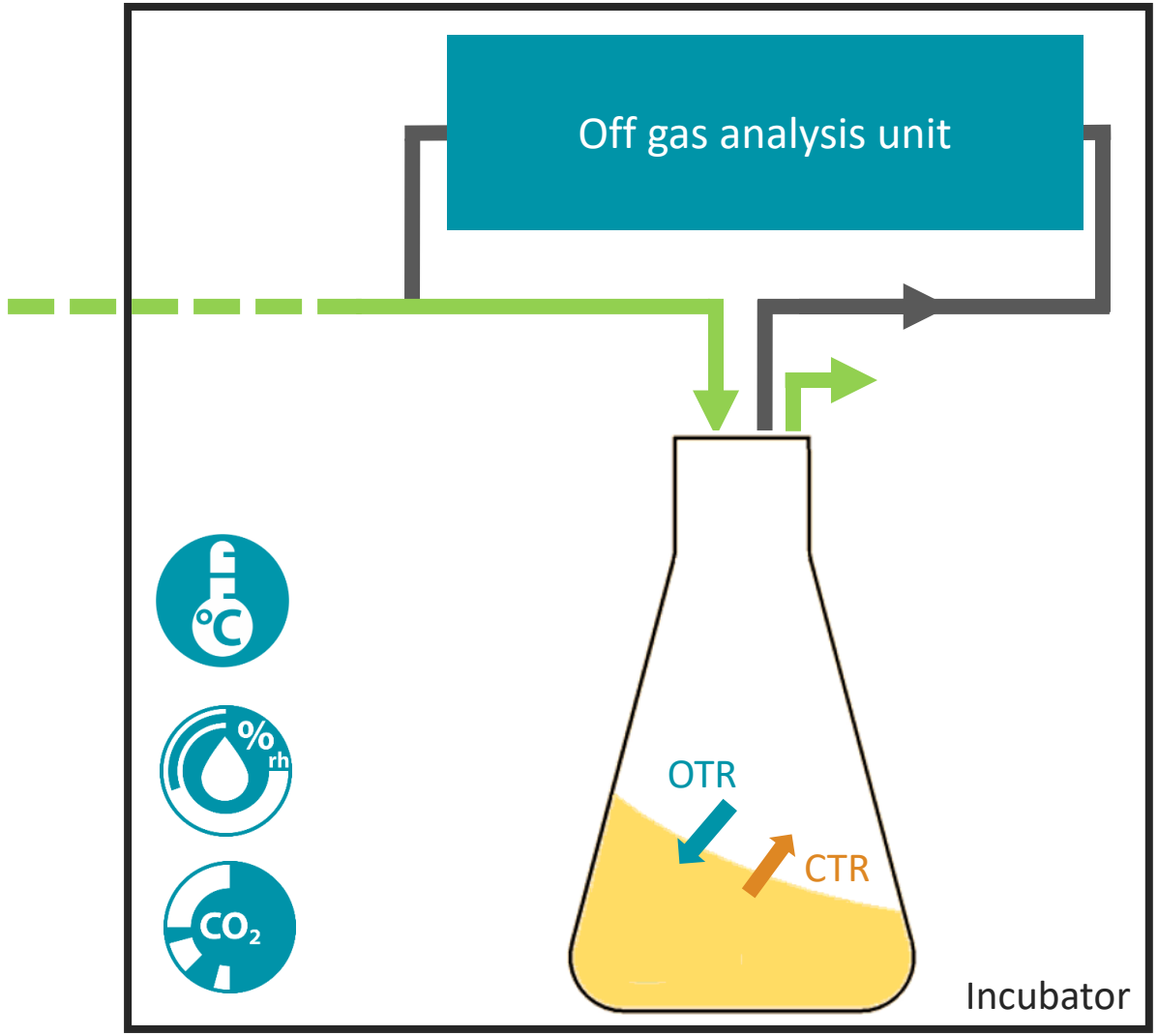


Active aeration

Variable aeration with

a) Compressed air (microbial application)

b) Conditioned incubator air (cell culture application)

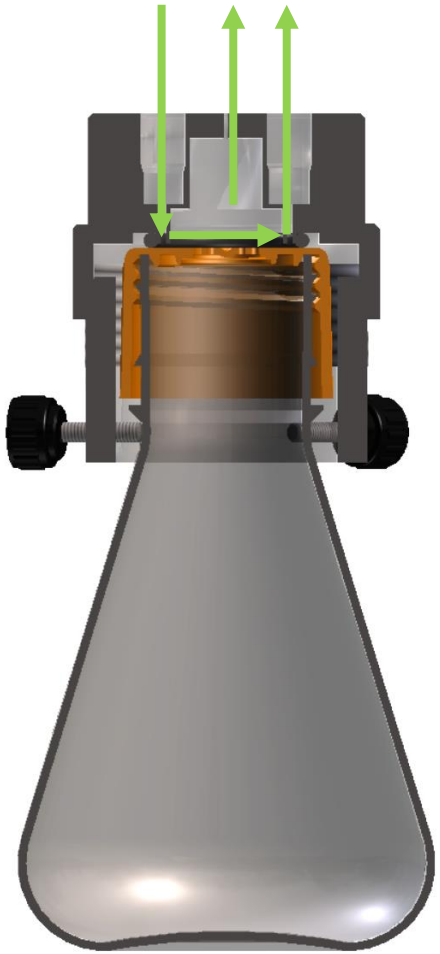


Single use flasks

Sterile vent cap stays in place

Simply use adapter ring for the specific flask size

Recommended for cell culture applications

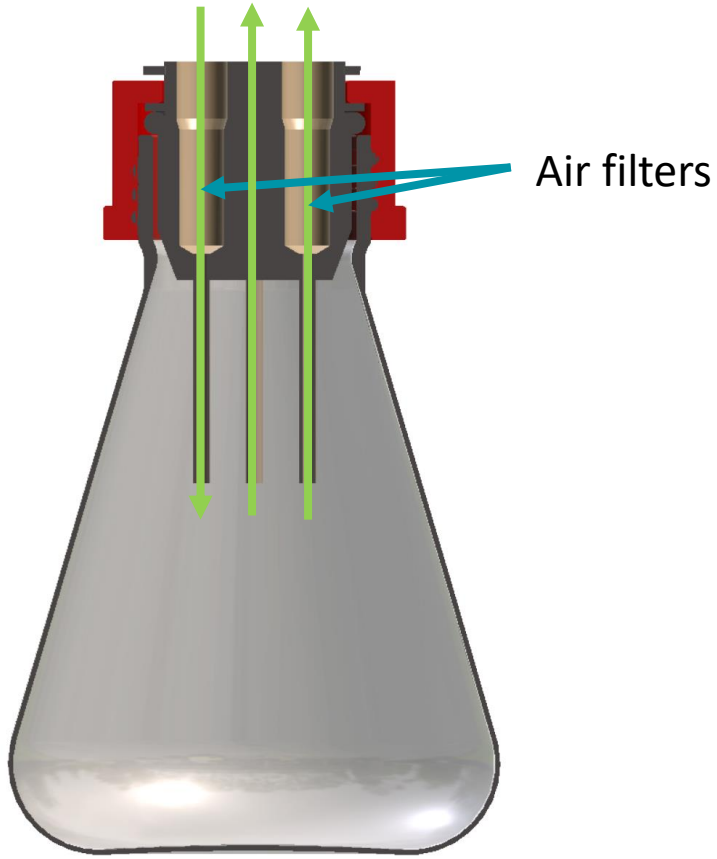


Autoclavable glass flasks

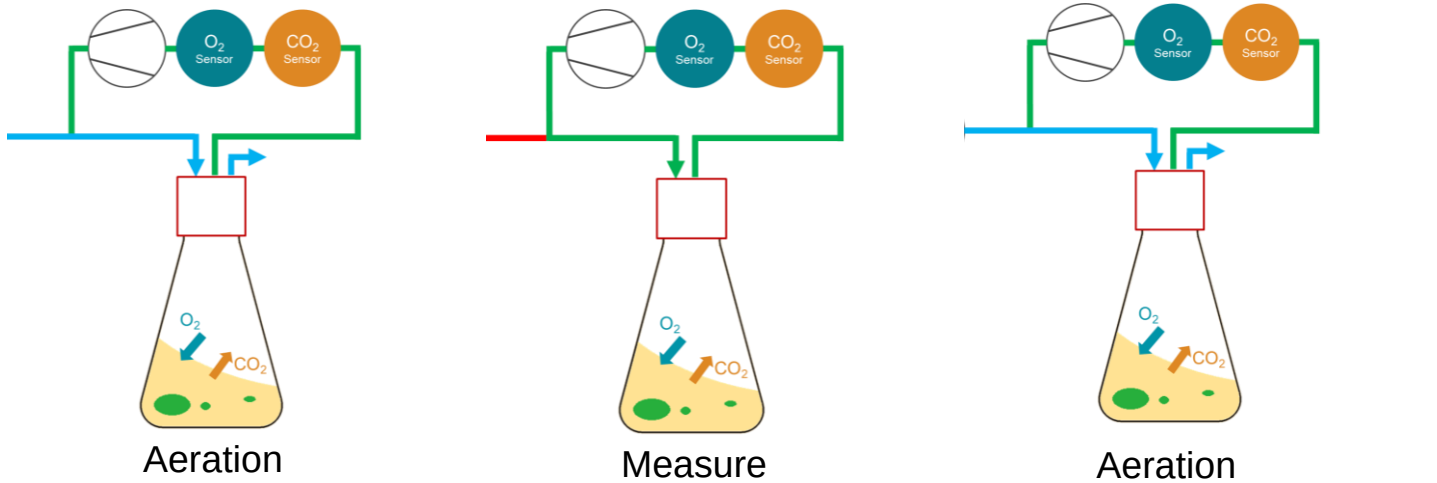
Glass flasks with thread are easy to use, autoclavable and reusable

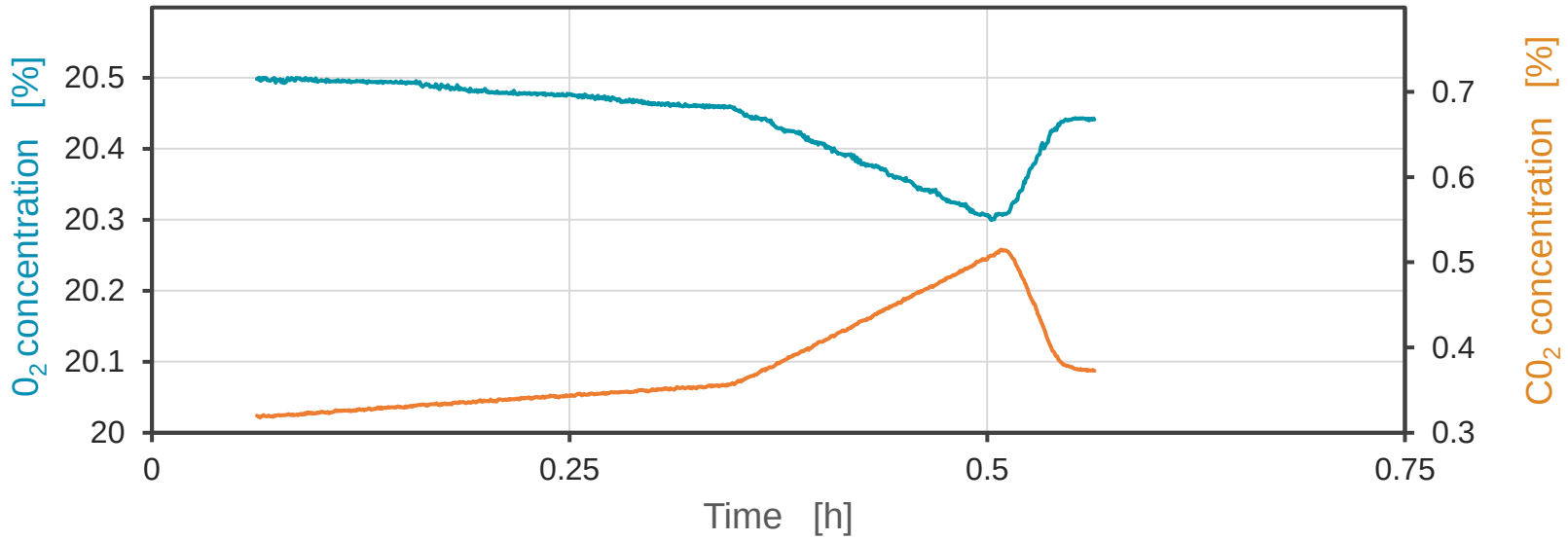
Direct aeration to the flasks via air filters

Recommended for microbial applications



Dynamic measurement for high accuracy





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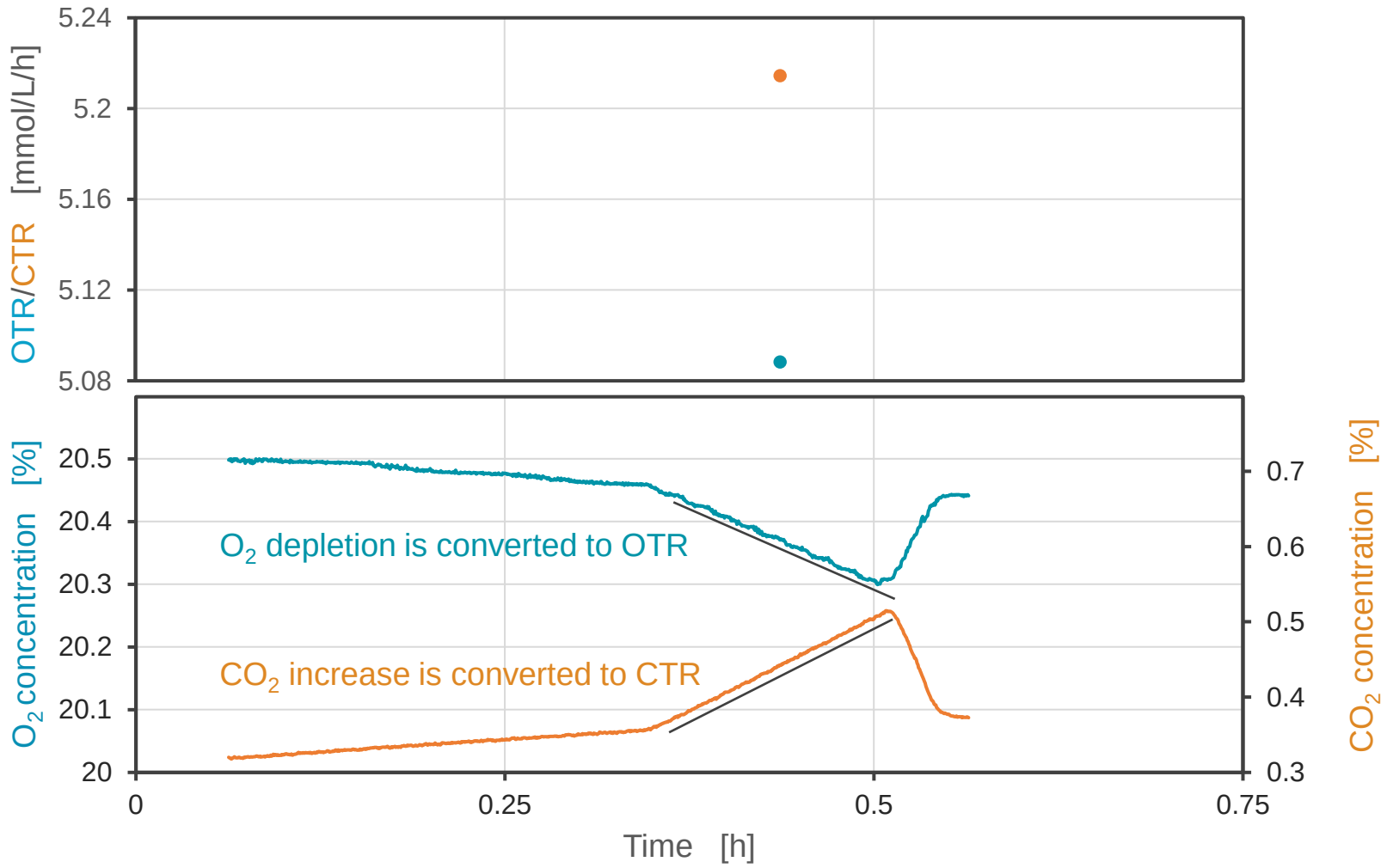

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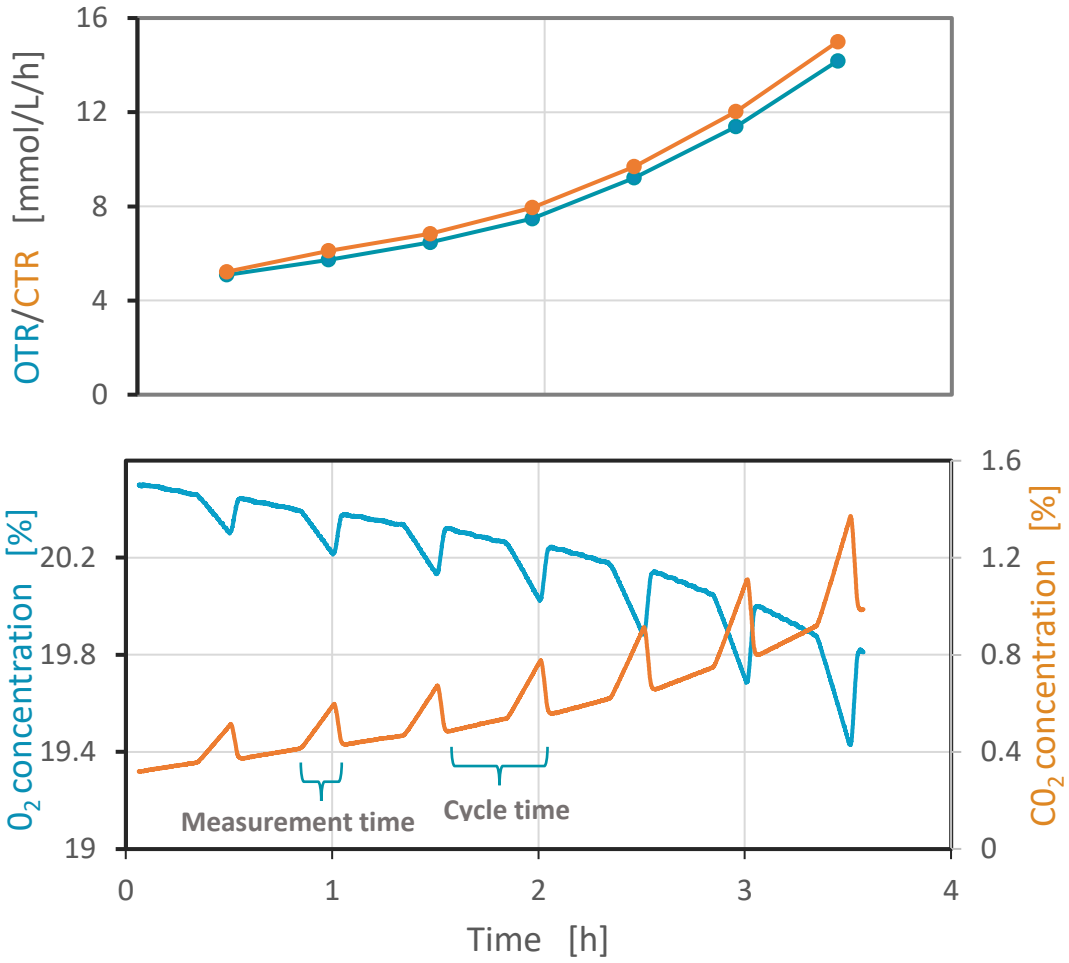
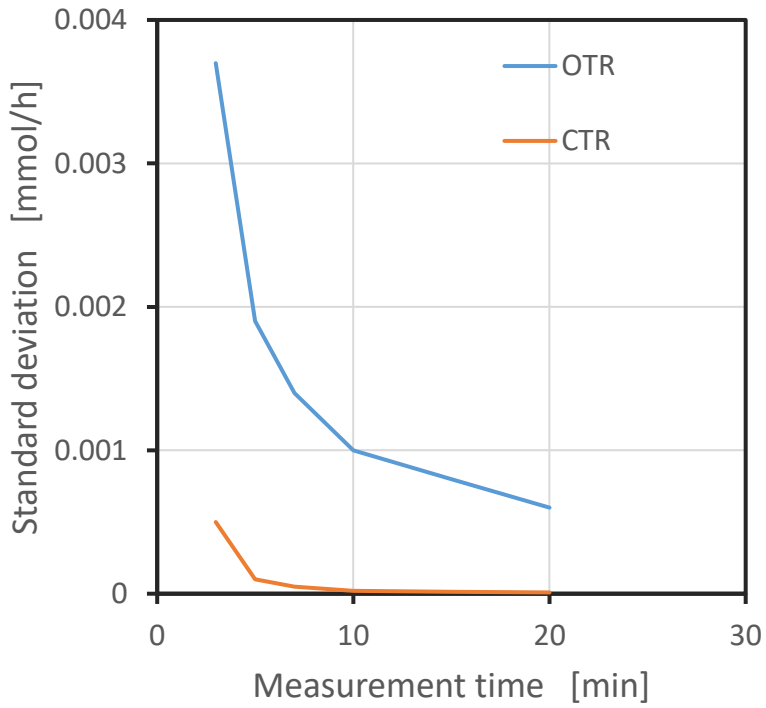
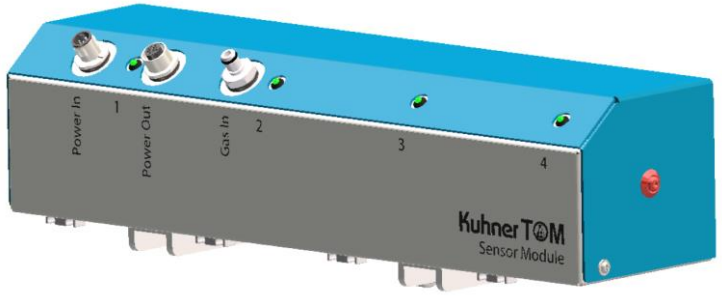




OTR (CTR) = mmol/L(liquid volume)/h

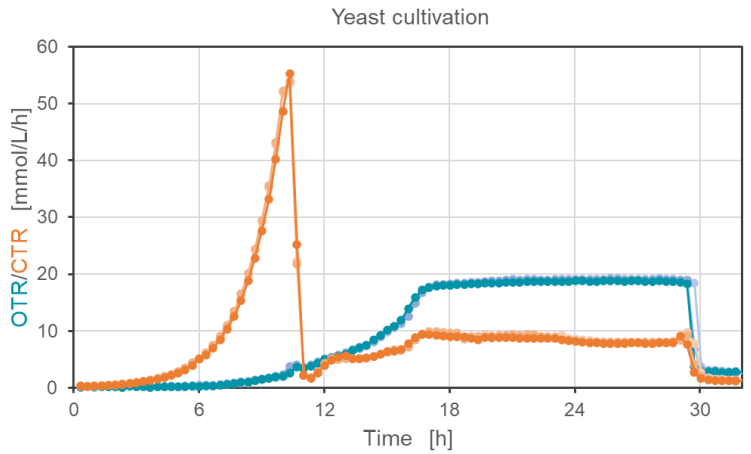
Long measurement time gives higher precision but less data points!



A single sensor module is ready for aeration and measurement in 4 individual flasks

Up to 4 sensor modules can be mounted in 1 shaker cabinet

TOM Control software for operation and visualization



Data export to .csv

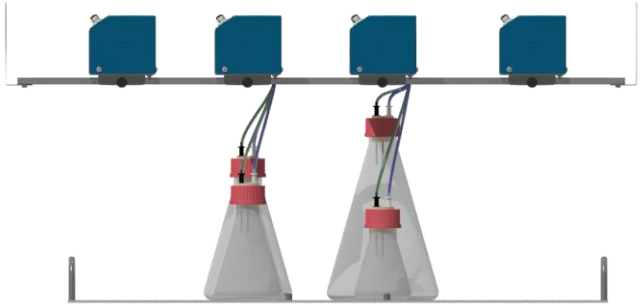
Flexible and modular design

Fits to any Kuhner incubator shaker





1-4 sensor modules (4-16 flasks)

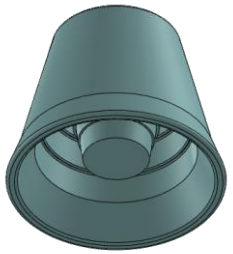


Variable flask size depending on shaker

Multiple flask types and sizes

(also ready for custom flasks)





We adapt to your shake flask

Kuhner glass erlenmeyer flask with GL45 thread:
250 mL, 500 mL, 1000 mL
2, 3, 5L upon request

Flasks compatible with Flexcap:

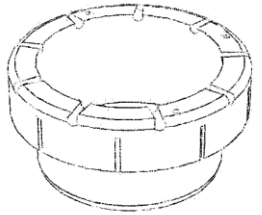
- 100 mL to 1 L wide neck glass erlenmeyer flask
- 250 mL to 5 L narrow neck glass erlenmeyer flask
- Bottom baffled GL45 flasks (non-splashing conditions)
- Ultrayield flask 250, 500, 1000 mL
- Corning 250 mL flask and 50 mL tubes for direct aeration
- ….to be continued, from inner diameter 25mm to outer diameter 55 mm

Cell culture Adapter Lid:

- Corning 125, 250, 500, 1000 mL flask
- 50 mL tubes

Custom made lids for special applications:

- E.g. 1.6, 2.8, 5 L Optimum growth flasks



Further information at:

https://kuhner.com/en/products/data/Add-ons_KuhnerTOM.php?highlight=TOM

- Scientific publications
- AppNotes
- DataSheets

Watch our latest TOM Video:

https://www.youtube.com/watch?v=sUd5scexzsk

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https://kuhner.com/en/contact/contact-and-offices.php

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Kuhner shaker

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