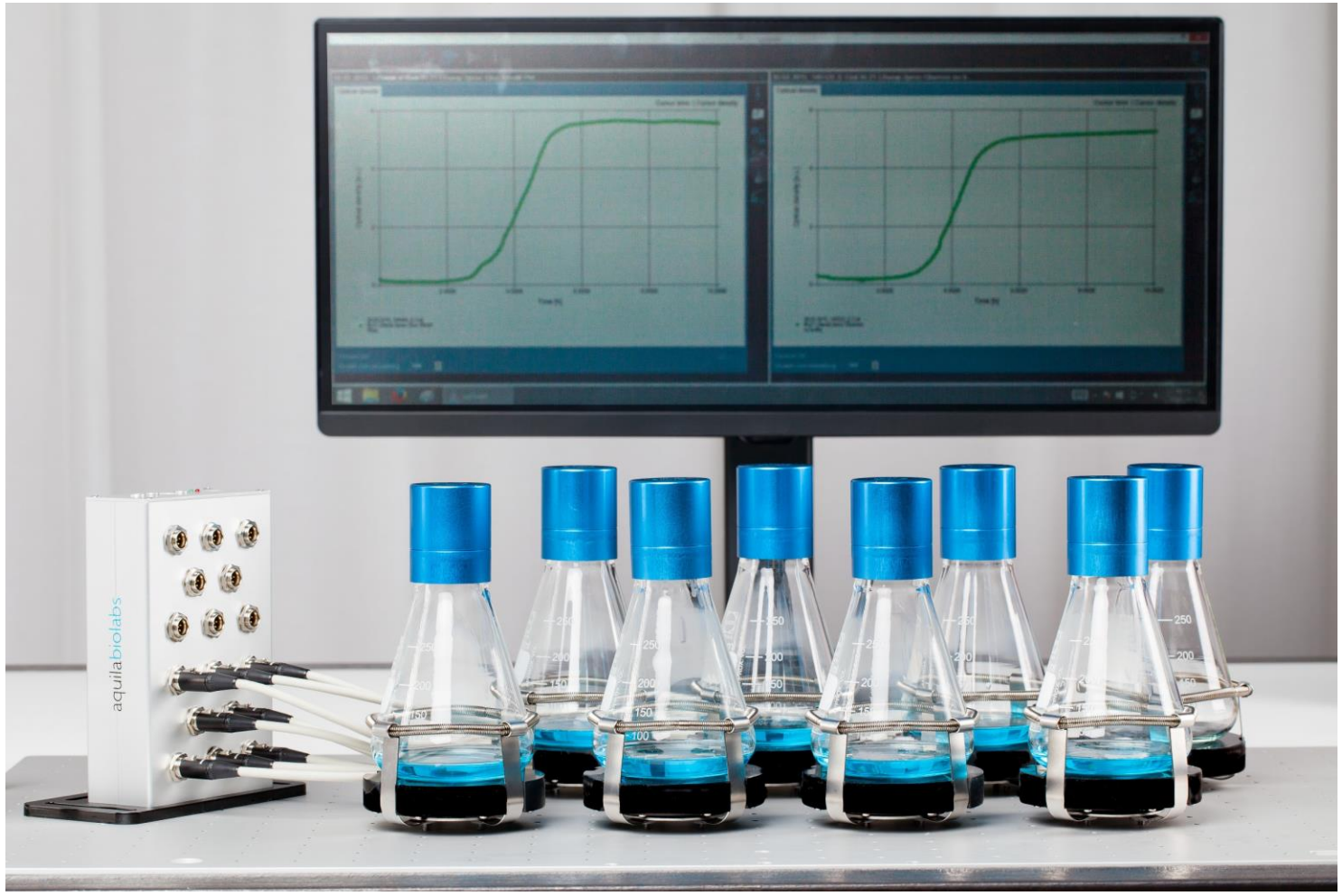
Cell Growth Quantifier (CGQ)

Online Biomass Monitoring in Shake Flasks

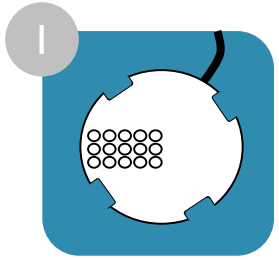
The Cell Growth Quantifier (CGQ) is a bioprocess analytical technology allowing for non-invasive online biomass monitoring in shake flask cultures.

The CGQ Technology



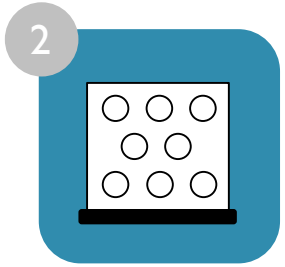
A CGQ system consists of three components:
The sensor plates, the base station and the software CGQuant.

Components of the CGQ System



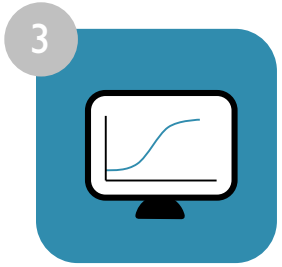
Sensor Plate

The sensor plates are positioned under the shake flask and measure the biomass non-invasively.



Base Station

The base station bundles the data from all monitored flasks and sends it to the software CGQuant.



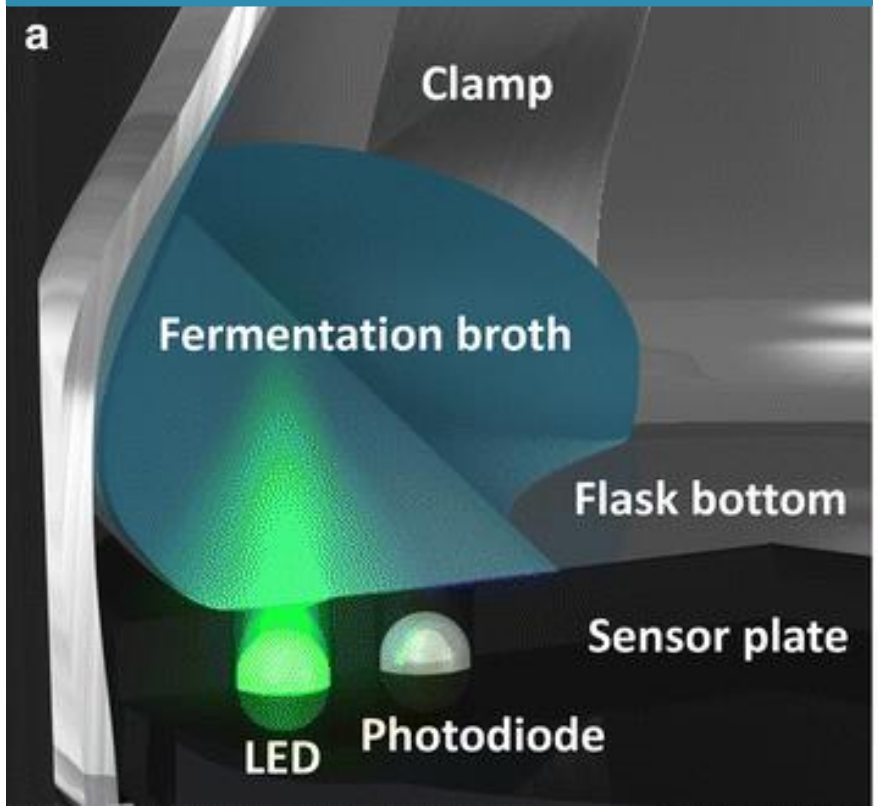
CGQuant

The software CGQuant analyzes and visualizes the biomass signal from all monitored shake flasks.

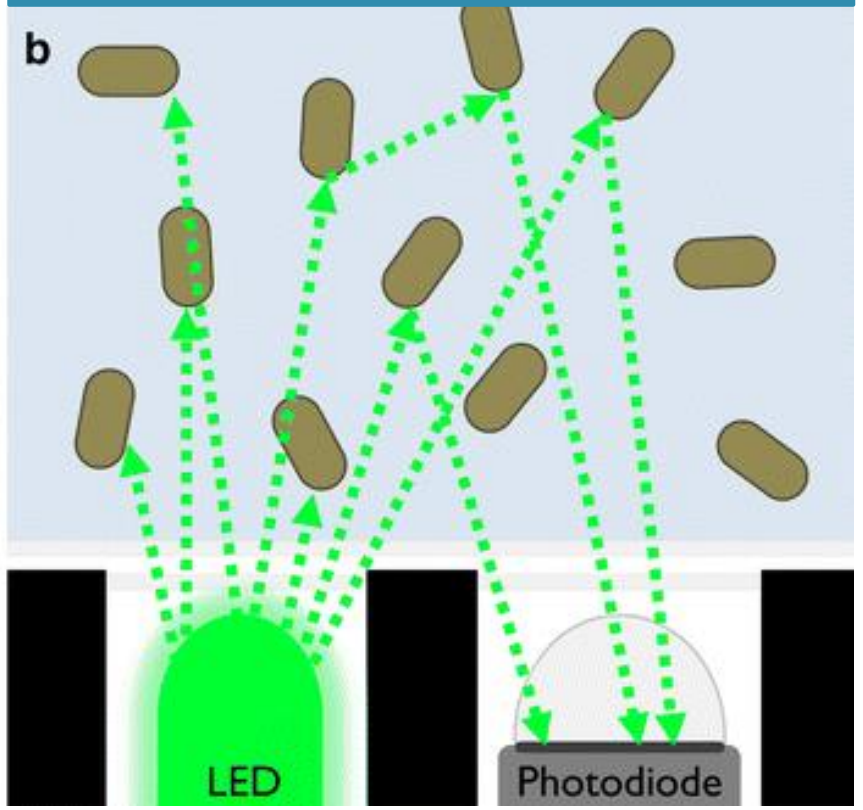
The CGQ implements a dynamic approach of backscattered light measurement, allowing for accurate biomass monitoring in shaken cultures.

The Principle of Measurement

CGQ Sensing Architecture



Biomass Monitoring by Backscattered Light Detection



aquila biolabs has developed a sensor capable of monitoring biomass non-invasively through the glass wall of a shake flask.

100 ml Sensor Plate

aquila biolabs' universal adapter system allows the customer to use the same sensor for various shake flask sizes.

The Model „One sensor for all shake flask sizes“

100 ml Sensor Plate

250 ml Universal Adapter

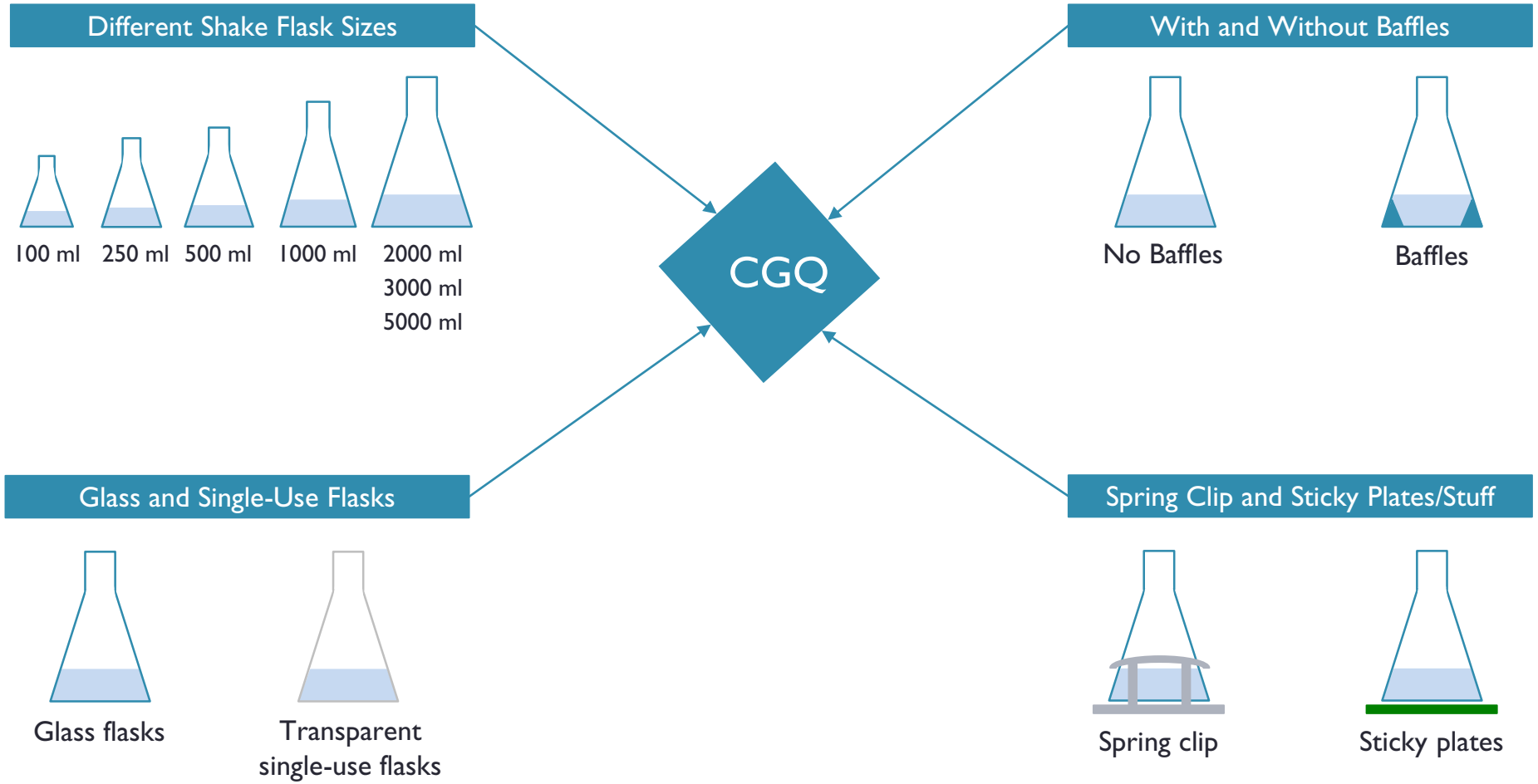
Sensor Plate for 250 ml Flask

Advantages

- Maximum flexibility: the same sensor plate can be used for different shake flask sizes.
- If an existing customer decides to monitor other flask sizes at one point, he now only needs to invest into adapters instead of buying additional sensor plates.

The CGQ is compatible with all sizes and kinds of shake flasks (and even other vessels) as well as every common type of shaker.

Compatible Laboratory Infrastructure



Various organisms ranging from bacteria and archaea over yeast to microalgae have been successfully monitored with the CGQ technology.

Successfully Monitored Organisms

Bacteria

- *Escherichia coli*
- *Corynebacterium glutamicum*
- *Bacillus subtilis*
- *Pseudomonas putida*
- *Gluconobacter oxydans*
- *Lactobacillus plantarum*
- *Vibrio natriegens*
- *Vibrio cholerae*
- *Staphylococcus aureus*
- *Klebsiella pneumoniae*
- *Actinobacillus pleuropneumoniae*
- *Chromobacterium violaceum*
- *Blautia producta*
- *Hungtatella hathewayi*
- *Prevotella copri*

Yeast

- *Saccharomyces cerevisiae*
- *Schizosaccharomyces pombe*
- *Pichia pastoris*
- *Yarrowia lipolytica*
- *Kluyveromyces lactis*
- *Hansenula polymorpha*
- *Ustilago maydis*

Filamentous organisms

- *Aspergillus fumigatus*
- *Aspergillus nidulans*
- *Aspergillus niger*
- *Streptomyces acidiscabies*
- *Streptomyces venezuelae*

Archaea

- *Haloferax volcanii*
- *Sulfolobus acidocaldarius*

Anaerobic organisms

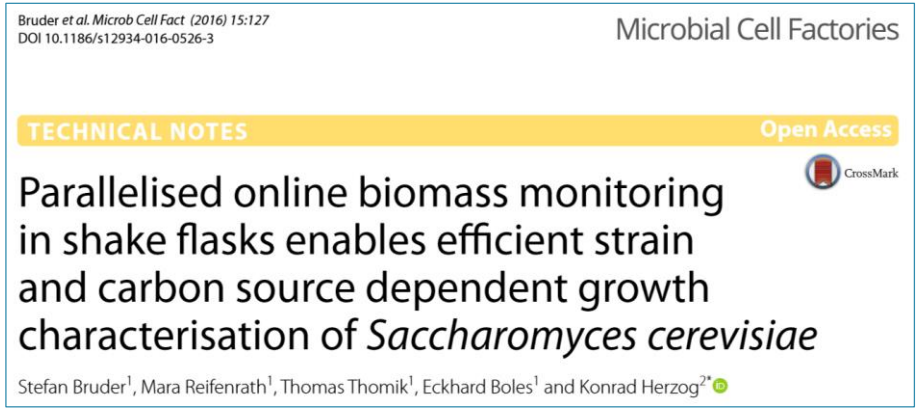
- *Acetobacterium woodii*
- *Clostridium aectobutylicum*
- *Clostridium ljungdahlii*
- *Clostridium difficile*

Phototrophic organisms

- *Chlorella vulgaris (green algae)*
- *Scenedesmus obliquus (green algae)*
- *Synechococcus elongatus (cyanobacteria)*
- *Nicotiana tabacum BY-2 (plant cells)*

The CGQ technology has already been used for several publications in renowned journals.

Exemplary Publications



Bruder *et al. Microb Cell Fact (2016) 15:127*
DOI 10.1186/s12934-016-0526-3

Microbial Cell Factories

TECHNICAL NOTES Open Access

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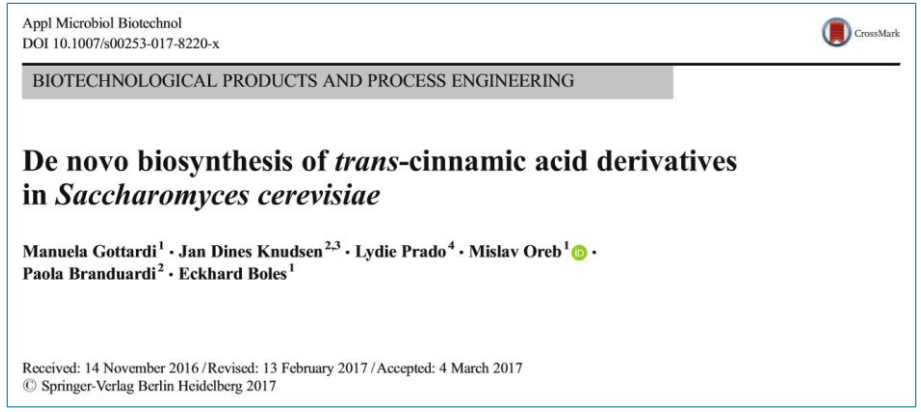
Parallelised online biomass monitoring in shake flasks enables efficient strain and carbon source dependent growth characterisation of *Saccharomyces cerevisiae*

Stefan Bruder[1], Mara Reifenrath[1], Thomas Thomik[1], Eckhard Boles[1] and Konrad Herzog[2*]



Appl Microbiol Biotechnol
DOI 10.1007/s00253-017-8220-x

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BIOTECHNOLOGICAL PRODUCTS AND PROCESS ENGINEERING

De novo biosynthesis of *trans*-cinnamic acid derivatives in *Saccharomyces cerevisiae*

Manuela Gottardi[1] · Jan Dines Knudsen[2,3] · Lydie Prado[4] · Mislav Oreb[1] · Paola Branduardi[2] · Eckhard Boles[1]

Received: 14 November 2016 / Revised: 13 February 2017 / Accepted: 4 March 2017
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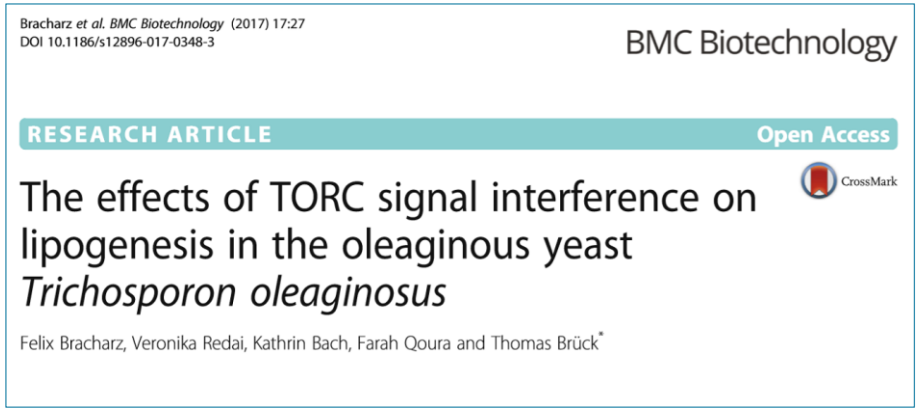

Bracharz *et al. BMC Biotechnology* (2017) 17:27
DOI 10.1186/s12896-017-0348-3

BMC Biotechnology

RESEARCH ARTICLE Open Access

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The effects of TORC signal interference on lipogenesis in the oleaginous yeast *Trichosporon oleaginosus*

Felix Bracharz, Veronika Redai, Kathrin Bach, Farah Qoura and Thomas Brück*

Biochemical Engineering Journal 120 (2017) 103–112

Contents lists available at ScienceDirect

Biochemical Engineering Journal

journal homepage: www.elsevier.com/locate/bej

ELSEVIER

Regular article

Improvement of the yeast based (*R*)-phenylacetylcarbinol production process via reduction of by-product formation

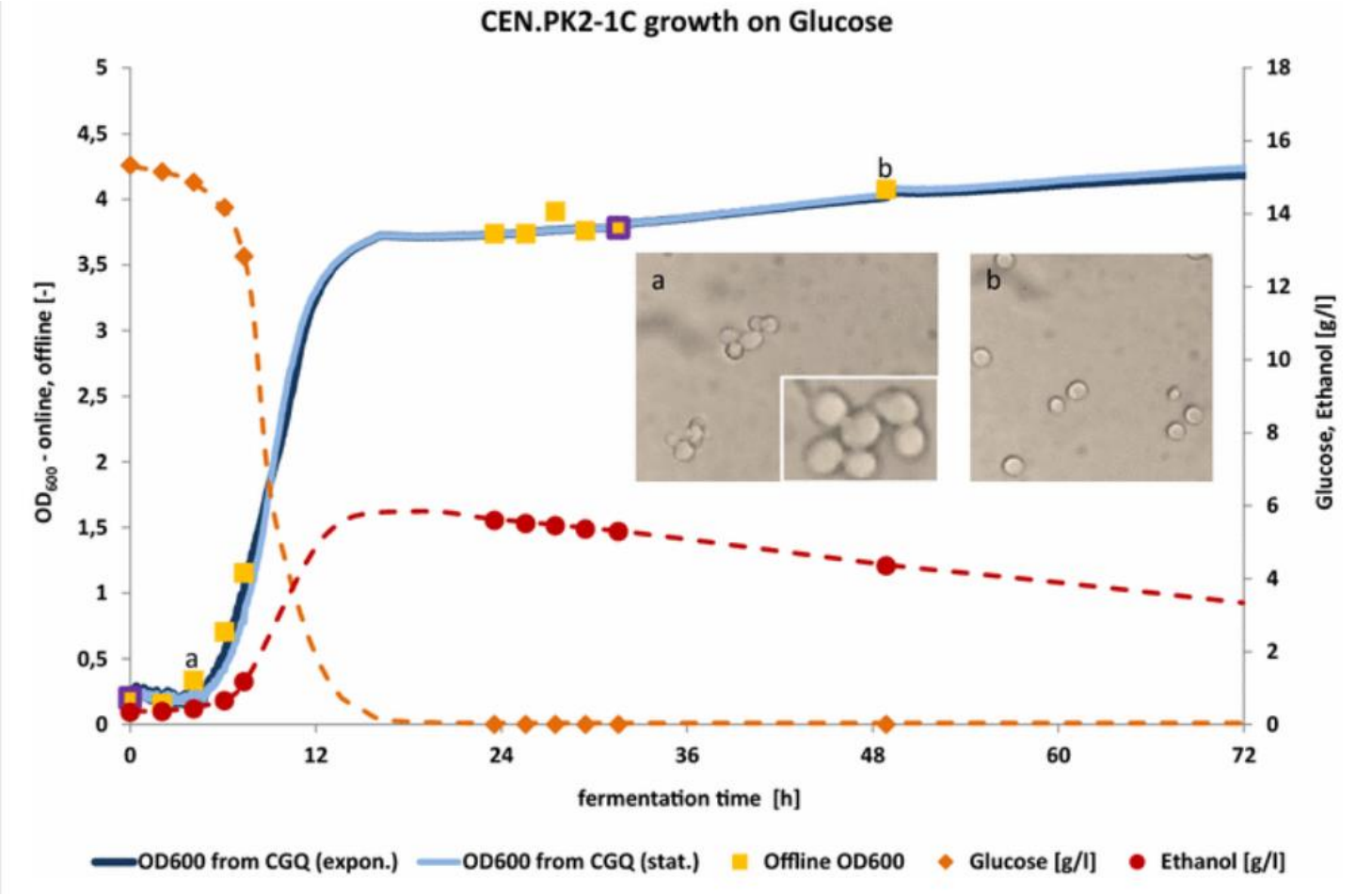
CrossMark

Stefan Bruder, Eckhard Boles*

Goethe University Frankfurt, Institute of Molecular Biosciences, 60438 Frankfurt am Main, Germany

The online biomass data generated by the CGQ correlates nicely with offline OD data.

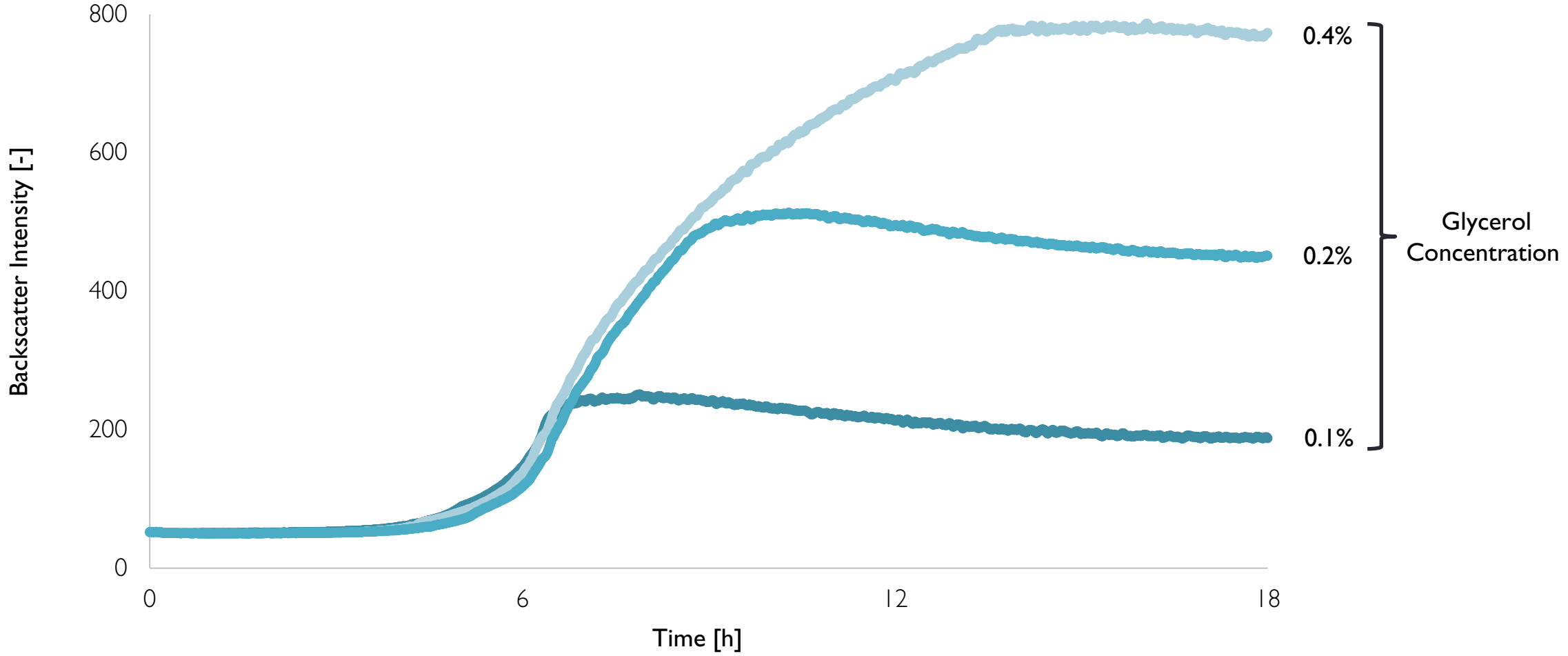
OD & CGQ Measurements (OD Calibrated): *Saccharomyces cerevisiae*



Bruder *et al.* (2016): Parallelised online biomass monitoring in shake flasks enables efficient strain and carbon source dependent growth characterisation of *Saccharomyces cerevisiae* (Microbial Cell Factories).

Parallelized online biomass monitoring with the CGQ allows for efficient screenings and growth characterizations.

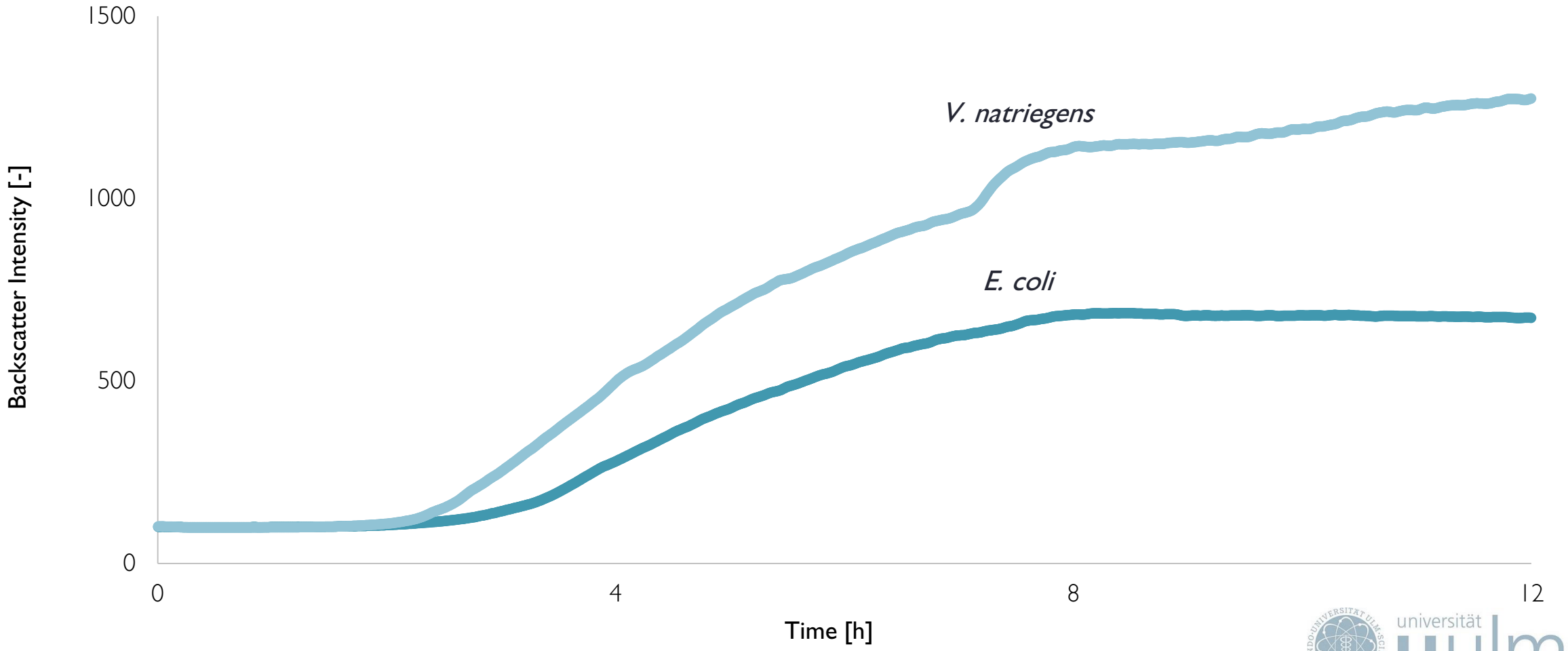
CGQ Measurements: *Escherichia coli* Growing on Different Glycerol Concentrations



Escherichia coli BL21-Gold (DE3) pET28a(+) EGFP Kan^{R}, 25 ml M9 Medium (+ 0.25 % Casamino Acids), 250 ml Shake Flasks, 37 °C, 250 rpm

The CGQ is ideal for growth rate comparisons of different organisms in shake flasks, for example *Vibrio natriegens* versus *Escherichia coli*.

CGQ Measurements: *Vibrio natriegens* and *Escherichia coli*



Escherichia coli & *Vibrio natriegens*, 25 ml LB Medium (*Vibrio*: + V2 Salts), 250 ml Shake Flasks, 37 °C, 180 rpm

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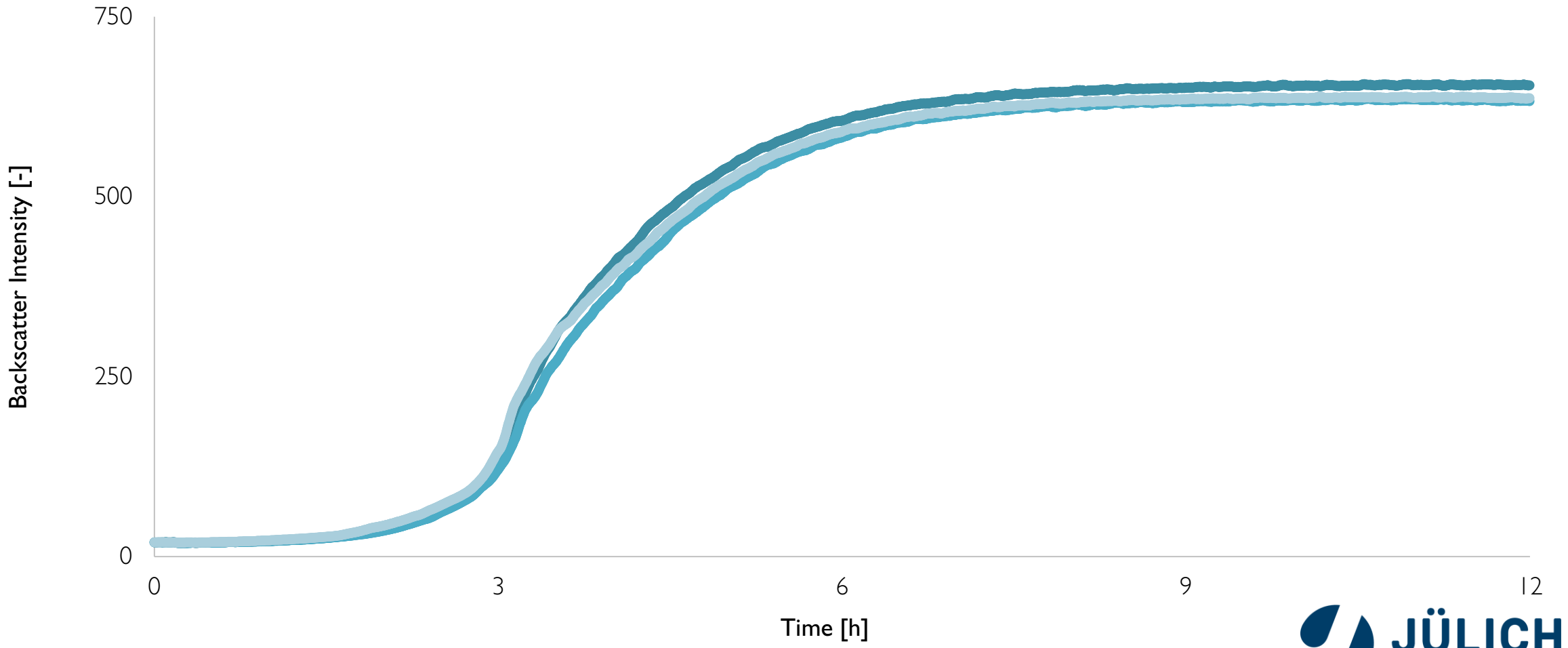
The CGQ is capable of precisely monitoring *Corynebacterium glutamicum* cultures in shake flasks.

CGQ Measurements: *Corynebacterium glutamicum* Triplicates



Corynebacterium glutamicum, 25 ml LB Medium, 250 ml Shake Flasks, 30 °C, 250 rpm

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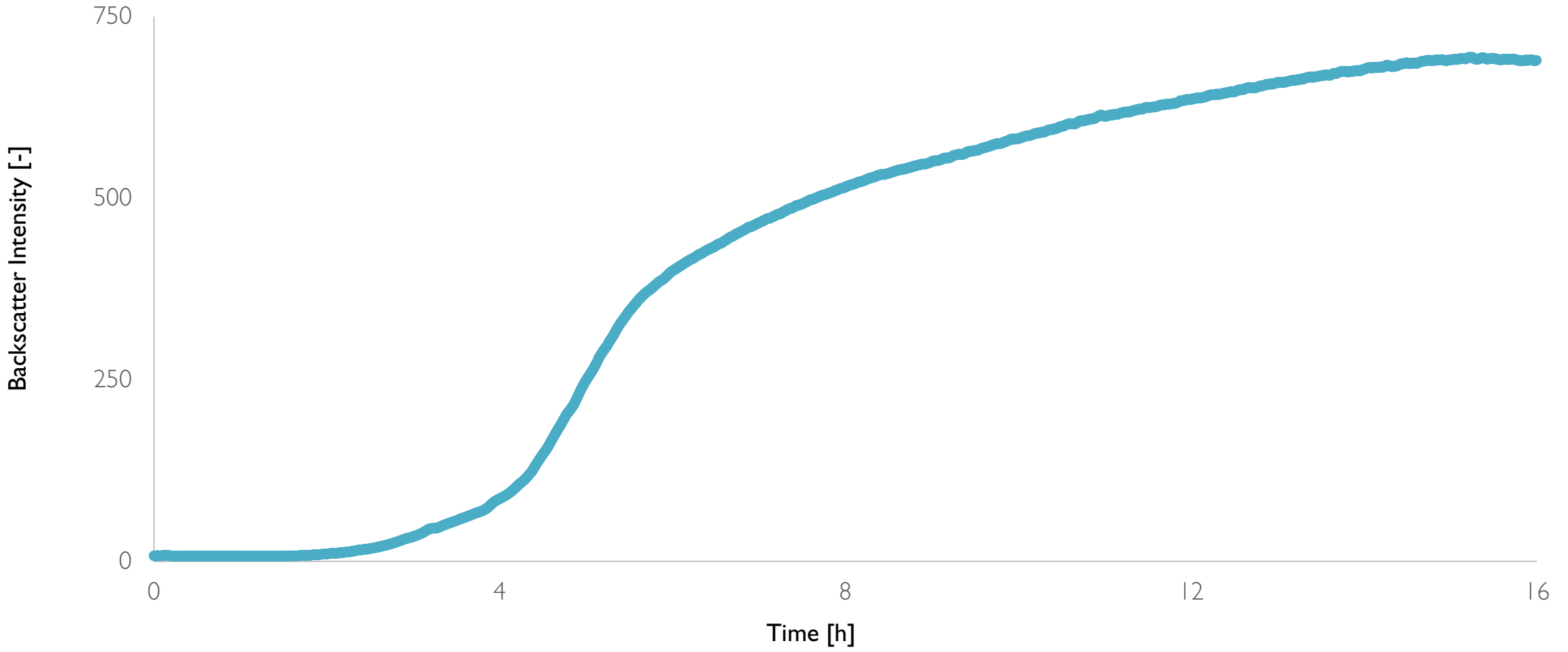
The CGQ is capable of precisely monitoring *Bacillus subtilis* cultures in shake flasks.

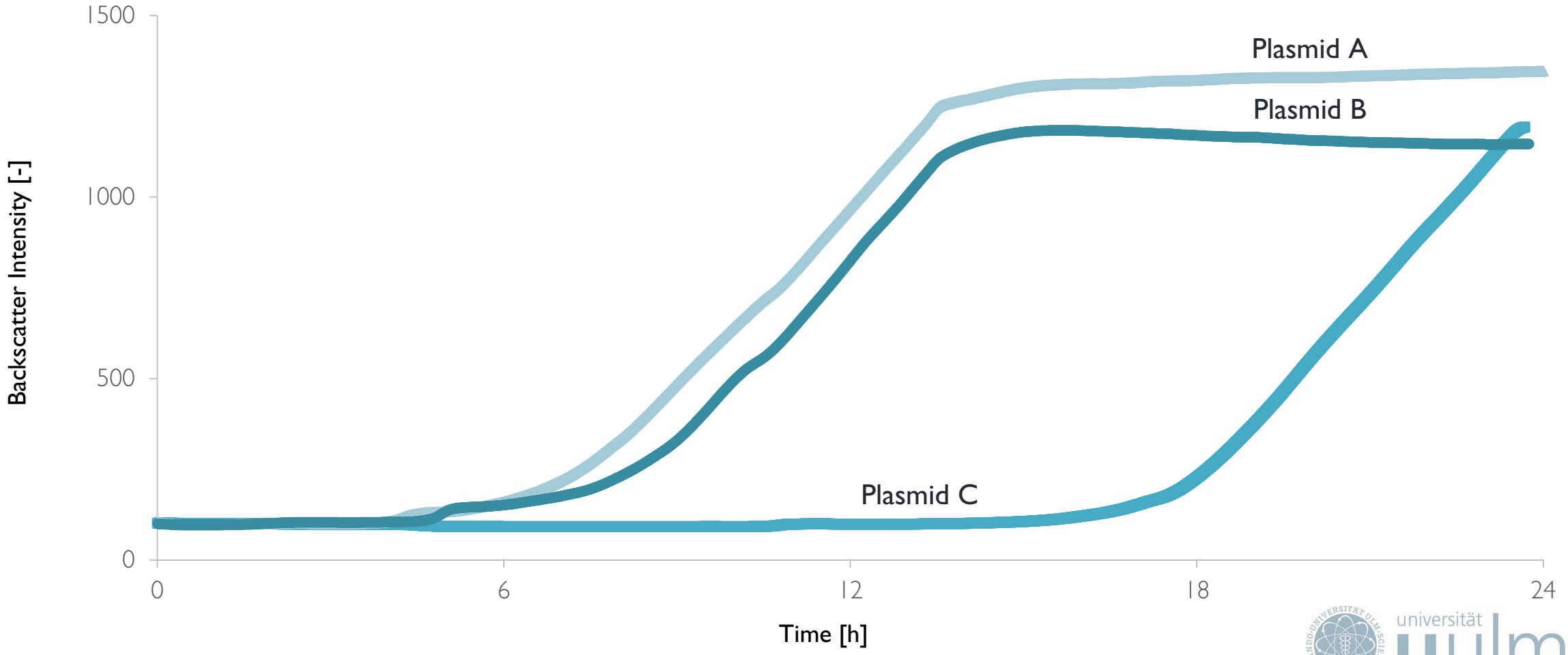
CGQ Measurement: *Bacillus subtilis*



Bacillus subtilis, 25 ml LB Medium, 250 ml Shake Flask, 37 °C, 250 rpm

The CGQ is ideal for quick and easy comparisons of different *Pseudomonas putida* strains.

CGQ Measurements: *Pseudomonas putida* Transformed with Different Plasmids



Pseudomonas putida, 25 ml Willems KPI Medium, 250 ml Shake Flasks, 30 °C, 200 rpm

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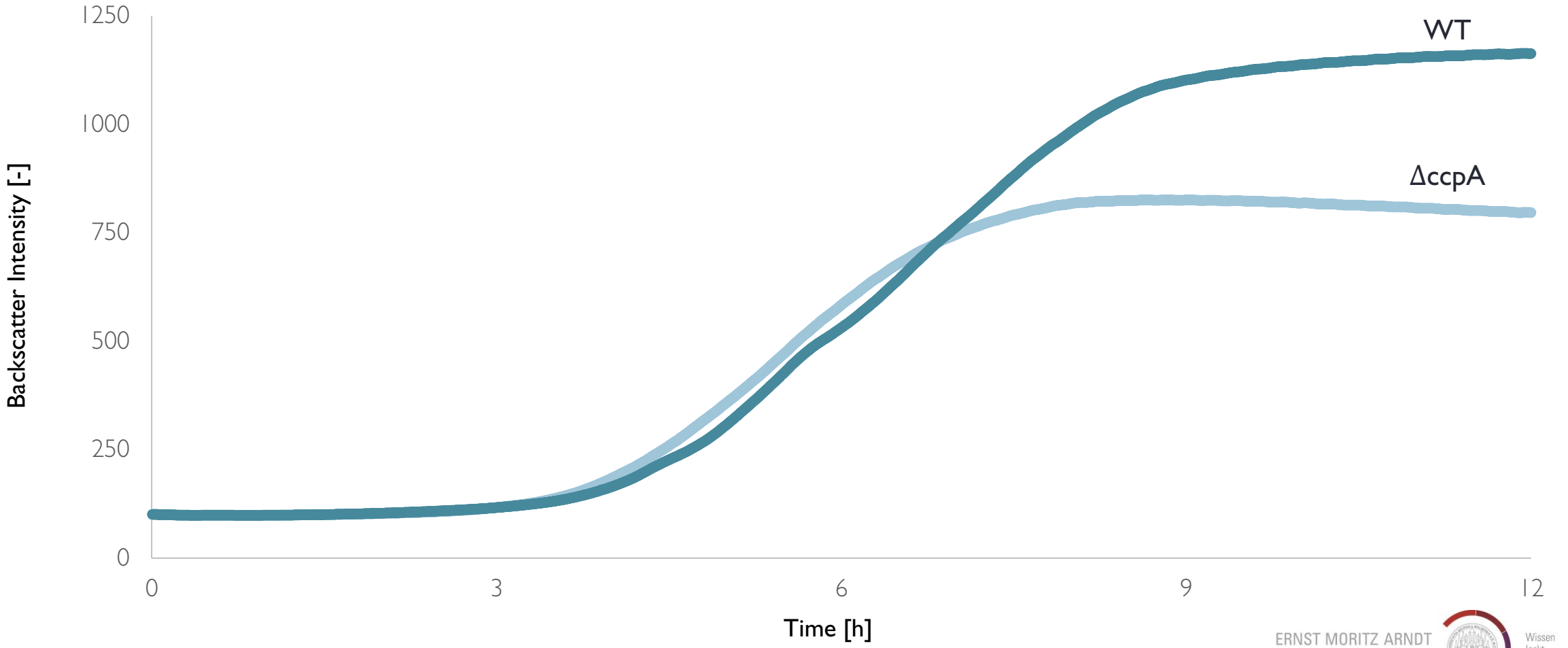
The CGQ is capable of precisely monitoring *Staphylococcus aureus* cultures in shake flasks.

CGQ Measurements: *Staphylococcus aureus* Wild Type and Deletion Mutant



Staphylococcus aureus, 20 ml LB Medium, 100 ml Shake Flasks, 37 °C, 180 rpm

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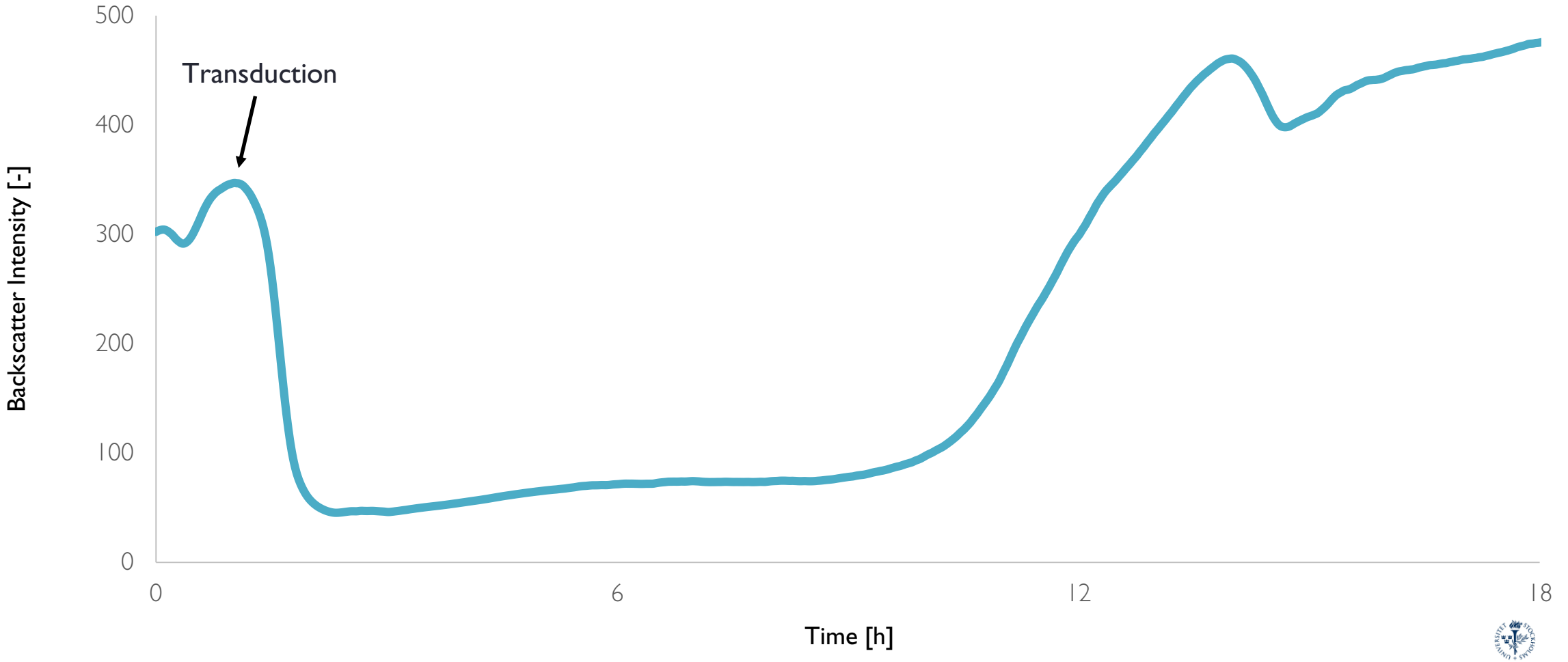
The CGQ is capable of precisely monitoring transduction of *Klebsiella pneumoniae* by phages

CGQ Measurements: *Klebsiella pneumoniae* with Phages



Klebsiella pneumoniae, 50 ml LB Medium, 250 ml Shake Flask, 37 °C, 150 rpm

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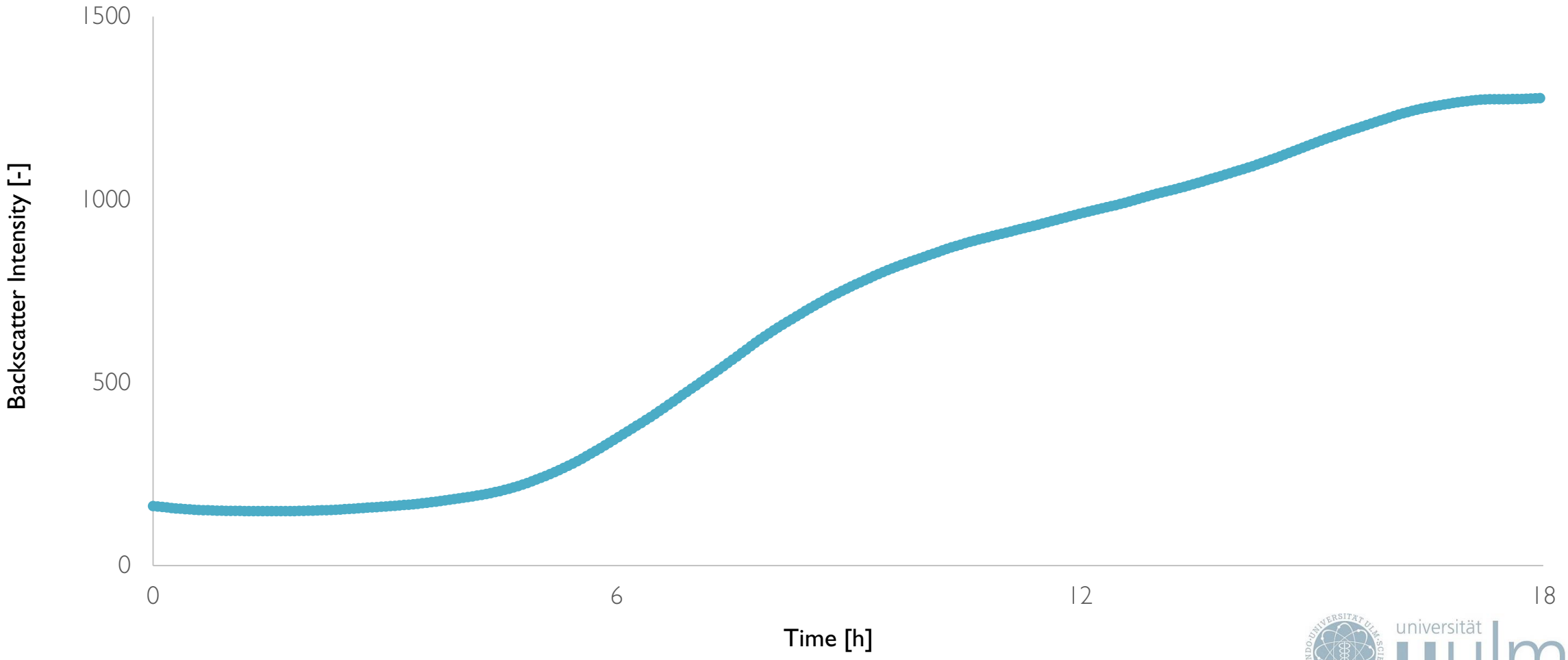
The CGQ allows for non-invasive and detailed biomass monitoring of thermophilic organisms such as *Haloferax volcanii* at 45 °C.

CGQ Measurement: *Haloferax volcanii*



Haloferax volcanii, 25 ml YPC Medium, 250 ml Shake Flask, 45 °C, 200 rpm

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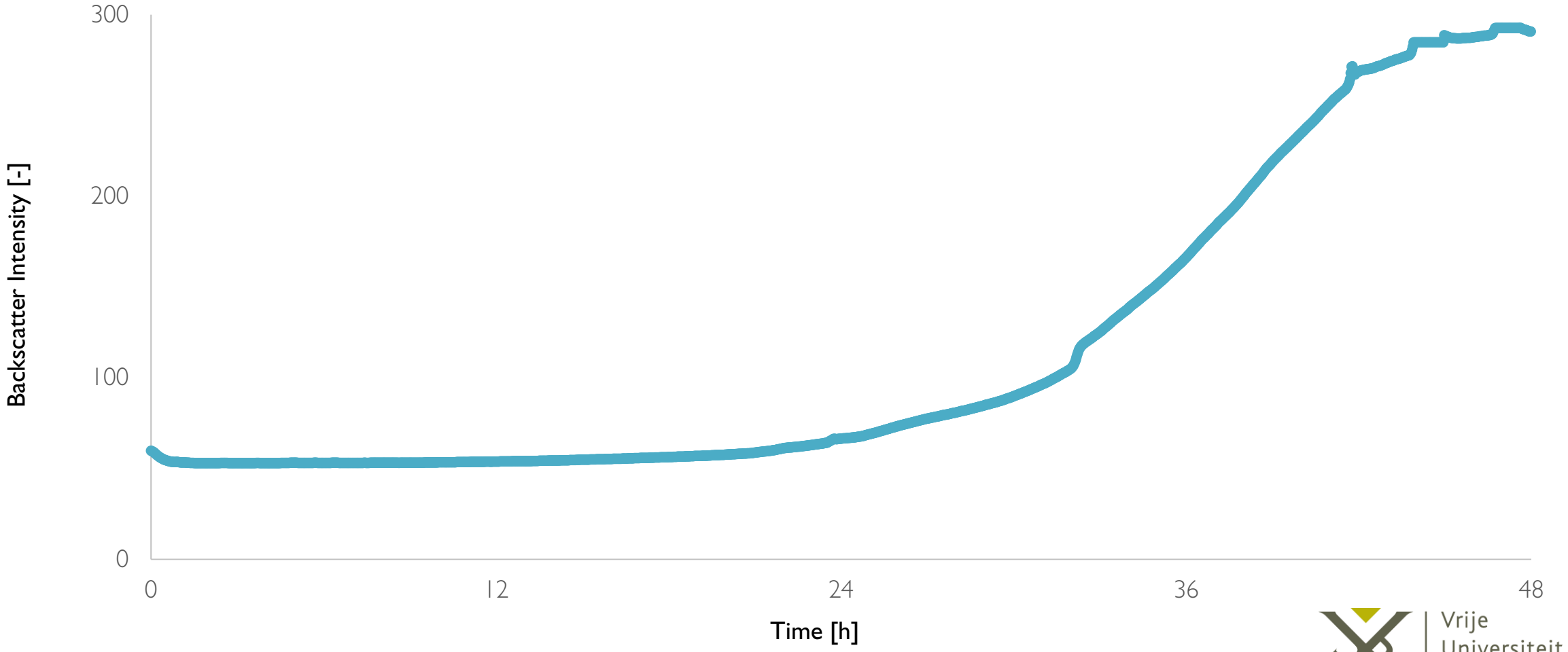
The CGQ allows for detailed biomass monitoring of hyperthermophilic organisms such as *Sulfolobus acidocaldarius* at 75 °C.

CGQ Measurement: *Sulfolobus acidocaldarius*



Sulfolobus acidocaldarius, 10 ml BROCK Medium (+ 0.1 % NZ + 0.3 % Dex), 100 ml Shake Flask, 75 °C, 180 rpm

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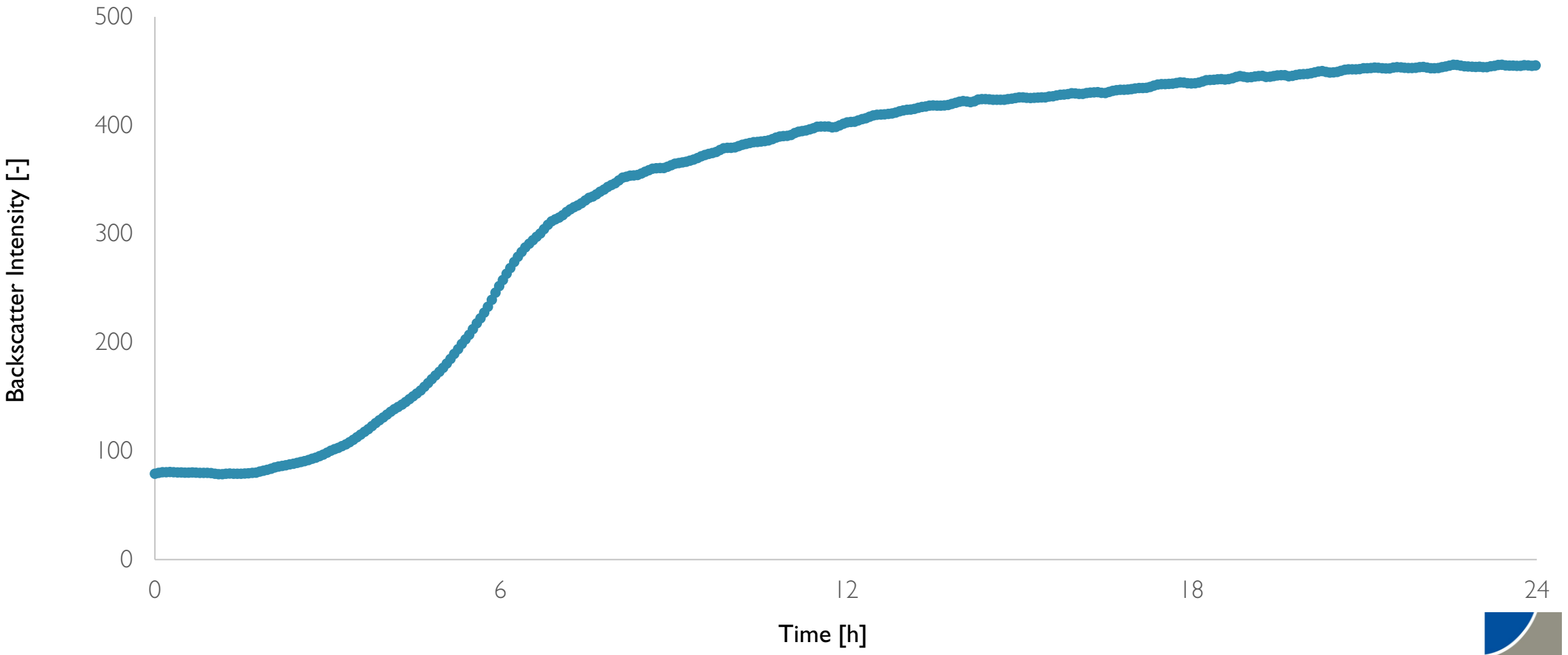
The CGQ allows for biomass monitoring of *Gluconobacter oxydans* cultures in shake flasks.

CGQ Measurement: *Gluconobacter oxydans*



Gluconobacter oxydans, 100 ml YM Media, 500 ml baffled Shake Flask, 30 °C. 140 rpm

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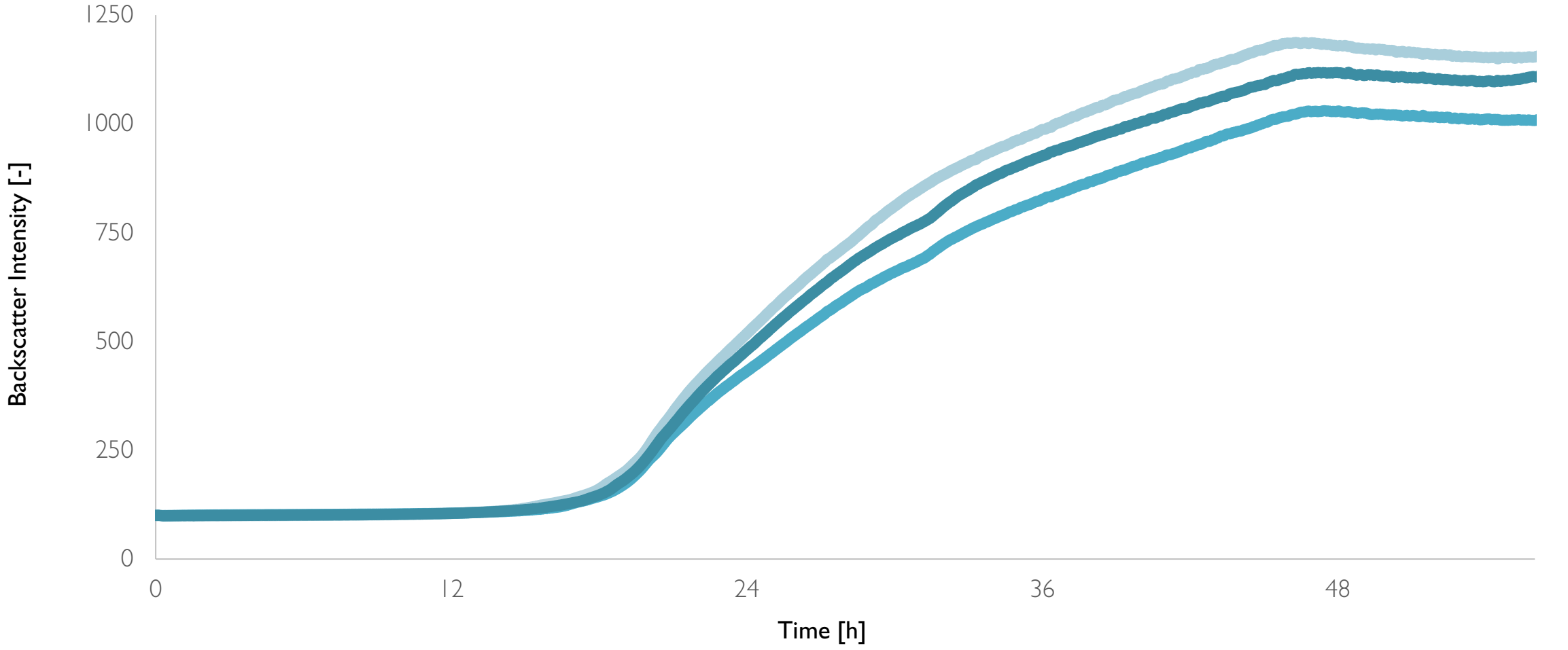
The CGQ is capable of precisely monitoring filamentous *Aspergillus niger* cultures in shake flasks.

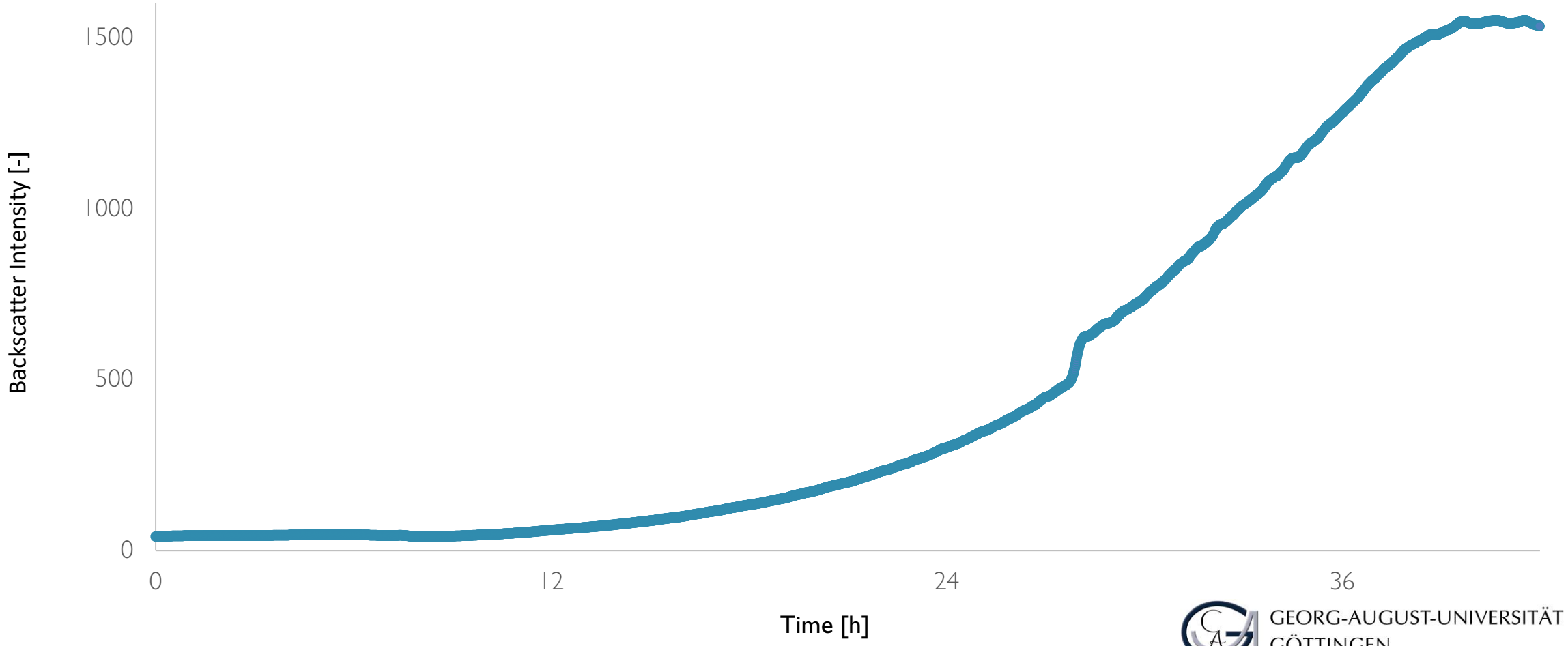
CGQ Measurement: *Aspergillus niger* Triplicates



Aspergillus niger, 50 ml LB Medium, 250 ml Shake Flasks, 25 °C. 250 rpm

The CGQ is capable of precisely monitoring filamentous *Aspergillus nidulans* cultures in shake flasks.

CGQ Measurements: *Aspergillus nidulans*



Aspergillus nidulans, 100 ml Minimal Medium, 250 ml Shake Flask, 30 °C, 150 rpm

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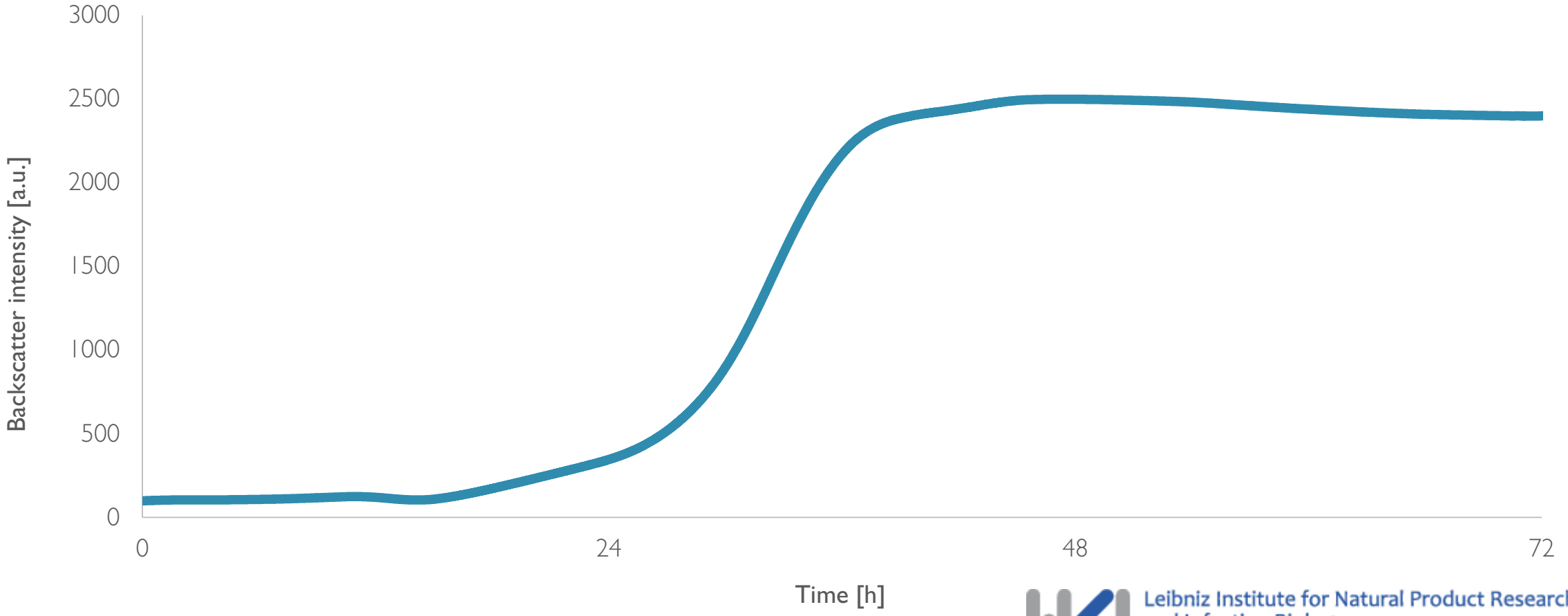
The CGQ is capable of precisely monitoring filamentous *Aspergillus fumigatus* cultures in shake flasks.

CGQ Measurements: *Aspergillus fumigatus*

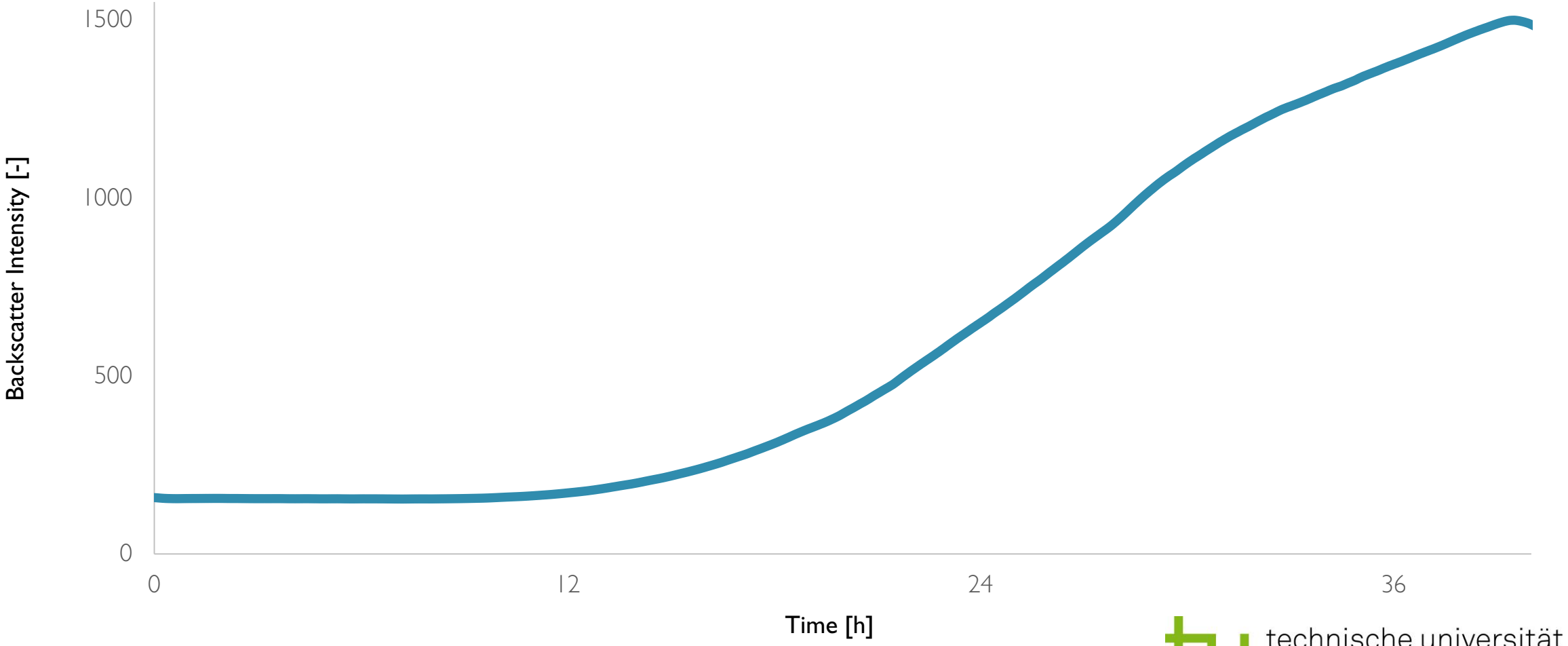


Leibniz Institute for Natural Product Research and Infection Biology
Hans Knöll Institute

Aspergillus fumigatus, 50 ml XAMM Medium, 250 ml Shake Flask, 37 °C, 200 rpm

The CGQ is capable of precisely monitoring *Streptomyces acidiscabies* cultures in shake flasks.

CGQ Measurements: *Streptomyces acidiscabies*



Streptomyces acidiscabies, 50 ml GYMS Medium, 250 ml Shake Flask, 30 °C, 160 rpm

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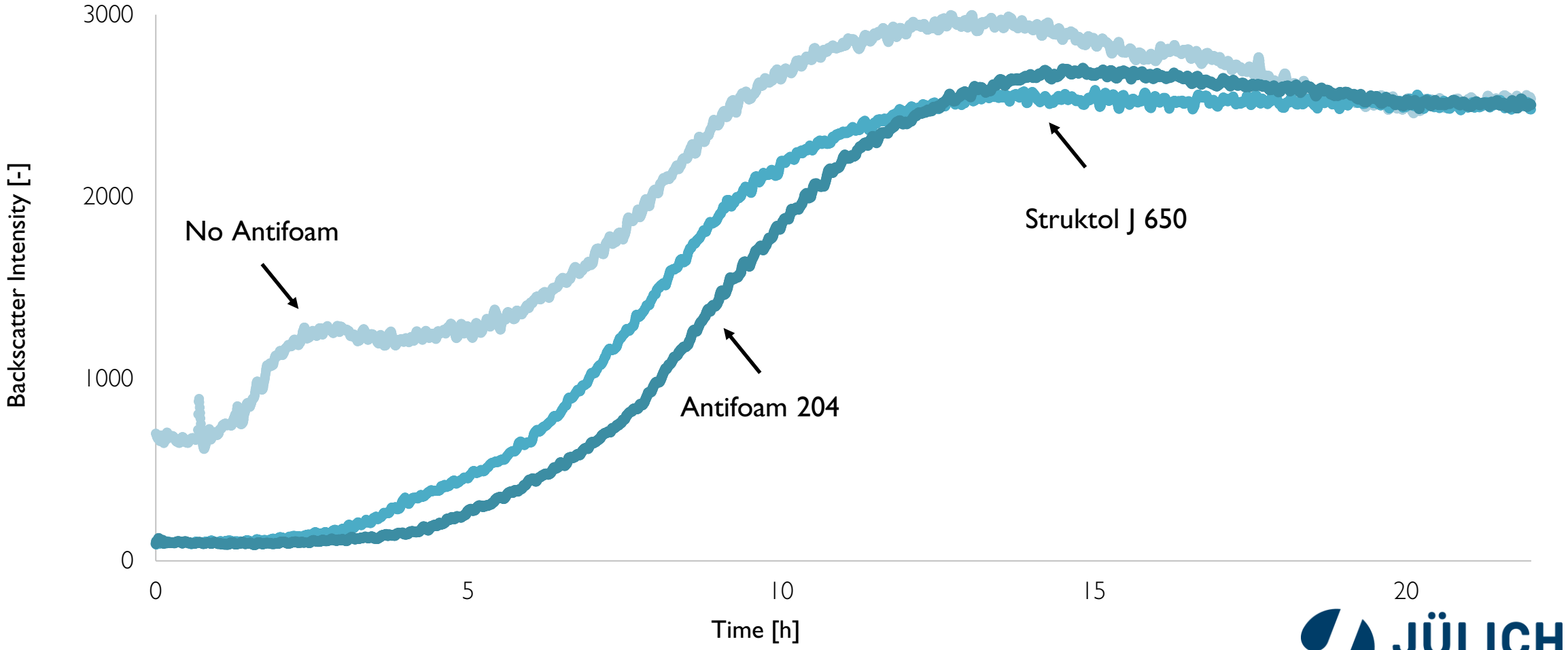
The CGQ is compatible with baffled shake flasks or foaming cultures, but antifoam should be used to avoid distorted measurement signals.

CGQ Measurements: Comparison of Different Anti-Foaming Agents



Corynebacterium glutamicum, 60 ml CGXII Medium (+ Glucose), 500 ml Baffled Shake Flasks, 30 °C, 130 rpm

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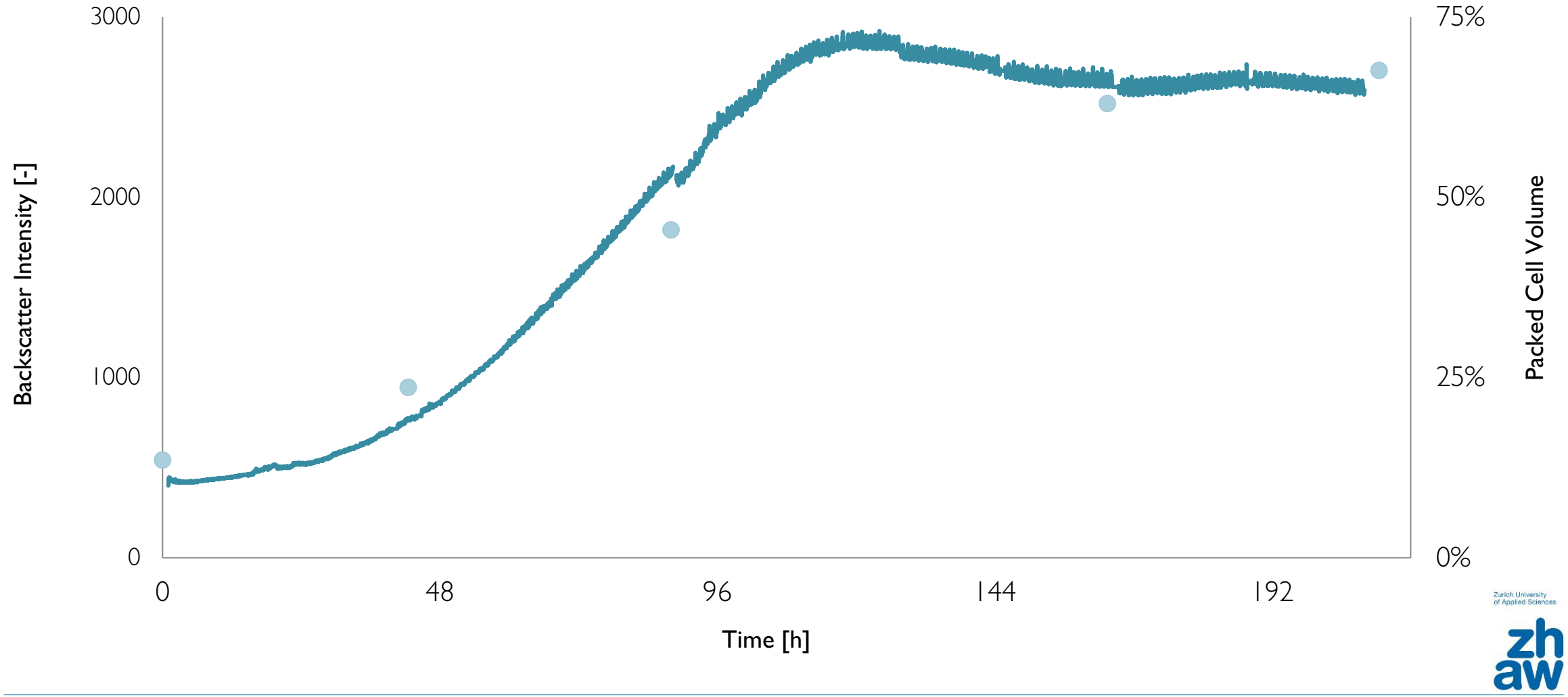
The CGQ allows for detailed biomass monitoring of plant cells and shows good correlation with "packed cell volume".

CGQ Measurement & Packed Cell Volume: *Nicotiana tabacum BY-2*



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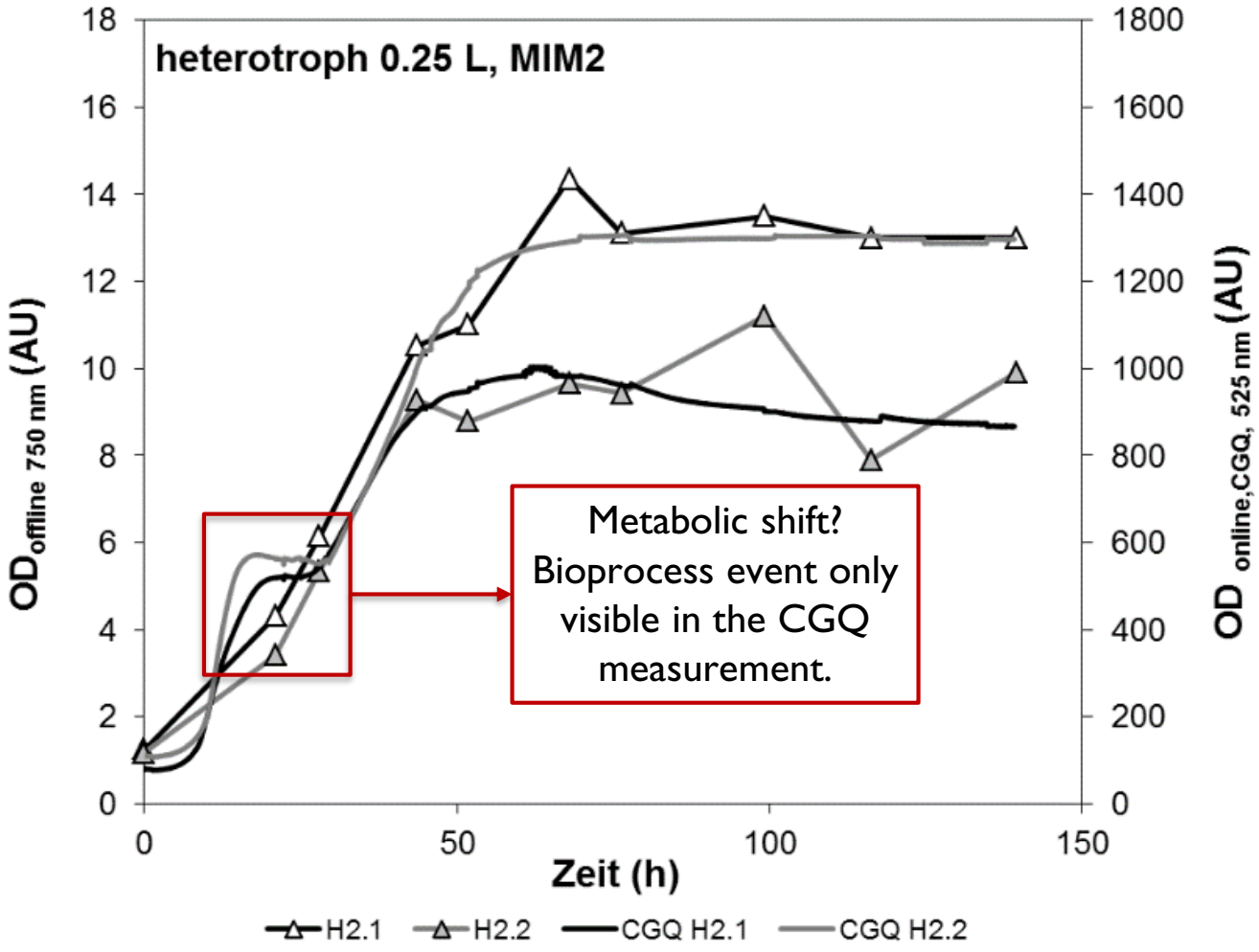
The CGQ allows for detailed bioprocess monitoring of microalgae and shows good correlation with offline OD.

CGQ & $OD_{750\ nm}$ Measurements: *Chlorella vulgaris*



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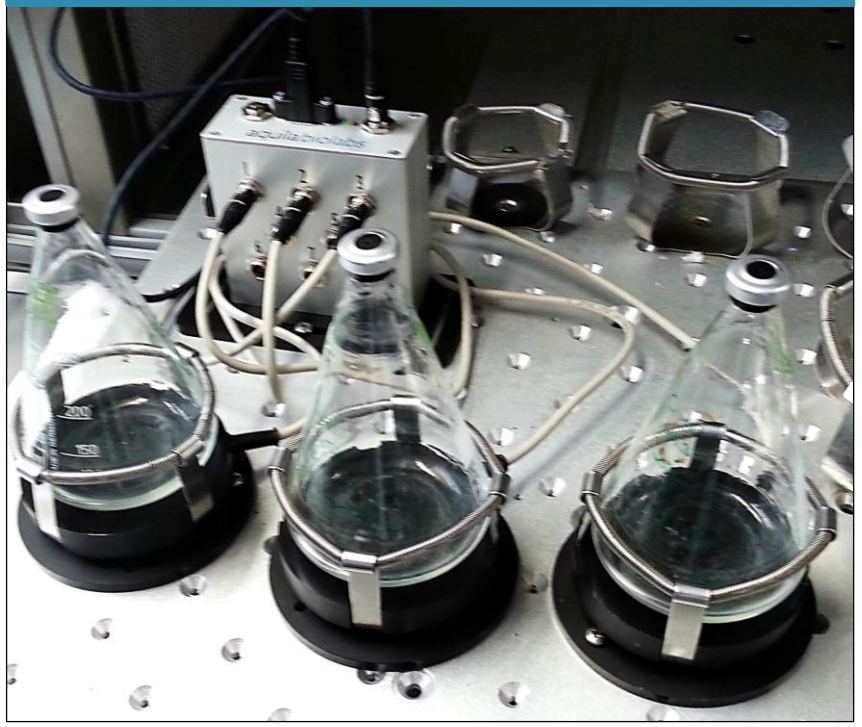
The CGQ is fully compatible with all typical anaerobic cultivation vessels such as serum bottles or anaerobic shake flasks.

CGQ for Anaerobic Cultivation Vessels

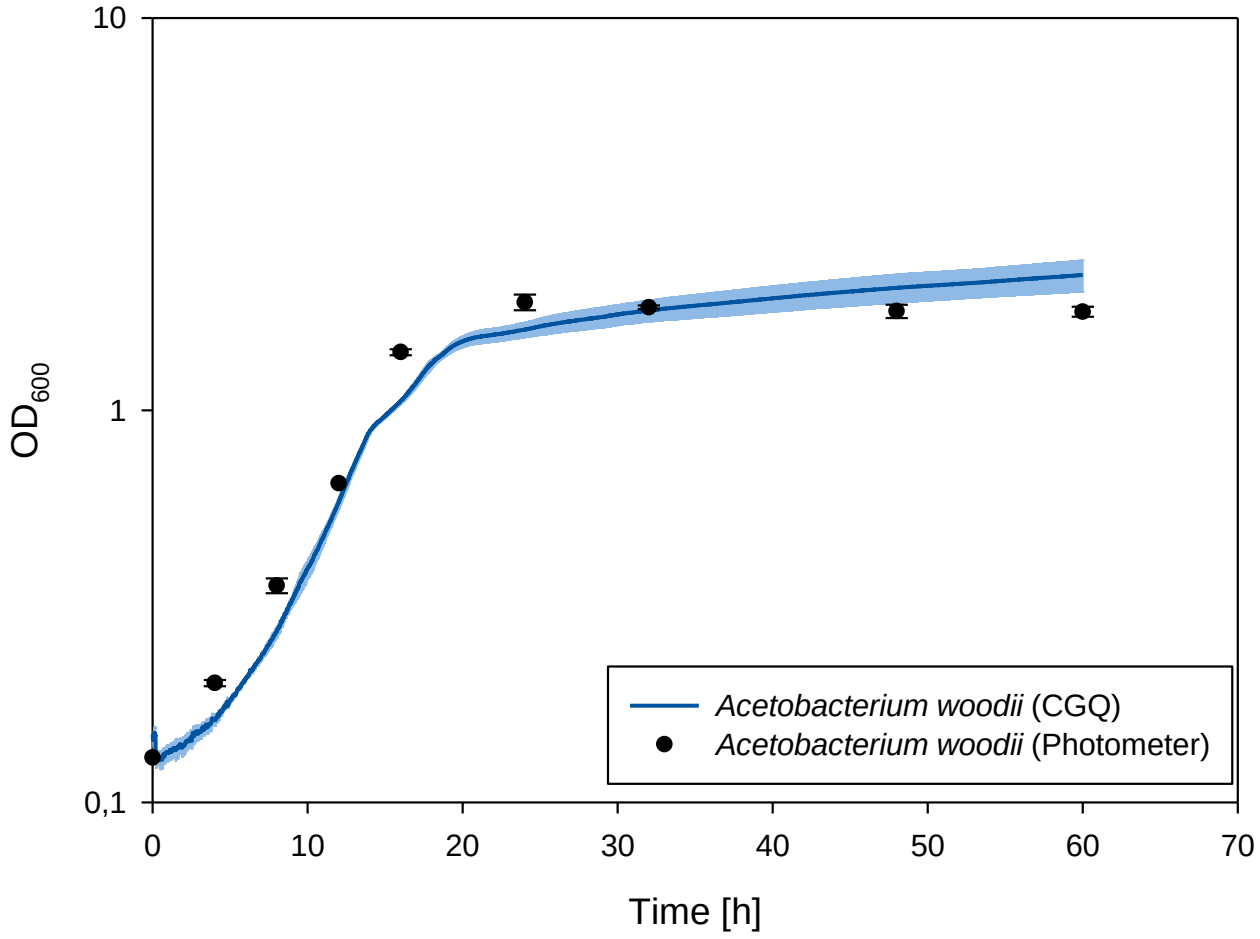
CGQ with Serum Bottles

CGQ with Anaerobic Shake Flasks



The CGQ is capable of precisely monitoring *Acetobacterium woodii* cultures in serum bottles and shows good OD correlation.

CGQ & OD_{600} Measurements: *Acetobacterium woodii* Triplicates



Acetobacterium woodii, 50 ml Acetobacterium Medium (+ Fructose), 100 ml Serum Bottle, 30 °C, 250 rpm

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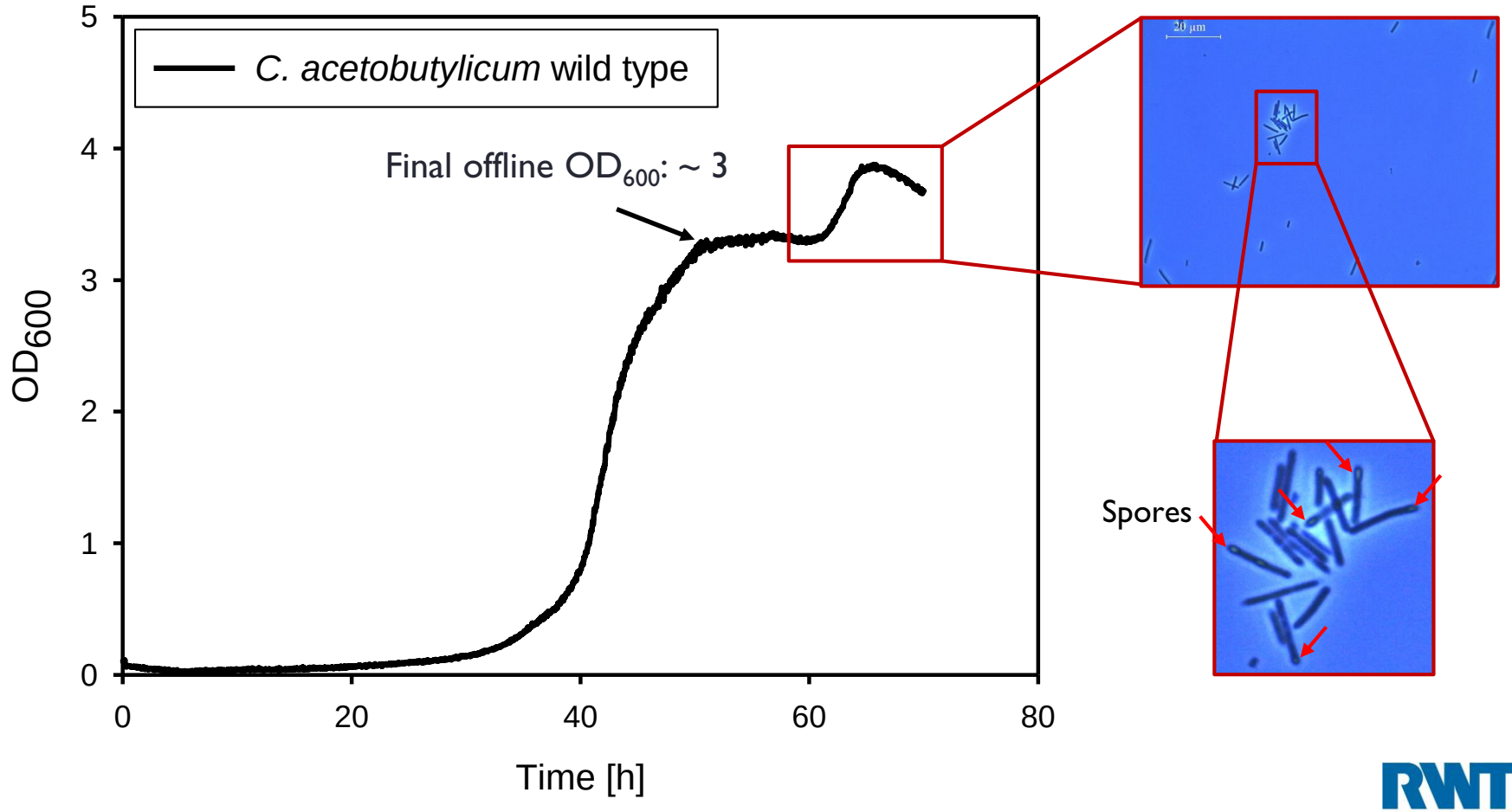
The CGQ allows for OD_{600} monitoring of anaerobic *Clostridium acetobutylicum* cultures and real time detection of spore formation.

CGQ Measurement & Microscopic Images: *Clostridium acetobutylicum*



Clostridium acetobutylicum, 50 ml MSM (+ MES), 100 ml Serum Bottle, 37 °C, 250 rpm

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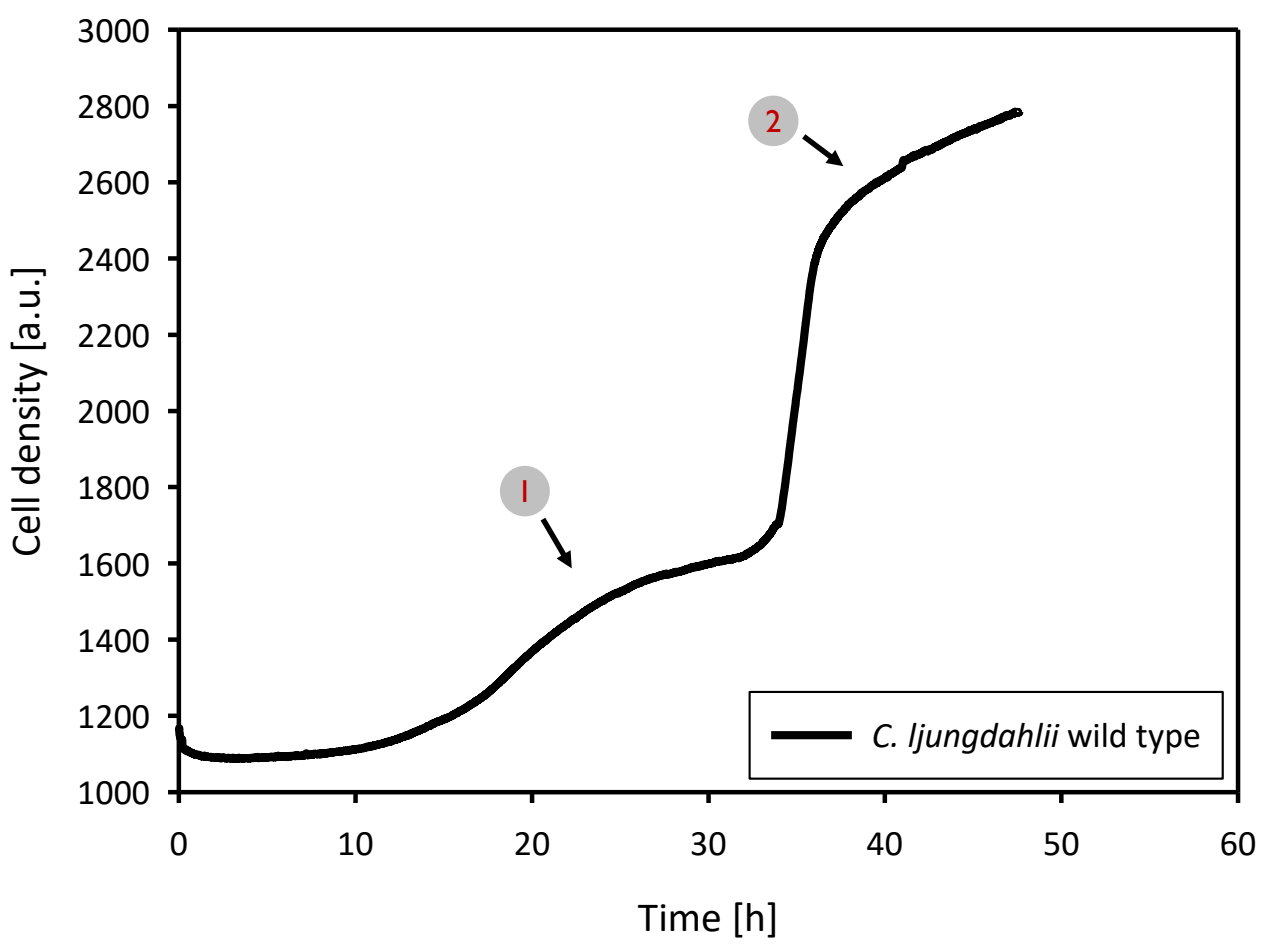
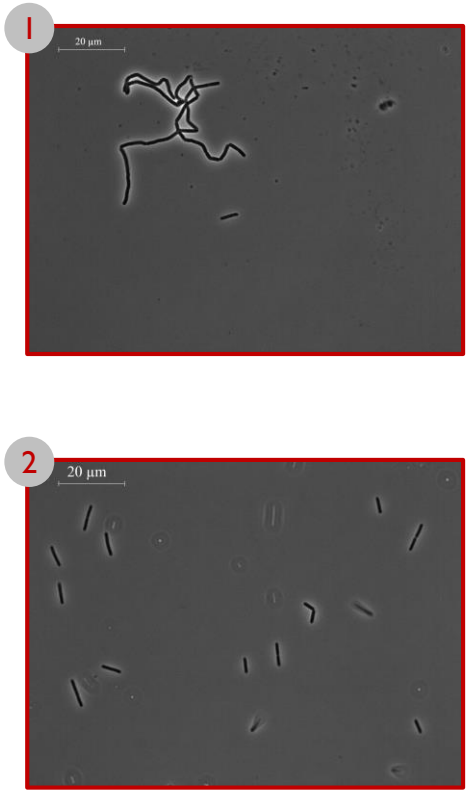
The CGQ allows for biomass monitoring of anaerobic *Clostridium ljungdahlii* cultures and detection of cell agglomeration.

CGQ Measurement & Microscopic Images: *Clostridium ljungdahlii*





Clostridium ljungdahlii, 100 ml RCM (+ Fructose), 200 ml Serum Bottle, 37 °C, 250 rpm

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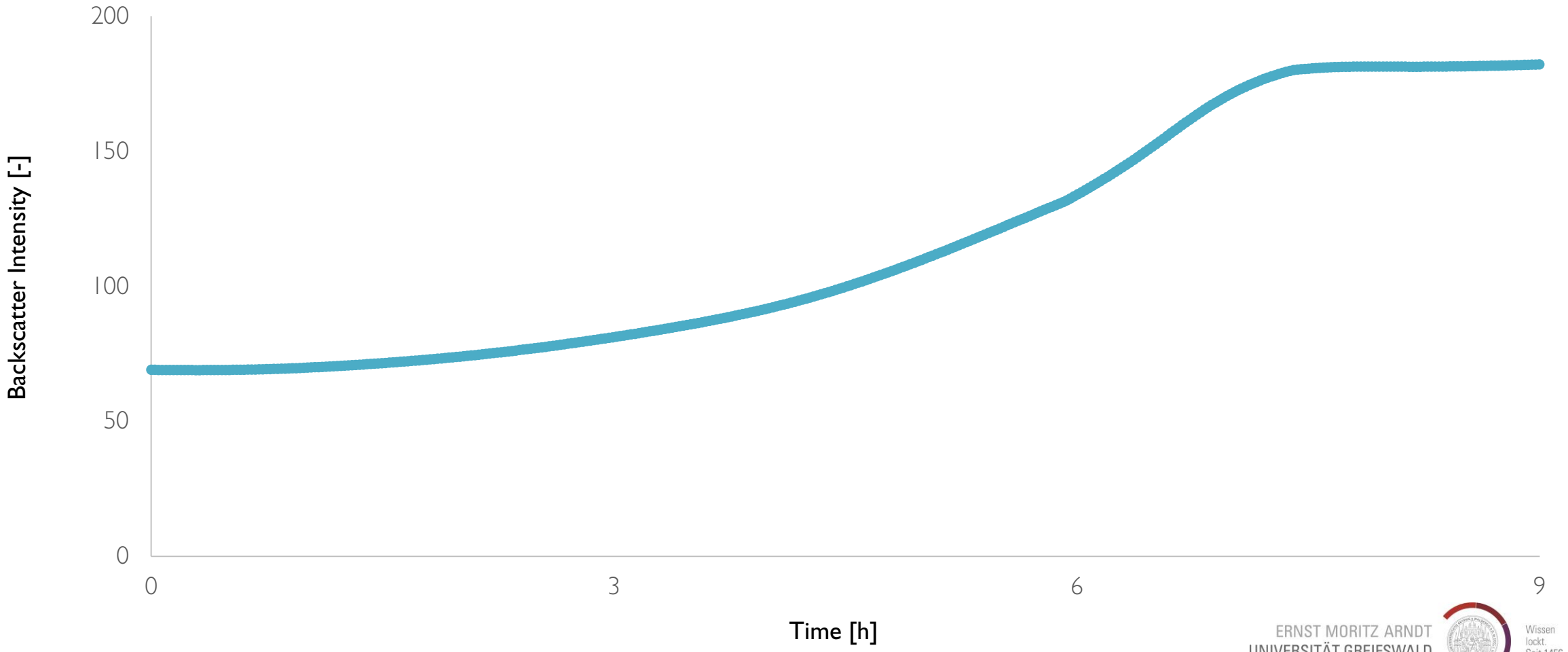
The CGQ is capable of precisely monitoring *Clostridium difficile* cultures in anaerobic shake flasks.

CGQ Measurements: *Clostridium difficile*



Clostridium difficile, 25 ml BHI Medium, 250 ml Sealed Shake Flasks, 37 °C, 180 rpm

ERNST MORITZ ARNDT
UNIVERSITÄT GREIFSWALD
Wissen lockt. Seit 1456

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