



# Non-contact Raman Spectroscopy for Bioprocess Monitoring of CHO Cell Cultivations

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## Introduction

The use of spectroscopic sensors for bioprocess monitoring is a powerful tool within PAT initiative of the FDA. In-line measurements are particularly important during cost-intensive manufacturing of biopharmaceuticals in order to facilitate early process fault detection, minimize the risk of contamination and observe real time product release. Spectroscopic sensors enable simultaneous in-line bioprocess monitoring of various critical process parameters (CPPs) including biological and chemical variables during the cell cultivation process. In this study, a new developed non-contact raman process probe (tecRaman probe by tec5) was evaluated for monitoring of CHO cell cultivations for monoclonal antibody production in a stirred tank bioreactor.

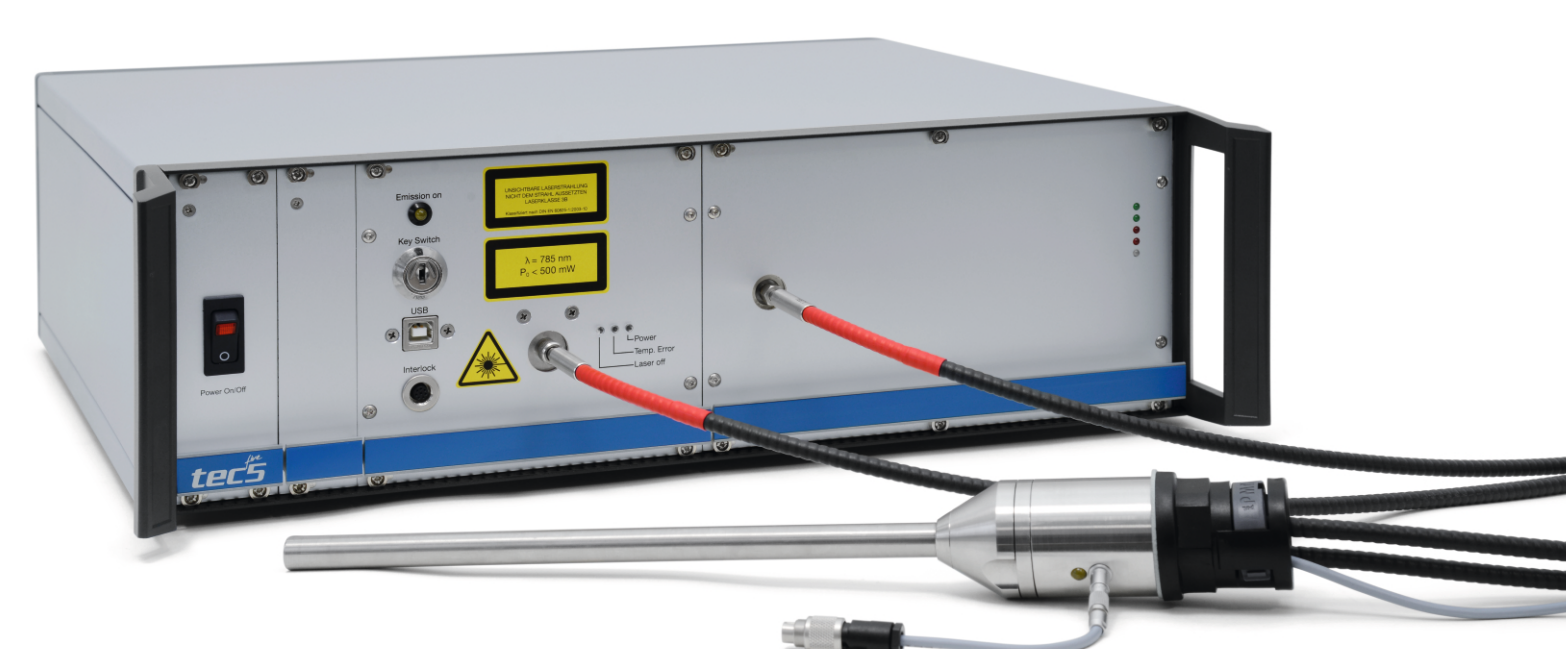
## Advantages of Non-contact Raman Spectroscopy

- No probe insertion, no risk of contamination
- Contact-free adaption
- Applicable with all commonly used glass components
- No biofilm formation
- Measurement through single-use bioreactor materials and glass

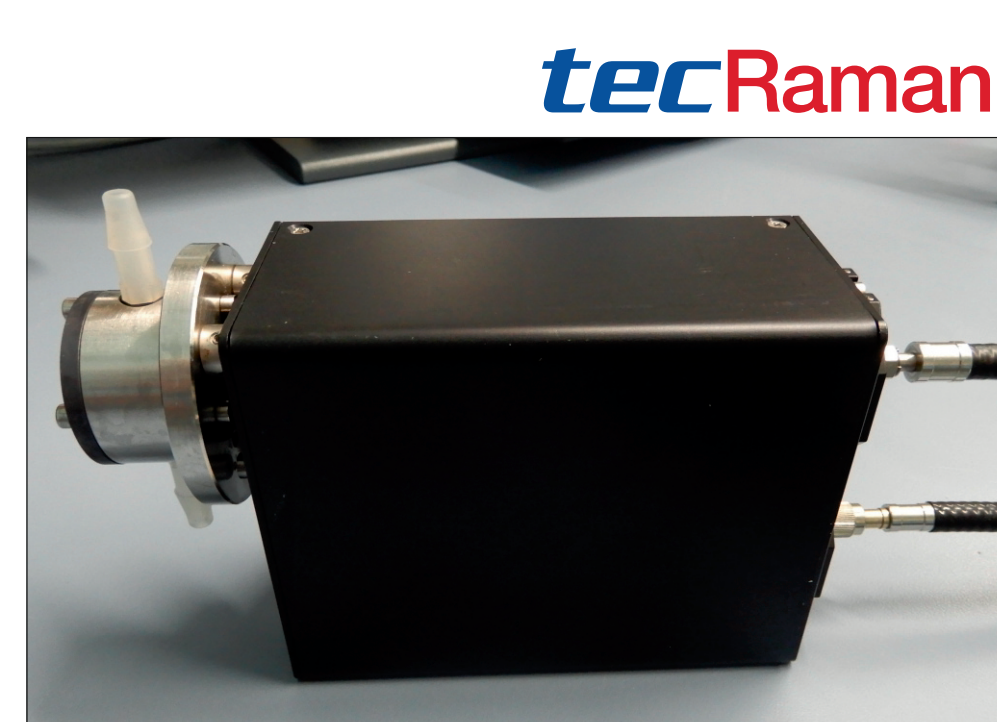
## Design of Experiments (DoE) - Multivariate Calibration

The selectivity and specificity of the non-contact raman probe was examined for relevant analytes in cell culture monitoring.

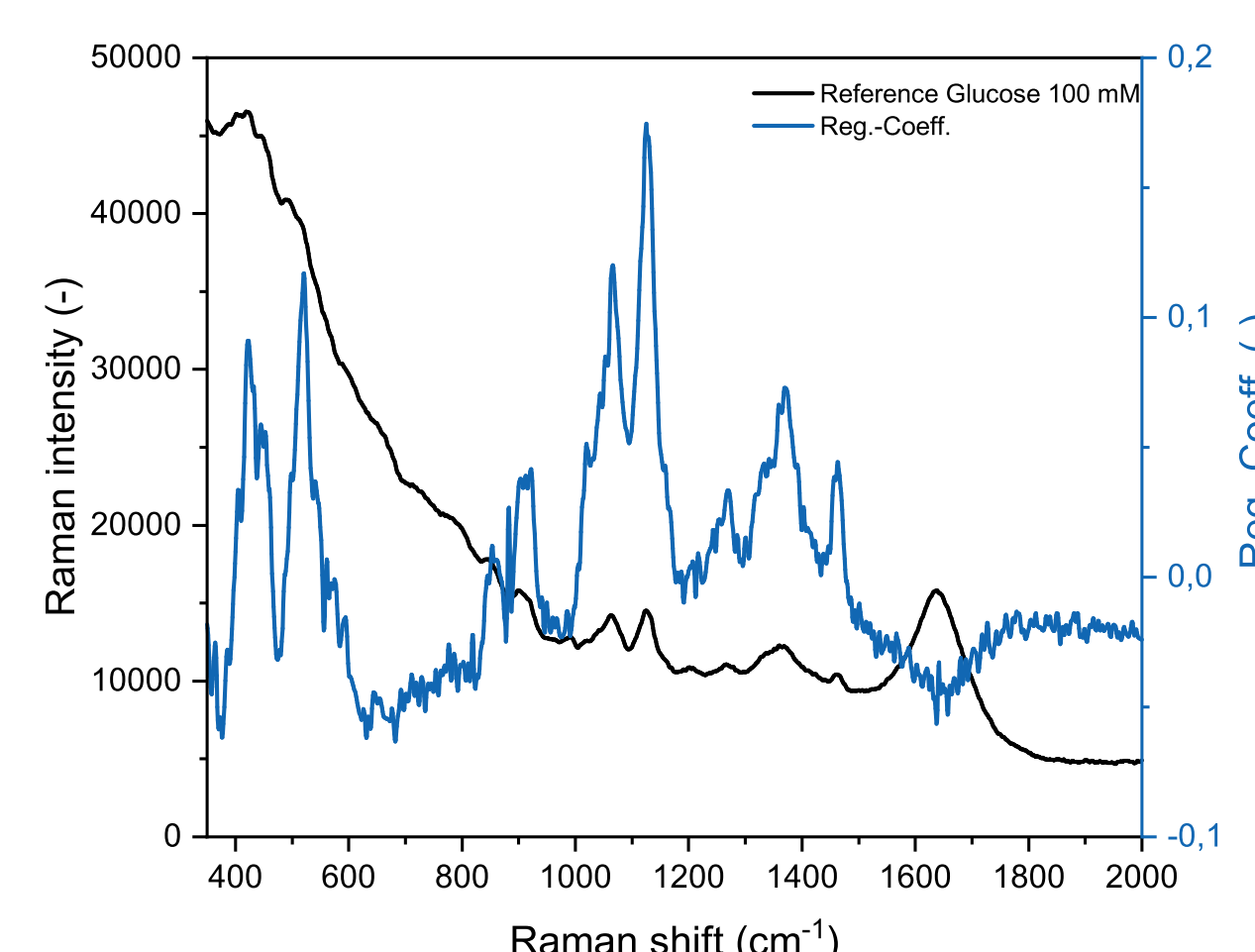
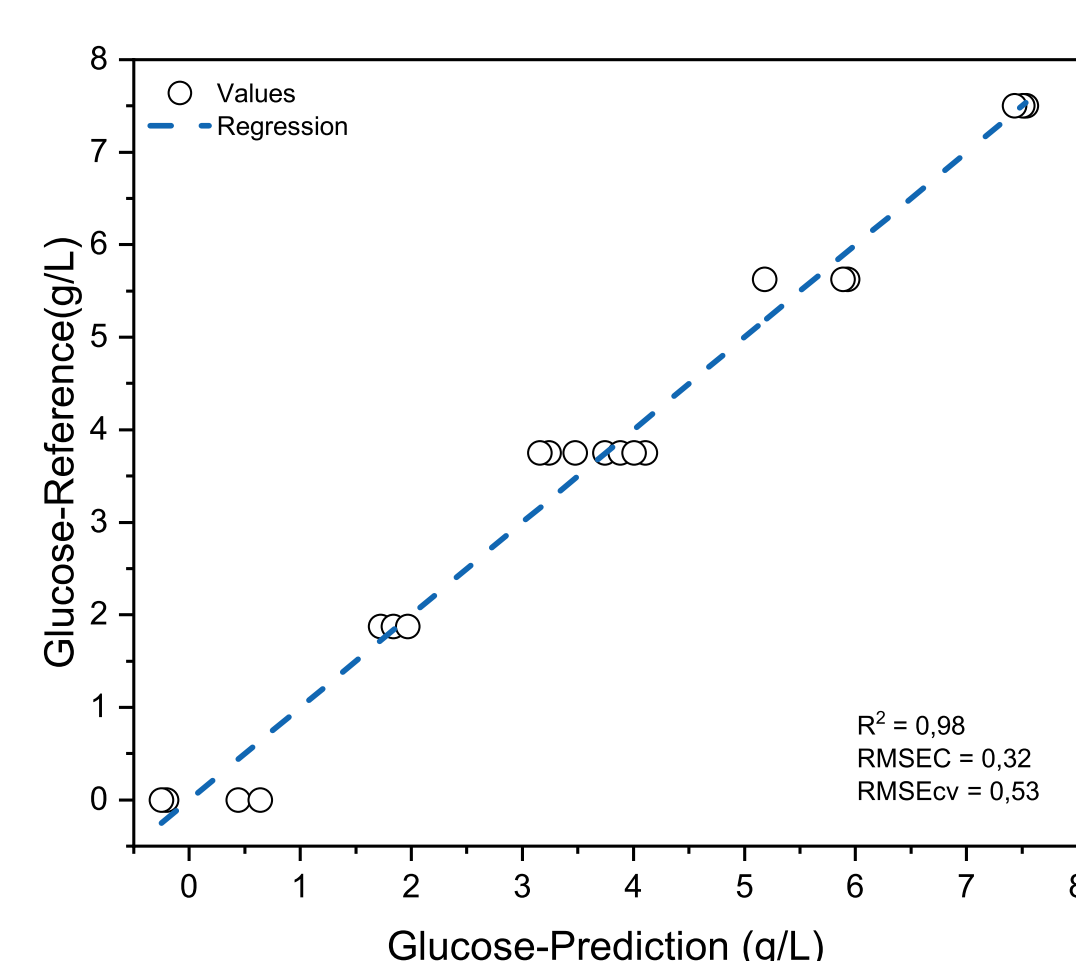
- 19 solutions
- 5 analytes (glucose, glutamine, glutamate, lactate, BSA)
- 4 level of concentrations not colinear
- Measurement through glass and single-use foil



tec5 MultiSpec® Raman Spectrometer System with Raman Probe Tidus



Bypass Flow-Cell; tecRaman non-contact Raman probe, Fiber optics



Analyte (g/L)	Pre-Processing	Factor	R²	RMSEC	RMSECV	LOD	LOQ
Glucose	SNV	2	0,98	0,32	0,53	0,19	0,29
Lactate	SNV	5	0,98	0,08	0,21	0,29	0,45
BSA	-	5	0,95	0,10	0,23	0,38	0,63

➡ Selective and specific measurement of glucose, lactate and protein

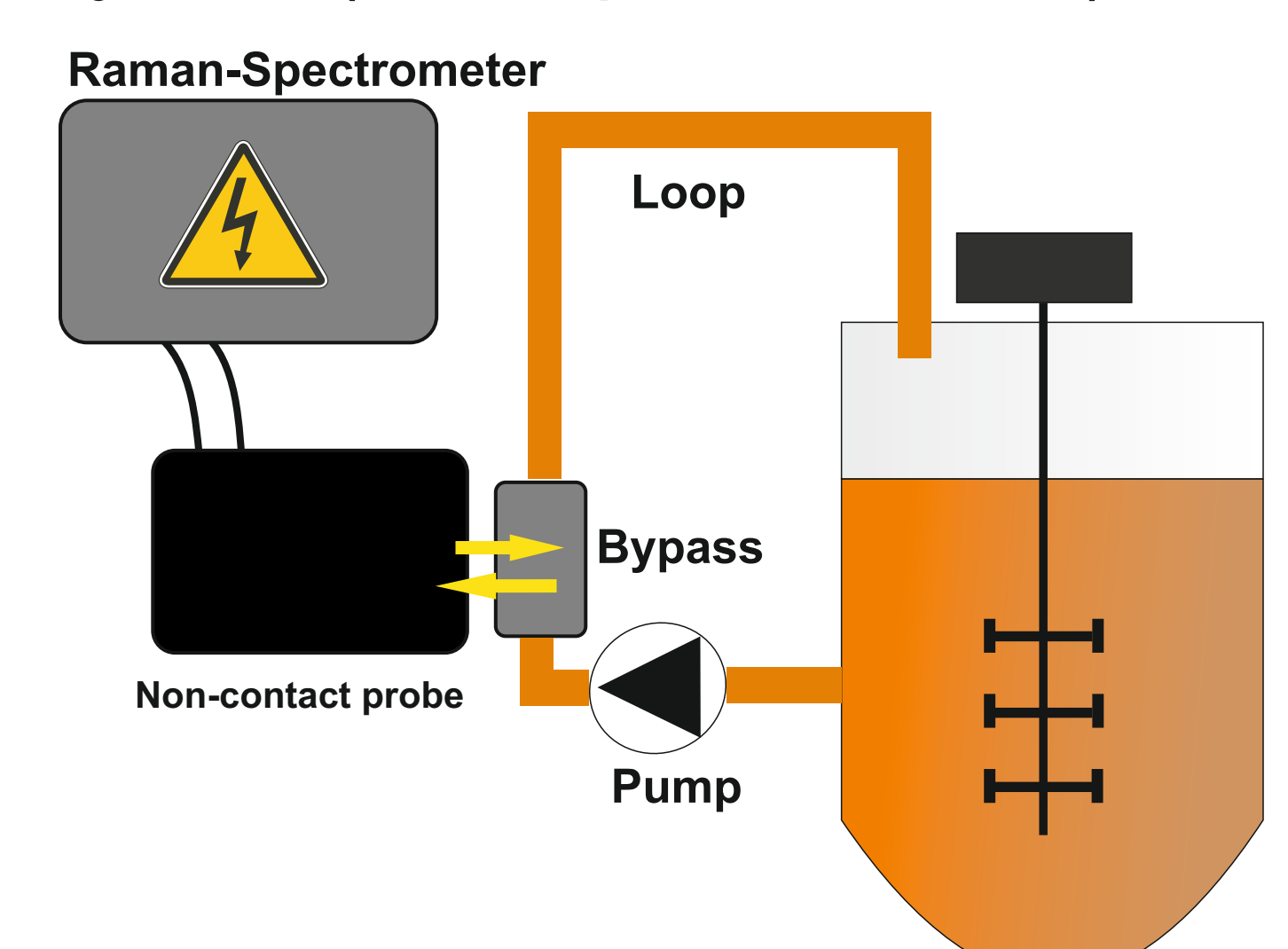
➡ Similar results for the measurement through single-use bioreactor foil and glass

## CHO Cell Cultivation

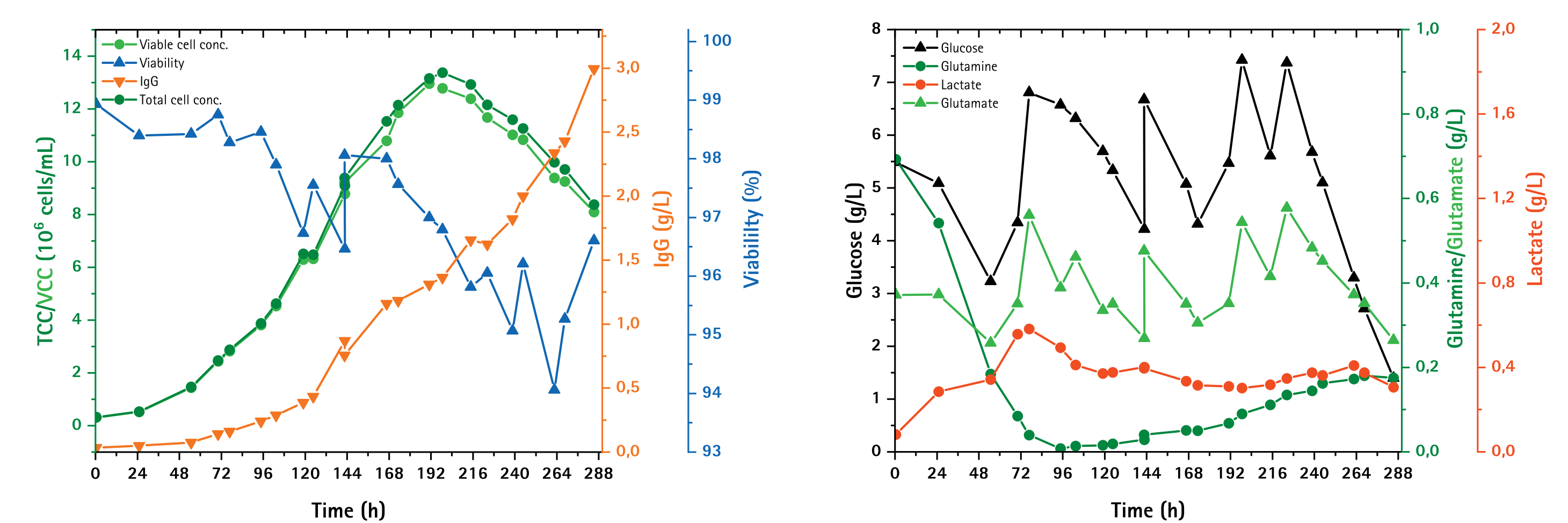
- 2 L benchtop Bioreactor (Sartorius Stedim Biotech)
- Closed-loop bypass with measuring chamber
- Non-contact measurement through the optical window
- Raman Process Spectrometer System (MultiSpec® Raman)

### Cultivation conditions:

Cell line: CHO-DG44  
Duration: 288 h  
Temperature: 37°C  
pH: 7.1 (CO<sub>2</sub>/Feed-Medium)  
pO<sub>2</sub>: 60% (gas mixture)  
Fed-Batch process  
mAb production

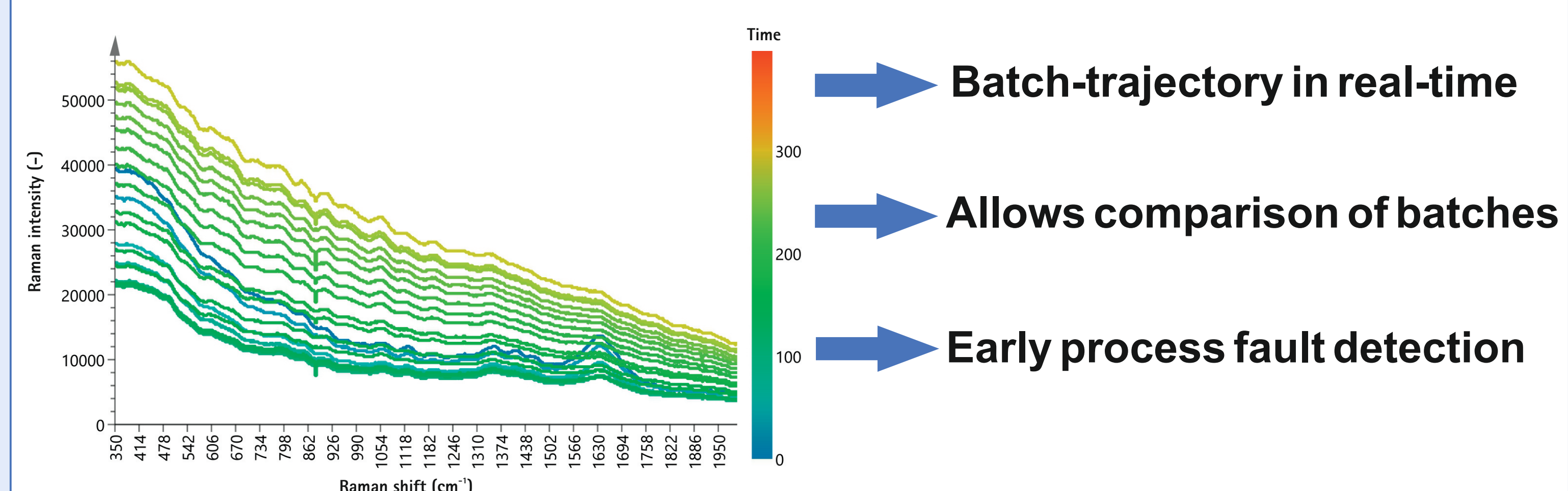


### Offline Measurements:



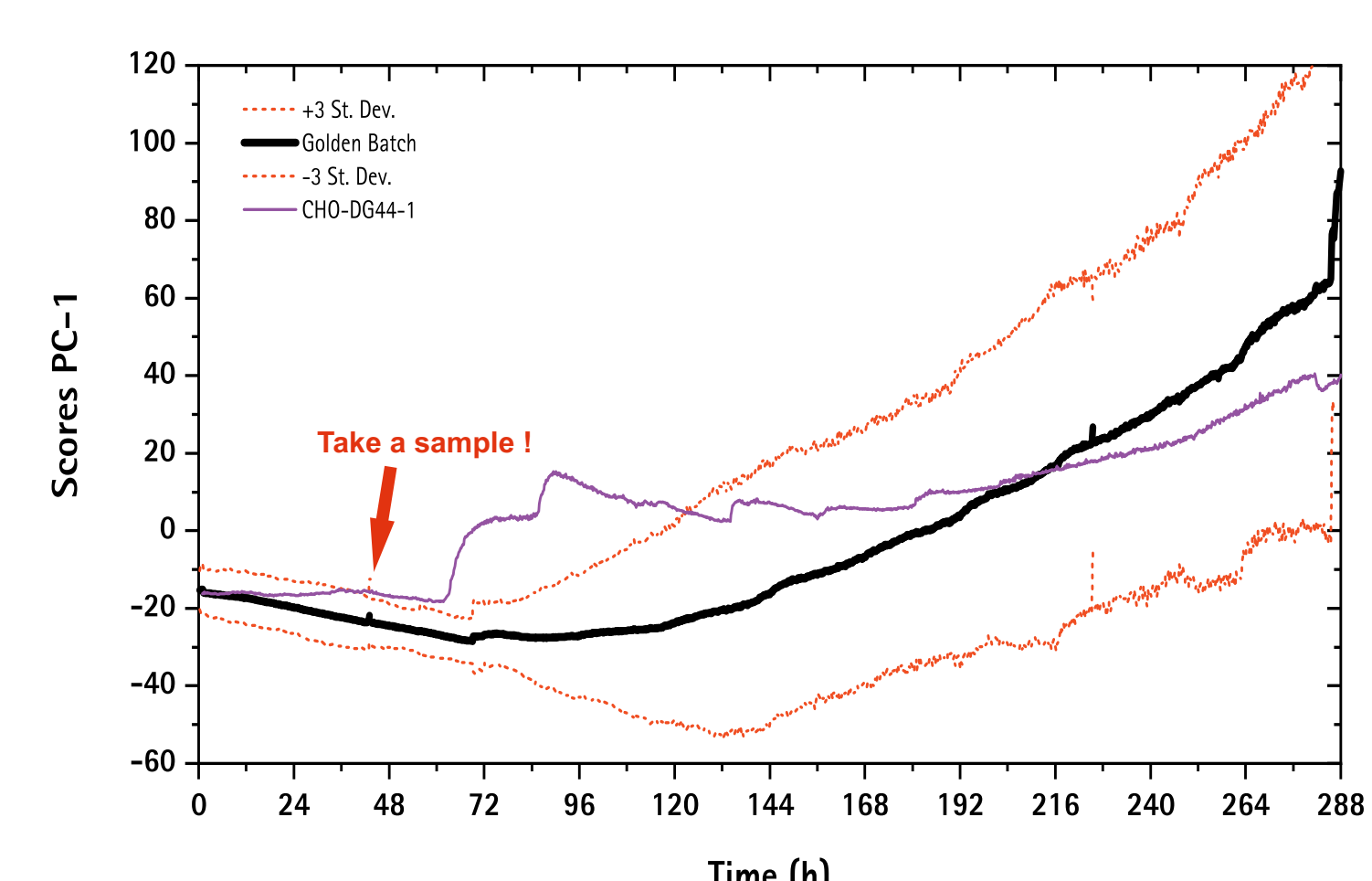
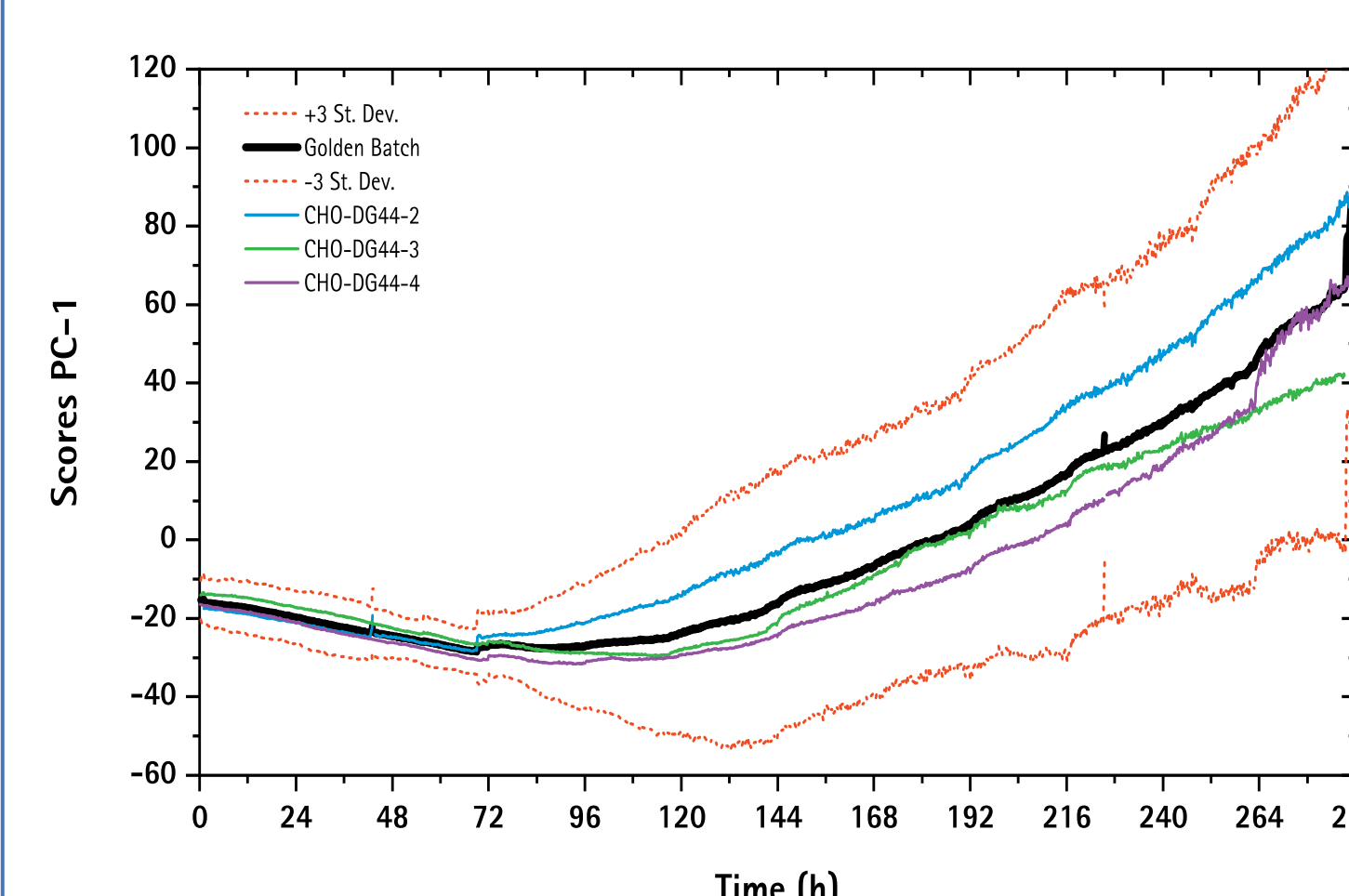
## Raman Spectra of the CHO Cell Cultivation

- Raman spectra obtain chemical information about the bioprocess
- Spectral trajectory can be measured through the glass
- Baseline shift comprises information about the cell concentration
- Data pre-processing necessary for quantitative models



## Batch-trajectory

- Raman data from three fed-batch processes
- No reference data needed - only spectral data
- Detect deviations from standard batches



## Conclusion

Raman Spectroscopy offers a great potential to be a powerful PAT tool for bioprocess monitoring.