Usage of Procellics Raman Analyzer in mRNA Manufacturing

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Agenda

01 Raman PAT Platform: Technology Overview

02 ProCellics™ Raman Analyzer in mRNA Manufacturing

03 Key Advantages

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Raman PAT Platform: Technology Overview

01

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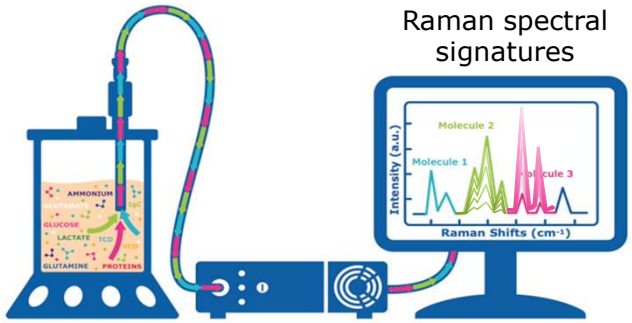
Raman PAT Platform: Technology Overview
Introduction

MOLECULE

Concentrations

Examples:

glucose, titer, VCD, aggregates, others…



Raman spectral signatures

Raman

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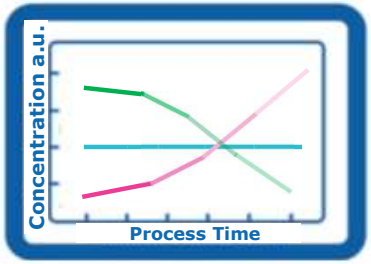
Quantitative Monitoring



- Process understanding
- Several process parameters measured simultaneously
- Excellent selectivity
- Non-destructive method
- Time and resource savings & fast decision-making

Introduction
Raman Effect: An Example

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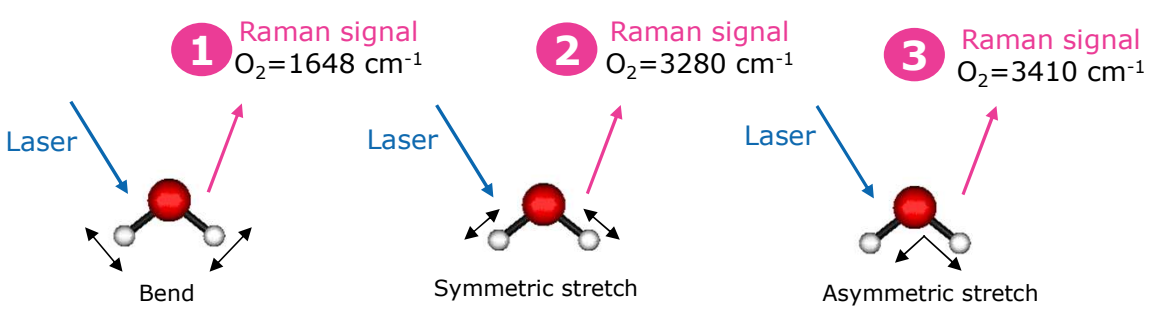
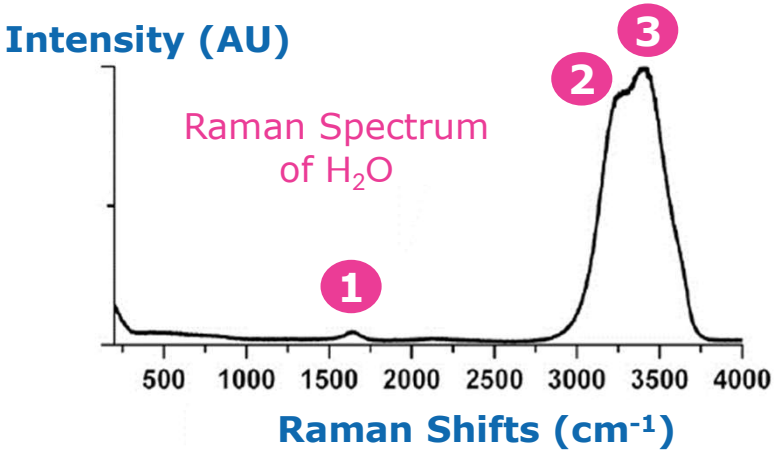
Molecular Vibrations of H_2O (water)





A Raman spectrum is a molecular fingerprint

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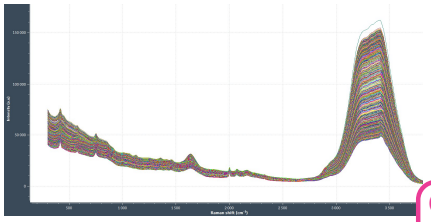
Raman for Bioprocess Monitoring

Raman Calibration Model: Let the Spectra Speak

Model Building

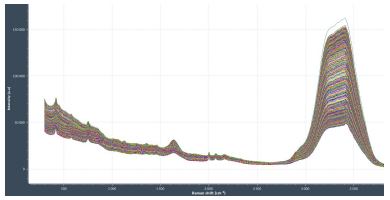
Monitoring

Real-time Raman measurements

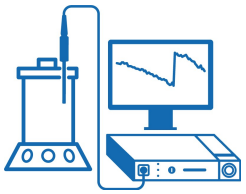


Raman spectra collection

Correlation between Raman spectra and off-line values with Partial Least Square (PLS)

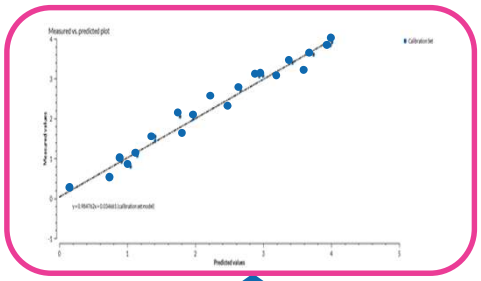


New Raman spectra collection in real-time & in-line

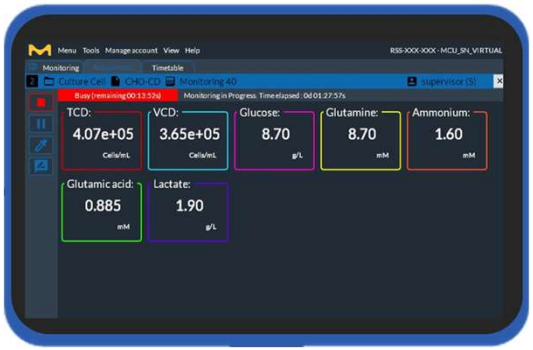


At least 3 batches or more for reliable monitoring

ProCellics™ Raman Analyzer with Bio4C® PAT Raman Software



Conversion of the Raman spectra



Display of real-time values

Sampling for off-line analysis

Off-line quantitation of parameters (in triplicate according to analytical best practices)

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ProCellics™ Raman analyzer in mRNA manufacturing

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ProCellics™ Raman Analyzer in mRNA Manufacturing
Which Steps Can Benefit from Raman Technology?

In vitro transcription

- **NTP bases**
  - Adenine
  - Guanine
  - Cytosine
  - Uracil
- **mRNA concentration**

Usage of Raman to Monitor the IVT Reaction
Case Study Introduction

Objective

- Demonstrate the **correlation** between spectral measures and the evolution of concentrations
- Demonstrate the **accuracy** of the analyzer to measure the NTPs and mRNA
- Demonstrate the **specificity** of the analyzer for each reagent

Samples

- Pure NTP solutions (ATP, GTP, CTP, UTP)
- Mixtures of NTPs at concentrations
- Pure mRNA, concentrations ranging from 0.1 – 3.5 g/L

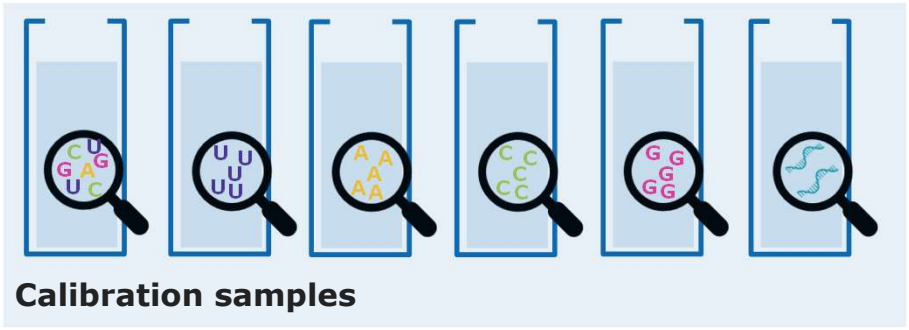
Experimental conditions

ProCellics™ External Measurement Unit

Cuvette holder
(interchangeable)

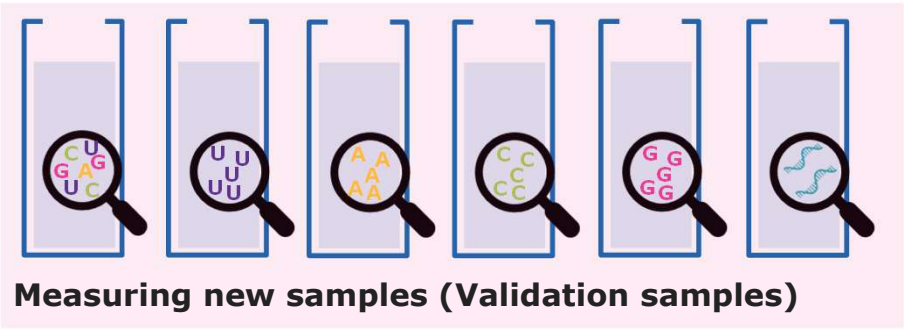
Quantitative Analysis

Usage of Raman to Monitor the IVT Reaction



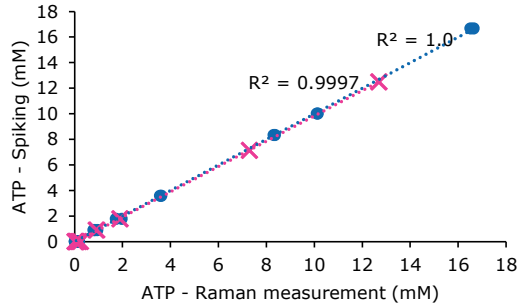
Bio4C® PAT Raman Software

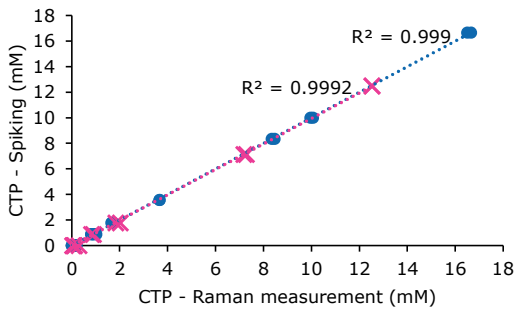
Create a **regression model** to correlate the Raman signal to the molecules concentrations

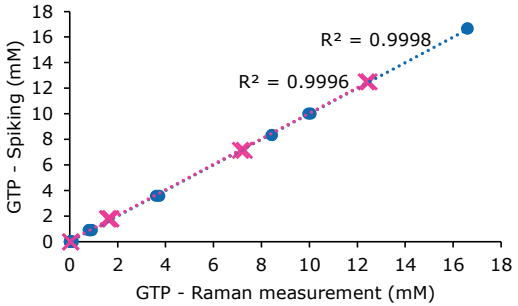


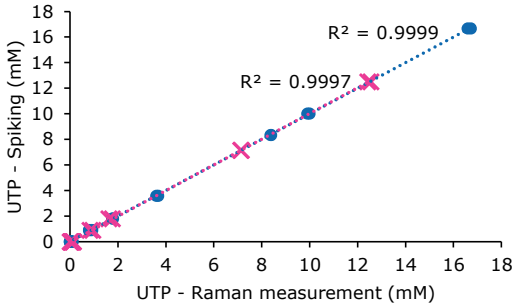
Quantitative Analysis: Partial Least Squares (PLS) Regression

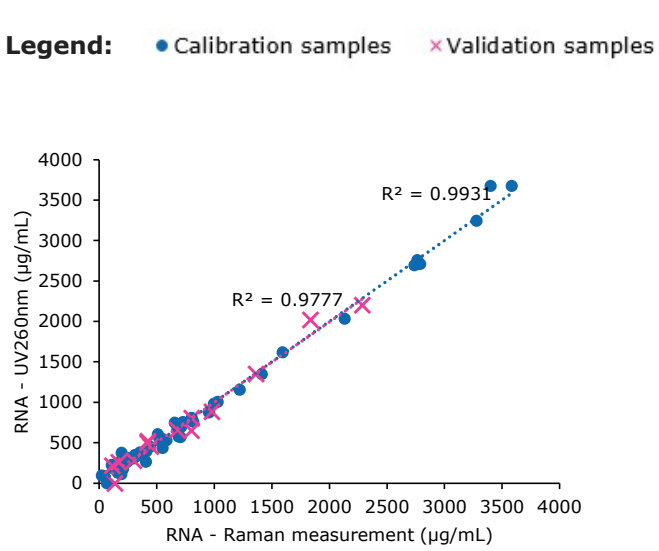
Usage of Raman to Monitor the IVT Reaction











	ATP (mM)	CTP (mM)	GTP (mM)	UTP (mM)	mRNA (µg/mL)
Calibration range	0 – 16.67	0 – 16.67	0 – 16.67	0 – 16.67	0 – 3586
RMSEP	0.11	0.12	0.10	0.07	95
Relative error	1%	1%	1%	1%	4%

Colored based on the error **< 10%** **< 15%** **< 20%** **Above 20%**

Usage of Raman to Monitor the IVT Reaction

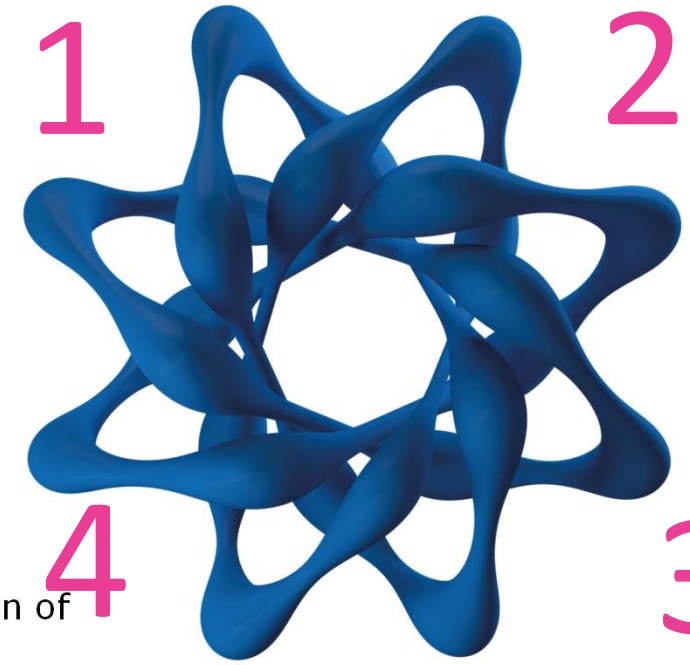
Advantages

1 Increase in productivity

Fast Raman measurements allows operators to take immediate action to ensure optimal process conditions

2 Cost savings

Non-destructive Raman measurements leads to cost savings in sampling



3 Accelerate process development

Raman allows for fast insights regarding reaction kinetics

4 Time savings

Raman allows detection of batches with higher productivity, which may be terminated faster then expected

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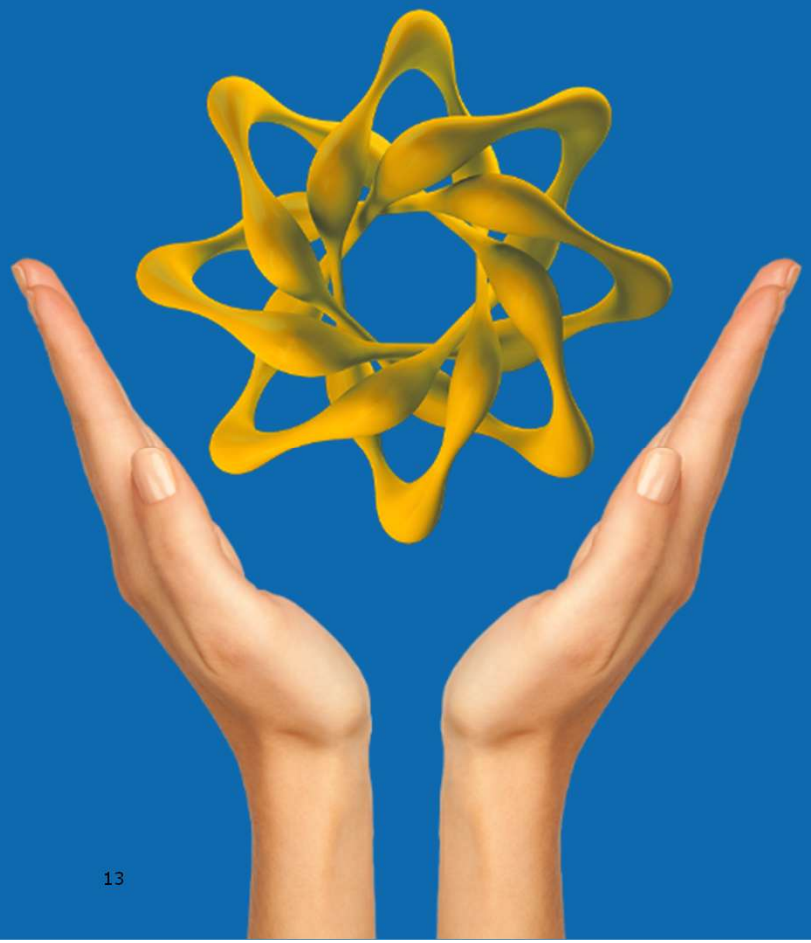

Thank you

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