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*"Reshaping the Future through Science and Technology"*

# Raman spectroscopy - an analytical tool for biologics

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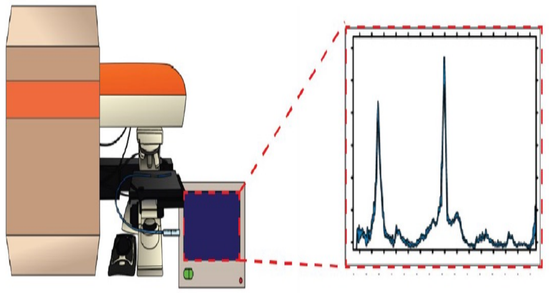
## ABSTRACT

Raman Spectroscopy (RS) is a non-invasive technique that analyses biomolecules qualitatively and quantitatively by measuring the inelastic scattering of light due to molecular vibrations. It can be applied to liquid, solid, or semi-solid forms of biological samples. The minimal sample preparation and non-invasive nature of RS can be applied for a process analytical technology (PAT) tool. We demonstrated qualitative and quantitative measurements of biologics with RS through our previous studies. Our results indicate that RS distinguishes various Gram-positive and Gram-negative bacteria, fungi, and a mixture of microbes and Chinese hamster ovary (CHO) cells, as well the concentration of viral samples.

## PRESENTER BIO INFORMATION

**Cindy Mayorga** received a B.S. degree in Food Engineering from Univ. Tecnologica de Panama. She completed her M.S. in Food Science from Purdue University in 2022 sponsored with a Fulbright scholarship. Currently, she is pursuing a PhD degree in ABE in Dr. Verma's Lab.



## BACKGROUND

Raman spectroscopy (RS) measures the inelastic scattering of light due to molecular vibrations. It is a non-invasive technique that analyses biomolecules qualitatively and quantitatively. RS can be applied to any physical form (liquid, solid, semi-solid) of the biological sample reducing the sample preparation measures.

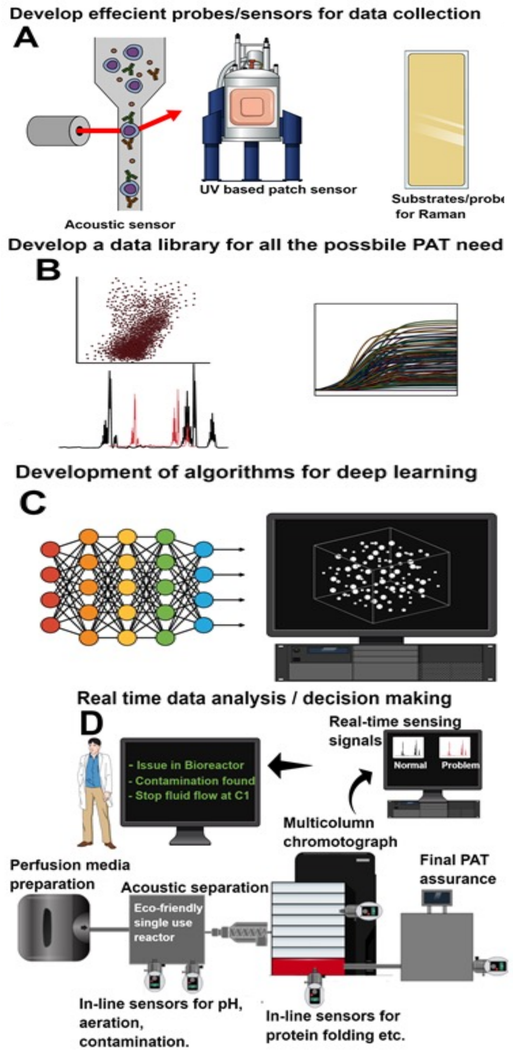
## MOTIVATION

Raman Spectroscopy can be used as an effective Process analytical technology (PAT) tool and as a diagnostic tool for detecting and characterizing biologics.

## WHERE ARE WE?

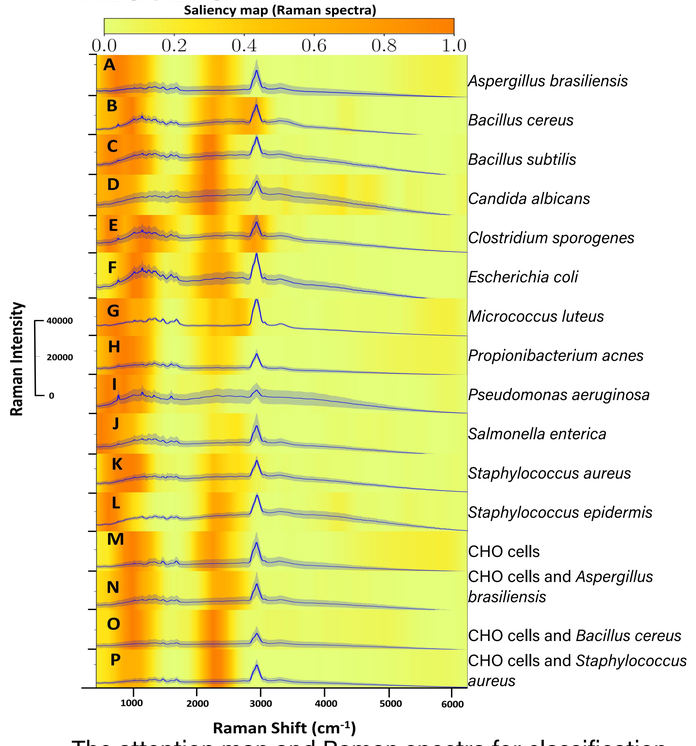
- Demonstrated that Raman Spectroscopy can be used qualitatively to distinguish between several different types of microbes (spanning over Gram-positive bacteria, Gram-negative bacteria, and fungi), and between microbes and CHO cells in a mixture (as shown in the Results).
- Quantified the concentration of viral samples (measles, mumps, rubella, and varicella-zoster viruses) using Raman spectroscopy and machine learning [3].

## METHODOLOGY




Steps for Implementing a Process Analytical Technology (PAT) for continuous manufacture of monoclonal antibodies (mAbs). (A) Sensor development; (B) data library based on model or historical process data; (C) development of deep learning algorithms; (D) real-time data analysis/decision-making for continuous processes. Figure reproduced from [1]

## RESULTS




The attention map and Raman spectra for classification of several microbes and CHO cells with microbes. The bold blue line indicates average spectra (6000 scans), and the shaded area standard deviation. The heatmap (yellow-orange) indicates the importance of different segments of the spectra according to the attention map. Figure reproduced from [2].

## RELEVANCE AND FUTURE WORK

Raman spectroscopy is applicable in pharmaceutical industry as a PAT tool to monitor in real-time and produce high-quality products without sample manipulation. We will continue to develop in-line probes and acoustic devices to improve the sensitivity of Raman spectroscopy and coupling RS with machine learning for other biological samples.

1. Maruthamuthu, M.K., Rudge, S.R., Ardekani, A.M., Ladisch, M.R., Verma, M.S. (2020) Process Analytical Technologies and Data Analytics for Manufacture of Monoclonal Antibodies Trends in Biotechnology. DOI: 10.1016/j.tibtech.2020.07.004
2. Maruthamuthu, M.K., Raffiee, A.H., De Oliveira, D.M., Ardekani, A.M., Verma, M.S. (2020) Raman spectra-based deep learning – a tool to identify microbial contamination MicrobiologyOpen DOI: 10.1002/mbo3.1122.
3. Boodaghidizaji, M., Milind Athalye, S., Thakur, S., Esmaili, E., Verma, M. S., & Ardekani, A. M. (2022). Characterizing viral samples using machine learning for Raman and absorption spectroscopy. MicrobiologyOpen (Weinheim), 11(6), e1336–n/a. https://doi.org/10.1002/mbo3.1336

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