



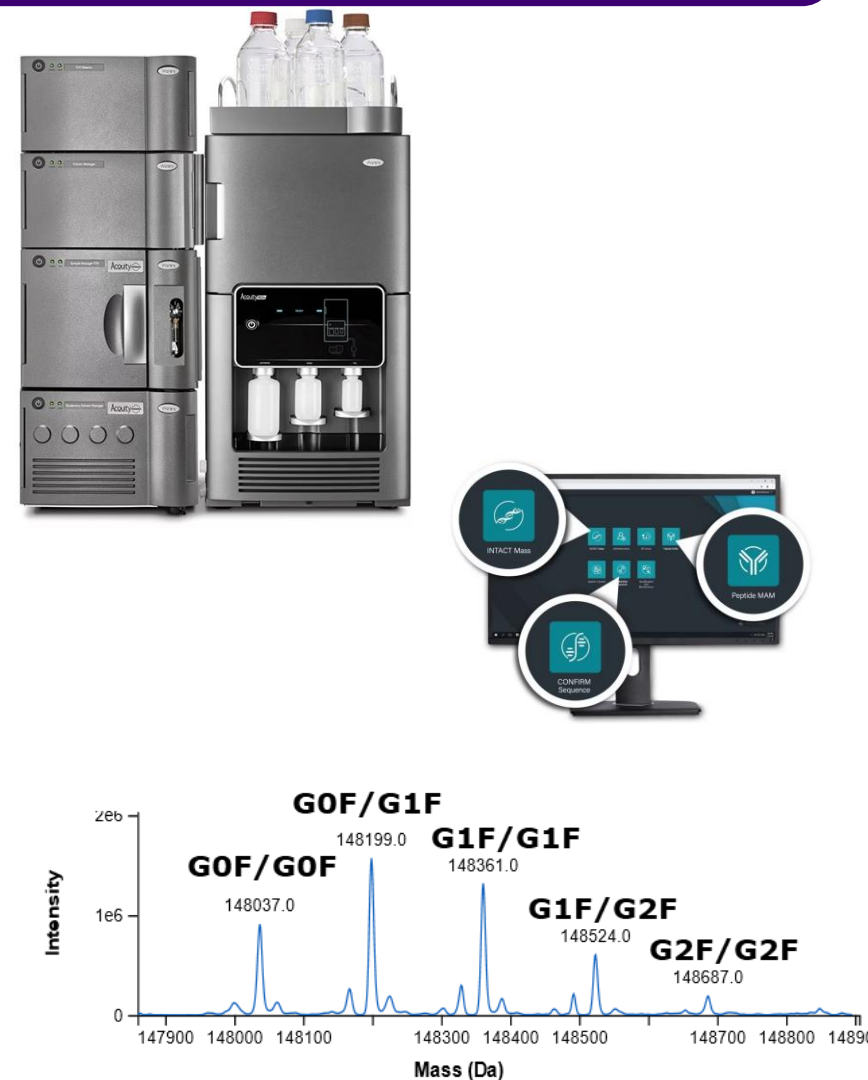
New Technologies



Chromatography and Separation Science Technologies

Waters BioAccord LC-MS System Evaluated by: Victoria Kennedy

- **Built for routine biotherapeutic analysis**
 - Dedicated application workflows:
 - Cell culture metabolites (amino acids, vitamins)
 - Intact mass analysis for product quality attributes from harvest
 - Relative glycoform/modification distributions
 - Peptide mapping and MAM, Released N-glycan analysis, Host-cell protein analysis
- **Smart Technology:**
 - **Automated Setup and Calibration:** minimal manual intervention, reducing the chances of user error
 - **System Health Monitoring:** continuously monitors the system parameters, helping ensure reliable operation and data integrity.
 - **Self-Diagnosis and Maintenance Alerts:** can self-diagnose certain issues, offers maintenance alerts and recommendations for corrective actions
- **Hardware and Software Overview:**
 - Comprised of Acquity Premier UPLC + Rda Time-of-Flight M
 - Smaller footprint than alternate MS systems
 - App based software packages for routine workflows,
- **Experience**
 - Simple hardware set-up and maintenance for all skill levels
 - App based acquisition and processing good fit for routine process development space and non-MS experts (*not available for all applications*)
 - New application implementation/s could require analytical SME due to potential complexity (especially with intact mass applications)



Relative Glycoform Abundance [Intact Mass Analysis]

Axcend Focus LC

Evaluated by: Victoria Kennedy

OVERVIEW

- Fully portable, compact high performance liquid chromatography system; microfluidic technology
 - Dimensions: 8.5 in x 14 in x 8 in, 17.6 pounds
- Utilizes tool-less and easily swappable cartridges
 - Contain commercially available capillary UPLC columns
 - Single wavelength on-column UV detection available
- Its design aligns with sustainability goals by minimizing solvent use and waste
- Small Interfaceable with ancillary devices (diode array detectors, compact MS, and more)

APPLICATIONS

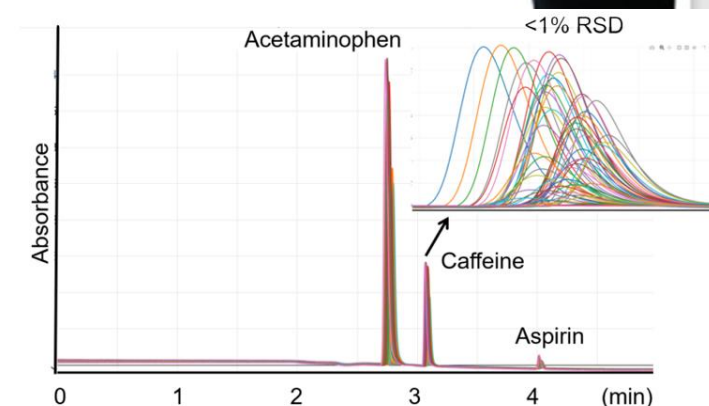
- Intact protein analysis
- Reaction monitoring
- API studies (e.g. dissolution)

EXPERIENCE

- Compatible with existing chromatographic data systems (i.e. Agilent OpenLab)
- Compact footprint advantageous for at-line monitoring
- Flexible cartridge design allows for screening of same chromatographic resins used at the analytical scale

FUTURE DEVELOPMENT

- Expanding biologics applications
- Vendor continued advancement of compact interfaceable devices (automated sampling, LC autosampler)



Ganymede AI Chromatography

Technology

Ganymede's "lab-as-code" approach provides a circular workflow that automates data movement between instruments and laboratory systems. They are able to use AI and machine learning to automate the analysis of chromatography data, which traditionally involves repetitive and manual data processing tasks. This includes steps like peak identification, baseline correction, and integration of chromatographic data.

Vendors

- Ganymede

Status

- Ganymede's AI for Chromatography software is in a late-stage development and pilot-testing phase.

Experience

Takeda is currently in the Legal agreement phase to be able to demo the software and possibly do a pilot of the software.

Webinar Link:

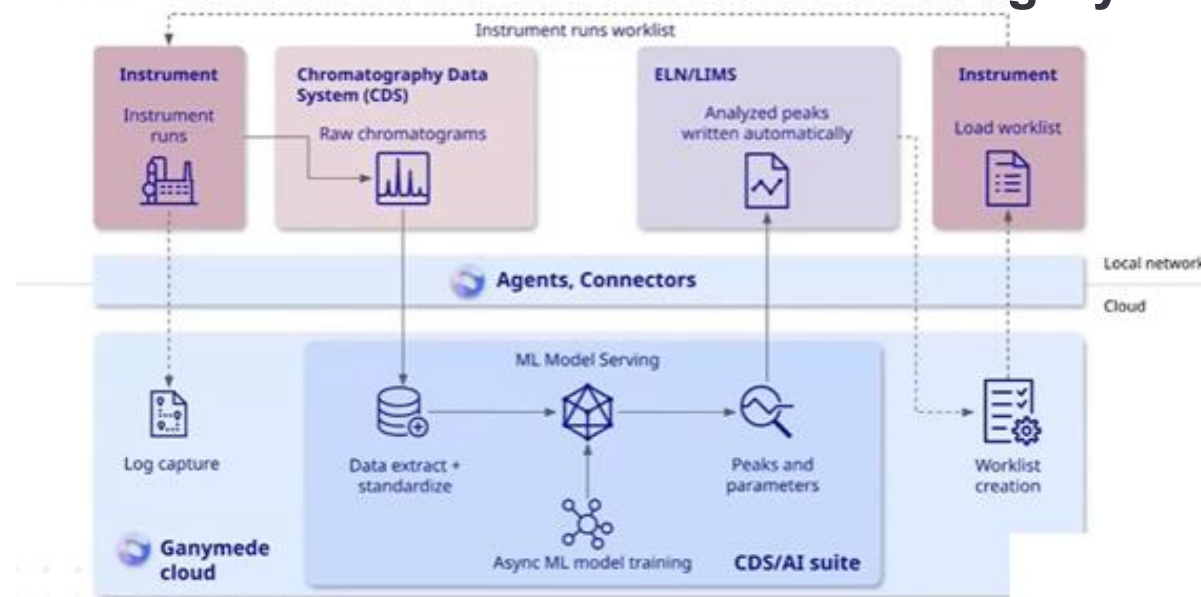
<https://www.linkedin.com/events/aiforchromatographydatasystems724222273586171904/about/>

Internal



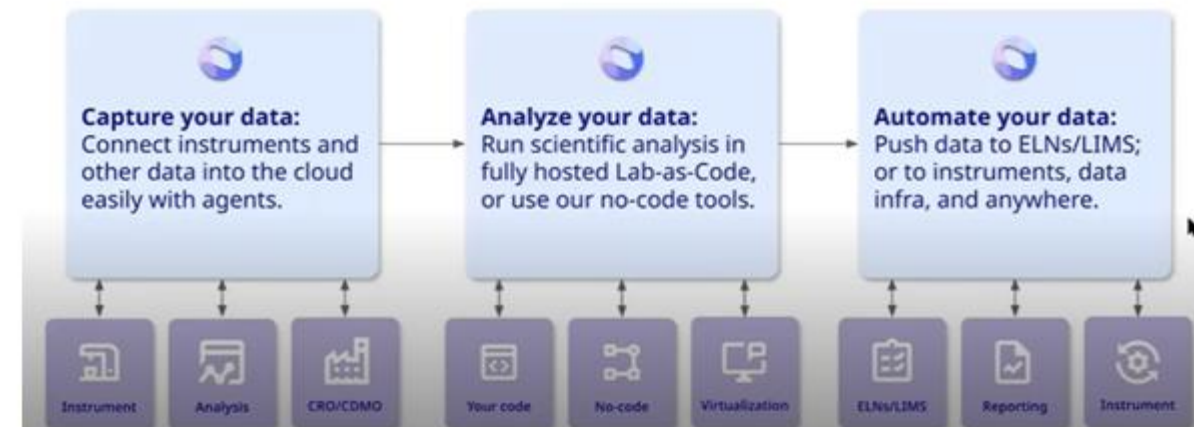
Gregory Pino

Ganymede's Solution



Ganymede's Paradigm

Ganymede is the Scientific Data Cloud (SDC) for instruments and apps like ELN/LIMS. Connect everything; turn data friction and risk into automated, traceable data via Lab-as-Code.



New Sensors/Analyzers

Online Product Quality (HMWS) Monitoring

Technology

Online High-Performance Liquid Chromatography (HPLC) refers to the direct integration of an HPLC system with a sample source, enabling continuous or automated sampling, separation, and analysis in nearly real-time.

Vendors

Agilent (would like to compare with other vendors)

Measured parameter

HMWS

Experience

Used in the purification and UFDF process development, qualified in GMP for CQA measurement



Light Scattering and Particle Size Characterization Technologies

In-Process LSP NanoFlowSizer

OVERVIEW

- Utilizes spatially resolved dynamic light scattering (SR-DLS)
- Based on low-coherence interferometry
- Non-invasive inline real-time nanoparticle size characterization.
- Measurements are performed through glass, preventing any direct contact or sample interference
- Superior to traditional dynamic light scattering due to:
 - capability to measure very broad turbidity range
 - unique sizing capabilities of flowing suspensions
 - wide range of containers that material can be in

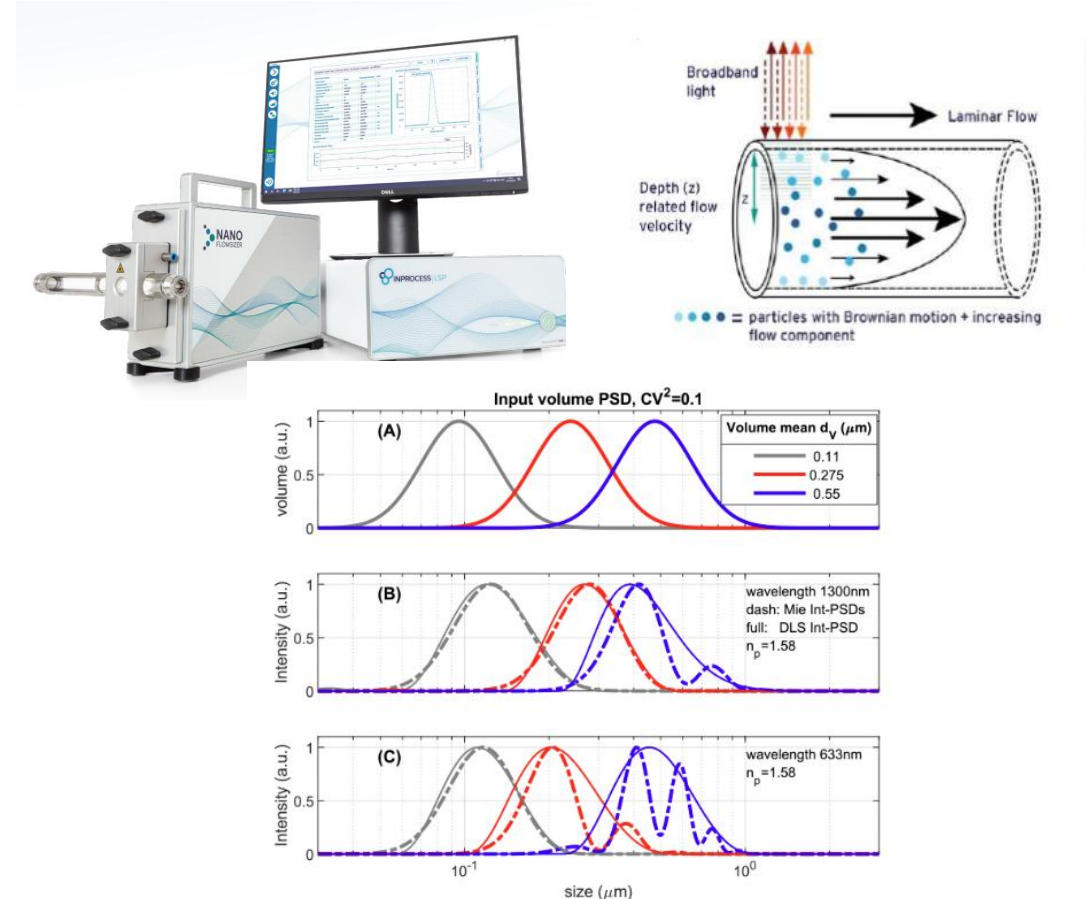
APPLICATIONS

- Particle size analysis
- Droplet size monitoring
- Liquid-based nanoparticles characterization
- Protein aggregation

EXPERIENCE

- Plan to demo in 2025

sanofi



<https://vimeo.com/558041547>

[Whitepaper: Lipid-based Nanoparticles – InProcess-LSP](#)

Real Time Multi Angle Light Scattering (RT-MALS)



Gregory Pino

Technology

Multiangle light scattering (MALS) describes a technique for measuring the light scattered by a sample into a plurality of angles. It is used for determining both the absolute molar mass and the average size of molecules in solution, by detecting how they scatter light.

Vendors

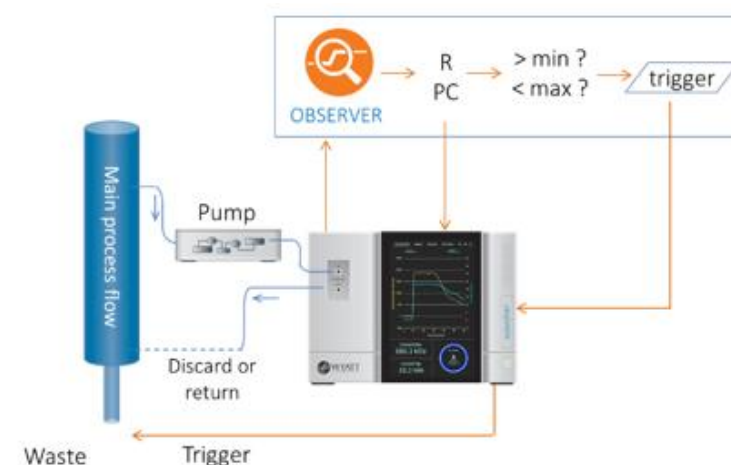
- Waters - Wyatt technologies

Measured parameters

- Average Molecular weight inline (Downstream)
- Average Radius of gyration inline (Downstream)

Experience

- Currently online set up ongoing for mAb polishing step



Source: <https://wyattfiles.s3.us-west-2.amazonaws.com/literature/white-papers/WP8007-RT-MALS-Real-time-product-attributes-from-lab-to-plant.pdf>



Spectroscopy Technologies

Nirrin Technologies

Overview

- Leverages **High-Precision Tunable Laser Spectroscopy (HPTLS)**, to provide higher signal sensitivity compared to FT-NIR broad-spectrum light source.
- Currently sold as an **at-line** instrument, with an **in-line** version in development
- Provides **out-of-the-box soft sensors** using a spectral library and least-square operations.

Applications

- Upstream Processing and Harvest (Glucose, Lactate, Titer, and VCD)
- Buffer Preparation (Excipients)
- Ultrafiltration/Diafiltration and Formulation (Titer, Excipients, and Surfactants)

Experience

- Tested Nirrin's in-line prototype on a formulation skid. After creating a protein spectral library, the instrument showed good accuracy for protein concentration, arginine, sucrose, and PS80. Histidine accuracy was good only in a protein-histidine matrix.



Monipa

Overview

- Leverages **Mid-Infrared Spectroscopy** with single-use silicon ATR crystal
- Currently sold as an **in-line** instrument. The vendor is experimenting with a membrane within the flow cell to allow selective diffusion of excipients.
- Provides **out-of-the-box soft sensors** using one-point calibration method based on a spectral library and known concentrations.

Applications

- Upstream Processing and Harvest (Glucose, Lactate, and Titer)
- Buffer Preparation (Excipients)
- Ultrafiltration/Diafiltration and Formulation (Titer, and Excipients)

Experience

- We tested Monipa on a formulation skid. Compared to other instruments, it showed moderate accuracy for protein concentration but low accuracy for excipients like histidine, arginine, and sucrose.



QCL-IR sensor development - Christian Doppler (CD)



Gregory Pino

Technology

The biggest caveat of using IR for Biologics PAT was its lack of sensitivity. The development of quantum cascade lasers (QCL) are a paradigm shift in laser design and enhance sensitivity by one order of magnitude. Further development of 1st generation QCL-IR technology aims to assess CQAs such as concentration and higher order structure in downstream monitoring

Vendors

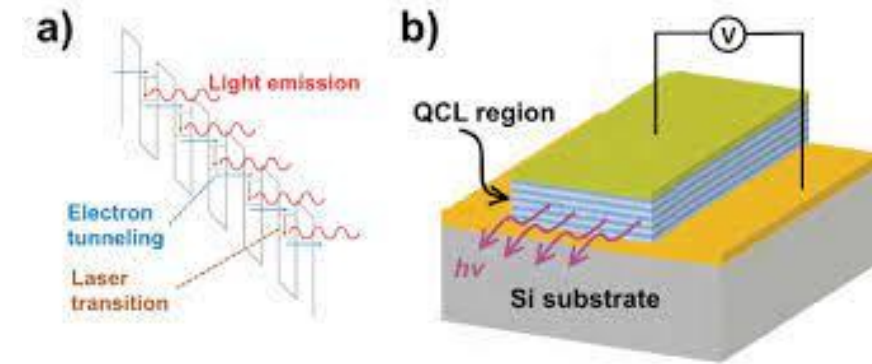
- Repligen - Culpeo

Status

- Christian Doppler Lab started operation in October 2024

Experience

- We recently installed Culpeo QCL-IR in our Äkta-PAT method development suite. Close collaboration with CD Lab to develop PAT solutions for downstream processing



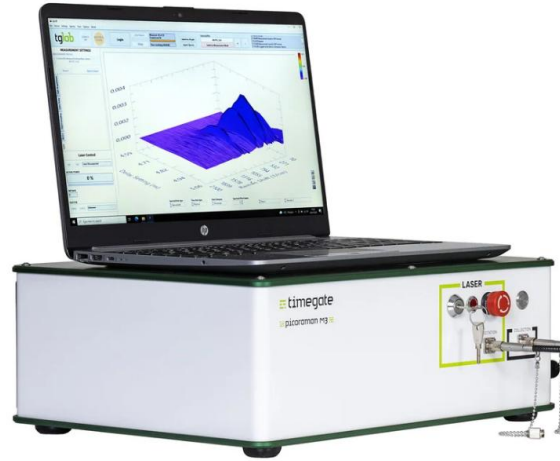
Source: https://www.photonics.com/Buyers_Guide/Products/Spectrometers/Culpeo_QCL-IR_Liquid_Analyzer/psp3766

Timegated Raman Spectroscopy



Professor Carl Anderson

- Time-gated Raman spectroscopy available from Timegate Instruments
- Primary technical advantage: ability to collect Raman spectroscopy while minimizing fluorescence
- Currently testing a system for upstream monitoring of bioreactions



[PicoRaman M3 | Timegated® Raman Technology](#)
Timegate Instruments



Diana Ritz

Points for Discussion

- Have any attendees evaluated this instrument?
- Does timegated Raman offer any major advantages and/or major improvements in prediction accuracy compared to traditional Raman for in-line bioprocess monitoring?
- How does sensitivity to ambient light interference compare to traditional Raman?

Measurement Gaps (can skip if there is no update from last year)

Inline Glucose Monitoring & Control

Current: inline Kaiser Raman together with atline Novaflex/Cedex Bio

Issues with current technology: not fast enough for control, and extensive modeling and maintaining efforts compared to the cost

Potential Solutions: Maven from 908, a diffusion based on glucose/lactate measurement



Other Technologies

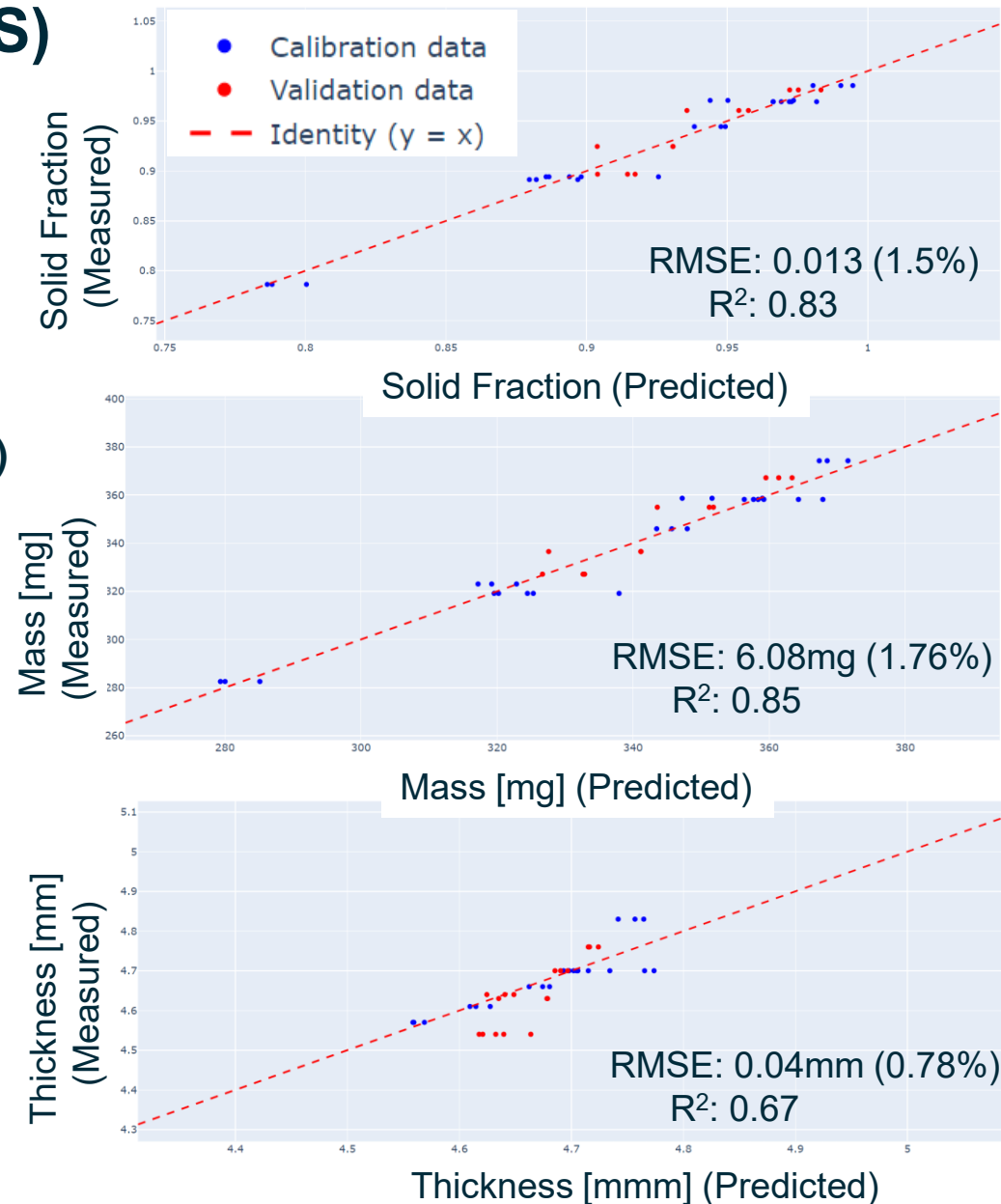
Real-time “combi-tester” for tableting (PICMES)

PICMES is a PAT tool for real-time tablet characterization:

- **Weight, Thickness, Hardness & Solid Fraction @ discharge chute**
- **Non-destructive testing** suitable for full batch characterization
- Better data for **Real Time Release Testing Models** (e.g. Dissolution)
- **Prototype built and IP filed PCT/EP2023/066694 (WO2023247572A1)**



PICMES



Phase contrast holography (Holloid)

Technology

Online phase contrast holography is based on recording of defocused images. Utilizing machine learning, numerical backpropagation generates a stack of pictures. This information is used to simulate different contrast methods which enables particle/cells/bacteria etc. characterization and distinction.

Vendors

- Holloid



Status

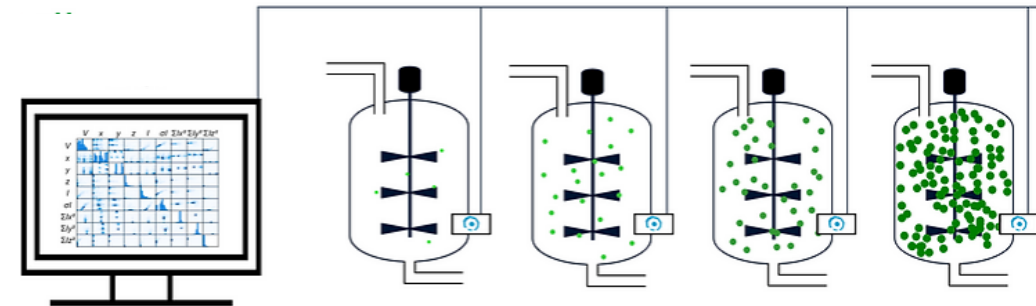
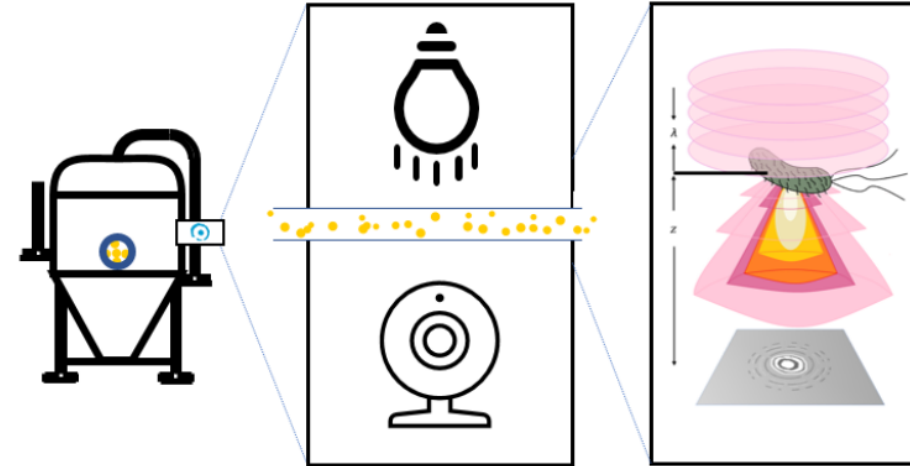
- Holloid has developed a prototype that can be used to measure viable and total cell density (two CPPs) simultaneously online and in realtime.

Co-development

- In addition to determine CPPs we want to use Holloids technology to co-develop an application to measure Bioburden (a CQA) including bacteria, yeast, mycoplasma etc. in bioreactors. Early detection of contamination is critical especially for continuous manufacturing.



Gregory Pino



Source: <https://www.holloid.com/>

Measurement Gaps

Inline pH Monitoring

Current: inline ph probe with drift determination strategy and initial calibration with offgas

Challenges with current technology: probe drifting is still not avoidable

Potential Solutions: Cleanfit H CPA475



New Sensors/Analyzers (can skip if there is no update from last year)

At-line Clade Mira IR and Bruker Benchtop NMR

Technology

mid-IR and NMR

Vendors

Clade /Bruker...(would like to compare with other vendors)

Measured parameter

Excipients (PS20, pH...)

Experience

Clinical pilot