Big Impact from Small Samples

Harnessing HPTLS for Complex Bioprocess Analysis

with Larissa Miropolsky

Nirrin Technologies aims to improve development and production of life-saving biotherapeutics with cutting-edge analytical tools that enhance accuracy, efficiency, and speed. Traditional near-infrared spectroscopy (NIR) methods, such as Fourier transform NIR (FT-NIR), have limitations related to power density and signal-to-noise ratio. By contrast, Nirrin's high-precision tunable laser spectroscopy (HPTLS) technology uses a tunable laser source that spans 300 nm, a range that is significantly broader than that of conventional tunable lasers. That broad spectral range, combined with high power density, enables accurate chemical analysis across a wide, dynamic range for all bioprocess analytes.

A key advantage of HPTLS is its low limits of detection with high precision. Compared with FT-NIR, HPTLS demonstrates 20× lower detection limits in a tenth of the time. Because FT-NIR requires extensive signal averaging, it can take up to 15 minutes to reach the same detection limits that HPTLS can achieve almost instantly. Larissa Miropolsky (senior director of data science at Nirrin Technologies) discussed HPTLS technology in her company's proprietary Atlas system during a January 2025 Ask the Expert webinar.

Miropolsky's Presentation

The Atlas system is designed for **real-time bioprocess monitoring** that operates through a simple workflow: A 15-µL sample is pipetted onto a pedestal, then sandwiched within two sapphire rods that create a 1-mm optical path. A background and a sample scan are combined to create an absorbance spectrum for analysis. Samples are scanned in seconds, yielding a fast workflow. The system includes a preloaded library of common bioprocess analytes that also can be expanded with custom chemicals. Analysis provides component concentrations and spectral residuals, allowing for precise chemical identification and quantitation.

The Atlas system uses an **iterative optimization technology (IOT) framework** to simplify data analysis. It integrates well-characterized noise sources directly into the system reference library, eliminating the need for extensive model development. Traditional partial least square (PLS) models require significant maintenance to account for variations in noise and sample conditions. By contrast, the IOT framework enables real-time, model-free analysis with high reliability, streamlining workflows and reducing the time needed for bioprocessing analytics.

Downstream Formulation Analysis: The Atlas system can achieve high selectivity in identifying different bioprocess components by deconvoluting sample spectra into individual-component spectra. That allows for accurate quantification of high-concentration proteins, surfactants, and stabilizers such as sucrose and histidine, overcoming challenges associated with traditional analytical techniques. Typically, obtaining such comprehensive bioprocess data would require high-performance liquid chromatography (HPLC), which involves extensive method development and multiple assays. By contrast, the Atlas system generates equivalent results using a small drop of sample, dramatically simplifying the workflow.

Another critical application of Atlas is the **rapid quantitation of surfactants** in complex matrices. Traditional HPLC methods often struggle with accuracy when measuring surfactants in protein-containing samples. In a comparison of HPLC and HPTLS performance, the former method showed significant under-recovery of surfactants in matrices containing sucrose, histidine, and high-concentration protein. HPTLS in the Atlas system accurately measured all sample types, making it a more reliable solution for surfactant quantification.

Whereas HPLC requires extensive sample preparation and condition optimization potentially taking up to two weeks to complete a full analysis, the Atlas technology delivers accurate results in under a minute with no sample preparation required. By leveraging HPTLS technology, the system provides unique quantitative data sets across bioprocessing operations that were previously difficult to generate due to time, cost, or complexity.

Questions and Answers

How is the Atlas system cleaned and maintained? We simply use water and lint-free wipes to clean the system pedestal. No other maintenance is required. The system also can be moved from one location to another without recalibration.

What prerequisites are needed for operating the Atlas system? Our system has a simple user interface that provides process steps in real time. After a short training session, operators will be ready to analyze samples.

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