



Please join Tornado Spectral Systems at the

IFPAC 2018 Annual Meeting

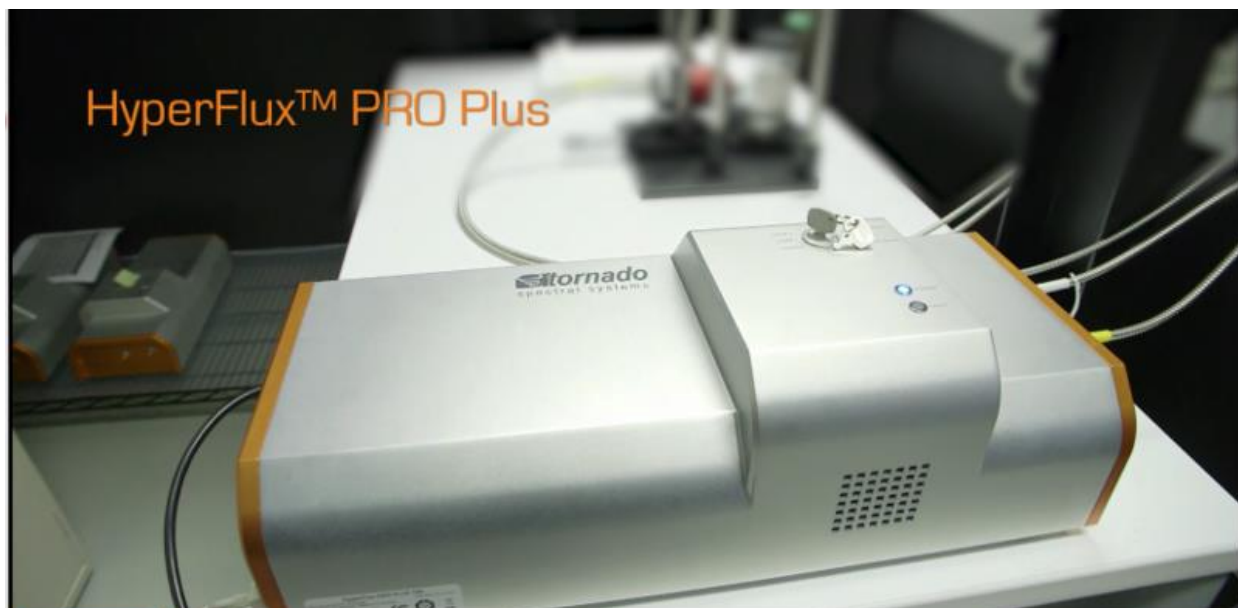
ADVANCING THE UNDERSTANDING & CONTROL OF
MANUFACTURING PROCESSES

February 12-14, 2018

Bethesda North Marriott | Bethesda, MD

Meet our experts and learn more about Tornado's HyperFlux™ PRO Plus

Visit us at **booth 209** and learn more about our **HyperFlux™ PRO Plus** Raman Spectroscopy system! Our team will demonstrate how you can achieve the best possible combinations of **signal strength** and **spectral resolution** in a dispersive spectrometer.



High Throughput Virtual Slit (HTVS™) Performance Advantage

Sensitivity, Speed and Safety

Tornado's proprietary HTVS design eliminates spectrometer slit losses while maintaining high spectral resolution.

What can be done with the HTVS performance advantage is game-changing:



(A) **10X Improvement** in Spectrometer Throughput and Signal Strength

(B) **3X to 6X Improvement in SNR** - *more accurate identification and quantitation for challenging mixtures and low concentration levels*

(C) **10X to 30X Faster Measurement** - *for precise tracking of rapid changes and transient features*

(D) **Lower Laser Power Operation** - *for improved safety and reduced sample damage*



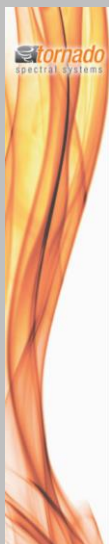
Featured Application Note

**9 Component Multivariate Calibration For
The Analysis Of Metabolites**

Featured Video

**Demonstrating the Speed & Sensitivity of
Tornado's HyperFlux PRO Plus: Real-time**

An assessment by Sanofi UK of the performance of the HyperFlux™ PRO Plus Raman Spectroscopy System for the quantitative analysis of biochemical components in a simplified chemically defined pseudo growth medium for mammalian cell culture.



Rapid Development of a 9 component Multivariate Calibration for the analysis of Metabolites in Chemically Defined Cell Culture Media

Marjorie Maquettias, Shehlin Hennessy and Dylan Jones
Chemical and Biotechnology Development, Sanofi, Haverhill, Suffolk, CB9 6PL, UK

This study assessed the performance of the HyperFlux™ PRO Plus Raman Spectroscopy System (Tornado Spectral Systems) for the quantitative analysis of biochemical components in a simplified chemically defined pseudo growth medium for mammalian cell culture. An experiment was designed to evaluate the ability of Raman Spectroscopy to directly measure individual components in a complex mixture at concentrations at or below the level of quantification of conventional Raman spectrometers. A set of samples with varying amounts of glucose, lactate, glycine, glutamate, serine, arginine, histidine, leucine, and phenylalanine were prepared so that co-absorbance between components was close to zero. The spectral collection and model development were completed in one day. The sample spectra were collected in a moving using fast acquisition times and powerful calibrations were developed in the afternoon using basic pre-treatments such as derivatives and normalisation.

Background

Real time analysis of biochemical components in bioreactors using Raman Spectroscopy has been widely discussed in the literature [1-4]. Having the ability to accurately monitor the consumption of starting materials, the formation of waste products, as well as provide the robust cell growth, ammonia, viable cell count and later cell death and provide responses in real time could provide valuable opportunities to better control the process and thereby improve process yield and consistency.

Raman spectroscopy has not yet been widely implemented in industrial bioreactors and this is due mainly to the complexity of the sample under analysis. There are many interfering signals arising from a cocktail of metabolites which require calibration model development challenges. A second factor is that in bioreactors, there are high levels of turbidity between samples to be processed, making it unclear sometimes whether the compounds of interest can be measured directly or via some differential means which in turn has implications for scalability. Finally, the acquisition of Raman information can be an issue as sample concentrations tend to be very dilute and Raman spectrometers are operating at the lower end of their capabilities. Measurement times of 10-20 minutes to obtain a signal are quoted in the literature [5].

In this analysis, a design space was generated to produce a multivariate calibration set for a chemically defined growth medium which contained no correlations between variables. The samples were then synthesized in the laboratory and analysed using the HyperFlux™ PRO Plus Raman Spectroscopy System.

Method

Sample Preparation

Using an experimental design which ensured orthogonality between the variables, a design space was mapped out with nine variables and five levels. A sample covariance plot between two variables is shown in Figure 1. Scatter graphs could be created for all combinations of variables.

Correlation plot between glucose and lactate

Level	Glucose	Lactate
1	0.00	0.00
2	0.05	0.05
3	0.10	0.10
4	0.15	0.15
5	0.20	0.20

Raman Spectroscopy of Propylene Glycol in Water

To demonstrate the sensitivity of the PRO Plus for making real-time process measurements or for reaction monitoring, we've performed a simple experiment where we add small quantities of propylene glycol to water and then monitor the mixture with a PRO Plus analyzer and immersion probe.



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Can't Make It To IFPAC?