Justin Neill Invited Oral Presentations – Fall 2019

SciX 2019 – Palm Springs Convention Center, Palm Springs, CA
Session: 19PMA04, Advanced Spectroscopic Techniques in Pharma
Chair: Sergey Arzhantsev, FDA

Wednesday, October 16, 2019 – 4:10-4:30 pm

"Enabling Faster Route Discovery and Process Optimization with Molecular Rotational Resonance Spectroscopy"

Molecular Rotational Resonance (MRR) spectroscopy is a powerful emerging technique for the characterization of small molecule mixtures. The core benefit of MRR over other techniques is that it analyzes mixtures without chromatographic separation, chemometrics, or reference standards. Because of its high resolution, MRR is able to identify and quantify components in a mixture quickly and easily, even isomeric compounds. By greatly shortening the both the time required for method development and the analysis-to-analysis cycle time, MRR can enable better chemical route development. In this talk, MRR is demonstrated both in an R&D laboratory as well as in on-line process instruments. In the R&D setting, each component can be unambiguously identified without prior reference standards using simple electronic structure calculations. For process monitoring, the MRR signatures of known compounds are measured in a fully automated analysis. No advance sample preparation is required for either instrument, and no chemometric models are required, so the measurement and results interpretation is extremely simple. We find that MRR gives comparable results to orthogonal techniques with significantly less method development, and can also perform analyses that are very difficult or impossible by other techniques. For example, MRR was used to determine the product distribution of an arylation reaction that produced a mixture of regioisomers. In addition to identifying and quantifying the major and minor components, MRR identified a third product that was not previously discovered by the chemists. MRR can be utilized in the pharmaceutical industry to accelerate understanding of the products, as well as the impurities, generated in synthetic processes. By eliminating complex method development and the need for expensive reference standards of impurities, MRR can dramatically shorten the time and cost required to bring small-molecule drugs to market.

Eastern Analytical Symposium – Crowne Plaza Princeton Conference Center, Princeton, NJ
Sesssion: EYES in the Process Line, Part 2
Chair: Jim Rydzak, Specere Consulting

Monday, November 18, 2019 – 1:40-2:20 pm

"Process Monitoring of Impurities using Molecular Rotational Resonance Spectroscopy"

In this talk, I will present case studies of the use of Molecular Rotational Resonance (MRR) spectroscopy in at-line and on-line monitoring applications, simplifying and accelerating process understanding and feedback. MRR identifies compounds in mixtures through their gas-phase pure rotational spectra, which are unambiguous fingerprints of molecular structure. Regioisomers, diastereomers, and isotopic substitutions change the MRR spectrum measurably, allowing direct resolution of complex mixtures without requiring chromatography or chemometrics. Enantiomers can also be resolved using a simple gas-phase chiral shift technique. This high structural selectivity means that isomeric composition can be determined quickly and easily and in conjunction with other impurities, adding critical new capabilities to the PAT toolbox. Key aspects of the MRR case studies that will be emphasized include at-line and on-line sampling integration, results workflow, automation, and the ease with which instruments can be configured to address a range of different analytical challenges in both laboratory and process environments.