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Raman spectroscopy as a real-time in situ analyzer for cell culture bioprocesses

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Production of recombinant proteins using mammalian cell lines is a commonly used bioprocess in the biopharmaceutical field. Improvements in cell media and process control have been important in realizing improvements in cell viability and productivity, but there are many opportunities to further advance cell culture bioprocesses. A key factor toward further advancing cell culture bioprocesses is incorporation of *in situ* process analytical technologies (PAT) to enable in-process control. Molecular techniques - such as Raman spectroscopy - are widely used for PAT applications because they provide *in situ* information in real-time. Raman spectroscopy is a vibrational spectroscopic technique that provides a chemical and physical "fingerprint" of a sample. The Raman spectroscopy "fingerprint" provides simultaneous, *in situ* measurements of multiple bioprocess assays within a cell culture or fermentation bioprocess. Raman spectroscopy enables a more thorough bioprocess understanding and real-time control of nutrients and metabolites. Representative examples show how Raman spectra were used to generate multi-component qualitative and quantitative predictive models. We demonstrate real-time prediction and process control of glucose, lactate, glutamine, glutamate, ammonium, and viable cell density. When combined with PID, closed-loop, or other feedback controls, *in situ* Raman measurements can optimize feeding strategies and improve yield and titer. Recent feedback control studies underscore the capability of Raman to not only provide *in situ* chemical information, but also control protein quality. We provide customer examples in how Raman-controlled glucose feeding can optimize post-translational target protein glycosylation and Raman-controlled lactate accumulation can improve titer. Together, these studies demonstrate the value of Raman spectroscopy as an *in situ* bioprocess analyzer from process development to GMP manufacturing.

Biography

Alexander Pitters is a Life-Science Engineer (M.Sc. - University of Technology and Economics Berlin), worked at Max Planck Institute for Molecular Genetics in Berlin as a Biologic-Technical Assistant, at Procter&Gamble Brussels Innovation Centre as a Process Development Engineer, and at Bayer Technology Services in Berkeley as a PAT-Biologics Engineer. He joined Kaiser as an Applications Scientist to analyze data, create chemometric models and develop business within the pharmaceutical industry.

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