

Raman Spectroscopy as a Real-Time *In Situ* Sensor for BioPharma



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INTRODUCTION

The past decade has seen a seemingly unquenchable demand for increased information about the bioprocessing environment with which we work. However, for most of the past ten years advancements in bioprocess analytics were few and far between, that is no longer the case. In recent years Kaiser Raman has redefined what it is we can expect to know about our bioprocesses. Gone are the excuses of “not enough ports”, “overcrowded headplates” and “not available yet”. Replaced instead with “yes, we can do that.”

Unlike most of the current bioprocess analyzers which have their origin in the hospital suite and not the bioprocessing suite, Kaiser Raman was born of bioprocessing. This is perhaps most obvious in the sensors which feature 316L S.S. wetted material, industry standard 12MM OD and are designed for SIP, CIP and/or Gamma sterilization. And while other analyzers require that you accept the risks to both sterility and reliability associated with automated sampling, the *in situ* nature of Kaiser Raman delivers real-time bioprocess measurements free of such risks.

Whether your application is Process Development, Pilot, or cGMP Manufacturing scale, Kaiser Raman is a solution that can meet or exceed your bioprocess measurement needs. But do not take our word for it, as this poster clearly illustrates many of our industry’s leading company’s are successfully deploying Kaiser Raman in their upstream bioprocessing applications, and these are just the ones we can share with you.

RAMAN SPECTROSCOPY

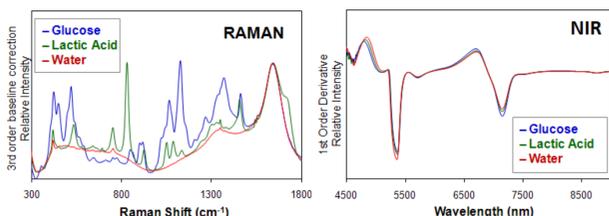
- Raman is a fundamental vibrational spectroscopic technique [1]
- Provides chemical and physical information from samples that can be used to generate multi-component qualitative and/or quantitative predictive models
- Requires no sample preparation, *in situ* capability
- Water presence does not pose as a spectral interference (like when using NIR)

SPECIFICITY

Specificity is a critical figure of merit during method validation

Raman spectroscopy has high chemical specificity to critical bioprocess constituents, such as glucose and lactate, without the typical water interference observed when using NIR process analyzers.

6 wt% Glucose and 2 wt% Lactic Acid



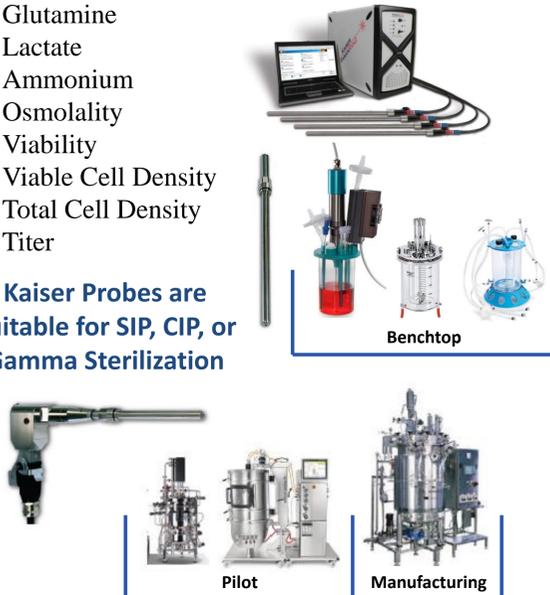
RAMANRXN SYSTEMS™
 REACTION ANALYSIS, MONITORING AND CONTROL

APPLICATIONS

One Probe, Multiple Measurements of the Bioprocess

- Glucose
- Glutamine
- Lactate
- Ammonium
- Osmolality
- Viability
- Viable Cell Density
- Total Cell Density
- Titer

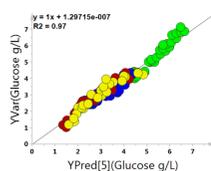
Kaiser Probes are Suitable for SIP, CIP, or Gamma Sterilization



MODELING

Raman spectra can be empirically correlated to off-line reference values by means of multivariate data analysis (MVA) predictive methods such as Partial Least Squares (PLS), using standard MVA software; for example SIMCA from Umetrics. Reference values should be obtained from qualified bio analyzers.

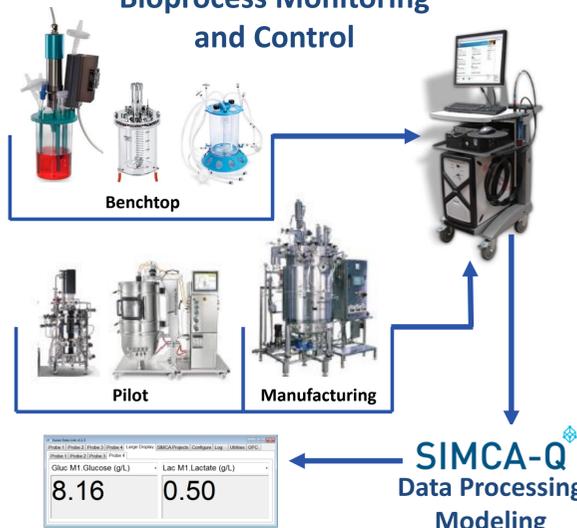
Glucose PLS Model



Each color represents a different batch

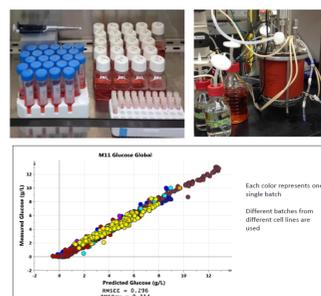
Predictive models can be easily imbedded via OPC connectivity to enable real-time monitoring and process control.

Bioprocess Monitoring and Control



CASE STUDY 1

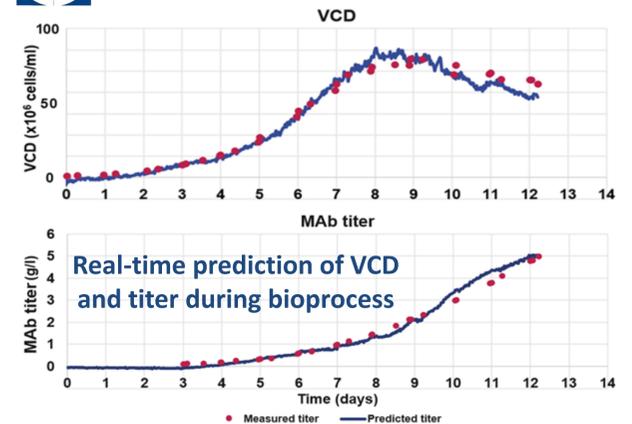
Pfizer, Intelliscient [2]



Generic or universal platform to monitor and control nutrients and metabolites in cell cultures

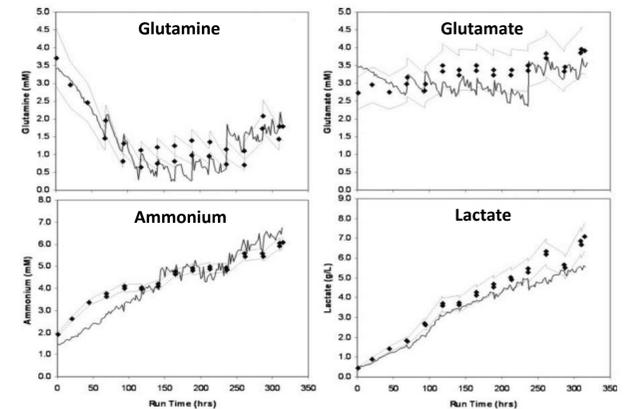
CASE STUDY 2

ucb Pharma [3]



CASE STUDY 3

Bristol-Myers Squibb [4]



Real-time prediction of glutamine, glutamate, ammonium, and lactate during bioprocess

CONCLUSIONS

Kaiser Raman has proven well suited for a host of applications commonly associated with upstream bioprocessing. This includes Benchtop, Pilot, and cGMP Manufacturing scale applications at some of our industry’s leading company’s. At the Benchtop scale Kaiser Raman optimize minimal headplate space to deliver maximum insights to your bioprocess, thereby enabling the full potential of QbD. While at the Pilot and cGMP Manufacturing scale Kaiser Raman can be a valued contributor to the goal of continuous bioprocessing.

As the data shared in this poster clearly illustrates, Kaiser Raman is redefining what it is to measure and control the modern bioprocess. Begging the question, What could Kaiser Raman do for you and your bioprocess?

REFERENCES

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2. H. Mehdizadeh “A Generic Platform Technology for Monitoring and Feedback Control of Nutrients and Metabolites in Biopharmaceutical Processes,” presented at *IFPAC*, January 24, 2014, Arlington, VA
3. D. Didion, A. L. Hantson, and E. Lecomte Norrant “PAT on mammalian cell culture – Comparison of two technologies: NIR and Raman,” presented at *3rd Annual Cell Culture & Bioprocessing Congress*, November 18th 2014
4. N. R. Abu-Absi, B. M. Kenty, M. E. Cuellar, M. C. Borys, S. Sakhamuri, D. J. Strachan, M. C. Hausladen, and Z.-J. Li, “Real Time Monitoring of Multiple Parameters in Mammalian Cell Culture Bioreactors Using an In-line Raman Spectroscopy Probe,” in *Biotechnology and Bioengineering*, May 2011, pp. 1215-1221.



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