

Raman-Based In-line Monitoring of Key Process Parameters in Mammalian Bioprocesses without the Need for Chemometric Model Building

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MAVERICK® Raman spectrometer device

The MAVERICK System provides Raman-based, in-line, continuous monitoring of mammalian (CHO, HEK293) bioprocess key parameters with a novel multivariate optical sensing technology. MAVERICK offers automated, non-destructive, and easy-to-integrate analysis of glucose, lactate and biomass with the ability to add feedback control loop to glucose feeding.

The components of MAVERICK are shown in Figure 1. One MAVERICK hub can be multiplexed to up to 6 modules (and thus 6 probes in bioreactors).



Figure 1. Components of MAVERICK: Optical immersion probe, measurement module and a central monitoring hub. One hub can manage up to 6 modules and bioreactors.

Rapid set-up of MAVERICK for glucose, lactate, and biomass measurements in cell culture

Figure 2 shows how setting up MAVERICK for in-line monitoring of process parameters is as simple as 1-2-3:

1. MAVERICK is calibrated using two calibration standards.
2. The probe is sterilized via autoclave.
3. MAVERICK can begin monitoring key process parameters in real time.

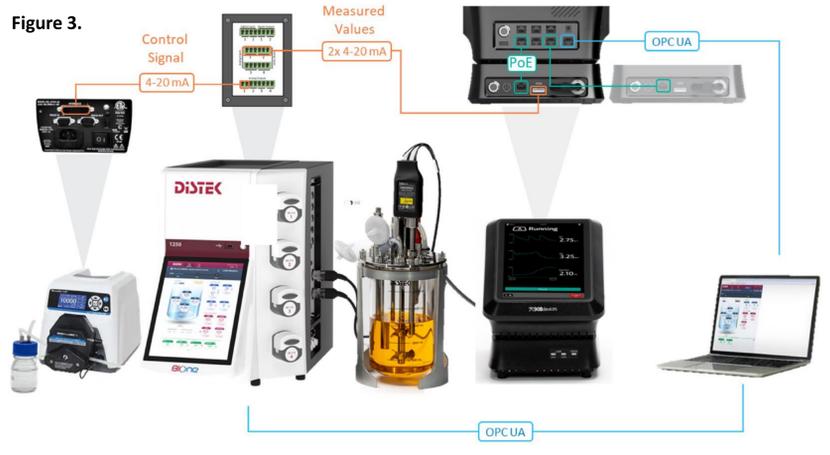
Figure 2.



1. Calibrate using the provided calibration standards following the on-screen prompts
2. Autoclave probe alone, or installed in the bioreactor
3. Start monitoring your bioprocess.

Established feed control with MAVERICK

Each MAVERICK measurement module can be connected directly to a feed pump to control the pump through a simple wired analog connection. MAVERICK supports pump control through either current or voltage signals. Configuring the pump control settings is easy as choosing an analyte to control (often glucose), a setpoint, a deadband, and the High Output % and Low Output % for the pump. Typically, the pump is switched off once the analyte under control exceeds the setpoint + deadband value. See Figure 3 for an example control connection.



Conclusion

The MAVERICK System demonstrates the advantages of in-line Raman PAT with monitoring and control of bioprocess for glucose, lactate, and biomass measurements. With MAVERICK, the analyte measurements are estimated with its *de novo* approach, meaning the user does not need to build chemometric models required for conventional process spectroscopy-based methods. Spectral data is available for additional parameter modeling.

Instant monitoring of CPPs in gene therapy bioprocess with MAVERICK

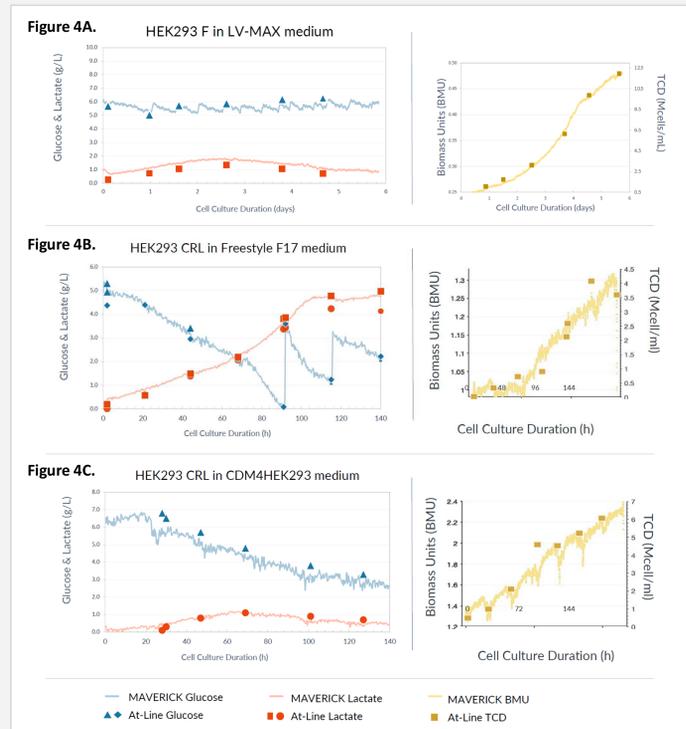
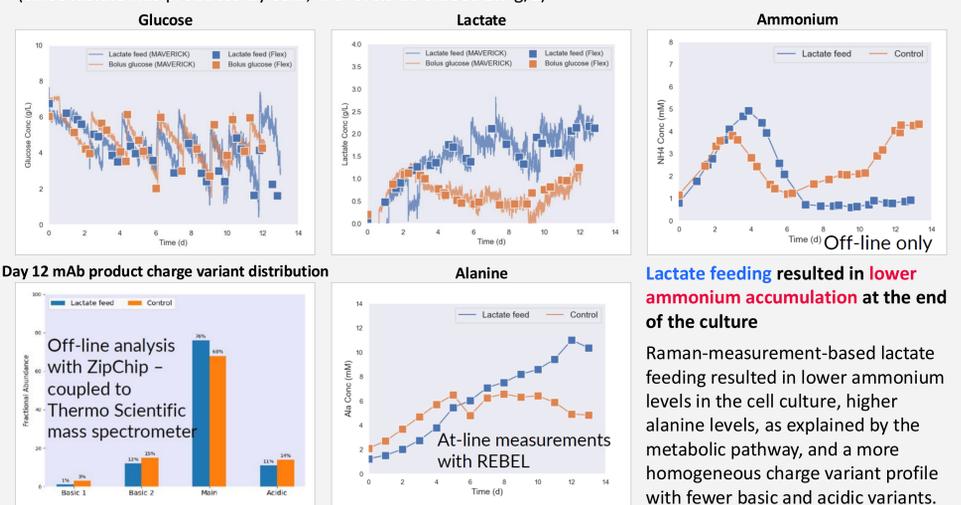


Figure 4. Glucose, lactate and biomass MAVERICK measurements and comparison to at-line measurements for (A) HEK293F in LV-MAX medium (Thermo Fisher Scientific), (B) HEK293 CRL in Freestyle F17 (Thermo Fisher Scientific) and (C) CDM4HEK293 media (Cytiva)^{1,2,3}

- Cell cultures: (A) Distek B1One 1250 dual 2L bioreactor; (B&C) Yokogawa BR1000 3L bioreactor.
- At-line glucose and lactate were measured daily using Bioprofile Flex2 analyzer (Nova Biomedical).
- TCD was measured daily with Cellometer (Nexcelom) (A), and ViCELL XR (Beckman Coulter) (B&C).
- MAVERICK measurements align well with the at-line glucose, lactate and TCD measurements in all three cultures, including two different HEK 293 cell lines, three media, and two bioreactor scales. MAVERICK was not trained on any of these bioprocesses.^{1,2,3}

Lactate level control with MAVERICK to avoid ammonium build-up

Raman-based lactate feeding for decreased ammonia accumulation in CHO cell culture. Comparing 1.5 g/L lactate set point (if falling below 1.5 g/L, add lactate to 1.5 g/L) to no lactate feed. Both conditions had glucose bolus feed. (Since lactate was produced by cells, the levels do exceed 1.5 g/L)⁴



Lactate feeding resulted in lower ammonium accumulation at the end of the culture

Raman-measurement-based lactate feeding resulted in lower ammonium levels in the cell culture, higher alanine levels, as explained by the metabolic pathway, and a more homogeneous charge variant profile with fewer basic and acidic variants.

References and more information

1. Application Note: *Instant Implementation of Raman-based PAT with MAVERICK for Monitoring Glucose and Lactate* (DOC0537)
2. Application Note: *Determining Total Cell Count with MAVERICK Biomass Measurements* (DOC0532)
3. Application Note: *Instant PAT Implementation with Raman-based MAVERICK across Cell Lines, Media, and Scales* (DOC0535)
4. Webinar: *Instant Implementation of Raman-based Monitoring and Control for Key Upstream Bioprocessing Parameters* (VD0136)



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