Raman-based In-line monitoring of key process parameters in mammalian bioprocesses without the need for chemometric model building

Colin Gavin[1], Steve Driscoll[1], Nick Randall[1],Richard Marx[2], Jaeweon Lee[2], Maurizio Cattaneo[2], Seongkyu Yoon[2], Scott Miller [1], Graziella Piras [1], Chris Brown[1]

[1]908 Devices Inc., Boston, MA; [2] Department of Chemical Engineering, University Massachusetts Lowell, MA

MAVERICK Raman spectrometer device

MAVERICK 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 probes in bioreactors).

Figure 1.

***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 of 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 autoclaved.
(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

MAVERICK measurements in fresh media panel – standard addition

To evaluate the consistency, linearity, and selectivity of MAVERICK measurements, known quantities of glucose and lactate were serially spiked into a range of mammalian cell culture media samples. We tested more than 15 media types (Ref.1) used to support the growth of popular bioprocess cells, including CHO, HEK293, and T-cells. The measurements showed great linearity and correlation to off-line reference measurements (Figure 3). The measurements obtained with MAVERICK typically will provide a precision of <0.1 g/L for both glucose and lactate: fresh BalanCD HEK293 medium (FUJIFILM) was measured for 20h under stable conditions in a 3L bioreactor. MAVERICK measurements at 1 minute reporting interval showed a standard deviation of 0.09g/L for glucose and 0.04g/L for lactate.

The spiking experiments were also used to evaluate glucose and lactate measurement accuracy in fresh media: Across the 15 types of media % recovery was excellent (within ±20% (data shown in Ref 1) and comparable to the accuracy of the reference analyzer.

References and more information

Part of this work was conducted at the University of Massachusetts Lowell in Prof. Seongkyu Yoon's lab.

- Ref 1: 908 Devices MAVERICK Technote 2
- Ref 2: 908 Devices MAVERICK Technote 1
- For more information, please visit www.908devices.com/MAVERICK

MAVERICK measurement linearity & accuracy

Figure 3 A.

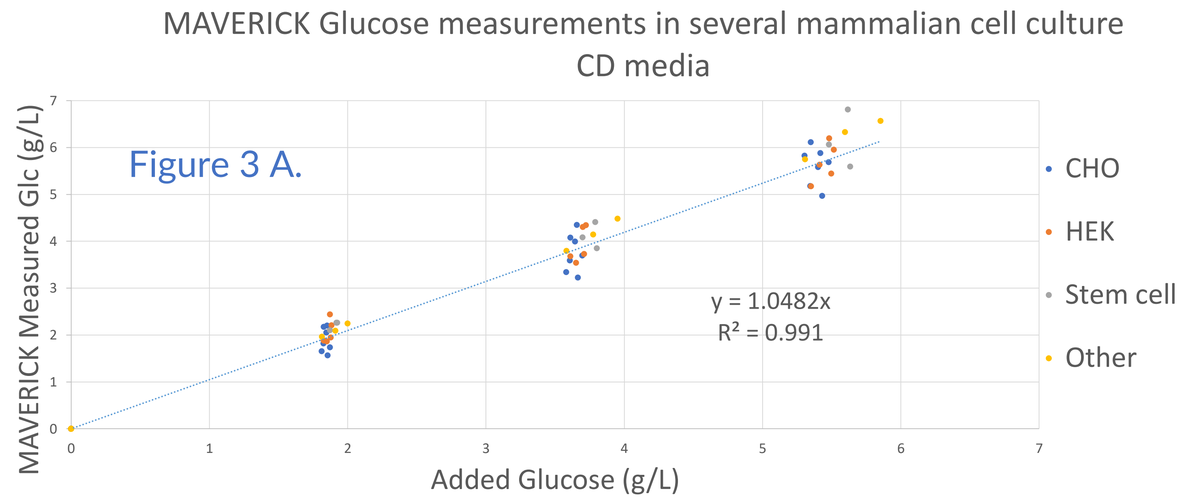

Figure 3 B.

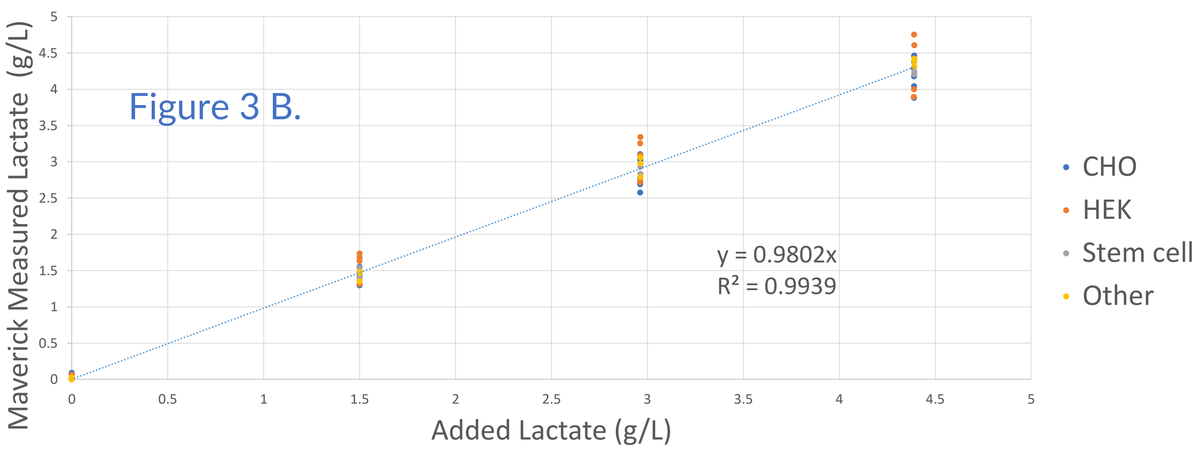

***Figure 3** Spiking known concentrations of glucose (A) and lactate (B) into mammalian cell culture media. Actual spike concentrations (x axis) plotted against the MAVERICK reported values (y axis)*

MAVERICK biomass measurement

To assess the linearity between biomass measurements using MAVERICK and off-line total cell densities, two cell lines (a CHO and a HEK293 cell line) were cultured for 14 days and 6 days respectively (for more details, please see Ref. 2). We saw great correlation between MAVERICK biomass data and off-line total cell counts for CHO (Fig. 4A) and HEK293 (Fig 4.B).

Figure 4 A.

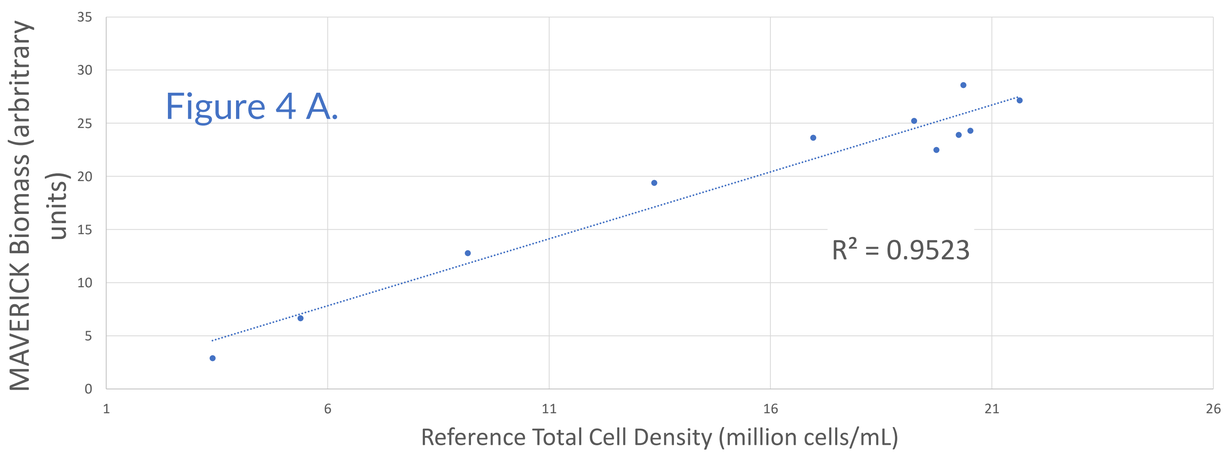

Figure 4 B.

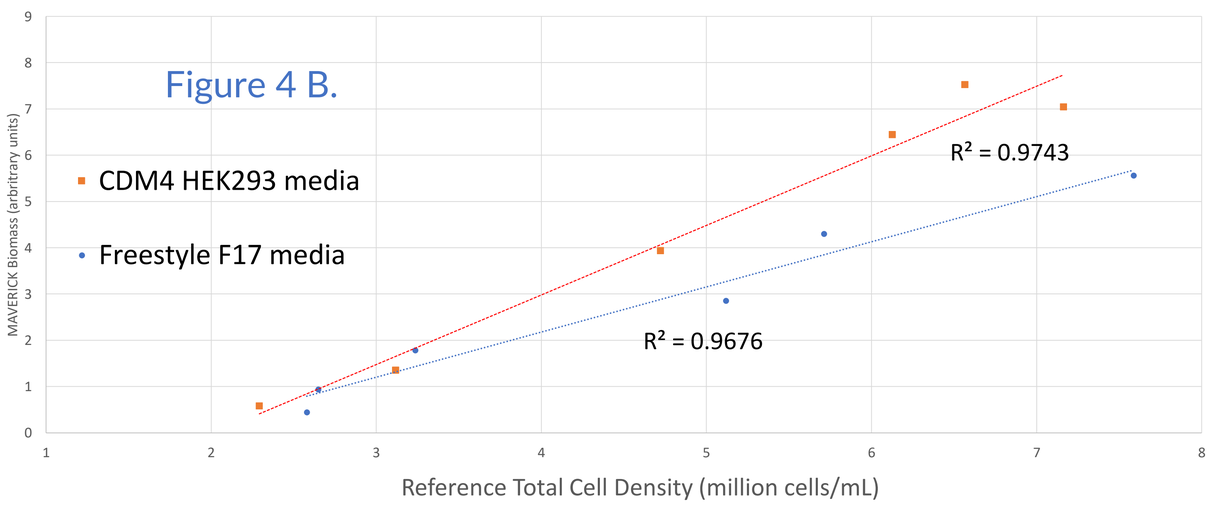

Figure 4 Correlation between MAVERICK biomass data and offline total cell counts for CHO (A), HEK293 cells in FreeStyle F17 (Thermo Fisher Scientific) and CDM4 HEK293 media (Cytiva) (B).

Conclusions

MAVERICK offers the advantages of in-line Raman process analytical technology (PAT) for glucose, lactate and biomass measurements without the cost and headaches inherent to the implementation of conventional process spectroscopy-based methods. Spectral data is available for additional parameter modeling.