DXCOVER

Dxcover Infrared Platform for Process Analytics

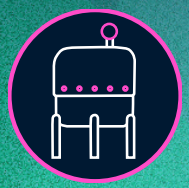
Large scale production of biologics is a high-cost process that requires precise monitoring. Process analytical technologies (PAT) focus on the measurement of key performance indicators to assess cell growth. The **Dxcover® Infrared Platform** provides a spectroscopic approach to process monitoring without the need for extensive preparation.

INTRODUCTION

Monitoring organism growth during bioproduction is critical to the success of the culture. Bioreactors are carefully monitored during cell expansion to measure key performance indicators, either by on-line, at-line, or off-line measurements. The progression towards continuous cell production at high volumes, lends itself to new PAT being introduced, that can provide real-time information from a cell culture. Key factors to be measured include pH, temperature, dissolved oxygen, and cellular metabolites.

During cell culture expansion, glucose levels are depleted in the cell medium as it serves as the main carbon source to the organisms. Conversely, lactate levels rise as by-products of anaerobic respiration. An insufficient supply of glucose may inhibit cell growth and reduce yield of a bioreactor, and an accumulation of lactate can lead to adverse decrease in pH which can be toxic to cell lines. In large scale and continuous cultures these key parameters must be closely monitored to ensure optimum metabolic rate and cell growth.

Infrared spectroscopy is a powerful technique for the measurement of cell and cell derivative samples[1]. The Dxcover Infrared Platform technology is highly adaptable for bioprocessing applications[2]. For at-line monitoring, the **Dxcover® Sample Slides** enable rapid sampling and can be disposed of or archived after analysis. The **Dxcover® Autosampler** automates this analysis, reducing user operating time. This **Dxcover® SIRE** technology (disposable Silicon Internal Reflection Elements) is also available for collaborative projects for in-line monitoring applications.



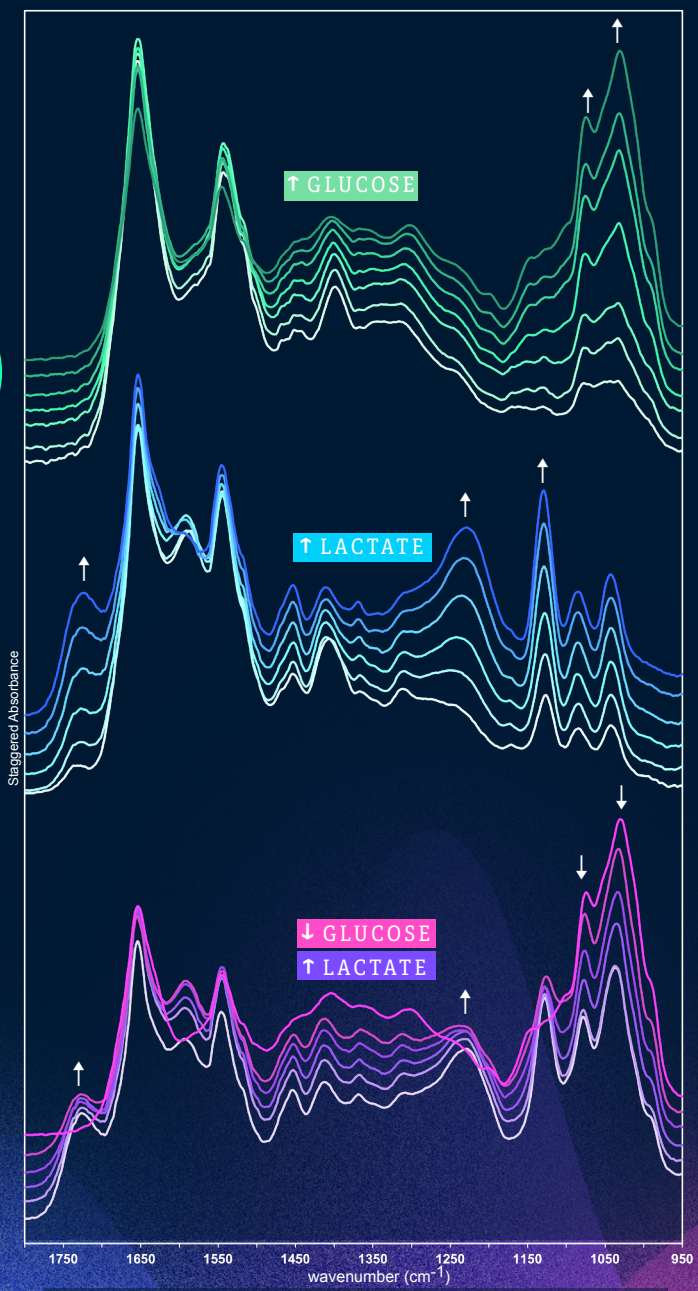


Figure 1. Spectra obtained from three metabolite concentration profiles; glucose at 0.78, 1.56, 2, 4, 6, 8, 12.5 mg/ml, lactate at 2, 4, 6, 8, 10 and 12 mg/ml, and a combined profile with decreasing glucose (12, 10, 8, 6, 4, 2 mg/ml) and increasing lactate (0, 2, 4, 6, 8, 10 mg/ml)

AIM

To characterise cell metabolites in cell media using the Dxcover Infrared Platform and to subsequently develop quantification models to predict glucose and lactate levels. This data depicts the suitability of the platform for bioprocess monitoring.

METHODS

To mimic indirect measurements within a bioreactor, cell media samples were analysed in this study. Dulbecco's Modified Eagle Medium (DMEM) that contained no inherent glucose was spiked with (i) glucose, (ii) lactate, and (iii) glucose and lactate to generate three concentration profiles. Five Dxcover Sample Slides were used per each concentration, with 4 microlitres of each sample deposited per Well. Sample Slides were dried in controlled conditions for 10 minutes prior to analysis. The Dxcover Autosampler was fitted to a Perkin Elmer Spectrum Two spectrometer, and slides were analysed using the Dxcover automated process.

RESULTS

The concentration profiles of gluocse and lactate in cell media show clear spectral changes as the concentrations increase (Fig. 1). For glucose, the C-O stretching modes can be seen between 1000-1100 cm^{-1}, with the two bands increasing relative to concentration. For lactate, the C-O-C stretching modes are the most apparent in the spectrum.

When combined and spiked at inverse concentrations, these patterns can be again discerned. As glucose decreases, the two peaks between 1000-1100 cm^{-1} decrease, whilst the C-O-C stretching modes of lactate begin to rise.

Partial least squares models were created using the spectral data from the concentration profiles. These were first calibrated, and then cross validated using a leave one out approach (Fig. 2). All models show a strong correlation between observed and predicted concentrations.

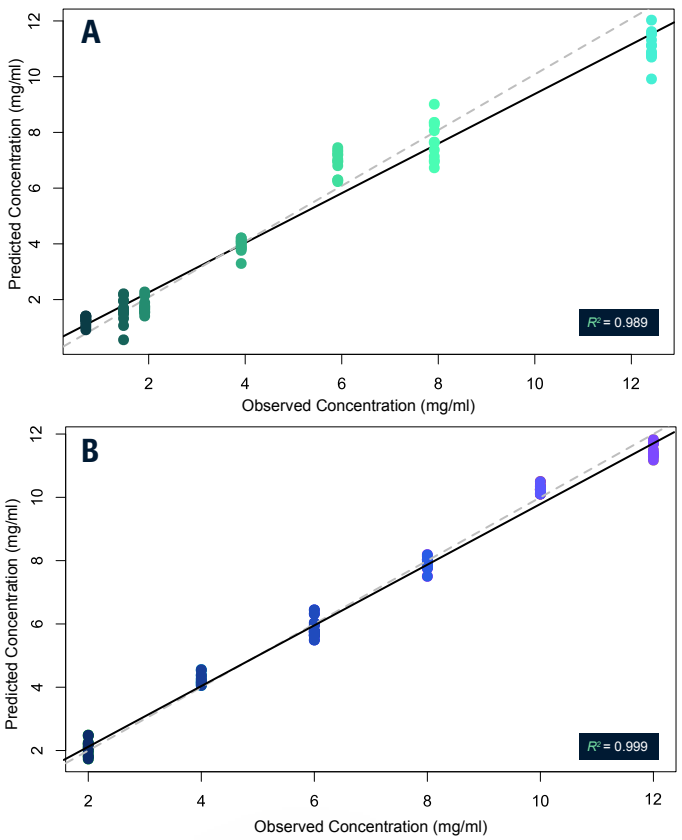


Figure 2. Leave one out cross-validation PLS models for predicting **(A)** glucose and **(B)** lactate

CONCLUSION

The Dxcover Platform is able to characterise and quantify metabolites directly from cell media, without the need for extensive sample preparation. The technology is well suited for at-line monitoring, and can be adapted to provide in- and on-line monitoring.

DISCOVER THE RANGE:

DXCOVER SAMPLE SLIDES

DXCOVER AUTOSAMPLER

DXCOVER MANUAL SAMPLER

To find out more about the Dxcover hardware range, speak to one of our representatives or info@dxcover.com

References: [1] Baker et al. 2014 *Nat. Protoc.* 9**(8)**:1771-1791, [2] Butler et al. 2019 *Nat. Comms.* 10**(1)**: 1-9