

# Know your process: on-line and at-line analytics for upstream bioprocess key nutrients

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## Overview

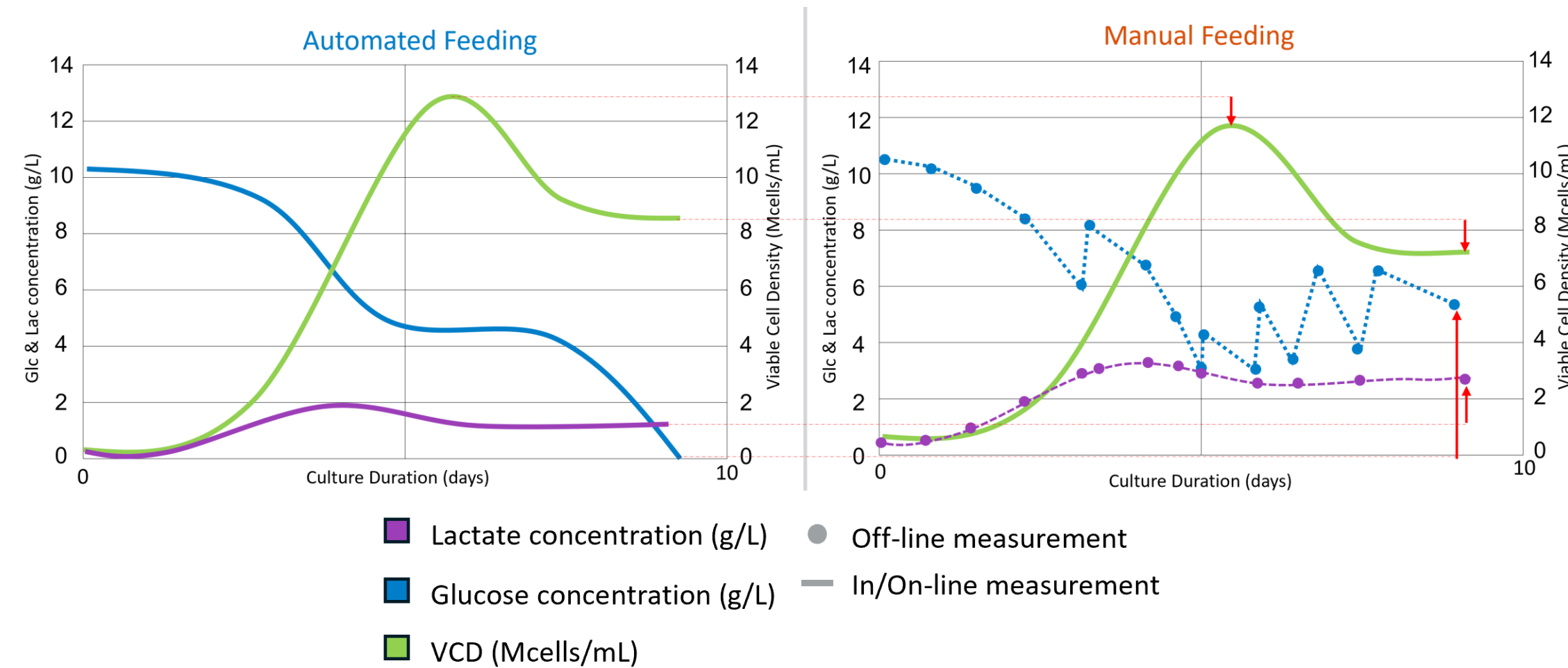
In bioprocess development, at-the-point-of-need analytics are required to monitor critical process parameters and to achieve desired product quality attributes. Here we present on- and at-line devices for data-driven and accelerated process optimization.

## Real-time monitoring of glucose and lactate with glucose control

Automated feeding enabled by frequent online measurement of glucose can be used to create very consistent and stable glucose levels in cell culture. This reduces the stress (alternating high-low - levels of nutrient) variable conditions often occurring in bolus-feeding strategies. The outcome of the optimized glucose feeding strategy is improved cell growth and viability (cell culture longevity and reproducibility) as well as reduced metabolite profiles.

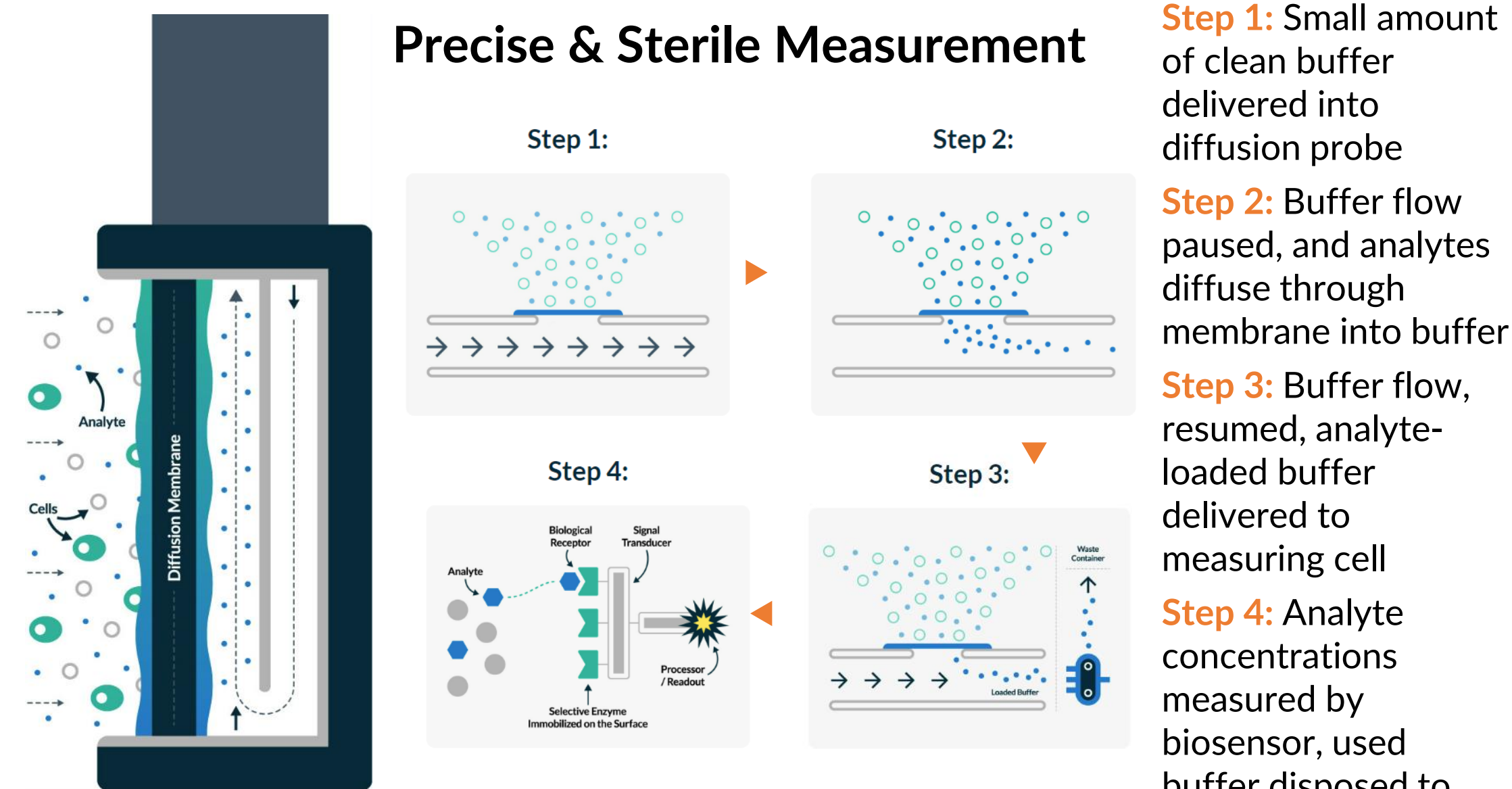
The MAVEN device uses an *in-situ* diffusion membrane probe, or perfusion flow cell, to collect biosensor-based measurements every 2 to 30 min throughout the bioprocess.

## Benefits of automated vs manual feeding



Sensitive, automated, on-line (sample-free) monitoring for glucose & lactate. The ability to adjust glucose feed rate benefits cell growth and viability. Lactate is a primary metabolite, or by-product, in cell culture. Lower metabolite accumulation may improve targeted glycosylation and charge variant profiles. Controlling glucose and lactate provides more consistent drug substance quality and yield.

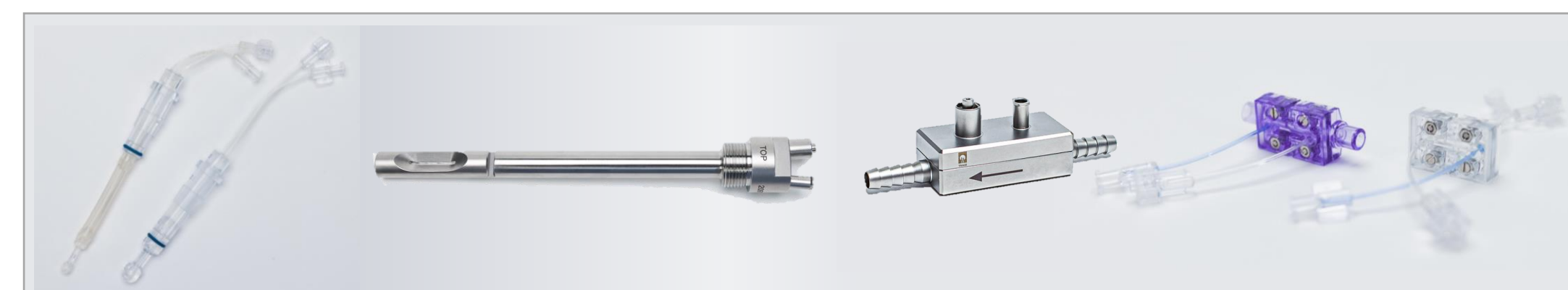
## MAVEN: On-line automated analysis and data processing with *in-situ* probe sampling



## Automatic, on-line glucose and lactate monitoring

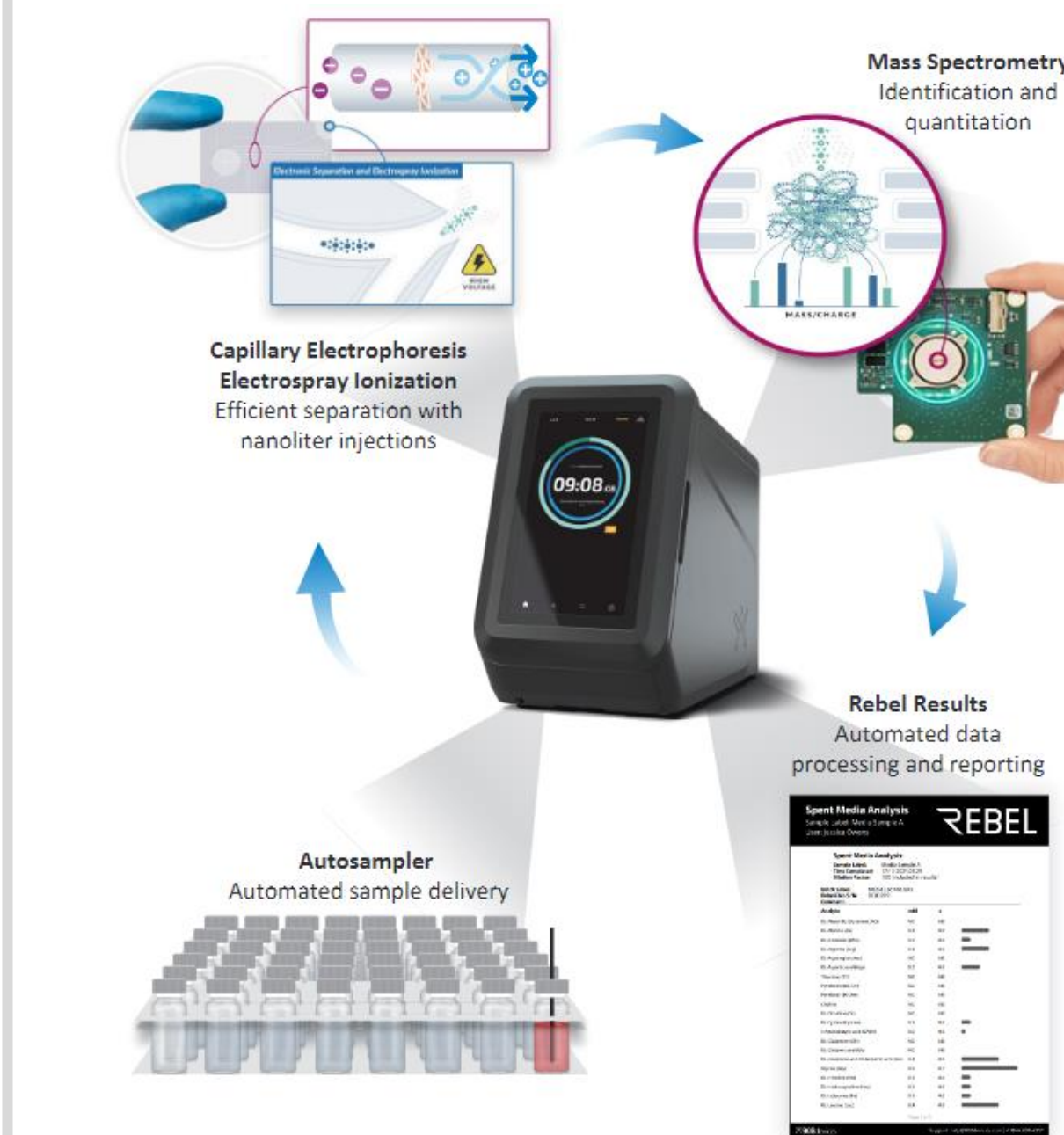
- No loss of bioreactor volume
- Enzyme-based biosensor detects glucose from 0.01 – 40.0 g/L and lactate from 0.05 – 10.0 g/L
- The biosensors are replaced after 5,000 measurements – sensor lifetime is dependent on measurement frequency
- Significantly reduced risk of contamination as compared to sample pulls
- Enables online analytics and glucose control by connecting to biosensor

## MAVEN *in-situ* probes and perfusion flow cells



Reusable and single-use probe options developed for stainless steel bioreactors and single-use bag bioprocesses + flow cells for perfusion processes

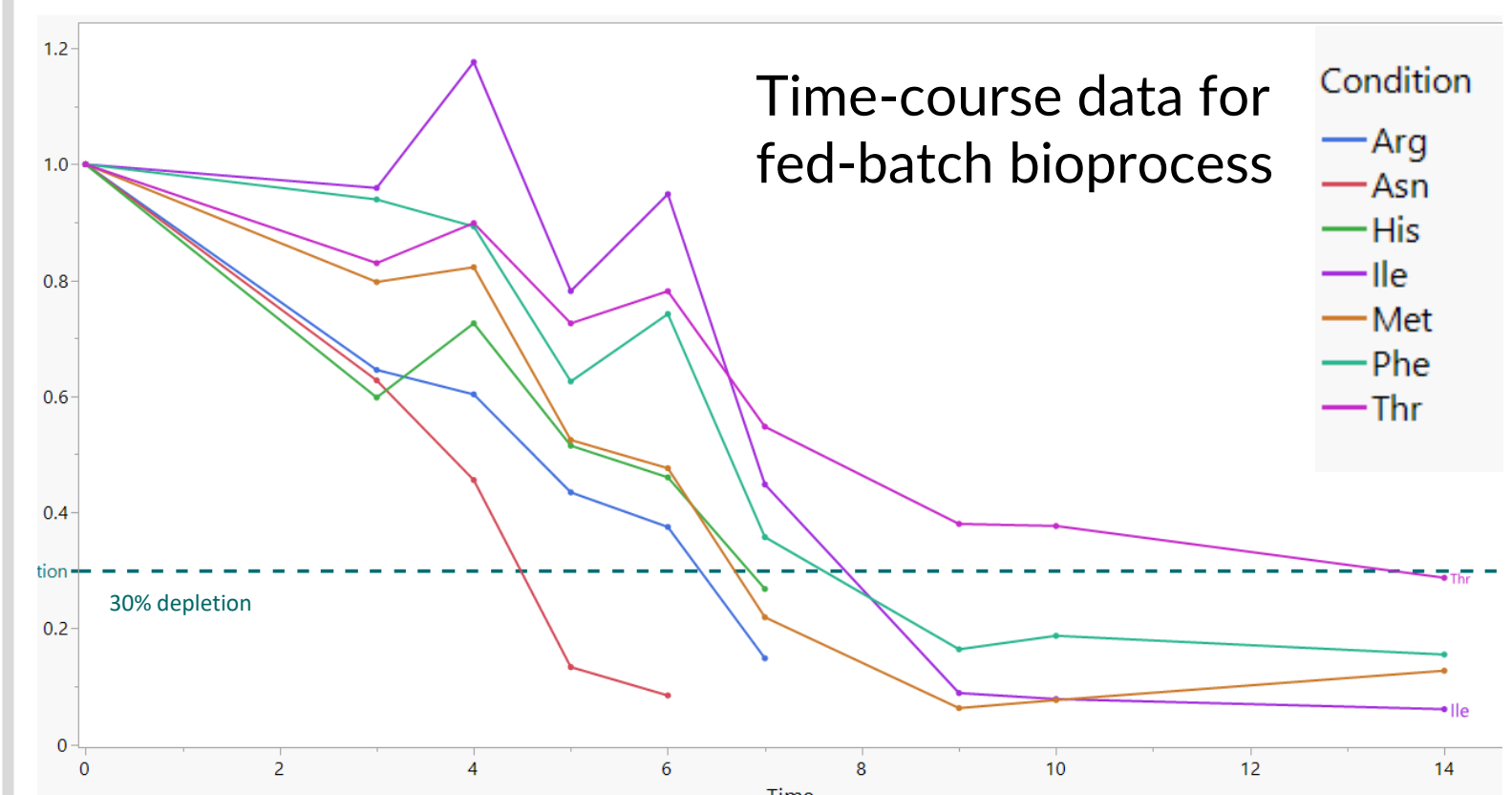
## REBEL: At-line cell culture media analyzer for AAA and more



### Spent Media Analysis:

- Bioprocess characterization, and media and feed strategy optimization
- Minimal sample requirement: as low as 10  $\mu$ L
- Simple sample prep: spin and filter, then dilute
- Integrated analyzer includes autosampler, separation, detection, analysis, and reporting
- Analysis run-time ~10 min per sample
- Consumable kit optimized for 200 replicate analyses

## REBEL provides vital statistics from spent media analysis



### What happens during the bioprocess?

- REBEL can be used at frequent time points to measure the cell culture media components over duration of bioprocess  
 - REBEL can also help assess media components as a function of multiple conditions

- Here, the data for the different analytes is normalized to the start concentration
- Some AA's depleted below 30% of the starting condition **before the mid-point of the process**
- Depletion may hinder cell growth or cause misincorporations in the final product