

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

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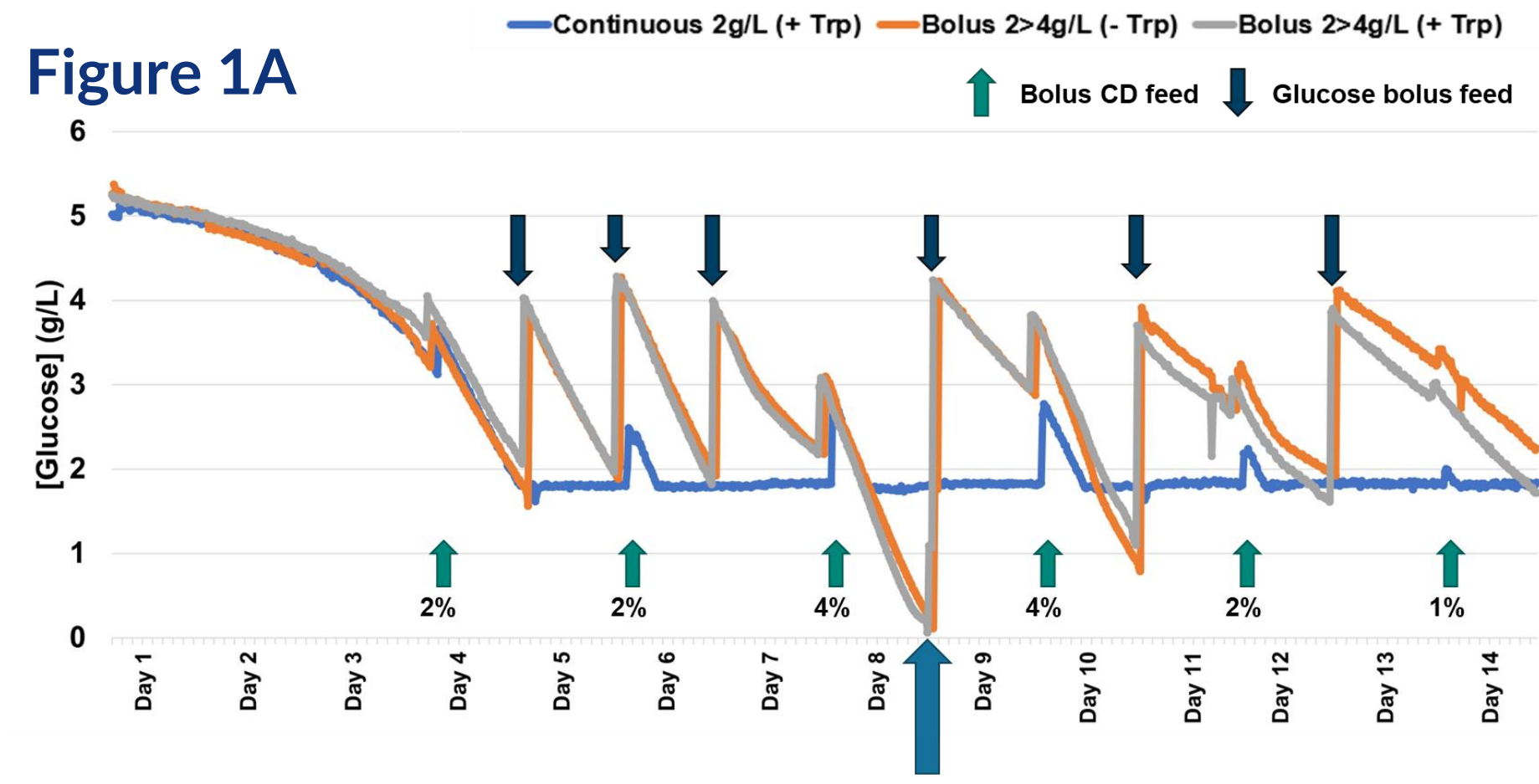
## Overview

In bioprocess development, at the point of need analytics are required to monitor critical process parameters and achieve desired product quality attributes. 908 Devices enables data-driven and accelerated process optimization with the following analytical bioprocess devices: On-line MAVEN for glucose and lactate and REBEL for spent media analysis.

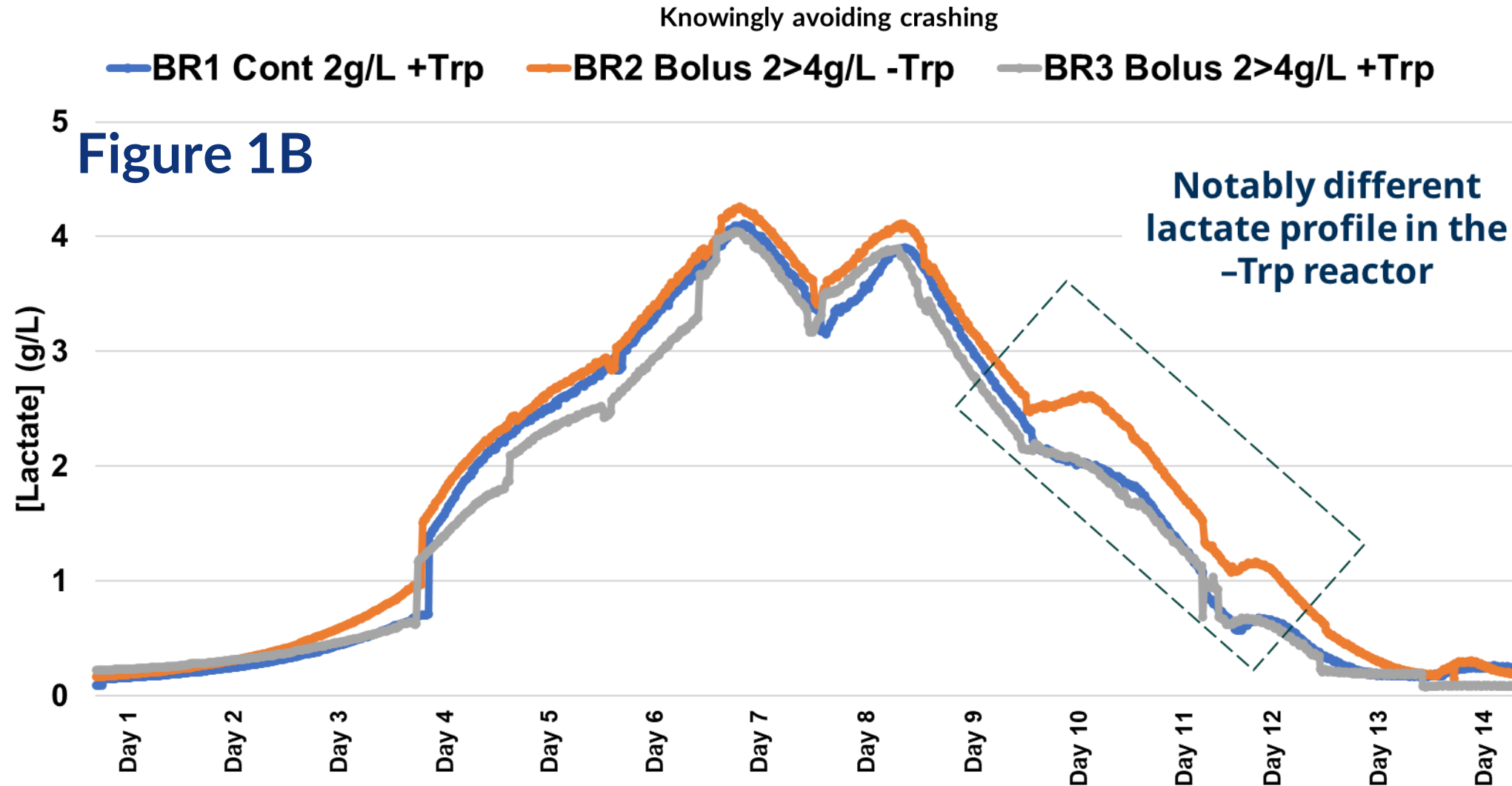
Automated monitoring of glucose and lactate plus glucose levels controlled at low levels, with MAVEN, together with understanding the amino acid consumption profiles with REBEL, can lead to higher growth/viability, lower lactate, and decreased COGS. Defined control strategies enable more intensified and stable cell cultures processes such as perfusion which may see dramatically improved productivity. This results in a more efficient and profitable process for biopharmaceuticals manufacturing.

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

Automated feeding enabled by frequent on-line measurement of glucose can be used to create very consistent and stable glucose levels in cell culture. This reduces the stress variable (alternating high-low levels of nutrient) 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.



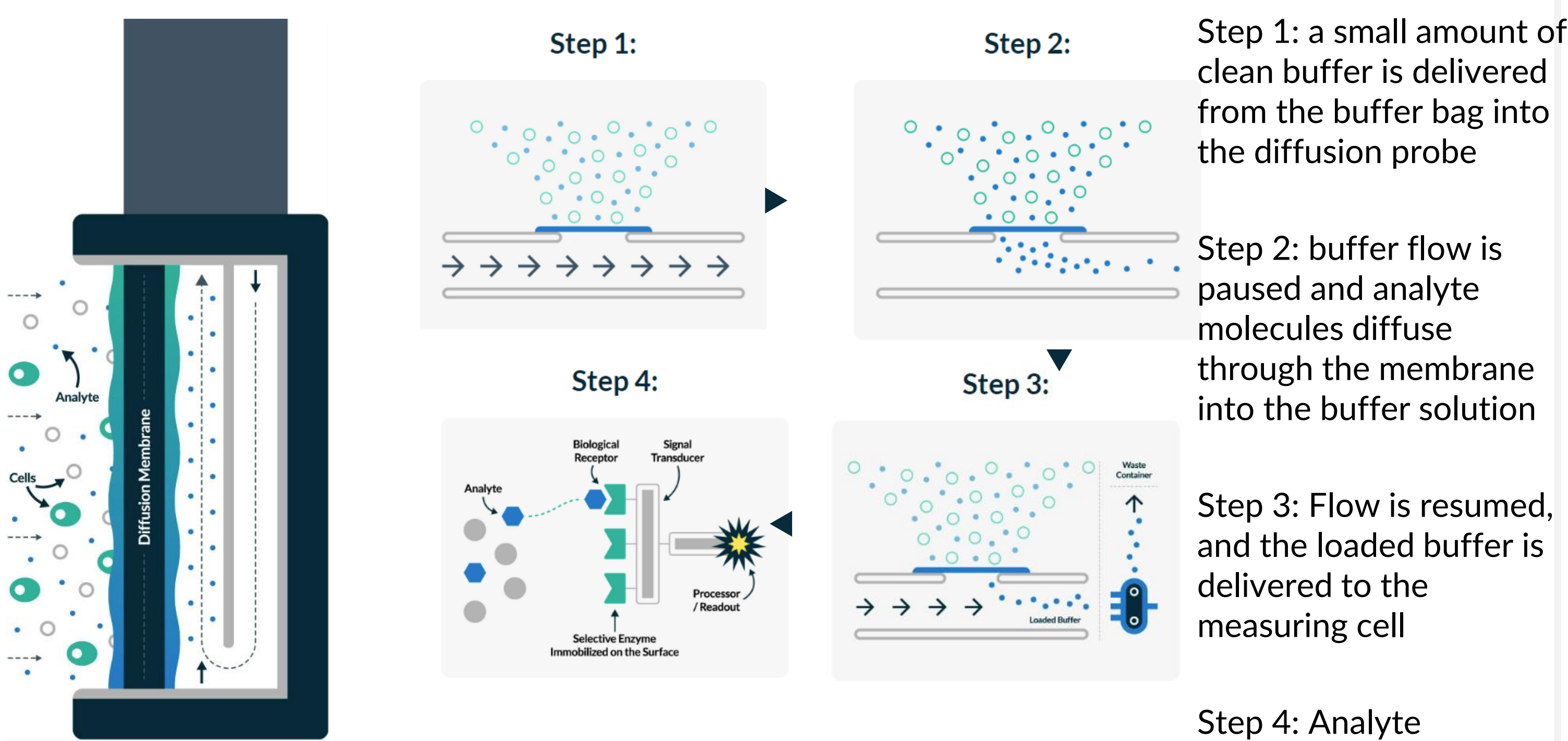
**Figure 1A.** Glucose measurements using the MAVEN in a CHO 10L bioreactor run: bioreactor 1 (continuous 2g/L glucose controlled by MAVEN), bioreactor 2 (bolus 2 to 4 g/L glucose (-Trp) and bioreactor 3 (bolus 2 to 4 g/L glucose (+Trp)). On day 8 the glucose levels dropped close to zero in bioreactors 2 and 3. A potential cell culture crash was avoided by monitoring the glucose levels closely with the MAVEN real-time measurements and adjustment of glucose feeding time.



**Figure 1B** Lactate profiles in run 1 for all three bioreactors. The real-time measurements showed a shift in the days 9-13 for the bioreactor that was not fed extra tryptophan in the amino acid mix.

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

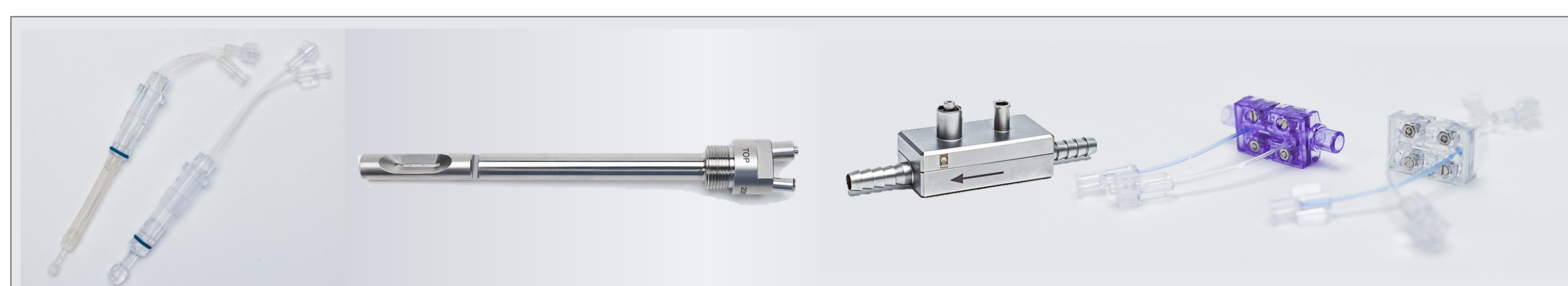
### Figure 2 - Precise & Sterile Measurements



### Automatic, on-line glucose and lactate monitoring

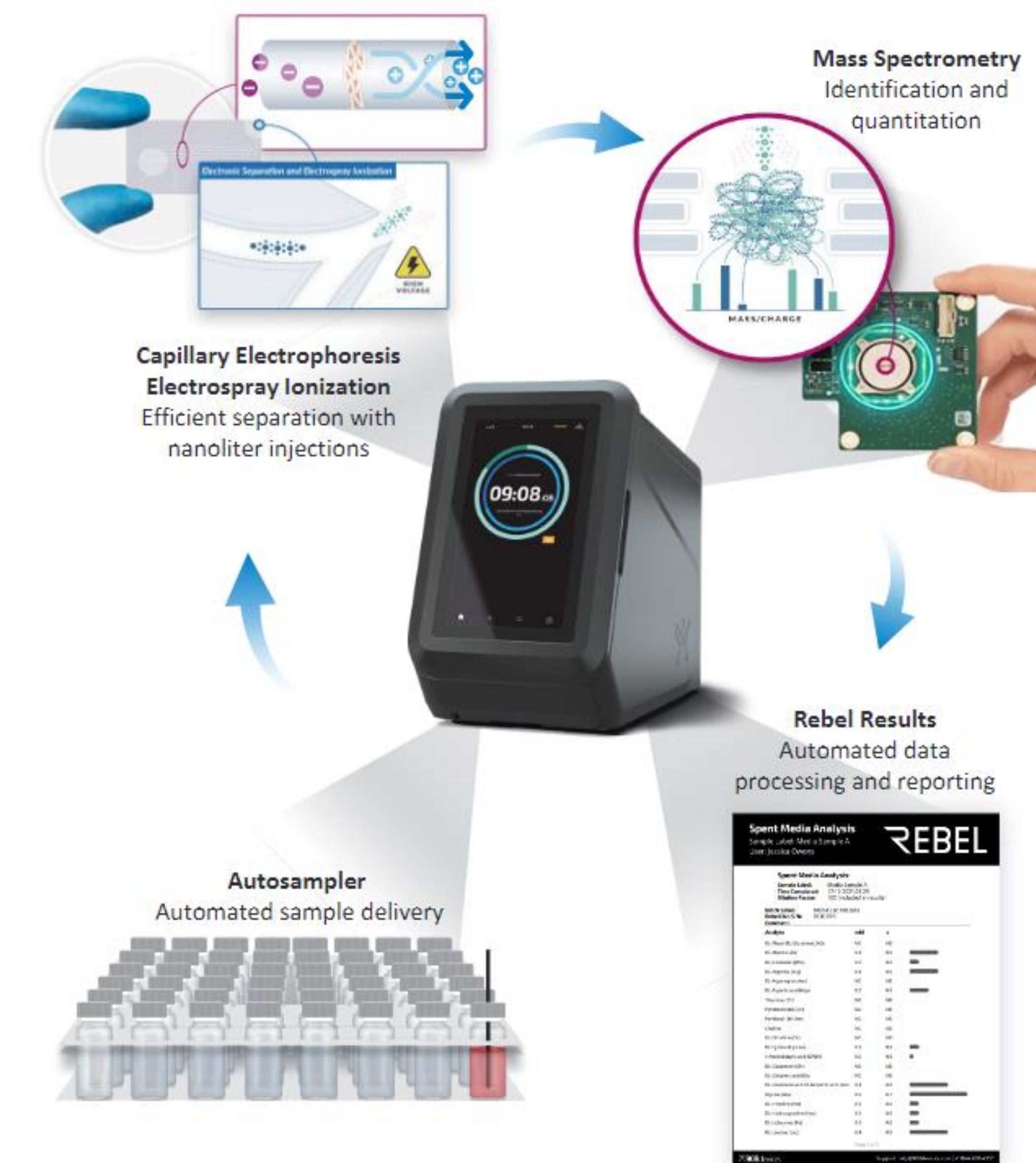
- Diffusion probe installed in bioreactor connects to biosensor
- Enzyme-based biosensor detects glucose to 0.01 g/L and lactate to 0.05 g/L
- Small molecules diffuse through the semipermeable membrane into the buffer solution
- The biosensors are replaced after 5,000 measurements, and therefore the lifetime of a sensor is dependent on the measurement frequency.
- No loss of bioreactor volume
- Significantly reduced risk of contamination as compared to sample pulls
- Enables on-line analytics and process control

### Figure 3 - MAVEN bioreactor *in-situ* probes and perfusion flow cells



Diffusion probes have been developed for stainless steel bioreactors and for single-use bag bioprocesses. The probes are autoclaved together with other bioprocess materials. Using the probe for frequent measurements reduces the risk of contamination from sample pulls and the manual work involved.

## The REBEL at-line cell culture media analyzer: Actionable information on your bioprocess at the point of need



- Spent media analysis:** Process & media optimization
- Fresh media analysis:** Media "fingerprinting", screening, and stability
- Process Modeling:** Mechanistic Data driven

### REBEL Spent Media Analysis Kit

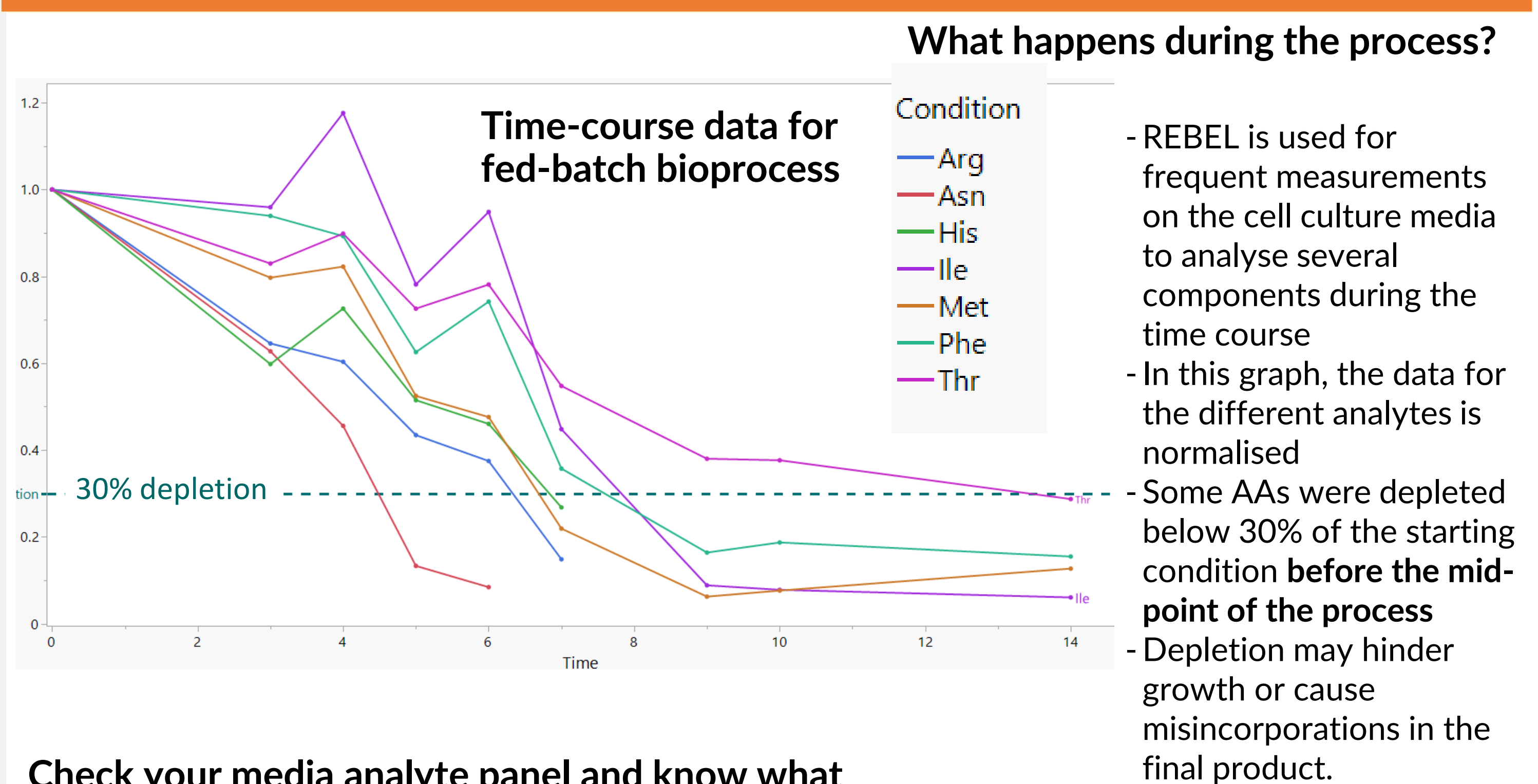


- Minimal sample requirement as low as 10  $\mu$ L
- Simple sample prep: spin and filter then dilute
- Integrated analyzer includes autosampler, separation, detection, analysis, and reporting
- Analysis run-time ~10 min per sample
- Consumable kit optimized for 200 replicate analyses

## REBEL analyte panel

Amino Acids						
Alanine	Asparagine	Glutamic Acid	Histidine	Lysine	Proline	Tryptophan
Alanyl-Glutamine	Aspartic Acid	Glutamine	Isoleucine	Methionine	Serine	Tyrosine
Arginine	Cystine	Glycine	Leucine	Phenylalanine	Threonine	Valine
Vitamins etc.						
Choline	Nicotinamide	Pyridoxal	Pyridoxine	Thiamine	Betaine	
Amines						
$\beta$ -Alanine	Citrulline	GABA	Hydroxy-proline	Methyl-Histidine	Sarcosine	

## REBEL provides critical bioprocess data



### Check your media analyte panel and know what you're dealing with!

- Analysis of common commercial media reveal analyte diversity
- Some CHO cell line strains and populations have different basal and feed media needs, - what is right for your bioprocess?
- Test diverse media with a variety of component levels/ concentrations

