

Automated Sampling Systems

Cell Culture and Fermentation



- 25 employees in Massachusetts
- 8 representatives across the US
- 13 distributor partnerships throughout Europe and Asia Pacific

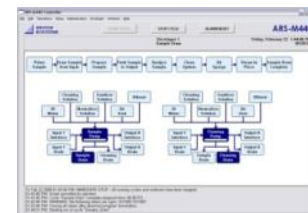


Optimization
of
Fermentation
or
Cell Culture

Sanitary
Reactor
Barrier

Phase 1

Automated
Closed
Loop
Solution



Sample
Draw,
Prep
And
Delivery

Feedback
to
Controller

Data
Analysis



Agilent Technologies



Phase 2



Phase 3



Collaborations with Industry Leaders

Providing Sample Draw, Prep and Analysis

HPLC  **Agilent Technologies**

Nutrient Monitoring



Cell Viability



Fraction Collection



Automated Sampling

Automated Delivery

Automated Analysis



HPLC Systems

Fraction Collector

Nutrient Monitors

Cell Viability

Agilent Technologies



GROTON BIOSYSTEMS



YSI



BECKMAN COULTER



Split Delivery
One Sample – Four Analyses

Fraction Collector



- The ARS-M delivers samples to sterile vials in the Fraction Collector for post run analysis.
 - Peltier Temperature Control
 - Maintains Temperature in a Range of 4°C to 37°C
- Optional Subzero Cooling with -40°C Chiller

		Vial Size
Fraction Collector	60 Chilled Positions	15 ml
Fraction Collector	96 Chilled Positions	2 ml
Fraction Collector	24 Chilled Positions	50 ml
Fraction Collector	Non-Refrigerated	50 ml
Autosampler	60 Position Chilled Tray	15 ml



Manual Sampling

Minimal Data Points



Around-the-Clock Online Sampling

All Day, All Night, All by Itself

ARS-M SERIES AUTOMATED REACTOR SAMPLER



ARS-M 840
ARS-M 440
ARS-M 140

Eight Inputs to 4 Instrument Outputs
Four Inputs to 4 Instrument Outputs
One Input to 4 Instrument Outputs

Inputs

Sample

Waste

Sample

1 2 3 4

5 6 7 8

Input ports 1 through 8 are arranged in two columns. The left column (Sample) has ports 1, 2, 3, and 4. The right column (Sample) has ports 5, 6, 7, and 8. A central vertical strip (Waste) contains four black ports. Yellow tubing is connected to ports 1 and 5. A red tube is connected to port 1. A white tube is connected to port 2.

Outputs

Waste

Sample

A B C D

Output ports A, B, C, and D are arranged in a vertical column with black caps. Yellow tubing is connected to ports A and B. A black tube is connected to port B. A white tube is connected to port A.

Power



CLEAN

RINSE

STABILIZE

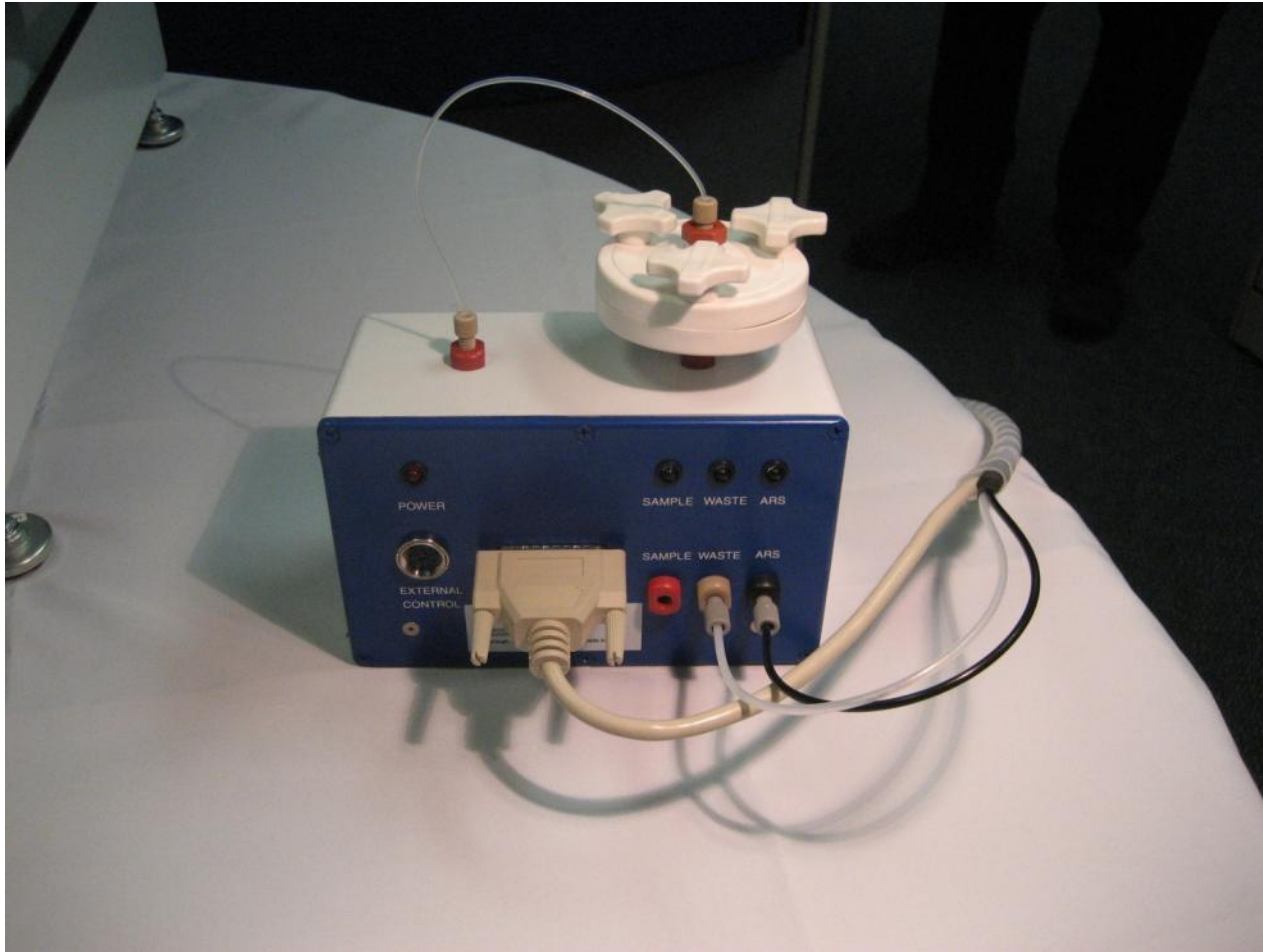
NEUTRALIZE

DILUTE

Function buttons are arranged vertically on the right side. CLEAN (white), RINSE (blue), and STABILIZE (green) have tubes connected to them. NEUTRALIZE (red) and DILUTE (yellow) are unconnected.

Waste Drain





iRIM
(Input Connections)

oRIM
(Output Connections)

1



5

2



6

3



7

4



8

A



B



C



D



100-240 VAC
50/60 Hz 2.5
GROTON BIOSYSTEMS
Boxborough, MA 01719 USA



COM 1



COM 2



COM 3



COM 4

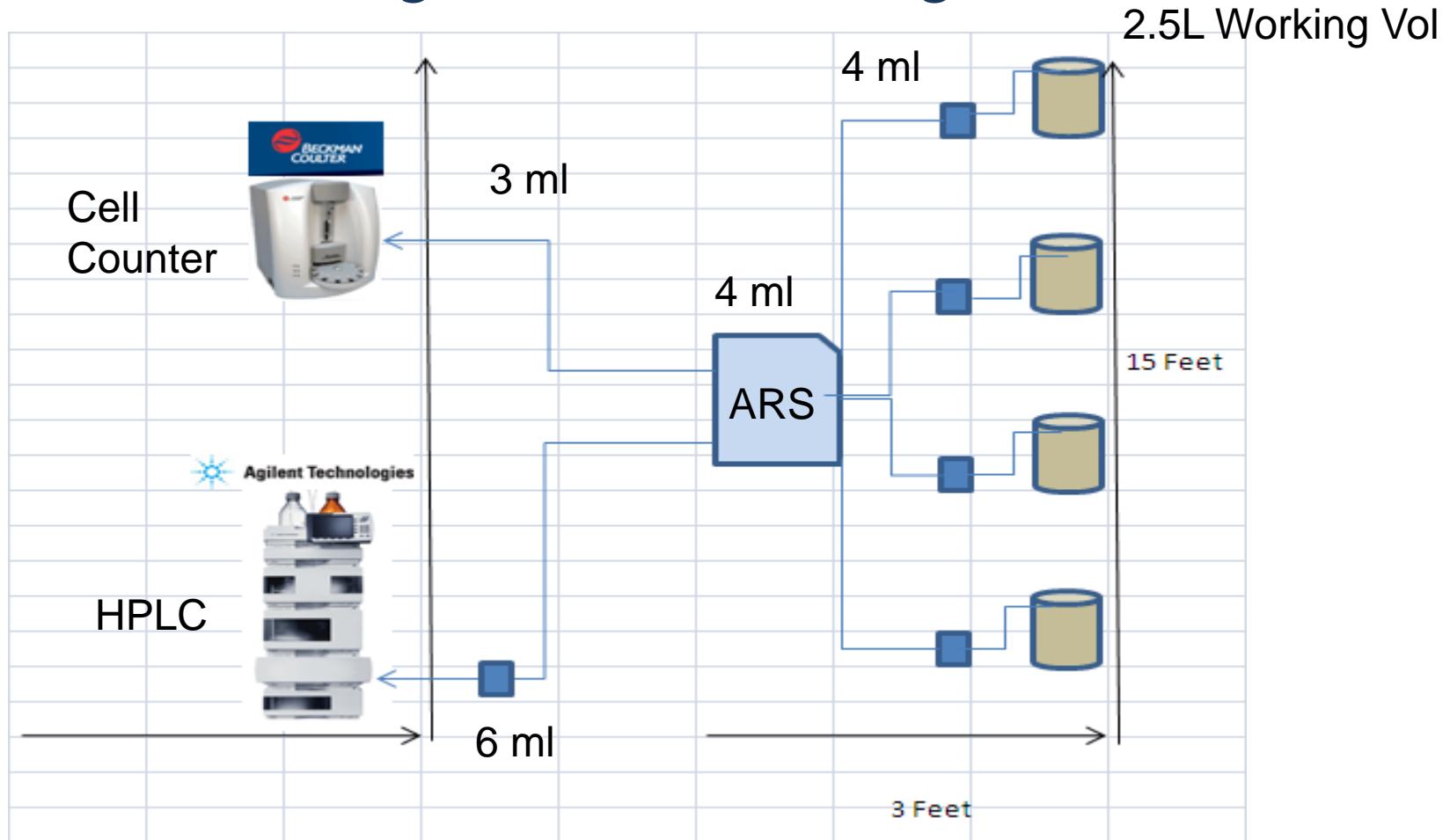


Ethernet

Model: ARS-M Series 840
Serial No: ARS-M840-005-Rev A



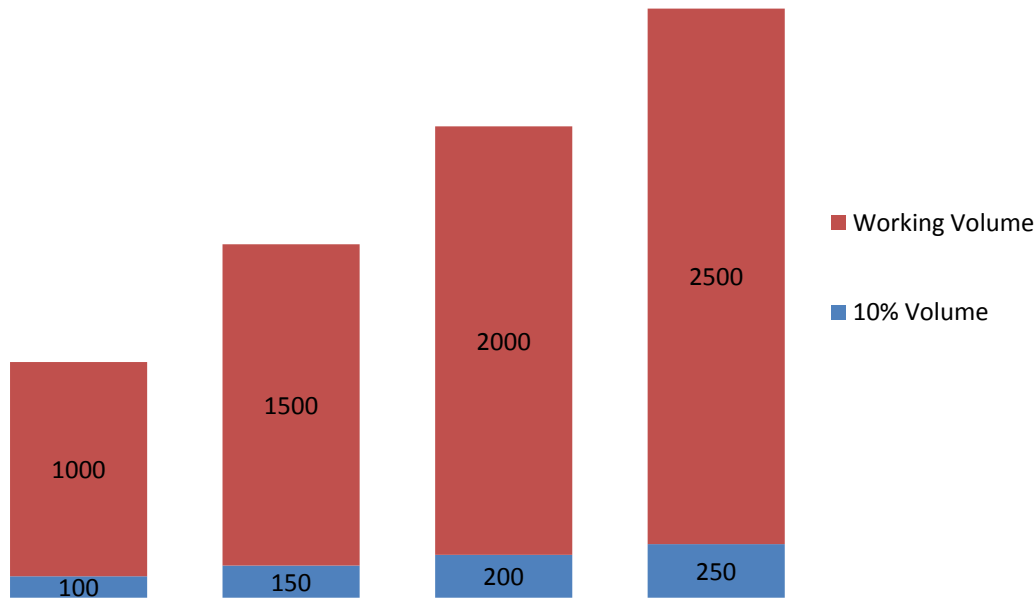
Volumes needed for analytical analysis



Reactor Sampling Volume

Goal is to limit total volume removed to be <10% of initial working volume

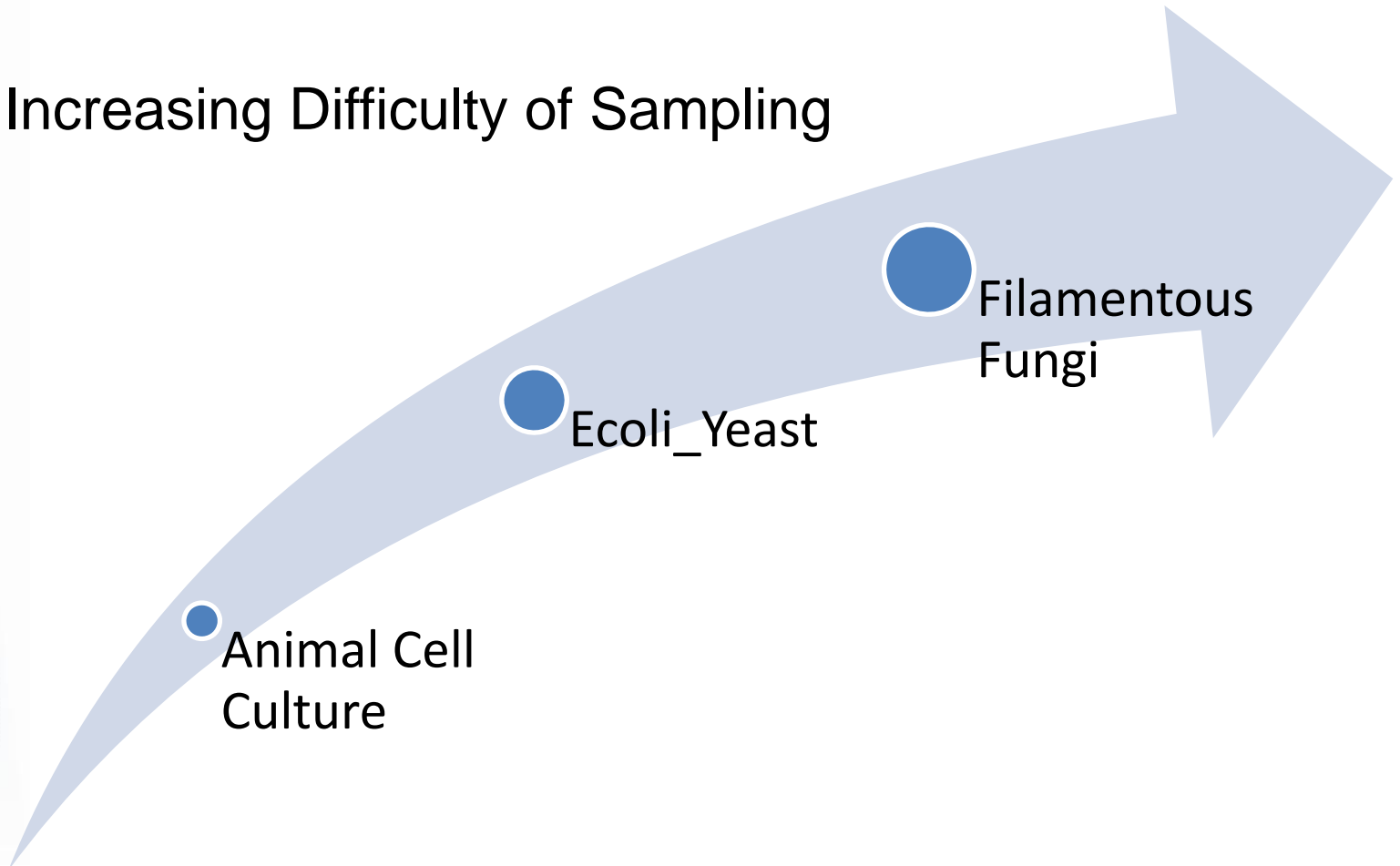
Volume Available for Sampling, ml



Reactor Size
Limitation on
Sampling

Biopharma

Increasing Difficulty of Sampling



Diptube

Cell containing sampling

Glass or
S.S.
Bioreactor

Connect by sanitary QC or tube welder

Clamp/valve

Diptube

RIM

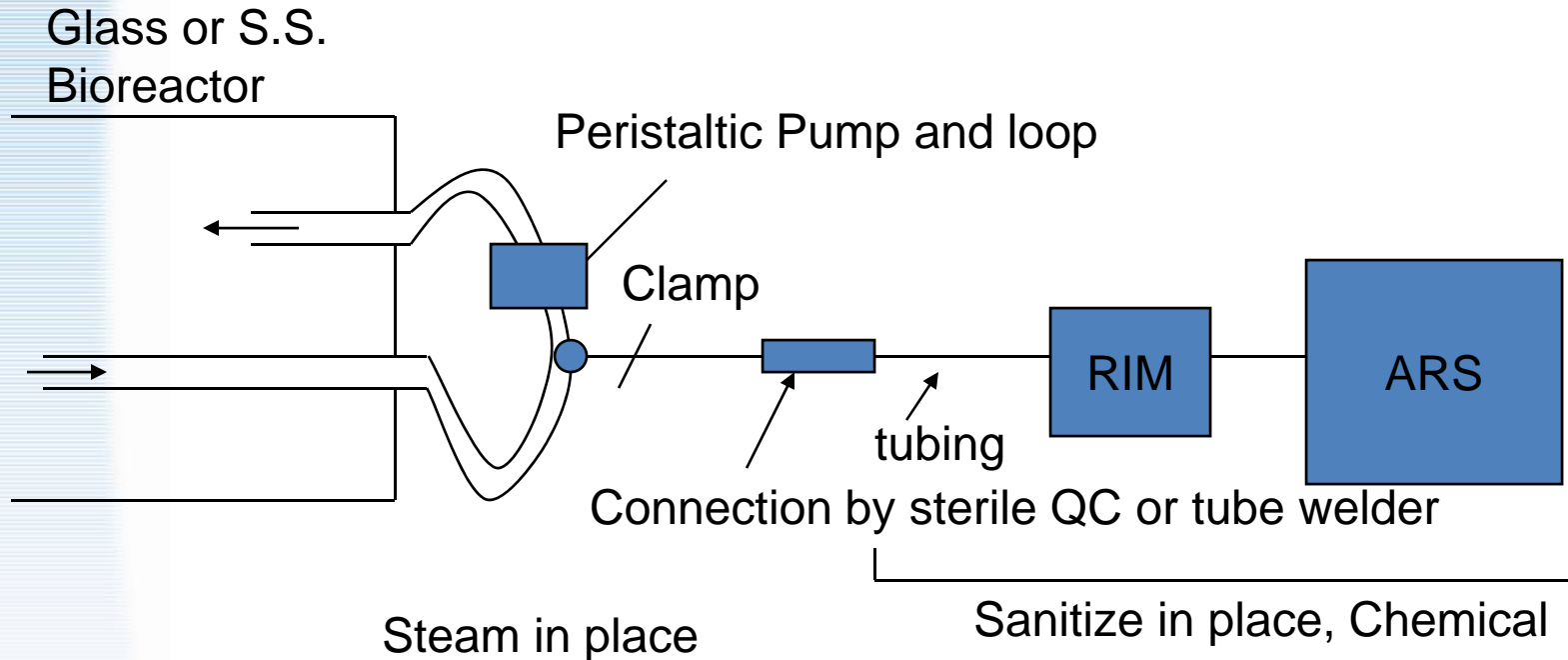
ARS

Tubing sized to sample
viscosity

Autoclave

Sanitize in place, chemical

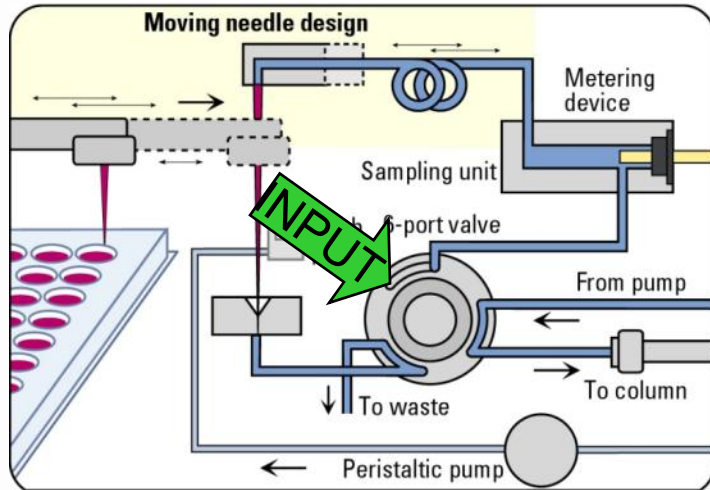
Using dip tube-peristaltic loop for viscous samples



Note: Peristaltic loop can be connected to top of head plate for Autoclaved Glass reactors. In line filtering available for cell free sampling.

On line HPLC

Groton-Agilent Online HPLC Assay System

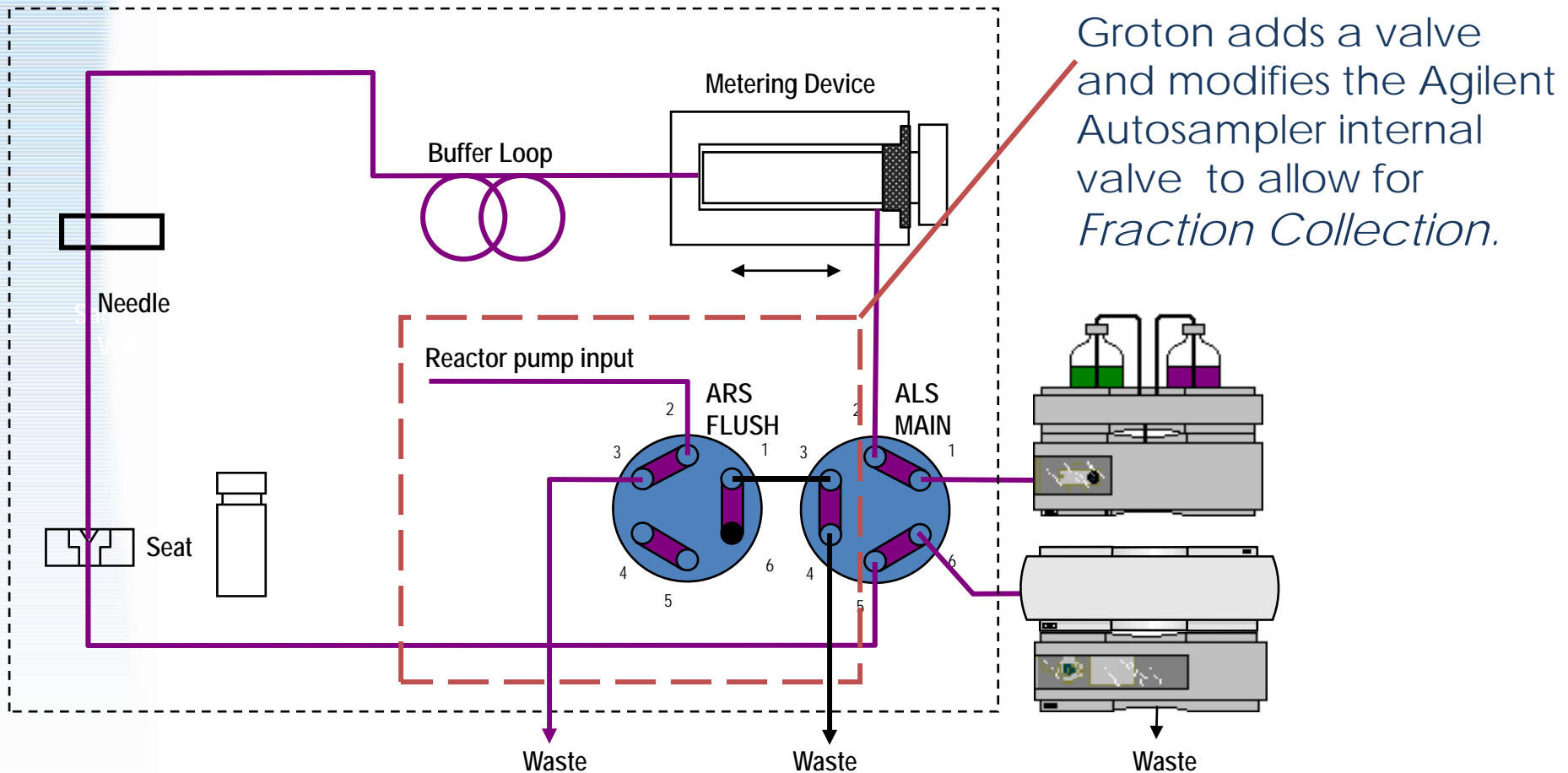


- The Groton **AAMK** (Agilent Autosampler Modification Kit) turns the Agilent Autosampler into a Simple Fraction Collector.
- Once a fraction is collected in a vial or well plate the ARS-M starts the Agilent ChemStation and the 1200 technology is standard.

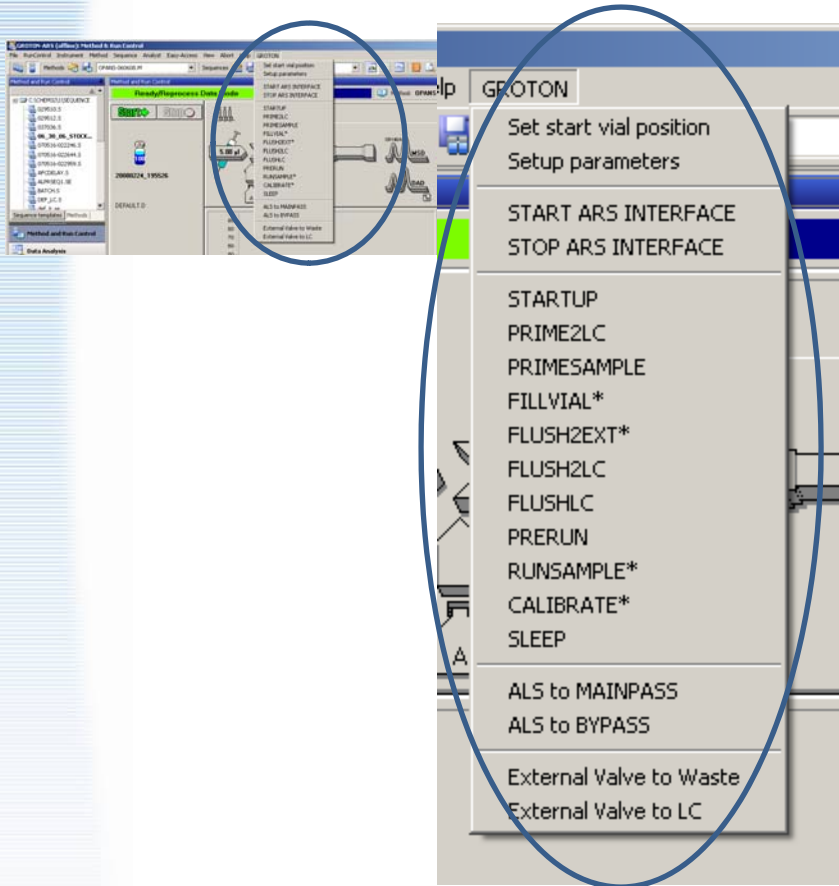
*Fully Programmable, Fully Automatic
24 Hours a Day, 7 Days a Week of Sampling*

ARS-M Hardware Upgrade Kit for Agilent 1200 Autosamplers

Internal plumbing of G1367D Hi-Performance Automated Liquid Sampler (Hi-P ALS)



ChemStation Integration



Set vial position where next fraction from ARS-M will be collected.

Set ChemStation methods for running samples, etc. within ARS-M commands.

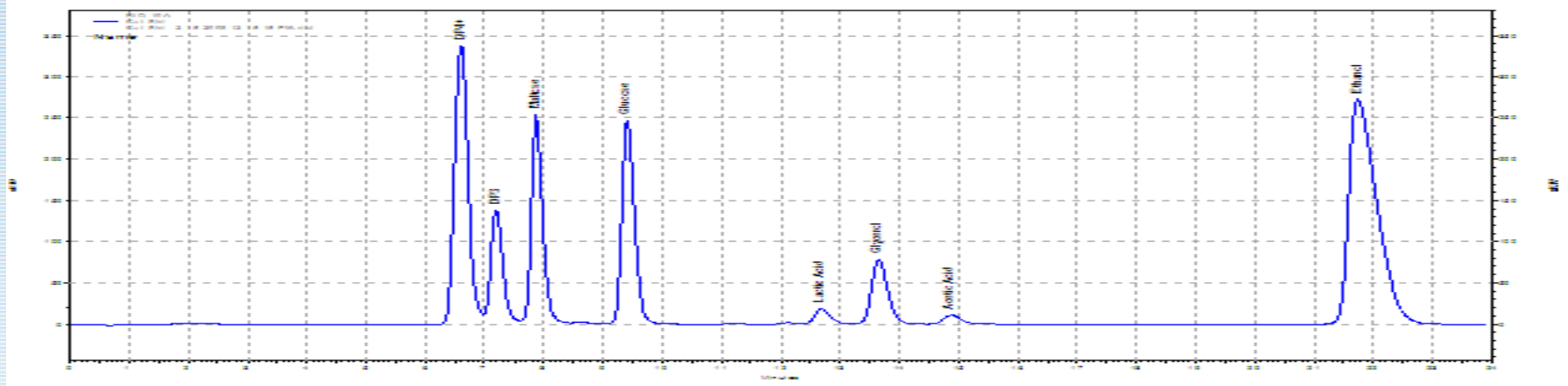
Start listening for commands from ARS.

Stop listening to commands from ARS.

Manually execute an ARS-M command.

When ChemStation is not listening for commands from the ARS-M, it can be used in regular analytical mode as a standalone instrument.

On Line HPLC- Biofuel or Biopharma



LC: Agilent 1200 Series Rapid Resolution LC

Column: Agilent ZORBAX RRHT Eclipse Plus-C18, 2.1 x 50 mm, 1.8 μ m

Detector: Agilent 1200 Series Fluorescence Detector

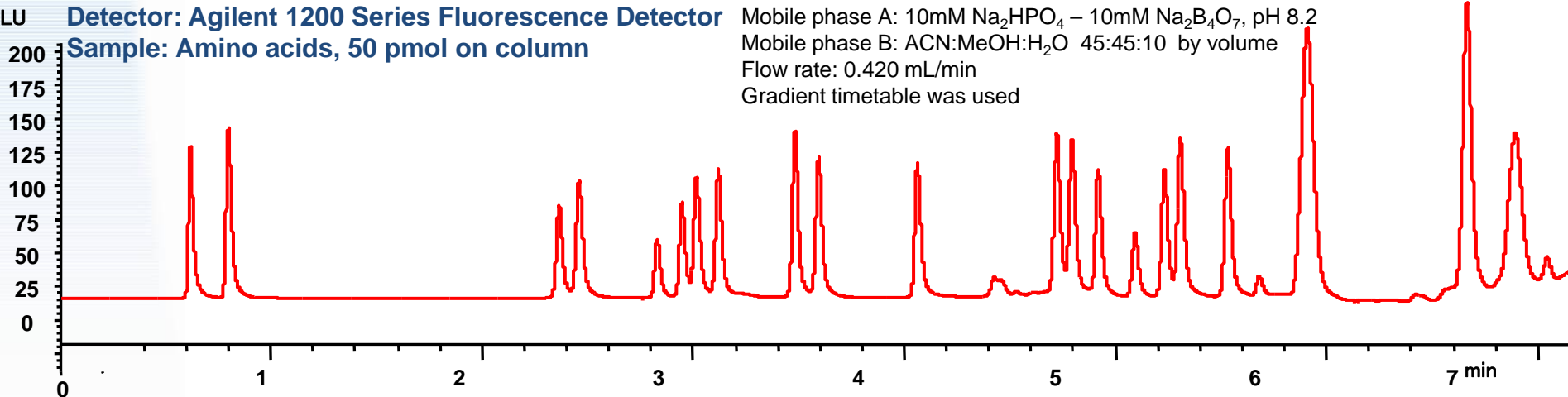
Sample: Amino acids, 50 pmol on column

Mobile phase A: 10mM Na_2HPO_4 – 10mM $\text{Na}_2\text{B}_4\text{O}_7$, pH 8.2

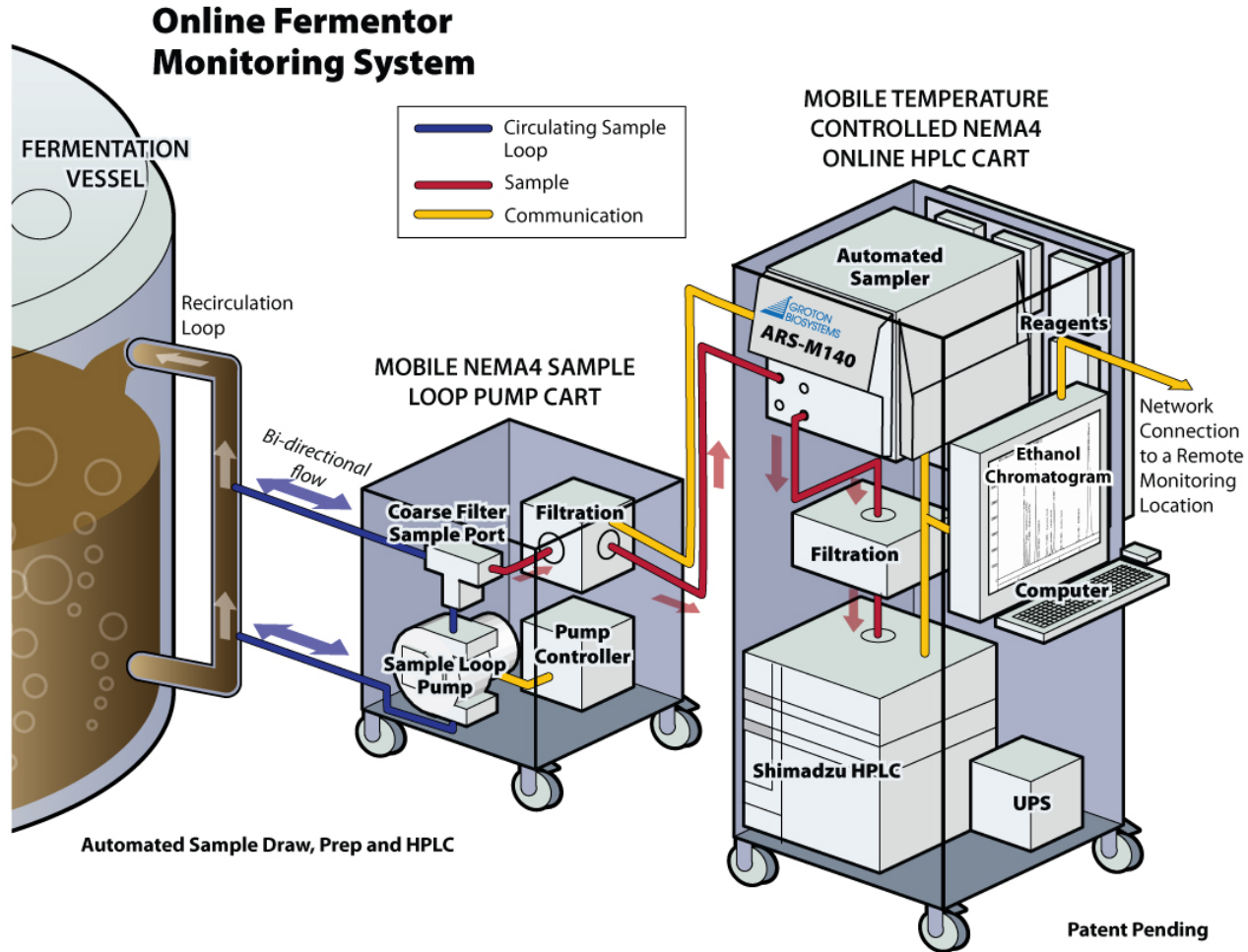
Mobile phase B: ACN:MeOH:H₂O 45:45:10 by volume

Flow rate: 0.420 mL/min

Gradient timetable was used



AUTOMATION FOR ETHANOL PRODUCTION



Biofuel System for On-line HPLC



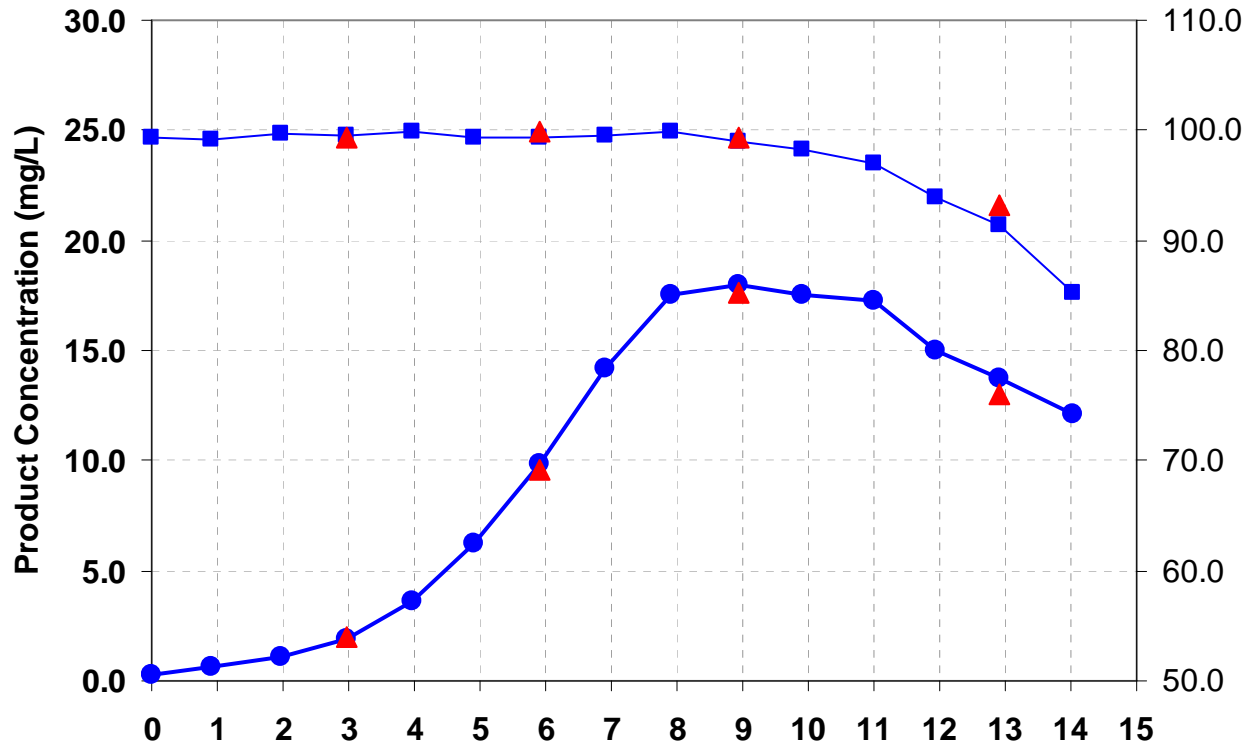
Biopharma Case Study

Automation vs Manual Sampling

30 Liter B.Braun - 25 mm Ingold Side Port SIP Valves for Autosampling

Analysis	Accuracy / Precision
Fraction Collector	2ml – 15 ml
Viable Cell Count	≤ 5%
Viability	≤ 2%
pH	≤ 0.035 Units
pO2	≤ 7%
pCO2	≤ 7%
Glucose, Lactate	NH4 ≤ 7%
Amino Acids	≤ 10%

Cedex Interface



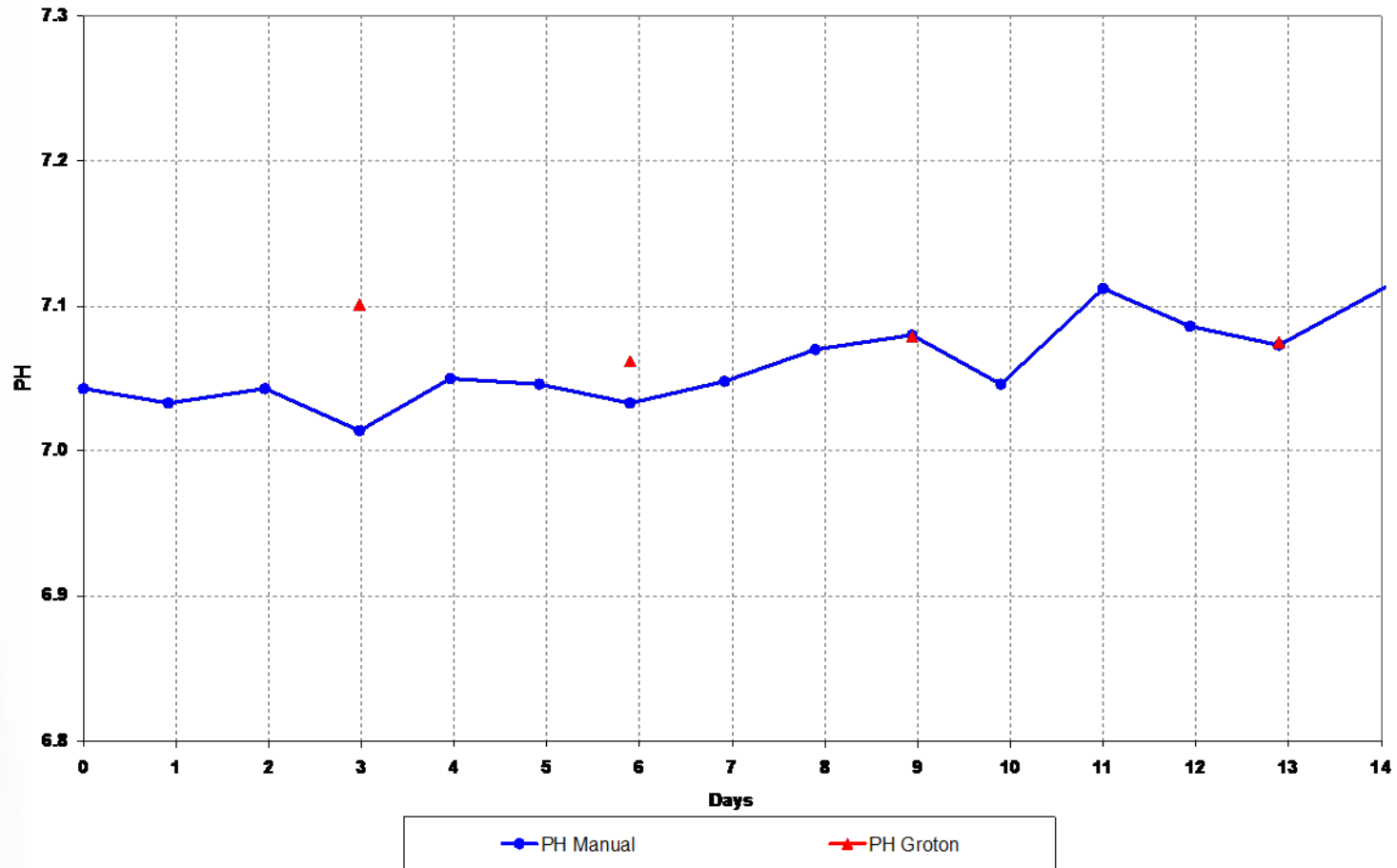
● Cedex VCC Manual

▲ Cedex VCC Groton

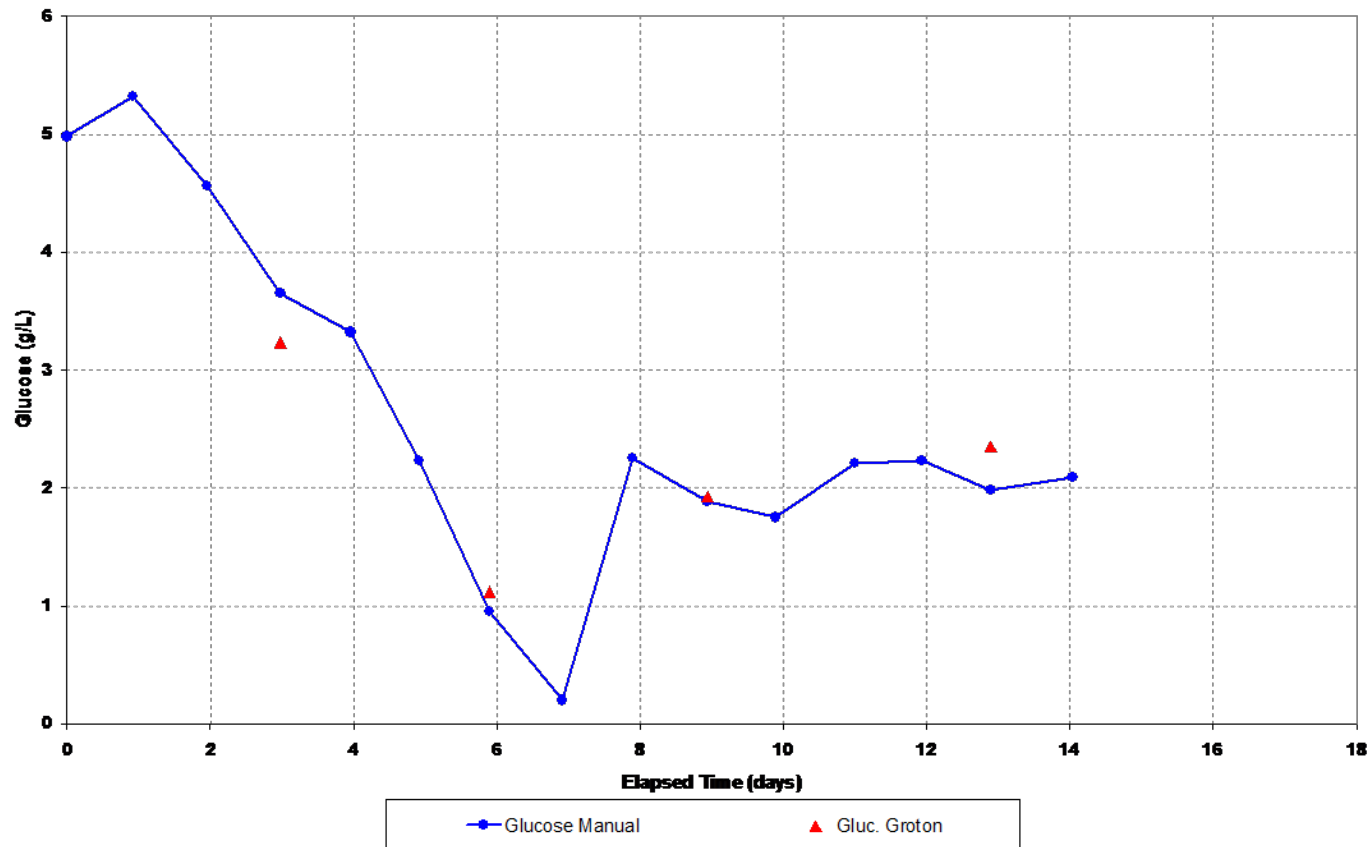
■ Cedex Via Manual

▲ Cedex Via

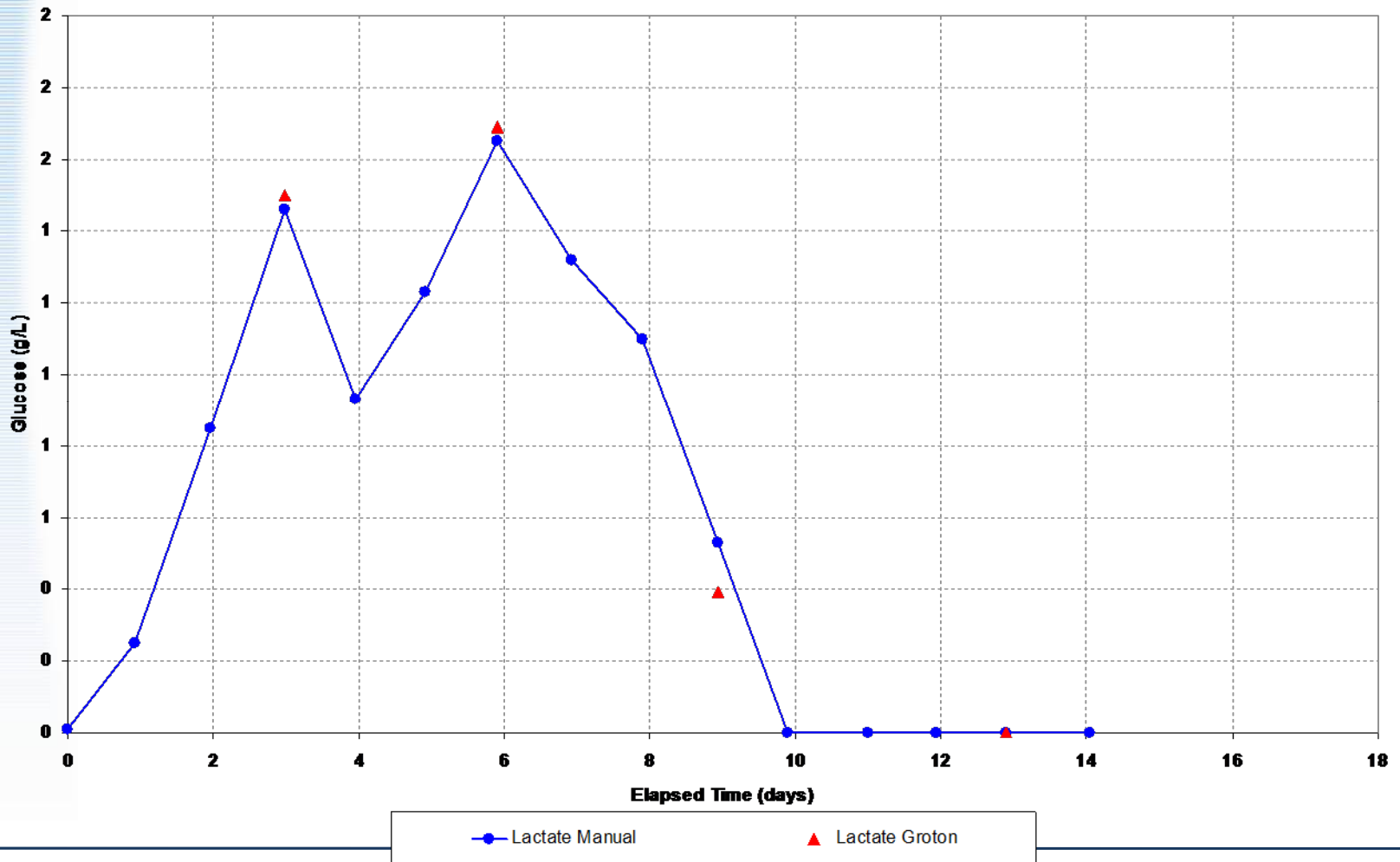
PH Evaluation



Glucose Evaluation



Lactate Evaluation



Future of Bioreactor Sampling

- Biopharm: Measurement of critical process parameters (i.e. amino acids) along with product, ie. Glycosylated proteins. Feedback control
- Biofuel: Measurement of both fermentation and saccharification process. Enzyme monitoring