

ADVA X3[®] - REVOLUTIONIZING THE MANUFACTURE OF LIFE-SAVING ADVANCED THERAPIES

Ohad Karnieli (PhD, MBA)

Founder & CEO

ohad@advabio.com

+972-502060616

www.advabio.com



More
Therapies

More
Savings

At More
Locations

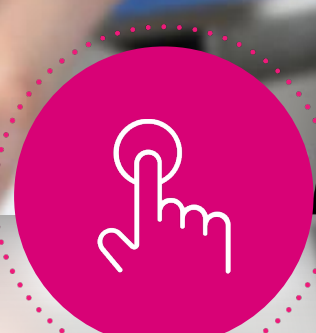
PLATFORM ATTRIBUTES



Manufacturing and logistics cost reduction - Automation



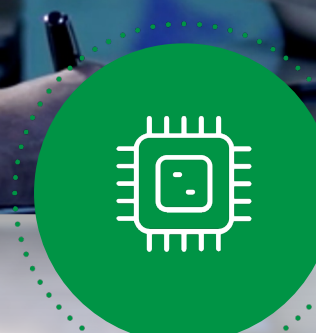
Flexibility
CAR T, TCR, NK,
TILs, Exosomes...



Simplicity



Reproducibility and predictability



AI, Machine learning with 14 controlled parameters



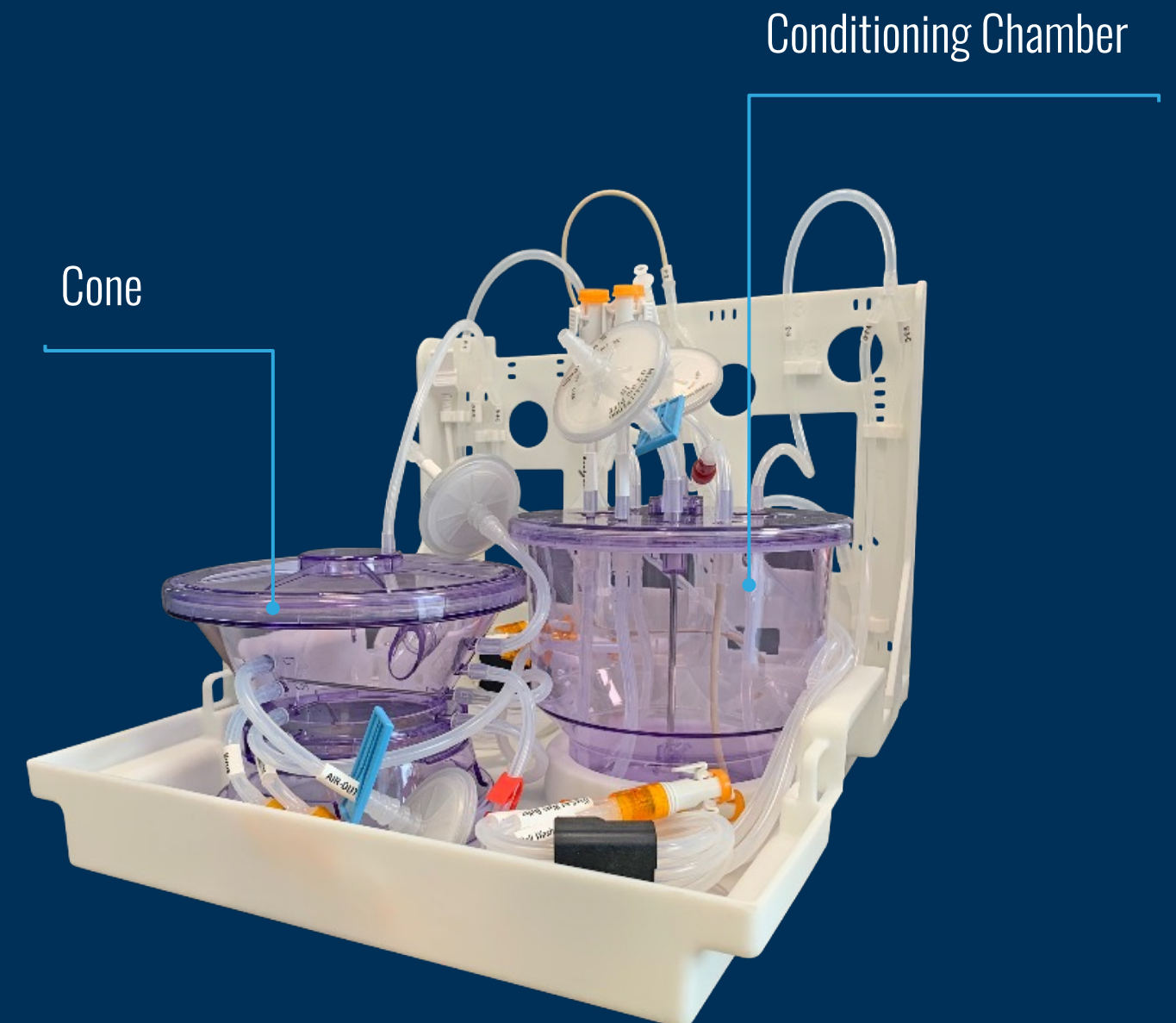
Remote access and control

ADVA X³ CELL MANUFACTURING PLATFORM



Proprietary & Confidential

DUAL CONTROLLED SINGLE USE UNITS



SPECIFICATIONS



CONTROLLED PARAMETERS

1. pH
2. Dissolved Oxygen
3. Glucose
4. Lactate
5. Glutamine
6. Glutamate
7. Pressure
8. Flow rates
9. Temperature
10. Volume
11. O₂
12. Nitrogen
13. Air
14. CO₂

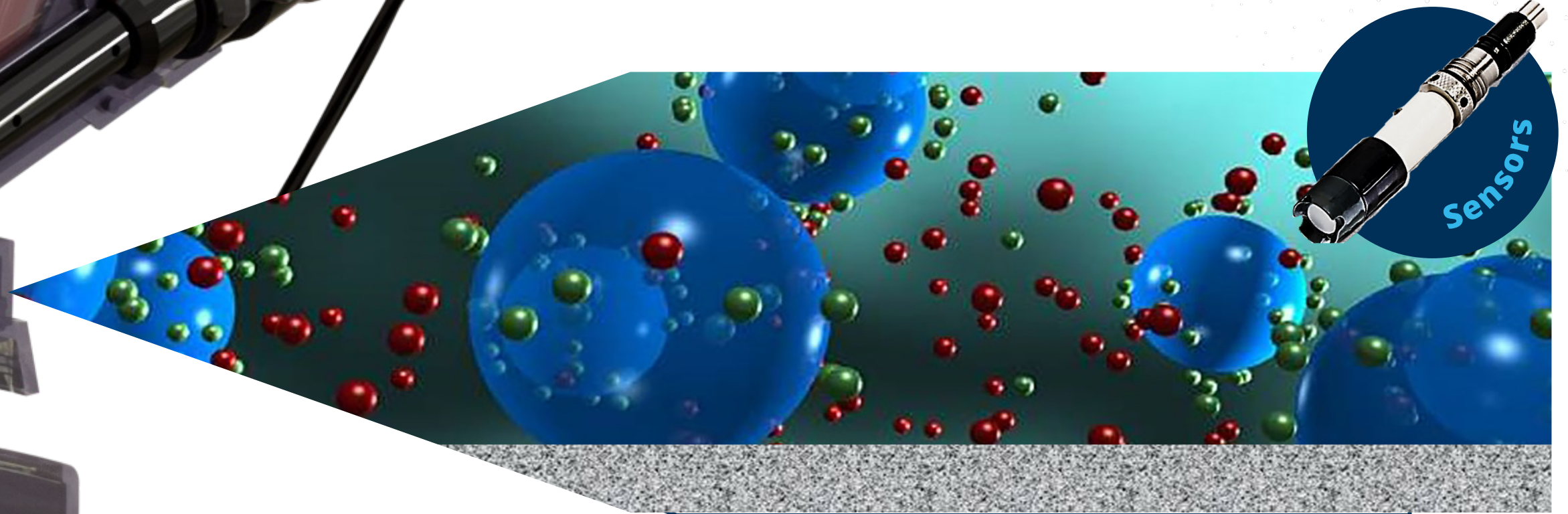
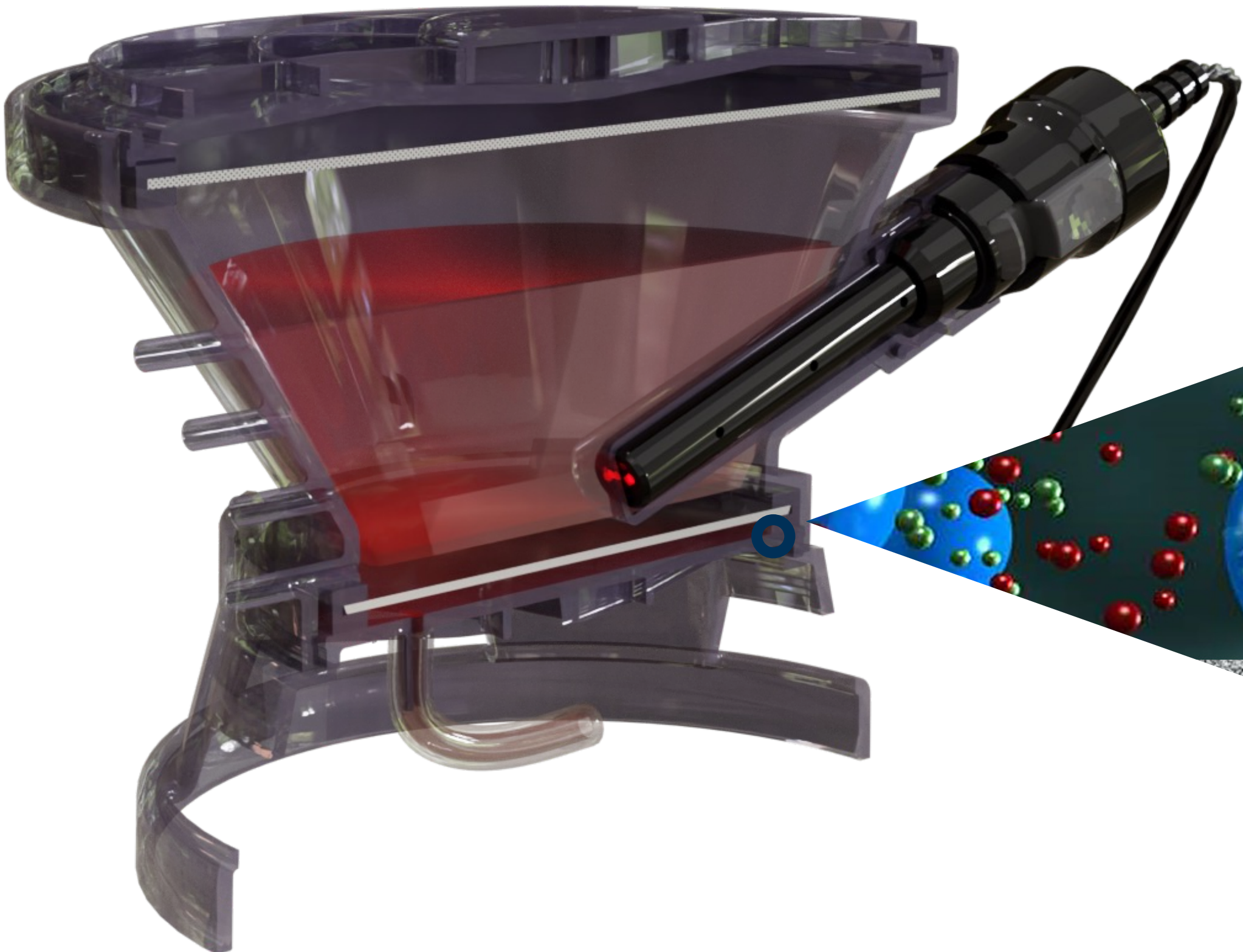
SPECIFICATIONS

- Flexible volume of **100-2700 ml** and then **perfusion**.
- Cone chamber culture - **10 million to 20 Billion cells**
- Weldable tubes or **sterile connectors**.
- Easy **programmable** controlled automated processes
- **Flexible** media and supplement option



ADVA CONE FLOW PATH

PROPRIETARY STRUCTURED MEMBRANE WITH MEDIA FLOW FROM BOTTOM TO THE TOP RESULTING IN A UNIFORM DIFFUSION FLOW WITHOUT SHEER



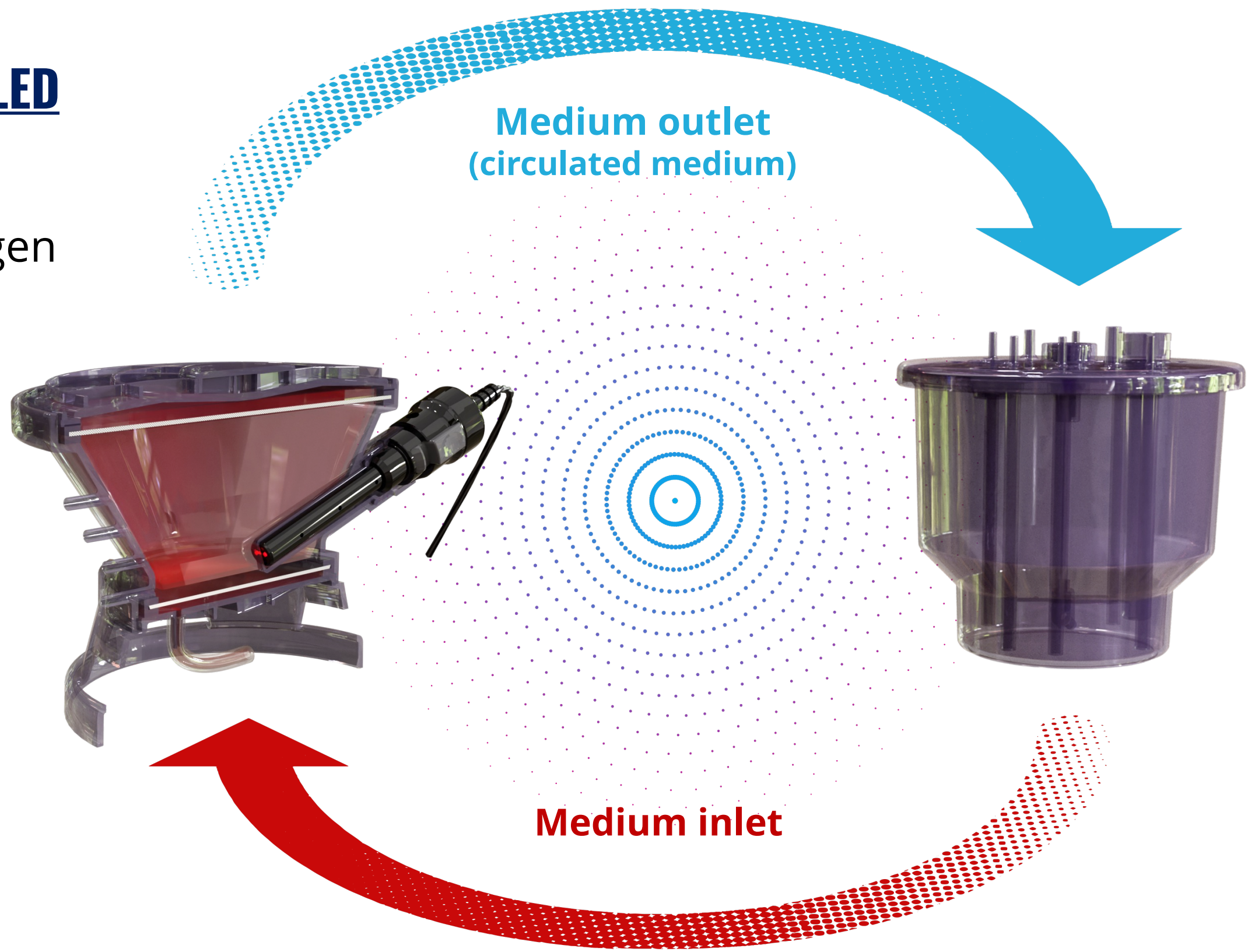
CAMP® Technology

CONTINUES ADAPTIVE MULTIPARAMETER CONTROL



CONTROLLED

- ✓ pH
- ✓ Dissolved Oxygen
- ✓ Glucose
- ✓ Lactate
- ✓ Glutamine
- ✓ Glutamate
- ✓ Pressure
- ✓ Flow rates
- ✓ Temperature
- ✓ Volume
- ✓ O₂
- ✓ Nitrogen
- ✓ Air
- ✓ CO₂

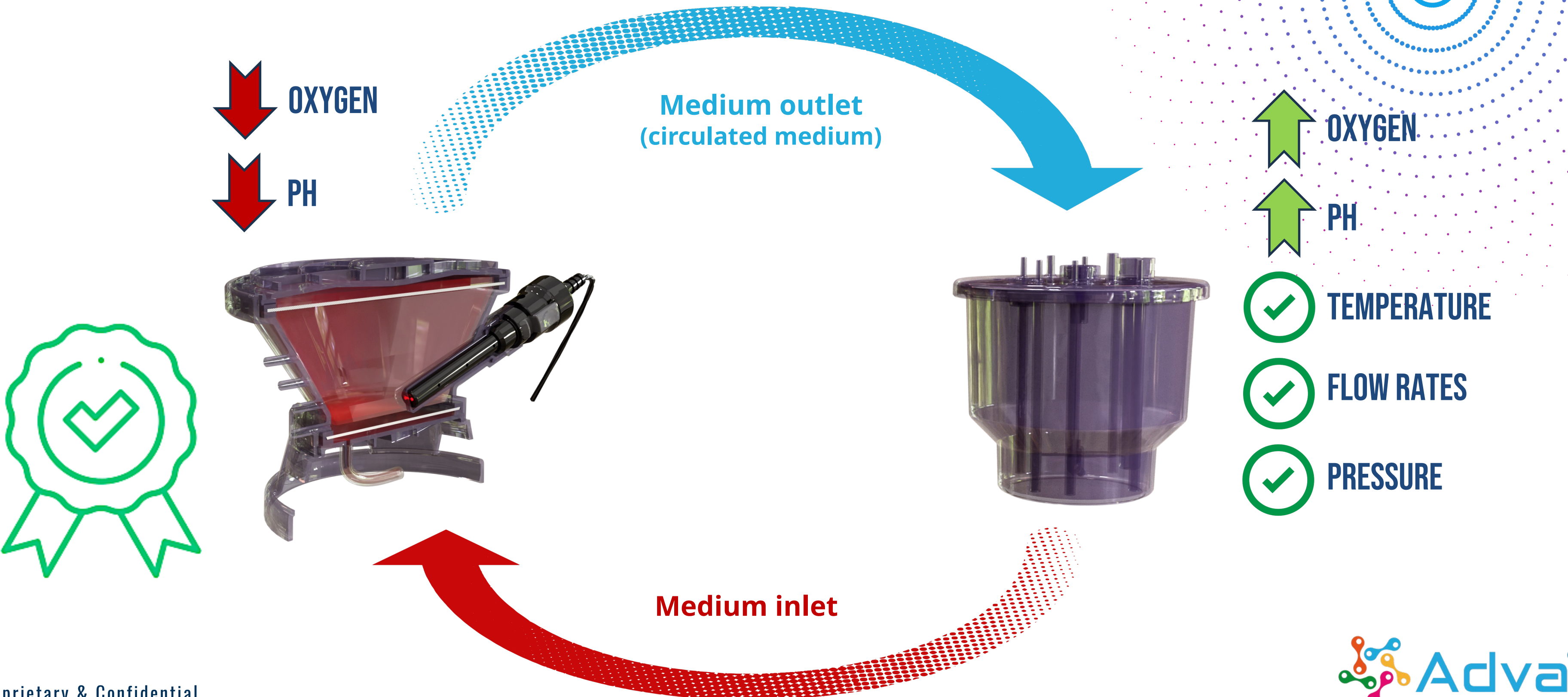


DYNAMIC

- ⏮ pH
- ⏮ Dissolved Oxygen
- ⏮ Glucose
- ⏮ Lactate
- ⏮ Glutamine
- ⏮ Glutamate
- ⏮ Pressure
- ⏮ Flow rates
- ⏮ Temperature
- ⏮ Volume
- ⏮ O₂
- ⏮ Nitrogen
- ⏮ Air
- ⏮ CO₂

CONTROL SCHEME

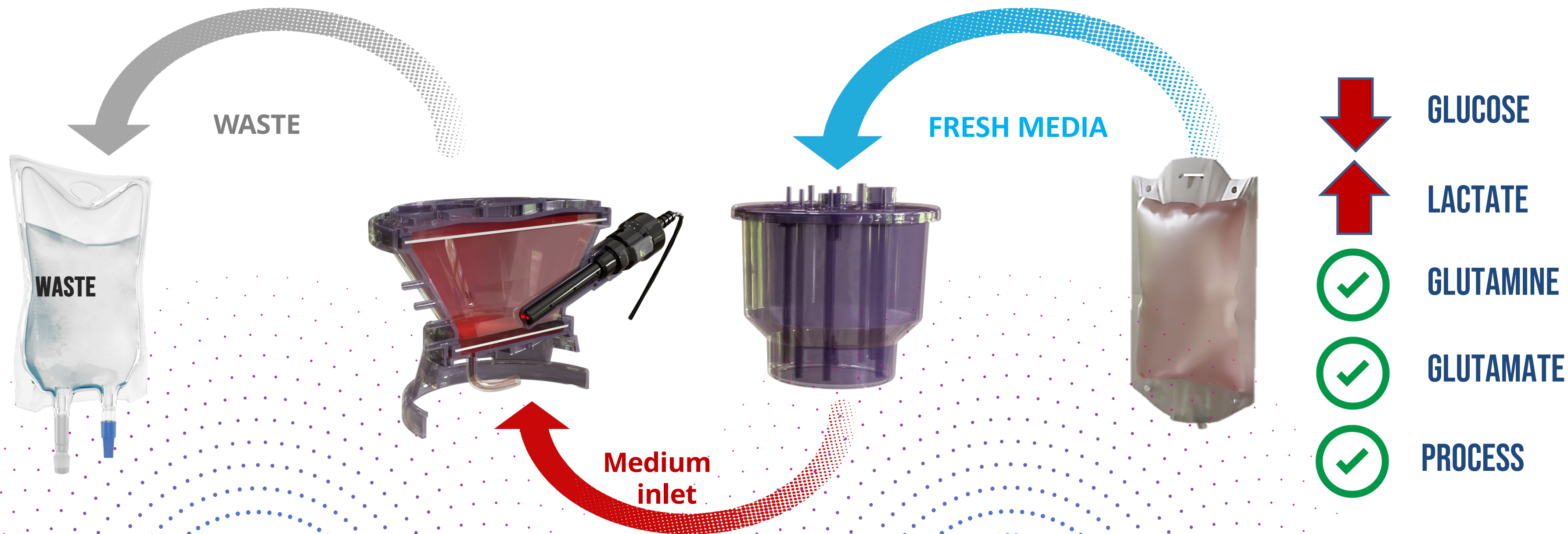
MEDIUM FLOWS INTO THE BIOREACTOR IN A CLOSED CYCLE



CONTROL SCHEME

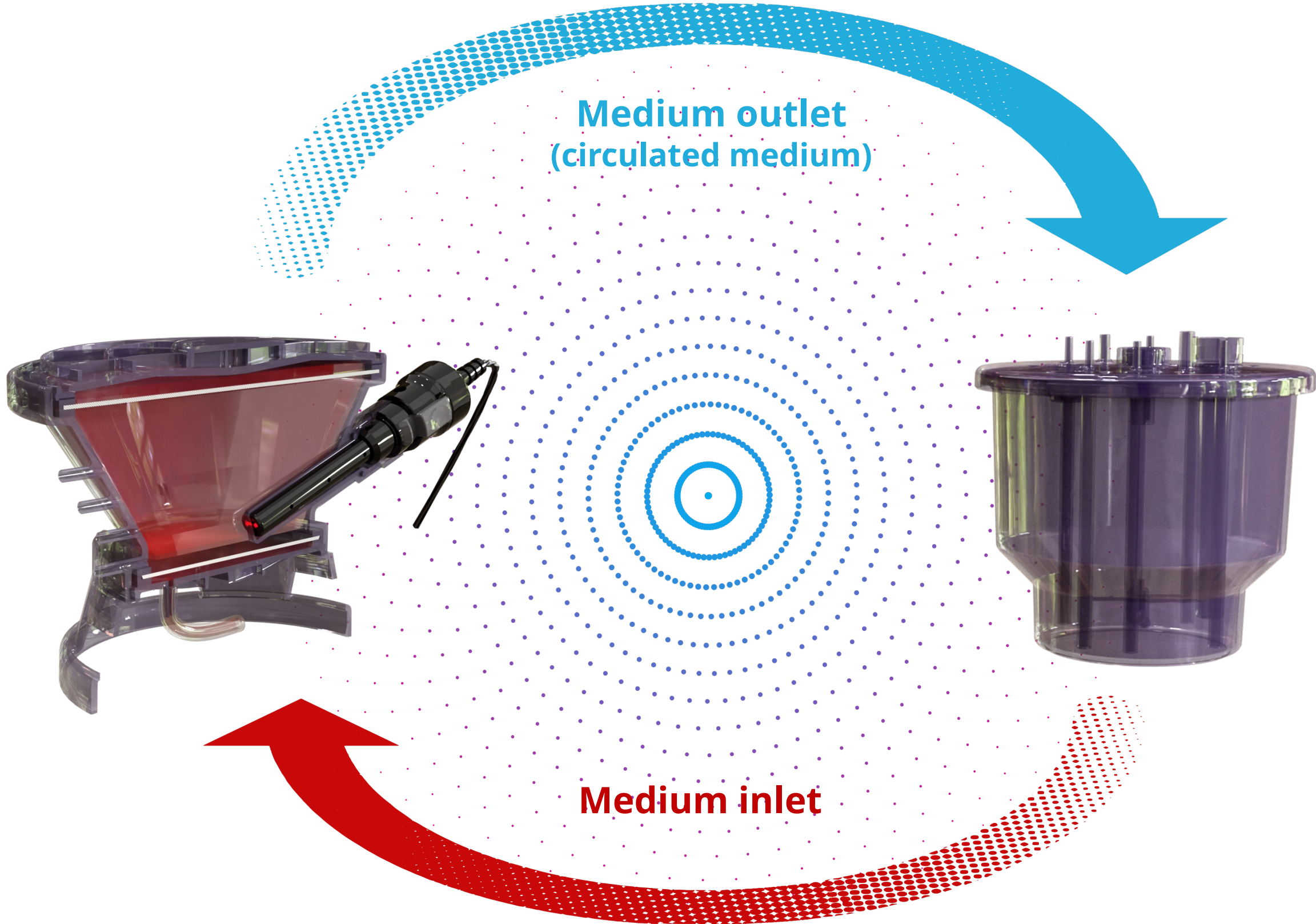
USED MEDIA FLOWS CONTINUOUSLY INTO THE WASTE UNTIL THE SET POINT IS REACHED

FRESH MEDIA FLOWS CONTINUOUSLY INTO THE CHAMBER UNTIL THE SET POINT IS REACHED



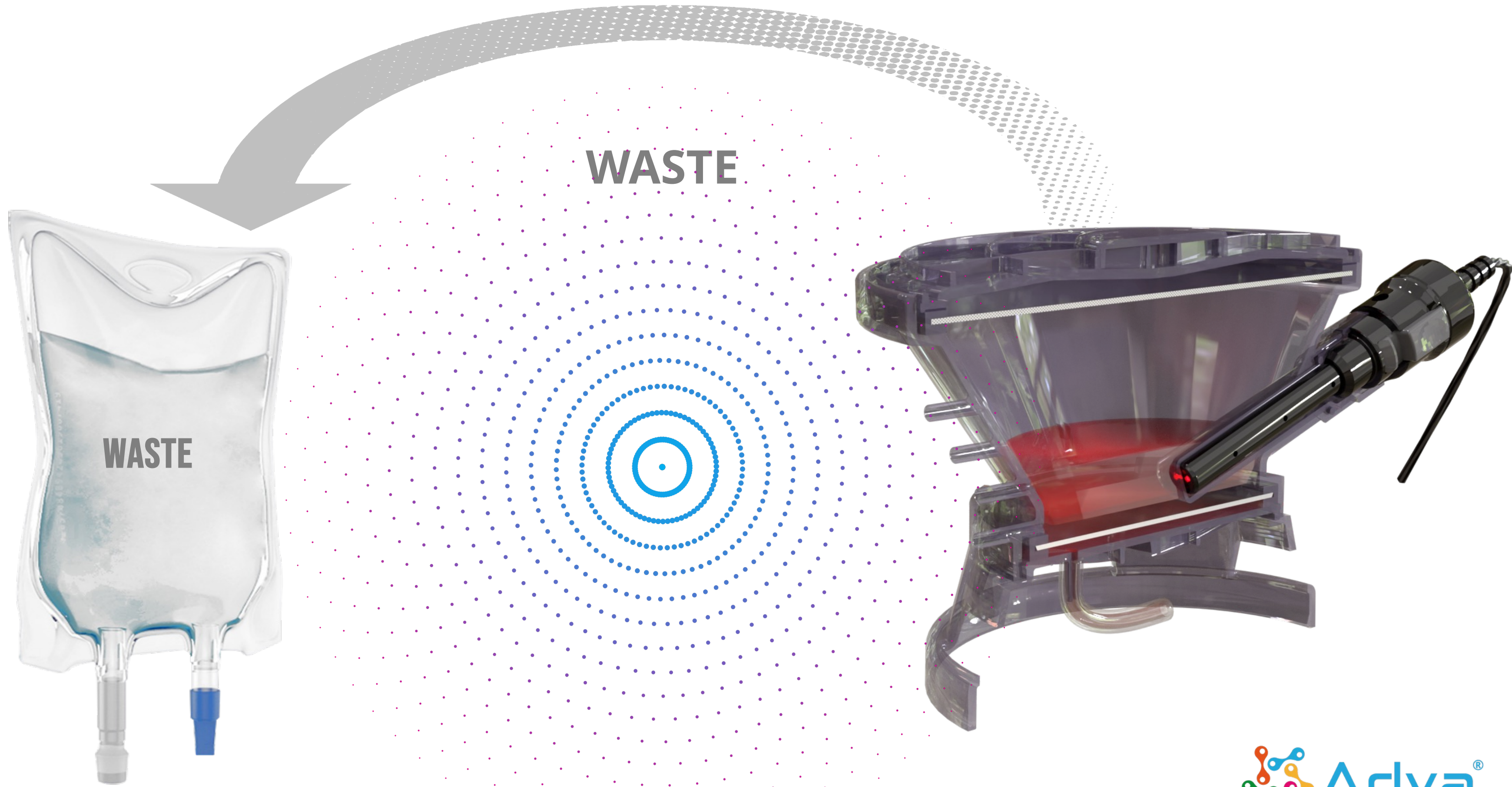
CONTROL SCHEME

MEDIUM FLOWS INTO THE BIOREACTOR IN A CLOSED CYCLE



- ✓ OXYGEN
- ✓ PH
- ✓ TEMPERATURE
- ✓ FLOW RATES
- ✓ PRESSURE

VOLUME REDUCTION

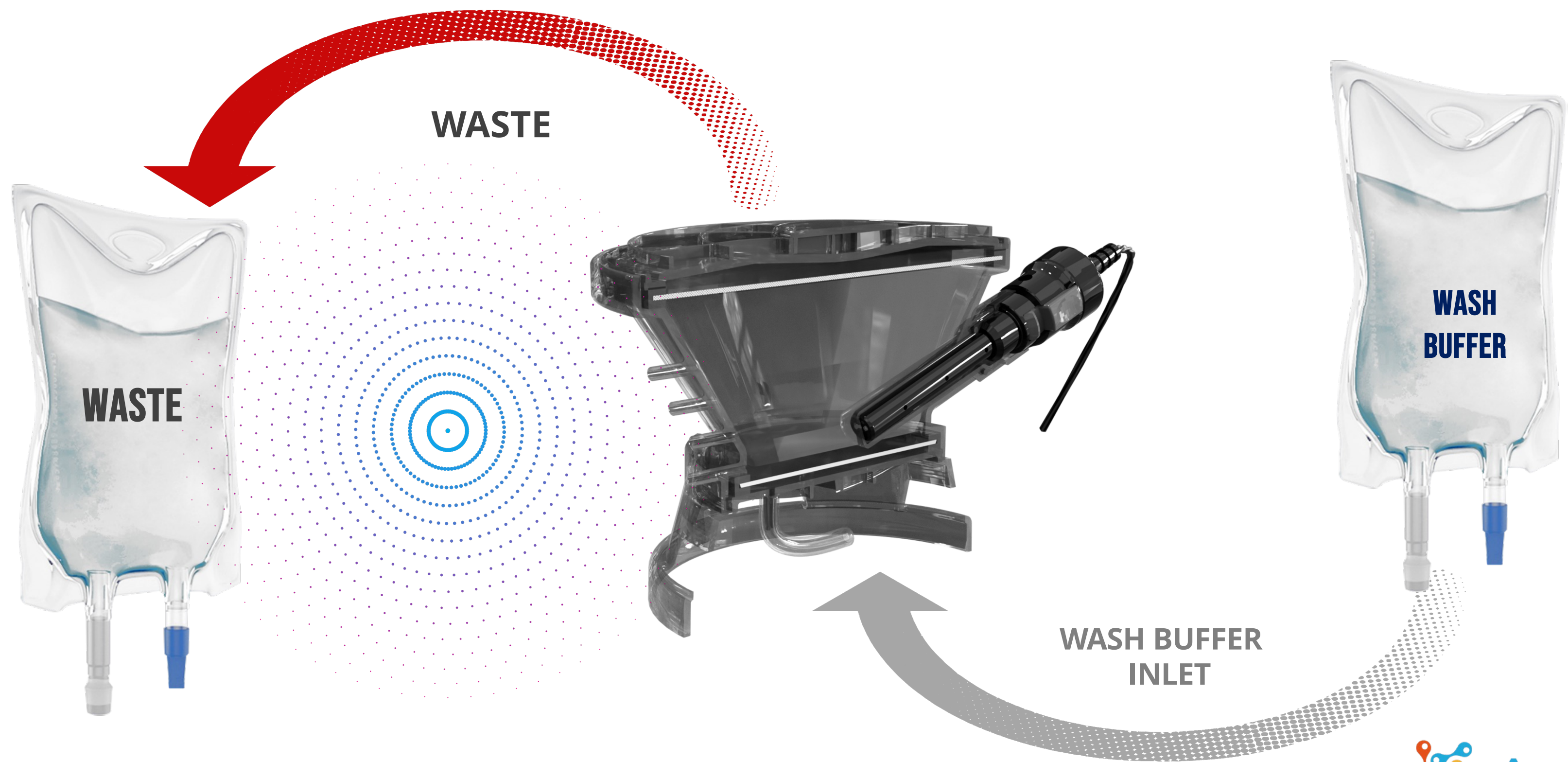


WASTE

WASTE

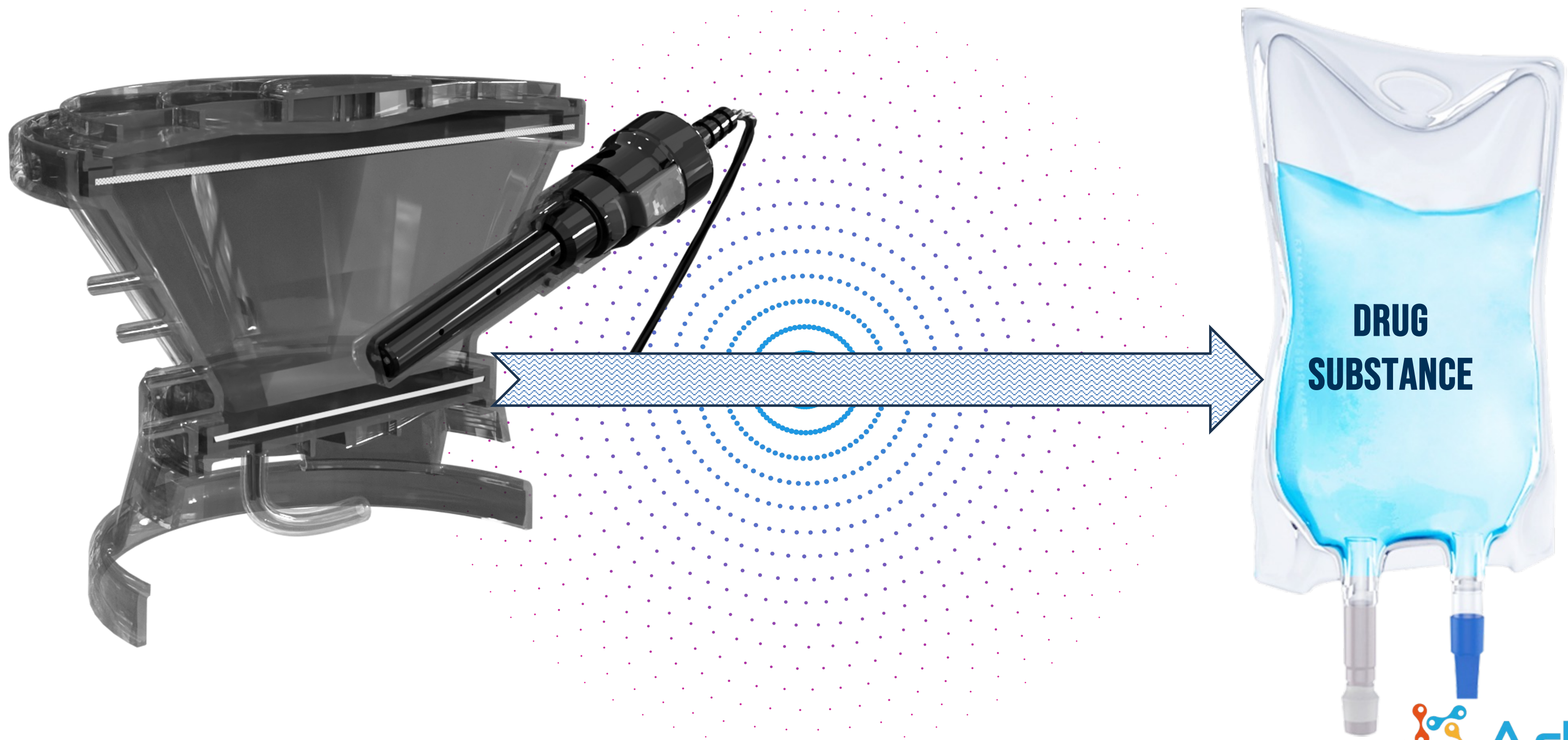
WASH AND FORMULATE

WASH BUFFER FLOWS INSIDE AND DILUTES OUT THE MEDIA



WASH AND FORMULATE

VOLUME REDUCTION AND FINAL PRODUCT COLLECTION



GMP USER INTERPHASE

Menu

Process Detail

Process Trends

Admin

Run Name : Bio-314 Broaden

Patient ID : B

Wed 19 Oct 2022 01:22:54

Log out

User : adva_admin

PROCESS DAY
3

No Macros Are Running

Glucose 1 -0.1 mg/dL
Glucose 2 0.48 mg/dL

Lactate 1 0 mM
Lactate 2 0.01 mM

INCUB DOOR
Incub Temp 35.5 °C

COOLER DOOR
Cooler Temp 26.6 °C

SU KIT PRESSURE 0.1 psi

STOP ALL

TAKE SAMPLE

66.14 %
Adva Cone DO

7.17
Adva Cone pH

36.71 °C
Adva Cone Temp

Cell Expansion


95.41 %
Media DO

7.25
Media pH

36.44 °C
Media Temp


USER MENU


Menu Dashboard Process Trends


 Admin


Run Name : -Idle-
Patient ID : -None-
Tue 01 Aug 2023 11:28:40


Log out
User : adva_admin


 Process Details


 Run Management


 Calibrations


 Macros


 Alarms


 Notifications


 Run Report

 Historical Trends

 Data Logs


 System Set-up

 Run Set-up

 User Management

DEVELOPER USER INTERPHASE

Menu
Dashboard
Process Trends



Run Name : Bio-314 Broaden
Patient ID : B
Wed 19 Oct 2022 04:04:06

Admin
Log out
User : adva_admin

Incub Door

Incubator Temperature

PV	37.0 °C
SP	37.0 °C

P2 - Manual
5.0 mL/min

WASTE

Details

Air pH/1	0.0 mL/min
CO2 pH/2	0.0 mL/min

Adva Cone DO

PV	66.5 %
SP	65.0 %

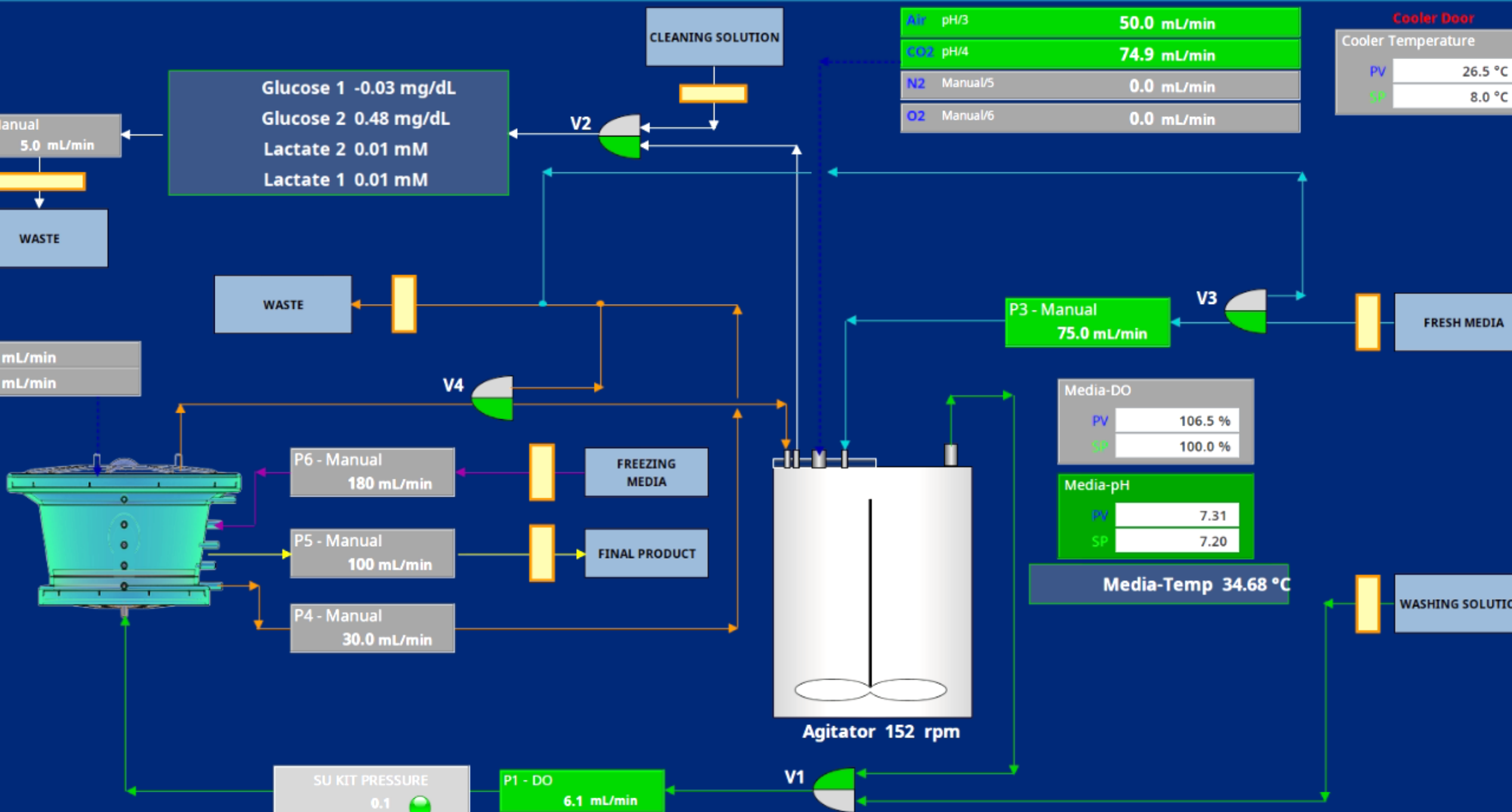
Adva Cone pH

PV	7.08
SP	7.20

Adva Cone Temperature

PV	37.3 °C
SP	37.0 °C

Stop All



Glucose 1 -0.03 mg/dL
Glucose 2 0.48 mg/dL
Lactate 2 0.01 mM
Lactate 1 0.01 mM

CLEANING SOLUTION

Media-DO

PV	106.5 %
SP	100.0 %

Media-pH

PV	7.31
SP	7.20

Media-Temp 34.68 °C

Agitator 152 rpm

SU KIT PRESSURE 0.1

P1 - DO 6.1 mL/min

P3 - Manual 75.0 mL/min

WASTE

FREEZING MEDIA

FINAL PRODUCT

WASHING SOLUTION

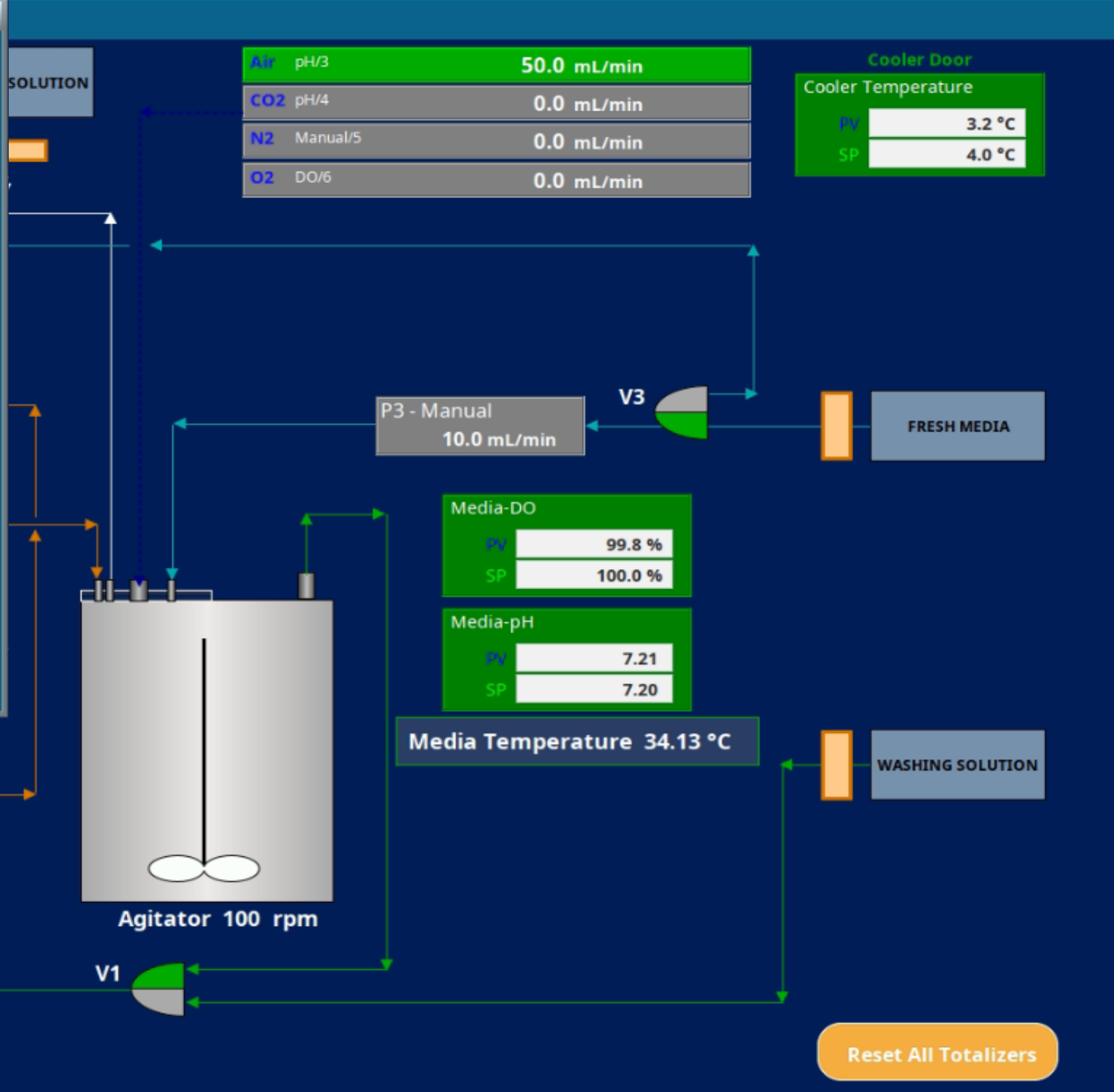
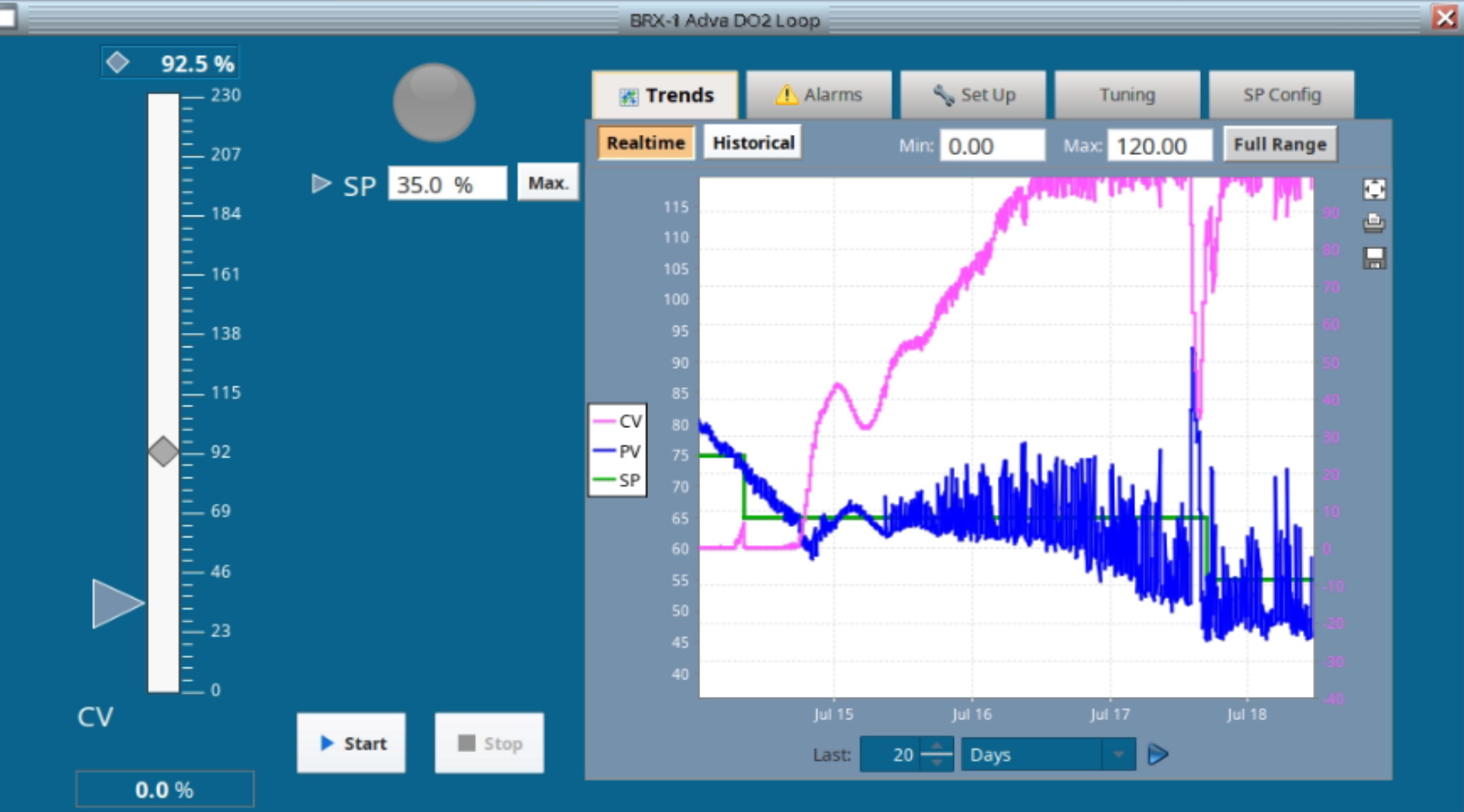
Cooler Door

Cooler Temperature

PV	26.5 °C
SP	8.0 °C

Air pH/3 50.0 mL/min
CO2 pH/4 74.9 mL/min
N2 Manual/5 0.0 mL/min
O2 Manual/6 0.0 mL/min

Reset All Totalizers



OUR SOLUTION

THE **ADVA X3**[®] AN AUTOMATED, CONTROLLED, MODULAR, CELL-THERAPY MANUFACTURING PLATFORM – ENABLING EFFICIENT DECENTRALIZED MANUFACTURING



Savings

70-80% of the current manufacturing costs

Simple

Technician level operator Minimal infrastructure scalability,

Smart

14 controlled parameters with **AI & ML** capabilities

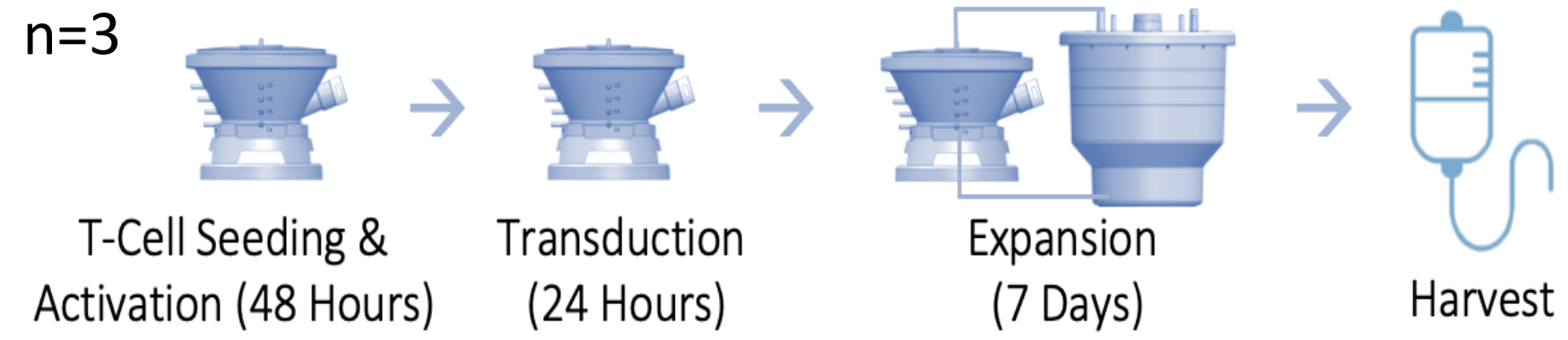
Flexible

Manufactures **CAR-T, TCR, NK, TILs, Viruses** And more

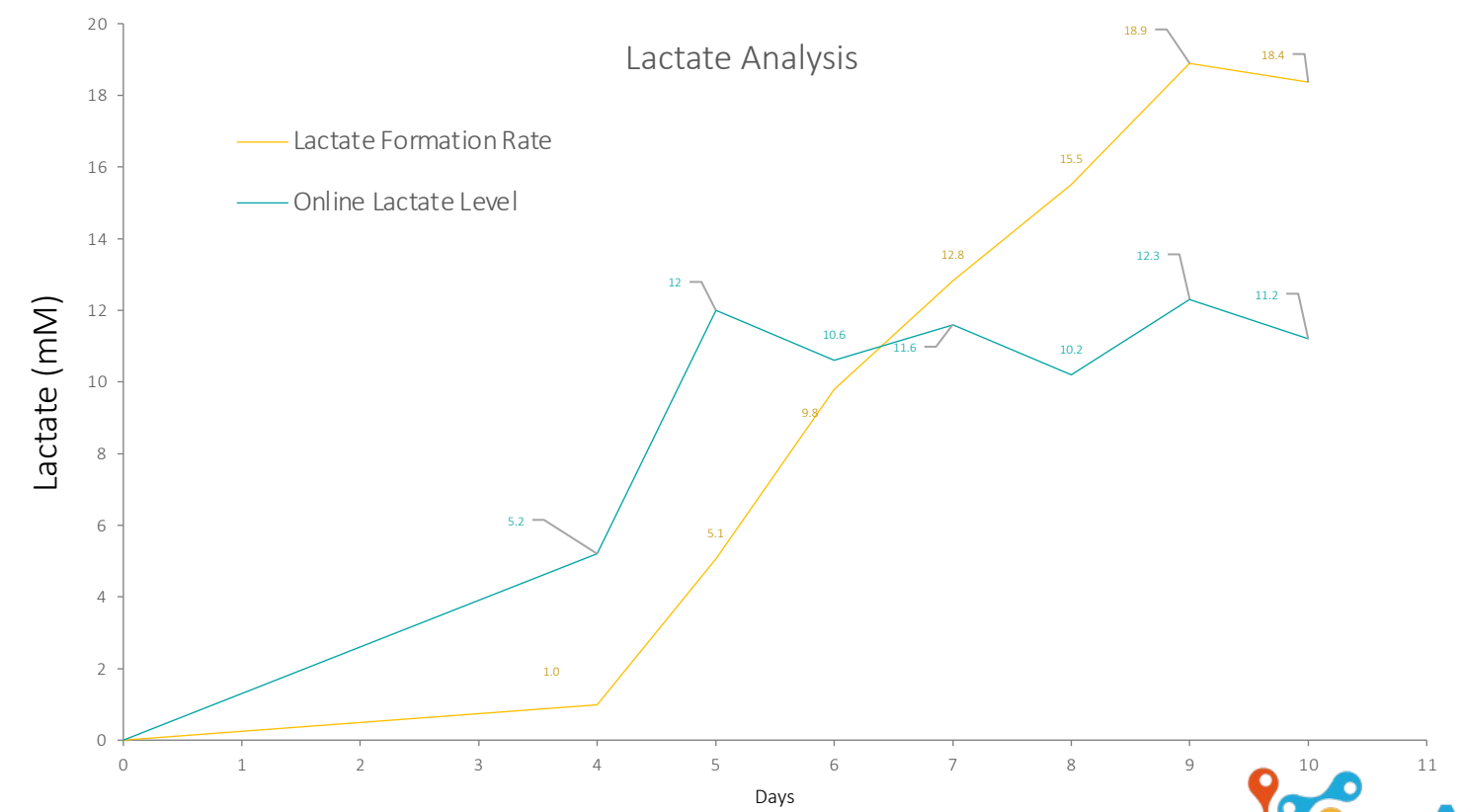
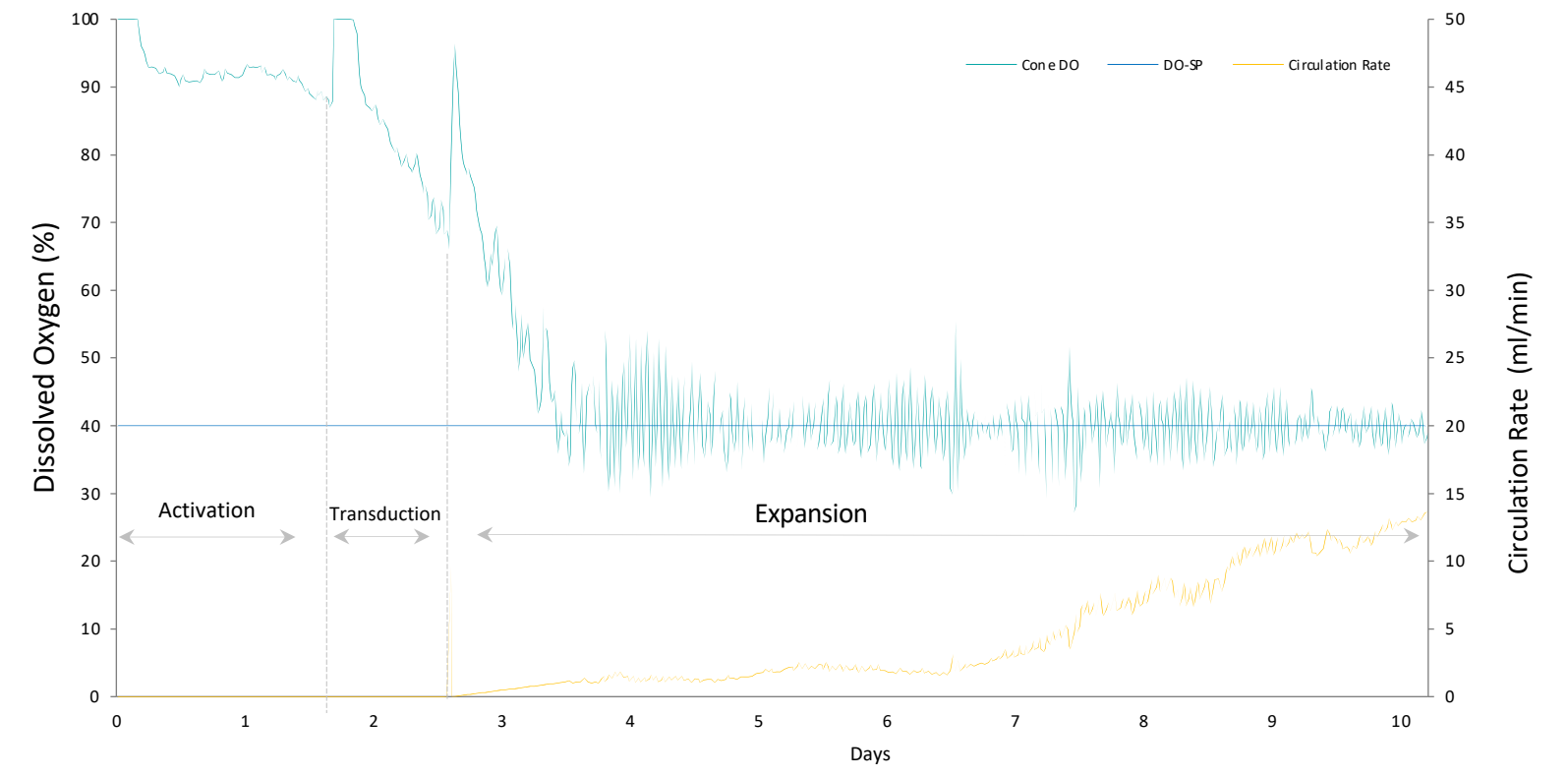
Productive/Scalable

10X more cells, the **only device** that can be used for **solid tumors**

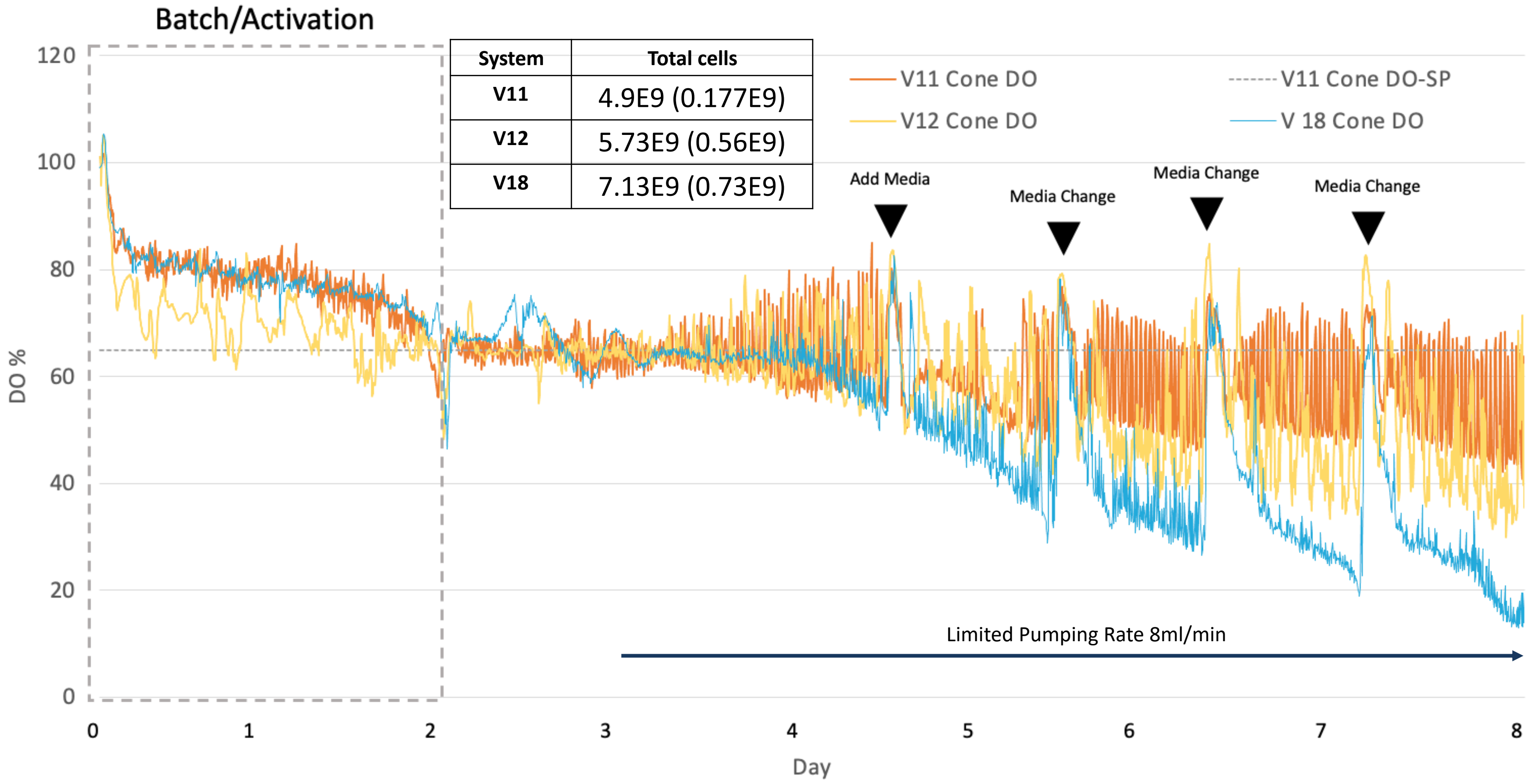
CLASSICAL CAR-T PROCESS



	ADVA-X3#	Gold Standard
Seeding Cells	60E6	60E6
Process Days	10	10
Harvest	8.1E9 ± 0.45E9	3.7E9 ± 0.24E9
Cells Viability	95%	92%
Fold Increase	140	66



Predicted Variation



Machine Learning

Machine Learning (ML) is an umbrella term for solving problems for which development for algorithms by humans is cost prohibitive, instead the problem are solved by helping machines “discover” their own algorithms



Supervised Machine Learning

- Diagnostics
- Predictions (cell growth/phenotype)
- Process Optimization

Unsupervised Machine Learning

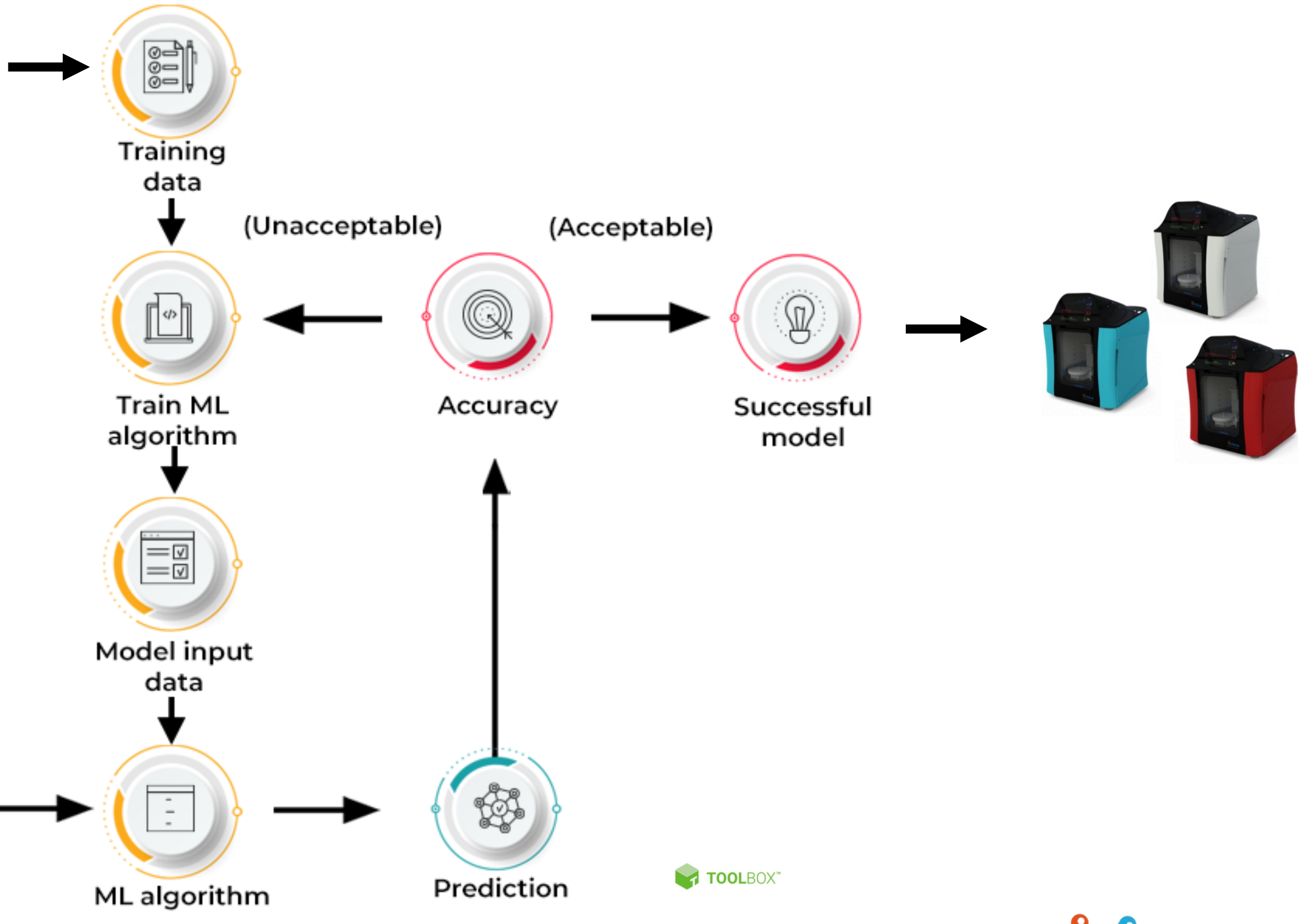
- Anomalies
- Correlations
- Segmentations
- Meaningful comparisons

Semi-Supervised Learning

Reinforcement Learning

- Realtime decisions
- Accuracy

Machine Learning



Unified Name Space Analytics



Sensor intensity and device performance
Blinded process data (pH, DO, Temp...)

Secure Data Flow

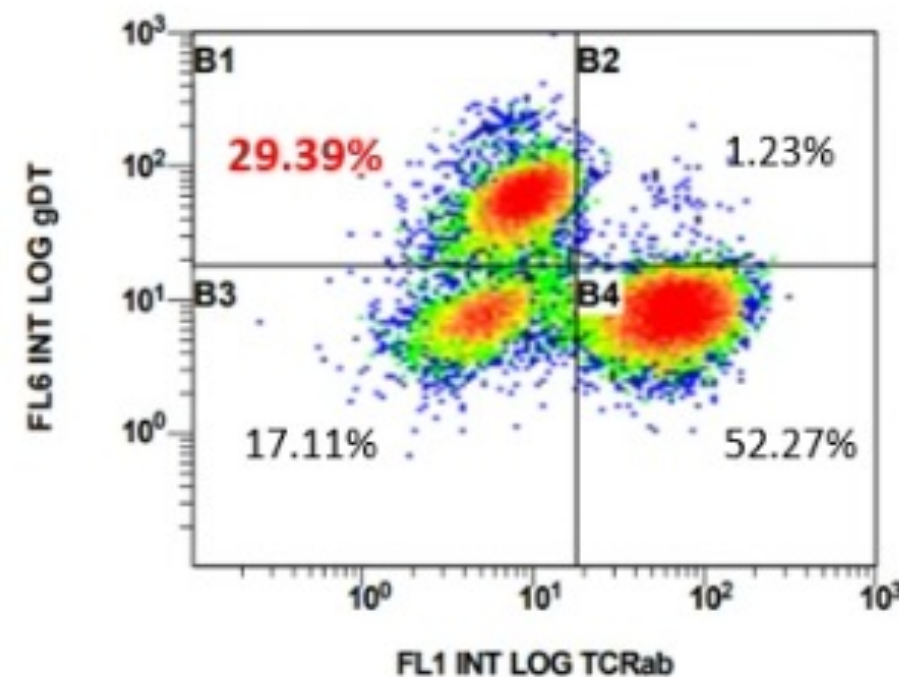


Use Case

Correlation and predictability between donors on cell phenotype and yield by process parameters

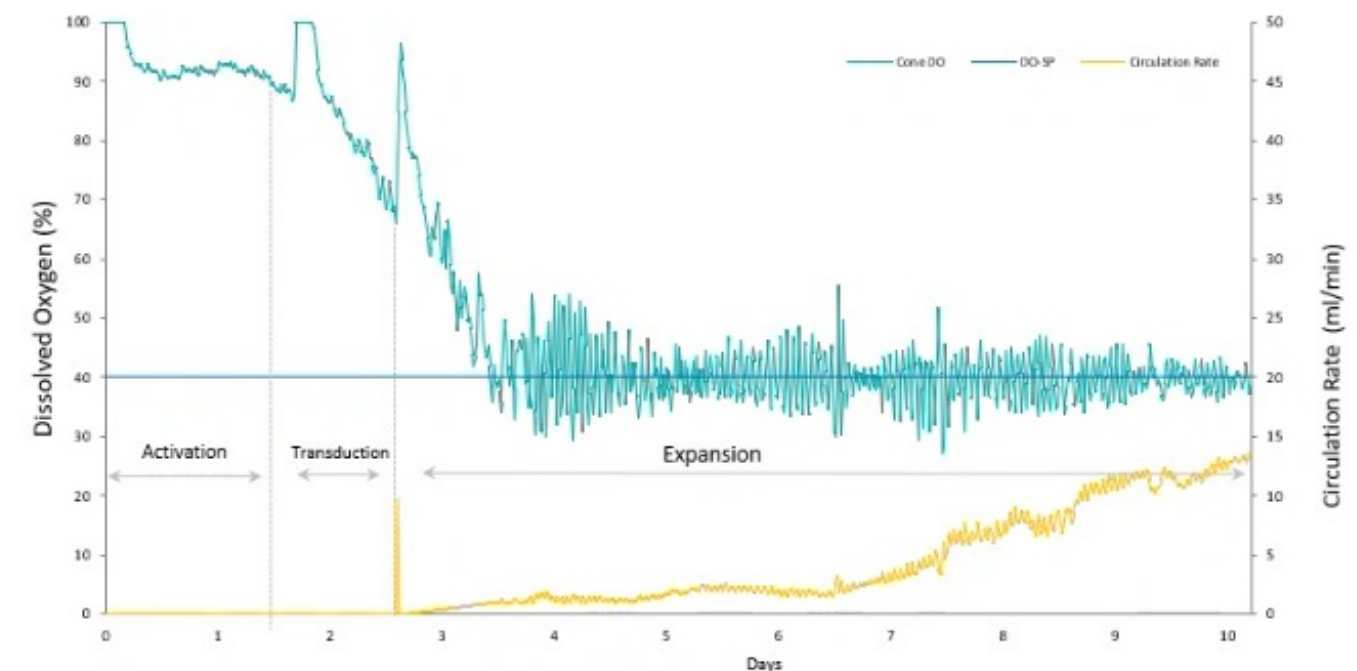
Maximize Cell Growth by Phenotype (CD8/CD4, # cells, Activation/exhaustion)

- Complex set of multiple variables
- Effected by doner materials, environment
- Time series data

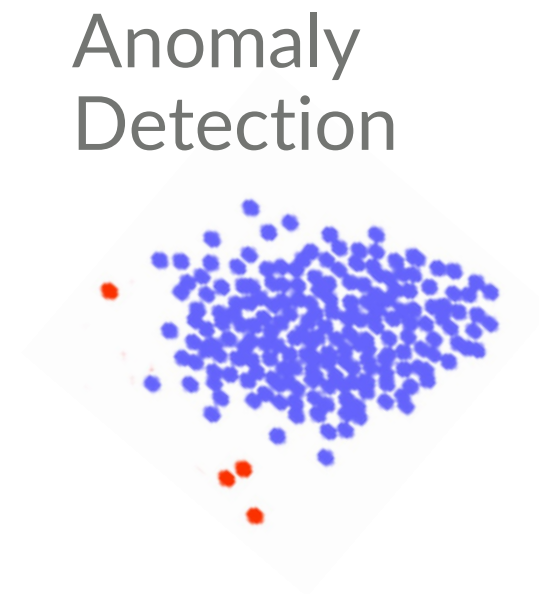
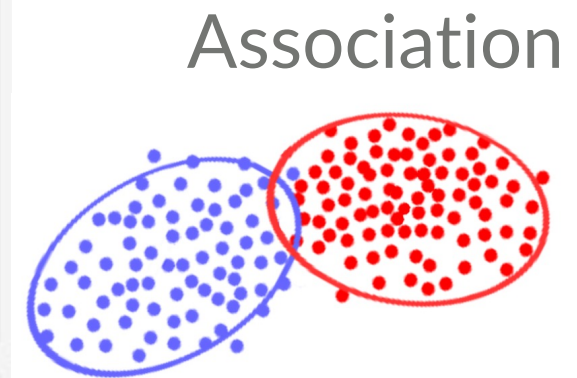
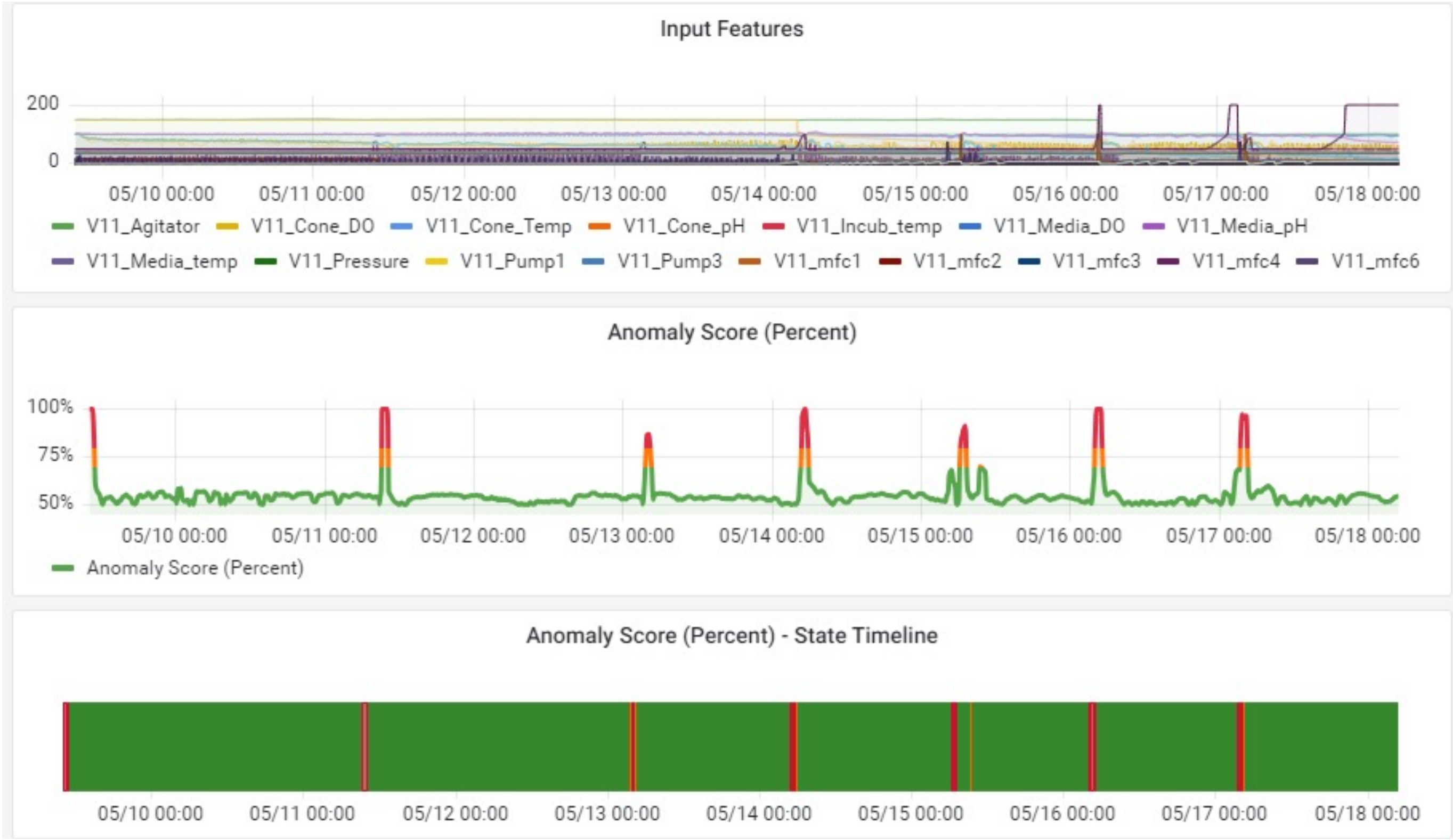


Inputs – Endless data

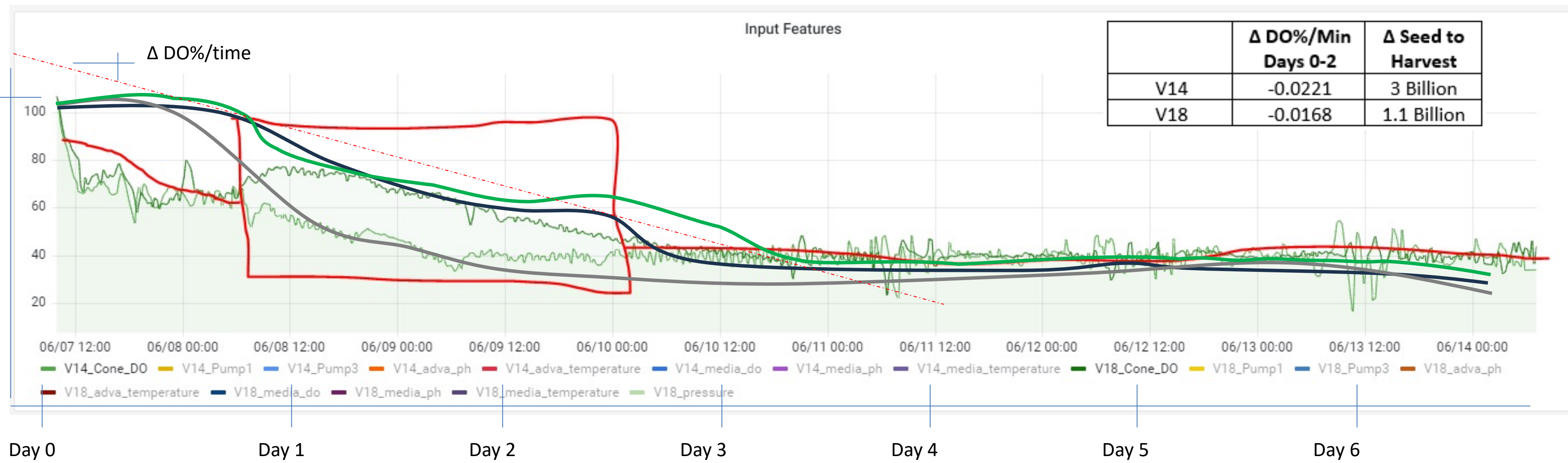
- DO%, media pump rate, lactate, cell count....
- Pre/post culture Phenotype, duration...
- Identify indicators that lead to best ratio of healthy cells by type



Unsupervised Learning

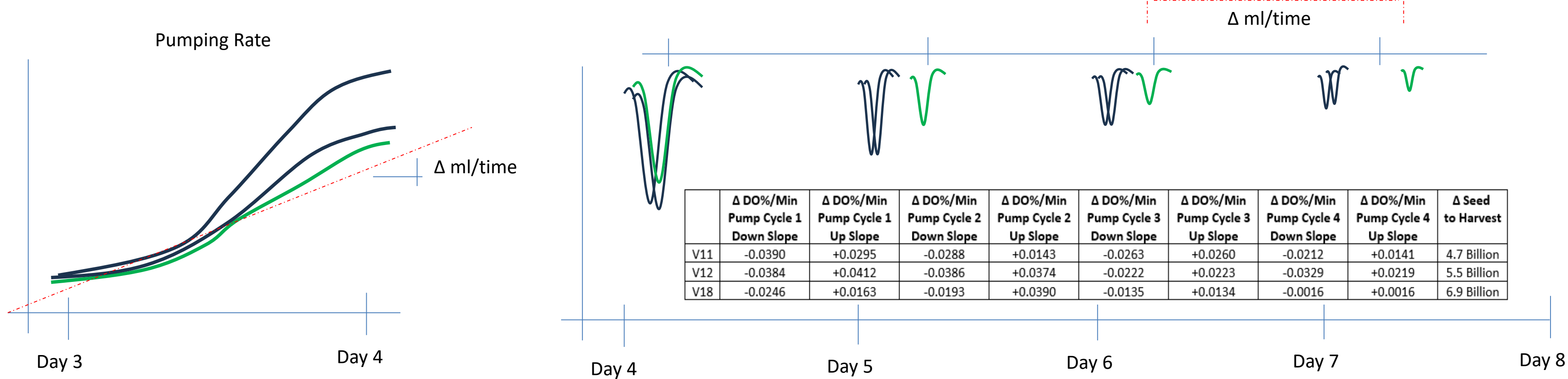
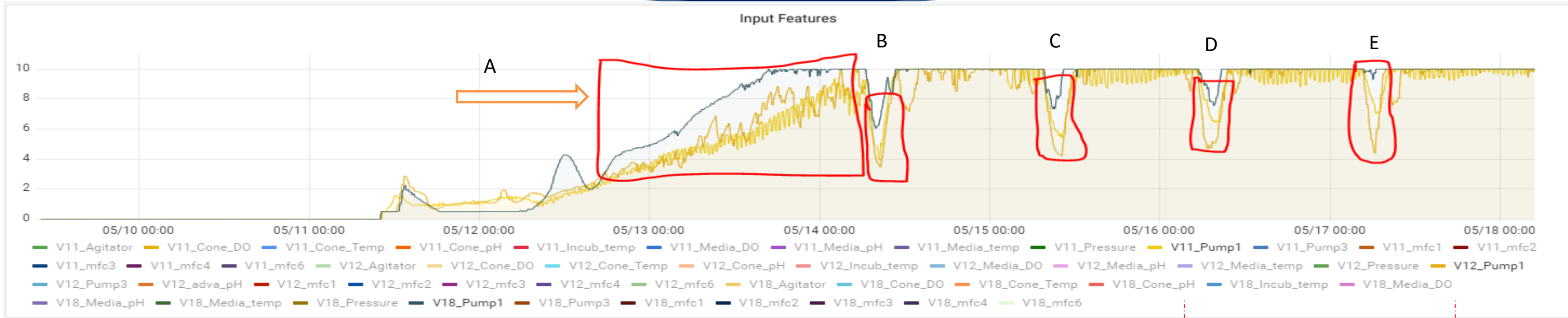


Clustering and Association



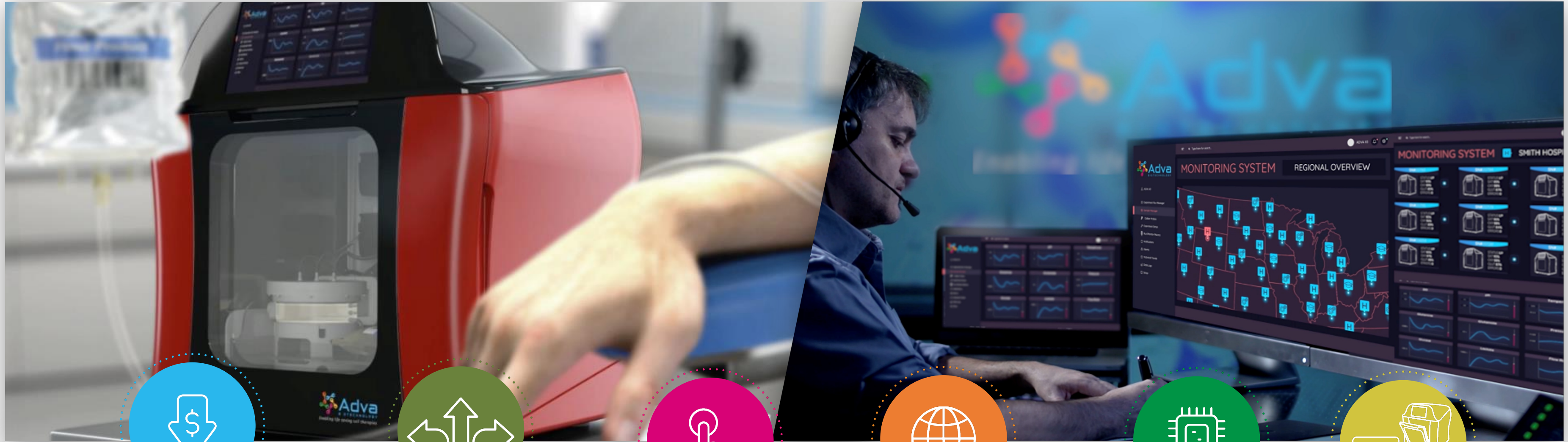
- Simple correlation; the greater the slope of DO production during the activation and transduction (especially after 20+hours), results in higher “preferred” cell yields. Likewise, a more rapid pump response can yield higher cell counts.

Regression



A more intense media pump response after each media change and the extended steadiness between media changes shows a correlation to higher “preferred” cell yield.

PLATFORM ATTRIBUTES



Manufacturing and logistics cost reduction - Automation



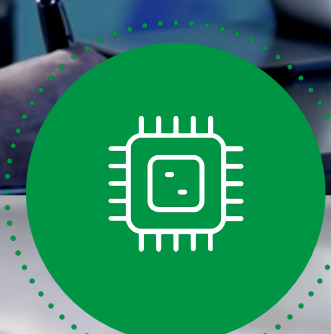
Flexibility
CAR T, TCR, NK,
TILs, Exosomes...



Simplicity



Reproducibility and predictability



AI, Machine learning with 14 controlled parameters



Remote access and control



READY TO SCALE



ADVAX³-INDUSTRIAL



ADVA X3[®]

MANUAL TO
AUTOMATED **GMP**

IN 3 MONTHS



METABOLIC SENSING & AI

Thank You!

From the ADVA Biotechnology Team

