Simplifying Progress

Application of the BioPAT® Viamass Capacitance Sensor in Bioprocesses

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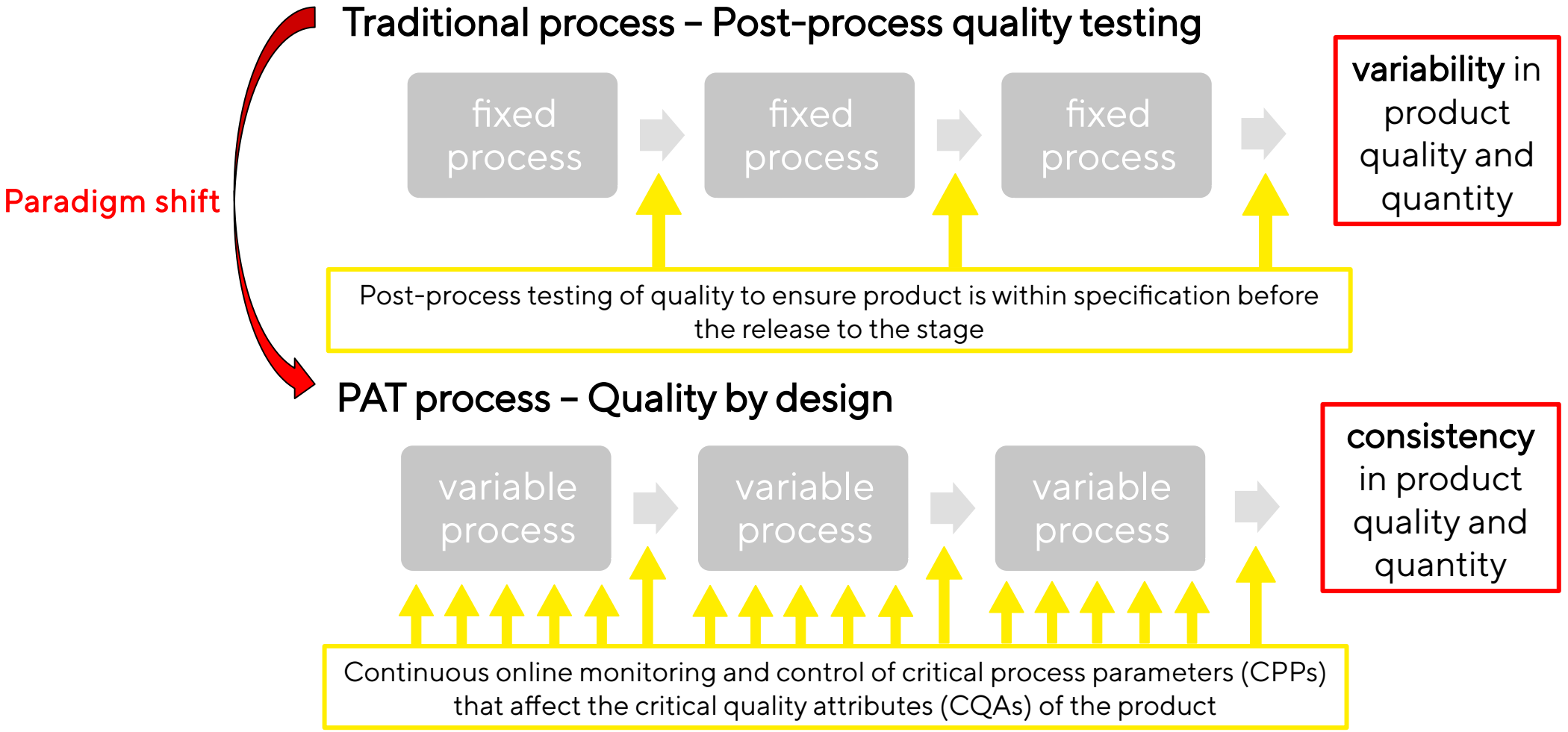
Agenda

1. **Introduction to Process Analytical Technology (PAT)**
2. Working principle of BioPAT® Viamass
3. Applications of BioPAT® Viamass
4. Process Control with BioPAT® Viamass

How does PAT improve a bioprocess?



Source: Svea Grieb, Kai Touw, Dan Kopec, 'What's beyond the bioprocess automation starting line', The Medicine Maker, July 2019

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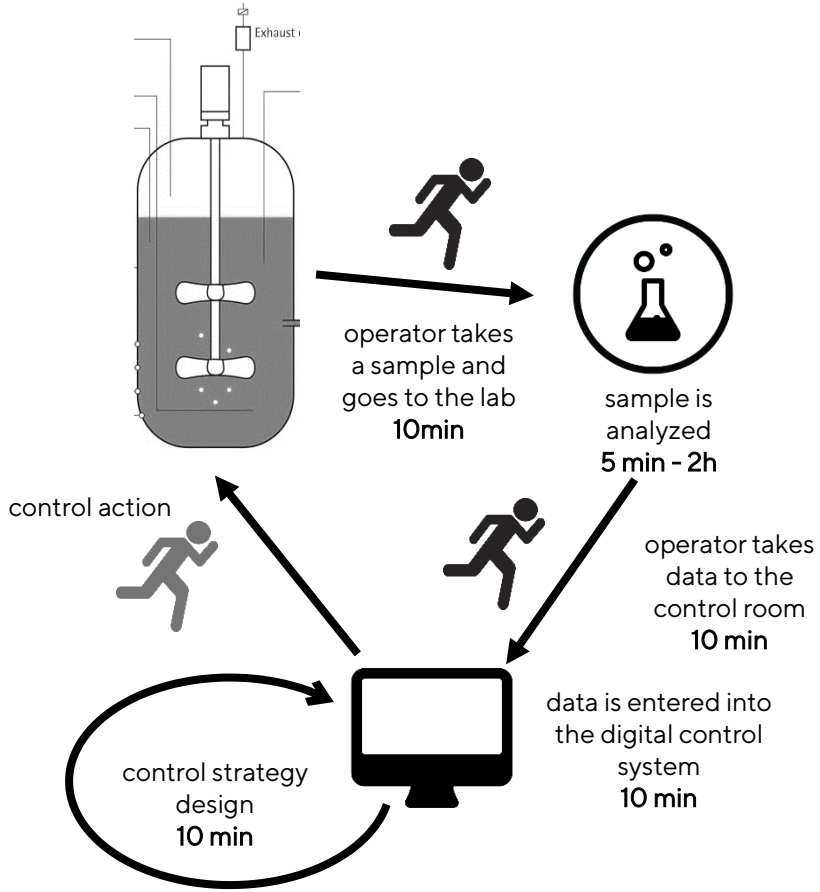
How does PAT improve a bioprocess?

Traditional process without PAT



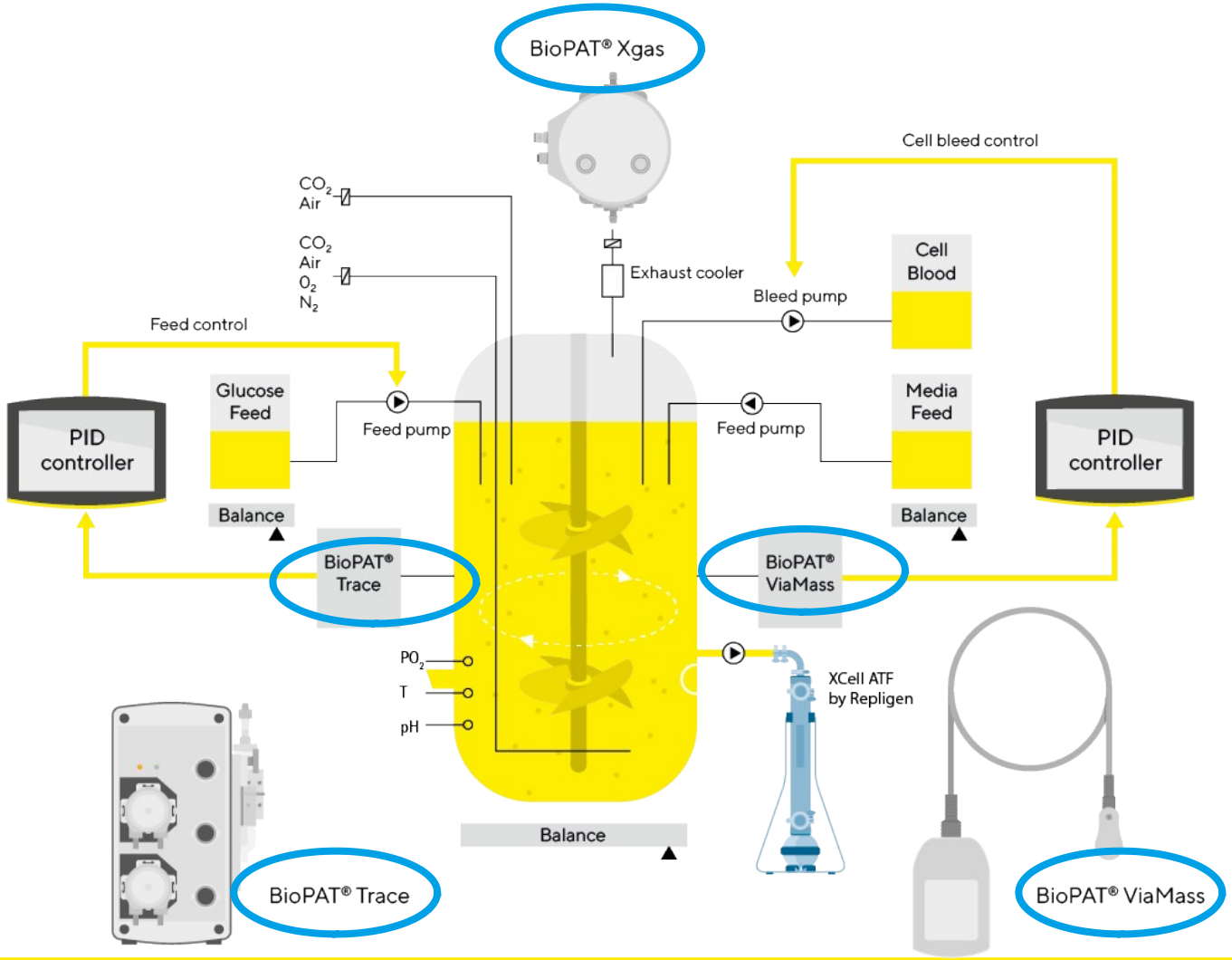
Problems / Risks

- Contamination risk through sampling
- Sample might change after removal from the reactor
- Reactor volume is lost
- Manual steps are prone to operator errors
- Up to 3h time delay between measurement and response
- No sampling over night / on weekends

Process with PAT

- ➢ Manual sampling not required
- ➢ Sample is not removed
- ➢ Reactor volume is unaffected
- ➢ Automation eliminates risk of operator errors
- ➢ Faster measurement results through data integration
- ➢ 24|7 monitoring and control

Sartorius has a comprehensive PAT portfolio



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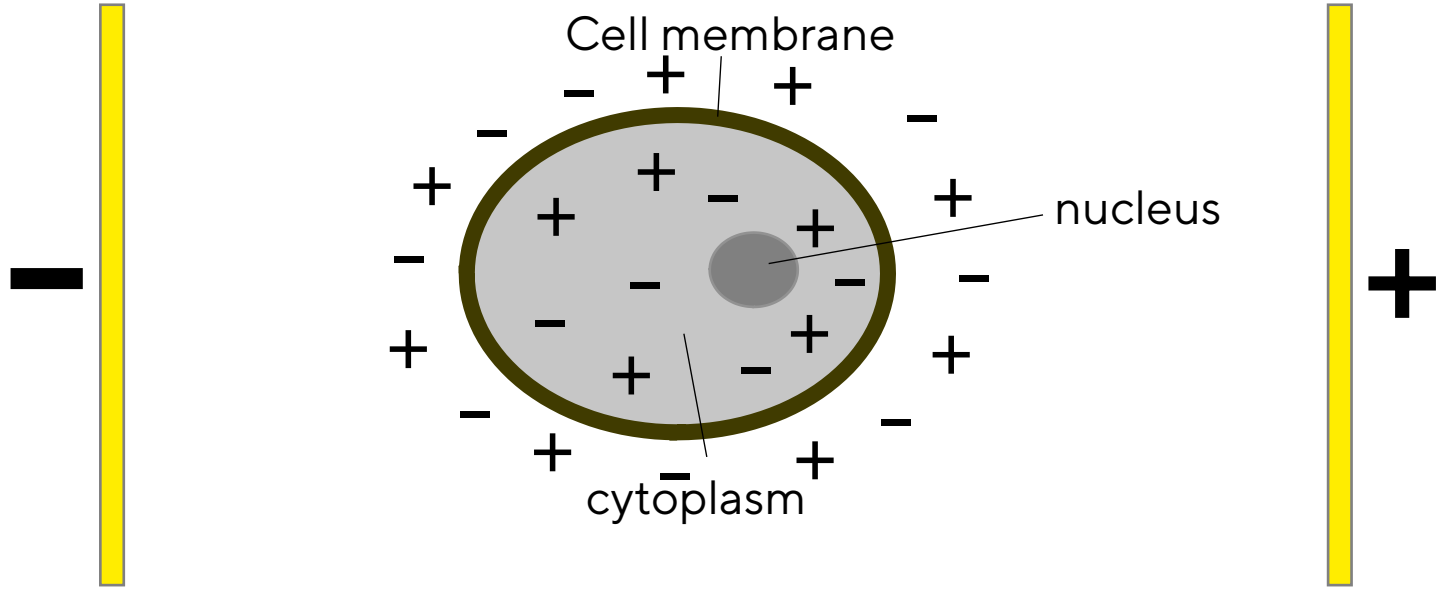
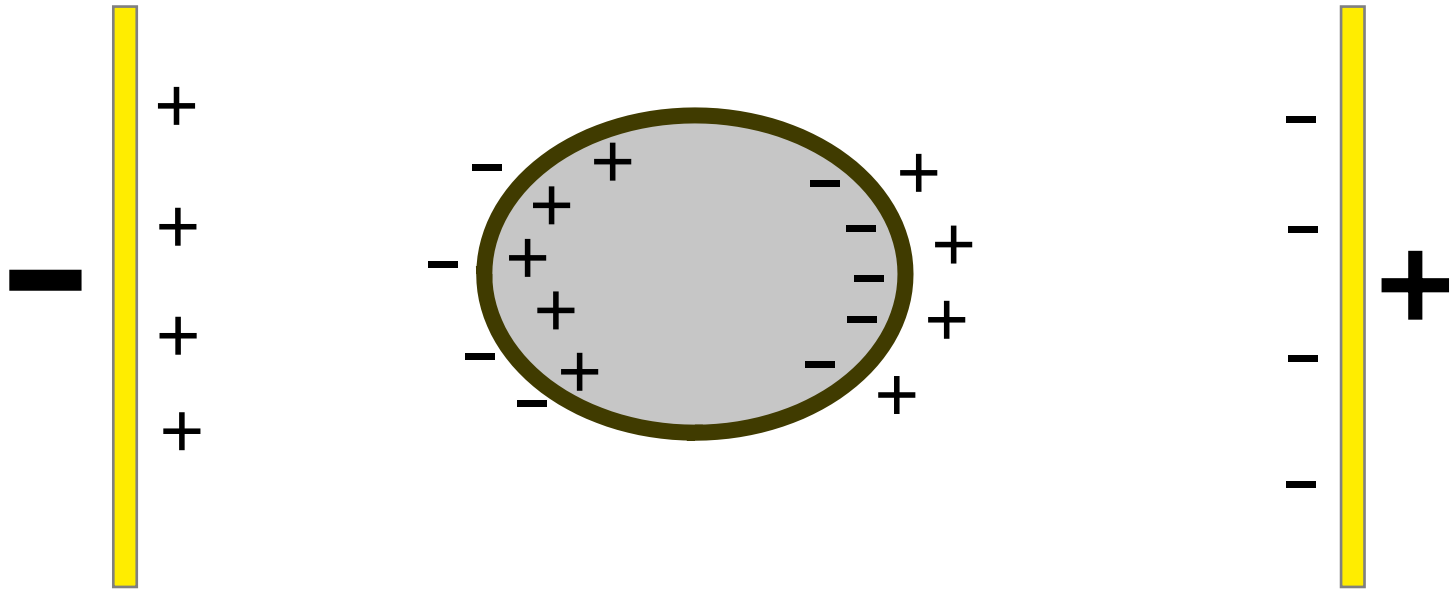
BioPAT® Viamass measures the viable cell volume through capacitance

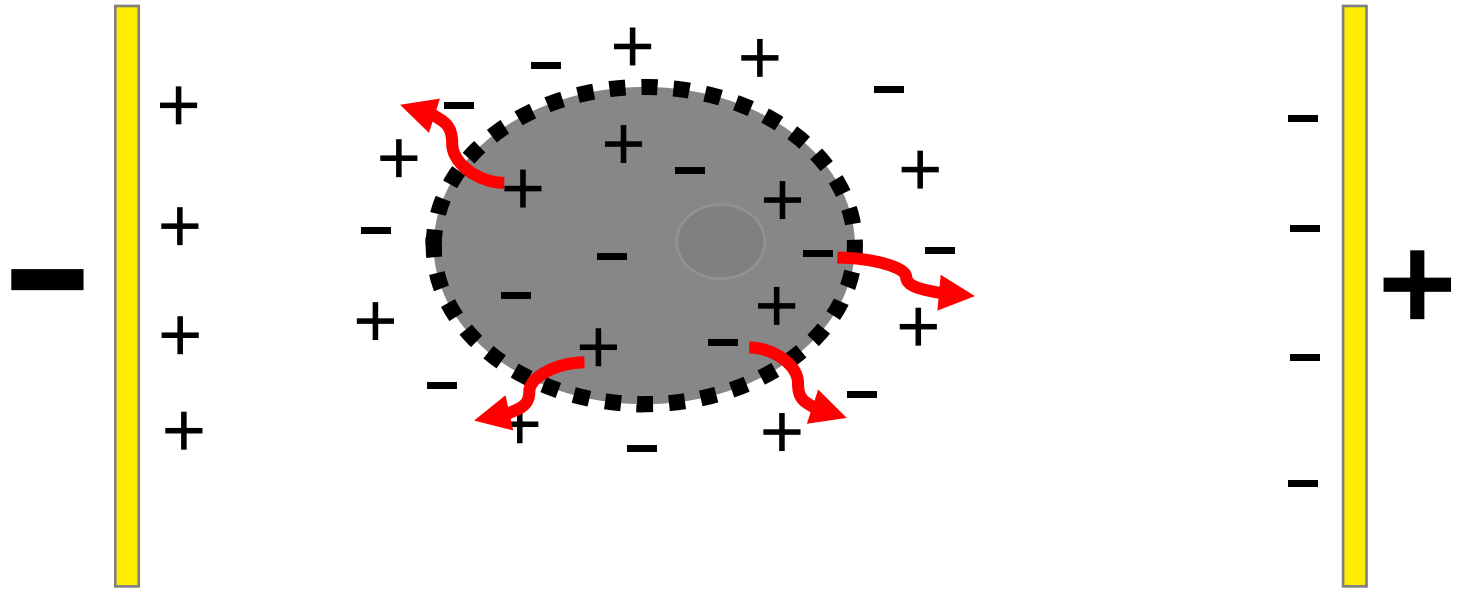


BioPAT® Viamass measures the viable cell volume through capacitance



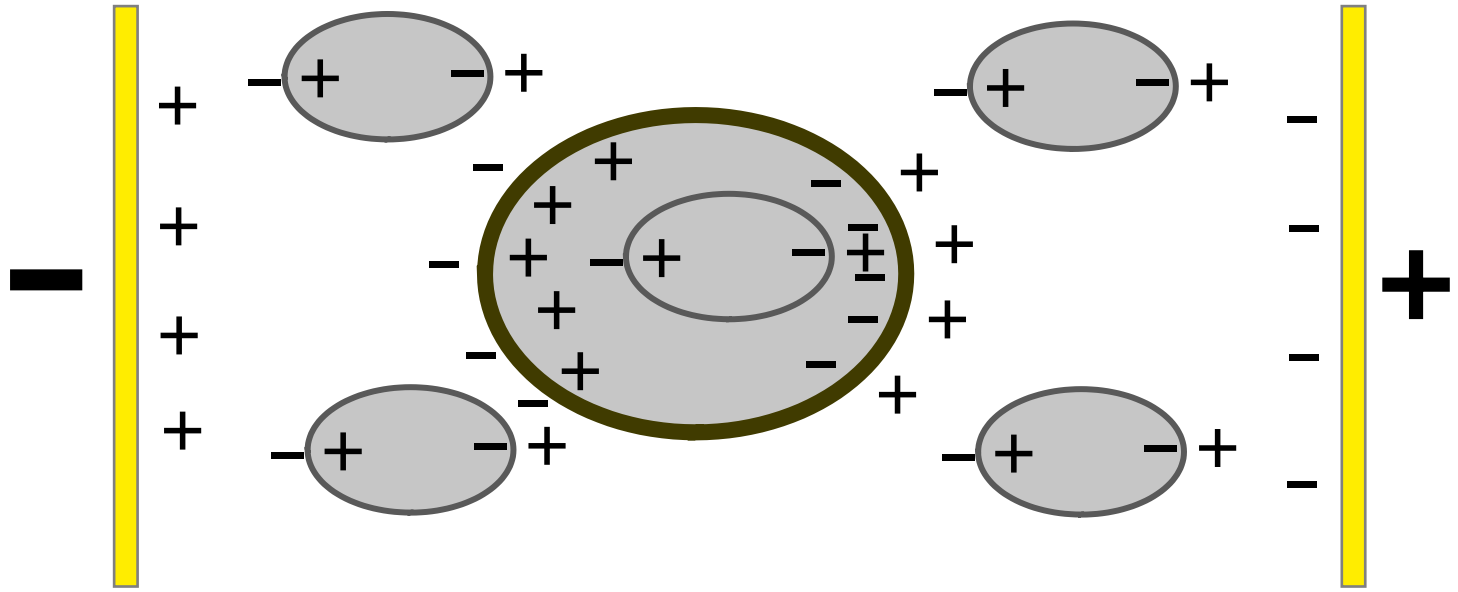
→ Living cells are polarized by the electric field and behave like a capacitor

BioPAT® Viamass selectively measures viable cells



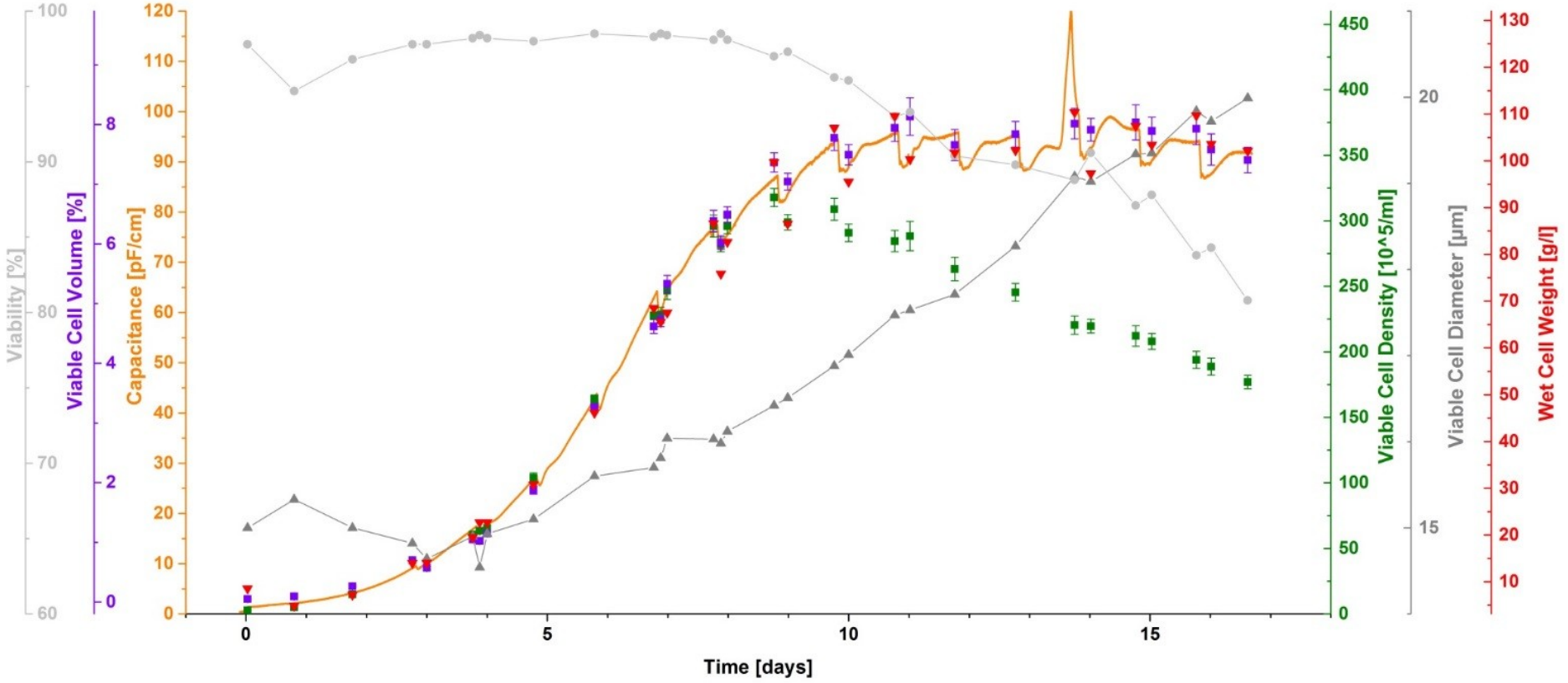
→ Dead cells cannot be polarized and do not contribute to the capacitance signal

BioPAT® Viamass measures the viable cell volume through capacitance



→ Capacitance measures the viable cell volume NOT the cell density
→ The more cells the higher the capacitance signal
→ The bigger the cells, the higher the capacitance signal

BioPAT® Viamass is a SU capacitance probe for measuring viable cells



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BioPAT® Viamass is a SU capacitance probe for measuring viable cells

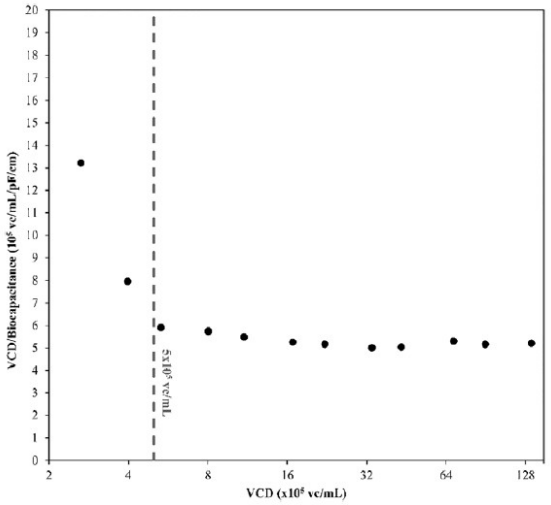
BioPAT® Viamass SU in Biostat® STR

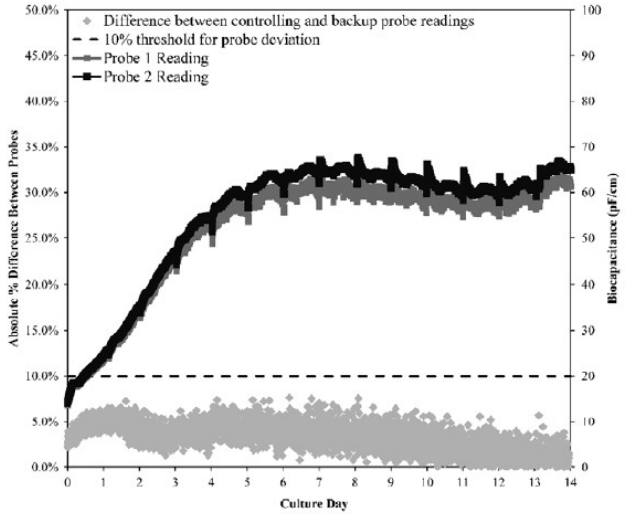
BioPAT® Viamass SU in Biostat® RM

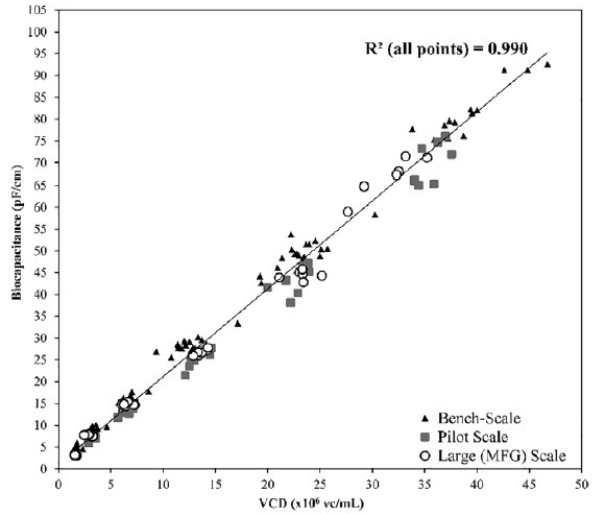
BioPAT® Viamass MU in Biostat® Univessel and stainless steel

Plug and play integration in the Sartorius Digital Control Unit (DCU) and Biobrain®

Implementation of bio capacitance for process control in a commercial GMP CHO manufacturing process







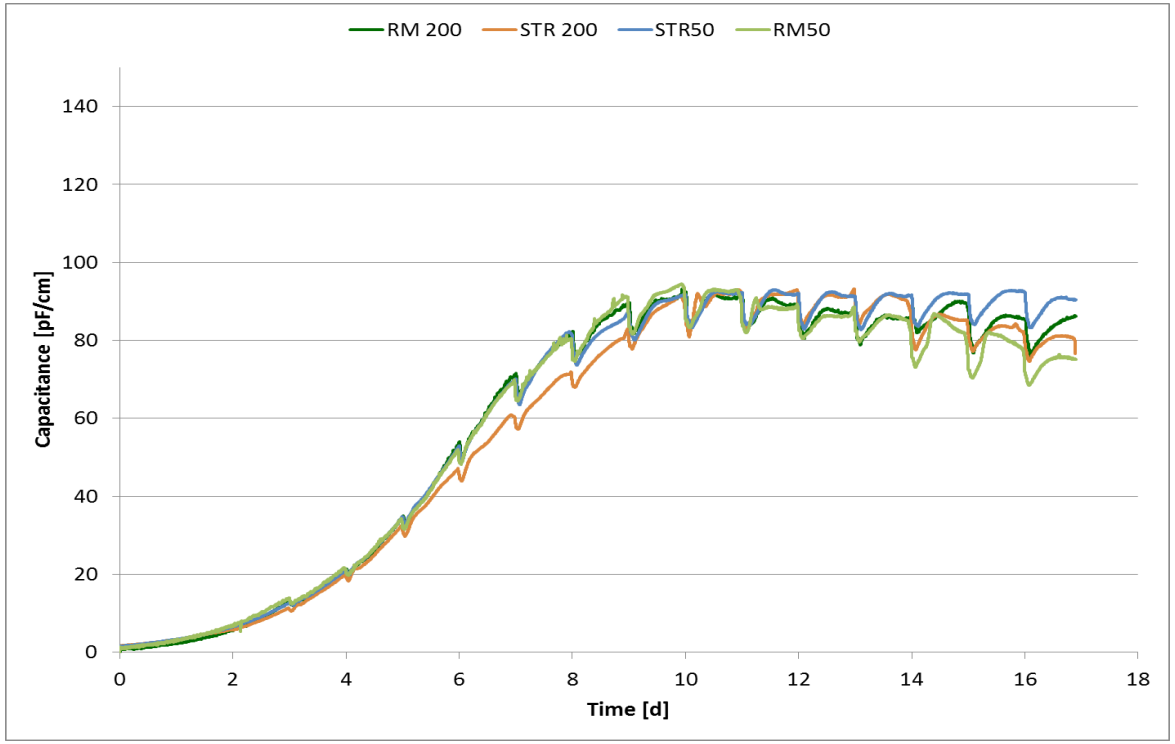
Limit of quantification
- For CHO cell process
- linear relation between VCD and capacitance
- LOQ: 50,000 cells/mL

Probe to probe variability
- 2 probes installed in same 15k bioreactor
- average difference: 3.6%
- Max. observed difference: 10%

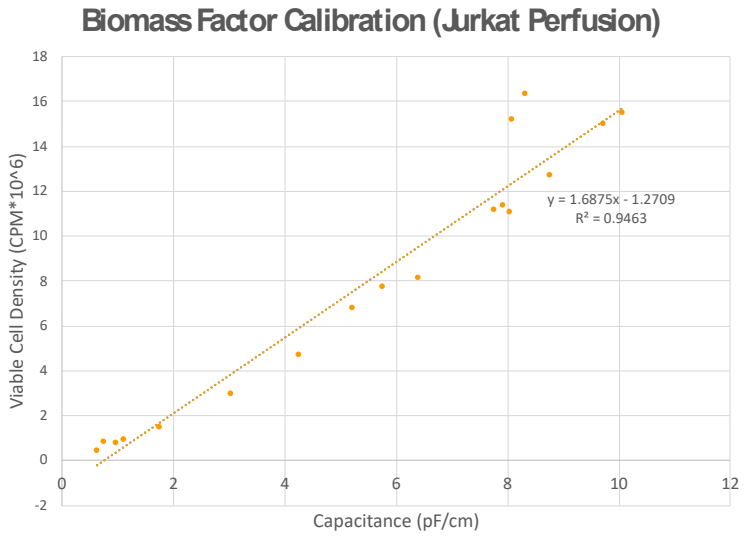
Scalability
- bench scale (5L), pilot scale (200-315L), large scale (15,000L)
- strong linear correlation of capacitance and VCD across all scales

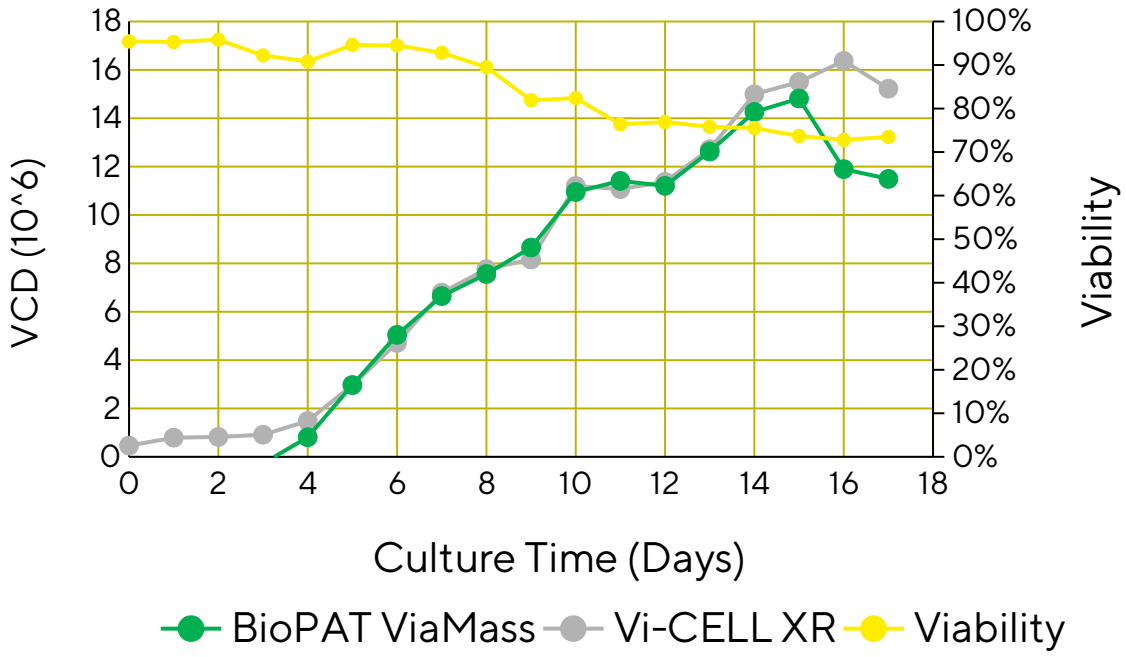
Source: Moore B, Sanford R, Zhang A., **Biogen**, Case study: The characterization and implementation of dielectric spectroscopy (biocapacitance) for process control in a commercial GMP CHO manufacturing process. Biotechnol Progress. 2019;e2782. https://doi.org/10.1002/btpr.2782

BioPAT® Viamass works reliably across scales and bioreactor types



BioPAT® Viamass in cell and gene therapies applications



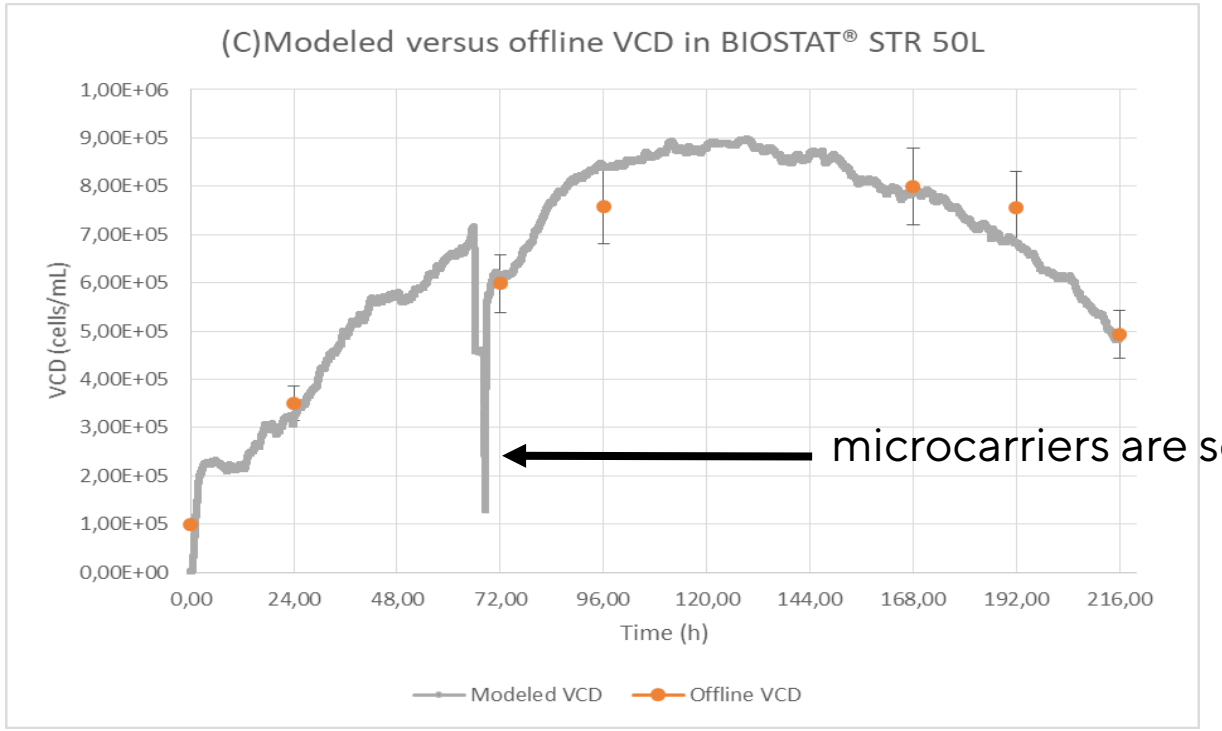


Reliable prediction of VCD for Jurkat cell line in a 2L rocking motion system

- Inoculation cell density: 500,000 cells per mL
- Maximum cell density: 16 million cells per mL
- Perfusion rate: 0.5 VVD starting day 4

Source: Poster by J. Bown, S. Chahine, & J. Sonico, Kegg Graduate Institute, 'Analysis of Dielectric Biomass Measurements in Jurkat Dead-End Perfusion'

BioPAT® Viamass in microcarrier-based viral vaccine processes



microcarriers are settling

Reliable prediction of VCD of cells growing on microcarriers

- Maximum cell density: 90,000 cells per mL

Source: Sartorius Application Note: 'Control and scale-up of a microcarrier-based viral vaccine process using BioPAT® ViaMass for inline viable cell density measurement', Juanola S., Garcia L., Mouriño M., Urniza A., Grieb S., Scholz J., Boulais A.

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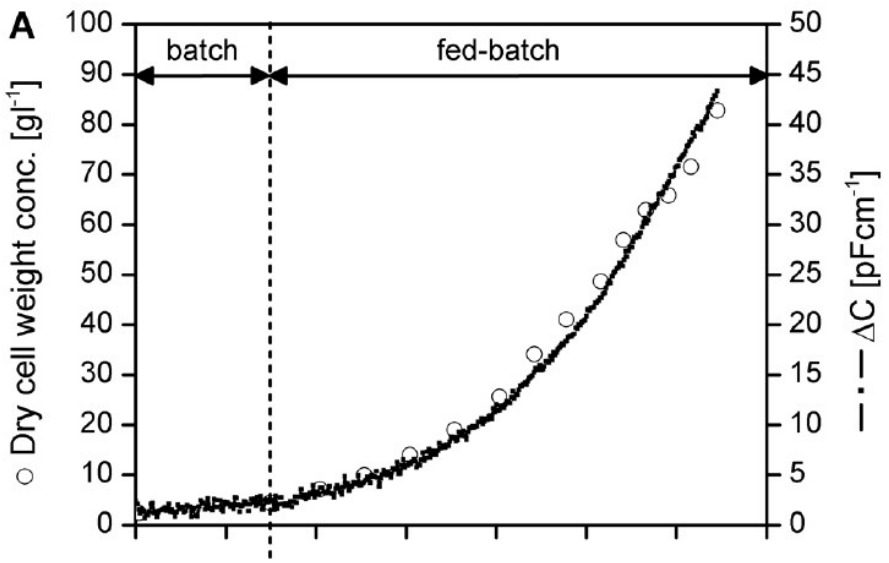
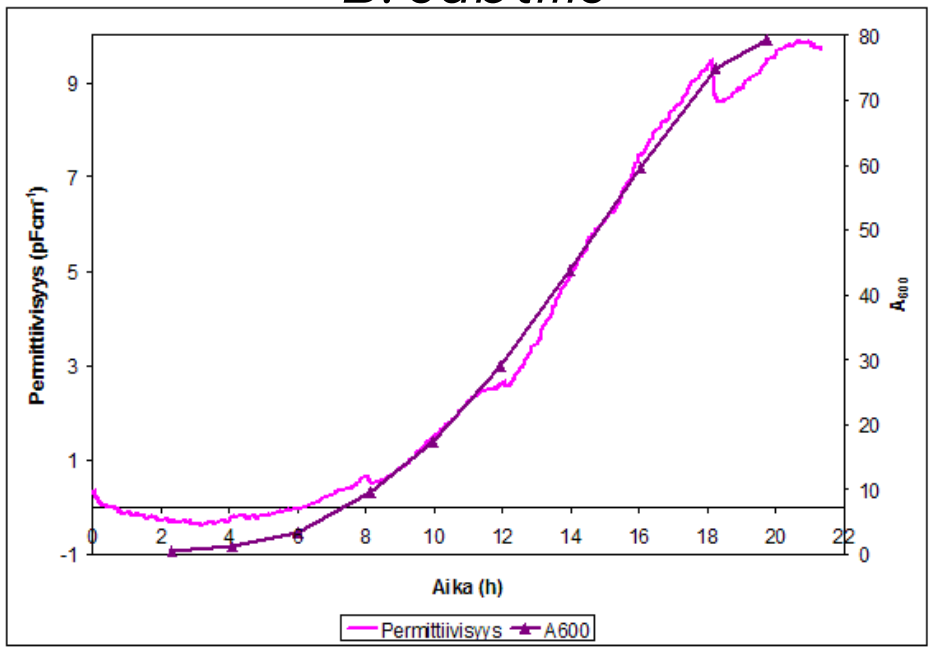
BioPAT® Viamass in microbial applications

E. coli



B. subtilis



Reliable prediction of biomass for gram-positive and gram-negative bacteria

Source: Courtesy af ABER Technologies

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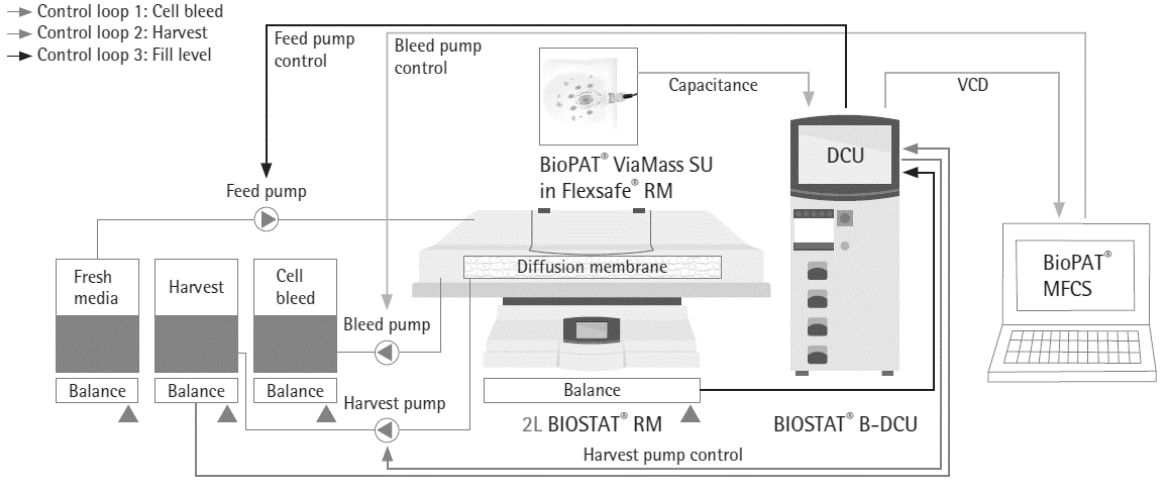
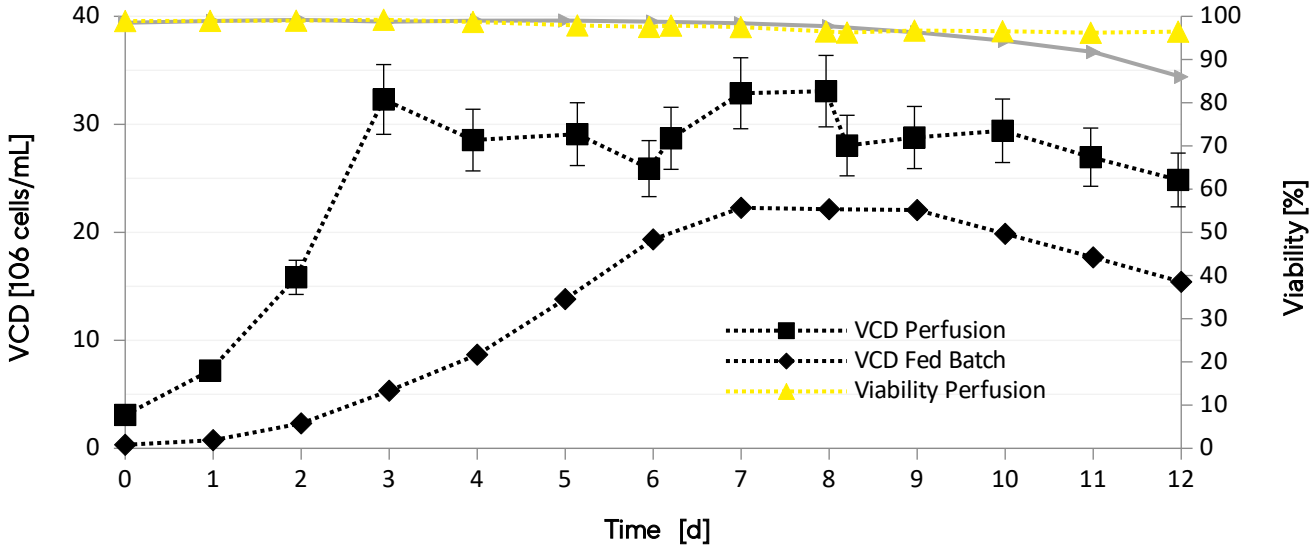
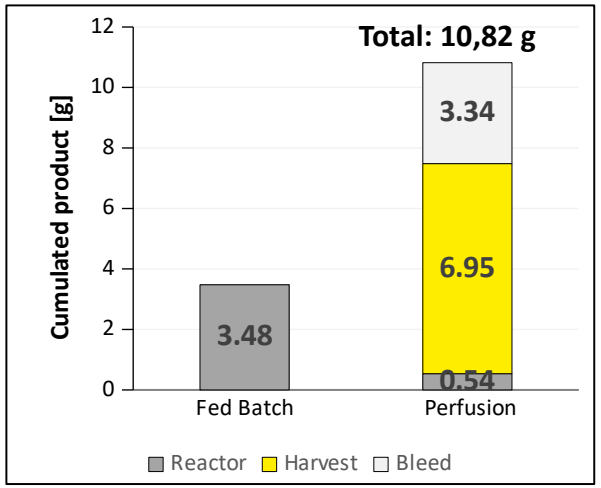
BioPAT® Viamass can control the perfusion rate in intensified processes





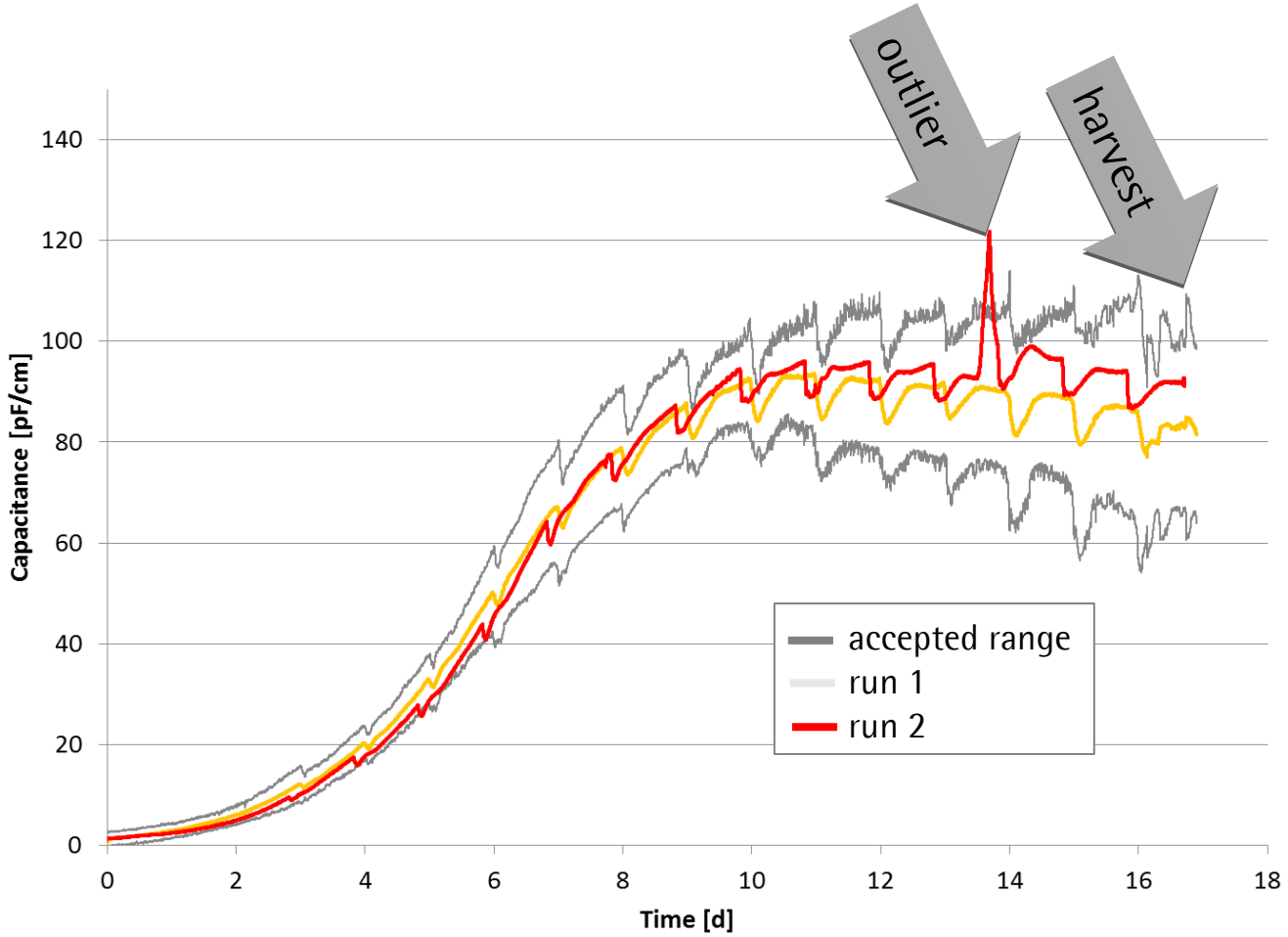


Cell bleed control with BioPAT® Viamass

- Automatic control of VCD at 30 million cells/mL
- Perfusion process in a 2L RM system
- Tripled the yield through perfusion

Source: Sartorius Application Note 'Automated Cell Bleed Control in an Intensified SU Rocking Motion Bioreactor Through the SU Capacitance Sensor BioPAT® ViaMass' , S. Grieb, J. Lemke, M. Schulze, and J. Matuszczyk

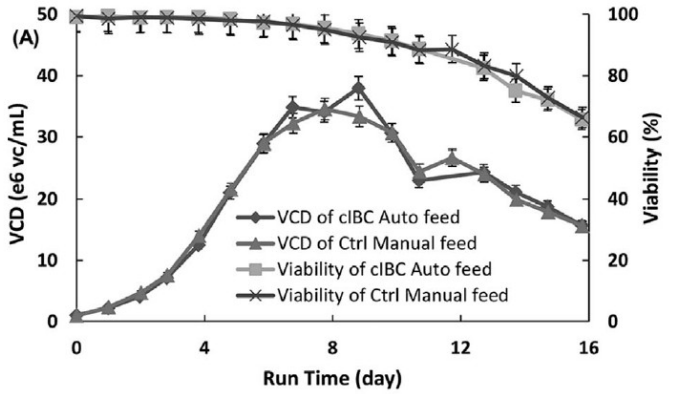
Trajectory monitoring allows for early detection of process deviations and optimal harvest point prediction

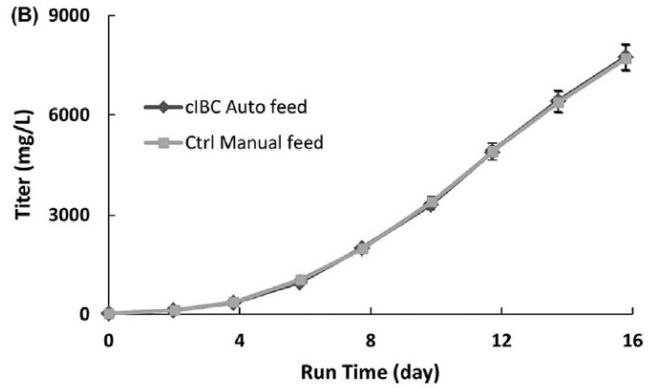


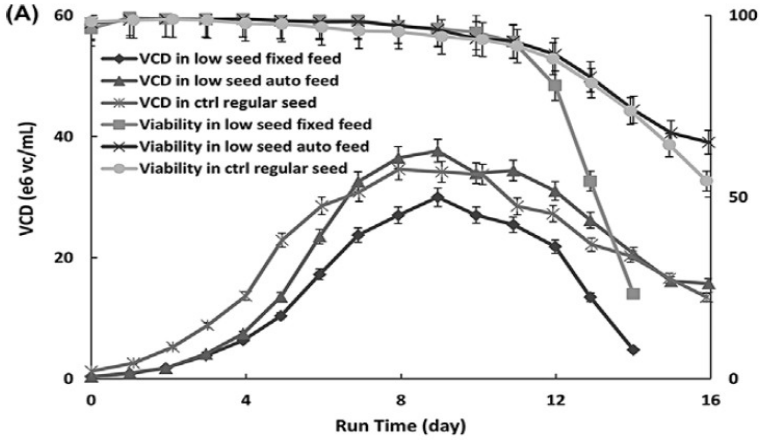
BioPAT® Viamass:

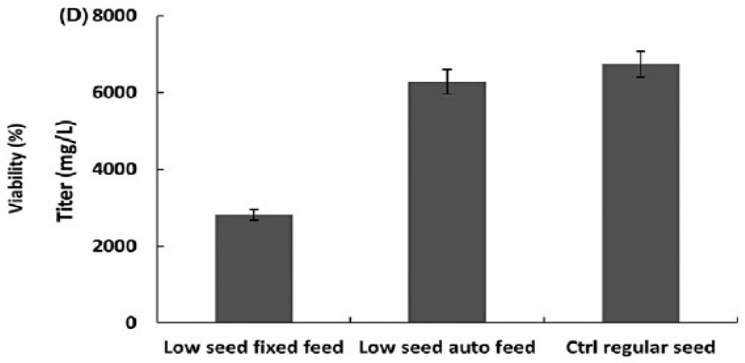
- detects abnormalities in a timely fashion and allows for intervention
- day 13: oxygen supply was interrupted
- growth trajectory can be used to predict the optimal harvest point

Feed control with BioPAT® Viamass ensures robust and consistent processes









Example 1: Regular process

- automated feed based on bio-capacitance control can reproduce results obtained with manual feeding

Example 2: Underseeded process

- an underseeded culture gets overfed by a regular, manual feed
- accumulation of unwanted byproducts decrease peak VCD, process time and titer
- automated feed based on bio-capacitance can rescue an underfed culture and yield the same results as a regular process

Source: Advanced process monitoring and feedback control to enhance cell culture process production and robustness. Zhang et al., **Biogen**, Biotec and BioEng, 2015

Thank you.

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