

# Scale up

Scaling is an important aspect with respect to any cell culture process which involves transferring a bioprocess from one bioreactor size to another which can include scale-up and scale-down. Scale-up is required when a process is being developed for smaller, easy to handle volumes, with the final goal of commercial manufacturing at a much larger scale. Scale-down on the other hand is critical to troubleshoot large scale processes, for producing smaller quantities of product and to verify process condition changes.

When moving from a small scale system to commercial manufacturing, the critical quality attributes of the product being developed and manufactured should be identical. Therefore, it is imperative that the key parameters and performance during the scaling process are kept constant.

As an example of how Aber's capacitance technology is scalable, Figure 1 and 2 show cultivations in RM 50, RM 200, STR 50, STR 200 and STR 1000 platforms (Sartorius, Germany) using capacitance to monitor biomass. Capacitance trends measured using the single use BioPAT Viamass were observed to be comparable across these platforms, thus indicating successful scale up. This demonstrates that not only can Radio Frequency Impedance measurements be used across platforms, but can also be used to determine the success of the scaling strategy across different platforms.

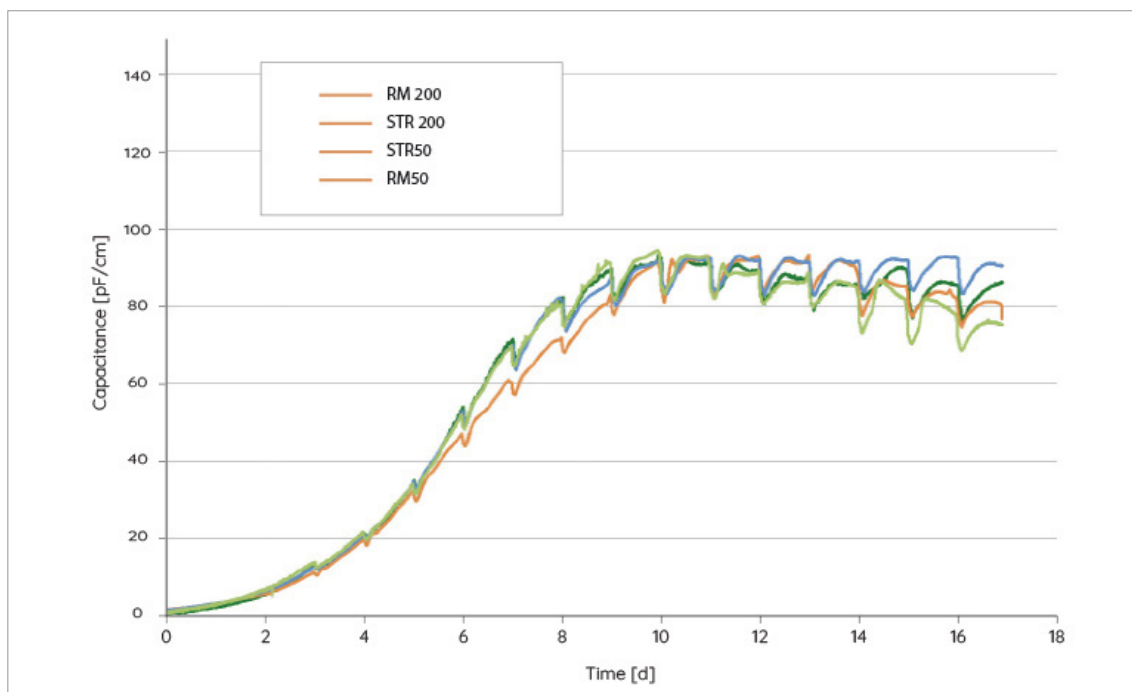


Figure 1 - Example of cultivations in SSB RMA 50, RM 200, STR 50 and STR 200 platforms using the BioPat Viamass sensor (Data Courtesy of Sartorius, Germany)

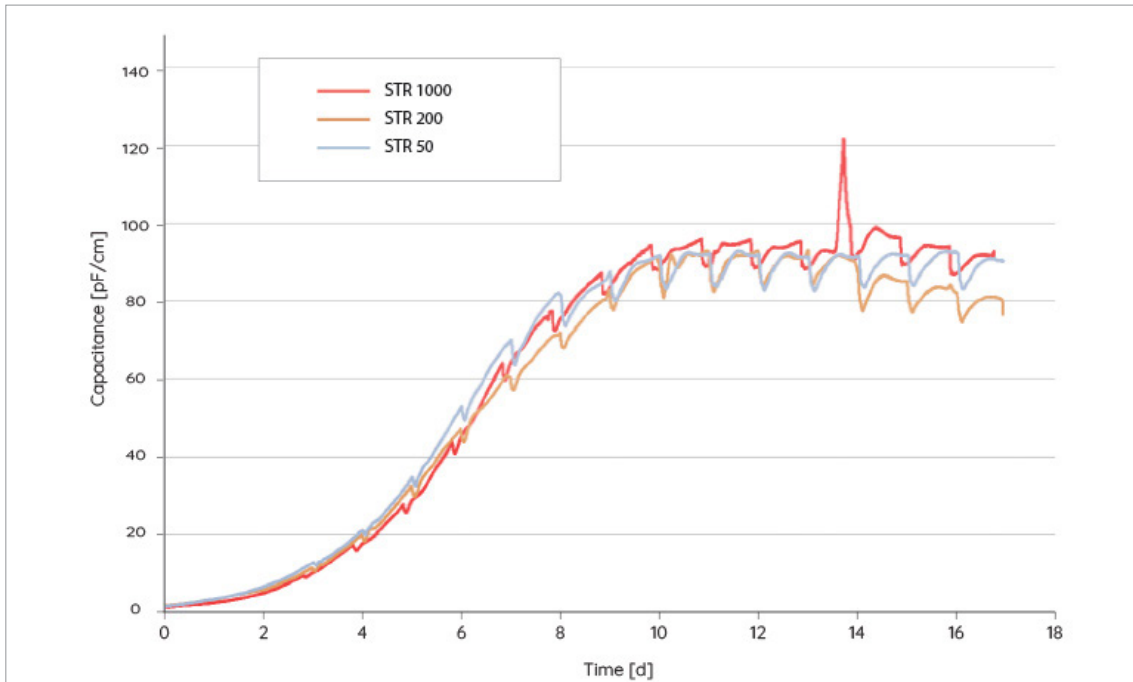


Figure 2 - Example of cultivations in SSB STR 50, STR 200 and STR 1000 platforms using the BioPat Viamass sensor (Data Courtesy of Sartorius, Germany)

In a further study conducted by Metzke *et al.* (2020), the scalability and transferability of the capacitance measurement from small scale to large scale single use bioreactors up to 2000L was investigated using a single use capacitance probe (BioPAT® ViaMass, Sartorius Stedim Biotech) for the single use applications and a 12 mm annular Futura system for multi-use applications (Aber Instruments).

The results of this study showed that measuring online Permittivity (a term used interchangeably with capacitance) allows Key Performance Indicators for biomass dynamics during process scale up to be identified across bioreactor scales ranging between 50L up to 2000L. In this study the benefits of using Permittivity measurements for scale up was also observed in the scale up of various CHO cell lines and display good correlation across all scales with Viable Cell Volume (VCV).

### Summary of the benefits:

- Use the technology across different platforms and scales successfully
- Key performance indicator for scale-up success
- Monitor cells in situ and in real time in a variety of bioreactor platforms (reusable and single use)
- Eliminates/reduces need for sampling
- Perform cell density measurements non-disruptively
- Obtain fingerprint of the process in real time
- Can be used to measure a variety of processes – batch, fed batch, perfusion, continuous processes
- Troubleshoot the process
- Control critical events during the process
- Automatic cell concentration control
- Automatic complex nutrient feed control
- Improve productivity and process consistency

### References:

Metze, S., Ruhl, S., Greller, G., Grimm, C. and Scholz, J., 2020. Monitoring online biomass with a capacitance sensor during scale-up of industrially relevant CHO cell culture fed-batch processes in single-use bioreactors. *Bioprocess and biosystems engineering*, 43(2), pp.193-205.

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