

## ONLINE CAPACITANCE MEASUREMENT FOR BIOMASS MONITORING OVER CULTIVATION SCALES AND PLATFORMS

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### Topic:

1. Sensors and their integration/use with single use technology
2. Challenges of scale-up of single use

Online capacitance measurement has become a well-established PAT tool in biopharmaceutical applications using traditional multi-use (MU) bioreactor and fermentation equipment. According to “Aspen Brook Report 2013” and “Report and Survey of Biopharmaceutical Manufacturing Capacity and Production (2015)”, over 40% of the biomanufacturing responders’ use this technology for process monitoring or control.

Simultaneously, as this PAT tool emerges in MU processes, there is a clear trend to single-use (SU) cultivation equipment in process development up to production. Consequently, prototypes of SU capacitance sensors for viable biomass detection have been developed and presented to the community throughout the past years. In 2015, SU capacitance measurement has become commercially available with significant uptake in market place.

Upstream capacity adaptation and bioprocess transfer is a necessary and challenging procedure in process development. During the scaling process, different types of bioreactors are used. Today, SU cultivation equipment is available with good scalability from small process development to production scale. Here, aligned geometrical aspect ratios and well characterized process parameters are the key for good comparability. In this scale-up context, online capacitance measurement for viable biomass monitoring can be a key parameter to monitor consistent cell growth and support the verification of process scaling.

CHO cultivation experiments were carried out in SU and MU bioreactors using different scales from 5 L to 2000 L working volume. Two different CHO fed-batch processes have been evaluated.

The comparison of the different scales results show scalability of the two model process. This was demonstrated by offline sample analysis (e.g. VCD and titer trends) as well as by the online capacitance signals. Here, the online viable biomass measurement in terms of capacitance detection showed to be an attractive tool to support scaling and process characterization.

The experiments and results will be presented and comparability between scales/systems as well as specific differences will be discussed.