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# PAT and chemometric models on CHO cell culture lines

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At the present moment, vaccine manufacturing processes are mostly done in a fed-batch culture (i.e., nutrients are fed daily to the bioreactor). Feeding occurs at determined intervals and the volumes fed do not take into account possible changes in cell concentration and nutrients in real time. This can lead to variability in cell culture batches and scalability may also be an issue, as it is difficult to guarantee the same or similar behavior of cell cultures between small-scale batches and large-scale batches. To monitor a cell culture in a bioreactor, samples are taken to follow the evolution of cell density and determine the final antigen production. However, critical quality attributes (CQAs) such as metabolites, amino acids and antigen content are generally not monitored.

To address these issues, Process Analytical Technologies (PATs), such as Raman spectroscopy or capacitance, can be directly integrated into the bioreactor via probes, enabling real-time monitoring of key attributes by acquiring fast, cheap and non-destructive measurements and also enhancing process understanding. Using PAT measurements, chemometric models can be built to not only determine the concentration of critical quality attributes and critical process parameters (CPPs) but also monitor and control the manufacturing process via Multivariate Statistical Process Monitoring (MSPM) models. The chemometric models require collecting data from a number of off-line samples, including concentrations for analytes of interest (e.g., glucose, lactate, amino acids, antigen content, etc.) for each sample (i.e., reference) and aligning them with the corresponding on-line spectra collected by a Raman probe. The MSPM models require data from a number of process parameters (e.g., temperature, pH, pO2, pCO2, air overlay, bag weight, etc.)

The resulting data is then preprocessed to filter out irrelevant and redundant information or noisy and unreliable data and can then be used to develop chemometric models that relates the Raman spectra to the concentration of key attributes and MSPM models that can be used to better monitor and control the manufacturing process. These models can be used to accurately predict the concentration of new samples in real-time based on PAT measurements.

## Type of presentation

Contributed Talk

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