Towards Model-Based Control of Granule Moisture Content during Continuous Wet Granulation
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Purpose
Controlling moisture level and moisture distribution of granules after continuous wet granulation is crucial because of the impact on final tablet quality. In addition, steering size-related metrics of the granules also requires accurate moisture regulation. The purpose of this study is to extend the regulatory control layer of the ConsiGma-25 continuous high-shear wet granulation system by adding a supervisory loop for efficient moisture control.

Methods
An in-line SentroPAT FO diode-array near infrared spectrometer is used for monitoring the moisture level. Next, a nearest-neighbour based outlier detection method is applied to fine tune the suboptimal process analyser interfacing device. Following classification, the spectral observations are projected on a latent variable space and used for moisture content prediction which is subsequently used to calculate the required feedback control action. To achieve the latter and assure effective control, the dynamic system behaviour over the entire operating range needs to be identified and used.

Results
For pre-processing of the spectral signal, the classifier is capable of making a good separation of the outlying observations. Next, a partial least squares regression model with good prediction accuracy is obtained which can predict the liquid flow rate from NIR spectral data. Results exhibit the transient behaviour of the system after stepwise excitation of the liquid flow. As a linear regression model is used for mapping the observations, the dynamic behaviour can also be approximated using a dynamic linear model which is also confirmed by the results. Regarding control, first indications of using the SentroPAT spectrometer in a process control related context are promising. Validation experiments of the proposed strategy are ongoing.

Conclusion
This study shows that common control engineering practices such as system identification and model-based control can be readily used in combination with PAT measurement tools for advanced control of a high-shear wet granulation process. Given these promising results, future steps will focus on the development of model-based controllers of additional quality attributes such as particle size distribution, leading towards a more powerful multivariable control system.