# Test Event

# Report of Contributions

Contribution ID: **3** Type: **not specified**

# Defining process operating space under uncertainty: Bayesian Design Space for complex kinetic reactions

*Thursday, 5 June 2025 08:40 (20 minutes)*

Design of experiments for process scale-up can be described as a double-edged sword for the pharmaceutical industry: intensification of experiments expands the knowledge of the process (uncertainty reduction) but increases resource expenditure. On the other hand, moving forward without enough process understanding is the first stone in a path of deviations, lack of quality, and even safety concerns.
In the past years, Bayesian sampling methodologies have surfaced to incorporate uncertainty and lead to better guided risk/optimal decision making in terms of process conditions, and reduction of required experiments. Utilizing Bayesian sampling for design space offers several significant advantages: First, it allows for the incorporation of prior knowledge, leading to more informed and efficient experimental designs [1]. Secondly, by continuously updating beliefs with new data, Bayesian sampling enables a dynamic and adaptive approach, enhancing the accuracy and reliability of results. This method also provides a rigorous framework for quantifying uncertainty, ensuring robust decision-making even in complex scenarios [2]. Additionally, Bayesian sampling can effectively identify the probability space with reduced experimental work, leading to an earlier definition of a Normalized Operating Range (NOR) within a scale-up approach to a pharmaceutical process.
In this work, a batch gas generating process with 10 different reactions occurring (reagents, products and by-products) is evaluated with the proposed Bayesian Design Space [1], with different pro-
cess parameters defined (time, temperature, reagent“A”initial concentration and reagent/solvent “B”initial concentration) and consumption CQA’s required for the same process. The results showed that a reduced amount of experiment (less than 6) were required to achieve an acceptable NOR for the process, and the outcome allowed for a safe transfer to a higher volume unit (manufacturing) with all safety and quality requirements achieved.
[1]–Kusumo, K. et al.,“Bayesian Approach to Probabilistic Design Space Characterization: A Nested Sampling Strategy”, I&EC research, 2019
[2]–Kennedy, P. et al.,“Nested Sampling Strategy for Bayesian Design Space Characterization”
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Comp. Aided Chem. Eng., 2020

## Type of presentation

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**Session Classification:** Fake Session

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# Multiscale interval PLS for spectral data modeling

*Thursday, 5 June 2025 08:20 (20 minutes)*

Process analytic technologies (PAT) are routinely used to rapidly assess quality properties in many industrial sectors. The performance of PAT-based models is, however, highly related to their ability to pre-process the spectra and select key wavebands. Amongst the modeling methodologies for PAT, partial least squares (PLS) (Wold, Sjöström and Eriksson, 2001) and interval partial least squares (iPLS) (Nørgaard et al., 2000) models coupled with well-known chemometric pre-processing approaches are the most widespread due to their ease of use and interpretability. As an alternative to classical pre-processing approaches, wavelet transforms (Mallat, 1989) provide a fast framework for feature extraction by convulsion of fixed filters with the original signal.
The proposed Multiscale interval Partial Least Squares (MS-iPLS) methodology aims to combine the ability of wavelet transforms for feature extraction with those of iPLS for feature selection. To achieve this, MS-iPLS makes use of wavelet transforms to decompose the spectrum into wavelet coefficients at different time-frequency scales, and, afterward, the relevant wavelet coefficients are selected using either Forward addition or Backward elimination algorithms for iPLS. As the wavelet filters are linear, the MS-iPLS model can also be equivalently expressed in the original spec-
tral domain, and thus, the standard PLS approaches can be applied for the sake of interpretability and feature analysis.
In this study, 10 MS-iPLS models variants were constructed using five types of wavelet transforms and two iPLS selection algorithms and compared against 27 PLS benchmarks variants using different chemometric pre-processing and interval selection algorithms. The models were compared in two case studies, addressing a regression problem and a classification problem with real data.
The results show that MS-iPLS models can either match or overcome the performance of the PLS benchmark models. For the regression problem, the PLS benchmark models were able to attain the lowest root mean squared error (RMSE), but their performance range was also wider, from an average RMSE of 0.11 (best model) to 2.46 (worst model), with most models being on the lower end. In contrast, the MS-iPLS models were consistently on the upper end, with an average RMSE ranging from 0.13 (best model) to 0.50 (worst model).
In the classification problem, MS-iPLS attained the best performance with an average accuracy of 92.7%, while the best PLS benchmark model had an average accuracy of 89.0%.
Similarly to the PLS benchmarks models, MS-iPLS still requires an exhaustive search for the optimal wavelet transform for each case study. However, with MS-iPLS the number of models to explore was significantly reduced (by a factor of 3, i.e., 1/3) without compromising on performance or interpretability.

## Type of presentation

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Contribution ID: **10** Type: **not specified**

# ONLINE MONITORING AND OPTIMIZATION OF REACTIVE EXTRUSION PROCESSES

*Thursday, 5 June 2025 08:00 (20 minutes)*

Online analysis has been widely developed to monitor the chemistry or the physics on batch or continuous processes. One of the major issues concerns the sampling part to integrate the analytical solution into the process. Optical spectroscopy is one of the most used technologies as it can be implemented directly inline and does not necessary required a sampling loop to adapt the process to the analyzer. The main advantage is the possibility to use probes or flow cells that can be immerged directly into the process. A wide range of probes exists to be able to fit with the process conditions like the temperature, pressure, or rotation speed. The possibility of using optical fibers allows to deport the analyzer from the processes to protect the sensitive part of it.
In the case of reactive extrusion processes, online analysis is not commonly used as the constraints have some difference from the classical batch or continuous processes. Harsh conditions like high temperature and pressure, melt product with high viscosity make sampling part challenging. Optical spectroscopy can monitor most of the reaction done inside an extruder and the objective here is to present how optical spectroscopy probes can be implemented directly inline. Reactive extrusion like grafting onto a polymer, depolymerization or even homogeneous mixing of polymers are presented to demonstrate its interest.
Online analysis into extruder can be used to do optimization of the process conditions to find the best quality product. An approach using near infrared spectroscopy, chemometrics tools like the PCA (Principal Component Analysis) and a design of experiments based on Bayesian optimization is also presented here. This approach allows to put in place self-optimization of the processes.

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