Towards optimal model selection: a trade-off between calibration effort and prediction accuracy

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Quantitative models have been progressively adopted as suitable supporting tool for pharmaceutical modernization, with the final goal of streamlining process development and decision making. Regulatory bodies frequently require interpretable computational modeling to justify a new healthcare product (Braakman et al., 2022; Destro and Barolo, 2022), but researchers may have several competing models available for the same system. The focus is on the model prediction capability with respect to product critical quality attributes and key performance indicators – herein generically referred to as key indicators (KIs). The required confidence towards the prediction of a target KI strongly impacts the selection of a suitable candidate model. Recalling that the predictive capability of a given model largely depends on the precision of the model parameter estimates, we can select the one which ensures that the prediction of the KI of interest falls within the range of preset tolerance, while simultaneously needs the lower experimental effort for the estimation of its model parameters.

In this study, we propose a workflow to support the critical selection of one candidate model. The methodology combines tools typically adopted for parameter estimation purposes – i.e., model-based design of experiments (MBDoE) – with techniques based on data analytics, which enhance readability and interpretability of results (Geremia et al., 2023). Two pharmaceutical models are used as case studies. The implementation of the methodology is critically discussed, demonstrating the effectiveness of the approach and the benefits of the proposed techniques. Results show that when the tolerance requirements on the prediction of model KIs are not strict, a simplified model can be enough, i.e., a low number of experiments is sufficient. Instead, if strong reduction of uncertainty in model prediction is required, a more complex model is typically the only possible choice to satisfy the KI requirements with a feasible number of experimental runs. We also demonstrate how the choice of the model may be influenced by the available instrumentation, as achieving preset fidelity in model predictions may require advanced measurement devices.

Keywords: *model selection, parameter estimation, prediction fidelity, experimental effort.*

References

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