BIO PROCESS AND SYSTEMS ENGINEERING TUHH
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# Model-assisted design of an immobilized enzyme process

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## Objective

- The **design and optimization** of biotechnological processes is still time- and cost-intensive[1].
- **Model-assisted Design of Experiments (mDoE)** can be used to mathematically model bioprocesses and efficiently investigate the experimental space[2].
- In this work, **mDoE** is used to predict optimal process conditions under uncertainty, **increase process knowledge** and **reduce the final experimental effort** for an immobilized enzyme process.

## Immobilized enzyme process

- **Two-step reaction:** N-acetyl-D-glucosamine to N-acetylneuraminic acid (Neu5Ac)[3]
- First reaction step (uni-uni mechanism): **Epimerisation**

  N-acetyl-D-glucosamine ⇌ N-acetyl-D-mannosamine

- Second reaction step (ordered bi-uni mechanism): **Aldol condensation**

  N-acetyl-D-mannosamine + sodium pyruvate ⇌ N-acetylneuraminic acid

- The reaction is performed in a **continuous flow reactor system**

## Mathematical process model

- Use of a **diffusion-convection-reaction model** (including enzyme kinetics) and "Method of Lines" approach to model a biocatalytical process in a continuous flow reactor[4]
- Description of **location- and time-dependent changes** in substrate and product concentrations
- Reactor length is equally segregated into ***n* number of grid-nodes** in axial direction (consecutive calculation)

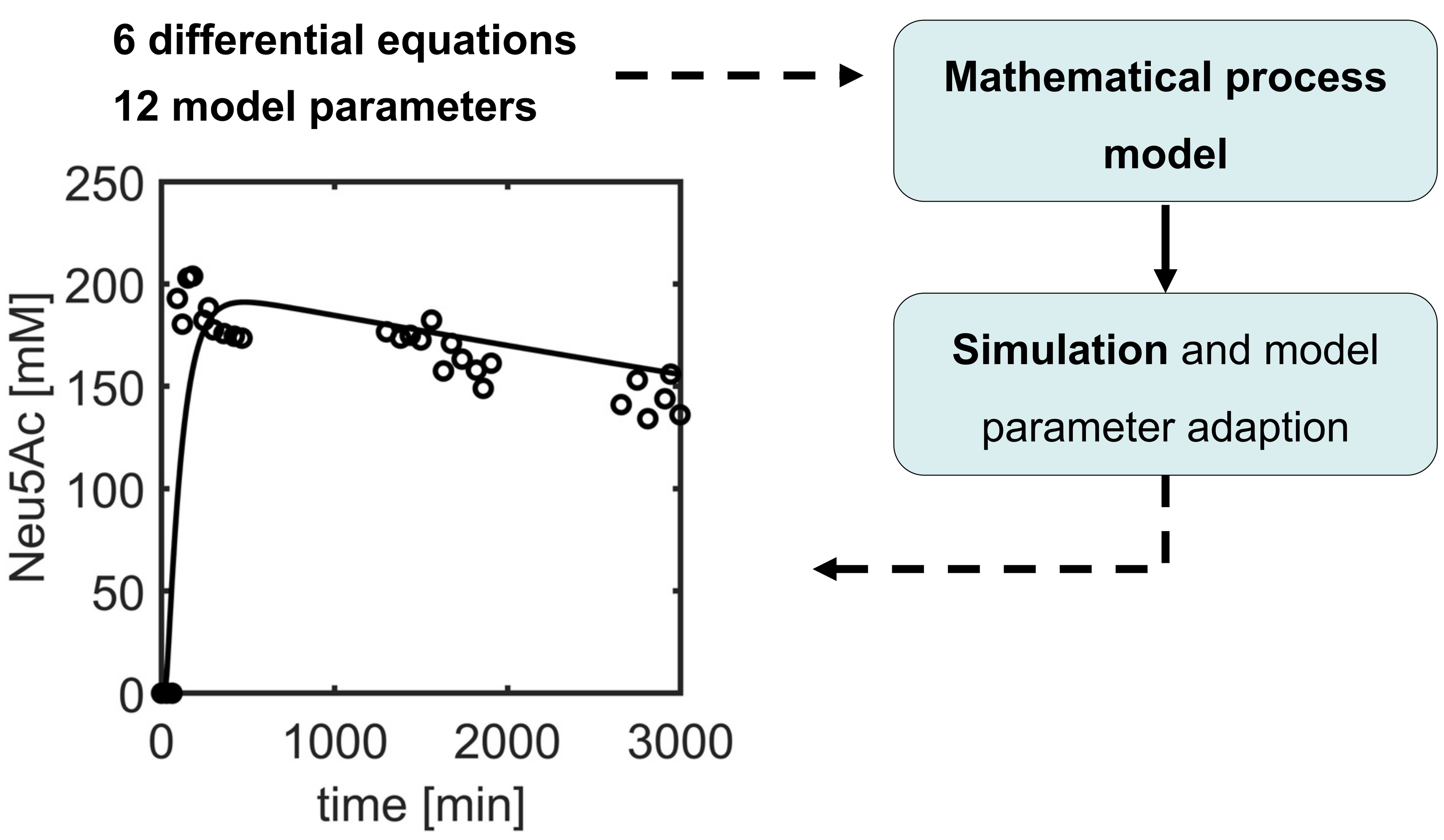
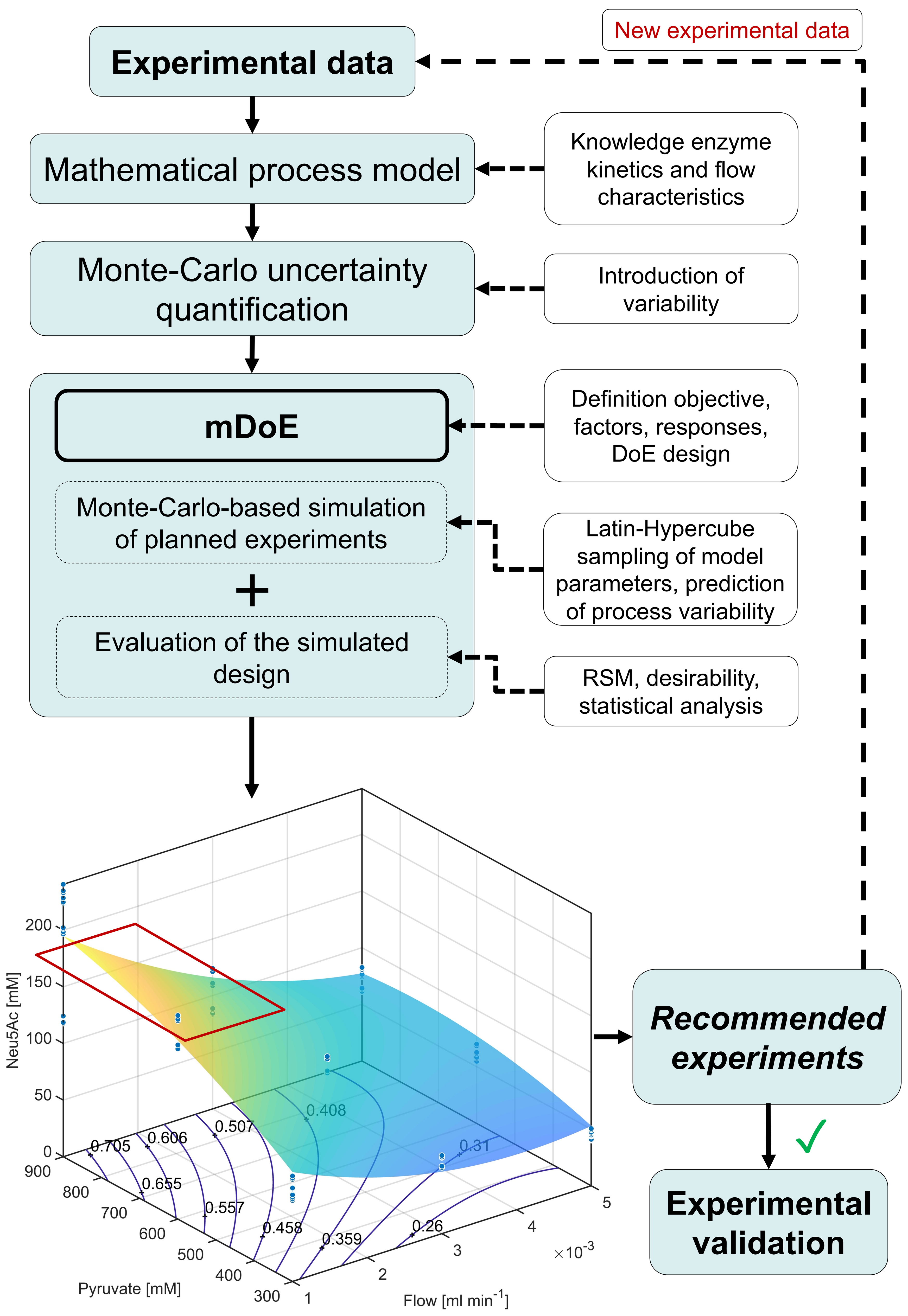



**Figure 2:** Neu5Ac concentration measured at reactor outlet, reactor length: 30.3 cm, flow rate: 2 mL min$^{-1}$, T= 40°C, pH= 8, 4044 U epimerase, 3479 U lyase, - simulated data, ∘ experimental data

## Model-assisted design

**Aim: Application** of a model-assisted design procedure based on a mathematical process model and statistical analysis to an **immobilized biocatalytical process**.




## Summary and Outlook

- Kinetic model and "Method-of-lines" approach **applicable to simulate flow** and **describe the process dynamics** of the two-step reaction system ✓
- Number of experiments can be **significantly reduced by mDoE** ✓
- **Process knowledge increased** ✓

➔ Application of workflow to biocatalytic processes, e.g., under hydrostatic pressure

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**References**

**[1]** Moser et al. (2021), doi.org/10.1007/s00449-020-02478-3
**[2]** Möller et al. (2020), doi.org/10.1016/j.compchemeng.2019.106693
**[3]** Zimmermann et al. (2007), doi.org/10.1007/s00253-007-1033-6
**[4]** Hamdi et al. (2007), doi.org/10.4249/scholarpedia.2859

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