

Digital Twin Development for Cascade Reactions in Continuous Flow

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Background

Cascade (tandem) reactions

- multiple reactions involved
- attractive route to intensified chemical manufacturing
- complex interplay of operating conditions, reaction steps, and design choices
- typically performed as one-pot batch processes
- limited range of conditions that can be explored

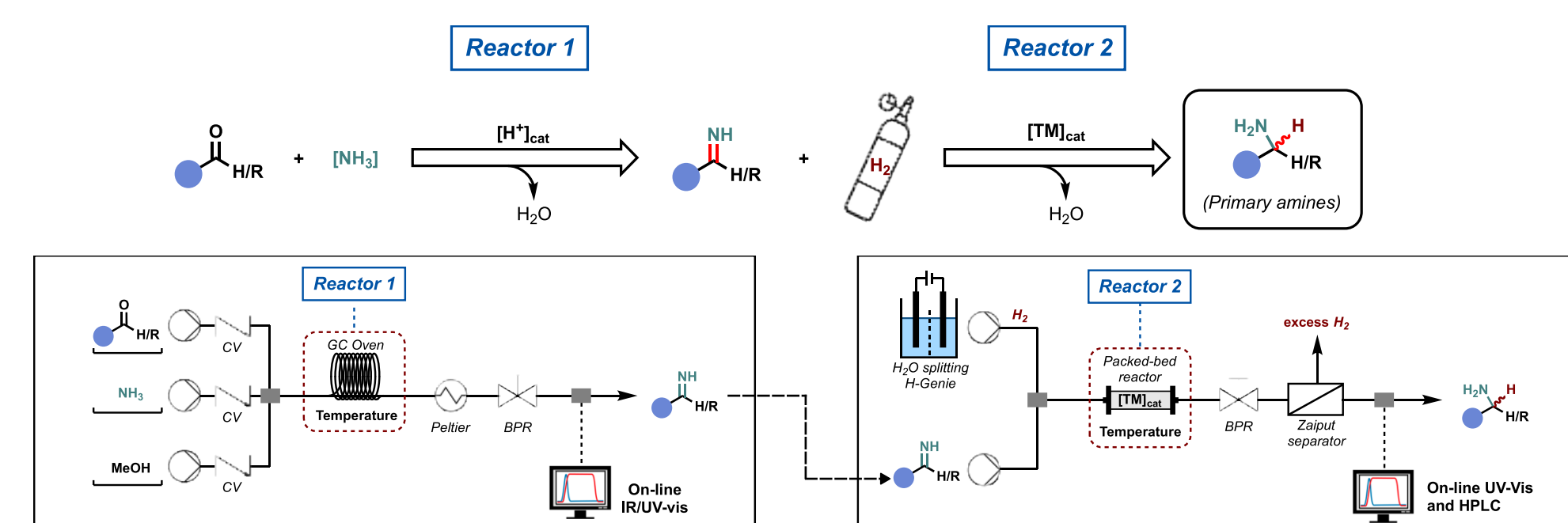
Continuous flow chemistry

- allows rapid investigation of broad range of operating conditions
- inherently safer
- fully automated experimental setup and data processing

Chemistry of interest: reductive amination

- amines are key building blocks in many industrial sectors
- carbon–nitrogen bond formation + hydrogenation

Experimental setup



Digital twin development

A **digital twin** is a virtual representation of a physical system or process, connected to its real-world counterpart through real-time data

Applications

- scale-up
- process monitoring
- real-time process optimization
- operator training

Development strategy

- reaction steps decoupled and analyzed separately
- initial focus on C–N bond formation

Fully data-driven modeling

Gaussian Process (GP) models

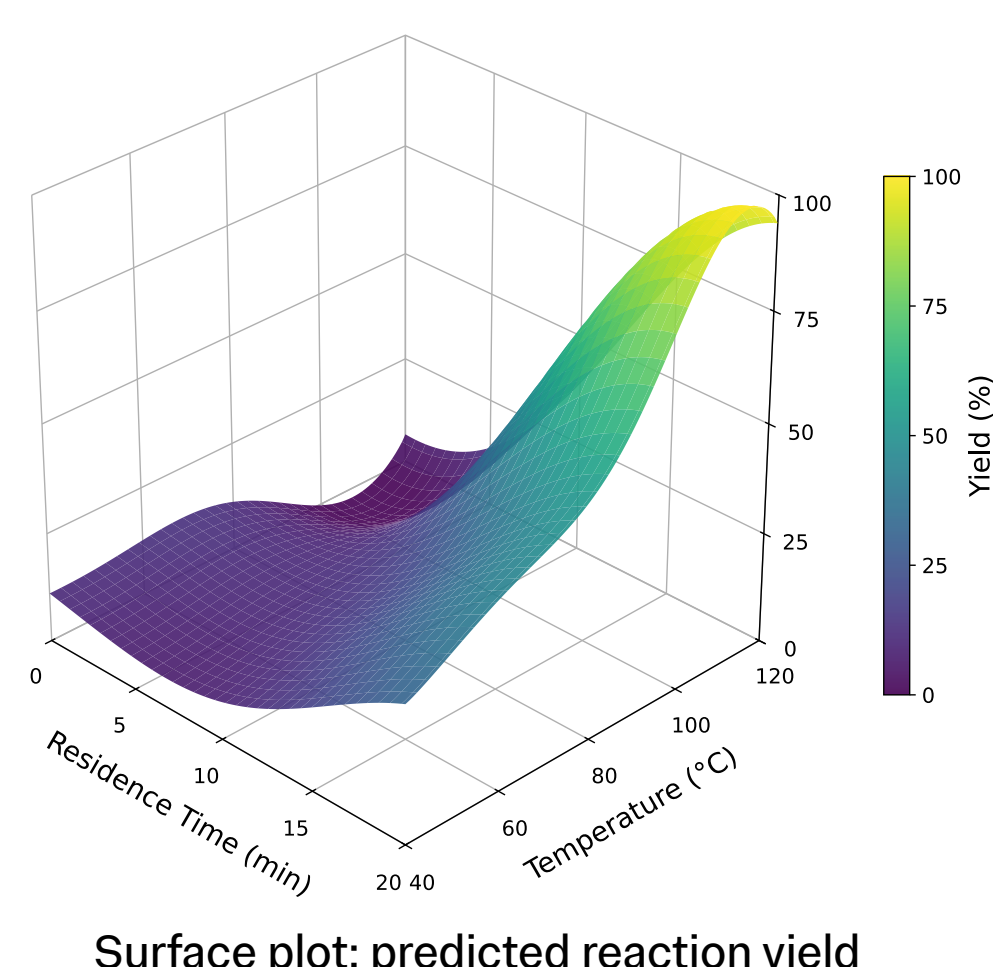
- simple structure: mean and covariance functions
- computationally cheap
- work well with small datasets

Drawbacks

- provide limited insight into the process
- cannot extrapolate beyond observed data

Available data

- input: flow data
- output: HPLC chromatograms



Motivations for mechanistic modeling

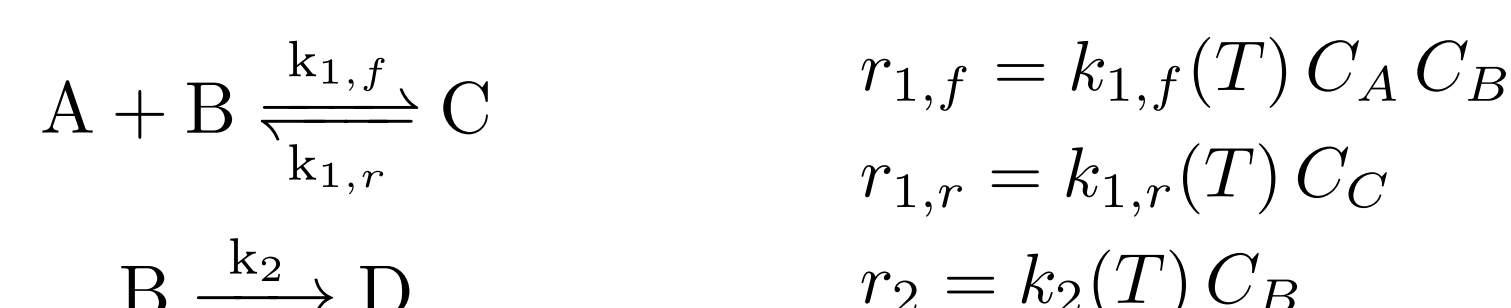
Experimental observations

- nitrogen source degrades, particularly at high residence time and temperature
- hysteresis effects: output data depend on reaction history
- part of the inlet piping is installed inside the heated reactor, worsening the degradation issue

Solution

- incorporate mechanistic information in the form of kinetic rate expressions
- explicitly model the reactant degradation
- apply residence time deconvolution twice to account for the upstream decomposition

Modeled reactions



Additional considerations

- Arrhenius dependence on temperature
- only the outlet concentrations of A and C are available
- density functional theory calculations used to assist parameter estimation

Hybrid digital twin

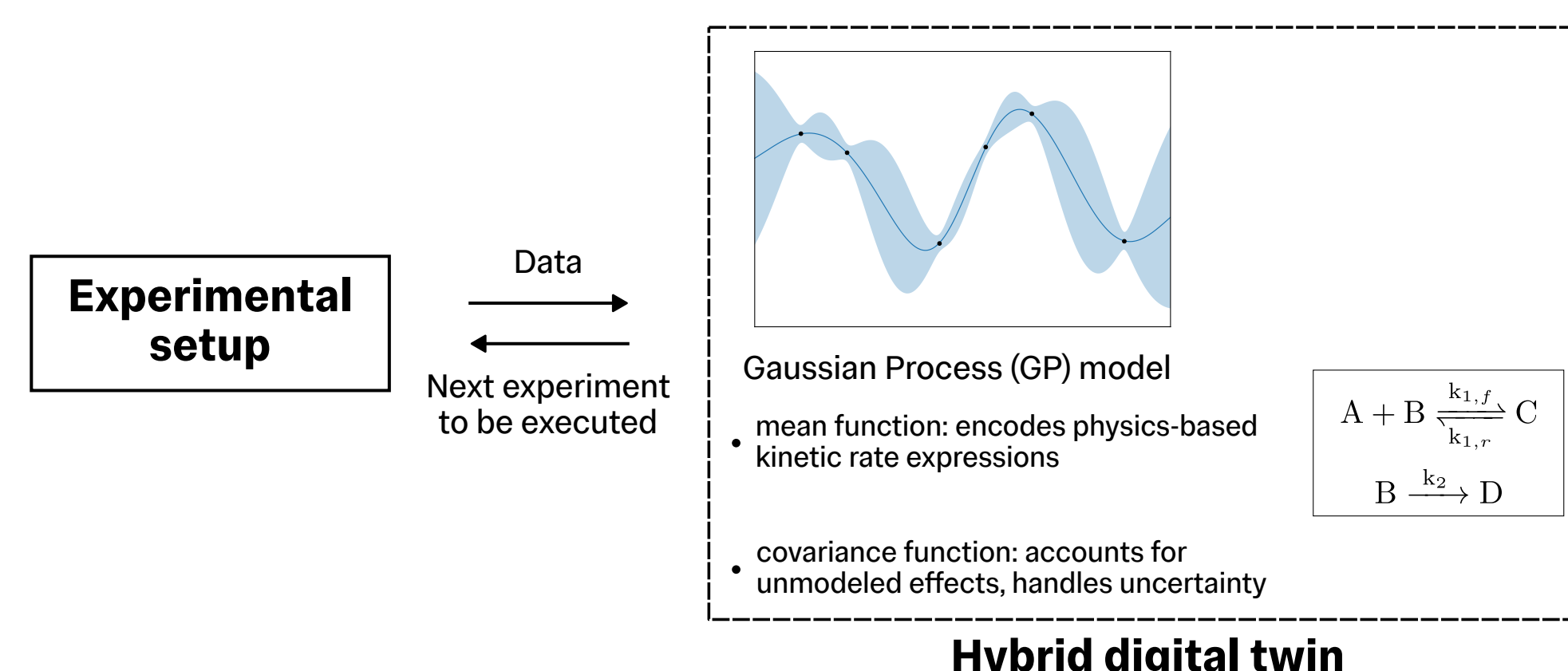
Integration of data-driven and mechanistic components

- estimate the model parameters first, then train the GP model on the uncertainty
- use mechanistic information as GP mean, fit all hyperparameters together

Objectives

- exploit the two-way connection between digital twin and experimental setup
- apply Bayesian optimization, model-based design of experiments to further accelerate the development

Digital twin structure



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