Real-Time Kinetic Hard-Modelling for the Optimisation of Reaction Conditions and the Detection of Process Upset in Semi-Batch Reactors

Julien Billeter\textsuperscript{1}, Yorck-Michael Neuhold\textsuperscript{1}, Graeme Puxty\textsuperscript{2}, Konrad Hungerbühler\textsuperscript{1}

\textit{Contact: julien.billeter@chem.ethz.ch}

\textsuperscript{1}ETH Zürich, Institute for Chemical and Bioengineering, Safety and Environmental Technology Group, Zürich, Switzerland.
\textsuperscript{2}CSIRO Energy Technology, PO Box 330, Newcastle NSW 2300, Australia
Motivation

- **Loss of productivity**: Fluctuations in reaction processes are partly due to variations in the concentration of initial reactants (sub-optimal operating conditions).

Another source of fluctuations comes from impurities present in the initial reactants causing unexpected side reactions.

- **Loss of time**: Initial concentrations are often determined by offline analysis (e.g. HPLC, spectroscopy) and can result in delaying the batch start.
Trends in favour of online Kinetic Hard-Modelling (KHM)

- **Improving knowledge**: Fine chemical industries try to improve manufacturing by elucidating the underlying kinetic model (rate law) of processes whose patents have expired.

- **Multivariate on-line sensors**: Recent progress in Process Analytical Technology (PAT) allows now the monitoring of processes in real time using multivariate probes.
KHM in Research phase

- Kinetic hard-modelling compares a measured signal with a modelled one obtained from a 1st principle hard model (rate law). The residuals are used as driving force for the least-square optimisation of the kinetic parameters.

\[
\text{Hard model} = \text{function} \left( \text{kinetic parameters, IC, CV, NCV} \right)
\]

- IC Initial Conditions e.g. initial concentrations
- CV Control Variables e.g. dosing rate, temperature
- NCV Non-Controlled Variables e.g. concentration of the dosing agent

- Our kinetic hard-modelling approach is a calibration free method in the sense that the calibration (the absorptivity spectra) is nested into the non-linear optimisation and linearly fitted at each iteration.
Online KHM in Production phase

- In production phase, differences between batches result from different IC and/or NCV that can be optimised in a non-linear way, setting the kinetic parameters to the values found during the research phase.

- Subsequently, Control Variables (e.g. dosing flow rate) can be optimised and/or the process can be monitored for detection of possible faults.
Concept of online KHM

Phase 1: OPTIMISATION OF THE IC/NCV AND PROCESS UPSET DETECTION

Optimisation of IC/NCV (e.g. $c_{0,\text{react 1}}$ and $c_{\text{dos, react 2}}$) with kinetic parameters fixed.
Possible Process Fault is detected.

Phase 2: OPTIMISATION OF THE CV

Extrapolation to a future time and optimisation of future CV under constraints to maximise $\Psi$ (= Yield, Selectivity or Conversion).

\[
\max_{f(t)} \Psi(t_{\text{end}}) \\
\text{s.c. } V(t_{\text{end}}) \leq V_{\max} \\
f_{\min} \leq f(t) \leq f_{\max}
\]

Phase 3: OBSERVATION PHASE

Process running under optimal CV.

---

$\bar{c}_{0,\text{react 1}}$ = mean initial concentration,
$f_{\text{opt}}(\bar{c}_{0,\text{react 1}})$ = optimum dosing rate for $\bar{c}_{0,\text{react 1}}$
Kinetic model

Absorptivity spectra

Heat released
modelled:
\[ \Delta H_{r1} = -10.0 \text{ kJmol}^{-1} \]
\[ \Delta H_{r2} = -5.0 \text{ kJmol}^{-1} \]
unmodelled:
\[ \Delta H_{r3} = -10.0 \text{ kJmol}^{-1} \]

modelled:
\[ A + B \quad k_1 = 0.0656 \rightarrow C \]
\[ A + C \quad k_2 = 0.0383 \rightarrow D \]
unmodelled:
\[ B + I \quad k_3 = 0.0468 \rightarrow S \]

A : dosed
C : wanted product
D : side product
I : contaminant in A

UV-vis
mid-IR

Calorimeter

A, I (as contaminant)
Base Case simulation
Mean IC / NCV
No process fault

\[
\begin{align*}
IC: \bar{c}_0 &= \begin{bmatrix} 0 & 1 & 0 & 0 & 0 & 0 \end{bmatrix} \\
NCV: \bar{c}_{dos} &= \begin{bmatrix} 2 & 0 & 0 & 0 & 0 & 0 \end{bmatrix} \\
f_{opt} (\bar{c}_0, \bar{c}_{dos}) &= 0.025
\end{align*}
\]
Base case

IC: $c_0 = [0 \ 1 \ 0 \ 0 \ 0 \ 0 \ 0]$

$A \ B \ C \ D \ I \ S$

NCV: $c_{dos} = [2 \ 0 \ 0 \ 0 \ 0 \ 0]$

Concentration profiles

$V_0 = 0.3, \ V_{end} = 0.6 \ (V_{max} = 1)$

Time normalised to normal batch duration (1: one normal batch duration)

Dosing rate (a CV)

$f_{opt}(\bar{c}_0, \bar{c}_{dos}) = 0.025 \ (f_{max} = 1)$

Spectroscopy

$\Psi = \text{Yield}$

Calorimetry

$\Psi(t_{end}) = \text{Yield}_{C/A, \ opt}(\bar{c}_0, \bar{c}_{dos}) = 46.98\%$
Optimisation of the **Initial Conditions (IC)** and **Non-Controlled Variables (NCV)**

and subsequent optimisation of the **Control Variables (CV)**

\[
\text{IC: } \bar{c}_0 - 15\% = [0 \ 0.85 \ 0 \ 0 \ 0 \ 0] \\
\text{NCV: } \bar{c}_{dos} + 15\% = [2.30 \ 0 \ 0 \ 0 \ 0 \ 0] \\
\]

\[
f_{\text{opt}} (\bar{c}_0 - 15\%, \bar{c}_{dos} + 15\%) = ?
\]
Optimisation of the Control Variables (CV)

**Spectroscopy**

- Yield incr.%
- Error of prediction %

**Calorimetry**

- Yield incr. %
- Error of prediction %

<table>
<thead>
<tr>
<th>Parameter</th>
<th>UV-vis</th>
<th>Calorimetry</th>
</tr>
</thead>
<tbody>
<tr>
<td>Time of calculation</td>
<td>0.516</td>
<td>0.616</td>
</tr>
<tr>
<td>$\sigma_p/p$</td>
<td>$\leq0.20%$</td>
<td>$\leq1.70%$</td>
</tr>
<tr>
<td>Calculated dosing rate</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>Yield increase</td>
<td>+4.05%</td>
<td>+3.30%</td>
</tr>
<tr>
<td>Maximum Yield increase</td>
<td>+4.08%</td>
<td>+4.08%</td>
</tr>
</tbody>
</table>

Extrapolation time = 0.0167
### CV optimisation and comparison with offline analysis

<table>
<thead>
<tr>
<th>IC</th>
<th>NCV</th>
<th>Signal</th>
<th>Yield increase</th>
<th>Error of prediction</th>
<th>Time criterion for online KHM to be more efficient than offline analysis</th>
</tr>
</thead>
<tbody>
<tr>
<td>0% (base case)</td>
<td>0% (base case)</td>
<td>Spectroscopy</td>
<td>0.09%</td>
<td>+0.00%</td>
<td>always</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Calorimetry</td>
<td>0.09%</td>
<td>+0.00%</td>
<td>always</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Offline</td>
<td>0.09%</td>
<td>-</td>
<td>-</td>
</tr>
<tr>
<td>-15%</td>
<td>+15%</td>
<td>Spectroscopy</td>
<td>4.05%</td>
<td>+0.02%</td>
<td>0.02%</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Calorimetry</td>
<td>3.30%</td>
<td>+0.30%</td>
<td>0.75%</td>
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<tr>
<td></td>
<td></td>
<td>Offline</td>
<td>4.08%</td>
<td>-</td>
<td>-</td>
</tr>
<tr>
<td>-30%</td>
<td>+30%</td>
<td>Spectroscopy</td>
<td>11.06%</td>
<td>+0.15%</td>
<td>3.30%</td>
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<tr>
<td></td>
<td></td>
<td>Calorimetry</td>
<td>8.47%</td>
<td>+0.45%</td>
<td>5.76%</td>
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<tr>
<td></td>
<td></td>
<td>Offline</td>
<td>14.72%</td>
<td>-</td>
<td>-</td>
</tr>
</tbody>
</table>
Optimisation of the CV

- For this particular mechanism and these pure component spectra, spectroscopy can be used to optimise online the CV.

- Due to its univariate nature, calorimetry produces a low improvement in yield when used in online KHM.

- For extreme variations in the IC/NCV, online KHM is only better than offline analysis if the time required for the offline analysis largely delays the batch start.

- For this particular mechanism, the concentration of the dosing agent has the most impact on the yield.
Process Fault Detection (PFD) or Process Upset Detection

\[ A B C D I S \]
\[ IC: \overline{c}_0 = [0 \ 1 \ 0 \ 0 \ 0 \ 0] \]
\[ NCV: \overline{c}_{dos} + I = [2 \ 0 \ 0 \ 0 \ c_{dos}, I \ 0] \]
\[ f_{opt} (\overline{c}_0, \overline{c}_{dos}) = 0.025 \]
SSQ and Standard deviation of the residuals as Process Fault indicators

**SSQ**

**σ\(_{\text{residuals}}\)**
Known absorptivity spectra (in eigen-space) as Process Fault indicators

$$SV^T$$ (benchmark: spectrum of C)

Without fault

With fault ($c_{dos, i} = 0.1$)

$$\sigma_p / p \leq 0.7\%$$

<table>
<thead>
<tr>
<th>Spectrum selected for PFD</th>
<th>$PVE_A$ at $t_{end}$</th>
</tr>
</thead>
<tbody>
<tr>
<td>Spectrum of A</td>
<td>85.51%</td>
</tr>
<tr>
<td>Spectrum of B</td>
<td>98.50%</td>
</tr>
<tr>
<td>Spectrum of C</td>
<td>78.33%</td>
</tr>
<tr>
<td>Spectrum of D</td>
<td>69.82%</td>
</tr>
</tbody>
</table>

$PVE_A$
Known reaction enthalpies as Process Fault indicator

\[ \Delta H_{r,1} \]

\[ \Delta H_{r,2} \]

With fault
\( c_{dos,i}=0.5 \)

Without fault

\( c_{dos,i}=0.5 \)
Process Fault Detection

- Spectroscopy and calorimetry can be used to detect Process Faults

- The best process fault indicators are generally the ones based on a priori information, i.e. the absorptivity spectra and the reaction enthalpies
Conclusion

- The capabilities of online KHM have been demonstrated by:
  - Optimisation of the Initial Conditions (IC) and Non-Controlled Variables (NCV)
  - Subsequent optimisation of the Control Variables (CV)
  - And constant Detection of possible Process Faults (PFD)
- Next, online KHM will be applied on experimental data for a simple chemical system.
Thank you for your attention