Cognitive Chemical Manufacturing

Dial-a-Molecule Annual Meeting 2018: Enabling Synthesis

9-10th July

i-HUB, Imperial College, White City Campus

Dr Tom Chamberlain & Dr Federico Galvanin
What is “cognitive chemical manufacturing”?

• **Cognitive chemical manufacturing** is an *information framework* where data across chemical systems, equipment and processes are utilised to derive actionable insight across the entire value chain from design through manufacture to support.

• Cognitive manufacturing drives at **key productivity improvements** in quality, efficiency, and reliability of the manufacturing environment.

• It employs **cognitive technologies**, including
  - **Intelligent assets and equipment**: utilizing connected sensors, analytics, and cognitive capabilities to sense, communicate and self-diagnose issues in order to optimize performance and reduce unnecessary downtime
  - **Cognitive processes and operations**: analyzing a variety of information from workflows, context, process, and environment to drive quality, enhance operations and decision-making
  - **Smarter resources and optimization**: combining various forms of data from individuals, location, usage, and expertise with cognitive insight to optimize and enhance resources such as labor, workforce, and energy
Cognitive Chemical Manufacturing

• £2.5M Project using Machine Learning to Optimise Chemical Manufacturing starting July-Sept 2018
• EPSRC call on ‘Digital Manufacturing Potential’
• Led by IPRD Leeds (PI: Richard Bourne)
• Academic Partners: University College London, University of Nottingham, Hartree Centre
• Industrial Support: IBM, AstraZeneca, Swagelok and Promethean Particles
• 4 year project with 14 years of PDRA time
Partner Roles

Swagelok
Reactor Design

Lab-Bot Design
Pilot-Bot Design
Integration of External Algorithms
Organic Synthesis Experiments
Cognitive Systems
Pilot Demonstration (Alfa Laval)

University of Nottingham
Nanoparticle Synthesis

IBM
Bayesian Optimisation Algorithm
Cloud-based Experimental Marketplace

AstraZeneca
Industrial Demonstration Model Case Studies

Promethean Particles
Industrial Demonstration Model Case Studies
Pilot Studies

UNIVERSITY OF LEEDS

UCL
Kinetic Models and Parameterisation Sim-Bot Development
Project Vision

- Experiments are performed by a linked network of multiple reactor systems – like multi threaded computer cores.
- Individual reactions are allocated from the cloud based on reactor capability and the efficiency of performing experiments.
Synthesis in flow

API synthesis
Lab scale
• Leeds University
• AZ

Plant scale
• Leeds University

Nanomaterial synthesis
Lab scale
• Leeds University
• Nottingham University

Plant scale
• Promethean Particles
• Algorithmic approach to optimising chemical reactions.
• New experiments generated based on previous results *via* a feedback loop (from the cloud).
• Optimum is verified by experiment.
Optimisation Limits

<table>
<thead>
<tr>
<th></th>
<th>Ester flow</th>
<th>MeNH₂</th>
<th>Temperature</th>
</tr>
</thead>
<tbody>
<tr>
<td>Lower</td>
<td>0.1 mL/min</td>
<td>1 eq</td>
<td>0 °C</td>
</tr>
<tr>
<td>Upper</td>
<td>0.4 mL/min</td>
<td>10 eq</td>
<td>130 °C</td>
</tr>
</tbody>
</table>
Optimum Conditions:
8.57 min, 10 °C,
10 eq MeNH₂, 94%

21 experiments
< 11 hours
Design of Experiment
Central Composite Faced Design (CCF)

18 experiments
5.5 hours
Design of Experiments
Contour Plot (0 °C)

Model Optimum:
9.85 min, 7.6 °C, 9.79 eq MeNH₂, 96 %

Self-Optimisation:
8.57 min, 10 °C, 10 eq MeNH₂, 94%

Predictor: 96%
iPRD focus:
“Supporting chemical companies of all sizes by providing understanding and solutions for product and process development”

• Pre competitive fine chemical manufacture related R&D delivering process understanding & new technology
• Research focus driven by challenges in manufacturing
• Generate students with an aptitude for process R&D
• Facilities
  • Industrial standard development lab with Pilot Scale capabilities
  • 20 L scale kg laboratory funded by Yorkshire Forward/EU (ERDF)
  • 5 m FC for flow processing
NP synthesis - in flow using a new Lab-Bot
NP synthesis - in flow using a new Lab-Bot

- Metal oxides
- Core shell NPs
- Hybrid materials
NP synthesis - Scale up

- Printed electronics
- Metal Organic Frameworks (MOF)
- Green energy and catalysts
- Healthcare/medical
- Nanocomposites (incl. plastics & coatings)
Kinetic models and parametrisation

Simbot
• UCL

Control/monitoring
Lab and plant scale
• University of Leeds

Kinetic modelling
• UCL
LabBots (Leeds, Nottingham, Swagelok)

SimBots (UCL)

CLOUD PLATFORM (IBM)

Focus
- Integration of information fluxes/data
- Integration of experimental and simulation activities

Generation of Scalable and Sustainable Industrial Chemical Processes (AZ, PP)

PilotBots (Leeds/Promethean Particles)
The UCL Team

Dr. Federico Galvanin (UCL Lead)

- Design of Experiments (DoE) and statistical planning
- Model-based Design of Experiments (MBDoE)
- Kinetic modelling in catalytic systems
- Machine learning applications to model identification
- Modelling of stochastic systems

Dr. Michail Stamatakis

- Computational catalysis
- Chemical reaction engineering
- Multiscale modelling
- Microkinetic modelling
- Kinetic Monte Carlo
UCL Team Contribution to the Project

Co-supervision (with Michail) of a 4-year PDRA at UCL

Main goal of the UCL team: to develop a SimBot platform for the automated generation and identification of kinetic models based on kinetic motifs.

The Simbot will be developed in a high level programming language, and it will integrate:

• Automated generation of kinetic motifs/model structure generation
• Online model-based design of automated experiments
• Data analysis
• Process simulation
• Machine learning techniques for model identification

The Simbot will be integrated in the cloud systems for the easy simulation, identification and optimisation of process models.
Development of the Simbot

Online design of experiments for model identification

Generation and analysis of complex reaction networks

Online design of experiments for fast identification of kinetic models

Online design of experiments for model identification

Identification of a suitable kinetic model structure

Identification of the kinetic parameters

Set of an optimal experiment

MBDoE for kinetic model discrimination

MBDoE for improving parameter precision

Optimally informative

Feasible

Operability
Controllability
Safety
Process Economics

Minimisation of the experimental effort

Framework for the online identification of parametric models

Identification requires:
- a precise estimation of $\theta$
- the conditions $u \in U$ where the model is reliable, i.e. the domain of validity

approximated model structure $\hat{y} = g(\theta, u)$

The procedure continues until a pre-defined statistical quality of parameters is achieved

$\text{Parameter statistics} \quad \text{Model-Based Data Mining} \quad \text{Model Reliability Map} \quad \text{Constrained MBDoE}$

$\theta_1 \quad \theta_2 \quad 95\%$ confidence ellipsoid

$\hat{y} = g(\theta, u)$

$R(u) = 0$

$R > 0$

$R < 0$

$I(u)$

optimal conservative experimental conditions for improving parameter statistics

additional experimental data

1M. Quaglio, E.S. Fraga, E. Cao, A. Gavriilidis, F. Galvanin (2018), Chemometrics and Intelligent Laboratory Systems, 12, 134-149.
Overall vision

• Individual reactions are allocated from the cloud based on reactor capability and the efficiency of performing experiments

• Outputs
  • Optimal design of experimental conditions/kinetic modelling (speed/resource/cost)
  • Demonstration of optimisation using pilot scale flow reactors (IPRD/Promethean Particles)
  • Reactors will be cognitive, capable of detecting possible future failures and performing experiments in reaction to previous results
  • Model-based process design and optimisation
Cognitive Chemical Manufacturing

- Federico Galvanin (UCL)
- Michail Stamatakis (UCL)
- Frans Muller (Leeds)
- Richard Bourne (Leeds)
- Tom Chamberlain (Leeds)
- Edward Lester (Nottingham)
- Brian Taylor (AstraZeneca)
- Graeme Clemens (AstraZeneca)
- Selina Ambrose (Promethean Particles)
- Edward Pyzer (IBM/Hartree)