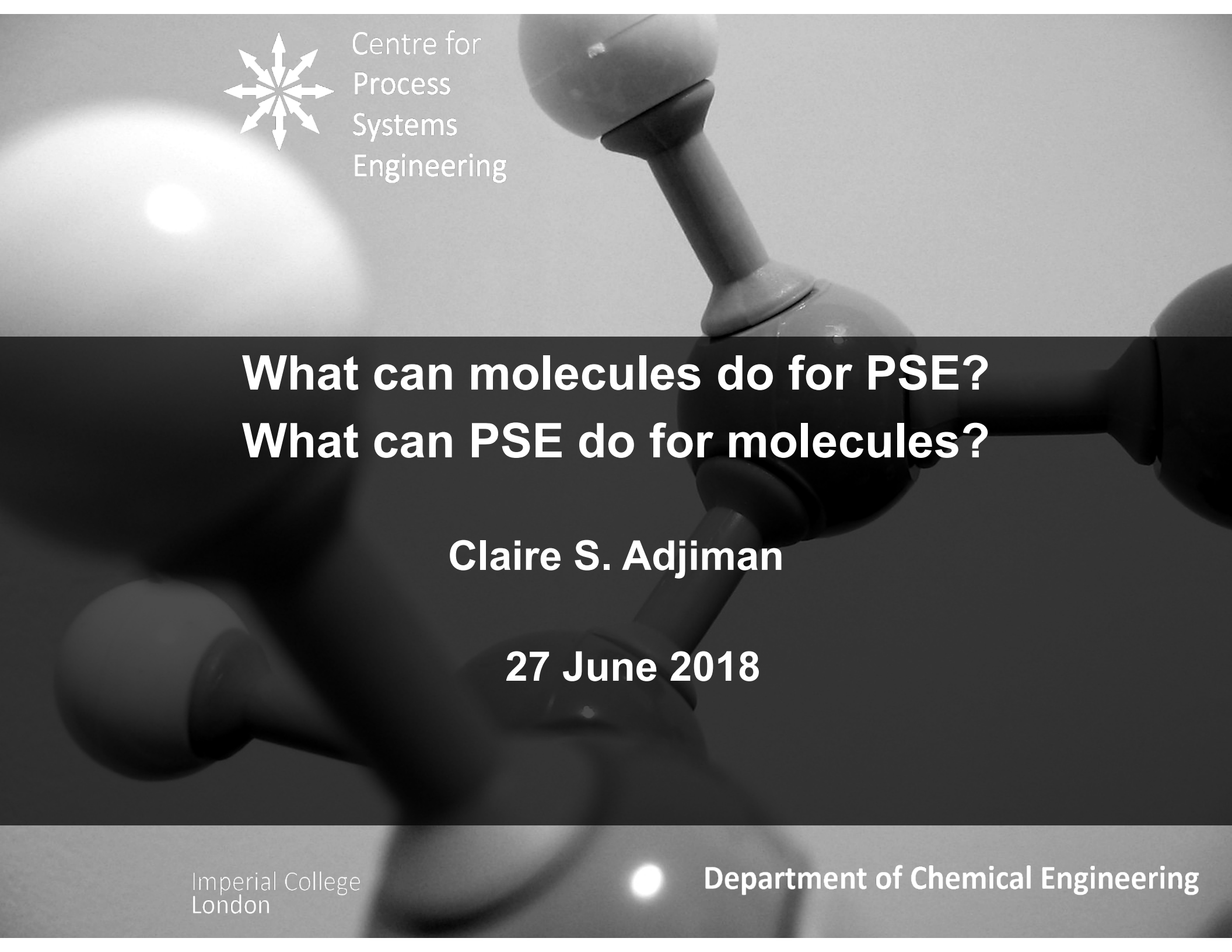


Centre for Process Systems Engineering

What can molecules do for PSE?
What can PSE do for molecules?

Claire S. Adjiman

27 June 2018

Imperial College London

Department of Chemical Engineering

Let's define "Molecules"

Processing materials

- For separation, transport, reaction, heat control
  - Solvents, adsorbents, membranes
  - Catalysts, additives
  - Heat transfer fluids

Chemical products

Gani, Ng, *Comp Chem Eng*, 2015, **81**, 70

- Molecular products
  - API, plastic
- Formulated products
  - Drug product, personal care products, paints
- Devices / Functional products (barriers, delivery)
  - transdermal patch, filter cartridge

Outline

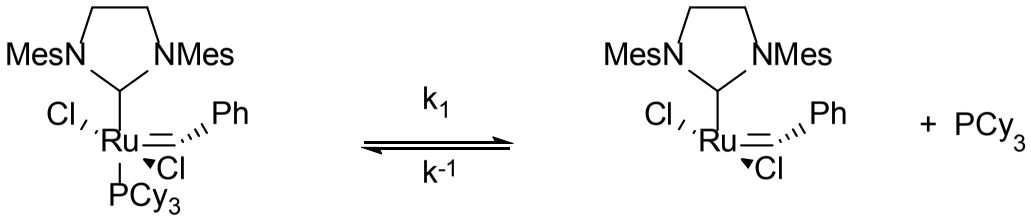
- What molecules can do for PSE
  - Why design processing materials?
  - Challenges in integrated molecule and process design
- What PSE can do for molecules?
  - “Simple” mixtures
  - Embedding experiments in product design

IMPACT OF PROCESSING MATERIALS ON PROCESS PERFORMANCE

Process feasibility

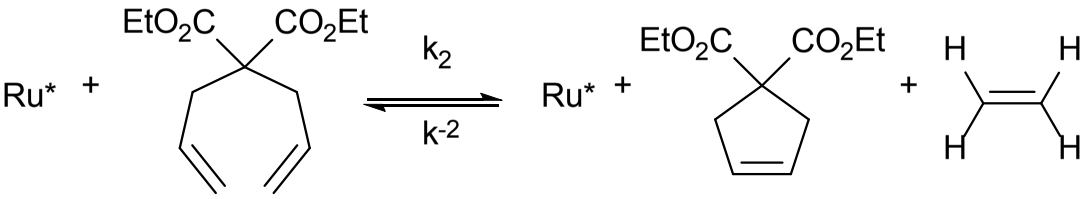
Ring-closing metathesis with a Grubbs II catalyst

Initiation



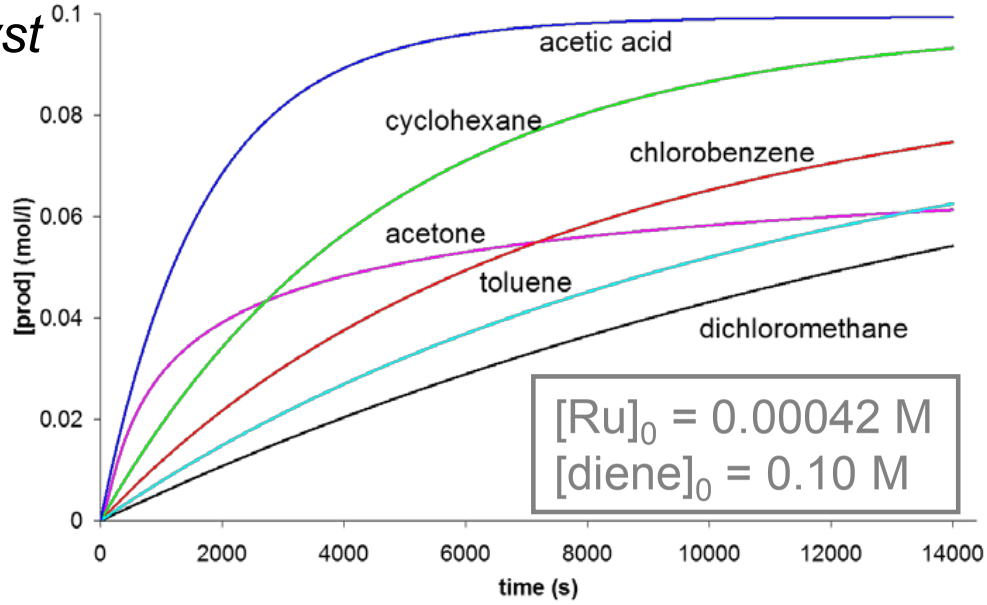
Ru **Ru***

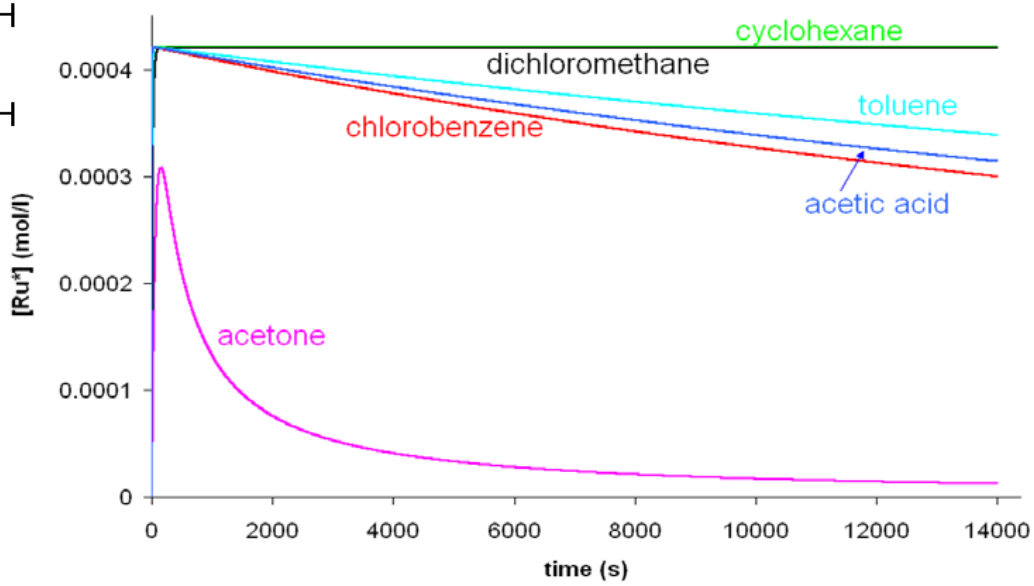
Metathesis



diene **prod**

Deactivation



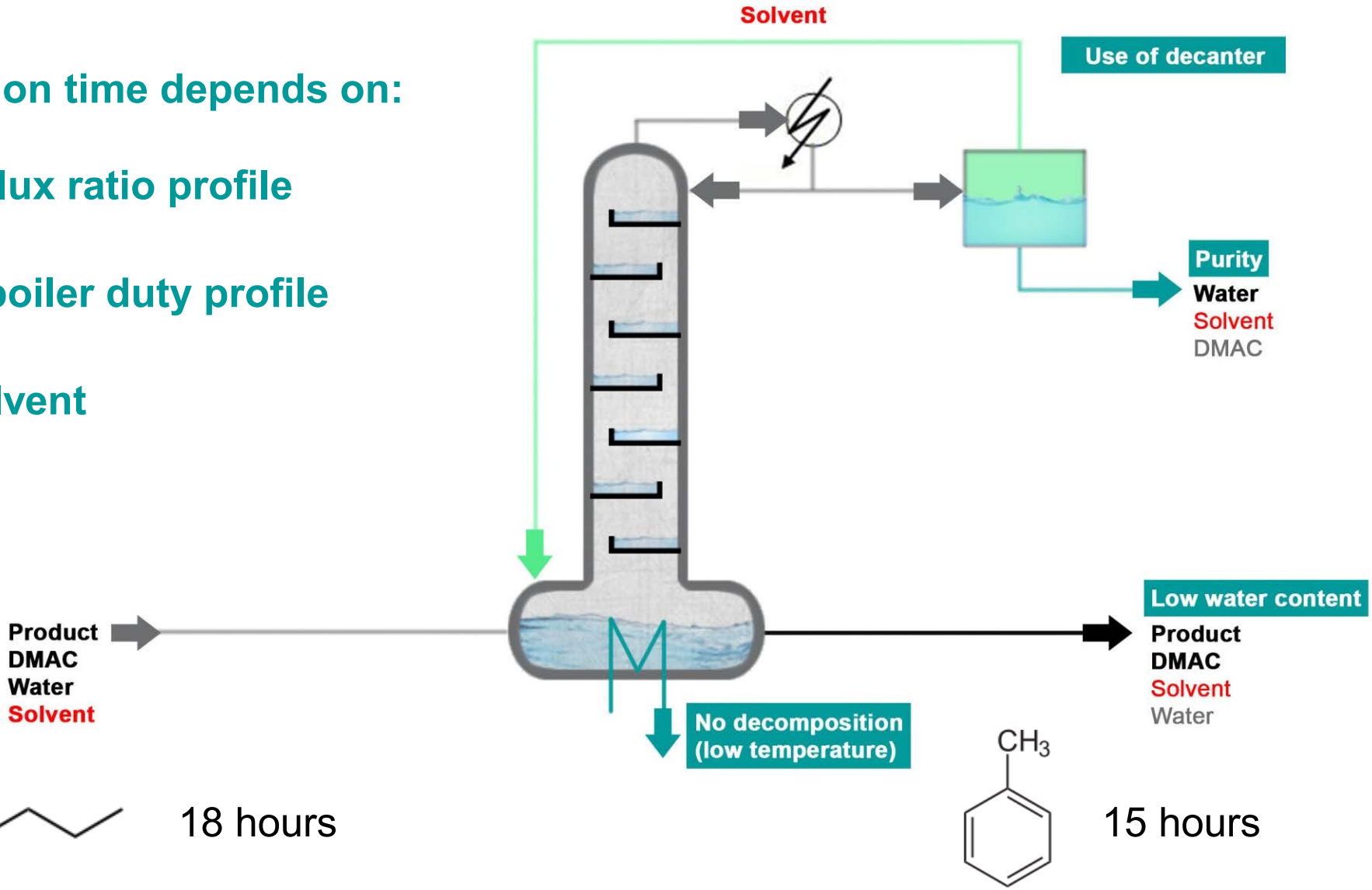


Productivity

Batch extractive distillation

Separation time depends on:

- **the reflux ratio profile**
- **the reboiler duty profile**
- **the solvent**

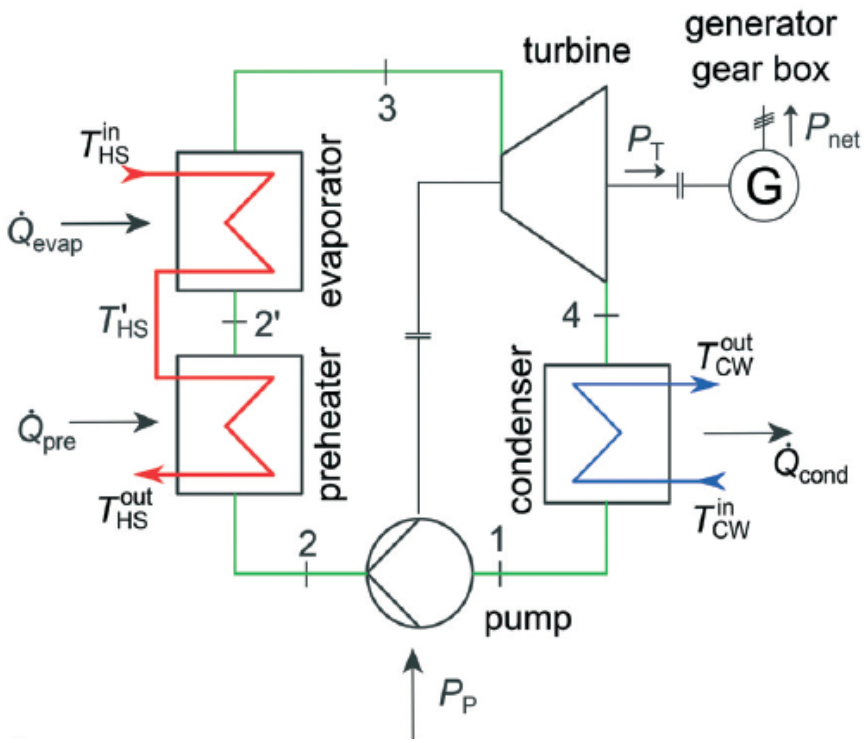


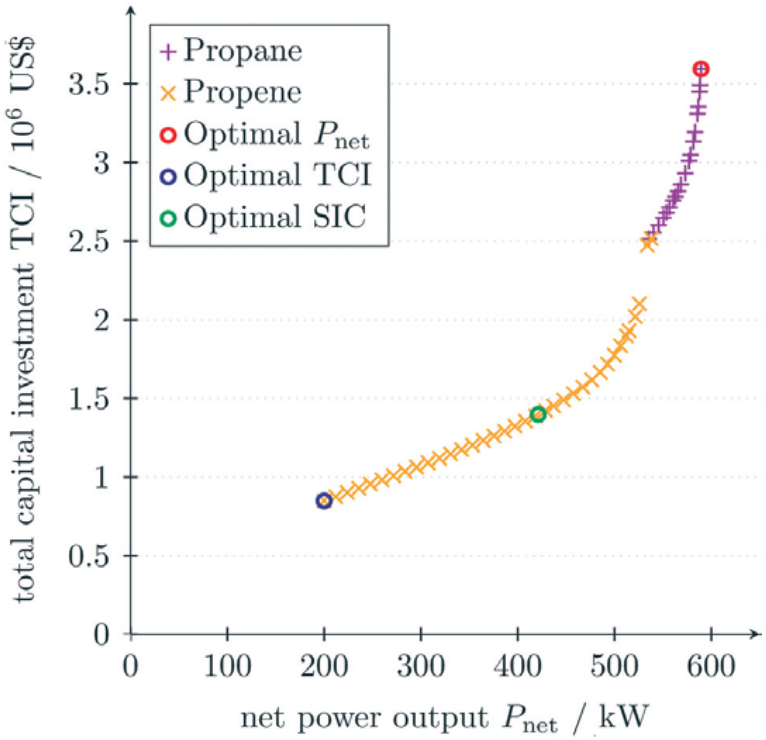
18 hours

15 hours

Giovanoglou, Barlatier, Adjiman, Pistikopoulos, Cordiner, *AIChE J.*, 2003, 49, 3095.

Capital cost

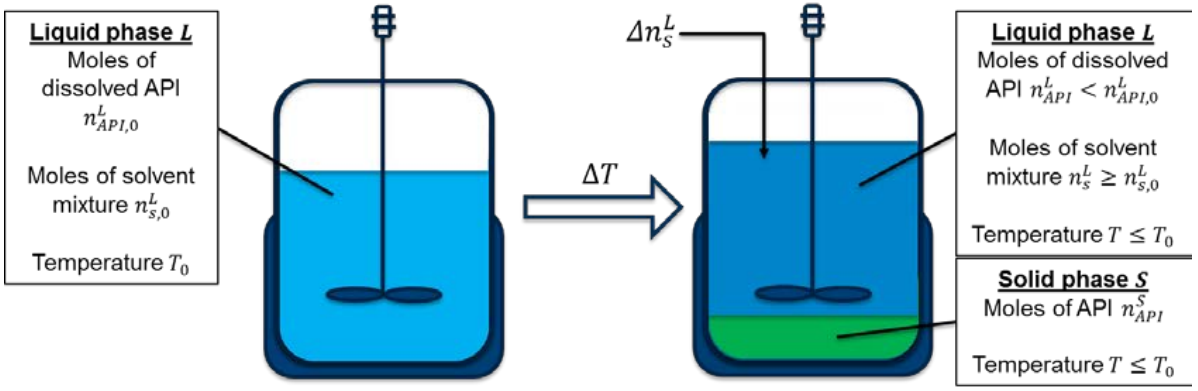




Schilling, Tillmanns, Lampe, Hopp, Gross, Bardow, *Mol Sys Des Eng*, 2017, **2**, 301

Environmental impact

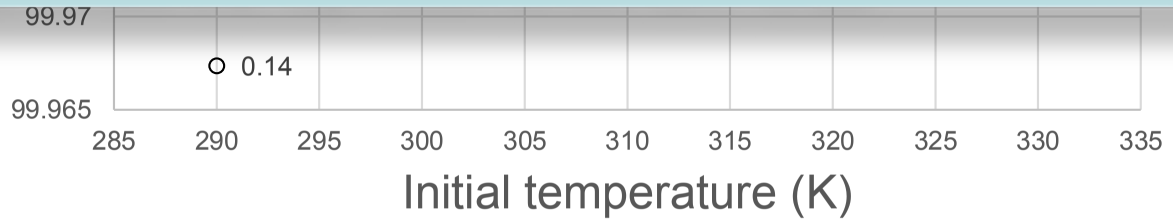
Anti-solvent / cooling crystallisation



Solvents as problem

- 4 kg solvent / kg API
- millions of tons used annually
- 60% of energy used in API production
- 50% of GHG emissions

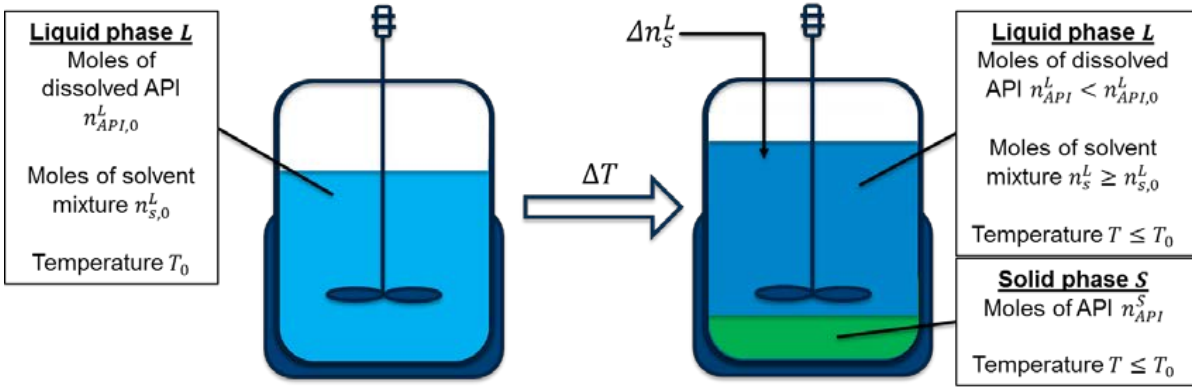
Jiménez-González, Curzons, Constable, Cunningham, *Clean Tech Env Pol*, 2005,
Jiménez-González et al., *Org Process Res Dev.,* 2011, 15, 900.

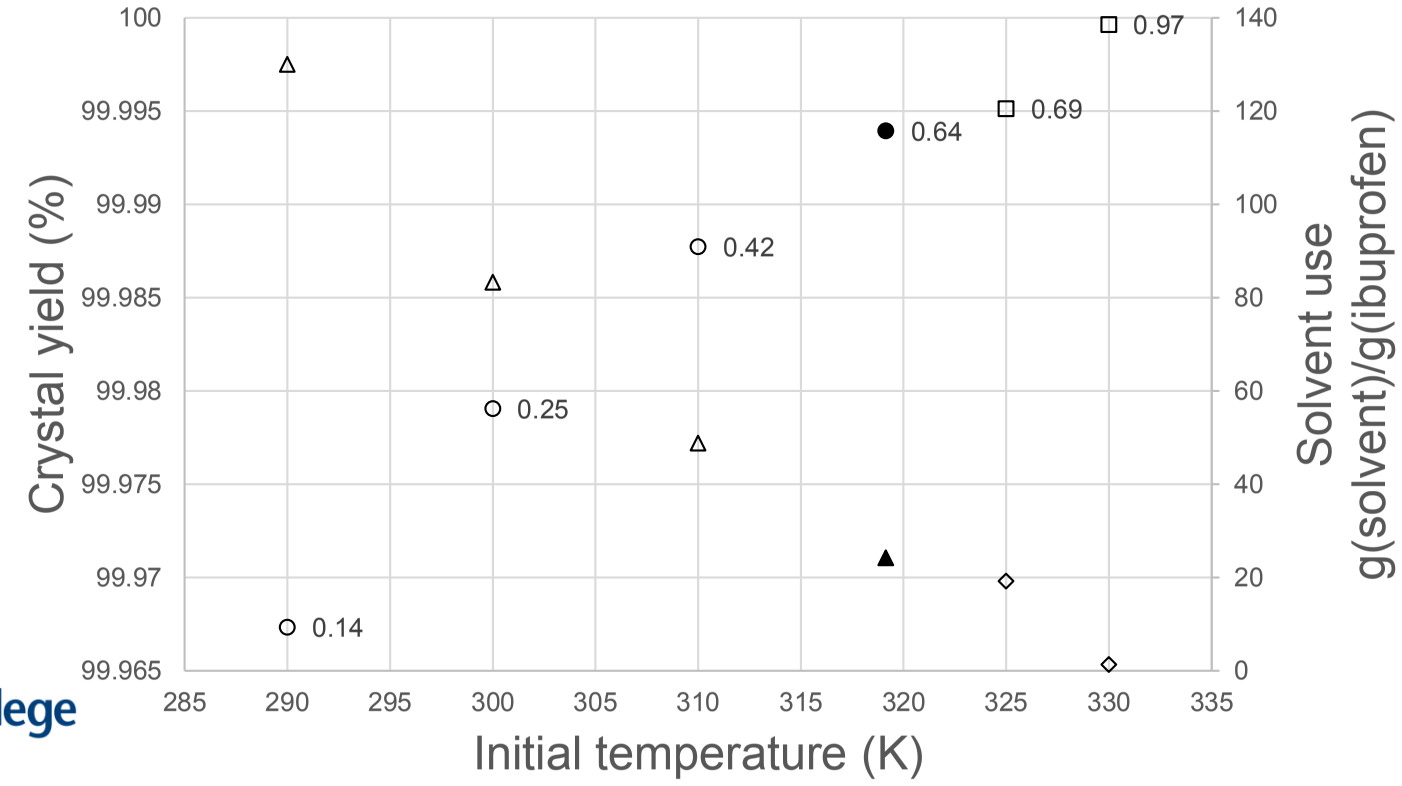


etone/water:
d
anol/water:
d

Environmental impact

Anti-solvent / cooling crystallisation

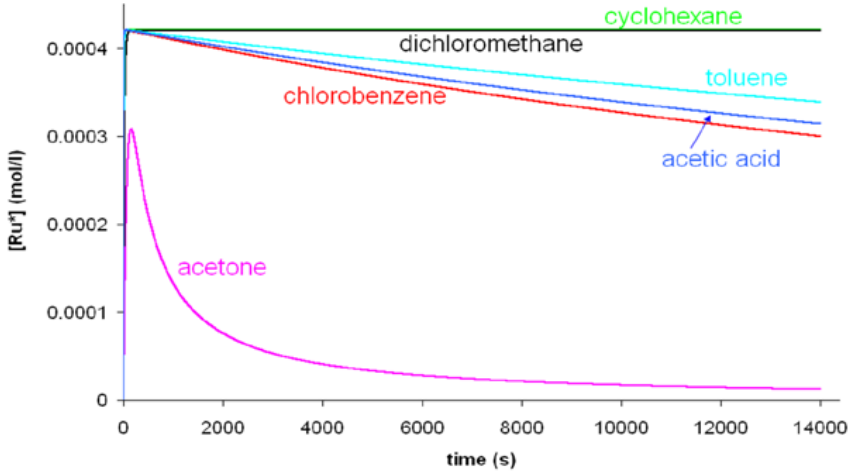




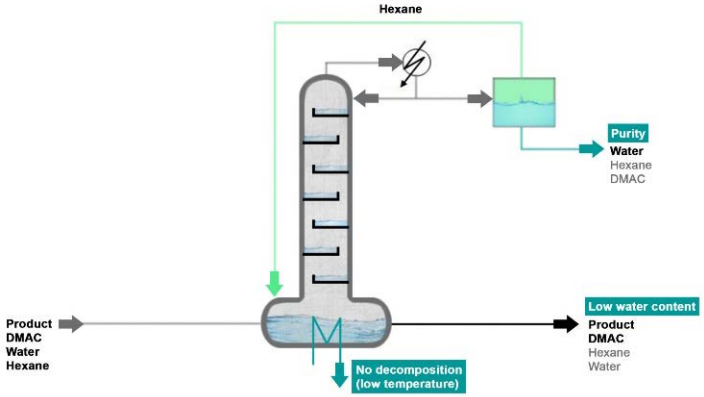
- ○ Acetone/water: yield
- □ Ethanol/water: yield
- △ Acetone/water: solvent use
- ◇ Ethanol/water: solvent use

The choice of processing materials can impact all aspects of process performance

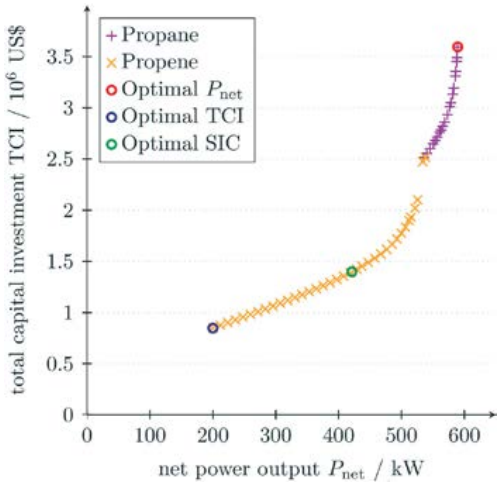
feasibility



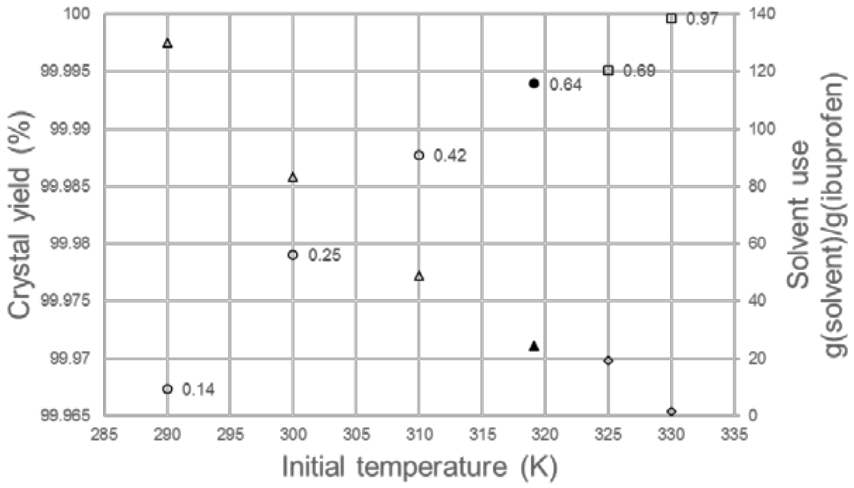
productivity



capital cost



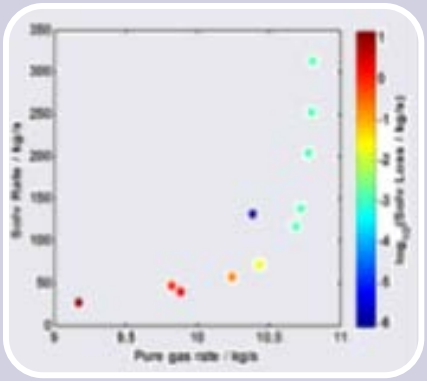
environmental impact



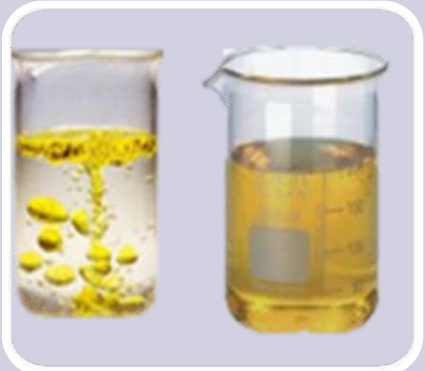
DESIGNER MOLECULES FOR DESIGNER PROCESSES?

The research goal

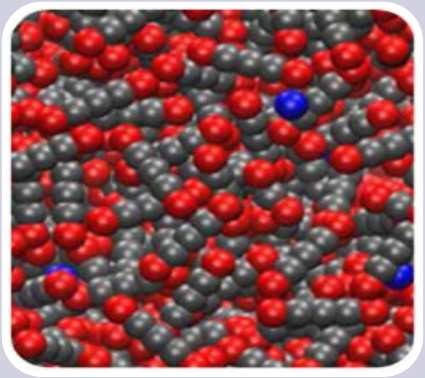
Can we develop PSE tools that embed molecular decisions as an integral part of process synthesis / design?



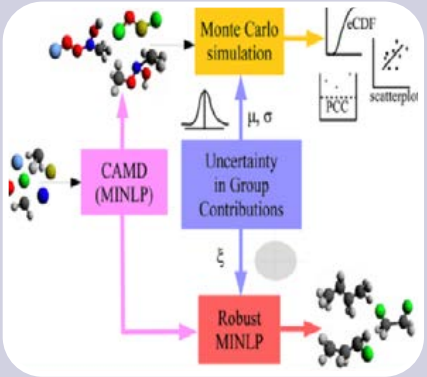
Definition and quantification of meaningful design metrics



Algorithms: complexity, nonconvexity, infeasibility



Integration of advanced property prediction methods in overall design problem



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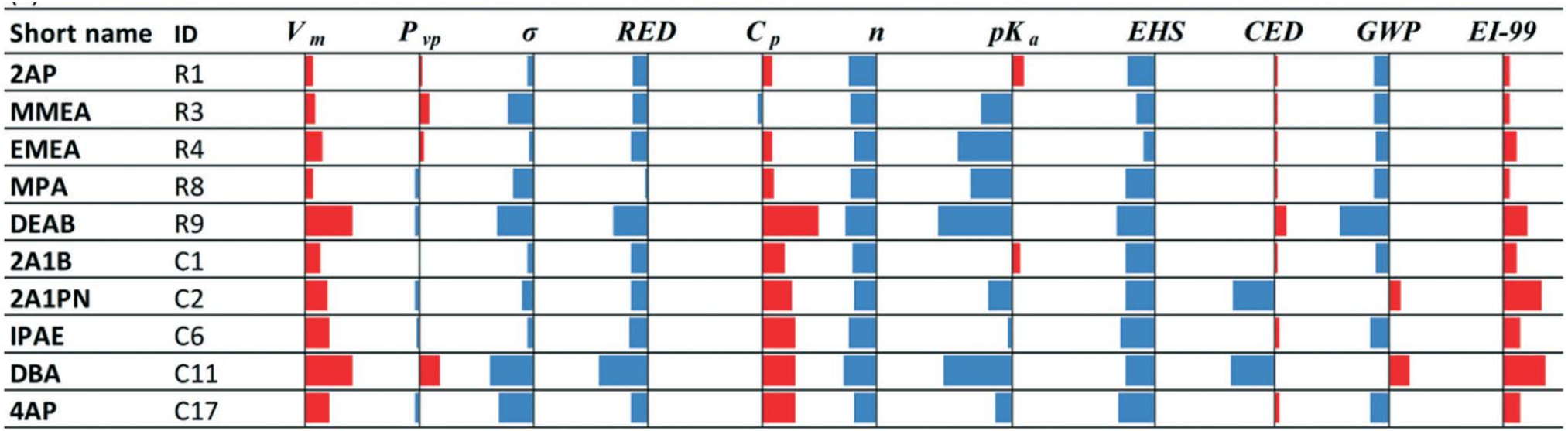
Quantification / mitigation of the impact of uncertainty in property prediction on design

What makes a good metric?

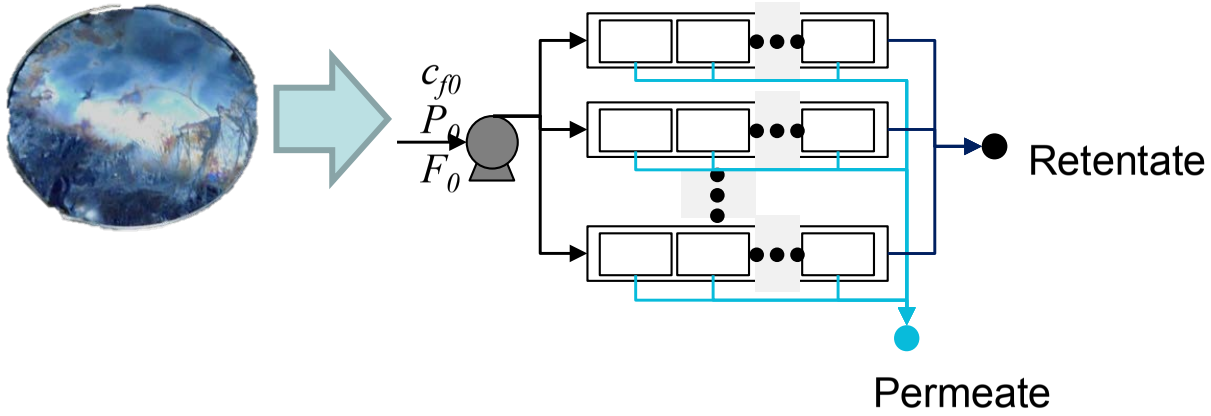
- Many advances have been based on property metrics
  - they are easiest to aim for and intuitive
  - they are of limited value in the context of process design
- It can be difficult to trade-off competing objectives
  - CO_2 capture by chemisorption

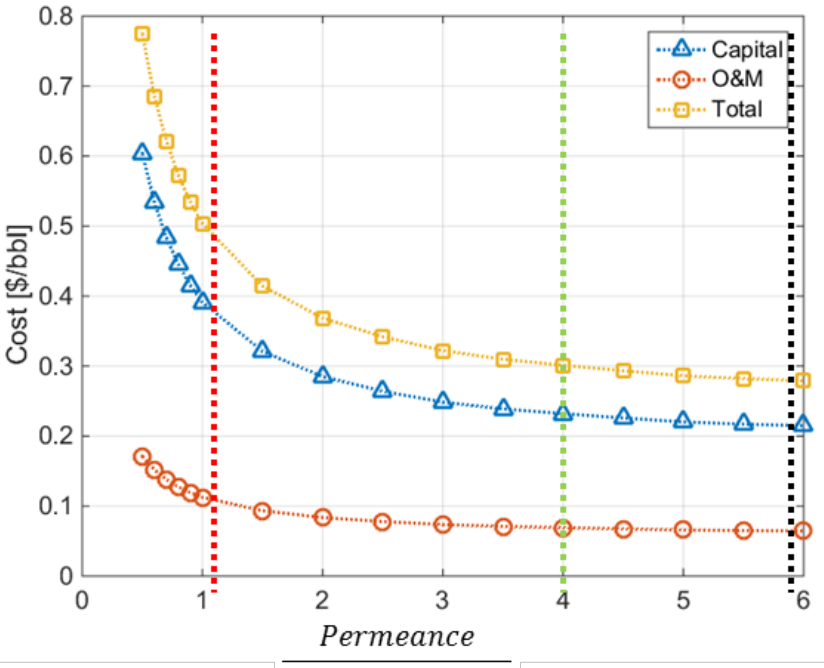


Papadopoulos et al, *MSDE*, 2016

What makes a good metric?

- Much of the literature is based on property metrics
  - they are easiest to aim for and intuitive
  - they are of limited value in the context of process design
- Difficult to trade-off competing objectives
- Improvements in properties do not necessarily lead to improvements in process performance





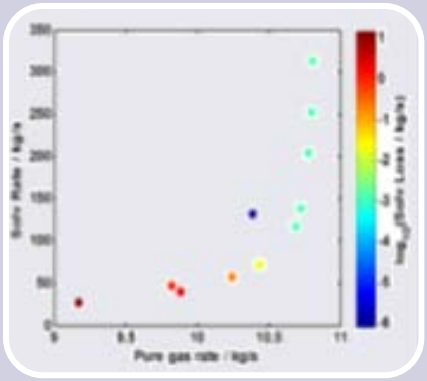
Gu, PhD thesis, 2016

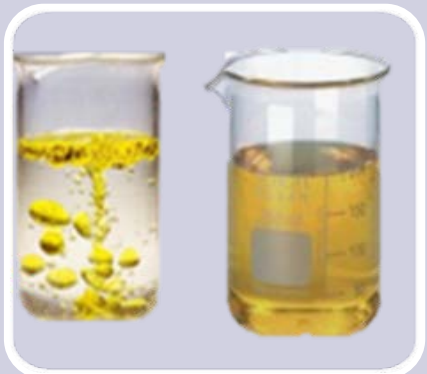
Metrics for molecular and process design

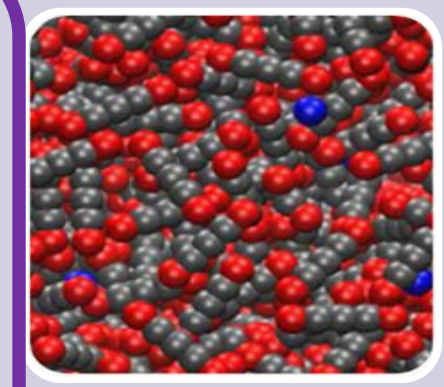
- Molecular structure is just another process variable
- The same performance metrics apply as for process optimisation
  - properties don't have an intrinsic value
- We face the same challenges as for other process optimisation problems
  - cf. yesterday's discussion; sustainability of industrial systems?
  - key question is how to estimate the sustainability of processes containing novel processing materials
    - standard green chemistry concepts are not sufficiently holistic

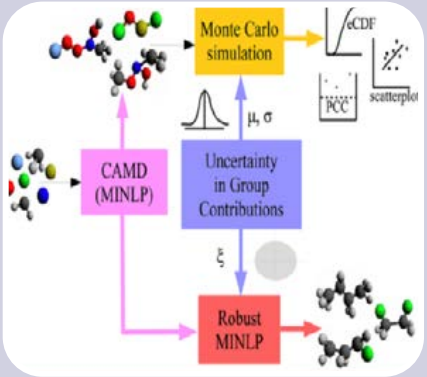
The research goal

Can we develop PSE tools that embed molecular decisions as an integral part of process synthesis / design?









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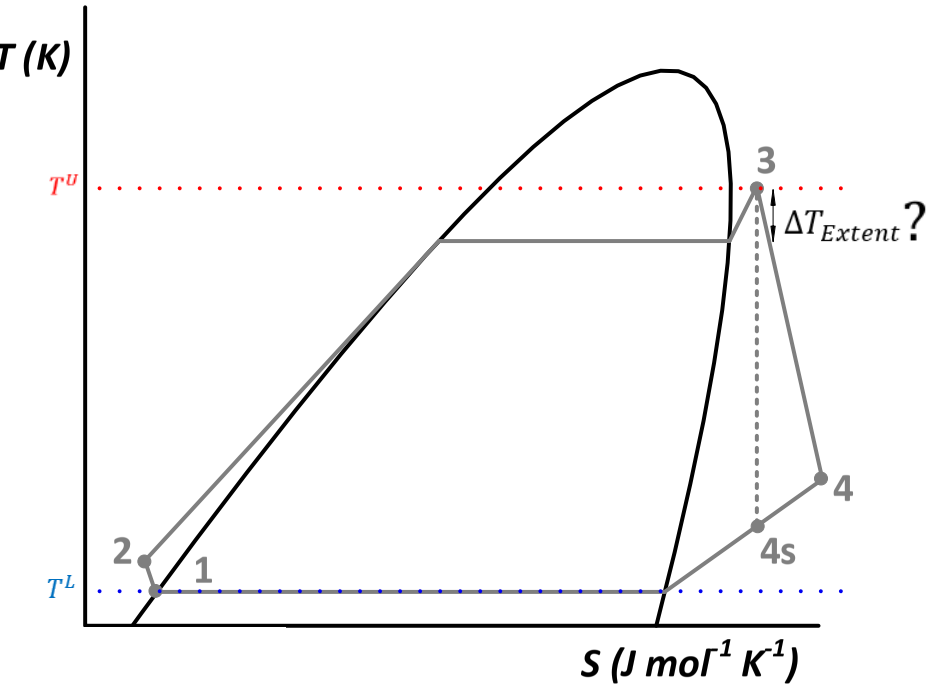
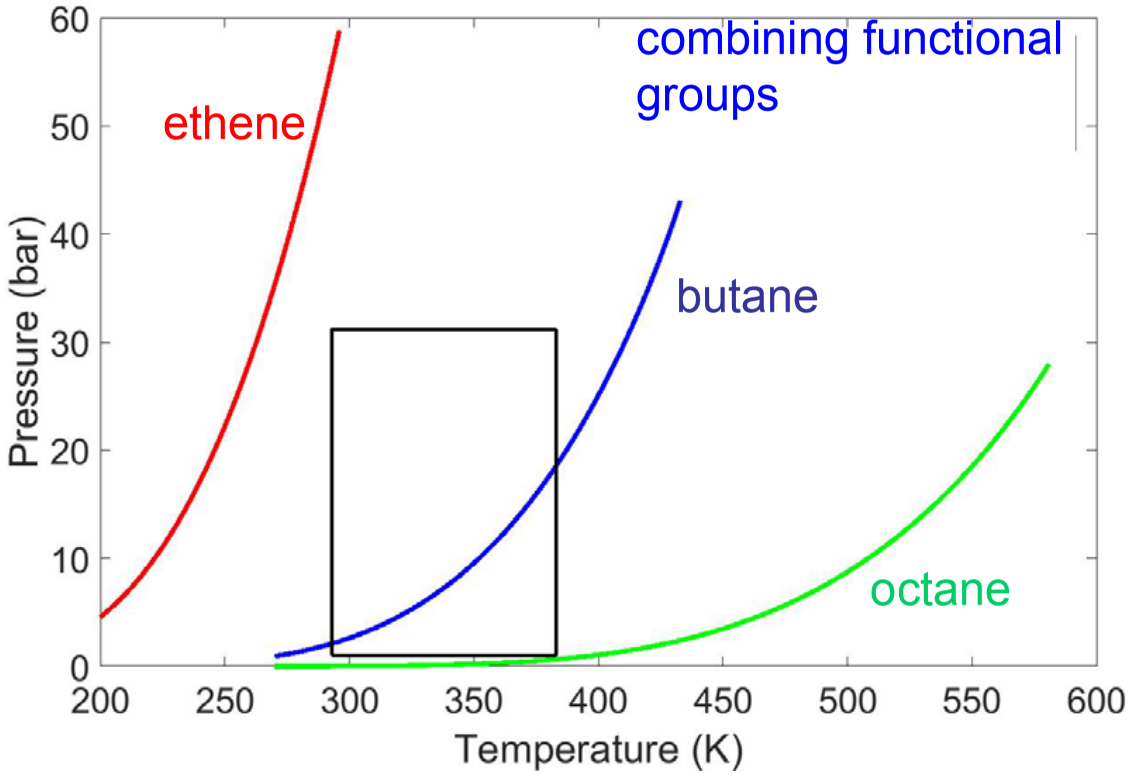
ORC fluid and cycle design



3,175 "feasible" molecules from combining functional groups

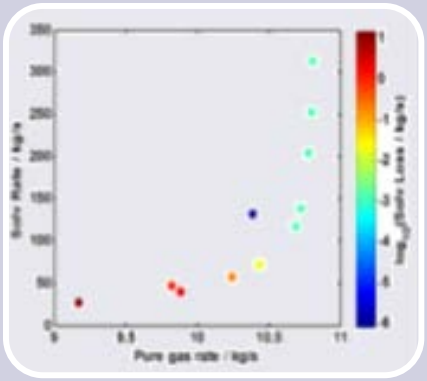


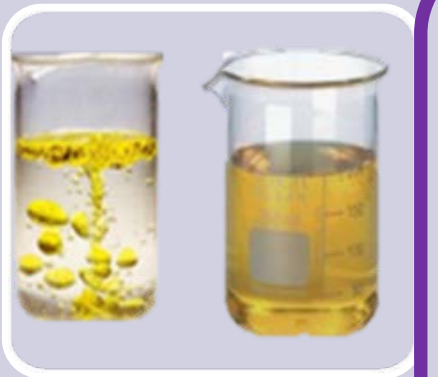
	Case Study 1 [20°C-110°C]	Case Study 2 [20°C-200°C]	Case Study 3 [35°C-80°C]
% **infeasible** fluids in the design space based on feasibility tests	98.4%	91.6%	99.1%

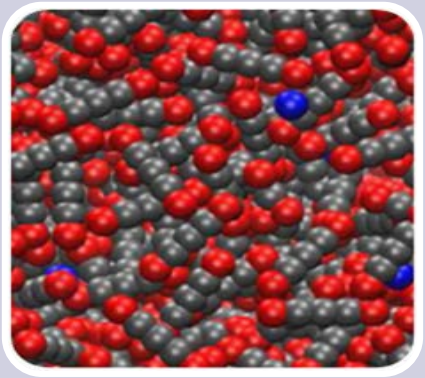
- Can we design algorithms to explore the design space reliably and efficiently?

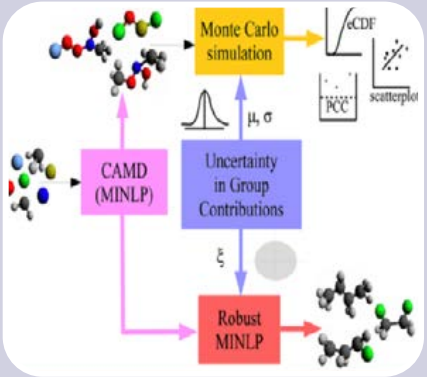
The research goal

Can we develop PSE tools that embed molecular decisions as an integral part of process synthesis / design?









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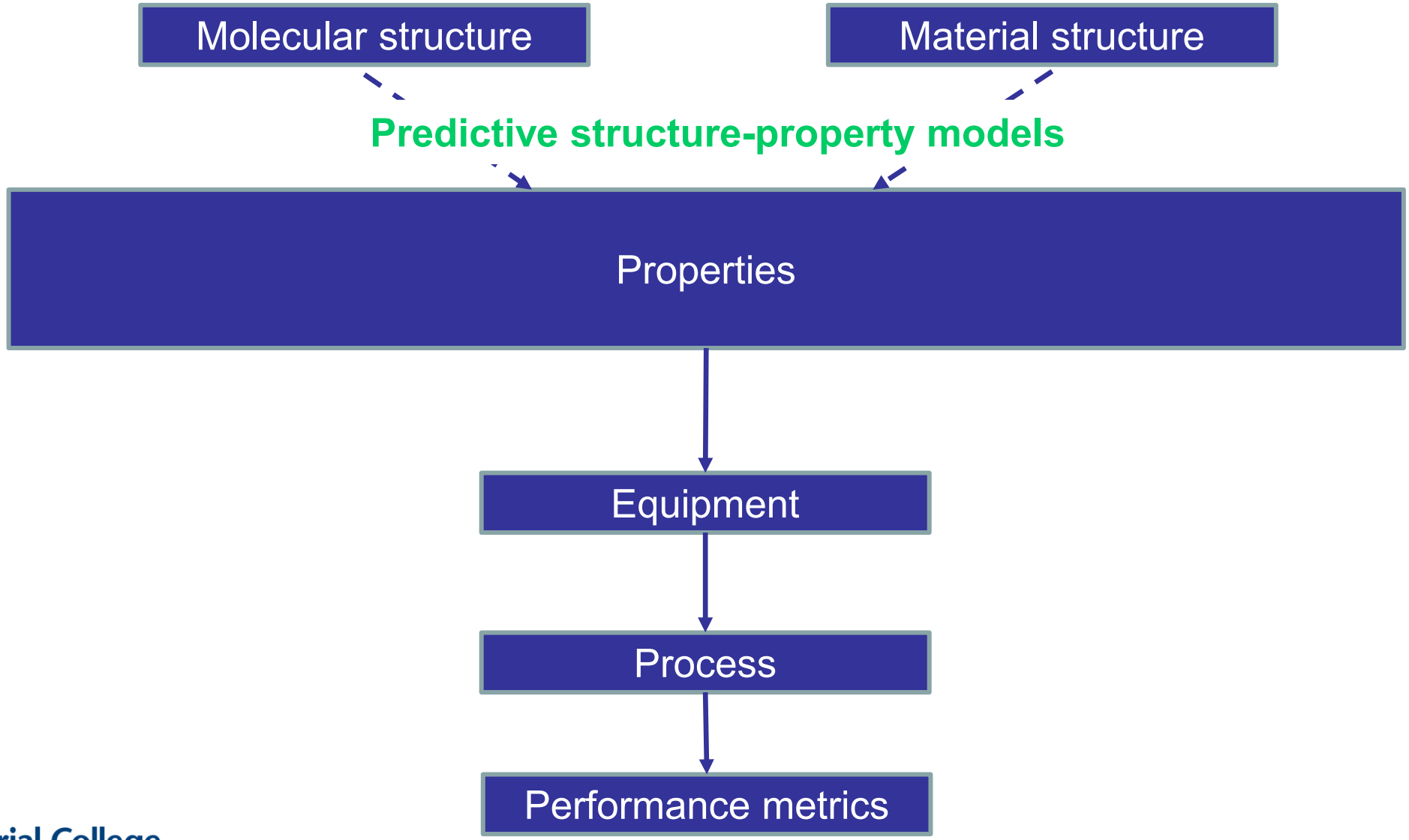
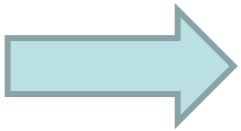
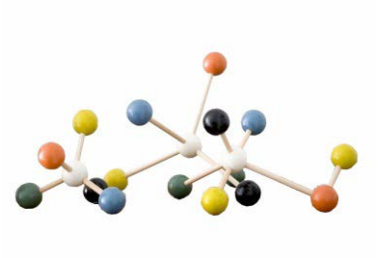
Property prediction needs in molecular and process design

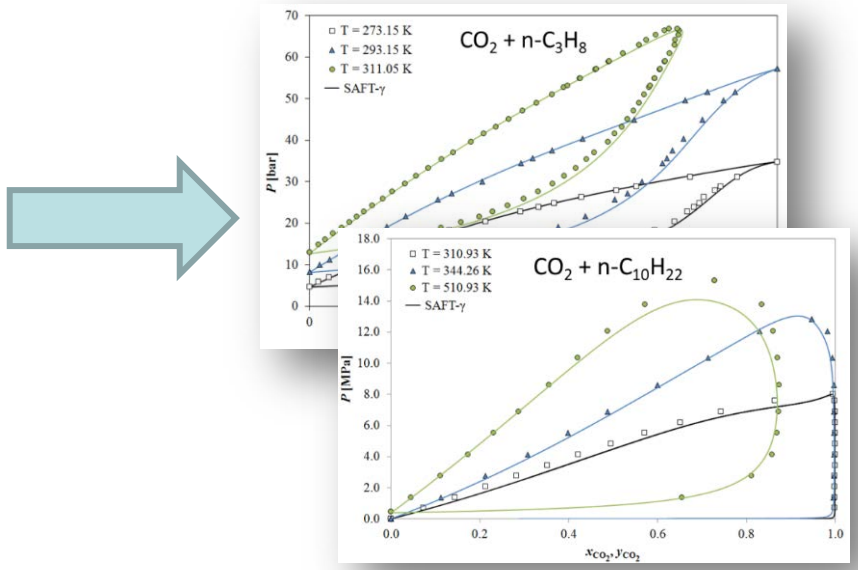


Transferability in structure-property models

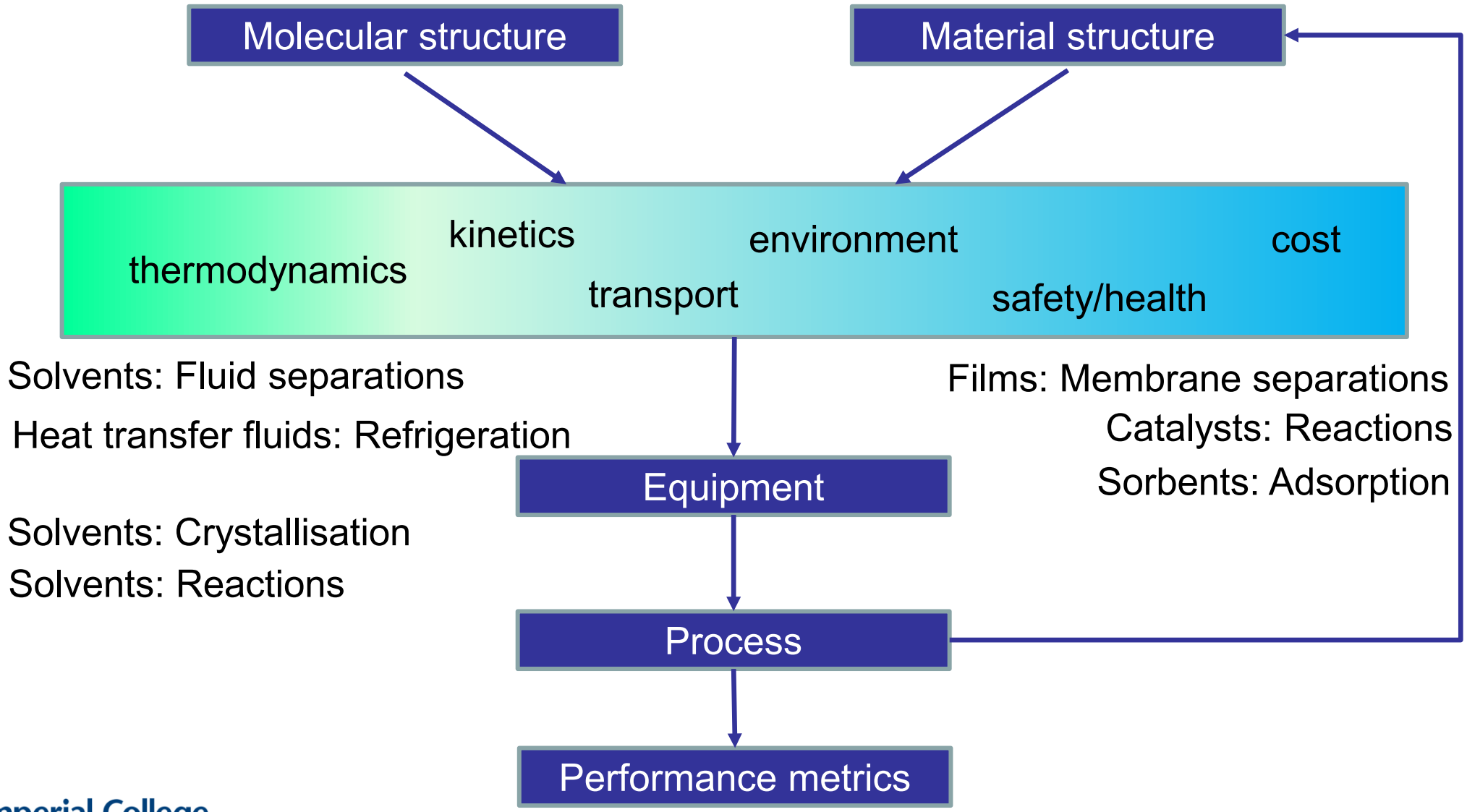
- Transferable models central to computer-aided molecular design
  - Quantum mechanics
  - Molecular simulations (Monte Carlo, Molecular Dynamics)
  - Coarse-grained simulations
  - Group contribution methods





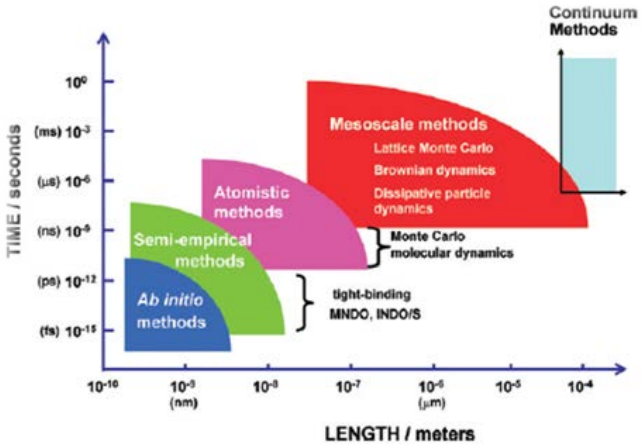


Property prediction needs in molecular and process design



Recent progress in property prediction

"Rapid improvements in our ability to model physical and chemical processes at the atomistic scale over the last two decades …"
Gubbins & Moore



gure 1. Theory and simulation scales for ab initio (electronic), semiem-
ical, atomistic, mesoscale, and continuum scales.

"Admittedly, the slowness of MD precludes replacing group contribution methods in a combinatorial approach to molecular design"
Maginn & Elliott

"One also sees fertile interactions developing between molecular simulators and "systems" (process design and optimization) researchers. There is very much to be gained if these communities join forces to address complex process and product design problems with the help of MC simulations"
Theodorou

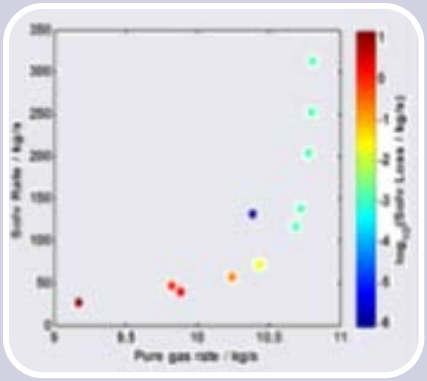
Key challenges

- Many property prediction methods are not well-behaved
  - high computational cost (from simulations to QM)
  - non-differentiable (MC)
  - require the solution of one or more optimisation problems (MM, QM, or even an equation of state!)
  - ➢ how do we embed them in process models?
  - ➢ how do we solve the resulting optimisation problems?

- Many prediction methods are lacking or not sufficiently well developed
  - there are great opportunities for PSE researchers to get involved in property prediction, as users **and as developers**
  - collaboration with physical chemists, molecular simulators
    - property prediction methods are not usually designed with process modelling in mind

The research goal

Can we develop PSE tools that embed molecular decisions as an integral part of process synthesis / design?



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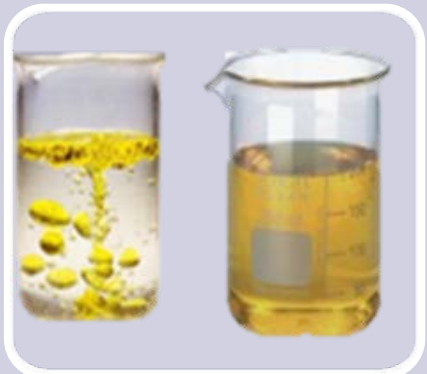

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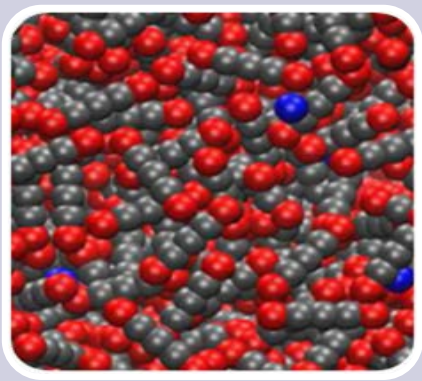
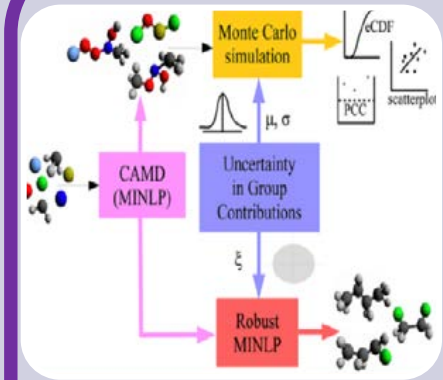


Integration of advanced property prediction methods in overall design problem



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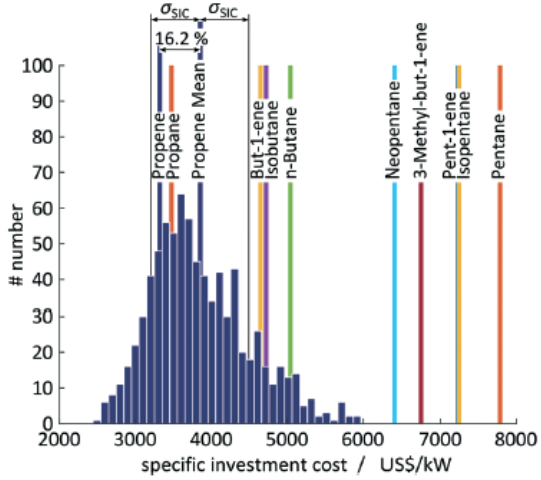
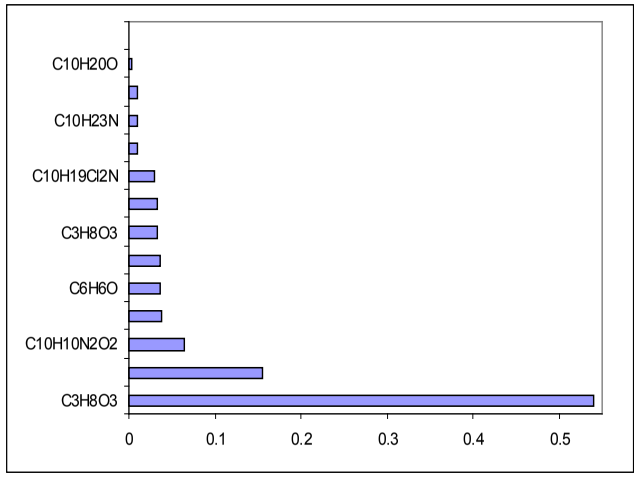
Quantification / mitigation of the impact of uncertainty in property prediction on design

Quantifying / mitigating the impact of uncertainty

- The usual questions apply
  - Uncertainty quantification, robust design



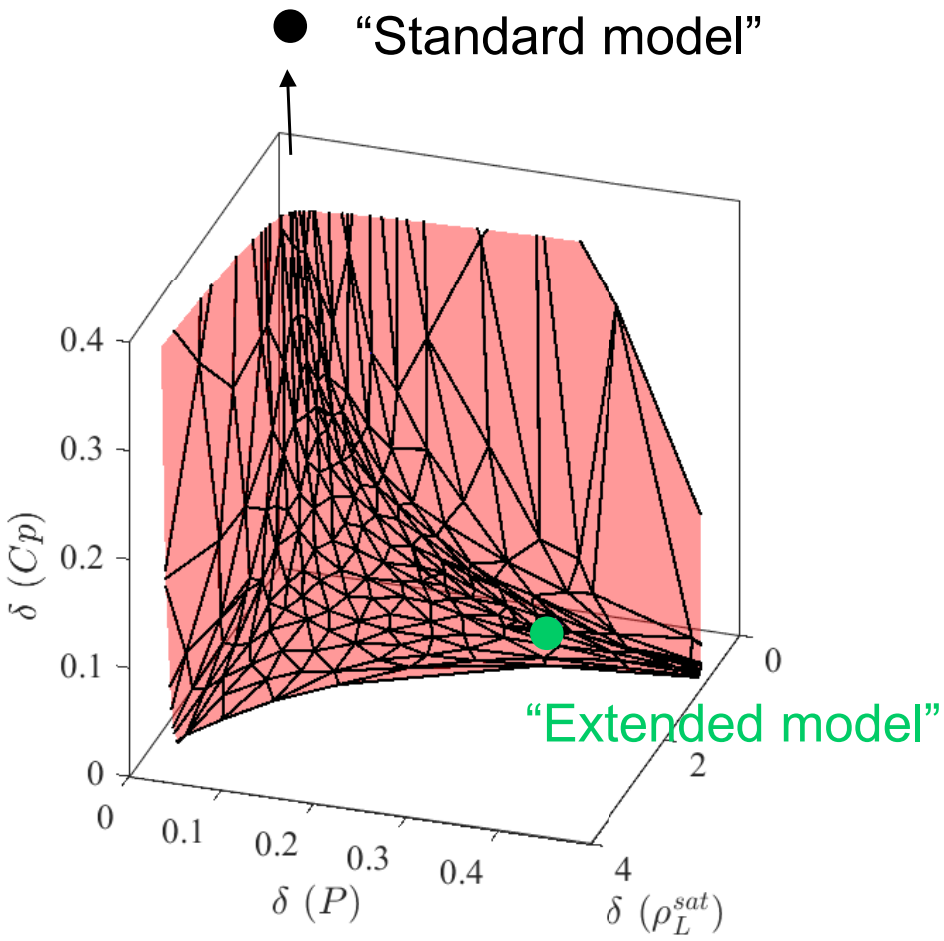


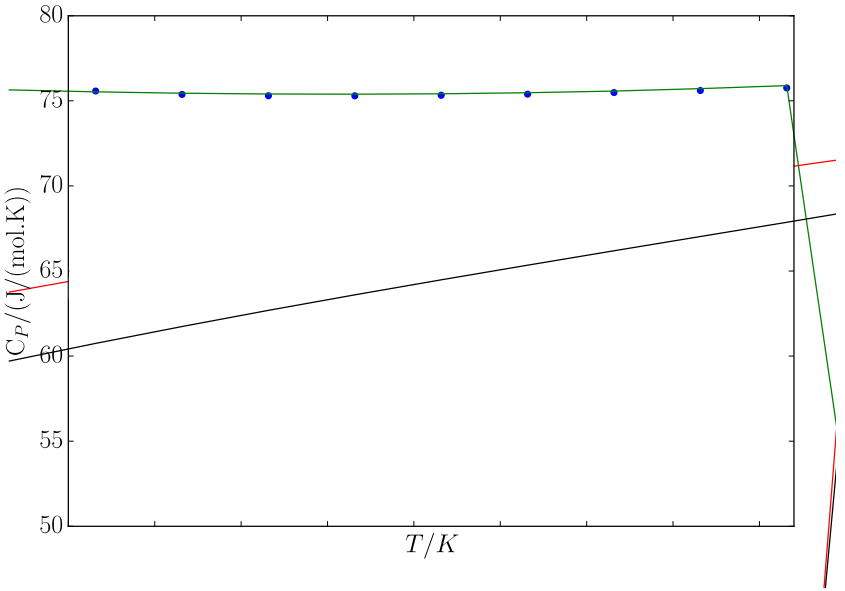
  - From Monday: goal-oriented uncertainty modelling; uncertainty propagation among subsystems

- In addition, when it comes to property models, accuracy is (sometimes) a matter of choice
  - How to choose or even develop structure-property models that minimise uncertainty for the problem of interest?

Models of water

- Which properties were used in developing the model?
- What impact does this have on the performance of the model?

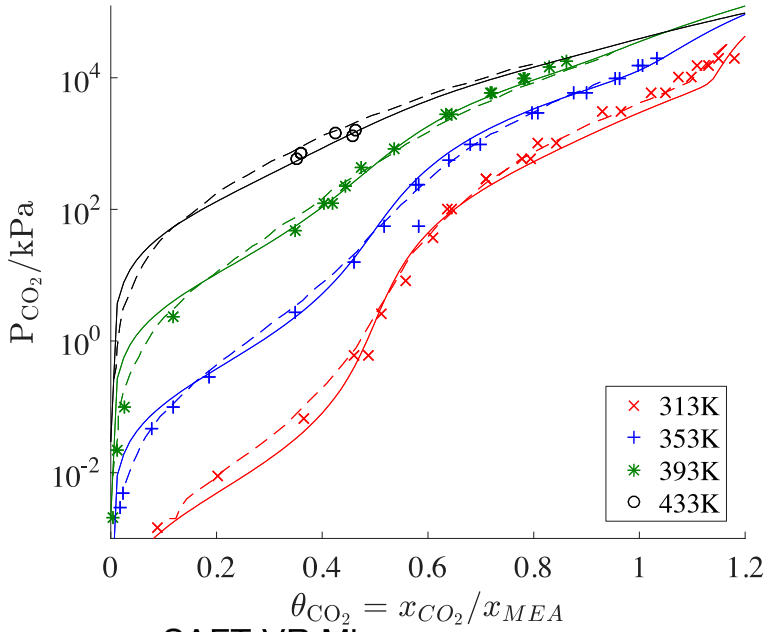




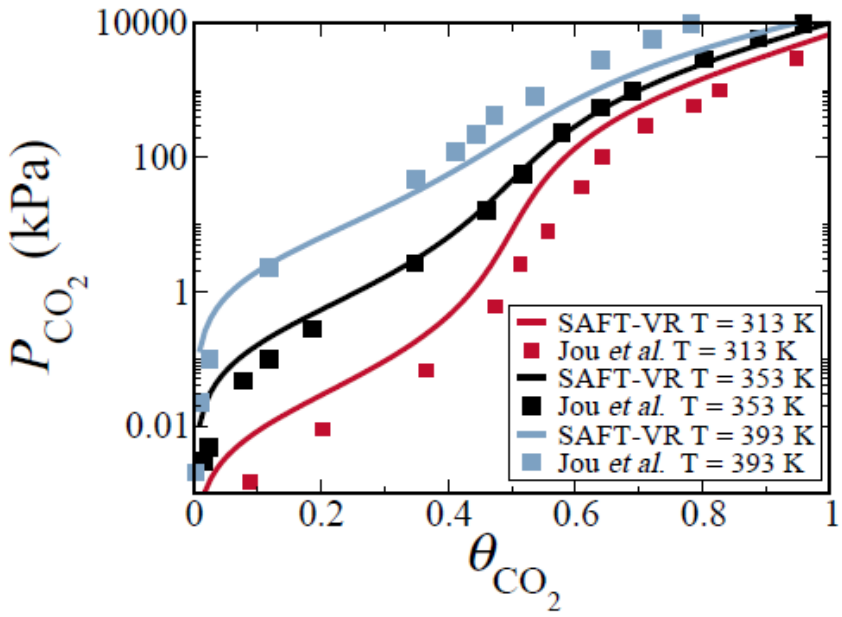
Property	ρ_L	P	C_P
AAD (%)	1.1	0.34	0.04

Effect on mixture properties – water + CO_2 + monoethanolamine

Extended model

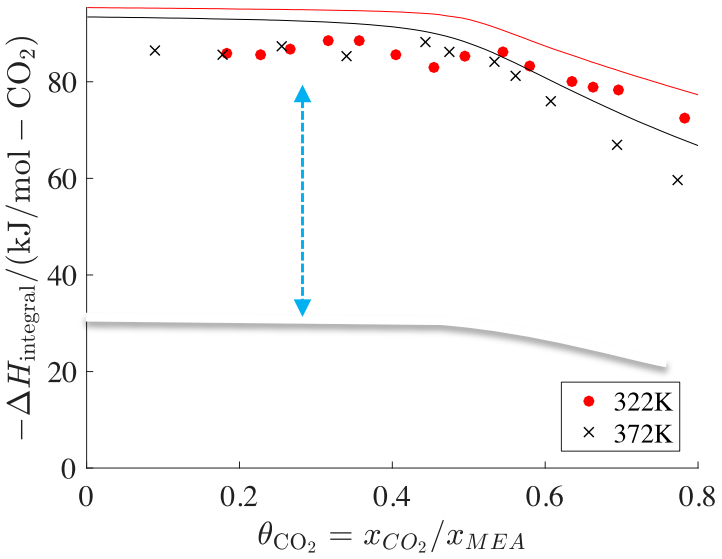


Standard model



SAFT-VR Mie

Full Speciation model, Zhang et al.



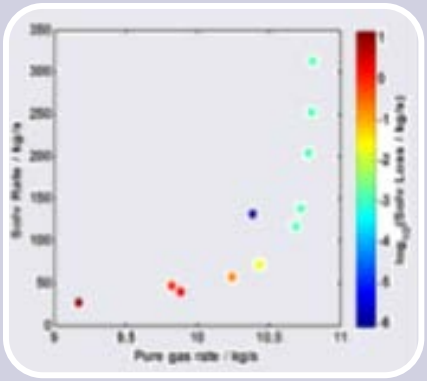
Not so transferable models

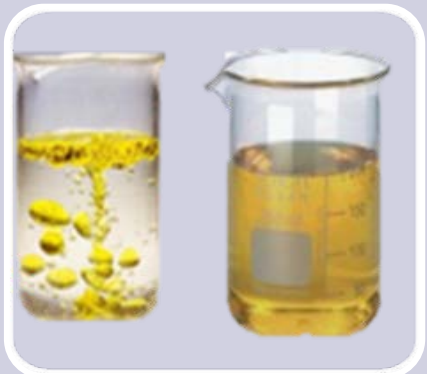
- How do we choose the right model for our purpose?
  - iterative design from a generic model to a more targeted model
  - a library of Pareto-optimal models
  - automatic re-estimation of transferable parameters

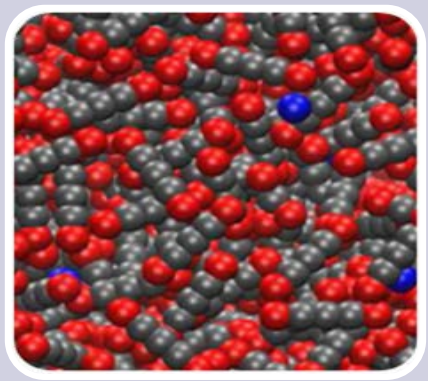
  - can we base our choice on process metrics rather than property metrics?

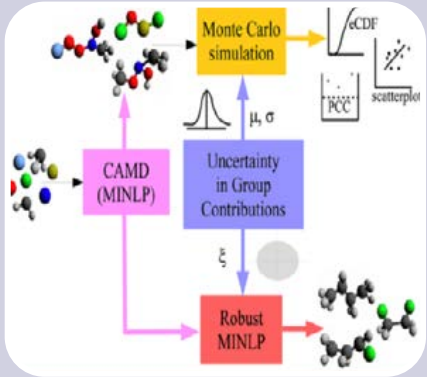
Four challenges along the way

Can we develop PSE tools that embed molecular decisions as an integral part of process synthesis / design?









Andres-Martinez & Flores-Tlacuahuac

Definition and quantification of meaningful design metrics

Algorithms: complexity, nonconvexity, infeasibility

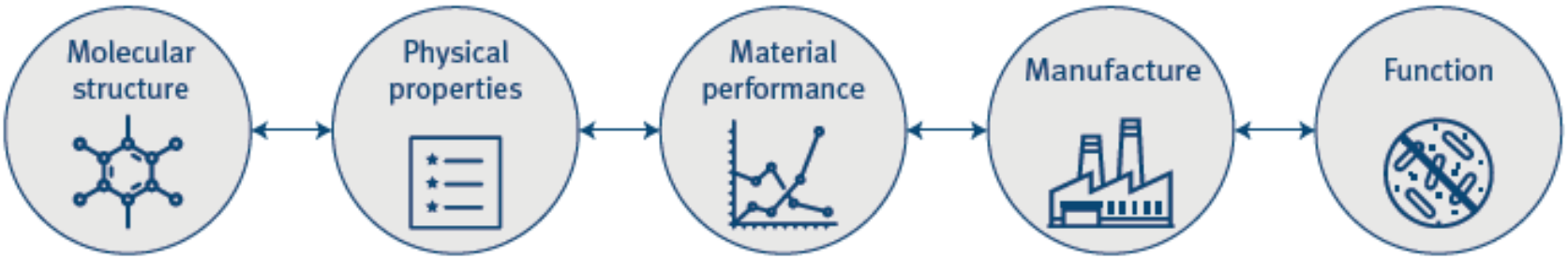
Integration of advanced property prediction methods in overall design problem

Quantification / mitigation of the impact of uncertainty in property prediction on design

WHAT CAN PSE DO FOR MOLECULES?

The discovery process

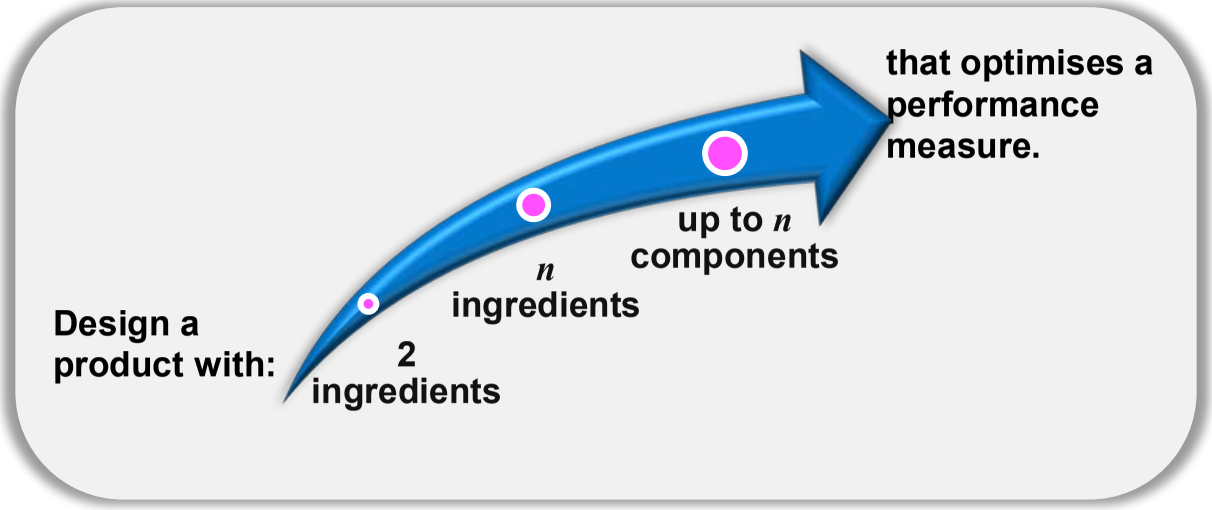
Designing a product that does the right thing
and can be manufactured … optimally



Adjiman et al., 2017, http://hdl.handle.net/10044/1/53609

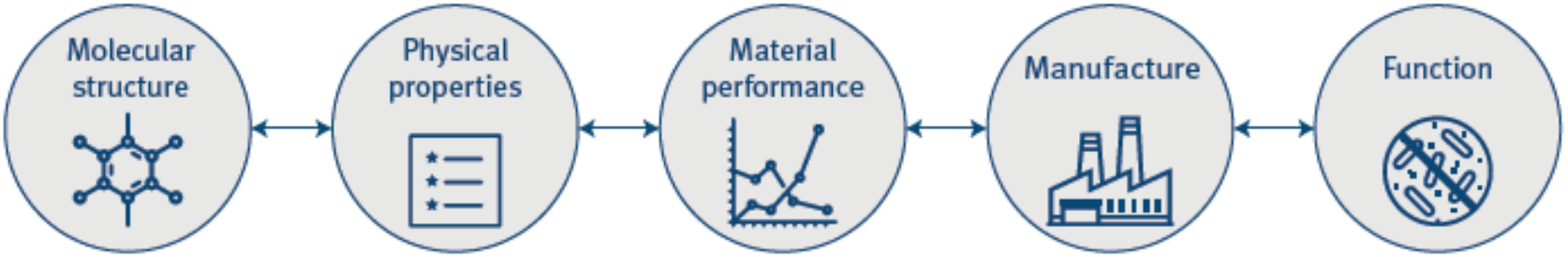
- Current limitations:
  - Costly, time-consuming, highly iterative process
  - Lack of fundamental understanding of key physical phenomena limits innovation

"Simple" mixture design



- Where the relevant structure-property models exist, we can formulate a design problem
  - applications to solvent design, adhesive design, lubricant design
  - key challenges in algorithm design
    - combinatorial nature of problem
    - high degree of nonlinearity
    - solutions are unlikely to be optimal
    - ➢ need a step change in numerical methods
  - what about manufacturability?

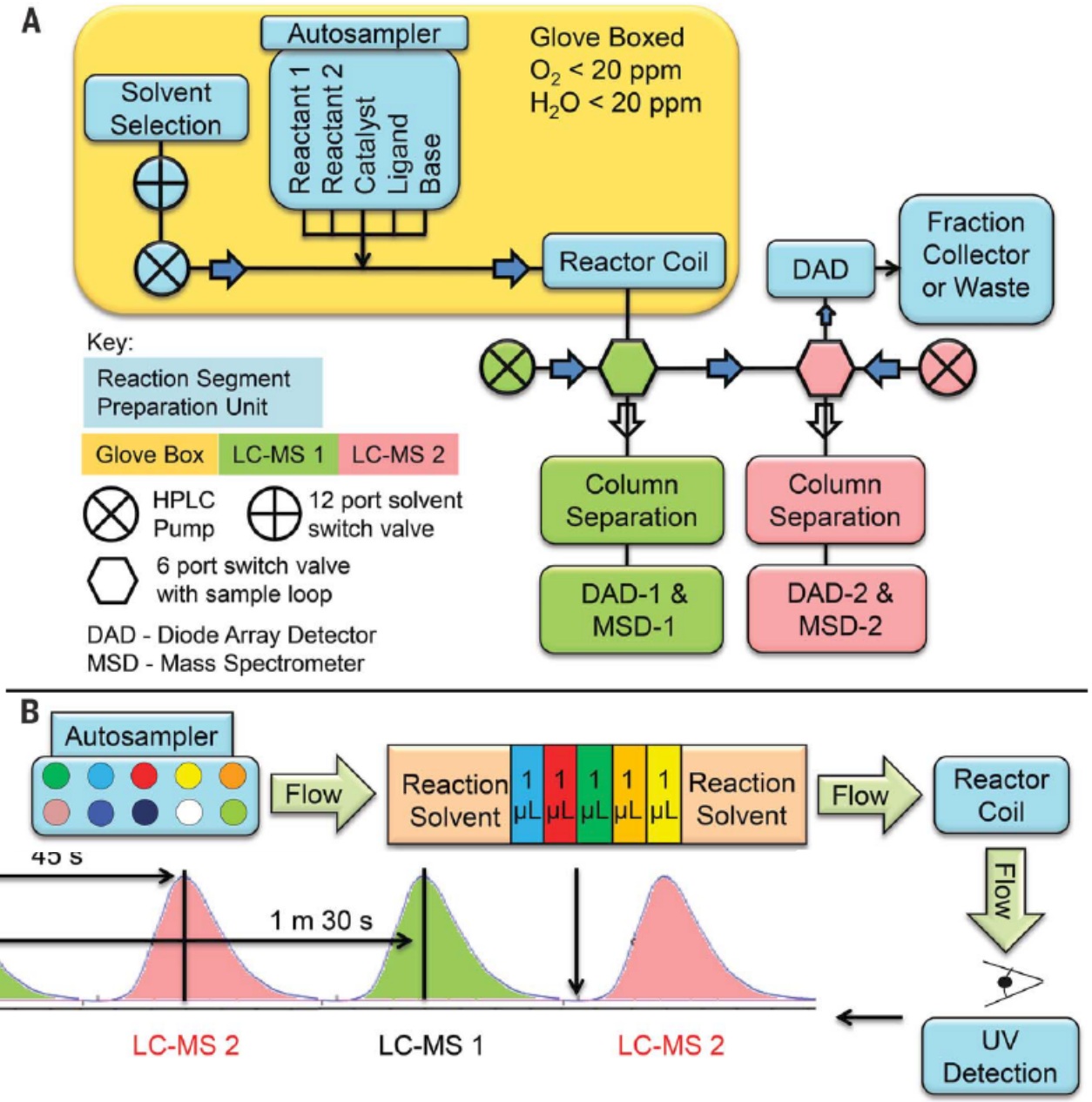
Towards manufacturability / structured products



- Predictive challenges along the chain:
  - molecular structure - material structure
  - structure-processing-function
  - material stability
- How do we know how easy it will be to make a novel molecule or material?
  - measuring manufacturability
  - predicting manufacturability

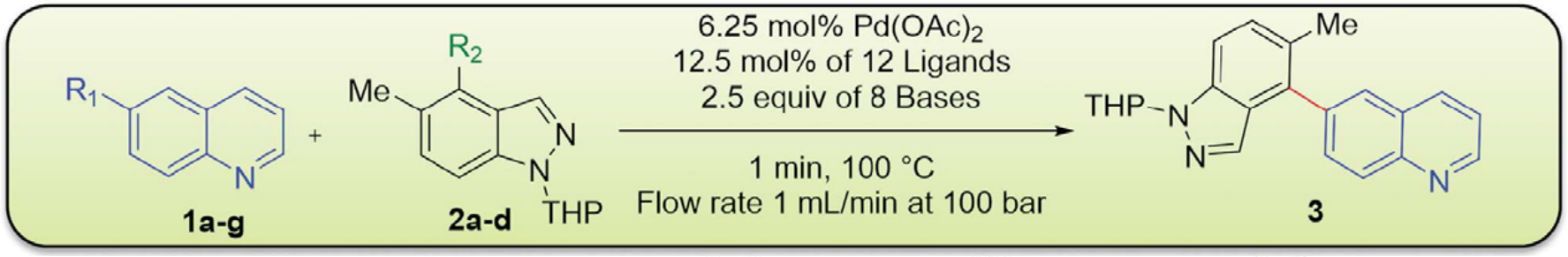
Discovering "manufacturable" drug candidates

- How to provide sufficient quantities of material for early stage screening of drugs?
- Continuous set-up for reaction screening

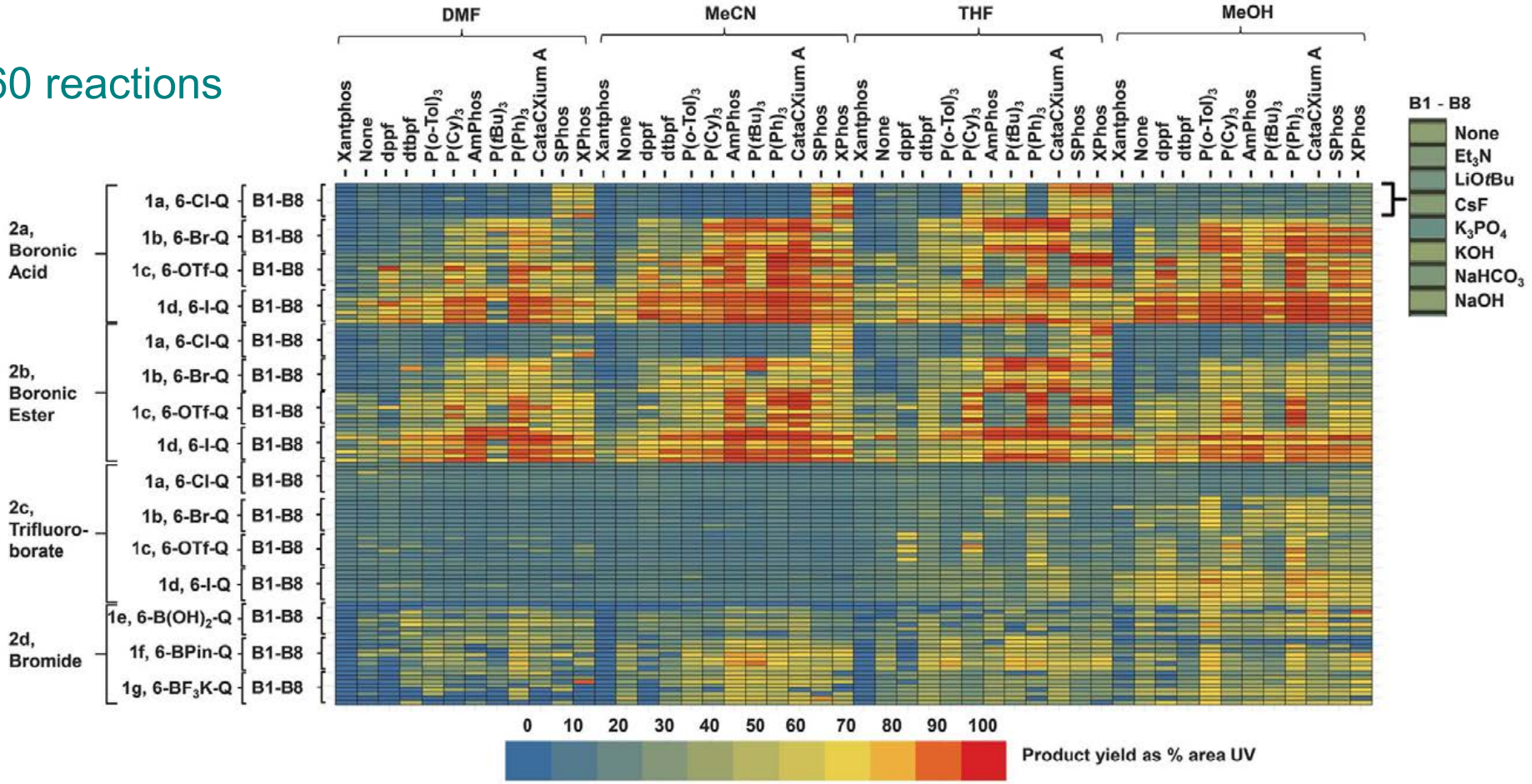


Perera et al., *Science,* 2018

High throughput reaction "optimisation"



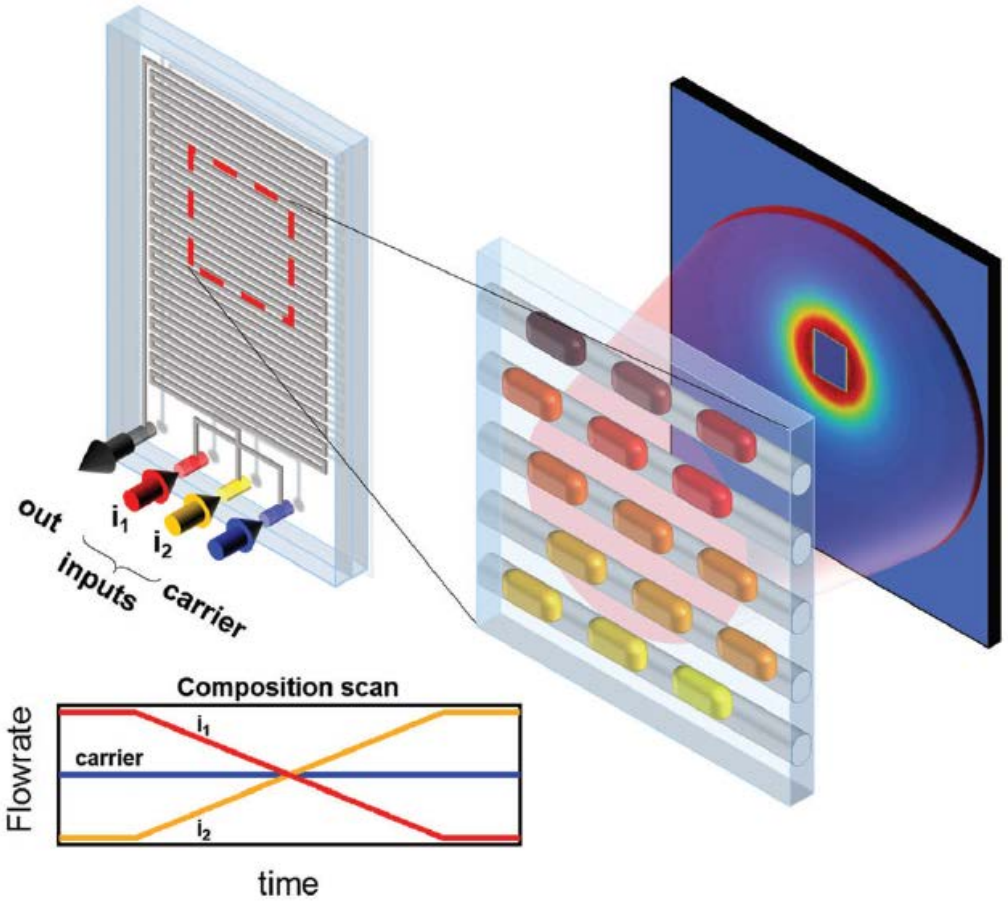
5760 reactions



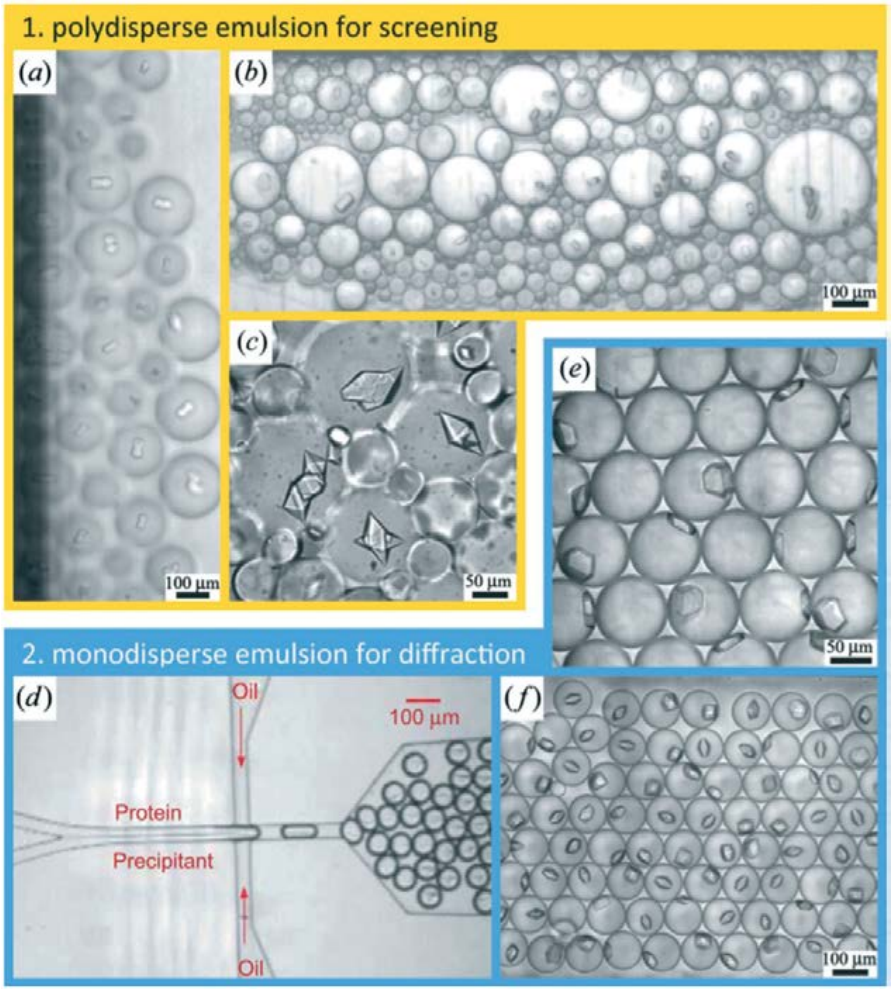
Perera et al., *Science,* 2018

Discovering structured products

- High throughput microfluidic SAN/XS (Small-Angle Neutron / X-ray Scattering)



Adamo et al., *Soft Matter*, 2018



Heymann et al., *IUCJR*, 2014

High throughput experimental (HTE) platforms

- An exciting opportunity to acquire much needed data, including data relating structure and processing
- Currently used principally to gather a lot of data and obtain insights or maps of behaviour

- PSE questions
  - what is the best set of experiments?
  - how can we use the data to build models that support product design?
  - product design with HTE in the loop?

- More questions – data processing
  - too much data goes to waste
  - how can it be interpreted

Concluding remarks

- Molecules/materials as process variables
  - Metrics and algorithms: a twist on the usual PSE challenges
  - Property prediction:
    - how can we make further use of state-of-the-art property prediction techniques?
    - do we need to engage in the development of new or modified methods for structure-property models?
    - what is a good property model? Tailoring transferable models to reduce uncertainty
- Product design
  - Metrics (manufacturability) and algorithms
  - Embedding emerging HTE techniques into PSE tools

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