



ADVANCED PROCESS MODELLING FORUM

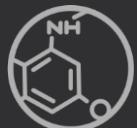
22-23 APRIL 2015

APM for Formulated Products

Systems-based Pharmaceutics and Digital Design developments

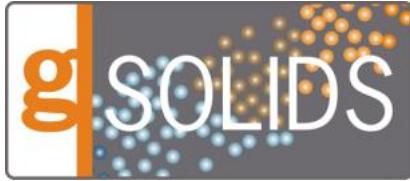
Sean Bermingham, Vice-President

PSE Life Sciences, Food, Consumer Goods, Specialty & Agrochemicals



Develop and deploy
Advanced Process Modelling (APM) tools
to allow
formulated products and their
manufacturing processes
to be designed and optimised
with fewer resources and
for better end-use performance

Progress made with respect to “Develop and deploy Advanced Process Modelling (APM) tools”



First PSE tools
aimed at domain experts,
not necessarily modelling experts

This has resulted in new insights
and new requirements, in particular
with respect to workflows

The screenshot displays three software windows side-by-side:

- gCRYSTAL 4.2.0 (dev):** Shows a process flowsheet for a continuous cooling stage with various components like tanks, pumps, and sensors. It includes several plots showing temperature, pressure, and flow over time.
- gSOLIDS 4.1.0 (dev):** Shows a spray drying process flowsheet. A central plot shows the spray drying process with a fluid bed dryer and a cyclone. Below it, a diagram of a stomach and intestines is shown with a graph of mass fraction versus time, illustrating drug dissolution and absorption.
- gCOAS Developer 1.1.0:** Shows an execution output for Ketoprofen tables. It features a large diagram of the human GI tract with a graph of mass fraction versus time. The graph shows the cumulative fraction dissolved (red line) and the fraction of permeating species absorbed in GI (blue line).

A vertical toolbar on the right contains icons for Annotations, gCOAS Dosage Forms, gCOAS Fundamentals, gCOAS GI Tracts, and gCOAS Pharmacokinetics. The bottom of the interface shows tabs for Output, Topology: Flowsheet, Stream tables: Flowsheet, Reports: Flowsheet, and Properties.

Progress made with respect to “Develop and deploy Advanced Process Modelling (APM) tools”



1.0

2.0

3.0

4.0

4.1

4.2



AstraZeneca

Boehringer
Ingelheim

TATE & LYLE

AJINOMOTO



SAINT-GOBAIN



1.0

2.0

3.0

3.1

4.0

4.1

VERTEX[®]Boehringer
Ingelheim

Genentech

SAINT-GOBAIN



1.0

1.2

2011

2012

2013

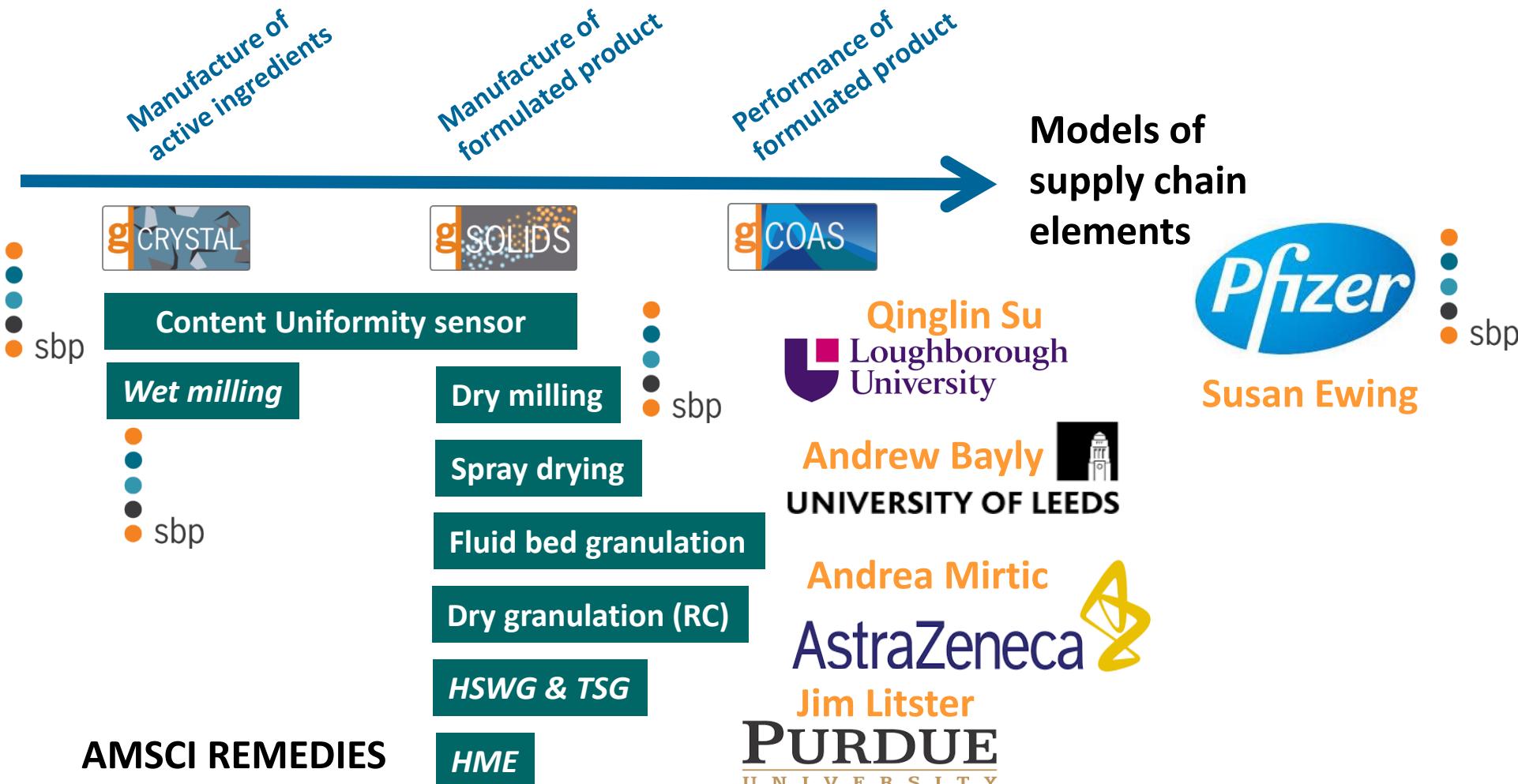
2014

2015

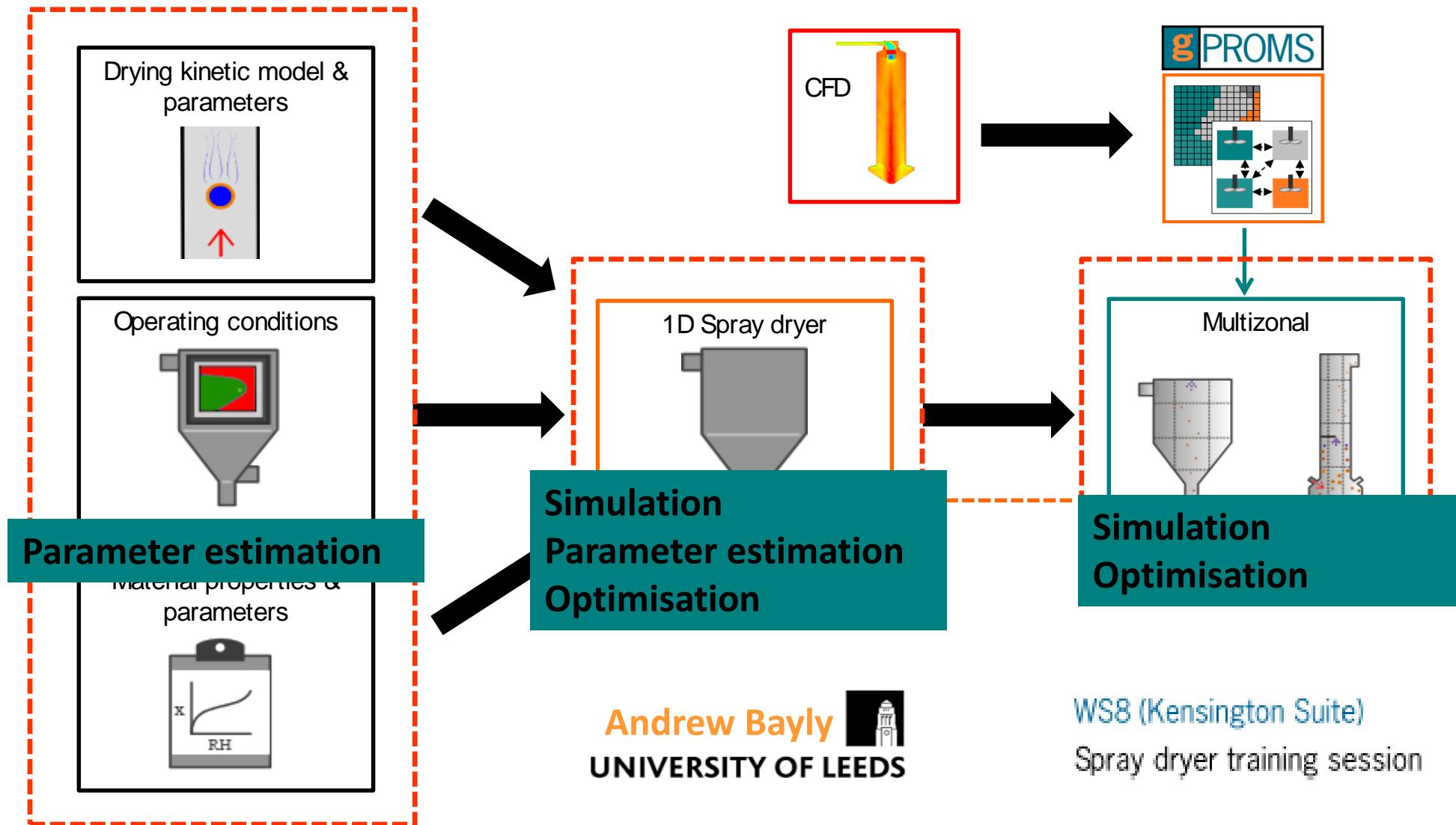
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Development dimensions for PSE's APM tools for formulated products

New models of supply chain elements



Multi-fidelity modelling of spray drying processes and integrated workflow for experimentation and modelling



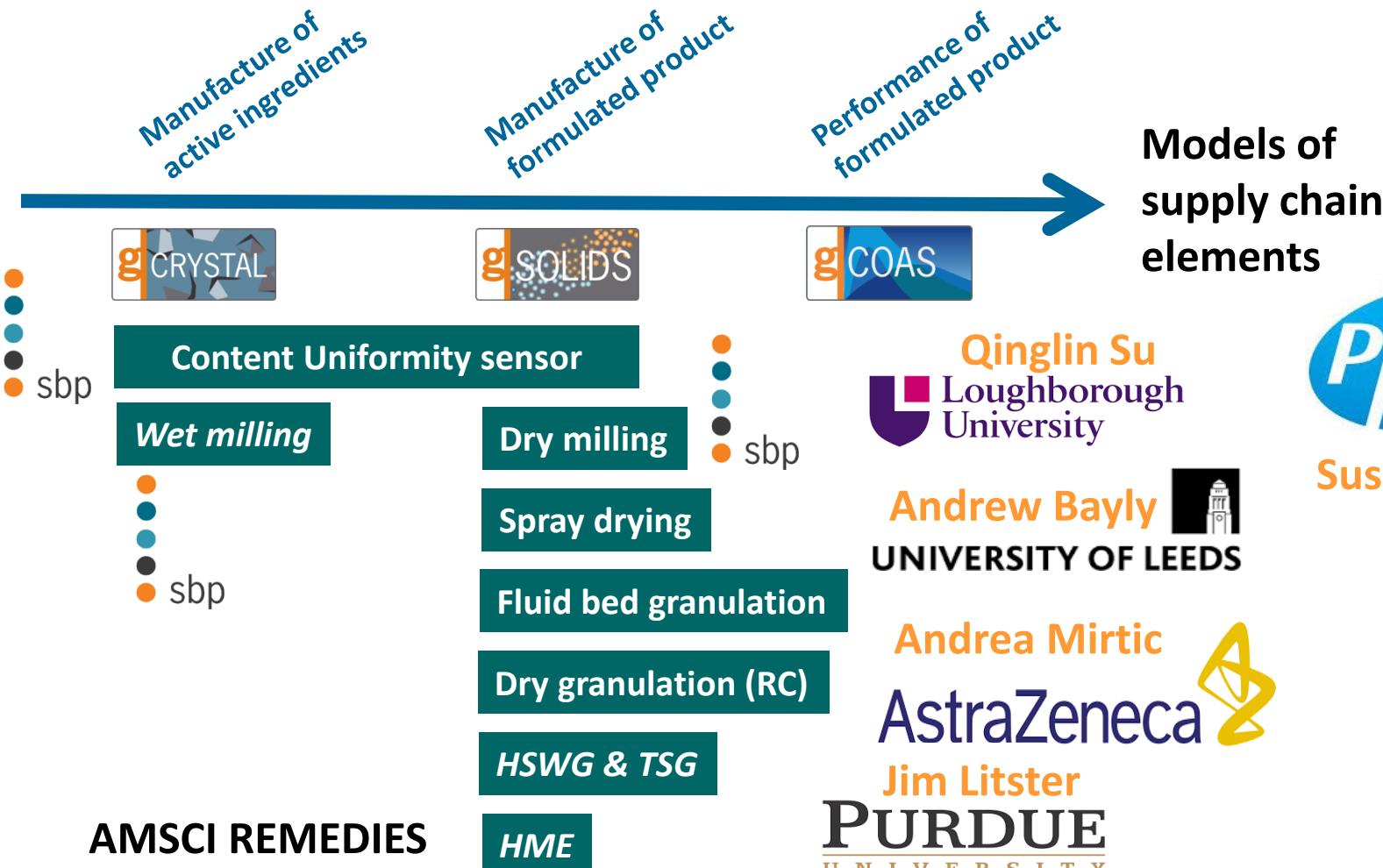
Andrew Bayly
UNIVERSITY OF LEEDS



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Development dimensions for PSE's APM tools for formulated products

Models of supply chain elements



Qinglin Su
Loughborough
University

Andrew Bayly
UNIVERSITY OF LEEDS

Andrea Mirtic
AstraZeneca
Jim Litster
PURDUE
UNIVERSITY

Pfizer
Susan Ewing

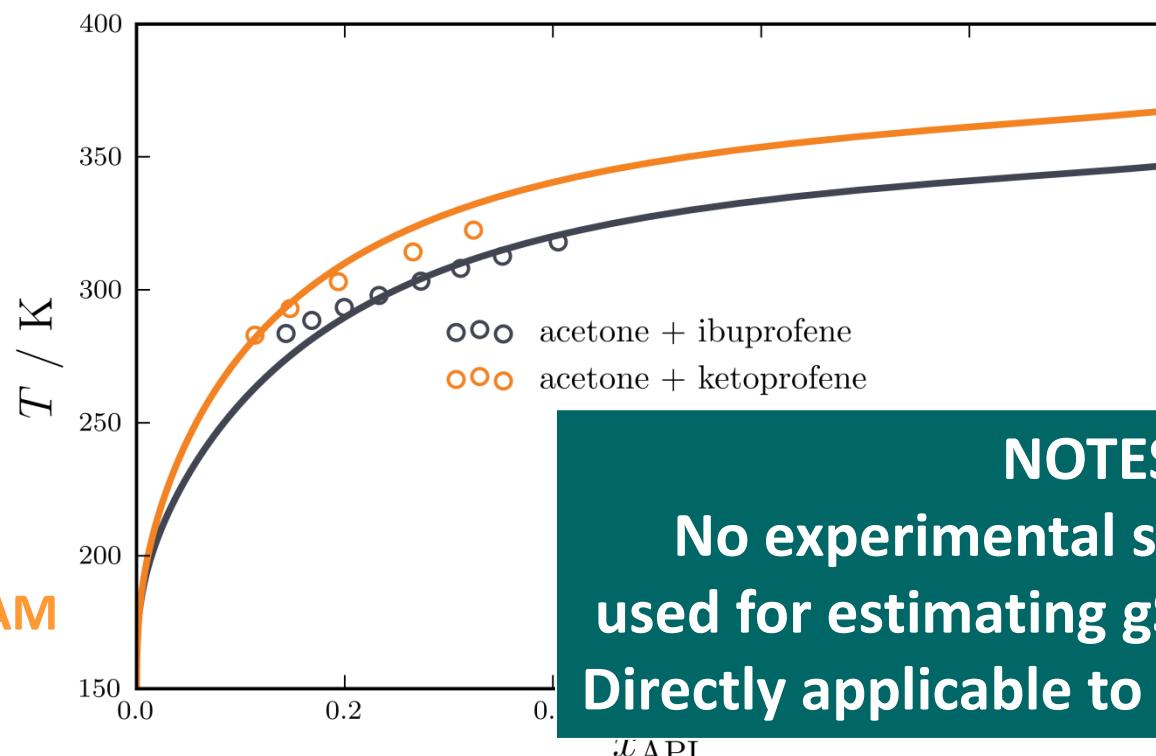
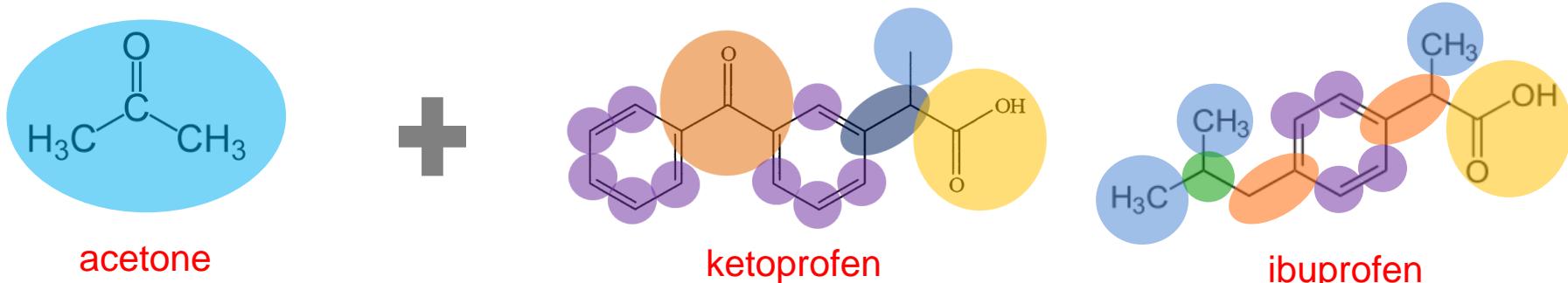
sbp



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gSAFT for pharmaceutical compounds

solubilities of APIs in acetone

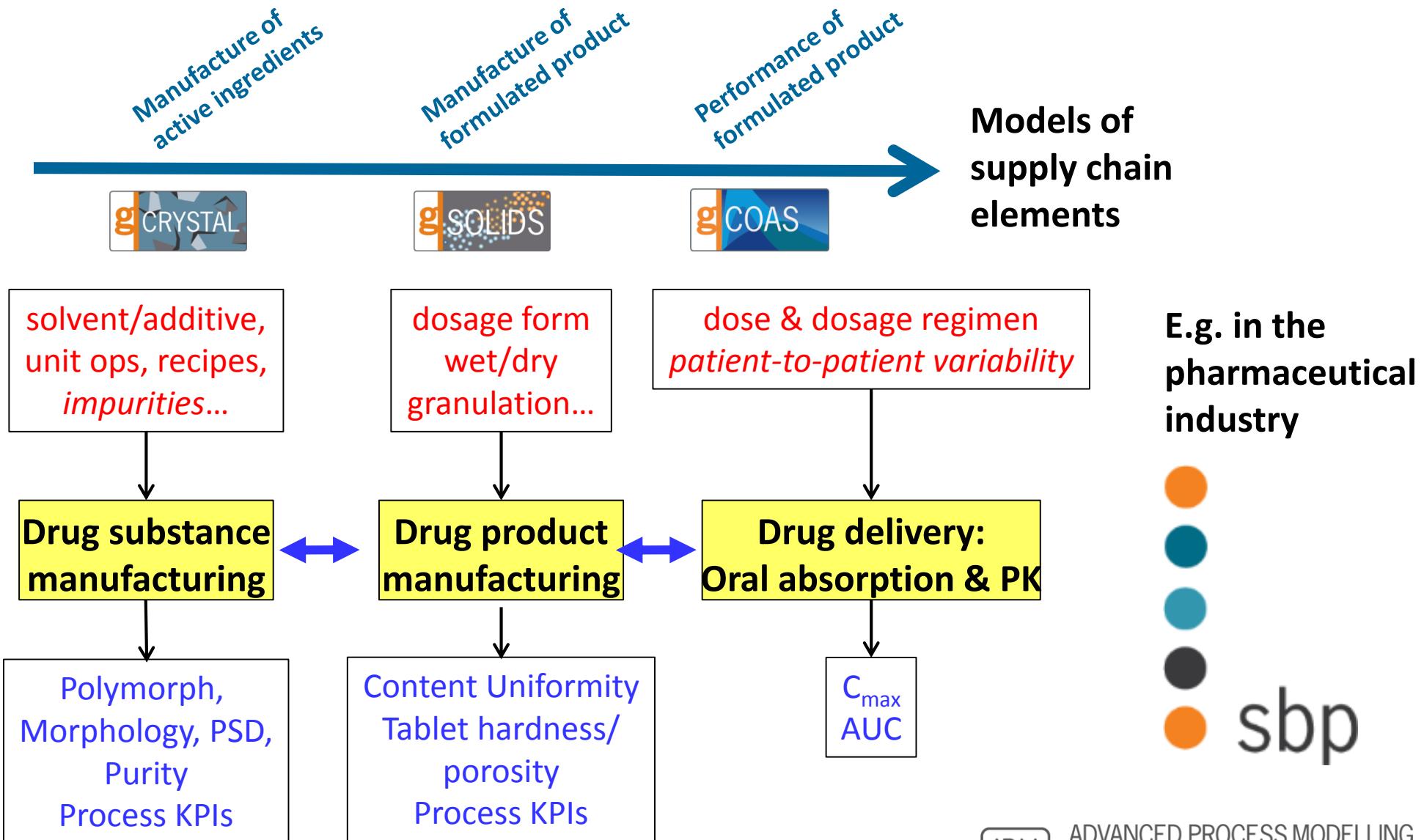


Tom Lafitte, Thu AM

NOTES
No experimental solubility data
used for estimating gSAFT parameters
Directly applicable to solvent mixtures

Development dimensions for PSE's APM tools for formulated products

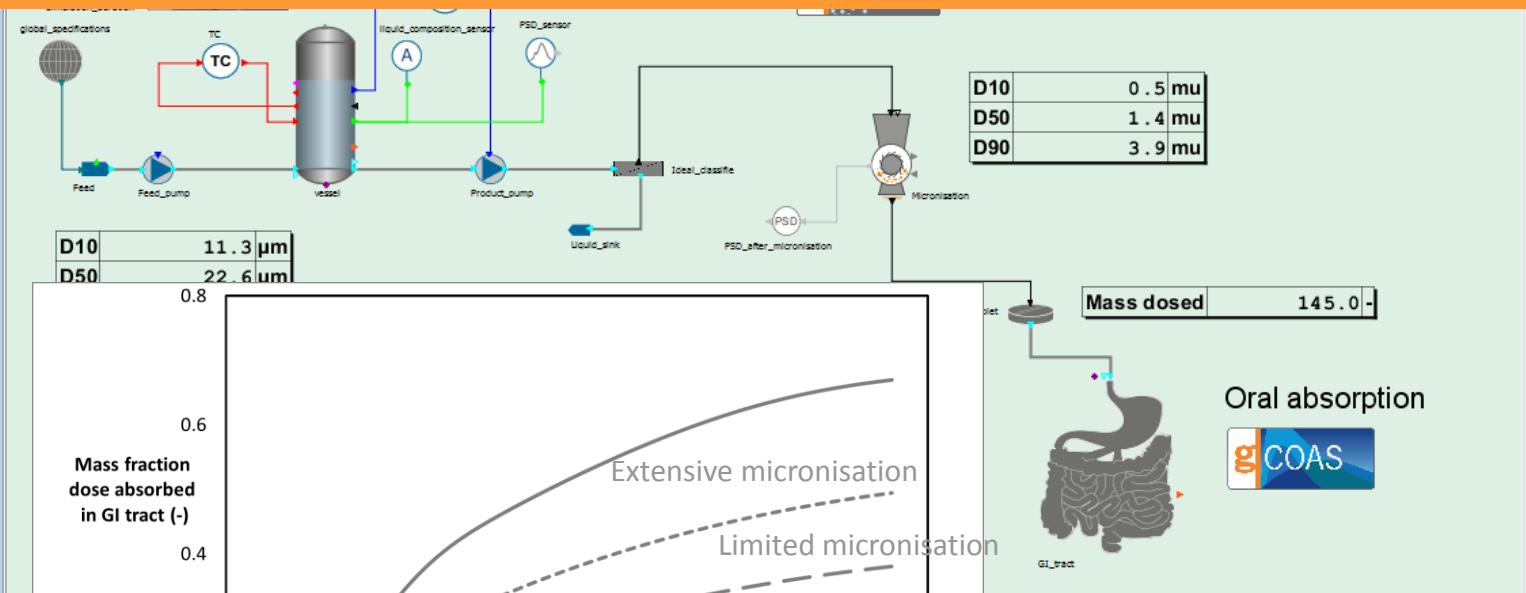
Interoperability to enable holistic approaches to design



Systems-based Pharmaceutics

Impact of manufacturing decisions / disturbances on fraction absorbed

A holistic approach for the optimal design of a drug product's formulation subject to manufacturing constraints (flowability, content uniformity, ...). Reduce iterations between formulators and drug product manufacturing.



Creating a flexible and robust interoperable modelling tool covering manufacture processes and product performance is challenging and provides great opportunities

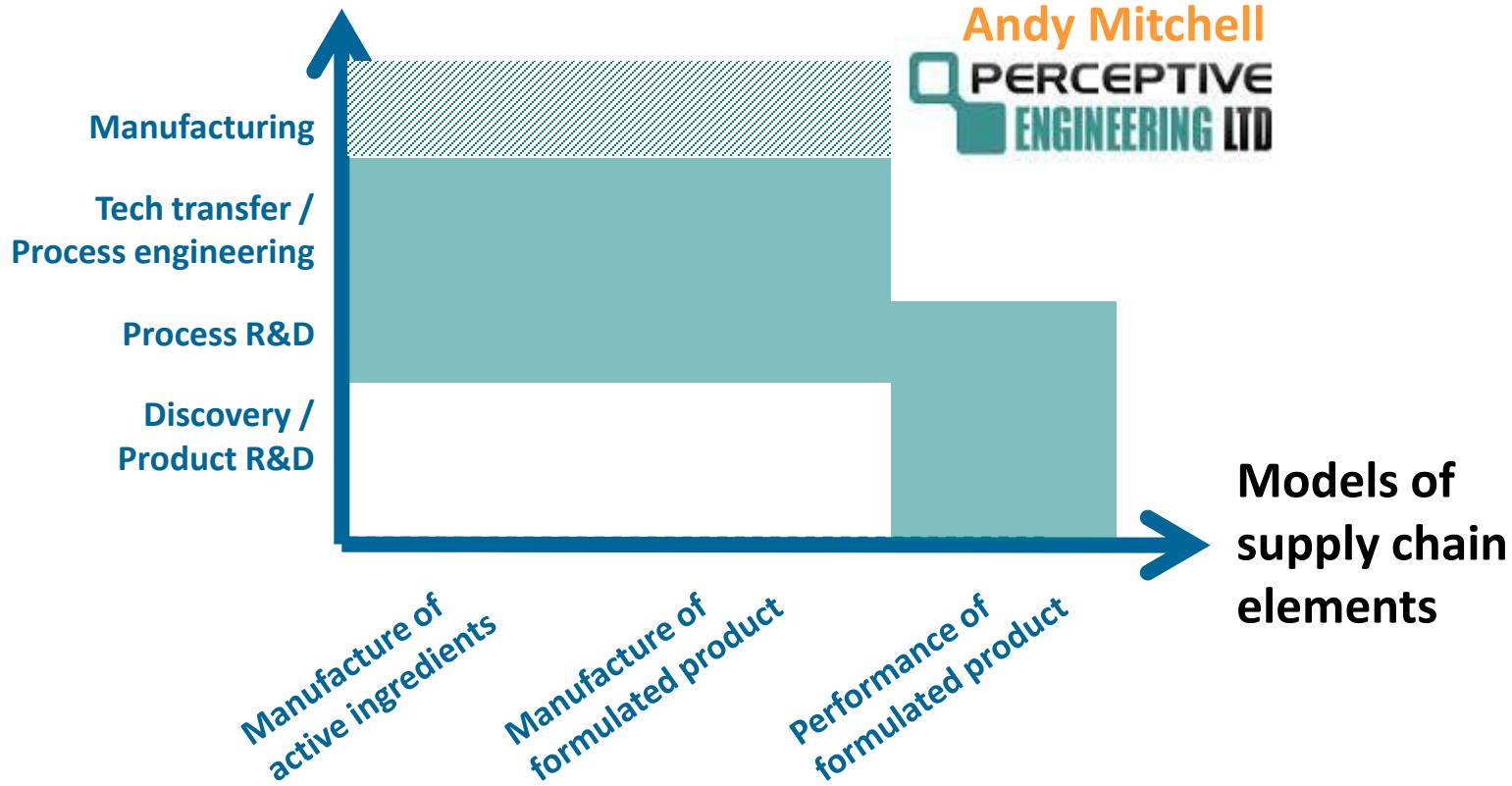
Frances Pereira, Thu AM

Development dimensions for PSE's APM tools for formulated products

Different stages of the product and process lifecycle

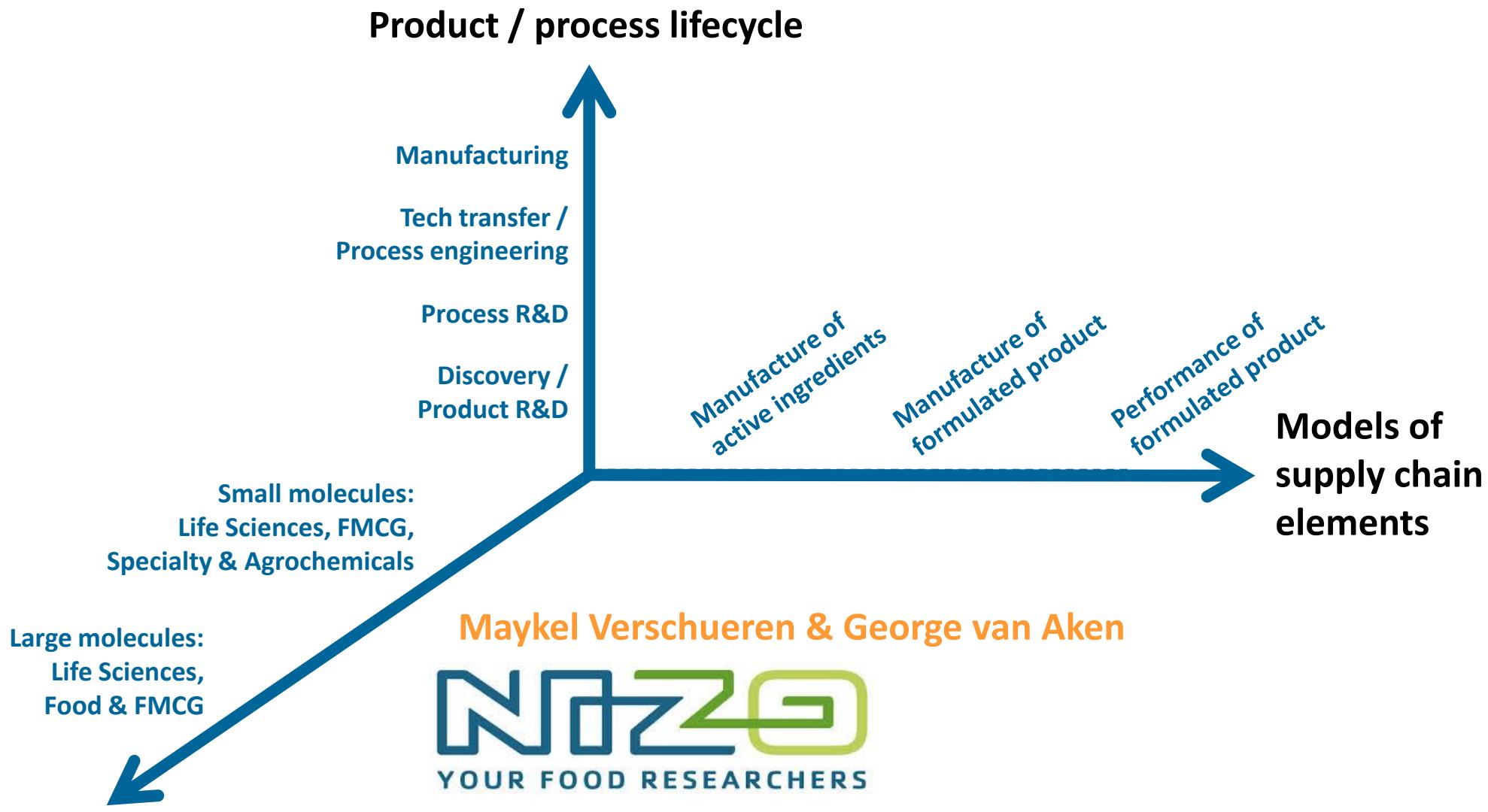


Product / process lifecycle



Development dimensions for PSE's APM tools for formulated products

A wide range of formulated product industries



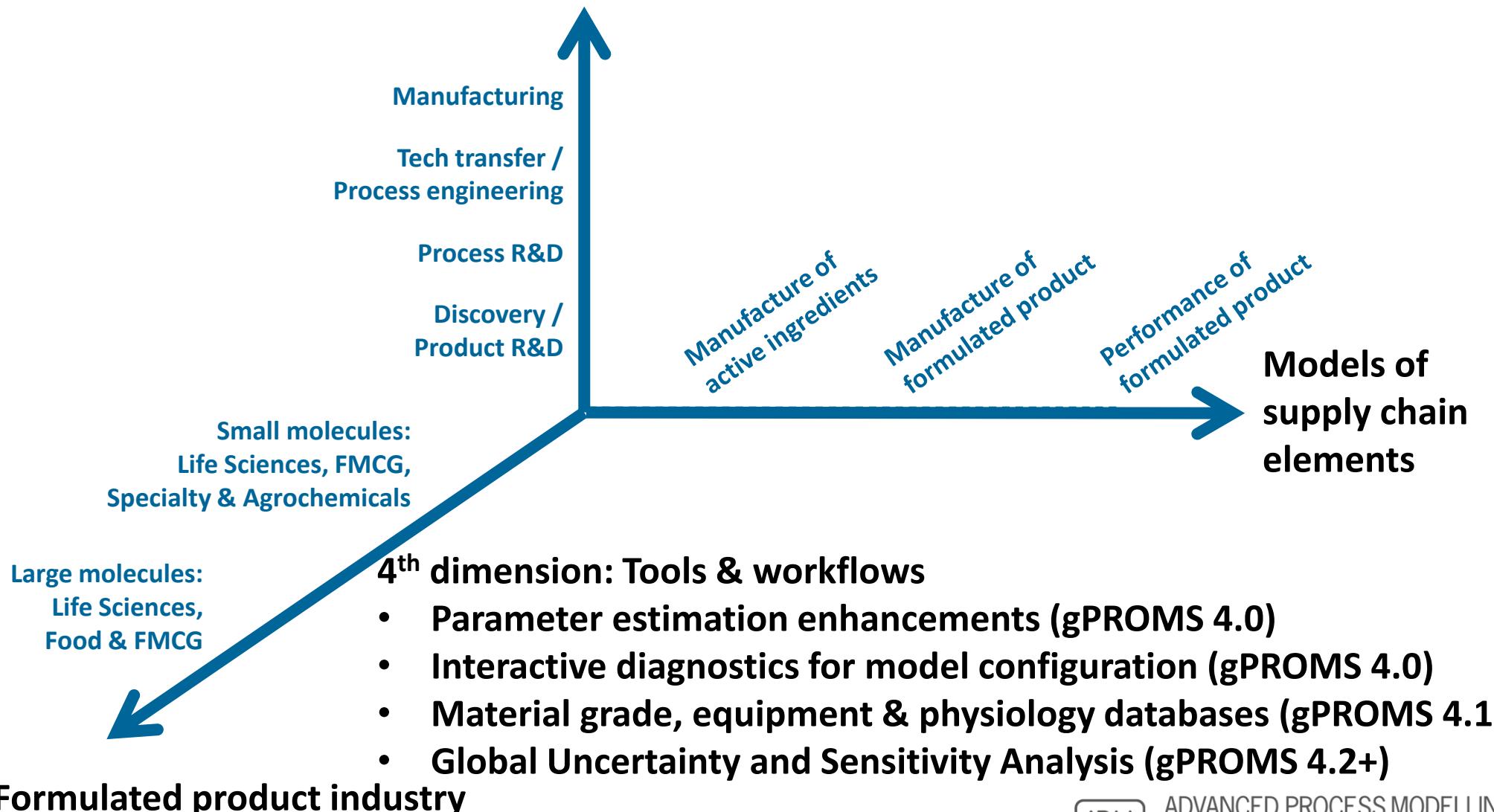
Formulated product industry



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Tools and workflows

Product / process lifecycle

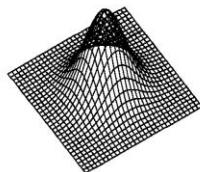


From Uncertainty Quantification to Risk Management



2. Reduce variability in environmental inputs

where possible
& as indicated by Global Sensitivity Indices



- Environmental inputs
- External disturbances
 - Commercial environment

Variability

3. Revise decisions to improve system robustness

Robust Optimization technology

- Decisions
- Design
 - Operational

Decisions

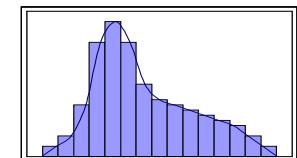
System

4. Modify system

e.g. by allowing operational
decisions to be manipulated
by control system

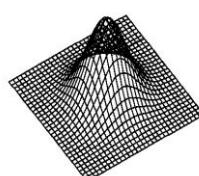
KPIs

- Product quality / performance
- Operability
- Safety
- Environmental impact
- Economic performance



1. Improve model and/or quality of data, reduce parameter uncertainty

R&D focus guided by
Global Sensitivity Indices



Model parameters

Uncertainty

Model

Innovate UK
Technology Strategy Board

June 2014 – May 2016
Britest, AZ, GSK and Pfizer

Costas Pantelides, Thu AM



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- Good progress in development and deployment of targeted tools (gCRYSTAL, gSOLIDs and gCOAS)
- Much more progress is on its way.
 - four years ago when we started development: 2 developers.
 - now: 6 developers
 - AMSCI Digital Design: further 5 developers
- Interoperability is a key *functionality* for the optimal design of formulated products and their manufacturing processes with fewer resources and better end-use performance
- Work in parallel on *usability and workflows* is paramount for widespread adoption of these tools

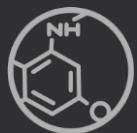
Acknowledgments

- Advisory Board
 - AstraZeneca, BASF, DuPont, Eli Lilly, GSK, Nestle, Novozymes, P&G, Pfizer, Solvay, Purdue U., Sheffield U., TU Delft,
- PSE Software Technology group for platform developments
- PSE Formulated Products team ...



... always prepared for the unexpected (but not for this photo)

Thank you



- Interoperability → holistic approach
 - e.g. Systems-based Pharmaceutics
- Further development of mechanistic models
 - dry and wet milling models (SbP)
 - better description of fragment PSD
 - relating breakage behaviour to more intuitive input parameters
 - oral absorption (Susan Ewing; Pfizer)
 - HSWG & TSG
 - HME (AMSCI REMEDIES)
 - CheK – CLOS slides
 - Food processing and properties (NIZO presentation)
- Model-based applications
 - GSA to assess robustness of product and process performance (IUK Digital Design)
- Workflows and usability
 - Content uniformity (SbP)
 - multi-fidelity models, e.g. spray drying (workshop Thursday PM)
 - PE work flows (SbP)
- Taking models on-line to support operations (PEL presentation)

gPROMS product family



General mathematical modelling



gPROMS ModelBuilder
Advanced process
modelling environment

Sector-focused modelling tools

Chemicals & Petrochemicals



gPROMS ProcessBuilder
Advanced process
simulation

Life Sciences, Consumer, Food, Spec & Agrochem



Solids process
optimisation



Crystallization
process optimisation



Oral absorption

Power & CCS



CCS system modelling

Oil & Gas



Flare networks &
depressurisation

Wastewater Treatment



Wastewater systems
optimisation

Fuel Cells & Batteries



Fuel cell stack &
system design



The gPROMS platform

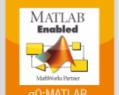
Equation-oriented modelling & solution engine

Materials modelling



Model deployment tools

Enterprise Objects



Deploy models in common engineering software

Logos & icons



Corporate



APM Forum

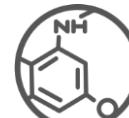


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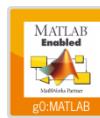
Products



Sector icons



gPROMS Objects



Enterprise



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