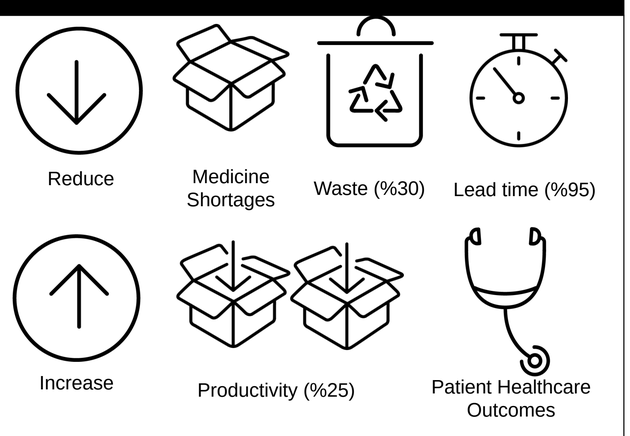
DM² Platform II: AI-Assisted Optimization of Oral Solid Dosage Form Development

Salehian M, Moores J, Abbas F, Markl D
Centre for Continuous Manufacturing and Advanced Crystallisation (CMAC) & Strathclyde Institute of Pharmacy and Biomedical Sciences (SIPBS), University of Strathclyde

Introduction to DM² Platform II

Platform II uses AI to develop an autonomous workflow for drug product manufacturing and testing system by identifying critical material attributes (CMAs) and associated critical process parameters (CPPs) that result in targeted critical quality attributes (CQAs). We aim to collect and use a database of 100s historical/new experiments to de-risk and accelerate drug product development while reducing experiments, development time, and materials use by 30%.



Overview of Manufacturing Optimisation

The goal is to maximize the value of information from each experiment while minimizing the material consumption in order to 1) make the right material and 2) test the right property at the right time. The iterative, model-based optimization consists of smartly designing the experiments that drive the automated manufacturing and testing system, collecting multi-scale and –point data, and updating the model to learn from the experiments. Bayesian optimization will be employed to execute this loop and it continues until the targets are achieved.

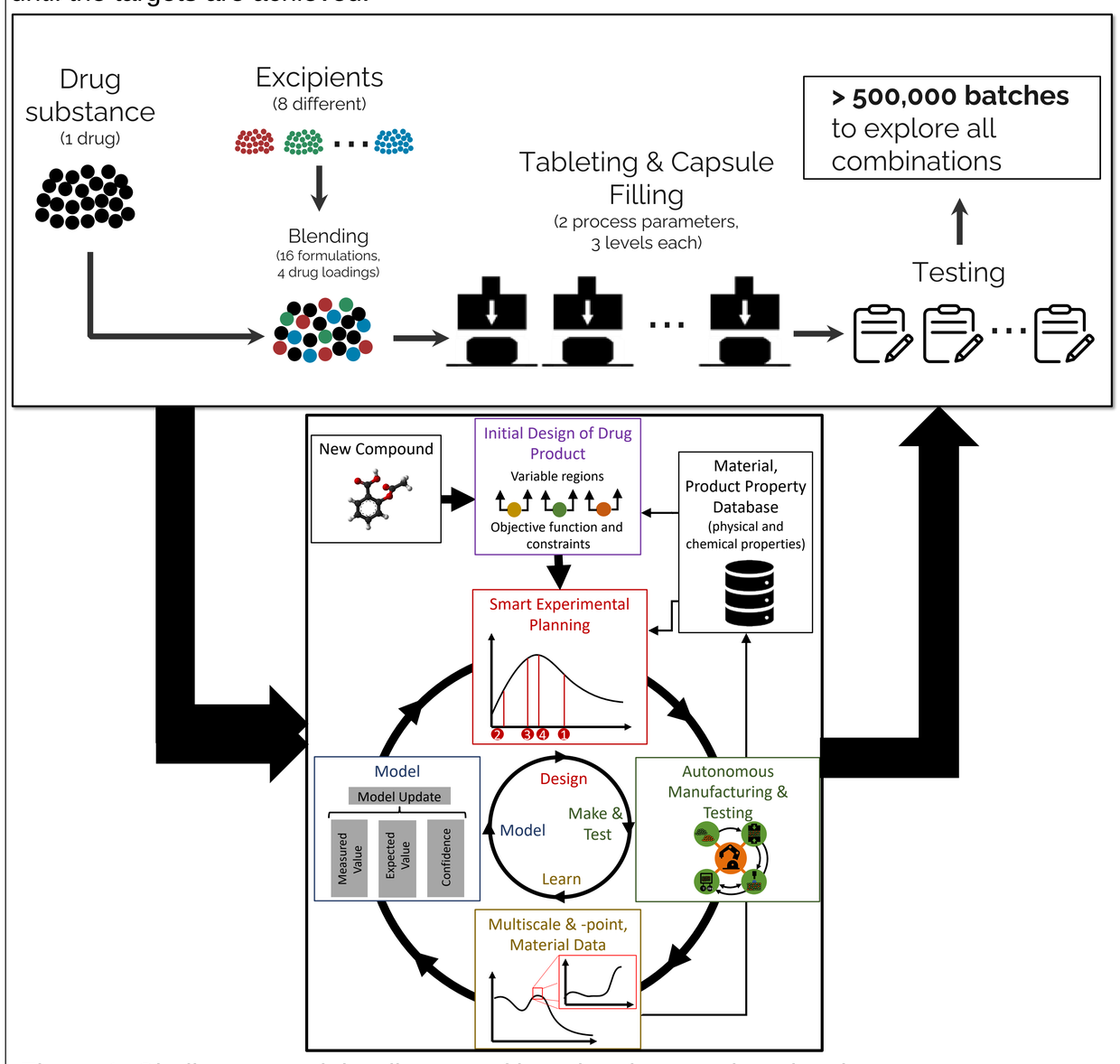


Figure 1: Challenges and the diagram of iterative drug product development process.

Modelling of Tablet & Capsule Attributes

To predict the product attributes, a hybrid machine is being developed to utilize historical data of raw material and blends imported into both domain knowledge (empirical/mechanistic models) and AI-based models (where domain knowledge is not available/reliable).

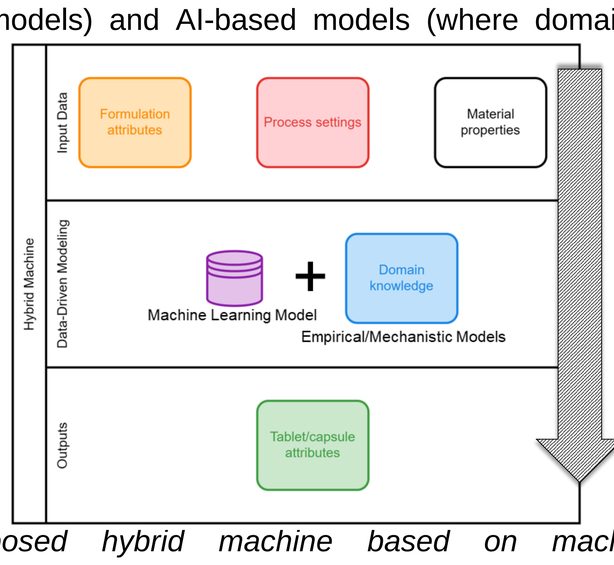


Figure 2: The proposed hybrid machine based on machine learning and empirical/mechanistic models to predict tablet/capsule attributes.

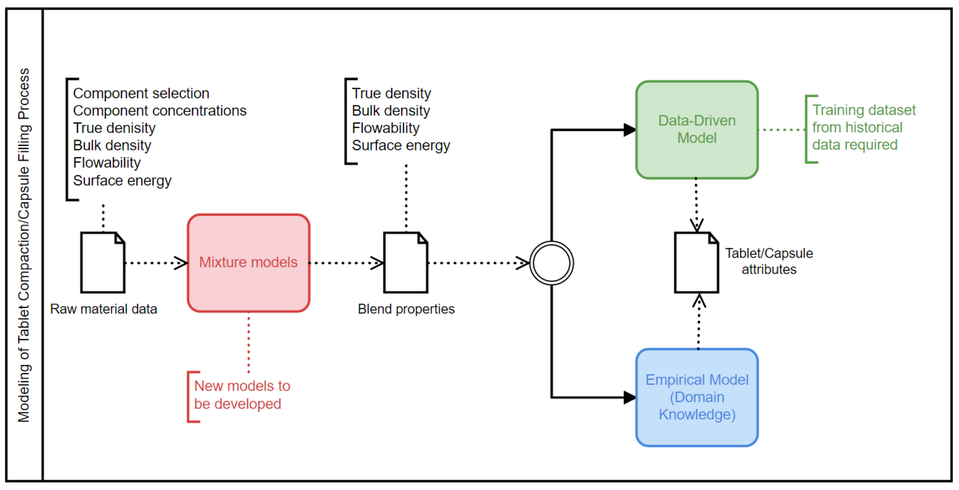


Figure 3: Hybrid use of raw material/blend data for compaction modelling and optimization.

Problem Definition for Manufacturing Optimisation

Different use cases were identified based on the specified input parameters, constraints, objectives and decision parameters. The framework is divided into two sub-problems, process and formulation optimization, where an outer loop (process optimization) is followed by an inner loop (formulation optimization). The goal is to enable flexible choice of different objectives/constraints at each level based on their relative importance.

Decision parameters

	Property	Type	e.g. Value
Process settings	Punch gap setpoint	Scalar	2 - 3 mm
	Rotation speed setpoint	Scalar	20-90 rpm
	Blending time setpoint	Scalar	20 min
Formulation attributes	Drug loading	Scalar	1, 10, 20, 40%
	Excipient selection	Categorical	MCC, DCPA, Lactose, Mannitol
	Excipient concentrations	Scalar	1-99%

Input parameters

Property	Type
True density	Scalar
Bulk/Tapped density	Scalar
Solubility	Scalar
Flowability	Scalar
Particle shape	Scalar
Particle size	Scalar
Surface energy	Scalar
Hygroscopicity	Scalar

Hybrid Machine

Objectives

Property	Type	e.g. Value
Minimise disintegration time	Scalar	< 5 min
Maximise dissolution	Scalar	Release of > 80% within 30 min
Maximise porosity	Scalar	10 - 20%
Maximise drug loading	Scalar	50%

Constraints

Content / weight uniformity	Scalar	< 5% RSD
Tensile strength	Scalar	> 2 MPa
Size/dimensions	Scalar	Thickness: 2 - 7 mm Diameter: 9 mm

Figure 4: Schematic representation of the optimization workflow based on hybrid machine, including different decision and input parameters, objectives, constraints, and objectives.

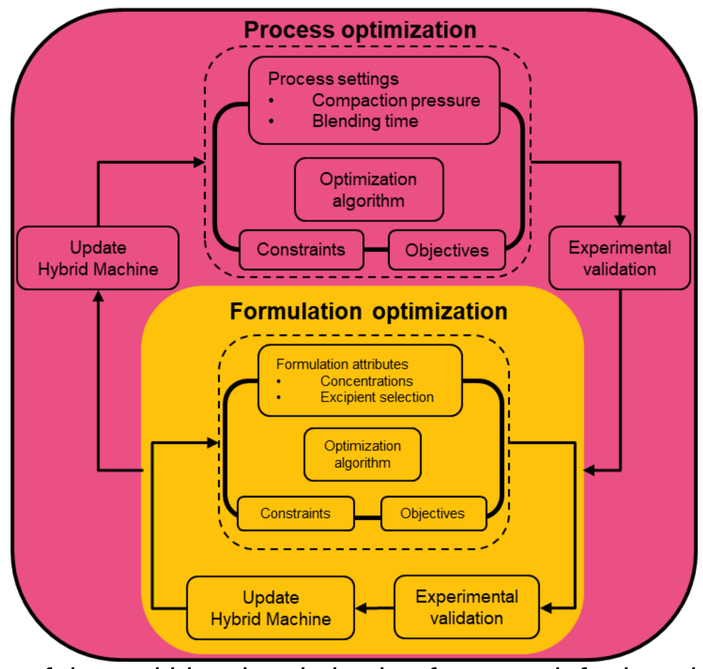


Figure 5: Flow diagram of the multi-level optimization framework for iterative, simultaneous optimization of process

Use Case 1: Optimization of Tablet Porosity

In the use case 1, compaction data is used to predict porosity based on the peak compression pressure. The Gurnham (empirical) model is used to fit the historical (existing) data. A smart experiment planning procedure is designed to minimize experimental workload and material use while estimating the model parameters. Analysing the uncertainty of fit (i.e. confidence interval) shows that adding 1 data point results in 20-fold improvement in the accuracy of prediction, while adding 8 more data points leads to minimal improvement, highlighting the significance of here-developed smart experimental planning procedure in achieving good prediction accuracy at minimal experimental cost.
The historical/existing data will be used to compute the model parameters for different blends and create a database, for which a data-driven model will be developed to estimate the model parameters of new blends (figure 3). Research is ongoing to utilize mixture models to account for raw material data with different properties such as type of component, concentrations, bulk/true density, flowability, surface energy, etc.

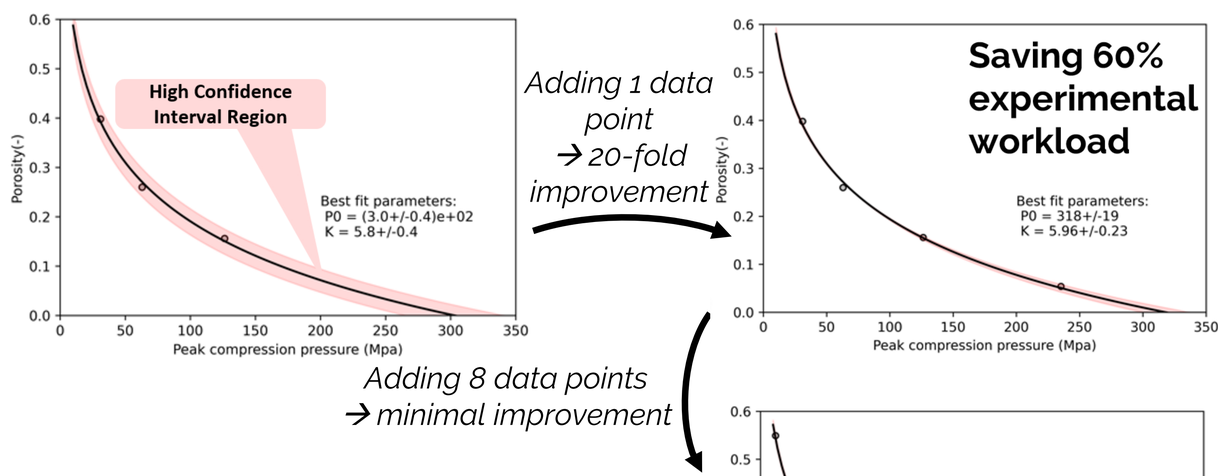


Figure 6: Example for smart experimentation planning by analysing uncertainty of fit and suggesting the next experiment to improve the accuracy of fit as much as possible.

SCAN ME

MADE SMARTER INNOVATION

DM² Digital Medicines Manufacturing