CMAC

System Model Driven Optimisation of Directly Compressed Tablets Development Processes

DM² Digital Medicines Manufacturing

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¹ Challenges & Motivations

- ? *Find the optimum formulation and process conditions*
- ? *Maximise drug product quality attributes*
- ✓ *Use models and algorithms to reduce material waste*
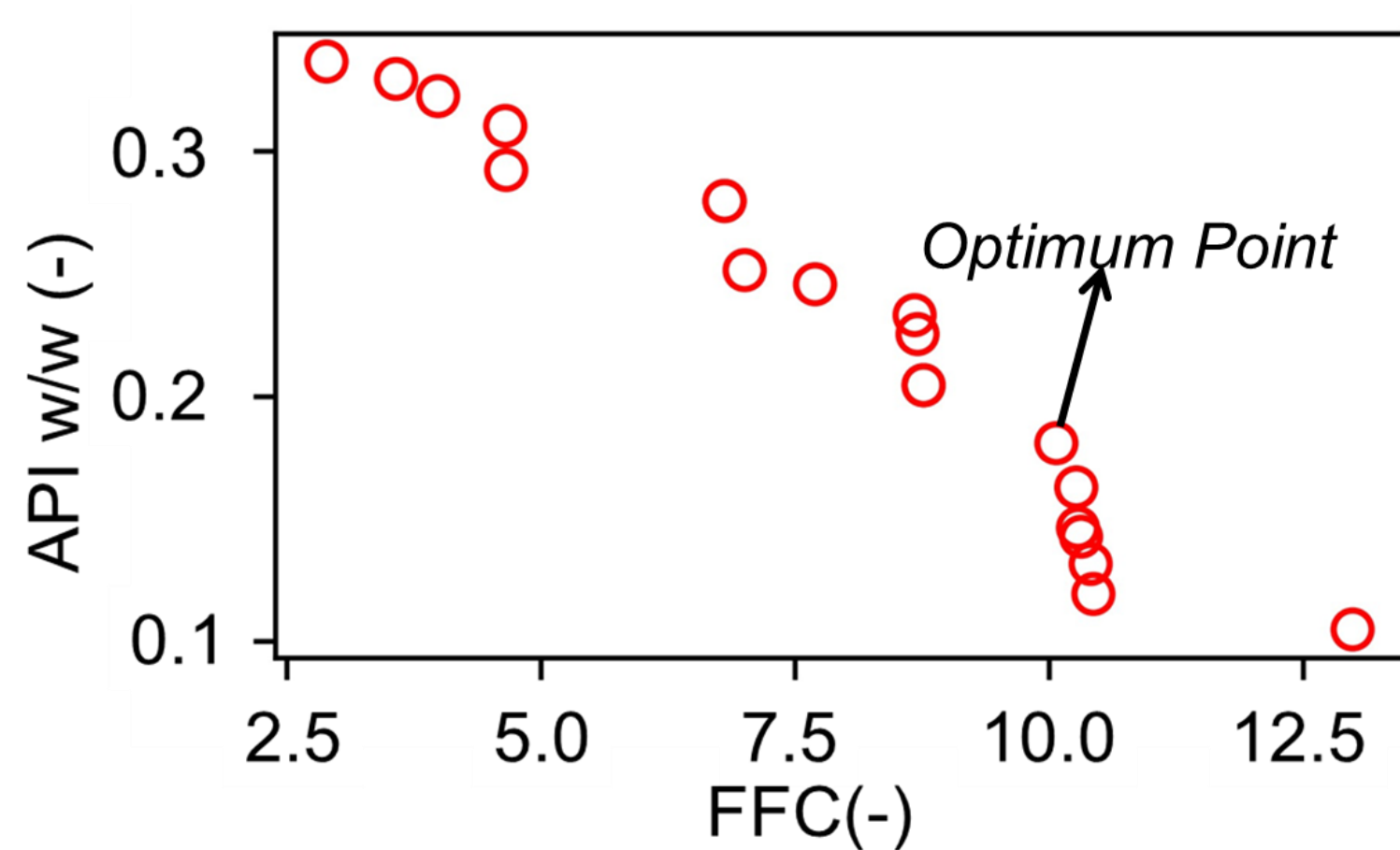- ✓ *Slash the development time of new drug products*

² Formulation and Process Development

Formulation Settings
API
Excipients
Blending

Process Settings

Objectives/Constraints
Porosity
Drug Loading
Tensile Strength
Flowability

Testing

⁴ Self-Optimisation
A Multi-Objective Case Study

Objectives:
Maximum Drug Loading
Maximum Flowability
Constrains:
Porosity > 12%
Tensile Strength > 2 MPa

Optimum Point — API w/w (-) vs FFC(-)

Raw material attributes:
- *True density*
- *Bulk density*
- *Particle size distribution*
- *Particle shape distribution*

Mechanistic Model

$f(x)$ — Particle size distribution of mixture
$f(x)$ — Aspect ratio distribution of mixture
$f(x)$ — True density of mixture
$f(x)$ — Bulk density of mixture

PCA → • PC1 • PC2 • PC3
PCA → • PC1 • PC2 • PC3

AI — *Data-Driven Model*

Tapped density of mixture
Flowability of mixture
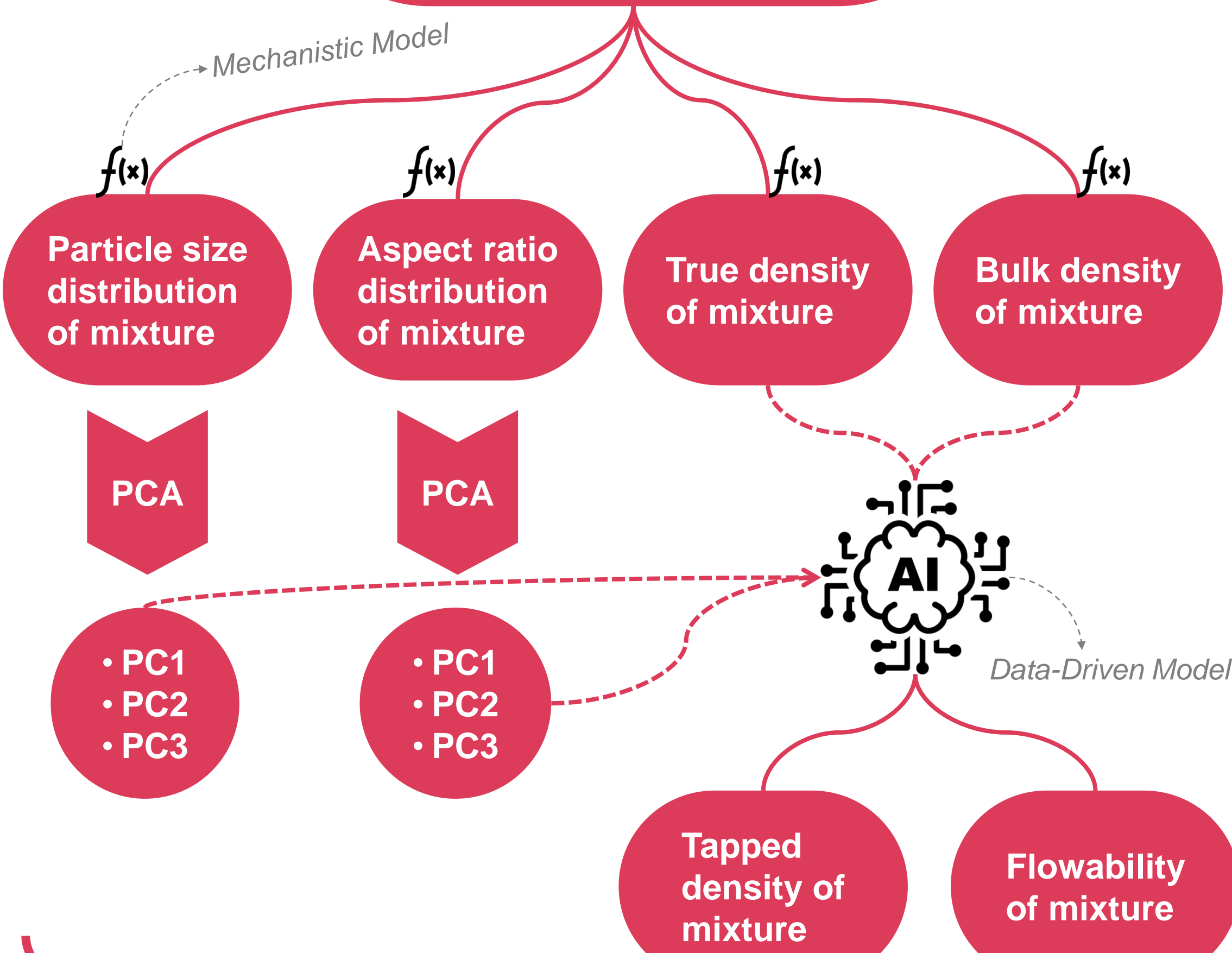
Process conditions
Formulation
Blend properties

Process models
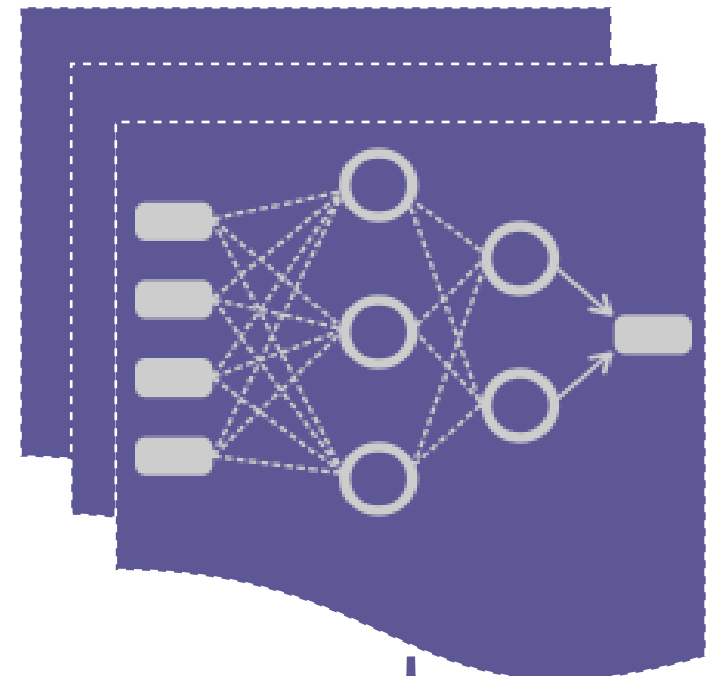
Porosity
Tensile Strength

³ System of Models

3.1 Mixture Models
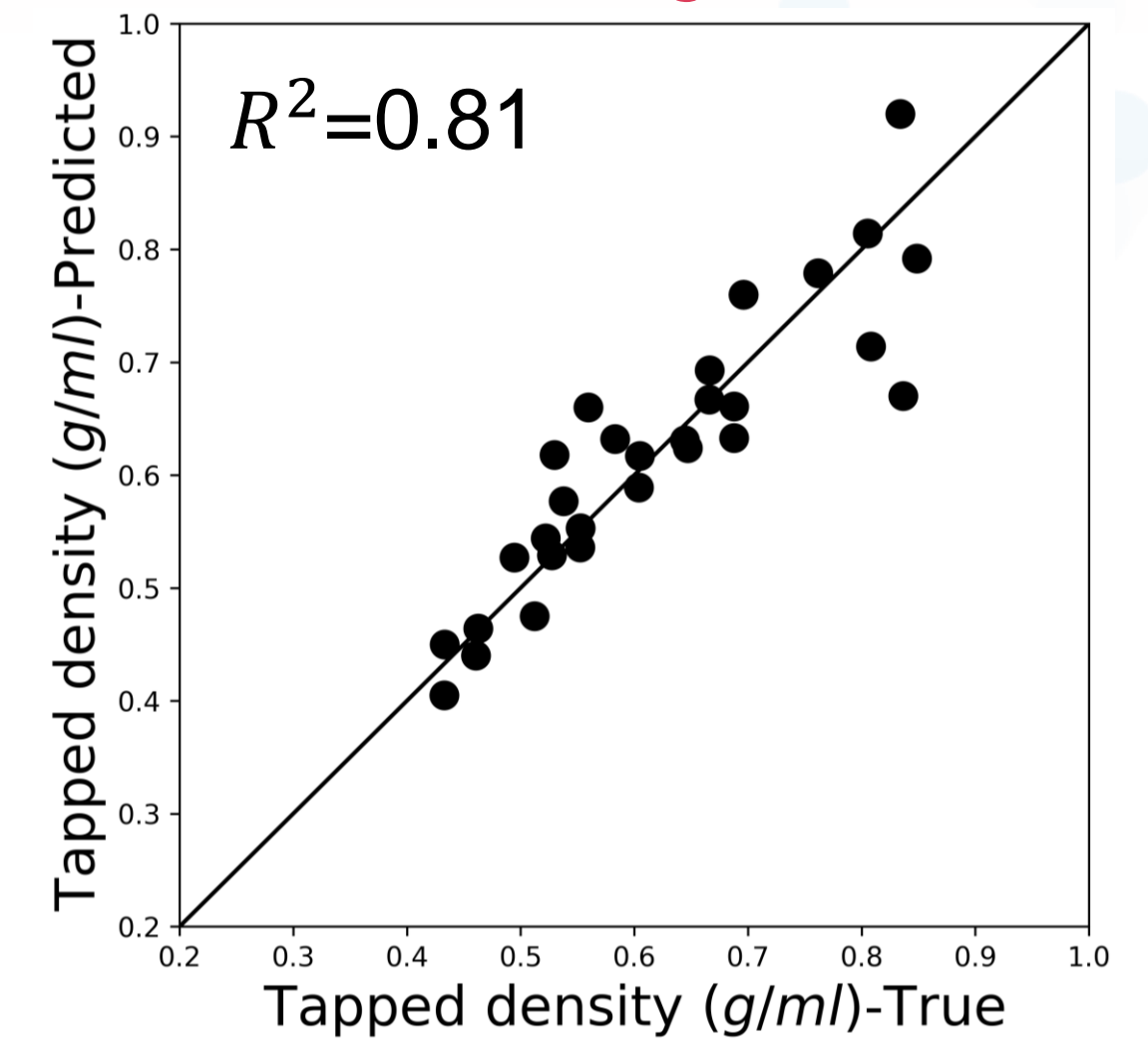*From Raw Components to Blend Properties*

True Density
Harmonic Mean
$R^2 = 0.98$
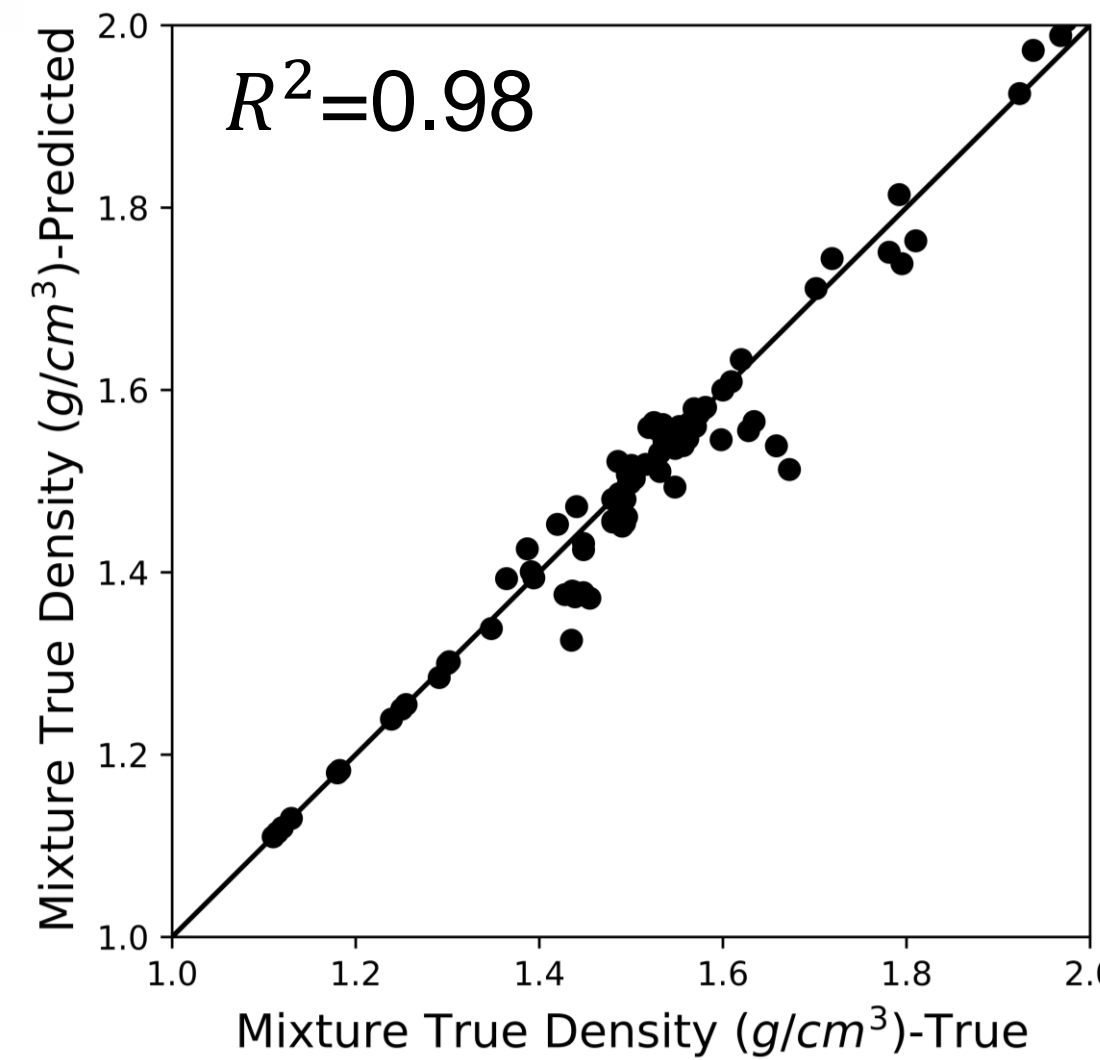
Bulk Density
Mass-based Arithmetic Mean
$R^2 = 0.89$
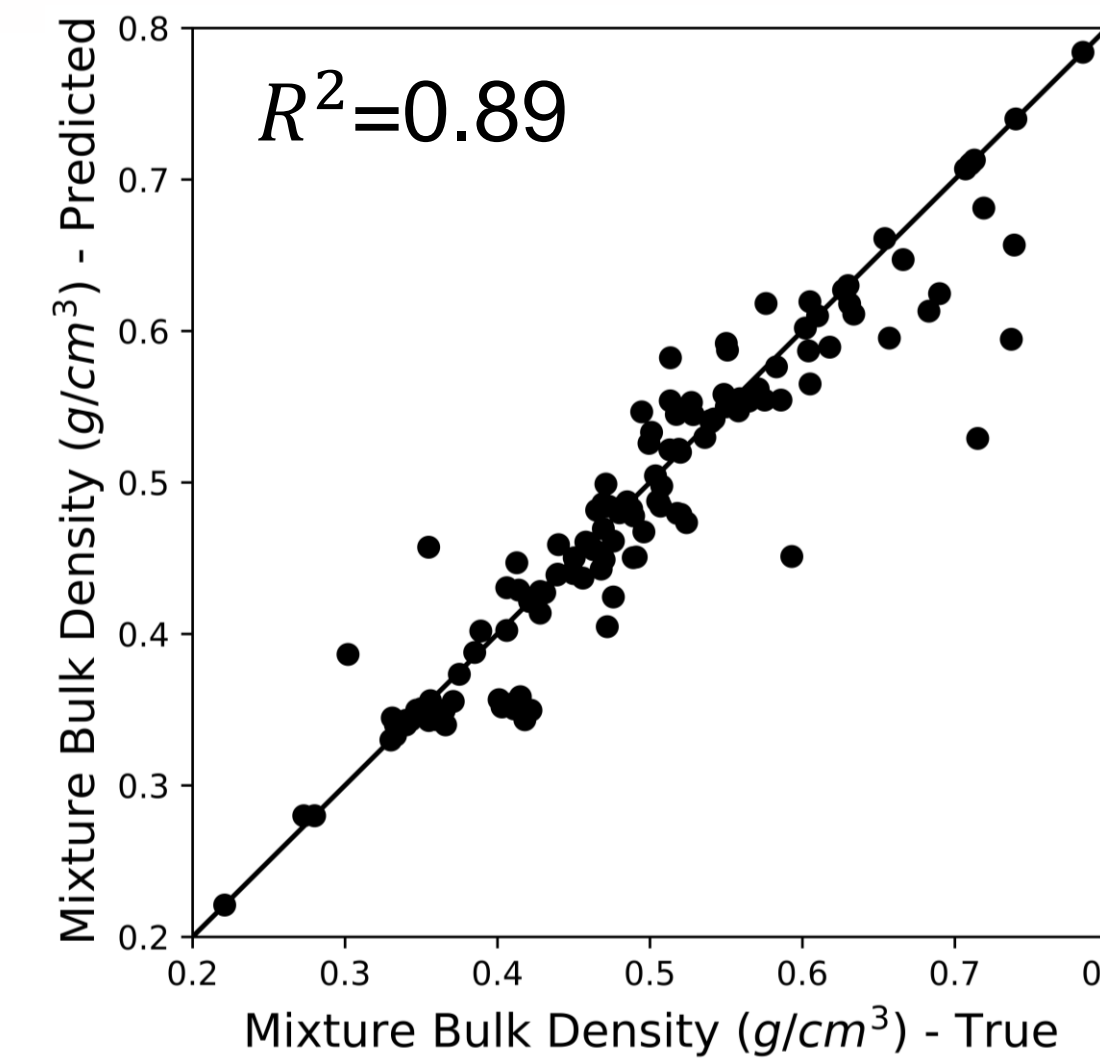
Tapped Density
XGBoost Regression
$R^2 = 0.81$

Particle Size
Probabilistic-Mechanistic Model
APAP-CCS1-MCC1-MgSt1-blend 1 model
APAP-CCS1-MCC1-MgSt1-blend 1 measured
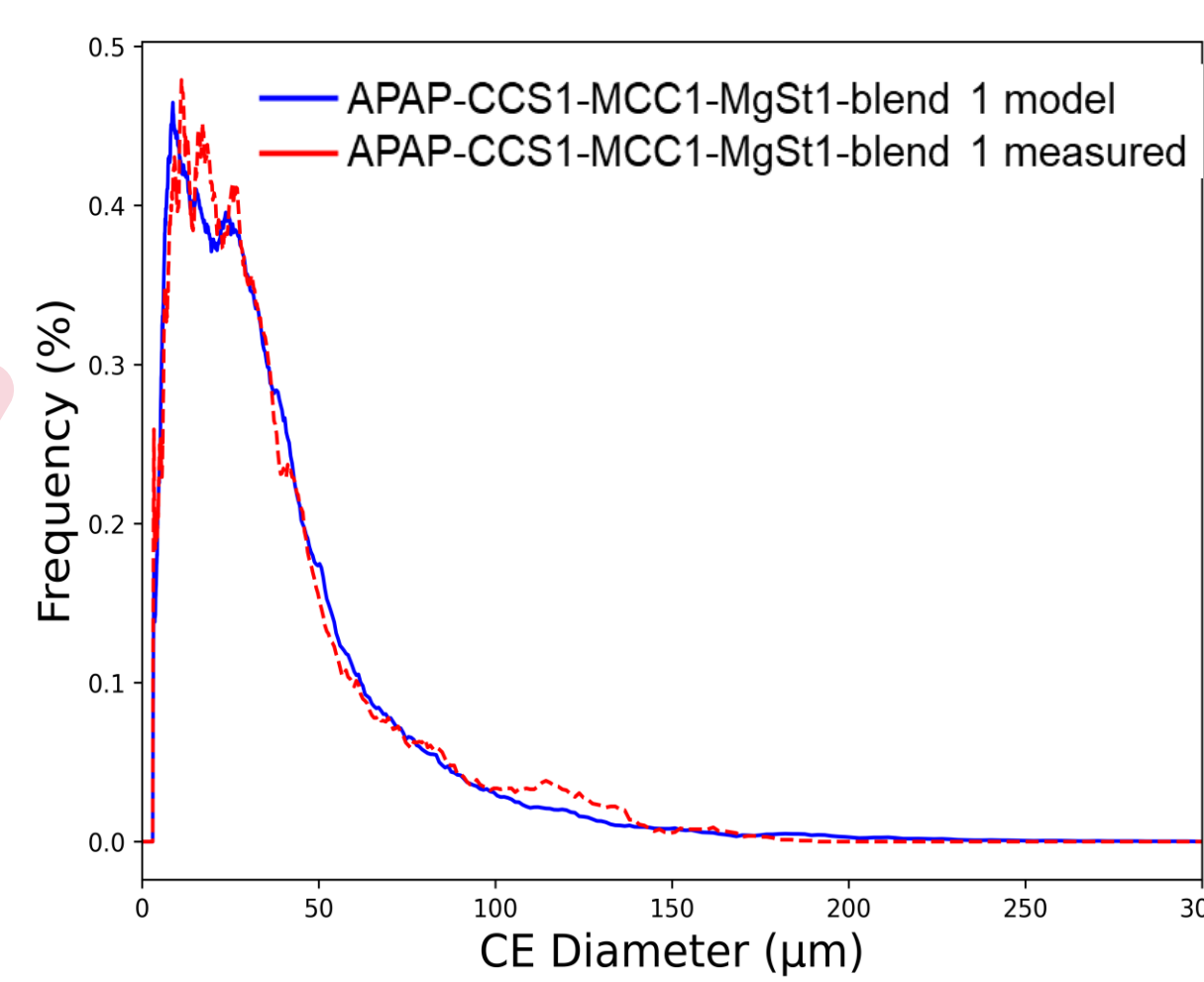
Particle Shape
Probabilistic-Mechanistic Model
APAP-CCS1-MCC1-MgSt1-blend 1 model
APAP-CCS1-MCC1-MgSt1-blend 1 measured
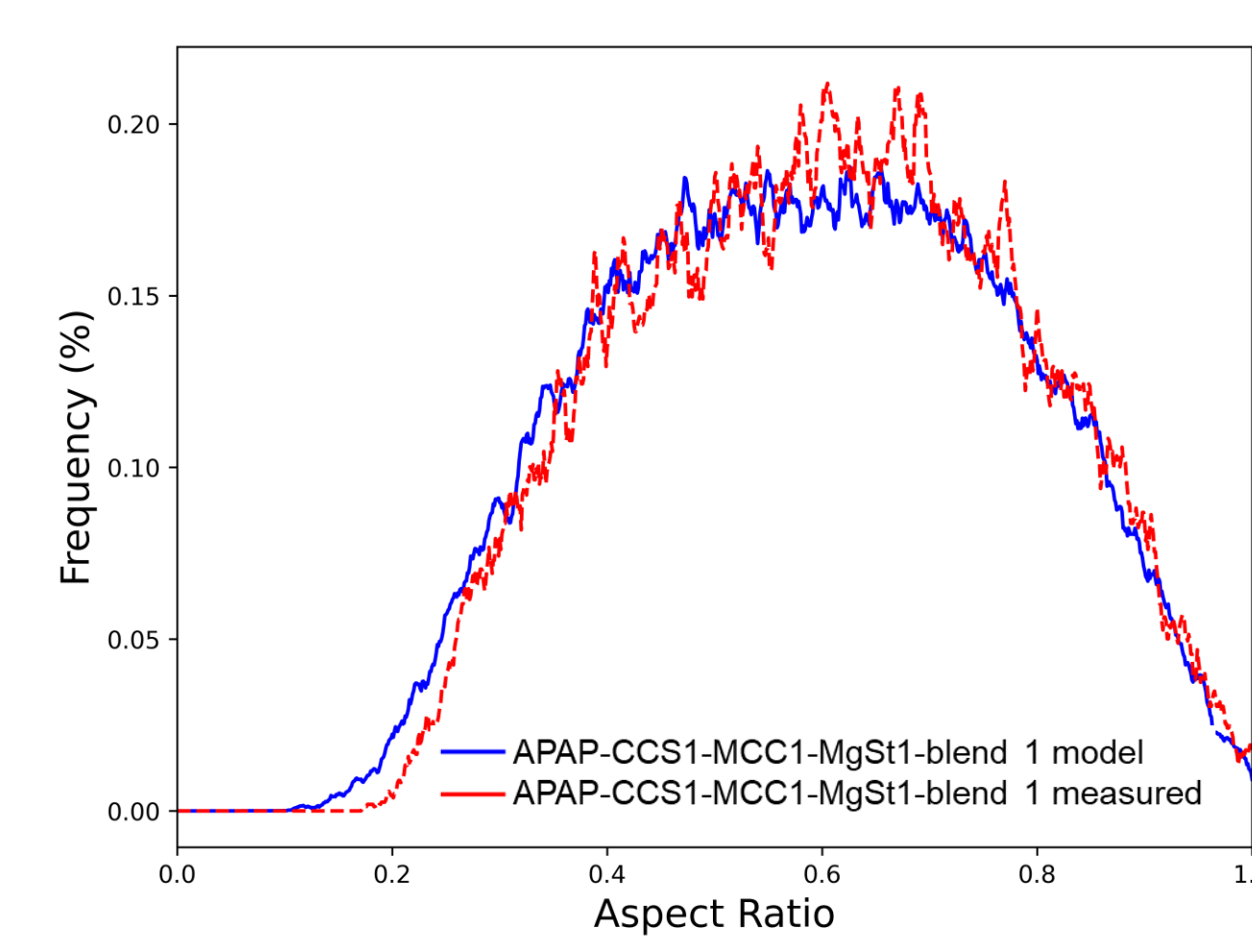
Flowability
Random Forest Regression
$R^2 = 0.93$
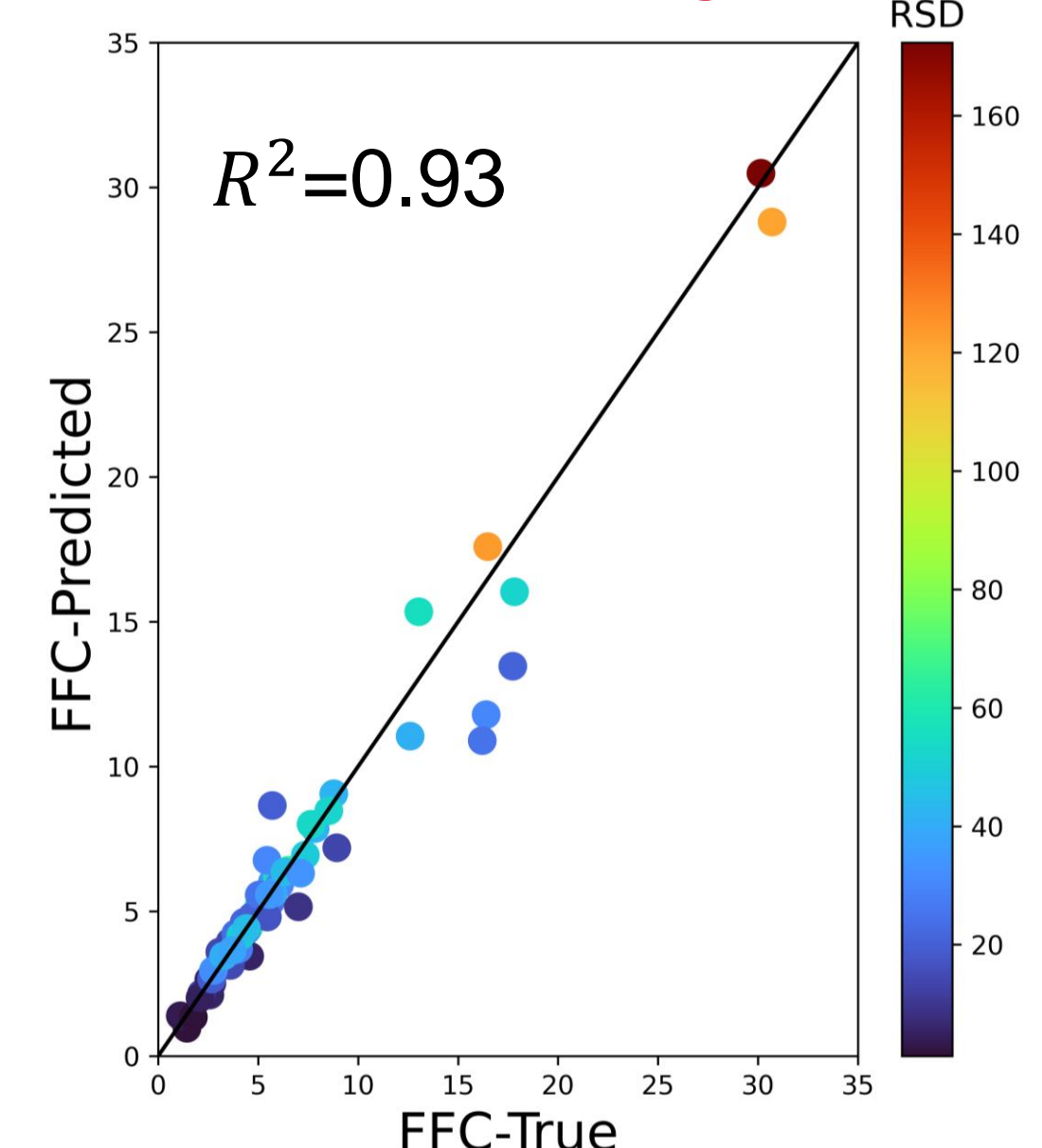
3.2 Process Models
From Blend Properties to Tablet Attributes

Tablet Porosity
Deep Neural Networks
$R^2 = 0.91$
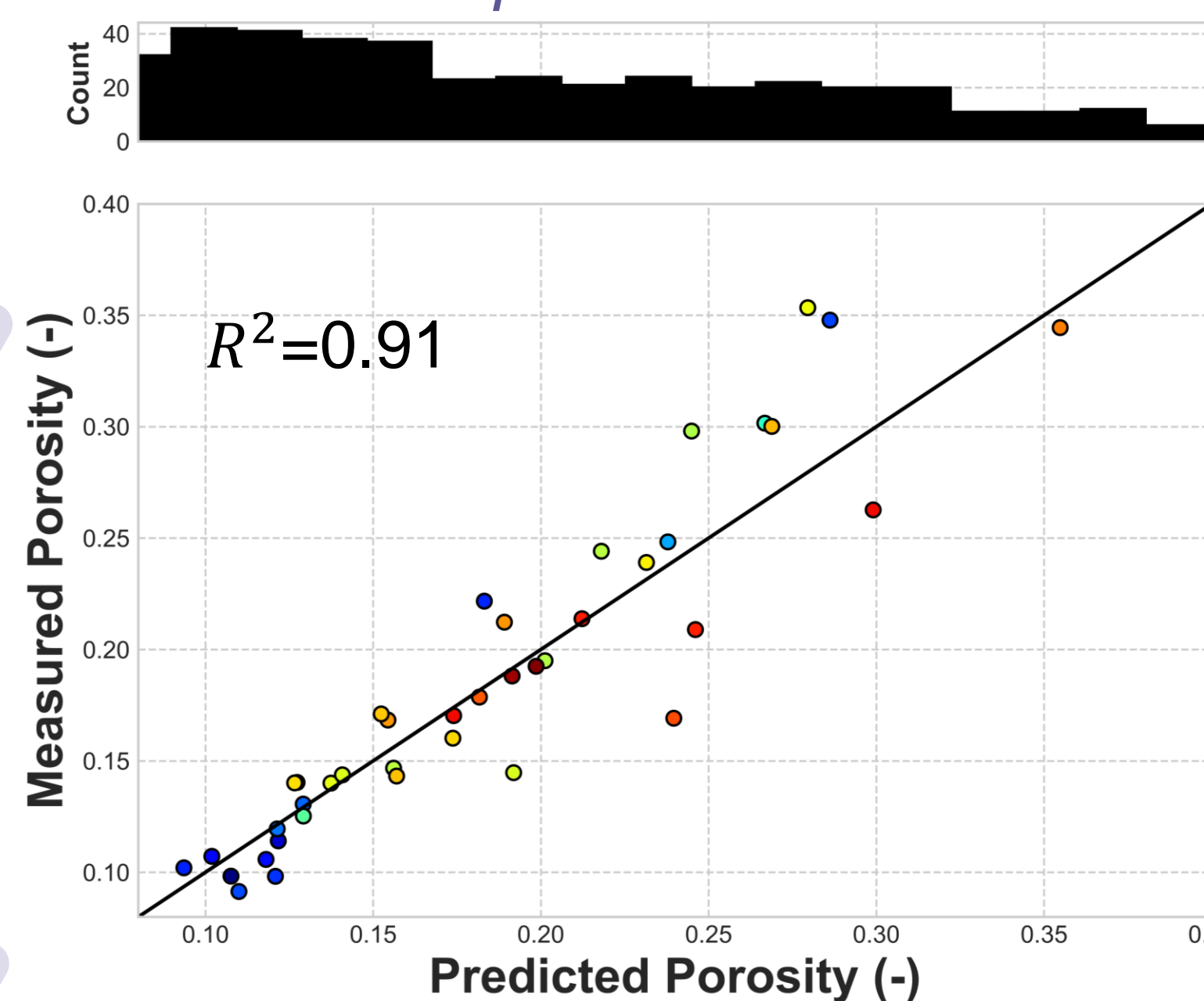
Tablet Tensile Strength
Deep Neural Networks
$R^2 = 0.95$
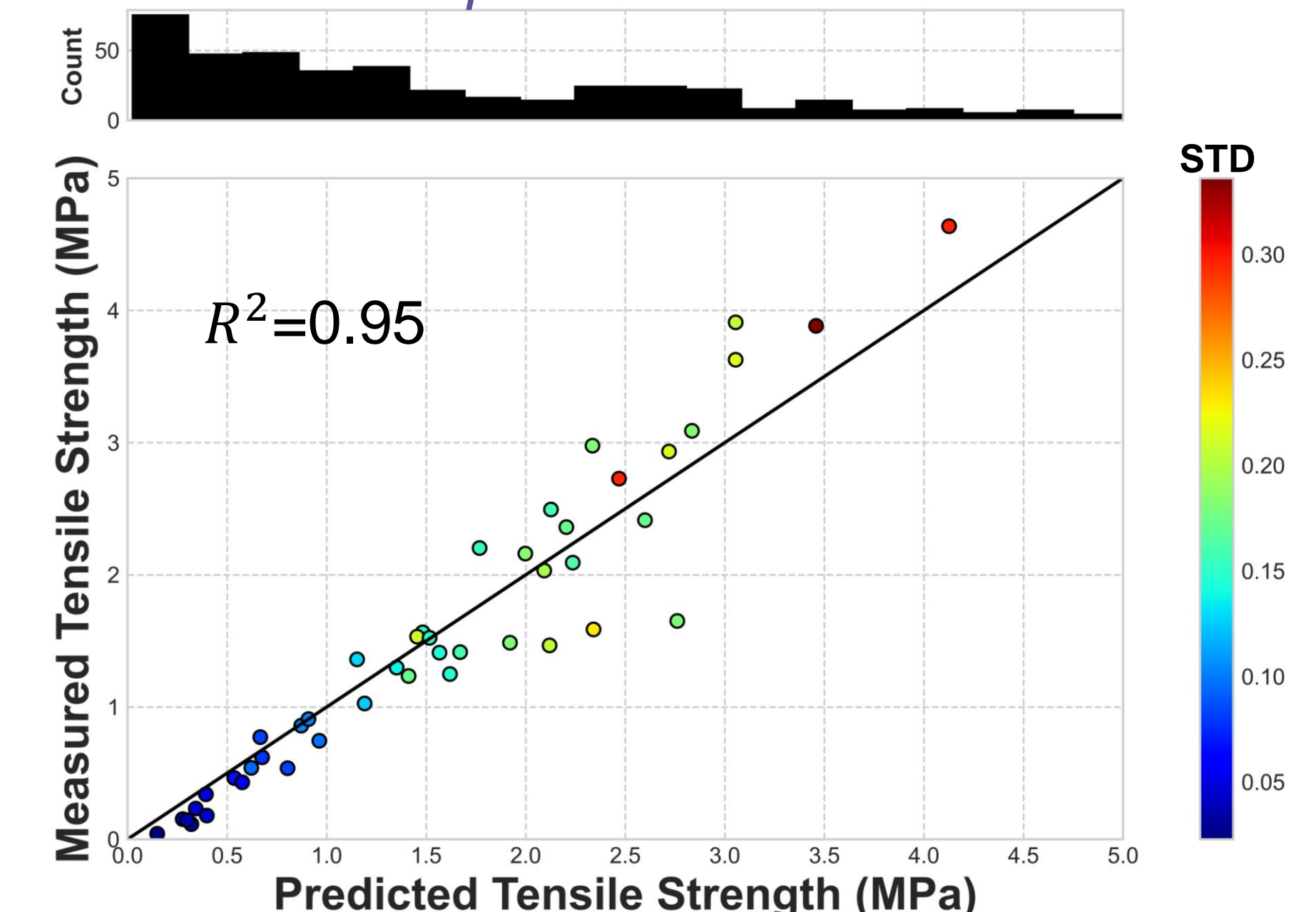
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