AI-based Inline Prediction of Tablet Properties for Accelerating Formulation Development

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INTRODUCTION AND AIM

Development of solid oral dosage forms depends on timely knowledge of critical quality attributes (CQAs) such as tablet hardness, tensile strength, solid fraction, and tablet weight. These CQAs are traditionally obtained by destructive offline tests that consume material and slow down iteration. A machine learning model was trained to predict these properties inline from process features during compaction. It enables faster screenings of blends and process settings while reducing reliance on destructive end-testing.

MATERIALS AND METHODS

The model development followed a structured data science workflow[1]. First, business and process understanding were established to define prediction targets (CQAs). This was followed by data understanding, including exploratory analysis of datasets with more than 300,000 tableting cycles, 200 punch profiles and 30 machine simulation profiles. During this step, erroneous, implausible or inconsistent records e.g., missing reference values or corrupted sensor streams were identified and excluded. In the data preparation phase, relevant force–displacement and tablet energy features like plastic, elastic and ejection energy were extracted, engineered and normalized. Subsequently, different machine learning regression models were trained and benchmarked in the modelling phase. A model performance of R^2 with 0.95 and mean absolute percentage error of 15% was achieved using time-separated splits to avoid data leakage. The model was validated with an external dataset of 9,364 tablets from 73 blends, using 36 machine and 67 punch profiles.

In a representative case study, an API-containing customer formulation was compressed on a STYL'One Evo equipped with 12 mm round EU-B tooling and configured to emulate a KORSCH XL 400[4] at 100 min^{-1} turret speed. 12 tablets were compressed at a main compaction force ranging from 6.7 to 13.5 kN. The machine learning model was used to predict the CQAs directly from compaction data. Destructive reference measurements (hardness, weight, diameter, height) were taken on a Kraemer LAB.line P5 tablet tester and compared to the predictions.

RESULTS & DISCUSSION

Using a prediction model reduces reliance on destructive tests and provides actionable, early-stage feedback on hardness, tensile strength, solid fraction, and weight. The relative deviation of predicted hardness vs. measured hardness across the validation set is centered around zero percent, but reveals increased errors at the boundaries probably caused by training data sparsity in extreme regions and historical unsystematic acquisition patterns (Figure 1).

The predicted vs. measured scatterplots for an API-containing customer product confirm high agreement in the investigated range (Figures 2 and 3), while the graphical user interface illustrates immediate usability in development workflows (Figure 4).

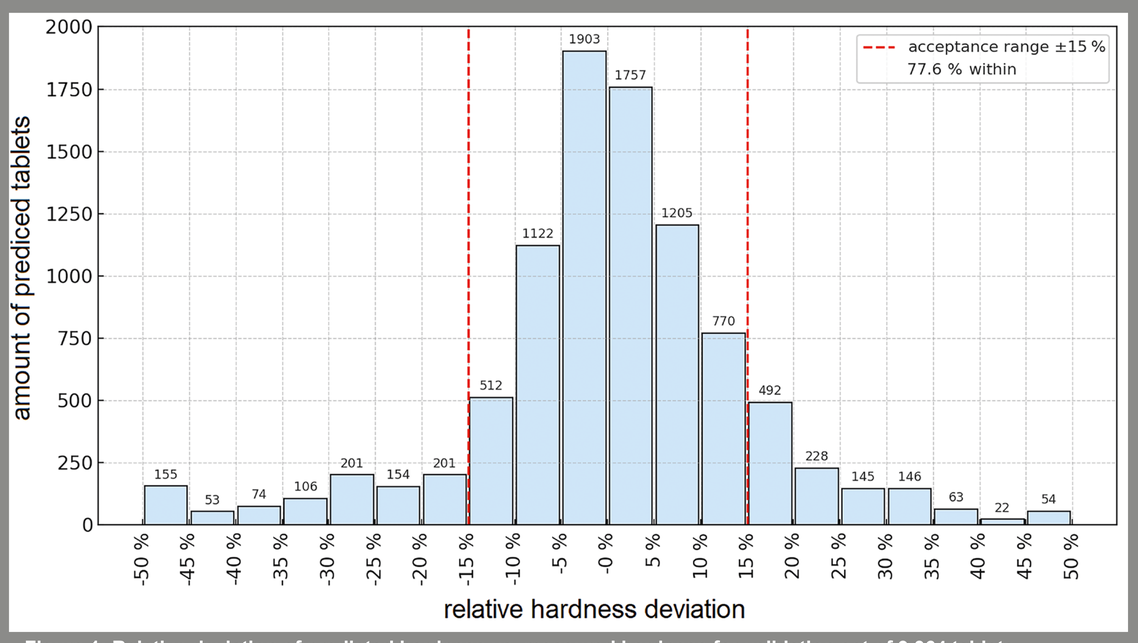

Figure 1: Relative deviation of predicted hardness vs. measured hardness for validation set of 9,364 tablets.

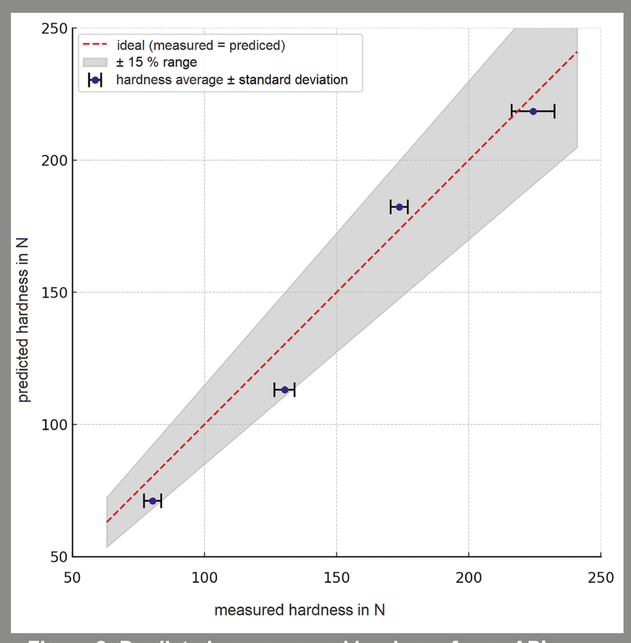

Figure 2: Predicted vs. measured hardness for an API-containing customer product.

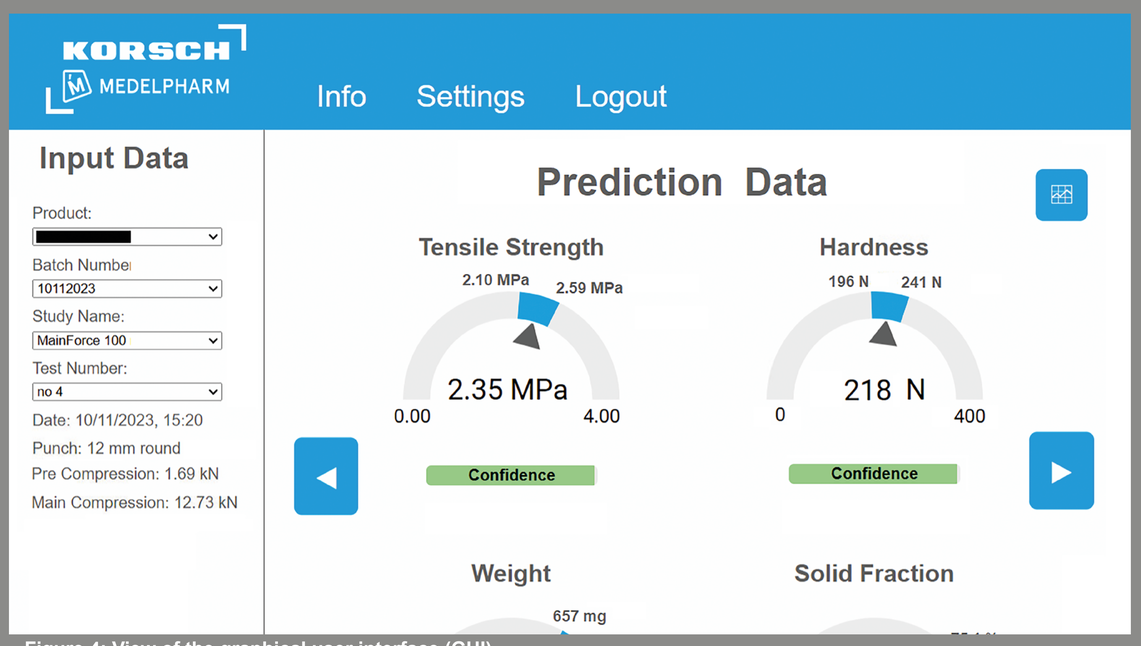

Figure 4: View of the graphical user interface (GUI).

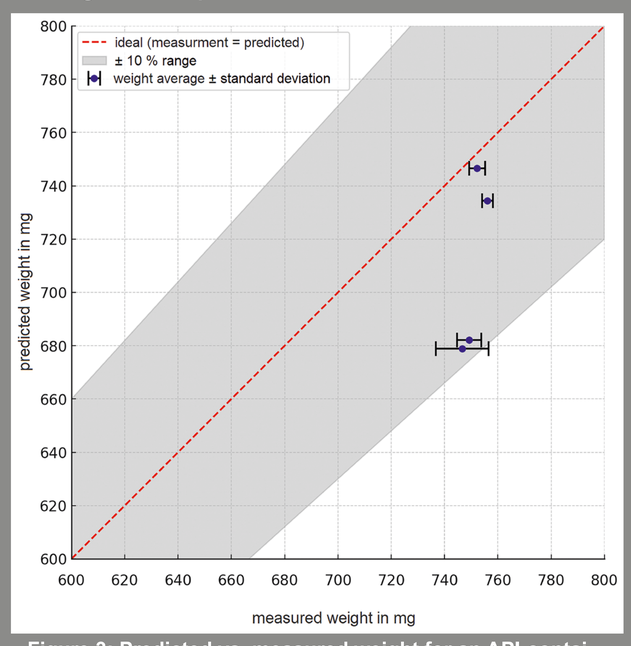

Figure 3: Predicted vs. measured weight for an API-containing customer product.

OUTLOOK

Future work will expand and refine the machine learning model prediction by densifying training data in boundary regions, where current predictions are less accurate. Furthermore, adopting an ensemble composition of neural networks is expected to improve robustness[2]. Finally, the CQAs will be expanded to include disintegration time and friability, providing a more comprehensive prediction framework for pharmaceutical development.

[1] M. J. Neuer, Machine Learning for Engineers - Introduction to Physics-Informed, Explainable Learning Methods for AI in Engineering Applications, Düsseldorf: Springer-Verlag GmbH, 2023, p. 17.
[2] A. Cosmin, B. I. Ates und T. Rabczuk, „Physics-Informed Neural Networks: Theory and Applications," in Machine Learning in Modeling and Simulation: Methods and Applications, Munich, Weimar, Springer Nature Switzerland AG, 2023, p. 179.