

Leveraging Machine Learning to Decode Polymeric Long-Acting Injectables and Predict Their Performance

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Introduction

Background: Long-acting injectables (LAIs) improve treatment for chronic diseases by extending drug release, but development is slow due to complex formulation testing. Machine learning (ML) can accelerate this by predicting release kinetics.

Challenges:

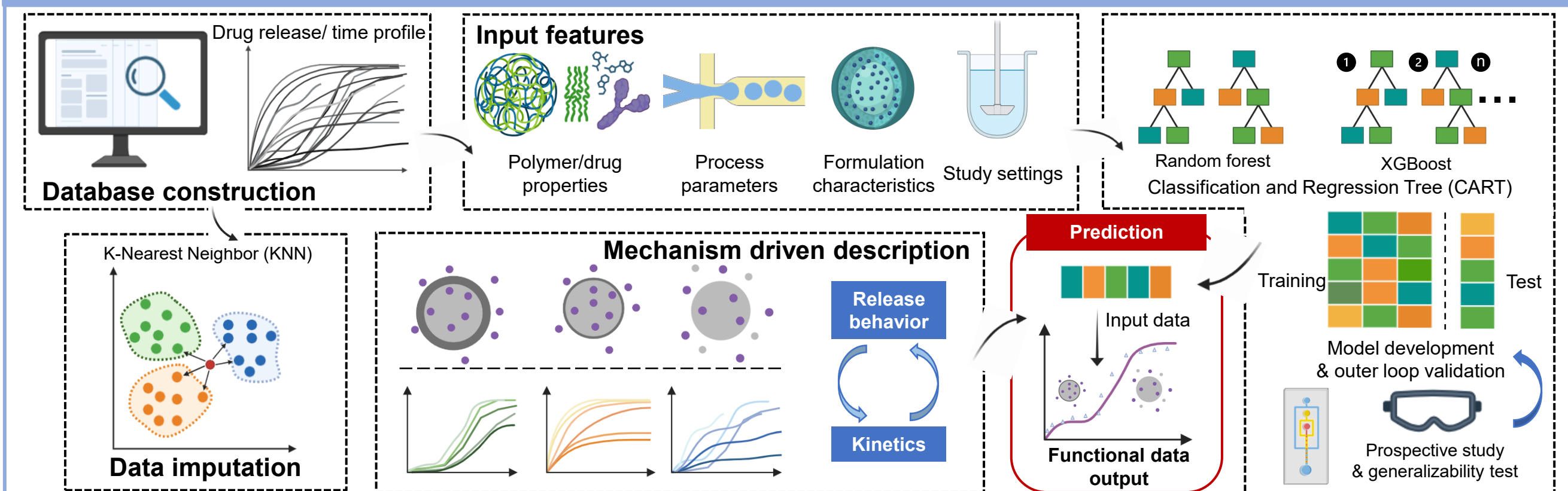
- Release profiles are time-series data (harder to predict than single values)
- Small, inconsistent datasets with missing values

Solution:

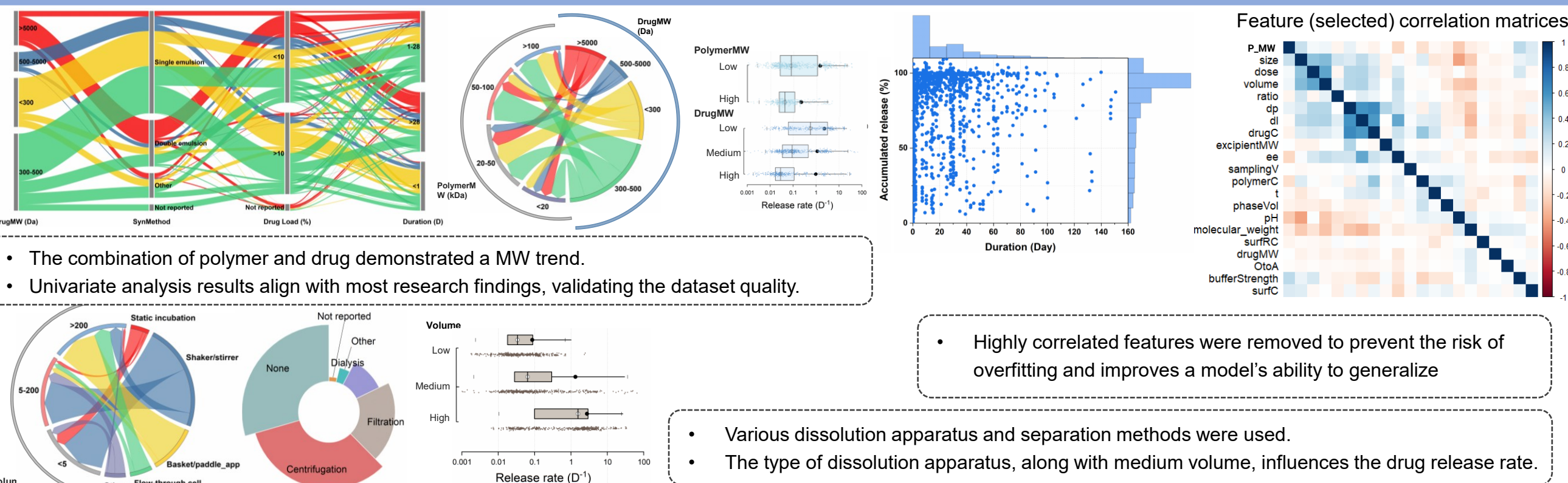
- Built a database of 1,500+ LAI release profiles
- Use KNN imputation to fill missing data
- Integrate the mathematical release models into predictive ML model
- Trained CART, Random Forest, and XGBoost models to predict release curves

Identified key release drivers (drug/polymer properties, particle size) and created a tool to speed up LAI development.

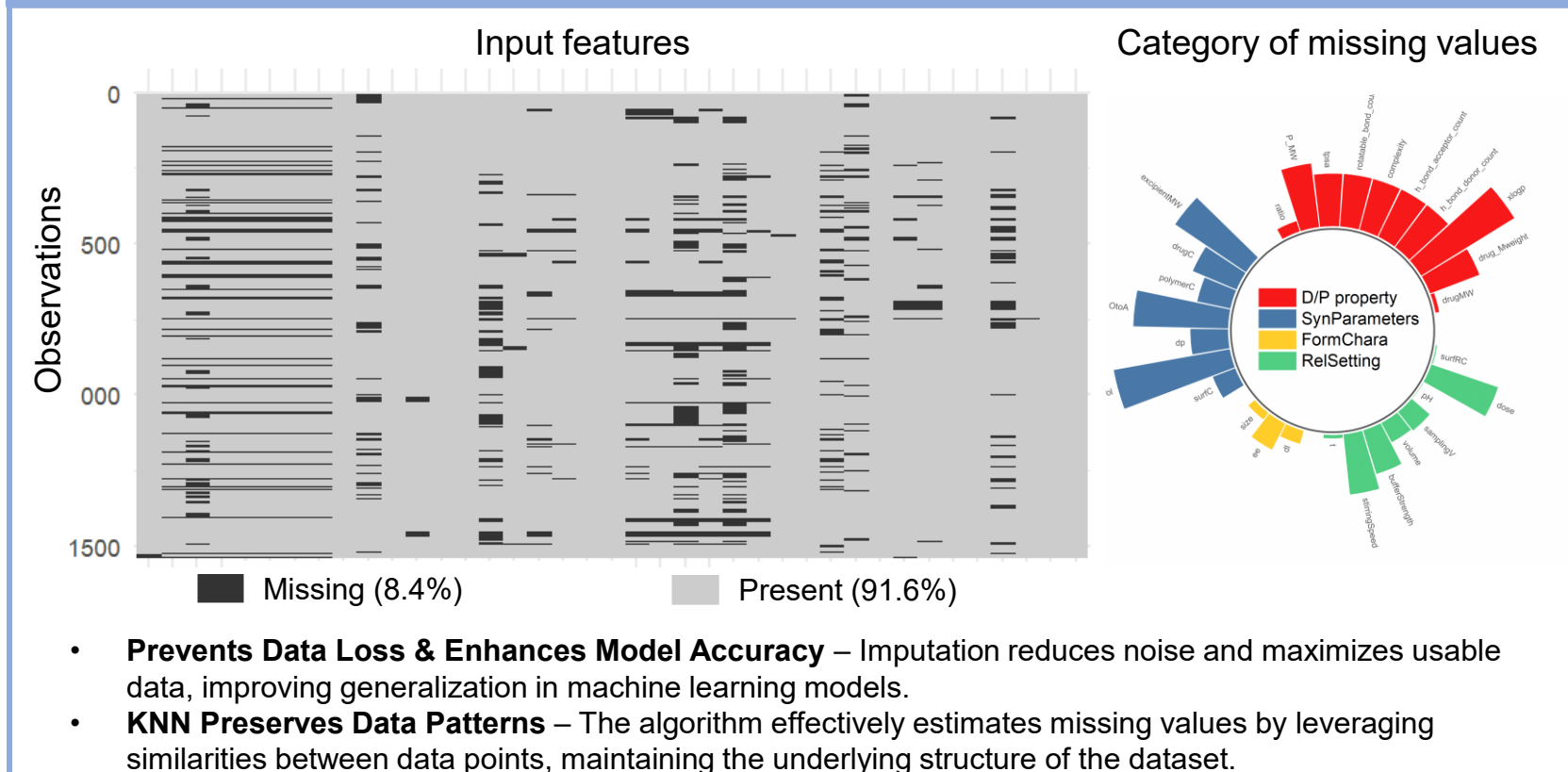
Methodology



Data exploration



Data imputation



Mathematical release models

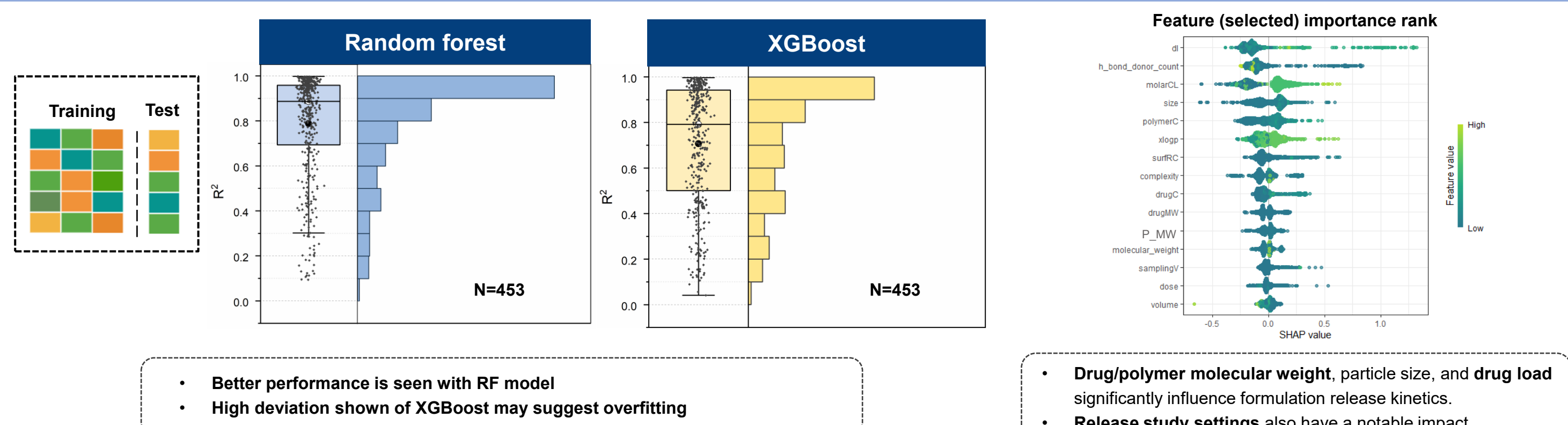
Single model:

- Zero order:** $F = kt$ F: Fractional drug release, t: Time
- First order:** $F = 1 - e^{-kt}$ k: release constant
- Higuchi:** $F = kt^{1/2}$
- Hixson-Crowell:** $F = 1 - (1 - kt)^3$
- Korsmeyer Peppas:** $F = kt^n$
- Weibull model:** $F = 1 - e^{-(\frac{t}{b})^k}$
- Hyperbolic tangent:** $F = \tanh(kt^2 + b)$

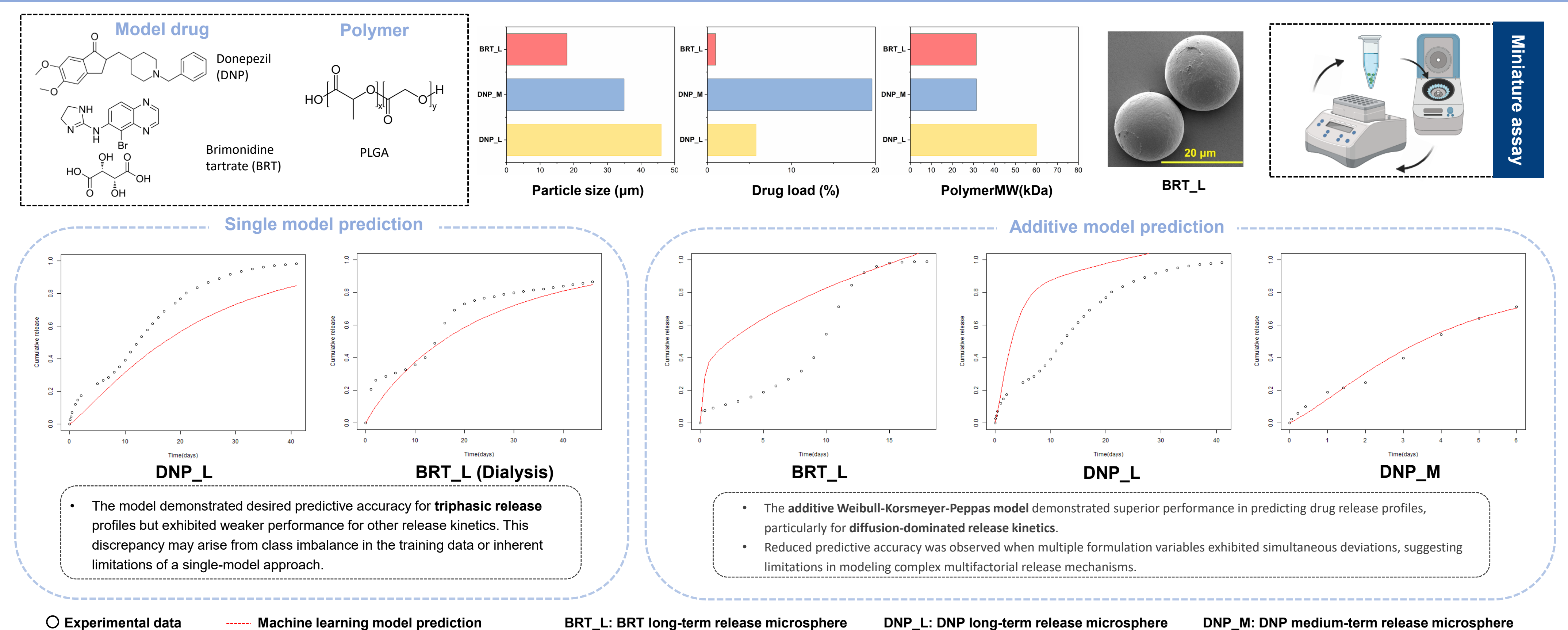
Additive model:

$$F = k_1 t^{a_1} + k_2 (1 - e^{-a_2 t^{a_3}})$$

Model validation – Retrospective study



Model validation – Prospective study



Conclusion

This study developed machine learning models to predict drug release kinetics from polymeric LAIs, addressing key challenges in formulation development.

- Developed a comprehensive database containing 1,500+ LAI release profiles with 30+ critical formulation parameters
- Established machine learning models for complex drug release kinetics prediction
- Demonstrated model validity through both retrospective analysis and prospective studies
- Identified key formulation parameters enabling optimized LAI design

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The Wacker Lab