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ANNUAL MEETING & EXPOSITION
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THE FUTURE OF DELIVERY SCIENCE

Innovation Showcase

Shortening development cycles with microstructure-based prediction of drug release

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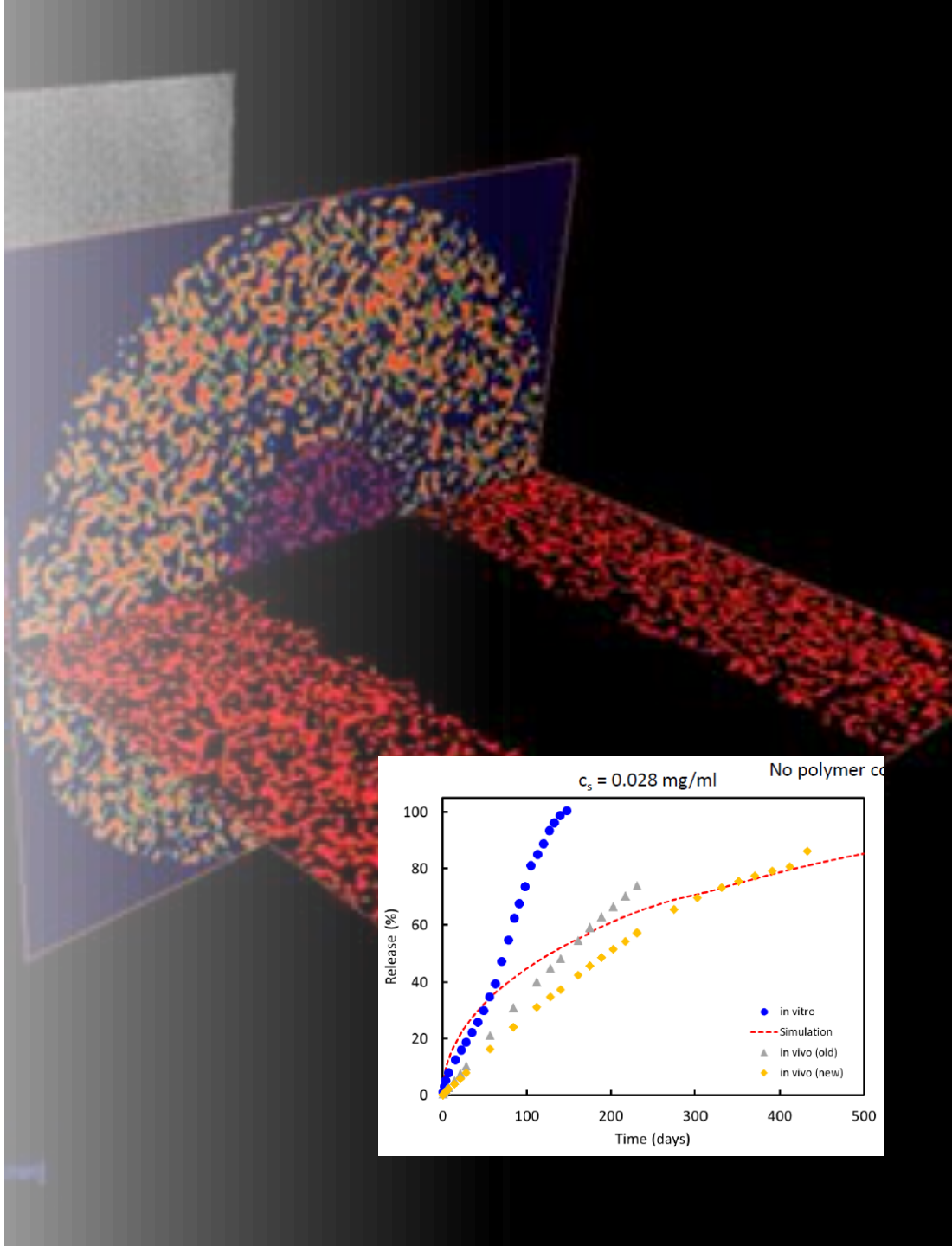
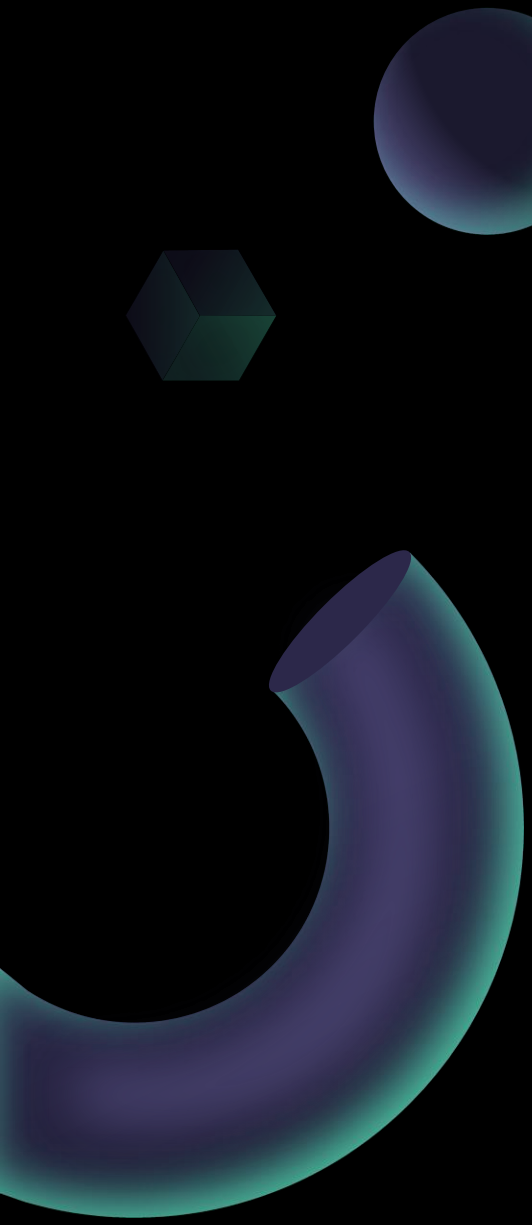
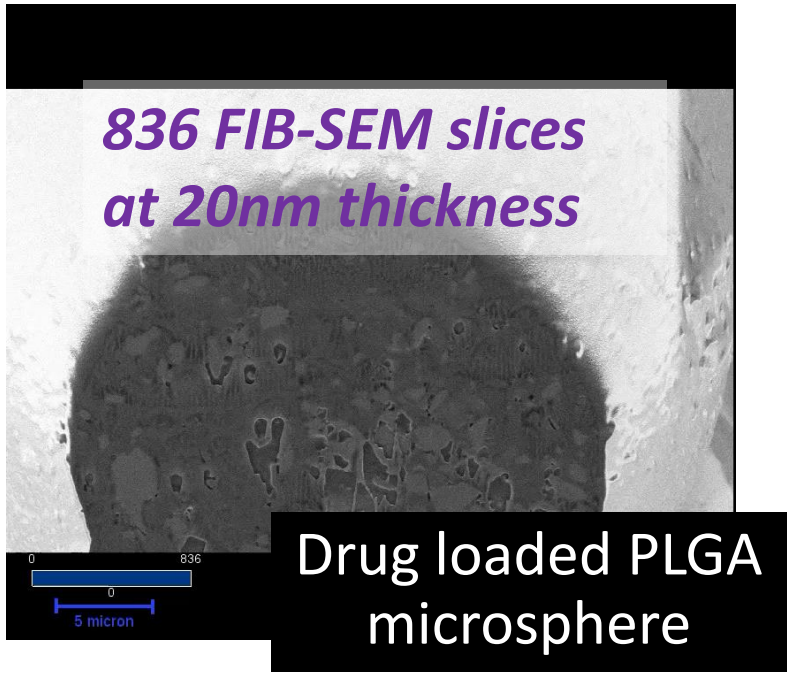




What if we could simulate drug release profiles, based on the actual structures driving release?

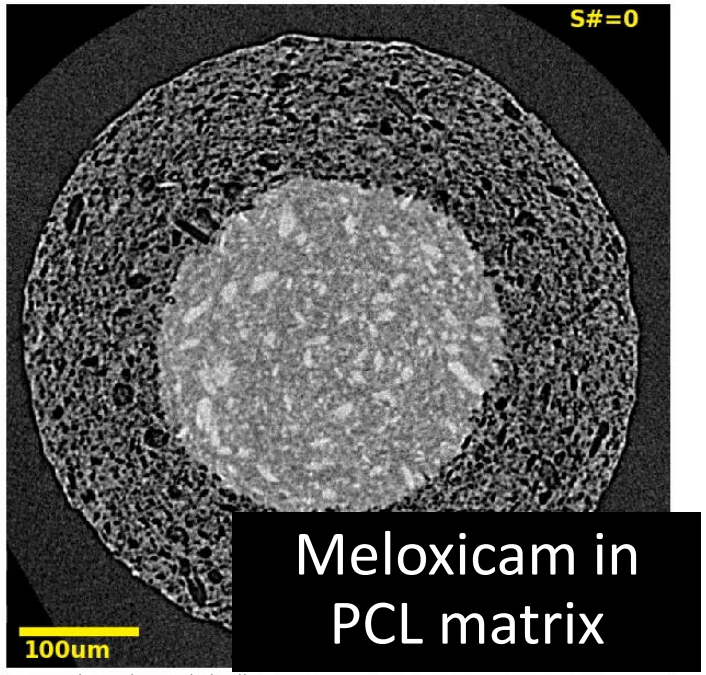
We can! It all starts with imaging the structure in 3D…

3D FIB-SEM



Drug loaded PLGA microsphere

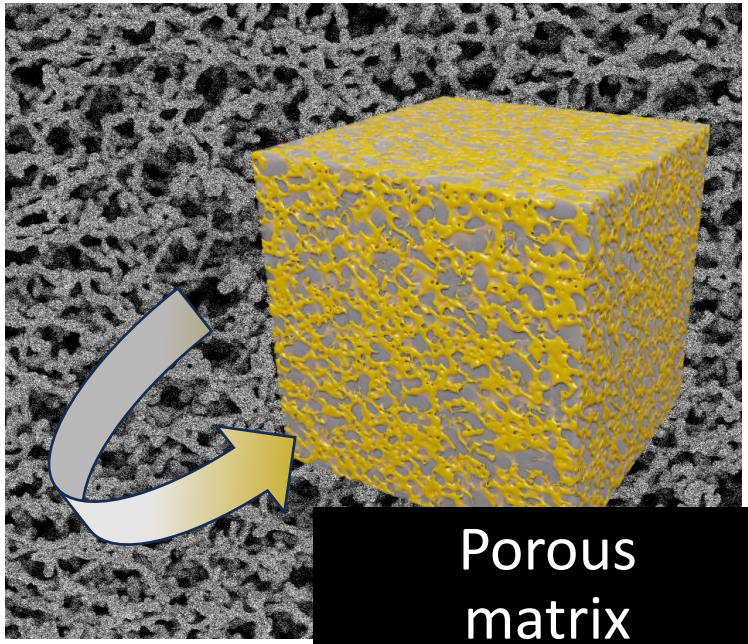
3D X-ray Microscopy
(X-ray micro-CT)



Meloxicam in PCL matrix

With Purdue and Eli Lilly
https://doi.org/10.1016/j.jconrel.2023.05.049

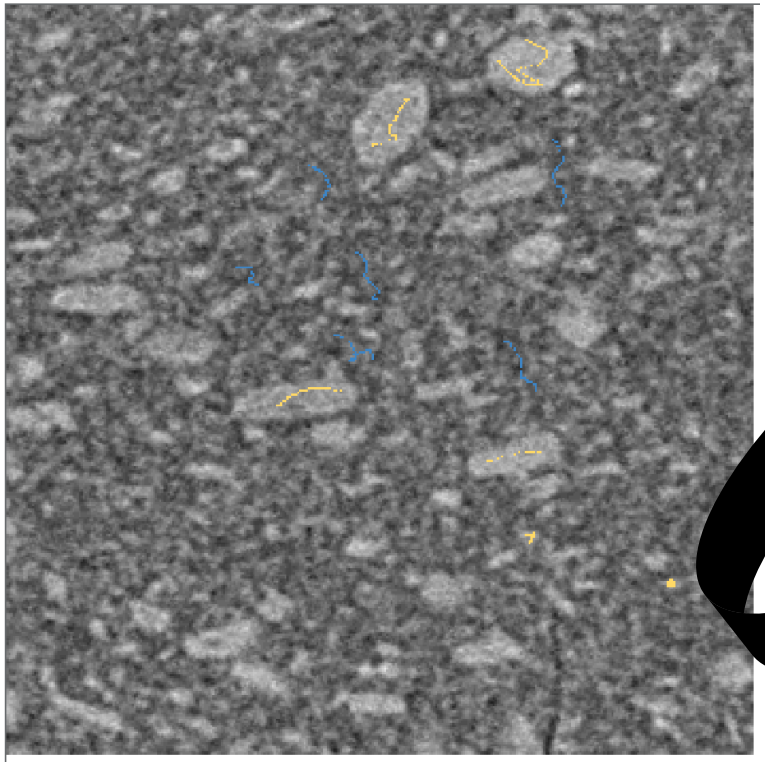
2D to 3D with Generative AI



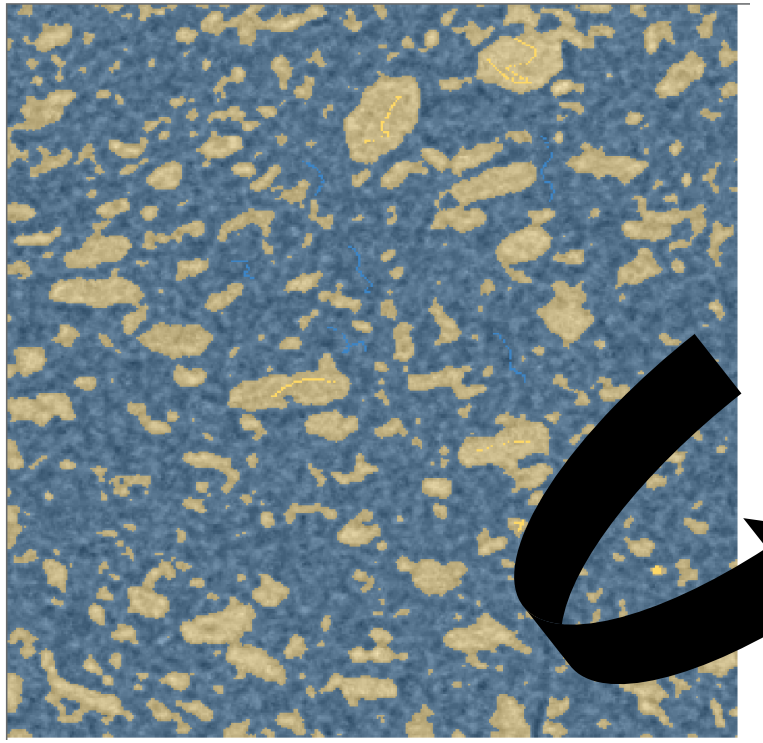
Porous matrix

Obtaining the structure provides a real input without assumptions about porosity/particle arrangement

To simulate from the imaged structure we need to classify each material domain

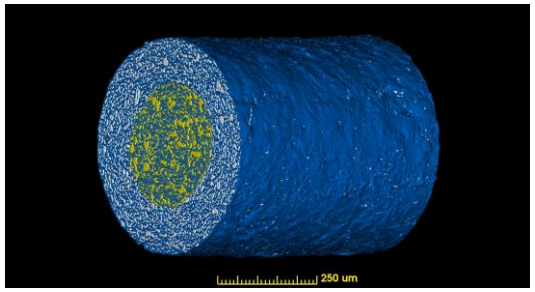


Supervised machine learning



Meloxicam particle network

PCL polymer matrix



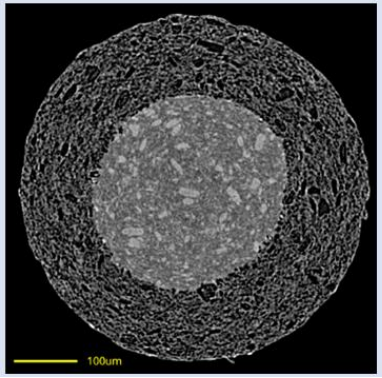
Applied to entire scanned 3D structure

With Purdue and Eli Lilly
https://doi.org/10.1016/j.jconrel.2023.05.049

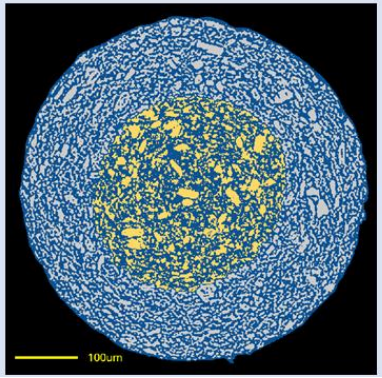
After classification, a library of structural properties can be computed (PSD, spatial distribution, surface area, connectivity)

Lastly, we simulate drug release on the classified pixels

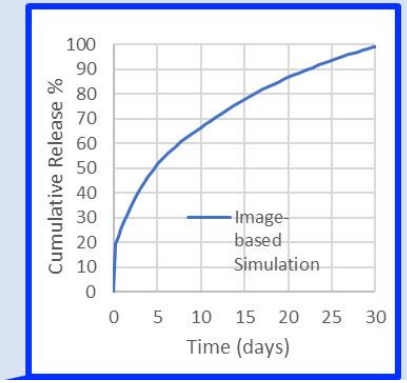
1. XRM Imaging



2. A.I. Image Analytics

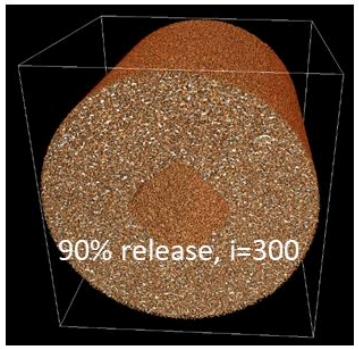


3. Image-based Simulation



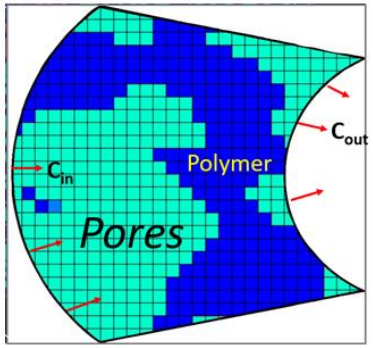
a. Percolation Simulation

Drug Release at Each Step



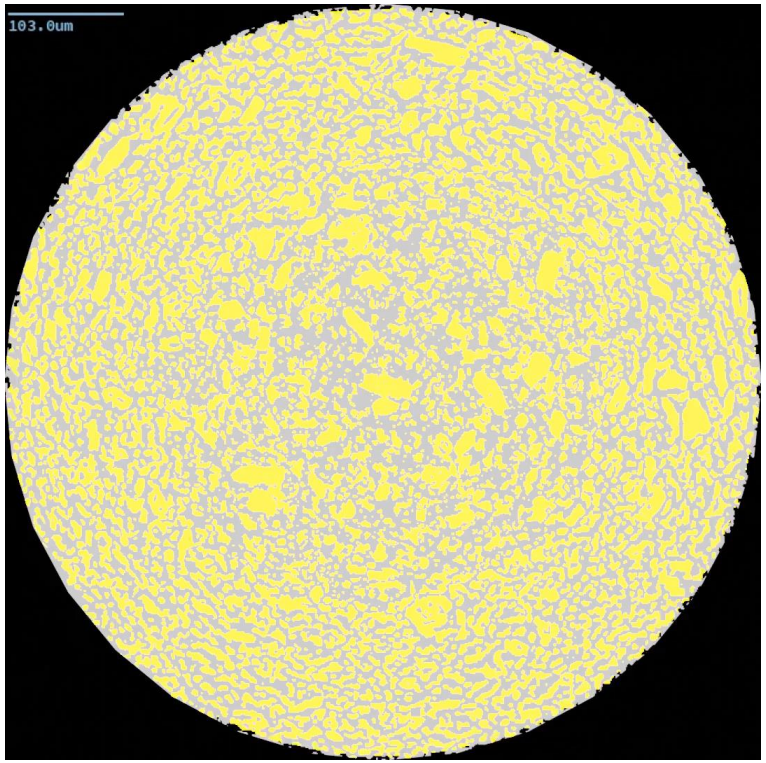
b. Effective Diffusivity

Dynamic Fick's Diffusion



c. Time Conversion

$$\frac{V_i}{V_\infty} + \left(1 - \frac{V_i}{V_\infty}\right)\ln\left(1 - \frac{V_i}{V_\infty}\right) = 4\left(\frac{c_s}{c_0}\right)\frac{D_i T_i}{R^2}$$



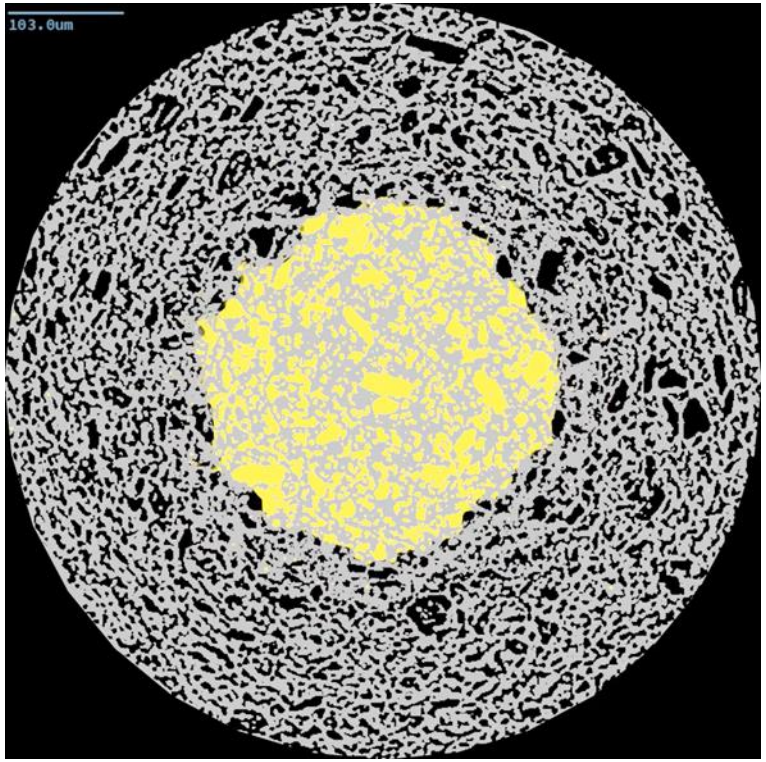
This simulation is on a biostable system → there are also models for biodegradable systems

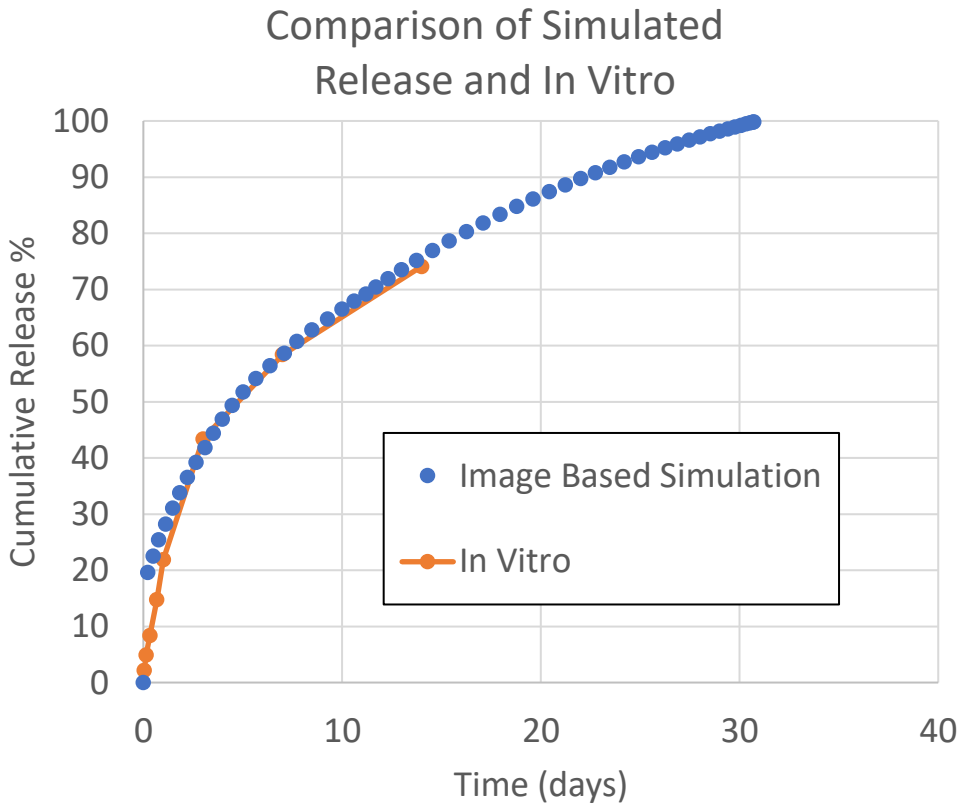
With Purdue and Eli Lilly
https://doi.org/10.1016/j.jconrel.2023.05.049

What are the other inputs, and how does predicted release compare to *in vitro*?

External inputs for simulation:

- Bulk diffusion coefficient
- Drug load
- Drug solubility
- Diameter





Blind simulation provides highly precise prediction without any data fitting or adjustments

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What are the implications?

Use of this workflow can help solve a number of the biggest challenges in controlled release development…

- Accelerate Formulation Selection
- Optimize Manufacturing and Scale Up
- Shorten Lengthy *In Vitro T*esting
- Easier Troubleshooting
- Seek *In vitro-In Vivo* Correlation
- Demonstrate Generic Equivalence with RLD