Design of PLGA-based drug delivery systems through a molar mass-dependent sustained release model

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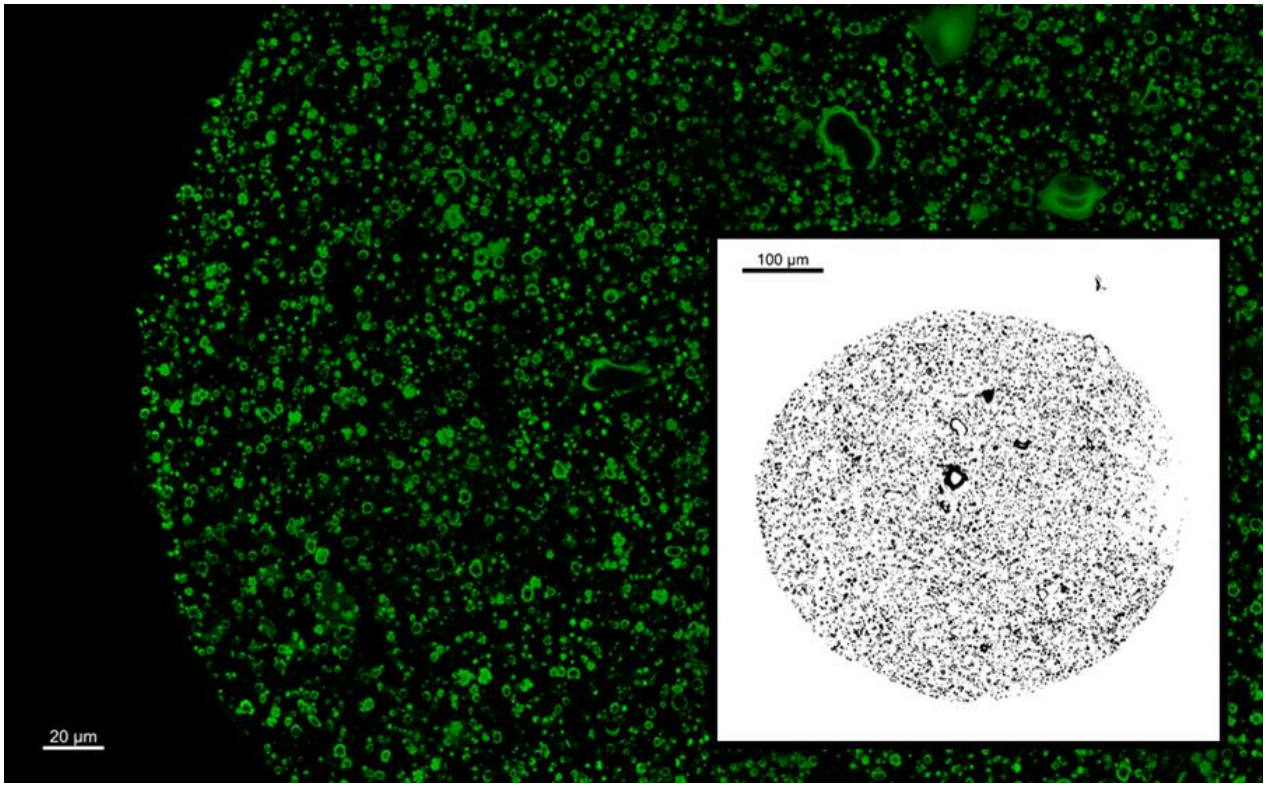
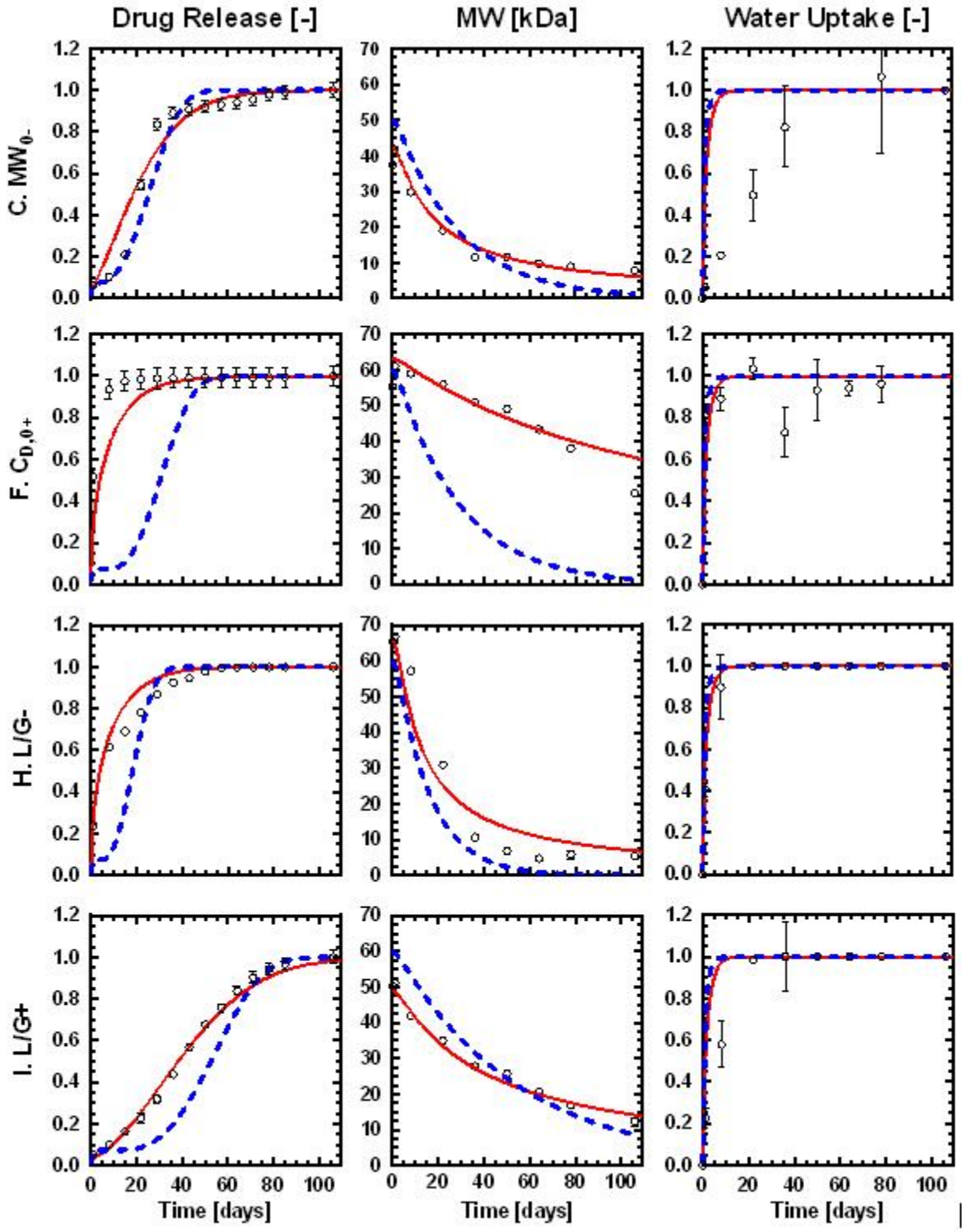
Improvements to a drug-release model are validated by comparing model prediction to *in vitro* experiments on a novel, industrially relevant PLGA controlled release system from Genentech. Combining parameter estimations from literature and comparisons to an extensive data base, this study enables *a priori* design of controlled drug release from a model PLGA system. Model predictions were validated against formulations of FITC-labeled dextran, a model surrogate for biopharmaceutical drugs, in PLGA rods with a broad range of parameters. While successful, deviations were noted for several model formulations with significant first-phase drug release. Supported by cross-sectional florescence microscopy images of the FITC-dextran distribution within the rods, this first-phase release was attributed to a combination of factors: (1) percolation of the drug particles and (2) swelling and pore formation due to water uptake. These observations indicate the importance of careful selection of the PLGA polymer grade when designing drug release systems. Adapting model parameters, without modifying the physical processes included in the model, enabled accurate fitting of the experimental data for all formulations, highlighting the wide applicability of the model. Areas for model improvement were identified and supplemented by X-ray computed tomography images of the PLGA spatial distribution during early stage of drug release.




Drug Release [-]
MW [kDa]
Water Uptake [-]
C. MW0-
F. CD,0+
H. L/G-
I. L/G+
Time [days]
Time [days]
Time [days]