

AI-Assisted Tool to Improve the Quality and Assessment of PLGA Formulations

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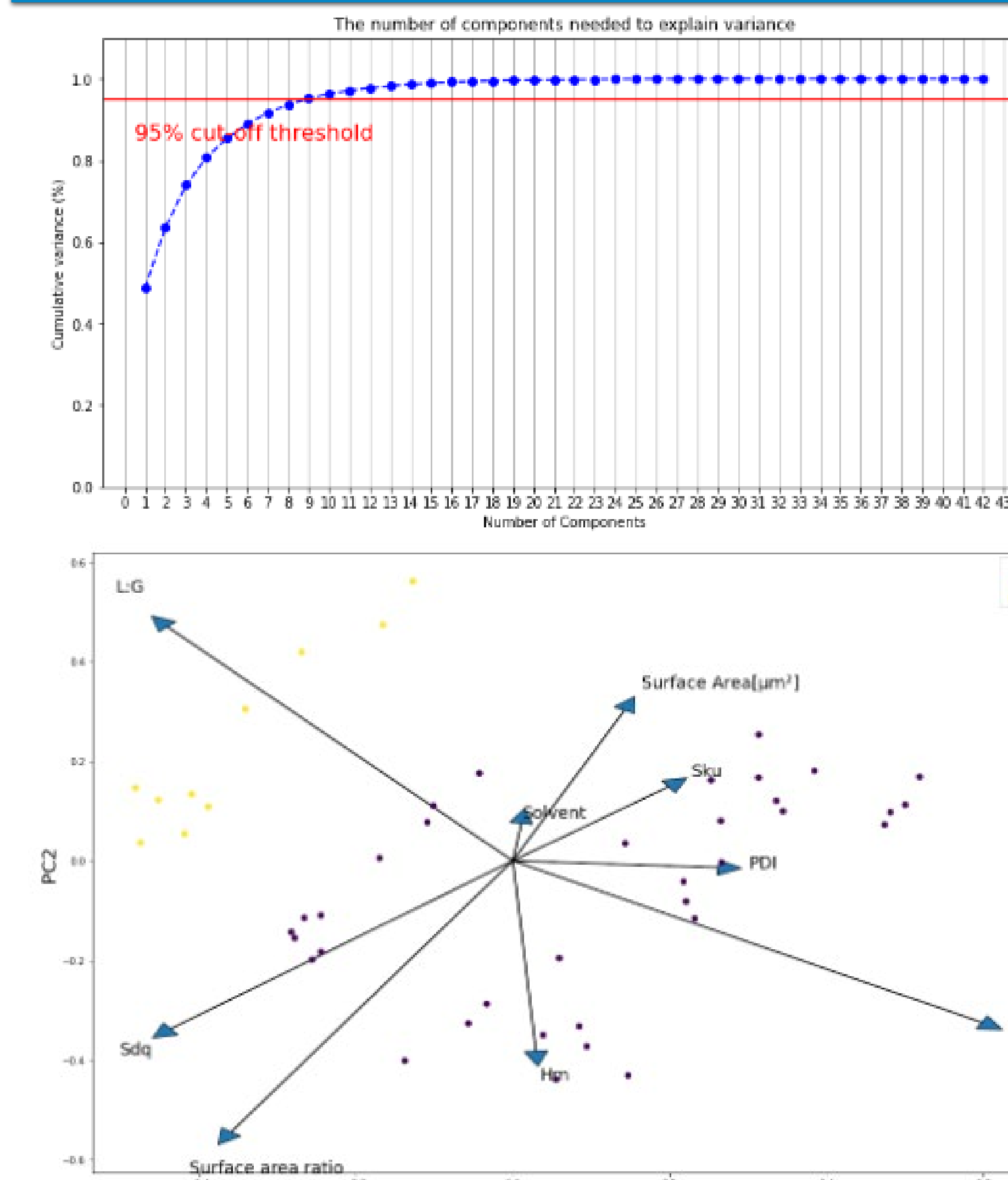
SUMMARY

- The AI-based method provides high-throughput analysis of PLGA (poly (lactic-co-glycolic acid))-based long-acting injectable (LAI) formulations to establish a correlation between material attributes, processing conditions, and product quality/performance.
- This AI method may serve as a tool in the future to evaluate the sameness of proposed generic products to reference listed drugs (RLD) by analyzing feature similarity across different formulations.

METHODS

- The study has compiled a comprehensive dataset of PLGA formulations from a previous FDA-funded research project [1].
- The dataset includes different formulation details, corresponding manufacturing data, detailed surface topographical characterization data due to solvent changes, and *in vitro* release testing data [1].

RESULTS



Sdq	1	-0.71	0.84	-0.46	0.21	-0.038	0.023	-0.45	-0.31	0.96	0.94	0.71	0.76	-0.8	0.81
Sku	-0.71	1	-0.55	0.22	-0.21	-0.047	0.11	0.31	0.14	-0.69	-0.77	-0.64	-0.6	0.62	-0.57
Surface area ratio	0.84	-0.55	1	-0.22	0.063	0.024	0.33	-0.59	-0.19	0.76	0.71	0.31	0.45	-0.85	0.66
Manufacturing Method	-0.46	0.22	-0.22	1	-0.54	2e-16	0.17	0.029	0.49	-0.55	-0.45	-0.51	-0.52	0.2	-0.62
L:G	-0.21	-0.21	0.063	-0.54	1	-1.4e-1	-0.22	-0.011	-0.22	0.24	0.27	0.22	0.25	-0.1	0.27
Solvent	-0.038	0.047	0.024	2e-14	4e-16	1	0.086	0.048	3e-17	0.014	0.051	0.066	0.12	0.0061	0.18
Hm	-0.023	0.11	0.33	0.17	-0.22	-0.086	1	-0.17	-0.18	-0.04	-0.18	-0.29	-0.18	-0.12	-0.18
Surface Area[μm²]	-0.45	0.31	-0.59	0.029	0.011	0.48	-0.17	1	0.093	-0.36	-0.32	-0.073	-0.14	0.82	-0.3
PDI	-0.31	0.14	-0.19	0.49	-0.22	3e-1	-0.18	0.093	1	-0.35	-0.27	-0.31	-0.33	0.18	-0.33
Sd[μm]	0.96	-0.69	0.76	-0.55	0.24	0.014	-0.04	-0.36	-0.35	1	0.94	0.82	0.89	-0.74	0.88
Sz[μm]	0.94	-0.77	0.71	-0.45	0.27	0.051	-0.18	-0.32	-0.27	0.94	1	0.78	0.8	-0.72	0.85
Sk[μm]	0.71	-0.64	0.31	-0.51	0.22	0.066	-0.29	-0.073	-0.31	0.82	0.78	1	0.95	-0.42	0.66
[μm³/μm²]	0.76	-0.6	0.45	-0.52	0.25	0.12	-0.18	-0.14	-0.33	0.89	0.8	0.95	1	-0.52	0.76
Area[μm²]	-0.8	0.62	-0.85	0.2	-0.1	0.0061	-0.12	0.82	0.18	-0.74	-0.72	-0.42	-0.52	1	-0.61
Vmc[μm³/μm²]	0.81	-0.57	0.66	-0.62	0.27	0.18	-0.18	-0.3	-0.33	0.88	0.85	0.66	0.76	-0.61	1

Fig 3: Principal component analysis (PCA) on the left and correlation matrix study on the right to find significant parameters

(A) Prediction of Formulation Conditions

Machine Learning Techniques	MSE	MAE	Accuracy (%)
Linear Regression	0.001	0.02	99.5002
Decision Tree	0	0	100
Random Forest	0.3439	0.4	90
Extra Trees Regressor	0.0042	0.0289	99.2778

(B) Prediction of L:G Ratios from PLGA Formulations

Placeholder for data related to L:G ratio prediction.

Table 1: Different machine learning (ML) algorithms were applied (A) to predict the formulation conditions and (B) to predict L:G ratios

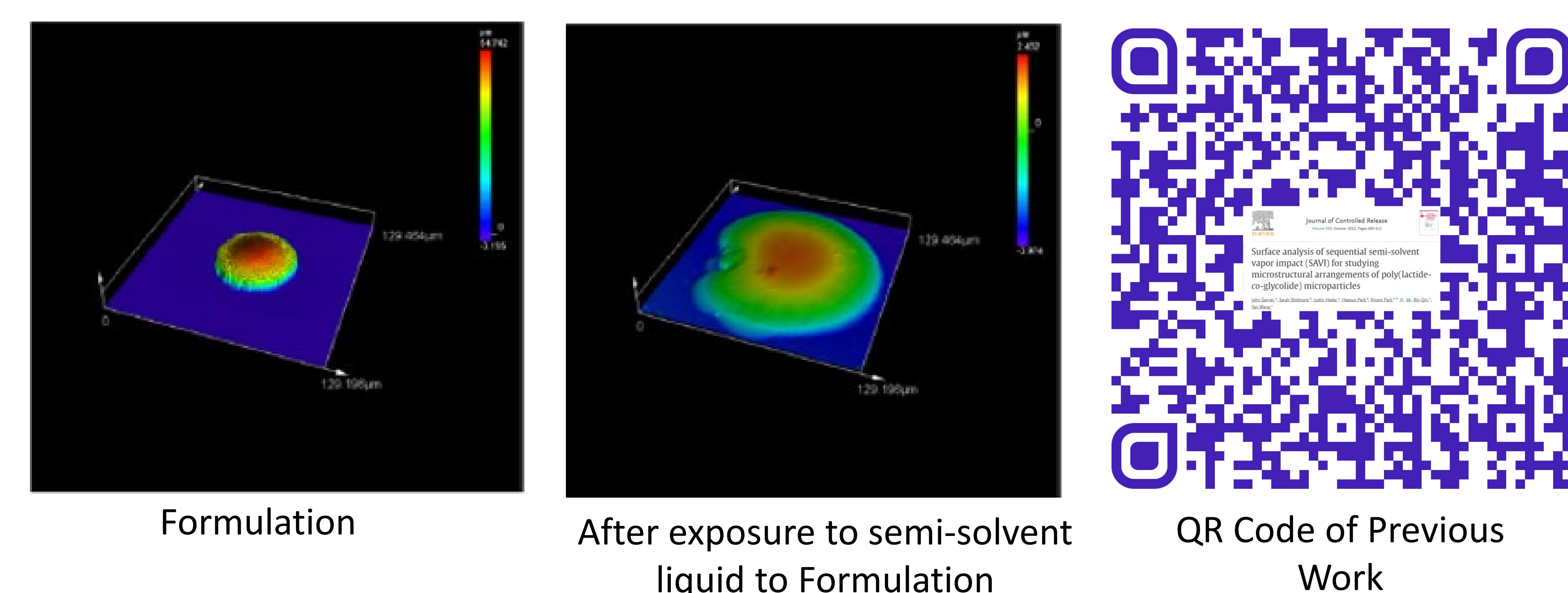


Fig 1: Microparticles of formulations in the dry state and after exposure to a semi-solvent liquid at 0°C for 1 min and details of previous work in the QR code [1]

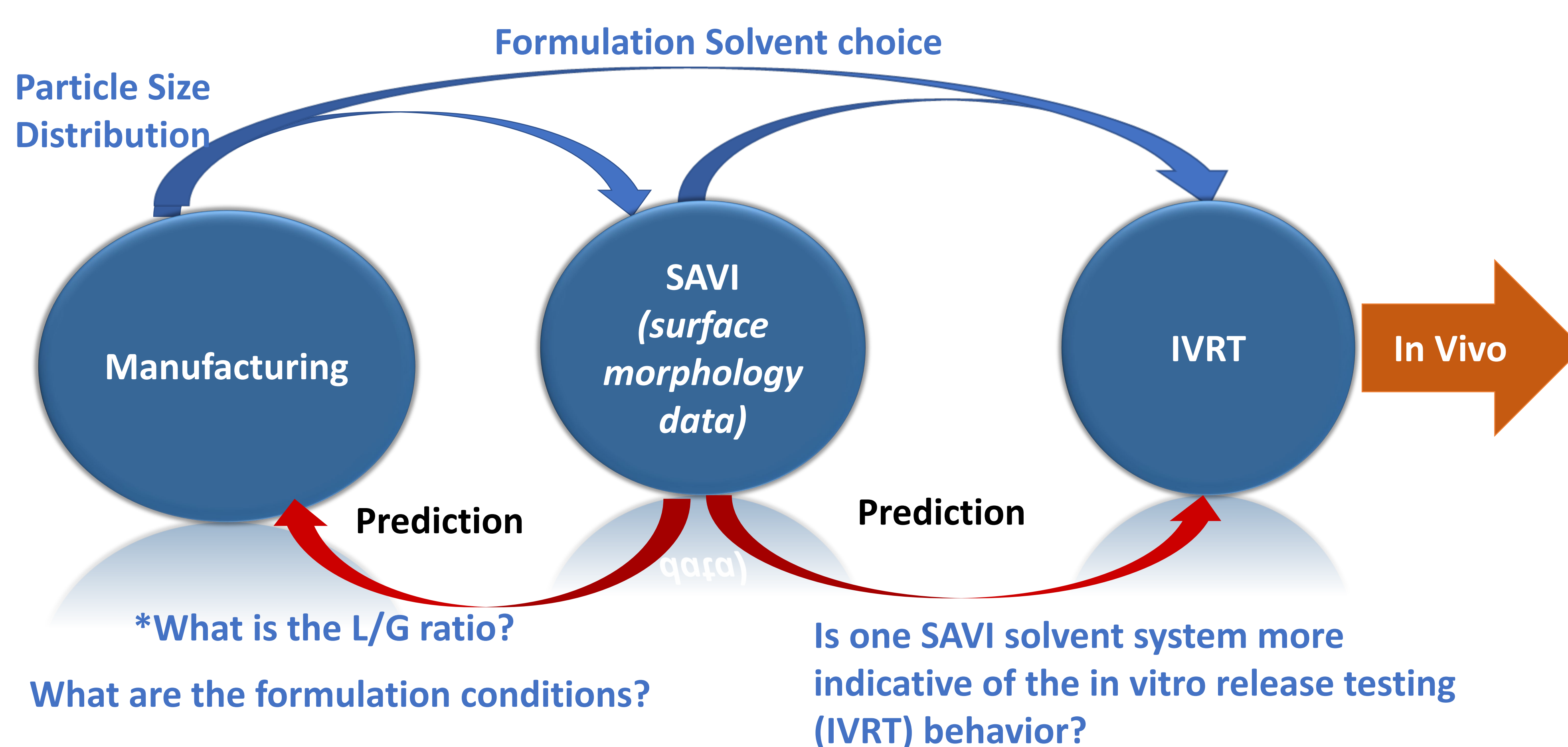


Fig 2: Functional flow of the work

REFERENCE

1. Surface analysis of sequential semi-solvent vapor impact (SAVI) for studying microstructural arrangements of poly (lactide-co-glycolide) microparticles; John Garner, Sarah Skidmore, Justin Hadar, Haesum Park, Kinam Park, Bin Qin, Yan Wang; Journal of Controlled Release, 2022, 350, 600-612

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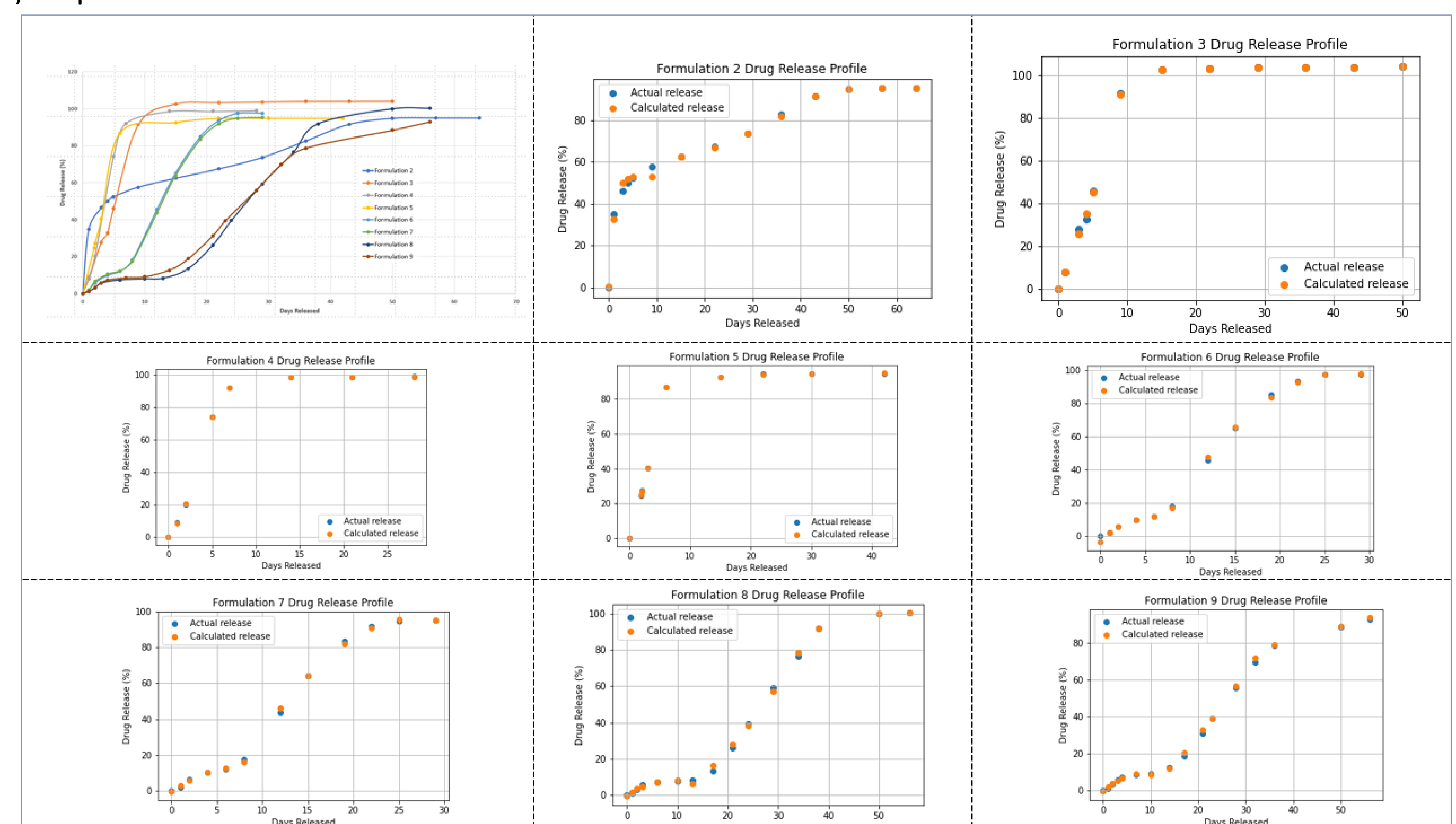


Fig 4: Prediction of IVRT profiles and compared with experimental release profiles

DISCLAIMER

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