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Thudichum award lecture

From computational design of responsive liposomal depots to predictive microfluidic manufacturing

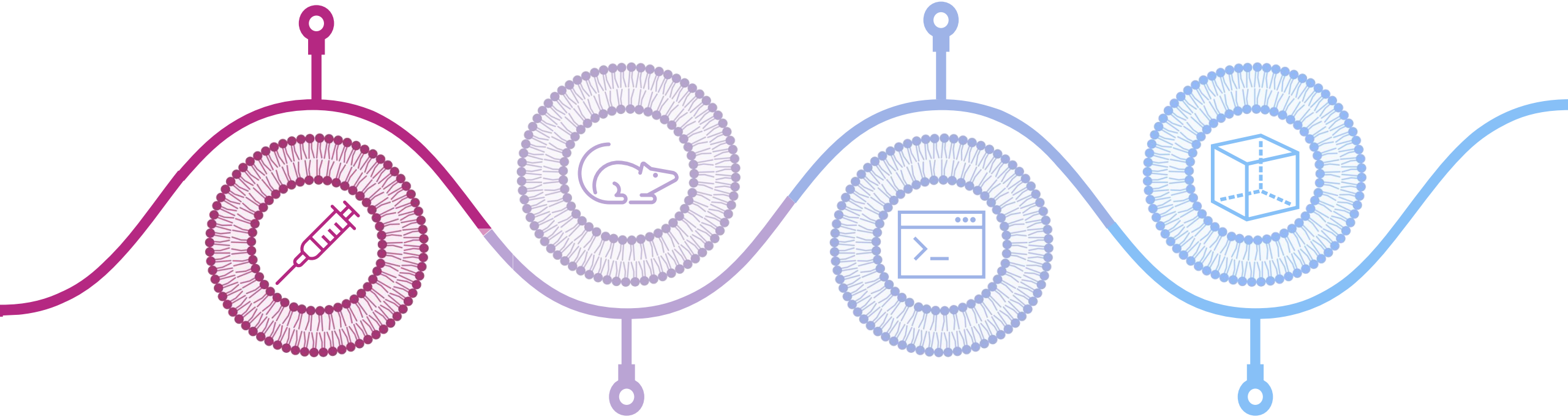
Presented by Remo Eugster, PhD

Computational design

Physiologically controlled release from an in situ forming liposomal depot

Predictive manufacturing

Streamlining the development of liposomal drug delivery systems



New alternative methods

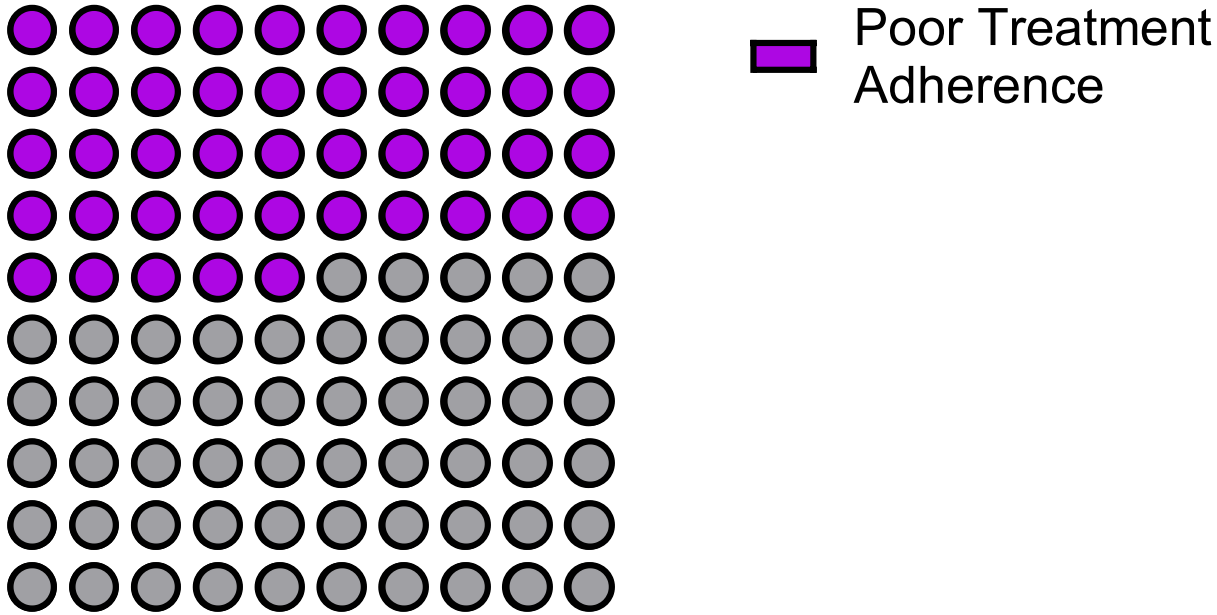
Replace, refine and reduce animal testing

Advanced delivery

Developing composite drug delivery systems

The silent epidemic

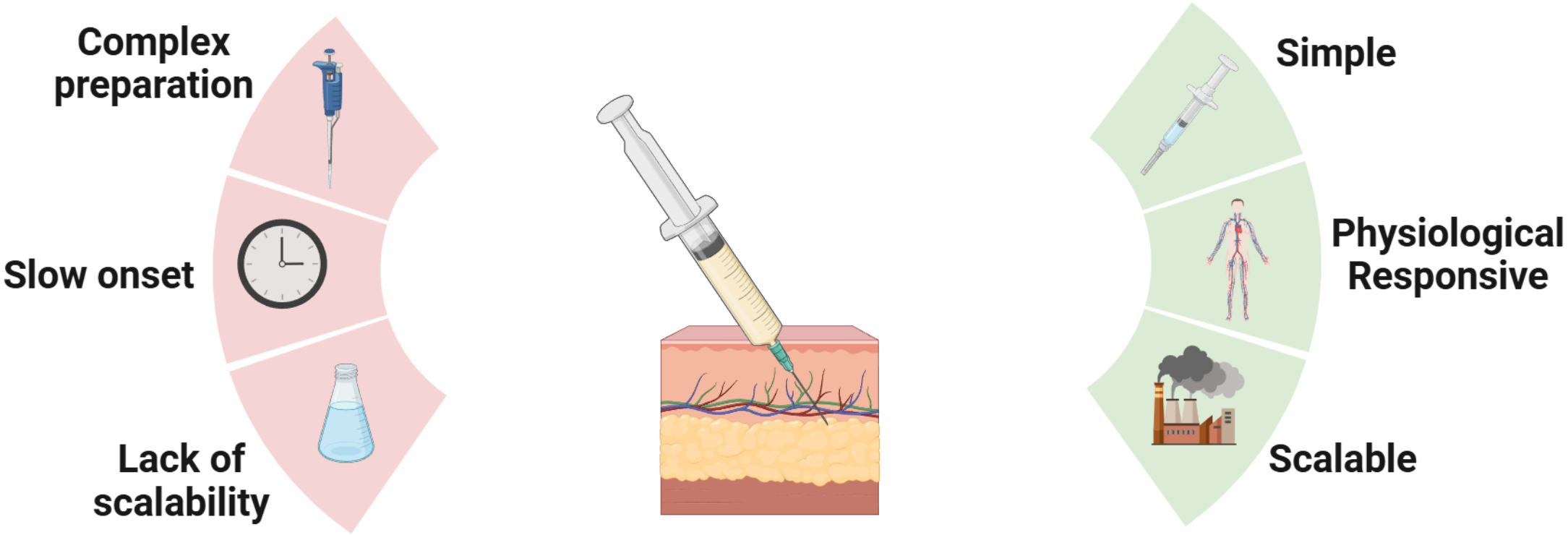
Poor treatment adherence continues to compromise outcomes across human and veterinary medicine. Today's treatments are frequent, invasive and inconvenient



Adherence to long term therapies: evidence for action. WHO. 2003

The opportunity in prolonged-acting injectables

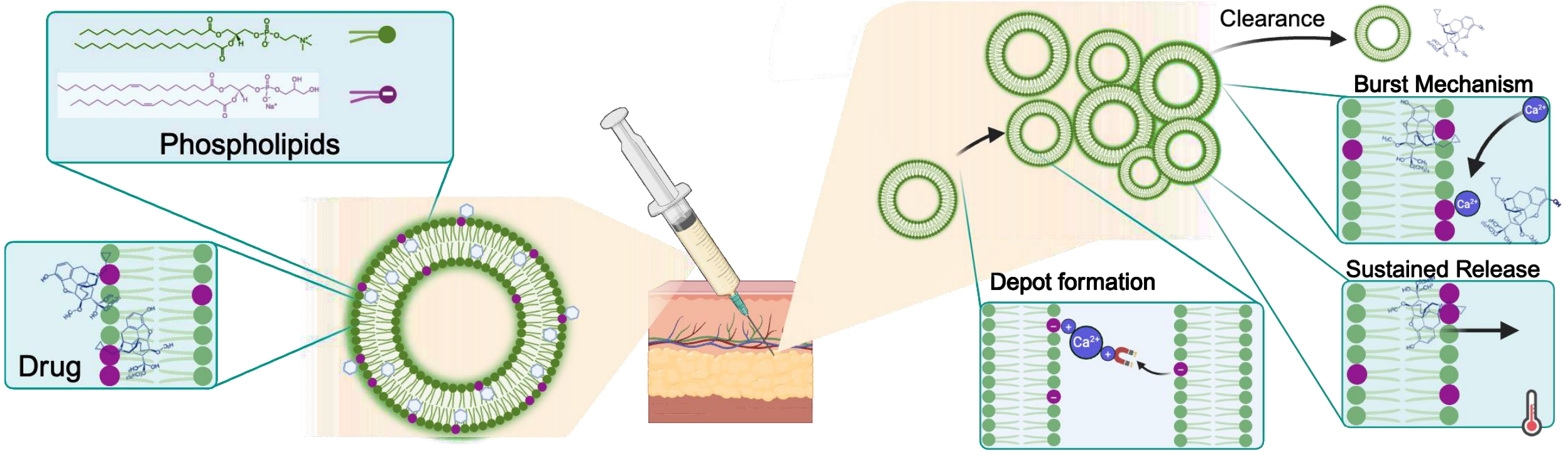
Leverage subcutaneous (s.c.) space for depot formulations and overcome current barriers



Tomasini et al. Subcutaneous drug delivery from nanoscale systems Nat. Rev. Bioeng. 2024

Solving delivery challenges: TILD

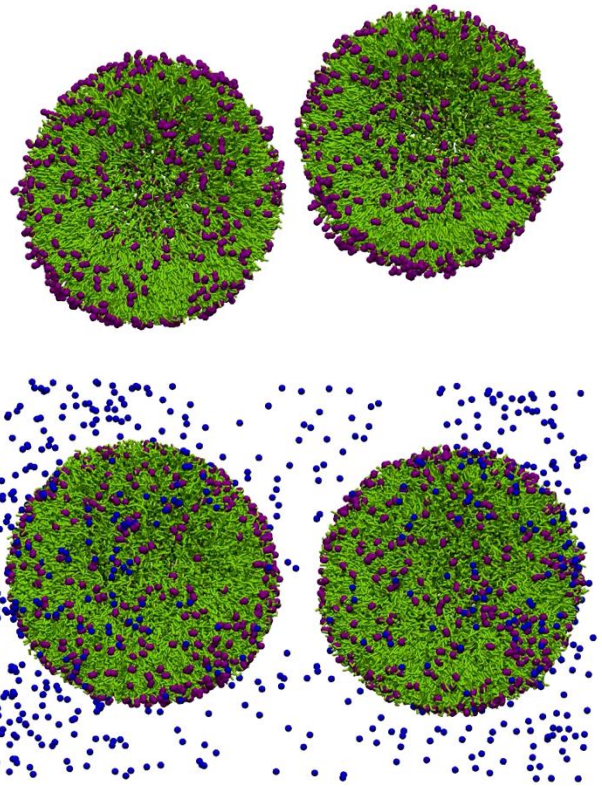
Thermoresponsive **i**n-situ forming **L**iposomal **D**epot (TILD) with dual-phase drug release

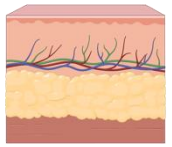


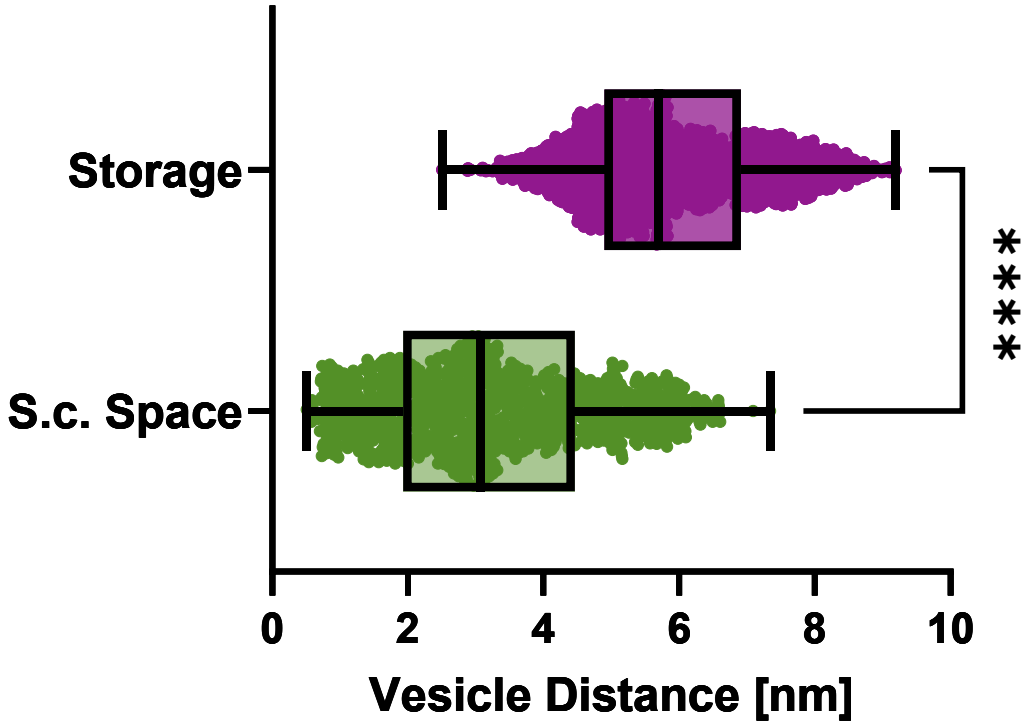
Eugster et al. J Control. Rel. 2026. 392. 114739
European Patent Application No 25186092.0; Charged Liposome Composition

Mechanistic Computational Design

Computational design and simulation of s.c. space guide and validate drug lipid interactions and depot formation induced by subcutaneous cations







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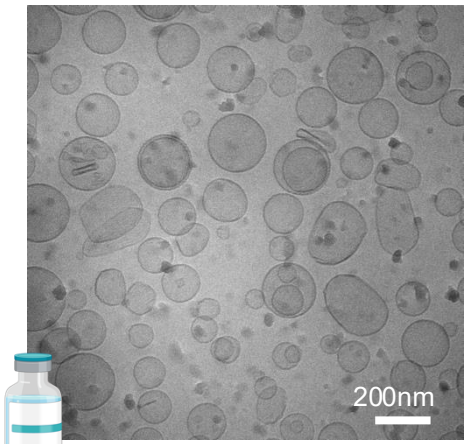
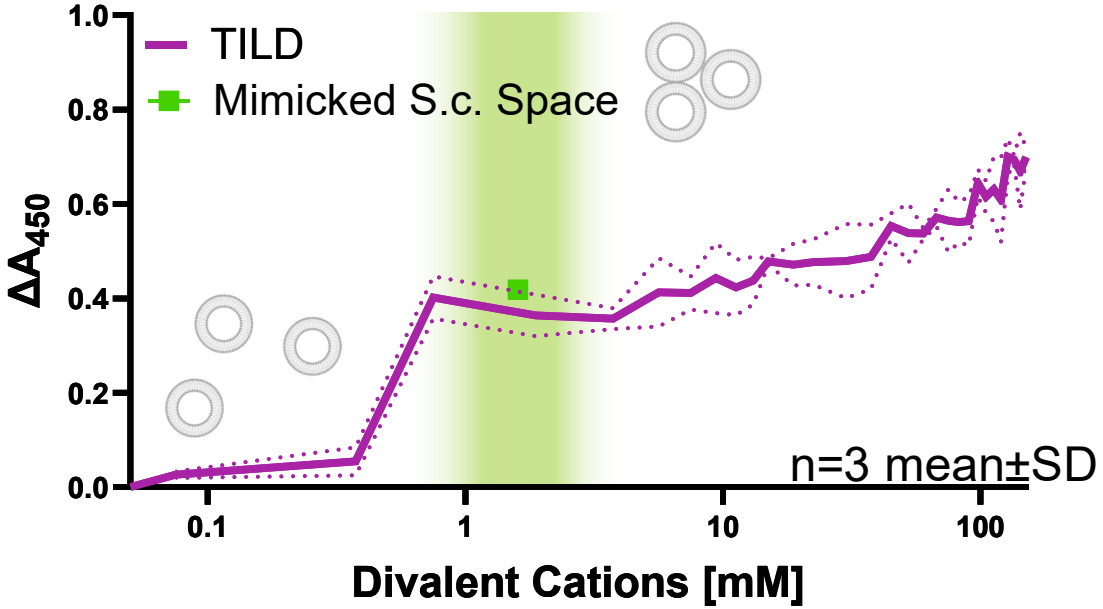
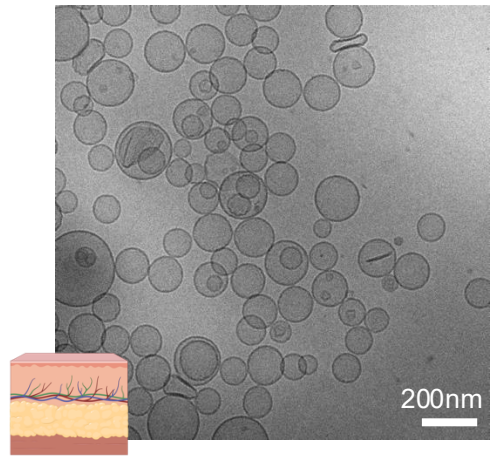
Experimental Validation: Depot formation

In-situ forming depot by aggregating liposomes while maintaining their integrity



Storage



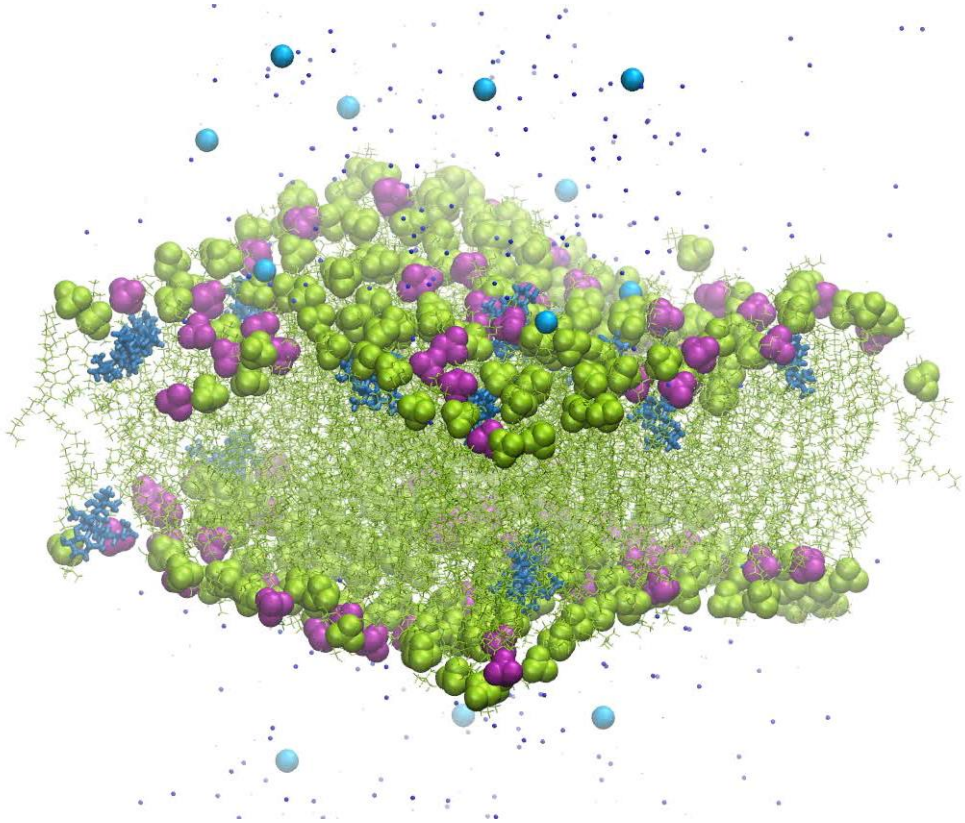


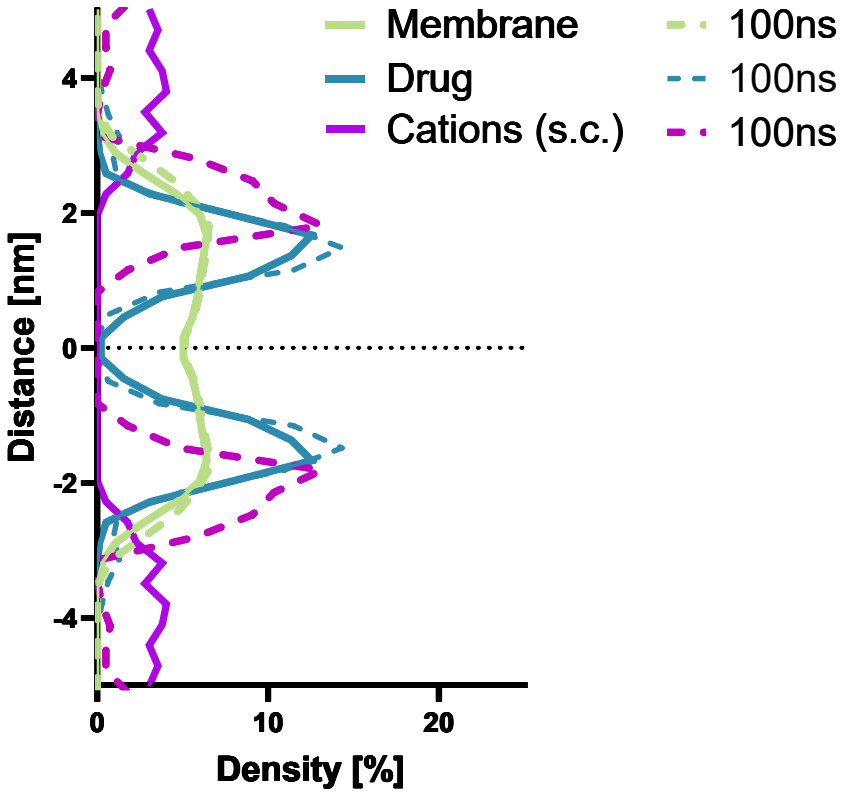
S.c. Space

Eugster et al. J Control. Rel. 2026. 392. 114739
European Patent Application No 25186092.0; Charged Liposome Composition

Mechanistic Computational Design

Simulation of membrane system within modeled s.c. space indicate drug release driven by physiological cations





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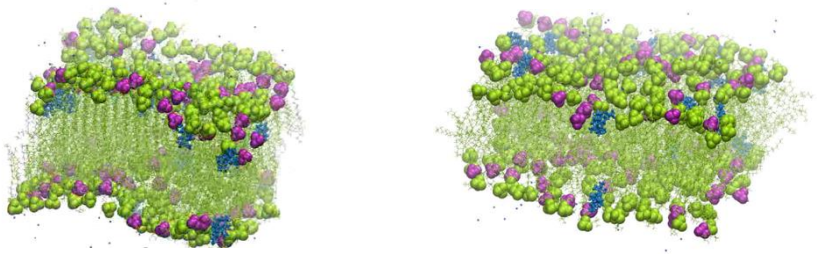
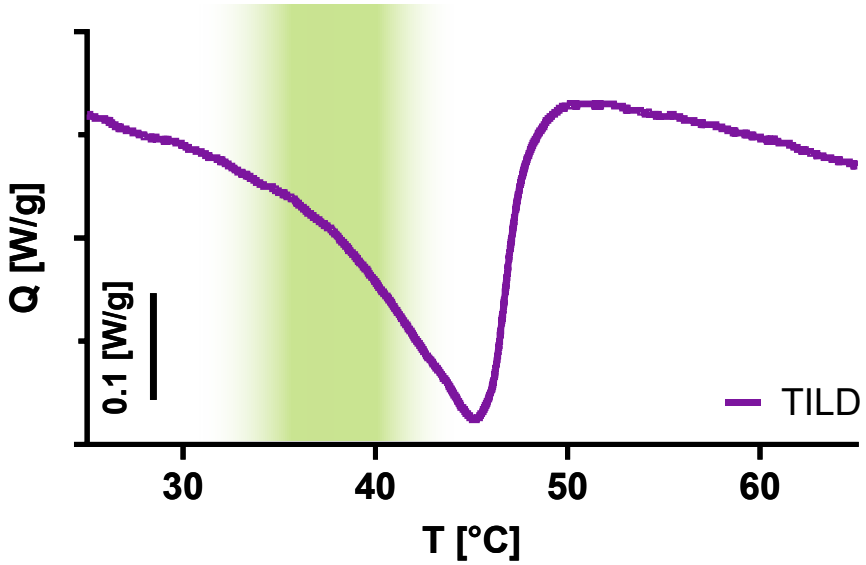
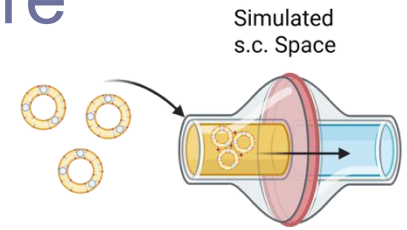
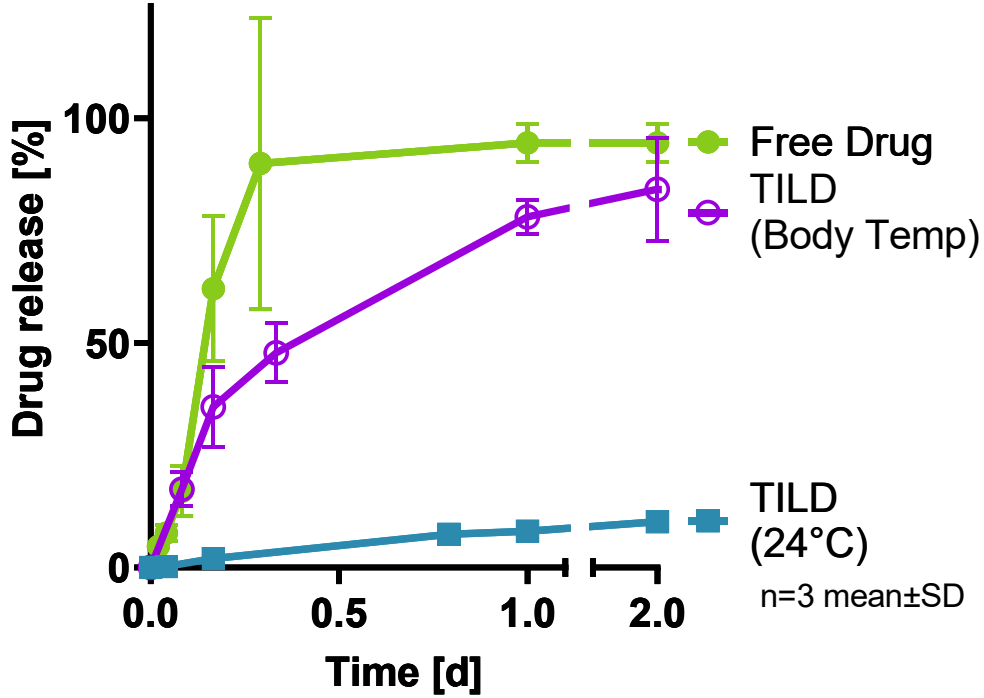
Experimental Validation: Temperature trigger

Sustained drug release driven by body temperature









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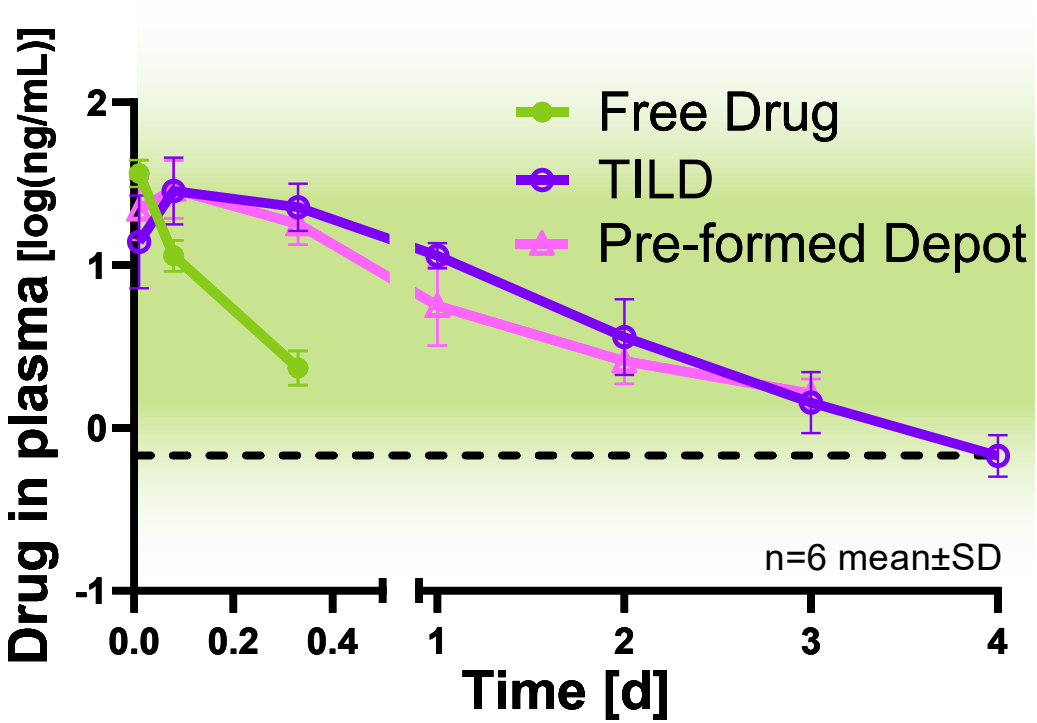
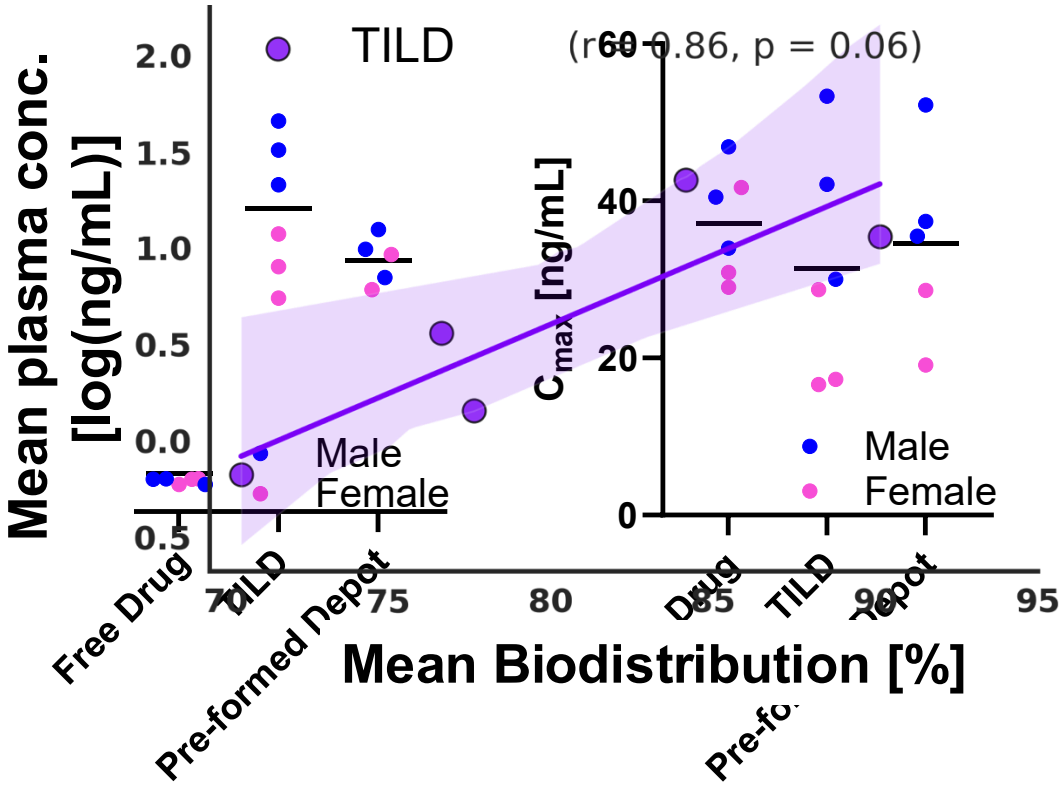
Proof of concept

Pharmacokinetic studies demonstrate maintenance of therapeutic window for 3-4 days





Eugster et al. J Control. Rel. 2026. 392. 114739
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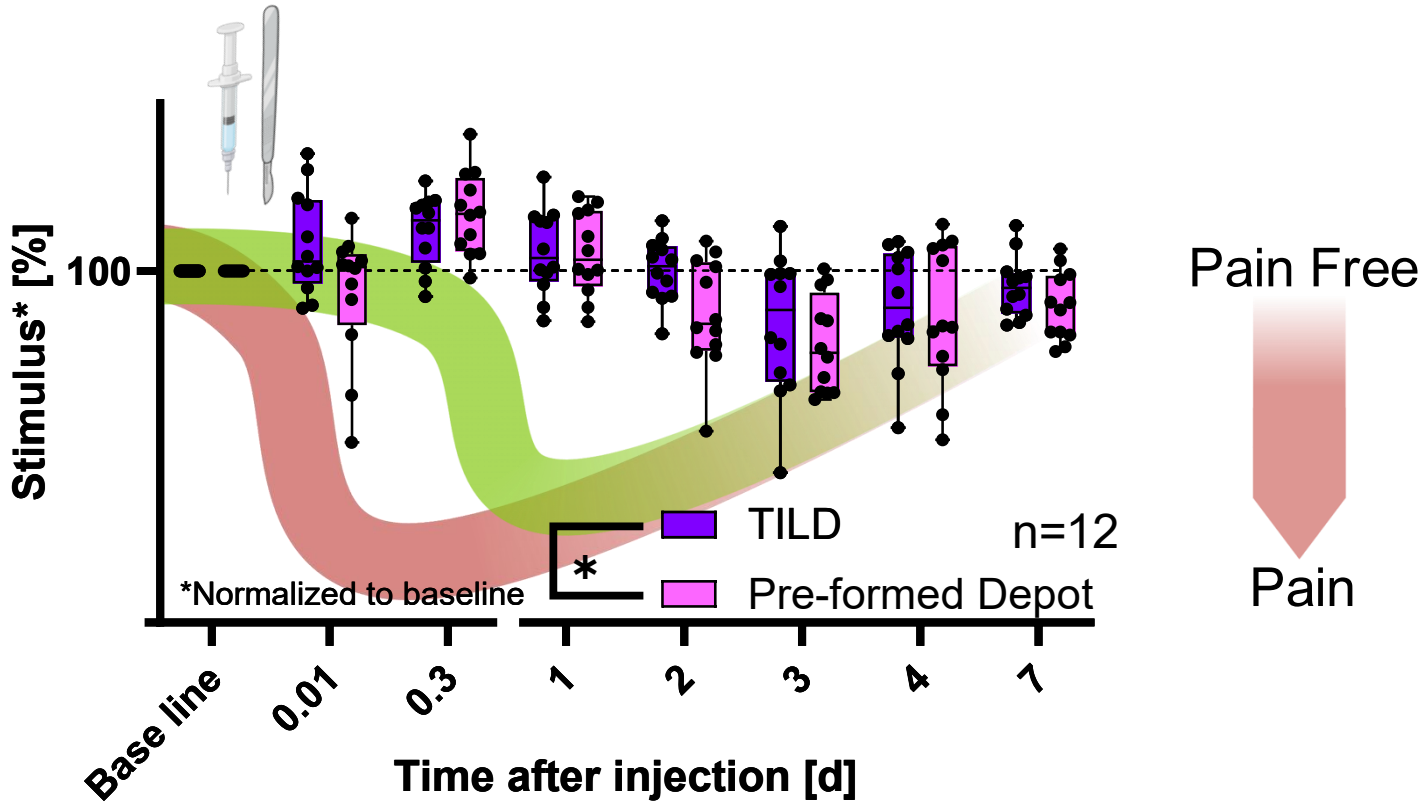
Therapeutic translation

Surgical incision models in rats demonstrate pain relief over 3 days outperforming current options



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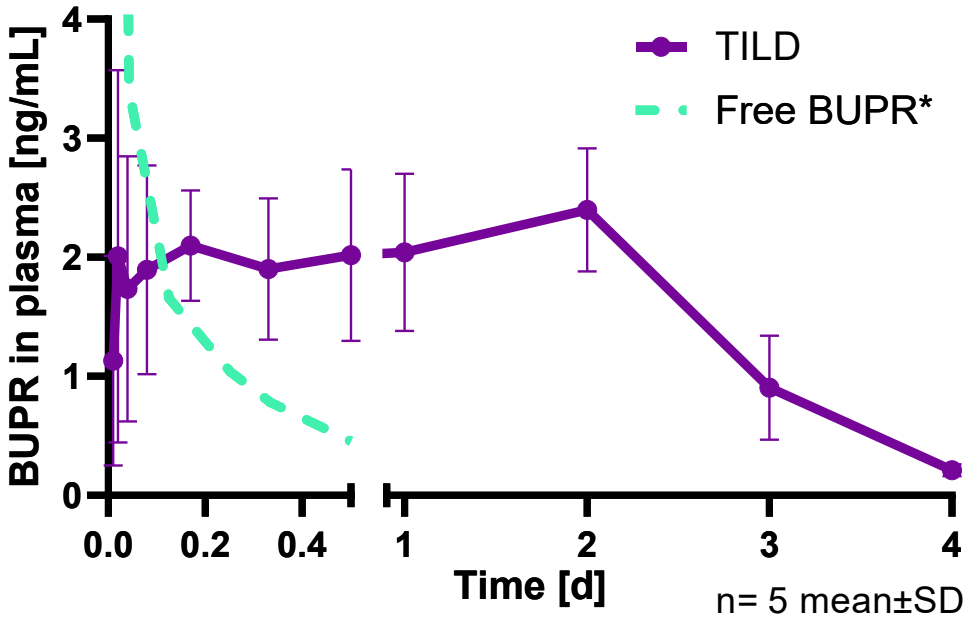
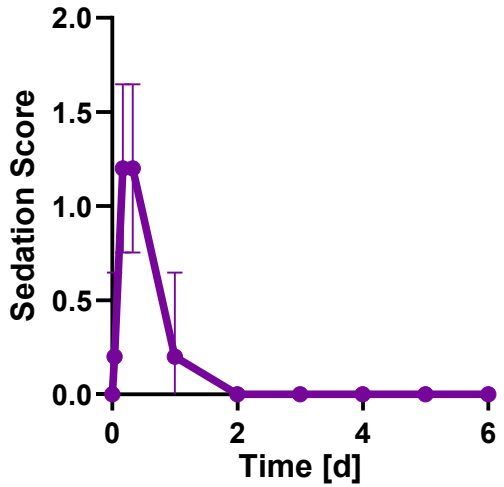
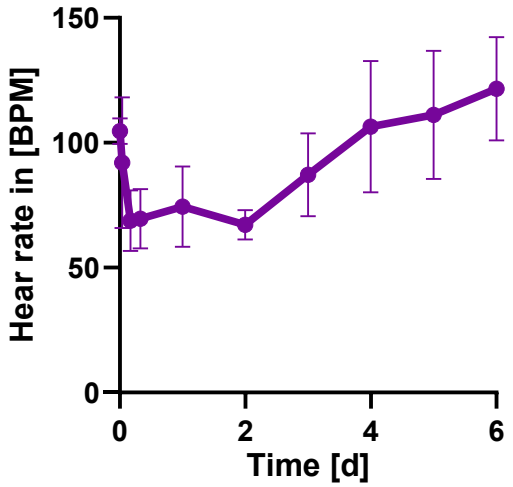
Validation in dogs

Sustained therapeutic levels for up to 3 days while remaining tolerable and safe







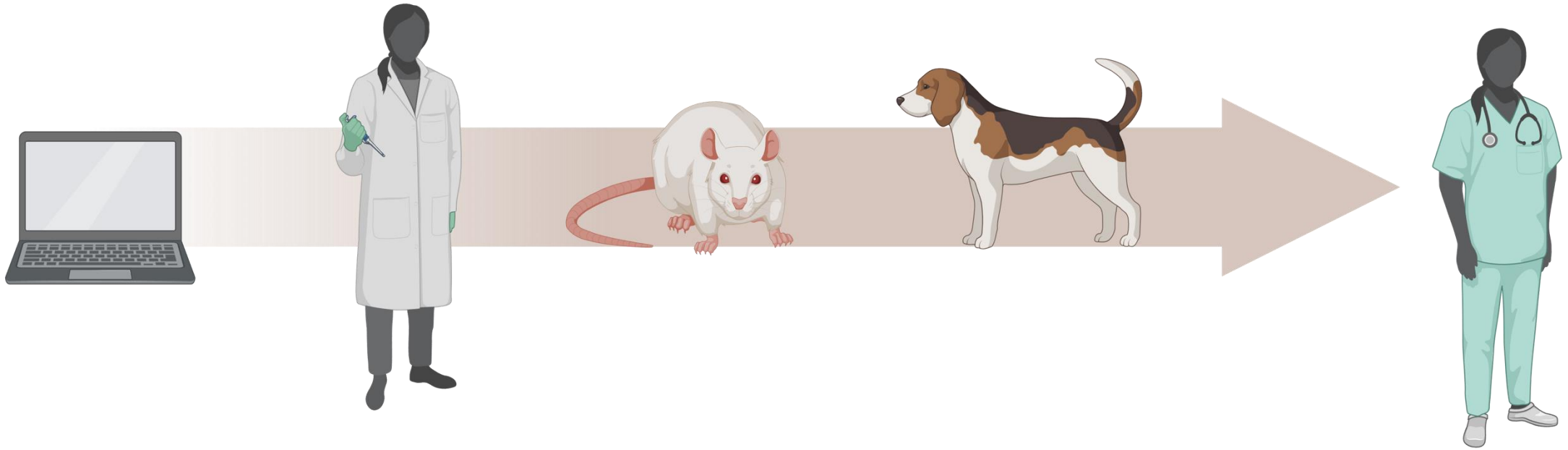
*Nunamaker et al. 2014

BUPR: Buprenorphine

Eugster et al. J Control. Rel. 2026. 392. 114739
European Patent Application No 25186092.0; Charged Liposome Composition

From screen to clinics

Strong alignment between design and outcome, successful translation from lab to different species - Next steps: Clinical Pilots

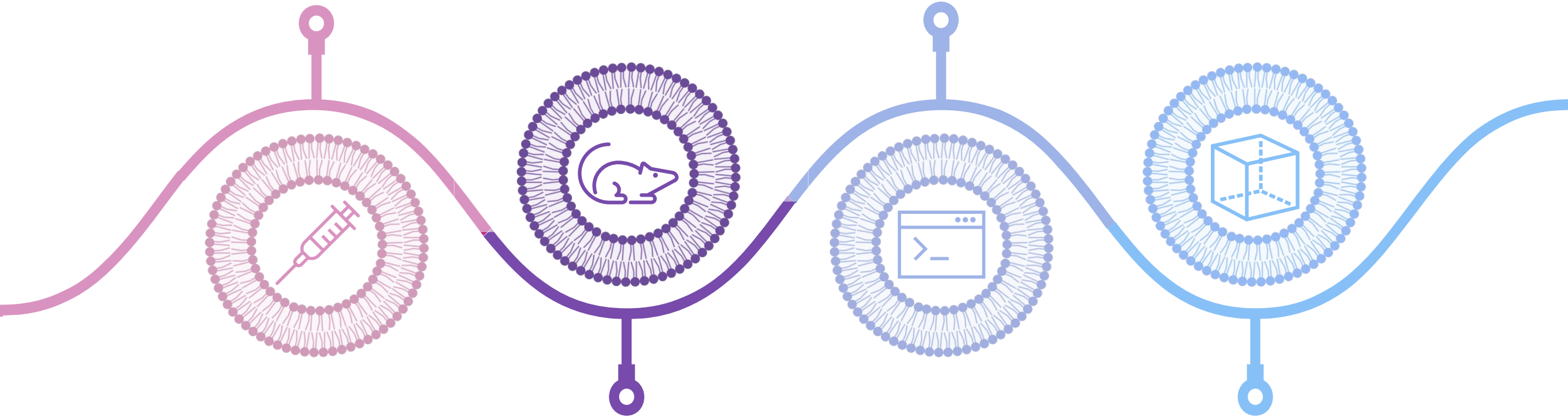


Computational design

Physiologically controlled release from an in situ forming liposomal depot

Predictive manufacturing

Streamlining the development of liposomal drug delivery systems



New alternative methods

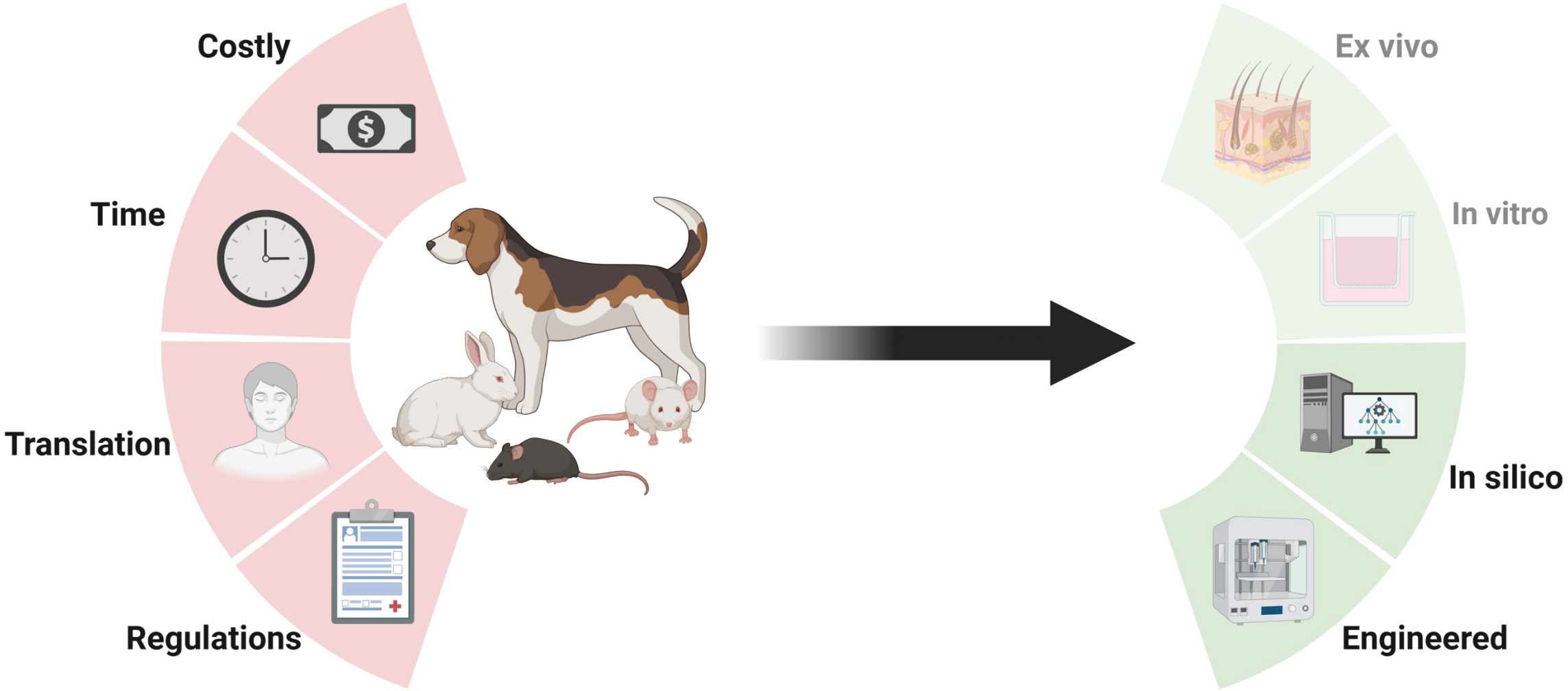
Replace, refine and reduce animal testing

Advanced delivery

Developing composite drug delivery systems

New alternative methods for animal models

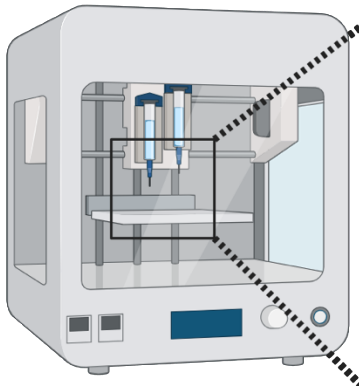
These methods together form an ethically aligned, more predictive, and more cost-effective alternative pipeline for evaluating s.c. formulations



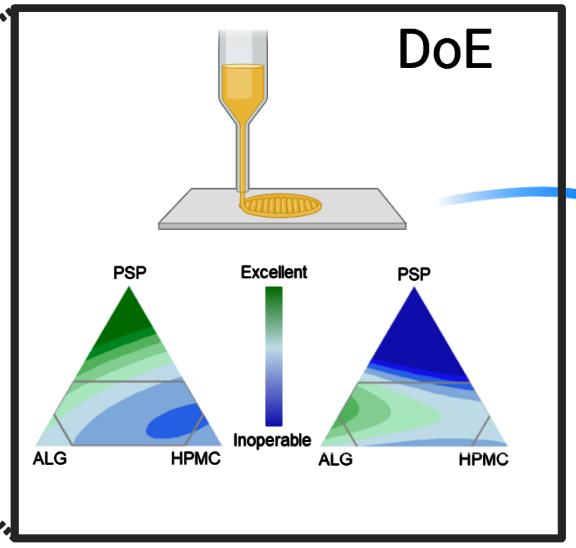
Richter et al. Lab Anim. 2024; 53:9-12

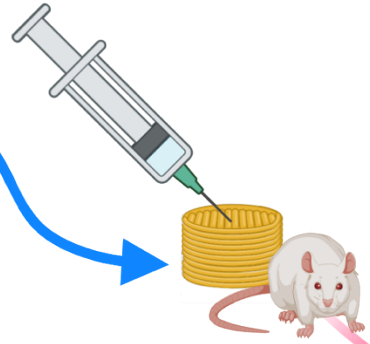
3D-printed artificial s.c. tissue

Printed constructs reduce biological variability and can be stored, standardized, and reproduced on demand.

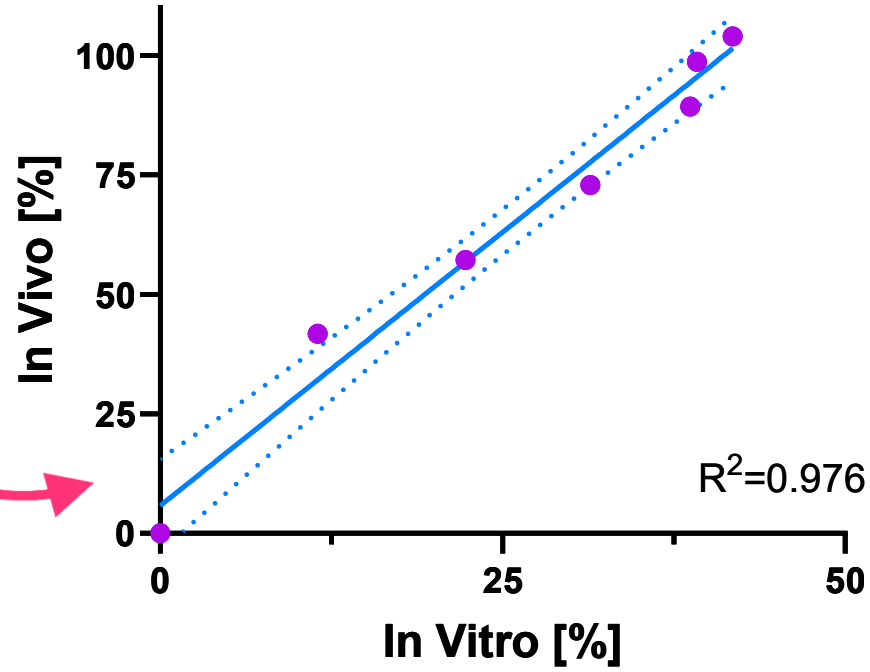


3D Printing





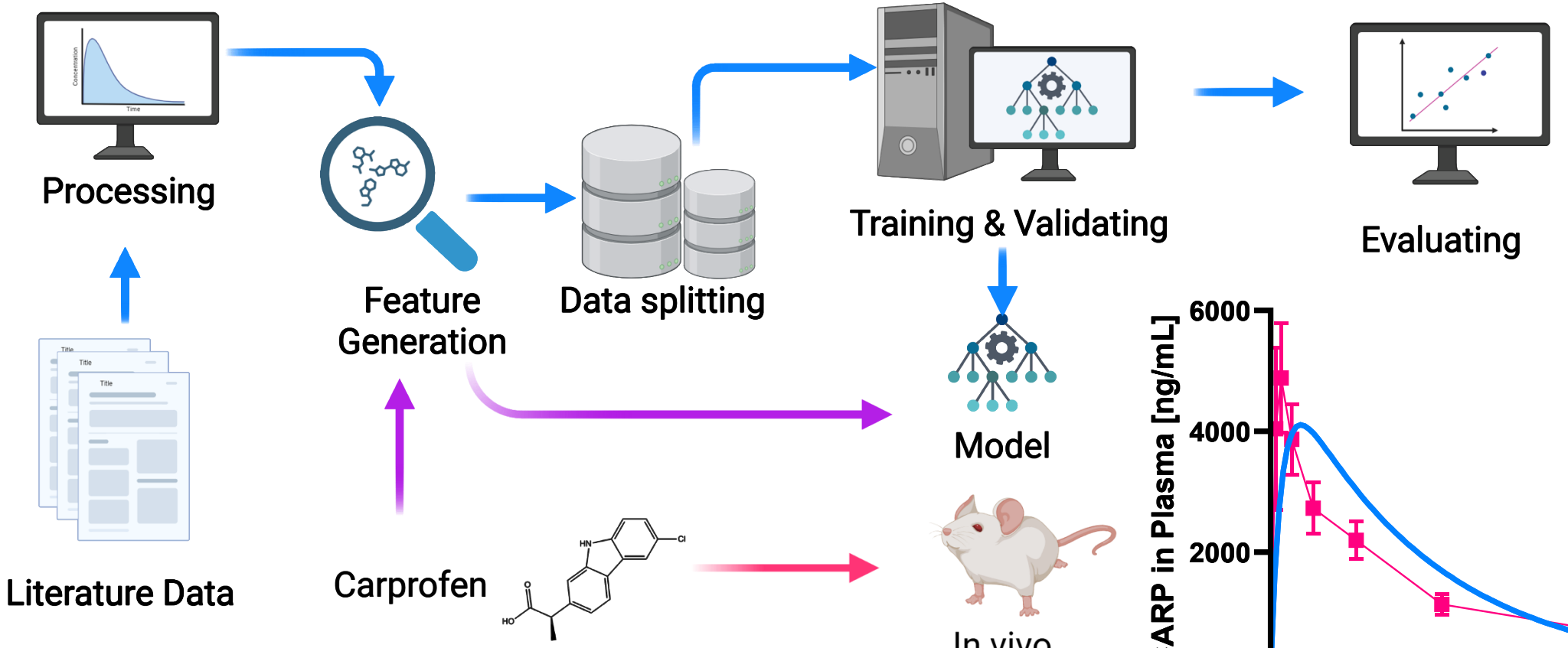
Injection
(Rodent vs. Artificial Tissue)

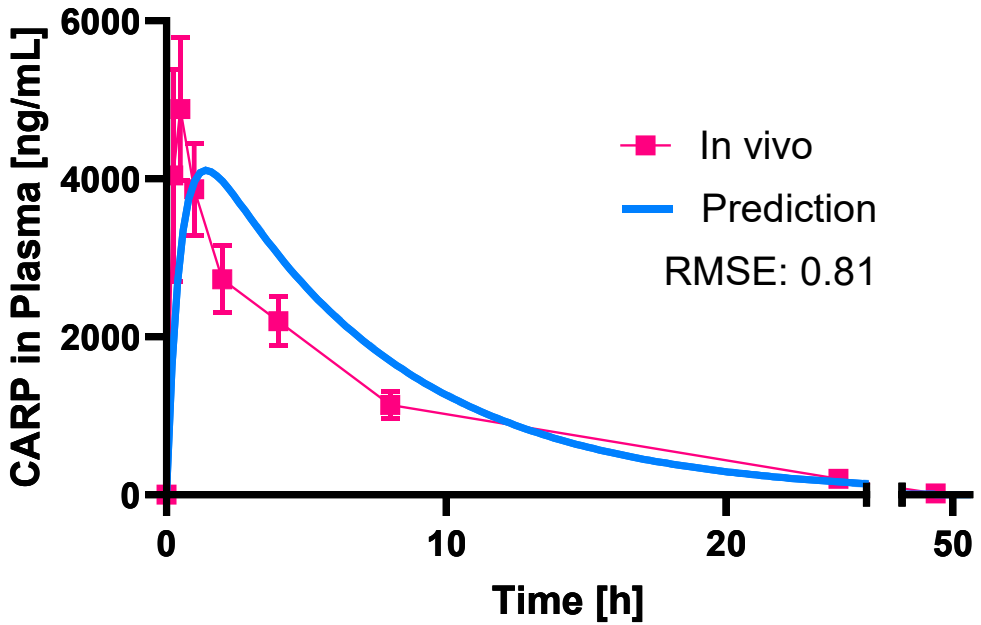


Eugster et al. J. Control. Release. 2026; 394:114863

Machine learning to predict s.c. pharmacokinetics

Models trained on curated rodent datasets predict V, Cl, and ka, thereby reducing exploratory animal studies.



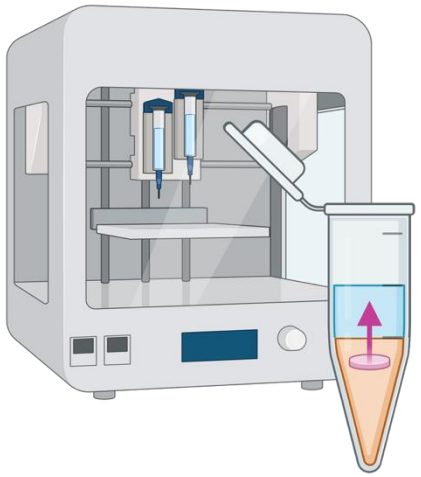


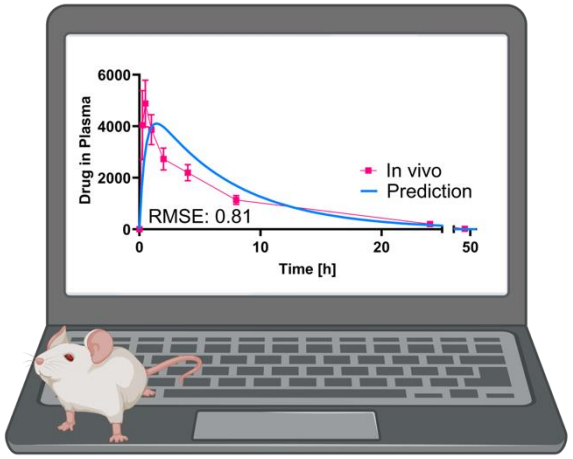
RMSE: Root Mean Squared Error

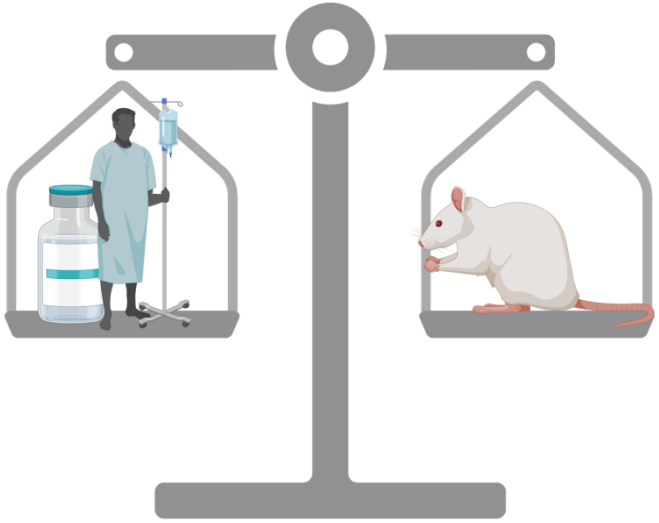
Eugster et al. J. Control. Release. 2026; 394:114863

From flesh to digits

Together the models form an ethically aligned, more predictive pipeline for developing long-acting s.c. formulations.







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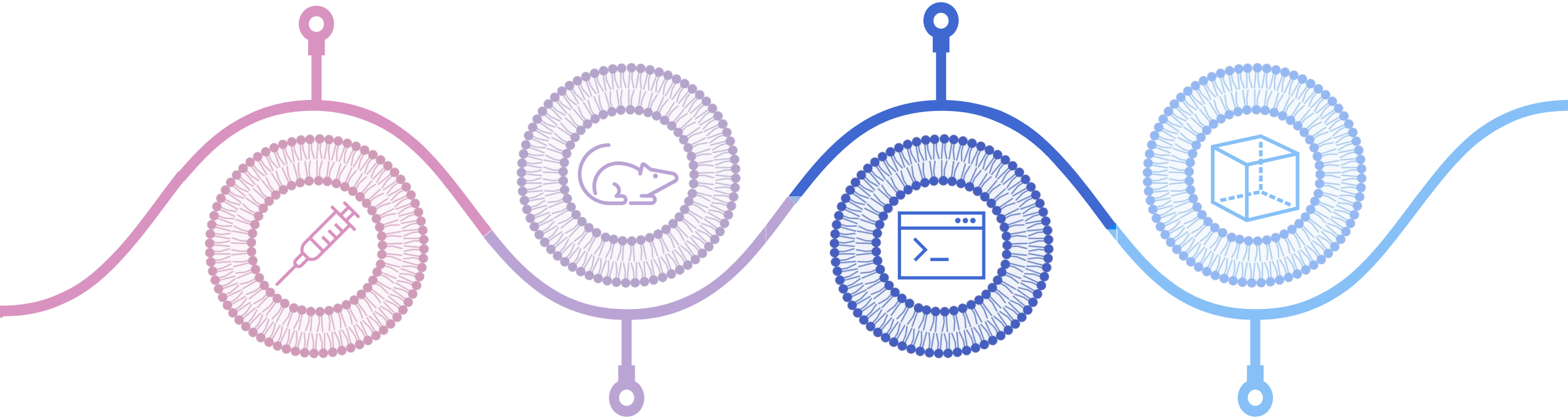

New alternative methods

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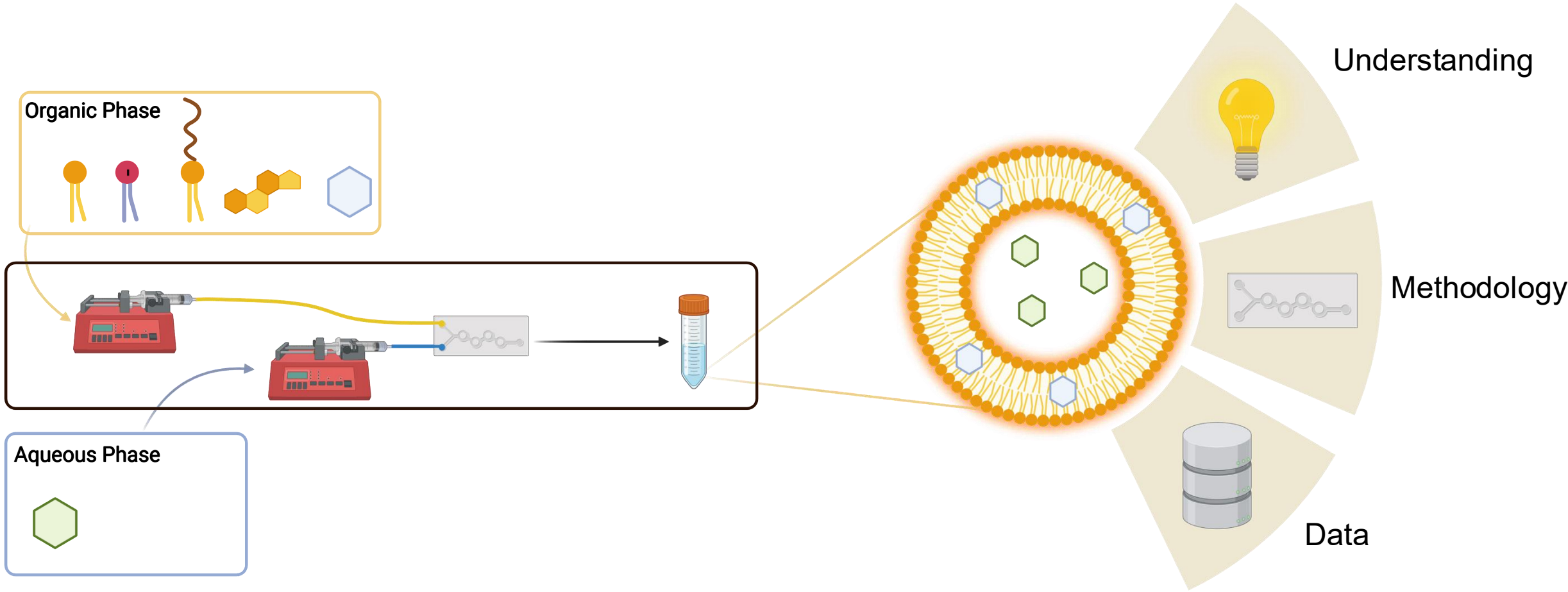
Advanced delivery

Developing composite drug delivery systems

The bottleneck in liposome development

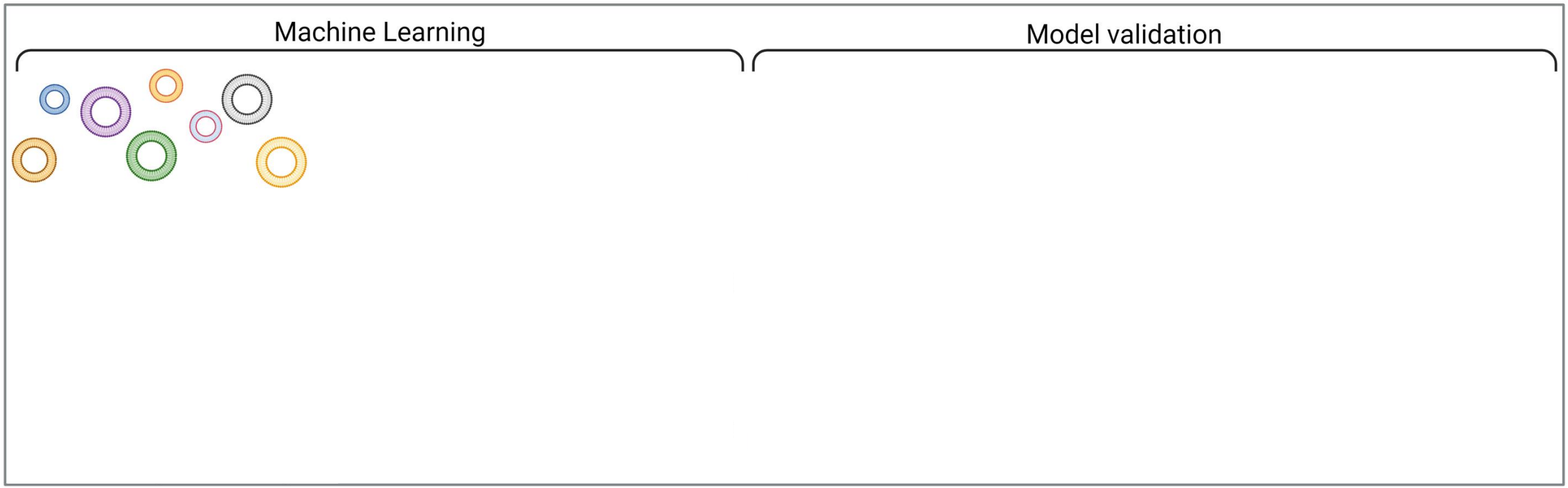
Microfluidic liposome production still relies on intuition, trial-and-error, and incomplete mechanistic understanding.



Eugster et al. J. Control. Release. 2024; 376:1024-38

A data-driven path to predictable microfluidics

We built a harmonized dataset integrating formulation and process parameters to model liposome outcomes.



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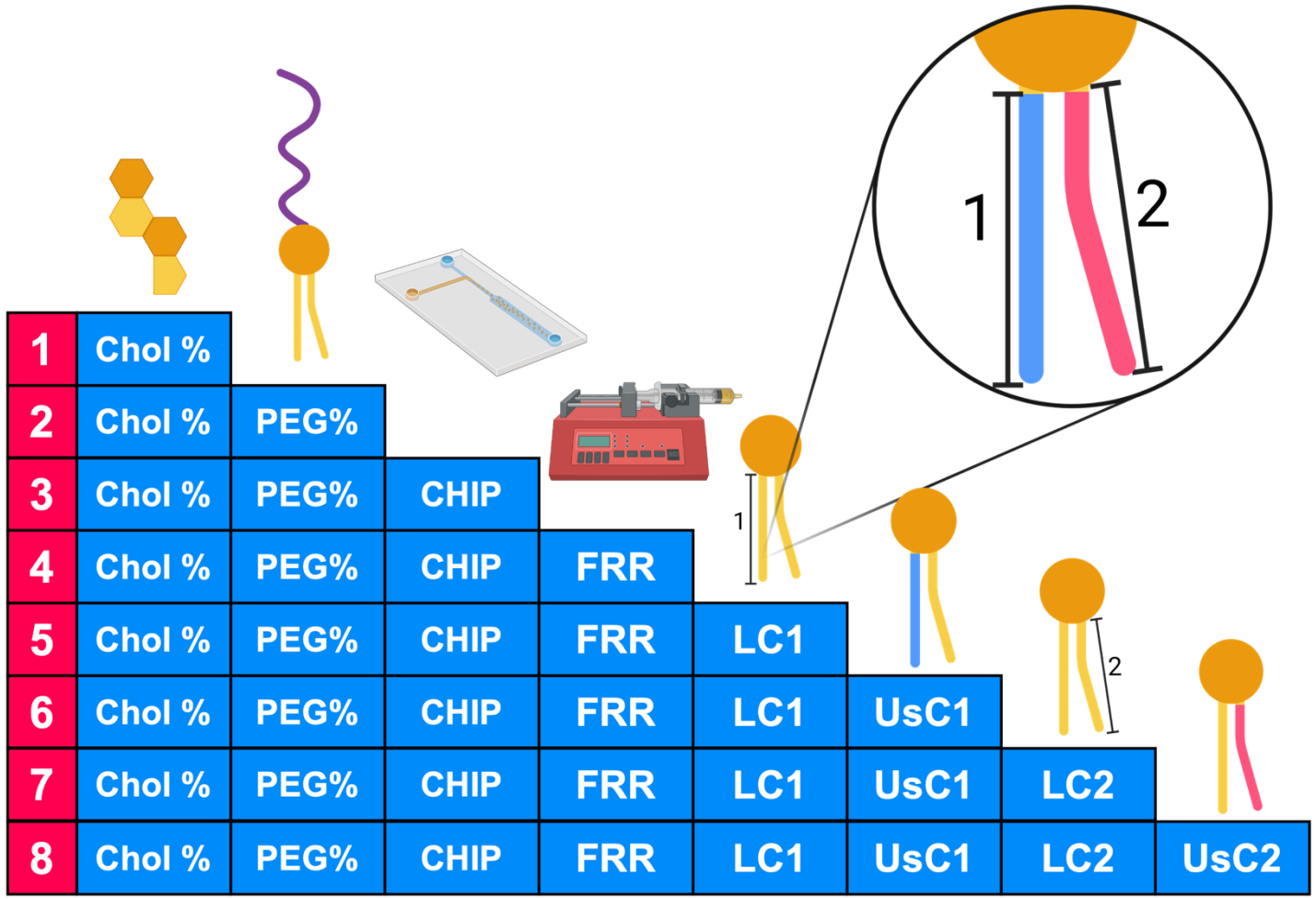
Feature selection

Identifying and selecting most relevant features in dataset, associated with microfluidic liposome production

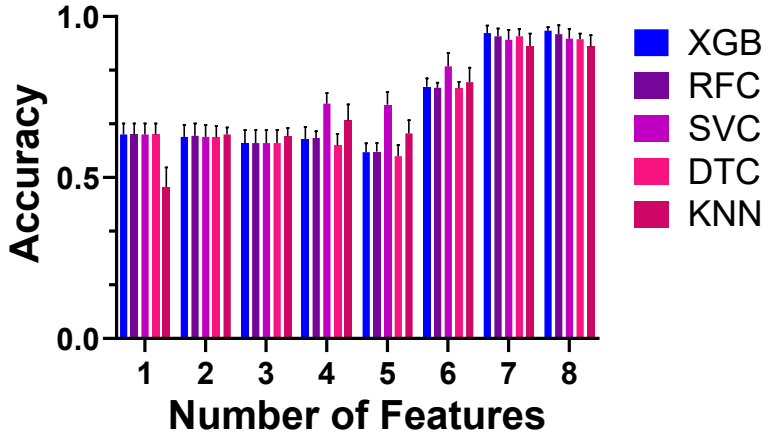


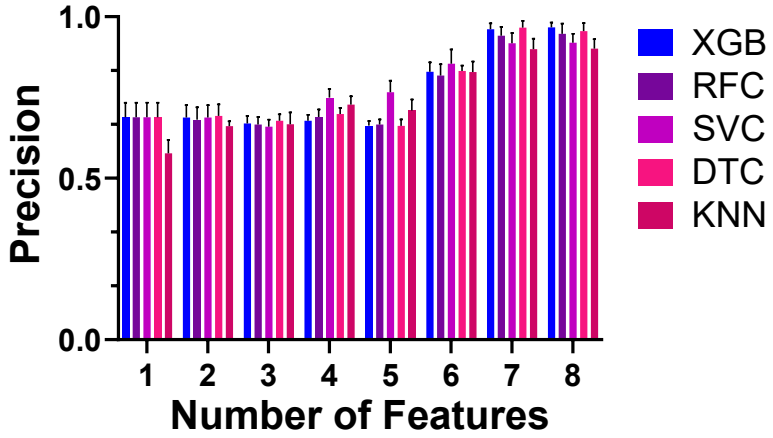
Chol: Cholesterol, PEG: PEGylated lipi, FRR: Flow rate ratio, LC: lipid chain, UsC: Unsaturation Chain

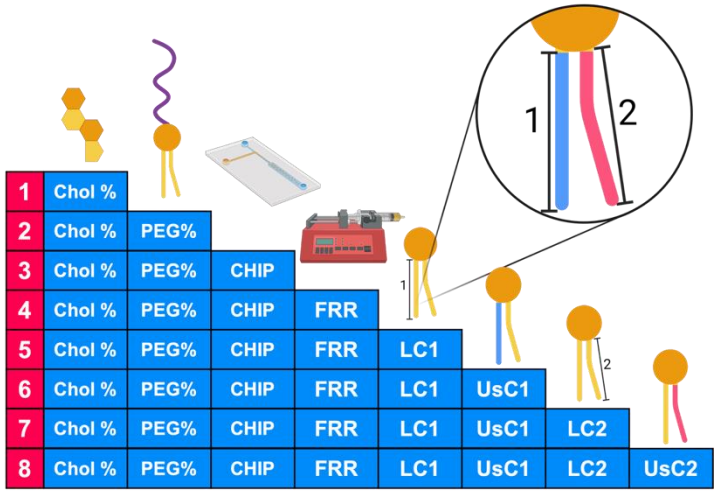
Eugster et al. J. Control. Release. 2024; 376:1024-38

Predicting formation of liposomes

Model after incremental feature addition - XGB performing best.







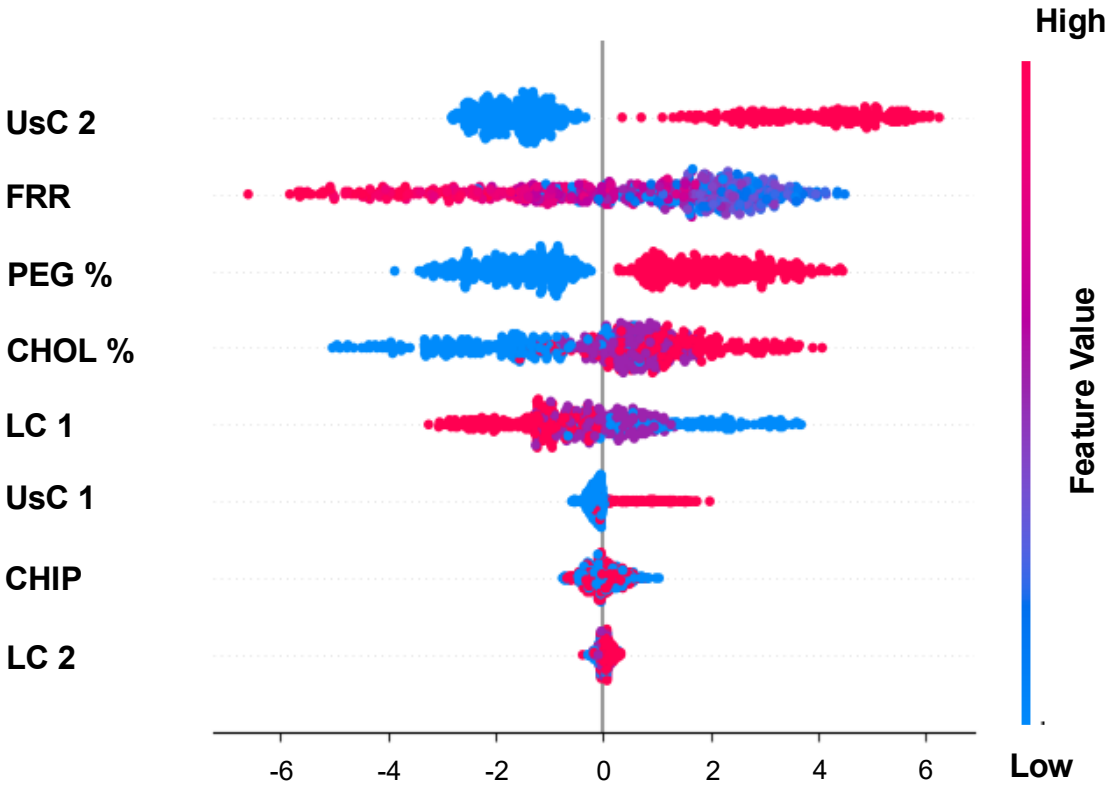
XGB: Extreme gradient boosting, RFC: Random forest classifier, SVC: Support vector classifier, DTC: Decision tree classifier, KNN: K-nearest neighbour

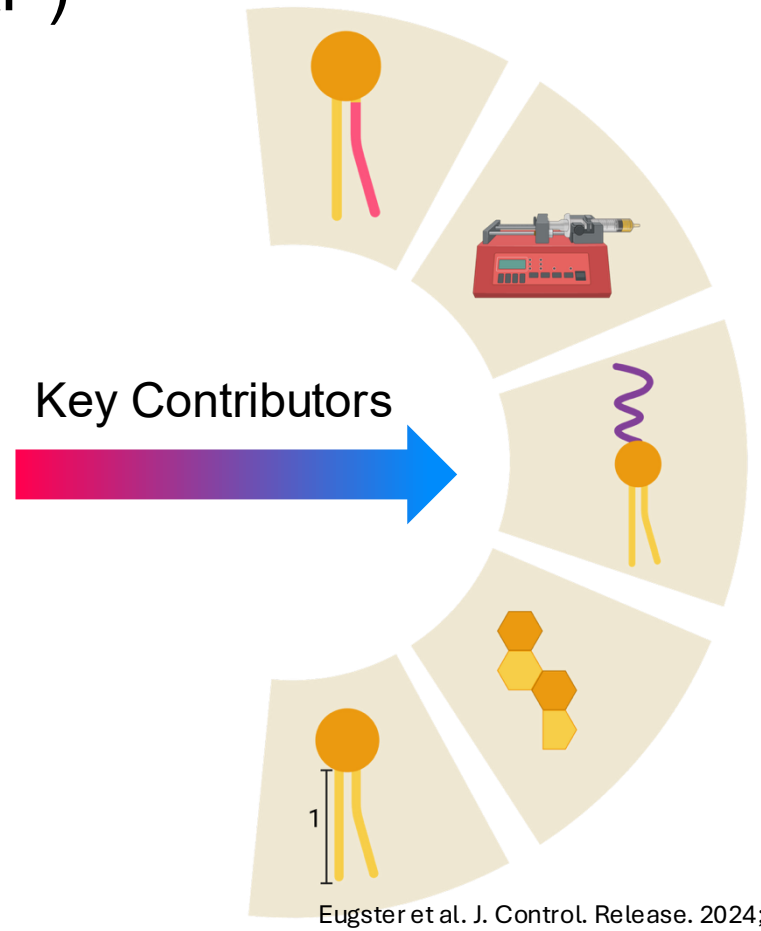
Eugster et al. J. Control. Release. 2024; 376:1024-38

Predicting formation of liposomes

Explainable AI, allows to extract information from black-box models and provide more transparency to the predictions

Shapley additive explanations (SHAP)





Chol: Cholesterol, PEG: PEGylated lipi, FRR: Flow rate ratio, LC: lipid chain, UsC: Unsaturation Chain

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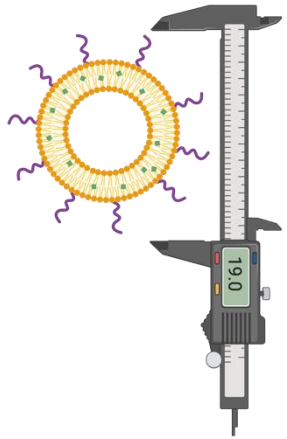
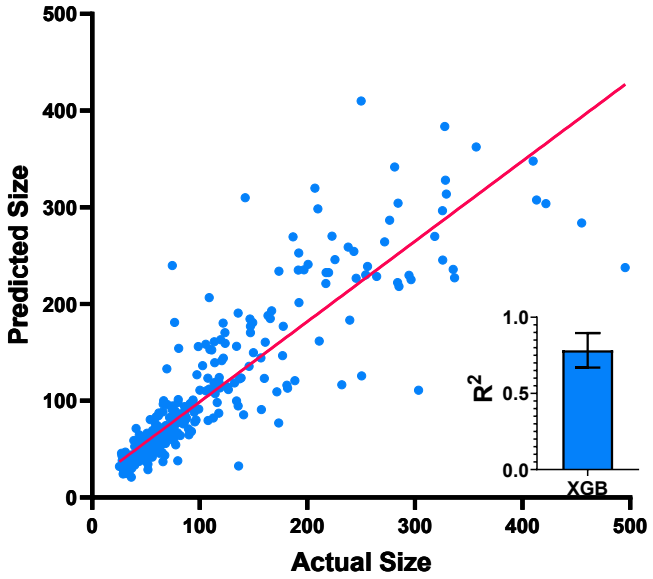
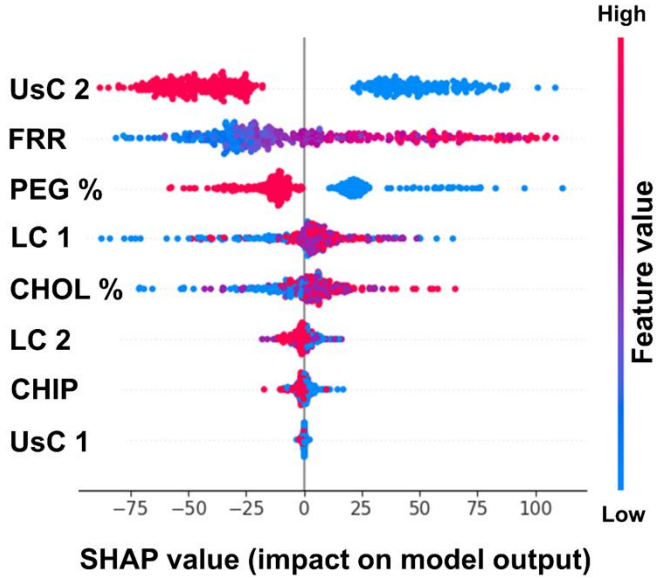
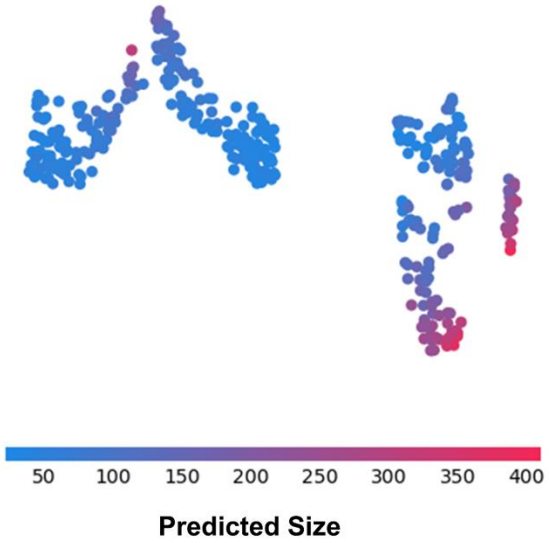
Predicting Size

A parameter of paramount importance in parenteral drug delivery









Chol: Cholesterol, PEG: PEGylated lipi, FRR: Flow rate ratio, LC: lipid chain, UsC: Unsaturation Chain, XGB: extreme gradient boosting

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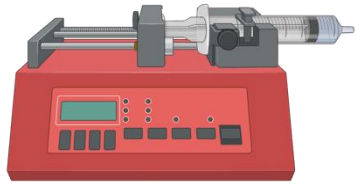
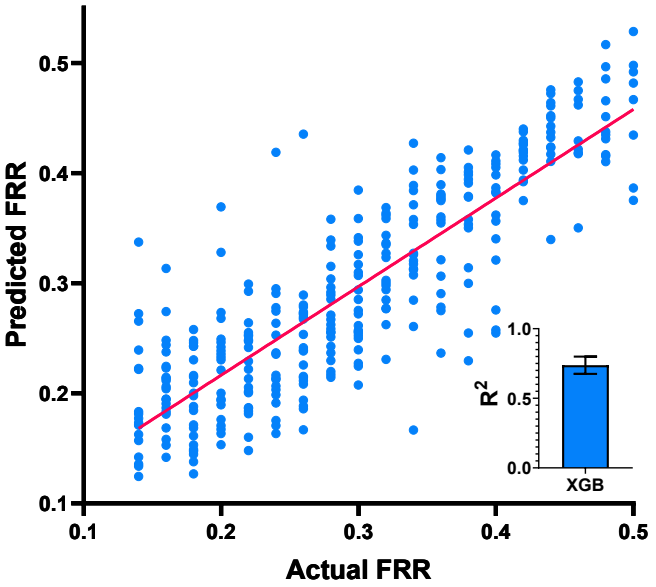
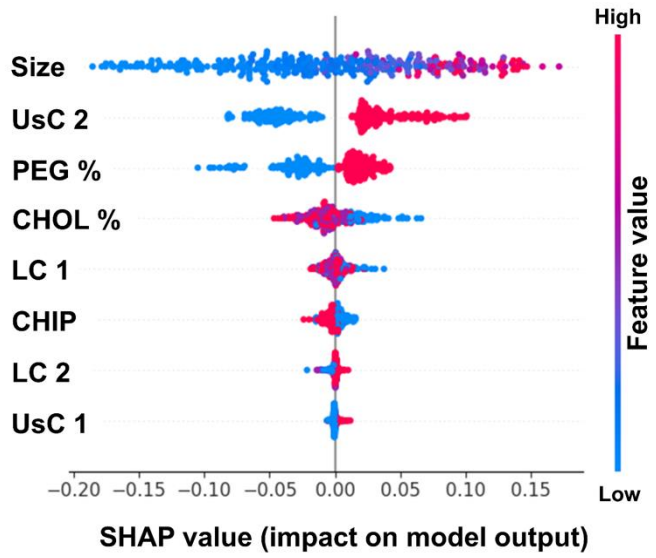
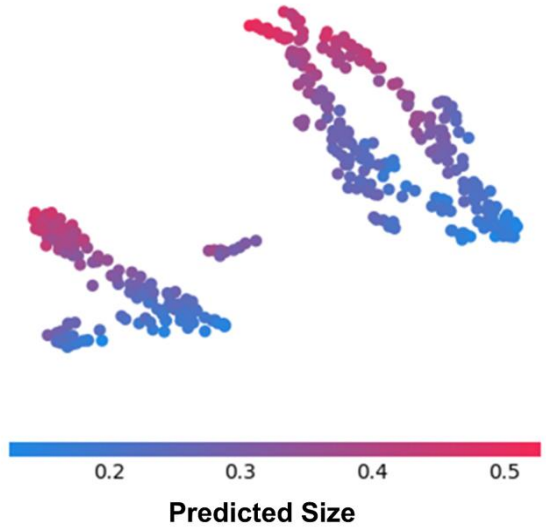
Predicting FRR

Scaling liposome production is challenging, often requiring a shift towards microfluidics as traditional methods fail to scale.









Chol: Cholesterol, PEG: PEGylated lipi, FRR: Flow rate ratio, LC: lipid chain, UsC: Unsaturation Chain, XGB: extreme gradient boosting, FRR: Flow rate ratio

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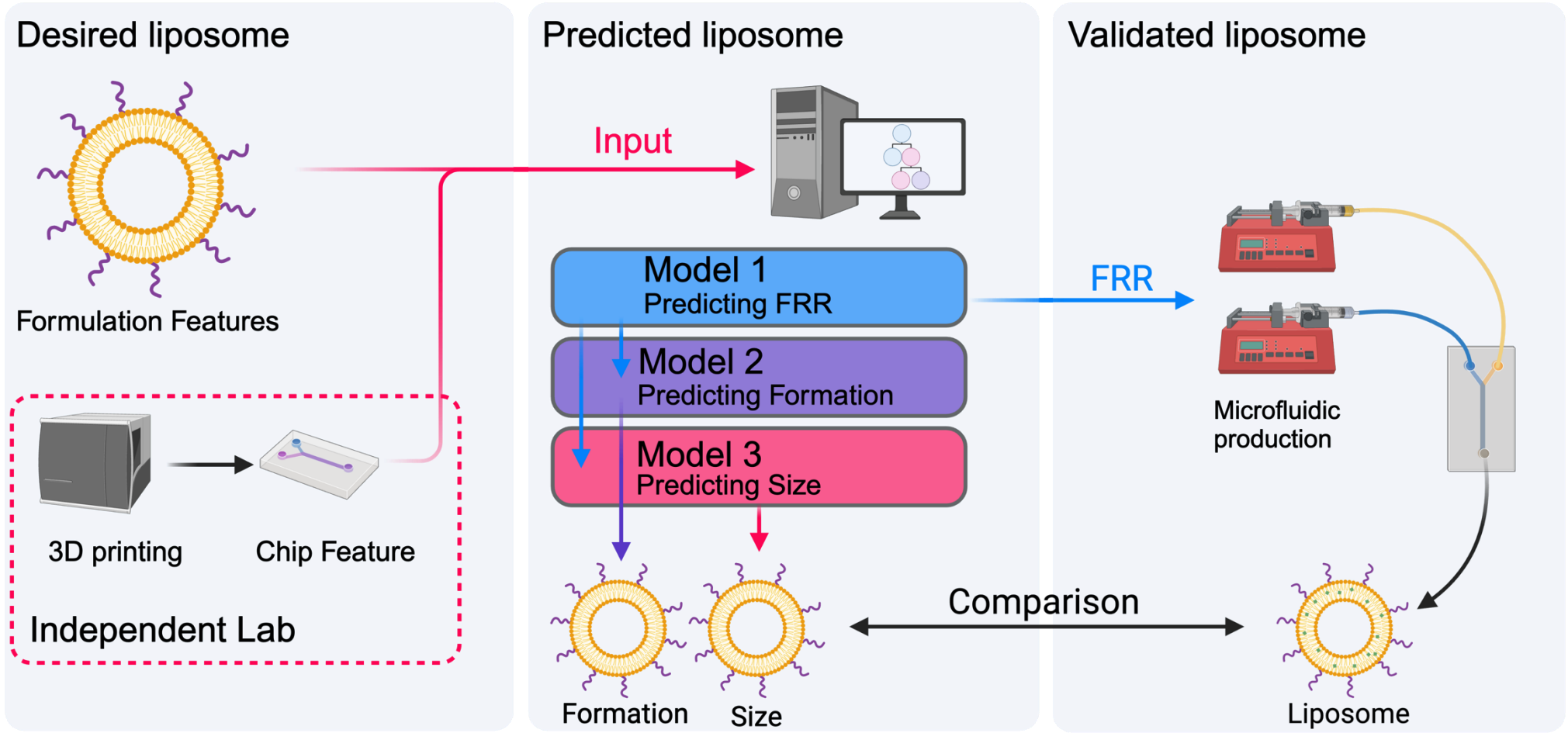
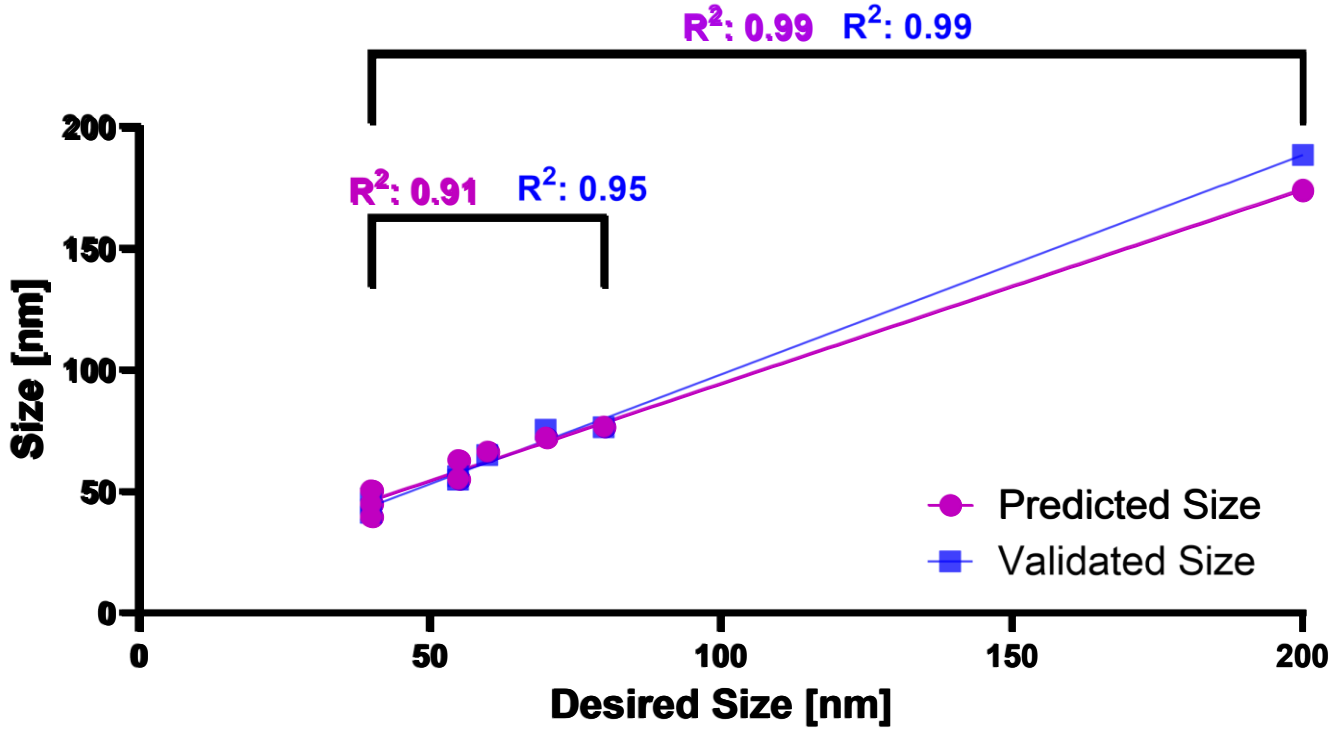
Wet lab validation



FRR: Flow rate ratio

Wet lab validation

The model reliably identified robust production regions, reducing trial-and-error.



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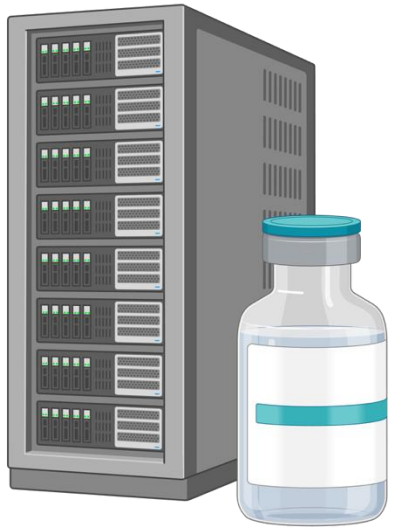
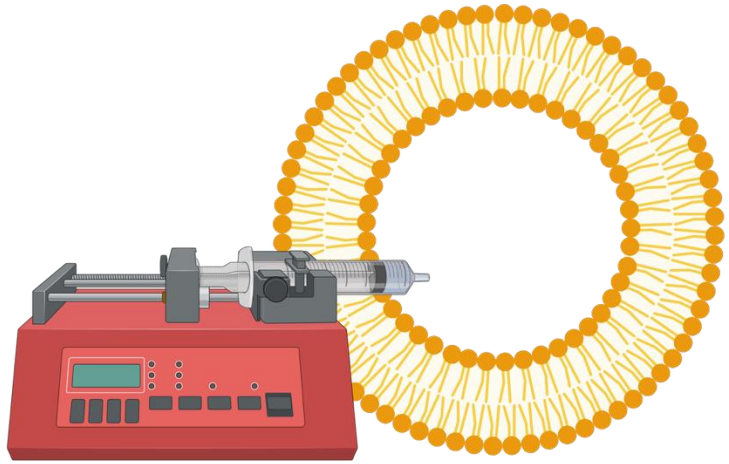
From labs to computers

Predictive models reduce experimental burden, accelerate development, and de-risk the scale-up from batch to microfluidics.





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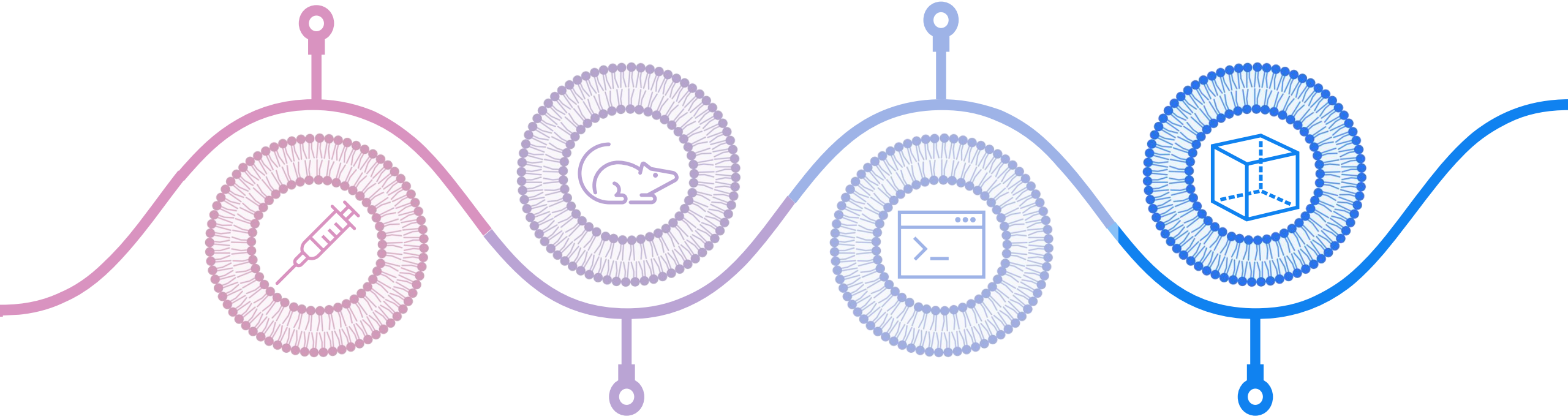
Computational design

Physiologically controlled release from an in situ forming liposomal depot

Predictive manufacturing

Streamlining the development of liposomal drug delivery systems



New alternative methods

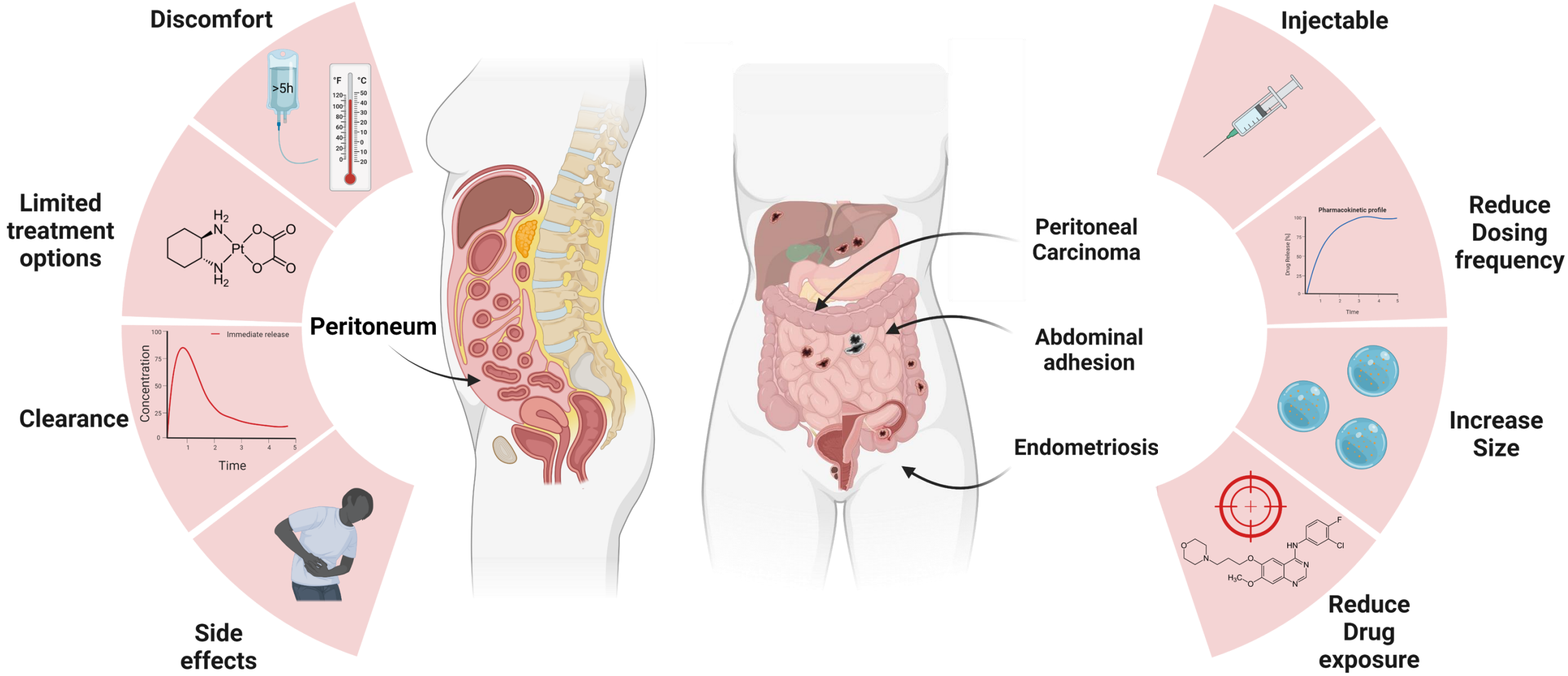
Replace, refine and reduce animal testing

Advanced delivery

Developing composite drug delivery systems

Challenges of Peritoneal Drug Delivery

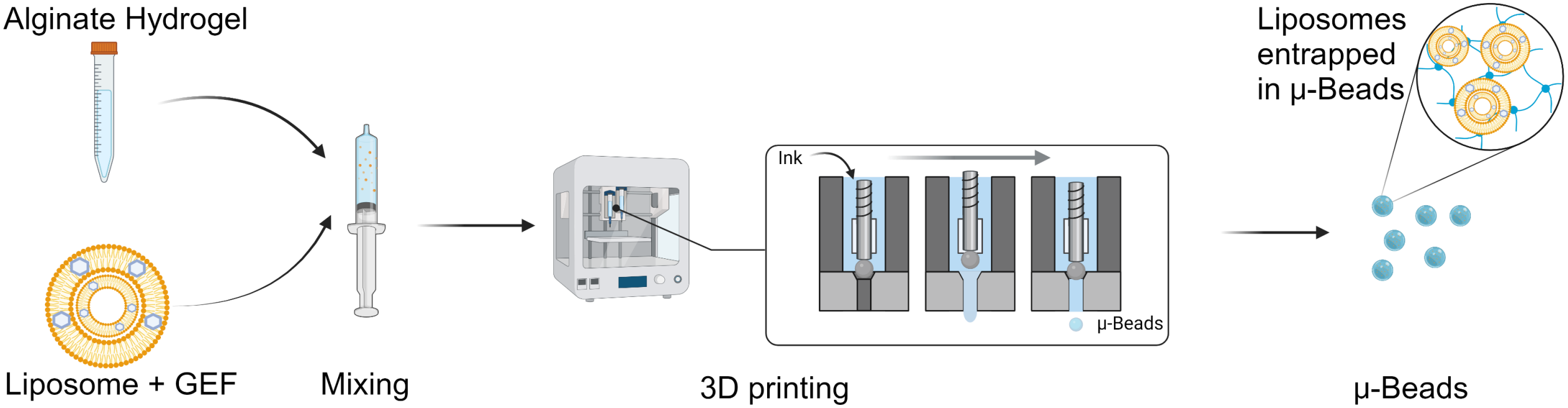
Peritoneal diseases, pose treatment challenges



Zindel et al. Nat. Commun. 2021;12:7316-7330 | Celen et al. Cancers. 2021; 31:3114-3130

Liposome loaded beads – A novel approach

Tackling drug delivery hurdles to the peritoneal cavity



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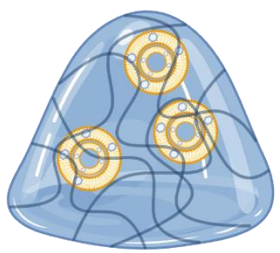
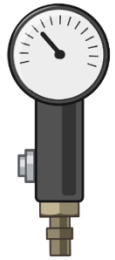
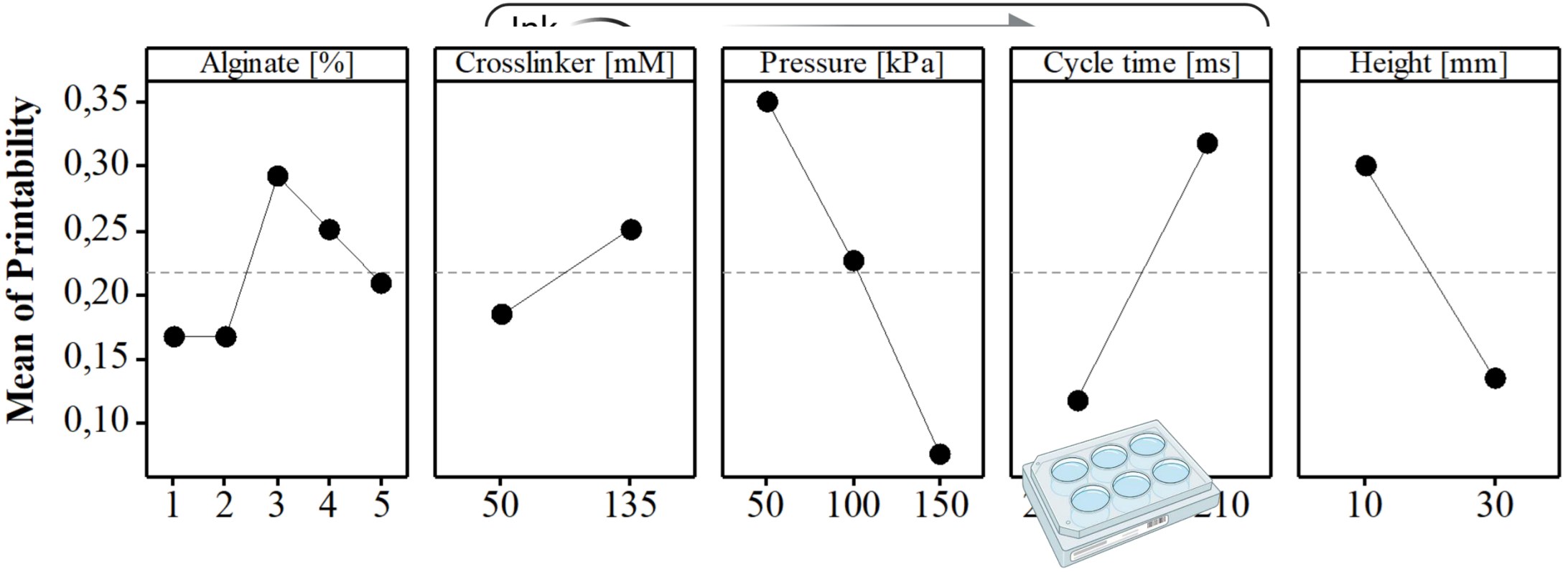
Drug product ink

EMD printhead overcoming limitations of µ-bead synthesis







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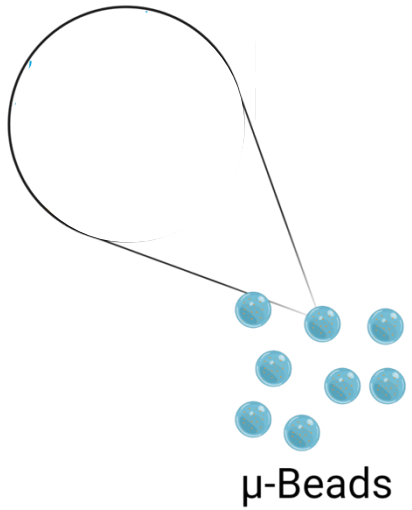
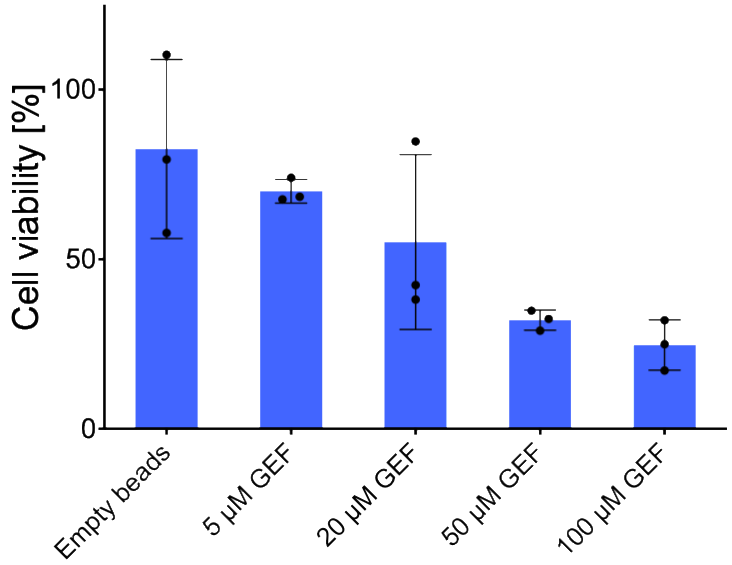
Therapeutic potential

Assessing the μ-beads in a model of human hepatic cancer underscores the efficacy of the composite formulation





GEF: Gefitinib

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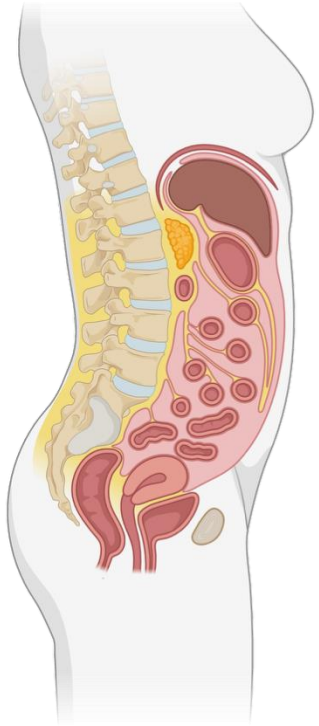
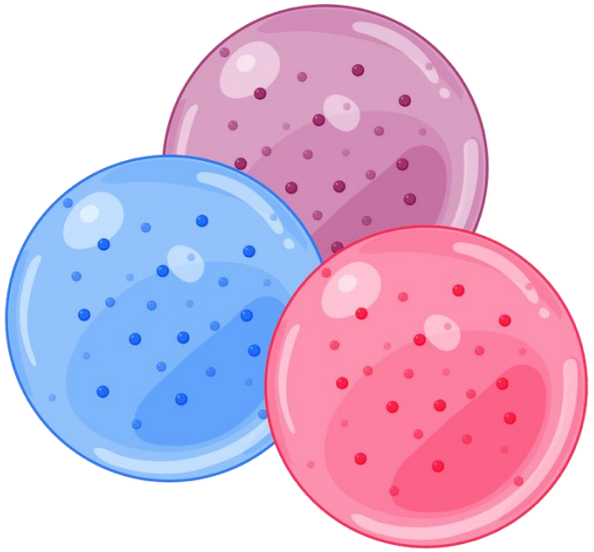
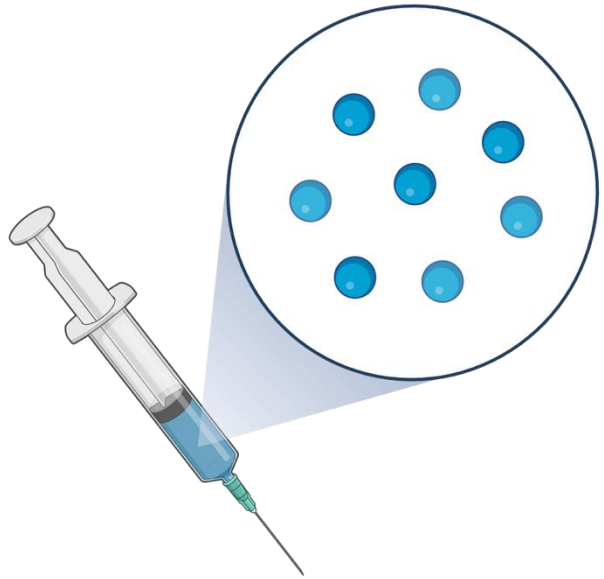
Toward patient-centric peritoneal therapy

3D-printed microbeads offer localized treatment, tunable kinetics, and compatibility with diverse drugs.







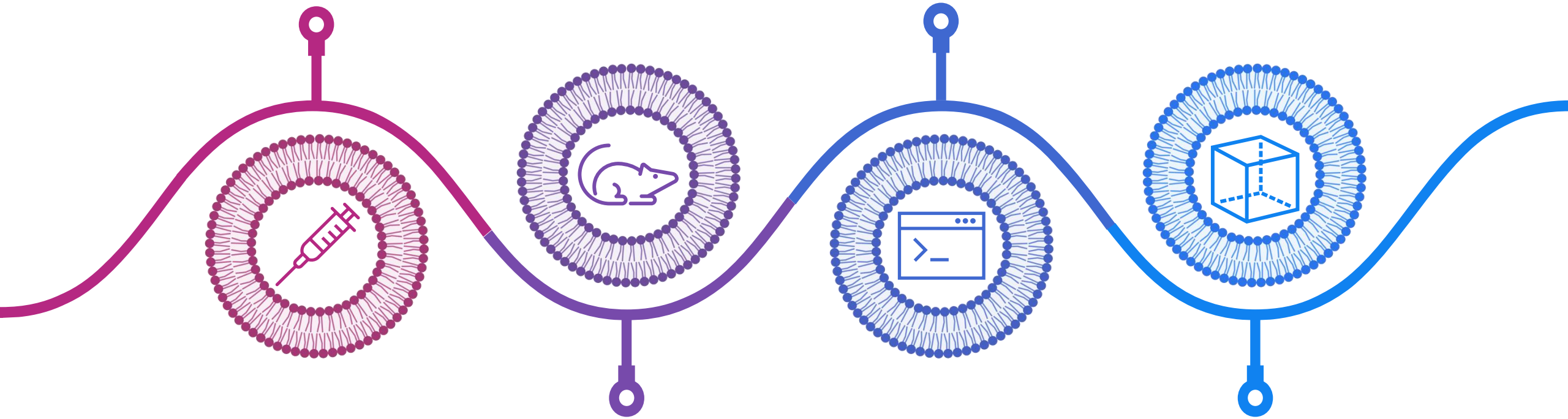
Digital, ethical, and translational drug delivery

Computational design

A computationally designed in situ liposomal depot demonstrated how digital tools can rationally accelerate formulation development and achieve translational performance.

Predictive manufacturing

Machine learning extended this digital paradigm by predicting microfluidic liposome formation, reducing experimentation and enabling scalable, continuous manufacturing.



New alternative methods

New experimental and computational models showed that data-driven approaches can replace animal studies while improving mechanistic insight into s.c. drug delivery.

Advanced delivery

Additive manufacturing further expanded digital formulation design, enabling precise fabrication of liposomal microbeads and stents.

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Prof. Dr. Giulia Rossi
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Dr. Giorgio Buttitta

University of Urbino
Prof. Dr. Luca Casettari
Dr. Mattia Tiboni

ETH Zurich
Prof. Dr. Raffaele Mezzenga
Dr. Laura Baraldi

PhD Exam Committee
Prof. Dr. Carole Bourquin
Prof. Dr. Andera Allmendinger
Prof. Dr. Paola Luciani

Mentors
Prof. Dr. Thierry Langer
Prof. Dr. Oliver Germershaus
Prof. Dr. Martin Albrecht
Prof. Dr. Thomas Lee Moore
Dr. Hicham Majid

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Cats
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