Spatiotemporal Prediction of Targeted Nanomedicine Kinetics and Drug Release using Deep Learning and Quantitative MRI

Revin Toquero, MSc[1]; Edward Taylor, PhD[1]
[1]Toronto Metropolitan University

2026 JULY 19–22 VANCOUVER, BC
JOINT AAPM | COMP MEETING

ABSTRACT

The clinical efficacy of systemic chemotherapy is severely constrained by a narrow therapeutic window. Thermally triggered liposomes can release drugs inside tumors via localized hyperthermia, but heterogeneous tumor microvasculature makes predicting local drug accumulation difficult. To bridge this gap, we implement a Physics-Informed Neural Network (PINN) that embeds governing mass transport equations directly into the model, constraining the model with a known, spatially heterogeneous capillary surface area density derived from microvascular imaging data. This framework is executed across a multi-phased pipeline where we first train the deep learning model to determine liposome accumulation kinetics using simulated synthetic tumor image data. We then validate these predicted accumulation profiles through *in vivo* preclinical studies comparing non-triggered and thermally triggered liposomes. Finally, we use this validated predictive model to personalize treatment protocols, maximizing the tumor-to-normal tissue drug uptake ratio. By merging transport physics with deep learning and microvascular image information, this model should provide a robust tool to optimize localized drug delivery and actively widen the therapeutic window for chemotherapy.

Toronto Metropolitan University

CONTACT

Revin Toquero, BSc., MSc.
Toronto Metropolitan University
350 Victoria Street, Toronto,
ON M5B 2K3
revin.toquero@torontomu.ca
+1 (416) 553-7559

INTRODUCTION

Conventional chemotherapies have a narrow therapeutic window due to systemic toxicities that limit effective intratumoral dosing. Thermally triggered liposomes can selectively release drugs inside tumors via localized hyperthermia[1], but heterogeneous tumor microvasculature makes predicting local drug accumulation difficult. Traditional transport models are too oversimplified, while standard deep learning models lack physical constraints. To bridge this gap, we implement a Physics-Informed Neural Network (PINN) that embeds governing mass transport equations into a model[2,3] (Fig. 1). We hypothesize that spatiotemporal liposome accumulation curves can be predicted by a PINN model constrained by a known, spatially heterogeneous capillary surface area density derived from high-resolution microvascular imaging data using DCE-MRI. By predicting the maximum liposome accumulation within the tumour, combined with the thermal release of chemotherapeutic drug, the therapeutic window for chemotherapy can be widened.

METHODOLOGY

To achieve the goals of this project, a computational and experimental pipeline was developed across four distinct phases. First, synthetic tumor microenvironments were computationally generated to simulate heterogeneous microvasculature, providing a robust "ground truth" dataset of interstitial fluid pressure (IFP) and liposome transport. Second, a PINN model will be developed and trained to predict spatiotemporal liposome concentration curves using known parameters and the model's loss function will be constrained by mass transport partial differential equations (Fig. 2) alongside specific capillary surface area densities. Third, the predictive machine learning model will be validated through *in vivo* preclinical studies, using quantitative magnetic resonance imaging (qMRI) to extract physiological perfusion and tissue parameters for direct spatial comparison. Finally, an *in silico* clinical trial and comprehensive sensitivity analysis will be conducted, systematically varying vascular and transport properties to evaluate model stability, refine parameter dependencies, and optimize personalized hyperthermia protocols.

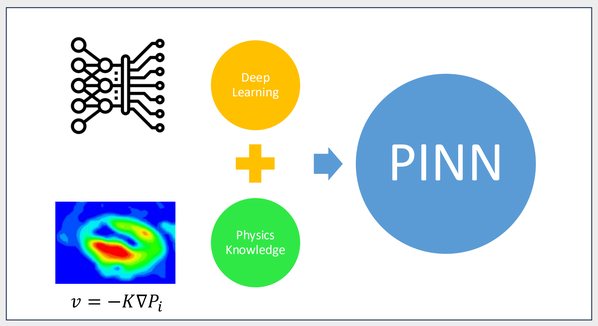

Figure 1. Physics-informed neural network Combines deep learning with the constraints of physical knowledge to solve complex mathematical and physical problems.

RESULTS

Initial results focus on the generation and mathematical validation of the 2D synthetic tumor microenvironment, establishing the essential baseline "ground truth" data required to train the PINN machine learning model. Computational simulations were used to map heterogeneous microvasculature, capturing localized variations in tissue geometry shown in Fig 3.

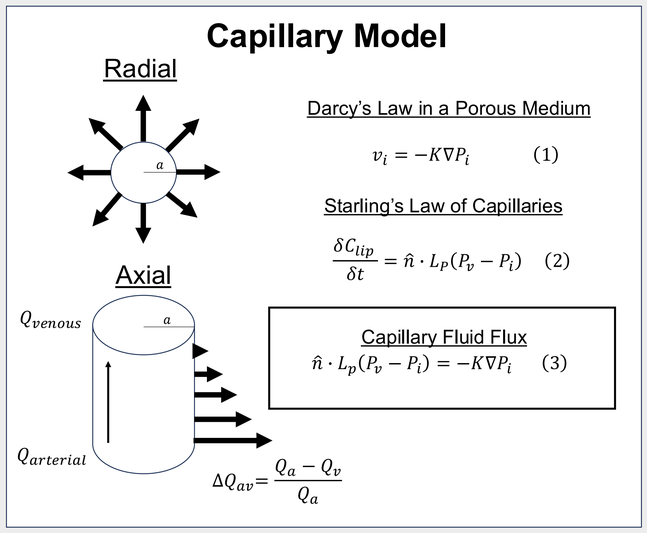

Figure 2. The synthetic tumour model was generated using Darcy's Law (Eqn. 1) for bulk fluid flow in the interstitium and Starling's law (Eqn. 2) for liposome leakage flux from the capillaries. The interstitium is dependent on the interstitial hydraulic conductivity (K), while the leakage flux is dependent on the capillary's vascular permeability (L_p).

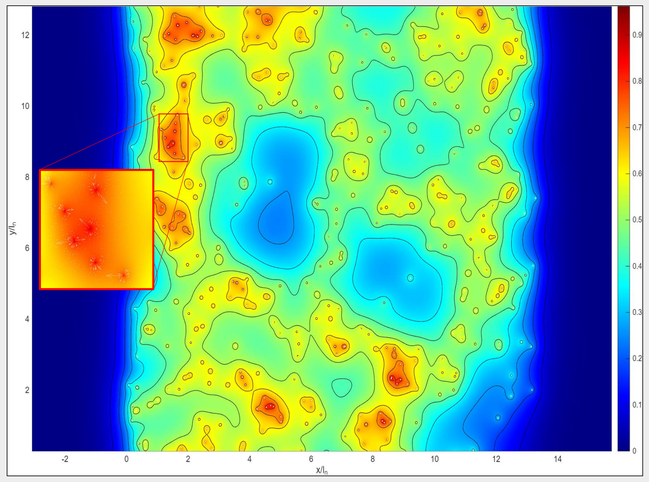

Figure 3. A synthetic tumour (center) model surrounded by normal tissue (left and right) showing IFP generated by the pressure build up of the capillaries. Magnified image shows micro-convection produced by the IFP. The simulation was non-dimensionalized by $l_h = \frac{K}{L_p}$.

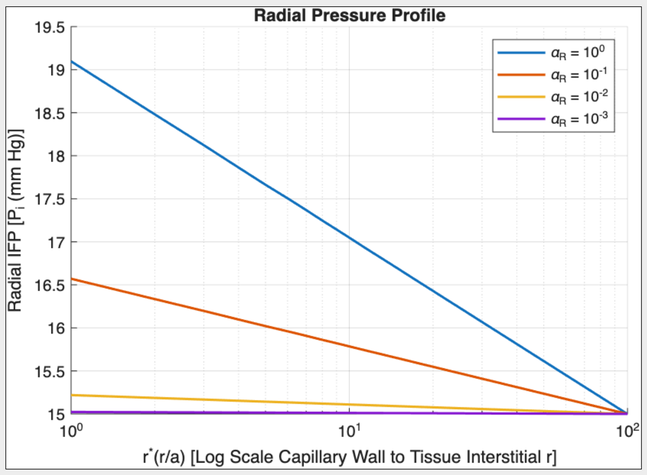

Figure 4. Radial pressure profile of a single capillary model from the capillary wall to the tumour interstitium r. The $\alpha_R\left(\frac{L_p}{K}\right)$ parameter shows varying permeability of the capillary and tumour interstitium.

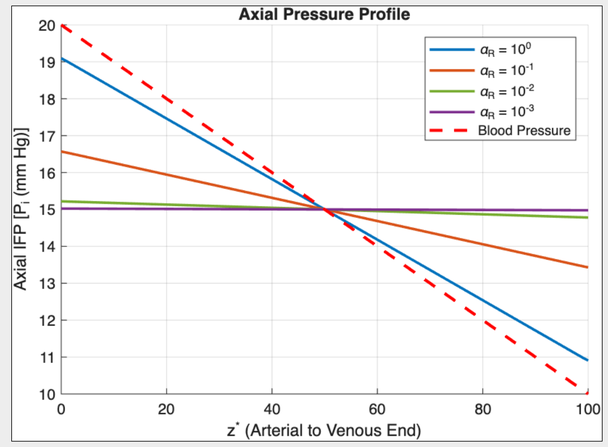

Figure 5. Axial pressure profile from the arterial to venous end with varying permeability.

DISCUSSION

Finite element model analysis of the synthetic tumour model demonstrated a physically accurate logarithmic drop in IFP (P_i) moving radially outward from the capillary wall $(P_i \propto \ln(r^*))$ as shown in Fig. 4. For highly permeable vascular regions $(\alpha_R = 1)$, the local IFP near the vessel wall correctly elevated toward the intravascular blood pressure (P_v) (~19 mm Hg), whereas tight, low-permeability boundaries $(\alpha_R = 10^{-3})$ remained isolated near the background tissue equilibrium baseline (15 mm Hg) as shown in Fig. 5. This alignment between our simulated microenvironment and analytical transport equations confirms that the synthetic data captures real world physiological boundary constraints, providing a mathematically sound foundation for training the PINN model.

CONCLUSIONS & FUTURE WORK

This work establishes a 2D synthetic tumor microenvironment that accurately captures heterogeneous microvasculature and follows foundational liposome transport physics. By verifying that our simulated IFP closely match analytical logarithmic decay profiles, we have generated a mathematically sound "ground truth" dataset required for neural network training.

The future work will be to fully train the PINN model on these validated spatiotemporal datasets to predict localized liposome concentration curves and compare that to the "ground truth" from the synthetic tumour before moving on to *in vivo* preclinical studies.

REFERENCES

[1] Tagami T, et al. *J Control Release*. 2011
[2] Meaney et al. *Sci Rep.* 2023
[3] Chapman SJ, et al. *Bull Math Biol.* 2008

© Poster Template by Genigraphics® 1.800.790.4001 www.genigraphics.com