PULSE: Uncertainty-Aware AI Learning for Drug Diffusion Across Hydrogel Blood-Brain Barrier Systems (Predictive Uncertainty-aware Learning for Synthetic Endothelial Barriers)

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Hemorrhagic stroke occurs when a cerebral blood vessel ruptures, creating an urgent need for intervention to prevent fatality. Developing a neuroprotectant designed to form a synthetic barrier around damaged vessels requires understanding how drugs diffuse across the blood-brain barrier (BBB), which varies in thickness under different conditions. This study investigates the use of hydrogel-based models to examine how BBB thickness influences drug transport. Alginate hydrogel disks infused with methylene blue were 3D printed to simulate localized drug delivery, then embedded within agarose hydrogels of varying thicknesses to simulate attenuated, typical, & inflamed BBB conditions. The constructs were placed in a modified United States Pharmacopeia apparatus 5 containing a diffusion medium mimicking extracellular fluid. Drug accumulation & diffusion rates were measured using UV-Vis spectrophotometry. Additionally, a neural network model was trained on the experimental data to predict diffusion behavior across the thicknesses tested, incorporating prediction uncertainty. Results showed that the typical BBB model exhibited the highest methylene blue accumulation, while the attenuated model demonstrated the fastest diffusion rate, with the inflamed model showing intermediate values. AI predictions closely aligned with experimental trends extend the model's applicability to untested thicknesses. These findings suggest that the alginate-agarose hydrogel system accurately reflects thickness-dependent diffusion governed by the BBB basement membrane, while endothelial transport mechanisms influence drug accumulation. This experimental and computational framework offers a scalable approach for evaluating neuroprotective drug delivery and optimizing therapeutic strategies.

Awards Won:

NC State College of Engineering: Alternates (not read aloud)