INDIAN INSTITUTE OF TECHNOLOGY GUWAHATI
SHORT ABSTRACT OF THESIS

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Programme of Study : Ph.D.

Thesis Title: On the penetration and distribution of drugs into biological tissues: A multiscale approach

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Thesis Submitted to the Department/ Center : Mathematics

Date of completion of Thesis Viva-Voce Exam : August 18, 2022

Key words for description of Thesis Work : Drug penetration, multiscale, drug delivery, mathematical modelling

SHORT ABSTRACT

In this thesis, a finite volume heterogeneous multiscale method (FV-HMM) is propounded to study drug transport into biological tissues by considering cell scale heterogeneity. The partition coefficient is incorporated in the diffusion-based drug transport model as the first objective. A new upscaling technique is devised to evaluate the effective drug transport at the macro level. Next, the FV-HMM is improvised (to FVHMM-p) to incorporate the passive diffusion across the cell membrane. The permeable cell membrane treated in the microscale model incorporates the solute diffusivity, membrane thickness, and partition coefficient. For the microscale model simulation, a novel permeable interface method (PIM) based on the central-type finite difference discretization is developed. Further, the FVHMM-p is reconstructed to investigate the effects of biological cell orientation on the penetration and distribution of a drug in tissues. The simulation results reveal that the biological cell orientation is an important factor, which can potentially affect the drug penetration and distribution in the tissues. In the next objective, the FVHMM-p incorporates the fluid flow and drug metabolism effects on drug transport. On treating the tissue as a porous medium, Darcy's law is used for fluid flow, and the drug metabolism is calculated using the Michaelis-Menten equation. It is observed that the particles of sizes 10 and 100 nm can penetrate the tissue in fluid flow regions. Furthermore, local sensitivity analysis is also performed to determine the model response to the input parameters. It is observed that the parameters such as fluid velocity, extracellular diffusivity, and microscale domain size are the most sensitive to the model outcome. Finally, the last multiscale model is employed to study the tissue penetration and distribution efficacy of chemotherapeutic agents, such as fluorouracil, carmustine, cisplatin, methotrexate, doxorubicin, and paclitaxel. The physical properties of drugs are incorporated in the model to understand the effects under different situations. It is observed that carmustine penetrates deeper into the tissue, followed by paclitaxel, methotrexate, fluorouracil, doxorubicin, while cisplatin penetrates least.