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Mathematical Model of Doxorubicin Transport within Solid Tumours

The efficacy of treating tumours with chemotherapeutic agents, such as doxorubicin, is dependent on how much drug reaches the regions most distant from drug supply in sufficient concentrations. Primerau et al. [1] show that the concentration of doxorubicin decreases exponentially with the distance from the nearest blood vessel. It is therefore important to understand how drug penetrates through cancerous tissue and how the penetration depends on treatment constraints, such as the pharmacokinetic profile or the dose of the injection.

Evans et al. [2] develop a mathematical model for the drug penetration through a multicellular layer, incorporating the "flip-flop" mechanism as a form of transport to and from cells and a Pgp-pump mechanism, which is thought to be the leading mechanism for the increased drug resistance of cancer cells. Because the model is bespoke to a transwell geometry, it has been successfully validated by experiments and important transport rates have been estimated.

Building on the work of Evans et al. [2], a model is presented for a geometry closer to that encountered *in-vivo*: a cylindrical blood vessel surrounded by multiple layers of cancerous cells. Moreover, the limited amount of membrane proteins that facilitate the transport of the drug is incorporated into the model, leading to Michaelis-Menten transport terms. Using this model, the effect of different pharmacokinetic profiles representing bolus injections, repeated bolus injections of lower concentration and infusions over several hours are assessed for their ability to deliver drug to the outer layers in the most efficacious manner.

References

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