Ultrasound responsive drug delivery systems: coupling wave propagation and drug diffusion

José A. Ferreira
Department of Mathematics, University of Coimbra, Portugal.
ferreira@mat.uc.pt

Daniela Jordão
Department of Mathematics, University of Coimbra, Portugal.
djordao@mat.uc.pt

Luís Pinto
Department of Mathematics, University of Coimbra, Portugal.
luisp@mat.uc.pt

Abstract

Stimuli responsive drug delivery systems (SRDDS) have been the object of intense laboratory and clinical research in different disease scenarios, such as cancer [4]. SRDDS aim to avoid the drawbacks of the traditional drug administration systems and controlled drug delivery systems. In medical applications, the drug is transported to the target tissue, using nanocarriers or by implanting the device directly in contact with the target tissue. In both cases, a stimulus is used to disrupt the drug reservoir, in general composed by a polymeric matrix where the drug is entrapped, and physiological barriers and force or enhance the drug release and its absorption. Promising results have been reported in the literature [1].

A set of complex phenomena are involved in the drug release that occurs in the polymeric matrix and target tissue: solvent absorption, swelling, biodegradation, dissolution, diffusion, active transport and stimulus propagation. We observe that the literature on mathematical modelling of drug release from SRDDS is fragmented and very few models (taking into account few phenomena) have been proposed. To the best of our knowledge, no mathematical models combining significant phenomena for the enhanced drug release were published [2],[3].

In this talk, we are mainly interested in SRDDS based on ultrasound stimulus. The behaviour of ultrasound propagation is described by a general telegraph equation whose coefficients and reaction term are specified in function of the particular application (polymer and target tissue). Ultrasound induces an active drug transport through the polymeric

matrix onto the target tissue. The drug release and drug absorption are then described by convection-diffusion reaction equation that is coupled with the telegraph equation for the stimulus. In this work this system is studied from analytical and numerical point of view.

Keywords: Ultrasound, wave equation, drug concentration, convection-diffusion equation.

References

[1] S. Ahmed, A. Martins, G. Husseini. The Use of Ultrasound to Release Chemotherapeutifc Drugs from Micelles and Liposomes. Journal of Drug Targeting, 23 (1): 1–27, 2015.

[2] L. Lentacker, I. De Cock, R. Deckers, S. De Smedt, C. Moonen. Understanding Ultrasounds Induced Sonoporation: Defintions and Underlying Mechanisms. Advanced Drug Delivery Reviews, 72:49–64, 2014.

[3] A. Pulkkinen, B. Werner, E. Martin, K. Hynynen. Numerical Simulations of Clinical Focused Ultrasound Functional Neurosurgery.Physics in Medicine and Biology, 59 (7):1679–1700, 2014.

[4] A. Wood, M. Sehgal. A Review of Low-Intensity Ultrasound for Cancer Therapy. Ultrasound in Medicine and Biology, 41(4):905–928, 2015.