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Title: A mathematical model of cellular drug binding within in-vitro cell culture systems

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Abstract: Local drug delivery is becoming an increasingly important tool to clinicians, with devices such as drug-eluting stents, transdermal patches and drug-releasing orthopaedic implants all now routinely used in practice. This is currently an area of intense research activity due to the desire to improve current local drug delivery devices and develop new devices with novel applications. However, there is currently an incomplete understanding of drug redistribution in biological tissue following delivery. Depending on the application, once released, the drug may diffuse through bodily fluid, undergo advection due to pressure gradients and bind with specific and/or non-specific binding sites within tissue and/or on cells. Several models of drug binding to tissue have been proposed in the literature but the validation of these models is limited by the difficulty in experimentally determining the many parameters of the models. In particular, drug binding-on and binding-off rates as well as the density of binding sites can be extremely difficult to measure directly. However, by making use of relatively simple in-vitro cell culture systems, experimental measurements can in principle be made of drug bound to cells as a function of time. When compared with a mathematical model of the experiment, it may be possible to not only validate the model, but also to reliably estimate the unknown parameters of the model. These could, in turn, feed into more sophisticated models of the in-vivo system.

In this talk we present a mathematical model of cellular drug binding within in-vitro cell culture systems. The components to which the drug binds could be, for example, non-specific general extracellular matrix binding sites or specific binding sites on the surface of cells. We consider both a linear and a non-linear model of drug binding and discuss the pros and cons of each. An analytical solution is derived for the linear model. It is then shown how the non-linear model results in a Volterra integro-differential equation which we solve numerically and also by way of perturbation techniques. Small and large t solutions are derived and are in excellent agreement with the numerics.