The chemistry in a flow cell.

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Introduction

During the last years, the use of biosensor technology with the purpose of determining the rate constants for reversible reactions between biological macromolecules has known a considerable development. These studies are done in flow cells (for example the BIACORE). It consists in a very thin channel in which there is a Poiseuille flow. The dimensions are (l=2.4mm, w=0.5mm, h=0.005mm). At one of the walls there is the chemical reaction. In the literature, there are different models that permit the numerical computation of the concentrations values when the rate constants are known. We revisit this problem, we propose and solve a model of coupled Ordinary Differential Equation and Partial Differential Equation. This model includes the most dominant parts of the physical and chemical phenomena. We validate an asymptotic result of Edwards (1999) and extend a simple description known as the "equilibrium model" (Myszka *et al* (1998)).

The chemistry in the BIACORE

The chemical first reaction is the reaction of "c" convected by the flow with "d" which is bounded at the wall. The product is "b" at the wall. The equation for the reaction product's formation "b" (K is the ratio of the constant of reverse and direct reaction) is:

$$\frac{\partial \bar{b}}{\partial \tilde{t}} = \bar{c}(1-\bar{b}) - K\bar{b}.$$

Flow chambers are designed to provide an excess of $\bar{c}$. The solution of *b* does not depend of the position and is written B_0:

$$B_0(\tilde{t}) = (1-\exp(-(1+K)\tilde{t})/(1+K).$$

We want to focus on the effect of the flow on this first order solution, so "c" will depend on the position in the flow and "b" on the position at the wall.

The asymptotic non dimensionalized convection-diffusion equation for the free reactant "c" injected in the Poiseuille flow is:

$$\bar{y}(1-\bar{y})\frac{\partial \bar{c}}{\partial \bar{x}} = \frac{1}{Pe}\frac{\partial^2 \bar{c}}{\partial \bar{y}^2},$$

(Pe>>1 is the Péclet number constructed with the mean velocity, h, and the diffusivity coefficient D, see Edwards (1999)). The 2D approximation holds because of the large aspect ratio. The PDE and the ODE are linked through a flux type boundary condition at the wall $\bar{y}$=0:

$$\frac{\partial}{\partial \bar{y}}\bar{c}(\bar{x},0,\tilde{t}) = Da(\bar{c}(1-\bar{b}) - K\bar{b}),$$

with Da the Damkhöler number ($Da=khR_T/D$, k is the direct reaction constant, R_T is the reference value for "d"). This system may be solved in the case of very large Pe, small Da $Pe^{-1/3}$. Edwards showed that the solution for the averaged value of $\bar{b}$, over the reactor length is

$$B(\tilde{t}) = B_0(\tilde{t}) + (DaPe^{-1/3})B_1(\tilde{t}) + \ldots$$

where B_0 has been already defined and B_1 is another explicit function with exponentials in time. The system that we propose is solved numerically for typical values of Da, K and Pe. In the case of small values of $DaPe^{-1/3}$ (lesser than one) the agreement with Edward formula is excellent (see figure).

Furthermore, we revisit the analysis of Myszka *et al* (1998) and conclude that there are not enough points in their computation to describe correctly the entrance effects. We also revisit their so called equilibrium model and show that it must be corrected to obtain the Edward formula. This model is:

$$\frac{\partial B}{\partial \tilde{t}} = (1-B)\frac{KB + \gamma(DaPe^{-1/3})^{-1}}{1-B+\gamma(DaPe^{-1/3})^{-1}} - KB,$$

with the coefficient γ that comes from the choice of the exchange coefficient at the wall: γ=0.870 if we have $(DaPe^{-1/3})<0.5$ and γ=0.807 if $(DaPe^{-1/3})>1$. The main advantage of our formulation is that Da $Pe^{-1/3}$ has not to be small.

Conclusion and perspectives

We have presented a model (Lagrée & Fernolendt (2004)) of the reacting flow in "flow cell", this gives the limit of validity of the previous approaches. Finally, as we will apply the preceding computation to an artery (with some very strong approximations). We will suppose that as the ligand "b" is formed, the shape of the artery will change by the amount of the formed ligand. Examples of simulation of the growth of a stenosis will be presented.

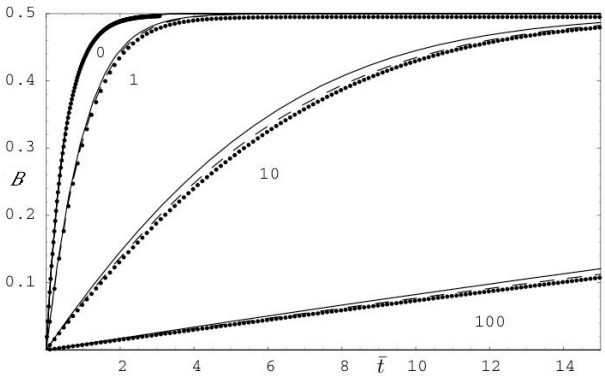

Figure: Response of the formed ligand concentration $\tilde{B}(\tilde{t})$ versus time for K=1, $DaPe^{-1/3}$=0, 1, 10 and 100. Points: the numerical resolution of the coupled PDE and ODE, Dashed /full line: the two integral models.

References:

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Myszka DG, He X, Dembo M, Morton TA, & Goldstein B (1998): *Biophysical Journal* 75:8:583-594.
Lagrée PY & Fernolendt A (2004), *Europ. Jourrnal of Physics, AP*, 26:133 -143.