The chemistry in the BIACORE cell.

Lagrée P-Y, Ivan- Fernolendt A.
L.M.M. UMR CNRS 7607
Université PARIS VI, FRANCE

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: a device named BIACORE is used for that. 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 which permit the numerical computation of the concentrations values when the rate constants are known.

We propose and solve a model of coupled Ordinary Differential Equation and Partial Differential Equation which 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 asymptotic non dimensionalized model for the chemistry consists in the convection-diffusion equation for the free reactant "c" injected in the Poiseuille flow:

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

(Pe>>1 is the Péclet number, see Edwards (1999)). The 2D approximation holds because of the large aspect ratio. The reaction of "c" with "d" which is bounded at the wall gives a product "b". The equation for the reaction product's formation "b" (K is the ratio of the constant of reverse and direct reaction) is:

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

The PDE and the ODE are linked through a flux type boundary condition at the wall $\bar{y}=0$:

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

with Da the Damkhöler number. This system may be solved in the case of very large Pe, small Da $Pe^{-1/3}$ and Edwards showed that the solution for the averaged value of $\bar{b}$, over the reactor length is

$$\tilde{B}(t) = \tilde{B}_0(t) + (Da\ Pe^{-1/3})\tilde{B}_1(t) + \ldots$$

where B_0 and B_1 are 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:

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

with the coefficient γ which comes from the choice of the exchange coefficient at the wall: $\gamma=0.870$ if we have $(DaPe^{-1/3})<0.5$ and $\gamma=0.907$ 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 of the reacting flow in "flow chambers", this as allowed us to find the limit of validity of the previous approaches, comparisons with real measurements in BIACORE chamber are on work. 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.

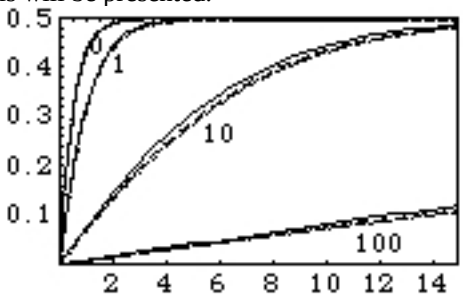

Figure: Response of the formed ligand concentration B(t) versus time for K=1, $DaPe^{-1/3}$=0, 1, 10 and 100. Points: the numerical resolution of the coupled PDE and ODE, Dashed /full line: the two integral models.

References:

Edwards DA (1999): *IMA J. Appl. Math* 63:89 -112,
Myszka DG, He X, Dembo M, Morton TA, Goldstein B (1998): *Biophysical Journal* 75:8:583-594.