ANALYSIS OF A CONVECTION-DIFFUSION-REACTION PROBLEM IN A SURFACE-BASED BIOSENSOR USING THE METHOD OF LINES

Carlos Adriano Moreira da Silva, carlos.silva@itec.ufpa.br
Emanuel Negrão Macêdo, enegrao@ufpa.br
João Nazareno Nonato Quaresma, quaresma@ufpa.br
Process Simulation Laboratory, School of Chemical Engineering, Institute of Technology, LSP/FEQ/ITEC
Universidade Federal do Pará, UFPA, Campus Universitário do Guamá, 66075-110, Belém, PA, Brazil

Abstract. *The Method of Lines (Mol) was used to study the process of mass transport and binding kinetics of biomolecules on a surface, which was monitored through the technology of an optical biosensor by the technique of Surface Plasmon Resonance (SPR). We consider that the receptors are directly immobilized on the sensor surface, i.e., the reaction in the hydrogel phase of the biosensor is neglected and the hydrogel is treated as a planar surface with the receptors. The mathematical modeling of the problem is accomplished along the flow chamber for the laminar flow, in which occurs diffusion both perpendicular and parallel to sensor surface. Furthermore a reversible chemical reaction between analyte and immobilized reactant takes place on the sensor surface. Together with the mass transport equation, a kinetic equation was used in the case of one-site binding where each receptor unit on the surface can accommodate one analyte molecule. The parameter values used for the simulation were chosen from the literature data that lead to transport-influenced binding kinetics, as well as parameter values where such effects are negligible. Therefore, the mathematical model is proposed to describe the mass transport and kinetics process of biomolecular interactions in the optical biosensor. A computer code in programming language FORTRAN 95/90 was developed to solve the model numerically using the subroutine DIVPAG from the IMSL Library. Numerical results for the average concentration of bound analyte and average free analyte concentration at the sensor surface were computed from data previously reported in the literature for typical cases.*

Keywords*: Biosensor, Convection-diffusion-reaction model, Mass transport, Method of Lines, Mathematical modeling.*

1. INTRODUCTION

The study of molecular interactions between proteins, nucleic acids, lipids, carbohydrates, antibody-antigen, and others is important for understanding the molecular recognition, biological functions and provide a chemical basis for all cellular processes (Myszka, 1997 and Sikavitsas *et al.*, 2002). Therefore, for studying these molecular interactions, a new technology of optical sensors based on an optical phenomenon called Surface Plasmon Resonance (SPR) has been widely used, the biosensors. The optical biosensors allow to analyze the binding kinetics of molecules in solution with immobilized molecules on the surface in a quick way easy to operate, efficient and in real-time. Although there are several types of optical biosensors currently available, the instrument BIACORE continues to be the most widely used.

The instrument BIACORE monitors through SPR the changes in the index of refraction caused by mass changes that affects the intrinsic optical properties at the sensor surface by bound macromolecules in the vicinity of a thin gold film. The signal provided by the instrument in Resonance Units (RU) is directly related with analyte bound concentration at sensor surface, providing an indication of the extent of reaction, or more precisely the kinetics of interaction between molecules of analyte and the receptor immobilized.

In BIACORE instrument one of the reactants is immobilized on a sensor chip and this reactant is called receptor. The other reactant, called analyte is injected and flows past into the solution over the chip. When the analyte and the receptor interact to compose the bound analyte-receptor complex, a binding response is generated and it is possible to interpret information about the interaction kinetics (Myszka, 1997). The instrument on detection starts with the formation of analyte-receptor complex to a surface of the biosensor, and the kinetics binding and dissociation can be influenced by the transport of analyte to the surface. If the chemical reaction is slow compared to transport of analyte to the sensor surface, the kinetics binding is unaffected by transport and the system acts as if it were well mixed. If the chemical reaction is fast, due to the high receptor concentration or high values of the constant of association rate, the binding kinetics will be affected or even dominated by transport (Mason *et al.*, 1999). In practical applications is very important to know and distinguish between these mechanisms, it allows to introduce small errors in the estimates of the experimental values (Myszka *et al.*, 1998).

The response generated by the instrument is result of combining the processes of mass transport by diffusion and convection, and the reaction process, requiring a model that reproduces adequately theses processes to estimate the constant of association and dissociation rate (Myszka *et al.*, 1998), other experimental parameters, optimize the experimental conditions, extend the applicability of the technique, understanding the intrinsic phenomena governing the transport of mass and the binding reaction and comprehending the mechanism of interaction between biomolecules.

Constant rates that characterize the kinetics of binding and dissociation between biomolecules carry fundamental information about the biological processes in which these molecules are involved (He *et al.,* 2006).

In this paper, we present a mathematical model involving the mass transport equation with terms of diffusion and convection coupled with a reversible chemical reaction equation that can simulate BIACORE binding experiments, involving binding of monovalent analyte to monovalent receptor. The process of mass transport of the analyte to the sensor surface followed by chemical reaction is developed in laminar flow inside the geometry of the BIACORE cell. We consider only simulation of experiments in which the properties of the hidrogel layer do not influence the binding kinetics, i.e., where the receptors are coupled directly to the sensor surface (illustrated in Fig. 1). Several experimental studies on the kinetics of binding have been performed both with the BIACORE instrument with receptors coupled to hidrogel layers and receptors directly coupled to the sensor surface (Myszka *et al.*, 1996; Karlsson and Fält, 1997; Parsons and Stockley, 1997). These experiments demonstrate that under appropriate experimental conditions (i.e., low concentration of immobilized receptors) the hidrogel layer has no significant effect on the binding kinetics. Therefore, is important to develop analysis on mathematical modeling for these conditions.

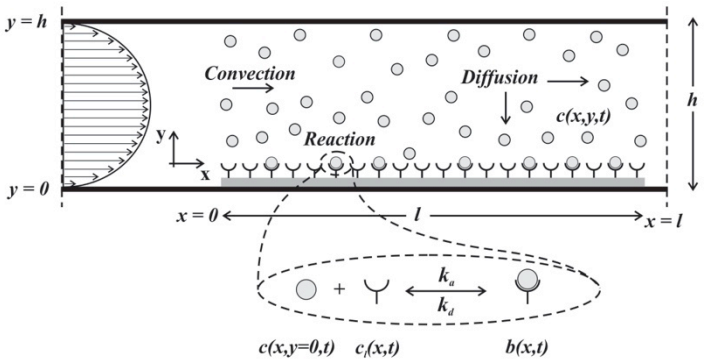


Figure 1. Schematic view of a BIACORE flow cell. In the channel, the transport of analyte occurs by diffusion and convection. At sensor surface the receptors are immobilized where the reaction of association and dissociation occur.

We used the Method of Lines (MOL) proposing a fixed rectangular grid to solve numerically the system of Partial Differential Equations (PDEs) of the proposed model. In the application of MOL, it results in a system of Ordinary Differential Equations (ODEs), which was numerically solved using the subroutine DIVPAG from the IMSL Library (1991) with a computer code developed in the programming language FORTRAN 90/95. Numerical results were generated for the average free analyte concentration and average concentration of bound analyte-receptor complex, showing the association and dissociation phases. The solution methodology used in this work will be compared and validated with parameter values and methodologies developed by other works, using graphical comparisons of the results.

2. MATHEMATICAL MODEL

The quantity more important to analyze in a BIACORE flow cell is the concentration of the analyte bound to the receptor, i.e., the concentration of analyte-receptor complex over time at sensor surface. In modeling this physical problem, it is proposed an analyte transport equation in the flow channel coupled with a reversible binding reaction equation. Figure 1 shows schematically the BIACORE flow channel used in the simulations. The biosensor is composed of two regions, the analyte flow channel and the hydrogel. The transport of the analyte occurs in a channel of rectangular cross section geometry (length l, height h, width w). The free and bound analyte concentrations are denoted by $c(x,y,t)$ and $b(x,t)$, respectively. The analyte is transported by diffusion and convection to the sensor surface. In this study, we consider that the properties of the hydrogel layer do not influence the binding kinetics, i.e., where the binding can be treated as if the receptors are coupled directly to the sensor surface. Fully developed laminar flow along the chamber is considered, essentially over its entire length. The velocity profile is parabolic, subject to the following boundary conditions, $v=0$ at $y=0$ and $y=h$, resulting in $v_x(y)=6v_{ave}\,(y/h)[1-(y/h)]$, where v_{ave} is the average velocity and it is set as $v_{ave}=2v_{max}/3$, and v_{max} is maximum flow velocity or at the center of channel, $(h/2)$. Due to the instrument's flow chamber is 10 times wider than it is high, variations in concentration across width of the channel can be neglected. Therefore the mathematical model is proposed of an analyte of mass transport equation, Eq. (1), involving the diffusion and convection terms, coupled with an equation to describe the interaction bimolecular processes, Eq. (2), subject to the initial and boundary conditions below:

$$\frac{\partial c}{\partial t} = D\left(\frac{\partial^2 c}{\partial x^2} + \frac{\partial^2 c}{\partial y^2}\right) - 6\,v_{ave}\,(y/h)\left(1 - y/h\right)\frac{\partial c}{\partial x};\quad 0 < x < l,\quad 0 < y < h,\quad t > 0$$

$$\frac{\partial b}{\partial t} = k_a\,c\,(x, y = 0, t)(C_T - b) - k_d\,b,\quad 0 \le x \le l;\quad t > 0$$

$$c\left(x, y, t = 0\right) = 0,\quad 0 < x \le l;\quad 0 \le y \le h$$

$$b\left(x, t = 0\right) = 0,\quad 0 \le x \le l;\quad t > 0$$

$$c\left(x = 0, y, t\right) = C_0\,(t),\quad C_0\,(t) = \begin{cases} C_0\,; & 0 \le t \le t_{inj} \\ 0; & t > t_{inj} \end{cases},\quad 0 \le y \le h; \tag{1-8}$$

$$\left.\frac{\partial c}{\partial x}\right|_{x=l} = 0,\quad 0 \le y \le h;\quad t > 0$$

$$D\left.\frac{\partial c}{\partial y}\right|_{y=0} = \frac{\partial b}{\partial t},\quad 0 \le x \le l;\quad t > 0$$

$$\left.\frac{\partial c}{\partial y}\right|_{y=h} = 0,\quad 0 \le x \le l;\quad t > 0$$

Equations (3) to (4) establishes that there are no free analyte in the channel and bound analyte to receptor at *t=0*. Equation (5) establishes that during the binding phase the analyte concentration is constant and equal to the injection concentration, C_0; that occurs during a period of time t_{inj}. In the dissociation phase $C_0=0$. Equation (6) considers the analyte exit as if it were due entirely in convective flow. Although this is an approximation, expect the imposed convective flow to be fast compared to diffusion, and the errors introduced by using Eq. (6) tend to propagate in the direction of flow, outside of the channel computational domain (Mason *et al.*, 1999). Equation (7) establishes that the analyte flux at sensor surface should equal the time of rate of change of the amount bound at the surface, i.e., it is assumed that the binding reaction occurs over the surface region channel at the bottom of the flow channel, where *c(x,y=0,t)* is the free concentration at position x just above the sensor surface. Equation (8) states that the flux vanishes at the top boundary because the channel surface is impenetrable and nonreactive there.

It is useful to write Eqs. (1) to (8) in dimensionless form, therefore, for this purpose, the following dimensionless groups are defined:

$$\begin{aligned} &X = x/l;\ Y = y/h;\ \tau = tD/h^2\ ;\ C = c/C_0\ ;\ B = b/C_T\ ;\ P = 6\,v_{ave}\,h/D \\ &v_x\left(Y\right) = v_x\left(y\right)/v_{av}\ ;\ \varepsilon = h/l;\ Ka = k_a\,C_0\,h^2/D;\ K_d = k_d\,h^2/D;\ \sigma = hC_0/C_T\ ; \end{aligned} \tag{9-19}$$

Then, the mathematical formulation in dimensionless form is written as:

$$\frac{\partial C(X,Y,\tau)}{\partial \tau} = \varepsilon^2\,\frac{\partial^2 C(X,Y,\tau)}{\partial X^2} + \frac{\partial^2 C(X,Y,\tau)}{\partial Y^2} - \varepsilon PY(1-Y)\frac{\partial C(X,Y,\tau)}{\partial X};\quad \begin{cases} 0 < X < 1 \\ 0 < Y < 1 \end{cases},\quad \tau > 0$$

$$\frac{\partial B(X,\tau)}{\partial \tau} = KaC(X, Y = 0, \tau)(1 - B(X,\tau)) - K_d\,B(X,\tau);\quad 0 < X < 1,\ \tau > 0$$

$$C(X, Y, \tau = 0) = 0;\quad 0 < X \le 1,\quad 0 \le Y \le 1$$

$$B(X, \tau = 0) = 0;\quad 0 \le X \le 1$$

$$C(X = 0, Y, \tau) = C_0\,(\tau);\ C_0\,(\tau) = \begin{cases} 1, & 0 \le \tau \le \tau_{inj} \\ 0, & \tau > \tau_{inj} \end{cases};\quad 0 \le Y \le 1 \tag{20-27}$$

$$\left.\frac{\partial C(X,Y,\tau)}{\partial X}\right|_{X=1} = 0;\quad 0 \le Y \le 1,\quad \tau > 0$$

$$\left.\frac{\partial C(X,Y,\tau)}{\partial Y}\right|_{Y=0} = \frac{1}{\sigma}\frac{\partial B(X,\tau)}{\partial \tau};\quad 0 \le X \le 1,\quad \tau > 0$$

$$\left.\frac{\partial C(X,Y,\tau)}{\partial Y}\right|_{Y=1} = 0;\quad 0 \le X \le 1,\quad \tau > 0$$

3. SOLUTION METHODOLOGY

To solve the proposed mathematical model in the dimensionless form, a procedure will be developed based on the Method of Lines (MOL). The MOL is a methodology based on Finite Difference Method (FDM) for solving partial differential equations (PDEs) in heat, mass, and momentum transport rather consolidated in the literature. The FDMs are simple to formulate, can be readily extended to two or three-dimensional problems, and are very easy to learn and apply to the solution of PDEs encountered in the modeling of engineering problems. Despite the simplicity of the finite-difference representation of governing PDEs, it requires considerable experience and knowledge to select appropriate finite-difference scheme for a specific problem in hand (Özisik, 1993).

The main purpose of the MOL is to replace the spatial derivatives through finite-difference formulae Once this is done, the spatial derivatives are no longer expressed explicitly in terms of independent spatial variables. Thus, only the temporal variable remains in the physical problem, resulting in a system of ordinary differential equations (ODEs) dependent on time. The elimination of spatial variations allows for applying any integration algorithm for the system of ODEs of initial value in order to compute an approximate numerical solution.

The axial and transverse variables of the concentration fields were divided in N_{IX} and N_{IY} intervals, respectively, as shown in Fig. 2. Differently of Mason *et al*. (1999), here it will be used a uniform or regular mesh, by making $N_{IX} = N_{IY}$, keeping the *X* grid size equal to the *Y* grid size, i.e., $\Delta X = \Delta Y$. The diffusive terms were discretized by central finite-differences of second order based on three-point formulas and the convective term using first order up-winding based on two-point formulas. This procedure is valid for nodes $1 \le i \le M_X$ and $1 \le i \le M_Y$, where $M_X = N_{IX}-1$ and $M_Y = N_{IY}-1$. For nodes $i=j=0$, $i=N_{IX}$ and $j=N_{IY}$, the boundary conditions were discretized by finite-differences of first order based on three-point formulas. For nodes $i=j=0$ the discretizations were made with forward finite-difference and for the nodes $i=N_{IX}$ and $j=N_{IY}$, the discretizations were made with backward finite-difference.

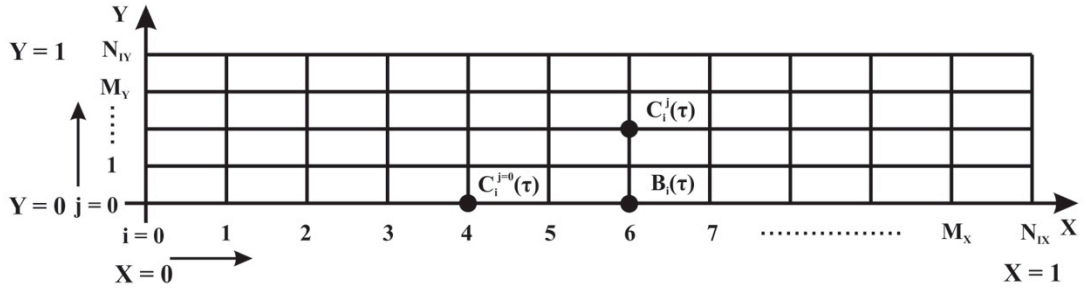


Figure 2. Scheme of discretization of the spatial variables for the fields C(x,y,t) and B(x,t).

Therefore, the system of ODEs, resulting from the MOL procedure, is given by:

$$\frac{dC_i^j}{d\tau} = \varepsilon^2 \delta_{Xi}{}^j + \delta_{Yi}{}^j - \Gamma_{Xi}{}^j; \quad 1 \le i \le M_X; \quad 1 \le j \le M_Y; \quad \frac{dB_i}{d\tau} = f_i(\tau); \quad 0 \le i \le N_{IX}$$

$$C_i^j(\tau = 0) = 0; \quad 0 \le i \le N_{IX}; \quad 0 \le j \le N_{IY}; \quad B_i(\tau = 0) = 0; \quad 0 \le i \le N_{IX}$$

$$C_{i=0}^j(\tau) = C_0(\tau); \quad C_0(\tau) = \begin{cases} 1, & 0 \le \tau \le \tau_{inj} \\ 0, & \tau > \tau_{inj} \end{cases}; \quad 0 \le j \le N_{IY} \tag{28-35}$$

$$C_{i=N_{IX}}^j(\tau) = (4C_{N_{IX}-1}^j(\tau) - C_{N_{IX}-2}^j(\tau))/3; \quad 0 \le j \le N_{IY}$$

$$C_i^{j=0}(\tau) = (4C_i^{j=1}(\tau) - C_i^{j=2}(\tau) + \alpha K_d B_i(\tau))/\gamma; \quad 0 \le i \le N_{IX}$$

$$C_i^{j=N_{IY}}(\tau) = (4C_i^{N_{IY}-1}(\tau) - C_i^{N_{IY}-2}(\tau))/3; \quad 0 \le i \le N_{IX}$$

where, the following terms are defined:

$$\delta_{Xi}{}^j = (C_{i-1}^j(\tau) - 2C_i^j(\tau) + C_{i+1}^j(\tau))/\Delta X^2; \quad 1 \le i \le M_X; \quad \delta_{Yi}{}^j = (C_i^{j-1}(\tau) - 2C_i^j(\tau) + C_i^{j+1}(\tau))/\Delta Y^2; \quad 1 \le i \le M_Y$$

$$\Gamma_{Xi}{}^j = \begin{cases} U_J(C_i^j(\tau) - C_{i-1}^j(\tau))/\Delta X & \therefore U_J > 0 \\ U_J(C_{i+1}^j(\tau) - C_i^j(\tau))/\Delta X & \therefore U_J < 0 \end{cases}; \quad f_i(\tau) = K_a(1 - B_i(\tau))C_i^{j=0}(\tau) - K_d B_i(\tau); \quad 0 \le i \le N_{IX}; \tag{36-42}$$

$$\alpha = 2\Delta Y/\sigma; \quad \gamma = \alpha K_a(1 - B_i(\tau)) + 3; \quad U_J = \varepsilon PY(1 - Y)$$

Equations (28) to (42) form a coupled system of ODEs in the dimensionless time variable to compute the fields $C(X,Y,\tau)$ and $B(X,\tau)$ within of precision required to achieve a convergence of numerical results obtained.

4. RESULTS AND DISCUSSION

A computational code was developed in the FORTRAN 90/95 programming language. The subroutine DIVPAG for initial value problems, with a relative error target of 10^{-8}, was used together with the subroutines DCSINT and DCSITG, all from the IMSL Library (1991), for the solution of the ordinary differential equations system, Eq. (28) to (35), resulting from the application of Method of Lines (MOL) to a regular grid or uniform. Numerical results for the average free analyte and average analyte-receptor complex concentrations are then computed, and compared with those of solution methodologies of works available in the literature.

The convergence behavior of the present solution is illustrated in Tab. (1) with parameters obtained by Myszka *et al*. (1998). A simulation in a BIACORE binding study using the values of parameters previously determined for interleukin-2 (IL-2), flowing past and interacting with its immobilized low-affinity receptor, IL-2Rα, as shown in the table below. As shown in table, the computational algorithm was truncated at various numbers of intervals for the axial and transverse coordinates. The goal of building a table of convergence is to seek a numerical convergence for potential merger and know the limitations of computer code. It is observed that local and averages concentrations show good convergence to the intervals between $N_{IX}=N_{IY}$=80-100, where it was reached with five and six significant digits.

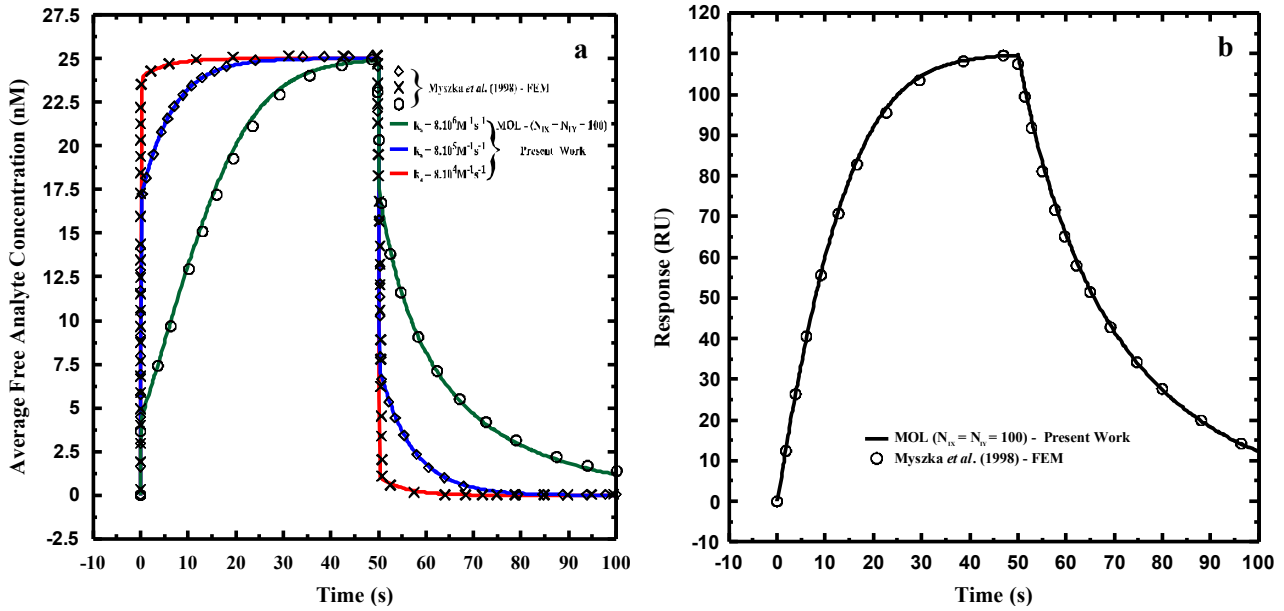
Table 1. Convergence behavior for free analyte concentration in nM and for concentration of bound analyte-receptor complex in RU. In the simulation: $k_a=8.0\text{x}10^6\text{M}^{-1}\text{s}^{-1}$, $k_d=0.2\text{s}^{-1}$, $C_0=25.0$nM, $v_{max}=5.0$cm/s, $D=1.0\text{x}10^{-6}\text{cm}^2/\text{s}$, $C_T=1.25$nMcm, MW IL-2=14,000. A standard flow cell was assumed, with $h=5.0\text{x}10^{-3}$cm, $w=5.0\text{x}10^{-2}$cm e l=0.24cm.

$N_{IX} = N_{IY}$	c (x = 0.2; y = 0)		c (x = 0.4; y = 0)		c_{ave}	
	t = 25s	t = 50s	t = 25s	t = 50s	t = 25s	t = 50s
40	24.063	24.991	22.912	24.961	22.426	24.916
50	23.987	24.990	22.784	24.956	22.314	24.908
60	23.929	24.989	22.700	24.952	22.242	24.902
70	23.887	24.988	22.644	24.949	22.194	24.898
80	23.855	24.987	22.605	24.947	22.161	24.895
90	23.832	24.987	22.577	24.946	22.137	24.893
100	23.815	24.986	22.556	24.944	22.119	24.891
$N_{IX} = N_{IY}$	b (x = 0.2)		b(x = 0.4)		b_{ave}	
	t = 25s	t = 50s	t = 25s	t = 50s	t = 25s	t = 50s
40	106.253	109.961	102.332	109.851	100.842	109.708
50	105.976	109.957	101.917	109.834	100.481	109.682
60	105.774	109.953	101.652	109.821	100.253	109.663
70	105.630	109.950	101.478	109.812	100.102	109.650
80	105.526	109.947	101.357	109.805	99.998	109.641
90	105.448	109.945	101.270	109.800	99.923	109.635
100	105.389	109.944	101.206	109.796	99.867	109.630

Figure 3 provides a comparative analysis between the present MOL results for the average free analyte concentration and average concentration of bound analyte-receptor complex just above the sensor surface, against those obtained by Myszka *et al*. (1998) for a number of intervals $N_{IX}=N_{IY}=100$. Myszka *et al*. (1998) solved numerically the PDEs using a computational code based on the Method of Finite Elements (FEM). A good agreement is observed, for all the conditions analyzed. These averages concentrations, $c_{av(y=0,t)}$ and b_{av} are performed only about the axial coordinate, since as this concentration are evaluated on the lower surface of the biosensor, i.e., at y=0. An integration was performed with respect to the axial coordinate of the potentials $c(x,y=0,t)$ and $b(x,t)$. And as in BIACORE instruments, the SPR detector is centered in the middle of the flow cell, it becomes necessary to obtain the results of the average concentration of the analyte-receptor complex in this region, as shown in Fig. (3b). In Fig. (3a), it is shown that when the association rate decreases, the effects of transport become negligible, i.e., the free analyte concentration becomes constant in time. In these cases of rapid mixing model, i.e., when $c(x,y=0,t)=C_0$, in Eq. (2), becomes a good description of binding kinetics. In Fig. (3a), it is also observed that the free analyte concentration near the sensor surface is not constant during the association phase or zero during the dissociation phase, as it is often assumed. In Fig. (3b), we show the concentration of analyte-receptor complex converted to resonance units (RU).

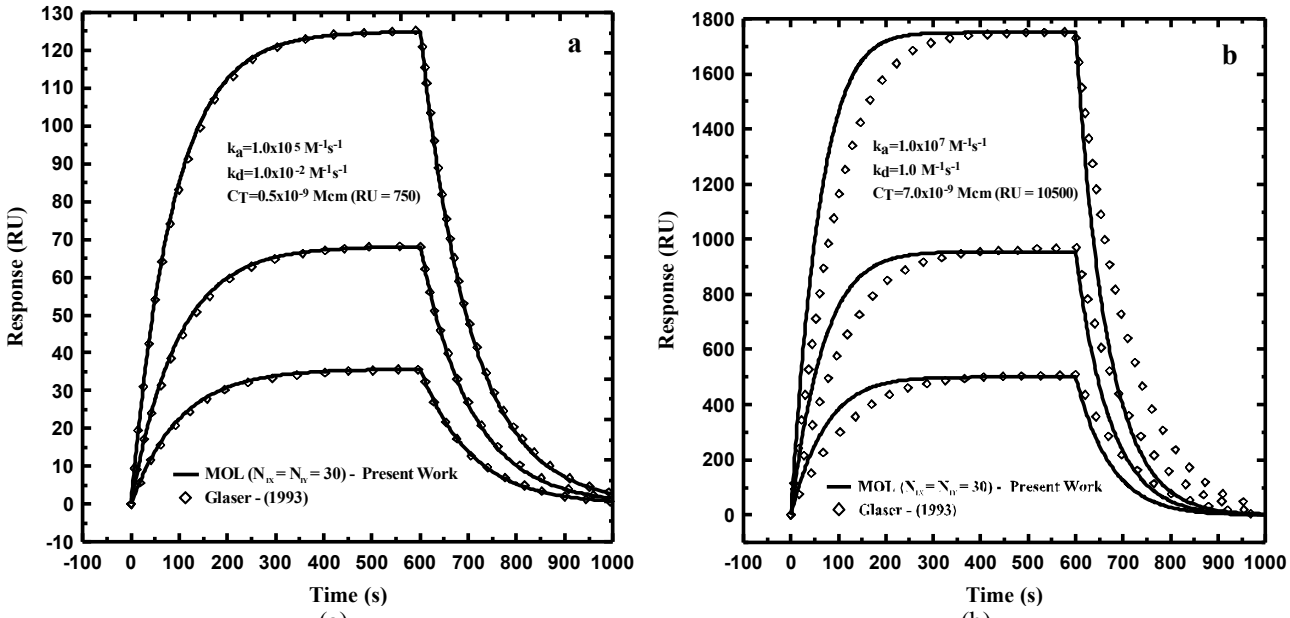
In Fig. 4, it is shown a comparison of the results obtained by this present work against those obtained by Glaser (1993) for the average concentration of analyte-receptor complex converted to resonance units (RU). Glaser (1993) solved the same mathematical model, but neglecting diffusion in the direction of flow of the analyte and used other values of parameters to simulate conditions where there are limitations of the reaction (Fig. 4a), and for conditions where there are mass transport limitations of the analyte to the surface (Fig. 4b). According Sikavitsas *et al.* (2002), the diffusion in the flow direction may be important under certain conditions, which cause rapid depletion of the free analyte due the bond on the surface with the immobilized receptor, i.e., for conditions where there are limitations in

mass transport. For conditions where there are reaction limitations (lower concentrations of immobilized receptors), the model developed by Glaser (1993) and the presented in this paper coincide significantly, as shown in Fig. (4a), and for conditions where there are limitations to mass transport of the analyte (higher concentrations of immobilized receptors), the model developed by Glaser (1993) and that presented in this work do not significantly overlap as shown in Fig. (4b).



(a) (b)

Figure 3. Comparison of the present Method of Lines results (MOL) and those of Myszka *et al*. (1998) for prediction of: (a) the average free analyte and (b) average bound analyte concentration at the sensor surface. C_0=25nM, v_{max}=5.0cm/s, C_T=1.25nMcm, MW IL-2=14000, h=5x10^{-5}cm, l=0.24cm, k_a=8x10^6 M^{-1}s^{-1} and k_d=0.2s^{-1}.

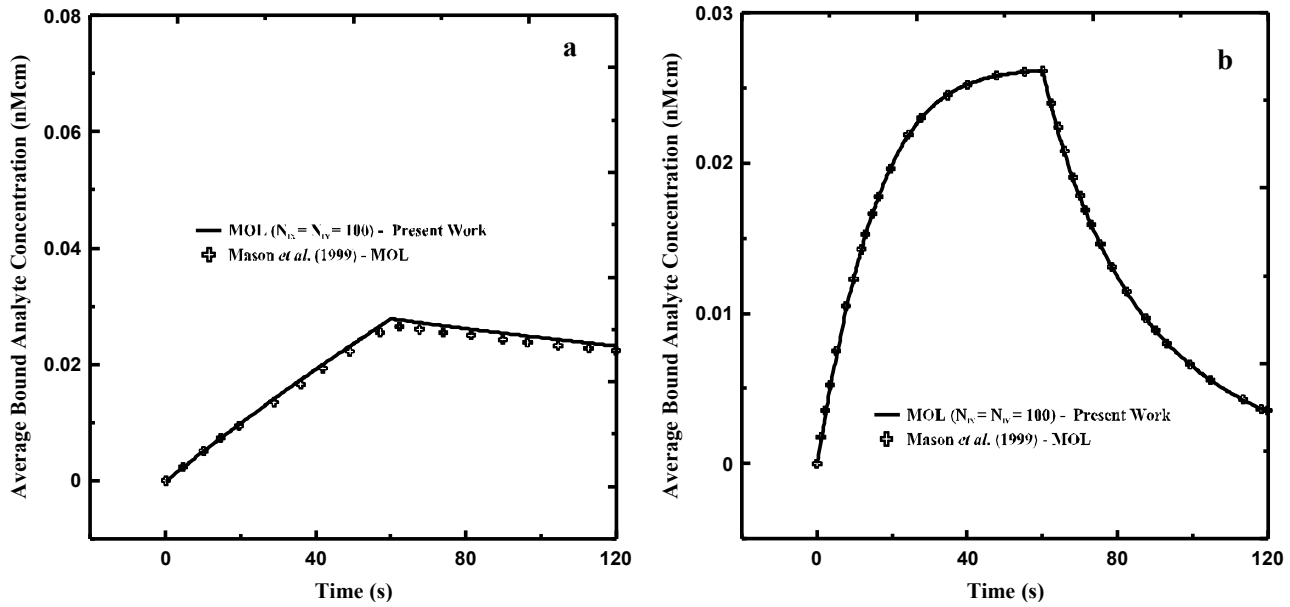


(a) (b)

Figure 4. Comparison of the present Method of Lines results (MOL) against those obtained by Glaser (1993) for prediction of the average bound analyte concentration at the sensor surface. C_0=5, 10, and 20nM, MW=150000, h=5.0x10^{-3}cm, l=0.08cm, v_{ave}=0.3333cm/s.

Figure 5 shows a comparison of the results obtained by this present work against those obtained by Mason et al. (1999) for the average concentration of analyte-receptor complex. As already mentioned, Mason *et al*. (1999) believes that because most of the variation in analyte concentration occurs near the sensor surface (y=0), the domain must be discretized using a non-uniform grid which concentrates the grid points near y=0, and it is necessary to predict the

concentration of the analyte-receptor complex. Therefore, Mason *et al*. (1999) solved the same mathematical model using the MOL proposing a non-uniform grid and other parameters used to simulate conditions where there are limitations in the mass transport. As shown in Fig. (5), there is a good agreement between the results obtained by present work and Mason et al. (1999). Therefore, a small difference is observed when proposing a uniform grid and non-uniform grid, given that the use of a non-uniform grid makes the process of discretization or applying of MOL more complicated than using a uniform grid.



(a) (b)

Figure 5. Comparison of the present Method of Lines results (MOL) against those obtained by Mason *et al*. (1999) for prediction of the average concentration of analyte-receptor complex at the sensor surface. C_0=0.889nM, v_{max}=10.0cm/s, k_a=1.0x10^{8}M^{-1}s^{-1}, k_d=8.0x10^{-2}s^{-1}, h=5.0x10^{-3}cm, l=0.24cm. In (a) C_T=0.167nMcm and D=1.0x10^{-7}cm²/s and (b) C_T=0.05nMcm and D=1.0x10^{-6}cm²/s.

5. CONCLUSIONS

In this work, it was developed a theoretical study of mass transport process and of binding kinetics process of biomolecules on the surface based on a biosensor, which uses the SPR technique to generate a signal on the interaction process. We performed a mathematical modeling based on a convection-diffusion-reaction formulation. Mass conservation and reversible bimolecular chemical reaction equations were solved with the application of Method of Lines (MOL), yielding a system of ordinary differential equations with low-cost computational simulations. A computer code based in FORTRAN 90/95 programming language using the subroutine DIVPAG from IMSL library was developed to numerically solve the system of ODEs. Typical results of present work for the average concentration of bound molecules at sensor surface were presented and compared with those obtained with other solution methodologies and values of parameters reported in the literature. The approach applied in this work was adequate to predict the average free analyte concentration in the flow channel and the average concentration of bound analyte-receptor complex for the conditions analyzed and shown to be in good agreement with results obtained in the literature.

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Conselho Nacional de Desenvolvimento Científico e Tecnológico (CNPq).

7. REFERENCES

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