Available online at www.sciencedirect.com

SciVerse ScienceDirect

Procedia Engineering 47 (2012) 957 – 960

Procedia Engineering

www.elsevier.com/locate/procedia

Proc. Eurosensors XXVI, September 9-12, 2012, Kraków, Poland

Analysis of the Influence of Competitive Adsorption and Mass Transfer on Adsorbed Mass Fluctuations in Affinity-Based Biosensors

M. Frantlović[a,] *, I. Jokić[a], Z. Djurić[b], K. Radulović[a]

[a]*ICTM – Institute of Microelectronic Technologies and Single Crystals, University of Belgrade, Njegoševa 12, Belgrade 11000, Serbia*

[b]*ITN – Institute of Technical Sciences SANU, Serbian Academy of Sciences and Arts, Knez Mihailova 35, Belgrade 11000, Serbia*

Abstract

We analyze the fluctuations of the equilibrium adsorbed mass in affinity-based biosensors, caused by both the random nature of adsorption-desorption and mass transfer processes of two molecular species (the target and the competitor molecules) which bind to the probe molecules. The analytical expression for the fluctuations spectral density is derived. The calculations show the significant influence of both the competitive adsorption and the mass transfer on the fluctuations spectrum. The theory provides a more realistic estimation of limiting performance of biosensors, and is useful for their improvement.

Keywords: Biosensor; competitive adsorption; mass transfer; adsorbed mass fluctuations

1. Introduction

In affinity-based biosensors, selective detection of target molecules in a solution is based on their highly specific binding to probe molecules immobilized on the sensing surface. Biological samples often contain other molecular species which compete with target molecules for the same capturing probes [1]. Fluctuations of the number of adsorbed molecules can be a dominant noise component in affinity-based biosensors and thus a limiting factor for sensor's performance. The fluctuations arising from the random

* Corresponding author. Tel.: +381112638188; fax: +381112182995.
E-mail address: frant@nanosys.ihtm.bg.ac.rs.

doi:10.1016/j.proeng.2012.09.305

nature of adsorption–desorption (AD) process of particles from the surrounding medium on the sensor's surface and also from the particles' mass transfer process are considered in previous works [2, 3]. An analysis of the influence of interference binding on the signal-to-noise ratio in biosensors is performed in [4]. In this paper we derive a simple mathematical model of adsorbed mass fluctuations in equilibrium, considering effects of both the AD and the mass transfer processes of the target and of the competitor molecules. It enables investigation of both the separate influences of these processes and their combined effect. The model is applicable for biosensors in which the spatial distribution of adsorbates concentrations in the reaction chamber can be approximated using the two-compartment model (typically in surface plasmon resonance (SPR) sensors, and also in other flow-through devices, such as quartz crystal microbalance (QCM) sensors and thin film bulk acoustic resonator (FBAR) sensors) [3, 5].

2. Theory

In the surface based biosensing techniques analyzed in this work, a sensing element, whose surface is functionalized for selective binding of target molecules, is located in a reaction chamber, where laminar flow of the sample solution exists. In the ideal case, only the target molecules bind to the capturing probes. However, in real situations other molecular species from a sample solution can bind to the same capturing probes [1], thus affecting the biosensor's response. We consider the case of binding of two different species of molecules (target and competitor molecules) to the same probes. In the reaction chamber the following processes occur: (1) mass transfer processes, i.e. the transport of target and competitor particles by diffusion and flow to and from the binding sites on the sensing surface, and (2) reversible (AD) reactions taking place on the sensor's surface between the both types of molecules from the solution and immobilized capturing probes. We assume a simple one-to-one reaction model, absence of any reaction between target and competitor molecules, and equivalence of all surface binding sites (whose total number is N_m on the sensing surface of area A).

The analysis starts from the equations describing the time change of the number of adsorbed target (N_T) and competitor molecules (N_C)

$$dN_T / dt = k_{fT} C_{ST}(t)(N_m - N_T - N_C) - k_{rT} N_T \,,\; dN_C / dt = k_{fC} C_{SC}(t)(N_m - N_C - N_C) - k_{rC} N_C \,. \quad (1)$$

Here k_f and k_r are the association and dissociation rate constants, respectively, and k_m is the mass transfer coefficient. Indices "T" and "C" refer to the target and competitor molecules, respectively. The adsorbates concentrations in the immediate vicinity of the capturing probes ($C_{ST}(t)=(k_{mT}AC_T+k_{rT}N_T)/(k_{mT}A+k_{fT}(N_m-N_T-N_C))$ and $C_{SC}(t)=(k_{mC}AC_C+k_{rC}N_C)/(k_{mC}A+k_{fC}(N_m-N_T-N_C))$), are determined by using the two-compartment model [3], which is justified in biosensors where the thin layer depleted of adsorbing molecules is formed close to the sensing surface. C_T and C_C are the concentrations of molecules in the solution. Assuming small fluctuations of the number of adsorbed molecules of both species (ΔN_T, ΔN_C) around the corresponding equilibrium values ($N_{Te}=N_m k_{fT} C_T/k_{rT}/D$, $N_{Ce}= N_m k_{fC} C_C/k_{rC}/D$, $D=1+k_{fT} C_T/k_{rT}+k_{fC} C_C/k_{rC}$), linearization of Eqs. (1) is performed, yielding the equations for fluctuations in the Langevin form

$$d\Delta N_T / dt = -\Delta N_T / \tau_{11} - \Delta N_C / \tau_{12} + \xi_1 \,,\; d\Delta N_C / dt = -\Delta N_T / \tau_{21} - \Delta N_C / \tau_{22} + \xi_2 \,. \quad (2)$$

The Langevin source functions, ξ_1 and ξ_2, are mutually statistically independent and their power spectra are white and equal to $\Xi_1^2=4k_{rT}N_{Te}$ and $\Xi_2^2=4k_{rC}N_{Ce}$, respectively. Since the total adsorbed mass is $m_a(t)=M_TN_T(t)+M_CN_C(t)$, where M_T and M_C are the molecular masses of the target and competitor molecules, respectively, the spectral density of the mean squared value of the fluctuations of the adsorbed mass is given by

$$\overline{\Delta m_a^2(\omega)} = M_T^2\overline{\Delta N_T^2(\omega)} + M_C^2\overline{\Delta N_C^2(\omega)} + M_TM_C(\overline{\Delta N_T(j\omega)\Delta N_C(-j\omega)} + \overline{\Delta N_C(j\omega)\Delta N_T(-j\omega)}) \,. \quad (3)$$

From Eqs. (2) and (3) the power spectrum of the adsorbed mass fluctuations is obtained in the form

$$S_{CA,MT}^2(\omega) = \overline{\Delta m_a^2(\omega)} = K\left(1+\omega^2\tau_{III}^2\right)/\left[\left(1+\omega^2\tau_I^2\right)\left(1+\omega^2\tau_{II}^2\right)\right], \quad (4)$$

where K and τ_I-τ_{III} are functions of the association and dissociation rate constants of both adsorbing species, their concentrations, molecular masses and mass transfer coefficients, and the density of capturing probes, $n_m=N_m/A$. The derived model enables the dependence of the adsorbed mass fluctuations spectrum on each of these parameters to be examined.

3. Numerical Calculations

The numerical calculations are performed using the parameter values corresponding to realistic experimental conditions in biosensors: $k_{fT}=8\cdot10^7$ 1/(Ms), $k_{rT}=0.08$ 1/s, $k_{mT}=8\cdot10^{-5}$ m/s, $M_T=5000$ Da, $k_{fC}=8\cdot10^6$ 1/(Ms), $k_{rC}=0.08$ 1/s, $k_{mC}=2\cdot10^{-5}$ m/s, $M_C=30000$ Da, $C_C=1\cdot10^{-9}$ M, $n_m=1\cdot10^{-11}$ Mm (1 M=1000 mol/m^3, 1 Da=1.66·10^{-27} kg). Fig. 1 shows the dependence of the adsorbed mass fluctuations spectrum ($S_{CA,MT}(f)$, $f=\omega/(2\pi)$) on the target molecules concentration, which takes into account competitive adsorption (CA) and the mass transfer processes (MT). At lower concentrations C_T the spectrum has the Lorentzian shape, as in the case of adsorption of only target molecules. At higher C_T two corner frequencies are observed, showing the presence of AD process of additional molecular species. Fig. 2a shows the ratio of the spectrum considering only adsorption and mass transfer of target molecules and the spectrum obtained by neglecting both mass transfer of target molecules and competitive binding effects ($S_{MT}(f)$/S(f)). The ratio $S_{CA,MT}$(f)/S(f) is shown in Fig. 2b. The significant influence of both the mass transfer and the competitive binding on the adsorbed mass fluctuations spectrum can be observed.

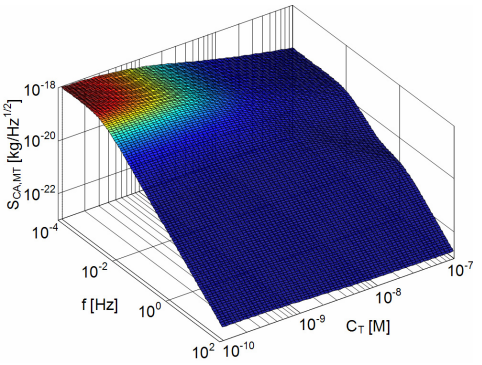
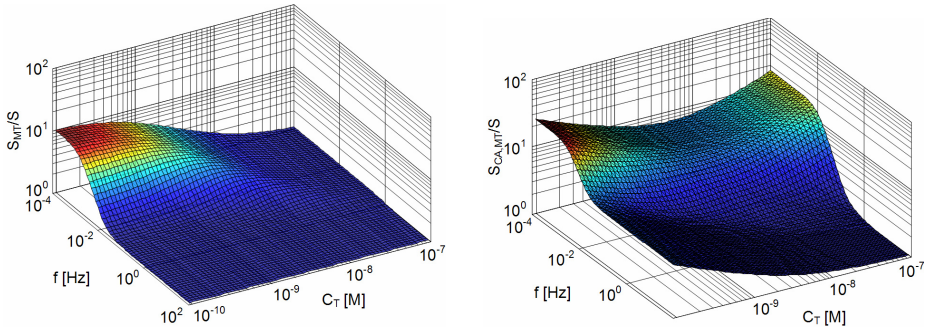


Fig. 1. Dependence of the spectrum of the adsorbed mass fluctuations on both the frequency f and the target molecules concentration C_T. Both the AD and the mass transfer processes of the target and of the competitor molecules are taken into account.



(a) (b)

Fig. 2. The ratio of: (a) the fluctuations spectrum calculated considering only the target molecules mass transfer and the spectrum obtained by neglecting mass transfer and competitive binding effects; (b) the adsorbed mass fluctuations spectrum obtained by taking into account the stochastic AD and mass transfer processes of both adsorbing molecular species and the spectrum obtained when the mass transfer and the competitive binding effects are neglected.

4. Conclusion

The performed analysis shows that both the mass transfer and the competitive binding significantly influence the adsorbed mass fluctuations spectrum in affinity-based biosensors. The presented model of fluctuations enables a more accurate estimation of biosensors limiting performance, which is important for improvement of existing methods for detection of biomolecules. The model is also useful for development of new detection methods and for characterization of bimolecular binding processes, based on frequency domain analysis of fluctuations of biosensor output signal.

Acknowledgements

This work has been partially supported by the Serbian Ministry of Education and Science within the framework of the Project TR32008.

References

[1] Baerga-Ortiz A, Bergqvist S, Mandell JG, Komives EA. Two different proteins that compete for binding to thrombin have opposite kinetic and thermodynamic profiles. *Protein Science* 2004;**13**:166–76.

[2] Djurić Z, Jokić I, Frantlović M, Jakšić O. Fluctuations of the number of particles and mass adsorbed on the sensor surface surrounded by a mixture of an arbitrary number of gases. *Sens Actuators B* 2007;**127**:625–31.

[3] Jokić I, Djurić Z, Frantlović M, Radulović K, Krstajić P, Jokić Z. Fluctuations of the number of adsorbed molecules in biosensors due to stochastic adsorption–desorption processes coupled with mass transfer. *Sens Actuators B* 2012;**166–167**:535–43.

[4] Hassibi A, Vikalo H, Hajimiri A. On noise processes and limits of performance in biosensors. *J Appl Phys* 2007;**102**:014909 1–12.

[5] Squires TM, Messinger RJ, Manalis SR. Making it stick: convection, reaction and diffusion in surface-based biosensors. *Nat Biotechnol* 2008;**26**:417–26.