Affinity sensors in non-equilibrium conditions: highly selective chemosensing by means of low selective chemosensors

Vladimir M. Mirsky

University of Regensburg, Institute of Analytical Chemistry, Chemo- and Biosensors,
D-93040 Regensburg, Germany. E-mail: vladimir.mirsky@chemie.uni-regensburg.de

Abstract: The selectivity of measurements by means of affinity sensors in (quasi)equilibrium conditions and in non-equilibrium conditions was compared. The results show that the measurements in non-equilibrium conditions can reduce or even eliminate a relative contribution of interferents to a sensor signal.

Key words: affinity sensors, kinetics, selectivity

Introduction

Affinity sensors represent one of the largest group of chemical and biological sensors [1 - 6]. Such sensors consist of an immobilized receptor layer (containing, for example, ionophores, antibodies, oligonucleotides or other chemical or biological receptors) and deliver a signal which depends on the adsorbed amount of species on the electrode. A type of this dependence (usually, a proportionality) is determined by the transducer used and by physical or/and chemical properties (mass, dielectrical or optical properties, etc.) of the adsorbed species.

Such sensors are usually used in quasi-equilibrium conditions, where the amount of adsorbed species is completely determined by the binding constant of a receptor. An intensive development of flow-injection analysis [7] during last decade provides a perfect instrumental feasibility to perform measurements under precisely controlled non-equilibrium conditions. As we show in this paper, it can provide a considerable improvement of selectivity of analysis.

Model

Let us consider a simple model of adsorption, where reactions at the interface are limiting stages of the whole process. Adsorption rates for a competitive adsorption of an analyte A and of an interfering specie B onto identical binding sites (according to Langmuir's adsorption isotherm) can be described as following:

$$\frac{d\Theta_A}{dt} = k_{A,a} c_A \left(1 - \Theta_A - \Theta_B\right) - k_{A,d}\Theta_A,$$

$$(1)$$

$$\frac{d\Theta_B}{dt} = k_{B,a} c_B \left(1 - \Theta_A - \Theta_B\right) - k_{B,d}\Theta_B$$

where Θ_A and Θ_B are molar fractional coverages of sensor binding sites by the species A and B. Correspondingly, $k_{A,a}$ and $k_{B,a}$ are the adsorption rate constants for A and B, while $k_{A,d}$ and $k_{B,d}$ are desorption rate constants for A and B and c_A and c_B are bulk concentration of A and B, respectively.

By analogy to a selectivity definition used in chromatography and recommended by IUPAC [8], let us define a selectivity of affinity sensors as a ratio of an amount of reagent and of interferent associated with receptor, i.e. a selectivity of a sensor to a reagent A relative interfering reagent B is

$$S_{A/B} = \frac{\Theta_A}{\Theta_B} \qquad\qquad (2)$$

Another approach to define the selectivity of affinity sensor as a ratio of partial selectivities related to an analyte and to interfering compounds [9, 10] or by using of a linearized analogue of the Nikolski equation [1] would give a value differing from (2) by a constant factor only. This correction is not essential for the comparative analysis presented here.

Measurements under (quasi)equilibrium conditions

A solution of (1) and (2) for equilibrium conditions ($\frac{d\Theta_A}{dt} = \frac{d\Theta_B}{dt} = 0$) results in a sensor selectivity under equilibrium $S_{A/B(equ)}$:

$$S_{A/B\ (equ)} = \frac{\Theta_{A,equ}}{\Theta_{B,equ}} = \frac{c_A\ k_{A,a}\ k_{B,d}}{c_B\ k_{A,d}\ k_{B,a}} \qquad\qquad (3)$$

where $\Theta_{A,equ}$ and $\Theta_{B,equ}$ are molar fractional coverages by the species A and B at equilibrium conditions.

This selectivity value is valid for most of the measurements by means of affinity sensors that are described so far.

Measurements during an adsorption phase

In some cases, especially if adsorption rates are slow and an equilibrium can not be reached during a reasonable time, measurements are performed during the initial phase of adsorption; in such conditions, the effects of a competitive adsorption and the effects of a desorption are negligible, and a solution of (1) and (2) results in a value of selectivity for the initial phase of adsorption $S_{A/B(ads)}$:

$$S_{A/B\,(ads)} = \frac{c_A k_{A,a}}{c_B k_{B,a}} \tag{4}$$

Therefore,

$$\frac{S_{A/B\,(ads)}}{S_{A/B\,(equ)}} = \frac{k_{A,d}}{k_{B,d}} \tag{5}$$

Therefore, a measurement at an initial phase of adsorption kinetics leads to an increase of the selectivity, if a desorption rate for analyte exceeds a desorption rate for interfering species.

Measurements during a desorption phase

Let us consider a selectivity of measurements during desorption of species A and B from the electrode after an equilibrium has been reached. At zero initial bulk concentrations of A and B its desorption kinetics can be described as:

$$\Theta_A = \Theta_{A,equ}\, exp\left(-k_{A,d}t\right)$$

$$\Theta_B = \Theta_{B,equ}\, exp\left(-k_{B,d}t\right) \tag{6}$$

Therefore, the selectivity of measurement after a desorption time t_d can be calculated from (2) and (6) with substitution $\Theta_{A,equ}/\Theta_B$ from (3):

$$S_{A/B(des)} = \frac{c_A k_{A,a} k_{B,d}}{c_B k_{B,a} k_{A,d}} \quad \left[\left(k_{B,d} - k_{A,d}\right) t_d\right] \tag{7}$$

The increase of the selectivity of measurement is described as

$$\frac{S_{A/B(des)}}{S_{A/B(equ)}} = exp\left[\left(k_{B,d} - k_{A,d}\right) t_d\right] \tag{8}$$

If the desorption time t_d corresponds to a desorption of 50 % of the analyte A,

$$\frac{S_{A/B(des)}}{S_{A/B(equ)}} = 2^{\left(\frac{k_{B,d}}{k_{A,d}} - 1\right)} \tag{9}$$

For affinity sensors which have a proportional dependence between their signal and occupation of binding sites, this result means that a desorption of analyte corresponding to only 50% decrease of the sensor signal can lead to an essential increase of selectivity of measurement: the ratio of the desorption rate constants of A and B of 4, 10 or 16 times results in an increase in selectivity over the conventional equilibrium selectivity by a factor of 8, 512 or 32768 respectively.

Results of the numerical calculation of selectivities during several adsorption/desorption cycles are illustrated in Fig 1. If a (quasi)equilibrium adsorption was not achieved during the first adsorption cycle, a maximal selectivity can be increased by using of several adsorption/desorption cycles.
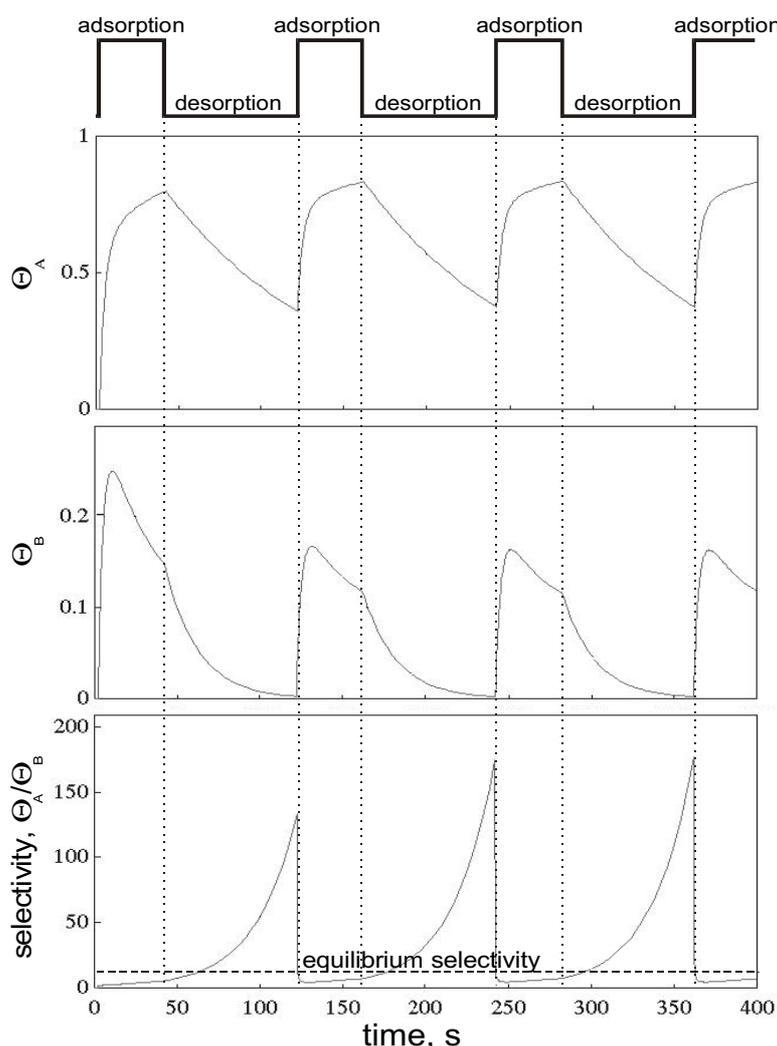
Figure 1. Calculated fractional coverages of receptor layer (Θ_A and Θ_B) and its ratio (Θ_A / Θ_B) for competitive adsorption of species A and B during several adsorption/desorption cycles. Parameters: $c_A k_{A,a} = 0.2$, $c_B k_{B,a} = 0.1$, $k_{A,d} = 0.01$, $k_{B,d} = 0.05$.

Analytical aspects

This article demonstrates that a selectivity of analysis performed by means of affinity chemo- and biosensors depends on the mode of analysis. Measurements under non-equilibrium conditions can

provide a higher selectivity than under equilibrium ones. A choice of optimal measurement conditions depends on desorption rate constants for analyte and interfering species.

If the rate constant of analyte desorption is higher than that of interfering species, an analysis during an initial part of adsorption stage provides some increase of selectivity. This increase is equal to the ratio of the respective rate constants.

If the desorption of an analyte is slower than that of interfering species, one can reach a considerable improvement of selectivity performing an analysis after partial desorption of species bond to a sensor surface. A quantitative value of this selectivity improvement depends on desorption rates and desorption time and is limited only by an acceptable attenuation of a sensor signal due to desorption of analyte. This idea can be applied to any type of affinity chemosensors and biosensors, including biosensors with amplification cascades. Applications in flow-injection immunosensors and gene sensors, in which desorption processes are slow enough to be monitored and controlled quite precisely, seem to be particularly useful.

Acknowledgements

References

1. Wolfbeis, O. S. *Fiber Optic Chemical Sensors and Biosensors*. CRC: Boca Raton, 1991.

2. Janata, J. *Principles of Chemical Sensors*. Plenum Press: New York - London, 1989.

3. Scheller, F.; Schubert, F. *Biosensoren*. Birkhäuser Verlag: Basel, 1989.

4. Hall, E. A. H. *Biosensors*. Open University Press: Cambridge, 1990.

5. Taylor, R. F.; Schultz, J. S. eds. *Handbook of Chemical and Biological Sensors*. Institute of Physics Publishing: Bristol - Philadelphia, 1996.

6. Turner, A. P. F.; Karube, I.; Wilson, G. S. eds. *Biosensors. Fundamentals and Applications*. Oxford University Press: Oxford, 1987.

7. Ruzicka, J.; Hansen, E. H. *Flow Injection Analysis*. John Wiley & Sons: New York, 1988.

8. IUPAC Nomenclature for chromatography.
   http://www.merck.de/english/services/chromatographie/iupac/5_5_02.htm

9. Göpel, W.; Schierbaum, K.-D. *Definition and Typical Examples*. In: Sensors. A comprehensive survey. Vol. 2 Part. I. Ed. by W. Göpel et al. WCH: Weinheim, 1991.

10. Horvai, G. *Sensors and Actuators B* **1997**, 43, 94-98.

Sample Availability: Available from the author.