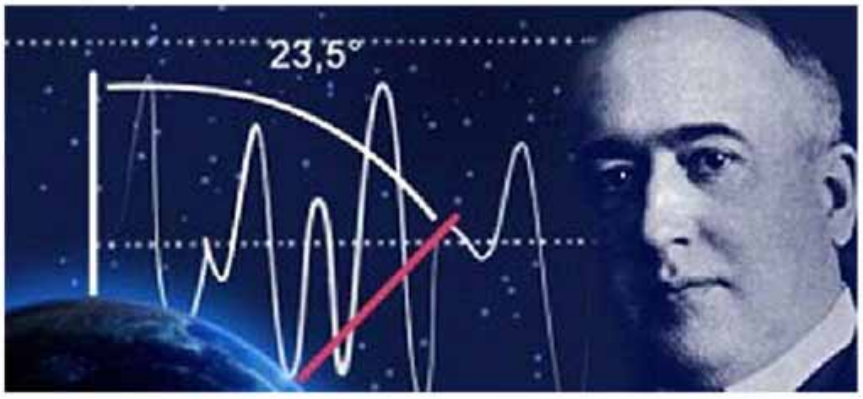
OTEH2018

8th International Scientific Conference on Defensive Technologies



Milutin Milankovic (1879 — 1958)

PROCEEDINGS

ISBN 978-8681123-88-1

Belgrade, 11-12 October 2018
MILITARY TECHNICAL INSTITUTE
Belgrade, Serbia

Publisher
The Military Technical Institute
Ratka Resanovića 1, 11030 Belgrade

Publisher's Representative
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Printed by
The Military Technical Institute
Ratka Resanovića 1, 11030 Belgrade
300 copies

CIP - Каталогизација у публикацији
Народна библиотека Србије, Београд

623.4/.7(082)(0.034.2)
66.017/.018:623(082)(0.034.2)

INTERNATIONAL Scientific Conference on Defensive Technologies (8th ; 2018 ; Beograd)
Proceedings [Elektronski izvor] / 8th International Scientific Conference on Defensive Technologies, OTEH 2018, Belgrade, 11-12 October 2018 ; organized by Military Technical Institute, Belgrade ; [editor Miodrag Lisov]. - Belgrade : The Military Technical Institute, 2018 (Beograd : The Military Technical Institute). - 1 elektronski optički disk (CD-ROM) ; 12 cm

Sistemski zahtevi: Nisu navedeni. - Nasl. sa naslovne strane dokumenta. - Tiraž 300. - Bibliografija uz svaki rad.

ISBN 978-8681123-88-1

1. The Military Technical Institute (Belgrade)
a) Војна техника - Зборници b) Технички материјали - Зборници

COBISS.SR-ID

8th INTERNATIONAL SCIENTIFIC CONFERENCE

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8th INTERNATIONAL SCIENTIFIC CONFERENCE
ON DEFENSIVE TECHNOLOGIES
OTEH 2018
Belgrade, Serbia, 11 – 12 October 2018

MEMS/NEMS SENSORS OF CHEMICAL AND BIOLOGICAL AGENTS: APPLICABILITY OF DIFFERENT MODELS FOR STEADY-STATE ANALYSIS OF SENSOR TIME RESPONSE AND NOISE

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Abstract: *We analyze the time response of MEMS/NEMS sensors of chemical and biological agents and its noise, by using two mathematical models. One of them is commonly used in the literature on MEMS/NEMS adsorption-based chemical and biological sensors, while the other one, which is more elaborate, and takes into account additional relevant physical processes, has been developed by us. We also investigate the limits of applicability of the two models as a function of the target substance concentration, especially having in mind the decrease of the minimal detectable concentration in the new sensor generation.*

Keywords: *chemical sensor, biosensor, time response, adsorption-desorption noise, steady-state analysis.*

1. INTRODUCTION

Detection of chemical or biological agents in the environment is very important in the world today. Chemical and biological sensors based on micro/nano-electromechanical systems (MEMS/NEMS) technologies have a great potential for both civilian and military applications [1].

Adsorption-based sensors constitute a large group of MEMS/NEMS sensors of chemical and biological agents, and they are the subject of this work. In order to achieve the most accurate interpretation of measurement results in the detection of substances present in extremely small amounts, as well as for the optimal sensor performance (regarding the minimal detectable concentration), there is a need for improved mathematical models of time response and noise of such sensors. In order to capture the intrinsic random nature of the sensor response and to enable noise analysis, stochastic response models are needed.

In adsorption-based sensors the basic model of time response considers only the adsorption-desorption (AD) process of target analyte particles as relevant for a generation of useful sensor signal. In the case of a closed sensor chamber, the simplest model assumes that the target substance concentration is high enough to be considered as constant during adsorption, and that the diffusion of target particles towards the adsorption sites on the sensing surface is sufficiently fast for its effects to be neglected [2]. A somewhat more complex model takes into account the depletion of the closed chamber due to the adsorption of the target particles [3], while a more elaborate model also includes diffusion [4]. In the case of a flow-through sensor chamber, stochastic models of sensor response usually neglect the influence of mass transfer (convection and diffusion). In the paper [5] we presented a model of time response of adsorption-based sensors that takes into account the effect of the stochastic AD process coupled with both convection and diffusion in a flow-through chamber. By using this model, the time evolution of the expected value of stochastic response was analyzed [5, 6].

In this paper we analyze the steady-state response and noise of a sensor with a flow-through chamber by using a

stochastic model that takes into account convection and diffusion [5], and the model that neglects them. We first give a short review of two models of response of adsorption-based sensors with a flow-through chamber. Then, we present a steady-state analysis of the expected value of sensor response and of its adsorption-desorption noise, depending on the target substance concentration. We investigate how pronounced is the influence of mass transfer on these statistical parameters of the response at various concentrations. We also examine the limits of applicability of the two models as a function of the target substance concentration, especially having in mind the decrease of the minimal detectable concentration in the new sensor generation.

2. REVIEW OF THE TIME RESPONSE MODELS OF SENSORS WITH FLOW-THROUGH REACTION CHAMBER

The time response of adsorption-based sensors is a function of the number of adsorbed particles of the substance to be detected. We assume a linear relation between the sensor's output signal and the number of adsorbed particles, which is desirable for this kind of sensors. Thus, the analysis of sensor time response and AD noise can be performed in terms of time evolution of the number of adsorbed particles and its fluctuations. Since the expected value describes the random process kinetics, while the variance is a measure of fluctuations (i.e. the noise), a mathematical model is needed for the expected value (<N>) and the variance (v) of the number of adsorbed particles (i.e. the random process $N(t)$). In [5] a detailed derivation of the mathematical model is presented for these two statistical parameters of sensor random response, taking into account the influence of coupled AD process, convection and diffusion on the stochastic change of the number of adsorbed particles. Here we will only mention that the model was obtained by the use of the master equation for gain-loss processes ($N(t)$ is a gain-loss process), in which the transition probabilities (i.e. the probabilities of increase and of decrease of the number of adsorbed particles by one in unit time) encompass the influences of AD and MT processes through the two-compartment model approximation. The equations of the model are

$$\frac{d\langle N\rangle}{dt}=\frac{k_aC(N_m-\langle N\rangle)-k_d\langle N\rangle}{1+(N_m-\langle N\rangle)k_a/(k_mA)} -\frac{k_a}{k_mA}\frac{N_mk_ak_d/(k_mA)+k_aC+k_d}{\left[1+(N_m-\langle N\rangle)k_a/(k_mA)\right]^3}\cdot v \tag{1}$$

$$\frac{dv}{dt}=\frac{k_a(C+2\frac{k_d}{k_mA}\langle N\rangle)(N_m-\langle N\rangle)+k_d\langle N\rangle}{1+\frac{k_a}{k_mA}(N_m-\langle N\rangle)} -\frac{\frac{k_ak_d}{k_mA}N_m+k_aC+k_d}{\left[1+\frac{k_a}{k_mA}(N_m-\langle N\rangle)\right]^3}\left\{2\left[1+\frac{k_a}{k_mA}(N_m-\langle N\rangle)\right]+\frac{k_a}{k_mA}\right\}\cdot v \tag{2}$$

where k_a and k_d are the adsorption and desorption rate constants, C is the concentration of target particles in the analyzed sample, N_m is the number of adsorption sites on the sensing surface, A is the sensing surface area, and k_m is the mass transfer coefficient (according to the two-compartment model [7] of the target substance concentration in a microfluidic sensor chamber, k_m models the combined effect of diffusion and convection on particle transport to the adsorption sites and from them). The system of Eqs. (1) and (2) in the steady-state yields analytical expressions for the expected value and variance of $N(t)$

$$\langle N\rangle_{AD+MT,s}=\frac{N_mk_aC}{k_aC+k_d\left(1+\frac{k_a}{k_mA}\right)} \tag{3}$$

$$v_{AD+MT,s}=k_dk_aCN_m \cdot\frac{\left[k_aC+k_d\left(1+\frac{k_a}{k_mA}\right)\left(1+\frac{k_a}{k_mA}N_m\right)\right]^2}{\left[k_aC+k_d\left(1+\frac{k_a}{k_mA}\right)\right]^3\left[k_aC+k_d\left(1+\frac{k_a}{k_mA}N_m\right)\right]} \tag{4}$$

The other model that we use in this study neglects the mass transfer influence, so it considers the stochastic change of the number of adsorbed particles only as a result of inherently random AD process. The equations of that model for the expected value and variance of $N(t)$ are

$$\frac{d\langle N\rangle}{dt}=k_aC(N_m-\langle N\rangle)-k_d\langle N\rangle \tag{5}$$

$$\frac{dv}{dt}=k_aC(N_m-\langle N\rangle)+k_d\langle N\rangle-2(k_aC+k_d)\cdot v \tag{6}$$

and the solutions in the steady-state are

$$\langle N\rangle_{AD,s}=\frac{k_aCN_m}{k_d+k_aC} \tag{7}$$

$$v_{AD,s}=\frac{k_dk_aCN_m}{(k_d+k_aC)^2} \tag{8}$$

Analysis of the conditions that lead to either matching or significant mismatch of the results obtained according to the two models can yield the criteria for application of the simpler model instead of the more complex model, and it can identify the circumstances that necessitate the use of the more complex model.

By comparing the Eq. (3) with Eq. (7) it can be seen that the second equation can be obtained from the first when

$$\frac{k_a}{k_mA}<<1 \tag{9}$$

Similarly, when

$$\frac{k_an_m}{k_m}<<1 \tag{10}$$

(n_m=N_m/A) the expression on the right side of Eq. (4) equals the one on the right side of Eq. (8). Therefore, in the case of fast mass transfer (sufficiently high value of k_m) the model

we developed matches the model that neglects mass transfer, so it is applicable in a wider parameter range, i.e. at both high and low k_m values. However, the considerations to this point did not reveal the influence of the target substance concentration on the conditions under which the two models match or on the applicability limits of the simpler model. That influence will be investigated in this work, having in mind both the decrease of the minimal detectable concentration and device miniaturization in the new sensor generation.

3. RESULTS OF THE ANALYSIS AND DISCUSSION

In order to analyze the applicability conditions of the model that neglects the mass transfer influence, we compare the results obtained by using that model (Eqs. (7) and (8)) and the model that takes into account mass transfer (Eqs. (3) and (4)).

Figure 1 shows the steady-state expected value of the number of particles (e.g. protein molecules) adsorbed on the surface of biosensor, as a function of target substance concentration, and for different sensing surface areas ($5\cdot10^{-11}$ m^2, $5\cdot10^{-12}$ m^2, $5\cdot10^{-13}$ m^2, $5\cdot10^{-14}$ m^2), according to the two models of sensor response. The parameter values are: $k_a=8\cdot10^7$ 1/(Ms), $k_d=0.04$ 1/s, $k_m=1\cdot10^{-6}$ m/s, $n_m=N_m/A=5\cdot10^{-11}$ mM (1 M = 1 mol/dm^3). The curves that correspond to the model that takes into account mass transfer are shown as solid lines, while dashed lines correspond to the model that neglects mass transfer.

As it can be seen in Figure 1, the difference between the expected values as predicted by the two models is significant only for the smallest sensing area ($5\cdot10^{-14}$ m^2), and it becomes negligible as the concentration increases. The same holds true for the influence of slow mass transfer on the expected value: it is significant only for small sensing areas and low concentrations. This implies that the target substance concentration does influence the applicability of the model that neglects mass transfer, although that is absent from the condition given by Eq. (9). The diagram shows that even when the condition (Eq. (9)) is not fulfilled (the case when $A=5\cdot10^{-14}$ m^2), at concentrations higher than $5\cdot10^{18}$ 1/m^3 the simpler model (given by Eqs. (7) and (8)) is applicable. And really, by observing the ratio $\langle N\rangle_{AD+MT,s}/\langle N\rangle_{AD,s}= 1+k_a/(k_mA)/(1+k_aC/k_d)$, a condition can be defined for obtaining approximately equal expected values (which is the applicability condition for the model that neglects mass transfer) in the form $k_a/(k_mA)/(1+k_aC/k_d)<<1$, that depends on the target substance concentration. It implies that for $k_a/(k_mA)>1$ the simpler model is applicable when

$$C >> \frac{k_d}{k_a}\left(\frac{k_a}{k_m A}-1\right) \qquad (11)$$

For $A=5\cdot10^{-14}$ m^2, the condition given by Eq. (11) yields approximately $C>>5\cdot10^{17}$ 1/m^3, which is in accordance with the conclusion made based on the diagram.

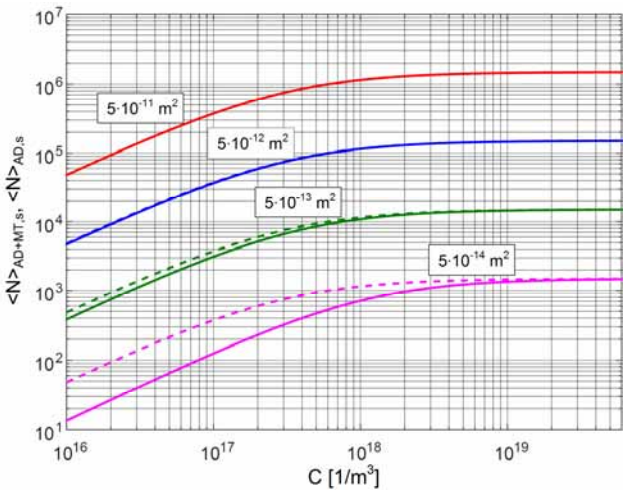

Figure 1. The steady-state expected value of the number of adsorbed particles as a function of the target substance concentration for sensors of different sensing surface areas, according to the model that takes into account mass transfer (solid lines) and according to the model that neglects it (dashed lines)

Figure 2 shows the concentration dependence of the steady-state variance of the number of adsorbed particles, for the same set of parameter values, and the same four sensing areas as for Figure 1. These curves are also obtained by using the two models (solid lines correspond to the model that takes into account mass transfer, and dashed lines to the model that neglects it). It can be seen that there is a significant difference between the results obtained by applying the two models for all the sensing areas, and also that it depends on the concentration.

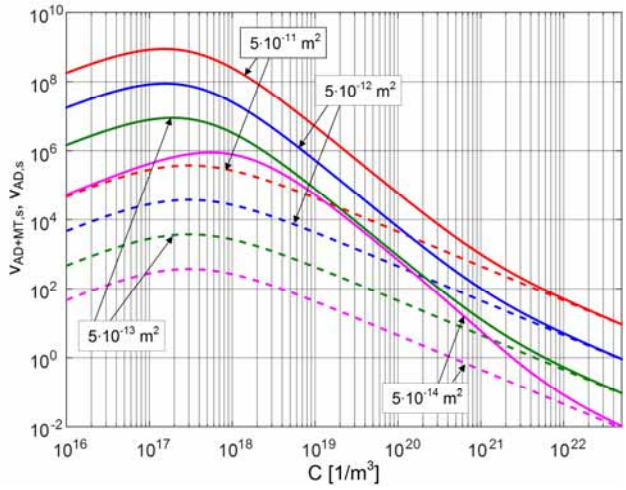

Figure 2. The steady-state variance of the number of adsorbed particles, as a function of concentration (sensing surface area is used as a parameter). Theoretical model that takes into account mass transfer (solid lines) and the model that neglects it (dashed lines) were applied

By determining the ratio of steady-state variances, $v_{AD+MT,s}/v_{AD,s}$, it can be shown that it approximately equals 1 when $[1+N_m+k_aN_m/(k_mA)]k_a/(k_mA)/(1+k_aC/k_d)<<1$. This inequation defines the concentration-dependent condition for validity of the simpler model, i.e. the condition under which the mass transfer influence on the steady-state

variance (and also on the sensor's AD noise) is negligible. It can be expressed in the following form

$$C >> \frac{k_d}{k_a}\left[\frac{k_a}{k_m A}\left(1+N_m+\frac{k_a}{k_m A}N_m\right)-1\right] \approx \frac{k_d}{k_a}\left[\frac{k_a n_m}{k_m}\left(1+\frac{k_a}{k_m A}\right)-1\right] \quad (12)$$

which determines the minimal concentration at which the simpler model becomes applicable, even if $k_a n_m/k_m << 1$ is not valid. This condition for $A=5\cdot10^{-14}$ m^2 is $C>>4.38\cdot10^{21}$ 1/m^3, and for the remaining three analyzed surface areas $C>>1.2\cdot10^{21}$ 1/m^3. It can be noticed that the condition given by Eq. (12) depends on A, contrary to the condition given by Eq. (10).

The conditions given by Eqs. (11) and (12) are less stringent for the applicability of the simpler model than the conditions represented by Eqs. (9) and (10), and they also reveal the influence of both the sensing surface area and the concentration.

4. CONCLUSION

In this work the steady-state analysis of the time response and adsorption-desorption noise of MEMS/NEMS sensors of chemical and biological agents has been presented. Both the mathematical model that takes into account mass transfer and the model that neglects it were used. The difference between the steady-state responses according to the two models was observed only in sensors of extremely small sensing areas, which means that in such sensors mass transfer influences the output signal. It has been shown that the amount of this influence depends on the target substance concentration. The influence of mass transfer on sensor's adsorption-desorption noise is pronounced even when it does not influence the steady-state response, and it is also concentration-dependent. The applicability conditions have been determined for the two mathematical models, as a function of the target substance concentration.

Acknowledgment

This work has been funded by the Serbian Ministry of Education, Science and Technological Development (Project TR 32008) and by the Serbian Academy of Sciences and Arts (Project F-150).

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