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ANALYSIS OF RESPONSE AND ADSORPTION-DESORPTION FLUCTUATIONS SPECTRUM OF MEMS/NEMS CHEMICAL AND BIOLOGICAL SENSORS

IVANA JOKIĆ
IHTM – Institute of Microelectronic Technologies and Single Crystals, University of Belgrade, 11000 Belgrade, Serbia, ijokic@nanosys.ihtm.bg.ac.rs

ZORAN DJURIĆ
IHTM – Institute of Microelectronic Technologies and Single Crystals, University of Belgrade, 11000 Belgrade, Serbia, zdjuric@nanosys.ihtm.bg.ac.rs

KATARINA RADULOVIĆ
IHTM – Institute of Microelectronic Technologies and Single Crystals, University of Belgrade, 11000 Belgrade, Serbia, kacar@nanosys.ihtm.bg.ac.rs

MILOŠ FRANTLOVIĆ
IHTM – Institute of Microelectronic Technologies and Single Crystals, University of Belgrade, 11000 Belgrade, Serbia, frant@nanosys.ihtm.bg.ac.rs

PREDRAG KRSTAJIĆ
IHTM – Institute of Microelectronic Technologies and Single Crystals, University of Belgrade, 11000 Belgrade, Serbia, pkrstajic@nanosys.ihtm.bg.ac.rs

Abstract: *There is a great interest for chemical and biological sensors intended for environmental monitoring and defense. Micro/nanoelectromechanical (MEMS/NEMS) sensors, whose principle of operation is based on adsorption-desorption process, are highly sensitive, selective, small and portable. In this paper the theoretical analysis is presented of both the response and the spectrum of adsorption-desorption noise of such sensors intended for detection of substances present in gas or in liquid phase.*

Key words*: adsorption-desorption, MEMS/NEMS, sensors.*

1. INTRODUCTION

Detection and identification of chemical substances and biomolecules present in gas or in liquid phase are of great importance in medicine, environmental protection and defense. Highly sensitive and selective, and at the same time small and portable chemical and biological sensors which enable obtaining information about presence and concentration of specific substances anytime and anywhere, would be helpful in solving various problems in these fields.

When a chemical or biological sensor is realized as a self-contained integrated analytical device, it consists of three basic functional parts: the sensitive element, the transducer and the signal processing electronics. The sensitive element (a certain chemical functional group, atom, molecule or biological specimen used for functionalization of the sensor) recognizes the target analyte and interacts with it, while transducer converts this event into a measurable signal. A large group of sensors exists for detection of certain target substances utilizing the principle of affinity-based binding between analyte particles and the sensitive element. When the sensitive elements are immobilized on the transducer's surface, the term adsorption is usually used for the process of analyte binding. In this paper we will use the terms "recognition probes" or "capturing probes" for sensitive elements which define the adsorption sites on the sensor surface. The described principle of operation is used in very sensitive mechanical sensing devices, such as quartz crystal microbalance and sensors based on MEMS/NEMS cantilever platform, as well as in optical techniques such as those based on surface plasmon resonance (SPR), or fluorescence microscopy and reflection interference spectroscopy [1-3]. An adsorption process is monitored indirectly, by measuring the change of a quantity that is a known function of the coverage of the adsorption sites by adsorbed analyte particles, which

is also a function of time. For example, that can be the deflection or the resonant frequency of a micro/nano-cantilever, or the optical refractive index of an SPR sensor surface. Nowadays, the comparison between the theoretically calculated time dependent number of adsorbed particles and the same dependence obtained experimentally is used for determination of analyte concentration, for development of methods for analyte identification, and also for investigation of the adsorption (and desorption) process kinetics.

Fluctuations of the measured signal, caused by fluctuations of the number of adsorbed analyte particles, have traditionally been regarded as noise – they degrade the sensor resolution. However, fluctuations can also provide information about molecular interaction processes and their kinetics. Attempts have already been made to develop methods for identification of chemicals or biomolecules present in a gaseous environment or in a solution, using the analysis of the spectrum of fluctuations [4].

In this paper the theoretical analysis of both the response and the spectrum of adsorption-desorption (AD) induced fluctuations of MEMS/NEMS chemical and biological sensors will be presented. The emphasis will be on the difference between the analysis performed in the case of detection of substances in liquids and the analysis when the target substance is in the gas phase.

2. THEORY OF ADSORPTION-DESORPTION PROCESS ON SENSOR'S SURFACE

Chemical and biological MEMS and NEMS sensors have attracted considerable attention over the last decade because of their potential as a highly sensitive platform for detection of chemicals and biomolecules. They are capable of real-time sensing in extremely small volumes of samples. The MEMS technology also enables integration of transducers with read-out and signal processing electronic circuits, decreasing the device size, detection time and cost and making the sensor portable. Sensors with MEMS/NEMS cantilevers for detection of various air-borne and water-borne pollutants (Fig. 1), explosives, biological weapons (e.g. anthrax) and other chemical and biological substances are described in the literature [5-7].

In our analysis of MEMS/NEMS sensors response we assume that all the adsorption sites on the transducer's surface are identical, which means that the rate constants of both the processes of association, k_a, and dissociation, k_d, between capturing probes and analyte particles, have an uniform value across the surface. We also assume that only one analyte particle can be adsorbed on one adsorption site and that the analyte particles do not interact with each other. Since the response of these sensors is related to the number of adsorbed particles, N, the starting equation we use for the analysis describes the time dependence of that quantity:

$$\frac{dN(t)}{dt} = k_a C_s(t)\left(N_m - N(t)\right) - k_d N(t) \qquad (1)$$

Here N_m is the number of adsorption sites on the sensor's surface, and C_S is the concentration of analyte particles in the immediate vicinity of the sensor's surface. In a general case, C_S changes during time due to the transport (convection and diffusion) of analyte particles relative to the surface of the sensor and also due to the reaction of association and dissociation taking place on the sensor's surface. In order to solve Eq. (1), it is necessary to know the dependence $C_S(t)$. This requires solving of the partial differential equation:

$$\frac{\partial C(t,x,y,z)}{\partial t} = -div\vec{j}(t,x,y,z) \qquad (2)$$

which, together with boundary conditions [8], defines the spatial distribution of the analyte concentration C at the moment t ($\vec{j}$ is the net flux due to analyte convection and diffusion), and C_S equals C for z=0, where z is the distance from the sensor's surface in the direction perpendicular to the surface. The previous equation can be solved by using a numerical method. However, since we are interested in an analytical solution which we can use in the further analysis, it is necessary to introduce certain approximations.

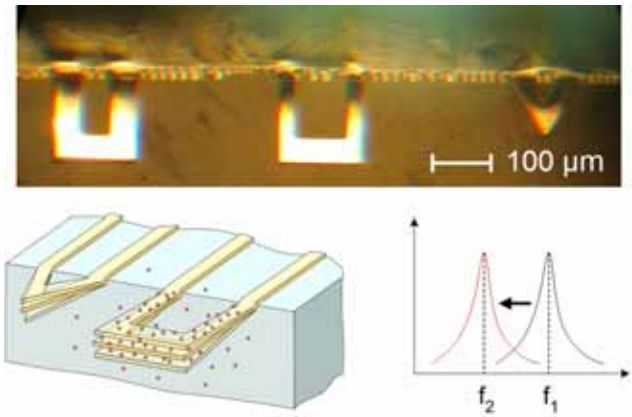

Figure 1: Photography of MEMS cantilevers for detection of mercury vapor, developed and fabricated at IHTM (above). Principle of operation is based on adsorption of mercury from the gas phase, resulting in the change of the oscillating cantilever's mass and consequently its resonant frequency (below).

We will consider two cases corresponding to the real experimental conditions: the first is detection of substances present in the gas phase, and the second is detection in liquids. For each of them an approximation is introduced which significantly simplifies the solving of the set of equations (1) and (2).

When the transport is fast compared to the adsorption process, the analyte concentration in the reacting chamber after injection rapidly becomes uniform in space and constant in time, equal to C_0. Then C_S=C_0 can be replaced in Eq. (1) and the equation can be solved for $N(t)$. In this case the binding process kinetics (i.e. the time needed for binding process on the sensor's surface to reach the equilibrium), which influences the response time of the sensor, is reaction-limited. This case corresponds well to AD processes of particles from the gas phase. In the

second case, typical for AD processes occurring from liquid phase, the transport of analyte particles is slow, thus it influences the sensor's response time and can even dominate the AD process kinetics (the transport-limited case). Then a simplification is done by using the two-compartment model for the analyte concentration dependence on spatial coordinates [8]. The model assumes that $C_S(t)$ is the concentration in the compartment near the surface of the sensor (the inner compartment), and C_0 is the concentration in the remaining part of the sensor's reacting chamber (the outer compartment), which is constant in time and uniform in space. According to the model, the values of all the variables are averaged over the sensor's surface. In that case, Eq. (2) applied to the inner compartment, simplifies to the form which in the quasi-steady state [5] yields:

$$C_S(t) = \frac{C_0 + \frac{k_d N(t)}{k_m A}}{1 + \frac{k_a (N_m - N(t))}{k_m A}} \tag{3}$$

where k_m is the mass transfer coefficient, which characterizes the mass transport between the inner and the outer compartment, and A is the functionalized surface area of the sensor. After substitution of this expression in (1), we obtain the equation which we use for the analysis of adsorption processes in chemical and biological sensors operating in liquids, i.e. their response and response fluctuations.

It is possible now to determine the number of adsorbed particles in equilibrium, N_e, which is established when all transient processes are finished. By using the previously described approximation for both mentioned cases, the following expression is obtained:

$$N_e = \frac{k_a C_o N_m}{k_d + k_a C_o}. \tag{4}$$

The time needed to reach this value is determined by the time constant of the system, τ, which depends on the rates of processes included in the transport of analyte particles and their binding to the capturing probes. However, after reaching the equilibrium state, the number of adsorbed particles still fluctuates due to the stochastic nature of AD and mass transfer processes.

In order to perform the analysis of fluctuation phenomena it is generally possible to divide the fluctuation processes in two categories. The first category includes the processes that are independent of spatial coordinates. This is often the case in spatially homogeneous systems whose total number of constituents fluctuates. As it is shown by A. van der Ziel [9] and in more details by K. M. van Vliet [10], carrier fluctuations in semiconductors, arising from the generation, recombination or trapping of carriers, belong to this class. The resulting noise is called generation-recombination (GR) noise.

Fluctuations in a spatially continuous system, in which both the spatial and time dependences of variables exist, belong to the second category. Here the fluctuation quantities are described by diffusion equations for time intervals larger than the basic collision times. In this case, fluctuations may arise due to both transitions between states and transport.

The phenomenon of fluctuations in the response of chemical and biological sensors generally belongs to the second category. However, the simplifications introduced by using the rapid mixing model and the two-compartment model approximations enable us to treat the stochastic binding process coupled with mass transfer as the phenomenon belonging to the first category. Thus the fluctuations in the number of adsorbed particles in sensors are considered to be analogous to the fluctuations in the number of carriers due to GR processes in semiconductors [11]. Therefore Eq. (1) can be expressed in the form:

$$\frac{dN(t)}{dt} = g\big(N(t)\big) - r\big(N(t)\big) \tag{5}$$

where g and r denote the rates of the processes which increase the number of adsorbed particles (equivalent to generation) and the processes which results in decrease of the adsorbed particles number (equivalent to recombination), respectively. It is obvious that in equilibrium $g(N_e)=r(N_e)$. According to the analogy with GR processes [12], the time constant which determines the rate of the steady state establishment can be obtained from:

$$\frac{1}{\tau} = \left(\frac{\partial g}{\partial N} - \frac{\partial r}{\partial N} \right)\Bigg|_{N=Ne} \tag{6}$$

which, based on both Eq. (1) and the rapid-mixing model approximation ($C_S=C_0$), yields:

$$\tau_g = \frac{1}{k_d + k_a C_o}. \tag{7}$$

When the influence of mass transfer cannot be neglected, using (1) and the two-compartment model approximation (Eq. (3)) yields:

$$\tau_l = \frac{1}{k_d + k_a C_o} + \frac{k_d k_a N_m}{(k_d + k_a C_o)^2 k_m A}. \tag{8}$$

By using the analogy [12] between AD and GR processes, the spectral density of the mean square value of fluctuations of the number of adsorbed particles around equilibrium value has the form:

$$\overline{\Delta N^2(f)} = \frac{4 k_d N_e \tau^2}{1 + 4\pi^2 f^2 \tau^2}, \tag{9}$$

since $g(N_e)=k_d N_e$. In the cases when mass transfer is fast enough that its effect is negligible, the spectrum of fluctuations is obtained by introducing $\tau=\tau_g$ in the Eq. (9), while in the cases when transport influences binding kinetics, $\tau=\tau_l$ should be substituted in (9) in order to obtain the spectrum.

3. RESULTS OF THE ANALYSIS AND DISCUSSION

The analysis of both the response and the spectrum of fluctuations in MEMS/NEMS chemical and biological sensors is performed for the cases when the sensor is used for detection of substances in gaseous environments, as well as when it is intended for detection in liquids. The parameter values used in the analysis are within the range that corresponds to realistic experimental and practical conditions, assuming that the goal is to detect a small concentration of a certain substance.

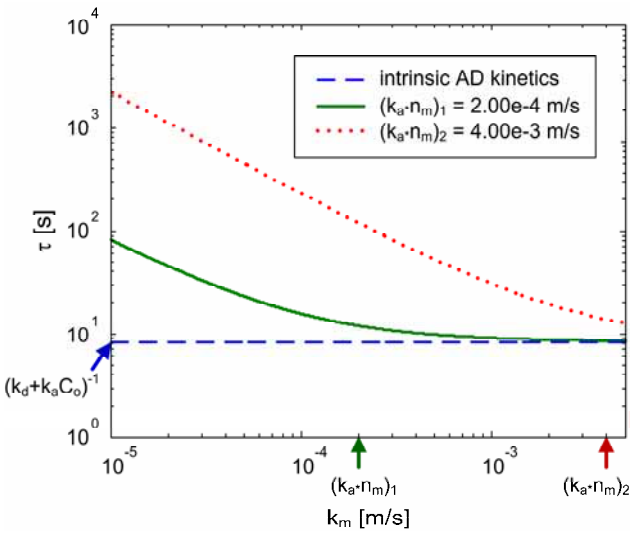

Figure 2: Dependence of the time constant of the system on the mass transfer rate constant for two different values of the adsorption rate ($k_a n_m$).

After injection of gaseous or liquid sample containing the analyte particles in the sensor's chamber, the number of adsorbed particles on the functionalized surface starts to rise approximately exponentially until the steady state is reached. Then the value of the sensor's output signal is recorded as a measure of the analyte concentration in the tested sample. From the presented theory (Eqs. (7) and (8)) it is obvious that the rates of the steady state establishment, i.e. the sensor response speeds, are different for sensors used in a gas and those used in a liquid. The dependence of the time constant of the system on the mass transfer coefficient is shown in Fig. 2. It is obtained for the following values of parameters: k_a=8·10^7 1/(Ms), k_d=0.08 1/s, C_o=5·10^{-10} M, and two different values of the surface density of capturing probes, n_{m1}=N_{m1}/A=2.5·10^{-12} Mm and n_{m2}=N_{m2}/A= 5·10^{-11} Mm (1 M = 1 mol/dm^3). The third line (dotted in the diagram) corresponds to the value of the time constant determined only by intrinsic kinetics of AD process occurring on the sensor's surface (i.e. by rate constants k_a and k_d). However, it can be seen from the diagram shown in Fig. 2 that, when the rate of adsorption ($k_a n_m$) is greater than the mass transfer rate ($k_a n_m$>k_m), which is often the case in liquids, the rate of establishment of the equilibrium value of sensor's response (for the parameters values used in the analysis) can be roughly two orders of magnitude lower than the value determined only by intrinsic kinetics of AD process. As the ratio $k_a n_m/k_m$ increases, the influence of mass transfer increases, i.e. it decelerates the sensor response. By lowering the adsorption sites density (n_m), the sensor's response speed can be increased, but at the same time the sensor's signal (proportional to N_e) would decrease, which must be kept in mind. When the value of k_m is sufficiently high (k_m>$k_a n_m$), as it is the case in gases, it can be assumed that the time constant of the sensor response equals τ_g, i.e. the value of the time constant corresponds to that of the dotted line. Then τ depends only on the intrinsic rates of adsorption and desorption processes. Adsorption of gases can be described by the part of the curves (shown by the solid and the dotted line in Fig. 2) where they approach the dashed line.

It is also known that AD process intrinsic rate constants can be obtained from the sensor's output signal measured during the time interval of steady state establishment [8]. Their values are useful because they can provide additional information about the detected analyte, for example, those necessary for identification of the analyte if several substances have the affinity for binding to the same capturing probes. If the influence of mass transfer really exists, and if it is neglected during determination of k_a and k_d from the measured time response, the obtained values will deviate from the real values. This can lead to misinterpretation of the result, to wrong identification of the analyte and to wrong determination of its concentration.

As it is already stated, fluctuations of the number of adsorbed particles also contain information about reacting molecules, their interaction processes and kinetics of the process. It is necessary to investigate the influence of mass transfer kinetics on the spectrum of fluctuations.

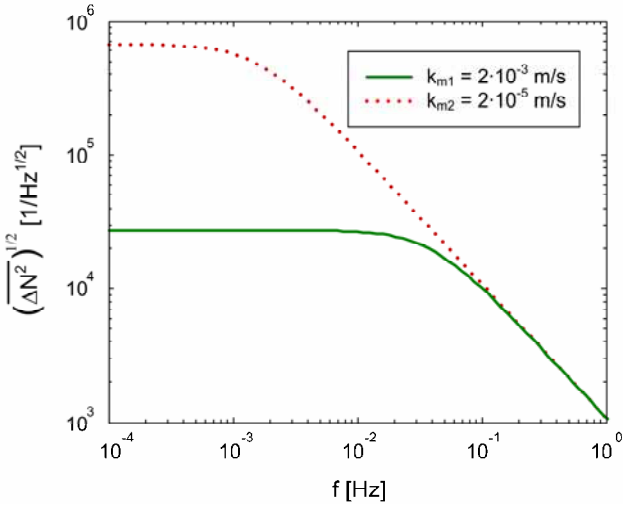

Figure 3: The spectrum of fluctuations of the number of adsorbed particles per unit area for two different values of the mass transfer coefficient.

Fig.3 shows the spectral density of fluctuations of the number of adsorbed particles per unit area for two different values of mass transfer coefficient: k_{m1}=2·10^{-5} m/s and k_{m2}=2·10^{-3} m/s. The parameter values common for both curves are k_a=8·10^7 1/(Ms), k_d=0.08 1/s, C_o=5·10^{-10} M and n_m=1·10^{-11} Mm.

The diagram in Fig. 3 shows that mass transfer process can significantly influence the fluctuations spectrum. Slower mass transfer (lower k_m) results in both the higher fluctuations magnitude and the lower knee frequency of the spectrum curve (which depends on the time constant of the sensor's response). It can be concluded that the fluctuations in sensor's response are a result of the combined effect of the stochastic AD process and the mass transfer process. Therefore, contrary to sensors used for detection in the gas phase, in sensors intended for use in liquids it is necessary to take into account the influence of mass transfer when the analysis of spectrum of fluctuations is performed in order to obtain additional information about the analyte or about the process of binding to capturing probes, as well as for development of methods for detection of substances, based on noise spectroscopy.

4. CONCLUSION

Using the presented theory, the influence of the transfer rate of analyte particles on adsorption sites on a MEMS/NEMS sensor surface on both the response of the sensor and the fluctuations in the number of adsorbed particles is investigated in this paper. It is shown that the mass transfer rate, which is significantly lower in liquids than in gases, influences the kinetics of binding of analyte particles to capturing probes, so it can significantly increase the value of the time constant and thus decrease the speed of sensor's response. The spectrum of fluctuations of the number of adsorbed particles contains information not only about the concentration of the substance to be detected and about the binding process kinetics, but also about the speed of the mass transfer. When the intrinsic adsorption rate is higher than the rate of mass transfer, the spectrum of fluctuations has a higher magnitude and a lower knee frequency than in a case when the influence of mass transfer is negligible. This should be kept in mind when results of measurements in a liquid are analyzed, because not taking into account the influence of mass transfer rate (if it actually exists) can lead to incorrect interpretation of the results. Both the theory and the analysis presented in this paper can be applied in development of noise spectroscopy methods in MEMS/NEMS sensors.

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