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INTRINSIC NOISE EQUIVALENT CONCENTRATION OF DYNAMIC MODE MICROCANTILEVER BIOSENSORS

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Abstract

The presented theory enables systematic investigation of the dependence of the minimal detectable concentration of the target analyte, determined by the cantilever intrinsic noise, on various parameters. Inclusion of the influence of effects such as the mass transfer in noise considerations results in a more accurate noise model, which is necessary when methods based on noise measurements are developed.

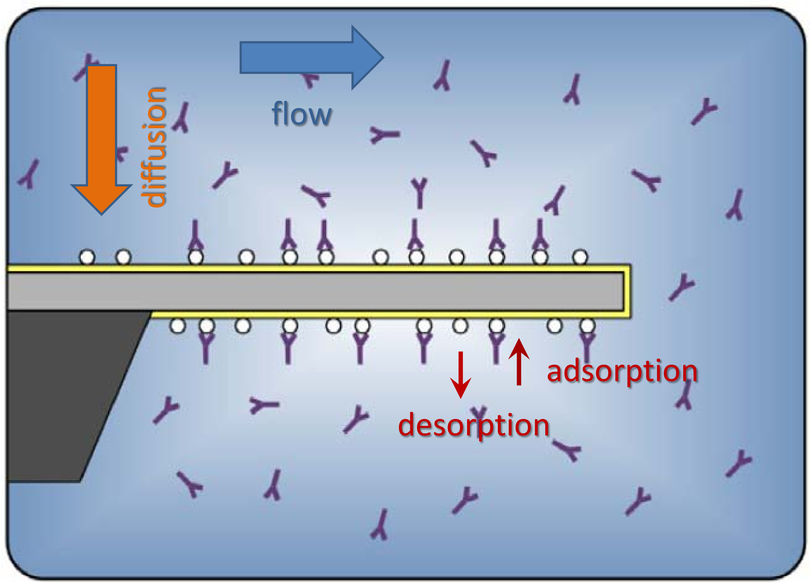

Figure 1 An illustration of a microcantilever sensor for detection of an analyte in liquids. In the measurement chamber the following processes occur: (1) the mass transfer processes, i.e. the transport of analyte particles by diffusion and flow, to and from the adsorption sites on the cantilever's surface, and (2) reversible (adsorption–desorption) reaction taking place on the sensor's surface between analyte particles and immobilized capturing probes used for functionalization.

Symbol	Parameter	Value
c	the target analyte concentration in the bulk	
c_S	the concentration of the target molecules in the immediate vicinity of the receptors	
k_f	the intrinsic adsorption rate constant	8e7 1/Ms
k_r	the intrinsic desorption rate constant	0.08 1/s
k_m	mass transfer coefficient	2e-5 m/s
n_m	the surface density of adsorption sites	5e-12 Mm
n	the surface density of adsorbed particles	
L, w, t, f_0, m_0	Cantilever length, width, thickness, resonant frequency, mass	_, 10μm, 100nm ,_ , _ ,
Q	Q factor	5

Theoretical approach – mass transfer effects

The transport in the bulk of the reactor is described by a convection-diffusion equation:

$$\frac{\partial c}{\partial t}+\nabla\left(-D\nabla c+c\vec{u}\right)=0$$

The reaction at the active surface is given as:

$$\frac{\partial n}{\partial t}=k_a c_s\left(n_m-n\right)-k_d n$$

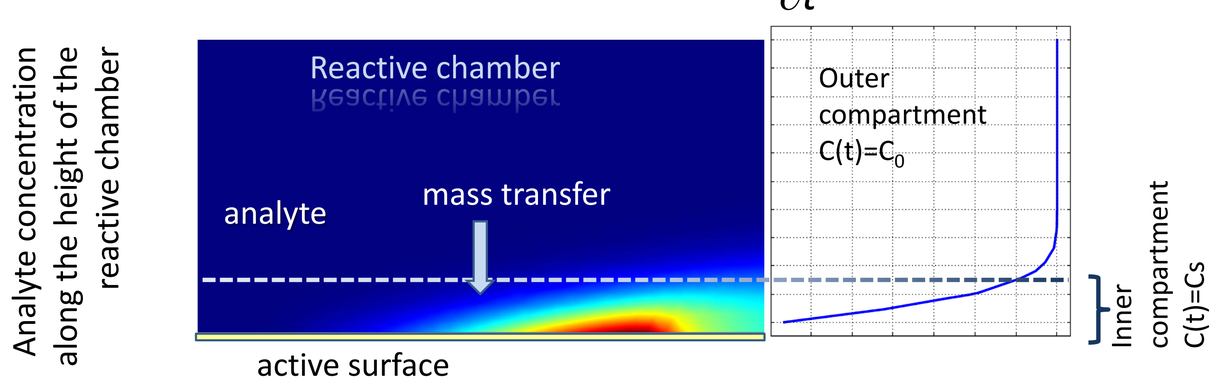

Figure 2 Distribution of the analyte (target) species concentrations in the case of diffusion-limited situations. The complete transport problem with a bimolecular reaction at one surface is simulated by finite element methods implemented in Comsol Multiphysics. In the case when diffusion time scale is much greater than the axial convection time scale, a mass transfer boundary layer in the vicinity of the cantilever active surface appears, such that the two-compartment model of spatial distribution of the analyte concentration in the solution has been used in analysis of kinetics of various molecular binding reactions.

Theoretical approach – Intrinsic noise equivalent concentration

We calculated the cantilever intrinsic frequency noise in the measurement bandwidth *B* by considering *two dominant intrinsic noise mechanisms* in microcantilever biosensors:

- the thermomechanical noise and
- the AD noise

Based on the determined sensitivity and the intrinsic noise of the sensor, the minimal detectable concentration of the target analyte (*Cmin)* in the sample is obtained as the intrinsic noise equivalent concentration:

$$\frac{4k_r\left(k_r+k_fC\right)}{k_fCN_m}\frac{\tau}{\pi}arctg\left(\pi\tau B\right)+\frac{2\left(k_r+k_fC\right)^2}{\left(k_fCN_mf_0\right)^2}\frac{m_0^2}{M_a^2}\frac{D_\varphi^2}{\pi^3}\left(\frac{\pi B}{D_\varphi}-arctg\left(\frac{\pi B}{D_\varphi}\right)\right)=1$$

$$\tau=\left(k_r+k_fC+k_fk_rn_m/k_m\right)/\left(k_r+k_fC\right)^2,\quad D_\varphi=k_BT/\left(2\pi f_0m_0A_0^2Q\right)$$

Numerical results

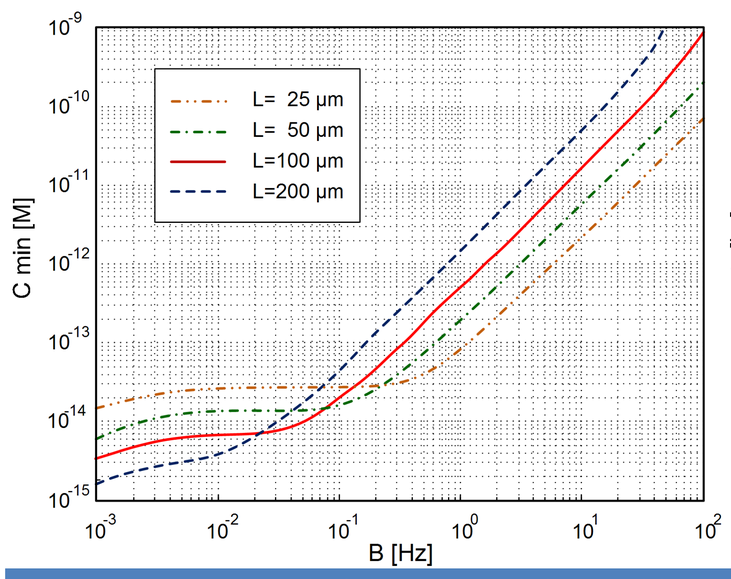

Figure 3 Dependence of the minimal detectable concentration on the measurement bandwidth, for four microcantilevers of different lengths. The parameters are given in Table.

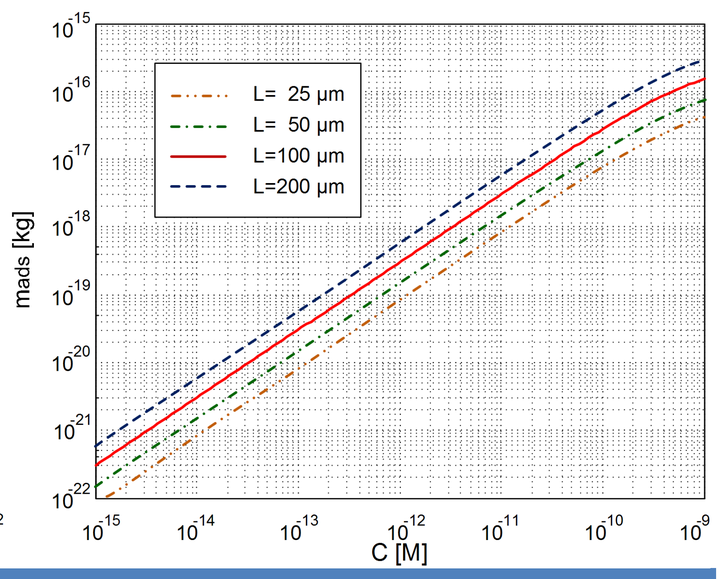

Figure 4 The mass adsorbed on the cantilevers as a function of the target analyte concentration. The values of the parameters are the same as for Fig. 3.

Conclusion

The presented theory enables systematic investigation of the dependence of the minimal detectable concentration of the target analyte, determined by the cantilever intrinsic noise, on various parameters, thus providing the guidelines for improvement of the limits of detection of microcantilever sensors operating in liquids. Inclusion of the influence of effects such as the mass transfer in noise considerations results in a more accurate noise model, which is necessary when a methods based on noise measurements are developed. On the other hand, the minimal detectable signal is a very important parameter for the assessment of measurement uncertainty.

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Acknowledgement

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