MODELLING OF A MICROREACTOR ON HETEROGENEOUS SURFACE AND AN INFLUENCE OF MICROREACTOR GEOMETRY

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Abstract

A model of an action of the amperometric biosensors based on carbon paste electrodes encrusted with single microreactor is analyzed. The model is based on non stationary diffusion equations containing non-linear term related to the enzymatic reaction. The biosensors current, which is a function of the concentration gradient of the reaction product on the electrodes, is used for analyzing of dynamics of the reaction. An influence of a size of microreactor, a geometrical form of microreactor and a position of microreactor on the biosensors action is investigated.

Key words: biosensor, microreactor, diffusion-reaction, modelling

INTRODUCTION

Recently the amperometric biosensors based on carbon paste electrodes encrusted with single microreactor (MR) have been constructed for the determination of glucose and a digital model of the biosensors action has been designed. The model is based on non stationary diffusion equations containing a non-linear term related to the enzymatic reaction. In the simplest case this term is expressed by Michaelis-Menten equation:

$$\frac{du}{dt} = \frac{a\,u}{b+u} \tag{1}$$

where a represents maximal enzymatic rate, b - Michaelis constant and u - substrate concentration.

The task of this research is an investigation of an influence of geometry of microreactor on the biosensors action.

MODEL DEFINITION AND REALIZATION

The biosensors action includes heterogeneous enzymatic process (reaction) and diffusion. The model has been described by a system of non-linear differential equations of reaction-diffusion type. Due to symmetry, the model in spherical coordinates can be expressed in two space dimensions

$$\frac{\partial u}{\partial t} = d\left(\frac{1}{r^2}\frac{\partial}{\partial r}\left(r^2\frac{\partial u}{\partial r}\right) + \frac{1}{r^2\sin(\vartheta)}\frac{\partial}{\partial \vartheta}\left(\sin(\vartheta)\frac{\partial u}{\partial \vartheta}\right)\right) - f(u)\,, \qquad (2)$$

$$\frac{\partial v}{\partial t} = d\left(\frac{1}{r^2}\frac{\partial}{\partial r}\left(r^2\frac{\partial v}{\partial r}\right) + \frac{1}{r^2\sin(\vartheta)}\frac{\partial}{\partial \vartheta}\left(\sin(\vartheta)\frac{\partial v}{\partial \vartheta}\right)\right) + f(u)\,, \qquad (3)$$

$(r,\vartheta) \in \Omega, t > 0\,,$

where u - substrate concentration, v - concentration of the reaction product, t - time,

$$\Omega = \{(r,\vartheta) : 0 \le r \le R, 0 \le \vartheta \le \pi/2\},$$

$$f(u) = \begin{cases} a \cdot u/(b+u)\,, & (r,\vartheta) \in \Omega_0 \\ 0\,, & (r,\vartheta) \in \Omega \setminus \Omega_0, \end{cases}$$

$$\Omega_0 = \{(r,\vartheta) : 0 \le r \le R_0, 0 \le \vartheta \le \pi/2\}.$$

The initial conditions ($t=0$)

$$u\big|_{\Omega_0} = 0,\ u\big|_{\Omega \setminus \Omega_0} = u_0,\ v\big|_{\Omega} = 0\,. \qquad (4)$$

The boundary conditions ($t>0$)

$$\frac{\partial u}{\partial r}\bigg|_{r=0} = \frac{\partial u}{\partial r}\bigg|_{r=R} = \frac{\partial u}{\partial \varphi}\bigg|_{\varphi=0} = \frac{\partial u}{\partial \varphi}\bigg|_{\varphi=\pi/2} = 0,$$

$$v\big|_{\varphi=\pi/2} = 0, \quad \frac{\partial v}{\partial r}\bigg|_{r=0} = \frac{\partial v}{\partial r}\bigg|_{r=R} = \frac{\partial v}{\partial \varphi}\bigg|_{\varphi=0} = 0. \tag{5}$$

Here R_0 represents a size (radius) of MR solid, R - a size (radius) of a buffer solution that was about 100 times larger then radius of MR, a is the maximal enzymatic rate, d - diffusion rate and u_0 - initial substrate concentration.

So the model (2)-(5) represents a reaction which performs in a relatively large capacity. The capacity has been filled by some substrate and a reason of the reaction is a small microreactor was immersed into the capacity and placed on a base of capacity.

The finite difference technique [3] has been used for discretisation of the model (2)-(5). We introduced the non-uniform discrete grid to avoid an overloading of calculations due to the condition $R_0 << R$. An increasing in geometrical progression step of the grid was used in r direction though a constant step was used in φ and t directions.

A system of linear equations of finite difference implicit schemes has been written as a result of appliance of the difference approximation. For decreasing an order of the system of linear equations the variable direction method [3] has been used. Taking action the system of equations was reformulated into an iteration process.

The biosensors current is measured to understand dynamics of reaction-diffusion in real experiment. The biosensors current has been expressed as

$$I = n \cdot F \cdot d \cdot \iint\limits_{\substack{0 \le r \le R, \\ 0 \le \varphi \le 2\pi}} \frac{\partial v}{\partial \varphi}\bigg|_{\varphi=\pi/2} r\, dr\, d\varphi \quad , \tag{6}$$

where $n = 2$ - a number of electrons, $F \approx 9.65 \cdot 10^4$ C/mol - Faraday's constant.
The calculated biosensor current was compared with the experimental data.

The model (2)-(5) has been used in numeric experiments at the following values of the parameters:

$$R = 1\,\text{cm}, R_0 = 0.032\,\text{cm}, d = 6.7 \cdot 10^{-6} \ \text{cm}^2\big/\text{s},$$

$$a = 4.4 \cdot 10^{-5} \ \text{mol}\big/\text{cm}^3\text{s}, b = 8.3 \cdot 1.0^{-5} \ \text{mol}\big/\text{cm}^3, u_0 = 10^{-6}\,\text{mol}\big/\text{cm}^3. \tag{7}$$

The model has been realized in C/C++ programming language, compiled by IBM VisualAge C++ for OS/2 compiler and it was tested in environment of operating system OS/2 Warp. The program runs about 20 min to simulate an reaction during 100 s on a PC based on Intel Pentium 200 MHz with MMX microprocessor.
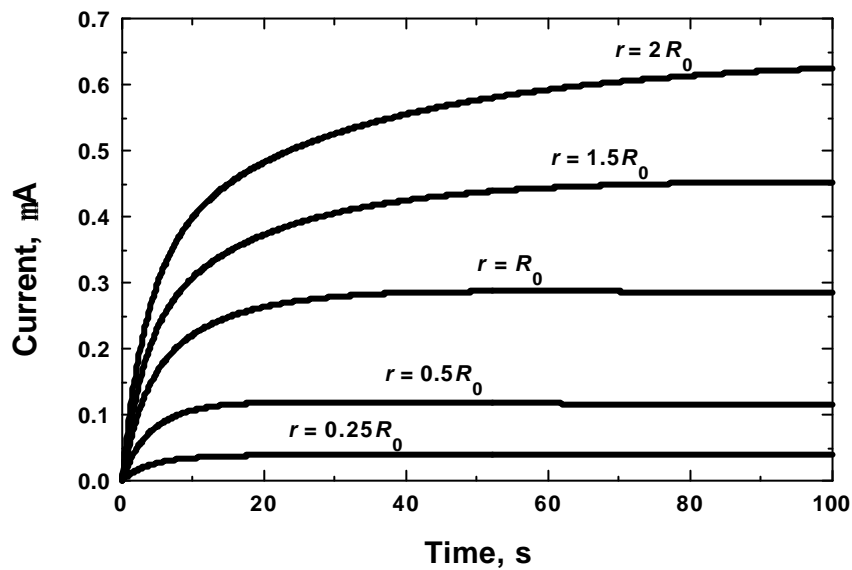
INFLUENCE OF A SIZE OF MICROREACTOR

Fig. 1. Dependence of the current on a size of microreactor solid. The microreactor was modelled as one half of a sphere of radius r, where r is from a set $\{0.25R_0$; $0.5R_0$; R_0; $1.5R_0$; $2.0R_0\}$, R_0 and values of all the other parameters are defined above (7).

A dependence of the MR action on a size of the MR solid was considered. The model has been tested in case when all the geometric data (a radius of the MR R_0 and a radius of a capacity R) are scaled up or down to some value x and respectively the diffusion rate d is multiplied by x^2. In such case due to symbolic model we must get values of the current which are multiplied by x^3 to compare to the former values, i.e. if $I[R_O,R,d](t)$ is a function of an argument t and of parameters R_O, R, d, which defines the current in time t and

$$R_0'' = xR_0', \ R'' = xR', \ d'' = x^2 d'$$

then

$$I\left[R_0'', \, R'', \, d''\right](t) = \, x^3 I\left[R_0', \, R', \, d'\right](t)$$

or

$$I\left[xR_0', \, xR', \, x^2 d'\right](t) = \, x^3 I\left[R_0', \, R', \, d'\right](t).$$

Calculations corroborated it - tested values did not exceed an error of calculations.

Dynamics of the current was considered in a parametrization of a radius of the MR only, i.e. a dependence on a size of microreactor solid was considered when the value of the diffusion rate d and values of all the other parameters were the same as defined above (7). The MR was one half of a sphere as it is defined in the model definition (2)-(5). An evolution of the current for the following values of the radius of MR $\{0.25R_0; \, 0.5R_0; \, R_0; \, 1.5R_0; \, 2.0R_0\}$, where R_0 is the same as above (7), is presented in fig. 1.

As it is possible to notice values of the current (including the maximal current) grows up if a radius of the microreactor grows and this growth is not linear.2

INFLUENCE OF A FORM OF MICROREACTOR

Several geometrical figure of the MR solid have been used instead of one half of a sphere to analyze a dependence of MR action on a form of the MR.

MR has been modelled as a half of a rotation ellipsoid at first. A half of the rotation ellipsoid, which was used in the investigation, can be expressed in the orthogonal coordinates as

$$\frac{x^2}{a^2} + \frac{y^2}{a^2} + \frac{z^2}{c^2} \leq 1, \, z \geq 0, \tag{8}$$

where a and c are semi-axises of the rotation ellipsoid. The current has been calculated at several different semi-axis a and c of a rotation ellipsoid. Volumes of all the rotation ellipsoids were identical to the volume of a sphere of radius R_0 to have the same volume of MR which was used in real experiments and in test calculations. So, volume of the MR was not changed, just a geometrical form has been changed. The following variants were analyzed:

a) a semi-axis c equal to one fourth of a semi-axis a;

b) a semi-axis c equal to one second of a semi-axis a;

c) a semi-axis c equal to a semi-axis a;

d) a semi-axis c equal to double a semi-axis a;

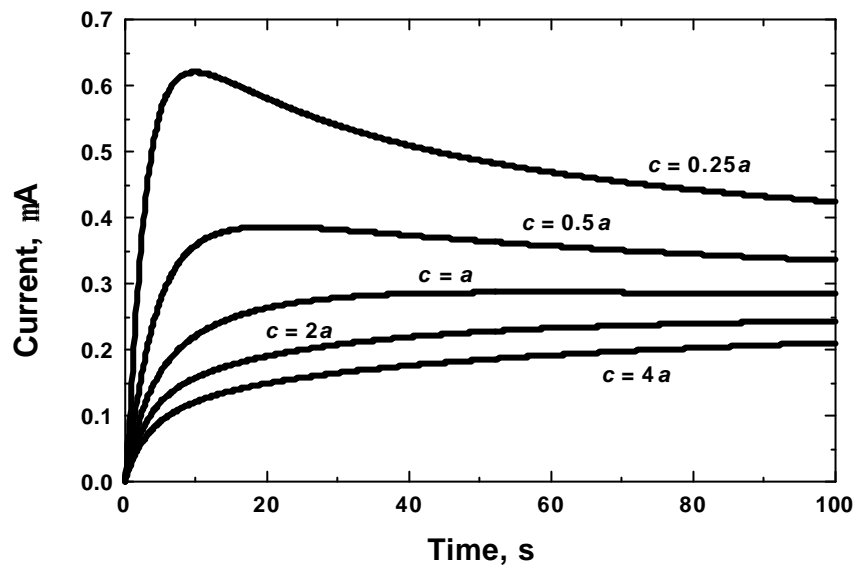e) a semi-axis c equal to four times a semi-axis a.

Fig. 2. Dynamics of the current when microreactor is one half of a rotation ellipsoid. a and c are semi-axises of an rotation ellipsoid in x and z directions respectively (see (8)). The volumes of all the rotation ellipsoids are identical to the volume of a sphere of radius R_o.

A result of calculations at these cases is presented in fig. 2. As it is possible to notice a form of a MR is important enough for the current and it is especially important in the beginning of the reaction. In the beginning of the reaction the current grows faster if an area of a base of the MR solid is greater. Later this importance decreases. A size of an area of a base of MR is important for maximal current and time of the maximal current. The maximal current increases and time of the maximal current decreases if the are of the base of the MR increases even if volume of MR does not change.
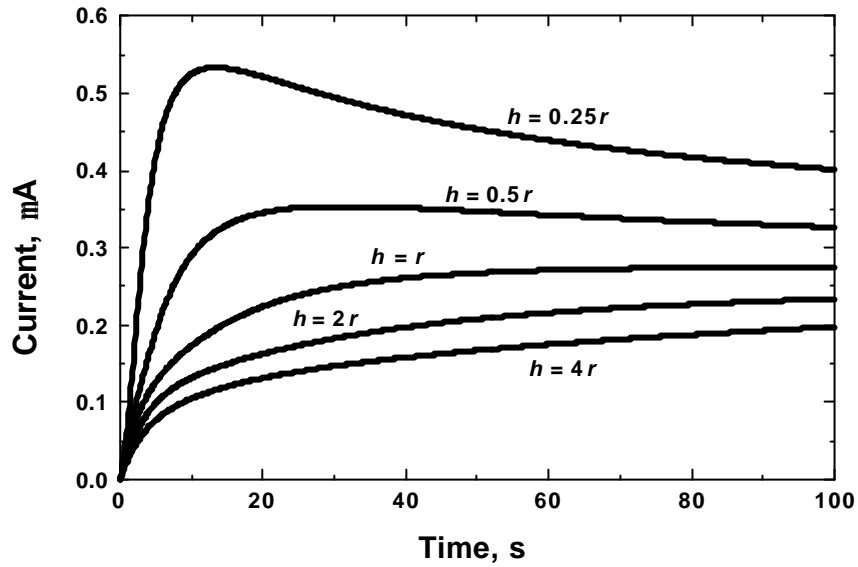
Fig. 3. Dynamics of the current when microreactor is a right round cylinder. r is a radius of a base of a cylinder and h is an altitude of the cylinder. The base of the cylinder is on a plane $z = 0$ and an axis of the cylinder is on Z-axis (in orthogonal coordinates). The volumes of all the cylinders are identical to the volume of one half of a sphere of radius R_o (7).

A right round cylinder was the next geometrical figure used in modelling of MR. Let us assume that r is a radius of a base of a cylinder and h is an altitude of the cylinder. The base of the cylinder is on a plane $z = 0$ and an axis of the cylinder is on Z-axis. Actions of microreactors in form of a cylinder at different radiuses r and altitudes h have been simulated. Volumes of all the right round cylinders were the same as it was in real experiment. The result of calculations is presented in fig. 3.

A microreactor was modelled as a right circular cone as well. Let us assume that r is a radius of a base of a cone and h is an altitude of the cone. The base of the cone is on a plane $z = 0$ and an axis of the cone is on Z-axis. Action of microreactors in a cone form at different radiuses r and altitudes h was simulated. Volumes of microreactors at all the values of r and h were the same as a volume of the real MR. The result of calculations is presented in fig. 4.

A half of torus was used as the next geometrical figure of the MR. Let us assume that r is a radius of a circle which is used in rotation to get the torus and R is a radius of that

rotation about an Z-axis, i.e. R is a distance between the Z-axis and a center of circle which is rotated around the Z-axis. The center of the circle, which is rotated, is
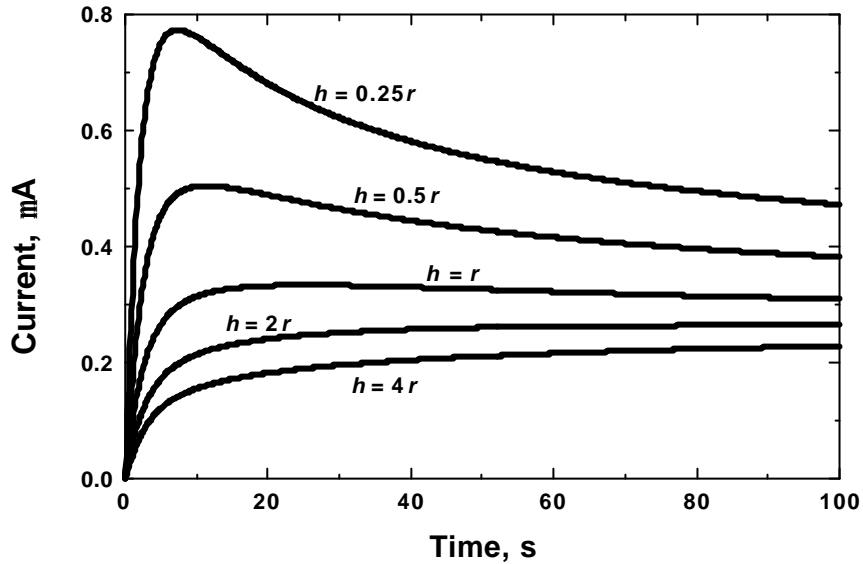

Fig. 4. Dynamics of the current when microreactor is a right circular cone. r is a radius of a base and h is an altitude. A base of the cone is on a plane $z = 0$ (in orthogonal coordinates). The volumes of all the cones are identical to the volume of one half of sphere of radius R_o (7).

on a plane $z = 0$. Toruses at several different values of both radiuses r and R have been used to see a dependence of the current on such geometrical form of MR. Volumes of all the toruses were identical to the volume of a sphere of radius R_o (7). Microreactors in form of one half of a torus defined by condition $z \geq 0$ have been used in calculations. In special case when $R = 0$, a MR is a half of a sphere. Dynamics of the current when MR was modelled as one half of a torus is depicted in fig. 5.

We have ordered all the geometrical figures by three criterions: the maximal current, the current integral at time [0, 100] (s) and time of the maximal current. The sequences of geometrical figures (microreactors) are depicted in table 1. As it is possible to notice the sequences of the geometrical figures ordered by the maximal current and by the current integral are rather similar. The sequence ordered by time of the maximal current is similar to an invert sequence ordered by the maximal current, i.e. in many cases the larger maximal current is reached in shorter time.
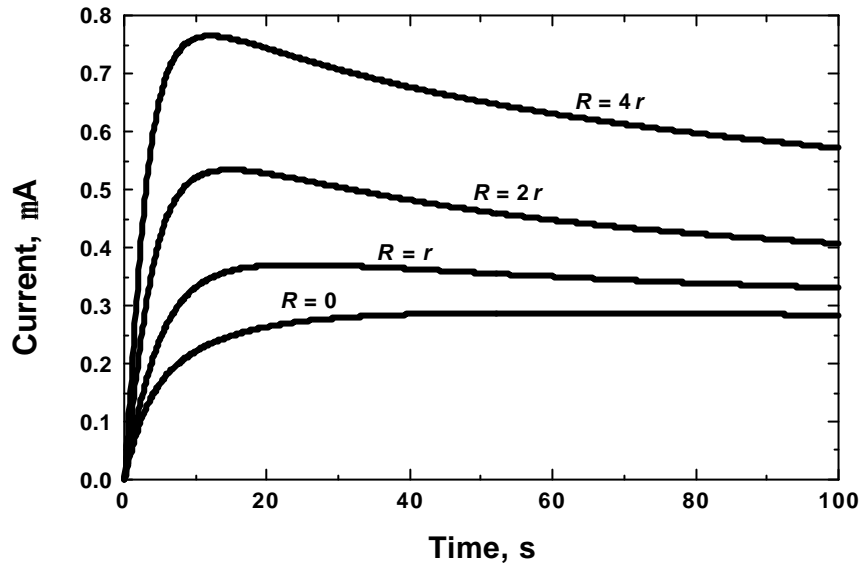
Fig. 5. Dynamics of the current when microreactor is one half of a torus. r is a radius of a circle which is rotated to get the torus and R is a radius of that rotation around an Z-axis (in orthogonal coordinates). The center of the circle which is rotated is on a plane $z = 0$. The volumes of all the toruses are identical to the volume of a sphere of radius R_o (7). (torus.wmf)

Figures ordered by maximal current	Figures ordered by current integral	Figures ordered by time of maximal current
ellipsoid ($c = 2a$)	cylinder ($h = 4r$)	cone ($h = 0.25r$)
cylinder ($h = 2r$)	ellipsoid ($c = 4a$)	ellipsoid ($c = 0.25a$)
ellipsoid ($c = 4a$)	cylinder ($h = 2r$)	cone ($h = 0.5r$)
cone ($h = 4r$)	cone ($h = 4r$)	torus ($R = 4r$)
cylinder ($h = 4r$)	ellipsoid ($c = 2a$)	cylinder ($h = 0.25r$)
cone ($h = 2r$)	cylinder ($h = r$)	torus ($R = 2r$)
cylinder ($h = r$)	cone ($h = 2r$)	ellipsoid ($c = 0.5a$)
ellipsoid ($c = a$)	ellipsoid ($c = a$)	torus ($R = r$)
cone ($h = r$)	cone ($h = r$)	cone ($h = r$)
cylinder ($h = 0.5r$)	cylinder ($h = 0.5r$)	cylinder ($h = 0.5r$)
torus ($R = r$)	torus ($R = r$)	ellipsoid ($c = a$)
ellipsoid ($c = 0.5a$)	ellipsoid ($c = 0.5a$)	cylinder ($h = r$)

cone ($h = 0.5r$)	cone ($h = 0.5r$)	cone ($h = 2r$)
cylinder ($h = 0.25r$)	cylinder ($h = 0.25r$)	ellipsoid ($c = 2a$)
torus ($R = 2r$)	torus ($R = 2r$)	cylinder ($h = 2r$)
ellipsoid ($c = 0.25a$)	ellipsoid ($c = 0.25a$)	cone ($h = 4r$)
torus ($R = 4r$)	cone ($h = 0.25r$)	ellipsoid ($c = 4a$)
cone ($h = 0.25r$)	torus ($R = 4r$)	cylinder($h = 4r$)

Table 1. Sequences of geometrical figures (microreactors) sorted numerically in ascending order by the maximal current, the current integral at up to 100 s and time of maximal current.
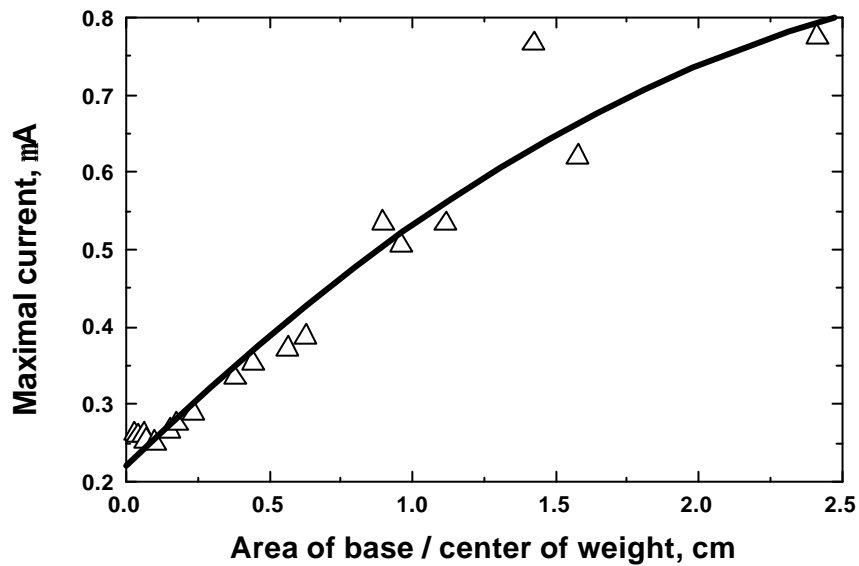

Fig. 6. Dependence of the maximal current on a ratio of a base area to a distance between a center of weight of the microreactor and the base of the microreactor. The open triangles shows values of the maximal current were calculated. The solid line is a polynomial of order two fit to that values of the maximal current.
(rmaxcurr.wmf)

Analysis of dynamics of the current in all the cases of geometry of microreactor grounded an idea that the dynamics of the current depends mainly on an area of a base of a microreactor and a distance between a center of weight of the microreactor and the base of the microreactor. A dependence of the maximal current on a ratio of a base area to a center of weight of the MR is shown in fig. 6 and a dependence of time of the

maximal current on the same ratio is presented in fig. 7. As it is possible to notice the maximal current grows polynomially and time of the maximal current decays
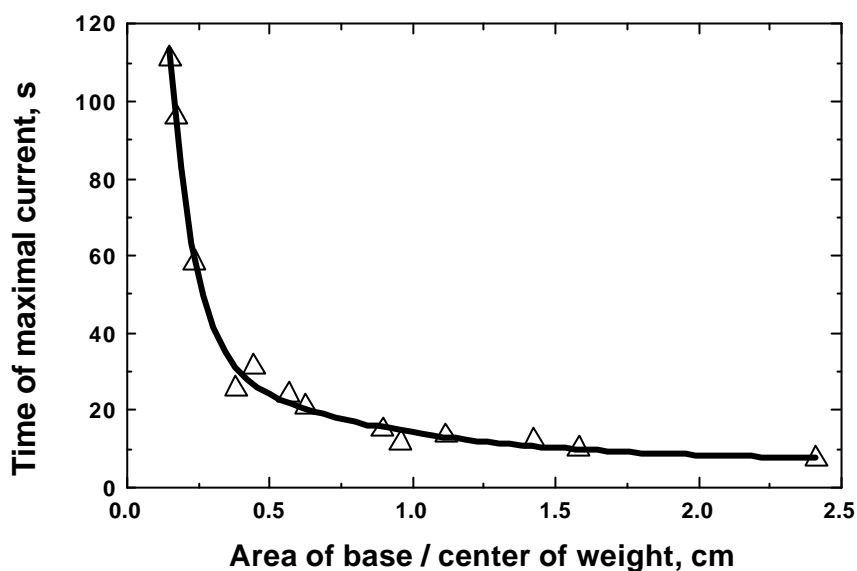

Fig. 7. Dependence of time of the maximal current on a ratio of a base area to a distance between a center of weight of the microreactor and the base of the microreactor. The open triangles shows values of time of the maximal current were calculated. The solid line is an exponential decay with offset fit to that values of the time of the maximal current.

exponentially if the ratio of a base area to a distance between a center of weight of the microreactor and the base of the microreactor increases.

INFLUENCE OF A POSITION OF MICROREACTOR

In all the numeric experiments discussed above and in the real experiments the MR was on a base of the capacity. We investigated the dynamics of the current when MR was lifted up. Because the current arises when some concentration of the reaction product appears on the base of the capacity, the current arises with delay if the MR solid is lifted up. The time of delay depends on a altitude. It was a reason why we simulated the reaction for a longer time than it was in previous numeric experiments. The MR in form of sphere was used for analyzing. A radius of the MR to be lifted up was derived from R_0, where R_0 is defined above (7), to have a volume of the MR the same as it was in test

experiments, when MR was modelled as one half of a sphere. Let us assume that h is a altitude of a MR, more precisely h is a distance between a center
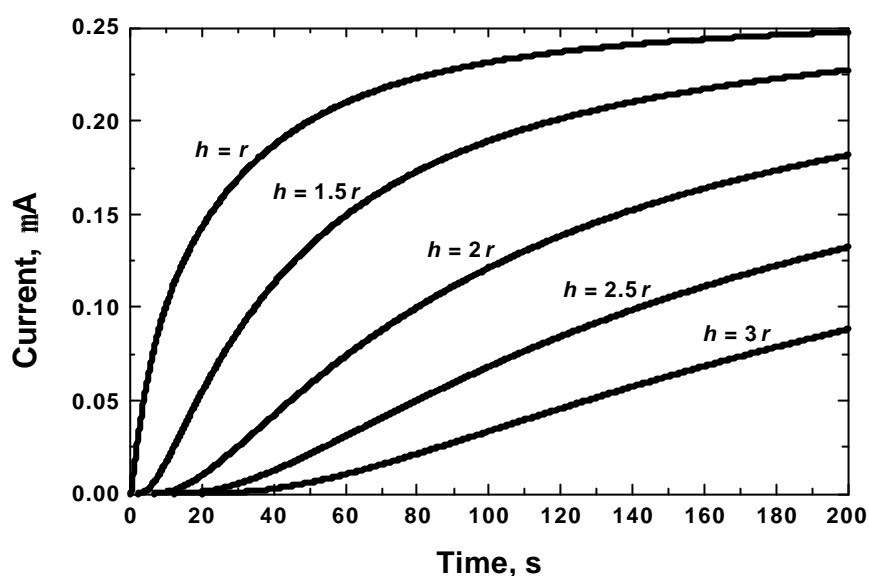

Fig. 8. Dynamics of the current when microreactor is lifted up a base of a capacity. A MR is a sphere of a radius r. A volume of the sphere is equal to a volume of one half of a sphere of radius R_o (7). h is a distance between a center of MR and a base of the capacity.

of MR and a base of the capacity. A result of numeric experiments at several values of the altitude h is shown in fig. 8. As it is possible to notice the altitude of MR is very important for dynamics of the current. The delay increases and the current grows much more slower if altitude increases.

REFERENCES

1. *Handbook of Chemistry and Physics*, 74 th edition (1993-1994), Lide, D.R. (Ed.), CRC Press, Boca Raton, Ann Arbor, London, Tokyo. p. 8-22.

2. N. K. Kotchetkov, A. F. Botchkov, B. A. Dmitriev, A. I. Usov, O. S. Tchizchov, V. N. Schibaev. *Chemistry of carbohydrates*, [in Russian], *Khimia*, Moscow, p. 32, 1967.

3. A. A. Samarskii, *Difference Scheme Theory*, [in Russian], Nauka, Moskow, 1989.

4. M. K. Weibel, H.J. Bright, *The glucose oxidase mechanism, J.Biol.Chem.* 246, p.2734-2744, 1971.