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Catalytic Semipermeable Membrane – Challenge and Possibilities

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Equations describing a multi-phase bioreactor with a catalytic membrane located on the boundary of phases, of which one is a substrate reservoir, are formulated. A model analysis of the process was carried out and the effect of main operating parameters of such a reactor, i.e. the catalytic layer thickness and the coefficients of diffusion mass transport in both phases, was determined.
Two periods with different methods of supplying the catalytic layer can be distinguished in the process. There is also a characteristic thickness of the catalyst layer and when it is exceeded the process duration is no longer shortened although not always full substrate conversion from the supply stream has a place. It is recommended to apply thin layers, because then the catalyst activity is fully used. The analyse of the influence of mass transfer showed that substrate mass transfer in acceptor phase to the catalyst layer has a slight effect on the process rate when the intensification of its transfer in donor phase could have a significance influence on process rate.

K e y w o r d s: biocatalyst layer, catalytic membrane, process modelling, multi-phase reactor

1. Introduction

Due to broad substrate specificity, biocatalysts (first of all enzymes) are more often used for catalyzing the reactions aiming at production of desired compounds or degradation of unfriendly for human life substances [1–4]. Due to high sensitivity to reaction media components, these applications are followed by numerous studies whose goal is to obtain preparations that will retain high catalytic activity for a relatively long time. There are different techniques of catalyst stabilization, among

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them the stabilization of protein molecule, by way of stiffening its structure due to immobilization.

If a biocatalyst is immobilized on the surface or inside membrane pores, the membrane whose main task is the selective separation of the system components, assumes additionally a catalytic character, and the catalytic reaction that takes place in the system can be related directly to the separation of reagents [5].

If the membrane is located on the boundary of two phases, it plays additionally the function of a phase contactor [6]. A particularly interesting case is the use of the membrane for the mass transport of chosen substances from donor to acceptor phase. In such a case, the donor phase can be the substrate reservoir from which it can be supplied in a controlled way to the reaction layer which, due to the biocatalyst properties, belongs usually to the acceptor phase.

Intensification of such processes should be directed towards a maximum use of the catalyst properties, particularly increase of its stability and maximization of substrate concentration in the reaction zone.

This paper is dedicated to the modelling of a process that takes place in a multiphase system (bioreactor) with a biocatalyst layer immobilized on the surface of a membrane that separates both phases. If we think about medicinal applications one from these phases is the body fluid.

2. Balance Equations of a Bioreactor with a Catalytic Membrane

In this case the considered system (Fig. 1), which main element is a membrane with a catalytic layer located on its surface, operates like well known in chemical engineering a column reactor with a concurrent/countercurrent flow of phases on both sides of the membrane. The system can work either in a batch or continuous regime.

Usually, because of a small value of the reacted substrate stream relative to the stream supplied to the column reactor, it is necessary to use circulation because a single flow of the substrate stream through the reactor does not ensure the required reaction degree.

The following reaction is considered:

$$S \xrightarrow{\text{enzyme}} P$$

It was assumed that products being formed had trifling effect on the mentioned reaction (for example no inhibition) and were not characterized by a limited solubility in the acceptor phase, so they did not affect the process. All reactants were transported by diffusion.

Figure 2 illustrates a differential element of the bioreactor with a catalytic membrane. For concurrent plug flow in the bioreactor, which is assumed in this paper, the mass balance of the substrate limiting the reaction is represented by the equations:

$$V_d \cdot c_d(h) - V_d \cdot c_d(h+dh) - n_1(c_d, c_a) \cdot dA = 0, \quad (1)$$

$$V_a \cdot c_a(h) - V_a \cdot c_a(h+dh) + n_2(c_d, c_a) \cdot dA = 0. \quad (2)$$

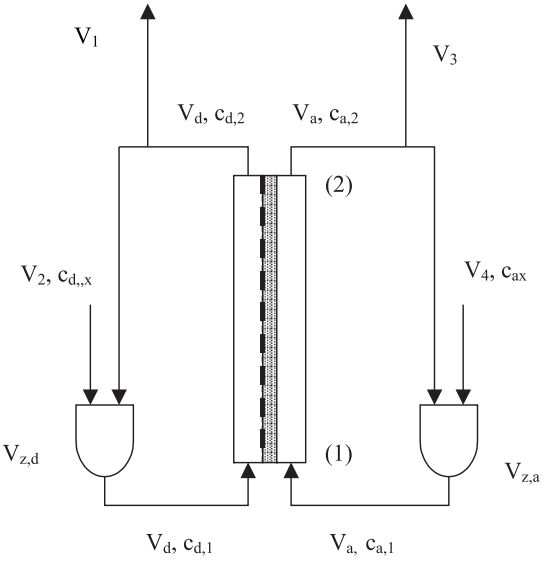

Fig. 1. Scheme of the system with the column bioreactor with catalytic membrane

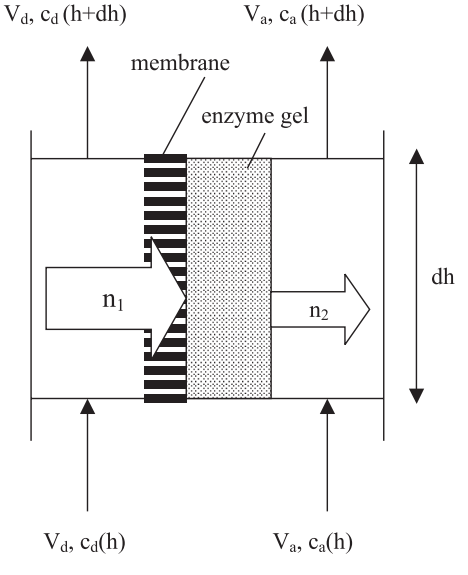

Fig. 2. The differential element of the column bioreactor with catalytic membrane

Relation between the mass stream density n_1, n_2 and concentration in bulk of both phases can be determined using mass transport coefficients. For example, for the membrane belonging to the acceptor phase (Fig. 3) the respective equations are:

$$n_1 = k_1 \cdot \left(\frac{c_d}{P} - c_a(x=0) \right), \tag{3}$$

$$n_2 = \beta_a \cdot (c_a(x=s) - c_a), \tag{4}$$

$$\frac{1}{k_1} = \frac{P}{\beta_d} + \frac{1}{\beta_a}. \tag{5}$$

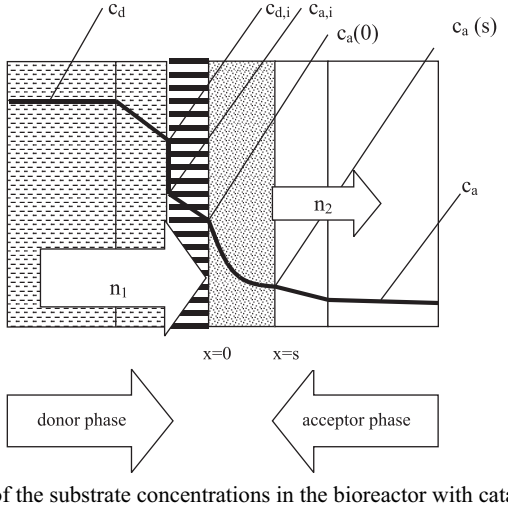

Fig. 3. Profile of the substrate concentrations in the bioreactor with catalytic membrane

For solving the presented balance equations values of n_1 and n_2 must be known. These can be determined from Trusek-Holownia model [8, 9]. Assuming that the reaction is of the first order, the equation of mass stream density is obtained:

$$n_1 = k_1 \cdot c_{s,o} \cdot \frac{\cosh\Phi - R + \dfrac{\beta_E}{\beta_w} \cdot \Phi \cdot \sinh\Phi}{(1 + \dfrac{P \cdot k_1}{\beta_w}) \cdot \cosh\Phi + (\dfrac{\beta_E}{\beta_w} \cdot \Phi + \dfrac{P \cdot k_1}{\beta_E \cdot \Phi}) \cdot \sinh\Phi}, \tag{6}$$

$$n_2 = k_1 \cdot c_{s,o} \cdot \frac{1 - R \cdot \cosh\Phi - R \cdot \dfrac{\beta_E}{P \cdot k_1} \cdot \Phi \cdot \sinh\Phi}{(1 + \dfrac{P \cdot k_1}{\beta_w}) \cdot \cosh\Phi + (\dfrac{\beta_E}{\beta_w} \cdot \Phi + \dfrac{P \cdot k_1}{\beta_w \cdot \Phi}) \cdot \sinh\Phi}, \tag{7}$$

$$n_r = n_1 - n_2, \tag{8}$$

where:

$$\Phi = \sqrt{\frac{k_r}{D}} \cdot s, \tag{9}$$

$$R = \frac{P \cdot c_{s,w}}{c_{s,o}}, \tag{10}$$

$$P = \frac{c^*_{s,o}}{c^*_{s,w}}, \tag{11}$$

$$\beta_E = \frac{D}{s}. \tag{12}$$

Upon integration of equations (1) and (2) for the initial conditions (Fig. 1):

$$c_d(h = 0) = c_{d,1}, \tag{13}$$

$$c_a(h = 0) = c_{a,1}, \tag{14}$$

the values of the limiting substrate concentrations in both phases at the outlet from the column reactor ($c_{d,2}$, $c_{a,2}$) are obtained.

In the case of a continuous operation, streams V_1 and V_3 are removed and streams V_2 and V_4 with properly selected composition are supplied to the system. In the general case (a continuous process), the mass balance of the limiting substrate in the reservoirs of both phases is given by the equations:

$$V_{z,d} \cdot c_{d,1}(t + dt) - V_{z,d} \cdot c_{d,1}(t) = (V_d - V_1) \cdot c_{d,2}(t) \cdot dt + V_2 \cdot c_{d,x}(t) \cdot dt - V_d \cdot c_{d,1}(t) \cdot dt, \tag{15}$$

$$V_{z,d} \cdot c_{a,1}(t + dt) - V_{z,a} \cdot c_{a,1}(t) = (V_a - V_3) \cdot c_{a,2}(t) \cdot dt + V_4 \cdot c_{a,x}(t) \cdot dt - V_a \cdot c_{a,1}(t) \cdot dt. \tag{16}$$

The solution of above equations allows us to determine the concentrations of both phases during the process duration.

3. The Verification of a Bioreactor Model

A model of the bioreactor with a catalytic membrane presented in Fig. 1 was verified by Trusek-Holownia in the isooctane-polyamide membrane-water system. Due to the hydrophilic character of the membrane, its pores were filled with the acceptor phase.

The biocatalyst (lipase from *Candida antarctica*) was immobilized on the membrane surface by a chemical bond using glutaraldehyde. The amount of the bound enzyme corresponded to the gel layer thickness equal to 0.53–0.92 micron [10]. The enzyme catalyzed the reaction of hydrolysis of glycidyl butyrate, a compound which partition coefficient in the tested system is equal to 1.74. Constants of the kinetic equation were determined in separate experiments [10]. For the low substrate concentration, the kinetics of enzymatic reaction could be described by the first order equation according to substrate kinetics:

$$r = k_r \cdot c. \tag{17}$$

In this case the constant is equal to 1.0 s^{-1} for R-enantiomer and 0.49 s^{-1} for S-enantiomer of glycidyl butyrate. During the process, the amount of butyric acid (one of the reaction products that whole mass was concentrated in the acceptor phase ($P \ll 1$)) was monitored.

For the known hydrodynamic conditions the mass transfer coefficients in both phases and in the membrane were calculated. Theoretical correlations were verified on the basis of the experimentally determined mass transport coefficients [11].

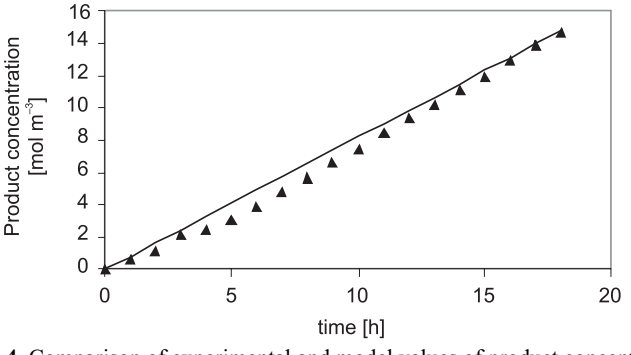

Fig. 4. Comparison of experimental and model values of product concentration

Table 1. Process parameters used for the verification and modeling of the process

Parameter		Value	
		verification	simulation
D	$m^2 s^{-1}$	$3.0 \cdot 10^{-12}$	$3.0 \cdot 10^{-12}$
k_r	s^{-1}	0.10	0.10
P		1.74	1.74
k_1	$m s^{-1}$	$2.9 – 5.1 \cdot 10^{-5}$	$1 \cdot 10^{-7} – 1 \cdot 10^{-4}$
β_a	$m s^{-1}$	$5.1 \cdot 10^{-5}$	$1 \cdot 10^{-10} – 1 \cdot 10^{-4}$
s	m	$5.3 – 9.2 \cdot 10^{-7}$	$1 \cdot 10^{-7} – 4 \cdot 10^{-5}$
$c_a(t=0)$	$mol m^{-3}$	0	0
$c_d(t=0)$	$mol m^{-3}$	40	60
A	m^2	0.014	0.014
H	m	0.10	0.10

Figure 4 shows an example of the comparison of the experimental values of the reaction product concentration in the water phase and the model values. Good agreement of the compared values enables the application of the proposed model in a simulation of the process in the reactor with a catalytic membrane.

Table 1 gives parameters used for the verification and modelling of the process.

4. Discussion of the Model

The subject of modelling was a batch process which can be more widely applied in medicine than the continuous one. In this presentation it was assumed that at the beginning of the process the whole substrate mass was located in the donor phase. When analyzing typical concentrations of substrate in both phases for a broad range of parameters (Fig. 5), it was found that the process could be divided into two characteristic periods. In the first period, the phases are far from the extraction equilibrium state, the stream of substrate mass (n_1) flowing to the catalytic layer is large, the substrate concentrations in the catalytic layer are high and therefore the stream of the reacted substrate is significant. Depending on the thickness and reactivity of the catalytic layer, part of the substrate mass (n_2) can not react and penetrates the acceptor phase thus increasing the substrate concentration. This period of the process is usually short.

After reaching the state close to interface equilibrium, the process slows down (it enters the second period). At the boundary of both periods, there is a maximum of the substrate concentration in the acceptor phase. This implies a very interesting property of the system, that consists in a change of the direction of substrate mass stream n_2. In the second period of the process, the catalyst layer is supplied with the substrate from both surrounding phases. In a typical case, when the donor phase is

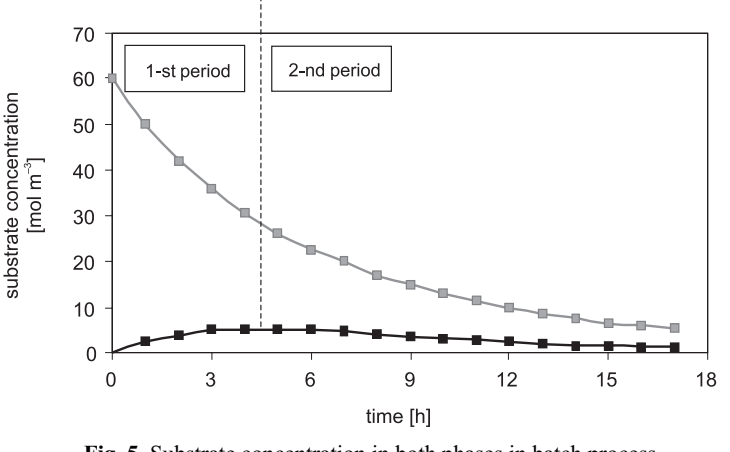

Fig. 5. Substrate concentration in both phases in batch process

a substrate reservoir, the value of stream n_2 in the second period of the process duration is much lower than the value of stream n_1.

Figure 6 shows schematically the substrate concentration in the catalyst layer and in the acceptor phase layer in both periods considered (for the sake of figures clarity the scale was not kept). Parallel to the change of stream direction n_2, the substrate concentration in the catalyst layer reveals its minimum. Its size and location depend on the thickness of the catalytic layer and the size of streams n_1 and n_2. The relation between streams n_1 and n_2 depends on the catalytic layer thickness and mass transfer coefficients on both sides of the enzyme gel.

The main process parameters that can control the work of the analyzed bioreactor include k_1, β_w and s. The effect of these parameters is shown below. There is the most interesting to determine an influence of the enzyme layer thickness on the stream of mass transported through the catalytic membrane and value of conversion degree in the biocatalyst layer.

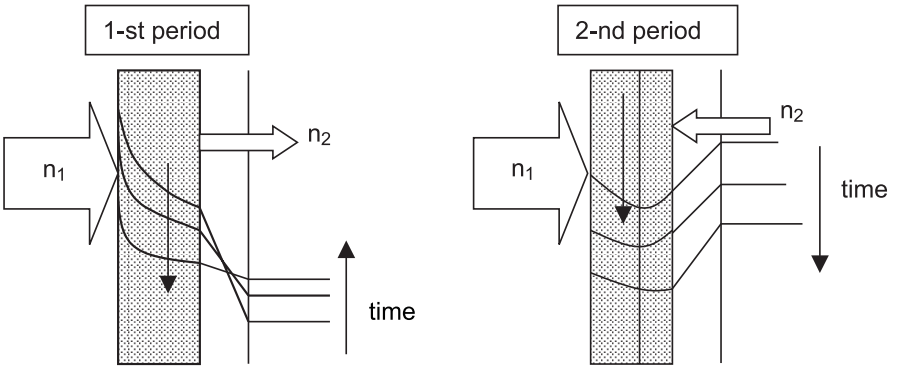

Fig. 6. Profile of substrate concentration in both periods

The catalyst layer thickness is particularly important, because on the one hand, its increase causes an increase of the amount of the catalyst applied which makes the reaction faster , and on the other hand induces an increase of substrate mass transfer resistance in the gel layer.

When analysing flux n_1 it is suitable to refer it to a comparative value. Let it be the density of mass flux during the mass transport through the membrane without the biocatalyst layer (i.e. the classical membrane contactor), as described by the equation:

$$n_1^{\circ} = k_1 \cdot c_d \cdot \frac{1-R}{1+M_2}. \tag{18}$$

Hence, the equation (19) will characterise changes in the flux n_1 resulting from the presence of the biocatalyst layer:

$$\frac{n_1}{n_1^\circ} = \frac{1+M_2}{1-R} \cdot \frac{1+M_1 \cdot \Phi \cdot \tanh\Phi - \dfrac{R}{\cosh\Phi}}{1+M_2+(M_1 \cdot \Phi + \dfrac{M_2}{M_1 \cdot \Phi}) \cdot \tanh\Phi}, \tag{19}$$

where

$$M_1 = \frac{\beta_E}{\beta_a}, \tag{20}$$

$$M_2 = \frac{P \cdot k_1}{\beta_a}. \tag{21}$$

Figure 7 illustrates the ratio of streams given by equation (19) as a function of Thiele modulus for case $c_a = 0$. For small values of Thiele modulus the mentioned ratio is smaller than unit and increases with this argument. For $\Phi > 4$ the analyzed function reaches plateau what means that the substrate stream is independent on the biocatalyst layer thickness. In the border the relative stream (eq. 19) is always higher then unit.

$$\lim_{\Phi\to\infty} \frac{n_1(c_{s,a}=0)}{n_1^\circ(c_{s,a}=0)} = 1+M_2. \tag{22}$$

Conversion degree is catalytic layer is described by equation

$$\alpha = 1-\frac{n_2}{n_1} = 1-\frac{1-R\cdot(\cosh\Phi+\dfrac{M_1}{M_2}\cdot\Phi\cdot\sinh\Phi)}{\cosh\Phi+M_1\cdot\Phi\cdot\sinh\Phi-R}. \tag{23}$$

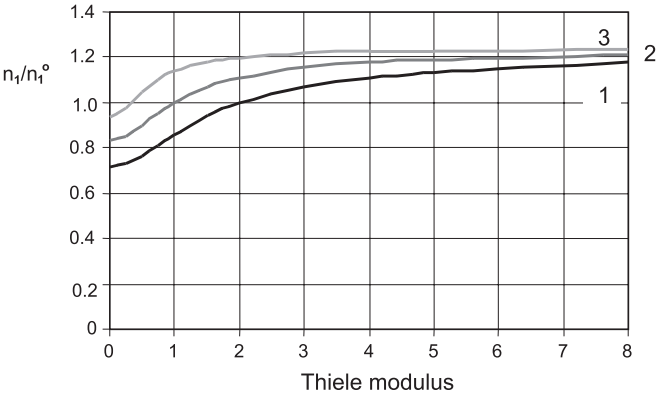

Fig. 7. The ratio of the substrate streams from donor phase (eq.19) vs. Thiele modulus. 1 – $M_1 = 0.5$, 2 – $M_1 = 1.0$, 3 – $M_1 = 3.0$

The influence of value Thiele modulus (gel thickness) for conversion degree is shown in Fig. 8. There is characteristic that for value of Thiele modulus higher then 4 practically full conversion of the substrate is observed. For typical values of the diffusion coefficient and the reaction rate constant a very high conversion is reached for the biocatalyst gel thickness smaller than several microns.

It was observed that there was a characteristic thickness of the catalyst layer, above which a further increment of the catalyst amount does not cause a shortening of the process duration. In practice this values does not depend on mass transport coefficient k_1. This follows from the fact that at this layer thickness the raw material contained in streams n_1 and n_2 reacts completely. A further increase of the layer thickness does not cause an increase of the process rate which is controlled in this case by the diffusion rate. It is very important for the process economy to determine this characteristic layer thickness.

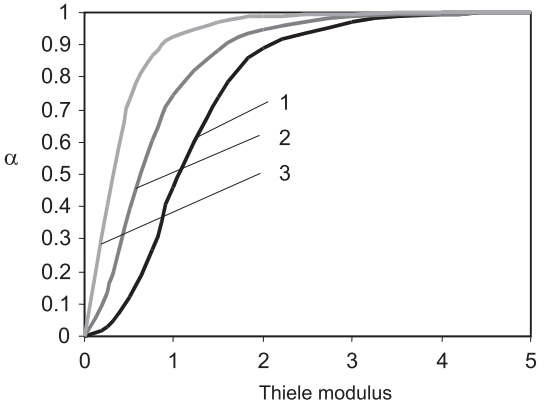

Fig. 8. Influence of Thiele modulus on conversion degree. 1 – M_1= 0.2; 2 – M_1=2.0; 3 – M_1=10.0

The growth of parameter R causes a strong monotonic increase of the conversion degree. Analysis of the impact that the value of Thiele modulus has on the conversion degree shows that when the substrate concentration in the acceptor phase is different than zero, the conversion degree increases much more rapidly as a function of Thiele modulus than in the case of zero product concentration in the water phase. Hence, to reach a high conversion, thin biocatalyst gel layers are sufficient. The high degree of the conversion in the layer results also from a decrease of the substrate flux at the inlet to the reaction zone.

With a decrease of the catalyst layer thickness a growth of the reaction time is observed. Starting from a certain value this relation is very distinct. The role of coefficient k_1 is interesting. With its decrease, for a given layer thickness, the process duration is prolonged. A hypothetical reaction time was calculated for the case when no mass transport resistance occurred for the stream n_1 ($k_1 \rightarrow \infty$). This hypotheti-

cal time does not differ much from the process time at high and medium values of $k_1 (> 5 \cdot 10^{-7}$ m s$^{-1})$. This means that for these values of k_1 the catalytic activity of the layer is used at maximum.

A decrease of coefficient k_1 induces two reasons for which the process duration is increased. The stream of the substrate supplied to the reaction layer by diffusion is decreased and the concentration gradient in the near-wall region increases, so the substrate concentration in the reaction layer is reduced. This means that the catalytic abilities of the gel layer are not fully used.

The analyzed relations allow us to determine an optimum region of the reactor operation. An increase of the catalyst layer is unjustified in many cases. Thin layers are recommended, then the second period of the process appears very quickly and the catalytic layer is supplied from both the phases, hence the catalyst activity is fully used. It is important that the coefficient k_1 should be high enough.

5. Conclusions

As a result of the model analysis of the process that takes place in a multi-phase reactor with a catalytic membrane located at the boundary of the phases, it was found that:

1. Two periods with different methods of supplying the catalytic layer can be distinguished in the process. In the first period, the substrate is supplied to the layer only from its reservoir (donor phase), while in the second one from both phases that surround it.
2. There is a characteristic thickness of the catalyst layer – when it is exceeded the process duration is no more shortened. It is recommended to apply thin layers, because then the catalyst activity is fully used.
3. The process of the substrate mass transport by diffusion from its reservoir to the catalyst layer should be intensified, but there is some boundary value of transfer coefficient k_1, which when exceeded, does not cause an increase of the process rate.
4. Transport of the substrate mass from the donor phase to the catalyst layer has a slight effect on the process rate and there is not need to intensify it.
5. The catalytic membrane stabilizes transmembrane flux.
6. High conversion in a thin (several microns) layer of the biocatalyst creates a possibility for the system miniaturization.

6. Symbols

A	membrane surface, m^2
c	substrate concentration, mol m^{-3}
D	diffusion coefficient, m^2 s^{-1}
h	current length of the column reactor, m

k_1 mass transfer coefficient to the catalysts gel, m s^{-1}
k_r reaction rate constant, s^{-1}
M_1, M_2 model parameters
n_r stream density of the converted substrate, mol $m^{-2}s^{-1}$
n_1 stream density of the entering substrate mass, mol $m^{-2}s^{-1}$
n_2 stream density of the nonconverted substrate mass, mol $m^{-2}s^{-1}$
P partition coefficient
R relation of both phases concentration
r reaction rate, mol $m^{-3}s^{-1}$
s thickness of the gel layer, m
t time, s
V flux, m^3 s^{-1}
$V_{z,d}$ volume of the donor phase tank, m^3
$V_{z,a}$ volume of the acceptor phase tank, m^3
x current thickness of the gel layer, m
α conversion degree
$ß$ mass transfer coefficient, m s^{-1}
Φ Thiele modulus

subscripts:

a acceptor phase
d donor phase
E enzyme
m membrane
1,2 cross-section of the column reactor

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