May Active Solute Flux Control the Cell Volume in the Steady State?

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Abstract. The dynamics of a bioreactor with a variable volume and an active solute flux based on the thermodynamics of irreversible processes and stability analysis was studied. The active solute flux may control both the bioreactor volume and the hydrostatic pressure as well as the concentration of the solute inside the cell in the steady state. The range of the active solute flux is limited by amplitudes (j_0^1, j_0^2) of the active transport depending on the membrane transport parameters. The dynamic system is stable for $j_0 > j_0^{th}$.

Key words: Dynamics of bioreactor — Active solute flux — Variable volume — Nonelectrolyte transport

Introduction

Cells may control their volume, osmotic and turgor pressures by means of passive and active solute transport, chemical reactions associated with the cell metabolism as well as by elastic properties of the membrane and the cell wall (Barry 1970; Coster et al. 1976; Zimmermann and Steudle 1978; Zimmermann 1977, 1978, 1980; Ludwików 1981; Gutknecht et al. 1978; Fiscus 1975).

Plant cells volume is regulated by a turgor pressure transducer the nature of which has not been completely understood (Coster et al. 1976; Zimmermann 1977; Gutknecht et al. 1978). Cells devoid of cell wall regulate their volume through changes in transport properties of ionic pumps of different kinds (Dainty 1963, 1976; Macknight and Leaf 1978).

Recently a mathematical model of a bioreactor with a variable volume has been presented (Dvorak and Markevich 1979).

The authors found that such a system is entirely stable and posseses only one steady state which is independent of the system parameters. However, they did not account for the active transport processes. This problem has been studied theoretically by Wierzchaczewski (1983).

A new experimental method for the determination of concentration gradient induced volume flow and the filtration coefficient of the volume measured on a spherical membrane was described (Langner et al. 1986).

In the present paper we consider a volume changing over time. As a working hypothesis we shall assume that the active transport flux is independent of the solute concentrations. We shall consider a new simple model of an elastic cell with active transport and a variable volume and study the stability of the presented model.

The model

A homogeneous membrane divides the system in two phases. The membrane contains an active solute uptake mechanism.

The reactor is spherical in shape and has a radius r (Fig. 1). In both phases, a binary solute nonelectrolyte is present. The solute is transported through the membrane actively and passively.

Let V and V_0 denote the volume of the reactor and the external phase ($V_0 \gg V$) respectively. We assume that the internal and external hydrostatic pressure, p_i, p_0, and the solute concentrations, c_i, c_0, are different.

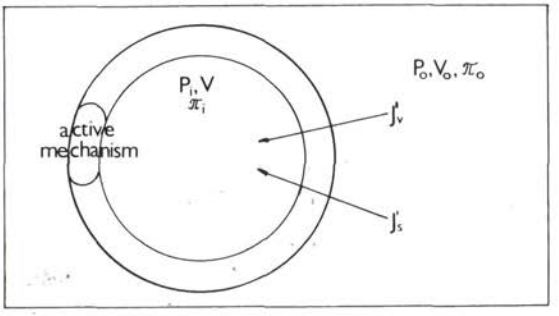

Fig. 1. A bioreactor with a variable volume containing an active solute uptake mechanism.

The differences Δc, and Δp are small. The system is isothermal. The internal and external osmotic pressure π_i, π_0 is given by the van't Hoff relations:

$$\pi_0 = RTc_0 \tag{1}$$

$$\pi_i = RTc_i \tag{2}$$

where R is the universal gas constant, T is the absolute temperature.

The volumetric elastic modulus, ε, can be described by the equation introduced by Philip (Philip 1958):

$$\varepsilon = V\left(\frac{dP}{dV}\right) \tag{3}$$

where V is the reactor volume and P is the turgor pressure:

$$P = p_i - p_0$$

For a plant cell $P > 0$ whereas for a red blood cell $P = 0$. However, under the condition of an osmotic shock, $P > 0$. Although the elasticity coefficient ε is a complex function of P and V (Coster et al. 1976; Hellebust 1976; Zimmermann et al. 1976; Zimmermann 1977, 1978) we may assume that $\varepsilon = \text{const}$ (Philip 1958).

The surface area of the cell is related to its volume, which, in turn, is related to the turgor pressure and the elastic modulus of the cell membrane. The Philip equation relating these quantities is:

$$V = V_0 \exp\left(\frac{P}{\varepsilon}\right) \tag{4}$$

where V_0 is the cell volume at $P = 0$.

Assuming a spherical cell, equation (4) can also be written in terms of the radius of the bioreactor:

$$r = r_0 \exp\left(\frac{P}{3\varepsilon}\right) \tag{5}$$

where r_0 is the radius at $P = 0$.

Dynamical equations

The linear, practical equations for a binary mixture of a solvent and one nonelectrolyle solute describing fluid movements through a membrane are based on the irreversible thermodynamics (Kedem and Katchalsky 1958; Katchalsky and Curran 1967).

$$J_v = L_p[(p_0 - p_i) - \sigma(\pi_0 - \pi_i)] \tag{6}$$

$$J_s = (1 - \sigma)\bar{c}_s J_v + \omega(\pi_0 - \pi_i) \tag{7}$$

where L_p is the hydraulic conductivity, σ is the reflection coefficient, ω is the coefficient of the permeable solute, J_v is the volume flow into the reactor, and J_s is the solute flux.

The average concentration, $\bar{c}_s$, is defined as:

$$\bar{c}_s = \frac{c_0 - c_i}{\ln \frac{c_0}{c_i}} \tag{8}$$

Assuming that the concentration difference is small, we may write:

$$\bar{c}_s = \frac{1}{2}(c_0 + c_i) \tag{9}$$

We assume here that the phenomenological coefficients L_p, ω, and σ are independent of the turgor pressure.

In addition to the active component of the uptake j_s, the total flux, J'_s, has then two additional components: a diffusive component, and a drag component. For such a system, we may write:

$$J'_s = J_s + j_s \tag{10}$$

$$J'_v = J_v + \bar{v}_s j_s \tag{11}$$

The second term on the right side depends on the metabolic energy.

Fundamental physical ideas in modelling the active transport system were presented by Heinz (1978); Monticelli and Celentano (1983); Patlak et al. (1963); Gałdzicki and Miękisz (1975); and Hill (1977).

The active solute flux may be a nonlinear function of the solute concentrations (Heinz 1978; Gałdzicki and Miękisz 1975). We assume according to Fiscus (1975) that the active solute flux is independent of both the hydrostatic and the osmotic pressure.

Transmembrane fluxes elicit changes in the reactor volume which result in changes in the hydrostatic pressure. Changes in the bioreactor volume and the number of moles of the solute, n_i, are connected with transmembrane fluxes by relations:

$$\frac{dV}{dt} = AJ'_v \tag{12}$$

$$\frac{dn_i}{dt} = AJ'_s \tag{13}$$

where: A is the reactor surface, n_i is the number of moles of the solute inside the bioreactor $n_i = c_i V$.

Taking into account Eq. (3), (12), (13) we may write:

$$\frac{dP}{dt} = \frac{A}{V}\varepsilon J_v' \tag{14}$$

$$\frac{dc_i}{dt} = \frac{A}{V}(J_s' - c_i J_v') \tag{15}$$

Using the relations (1)—(15) and introducing transformation of time variables

$$X = \frac{p_i}{p_0}$$

$$Y = \frac{c_i}{c_0}$$

$$\tau = p_{at}\frac{A_0}{V_0}L_p t$$

where A_0 is the cell area for $P = 0$, we obtain equations describing the dynamics of the system studied:

$$\frac{dX}{d\tau} = \exp\left\{\frac{b}{3\varepsilon}(1 - X)\right\}\varepsilon'\left\{(1 - X) - \frac{k_2}{b}(1 - Y) + \frac{a_2}{b}j_0\right\} \tag{16}$$

$$\begin{aligned}\frac{dY}{d\tau} = \exp\left\{\frac{b}{3\varepsilon}(1 - X)\right\}\Bigg\{nb(1 + Y)\left[(1 - X) - \frac{k_2}{b}(1 - Y)\right] \\ + k_3(1 - Y) + a_3 j_0 - bY\left[(1 - X) - \frac{k_2}{b}(1 - Y) + \frac{a_2}{b}j_0\right]\Bigg\}\end{aligned} \tag{17}$$

where

$$\begin{aligned} \varepsilon' &= \frac{\varepsilon}{p_{at}}, & k_2 &= \frac{RT\sigma c_0}{p_{at}} \\ b &= \frac{p_0}{p_{at}}, & k_3 &= \frac{RT\omega}{L_p p_{at}} \\ a_2 &= \frac{\bar{v}_s}{L_p p_{at}}, & n &= \frac{1}{2}(1 - \sigma) \\ a_3 &= \frac{1}{L_p p_{at} c_0}, & g(X) &= \exp\left\{\frac{b}{3\varepsilon'}(1 - X)\right\} \end{aligned} \tag{18}$$

p_{at} is the atmospheric pressure.

Stability analysis

The system of equations (16) and (17) has only one steady solution $X = X_0$, $Y = Y_0$

$$X_0 = 1 - \frac{k_2}{b}(1 - Y_0) + \frac{a_2}{b} j_0 \tag{19}$$

$$Y_0 = \frac{k_3 - (a_3 - na_2)j_0}{k_3 + na_2 j_0} \tag{20}$$

The steady state (X_0, Y_0) is independent of ε'.

We see from (18)—(20) that X_0 and Y_0 depend on the parameters $\bar{v}_s$, ω, σ, c_0, T, and the active solute flux j_0. If $j_0 = 0$ the dynamic system has only one steady state

$$\begin{aligned} X_0 &= 1 \\ Y_0 &= 1 \end{aligned} \tag{21}$$

A classical stability analysis (Iooss and Joseph 1980) of the steady state, (i.e. linearization of the equations of motion in terms of small deviations from the steady state solution) gives the variational equation

$$\hat{\omega}^2 - Tr\hat{\omega} + \Delta = 0 \tag{22}$$

where Tr is the trace, Δ is the determinant of the matrix of coefficients, and $\hat{\omega}$ is the characteristic value

$$Tr = \left(\frac{\partial \dot{X}}{\partial X}\right)_0 + \left(\frac{\partial \dot{Y}}{\partial Y}\right)_0 \tag{23}$$

$$\Delta = \left(\frac{\partial \dot{X}}{\partial X}\right)_0 \left(\frac{\partial \dot{Y}}{\partial Y}\right)_0 - \left(\frac{\partial \dot{X}}{\partial Y}\right)_0 \left(\frac{\partial \dot{Y}}{\partial X}\right)_0 \tag{24}$$

The roots $\hat{\omega}_\pm$ are given by the solution of (22)

$$2\hat{\omega}_\pm = Tr \pm \sqrt{Tr^2 - 4\Delta} \tag{25}$$

Thus, we see from (25) that the steady state will be asymptotically stable, if and only if both $Tr < 0$, and $\Delta > 0$. Differentiating (16) and (17) we get:

$$\begin{aligned} Tr &= g(X_0)\{ - \varepsilon' + nb(1 - X_0) + 2nk_2 Y_0 - k_3 - k_2 Y_0\} \\ \Delta &= - g^2(X_0)\varepsilon'\{nb(1 - X_0) + 2nk_2 Y_0 - k_3 + nk_2(1 - Y_0)\} \\ D &= Tr^2 - 4\Delta \end{aligned} \tag{26}$$

Using relations (19), (20) the equations (26) can be written in the form:

$$Tr = g(X_0)Z_1(j_0) \tag{27}$$

$$\Delta = g^2(X_0)\varepsilon' Z_2(j_0) \tag{28}$$

$$D = g^2(X_0)Z_3(j_0) \tag{29}$$

where

$$Z_1 = \{-\varepsilon' + (n-1)k_2 Y_0 + nk_2 - (na_2 j_0 + k_3)\} \tag{30}$$

$$Z_2 = na_2 j_0 + k_3$$

$$Z_3 = Z_1^2 - 4\varepsilon' Z_2$$

$$g(X_0) = \exp\{\frac{b}{3\varepsilon'}(1 - X_0)\}$$

Y_0 is given, by eq. (20)

The system is entirely stable if:

$$Z_1 < 0$$

and (31)

$$Z_2 > 0$$

because $g(X_0) > 0$.

The behaviour of the system is non-oscillating when conditions (31) and $Z_3 > 0$ are fulfilled.

We have shown that active transport may control both the cell volume and the solute concentration as well as the hydrostatic pressure inside the bioreactor.

In our calculations we assume that

$$p_{at} = 10^5 \,\mathrm{N \cdot m^{-2}}$$

$$R = 8314 \,\mathrm{J(kmol \cdot K)^{-1}}$$

$$\bar{v}_s = 0.018 \,\mathrm{m^3(kmol)^{-1}}$$

$$\sigma = 0.5$$

$$c_0 = 0.003 \,\mathrm{kmol(m)^{-3}}$$

$$k_3 = 7.5 \times 10^{-2}$$

Results and Discussion

The nonlinear differential equations (16) and (17) describe the dynamics of a bioreactor with a variable volume and with an active solute flux.

For $0 < c_i < 2c_0$, we obtain from equation (20) two different values of the active solute amplitudes determining the range of the active solute flux j_0.

$$j_0^1 = -k_3(a_3 - na_2)^{-1}$$

$$j_0^2 = +k_3(a_3 - 3na_2)^{-1}$$

Both parameters $j_0^{1,2}$ are independent of the membrane elasticity ε.

The amplitudes $j_0^{1,2}$ depend on the reflextion coefficient, σ, the solute permeability, ω, the solute concentration, c_0, and the partial molar volume, $\bar{v}_s$, respectively.

We analysed the dynamic system in a range (j_0^1, j_0^2) of active solute fluxes.

The system of equations (16) and (17) has only one steady state (X_0, Y_0) (see eq. (19) and (20)) which depends on the active solute flux and the parameters σ, ω, c_0, $\bar{v}_s$, but is independent of membrane elasticity ε.

In Figure 2 the dependences of both X_0 and Y_0 on the active solute flux j_0 are plotted.

It is seen that X_0 and Y_0 are monotonically increasing functions of j_0.

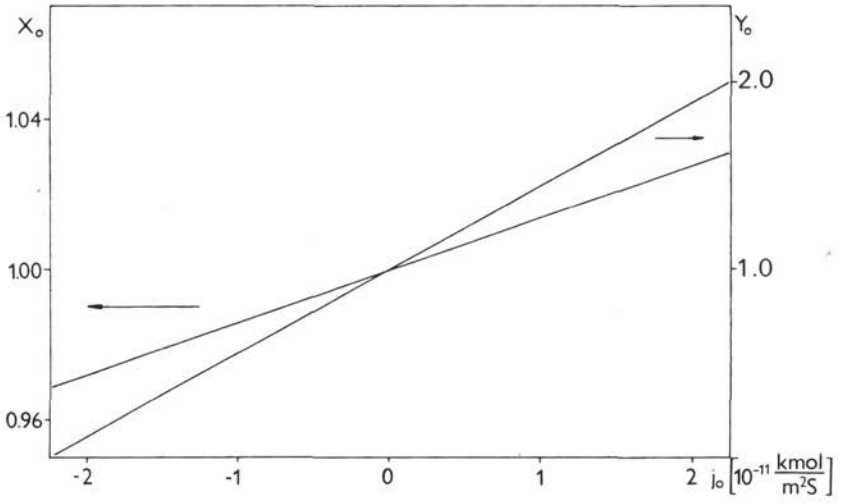

Fig. 2. The dependence of $X_0 = \frac{p_i}{p_0}$ and $Y_0 = \frac{c_i}{c_0}$ on the active solute flux j_0; $\varepsilon' = 10$; $\sigma = 0.5$; $L_p = 10^{-12}\,\mathrm{m^3(N.s)^{-1}}$; $k_3 = 0.075$; $c_0 = 0.003\,\mathrm{kmol.(m)^{-3}}$; $b = 1.2$.

It is important to note that for $0 < j_0 < j_0^2$, $X_0 > 1$, $Y_0 > 1$ and $p_i > p_0$, $c_i > c_0$, moreover, for $j_0^1 < j_0 < 0$ we have

$$X_0 > 0, \qquad Y_0 > 0$$

$$p_i < p_0, \qquad c_i < c_0$$

The steady state (X_0, Y_0) is independent of the dynamic system parameters for $j_0 = 0 (X_0 = 1, Y_0 = 1)$.

The stability of the steady state (X_0, Y_0) is determined by $Tr < 0$ and $\Delta > 0$.

The two conditions for stability of the steady state are given $Z_1(j_0) < 0$, $Z_2(j_0) > 0$

They determine the threshold value of the active solute flux j_0^{th}

$$j_0^{th} = k_3\{\varepsilon' + k_2(1 - 2n)\}$$
$$\{k_2(n-1)(a_3 - na_2) - na_2(nk_2 + \varepsilon')\}^{-1}$$

For $j_0 > j_0^{th}$ the dynamic system is stable.

It is interesting to note that j_0^{th} depends on the membrane transport parameters ω, σ and on the cell elasticity ε' (Figure 3).

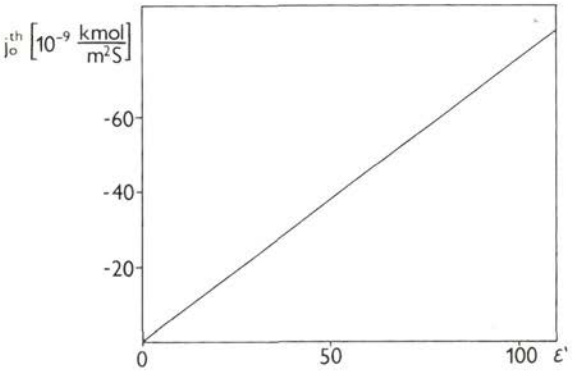

Fig. 3. The dependence of the threshold value amplitude, j_0^{th}, on the volumetric elastic modulus $\varepsilon' = \frac{\varepsilon}{p_{at}}$; $L_p = 10^{-12}\,m^3\,(N.s)^{-1}$; $\sigma = 0.5$; $k_3 = 0.075$.

The damped oscillation in the system is determined by

$$Z_1 < 0, Z_2 > 0 \text{ and } Z_3 < 0$$

The behaviour of the system is non — oscillatory when the conditions

$$Z_1 < 0, Z_2 > 0 \text{ and } Z_3 > 0 \text{ are fulfilled.}$$

In Figure (4) the dependences of Z_1, and Z_3 one the active solute flux j_0 are plotted in the range (j_0^1, j_0^2) for a red blood cell $\varepsilon' = 10$.

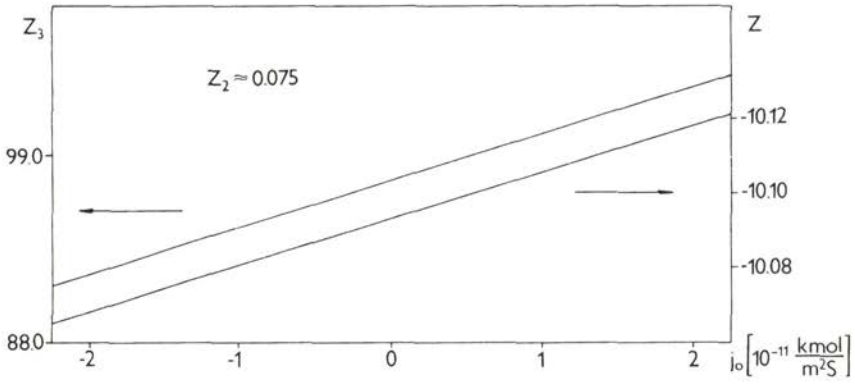

Fig. 4. The dependence of the functions Z_1, Z_3 on the active solute flux j_0; $\varepsilon' = 10$; $\sigma = 0{,}5$; $L_p = 10^{-12}\,\mathrm{m^3(N.s)^{-1}}$; $k_3 = 0.075$; $c_0 = 0.003\,\mathrm{kmol(m)^{-3}}$; $b = 1.2$.

In the range (j_0^1, j_0^2) of the active solute flux the dynamic system has only one steady state (X_0, Y_0) and a stable node solution.

Table 1 lists the values of elasticity ε', and the hydraulic conductivity L_p corresponding to the plant and the red blood cell. These values were subsequently used to calculate j_0^{th}, the range (j_0^1, j_0^2) of the active solute flux, and the corresponding solutions (Z_1, Z_2, Z_3).

Table 1. The limited range (j_0^1, j_0^2), j_0^{th}, and the solutions for plants and red blood cells.

ε'	L_p $\left[10^{-12}\frac{m^3}{N^s}\right]$	j_0^1 $\left[10^{-11}\frac{kmol}{m^2 s}\right]$	j_0^2 $\left[10^{-11}\frac{kmol}{m^2 s}\right]$	j_0^{th} $\left[10^{-8}\frac{kmol}{m^2 s}\right]$	Solutions
10	1	−2.25	+2.25	−0.79	stable node
10	0.1	−0.23	+0.23	−0.08	stable node
100	1	−2.25	+2.25	−7.65	stable node
100	0.1	−0.23	+0.23	−0.76	stable node

In Figure (5) the volume ratio $\left(\frac{V}{V_0}\right)_0$ and the radius ratio $\left(\frac{r}{r_0}\right)_0$ are plotted

as functions of X_0 in the steady state. $\left(\frac{V}{V_0}\right)_0$ and $\left(\frac{r}{r_0}\right)_0$ increase linearly with the increasing X_0. The range of X_0 is related to the range (j_0^1, j_0^2) of the active solute flux.

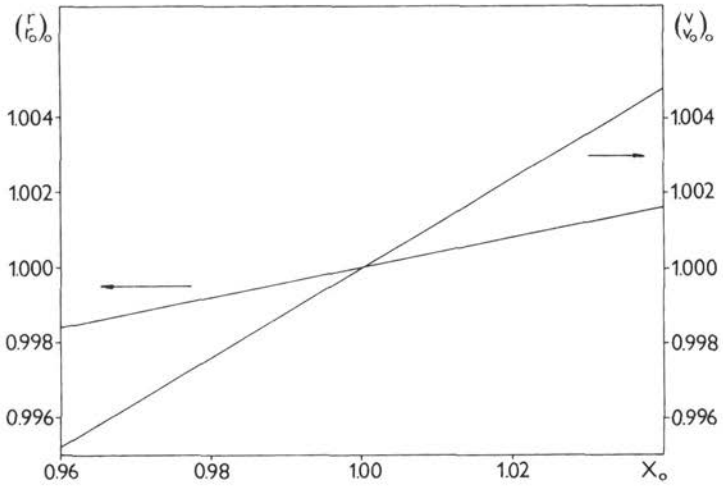

Fig. 5. The dependence of $f_1 = \left(\frac{r}{r_0}\right)_0$ and $f_2 = \left(\frac{V}{V_0}\right)_0$ in the steady states (X_0, Y_0) on X_0

$\varepsilon' = 10$; $b = 1.2$.

It is seen that for $X_0 > 1$, $V > V_0$ and $r > r_0$ for $X_0 < 1$ we have $V < V_0$ and $r < r_0$ moreover, for $j_0 = 0$, $X_0 = 1$ and

$$\left(\frac{V}{V_0}\right)_0 = 1, \quad \left(\frac{r}{r_0}\right)_0 = 1$$

In this paper we have not specified the mechanism of the active solute transport simply assuming it to be independent of both the hydrostatic pressure and the solute concentration. The results of the present paper show that already under the conditions of our simple model, active solute flux may control both the bioreactor volume and the solute concentration, as well as the hydrostatic pressure inside a cell.

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