

Concentration Dependent Active Transport, Osmotically Active Nonpermeable Component and Bioreactor Volume Regulation

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In a previous paper (Wierzychaczewski 1988) a model of (two-component) bioreactor volume regulation has been considered in which the active solute (nonelectrolyte) flux was assumed to be concentration independent, whereas the passive transport across the membrane was described by the Kedem-Katchalsky equations. The stability of the system has been analysed. It has been shown that the active solute flux may control both the bioreactor volume and the solute concentration, as well as the hydrostatic pressure inside the bioreactor. The steady state of the system was shown to be independent of the elasticity coefficient. In the present paper we make a more realistic assumption that the active solute flux is a (nonlinear) function of its concentrations c_i and c_o inside and outside the bioreactor, respectively. We also take into account a presence of an osmotically active non-permeating species. Thus, in the background equations of the model we make the following changes:

i) we replace Eq. (6) of (Wierzychaczewski 1988) by

$$J_V = L_P[(p_o - p_i) - (\sigma\pi_o - \pi_i) - (\pi_o^* - \pi_i^*)] \quad (1)$$

where π_o^* and π_i^* are the external and internal osmotic pressure of the non-permeating component, respectively (the reflection coefficient of the nonpermeable component being equal to 1). Both quantities are assumed to be given by the van't Hoff relation. All the remaining symbols preserve their previous meaning (Wierzychaczewski 1988)

ii) the equations are supplemented by the following one describing the active solute flux j_s (Heinz 1978):

$$j_s = J_m [c_o(K' + c_o)^{-1} - c_i(K' + c_i)^{-1}] \quad (2)$$

where J_m is the maximum active flux and K' is the apparent Michaelis constant.

The two changes naturally cause a corresponding change in the equations describing the dynamics of the system considered. The augmented system of equations is investigated in a way completely analogous to that presented by Wierchaczewski (1988), i. e. with the employment of classical stability analysis (Iooss and Joseph 1980).

If

$$K'/c_0 \neq 0$$

and

$$J_m \neq 0$$

the dynamic system has two steady states, one in which the active solute flux j_s is different from zero, and another in which the flux vanishes. Naturally, the second possibility corresponds to thermodynamic equilibrium.

Assuming that $(j_s)_0 \neq 0$ (i. e. that the active flux is different from zero in the steady state), we get for the steady state:

$$Y_0 \equiv (c_1/c_0)_0 = [(a_3 - na_2)J_m K + k_3 K(K + 1)][na_2 J_m K - k_3(K + 1)]^{-1} \quad (3)$$

where:

$$K \equiv K'/c_0$$

and where the symbol $(\)_0$ refers to the steady state value. All the remaining symbols have their original meaning (Wierchaczewski 1988).

To get an analytic expression for the corresponding steady state coordinate X_0 , we make now the following assumption:

$$b/\varepsilon' \ll 1 \quad (4)$$

which is always true for any realistic value of the coefficients.

Making use of (4), we may write:

$$Z_0 \equiv (C_1^*/C_0^*)_0 = a_1 \exp[(b/\varepsilon')(1 - X_0)] \approx a_1 [1 + (b/\varepsilon')(1 - X_0)] \quad (5)$$

where

$$a_1 \equiv C_1^*(0)/C_0^*, \quad X_0 \equiv (p_i/p_0)_0$$

and where C_1^* and C_0^* are the internal and the external concentration of the non-permeating component, respectively, and $C_1^*(0)$ is the internal concentration of the component at turgor pressure P equal to zero ($P \equiv p_i - p_0$, p_i and p_0 being the internal and the external pressure, respectively).

Under approximation (5) we get, with a relative error much smaller than 1 %, the following expression for steady state coordinate X_0 :

$$X_0 = 1 - b^{-1} [k_2(1 - Y_0) - a_2 J_m K(1 - Y_0)(K + 1)^{-1}(K + Y_0)^{-1} + k_1(1 - a_1)][1 + k_1 a_1 (\varepsilon')^{-1}]^{-1} \quad (6)$$

where:

$$k_1 \equiv RTC_o^*/p_{at}$$

R being the gas constant, T the absolute temperature and p_{at} the atmospheric pressure.

Thus, under the assumption that $(j_i)_0 \neq 0$, the dynamic system has only one steady state (X_0, Y_0) and the active transport controls the volume of the bioreactor, as in the case considered by Wierzbaczewski (1988), where the active flux was set constant and the nonpermeable solute was absent. However, in the present model the hydrostatic pressure inside the bioreactor and the volume are controlled also by the non-permeating component as well as by the elasticity coefficient.

If the active solute flux is zero in the steady state, or the active transport is absent (i. e., $J_m = 0$), we obtain from the dynamic equations of the model the steady state given by:

$$Y_0 = 1 \quad (7)$$

$$X_0 = 1 - b^{-1} [k_1(1 - a_1)][1 + k_1 a_1 / \varepsilon']^{-1}$$

From. Eqs. (7) it is seen that X_0 need not be 1, and that the quantity depends in this special case (thermodynamic equilibrium) on the parameters a_1 and $b = p_o/p_{atm}$ as well as on the elasticity coefficient. In the previous description (Wierzbaczewski 1988) switching off the active transport would result in achieving a steady state in which $X_0 = Y_0 = 1$. In the present model the same is obtained when in the absence of active transport parameter a_1 is set 1 (i. e. when the internal osmotic pressure of the nonpermeable component at zero turgor pressure is equal to the external osmotic pressure of the component). It is important to note that if $J_m = 0$, the steady state given by Eqs. (7) becomes the only one in the system.

We will now restrict our considerations to the first, more interesting case when the active flux in the steady state of the system is different from zero. For $0 < c_i < 2c_o$, we obtain from Eq. (3) the range of the maximum active flux (J_m^1, J_m^2). We do not present the respective equations here, restricting ourselves to note that the range itself does not depend on either the elasticity coefficient or the hydraulic permeability L_p .

Next, in a way presented by Wierzbaczewski (1988), we determine the threshold value of the maximum active solute flux J_m^{th} , the quantity being a

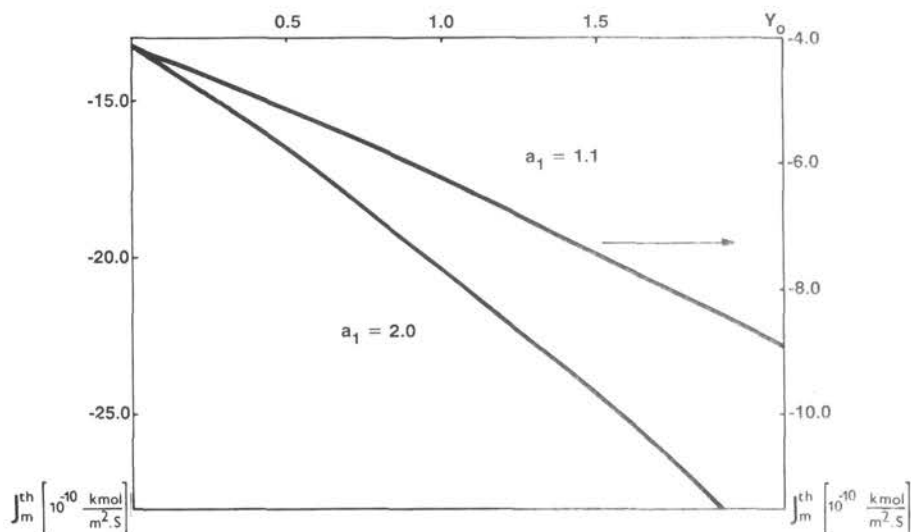


Fig. 1. The dependence of the threshold value of maximum active flux von $Y_o = (c_i/c_o)_o$ for $\varepsilon' = 10$, $L_p = 10^{-12} \text{ m}^3(\text{Ns})^{-1}$, $\sigma = 0.5$, $K = 4.0$, $k_3 = 0.075$, $c_o = 0.01 \text{ kmol m}^{-3}$, $C_o^* = 0.01 \text{ kmol m}^{-3}$, $v_s = 0.1117 \text{ m}^3 \text{ kmol}^{-1}$.

function of both X_o and Y_o :

$$J_m^{\text{th}} = \{[nk_1(1 - Z_o) - \varepsilon' - k_3]k_1 Z_o + \varepsilon'(k_1 - k_3)\} \quad (8)$$

$$* \{na_2 u_1 + [a_3 - na_2(1 + Y_o)]u_2\}^{-1} (k_1 Z_o + \varepsilon')^{-1}$$

where

$$u_1 \equiv K(1 - Y_o)(1 + K)^{-1}(K + Y_o)^{-1}, \quad u_2 \equiv K(K + Y_o)^{-2}$$

The dynamic system is stable for $J_m > J_m^{\text{th}}$ and has a stable node solution (there are no damped oscillations in the system). From Eq. (8) it is seen that J_m^{th} depends on the elasticity coefficient, the (dimensionless) constant K as well as on the transport parameters of the membrane. It should be stressed that J_m^{th} depends also on the quantity Z_o defined above, i.e. the stability area of the dynamic system is strongly controlled by the nonpermeable species osmotic pressure ratio. In accordance with the physiological situation, for the assumed values of the membrane transport parameters the system is stable only for $a_1 \geq 1$. To illustrate the properties of the model in a more quantitative way, a plot of the threshold value of the maximum active flux J_m^{th} as a function of the parameter Y_o for two different values of parameter a_1 ($K = 4$, $\varepsilon' = 10$) is shown in Fig. 1.

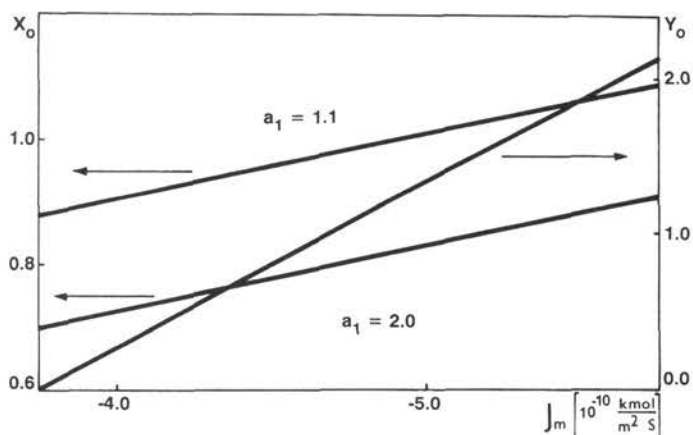


Fig. 2. The dependences of $X_o = (p_i/p_o)_o$ and $Y_o = (c_i/c_o)_o$ on the maximum active solute flux J_m . Same parameters as in Fig. 1.

Finally, in Fig. 2 we plot the dependence of both Y_o and X_o on the maximum active flux J_m (for two different values of the parameter a_1). It should be added that if parameter a_1 is set 1, the system is stable only for $Y_o \geq 1$, $X_o \geq 1$. This means that in this special case a stationary state will be achieved only when both the internal pressure and the internal permeable solute concentrations are not smaller than their respective external values. From Fig. 2 it is seen how the internal hydrostatic pressure and the internal solute concentration as well as the bioreactor volume are controlled by the active flux. Fig. 2 shows also the way in which the nonpermeating species concentration ratio controls the hydrostatic pressure and the volume.

It is easily seen that the present model has many properties of a "double Donnan" system (Macknight and Leaf 1978) where the steady state is maintained by metabolism in such a way that the active transport-dependent concentration gradient gives a contribution to the total osmotic pressure (see Eq. (1)) to counterbalance the intracellular osmotic pressure arising from the presence of nonpermeable components. The role played in real cells by (sodium) ions has been ascribed here to the permeating nonelectrolyte.

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