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A THREE-COMPARTMENT REACTION SYSTEM WITH THE EFFECT OF DIFFUSION AND TIME DELAY

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INTRODUCTION

It has been proposed by Jacob and Monod [3] that genes control certain biochemical pathways in cells by a negative feedback mechanism or repression. Mathematical models for the biochemical control of the genes were first proposed by Goodwin [1,2]. These Goodwin models were based on spatially homogeneous biochemical kinetics with time-delays although Goodman suggested that spatial effects and diffusion should be taken into consideration. In a recent paper, Mahaffy and Pao [4] extended Goodman's models for a two- and a three-interacting compartments which incorporate both time delays and diffusion. These models are formulated using a combination of the biochemical techniques and compartmental analysis to account for spatial effects. In this note we give some analytical results for the three-interacting compartment model. Proofs of these results are based on the monotone argument and the associated upper-lower solutions and will appear elsewhere (cf. [5]).

THE MATHEMATICAL MODEL

In the three-interacting compartment model, the first and third compartments are well-mixed with differential delay equations governing the reaction. The second compartment, connecting the first and third, is nonreacting except for decay of the chemical species and accounts for spatial differences between the first and third compartments. Using the standard theory from compartment analysis and biochemical kinetics the differential equations governing the chemical species (u_i, v_i) in the i-th compartment are given by (cf. [4])

$$\begin{aligned}
&u_1' + (a_1 + b_1)u_1 = a_1u_2(0,t) + f(v_1(t - r_1)) \\
&v_1' + (a_1 + b_2)v_1 = a_1v_2(0,t) \\
&(u_2)_t - D_1(u_2)_{xx} + b_1u_2 = 0 \qquad (t > 0, 0 < x < \ell) \qquad (1) \\
&(v_2)_t - D_2(v_2)_{xx} + b_2v_2 = 0 \\
&u_3' + (a_3 + b_1)u_3 = a_3u_2(\ell,t) \\
&v_3' + (a_3 + b_2)v_3 = a_3v_2(\ell,t) + c_0u_3(t - r_2)
\end{aligned}$$

where $u_i' = du_i/dt$, $(u_i)_t = \partial u_i/\partial t$ etc., and a_i, b_i, D_i, r_i and c_0 are physical constants. The function $f(v_1)$ is a continuous nonnegative function representing the controlled production of u_1 by v_1 and is often given in the form

$$f_0(v_1) = \sigma(1 + kv_1^\rho)^{-1}$$

where σ, k, ρ are positive constants and $\rho \geq 1$ is the order of repression. On the interface between compartments 1 and 2, and between compartments 2 and 3 the concentrations u_i, v_i are related by the boundary condition

$$\begin{aligned}
&-(u_2)_x(0,t) + \beta_1u_2(0,t) = \beta_1u_1(t) \\
&(u_2)_x(\ell,t) + \beta_2u_2(\ell,t) = \beta_2u_3(t) \\
&-(v_2)_x(0,t) + \beta_1^*v_2(0,t) = \beta_1^*v_1(t) \qquad (t > 0) \qquad (2) \\
&(v_2)_x(\ell,t) + \beta_2^*v_2(\ell,t) = \beta_2^*v_3(t) .
\end{aligned}$$

The initial condition for the system is given by

$$\begin{aligned}
&u_1(0) = \xi_1, \quad v_1(t) = \eta_1(t) \quad (-r_1 \leq t \leq 0) \\
&u_2(x,0) = \xi_2(x), \quad v_2(x,0) = \eta_2(x) \quad (0 < x < \ell) \qquad (3) \\
&u_3(t) = \xi_3(t), \quad v_3(0) = \eta_3 \quad (-r_2 \leq t \leq 0) .
\end{aligned}$$

In the boundary and initial conditions, $\beta_i > 0$, $\beta_i^* > 0$, $\xi_1 \geq 0$, $\eta_3 \geq 0$, $i = 1,2$, are constants and ξ_2, ξ_3, η_1, η_2 are given continuous nonnegative functions of their respective arguments (see [4] for more detailed discussions). A novelty of the system (1) - (3) is that the coupling of the various concentrations is through the boundary condition.

EXISTENCE AND STABILITY

As little is known about coupled systems of reaction-diffusion equations with time delays, especially about systems with coupled boundary conditions, it is essential to establish the existence and uniqueness of a global solution. Using the method of upper-lower solutions we have the following result.

Theorem 1. Suppose $f \in C^1(R^+)$ and

$$f(v_1) \geq 0 \text{ and } f'(v_1) \leq 0 \text{ for } v_1 \in R^+ \equiv [0,\infty). \tag{4}$$

Then the coupled system (1) - (3) has a unique global solution (u_i, v_i). Moreover there exist positive constants ρ_i, ρ_i^*, $i = 1,2,3$, such that

$$\begin{aligned} &0 \leq u_i(t) \leq \rho_i, \quad 0 \leq v_i(t) \leq \rho_i^* \quad (t \in R^+) \quad i = 1,3 \\ &0 \leq u_2(t,x) \leq \rho_2, \quad 0 \leq v_2(t,x) \leq \rho_2^* \quad ((t,x) \in R^+ \times [0,\ell]) \end{aligned} \tag{5}$$

The result in Theorem 1 implies that under condition (4) the time-dependent problem has a unique bounded nonnegative solution, independent of the time-delays r_1, r_2. The next theorem shows that if f satisfies a suitable growth condition then the steady-state solution is globally asymptotically stable (with respect to nonnegative initial perturbations).

Theorem 2. Let (u_i^s, v_i^s) be a nonnegative steady-state solution of (1.1) (1.2) and let f satisfy condition (4). If, in addition,

$$\sup_{v_1 \geq 0} [-f'(v_1)] < b_1 b_2 / c_o \tag{6}$$

then for any time delays r_1, r_2, (u_i^s, v_i^s) is globally asymptotical stable.

Proofs of Theorems 1 and 2 have been given in [5] where an existence-comparison theorem is established and suitable comparison functions are constructed. It is to be noted that when $f = f_0$ condition (4) is trivially satisfied and condition (6) is reduced to

$$\begin{aligned} &\sigma k < b_1 b_2/c_0 && \text{when } \rho = 1 \\ &\sigma k^{1/\sigma}\rho^{-1}(\rho - 1)^{1-1/\rho}(\rho + 1)^{1+1/\rho} < 4b_1 b_2/c_0 && \text{when } \rho > 1. \end{aligned} \tag{7}$$

In this situation we have the following existence-uniqueness result for the steady-state problem.

Theorem 3. The steady-state problem (1) (2) with $f = f_0$ has a unique positive solution (u_1^s, v_1^s). This steady-state is globally asymptotically stable when condition (7) holds.

A proof of the existence-uniqueness result can be found in [4]. The stability result follows from Theorem 2.

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