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OPTIMAL CONTROL OF A CHEMOTAXIS SYSTEM

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Abstract. Chemotaxis is the process by which cells aggregate under the force of a chemical attractant. The cell and chemoattractant concentrations are governed by a coupled system of parabolic partial differential equations. We investigate the optimal control of the proportion of cells being generated in two settings. One involves harvesting the actual cells and the other depicts removing a proportion of the chemoattractant. The optimality system for each problem contains forward and backward reaction-diffusion and convection-diffusion equations. Numerical results are presented.

1. Introduction. Chemotaxis is understood as the movement of an organism toward or away from a relatively high concentration of a chemical stimulus. In the early work of Keller and Segel [12], they discuss the chemotactic response of amoebae to bacteria in a cellular slime mold. In addition, they investigate the chemical sensitivity of *E. coli* in the context of Brownian motion. From their theoretical setting, they see that both chemotactic waves of bacteria and the genesis of aggregation of cells can occur [13, 14]. Other authors have addressed the concept of chemotaxis in ecology [4, 15, 25, 26], medicine and biology [1, 2, 3, 7, 16, 17, 23], and in mathematical issues as existence of solutions and chemotactic collapse [10, 11, 22].

In this work, we consider the system which is addressed in a manuscript by Fisackerly and McCartin [6]. This model has also been investigated by Oster and Murray [24]. They discuss pattern formation of cartilage condensation in a vertebrate limb bud. There is a balance between the effect of the random dispersion of cells and the aggregation of cells. They describe the chemotactic process as autocatalytic since the more the cells aggregate the stronger the emission of attractant. Hence, patterns form establishing the cartilage regeneration if the chemotactic response is greater than the dispersive motility coefficient.

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Since chemotaxis results from the interaction of cells and chemical as the cells move and the chemical diffuses, a focus of this paper is to determine if the patterns that form from this ebb and flow dynamics between the cells and the chemoattractant can be controlled in an optimal fashion. Through harvesting a portion of the cells or chemoattractant, we determine an appropriate bilinear harvesting control so that the cartilage in a limb bud, for example, expands to and remains in a target zone with minimal chemoattractant concentration. Another motivation for optimal control can also be viewed in controlling the removal of a proportion of the chemical concentration through the use of drug treatment. In Orr *et. al* [23], they studied the migration of tumor cells toward the bone in which the cells moved chemotactically. Optimal control strategies can be used to find an optimal drug treatment that reduces the chemical concentration while minimizing the metastasized tumor cell burden.

We investigate the model with $u(x,t)$ and $c(x,t)$ representing the concentration of the cells and the chemoattractant, respectively. The cells and the chemoattractant are governed by a convection-diffusion equation and a reaction-diffusion equation as

$$\begin{aligned} u_t &= Mu_{xx} - a(uc_x)_x && \text{on } [0,L]\times[0,T] \\ c_t &= Dc_{xx} + \tfrac{bu}{u+h} - \mu c \\ u(x,0) = u_0(x), &\quad c(x,0) = c_0(x) && \text{for } x \in [0,L] \\ u_x(0,t) = u_x(L,t) &= c_x(0,t) = c_x(L,t) = 0 && \text{for } t \in [0,T]. \end{aligned} \tag{1.1}$$

In (1.1), we have several parameters. M and D represent the diffusion coefficients of the cells and the chemoattractant. Here, a is the chemoattractant coefficient which monitors the chemical gradient attraction of the cells. The Michaelis-Menten term, $\frac{bu}{u+h}$, represents a response of the chemoattractant to a maximum carrying capacity or saturation rate, assuming $b, h > 0$. We incorporate a decay term where μ denotes the degradation rate. In addition, we have assumed that there is no flux of the concentrations across the boundary. Moreover, we give initial concentrations for the cells, $u_0(x)$, and the chemoattractant, $c_0(x)$.

To analyze this system we incorporate the non-dimensionalization of Fisackerly and McCartin [6]. We also introduce a linear control in which we desire to control either the proportion of the cells or the proportion of the chemoattractant that is being generated. Specifically this term is modeled by either $-fu$ in the $u(x,t)$ equation or $-fc$ in the $c(x,t)$ equation.

Our non-dimensionalized system is either

$$\begin{aligned} u_t &= Mu_{xx} - (uc_x)_x - fu && \text{on } Q \\ c_t &= Dc_{xx} + \tfrac{u}{u+1} - c \\ u(x,0) = u_0(x), &\quad c(x,0) = c_0(x) && \text{for } x \in \Omega \\ u_x(0,t) = u_x(L,t) &= c_x(0,t) = c_x(L,t) = 0 && \text{for } t \in [0,T] \end{aligned} \tag{1.2}$$

which incorporates the control of the cells u, or

$$\begin{aligned} u_t &= Mu_{xx} - (uc_x)_x && \text{on Q} \\ c_t &= Dc_{xx} + \tfrac{u}{u+1} - (1+f)c \\ u(x,0) &= u_0(x), \quad c(x,0) = c_0(x) && \text{for } x \in \Omega \\ u_x(0,t) &= u_x(L,t) = c_x(0,t) = c_x(L,t) = 0 && \text{for } t \in [0,T] \end{aligned} \tag{1.3}$$

which incorporates the control of the chemoattractant c. We have used the same notation in the renaming process. Note that $\Omega = [0, L]$ and that $Q = \Omega \times [0, T]$.

The admissible control set is $A = \{f(x,t) \in L^\infty(Q) \mid 0 \leq f(x,t) \leq 1 \text{ a.e. in Q}\}$. Furthermore, the following objective functional is to be minimized over A,

$$J(f) = \frac{1}{2} \int_0^T \int_0^L \left[(u - z_0)^2 + 2A_1 c + f^2\right] \, dx \, dt \tag{1.4}$$

where z_0 is a target of the pattern formation of the cells. We minimize the deviations of the cells from the target formation, the amount of chemoattractant and the cost associated with controlling the concentration of the cells. Our goal is to characterize an optimal control, f^*, such that $\min_{f \in A} J(f) = J(f^*)$.

In the framework of this paper, we investigate the existence and uniqueness of the state system along with regularity properties in Sec. 2. In addition, existence of an optimal control that minimizes our objective functional is proven in that section. In Sec. 3, we discuss the optimality conditions. Specifically, we develop the sensitivity analysis of the state concentrations. Then we find the characterization of the optimal control in terms of the solution to the optimality system, which is the state system coupled with the adjoint system. We prove the uniqueness of this optimality system for small time. In Sec. 4, we develop a numerical scheme for the optimality system and in Sec. 5 we graphically demonstrate control of chemotaxis.

2. Existence. In Theorem 2.1, we prove the existence of a unique solution to the chemotaxis system (1.2) using semigroup theory. Then we characterize the weak solution format to (1.2). Using this format, we then prove the existence of an optimal control that minimizes the objective functional (1.4) via a minimizing sequence argument. These results also hold for the second chemotaxis system (1.3).

2.1. *Existence of State Solutions.* Using the standard notation $H^k(\Omega)$ to represent the Sobelev space $W^{k,2}(\Omega)$, let $H^{k+\theta}(\Omega)$ denote the intermediate space between $H^k(\Omega)$ and $H^{k+1}(\Omega)$ for any $0 < \theta < 1$. Let I be an interval in $[0, \infty)$. The space $L^p(I; X)$ is the L^p space of measurable functions in I with values in the Banach space X. The space $C^m(I; X), m = 0, 1, 2, \ldots$ is the space of $m-$times continuously differentiable functions in I with values in X, while the space $C^\theta(I; X), 0 < \theta < 1$ is the space of Hölder-continuous functions in I with values in X.

THEOREM 2.1. If $u_0, c_0 \in H^{1+\varepsilon}(\Omega)$ for $0 < \varepsilon \leq 1$, and $u_0(x) \geq 0$, $c_0(x) \geq \overline{c}_0 > 0$ on $\overline{\Omega}$, then a real unique local solution u, c of (1.3) exists on an interval $[0, T]$ such that

$$u, c \in C^\eta\left([0,\infty); H^{1+\varepsilon_1}(\Omega)\right) \cap C\left([0,T); H^2(\Omega)\right) \cap C^1\left([0,T); L^2(\Omega)\right)$$

with $0 < \varepsilon_1 < \min(\varepsilon, \frac{1}{2})$ and $0 < \eta < \min\left(\frac{\varepsilon-\varepsilon_1}{2}, \frac{1-2\varepsilon_1}{4}\right)$. The solution satisfies the lower bounds

$$u(x,t) \geq 0, \quad c(x,t) \geq \bar{c}_0 e^{-t} \quad \text{on } [0,T].$$

Proof. The system (1.2) can be formulated as an abstract quasilinear equation

$$\begin{aligned} \frac{du}{dt} &+ A(u)u = f(u) \qquad 0 < t < \infty \\ u(0) &= u_0 \end{aligned}$$

on the Banach space $L^2(\Omega) \times L^2(\Omega)$. Let $X = L^2(\Omega) \times L^2(\Omega)$ and $Z = H^{1+\varepsilon}(\Omega) \times H^{1+\varepsilon}(\Omega)$, $u_0 = \binom{u_0}{c_0}$, $u = \binom{u}{c}$. Clearly $u_0 \in Z$.

Let $A(u)$ be the linear operator in X such that

$$A(u)\hat{u} = \begin{pmatrix} -(M\hat{u}_{xx} - (u\hat{c}_x)_x) + f\hat{u} \\ -D\hat{c}_{xx} + \hat{c} \end{pmatrix}$$

with domain

$$D(A(u)) = \left\{ \hat{u} \in H^2(\Omega) \times H^2(\Omega); \hat{u}_x = \hat{c}_x = 0 \text{ on } \partial\Omega \right\}.$$

Let $F(u)$ be the function

$$F(u) = \begin{pmatrix} 0 \\ \frac{u}{u+1} \end{pmatrix}.$$

This system has all of the properties of the one considered by Yagi [28]. Application of his Theorems 2.1 and 3.4 yields our result. □

We mention that the results from Childress and Percus [5] imply that our one dimensional problem does not possess chemotactic collapse, which refers to the concentration of the cells into a single point in finite time.

COROLLARY 2.1.

$$\|u\|_{L^\infty(Q)}, \ \|c_x\|_{L^\infty(Q)} < \infty.$$

Proof. Recall that for $\Omega \subset \mathbb{R}^n$, the regularity properties of $H^k(\Omega)$ imply that

$$\begin{aligned} H^{1+\varepsilon}(\Omega) &\subset C^0(\overline{\Omega}) \quad \text{n=1,2} \\ H^2(\Omega) &\subset C^1(\overline{\Omega}) \quad \text{n=1} \\ H^2(\Omega) &\subset C^0(\overline{\Omega}) \quad \text{n=2,3} \end{aligned}$$

[19, Thm 11.9.1, Cor. 1.9.1], where Ω satisfies the smoothness property of [19, Thm. 1.7.10-11]. Thus

$$\|u\|_{L^\infty(Q)} < \infty.$$

Since $c \in C^1\left((0,T]; L^2(\Omega)\right)$, the differential equation $c_t = Dc_{xx} + \frac{u}{u+1} - c$ implies that $c_{xx} \in L^2(\Omega)$. It follows that

$$\|c_x\|_{L^\infty(Q)} < \infty.$$

□

2.2. *Existence of Optimal Control.* In the discussion of existence of an optimal control, we consider the variational formulation of the state system (1.2). We define our weak solutions $(u, c) \in W \times W$ where $W = L^2\left((0,T): H^1(\Omega)\right)$. We note that W is a subset of the solution space for the chemotaxis system as designated in Theorem 2.1.

$$\begin{aligned} \int_0^T \langle u_t, \phi\rangle \, dt &+ M\int_0^T\int_0^L u_x\phi_x \, dx\, dt - \int_0^T\int_0^L u\, c_x\phi_x \, dx\, dt \\ &= -\int_0^T\int_0^L f u\phi \, dx\, dt \\ \int_0^T \langle c_t, \phi\rangle \, dt &+ D\int_0^T\int_0^L c_x\phi_x \, dx\, dt - \int_0^T\int_0^L \frac{u}{u+1}\phi \, dx\, dt \\ &= -\int_0^T\int_0^L c\phi \, dx\, dt \end{aligned} \tag{2.1}$$

for all $\phi \in W$ where $\langle , \rangle$ denotes the duality between $\left(H^1(\Omega)\right)^*$ and $H^1(\Omega)$.

We recall that the admissible set is

$$A = \{f(x,t) \in L^\infty(Q) \mid 0 \le f(x,t) \le 1 \text{ a.e. in Q}\}.$$

Also, the objective functional is

$$J(f) = \frac{1}{2}\int_0^T\int_0^L \left[(u - z_0)^2 + 2A_1 c + f^2\right] \, dx\, dt.$$

THEOREM 2.2. There exists an optimal control in A that minimizes the functional $J(f)$.

Proof. Since the state variables and the controls are bounded below, there exists a minimizing sequence $\{f_n\} \in A$ such that

$$\lim_{n\to\infty} J(f_n) = \inf\{J(f) | f \in U\} = \delta \text{ for } \delta \ge 0.$$

By the existence and uniqueness to the state system (1.2), we define $u^n = u(f_n)$ and $c^n = c(f_n)$ for each n. Using the weak formulations to the state system (2.1) for u^n and c^n, we develop estimates in order to discuss convergence of our sequences. First, we add the weak formulations with appropriate test functions to obtain

$$\begin{aligned} \int_0^t \left[\langle u_t^n, u^n\rangle + \langle c_t^n, c^n\rangle\right] \, dt &+ M\int_0^t\int_0^L (u_x^n)^2 \, dx\, dt \\ + D\int_0^t\int_0^L (c_x^n)^2 \, dx\, dt &- \int_0^t\int_0^L u^n c_x^n u_x^n \, dx\, dt \\ = \int_0^t\int_0^L \frac{u^n}{u^n+1}c^n \, dx\, dt &- \int_0^t\int_0^L f^n(u^n)^2 \, dx\, dt - \int_0^t\int_0^L (c^n)^2 \, dx\, dt. \end{aligned} \tag{2.2}$$

If we define $m = \min(M, D)$ and recognize that $\frac{u^n}{u^n+1} < 1$ for $u^n \geq 0$ for each n, then we can estimate (2.2) as

$$\begin{aligned} & \frac{1}{2}\int_\Omega \left\{ [u^n(x,t)]^2 + [c^n(x,t)]^2 \right\} dx + m\int_0^t \int_0^L \left[(u_x^n)^2 + (c_x^n)^2 \right] dx\, dt \qquad (2.3) \\ \leq \; & K\int_0^t \int_0^L \left[(u^n)^2 + (c^n)^2 \right] dx\, dt + \frac{\varepsilon}{2}\int_0^t \int_0^L \left[(u_x^n)^2 + (c_x^n)^2 \right] dx\, dt \\ & + \frac{1}{2}\int_\Omega \left[u_0^2(x) + v_0^2(x) \right] dx \end{aligned}$$

where we apply Cauchy's inequality for $\varepsilon > 0$ and we recognize that K is dependent on the bound of u^n. Next, we apply Gronwall's inequality and choose $\varepsilon < 2m + 1$ to obtain

$$\begin{aligned} \sup_{0\leq t\leq T} \Bigg\{ \int_\Omega \left\{ [u^n(x,t)]^2 \right. & + \left. [c^n(x,t)]^2 \right\} dx + m\int_0^t \int_0^L \left[(u_x^n)^2 + (c_x^n)^2 \right] dx\, dt \\ & \leq \; e^{2KT} \int_\Omega \left[u_0^2(x) + v_0^2(x) \right] dx \Bigg\}. \end{aligned}$$

Since f^n is L^∞ bounded in Q, then by weak compactness, there exists a subsequence f^n (we've used the same notation for convenience) such that $f^n \rightharpoonup f^*$ in $L^2(Q)$. From the boundedness of u^n and c^n in W, we can also extract subsequences such that $u^n \rightharpoonup u^*$ and $c^n \rightharpoonup c^*$ in W. If we again use the boundedness of u^n and c^n and the system (1.2), we see that u_t^n and c_t^n lie in a bounded subset of $L^2\left((0,T); \left(H^1(\Omega)\right)^*\right)$. Hence $u_t^n \rightharpoonup u_t^*$ and $c_t^n \rightharpoonup c_t^*$ in $L^2\left((0,T); \left(H^1(\Omega)\right)^*\right)$.

Using the fact that $L^2\left((0,T); H^1(\Omega)\right)$ compactly imbeds into $L^2(Q)$ and employing a compactness result in Simon [27], we have that $u^n \to u^*$ and $c^n \to c^*$ strongly in $L^2\left((0,T); H^1(\Omega)\right)$. With $c_x^n \rightharpoonup c_x^*$ in $L^2(Q)$, we also have the $u^n c_x^n \rightharpoonup u^* c_x^*$ in W.

Using the above convergences, we can pass to the limit in (2.2) if we recognize that

$$\int_0^T \int_0^L \frac{u^n}{u^n+1}\phi\, dx\, dt \to \int_0^T \int_0^L \frac{u^*}{u^*+1}\phi\, dx\, dt \quad \text{in W.}$$

We see that $\int_0^T \int_0^L \left(\frac{u^n}{u^n+1}\right)^2 dx\, dt < \infty$. Consequently, we know that $\frac{u^n}{u^n+1}$ converges weakly to some $\beta \in W$. Since $u^n \to u^*$ strongly in W and u^n is bounded below for each n, then we obtain that $\beta = \frac{u^*}{u^*+1}$.

As we now pass to the limit in the (u^n, c^n) state system in (2.2) we determine that (u^*, c^*) is a weak solution to (1.2) associated with f^*. In order to verify that f^* is an optimal control that minimizes our functional, we must show that $J(f^*) \leq \inf_{f\in U} J(f)$. We employ the lower semicontinuity of the functional with respect to weak convergences.

Hence,

$$\begin{aligned} J(f^*) &= \frac{1}{2}\int_0^T\int_0^L (u^* - z_0)^2 \, dx\, dt + \int_0^T\int_0^L A_1 c^* \, dx\, dt \\ &\quad + \frac{1}{2}\int_0^T\int_0^L (f^*)^2 \, dx\, dt \\ &\leq \lim_{n\to\infty} \int_0^T\int_0^L \frac{1}{2}\left[(u^n - z)^2 + 2A_1 c^n + (f^n)^2\right] dx\, dt \\ &\leq \lim_{n\to\infty} J(f^n) = \inf_{f\in U} J(f). \end{aligned}$$

Consequently, f^* is an optimal control that minimizes $J(f)$. □

A similar existence result holds if we consider the second chemotaxis system (1.3).

3. Optimality Conditions. In this section, we derive the optimality conditions for the chemotaxis system. First, we must develop the sensitivity analysis since we must differentiate the functional with respect to the controls. Secondly, we prove the necessary conditions for the optimal control problem. We determine the adjoint solutions to (1.2) associated with (1.4) as well as the representation for an optimal control. Finally, we prove the uniqueness of the optimality system, and hence, the uniqueness of our optimal control.

THEOREM 3.1. The mapping $f \in A$ $(u, c) \in W \times W$ is differentiable in the following sense:

$$\begin{aligned} \frac{u(f+\varepsilon h) - u(f)}{\varepsilon} &\rightharpoonup \psi \quad \text{in W} \\ \frac{c(f+\varepsilon h) - c(f)}{\varepsilon} &\rightharpoonup \phi \quad \text{in W} \end{aligned}$$

as $\varepsilon \to 0^+$ for any $f \in A$ and $h \in L^\infty(Q)$ such that $(f + \varepsilon h) \in A$. Also ψ and ϕ satisfy

$$\begin{aligned} \psi_t = M\psi_{xx} - (u\phi_x)_x - (\psi c_x)_x - f\psi - hu \quad &\text{in } Q \\ \psi_x(0,t) = \psi_x(L,t) = 0 \quad &\text{for } 0 \leq t \leq T \\ \psi(x,0) = 0 \quad &\text{for } 0 \leq x \leq L \\ \phi_t = D\phi_{xx} + \tfrac{\psi}{(u+1)^2} - \phi \quad &\text{in } Q \\ \phi_x(0,t) = \phi_x(L,t) = 0 \quad &\text{for } 0 \leq t \leq T \\ \phi(x,0) = 0 \quad &\text{for } 0 \leq x \leq L. \end{aligned} \tag{3.1}$$

The proof can be found in the Appendix.

To derive the optimality system and to characterize our optimal control, we must investigate the adjoint variables as well as the adjoint of the operator associated with the (ψ, ϕ) system.

THEOREM 3.2. Given an optimal control f^* and corresponding solutions u and c of (1.2), there exists a weak solution $(p, q) \in W \times W$ satisfying the adjoint system

$$\begin{aligned} -p_t - Mp_{xx} - p_x c_x &= (u - z_0) - f^* p + \tfrac{q}{(u+1)^2} && \text{in } Q \\ -q_t - Dq_{xx} + (up_x)_x &= A_1 - q && \text{in } Q \\ p(x,T) = q(x,T) &= 0 && \text{on } 0 \le x \le L \\ p_x(0,t) = p_x(L,t) = q_x(0,t) &= q_x(L,t) = 0 && \text{for } 0 \le t \le T \end{aligned} \tag{3.2}$$

where $f^* = \min(1, (up)^+)$.

Proof. Let f be an optimal control and (u, c) be its corresponding solution. Let $f + \varepsilon h \in U$ for $\varepsilon > 0$ and u^ε and c^ε be the corresponding weak solution for the state equations (1.2). Application of the technique used to establish existence of solutions to the state system leads to a similar existence result for the adjoint system (3.2). We compute the directional derivative of the cost functional $J(f)$ with respect to f in the direction of h. Since $J(f)$ is the minimum value, we have with the equations (3.1 and 3.2) and integration by parts that

$$\begin{aligned} 0 \;\le\; & \lim_{\varepsilon \to 0^+} \frac{J(f + \varepsilon h) - J(f)}{\varepsilon} \\ =\; & \lim_{\varepsilon \to 0^+} \left[\frac{1}{2} \int_0^T \int_0^L \frac{(u^\varepsilon - z_0)^2 - (u - z_0)^2}{\varepsilon} \, dx\, dt + \int_0^T \int_0^L A_1 \left(\frac{c^\varepsilon - c}{\varepsilon} \right) dx\, dt \right. \\ & \left. + \frac{1}{2} \int_0^T \int_0^L \frac{(f + \varepsilon h)^2 - (f)^2}{\varepsilon} \, dx\, dt \right] \\ =\; & \int_0^T \int_0^L ((u - z_0)\psi + A_1 \phi + fh) \; dx\, dt \\ =\; & \int_0^T \int_0^L (p\psi_t + Mp_x \psi_x - p_x c_x \psi - p_x u \phi_x) \; dx\, dt \\ & + \int_0^T \int_0^L (q\phi_t + Dq_x \phi_x) \; dx\, dt + \int_0^T \int_0^L fh \; dx\, dt \\ & + \int_0^T \int_0^L (p, q) \begin{pmatrix} f & 0 \\ -\frac{1}{(u+1)^2} & 1 \end{pmatrix} \begin{pmatrix} \psi \\ \phi \end{pmatrix} dx\, dt \\ =\; & \int_0^T \int_0^L h\,(f - up) \; dx\, dt. \end{aligned}$$

By standard optimality techniques [18, 8], we find that $f^* = \min(1, (up)^+)$. □

Using the relationship associated with the optimal control and the solution to the chemotaxis system (1.2) and the adjoint system (3.2), we can formulate the optimality system. We note that the chemotaxis system is a system moving forward in time while the adjoint

system is a system marching backward in time.

$$\begin{aligned} u_t - Mu_{xx} + (uc_x)_x &= -\min(1,(up)^+)u \qquad \text{in } Q && (3.3)\\ c_t - Dc_{xx} &= \frac{u}{u+1} - c && (3.4)\\ -p_t - Mp_{xx} - p_x c_x &= (u - z_0) - \min(1,(up)^+)p + \frac{q}{(u+1)^2} && (3.5)\\ -q_t - Dq_{xx} + (up_x)_x &= A_1 - q && (3.6) \end{aligned}$$

subject to

$$\begin{aligned} &u_x(0,t) = u_x(L,t) = c_x(0,t) = c_x(L,t) = 0 && (3.7)\\ &p_x(0,t) = p_x(L,t) = q_x(0,t) = q_x(L,t) = 0 \qquad \text{for } 0 \le t \le T\\ &u(x,0) = u_0(x),\ c(x,0) = c_0(x)\\ &p(x,T) = q(x,T) = 0 \qquad \text{for } 0 \le x \le L. \end{aligned}$$

If we consider instead the second chemotaxis system (1.3), we can establish in a similar manner that the optimality system is

$$\begin{aligned} u_t - Mu_{xx} + (uc_x)_x &= 0 \qquad \text{in } Q && (3.8)\\ c_t - Dc_{xx} &= \frac{u}{u+1} - (1 + \min(1,(cq)^+))c && (3.9)\\ -p_t - Mp_{xx} - p_x c_x &= (u - z_0) && (3.10)\\ -q_t - Dq_{xx} + (up_x)_x &= A_1 - (1 + \min(1,(cq)^+)q && (3.11) \end{aligned}$$

subject to

$$\begin{aligned} &u_x(0,t) = u_x(L,t) = c_x(0,t) = c_x(L,t) = 0 && (3.12)\\ &p_x(0,t) = p_x(L,t) = q_x(0,t) = q_x(L,t) = 0 \qquad \text{for } 0 \le t \le T\\ &u(x,0) = u_0(x),\ c(x,0) = c_0(x)\\ &p(x,T) = q(x,T) = 0 \qquad \text{for } 0 \le x \le L. \end{aligned}$$

THEOREM 3.3. For T sufficiently small, the weak solution of the optimality system (3.3–3.7) is unique.

Proof. Suppose (u,c,p,q) and $(\overline{u},\overline{c},\overline{p},\overline{q})$ are two weak solutions. We first make a change of variables where $\lambda > 0$ is to be chosen,

$$\begin{aligned} u &= e^{\lambda t}w\ , \quad \overline{u} = e^{\lambda t}\overline{w}\ , \quad c = e^{\lambda t}v\ , \quad \overline{c} = e^{\lambda t}\overline{v}\\ p &= e^{\lambda t}y\ , \quad \overline{p} = e^{\lambda t}\overline{y}\ , \quad q = e^{\lambda t}\xi\ , \quad \overline{q} = e^{\lambda t}\overline{\xi}\\ f &= \min(1,(up)^+) \quad \text{and} \quad \overline{f} = \min(1,(\overline{u}p)^+). \end{aligned}$$

We consider the weak formulations of $w - \overline{w}$, $v - \overline{v}$, $y - \overline{y}$, and $\xi - \overline{\xi}$. Then for each of the four representations, we select an appropriate test function. We add the four formulations together and estimate. The details can be found in the Appendix. After

careful simplification, we have with assuming $\theta = \min(M, D)$,

$$\begin{aligned} &\tfrac{1}{2}\int_0^L \left[(w(x,T)-\overline{w}(x,T))^2 + (v(x,T)-\overline{v}(x,T))^2 \right. \\ &\left. + (y(x,0)-\overline{y}(x,0))^2 + \left(\xi(x,0)-\overline{\xi}(x,0)\right)^2\right] dx\,dt \\ &+ \left(\theta - e^{\lambda T}C_7\varepsilon\right)\int_0^T\int_0^L \left[(w-\overline{w})_x^2 + (v-\overline{v})_x^2 + (y-\overline{y})_x^2 + \left(\xi-\overline{\xi}\right)_x^2\right] dx\,dt \\ &+ \left(\lambda - \left(C_8 + C_\varepsilon e^{2\lambda T}\right)\right)\int_0^T\int_0^L \left[(w-\overline{w})^2 + (v-\overline{v})^2 + (y-\overline{y})^2 + \left(\xi-\overline{\xi}\right)^2\right] dx\,dt \\ &\leq 0, \end{aligned} \tag{3.13}$$

where C_ε depends on $\varepsilon > 0$ and the coefficients. Also C_7 and C_8 depend on the coefficients and the bounds of the solutions and their spatial derivatives. We note that the norms on the spatial derivatives are bounded according to the results of Corollary 2.1. In order to establish uniqueness of the solution to the optimality system (3.3–3.7), we choose ε, λ, and T appropriately. First, we choose $\varepsilon < \dfrac{\theta}{C_7}$, then $\lambda > C_8 + C_\varepsilon$. Lastly we have $T < \dfrac{1}{\lambda}\min\left(\dfrac{1}{2}\ln\left(\dfrac{\lambda - C_8}{C_\varepsilon}\right), \ln\left(\dfrac{\theta}{C_7}\right)\right)$. □

A similar argument establishes that the optimality system (3.8–3.12) is also unique.

4. Numerical Scheme. Let us consider the first optimality system (3.3–3.7). In order to characterize the optimal proportion of cells being generated in our model, the optimality system must be solved for the optimal cell and chemoattractant concentrations, and the adjoint variables. There are two issues that must be addressed carefully in the numerical scheme. The first is the opposite orientations of the differential equations. The second is the convection-reaction-diffusion aspect of the system.

The state equations move forward in time from an initial condition, while the adjoint equations move backward in time from a final condition. Following Hackbusch [9], we use the iterative scheme to solve the optimality system (3.3–3.7)

(1) Initialize the adjoint variables, e.g., $p^0(x,t) = q^0(x,t) = 0$.
(2) Using the current adjoint variables p^{j-1}, q^{j-1}, solve the state equations (3.3–3.4) for the state variables u^j, c^j.
(3) Using the current state variables u^j, c^j, solve the adjoint equations (3.5–3.6) for the adjoint variables p^j, q^j.
(4) Repeat 2 & 3 until $\left\|u^{j-1}-u^j\right\|, \left\|c^{j-1}-c^j\right\|, \left\|p^{j-1}-p^j\right\|, \left\|q^{j-1}-q^j\right\| \to 0$.

In order to use this scheme, we must choose an appropriate norm with which to measure convergence. In the examples that follow we will use an approximation to the L^2-norm over $(0,T)\times(0,L)$.

In the optimality system, equations (3.3) and (3.6) are both convection-diffusion equations, while (3.4) and (3.5) are reaction-diffusion equations. The nature of these equations limits the type of numerical scheme that we can use to solve them. In particular, the size of the spatial and temporal discretizations must be chosen with great care in order to avoid the introduction of numerical error. For both the convection-diffusion equations and the reaction-diffusion equations, we use exponential fitting in space, which is a fitted operator method, to approximate the spatial derivative. Fitted operator methods

consist of fitted finite difference operators on uniform meshes—see Miller, O'Riordan and Shishkin [21]. Analysis similar to that of McCartin and Fisackerly [20] shows that their use leads to a more stable numerical scheme than, for example, the use of central differences. Since the state equations and adjoint equations have opposite temporal orientations, we will use forward and backward differences in time, respectively.

Choosing a spatial mesh size $\Delta x = L/n$ and a temporal mesh size of $\Delta t = T/m$, we let

$$\begin{aligned} x_i &= i\Delta x, \quad x_{i+1/2} = (i+1/2)\Delta x, \quad i = 0, \ldots, n \\ t_k &= k\Delta t, \quad k = 0, \ldots, m \\ u_{i,k} &\approx u(x_i, t_k), \quad c_{i,k} \approx c(x_i, t_k), \\ p_{i,k} &\approx p(x_i, t_k), \quad q_{i,k} \approx q(x_i, t_k). \end{aligned}$$

The first state equation in the optimality system can be written in the form

$$u_t = M\left(u_x - uc_x/M\right)_x + F,$$

where $F = -\min(1, (up)^+)u$. This is a convection-diffusion equation which we discretize using forward differences in time and exponential fitting in space, giving

$$\begin{aligned} u_{i,k+1} &= u_{i,k} + \frac{M\triangle t}{(\triangle x)^2}\Big[B\left(-\eta_{i-1/2}\right)u_{i-1,k} + B\left(\eta_{i+1/2}\right)u_{i+1,k} \\ &\quad - \left(B\left(\eta_{i-1/2}\right) + B\left(-\eta_{i+1/2}\right)\right)u_{i,k}\Big] + \triangle t F_{i,k} \end{aligned}$$

where $\eta_{i-1/2} = (c_i - c_{i-1})/M$, and $\eta_{i+1/2} = (c_{i+1} - c_i)/M$ are the cell peclet numbers, and

$$B(x) = \begin{cases} \frac{x}{e^x - 1} & \text{for} \quad x \neq 0 \\ 1 & \text{for} \quad x = 0 \end{cases}$$

is the Bernoulli generating function [21].

The second state equation in the optimality system can be written in the form

$$c_t = Dc_{xx} - c + G,$$

where $G = u/(u+1)$. This is a reaction-diffusion equation which we also discretize using forward differences in time and exponential fitting in space, giving

$$\begin{aligned} c_{i,k+1} &= c_{i,k} + \frac{D\left(\triangle t\right)}{(\triangle x)^2}\frac{z^2}{2\left(\cosh(z) - 1\right)}\left[c_{i-1,k} - 2c_{i,k} + c_{i+1,k}\right] \\ &\quad -(\triangle t)c_{i,k} + (\triangle t)G_{i,k} \end{aligned}$$

where $z = \triangle t/\sqrt{D}$.

The adjoint equations must also be discretized with care, particularly because of the fact that they are backward in time. The adjoint equations can be written in the form

$$\begin{aligned} -p_t &= Mp_{xx} - (-c_x)p_x + H, \\ -q_t &= Dq_{xx} - q - (up_x)_x + A_1, \end{aligned}$$

where $H = (u - z_0) - \min(1, (up)^+)p + q/(u+1)^2$. The first is a reaction-diffusion equation, while the second is a convection-diffusion equation. We discretize using backward

differences in time and exponential fitting in space, giving

$$\begin{aligned} p_{i,k-1} &= p_{i,k} - \frac{M\triangle t}{(\triangle x)^2}\Big[B\left(-\eta_{i-1/2}\right)p_{i-1,k} - 2\left(B\left(\eta_{i-1/2}\right) + B\left(-\eta_{i+1/2}\right)\right)p_{i,k} \\ &\quad + B\left(\eta_{i+1/2}\right)p_{i+1,k}\Big] - H_{i,k}(\triangle t) \\ q_{i,k-1} &= q_{i,k} - \frac{(\triangle t)}{2\left(\cosh(z)-1\right)}\left[q_{i-1,k} - 2q_{i,k} + q_{i+1,k}\right] + (\triangle t)\left[q_{i,k} - A_1\right] \\ &\quad + \frac{(\triangle t)}{4(\triangle x)^2}\Big[\left(u_{i-1,k} + 4u_{i,k} - u_{i+1,k}\right)p_{i-1,k} - 8u_{i,k}p_{i,k} \\ &\quad + \left(-u_{i-1,k} + 4u_{i,k} + u_{i+1,k}\right)p_{i+1,k}\Big]. \end{aligned}$$

The flux boundary conditions for all of the variables can easily be accommodated by the numerical scheme. All of the approximations are first order in time and second order in space provided that the stability conditions

$$\Delta t < \frac{(\Delta x)^2}{D(B(-\eta) + B(\eta))}$$

$$\Delta t < \frac{(\Delta x)^2}{2D}\frac{2(\cosh(z)-1)}{z^2}$$

where $\eta = (\Delta x)c_x/M$ is the cell peclet number and $z = \Delta x/\sqrt{D}$, are satisfied.

This scheme can readily be adapted for use with the second optimality system (3.8–3.12).

5. Examples. In each of the examples that follow, we consider cells and a chemoattractant with diffusion coefficients of $M = 0.7$ and $D = 1$, respectively. We set $A_1 = 1$ in our objective functional and define a spatial mesh size of $\Delta x = 1/30$ and a temporal mesh size of $\Delta t = 0.00005$.

In the first example

$$u_0 = 1.5 + 5.9e^{-55.262(x-.2)^2},\ c_0 = 0.5 + 5.9e^{-55.262(x-.25)^2},$$
$$z_0 = 0.9 + 0.1e^{-55.262(x-.2)^2},$$

we attempt to move the area of highest cell concentration and reduce the number of cells present. Figure (1) shows the chemotaxis system in the absence of any control terms. Figure (2) illustrates the optimal controls for the linear control of cells and chemoattractant. In both cases, the optimal control is zero, indicating that linear control of the cells or chemoattractant has no impact on the chemotaxis system.

In the second example

$$u_0 = 10.5,\ c_0 = 2.5 + 1.1e^{-55.262(x-.5)^2},\ z_0 = 10.5$$

we attempt to maintain a constant cell distribution in the presence of a nonconstant chemoattractant distribution. Figure (3) shows the chemotaxis system in the absence of any control terms. Figure (4) show the optimal controls for the linear control of cells and chemoattractant. In both cases, the optimal control is only nonzero for a brief period of time. The rapid decay to zero of the optimal control indicates that the control has

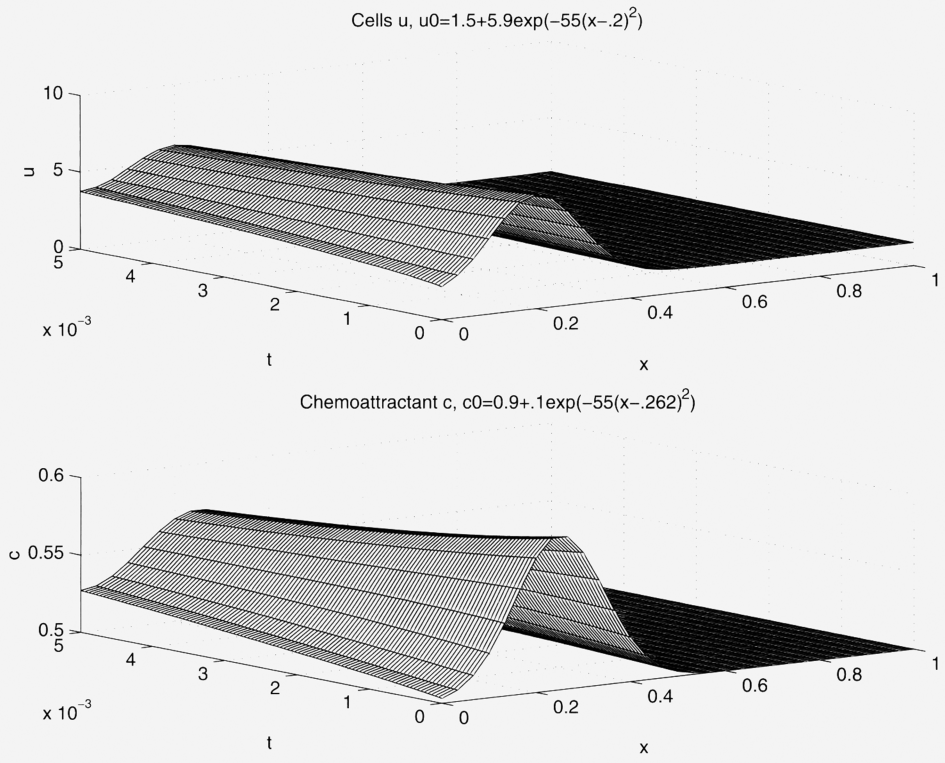

FIG. 1. Chemotaxis system for Example 1.

a minimal effect on the chemotaxis system, and comparison of the solutions at the final time confirms this.

Theoretically, the introduction of linear control terms in a chemotaxis system should facilitate the control of such a system. However, these examples indicate that the introduction of linear control terms is not sufficient in order to effectively control the chemotaxis system. Preliminary investigations suggest that a nonlinear control will lead to more practical results.

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6. Appendix. We address the details of the proof of Theorem 3.1 and the weak formulation of the optimality system needed in the proof of Theorem 3.3 here.

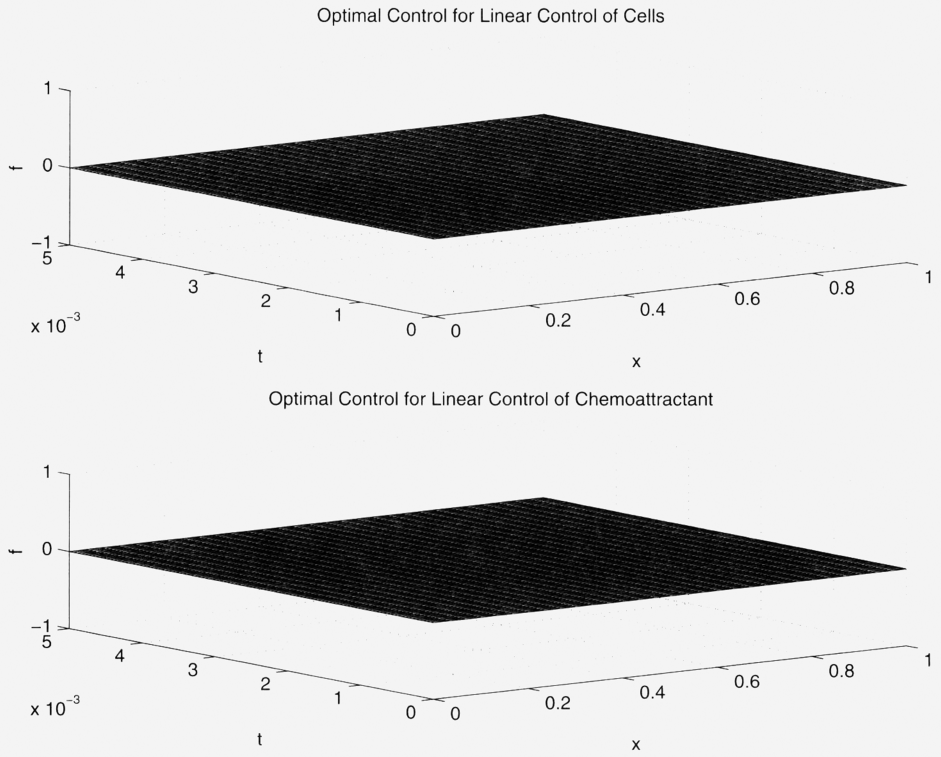

FIG. 2. Optimal Controls for Example 1.

THEOREM 6.1. The mapping $f \in A\,(u, c) \in W \times W$ is differentiable in the following sense:

$$\frac{u(f+\varepsilon h) - u(f)}{\varepsilon} \rightharpoonup \psi \quad \text{in W}$$
$$\frac{v(f+\varepsilon h) - c(f)}{\varepsilon} \rightharpoonup \phi \quad \text{in W}$$

as $\varepsilon \to 0^+$ for any $f \in A$ and $h \in L^\infty(Q)$ such that $(f + \varepsilon h) \in A$. Also ψ and ϕ satisfy

$$\begin{aligned} \psi_t &= M\psi_{xx} - (u\phi_x)_x - (\psi c_x)_x - f\psi - hu \quad \text{in } Q \\ \psi_x(0,t) &= \psi_x(L,t) = 0 \quad \text{for } 0 \le t \le T \\ \psi(x,0) &= 0 \quad \text{for } 0 \le x \le L \\ \phi_t &= D\phi_{xx} + \tfrac{\psi}{(u+1)^2} - \phi \quad \text{in } Q \\ \phi_x(0,t) &= \phi_x(L,t) = 0 \quad \text{for } 0 \le t \le T \\ \phi(x,0) &= 0 \quad \text{for } 0 \le x \le L. \end{aligned} \tag{6.1}$$

Proof. We establish the necessary convergences by analyzing the weak forms of the solutions for $\frac{u^\varepsilon - u}{\varepsilon}$ and $\frac{c^\varepsilon - c}{\varepsilon}$ where $u^\varepsilon = u(f + \varepsilon h)$, $c^\varepsilon = c(f + \varepsilon h)$, $u = u(f)$, $c = c(f)$ with $h \in L^\infty$ and ε small. First, we let $u^\varepsilon = e^{\lambda t} w^\varepsilon$, $c^\varepsilon = e^{\lambda t} z^\varepsilon$, $u = e^{\lambda t} w$, and $c = e^{\lambda t} z$

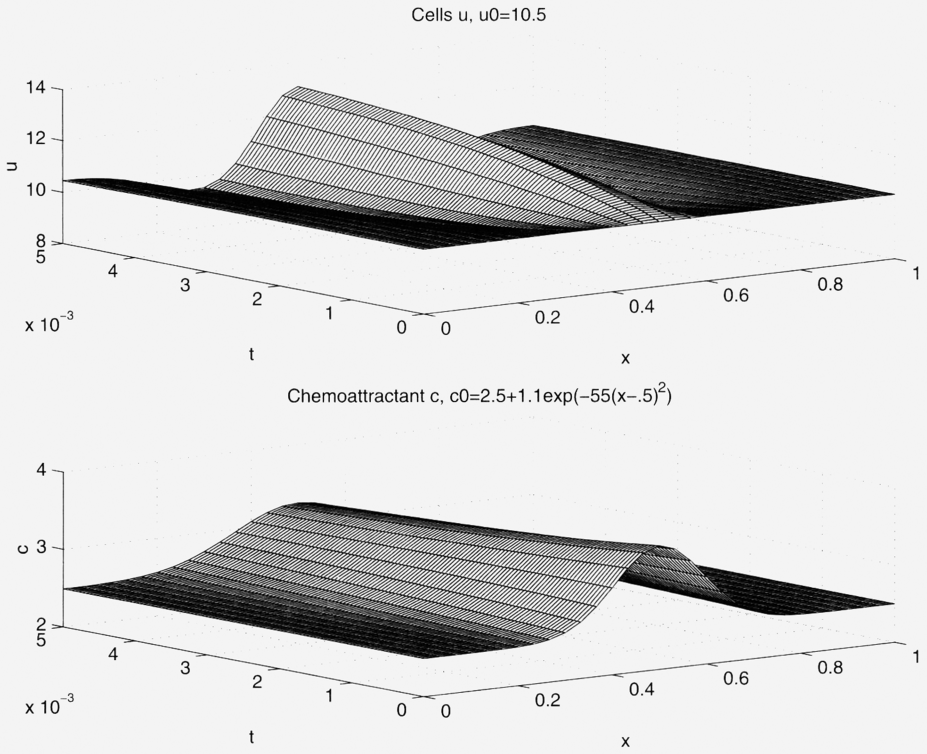

FIG. 3. Chemotaxis system for Example 2.

for $\lambda > 0$ to be chosen. Then we sum the weak forms for the $\frac{w^\varepsilon - w}{\varepsilon}$ and $\frac{z^\varepsilon - z}{\varepsilon}$ equations.

$$\begin{aligned}
&\tfrac{1}{2}\int_0^L \left[\left(\tfrac{w^\varepsilon - w}{\varepsilon}\right)^2(x,t) + \left(\tfrac{z^\varepsilon - z}{\varepsilon}\right)^2(x,t)\right]\,dx + M\int_0^t\int_0^L \left[\left(\tfrac{w^\varepsilon - w}{\varepsilon}\right)_x\right]^2\,dx\,dt \qquad (6.2)\\
&\quad + \int_0^t\int_0^L D\{\left[\left(\tfrac{z^\varepsilon - z}{\varepsilon}\right)_x\right]^2 - \tfrac{1}{\varepsilon}\left[\left(e^{\lambda t}w^\varepsilon z_x^\varepsilon\right) - e^{\lambda t}wz_x\right]\left(\tfrac{w^\varepsilon - w}{\varepsilon}\right)_x\}\,dx\,dt\\
+\lambda\int_0^t\int_0^L &\left[\left(\tfrac{w^\varepsilon - w}{\varepsilon}\right)^2 + \left(\tfrac{z^\varepsilon - z}{\varepsilon}\right)^2\right]\,dx\,dt - \int_0^t\int_0^L \tfrac{1}{\varepsilon}\left[\tfrac{w^\varepsilon}{e^{\lambda t}w^\varepsilon + 1} - \tfrac{w}{e^{\lambda t}w + 1}\right]\left(\tfrac{z^\varepsilon - z}{\varepsilon}\right)\,dx\,dt\\
&= -\int_0^t\int_0^L \left[\tfrac{(f+\varepsilon h)w^\varepsilon - fw}{\varepsilon}\right]\left(\tfrac{w^\varepsilon - w}{\varepsilon}\right) - \left(\tfrac{z^\varepsilon - z}{\varepsilon}\right)^2\,dx\,dt.
\end{aligned}$$

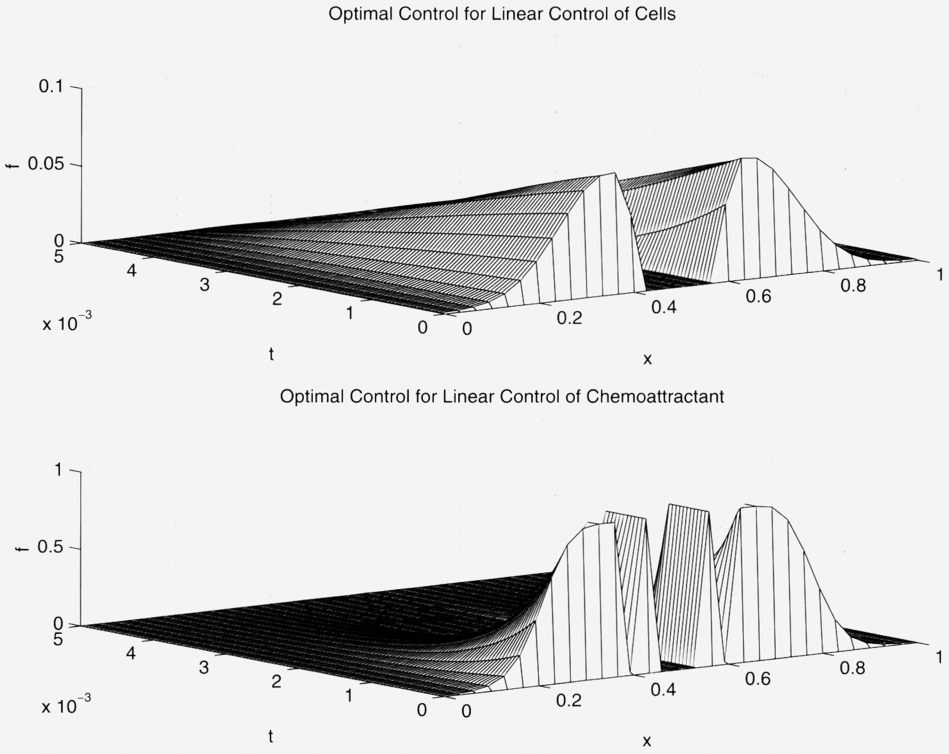

FIG. 4. Optimal Controls for Example 2.

Applying Cauchy's inequality, using the L^∞ bounds on w^ε and z_x, we obtain with $m = \min(M, D)$ that

$$\begin{aligned} &\frac{1}{2}\int_0^L \left[\left(\frac{w^\varepsilon(x,t)-w(x,t)}{\varepsilon}\right)^2 + \left(\frac{z^\varepsilon(x,t)-z(x,t)}{\varepsilon}\right)^2\right] dx \qquad (6.3)\\ &+(\lambda - C_4 e^{\lambda T} - C_1)\int_0^t\int_0^L \left[\left(\frac{w^\varepsilon - w}{\varepsilon}\right)^2 + \left(\frac{z^\varepsilon - z}{\varepsilon}\right)^2\right] dx\,dt\\ &+(m - e^{\lambda T}C_3\varepsilon)\int_0^t\int_0^L \left(\left[\left(\frac{w^\varepsilon - w}{\varepsilon}\right)_x\right]^2 + \left[\left(\frac{z^\varepsilon - z}{\varepsilon}\right)_x\right]^2\right) dx\,dt\\ \leq\quad & C_2\int_0^T\int_0^L h^2\, dx\,dt \end{aligned}$$

where C_1, C_2, C_3, and C_4 depend on the coefficients and the bounds of the concentrations. By choosing $e < \frac{m}{C_3}$ and $\lambda > C_1 + C_4$, then we conclude that

$$\left\|\frac{w^\varepsilon - w}{\varepsilon}\right\|_W + \left\|\frac{z^\varepsilon - z}{\varepsilon}\right\|_W \leq C_2\int_0^T\int_0^L h^2\, dx\,dt. \qquad (6.4)$$

Since $\frac{w^\varepsilon - w}{\varepsilon}$ and $\frac{z^\varepsilon - z}{\varepsilon}$ are bounded in W, then we can extract a weakly convergent subsequence. Moreover, we have

$$\frac{u^\varepsilon - u}{\varepsilon} \rightharpoonup \psi \quad \text{and} \quad \frac{c^\varepsilon - c}{\varepsilon} \rightharpoonup \phi \quad \text{in } W.$$

Similar to Theorem 2.2 we see that

$$\frac{u^\varepsilon - u}{\varepsilon} \psi \quad \text{and} \quad \frac{c^\varepsilon - c}{\varepsilon} \phi \quad \text{in } L^2(Q).$$

We can also obtain that $u^\varepsilon \; u$ and $c^\varepsilon \; c$ in W from (6.4). Essentially,

$$\|w^\varepsilon - w\|_W + \|z^\varepsilon - z\|_W \leq C_2 \varepsilon^2 \int_0^T \int_0^L h^2 \, dx \, dt.$$

Thus $w^\varepsilon \to w$ and $z^\varepsilon \to z$ in W, and hence $u^\varepsilon \to u$ and $c^\varepsilon \to c$ in W. It is noted that strong convergence for $u^\varepsilon \to u$ is needed when we pass to the limit in the equations satisfied by $\frac{u^\varepsilon - u}{\varepsilon}$ and $\frac{c^\varepsilon - c}{\varepsilon}$. Therefore, when we pass to the limit in this system (6.2), ψ and ϕ solve the system (6.1). □

LEMMA 6.2. The appropriate weak formulation for estimation of the optimality system (3.3–3.7) is proven.

Proof.

$$\begin{aligned}
&\int_0^T \int_0^L \left[(w-\overline{w})_t (w-\overline{w}) + (v-\overline{v})_t (v-\overline{v}) - (y-\overline{y})_t (y-\overline{y}) - \left(\xi - \overline{\xi}\right)_t \left(\xi - \overline{\xi}\right) \right] dx\, dt \\
&\quad + M \int_0^T \int_0^L \left[(w-\overline{w})_x^2 + (y-\overline{y})_x^2 \right] dx\, dt + D \int_0^T \int_0^L \left[(v-\overline{v})_x^2 + \left(\xi - \overline{\xi}\right)_x^2 \right] dx\, dt \\
&\quad + \lambda \int_0^T \int_0^L \left[(w-\overline{w})^2 + (v-\overline{v})^2 + (y-\overline{y})^2 + \left(\xi - \overline{\xi}\right)^2 \right] dx\, dt \\
&= \int_0^T \int_0^L e^{\lambda t} (w v_x - \overline{w}\overline{v}_x)(w-\overline{w})_x \, dx\, dt - \int_0^T \int_0^L e^{\lambda t} \left(fw - \overline{f}\overline{w}\right)(w-\overline{w}) \, dx\, dt \\
&\quad + \int_0^T \int_0^L \left(\frac{w}{e^{\lambda t} w + 1} - \frac{\overline{w}}{e^{\lambda t}\overline{w} + 1} \right)(v-\overline{v}) \, dx\, dt - \int_0^T \int_0^L e^{\lambda t} (v-\overline{v})^2 \, dx\, dt \\
&\quad + \int_0^T \int_0^L e^{\lambda t} \left[y_x v_x - \overline{y}_x \overline{v}_x \right](y-\overline{y}) \, dx\, dt + \int_0^T \int_0^L e^{2\lambda t} (w-\overline{w})(y-\overline{y}) \, dx\, dt \\
&\quad - \int_0^T \int_0^L \left(fy - \overline{f}\overline{y}\right)(y-\overline{y}) \, dx\, dt \\
&\quad + \int_0^T \int_0^L \left(\frac{\xi}{(e^{\lambda t} w + 1)^2} - \frac{\overline{\xi}}{(e^{\lambda t}\overline{w} + 1)^2} \right)(y-\overline{y}) \, dx\, dt \\
&\quad + \int_0^T \int_0^L e^{\lambda t} \left[y_x w - \overline{y}_x \overline{w} \right] \left(\xi - \overline{\xi}\right)_x \, dx\, dt - \int_0^T \int_0^L \left(\xi - \overline{\xi}\right)^2 \, dx\, dt.
\end{aligned}$$

The first term on the right hand side of the previous equation is estimated,

$$\begin{aligned}
&\int_0^T \int_0^L e^{\lambda t} (w v_x - \overline{w}\overline{v}_x)(w-\overline{w})_x \, dx\, dt \\
= \; &\int_0^T \int_0^L e^{\lambda t} \left[(w-\overline{w}) v_x (w-\overline{w})_x + \overline{w} (v-\overline{v})_x (w-\overline{w})_x \right] dx\, dt \\
\leq \; &e^{\lambda t} \widetilde{C} \int_0^T \int_0^L \left[(w-\overline{w})^2 + \frac{\varepsilon}{2} (w-\overline{w})_x^2 \right] dx\, dt \\
&+ e^{\lambda t} \widehat{C} \int_0^T \int_0^L \left[C_\varepsilon (v-\overline{v})_x^2 + \frac{\varepsilon}{2} (w-\overline{w})_x^2 \right] dx\, dt
\end{aligned}$$

where $\widetilde{C}$, $\widehat{C}$ depend on the L^∞ norms of v_x and w. The norms of v_x and w are bounded according to the results in Corollary 2.1. We use similar concepts to bound the other terms. □

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