Effects of Diffusivity and Chemotaxis on Cell Growth

Project for Math 447/647
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1 Introduction

We are interested in the effects of diffusivity and chemotaxis on the competition of several species for a limited resource. Diffusivity of cells is also called motility in some engineering literature. Chemotaxis is the oriented movement of cells in response to the concentration gradient of chemical substances in their environment. It is "anti-diffusion". It was observed experimentally that motility and chemotaxis of cells play a dominant role in the cell growth: when several species of cells compete for a limited resource, the species with smaller diffusion rate and larger chemotaxis rate enjoys better growth, even when the other species have superior growth kinetics.

The mathematical modeling on chemotaxis by using PDE's started only in 1970 by Keller and Segal (see [KS]). To illustrate the general idea involved, consider a species of cells which responds chemotactically to a chemical which attracts the cells. Let $u(x,t)$ and $v(x,t)$ be the concentration of the chemical and density of cells, respectively. The chemical is assumed to be diffusive with diffusion coefficient $= D_1$; The cells are assumed both diffusive and chemotactic with diffusion coefficient $= D_2$; The chemotaxis flux of cells is assumed to have the form

$$\overrightarrow{J}_{chemo} = \chi v \phi'(u) \nabla u, \tag{1.1}$$

where χ is a nonnegative constant, called chemotaxis coefficient; $\phi'(u) > 0$, and ∇u is the gradient of u with respect to the spatial variable x.

Question 1. Explain (or speculate) the rationale of (1.1): Why is the chemotaxis flux in the same direction of ∇u? Why is the flux proportional to v? In the engineering literature, typical choices for $\phi(u)$ are $\phi(u) = u$, $\phi(u) = \ln(c+u)$ (c being a positive constant), etc. What is the reason for each of these choices?

Now we have a system of two PDE's for u and v:

$$\begin{cases} u_t = D_1 \Delta u + h(u,v), \\ v_t = \nabla \cdot (D_2 \nabla v - \chi v \phi'(u) \nabla u) + k(u,v) \end{cases} \tag{1.2}$$

where $h(u, v)$ is the creation-degradation rate of the chemical, and $k(u, v)$ is the birth-death rate of cells.

Question 2. Use the transport equation to derive (1.2).

Physiologists are interested in the effects of cell motility and chemotaxis on the population growth. To elucidate such effects, Lauffenburger, Aris and Keller [LAK] proposed a mathematical model for the situation of a single bacterial population in a one-dimensional medium with finite lenth, with growth limited by a nutrient diffusing from an adjacent phase not accesible to the bacteria. Their non-dimensionalized model is

$$\begin{cases} u_t = u_{xx} - f(u)v, & 0 < x < 1,\ t > 0, \\ v_t = (d_1 v_x - \chi v \phi'(u) u_x)_x + (kf(u) - \theta)v, & 0 < x < 1,\ t > 0, \\ u_x(0,t) = 0, \quad u_x(1,t) = h(1 - u(1,t)), & t > 0, \\ d_1 v_x - \chi v \phi'(u) u_x = 0, & x = 0, 1,\ t > 0 \end{cases} \tag{1.3}$$

Intuitively, this models bacteria in a lake where $x = 0$ represents the floor of the lake and $x = 1$ its surface. Here u is the concentration of the nutrient(e.g., oxygen) and v the density of the bacteria; $f(u)$ is the consumption rate of the nutrient per cell; the term $(kf(u) - \theta)v$ in the v-equation represents the fact that the bacteria have a Malthusian growth with $kf(u)$ and the positive constant θ measuring the respective birth and death rates; in the adjacent phase (i.e., the interval $(0, \infty)$) the (non-dimensionalized) concentration of nutrient (oxygen) is $u \equiv 1$; h is a positive constant, called transport coefficient. $u(1, t)$ is understood as $\lim_{x \to 1^-} u(x, t)$.

Question 3. Interpret the boundary conditions in plain English (so people on the street can understand you).

$f(u)$ is assumed to satisfy $f(0) = 0$ and $f'(u) > 0$.

Question 4. What is the rationale of this assumption?

We shall proceed to study the effects of diffusivity d_1 and chemotaxis coefficient χ on the solutions (u, v) of the system (1.3) in the following section; after that, we shall modify the model to study "competition-exclusion" and co-existence of two species of cells competing for the same nutrient.

2 Single species model (1.3)

Since (u, v) represent concentration and density (resp.), we will be only interested in the nonnegative solutions of (1.3). The simplest solutions of (1.3) are the ones that are independent of time t; such solutions are called *steady states*.

Question 5. Check that the constant function $(u, v) \equiv (1, 0)$ is a steady state of (1.3). What is meaning of this steady state? Show that the only constant(in x-variable) steady state is $(1, 0)$.

This constant steady state is called a trivial steady state. We are interested in non-trivial ones. Zeng [Z] proved that nontrivial steady states exist if $kf(1) > \theta$, and do not exist if $kf(1) \leq \theta$. The existence proof is beyond the scope of this project, but the non-existence proof is an exercise in Calculus.

Question 6. Let $(u(x), v(x)$ be an arbitrary nonnegative steady state. (i) Prove that $u'(x) \geq 0$ and $u(x) \leq 1$ for $x \in [0, 1]$; (ii) If $kf(1) \leq \theta$, prove that $v \equiv 0$ and $u \equiv 1$ on $[0, 1]$, i.e., in this case, the only steady state is the trivial one.

It is proved by Wang [W] that if $kf(1) \leq \theta$, then any time-dependent solution of (1.3) converges to the trivial steady state as $t \to \infty$ (i.e., the trivial steady state is a global attractor). On the other hand, the nontrivial steady state (that exists when $kf(1) > \theta$) must be positive (i.e, $u(x) > 0$ and $v(x) > 0$ on [0,1]) and strictly increasing, as proved by Zeng [Z]; and this steady state is *believed*(not proved) to be a global attractor.

Question 7. Numerically simulate what is said in the above paragraph. You may choose the functions and parameters in (1.3) as follows

$$f(u) = u, \quad \phi'(u) = 1, \quad h = 4 \tag{2.1}$$

(the case investigated by former Tulane math major Brandon Chabaud [C]). Choose your own d_1, χ, k, θ and initial value $(u(x, 0), v(x, 0))$ (remember u, v are concentration and density and therefore must be at least nonnegative). You should simulate on several initial values, to be convincing. You may use a built-in PDE solver on Matlab, called pdepe. See
http://www.mathworks.com/access/helpdesk/help/techdoc/ref/pdepe.html
for details.

Wang [W] studied the behavior of positive steady states (recall they only exist when $kf(1) > \theta$) as the important parameters d_1 and χ vary. In particular, Wang proved when either diffusivity is small (i.e., as $d_1 \to 0$) or chemotaxis is large(i.e., $\chi \to \infty$), $u(x)$ is close to be the constant c such that $kf(c) = \theta$, and $v(x)$ concentrates at the boundary point $x = 1$ like half of the δ-function centered at that point; moreover, the total bacteria population $\int_0^1 v(x)dx$ is close to $kh(1-c)/\theta$, which is the maximum of $\int_0^1 v(x)dx$. Wang also proved that in the opposite scenario when diffusivity is large and chemotaxis is small: $d_1/\chi \to \infty$, then $v(x)$ converges to a positive constant on $[0, 1]$.

Question 8. Simulate what is said in the above paragraph. In case you can't find a solver for the steady state problem, just run the time-dependent simulation of (1.3) with long enough time.

Question 9. What insights have you gained? For example, explain heuristically why it is an advantage for bacteria to have small diffusivity and/or large chemotaxis?

3 Two-species competition model

In this section, we consider the situation of two species of bacteria competing for the same nutrient, where the growth kinetics of both species are identical but their diffusion and chemotaxis coefficients are different. The interest is in the possibility of "competition exclusion" and stable coexistence, attributable solely to diffusivity and chemotaxis. Let the competing species have density function w and to *focus solely on the effect of diffusivity and chemotaxis, we assume that both species have the same consumption rate of the nutrient, and the same birth and death rates.* The model is

$$\begin{cases} u_t = u_{xx} - f(u)(v+w), & 0<x<1, t>0, \\ v_t = (d_1 v_x - \chi_1 v\phi'(u)u_x)_x + (kf(u)-\theta)v, & 0<x<1, t>0, \\ w_t = (d_2 w_x - \chi_2 w\phi'(u)u_x)_x + (kf(u)-\theta)w, & 0<x<1, t>0, \\ u_x(0,t)=0, \;\; u_x(1,t) = h(1-u(1,t)), & t>0, \\ d_1 v_x - \chi_1 v\phi'(u)u_x = 0 = d_2 w_x - \chi_2 w\phi'(u)u_x, & x=0,1, \; t>0. \end{cases} \tag{3.1}$$

Similar to the case of single species, if $kf(1) \le \theta$ then the only nonnegative steady state of (3.1) is the trivial one: $(u, v, w) = (1, 0, 0)$; if $kf(1) > \theta$, then in addition to the trivial steady state, we have two semi-trivial steady states: $(u_1(x), v_1(x), 0)$ and $(u_2(x), 0, w_2(x))$, where $u_{1,2}(x)$, $v_1(x)$ and $w_2(x)$ are positive on $[0, 1]$. Again, as in the case of (1.3), when $kf(1) \le \theta$ all time-dependent solutions of (3.1) converge to the trivial steady state $(1, 0, 0)$; and thus both species go extinct in the long run. This effect is not due to diffusion and chemotaxis, rather, it is due to the defect in their growth kinetics k,, f, and θ.

So from now on, assume $kf(1) > \theta$.

Wang and Wu [WW] proved results that indicate what are illustrated in the diagrams attached. In the remainder of this project, we simulate these theoretical results. You should use the following parameters:

$$f(u) = u, \quad \phi'(u) = 1, \quad h = 4, \quad k = 13, \quad \theta = 2.5 \tag{3.2}$$

Question 10 (*Effects of diffusion in the non-chemotactic case*). Set $\chi_1 = 0 = \chi_2$. Simulate both cases $d_1 < d_2$ and $d_1 > d_2$. Use initial values $(u(x,0), v(x,0)$ that are boring as well as ones with one component much larger than the other. Do you see the semi-trivial steady states? Tell the moral of the story.

Question 11 (*Effects of chemotaxis*). Set $d_1 = d_2 = 1$. Simulate both cases $\chi_1 < \chi_2$ and $\chi_1 > \chi_2$...(see Question 10 for requirements).

Question 12 (*Combined Effects of diffusion and chemotaxis*). For the case when $(d_1, \chi_1) = (1, 0)$, numerically find a pair (d_2, χ_2) in each of the Regions A, B and C (see the attached figure)–you need to use graphs of solutions of (3.1) to back you up. Do the same for the case when $(d_1, \chi_1) = (1, 0.2)$, for this case also find d_0.

References

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