# EFFECTS OF CELL MOTILITY AND CHEMOTAXIS ON MICROBIAL POPULATION GROWTH

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ABSTRACT A mathematical model is developed to elucidate the effects of biophysical transport processes (nutrient diffusion, cell motility, and chemotaxis) along with biochemical reaction processes (cell growth and death, nutrient uptake) upon steady-state bacterial population growth in a finite one-dimensional region. The particular situation considered is that of growth limitation by a nutrient diffusing from an adjacent phase not accessible to the bacteria. It is demonstrated that the cell motility and chemotaxis properties can have great influence on steady-state population size. In fact, motility effects can be as significant as growth kinetic effects, in a manner analogous to diffusion- and reaction-limited regimes in chemically reacting systems. In particular, the following conclusions can be drawn from our analysis for bacterial populations growing at steady-state in a confined, unmixed region: (*a*) Random motility may lead to decreased population density; (*b*) chemotaxis can allow increased population density if the chemotactic response is large enough; (*c*) a species with superior motility properties can outgrow a species with superior growth kinetic properties; (*d*) motility effects become greater as the size of the confined growth region increases; and (*e*) motility effects are diminished by significant mass-transfer limitation of the nutrient from the adjacent source phase. The relationships of these results for populations to previous conclusions for individual cells is discussed, and implications for microbial competition are suggested.

## INTRODUCTION

In studying the dynamics of microbial populations, investigators have focused primarily on well-mixed, spatially uniform systems. The chemostat has been the most widely used experimental device for studies of growth and growth-associated processes and of interactions between mixed populations. Hence, the mathematical models used to interpret and predict experimental results have been developed under the assumption of uniform spatial distribution of chemical concentration and cell population density. These models have led to great progress in the understanding of cell growth, nutrient utilization, and product-formation kinetics. This information regarding microbial reaction kinetics has been usefully applied to many problems of biochemical and ecological importance.

The fact remains, however, that in numerous situations of engineering interest the environment is not well-mixed, so that spatial gradients in chemical concentration and cell population density may exist. Such a condition may be common in natural microbial environments, such as soil, films, and bodies of water, and mammalian hosts. Important contemporary problems that might fall into the category of spatially distributed cell population systems are the ecology of pathogenic bacteria in mammalian hosts, microbial degradation of oil spills, and microbial fouling of marine surfaces.

Further, motility (i.e., self-propelled movement requiring utilization of energy) is extremely common among microbial species, and the phenomenon of chemotaxis is widespread in motile species (1–3). Motility in its basic form is random, roughly analagous to Brownian motion (4). Chemotaxis is complex movement in which the net direction of cell movement is biased by the concentration gradient of some chemical substance (4). The substance is an attractant (positive chemotaxis) if the net cell movement is toward higher chemical concentration; it is a repellent (negative chemotaxis) if the movement is toward lower concentration. Attractants are commonly substances favorable for cell growth, while repellents are often substances with some harmful effect (1–3, 5). For example, oxygen is often an attractant for aerobic bacteria and a repellent for anaerobic bacteria (2). To emphasize the widespread occurrence of chemotactic responses by common bacterial species to a variety of important chemical species, we have presented in Table I a list of some responses compiled from literature sources.

We thus note that (*a*) many situations of biological importance can allow nonuniform spatial distribution of

TABLE I
CLASSIFICATION OF SOME BACTERIAL CHEMOTACTIC RESPONSES

| Genus | Classes of attractants | Classes of repellents |
|---|---|---|
| *Escherichia* | sugars | pH extremes |
| | amino acids | aliphatic alcohols |
| | $O_2$ | |
| *Pseudomonas* | sugars | inorganic ions |
| | amino acids | pH extremes |
| | nucleotides | amino acids |
| | vitamins | |
| | $O_2$ | |
| | ammonium ions | |
| *Bacillus* | sugars | inorganic ions |
| | amino acids | pH extremes |
| | $O_2$ | metabolic poisons |
| *Salmonella* | sugars | aliphatic alcohols |
| | amino acids | |
| | $O_2$ | |
| *Vibrio* | amino acids | |
| | $O_2$ | |
| *Spirillum* | sugars | inorganic ions |
| | amino acids | pH extremes |
| | $O_2$ | |
| *Rhodospirillum* | nucleotides | pH extremes |
| | sulfhydryl compounds | poisons |
| *Clostridium* | | $O_2$ |
| *Bdellovibrio* | amino acids | |
| *Proteus* | sugars | inorganic acids |
| | amino acids | pH extremes |
| | $O_2$ | |
| *Erwinia* | sugars | inorganic ions |
| | | pH extremes |
| *Sarcina* | | inorganic ions |
| | | pH extremes |
| *Serratia* | sugars | inorganic ions |
| | amino acids | pH extremes |
| | $O_2$ | |
| *Bordetella* | $O_2$ | |
| *Pasteurella* | $O_2$ | |
| *Marine bacteria* | algal culture filtrates | heavy metals |
| | | toxic hydrocarbons |

The data of this summary was compiled from references 1–3.

cell population densities and chemical concentrations; and (*b*) many common bacterial species are motile and chemotactic to a variety of chemicals. The obvious question is whether the motility properties of bacteria have a significant effect on population growth and interactions in such systems. This question has been the subject of speculation in microbiological literature (1, 3, 6, 7), and there are limited experimental data indicating that motility properties may not only be an important factor in governing population growth and interactions, but sometimes can be the dominant factor. In a well-mixed environment, immotile *Acinetobacter* will outgrow aerotactic (positively chemotactic to oxygen) *Pseudomonas* when the two species compete for oxygen; in a similar but unmixed environment *Pseudomonas* dominates (8). An aerotactic parent strain of *Pseudomonas* and an immotile mutant grow to equal population sizes in a well-mixed vessel, but in an unmixed vessel the parent outgrows the mutant by a factor of 10–30 within 24 h (9). Similary, an aerotactic strain of *Salmonella* multiplied over a thousand times faster than an immotile strain in a static aerobic broth (10). A species of *Proteus* chemotactically attracted by amino acids prevails against a randomly motile mutant in a semi-solid agar medium, although both grow equally well in a shaken broth (11). Freter et al. (12) have presented results showing that the ability of bacterial species to establish themselves in the mammalian gut flora can depend critically upon whether the species is chemotactic, randomly motile, or immotile, as well as on growth and adhesion properties.

Though it is therefore apparent that motility properties can be key factors in microbial growth and interactions, the important parameters and parameter relationships are not known. That is, it cannot be predicted for a given situation what population sizes and distributions will occur. Further, even when experimental results are available their interpretation is unclear. The biochemical reaction processes (cell growth and death, chemical species utilization and production) are fairly well studied but the effects of coupling with the biophysical transport processes (chemical diffusion, cell motility and chemotaxis) are not.

In this work we begin to address the question of the combined effects of reaction kinetics and transport phenomena in microbial reacting systems. We investigate here a simple problem—the growth of a single bacterial population in a stagnant medium of finite length in one dimension, with growth limited by a nutrient diffusing from an adjacent phase not accessible to the bacteria. This is referred to as "confined growth." It might describe, for example, the growth of a single cell population in water, limited by the supply of oxygen from an adjacent air source.

## MATHEMATICAL MODEL

Consider a population of bacterial cells in a finite one-dimensional region of length $L$, with a diffusible, growth-rate–limiting chemical substrate entering the region from the boundary at $x = L$, as shown in Fig. 1. We can write continuum conservation equations for cell biomass density, $b$, and substrate concentration, $s$, within the region $0 \le x \le L$:

$$\frac{\partial b}{\partial t} = -\frac{\partial J_b}{\partial x} + G_b \tag{1}$$

$$\frac{\partial s}{\partial t} = -\frac{\partial J_s}{\partial x} - G_s \tag{2}$$

where $J_b$ and $J_s$ are the cell and substrate fluxes and $G_b$ and $G_s$ are the net generation and consumption rates of bacteria and substrate, respectively.

For the cell generation rate, we use Monod's model for exponential growth, with utilization of biomass representing cell death (13)

$$G_b = f(s)\, b - k_e b = \frac{ks}{K + s} b - k_e b. \tag{3}$$

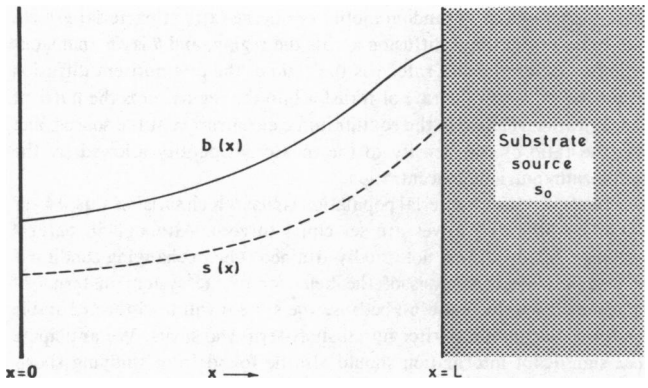


FIGURE 1 Illustration of model one-dimensional growth system. The bacteria are confined to the region between $x = 0$ and $x = L$. The substrate enters the system at $x = L$.

Growth inhibition at high bacterial densities is not considered here. The substrate consumption rate is determined by uptake by the cells:

$$G_s = \frac{1}{Y} f(s)\, b = \frac{1}{Y} \frac{ks}{K + s} b. \tag{4}$$

For the substrate flux expression we use Fick's law for chemical diffusion:

$$J_s = - D \frac{\partial s}{\partial x}. \tag{5}$$

If the volume fraction of cells is large the diffusivity $D$ should be replaced by an effective diffusivity through heterogeneous media, such as the expression developed by Fricke (14). This effective diffusivity may be slightly smaller than the pure solution diffusivity if the diffusivity within the cell is less than in solution.

The cell flux can be expressed phenomenologically as the combination of random and chemotactic movement (15)

$$J_b = - \mu \frac{\partial b}{\partial x} + b \chi \frac{\partial s}{\partial x}. \tag{6}$$

For attractants $\chi$ is positive; for repellents $\chi$ is negative. $\mu$ is the random motility coefficient for the cells, analogous to the chemical diffusivity. For common flagellated bacteria such as *Escherichia* and *Pseudomonas*, it has a value $\sim 10^{-7}$–$10^{-5}$ cm$^2$/s (16). Thus it can sometimes be as large as chemical diffusivity, suggesting that when nutrient diffusion is important cell motility may be also. Immotile cells exhibit Brownian motion as do inanimate particles. In this case, $\mu$ is much smaller, on the order of $10^{-9}$ cm$^2$/s (16).

$\chi$ is the chemotactic coefficient, representing the strength of the chemotactic movement caused by a unit chemical concentration gradient. Chemotaxis essentially results in a population drift velocity, as can be seen by rewriting the cell flux expression:

$$J_b = - \mu \frac{\partial b}{\partial x} + V_d b$$

where $V_d = \chi\, (\partial s/(\partial x)$. In this work we will assume $\mu$ and $\chi$ to be constant parameters.

If the cell speed or turning frequency depends upon the chemical substrate concentration, a phenomenon called chemokinesis, the cell flux expression is more complicated. Essentially, $\mu$ is a function of $s$, although the Fickian form may also not be retained. The sensitivity of the chemotactic response is generally considered to depend upon attractant concentration, because the response mechanism involves binding of attractant molecules to cell receptors. A commonly accepted form is $\chi(s) = \chi K_d/(K_d + s)^2$, where $K_d$ is the binding dissociation constant (17). Constant $\chi$ will thus be a good assumption for $s << K_d$.

Substituting Eqs. 3–6 into 1 and 2, we obtain

$$\frac{\partial b}{\partial t} = \mu \frac{\partial^2 b}{\partial x^2} - \chi \frac{\partial}{\partial x}\left(b \frac{\partial s}{\partial x}\right) + [f(s) - k_e]\, b \tag{7}$$

$$\frac{\partial s}{\partial t} = D \frac{\partial^2 s}{\partial x^2} - \frac{1}{Y} f(s)\, b. \tag{8}$$

The boundary conditions are

$$\text{at } x = 0 \begin{cases} \dfrac{\partial b}{\partial x} = 0 & \text{(9a)} \\ \dfrac{\partial s}{\partial x} = 0 & \text{(9b)} \end{cases}$$

and

$$\text{at } x = L \begin{cases} \mu \dfrac{\partial b}{\partial x} - \chi b \dfrac{\partial s}{\partial x} = 0 & \text{(10a)} \\ D \dfrac{\partial s}{\partial x} = h(s_0 - s) & \text{(10b)} \end{cases}$$

where $s_0$ is the substrate concentration in equilibrium with the adjacent phase, and $h$ is an interfacial mass transfer coefficient.

To get useful analytical results for fundamental behavior of this system without changing the essential nature of the problem, we linearize the generation terms by approximating the Monod growth form by a

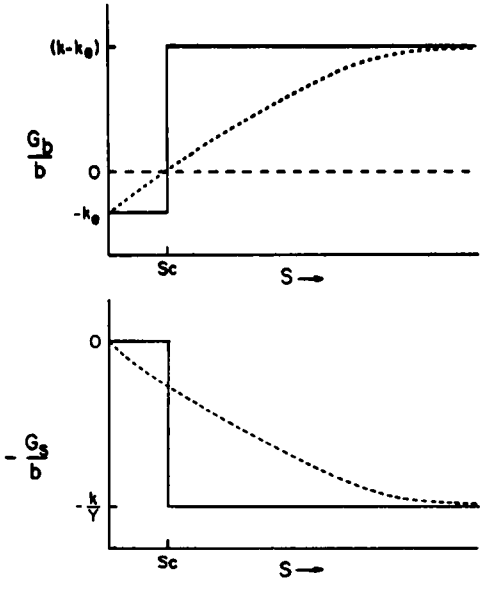


FIGURE 2 Illustration of the step-function approximation for the bacterial generation rate and substrate consumption rate. The common Monod expression for bacterial growth and substrate uptake (Eqs. 3 and 4) are represented by the dashed curves, and the step-function approximations (Eqs. 11 and 12) are represented by the solid lines.

step-function (see Fig. 2), $f(s) = kH(s - s_c)$, where $H(y)$ is the Heaviside step function, which is $H(y) = 1$ for $y > 0$, $H(y) = 0$ for $y \leq 0$. Then

$$G_b = \begin{cases} (k - k_e)\, b & s > s_c \\ -k_e\, b & s \leq s_c \end{cases} \tag{11}$$

$$G_s = \begin{cases} \frac{1}{Y} kb & s > s_c \\ 0 & s \leq s_c. \end{cases} \tag{12}$$

This is justified by assuming that there is a critical concentration level, $s_c$, below which the substrate cannot be utilized effectively for growth by the bacteria. The value of $s_c$ is related to the Monod constant $K$. If it is assumed that $s_c$ has a value such that $G_b = 0$ at $s = s_c$, then

$$s_c = K/(k/k_e - 1). \tag{13}$$

Support for such a concept is suggested by the experimental results of Caperon and Meyer (18). We emphasize, though, that the particular forms used here in Eqs. 11–13 to approximate the exact expression of Eqs. 3 and 4 are not crucial to the analysis or results presented here. Only minor quantitative differences are expected from using exact expressions instead, and the analysis is much less direct. In fact, numerical solutions to the original nonlinear set of equations have been obtained, using an orthogonal collocation procedure (19). The comparison with the analytical solutions developed in this paper is very good.

Because we desire to elucidate the effects of the motility parameters $\mu$ and $\chi$ upon bacterial growth, it is useful to rewrite the equations in dimensionless form. Defining the following quantities

$$u = \frac{s}{s_o} \quad v = \frac{b}{b_o} \quad b_o = \frac{Ys_oD}{kL^2} \quad \tau = \frac{Dt}{L^2} \quad \xi = \frac{x}{L}$$

$$\lambda = \frac{\mu}{D} \quad \kappa = \frac{kL^2}{D} \quad \theta = \frac{k_eL^2}{D} \quad \delta = \frac{\chi s_o}{\mu}$$

$$\gamma = \frac{D}{hL} \quad F(u) = \begin{cases} 1, & u > u_c \\ 0, & u \leq u_c \end{cases}$$

we obtain the dimensionless equations

$$\frac{\partial v}{\partial \tau} = \lambda \frac{\partial^2 v}{\partial \xi^2} - \delta\lambda \frac{\partial}{\partial \xi}\left(v \frac{\partial u}{\partial \xi}\right) + [\kappa F(u) - \theta]v \tag{14}$$

$$\frac{\partial u}{\partial \tau} = \frac{\partial^2 u}{\partial \xi^2} - F(u)v \tag{15}$$

with boundary conditions

$$\text{at} \quad \xi = 0 \qquad \frac{\partial y}{\partial \xi} = 0 \qquad \frac{\partial u}{\partial \xi} = 0 \tag{16a, b}$$

and

$$\text{at} \quad \xi = 1 \begin{cases} \dfrac{\partial v}{\partial \xi} - \delta v \dfrac{\partial u}{\partial \xi} = 0 & (17a) \\ \gamma \dfrac{\partial u}{\partial \xi} = 1 - u. & (17b) \end{cases}$$

Now the rates of the various kinetic and transport processes have been rescaled relative to the rate of nutrient diffusion across the region, $D/L^2$. $\lambda$ is the ratio of cell random motility to nutrient diffusivity, and $\delta$ is the ratio of chemotaxis to random motility. $\kappa$ is the ratio of bacterial growth rate to rate of nutrient diffusion across the region, and $\theta$ is an analogous ratio for bacterial death rate. $\gamma$ is the ratio of the rate nutrient diffusion across the region to the rate of transfer into the region. $u$ is the nutrient concentration relative to the equilibrium concentration at the source, and $v$ is the ratio of cell density to the maximum density allowed by the equilibrium nutrient concentration.

The steady-state bacterial population is that which satisfies Eqs. 14–17 when the time derivatives are set equal to zero. Although in natural systems a steady-state is not usually attained (due to changing conditions or genetic shifts), analysis of the behavior of the system in terms of steady-state results is useful, because the system will tend toward stable steady-state conditions after initial short-term transients. We anticipate that significant information should also be found from studying short-term results, as well as time-varying environmental conditions.

This work will consider the steady-state solution to Eqs. 24–27 for the following cases: (*a*) Random motility only ($\delta = 0$) in both the case where there is no mass transfer limitation ($\gamma \to 0$), and where there is mass transfer limitation ($\gamma > 0$).

(*b*) Chemotaxis ($\delta > 0$).

We will particularly be interested in the average steady-state bacterial population density,

$$B = \frac{1}{L}\int_o^L b(x)\, dx$$

$$B = \frac{Ys_oD}{kL^2} V \tag{18}$$

where

$$V = \int_o^1 v(\xi)\, d\xi. \tag{19}$$

## SOLUTIONS

We consider in order the cases outlined previously.

## Random Motility Only: $\delta = 0$

*No Mass Transfer Limitation: $\gamma = 0$.* This case has been presented in some detail previously (20). For this case, Eqs. 14–17 in the steady state are

$$0 = \lambda \frac{d^2v}{d\xi^2} + [\kappa F(u) - \theta]\, v \qquad 0 < \xi < 1 \tag{20}$$

$$0 = \frac{d^2u}{d\xi^2} - F(u)\, v \qquad 0 < \xi < 1 \tag{21}$$

$$\frac{dv}{d\xi} = 0, \qquad \frac{du}{d\xi} = 0 \qquad \xi = 0 \tag{22a, b}$$

$$\frac{dv}{d\xi} = 0, \qquad u = 1 \qquad \xi = 1. \tag{23a, b}$$

There is a position $\xi = \omega$ such that $u(\omega) = u_c$, so that there are two zones in the populated region:

zone I: "depleted zone" $0 < \xi < \omega$, $u < \mu_c$, $F(u) = 0$

zone II: "growth zone" $\omega < \xi < 1$, $u \geq u_c$, $F(u) = 1$.

Eqs. 20–21 can be solved in each zone, with the appropriate boundary conditions, and with the solutions matched at the interface $\xi = \omega$, so that $u_I(\omega) = u_{II}(\omega)$, $v_I(\omega) = v_{II}(\omega)$,

$$\frac{du_I}{d\xi}(\omega) = \frac{du_{II}}{d\xi}(\omega), \frac{dv_I}{d\xi}(\omega) = \frac{dv_{II}}{d\xi}(\omega).$$

The solutions are

$$u_I(\xi) = u_c \tag{24}$$

$$u_{II}(\xi) = 1 + C_0(1 - \xi) + B_0 \frac{1}{\beta^2}[1 - \cos\beta(1 - \xi)] \tag{25}$$

$$v_I(\xi) = A_0 \cosh \alpha\xi \tag{26}$$

$$v_{II}(\xi) = B_0 \cos\beta(1 - \xi) \tag{27}$$

where

$$\alpha = (\theta/\lambda)^{1/2}, \beta = [(\kappa - \theta)/\lambda]^{1/2}, \text{ and}$$

$$A_0 = \beta^2(1 - u_c)\cos\beta(1 - \omega)/M[\beta(1 - \omega)]\cosh \alpha\omega \tag{28}$$

$$B_0 = \beta^2(1 - u_c)/M[\beta(1 - \omega)] \tag{29}$$

$$C_0 = -\beta(1 - u_c)\sin\beta(1 - \omega)/M[\beta(1 - \omega)] \tag{30}$$

with

$$M(y) = y \sin y - 1 + \cos y \tag{31}$$

and $\omega$ is found from

$$\alpha \tanh \alpha\omega = \beta \tan\beta(1 - \omega). \tag{32}$$

Notice that there are now only two independent parameters that govern the system, $\alpha$ and $\beta$. $\alpha$ represents the ratio of bacterial death rate to random motility, and $\beta$ represents the ratio of bacterial growth rate to random motility.

Fig. 3 shows an example of the concentration and density profiles for this case. The total bacterial density is then found from using Eqs. 26 and 27 in 19, so that

$$V = (1 - u_c)\beta\left(1 + \frac{\beta^2}{\alpha^2}\right)\sin\beta(1 - \omega)/M[\beta(1 - \omega)]. \tag{33}$$

*Mass Transfer Limitation:* $\gamma > 0$. Eqs. 20–22 and 23 *a* remain applicable, but now the substrate boundary condition at $\xi = 1$ is 17 *b*. The solutions are similar to Eqs. 24–32; the only differences are that now Eq. 25 becomes

$$u_{II}(\xi) = 1 + C_0(1 + \gamma - \xi) + \frac{1}{\beta^2} B_0[1 - \cos\beta(1 - \xi)] \tag{34}$$

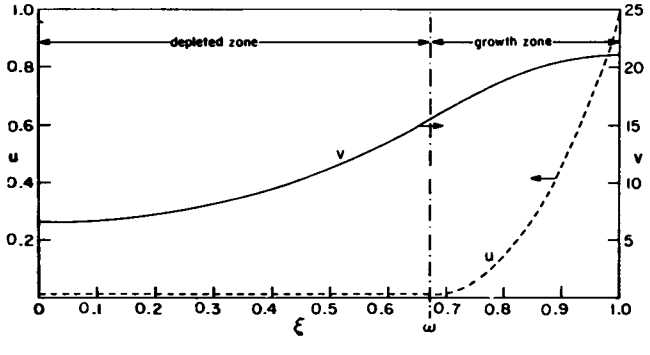


FIGURE 3 Example plot of dimensionless bacterial density, $v$, and substrate concentration $u$, profiles, as functions of dimensionless position, $\xi$, within the confined growth region. The substrate source is located at $\xi = 1$. $\xi = \omega$ is the position dividing the region into two zones (see Eq. 32). For $\xi > \omega$, $u > u_c$ so that bacterial growth can be supported; for $\xi < \omega$, $u \leq u_c$ so that growth cannot be supported. Parameter values used are $\kappa/\theta = 2$, $\lambda/\kappa = 10^{-1}$, $u_c = 10^{-2}$.

and Eq. 29 is now

$$B_0 = \beta^2(1 - u_c)/\{M[\beta(1 - \omega)] + \gamma\beta \sin\beta(1 - \omega)]\}. \tag{35}$$

Thus now

$$V = (1 - u_c)\beta\frac{\kappa}{\theta}\sin\beta(1 - \omega)/\{M[\beta(1 - \omega)] + \gamma\beta\sin\beta(1 - \omega)\}. \tag{36}$$

## Chemotaxis: $\delta > 0$

The substrate Eqs. 21, 22 *b*, 23*b* remain the same but here the bacteria equation becomes

$$0 = \lambda\frac{d^2v}{d\xi^2} - \delta\lambda v\frac{d^2u}{d\xi^2} - \delta\lambda\frac{dv}{d\xi}\frac{du}{d\xi} + [\kappa F(u) - \theta]\ 0 < \xi < 1 \tag{37}$$

and

$$\frac{dv}{d\xi} = 0 \qquad \xi = 0 \tag{38}$$

$$\frac{dv}{d\xi} - \delta v\frac{du}{d\xi} = 0 \quad \xi = 1. \tag{39}$$

Being nonlinear, these must ordinarily be solved numerically. However, we can obtain analytical results for the effect of chemotaxis with a perturbation method. That is, we write the solution as an asymptotic series in $\delta$:

$$v = v_0 + \delta v_1 + O(\delta^2) \tag{40}$$

$$u = u_0 + \delta u_1 + O(\delta^2) \tag{41}$$

$$\omega = \omega + \delta\omega_1 + O(\delta^2). \tag{42}$$

This solution will be a good approximation to the exact solution for small enough values of $\delta$. Substituting Eqs. 40–41 into 37–39 and 21, 22 *b*, and 23 *b*, and collecting the terms in like powers of $\delta$ allows sequential determination of the successive terms in 40–42. The solutions are still found for zones I and II individually, and now matched at $\xi = \omega$ by linearization around $\omega = \omega_0$. For example, the concentration $u$ is matched in the following manner (retaining only the first order power of $\delta$):

$$u_I(\omega_0 + \delta\omega_1) = u_{II}(\omega_0 + \delta\omega_1) = u_c$$

which implies

$$u_{I_0}(\omega_0) + \delta u_{I_1}(\omega_0) + \delta\omega_1\frac{du_{I_0}}{d\xi}(\omega_0) = u_{II_0}(\omega_0) + \delta u_{II_1}(\omega_0) + \delta\omega_1\frac{du_{II_0}}{d\xi}(\omega_0) = u_c.$$

The flux of $u$ and density and flux of $v$ are matched similarly.

As expected, the zero-order terms ($u_0$, $v_0$, $\omega_0$) are identical to the solution for the case of pure random motility with no mass transfer limitation. higher order terms are found easily analytically because the equations are now linear in each order. The expressions are rather lengthy, however, so they are given in the Appendix.

## RESULTS

The steady state in this model is created by the dynamic balance between the increase in cell biomass in the substrate-rich growth zone and the decrease in cell biomass in the substrate-poor depleted zone. This balance is mediated by the net movement of cells from the growth zone into the depleted zone caused by cell motility. This situation should be evident from Fig. 3.

Figs. 4 and 5 show computational results for the case of pure random motility with no mass transfer limitation. The steady-state population $B$ increases and growth zone thickness $(1 - \omega)$ decreases as $\kappa/\theta$ (growth/death) increases and $\lambda/\kappa$ (motility/growth) decreases. The reason for this behavior may be found in Fig. 6, which shows the effect of $\lambda/\kappa$ on cell density profiles. We see that as $\lambda/\kappa$ increases, the cells disperse more readily from the growth zone to the depleted zone, and are less likely to be in an environment favorable for growth. Therefore, $B$ decreases as $\lambda/\kappa$ increases. The key quantity is not the value of $\lambda$ (cell motility to nutrient diffusivity) but is rather the value of $\lambda/\kappa$ (cell motility to growth rate).

Because we are primarily concerned about the effects of random motility on population size, it is of interest to consider the limiting cases of very large and very small $\lambda/\kappa$.

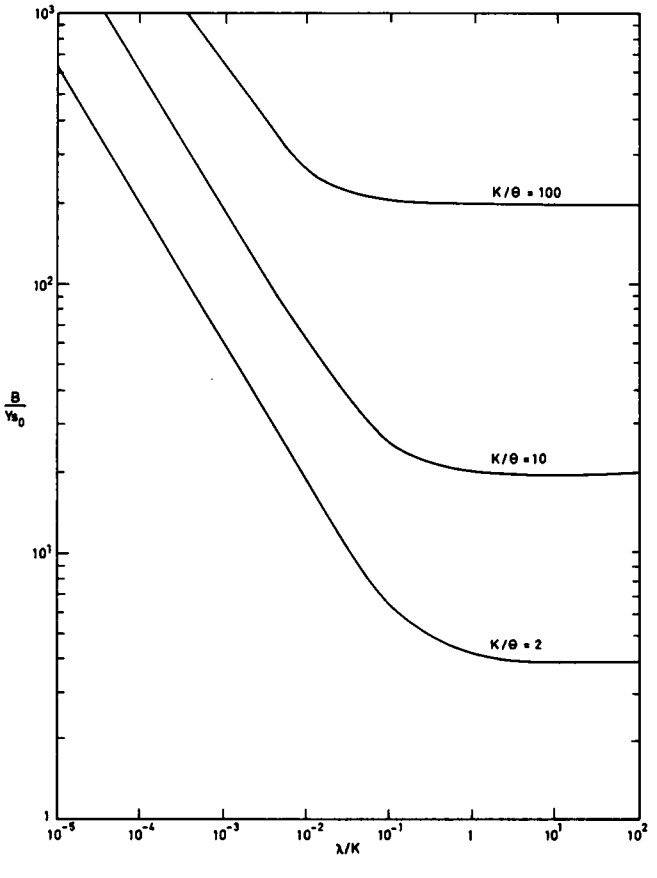


FIGURE 4 Plot of average bacterial density within the confined growth region, $B$, (see Eq. 18), as a function of the ratio of cell motility to growth rate, $\lambda/\kappa$, for various ratios of growth rate to death rate, $\kappa/\theta$, $u_c = 10^{-2}$.

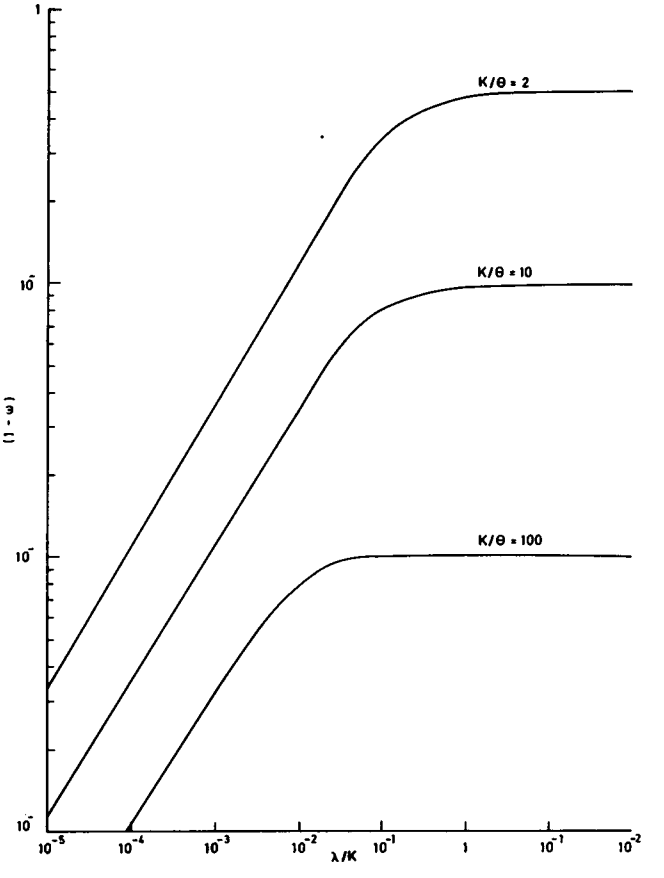


FIGURE 5 Plot of growth zone thickness, $1 - \omega$, (see Eq. 32), as a function of the ratio of cell motility to growth rate, $\lambda/\kappa$, for various ratios of growth rate to death rate, $\kappa/\theta$.

The limiting expressions (for the biologically reasonable assumption $\kappa >> \theta$) are

$$\frac{\lambda}{\kappa} >> 1, V \approx V_\infty \equiv 2(1 - u_c)\frac{\kappa^2}{\theta^2}, (1 - \omega) \approx (1 - \omega_\infty) \equiv \frac{\theta}{\kappa}$$

$$\frac{\lambda}{\kappa} << 1, V \approx \left(\frac{\theta}{\lambda}\right)^{1/2} V_\infty, (1 - \omega) \approx \left(\frac{\lambda}{\kappa}\right)^{1/2} (1 - \omega_\infty)^{1/2}.$$

For $\lambda/\kappa >> 1$, the cells can traverse the whole region many times in a given doubling time, so that the growth rate is effectively a function of an average substrate concentration. Thus the system acts almost well-mixed, microscopically, and the population attained depends only on the growth and death rate constants. For $\lambda/\kappa << 1$, the doubling time is very small relative to the rate of movement across the region, so the growth rate depends only on the local substrate concentration, and the system is clearly nonuniform. In this case population growth is very heavily influenced by the spatial distribution of cells, so the population attained depends upon the motility coefficient as well as upon the growth rate constant.

Fig. 7 presents some computational results for the case of, pure random motility with mass transfer limitation. The cell population decreases as $\gamma$ (nutrient diffusion/transfer)

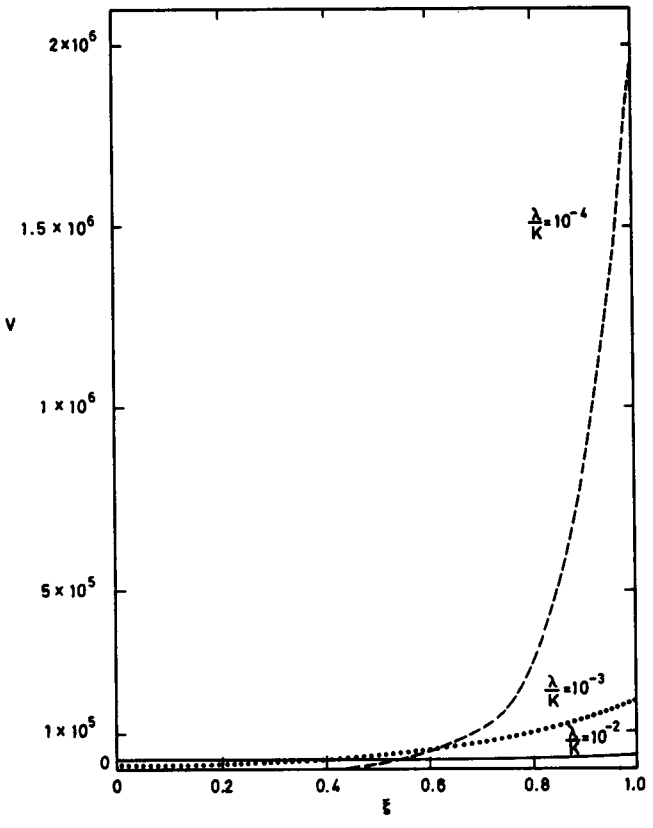


FIGURE 6 Example dimensionless cell density profiles within confined growth region, showing the effect of the ratio of cell motility to growth rate, $\lambda/\kappa$, for $\kappa/\theta = 100$ and $u_c = 10^{-2}$. As this ratio becomes very small, the density profiles become quite nonuniform, with great concentration of cells near the substrate source. As this ratio increases, the profiles become flat, representing essentially uniform bacterial densities within the region. In this case, profiles are unchanged for $\lambda/\kappa$ greater than $10^{-2}$. This corresponds to the flat portion of the $B$ vs. $\lambda/\kappa$ curve in Fig. 4 for this value of $\kappa/\theta$.

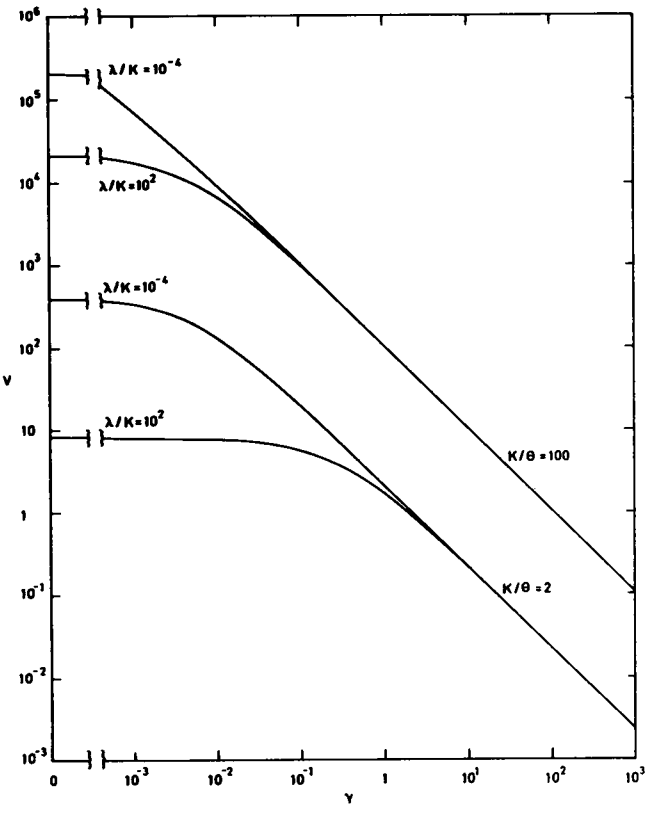


FIGURE 7 Plot showing the effect of substrate mass transfer limitation, described by the parameter $\gamma$, on dimensionless total bacterial population within the confined growth region, $V$ (see Eq. 36). Large values of $\gamma$ represent significant mass transfer resistance, and the figure shows that this eliminates the effect of cell motility. $u_c = 10^{-2}$.

increases, because the rate of nutrient uptake by the population is reduced. In fact, as $\gamma$ becomes very large, the population site becomes independent of the random motility coefficient. The quantitative effect of $\gamma$ can be seen more clearly from comparison of Eqs. 33 and 36, for if we define $V_0$ to be the value of $V$ in the former (i.e., with $\gamma = 0$) and $V_\gamma$ in the latter (with $\gamma > 0$), then

$$\frac{V_\gamma}{V_0} = \frac{1}{1 + \eta\gamma} \tag{43}$$

where

$$\eta = \{(1 - \omega) + [\cos\beta(1 - \omega) - 1]/[\beta \sin\beta(1 - \omega)]\}^{-1} = V_0/(\kappa/\theta). \tag{44}$$

We can again look at the limiting cases

$$\lambda/\kappa >> 1,\ V \approx V_{\gamma_\infty} = V_{0_\infty}/(1 + 2\gamma\kappa/\theta)$$

$$\lambda/\kappa << 1,\ V \approx V_{\gamma_\infty} \times (1 + \theta/2\gamma\kappa) = V_{0_\infty}/(2\gamma\kappa/\theta).$$

Notice that for this case $V$ does not increase indefinitely as $\lambda \to 0$, as it did for $\gamma = 0$. The key quantity for the effect of mass transfer limitation is $2\gamma\kappa/\theta$. For $2\gamma\kappa/\theta >> 1$, mass transfer limitation will act to significantly decrease the population size. For $2\gamma\kappa/\theta << 1$, the mass transfer limitation will have an insignificant effect.

Fig. 8 presents computational results for case of chemotaxis where we have neglected all terms in $\delta$ greater than first order. The dashed curves are only extrapolations of the perturbation solutions beyond their regions of validity. However, what is important is the general trend of these curves. Chemotaxis acts to increase population size, which is not surprising intuitively, but there is a subtlety that we will discuss later. The effect of this type of movement behavior on the cell density profile is illustrated in Fig. 9. Chemotaxis leads to increased population size because the tendency of cells to disperse away from the growth zone is opposed by the tendency to move in the direction of the increasing substrate concentration gradient. Notice that one particularly significant consequence of chemotaxis is that the gradient of cell population density at the nutrient source no longer needs to be zero.

## DISCUSSION

To understand the effects of cell motility properties on bacterial population growth, we have developed a mathe-

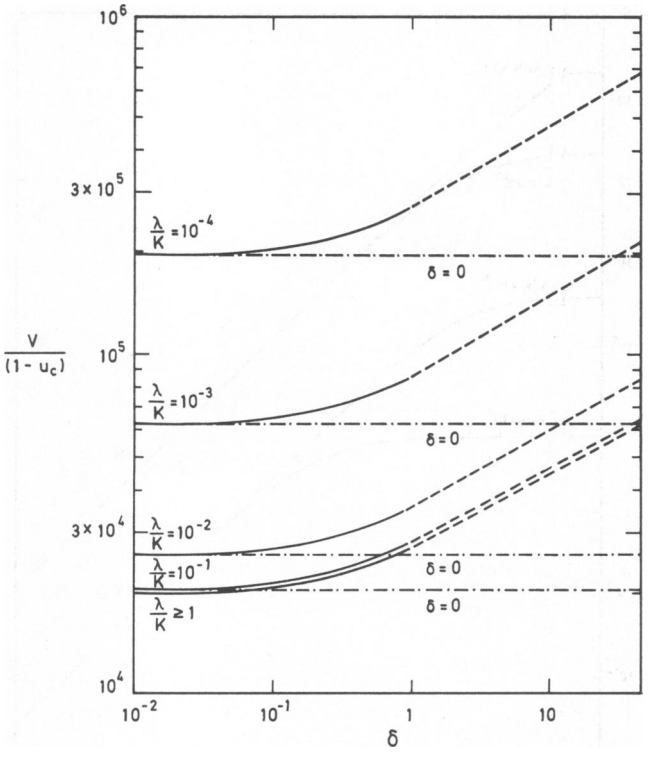


FIGURE 8 Plot showing the effect of cell chemotaxis, represented by the parameter $\delta$, on dimensionless total bacterial density within the confined growth region, $V$, for $\kappa/\theta = 100$. The dashed lines (---) are extrapolations of the perturbation solutions obtained in this paper, for $\delta > 1$. The different curves are for various values of $\lambda/\kappa$. It is clear that $\delta$ must be $>10^{-1}$ to have a noticeable effect on the population size, and that it must be $>1$ to have a significant effect.

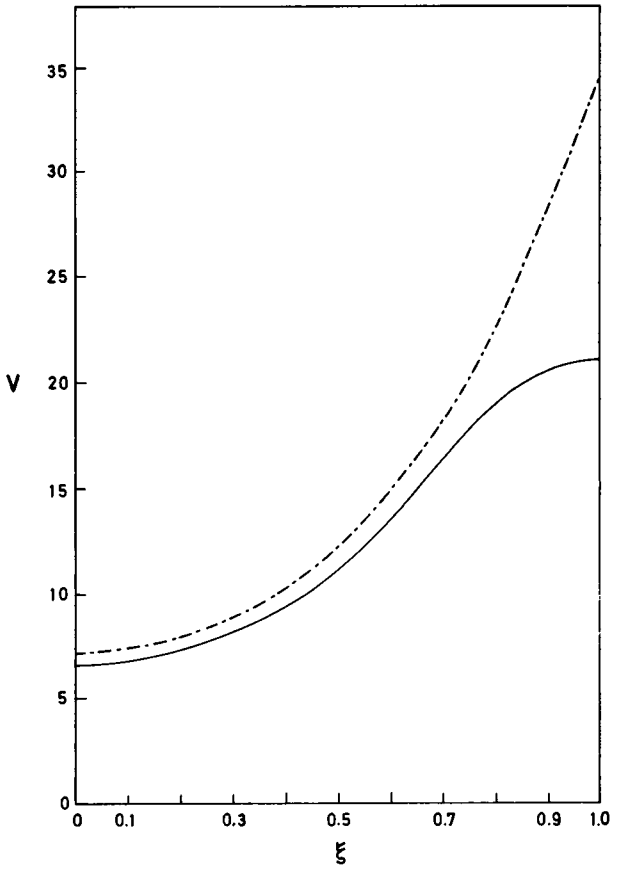


FIGURE 9 Effect of chemotaxis on the cell density profile within the confined growth region. In this example, $\kappa/\theta = 2$, $\lambda/\kappa = 10^{-1}$, $u_c = 10^{-2}$, and $\delta = 0.5$. Notice that the presence of chemotaxis allows a nonzero slope at $\xi = 1$.

matical model for growth of a single population in a confined, unmixed region, on a rate-limiting nutrient diffusing into the region from a boundary. This model may represent a number of important natural situations of biological importance. We have analyzed the steady-state population size that can be attained, being primarily interested in its dependence upon the following key parameters: $k$, cell growth rate constant; $k_e$, cell nonviability rate constant; $\mu$, cell random motility coefficient; and $\chi$, cell chemotaxis coefficient. Our analysis has yielded predictions we will now discuss.

In the absence of chemotaxis, random motility acts to reduce population size as the ratio $\mu/kL^2$ increases, where $L$ is the length of the confined region. Fig. 4 shows this result graphically. An important conclusion that can be drawn from this figure is that a species with a small enough random motility coefficient can grow to a larger population size than a second population with a greater growth rate constant. Consider two species, 1 and 2, growing separately under identical circumstances; that is, the same size region, same nutrient, and equal nutrient source concentration. Further, let the death rates and yield coefficients be equal. Now, if it is assumed that $k_1 > k_2$, then under well-mixed conditions we would expect that $B_1 > B_2$, where $B$ is the total steady-state population density. However, in an unmixed system, if $\mu_1$ is large enough relative to $\mu_2$, Fig. 4 shows that $B_2 > B_1$ is in fact possible. That is, a species with superior motility kinetic properties can outgrow a species with superior growth kinetic properties. The parameter relationships necessary for such an occurrence have been derived and discussed previously (20).

From our results here for constant $\mu$, we can predict that positive chemokinesis ($\mu$ increasing at higher nutrient concentration) should decrease the steady-state population size, and that negative chemokinesis ($\mu$ decreasing at higher nutrient concentration) should increase it. Calculations using a perturbation approach similar to that used here for the chemotaxis case have confirmed this suggestion (21). Thus we can formulate a rule for cell movement behavior: at high nutrient concentrations it is advantageous for cells to remain localized; at low nutrient concentrations it is advantageous for cells to disperse.

The presence of chemotaxis acts to increase the population size, according to the magnitude of the quantity $\delta = (\chi s_o)/(\mu)$, where $s_o$ is the nutrient source concentration (this assumes that the chemotaxis coefficient is indepen-

dent of attractant concentration). This result for chemotaxis is not qualitatively surprising; however, we are now in a position to make quantitative predictions about the consequences of chemotaxis for population growth. Some calculations for population size dependence upon $\delta$ are illustrated by Fig. 8. It is clear that we could again proceed to derive parameter relationships, now including $\delta$, that determine relative population sizes. Leaving that aside, it is of interest here to point out a significant and counterintuitive implication from Fig. 8. There is a minimum value of $\delta$ necessary for motility to be profitable. That is, a cell must be motile to be chemotactic, and the effect of increasing $\mu$ from the value for Brownian motion would be to diminish population size. Therefore, $\delta$ should be large enough to overcome this diminution. It follows that a chemotactic species may not always automatically grow to a greater population size than a nonchemotactic species. There is a relationship between the values of $\mu/kL^2$, $k/k_e$, and $\delta$ that will determine relative population sizes.

Fig. 8 also shows that, at least according to our perturbation solution, chemotaxis has no real effect on population size until, roughly, $\delta = 0.1$. At $\delta = 1$, the population size is increased by ~40% over that for $\delta = 0$. Very crude estimates of $\delta$ given in the literature fall in the range of ~1–10 (22, 23). So, we see that a considerable growth advantage should result for a species of given $\mu$, $k$, and $k_d$. However, it should be evident from Fig. 8 that such a value for $\delta$ is not necessarily great enough to overcome any given growth disadvantage relative to a faster growing or less motile species.

It should also be mentioned that numerical solutions obtained by using an orthogonal collocation method show excellent agreement with the perturbation results given here, at least up to $\delta = 1$ (19).

We must be careful not to conclude that random motility *per se* is generally detrimental to microbial population survival. For the confined growth situation considered here, that is the clear result. But in other situations, it may well be beneficial. For example, for a species inoculated in a nutrient environment of infinite extent, increasing values of $\mu$ might allow greater population growth because dispersal would be toward regions of greater nutrient concentrations. Also, travelling bands of randomly motile bacteria may allow population persistence via movement from depleted areas to plentiful areas (21, 24). Therefore, care must be exercised in predicting the effects of cell motility. The major point of this paper remains the same, however: that motility effects can be significant and even dominant factors in determining microbial population dynamics.

We would like to point out the relationship of the conclusions presented here for cell populations to those published previously for individual cells. Early authors suggested that motility, even random in nature, should always tend to enhance cell growth by increasing the rate of substrate uptake by an individual cell through a local convection mechanism (6, 7). That such an effect is in reality negligible in the case of bacteria feeding on chemical substrates has been demonstrated by Berg and Purcell (25) (although it may be significant for larger protozoa feeding on bacteria because of the smaller prey diffusivity). The rate of substrate uptake by a cell is governed by chemical diffusion, and so is always proportional to the local substrate concentration. The crucial consequence noted by Purcell (26) is that an important function of bacterial motility could therefore be to move a cell to a region of significantly different local chemical concentration (this could apply to both beneficial and harmful chemical species), to change the rate of diffusive flux to the cell. Our results for cell population are in perfect harmony with this reasoning, for the chief role of motility is to distribute the cell population in accordance with whatever physical law governs the cell population flux. Hence individual cells are situated in varying local levels of substrate concentration, and the net result of the growth of all cells is reflected in the population results.

The implications of our analysis for competition between microbial species are of potentially great significance. It seems possible that a species with inferior growth kinetic properties could prevail against a species with superior growth kinetic properties in direct competition for a nutrient, if the former has superior motility properties. Further, coexistence could now be a possible outcome of competition in an environment that is not well mixed. Spatial heterogeneity is often suggested as an explanation for violation of the competitive exclusion principle, as for example by Stephanopoulos and Fredrickson (27). In our confined growth competition situation, heterogeneity is provided by the interaction of diffusion, motility, growth, and uptake kinetics.

If there is a significant transfer resistance for the diffusion of nutrient from the adjacent source phase into the bacterial growth region, the influence of motility is diminished. The key quantity here is the ratio $2Dk/k_e hL$, where $D$ is the nutrient diffusivity and $h$ is the nutrient interfacial transfer coefficient. As this ratio becomes large, the motility effects discussed above become insignificant. The quantitative relationship is shown in Fig. 7. When $h$ becomes small, nutrient diffusion from the interface into the growth region is rapid relative to the transfer of nutrient across the interface. This results in a very flat, almost uniform nutrient concentration profile within the confined region. Consequently, regardless of cell movement properties, the system behaves as if well-mixed. Even under stagnant conditions, then, mass transfer limitations may prevent cell motility from playing a signficant role in population dynamics. An example might be the case of microbial growth, rate-limited by oxygen in an aqueous growth medium. With estimated parameter values $D = 10^{-5}$ cm$^2$/s, $k = 1$ h$^{-1}$, $k_e = 10^{-2}$ h$^{-1}$, and $h = 10^{-2}$ cm/s, then $\kappa/\theta = 100$ and $\gamma = 10^{-3}/L$ where $L$ has units of cm. Thus, if $L = 1$ cm, $\gamma = 10^{-3}$ and Fig. 7 shows that cell motility can have a significant effect. If $L = 10^{-1}$ cm, then

$\gamma = 10^{-2}$ and the same figure shows that the effect of cell motility will be very small. The ratio $2Dk/k_c hL$ takes the value 0.2 in the first case, and 2.0 in the second. The size of this ratio relative to unity is the critical consideration.

A remark is in order here concerning the assumption that our confined growth medium is stagnant. Convection currents and even some organized flow may be expected in most real systems. Might these not mitigate the effects of chemical diffusion and cell motility? There is experimental evidence that in a particular system cell motility and chemotaxis can significantly affect the net cell flux in the presence of convective flow up to ~2 cm/min (28). This would suggest that such ideas as presented here should find application not only in quiescent environments but also in those with a small convective flow present.

Finally, it is of interest to mention that some recently published experiments have been directed toward quantitative study of bacterial density profiles in spatially distributed growth media (29). These are just the sorts of experiments that will be appropriate for further investigation of the theoretical predictions made here.

## APPENDIX

For the case of Chemotaxis (*b*), with $\delta \neq 0$, the solution to Eqs. 21 and 37 may be written as an asymptotic series in $\delta$, as $\delta \to 0$:

$$u_{\mathrm{I}} = u_{\mathrm{I}_0} + \delta u_{\mathrm{I}_1} + 0(\delta^2)$$

$$v_{\mathrm{I}} = v_{\mathrm{I}_0} + \delta v_{\mathrm{I}_1} + 0(\delta^2)$$

for $0 < \xi < \omega$, and

$$u_{\mathrm{II}} = u_{\mathrm{II}_0} + \delta u_{\mathrm{II}_1} + 0(\delta^2)$$

$$v_{\mathrm{II}} = v_{\mathrm{II}_0} + \delta v_{\mathrm{II}_1} + 0(\delta^2)$$

for $\omega < \xi < 1$. We must also write $\omega = \omega_0 + \delta\omega_1 + 0(\delta^2)$. $u_{\mathrm{I}_0}$, $u_{\mathrm{II}_0}$, $v_{\mathrm{I}_0}$, $v_{\mathrm{II}_0}$ and $\omega_0$ are identical to the results obtained for case *a*, where $\delta = 0$. The first-order terms are given by

$$u_{\mathrm{I}_1} = 0$$

$$v_{\mathrm{I}_1} = A_1 \cosh \alpha\xi$$

$$u_{\mathrm{III}} = C_1(1 - \xi) + B_1 \frac{1}{\beta^2}[1 - \cos\beta(1 - \xi)]$$

$$+ \frac{1}{12\beta^4} B_0 [\cos 2\beta(1 - \xi) - 1]$$

$$- \frac{1}{2\beta^2} B_0 C_0 (1 - \xi) \cos\beta(1 - \xi)$$

$$+ \frac{1}{2\beta^3} B_0 C_0 \sin\beta(1 - \xi)$$

$$v_{\mathrm{III}} = B_1 \cos\beta(1 - \xi) + \frac{1}{2\beta} B_0 C_0 \sin\beta(1 - \xi)$$

$$+ (1/2) B_0 C_0 (1 - \xi) \cos\beta(1 - \xi)$$

$$- \frac{1}{3\beta^2} B_0^2 \cos 2\beta(1 - \xi).$$

$A_0$, $B_0$, and $C_0$ have the same values as in case 1 *a*. $A_1$, $B_1$, $C_1$, and $\omega_1$ are obtained from the matrix equation

$$M y = q$$

where

$$y^{\mathrm{T}} = [A_1\ B_1\ C_1\ \omega_1] \text{ and } q^{\mathrm{T}} = [q_1\ q_2\ q_3\ q_4],$$

with

$$q_1 = 1/2\, B_0 C_0 (1 - \omega_0) \cos\beta(1 - \omega_0)$$

$$+ B_0 C_0 \frac{1}{2\beta} \sin\beta(1 - \psi_0)$$

$$- B_0^2 \frac{1}{3\beta^2} \cos 2\beta(1 - \omega_0)$$

$$q_2 = -B_0^2 \frac{2}{3\beta} \sin 2\beta(1 - \omega_0) - B_0 C_0 \cos\beta(1 - \omega_0)$$

$$+ B_0 C_0 \frac{\beta}{2} (1 - \omega_0) \sin\beta(1 - \omega_0)$$

$$q_3 = B_0^2 \frac{1}{12\beta^4} + B_0 C_0 \frac{1}{2\beta^2} (1 - \omega_0) \cos\beta(1 - \omega_0)$$

$$- B_0^2 \frac{1}{12\beta^4} \cos 2\beta(1 - \omega_0) - B_0 C_0 \frac{1}{2\beta^3} \sin\beta(1 - \omega_0)$$

$$q_4 = B_0^2 \frac{1}{6\beta^3} \sin 2\beta(1 - \omega_0) - B_0 C_0 \frac{1}{2\beta} (1 - \omega_0) \sin\beta(1 - \omega_0).$$

Finally, $M$ is a 4 by 4 matrix with elements $M_{ij}$, where $i$ is the row number and $j$ the column number, and

$$M_{11} = \cosh \alpha\omega_0$$

$$M_{12} = -\cos\beta(1 - \omega_0)$$

$$M_{14} = \alpha A_0 \sinh \alpha\omega_0 - \beta B_0 \sin\beta(1 - \omega_0)$$

$$M_{21} = \alpha \sinh \alpha\omega_0$$

$$M_{22} = -\beta \sin\beta(1 - \omega)$$

$$M_{24} = \alpha^2 A_0 \cosh \alpha\omega_0 + \beta^2 B_0 \cos\beta(1 - \omega_0)$$

$$M_{32} = \frac{1}{\beta^2}[1 - \cos\beta(1 - \psi_0)]$$

$$M_{33} = 1 - \omega_0$$

$$M_{42} = \frac{1}{\beta} \sin\beta(1 - \omega_0)$$

$$M_{43} = 1$$

$$M_{44} = -B_0 \cos(1 - \omega_0)$$

$$M_{13} = M_{23} = M_{31} = M_{34} = M_{41} = 0.$$

The total dimensionless population density is then

$$V = \frac{1}{\alpha} A_0 \sinh \alpha\omega + \frac{1}{\beta} B_0 \sin \beta(1 - \omega)$$
$$+ \delta \left\{ \frac{1}{\alpha} A_1 \sinh \alpha\omega + \frac{1}{\beta} B_1 \sin \beta(1 - \omega) \right.$$
$$- \frac{1}{6\beta^3} B_0^2 \sin 2\beta(1 - \omega)$$
$$+ B_0 C_0 \left[ \frac{1}{2\beta^2} \right.$$
$$\{1 - \cos \beta(1 - \omega) + \beta(1 - \omega) \sin \beta(1 - \omega)\}$$
$$\left. \left. + 1/4 \{1 - 2(\omega - 1/2\,\omega^2) \cos \beta(1 - \omega)\} \right] \right\}.$$

The work of Barbara Calcagno in performing some numerical computations related to these results is greatly appreciated.

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