Neural, Parallel, and Scientific Computations 25 (2017) 307-312

BAND FORMATION IN BACTERIAL AEROTAXIS

VASILIOS ALEXIADES[1], MUSTAFA ELMAS[1], AND GLADYS ALEXANDRE[2]

[1]Mathematics, University of Tennessee, Knoxville, TN 37996, USA
[2]Biochemistry, Cellular and Molecular Biology, University of Tennessee, Knoxville, TN 37996, USA

ABSTRACT. We study a model of bacterial aerotaxis of Azospirillum brasilense bacteria. The model consists of a system of diffusion-reaction and advection-reaction PDEs describing diffusion of oxygen in water and chemotactic movement of bacteria towards where oxygen concentration is most desirable for them. They preferentially concentrate about that location forming a 'band' that becomes visible in experiments. We present simulations that show the effect of some of the parameters on the formation of the band.

AMS (MOS) Subject Classification. 92C17, 35L50, 35K57.

1. Chemotaxis and aerotaxis

Bacterial **chemotaxis** is the movement of motile bacteria towards higher attractant concentrations and/or away from repellents [6]. Stimuli can be various chemicals, such as nutrients (sugars) or oxygen. The motion of motile bacteria is driven by rotation of flagella attached to the cell body. They move by straight **runs** and **tumbles**, executing a sort of biased random walk. When the flagella rotate counterclockwise (CCW), they form a bundle that propels the bacterium in a smooth motion (straight **runs**). When the flagella rotate clockwise (CW), the bundle flies apart and the bacterium **tumbles**, changing the direction of the subsequent run. Biasing the movement towards desirable concentrations is accomplished by how often the bacterium tumbles, so by the frequency of reversals between clockwise and counterclockwise flagellar rotation. When in a desirable attractant concentration, the reversal frequency increases, thus tumbling more, preventing long runs. On the other hand, in unfavorable environment reversal frequency decreases enabling longer straight movement to escape away.

Aerotaxis is a particular type of taxis in which oxygen acts as both attractant and repellant. Very low and very high oxygen concentrations act as repellants, whereas some intermediate concentrations are favorable. More bacteria stay there longer, piling up in a narrow region, called a **band**, as seen in Fig.1. The location

Received June 1, 2017 1061-5369 $15.00 ©Dynamic Publishers, Inc.

and width of a band are primary observable and measurable quantities in aerotaxis experimants.

Most of chemotaxis studies are on E.coli bacteria. Here we study the single-cell micro-aerophilic soil bacteria *Azospiriullum brasilense* (Azo.b.) They live in rhizospheres at roots of many cereals and grasses, promoting plant growth by fixing nitrogen under low oxygen conditions [1], [2], [3]. They seek favorable oxygen concentration, which is crucial to their metabolism and growth. Moreover, they consume Oxygen, thus depleting its concentration.

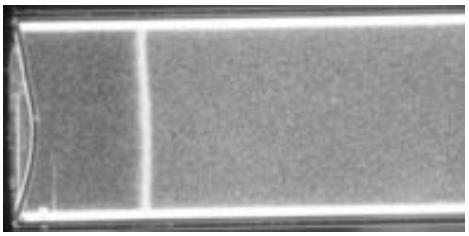

FIGURE 1. Aerotactic band of Azo.b. in capillary tube at 40× magnification. From [3].

2. **Mathematical model for aerotaxis**

Modeling approaches for chemotaxis include: ODE models for signaling pathways [4], PDE models of various types for chemotactic movement, most commonly Keller-Segel type models, stochastic models of many types, and agent based models.

A model particularly appropriate for aerotaxis was developed by Mazzag-Zhulin-Mogilner [5]. It is *not* of Keller-Segel type and, unlike those, it incorporates experimentally measurable parameters, namely swimming speed and frequency of reversals, as described below.

Consider a capillary tube of length X_{end} occupying the interval $[0, X_{end}]$. It is filled with water and a (large number) of bacteria at some concentration B_0. The left end $x = 0$ is exposed to a specified Oxygen concentration $C(0,t) = C_0(t)$, and the right end $x = X_{end}$ is closed, so $\frac{\partial C(X_{end},t)}{\partial x} = 0$. Initially there is no Oxygen in the water, so $C(x,0) = 0$ everywhere.

The Oxygen concentration $C(x,t)$ is governed by the diffusion-reaction equation

$$\frac{\partial C(x,t)}{\partial t} = D\frac{\partial^2 C(x,t)}{\partial x^2} - \theta(C)KB(x,t), \tag{2.1}$$

with D the diffusion coefficient of Oxygen in water, K the rate of consumption of oxygen by bacteria, $\theta = 1$ if $C(x,t) > 0$ and $\theta = 0$ if $C(x,t) \le 0$, and $B(x,t)$ the concentration of bacteria.

The movement of bacteria is described by advection-reaction equations separately for $R(x,t)$ = right moving bacteria and for $L(x,t)$ = left moving bacteria, with

$B(x,t) = R(x,t) + L(x,t)$, as follows:

$$\frac{\partial R(x,t)}{\partial t} + v\frac{\partial R(x,t)}{\partial x} = -f_{RL}\, R(x,t) + f_{LR}\, L(x,t), \tag{2.2}$$

$$\frac{\partial L(x,t)}{\partial t} - v\frac{\partial L(x,t)}{\partial x} = +f_{RL}\, R(x,t) - f_{LR}\, L(x,t), \tag{2.3}$$

where $v > 0$ is the (constant) swimming speed, f_{LR} and f_{RL} are the frequencies of reversals from to Left to Right and from Right to Left, respectively, given by

$$f_{LR} = \begin{cases} f & if\ C < C_{min}\ or\ C > \widehat{C}_{max}, \\ F & if\ \ C_{min} < C < \widehat{C}_{max}, \end{cases} \tag{2.4}$$

$$f_{RL} = \begin{cases} f & if\ C < \widehat{C}_{min}\ or\ C > C_{max}, \\ F & if\ \ \widehat{C}_{min} < C < C_{max}, \end{cases} \tag{2.5}$$

with $f < F$ specified reversal frequencies and $\widehat{C}_{min} < C_{min} < C_{max} < \widehat{C}_{max}$ specified switch values of Oxygen concentration C at which frequencies change from low f to high F and vice versa. The formulas are depicted in Fig.2.

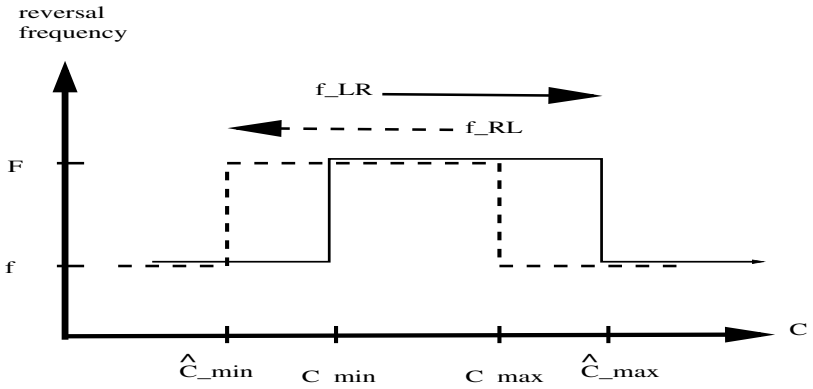

FIGURE 2. Frequencies of reversals from Left to Right, f_{LR} in (2.4), and from Right to Left, f_{RL} in (2.5).

Initially, $R(x,0) = L(x,0) = B_0/2$. At the left boundary $x = 0$, all Left-moving cells turn Right, and at the right boundary $x = X_{end}$, all Right-moving cells turn Left:

$$R(0,t) = L(0,t),\ \ R(X_{end},t) = L(X_{end},t) \tag{2.6}$$

The total number of bacteria in the capillary should remain constant:

$$\int_0^{X_{end}} B(x,t)dx = const. = B_0. \tag{2.7}$$

Thus, the model consists of the coupled system of PDEs (2.1), (2.2), (2.3) with appropriate initial and boundary conditions mentioned above. The PDEs are discretized by Finite Volumes in space, and by Forward Euler in time, subject to an appropriate CFL condition.

Experimentally, only the location and width of a band are directly observable (under the microscope). Moreover, v, f, F can be estimated from video of an experiment using appropriate cell-tracking software (CellTrak). Computationally, a *band* would appear as a "bump" in the profile of bacterial concentration $B(x,t)$ vs x, at any time t, if any. Quantifying the width of such a bump is ambiguous. We take it to be the Full-Width-at-Half-Maximum (FWHM), commonly used to characterize laser pulses. This is done by finding $maxB(x)$ and $minB(x)$, setting the cut-off B_{half} at half height, and then locating the left (xL) and right (xR) intersections of $B(x)$ with B_{half}. The band width is $xR - xL$ and its location is the midpoint $\frac{xL+xR}{2}$. These are the primary Quantities of Interest in the simulations, to be matched to experiments.

The model contains 10 main parameters (B_0, D, K, v, f, F, $\widehat{C}_{min}, C_{min}, C_{max}, \widehat{C}_{max}$). Of these, D, K are known, and B_0, v, F can be estimated in each experiment. The rest need to be found computationally so as to match the quantities of interest, namely, band location and band width. This is a tough *inverse problem* of parameter identification.

3. **Simulation of aerotactic assay**

We present here results of simulations of actual experiments with wild type Azo.b. grown in malate (as food source), and exposed to air with 21% Oxygen (at left end of capillary tube). Experimentally measured parameters were $v = 20\ \mu m/s$, $F = 0.96\ reversals/s$, and measured band location and width were 407 and 132 μm. Taking $C(0,t) = 21\%$ as boundary value for Oxygen, we determined the rest of the parameters and produced remarkably close values of 406 and 131 μm for band location and width.

Fig.3 shows computed profiles of bacteria concentration $B(x,t)$ at times 50 s and 300 s. Note that $B(x,t)$ is normalized by the initial value B_0, so $B = 1$ is the initial concentration (assumed uniform), in this case $B_0 = 7 \times 10^8$ cells/mL.

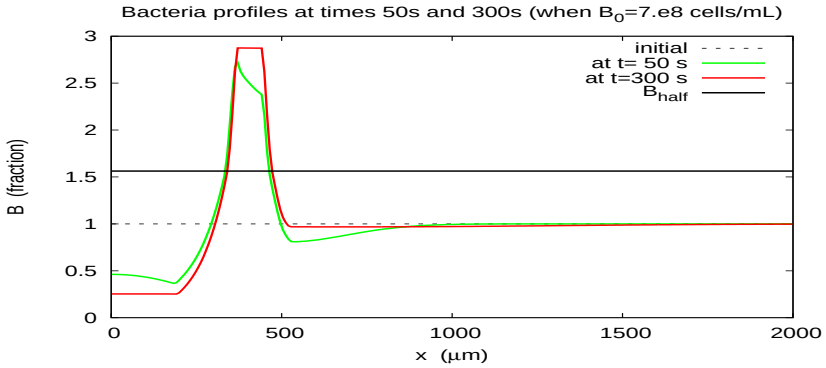

FIGURE 3. Profiles of (normalized) $B(x,t)$ at time 50 s (green) and 300 s (red). Width is found at height B_{half} (black). $B(x,t)$ is normalized by the initial value B_0.

Fig.4 shows the evolution of the band in time, up to 600 s. The band forms very soon, within a mimute, and remains stationary ever after, exactly as observed in experiments.

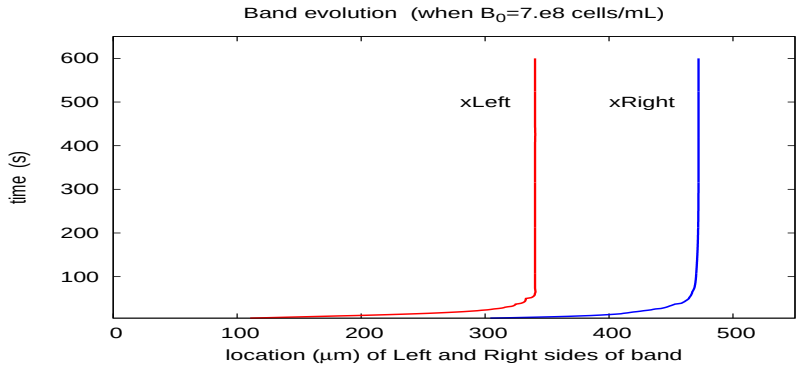

FIGURE 4. Band evolution in time. Location 406, width 131 μm.

We present a couple of examples of using the model for parametric studies.

Effect of Oxygen level at capillary opening: In the above, the boundary value C_0 was 21%, normal air. Reducing C_0 to 10% Oxygen, we find that the band now forms at location 226 μm, whereas the width remains the same (132 μm). Increasing C_0 to 40% Oxygen, moves the location to 638, with width 125 μm. Thus, C_0 affects the band location (monotonically), but does not affect the band width.

Effect of bacterial density B_0: Decreasing the initial bacteria concentration by an order of magnitude to $B_0 = 7 \times 10^7$ cells/mL, we can still find switch parameters ($\widehat{C}_{min}, C_{min}$, etc) that produce the same band location and width, see Fig.5, Fig.6. In this case, the band takes several mimutes to attain its width and it does not stay at the same location. The slowdown is consistent with the profile in Fig.5 which shows cells from as far away as 2500 μm coming into the band, so it takes longer to form the band (compare with profile in Fig.3 where, the more abundant cells, come from the left side). Regarding the receding of the band towards the opening after 300s, we note that in Fig.5 bacterial density $B(x)$ rises very high in the band (up to 8 times B_0), thus much more oxygen is consumed there; this makes the $C(x)$ curve steeper, so the preferred oxygen zone moves left and the band follows it.

ACKNOWLEDGMENTS

Partially supported by NSF Grant R01-1052148.

REFERENCES

[1] Gladys Alexandre, More than one way to sense chemicals, *Bacteriology*, 183:4681-4686, 2001.

[2] Gladys Alexandre, Coupling metabolism and chemotaxis-dependent behaviours by energy taxis receptors, *Microbiology*, 156, 22832293, 2010.

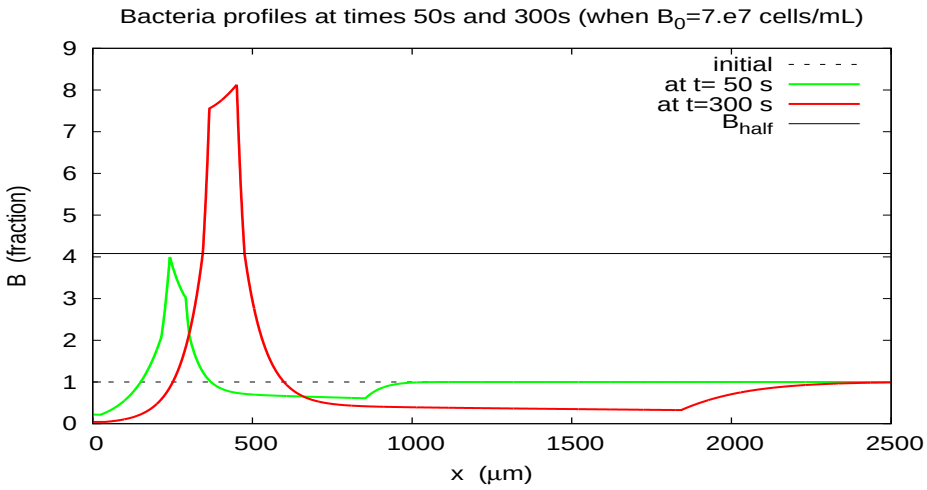

FIGURE 5. Profiles of (normalized) $B(x,t)$ at time 50 s (green) and 300 s (red), when $B_0 = 7 \times 10^7$ cells/mL.

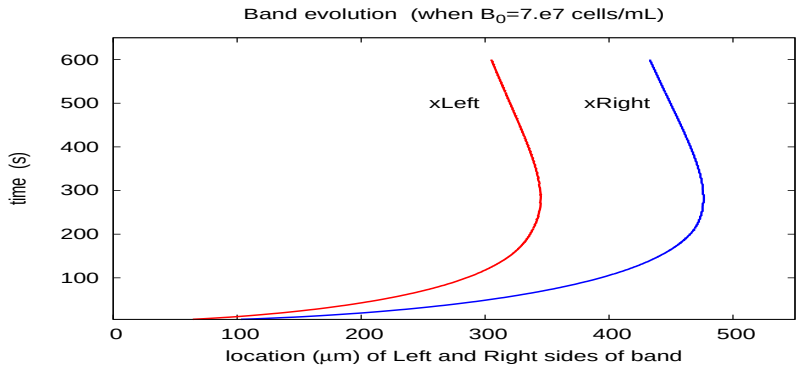

FIGURE 6. Band evolution for fewer bacteria: $B_0 = 7 \times 10^7$ cells/mL. Location 407, width 130 μm.

[3] AN Bible, Characterization of the Function of the Azospirillum brasilense Che1 Chemotaxis Pathway in the Regulation of Chemotaxis, Cell Length and Clumping, *PhD dissertation*, University of Tennessee, 2012.

[4] M Elmas, T Mukherjee, V Alexiades, G Alexandre, A two pathways model for chemotactic signaling in Azospirillum Brasilense, *in this volume*.

[5] BC Mazzag, IB Zhulin, and A Mogilner, Model of Bacterial Band Formation in Aerotaxis, *Biophysical J.*, 85(6): 3558-3574, 2003.

[6] GH Wadhams and JP Armitage, Making sense of it all: bacterial chemotaxis, *Nature Rev. Mol. Cell. Biol.*, 5:10241037, 2004.