Simulation of Bacterial Chemotaxis by the Random Run and Tumble Model

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Simulation of Bacterial Chemotaxis by the Random Run and Tumble Model

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***Abstract*—*In this paper, the movement of bacteria, i.e. E. coli, is simulated based on the run and tumble model. The random walk parameters, such as the speed, tumbling frequency, run duration, and the turn angle between two successive runs were taken from experimental measurements; and use them to simulate the bacteria movement in cases of three different uniform chemical concentration distributions. The motility coefficient is computed to characterize the migration responses. Furthermore, a case of chemical attractant gradient distribution in the environment is designed to validate the run and tumble model. It is found that bacteria move with higher motility coefficient in higher chemical concentrations. Simulation results suggested that bacterial run and tumble model can be used to describe real bacteria movement.*

Keywords-the run-and-tumble model, motility coefficient, random walk, attractant.

I. INTRODUCTION

The process, in which an individual bacterium moves in a chemical stimulus gradient is called bacterial chemotaxis. The trajectories of movement appear as an alternating random sequence of movements during which changes in direction are gradual or abrupt, we call these runs and tumbles. This series of run movements, tumble and turn angle are illustrated in Figure 1. The bacterium swims in a series of smooth straight trajectories. Then the bacterium tumbles, orients itself and selects a new direction to start another smooth run. This gives the cells nearly a random reorientation from which to begin the next run [1]. This alternating series of runs and tumbles, the bacterium traces out a random walk trajectory.

Motility of *E. coli* is generated by a reversible rotary motor located at the flagella filament. When the flagella rotary motors rotate in the counterclockwise direction, the 6 to 8 flagella on *E. coli* tend to form a coordinated bundle according to the flagella left-handed helicity, and as a result form a nearly constant propulsion and drive the cell in a smooth track. On the contrary, a clockwise rotation of the flagellum results in a disruption of the coordinated bundle which causes the cell tumble [2, 3].

For an individual cell, motility can be further interpreted in terms of its speed, tumbling frequency, the reciprocal mean run length time, and the run of directional persistence [4]. Speed is defined as the cell's linear velocity magnitude during a run. Due to the Poisson process of the underlying random processes, the inverse mean run length time is related to the tumbling frequency or the tumbling probability. The run of directional persistence is related to the turn angle; that is, the turn angle between two successive runs. Further, the dispersion of a population of cells in an isotropic medium can be described in terms of a random motility coefficient for the microscopic level [4, 5].

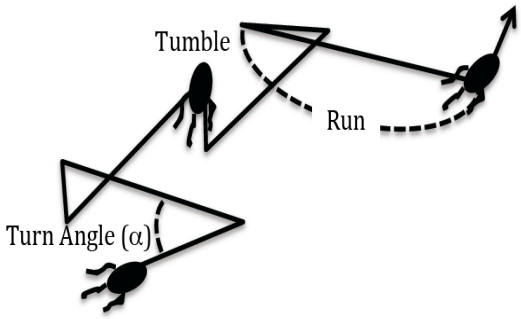


Figure 1. An illustration of bacterial runs, tumbles and turn angle

In this study, we develop hypotheses for the parameter distributions from the literature and use them to simulate bacteria random walks. Then we can validate and compare the stochastic model by computing the simulated random motility coefficient, under different concentration of L-serine. Our goal is to employ a mathematical model of chemotaxis that can help understanding the mechanism of bacterial movement that allow for model validation. The parameters used in the present study for *E .coli* AW405 have been measured at microscopic individual cell.

This paper is organized as follows. In Section II, we describe the parameters used in simulating the *E. coli* movement, and define the motility coefficient. In Section III, we discuss the random walk simulation results for three different uniform concentration distributions, and a case of non-uniform concentration distribution. In Section IV, we present our conclusion and discussion.

II. PARAMETERS FOR *E.COLI* MOTILITY

On cellular level, individual bacterial cell movement was thoroughly studied by using a three-dimensional

tracking microscope to track *E. coli AW405* in an isotropic solution and in the presence of aspartate and serine gradients [1]. On the molecular level, advacned physical method, such as the bioluminescence resonance energy transfer technique, is used to investigate the bacterial flagellar motor [6]. In this section, we follow the conventional approach assuming that the motion of the bacterial is completely defined by the cell speed, cell run length time, and the turn angle [7]. Also, our random walk simulation assumed that motion of the cell can be very well approximated by two dimensional movement.

A. Cell speed

The cell's linear speed during a run to run is denoted as ν. The speed distribution for cell swimming in the absence of serine is shown in Figures 2. The cell speed is assumed to follow a normal distribution with a mean of 24.1 ± 6.8 μm/s [8]. We can consider the speed as consant for the reason that all of the filaments rotate in the same direction, and the total propulsion can be seen as a constant. Figure 3 shows the record of experiment real speed. The measured data were gathered only when a cell was observed to tumble, run and making turns. It is rare random motility parameters for an individual cell is measured more than once.

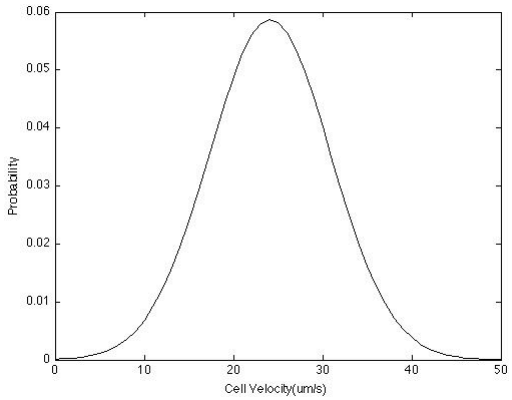


Figure2. Distribution of cell speed. The run speed is simulates as a normal distribution (μ=24.1μm/s, σ=6.8μm/s).

Experimental determined cell speed of the *E. coli* AW405 is given in Figure 3.

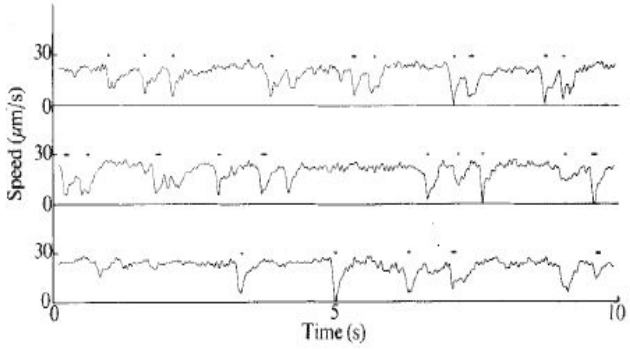


Figure 3. The real speed of the E. coli AW405 reported in Ref. 1.

B. Cell run length time

The theoretical models of Refs. 4 and 5 are assumed, that is, the cell tumbling events are the result of a Poisson process [9] with rate interval, λ_τ [4, 5].

Let T_1 denotes the time beteween cell tumble, then the cumulative probability of T_1 occurs at a time less than t is given by [8],

$$p[T_1 \le t] = 1 - p[T_1 > t] = 1 - e^{-\lambda_\tau t} \quad (1)$$

The run length time distribution for bacteria swimming in the absence of serine is show in Figure 4. The data are distributed exponentially with a mean of 0.84 ± 0.71 s. In this case the tumbling probability was found to be 1.37 per second. Figure 4 is a plot of run length time Poisson probability distribution.

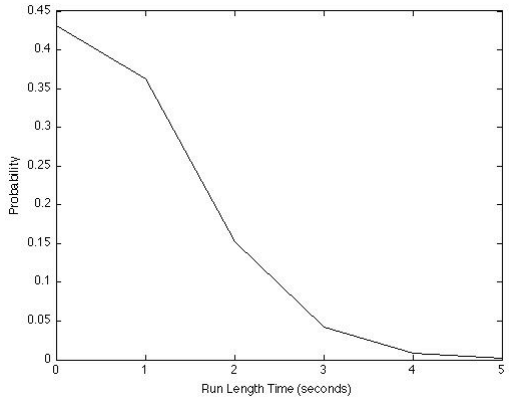


Figure 4. Possion distribution of cell run length time.

Cell run distance D is defined as the cell's displacement between two continuous tumbles, which is given by,

$$D = v \times T_1 \quad (2)$$

Both of the run distance D and T_1 follow the Possion distribution. Furthermore, it is assumed that the cell run distances of successive runs are not correlated [10, 11].

C. Cell turn angle

Angle α is the cell turn angle from run to run. The *E. coli* will start a new run, the direction of the new run is chosen nearly at random. The cell chooses a new run direction at random, and we can assume its distribution to be a uniform distribution between 0 to π. The mean of α is π and mean of cos α is -1 [11]. If α is concentrated around 0, the mean of cos α is around 1 (see Figure 5). This means a high degree of the persistence of the direction from run to run. In this paper, we will use Ref. 1 results, which reported *E. coli* AW405 turn angle experiment data, showed in Figure 6, as the simulation parameter.

When the cell selects an angle (normal distributed at 68^0 with a standard deviation of 36^0), the decision of whether it is upward or downward depends on the Bernoulli

random valuable with the probability for upward equals to the probability for downward. During the next selection of turn angle, the above procedure is repeated with the last selected direction set to zero. In other words, the coordinate system is re-oriented for every step of simulation.

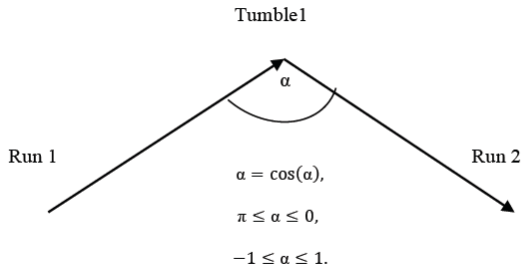


Figure 5. Run to run angle was purely random, turn angle α would have an expected value of π, resulting in a value of cos α equals to -1.

Figure 6 is the reported *E. coli* AW405 turn angle experiment data. As a good approximation in the simulation, the turn angle distribution assumed to follow the normal distribution.

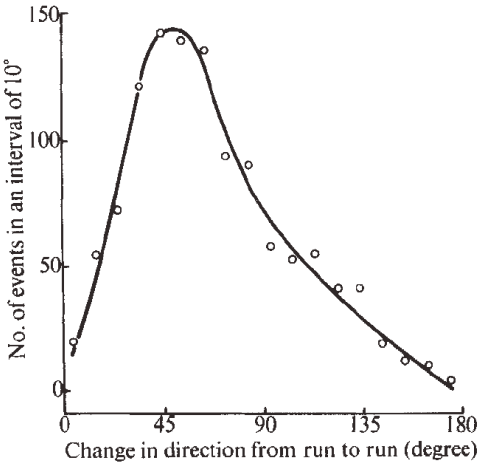


Figure 6. Distribution of cell changes in direction from the end of one run to the beginning of the next for the *E. coli* AW405 (μ=62°, σ=26°) [1].

Parameters used in the present work for different concentration environments are shown in Table 1. The turn angle used in Table 1is 68±36 which is taken from Ref. [1] Table 1.

Table 1. Physical parameters used for the simulation at different concentration environment [1].

L-Serine Concentration (10^{-6} Molar)	Cell Speed (μm/s)	Run Length Time(s)	Turn Angle (degrees)	Tumbling Frequency (1/s)
0	24.1±6.8	0.84±0.71	68±36	1.37
67	30.7±7.1	1.00±0.87	68±36	1.15
1000	30.2±5.2	1.35±1.02	68±36	0.67

D. Motility coefficient

At the cellular level, the cell population random motility coefficient (MC) can be related to individual cell parameters, which is given by [4, 5].

$$\mu_0 = \frac{v^2}{n_d \lambda_t (1-(Cos\alpha))} \tag{3}$$

where μ_0 is the random motility coefficient, ν is the individual cell swimming speed, λ_t is the tumbling frequency or reciprocal run length time, n_d is the number of spatial dimension, and α is the turn angle between successive runs. The stochastic model assumes that the probability of tumbling. λ_t is the rate intensity of a Poisson process. Angle α accounts for the angle a cell's path takes between adjacent runs. If the angle between run is random, the mean run to run angle will be 90 degrees. If the mean turn angle approaches the extreme value 180 degrees, then on average a cell would swim in the opposite direction. The motility coefficient has a physical dimension of $(\mu m)^2/s$, which can interpreted as the two-dimensional areas swap out per second by the baceteria.

III. SIMULATION FOR DIFFERENT CONCENTRATION CASES

A. Random walk simulation of different concentration

The random walk simulation for bacteria swimming is performed within a circular spatial region of 6 cm in diameter under three different concentrations, i.e. 0 μM, 67 μM and 1000 μM are presented in Figures 7 (a), (b) and (c) respectively. For the purpose of comparing with the experimental result reported in Ref. [1], the simulations are performed using 26 run and 25 tumbles, and the rest of the parameters are taken from Table 1.

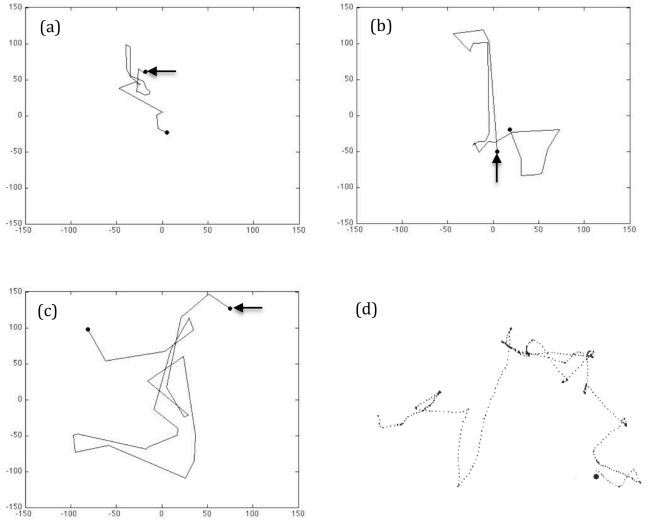


Figure 7. Simulation of the random walk for *E. coli* under different concentrations. The random walk simulations are performed with 26 run and 25 tumbles. Figure (a) The concentration is 0 (10^{-6} Molar), (b) the concentration is 67 (10^{-6} Molar), (c) the concentration is 1000 (10^{-6} Molar), and (d) The *E. coli* AW405 was tracked in 29.5 seconds and mean speed 27.1 μm/s. The arrow indicates the bacterium final stopping point. Figure 7 (d) was adapted from Ref. 1.

From Figures 7 (a) – (c), it is found that the spatial extension of the bacterium movement is larger for higher concentration. This is expected because the bacterium run length time is the highest and the tumble frequency is the lowest at the 1000 μM concentration level. Figure 7 (d) is the experimental plot taken from Ref. 1. The results of the random walk simulation indicated that bacteria swimming behave like real *E. coli* AW450.

The simulation numerical results of the MCs for bacteria swimming in three different concentrations are given in Table 2. The simulations are performed with 20 run and 19 tumbles for 5000 times, i.e. a total of 10^5 runs. The MC at the 67 μM and 1000 μM levels are about twice and three times larger than the 0 μM level respectively. That means bacteria tend to move in a higher speed in higher concentration. The last column in Table 2 reports the coefficient of variation (*CV*), i.e. standard deviation divided by the mean value, for MC. It is found that the *CV* values remain close to 0.30 which is rather independent of the concentration.

Table 2. The simulation results of motility coefficients for three different environment concentrations .

L-Serine Concentration (μM)	Cell Speed (μm/s)	Turn Angle (degree)	Tumbling Frequency (1/s)	Motility Coefficient ((μm)^2/s)	*CV* of MC
0	24.1±6.8	68±36	1.37	203±62	0.305
67	30.7±7.1	68±36	1.15	393±116	0.295
1000	30.2±5.2	68±36	0.67	657±194	0.295

Figure 8 is the bar-chart plots of the number of occurrence versus the MC. The frequency of occurrence distribution of motility coefficient plot indicates that it can be approximated by a normal distribution with long tails. The higher the chemical concentrations, the higher the portion of bacteria have higher MCs. Both of the 67 μM and 1000 μM plots start with a finite MC, and they have long-tailed distributions as well.

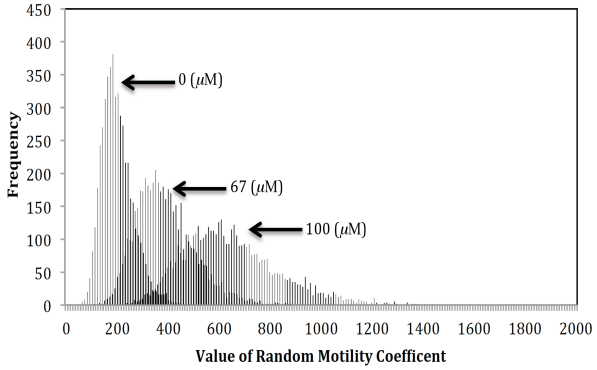


Figure 8. Bar-chart plots of the number of occurrence versus the motility coefficient under three different concentrations.

These two features can be used to distinguish between the zero and high concentration levels. For instance, if the MC is less than 200 (μm)^2/s, then the bacteria are moving under the unbiased condition. On the other hand, if the MC is above 800 (μm)^2/s, then the bacteria are swimming under high concentration level.

B. Random walk simulation of different concentration distributions

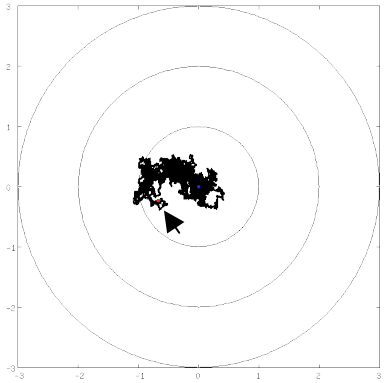
In addition, we also designed a case of chemical attractant gradient environment distributions in order to validate the random run and tumble model. The chemical concentration distribution is 0 μM, 67 μM and 1000 μM for the inner, middle and outer circles respectively. Radius of the inner, middle and outermost circle is 1, 2 and 3 cm respectively.

The simulation is performed for a range of runs from 10^5 to $3x10^5$ in step of $0.5x10^5$. The simulation is repeated for 3000 times, that is, the total number of runs ranges from $3x10^8$ to $9x10^8$. The results of the simulation are given in Table 3. Among the 3000 samples, 4.5% of the time the bacteria finally stopped at the 1000μM concentration circle after 10^5 runs. As the number of runs increased to $3x10^5$ runs, the percentage raises to 22.5 %. On the other hand, the percentage of samples drops from 70.0% to 38.1% for the 0μM concentration inner circle. The last column in Table 3 is the average and standard deviation of the motility coefficient over 3000 samples. In case of 0μM concentration and 10^5 runs, the value of MC is 229 (μm)^2/s, which is a little above the unbiased value, i.e. 203 (μm)^2/s, this is because the bacteria is moving at a higher linear speed at the 67 μM and 1000 μM concentration levels at 25.5% and 4.5% of time respectively. As the number of runs increase, the value of MC is further increased, and reaches 301 (μm)^2/s. This value is still less than 393 (μm)^2/s compared to the 67 μM uniform distribution case.

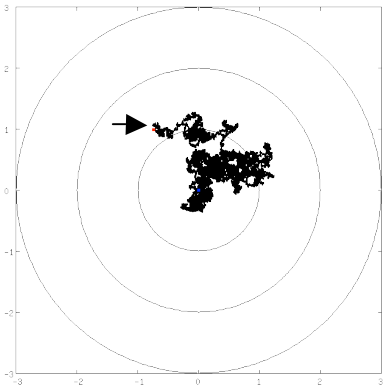
Table 3. Distribution of parameters different concentration environment [1].

Number of runs and tumbles	0μM	67μM	1000μM	Motility Coefficient
$1x10^5$, $1x10^5$-1	70.0%	25.5%	4.5%	229.4±41.9
$1.5x10^5$, $1.5x10^5$-1	58.3%	32.3%	9.4%	248.7±57.4
$2x10^5$, $2x10^5$-1	47.7%	36.5%	15.8%	269.8±71.2
$2.5x10^5$, $2.5x10^5$-1	40.8%	38.4%	20.8%	289.7±78.3
$3x10^5$, $3x10^5$-1	38.1%	39.4%	22.5%	301.6±80.3

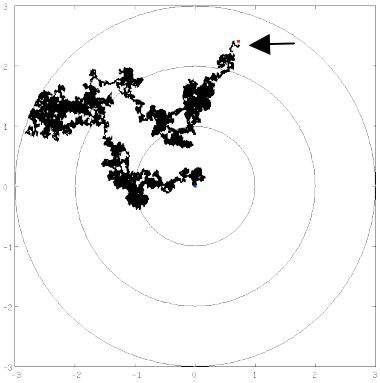
Figures 9 (a), (b), and (c) present the random walk trajectories of a bacterium for $3x10^5$ runs. The bacterium starts moving from the origin, i.e. (0, 0). Figures 9 (a) , (b), and (c) shown that the bacterium stays at the inner, middle and outermost circle respectively. The arrow indicates the final stopping point of the bacterium.



(a)



(b)



(c)

Figure 9. Simulated of the random walk for *E. coli* AW405 under different concentration. In this figure there are 3 x10^5 runs. The arrow indicates the bacterium final stopping point. (a) final position of the bacterium stops at the inner circle, (b) bacterium stops at the middle region, and (c) bacterium stops at the outermost circle.

In Figure 10, the distribution of the number of samples versus the motility coefficient for five different numbers of runs is presented. In case of the simulation is performed with 10^5 runs, the peak of the sample frequency occurs at a MC value of 200 μm^2/s. In other words, bacteria tend to stay at the innermost region. In case of a MC value of 200 μm^2/s, it is observed the number of samples decrease for the 1.5x10^5, 2x10^5, 2.5x10^5 and 3x10^5 runs. That means in some of the samples, the bacterium has a higher MC value. The long-tailed part of the distribution in Figure 10 impies that it is only the 3x10^5 runs contribute to higher MC values This means that bacteria tend to move to the outermost circle in most of the samples, i.e. 22.5%.

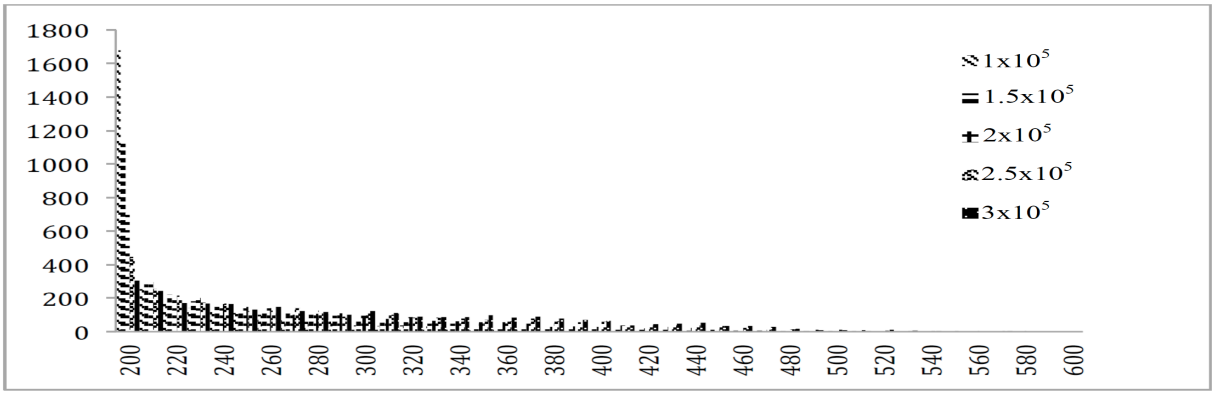


Figure 10. The distribution of number of samples versus the motility coefficient for five different numbers of runs, i.e. 1x10^5 to 3x10^5 in steps of 0.5x10^5

IV. Conclusion and Discussion

In this study, the movement of bacteria, i.e. E. coli, for three different attractant gradient distributions is simulated in order to validate the run and tumble model. The single-cell random walk parameters, such as the speed and turn angle are assumed to follow the normal distribution, whereas tumbling frequency, and run duration are assumed to follow the Poisson distribution. The MC is computed to characterize the migration responses. A case of chemical

attractant gradient distributions in the environment is designed to validate the run and tumble model. It is found that bacteria tend to move with higher MC in higher chemical concentrations.

Our simulation results suggested that bacteria random walk movement behave like real bacteria swimming, and the random MC is generated by a reversible rotary motor located at the base of each flagella filament. In summary, the results indicated that it is possible that we can understand the bacteria swimming process.

Chemotaxis is one of the biologically inspired methods which found applications in (i) the problem of inverse airfoil design [7], and (ii) environmental monitoring and studies of the ecosystem [12]. There are several directions one can extend the current work in the future; (i) simulate the bacteria movement in a continuously changing chemical attractant gradient distribution, (ii) consider chemical repellant gradient distribution, and (iii) conduct *in vitro* experiments in order to confirm simulated results.

ACKNOWLEDGMENT

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REFERENCES

[1] H.C. Berg and D.A. Brown, “Chemotaxis in escherichia coli analysed by three-dimension tracking,” Nature, 239, 500, 1972.

[2] S. H. Larsen, R. W. Reader, E. N. Kort, W.-W. Tso, and J. Adler, “Change in Direction of Flagellar Rotation is the Basis of the Chemotactic Response in Escherichia coli,” Nature, 249, 74, 1974.

[3] R. M. Macnab and M. K. Ornston, “Normal-to-Curly Flagellar Transition5 and their Role in Bacterial Tumbling. Stabilization of an AlternaLive Quaternary Structure by Mechanical Force,” J. Mol. Biol., 112, l, 1977.

[4] H. G Othmer, S. R. Dunbar, and W. Alt, “Models of Dispersal in Biological Systems,” J. Math. Biol., 26, 263, 1988.

[5] H. A. Rivero, H. M. Buettner, R. T. Tranquillo, and D. A. Lauffenburger,“Transport Models for Chemotactic Cell-Populations Based on Individual Cell Behavior,” Chem. Eng. Sci., 44, 2881, 1989

[6] Thomas S. Shimizu, Nicolas Delalez, Klemens Pichler, and Howard C. Berg. “Monitoring bacterial chemotaxis by using bioluminescence resonance energy transfer”, Proc Nat Acad Sci, 103, 2093, 2006.

[7] Sibylle D. Müller, Jarno Marchetto, Stefano Airaghi, and Petros Koumoutsakos, “Optimization Based on Bacterial Chemotaxis”, IEEE Trans. Evolutionary Computation, 6(1), 16, 2002

[8] B. R. Phillips, J. A. Quinn, and H. Goldfine, “Random motility of swimming bacteria: single cells compared to cell populations,” AIChE Journal, 40, 1923, 1994.

[9] S. M. Ross. Introduction to Probability Models, 3rd ed., Academic Press, Inc , San Diego, CA, 1985.

[10] P. Lewus and R.M. Ford, “Quantification of random motility andchemotaxis bacterial transport coefficients using individual-cell andpopulation-scale assays,” Biotechnology and Bioengineering, 75, 292, 2001.

[11] Z. Wang, M. Kim, and G. Rosen, "Validating models of bacterial chemotaxis by simulating the random motility coefficient", Proceedings of Bioinformatics and Bioengineering, 1-5, 2008

[12] Amit Dhariwal, Gaurav S . Sukhatme and Aristides A. G. Requicha, “Bacterium-inspired Robots for Environmental Monitoring”. Proceedings of the 2004 IEEE International Conference on Robatics and Automation, New Orleans. LA, 1436, 2004.