ADVANCES IN BACTERIA MOTILITY MODELLING VIA DIFFUSION ADAPTATION

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ABSTRACT

In this paper we model the biological networks of bacteria and antibacterial agents and investigate the effects of cooperation in the corresponding self-organized networks. The cooperative foraging of the bacteria has been used to solve non-gradient optimization problems. In order to obtain a more realistic model of the process, we extend the previously introduced strategies for bacteria motility to incorporate the effects of antibacterial agents and bacterial replication as two key aspects of this network. The proposed model provides a more accurate understanding of bacterial networks. Moreover, it has applications for various regenerative networks where the agents cooperate to solve an optimization problem. The model is examined and the effects of bacterial growth, diffusion of information and interaction of antibacterial agents with bacteria are evaluated.

Index Terms— Biological networks, bacterial motility, diffusion adaptation, optimization.

1. INTRODUCTION

Biological networks are representations of biological systems and the study of these networks can increase our understanding of such systems. In these networks, species with poor foraging behaviors are not able to survive and will be eliminated over time through natural selection. In order to survive, a species has to optimize the energy it spends foraging under several environmental and physiological constraints [3]. Therefore, modeling the behavior of such networks can be considered as an optimization problem. In particular, these networks can be helpful in solving non-gradient optimization problems, where there is no measurement or analytical description of the field gradient [1].

One of these foraging networks is the bacterial network. Bacteria have the ability to move in response to specific chemical stimuli in their surrounding environment. This phenomenon, which is called chemotaxis, can assist the bacteria to find sources of nutrition or to flee from poisons and antibacterial agents. In this process, the bacteria sense the gradient of chemical stimuli as they move and this gradient affects their movement at each time instant [4]. Bacterial movement can occur through various mechanisms. In order to move and swim through fluids, a bacterium can use its cylindrical structures (the flagella), while gliding and twitching can help it move across surfaces [5, 6]. Bacteria have also the ability to communicate with each other in order to gain more information about their environment. They can emit chemical signals which can be sensed by other bacteria and assist them in perceiving their surroundings [7].

The motility and cooperation of bacterial agents have been modeled based on the physiological behavior of these single-cell microorganisms [1, 2]. However, reproduction among the agents of this network has not been considered and the population size is fixed in the previous models. A network of bacteria undergoes an exponential growth in which the growth rate of the bacterial population is proportional to its current value. The number of bacteria increases in this manner until the concentration of nutrients falls below a certain level [8]. Another important issue that must be taken into consideration is the role of antibacterial agents in this network, which has not been studied in the previous models [1, 2]. Such agents have the ability to kill bacteria, resulting in loss of motility and biochemical signaling of the killed bacteria.

The objective of this paper is to provide a more realistic model for the bacterial network by considering the reproduction of bacteria as well as the role of killer agents in this network. Considering the population growth in the cooperative networks is of crucial importance because it can affect the level of cooperation and therefore, the movement and behavior of the entire network. Moreover, we consider the ability of antibacterial agents to kill the bacteria which plays an important role in the behavior and outcome of the network. Our proposed model of the bacterial network not only promotes our understanding of this network, but is also useful in solving optimization problems in regenerative networks with killer agents and several other constraints.

2. PROBLEM FORMULATION

To realistically model the network of bacteria, we consider bacterial growth, bacterial movement and antibacterial agents. First, we introduce a motility model of bacteria using

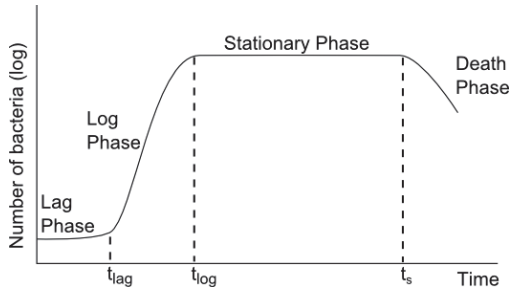


Fig. 1. Bacterial growth curve [8].

diffusion adaptation. We then model the bacteria reproduction and the role of antibacterial agents.

2.1. Motion Model

To model bacterial motion, we use the motion model in [2] which is based on the realistic movement of bacteria. In this model, a bacterium has two types of movement, namely, running and the tumbling. In the running movement, the bacterium moves forward and maintains a relatively fixed moving direction, while in tumbling the bacterium has a random movement whose direction changes randomly. In addition to these two types, the movement of bacteria is also affected by Brownian motion which arises from the nature of the surrounding medium. Brownian motion is usually much smaller than the self-driven motion of the bacterium and can affect the movement of a bacterium in both running and tumbling.

A bacterium can decide to run or tumble at each time instant. We consider $e_k(t)$ as the decision of the kth bacterium at time t which can be either 0 or 1. This variable is the key variable governing the motion model of the bacterium, and its status depends on several inputs such as nutrition sources and information of the other bacteria [9]. When $e_k(t) = 0$ the bacterium tumbles and when $e_k(t) = 1$ the bacterium is in the running mode and moves in the same direction. Consider $I_n(\omega_{k,t})$ to be the density of the nutrition at location $\omega_{k,t}$. The goal of each bacterium is to move towards the maximum of the nutrition density, I_n. Therefore, each bacterium chooses $e_k(t)$ at each time instant such that it moves toward the maximum of nutrition intensity. To achieve this goal, the bacterium measures $I_n(\omega_{k,t}) - I_n(\omega_{k,t-1})$ and chooses $e_k(t)$ based on this gradient [1].

In addition to each bacterium sensing the nutrition density, the bacteria form a network and communicate with each other, sharing their information about the food source through biochemical signaling. A bacterium can release a chemical in the environment which can be sensed by its neighbors and help them move toward the food source.

Considering all of these properties, the motion of a bacterium can be modeled as [2]:

$$\omega_{k,t} = \omega_{k,t-1} + h\frac{u_{k,t}^*}{\|u_{k,t}\|}e_k(t) + b_{k,t}. \quad (1)$$

where $\omega_{k,t} \in \mathbb{R}^2$ is the position of the kth bacterium at time t, h is the movement step size, $u_{k,t}$ defines the direction of the kth bacterium at time t and is a row vector, and $b_{k,t} \in \mathbb{R}^2$ models the Brownian motion and is an i.i.d Gaussian random vector. It should also be noted that $u_{k,t}^*$ is the Hermitian transpose of $u_{k,t}$.

As stated in [2], the orientation of the bacterium can be obtained through a recursion of $u_{k,t}$:

$$u_{k,t+1}^* = h\frac{u_{k,t}^*}{\|u_{k,t}\|}e_k(t) + b_{k,t}. \quad (2)$$

When a bacterium tumbles $e_k(t) = 0$; therefore, $u_{k,t+1}^* = b_{k,t}$ and the movement direction changes randomly. When the bacterium is running $e_k(t) = 1$ and its direction is relatively fixed, since $h \gg \|b_{k,t}\|$.

2.2. Bacterial Growth

Bacterial growth is the result of dividing or splitting of one or more bacteria each into two daughter cells. These daughter cells are identical to the original bacterium genetically and can undergo division themselves. One of the most common models for the bacterial growth consists of four different phases: lag phase, log phase, stationary phase and death phase [10]. Figure 1 shows the bacterial growth curve and the four different phases [8].

During the lag phase, the existing bacteria adapt themselves to the environment and the number of bacteria remains constant. After this phase, they go through the log phase in which the population of bacteria grows exponentially. Because of limiting growth factors, such as nutrition sources, the population of bacteria reaches a maximum in the stationary phase and at the end, due to lack of growth factors the bacteria enter the death phase. To model bacterial growth we consider K_i as the initial number of bacteria in the environment and K_m as the maximum number of bacteria. The number of bacteria during the log phase can be estimated by:

$$k_{\log}(t) = K_i(1 + q_0)^{-\frac{\mu}{v}}(1 + q_0\exp(vt))^{\frac{\mu}{v}}. \quad (3)$$

where $k_{\log}(t)$ is the number of bacteria at time t during the log phase, and $q_0, \mu,$ and v are constant values which represent respectively the total critical substance at $t = 0$, maximum specific growth rate, and growth rate of the critical substance [10]. We assume that the number of bacteria is K_i in the lag phase and increases based on (3) till it reaches K_m and remains constant in the stationary phase. Assuming the bacteria do not go through the death phase, the number of bacteria can be obtained as:

$$k(t) = \begin{cases} K_i, & t < t_{\text{lag}} \\ K_i(1 + q_0)^{-\frac{\mu}{v}}(1 + q_0\exp(vt))^{\frac{\mu}{v}}, & t_{\text{lag}} \le t < t_{\log} \\ K_m, & t_{\log} \le t \end{cases}. \quad (4)$$

where t_{lag} and $t_{\log}$ refer respectively to the beginning and end of the log phase in Figure 1.

2.3. Antibacterial Model

Antibacterial agents can be divided into two major groups in terms of their biological activities: bactericidal and bacteriostatic agents. The bactericidal agents kill bacteria and the bacteriostatic agents slow down the growth of bacteria. The activity of antibacterial agents depends on the phase of bacterial growth and their concentration [11]. In this study, we focus on bactericidal agents. The concentrations of the bactericidal agents should be above a certain level to kill bacteria, called minimum inhibitory concentration [12]. To model the bactericidal agents, we consider $I_h(\omega, t)$ as the concentration of bactericide in location ω at time t. The kth bacterium will be killed by the bactericidal agents at time t if the concentration of bactericide at its location, i.e. $I_h(\omega_{k,t}, t)$, is higher than the minimum inhibitory concentration. In this model, when a bacterium is killed through this process, it loses its motility and thus remains at the same location. Additionally, the killed bacterium no longer emits chemical signals and does not play a role in the cooperation process.

3. DIFFUSION BASED MODELING

The collection of bacteria forms an adaptive network, where the agents cooperate with each other by propagating signals that stem from biochemical reactions. In the simulation results we show that the diffusion of information helps them adapt their performance, survive, and locate the food sources more efficiently.

At every time instant, each bacterium in the network has a noisy estimate of the nutrition intensity. This estimate is a scalar measure which depends on the distance of the bacterium from the source of nutrition, represented by:

$$d_k^n(t) = I_n(\omega_{k,t}) + v_k^n(t). \tag{5}$$

where $d_k^n(t)$ represents the nutrition density observed by the kth bacterium at time t and n refers to nutrition. $v_k^n(t)$ is the observation noise which is assumed to be an i.i.d Gaussian random variable.

Additionally, each bacterium has access to the information emitted by other bacteria in the network. The nature of this information arises from the chemicals bacteria are able to release in their surrounding environment [2]. We can model this information sharing as:

$$I_c(\omega_{k,t}, t) = \lambda_c I_c(\omega_{k,t}, t-1) + \sum_{l=1}^{k(t)} I_b(\omega_{k,t}, \omega_{l,t}) s_l^n(t). \tag{6}$$

where $I_c(\omega_{k,t}, t)$ represents the chemical intensity in the location of the kth bacterium at time t, λ_c is a factor that indicates the decay of the chemical field over time, $I_b(\omega, \omega_{l,t})$ is the chemical signal released by the lth bacterium, and $s_l^n(t)$ can be 0 or 1. The parameter $s_l^n(t)$ in (6) indicates whether the lth bacterium shares its information about the food source at time t which can be defined as:

$$s_k^n(t) = \begin{cases} 1, & I_n(\omega_{k,t-1}) - I_n(\omega_{k,t-2}) \geq \sigma_n \\ 0, & I_n(\omega_{k,t-1}) - I_n(\omega_{k,t-2}) < \sigma_n \end{cases}. \tag{7}$$

where σ_n is a positive threshold that defines the minimum necessary nutrition gradient that stimulates the bacterium to share information.

Similar to information of bacteria about the nutrition intensity, the estimated chemical intensity by each bacterium can be noisy. Hence, the measured chemical intensity by the kth bacterium at time t, i.e. $d_k^c(t)$, is:

$$d_k^c(t) = I_c(\omega_{k,t}, t) + v_k^c(t). \tag{8}$$

where $v_k^c(t)$ is measurement noise and is assumed to be an i.i.d Gaussian random variable.

Based on these two items of information, $I_n(\omega_{k,t})$ and $I_c(\omega_{k,t}, t)$, each bacterium can decide whether to diffuse information to the network or not. This decision is represented by $e_k(t)$ for every time instance:

$$e_k(t) = \lambda_l s_k^n(t) + (1-\lambda_l) s_k^c(t). \tag{9}$$

where $0 \leq \lambda_l \leq 1$ is a coefficient that determines the level of cooperation, and $s_k^c(t)$ indicates the chemical gradient and can be defined as:

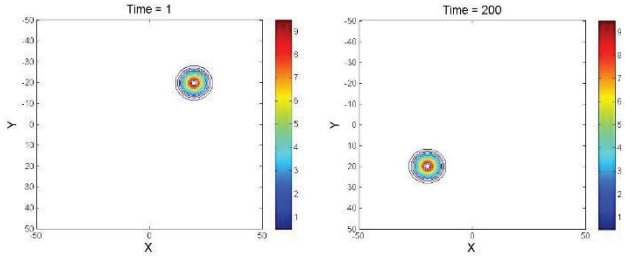
$$s_k^c(t) = \begin{cases} 1, & I_c(\omega_{k,t-1}) - I_c(\omega_{k,t-2}) \geq \sigma_c \\ 0, & I_c(\omega_{k,t-1}) - I_c(\omega_{k,t-2}) < \sigma_c \end{cases}. \tag{10}$$

where σ_c is the minimum necessary chemical gradient to stimulate the bacterium to share information and is a positive threshold. As stated, different values of λ_l can affect the cooperation among the network agents. For instance, when $\lambda_l = 1$, the emphasis is only on the nutrition and each bacterium decides about its movement only based on its own sense about the nutrition intensity. On the other hand, when $\lambda_l = 0$, the emphasis is on biochemical signaling and the information shared by other agents. In the next section, we evaluate the performance of the network for various values of λ_l.

4. SIMULATION RESULTS

In this section we simulate the growing network of bacteria moving in the presence of antibacterial agents. The results for different cooperation strategies are demonstrated to comprehend the role of diffusion adaptation.

To model the growth of bacteria, we use (4) with K_i=30 and K_m=90, i.e. the number of bacteria is 30 at the beginning and grows up to 90. For convenience, we assume $t_{\text{lag}} = 0$ which means the bacteria start to grow as the time begins and $t_s = \infty$ which means that a bacterium dies only if it gets close enough to the antibacterial agents during the simulation and does not go through the death phase by itself. The parameter $t_{\log}$ is the time when the number of bacteria reaches 90. The values of q_0, μ, and v are assumed to be 0.5, 0.1 and 0.2 respectively [10].



(a) Initial stage (t=1) (b) Final stage (t=200)

Fig. 2. Distribution and dynamic movement of antibacterial agents based on (11).

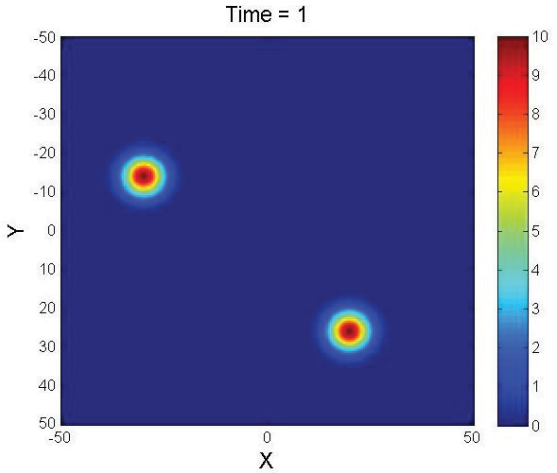


Fig. 3. Distribution of nutrition intensity.

The bactericidal field can be modeled using a two dimensional Gaussian distribution. Therefore, the intensity of bactericidal at location $\omega = (x, y)$ and time t can be obtained by:

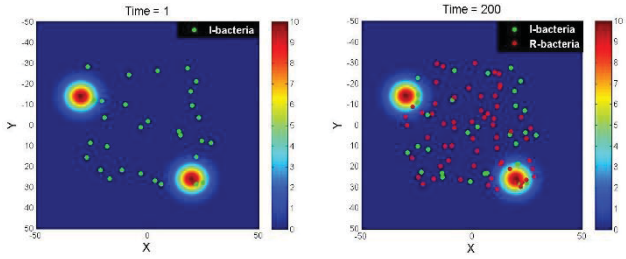
$$I_h(\omega, t) = a_{max} \exp\left(-\frac{(x-(x_h-t/10))^2+(y-(y_h+t/10))^2}{2\sigma_a^2}\right). \quad (11)$$

where $a_{max} = 10$, $(x_h, y_h) = (20, -20)$, and $\sigma_a = 4$. It should be noted that the center of the distribution changes slightly with time in order to allow for slow movement of bactericide. As it can be seen from (11) the movement step size is 0.1. The bactericidal field for $t = 1$ and $t = 200$ are shown in Figure 2.

To model the nutrition intensity, two identical nutrition sources with two-dimensional Gaussian distribution are located at (x_1^n, y_1^n) and (x_2^n, y_2^n). We assume that the nutrition intensity does not change over time. Thus, the nutrition intensity at location $\omega = (x, y)$ can be obtained from:

$$I_n(x, y) = b_{max} \exp\left(-\frac{(x-x_1^n)^2+(y-y_1^n)^2}{2\sigma_b^2}\right) + b_{max} \exp\left(-\frac{(x-x_2^n)^2+(y-y_2^n)^2}{2\sigma_b^2}\right). \quad (12)$$

where $b_{max} = 10$, $(x_1^n, y_1^n) = (-30, -14)$, $(x_2^n, y_2^n) = (20, 26)$, and $\sigma_b = 4$. Figure 3 shows the nutrition intensity.



(a) Initial stage (t=1) (b) Final stage (t=200)

Fig. 4. Location of bacteria; The population of bacteria changes based on (4).

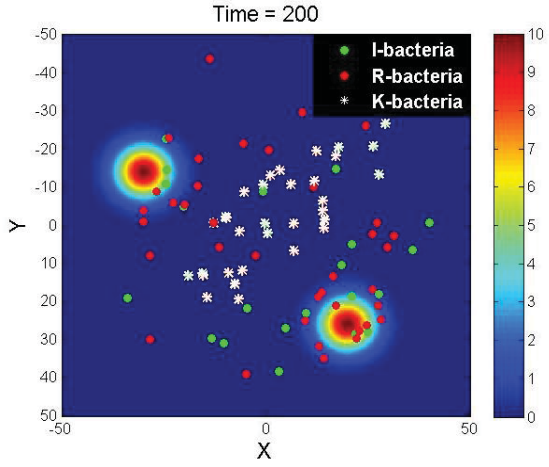


Fig. 5. Regenerative network of bacteria; dynamic behavior based on (9) when $\lambda_l = 1$ and there is no cooperation.

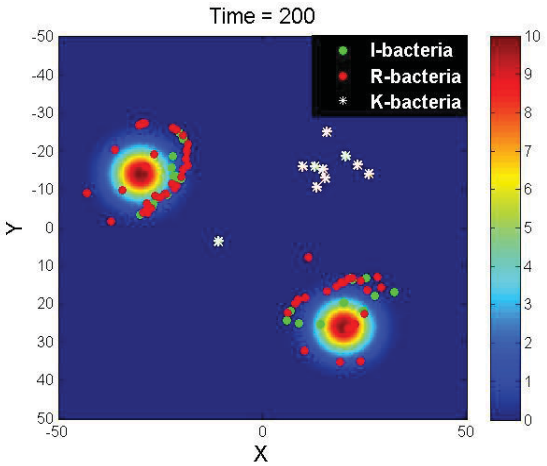


Fig. 6. Regenerative network of bacteria; dynamic behavior based on (9) when $\lambda_l = 0.8$ and there is cooperation among bacteria.

The chemical signal released by the kth bacterium, i.e. $I_b(\omega, \omega_{k,t})$, is also assumed to follow a two dimensional Gaussian distribution:

$$I_b(\omega, \omega_{k,t}) = c_{max} \exp\left(-\frac{(x-x_{k,t})^2+(y-y_{k,t})^2}{2\sigma_c^2}\right). \quad (13)$$

where $\omega = (x, y)$, $\omega_{k,t} = (x_{k,t}, y_{k,t})$ is the location of the kth bacterium at time t. We empirically selected $c_{max} = 5$, and $\sigma_c = 5$. According to (6), all these chemical signals are accumulated to form the chemical intensity which decays with λ_c=0.9. Moreover, the noise components $v_k^n(t)$ and $v_k^c(t)$ in (5) and (8) are modeled as i.i.d Gaussian random variables with zero mean and unit variance and σ_n and σ_c in (7) and (10) are 0.1.

The bacteria are assumed to be distributed randomly and uniformly over a 60 × 60 rectangle centered at the origin $(0, 0)$ at $t = 1$. The regenerated bacteria are also assumed to follow the same distribution. Figure 4 shows the locations of bacteria at $t = 1$ and at the final stage when the number of bacteria has reached its maximum. To model the motion of bacteria based on (1) and (2), h and $b_{k,t}$ are respectively set as 1 and i.i.d two dimensional Gaussian random variables with zero mean and 0.1 standard deviation. It should be mentioned that I-bacteria in Figure 4 represents the initial K_i bacteria existing since the beginning of the process, while R-bacteria represents the reproduced bacteria over time.

To investigate the behavior of the network for various diffusion cases, we simulated and demonstrated the results for 200 time steps. Figure 5 shows the simulation results of the final stage for the case where there is no cooperation between the bacteria. In other words, in this case $\lambda_l = 1$ in (9) and the decision of each bacterium depends only on its own knowledge about the nutrition intensity. In contrast, Figure 6 illustrates the results of simulation when $\lambda_l = 0.8$ and bacteria are cooperating and sharing their information in order to reach higher nutrition intensity. In Figure 5 and Figure 6, K-bacteria represents the bacteria that have been killed by the antibacterial agents.

It can be seen by comparing Figure 5 and Figure 6 that in the cooperation case most of the bacteria reach the source of nutrition despite the noisy conditions. However, the performance of the network is not as successful when the bacteria are not cooperating. Without cooperation, most of the bacteria are not able to find their way to the nutrition source and the number of bacteria killed by the antibacterial agents is larger compared to the case with cooperation. The main reason is that in this situation the movement of bacteria is mostly Brownian motion in which the location of bacteria changes slowly. Therefore, the bacteria stay in the central area which is farther from the nutrition source and closer to the antibacterial field. However, in the case of cooperation among bacteria, the chemical communication in the network leads the bacteria toward nutrition and away from the antibacterial agent, resulting in a higher survival rate.

5. CONCLUSION

In this paper we model the behavior of the regenerative network of bacteria in the presence of antibacterial agents which models the entire process more realistically compared with that presented in [2]. The performance of this self-organized network is compared for two cases, with and without cooperation among the bacteria. Cooperation among agents of the network can be successfully modeled using diffusion adaptation. It is shown that cooperation is beneficial for the network of bacteria in terms of tracking the nutrition source and fleeing from antibacterial agents. This method can be used to model the growth of infection and the role of antibacterial agents in controlling infection. The proposed model can also be helpful in solving non-gradient optimization problems, where measurements or analytical descriptions of the field gradient are not available.

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