Distance Estimation for Molecular Communication in Blood Vessel

Yu Li[1], Zhongke Ma[2], Hao Yan[2(✉)], Jie Luo[1], and Lin Lin[1]

[1] College of Electronics and Information Engineering, Tongji University, Shanghai, China
{1930703,2132942,fxlinlin}@tongji.edu.cn
[2] School of Electronic, Information and Electrical Engineering, Shanghai Jiao Tong University, Shanghai, China
yan_hao@sjtu.edu.cn

Abstract. Molecular communication (MC) is proposed as a promising communication paradigm for nanonetworks. The knowledge of the distance between transmitter and receiver is of great importance in MC to achieve good system performance. The distance estimation work has been carried out based on the free diffusion channel of MC. The blood vessel, which is different from the free diffusion channel, is also very important for many MC applications such as drug delivery. However, the distance estimation schemes for the channel of blood vessel have not been investigated. In this work, we propose a distance estimation scheme for the blood vessel channel of MC. A more realistic model of the flow velocity in the blood vessel is presented. The corresponding channel impulse response (CIR) of the blood vessel channel is derived. Moreover, the effectiveness of the proposed distance estimation scheme is validated by simulations.

Keywords: Molecular communication · Blood vessel · Blood velocity · Distance estimation

1 Introduction

Molecular communication (MC) is a promising paradigm to interconnect nanomachines in a nanonetwork due to its advantages of bio-compatibility and energy efficiency [4,16]. One of the most important applications of the MC is the drug delivery system where drug particles (micro- or nano- meter in size) propagate from the injected site to the targeted site via blood vessels [10]. However, the study of MC in the channel of blood vessel is quite limited. Therefore, it is very necessary and important to investigate MC system in the blood vessel channel.

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In MC, the distance between the transmitter and the receiver is quite an important parameter [11]. Different distance between nanomachines results in different channel impulse response (CIR) which has great impacts on the performance of the MC system [7]. For example, the distance has to be known in order to achieve clock synchronization among nanomachines [12]. The distance is also a key parameter to determine the transmission rate and the number of molecules to be released for the optimal channel capacity [17]. In the MC applications such as the drug delivery system, the distance between the drug carrier nanomachine and the destination is quite important. Therefore, the distance between the transmitter and the receiver is of great importance and appropriate distance estimation schemes are quite necessary.

The studies on the distance estimation schemes in MC mainly focus on the distance estimation in free diffusion channel. For the free diffusion channel, the scheme based on the peak concentration of the received signal is the most frequently used method [6,13]. The receiver measures the concentration of the molecules and records the time when the concentration reaches its maximum. The distance is then calculated with the peak time and the concentration value. Another scheme is to use the energy to estimate the distance [18]. It performs better in accuracy compared with the peak concentration scheme, though it is more complex. In [15], round trip time and signal attenuation protocols are proposed. These two schemes estimate distance by measuring the round trip time or the signal attenuation of the received feedback signal. These schemes are designed for the free diffusion channel. However, the blood vessel is neither a simple free diffusion channel nor a flow-assisted channel with a constant flow speed. The velocity of the blood flow in blood vessels changes periodically [3]. Therefore, the state-of-the-art distance estimation schemes designed for free diffusion channel are not suitable for blood vessel channels. To the best of our knowledge, there is no specific distance estimation scheme for the blood vessel channel. The investigation of distance estimation schemes in blood vessel channels is quite necessary.

In this paper, we propose a distance estimation scheme for the channel of the blood vessels in the MC system. We establish a more realistic model of the blood velocity in vessels for MC. Based on the proposed blood velocity model, the CIR of the blood vessel is derived. We find that both the periodical property of the blood velocity and the molecule releasing time relative to the period of the blood velocity affect the CIR. By acquiring the period of the blood velocity and the molecule releasing time relative to the period, the distance is accurately estimated. The effectiveness of the proposed scheme is validated by the simulation.

The remainder of the paper is organized as follows. In Sect. 2, we put forward the blood velocity pattern and introduce the system model. Section 3 proposes the scheme for the estimation of the distance between the transmitter and the receiver. Simulation results are shown in Sect. 4. Finally, the conclusion is drawn in Sect. 5.

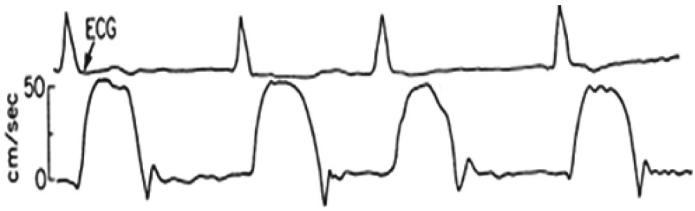

Fig. 1. The blood velocity in human beings' pulmonary artery. ECG means electrocardiogram.

2 System Model

2.1 Model of Blood Velocity

Considering the fact that the heart beats periodically, the pressure difference at the two ends of the vessel also changes periodically. Accordingly, the blood velocity changes periodically. Figure 1 shows an example of the blood velocity pattern in a human being's pulmonary artery [5]. The upper curve is the ECG curve, and the lower curve is the velocity pattern. The blood velocity changes periodically and its waveform is close to a rectangle wave. According to [5], no matter how long the period is, the duty cycle of the blood velocity is always about 37.5% of the period.

In the state-of-the-art MC studies, the blood velocity is always modeled as a constant velocity, and the channel of the blood vessel is correspondingly considered as a flow-assisted diffusion channel with a constant flow velocity. Such approximation is quite different from reality and not accurate at all. Herein, we propose a more accurate model of the blood velocity. As the blood velocity curve in Fig. 1 is close to a rectangle wave, we adopt the rectangle wave as the approximation shown in Fig. 2 to better model the blood velocity in vessels. Its period is defined as T and the amplitude is V_0. Assume the signal molecules are released at $t = 0$. τ is the time duration between the initial time $t = 0$ and the first rising edge of the periodical rectangle wave. This parameter is useful in the distance estimation scheme in Sect. 3. The function of the modeled blood velocity can be written as

$$V(t) = \begin{cases} V_0 & kT + \tau < t < kT + 0.375T + \tau, \\ 0 & kT + 0.375T + \tau < t < kT + T + \tau, \end{cases} \tag{1}$$

where $k = 0, 1, 2, 3, \ldots$ and the duty cycle is 37.5%.

For a particular vessel, V_0 is a fixed value. For example, in human beings' capillary vessels, the approximate amplitude is $V_0 = 0.4\,\text{mm/s}$ [9]. But the period of the blood velocity T is variable. This is because that the heart rate differs among people. And even for the same person, the heart rates are different in different body states, such as when people are resting or doing exercise.

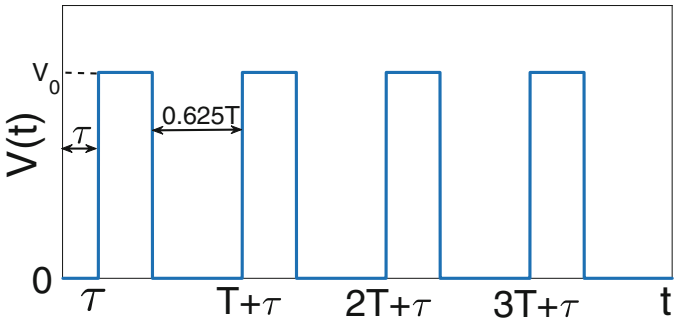

Fig. 2. The proposed model of the blood velocity in blood vessel.

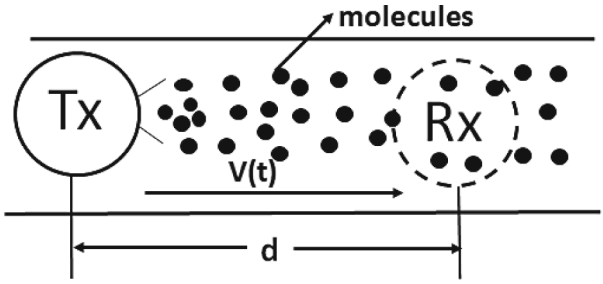

Fig. 3. Illustration of an end-to-end MC system in a 3D fluid environment.

2.2 System Model

An end-to-end MC system in a 3D fluid environment is considered in this paper. It is illustrated in Fig. 3. A passive receiver is located at a Euclidean distance of d from the transmitter. The synchronization between the transmitter and the receiver is assumed to be achieved [14]. The transmitter releases N molecules into the channel. The molecules propagate in the channel affected by both the diffusion and blood velocity $V(t)$. Finally, the molecules arrive at the receiver at different times. The passive receiver detects the concentration of the molecules that enter its sensing range, but does not affect the movement of the molecules. Based on the detected signal, the distance d is estimated by the scheme proposed in Sect. 3. In the system, the time instant that the transmitter releases the molecules is set as $t = 0$. Usually the time interval τ between the releasing time and the time of the first rising edge of the blood velocity is stochastic, because the transmitter can release molecules at any time which is irrelevant to the blood flow.

In a free diffusion channel, the channel impulse response (CIR) at the receiver is given in [8] as

$$h(t) = \frac{1}{(4\pi Dt)^{\frac{3}{2}}} exp(-\frac{d^2}{4Dt}), \tag{2}$$

where D is the diffusion coefficient. In the channel of blood vessel where exist both free diffusion and blood flow assisted diffusion with velocity $V(t)$ in (1), the CIR can be derived as

$$h(t) = \frac{1}{(4\pi Dt)^{\frac{3}{2}}} exp\{-\frac{[d - \int_0^t V(t)\, dt]^2}{4Dt}\}. \tag{3}$$

If the transmitter releases N signal molecules, the concentration of the signal molecules detected by the receiver then comes to

$$C(t) = \frac{N}{(4\pi Dt)^{\frac{3}{2}}} exp\{-\frac{[d - \int_0^t V(t)\, dt]^2}{4Dt}\}. \tag{4}$$

An example of signal concentration detected by the receiver is shown in Fig. 4, associated with $V(t)$ to illustrate their relationship. When $V(t) = 0$, due to the free diffusion, the molecules perform Brownian motion. When $V(t) \neq 0$, the drift with velocity V_0 dominates the movement of molecules. The diffusion still takes effect, but its impact is quite limited. Affected by such $V(t)$, it is noticed that the plot of signal concentration in Fig. 4 is quite different from the signal concentration in free diffusion channel or that in the constant flow-assisted channel. The concentration curve in Fig. 4 looks like cutting the concentration curve of constant flow-assisted channel into several pieces and connecting these pieces with line segments which are parts of the concentration curve of free diffusion channel where concentration changes slowly. These two different types of pieces appear alternately and correspond to the time that $V(t) = V_0$ and $V(t) = 0$ respectively. The amplitude changes at $V(t) = V_0$ are faster than the amplitude changes at $V(t) = 0$. We define these points at the junction of the two types of pieces as feature points of the concentration curve. Hence, at the feature points, the change of its first derivative is relatively larger than that of other parts.

The concentration curve in the bottom panel of Fig. 4 is an example of the channel response in blood vessels with fixed values of parameter T and τ. Different from the response in the free diffusion channel and constant flow-assisted channel with fixed d, the CIR for the channel with periodic blood velocity also varies with different values of T and τ.

3 Distance Estimation Scheme

As discussed in Sect. 2, the CIR of the blood vessel channel is different from the CIRs of free-diffusion channel and constant flow-assisted channel. Therefore, the distance estimation schemes for free-diffusion channel and constant flow-assisted channel are not applicable to the blood vessel channel. Herein, we propose a distance estimation scheme for the blood vessel channel.

Our proposed scheme utilizes the CIR of blood vessel channel in (3) to estimate the distance in blood vessels. The transmitter releases N molecules which propagate in the blood vessel. The receiver measures the concentration $C(t)$

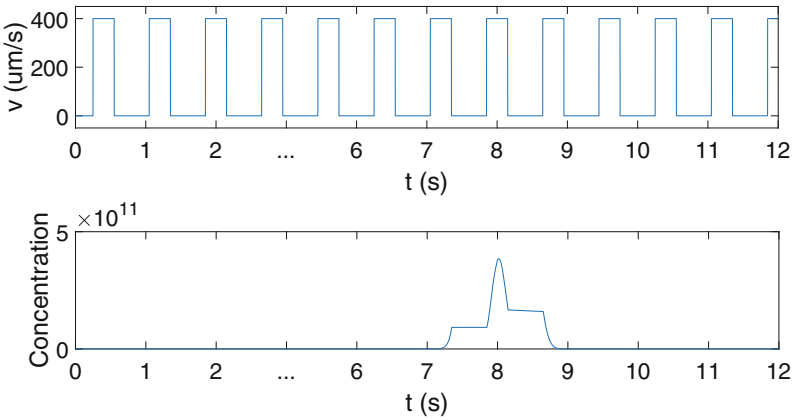

Fig. 4. The concentration curve of the blood vessel and the corresponding $V(t)$.

of signal molecules and records the corresponding time when the concentration reaches its maximum. The problem is that $V(t)$ is unknown in (3). In order to calculate the distance d, $V(t)$ should be estimated first. With the peak time, peak concentration, and $V(t)$, the distance is calculated through the CIR in (3).

The whole scheme includes two parts: 1. Calculate variables T and τ to obtain $V(t)$ in (1); 2. Estimate the distance d with (3). In this paper, the situation that $d < V_0 \times 0.375T$ is not considered. That is to say, we do not consider the situation that the transmitter and receiver locate too close such that the peak concentration of molecules arrives within a single period of blood velocity.

The receiver measures the concentration of signal molecules and records the time when the concentration reaches its maximum.

3.1 Calculate T and τ

To calculate T in (1), our strategy is to find the feature points of the concentration curve. The time interval between two feature points at two neighboring rising edges or two neighboring falling edges is the period of the blood velocity T.

Firstly, we discuss how to find the feature points. The receiver takes samples of the concentration of signal molecules around it. We denote the sampling values as C(Δ), C(2Δ), C(3Δ), ..., C(nΔ), where Δ is the sampling interval. Since there are noises in the MC system which affect the accuracy of the received signal. Therefore, smoothing is performed in the first step. After smoothing, the first and second derivatives of the concentration are calculated as

$$S(i) = \frac{C[(i+1)\Delta] - C(i\Delta)}{\Delta}, \tag{5}$$

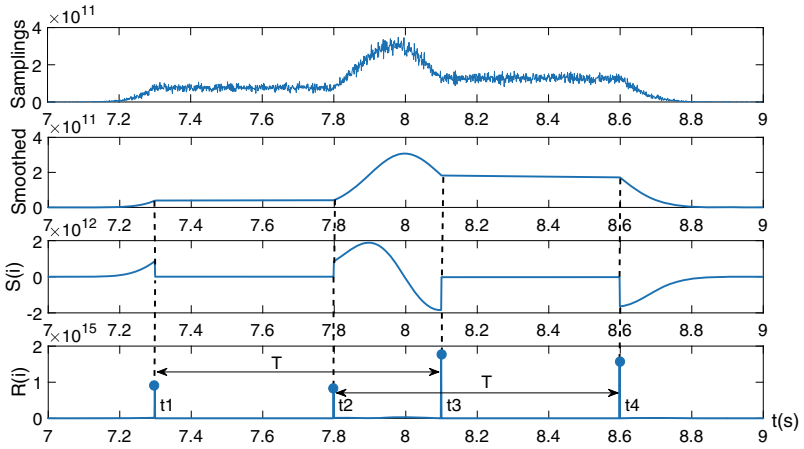

Fig. 5. Illustration of the calculation process of T. The plot of the concentration $C(i)$, the first derivative $S(i)$, and the absolute value of the second derivative $R(i)$ are shown in the top two panels, the middle and bottom panels respectively in the figure. The real distance is 1270 µm and other parameters are the same as defined in Table 1.

and

$$R(i) = \frac{S[(i+1)\Delta] - S(i\Delta)}{\Delta}, \tag{6}$$

where i $= 1, 2, 3, \ldots$

Figure 5 is used to illustrate the above processes. The top panel shows the sampled concentration with noise at the receiver. The second panel is the smoothed signal of the concentration curve. The third and bottom panels are the first derivative and the absolute of the second derivative of the smoothed signal. It is seen that the absolute values of the second derivative at the feature points are much higher than those at non-feature points. We also find that among all feature points before or after the peak concentration, those feature points closer to the peak concentration have larger second derivative values than the feature points further away from the peak. This is because the amplitude of the concentration curve far away from the peak is lower and changes more slowly. The first derivative of the feature point far away from the peak is smoother and the second derivative is smaller. The greater the amplitude of the concentration curve near the peak, the more drastic the change in the first derivative, and therefore the greater the second derivative.

Thus, it can be seen that the feature points of the four largest second derivatives are consecutive feature points around the peak of concentration curve as shown in Fig. 5. If we arrange their time values in chronological order as t_1, t_2, t_3, and t_4 such that $t_1 < t_2 < t_3 < t_4$, we have that $T = t_4 - t_2 = t_3 - t_1$. For accuracy, t_1, t_2, t_3, and t_4 are all used in the calculation of the period of blood velocity T as

Table 1. Simulation parameters

Parameter	Symbol	Value
Diffusion coefficient of information molecules	D	10^{-10} m^2/s [1]
Number of molecules	N	1.1×10^{10}
Volume of spherical reception space of receiver	V_R	$0.0056\,\mu$m^3
Real distance	d	300–2100 μm
Interval between releasing time and rising edge	τ	0.1–0.7 s [2]
Symbol interval	T_b	2.7 ms

$$T = \frac{(t_4 - t_2) + (t_3 - t_1)}{2}. \tag{7}$$

The relationships between t_1, t_2, t_3, and t_4 are also used in the calculation of τ. We have prior knowledge that the duty cycle is 37.5%. Therefore, the feature points are not equally spaced. According to such property of the duty cycle, in the case that $t_4 - t_3 > t_3 - t_2$, t_2 and t_4 are the time of rising edges. In the case that $t_4 - t_3 < t_3 - t_2$, t_1 and t_3 are the time of rising edges. According to the definition of τ, it is the time interval between the releasing time of molecules and the time of the first rising edge of the blood velocity. Therefore, the remainder of any rising edge time divided by the period T is the required τ, which can be expressed as

$$\tau = \begin{cases} t_2 - \lfloor t_2/T \rfloor \times T & \text{if } t_4 - t_3 > t_3 - t_2, \\ t_1 - \lfloor t_1/T \rfloor \times T & \text{if } t_4 - t_3 \leq t_3 - t_2, \end{cases} \tag{8}$$

where $\lfloor \cdot \rfloor$ denotes the floor function.

With T calculated in (7) and τ in (8), $V(t)$ in (1) and (3) is obtained.

3.2 Distance Estimation

The receiver takes samples of the concentration. After smoothing is performed to remove the noise, the time t_{max} and the amplitude C_{max} when the concentration reaches its maximum are recorded. And $V(t)$ is calculated as discussed in Sect. 3.1. With $V(t)$, C_{max}, and t_{max}, the distance d is calculated by (3) as

$$d = \sqrt{-4Dt_{max} ln[\frac{C_{max}}{N}(4\pi Dt_{max})^{\frac{3}{2}}]} + \int_0^{t_{max}} V(t)\,dt. \tag{9}$$

4 Simulation Results

In this section, the proposed distance estimation scheme for blood vessel channel is examined through Monte Carlo simulation. The system parameters in Table 1 are adopted as default parameters without stated otherwise.

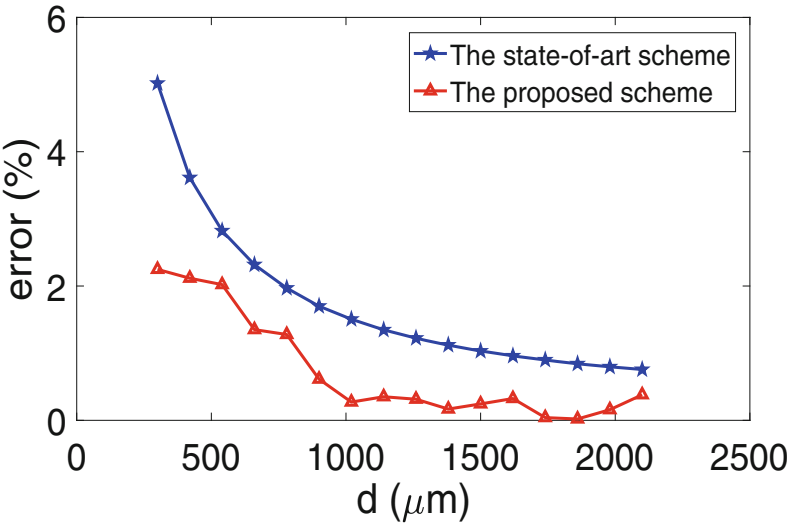

Fig. 6. Comparison of our proposed scheme with the existing constant flow-assisted scheme [6].

To quantitatively evaluate the performance of the proposed scheme, the relative estimation error (error for short in the following part) is used as the performance metric which is defined as

$$error = \frac{|d_{est} - d|}{d}, \tag{10}$$

where d_{est} is the estimated distance by the proposed scheme. A smaller error indicates a better performance.

The effectiveness of the proposed distance estimation scheme is investigated by comparing it with the state-of-art distance estimation scheme in [6]. In the comparison scheme, the blood velocity $V(t)$ is set as a known constant as in the state-of-the-art MC studies. The constant velocity value is set as the average of the blood velocity which is $V(t) = V_0 \times 0.375$. In such a case, the channel is a constant flow-assisted channel. The receiver measures the concentration of the molecules and records the time when the concentration reaches its maximum. The distance is calculated with the peak time and concentration value through the CIR in (3) with a known velocity $V(t) = V_0 \times 0.375$.

The result is shown in Fig. 6. The proposed distance estimation scheme with a more realistic model of the blood vessel channel performs better than the comparison scheme. The effectiveness of the proposed scheme is demonstrated. The result also shows that, when the distance becomes larger, the error decreases and the difference between the state-of-art scheme and the proposed one becomes smaller. This is because as the distance becomes larger, the arriving time of molecules becomes longer and more periods are covered before arrival. The overall inaccuracy of approximating the blood velocity with its average is reduced.

But, for distances not long enough, the proposed scheme has an obvious advantage over the state-of-art scheme.

5 Conclusion

In this work, a distance estimation scheme for the blood vessel channel is proposed for the MC system. Due to the periodical property of the blood velocity, the CIR of the blood vessel channel is not fixed and more complicated. The state-of-art distance estimation schemes are not applicable anymore. We propose a distance estimation scheme for the blood vessel channel. In the proposed scheme, the blood velocity is estimated first to obtain the CIR. With the accurate CIR, the distance between the transmitter and receiver is accurately estimated. The effectiveness of the proposed scheme is validated by simulation investigation.

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