



# Clock Synchronization for Mobile Molecular Communication in Nanonetworks

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**Abstract.** Molecular communication (MC) is an emerging communication method using molecules or particles as signal carriers, which enables nanomachines to send messages at the nano- or micro-nano scale for information exchange and collaboration. Clock synchronization between nanomachines plays an important role in collaboration. The current researches on the synchronization between nanodevices mainly focus on fixed MC systems. However, the movement of nanodevices is widespread in MC systems. A simple but effective scheme for clock synchronization between mobile nanodevices in mobile MC systems based on diffusion is proposed. In an equivalent diffusion mobile MC system model, the number of molecules received by the receiver is related to the transmission time of molecules and the distance between transmitter and receiver at the moment that molecules are released. Based on the detected molecular information, the clock offset and the distance between mobile nanodevices in nanonetworks are estimated by the least-square method. By using different types of molecules, the challenge of the varying synthesis time of the molecule is overcome. The simulation results show the effectiveness of the proposed algorithm.

**Keywords:** Clock synchronization · Clock offset · Mobile molecular communication · Least-square method

## 1 Introduction

The development of nanotechnology has made various applications of nanomachine-based nanonetworks possible. Nevertheless, the functions of a single nanomachine are limited. Molecular communication (MC) is a new communication mechanism at the nano-scale or micro-scale [6]. The molecules carrying information are released from the transmitter and propagate to the receiver via

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diffusion. Molecular communication makes nanomachines promising to expand the capabilities through information exchange and collaboration. For example, in the targeted drug delivery application in the medical field [17], multiple nanomachines exchange or share information through MC, and release drugs to attack cancer cells simultaneously.

Clock synchronization between nanomachines plays an essential role in collaboration. In the process of collaboration, the time and sequence of the nanomachine's action response will affect the collaboration. For example, in a targeted drug delivery application, if the clocks of the nanomachines are not synchronized when multiple nanomachines release drugs to attack cancer cells simultaneously, nanomachines cannot respond at the same time, and the drug treatment effect will be affected. In current researches, it is always assumed that the transceivers in the MC system are synchronized. In [5], based on the assumption of clock synchronization, signal detection in a mobile MC system is proposed.

However, the clocks of nanomachines are not all synchronized automatically. The clocks of different nanomachines may be different. There may be a clock offset between different nanomachines. Some mechanisms for achieving the synchronization of MC systems have been proposed. In [24], the authors proposed a method for synchronizing the system by using external noise common to all cells of a multicellular system. In [1, 2], the authors proposed using the quorum sensing mechanism of bacteria to achieve the synchronization of cluster nodes in nano-networks. Inhibitory molecules are used to achieve clock synchronization in [20, 21]. A nanomachine releases inhibitory molecules into the environment, making it impossible for other nanomachines in the environment to release molecules. However, all of these synchronization methods need to correspond to specific molecules or cells.

In [15], the authors proposed a two-way message exchange clock synchronization model, which estimates the clock offset and clock skew by forwarding multiple sets of handshaking. The authors used a SIMO system to implement clock difference estimation in systems with uniformly distributed random noise in [13, 18]. In [15, 18], both the transmitter and the receiver in the MC system are fixed, and synchronization between the nanomachines is realized by multiple rounds of transmission of molecules. In those scenarios, the distance between the transmitter and the receiver does not change. In [16], the authors consider the clock synchronization of the MC system with drift. It also focuses on the static MC system.

The mobile MC system is also a very important scenario that has many potential applications and has been investigated in literature such as [4, 8, 9, 14, 22]. In mobile MC systems, in addition to the diffusion of molecules, the transmitter and receiver also move due to Brownian motion so that the distance between the transmitter and the receiver change over time. Although there have been so many synchronization algorithms in fixed MC systems, the synchronization algorithm for mobile MC systems is rare. Because the distance in a mobile MC system is a variable rather than a constant, it is not possible to implement clock synchronization directly in a mobile scenario using synchronization algorithms for fixed MC systems.

In [19], the authors proposed a clock synchronization model for a communication system in which a nanodevice is mobile, and the other is fixed. Assuming that the propagation time of a molecule is proportional to the transmission distance, two types of signal molecules are used for bidirectional transmission to estimate the propagation time. However, multiple rounds of bidirectional transmission of signals take a long time. At the same time, the molecular synthesis time is not taken into account. Also, in general, it is common both the transmitter and the receiver are mobile in mobile communication systems. But so far, a synchronization algorithm that is directly applied to a scenario where nanomachines are all mobile has not been proposed.

This paper proposes a simple but effective clock synchronization mechanism for mobile communication systems in nanonetworks where the transmitter nanomachine and receiver nanomachine are constantly moving. In a mobile communication system, since the transmitter and the receiver are constantly moving, the distance between two nanomachines is constantly changing, and the propagation time of molecules at different distances is also changing. The existing synchronization algorithms are not necessarily used in such scenarios. In this paper, the clock value of the transmitter is encoded into the information molecule using M-ary Mosk [11]. However, different clocks will get different molecular structures, so that the diffusion coefficient of the molecule containing clock information is uncertain. Besides, encoding the clock value into molecules takes time, which means that the release time of molecules is later than the encoded clock time of the transmitter. Therefore, to achieve clock synchronization in mobile scenarios, all these issues will be challenges.

To solve these problems, other different types of molecules with known diffusion coefficients that have been synthesized in advance are released at the clock time of the transmitter which is encoded into the molecules are used. Because distance changes over time, to reduce the impact of the change of distance, all types of molecules are released only once. The receiver estimates the clock offset between the transmitter and the receiver by detecting the clock information in the molecules containing clock information and the number of other types of molecules with known diffusion coefficients which have been synthesized in advance. The contributions of this paper are as follows:

1. In the clock synchronization process, the synthetic time when the transmitter encodes the clock into the molecule and the effect of the molecular structure change on the diffusion coefficient are considered. By using different types of molecules released at the clock time of transmitter which is encoded into molecules, the challenge for the practical varying molecular synthesis time and diffusion coefficient are solved.
2. Based on the waveform of the molecular signal, by using the least-square method, the clock offset and the initial distance between the transmitter and the receiver is estimated.

Combining the above two points, clock synchronization in a mobile scenario is achieved.

The rest of the article is organized as follows. Section 2 presents the system model. The clock synchronization mechanism is proposed in Sect. 3. Section 4 presents the simulation results. Section 5 finally summarizes the article.

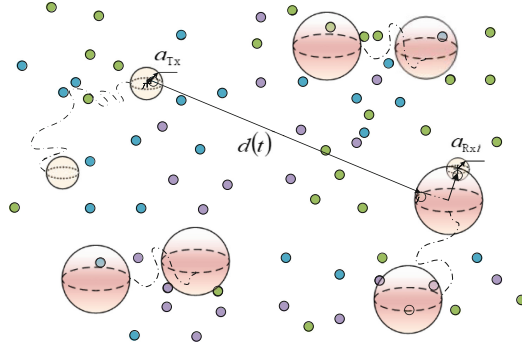
## 2 System Model

We consider an unbounded three-dimensional fluid environment with constant temperature and viscosity. The entire nanonetwork includes a clock reference nanomachine and multiple nanomachines that require clock correction. In this paper, the clock reference nanomachine is modeled as a moving spherical transmitter with radius  $a_{\text{Tx}}$ , denoted by Tx; the nanomachines that require clock correction are modeled as receivers with multiple receiving antennas which are passive observers with radius  $a_{\text{Rxi}}$ , denoted by Rx. Molecules can enter and leave the passive observers freely. The transmitter nanomachine and the receiver nanomachines obey the Brownian motion with the diffusion coefficients  $D_{\text{tx}}$  and  $D_{\text{rx}}$ , respectively. In order to form our system, we make the following assumptions about the system:

1. It is assumed that the nanomachines in the network do not collide with each other, or affect the movement of molecules in the environment.
2. The transmitter can release multiple types of molecules simultaneously. The receiver has multiple receiving antennas, and each antenna can detect multiple types of molecules simultaneously. The idea of multiple antennas was proposed in [18]. It is assumed that the distance between the nanomachines is much larger than the radius of the nanomachines. Therefore, the distances between the transmitter nanomachine and each receiving antenna on receiver nanomachines are the same.
3. The signal molecules are released from the center of the spherical transmitter, and the molecules can propagate to the receiver by diffusion. The diffusion process of each molecule in the environment is independent of each other, and the impact of collisions between molecules is negligible.
4. The time interval between the two clock synchronizations of the network is long enough, and there is no inter-symbol interference.

Because the movement of molecules is independent of the nanomachines in the network, the clock reference nanomachine calibrates all nanomachines in the network independently. At the same time, the receiver nanomachines in the nanonetwork do not affect the detection of molecular signals by other receiver nanomachines. We only consider the case where the clock reference nanomachine corrects the clock of one of the receiver nanomachines in the network. Due to Brownian motion, the positions of the transmitter and receiver change over time.  $d(t)$  is used to denote the distance between the transmitter and the receiver when the transmitter clock time is  $t$ , as shown in Fig. 1.

The transmitter releases a molecular pulse at any time  $t$ , with the number of released molecules  $Q$ , and the diffusion coefficient  $D_{\text{m}}$ . At this time, the initial distance between the receiving antenna and the transmitter is  $d(t)$ . After the



**Fig. 1.** Mobile communication system model for synchronization. Colorful balls represent different types of molecules. (Color figure online)

propagation time  $\tau$ , the receiver receives information molecules. The channel impulse response at each receiving antenna given  $Q$  released molecules can be expressed as [7]

$$s_i(t, \tau) = \frac{v_{\text{obs}} Q}{(4\pi D' \tau)^{\frac{3}{2}}} \exp\left(-\frac{d^2(t)}{4D' \tau}\right), \quad (1)$$

where  $v_{\text{obs}} = \frac{4\pi}{3} a_{\text{Rx}i}^3$ , and  $s_i(t, \tau) = 0$ , for  $\tau \leq 0$ . Here  $D'$  is the equivalent diffusion coefficient of the relative motion of the signal molecule and the receiver,  $D' = D_{\text{rx}} + D_{\text{m}}$  [3].  $s_i(t, \tau)$  is the average number of molecules received by the  $i$ th antenna.

The noise exists due to the free diffusion of the molecules governed by Brownian motion. Assuming that the time between two network synchronization operations of the network is very long. We do not consider the influence of the signal molecules sent by the source transmitter. As for the Brownian noise, it is usually modeled by binomial distribution [23]. According to [4], the Brownian noise  $n_i(t, \tau)$  received by  $i$ th antenna is modeled as a Gaussian distribution with a mean of 0 and a variance of  $s_i(t, \tau)$  when  $s_i(t, \tau)$  is very large, i.e.

$$n_i(t, \tau) \sim \mathcal{N}(0, s_i(t, \tau)). \quad (2)$$

The noise is non-stationary and signal-dependent [10]. Therefore, after propagation time  $\tau$ , the number of molecule arriving at the receiver is

$$S'_i(t, \tau) = s_i(t, \tau) + n_i(t, \tau). \quad (3)$$

It is assumed that the receiver has  $M$  receiving antennas. The signal received by the receiver is the average of the signals received by the  $M$  antennas. Hence,

$$S(t, \tau) = \frac{1}{M} \sum_{i=1}^M S'_i(t, \tau) = s(t, \tau) + \frac{1}{M} \sum_{i=1}^M n_i(t, \tau), \quad (4)$$

where

$$s(t, \tau) = \frac{v_{\text{obs}}Q}{(4\pi D'\tau)^{\frac{3}{2}}} \exp\left(-\frac{d^2(t)}{4D'\tau}\right), \quad (5)$$

where  $S(t, \tau)$  represents the average number of observed molecules of the receiver after the propagation time  $\tau$  of molecules.  $s(t, \tau)$  is the number of molecules after the propagation time  $\tau$  in theory. Since  $n'(t, \tau)$  is independent and identically distributed Gaussian noise, according to the law of large numbers, when the number of antennas is close to infinity,  $\frac{1}{M} \sum_{i=1}^M n_i(t, \tau)$  is close to 0. Thus the influence of noise on the signal is weakened. According to (5), when the number of signal molecules received by the receiver reaches the maximum, the corresponding theoretical peak time is

$$t_{\text{peak}} = \frac{d^2(t)}{6D'}, \quad (6)$$

which is defined as the propagation delay.

### 3 Proposed Clock Synchronization Mechanism

In order to synchronize the clock of the transmitter and the receiver, the clock offset  $\phi$  is needed. When the MC system starts clock synchronization process, it is assumed that the clock of the transmitter at this time is  $T_{t0}$ , the clock of the receiver is  $T_{r0}$  and the initial distance between transmitter and the receiver is  $d(T_{t0})$ . The clock offset  $\phi$  is defined as

$$\phi = T_{r0} - T_{t0}. \quad (7)$$

We consider sending the clock value  $T_{t0}$  of the transmitter to receivers, and receivers adjust their clocks so that the clocks of the nanomachines in the entire system are the same. Like other research papers on clock synchronization [15], [18], the clock value of the transmitter is encoded into the information molecule using M-ary Mosk [11]. Each information molecule includes a head, a tail, and  $n$  chemical bit elements, where  $n = \log M$ . All these parts are linked to the same molecule by chemical bonds. Assume that the synthesized molecule is molecule A with diffusion coefficient  $D_A$ .

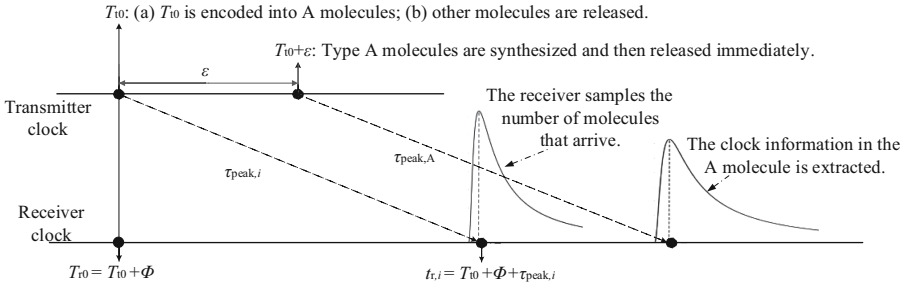
However, encoding the transmitter clock into A molecules takes time  $\varepsilon$ , that is, the release time of A molecules is later than the encoded clock time  $T_{t0}$  of the transmitter. Different clocks will get different molecular structures so that the diffusion coefficient  $D_A$  is uncertain. As described in [12], the synthesis time required for the same molecule is different, which means the synthesis time  $\varepsilon$  of a molecule is uncertain. Besides, in a MC system, molecules are released from a transmitter to a receiver through diffusion, and the propagation time of a signal cannot be ignored. Therefore, in a MC system, before the receiver nanomachine corrects its clock based on the received transmitter clock value, the propagation time of the molecule also needs to be obtained.

Suppose that after the propagation time of A molecules  $\tau_A$ , the receiver clock is  $t_{r,A}$ . Then the clock offset  $\phi$  between the transmitter and the receiver can be expressed as

$$\phi = t_{r,A} - \tau_A - T_{t0} - \varepsilon. \quad (8)$$

The receiver detects and extracts the clock  $T_{t0}$  of the transmitter in A molecules, and the clock of the receiver is known. If only A molecules are used to get the clock offset between the transmitter and the receiver,  $\phi$ ,  $\varepsilon$ , and propagation time are needed. However, both  $\phi$  and  $\varepsilon$  are random numbers, and the distribution of them cannot be obtained. Therefore, even if the propagation time of the A molecule is known, clock offset is difficult to obtain.

In this paper, in order to obtain the clock offset  $\phi$ , in addition to the A molecule, another different  $I$  types of molecules with diffusion coefficient  $D_i$   $\{i = 1, 2, \dots, I\}$  are also used, which have been synthesized and can be released at transmitter clock  $T_{t0}$ . That means  $I + 1$  types of molecules will be released from transmitter. As shown in Fig. 2, when the system starts clock synchronization, the A molecules begin to synthesize. At the same time, other  $I$  types of molecules are simultaneously released. The number of  $I$  types of molecules and A molecules released by the transmitter are  $Q$ .



**Fig. 2.** The clock relationship between transmitter and receiver.  $\varepsilon$  is the synthesis time of A molecules. The receiver uses the sampling results of other molecules and the clock information  $T_{t0}$  extracted from the A molecule, and uses the least-square method to estimate the clock offset and the distance between the transmitter and the receiver.

Type A molecules are only used to transmit the clock  $T_{t0}$  of the transmitter. The another  $I$  types of molecules are used to estimate clock offset and distance. Since the  $I$  types of molecules are released simultaneously, the initial distance between the transmitter and the receiver is the same. The receiver detects molecules in the environment. The clock information  $T_{t0}$  carried in the molecule A is extracted. And the receiver counts the number of  $I$  types of molecules arriving at the receiver. Suppose the propagation time of type- $i$  molecules is  $\tau_i$ , the receiver clock is  $t_{r,i}$ . Then the clock offset  $\phi$  between the transmitter and the receiver can be expressed as

$$\tau_i = t_{r,i} - \phi - T_{t0}. \quad (9)$$

Substitute (9) into (5),

$$s(T_{t_0}, \tau_i) = \frac{v_{\text{obs}} Q}{(4\pi D'_i(t_{r,i} - \phi - T_{t_0}))^{\frac{3}{2}}} \exp\left(-\frac{d^2(T_{t_0})}{4D'_i(t_{r,i} - \phi - T_{t_0})}\right), \quad (10)$$

where  $D'_i = D_{\text{rx}} + D_i$ ,  $T_{t_0}$  is the clock of the transmitter when the type- $i$  molecules are released.

For the  $I$  types of molecules, the receiver counts the molecules arriving at the receiver at the receiver clock time  $t_{r,i} = \{t_{r1,i}, \dots, t_{rm,i}\}$   $\{i = 1, 2, \dots, I\}$ . Then  $mI$  observations of  $I$  types of molecules are obtained, denoted by  $\{S_{1,i}, \dots, S_{m,i}\}$   $\{i = 1, 2, \dots, I\}$ . There are two unknowns parameters in (10),  $\phi$  and  $d(T_{t_0})$ . To obtain the unknown parameters, the least-square method can be used. For type- $i$  molecules,  $\{S_{1,i}, \dots, S_{m,i}\}$  are used.

$$\{\hat{d}'_i(T_{t_0}), \hat{\phi}'_i\} = \arg \min_{d(T_{t_0}), \phi} \sum_{j=1}^m \left( \frac{v_{\text{obs}} Q}{(4\pi D'_i(t_{r,i} - T_{t_0} - \phi))^{\frac{3}{2}}} \exp\left(-\frac{d^2(T_{t_0})}{4D'_i(t_{r,i} - T_{t_0} - \phi)}\right) - S_{j,i} \right)^2. \quad (11)$$

For the type- $i + 1$  molecules,  $\hat{\phi}'_i$  and  $\hat{d}'_i(T_{t_0})$  can be used as the initial values of the least-square method, where

$$\hat{\phi}'_i = \frac{(i-1)\hat{\phi}'_{i-1} + \hat{\phi}_i}{i}, \quad (12)$$

$$\hat{d}'_i(T_{t_0}) = \frac{(i-1)\hat{d}'_{i-1}(T_{t_0}) + \hat{d}_i(T_{t_0})}{i}. \quad (13)$$

The final estimated clock offset and distance are

$$\hat{\phi}'_I = \frac{(I-1)\hat{\phi}'_{I-1} + \hat{\phi}_I}{I}, \quad (14)$$

$$\hat{d}'_I(T_{t_0}) = \frac{(I-1)\hat{d}'_{I-1}(T_{t_0}) + \hat{d}_I(T_{t_0})}{I}. \quad (15)$$

As stated in Sect. 2, the received signal is affected by additive Gaussian noise. To mitigate the influence of the noise, one receiver is considered to have 20 antennas.

## 4 Simulation Results

In order to evaluate the performance of the proposed synchronization mechanism, the simulation results using MATLAB will be presented in this section. The effect of different parameters on the accuracy of the clock offset estimation will also be analyzed. The simulation parameters are given in Table 1.

The mean square error (MSE) is a measure that reflects the degree of difference between the estimate and the actual value. The smaller the mean square

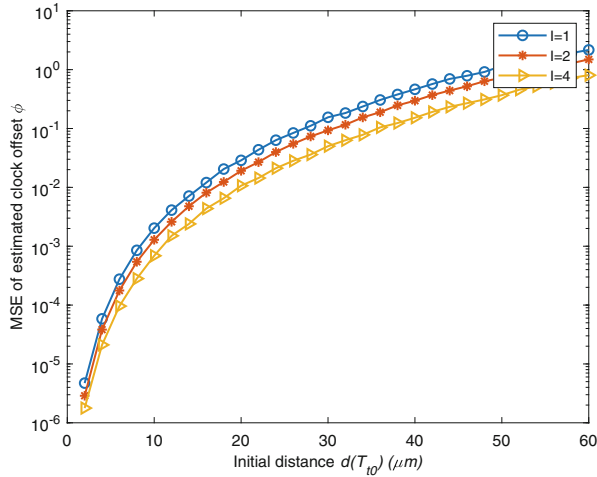
**Table 1.** System parameters used for numerical results

Parameter	Definition	Value
$D_{tx}$	Diffusion coefficient of transmitter	$50 \mu\text{m}^2/\text{s}$
$D_{rx}$	Diffusion coefficient of receiver	$30 \mu\text{m}^2/\text{s}$
$D_i$	Diffusion coefficient of A molecule	$100 \mu\text{m}^2/\text{s} - 1000 \mu\text{m}^2/\text{s}$
$a_{Tx}$	Radius of transmitter	$0.2 \mu\text{m}$
$a_{Rxi}$	Radius of antenna	$0.4 \mu\text{m}$
$Q$	Number of A molecule released by the transmitter	5000
$\phi$	Preset value of clock difference	15 s
$\varepsilon$	Synthesis time of A molecule	3 s

error, the closer the representative estimator is to the estimated amount. For  $l$  actual values  $x_i$   $i = 1, \dots, l$  and corresponding estimated values  $\hat{x}_i$   $i = 1, \dots, l$ , the mean square error is

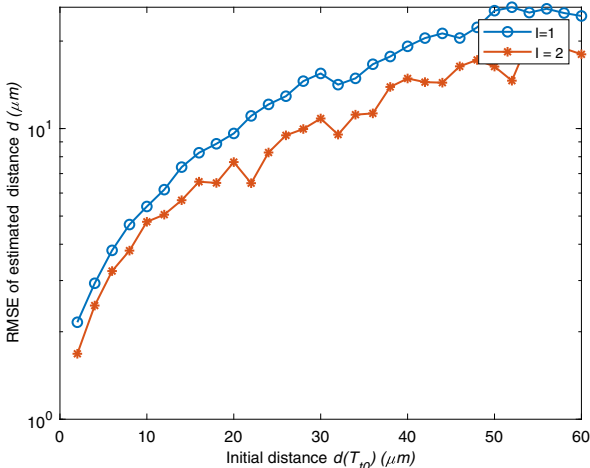
$$MSE = \frac{1}{l} \sum_{i=1}^l (x_i - \hat{x}_i)^2. \quad (16)$$

The simulation results mainly evaluate the performance of the synchronization mechanism and the influence of various parameters on the system performance by using the mean square error.



**Fig. 3.** The relationship between the initial distance  $d(T_{t0})$  and the MSE of estimated  $\phi$ .  $l$  indicates the number of other types of molecules used.

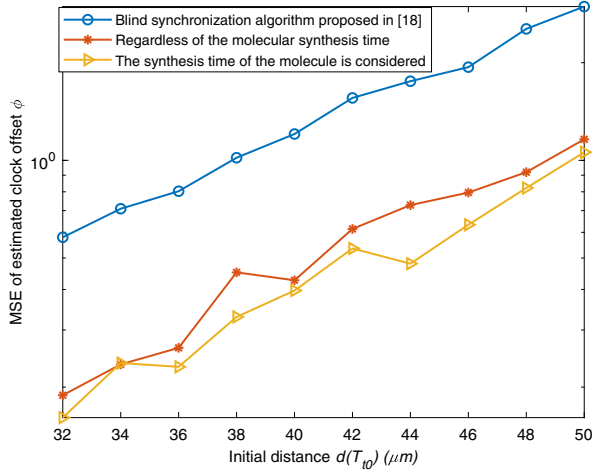
Figure 3 shows that the performance of the proposed clock offset estimation algorithm for  $\phi$ . The performance of the algorithm is mainly related to the distance between the transmitter and the receiver when molecules are released. As the distance increases, the MSE of the estimated  $\phi$  increases. This is because as the distance gradually increases, the number of signal molecules received by the receiver gradually decreases, and the received signal is gradually increased by the influence of noise. Also, the type of molecules released will also affect the performance of the algorithm. The more types of molecules released, the better the estimation performance of the algorithm. This is because the  $I$  types of molecules are released at the same time, and the initial distance  $d(T_{t0})$  and clock offset  $\phi$  between the transmitter and the receiver are the same. Different molecules are affected by noise differently. Using multiple types of molecules can reduce the effect of noise on overall synchronization performance.



**Fig. 4.** The RMSE of estimated initial distance  $d(T_{t0})$ .

In Fig. 4, the root mean square error (RMSE) of the proposed clock offset estimation algorithm for  $d(T_{t0})$ . As with the estimation of the clock offset, the RMSE of estimated distance is also mainly affected by the distance between the transmitter and the receiver at the moment of molecular release. And the more types of molecules released, the better the estimation performance of the algorithm.

In Fig. 5, the algorithm proposed in this paper is applied in two scenarios. One scenario does not consider the synthesis time of the molecule, and the other scenario considers the synthesis time of the molecule. It can be seen that the clock synchronization performance obtained after considering the effect of molecular synthesis time is better. Also, the algorithm proposed in this paper is also compared with the current synchronization algorithms in fixed MC systems.



**Fig. 5.** The algorithm proposed in this paper is applied to two different scenarios, one considers the synthesis time of molecules and the other does not consider the synthesis time of molecules. And the blind synchronization algorithm proposed in [18].

Compared with the blind synchronization algorithm used in [18], the proposed synchronization algorithm in this paper has better performance. This is because more types of molecules are used in this paper and the clock of the transmitter is directly transmitted to the receiver. As Fig. 5 shown, three types of molecules are used. This relatively increases the requirements for the functions of transmitter and receiver nanomachines.

The above simulation results show that the synchronization mechanism proposed in this paper has good performance in a certain range. However, when the distance between the transmitter and receiver is large enough, the MSE of estimated  $\phi$  will also be very large so that the estimated clock offset is not accurate. To obtain better performance, more types of molecules can be used. But it will improve the requirements for the functions of the transmitter and receiver. From both Figs. 3 and 4, it can be seen that, for the proposed clock synchronization mechanism, the effect of distance between the transmitter and the receiver is greater than that of the number of types of molecules released.

## 5 Conclusion

In this paper, we investigate the clock synchronization between the transmitter and the receiver in a mobile MC system. The clock offset and the distance between transmitter and receiver is estimated by releasing multiple types of molecules. The transmitter clock value is encoded into signal molecules. The synthesis time of molecules is taken into account. The clock offset between the transmitter and receiver is estimated by the least-square method. The initial

distance, and the number of the type of molecules released will affect the performance of the MC system. Simulation results show that the synchronization mechanism proposed in this paper has good performance. In our future work, we will continue to study clock synchronization mechanisms and performance in more practical mobile MC systems in nanonetworks.

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