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Diffusion-Based Reference Broadcast Synchronization for Molecular Communication in Nanonetworks

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ABSTRACT Molecular communication is a novel inter-disciplinary communication methodology at the nanoscale, which uses chemical or biological molecules as the information carriers. For many prospective molecular communication applications, the clock synchronization is a major issue. However, the existing solutions use the molecule releasing time for the clock synchronization schemes but ignore the molecule synthesizing time, which is not practical. To overcome this issue, in this paper, we propose a reference broadcast synchronization scheme. One nanomachine sends a broadcast beacon and the other two nanomachines records their receiving times. The receiving times are exchanged by that two nanomachines, then, the clocks between these two nanomachines can be synchronized. Owing to the fact that the information molecules propagate slowly with a large propagation delay, which also depends on the transmitter–receiver distance, so a delay estimation method is adopted in the synchronization scheme. The simulation results evaluate proposed synchronization scheme and show that the proposed scheme outperforms other clock synchronization schemes for molecular communication.

INDEX TERMS Molecular communication, nanonetworks, clock synchronization.

I. INTRODUCTION

Molecular communication (MC) networks, combining the techniques of nanotechnology, biotechnology and electrical engineering, become an interesting and important research area recently [1], [2]. There are many potential applications for the MC networks in the fields of biomedical engineering, biomedicine, and life science [1], [3]. In these applications, the nanomachines/nano-devices do not work independently, but collaborate with each other in a distributed manner [4]. Similar to many research works about distributed networks, the collaborations require all the nanomachines running on an identical time frame, i.e., they are synchronized within the MC network.

Many existing research works about the MC networks assume that the clock is perfect synchronized [5]–[11]. In [6], the authors assume an ideal synchronization between the transmitter nanomachine (TN) and the receiver nanomachine (RN) by default to set up a physical end-to-end model of the MC system. In [7], the authors assume that the TN is synchronized with the RN in one-way message communication, under which assumption, the distance between the TN and the RN is estimated by a function of the number of molecules. However, the clocks in the real MC networks are not synchronized automatically. The MC networks consist of many nanoscale devices and all these devices run their own clocks. Therefore, it is necessary for the researchers to design the clock synchronization algorithms to synchronize the MC networks such that other functionalities can be performed based on the uniform synchronized clock.

The studies on the implementation of the clock synchronization have been done since recently. In [12], the authors have used two genes in Vibrio fischeri to synchronize a synthetic gene regulatory network (SGN). The variance of extracellular noise is used to synchronize the cells by using the same fluctuations. In [13] and [14], a bacterial quorum sensing mechanism has been proposed for oscillating the nanomachines. The self-induced molecules are released

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by one nanomachine, and trigger another nanomachine to release the same molecules. When the concentration of the inducer particles in the environment reaches a certain fixed threshold at a moment, the entire nanonetworks achieves one synchronization. In [15] and [16], the synchronization has been realized by inhibitory molecules. These molecules are released by a nanomachine, and inhibit the release of similar molecules from other nanomachines in the nanonetworks. When the concentration of molecules falls below a certain threshold, those molecules can be released again. The release pulse of inhibitory molecules can be considered as the synchronization pattern in the MC networks. The above works try to oscillate the nanomachines by resonance rather than synchronize the clock. In [17], a blind algorithm for the synchronization has been proposed by using non-decision directed maximum likelihood. The clock sequence is calculated by the RN based on the analysis of the molecular channel delay. But the authors have only designed the sampling sequences of the RN. They did not further discuss how to synchronize the clock between the TN and the RN.

As mentioned in [18], the synchronization can be classified into three types: synchronization of oscillation, time/clock synchronization, and symbol synchronization. In this paper we focus on the time/clock synchronization, which is crucial and indispensable in various applications of the nanonetworks. Here, we define clock as the time reading from the engineered nanomachine. According to [18], the clock synchronization refers to making the time/clock readings the same for different nanomachines. In [19], a clock synchronization algorithm using maximum likelihood (ML) estimation between two nanomachines is proposed. The inverse Gaussian distribution is used to approximate the propagation delay. The clock offset between two nodes is estimated. Similar ideas have been proposed for different scenarios [20]–[23]. In these state-of-the-art works, the time instant for clock synchronization is embed into a chemical molecule by M-ary molecular shift keying (MoSK) by the nanomachine. The nanomachines do not store the M types of molecules, but synthesize the corresponding type of molecule whenever a specific time instant is needed to transfer. The molecule synthesis cannot be completed instantaneously but takes time. However, the current works [20]–[23] assumed that the molecule synthesizing time, which is the time duration to synthesize the molecules containing the time instant, is ignored. This is not the real case. Firstly, the time duration for synthesizing molecules is not small enough to be ignored [24]. Secondly, the synthesis time varies with different conditions, such as whether the energy or materials for molecule synthesis are sufficient or not. Therefore, the synthesis time cannot be ignored. Current treatment of the synthesis time brings errors in the real clock synchronization scheme.

To overcome this problem, we proposes a diffusion-based reference broadcast synchronization scheme. In this scheme, one more nanomachine releases a reference broadcast beacon is introduced into the system. The other two nanomachines record the receiving time and they exchange the recorded time stamp for the clock synchronization. The difference of the signals received the two nanomachines helps to alleviate the influence of the synthesis time on the clock synchronization and improves the clock synchronization accuracy. One important difference between the MC scenario and the conventional wireless communication scenario is that: in conventional wireless channel, the electromagnetic wave propagates very fast so that the propagation delay between the wireless nodes can be ignored. However, the molecules in the MC propagate very slowly in the channel, so that the propagation delay cannot be ignored. In this work, the propagation delay is also estimated in the synchronization scheme such that the scheme can be applied to any deployment of the nanomachines. In summary, the contributions of this paper include:

1) Considering the non-negligible synthesis time, a practical synchronization scheme using reference broadcast is proposed.

2) The propagation delay method is integrated into the synchronization scheme so that the scheme can be applied to any arbitrary deployment of nanomachines.

3) The performance of the proposed scheme is evaluated by simulations and is compared with existing scheme.

The rest of this paper is organized as follows. The system model for the MC networks is presented in Section II. Section III provides the details about the proposed clock synchronization scheme with mathematical equations. The simulation results are given in Section IV. Section V concludes the paper.

II. SYSTEM MODEL

A three-node MC network with an arbitrary deployment is considered in our scenario, as shown in Fig. 1. It consists of a parent nanomachine denoted by node P and two children nanomachines denoted by node A and node B. Each node can send and sense information molecules. The distance between node P and node A is denoted by d_{AP}, and the distance between node P and node B is denoted by d_{BP}.

Node A and node B have multiple receiving antennas. The idea of multiple molecular antennas was proposed in [25] and is adopted here. It is assumed that the distance between the nanomachines is much larger than the radius of the nanomachine (e.g., the distance is larger than ten times of the nanomachine radius) and the information molecules are released from the center of the nanomachine. Therefore, the distances between the molecule-releasing nanomachine P and each receiving antenna on node A (or node B) are the same.

In the research works of the clock synchronization for MC such as [20]–[22], time instants are encoded into molecules by M-ary MoSK [23]. Each molecule is composed of a header, a trailer, and n chemical bit elements, where $n = \log_2 M$. All these parts are linked using chemical bonds. Theoretically, there is no limit on the number of chemical bit elements, so the modulation order M can be infinite. This paper also adopts this kind of modulation method.

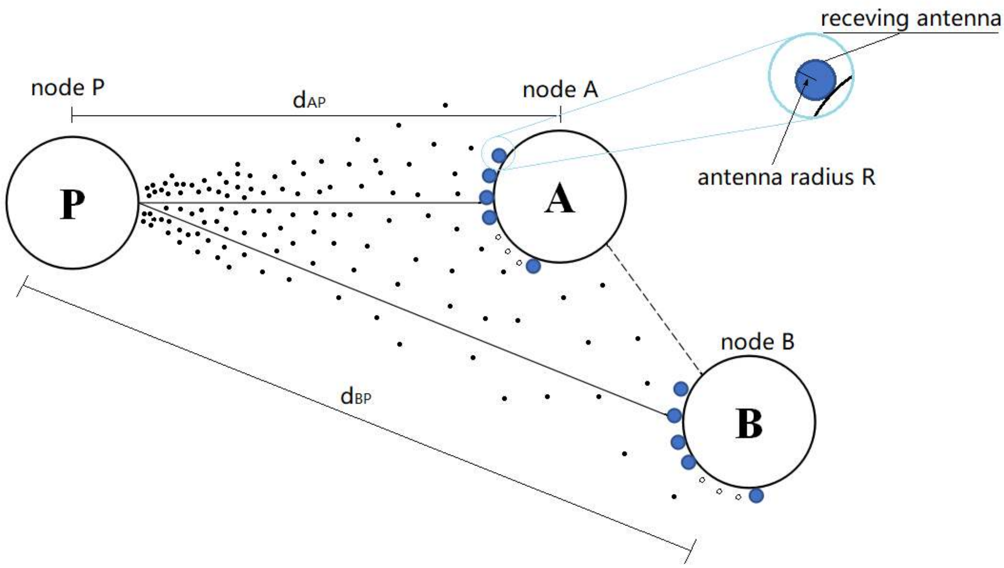


FIGURE 1. System model. The scenario is composed of three nanomachines with an arbitrary deployment. Node P is the reference nanomachine. Node A and node B are the nanomachines which will be synchronized. The nanomachines can send signals by releasing information molecules. These molecules diffuse in the environment based on Brownian motion. Node A and node B with multiple antennas can observe the number of molecules within their observing volume.

In those works like [20]–[22], the molecule synthesizing time is always ignored, which does not match reality and brings error in clock synchronization. In this paper, the molecule synthesizing time is taken into account. To send signals with molecules, the nanomachine firstly synthesizes the molecules which takes a period of time. Once the molecules are synthesized, the node will release them into the environment.

The released molecules diffuse freely in the channel, which is governed by the Fick's second law of diffusion with the equation [26]

$$\frac{\partial c(t)}{\partial t} = D \times [\frac{\partial^2 c(t)}{\partial x^2} + \frac{\partial^2 c(t)}{\partial y^2} + \frac{\partial^2 c(t)}{\partial z^2}], \tag{1}$$

where D is the diffusion coefficient, which is determined by the channel environment and the property of the molecules. In this paper, D is a constant.

The nanomachines A and B are "passive" nanomachines which can sense the concentration within its antennas volume but does not impede the diffusion of the molecules. This assumption has been widely used in the literature in the MC field such as [27]. It is also assumed that the delay of the sensing behavior is negligible. The channel impulse response at each receiving antenna given Q released molecules can be expressed as [28], [29]

$$N(t) = \frac{V_R Q}{(4\pi D t)^{\frac{3}{2}}} e^{(\frac{-d^2}{4Dt})}, \tag{2}$$

where $N(t)$ represents the average number of observed molecules at time instant t. d is the distance between the receiving antenna and the transmitter, V_R is the volume of the spherical receiving antenna expressed as

$$V_R = \frac{4}{3}\pi R^3, \tag{3}$$

where R is the radius of the antenna.

The noise exists due to the free diffusion of the molecules governed by Brownian motion. To describe the noise, we denote the number of observed molecules as $\hat{N}(t)$, which is different from the average number of observed molecules $N(t)$. $\hat{N}(t)$ is usually modeled by binomial distribution [30]. For moderately large number of molecules, Poisson distribution is used as an approximation [31], [32] with both expectation and variance equal to $N(t)$. Furthermore, it is a reasonable assumption that $N(t) \gg 100$ [32]. Then the Gaussian approximation of the Poisson distribution can be used, i.e., $\hat{N}(t) \sim \mathcal{N}(N(t), N(t))$. The noise $n_b(t)$ can be expressed as $n_b(t) \sim \mathcal{N}(0, \sigma^2(t))$, where $\sigma^2(t) = N(t)$ is the variance of $n_b(t)$. Many literature adopts the Gaussian distributed additive noise with zero mean as a reasonable approximation of such noise [33], [34]. The noise is non-stationary and signal-dependent [32].

Considering the noise, the number of observed molecules at different receiving antennas $(R_{x1}, R_{x2}, \ldots, R_{xm})$, where $x \in \{A, B\}$, can be expressed as

$$\begin{bmatrix} N'_1(t) \\ N'_2(t) \\ \vdots \\ N'_m(t) \end{bmatrix} = N(t)1_m^{\mathrm{T}} + \begin{bmatrix} n_{b_1}(t) \\ n_{b_2}(t) \\ \vdots \\ n_{b_m}(t) \end{bmatrix}, \tag{4}$$

where m denotes the mth of receiving antennas. 1_m is the $1 \times m$ vector with all values equal to 1. Superscript T is vector transpose. $n_{b_1}(t), n_{b_2}(t), \ldots, n_{b_m}(t)$ can be considered independent and identically distributed random noise.

III. CLOCK SYNCHRONIZATION SCHEME

In this section, the clock synchronization scheme is presented. The aim of the clock synchronization is to synchronize the clocks between node A and node B. In Section III-A, the problem for the current clock synchronization scheme is briefly discussed, then in Section III-B, the proposed solution to overcome that problem is presented.

A. PROBLEM FOR CURRENT CLOCK SYNCHRONIZATION SCHEME

To synchronize the clocks between node A and node B, the straightforward idea is that: node A sends a message with its time stamp to node B. Once node B receives this message, it updates its own clock with the time stamp contained in the message sent by node A immediately (see Fig. 2a). However, the propagation delay is one of the major sources of error for the synchronization. It becomes much more serious in MC than in wireless communication, because the information molecules propagate much more slowly than the electromagnetic wave (see Fig. 2b).

The authors in [22] proposed a scheme which takes the propagation delay into consideration. In that synchronization scheme, the distance between node A and node B d_{AB} and molecular diffusion coefficient D are assumed to be known in order to calculate the propagation delay T_{del}. As soon as node B receives the message sent by node A, it updates its own clock with the time stamp contained in the message T_A and the propagation delay T_{del} as

$$T_{\text{update}} = T_A + T_{\text{del}}. \tag{5}$$

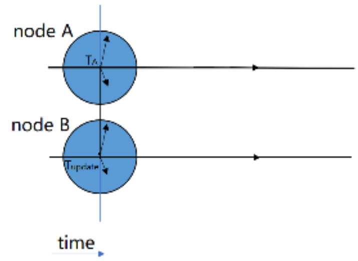
Then the synchronization between node A and node B can be achieved.

However, the scheme in [22] is still not prefect. This is because in the state-of-the-art clock synchronization works for MC like [19]–[22], the time duration of the molecule synthesis T_{syn} is not considered and but ignored. However, the molecule synthesis indeed takes time, which cannot be negligible [24] and is hard to estimate. In these schemes, the nanomachine takes uncertain length of time to synthesize molecules which is embedded with the instantaneous time instant. Therefore, the actual molecule releasing time is T_{syn} after that embedded time instant plus the synthesize time. Hence, if (5) is used to perform synchronization, the ignorance of the synthesis time duration causes error (see Fig. 2c).

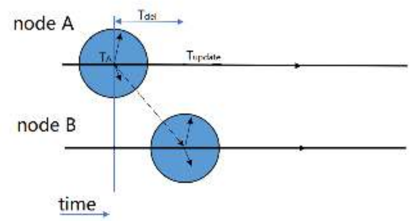
In Section III-B, a clock synchronization scheme taking the molecule synthesis time into consideration is proposed.

B. PROPOSED CLOCK SYNCHRONIZATION SCHEME

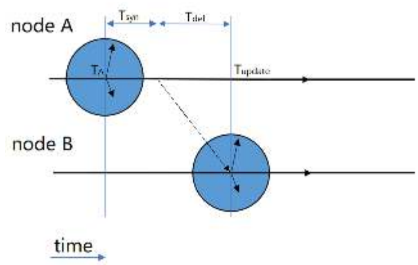
To overcome the errors in the synchronization caused by the molecule synthesis time duration, a reference broadcast synchronization scheme is proposed by introducing another nanomachine node P (see Fig. 2). The procedure of the proposed synchronization scheme is shown in Fig. 3. At the



(a) Node A sends a time stamp to node B. It is assumed there is no propagation delay. Node B receives the time stamp and updates its own clock immediately.



(b) The propagation delay is considered. Node A sends a time stamp with information molecules. The molecules propagate and arrive at node B with the delay T_{del}. Node B updates its own clock with the value $T_A + T_{\text{del}}$.



(c) The propagation delay and the time duration for molecule synthesis are considered. If $T_A + T_{\text{del}}$ is used for node B to update its clock, there incurs error.

FIGURE 2. Three different assumptions during the clock synchronization process. (a) The message propagation delay is assumed to be zero. (b) There is an unknown propagation delay for the message transmitted from node A to node B. (c) Based on (b), the time duration for molecule synthesis is considered.

beginning of the synchronization, node P broadcasts a beacon message by releasing a number of molecules. There is no need to encode any time information into the molecules. Then these molecules propagate in the medium in a free diffusion manner, and finally they will arrive at node A and node B. The time instant for the maximum concentration at node A or node B is considered as the receiving time instant. The propagation delay is denoted as T_{del_m}, where $m \in \{A, B\}$.

It is assumed that the clock reading of node A at the start of the synchronization, i.e., the moment node P begins to synthesize molecules, is denoted by T_A. Similarly, the clock reading of node B at the start of the synchronization is denoted by T_B. Once the molecule concentration reaches maximum

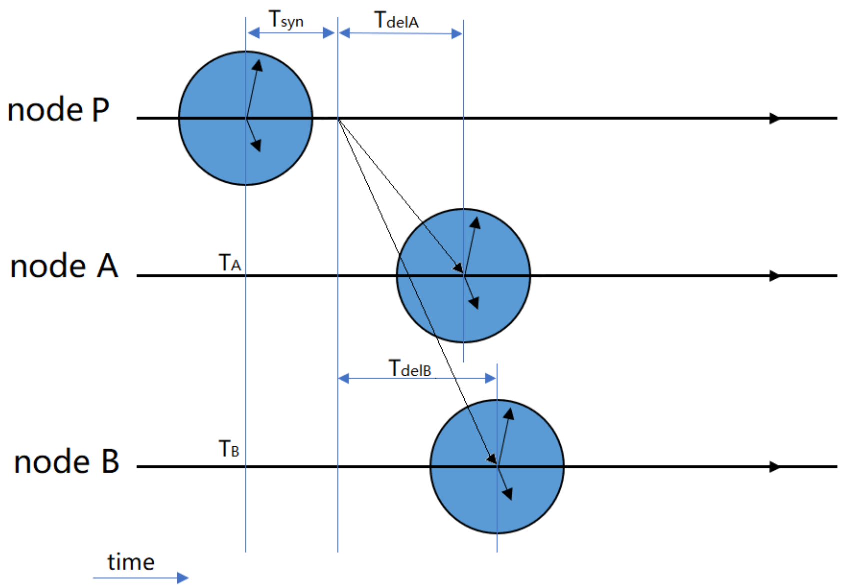


FIGURE 3. The proposed reference broadcast clock synchronization scheme. Node P would like to send a beacon message with a number of molecules. It costs some time to synthesize the molecules. Once finished, node P releases the molecules into the environment. The molecules diffuse and arrive at node A and node B. Node A and node B record their clock readings when the molecular concentrations reach the maximum. They estimate the propagation delays from the temporal sensed concentration. Using the estimated propagation delay and the recorded clock readings, the clock offset between node A and node B can be calculated.

at node A, node A records its time reading as T_{r_A}. Similarly, once the molecule concentration reaches maximum at node B, node B records its time reading as and T_{r_B}. Then we have the following equations

$$T_{r_A} = T_A + T_{\text{syn}} + T_{\text{del}_A}, \quad (6)$$
$$T_{r_B} = T_B + T_{\text{syn}} + T_{\text{del}_B}. \quad (7)$$

T_{syn} is a variable, whose value is unknown by the nanomachines. The clock difference between node A and node B can be given by

$$T_A - T_B = T_{r_A} - T_{r_B} + T_{\text{del}_A} - T_{\text{del}_B}. \quad (8)$$

If $T_A - T_B$ is calculated, then the synchronization between node A and node B can be achieved.

From (8), it can be seen that the clock difference is not influenced by the molecule synthesizing time. which is excluded from the critical path. T_{r_A} and T_{r_B} are clock readings by the node A and node B. Therefore, the key to obtain the clock difference $T_A - T_B$ is to calculate the molecule propagation delay T_{del_A} and T_{del_B}. Next, we will present the method for the propagation delay estimation.

C. ESTIMATION OF T_{del_A} AND T_{del_B}

In this subsection, the propagation delay estimation is presented. Since the propagation delay is estimated in the proposed scheme, there is no requirement for the deployment of the nanomachines. To estimate the propagation delay, we take derivative of (1) with respect to t and set it to zero. We have

$$T_{\text{del}} = \frac{d^2}{6D}. \quad (9)$$

However, the parameters D and d are usually unknown in the real MC system. So, we take serval samples of the signals at the receiver side temporally to calculate them. For a given sample $(t_i, N_i(t_i))$, it is not a solution to the function

$$N(t) = \frac{V_R Q}{(4\pi D t)^{\frac{3}{2}}} e^{(\frac{-d^2}{4Dt})}, \quad (10)$$

because the transmitter and the receiver are not synchronized when sampling. Hence, (10) is transformed into

$$N(t) = \frac{V_R Q}{[4\pi D(t-t_0)]^{\frac{3}{2}}} e^{(\frac{-d^2}{4D(t-t_0)})}, \quad (11)$$

where t_0 is the time instant after the molecules are released into the environment based on node A's clock or node B's clock. There are three unknown parameters in (11), i.e., D, d, and t_0. Hence, we need at least three samples $(t_i, N_i(t_i))|_{i=1,2,3}$ to solve it, shown as

$$\begin{cases} N(t_1) = \dfrac{V_R Q}{[4\pi D(t_1-t_0)]^{\frac{3}{2}}} e^{(\frac{-d^2}{4D(t_1-t_0)})} \\ N(t_2) = \dfrac{V_R Q}{[4\pi D(t_2-t_0)]^{\frac{3}{2}}} e^{(\frac{-d^2}{4D(t_2-t_0)})} \\ N(t_3) = \dfrac{V_R Q}{[4\pi D(t_3-t_0)]^{\frac{3}{2}}} e^{(\frac{-d^2}{4D(t_3-t_0)})}. \end{cases} \quad (12)$$

We can use the least square method to do the approximation:

$$\{\hat{D}, \hat{d}, \hat{t_0}\} = \arg\min_{D,d,t_0} \sum_{i=1}^{3} \left\{ \frac{V_R Q}{[4\pi D(t_i-t_0)]^{\frac{3}{2}}} e^{(\frac{-d^2}{4D(t_i-t_0)})} - N(t_i) \right\}^2. \quad (13)$$

TABLE 1. Simulation parameters.

Parameters	Symbol	Values
The number of the receiving antennas	m	$1-10$
The distance between node P and node A	d_{AP}	100-160 μm
The distance between node P and node B	d_{BP}	100-160 μm
The distance between node A and node B	d_{AB}	80 μm
The clock offset between node A and node B	T^{AB}	10-100 μs
The number of molecules released by the transmitter	Q	1×10^7-5×10^7
The diffusion coefficient	D	10-30 μm^2/ms
The antenna radius	R	5 μm
The time duration of the molecule synthesis	T_{syn}	30 ms

Then T_{del_A} and T_{del_B} can be calculated as

$$T_{\text{del}_A} = \frac{\hat{d_{AP}}^2}{6\hat{D}_A}, T_{\text{del}_B} = \frac{\hat{d}_{BP}^2}{6\hat{D}_B}. \tag{14}$$

Substituting (14) in (8), $T_A - T_B$ can be calculated. Then the clock synchronization can be achieved.

D. MOLECULAR SIMO FOR MITIGATING NOISE

Equation (14) is the theoretical result without considering the noise. As stated in Section II, the received signal suffers an additive Gaussian noise. We adopt the SIMO structure [22] to mitigate the influence of the noise. Several receiving antennas get samples spatially and take average to them. Hence, we have

$$\bar{N}(t_i) = \frac{1}{m}\sum_{j=1}^{m} N_j'(t_i) = N(t_i) + \frac{1}{m}\sum_{j=1}^{m} N_{b_j}(t_i), \tag{15}$$

where $\bar{N}(t_i)$ represents the average number of observed molecules of the antennas for the ith temporal sample. $N_j'(t_i)$ represents the number of observed molecules at the jth antenna for the ith temporal sample which is composed of $N(t_i)$ and $n_{b_j}(t_i)$. $N(t_i)$ is the number of molecules at time t_i in theory. $n_{b_j}(t_i)$ is the corresponding noise. Since $n_{b_j}(t_i)$ is independent and identically distributed Gaussian noise, according to the law of large numbers, $\frac{1}{m}\sum_{j=1}^{m} N_{b_j}(t_i)$ approaches zero as the number of antennas tends to infinity. In this way the noise can be mitigated. Taking $\{(t_i, \bar{N}(t_i))\}_{i=1}^{3}$ into the scheme proposed in Section III-C, we can estimate the propagation delay more precisely and achieve the clock synchronization more accurately.

IV. SIMULATION RESULTS AND DISCUSSION

In this section, simulations are performed in MATLAB to validate the performances of our proposed diffusion-based broadcast reference clock synchronization scheme. The proposed scheme is compared with a typical and latest clock synchronization scheme for MC [22] in terms of accuracy. The synchronization schemes with and without propagation delay are evaluated. What is more, the influences of the number of antennas, the number of released molecules, the initial clock offset, the distances, and the diffusion coefficient on the synchronization accuracy are simulated and analyzed.

The parameters used in the simulations are listed in Table 1. Unless stated otherwise, the default parameters are: the number of the receiving antennas on node A and node B, m, is set as 5 [22]. The distance between node P and node A is 100 μm. The distance between node P and node B is 150 μm. The distance between node A and node B is 80 μm. The initial clock offset between node A and node B, T^{AB}, is set to 20 μs. The number of molecules released by the transmitter Q is set to 2.5×10^7 [35]. The diffusion coefficient D is set as 10 μm^2/ms [36], The antenna radius R is set as 5 μm [22]. The time duration of the molecule synthesis T_{syn} is set as 30 ms.

The absolute error and the mean squared error (MSE) are used to measure the difference between the estimated clock offset and the real clock offset. The absolute error of the clock offset is defined as

$$Error = \frac{1}{M}\sum_{i=1}^{M} |t_i^{AB} - T^{AB}|, \tag{16}$$

where t_i^{AB} is the estimated clock offset of a simulation and M is the number of simulations with constant parameters. The MSE of the estimated clock offset is given as

$$MSE = \frac{1}{M}\sum_{i=1}^{M} (t_i^{AB} - T^{AB})^2. \tag{17}$$

In Fig. 4, we compare our proposed scheme with the scheme in [22] in terms of accuracy for different time durations of the molecule synthesis. The same parameters are set for the two schemes. The number of antennas $m = 5$, the number of molecules released by the transmitter $Q = 2.5\times10^7$. The clock offset between node A and node B is set as 20 μs. The diffusion coefficient D is set as 10 μm^2/ms. The distance between node A and node B is 80 μm. The time duration of the molecule synthesis T_{syn} is set from 20 to 60 ms. From the figure, it can be seen that the error of the clock synchronization in our scheme is much smaller than that of the scheme in [22]. The accuracy of the proposed scheme is almost not influenced by T_{syn}, while the accuracy of the scheme in [22] is influenced by T_{syn} significantly. For the scheme in [22], the error increases with the increase of T_{syn}. The reason is that the scheme in [22] does not take the molecule synthesis time into account. One can simply think that the scheme in [22] is equivalent to using (5). But if the

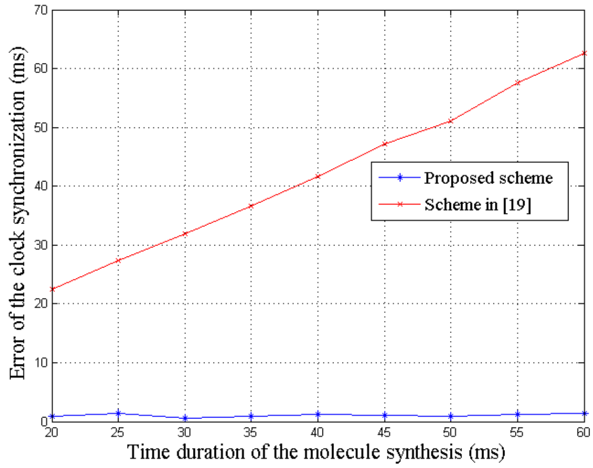


FIGURE 4. The error of the clock synchronization versus the time duration of the molecule synthesis for two schemes of the clock synchronization.

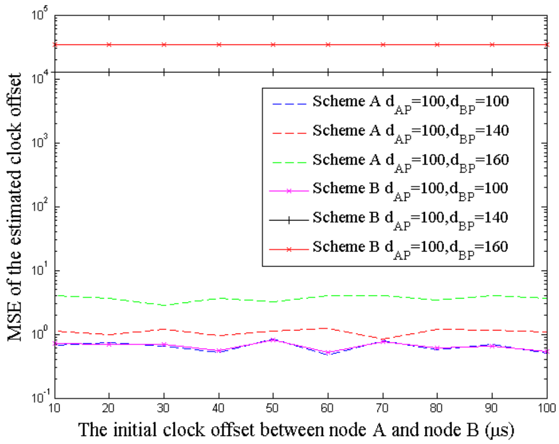


FIGURE 5. MSE of the estimated clock offset versus the initial clock offset between node A and node B for different distances {d_{AP},d_{BP}}.

molecule synthesis time duration is not equal to zero, then the correct updated time should be

$$T_{\text{update}} = T_A + T_{\text{del}} + T_{\text{syn}}. \quad (18)$$

From Fig. 4, it is seen that the error is indeed very close to the time duration of the molecule synthesis. While the proposed scheme use another reference nanomachine node P to exclude the molecule synthesis time as critical path. So the error of the clock synchronization is close to zero and not influenced by the time duration of the molecule synthesis.

In Fig. 5, the MSEs of the estimated clock offset versus the initial clock offset between node A and node B for different distances {d_{AP}, d_{BP}} are plotted. Two reference broadcast synchronization schemes are simulated. Scheme A includes the molecule propagation delay estimation and subtraction as shown in (8). Scheme B does not include the propagation delay estimation and subtraction process, which can be expressed as

$$T_A - T_B = T_{r_A} - T_{r_B}. \quad (19)$$

This is a typical way in the clock synchronization scheme for wireless communication networks, because electromagnetic wave propagates very fast, then the propagation delay can be ignored.

The parameters are: the number of antennas $m = 5$, the number of molecules released by the transmitter $Q = 2.5 \times 10^7$. And the clock offset between node A and node B is set from 10 to 100 μs. The different distances {d_{AP}, d_{BP}} are set as {$d_{AP} = 100\,\mu$m, $d_{BP} = 100\,\mu$m}, {$d_{AP} = 100\,\mu$m, $d_{BP} = 140\,\mu$m}, {$d_{AP} = 100\,\mu$m, $d_{BP} = 160\,\mu$m}. The MSEs of the estimated clock offset are calculated based on (17). It is obvious that the MSEs of the estimated clock offset for all curves are relatively stable. This result shows that the accuracy is not affected by the initial clock offset between node A and node B.

It can also be seen from Fig. 5 that if d_{AP} keeps the same while increasing d_{BP}, the average MSE of the estimated clock offset increases no matter scheme A or scheme B is adopted. The reason is that increasing the distance makes the channel impulse response more ''flat'', and further leading to the inaccuracy of the estimation of the propagation delay. Therefore, the MSE of the estimated clock offset becomes larger.

It is also seen from the figure that the MSE of the estimated clock offset for scheme A is smaller than scheme B for the case {$d_{AP} = 100\,\mu$m, $d_{BP} = 140\,\mu$m}, {$d_{AP} = 100\,\mu$m, $d_{BP} = 160\,\mu$m}. This result can be easily understood that because scheme B does not include the propagation delay estimation and subtraction process, so the accuracy is worse than scheme A. It should be also noted that for the case {$d_{AP} = 100\,\mu$m, $d_{BP} = 100\,\mu$m}, the MSE of the estimated clock offset for scheme A is almost the same as that of scheme B. This is because if $d_{AP} = d_{BP}$, then the propagation delay from node P to node A will be the same as the propagation delay from node P to node B, i.e., $T_{\text{del}_A} = T_{\text{del}_B}$. So (8) becomes (19). Therefore, even if scheme B does not include the propagation delay estimation and subtraction process, the accuracy will not be affected.

The MSE of the estimated clock offset versus the number of molecules sent by node P in the clock synchronization process for different numbers of receiving antennas is shown in Fig. 6. The number of molecules Q is set from 1×10^7 to 5×10^7. The number of receiving antennas is set to be $m = 1$ (single antenna), 2, 5, 10, respectively. It can be seen from the figure that the MSE of the estimated clock offset decreases as the increase of the number of molecules Q. Actually, as a beacon message, the number of released molecules should not affect the clock synchronization. However, the number of released molecules affects the accuracy of the estimation of the propagation delay. Since the estimation of the clock difference is related to the propagation delay as in (8), the accuracy of the clock synchronization will be affected. In our case, the increase of the number of released molecules by node P improves the accuracy of the estimation of the propagation delay, and further improves the accuracy of the clock synchronization.

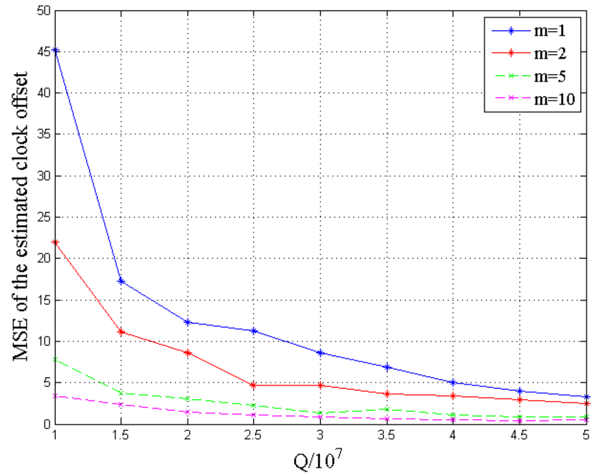


FIGURE 6. MSE of the estimated clock offset versus the number of molecules *Q* for different numbers of antennas *m*.

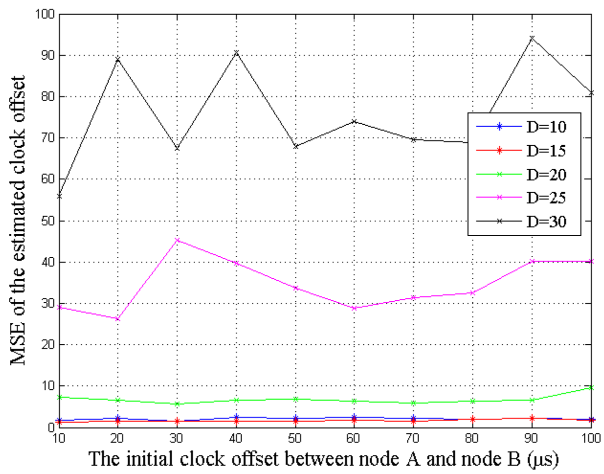


FIGURE 7. MSE of the estimated clock offset versus the clock offset between node A and node B for different diffusion coefficients *D*.

Focusing on different curves which represent different number of receiving antennas, it can be seen that for any specific number of released molecules Q, the MSE of the estimated clock offset decreases as the increase of the number of receiving antennas m. This is because the increase of the number of receiving antennas can obtain better performance of noise mitigation according to (15). Then the estimation of the propagation delay becomes more accurate, and further the MSE of the estimated clock offset becomes smaller.

In Fig. 7, the MSEs of the estimated clock offset versus the initial clock offset between node A and node B for different diffusion coefficients D are plotted. The parameters are set as: the number of antennas $m = 5$, the number of molecules released by the transmitter $Q = 2.5 \times 10^7$. The clock offset between node A and node B is set from 10 to 100 μs. And the diffusion coefficient is set to be $D = 10, 15, 20, 25$ and 30 μm^2/ms, respectively. From this figure, smaller diffusion coefficient D leads to smaller MSE of the estimated clock offset for a specific initial clock offset between node A and node B. The reason is: if D is smaller, the channel varies more slowly and the amplitude of the samples becomes larger for a constant time instant. Then the SNR becomes larger. The larger SNR makes the estimations of D and d become more accurate, and the estimation of the clock offset becomes more accurate.

V. CONCLUSION

The existing clock synchronization schemes for MC do not consider the molecule synthesis time and assume that it is equal to zero, which is not practical. If those clock synchronization schemes were applied in the real MC system, errors incur. This paper proposes a reference broadcast synchronization scheme by introducing a reference nanomachine. This reference nanomachine sends a beacon message with a number of molecules. The other two nanomachines record the receiving time, and estimate the propagation delay. Using these information, the nanomachines manage to calculate the clock offset between those two nanomachines and achieve the clock synchronization.

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