Non-Uniform BCSK Modulation in Nutrient-Limited Relay-Assisted Molecular Communication System: Optimization and Performance Evaluation

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Abstract

In this paper, a novel non-uniform Binary Concentration Shift Keying (BCSK) modulation in the course of molecular communication is introduced. We consider the nutrient limiting as the main reason for avoiding the nanotransmitters to release huge number of molecules at once. The solution of this problem is in the utilization of the BCSK modulation. In this scheme, nanotransmitter releases the information molecules non-uniformly during the time slot. To boost the bit error rate (BER) performance, we consider a relay-assisted molecular communication via diffusion. Our computations demonstrate how the pulse shape of BCSK modulation affects the BER, and we also derive the energy consumption of non-uniform BCSK in the closed-form expression. We study the parameters that can affect the BER performance, in particular the distance between the nanotransmitter and the nanoreceiver, the drift velocity of the medium, and the symbol duration. Furthermore, we propose an optimization problem that is designed to find the optimal symbol duration value that maximizes the number of successful received bits. The proposed algorithm to solve the optimization problem is based on the bisection method. The analytical results show that non-uniform BCSK modulation outperforms uniform BCSK modulation in BER performance, when the aggregate energy is fixed.
Index Terms

Molecular Communication, Nutrient Limiting, Binary Concentration Shift Keying Modulation, Bit Error Rate, Optimization

I. INTRODUCTION

In nanonetworks, Molecular Communication (MC) is used for communication between nanotransmitters and nanoreceivers. The electromagnetic-based communication is not proficient when the communication between microscale and/or nanoscale robots comes into the account [1], [2]. Optical communication is also not useful for these microscale and nanoscale applications because the optical signal requires guided medium or line of sight links [3]. This problem is already solved in nature. In the natural world, chemical signals are used for inter- and intracellular communication at micro- and nanoscales [4]. Therefore, chemical signals are a good candidate for communication at both the macro- and microscopic scales. This is the base of MC. It is one of the most competent approach in nanonetworks for communication between nanomachines. In this communication paradigm, nanomachines use molecules to communicate with each other. Moreover, MC signals are biocompatible, and require very low energy, in the order of a femto-Joule (fJ), for transmitting a bit [3].

Inspired by the communication methods used by biological systems, a variety of MC frameworks are proposed in the literature [5]–[8]. Among them, microtubule MC is imagined for short-range communication [6], and ion signaling and MC via diffusion are proposed for short to medium range communication [7], [8]. In this article, we focus on the MC via diffusion (MCvD). This framework can improve the bit error probability (BER) performance using relaying with decode and forward (DF) technique [9].

As a part of the biological systems, the modulation process in MC systems demands the oscillatory behavior in nanotransmitters. This oscillation needs ON/OFF mechanism [10]. The nutrient limiting avoid nanotransmitters to synthesize huge number of information molecules (the molecules that are released from the transmitter node to convey the information) at once [11]. This problem, in nature, has been solved by spreading the releasing time of molecules. This is the main idea behind BCSK (Binary Concentration Shift Keying) modulation concept. In standard BCSK, the molecules are released uniformly during the time. Despite uniform BCSK, in this paper, we employ non-uniform pulse shapes in BCSK, and show that the manner of releasing the molecules in time, is going to significantly affect the performance of MC systems.
Different modulation techniques are introduced in MCvD. Mahfuz et al. employ two modulation techniques [12]. In the first technique, they consider transmitting bit “1” along the concentration of \( Q \) (number of) molecules, when for bit “0”, no molecule is transmitted. In the second modulation technique, they consider information-carrying particles being released as sinusoidal signals with predefined frequency. In [13], Kuran et al. propose two new modulation techniques, namely Concentration Shift Keying (CSK) and Molecule Shift Keying (MoSK). In CSK, the information is modulated using the concentration of the identical molecules, while different types of molecules are considered in MoSK. This idea is extended to use isomer as messenger molecules by Kim et al. [14].

In this paper, the BER of the introduced non-uniform BCSK modulation is derived in closed form expression, and the analytical results reveal that the non uniformity of the molecules concentration shape can potentially improve the BER.

In the second part of the paper, the energy model of the MC, when the capacity of the vesicle is not constant, is considered. As the number of the released molecules increases, the BER decreases with the cost of spending more energy. Considering the limited energy per bit, we show the non-uniform BCSK has better BER compared to the uniform BCSK. We also study the trade off between the transmission rate and the probability of successfully receiving a bit. The molecules are transmitting in equal time slots, called the symbol duration. An optimization problem is designed to find the optimum symbol duration by maximizing the number of successful received bits. We propose an algorithm based on the bisection method to find the optimal value of the symbol duration.

The rest of the paper is organized as follows. In Section II, we study the system model including the channel model and BER analysis. In this section, we derive the mean and the variance of the number of the received molecules and derive a closed-form expression for bit error probability. In Section III, we study the energy model to evaluate the BER performance in terms of energy. In Section IV, we propose the optimization problem to find the optimal value of symbol duration by utilizing the bisection method. the In Section V the numerical result is shown. The paper is concluded in Section VI

**Notation:** In this paper, \( \exp(x) \) and \( \text{B}(k,l) \) denote the natural exponential function and the binomial distribution with \( k \) total number of experiments and the probability of \( l \) that each experiment yielding a successful result, respectively. The notation \( \mathcal{N} (\mu, \sigma^2) \) stands for the normal distribution with mean \( \mu \) and variance \( \sigma^2 \). In addition, \( \Psi(x) \) is the standard Gaussian cumulative
distribution function (CDF) which is given by
\[ \Psi(x) = \frac{1}{\sqrt{2\pi}} \int_{-\infty}^{x} \exp\left(-\frac{y^2}{2}\right) dy. \]
The notations erf\(x\) and Pr\(X\), refer to error function which is
\[ \text{erf}(x) = \frac{1}{\sqrt{2\pi}} \int_{0}^{x} \exp\left(-y^2\right) dy, \]
and the probability of happening the \(X\) event, respectively.

II. SYSTEM MODEL

In this paper, we adopt Brownian motion [15], to model the movement of the molecules in
the medium and consider positive drift due to the fact that particles are propagated throughout
the blood vessels. It is also assumed the receiver is downstream from the transmitter. The nanotransmitter, transmits the information in equal symbol durations. The inter-symbol interference (ISI) is defined as the received molecule during the current symbol duration that is transmitted in the previous symbol durations. The noise is created by molecules from the other sources which is accounted in the receiver. The maximum-a-posterior (MAP) rule is employed in the receiver to detect the transmitted information.

In the employed model, we have three nodes, namely a nanotransmitter (node S), a nanoreceiver in the destination (node D), and a relay nanomachine (node R). The model is illustrated in Fig. 1.

This system acts as a relay-assisted MCvD system. Node S is assumed to be a point source. It is also assumed that the nodes do not have any mobility. During the transmission node R is located between nodes S and D. It has full-duplex transmission and utilizes the DF strategy. We assume node S transmits information to node R in the \(n\)th time slot, node R decodes the received message from node S at the end of the \(n\)th time slot, and retransmits it to node D in the \((n + 1)\)th time slot. Finally, node D detects the information at the end of the \((n + 1)\)th time slot. The medium has positive drift velocity, i.e., the receiver is downstream from the transmitter, and
The BCSK modulation technique is based on releasing the same number of molecules in each sub slot of a time slot [17]. We propose a new BCSK modulation in which the pulse shape of molecules is non uniform. We divide each time slot into $I$ identical sub slots, and the time slot duration is denoted by $t_s$. Therefore, each sub slot has $\left( \frac{1}{I} \times t_s \right)$ duration. In Fig. 2, $g(i)$ is the packet of molecules for each sub slot $i$. We should shape $g(i)$ with specific function. In Fig. 2 we plot non-uniform BCSK with different pulse shapes. In the introduced scheme, $N$ molecules with the pulse shape of $g(i)$ are released into the medium to represent transmitting bit “1”. In the proposed modulation model, the transmitter does not release any molecule to represent transmitting bit “0” [12]–[14], [18].

In the relay-assisted MCvD system, we should use two different molecules in order to reduce ISI which are denoted by $T$ and $U$ at the transmitter and relay node, respectively.

Fig. 2. Modulation scheme to send bit “1”, a). Exponentially function for non-uniform BCSK, b). Sinc function for non-uniform BCSK, c). Cosine function for non-uniform BCSK, d). uniform pulse BCSK modulation scheme (the number of molecules to send bit “1” in (a), (b), (c) and (d) are equal).
A. Channel Model

In this paper, the Brownian motion of the released molecules into the medium is biased in positive drift. We follow the channel model from [16]. The operation of propagating is administered by both diffusion and drift as a result of the external active mobility. Therefore, we need to consider the Brownian motion with drift in the channel model. We assume no collision occurs between the molecules that are propagating. The released molecules can be diffused with positive drift in the medium continuously. We assume when they hit the receiver, they are absorbed and removed from the medium. In this paper, we consider the positive drift velocity is in the direction of the molecules transmitted from the transmitter toward the receiver.

We use 1D Brownian motion in a fluid medium with positive drift velocity. The absorption time \( t \) for molecule of type \( T \), which is the first hitting time of molecule type \( T \) by receiver, follows the probability density function (pdf) as [19], [20]

\[
f(t) = \frac{d}{\sqrt{4\pi D_T t^3}} \exp\left(\frac{-(vt - d)^2}{4D_T t}\right),
\]

where \( d \) is the distance between the transmitter and the receiver, \( D_T \) is the diffusion coefficient of \( T \) molecules in the medium, and \( v \) is the medium drift velocity. The value of \( D_T \) depends on the temperature\(^1\), viscosity of the fluid\(^2\) and the Stokes radius of \( T \) molecules [22].

The CDF of the absorption time that is the probability that the molecules of type \( T \) hit the receiver, within time \( t \), is given by [20], [21]

\[
F(t) = \Psi\left(\frac{d}{\sqrt{2D_T t}}\left(\frac{vt}{d} - 1\right)\right) + \exp\left(\frac{vd}{D_T}\right)\Psi\left(\frac{-d}{\sqrt{2D_T t}}\left(\frac{vt}{d} + 1\right)\right).
\]

The CDF in (2) is a function of medium velocity, diffusion coefficient of \( T \) molecules, distance, and time. Thus, we can rewrite \( F(t) = P_{\text{hit}}(v, D_T, d, t) \), where \( P_{\text{hit}} \) is the probability of hitting the \( T \) molecules by the receiver, within time \( t \).

Let \( M_{s,r}^T[n] \) denote the total number of \( T \) molecules absorbed by node R, located at distance of \( d_{sr} \) away from node S and absorbed by node R at the end of the \( n^{th} \) time slot. The total number of molecules, denoted by \( M_{s,r}^T[n] \) is given by [13], [23]

\[
M_{s,r}^T[n] = N_{Cs,r}^T[n] + N_{Ps,r}^T[n] + N_{Nos,r}^T[n] + N_{NCS,r}^T[n],
\]

\(^1\)Body temperature is 310 k [21].

\(^2\)Viscosity of blood at body temperature is \( 2.46 \times 10^{-3} \) kg/sec.m [21].
TABLE I
SPECIFICATION OF DENOTED TERMS FOR THE RECEIVED MOLECULES

| Specification                                                                 | Denoted Term          |
|-------------------------------------------------------------------------------|-----------------------|
| the number of molecules transmitted and received during the current time slot  | $N_{Cs,r}[n]$         |
| the number of molecules transmitted in the previous time slot while they are   | $N_{Ps,r}[n]$         |
| received during the current time slot (ISI)                                   |                       |
| the number of molecules from other sources which act as noise                 | $N_{Nos,r}[n]$        |
| the error in the counting of the absorbed molecules by node R                 | $N_{NCs,r}[n]$        |

where $N_{Cs,r}[n]$, $N_{Ps,r}[n]$, $N_{Nos,r}[n]$, and $N_{NCs,r}[n]$, are explained at Table I.

As regard the independent movement of the messenger molecules with specific probability of hitting the receiver, $N_{Cs,r}[n]$ obeys a binomial distribution as [13], [21], [23], [24]

$$N_{Cs,r}[n] \sim \sum_{i=0}^{I-1} B(x_s[n]g(i), P_{1,i}),$$  \hspace{1cm} (4)

where $x_s[n]$ represents the bit transmitted by node S at the $n$th time slot. In (4) $P_{j,i} = P_{hit}(v, D, d, t_{j,i})$ is the probability of hitting the molecules within time $t_{j,i}$, where $t_{j,i} = (jt_s - \frac{it_s}{I})$, is the time of each sub slot $i$ of the $j$th time slot.

The ISI length is finite because we can ignore the ISI effect after a finite number of previously transmitted symbols [25]. Therefore, we can write $N_{Ps,r}[n]$ as

$$N_{Ps,r}[n] \sim \sum_{j=1}^{J} \sum_{i=0}^{I-1} B(x_s[n-j] g(i), q_{j,i}),$$  \hspace{1cm} (5)

where $J$ indicates the ISI length, $x_s[n-j]$ represents the bit transmitted by node S at the $(n-j)$th time slot and $q_{j,i} = P_{j+1,i} - P_{j,i}$

We can approximate the binomial distribution in (4) and (5) by a normal distribution, if $g(i)$ in each sub slot is large enough, and $g(i)P_{hit}(v, D_T, d, t)$ is not zero [24]. We know the mean and variance of the sum of independent normal distributions are the sum of their means and variances, respectively. Therefore, $N_{Cs,r}[n]$ obeys a normal distribution given by

$$N_{Cs,r}[n] \sim \mathcal{N}\left(x_s[n] \sum_{i=0}^{I-1} g(i) P_{1,i}, x_s[n] \sum_{i=0}^{I-1} g(i) P_{1,i}(1 - P_{1,i})\right).$$  \hspace{1cm} (6)

Then, $N_{Ps,r}[n]$ becomes

$$N_{Ps,r}[n] \sim \mathcal{N}\left( \sum_{j=1}^{J} \sum_{i=0}^{I-1} x_s[n-j] g(i) q_{j,i}, \sum_{j=1}^{J} \sum_{i=0}^{I-1} x_s[n-j] g(i) q_{j,i}(1 - q_{j,i})\right).$$  \hspace{1cm} (7)
We assume the distribution of $N_{\text{Nos},r}[n]$ is normal as

$$N_{\text{Nos},r}[n] \sim \mathcal{N}(\mu_{\text{Nos},r}, \sigma^2_{\text{Nos},r}), \quad (8)$$

where $\mu_{\text{Nos},r}$ and $\sigma^2_{\text{Nos},r}$ are the mean and variance of noise, respectively. The distribution of counting noise $N_{\text{NCs},r}[n]$ is considered as

$$N_{\text{NCs},r}[n] \sim \mathcal{N}(0, \sigma^2_{\text{NCs},r}), \quad (9)$$

where $\sigma^2_{\text{NCs},r}$ is the variance of counting noise and is dependent on the mean values of the molecules received by node R as $\mu_{\text{Nos},r}$.

Since the distributions of $\mathcal{N}(6), \mathcal{N}(7), \mathcal{N}(8), \text{and } \mathcal{N}(9)$ are normal, $M_{s,r}^T[n]$ obeys the normal distribution as follows

$$\text{Pr}(M_{s,r}^T[n] \mid x_s[n] = 0) \sim \mathcal{N}(\mu_{0s,r}, \sigma^2_{0s,r}), \quad (10)$$

$$\text{Pr}(M_{s,r}^T[n] \mid x_s[n] = 1) \sim \mathcal{N}(\mu_{1s,r}, \sigma^2_{1s,r}), \quad (11)$$

where $\mu_{0s,r}, \sigma^2_{0s,r}, \mu_{1s,r}$ and $\sigma^2_{1s,r}$ are derived from $\mathcal{N}(6), \mathcal{N}(7), \mathcal{N}(8), \text{and } \mathcal{N}(9)$, respectively as follows

$$\mu_{0s,r} = \pi_1 \sum_{j=1}^{J} \sum_{i=0}^{I-1} g(i) q_{j,i} + \mu_{\text{Nos},r}, \quad (12)$$

$$\mu_{1s,r} = \pi_1 \sum_{j=1}^{J} \sum_{i=0}^{I-1} g(i) q_{j,i} + \pi_1 \sum_{i=0}^{I-1} g(i) P_{1,i} + \mu_{\text{Nos},r}, \quad (13)$$

$$\sigma^2_{0s,r} = \pi_1 \sum_{j=1}^{J} \left\{ \sum_{i=0}^{I-1} g(i) q_{j,i} (1 - q_{j,i}) + \pi_0 \left( \sum_{i=0}^{I-1} g(i) q_{j,i} \right)^2 \right\} + \sigma^2_{\text{Nos},r} + \mu_{0s,r}, \quad (14)$$

$$\sigma^2_{1s,r} = \pi_1 \sum_{j=1}^{J} \left\{ \sum_{i=0}^{I-1} g(i) q_{j,i} (1 - q_{j,i}) + \pi_0 \left( \sum_{i=0}^{I-1} g(i) q_{j,i} \right)^2 \right\} + \sum_{i=0}^{I-1} g(i) P_{1,i} (1 - P_{1,i}) + \sigma^2_{\text{Nos},r} + \mu_{1s,r}, \quad (15)$$

where $\text{Pr}(x_s[n] = 1) = \pi_1$ and $\text{Pr}(x_s[n] = 0) = \pi_0$. The details of the calculation for mean and variance of $N_{p_{s,r}}^T$ are provided in Appendix A.

Relay-node (node R) decides based on the MAP rule in detection as below

$$\hat{x}_r[n] = \begin{cases} 1 & \text{if } M_{s,r}^T[n] \geq \tau_R \\ 0 & \text{if } M_{s,r}^T[n] < \tau_R \end{cases}, \quad (16)$$

where $\tau_R$ is the detection threshold at node R, and $\hat{x}_r[n]$ is the information bit detected by node R at the end of the $n$th time slot.
Since our system is a relay-assisted MCvD system, node R has to forward the information bit detected at the end of the \( n \)th time slot. Similar to the mathematical manipulations derived for node S and node R, the distribution of the total number of \( U \) molecules absorbed by node D, denoted by \( M_{r,d}^U[n+1] \), which detected at the end of the \((n+1)\)th time slot can be derived from

\[
\Pr(M_{r,d}^U[n+1] \mid x_r[n+1] = 0) \sim \mathcal{N}(\mu_{0r,d}, \sigma_{0r,d}^2),
\]

\[
\Pr(M_{r,d}^U[n+1] \mid x_r[n+1] = 1) \sim \mathcal{N}(\mu_{1r,d}, \sigma_{1r,d}^2),
\]

where \( x_r[n+1] \) is the transmitted bit at the beginning of the \((n+1)\)th time slot from node R. The calculation of mean and variance values of molecules transmitted by node R and received by node D (\( \mu_{0r,d}, \sigma_{0r,d}^2, \mu_{1r,d}, \) and \( \sigma_{1r,d}^2 \)), is similar to the calculation of mean and variance values of molecules which are transmitted by node S and received by node R, and are therefore omitted here.

### B. BER Analysis

We study the BER analysis of the relay-assisted MCvD system, which is introduced in [16]. The probability of error between two nodes for the \( n \)th transmitted bit is calculated as follows

\[
P_e[n] = \Pr(x_s[n] = 1) \Pr(\hat{x}_d(n+1) = 0 \mid x_s[n] = 1) \\
+ \Pr(x_s[n] = 0) \Pr(\hat{x}_d(n+1) = 1 \mid x_s[n] = 0).
\]  
(19)

Before the calculation of BER, we should determine the \( \Pr(x_r[n] = 1) \), which is given by

\[
\Pr(x_r[n] = 1) = \pi_1 \Pr(\hat{x}_r[n-1] = 1 \mid x_s[n-1] = 1) \\
+ \pi_0 \Pr(\hat{x}_r[n-1] = 1 \mid x_s[n-1] = 0),
\]  
(20)

where \( \Pr(x_s[n-1] = 1) \) and \( \Pr(x_s[n-1] = 0) \) are \( \pi_1 \) and \( \pi_0 \), respectively. We consider the MAP rule detection in (16) and use (12), (13), (14) and (15) to calculate (20) as follows:

\[
\Pr(\hat{x}_r[n-1] = 1 \mid x_s[n-1] = 1) \\
= \Pr(M_{s,r}^T[n-1] \geq \tau_R \mid x_s[n-1] = 1) \\
= \frac{1}{2} \left( 1 - \text{erf} \left( \frac{\tau_R - \mu_{1s,r}}{\sqrt{2} \sigma_{1s,r}^2} \right) \right),
\]  
(21)
\[
\Pr(\hat{x}_r[n-1] = 1 \mid x_s[n-1] = 0)
= \Pr(M^T_{s,r}[n-1] \geq \tau_R \mid x_s[n-1] = 0)
= \frac{1}{2} \left(1 - \text{erf}\left(\frac{\tau_R - \mu_{0s,r}}{\sqrt{2} \sigma_{0s,r}^2}\right)\right).
\]

(22)

Now we can calculate (19) from (21) and (22). At the final step we can write BER for the direct transmission from (19)-(22) given by

\[
P_{eD}[n] = \frac{1}{2} + \frac{1}{4} \left[\text{erf}\left(\frac{\tau_D - \mu_{1s,d}}{\sqrt{2} \sigma_{1s,d}^2}\right) - \text{erf}\left(\frac{\tau_D - \mu_{0s,d}}{\sqrt{2} \sigma_{0s,d}^2}\right)\right],
\]

(23)

and for the relay-assisted transmission as

\[
P_{esR}[n] = \frac{1}{2} + \frac{1}{8} \left[\text{erf}\left(\frac{\tau_R - \mu_{1s,r}}{\sqrt{2} \sigma_{1s,r}^2}\right) - \text{erf}\left(\frac{\tau_R - \mu_{0s,r}}{\sqrt{2} \sigma_{0s,r}^2}\right)\right] \times \left[\text{erf}\left(\frac{\tau_D - \mu_{0r,d}}{\sqrt{2} \sigma_{0r,d}^2}\right) - \text{erf}\left(\frac{\tau_D - \mu_{1r,d}}{\sqrt{2} \sigma_{1r,d}^2}\right)\right],
\]

(24)

where \(P_{eD}\) and \(P_{esR}\) denote the bit error probability for the direct transmission and the bit error probability for the relay-assisted transmission, respectively.

III. ENERGY MODEL

In a communication via a diffusion system, energy is consumed for the production of the messenger molecules and releasing them toward the destination nanomachine [5]. In our energy model, the energy cost for sending bit “1”, is considered as the sum of the total energy of each sub slot \(i\) in \(g(i)\) pulse shape. The steps of the messenger molecule production and releasing known as exocytosis are [4]:

- Synthesis of the messenger molecules from their building blocks: The energy cost of a single messenger molecule is denoted by \(E_S\). Since we should consider the synthesis of \(g(i)\) packets in the energy model, the energy cost of it would be \(g(i)E_S\).
- Production of a secretory vesicle, which is a packet of the messenger molecules [5]: We use one vesicle for each \(g(i)\) packet of the molecules and the energy cost is denoted by \(E_V(i)\). Since we use one vesicle for each \(g(i)\), we would have \(C_v = g(i)\) where \(C_v\) is the capacity of each vesicle and its unit is the number of molecules.
- Carrying the secretory vesicles to the cell membrane: The energy cost of it denoted by \(E_C\).
- Releasing the molecules via the fusion of the vesicle and the cell membrane: The energy cost of extraction of a vesicle to the medium denoted by \(E_E\), which is provided in Table [II]
The capacity of each vesicle $C_v$ can be approximated by \[5\]:

$$C_v = \left( \frac{r_v}{r_{mm} \sqrt{3}} \right)^3 = g(i),$$

(25)

where $r_v$ is the radius of a vesicle and $r_{mm}$ is the radius of the messenger molecule. Note that the value of $r_v$ differs for each $g(i)$ due to non-uniform BCSK assumption. Therefore, $r_v$ is not constant in our energy model and we should change $r_v$ to $r_v(i)$ which can be calculated as

$$r_v(i) = \sqrt{3} r_{mm} \times \sqrt[3]{g(i)}.$$  

(26)

In this paper, we use proteins as messenger molecules. Proteins are produced by combining amino acids to create a specific amino acid chain at the subunit plant. The energy cost of each step to transmit proteins as messenger molecules that are explained above can be obtained as follows \[5\]:

$$E_S = E_{AM} (N_{aa} - 1),$$

(27)

$$E_v(i) = E_{SY} \left( 4\pi r_v^2(i) \right),$$

(28)

$$E_C = E_{PH} \left[ \frac{r_{unit}/2}{8} \right],$$

(29)

where $[X]$, $N_{aa}$, $r_{unit}$ are the ceiling function which maps $X$ to the least integer greater than or equal to $X$, the number of amino acids, the radius of the transmitter unit in nanometer scale, respectively. The values of parameters $E_{AM}$, $E_{SY}$, and $E_{PH}$ are provided in Table II. The zJ term in the aforementioned table is the zepto Joule whose value is $10^{-21}$ Joules.

By using all of the energies given above and (26), the total energy for sending each $g(i)$ is derived as

$$E_{T_i} = E_{AM} (N_{aa} - 1) g(i) + \left( E_{SY} \left( 4\pi \sqrt{3} r_{mm} \sqrt[3]{g(i)} \right)^2 \right) + E_{PH} \left[ \frac{r_{unit}/2}{8} \right] + E_E.$$  

(30)

According to (30), the total energy for sending bit “1” in non-uniform BCSK modulation is

$$E_T = \sum_{i=0}^{l-1} E_{T_i}.  

(31)$$

$E_T$ is directly proportional to pulse shape in non-uniform BCSK modulation as seen in (30) and (31).
Fig. 3. BER of the MCvD system with the relay node for exponentially, sinc, cosine and uniform pulse shape in non-uniform BCSK modulation, as a function of the detection threshold at the receiver for different values of distance between node S and node D ($\sum_{i=0}^{I-1} g(i) = 3000$, $v = 0.5$ mm/s, $t_s = 5$ ms and $d_{sd} = 2$ $\mu$m).

| Parameter                                                                 | Term | Values  |
|---------------------------------------------------------------------------|------|---------|
| Energy cost for adding a single amino acid to an amino acid chain          | $E_{AM}$ | 202.88 zJ [5] |
| The cost of synthesizing                                                  | $E_{SY}$ | 415 zJ [1], [26] |
| The cost of phosphorylation                                               | $E_{PH}$ | 83 zJ [1], [26] |
| The cost of releasing molecules into the medium                            | $E_{RE}$ | 830 zJ [27] |

IV. SYMBOL DURATION OPTIMIZATION PROBLEM

In this section we introduce the optimization problem to find the optimal value of the symbol duration. The transmission data rate, denoted by $R$, is

\[ R = \frac{1}{t_s} \]  

By increasing the symbol duration, the achievable data rate decreases. There is a trade off between $t_s$ and BER, as $t_s$ increases, BER decreases [19]. The product of the success probability of a
TABLE III
PROPOSED ALGORITHM BASED ON THE BISECTION METHOD

Initialization:
Set $0 < \epsilon < 1$, Lower bound = 0, and Upper bound = a sufficiently large number, e.g., $10^3$ in our setting.

Iterations:
Step 1: $l = \frac{\text{Lower bound} + \text{Upper bound}}{2}$.
Step 2: Solve the concave feasibility problem (36).
Step 3: If (36) is feasible,
    Lower bound = $l$,
    else
    Upper bound = $l$.
Step 4: If $|\text{Upper bound} - \text{Lower bound}| \leq \epsilon$,
    stop,
    else
    go back to Step 1.

received bit and data rate gives the aforementioned tradeoff. Based on our system model, the probability of successful reception, denoted by $P_{\Upsilon}[n]$, is 

$$P_{\Upsilon}[n] = 1 - 2P_{\text{sr}}[n]. \quad (33)$$

We formulate the optimization problem to find the optimal value of $t_s^*$ as follows:

$$\max_{t_s} P_{\Upsilon}[n](t_s) \cdot R(t_s). \quad (34)$$

It could be shown that the objective function in (34) is not a concave function, therefore, the optimization problem is not concave. However, its domain and all its sublevel sets are concave (see Fig. 8), hence, our optimization problem is quasi-concave [30]. Thus, we employ the bisection method to solve the optimization problem (34), in which the optimal symbol duration is determined by solving a concave feasibility problem at each step. The $l$-sublevel set ($l \in \mathbb{R}$) of a function $f: \mathbb{R}^n \to \mathbb{R}$ is defined as [30]

$$\zeta_l = \{x \in \text{dom } f \mid f(x) \geq l\}. \quad (35)$$
Note that \( \mathbb{R} \) is the set of real numbers. Thus, the new optimization problem by considering the \( l \)-sublevel set of the objective function in (34) as constraint, is

\[
\text{Find} \quad t_s \\
\text{s.t} \quad P_T[n](t_s) \cdot R(t_s) - l > 0.
\]

We provide the proposed algorithm based on the bisection method for solving the optimization problem in Table III, where \( \epsilon \) is some positive small number.

V. NUMERICAL RESULT

In this section, we show the numerical results to calculate the error probability performance of a relay-assisted MCvD system with drift for BCSK modulation and evaluate the BER in terms of the budget of energy. Also, we present how the MCvD system parameters influence the performance.

The proposed system parameters used in the analysis of BER and energy are provided in Table IV. We use capillaries with diameter ranging from 10 \( \mu \)m to 20 \( \mu \)m as the propagating medium whose velocities are between 0.3 and 1 mm/s [31], [32]. Note that the diameter of capillaries have no compliance with the assumption of the distance between the transmitter node and the destination node. We also consider protein based messenger molecules in our system. The number of amino acids that are required to form a protein depends on the size of protein. Furthermore, adding a single amino acid to an amino acid chain, regardless of the type of the amino acid, has a constant cost of energy [33]. We assume that the diffusion coefficient of \( T \) and \( U \) molecules are equal. We also assume \( I = 10 \), because the ISI effect for more than 10 previous symbols is small, which can be ignored [16].

At first, we assume that node R is located at the middle of nodes S and D. Note that node R has the same modulation scheme as node D. Without loss of generality, it is assumed that the mean and variance values of molecular noise are considered as 100.

The BER performance of MCvD system for exponential, sinc, cosine, and uniform pulse shapes as a function of the detection threshold at the receiver are presented in Fig. 3. Detection threshold provides a good comparison for BER performance. Because a fair comparison the number of molecules to send bit “1” for the four aforementioned pulse shapes are identical \( (\sum_{i=0}^{I-1} g(i) = 3000) \). In the numerical result, we observe from Fig. 3 that BER performance for uniform pulse shape in BCSK modulation has no admirable performance and is outperformed by...
non-uniform BCSK modulation scheme. In this figure, the BER performance of exponentially pulse shape has the best performance among others, because the effect of ISI has less impact on exponential pulse shape. After exponential pulse shape, the uniform pulse shape has better BER performance among others and then sinc function has better BER performance in compare to cosine function. The mentioned pulse shapes have no advantage as a function of detection threshold, compared to the exponential pulse shape. The main reason is that these pulse shapes are vulnerable against ISI effect.

In Fig. 4, we present the BER performance of non-uniform BCSK modulation as a function of the distance between nanotransmitter (node S) and nanoreceiver (node D). We can observe that by increasing the distance, the BER increases. It is due to the fact that by increasing the distance between the transmitter and the receiver nodes, the probability of hitting the molecules by the receiver decreases. Also, as shown in Fig. 4, the exponential pulse shape for non-uniform BCSK modulation has the best BER performance among other examples.

In Fig. 5, the BER performance of pulse shape examples for non-uniform BCSK modulation for different values of drift velocity is shown. We can see that increasing the drift velocity can improve the BER performance, because the drift velocity can make the diffusion and propagating molecules faster. Thus, increasing the drift velocity can improve the hitting probability of

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**TABLE IV**

**VALUES AND RANGES OF MCvD SYSTEM PARAMETERS**

| Parameter                        | Variable | Values         |
|----------------------------------|----------|----------------|
| Diffusion Coefficient            | $D_T$, $D_U$ | $79 \, \mu m^2/s$ |
| Drift Velocity                   | $v$      | $[0.4, 0.7] \, mm/s$ |
| Distance between nodes S and D   | $d_{sd}$ | $[2, 8] \, \mu m$ |
| Symbol duration                  | $t_s$    | $[1, 6] \, ms$ |
| Molecular noise mean             | $\sigma^2_{nos,r}$, $\sigma^2_{nor,d}$ | $100$ |
| Molecular noise variance         | $\mu_{nos,r}$, $\mu_{nor,d}$ | $100$ |
| Probability of sending bit “1”   | $\pi_1$  | $0.5$ |
| The ISI length                   | $J$      | $10$ |
| The number of i sub slot         | $I$      | $10$ |
| Number of amino-acids            | $N_{aa}$ | $51$ |
| Stokes’ radius of insulin        | $r_s$    | $2.68 \, nm$ [34] |
| Radius of insulin molecule       | $r_{mm}$ | $2.5 \, nm$ [31] |
| Radius of the transmitter        | $r_{unit}$ | $10 \, \mu m$ [45] |
molecules and which results in the BER performance improvement. Increasing the drift velocity also impacts the number of molecules received from other sources, which are denoted by $N_{Nos,r}[n]$ and treated as noise. Furthermore, BER is improved by increasing the drift velocity as shown in Fig. 5, which means that the impact of received molecules during the current time slot overcomes the noise and ISI effects.

In Fig. 6 we show the BER performance as a function of the symbol duration for pulse shape examples in non-uniform BCSK modulation. We can see that in this figure, with increasing the symbol duration value, the BER performance is improved because increasing the symbol duration implies the molecules have more time to arrive the receiver. Increasing the symbol duration can also enhance the probability of hitting molecules and also the BER performance.

In Fig. 7 we present the BER performance of pulse shape examples in non-uniform BCSK modulation as a function of energy in each time slot. We observe with increasing the energy in each time slot, BER performance improves, but for sinc function, cosine function and uniform pulse, there is no significant change in BER. This problem is because of the ISI effect. Increasing energy will increase the number of molecules, since the ISI effect has direct proportion to the
number of molecules, therefore, the mentioned functions do not have a good performance in BER. On the other hand, the advantage of the exponential function is increased by increasing the budget of energy.

The performance of the proposed algorithm to obtain the optimal value of the symbol duration is demonstrated in Fig. 8. We consider four cases for the mixture of distance between transmitter and destination nodes ($d_{sd}$) and velocity of the medium ($v$) when the pulse shape is exponential. As we discussed, the optimal symbol duration obtains the maximum number of successful received bits. By considering the velocity drift as 0.52 mm/s, $d_{sd} = 4 \mu m$, and optimal symbol duration as 3.47 ms, the number of successful received bits reach to 283. We observe that by increasing the velocity of the medium in fixed distance between transmitter and destination node, the optimal symbol duration is decreased. This is due to the Brownian motions behavior. Increasing drift velocity causes faster propagation of the molecules into the medium. In addition, the number of molecules that are received to the receiver node are increased. Therefore, we can find the smaller value of the symbol duration to reach the minimum BER.

Note that we use MAP rule detection in Fig. 4, Fig. 5, Fig. 6 and Fig. 7 at receiver node. We can observe from Fig. 4, Fig. 5, Fig. 6 and Fig. 7 that the pulse shaping in BCSK modulation
Fig. 6. BER of the MCvD system with the relay node for exponentially, sinc, cosine and uniform pulse shape in non-uniform BCSK modulation, as a function of the symbol duration ($\sum_{i=0}^{L-1} g(i) = 3000$, $d_{sd} = 2 \mu m$ and $v = 0.5$ mm/s).

can make a significant difference in BER performance considering parameters of MCvD system and budget of energy.

VI. CONCLUSION

The nutrient limiting is the main reason to utilize the BCSK modulation in MC systems. In this paper, we proposed a new non-uniform BCSK modulation and analyzed the BER of a relay-assisted MCvD system with drift with respect to the energy in nanotransmitter. We also derived closed-form expression for the means and the variances of the number received molecules to calculate BER in the direct and the relay-assisted transmission. In addition, we studied the effect of the system parameters such as the distance between nanotransmitter and nanoreceiver, drift velocity of medium and symbol duration on the BER performance. We also employed an iterative algorithm to find the optimal value of symbol duration in terms of maximizing the number of successfully received bits. Finally, we compared the difference between uniform and non-uniform BCSK modulation considering the energy and BER performance. As a future work, one can optimize the pulse shape in the introduced modulation model to minimize the BER in a channel with degradation of molecules. The other future works can focus on the outage...
Fig. 7. BER of the MCvD system with the relay node for exponentially, sinc, cosine and uniform pulse shape in non-uniform BCSK modulation, as a function of energy in time slot ($d_{sd} = 2 \mu m$, $v = 0.5$ mm/s and $t_s = 5.8$ ms).

performance, subject to the evaluation of the Signal-to-Noise-Ratio (SINR) or other goodputs, such as the capacity of the channel. One can also optimize the other parameters of the system, such as the number of allocated molecules to the transmitter node. Furthermore, interested readers can investigate applications of MC, e.g., the mobile MC and drug delivery system on the basis of the introduced non-uniform BCSK modulation.

APPENDIX A
THE CALCULATIONS OF MEAN AND VARIANCE FOR ISI

In this appendix, the details for calculation of mean and variance values of $N_{P_s,r}^T$ in (7), are provided.

We approximate the binomial distribution of each sub slot $i$ in every time slot $j$ to normal distribution in (7), in terms of $g(i)$ is large enough and $g(i) \times q_{j,i}$ is not zero. The mean of ISI for the $j^{th}$ time slice is calculated as follows:

$$E(N_{P_s,r}^T[n,j]) = \pi_0 E(N_{P_s,r}^T[n,j] \mid x_s[n-j] = 0) + \pi_1 E(N_{P_s,r}^T[n,j] \mid x_s[n-j] = 1)$$

$$= \pi_1 \sum_{i=0}^{l-1} g(i)q_{j,i}. \quad (37)$$
The variance value of $N_{P_{s,r}}^T$ for $j$th time slice is calculated as

$$\text{var}(N_{P_{s,r}}^T[n,j]) = E((N_{P_{s,r}}^T[n,j])^2) - E^2(N_{P_{s,r}}^T[n,j]),$$

(38)

where $\text{var}(X)$ denotes the variance of random variable $X$ and $E((N_{P_{s,r}}^T[n,j])^2)$ can be calculated as follows:

$$E((N_{P_{s,r}}^T[n,j])^2) = \pi_0 E((N_{P_{s,r}}^T[n,j])^2 | x_s[n - j] = 0) + \pi_1 E((N_{P_{s,r}}^T[n,j])^2 | x_s[n - j] = 1)$$

$$= \pi_1 \left( \sum_{i=0}^{L-1} g(i)q_{j,i}(1 - q_{j,i}) + \left( \sum_{i=0}^{L-1} g(i)q_{j,i} \right)^2 \right).$$

(39)

Therefore, $\text{var}(N_{P_{s,r}}^T[n,j])$ becomes

$$\text{var}(N_{P_{s,r}}^T[n,j]) = \pi_1 \left( \sum_{i=0}^{L-1} g(i)q_{j,i}(1 - q_{j,i}) + \left( \sum_{i=0}^{L-1} g(i)q_{j,i} \right)^2 \right) - \left( \pi_1 \sum_{i=0}^{L-1} g(i)q_{j,i} \right)^2$$

$$= \pi_1 \left( \sum_{i=0}^{L-1} g(i)q_{j,i}(1 - q_{j,i}) \right) + \pi_0 \pi_1 \left( \sum_{i=0}^{L-1} g(i)q_{j,i} \right)^2.$$

(40)
The mean and variance values for ISI are, respectively, derived as

\[
E(\mathcal{N}_{P_{s,r}}^T[n]) = \sum_{j=1}^{J} E(\mathcal{N}_{P_{s,r}}^T[n, j]), \quad (41)
\]

\[
\text{var}(\mathcal{N}_{P_{s,r}}^T[n]) = \sum_{j=1}^{J} \text{var}(\mathcal{N}_{P_{s,r}}^T[n, j]). \quad (42)
\]

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