Modulation Techniques for Molecular Communication via Diffusion

H. Birkan Yilmaz, Na-Rae Kim and Chan-Byoung Chae

Abstract Molecular Communication via Diffusion (MCvD) is an effective and energy efficient method for transmitting information in nanonetworks. In this chapter, we focus on the modulation techniques in a diffusion-based communication system. We mainly assume the first hitting process for the reception of the signal and it affects the design of the modulation techniques. As observed in the nature, whenever an information carrying molecule hits to the receiver it is removed from the environment. These information molecules are called messenger molecules and can be of many types of chemical compounds such as DNA fragments, proteins, peptides or specifically formed molecules. Information is modulated on one or more physical properties of these molecules or the release timing. In this chapter, we mention four novel modulation techniques, i.e., concentration, frequency, molecular-type, and timing-based modulations for MCvD in a single transmitter and single receiver environment. We also exemplify a systematic realization for molecular-ratio-based modulation using isomers as messenger molecules for MCvD. Next, we compare the pros and cons of the modulation techniques for an absorbing receiver that are studied in the literature. Knowing the workings and the properties of these modulation techniques enables us to use them in combination whenever it is possible.

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J. Suzuki et al. (eds.), *Modeling, Methodologies and Tools for Molecular and Nano-scale Communications*, Modeling and Optimization in Science and Technologies 9, DOI 10.1007/978-3-319-50688-3_5

1 Introduction

Operating in the nano-scale is expected to require high cooperation among multiple devices to make an impact on the macro scale. Nanonetworking is to interconnect several nanoscale machines that has molecular communication as one of the most promising mechanisms [1, 9, 20, 21]. Molecular Communication via Diffusion (MCvD) which is a new paradigm of nano communication networks enables transmitting desired information using biological molecules. On its most basic definition, MCvD deals with communication systems between transmitter-receiver couples; exchanging information via a shared medium using molecules that represent the data. MCvD absent of the need for infrastructural deployment, can be utilized for both intra- and inter-cellular communication. The molecules, called messenger/information molecules, function both as a information and a carrier. These molecules can be of many types of chemical compounds such as DNA fragments, proteins, peptides or specifically formed molecules. Generally, the information is modulated on any physical property or the release timing of the messenger molecules with certain method, which physically travel to a receiver side. Therefore, the modulation techniques are required to properly modulate the desired information.

In this chapter, we mention four novel modulation techniques, i.e., concentration, frequency, molecular-type, and timing-based modulations for MCvD in a single transmitter and single receiver environment [14, 16, 24]. We also investigate molecular-ratio-based modulation using isomers as messenger molecules for MCvD [11]. There is a literature proposing modulation techniques using concentration and types of messenger molecules only conceptually using hydrocarbon molecules. On the other hand, isomers are molecules composed of the same number and types of atoms, and have advantages in terms of complexity and systematic analysis that can be applied into practical systems.

Next, we compare the pros and cons of the aforementioned modulation techniques. For example, the molecular-type-based modulation would have higher transmitter complexity since the transmitter synthesizes multiple types of molecules while only one for the concentration-based method. Nevertheless, it can be more robust with distortion materials in propagating medium than other techniques. There exists modulation techniques those are mutually complementary to each other, the combination of several methods can be chosen depending on system conditions. It is also possible to analyze the achievable data rate performances in specific scenarios.

To make nano communication feasible in practice, proper modulation techniques are one of the important issues to be investigated further. Thus, this chapter will cover the previous work regarding a variety of modulation techniques, and even analyze the system with more complicated and practical situations.

2 Molecular Communication via Diffusion

The messenger molecules are the information particles in molecular scale. In this scale, the movement of particles inside a fluid is modeled by Brownian motion or diffusion process. The motion is governed by the combined forces applied to the messenger molecule by the molecules of the liquid due to thermal energy. In nature, whenever a messenger molecule's body coincides with the body of the receiver, the molecule is received and removed from the environment. Therefore, after that point that molecule cannot move further and constitutes the signal just once. This process is named first passage or hitting process and we are concerned with the probability that a diffusing particle first reaches a specified site or sites at a specified time [23]. If we are dealing with first hitting process, considering the concentration formulation, $C(r, t)$, is not the correct way of finding the hitting time histogram. Using $C(r, t)$ as the channel transfer function, implicitly assumes that the receiver node does not affect the MCvD system, which means molecules are freely moving in the environment and inside the receiver, also passing through the receiver boundary without any resistance. Hence, using first hitting process is more realistic compared to just using propagation process. Some works in the literature consider first hitting and derive channel functions which are inverse Gaussian [6, 24, 25].

The MCvD system for distance d is depicted in Fig. 1, where the radii of transmitter and receiver nodes are denoted by r_{TN} and r_{RN}, respectively. In this communication system, information is sent using a sequence of symbols which are spread over sequential time slots with one symbol in each slot. The symbol sent by the transmitter is called the "intended symbol", and the demodulated symbol at the receiver is called the "received symbol". An MCvD system has five main processes: encoding, emission, propagation, absorption, and decoding [13]. We mainly focus on emission, propagation, and absorption processes in this chapter.

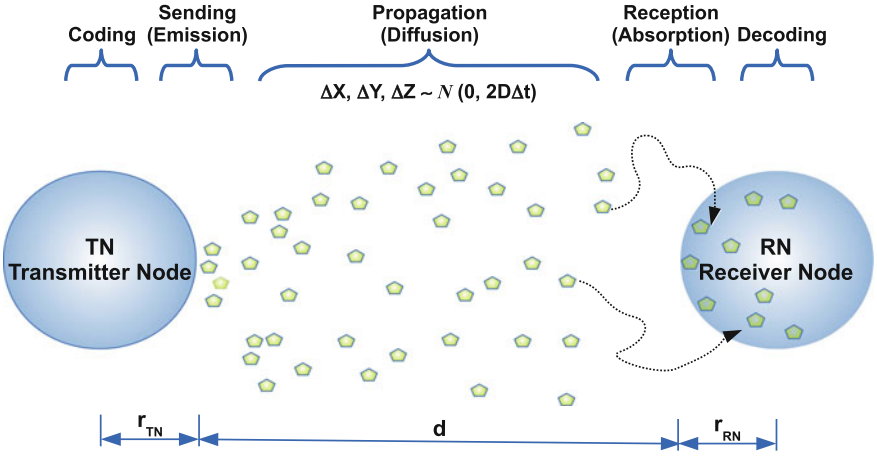

Fig. 1 MCvD system model and processes in a 3-D environment

2.1 Propagation Process

In an n-dimensional space, the total displacement, $\mathbf{r}$ in one time step can be found as

$$\mathbf{r} = (\Delta x_1, \ldots, \Delta x_n) \tag{1}$$

where Δx_i is the displacement at the ith dimension. Movement at each dimension in one time step is modeled independently and follows a Gaussian distribution

$$\Delta x_i \sim \mathcal{N}(0, 2D\Delta t) \quad \forall i \in \{1, \ldots, n\} \tag{2}$$

where Δt and D are the step time and the diffusion coefficient, respectively. Molecules propagate in the environment according to these dynamics. We model the transmitter, the receiver and the messenger molecules as spherical bodies. Our model ignores collisions between the messenger molecules, as done in the literature for simplicity [19]. If the transmitter node is not a point source, then it is a reflecting boundary for messenger molecules, that makes the closed form solution more harder since it changes the symmetry for the solution. Therefore, we simulate the first hitting process by moving messenger molecules according to (2) and reflecting or removing the particles that hit to transmitter or receiver, respectively. While wandering in the environment, a single molecule has a certain hitting probability at the receiver.

2.2 Emission and Reception Processes

The task of the particle emission process is to modulate the particle concentration $N_{Tx}(t)$ at the transmitter according to the input symbol $S_{Tx}(t)$, modulation type, and the waveform of the signal. In one symbol duration, t_s, the number of released molecules may be spike like at the start of the slot or may be spread over the slot. This behavior depends on the capabilities of the transmitter node, input signal, and the sampling period (t_s^{smp}) of the transmitter node.

Releasing all the molecules for a symbol may be better compared to spreading it over the symbol slot in terms of symbol demodulation and this claim is studied in [8]. The capabilities of the transmitter node, however, may necessitate the spreading it over the symbol duration. Peak-to-Average-Molecule-Ratio (PAMR) at the transmitter node is defined in [26] as

$$\mathrm{PAMR}_{Tx} = \frac{\max N_{Tx}(t)}{\operatorname{avg} N_{Tx}(t)}\,. \tag{3}$$

PAMR is a similar concept to Peak-to-Average-Power-Ratio (PAPR) in an OFDM system. If the transmitter node has less space for storing the synthesized messenger molecules, it would necessitate sending the synthesized messenger molecules before the storage areas are full. Hence, depending on the capabilities of the transmitter node, sending one peak at the start of the symbol duration may be possible or not. Having high PAMR value may violate the transmitter node constraints due to capabilities. Similarly, PAMR at the receiver side can be defined and determines the capabilities/constraints of the RN.

On the other hand, whenever a messenger molecule hits the receiver it is directly absorbed and removed from the environment. Demodulation takes place during the reception process. Demodulating the information is achieved by detecting and classifying one or more physical properties of the arriving messenger molecules on which the information is modulated.

Since the molecules propagating through the environment exhibit Brownian motion, a single molecule has a certain hitting probability at the receiver. This probability, $P_{hit}(d, t_s)$, depends on the distance between the transmitter and the receiver, and the symbol duration. Modeling the arrival process as a binomial distribution gives us the model for the received number of molecules, N_{Rx}.

$$N_{Rx} \sim B(N_{Tx}, P_{hit}(d, t_s)) \tag{4}$$

In (4), $B(n, p)$ stands for binomial distribution with parameters n and p. Instead of binomial modeling Gaussian approximation can also be used when N_{Tx} is large enough. Poisson modeling, however, can only be considered when $P_{hit}(d, t_s)$ is very small. Poisson modeling is better than Gaussian modeling when the number of arriving molecules is small enough that Gaussian model's left tail causes error.

3 Modulation Techniques for MCvD

Symbols can be modulated over various "messenger molecule emission properties" at the sender, e.g., concentration, frequency, phase, molecule type, to form a signal. Some of the modulation techniques utilizes carrier waves, however, some do not. Using carrier waves makes the handling of Inter Symbol Interference (ISI) more complex. In this section, we classify four main modulation techniques and elaborate

the details of them. Most of the modulation techniques mentioned in this section are studied thoroughly in [12, 26] and some of the results are given to supplement the theory.

3.1 Amplitude-Based Modulations

The concentration of the sent/received messenger molecules is used as the amplitude of the signal in Concentration Shift Keying (CSK), hence it represents data as variations in the amplitude of a carrier wave or pulse. CSK is analogous to Amplitude Shift Keying (ASK) in classical communication. Representing b bits requires 2^b different amplitudes. If the carrier wave is a single point pulse and we use presence and absence of the carrier wave to indicate binary "1" and "0", respectively, it is called Molecular Concentration On-off Keying (MC-OOK) which is a special type of Binary CSK (BCSK). BCSK symbols may also be modulated on a square wave. If there are four amplitude levels for two bit symbols then it is called Quadrature CSK (QCSK). These modulations are depicted in Fig. 2. In all cases, one of the symbols is represented by no emission for reducing the energy consumption and the mean energy consumption is same for all modulations in Fig. 2. Therefore, in MC-OOK that uses a pulse, the transmitter node emits much more molecules just at the start of the symbol slot. MC-OOK requirement in terms of PAMR_{Tx} is higher compared to other modulations using square or cosine wave as a carrier. MC-OOK is imple-

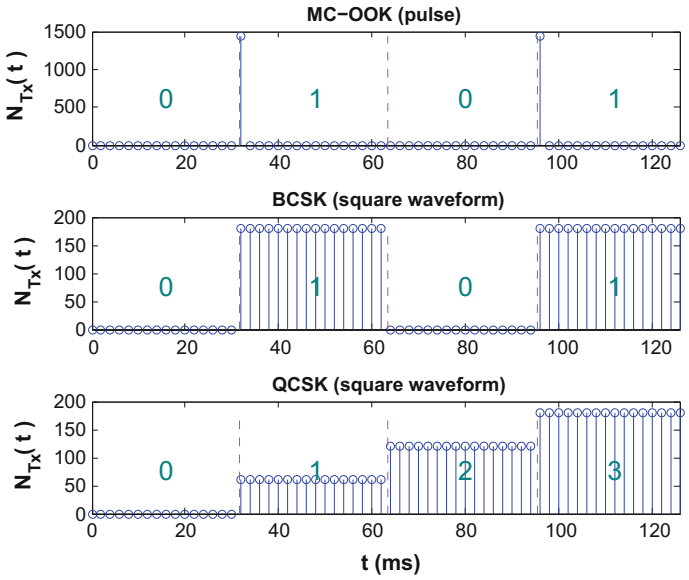

Fig. 2 $N_{Tx}(t)$ for amplitude-based modulations

mented for the tabletop testbed that is introduced in [5]. Because communication is performed through chemical signals, and a limited amount of signaling chemical can be stored in a container at the receiver, the modulation and demodulation scheme should minimize the amount of chemical used. Therefore, authors used zero emission for symbol "0" to reduce the energy cost as mentioned before.

If the data is modulated on the amplitude variations, a thresholding is employed for detecting symbols. For example, demodulating MC-OOK or BCSK symbols requires one threshold. The receiver decodes the intended symbol as "1" if the number of messenger molecules arriving at the receiver during a time slot exceeds a threshold τ, "0" otherwise. The MCvD system using CSK technique can be affected adversely from ISI which can be caused by the surplus molecules from previous symbols. Due to diffusion dynamics, some messenger molecules may arrive after their intended time slot. These molecules may cause the receiver to decode the next intended symbol incorrectly. It is shown in [14] that in the MCvD system, only the previous symbol has a significant ISI effect over the current symbol if the symbol duration is selected appropriately. The severity of this ISI related error depends on the symbol duration, distance, and diffusion channel parameters [15].

In [22], authors proposed Zebra-CSK to overcome ISI problem via utilizing inhibitor molecules. The proposed Zebra-CSK selectively suppresses ISI causing molecules. Numerical results show that Zebra-CSK not only enhances capacity of the molecular channel but also reduces symbol error probability observed at the receiver nanomachine. In [10], authors proposed four methods for a receiver in the molecular communication to recover the transmitted information distorted by both ISI and noise. They introduce sequence detection methods based on maximum a posteriori (MAP) and maximum likelihood (ML) criterions, a linear equalizer based on minimum mean-square error (MMSE) criterion, and a decision-feedback equalizer (DFE) which is a nonlinear equalizer. The results show that using these methods significantly increases the channel capacity in the molecular communication.

3.2 Molecule Type-Based Modulations

Molecule type is used to represent information in Molecular Shift Keying (MoSK). Representing b bits requires 2^b different molecules with similar properties. The transmitter releases one of these molecules based on the current intended symbol. The receiver decodes the intended symbol based on the type and the concentration of the molecule received during a time slot. If the concentration of only one molecule type exceeds the threshold τ at the receiver, the symbol is decoded based on the bit sequence corresponding to this molecule type. Another decoding strategy may decide the intended symbol depending on the majority logic. For the first strategy, an error is assumed if the concentration of any molecule types does not exceed the threshold or the concentration of more than one molecule type exceeds the threshold.

Inspired by [7], hydrofluorocarbons can be used as the messenger molecule structure for systematically designing 2^b different molecules for b bit logical information

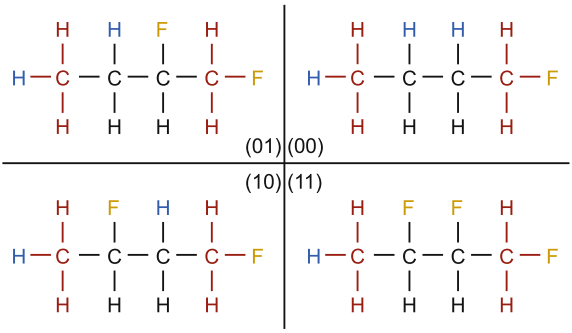

Fig. 3 Constellation of QMoSK using hydrofluorocarbon based messenger molecules

representation. Based on the message to be transmitted, a special messenger molecule is synthesized using three parts: header, trailer, and the chemical bit element. A single header and a single trailer are present in each molecule representing the start and the end of the message. For each bit of information, a chemical bit element is synthesized. A chemical bit element has two forms: one for representing "0" and another one for "1". All of these parts are linked to each other using chemical bonds to form a single messenger molecule. In Fig. 3, we depict a 2-bit constellation realization of this modulation technique called Quadruple MoSK (QMoSK). These molecules are flammable, hence the usage areas may be limited. This constellation is just a hypothetical one and can be done via more appropriate messenger molecules such as isomers [11].

Similar to the CSK technique, the surplus molecules from the previous symbols also cause ISI when MoSK technique is used. However, MoSK is less susceptible to ISI effects than the CSK technique when the bits per symbol is greater than 1. In this case, a single threshold is used for MoSK whereas $2^b - 1$ thresholds are required for CSK. This advantage of the MoSK technique, however, comes at the cost of the requirement for complex molecular mechanisms at both the transmitter and the receiver for messenger molecule synthesis and decoding purposes, respectively. Also, a corruption in such a messenger molecule may cause some or all of the information in the symbol to get lost. This information corruption must be taken into account, since a corruption may still represent some information albeit not the one sent by the transmitter.

In [3], authors combined MoSK and CSK to overcome the ISI problem of CSK. The proposed scheme utilizes two types of molecules and uses them in an alternating fashion. Therefore, ISI on the CSK modulated symbols is reduced significantly. This is due to the fact that the decoding of the current symbol in the proposed scheme does not encounter propagation of error, as the decoding of the current symbol does not depend on the previously transmitted and decoded symbols.

In order to evaluate the performance of different modulation techniques, we consider a channel model as depicted in Fig. 4. Channel model for binary and quadruple modulations are depicted with correct and incorrect demodulations. Modeling

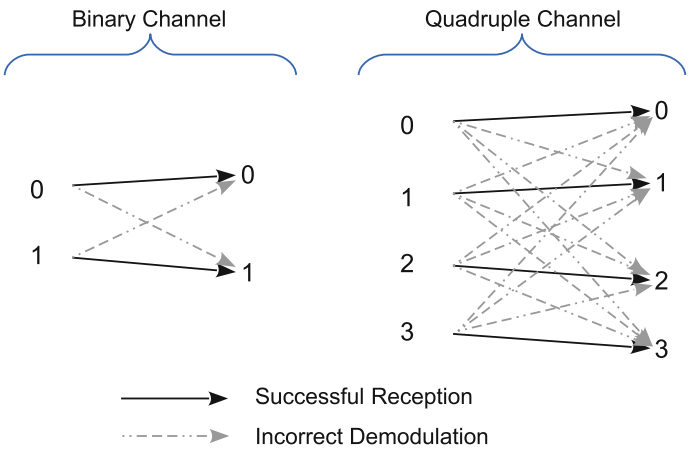

Fig. 4 Channel models

arrival process as in (4) enables us to derive the successful reception and incorrect demodulation probabilities.

Using these probabilities, we can find the mutual information, $I(X;Y)$, given the values for thresholds, distance, and the probability of hit during the current and next symbol durations [2]. By selecting ideal threshold values, the channel capacity (C) can be calculated using the maximum of mutual information as in (5), where b stands for the number of bits per symbol.

$$\begin{aligned} C &= \max_{\tau} I(X,Y) \\ &= \max_{\tau} \sum_{Y=0}^{2^b-1} \sum_{X=0}^{2^b-1} \mathbf{P}_{X,Y}(x,y) \log_2 \frac{\mathbf{P}_{X,Y}(x,y)}{\mathbf{P}_X(x)\mathbf{P}_Y(y)} \end{aligned} \tag{5}$$

Using $P_{hit}(d,t_s)$, arrival model, and channel model, the channel capacities of BCSK, BMoSK, QCSK, and QMoSK implementations with pulse carriers under various Signal-to-Noise Ratio (SNR) values are evaluated. SNR is defined as the square of the reciprocal of the coefficient of variation of the received signal. According to the results given in Fig. 5, all modulation techniques attain their theoretical channel capacity limits when the SNR level is high. As SNR decreases, in case of the binary implementations, BCSK with pulse carrier (a.k.a. MC-OOK) offers more robustness compared to BMoSK. Same amount of noise is applied to both molecule types in BMoSK, since the noise in the channel is AWGN. Thus, BMoSK is more affected by the noise than BCSK.

In case of quadruple implementations (QCSK and QMoSK), this trend changes and QMoSK exhibits higher noise tolerance than QCSK. This behavior is due to the number of threshold values used in these quadruple implementations. Since QMoSK uses a single threshold value, the channel capacity can be kept high by choosing a

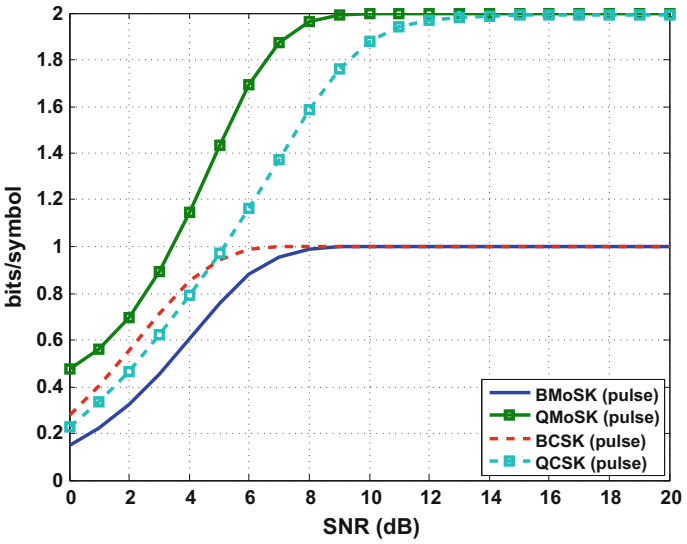

Fig. 5 Channel capacity of different modulation techniques ($N_{Tx} = 1500$ molecules, $D = 79.4\,\mu m^2/s$, $d = 16\,\mu m$, $t_s = 5.9\,s$, $r_{TN} = r_{RN} = 10\,\mu m$)

suitable threshold value even when the noise level is high. On the other hand, finding suitable threshold levels to keep the same channel capacity becomes harder as the noise level increases in QCSK.

3.3 Frequency-Based Modulations

Representing the data through discrete frequency changes of a carrier wave of number of messenger molecules is called Molecular Frequency Shift Keying (MFSK). In this modulation scheme, number of molecules sent is not constant during the symbol duration and changes according to cosine wave. Since we cannot send negative number of molecules, we have to shift the amplitude in y-axis up.

If the carrier wave is a cosine wave and there are two frequencies, then it is called Binary MFSK (BMFSK). Similarly, if there are four frequencies for two bit symbols, then it is called Quadrature MFSK (QMFSK). These modulations are illustrated in Fig. 6.

General formula for $N_{Tx}^{s_i}(t)$ with MFSK modulations on cosine waveform is as follows

$$N_{Tx}^{s_i}(t) = \mu_a + \mu_a * \cos(2\pi f_i t) \quad i = 0, \ldots, m \tag{6}$$

where s_i,f_i and μ_a are symbol i, frequency for s_i, and mean amplitude, respectively. If the data is modulated on the frequency variations, the received symbol at the receiver

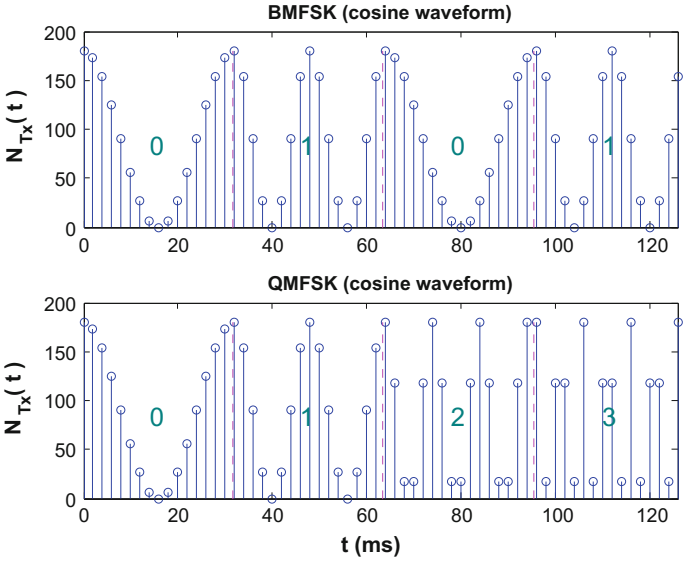

Fig. 6 $N_{Tx}(t)$ for frequency-based modulations

side can be detected via correlating the received signal with the symbol waveforms after synchronizing the signals. You can also look at the received signal in the frequency domain and correlate to the symbol frequency signatures. The MCvD system using MFSK-based modulation is affected less from the ISI, however, CSK-based symbols are easier to detect.

For analyzing symbol detection and false alarm probabilities we compare Receiver Operating Characteristics (ROC) curves. In Fig. 7, ROC curves for symbol "1" of binary modulations are depicted for 3 and 9 dB SNR values. $P_d(\text{Sym} = 1)$ represents the probability of demodulating the received symbol as "1" when the transmitted symbol is actually the symbol "1". Similarly, $P_f(\text{Sym} = 1)$ corresponds to the probability of demodulating the received symbol as "1" when the transmitted symbol is actually the symbol "0", hence it can be seen as false alarm of saying demodulated result is the symbol "1". In Fig. 7, MC-OOK stands for BCSK modulated on pulse at the start of a symbol slot and BCSK stands for BCSK modulated on square wave. Energies spent at a time slot are equal, hence PAMR_{Tx} value of MC-OOK is higher than other modulation techniques.

In Fig. 7, for a given false alarm constraint, achievable detection probability can be compared. For $P_f(\text{Sym} = 1) = 0.05$, we have nearly 0.3, 0.98, and 1 as a detection probability for symbol "1" for 3 dB case for BMFSK, BCSK, and MC-OOK, respectively. Increasing SNR results in better detection probability. Hence, with the same false alarm constraint we have 0.72, 1, and 1 as a detection probability for symbol "1" for 9 dB case for the same order of modulations. MC-OOK has the best performance

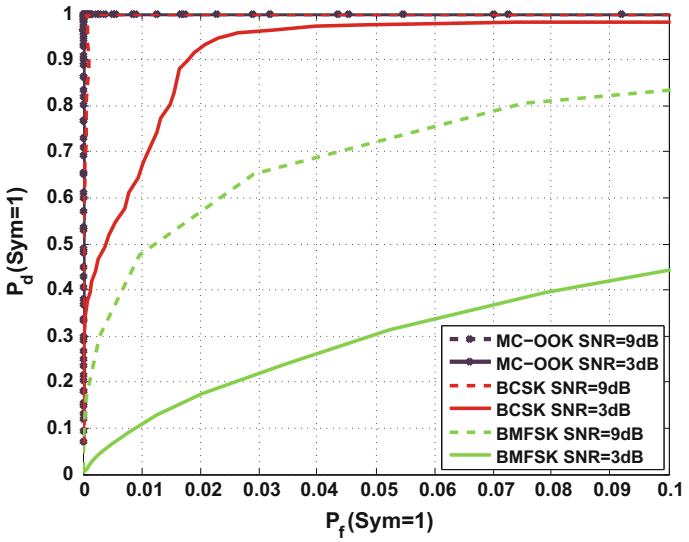

Fig. 7 ROC curves for symbol "1" of binary modulations ($\mu_a = 90$ molecules, $D = 79.4\,\mu\text{m}^2/\text{s}$, $d = 1\,\mu\text{m}$, $t_s = 0.032\,\text{s}$, $t_s^{smp} = 0.002\,\text{s}$, $r_{\text{TN}} = r_{\text{RN}} = 10\,\mu\text{m}$)

in terms of $P_d(\text{Sym} = 1)$ with given $P_f(\text{Sym} = 1)$ constraint. BCSK has comparable performance for 9 dB SNR while 3 dB case can also be satisfactory for some cases.

In Fig. 8, Symbol Error Rate (SER) plots of amplitude and frequency based modulations without ISI filtering are depicted. Without ISI filtering, even BCSK with a square carrier has an error floor. In high SNR regime, BMFSK performs better than BCSK. MC-OOK performs better than all of the modulations compared.

In Fig. 9, SER plots of amplitude and frequency based modulations with ISI filtering are depicted. ISI filter increases the performance of amplitude-based modulations significantly. BCSK with a square carrier wave has an error floor due to ISI and it is eliminated effectively when an ISI filter is applied. MC-OOK has the best performance compared to the BCSK modulated on a square wave and BMFSK modulated on a cosine wave. MC-OOK, however, has the highest PAMR_{Tx} value (32 times higher compared to other modulations for given parameters) while the BCSK, when ISI filter is applied, has an acceptable SER and PAMR_{Tx} value.

In Table 1, we summarize the performances and the capabilities of the modulation schemes. In terms of SER, MC-OOK performs better than the other schemes, however, in terms of PAMR_{Tx} it is the far worse than the others. These results and the summary table can help to the system designers in nanonetworking domain for research and implementation issues.

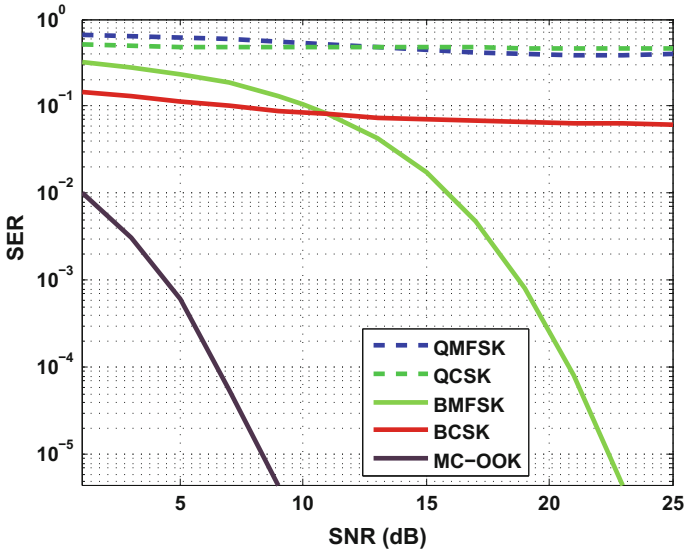

Fig. 8 SER plots of modulation techniques without ISI filtering ($\mu_a = 90$ molecules, $D = 79.4\,\mu\text{m}^2/\text{s}$, $d = 1\,\mu\text{m}$, $t_s = 0.032\,\text{s}$, $t_s^{smp} = 0.002\,\text{s}$, $r_{\text{TN}} = r_{\text{RN}} = 10\,\mu\text{m}$)

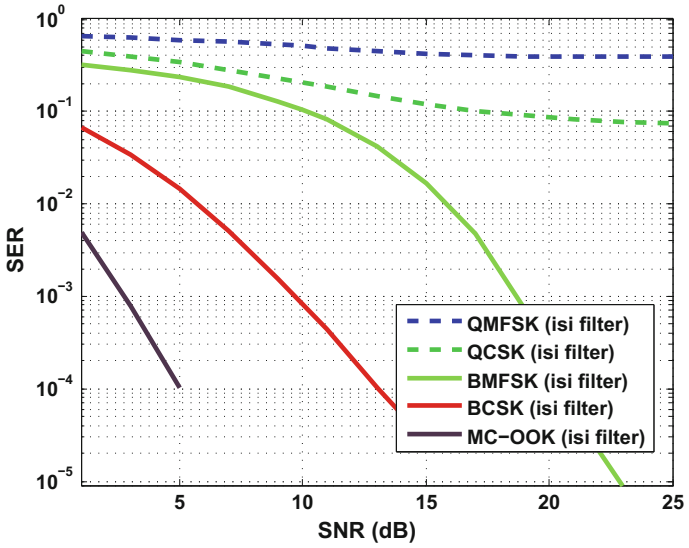

Fig. 9 SER plots of modulation techniques with ISI filtering ($\mu_a = 90$ molecules, $D = 79.4\,\mu\text{m}^2/\text{s}$, $d = 1\,\mu\text{m}$, $t_s = 0.032\,\text{s}$, $t_s^{smp} = 0.002\,\text{s}$, $r_{\text{TN}} = r_{\text{RN}} = 10\,\mu\text{m}$)

Table 1 Modulation comparison matrix

Metric	MC-OOK	BCSK	BMFSK	QCSK	QMFSK	MoSK
SER	Low	Moderate	Moderate	High	High	Moderate
ISI resilience	High	Moderate	High	Low	Moderate	High
PAMR_{Tx}	High	Low	Low	Low	Low	Low
Node complexity	Low	Moderate	High	Moderate	High	Moderate

3.4 Timing-Based Modulation

The information can also be modulated on the timing of the molecule releases. In [24], this kind of modulation is considered with infinite length receiver in a 2-D environment, which reduces the problem to 1-D projection. The transmitter is assumed to be a point source, which releases identical molecules that only react with the absorbing boundary.

The transmitter modulates the information on the time of release. The transmitter does not affect the propagation of the molecules once they are released. Since the propagation is 1-D projection, it has a closed form solution for first hitting time distribution that exhibits an inverse Gaussian distribution [4, 23]

$$f_N(n) = \begin{cases} \sqrt{\frac{\lambda}{2\pi n^3}} \;\; e^{-\frac{\lambda(n-\mu)^2}{2\mu^2 n}}, & n > 0 \\ 0, & n \leq 0 \end{cases} \tag{7}$$

Under this assumption, the symbol $X = t$ represents a release of a single molecule at time t and the corresponding arrival time is

$$Y = t + N \tag{8}$$

where N is the first arrival of the 1-D Wiener process. The probability density of observing channel output $Y = y$ given channel input $X = t$ is given by

$$f_{Y|X}(y|X = t) = \begin{cases} \sqrt{\frac{\lambda}{2\pi(y-t)^3}} \;\; e^{-\frac{\lambda(y-t-\mu)^2}{2\mu^2(y-t)}}, & y > t \\ 0, & y \leq t \end{cases} \tag{9}$$

As an example of an MCvD system using timing modulation of m symbols, the message alphabet would be $\chi = \{t_1, t_2, \ldots, t_m\}$. The receiver computes an estimate $\hat{X}$ of the transmitted message from Y. The transmission is successful when $\hat{X} = t_i$ and the transmitted message is t_i.

Considering these distributions and maximum likelihood estimator as a receiver yields;

$$\hat{X}_{ML} = y + \frac{\mu^2}{\lambda}\left(\frac{3}{2} - \sqrt{\frac{9}{4} + \frac{\lambda^2}{\mu^2}}\right) \tag{10}$$

where λ and μ are the parameters of the inverse Gaussian distribution. This estimation at the receiver side is valid for infinite length symbol duration. Repeated channel use can also be considered by taking ISI into account. Amplitude-based modulations with appropriate symbol duration can easily be coupled with the timing-based modulations.

3.5 Realization with Isomers

In Sect. 3.2, hydrocarbons are used as messenger molecules only to conceptually explain the MoSK technique. The molecules, however, are known to be highly flammable, which makes them less feasible in practical systems, especially for in-vivo applications. Therefore, it is another important thing to be considered in molecular communication systems to choose the proper type of messenger molecules. The authors in [11] propose three isomer-based modulation techniques to use in practical applications, i.e., isomer-based concentration shift keying (ICSK), isomer-based molecule shift keying (IMoSK), and isomer-based ratio shift keying (IRSK).

An important thing when designing messenger molecules is that they have to be non-toxic to the human body. For several reasons, isomers could be potential candidates for messenger molecules which are composed of the same number and types of atoms [17]. First of all, this method can reduce the burden to the transmitter nanomachine that synthesizes messenger molecules since isomers consist of the same type of atoms. Moreover, they have the same physical properties that makes more systematic analysis. Especially in MoSK technique, it is possible to apply the same diffusion coefficient value in spite of using different messenger molecules (or isomers) to represent different information. Here, aldohexoses (i.e., aldose forms of hexoses) are mostly deployed for numerical analysis. Note that other aldoses family (e.g., pentoses, tetroses, or trioses) can also be utilized depending on the required modulation order.

Aldohexoses are monosaccharides that have the chemical formula of $C_6H_{12}O_6$. They have four chiral (not superposable on the mirror images) carbon atoms, which give them 16 ($=2^4$) stereoisomers [18]. Figure 10 illustrates eight kinds of D-form aldohexeses, and enantiomers (mirror images as shown in Fig. 11) of each molecule compose L-form aldohexoses. Therefore, aldohexoses have 16 different structures. When each isomer is dissolved in an aqueous solution, however, each D- and L-type aldohexoses change the structure into two kinds of cyclic molecules. These are named as α- and β-forms as described in Fig. 12. Thus, by deploying hexoses group into the system, we consider 32 different isomers in total, and three modulation techniques can be used using them as described in Figs. 13, 14 and 15.

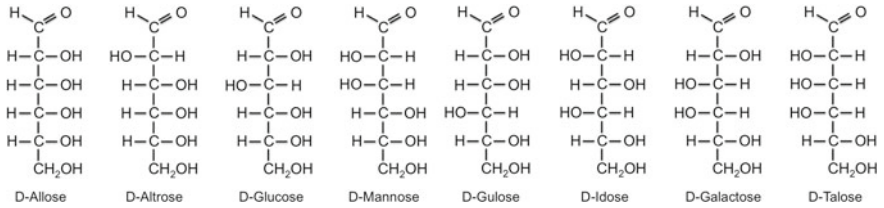

Fig. 10 D-form isomers of aldohexoses

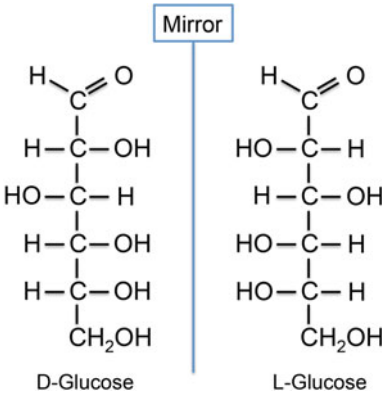

Fig. 11 L- and D-form of glucose that are enantiomers

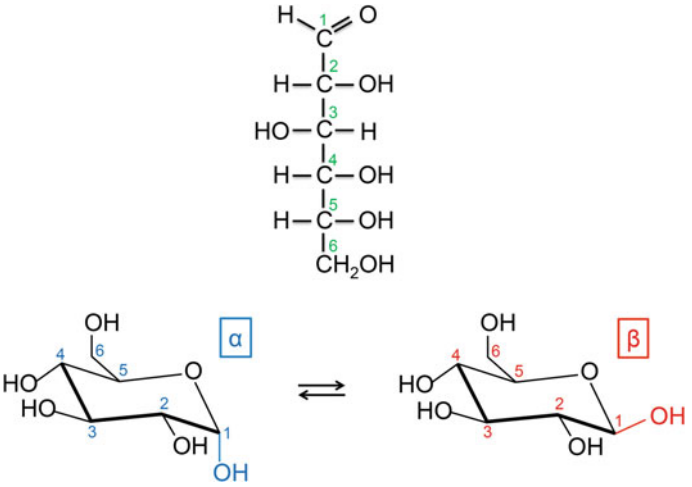

Fig. 12 D-glucose and its α- and β-form isomers in an aqueous solution

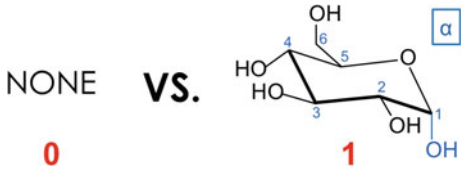

Fig. 13 Conceptual figure of ICSK

Fig. 14 Conceptual figure of IMoSK

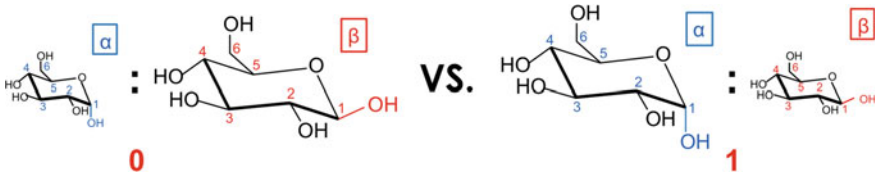

Fig. 15 Conceptual figure of IRSK

First, for realization of concentration-based modulation using isomers, or ICSK, one of the hexose family can be utilized with different concentrations, and basically, the concept is the same as CSK technique. Next, for IMoSK, we can choose one among the several aforementioned isomer sets (e.g., hexoses, pentoses, tetroses, or trioses); a modulation order can be determined by the sets used. For instance, hexoses have a modulation order of up to 32, and trioses of 4 (i.e., we consider 4 isomers for trioses). It has an advantage over MoSK in terms of system complexity since only one diffusion coefficient value is used. Lastly, a new type of modulation technique is proposed using isomers, i.e., ratio-based modulation or IRSK, which encodes information based on the ratios of two isomers. It is basically similar to ICSK except that IRSK uses two, or more, types of isomers. Thus, it can be more robust when the medium has some distortion molecules that have a negative effect to messenger molecules.

Each modulation has pros and cons, and one can be chosen considering system conditions. For example, achievable rates for IMoSK systems can be better for IMoSK systems unless it is binary case. This is because ICSK and IRSK systems have more thresholds, which means shorter minimum distance (i.e., concentration difference) between symbols. The IMoSK system, however, has to generate and detect multiple kinds of messenger molecules whereas ICSK and IRSK systems

need to generate only one or two. Thus, transmitter and receiver complexities are higher in IMoSK systems. Thus, the most appropriate technique can be found with different situations.

4 Research Challenges

In this section, we discuss the research issues and challenges from a communications perspective. We start by focusing on physical layer and continue with modulation and demodulation issues.

Most crucial challenge in this domain is to characterize and model the propagation of information-carrying molecules. In the scope of wireless communications, many models and characterizations are developed for electromagnetic waves. To predict and understand the channel response, it is necessary to develop the propagation and arrival modeling in nanonetworking domain. The diffusion dynamics and modeling are mature research areas, however when the receiver is an absorber, problem becomes much more complex. In general, molecular communication systems and receptors are designed to guarantee that each molecule contributes to the signal only once. Therefore, first passage processes are studied to form the basis of the channel characteristics [23].

After physical channel problems are studied and practiced, more predictable and robust modulation techniques can be proposed and implemented. Some of the modulation techniques are introduced in this chapter, however there are unrealistic assumptions including perfect modulation, demodulation, and synchronization. Nanonetworking-enabled nodes are assumed to be capable of synthesizing the required molecules and to be able to store as much as required. There may be constraints on the transmitter receiver pairs for more realistic scenarios [26]. These assumptions should be relaxed in the future in order to make these modulation schemes more feasible.

Another issue in molecular communication domain is the interference. Sources of interference may differ, however due to channel characteristics, ISI is at a crucial point. Therefore, ISI mitigation techniques compatible with nanonetworking-enabled nodes should be designed and implemented. Arrival of diffusing particles spans a huge duration, however on the other hand we are trying to shorten the symbol duration. Therefore, ISI becomes an important problem to be solved. Considering the simplicity and the expected outcomes of the nanomachines, one can deduce that these nonomachines should cooperate and communicate. Their collaborative actions are expected, therefore multi user interference should also be considered.

Other research challenges for modulation issues can be listed as; channel modeling, formulating channel capacity, hardware and device designs, bio-compatibility for in vivo applications, and analyzing the effects of receptor heterogeneity.

5 Conclusions

In this chapter, four types of modulation techniques are introduced for MCvD systems. First, molecular concentration, or amplitude, can be utilized to make CSK or MC-OOK systems using one kind of messenger molecule. When two or more types of messenger molecules are available, MoSK systems are one of possible candidates that encodes information into the type of messenger molecules. Also, frequency of concentration wave can represent information which makes MFSK systems. On the other hand, timing-based method does not utilize the chemical or physical properties of messenger molecules. It encodes information into the release timing of messenger molecules at the transmitter side, instead.

Moreover, the modulation techniques can be realized using isomers as messenger molecules. Isomers have several advantages such as transmitter/receiver complexity and analysis complexity since they have the same physical properties with different structures. Different isomer sets can be chosen depending on the required modulation order or SNR. To sum up, all the techniques explained in this chapter have both advantages and disadvantages, and a proper method has to be applied based on the system conditions and requirements.

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