Molecular Communication with DNA Cellular Storage System

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ABSTRACT

In this paper, we construct a DNA Cellular Storage System (DCSS) that allows rewritable and reliable DNA storage and retrieval. To demonstrate the applicability of our proposed DCSS, we embed it into a molecular communication system and propose a new signal modulation scheme called DNA-molecule shift keying (DNA-MoSK). In our proposed modulation scheme, DNA sequences are used to encode data in molecules, providing higher scalability than other existing modulation schemes, such as concentration shift keying (CSK), molecule shift keying (MoSK), and depleted-molecule shift keying (D-MoSK). Through numerical analyses, we show that the performance of DNA-MoSK is comparable to the performance of D-MoSK which, in turn, performs better than both MoSK and CSK, in terms of the achievable rate (AR) and the symbol error rate (SER). Overall, DNA-MoSK is capable of achieving high channel capacity values, suggesting it as a better modulation technique for high scalability.

CCS CONCEPTS

•Computing methodologies → Bio-inspired approaches; •Computer systems organization → Molecular computing; •Hardware → Biology-related information processing; •Applied computing → *Biological networks;*

KEYWORDS

DNA computing, DNA storage, molecular communication

1 INTRODUCTION

In a data-driven technological world, there is a greater need for huge data storage centers. The need for data is exceeding Moore's Law and conventional technology is failing to keep up: the total data usage of the planet will exceed 40 zettabytes by 2020 [8]. Modern hardware systems are based on magnetic and silicon storage technology, which can store data with a density of up to 24 gigabytes per cubic millimeter. Already, modern data centers can use as much electricity as a small town in the United States, and can require up to 10 acres of land. With the large-scale data storage needs of the future, the physical space and energy required for large-scale storage systems will continue to grow at an unsustainable rate.

In order to meet the needs of large-scale data storage, advances in storage technology should use less physical space and energy than the current one. Instead of developing new hardware storage systems, nature already suggests the possibility to utilize micro-scale molecules to encode information and store huge amounts of data. For example, DNA sequences can compactly and reliably store data with a density of up to 1 exabyte per cubic millimeter with a half life of over 500 years [7, 9, 17]; this is orders of magnitude above the capacities of traditional hardware. Consequently, in this paper, we propose a rewritable and reliable DNA Cellular Storage System (DCSS) that utilizes DNA sequences to store information; this system allows long lasting storage of large amounts of data and reliable data retrieval.

Recent advancements in synthetic and systems biology enable us to build computational devices using genetic circuits [4]. They have shown great promise in a variety of applications such as drug delivery [5, 14] and molecular communication [6]. Bonnet et al. in [2] propose a rewritable recombinase addressable data (RAD) system that allows to dynamically address and rewrite data in DNA; they show that creating a system that allows rapid modification of stored DNA information is possible and practical. Bornholt et al. [3] describe a method for encoding data in DNA; this allows for data redundancy, as well as parity for error detection and correction. The authors also describe an architecture for a DNA-based archival storage system, which leverages common biochemical techniques to provide random access to DNA encoded data. We note that, although these systems demonstrate how to store data on DNA sequences, they do not describe a mechanism for retrieving the stored information.

Since conventional data retrieving methods (e.g. hard disk read and write) cannot be applied to cellular storage systems, we propose a novel mechanism to retrieve data. Our proposed DCSS consists of two parts: a genetic address translation and a cellular information retrieval, as in Fig. 1. More specifically, we first translate a binary address into a genetic address in the form of a DNA sequence; this process can be realized by using unidirectional DNA transport across semipermeable membranes [13, 15]. Next, the constructed DNA sequence is sent to the cellular storage system in order to retrieve the cells that contain the same unique address for future computations.

To demonstrate the applicability of our proposed DCSS, we embed it into a molecular communication (MC) system [1, 16] with our

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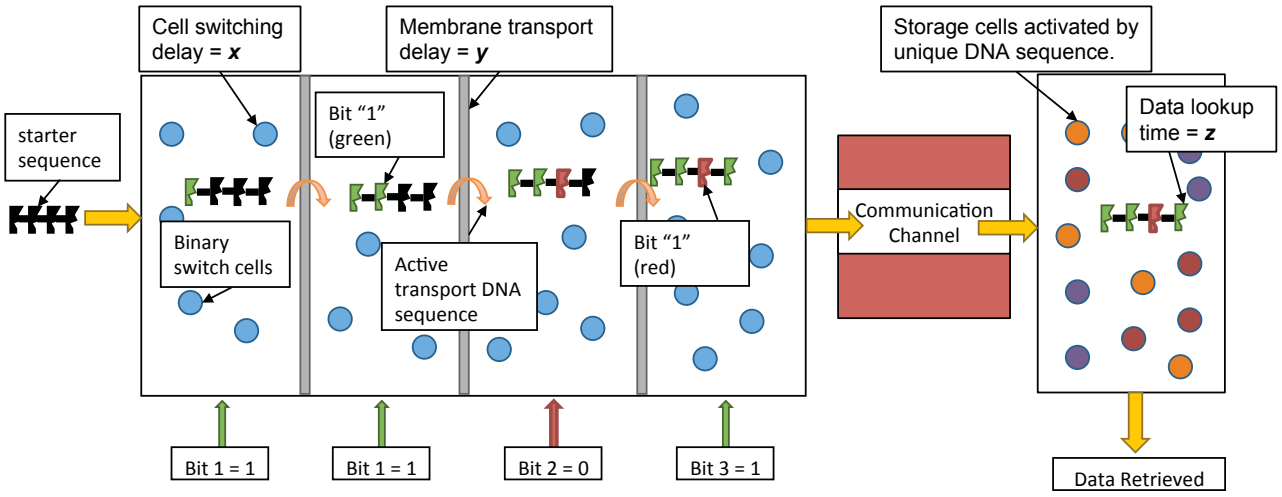

Figure 1: A visual example of the proposed system. First, either an activator protein (shown with green arrows from bottom of system) or a repressor protein (shown with red arrows) are inserted into each layer. Then, when the system reaches steady states as the binary cells (shown as blue cells) switch, a starter sequence, which is an empty DNA sequence, is inserted into the first layer, where the first segment of the sequence is modified and transported to the next layer, shown as a change in color in the sequence; this action occurs in each layer in the structure, until the DNA sequence reaches the final layer. The sequence is then sent across a communication channel to the destination. At the data retrieval module, the DNA sequence is matched with a cell containing the data to be extracted, represented by the uniquely colored cells. Each color corresponds to a different DNA sequence; similarly to a key-value data structure, each distinct DNA sequence accesses a unique storage cell.

proposed novel modulation scheme. In our proposed MC scheme, the transmitter first releases the information encoded by DNA molecules into the environment and then the DNA molecules propagate via diffusion dynamics to the receiver. After receiving the message, the receiver decodes it and retrieves the information from the cellular storage system [12].

Recently, several different signal modulation schemes that are suitable for MC have been proposed in order to achieve low error rate and high throughput of the MC system. Concentration shift keying (CSK) encodes symbols based on the concentration levels of the messenger molecules. Molecule shift keying (MoSK) uses different types of molecules for encoding; for the M-ary MoSK, M different types of molecules are used for encoding [12]. Depleted molecule shift keying (D-MoSK) is an improvement over MoSK for reducing the number of types of molecules. While a numerical analysis of D-MoSK shows that it is effective in reducing the number of types of molecules compared to MoSK [10], it still faces problems regarding scalability since the number of different types of molecules suitable for MC is limited.

To this end, we propose a novel encoding scheme where symbols are encoded into DNA sequences (DNA-MoSK) based on the DCSS; this can not only reduce the number of different molecules being used, but also provide a higher throughput for the communication process. Taken together, our contributions are three folds:

- First, we develop the DCSS which encodes digital data onto DNA sequences and allows for reliable data retrieval.
- Second, we analytically show that our proposed system can operate with low energy consumptions and moderate latency for data retrieval.
- Third, we embed our proposed DCSS into a MC system, and show that our proposed modulation scheme outperforms other existing modulation schemes in terms of achievable rates and scalability.

The remainder of this paper is organized as follows. Section 2 focuses on the DCSS mathematical modeling of and its application to MC. Section 3 shows the experimental results of our proposed system. Section 4 discusses and compares our solution with other signal modulation schemes in MC. Conclusions are drawn in section 5.

2 MATHEMATICAL MODELING OF THE DCSS AND MC

Our proposed DCSS consists of two parts: a DNA sequence translation module and a data retrieval module. More specifically, constructing a M bit binary DNA sequence requires M layers in the address translation module, where each layer modifies a different part of the DNA sequence. For example, if $M = 4$, then the system is using a 4-bit address space. Each layer contains several cells engineered to modify a particular location in the DNA sequence. Cells in each layer can be toggled by the addition of either the activator or the repressor protein which can be viewed as a "1" or "0" signal, respectively (shown as green and red arrows at the bottom of Fig. 1, respectively). Once the system reaches steady state, several start sequences (essentially empty DNA sequences) will be inserted into the first layer (i.e., the black sequence at the left of Fig. 1). The first layer then encodes the first digital bit into the beginning of the sequence, and the DNA sequence is passed onto the next layer through the unidirectional membrane. Note that since the activator

Event	Symbol	Description	Ball-park Magnitude
Transcription	α_m	Rate of mRNA synthesis	few nM/min < 60 nM/min
mRNA Degradation	β_m^{-1}	Average mRNA lifetime	few min < 20 min
Translation	α_p	Translation rate	few mRNA/min
Protein Degradation	β_p^{-1}	Average protein lifetime	doubling time (dilution)

Table 1: The parameters that govern the rate of protein synthesis and degradation

and repressor proteins are too large to pass through the unidirectional membrane, only DNA sequences can pass through.

The completed DNA sequence (mapped to a digital address) is then passed to the data retrieval module, where specialized cells read the DNA sequence, check to see if they map to the encoded address, and if they do, then they release data in the form of drugs, proteins or other DNA sequences.

2.1 Single Cell Modeling

We first mathematically model the behavior of a single layer; this represents a binary switch that encodes data onto the DNA sequence. As shown in Fig. 1, each layer can be toggled by inserting either activator or repressor proteins. For example, if we want to switch the states from 1 to 0, we need to add repressor proteins into the environment, as seen in the third layer of Fig. 1.

To model this switching, we need to characterize the protein concentrations changes over time. Based on the work in [18], the dynamics of the on-off switch can be modeled by the ordinary differential equations (ODEs) that describe protein and mRNA concentrations in an *E. coli* cell [18]. The model is defined by eq. (1) and (2) shown below:

$$\frac{dm}{dt} = \alpha_m - \beta_m m \tag{1}$$

$$\frac{dp}{dt} = \alpha_p - \beta_p p \tag{2}$$

where m represents the mRNA, and p represents the activator and repressor proteins. Approximate values for these constants are listed in Table 1. Both the activator and repressor proteins can be modeled using the same parameters, even though they have inverted responses.

In *E. coli*, the mRNA typically degrades much faster than the protein, so $\beta_m >> \beta_p$; this simplification allows a numerically solvable differential equation relating the activator and repressor proteins, shown in eq. (3):

$$\frac{dr_i}{dt} = \gamma^0 g_R(r_j) - \beta_p r_i \tag{3}$$

where r_i, r_j represent the repressor and activator proteins, respectively. In this case, $g_R(r_j)$ is modeled by the logistic function as a representation of the protein promoter activity function, $\gamma^0 = \alpha_p \alpha_m / \beta_m$. This equation governs the rate of repressor and activator protein synthesis, describing the concentration of activator and repressor proteins through time.

2.2 DNA Sequence Construction Mechanism

As shown in Fig. 1, the DNA sequence can be constructed through layers that are separated by unidirectional membranes [13]; this unidirectional membrane serves as an active transport mechanism, and facilitates the *one-way* transport of DNA sequences between layers [13, 15]. The complete sequences will then be passed to the data retrieval module, through the communication channel, where they will be decoded and used to release the corresponding data from the corresponding data storage cells.

As shown in Fig. 1, the data retrieval module stores large amounts of data cells, where each color corresponds to a different "address" if a DNA sequence maps to a given address that exists in the decoder, then cells of that color will release their stored data in the form of proteins, drugs, or longer, more intricate DNA sequences.

To quantify the performance of the DCSS, we calculate the propagation delay through the entire process. The total propagation delay, D, scales with the number of bits as in eq. (4).

$$D = x + (y * M) + l_u \tag{4}$$

where delay, x, is modeled by the on-off switching as described earlier. The membrane active transport time, y, is 200-300 base pairs per second and is modeled from the third stage of *E. Coli* RNA polymerase [19]. M is the number of layers and l_u is the look up time in the receiver.

Note that we only have to count the cell switching time once, as we insert all proteins simultaneously (in parallel) and wait for the system to reach steady state.

In Section 3, we simulate the full propagation of the DNA sequence, and measure our success based on system latency vs. total data storage.

2.3 Communication Modeling

To demonstrate the applicability of our proposed DCSS, we embed the DCSS into the MC context. More specifically, the transmitter is equipped with a DNA sequence constructor that can encode the symbols using DNA sequences. On the other hand, receiver is equipped with a data retrieval module that can retrieve the stored data after receiving the symbols; this results in a completely novel modulation technique, DNA-MoSK, which utilize DNA sequences that is more scalable in terms of number of bits than other existing modulation schemes.

For example, in the D-MoSK technique [10], each bit is encoded as the existence or omission of a particular molecule. A particular molecule is released from its bin if the bit is 1 and not released otherwise. The receiver is equipped with different types of receptors for different types of molecules, so decoding is done by detecting whether the number of molecules received is larger than some predefined threshold. However, as the number of different types of molecules suitable for MC is limited, this is not a scalable modulation technique.

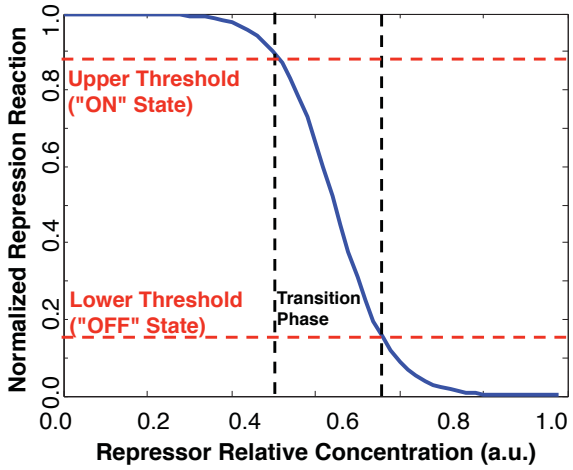

Figure 2: Repressor protein action as a function of relative protein level. At low levels of the repressor protein, the state of the layer is 1. This drops off sharply at the transition threshold and levels out to a state of 0 following a logistic function.

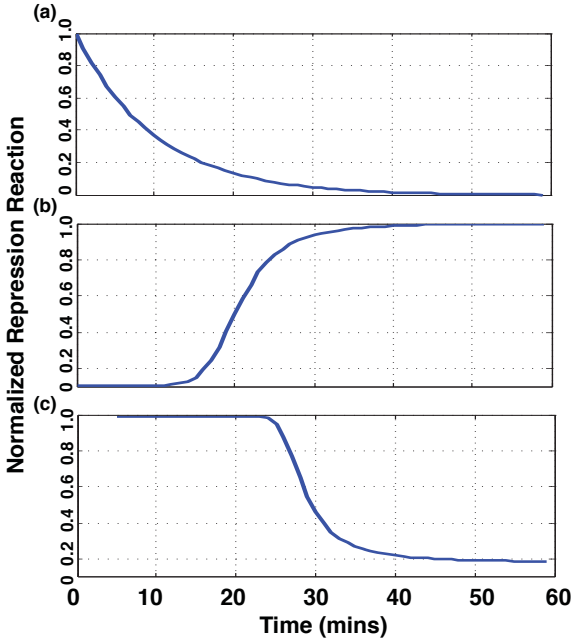

Figure 3: Propagation of a signal over time between cells with protein degradation.

In this paper, we assume that the receiver detection threshold for our DNA-MoSk modulation scheme is the same as the one being used in D-MoSk for fair comparison. Additionally, we use a binomial distribution to model the reception of DNA sequence molecules as follows: N~$Binomial(n,p)$, where N represents the number of molecules received, p is the probability a molecule reaches the destination within a fixed time (T_s), and n is the total number of molecules sent by the transmitter.

To model the symbol error rate (SER), we use the general form of the symbol error probability: $\sum_{i=0}^{M-1} q_i p_i$, where q_i is a *priori* probability of transmitting the i-th symbol. Here, the probabilities are calculated using the same scheme as that used to calculate the probabilities of reception for the D-MoSK modulation technique [10]. The probability of the SER is calculated as:

$$\text{SER} = P_e = 1 - Q(U) \tag{5}$$

where Q is the tail probability of a Gaussian distribution and U is as follows:

$$U = z - \frac{np}{\sqrt{np(1-p)}}. \tag{6}$$

where z is the threshold number of received molecules.

We consider the probability of DNA sequences being corrupted in transit to be negligible, so the SER is dictated solely by the diffusion mechanisms through the environment.

Similarly, to model the achievable rate (AR), we look at the mutual information between the transmitted symbol X and the received symbol Y:

$$AR = \max_{z} I(X;Y) \tag{7}$$

with

$$I(X;Y) = \sum_{X\in\{s_i\}} \sum_{Y\in\{s_i\}} P(X,Y) log_2 \frac{P(X,Y)}{P(X)P(Y)} \tag{8}$$

where we make the same assumptions as above: the probability of DNA sequences being corrupted in transmission is negligible, so the AR is dictated solely by the diffusion mechanisms of the environment.

2.3.1 Energy Efficiency. The energy budget of the transmitter limits the rate at which the transmitter can emit symbols. The energy requirements of the transmitter grow as the number of molecules emitted by the transmitter grows [11]; this can be modeled by:

$$n_{DNA-MoSK} = k * n_d \tag{9}$$

where $n_{DNA-MoSK}$ is the total number of molecules emitted by the transmitter, k is a proportionality constant, n_d is the number of DNA sequences released at a time.

However, we also need to take into account the energy required to encode a DNA sequence ($E_{encoding}$) given the binary data. This includes the energy required to encode a single bit in the DNA sequence, s, and the energy required for active transport across the unidirectional semi-permeable membrane, l; this is modeled by adding a linear term to the energy calculation:

$$E_{encoding} = (s * l) * b \tag{10}$$

The total energy E_{total} required for this modulation scheme, including the DNA sequence construction, is given by:

$$E_{total} = k * n_d + n_d * (s * l) * b \tag{11}$$

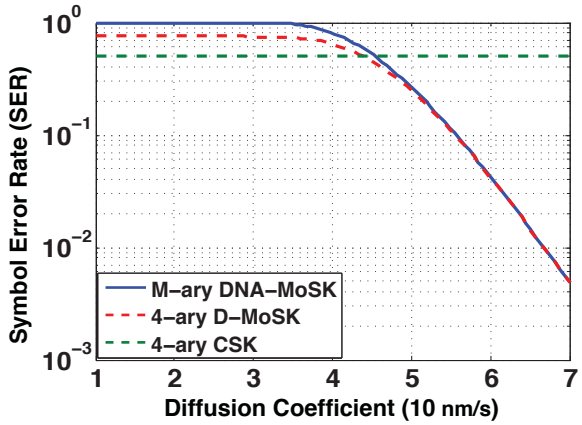

Figure 4: Symbol error rate vs. Diffusion coefficient for three different modulation schemes.

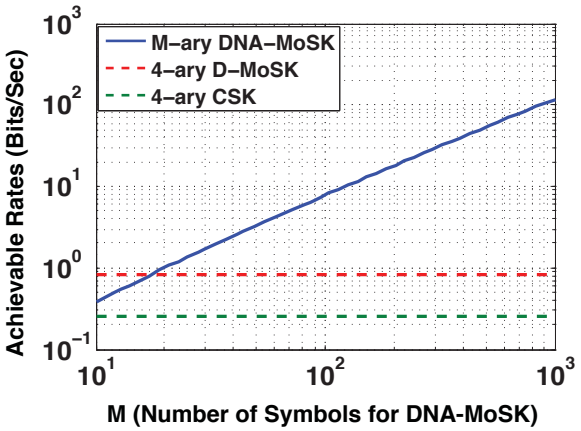

Figure 5: After M > 17 symbols, DNA-MoSK outperforms both CSK and D-MoSK in the achievable rate.

Cell Switching Time (x)	*2 minutes*
Signal Propagation Time y	*< 1 second*
Lookup Time (l_u)	*5-10 seconds*
Total Latency (D)	*≈ minutes*

Table 2: A summary of the timing from the proposed architecture

where s is the energy required to encode a single part of the sequence, b is the number of bits encoded by the DNA sequence, and l is the energy required for active transport across the unidirectional semi-permeable membrane.

3 EXPERIMENTAL RESULTS

3.1 DNA Sequence Construction Latency

Experimental results are obtained via a full system simulation built in Python. We first simulate single cell dynamics (i.e., the toggle switch); this is done by solving the ODEs in eqs. (1), (2), and (3) mentioned in Section 2.1.

As shown in Fig. 2, the simulated response of the toggle switch is normalized within 0 and 1. Since the repressor protein can deactivate the cells, the toggle switch turns off as the amount of repressor protein increases, and turns on as the the amount of activator protein increases. If the cell toggle switch is in state 0, it will encode a binary 0 onto the DNA sequence, and if the cell toggle switch is in state 1, it will encode a binary 1 into the DNA sequence.

However, there exists a transition phase where neither a bit 0, nor 1 is defined. To avoid encoding the incorrect bit onto the DNA sequence, we must avoid sending the starter sequence during this period. By waiting for a sufficient amount of time after the activator and repressor protein insertion, we can reduce the probability of errors in the DNA encoding sequences.

As shown in Fig. 3, the inserted activator and repressor proteins cause a signal propagation after initial insertion in Fig. 3(a). This protein concentration gradually declines over time as the initial protein degrades. Fig. 3(b) shows the delayed activation of the next layer, while Fig. 3(c) shows the delayed activation of the layer after that.

As can be seen in Table 2, the longest latency in the DCSS is caused by the cell switching delay (x). The active transport membrane can transport the data across the membrane at 200-300 base pairs per second [19]. Since the DNA sequence is usually a small length with $M < 100$, the membrane transport will take under a second for any practical DNA encoding sequences; this shows that the system is best suited for a very large address space, as it takes full advantage of the low latency on size of base pairs and large overhead in cell switching.

3.2 Communication Model Performance Analyses

We simulate the MC system by incorporating the DNA sequence constructor and data retrieval module from our proposed DCSS. We use the same constants as in [10] for a fair comparison. We assume the radius of the communication channel to be $r = 20 \times 10^{-9} m$. To calculate SER and AR of the DNA-MoSK communication channel, we require molecules be seen within $T_s = 2s$. In the simulation, the total number of molecules emitted from the transmitter (n) is set to 100, and the receiver detection threshold (z) is set to 20 molecules [10].

The SER was simulated for varying values of the diffusion coefficient. As diffusion coefficient rises, the probability a molecule reaching the end of the channel increases. As can be seen in eq. (6), increasing the probability of seeing a molecule in a given time will decrease the SER. As shown in Fig. 4, the SER of all modulation schemes decrease inversely with diffusion coefficient. With a higher diffusion coefficient, the SER of DNA-MoSK reaches the same point as D-MoSK, and is significantly lower than CSK. In summary, as the diffusion coefficient grows and the advantages of D-MoSK are evident, it is clear that DNA-MoSK has the same advantages over CSK.

For the simulation of AR, which is calculated from eq. (8), DNA-MoSK are compared against D-MoSK and CSK with 4 symbols due to scalability issues. A delay was added to DNA-MoSK as the construction method is expected to take around 2 minutes as

seen in Table 2, where in D-MoSK and CSK the molecules can be sent instantly. As shown in Fig. 5, the benefits of DNA-MoSK can be seen at high levels of symbols. After $M > 17$ symbols, DNA-MoSK's AR is higher than that of D-MoSK. It is far more practical to have a large number of symbols with DNA-MoSK than with D-MoSK, since DNA-MoSK does not have to store every molecule beforehand. Thus, DNA-MoSK is more scalable than D-MOSK.

4 DISCUSSION

In this paper, we have proposed a novel method for translating a binary address to a DNA sequence, and showcased the advantages this system has over the silicon technology by using the system in a MC context. DNA is capable of extremely high data density, so we are able to leverage the density and flexibility of our system to develop a scalable molecular communication modulation technique.

We have shown that the proposed DCSS can achieve high density and durability due to its use of DNA in data storage, but there are still areas for improvement. For instance, the silicon storage technology is considerably faster than its DNA-based counterpart in terms of read/write time. Additionally, there is also a significant wait time for reuse of the DCSS since we have to wait for the activator and repressor proteins to degrade. Without this wait-time, the DCSS's previous process will affect the current process, since remaining proteins may send the wrong signal to cells in the DNA sequence translation module. This can be mitigated by parallelizing this encoding process where multiple address translator systems are used in conjunction with a single storage unit to hide latency.

In terms of the application to MC, our proposed DNA-MoSK shows promise to outperform D-MoSK due to the much higher scalability with the possible number of symbols. Using D-MoSK with a large molecule count is infeasible due the high likelihood of symbol errors, so this method builds off of the MoSK technique to maintain a low symbol error rate and achieve much higher bitrate. However, D-MoSK relies on pre-made bins with unique molecules which makes it unscalable. Using our method, the molecules would be created dynamically, and would therefore allow much higher scalability. Future research in this area will aim at reducing the base delay associated with the DNA sequence construction and will look into the technical feasibility of such a design.

5 CONCLUSIONS

In this work, we have introduced a novel method of data storage based on DNA encoding: We have also demonstrated the applicability of our proposed memory system by incorporating it into a molecular communication system. Getting into details, we have first proposed and analyzed a simple cell-based toggle switch. We have then proposed an efficient mechanism for encoding digital data onto DNA sequences using layers separated by unidirectional, semipermeable membranes. Finally, we have applied this encoding scheme to molecular communication by proposing a modification on MoSK; we have compared the results against existing modulation techniques such as CSK, MoSK, and D-MoSK.

In terms of the experimental results, the cell model shows a latency of around 2 minutes when modeled using binary toggle switches. The error rate of the system shows a similar asymptotic behavior to D-MoSK; this is a promising alternative to D-MoSK. The achievable rate shows that with $M > 17$ symbols, DNA-MoSK outperforms D-MoSK with 4 symbols; these results show promise that this method can scale better than D-MoSK.

The data storage needs of the future cannot be done by traditional silicon and magnetic storage technology; the data requirements are too large for traditional storage solutions. For example, emerging quantum computers are said to hold massive computing power, but require an immense amount of data storage and sizes that cannot be met with commercial system right now. On the contrary, DNA is much more dense and durable than traditional storage technology, and may be the key to long term, compact data storage in the future. We envision our proposed DNA cellular storage system can be used for such large-scale computations.

6 ACKNOWLEDGMENTS

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