On the tradeoff between data rate and error probability in discrete microfluidics

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ABSTRACT

The recent advancements in synthetic biology, and specifically in genetic engineering of bacteria, have enabled the use of bacterial populations to define and design a communication system for nano-machines in biological applications. The need for providing communication strategies in these challenging environments where electromagnetic waves cannot be used, has brought attention of researchers towards molecular communications. In particular, the possibility of moving very small amounts of matter inside microfluidic systems can be exploited to exchange information between micro- and nano-scale devices. Simple modulation techniques such as on-off keying, or alternative strategies such as time-elapse communication (TEC) and following enhancements (e.g. SMART-TEC), have been introduced in microfluidic systems. However, the data-rate of these schemes is extremely low, due to the specific microfluidic approach utilized. In this paper we demonstrate that such a low data rate can be improved by several orders of magnitude by exploiting the advantages of both droplet-based microfluidics and bubble-logic. We provide an analytical study of the achievable data rates for molecular communications in discrete microfluidics and evaluate the tradeoff between data rate and error probability.

1. INTRODUCTION

There are many environments, such as underground or underwater tunnels, human body or biological tissues, or applications such as biomedical nanorobots or biological synthetic systems, where data transmission cannot be achieved through electromagnetic waves. A possible way to communicate in these scenarios is through bio-inspired molecular communications which use small amounts of matter (e.g., molecules) to encode messages and propagate them through a fluid medium [18, 13]. In nature, plants and animals use chemical signals for long range communications between members of the same species, such as insects that use pheromones [9]. Another interesting example of molecular signaling is given by many species of bacteria which communicate through a system, called *quorum sensing*, of chemical stimuli and responses correlated to population density [1]. So, taking the cue from these examples, chemical signals can be used for communications at both macroscopic and microscopic scales.

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In particular, at microscopic scales, molecular signaling in microfluidic environments has been investigated as an effective strategy for communications between micro and nano-machines [13]. More specifically, microfluidic systems consist of a series of micro channels with a diameter in the order of micrometers [21]. The advantages of using microfluidics rely on the dominance, at the micro scale, of physical parameters, such as surface tension, energy dissipation and viscosity: these parameters influence the behavior of fluids, so that they flow in laminar streams without mixing together, and make possible the motion control. Relevant examples of microfluidic systems are Labs-on-a-Chip (LoCs) [14] which are devices where small volumes of fluids are manipulated, typically for chemical and biological analysis and synthesis (e.g. biomolecule synthesis, drug delivery, DNA sequencing, diagnostic testing, etc.) [19, 10].

The mainstream approach to microfluidics has been based on the manipulation of continuous liquid flow through micro channels. However, promising opportunities and applications are offered by the introduction of an emerging approach named droplet-based microfluidics [20, 22]. In droplet microfluidics, a sequence of droplets or bubbles (called *dispersed phase*) are dispersed into another fluid (called *continuous phase*), immiscible with them. The generation of droplets [2], as well as their fission, fusion and motion [17, 6], can be reliably controlled, so that sequences of droplets can be used to encode information (e.g. presence/absence of droplets, distance between consecutive droplets, size or composition, etc.). The benefits of such a discrete approach come from the possibility of highly controlling the molecular processes occurring inside a droplet, which can be considered as an environment where reactions occur (almost) in isolation.

Molecular communications in continuous microfluidics have been investigated in [11], where simple modulations such as on-off keying, and alternative strategies, such as time-elapse communication (TEC) and following enhancements (e.g. SMART-TEC), have been defined. More specifically, in [11] molecular communication is realized by housing populations of E. coli bacteria in micrometer sized chambers inside an experimental microfluidic system. The E. coli bacterium utilized is engineered to exhibit fluorescence when stimulated by a specific signaling molecule (N-(3-Oxyhexanoyl)-L-homoserine lactone, or C6-HSL). However, such a technique in this context shows very poor performance in terms of data rates, which remains as low as 10^{-4}bps. The low data rate limits the target of these techniques to super-slow networks. The reason of such poor performance is due to the extremely large bit period involved, which is related to the period of time during which the bacteria populations exhibit fluorescence, which was found to be 435 min. In this paper we will demonstrate that such a low data rate can be

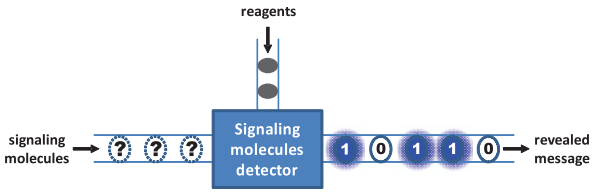


Figure 1: Generic chemi- or bio-luminescence detection

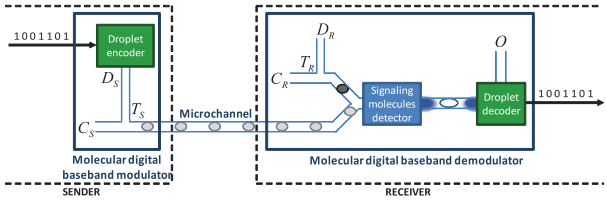


Figure 2: Scheme of a microfluidic system for molecular communications in discrete microfluidics

improved by several orders of magnitude by adopting a discrete approach which decouples the bit period from the bacterial luminescence period.

To this purpose, in this paper, we consider a molecular communication scheme which exploits the advantages of both droplet-based microfluidics and bubble-logic [15]. The idea is to enclose the signaling molecules inside droplets that are delivered, through microchannels, to the destination. A particular encoding scheme is considered where the information is encoded in the composition of the droplets, i.e. in the presence or absence of particular signaling molecules inside the droplets. Once the droplets containing the signaling molecules reach the receiver, they are combined with specific reagents. Inside the droplets, biological processes or chemical reactions (e.g. bio- or chemiluminescence) can occur in isolation and change their status while droplets are stored at the receiver side. As a consequence, the bit period and the achievable data rate are related to the generation process of the droplets, rather than to the time period needed for the chemical reactions (or the luminescence phenomenon).

The contribution of this work is twofold. First, we provide an analytical study of the achievable data rates for molecular communications in discrete microfluidic systems. We show that data rates of a few tens of bits per second are achievable which, as compared with the results in [11], correspond to an improvement of five orders of magnitude. We evaluate a tradeoff between data rate and error probability, and we discuss some design guidelines for the best choice of the bit period.

The rest of the paper is organized as follows. In Section 2, we will present a molecular communication scheme that can be used as a reference for the analysis of a discrete microfluidics system. A possible encoding strategy to represent information will be considered in Section 3. Then, in Section 4, we will evaluate the data rate that can be achieved with the proposed approach and the error that may occur. Additionally, we will derive some guidelines for the choice of the bit period as a tradeoff between maximization of the data rate and minimization of the error probability. Finally, we will draw our conclusions in Section 5.

2. THE REFERENCE SYSTEM

In this section, we present a molecular communication scheme that can be used as a reference for the analysis of a discrete microfluidics system. As well known, molecular communications exploit the possibility of using small amounts of molecules to encode messages and propagate them through a fluid medium. The idea in this work is to enclose the signaling molecules inside droplets that are delivered to the destination through micro channels.

The message to be delivered is encoded (according to specific molecular encoding schemes that we will discuss later in Section 3) in a train of droplets containing the signaling molecules. Since the message is contained in the chemical composition of droplets, i.e. in the presence or absence of signaling molecules, once the message reaches the destination, detectors for the chemical content of the droplets have to be used to reveal the message. To this purpose, chemi- or bio-luminescence can be exploited to reveal the presence or absence of signaling molecules and easily perform decoding operations (see Fig. 2). More specifically, the signaling molecules are chosen among chemical substances which produce, after being combined with specific reagents, bio- or chemi-luminescence phenomenon, i.e. the emission of visible light from living organisms or as a result of a chemical reaction, respectively. Examples of bioluminescence are given by some species of bacteria. Conversely, an example of chemiluminescence is the luminol test used by forensic investigators to detect traces of blood left at crime scenes. Another example of chemiluminescence is given by the light sticks (or glow sticks) often used for recreational purposes, or as short-term light sources and light markers by military forces and recreational divers, or, as well, as the only safe light source to be used immediately after a catastrophic emergency.

Once the droplets containing the signaling molecules reach the receiver, the message is decoded by revealing the composition of droplets through their combination with reagents that activate the luminescence phenomenon (see Fig. 2). Such a combination of reactants is performed by generating at the receiver side, a second train of droplets containing the reagents to be used for the detection of the signaling molecules (see Fig. 2). As an example, in the case of bacteria communications, populations of bacteria can be used as reagents while the inducers that activate the bioluminescence process can be used as signaling molecules: in this way, by combining droplets containing or not the inducers with droplets containing bacteria, a train of luminescent and non-luminescent droplets can be obtained at the receiver side.

The system used for this purpose is depicted in Fig. 2. The *Molecular digital baseband modulator* conveys the digital bit stream encoding the message inside a molecular signal, in the form of a sequence of droplets that can be physically transmitted in a microfluidic channel. Inside the Molecular digital baseband modulator, two inlets, labeled as D_S and C_S, are used for the dispersed phase and the continuous phase, respectively. Note that the dispersed phase contains the signaling molecules. The T-junction topology in T_S is used to generate the droplets enclosing the signaling molecules. The flow rate or the concentration of the dispersed phase is controlled by the *droplet encoder* according to the desired modulation scheme.

The so generated train of droplets is transported by the continuous phase, through a microchannel, to the receiver. Here the *Molecular digital baseband demodulator* is used to perform demodulation operations. More specifically, first, droplets coming from the microchannel are combined with specific reagents in order to activate the luminescence process and reveal, in this way, the droplet chemical contents. Then, the revealed message is converted to the original digital bit stream encoding the message. In order to real-

ize these operations, a second train of droplets is generated inside the Molecular digital baseband demodulator. To this purpose, a fluid containing specific reagents is introduced in the circuit, as dispersed phase, through the inlet labeled as D_R, whereas continuous phase is introduced through the inlet labeled as C_R. The T-junction labeled as T_R is used to generate the droplets. The droplets containing the signaling molecules, together with the droplets containing reagents, are piped towards the *Signaling molecule detector*, where droplets belonging to the two trains join together, so that the combination between the signaling molecules with the reagents activates the luminescence process and allows to reveal the message. Once reagents are mixed together, chemical reactions inside the droplet usually take some time to occur. For this reason, the use of storage devices inside the Signaling molecule detector has to be considered for the time needed by the chemical reactions to produce the desired effects. Let us note, however, that chemi- and bio-luminescence are evanescent phenomena, whose duration limits the lifetime of the revealed message. The duration of luminescence can be extended or shortened by adjusting the concentration of reactants, taking into account that the brightness is affected as a counterpart of this choice. Finally, once the message has been revealed, the droplet encoder is used to convert the sequence of luminescent and non-luminescent droplets in the original digital bit stream encoding the message. Then, droplets are discarded through the outlet O.

3. INFORMATION REPRESENTATION AND MODULATION TECHNIQUES

In this section we discuss how the system described in Section 2 can be used for achieving molecular communications in discrete microfluidic scenarios. As already said so far, the idea is to use droplets containing signaling molecules to deliver a message through the microfluidic channel. More specifically, given a source encoded (or even a channel encoded) message in the form of a string of bits, a *molecular* digital baseband modulation (or *droplet* line encoding) is performed in order to convert the sequence of bits in a sequence of droplets containing the message. Once the message reaches the destination, by using specific reagents that enable bio- or chemiluminescence processes inside droplets, the encoded message is revealed and decoded.

To this aim, several encoding, revealing and decoding strategies can be used. In this work, we assume that the signaling molecules are dissolved in a fluid that is introduced in the microfluidic system as dispersed phase, i.e. droplets containing signaling molecules are generated and dispersed in the continuous phase. The content of the dispersed phase, i.e. the presence of the signaling molecules inside droplets, is controlled and varied through the droplet encoder, according to the message. More specifically, given a stream of bits encoding the message, at regular time interval of duration T_b, at the T-junction T_S in Fig. 2, a droplet containing signaling molecules is generated for the bit '1', whereas a droplet containing only the medium, where the signaling molecules can be dissolved, is generated for the bit '0'. In other words, the information is contained in the chemical composition of droplets generated at the T-junction. Such a sequence of droplets represents the line coded signal and is composed by droplets all of the same size, and with constant droplet rate. At the receiver side, a droplet of reagents is generated in each time slot (i.e. with the same droplet rate of the message). Then, in each time slot, two droplets enter the signaling molecule detector, one from the message and one of reagents, and a merged droplet is produced. Inside this droplet, the luminescent process takes place or not, according to the presence or absence of signaling molecules. Thus, downstream the signaling molecule detector, a sequence of luminescent and non luminescent droplets is produced, where the luminescent droplet represents the bit '1' and the non-luminescent droplet represents the bit '0'.

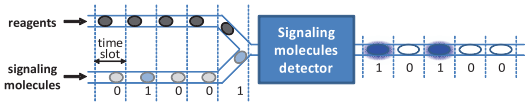


Figure 3: Graphic representation of the adopted encoding approach

4. DATA RATE ANALYSIS

In this section we evaluate the data rate that can be achieved with the proposed approach and the error that can occur. Additionally, we will derive some guidelines for the choice of the time slot as a tradeoff between maximization of the data rate and minimization of the error probability. In Section 3, we have described a possible encoding approach, where, given a stream of bits encoding the message, we have considered a discrete time domain, with time slots of equal duration associated to each bit of the message. More specifically, one droplet is associated to each bit of the message, so that one droplet is generated in each time slot.

Let D_0 be the distance between two adjacent droplets of the message, from the rear end of the downstream droplet to the front end of the upstream one, let L_S be the length of the droplets from the most advanced point in the front of the droplet to the most backward one in the rear, and let v denote the velocity of the droplets in the microfluidic channel. Therefore, in order to regularly place one droplet in each time slot of duration T_b (see Fig. 4(a)), the following relationship must hold:

$$T_b = \frac{L_S + D_0}{v} \tag{1}$$

where the numerator in (1) represents the distance between the centers of two adjacent droplets, by considering all the droplets of the same size, as expected when using the proposed encoding approach.

Now, the data rate that can be achieved with the described encoding approach is given by:

$$r = \frac{1}{T_b} = \frac{v}{L_S + D_0} \tag{2}$$

Obviously, the choice of short time slots, which means in turn high droplet velocity v and short distance D_0 between adjacent droplets, results in high information capacity. However, the droplet velocity is bounded by the droplet generation process and the properties of the fluid phases [7]. At the same time, the distance between two droplets cannot be chosen too short in order to avoid interaction between droplets which may results in droplet coalescence [3].

Additionally, it has been experimentally observed that the distance between pairs of droplets, flowing through a microfluidic channel, suffers variations due to a large number of physical factors, including viscosity of the fluid phases, pressure fluctuations, irregularity and roughness of the microfluidic channels [16, 8]. As a consequence, errors can occur when such a distance decreases or increases enough to cause either droplet coalescence, or misplacement of the droplets in wrong time slots. Therefore, in this study, such a variation of the distance between pairs of droplets will be identified with the *noise* in the microfluidic channel. In [5, 4, 12], such a variation has been statistically characterized.

In the following, we first resume the statistical characterization of distance variation between pairs of droplets (Section 4.1), then we evaluate the non-zero error conditions for the proposed system (Section 4.2) and investigate how to design the time slot duration to trade off data rate maximization and error reduction (Section 4.3).

4.1 Statistical characterization of the distance variation between pairs of droplets

As mentioned before, in this section we present the statistical characterization of the distance variation between pairs of droplets. More specifically, let D_0 be the distance between two adjacent droplets when they are generated (i.e. measured at the T-junction T_S, when the second droplet is generated), and let D be the distance between the two droplets, measured in a generic section of the channel, (i.e. measured when the second droplet crosses that section). Let $E = D - D_0$ be the difference between the above distances. It has been experimentally observed that the distribution function of the difference E fits the distribution function of a Gaussian random variable [5, 4]. This result is expected given that E is the effect of the interactions between a huge number of particles. Furthermore, the Gaussian distribution of E is characterized by a mean μ_E equal to zero and a variance σ_E^2 which does not depend on the distance of the observation point from the droplet generation point. The probability density function of E is thus:

$$f_E(t) = \frac{1}{\sqrt{2\pi\sigma_E^2}} e^{-\frac{t^2}{2\sigma_E^2}} \tag{3}$$

In the case of no interactions between droplets, the difference E can be modeled as an additive noise independent from the distance D_0 of the two droplets at the generation point. As a consequence, the distance D between two droplets, in a generic section of the microfluidic channel, can be described as a random variable, and, more specifically, it is a function of the distance D_0 at the generation point plus the additive gaussian noise E, that is:

$$D = D_0 + E \tag{4}$$

Therefore, its probability density function $f_D(x)$ is:

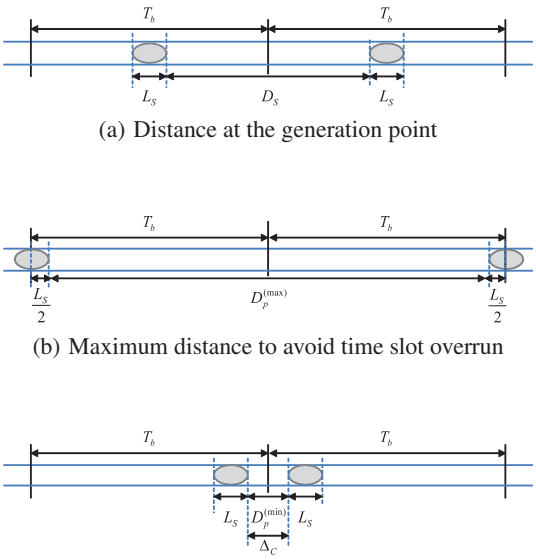
$$f_D(x) = \frac{1}{\sqrt{2\pi\sigma_E^2}} e^{-\frac{(x-D_0)^2}{2\sigma_E^2}} \tag{5}$$

4.2 Non-zero Error Conditions

In this Section we examine the possible errors affecting the successful transmission of a message in case the proposed encoding methodology is adopted, and we investigate how to trade off data rate maximization and error reduction.

According to (1) and (2), the maximum achievable data rate is affected by the choice of the time slot duration T_b, which in turn is related to the distance D_0 between two adjacent droplets. However, in order to reduce the error probability, the variation of the distance between a pair of droplets should be taken into account for the selection of the most convenient time slot duration T_b. To this purpose, two possible types of errors may occur:

- *time slot overrun* - when the distance between two droplets increases, droplets may move beyond their own time slot. If such a misplacement happens right when the misplaced droplets reach the receiver, the decoder would erroneously find an empty time slot, that we can assume would be interpreted as an additional bit '0', not present in the original message. Therefore, an error of one bit is introduced, when



(a) Distance at the generation point

(b) Maximum distance to avoid time slot overrun

(c) Minimum distance to avoid droplet coalescence

Figure 4: Distance between adjacent droplets

the time slot overrun occur. In order to reduce the bit error probability, the time slot duration T_b, or the distance D_0 between adjacent droplets at the generation point, should be designed such that droplets do not overrun their own time slot even when they are at their maximum distance. Note, however, that such a distance is Gaussian distributed, and thus not limited. Therefore, let us define $D_p^{(max)}$ as the value such that the distance D between two adjacent droplets is greater than or equal to $D_p^{(max)}$ with probability p, that is:

$$prob(D \geq D_p^{(max)}) = \int_{D_p^{(max)}}^{+\infty} f_D(x)dx = p \tag{6}$$

Accordingly, the condition to avoid time slot overrun with probability higher than or equal to $1-p$ can be written as (see Fig. 4(b)):

$$2T_b \geq \frac{L_S + D_p^{(max)}}{v} \tag{7}$$

Later in this section we will derive $D_p^{(max)}$ as a function of D_0.

- *droplet coalescence* - when the distance between two droplets decreases and becomes lower than a critical value Δ_C (depending on the radius of the capillary channel, velocity of motion, surfactant concentration and type of surface forces, among other physical factors [3]), droplets interact with each other. As a result of such interactions, the relative position of droplets may vary significantly and even the coalescence (i.e. fusion) of droplets may occur: if two droplets undesirably join in a single one, one of the two original bits, associated to the two droplets, will be missing and the message will be corrupted. More specifically, let us note that two adjacent droplets may encode any possible string of two bits, i.e. '00','01','10','11'. The droplet coalescence instead will produce an empty time slot that would be decoded as '0', and a large droplet that, in case the original string is '00', does not contain signaling molecules and would be decoded

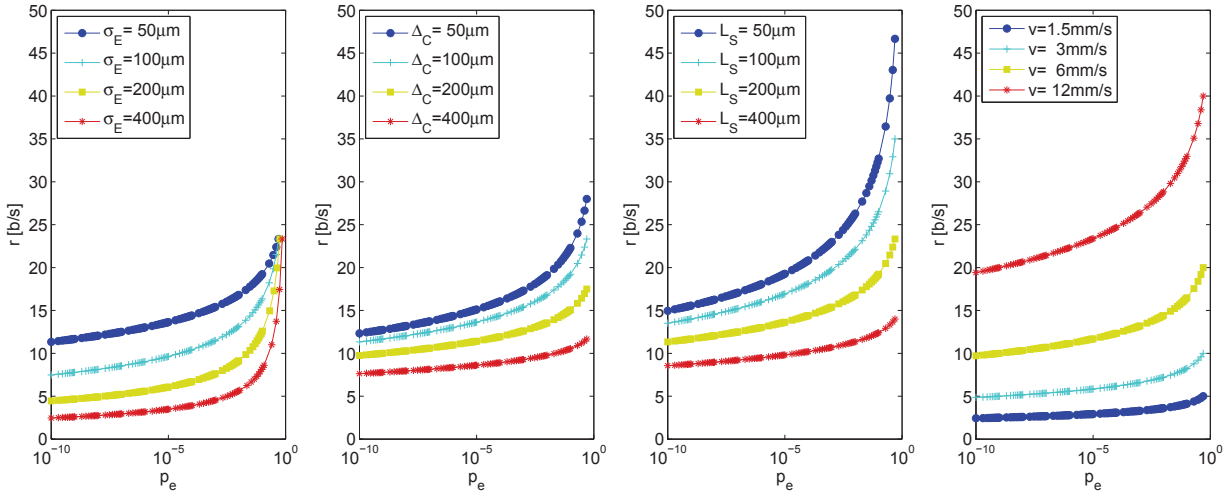


Figure 5: Maximum achievable data rate r vs. bit error probability p_e

as '0'. In case one of the two original bits is '1', it contains signaling molecules and would be decoded as '1'. Therefore the bit string '00', would not be corrupted, whereas all the other bit strings would be decoded as '10' or '01', depending on the placement of the coalesced droplet in one of the two time-slots, so producing, in any case, an error of at most one bit. Obviously, errors produced by these events can be reasonably avoided by generating droplets at a distance greater than the critical value (though not too large, not to degrade the data rate). More specifically, the minimum distance between two droplets should be greater than Δ_C. Therefore, let us define $D_p^{(min)}$ as the value such that the distance D between two adjacent droplets is lower than or equal to $D_p^{(min)}$ with probability p, that is:

$$prob(D \leq D_p^{(min)}) = \int_{-\infty}^{D_p^{(min)}} f_D(x)dx = p \tag{8}$$

Accordingly, the condition to avoid droplet coalescence with probability higher than or equal to $1-p$ can be written as:

$$D_p^{(min)} \geq \Delta_C \tag{9}$$

Let us note that, by considering (4), and exploiting the symmetry of the Gaussian distribution, $D_p^{(max)}$ and $D_p^{(min)}$ can be derived as:

$$\begin{aligned} D_p^{(max)} &= D_0 + E_p \\ D_p^{(min)} &= D_0 - E_p \end{aligned} \tag{10}$$

where E_p is the value such that E is greater than or equal to E_p with probability p.

4.3 Design guidelines

In the previous section we have considered the possible types of error affecting the transmission of a message and we have derived some conditions to reduce the bit error probability. In this section, we will analyze such conditions and obtain design guidelines. More specifically, we will investigate the best choice of the time slot duration T_b, or alternatively, the distance D_0 between two droplets at the generation point, in order to maximize the data rate and reduce the error probability.

To this end, let us consider the condition in (7), to avoid time slot overrun, which combined with (1) and (10), becomes:

$$D_0 \geq E_p - L_S \tag{11}$$

Analogously, the condition in (9), to avoid droplet coalescence, combined with (10), becomes:

$$D_0 \geq \Delta_C + E_p \tag{12}$$

Note that the condition in (11) is included in the condition in (12).

Time slot overrun and droplet coalescence, are pairwise disjoint events. Moreover they all produce an error of, at most, one bit. In other words, when one of the above events occurs, a bit error may or may not be produced. Accordingly, let us consider the worst case where one bit error is produced whenever one of the above events occur, that is let us assume that the conditional probability of bit error given one of the above events is equal to 1. Therefore, for the law of total probability, we can derive the bit error probability p_e as:

$$\begin{aligned} &p_e = p_{overrun} + p_{coalescence} = \\ &= prob(D \geq 2T_b v - L_S) + prob(D \leq \Delta_C) = \\ &= \int_{2D_0+L_S}^{+\infty} f_D(x)dx + \int_{-\infty}^{\Delta_C} f_D(x)dx = \\ &= \tfrac{1}{2} erfc\left(\tfrac{D_0+L_S}{\sqrt{2\sigma_E^2}}\right) + \tfrac{1}{2} erfc\left(\tfrac{D_0-\Delta_C}{\sqrt{2\sigma_E^2}}\right) \end{aligned} \tag{13}$$

where $p_{overrun}$ and $p_{coalescence}$ are the probabilities of time slot overrun and droplet coalescence, respectively. Furthermore, by considering (12) when $D_0 = \Delta_C + E_p$, (13) becomes:

$$\begin{aligned} &p_e = \tfrac{1}{2} erfc\left(\tfrac{\Delta_C+L_S+E_p}{\sqrt{2\sigma_E^2}}\right) + \tfrac{1}{2} erfc\left(\tfrac{E_p}{\sqrt{2\sigma_E^2}}\right) = \\ &= \tfrac{1}{2} erfc\left(\tfrac{\Delta_C+L_S+E_p}{\sqrt{2\sigma_E^2}}\right) + p \end{aligned} \tag{14}$$

Note that, the selection of D_0 after imposing, through the probability p, the maximum range of variation for the distance between

adjacent droplets, allows to limit the bit error probability p_e, which is always:

$$p_e \leq 2p \tag{15}$$

as can be easily demonstrated. Obviously, the relationship in (15) is worth considering only for small values of p. Also note that p corresponds to the probability of droplet coalescence $p_{coalescence}$.

The analysis conducted so far allows to identify a trade off between the maximum achievable data rate and the bit error probability reduction. More specifically, the choice of $D_0 = \Delta_C + E_p$ determines, through (2), the maximum data rate which, according to (14), can be achieved at the cost of the bit error probability p_e. Fig. 5 shows the maximum achievable data rate r vs. the bit error probability p_e, when $\sigma_E = 50\mu m$, $v = 7mm/s$, $\Delta_C = 100\mu m$, $L_S = 200\mu m$ (if not otherwise specified in the legends). The results show that high values of the bit error probability strongly affect the achievable data rate. However, as lower values of bit error probability are considered, the reduction of the achievable data rate is less severe. Additionally, Fig. 5 shows the impact of each of the above parameters on the achievable data rate. More specifically, as expected, results show that the achievable data rate decreases as σ_E, Δ_C and L_S increase, whereas increases as v increases as well.

Let us note, that data rates of a few tens of bits per second are achievable, with low error probability, in almost all the considered cases. These results, compared with those in [11], show an increase of the data rate of five orders of magnitude and demonstrate that a great improvement is possible by exploiting the advantages of discrete microfluidics.

5. CONCLUSIONS

In this work we have presented a molecular communication scheme which exploits the advantages of both droplet-based microfluidics and bubble-logic. More specifically, we have considered a particular encoding scheme, where the information is encoded by enclosing signaling molecules inside droplets that are delivered, through microchannels, to the destination. Then, we have provided an analytical study of the achievable data rates and we have shown that data rates of a few tens of bits per second are achievable, which compared with the results in [11] correspond to an improvement of five orders of magnitude. Additionally, we have derived some guidelines for the choice of the best bit period as a tradeoff between maximization of the data rate and minimization of the error probability.

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