Microfluidic QCSK Transmitter and Receiver Design for Molecular Communication

Dadi Bi, Graduate Student Member, IEEE, and Yansha Deng, Member, IEEE

Abstract—The components with molecular communication (MC) functionalities can bring an opportunity for emerging applications in fields from personal healthcare to modern industry. In this paper, we propose the designs of the microfluidic transmitter and receiver with quadruple concentration shift keying (QCSK) modulation and demodulation functionalities. To do so, we first present an AND gate design, and then apply it to the QCSK transmitter and receiver design. The QCSK transmitter is capable of modulating two input signals to four different concentration levels, and the QCSK receiver can demodulate a received signal to two outputs. More importantly, we also establish a mathematical framework to theoretically characterize our proposed microfluidic circuits. Based on this, we first derive the output concentration distribution of our proposed AND gate design, and provide the insight into the selection of design parameters to ensure an exhibition of desired behavior. We further derive the output concentration distributions of the QCSK transmitter and receiver. Simulation results obtained in COMSOL Multiphysics not only show the desired behavior of all the proposed microfluidic circuits, but also demonstrate the accuracy of the proposed mathematical framework.

Index Terms—AND gate, chemical reactions, microfluidics, molecular communication, QCSK modulation and demodulation, signal processing.

I. INTRODUCTION

OVER the past few years, molecular communication (MC) has attracted increasing attention as it can wave revolutionary and interdisciplinary applications ranging from healthcare, to industry, and military [2], [3]. The wide range of applications inspired a bulk of research centering around theoretical characterizations of MC, such as transmission schemes [4], [5], propagation characterizations [6], [7], reception models [8], [9], and detection strategies [10], [11]. To ensure successful information transmission, signal processing units are essential components for MC transmitter and receiver to facilitate modulation-demodulation and encoding-decoding functionalities. However, how to practically realize these basic signal processing functions in microscale/nanoscale has been rarely studied.

The signal processing functions realized in existing MC works were performed over electrical signals using electronic devices. In [5], [12]–[15], the transmitted bit sequence was modulated over the concentration of signaling molecules via the on/off of an air tank [5], [12], [13], electronic spray [14], and light-emitting diode (LED) controlled by Arduino microcontroller boards and laptops [15]. Their high dependency on electrical signals/devices can hardly fulfill the biocompatible and non-invasive requirements of biomedical applications, such as disease diagnosis and drug delivery [16]. Meanwhile, the size of electronic devices can hardly meet the requirement of intra-body healthcare applications promised by MC, where fully MC functional devices are expected to be miniaturized into microscale/nanoscale [2].

In nature, signal processing functions can be realized in molecular domain by exploiting a gene expression process, where transcription factors bind with genes to either activate or repress their expression into proteins [17]. If the transcription factor activates protein expression, the gene expression process can function as a buffer gate [18]. On the contrary, if the transcription factor represses protein expression, the gene expression process can function as a NOT gate [19]. The signal processing nature of gene expression process motivates biologists to design more complex artificial genetic circuits to manipulate molecular concentrations using synthetic biology [20]. One type of artificial genetic circuit with computing functions is the Boolean inspired digital logic device. The sharp state change between a low concentration and a high concentration is ideal for reliable state transitions and signal integration, making digital logic particularly useful in decision-making circuits [21]. For example, the authors of [19] designed an orthogonal AND gate and coupled it to nonspecific sensors to increase selectivity [22]. The authors of [23] constructed a simple NOR logic gate and spatially configured multiple NOR gates to produce all possible two-input gates, which have found their utilities in biotechnological applications [24].

Although the aforementioned genetic circuits have advantages in biocompatibility and miniaturization over electric circuits, the experimental realization of genetic circuits faces challenges, such as slow speed, unreliability, and non-scalability [25]. These challenges motivate our initial work on chemical reactions-based microfluidic circuits [26]–[28]. Unlike genetic circuits, chemical circuits are much easier to be controlled. Moreover, the integration of chemical reactions

0090-6778 © 2022 IEEE. Personal use is permitted, but republication/redistribution requires IEEE permission. See https://www.ieee.org/publications/rights/index.html for more information.
with microfluidic systems not only endows chemical circuits with advantages of rapid analysis and low reagent costs due to a reduction of circuit size [29], but can also benefit from an additional space level of chemical control through applying and regulating chemical reactions in different regions of a microfluidic device. In [26] and [27], we designed an MC microfluidic transceiver based on chemical reactions to successfully realize binary concentration shift keying (BCSK) modulation and demodulation functions. The signal processing capability of chemical reactions-based microfluidic circuits was further exploited in [28], where we provided the designs of AND, NAND, OR, NOR, and XOR gates. These logic computation units can be applied to environmental monitoring. For example, the AND microfluidic circuit can improve the selectivity of a biosensor by producing a measurable signal only in the presence of multiple chemical signals. As we discussed in [28], one challenge in realizing signal processing functions via chemical reactions-based microfluidic circuits is the theoretical characterization of a logic gate, which facilitates the selection of design parameters for expected gate outputs. Although we mathematically modeled the dynamics of molecular species in microfluidic channels in [26] and [27], this analysis is not scalable with the increase in the number of microfluidic circuits. Motivated by above, the objective of this paper is to employ microfluidic logic gates to achieve QCSK modulation-demodulation function and establish a mathematical framework to analyze any microfluidic MC circuit. The main contributions of this paper are as follows:

- We first present a chemical reactions-based microfluidic AND gate design, based on which, we design the microfluidic transmitter and receiver with quadruple concentration shift keying (QCSK) modulation and demodulation functionalities, to show how logic computations can process molecular concentrations and realize communication functionalities. The QCSK transceiver design largely expands the brief investigation of the digital signal processing capability of microfluidic circuits in [1]. Most importantly, we show how digital electronics theory can be applied to and facilitate microfluidic circuit design, which serves as a foundation for utilizing simple microfluidic logic gates to achieve more complex MC functions.

- We develop a novel mathematical framework to characterize our proposed microfluidic circuits, which can be applied to analyze other new and more complicated microfluidic circuits. As in [1], we first analyze the concentration and velocity changes under fluid mixing, but in this work we also consider the fluid separation scenario. Then we derive the impulse response of a straight convection-diffusion channel. Based on these, we derive the spatial-temporal concentration distribution of a convection-diffusion-reaction channel with either a thresholding reaction or an amplifying reaction.

- To evaluate our proposed microfluidic designs, we identify four elementary microfluidic blocks of the basic AND gate, and define five corresponding operators to represent the output concentration distribution of each elementary block. Relying on these, we derive not only the output concentration distribution of the proposed AND gate, but also the output distributions for our designed QCSK transmitter and receiver. The functionalities of our proposed microfluidic designs and the corresponding theoretical results are validated via simulations performed in COMSOL Multiphysics finite element solver. The remainder of this paper is organized as follows. In Sec. II, we provide the basic microfluidic channel analysis. In Sec. III, we establish a mathematical framework to theoretically characterize our proposed AND gate. In Sec. IV, we propose the designs and analysis of the QCSK transmitter and receiver. Numerical results in Sec. V validate the proposed microfluidic designs and their theoretical analyses. Finally, Sec. VI concludes the paper.

II. BASIC MICROFLUIDIC CHANNEL ANALYSIS

With the ultimate goal of designing and analyzing a microfluidic system with modulation and demodulation functionalities, the basic characteristics of fluids in microfluidic channels must be first understood. To do so, we analyze and derive the concentration and velocity changes for a general microfluidic device with combining channels (Sec. II-A) and separation channels (Sec. II-B), which are not fully investigated in the existing literature. We present the new results as lemmas in order to distinguish them from the known results in fluid dynamics. In particular, these lemmas hold under the assumption that the flow is laminar, viscous, and incompressible. The results provided in this section serve as the foundation for the analysis in the following sections.

For a Poiseuille flow traveling along the $x$ direction of a microfluidic channel with rectangular cross-section, the average velocity can be expressed in terms of volumetric flow rate $Q$ and cross-sectional area as [30, eq. (5)]

$$\bar{v} = \frac{Q}{wh},$$

where $w$ and $h$ are the width and the height of the cross-section.

A. Fluid Mixing at Combining Connections

In a microfluidic circuit, fluids flowing in different channels can mix to a single flow at a combining connection, and we name this behavior as fluid mixing for simplicity.

1) Concentration Change: Let us consider a microfluidic device with $n$ inlets and $n$ combining channels as shown in Fig. 1. We assume that a solution containing species $S_i$ ($1 \leq i \leq n$) is constantly injected into Inlet $i$ with concentration $C_{S_i}$, average velocity $\bar{v}$, and volumetric flow rate $Q_i$. According to the well-known analogy between Hagen-Poiseuille’s law and Ohm’s law, the pressure drop, the flow rate, and the flow resistance in hydraulic circuits are analogous to the voltage drop, the electric current, and the electric resistance in electric circuits, respectively. On the one
hand, this analogy enables a sound engineering estimate of steady-state pressure drops, flow rates, and hydraulic resistance of 1D long and straight microchannels, and is still effective even for channels with non-circular cross-sections that are neither perfectly straight nor infinite in extent. On the other hand, this analogy enables the application of electric circuit theory to microchannel network analysis [30]. Based on the Kirchoff’s Current Law, the volumetric flow rate in the \( n \)th combining channel \( Q_{CHn} \) is the summation of coming flow rates, such that

\[
\begin{align*}
Q_{CH1} &= Q_1, \\
Q_{CH2} &= Q_{CH1} + Q_2 = \sum_{i=1}^{2} Q_i, \\
& \quad \cdots, \\
Q_{CHn} &= Q_{CH(n-1)} + Q_n = \sum_{i=1}^{n} Q_i.
\end{align*}
\]

(2)

Therefore, the mixed concentrations of species \( S_1 \) and \( S_2 \) in the second combining channel are [30]

\[
\begin{align*}
C_{S12}^{CH2} &= \frac{Q_1}{Q_1 + Q_2} C_{S10}, \\
C_{S22}^{CH2} &= \frac{Q_2}{Q_1 + Q_2} C_{S20}.
\end{align*}
\]

(3)

Then, when \( n \geq 3 \), the mixed concentrations of species \( S_1, S_2, \cdots, S_n \) in the \( n \)th combining channel become

\[
\begin{align*}
C_{S1}^{CHn} &= \frac{Q_{CH(n-1)}}{Q_{CH(n-1)} + Q_n} C_{S1}^{CH(n-1)} = \sum_{i=1}^{n-1} \frac{Q_i}{Q_i + Q_n} C_{S1}^{CH(n-1)}, \\
C_{S2}^{CHn} &= \frac{Q_{CH(n-1)}}{Q_{CH(n-1)} + Q_n} C_{S2}^{CH(n-1)} = \sum_{i=1}^{n-1} \frac{Q_i}{Q_i + Q_n} C_{S2}^{CH(n-1)}, \\
& \quad \cdots, \\
C_{Sn}^{CHn} &= \frac{Q_n}{Q_{CH(n-1)} + Q_n} C_{S0}^{CHn0} = \sum_{i=1}^{n-1} \frac{Q_i}{Q_i + Q_n} C_{S0}^{CHn0}.
\end{align*}
\]

(4)

**Lemma 1:** For the fluid mixing from \( n \) inlets to one combining channel, the mixed concentration of species \( S_i \) (\( 1 \leq i \leq n \)) can be derived as

\[
C_{Si}^{CHn} = \frac{Q_i}{\sum_{i=1}^{n} Q_i} C_{S0}^{CHn0},
\]

where \( Q_i \) and \( C_{S0}^{CHn0} \) are the volumetric flow rate and the species concentration injected into Inlet \( i \). If all the species are injected with volumetric flow rate \( Q \) (i.e., \( Q_1 = \cdots = Q_n = Q \)), species \( S_i \) will be diluted to \( 1/n \) of its injected concentration in the \( n \)th combining channel, that is

\[
C_{Si}^{CHn} = C_{S0}^{CHn0}/n.
\]

(6)

**Proof:** The last line of (4) can be reduced to (5) using (3) and other equations in (4).

**Remark 1:** From (6), we can conclude that a higher volume of injected fluids can lead to a decrease of the output concentration of each species.

2) Velocity Change: Injecting fluids into a combining channel influences not only the species concentration but also the flow velocity.

**Lemma 2:** For the fluid mixing from \( n \) inlets to one combining channel, the flow rate in the \( n \)th combining channel can be expressed in terms of average velocity and channel geometry as

\[
w_{CHn} h_{CHn} v_{eff}^{CHn} = w_{CH(n-1)} h_{CH(n-1)} v_{eff}^{CH(n-1)} + w_n h_n v_{eff}^n,
\]

(7)

where \( v_{eff}^n, w_n, \) and \( h_n \) are the average velocity, the width, and the height of Inlet \( n \), and \( v_{eff}^{CHn}, w_{CHn}, \) and \( h_{CHn} \) are the average velocity, the width, and the height of the \( n \)th combining channel, respectively. If all inlets and combining channels share the same geometry and the same average velocity \( v_{eff} \), the average velocity in the \( n \)th combining channel becomes

\[
v_{eff}^{CHn} = n v_{eff}.
\]

(8)

**Proof:** Based on the Kirchoff’s Current Law and (1), we can obtain (7). □

**Remark 2:** It is revealed in (8) that a higher volume of injected fluids can lead to an increase of the average velocity.

**B. Fluid Separation at Bifurcation Connections**

In a microfluidic circuit, a single flow can be separated into different flow streams at a bifurcation connection, and we name this behavior as fluid separation for simplicity. Let us consider a microfluidic device with one inlet and \( n \) outlets as shown in Fig. 2(a), where a single flow is separated into \( n \) streams travelling over \( n \) daughter channels. Assuming that the solution containing species \( S_1 \) is injected with concentration \( C_{S10} \) and average velocity \( v_{eff} \), the concentration at each outlet is the same as \( C_{S10} \), because species \( S_1 \) is not diluted by other species. However, the average velocity in each outlet varies for different geometry of its daughter channel. To derive the outlet velocities, we establish the hydraulic circuit model in Fig. 2(b). Analogous to current division in electric circuits, the relationship between the volumetric flow rate \( Q_i \) (\( 1 \leq i \leq n \)) and the supplied volumetric flow rate \( Q \) can be described by [30, eq. (18)]

\[
Q_i = R_{eq} Q / R_i,
\]

(9)

where \( R_i \) is the hydraulic resistance of the \( i \)th daughter channel and \( R_{eq} \) is the equivalent resistance of all daughter channels. Let us denote \( L_{DI} \) as the length from the crosspoint Node A in Fig. 2(b) to outlet \( i \), and \( w_i \) and \( h_i \) as the geometry width and height of the \( i \)th daughter channel, \( R_i \) [30, eq. (10)] and \( R_{eq} \) [30, eq. (13)] can be calculated as

\[
R_{eq} = \frac{1}{(1/R_1 + 1/R_2 + \cdots + 1/R_n)},
\]

(10)

and

\[
R_i = \frac{12 \eta L_{DI}}{w_i h_i^3 \sum_{i=1}^{3,5,\cdots} 10^2 h_i^2 \tan h_i (\frac{s_i w_i}{2 h_i})},
\]

(11)
and undergoes a depletion by species

Moreover, we assume that the flows carrying chemical

As shown in Fig. 3, the proposed AND gate consists of the

Substituting (1) into (9), we can obtain (12). When

We present our proposed AND gate design in Fig. 3.

A. Convection-Diffusion Channel

Although (16) has been solved in [27], the complex expression of the solution does not allow the cascaded channels to be mathematically solvable in closed-form. This shortcoming

1The rectangular-shaped cross-section is a common geometry considered in MC literature [32]–[34]. The methodology presented in this paper can be also applied to other cross-section shapes.
motivates us to derive the impulse response of a microfluidic channel so that the output of a microfluidic circuit can be written as the convolution of an input and a cascade of the impulse response of each channel. We solve the impulse response in the following theorem.

**Theorem 1:** The impulse response of a straight convection-diffusion channel is derived as

\[
H(x, t) = \frac{1}{2\pi} \int_{0}^{\infty} [e^{-j\omega x} C_{S_i}(x, \omega) + e^{j\omega x} \overline{C_{S_i}(x, \omega)}] d\omega,
\]

where

\[
\overline{C_{S_i}(x, \omega)} = \exp \left[ \left( v_{\text{eff}} x / 2D_{\text{eff}} \right) - \sqrt{x^2 (v_{\text{eff}}^2 + 4j\omega D_{\text{eff}}) / 4D_{\text{eff}}^2} \right]
\]

and \( C_{S_i}(x, \omega) \) is the complex conjugate of \( C_{S_i}(x, \omega) \).

**Proof:** Please refer to the Appendix A.

From **Theorem 1**, the concentration of species \( S_i \) can be expressed as

\[
C_{S_i}(x, t) = C_{S_{i0}}(t) * H(x, t),
\]

where \( C_{S_{i0}}(t) \) is the input concentration of species \( S_i \) at channel inlet and *\( *\) denotes the convolution operator.

**B. Reaction Channel With a Thresholding Reaction**

When a microfluidic channel contains a thresholding reaction \( S_i + S_j \rightarrow S_k \), according to (14) and [35, eq. (9.13)], the spatial-temporal concentration distributions of reactant and product are

\[
\frac{\partial C_{S_i}(x, t)}{\partial t} = D_{\text{eff}} \frac{\partial^2 C_{S_i}(x, t)}{\partial x^2} - v_{\text{eff}} \frac{\partial C_{S_i}(x, t)}{\partial x} - k C_{S_i}(x, t) C_{S_j}(x, t),
\]

\[
\frac{\partial C_{S_k}(x, t)}{\partial t} = D_{\text{eff}} \frac{\partial^2 C_{S_k}(x, t)}{\partial x^2} - v_{\text{eff}} \frac{\partial C_{S_k}(x, t)}{\partial x} + k C_{S_i}(x, t) C_{S_j}(x, t).
\]

Compared with the convection-diffusion equation in (16), the newly introduced reaction term is fully coupled with convection and diffusion process, which complicates the resolution of (20) and (21). A strategy to tackle this coupling is to apply the "operator splitting" method. It first divides an original differential equation into several sub-equations, which are solved separately to give their individual solutions. Then, the solutions for sub-equations are combined to form a solution for the original equation [36]. The derived impulse response of a convection-diffusion channel in **Theorem 1** motivates us to separate a convection-diffusion-reaction equation into a reaction term and a convection-diffusion term. This separation can be achieved via 1) assuming the reactants are added into a virtual reactor, and the unconsumed reactants and generated product flow into a convection-diffusion channel as soon as the reaction stops; and 2) treating the solution of the reaction term as the initial input for the convection-diffusion part.

With species \( S_i \) and \( S_j \) continuously flowing into a channel, we regard that \( S_i \) and \( S_j \) are continuously added into a virtual reactor, where the continuous reactant supply is a superposition of reactant addition with constants at different times. To solve the reaction part, we consider the following two scenarios:

- **Scenario 1:** species \( S_i \) and \( S_j \) are only added at \( t = 0 \) with concentration \( C_{S_{i0}} \) and \( C_{S_{j0}} \).
- **Scenario 2:** species \( S_i \) and \( S_j \) are added continuously with concentration \( C_{S_{i0}}(t) \) and \( C_{S_{j0}}(t) \).

We first derive the concentration changes of reactants and product for **Scenario 1**, which will then be applied to **Scenario 2** to derive the solutions of the separated reaction term.

1) **Scenario 1:** Let \( c(t) \) denote the consumed concentration of reactant \( S_i \) or \( S_j \) during the reaction. Note that \( c(t) \) can also represent the concentration of product species \( S_k \) due to a one-to-one stoichiometric relation between reactants and product. The remaining concentrations of species \( S_i \) and \( S_j \) can be expressed as

\[
\begin{align*}
C_{S_i}(t) &= C_{S_{i0}} - c(t), \\
C_{S_j}(t) &= C_{S_{j0}} - c(t).
\end{align*}
\]

Then, the reaction equation can be expressed as [35, eq. (9.13)]

\[
d[C_{S_{i0}} - c(t)]/dt = -k[C_{S_{i0}} - c(t)][C_{S_{j0}} - c(t)].
\]

After rearrangement, eq. (23) becomes

\[
\frac{dc(t)}{[C_{S_{i0}} - c(t)][C_{S_{j0}} - c(t)]} = k dt.
\]

By taking the integral of the two sides of (24), we yield

\[
c(t) = \begin{cases} 
C_{S_{i0}} \exp \left[ (C_{S_{i0}} - C_{S_{j0}}) kt \right] - C_{S_{i0}} C_{S_{j0}}, \\
C_{S_{j0}} \exp \left[ (C_{S_{i0}} - C_{S_{j0}}) kt \right] - C_{S_{i0}}, \\
C_{S_{i0}} C_{S_{j0}} \exp \left[ (C_{S_{i0}} - C_{S_{j0}}) kt \right] - C_{S_{i0}} C_{S_{j0}}, \\
C_{S_{i0}} C_{S_{j0}} \exp \left[ (C_{S_{i0}} - C_{S_{j0}}) kt \right] - C_{S_{i0}} C_{S_{j0}},
\end{cases}
\]

\[
C_{S_{i0}} \geq C_{S_{j0}}.
\]

**Remark 4:** It can be observed from (25) that \( c(t) \) is proportional to the rate constant \( k \). The higher the rate constant is, the faster a reactant is consumed and decreased to zero.

**Lemma 4:** For reaction \( S_i + S_j \rightarrow S_k \), when reaction rate \( k \rightarrow \infty \), the consumed concentration \( c(t) \) of reactant can be derived as

\[
\lim_{k \to \infty} c(t) = \varphi(C_{S_{i0}}, C_{S_{j0}}),
\]

where \( C_{S_{i0}} \) and \( C_{S_{j0}} \) are the initial concentrations of species \( S_i \) and \( S_j \), and \( \varphi(\cdot, \cdot) \) is defined as

\[
\varphi(x, y) = \min \{x, y\}.
\]

**Proof:** With \( k \to \infty \), eq. (25) can be easily reduced to (26).
Algorithm 1 The Calculation of Remaining Concentrations of Species $S_i$ and $S_j$

**Input:** The input concentrations $C_{S_{i0}}(t)$ and $C_{S_{j0}}(t)$. The time step $\Delta t$.

1. Initialization of $C_{S_{i0}}^0 = C_{S_{i0}}^{0,a}$ and $C_{S_{j0}}^0 = C_{S_{j0}}^{0,a}$.
2. for $n = 1, \lfloor T/\Delta t \rfloor$ do
   3. Calculate the consumed concentration $C_{i} C_{\Delta t}^{n} C_{j} C_{\Delta t}^{n} C_{i}$ during $[(n - 1)\Delta t, n\Delta t]$ according to (25) by interchanging $C_{S_{i0}} \rightarrow C_{S_{i0}}^{n, -1}$ and $C_{S_{j0}} \rightarrow C_{S_{j0}}^{n, -1}$.
   4. Update the remaining concentration $C_{S_{i}, r}^{n} = C_{S_{i}}^{n, -1} - C_{i} C_{\Delta t}^{n-1}$ and $C_{S_{j}, r}^{n} = C_{j} C_{\Delta t}^{n-1} - C_{j} C_{\Delta t}^{n-1}$.
   5. Update the initial concentration $C_{S_{i0}}^{n} = C_{S_{i}}^{n, -1} C_{i} C_{\Delta t}^{n} C_{j} C_{\Delta t}^{n}$ and $C_{S_{j0}}^{n} = C_{S_{j}}^{n, -1} C_{i} C_{\Delta t}^{n} C_{j} C_{\Delta t}^{n}$ for $[n\Delta t, (n + 1)\Delta t]$.
3. end

2) Scenario 2: Now, we consider the continuous injection of species $S_i$ and $S_j$ with concentrations $C_{S_{i0}}(t)$ and $C_{S_{j0}}(t)$. Scenario 2 can be regarded as a superposition of Scenario 1 in time domain. To apply the analysis of Scenario 1, we first discretize the reaction process into many time intervals with step $\Delta t$. Thus, the added concentration of species $S_i$ can be denoted as $C_{S_{i0}}^{0,a} = C_{S_{i0}}(n\Delta t) \ (n \geq 0)$, where the subscript $a$ refers to addition. We also denote $C_{S_{i0}}^{n}$ and $C_{S_{i}, r}^{n}$ as the initial and the remaining concentrations of $S_i$ at $t = n\Delta t$, respectively. The same notations are also applied to species $S_j$.

We propose Algorithm 1 to numerically calculate the remaining concentrations of $S_i$ and $S_j$ for reaction $S_i + S_j \rightarrow S_k$. Algorithm 1 describes that for any time interval $[n\Delta t, (n + 1)\Delta t]$, the consumed concentration can be calculated according to (25), but with different initial concentrations $C_{S_{i0}}^{0,a}$. The difference in the initial concentration is due to the fact that the initial concentration of any time interval is influenced not only by the newly added concentration, but also by the incompletely consumed concentration that added in previous intervals. For instance, the initial concentration $C_{S_{i0}}^{0,a}$ for the time interval $[\Delta t, 2\Delta t]$ is the sum of the newly added concentration $C_{S_{i0}}^{1,a}$ and the remaining concentration $C_{S_{i}, r}^{1}$ that added at $t = 0$.

The value of rate constant $k$ influences the approximation accuracy. The smaller the $k$ is, the larger volume of reactants remain. The unconsumed reactants accumulate in reactor and would participate into the reaction in the following time interval, which introduces correlation between different time intervals. By contrast, this correlation does not exist in practical scenario. As shown in Fig. 4, for time interval $[\Delta t, 2\Delta t]$, the flowing fluid carries remaining reactants added at $t = 0$ and $t = \Delta t$ forward, preventing them from interacting with each other. Therefore, in the virtual reactor, we should make rate constant approach infinity to ensure that reaction is always complete inside any time interval, thus eliminating the correlation.

3) With $\Delta t \to 0$, the remaining concentrations of $S_i$ and $S_j$ calculated in Algorithm 1 reduce to

$$C_{S_{i}, r}(t) = C_{S_{i0}}(t) - \varphi[C_{S_{i0}}(t), C_{S_{j0}}(t)], \quad (28a)$$

$$C_{S_{j}, r}(t) = C_{S_{j0}}(t) - \varphi[C_{S_{i0}}(t), C_{S_{j0}}(t)], \quad (28b)$$

where $\varphi(\cdot, \cdot)$ is given in (27).

We derive the output concentrations of species $S_i$, $S_j$ and $S_k$ in the following lemma.

**Lemma 5:** For a straight reaction channel with thresholding reaction $S_i + S_j \rightarrow S_k$, the output concentrations of species $S_i$, $S_j$, and $S_k$ can be derived as

$$C_{S_{i}}(x, t) = C_{S_{i}, r}(t) * H(x, t), \quad (29a)$$
$$C_{S_{j}}(x, t) = C_{S_{j}, r}(t) * H(x, t), \quad (29b)$$
$$C_{S_{k}}(x, t) = [C_{S_{i0}}(t), C_{S_{j0}}(t)] * H(x, t), \quad (29c)$$

where $C_{S_{i}, r}(t)$, $C_{S_{j}, r}(t)$, $H(x, t)$, and $\varphi(\cdot, \cdot)$ are given in (28a), (28b), (17), and (27), respectively.

**Proof:** Recall that we separate a convection-diffusion-reaction equation into a reaction part and a convection-diffusion part, we consider the remaining concentrations of $S_i$ in (28a) and $S_j$ in (28b) as inputs to a straight convection-diffusion channel. According to (19), we can obtain (29a) and (29b). The derivation of (29c) can see Appendix B.

C. Reaction Channel With an Amplifying Reaction

**Lemma 6:** For a straight reaction channel with amplifying reaction $S_i + Amp \rightarrow S_i + O$, the output concentration of species $O$ can be derived as

$$C_{O}(x, t) = [C_{Amp_{o}}(t) * \mathbb{1}_{\{C_{S_{i0}}(t) > 0\}}] * H(x, t), \quad (30)$$

where $C_{Amp_{o}}(t) = C_{Amp_{o0}}(t)$ and $C_{S_{i0}}(t)$ are the injected concentrations of species $Amp$ and $S_i$, $u(t)$ is the Heaviside step function, $\mathbb{1}_{\{\}}$ is the indicator function that represents the value 1 if the statement is true, and zero otherwise.

**Proof:** To analyze a straight microfluidic channel with amplifying reaction $S_i + Amp \rightarrow S_i + O$, we also separate it into a reaction term and a convection-diffusion term. For the reaction term, as species $O$ is only produced in the presence of $S_i$ and the concentration of species $O$ equals the injected concentration of species $Amp$ [31], the reaction solution can be expressed as $C_{Amp_{o}}(t) * \mathbb{1}_{\{C_{S_{i0}}(t) > 0\}}$. Taking the reaction solution as the initial input for a convection-diffusion channel, we derive the concentration of product $O$ in (30).

Throughout this paper, the superscript for concentration $C$ does not represent a mathematical operation.
D. Elementary Blocks

Relying on the analyses of fluid mixing in Lemma 1 and 2, convection-diffusion channel in Theorem 1, and convection-diffusion-reaction channel in Lemma 5 and 6, we focus on the analysis of four elementary blocks of our designed AND gate (Fig. 3) in Table I. Meanwhile, to simplify the output expression of a microfluidic circuit, we also define five typical operators for the four elementary blocks. As shown in Table I, the operator $T[\cdot]$ represents the output of a convection-diffusion channel with length $L_T$, and can be expressed as

$$T[C_{S_i}(t), n] \triangleq C_{S_i}(t) \ast H_n(L_T, t),$$

(31)

where the subscript $n$ of $H_n$ indicates that the average velocity in the channel is $n v_{\text{eff}}$.

For the block with thresholding reaction $S_i + S_j \rightarrow S_k$, solutions containing species $S_i$ and $S_j$ are injected to a channel with length $L_C$ from two inlets. The initial concentrations of species $S_i$ and $S_j$ are $C_{S_{i0}}(t)$ and $C_{S_{j0}}(t)$, and the injection speeds of species $S_i$ and $S_j$ are $(n-1)v_{\text{eff}}$ and $v_{\text{eff}}$. The combining of two solutions will result in a concentration dilution, and the diluted concentrations of $S_i$ and $S_j$ are $(n-1)C_{S_{i0}}(t)/n$ and $C_{S_{j0}}(t)/n$ following (5) in Lemma 1, respectively. Meanwhile, the average velocity will increase to $nv_{\text{eff}}$ following (7) in Lemma 2. Then, species will flow to a buffer channel before the convection-diffusion-reaction channel filled with grey-gradient color.4 The buffer channel allows reactants to be well mixed before a reaction, and the reactant mixing along the radial direction only relies on diffusion. The minimum buffer length $L_B$ can be estimated as

$$L_B = \frac{w^2 + h^2}{D} v_{\text{eff}}. $$

(32)

The term $\frac{w^2 + h^2}{D}$ quantifies the time required for molecules to be transported over distance $\sqrt{w^2 + h^2}$ along the radial direction to achieve a fully diffusional mixing, and (32) represents how far molecules have traveled along the axial direction by convection. We define operator $G[\cdot]$ to describe the concentration of product $S_k$, and according to (29c), operator $G[\cdot]$ can be expressed as

$$G[C_{S_{i0}}(t), C_{S_{j0}}(t), n] \triangleq \varphi[(n-1)C_{S_{i0}}(t)/n, C_{S_{j0}}(t)/n] \ast H_n(nL_B + L_C, t) \ast H_n(L_R, t).$$

(33)

For the same reaction, we define operator $R[\cdot]$ to characterize the residual concentration of $S_i$. According to (29a), operator $R[\cdot]$ can be expressed as

$$R[C_{S_{i0}}(t), C_{S_{j0}}(t), n] \triangleq [(n-1)C_{S_{i0}}(t)/n - \varphi[(n-1)C_{S_{i0}}(t)/n, C_{S_{j0}}(t)/n]] \ast H_n(nL_B + L_C, t) \ast H_n(L_R, t).$$

(34)

For the amplifying reaction $S_i + \text{Amp} \rightarrow S_i + O$, operator $A[\cdot]$ describes the concentration of product $O$, and can be expressed using Lemma 6 as

$$A[C_{S_{i0}}(t), C_{\text{Amp0}}(t), n] \triangleq [(C_{\text{Amp0}}(t)/n \ast H_n(nL_B + L_C, t) \cdot I_{\{[(n-1)C_{S_{i0}}(t)/n] < H_n(nL_B + L_C, t)\}}) \ast H_n(L_R, t).$$

(35)

As seen in the AND gate design in Fig. 3, a threshold reaction is cascaded with an amplifying reaction; thus, we define operator $F[\cdot]$ as a combination of operators $R[\cdot]$ and $A[\cdot]$, which represents the concentration of product $O$ with $S_i + S_j \rightarrow S_k$ and $S_i + \text{Amp} \rightarrow S_i + O$ as

$$F[C_{S_{i0}}(t), C_{S_{j0}}(t), C_{\text{Amp0}}(t), n] \triangleq A[R[C_{S_{i0}}(t), C_{S_{j0}}(t), n], C_{\text{Amp0}}(t), n + 1].$$

(36)

E. AND Logic Gate Analysis

We denote the initial concentrations of input species $I_1$ and $I_2$ as $C_{I_{10}}(t)$ and $C_{I_{20}}(t)$. Remind that we use non-zero concentration to represent HIGH state (bit-1), and zero concentration to represent LOW state (bit-0). Therefore, at any time $t$, $C_{I_{10}}(t)$ and $C_{I_{20}}(t)$ are either greater than or equal to 0. Species $M$, $ThL$, and $\text{Amp}$ are injected continuously;

| Operator | Elementary Block | Operator Output |
|----------|-----------------|-----------------|
| $T[C_{S_i}(t), n]$ | $L_C$ | $C_{S_i}(t)$: The output of a convection-diffusion channel with length $L_T$ |
| $G[C_{S_{i0}}(t), C_{S_{j0}}(t), n]$ | $L_C$ | $C_{S_k}(t)$: The concentration of product $S_k$ with $S_i + S_j \rightarrow S_k$. |
| $R[C_{S_{i0}}(t), C_{S_{j0}}(t), n]$ | $L_C$ | $C_{S_i}(t)$: The remaining concentration of $S_i$ with $S_i + S_j \rightarrow S_k$. |
| $A[C_{S_{i0}}(t), C_{\text{Amp0}}(t), n]$ | $L_C$ | $C_{O}(t)$: The concentration of product $O$ with $S_i + \text{Amp} \rightarrow S_i + O$. |
| $F[C_{S_{i0}}(t), C_{S_{j0}}(t), C_{\text{Amp0}}(t), n]$ | $L_C$ | $C_{O}(t)$: The concentration of product $O$ with $S_i + S_j \rightarrow S_k$ and $S_i + \text{Amp} \rightarrow S_i + O$. |

**Table I**

Four Elementary Blocks

---

In practice, by cooling the buffer channel while heating the corresponding reaction channel, it would allow us to keep the buffer channel thermally isolated from the reaction channel, which ensures that pre-mixed reactants do not react until they reach the reaction channel [37].
thus, their initial concentrations follow $C_{M_0}(t) = C_{M_0}u(t)$, $C_{ThL_0}(t) = C_{ThL_0}u(t)$, and $C_{Amp_0}(t) = C_{Amp_0}u(t)$. For simplicity, all reactants are injected using the same average velocity $v_{eff}$.

**Theorem 2:** The concentration of product species $O$ in our designed AND gate in Fig. 3 can be derived as

$$C_O(x_5, t) = F\{T[C_N(x_3, t), 4], T[C_{ThL_0}(t), 1], T[C_{Amp_0}(t), 1], 5\},$$

(37)

where

$$C_N(x_3, t) = \frac{1}{2}\left\{G[T[C_{I_{10}}(t), 1], T[C_{M_0}(t), 1], 2] + G[T[C_{I_{20}}(t), 1], T[C_{M_0}(t), 1], 2]\right\} \ast H_2(L_{A2}, t).$$

(38)

In (37) and (38), operators $T[\cdot], G[\cdot], F[\cdot]$ are defined in Table I. $L_{A2}$ is the travelling distance of the laminar located at the centre channel from $x_2$ to $x_3$ in Fig. 3.

**Proof:** To facilitate the understanding of the derivation, we illustrate the flow velocity changes and the mathematical descriptions of some elementary blocks in Fig. 5. At position $x = x_1$, the concentrations of species $I_1$ and $I_2$ can be expressed as $T[C_{I_{10}}(t), 1]$ and $T[C_{I_{20}}(t), 1]$, respectively. Then, species $I_1$ (or $I_2$) and $M$ flow into the second elementary block defined in Table I, and the output product species $N$ can be described using operator $G[\cdot]$, that is: $G[T[C_{I_{10}}(t), 1], T[C_{M_0}(t), 1], 2]$. The species $N$ separately generated by inputs $I_1$ and $I_2$ merge with each other at position $x = x_3$. The concentration of species $N$ at $x = x_3$ can be derived as (38), where the coefficient $1/2$ explains the dilution of species $N$ generated in the upper branch by the flow in the lower branch, or vice versa. Finally, species $N$ travels over a convection-diffusion channel and enters the elementary block $F[\cdot]$ consisting of reactions $N + ThL \rightarrow W$ and $N + Amp \rightarrow N + O$ to produce the gate output $O$. According to the definition of $F[\cdot]$ in (36), the concentration of species $O$ at location $x = x_5$ can be derived as (37).

For the thresholding reaction $N + ThL \rightarrow W$ in Fig. 5, $C_{ThL_0}$ directly determines the gate function. We derive the constraint for $C_{ThL_0}$ in the following lemma.

**Lemma 7:** To ensure that the designed microfluidic circuit exhibits AND logic behavior, the concentration of species $ThL$ needs to satisfy

$$C_{Con} < C_{ThL_0} < 2C_{Con},$$

(39)

where

$$C_{Con} = \lim_{t \to \infty} \frac{4}{5} \cdot \frac{1}{2} \cdot G\{T[C_0u(t), 1], T[C_{M_0}u(t), 1], 2\} \ast q(t),$$

(40)

In (40), $C_0$ is the HIGH concentration of input species $I_1$ and $I_2$, $C_{M_0}$ is the HIGH concentration of species $M$, $q(t) = H_2(L_{A2}, t) \ast H_4(L_T, t) \ast H_5(5L_B + L_C, t)$, $H(x, t)$ is the impulse response derived in (17), and $T[\cdot]$ and $G[\cdot]$ are defined in (31) and (33), respectively.

**Proof:** Let $C_1$ and $C_{ThL}$ denote the steady-state concentrations of species $N$ and $ThL$ at location $x = x_4$, respectively. Fig. 6 plots the concentration of species $N$ before and after reaction $N + ThL \rightarrow W$. When only one input is HIGH, the steady-state concentration $C_1$ can be expressed as

$$C_1 = \lim_{t \to \infty} \frac{4}{5} \cdot \frac{1}{2} \cdot G\{T[C_0u(t), 1], T[C_{M_0}u(t), 1], 2\} \ast q(t),$$

(41)

where the coefficient $4/5$ explains the dilution of species $N$ by species $ThL$. When both inputs are HIGH, the steady-state concentration becomes $2C_1$. For species $ThL$, its steady-state concentration $C_{ThL}$ at $x = x_4$ can be expressed as

$$C_{ThL} = \lim_{t \to \infty} \frac{1}{5} T[C_{ThL_0}u(t), 1] \ast H_5(5L_B + L_C, t),$$

(42)

where the coefficient $1/5$ explains the dilution of species $ThL$ by the flow coming from location $x_3$. As shown in Fig. 6, the blue region represents that both two inputs are HIGH, and the yellow region represents that only one input is HIGH. The relationship between $C_1$ and $C_{ThL}$ has three cases:

1. $C_{ThL} < C_1$: After reaction, the remaining concentration of species $N$ contains the region where one or both the inputs are HIGH.
2. $C_1 < C_{ThL} < 2C_1$: After reaction, the remaining concentration of species $N$ only contains the region where both two inputs are HIGH.
3. $2C_1 < C_{ThL}$: After reaction, species $N$ is completely depleted.

Therefore, to capture the region where both the inputs are HIGH, the concentration of species $ThL$ needs to satisfy the condition $C_1 < C_{ThL} < 2C_1$. Combined with (41) and (42), we can obtain (39) and (40).
IV. MICROFLUIDIC QCSK TRANSMITTER AND RECEIVER

In this section, we present the microfluidic designs to show how logic computations can process molecular concentration so as to achieve QCSK modulation and demodulation. Meanwhile, we also theoretically characterize the output concentration distributions of the proposed QCSK transmitter and receiver. At the end, we discuss the synchronization of molecular species in microfluidic circuits.

A. QCSK Transmitter

1) QCSK Transmitter Design: QCSK modulation represents two digital inputs as four concentration levels of an output signal, which is analogous to the Amplitude Shift Keying (ASK) modulation in wireless communication [4].

A challenge of implementing a QCSK MC transmitter is how to control the output concentration via four different input combinations (i.e., “00”, “01”, “10”, and “11”). We solve this challenge by borrowing the mechanism of an electric 2:4 decoder. In electric circuits, a 2:4 decoder, which has 2 inputs and 4 outputs, selects exactly one of its outputs according to the input combination. Fig. 7 presents the truth table and an implementation of the electric 2:4 decoder, where four AND gates receive the HIGH or the LOW of inputs $I_1$ and $I_2$.

Inspired by the electric 2:4 decoder, we propose a chemical reactions-based microfluidic 2:4 decoder (with a combiner) to realize QCSK modulation as shown in Fig. 8. The proposed microfluidic device is made up of four microfluidic units corresponding to four different concentration outputs. For ease of reference, these four units are named as Unit 4, Unit 3, Unit 2, and Unit 1 from top to bottom. Analogous to the electric 2:4 decoder in Fig. 7, the AND gate in each unit takes either $I_1$ and $I_2$ or their complementary species $P_1$ and $P_2$ as its inputs. Species $P_1$ and $P_2$ are supplied continuously with a HIGH state so that after reactions $I_1 + P_1 \rightarrow W_1$ and $I_2 + P_2 \rightarrow W_2$, the remaining concentrations of species $P_1$ and $P_2$, i.e., $C_{P_1/P_2}(x_1,t)$, can represent the complementary states of species $I_1$ and $I_2$, thus achieving the NOT gate. Unlike an electric 2:4 decoder that an identical voltage level is realized, the proposed chemical 2:4 decoder will output different concentration levels. As each unit output $C_{O_i}^t(t)$ is influenced by $C_{Ampo}^t(t)$ through an amplifying reaction, the concentration variation of transmitted signals is represented via different concentrations of injected species $Amp$ as $C_{Ampo}^t(t) = C_{Ampo}^t(t)$ (1 ≤ $i$ ≤ 4) for different units. Here, we set $C_{Ampo}^4 > C_{Ampo}^3 > C_{Ampo}^2 > C_{Ampo}^1$ to ensure $\max\{C_{O_1}^i(t)\} > \max\{C_{O_2}^i(t)\} > \max\{C_{O_3}^i(t)\} > \max\{C_{O_4}^i(t)\}$. The combiner acts as a transmitter-channel interface and merely combines the four outputs $C_{O_i}^t(t)$. We highlight that it does not have an impact on the QCSK modulation function. Thus, for simplicity we will not consider it in the following analysis, which also brings flexibility to test each unit of our proposed design.

2) QCSK Transmitter Analysis: The objective of the following analysis is to derive the transmitter output $C_{O_i}^t(t)$ of the design in Fig. 8. We first derive the inputs of an AND gate, i.e., the concentrations of $I_1$, $I_2$, $P_1$, and $P_2$ at location $x = x_1$. When input species $I_1$ and $I_2$ directly flow into an AND gate, their concentrations can be expressed as

$$C_{I_1/I_2}(x_1,t) = \left[ T[C_{I_1/I_2}(t), 1] \right] = H_2(L_C + L_{B1} + L_R, t)/2,$$

where $C_{I_1/I_2}(t)$ is the concentration of input species $I_1$ or $I_2$, operator $T[\cdot]$ is defined in Table I, the coefficient $1/2$ explains the dilution of species $I_1$ by species $P_1$ (or $I_2$ by $P_2$). When the complementary species $P_1$ and $P_2$ flow into an AND gate, their concentrations can be expressed as

$$C_{P_1/P_2}(x_1,t) = R\{ T[C_{P_1/I_2}(t), 1], T[C_{I_1/I_2}(t), 1], 2 \},$$

where $C_{P_1/I_2}(t)$ is the input concentration of species $P_1$ or $P_2$, and operator $R[\cdot]$ is defined in Table I.

With the derived AND gate inputs $C_{I_1/I_2}(x_1,t)$ and $C_{P_1/P_2}(x_1,t)$ in (43) and (44), the transmitter output $C_{O_i}^t(t)$ can be expressed by Theorem 2 by interchanging the parameters

- in (38) via: $T[C_{I_1/I_2}(t), 1] \rightarrow C_{I_1/I_2}(x_1,t)$ if an AND gate input is $I_1/I_2$, $T[C_{I_1/I_2}(t), 1] \rightarrow C_{P_1/P_2}(x_1,t)$ if an AND gate input is $P_1/P_2$, $n = 2 \rightarrow n = 3$, $H_2(L_{A_2}, t) \rightarrow H_3(L_{A_2}, t)$;
- in (37) via: $T[C_{N}(x_3,t), 4] \rightarrow T[C_{N}(x_3,t), 6]$, $C_{Ampo}(t) \rightarrow C_{Ampo}(t), n = 5 \rightarrow n = 7$.

B. QCSK Receiver

1) QCSK Receiver Design: From the communication perspective, the QCSK microfluidic receiver is required to distinguish different concentration levels from different input combinations to achieve demodulation. In this paper, we consider a Gaussian signal $C_{O_i}^t(t)$ as the input for the receiver, which can be expressed as

$$C_{O_i}^t(t) = \frac{C_{O_i}^0}{\sqrt{2\pi\sigma^2}} e^{-\frac{(t-\mu)^2}{2\sigma^2}} (1 \leq i \leq 4),$$

where the superscript $t$ indicates the four concentration levels of QCSK, $\mu$ is the mean, and $\sigma$ is the standard deviation. For simplicity, we use $C_{O_i}^t(t)$ to denote the general receiver input. The motivation of using Gaussian signal as the receiver input is that it can reveal the dispersion effect of molecule diffusion (i.e., Taylor dispersion) on the transmitted rectangular signals, thus representing the distortion of transmitted signals occurred in the propagation channel between a transmitter and a receiver. For more details on Taylor dispersion, we refer readers to [29]. To focus on the fundamental principle and
mechanism of our proposed QCSK transceiver, we leave the analysis of the propagation channel between transmitter and receiver for our future work. We also denote \( C_{Y_1}(t) \) and \( C_{Y_2}(t) \) as the final demodulated concentration signals, which correspond to the transmitter concentration inputs \( C_{I_{10}}(t) \) and \( C_{I_{20}}(t) \), respectively.

To detect four concentration levels, we first design three detection units in Fig. 9 to serve as a front-end processing module. Each channel is labeled with a channel number to denote channel length as \( L_{\text{number}} \). By setting \( \max \{ C_{Y_1}(t) \} < C_{T_{10}}^i < \max \{ C_{D}^{i+1}(t) \} \), the front-end processing module can distinguish four concentration regions.

Fig. 9. Three detection units [27] serve as a front-end processing module. Each channel is labeled with a channel number to denote channel length as \( L_{\text{number}} \).

To detect four concentration levels, we first design three detection units in Fig. 9 to serve as a front-end processing module for the QCSK receiver. Each detection unit follows the receiver design in our initial work [27] and is capable of generating a rectangular signal if the maximum concentration of a received signal exceeds a predefined threshold. As shown in Fig. 9, the only difference among three detection units is the injected concentration \( C_{I_{10}}^i(t) = C_{I_{10}}^i u(t) \) \( (1 \leq i \leq 3) \) of thresholding reactant \( T_1 \). By setting \( \max \{ C_{O}^{i}(t) \} < C_{T_{10}}^i < \max \{ C_{D}^{i+1}(t) \} \), the concentration region of \( C_{O}(t) \) can be identified for three-bit binary signals \( B_3B_2B_1 \) as shown in Fig. 9. For instance, if \( \max \{ C_{O}(t) \} > C_{T_{10}}^i \), all detection units will produce a HIGH state with \( B_3B_2B_1 = 111 \).

The three detection units in Fig. 9 can only demodulate \( C_{O}(t) \) to three concentration signals \( C_{B}^{i}(t) \), \( C_{B}^{i+1}(t) \), and \( C_{B}^{i+2}(t) \) instead of \( C_{Y_1}(t) \) and \( C_{Y_2}(t) \), which means extra signal processing units are required. Consider the output of front-end module \( C_{B}(t) \) exhibits a rectangular concentration profile and its digital characteristic is ideal to perform logic computations [19], this motivates us to design logic circuits to transform \( C_{B}^{i}(t) \) to desired outputs \( C_{Y_1}(t) \) and \( C_{Y_2}(t) \).

Table II, the relation between the receiver input \( C_{O}(t) \), front-end module output binary signal \( B \), and receiver output binary signal \( Y \).

| \( \max \{ C_{O}(t) \} \) | \( B_3 \) | \( B_2 \) | \( B_1 \) | \( Y_2 \) | \( Y_1 \) |
|-----------------------|-------|-------|-------|-------|-------|
| \([0, C_{T_{10}}^i] \)  | 0     | 0     | 0     | 0     | 0     |
| \([C_{T_{10}}^i, C_{T_{10}}^{i+1}] \) | 0     | 0     | 1     | 0     | 1     |
| \([C_{T_{10}}^{i+1}, C_{T_{10}}^{i+2}] \) | 0     | 1     | 1     | 0     | 0     |
| \([C_{T_{10}}^{i+2}, \infty] \) | 1     | 1     | 1     | 1     | 1     |

To theoretically characterize receiver outputs \( C_{Y_2}(t) \) and \( C_{Y_1}(t) \), we denote \( C_{[i]}^{i}(t) \) as the concentration of an injected species \([i] \), and \( L_i \) as the length of the microfluidic channel with number \( i \). Moreover,
we assume that the injection velocity of any flow is \( v_{\text{eff}} \).
In the following, we first derive the front-end processing output \( C_B(t) \) in Fig. 9, and then derive the QCSK receiver outputs \( C_{Y2}(t) \) and \( C_{Y1}(t) \) in Fig. 10. In addition, the location and channel number are in bold in the following so that readers can easily follow our derivation.

\( C_B(t) \) derivation: As shown in Fig. 9, each detection unit in the front-end processing module consists of a thresholding reaction \( O + T_1 \rightarrow W \) and an amplifying reaction \( O + A_1 \rightarrow O + B \). The output of a detection unit can be expressed using the operator \( F[\cdot] \) defined in Table I as

\[
C_B(x_5, t) = F\{T[C_{O}(t), 1], T[C_{T_1}(t), 1], T[C_{A_1}(t), 1], 2\},
\]

where \( C_{O}(t) \) is the receiver input concentration.

\( C_{Y2}(t) \) derivation: As shown in Fig. 10(a), \( C_B^1(t) \) and \( C_B^2(t) \) flow into an AND gate to produce \( C_{Y2}(t) \). At \( x = x_6 \), \( C_{Y2}(t) \) can be derived as

\[
C_{Y2}(x_6, t) = F\{T[\frac{1}{2} \sum_{j=1}^{2} C_B^j(x_5, t) * H_3(\frac{2L_2 + L_6 + h}{2}, 6) \times T[C_{T_2}(t), 1], T[C_{A_2}(t), 1], 7\},
\]

where 1/2 represents the dilution of \( C_B^1(x_5, t) \) by \( C_B^2(x_5, t) \) and vice versa, \( H_n(x, t) \) is given in Theorem 1 with \( n \) indicating that the average velocity is \( v_{\text{eff}} \), and the operator \( T[\cdot] \) is defined in Table I.

c) \( C_{Y1}(t) \) derivation: As shown in Fig. 10(b), an XNOR gate and an AND gate are linked to the front-end processing module to produce \( C_{Y1}(t) \).

- **XNOR Gate Analysis:** Relying on the fluid separation analysis in Lemma 3, at \( x = x_5 \), \( C_B^j(x_5, t) \) (\( j = 2, 3 \)) is equally separated from channel 9 to channels 10 due to the symmetrical microfluidic design from \( x_5 \) to \( x_9 \). Therefore, the confluence of \( C_B^3(x_5, t) \) and \( C_B^3(x_5, t) \) occurs, and then is diluted by species \( T_3 \) injected at \( x_7 \). Subsequently, the outer fluid performs reaction \( B + T_3 \rightarrow W \) to capture the region where both \( C_B^3(x_5, t) \) and \( C_B^3(x_5, t) \) are HIGH as the second case in Fig. 6, while the inner fluid flows forward without reaction \( B + T_3 \rightarrow W \). After reactions \( B + A_3 \rightarrow B + R_1 \) and \( B + A_4 \rightarrow B + R_2 \), the concentrations of products \( R_1 \) and \( R_2 \) at \( x = x_9 \) can be expressed as (50) and (51), shown at the bottom of the next page, where the superscript “Inner” and “Outer” represent the outer and inner fluids from \( x_7 \) to \( x_9 \), and 3/4 in (50) represents the dilution of species \( B \) by species \( T_3 \).

After reaction \( R_1 + R_2 \rightarrow W \), the remaining species \( R_1 \) at \( x = x_{10} \) will be HIGH when either \( C_B^3(x_5, t) \) or \( C_B^3(x_5, t) \) is HIGH, thus achieving an XOR gate.\(^5\) Relying on (29a) in Lemma 5, the remaining concentration

\({}^5\)Since there are three inlets in each unit of the front-end processing module and a flow at each inlet is injected with \( v_{\text{eff}} \), the average velocity in channel 4 is \( 3v_{\text{eff}} \).

\({}^6\)As the inner fluid does not perform any reaction from \( x_7 \) to \( x_8 \), after reaction \( B + A_3 \rightarrow B + R_1 \), species \( R_1 \) is HIGH when one or both \( C_B^3(x_5, t) \) and \( C_B^3(x_5, t) \) are HIGH, thus achieving an OR gate. By contrast, with reaction \( B + T_3 \rightarrow W \), after reaction \( B + A_3 \rightarrow B + R_2 \), species \( R_2 \) is HIGH only when both \( C_B^3(x_5, t) \) and \( C_B^3(x_5, t) \) are HIGH, thus achieving an AND gate. Therefore, the XOR gate is consisted of an OR gate, an AND gate, and a thresholding reaction \( R_1 + R_2 \rightarrow W \) as shown in Fig. 10(b).
of species $R_1$ is derived as

$$C_{R_1}(x_{10}, t) = \frac{1}{2} \left\{ C_{R_1}(x_{9}, t) - \phi[C_{R_1}(x_{9}, t), C_{R_2}(x_{9}, t)] \right\} * H_5(L_2 + L_9 + 2w, t) * H_{10}(L_{14}, t) * H_{10}(L_4, t),$$  \tag{52}$$

where $\phi[\cdot, \cdot]$ is given in (27). The cascaded reaction $R_1 + NOT \rightarrow W$ functions as a NOT gate similar to the reaction $I_1 + P_3 \rightarrow W$ in the QCSK transmitter in Fig. 8 in order to achieve the XNOR gate. At $x = x_{11}$, the concentration of $NOT$ can be expressed using the operator $R[\cdot]$ defined in Table I as

$$C_{2^k NOT}^{2k3}(x_{11}, t) = R\{ T[C_{NOT}(t), 1], C_{R_1}(x_{10}, t), 11 \} * H_{11}(2L_2 + L_{18} + h/2, t),$$  \tag{53}$$

where the superscript $2^k3$ represents the species $NOT$ generated by $C_B^2(x_5, t)$ and $C_B^2(x_5, t)$.

**AND Gate Analysis:** The calculation of receiver output $C_Y(t)$ also needs $C_B^1(x_5, t)$. To perform the AND gate, the product species $B$ (indicated by the red arrow) should be converted to molecular type $NOT$ via $B + V \rightarrow NOT$. At $x = x_{11}$, the concentration of species $NOT$ generated by $C_B^1(x_5, t)$ can be expressed using operator $G[\cdot]$ defined in Table I as

$$C_{NOT}^1(x_{11}, t) = G\{ C_B^1(x_5, t) * H_3(L_{16}, t), T[C_{V_0}(t), 1], 4 \} * H_4(2L_2 + 2L_{17} + L_{18} + h/2, t).$$  \tag{54}$$

Finally, we can derive the QCSK receiver output $C_Y(x_{12}, t)$ as

$$C_Y(x_{12}, t) = F\left\{ T[4/15 C_{NOT}(x_{11}, t) + 11/15 C_{2^k NOT}^{2k3}(x_{11}, t), \frac{4}{15}], T[C_{T_{40}}(t), 1], T[C_{A_{40}}(t), 1], 16, \right\},$$  \tag{55}$$

where $4/15$ represents the dilution of $C_{NOT}^1(x_{11}, t)$ by $C_{2^k NOT}^{2k3}(x_{11}, t)$, while $11/15$ represents the dilution of $C_{2^k NOT}^{2k3}(x_{11}, t)$ by $C_{NOT}^1(x_{11}, t)$.

C. Microfluidic Circuit Synchronization

There are mainly two synchronization cases that need to be taken into account: 1) species synchronization at the inlets of microfluidic circuits and 2) species synchronization inside microfluidic circuits. The first case refers to the simultaneous injection of different species to microfluidic circuits. In practice, we can deal with this synchronization issue by grouping syringe pumps with a microcontroller board (e.g., Arduino) and sending the release signal to syringe pumps at the same time. For the second case, one example is the synchronization of the two inputs (i.e., $C_{NOT}^1(x_{11}, t)$ and $C_{NOT}^1(x_{11}, t)$) of the AND gate used in Fig. 10(b). The synchronization of $C_{NOT}^1(x_{11}, t)$ and $C_{NOT}^1(x_{11}, t)$ requires that $C_{NOT}^1(x_{11}, t)$ and $C_{NOT}^1(x_{11}, t)$ should arrive at $x_{11}$ simultaneously, which can be achieved by ensuring the inputs $C_O(t)$ of three detection units have the same traveling time from the front-end module to position $x_{11}$ in Fig. 10(b).

Based on the fact that the convection effect is merely a shift of the molecular profile in time with average velocity and without any change of shape [39], the design should satisfy the following requirement

$$\sum_{i \in I} L_i/v_i = \sum_{j \in J} L_j/v_j,$$  \tag{56}$$

where $I$ is the set of the microfluidic channels used to generate $C_{NOT}^1(x_{11}, t)$, $J$ is the set of the microfluidic channels used to generate $C_{NOT}^1(x_{11}, t)$, and $L_i$ and $v_i$ are the channel length and the corresponding flow velocity of microfluidic channel with label $i$.

V. PERFORMANCE EVALUATION

In this section, we implement our proposed microfluidic AND gate, QCSK transmitter, and QCSK receiver design.

---

$$C_{R_1}(x_{9}, t) = A\left\{ T[3/2 \sum_{j=2}^3 C_B^j(x_{5}, t) * H_5(3L_2 + L_9 + 2L_{10} + L_{11} + h + 2w, t), 3] * \frac{3}{4} H_4(L_2 + L_{12} + L_4, t), T[C_{A_{40}}(t), 1], 5, \right\},$$  \tag{50}$$

$$C_{R_2}(x_{9}, t) = F\left\{ T[1/2 \sum_{j=2}^3 C_B^j(x_{5}, t) * H_5(3L_2 + L_9 + 2L_{10} + L_{11} + h + 2w, t), 3] T[C_{T_{40}}(t), 1], T[C_{A_{40}}(t), 1], 4. \right\}.  \tag{51}$$
in Fig. 3, Fig. 8, and Fig. 10 using COMSOL Multiphysics, which are then used to validate our corresponding theoretical analysis. The impulse response \( H(x, t) \) given in Theorem 1 is computed in Matlab using `quadgk`. As `quadgk` is only an approximation of \( H(x, t) \), the computed results may fluctuate around their steady values. If a computed value is slightly larger than steady value 0, it can induce an instant change on the output value of the indicator function in (30) from 0 to 1, which would further lead to a generation of output signals in undesired regions after an amplifying reaction. To avoid this phenomenon, we modify the statement of an indicator function \( C_{S_0}(t) > 0 \) as \( C_{S_0}(t) > \frac{1}{10} \max \{ C_{S_0}(t) \} \). By doing so, the width of a rectangular output is expected to be smaller than that of the corresponding simulation result. In COMSOL simulations, unless otherwise stated, we set \( v_{\text{eff}} = 0.1 \text{cm/s}, D = 10^{-6} \text{m}^2/\text{s}, w = 20 \mu\text{m}, h = 10 \mu\text{m}, k = 400 \text{cm}^3/(\text{mol} \cdot \text{s}) \). Consider these values and water as solvent, the value of the Reynolds number is roughly 3, which is less than 2000 so that the laminar flow assumption is valid. Furthermore, we use “Ana.” and “Sim.” to abbreviate “Analytical” and “Simulation” in all figures.

### A. AND Logic Gate

Fig. 11 presents the COMSOL simulation results of the AND logic gate design depicted in Fig. 3. We set the parameters: \( C_{I_{10}}(t) = 8[u(t - 1) - u(t - 3)], C_{I_{20}}(t) = 8[u(t - 2) - u(t - 4)], C_{M_0}(t) = 8u(t), C_{Amp_0}(t) = 12u(t), L_T = 80 \mu\text{m}, L_C = 20 \mu\text{m}, L_R = 500 \mu\text{m}, L_{A2} = 120 \mu\text{m} \). In order to examine the impact of the injected concentration of species \( T_hL \) on the gate behavior, we consider three cases: \( C_{T_{hL0}}(t) = 5u(t), C_{T_{hL0}}(t) = 10u(t), C_{T_{hL0}}(t) = 20u(t) \), which correspond to the cases \( C_{T_hL} < C_1, C_1 < C_{T_hL} < 2C_1, \) and \( C_{T_hL} < 2C_1 \) in Fig. 6, respectively.

Fig. 11(a) plots the concentrations of species \( N \) and \( T_hL \) before reaction \( N + T_hL \rightarrow W \) in Fig. 3. We observe that the simulated concentration points agree with the analytical concentration curves, thus demonstrating the correctness of our analysis of the AND logic gate. In addition, for \( C_{T_{hL0}}(t) = 10u(t) \), the width of species \( O \) equals the width where both input species \( I_1 \) and \( I_2 \) are HIGH, demonstrating the desired behavior of an AND gate. Furthermore, due to the modification of the indicator function set, we can see the width of (37) is smaller than that of the simulation results.

### B. QCSK Transmitter

Fig. 12 plots the outputs of the proposed microfluidic QCSK transmitter design in Fig. 8 and their analytical values \( C_{\text{Q}_i}(t) \) in Sec. IV-A.2. Species \( I_1 \) and \( I_2 \) are injected with either \( 12[u(t - 1) - u(t - 3)] \) representing bit 1 or \( 0u(t) \) representing bit 0. For other molecular types, their injected concentrations are set as: \( C_{P_{i0}}(t) = C_{P_{i0}}(t) = 12[u(t - 1) - u(t - 3)], C_{M_0}(t) = 12u(t), C_{T_{hL0}}(t) = 16u(t), C_{Amp_0}(t) = 24u(t), C_{Amp_0}(t) = 16u(t), C_{Amp_0}(t) = 8u(t), \) and \( C_{Amp_0}(t) = 0 \). The buffer channels are configured with \( L_{B1} = 100 \mu\text{m}, L_{B2} = 150 \mu\text{m}, L_{B3} = 350 \mu\text{m}, \) and \( L_{B4} = 400 \mu\text{m} \).

As shown in Fig. 12, for any input combination, only one unit outputs a HIGH signal except from the case where both \( I_1 \) and \( I_2 \) are LOW due to \( C_{Amp_0}(t) = 0 \). In addition, for each unit, it is selected under a specific input combination (e.g., Unit 4 is only selected when both input species \( I_1 \) and \( I_2 \) are HIGH) so that the outputs for other three input combinations are all in a LOW state and the corresponding curves are completely overlapped. Moreover, the analytical curves always capture the simulation points, which again demonstrates the effectiveness of our theoretical analysis \( C_{\text{Q}_i}(t) \) in Sec. IV-A.2. As species \( Amp \) is supplied with different injected concentrations for each unit, we see that the selected unit reaches

**TABLE III**

| Molecular Type | Concentration (mol/cm²) |
|----------------|-------------------------|
| \( A_1 \)      | \( 8u(t) \)              |
| \( A_2 \)      | \( 20u(t) \)             |
| \( A_3 \)      | \( 20u(t) \)             |
| \( A_4 \)      | \( 5u(t) \)              |
| \( \text{NFF} \)| \( 22u(t) \) |

Fig. 11. The evaluation of an AND logic gate.
C. QCSK Receiver

To evaluate the proposed QCSK receiver design in Fig. 10, we consider Gaussian signals $C_O(t)$ with four peak amplitudes as the receiver input: $C_{O_1}^1 = 0$, $C_{O_2}^2 = 0.85$, $C_{O_3}^3 = 1.7$, and $C_{O_4}^4 = 2.55$, with the mean $\mu = 2$ and standard deviation $\sigma = 0.34$. Accordingly, to distinguish these four concentration levels, the concentration of species $T_1$ for three units in Fig. 9 are set as: $C_{T_0}^{3.0}(t) = 2.2u(t)$, $C_{T_0}^{2.1}(t) = 1.2u(t)$, and $C_{T_0}^{1.0}(t) = 0.8u(t)$. Other parameters and the geometry are summarized in Table III and IV.

Fig. 13 plots the outputs of the proposed QCSK receiver design in Fig. 10 and the corresponding analytical results of $C_Y(t)$ in (49) and $C_Y(t)$ in (55). First, we can see that although simulation curves are not in precise agreement with analytical curves, the close match can still confirm the correctness of the mathematical characterization of $C_Y(t)$ and $C_Y(t)$. Second, we observe that the width difference between analytical and simulation curves for $C_Y(t)$ is larger than that for $C_Y(t)$. This is because the modification of the statement of an indicator function results in the width difference in each amplifying reaction, and the more amplifying reactions are utilized to compute $C_Y(t)$ in Fig. 10(b), the bigger the width difference is. Third, we see that the proposed receiver design can well demodulate the received signal $C_O(t)$ to two outputs $C_Y$ and $C_Y(t)$. Recall that we use non-zero concentration to represent HIGH state (bit-1), and zero concentration to represent LOW state (bit-0). We also observe that the relationship between the maximum concentration of the receiver input $\max \{C_O(t)\}$, the concentration of species $T_1$, and binary signals $Y_2$ and $Y_1$ is in consistent with the truth table of Table II, which demonstrates the effectiveness of our proposed design.

VI. CONCLUSION

In this paper, we considered the realization of QCSK modulation and demodulation functionalities for MC using chemical reactions-based microfluidic circuits. We first presented an AND gate design to demonstrate the logic computation capabilities of microfluidic circuits, and then showed how to utilize logic computations to achieve QCSK modulation and demodulation functions. To theoretically characterize a microfluidic circuit, we established a general mathematical framework which is scalable with the increase of circuit scale and can be used to analyze other new and more complicated circuits. We derived the output concentration distributions of the AND gate, QCSK transmitter and receiver designs. Simulation results obtained from COMSOL Multiphysics showed all the proposed microfluidic circuits responded appropriately to input signals, and closely matched our derived analytical results. The QCSK design can be extended to general $n$th order CSK modulation scheme by using a microfluidic $n$ decoder constructed from $2^n$ AND gates. This extension reveals the scalability and extendibility of our proposed microfluidic circuit design. Thus, we believe that this paper provides not only a design principle and mathematical
framework for microfluidic MC circuits, but also a foundation for utilizing simple microfluidic logic gates to produce diverse and complex signal processing functions.

The proposed mathematical framework is a deterministic model and the COMSOL simulation results describe the deterministic responses of our proposed microfluidic circuits. Although COMSOL Multiphysics simulator can simulate flows in the most accurate way, proposing a statistical model for microfluidic circuit to provide more communication insights is an interesting direction for future work. This statistical model can include the noise caused by the mechanical limitations of the solution injections devices (e.g., syringe pump), the noise caused by the chemical reactions, and the noise caused by the external observation equipment (e.g., spectrometer or pH meter). Furthermore, the incorporation of transmitter-channel interface, propagation channel, and the channel-receiver interface into the model makes the model more comprehensive and complete.

APPENDIX A
PROOF OF THEOREM 1

To derive the impulse response \( H(x, t) \), we formulate the following initial and boundary conditions for (16)

\[
\begin{align*}
C_S(x, 0, t) & = \delta(t), \quad \text{(57a)} \\
C_S(x, 0, t) & = 0, \quad x \geq 0, \quad \text{(57b)} \\
\frac{\partial C_S(x, t)}{\partial x} |_{x=\infty} & = 0, \quad t \geq 0, \quad \text{(57c)}
\end{align*}
\]

where \( \delta(\cdot) \) is the Kronecker delta function. The Laplace Transform of (16) with respect to \( t \) is

\[
D_{\text{eff}} \frac{\partial^2 \tilde{C_S}(x, s)}{\partial x^2} - v_{\text{eff}} \frac{\partial \tilde{C_S}(x, s)}{\partial x} - s \tilde{C_S}(x, s) = 0,
\]

where \( \tilde{C_S}(x, s) \) is the Laplace Transform of \( C_S(x, t) \). The general solution for (58) can be expressed as

\[
\tilde{C_S}(x, s) = d_1 e^{\frac{\nu_{\text{eff}} + \sqrt{\nu_{\text{eff}}^2 + 4 D_{\text{eff}} s}}{2 D_{\text{eff}}}} + d_2 e^{\frac{\nu_{\text{eff}} - \sqrt{\nu_{\text{eff}}^2 + 4 D_{\text{eff}} s}}{2 D_{\text{eff}}}} x,
\]

where \( d_1 \) and \( d_2 \) are two constants. To determine \( d_1 \) and \( d_2 \), we also apply Laplace Transform to (57a) and (57c), which are

\[
\begin{align*}
\tilde{C_S}(0, s) & = 1, \quad \text{(60)} \\
\frac{\partial \tilde{C_S}(x, s)}{\partial x} |_{x=\infty} & = 0. \quad \text{(61)}
\end{align*}
\]

Constrained by these two conditions, we arrive at the particular solution for (58) as

\[
\tilde{C_S}(x, s) = e^{\frac{\nu_{\text{eff}} - \sqrt{\nu_{\text{eff}}^2 + 4 D_{\text{eff}} s}}{2 D_{\text{eff}}}} x. \quad \text{(62)}
\]

In order to obtain the impulse response, we need to calculate the inverse Laplace Transform of (62), i.e., \( \mathcal{L}^{-1} \{ \tilde{C_S}(x, s) \} \). In the following, we provide two methods to derive \( \mathcal{L}^{-1} \{ \tilde{C_S}(x, s) \} \). The first method relies on the table provided in [40]. According to [40, eqs. (1.3) and (5.58)], the inverse Laplace Transform\(^3\) can be derived as

\[
\mathcal{L}^{-1} \{ \tilde{C_S}(x, s) \} = \frac{x}{2 \sqrt{\pi D_{\text{eff}}}} e^{\frac{-x^2}{4 D_{\text{eff}}}} x. \quad \text{(63)}
\]

However, when we consider a much more practical scenario, e.g., a time-varying distribution of average velocity due to the imperfectness of syringe pumps, the first method may become infeasible. Therefore, the second method is more general. This method resorts to the Gil-Pelaez theorem and regards the distribution function (CDF) for \( \mathcal{L}^{-1} \{ \tilde{C_S}(x, s) \} \) as a probability density function whose characteristic function\(^3\) is \( \tilde{C_S}(x, \omega) \). The cumulative distribution function (CDF) for \( \mathcal{L}^{-1} \{ \tilde{C_S}(x, s) \} \) can be expressed as [41]

\[
F(x, t) = \frac{1}{2} - \frac{1}{\pi} \int_0^\infty e^{-j \omega x} \tilde{C_S}(x, \omega) - e^{j \omega x} \tilde{C_S}(x, \omega) \frac{d\omega}{2j\omega},
\]

where \( \tilde{C_S}(x, \omega) \) is the complex conjugate of \( \tilde{C_S}(x, \omega) \). Take the derivative of \( F(x, t) \) with respect to \( t \), we can arrive at (17).

APPENDIX B
THE DERIVATION OF THE CONCENTRATION OF PRODUCT SPECIES \( S_k \) IN (29c)

To derive the concentration of product \( S_k \), we combine (20) and (21) and denote \( C(x, t) = C_{S_k}(x, t) + C_{S_k}(x, t) \), which yields

\[
\frac{\partial C(x, t)}{\partial t} = D_{\text{eff}} \frac{\partial^2 C(x, t)}{\partial x^2} - v_{\text{eff}} \frac{\partial C(x, t)}{\partial x} . \quad \text{(65)}
\]

The sum concentration has the following initial and boundary conditions

\[
\begin{align*}
C(0, t) & = C_{S_k}(0, t), \quad \text{(66a)} \\
C(x, 0) & = 0, \quad x \geq 0, \quad \text{(66b)} \\
\frac{\partial C(x, t)}{\partial x} |_{x=\infty} & = 0, \quad t \geq 0. \quad \text{(66c)}
\end{align*}
\]

As these conditions are the same as (57a)-(57c), we can write

\[
C(x, t) = C_{S_k}(0, t) * H(x, t). \quad \text{(67)}
\]

Combined with (28a) and (29a), the concentration of product \( S_k \) is

\[
C_{S_k}(x, t) = C(x, t) - C_{S_k}(x, t) = \varphi(C_{S_k}(t), C_{S_k}(t)) * H(x, t). \quad \text{(68)}
\]

\(^3\)In Matlab, we need to manually set value 0 for (63) when \( t = 0 \) as Matlab returns the scalar “not a number” (NaN).

\(^4\)The Fourier Transform of a probability density function is its characteristic function. The Laplace Transform \( \tilde{C_S}(x, s) \) can be converted to the corresponding Fourier Transform \( \tilde{C_S}(x, \omega) \) via \( s = j\omega \).
