

A Crossbar Interconnection Network in DNA

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Abstract—DNA computers provide exciting challenges and opportunities in the fields of computer architecture, neural networks, autonomous micromechanical devices, and chemical reaction networks. The advent of digital abstractions such as the seesaw gates hold many opportunities for computer architects to realize complex digital circuits using DNA strand displacement principles. The paper presents a realization of a single bit, 2×2 crossbar interconnection network built using seesaw gates. The functional correctness of the implemented crossbar was verified using a chemical reaction simulator.

I. INTRODUCTION

A. DNA as a Computational Framework

Adleman used DNA sequences to solve the seven-city Hamiltonian path problem successfully demonstrating the usefulness of DNA as a computing substrate[1]. Subsequently, DNA strand displacement techniques[2] have been explored by researchers in a broad range of information processing devices. Boolean logic gates[3][4], chemical reaction networks[5][6], and neural networks[7] have been successfully demonstrated using the DNA circuit design paradigm. DNA strand displacement techniques use no additional components other than nucleotide sequences to engineer computational devices. DNA strand displacement circuits have also served in applications such as medical therapeutics in vivo[8], molecular instruments in situ[9], and biomedical diagnostics in vitro[10].

B. Seesaw Gates

A single strand of DNA can be used as a signal in DNA circuits. If a strand is bound by its complement, the signal is inhibited. A specific domain in a single stranded DNA, called the *toehold*, can bind to a partially double-stranded complex. On binding, a strand from the complex is released. The released single strand acts as the output signal generated from the input signal[11].

Scalable DNA circuits can be created using a DNA gate motif, the “seesaw” gate, proposed by Qian and Winfree[12]. The seesaw gate uses a reversible strand displacement reaction based on the principle of toehold exchange. The seesaw gate activity involves hybridization and branch migration between input signals and the gate signals to generate a distinctive output DNA signal. During a logic operation, DNA signals take up different roles in the seesaw gate. Input signals arrive at the gate to initiate a reaction; fuel signals catalyze the reaction and the output signals are generated by the gate. In a catalytic cycle, a seesaw gate can receive an input which transforms free fuel into output. Apart from these two, a threshold signal can be used in the seesaw gate to push the intrinsically analog signal toward either the ideal ON or OFF value.

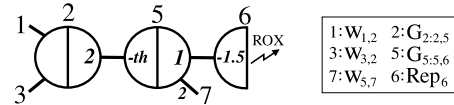


Fig. 1. A digital gate implemented using the DNA seesaw motif. 1, 3, and 7 are DNA signals. 2, 5, and 6 are seesaw gates. 2, *th*, *I*, 1.5 are relative concentrations of DNA signals.

Consider the digital logic gate implemented with the seesaw DNA motif shown in Figure 1. The logic gate consists of three seesaw gates represented by two circles (2 and 5) and a semicircle (6). The DNA signals present in the logic gate are represented by wires. The first seesaw gate (identified as gate 2) outputs a DNA signal whose concentration is the sum of the concentrations of both the input signals. This type of seesaw gate is called an integrating gate. The second seesaw gate, called the amplifying gate, produces an output if the concentration of the signal input to the gate is above a threshold value (*th*). The amplifying gate also takes in a fuel input (identified as 7) that catalyzes the generation of the output signal. The relative concentration of the outputs generated by individual seesaw gates are mentioned inside the gate at the output terminal (2 and *I*). The reporter gate (identified as 6) absorbs an input signal and generates fluorescence in proportion to the input signal. The fluorescence is generated by the ROX fluorophore.

The sequence of DNA reactions of the digital logic gate are shown in the Figure 2. The sequence of reactions in the amplifying gate are shown in Figure 2(a). Each DNA signal (eg. $w_{1,2}$) has two recognition domains (S1 and S2) around a central toehold domain (T). The recognition domains identify the two gates the DNA signal connects to ($w_{1,2}$ connects to gate 2). Each gate is associated with a gate base strand that has (the complement of) one recognition domain flanked by two toehold domains ($T^*S2^*T^*$). The base strand bound to a DNA signal ($S2-T-S5$) forms a gate:signal complex ($G_{2,2,5}$). The gate:signal complex has an uncovered toehold domain (T^*) that is the initiation point of the strand displacement reactions. The input DNA strands hybridize with the gate:signal complex at the uncovered toehold domain to release the bound DNA strand $w_{2,5}$. This reaction is reversible and is called seesawing. The output signal forms the input to the downstream amplifying gate.

The reactions involved in the amplifying gate are presented in Figure 2(b). The threshold species ($Th_{2,5,5}$) and the input signal ($w_{2,5}$) react by means of the exposed longer toehold ($S2^*T^*$) to produce only inert waste species. The excess

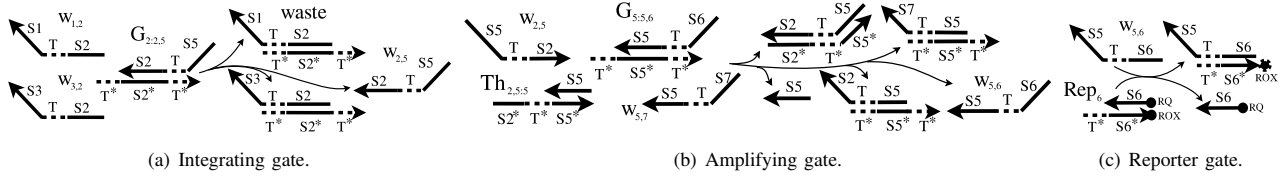


Fig. 2. Sequence of reactions in the digital logic gate structure that can be configured as an OR gate or an AND gate.

input strands hybridize with the $G_{5:5,6}$ gate:signal complex to generate the output signal $w_{5,6}$. Thresholding is much faster than the seesawing reaction as the length of the threshold dictates the reaction rate[13]. As a result, seesawing can happen only when the concentration of the input is greater than the concentration of the threshold signal. The excess DNA signal from the input reacts with the $G_{5:5,6}$ to release the output. The amplification of the output signal $w_{5,6}$ is catalyzed by the fuel signal $w_{5,7}$.

Translating the signal concentrations into a digital abstraction, a normalized concentration up to 0.2 is considered digital OFF and a concentration of 0.8 or higher is considered digital ON. To configure the logic gate in Figure 1 as an OR gate, the threshold value should be set such that seesawing occurs when either of the inputs has a normal concentration of 0.8 (digital ON). Similarly, to configure the gate as an AND gate, the threshold concentration should be such that seesawing reaction occurs only when both the inputs have a normal concentration of at least 0.8. Setting the threshold concentration value to 0.6 configures the logic gate structure as an OR gate and a value of 1.2 configures it as an AND gate[14].

The reporter gate is denoted by a semicircle with an arrow in Figure 1. The reporter species (Rep_6) is similar to a threshold signal, but is modified with a fluorophore (ROX) and quencher (RQ) pair. Rep_6 absorbs the input $w_{5,6}$ signal and generates a fluorescence signal (Figure 2(c)).

C. Contribution of the Paper

The proposed work uses seesaw gates working on the toehold exchange principles using reversible strand displacement[15] to demonstrate a working 2×2 crossbar interconnection network. The crossbar is the basic switching component in various interconnection networks, and Network-on-Chip routers[16]. A reference mux based crossbar implementation using AND, OR, NOT gates is presented in Figure 3(a). The dual rail logic implementation has been used to realize the equivalent DNA circuit. NOT gates are difficult to realize in a DNA circuit where digital ON or OFF is represented by presence or absence of DNA species. Hence dual rail logic implementation of digital circuits are used as a starting point in DNA circuit implementation. The seesaw gate circuit was designed using the Seesaw Compiler[17]. The composition of the DNA sequences involved in the reactions were also output by the Seesaw Compiler. The DNA circuit was simulated on the chemical reaction simulator, COPASI[18]. All the possible input combinations were tested and found to reach the appropriate output values. The crossbar network is

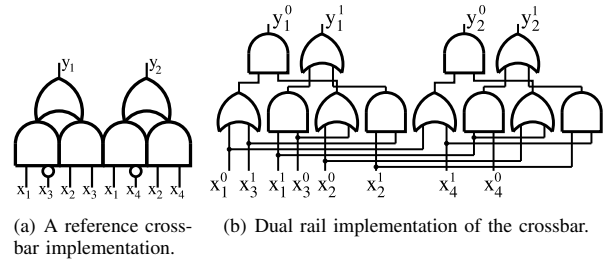


Fig. 3. (a) A 2×2 crossbar. x_1, x_2 : 1 bit inputs. x_3, x_4 : control inputs. $y_1 = x_1$ when $x_3 = 0$, x_2 otherwise, and (b) its dual rail logic AND-OR equivalent circuit. x_1^0, x_1^1 : digital 0 and 1 of x_1 .

one of the first proposals of the DNA strand displacement based implementation of an interconnection network.

D. Organization of the Paper

Section II presents the experimental framework and the results obtained in support of the working of the DNA based crossbar. Section II-C explains the reactions involving DNA signals in the seesaw gates of the crossbar DNA circuit. The papers concludes in Section III.

II. EXPERIMENTS AND RESULTS

Seesaw gates were used to simulate DNA strand based implementation of the crossbar network. The Seesaw compiler[17] was used to simulate the DNA strand implementation of the crossbar at the chemical reaction level. The Seesaw compiler automatically translates any feed forward logic circuit into its equivalent seesaw circuit. The compiler also generates (a) DNA sequences participating in the chemical reactions, (b) the DNA circuit's Mathematica code and (c) Systems Biology Markup Language (SBML)[19] representation of the DNA circuit. The Mathematica and SBML code can be used for simulations at the chemical reaction level. Apart from these, the compiler generates DNA strand displacement calculus (DSD)[20] code for visualization and simulation at the domain level.

A. Realization of the DNA based Crossbar

The AONtoAO module of the Seesaw compiler converts the crossbar (Figure 3(a)) into its equivalent dual rail logic circuit (Figure 3(b)). The dual rail AND-OR circuit was converted into its SBML representation using the dual rail to SBML module (AOTO SBML) of the compiler. The SBML script was

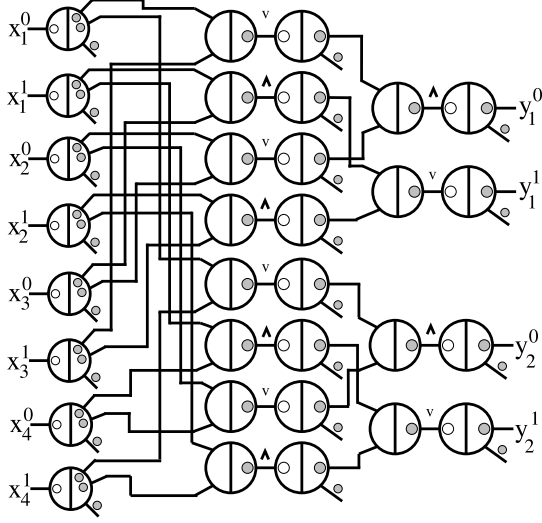


Fig. 4. The seesaw gate implementation of the dual rail 2×2 crossbar circuit.

imported and simulated in the chemical reaction simulator COPASI[18]. The AND-OR to seesaw module converts the dual rail logic circuit into its equivalent seesaw gate circuit (shown in Figure 4).

B. Results

For the chemical reaction simulation, a low initial concentration of 5×10^{-9} mol/l was considered as logic level 0. A higher concentration level of 4.5×10^{-8} was considered as logic level 1. The DNA strand displacement circuit for the 2×2 crossbar contained 44 initial DNA species.

Figure 5(a) to 5(d) plot the normalized transient concentrations of the DNA species corresponding to the output signals. For each of the 16 possible combinations from the four inputs, the outputs reached the expected concentrations, proving the functional correctness of the DNA realization of the crossbar. Each of the plots in Figure 5 correspond to each of the 4 possible output states that y_1 and y_2 can reach. Figure 5(a) plots the concentrations of the dual rail outputs y_1^0 , y_1^1 , y_2^0 , and y_2^1 that correspond to the output $(y_1, y_2) = (0, 0)$. The output $(0, 0)$ was obtained for the dual rail input sequences corresponding to $(x_1, x_2, x_3, x_4) = (0, 0, 0, 0)$, $(0, 0, 0, 1)$, $(0, 0, 1, 0)$, $(0, 0, 1, 1)$, $(0, 1, 0, 0)$, and $(1, 0, 1, 1)$.

C. The DNA Sequence Reactions

The composition of the DNA sequences corresponding to each of the possible inputs and outputs are shown in Table I. The seesaw gates involved in producing the y_1^0 output are shown in Figure 6. Each input is connected to an amplifying gate, whose output feeds into an OR gate whose output feeds into an AND gate. The output signal $w_{45,52}$ is connected to a reporter gate (not shown in the figure).

The reactions taking place in the amplifying gate are illustrated in the Figure 7. The single stranded output signal $w_{5,28}$ is generated in proportion to the input $w_{4,5}$. The threshold double strand ($Th_{4,5;5}$) hybridizes with the input signal to produce

TABLE I
THE COMPOSITION OF THE INPUT DNA SEQUENCES OF THE CROSSBAR.

In-put	Strand Id	Strand Composition	Out-put	Repeater Id.	Strand Composition
x_1^0	w _{4,5}	S ₅ -T-S ₄	y_1^0	Rep52-t	RQ S52
x_1^1	w _{6,7}	S ₇ -T-S ₆	y_1^1	Rep52-b	T* S52* ROX
x_2^0	w _{8,9}	S ₉ -T-S ₈	y_2^0	Rep54-t	FQ S54
x_2^1	w _{10,11}	S ₁₁ -T-S ₁₀	y_2^1	Rep54-b	T* S54* FAM
x_3^0	w _{12,13}	S ₁₃ -T-S ₁₂	y_1^0	Rep56-t	RQ S56
x_3^1	w _{14,15}	S ₁₅ -T-S ₁₄	y_1^1	Rep56-b	T* S56* TYE563
x_4^0	w _{16,17}	S ₁₇ -T-S ₁₆	y_2^0	Rep58-t	RQ S58
x_4^1	w _{18,19}	S ₁₉ -T-S ₁₈	y_2^1	Rep58-b	T* S58* TYE665

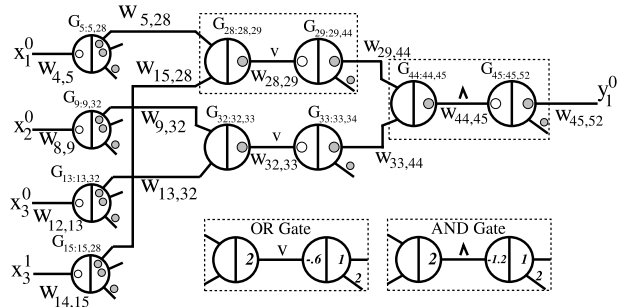


Fig. 6. Seesaw gates and DNA signals involved in the generation of the output y_1^0 .

the S4-T-S5 double strand and a single S5 strand. The S4-T-S5 double strand does not contribute to any further chemical reaction in the later stages of the circuit. The S5 single strand does not contain the toehold sequence and cannot initiate new reactions. The catalytic fuel strand ($w_{5,f}$) hybridizes with the double stranded gate:signal complex $G_{5,5,28}$ to produce the output signal, $w_{5,28}$ and a Sf-T-S5 double strand. The output signal contains a toehold flanked by two DNA sequences and initiates reactions in the next stage of the circuit.

The sequence of reactions continue in the OR gate with input signals $w_{5,28}$ and $w_{15,28}$ (Figure 8(a)). The input signals hybridize with $G_{28,28,29}$ to release $w_{28,29}$. Seesawing at the next gate can happen if the normalized input concentration is greater than 0.6.

The $w_{29,44}$ signal initiates reactions in the successive AND gate. After a series of chemical reactions similar to the OR gate, the AND gate output signal $w_{45,52}$ is released. This signal initiates the final sequence of reactions to release fluorescence

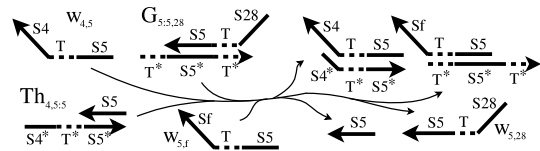


Fig. 7. DNA strand displacement reactions from the amplifying gate in Figure 6.

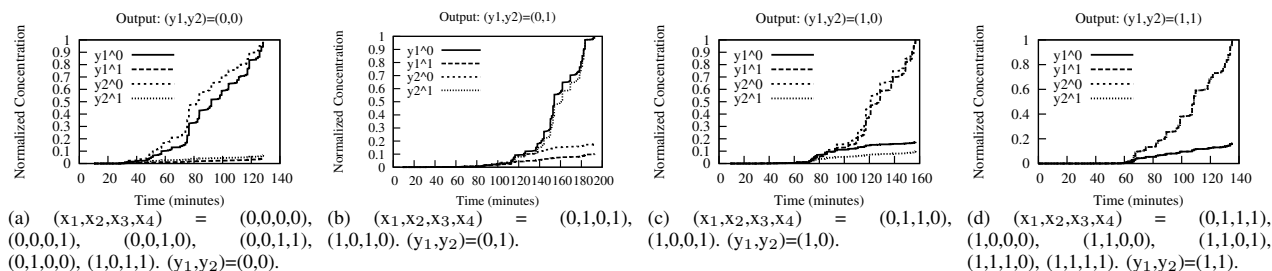


Fig. 5. Normalized concentrations of output signals during chemical reactions corresponding to all input combinations.

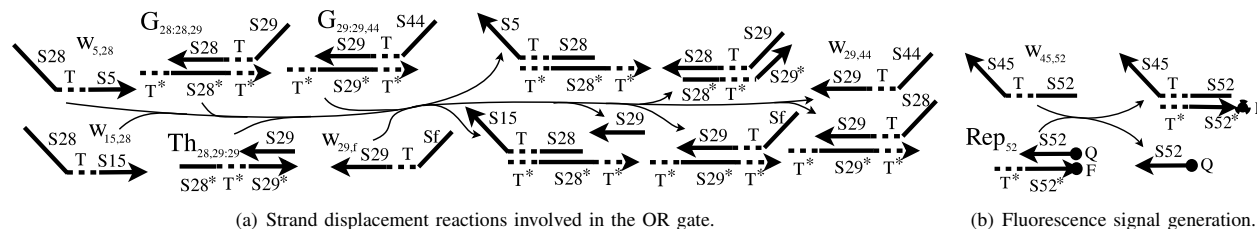


Fig. 8. DNA strand displacement reactions in the OR gate and the reporter gate.

from the reporter species (Rep_{52}). The fluorescence generation sequence is illustrated in Figure 8(b). The reporter strands used in the reactions are tabulated in Table I. The output signal $w_{45,52}$ hybridizes with the reporter to detach the quencher leaving the fluorophore to emit fluorescence.

III. CONCLUSION

DNA molecules provide exciting challenges and opportunities in various fields of computation and medicine[21]. Various computational and autonomous mechanical tasks have already been demonstrated using the DNA computing paradigm. The current work takes the first steps into realizing a DNA strand based interconnection network. The current work demonstrates the use of DNA strand displacement technology to realize a basic implementation of a single bit 2×2 crossbar. Seesaw gates working on the principle of toehold exchange were used to realize a dual rail implementation of the crossbar interconnection network. The DNA circuit was realized using the Seesaw compiler and its functional correctness was demonstrated using the chemical reaction simulator COPASI. All possible input combinations were simulated and the DNA signals reached the expected correct output in each of the input combination. The paper is the first step in a long journey towards realizing intelligent autonomous communication networks on the DNA substrate.

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