DNA strand displacement-based logic inverter gate design

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DNA-based circuits are considered as the possible replacement for the traditional silicon transistor based circuits for biomedical applications, especially for implantable medical devices because of their programmability, bio-compatibility, light weight, and small size. The seesaw DNA circuits, which uses DNA strand displacement operation lacks the logic inversion operation and uses a dual-rail design to overcome this issue. Here, a logic inverter gate using DNA strand displacement operations is introduced. This logic inverter gate is having a modular property and hence it can be used anywhere in the circuit. A gate enabling technique is used to achieve the modular design and the same can be used in analogue designs also. A full-adder circuit is developed to confirm the modularity property of the logic inverter gate. The DNA circuits were simulated in visual DSD software.

1. Introduction: The advancements in nanotechnology are paving the way for building the bio-compatible molecular devices in-vivo or in-vitro. Deoxyribonucleic acid (DNA) is considered as a suitable candidate for building such devices because of the small size, weight, bio-compatibility, and programmability. The computational power of DNA was first explored by Adleman in [1]. Different circuits were developed using the DNA strands since then. All these circuits are working on the basis of the toehold mediated DNA strand displacement operation. Similar to silicon transistor in a conventional digital computing device, the DNA strands can be used as the basic building blocks of a DNA computing device.

Enzyme-free DNA logic gates such as AND, OR, and majority gates are already available in the literature [2–8]. Among these logic gate designs, all of them are not suitable for the design of large complex circuits. A brief review of all the scalable digital DNA designs is given in [9]. Digital circuits made up of DNA strands can be used in nanomachines and devices such as DNA nanorobots [10–12]. Presently, most of these logic gate circuits lack the logic inverter or NOT operation. Hence, a dual-rail AND–OR or AND–OR–majority logic is considered for the scaling up of the digital circuits in such DNA circuits. In this Letter, we are introducing a new logic inverter gate or NOT gate design using enzyme-free DNA strand displacement operations. The use of DNA logic gate inverters in a circuit will reduce the number of unique strands required for that circuit into approximately half. A modular design of DNA subtraction operation is used for the design of the logic inverter gate.

2. DNA inverter gate design: The basic operation associated with any enzyme-free DNA circuit is the toehold mediated strand displacement operation. The DNA inverter can be developed from the subtraction gate proposed by Song *et al.* in [13], by treating the second input as a constant. The subtraction operation given in [13] is not having modularity property. Here, the second input itself is acting as the output of the subtraction gate. If a circuit is connected to this subtraction gate directly, then the input may get consumed before the inversion operation, and it may lead to inaccurate results. To make the subtraction operation modular, a switching circuit called gate enable is used. The gate enable can be considered as an electrical relay switch, which passes the signal when a control signal is present. The control signal is generated by the delay circuit [14]. The delay is programmable and hence, this control signal can be used to control the inversion operations in different levels. Such a subtraction gate is shown in Fig. 1. The DNA strands in the figure are drawn using visual DSD software [15].

The standard concentration of the inverter gate is considered as r_{min}. The input (I_{inv}) to the subtraction gate is a single-stranded DNA (ssDNA). The concentration of the DNA strand is considered as the signal. If the concentration is in the range $(0, 0.2 \times r_{inv})$, then the signal can be considered as a logic *low*. Similarly, if the input concentration is in the range $(0.8 \times r_{inv}, r_{inv})$, then the signal can be considered as a logic *high*. The DNA strands used in the logic inverter gate design (D_s and G_s) are similar to that given in [13] for the subtraction gate. The initial concentration of D_s and G_s is set at r_{inv}. The second input in this subtraction operation I_s is kept constant at logic high (r_{inv}) such that $I_{inv} \leq I_s$. The DNA reactions associated with the subtraction operation are reactions 3–5 given in Fig. 2. The output of the subtracting gate is the equilibrium concentration of the second input I_s. Hence, this subtracting gate is not modular. A delayed signal with a gate enable switch will make the subtraction gate into modular. The delayed signal is produced from a delay gate which uses an initiator (I_D), a source (S), and a delay (D) strand [14]. The DNA reactions associated with the delay gate are reactions 1 and 2 given in Fig. 2. Reaction 1 is having a very small rate constant. The *sp*13 strand produced from the reaction 1 bind to the D strand to produce two waste strands (*sp*23 and *sp*24). This reaction (reaction 2) is a faster reaction, and the D strand fully gets consumed by the *sp*13 strand. When the concentration of the D strand becomes zero, the *sp*13 signal can react with the *GE* strand and switch the gate enable to allow further reactions. The concentration of the D strand determines the delay of the signal *sp*13 to reach the *GE* strand. The delay is chosen in such a way that the subtraction operation is completed and the output of the subtraction operation is at equilibrium. The concentration of the initiator strand (I_D) and source strand (S) is very high ($\sim 1000 \times r_{inv}$).

The *sp*13 strand reacts with the *GE* strand to produce *sp*26 which can further react with the output of the subtraction gate. The *GE* strand prevents the subtraction gate output from reacting with the next level DNA strands until the subtraction operation is completed. Reactions 6 and 7 given in Fig. 2 represent the gate enable operation. The initial concentration of *GE* is also set at r_{inv}. The next level in the inverter design is a seesaw gate motif [2, 3], which consists of a threshold strand (*Th*), a gate strand (G) and a fuel strand (F). The detailed description of the seesaw gate motif operation can be found in [2, 3]. The concentration of G and F is set to r_{inv}, and that of threshold gate is set to $0.5 \times r_{inv}$. The seesaw gate operation consists of reactions 8–10. The output from the seesaw

gate is the strand *sp*36. This strand is further reacted with the reporter strand (R) to produce the output signal O_{inv}. This reaction is given in Fig. 2 as reaction 11.

3. Simulation results and discussion: The proposed DNA strand displacement-based circuits are implemented in visual DSD software using the programming language developed by Phillips and Cardelli [16]. The standard concentration r_{inv} of the design is selected as 50 nM ($1\times = 50$ nM). $0.2\times$ is considered as a logic *low* and $0.8\times$ is considered as a logic *high*. The toehold domain (t) is having a toehold dissociation rate constant of $26\,s^{-1}$ and a toehold binding rate constant of $5 \times 10^{-5}\,nM^{-1}\,s^{-1}$. The reaction rate constant of the slow reaction in the delay gate (reaction 1 in Fig. 2) is 3.6 nM/h. The initial concentration of the initiator strand (I_D) and the source strand (S) are set at $1000 \times r_{inv}$ to produce a delay of $\sim 1 \times 10^4$ s for a 30 nM concentration of the delay strand (D). The delay time linearly increases with an increase in the initial concentration of the D strand [14]. A MATLAB file is generated from the visual DSD software, and the simulations are performed in MATLAB. The concentration of the inverter output strand (O_{inv}) is observed for input (I_{inv}) logic low ($0.2\times$) and logic high ($0.8\times$) conditions and it is shown in Fig. 3.

To check the modular property of the proposed inverter gate, we use the logic inverter gate in the design of a full adder. The full adder takes three inputs, x, y, and z and produces the sum (S) and carry (C_{out}) outputs

$$S = x \oplus y \oplus z \tag{1}$$

$$C_{out} = xy + yz + xz \tag{2}$$

These functions can be implemented using a three-input majority gate (M3), a five-input majority gate (M5), and an inverter [17] as shown in Fig. 4. The abstract diagram of the full-adder seesaw circuit is shown in Fig. 5. Here, the three-input majority gate is designed by selecting the threshold as $1.4\times$ and five-input majority gate by selecting threshold as $2.8\times$. The control signal with a switch in the diagram indicates the gate enable operation. Subtraction operation is represented by a subtraction gate symbol as given in [13].

The simulation of full-adder circuit using majority gates and inverter gate for different input combinations is shown in Fig. 6. It can be noted that the C_{out} response is faster compared with the

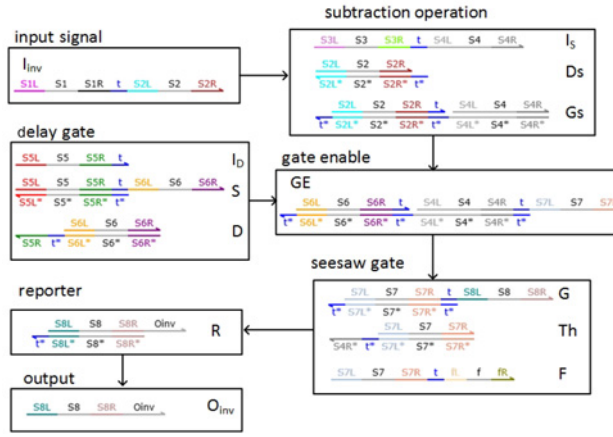

Fig. 1 *Block diagram of the proposed DNA inverter*

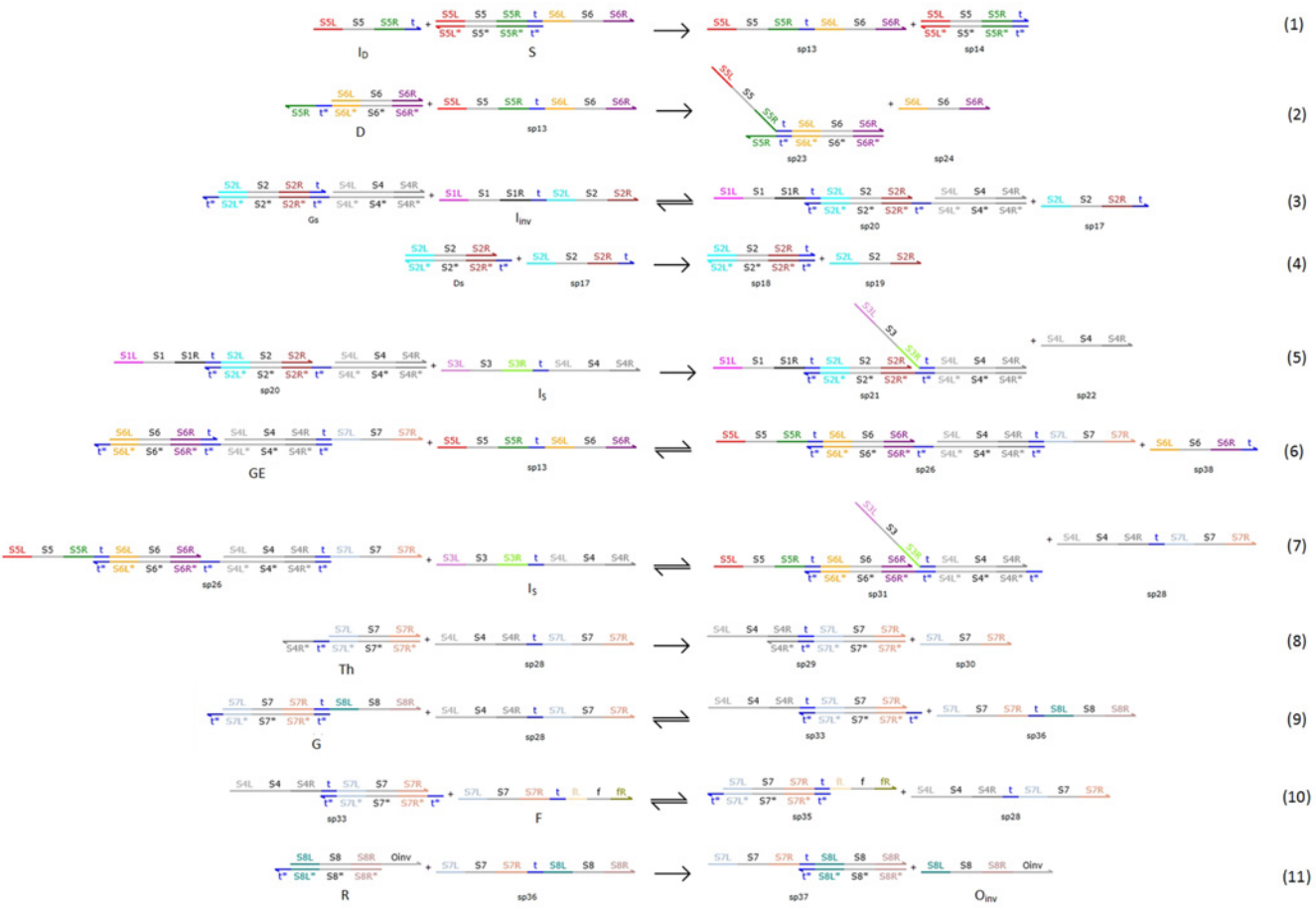

Fig. 2 *DNA reactions associated with the DNA inverter*

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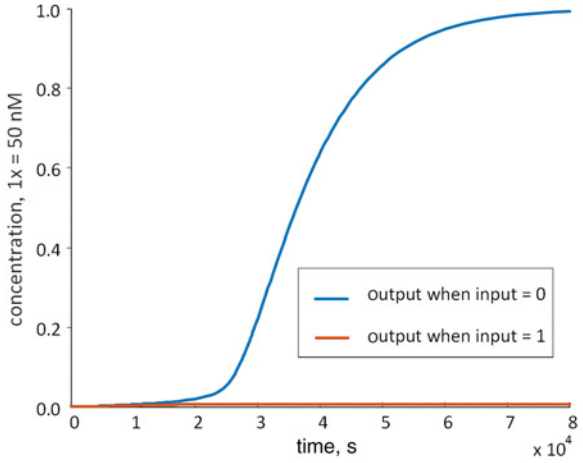

Fig. 3 *Simulation results of the proposed DNA inverter*

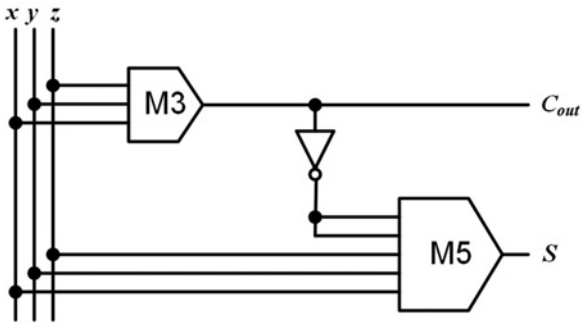

Fig. 4 *Full-adder circuit using majority gates and inverter*

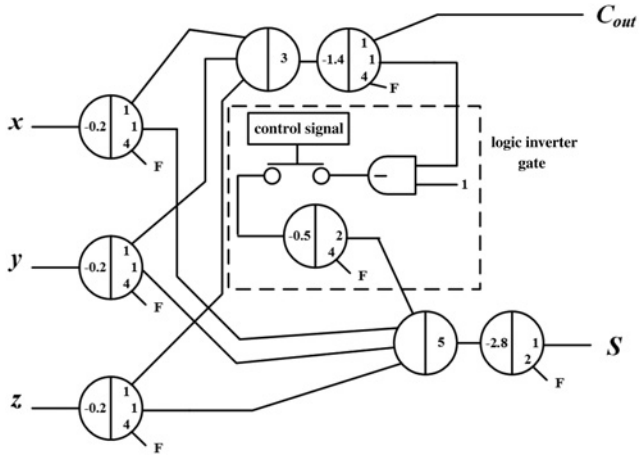

Fig. 5 *Full-adder abstract diagram using seesaw gates and inverter gate with gate enable*

S response. This is due to that fact that the S output is a function of $\overline{C_{\text{out}}}$. We can observe a faster response for S, when $x = 1$, $y = 1$ and $z = 1$, since the $\overline{C_{\text{out}}}$ has no effect in this particular case, and hence, no extra delay in the output.

The modular design approach proposed in this Letter is not limited to digital designs. It can also be used with the analogue circuits [13] and decision-making circuits [18] for the modular designs of the subtraction gate and the maximum operation, respectively. The proposed method can reduce the number of unique strands required for the seesaw DNA digital design into approximately half by removing the dual rail design.

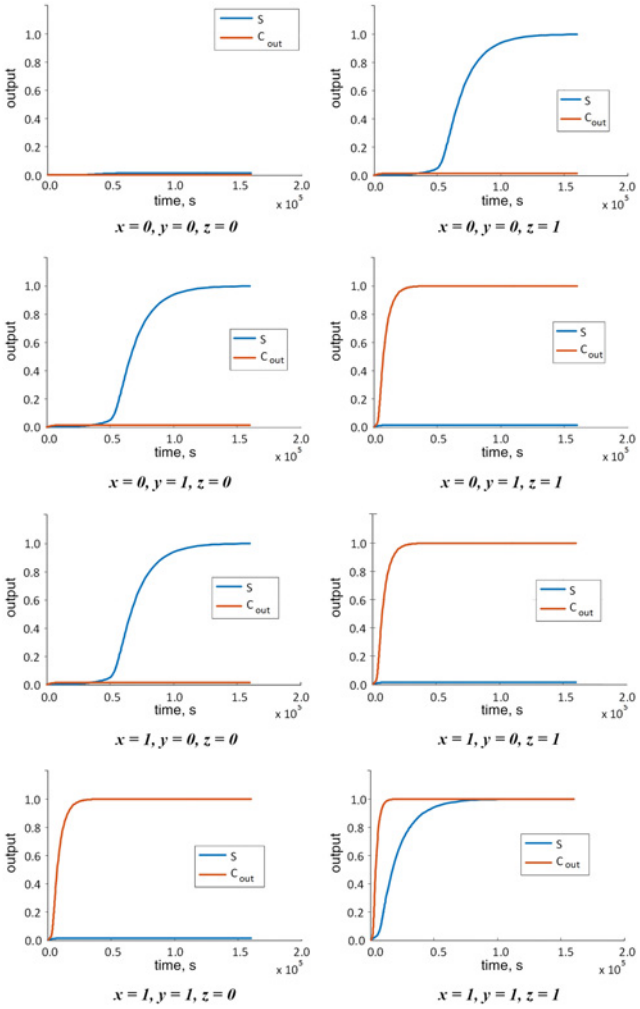

Fig. 6 *Full-adder simulation results for different input combinations*

4. Conclusion: A logic inverter gate using DNA strand displacement operation is proposed. A gate-enable switch which operates on a control signal from a delay circuit is employed to make the circuit modular. Approximately, 50% reduction in the number of DNA strands required for the DNA circuit design can be achieved by using the proposed approach. The logic inverter gate is modular and is capable of using anywhere in the circuit. The modularity property of the proposed logic inverter gate is tested by designing a full-adder circuit. The proposed gate-enable operation proposed in this work can be used in analogue circuits to give them the modular property.

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6 References

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