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A versatile DNA-supramolecule logic platform for multifunctional information processing

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Abstract

DNA-based logic units are rapidly being developed in molecular computation. However, because DNA cannot produce detectable signals, suitable signal reporters must be carefully selected, which is challenging, especially in advanced, multifunctional devices. By introducing a supramolecular reporter *MTC* [3,3'-di(3-sulfopropyl)-4,5,4',5'- dibenzo-9-methyl-thiacarbo-cyanine triethylammonium salt], we developed a simplified DNA-supramolecule platform. Owing to the multiple assembly states of *MTC*, the platform contains only one reporter block but can provide multiple parallel outputs and easily implement several types of information processing functions, including data filtration (binary and ternary INHIBIT gates), selection (multiplexer and demultiplexer) and verification (parity checker and comparator). In addition to combinational circuits, a fundamental sequential logic circuit, counter, has also been fabricated at the molecular level. With the advantages of high reconfigurability, flexibility and enormous parallelism, this DNA-supramolecule prototype may have a promising future in the field of molecular computing and multiplex chemical analysis.

Introduction

Molecular computation has attracted intense attention in widespread. scientific studies over the past few decades^{1–3}. Unlike traditional digital circuitry whose logic units are physically combined, molecular logic units are functional-combined by associating chemical or biochemical molecules^{4,5}. In molecular logic devices, DNA is endowed with unique advantages due to its strict base complementarity and controllable structural transitions. Hitherto, a series of advanced logic circuits, such as multiplexer/demultiplexer⁶, encoder/decoder^{7,8} and parity checker^{9,10}, have been constructed via DNA-based systems. These works not only promote the development of molecular computation but also show great application potential for biomedical imaging¹¹, data storage¹², medical diagnostics¹³, and biochemical analysis¹⁴.

Although great advancements have been achieved in DNA computation, the inherent drawback that DNA cannot generate detectable signals still exists. Therefore, the development of DNA-based circuits relies heavily on the design of ingenious signal reporters. Reported DNAbased logic systems mostly contain two independent components: (1) oligonucleotides in charge of logical function and (2) extrinsic reporters responsible for monitoring the "state" of the logic devices. This strategy works very well in simple logic circuits, such as basic Boolean logic gates and some single-output units^{9,15}. However, for advanced, multi-output logic circuits, selecting suitable reporters with distinguishable signals is still a challenge. For example, the DNA-based platform designed by Wang's group⁸ employed four different fluorescent reporters with partially overlapping signals to

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construct a 2-to-4 decoder. Obviously, the higher the complexity of the logic functions, the more difficult it is to find suitable reporters. To simplify the design of advanced logic circuits, we introduce a supramolecular reporter, which involves only one molecular block but is capable of displaying multiple assembly states^{16,17} and, consequently, represents multiple output channels.

Cyanine dye, a common fluorochrome, has been applied in various devices, such as biosensors¹⁸, components for nonlinear optics¹⁹, and data storage devices²⁰, owing to its unique photophysical and photochemical properties. Cyanines can assemble into various aggregates²¹, and each aggregate presents distinguishable spectral features, implying that they have the potential to simultaneously provide multiple independent output channels. In our previous work, we succeeded in constructing a 2-to-4 decoder based on a cyanine supramolecular system²². Another advantage of cyanines is that their assembly behavior can be regulated by various stimuli, including pH, metal ions and biomacromolecules, especially specific DNA structures^{23–28}, and the assembly conversions could be reversed by eliminating the stimuli. Herein, we developed a multifunctional logic platform based on DNA D1 (5'-GGTGGTGGTGGT-3'), D2 (5'-CCACCACCA-CAACCACCACCACCAAA-3'), and cyanine dye MTC

[3,3'-di(3-sulfopropyl)-4,5,4',5'-dibenzo-9-methyl-thia-

carbocyanine triethylammonium salt] (Fig. 1). By introducing stimuli that can regulate both the secondary structures of D1/D2 and the assembly states of MTC, the platform implemented several types of information processing functions, including data filtration, selection, verification, and accumulation.

Materials and methods

Chemicals and reagents

DNA oligonucleotides *D1* (5'-GGTGGTGGTGGTGGT-3') and *D2* (5'-CCACCACCACCAACCAACCAACCACCAC CAAA-3') were purchased from Sangon Biotechnology Co. Ltd. (Shanghai, China). The cyanine dye *MTC* was synthesized according to the methods of Hamer²⁹ and Ficken³⁰, and the purity was determined by MS, elemental analysis, NMR and absorption spectroscopy (shown in Figs. S1–S4 and Tables S1–S3). Lead chloride (PbCl₂), 18crown-6-ether (CE) and potassium nitrate (KNO₃) were purchased from Aldrich Ltd. (Shanghai, China). Silver nitrate (AgNO₃) and L-cysteine (Cys) were obtained from Sigma-Aldrich. All the chemicals are analytical reagent grade and used as received without further purification. Ultrapure water prepared by an ULUPURE (Chengdu,



China) ultrapure water system and was used throughout the experiments.

The stock solution of MTC was prepared by dissolving its powder in methanol and was stored in darkness. The DNA stock solutions were prepared by dissolving certain amounts of oligonucleotides in 10 mM Tris-HCl buffer solution. The D1D2 duplex was prepared by mixing D1and D2 in equimolar amounts and annealing the mixture in a thermocycler (first heated at 90°C for 5 min and then cooled slowly to room temperature). The DNA concentrations were determined by measuring the absorbance at 260 nm.

The fluorescence spectra were collected with a F-4600 spectrophotometer (HITACHI, Japan) in a 10 mm quartz cell. Xenon arc lamp was used as the excitation light source. Both the excitation and emission slits were 5 nm, the PMT voltage was 400 V, and the excitation wavelength was 530 nm. The absorption spectra were acquired with an EVOLUTION 201 spectrophotometer (Thermo SCIENTIFIC, USA) at room temperature in a 10 mm quartz cell.

Operations of the logic circuits

To better demonstrate the logic functions of the platform, the optimized input conditions were selected for each circuit. All samples were incubated in the dark at room temperature for 20 min before the measurement.

For the binary INHIBIT gate, $4 \mu M D1$ and $4 \mu M MTC$ in 10 mM Tris-HCl buffer solution (pH 7.0) were used as the initial state, and $10 \mu M$ PbCl₂ and $4 \mu M D2$ were employed as the inputs. With respect to the ternary INHIBIT gate, $4 \mu M MTC$ in 10 mM Tris-Ac buffer solution (pH 7.4) was used as the initial state, and $1 \mu M$ D1, $1 \mu M D1$ with 0.15 μM PbCl₂, $1 \mu M D2$, and $1 \mu M D2$ with $3 \mu M$ AgNO₃ were employed as the inputs.

For the 2:1 MUX, $4 \mu M D1$ and $4 \mu M MTC$ in 10 mM Tris-HCl buffer solution (pH 7.0) were used as the initial state; $10 \mu M$ PbCl₂ and 10 mM Tris-HCl buffer solution (pH 4.0) were employed as the data inputs; and $4 \mu M D2$ with 30 mM KCl was employed as the address input.

For the DEMUX and parity checker, $6 \mu M MTC$ in 10 mM Tris-HCl buffer solution (pH 8.5) was used as the initial state; 60 mM KCl was employed as the data input; and 50 mM CE and $6 \mu M D1$ were used as the address inputs in the 1:3 DEMUX. 10 mM Tris-HCl buffer solution (pH 4.0), 60 mM KCl, 10 μ M PbCl₂ and D1 were employed as the four binary bits of the examined numbers in the parity checker.

For the comparator, $6 \mu M MTC$ and $6 \mu M D1D2$ in 10 mM Tris-HCl (pH 8.5) were used as the initial state, and 30 mM KCl and 10 mM Tris-HCl buffer solution (pH 4.0) were employed as the inputs.

For the counter, $5 \mu M MTC$ in 10 mM Tris-HCl buffer solution (pH 8.5) was used as the initial state; 40 mM KCl

and 70 mM CE were selected as the cumulating and descending pulses, respectively.

Operations of the logic circuits in human serum

The human serum samples were supplied by Solarbio (China). The serum was centrifuged at 10,000 rpm for 3 min to remove precipitates, and the supernatants were diluted ten times using Tris-HCl (10 mM, pH 7.0) buffer before the logic operations. For the logic operations, all the samples contained 1000-fold diluted serum, and the input stimuli were consistent with the above description.

Results and discussion

As a typical cyanine, MTC presents several assembly behaviors under different conditions. In alkaline buffer solutions (such as pH 8.5, 10 mM Tris-HCl), it has a dominating absorption peak at 528 nm assigned to dimer (termed the D-band), while in acidic conditions (such as pH 4, 10 mM Tris-HCl) it self-assembles into J-aggregates (typical absorption peak at approximately 655 nm, termed the J-band)³¹, as shown in Supplementary Figs. S5 and S6. Some cations can also facilitate the self-assembly of MTC. For example, MTC can assemble into either J- or Haggregates (absorption peak in the range of 440-480 nm, termed the H-band) in the presence of potassium (Supplementary Fig. S7). In addition, we previously reported that certain DNA G-quadruplex structures can specifically disassemble MTC aggregates into monomers, accompanied by a dramatic fluorescence enhancement (maximum emission wavelength at 600 nm, termed the FI)^{32,33}. The unique assembly behavior of MTC can provide at least four distinguishable output signals (D-band, J-band, H-band, and FI), which makes it convenient for the construction of multi-output logic circuits.

In this paper, we defined the threshold of the output signals (normalized *MTC* J-band, H-band or FI) at 0.3 in all the binary logic devices. Any signal greater than the threshold was defined as "1", and those less than the threshold as "0". Similarly, the thresholds in the ternary gate were defined at 0.3 and 1.5. It is worth mentioning that all the inputs in this work can be eliminated by adjusting the complexing agents, so all the logic operations are reversible. For example, Pb^{2+} and Ag^+ can be complexed by cysteine (Cys), K⁺ can be complexed by 18-crown-6 (CE), and the G-quadruplexes can be unwound into a stable complex (Supplementary Figs. S8 and S9).

Data filtration: the binary and ternary INHIBIT gates

The INHIBIT gate (Fig. 2a) is one of the most widely used Boolean logic gates. A binary INHIBIT gate can only output the high level by inputting special one of the two inputs individually. This filtering function makes it to be applied widely in biochemical detection¹³. As mentioned above, *MTC* can recognize specific G-quadruplex structures against single-/double-stranded oligonucleotides. The G-rich oligonucleotide *D1* in a random single strand (under metal ion-free conditions) can induce only weak fluorescence signal of *MTC*, while its parallel Gquadruplex formation (induced by metal ions, such as K⁺ or Pb²⁺) can cause a strong fluorescence enhancement. In addition, the D1D2 complex can hardly induce fluorescence (Supplementary Fig. S8). By utilizing distinctive fluorescence patterns, both binary and ternary logic gates were constructed.

To construct a binary INHIBIT gate, we chose MTC and D1 as the initial state and Pb^{2+} and D2 as the input





stimuli (Fig. 2b). Pb²⁺ can facilitate the formation of the D1 G-quadruplex, while D2 has the opposite effect. As shown in Fig. 2d, in the initial state, MTC shows a weak fluorescence signal with single-stranded D1, while it emits a strong signal with PbCl₂ input. The addition of D2 complements D1 to D1D2 complex, which is stable and cannot be unwound by Pb²⁺, and reduces the signal to near zero. The normalized MTC FI values are plotted as a bar chart in Fig. 2c, and the result is accordance with the proper execution of the INHIBIT gate.

In binary logic systems, each bit is coded by "0" or "1", corresponding to a low and high signal, respectively. However, due to the complexity of information processing, sometimes it is difficult to identify certain and accurate states based on this low/high system. In contrast, multi-valued logic systems, which involve a switch between multiple states, show an overwhelming advantage in dealing with uncertain information. Ternary logic gates, as a typical representation of multi-valued logic systems, have three different output levels: low, medium and high, which correspond to logic values of "0", "1", and "2", respectively³⁴. With respect to *MTC*, its fluorescence signals can be induced to three different levels by D1 with certain structures, i.e., (1) a strong signal induced by the G-quadruplex (termed D1-G4), (2) a weak signal induced by the single-stranded structure (termed D1-ss) and (3) almost no signal induced by the D1D2 complex. Therefore, a ternary logic unit can be constructed based on this platform, and the outputs can be defined as "2", "1", and "0", according to the fluorescence strength.

As shown in Fig. 2e, *MTC* is defined as the initial state. With respect to the input *X*, *D1* is defined as "1" and further addition of Pb²⁺ as "2". With respect to the input *Y*, the mixture of *D2* and Ag⁺ is defined as "1" and *D2* alone as "2". In this system, there are five DNA motifs, including *D1-ss*, *D1-G4* induced by Pb²⁺, single-stranded *D2* (termed *D2-ss*), i-motif *D2* induced by Ag⁺ (termed *D2-i*) and the *D1D2* complex, and their stabilities are in the following order: D2-i > D1D2 > D1-G4 > D1-ss/D2-ss. The confirmation of each DNA structure and the thermal stability experiment results are shown in Supplementary Figs. S10–S13.

As shown in Fig. 2f and Supplementary Fig. S12, in the case of input X = "0", the system contains no DNA, D2-i or D2-ss with different input Y situations. Since neither D2-i nor D2-ss can induce MTC to generate a fluorescence signal, all the outputs are "0". In the case of input X = "1", owing to the absence of Pb²⁺, D1-ss causes a weak signal (output = "1") in the (1,0) input situation. For the input of (1,2), D1 is totally complemented by D2, and the D1D2 complex decreases the output signal to "0". For the input of (1,1), since D2-i is more stable than D1D2, part of D1D2 is unwound by Ag⁺, and the released D1-ss causes a weak signal, which is similar to

the (1,0) input situation (output = "1"). In the case of input channel X = "2", the *D1-G4* induced by Pb²⁺ causes a strong signal (output = "2") in the (2,0) input situation. For the input (2,2), since *D1D2* is more stable than *D1-G4*, *D1-G4* is totally complemented by *D2*, which leads to no signal (output = "0"). For the input (2,1), which is similar to the case of (1,1), partial *D1* is released and forms the *G*-quadruplex in the presence of Pb²⁺. Since only some *D1-G4* is formed, the signal of *MTC* is still weak compared with that observed in the case of (2,0), and the output is "1". The normalized *MTC* FI values are plotted as a bar chart in Fig. 2g, and the results are accordance with the proper execution of a ternary INHIBIT gate.

Data selection: the multiplexer and demultiplexer

The multiplexer (MUX) and demultiplexer (DEMUX) are controlled rotary switches and play key roles in electronic, telecommunication, and signal processing systems³⁵. They involve a couple of data input/output channels and an additional address (A) control. Depending on the state of A, data can be transmitted between certain input and output channels. To date, several MUX/ DEMUX systems have been designed based on organic molecules, enzyme reactions, or DNA platforms^{8,35–37}. Among them, an oligonucleotide-triggered DNA conformational change is a common strategy. However, the interference among DNA strands increases the difficulty of the implementation process and limits the operational performance. In this work, owing to the multiple assembly states of MTC, a series of MUX and DEMUX was constructed in a simple manner.

The simplest MUX contains two data inputs, one output channel, and an A control (termed 2-to-1 MUX). The function of the 2-to-1 MUX is selecting one certain of the two data inputs according to the "state" of A (Fig. 3d). Figure 3a presents the schematic illustration of the constructed 2-to-1 MUX. The mixture of MTC and D1 is considered the initial state, and D2 is the A control. To balance the output signal, the D2 sample contains 30 mM KCl, which can facilitate the formation of D1-G4. Two ions, i.e., Pb^{2+} , which can induce *D1* to fold into the Gquadruplex, and H^+ , which can induce D2 to fold into the i-motif, are chosen as the two data input stimuli. In the case of A = "0", inputting Pb²⁺ promotes the formation of D1-G4 and turns on the fluorescence of MTC, while inputting H^+ cannot change the structure of D1 nor the *MTC* fluorescence (Fig. 3b). In this way, the input of Pb^{2+} is transmitted into the MTC fluorescence signal, and the H^+ channel has no influence on the output. In the case of A ="1", the presence of *D2* induces the formation of the D1D2 complex, which can be unwound by H⁺ but not Pb² ⁺. Therefore, only the acidic condition can release D1. The D1-G4 induced by KCl can turn on the MTC



fluorescence, while the Pb^{2+} channel cannot influence the output. The conformational changes in MUX were confirmed by circular dichroism (CD) and native polyacrylamide gel electrophoresis (PAGE) experiments (Supplementary Figs. S14 and S15). The normalized *MTC* FI values are plotted as a bar chart in Fig. 3c, which satisfy the logic requirement of the 2-to-1 MUX. (The truth table is shown in Fig. 3e).

Any ion pairs capable of inducing the corresponding structural changes of D1/D2 can be considered as inputs the 2-to-1 MUX. To demonstrate the adaptability of the platform, we also constructed another 2-to-1 MUX by changing H⁺ to Ag⁺. The result is shown in Supplementary Fig. S16, and it demonstrates that the platform can be applied for parallel detection of heavy-metal Pb²⁺ and Ag⁺.

In contrast to MUX, the function of DEMUX is detangling data streams from a compressed signal. In this

work, a 1-to-3 demultiplexer was also fabricated in a similar strategy (Fig. 4).

Potassium can induce MTC to form several aggregations by increasing its effective dielectric constant³⁸, for example, 60 mM KCl can induce MTC to form Haggregates (Supplementary Fig. S7). Herein, KCl is chosen as the data input and the H-band is considered the first output channel. CE, which can chelate K^+ and reduce its active concentration, is chosen as one address control (A₁). When $A_1 = "1"$, inputting KCl leads to the formation of MTC J-aggregates. The featured J-band is considered the second output channel. In the same way, D1, which can be transformed into the G-quadruplex by KCl and disassemble MTC aggregates into monomers, is considered another kind of address control (A_2) , and *MTC* FI is defined as the third output channel. The absorption and fluorescence spectra are shown in Fig. 4c, d, respectively. The normalized outputs are plotted as bar charts (Fig. 4e),



and the obtained truth table (Fig. 4f) presents the input data leads to three different output channels according to the A conditions.

Data verification: the parity checker and comparator

In data transmission, an inevitable problem is incorrect bits³⁹, which have serious effects on the stable performance of logic computing, especially in sophisticated circuits. A parity checker is a logic unit that can determine erroneous bits and maintain data validity. To develop a parity checker on this platform, we exploited the logic devices mentioned above with slight modifications to distinguish odd and even numbers from natural numbers between 0 and 9 (Fig. 5). The decimal numbers are encoded into four-bit binary numbers (N_1 , N_2 , N_3 , and N_4), and H^+ , K^+ , Pb^{2+} , and D1 are assigned to the corresponding bits for computation (Fig. 5e). Only the input situations containing D1 can produce the *MTC* fluorescence signal (Fig. 5b, c). Therefore, the corresponding fluorescence signals of all the odd numbers are extremely low, i.e., false outputs, while the even numbers produce dramatic fluorescence signals, i.e., true outputs. It is worth mentioning that the parity of a natural number, regardless of odd or even, is determined by the digit in the unit position. Thus, the logic system fabricated here can distinguish all the even numbers from the odd ones.

The comparator is another important device in signal processing systems, and it is widely used in



telecommunication interfaces, analog-digital converters and sensory circuits. In this work, K^+ and H^+ are chosen as the two numbers for comparison (A and B), and a digital comparator is constructed based on the structural change of *D1D2* and corresponding assembly state of *MTC* (Fig. 6).

Under our experimental conditions, KCl at certain concentrations can induce MTC to form a mixture of H- and J-aggregates, while H⁺ can induce MTC to form Jaggregates. The two assembly states of MTC (J- and Haggregates) are employed as the two output channels (O₂ and O₁), respectively. The former indicates whether $A \neq B$, and the latter indicates whether A > B. There are two input situations, i.e., (0, 0) and (1, 1), that lead to the result A = B. For the (0, 0) situation, the *D1D2* complex shows little interaction with MTC and MTC remains in the dimer form. For the (1, 1) situation, H⁺ unwinds *D1D2*, and the released *D1* is induced into the G-quadruplex by K⁺. Consequently, MTC is disassembled into monomers by *D1-G4*. In both situations, J- or H-aggregates do not form, indicating that both outputs are "0". In the case where A and B are not equal, there is no formation of *D1-G4*, and the assembly states of *MTC* are determined by the cations in the system. If A > B, there is only K⁺ in the system, and *MTC* exists as a mixture of J- and H-aggregates, thus, both outputs are "1". If A < B, there is only H⁺ in the system, and *MTC* is induced to completely form J-aggregates, resulting in $O_1 = 1$ and $O_2 = 0$ (Fig. 6b, c). The conformational changes were confirmed by CD and PAGE experiments (Supplementary Figs. S14 and S15). The obtained truth table (Fig. 6e) presents the comparison results of the two digits, $(O_1 = O_2 = 0)$ presents A = B, $(O_1 = O_2 = 1)$ presents A > B and $(O_1 = 1, O_2 = 0)$ presents A < B.

Data accumulation: the counter

In addition to combinatorial logic, sequential logic is another primary class of logic devices widely used in modern computers⁴⁰. The counter is a fundamental sequential logic circuit, which is used to count stimuli pulses, frequency division, timing, and arithmetic (or logical) operations. To construct a counter on the molecular level, a logic system must fulfill the following



requirements: (1) multi-channel compatibility; (2) transformations among different output channels triggered by the same stimulus at different amounts; (3) availability of chemical or biochemical pairs with opposite reactions to the system. These requirements are so challenging to simultaneously satisfy that there are few works on the construction of a molecular counter. Here, on the *MTC* platform, we designed a two-bit counter that can perform both cumulating and descending operations (Fig. 7).

As shown in Fig. 7e, the assembly states of MTC, i.e., Jand H-aggregates, are assigned as the two bits of counted number (R), while K⁺ and CE are chosen to represent the cumulating and descending operations, respectively. For the accumulating operation, inputting KCl pulses would induce MTC to form J-aggregates alone, a mixture of Jand H-aggregates or H-aggregates alone step by step, indicating that the values of R cumulate from 0 to 3, respectively (Fig. 7c). With respect to the descending operation, CE is gradually inputted to chelate K^+ , and the assembly states of *MTC* are induced backward, i.e., from H-aggregates alone to a mixture of J- and H-aggregates, J-aggregates alone, and finally to dimers, indicating that the values of *R* descend from 3 to 0, respectively (Fig. 7f). The normalized *MTC* J- and H-bands are plotted as a bar chart in Fig. 7d, and the obtained truth table (Fig. 7e) demonstrates that the assemble states of *MTC* could indicate both cumulating and descending results. The results show that cumulating/descending operations can be performed at any stage of counting *R* values in the range of 0–3.

Application perspectives

From the viewpoint of practical applications, the developed DNA-supramolecule logic platform not only performs diverse intelligent logic functions but also shows



Fig. 7 Schematic illustration of the counter. **a** schematic illustration of the implementation of the counter. **b** The equivalent switching device of the counter. **c** The absorption spectra of *MTC* with different input conditions and (**d**) the normalized *MTC* J-band and H-band as the outputs of the cumulating process. **f** The absorption spectra of *MTC* with different input conditions and (**g**) the normalized *MTC* J-band and H-band as the outputs of the descending process. **e** The truth table of the counter logic operation



great potential for applications in multiplex chemical analysis. For example, the binary INHIBIT gate can analyze Pb^{2+} with high efficiency, and the MUX can parallelly discriminate Pb²⁺ and Ag⁺. As highly poisonous metal elements, lead harms almost every organ and system in organisms, especially the nervous system⁴¹, while silver can cause severe damage to cell membranes via extracellular mechanisms, inducing skin irritation, organ edema, and stomach distress^{42,43}. Excessive amounts of both ions are lethal. Lead, silver, and their compounds are prevalently applied in electrical, electronic, biomedical, jewelry, imaging industries, and manufacturing fungicides, and they usually coexisting in various sources like water, soil, and industrial waste. Therefore, integrated sensing methods that can parallelly detect these heavy-metal ions show much wider application prospects than single-target methods for these individual metals. To date, only a few parallel detection methods have been reported⁴⁴⁻⁴⁶. For example, Pei et al.⁴⁶ designed a DNA nanostructured microarray (DNM) that could sensitively and selectively detect multiple heavy-metal ions (Hg $^{2+}$, Pb $^{2+}$, and Ag $^+$). The 2-to-1 MUX constructed in this work can be applied to analyze Pb^{2+} or Ag^+ , and the method is efficient, lowcost and convenient for on-site detection. Moreover, the two MUX circuits with different inputs indicate the flexibility and wide adaptability of this platform for multiplex chemical and biochemical analyses.

Furthermore, the development of DNA-based logic systems will be crucial for applications in complex biological environments. To expand the potential application scenarios of the *MTC*-DNA platform, the binary INHI-BIT, 2-to-1 MUX and parity checker were also operated in diluted human serum. As shown in Fig. 8, all the results satisfy the logic requirements, and all the logic devices present the same threshold value (spectral results shown in Supplementary Fig. S17). The results suggest that the proposed logic platform shows great adaptability for complex biological environments and has potential for clinical diagnosis applications.

Conclusions

In conclusion, by combining DNA structural changes with supramolecule assembly, we developed a versatile logic platform to construct combinational and sequential logic circuits for information processing, including binary and ternary INHIBIT gates, two 2-to-1 MUX, a 1-to-3 DEMUX, a parity checker, a comparator and a counter. Since the DNA structures and supramolecule assembly states can be simultaneously regulated by the inputs, all the logic operations were implemented with high efficiency (all logic operations completed within 30 min) and excellent performance (constant threshold as low as 0.3). Furthermore, the logic system not only performs various intelligent logic functions but also shows potential applications for multiplex chemical analysis and clinical diagnosis. The developed DNA-supramolecule platform provides a novel prototype for the design of multifunctional molecular logic circuits, which may bridge the gap between molecular devices and silicon-based electronics owing to its high reconfigurability, flexibility, parallelism, scalability, and considerable application prospects.

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Conflict of interest

The authors declare that they have no conflict of interest.

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