Electronic Supplementary Information

Experimental section

Chemicals and apparatus. All oligonucleotides were synthesized and HPLC-purified by Sangon Biotech. Co., Ltd. (China). Their sequences are listed in Table S1. Exo III was ordered from Fermentas (Canada). Hemin and luminol with analytical grade were purchased from Aladdin Chemistry Co., Ltd. (China), which were used as received without further purification. Ultrapure water was used throughout the experiments.

The CL imaging experiments were performed on a K6000 mini chemiluminescent imaging system (Beijing kcrx bio-company, China). The gel electrophoresis was carried out on a Tanon 2500R electrophoresis analyzer (China).

Native polyacrylamide gel electrophoresis (PAGE). The 15% non-denaturing PAGE was first prepared by mixing 4 mL of 30% acrylamide/bis-acrylamide gel solution (29:1), 160 μL of 50×TAE/Mg^{2+} buffer, 80 μL of 10% ammonium persulfate (APS), 4 μL of N,N,N',N'-tetramethylethylenediamine (TEMED), and 3.756 mL of deionized water. The gel was polymerized for 1 h at room temperature and was soaked in 1× TAE/Mg^{2+} buffer (pH 8.0). And then, 12 μL of each sample was mixed with 2 μL of 10× loading buffer. Electrophoresis was carried out at 170 V for 5 min and 110 V for 1 h at room temperature. After staining in diluted 4S Red Plus solution (Sangon Biotech. Co., Ltd., China) for 40 min, the gel was scanned using a Tanon 2500R gel imaging system.

Exo-TRA for input DNA detection ("signal-on" for "YES" gate and "signal-off" for "NOT" gate). For "YES" gate configuration, 10 μL of (1) (10^{-6} M) were mixed with 10 μL of (2) (10^{-6} M),

followed by annealing at 90 °C for 10 min and cooling to room temperature to yield the hybrid I. Then, 10 μL of input DNA with different concentrations were added. The Exo-TRA was initiated upon introducing 3 μL of 10× reaction buffer (660 mM Tris-HCl and 6.6 mM $MgCl_2$, pH 8.0) containing 50 units of Exo III. After incubation at 25 °C for 30 min, 10 μL of hemin (1×10^{-6} M) was added to the resultant solution, followed by reaction for another 30 min at 25 °C. Finally, the CL images were recorded upon the addition of 50 μL of luminol (10 mM) and 40 μL of H_2O_2 (300 mM).

For NOT gate, hemin/(5) complex (1×10^{-8} M) was previously prepared by mixing equal volume of hemin and (5) at 25 °C for 30 min, which was used to react with the product of the "NOT" gate. In addition, hybrid II consisting of strands (3) and (4) was constructed as hybrid I. Other procedures were the same as those of "YES" gate.

Operations of "AND", "OR", and "INHIBIT" gates. For AND gate, strands (6) was first annealed at 90 °C for 5 min and gradually cooled to room temperature to form the hairpin structure. The annealed strand (6) was then hybridized with strand (7) to yield hybrid III. Subsequently, the inputs (10^{-10} M for each) corresponding to different states ([0,0], [1, 0], [0, 1] and [1, 1]) were introduced into the system. Other reaction conditions were the same as those mentioned in "YES" gate. The operation procedures of "OR" and "INHIBIT" gates were similar to "AND" gate except that different DNA hybrids were formed corresponding to respective logic gates.

Operations of "NOR" and "IMPLICATION" gates. For "NOR" and "IMPLICATION" logic gates, hemin/(5) complex was previously prepared by mixing equal volume of hemin and (5) at 25 °C for 30 min, which was used to react with the product of corresponding gate. The concentration

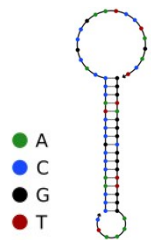
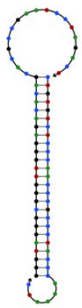
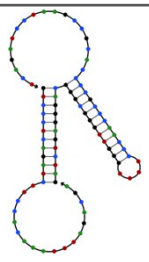
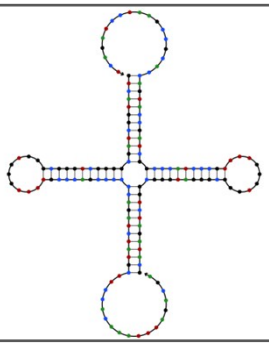
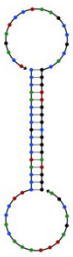
of each input was 10^{-8} M. Other procedures were similar to "AND" gate except that different DNA hybrids were formed corresponding to respective logic gates. It should be noted that strands (8), (9), (12) and (13) should be respectively annealed to obtain the hairpin structures before hybridization to form corresponding DNA hybrids.

Table S1. DNA sequences used in this work[a]

name	sequences (5'-3')
input or input 1	AGTCTAGGATTCGGCGTGATATA
input 2	TCGTCTAAATTTGTGGAAGGAAA
(1)	GGGTAGGGCGGGTTGGGAAAATC
(2)	CCCAACCCGCCCTACCCCACGCCGAATCCTAGACT
(3)	CTGTGTCTCCCAACCCGCCCTACCCAAAATC
(4)	GGGTAGGGCGGGTTGGGAGACACAGCACGCCGAATCCTAGACT
(5)	GGGTAGGGCGGGTTGGGAGACACAGAAAAA
(6)	GATCTGAGGGACGGGCGGGTTGGGTTTTCCCAACCCGCCCCACGCCGAATCCTAGACT
(7)	GTCCCTCAGATCTTCCACAAATTTAGACGA
(8)	GCATAGATCTGGCGGGTAGGGCGGGTGGGTTTTGCCCTACCCGGCTAGCCATGACCACG CCGAATCCTAGACT
(9)	GTCATGGCTAGCGGGGCTGGGCGGGTGGGTTTTGCCCAGCCCCCCAGATCTATGCTTCC ACAAATTTAGACGA
(10)	GGGTAGGGCGGGTTGGGCACGCCGAATCCTAGACT
(11)	CCCAACCCGCCCTACCCTTCCACAAATTTAGACGA
(12)	GCATAGATCTGGCTGTGTCTCCCAACCCGCCCTACCCTTTTCGGGTTGGGAGACACAGGC TAGCCATGACCACGCCGAATCCTAGACT
(13)	GTCATGGCTAGCCTGTGTCTCCCAACCCGCCCTACCCTTTTCGGGTTGGGAGACACAGCC AGATCTATGCTTCCACAAATTTAGACGA
(14)	CTGTGTCTCCCAACCCGCCCTACCCCACGCCGAATCCTAGACT
(15)	GGGTAGGGCGGGTTGGGAGACACAGTTCCACAAATTTAGACGA

[a] The sequence color is accord with that in the schemes.

Table S2. Secondary structures of the hybrids used in logic gates (http://www.nupack.org).

hybrid I (1)/(2) for YES gate	hybrid II (3)/(4) for NOT gate	hybrid III (6)/(7) for AND gate	hybrid IV (8)/(9) for OR gate	hybrid V (10)/(11) for INHIBIT gate
				

Real sample analysis

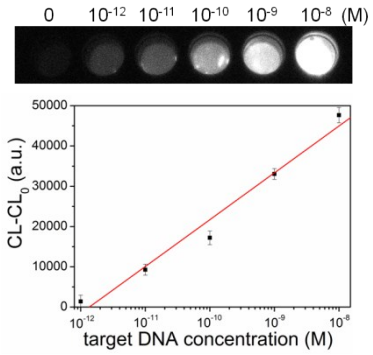


Fig. S1 CL images and corresponding calibration curve generated by target DNA with various concentrations that are spiked into 10-fold diluted human serum samples. The error bars represent the standard deviation obtained from three independent experiments.

Selectivity of the "NOT" gate

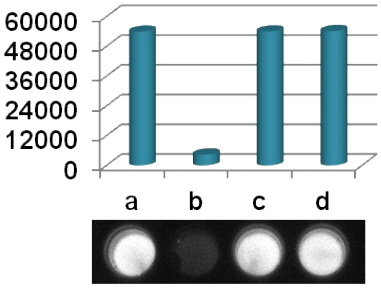


Fig. S2 CL images and intensities of the "NOT" gate in response to different input DNAs. (a) Blank, (b) perfectly complementary input, (c) one-base mismatched input, and (d) non-complementary input. The concentration of each input is 10^{-8} M.

"OR" gate

"OR" gate is constructed through hybridization hairpins (8) and (9) with each other with 3'-end overhangs to form hybrid IV as substrate and still using input 1 and input 2 as inputs. For an "OR" logic operation, the output 1 can be detected when either one or both inputs is 1. As shown in Fig. S3a, the HRP-mimicking DNAzyme sequences are caged in the stems of (8) and (9), respectively, which thus cannot fold into G-quadruplex/hemin HRP-mimicking DNAzyme structure in the presence of hemin. Therefore, no CL signal can be readout (output 0) in the absence of inputs (0,0). Upon the introduction of either input 1 (1,0) or input 2 (0,1), the formation of duplex region initiates the activity of Exo III, resulting in the stepwise hydrolysis of mononucleotides from the blunt 3'-terminus of (8) or (9) in the direction of 3'-to-5' and liberating intact input 1 or input 2 to initiate a new cycle. After the duplex is fully consumed, the cleavage activity of Exo III is resisted when it meets the single-stranded loop domain of (8) or (9). As a result, the caged HRP-mimicking DNAzyme sequence is released, which assembles into the catalytically active HRP-mimicking DNAzyme in the presence of hemin. Thus, the DNAzyme catalyzes the oxidation of luminol by H_2O_2 to generate an amplified CL readout (output 1). When both inputs are present (1,1), both resulting blunt 3'-terminus of (8) and (9) are cleaved by Exo III simultaneously, leading to the autonomous production of G-quadruplex sequences and the generation of remarkable CL signal in the presence of hemin (output 1). Therefore, the output is 1 when the system is subjected to one input or two inputs, whereas 0 when neither input is 1, which corresponds to the "OR" gate. The CL images and signals of the "OR" gate and the corresponding truth table are shown as Fig. S3b and Fig. S3c, respectively.

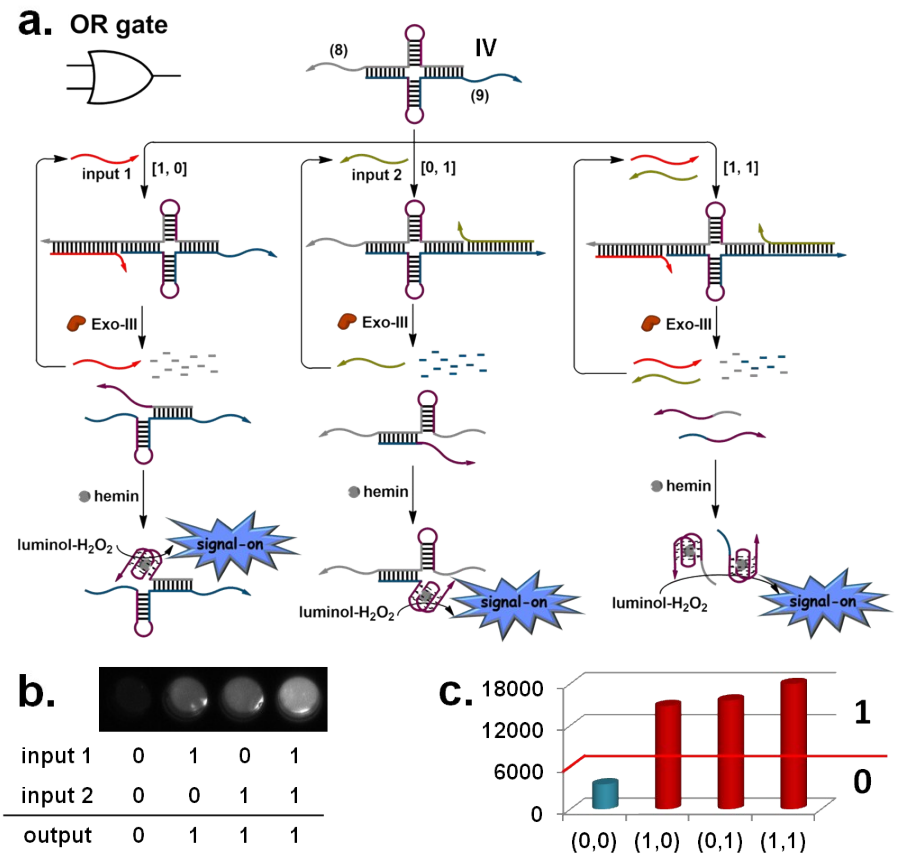


Fig. S3 The "OR" logic gate. (a) Schematic diagram, (b) CL images and truth table, and (c) column diagram of the CL intensities of the "OR" logic gate with different input combinations. The red solid line in (c) shows the threshold value as 6000.

"INHIBIT" gate

Another logic type, "INHIBIT" gate, is constructed by assembling a duplex (10)/(11) (hybrid V) as substrate with protruding regions at 3'-terminus of (10) and (11), respectively (Fig. S4a). This gate still utilizes input 1 and input 2 as inputs. The G-quadruplex sequence is caged in the double-stranded region. When input 2 is added, it hybridizes with the single-stranded domain of (10) to form a blunt 3'-terminus that is cleaved by Exo III to release the G-quadruplex sequence that folds into the HRP-mimicking DNAzyme in the presence of hemin, resulting in a great increase in CL intensity. Otherwise, for the situation of (1,0) or (1,1), the G-quadruplex DNAzyme sequence is

degraded by Exo III. Thus, the output 1 is produced only when input 2 is held at 1, which is equivalent to a logical "INHIBIT" operation. The results of this system are presented in Fig. S4b and Fig. S4c.

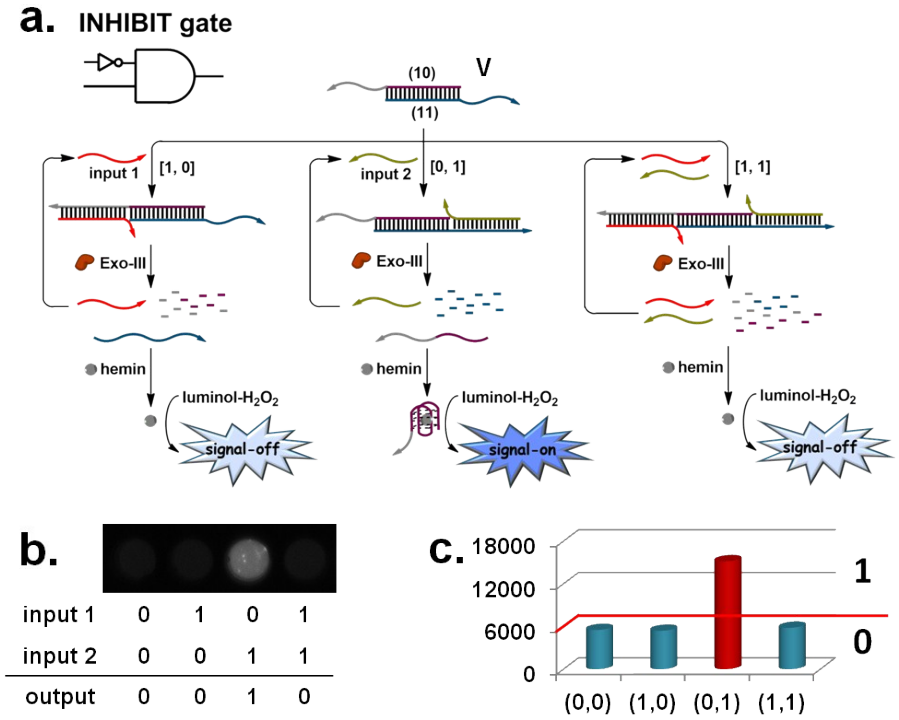


Fig. S4 The "INHIBIT" logic gate. (a) Schematic diagram, (b) CL images and truth table, and (c) column diagram of the CL intensities of the "INHIBIT" logic gate with different input combinations. The red solid line in (c) shows the threshold value as 6000.

"IMPLICATION" gate

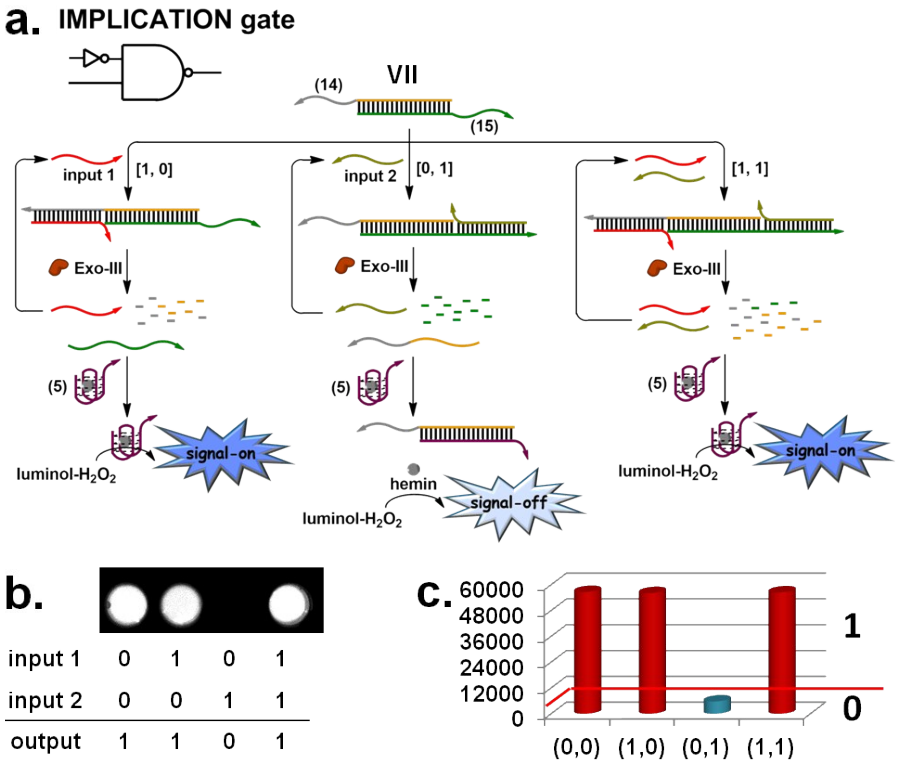


Fig. S5 The "IMPLICATION" logic gate. (a) Schematic diagram, (b) CL images and truth table, and (c) column diagram of the CL intensities of the "IMPLICATION" logic gate with different input combinations. The red solid line in (c) shows the threshold value as 6000.