

# **Construction of Scalable DNA Computing Nano-system for Large-scale and Complex Logical Operations**

Chunyang Zhou,<sup>a</sup> Yiwei Song,<sup>a</sup> Xiuyan Jin,<sup>a</sup> Bei Li,<sup>\*bc</sup> Chunying Pang<sup>\*a</sup>

<sup>a</sup> *Biomedical Engineering, School of Life Science and Technology, Changchun University of Science and Technology, Changchun, 130031, China. Email: 1281957328@qq.com*

<sup>b</sup> *Changchun Institute of optics, precision machinery and physics, Chinese Academy of Sciences, Changchun, 130031. Email: beili@ciomp.ac.cn*

<sup>c</sup> *University of Chinese Academy of Sciences, Beijing 100049.*

**Table S1.** Single-stranded DNA used for the construction of reaction platform.

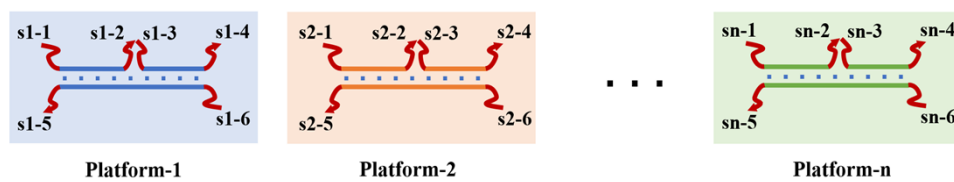
Platform (P1-P10)	Strand name	DNA Sequence (from 5' to 3')	Modification
P-1	P <sub>1</sub> -DNA	TGAAGTG TTATGAATG TT GTAATG TAATG TATGA	
	Q <sub>1</sub> -DNA	ATACAA TCATA CATT A CATTAC	3'-BQH1
	F <sub>1</sub> -DNA	CATTCATAACACTTCAATTACA	5'-FAM
P-2	P <sub>2</sub> -DNA	AAGTGATAATGTAATGTTGTAAAGTTAAAGATTGT	
	Q <sub>2</sub> -DNA	AATCAT ACAATCTTAACTTTAC	3'-BQH2
	F <sub>2</sub> -DNA	CATTACATTATCACTTCAATAC	5'-HEX
P-3	P <sub>3</sub> -DNA	TGTAATTGAAGTAATGTTGTAAAGTAAAGATTGTA	
	Q <sub>3</sub> -DNA	TAACTCTACAATCTTACTTTAC	3'-BQH1
	F <sub>3</sub> -DNA	CATTACTTCAATTACAAACATC	5'-FAM
P-4	P <sub>4</sub> -DNA	TGATATTGAAGTAATGTTGTAATGTATAGATATT	
	Q <sub>4</sub> -DNA	ACATTCAATATCTATACATTAC	3'-BQH2
	F <sub>4</sub> -DNA	CATTACTTCAATATCAACTTAA	5'-HEX
P-5	P <sub>5</sub> -DNA	AGAGATTAGTTGATAGTTGTATTGATAAGTGAAT	
	Q <sub>5</sub> -DNA	TCAACAATCACTTATCAATAC	3'-BQH1
	F <sub>5</sub> -DNA	CTATCAACTAATCTCTCACTAT	5'-FAM
P-6	P <sub>6</sub> -DNA	GAGAATAGAAGTTAAGTTGATTAGTAAGTGATTA	
	Q <sub>6</sub> -DNA	CTTATCTAATCACTTACTAATC	3'-BQH2
	F <sub>6</sub> -DNA	CTTAACTTCTATTCTCTCTTAA	5'-HEX
P-7	P <sub>7</sub> -DNA	GTTATGATATTGTATGTTGAATGTAATGATTAAT	
	Q <sub>7</sub> -DNA	TCCATAATTAATCATTACATTC	3'-BQH1
	F <sub>7</sub> -DNA	CATACAATATCATAACATCACT	5'-FAM
P-8	P <sub>8</sub> -DNA	GAGAATATGGATAATGTTGAATATGAAGTTGAAG	
	Q <sub>8</sub> -DNA	CATATCTTCAACTTCATATTC	3'-BQH2
	F <sub>8</sub> -DNA	CATTATCCATATTCTCACCTTA	5'-HEX
P-9	P <sub>9</sub> -DNA	TTAAGGTTGAATGTTGTTGTTAGTAATAAGATGT	
	Q <sub>9</sub> -DNA	TATCTAACATCTTATTACTAAC	3'-BQH1
	F <sub>9</sub> -DNA	CAACATTCAACCTTAATACACT	5'-FAM
P-10	P <sub>10</sub> -DNA	TGATGTATATGTATAGTTGTTAGATGTATGAAGA	
	Q <sub>10</sub> -DNA	CTACAATCTTCATACATCTAAC	3'-BQH2
	F <sub>10</sub> -DNA	CTATACATATACATCATTTCTCA	5'-HEX

**Table S2.** Sequence of input DNA used in the operation square root logic circuit.

Square root Input Library	Subset	DNA Sequence (from 5' to 3')
A	A1	AGTTAAGATTGTATGATT
	A2	TAACTCTACAATCTTACT
	A3	AAATCCTCAACAATTCGTATTGATAAGTGAAT TGGTGA
	A4	ATTAGATAAGTAAGAG
	A5	GAAGAATATGAAGTAA
	A6	CCTACTTATCTAACATGTAATAAGATGTTAGATA
	A7	CTACAATCTTCATACATC
	A8	ATTCAACCTTAATACACT
B	B1	AGTTAAGATTGTATGATT
	B2	TGTATAGATATTGAATGT
	B3	TAACTCTACAATCTTACT
	B4	CTCTTACTTATCTAATGATTAGTAAGTGATTAGATAAG
	B5	GAATTGTTGAGGATTT
	B6	GAAGAATATGAAGTAA
	B7	GTGAAATAAGGTGAGA
	B8	ATGTTAGATAAGTAGG
	B9	CTACAATCTTCATACATC
	B10	TGAGAATGATGTATATGT
C	C1	TG TAATG TATGATTGTAT
	C2	AATCAT ACAATCTTAACT
	C3	GAATTGTTGAGGATTT
	C4	TTACTTTCATATTCTTCGAATATGAAGTTGAAG AATATG
	C5	CCTACT TATCTAACAT
	C6	CTCTTACTTATCTAAT
D	D1	TG TAATG TATGATTGTAT
	D2	AGTAAGATTGTAGAGTTA
	D3	ACATTCAATATCTATACA
	D4	ATTAGATAAGTAAGAG
	D5	TAAGGTGAGAATATGGATAATGTCTCACCTTATTTTAC
	D6	GATGTATGAAGATTGTAG
	D7	AGTGTATTAAGGTGAAT
	D8	ACATATACATCATTCTCA

**Table S3.** Sequence of input DNA used in the operation cube root logic circuit.

Cube root Input Library	Subset	DNA Sequence (from 5' to 3')
A	A1	AGTTAAGATTGTATGATT
	A2	TTAAGTTGATATTGAAGTATCAACTTAAAAATCC
	A3	TCAACAATTCACCTATCA
	A4	AAGTAAATAGTGAGAG
	A5	GTGAAATTAAGAGAGA
	A6	TCCATAATTAATCATTAC
	A7	GAGAATAGTGATGTTA
	A8	TATCTAACATCTTATTAC
	A9	ATGTTTTGAGAATGAT
B	B1	AGTTAAGATTGTATGATT
	B2	GGATTTTTAAGTTGAT
	B3	ACATTCAATATCTATACA
	B4	TAAGAGGATGTTTGTA
	B5	TGATAAGTGAATTGTTGA
	B6	CTTATCTAATCACTTACT
	B7	CTCTCACTATTTACTT
	B8	AGTAGGTTAAGAGAGA
	B9	ATGAAGTTGAAGAATATG
	B10	TCCATAATTAATCATTAC
	B11	GTAATAAGATGTTAGATA
	B12	CTACAATCTTCATACATC
	B13	GGATAATGAGAATGAT
C	B1	AGTTAAGATTGTATGATT
	B2	TGTATAGATATTGAATGT
	B3	GATGTTTGTAATTGAAGTTACAAACATCCTCTTA
	B4	ATCAACTTAAAAATCC
	B5	AGTAAGTGATTAGATAAG
	B6	ATAGTGAGAGATTAGTTGCTCTCACTATTTACTT
	B7	TCAACAATTCACCTATCA
	B8	TTAAGAGAGAATAGAAGTTCTCTCTTAATTTAC
	B9	GTAATGATTAATTATGGA
	B10	CATATTCTCAACTTCAT
	B11	GATGTATGAAGATTGTAG
	B12	TGAGAATGATGTATATGTATCATTCTCAAAACAT
D	D1	TGTAATGTATGATTGTAT
	D2	AATCATACAATCTTAACT
	D3	TCAACAATTCACCTATCA
	D4	TTAAGAGAGAATAGAAGTTCTCTCTTAACCTACT
	D5	AGTGATGTTATGATATTGTAACATCACTATTCTC
	D6	TATCTAACATCTTATTAC
	D7	TGAGAATGATGTATATGTATCATTCTCATTATCC



**Fig. S1** Diagram of the combination of monomers forming the reaction platform. Each monomer consists of three single-stranded DNAs and can form up to six encodable sites. In the case of Platform-1, the encoded sites are s1-1, s1-2, s1-3, s1-4, s1-5 and s1-6, which remain single stranded. Each coding site can be modified by fluorophore or quenching group.

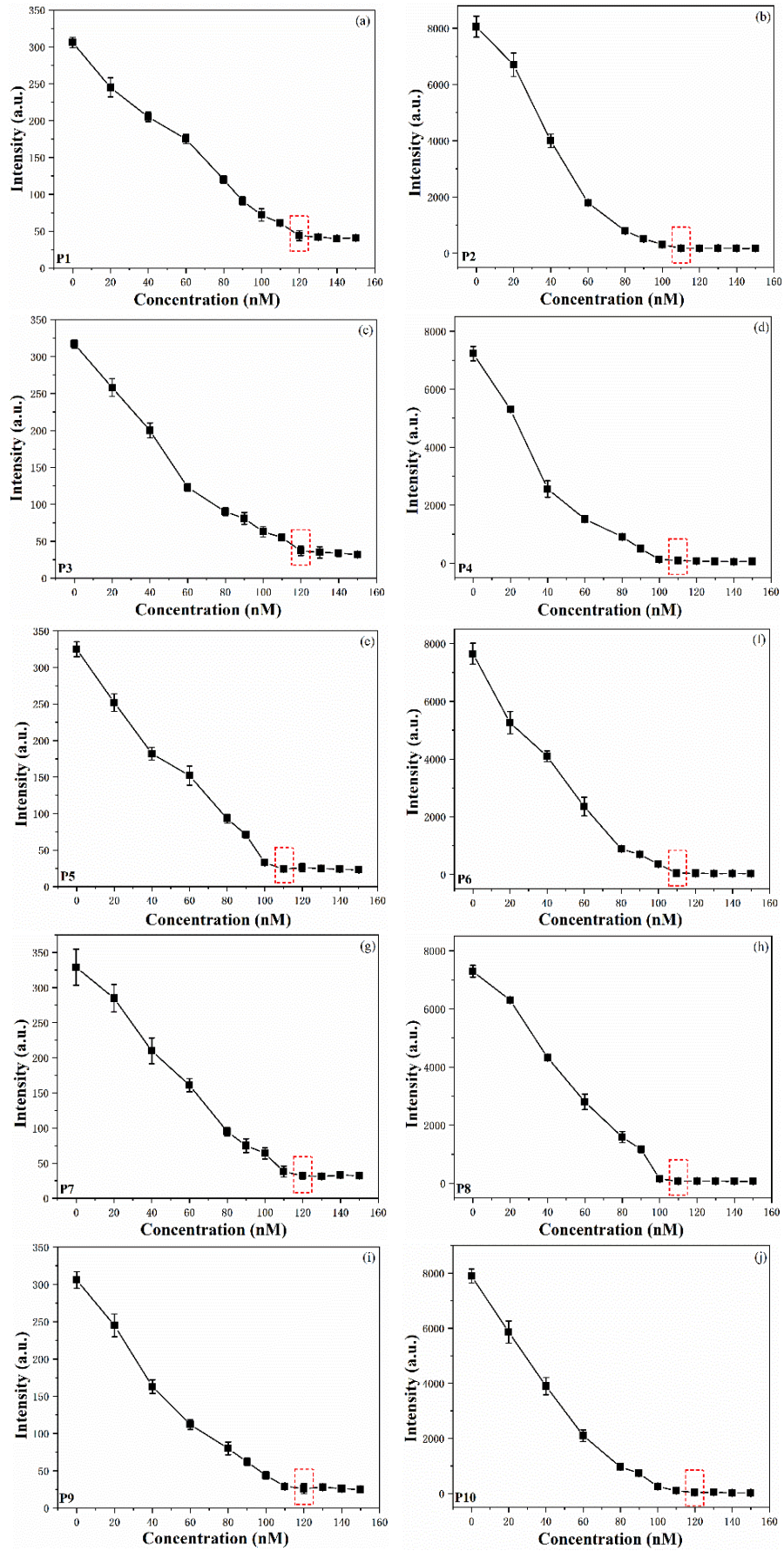
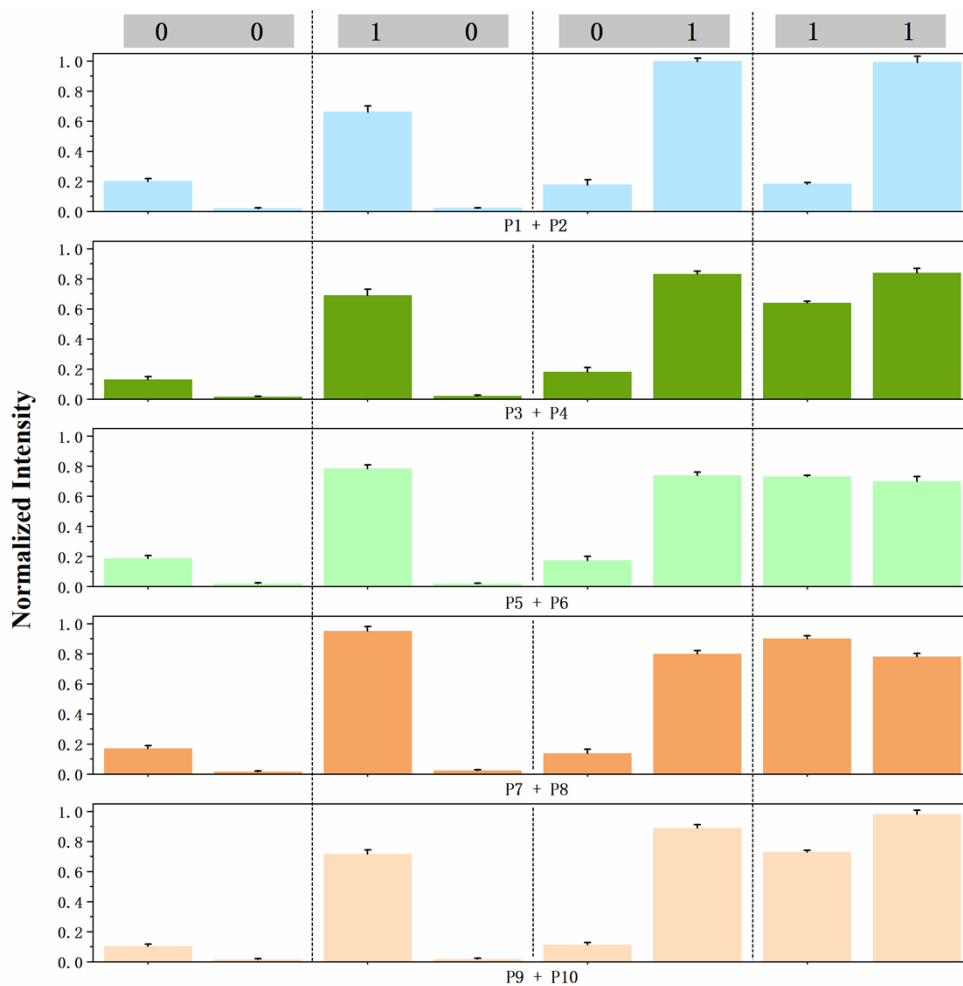


Fig. S2 Optimized concentrations of three single-stranded DNAs that consist of each platform

monomer. As shown in Fig. 2c, the original concentrations of P-DNA and F-DNA are set to 100 nm and mix preferentially, followed by the addition of Q-DNA. As shown in Fig. S3, as the concentration of Q-DNA gradually increases, the fluorescence intensity gradually decreases. When it drops to a minimum the corresponding concentration is the optimal concentration of Q-DNA, which is indicated in the red box in Fig. S3.



**Fig. S3** The fluorescence intensity changes before and after adding the input sequence into the five subsets. In the mixture of P1+P2, P3+P4, P5+P6, P7+P8, and P9+P10, the fluorescence intensity of each two monomers with the addition of no input DNA (0 0) is the low and ideal background signal. When the addition of the input DNA that can “turn on” any monomer (1 0/0 1) in each mixture, its fluorescence signal was significantly increased, while the fluorescence signal of the other monomer remained low. When the input sequences were added to light up both monomers in the mixture (1 1), both fluorescence signals were significantly improved.



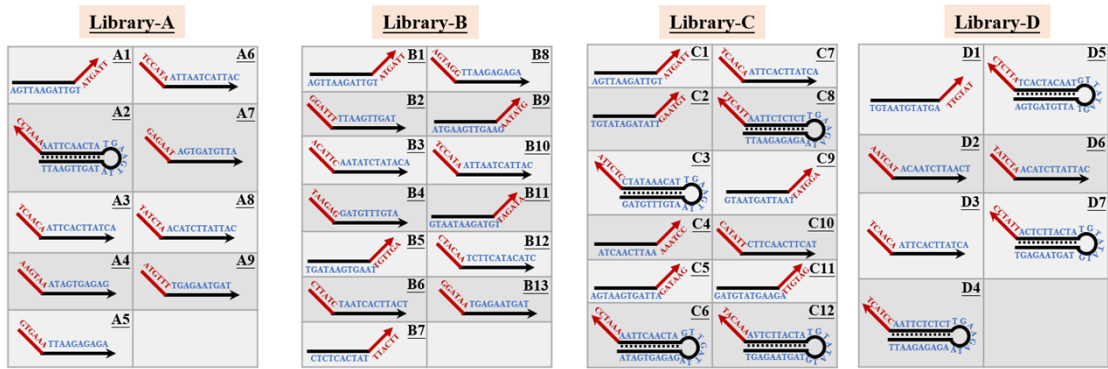
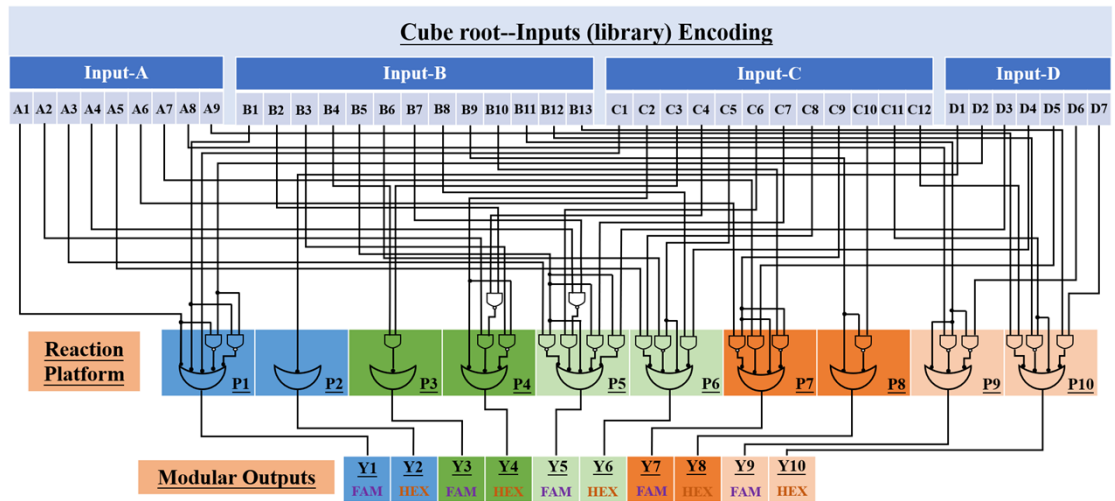
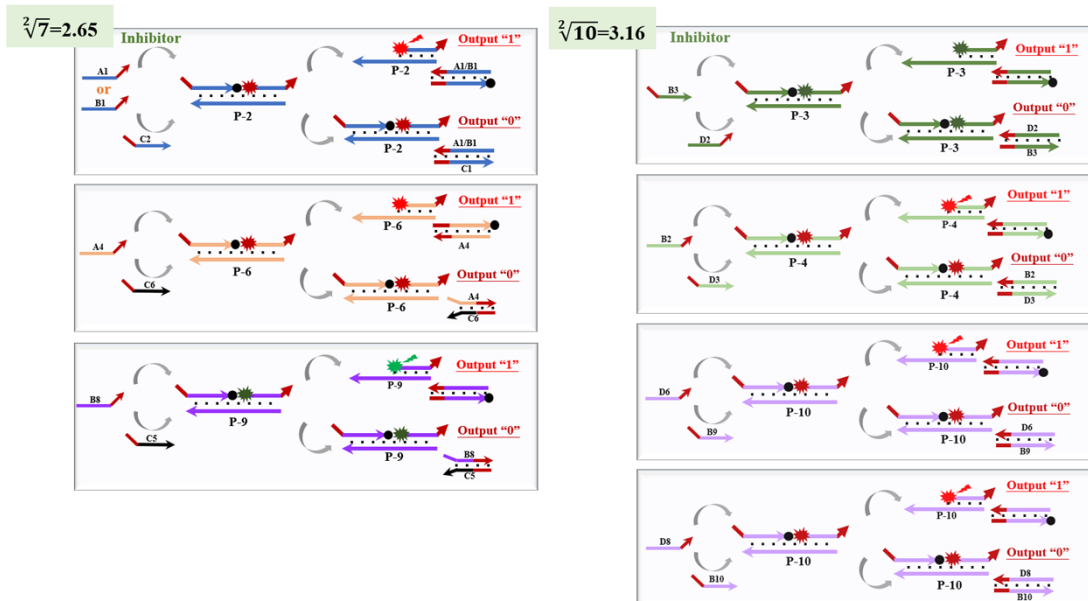


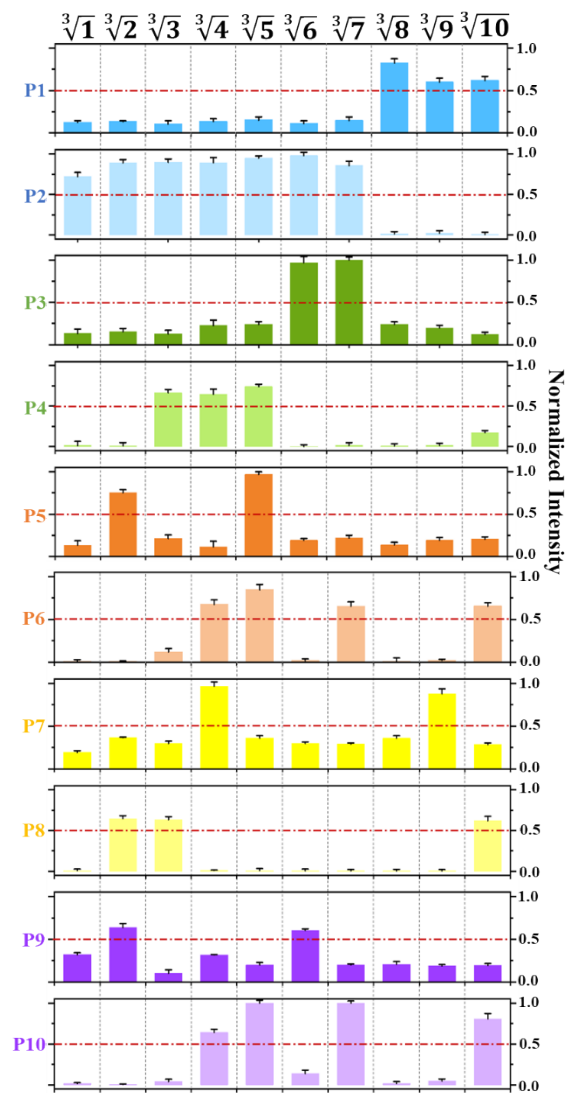
Fig. S4 Display of the input DNA library design for the cube root logic computing.



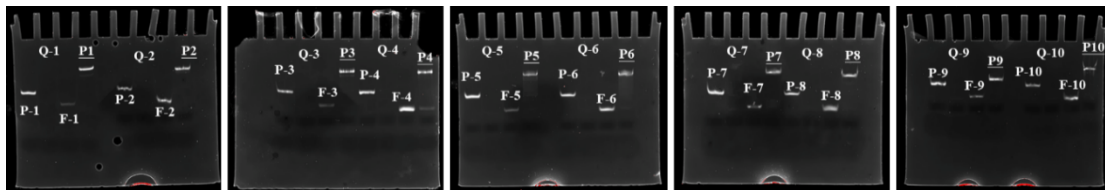
**Fig. S5** Logic circuit diagram for realizing cube root calculation.



**Fig. S6** Detailed work mechanism of bl-SW in the operation of “ $\sqrt[2]{7}=2.65$ ” and “ $\sqrt[2]{10}=3.16$ ”. The “ON” or “OFF” status of the fluorescence signal was monitored by contrast before and after adding the bl-SW to the reaction platform.



**Fig. S7** Histogram of normalized fluorescence output intensities of P1 to P10 within the calculation range of any integer up to “ $1 \leq x \leq 10$ ” in the cube root operation. The error bars are obtained via three independent experiments and donate standard deviation (S.D.).



**Fig. S8** Display of the raw gel images corresponding to Fig. 2e.