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Control of electrochemical signals from quantum dots conjugated to organic materials by using DNA structure in an analog logic gate

Qi Chen [a,1], Si-Youl Yoo [a,1], Yong-Ho Chung [c], Ji-Young Lee [a], Junhong Min [d,*], Jeong-Woo Choi [a,b,**]

[a] Department of Chemical and Biomolecular Engineering, Sogang University, 35 Baekbeom-ro, Mapo-gu, Seoul 121-742, Republic of Korea
[b] Interdisciplinary Program of Integrated Biotechnology, Sogang University, 35 Baekbeom-ro, Mapo-gu, Seoul 121-742, Republic of Korea
[c] Department of Chemical Engineering, Hoseo University, Hoseoro 79 bungil 20, Baebang, Asan, Chungnam 336-795, Republic of Korea
[d] School of Integrative Engineering, Chung-Ang University, Heukseok-dong, Dongjak-gu, Seoul 156-756, Republic of Korea

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ABSTRACT

Various bio-logic gates have been studied intensively to overcome the rigidity of single-function silicon-based logic devices arising from combinations of various gates. Here, a simple control tool using electrochemical signals from quantum dots (QDs) was constructed using DNA and organic materials for multiple logic functions. The electrochemical redox current generated from QDs was controlled by the DNA structure. DNA structure, in turn, was dependent on the components (organic materials) and the input signal (pH). Independent electrochemical signals from two different logic units containing QDs were merged into a single analog-type logic gate, which was controlled by two inputs. We applied this electrochemical biodevice to a simple logic system and achieved various logic functions from the controlled pH input sets. This could be further improved by choosing QDs, ionic conditions, or DNA sequences. This research provides a feasible method for fabricating an artificial intelligence system.

1. Introduction

Mobile electronic devices have been developed to receive and manipulate simple biological signals such as pulse frequency and body temperature [1,2]. In the near future, electronic devices may connect directly to tissues or organs in the body to receive and interpret sophisticated biological and chemical molecular information. Indeed, bioelectronic devices consisting of biomolecules could play a leading role in facilitating communications between electronic devices and biosystems. Communications between electronic devices and biosystems are usually expressed as signal transductions based on binary code. Binary code is a universal language in computing and digital communications. Binary code employs the digits "0" and "1" as the basic unit of information. Through serial combination of various binary logic gates such as "AND", "OR", and "NOT", logic processor circuits have been designed to execute Boolean logic functions [3–5]. Sophisticated integrations of rigid logic functions are required to realize flexible analog logic functions with silicon-based gates. Biomolecules possessing redox electrochemical properties and flexible structure are an attractive proposition in development of bioelectronic devices [6–8]. Most redox biomolecules such as metalloproteins also transport or store signals, electrons, or energy in biosystems [9,10]. The main advantages of biodevices compared to silicon-based devices are improved biocompatibility, bioaffinity, and flexibility. Silicon-based materials cannot represent intricate logic systems due to their structural rigidity and insufficient plasticity. Biodevices combined with biomaterials and a solid platform have the potential for new uses, such as evaluation of brain function or use in analog-type logic systems, even though it has been difficult to demonstrate practical device application owing to technical limitations. These properties are used directly in various bioelectronics devices, providing a promising alternative to silicon-based electronic devices [11–13].

In our previous studies, we investigated the electrochemical properties of various metalloproteins and applied them to developing bioprocessors and biomemory devices [14–17]. Self-assembled monolayers of metalloproteins were used to implement multifunctional information processing (write-read-erase) and applied in biomemory devices. Multiple-bit biomemory devices were also investigated to enhance computational ability and revolutionize biocomputing techniques. Au nanoparticles and quantum dots (QDs) were introduced in our studies to regulate signals [18,19]. However, these binary studies were based on two distinct forms (reduced and oxidized) of metalloproteins, and did not demonstrate the inherent characteristics of biosystems such as analogy, flexibility, and environmentally-dependent information processing with levels

* Correspondence to: J. Min, School of Integrative Engineering, Chung-Ang University, Seoul 156-756, Republic of Korea.
** Correspondence to: J.-W. Choi, Department of Chemical and Biomolecular Engineering, Sogang University, Seoul 121-742, Republic of Korea.
E-mail addresses: junmin@cau.ac.kr (J. Min), jwchoi@sogang.ac.kr (J.-W. Choi).
[1] These authors contributed equally to this work.

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of gradation and threshold [20]. The extraordinary complexity of bio-systems calls for advanced compuatational methods to deal with the biological signals transduction network.

Therefore, we focused on the flexibility of structure and redox characteristics of nucleic acids. These biopolymers are good candidate molecules for bioelectronics because of their sequence flexibility, which guarantees infinite computational capacity. The structures of G-rich sequences are known to be switchable by pH and certain target molecules, which have been applied in biosensors and nanostructures [21–23]. The photoelectric bioswitch concept for highly charged transfers was demonstrated by conjugation of QDs to DNA [24–27].

Here, we propose a simple biologic device that could be formed by controlling the distance between QDs and gold electrodes through the DNA structure. A flexible electrochemical bio-logic gate was prepared using two independent logic units consisting of G-rich DNA conjugated to QDs. We merged electrochemical signals from two logic units under various pH conditions (input sets) into a single electrochemical output signal, which facilitated the development of diverse logic functions. This provided a feasible way to develop an advanced bioelectronics device as a tool to illustrate the communication between technique and bio-systems.

2. Materials and methods

2.1. Chemicals

Complementary DNA sequences were synthesized by Bioneer Co. (Korea): 5′-HS-$(CH_2)_6$-TTT TTT TTT TGG GTT AGG GTT AGG GTT AGG G-NH_2-3′ (S-DNA); 5′-CCC TAA CCC TAA CCC TAA CCC AAA AAA AAA A-3′ (C-DNA).

CdSe/ZnS quantum dots (610 nm emission wavelength), dithiothreitol (DTT), 2-mercaptoacetic acid (MAA), ethylenediamine (EDA), and other reagents were purchased from Sigma-Aldrich (USA). A sylgard 184 silicon elastomer kit (Dow Corning, USA) containing a polydimethylsiloxane (PDMS) base and a curing agent was used.

2.2. Fabrication of logic units

Schematic 1a shows the fabrication of logic units: S-DNA treated with 1 mM DTT was incubated with clean Au surfaces at room temperature (RT) for 4 h. S-DNA on Au was then conjugated with MAA-capped QDs in the presence of 50 mM 1-ethyl-3-(3-dimethylaminopropyl) carbodiimide (EDC) and N-hydroxysuccinimide (NHS) at RT for 2 h [28]. Logic unit "A" composed of S-DNA/QD/MAA was fabricated. The other logic unit, "B," which was composed of S-DNA/QD/MAA/EDA was fabricated from logic unit A by modifying another layer of EDA on MAA-capped QDs with the help of EDC and NHS.

2.3. Platform design and fabrication

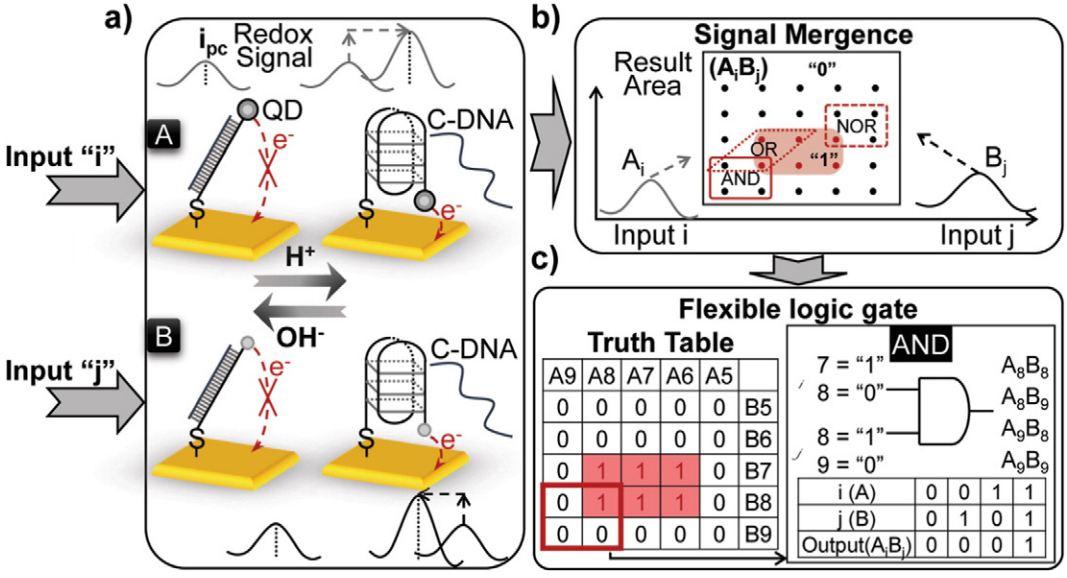
A silicon substrate was deposited with two parallel working electrodes (W_A and W_B) and a common counter electrode. The substrate was cleaned with piranha solution, then placed in a designed cell compartment (PDMS). A working electrochemical cell named "A" was used to connect W_A and the facing fragment of the counter electrode by saturating the cell with 100 L phosphate buffered saline (PBS, various pH). Working cell "B" was used to connect W_B and the counter in the same method. Cells A and B were symmetrically separated from the reference cell using 1% agarose gels. The reference cell used was a commercial Ag/AgCl electrode immersed in saturated 200 L NaCl (1 M) solution.

2.4. Morphological characterization

Modification of logic unit A (S-DNA/QD/MAA) on Au was investigated by examining morphological changes. Morphological characterization was performed using AFM (Multimode, Veeco, USA) by varying the frequency of its cantilever in tapping mode. A cantilever (257–319 kHz resonance frequency) fabricated using phosphorus (n) doped silicon was utilized. The tip velocity was 2.0 μm s^{-1} and the scan size was 500 nm × 500 nm.

2.5. Analysis of electrochemical properties

Electrochemical investigations were performed using an electrochemical analyzer (CHI 660, USA). The electrochemical properties were studied using a three-electrode system composed of a platinum counter electrode, Ag/AgCl double junction reference electrode, and a logic unit on a modified gold substrate with a 0.25 cm^2 area as a working electrode. The electrolyte was 5 mL PBS buffer of quartz. The patterned W_A or W_B, the patterned counter, and the dipped reference electrode comprised the three-electrode system on the chip. Signals generated by A and B cells under various pH conditions



A9	A8	A7	A6	A5	
0	0	0	0	0	B5
0	0	0	0	0	B6
0	1	1	1	0	B7
0	1	1	1	0	B8
0	0	0	0	0	B9

i (A)	0	0	1	1
j (B)	0	1	0	1
Output(A_iB_j)	0	0	0	1

Schematic 1. Analog logic gates via signal processing of two logic units. a) Illustration of pH conducted DNA transformation and related redox signal variation. b) Mapping of merged output signals (A*i*B*j*) in response to individual pH inputs in A (*i*) and B (*j*) platforms. c) Obtained flexible logic gate with a function determined by choosing the input of pH sets.