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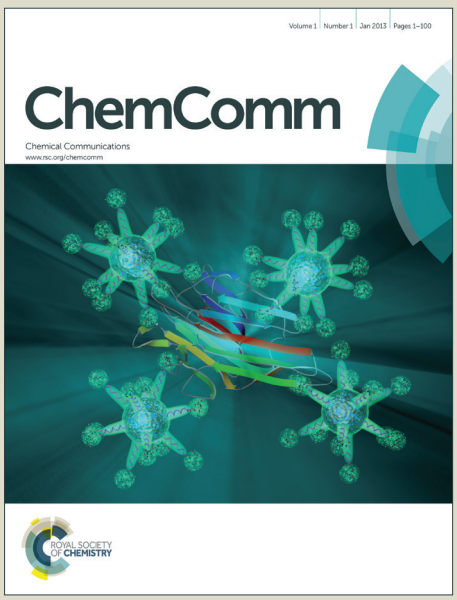

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COMMUNICATION

Molecular Encoder - Decoder Based on Assembly of Graphene with Dye-labeled DNA

Cite this: DOI: 10.1039/xoxxoooooox

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A general strategy was developed to fabricate 2-to-1, 4-to-2, 8-to-3 molecular encoders and 1-to-2 decoder by assembling graphene oxide with various dye-labeled DNA.

Molecular computing, performed by small organic molecules, bio-macromolecules (e.g. DNA, protein/enzymes), cells, and other living organisms for the fabrication of chemical and/or biological computers, has attracted a great deal of scientific interest[1]. As an alternative route to silicon-based computing, molecular computing process information according to chemical or biochemical means. To realize molecular computing, one of the key factors is the choice of suitable materials. DNA, a powerful medium for data storage and information processing, has been regarded as promising materials for molecular computing due to their well-regulated structures and ease of self-assembly with desired folding pathways and conformation changes[2]. To date, DNA-based logic gates, keypad lock, and molecular switches have been experimentally demonstrated via utilizing different input and output signals, which have been used for environmental monitoring, drug delivery, and intelligent medical diagnostics[3]. For example, Willner and co-workers reported a pH-programmable system for the emulation of Boolean logic functions using libraries of DNAzyme subunits and their substrates as functional constituents[4]. Wang's group developed an enzyme-free unlabeled DNA logic circuits based on toehold-mediated strand displacement and split G-quadruplex enhanced fluorescence of protoporphyrin IX[5]. Most recently, Li and co-workers realized three-input majority logic gate with programmed DNA strand displacement reactions and demonstrated that it reliably produced all the correct outputs with different combinations of the inputs[6]. By linking two three-input majority gates together, they further constructed a five-input computing circuit implemented solely. Although molecular encoders and decoders play more important roles in molecular computing because they could convert data/code into a code/data, relatively few studies have been reported compared with logic gates. Gust's group reported a molecular triad consisting of a dithienylethene covalently linked to two fulgimide photochromes that performed as an all-photonic single-bit 4-to-2 encoder and 2-to-4 decoder[7]. Balzani and coworkers employed the optical and electronic properties of $[Ru(bpy_{)3}]^{2+}$, constructing 4-to-2 encoder and 2-to-4 decoder[8]. The reported work employed unique molecules that could respond external stimuli, which needed elaborate synthesis or screen. Also, the proposed strategy could not realize more complex encoders and decoders such as 8-to-3 encoder, limiting encoders and decoders for performing advanced and complex molecular computing. Thus current work is at proofs of concept stage. It still remains a great challenge for the construction of more complex, multi-component molecular devices or logic circuits for improving computational complexity and realizing realistic DNA-based information processing systems with a simple and general strategy.

Graphene and their derivatives, due to their unique optical, thermal, electronic, and catalytic properties, have received much attention recently in materials science and biotechnology[9]. For instance, graphene oxide (GO) can not only quench the fluorescence of various dyes through the long-range energy transfer, but also interact differentially with DNA oligonucleotides with different length and structure, thus they have served as nano/bio interfaces and sensing platforms for biosensing, biomedical applications, and molecular computing[10]. Although GO have been used to fabricate logic gates by taking advantage of metal ions and organic molecules as input and fluorescent signals as their readouts, further application of this novel 2D nanomaterial for fabrication of molecular encoders and decoders was not explored.

Herein, we report for the first time a novel strategy to fabricate 2-to-1, 4-to-2, 8-to-3 molecular encoders and 1-to-2 decoder by assembling GO with dye-labeled DNA based on the differential interaction of the single stranded DNA (ssDNA) and duplex DNA with GO and fluorescent quenching effect of dyes by GO, realizing advanced molecular computing. These devices involved one, two, or more sequence-specific DNA labeled with different dyes as probes. When integrated together, these probes could serve as encoders, converting patterns encoded by the presence or absence of specific DNA sequences into specific optical outputs (fluorescence emission). Furthermore, a 1-to-2 decoder was also successfully fabricated according to the combination of signal-on and signal-off probes.

A digital encoder converts data into a code, which is useful to compress information for transmission or storage. To demonstrate the molecular encoders, a 2-to-1 molecular encoder was firstly designed, which compressed 2 input sates into 1 output sate (Fig. 1). The proposed molecular encoder was composed by GO and carboxyl fluorescein (FAM) labeled ssDNA probe (P1, Table S1, ESI). In the absence of complementary target DNA (D_0), P1 is adsorbed on the surface of GO and its fluorescence is quenched by GO via the long-range energy transfer, producing a very weak fluorescence emission at 516 nm with the excitation wavelength of 492 nm.

The attractive forces between DNA and GO include π–π stacking, hydrophobic interaction, hydrogen bonding, and van der Waals forces [9]. Moreover, DNA adsorption is reversible. Adsorbed DNA can be desorbed by adding its complementary DNA to form a duplex because the affinity of a double-stranded DNA (dsDNA) with GO is much weaker than that of ss-DNA[11]. Therefore, in the presence of complementary target DNA (D_1), P1 will hybridize with its complementary target DNA to form dsDNA. And the dsDNA will desorb from the surface of GO, generating a strong fluorescence emission at 516 nm.

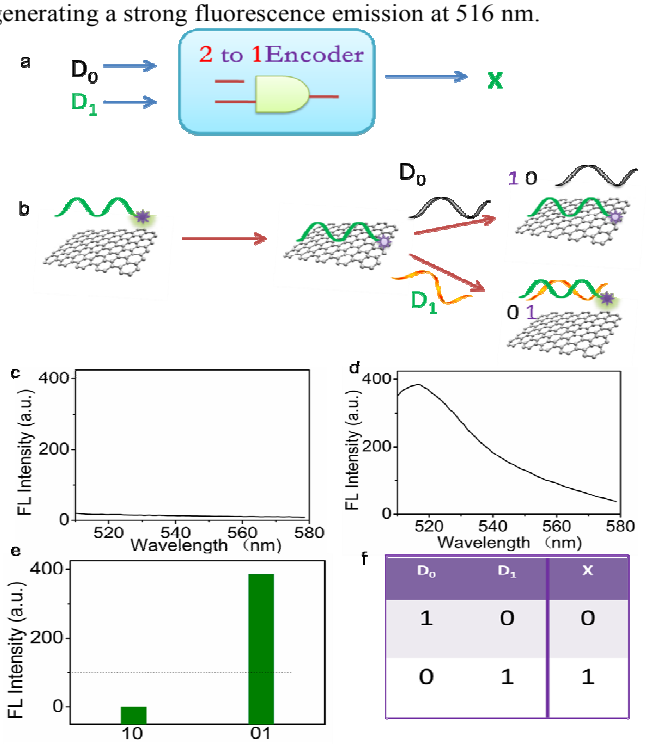

Fig. 1. Schematic representation for 2-to-1 encoder (a, b). Fluorescence spectra of the system of GO and P1 in the presence of D_0 (c) and D_1 (d) and fluorescence response (e) in presence of different input signals with excitation wavelength of 492 nm. Truth table (f) of 2-to-1 encoder.

The concentration of various DNA targets and fluorescence signal of FAM is defined as inputs and outputs, respectively. For input, the presence of >100 nM DNA targets is defined as 1 state, and lower (to 0) concentrations 0 state, respectively. For output, the fluorescent intensity at 516 nm greater than 100 and less than 100 is defined as 1 and 0 states, respectively. Two DNA targets, D_0 (R sequence, Table S1) and D_1 (T1 sequence), are compressed into one optical output, X, which is the fluorescent signal of FAM. D_0 does not hybridize with P1, exhibiting a low fluorescent signal (X=0). In contrast, D_1 is complementary to the probe, increasing the fluorescent signal (X=1). All in all, these operations result in a truth table characteristic of the 2-to-1 encoder (Fig. 1).

Based on the initial studies of the 2-to-1 encoder, a 4-to-2 encoder was fabricated. Another 6-carboxy-X-rhodamine (ROX) labeled single DNA probe (P2, Table S1) was added as a second optical reporter except FAM, which was also adsorbed on the surface of GO in the absence of the corresponding complementary DNA, providing a second and independent output signal. Similar to 2-to-1 encoder, the presence of each DNA at concentrations > 100 nM is defined as 1 state, and lower (to 0) concentrations as 0 state. As outputs, the fluorescent intensity greater than 30 and less than 30 is defined as 1 and 0 states, respectively. Four DNA sequence inputs, D_0 to D_3, are compressed into two optical outputs, X and Y, which correspond to fluorescent signal of FAM and ROX, respectively. D_0 (R sequence), does not hybridize with both of the probes so that it does not alter the fluorescent signals of FAM (X=0) or ROX (Y=0). D_1 (T1 sequence), complementary to P1, increases the fluorescent signal of FAM (X=1), but does not change the fluorescent signal of ROX (Y=0). D_2, complementary to P2 (T2 sequence, Table S1), does not affect the fluorescent signal of FAM (X=0), but enhances the fluorescent signal of ROX (Y=1). D_3 (T1-T2 sequence), complementary to both of P1 and P2, increases both of fluorescent signals (X=1, Y=1). These operations obtain a truth table of the 4-to-2 encoder as shown in Fig. 2.

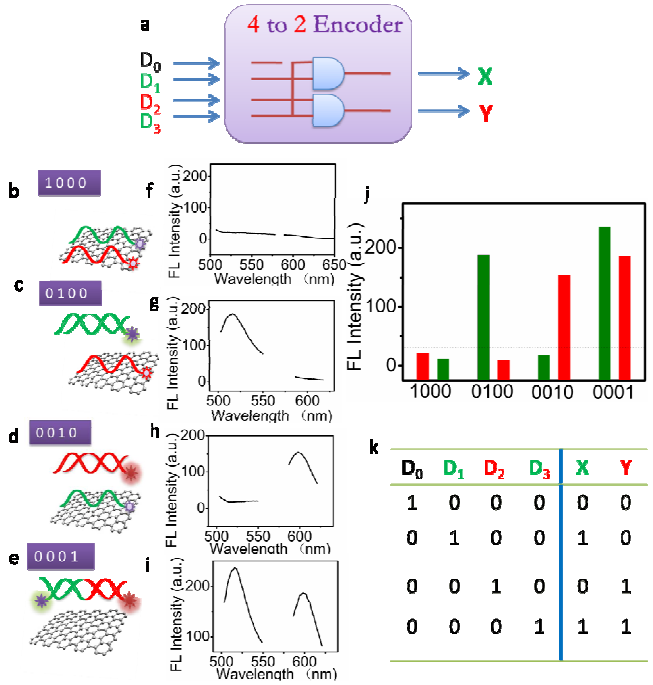

Fig. 2. Schematic representation (a-e) for 4-to-2 encoder and fluorescence spectra of the system of GO, P1 and P2 in the presence of different input signals: (f) D_0, (g) D_1, (h) D_2, (i) D_3.Fluorescence response (j) in presence of different input signals for 4-to-2 encoder. Truth table (k) of 4-to-2 encoder.

To further demonstrate the feasibility of our molecular computing system, an 8-to-3 encoder was also developed. Cyanine 5 (Cy5) labeled DNA probe (P3, Table S1) was added as a third output signal. For inputs, the presence of each DNA at concentrations > 1 μM is defined as 1 state and lower (to 0) concentrations as 0 state. Eight DNA sequence inputs, D_0 to D_7, are compressed into three optical outputs, X, Y, and Z, corresponding to the fluorescence signal of FAM, ROX, and Cy5 (Fig. S3), respectively. Similar to the 4-to-2 encoder, D_0 (R sequence) does not hybridize with none of the three probes and does not alter the fluorescent signals of FAM (X=0), ROX (Y=0), and Cy5 (Z=0). D_1 (T1 sequence), complementary to P1, increases the fluorescent signal of FAM (X=1), but does not change the fluorescent signal of ROX (Y=0) and Cy5 (Z=0). D_2 (T2 sequence), complementary to P2, does not affect the fluorescent signal of FAM (X=0) and Cy5 (Z=0), but enhances the fluorescent signal of ROX (Y=1). D_3 (T3 sequence), complementary to P3, does not alter the fluorescent signal of FAM (X=0) and ROX (Y=0), but increases the fluorescent

signal of Cy5 (Z=1). D_4 (T1-T2 sequence), complementary to both of P1 and P2, increases both fluorescent signals of FAM and ROX (X=1, Y=1), but does not affect the fluorescent signal of Cy5 (Z=0). D_5 (T1-T3 sequence), complementary to both of P1 and P3, increases both fluorescent signals of FAM and Cy5 (X=1, Z=1), but does not change the fluorescent signal of ROX (Y=0). D_6 (T2-T3 sequence), complementary to both of P2 and P3, increases both fluorescent signals of ROX and Cy5 (Y=1, Z=1), but does not change the fluorescent signal of FAM (X=0). D_7 ((T1-T2-T3 sequence), complementary to all the three probes, increases the fluorescent signals of FAM, ROX, and Cy5 (X=1, Y=1, Z=1). For outputs, the signal change of greater than 56% and less than 56% is defined as 1 and 0 states, respectively. Based on the above definitions, an 8-to-3 encoder operation is realized by controlling the concentrations of complementary DNA sequence for the FAM- , ROX-, and Cy5-labeled DNA probes. The corresponding truth table and schematic representation of the 8-to-3 encoder are presented in Fig. S4. The results indicate that our molecular computing system can realize a relatively complex encoder.

In digital electronics, a decoder is a device which does the reverse operation of an encoder, undoing the encoding so that the original information can be retrieve. The proposed molecular computing system is also able to act as a 1-to-2 decoder. The 1-to-2 decoder consists of GO, duplex DNA formed by the partially hybridization of P1 with a distinct DNA sequence (P-C-P1, Table S1, ESI), and P2. For input, the presence of DNA at concentration > 100 nM is defined as 1 state and lower (to 0) this concentration as 0 state. For output, the fluorescent intensity of FAM less than 560 and greater than 560 is defined as 1 and 0 states, respectively. Fluorescent intensity of ROX greater than 100 and less than 100 is defined as 1 and 0 states, respectively. When no input is applied, the signal of FAM is relatively strong (X=0) and the signal of ROX is very weak (Y=1). When D_0 (T4 sequence, Table S1), fully complementary to both of P-C-P1 and P2, is added as the input, DNA strand displacement reaction between D_0 and duplex DNA occurs, which leads to the release of P1 from duplex DNA. Subsequently, P1 will be adsorbed on the surface of GO as shown in Fig. 3. Therefore, the fluorescent intensity of FAM decreases (X=1), while fluorescent intensity of ROX increases (Y=0). Overall, these operations result in a truth table of a 1-to-2 decoder as shown in Fig. S5.

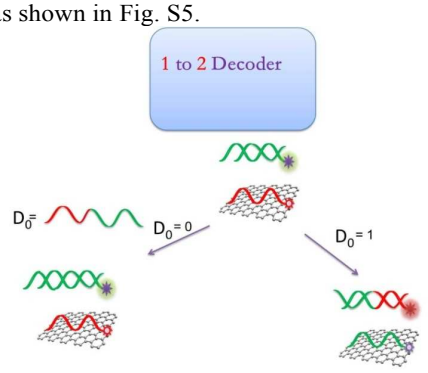

Fig. 3. Schematic representation for 1-to-2 decoder.

In summary, a set of relatively complex and multi-component molecular devices based on assembly of GO with dyes labeled DNA has been successfully designed and demonstrated, including molecular encoders (2-to-1, 4-to-2 and 8-to-3) and decoder (1-to-2). These devices convert DNA molecular information into optical output, realizing advanced molecular computing. Moreover, the developed molecular computing system is general strategy, which is readily expanded to other molecular device and more complex molecular computing according to the rational design of DNA sequence and GO. This work for the first time demonstrates that advanced molecular computing can be carried out by virtue of facile and smart assembly of GO with dye-labeled DNA, which reduces the gap between molecular computing and silicon-based electronics. The proposed molecular encoders and decoder hold great promising applications in sensing, intelligent medical diagnostics, and data processing.

Support of this research by the National Natural Science Foundation of P. R. China (Grant Nos. 21173201, 21075115 and 20625517) is gratefully acknowledged.

Notes and references

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