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Fluorescent Polymeric AND Logic Gate with Temperature and pH as Inputs

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Molecular logic gates which can simultaneously treat multiple inputs have been extremely interesting as intelligent "bottom-up" materials.[1] In particular, a fluorescence signal can be detected even in one molecule,[2] and therefore many fluorescent logic gates showing AND,[3] OR,[4] XOR,[5] NAND,[6] and INHIBIT[7] functions were reported as molecular-level devices.[8] However, the inputs to these fluorescent logic gates have been limited to chemical species such as ions or molecules. Nevertheless, these serve a valuable role as smart sensors for such species. Current sensor research has the benefit of several molecular[2b,9] and supramolecular[8b,10] designs. Here, we demonstrate the first use of the most physically important parameter "temperature" as one of the inputs to a fluorescent logic gate or smart sensor, where a sharp thermal response has been designed in. This AND logic gate with the physiologically useful inputs of temperature and pH is based on a general polymeric design. Polymeric materials[11] can have advantages over small molecule systems.

Figure 1A indicates a novel design of fluorescent polymeric logic gates consisting of *N*-alkylacrylamide and fluorophore units. This logic gate uses the three following principles: (I) The polymeric structure of *N*-alkylacrylamide units (blue part) senses the change in temperature in water solution.[12] The microenvironmental polarity near the *N*-alkylacrylamide units decreases at high temperature, and vice versa.[13] (II) The ionizable moiety in the copolymer (pink part) prevents the copolymer from intermolecular aggregation and subsequent insolubilization.[14] Moreover, its ionization affects the hydrophobicity/hydrophilicity balance of the polymer chain, which is significantly related to the thermosensitivity of the copolymer.[15] In other words, this part produces the sensitivity to the pH value. (III) The polarity-sensitive fluorophore unit in the copolymer (green part) detects the change in the microenvironmental polarity near the *N*-alkylacrylamide units to result in fluorescence as output. The number of the polarity-sensitive units in the copolymer should be much less than that of *N*-alkylacrylamide units so as not to affect the thermosensitivity of the copolymer. *N*,*N*-Dimethylaminopropylacrylamide (DMAPAM) and *N*-*t*-butylacrylamide (NTBAM) were adopted as the component *N*-alkylacrylamide monomers. DMAPAM has an amino group in its structure, and therefore it becomes more hydrophilic in acidic medium. As for a fluorophore unit, a benzofurazan group[16] which has a higher emission quantum yield in nonpolar medium[17] was selected, and 4-*N*-(2-acryloyloxyethyl)-*N*-methylamino-7-*N*,*N*-dimethylaminosulfonyl-2,1,3-benzoxadiazole (DBD-AE) with a vinyl group was used as a comonomer of the copolymer. Using these comonomers, poly(DBD-AE-*co*-DMAPAM-*co*-NTBAM) (Figure 1B) was obtained, and its fluorescence characteristics were investigated.

First, we show the function of poly(DBD-AE-*co*-DMAPAM-*co*-NTBAM) as a fluorescent molecular thermometer by fixing pH condition. Related work using the thermosensitive poly(*N*-isopropylacrylamide) and the polarity-responsive DBD-AE is available.[18] Figure 2A indicates the fluorescence intensity−temperature diagram of poly(DBD-AE-*co*-DMAPAM-*co*-NTBAM) (the composition of the copolymer is 0.1/20/80). This shows the fluorescence intensity of the copolymer is significantly increased with heating from 8 to 40 °C. The fluorescence quantum yields (Φ_f) at 10 and 40 °C were 0.016 and 0.12, respectively. The maximum emission wavelength of the copolymer was also changed from 550 to 530 nm with heating (Figure 2A, inset), indicating that the microenvironmental polarity near the DBD-AE unit decreased as designed. It is noteworthy that this copolymer maintains high solubility even at the higher temperature (Figure 2B) (cf., conventional LCST (lower

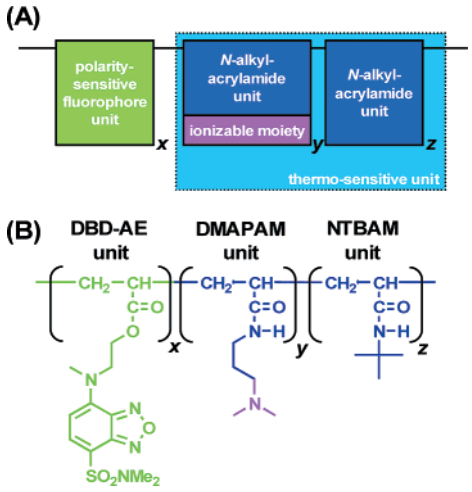

Figure 1. Design of a fluorescent logic gate with temperature and pH as inputs. (A) General structure. (B) Specific chemical structure. Each unit is randomly arranged along the polymer chain. For an original name of each unit, see the text.

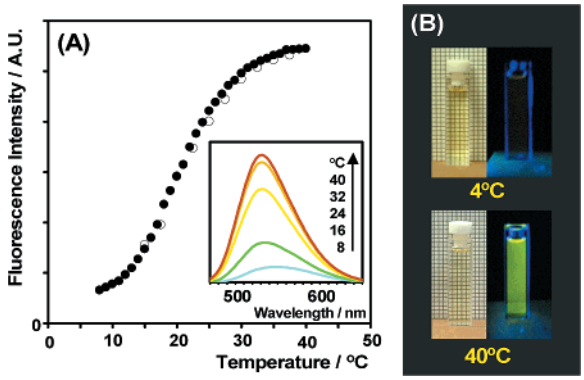

Figure 2. Behavior as a highly soluble fluorescent molecular thermometer. (A) Fluorescence intensity−temperature diagram of poly(DBD-*co*-DMAPAM-*co*-NTBAM) (0.1/20/80) in buffer (pH 7). ●, heating; ○, cooling. Excitation: 444 nm. Inset: fluorescence spectra. (B) Visual and fluorescent images. The former clearly shows the transparency of the sample.

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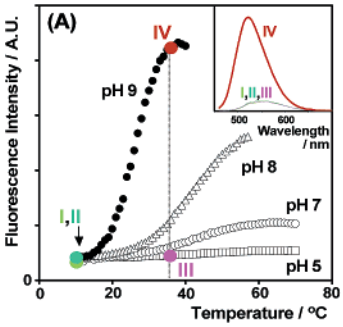

(B)

	input$_1$ (temp.)	input$_2$ (pH)	output (FI[a])
I	0 (10°C)	0 (5)	0 (0.097)
II	0 (10°C)	1 (9)	0 (0.11)
III	1 (35°C)	0 (5)	0 (0.099)
IV	1 (35°C)	1 (9)	1 (1.0[b])

[a] Relative fluorescence intensity. [b] $\Phi = 0.10$

Figure 3. AND logic operation. (A) Fluorescence intensity−temperature diagram of poly(DBD-*co*-DMAPAM-*co*-NTBAM) (0.1/30/70). Excitation: 444 nm. Inset: fluorescence spectra. (B) Truth table.

critical solution temperature) type polymers[12,18]). This unusual transparency is clearly due to the ionization of the amino moiety in the DMAPAM unit (cf., the pK_a value of trimethylamine is ∼9.8) and is useful for applications involving the temperature monitoring of small biological spaces. Furthermore, the prevention of the intermolecular aggregation by the ionized moiety enables the copolymer to work as a true molecular-level device without any intermolecular interactions. Therefore, a totally reversible response to the change in temperature was observed without hysteresis (Figure 2A) (cf., the relative standard deviations of the fluorescence intensities at 10, 20, 30, and 40 °C were only 1.7%, 0.89%, 1.0%, and 0.52%, respectively, during experiments repeated 10 times).

Next, we demonstrate the logic operation of poly(DBD-AE-*co*-DMAPAM-*co*-NTBAM) with temperature and pH as the inputs. Figure 3A shows the fluorescence intensities of poly(DBD-AE-*co*-DMAPAM-*co*-NTBAM) (0.1/30/70) at varying temperature and pH. It can be seen that the copolymer senses the change in the temperature at pH = 9 but not at pH = 5. With the increase in pH, the amino moiety in the DMAPAM unit is less ionized, and therefore its hydrophobicity increases. This increase in the hydrophobicity of the *N*-alkylacrylamide units results in the high sensitivity toward the change in temperature at high pH because the thermosensitivity of the copolymer is determined by the hydrophobicity/hydrophilicity balance of the *N*-alkylacrylamide units.[15] In brief, the change in pH of the medium plays a key role in the off−on switching of the fluorescent molecular thermometer. To indicate clearly the function of the copolymer as a logic gate, the four situations (I−IV in Figure 3A) are examined, in which temperature (Input$_1$) is 35 °C (high, binary 1) or 10 °C (low, 0) and pH (Input$_2$) is 9 (high, 1) or 5 (low, 0). As shown in Figure 3A and 3B, the fluorescence intensity (Output) of the copolymer is distinctly high (1) only when (Input$_1$, Input$_2$) is (1, 1). In contrast, the fluorescence intensity holds a low level when (Input$_1$, Input$_2$) is (0, 0), (0, 1), or (1, 0). The fluorescence intensity at Output = 1 is over 9-fold that at Output = 0. Needless to say, the response of this logic gate is reversible. These results show that the poly(DBD-AE-*co*-DMAPAM-*co*-NTBAM) performs the AND logic operation with the two inputs, temperature and pH.

We showed above an AND logic gate functioning with temperature and pH as the inputs based on a general polymeric design. Our design can be developed further because other functional logic gates can also be easily obtained by altering each component in the copolymer. For example, we can substitute the benzofurazan fluorophore units with quinoxalinone units which strongly fluoresce in a polar medium.[19] The output of the resulting logic gate must then be reversed as 1 → 0 and 0 → 1 to perform a NAND logic operation. Also, the change of the poly(*N*-alkylacrylamide) component into units which show an UCST (upper critical solution temperature) type conformational change provides an INHIBIT logic gate. We can also reverse the pH sensitivity by the replacement of the DMAPAM units in the copolymer by the *N*-alkylacrylamide units bearing a carboxylic group to make another INHIBIT logic gate. The mixture of these two INHIBIT logic gates in water solution can behave as a XOR logic gate which is required for molecular-scale arithmetic.[20] Similarly, NOR and OR logic gates can be developed by the change of two or three components of the copolymer. Thus, a general design platform for polymeric logic gates becomes available.

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Supporting Information Available: Experimental details (PDF). This material is available free of charge via the Internet at http://pubs.acs.org.

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