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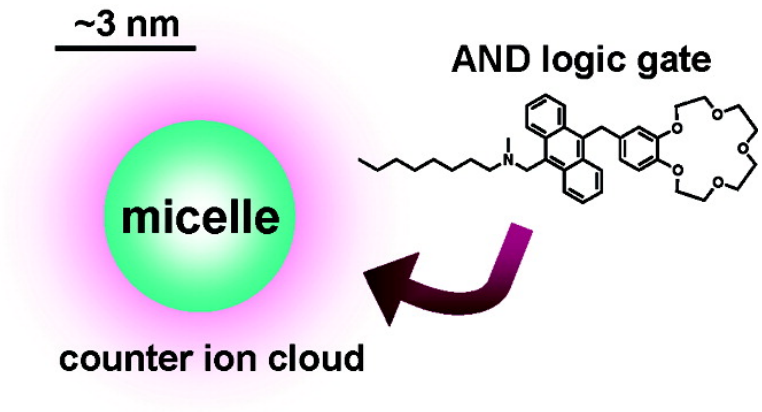

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Membrane Media Create Small Nanospaces for Molecular Computation

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Information processing,[1] storing,[2] and gathering[3] are important functions of molecular devices and machines.[4] In particular, chemical computation by molecular devices is an ultimate challenge of future technology. Although a semiconductor feature can be downsized to 65 nm,[5] it will be difficult to approach the molecular size. In molecular computation, fluorescent logic gates[1] play pivotal roles because they are detectable as a single molecule[6] and can simultaneously handle multiple inputs.[7] Here, we show for the first time that a designed fluorescent logic gate can operate in a small nanospace. The AND logic gate **1**[8] (Figure 1) is restricted to a tetramethylammonium dodecyl sulfate[9] (TMADS, Figure 1) micelle and gives fluorescence as an output only when both H^+ and Na^+ ions exist nearby. The volume needed for this operation has a radius of ~3 nm,[10] which is much smaller than that of a molecular electronic-based logic device (dimensions = 100 μm × 100 μm × 100 nm[11]). From a biological viewpoint, this system mimics a cell membrane where both ions are handled by a two-input logic device, Na^+/H^+ antiporter.[12] Biology has many examples of simple computation in membrane-bound nanospaces.

The logic gate **1** consists of the following components. (i) The anthracene (blue part) is a fluorophore. (ii) The trialkylamino and benzo-15-crown-5 moieties (green) are selective H^+ and Na^+ receptors, respectively. Moreover, their interaction with ions allows the fluorescence switching by controlling the photoinduced electron transfer (PET) processes[3a] from the receptors to the fluorophore.[7a] A strong fluorescence signal can be observed only when both receptors catch the correct ions. (iii) Short methylene spacers (red) are suitable for the efficient fluorescence switching.[13] (iv) Due to the long alkyl chain (orange), this logic gate is anchored in micelles and away from the bulk water.

Then, we demonstrate the AND logic operation with **1** in TMADS micelles. The radius of a TMADS micelle from the center to the edge of a tetramethylammonium ion cloud has been estimated to be ~3 nm.[10] This nanospace associated with TMADS aqueous solution is the domain of **1**. Figure 2 shows the fluorescence characteristics of **1** in TMADS aqueous solution under four different conditions (I−IV),[14] in which H^+ concentration ($input_1$) is 10^{-11} M (low, binary 0) or 10^{-3} M (high, 1) and Na^+ concentration ($input_2$) is 0 M (low, 0) or 4 × 10^{-1} M (high, 1). As shown in Figure 2, a strong fluorescence signal is observed (output = 1) only when both ion concentrations are kept high, that is, ($input_1$, $input_2$) = (1, 1). In contrast, the fluorescence signal is very weak (output = 0) in the other cases. The fluorescence quantum yield (Φ_f) at output = 1 is over 7-times higher than that at output = 0.

To remove the possibility that nonspecific salt-induced environmental change of the micelles resulted in the fluorescence "off−on" switching of **1** under sufficient H^+ ion (II→IV), the Φ_f−pNa diagrams for **1** and a control compound **2**[16] are obtained (Figure 3). Since **2** bears a dimethoxybenzene moiety, which cannot bind Na^+ ion, the PET process occurs from the dimethoxybenzene moiety to the fluorophore regardless of the Na^+ concentration. If the salt-induced environmental change of the micelles caused the increase in the Φ_f of **1**, similar fluorescence enhancement should be seen in the Φ_f−pNa diagrams for **2** in Figure 3, as well. Nevertheless, such enhancement is not observed, and the Φ_f value of **2** is kept low by the PET process.

For the AND logic operation with **1** shown in Figure 2, the appropriate micelle (i.e., TMADS) is necessary. This is the key evidence that **1** is operating in the micelle-bounded nanospace. Other micelles, such as Triton X-100, octyl β-D-glucopyranoside (OG), and cetyltrimethylammonium chloride (CTAC), do not display a distinct AND logic operation because these micelles cannot afford a large fluorescence enhancement with increasing

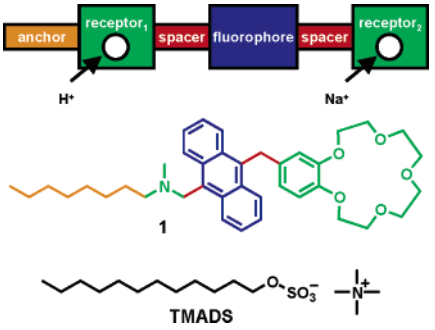

Figure 1. Structures of AND logic gate **1** and TMADS. In **1**, if H^+ is absent, the PET process from the trialkylamino moiety to the fluorophore is involved in nonradiative relaxation pathways of the excited anthracene, resulting in weak fluorescence. Even when H^+ is present, another PET occurs from the benzocrown moiety to the fluorophore, which can be suppressed by Na^+ addition. Therefore, strong fluorescence can be observed from **1** only when H^+ and Na^+ are available.

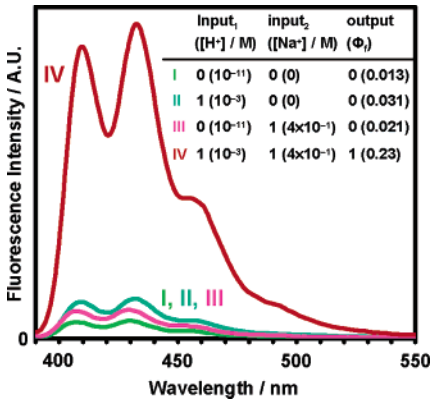

Figure 2. AND logic operation in a small nanospace. Fluorescence spectra and truth table of **1** (5 μM) with TMADS (20 mM[15]) in water at four different conditions. All concentrations are bulk values. Excitation = 378 nm.

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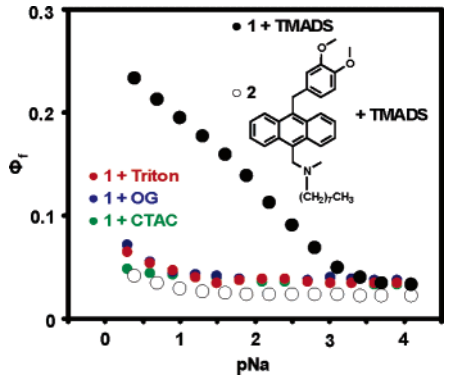

Figure 3. Fluorescence quantum yield (Φ_f) − Na^+ concentration (pNa) diagrams in different micelle systems. The bulk H^+ concentration is sufficient (pH = 3) to suppress one PET process from the trialkylamino moiety. Concentrations of TMADS, Triton X-100, OG, and CTAC are 20, 0.52, 34, and 5.0 mM, respectively.[15,17]

Na^+ concentration, as shown in Figure 3. The log β_{Na^+} value[18] for **1** and Na^+ (i.e., logarithm of the binding constant) in TMADS micelles is ∼1.9, whereas the estimated log β_{Na^+} values in Triton X-100, OG, and CTAC micelles and bulk water[19] are less than 0.5. These values indicate that Na^+ ion is more available for **1**, which is restricted to the TMADS micelle, than in the other micelles and even in bulk water. Na^+ ion is electrostatically concentrated near the surface of anionic TMADS micelles, while this effect cannot be expected for the other neutral and cationic micelles. The hydrophilic benzocrown moiety of **1** is located near the headgroup of TMADS and, therefore, binds concentrated Na^+ ions. Such an amplifying effect of ionic micelles on the local ion concentration has been observed,[20] only for the specific case of H^+ amplification by anionic micelles, which results in the positive shift in pK_a values. In this study, the pK_a value (8.6) for **1** and H^+ in the TMADS micelles under sufficient Na^+ ion is higher than that in the other neutral and cationic micelles (5.5, 5.6, and 5.5 in Triton X-100, OG, and CTAC, respectively), though similar to that (9.0−9.2[21]) in bulk water. The TMADS-induced pK_a shift in comparison with water is less than the corresponding log β_{Na^+} shift because the position of the H^+ and Na^+ receptors are different in the steeply varying fields of dielectric, electric, and specific effects in this small membrane-bounded nanospace.

In summary, **1** works as an AND logic gate with H^+ and Na^+ ions within TMADS micelles with the radius of ∼3 nm. This is the first report of a simple molecular computation with plural inputs in a small nanospace. This strategy should be easily generalizable to all the other types of molecular computation in the literature.[1,7]

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(8) **1** was synthesized as follows. *N*-Methyloctylamine (200 μL, 1.10 mmol) and 4-(10-bromomethylanthracen-9-ylmethyl)benzo-15-crown-5-ether[7c] (471 mg, 0.85 mmol) were dissolved in benzene (10 mL). Potassium carbonate (1 g) was added to the solution, and the suspended mixture was heated to 60 °C for 16 h. After the reaction, the remaining potassium carbonate was filtered, and then the mixture was evaporated under reduced pressure. The solid obtained was purified by recrystallization from ethanol to afford **1** (301 mg, 0.49 mmol) as a yellow powder. Yield 57%. Mp 93−94 °C. ^{1}H NMR ($CDCl_3$): δ 8.57 (2H, d, J = 8.4 Hz), 8.21 (2H, d, J = 8.4 Hz), 7.41−7.52 (4H, m), 6.73 (1H, s), 6.66 (1H, d, J = 8.2 Hz), 6.52 (1H, d, J = 8.2 Hz), 4.93 (2H, s), 4.44 (2H, s), 4.03 (2H, t, J = 4.3 Hz), 3.96 (2H, t, J = 4.3 Hz), 3.80−3.86 (4H, m), 3.72 (8H, m), 2.61 (2H, t, J = 7.3 Hz), 2.23 (3H, s), 1.59−1.69 (2H, m), 1.23 (10H, m), 0.87 (3H, t, J = 6.8 Hz). HR-LSIMS m/z: Calcd for $C_{39}H_{51}NO_5$ (M^+) 613.3767. Found 613.3756.

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(16) As a brown powder from the corresponding bromide by the procedure similar to that for **1**. Yield 63%. Mp 95 °C. ^{1}H NMR ($CDCl_3$): δ 8.58 (2H, d, J = 8.0 Hz), 8.24 (2H, d, J = 8.0 Hz), 7.42−7.53 (4H, m), 6.79 (1H, s), 6.65 (1H, d, J = 8.2 Hz), 6.49 (1H, d, J = 8.2 Hz), 4.96 (2H, s), 4.46 (2H, s), 3.78 (3H, s), 3.73 (3H, s), 2.61 (2H, t, J = 7.3 HZ), 2.24 (3H, s), 1.57 (2H, m), 1.24 (10H, m), 0.87 (3H, t, J = 6.8 Hz). LSIMS m/z: 483 (M^+). Anal. Calcd for $C_{33}H_{41}NO_2$: C, 81.94; H, 8.54; N, 2.90. Found: C, 81.99; H, 8.44; N, 3.03.

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(18) The log β_{Na^+} values were obtained by the equation, $\log[(FI_{max} - FI)/(FI - FI_{min})] = pNa - \log \beta_{Na^+}$, where FI is the observed fluorescence intensity at a fixed wavelength. FI_{max} and FI_{min} are the corresponding maximum and minimum, respectively. The pK_a values were determined by using the corresponding equation with pH as the independent variable.

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