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Switching between molecular switch types by module rearrangement: Ca^{2+}-enabled, H^+-driven 'Off–On–Off', H^+-driven YES and PASS 0 as well as H^+, Ca^{2+}-driven AND logic operations

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Several logic gates and switches can be accessed from two different combinations of a single set of fluorophore, receptor and spacer components.

During the formative phase of molecular-scale computational devices, it is important to explore the flexibility of current designs.[1] We now use our photoionic design[2] based on photoinduced electron transfer[3] (PET) and fluorescence as a platform to demonstrate an enabled 'Off–On–Off' function[4,5] in water. The present illustration means that a microscopic region containing a H^+ concentration within a chosen window and a Ca^{2+} concentration exceeding a chosen threshold can be directly visualized. This case is not only biocompatible,[6] but it can be switched to conventional YES, PASS 0 or AND logic behaviour[3,7] by changing an input level or by reformatting its components. The latter method of switching between molecular switch types is unprecedented, though cases of reconfiguring logic with wavelength,[1e–f,8] the level[9,10a] and nature[7d,10b] of the chemical input as well as the output level[10a] are known.

Molecular photoionic AND logic gates can be constructed by joining a fluorophore with two selective receptors by using two spacers. This corresponds to 'fluorophore–spacer$_1$–receptor$_1$–spacer$_2$–receptor$_2$'[2] or 'receptor$_1$–spacer$_1$–fluorophore–spacer$_2$–receptor$_2$'[11] formats. The latter minimizes the distances over which PET must occur.[12] We use a tertiary amine receptor for H^+ as receptor$_1$, Tsien's BAPTA receptor[13] for Ca^{2+} as receptor$_2$ and anthracene as the fluorophore. PET occurs to the fluorophore from each receptor when ion free. A methylene group each is used for spacer$_1$ and spacer$_2$. Spacers longer than one methylene group begin to retard PET (and hence reduce fluorescence switching efficiency) in 'anthracene–spacer–amine' systems.[14] The more electron-rich BAPTA receptor is expected to perform better at longer separation distances from the fluorophore, especially if folded conformers can be arranged. The other combinatorial possibility of the 'fluorophore–spacer$_2$–receptor$_2$–spacer$_1$–receptor$_1$' format is not examined for this reason. Switches **1**[†] and **2**[†] are designed and synthesized on this basis.

As expected for modular PET systems, **1** and **2** show typical anthracenic fluorescence (Table 1) when the two PET-active receptors are separately blocked with H^+ and Ca^{2+}. Hence, AND logic gate action can be seen for both **1** and **2** if we take excitation light as the power supply, H^+ as input$_1$ (high = $10^{-6.7}$ M and low = $10^{-9.7}$ M), Ca^{2+} as input$_2$ (high = $10^{-2.3}$ M and low = 0 M) and fluorescence as the output (Fig. 1). However if we choose high H^+ as $10^{-4.5}$ M then **1** becomes, at the simplest level, a H^+-driven YES gate whose main dependence on the Ca^{2+} input is in the pK_a value. We do not develop the possibility of multistable output[18] in this paper. Taking high H^+ as $10^{-4.5}$ M, **2** can be seen as a H^+-driven PASS 0 gate essentially independent of Ca^{2+}. The logic table in the Fig. 1 codes input$_1$ (H^+) as v. high ($10^{-4.5}$ M), high ($10^{-6.7}$ M) and low ($10^{-9.7}$ M).

When we look across the whole range of pH values, **2** clearly shows a maximum fluorescence emission at pH 6.7 in the presence of Ca^{2+} (Fig. 1). The emission is far lower in the absence of Ca^{2+}. This is Ca^{2+}-enabled, H^+-driven 'Off–On–Off' action. What causes the sharp fall of fluorescence at lower pH values? The anthracene unit is separated by a three-atom chain from the proximal oxyaniline. This is optimal[19] for the approach of the phenyliminodiacetic acid moiety to the anthracene during its excited state lifetime. Intramolecular quenching of anthracene emission by carboxylic acid groups is known.[20] The distal oxyaniline and its acetic acid appendages are less likely to be involved in the quenching owing to the lower folding probability.[21] An effect similar to that seen in **2** cannot occur for **1** since the anthracene unit is held apart from the proximal oxyaniline by a single methylene group.

The maximum quantum yield of fluorescence seen for **1** is low whereas **2** is normal in this regard. Protonated aminomethyl groups are strongly electron withdrawing[11] and hence this allows a residual PET to occur from the protonated oxyaniline to the electron-deficient anthracene. This effect cancels out in the case of **2** since the protonated aminomethyl group affects the anthracene and the protonated oxyaniline equally.

To conclude, the general PET design of AND logic gates can be modulated by structure-specific effects, particularly at low pH values, in logically useful ways.[‡]

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Table 1 Electronic spectral and ion-binding properties of **1** and **2**[a]

Property	1	2
λ_{abs}/nm	398, 377, 359[b]	389, 367, 350[b]
$10^3\varepsilon_{max}$/mol^{-1} dm^3 cm^{-1}	10.8, 10.8, 8.0[b]	9.8, 11.6, 8.7[b]
λ_{exc}/nm	377	369
λ_{flu}/nm	408, 428, 453	400, 419, 443
ϕ_{flu} at pH 6.7	0.023	0.25
log $\beta_{Ca^{2+}}$ (low H^+)[c]	6.6[d]	6.2
log $\beta_{Ca^{2+}}$ (high H^+)[c]	6.6[d]	6.0

[a] 10^{-5} M **1** and **2** in water. Data such as fluorescence quantum yields (ϕ_{flu}) which can be deduced from the Fig. are not repeated here. The binding constant data are obtained from the analysis of fluorescence intensity–ion concentration profiles[11] (Fig.). [b] Average values in the four input states created by high and low Ca^{2+} and H^+. The λ_{abs} values have a SD = 1 nm and the ε_{max} values have a SD = 600 mol^{-1} dm^3 cm^{-1}. [c] See concentration conditions in the main body of the text. [d] Value obtained[15] for a closely related structure lacking the diethylamino substituent on the anthracene at pH = 7.2, I = 0.1 M (KCl).

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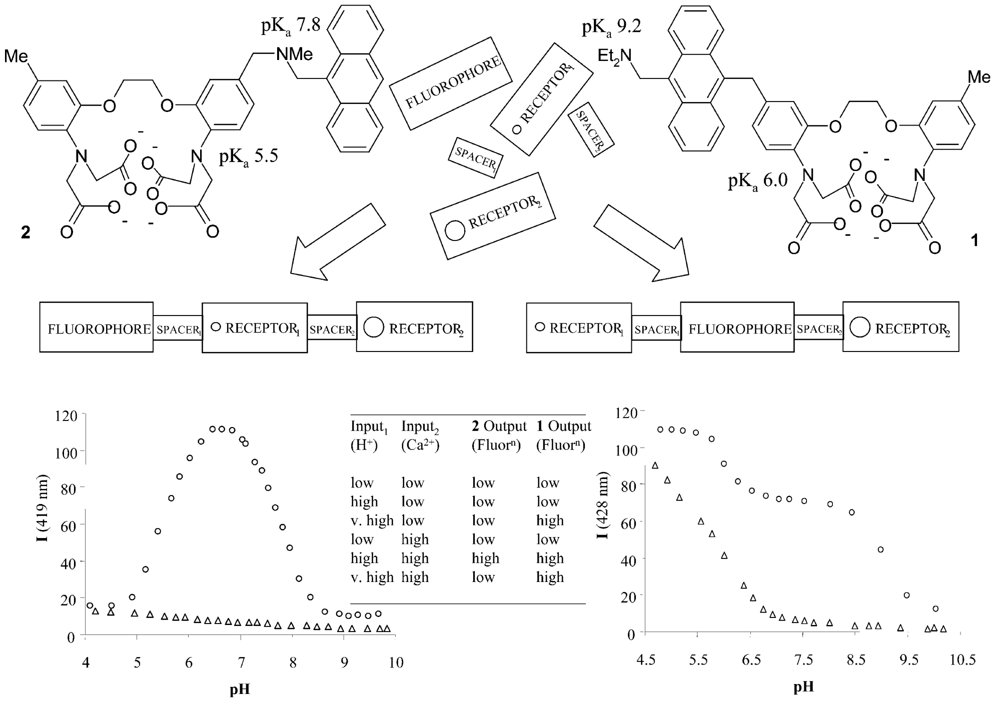

Input₁ (H⁺)	Input₂ (Ca²⁺)	**2** Output (Fluorⁿ)	**1** Output (Fluorⁿ)
low	low	low	low
high	low	low	low
v. high	low	low	high
low	high	low	low
high	high	high	high
v. high	high	low	high

Fig. 1 Two module combinations, formulae and fluorescence intensity (*I*)–pH profiles (triangles: no Ca^{2+}; circles: high Ca^{2+}). Logic tables for these are shown between the two streams. The pK_a values (determined under high Ca^{2+} conditions) are given next to the appropriate groups in the formulae.

Notes and references

† Switch **1** was prepared as follows: BAPTA tetramethyl ester[13] was alkylated with 9-anthracenylmethyl bromide using $ZnBr_2$.[15] The diethylaminomethyl group was attached by the sequence of Vilsmeier formylation ($POCl_3$, DMF), reduction ($NaBH_4$), chlorination ($SOCl_2$) and amination ($HNEt_2$). The tetramethyl ester of **1** was hydrolyzed with KOH to yield **1**. Switch **2**[16] was obtained by alkaline hydrolysis of its tetramethyl ester which was made by reductive amination of BAPTA tetramethyl ester aldehyde[13] with 9-(*N*-methylaminomethyl)anthracene.[17]

‡ Resetting of photoionic gates is possible by adding complexants for a given ion input or by washing of solid-bound gates.

1 Recent reviews: (*a*) A. P. de Silva, N. D. McClenaghan and C. P. McCoy, in *Molecular Switches* (Ed. B. L. Feringa), Wiley-VCH, Weinheim, 2000, p. 339; (*b*) F. M. Raymo, *Adv. Mater.*, 2002, **14**, 401; (*c*) V. Balzani, M. Venturi and A. Credi, *Molecular Devices and Machines*, Wiley-VCH, Weinheim, 2003, Ch. 9; (*d*) A. P. de Silva and N. D. McClenaghan, *Chem. Eur. J.*, 2004, **10**, 574; (*e*) Recent papers: F. M. Raymo and S. Giordani, *J. Am. Chem. Soc.*, 2002, **124**, 2004; (*f*) F. M. Raymo, R. J. Alvarado, S. Giordani and M. A. Cejas, *J. Am. Chem. Soc.*, 2003, **125**, 2361; (*g*) H. Tian, B. Qin, R.-X. Yao, X.-L. Zhao and S.-J. Yang, *Adv. Mater.*, 2003, **15**, 2104; (*h*) H.-M. Wang, D.-Q. Zhang, X.-F. Guo, L.-Y. Zhu, Z.-G. Shuai and D.-B. Zhu, *Chem. Commun.*, 2004, 670.

2 A. P. de Silva, H. Q. N. Gunaratne and C. P. McCoy, *Nature*, 1993, **364**, 42.

3 *Handbook of Electron Transfer in Chemistry*, (Ed. V. Balzani), Wiley-VCH, Weinheim, 2000.

4 S. A. de Silva, B. Amorelli, D. C. Isidor, K. C. Loo, K. E. Crooker and Y. E. Pena, *Chem. Commun.*, 2002, 1360.

5 (*a*) A. P. de Silva, H. Q. N. Gunaratne and C. P. McCoy, *Chem. Commun.*, 1996, 2399; (*b*) S. A. de Silva, A. Zavaleta, D. E. Baron, O. Allam, E. V. Isidor, N. Kashimura and J. M. Percarpio, *Tetrahedron Lett.*, 1997, **38**, 2237; (*c*) L. Fabbrizzi, M. Licchelli, A. Poggi and A. Taglietti, *Eur. J. Inorg. Chem.*, 1999, 35.

6 (*a*) R. Y. Tsien, *Am. J. Physiol.*, 1992, **263**, C723; (*b*) R. P. Haugland, *Handbook of Fluorescent Probes and Research Products*, 9th Edn., Molecular Probes, Eugene, OR, 2002; (*c*) A. P. de Silva, D. B. Fox, T. S. Moody and S. M. Weir, *Trends Biotechnol.*, 2001, **19**, 27.

7 (*a*) C. R. Cooper and T. D. James, *J. Chem. Soc., Perkin Trans. 2*, 2000, 963; (*b*) H. Miyaji, S. R. Collinson, I. Prokes and J. H. R. Tucker, *Chem. Commun.*, 2003, 64; (*c*) A. P. de Silva, G. D. McClean and S. Pagliari, *Chem. Commun.*, 2003, 2010; (*d*) A. Saghatelian, N. H. Völcker, K. M. Guckian, V. S.-Y. Lin and M. R. Ghadiri, *J. Am. Chem. Soc.*, 2003, **125**, 346; (*e*) A. S. Lukas, P. J. Bushard and M. R. Wasielewski, *J. Am. Chem. Soc.*, 2001, **123**, 2440; (*f*) *cf.* C. A. Hunter and L. D. Sarson, *Tetrahedron Lett.*, 1996, **37**, 699.

8 (*a*) R. Ballardini, V. Balzani, A. Credi, M. T. Gandolfi, F. Kotzyba-Hibert, J.-M. Lehn and L. Prodi, *J. Am. Chem. Soc.*, 1994, **116**, 5741; (*b*) H. T. Baytekin and E. U. Akkaya, *Org. Lett.*, 2000, **2**, 1725; (*c*) K. Rurack, A. Koval'chuck, J. L. Bricks and J. L. Slominskii, *J. Am. Chem. Soc.*, 2001, **123**, 6205; (*d*) A. P. de Silva and N. D. McClenaghan, *Chem. Eur. J.*, 2002, **8**, 4935; (*e*) N. B. Sankaran, S. Banthia, A. Das and A. Samanta, *New J. Chem.*, 2002, **26**, 1529.

9 S. Alves, F. Pina, M. T. Albelda, E. Garcia-Espana, C. Soriano and S. V. Luis, *Eur. J. Inorg. Chem.*, 2001, 405.

10 (*a*) K.-P. Zauner and M. Conrad, *Soft Comput.*, 2000, **5**, 39; (*b*) A. S. Deonarine, S. M. Clark and L. Konermann, *Future Gener. Comput. Syst.*, 2003, **19**, 87.

11 A. P. de Silva, H. Q. N. Gunaratne and C. P. McCoy, *J. Am. Chem. Soc.*, 1997, **119**, 7891.

12 G. L. Closs and J. R. Miller, *Science*, 1988, **240**, 440.

13 (*a*) R. Y. Tsien, *Biochemistry*, 1980, **19**, 2396; (*b*) G. Grynkiewicz, M. Poenie and R. Y. Tsien, *J. Biol. Chem.*, 1985, **260**, 3440.

14 (*a*) J. C. Beeson, M. E. Huston, A. Douglas, T. K. Pollard and A. W. Czarnik, *J. Fluoresc.*, 1993, **3**, 65; (*b*) See also M. Onoda, S. Uchiyama, T. Santa and K. Imai, *Luminescence*, 2002, **17**, 11.

15 A. P. de Silva and H. Q. N. Gunaratne, *Chem. Commun.*, 1990, 186.

16 A. P. de Silva and N. D. McClenaghan, *J. Am. Chem. Soc.*, 2000, **122**, 3965.

17 C. Sangoe and E. Zimerson, *J. Liq. Chromatogr.*, 1980, **3**, 971.

18 (*a*) R. Grigg and W. D. J. A. Norbert, *J. Chem. Soc., Chem. Commun.*, 1992, 1298; (*b*) L. Fabbrizzi, M. Licchelli and P. Pallavicini, *Angew. Chem., Int. Ed.*, 1998, **37**, 800; (*c*) C. Di Pietro, G. Guglielmo, S. Campagna, M. Diotti, A. Manfredi and S. Quici, *New J. Chem.*, 1998, **22**, 1037; (*d*) F. Pina, M. J. Melo, M. A. Bernardo, S. V. Luis and E. Garcia-Espana, *J. Photochem. Photobiol., A: Chem.*, 1999, **126**, 65; (*e*) G. Dilek and E. U. Akkaya, *Tetrahedron Lett.*, 2000, **41**, 3721.

19 F. Hirayama, *J. Chem. Phys.*, 1965, **42**, 3165.

20 R. A. Bissell, *PhD Thesis*, Queen's University, Belfast, 1990.

21 M. A. Winnik, *Chem. Rev.*, 1981, **81**, 491.