Proof-of-Principle of Molecular-Scale Arithmetic

A. Prasanna de Silva* and Nathan D. McClenaghan

School of Chemistry, Queen's University
Belfast BT9 5AG, Northern Ireland

Received November 22, 1999
Revised Manuscript Received February 22, 2000

Arithmetic is the most universally recognizable form of computation whether it is performed by human brains or by computing machines. Addition is the primeval form of arithmetic and can lead to other operations.[1] Arithmetic and logic operations are the twin pillars on which the entire information technology revolution has been built. Arithmetic operations are currently implemented in semiconductor technology by combining AND and XOR logic gates in parallel. Now we demonstrate this combination at the far smaller molecular-scale. Elementary molecular arithmetic operations therefore arise naturally. Although several approaches with potential for molecular-scale arithmetic are available,[2−7] small designed molecules intrinsically endowed with numeracy are unprecedented.

Elementary logic operations at the molecular-scale have been a reality for some time.[8−16] These function with chemical inputs and optical outputs. We and others have previously demonstrated supramolecular systems[17] acting as AND logic gates, some of which are ready for use in arithmetic operations.[9,13,15] Balzani, Stoddart, and their colleagues demonstrated the first XOR logic operation.[10] However, this XOR gate employs chemical inputs which annihilate one another and cannot therefore be used as-is in an arithmetic context. We now demonstrate a general approach to XOR logic without this annihilation problem so that arithmetic becomes accessible.

Push−pull system **1** (Figure 1) has selective cation receptors at both terminals. The energy of the internal charge transfer (ICT) excited state of **1** will naturally be perturbed by occupancy of either receptor by its chosen cation. Push−pull systems with a single receptor have enabled the visualization of intracellular messengers such as Ca^{2+}.[18] However, occupancy of receptor$_2$ will destabilize the ICT excited-state, that is, blue-shift the lowest-energy band in its electronic absorption spectrum. On the other hand, occupancy of receptor$_1$ causes the opposite effect, that is, a red shift. In favorable cases, occupancy of both receptors by their respective cations causes almost no net shift of the spectrum from its original cation-free position.

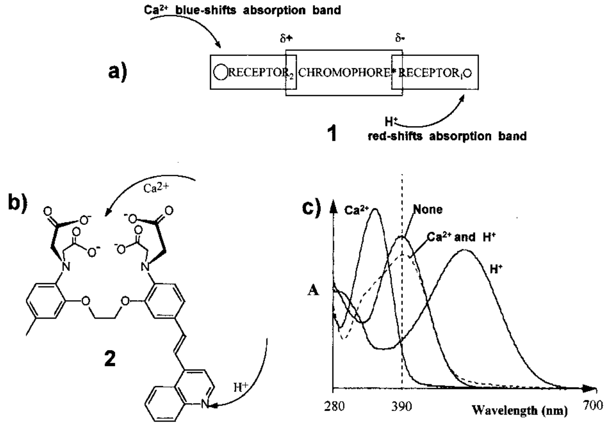

Figure 1. (a) Design principle, (b) molecular-scale implementation, and (c) experimental demonstration of XOR logic gate **2** suitable for arithmetic operations.

A molecular-scale implementation of these ideas can be arranged in **2** which combines well-known receptors for Ca^{2+} [19] and H^{+} [20] within a push−pull chromophore. A report on the protonation behavior exhibited by a relative of the parent chromophore[21] gave us early confidence about this design. Observation at 390 nm (a wavelength close to the original cation-free absorption maximum) then produces the following truth table (Table 1). If the output is viewed as absorbance, XNOR logic is produced. If the output is viewed as transmittance, XOR logic is the result. We choose the latter for the present arithmetic application, especially because the output of our AND gate is also light (see later), except that it is by emission rather than by transmission.

With the XOR logic gate in hand, we now require an AND gate which is fully compatible with the former in terms of chemical inputs, optical outputs, and power supplies. Mutual interference must also be minimized. Drawing on our early design **3** (Figure 2),[9] molecule **4** responding to Ca^{2+} and H^{+} could be constructed. Both receptor$_1$ and receptor$_2$ must be occupied by their respective cations before bright fluorescence output is produced, that is, showing AND logic (Table 1: last column). If not, photoinduced electron transfer (PET)[22−24] from either receptor to the fluorophore takes place as an energy-draining pathway.

Now we operate XOR gate **2** and AND gate **4** in parallel for the purpose of binary addition. This can be represented as **5** by conventional electronic symbols (Figure 3). The first binary number is coded for by the presence (01) or absence (00) of H^{+} input. The second binary number is coded for by the presence (01) or absence (00) of Ca^{2+} input. The sum digit is coded for by the transmitted light intensity output at 390 nm when high (1) or low (0). The carry digit is coded for by the emitted light intensity

* E-mail; a.desilva@qub.ac.uk.

(1) Malvino, A. P.; Brown, J. A. *Digital Computer Electronics*, 3rd ed.; Glencoe: Lake Forest, 1993.
(2) Wild, U. P.; Bernet, S.; Kohler, B.; Renn, A. *Pure Appl. Chem.* **1992**, *64*, 1335.
(3) Bissell, R. A.; Cordova, E.; Kaifer, A. E.; Stoddart, J. F. *Nature* **1994**, *369*, 133.
(4) Adleman, L. M. *Science* **1994**, *266*, 1021.
(5) Gershenfeld, N.; Chuang, I. *Science* **1997**, *275*, 350.
(6) Fahmy, A.; Havel, T. *Proc. Natl. Acad. Sci. U.S.A.* **1997**, *94*, 1634.
(7) Sauvage, J.-P. *Acc. Chem. Res.* **1998**, *31*, 611.
(8) Hosseini, M. W.; Blacker, A. J.; Lehn, J.-M. *J. Am. Chem. Soc.* **1990**, *112*, 3896.
(9) de Silva, A. P.; Gunaratne, H. Q. N.; McCoy, C. P. *Nature* **1993**, *364*, 42.
(10) Credi, A.; Balzani, V.; Langford, S. J.; Stoddart, J. F. *J. Am. Chem. Soc.* **1997**, *119*, 2679.
(11) Inouye, M.; Akamatsu, K.; Nakazumi, H. *J. Am. Chem. Soc.* **1997**, *119*, 9160.
(12) Parker, D.; Williams, J. A. G. *Chem. Commun.* **1998**, 245.
(13) Pina, F.; Maestri, M.; Balzani, V. *Chem. Commun.* **1999**, 107.
(14) Roque, A.; Pina, F.; Alves, S.; Ballardini, R.; Maestri, M.; Balzani, V. *J. Mater. Chem.* **1999**, *9*, 2265.
(15) de Silva, A. P.; Dixon, I. M.; Gunaratne, H. Q. N.; Gunnlaugsson, T.; Maxwell, P. R. S.; Rice, T. E. *J. Am. Chem. Soc.* **1999**, *121*, 1393 and references therein.
(16) Gunnlaugsson, T.; MacDonail, D. A.; Parker, D. *Chem. Commun.* **2000**, 93.
(17) (a) Lehn, J.-M. *Supramolecular Chemistry*; VCH: Weinheim, 1995. (b) Balzani, V.; Scandola, F. *Supramolecular Photochemistry*; Ellis-Horwood: Chichester, 1991.
(18) Tsien, R. Y. *Am. J. Physiol*. **1992**, *263*, C723.
(19) Grynkiewicz, G.; Poenie, M.; Tsien, R. Y. *J. Biol. Chem.* **1985**, *260*, 3440.
(20) Morrison, R. T.; Boyd, R. N. *Organic Chemistry*, 4th ed.; Allyn and Bacon: Boston, 1983.
(21) Wang, S. L.; Ho, T. I. *Chem. Phys. Lett.* **1997**, *268*, 434.
(22) de Silva, A. P.; Gunaratne, H. Q. N.; Gunnlaugsson, T.; Huxley, A. J. M.; McCoy, C. P.; Rademacher, J. T.; Rice, T. E. *Chem. Rev.* **1997**, *97*, 1515.
(23) *Chemosensors for Ion and Molecule Recognition*; Czarnik, A. W.; Desvergne, J.-P.; Eds.; Kluwer: Dordrecht, 1997.
(24) Fabbrizzi, L.; Licchelli, M.; Pallavicini, P. *Acc. Chem. Res.* **1999**, *32*, 846.

10.1021/ja994080m CCC: $19.00
Published on Web 04/07/2000

Table 1. Truth Tables for Logic Gates **2** and **4** When Operated Separately[a]

input$_1$ H^+	input$_2$ Ca^{2+}	output **2**; XNOR (A_{390})	output **2**; XOR (% transmittance at 390 nm)	output **4**; AND (fluorescence at 419 nm)
0	0	1(high; 13000[b])	0(low; 5[c])	0(low; 4[d], 0.006[e])
0	1	0(low; 3100[b])	1(high; 49[c])	0(low; 10[d], 0.020[e])
1	0	0(low; 4100[b])	1(high; 39[c])	0(low; 9[d], 0.018[e])
1	1	1(high; 11400[b])	0(low; 7[c])	1(high; 100[d], 0.21[e])

[a] 10^{-5} M **2** or **4** in H_2O, **2** monitored at 390 nm by absorbance or transmittance**.** The lowest energy absorption maxima are 393, 347, 492, and 396 nm under (input$_1$, input$_2$) conditions of (0,0), (0,1), (1,0), and (1,1), respectively. **4** excited at 369 nm, fluorescence emission maxima are at 400, 419, and 443 nm. 0 and 1 are digital representations of low and high signal levels, respectively. The low input level corresponds to $10^{-9.5}$M for H^+ and $<10^{-9}$M for Ca^{2+}. The high input level corresponds to 10^{-6}M for H^+ and $10^{-2.3}$M for Ca^{2+}. Logarithms of ion binding constants under the experimental conditions (log β, concentrations in M); **2**-H^+ = 7.0 (low Ca^{2+}), 6.4 (high Ca^{2+}), **2**-Ca^{2+} = 5.9 (low H^+), 5.8 (high H^+), **4**-H^+ = 8.4 (low Ca^{2+}), 7.8 (high Ca^{2+}), **4**-Ca^{2+} = 6.2 (low H^+), 6.0 (high H^+). [b] Extinction coefficient. [c] 10 cm optical path length. [d] Intensity in arbitrary units. [e] Quantum yield

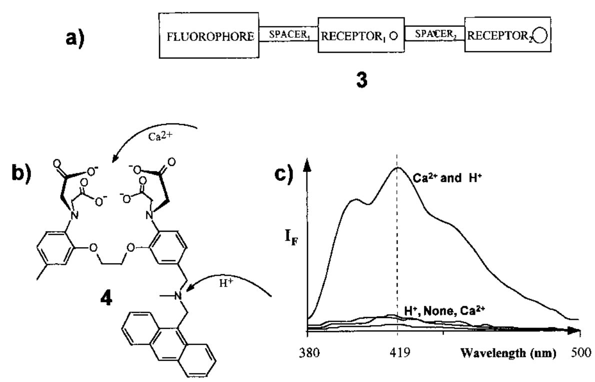

Figure 2. (a) Design principle, (b) molecular-scale implementation, and (c) experimental demonstration of AND logic gate **4** compatible with the XOR gate of Figure 1.

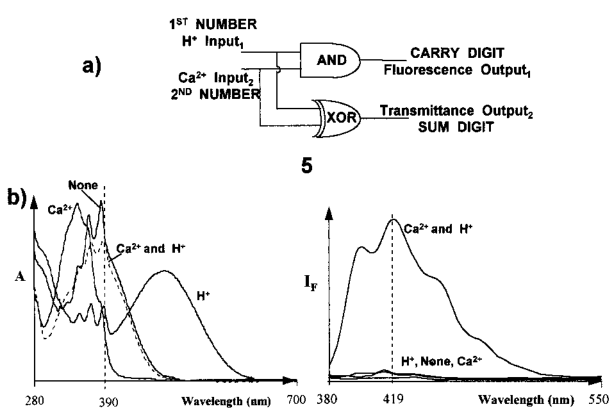

Figure 3. Addition of binary numbers by parallel operation of XOR gate **2** and AND gate **4**: (a) design principle and (b) experimental demonstration.

output at 419 nm when high (1) or low (0). Table 2 shows that the molecular world is capable of carrying out the following binary additions: 00 + 00 = 00, 00 + 01 = 01, 01 + 00 = 01, and 01 + 01 = 10. In the universally recognizable decimal number system, these operations become: 0 + 0 = 0, 0 + 1 = 1, 1 + 0 = 1, and 1 + 1 = 2. The commutative nature of addition is also clear. Overall, this lets the combined molecules **2** and **4** emulate the half-adder found in electronic calculators and computers.

Table 2. Truth Tables for Combined Logic Gates **2** and **4** When Operated in Parallel[a]

first number Input H^+	second number Input Ca^{2+}	added number: carry digit output (fluorescence at 419 nm)	added number: sum digit output (% transmittance at 390 nm)
00	00	0(low; 2[b], 0.003[c])	0(low; 8[d])
00	01	0(low; 5[b], 0.009[c])	1(high; 40[d])
01	00	0(low; 5[b], 0.005[c])	1(high; 33[d])
01	01	1(high; 100[b], 0.10[c])	0(low; 12[d])

[a] Experimental conditions and input signal levels as for Table 1, except that H^+ and Ca^{2+} code for binary numbers in this case. [b] Intensity in arbitrary units. [c] Apparent quantum yield. [d] 10 cm optical path length.

Several features of system **2** and **4** and others of this genre must be noted: (a) It operates in wireless mode on the molecular-scale in room-temperature water and responds to physiological levels of Ca^{2+} and H^+. (b) Fluorescent **4** lends itself easily to single-molecule operations,[25] whereas **2** would require special modulation techniques.[26] (c) Since ion−ligand interactions are reversible, reset is best achieved by washing polymer-bound systems[27] in a flow regime. (d) Three-dimensional ionic diffusion in solution is currently a speed limiter, although the potential exists to use photo-decoordination methods[28] to provide the chemical inputs to the logic system within picoseconds. (e) The principles outlined here are general, and the number of inputs are not limited to two. In fact, three-input molecular logic is available.[15] (f) Logic systems with ionic inputs and fluorescence outputs can in principle be “wired” together via intermediate units having optical inputs and ionic outputs. The latter are available by design[29] and in nature.[30] Nevertheless, small-scale integration of two molecular logic functions without “wiring” of gates was demonstrated in 1999.[15] (g) Logic predates electronic computation. Thus, the definition of general logic operations are not bound by electronic requirements such as wiring and circuitry. In fact, the earliest applications of molecular-scale computational elements will probably arise in cellular and chemical sciences.

To conclude, we have demonstrated prototypical arithmetic operations with designed molecules using chemical inputs and optical outputs. Children learn that 1 + 1 = 2 via molecule-based processes in their brains. It is remarkable that molecules **2** and **4** now know that too.

Acknowledgment. We thank the Department of Education in Northern Ireland and Dr. C. Hardacre for their support and Dr. W. D. J. A. Norbert for valuable discussions.

Supporting Information Available: Details concerning synthesis and characterization of **2** and **4** (PDF). This material is available free of charge via the Internet at http://pubs.acs.org. See any current masthead page for ordering information and Web access instructions.

JA994080M

(25) Weiss, S. *Science* **1999**, *283*, 1676.
(26) (a) Moerner, W. E.; Basche, T. *Angew. Chem., Int. Ed. Engl.* **1993**, *32*, 457. (b) Bornemann, R.; Thiel, E. *Abstr. VI Int. Conf. Methods Appl. Fluoresc. Spectrosc.* Paris, **1999**, P7.
(27) Daffy, L. M.; de Silva, A. P.; Gunaratne, H. Q. N.; Huber, C.; Lynch, P. L. M.; Werner, T.; Wolfbeis, O. S. *Chem. Eur. J.* **1998**, *4*, 1810.
(28) Martin, M. M.; Plaza, P.; Meyer, Y. H.; Badaoui, F.; Bourson, J.; Lefebvre, J. P.; Valeur, B. *J. Phys. Chem.* **1996**, *100*, 6879.
(29) Shinkai, S.; Manabe, O. *Top. Curr. Chem.* **1984**, *121*, 67.
(30) El-Sayed, M. A.; Griffiths, J.; Song, L.; Zhang, N. *Pure Appl. Chem.* **1995**, *67*, 149.