Integration of Logic Functions and Sequential Operation of Gates at the Molecular-Scale

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Despite a lot of effort[1] and expectations,[2] molecular-scale electronics/photonics is undergoing a gradual evolution[3] via wires,[4] switches,[5] and diodes[6] with logic gates being beyond the current horizon. On the other hand, it has been possible to leapfrog directly to molecular logic gates by combining chemical and photonic signals[7–9] according to principles of supramolecular chemistry.[10] Similar jumps to potentially useful systems such as controllable molecular abacuses have been made.[11,12] Nevertheless, integration of relatively simple molecular logic systems into higher-level devices remains an important goal. Both our brains and modern silicon-based electronics technology rely heavily on integration. Structural integration of molecular systems is possible in principle, especially given the encouraging developments in ion channel research,[13] but the practical prospects are daunting. We now demonstrate that functional integration of molecular logic is feasible. First, NOT and OR logic are integrated within single supermolecules[14] to result in NOR gates according to two separate design principles. Next, AND and NOT functions are combined so as to produce the INHIBIT operation. All three molecular logic devices depend on chemically induced luminescent signaling.[15] We also outline how these molecular logic gates can be operated sequentially by exploiting the sluggishness of certain luminescence processes and their susceptibility to quenching.
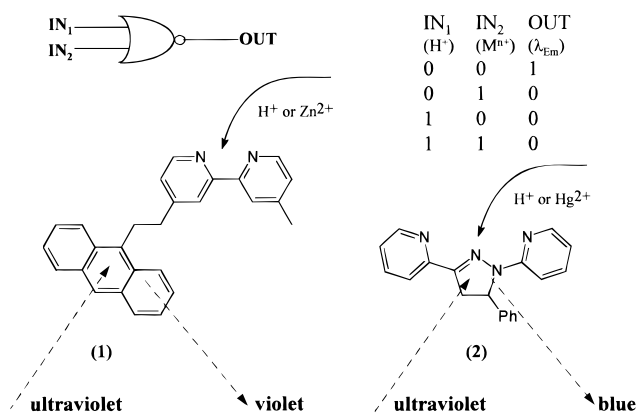
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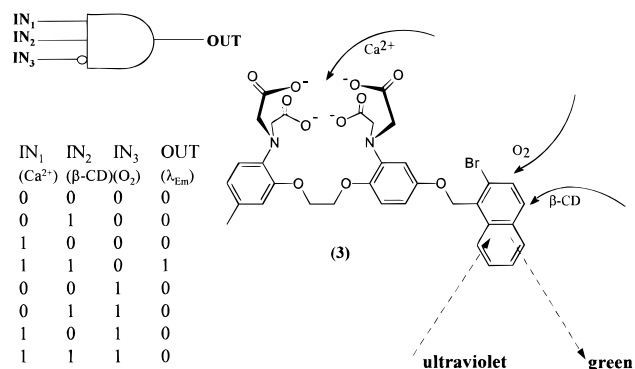(14) de Silva, A. P.; Gunnlaugsson, T.; McCoy, C. P. *J. Chem. Educ.* **1997**, *74*, 53.

Figure 1. Molecular-scale implementation of NOR logic gates.

Table 1. Truth Tables for Logic Gates **1–3**[a]

gate	chemical input (concentration, M)			luminescence output
1	H^+ (10^{-7})	0		1.0 (standard)
1	H^+ (10^{-7})	Zn^{2+} (10^{-3})		0.13
1	H^+ (10^{-2})	0		0.13
1	H^+ (10^{-2})	Zn^{2+} (10^{-3})		0.12
2	0	0		1.0 (standard)
2	0	Hg^{2+} (1.5×10^{-3})		0.11
2	H^+ (10^{-3})	0		0.02
2	H^+ (10^{-3})	Hg^{2+} (1.5×10^{-3})		0.01
3	0	0	O_2 ($<10^{-6}$ M)	1.0 (standard)
3	0	β-CD (5×10^{-3})	O_2 ($<10^{-6}$ M)	1.0
3	Ca^{2+} (10^{-3})	0	O_2 ($<10^{-6}$ M)	1.6
3	Ca^{2+} (10^{-3})	β-CD (5×10^{-3})	O_2 ($<10^{-6}$ M)	25
3	all 4 combinations of Ca^{2+} ...	... and β-CD immediately above	O_2 (3.0×10^{-4} M)	1.0 ± 0.5

[a] 10^{-5} M **1** in $CH_3OH:H_2O$ (1:1 v/v), excited at 368 nm, fluorescence emission maxima are 405, 425, and 440 nm. 0.5×10^{-5} M **2** in CH_3CN, excited at 374 nm, fluorescence emission maximum is 440 nm. 10^{-5} M **3** in H_2O at pH 7.2, excited at 287 nm, phosphorescence emission maxima are 505 and 530 nm, observation delay time 0.1 ms and gate time 3.0 ms. Logarithms of apparent host–guest binding constants under the experimental conditions (log β); **1**–Zn^{2+} = 5.2, **1**–H^+ = 4.2, **2**–Hg^{2+} = 3.7, **2**–H^+ [measured in $CH_3OH:H_2O$ (1:1 v/v)] = 4.8, **3**-β-CD = 2.1 ± 0.2, **3**–Ca^{2+} = 7.2.

The 2,2′-bipyridyl receptor within "fluorophore-spacer-receptor" system **1** (prepared according to ref 16) (Figure 1) can complex either H^+ or Zn^{2+}.[17] Complexation or "input" of either cation is expected to quench fluorescence output, because the cation-bound receptor is sufficiently electron deficient and planarized[18] so as to allow a rapid PET process from the anthracene fluorophore. In the event, fluorescence output is quenched by nearly an order of magnitude (Table 1 and Figure 3A). The pattern of fluorescence intensity as a function of cation input is read as a NOR logic response according to the truth table in Figure 1.

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IN$_1$	IN$_2$	IN$_3$	OUT
(Ca^{2+})	(β-CD)	(O$_2$)	(λ_{Em})
0	0	0	0
0	1	0	0
1	0	0	0
1	1	0	1
0	0	1	0
0	1	1	0
1	0	1	0
1	1	1	0

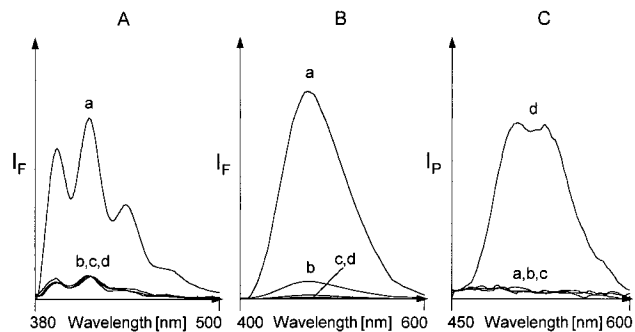**Figure 2.** Molecular-scale implementation of INHIBIT logic gates.

Figure 3. (A) Fluorescence emission spectra for **1** under different input conditions (a, blank; b, H$^+$; c, Zn^{2+}; d, H$^+$ and Zn^{2+}). (B) Fluorescence emission spectra for **2** under different input conditions (a, blank; b, Hg^{2+}; c, H$^+$; d, H$^+$ and Hg^{2+}). (c) Phosphorescence emission spectra for **3** after deaeration under different input conditions (a, blank; b, Ca^{2+}; c, β-CD; d, Ca^{2+} and β-CD). Details are given under Table 1. All intensities are in arbitrary units. Excitation is carried out at the relevant isosbestic point.

We note that NOR logic is achieved with H$^+$ and Zn^{2+} which are not intrinsic quenchers according to paramagnetic or heavy atom mechanisms. Thus H$^+$ and Zn^{2+} can be simultaneously supplied as inputs, say, to an AND gate for operation in parallel with NOR gate **1**. Gates operating in parallel have obvious implications for computation.

This approach to a higher-level gate which integrates NOT and OR logic can be generalized to include distinctly different architectures and mechanisms. Molecule **2** (Figure 1) is a spatially overlapping "fluorophore-receptor" system.[15] Its receptor, which is reminiscent of 2,2′;6′,2″-terpyridyl, complexes H$^+$ or Hg^{2+}.[17] The fluorescence output of **2** is seriously quenched by either cation (Figure 3B) and the NOR truth table is again obeyed. The mechanism of fluorescence quenching with Hg^{2+} probably involves a nonemissive ligand-to-metal charge transfer (LMCT) excited state. The observation of quenching with H$^+$ is easily understandable since 1,3-diaryl-Δ^2-pyrazolines such as **2** show fluorescence quenching when the lone electron pair on N-2 interacts with hydrogen centers.[19]

The concept of functional integration is simple in these cases: NOT logic involves fluorescence quenching upon complexation of a chemical guest.[7] OR logic specifies that two (or more) chemical guests should cause a similarly strong revival of a previously extinguished fluorescence.[7,9] Thus NOR logic must be a nonselective quenching of fluorescence by at least two

chemical guests. Once we are armed with such a simple concept, some older reversible fluorescence phenomena can now be interpreted as NOR logic for the first time.[20]

Functional integration also succeeds in achieving the much more complex INHIBIT logic operation with a rather simple supermolecule **3** (Figure 2). **3** contains a tetracarboxylate receptor that can bind Ca^{2+} [21] and a 2-bromonaphthalene phosphor which can be enveloped by β-cyclodextrin (β-CD).[22] The extinguished phosphorescence emission of **3** is not revived by the addition of Ca^{2+} and β-CD in any of the four combinations if O$_2$ is allowed to be present. However, if O$_2$ is purged, strong phosphorescence is generated but only if Ca^{2+} and β-CD are simultaneously present (Figure 3C). This behavior pattern (summarized in Table 1) exactly fits the INHIBIT truth table (Figure 2). System **3** shows no phosphorescence when free of guests because of PET from the tetracarboxylate receptor to the 2-bromonaphthalene phosphor.[23] Ca^{2+} binding arrests this PET process. However, phosphorescence is not seen because the phosphor excited state requires protection against bimolecular triplet−triplet annihilation by enveloping with β-CD. Still, the conditions are not met for strong phosphorescence because ambient levels of O$_2$ can quench the bromonaphthalene triplet−β-CD assembly. It is only when O$_2$ is removed that the phosphorescence becomes strong, i.e., O$_2$ serves as the disabling input$_3$, while Ca^{2+} and β-CD inputs combine according to AND logic (Figure 2).

The characteristics of the two sets of gates presented here are strikingly different. The fluorescent output of **1** and **2** is of nanosecond duration and is negligibly quenched by ambient levels of O$_2$. The phosphorescence output of **3** has a lifetime of 0.14 ms besides being efficiently disabled by O$_2$. We are thus presented with a simple approach to select a given gate from an ensemble. Gate **3** can be operated without interference from **1** or **2** by using flash excitation, a delay of 0.1 ms (the shortest delay available to us) before observation of emission[23,24] and deaerated conditions. Conversely, **1** or **2** can be operated without interference from **3** by using prompt observation and aerated conditions. The excitation/emission wavelengths and the various chemical species as inputs are additional controllable variables to aid the gate selection. Since molecular-scale logic gates are not hard-wired to their inputs, outputs, and power supplies, such freedom to address gates in any sequence within an ensemble is essential if more complex computational operations are to evolve.

More generally, the angstrom size of these molecular logic devices and their ability to be operated in parallel with optically readable outputs can lead to unique applications especially when they are incorporated into small spaces such as polymer beads featuring combinatorial chemistry.

Supporting Information Available: Details concerning synthesis and characterization of **2** and **3** (PDF). This material is available free of charge via the Internet at http://pubs.acs.org.

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