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Molecules that add up

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As information technology encroaches more and more into our lives, attention is turning to how the revolution started by silicon logic gates can be carried forward. Smaller-scale information processors is one approach to which chemical solutions can be imagined. The first molecular logic gates were built in Belfast a few years back. These artificial systems use chemical inputs and light output, reversing the natural roles existing within the eye. They can now do simple addition.

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HOW MUCH IS 1 PLUS 1? This question seems trivial at first sight, but it represents the way in which most of us were introduced to numeracy on our mothers' knee.[1] The word 'us' includes not only virtually everyone alive today but all of those who walked this planet over the past three millennia at least. While the basis of human numeracy[2] is likely to remain mysterious for a while yet, it is clear that molecular systems in the brain are involved in one way or another. It is, therefore, quite a challenge to persuade laboratory molecules to go down the numerical road. Of course, devices used in computing – abacuses, electromagnetic relays, vacuum tubes and semiconductor transistors[3] – have travelled this path at various points in history. Their success has shaped societies and even human behaviour. However, they have not relied on molecular processes.[4]

Nevertheless, in recent decades, quite a few researchers have considered how to exploit molecular properties, with their intrinsic diversity, to create minuscule systems that could carry out computational operations – as electrons do in the ubiquitous silicon structures found in modern processing devices. Indeed, 30 years ago, the area of molecular electronics – encouraged by the visionary thinking of early proponents such as Ari Aviram of IBM and Forrest Carter of the US Naval Research Laboratory – seemed to have great potential. However, suggestions, for example, of exploiting the electronic mobility within conjugated structures never materialised into workable devices. Consequently, computer companies largely lost interest.

Today, however, there is renewed enthusiasm for coaxing molecules to carry out information processing. This is partly because of the commercial drive to increase computer power by packing ever more transistors onto a chip, and partly because from the early 1990s onwards, researchers were starting to demonstrate a variety of imaginative model systems. For instance, Robert Birge at Syracuse University in New York State has described an optical memory device based on the light-sensitive protein dye bacteriorhodopsin; and the British chemist Fraser Stoddart, now at UCLA, has constructed rotaxanes – intriguing hoop-shaped molecules threaded onto a rod along which they could slide like beads to create a switching device. Our group in Belfast developed the first molecular system suited to small-scale computational processing. It is based on photo-induced electron transfer in which the fluorescence emitted by a chromophore can be modulated by introducing one or more chemical species. Thus, using this simple strategy, we have been able to address our opening question.

Molecular logic gates

Our molecular approach has followed the computational tradition of achieving number processing via Boolean logic operations.[3] These rely on the binary 'yes-no, true-false, 1-0' concept to create logic gates which carry out a specific operation on an input to create an output. For example, a YES gate has an output of 1 for an input of 1; a NOT gate reverses the input of 1 to produce an output of 0; an AND gate requires two inputs of 1 to give an output of 1; and a XOR gate has two inputs but they must differ to give an output of 1, otherwise they give an output of 0. To add 1 plus 1 (1+1 = 10 in binary), AND and XOR logic gates can be combined to give the two digits of the sum (two digital-1 inputs will give outputs 1 and 0 for AND and XOR, respectively). This is the simplest form of addition done by a device called a half-adder. Let's see how molecules can perform this binary logic.

• *The YES logic operation*

Starting with the simplest 1-input YES logic operation, compound **1** in Figure 1 shows our molecular version.[5] It is conceptually a modular 'lumophore-spacer-receptor' system based on an aromatic unit (the lumophore) with an electron-rich amine sidechain (receptor).[6,7] The excited lumophore will not emit light because the receptor engages in photo-induced electron transfer (PET)[8] by launching an electron across the spacer into the lumophore. When thermodynamically allowed,[6,7] PET can be so fast[9] that light emission from the lumophore is strongly quenched (output 0). However, the arrival of the correct guest as input into the receptor site stops PET and the excited lumophore emits unimpeded ($output_1$). Specifically, **1** uses a proton as an input; blue fluorescence is the output; and the ultraviolet radiation used to excite the molecule is the power supply. Simple though it is, the processing device **1** manages[10] its interactions with three entities and can work as a single molecule.[11]

• *The AND logic operation*

The two-input AND logic operation requires that two inputs are both applied as digital 1 to the appropriate points of the gate in order to elicit an output of digital 1 (Figure 2). This can be translated to the molecular arena1[2] with system **2** which has an additional crown ether attached to

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provide the second receptor. H^+ is $input_1$, Na^+ is $input_2$, blue fluorescence is the output and ultraviolet excitation is the power supply. System **2** is designed as a modular 'lumophore-spacer$_1$-receptor$_1$-spacer$_2$-receptor$_2$' system, where each receptor module is capable of transferring an electron to the excited lumophore. However, each receptor becomes unable to achieve PET to the lumophore when bound to its respective guest. Since even one PET process can kill off light emission, it's no wonder that emission output achieves digital 1 only if both receptors are bound up with their corresponding guest inputs. System **2** succeeds as a logic device by marshalling four entities: H^+, Na^+, blue photons and ultraviolet photons.

• *The XOR logic operation*

The 2-input XOR logic operation passes an output of digital 1 only if the inputs are digitally different (Figure 3). A luminescent molecular version of the XOR gate was reported in 1997 by Vincenzo Balzani (in the University of Bologna), Stoddart and colleagues.[13] However, its use of cross-reactive input guests can be problematic for the operation of other gates in parallel, so for this purpose we use optical transmittance (rather than luminescence) at a chosen wavelength. The integrated 'receptor$_1$-chromophore-receptor$_2$' system has H^+ as $input_1$, Ca^{2+} as $input_2$, the transmitted violet light as output and violet excitation light as the power supply. Upon excitation to its internal charge transfer (ICT) state,[7] the chromophore within molecule **3** separates substantial fractional charges, which naturally interact with ionic guests lodging in the receptors. The latter are deliberately positioned at opposite termini of the chromophore so that the two cationic guests elicit opposite energetics upon interaction with the ICT state. Thus, the UV-VIS absorption spectrum of **3** is pulled in opposite wavelength directions by the two guest inputs. The simultaneous presence of both inputs leads to a balance of power, and the UV-VIS spectrum is largely unaltered. Measuring transmittance at a violet wavelength then produces the XOR truth table as shown in Figure 3b.

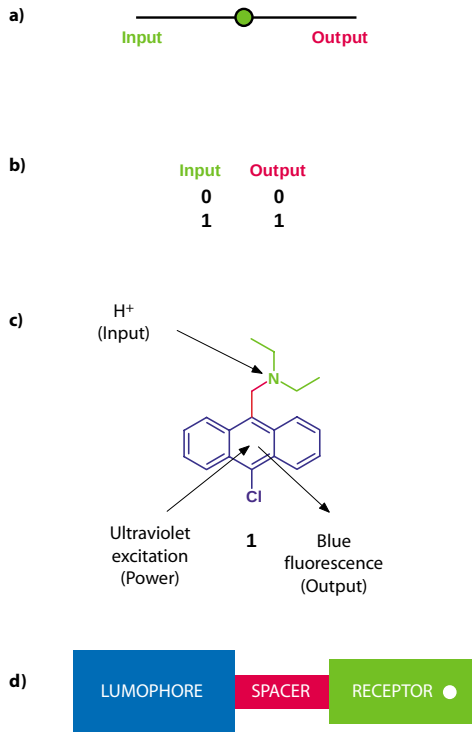
• *A molecular half-adder*

The half-adder (Figure 4) arises when we simply mix aqueous solutions of XOR gate **3** and a compatible AND gate **4** (identical in concept to **2**).[14] The binary numbers, 1 plus 1, to be added are represented by the combination of H^+ as $input_1$ and Ca^{2+} as $input_2$. The result is read as the two-bit number '$output_1$ $output_2$' (1 from the AND gate and 0 from the XOR gate to give the answer 10), which thus correctly answers our opening question. So here is the first step in intrinsic molecular numeracy. Like most first steps it is a very small one – nevertheless, the combination of **3** and **4** is a small-scale information processor in terms of its numerical capability.

The future

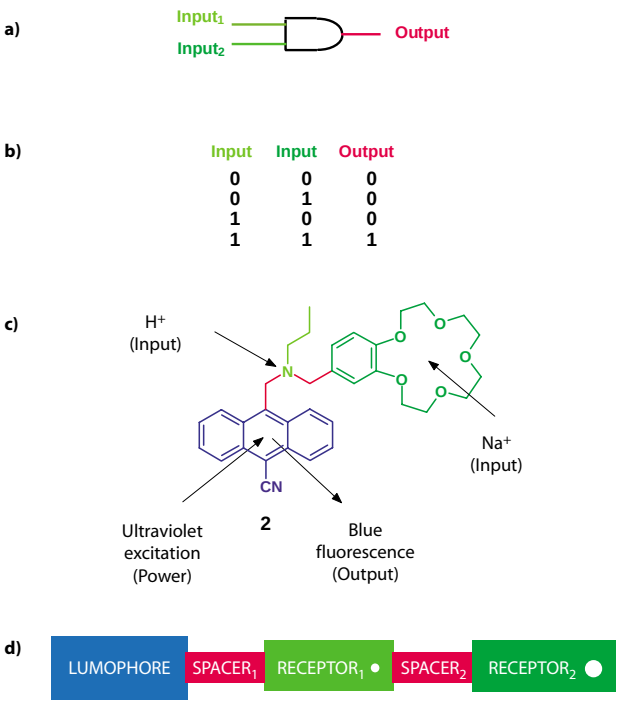
Issues of component integration have to be addressed for further progress to be made in line with computational tradition. While a degree of integration is already subsumed within individual gates, increasingly complex gate arrays are appearing within a number of molecular systems.[15] One advantage of our system is that it does not require any connecting wires between the two component gates – a major problem to be overcome in the molecular electronics field. Our system is, of course, in solution – so while it is a good demonstrator for the principle of molecular computing, it is unlikely to integrate well with traditional solid-state systems. Nevertheless, it may be possible in the future to design 'wet' computers that work more like the brain, relying on membrane-bound molecular processors similar in nature to ours.

Figure 1



a) Physical electronic symbol of 1-input YES logic gate, b) the truth table, c) molecular version, d) generalisation

Figure 2



a) Physical electronic symbol of 2-input AND logic gate, b) the truth table, c) molecular version, d) generalisation

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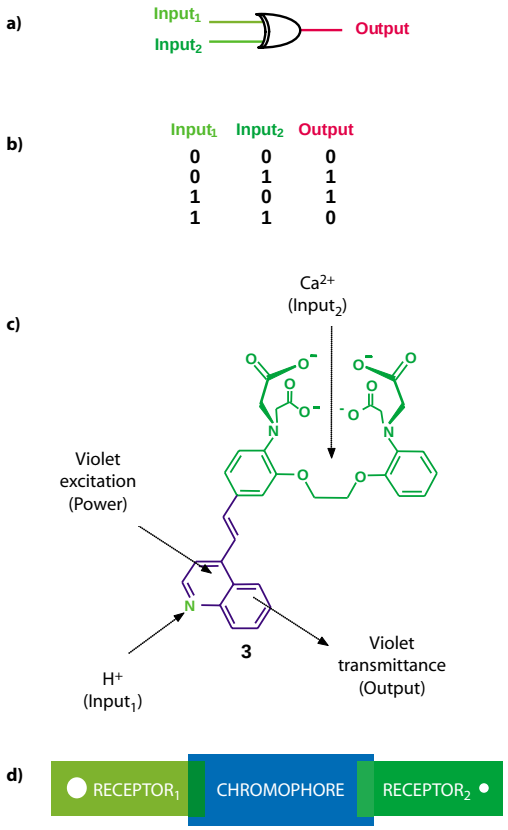
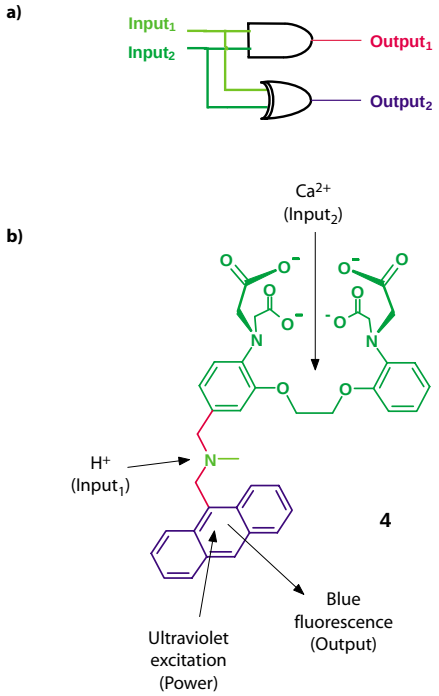
Figure 3



a) Physical electronic symbol of 2-input XOR logic gate, b) the truth table, c) molecular version, d) generalisation

Figure 4



a) Physical electronic representation of a half adder, b) AND gate 4 compatible with XOR gate 3 so that the pair serve as a half-adder

In the meantime, we should bear in mind that simple logic operations are not just used in computers. As well as processing information, our system can be used for information gathering – in other words as a miniaturised diagnostic system capable of working under physiological conditions. Indeed, information systems based on wet molecular logic are likely to be applied increasingly in the medical sphere.

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