Molecular Logic Elements

DOI: 10.1002/anie.200603990

Chemical Approaches to Molecular Logic Elements for Addition and Subtraction

*Uwe Pischel**

Keywords:
electron transfer · energy transfer · fluorescence · logic gates · molecular devices

Molecular and supramolecular logic gates are candidates for computation at the nanoscale level. Nowadays all common logic operations can be mimicked with molecular devices based on chemical approaches. One step further towards molecular systems with increased logic capabilities is the addition or subtraction of binary digits. This Minireview describes recent developments to attain this goal, including bioinspired systems based on DNA and enzymes. Furthermore, chemical molecular logic gates are discussed and compared critically with regard to alternative concepts.

1. Introduction

In the light of the increasing demands of information technology (IT) in terms of miniaturization, chemistry plays a key role in the so-called bottom-up approach.[1] This approach consists of the controlled design of nanoscale structures using first principles of supramolecular chemistry or advanced strategies of polymer synthesis. For the directed implementation of functions, molecular and supramolecular building blocks, which can be addressed by external stimuli (input; for example, photons, electrons, chemical entities) and which generate one or more answer signals (output; for example, light emission, changes in electronic or electrochemical properties, chemical reactions) are required.

One predominant feature of IT is the processing of input signals by means of combinatorial operations, using so-called logic gates.[2] Based on early ideas to use molecules as logic gates,[3] one of the first examples, a molecular AND gate, was reported in 1993 by de Silva et al.[4] Data processing in conventional computers based on silicon circuitry requires the binary encoding of information contained in electrical signals; for each signal a threshold value and a logic convention are defined. Positive logic convention relates to 0 for a signal value below the threshold and to 1 for a value above the threshold. Negative logic convention leads to the reverse situation. It should be noted that binary logic is a general concept and applies therefore to any type of signal, including chemical and optical ones. This makes it possible to use molecular systems for mimicking logic functions.

In an extension of previously reviewed chemical concepts for basic Boolean logic at the molecular level,[5–8] this Minireview will describe very recent approaches to refined molecular systems that can mimic comprehensive arithmetic operations like addition or subtraction of binary digits. This requires the integration of several basic logic gates in circuits of higher complexity.[9] Although molecules able to encode $1+1=2$ or $1-1=0$ are hardly serious competitors for present silicon-based microprocessors, the reported examples constitute a proof-of-principle and important efforts within the framework of molecular computing. The Minireview will conclude with a brief discussion of the present status of molecular logic and a critical evaluation of the impact of the herein discussed concepts.

2. Principal Elements of Molecular Calculators

A half adder is a device that adds two binary digits (bits). As shown in Scheme 1, half adders require the parallel implementation of AND and exclusive OR (XOR) logic gates. The two gates share the same inputs (I1 and I2) and produce outputs that code for the CARRY (C) and SUM (S) digits. These digits stand for the binary realization of $0+0=0$, $1+0=1$, and $0+1=1$. In the case of $1+1$ the SUM is 0, but the CARRY is set to 1, yielding $1+1=2$.

The first molecular XOR operation was demonstrated by Balzani, Stoddart, and co-workers.[10] They made use of the assembly/disassembly of a pseudorotaxane, initiated by inputs in form of acid and an amine. Their pseudorotaxane consists

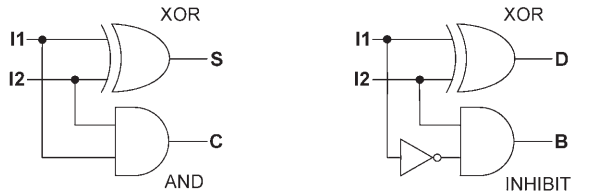
[*] Dr. U. Pischel
Instituto de Tecnología Química
Universidad Politécnica de Valencia
Av. de los Naranjos s/n, 46022 Valencia (Spain)
Fax: (+34) 96-3877-809
E-mail: upischel@itq.upv.es

a)

I1	I2	C	S
0	0	0	0
0	1	0	1
1	0	0	1
1	1	1	0

b)

I1	I2	B	D
0	0	0	0
0	1	1	1
1	0	0	1
1	1	0	0



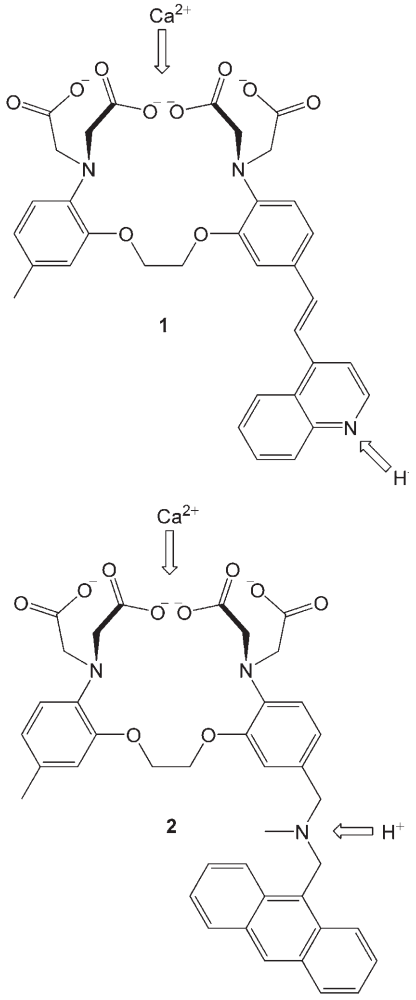
Scheme 1. Truth table and logic representation of a) a half adder and b) a half subtractor.

of an electron-poor thread (2,7-dibenzyldiazapyrenium dication) and an electron-rich macrocycle (2,3-dinaphtho[30]-crown-10), which form a charge-transfer complex, resulting in quenched naphthalene fluorescence (output signal). Addition of acid or amine leads to dethreading of the pseudorotaxane and recovery of the fluorescence. However, annihilation of both inputs by acid–base neutralization impedes the implementation of this gate in a half adder.

De Silva and McClenaghan developed an interesting approach towards XOR logic, avoiding input annihilation.[11,12] System **1**, shown in Scheme 2, consists of a push–pull chromophore with receptor sides for Ca^{2+} and H^+. The internal charge-transfer (ICT) excited state is perturbed by the presence of either input, which leads to changes in the absorption spectrum. By clever selection of the optical output signal (transmittance) no net effect is observed when both inputs are present simultaneously.

As a result of the efforts towards molecular calculators, more and more XOR gates have been reported. Beside the ones discussed in this Minireview,[11,13–26] others without integration in arithmetic logic systems have been published.[10,12,27,28] The second logic element needed for a half adder is the AND gate, for which numerous examples are known.[4,29–31]

Uwe Pischel studied chemistry at the Technical University Dresden and the Humboldt University Berlin. He received his PhD from the University of Basel in 2001 for work with W. M. Nau. After a postdoctoral stay (2002) at the Polytechnical University Valencia with M. A. Miranda he assumed a position as junior research team leader at the University of Porto (2003–2006). Since 2006 he has been a Ramón y Cajal researcher at the Polytechnical University Valencia. In 2003 he received the Albert Weller Prize of the Photochemistry Division of the German Chemical Society. His current research interests include supramolecular photochemistry and chiral phenomena in photochemistry.



Scheme 2. A half adder composed of **1** and **2** with Ca^{2+} and H^+ as inputs.

Half subtractors are composed of an INHIBIT and an XOR gate. They produce a BORROW (B) and a DIFFERENCE (D) output (Scheme 1), resulting in the following operations (I1–I2): $0-0=0$, $1-0=1$, and $1-1=0$. In the case of $0-1$, a 1 is borrowed from a higher stage, which makes the difference become $2-1=1$. INHIBIT gates rely basically on AND operations with one of the inputs being inverted. Several examples for molecular INHIBIT gates are known, including luminescent lanthanide complexes, fluorophore/cation receptor dyads with emissive ICT states, or fluorescence phenomena related to host–guest complexes.[12,28,32–34] More INHIBIT gates will be described in the context of this Minireview.[14,17,19,20,22,24,25,35]

For the sake of completeness it should be mentioned that binary multiplication follows the same rules as the truths of an AND gate ($0\times0=0$, $1\times0=0$, $0\times1=0$, $1\times1=1$), while binary division is the result of repeated subtraction, the same as decimal division.

3. Half Adders and Full Adders

The first molecular half adder by de Silva et al. used a combination of **1** as an XOR gate and **2** (cf. Scheme 2).[11] The latter works as an AND gate, combining receptors for Ca^{2+} and H^+, which contain electron-donating amino functions. This results in anthracene fluorescence quenching by the noncomplexed receptors by means of photoinduced electron transfer (PET). Only in the presence of both inputs is this deactivation pathway blocked and intensive fluorescence observed.

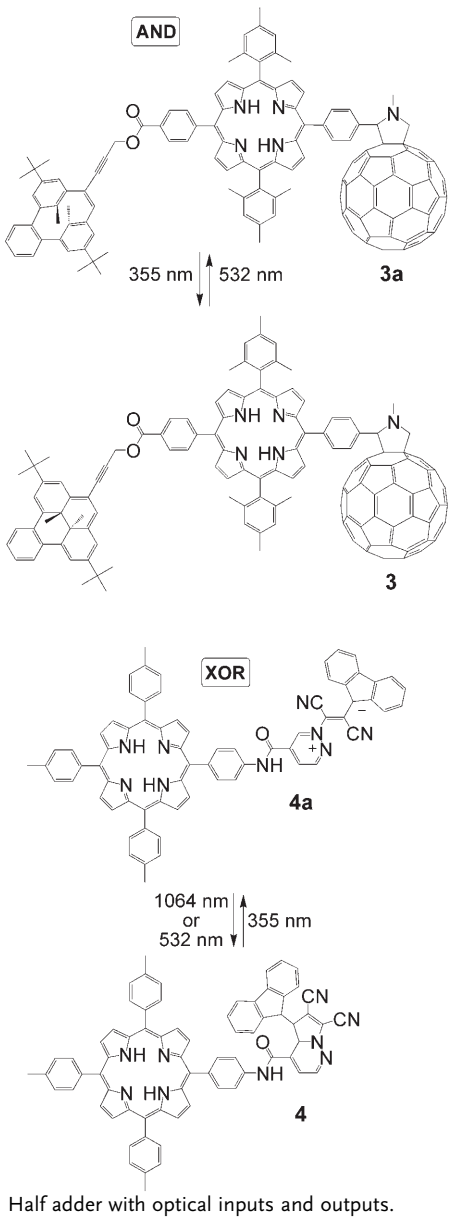
A drawback of many molecular logic gates is that input information is often applied in the form of chemical entities. This limits their application to fluid media. This disadvantage can be overcome with all-optical systems, in other words, systems using exclusively optical inputs and outputs. Contrary to the half adder composed of **1** and **2**, which works with chemical inputs and optical outputs, all-optical logic elements provide input/output homogeneity. Furthermore, optical signals allow in principle the communication between different logic devices, a strategy that will be further considered in Section 6. Gust and co-workers introduced an all-optical half adder, based on the dihydropyrene–porphyrin–fullerene (DHP-P-C_{60}) triad **3** and the porphyrin–dihydroindolizine (P-DHI) dyad **4** (Scheme 3).[15] Triad **3** contains a photochromic DHP unit. Irradiation at 532 nm leads to **3a**, and the reaction can be reversed by irradiation at 355 nm.[34] Furthermore, a long-lived charge-separated state (DHP$^{\bullet+}$-P-$C_{60}^{\bullet-}$), characterized by the transient absorption of the C_{60} radical anion at 1000 nm, is formed upon excitation of P in **3** at 650 nm (probe wavelength).[36] However, **3a** results only in a short-lived transient absorption for $C_{60}^{\bullet-}$.

To implement an AND gate, one has to start with **3a**, and laser light with wavelengths of 1064 nm and 532 nm is used as inputs. Neither wavelength leads to photoisomerization; therefore only a short-lived C_{60} radical anion is produced when 650-nm laser light is used as the probe. However, simultaneous application of both input wavelengths and use of a third-harmonic-generating crystal (THG) yields light of wavelength 355 nm. This results in the formation of **3** and consequently a long-lived transient at 1000 nm.

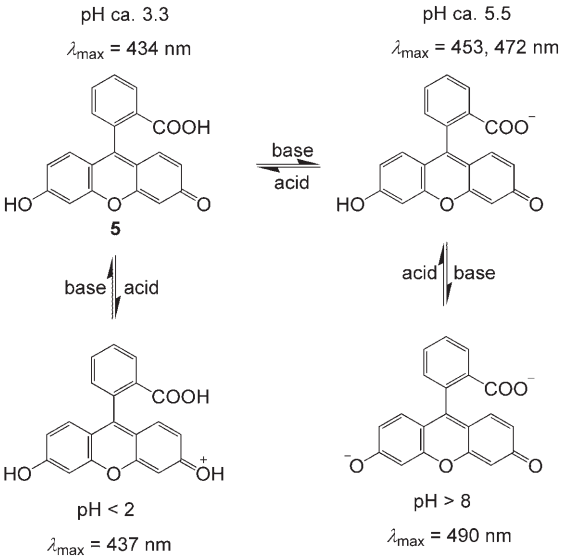
Dyad **4** contains DHI as the photochromic unit and can be converted to **4a** by 355-nm light.[34] The back reaction to **4** proceeds by irradiation at 532 nm (photoisomerization) or 1064 nm (thermal isomerization). Upon excitation of **4** at 650 nm, the porphyrin P shows strong fluorescence (output, 720 nm). However, this emission is quenched by PET in **4a**. Using the dyad as an XOR gate requires **4a** as the initial state. Application of 1064-nm or 532-nm laser light isomerizes **4a** to **4** and results in fluorescence, while simultaneous application of both irradiation wavelengths (i.e., 355 nm via the THG) leads to no changes. As an additional asset, the half adder can be reset by inducing back isomerization of the photochromic units to their initial states.

An interesting approach to molecular arithmetic systems with reset capability was presented by Shanzer and co-workers.[19,22] They used the pH-controlled switching between the monocationic, neutral, monoanionic, and dianionic forms of fluorescein (**5**, Scheme 4). These ionization states have different absorption spectra, which allows the unimolecular implementation of XOR and AND gates by the choice of appropriate readout wavelengths (output). As inputs two equimolar solutions of NaOH are used. Note that XOR and AND gates are insensitive to this degeneracy of inputs. Half adders based on **5** can be operated with different initial states, for example, pH < 2 (monocationic form) or pH 3.3 (neutral form), and appropriately chosen optical outputs (transmittance or absorbance). Further, the system can be reset by acid–base neutralization.

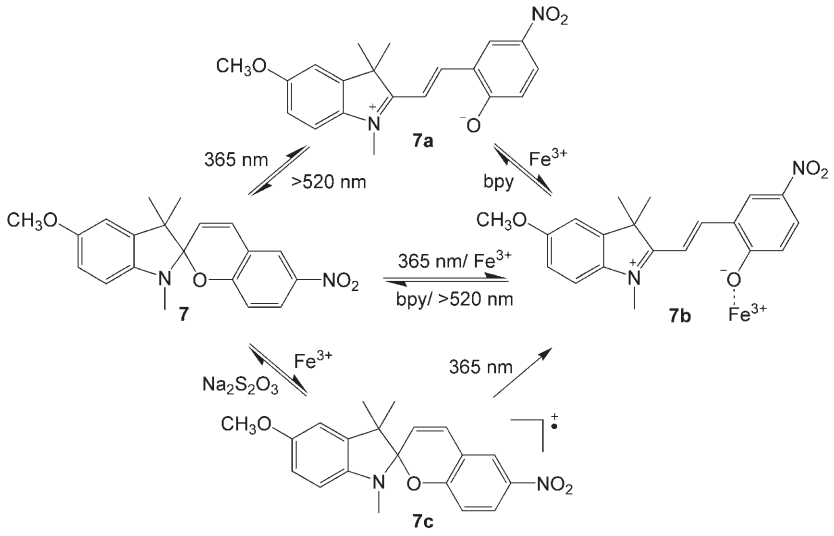
In general, other pH indicators can also be imagined as potential candidates for molecular calculators. For instance, Liu et al. recently exploited the imidazophenanthroline derivative **6** as a pH-sensitive fluorophore, which shows well-distinguished emission spectra in the different states of ionization.[24] Other examples (**14** and **15**) are described in Section 4.



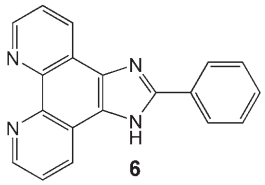
Scheme 3. Half adder with optical inputs and outputs.



Scheme 4. Ionization states of the pH indicator fluorescein (**5**) and the maxima of their respective absorption spectra.



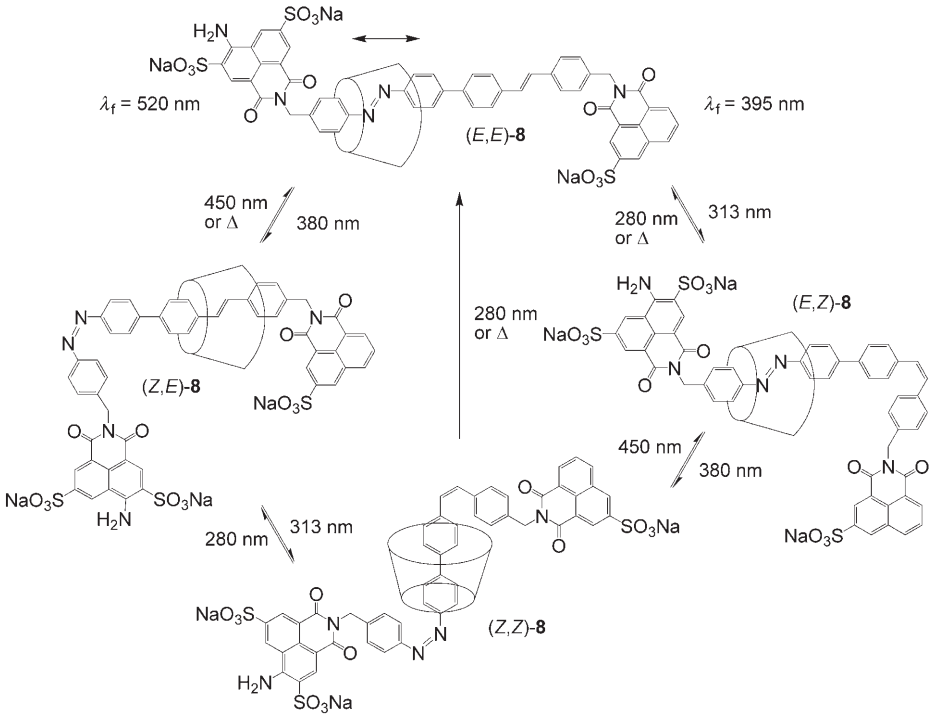
Scheme 5. Switching between photochromic forms of **7**; Fe^{3+} was used in excess (5 equiv). bpy: 2,2′-bipyridine.



For a well-defined arithmetic operation, interferences between the integrated logic gates must be avoided. In this respect the unimolecular realization of reconfigurable logic functions is a further step towards molecular circuits with extended processing capabilities. The half adder **5** addresses this point; other systems will be discussed in the following paragraphs.

Zhu and co-workers introduced the spiropyran **7** as a half adder, which has Fe^{3+} ions and UV irradiation at 365 nm as inputs (cf. Scheme 5).[16] The required XOR and AND gates are reconfigurable by a simple change of the UV/Vis absorption wavelength of the output ($\lambda_{abs} = 420$ or 520 nm). The absorption at 520 nm is dominated by the merocyanine **7a** and the radical cation **7c** and is highest if either 365-nm light or Fe^{3+} is applied. On the other hand, the absence or simultaneous presence of both inputs yields lower output signal intensities at 520 nm. This behavior is compatible with XOR logic. The shorter output wavelength (420 nm) corresponds mainly to the absorption of the Fe^{3+}-complexed merocyanine **7b**, which is formed only in the presence of 365-nm light and Fe^{3+}, in accord with AND logic.

Also mechanically interlocked supramolecular assemblies have been used as half adders. Tian and co-workers reported the [2]rotaxane **8** (Scheme 6), composed of a thread with two photoisomerizable stations (an azobenzene and a stilbene unit), fluorescent 1,8-naphthalimide stoppers, and an α-cyclodextrin (α-CD) macrocycle.[21] The system works on an all-optical basis, using different irradiation wavelengths (313 nm: $E \rightarrow Z$ conversion of the stilbene unit, 380 nm: $E \rightarrow Z$ conversion of the azobenzene unit) as inputs and changes of UV absorbance and fluorescence as outputs. The initial situation consists of the *E*,*E* arrangement of the thread. The largest variations in the absorption spectrum are detected



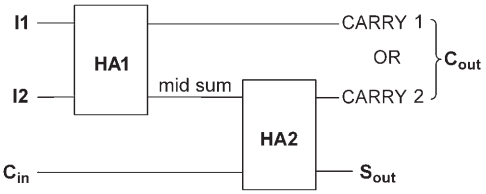
Scheme 6. Photoisomerization processes of rotaxane **8** and corresponding position of the α-CD macrocycle. λ_f = fluorescence wavelength.

when both stations are in their *Z* arrangement, which is achieved only by parallel irradiation with both input wavelengths, corresponding to AND logic. The XOR gate is implemented by using the total change in fluorescence as the output. Irradiation at either input wavelength alone (313 nm or 380 nm) locks the α-CD at the station that remains in the *E* arrangement. The resulting rigidity increase causes fluorescence enhancement of the nearby stopper. Simultaneous irradiation with both input wavelengths yields the *Z*,*Z* isomer, without significant fluorescence changes. Interestingly, this unimolecular system combines all-optical performance of the XOR and the AND gate with reset capability by means of photoinduced or thermal back isomerization.

Remacle, Levine, and co-workers reported an elegant example of an unimolecular half adder based on 2-phenylethyl-*N*,*N*-dimethylamine (**9**). The authors also stated that their concept is in principle generally applicable for aromatic and conjugated molecules. One- and two-photon UV absorption yields fluorescence and amine fragmentation (by means of photoionization followed by charge transfer), respectively (Scheme 7).[23] The inputs are defined by the two UV photons, which, for example, can be provided by two different lasers. Absorption of either photon leads to fluorescence, while the two-photon absorption causes photoionization without observed fluorescence. Thus, the XOR gate is defined by fluorescence as output, and the AND gate output is related to amine fragmentation. As a disadvantage, the molecule is destroyed by the photoionization, which prevents repeated arithmetic cycles. On the other hand, even a few ions can be detected with good signal-to-noise ratios, thereby manifesting a remarkable sensitivity and the potential to scale-down large molecule ensembles to few molecules (about 100), given that absorption cross-sections are large enough.

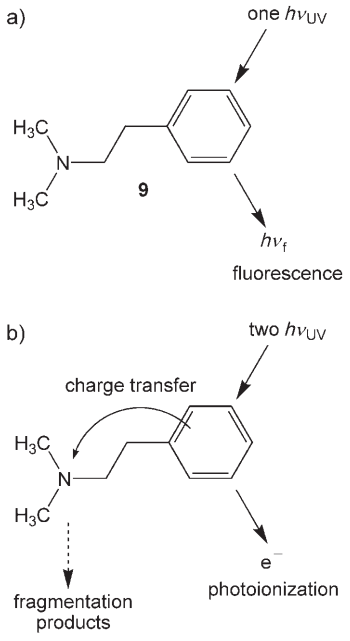
Interestingly, **9** was also explored for full-adder arithmetic.[23] A full adder can sum three binary digits: two inputs (I1 and I2) and the CARRY IN (C_{in}) from the previous addition. This requires two half adders with the sum output of the first half adder HA1 (mid-sum) being one input of the second half adder HA2 (Scheme 8). The result of the addition is defined by the CARRY OUT (C_{out}) and the SUM OUT (S_{out}). The only output combination that a full-adder does not have in common with a half adder is $C_{out} = S_{out} = 1$, corresponding to $1+1+1=3$. In the example of **9**, two inputs are again constituted by two UV photons, while the C_{in} is defined by the absorption of two green photons of sufficient energy to populate the fluorescent first excited singlet state. These two green photons can also fragment the phenyl radical cation, which is formed by two-photon UV absorption (see above).

I1	I2	C_{in}	C_{out}	S_{out}
0	0	0	0	0
0	1	0	0	1
1	0	0	0	1
1	1	0	1	0
0	0	1	0	1
0	1	1	1	0
1	0	1	1	0
1	1	1	1	1

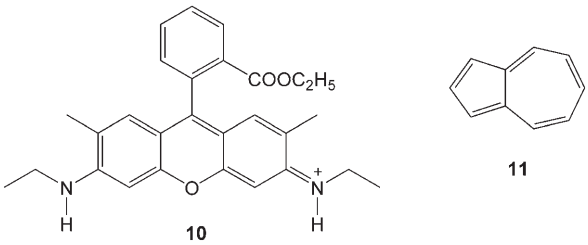


Scheme 8. Truth table and simplified scheme of a full adder. C_{out} results from the logic OR combination of the carry outputs of the individual half adders HA.

A different strategy for a full adder is the concatenation of two half adders, as has been demonstrated by Levine and coworkers.[13] They used an energy donor–acceptor pair composed of rhodamine 6G (**10**) and azulene (**11**). Each of the compounds acts as a half adder and uses two photons of similar energy (provided by two different lasers) as inputs and emission from the first (S_1) or second electronically excited singlet state (S_2) as outputs of the XOR and the AND gate, respectively. The concatenation is achieved by fast intermo-



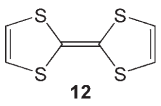
Scheme 7. One- and two-photon processes in **9**.



lecular energy transfer between donor **10** and acceptor **11**. Generally the efficiency of the energy transfer is dependent on the relative spatial orientation of the energy donor and acceptor. In that sense, the linking of energy donor–acceptor pairs by rigid spacers might be an interesting approach to facilitate communication between logic gates and improve energy transfer concatenation.[37] Other strategies for digital communication at the molecular level will be discussed in Section 6.

The half adder **5** described by Shanzer and co-workers can be extended to a full adder by introducing an additional input (a third equimolar solution of NaOH) and setting the initial state of the system to the monoprotonated form of **5**, which exists at $pH < 2$ (Scheme 4).[22] In this case, the outputs are defined as transmittance at 447 nm (S_{out}) and absorbance at 474 nm (C_{out}).

Finally, Zhou et al. demonstrated that consecutive one-electron processes of simple tetrathiafulvalene (**12**) involving electrochemical and chemical oxidation can be interpreted in terms of a half adder.[26] Their approach makes use of the well-differentiated absorption spectra of **12**, its radical cation, and its dication as the read-out signals. Further, owing to the reversible electrochemistry of **12**, the system can be reset easily without chemical reactions, the products of which would accumulate with increasing cycle numbers, as is the case for chemical inputs in form of acid or base. This advantage applies also to the discussed all-optical systems **3**/**4** and **8**.

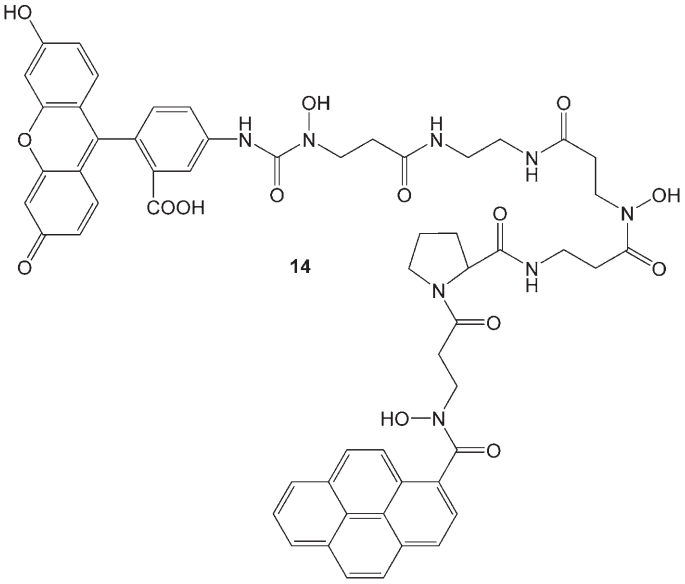


12

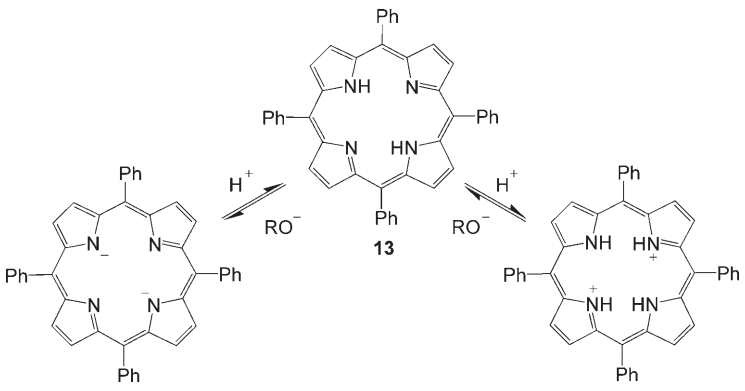
4. Half Subtractors and Full Subtractors

In 2003 Langford et al. realized the first molecular half subtractor based on a surprisingly simple compound: 5,10,15,20-tetraphenylporphyrin (**13**).[14,38] The amphiphilic nature of **13** enables the generation of the dicationic and dianionic forms of the porphyrin by protonation and deprotonation, respectively (Scheme 9). The ionized forms and neutral **13** have quite different absorption and fluorescence properties. While **13** has its Soret band at 417 nm, addition of strong acid (HCl) or base (*t*BuOK) results in a red shift by approximately 20 to 30 nm. However, the simultaneous presence of acid and base leads to neutralization of the inputs without changes in the absorption spectrum. Thus, the definition of the transmittance at 417 nm as the readout signal is compatible with XOR logic. The logic function of the system can be reconfigured by alteration of the output to the fluorescence intensity of the dianionic form ($\lambda_{max,f} = 637$ nm). Because the neutral form and the dicationic form have no significant fluorescence output at this wavelength, an INHIBIT gate is obtained. Both gates are implemented in parallel and addressed by the same inputs, thus fulfilling the requirements for a half subtractor. Interestingly, the realization of the 1−1 arithmetic operation is very intuitive, because it is achieved by acid–base neutralization of the two inputs.

Another half subtractor, which is based solely on fluorescence outputs, was introduced by Shanzer and co-workers.[17] The siderophore-like compound **14** contains two fluorophores: pyrene and fluorescein. With acid (HCl) and base (sodium acetate) as inputs, the Fe^{3+} complex of **14** can perform XOR and INHIBIT logic operations in a reconfigurable manner. Both gates function in the fluorescence mode; the fluorescein emission at 525 nm (INHIBIT) and the simultaneous emissions of pyrene at 390 nm and fluorescein at 525 nm (XOR) serve as outputs. In absence of both inputs, metal-induced fluorescence quenching results. Addition of sufficient amounts of base ($pH > 8$) leads to the dianionic form of fluorescein (Scheme 4) and its green fluorescence induced by electronic energy transfer from the selectively excited pyrene. On the other hand, addition of acid favors the formation of free **14**, which contains fluorescein in its protonated form. Energy transfer is not feasible under these conditions, and the blue fluorescence of the pyrene unit (390 nm) is observed. If both inputs are present simultaneously, a buffer is formed and no significant changes of the output signals are observed.



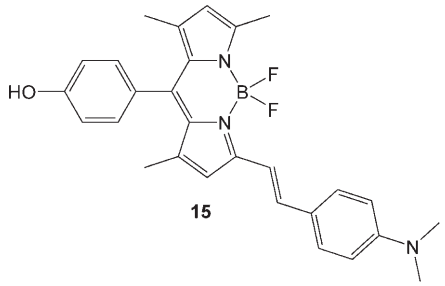
14



Scheme 9. Amphiphilic behavior of porphyrin **13**.

When HCl is replaced with the weaker acid and metal-ion chelator *N*,*N*,*N*′,*N*′-ethylenediaminetetraacetic acid, the fluorescence behavior of the Fe^{3+} complex of **14** can be interpreted as an AND logic gate (fluorescein emission at 525 nm).[17] This, along with the XOR gate described above, can conceivably lead to a half adder. However, this is hypothetical, because two different sets of inputs would have to be applied in parallel.

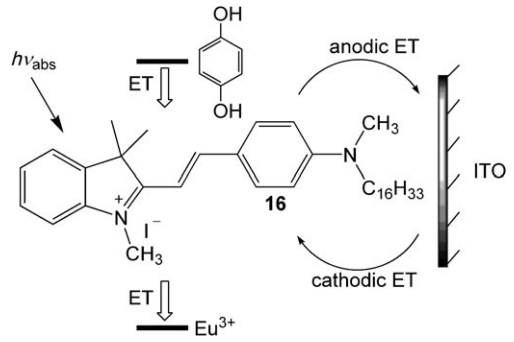
Borondipyrromethenes, also known as BODIPY dyes, are a very popular class of fluorophores applied in molecular sensors and switches. Akkaya and co-workers reported recently the derivative **15**, containing pH-sensitive groups,



15

whose protonation/deprotonation has a considerable impact on the fluorescence properties of the compound.[35] In the absence of acid and base, the moderate red fluorescence of an ICT state (at 660 nm) is observed, which defines the output of an XOR gate (application of a negative logic convention to the output). Expectedly, protonation of the amino group leads to perturbation of the ICT state, resulting in a blue-shifted and intense fluorescence at 565 nm (output of the INHIBIT gate). Deprotonation of the phenolic OH group by addition of the base *t*BuOK does not result in a shift of the fluorescence band but rather PET-induced fluorescence quenching of the ICT state. Again, the simultaneous presence of acid and base results in self-cancellation of the inputs by neutralization.

Li et al. reported a half subtractor based on photocurrent outputs.[20] They used a modified indium–tin oxide (ITO) electrode with a Langmuir–Blodgett monolayer of hemicyanine **16** (Scheme 10). An electron donor (hydroquinone)



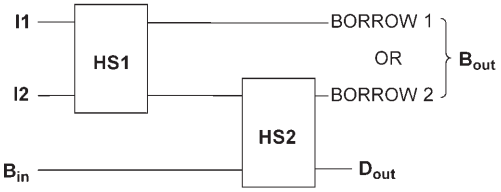
Scheme 10. Hemicyanine **16** on an ITO electrode. Photoelectrochemical behavior upon addition of hydroquinone as electron donor or Eu^{3+} as electron acceptor. ET: electron transfer.

and an electron acceptor (Eu^{3+}) were chosen as inputs. The largest cathodic photocurrent (INHIBIT gate) is observed for the combination hydroquinone/**16**. On the other hand, the absolute value of the photocurrent is high in presence of either electron donor or acceptor but low in the absence or simultaneous presence of both inputs (XOR gate).

Fluorescein (**5**) was demonstrated by Shanzer and co-workers to function also as a half and a full subtractor.[19,22] The half subtractor is constituted by neutral **5** as the initial state, acid (HCl) and base (NaOH) as inputs, and absorbance changes at 447 nm (XOR) and 474 nm (INHIBIT) as outputs. Upon addition of HCl, the monocationic state of **5** is formed, while addition of appropriate amounts of NaOH leads to the monoanionic species. The pH-dependent changes in the absorption spectrum of the phenanthroline derivative **6** can be also interpreted in terms of a half subtractor.[24]

A full subtractor requires two half subtractors, as shown in Scheme 11 together with the corresponding truth table. The difference output of the first half subtractor HS1 is one input

I1	I2	B_{in}	B_{out}	D_{out}
0	0	0	0	0
0	1	0	1	1
1	0	0	0	1
1	1	0	0	0
0	0	1	1	1
0	1	1	1	0
1	0	1	0	0
1	1	1	1	1



Scheme 11. Truth table and simplified scheme of a full subtractor (inverted INHIBIT inputs: I1 and DIFFERENCE of HS1).

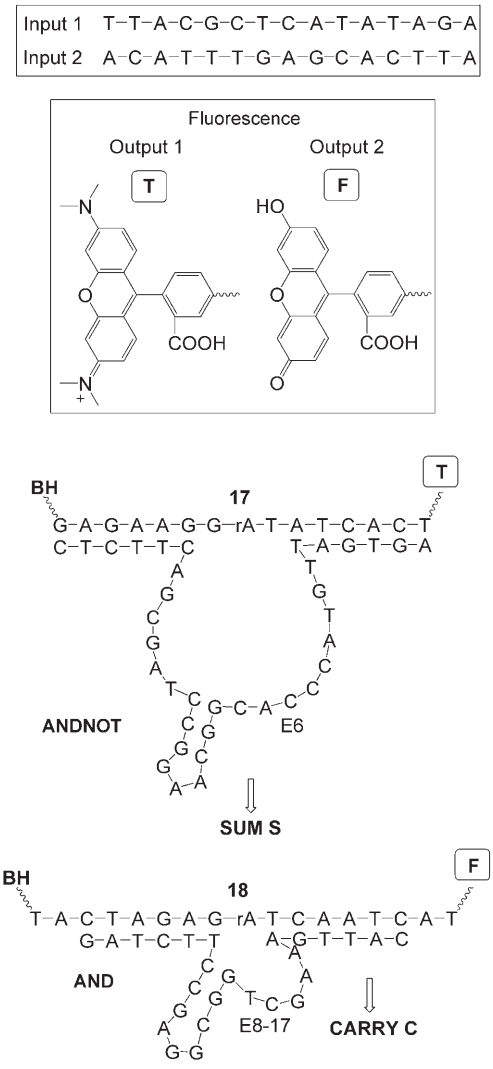
of the second (HS2). The final outputs are the BORROW OUT (B_{out}) and the DIFFERENCE OUT (D_{out}). The former is the result of the logic OR combination of the borrow outputs of the individual half subtractors. Note that in the case of a high borrow ($B_{out} = 1$) the DIFFERENCE OUT takes an addition of 2 into account, akin to a half subtractor. Very recently, the application of three inputs (two equimolar NaOH solutions and a HCl solution) to fluorescein **5** was shown to lead to the first molecular full subtractor.[22]

5. Biocompatible Molecular Arithmetic

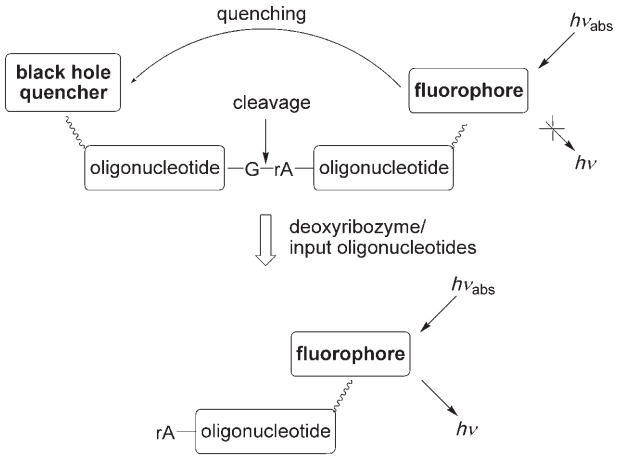
This section is dedicated to the demonstration of arithmetic functions based on bioinspired systems.[8] Logic gates (for example, NOT, OR, AND, INHIBIT, NAND, XOR) using DNA,[18,39–42] enzymes,[25,43,44] peptides, and proteins

have been described.[45] Biocompatibility provides also additional value in terms of applications of molecular logic devices as controlling elements of diagnostic and therapeutic agents. However, only few systems are known that can perform arithmetic functions like addition or subtraction.

In 2003 Stojanovic and Stefanovic exploited an array of three deoxyribozyme-based logic gates: two ANDNOT gates and an AND gate.[40] The two ANDNOT gates behave like an XOR element, which, together with the AND gate, defines a half adder. Two oligonucleotide strands serve as inputs (Scheme 12), which activate two deoxyribozymes (E6 and E8-17) by hybridization with their loop sequences (not shown in Scheme 12). This results in the cleavage of substrates **17** and **18** and is followed by the light emission of fluorophores (fluorescein and tetramethylrhodamine) attached at the 5′ ends of the substrates. In the intact substrate strands the fluorescence is reduced by black hole quenchers (BH), as shown in Scheme 13. Very recently, this approach has been extended to a full adder.[42]

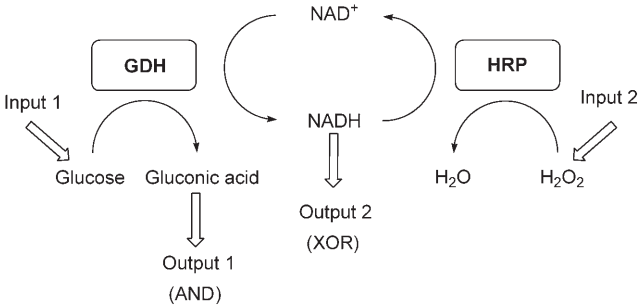


Scheme 12. Logic gates based on deoxyribozyme cleavage of substrates **17** and **18**. T: tetramethylrhodamine, F: fluorescein.



Scheme 13. Generation of fluorescence outputs upon oligonucleotide cleavage. rA = adenosine ribonucleotide.

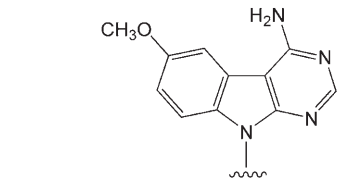
Willner and co-workers developed a biocatalytic system (Scheme 14) based on horseradish peroxidase (HRP) and glucose dehydrogenase (GDH) which can be used as a half



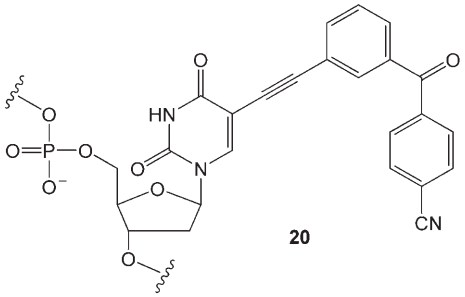
Scheme 14. NAD^+/NADH-coupled enzyme system of glucose dehydrogenase (GDH) and horseradish peroxidase (HRP).

adder or half subtractor.[25,46] Chemical inputs are substrates that are converted by these two enzymes: hydrogen peroxide and glucose, respectively. Furthermore, the two enzymes are coupled by the NAD^+/NADH cofactor system. The output information of the AND gate is monitored as changes in UV/Vis absorbance resulting from a colorimetric reaction of the formed gluconic acid. XOR logic behavior is achieved by starting with an equimolar mixture of NAD^+ and NADH, and absorbance changes due to NADH serve as the output signal. When the initial state of the system is changed to the presence of NADH alone, instead of NAD^+/NADH, the INHIBIT logic is mimicked; this logic element can be integrated into a half subtractor.[25,44] The partial gates are realized in separate compartments. For the half adder this can be overcome with a more complex system including glucose oxidase (GOx) and catalase (Cat) in addition to GDH and HRP, as demonstrated by the same authors.[25]

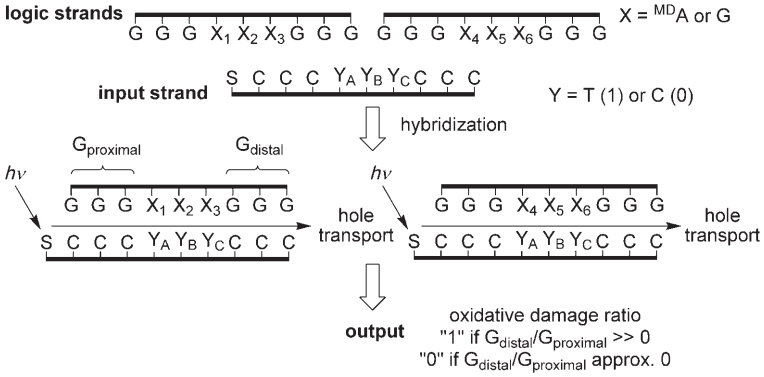
Okamoto, Saito, and Tanaka realized a full adder relying on the significantly different hole-transport properties of ^{MD}A/T, ^{MD}A/C, G/C, and G/T base pairs (^{MD}A: methoxybenzodeazaadenine, **19**), integrated in a DNA logic system.[18]



19



20



Scheme 15. Conceptual approach to logic circuits based on photosensitized oxidative damage of DNA.

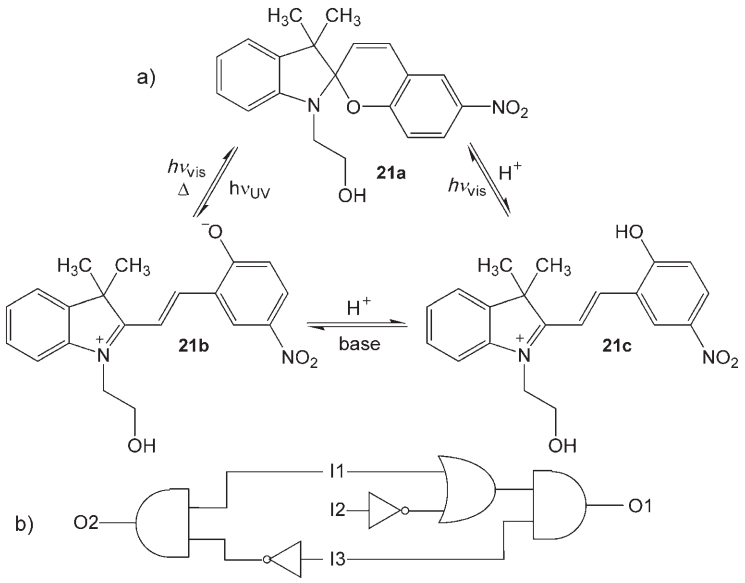
Input information is given by certain combinations of pyrimidines (T and C) in an "input strand", while the "logic strands" contain the artificial nucleobase ^{MD}A and G (Scheme 15). The output information relates to the GGG-site-selective oxidative strand cleavage (defined by the $G_{distal}/G_{proximal}$ ratio) induced by the cyanobenzophenone-derived photosensitizer **20**.

6. Molecular Logic: Quo Vadis?

The relative position of these chemical approaches to molecular logic within the context of molecular computing will be examined in the last part of this Minireview. First of all, it should be emphasized that the discussed logic functions result from the statistical distribution of chemical or physical events (fluorescence, chemical reactions, electrochemical processes) caused by the simultaneous stimulation (chemical, electrical, or optical inputs) of large molecule ensembles in solution. Therefore, they surely constitute a proof of principle but do not offer an immediate solution to the problem of miniaturization. Further, most systems are not based on input/output homogeneity, meaning that, for instance, an optical input signal should cause an optical output of sufficient signal intensity to operate a second logic gate and so on. Some of the described all-optical systems could potentially fulfill this requirement, while the often encountered combination of chemical inputs and optical output clearly does not.

How can logic gates communicate with each other? This is one of the central questions associated with the development of molecular computers. Gate-to-gate communication, where the output of one logic element is used as input for a second one, is necessary to achieve the flexible and modular design of elaborate logic circuits. At first glance this problem can be avoided, at least partially, at the level of elementary operations by the implementation of reconfigurable and superposed logic functions in unimolecular systems, as explored in some of the examples discussed above. Very inventive chemists have been able to develop systems whose logic behavior integrates up to 20 basic gates.[47] This was possible by concatenation (wiring) of logic elements which is without a doubt a major hurdle to be overcome in the development of molecular computers. Wiring by optical signaling could be an interesting approach. In comparison to electrical signals (see below), optical signals allow, in principle, a drastic reduction of computation times by parallel processing of multiple data streams. This is based on the non-interacting character of optical signals, which does not apply to electrical signals.

In this context, Raymo et al. have described several examples of optical wiring, where emitted photons of aromatic fluorophores (such as pyrene) are reabsorbed in dependence on the state of a photo- and acidochromic switch **21a–c** (Scheme 16).[48,49] These and related investigations led to interesting optical communication networks with integrated logic and the demonstration of logic-gate-linking in a

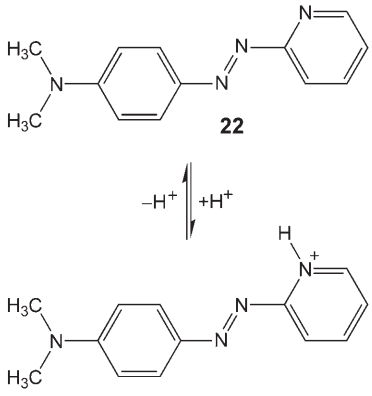


Scheme 16. a) Three-state molecular switch and b) corresponding representation of the integrated logic circuit. $I1 = h\nu_{UV}$, $I2 = h\nu_{vis}$, $I3 = H^+$.

modular approach.[47,50] However, it should be kept in mind that light is a multidirectional signal, and specific communication between two molecules by means of a random emission/reabsorption mechanism is rather inefficient.

Concatenation by fast intermolecular energy transfer between two half-adder molecules has been explored by Levine and co-workers and resulted in the full adder composed of the compounds **10** and **11**.[13] Connecting energy donor–acceptor pairs by rigid spacers can be foreseen to improve the energy-transfer efficiency. In the so-called superexchange mechanism, molecular orbitals of the spacer are actively involved;[51] this could be used for directed wiring of all-optical logic gates. In this way the disadvantage of the multidirectional nature of light, which determines energy transfer by the trivial emission/reabsorption mechanism, could be overcome.

Based on the system **21a–c**, Raymo et al. devised a strategy to achieve communication between molecular switches by photoinduced proton transfer with acidochromic azopyridines (for example, **22** in Scheme 17).[52] A drawback



Scheme 17. Protonation of the azopyridine switch **22**.

of the described examples is the rather long response time on the order of minutes to hours. Guo et al. published a related approach using a spiropyran and a fluorescent pyrene switch.[53] However, in general the use of chemical entities to code input and/or output information and to communicate between logic gates is rather limited, because transport by diffusion in liquid phase is required, and this is difficult to control and direct at the molecular level. Furthermore, in the course of resetting by chemical manipulations, waste products accumulate; this limits the number of switching cycles of the logic device. Ultimately, the generation of chemical output signals might lead to the destruction of the logic gate. Thus, the encoding of input and output information in the form of chemical signals is certainly not an ideal strategy.

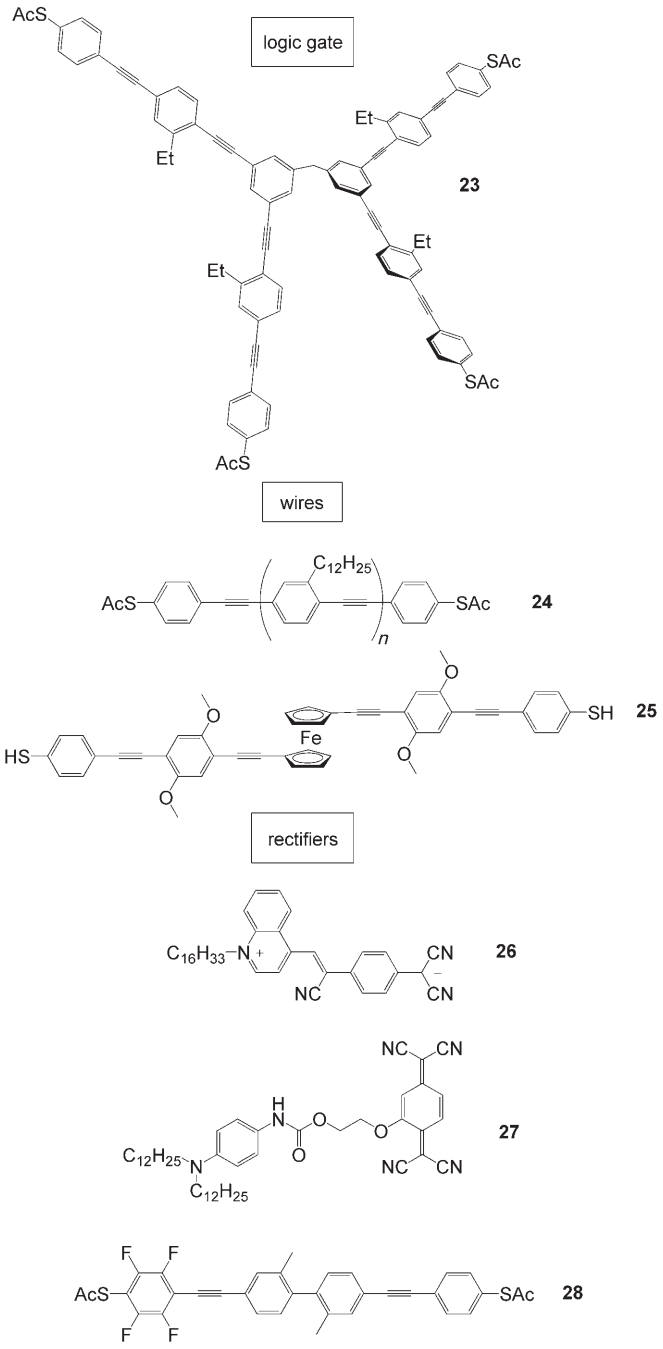
Despite their drawbacks, chemical approaches to molecular logic should not be underestimated. Several aspects, such as reconfigurability and superposed logic, show the potential of this relatively recent field.[7] Superposed logic is inherently unknown for silicon-based electronic circuits but has been demonstrated for optical molecular logic systems: Different output wavelengths (absorbance, transmittance, or fluorescence), which correspond to distinct logic gates, are monitored simultaneously.[12] Some combinations of superposed logic gates can lead to adders or subtractors, as shown, for example, for **5** (absorbance) and **15** (fluorescence). However, it should be clear that the future of molecular logic elements is strongly connected to the avoidance of large molecule ensembles in solution and the successful transfer of logic principles to solid and polymer supports,[33,41,54] electrodes,[55–58] and confined environments.[31] Naturally, this complicates the application of chemical signals, but the solid-phase approach should be less problematic for the operation of all-optical molecular logic elements[13,15,30,59] and those with electrical inputs and outputs. The latter perspective leads directly to the field of molecular electronics.

A strong point of molecular electronics is input/output homogeneity; in other words, electrical signals are used both to address and readout logic devices. Another advantage is that these systems are immobilized on electrode surfaces or trapped between metallic nanowires. This may be a viable approach to the problem of gate-to-gate communication and could provide answers to the question of how to implement interface strategies for addressing logic gates from the macroscopic level of the user (see below).

Nowadays, a broad range of functional molecules that mimic electronic building blocks like rectifiers,[60,61] wires,[62,63] and switches[55–57,64,65] are synthetically accessible and physically well-characterized (some examples are given in Scheme 18). At the molecular level, synthetic combinations of rectifiers and molecular wires provide an acceptable solution for the integration of logic gates in unimolecular circuits. This approach has been followed by Ellenbogen et al. for the design of molecular AND, XOR, and OR gates (Scheme 19) and combinatorial logic circuits, which are capable of half- and full-adder operations.[65] Specifically, they suggested embedding molecular rectifiers in a backbone of Tour-type oligo(phenylene ethynylene) wires[62] by substitution with electron-donor and -acceptor groups, in analogy to the pioneering concept of Aviram and Ratner.[66]

Towards the goal of miniaturization, two steps have to be considered: a) realization of logic functions at the level of individual or, at most, few molecules and b) assembly of individual functional molecules in devices with high circuit density (a factor of 10^6–10^7 relative to that achieved by conventional lithographic techniques can be estimated). In other words, arrays of wired molecular components that can be selectively addressed from the macroscopic level will be needed for the realization of molecular computers. If electrical signals are considered as in- and output, the design of such arrays makes electrical gate-to-gate wiring with nanoelectrodes necessary, because classical organic synthesis, creating covalent bonds, would be highly inefficient to produce molecular logic elements above a certain level of complexity and with the needed flexibility.

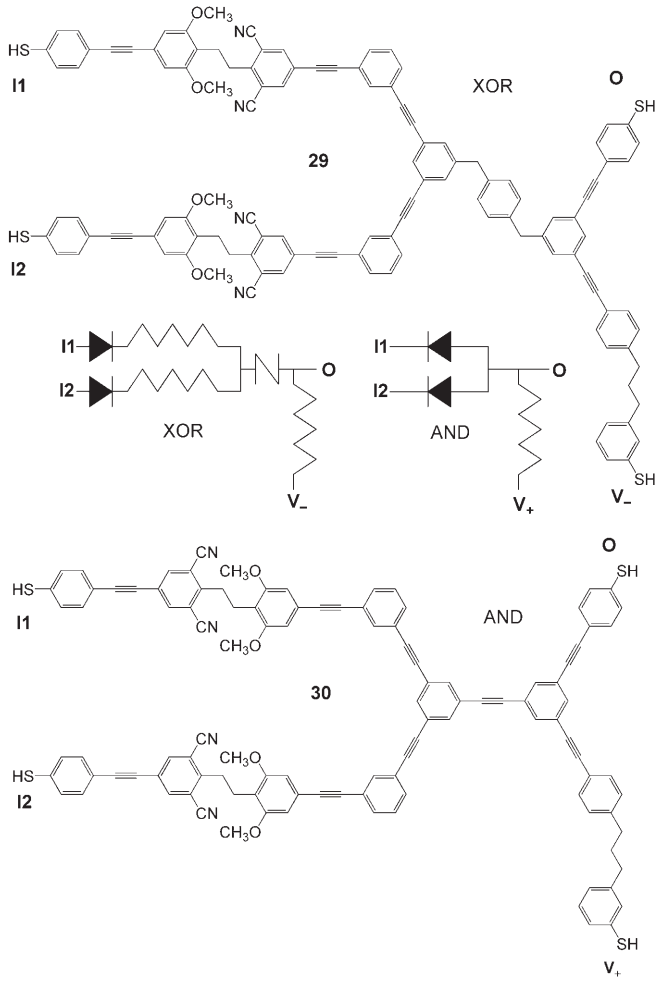
To reach the described goals, several strategies are followed in molecular electronics. One approach is the insertion of individual or very few molecules in a nanometer-sized gap between two electrodes (Scheme 20). Tremendous research efforts have been undertaken to understand and improve junctions between metal electrodes and



Scheme 18. Examples of molecular logic gates, wires, and rectifiers.

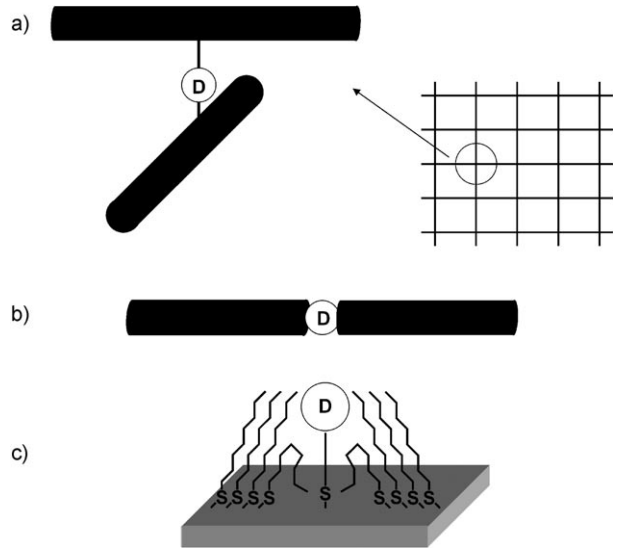
molecules. Thus, individual molecules have been addressed in experimental and theoretical investigations with the aim to demonstrate electrical conductance, diode function, and logic behavior, to name a few relevant examples.[61,63,67,68] However, potential problems, such as controlling the number, purity, and configuration of the molecules and fabricating the nanowires, need to be addressed further. The crossbar structure shown in Scheme 20a has been suggested as a possible architecture for an electrically wired array, in which each molecular device can be addressed individually.[56]

Other strategies follow the ordering of molecular devices on macroscopic electrode surfaces by Langmuir–Blodgett

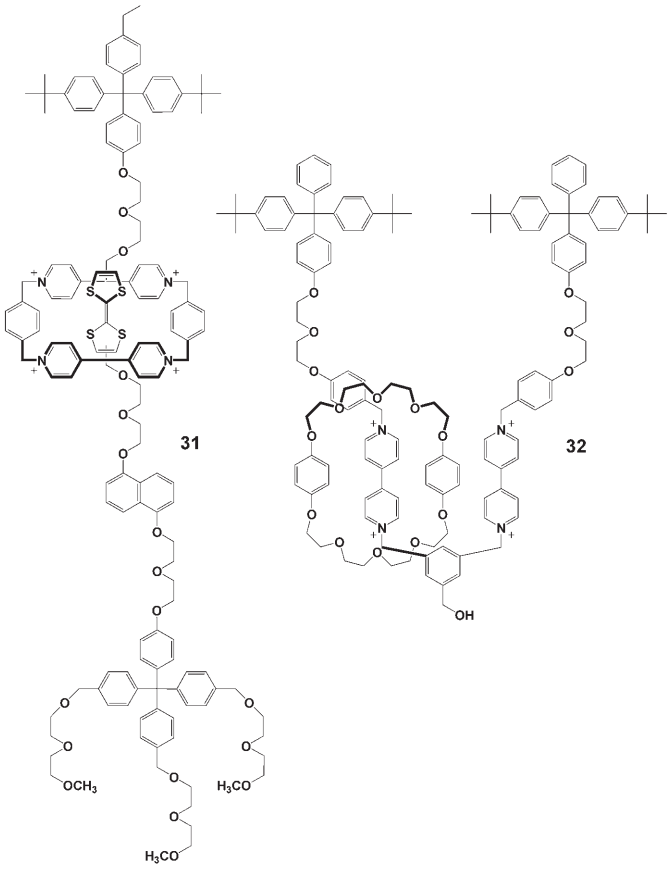


Scheme 19. Logic gates based on a combination of molecular rectifiers and wires, and their electronic equivalents. The gates can be further combined in a modular manner resulting in unimolecular half and full adders.[65]

physisorption or the formation of self-assembled monolayers (SAMs) by covalent bonding (for example, thiols on gold surfaces, Scheme 20c). On such modified surfaces, individual molecules can be visualized and addressed from the macroscopic level by means of scanning tunneling microscopy (STM) and atomic force microscopy (AFM). The interaction between the logic device and the macroscopic interface can be mediated by molecular wires, whose capability to be addressed selectively by STM has been demonstrated by Tour et al.[68] The teams led by Stoddart and Heath developed an interesting approach based on [2]rotaxanes as supramolecular structures,[55–57] which can be organized as Langmuir–Blodgett films on gold electrodes and electrically switched, implementing thereby for instance XOR (**31**)[57] and AND (**32**)[55] logic functions. It should be noted that if it is possible to integrate both gates in one device, a half adder could be realized. However, despite the promising progress in the field of molecular electronics, many potential problems like defect tolerance and heat dissipation in assemblies of high circuit density still need to be addressed in more detail. Also the issue of the occasional degradation of individual molecules



Scheme 20. Examples of architectures based on combinations of molecular devices D (for example, logic gates, switches, wires, rectifiers) and electrodes (in black or gray): a) crossbar structure, b) molecule–metal junction, c) self-assembled monolayer on a gold electrode, containing a molecular device electrically insulated by long alkyl chains.



has to be taken into account; one solution here might be making the answer of a logic element dependent on more than only one molecule.

So far, we have considered wiring by photophysical processes, chemical reactions (protonation), molecular wires, and electrodes. One potentially powerful approach in terms of diversity and "synthetic" flexibility has received less attention for the aim of molecular computing: the assembly and wiring of logic gates by using first principles of supramolecular interactions, for example, hydrogen bonding, electrostatic interactions, metal–ligand interactions, charge-transfer interactions, and π–π interactions. The currently available set of optimized photo- or electroactive molecular building blocks could give access to a large variety of tailored devices. Photoinduced electron and energy transfer in noncovalently coupled donor–acceptor supramolecules have been discussed for various examples[69] and have led to the suggestion of molecular wires based on a modular supramolecular approach. In large supramolecular arrays for computing, electrons and electronic excitation energy will have to be controlled. First examples of directional control of electron and energy transfer have shown that this is in principle possible.[70]

Interestingly, Lehn's metallosupramolecular grid-type complexes resemble, on the supramolecular level, the crossbar structure shown in Scheme 20 a.[71] Promising experiments using STM and scanning tunneling spectroscopy (STS) demonstrated the possibility of addressing individual metal-ion centers in these arrays.[72] These first results and the rich electronic and optical properties of transition-metal ions strongly suggest applications of grid-type complexes in molecular electronics.

An approach differing conceptually from molecular electronics is the unimolecular implementation of basic and combinatorial logic functions in individual or few molecules to be addressed by ultrafast pump–probe spectroscopy using lasers for stimulation. Some aspects of this strategy have been discussed above in the context of full adders and concatenation of logic gates. However, this approach bears also another interesting facet, namely its potential for miniaturization. With single-molecule spectroscopy[73] it has been shown that individual molecules can be cycled repeatedly in photophysical processes. In addition, highly sensitive readout methods, like the detection of photoionized fragments (cf. **9**), make it possible to work with few molecules. The implementation of molecular logic in this strategy relies on molecular photophysical and photochemical processes (fluorescence, photoionization, photoisomerization, photodissociation, multiphoton processes).[6,13,23,74] Basic logic gates, combinatorial logic circuits like adders, and a more elaborate finite-state logic machine with an internal memory have been developed on this basis.[75] However, these experiments have been mainly restricted to the gas phase; there is still a long road ahead to devices that address issues like wiring and interfacing in a practical sense.

A less directly related, but promising concept that should be not forgotten in this brief discussion is quantum computing.[76] In the classical computation approach a bit can exist in only one of two states: 0 or 1. However, a quantum bit (qubit) exists not only in these classical states but also in a coherent superposition of them, which can be imagined as a 0 in one universe and a 1 in another universe. Every operation on a

qubit will therefore act on both values in parallel; this is referred to as quantum parallelism. Thus, an operation on an *n*-qubit system would be performed on 2^n values at the same time, which makes a quantum computer a powerful tool for the rapid processing of large numbers. It should be noted that chemical systems capable of superposed logic constitute in this context a related case from the classical molecular world.[12] The main problem of the quantum computer is its instability, which is related to decoherence. As soon as a coherent state interacts with its environment, for example, while the computing result is being read out, it will decohere and degrade to one of the classical states, 0 or 1. As a concept, quantum computing is very powerful, but because of the extremely fragile nature of qubits it remains to be seen whether quantum computers will have a future as generally applicable desktop devices.

7. Conclusions

In this Minireview, molecular, supramolecular, and biocompatible approaches towards logic elements with addition and subtraction functions have been discussed. Several aspects, like avoiding interferences between logic gates by the unimolecular implementation of logic functions, resetting the logic device, and using optical input and output signals, have been addressed. The approaches were further analyzed with respect to their feasibility as alternative concepts to molecular computers. In particular, downscaling to few molecules, immobilization onto solid supports, gate-to-gate communication, and selective addressing of logic gates from the macroscopic user level have been identified as main problems.

It is certainly difficult to predict which strategy will constitute the key approach to molecular computers. Approaches to molecular logic using chemical and optical signals rely on a broad foundation of long-known chemical concepts paired with the understanding of supramolecular interactions. Although these interesting laboratory experiments have not yet reached a state of maturity that would put a molecular computer within reach, they provide examples of how to see "established" chemistry with different eyes.

Molecular electronic appears to be more advanced: problems like gate-to-gate communication, selective addressing of individual molecular logic elements, and interfacing strategies constitute strong driving forces in that field. The logic gates described by Stoddart and Heath relying on [2]rotaxanes as supramolecular entities self-assembled on metal electrodes are very nice examples for the fruits of these efforts. Perhaps such a combination of molecular electronics and classical chemical concepts will lead to the final success. Also the use of optical signaling, and its potential for parallel processing, should be not discarded. However, strategies to direct optical signals and excited-state energy have to be encountered and integrated within the concept of molecular logic.

When imagining computers we tend to think about electronic machines. But we should not forget that the human body performs highly efficient information processing that ultimately relies on chemical, optical, and electrical signals. A very elegant example is the vision process. In that sense, we should be open to every approach that could bring us closer to molecular computers.

U.P. thanks the Spanish Ministry for Education and Science, Madrid, for a Ramón y Cajal grant and the Instituto de Tecnología Química, Valencia, for financial support.

Received: September 28, 2006
Revised: January 19, 2007

Please note: Minor changes have been made to this manuscript since its publication in *Angewandte Chemie*, Early View. The Editor.

Published online: March 27, 2007

[1] a) V. Balzani, A. Credi, F. M. Raymo, J. F. Stoddart, *Angew. Chem.* **2000**, *112*, 3484; *Angew. Chem. Int. Ed.* **2000**, *39*, 3348; b) V. Balzani, A. Credi, M. Venturi, *Chem. Eur. J.* **2002**, *8*, 5524.
[2] P. Ball, *Nature* **2000**, *406*, 118.
[3] A. Aviram, *J. Am. Chem. Soc.* **1988**, *110*, 5687.
[4] A. P. de Silva, H. Q. N. Gunaratne, C. P. McCoy, *Nature* **1993**, *364*, 42.
[5] a) A. P. de Silva, N. D. McClenaghan, C. P. McCoy in *Molecular Switches* (Ed.: B. L. Feringa), Wiley-VCH, Weinheim, **2001**, p. 339; b) A. R. Pease, J. F. Stoddart, *Struct. Bonding (Berlin)* **2001**, *99*, 189; c) F. M. Raymo, *Adv. Mater.* **2002**, *14*, 401; d) V. Balzani, A. Credi, M. Venturi, *Molecular Devices and Machines*, Wiley-VCH, Weinheim, **2003**; e) V. Balzani, A. Credi, M. Venturi, *ChemPhysChem* **2003**, *4*, 49; f) A. P. de Silva, Y. Leydet, C. Lincheneau, N. D. McClenaghan, *J. Phys. Condens. Matter* **2006**, *18*, S1847.
[6] D. Steinitz, F. Remacle, R. D. Levine, *ChemPhysChem* **2002**, *3*, 43.
[7] A. P. de Silva, N. D. McClenaghan, *Chem. Eur. J.* **2004**, *10*, 574.
[8] I. K. Cheah, S. J. Langford, M. J. Latter, *Supramol. Chem.* **2005**, *17*, 121.
[9] a) G. J. Brown, A. P. de Silva, S. Pagliari, *Chem. Commun.* **2002**, 2461; b) A. P. de Silva, *Nat. Mater.* **2005**, *4*, 15.
[10] A. Credi, V. Balzani, S. J. Langford, J. F. Stoddart, *J. Am. Chem. Soc.* **1997**, *119*, 2679.
[11] A. P. de Silva, N. D. McClenaghan, *J. Am. Chem. Soc.* **2000**, *122*, 3965.
[12] A. P. de Silva, N. D. McClenaghan, *Chem. Eur. J.* **2002**, *8*, 4935.
[13] F. Remacle, S. Speiser, R. D. Levine, *J. Phys. Chem. B* **2001**, *105*, 5589.
[14] S. J. Langford, T. Yann, *J. Am. Chem. Soc.* **2003**, *125*, 11198.
[15] J. Andréasson, G. Kodis, Y. Terazono, P. A. Liddell, S. Bandyopadhyay, R. H. Mitchell, T. A. Moore, A. L. Moore, D. Gust, *J. Am. Chem. Soc.* **2004**, *126*, 15926.
[16] X. Guo, D. Zhang, G. Zhang, D. Zhu, *J. Phys. Chem. B* **2004**, *108*, 11942.
[17] D. Margulies, G. Melman, C. E. Felder, R. Arad-Yellin, A. Shanzer, *J. Am. Chem. Soc.* **2004**, *126*, 15400.
[18] A. Okamoto, K. Tanaka, I. Saito, *J. Am. Chem. Soc.* **2004**, *126*, 9458.
[19] D. Margulies, G. Melman, A. Shanzer, *Nat. Mater.* **2005**, *4*, 768.
[20] F. Li, M. Shi, C. Huang, L. Jin, *J. Mater. Chem.* **2005**, *15*, 3015.
[21] D.-H. Qu, Q.-C. Wang, H. Tian, *Angew. Chem.* **2005**, *117*, 5430; *Angew. Chem. Int. Ed.* **2005**, *44*, 5296.
[22] D. Margulies, G. Melman, A. Shanzer, *J. Am. Chem. Soc.* **2006**, *128*, 4865.
[23] F. Remacle, R. Weinkauf, R. D. Levine, *J. Phys. Chem. A* **2006**, *110*, 177.

[24] Y. Liu, W. Jiang, H.-Y. Zhang, C.-J. Li, *J. Phys. Chem. B* **2006**, *110*, 14231.
[25] R. Baron, O. Lioubashevski, E. Katz, T. Niazov, I. Willner, *Angew. Chem.* **2006**, *118*, 1602; *Angew. Chem. Int. Ed.* **2006**, *45*, 1572.
[26] Y. Zhou, H. Wu, L. Qu, D. Zhang, D. Zhu, *J. Phys. Chem. B* **2006**, *110*, 15676.
[27] a) F. Pina, M. J. Melo, M. Maestri, P. Passaniti, V. Balzani, *J. Am. Chem. Soc.* **2000**, *122*, 4496; b) G. Bergamini, C. Saudan, P. Ceroni, M. Maestri, V. Balzani, M. Gorka, S.-K. Lee, J. van Heyst, F. Vögtle, *J. Am. Chem. Soc.* **2004**, *126*, 16466; c) K. Szaciłowski, W. Macyk, G. Stochel, *J. Am. Chem. Soc.* **2006**, *128*, 4550.
[28] L. F. O. Furtado, A. D. P. Alexiou, L. Gonçalves, H. E. Toma, K. Araki, *Angew. Chem.* **2006**, *118*, 3215; *Angew. Chem. Int. Ed.* **2006**, *45*, 3143.
[29] a) A. P. de Silva, H. Q. N. Gunaratne, C. P. McCoy, *J. Am. Chem. Soc.* **1997**, *119*, 7891; b) A. P. de Silva, G. D. McClean, S. Pagliari, *Chem. Commun.* **2003**, 2010; c) J. F. Callan, A. P. de Silva, N. D. McClenaghan, *Chem. Commun.* **2004**, 2048; d) S. Uchiyama, N. Kawai, A. P. de Silva, K. Iwai, *J. Am. Chem. Soc.* **2004**, *126*, 3032; e) J. Andréasson, Y. Terazono, B. Albinsson, T. A. Moore, A. L. Moore, D. Gust, *Angew. Chem.* **2005**, *117*, 7763; *Angew. Chem. Int. Ed.* **2005**, *44*, 7591; f) B. Bag, P. K. Bharadwaj, *Chem. Commun.* **2005**, 513; g) S. J. M. Koskela, T. M. Fyles, T. D. James, *Chem. Commun.* **2005**, 945; h) D. C. Magri, G. J. Brown, G. D. McClean, A. P. de Silva, *J. Am. Chem. Soc.* **2006**, *128*, 4950; i) G. Zhang, D. Zhang, Y. Zhou, D. Zhu, *J. Org. Chem.* **2006**, *71*, 3970.
[30] M. Andersson, L. E. Sinks, R. T. Hayes, Y. Zhao, M. R. Wasielewski, *Angew. Chem.* **2003**, *115*, 3247; *Angew. Chem. Int. Ed.* **2003**, *42*, 3139.
[31] S. Uchiyama, G. D. McClean, K. Iwai, A. P. de Silva, *J. Am. Chem. Soc.* **2005**, *127*, 8920.
[32] a) A. P. de Silva, I. M. Dixon, H. Q. N. Gunaratne, T. Gunnlaugsson, P. R. S. Maxwell, T. E. Rice, *J. Am. Chem. Soc.* **1999**, *121*, 1393; b) T. Gunnlaugsson, D. A. Mac Dónail, D. Parker, *Chem. Commun.* **2000**, 93; c) T. Gunnlaugsson, D. A. Mac Dónaill, D. Parker, *J. Am. Chem. Soc.* **2001**, *123*, 12866; d) K. Rurack, A. Koval'chuck, J. L. Bricks, J. L. Slominskii, *J. Am. Chem. Soc.* **2001**, *123*, 6205; e) M. de Sousa, M. Kluciar, S. Abad, M. A. Miranda, B. de Castro, U. Pischel, *Photochem. Photobiol. Sci.* **2004**, *3*, 639; f) S. H. Lee, J. Y. Kim, S. K. Kim, J. H. Lee, J. S. Kim, *Tetrahedron* **2004**, *60*, 5171; g) X. Guo, D. Zhang, H. Tao, D. Zhu, *Org. Lett.* **2004**, *6*, 2491; h) J.-M. Montenegro, E. Perez-Inestrosa, D. Collado, Y. Vida, R. Suau, *Org. Lett.* **2004**, *6*, 2353; i) S. Banthia, A. Samanta, *Eur. J. Org. Chem.* **2005**, 4967; j) D. Jiménez, R. Martínez-Máñez, F. Sancenón, J. V. Ros-Lis, J. Soto, A. Benito, E. García-Breijo, *Eur. J. Inorg. Chem.* **2005**, 2393; k) A. Petitjean, N. Kyritsakas, J.-M. Lehn, *Chem. Eur. J.* **2005**, *11*, 6818; l) M. de Sousa, B. de Castro, S. Abad, M. A. Miranda, U. Pischel, *Chem. Commun.* **2006**, 2051.
[33] D. A. Leigh, M. A. F. Morales, E. M. Pérez, J. K. Y. Wong, C. G. Saiz, A. M. Z. Slawin, A. J. Carmichael, D. M. Haddleton, A. M. Brouwer, W. J. Buma, G. W. H. Wurpel, S. León, F. Zerbetto, *Angew. Chem.* **2005**, *117*, 3122; *Angew. Chem. Int. Ed.* **2005**, *44*, 3062.
[34] S. D. Straight, J. Andréasson, G. Kodis, S. Bandyopadhyay, R. H. Mitchell, T. A. Moore, A. L. Moore, D. Gust, *J. Am. Chem. Soc.* **2005**, *127*, 9403.
[35] A. Coskun, E. Deniz, E. U. Akkaya, *Org. Lett.* **2005**, *7*, 5187.
[36] P. A. Liddell, G. Kodis, J. Andréasson, L. de la Garza, S. Bandyopadhyay, R. H. Mitchell, T. A. Moore, A. L. Moore, D. Gust, *J. Am. Chem. Soc.* **2004**, *126*, 4803.
[37] S. Speiser, *J. Lumin.* **2003**, *102–103*, 267.
[38] S. J. Langford, T. Yann, *J. Am. Chem. Soc.* **2003**, *125*, 14951.
[39] a) M. N. Stojanovic, T. E. Mitchell, D. Stefanovic, *J. Am. Chem. Soc.* **2002**, *124*, 3555; b) A. Saghatelian, N. H. Völcker, K. M. Guckian, V. S.-Y. Lin, M. R. Ghadiri, *J. Am. Chem. Soc.* **2003**, *125*, 346; c) H. Yan, L. Feng, T. H. LaBean, J. H. Reif, *J. Am. Chem. Soc.* **2003**, *125*, 14246; d) M. N. Stojanovic, S. Semova, D. Kolpashchikov, J. Macdonald, C. Morgan, D. Stefanovic, *J. Am. Chem. Soc.* **2005**, *127*, 6914; e) D. M. Kolpashchikov, M. N. Stojanovic, *J. Am. Chem. Soc.* **2005**, *127*, 11348; f) X. Chen, Y. Wang, Q. Liu, Z. Zhang, C. Fan, L. He, *Angew. Chem.* **2006**, *118*, 1791; *Angew. Chem. Int. Ed.* **2006**, *45*, 1759; g) J. Liu, Y. Lu, *Adv. Mater.* **2006**, *18*, 1667; h) G. Seelig, D. Soloveichik, D. Y. Zhang, E. Winfree, *Science* **2006**, *314*, 1585.
[40] M. N. Stojanovic, D. Stefanovic, *J. Am. Chem. Soc.* **2003**, *125*, 6673.
[41] Y. Weizmann, R. Elnathan, O. Lioubashevski, I. Willner, *J. Am. Chem. Soc.* **2005**, *127*, 12666.
[42] H. Lederman, J. Macdonald, D. Stefanovic, M. N. Stojanovic, *Biochemistry* **2006**, *45*, 1194.
[43] R. J. Amir, M. Popkov, R. A. Lerner, C. F. Barbas III, D. Shabat, *Angew. Chem.* **2005**, *117*, 4452; *Angew. Chem. Int. Ed.* **2005**, *44*, 4378.
[44] R. Baron, O. Lioubashevski, E. Katz, T. Niazov, I. Willner, *Org. Biomol. Chem.* **2006**, *4*, 989.
[45] a) G. Ashkenasy, M. R. Ghadiri, *J. Am. Chem. Soc.* **2004**, *126*, 11140; b) S. Muramatsu, K. Kinbara, H. Taguchi, N. Ishii, T. Aida, *J. Am. Chem. Soc.* **2006**, *128*, 3764.
[46] R. Baron, O. Lioubashevski, E. Katz, T. Niazov, I. Willner, *J. Phys. Chem. A* **2006**, *110*, 8548.
[47] K. Szaciłowski, *Chem. Eur. J.* **2004**, *10*, 2520.
[48] a) F. M. Raymo, S. Giordani, *J. Am. Chem. Soc.* **2001**, *123*, 4651; b) F. M. Raymo, S. Giordani, A. J. P. White, D. J. Williams, *J. Org. Chem.* **2003**, *68*, 4158.
[49] a) F. M. Raymo, S. Giordani, *Org. Lett.* **2001**, *3*, 1833; b) F. M. Raymo, S. Giordani, *J. Am. Chem. Soc.* **2002**, *124*, 2004.
[50] F. M. Raymo, S. Giordani, *Proc. Natl. Acad. Sci. USA* **2002**, *99*, 4941.
[51] S. Speiser, *Chem. Rev.* **1996**, *96*, 1953.
[52] a) F. M. Raymo, S. Giordani, *Org. Lett.* **2001**, *3*, 3475; b) F. M. Raymo, R. J. Alvarado, S. Giordani, M. A. Cejas, *J. Am. Chem. Soc.* **2003**, *125*, 2361.
[53] X. Guo, D. Zhang, Y. Zhou, D. Zhu, *Chem. Phys. Lett.* **2003**, *375*, 484.
[54] a) J. Matsui, M. Mitsuishi, A. Aoki, T. Miyashita, *Angew. Chem.* **2003**, *115*, 2374; *Angew. Chem. Int. Ed.* **2003**, *42*, 2272; b) S. Giordani, F. M. Raymo, *Org. Lett.* **2003**, *5*, 3559; c) A. P. de Silva, M. R. James, B. O. F. McKinney, D. A. Pears, S. M. Weir, *Nat. Mater.* **2006**, *5*, 787.
[55] C. P. Collier, E. W. Wong, M. Belohradský, F. M. Raymo, J. F. Stoddart, P. J. Kuekes, R. S. Williams, J. R. Heath, *Science* **1999**, *285*, 391.
[56] A. R. Pease, J. O. Jeppesen, J. F. Stoddart, Y. Luo, C. P. Collier, J. R. Heath, *Acc. Chem. Res.* **2001**, *34*, 433.
[57] Y. Luo, C. P. Collier, J. O. Jeppesen, K. A. Nielsen, E. Delonno, G. Ho, J. Perkins, H.-R. Tseng, T. Yamamoto, J. F. Stoddart, J. R. Heath, *ChemPhysChem* **2002**, *3*, 519.
[58] R. Gill, F. Patolsky, E. Katz, I. Willner, *Angew. Chem.* **2005**, *117*, 4630; *Angew. Chem. Int. Ed.* **2005**, *44*, 4554.
[59] A. S. Lukas, P. J. Bushard, M. R. Wasielewski, *J. Am. Chem. Soc.* **2001**, *123*, 2440.
[60] a) C. Zhou, M. R. Deshpande, M. A. Reed, L. Jones II, J. M. Tour, *Appl. Phys. Lett.* **1997**, *71*, 611; b) R. M. Metzger, B. Chen, U. Höpfner, M. V. Lakshmikantham, D. Vuillaume, T. Kawai, X. Wu, H. Tachibana, T. V. Hughes, H. Sakurai, J. W. Baldwin, C. Hosch, M. P. Cava, L. Brehmer, G. J. Ashwell, *J. Am. Chem. Soc.* **1997**, *119*, 10455; c) R. M. Metzger, *Acc. Chem. Res.* **1999**, *32*, 950.
[61] M. Elbing, R. Ochs, M. Koentopp, M. Fischer, C. von Hänisch, F. Weigend, F. Evers, H. B. Weber, M. Mayor, *Proc. Natl. Acad. Sci. USA* **2005**, *102*, 8815.

[62] J. M. Tour, *Acc. Chem. Res.* **2000**, *33*, 791.
[63] S. A. Getty, C. Engtrakul, L. Wang, R. Liu, S.-H. Ke, H. U. Baranger, W. Yang, M. S. Fuhrer, L. R. Sita, *Phys. Rev. B* **2005**, *71*, 241401.
[64] J. M. Tour, M. Kozaki, J. M. Seminario, *J. Am. Chem. Soc.* **1998**, *120*, 8486.
[65] J. C. Ellenbogen, J. C. Love, *Proc. IEEE* **2000**, *88*, 386.
[66] A. Aviram, M. A. Ratner, *Chem. Phys. Lett.* **1974**, *29*, 277.
[67] a) L. A. Bumm, J. J. Arnold, M. T. Cygan, T. D. Dunbar, T. P. Burgin, L. Jones II, D. L. Allara, J. M. Tour, P. S. Weiss, *Science* **1996**, *271*, 1705; b) S. Ami, M. Hliwa, C. Joachim, *Chem. Phys. Lett.* **2003**, *367*, 662.
[68] M. T. Cygan, T. D. Dunbar, J. J. Arnold, L. A. Bumm, N. F. Shedlock, T. P. Burgin, L. Jones II, D. L. Allara, J. M. Tour, P. S. Weiss, *J. Am. Chem. Soc.* **1998**, *120*, 2721.
[69] a) M. D. Ward, *Chem. Soc. Rev.* **1997**, *26*, 365; b) J. M. Haider, Z. Pikramenou, *Chem. Soc. Rev.* **2005**, *34*, 120.
[70] a) S. Serroni, S. Campagna, R. Pistone Nascone, G. S. Hanan, G. J. E. Davidson, J.-M. Lehn, *Chem. Eur. J.* **1999**, *5*, 3523; b) N. Armaroli, J.-F. Eckert, J.-F. Nierengarten, *Chem. Commun.* **2000**, 2105; c) S. Abad, M. Kluciar, M. A. Miranda, U. Pischel, *J. Org. Chem.* **2005**, *70*, 10565; d) A. C. Benniston, *Chem. Soc. Rev.* **2004**, *33*, 573.
[71] M. Ruben, J. Rojo, F. J. Romero-Salguero, L. H. Uppadine, J.-M. Lehn, *Angew. Chem.* **2004**, *116*, 3728; *Angew. Chem. Int. Ed.* **2004**, *43*, 3644.
[72] M. S. Alam, S. Strömsdörfer, V. Dremov, P. Müller, J. Kortus, M. Ruben, J.-M. Lehn, *Angew. Chem.* **2005**, *117*, 8109; *Angew. Chem. Int. Ed.* **2005**, *44*, 7896.
[73] W. E. Moerner, M. Orrit, *Science* **1999**, *283*, 1670.
[74] K. L. Kompa, R. D. Levine, *Proc. Natl. Acad. Sci. USA* **2001**, *98*, 410.
[75] F. Remacle, R. D. Levine, *J. Chem. Phys.* **2001**, *114*, 10239.
[76] P. Ball, *Nature* **2006**, *440*, 398.