# Molecular devices and machines

The bottom-up design, construction, and operation of devices and machines on the molecular scale is a topic of great interest in nanoscience and a fascinating challenge for nanotechnology. Species made of interlocked molecular components are most attractive candidates for these purposes. In recent times, the evolution of the structural and functional design of such systems has led to the construction and operation of complex molecular devices and machines that, in some cases, are able to perform specific tasks.

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The progress of human civilization has always been related to the construction of novel devices and machines. Depending on their use, devices and machines can be very big or very small. The general trend in our 'knowledge age' is that of reducing the size and weight of the components employed as much as possible, particularly in the field of information technology.

The miniaturization of components for the construction of devices and machines is currently pursued by a 'top-down' approach. This approach, which is in the hands of physicists and engineers, consists of manipulating progressively smaller pieces of matter by photolithography and related techniques. Although semiconductor devices of 65 nm are already on the market<sup>1,2</sup> and devices of 45 nm have been reported<sup>3</sup>, it is becoming clear that the top-down approach is subject to drastic limitations, including a severe cost escalation when the components approach the nanometer dimension<sup>2,4,5</sup>. But "there is plenty of room at the bottom" for further miniaturization, as Richard P. Feynman stated<sup>6</sup> in his famous address to the American Physical

Society on December 29, 1959. To proceed toward miniaturization at the nanometer scale, science and technology need to find new avenues.

A promising strategy to exploit science and technology at the nanometer scale is the 'bottom-up' approach, which starts from nanoor subnano-scale objects (namely atoms or molecules) to build up nanostructures.

#### Bottom-up atom-by-atom

The idea that atoms could be used to construct nanoscale machines was first raised by Feynman ("The principles of physics do not speak against the possibility of maneuvering things atom by atom")<sup>6</sup> and depicted in a visionary way in the mid-1980s by K. Eric Drexler<sup>7</sup>. He claimed that it would be possible to build a general purpose 'nanorobot', nicknamed an assembler. Such a device could, in principle, build almost anything atom-by-atom, including copies of itself.

The fascinating but, admittedly, abstract ideas of Drexler<sup>8</sup> are viewed with skepticism by a large part of the scientific community<sup>9-12</sup>.

In particular, the concept of a universal assembler, i.e. a nanorobot that can manipulate and build things atom-by-atom, is considered unrealistic for at least three well-grounded reasons<sup>10,11</sup>: (i) the fingers of a hypothetical manipulator arm should themselves be made out of atoms, which implies that they would be too fat to have control of the chemistry in the nanometer region; (ii) such fingers would also be too sticky – the atoms of the manipulator hands would adhere to the atom that is being moved, so that it would be impossible to place it in the desired position; (iii) the continual shaking to which every nanoscale structure is subject because of collisions with the surrounding molecules would prevent precise nanoengineering. Therefore, the idea of an atom-by-atom bottom-up approach to nanotechnology, which seems so appealing to physicists, does not convince chemists who are well aware of the high reactivity of most atomic species, the subtle aspects of the chemical bond, and the properties of molecules. It should be recognized, however, that Drexler's visionary ideas have had at least the merit to draw the attention of nonscientists and influence many scientists to direct their research projects toward the fascinating world of nanotechnology.

### Bottom-up molecule-by-molecule

In the late 1970s, in the frame of research on supramolecular chemistry<sup>13-15</sup>, studies on molecular electronic devices began to flourish<sup>16-18</sup> and the idea arose in a few laboratories<sup>15,19-21</sup> that molecules could be much more convenient building blocks than atoms to construct nanoscale devices and machines. This idea is based on the

following points: (i) molecules are stable species, whereas atoms are difficult to handle; (ii) nature uses molecules not atoms to construct the great number and variety of nanodevices and nanomachines that sustain life<sup>22,23</sup>; (iii) most laboratory chemical processes deal with molecules, not atoms; (iv) molecules are objects that already exhibit distinct shapes and carry device-related properties (e.g. properties that can be manipulated by photochemical and electrochemical inputs); and (v) molecules can self-assemble or can be connected to make larger structures.

In the following years, supramolecular chemistry grew very rapidly<sup>24</sup> and it became clear that the supramolecular bottom-up approach opens virtually unlimited possibilities (Fig. 1)<sup>25,26</sup> concerning the design and construction of artificial molecular devices and machines<sup>27</sup>. Furthermore, it became more and more evident that such an approach could make invaluable contributions to our understanding of the molecular aspects of the extremely complicated devices and machines that are responsible for biological processes<sup>22,23,28</sup>. These systems constitute, in fact, a straightforward demonstration of the feasibility and utility of nanotechnology.

### **Devices and machines**

In the macroscopic world, devices and machines are assemblies of components designed to achieve a specific function. Each component of the assembly performs a simple act, while the entire assembly performs a more complex, useful function, characteristic of that particular device or machine. For example, the function performed by a hairdryer is the result of operations performed by a switch, a heater,



Fig. 1 Two examples of complex and beautiful artificial multicomponent molecules. (a) A coordination cage obtained<sup>25</sup> by self-assembly of four triazine-based bridging ligands and six Pd(diamine) complexes. (b) Molecular borromean rings, synthesized<sup>26</sup> by using, in concert, coordination, supramolecular, and dynamic covalent chemistry. (Crystal structure courtesy of J. Fraser Stoddart, University of California, Los Angeles.)

and a fan, suitably connected by wires and assembled in an appropriate framework. The macroscopic concepts of a device and a machine can be extended to the molecular level<sup>27,29</sup>. A molecular device can be defined as an assembly of a discrete number of molecular components designed to achieve a specific function. Each molecular component performs a single act, while the entire supramolecular assembly performs a more complex function, which results from the cooperation of the various components. A molecular machine is a particular type of molecular device in which the component parts can display changes in their relative positions as a result of some external stimulus<sup>30</sup>. Molecular-level devices and machines operate via electronic and/or nuclear rearrangements and, like macroscopic devices and machines, need energy to operate and signals to communicate with the operator. The extension of the concepts of a device and a machine to the molecular level is of interest not only for basic research, but also for the growth of nanoscience and the development of nanotechnology.

It should be pointed out that nanoscale devices and machines cannot be considered merely as 'shrunk' versions of macroscopic counterparts because physics is different at the nanoscale<sup>31</sup>. Several phenomena at the nanoscale are governed by the laws of quantum mechanics and, most important, some intrinsic properties of molecularlevel entities are quite different from those of macroscopic objects. For example: (i) molecules are in a state of constant random motion and are subjected to continual collisions (Brownian motion); (ii) in the nanoworld, things are somewhat floppy and stick strongly to each other because of electromagnetic interactions; and (iii) the dimensions of molecules are much smaller than the wavelengths of the light used to supply energy or to obtain information.

The (physical) top-down approach has allowed the construction of a variety of solid-state microelectronic devices<sup>2,5</sup> and microelectromechanical systems<sup>32,33</sup>. It is now expected that the (chemical) bottom-up approach will move science and technology not only from the micro- to nanoscale, but also from electronics to photonics and chemionics since light and chemical inputs are convenient ways to power molecular devices and to exchange information at the molecular level<sup>34</sup>. Furthermore, the bottom-up approach, taking inspiration from natural nanoscale devices<sup>35</sup>, could displace the interest of scientists from the solid state to solution and soft matter<sup>31</sup>.

### Energy supply, signal exchange, and other features

Molecular devices and machines are chemical systems and therefore operate by means of chemical reactions that, broadly speaking, imply both electronic and nuclear rearrangements. In some cases, however, the function performed is essentially based on the transfer of electrons or electronic energy without substantial nuclear rearrangements. In other cases, the operation is based on the occurrence of more or less extensive nuclear displacements caused by electronic rearrangements. As in the macroscopic world, molecular-level devices and machines need energy to operate and signals to communicate with the operator. The energy needed for the operation of a molecular device or machine can be supplied in the form of (i) a chemical reagent, (ii) an absorbed photon, or (iii) addition or subtraction of an electron. In view of the shortage of chemical fuels and increasing environmental problems, the ideal primary energy source is sunlight and the worthiest processes are those that do not form waste products. Indeed, even in a knowledge-based society the consumption of nonrenewable energy resources and accumulation of waste will continue to pose very difficult problems<sup>36</sup>.

In order to control and monitor the operation of a molecular device or machine, a suitable signal is needed. Since at least one molecular component of the system changes its state on performing the required function, any signal related to such component changes can be used. In this regard, a variety of chemical and physical techniques can be valuable. Most frequently, control of the state of the system is performed by a spectroscopic method (nuclear magnetic resonance or NMR, ultraviolet-visible absorption, luminescence, etc.). For some systems, e.g. those based on donor-acceptor interactions, electrochemistry<sup>37</sup> can be profitably employed.

Since a device and a machine have to work by repeating cycles, an important requirement is reset. This means that any chemical reaction involved in the operation has to be reversible. Although no chemical reaction is fully reversible, this requirement is met reasonably well by energy transfer, electron-transfer (redox), and proton-transfer (acidbase) processes, and by some types of photoisomerization and metalligand coordination reactions.

The operation time scale of a molecular device and machine can range from less than picoseconds to days, depending on the nature of the processes involved. Energy-, electron-, and proton-transfer processes, and isomerization reactions can be very fast, but large and complex movements of component parts may be much slower. Information on rate constants can be obtained by conventional kinetic methods in the case of slow processes, by electrochemistry and stopped flow techniques for relatively fast processes, and by flash spectroscopy (on different time scales) for very fast processes.

The functions that could be performed by molecular devices and machines are various. They may be related to signal transfer (in the form of energy, electrons, protons, etc.)<sup>34,38</sup>, information processing (e.g. by molecular-level logic gates)<sup>39</sup>, energy conversion (e.g. conversion of light into an electrochemical potential<sup>40,41</sup> or a chemical fuel<sup>42</sup>), and a wide range of mechanical-like aspects (e.g. transportation of a cargo through a membrane).

In an attempt to develop a set of molecular-level components for information processing, chemical species capable of mimicking the role of wires<sup>43</sup>, switches<sup>44</sup>, memories<sup>45</sup>, sensors<sup>46</sup>, antennas<sup>47,48</sup>, plug-socket<sup>49,50</sup> and extension cable<sup>51</sup> systems, and logic gates<sup>39,52,53</sup> at the nanoscale have been reported. In particular, the study of molecular species capable of performing binary logic operations<sup>39,52-55</sup> could lead to practical applications such as tagging<sup>56</sup> of very small objects

and, in the long term, to the design and construction of a molecular computer<sup>57,58</sup>. It is worth noting that all fundamental logic operations have been implemented with molecular systems<sup>39</sup>, leading to the recent laboratory demonstration of binary arithmetics<sup>59</sup> with molecular full-adder<sup>60</sup> and full-subtractor<sup>60,61</sup> devices. These systems, which employ light, molecules, and ions as input/output signals<sup>34</sup>, operate in solution and take inspiration from information processing in living organisms.

Regardless of the possibility of short-term applications, the development of a set of molecular-level devices and machines appears to be a worthwhile investment. Many reviews on this topic are available<sup>30,62-72</sup> and an exhaustive monograph<sup>38</sup> has been published. In this review, some recent achievements in the field will be illustrated, using recent examples of molecular machines taken from our own work in collaboration with the group of J. Fraser Stoddart at the University of California, Los Angeles.

### Mechanically interlocked molecules as nanoscale machines

In principle, molecular machines can be designed starting from several kinds of molecular and supramolecular systems<sup>38,62–71</sup>, including DNA<sup>73-75</sup> (see the review by Tim Liedl *et al.* on page 36 of this issue). However, for the reasons mentioned below, most of the artificial systems constructed so far are based on interlocked molecular species such as rotaxanes, catenanes, and related species. The names of these compounds derive from the Latin words *rota* and *axis* for wheel and axle, and *catena* for chain. Rotaxanes<sup>76</sup> are composed of a dumbbell-shaped molecule surrounded by a macrocyclic compound (the 'ring') and terminated by bulky groups ('stoppers') that prevent disassembly (Fig. 2a, 2b). Catenanes<sup>76</sup> are made of (at least) two interlocked macrocycles (Fig. 2c). Important features of these systems derive from noncovalent interactions between components that contain complementary recognition sites. Such interactions, that are also responsible for the efficient template-directed syntheses<sup>77,78</sup> of

Fig. 2 Schematic representation of the intercomponent motions that can be obtained with simple interlocked molecular architectures: ring shuttling in rotaxanes (a), and ring rotation in rotaxanes (b) and catenanes (c). (Reproduced with permission from<sup>70</sup>. © 2006 The Royal Society of Chemistry.)

rotaxanes and catenanes, include charge-transfer (CT) ability, hydrogen bonding, hydrophobic-hydrophilic character,  $\pi$ - $\pi$  stacking, electrostatic forces and, on the side of the strong interaction limit, metal-ligand bonding.

Rotaxanes and catenanes are appealing systems for the construction of molecular machines because (i) the mechanical bond allows a large variety of mutual arrangements of the molecular components, while conferring stability to the system; (ii) the interlocked architecture limits the amplitude of the intercomponent motion in the three directions; (iii) the stability of a specific arrangement (co-conformation) is determined by the strength of the intercomponent interactions; and (iv) such interactions can be modulated by external stimulation. The large-amplitude motions that can be achieved with rotaxanes and catenanes are represented schematically in Fig. 2. Particularly, two interesting molecular motions can be envisaged in rotaxanes, namely (i) translation, i.e. shuttling, of the ring along the axle, and (ii) rotation of the ring around the axle. Hence, rotaxanes are good prototypes for the construction of both linear and rotary molecular motors. Systems of type (i), termed molecular shuttles<sup>79</sup> (Fig. 2a), constitute the most common implementation of the molecular machine concept with rotaxanes.

## Chemically controllable molecular shuttles and elevators

Since the first example, reported in 1994<sup>80</sup>, many controllable molecular shuttles relying on chemical, electrochemical, and photochemical stimulation have been described<sup>38,62-71</sup>. A chemically driven system with good performance in terms of switching and stability is compound 1-H<sup>3+</sup> (Fig. 3)<sup>81</sup>. It is made of a dumbbell component containing an ammonium and an electron acceptor 4,4'-bipyridinium units that can establish hydrogen-bonding and CT interactions, respectively, with the ring component dibenzo-24-crown-8 (DB24C8), a crown ether with electron donor properties. An anthracene moiety is used as a stopper because its absorption, luminescence, and



Fig. 3 Schematic representation of the operation of rotaxane  $1-H^{3+}$  as a reversible molecular shuttle controlled by acid-base chemical stimulation in CH<sub>3</sub>CN solution<sup>81</sup>. For a description of parts a-d, see main article. (Reproduced with permission from<sup>38</sup>. © 1998 Wiley-VCH.)



Fig. 4 Chemical formula (a) and operation scheme in CH<sub>3</sub>CN solution (b, c) of the molecular elevator<sup>84,85</sup> **2**-H<sub>3</sub><sup>9+</sup>. According to molecular models, the elevator is approximately 2.5 nm high and 3.5 nm wide. (Reproduced with permission from<sup>70</sup>. © 2006 The Royal Society of Chemistry.)

redox properties are useful to monitor the state of the system. Since the N+-H-O hydrogen-bonding interactions between the macrocyclic ring and the ammonium center are much stronger than the CT interactions of the ring with the bipyridinium unit, the rotaxane exists as only one of the two possible translational isomers (Fig. 3a, state 0). Deprotonation of the ammonium center of  $1-H^{3+}$  with a base (Fig. 3b) weakens the hydrogen bonding interactions and causes the quantitative displacement of the DB24C8 ring by Brownian motion to the bipyridinium unit (Fig. 3c, state 1). Reprotonation of  $1^{2+}$  with an acid (Fig. 3d) directs the ring back on the ammonium center. This switching process has been investigated in solution by <sup>1</sup>H NMR spectroscopy and by electrochemical and photophysical measurements<sup>81</sup>. Recently, the kinetics of ring shuttling in solution<sup>82</sup> and the properties of Langmuir-Blodgett films<sup>83</sup> containing 1-H<sup>3+</sup> have also been studied. The full chemical reversibility of the energy-supplying acid-base reactions guarantees the reversibility of the mechanical movement despite the formation of waste products. Notice that this rotaxane is a bistable system and in principle could be used to store binary information.

By incorporating the architectural features of the acid-base switchable rotaxane  $1-H^{3+}$  (Fig. 3)<sup>81</sup> into those of a triply threaded two-component supramolecular bundle<sup>84</sup>, we designed and constructed a two-component molecular device,  $2-H_3^{9+}$  (Fig. 4a), that behaves like a nanoscale elevator<sup>85</sup>. This nanomachine, which is ~2.5 nm high and has a diameter of ~3.5 nm, consists of a tripod component containing two different notches – one ammonium center and one 4,4'-bipyridinium unit – at different levels in each of its three legs. The latter are interlocked by a tritopic host, which plays the role of a platform that can be made to stop at the two different levels. The three legs of the tripod have bulky feet that prevent the loss of the platform. Initially, the platform resides exclusively on the 'upper' level<sup>§</sup>, i.e. with the three rings surrounding the ammonium centers (Fig. 4b, state 0). This preference results from strong N+-H-O hydrogen bonding and weak stabilizing  $\pi$ - $\pi$  stacking forces between the aromatic cores of the platform and tripod components. Upon addition of a strong, non-nucleophilic phosphazene base to an acetonitrile solution of  $2-H_3^{9+}$ , deprotonation of the ammonium center occurs and, as a result, the platform moves to the 'lower' level, that is with the three DB24C8 rings surrounding the bipyridinium units (Fig. 4c, state 1). This structure is stabilized mainly by CT interactions between the electron-rich aromatic units of the platform and the electron-deficient bipyridinium units of the tripod component. Subsequent addition of acid to 26+ restores the ammonium centers and the platform moves back to the upper level. The 'up and down' elevator-like motion, which corresponds to a quantitative switching and can be repeated many times, can be monitored by <sup>1</sup>H NMR spectroscopy, electrochemistry, and absorption and fluorescence spectroscopy<sup>86</sup>.

It should be noted that the acid-base controlled mechanical motion in  $2-H_3^{9+}$  is associated with interesting structural modifications, such as the opening and closing of a large cavity and control of the positions and properties of the bipyridinium legs. This behavior can in principle be used to control the uptake and release of a guest molecule, a function of interest for the development of drug delivery systems.

### A molecular shuttle powered by sunlight

The chemically powered artificial nanomachines described in the previous section are *not autonomous* since, after the mechanical movement induced by a chemical input, they need another, opposite chemical input to reset, which also implies generation of waste products. However, addition of a reactant (fuel) is not the only means by which energy can be supplied to a chemical system. In fact, nature shows that, in green plants, the energy needed to sustain the machinery of life is ultimately provided by sunlight. Energy inputs in the form of photons can indeed cause mechanical movements by

<sup>&</sup>lt;sup>§</sup>The molecular elevator operates in solution, i.e. with no control of the orientation of the molecules relative to a fixed reference system. Therefore, in the present context the words 'upper' and 'lower' are used only for descriptive purposes.

reversible chemical reactions without the formation of waste products. As mentioned above, the use of a renewable energy source to power nanomachines is a worthwhile objective.

The design and construction of molecular shuttles powered exclusively by light energy is therefore a fascinating yet challenging subject. On the basis of the experience gained with previous studies on pseudorotaxane model systems<sup>87-89</sup>, rotaxane **3**<sup>6+</sup> (Fig. 5) has been specifically designed to achieve photoinduced ring shuttling in solution. This compound<sup>90</sup> is made of the electron donor ring R and a dumbbell component that contains several units: a ruthenium(II) polypyridine complex (P<sup>2+</sup>), which plays the dual role of a light-fueled power station<sup>91</sup> and a stopper, a *p*-terphenyl-type rigid spacer (S), a 4,4'-bipyridinium unit (A<sub>1</sub><sup>2+</sup>) and a 3,3'-dimethyl-4,4'-bipyridinium unit (A<sub>2</sub><sup>2+</sup>) as electron accepting stations, and a tetraarylmethane group as the second stopper (T). The stable translational isomer of rotaxane **3**<sup>6+</sup> is the one in which the R component encircles the A<sub>1</sub><sup>2+</sup> unit, in keeping with the fact that this station is a better electron acceptor than the other one.

The strategy devised in order to obtain the photoinduced abacuslike movement of the R macrocycle between the two stations  $A_1^{2+}$  and  $A_2^{2+}$ , illustrated in Fig. 6, is based on the following four operations: (a) *Destabilization of the stable translational isomer*: light excitation of the photoactive unit P<sup>2+</sup> (process 1) is followed by the transfer of an electron from the excited state to the  $A_1^{2+}$  station, which is encircled by the ring R (process 2), with the consequent 'deactivation' of this station; such a photoinduced electron-transfer process has to compete with the intrinsic decay of the  $P^{2+}$  excited state (process 3);

- (b) *Ring displacement*: the ring moves (process 4) for 1.3 nm from the reduced station  $A_1^+$  to  $A_2^{2+}$ , a step that has to compete with the back electron-transfer process from  $A_1^+$  (still encircled by R) to the oxidized unit P<sup>3+</sup> (process 5);
- (c) *Electronic reset*: a back electron-transfer process from the 'free' reduced station  $A_1^+$  to the oxidized unit  $P^{3+}$  (process 6) restores the electron acceptor power to the  $A_1^{2+}$  station;
- (d) Nuclear reset: as a consequence of the electronic reset, back movement of the ring from  $A_2^{2+}$  to  $A_1^{2+}$  takes place (process 7). Steady-state and time-resolved spectroscopic experiments together with electrochemical measurements in acetonitrile solution have shown<sup>92</sup> that the absorption of a visible photon by  $3^{6+}$  can cause the occurrence of a forward and back ring movement, that is, a full mechanical cycle according to the mechanism illustrated in Fig. 6. It has been estimated that the fraction of the excited state energy used for the motion of the ring amounts to ~10%, and the system can generate a mechanical power of  $\sim$ 3 x 10<sup>-17</sup> W per molecule. The somewhat disappointing quantum efficiency for ring shuttling (2% at 30°C) is compensated for by the fact that the investigated system gathers together the following features: (i) it is powered by visible light (in other words, sunlight); (ii) it exhibits autonomous behavior, like motor proteins; (iii) it does not generate waste products; (iv) its operation can rely on intramolecular processes alone, in principle allowing operation at the single-molecule level; (v) it can be driven at a



Fig. 5 Chemical formula (a) and schematic representation (b) of the rotaxane  $3^{6+}$ , showing its modular structure<sup>90</sup>. Molecular models show that the rotaxane molecule is approximately 5 nm long and has a ring diameter of ~1.3 nm. (Reproduced with permission from<sup>67</sup>. © 2006 CSIRO Publishing.)



Fig. 6 Operation scheme of rotaxane  $3^{6+}$  as an autonomous 'four stroke' molecular shuttle powered by light<sup>92</sup>.

frequency of ~1 kHz; (vi) it works in mild environmental conditions (i.e. fluid solution at ambient temperature); and (vii) it is stable for at least  $10^3$  cycles. Although the system in its present form could not develop a net mechanical work in a full cycle of operation<sup>93</sup>, it shows that the structural and functional integration of different molecular subunits in a multicomponent structure is a powerful strategy to construct nanoscale machines. Because of its modular design, rotaxane **3**<sup>6+</sup> is amenable to structural modification to try to improve its performance as a light-driven molecular shuttle<sup>94</sup>.

### Summary and outlook

The construction of simple prototypes of molecular devices and machines has been achieved by using careful incremental design strategies, the tools of modern synthetic chemistry, and the paradigms of supramolecular chemistry - together with some inspiration from natural systems and processes. The systems described here operate in solution, individually, and incoherently. For some kinds of applications, they will need to be interfaced with the macroscopic world by ordering them in some way, for example at interfaces<sup>83</sup> or on surfaces<sup>95,96</sup>, so that they can behave coherently either in parallel or series. It has been shown recently<sup>97,98</sup> that the collective operation of artificial nanomachines in carefully engineered surface-deposited monolayers can develop mechanical work at a larger scale. A detailed discussion of this and related topics is beyond the scope of this article. Apart from more or less futuristic applications, the extension of the concept of a device or machine to the nanoscale is a fascinating topic for basic research. Looking at molecular and supramolecular species from the

viewpoint of functions with reference to devices in the macroscopic world is a very interesting exercise that introduces novel concepts into chemistry as a scientific discipline.

The fast growth rate of this research field allows us to be optimistic that molecular devices and machines of practical use will see the light of day in the not too distant future. In this regard, it is to be hoped that nanoscience and nanotechnology will contribute to the finding of solutions to the four big problems that face a large part of the Earth's population: food, health, energy, and environment. While developing nanoscience and nanotechnology, however, we should not forget the 'great asymmetry' principle<sup>99</sup>: "The essential human tragedy, and the true source of science's potential misuse for destruction, lies in a great asymmetry in our universe of natural laws. We can only reach our pinnacles by laborious steps, but destruction can occur in a minute fraction of the building time, and can often be truly catastrophic. A day of fire destroyed a millennium of knowledge in the library of Alexandria, and the shot of one assassin can launch a preventable war... We have no choice, for humans must wonder, ask, and seek - and science must break through the strictures of custom - to become either our greatest glory, and our most potent engine of benevolent change, or an accelerator of destruction on the wrong side of the great asymmetry." nt

### Acknowledgments

We would like to thank J. Fraser Stoddart and coworkers for a long lasting and very profitable collaboration. Financial support from EU (STREP 'Biomach' NMP2-CT-2003-505487) and the University of Bologna is gratefully acknowledged.

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