

from the 1G_4 state of the thulium ions. By comparison, a super-intense laser beam can assist in exciting the thulium ions, which are populated in the 3H_4 intermediate state through cross-relaxation, to higher-energy states. The combination of high-power excitation and cross-relaxation thus gives rise to enhanced upconversion emission of the nanoparticles.

The difference in upconversion intensity, induced by applying different power densities, is utilized by Jin and colleagues as a proof-of-concept demonstration for security printing. The researchers printed two different patterns on two layers using the nanoparticles doped with high and low activator concentrations, respectively. The pattern printed with the high activator concentration cannot be observed under weak illumination conditions and can only be visualized at a high power density. Furthermore, the combination of the high-power optical fibre and the heavily doped nanoparticles enables single-particle detection of these nanocrystals in solution within the hollow fibre. Two main factors contribute to the record high sensitivity: improved signal strength through the concentration enhancement effect, and background noise reduction.

A caveat of this work is that the lifetime data of 1G_4 versus thulium concentration were not included. Such information is essential for understanding the complex energy-transfer process in heavily doped nanoparticles. It would also be interesting to test nanoparticles doped with other activator ions, such as erbium and holmium. Nonetheless, Jin and colleagues present an important work that may be applied to rapid molecular sensing. Moreover, this fibre system may

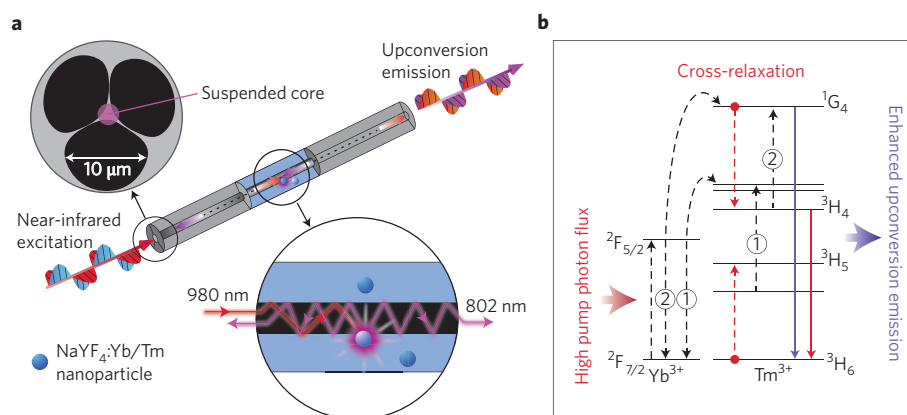


Figure 1 | An optical fibre coupled to upconversion nanoparticles. **a**, Schematic showing an optical sensor design that combines a suspended-core optical fibre with NaYF₄:Yb/Tm upconversion nanoparticles dispersed in the three hollow channels. A ray of light generated from a 980-nm diode laser is directed into the thin glass core of the fibre from one end and guided to the other end, which is immersed in a solution of upconversion nanoparticles. Note that only nanoparticles in close proximity to the glass core are excited by an evanescent wave. **b**, Simplified energy-transfer mechanism in NaYF₄:Yb/Tm nanoparticles under high-density excitation. Cross-relaxation (or self-quenching) between a pair of thulium ions (one in the excited state and the other in the ground state) dominates in nanoparticles with a high thulium dopant content, resulting in both thulium ions occupying two intermediate excited states. High pump power promotes optical transitions of the thulium ions from these intermediate states to higher-energy states by supplying high-density photons, leading to enhanced upconversion emission. The four main energy states for optical transitions in the thulium ion are 3H_6 , 3H_5 , 3H_4 and 1G_4 . The transition states of an ytterbium ion that absorb energy from a 980-nm laser are $^2F_{5/2}$ and $^2F_{7/2}$. Steps 1 and 2 represent two subsequent energy-transfer processes from the ytterbium to thulium ions.

help in the development of new imaging methods, for example, real-time *in vivo* endoscopic imaging.

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DNA COMPUTING

Molecules reach consensus

DNA molecules can be programmed to execute any dynamic process of chemical kinetics and can implement an algorithm for achieving consensus between multiple agents.

Ehud Shapiro and Tom Ran

The intersection of computer science and molecular biology is a fertile ground for new and exciting science. Two notable examples of this are molecular computing and molecular programming. Molecular computing is the use of molecules, and typically biological molecules, to create programmable

autonomous computing devices^{1–7}. Whereas molecular programming is the use of computer programming languages to describe, simulate, analyse and even engineer the behaviour of molecular systems, and typically systems made of biological molecules^{8–12}. Writing in *Nature Nanotechnology*, Georg Seelig

and colleagues¹³ at the University of Washington, Microsoft Research in Cambridge, the California Institute of Technology and the University of California, San Francisco have now shown that the fields of molecular computing and molecular programming can join forces to create programmable chemical controllers

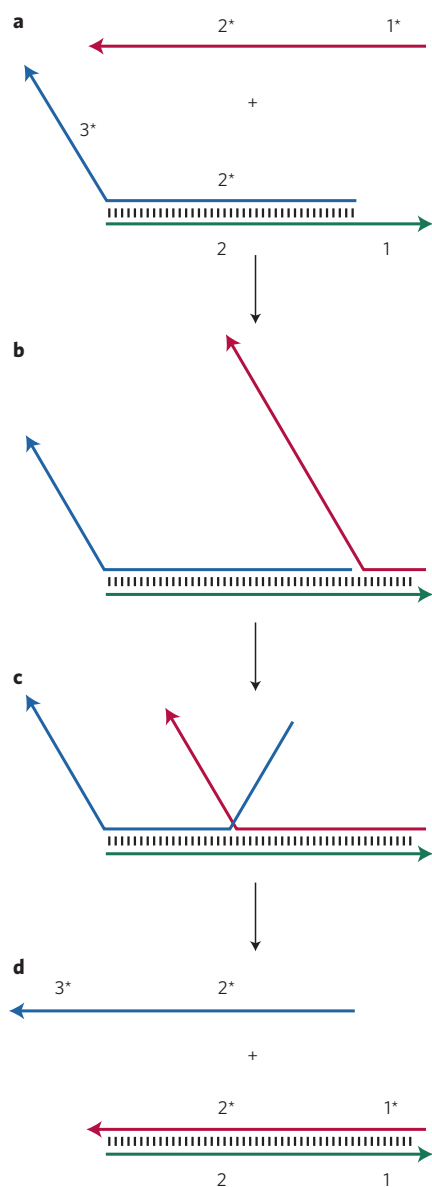


Figure 1 | DNA strand displacement.

a–d, A single-stranded DNA molecule (red) can be programmed to displace another (blue) within a double-stranded DNA molecule (blue-green). The displaced (blue) strand can then initiate a new strand displacement operation with a correspondingly designed molecule. The strand-displacement reaction is facilitated by the ‘toehold’ domains 1^* and 1 (**a**). The hybridization of these single-stranded toeholds co-localizes 1^* and 1 (**b**), and allows the 2^* domain to ‘branch migrate’ (**c**). Branch migration is the random walk process in which one domain displaces another of identical sequence through a series of reversible single nucleotide dissociation and hybridization steps. At the completion of branch migration, the red-green double-stranded DNA complex is formed and the blue strand is released (**d**). The reaction is driven forward thermodynamically by the entropic gain.

made of DNA, which can be programmed to reach consensus¹⁴.

From the field of molecular computing, Seelig and colleagues have employed the method of DNA strand displacement^{4,5,11}, in which one DNA strand is programmed to displace another within a double-stranded DNA molecule (Fig. 1). From the field of molecular programming, they have used Chemical Reaction Networks, a mathematical language for describing chemical reactions occurring in well-mixed solutions. Chemical Reaction Networks are used here as the programming language¹¹ for designing the DNA strand-displacement systems. Also from the field of molecular programming the researchers make use of the DNA strand-displacement calculus software tool¹⁰ for simulating, analysing and debugging these complex molecular systems.

DNA strand displacement has previously been used to create a variety of systems and devices including complex Boolean logic gates⁴, autonomous molecular motors and reconfigurable nanostructures (reviewed in ref. 5). As a fundamental mechanism for computation, DNA strand displacement has a number of attractive features. (1) The inputs and outputs of the system are single-stranded DNA molecules, which allow devices to be cascaded and combined into larger modules. (2) Devices made with the approach are autonomous and operate spontaneously when all components are present. (3) The system is programmable and, as illustrated by Seelig and colleagues, supports the use of Chemical Reaction Networks as a programming language, which is naturally suited to the direct specification and programming of simple molecular systems and can easily express their inherent analogue and temporal dynamics. (4) Any computation that can be specified by a Chemical Reaction Network can, in principle, be realized using the set of uniformly constructed double-stranded DNA molecules employed by Seelig and colleagues, which have only two domains and a nick (a discontinuity) at one of the strands⁷. (5) Finally, the DNA strand-displacement architecture used by the researchers supports ‘garbage collection’, which is the ability to reclaim resources that have fulfilled their contribution to a computation and is an essential feature of any realistic computing system. In electronic computers, garbage collection of memory locations allows very long computations to be completed using finite memory. In DNA strand-displacement computations, the uniform two-domain molecules allows single-stranded DNA that has fulfilled its mission to be reclaimed

by turning it into inactive waste, which ensures that the computation only progresses forward⁷.

One possible disadvantage of the DNA strand-displacement approach is its incompatibility with *in vivo* operation: the hostility of the eukaryotic cellular environment to short foreign DNA molecules might make it difficult for DNA strand-displacement devices to operate as ‘smart’ drugs^{3,6} and realize the vision of a ‘doctor in a cell’². Another disadvantage is the long time (hours) required for DNA strand-displacement computations to provide a result. In comparison, enzyme-based mechanisms require only a few seconds or minutes to yield a result³. There are also some limitations associated with Chemical Reaction Networks. Although the language of Chemical Reaction Networks is ideally suited for describing DNA strand-displacement systems, it lacks data structures and process structures, and therefore cannot naturally describe the dynamics of molecular processes^{8,9} such as DNA replication and methylation, RNA splicing, protein phosphorylation and membrane budding.

To illustrate the capabilities of their approach, Seelig and colleagues first show that they can implement different building-block reaction types: non-catalytic, catalytic and autocatalytic. Then, using an example from theoretical computer science, they combine these building blocks into a network that can implement a distributed algorithm for reaching consensus among mobile interacting finite-state machines. The Approximate Majority algorithm¹⁴ assumes a population of interacting 3-state machines that are initially in one of the three states (positive, negative and neutral, for example). If two machines of the same state meet, nothing happens. If a positive meets a negative, both turn neutral. If a neutral meets a positive it also turns positive and, similarly, when a neutral meets a negative it turns negative. The algorithm guarantees that it will switch the majority (of positives or negatives) into a totality in a way that is fast, reliable and robust.

Although this elegant algorithm was conceived in a rather abstract mathematical setting, it is remarkable that it may in fact be at the core of the cell-cycle switch¹⁵ and that it naturally lends itself to implementation by a DNA strand-displacement system, as was previously shown theoretically¹² and has now been demonstrated experimentally by Seelig and colleagues. The researchers have, through the use of DNA biochemistry, combined the fields of molecular computing and

molecular programming with a dash of theoretical computer science, and provided a work that is the epitome of interdisciplinary research.

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ARTIFICIAL SPIN ICE

Crystal-clear order

Magnetic ordering in two-dimensional arrangements of nanomagnets can be repeatedly obtained by annealing an artificial spin ice.

Laura J. Heyderman

Spin ice crystals, such as rare-earth titanate pyrochlores, take their name from the resemblance of their spin configuration to the frustrated spatial arrangement of hydrogen atoms in frozen water. In artificial spin-ice systems, analogous frustrated magnetic configurations are created using lithographically fabricated arrangements of dipolar-coupled single-domain nanomagnets¹. Such artificial systems can be used to explore spin systems not found in nature and could provide answers to fundamental questions about the physics of magnetic frustration. They could also potentially be used to develop novel spintronic devices.

So far, research on artificial spin ice has focused on the study of nanomagnets with magnetic moments that are static at room temperature. In such cases, switching the moments requires the application of a magnetic field. However, systems with fluctuating moments would better mimic the behaviour of natural spin ice, and would allow the lowest energy states to be obtained in a controllable manner, which is desirable for studying novel phases of frustrated magnetic systems. Writing in *Nature*, Peter Schiffer and colleagues at Pennsylvania State University, University of Illinois, Los Alamos National Laboratory, University of Minnesota and University of Cambridge have now found a way to explore such an artificial spin ice in arrays of permalloy nanomagnets². To attain a regime where the moments fluctuate, the researchers heat the samples above the Curie temperature of permalloy and, after cooling, observe the magnetic

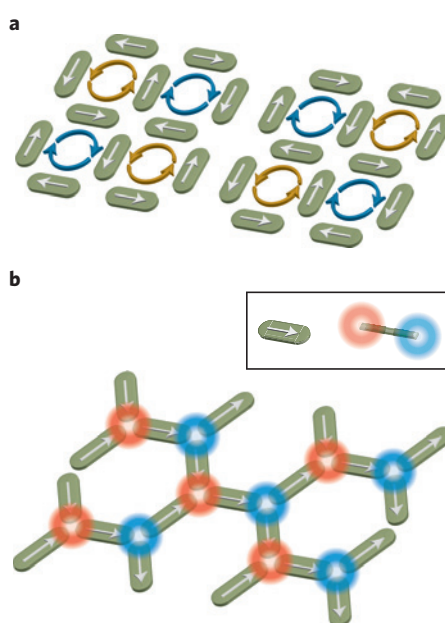


Figure 1 | Artificial spin-ice lattices. **a**, Ground state in artificial square ice with tiles of alternating chirality (represented by blue and orange arrows). As shown, this state is two-fold degenerate and experimentally results in ground state domains separated by boundaries. **b**, Remnant magnetic state in the artificial kagome spin ice. When replacing each magnetic dipole by a charge dumbbell (inset) and considering the net charge at each lattice vertex, this spin configuration corresponds to a charge-ordered phase with alternating positive and negative charges (shown in blue and red). This charge order can be achieved with a variety of different spin arrangements besides the example shown here. The white arrows represent the magnetic moments.

state with magnetic force microscopy. The work reports one of the first direct observations of the magnetic configurations in a thermally active artificial spin ice, and provides a method for repeatedly inducing the thermally driven states and for studying how these systems become ordered.

There are two key artificial spin-ice geometries: one has elongated single-domain nanomagnets placed on the sites of a square lattice (Fig. 1a) and the other has nanomagnets placed on the sites of the kagome lattice, in a hexagonal arrangement (Fig. 1b). For the elongated nanomagnets, minimization of the magnetic-stray-field energy causes the magnetic moment to point in one of two directions parallel to their long axis. Neighbouring nanomagnets prefer to have their magnetization aligned north pole to south pole, and in the square ice this results in a unique ground state with alternating tiles of clockwise and anticlockwise oriented moments. In the low-energy states, domains of opposite chirality are separated by boundaries.

Schiffer and colleagues fabricated several nanomagnet arrays on the same substrate, which were characterized by different values of the distance between nanomagnets, and found that the size of the domains in artificial square ice increased as the separation between the nanomagnets decreased. At small separations, the researchers achieved almost perfect magnetic ordering. This result goes far beyond previous attempts that used an alternating magnetic field to achieve the ground state in artificial square ice. The level of ordering achieved by Schiffer and colleagues has thus far been observed only