

Nano on reflection

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A number of experts from different areas of nanotechnology describe how the field has evolved in the last ten years.

A decade ago, ‘nano’ was a word of tomorrow, signifying the promise of a future enhanced and streamlined by the torrent of possibilities that would come from single-atom control over the material world. Apple had just blazed a now well-worn path of cashing in on this cultural sentiment, releasing its first-generation iPod Nano in September 2005. Nanotechnology was hailed as a panacea to the economic and ecological malaise of the early 2000s, with the promise of cost-effective and relatively easy-to-produce solutions to problems as diverse as the energy crisis, chemotherapy and cybersecurity.

Many of the contributions to this article reflect on the delivery of those promises. As a philosopher of science, however, I am interested in another set of promises that nano has, perhaps unwittingly, made. Nano is a science built around a scale, among the first of its kind. In gathering ideas under the umbrella of a length scale, nano has reshaped how scientists — and philosophers of science — understand the very nature of scientific concepts and the theories they comprise.

The trajectory of knowledge in those effects are miniscule compared with the dominant material behaviours of macroscopic materials.

Nano demands that scientific understanding of material behaviour be indexed to length, time and energy scales. This insight about the nature of scientific understanding promises to be as revolutionary as the realization that terrestrial and planetary bodies can be described by the same equations of motion. In the past decade, nano has shown definitively that scale constrains scientific activity from the conception and carrying-out of an experiment to the choice of theories, models and simulations used to predict and explain those experimental results. In the decades to come, nano will reshape the structure of scientific knowledge as scientists and philosophers recognize the import of systematically scale dependent investigations on our conceptual understanding of the material world.

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As the new millennium dawned, scientists physically connected the control of single atoms to new behaviour at the macroscale. their discoveries gave us the opportunity to engineer new materials, devices and systems through the hierarchical assembly of matter from the nanoscale. In the last decade, we have seen the frontier of nanoscience progress from uncovering nanoscale phenomena and synthesizing components of nanometric size to creating active nanostructures and integrated nanosystems for fundamentally new technologies and products. Now, we can envision creating new nanosystem architectures and converging technology platforms with ever-greater complexity and functionality.

I had the opportunity to propose the long-term scientific vision of nanotechnology on behalf of a group of experts in a 10 minute presentation at the White House in March 1999. To achieve that vision, the US established the National Nanotechnology Initiative (NNI), which mapped out the needed foundational knowledge, general-purpose simulation and manufacturing methods, and infrastructure.

President Clinton announced the NNI in January 2000, and he asked us to imagine the outstanding progress we might see 20–30 years later. His ambitious goal was to reach a stage where we could store all the information held in the Library of Congress in a memory element the size of a sugar cube. The

goal was met with some scepticism, but in 2012, nanotechnology-based prototypes did achieve this milestone. For example, the IBM group led by Andreas Heinrich demonstrated that 12-atom structures could be stored in a cm^3 volume (S. Loth, S. Baumann, C. P. Lutz, D. M. Eigler and A. J. Heinrich, *Science* 335, 196–199; 2012) and the group led by George Church at Harvard demonstrated that DNA structures could be stored in a mm^3 volume (G. M. Church, Y. Gao and S. Kosuri, *Science* 337, 1628; 2012). President Clinton also spoke of detecting cancer at the cellular level in 20–30 years, and now already we have several nanotechnology-enabled diagnostic and therapeutic agents, and many others in clinical trials (such as supported by the National Cancer Institute Alliance for Nanotechnology in Cancer programme; go.nature.com/2ctab0v). Again, nano research successfully enabled this capability well ahead of the predicted time. Today, over half of the semiconductors produced by US companies are the result of nanoscale research, and smartphones, new calculators and medical devices incorporate nanocomponents. In 2000, we evaluated that the world would have US\$1 trillion worth of products that incorporated nanotechnology by 2015, and we reached the US\$1 trillion mark in 2013. We are now about half way through the NNI plan, and in so many fields that incorporate nanotechnology, the ‘tomorrow’ we envisioned has already been reached not today, but yesterday.

The NNI started “as a new way to run an initiative” (C. West, NNI bi-annual review, President’s Council of Advisors on Science and Technology, White House, 2005) and has spread in the last decade to over 80 nations that have similar long-term research programmes on nano incorporated in national strategies. Nanotechnology has become a global scientific revolution for a foundation, general-purpose science and technology endeavour. By extending the S-development curve factual data of the last decade, the revenues from nanoscience has taken a very different path than the discovery of relativity or the last decade, the revenues from nanotechnology-based economy are estimated to exceed 10% of the gross domestic product by 2025 in the US and several other developed countries.

Four large National Science Foundation (NSF)-sponsored networks established in the interval 2005 to 2008 have been at the core of an international ecosystem addressing societal implications in the last decade. Over 10,000 students and teachers have been supported each year in the last decade by NSF, and the NNI physical user facilities have employed over 10,000 scientists annually. Together these individuals and organizations are creating a new scientific and engineering culture where fields converge to bring remarkable and valuable advances to our lives. In the future, advances in nanotechnology will continue to drive us toward frontiers that were not even possible to envisage until not too long ago — such as brain-like computing, digital manufacturing of nanosystems, addressing the water–energy–agriculture–environment nexus, and convergence with bio- and cognitive technologies — and will help shape exotic fields such as metamaterials, DNA editing and quantum information, overall increasing human potential.

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Among the disciplines supported by the National Natural Science Foundation of China (NSFC), three of them — namely solid-state physics, inorganic and non-metallic materials, and molecular biology — stand out in terms of the most progress made in the past 10 years. They are powered by a common driver: nanotechnology. Among the grants awarded by the NSFC, those with nano-related titles have grown from 569 in 2006 to 1,942 in 2015. The number of publications from mainland China in the category of nanoscience and nanotechnology according to the Web of Science increased dramatically from 1,639 in 2006 (14.74% world share) to 10,951 in 2015 (31.76% world share). The increase in the number of citations during the same period was even higher. The NSFC plays a pivotal role in funding nanotechnology in China.

The fast-growing activity is driven by multiple factors. First, the interdisciplinary nature of the field, linking physics, chemistry, biology and technology at the nanoscale, which results in the creation of new research interfaces. Second, the fact that phenomena can be examined across multiple length scales, from the atomistic, nanoscopic, mesoscopic and macroscopic. Last, interactions between

academics and enterprises, and between politicians and the general public. However, the expectations of disruptive technologies fuelled by nanoscience have not yet been fulfilled. A major breakthrough in nanoelectronics is elusive as a result of a slowdown in the post-Moore era; nanomaterials featuring nanotubes, bucky balls and graphene have not met their applications targets; nanomedicine is still in its infancy; nanomanufacturing faces insurmountable difficulties in efficiency.

Nevertheless, nanoscience and nanotechnology still promise new horizons. Nanostructures may be used in quantum devices or in neuroscience, and molecular chemistry will provide new tools for catalysis. One expects another decade of fast progress in nanotechnology. After a phase of nurturing ideas, of feverish and random explorations, and of creating technology pathways, there may be a phase of application breakthroughs before the realization of scalable and sustainable technology.

Nanotechnology has entered an era calling for breakthroughs in disruptive technology and for sustained public funding.

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Nanotechnology may be one of the few fields where the safety concerns of the public, government, academia and industry have led to worldwide scientific investigations into nanosafety being initiated at the initial stages of research before large-scale utilization. In China, the government has invested in fundamental nanosafety research since 2001 when the Chinese Academy of Sciences (CAS) approved the proposal of Yuliang Zhao to establish a Nanosafety Laboratory. When the National Nanotechnology Program of the National Basic Research Program of China was initiated in 2006 by the Ministry of Science and Technology of China (MOST), environmental health and safety had been recognized as a strategic priority and government investment supporting nanosafety studies accounted for ~7% of the nanotechnology budgets of both the NSFC and MOST.

From 2001 to 2008, nanosafety research mainly focused on the establishment of quantitative analytical methods to understand the absorption, distribution, metabolism, excretion and toxicology — known as ADME/Tox — of carbon and metal-containing inorganic nanomaterials. Accurate characterization of physicochemical properties of nanomaterials in vitro and in vivo is a key requirement for understanding and managing potential risks and human impact. Quantification and visualization methods of nanomaterials in vitro and in vivo based on isotope labelling and synchrotron radiation techniques have been established by Chinese scientists. These methods provide high sensitivity and low matrix interference, can be used for in situ detection, are non-destructive and have been adopted worldwide in related fields. For example, a quantitative analytical method for detecting contaminated metals in carbon nanotubes (CNTs) has been established and has been authorized as an international standard by the International Organization for Standardization (ISO) and the International Electrotechnical Commission (IEC). This method is the first ISO standard from China and is utilized for the certified reference nanomaterial single-walled CNTs by the National Institute of Standards and Technology of the US and the National Research Council of Canada. It has also been considered to “help end the long-time debate on the nanosafety issue [...] using this standard method” (B. Fugetsu et al., *J. Hazard. Mater.* 170, 578–583; 2009). Since 2008, approaches developed for use in occupational and consumer exposure scenarios have become a main research focus to construct guidelines for monitoring nanoparticle release in workplaces to help the government agencies and industry to draw up regulations and safeguards. In 2010, the Committee of Nanotoxicology including a multidisciplinary domestic consortium was officially launched by the Chinese Society of Toxicology to coordinate nationally related activities. Chinese scientists are also actively involved in international collaborations and activities, including with the ISO, the Organisation for Economic Co-operation and Development (OECD), the United Nations, the European Union’s Sixth and Seventh Framework Programmes (FP6 and FP7) and Horizon 2020, the European NanoSafety Cluster, and research groups in Canada, Denmark, Finland, France, Germany, the UK and the USA.

Since then, particular efforts have been made to understand the underlying mechanisms of the complicated and debated toxicological phenomena of nanomaterials by exploring correlations between

their toxic responses and nanocharacteristics.

In the future, a fundamental understanding of nanoscale materials interacting with living systems, quantitative approaches for hazard characterization of nanomaterials, certified reference nanomaterials and internationally standardized methodologies are all challenges that need to be addressed that will aid the issue of reproducibility of results. Finally, regulation of nanomaterials and public education on nanosafety will also be key to successful nanotechnology applications.

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The hype surrounding nanotechnologies between 2000 and 2010 has slowly faded. At the same time, the presence of engineered nanomaterials (ENMs) in consumer products has become commonplace. Changes have also taken place in the ways we look at the possible harmful health effects of ENMs. Currently, physicochemical features of a given ENM, and their effects on ENM toxicity, are much more in the focus. Careful characterization of ENMs has become more important, and new technologies have spread quickly in the research on nanosafety. At present, there is no common understanding of the toxicity mechanisms of ENMs (E. Valsami-Jones and I. Lynch, *Science* 370, 388–389; 2015). However, for ENM safety and risk assessment, understanding of the toxicity mechanisms of ENMs is crucial. This has led to an increased need to use state-of-the-art methods including omics and bioinformatics to enable the analysis of new toxicity pathways of ENMs (T. Hartung, *Nature* 460, 208–212; 2009).

The overall quality requirements of nanosafety research have also increased. Nowadays, research on nanosafety cannot be based on narrow expertise. Rather, a wide range of competences is required to successfully execute any research exploring safety and mechanisms of toxicity of ENMs. Competences as diverse as aerosol physics, bioinformatics, molecular biology, social sciences, environmental chemistry and physiology are required to solve new research challenges. This development has favoured the formation of large multinational consortia, an approach used for example by the European Union (EU). Large multinational consortia can include 20–30 research groups with more than a hundred scientists. The EU has adopted this paradigm for example in the Horizon 2020 programme. This all has greatly changed the way research is conducted, and stresses the importance of a party that coordinates research efforts and assures the societal impact of the research.

The European Commission's Directorate General for Research and Innovation also established in 2009 the NanoSafety Cluster (NSC) to harmonize the collaboration of EU-funded nanosafety research projects. Since then, membership of the NSC has been mandatory for such projects. The NSC has also supported the EU Commission by producing a research agenda for 2015–2025 (K. Savolainen et al., *Nanosafety in Europe 2015–2025: Towards Safe and Sustainable Nanomaterials and Nanotechnology Innovations* go.nature.com/2d31CoW; 2013), which has been used to identify new topics of nanosafety research in the Horizon 2020 calls. This reflects the enhanced focusing and coordination of nanosafety research in the EU to more effectively carry out research on nanosafety.

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Nature is the ideal example of a system that works perfectly on the nanometre scale with a high degree of optimization regarding involved materials, energy consumption and data handling. The emergence of scanning probe methods (SPM) in the field of nanotechnology has led to a revolutionary transformation in the understanding and perception of matter at its most fundamental level. The

scanning tunnelling microscope (STM) and atomic force microscope (AFM) have taken scientists into uncharted territory by offering the ability to image surfaces in 3D at the atomic scale.

The techniques have opened new avenues in physics, chemistry, biology and medicine, and still are inspiring researchers in a variety of different disciplines, as testified by the more than 460,000 scientific articles in peer-reviewed journals (according to the Web of Science), which is over 10 times more than 10 years ago. The enormous flexibility of the AFM and STM to image, probe and manipulate materials with unprecedented resolution and the option to be combined with other technologies made SPM the most powerful and versatile toolkit in nanoscience and nanotechnology today.

The number of applications of scanning probes has increased dramatically in the last 10 years. Just to name a few examples, high-speed AFM can now provide time-resolved information of chemical activity, and allows monitoring the cellular machinery at the nanoscale with millisecond resolution; the optimization of high-resolution non-contact AFM has allowed ultralow forces to be measured and superlubricity (frictionless interaction) to be observed at the nanoscale, and it is now possible to use AFM for 2D force–distance spectroscopy mapping in various fields of application.

Equally impressive have been the developments beyond imaging. Cantilevers can be used as chemical and biomedical sensors to observe adsorption processes on the cantilever surface, thereby converting biochemical activities into nanomechanical motion. Many application fields for cantilever sensors have been reported over the years, for example the detection of DNA hybridization with single-point-mutation sensitivity, protein and antibody recognition, and more recently, assessing patient eligibility for cancer treatment.

We feel confident that an ever-larger demonstration of scanning probes used for efficient diagnosis will be made in the next few years.

Christoph Gerber (co-inventor of the AFM) and Hans Peter Lang lead the cantilever array sensor group at the Swiss Nanoscience Institute, University of Basel, Switzerland.

The unique properties of nanomaterials could one day be used to improve patient healthcare. In my view, the final goal of nanotechnology in medicine is to realize ‘in-body hospitals’, that is, smart virus-sized nanomedicines can migrate into the microenvironments in the body to provide diagnostic and therapeutic functionalities 24 hours a day. There are four key research areas that, in my view, have evolved dramatically in the last decade and that will contribute to future changes in medicine.

The first is the targeting and eradication of intractable cancer. Systems based on paclitaxel-loaded albumin nanospheres (Abraxane) have achieved significant success in the treatment of several intractable cancers in the last

10 years. In 2015, their sales exceeded US\$800 million. Furthermore, novel formulations, including polymeric micelles and nanoparticles are currently in phase III clinical trials and are expected to get approval soon. Strategies to develop the next generation of anticancer nanomedicine have evolved to treat highly intractable cancers, such as brain tumours, metastatic cancers and cancer stem cells, based on the approach of active targeting, particularly using ligands to facilitate extravasation. Mechanisms of extravasation and tissue penetration of nanomedicines at tumour sites have been studied in detail in terms of in vivo imaging modalities such as intravital laser confocal microscopy (H. Cabral et al., *Nat. Nanotech.* 6, 815–823; 2011 and Y. Matsumoto et al., *Nat. Nanotech.* 11, 533–538; 2016), highlighting the importance of regulating the size of nanomedicines in the range 10–100 nm.

The second area is the search for an innovative methodology for the treatment of neurodegenerative diseases. The brain is protected by the blood–brain barrier (BBB), through which it is difficult to deliver biologically active substances. An effective therapeutic approach has not been established yet, though an ageing society is suffering from a high prevalence of neurodegenerative diseases, including Alzheimer’s disease. There has recently been interest in developing nanomedicines that can cross the BBB to deliver diverse biologically active substances directly into brain parenchyma, but the results are still preliminary.

The third area is nanomedicines for messenger RNA (mRNA) delivery. Developments in nanomedicine for delivering mRNA, the next-generation ‘nucleic acid-based therapeutics’, are in progress. By delivering mRNA to the necessary place at the necessary time to produce proteins that would improve and/or restore the functions of cells, treatment for many diseases, such as neurodegenerative and age-related motor and sensory disorders, can be realized. This approach opens a new field of non-cell-based regenerative medicine.

The last is theranostic systems for minimally invasive treatment of diseases. Here, the aim is to develop a diagnostic and therapeutic technology that can pinpoint the diseased tissue to enable its removal while minimizing damage to the healthy surrounding tissue by combining nanomedicines delivering imaging and therapeutic agents activatable by external energy, such as by light, ultrasound and neutron irradiation. Key achievements in the last decade are now being translated into clinics, leading to several clinical trials focusing on cancer treatment.

This combination of diagnosis and therapy in a single nanomedicine platform has led to the emergence of ‘theranostics’, one of the hot topics in the field of nanotechnology. However, nano-based imaging agents are needed for the personalized treatment of patients with nanomedicines, such as evaluating the enhanced permeation and retention effect of tumour capillaries, to increase the efficacy of treatment with nanomedicines.

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The ability to control matter at the nanoscale lies at the heart of nanotechnology, and is beautifully portrayed by the field generally known as DNA nanotechnology. When the structure of DNA was solved in 1953, and we learned how its non-covalent structure enabled information transfer, its unparalleled ability to self-assemble was also revealed. Although early researchers studied how this self-assembly underlay genetic inheritance, a later generation began to explore DNA self-assembly to build nanostructures with no reference to biological function. These structures encompassed molecular wires, substrates for computing, nanoscale building blocks for hierarchical assembly into complex architectures and in vitro evolved structures with synthetic function. The singular capacity of DNA to undergo programmed folding into any desired two-dimensional shape, that is, DNA origami, was revealed in an iconic paper in 2006 (P. W. Rothemund, *Nature* 440, 297–302). DNA origami was then extended to three dimensions, revealing its potential as a medium for 3D printing on the nanoscale.

An emphasis on the functionality of these nanostructures then arose. Origami was used as a nanoscale pegboard to position nanoparticles, small molecules and proteins for applications ranging from light-harvesting devices to enzyme cascades. Molecular computation was leveraged in diverse contexts ranging from pattern formation to molecule detection (C. Jung and A. D. Ellington, *Acc. Chem. Res.* 47, 1825–1835; 2014). The modularity of DNA was exploited for targeted delivery of diverse payloads in vivo. Exciting applications of DNA nanotechnology in quantitative and multiplexed imaging of biological systems emerged (K. Chakraborty et al., *Annu. Rev. Biochem.* 85, 349–373; 2016). Now, a rich vein is appearing where DNA/RNA-based information systems are merging with micro/nano fluidics to yield hybrid technologies for high-throughput optimization of biochemical reaction networks.

Other nucleic-acid-based biochemical technologies such as RNAi and sequencing have already successfully integrated non-RNA/non-DNA-based technologies to give hybrid technologies. In the case of sequencing, such hybrid nanotechnologies enabled whole-genome and single-cell sequencing, thus continuing to power breakthroughs in basic biology and clinical science. Additionally, robust, pre-assembled, yet easily customizable platforms for such hybrid technologies were made commercially available. Thus nanostructured DNA technologies stand to gain significantly by considering such approaches and synergizing with other nanoscale technologies.

DNA is highly charged: consequently, a Coulombic barrier must be overcome to compact it into

nanostructures. So far, this is achieved either by keeping structures relatively small or working with high cation concentrations. Nevertheless, DNA origami has uncovered certain architectural principles operating over long length scales of DNA that nature is probably exploiting endogenously, for example, RNA-mediated modulation of chromatin architecture. So, a worthy future challenge for the field is to reconnect with biology (S. Surana, A. R. Shenoy and Y. Krishnan, *Nat. Nanotech.* 10, 741–747; 2015). Given our growing realization of nucleic acid superstructure impinging on cell function, the coming decade seems poised for a revolution in nanostructured DNA-based hybrid technologies impacting diverse fields in science and medicine.

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Over the last ten years, many spin-out companies based on the broad area of nanotechnology have been founded and dissolved, or occasionally survived, as would be expected for such high-risk ventures. Large corporations have also increasingly highlighted nanoscience in their research and development programmes.

I have been directly involved with the commercialization of nanotechnology. My interest in the field comes in particular from my experience in single-molecule science. My group elaborated the oldest single-molecule approach, current recording through individual pores, by using emerging techniques, including new forms of protein engineering. Our work permitted protein nanopores to be used for the detection of a wide variety of individual molecules and for monitoring the covalent chemistry of single bond- making and bond-breaking events.

Oxford Nanopore was formed just over ten years ago to exploit single-molecule sensing and after an arduous struggle the company implemented nanopore DNA sequencing, brought to reality from the realms of science fiction. The portable, long-read MinION sequencer required a hugely multidisciplinary approach: protein and nucleic acid chemistry, polymer chemistry, surface chemistry, electronics, data collection and processing, and yes the sociology of data sharing and community-based technology improvement. Nanopore sequencing is a cheap push- button technology and we can expect more democratizing enterprises to emerge from nanotechnology over the coming years.

The decade-long venture required long- term investment, extraordinary tenacity by the Oxford Nanopore team and an excellent environment for progression and evolution of the company. In other words, ground- breaking science was only one piece of the puzzle, a lesson for others who have created innovative nanoscience.

Hagan Bayley is the Professor of Chemical Biology at the University of Oxford. In 2005, he founded Oxford Nanopore Technologies.

Nanoscience has been embraced in energy storage within the last decade, as a consequence of rethinking in the underpinning chemistry and materials science and the inevitable rush to ‘beyond-Li ion’ batteries. In the past, energy storage was focused on small-scale batteries driven by the market for portable devices. Now, however, there are urgent needs for larger-scale energy storage solutions to mitigate CO₂ emissions and urban pollution. The widespread integration of renewable, intermittent energy sources (wind, solar) is dependent on developing efficient low-cost energy storage for load-levelling the electric grid. The acceptance of electric vehicles hinges on safe, low-cost energy storage batteries to provide practical driving ranges. At the same time, traditional Li-ion batteries — which operate on the principle of reversible storage of electrons and Li ions in bulk materials — are approaching their limits. A challenge is to find electrochemical energy storage systems that are lower

cost, and provide higher energy density and/or high power. Nanoscience can help in this regard.

For Li-ion batteries, nanomaterials typically exacerbate deleterious surface reactions with the electrolyte at the positive electrode. Nonetheless, some new nanotechnology concepts are now providing significant gains in energy density. Advances in ‘core–shell’-gradient lithium metal oxide positive electrode materials — where compositional domains on the nanoscale are vital to their functioning — are helping to solve the conundrum of how to simultaneously achieve high cell voltage and safety. At the negative electrode, Si-based nanostructured ‘matrix’ materials are making inroads as future materials to replace graphitic carbons.

Many next generation, potentially exciting new technologies are even more reliant on nanoscience. They include multivalent intercalation batteries; chemical transformation batteries such as lithium–sulfur, lithium–oxygen and zinc–air; and supercapacitors. The sluggish kinetics that generally characterize divalent cation transport will undoubtedly require nanoscale path lengths to provide practical power densities, especially for Mg²⁺ ion aprotic cells. While Zn²⁺ transport is assisted by the incorporation of water, two recently reported aqueous Zn-ion batteries this year in Nature Energy also benefit from nanodimensional materials; one utilizes a nanoribbon metal oxide cathode (250 nm wide in the transport direction) to enable fast-rate, minimal structural-stress Zn²⁺ mobility (D. Kundu et al., Nat. Energy 1, 16119; 2016), and the other relies on conversion chemistry in nano fibres (H. Pan et al., Nat. Energy 1, 16039; 2016). Regarding chemical transformation batteries, while many barriers remain to realizing their full potential, it is clear that they require cleverly designed electrode nanomaterials and advanced electrode nanoarchitectures. Storage of sulfur or its lithium sulfide end product in the positive electrode in lithium–sulfur cells not only requires that these insulating materials be combined with electronically conductive materials at the nanoscale, but control of deposition of the intermediate polysulfides also necessitates chemistry at the host/sulfur interface that relies on nanoscience. The same is true in related aprotic lithium–air cells for storage of lithium peroxide, whereas rechargeable aqueous zinc–air cells rely on nanoelectrocatalysts.

Like in other fields, while nanoscience has been the victim of some overwrought hype that has failed to deliver real promise, it is equally clear that it has beneficially and irrevocably changed the way energy storage technology will move forward.

If the hurdles can be overcome, then energy storage technology has a much better opportunity to change the way we manage energy.

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Graphene and other 2D materials have been among the major players in nanotechnology in the last ten years. Since its isolation back in 2004, graphene continues to be the subject of a vast amount of fundamental research and experimental device implementations. The demonstration of the first proof-of-concept graphene-based field-effect transistor paved the way to large-scale chemical vapour deposition synthesis of graphene films on metallic substrates, followed by roll-to-roll production of conductive, transparent and flexible graphene coatings, limited in size only by the underlying substrate. This decade of graphene research, from micrometre- sized flakes cleaved with adhesive tape to litres of graphene inks prepared with commercial blenders, draws a timeline clearly indicating an evolution towards up- scalable manufacturing, accompanied by an increasing synergy between academia and industry. As a result, a growing number of enterprises, established companies and emerging spin- o s are seeking ways into the graphene market.

Graphene is only one member of the quickly expanding family of layered materials that can exist in an environmentally stable monolayer form. Each material offers a unique combination of structural, electronic, magnetic, optical and thermal properties, often different from those of its 3D counterpart, and complementary to those of other atomically thin materials. The combination of such monolayer building blocks

enables the fabrication of van der Waals heterostructures, whose functionalities can be engineered according to the individual components, thus opening endless opportunities for the design of a new generation of ‘materials on-demand’ with advanced functionalities.

The shift from academic research to commercialization that 2D materials is facing doesn’t come as a surprise, considering that the Graphene Flagship, one of the major initiatives aimed at funding and boosting the development of this emerging technology, has successfully completed its initial development phase. The future targets are clearly laid out: besides managing knowledge and intellectual property for a realistic exploitation of the available products, a strong effort will be dedicated to prototyping, standardization and benchmarking with respect to competing technologies.

The plethora of achievements reported thus far is impressive, and includes the use of 2D materials in radiofrequency devices for high-speed communication, light detectors, molecular biosensors, flexible RFID tags, smart windows and displays, multifunctional nanocomposites, batteries, supercapacitors and fuel cells. Needless to say, a significant reduction of the costs associated with material production combined with an increase in device performance will be key to realistically adopting 2D materials and embracing such an ambitious industrial shift.

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One of the most striking consequences of working at the nanoscale is emerging quantum behaviour. Thanks to breakthrough developments over the last 10–15 years, it is now possible to study and control the quantum state of individual charges, spins, phonons, photons and other ‘quanta’ in nanoscale devices. Increasingly, it becomes possible to apply this ability in so-called quantum technologies as progress builds on a long tradition of experiments studying quantum mechanical effects in bulk solid samples. These range from solid-state nuclear magnetic resonance experiments controlling ensembles of spins to transport measurements in mesoscopic devices that reveal quantum mechanical effects such as the interference of electron waves. Subsequently, taking the step from ensembles to individual quanta was made possible by two parallel developments.

First, a combination of improved materials and novel operating concepts has dramatically reduced the interaction between selected isolated quanta and their microscopic environment. For instance, by moving from III–V semiconductors to group IV materials such as diamond, silicon and isotopically enriched ^{28}Si , spin coherence times have increased by four orders of magnitude. In superconducting systems, clever qubit designs reducing sensitivity to dielectric loss and extrinsic noise have yielded similar improvements in coherence time.

Second, novel delicate tools and innovative techniques allowed probing and manipulating fragile quantum states in nanoscale devices. The art is to strike the right balance between access and control and isolation and unwanted side effects, such as cross-talk, heating, or worse. The state-of-the-art ability of working with individual quanta available to us now is beautifully used to test the limits and fundamentals of quantum physics.

For instance, nanoscale experiments continue to probe the boundary between the microscopic quantum world and the macroscopic classical world, and have been used to rule out a local realist description of the world.

Increasingly, the focus has shifted towards exploring new real-life technologies that rely on quantum superposition, measurement and entanglement. Tapping into this quantum behaviour allows more sensitive detectors, secure communication, efficient simulation of molecules and materials, and superfast quantum computers. Industry interest is rapidly growing and will propel further progress in the next decade to make quantum technology a reality.

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Nanoscience and nanotechnology have evolved and expanded rapidly as scientists have learned to communicate across their fields of origin, and to share challenges, approaches and tools. This process has made many practitioners and trainees uniquely suited to work across disciplines and to bring new perspectives to key challenges at the nanoscale and beyond. This agility to move across traditional boundaries has made it possible for researchers working in nanoscience and nanotechnology to develop the technologies of the future at all scales. While looking at materials at the smallest scales, the community has learned to ‘think big’. As a result, nanoscientists have made key contributions in proposing and laying out the roadmaps for the BRAIN and National Microbiome Initiatives in the United States and to proposals to address other grand challenges around the world.

While there are few products that can be described as ‘pure’ nanotechnology, many of them in increasingly diverse fields are ‘nano-enabled’, which is a consequence of nanoscientists and nanotechnologists looking beyond their own fields for solutions to a much broader set of problems. There may be no greater expansion than in biology and medicine, where the nanoscale is often the scale of function. There is still much to learn in this area, where the precise placement of chemical functionality, control of mechanical properties and dynamics as well as many other factors are all important for probing, manipulating, inducing and understanding biological function. Likewise, precision will play an important role in effectiveness, safety and regulatory approval for materials, diagnostics and therapeutics.

Our communication skills have not yet translated effectively into our interactions with the public, who ultimately pay for the majority of our research worldwide. We leave the perception of nanoscience and nanotechnology to science fiction writers and others at our own risk. One of the key goals of the next decade is to engage the broader community, to showcase the advances and opportunities that arise from research at the nanoscale and to proceed with due care to make the world a better, safer and healthier place.

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Shortly after the US National Nanotechnology Initiative (NNI) had been launched by President Clinton in January 2000, the social sciences and humanities (SSH) were invited to participate in the project. At that time, hardly anyone knew anything about nanotechnology other than Eric Drexler’s vision and the science fiction stories that both had circulated since the late 1980s under that label. The NNI picked not only Drexler’s term but also slogans such as ‘shaping the world atom by atom’ and made promises of ‘the next industrial revolution’ with a transhumanist touch. Avoiding failures of the Human Genome Project, the SSH were called on from the beginning to research the ‘societal and ethical implications of nanotechnology’. To many of us, that at first sounded like an invitation to academic science fiction writing.

However, the call from the NNI turned out to be extremely fruitful because it allowed new kinds of interdisciplinarity and SSH research perspectives that soon spread internationally. Once embedded in a science setting, SSH scholars learned to distinguish the real ethical from the fictitious issues, engaged in outreach activities (from science cafés to focus groups), studied the manifold science–society interactions, the role of visions and images in science popularizations and science policy, as well as the impact of nanotechnologies on the scientific landscape, the public image of science and the global development.

During the first decade, nanotechnology looked more like a global social movement rather than a developing research field. Because of vague definitions and unprecedented funding opportunities, nanotechnologies multiplied and grew at tremendous speed, largely by relabelling established research. If the hype had continued, the number of nano groups, centres and departments worldwide would

nowadays outnumber those of physics and chemistry together (J. Schummer, *Scientometrics* 70, 669–692; 2007). That did not happen though. Nanotechnology did not turn into a new discipline of its own comparable to materials science and engineering, nor was it a temporary appearance. Instead it has developed into a large set of specialized research fields, as diverse as nanopore DNA sequencing and functional nanomaterials, each of which has established a remarkably stable interdisciplinary setting of outstanding productivity.

At the end of the hype cycle, when public excitement vanishes, fields usually become more productive, albeit less visible. Although nanotechnology's current productivity, with potentially large impact on society, would require more SSH research, funding and interest therein have dropped. Perhaps one should rethink the role of the SSH within the hype cycle.

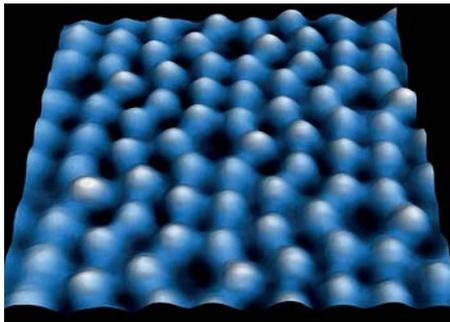
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Figures:

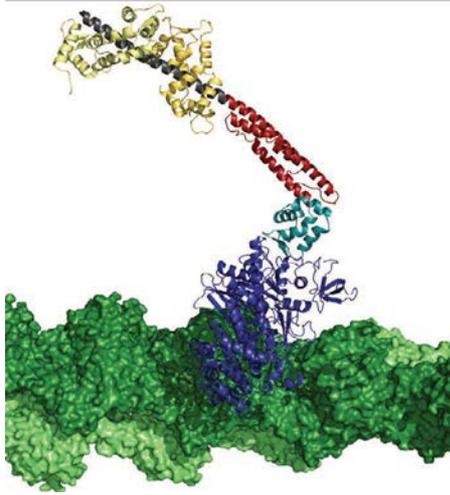


Nanoparticles destroying tumours.

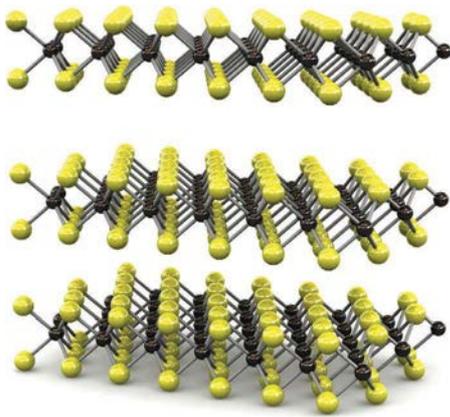
Image: Nicolle R. Fuller / Science Photo Library / Getty Images.



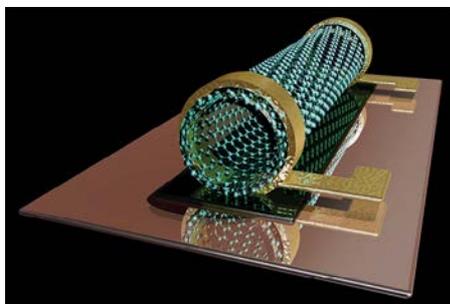
Atoms on a silicon surface. Image: Andrew Dunn / Alamy Stock Photo



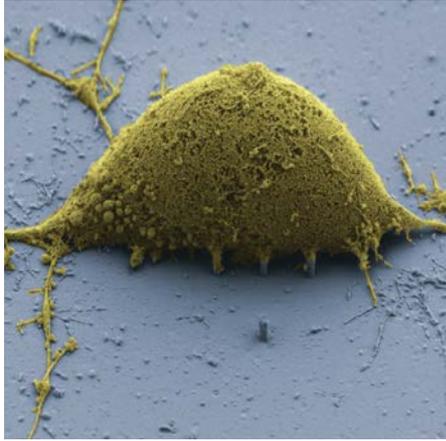
Molecular motor protein. Image from L. Chen et al., Nat. Nanotech. 7, 252–256 (2012), Nature Publishing Group.



The structure of molybdenum disulfide. Image from B. Radisavljevic et al., Nat. Nanotech. 6, 147–150 (2011), Nature Publishing Group.



Carbon nanotube transistor. Image: Martin McCarthy / E+ / Getty Images.



Neurons on nanowires. Image from
J. T. Robinson et al., *Nat. Nanotech.* 7, 180–184 (2012), Nature Publishing Group