Commercializing nanotechnology

Laura Mazzola

Nanotechnology has solid commercial prospects, but the process of converting basic discoveries into marketable products will be long and hard.

Nanotechnology has been showcased and revisited a number of times over the past decade, with each pass hinting at the promise of a revolutionary, ubiquitous technology. The editors of *Science* magazine fell under its spell in 2001, when they declared nanoelectronic circuits the breakthrough of the year[1]. Today, nanotechnology does have solid commercial prospects, but much of the media buzz is pure speculation, and most recent advances are closer to nanoscience than nanotechnology.

Though commercial nanotechnology is still in its infancy, the rate of technology enablement is increasing, in no small part as a result of the substantial government-mandated funds that have been directed toward nanotechnology. Nanotechnology is also receiving particular attention in academia, where new programs are being designed to accelerate the rate of innovation through interdisciplinary working teams (**Table 1**).

This article presents an overview of some of the early commercial efforts using nanotechnology in the life sciences (loosely termed nanobiotechnology). The earliest products applied tools from microscopy and microfluidics to manipulate materials at the nanometer scale (**Fig. 1**). These are being followed to the market by systems that use nanomaterials as molecular tags (*e.g.*, quantum dots), composite materials (*e.g.*, peptide-lipid assemblies) and biosensors (*e.g.*, carbon nanotube arrays). Though several years further from commercialization, products using nanostructured materials for drug delivery and tissue engineering are approaching the clinical testing phase. Farthest out on the commercial horizon are integrated nanoelectronic devices, which promise intriguing health-care applications such as implantable sensors that monitor and respond to health status. (More general information on nanotechnology can be obtained from the National Nanotechnology Initiative's (NNI) website: http://www.nano.gov/.)

> Given nanotechnology's nascent stage, there are understandably few investors taking the risk in early-stage innovation.

Challenges to commercialization

Along the path to commercialization, nanotechnology's biggest liability is its novelty. Inventions often attract attention because of their ingenuity, but a product must also be useful and compelling. Although most people can imagine how nanotechnology could transform personal medicine, the reality is that nanotechnology is years from being able to fulfill that demand. A more realistic goal would be to identify a market for the tools that nanotechnology can provide today.

The first step to product development is positioning the technology—what is nanotechnology's competitive edge? There is no simple answer to this question because of the enormous breadth of devices that can be built from nanoscale materials. Methods of synthesis and construction differ greatly, as do the performance aspects of each system.

The second step is to develop applications that leverage the unique aspects of the nanoscale system, whether in photovoltaics, memory storage or medical devices. Much of nanotechnology (particularly nanobiotechnology) is still at these early stages, requiring significant incubation for application and assay development.

Given nanotechnology's nascent stage, there are understandably few investors taking the risk in early-stage innovation. Many are waiting on the sidelines for an early indication in product development. Government funding has become the main source of early support for nanotechnology research and development (R&D), particularly since the establishment of the US NNI in 2000 (Arlington, VA, USA) and other initiatives like it around the world (see p. 1127).

Nanotechnology significantly extends our capabilities in resolution and sensitivity, but is there currently a need for these products? As outlined below, some of nanotechnology's tools are complementary to biotech's picks and shovels (*e.g.*, contact microprinting technology could permit the creation of new types of arrays with smaller feature size and greater sensitivity). In other areas, there is a clear indication that nanotechnology will outperform micron-scale technology platforms. For those nanotechnologies that offer what may be considered incremental performance, industries that have invested heavily over the past few years in other technology platforms may show significant resistance to adoption.

Large-scale production and manufacturing is another challenge. Can nanoscale systems be produced cheaply and in mass quantities? Nanoparticle synthesis has been adapted for bulk production, and several companies (such as Carbon Nanotechnologies, Houston, TX, USA, and Sumitomo, Tokyo, Japan) are already mass producing carbon fullerenes and nanotubes. But the production of integrated nanoscale devices is a formidable process, even using micron-scale tools.

Self assembly may provide a key to nanoscale device manufacturing. Nature has

Laura Mazzola is at Excellin Life Sciences, 755 East Capitol Avenue #0201, Milpitas, California 95035, USA, and chairs the Forum on NanoBioConvergence (www.nanobioconvergence.org). e-mail: ltmazzola@earthlink.net

Table 1 US universities with federally funded nanotechnology programs

University	Program	Government agency
Rice University (Houston, TX)	Nanoscience in Biological and Environmental Engineering	National Science Foundation (NSF)
Northwestern University (Evanston, IL)	Integrated Nanopatterning and Detection	NSF
Rensselaer Polytechnic Institute (Troy, NY)	Directed Assembly of Nanostructures	NSF
Cornell University (Ithaca, NY)	Nanobiotechnology, Science and Technology Center	NSF
Columbia University (New York, NY)	Center for Electron Transport in Molecular Nanostructures	NSF
University of California, Los Angeles (Los Angeles, CA)	Institute for Cell Mimetic Space Exploration	National Aeronautics and Space Administration (NASA, Washington, DC)
Texas A&M University (College Station, TX)	Institute for Intelligent Bio-nanomaterials and Structures for Aerospace Vehicles	NASA
Princeton University (Princeton, NJ)	Bioinspection, Design and Processing of Multifunctional Nanocomposites	NASA
University of California, Santa Barbara; Massachusetts Institute of Technology (MIT; Cambridge, MA); and California Institute of Technology (Caltech; Pasadena, CA)	Institute for Collaborative Biotechnology	US Army
MIT	Institute for Soldier Nanotechnologies	US Army

evolved the ultimate system for nanoscale engineering, supplying at once building blocks and self-replicating tools for molecular design. Using a similar process of chemical and physical recognition to guide nanocomponent assembly, the devices can evolve from a one-off, expert-guided process to a more robust means for nanocomponent assembly (**Box 1**).

The journey to market

Nanotechnology enables a broad range of products spanning research, medical and consumer goods. Some existing commercial technologies, such as liposomes or Affymetrix's (Santa Clara, CA, USA) oligonucleotide chips, fall under the working definition of nanotechnology. Other systems, such as nanosensors, are so novel that they are likely to be years away from commercial prototypes.

The use of nanotechnology can be categorized by application, in which the nanocomponents enhance performance in quite different areas. Here, I define the primary fields of application as bioanalysis, drug delivery and therapeutics, and biosensors and medical devices. There is clearly crossover between these areas, and in fact many of the developments in one category catalyze development in another.

Bioanalysis. The earliest commercial nanotechnology is atomic force microscopy, now known more generally as scanning probe microscopy (SPM). Using a silicon-based needle of atomic sharpness, this approach was first used to image the topography of surfaces with atomic-scale precision[2]. The probe, positioned so close to the surface that it interacts with the atoms as it scans the surface, can also be used to pick atoms up and move them around for bottom up nanoscale assembly (**Box 2**). The technology thus provides an accessible benchtop device for nanoscale engineering and analysis.

Although SPM is used primarily for analytical research, several companies have automated it for read-write capabilities (**Table 2**). NanoInk (Chicago, IL, USA) and

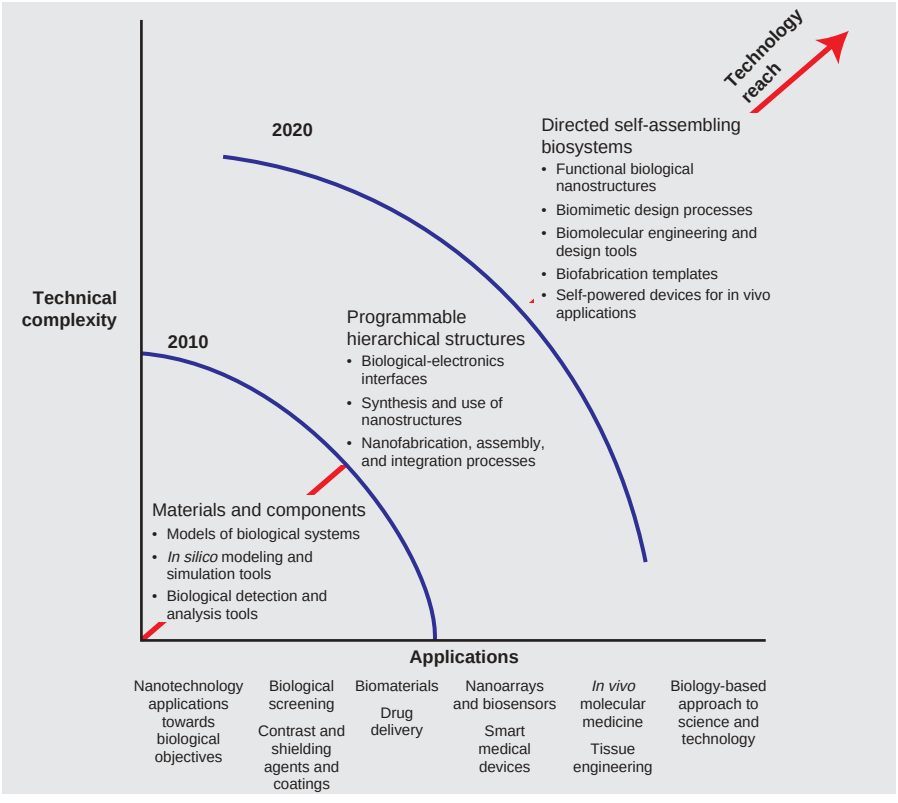

Figure 1 Nanobiotechnology: a continuum of opportunity for nanotechnology in the life sciences. Source: SRI Consulting Business Intelligence (SRIC-BC; Menlo Park, CA, USA).

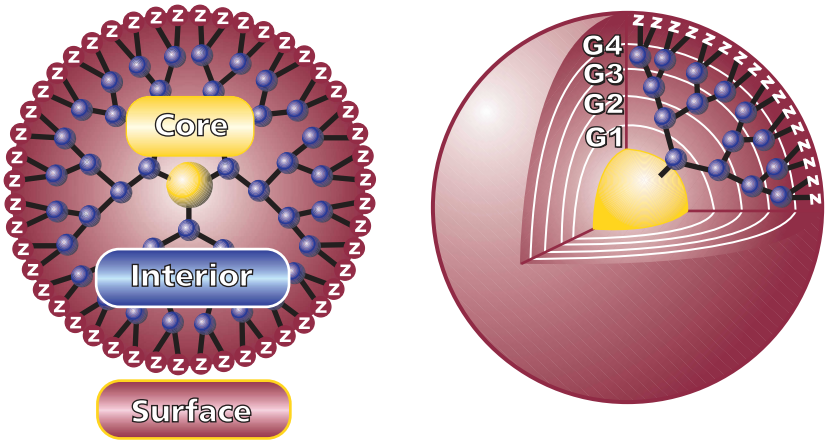

Figure 2 Dendrimer architecture in two and three dimensions. A dendrimer can be defined into a multitude of structures by tuning the three architectural components: the core (yellow), the interior area containing branch upon branch of repeat units (blue) and an exterior surface of terminal moieties attached to the outermost generation (red.) Source: Dendritic Nanotechnologies

BioForce Nanosciences (Ames, IA, USA) are creating truly nanoscale molecular arrays using SPM tools to print biomolecular array elements. Because the instrument has both print and read capability, these systems do not require molecular labeling for ultrahigh-throughput bioanalysis.

Some micron-scale technologies can be considered platforms for nanoscale bioanalysis, and these products have already proven their value in the marketplace. For example, Caliper Technologies' (Mountain View, CA, USA) microfluidic systems routinely transport nanoliter volumes of fluid for nucleic acid and protein analysis. Affymetrix's and Nanogen's (San Diego, CA, USA) microarray platforms manipulate subnanogram quantities of genetic material. These technologies are converging to submicron resolution because of the demand for increased sensitivity and throughput for genomics and proteomics. Nanomaterials and true nanoscale devices are also being developed to address the need for greater sensitivity in high throughput screening (**Box 3**).

Nanoparticles (dots, bars, dendrimers or colloids) provide molecular labels that are highly stable, readily multiplexed and comparable in size to the molecular components of interest. Quantum dots leverage semiconductor materials to provide robust quantum 'fluorescence,' with an array of colors that requires only a single illumination source. Quantum dots with a variety of conjugates and colors are currently available from Quantum Dot (Hayward, CA, USA) and Evident Technologies (Troy, NY, USA).

Nanobars, constructed from alternating layers of reflective metals, are currently in development at NanoPlex (Mountain View, CA, USA) and Nanosys (Palo Alto, CA, USA). Used as another form of molecular tag, they can be optically scanned as literal bar codes to differentiate molecular species. Such systems offer advantages over conventional labeling in that there are a large number of different labels that can be constructed, multiplexing is possible, and the signal is long-lived.

Colloidal gold and silver are used already in molecular detection and separation, where their size can be reproducibly engineered to submicron dimensions for controlled chemical architecture and high surface-to-volume loading capacity. Companies working in this area, such as Nanosphere (Chicago, IL, USA) and Genicon Sciences (San Diego, CA, USA), are taking advantage of the optical difference between solution-bound nanoparticles and

Table 2 Selected nanobiotechnology companies developing bioanalysis applications

Technology	Companies	Platform[a]
SPM	Hitachi High Technologies (London, UK)	Electron-beam lithography (on market)
	Imago Scientific Instruments (Madison, WI)	Leap atom probe microscope (on market)
	Veeco (Woodbury, NY)	Near-field scanning optical microscope (on market)
Arrays	Affymetrix (Santa Clara, CA)	High-density oligonucleotide (GeneChip) arrays (on market)
	BioForce Nanosciences (Ames, IA)	Nanoarrays ~10,000-fold smaller than conventional arrays (on market)
	Nanogen (San Diego, CA)	Oligonucleotide arrays with polarized features (on market)
	NanoInk (Chicago, IL)	Dip-pen nanolithography system (on market)
Molecular tags	Dendritic Nanotechnologies (Mt. Pleasant, MI)	Dendrimers (on market)
	Evident Technologies (available through Ocean Optics, Dunedin, FL, USA)	Semiconductor nanocrystal quantum dots (on market)
	Genicon Sciences (San Diego, CA)	Two-color microarray tool kit; resonance light-scattering detection and imaging instrument
	NanoPlex (Mountain View, CA)	Nano-bar-codes particle kit (on market)
	Nanosphere (Chicago, IL)	Gold nanoparticle probes and detection system
	Quantum Dot (Hayward, CA)	Quantum-dot conjugates (streptavidin, protein A, biotin) (on market)
Microfluidics	Caliper Technologies (Mountain View, CA)	Microfluidics (LabChip; on market)
	Fluidigm (South San Francisco, CA)	Multilayer soft lithography microfluidics
	Nanostream (Pasadena, CA)	High-throughput screening platforms
	Surface Logix (Brighton, MA)	High-throughput screening platforms using soft lithography and biosurface chemistry

[a]Unless otherwise specified in parentheses, platform under development. Locations are in United States unless otherwise stated.

aggregates formed by molecular affinity in designing assays.

Drug delivery and therapeutics. Because of their size, nanoscale assemblies offer unique opportunities in drug delivery and in therapeutics (**Table 3**). Early 'cosmeceutical' products have included liposomes (lipid-based vesicles) commonly used in topical lotions and titanium nanoparticles used in sunscreen produced by Procter & Gamble (Cincinnati, OH, USA) and L'Oréal (Westfield, NJ, USA).

Liposomes have been under development as delivery vehicles since the early 1990s. They have low toxicity, are versatile in size, composition and bilayer fluidity, and are capable of displaying drugs on their surface or encapsulating them within. However, they also have suffered from low delivery efficiencies (particularly in gene therapy applications) and high drug leakage (although the latter problem may be remedied by the introduction of colloidally stabilized liposomes). As liposomes have been covered in detail elsewhere, I will not discuss them further here.

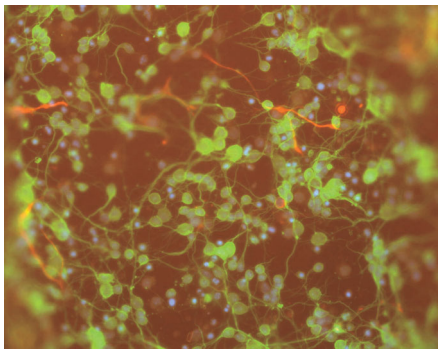

Figure 3 Neurons (neurons) penetrating into a three-dimensional network of the self-assembling nanofibers. Source: NanoMateria

The surface chemistry of nanoparticles can be modified to display high concentrations of a therapeutic drug and/or molecules for tissue-specific recognition. Dendrimers—polymeric macromolecules structured as concentric shells—are one type of nanoparticle that can be functionalized with chemical groups to allow attachment of drugs or molecules of interest (**Fig. 2**). Companies such as Dendritic Nanotechnologies (Mt. Pleasant, MI, USA) and Alnis Biosciences (Emeryville, CA, USA) are already marketing dendrimers for use in research. In July, a first dendrimer drug, developed by StarPharma (Melbourne, Australia) for use against HIV, received regulatory clearance for phase 1 clinical trials from the US Food and Drug Administration (FDA; Rockville, MD, USA). The drug is a topical gel containing an anionic polyamidoamine dendrimer that is postulated to interfere with the entry and fusion process of the HIV particle.

Other types of nanoparticle are also being developed for use in drug delivery. For example, C Sixty (Houston, TX, USA) is investigating fullerenes (clusters of 60 carbon atoms) as a means of delivering therapeutics, and Nanospectra Biosciences (Houston, Texas, USA) is developing nanoshells comprising a silica core and an ultrathin gold coat that will allow localized payload delivery or tissue ablation triggered by a secondary mechanism, such as light activation. Clearly, such platforms are

Box 1 Making things grow

Taking a page from nature, researchers are using biological molecules and structures as scaffolds for building and growing materials at the nanoscale. Exploiting the molecular recognition properties of DNA, for example, Chad Mirkin (Northwestern University, Evanston, IL, USA) and others have organized inorganic nanoparticles (such as colloidal gold) into ordered macrostructures[3]. Another approach that has seen some success is the use of viruses as templates for nanostructures. For Angela Belcher, a biochemist turned electrical engineer turned molecular biologist at the Massachusetts Institute of Technology (MIT; Cambridge, MA, USA), the inspiration came from abalone shells, in which proteins function as templates to control the deposition of calcium carbonate–based materials with precision and crystallographic specificity. Belcher wanted to be able to exert the same level of control over other types of material, particularly those with interesting electrical or optical properties. But, she notes, biological systems are equipped to handle only a few elements—most of the periodic table is virtually untouched, and untouchable, by nature. So she turned to phage display as a way to evolve and select proteins with the ability to recognize other elements, starting with some used in the semiconductor industry. She showed in 2000 that she could evolve peptides to bind a range of semiconductor surfaces with high specificity and with particular crystallographic orientation[4]. She has gone on to show that the bacteriophage M13 can be made to pick just about up anything and organize it into nanoscale structures. Recently, she showed that quantum-dot nanowires could be grown on the head of M13 virus particles, which self-assemble into different orientations and phases[5]. So perfect were the crystals, she says, that she could shine a laser through the film and see a diffraction pattern on the wall (**Fig. 4**). This kind of precision will be hard to achieve with other kinds of nanomanufacturing processes. In addition, Belcher is looking for routes to build new materials on the nanoscale using conditions that are environmentally friendly—no organic solvents, or extremes of temperature and pH.

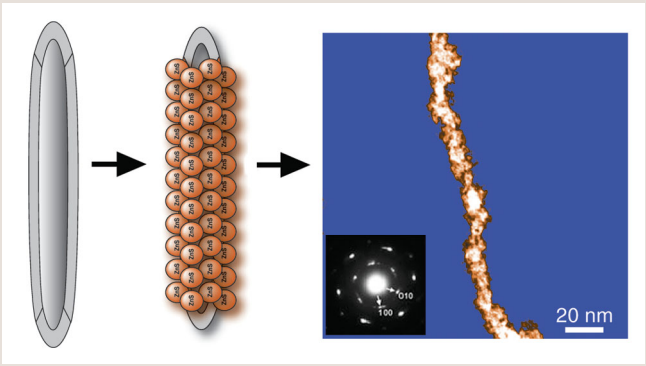

Figure 4 Images of engineered virus directing nanocrystal synthesis. (**a**) Wild-type virus (no engineered insert). (**b**) Engineered virus nucleating nanowires. (**c**) Scanning transmission electron microscope image of a straight region of a viral nanowire at high magnification showing tightly packed nanocrystal morphology. Insert: Electron diffraction pattern. Image courtesy of Angela Belcher, Massachusetts Institute of Technology.

Belcher has formed a company (Semzyme, Cambridge, MA, USA) to exploit her work with biomimetics, and she is part of the newly announced Institute for Biotechnology Collaboration, which joins researchers at MIT, Caltech (Pasadena, CA, USA) and the University of California, Santa Barbara (UCSB, Santa Barbara, CA, USA). *Laura DeFrancesco*

Box 2 Bottom-up or top-down?

Two distinct strategies have been used to explore the nanometer domain (*i.e.,* 1–100 nm)—often referred to as 'bottom-up' and 'top-down' development. For the former, nanoscale materials are assembled from smaller molecular and atomic components. Here, nanomaterials, such as quantum dots and nanobars, can be synthesized or designed layer by layer, blending techniques from chemical engineering and material science. The innovation lies in precise control of the material's size and resulting optical and electronic properties. Dendrimer and liposome technologies are derived from well-established bottom-up synthetic techniques, built to scale using chemistry and self-assembling lipids, respectively.

The top-down development path is guided to the nanoscale by fabrication tools from the electronics industry, where techniques of lithography, embossing and contact printing are used to create micron-scale array elements and fluidic pathways. These micron-sized components can be used to manipulate submicron (nanometer) amounts of material.

Ultimately, nanotechnology-based products will require a convergence of the two approaches for practical use, both to engineer the nanoscale device and to interface with the outside world. The bottom-up approach permits control of the chemical and structural architecture; however, manual assembly of individual nanometer-sized components is clearly prohibitive in time and cost. Top-down technologies provide a progressive interface from the real world (meters, millimeters, microns) to control at the nanometer scale. ***LM***

much earlier in development than liposomes.

Highly insoluble drugs may be reformulated as nanoparticles for more efficient and controlled uptake, as the small size may allow them to more readily diffuse through membranes. This approach was developed years ago by Elan Pharmaceuticals (Dublin, Ireland) through a top-down milling process, which is now being commercialized by NanoCrystal Technologies (King of Prussia, PA, USA). Other companies working in this field include NanoMed Pharmaceuticals (Lexington, KY, USA) and SkyePharma (London, UK), which use synthetic methods to more reliably engineer particle size.

And finally, there are some interesting applications of nanoparticles for cholesterol removal, nutritional supplements and antimicrobials, which are being pursued by companies such as BioSante Pharmaceuticals (Lincolnshire, IL, USA) and NanoBio Corporation (Ann Arbor, MI, USA).

Biosensors and medical devices. Nanotechnology holds great promise for innovation in biosensing, though integration and assembly may be stumbling blocks to early commercialization (**Table 4**). Nanotubes and nanowires have demonstrated unprecedented sensitivity for molecular detection, where surface-binding events detectably perturb the material's electronic properties.

Novel techniques of surface engineering and patterning also permit new methods of molecular detection, as shown in work using nanopore structures for single-molecule detection—with efforts from US Genomics (Woburn, MA, USA), Agilent (Palo Alto, CA, USA) and 454 Life Sciences (Branford, CT, USA).

Other applications of nanoparticles include their use as contrast agents for magnetic resonance imaging and X-ray imaging at companies such as Nanospectra Biosciences and Advance Magnetics (Cambridge, MA, USA) as well as some larger corporations, such as General Electric (Stamford, CT, USA) and Philips Medical Systems (Andover, MA, USA). Nanoparticle contrast agents can provide better image resolution, tissue-specific targeting and increased retention in the blood pool.

Nanomaterials also have an increasing role in tissue engineered materials and devices. For example, AngstroMedica (Newton, MA, USA) is using nanostructured materials to stabilize and regenerate bone matrix material from calcium and phosphate, and pSiMedica (The Malverns, UK) is using biodegradable silicon for bone implants. Other types of nanoscale architecture are being developed for nerve

Table 3 Selected nanobiotechnology companies developing drug delivery and therapeutic applications

Focus	Company	Platform[a]
Therapeutics	Alnis Biosciences (Emeryville, CA)	Polyfunctional nanoparticles
	ALZA (Mountain View, CA)	Lipid nanoparticles with polyethylene glycol coating; Doxil (doxorubicin liposome) on the market
	NanoCrystal Technologies (King of Prussia, PA)	NanoMill technology for creating nanocrystals
	NanoMed Pharmaceuticals (Kalamazoo, MI)	Nanotemplate engineering for drug and vaccine delivery systems
	Alnis Biosciences (Emeryville, CA)	Polyfunctional nanoparticles
	StarPharma (Melbourne, Australia)	VivaGel anti-HIV dendrimer (phase I)
Drug delivery	Advectus Life Sciences (West Vancouver, BC, Canada)	NanoCure system for delivery of anticancer drugs across blood-brain barrier
	BioDelivery Sciences (Newark, NJ)	BioOral nanocochleates cigar-shaped structures comprised of lipid bilayers
	BioSante Pharmaceuticals (Lincolnshire, IL)	Nanoparticulate platform (CAP) for drug delivery (phase I)
	C-Sixty (Houston, TX)	Fullerene-based drug delivery
	CytImmune Sciences (College Park, MD)	Tumor necrosis factor bound to colloidal gold nanocrystals for targeting tumors; vector with docking site for gene therapy
	NanoCarrier (Chiba, Japan)	NanoCap micellar nanoparticle for water-insoluble drugs (under development)
	NanoBio (Ann Arbor, MI)	Antimicrobial nanoemulsions (phase II)
	NanoSpectra Biosciences (Houston, Texas)	Nanoshells for optical therapies
	Targesome (Palo Alto, CA)	Injectable nanospheres for therapeutic or diagnostic agents

[a]Unless otherwise specified in parentheses, technology in preclinical development. Locations are in United States unless otherwise stated.

Box 3 Nanotechnology takes on microarrays

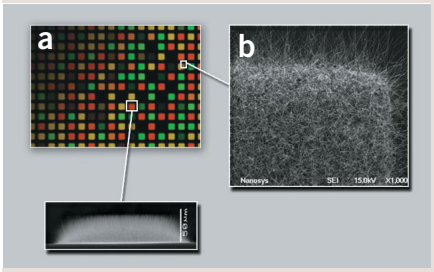

Figure 5 Nanosys nanostructured microarray. (**a**) Top-view scanning electron microscopy (SEM) micrograph of nanostructured array feature. (**b**) Side-view SEM micrograph of nanostructured array feature. Open architecture mesh wets evenly and allows analyte diffusion to binding sites. Source: Nanosys.

Although massively parallel platforms such as microarrays have engendered excitement because of their unprecedented throughput, they remain hampered by problems such as reproducibility, sensitivity and poor signal-to-noise ratios. Two companies are looking to nanotechnology to solve these problems. Nanosys has developed a nanomaterial (nanowire) to serve as a substrate for microarrays of DNA and proteins. According to Stephen Empedocles, Nanosys director of business development, the nanowire morphology (**Fig. 5**) provides a 100-fold higher binding area without reducing binding kinetics. Although other surfaces that increase binding capacity, and hence sensitivity, often exhibit considerably slower binding reactions, Empedocles claims this is not the case with nanowires. Nanosys's nanomaterial could be used to create arrays of any dimension, including at the nanoscale, but the company is fashioning its first product to be compatible with today's microarray platforms. The substrate can be mounted on conventional microscope slides, used with existing fluorescent assay chemistries and scanned using standard array readers. Nanosys will start alpha testing its system later this month.

BioTrove (Woburn, MA, USA) has taken a different approach to the sensitivity problem with microarrays, one that also does not require new or specialized equipment. The company has created a plate with over 24,000 one-nanoliter reaction chambers in which miniaturized PCR amplifications—the 'gold standard' according to company president and CEO Cloin Brenan, for increasing sensitivity in genomic experiments—can be carried out. With conventional technology, the cost of conducting thousands of PCR reactions could be prohibitive, but with BioTrove's platform (the 'LivingChip'), reaction volumes are 200 times smaller than in microplate screening systems, making PCR an affordable option, according to Brenan. The chip is designed to work with ordinary thermal cyclers and scanning devices. The company is set to release its first product, a SNP Chip that will be preloaded with PCR primers and assay buffers for 3072 reactions, to be released in the third quarter of 2004. *LD*

regeneration at NanoMateria (Chicago, IL, Fig. 3).

The use of nanotechnology in implantable devices is also attracting the attention of industry leaders, such as Guidant (Indianapolis, IN, USA) and Medtronic (Minneapolis, MN, USA). This is because nanoscale architecture can be used to enhance integration of artificial structures and living tissue, presenting a more size-appropriate interface to biological systems. Most of these devices are still years away from clinical trials, however. Companies developing such systems include iMEDD (Columbus, OH, USA), which is etching nanopores into implantable drug-delivery devices for controlled release of therapeutics. Elsewhere, collaborative programs at the National Aeronautics and Space Agency Ames Research Center (Moffet Field, CA, USA) and Stanford University (Stanford, CA, USA) are attempting to incorporate nanoporous electrodes into retinal implants to enable a functional interface with the nerves of the retina. In addition, companies such as Cymbet (Elk River, MN, USA) and NanoGram Devices (Fremont, CA, USA) are working on nanostructured materials that can manufacture their own electrical power.

Table 4 Selected nanobiotechnology companies developing medical devices (including tissue engineering)*

Focus	Company	Platform under development
Tissue engineering	AngstroMedica (Newton, MA)	Nanostructured hydroxyapatite artificial bone matrix
	NanoMateria (Chicago, IL)	Nanostructured material for heart, cartilage and nerve regeneration
	pSiMedica (The Malverns, UK)	BioSilicon for bone implants
Biosensors	Agilent (Palo Alto, CA)	Nanopore sequencing (in collaboration with Harvard University)
	454 Life Sciences (Branford, CT)	PicoTiter sequencing plate
	US Genomics (Woburn, MA)	Single-strand DNA sequencing
	Nanomix (Emeryville, CA)	Nanotube chemical/biosensors

*Locations are in United States unless otherwise stated.

Regulatory and safety issues

Companies require customers, and if a new technology is to survive, the public market must embrace it. It would be a mistake to underestimate the impact of public acceptance or the influence it has on the political process for funding early-stage development. Public outcry against genetically modified foods, somatic cell nuclear transfer and embryonic stem cell research demonstrates how a technology can stall when risks are oversimplified and concerns (some of them justified) are magnified through fear and uncertainty.

Much of the recent public debate on nanotechnology has foundered because the technology is too diverse and because there has not been enough real data for rational discussion. These issues surround any innovative technology at its early stage, when science fiction often captures more attention that the science itself. It would be naive to claim all applications of nanotechnology as potentially suspect, particularly since the

moniker encompasses so many different applications—some old, some new. The attitudes of watchdog groups such as Greenpeace and Canada's action group on Erosion, Technology and Concentration (ETC Group, Winnipeg, Canada) range from cautious to extreme, but these groups highlight the potency of public curiosity and concern.

The request for an in-depth environmental analysis of technology is reasonable, given previous concerns about transgenic organisms and the unpredicted environmental impact of materials such as asbestos and plastics. Issues relating to nanoparticle clearance and tolerance do need to be investigated—researchers, as well as the general public, will benefit from this information. Academic centers such as the Center for Biological and Environmental Nanotechnology (CBEN; Rice University, Houston, TX, USA) have been formed specifically to address the toxicology issues (see p. 1166). In the United Kingdom, the government has commissioned the Royal Society to study possible developments in nanotechnology and whether they are likely to raise new ethical, health and safety, or social issues. In addition, groups such as the NanoBusiness Alliance have formed task forces to specifically address the public perception about the risks of nanotechnology.

Conclusions

Nanotechnology is not so much an industry as a collection of tools and approaches, which will achieve commercial success only when compelling applications are found and adopted. Many nanotechnology applications are still at the concept level, requiring much more basic research before they can be incorporated into a viable product. Once designed, nanotechnologies must also overcome difficulties relating to robust production and large-scale manufacturing. It will also be necessary to follow through on rigorous safety studies to ensure public acceptance. Universal to each step in this process is the need for funding and support as a prerequisite. Government funds may provide the early-stage investment in this high-risk, high-payoff technology, but ultimately private or corporate investment will be required to carry the process to fruition.

Finally, nanotechnology is an international phenomenon. Although US-based companies are predominantly mentioned here, these companies reflect a supportive entrepreneurial culture rather than true market dominance. Nearly every economic center has developed an interest in nanotechnology, and some have made huge commitments toward research in step with US funding. Though the United States has a lead in commercial development, as shown by the number of companies involved in active development in this area, it is too early to decide where the ultimate profits in nanotechnology will be made. The blockbuster nanotechnology products will certainly address the health-care market, but whether these products will be as multinational as in the pharmaceutical market, it is far too early to guess.

1. Service, M. Molecules get wired. *Science* **294**, 2442–2443 (2001).
2. Binning, G. and Quate, C.F. Atomic force microscope. *Phys. Rev. Lett.* **56**, 930-933 (1986).
3. Mirkin, C.A. *et al.* A DNA-based method for rationally assembling nanoparticles into macroscopic materials. *Nature* **382**, 607–609 (1996).
4. Whaley, S.R. *et al.* Selection of peptides with semiconductor binding specificity for directed nanocrystal assembly. *Nature* **405**, 665–668 (2000).
5. Mao, C *et al.* Viral assembly of oriented quantum dot nanowires. *Proc. Natl. Acad. Sci. USA* **100**, 6946–6951 (2003).