

# Nanotechnology: convergence with modern biology and medicine

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The worldwide emergence of nanoscale science and engineering was marked by the announcement of the National Nanotechnology Initiative (NNI) in January 2000. Recent research on biosystems at the nanoscale has created one of the most dynamic science and technology domains at the confluence of physical sciences, molecular engineering, biology, biotechnology and medicine. This domain includes better understanding of living and thinking systems, revolutionary biotechnology processes, the synthesis of new drugs and their targeted delivery, regenerative medicine, neuromorphic engineering and developing a sustainable environment. Nanobiosystems research is a priority in many countries and its relevance within nanotechnology is expected to increase in the future.

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## Abbreviations

**FY** fiscal year  
**NNI** National Nanotechnology Initiative  
**NSET** Nanoscale Science and Engineering Technology  
**NSF** National Science Foundation

## Introduction

Nanotechnology is the ability to work at the atomic, molecular and supramolecular levels (on a scale of ~1–100 nm) in order to understand, create and use material structures, devices and systems with fundamentally new properties and functions resulting from their small structure [1\*\*]. All biological and man-made systems have the first level of organization at the nanoscale (such as a nanocrystals, nanotubes or nanobiomotors) where their fundamental properties and functions are defined. The goal of nanotechnology might be described by the ability to assemble molecules into objects, hierarchically along several length scales, and to disassemble objects into molecules. This is what nature already does in living systems and in the environment. Rearranging matter at the nanoscale using ‘weak’ molecular interactions, such as

van der Waal forces, hydrogen bonds, electrostatic dipoles, fluidics and various surface forces, requires low-energy consumption and allows for reversible or other subsequent changes. Such changes of usually ‘soft’ nanostructures in a limited temperature range are essential for bioprocesses to take place. Biosystems are governed by nanoscale processes that have been optimized over millions of years; examples of biostrategies have been surveyed [2]. Smalley [3] classified nanotechnology into two categories: ‘wet’ nanotechnology (including living biosystems) and ‘dry’ nanotechnology. Research on dry nanostructures is now seeking systematic approaches to engineer man-made objects at the nanoscale and to integrate nanoscale structures into large-scale structures, as nature does. Although the specific approaches may be different from the slowly evolving living systems in aqueous medium, many concepts such as self-assembly, templating of atomic and molecular structures on other nanostructures, interaction on surfaces of various shapes, self-repair, and integration on multiple length scales can be used as sources of inspiration.

Nanobiotechnology is defined as a field that applies the nanoscale principles and techniques to understand and transform biosystems (living or non-living) and which uses biological principles and materials to create new devices and systems integrated from the nanoscale. The integration of nanotechnology with biotechnology, as well as with infotechnology and cognitive science, is expected to accelerate in the next decade [4\*\*]. The convergence of nanoscale science with modern biology and medicine is a trend that should be reflected in science policy decisions [5\*\*,6]. The aim of this review is to highlight recent scientific advances, and on this basis to outline corresponding science and funding policy developments.

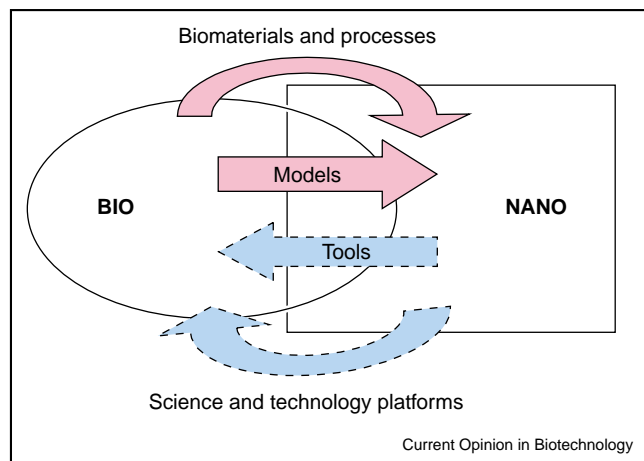
## Confluence of biology and nanotechnology

Nanotechnology provides the tools and technology platforms for the investigation and transformation of biological systems, and biology offers inspiration models and bio-assembled components to nanotechnology (Figure 1).

### Nanotechnology provides the tools to measure and understand biosystems

Investigative methods of nanotechnology have made inroads into uncovering fundamental biological processes, including self-assembly, cellular processes, and systems biology (such as neural systems). Key advances have been made in the ability to make measurements at the sub-cellular level and in understanding the cell as a highly organized, self-repairing, self-replicating, information-rich molecular machine [7,8]. Single-molecule measurements

Figure 1



Key interactions between fields of biology and nanotechnology.

are shedding light on the dynamics and mechanistic properties of molecular biomachines, both *in vivo* and *in vitro*, allowing the direct investigation of molecular motors, enzyme reactions, protein dynamics, DNA transcription and cell signaling. It has also been possible to measure the chemical composition within a single cell *in vivo*. Measurements of the intermolecular mechanics of a single protein molecule, polymer molecule or 'soft' nanoparticle have been performed with atomic force microscopy (AFM) [9]. Nanoscale instrumentation has also allowed measurements of small RNAs (also called 'nanoRNAs' or short stretches of RNA ranging in length between 21 and 28 nucleotides) and their significant effect on gene expression [10]. The discovery of these small RNAs was selected as the Science 'Breakthrough of the Year' in 2002. Furthermore, a biological force microscope, which is capable of quantitatively measuring interfacial and adhesion forces between living bacteria and mineral surfaces *in situ*, has been developed [11]. Another contribution of nanotechnology was the development of a nanoscale system that displays protein unfolding events as visible color changes [12]. This system will greatly enhance our ability to visualize structural changes of proteins in complex synthetic and living systems. Rectified Brownian motion has been used to explain several chemomechanical energy conversions typical to intracellular processes, as well as the kinesin motion along microtubules [13].

Spatial and temporal interaction among cells, including intracellular forces have also been measured. AFM has been used to obtain the intermolecular binding strength between a pair of molecules in physiological solutions, providing the quantitative evidence of their cohesive function [14]. Flow and forces around cells have been quantitatively determined and the mechanics of biomolecules are now better understood [15]. It is accepted that

cell architecture and macro behavior is determined by small-scale intercellular interactions.

Fluorescent semiconductor nanoparticles, or quantum dots, have been developed for use in imaging and have been employed as markers for biological processes. These nanoparticles offer several advantages over fluorescent dye molecules, as they photobleach much more slowly and their emission wavelength can be finely tuned [16]. Key challenges for the further development of quantum dots relate to their encapsulation with a biocompatible layer and the need to avoid nonspecific adsorption.

Understanding systems biology, such as the neural system [17], is enabled by measurements made at the level of developing interneuronal synapse circuits and their ~20 nm diameter synaptic vesicles. Advances in nanotechnology have allowed such measurements to be made.

Nanoscience investigative tools have helped us to understand self-organization, supramolecular chemistry and assembly dynamics, and have furthered our knowledge of the self-assembly of nanoscopic, mesoscopic and even macroscopic components in living systems [18,19\*\*]. However, current understanding of the biosystem building blocks at the nanoscale is far from complete. As an illustration, one cannot explain the anomalous behavior of water with small impurities that is an essential component in a living system. Also, key brain functions have yet to be discovered. Emerging areas in which nanotechnology is set to play a role include the realistic molecular modeling of soft matter [20], obtaining non-ensemble-averaged information at the nanoscale, understanding energy supply to and energy conversion in cells (e.g. using photons or lasers), and the study of tissue regeneration mechanisms.

#### Nanotechnology solutions for biotechnology, biomedicine and agriculture

Nanotechnology offers new solutions for the transformation of biosystems and provides a broad technological platform for applications in several areas: bioprocessing in industry; molecular medicine [21,22] (e.g. for the detection and treatment of illnesses, body part replacement and regenerative medicine, nanoscale surgery, synthesis and targeted delivery of drugs); investigating the health effect of nanostructures in the environment (e.g. pollution by nanoparticles [23] and eco-toxicology [24,25]); improving food and agricultural systems [26] (e.g. enhancing agricultural output, new food products, food conservation); and improving human performance (e.g. enhancing sensorial capacity, connecting brain and mind, integrating neural systems with nanoelectronics and nanostructured materials). Several examples of applications of nanotechnology are given in Box 1 [27,28\*\*,29–35].

**Box 1 Applications of nanotechnology to biotechnology, biomedicine and agriculture.**

Surface-directed nanobiotechnology techniques for the manipulation of molecules within cells, including use of bioselective surfaces, control of biofouling and cell culture [27].

Dendritic polymers [28\*\*,29] have been used for the production of diagnostics for the earlier detection of cancer. These polymers have also been used to develop new delivery methods for performing therapeutic functions *in vivo* and to construct nanostructured scaffolds for drug delivery with about 97% porosity.

The use of nanoparticles for DNA delivery into cells [30,31].

Biocompatible implants to replace damaged or worn body parts and tissue engineering at the nanoscale [32] to create bioartificial organs.

The rational production of precisely formulated nanobiological devices [33].

Biocompatible electronic systems for detection and control, including implants of wireless systems (plus information systems outside), neuroprostheses and parts of the neural system [34].

Nanotechnology promises to reduce genotyping by two orders of magnitude, allowing associations between genetic variations and diseases to be uncovered [35]. High-throughput single nucleotide polymorphism analysis is envisioned.

Agriculture and food system applications of nanotechnology [26]. These include 'smart' (spatially directed, time-controlled release, intelligent control — remotely regulated/preprogrammed/self-regulated) delivery of nutrients, transplanted cells protected by membranes, bioseparation, signal transducer, rapid sampling and animal health (such as the breeding of stock).

Nanotechnology has also enabled the development of biochips and has a role in green manufacturing (e.g. biocompatibility and biocomplexity aspects). Other applications have included the design of sensors for astronauts and soldiers, biofluidics (for handling DNA and other molecules), *in vitro* fertilization of live stock, nanofiltration, bioprocessing 'by design' and traceability of genetically modified food.

Exploratory areas for nanotechnology will include research into the condition and/or repair of the brain and other areas for regaining cognition. It might also find application in designing pharmaceuticals as a function of patient genotypes and in applying chemicals to stimulate production as a function of plant genotypes. The synthesis of more effective and biodegradable chemicals for agriculture and the production of implantable detectors could be aided by nanotechnology. Employing this technology it should also be possible to develop methods that use saliva instead of blood for the detection of illnesses or that can perform complete blood testing within one hour. Broader issues include economic molecular medicine, sustainable agriculture, conservation of biocomplexity, and enabling emerging technologies.

**Biosystems offer models of inspiration for nanotechnology**

Biomimetics is a frequently used term to describe the use of concepts and principles from nature and their application to creating new materials, devices and systems. Emulating the concepts and principles of biology has led to the controlled self-assembly of biopolymeric materials, of arrays of nanoparticles, of devices for use in nanoelectronics, and of macromolecular crystals. Inorganic systems have also been assembled at the nanoscale using bioagents [36\*\*]. Self-assembly and self-organization [37\*\*] have inspired ideas for 'bottom-up' manufacturing and other bioengineering methods at the nanoscale. Bottom-up manufacturing based on self-assembly is the most promising assembly method in the long term; however, the approach has not yet been successful in assembling more than one scale for useful systems. Biological models cannot be copied directly, because biosystems work on a much smaller time scale than usually necessary in industry and need water when most industrial processes take place in other media.

Creating larger molecular structures [19\*\*], structure replication [38], neuromorphic engineering [39], mimicking photosynthesis [40,41], and the development of bio-receptors and biomarkers, are further examples of creating artificial nanoscale devices and semibiological hybrids using biological paradigms.

**Biosystems offer bionanomaterials and nanoscale components for manufacturing**

Nature provides biologically assembled materials and biology's molecular toolbox has been used to develop biohybrid processes and products. Biostructures and bioprocessing offer a relatively large number of opportunities with industrial and medical relevance. These include the use of organic-inorganic hybrid materials and the creation of nanostructures as building blocks (so-called 'molecular Lego'), which can be used to make, for example, nano-devices for biosensing or coatings. Further examples are given in Box 2 [42–59].

Exploratory research in this area will focus on creating architectures in multiscale systems and on the creation of sensors with improved characteristics.

**Funding and policy implications****Research priorities and investments**

The United States have initiated a multidisciplinary strategy for the development of science and engineering fundamentals through the National Nanotechnology Initiative (NNI). Japan and Europe have broad programs and their current plans look ahead four to five years. More than 35 countries have developed programs in nanotechnology since 2000, illustrating the importance of this field of research. Research on biosystems has received increased support in 2002, as compared with previous

**Box 2 Examples of bionanomaterials and nanoscale components for manufacturing.**

Biostructures created in the natural environment as a result of biomineralization, and the assembly and deposition of nanoparticles and scaffolds [42].

The use of organic–inorganic hybrid materials and manufacturing methods.

A polymer–ceramic interface that provides superior control of the properties at the nanoscale has been proposed [43]. New developments are needed at the interface between organic and inorganic matter.

Creating nanostructures as building blocks (Lego-type) for the formation of hierarchical structures (i.e. the design of molecules as building blocks [44]).

- DNA-mediated artificial nanostructures and nanomotors [36\*\*, 45–47].
- Molecular recognition mediated fabrication of nanostructures using dip pen technology [48,49].
- Artificial cells and their assemblies [50].
- The design of proteins for efficient electron transport or with mechanical characteristics [51].

The formation and growth of nanostructures in living biosystems (e.g. the formation of gold nanoparticles by alfalfa plants [52]).

Using DNA [53], proteins [54] or other structures [21] for diagnostic and computational approaches.

Creating nanobiodevices and systems using biocomponents, for example, nanobiomotors or biochannels in membranes. These can then be assembled into nanosystems.

Bioagents may be used to create the first level of organization at the nanoscale in hybrid systems (biostructures/living or non-living with inert structures) [35]. The bioagents could increase the sensitivity of biosensors [55] or might act as switches [56], connectors or nanobiomotors [57–59].

years, in the US, UK, Germany, Switzerland and Japan [59,60]. Other significant investments in nanotechnology research programs with contributions to nanobiosystems have been made in the EC [61], Australia [62], Taiwan [63], Canada, Finland, Italy, Israel, Singapore and Sweden. Relatively large investments in nanotechnology with a small biosystems component have also been made in South Korea [64] and China [65]. Worldwide government funding of nanotechnology has increased about five times since 1997, exceeding \$2 billion in 2002 (see <http://nano.gov/international>). Differences among countries are observed in the research domain they are aiming for, the level of program integration into various industrial sectors, and in the time scale of their R&D targets.

In the US, the Federal Government investment in nanotechnology R&D increased from \$116 million in fiscal year (FY) 1997 to about \$697 million in FY 2002. The establishment of the NNI was announced on January 21st 2000, by then President Clinton [66], and has received support from President Bush's Administration [67]. It

includes fundamental research on nanobiosystems and three bio-related research 'grand challenges' on novel materials, health and nanobiodevices. The NNI currently coordinates the nanoscale research interests and programs of 17 organizations through the Nanoscale Science and Engineering Technology (NSET) subcommittee of the National Science and Technology Council (NSTC). NSET sets the long-term vision, plans, budgets and programs and carries out evaluations to ensure a successful initiative. The subcommittee is composed of representatives from each participating agency, the Office of Science and Technology Policy, and the Office of Management and Budget. The largest investments in FY 2002 were made by the National Science Foundation (NSF) (\$204 million), the Department of Defense (DOD) (about \$200 million), the Department of Energy (DOE) (\$89 million), the National Institutes of Health (NIH) (\$59 million), the National Institute of Standards Technology (\$77 million) and the National Aeronautics and Space Administration (NASA) (\$35 million). Other agencies with a nanotechnology investment in the same FY are the Departments of Agriculture (USDA), Justice (DOJ) and Transportation (DOT) and the Environmental Protection Agency (EPA). States, universities and industry have provided funding for infrastructure, education and small business development in an increasing trend.

The 10-year vision for nanotechnology published in Nanotechnology Research Directions [1\*\*] included the study of nanobiosystems in both fundamental research and in a section dedicated to nanotechnology applications to biology, medicine and health. The interdisciplinary NNI definition of nanotechnology has promoted the integration of physical, chemical, biological, material science and engineering aspects. Nanotechnology research represented about 0.6% in Federal R&D funding in the US in FY 2002. The NSF is the largest investor in nanoscale science and engineering with \$221 million in 2003, which represents about 5% of its overall R&D budget. Of the total NNI investment in 2002, about 12% is explicitly dedicated to nanobiosystems in two ways [66,68\*\*]. First, the implementation plan of the NNI has a focus on fundamental research on nanobiosystems (about 8% of the total NNI budget in FY 2002). Second, grand challenges on 'health issues' and 'bionanodevices' cover about 4% of the NNI budget. Additional investments have been made for development of the respective infrastructure in various centers including the Cornell Nanotechnology Center and Nanoscale Science and Engineering center at Rice University, in education and societal implications studies. In FY 2002, the nanobiodevices grand challenge was refocused on nanobiodetection and protection [67]. The NNI was evaluated by the National Research Council (NRC) and its findings published in June 2002 [5\*\*]. One of the recommendations was to expand research at the interface of nanoscale technology with biology, biotech-

Table 1

## Estimated government nanotechnology R&amp;D expenditure (in \$ millions/year).

Area	1997	1998	1999	2000	2001	2002	2003	2004
Western Europe	126	151	179	200	~225 (270) <sup>†</sup>	~400	~600	
Japan	120	135	157	245	~465	~700	~810	
USA*	116	190	255	270	422 (465) <sup>†</sup>	600 (653) <sup>†</sup>	774	849
Others	70	83	96	110	~380	~550	~750	
Total	432	559	687	825	1580	2303	2934	
% of 1997	100%	129%	159%	191%	365%	533%	679%	

\*Western Europe' includes countries in the EU and Switzerland. The rate of exchange \$1 = 1.1 Euro in 2002 and \$1 = 0.95 Euro in 2003; Japanese rate of exchange \$1 = 120 Yen in 2002. 'Others' includes Australia, Canada, China, Eastern Europe, FSU, Israel, Korea, Singapore, Taiwan and other countries with nanotechnology R&D. \*A financial year begins in the USA on October 1 of the previous calendar year and in most other countries six months before. <sup>†</sup>Denotes the actual budget recorded at the end of the respective FY. Estimations use the nanotechnology definition as defined in NNI (see [1\*\*]), and include publicly reported government spending.

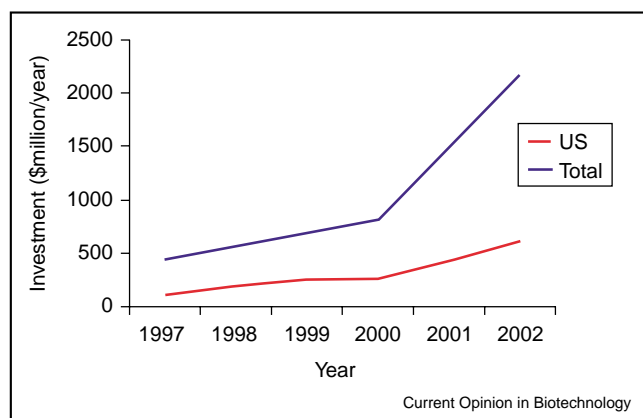
nology and life sciences. Such plans to extend nanobiosystems research are under way at the DOE, NIH, NSF and USDA. An NSF-Department of Commerce (DOC) report recommends a focus on improving physical and mental human performance [4\*\*]. NSF, NASA and the DOD have included aspects of converging technologies and improving human performance in their program solicitations. The Defense Advanced Research Projects Agency (DARPA) has a program on 'Engineered biomolecular nanodevices/systems'. A letter sent to the NIH director by seven senators recommends that the NIH increase funding in nanotechnology [69]. The White House budget request for FY 2004 lists 'nanobiosystems for medical advances and new products' as a priority within NNI.

The NNI has inspired or stimulated nanotechnology programs worldwide (see Table 1) [61,70]. As a reflection of its interdisciplinary characteristics, nanotechnology is supported by dedicated programs that cross a range of fields or in materials, life sciences, environmental issues

and electronics in both the EC and Japan (Table 1). Figure 2 shows increased funding after 1997, when the first worldwide study on nanotechnology was undertaken by the US Nanotechnology Working Group. An increased rate of investment is also seen after the announcement of NNI in January 2000 [59]. The timeline of the government announcements on R&D nanotechnology programs each exceeding \$100 million/year is shown in Figure 3.

The EC 6th Framework Programme (2002–2006) [61] includes an approximate \$700 million investment distributed over five years in thematic area 3, dedicated to nanotechnology and materials. Nanobiotechnology is included in this area in two sections: integration of biological and nonbiological systems at the nanoscale level and integration of new nanoscale materials and technology for improved security and quality of life, including tissue engineering, new biomimetic and biohybrid systems. Other EC thematic areas may include some support for nanobiotechnology. Of the approximate \$700 million allocated to nanotechnology in the 6th Framework, only

Figure 2



Government investment in nanotechnology between 1997 and 2002 (total worldwide investment including US, blue; US investment, red).

Figure 3

Preparation of NNI Broad definition, 10-year vision, worldwide study, investment plan				US NNI (Announced January 2000)			
				Japan (Announced April 2001)			
				South Korea (Announced July 2001)			
				EC - 6th Frame (Ann. March 2002)			
				Germany (Ann. May 2002)			
				Taiwan (Ann. Sept. 2002)			
1996	1987	1988	1999	2000	2001	2002	2003

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Comprehensive nanotechnology research programs with funding exceeding US \$100 million/year by national governments or EC, announced after 2000.

a relatively small fraction as compared with the US will be awarded to nanobiotechnology owing to competition with other areas.

Nanotechnology has been formally recognized as one of the science and technology priorities by the Federal German government in FY 2003, with a budget of about \$118 million (assuming \$1 = 0.95 Euro). This program was announced in May 2002. The focus is on nanoelectronics, nanoscale materials, and optical science and engineering. A lower importance is given to nanobiosystems, an area which is supported in a Virtual Nanotechnology Competence Center located in Munich. In FY 2002, the UK had a budget of about \$45 million allocated to nanotechnology, distributed throughout various government programs. While the areas of strong specialization are nanoelectronics, nanophotonics and molecular nanotechnology, the contribution of medical and pharmaceutical research is estimated to be about 5–7%. France had a FY 2002 investment estimated at \$35 million (\$50 million planned for FY 2003) for nanotechnology under a variety of programs, and the contribution of research on nanobiosystems is estimated to be in the same range of 5–7%.

The Japan Science and Technology Basic Plan, initiated on March 30 2001 [71,72] (Table 1), provides priority funding to 'Nanotechnology and Materials', of which about 6% is for 'nanobiology for novel medical care technology and biomaterials.

Australia [62] has created a national R&D program on nanotechnology including a focus area on biomimetics and biosensors. The Korean government has designed nanotechnology as one of six R&D national priorities [64], and in July 2001 announced the nanotechnology priority program of \$1.2 billion for 10 years. Then, a decision was taken to accelerate the investment from about \$87 million in 2001 to about \$170 million, of which about \$28 million was allocated to a centralized nanofabrication facility and \$7 million was allocated to education. The focus is on areas with highest commercial potential and competitiveness over industrialized countries. Nanobiotechnology has not received significant funding in Korea because of existing expertise and higher economical expectation for electronic and materials sectors. The formation of the Taiwan National Nanotechnology science and technology Priority Program [63] was announced in September 2002 and began in January 2003. The program has a total budget of about \$110 million/year for 6 years. One of the five research topics is nanoscale biology, with a focus on 'molecular detection and manipulation, bio and non-bio interface devices and materials, and drug delivery devices'. China has an increased budget for nanotechnology [65] estimated to be about \$80 million from the central government (and \$200 million including regional governments) in 2002 [65]. The focus is on nanoscale

materials and devices and there is a relatively small contribution to biosystems.

Nanobiosystems is an area of interest recognized in international studies on nanotechnology prepared by both the Asia-Pacific Economic Cooperation (APEC) [73] and the Organization for Economic Cooperation and Development (OECD) [60]. In a survey made by the UK Institute of Nanotechnology [60], experts identified the location of the most sophisticated nanotechnology developments in the 'Medical/Pharmaceutical area' in the US (48%), UK (20%), Germany (17%), Switzerland (8%), Sweden (4%), and Japan (3%). In FY 2003, the US NNI plans to devote about 12% of its R&D budget to nanobiosystems, Germany about 8%, and France about 6%. The biological route to nanotechnology may be the pathway of choice for countries with less developed economies, because the research facility investment is lower.

### Science and education policy implications

The NNI strategy is to support five complementary modes of research: fundamental research, grand challenges, research centers of excellence, fabrication and user facilities for developing physical infrastructure, and education and societal implications. The main components of other national programs have similar structures. The US, Japan, Korea, China and other countries have established coordinating nanotechnology offices at the national level.

The NNI was a bottom-up initiative that has advanced relatively quickly from its concept to implementation, because of a bold scientific vision and strong societal relevance. Fundamental research for biosystems has been recognized in all phases of the program. The NSF listed 'nanobiosystems at the nanoscale' as the first theme in the program solicitations for FYs 2001–2003. NRC reports on NNI '*Small wonders — Endless frontiers*' [5\*\*] and '*Implications of emerging micro and nanotechnologies*' [6] recommends research on biologically inspired materials and systems, and particularly research on potential applications for sensors, communications and improving human performance.

The second mode, known as the 'grand challenges', supports specific visionary R&D activities identified as having the potential to realize significant economic and societal implications [74,75]. Centers and networks can encourage the multidisciplinary research that is expected to contribute highly innovative approaches to new technology. Fifteen new multidisciplinary centers have been initiated throughout the country since 2001. Eight were funded by the NSF, three by the DOD, and four by NASA. A list of these centers with significant biosystems research is given in Table 2.

Fabrication and user facilities for physical infrastructure includes the National Nanotechnology User Network

Table 2

## Examples of NNI centers of excellence with biosystems research and education.

Center name	Funding agency	Institution
Nanoscience in Biological and Environmental Engineering (Nanoscale Science and Engineering Center – NSEC)	NSF	Rice University
Integrated Nanopatterning and Detection (NSEC)	NSF	Northwestern University
Directed Assembly of Nanostructures (NSEC)	NSF	Rensselaer Polytechnic Institute
Nanobiotechnology, Science and Technology Center	NSF	Cornell University
Institute for Cell Mimetic Space Exploration	NASA	UCLA
Institute for Intelligent Bio-nanomaterials and Structures for Aerospace Vehicles	NASA	Texas A&M
Bio-inspection, Design and Processing of Multifunctional Nanocomposites	NASA	Princeton

(NNUN) and the Network for Computational Nanotechnology sponsored by NSF, and a group of five large user-facility Nanoscience Centers established by DOE. Of these, the Lawrence Berkeley National Laboratory and Oak Ridge National Laboratory will have a focus on nanobiosystems research. In 2003, the NSF has opened the competition for the National Nanotechnology Infrastructure Network for a \$14 million/year investment for 2004–2013 to replace and expand the goals of the NNUN. It is planned that biosystems research will be a central research and education area in the new network.

The NNI provides funding for research that addresses the ethical, social, economic, and workforce impacts of nanoscience and nanotechnology. Examples of funded research areas include transforming individuals and social institutions, identifying impacts of legislation and regulation, reducing barriers to nanotechnology diffusion, and using nanotechnology for more effective education.

Education and training outreach activities must begin in primary and secondary schools. The National Nanotechnology Coordination Office, the secretarial office of NSET, has prepared a paper entitled, ‘*Extending Outreach Success for the National Nanoscale Science and Engineering Centers – a Handbook for Universities*’, which provides guidance for impacting the curricula development process.

Broader nanobiotechnology recognition is sought through outreach to the public through the media and museums, secondary and continuing education [73–76]. Increased interdisciplinarity in university education has been recommended to ensure a nanotechnology workforce [74–76]. Ethical and moral concerns also need to be addressed before new developments can be made in some areas, for example, neuroethics need to be investigated before brain and neural system research [77]. Research and education on nanobiosystems is expected to increase within the nanotechnology programs as our understanding of complex nanosystems develops and new tools become available.

### Concluding remarks

The ability to uncover the structure and function of biosystems at the nanoscale has stimulated research lead-

ing to improvements in biology, biotechnology, medicine and healthcare. The scientific confluence is reflected in government funding programs and science policies. The NNI plans to increase its financial contribution to programs dedicated to nanobiosystems over the current level of 12% [67], and similar trends to better recognize biosystems research within nanotechnology are noted in other countries, including the UK, Germany, Australia, Japan and Switzerland.

Nanoscale and biosystems research are merging with information technology and cognitive science [4\*\*], leading to completely new science and technology platforms such as those for genome pharmaceuticals, biosystems on a chip, regenerative medicine, neuroscience, neuromorphic engineering, and food systems. A key challenge is bringing together biologists, medical personnel and nanotechnologists. Another key challenge is forecasting and addressing possible unexpected ethical, environmental and health consequences of the revolutionary science and engineering developments in nanobiosystems. Priority science and technology goals may be envisioned for international collaboration in nanoscale research and education: better comprehension of nature, increasing productivity, sustainable development and improving human performance.

The nanoscale assembly of organic and inorganic matter leads to the formation of cells and to the most complex known systems — the brain and human body. Nanotechnology plays a key role in understanding these processes and in the advancement of biological sciences and biotechnology. Science policy aims to reflect the scientific dimensions, interdisciplinarity, partnerships and the broad implications of the developments in nanobiosystems science and technology.

### Update

Two draft bills on nanotechnology submitted in the current Congress address the need for coherent, multi-year planning with increased interdisciplinarity and inter-agency coordination. The Senate draft bill S189 ‘*21st Century Nanotechnology R&D Act*’ recommends a five year ‘National Nanotechnology Program’ [78]. It was introduced by a group of senators led by Ron Wyden and

George Allen. The draft bill in the House of Representatives HR 766 'Nanotechnologies R&D Act of 2003' was introduced by a group of representatives led by Sherwood Boehlert [79].

In March 2003, the President's Council of Advisors on Science and Technology (PCAST) decided to undertake a study of the NNI in 2003. PCAST will use in its evaluation three task forces (of which one is on nanotechnology and societal implications) and the NSET subcommittee.

## Acknowledgements

Opinions expressed in this review are those of the author and do not necessarily reflect the position of NSET or NSF.

## References and recommended reading

Papers of particular interest, published within the annual period of review, have been highlighted as:

- of special interest
- of outstanding interest

1. Roco MC, Williams RS, Alivisatos P (Eds): **Biological, medical and •• health applications**. In *Nanotechnology Research Directions*, Chapter 8. Boston: Kluwer Academic Publishers 2000. URL: <http://nano.gov>
- Provides a 10-year vision for various areas of nanotechnology, including the tools of nanotechnology, biotechnology and the medical field. This key NSET report has been at the foundation of the NNI and was used as a reference in programs established worldwide.
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4. Roco MC, Bainbridge WS (Eds): *Converging Technologies for •• Improving Human Performance*. NSF-DOC Report, 2002; Kluwer: Boston. URL: <http://wtec.org/ConvergingTechnologies>
- Convergence of nanotechnology, biotechnology, infotechnology and cognitive sciences is based on material and scientific unity at the nanoscale. This report underlines the theoretical background and its implications in key areas of human activity, including working, learning, aging, group interactions, defense, culture and human evolution.
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