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PERSPECTIVES

National Nanotechnology Initiative at 20 years: enabling new horizons

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Abstract A succession of breakthrough discoveries at the nanoscale and the transforming vision formulated in 1999, which inspired the National Nanotechnology Initiative (NNI) in the US and other research programs around the world, set in motion a global scientific, technological, and societal endeavor. NNI was announced by President Clinton in January 2000 and formalized as a long-term national initiative by the US Congress in December 2003. Over thirty US research and regulatory agencies participate with a cumulative public R&D investment of about $40 billion by 2023. The initiative aims to establish a general-purpose science and technology field for matter, energy, and life systems, with anticipatory governance of societal implications. The revenues from products where nanotechnology is a condition for competitiveness have been estimated to increase by about 25% annually on average from 2000 to 2020 reaching about $3 trillion worldwide, of which about one-fourth is in the US. This paper presents an overview of research investments and governance of NNI, its outcomes, and lessons learned. The unifying concepts and the convergence of nanoscale science and engineering with modern biology, information, cognition, and artificial intelligence (AI) have opened new horizons in knowledge and technology. Emerging technologies include platforms for quantum information systems, AI systems, advanced semiconductors, wireless communication, modern bioeconomy, and advanced manufacturing. New knowledge and solutions are created to address sustainable society, nanomedicine, cognition, personalized learning, augmenting human capabilities, and independent aging.

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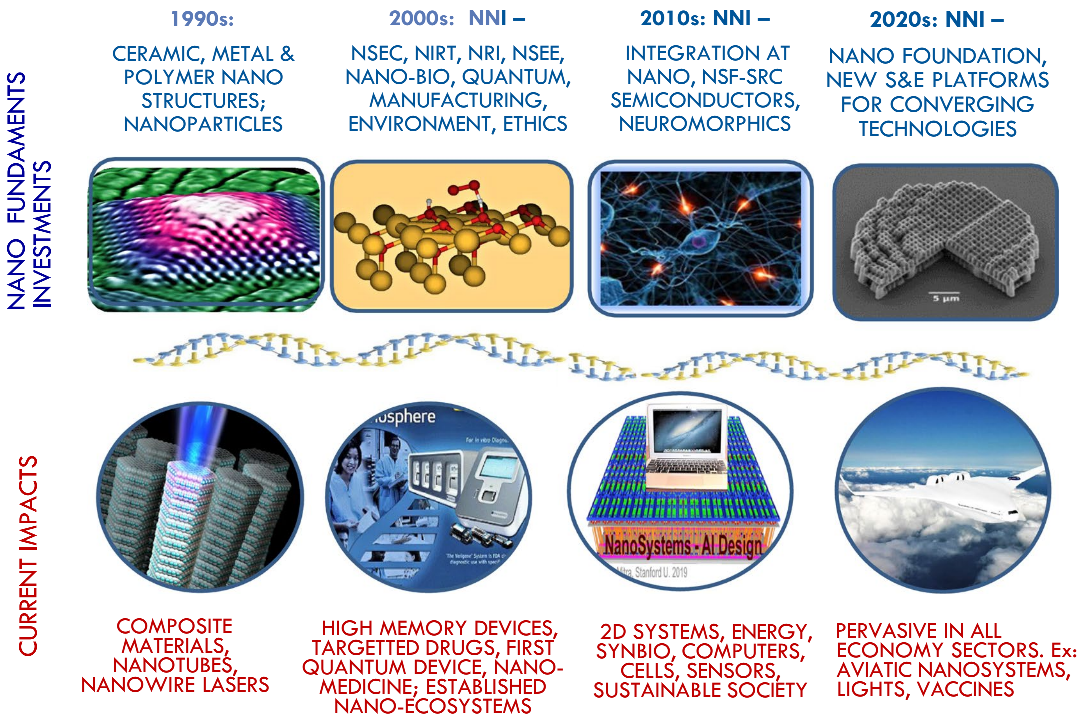
Graphical abstract



Keywords Nanoscale science and engineering · Research and education · International perspective · Governance · Emerging technologies · Global S&T system · Human development

Introduction

At the end of the last century, scientific discoveries in chemistry, physics, biology, materials, electronics, and optics and other disciplines have reached the atomic and molecular levels—the building blocks of matter. At this scale, the fundamental properties and functions of materials and devices are established and, once control is achieved, can be changed economically with less material, energy, and waste. Atoms with fixed properties can assemble in complex architectures to construct the rich diversity of nature and life. The transition from single atoms or molecule behavior to collective behavior of their assemblies is encountered in nature, and nanotechnology exploits this natural threshold.

NNI started as a bottom-up, science-driven opportunity to improve comprehension of nature, connect fields of knowledge, and change the foundation of technology. The unified definition of nanotechnology proposed in 1999 as part of NNI preparation [1–3] identified common nanoscale phenomena, methods of investigation, tools, and potential outcomes across all fields of science and technology:

> Nanoscale science, engineering, and technology, known in brief as 'nanotechnology', is the understanding and control of matter at the nanoscale, at dimensions between approximately 1 and 100 nanometers, where unique phenomena enable novel applications.

Nanotechnology covers the dynamic behavior of atomic and molecular systems that are dominated by large surface area, quantum interactions, self-assembly, surface recognition, confinement, and other specific forces and phenomena. Motion at the nanoscale, except for zero degrees Kelvin, is continued, fast, and inextinguishable and at times is described by average properties (of atoms, quantum dots, or other nanomodules) or probabilistic properties (of qubits).

Nanoscale is a length scale through which the material world's behavior can be connected. This has created conditions for the convergence of disciplines, synergy among areas of application, and cause-and-effect breakthrough transformations, and it allows for a holistic view in knowledge, technology, and education toward a new kind of Renaissance. Around the year 2000, nanoscale was called a "magic scale" because of its multifaced specific phenomena and potential transforming capabilities. "Going to the nanoscale" using microscopes has an exploratory flavor and scale difference from the human size similar to "going to the Moon" using telescopes, but in another direction.

The US National Science Foundation (NSF) established its first program dedicated to nanoparticles in 1991 [3] following a competition for emerging technologies. I had the opportunity to propose the program based on concepts seeded in my earlier nanoparticle research sponsored by NSF and IBM. The long-term vision for nanotechnology development was formulated by generalizing those concepts to all matter and all disciplines in 1999 in the report, *Nanotechnology Research Directions* [1], an official document of the US National Science and Technology Council (NSTC), which has received a high degree of international acceptance. NSTC also prepared a brochure "Nanotechnology - shaping the world atom by atom" to inform the public. With this foundation, and after benchmarking the international situation in the report *Nanostructure Science and Technology* [2], I had the opportunity to propose NNI at the White House on behalf of an interagency group (NSF, DOC, DOD, DOE, DOT, DoTreasury, NASA, and NIH) on March 10, 1999. The vision of NNI has been "*A future in which the ability to understand and control matter at the nanoscale leads to a revolution in technology and industry that benefits society*" [1, 3, 4]. The initial annual investment was approved by the OSTP, OMB, and PCAST (all in 1999) and by House and Senate in Congress (in 2020) after President Clinton's announcement on January 20, 2000 [5]. Tom Kalil, leading the Economic Council, co-organized the presidential competition for a new national R&D program for which NNI proposal was prepared. In July 2000, Neal Lane, Assistant to the President for Science and Technology, signed the NNI Implementation Plan for the program with the first annual budget of $464 million [6, 7]. In August 2000, I was named as the Chair of the White House Interagency Subcommittee (Nanoscale Science, Engineering, and Technology (NSET)) to implement the NNI. Jim Murday was appointed Director of the National Nanotechnology Coordinating Office (NNCO) to support NSET activities [8]. This was the beginning of the NNI, which, with cumulative funding from 2001 to 2023 of about $40 billion, became the largest bottom-up science national initiative.

National R&D programs on nanotechnology very soon announced by Japan (April 2001), South Korea (July 2001), the European Community (March 2002), Germany (May 2002), China (2002), and Taiwan (September 2002). International dimensions have become clear after about 80 countries developed nanotechnology activities by 2005, partially inspired or motivated by the NNI.

The US Senate formed a Nanotechnology Caucus lead by senators George Allen and Ron Wyden in 2003 that catalyzed participants from industry, government, and academic stakeholders to pass the "21st Century Nanotechnology Research and Development Act" for long-term support of nanotechnology, and President George W. Bush signed it in to Public Law 108–153 [9]. It took another 15 years for the next US R&D national initiative law to be approved by US Congress, the Quantum Information Systems, which is an outgrow of NNI.

Nanotechnology is a foundational S&T field

A long view of nanotechnology development is needed because nanotechnology is a foundational and general-purpose science and technology (S&T) field with broad connections and implications. Since its unifying definition and NNI vision were formulated about 2000, nanotechnology research has become a global science initiative and has inspired and enabled the global emerging S&T system (Fig. 1). This emerging system has five essential elements: atoms/qubits, genes, bits of information, neurons/synapsis, and logic steps. From these elements, corresponding foundational S&T fields—nanotechnology, bio, information, cognition, and system AI (labelled together as NBICA)—are

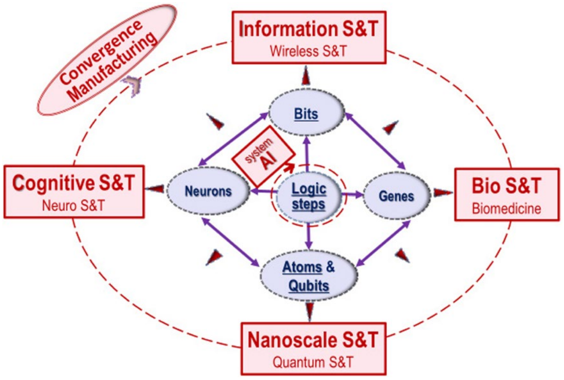


Fig. 1 Nanoscale S&T is a key component of the emerging S&T system, which is based on convergence of five essential building blocks (marked by *blue ellipses* in this figure) and the corresponding five foundational S&T fields (NBICA, *red rectangles*)

hierarchically built up. Other emerging S&T fields originate from this core through spin-offs and convergence among fields [10].

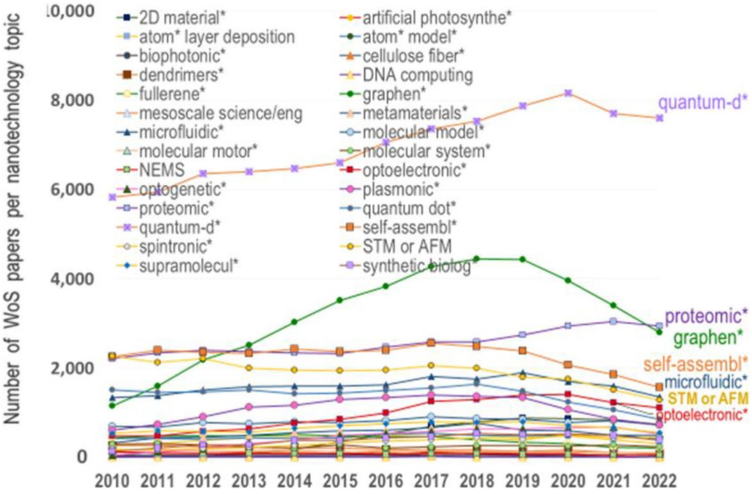
Nanotechnology today continues its growth with many spin-off areas such as metamaterials and quantum information systems, as well as through convergence at the interfaces with other foundational S&T fields such as synthetic biology and nanomedicine at the interface of nanotechnology with modern biology. Nanotechnology already has become a primary investment S&T platform as its methods of investigation, design, and manufacturing have advanced and become more efficient, more reliable, and readily available.

Indicators of nanotechnology development

Nanotechnology development has been characterized by several indicators: the most frequent topics covered in publications, number of papers and patent publications, number of supported people, estimated revenues, R&D funding, and venture capital. Title-abstract keyword searches have been used in the respective databases, with a similar set of keywords since 2000 [11, 12]. The keywords have been slightly updated as listed in Fig. 2 for searches completed after 2021 to account for increased contributions in several areas.

(i) *Nanotechnology topics* covered in publications have evolved from a focus on passive nanostructures in 2000 to active nanostructures after 2005, nanosystems after 2010, molecular nanosystems after 2015, and converging technologies after 2020. Several topics including quantum, graphene, proteomics, micro-/nanofluidics, and optoelectronics have larger contributions in 2020–2022 as compared to other topics. In the last 5 years, the largest number of nanotechnology papers published in Word of Science (WoS) from US-affiliated authors are for "quantum-d*" (quantum* excluding "quantum dot*" which is searched separately) and "graphen*" keywords (Fig. 2). The evolution tendencies in the USA and the world generally are similar. A difference is that "graphen*" is the most frequent topic for world-affiliated

Fig. 2 Number of WoS papers from the US-affiliated authors for nanotechnology topics in the interval 2010–2022



authors, peaking at about 38,000 papers in 2020 (while for the US-affiliated authors, "graphen*" is the second most frequent topic, peaking two years earlier in 2018), and "quantum-d* "is the most frequent topic for the US-affiliated authors, peaking at about 7800 papers in 2020 (while worldwide, this is the second most frequent topic, peaking one year later in 2021). The number of US "nano toxicity" papers reflecting the level of nano-EHS research activity reached a maximum of about 1185 papers in 2020 and decreased to 1002 in 2022.

(ii) *The number of WoS papers* reflecting discoveries in nanotechnology using keywords from [11] increased in the interval 2000 to 2020 about 11.5 times with an average worldwide annual growth rate of about 13%, which is almost five times faster than the average for all technology fields of about 3.3%. About 6% of WoS papers published worldwide in all areas in 2020 included nanoscale science and engineering aspects. The number of nanotechnology papers grew faster between 2000 and 2010 than in the following interval. The average growth rate for US authors is 8%, lower than the worldwide average, in part because the USA started with a larger base and public funding did not increase significantly after 2010. The increase is uneven per country or economy around the world, as illustrated by Fig. 3 for the interval 2010 to 2022. In recent years, the number of papers from P.R. China is the largest reflecting an increased number of nanotechnology researchers, followed by the EU and US. The US share of papers has decreased from 25% in 2010 to about 16% in 2020 and about 13% in 2022 after the pandemic. Authors from South Korea and Africa each reached the same number as Japan in 2020 and slightly exceeded Japan in 2022.

The citations reflecting the novelty of the papers have a different international distribution than the number of papers. For illustration, the number of nanotechnology papers by country published in 2022 in the top three journals with high citation index, that is *Nature*, *Proceedings of the US National Academy of Sciences (PNAS)*, and *Science*, is shown in Fig. 4. The keyword search was similar to [11]. US participation is about 65%, followed distantly by P.R. China, Germany, France, and Japan. The USA has maintained approximately this percentage from 2015 to 2022.

The US private sector has the largest contribution in WoS publications [13]. For example, in 2019, it had 1500 publications, and the total number of citations since 2000 was about 500,000. The second country is Japan with about 700 publications in 2019 and 200,000 citations since 2000. The average private sector WoS annual growth rate of number of papers in the interval 2000–2019 was about 8%. The leading five companies in that interval are IBM, NTT, Intel, Hitachi, and STMicroelectronics.

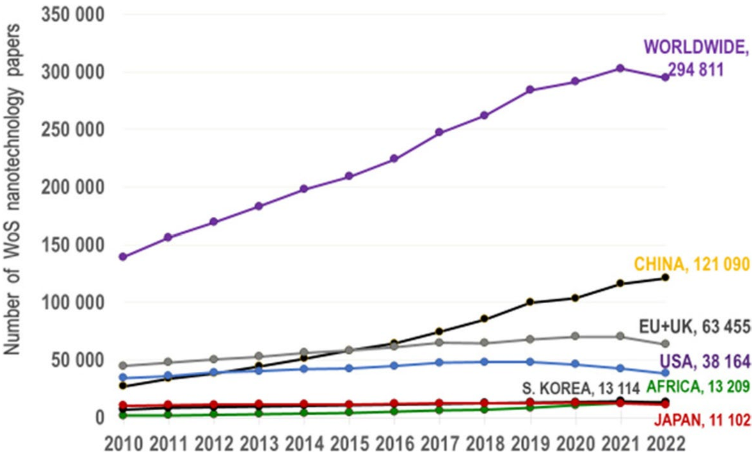


Fig. 3 Number of WoS nanotechnology papers in top five regions in the interval 2010–2022: data generated using a "title-abstract" search by nanotechnology keywords

(iii) *Nanotechnology patent applications* in the World Intellectual Property Office (WIPO)

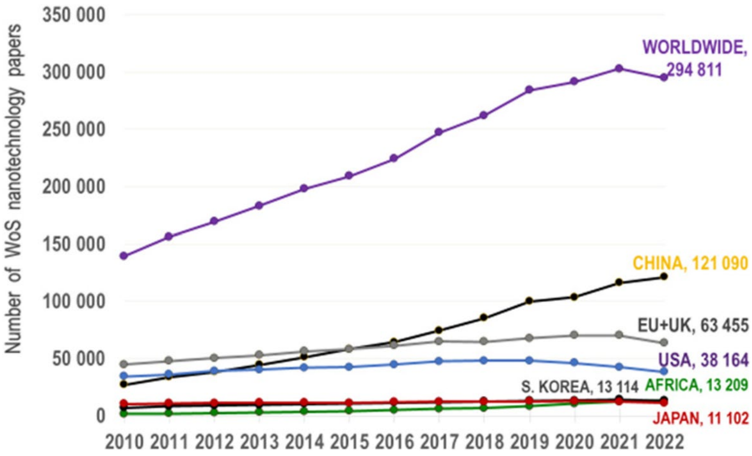


Fig. 4 Five countries' contributions to the top three journals with high citation index in 2022 (each article is assigned to multiple countries if its authors have different nationalities; therefore, the sum of percentages from five countries may exceed 100%)

database between 2000 and 2020 have increased at an average rate of about 19% for all countries (Fig. 5) and about 13% for US authors. The rate of 19% in nanotechnology is about 5.5 times larger than the respective average for patent application in all areas of 3.4%. It also is faster than the 13% annual growth rate of digitalization patent applications in the world, which has been identified as the largest innovation revolution at WIPO in the interval 2000–2020 [14]. A relatively small fraction of about 10% of all patent applications have overlapping claims (Fig. 5). The largest contributions of nanotechnology patent applications by the private sector were from Japan, the US, and South Korea in the first decade of this century and increasingly by P.R. China in the second decade. The leading five US companies in this interval for the number of nanotechnology-related papers are IBM, 3 M, HP, Intel, and Xerox, while the lead internationally is held by Samsung, Foxconn, and IBM [13].

The rate of increase of nanotechnology patent applications at the US Patent and Trade Office (USPTO), the largest national patent depository, has been about 13% from 2000 to 2020. US authors have the lead number of applications at USPTO, with about 41.5% of total in 2019/2020, followed by EU27 (12.3%), S. Korea (7.2%), Japan (5.4%), and P.R. China (4.4%).

Table 1 summarizes the evolution of primary nanotechnology workforce (as discussed in the following paragraph (iv)) and nanotechnology revenues) at the

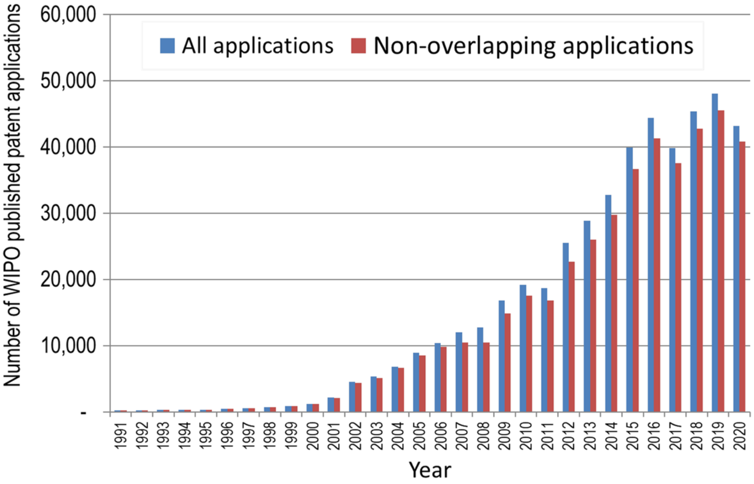


Fig. 5 Number of WIPO nanotechnology patent applications for all countries (1991–2020)

Table 1 Estimated revenues from products where nanotechnology is a condition for competitiveness and corresponding primary nanotechnology workforce (2000–2020): **world** (in bold letters) and the *US* (in italics letters, in parentheses) [15–22]

World (*US*)	People (primary nanotechnology workforce)	Revenues (estimate)
2000 (survey)	~**60,000** (*~25,000*)	~**$30 B** (*~$13 B*)
2010 (survey)	~**660,000** (*~220,000*)	~**$335 B** (*~$110 B*)
2013 (survey)	~**2.38 M** (*~568,000*)	~**$1190 B** (*~$284 B*)
2020 (survey)	~**6 M** (*~1.5 M*)	~**$3000 B** (*~$750 B*)
(2010–2020) average growth	~**25%** (*~21%*)	~**25%** (*~21%*)
(2000–2020) average growth	~**26%** (*~23%*)	~**26%** (*~23%*)

global level and in the US for two decades, 2000 to 2020 (discussed in paragraph (v)).

(iv) *The number of researchers and workers involved in at least one area of nanoscale science and engineering (primary workforce)* has been estimated by considering about $0.5 million/year revenues from nanoproducts per nanotechnology worker (Table 1). This conservative estimation of a relatively large production per worker is based on industry input [15, 16]. The revenues have increased in time via nanoscience-technology transition, expansion of nanotechnology use in traditional and emerging industries, and spin-off areas such as metamaterials, synthetic biology, nanostructured batteries, and quantum devices and systems. The average annual growth rates between 2000 and 2020 are about 26% worldwide and 23% in the USA for revenues from products where nanotechnology is a condition for their feasibility and competitiveness. Accordingly, the corresponding numbers of nanotechnology workers are estimated to grow by the same rates as the revenues in the same time interval. The estimation is 6 million nanotechnology workers worldwide in 2020, of which about 1.5 million in the USA. In addition, for each nanotechnology worker, it is that estimated 2.5 other related secondary jobs (called secondary workforce) are created if one extrapolates the experience from information technology. Accordingly, the corresponding secondary workforce is estimated at 15 million worldwide in 2020, of which 3.75 million in the US.

(v) *The estimated revenues from products that have nanotechnology as a condition for their feasibility and competitiveness* in 2000, 2010, 2013, and 2020 are given in Table 1 [15–22]. The trends were evaluated based on industry surveys of nanotechnology value chains and expert evaluations of the fractions of nanotechnology products and services from total reported production outputs (as illustrated for several industrial sectors in Table 2). The systematic studies by Lux Research covering all economic sectors [17–19] and NSF reports [2, 15, 20–22] have included experts in the respective areas from academia, government, and small and large companies with related R&D programs (such as IBM, Intel, Mobil, Mitsubishi Research Corporation, Hoechst, and Deutsche Bank).

Because of its technological and economic promise, nanotechnology has penetrated both the emerging and classical industries. Significant progress has been in nanoelectronics-semiconductors, nanostructured catalysts, pharmaceutics, nanomedicine, energy conversion and storage, aeronautics, sensors, and mRNA vaccines as reflected by the estimated level of adoption of nanotechnology in those industrial sectors (Table 2) [21]. For example, semiconductors with features under 100 nm represented about 60% (or $90 billion) of the total revenues of $150 billion from all semiconductors in 2010 and about 80–90% (or $350 billion) of total revenues of $410 billion from all semiconductors in 2020. The penetration rate of nanotechnology in key industries seems to correlate with the percentage of overall spending on R&D in the respective industry. This approach based on expert evaluation of fractional contribution of nanotechnology products from total production outputs is more reliable for evaluations at the national and global levels as compared to the summation approach from various individual production units where contributions are difficult to be identified and collected with local personnel.

Table 2 Examples of penetration of nanotechnology in several industrial sectors: estimations of the revenue percentages affected by nanotechnology

USA	2000	2010	2020
Semiconductor industry			
- With features less 100 nm	0%	~60%	~80–90%
- With nanoscale behavior	0%	~30%	~70–80%
New nanostructured catalysts	0%	~35%	~50%
Pharmaceutics (therapeutics and diagnostics)	0%	~15%	~50%
Wood cellulose processing	0%	0%	~3%
Aeronautic-nanocomposite content; carbon reinforced	~5%	~10%	~40%
mRNA therapy	0% (tests on animals)	0% (phase 1, RNA for human cancer)	100% mRNA vaccines*
COVID-19 testing (in the US)	0%	0%	~20%

*Used in COVID-19 vaccines (Pfizer, Moderna)

There are significant differences between countries concerning the rate of growth and their domains of relevance. On average, from 2000 to 2020, the global revenues are approximately doubling every 3 years because of the successive introduction of new products and expansion in new sectors of application. One notes that the estimations above are for revenues of the first level of integrated devices or systems that are competitive because of the respective nanocomponents; the values of nanocomponents alone, which are embedded in systems, are difficult to separate from the first level of system integration.

In 2000, a question raised in the community was when we would have the first products in nanotechnology. In 2001, global revenues from products that incorporate nanotechnology as a key for competitiveness in seven sectors of the economy were estimated to reach $1 trillion by 2015 [15]. In 2013, according to industry surveys [18, 19] these global revenue estimations of $1 trillion were reached of which about $284 billion were in the US.

The US had about 33% ($110 billion) of the world revenues of $335 billion in 2010, 33% in 2011, 28% in 2013, and an estimated 25% ($750 billion) of the world revenues of $3 trillion in 2020. It is estimated these US nanotechnology-related revenues to be about 3.6% of national GDP ($20.94 trillion) in 2020 [19–22].

(vi) *Global R&D investment by both public and private sources* increased at an average global rate of about 35% in the first 8 years being estimated at $15 billion in 2008, of which about $3.7 billion was in the US, before the 2009 financial crisis [3, 17]. After 2010, nanotechnology R&D and production are found in increasingly diverse private, government, and non-profit platforms, which have expanded in new application areas with different growth rates.

(vii) *Global venture capital investment in nanotechnology* reached about $1.4 billion in 2008, of which about $1.17 billion was in the US [3, 17]. After 2010, nanotechnology is found in increasingly diverse venture capital platforms, which have expanded in numerous relevance fields at different rates.

(viii) *The level of penetration of nanotechnology in knowledge and technology* publications is another indicator of nanotechnology development. The penetration of nanotechnology in the number of new NSF awards increased steadily until 2013 and remains at about 14% since 2014 (Fig. 6) [22]. The NNI and US funding agency–related award data refer to fiscal years (FY), which begin on October 1 of the previous calendar year, according to the US federal budget schedule, while paper and patent publications refer to the calendar's year. Nanotechnology-related publications in the top 20 journals with nanotechnology content reached about 12–13% on average between 2014 and 2020. Corresponding publications in three highly cited journals—*Nature*, *PNAS*, and *Sci-*

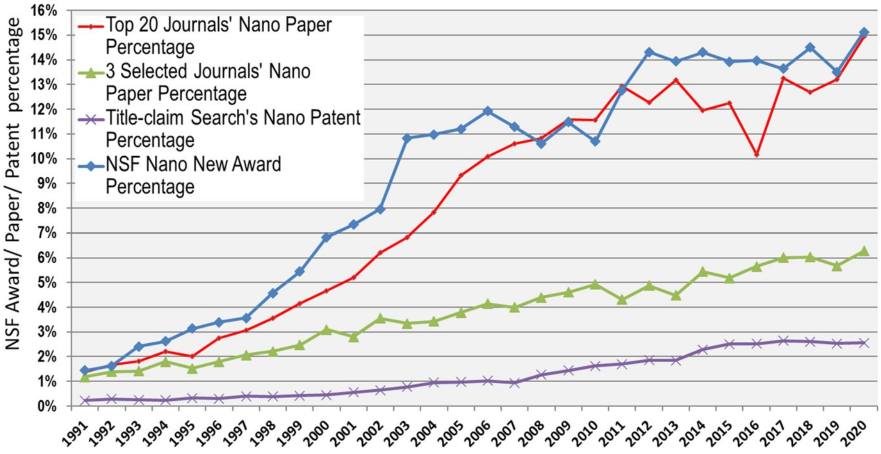


Fig. 6 Percentage rate of penetration of nanotechnology in the number of NSF awards, papers in 20 WoS journals with the largest nanotechnology contents, papers in three highly cited journals (*Nature*, *Science*, *PNAS*), and USPTO patent publications in the interval 1991–2020

ence—are at about 5–6% in the same interval. Nanotechnology-related patent publications at USPTO represent about 2.5% on average from 2015 to 2020. The rising nanotechnology percentage penetration curves follow each other in time, the first being the growing proportion in funding, then the proportion of papers, which is followed by the proportion of USPTO patents covering nanotechnology.

(ix) *Periodic expert evaluations*. Surveying publications and their citations generally show the level of research activity and innovation but not necessarily the breakthroughs or long-term scientific, technological, and other outcomes. NNI progress was subject to expert evaluations of the qualitative outcomes by nationally recognized organizations at the request of the US Congress, including by the Presidential Council of Advisors in Science and Technology (PCAST) [23–30], the National Academies (NASEM) with its arm National Research Council (NRC) [31–34], and the Government Accountability Office (GAO) [35]. The first PCAST letter of 1999 [23] recommended NNI to be supported by the President Clinton. The PCAST report (2005) completed after the passage of the 2003 "21st Century Nanotechnology Law" underlined the strong NNI outcomes after 5 years in research, education, and infrastructure [24]. In 2014, the fifth PCAST assessment of NNI highlighted the need to further support nanosystems and nanomanufacturing R&D and recommended a new vision for the following 15 years to 2030 [28]. The 2017 PCAST letter report recommends continuing a focus on grand challenges and especially on advanced nanomanufacturing [30].

The first evaluation of NNI by the National Academies was performed by the NRC (National Research Council) in 2002 with a report "Small Wonders, Endless Frontiers: A Review of the National Nanotechnology Initiative," which underlined the transformative long-term vision of the initiative [31]. The 2020 evaluation by the National Academies entitled "A Quadrennial Review of the National Nanotechnology Initiative: Nanoscience, Applications, and Commercialization" highlighted the significant outcomes of NNI after two decades, such as outgrowing the National Quantum Initiative for quantum information systems and underlined the importance of convergence of nanotechnology with other emerging fields [34].

NNI has produced important qualitative changes that are not fully reflected in numerical indicators:

- The creation of a vibrant multidisciplinary, multisector, international community of professionals and organizations engaged in various dimensions of the nanotechnology enterprise.
- Influencing the scientific research culture including energizing interdisciplinary academic research collaborations with industry and the medical field.
- Advancing unified concepts in understanding and transforming the material, energy, and biological systems in both research and education.
- Establishing advanced and flexible infrastructure for nanotechnology in academic and government

institutions, geographically distributed in all 50 states.

Four stages in nanotechnology development and diffusion in economy

The long-term view for establishing nanotechnology in the economy may be represented by a convergence-divergence cycle represented in Figs. 6 and 7. The convergence part originates with confluence of upstream knowledge, materials, and disciplinary tools (in the discovery/basic stage "a" in Fig. 7; in focus after about 2000) and continues with their assembling and integration at the nanoscale to form useful nanostructured assemblies, nanosystems, and technology platforms (in the integration stage "b"; in focus after about 2010). The divergence part begins with the creation of new processes and nanoproducts from the established technology and application platforms (stage "c"), from where new science and technology fields emerge by divergent differentiation and spin-off (stage "d"). An information and innovation spiral crosses the development platforms in time leading to new expertise, new architectures, new businesses, and new products. The divergence part of the cycle began about 2020. Here is where the most benefits are realized.

Each stage of the convergence-divergence cycle has several characteristics:

a. *Discovery/basic stage* (~2000–2010) is dominated by the confluence of disciplines, tools, and methods and activity sectors toward "control of matter at the nanoscale." Its main results are discovery of specific phenomena, properties, and functions at the nanoscale; creation of a library of nanostructures of most elements in the periodic table as building blocks for potential future applications; tool advancement; and improvement of existing products by incorporating relatively simple nanoscale components. The perceived higher risk areas of using nanostructured materials during this stage have been in cosmetics and food, as well as pharmaceutics and neuro-electronic interfaces.
b. *Integration at the nanoscale stage* (~2010–2020) led to new systems and generations of nanotechnology products. It had a focus on measurements with good time resolution and science-based design of fundamentally new products. The R&D emphasis shifted toward more complex nanosystems, new areas of relevance, and fundamentally new products. The perceived higher risk areas of using nanosystems were in nanorobotics, agriculture, and brain-machine interfaces.
c. *Innovation and divergence stage*. After about 2020, nanotechnology knowledge and technology begun to lead to multiple emerging technology platforms. Distributed and interconnected nanosystem networks and technologies across domains find applications for health, production,

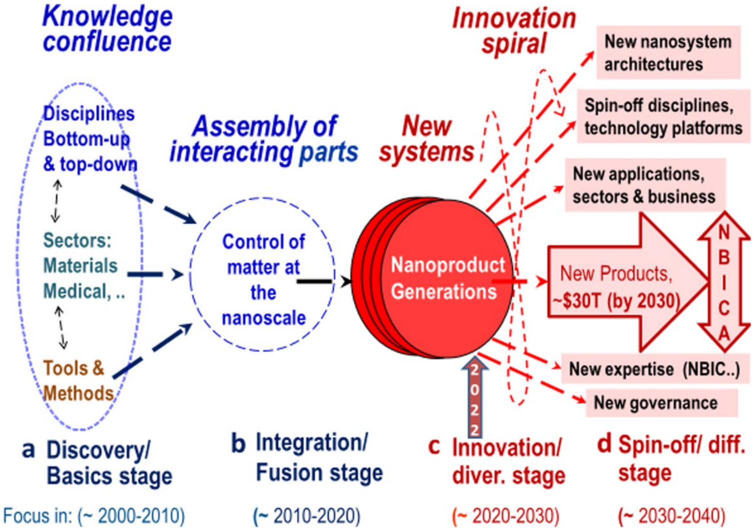


Fig. 7 2000–2040 convergence (a and b)-divergence (c and d) cycle for establishing nanotechnology

infrastructure, and services. The perceived higher risk areas of nanotechnology are using nano-bio-info-cogno-AI hybrid systems with increased integration and complexity.

d. *Spin-off and diffusion in the economy stage* is estimated to become dominant in 2030–2040. The developed research, design, and manufacturing tools will allow the application of nanotechnology to critical societal needs and inspire new S&T fields.

The introduction of new generations of nanotechnology-enabled product prototypes and services is shown on the right-hand-side of Fig. 8 [3, 22]). Nanotechnology between 2000 and 2020 encompasses four generations of new products with increasing structural and dynamic complexity: (1) passive nanostructures, (2) active nanostructures, (3) nanosystems, and (4) molecular nanosystems. Developments after 2020 are dominated by the creation of general capabilities and services and their deployment: (5) nano-inspired converging technology platforms, (6) nanosystem convergence networks, (7) emerging societal solutions, and (8) foundation for new S&T fields.

The vision and research directions for nanotechnology development in four stages have been formulated in several reports [1, 20, 36, 37]. The last three reports were developed with participation from more than 40 countries and have inspired programs at the national level in over 80 countries.

Various nanotechnology topics have "diverged" as spin-off activities and programs from core NNI research. The list includes the following:

- Quantum systems: to activities under the Quantum S&T Council in 2003 and later to establishing the National Quantum Initiative in 2018.
- Nano-environment, EHS, and ELSI: to NSF program solicitations beginning in 2001; grand challenge and NNI workshop in 2003; establishing NEHI working group in 2005.
- Metamaterials: a significant increase of NSF awards and outcomes after 2004.
- Plasmonics: a significant increase of NSF awards and outcomes after 2004.
- Nanomedicine: a strong focus for the National Institutes of Health (NIH) beginning with nanocancer research after 2004.
- Synthetic biology research: NSF/NNI and DARPA support research after 2004; SynBERC (Synthetic Biology Engineering Research Center) is established in 2006; Engineering Biology Research Consortium support after 2016.
- Advanced semiconductors: establishing the Nanoelectronics Research Initiative with the Semiconductor Research Corporation (SRC) after 2005; brain-like future of computing in 2015; National Microelectronics Leadership Strategy in 2020.

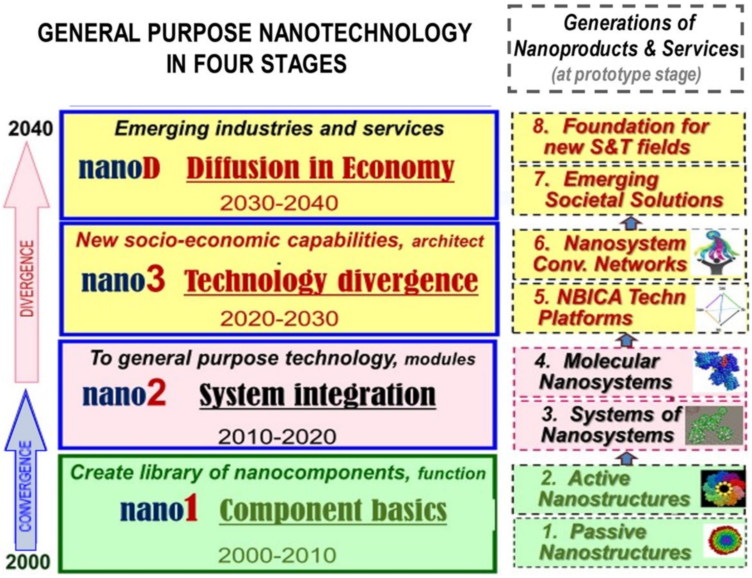


Fig. 8 Creating the nanotechnology field in four foundational stages: each stage includes two new generations of nanoproducts and services (updated from [20])

- Nano antennas and devices for wireless: a significant increase of NSF awards and outcomes after 2006.
- Modeling and simulation from the nanoscale up: to Materials Genome Initiative after 2011.
- Nanophotonics: to National Photonics Initiative after 2012.
- Twelve other spin-off topics are nanofluidics, carbon-based electronics, nano sustainability, wood nanofibers (nanocellulose), nanosystems for and by AI, DNA nanotechnology, protein nanotechnology, nano neurotechnology, nanosystems-mesoscale, quantum biology, nano- and micro-plastics, and nanoscale processes in plants and trees.

Over 30 federal agencies (20 departments and agencies if we group together the agencies from the same federal department) use NNI results on the control of matter at the nanoscale in their areas of relevance (Fig. 9).

All Fortune 500 companies dealing with materials, chemicals, pharmaceutical, aerospace, and other fields have programs on nanotechnology since 2015.

Setting priorities

The long-term view of nanotechnology development has several core ideas such as reaching systematic control of matter at the nanoscale, a focus on exploratory and transformative research, convergence principles in anticipatory and responsible governance, and incorporating emerging solutions in economy for societal benefit [1]. While the long-term vision has proven its viability after two decades, the strategic priorities and the approach to select them have evolved:

a. *Between 2001 and 2005*, NNI research priorities focused on “grand challenges” in nine R&D areas identified as having the potential to realize significant science and technology progress with economic, governmental, and societal impact [6]:

- Nanostructured materials by design
- Manufacturing at the nanoscale
- Chemical–biological–radiological–explosive detection and protection
- Nanoscale instrumentation and metrology
- Nano-electronics, nano-photonics, and nano-magnetics
- Healthcare, therapeutics, and diagnostics
- Efficient energy conversion and storage
- Micro craft and robotics
- Nanoscale processes for environmental improvement

Dedicated nanotechnology programs and major research and education centers and network initiatives

Fig. 9 Divergence of NNI created knowledge “control of matter at the nanoscale” to over thirty participating agencies (selected agencies are in this figure)

at NSF (with ten research and education networks including one with 19 Nanoscale Science and Engineering Centers and another around the Nanotechnology Center for Learning and Teaching), the Department of Energy (large-scale facilities in five Nanoscale Science and Engineering Centers), the Department of Defense (incorporated in DOD research facilities, including the Naval Research Laboratory's Institute of Nanoscience), NASA (e.g., four nanotechnology-serving space mission), NIH (e.g. National Cancer Institute's Nanotechnology Characterization Lab), NIST (Center for Nanoscale Science and Technology, NanoFabs), and other NNI agencies in the first 5 years led to the formation of the US nanoscale community, a strong R&D program portfolio, and new nanotechnology education programs. In the first 5 years of NNI, all engineering schools with accreditation had nanotechnology-related research, institutes or organized groups, and courses. Introducing foundational multidisciplinary research, education, and culture on nanotechnology has been a systemic change.

b. *Between 2006 and 2010*, NNI research focused on *four main goals* with their respective priorities [38, 39] and emphasized several program component areas. The goals were as follows: (1) advance a world-class research and development program; (2) foster the transfer of new technologies into products for commercial and public benefit; (3) develop and sustain educational resources, a skilled workforce, and the supporting infrastructure and tools to advance nanotechnology; and (4) support responsible development of nanotechnology. The NNI investment categories (originally seven categories, amended in 2007 to eight categories), called program component areas (PCAs), are as follows:

   - Fundamental nanoscale phenomena and processes
   - Nanomaterials
   - Nanoscale devices and systems
   - Instrumentation research, metrology, and standards for nanotechnology
   - Nanomanufacturing
   - Major research facilities and instrumentation acquisition
   - Environment, health, and safety
   - Education and societal dimensions

   NNI emphasized support of R&D for innovation and nanomanufacturing during this interval. In 2006, private nanotechnology R&D funding in the USA exceeded public funding, a trend growing continuously up to the present.

c. *Beginning in 2011*, the NNI introduced research and development "signature initiatives" for important application opportunities where collaboration among agencies is essential [40–42]. Three signature initiatives were established in 2011: Nanoelectronics for 2020 and Beyond (2011–2020), Nanotechnology Applications for Solar Energy (2011–2016), and Sustainable Nanomanufacturing (2011–2021). Other signature initiatives were adopted later: Nanotechnology Knowledge Infrastructure (2012–2018), Nanotechnology for Sensors (2012–2023), and Water Sustainability through Nanotechnology (2016–2023).
d. *In 2014, PCAST (2014) recommended a focus on grand challenges* [28]. The "Nanotechnology-Inspired Grand Challenge for Future Computing" was initiated. One outcome was the development of the concept of Intelligent Cognitive Assistants at NSF in collaboration with SRC [43] and the follow-up support of the research theme "Future of Work at the Human-Technology Frontier."
e. *In 2011–2020, NNI emphasized research on capabilities for a new generation of nanoproducts* such as those based on nanosystems, nano-bio assemblies, and self-powered nanodevices. There is an increased attention on nanoscale science and engineering integration with other knowledge and technology domains to create new nanosystem architectures and corresponding technology platforms [20, 21, 37]. Several research areas were strengthened such as nanobiomedicine and nanoneurology, exploiting probabilistic features at the nanoscale in stochastic magnets and entangled qubits, and nanotechnology for efficient energy conversion and storage. About one-third of the NSF's NNI awards in 2020 had an international dimension. One example of collaborative international activity on responsible nanotechnology is the US-EU Communities of Research (https://

us-eu.org/communities-of-research/). Another example is the annual US-Korea Forum on Nanotechnology focused on advancing emerging R&D areas.

f. *Focus after 2020 on societal nanotechnology challenges and diffusion of nanotechnology in science, technology, and the economy*. A primary research challenge remains the creation of hierarchical system architectures from the nanoscale and scaling-up modular NBICA manufacturing close to human dimension for various S&T platforms. Exploration of foundational principles at nanoscale that are not yet understood will be essential, including quantum entanglement and communication, gene editing in medicine and agriculture, and nano neurology. Special attention will be given to nanotechnology use in smart systems for general purpose AI and improving human capabilities. It is envisioned that convergence with other foundational technologies will bring more than half of the benefits. Nano-convergence will require specific risk governance measures and new organizations. The education pipeline needs to be expanded both in depth and cross-fields, be anticipatory for the opportunities in future economy and be inclusive. Nanotechnology sustainability will emphasize water, energy, materials, and clean environment resources. Growing topics are cleaning PFAS (per- and polyfluoroalkyl substances) from the environment with nanostructured catalysts, addressing global warming (see nano4Earth, https://www.nano.gov/National-Nanotechnology-Challenges), using distributed nanosensors and AI systems to monitor health and the environment, and reducing the risks of nano metals, nanocomposites, and nano-plastics. The new technologies from the nanoscale will require new responsibilities, including addressing the implications of emerging technologies and their products. Nano-EHS will address the safety of larger nanostructures and devices, as well as biosystems. Nano-ELSI will increase in importance for ethical, economic, legal, safety, and human development aspects.

The NNI's total R&D investment for nanotechnology increased about sevenfold in the first decade, from $270 million in 2000 to about $1.9 billion in FY2010 [3]. Funding has remained relatively steady after 2011 until 2021 when the core funding reached $2.065 billion. With supplemental funding of about $1.71 billion provided for BARDA (Biomedical Advanced Research and Development Authority) for COVID-19 diagnostics and vaccine research and devices using nanotechnology, the total reached about $3.780 billion [44]. The actual annual expenditures generally have exceeded the planned budgets because of additional contributions from other programs based on competitive scientific basis. For illustration, the NSF total budget for new awards in 2021 was planned to be about $425 million and the actual expenditure was about $620 million. This annual expenditure supported approximately 7000 multiyear active awards in all 50 states of which about ¼ are new awards made in 2021, funded over 30 centers and networks (including the National Nanotechnology Coordinated Infrastructure (NNCI) and Network for Computational Nanotechnology (NCN) and a large part of Materials Research Science and Engineering Centers (MRSECs), Engineering Research Centers (ERCs), and of other center programs), trained and educated over 10,000 students and teachers, and supported over 30 SBIR-STTR awards.

The convergence of nanotechnology with other emerging fields is a priority that was set up in 2001 [36, 45]. Table 3 shows the proportion of the number of NSF awards in 2020 and 2022 in eight emerging S&T sectors confluent with nanotechnology. The highest current confluence is with advanced bioeconomy (about 43% of the active nanotechnology awards), advanced manufacturing (about 25%), nanomedicine (about 24%), and advanced computing elements (about 20%). The most significant increases are for quantum information systems (from about 26 to 38%), digitization and AI systems (from 5.3 to 10%), and nano sustainability (from 11 to 18%). If one considers the new awards, the increases are even more pronounced for these three sectors. Moderate increases are seen for cognition and brain (from 5.4 to 6%) and for advanced wireless (from 1.7 to 2%).

Many nanotechnology projects contribute to more than one special area listed in Table 3. About 70% of the nanotechnology projects contribute to at least one of those areas in 2020–2022. If we limit the special S&T areas only to the foundational NBICA areas (nano, bio, info, cogno, AI), about 50% of all nanotechnology awards have contributions from them.

Table 3 Proportions of active research projects supported by NSF in 2020 and 2022 at the confluence with the six "industries of the future" identified in national R&D investments, as well as in other three sectors

Special S&T sectors (covered by the NSF nanotechnology awards)	2020 % of all active awards (% of new award)	2022 % of all active awards (% of new awards)
"Industries of the future"		
(i) Quantum information systems	**26%** (32%)	**38%** (40%)
(ii) Digitization and AI systems	**5.3%** (9.4%)	**10%** (14%)
(iii) Advanced computing elements	**19.3%** (21.7%)	**21%** (22%)
(iv) Advanced wireless (5G, 6G)	**1.7%** (2.0%)	**2%** (2%)
(v) Advanced bioeconomy	**44%** (53%)	**41%** (37%)
(vi) Advanced NBICA manufacturing	**25%** (23%)	**25%** (24%)
Other sectors		
(vii) Nano sustainability	**11%** (10%)	**14%** (18%)
(viii) Nanomedicine	**23%** (26%)	**25%** (26%)
(ix) Cognition and brain	**5.4%** (5.5%)	**6%** (7%)

Besides formulating the unifying definition, the long-term vision, governance principles, and a process for setting research priorities of nanotechnology from the beginning, the NNI has created a framework for advancing investments in physical infrastructure and education [1, 3, 20, 46, 47], environmental aspects [3, 20, 48, 49], translational research (e.g., [3, 7, 20, 50]), and outreach and international aspects [7, 16, 20, 51]. This scientific approach was positively evaluated by the National Academies and PCAST.

The NNI has been implemented during five US presidential administrations: Clinton, Bush, Obama, Trump, and Biden.

- President Clinton set up broad NNI priorities in his remarks made at the California Institute of Technology in January 2000: "Some of our research goals may take twenty or more years to achieve, but that is precisely why there is an important role for the federal government" [[5]. The NSET Subcommittee and NNCO were established in August 2000 to implement those goals [[52].
- President George W. Bush's administration further increased funding for nanotechnology to address several grand challenges. On 3 December 2003, President Bush signed into law the 21st Century Nanotechnology Research and Development Act. Public Law 108–153 [[9]. The annual budget of NNI increased 20–25% per year from 2000 to the end of 2008 during his administration.
- President Obama's administration highlighted nanotechnology support in several White House presentations and approved the 2015 PCAST report with a vision for development of nanotechnology to 2030 [[28].
- President Trump's administration supported increase funding of NNI with a focus on both basic research and emerging technologies to advance industries and communities of the future, in particular quantum, AI semiconductors, wireless communication systems, and mRNA vaccines [[33].
- President Biden's administration renewed the strategic plan for 2021–2026 [[7] and increased efforts to address environmental and climate concerns including the Climate Change National Nanotechnology Challenge and to mitigate the effects of nano- and micro-plastics in the environment.

Governance of nanotechnology

Five functions of anticipatory nanotechnology governance have been advanced at the beginning of the initiative: be visionary, transformative, responsible, inclusive, and advance convergence [34, 53, 54]. Combining innovative and responsible governance has been a priority [20]. Governance has been implemented at four levels: research and regulatory programs, funding agencies' principles, the national executive leadership (NSTC), and the legislative framework (US Congress).

Visionary and anticipatory governance of nanotechnology

The long view for nanotechnology development includes the following: (a) the 30–40-year perspective for establishing nanotechnology as a foundational, general-purpose science and technology field [1, 36], including the Public Law No. 108–153 in December 2003, which provides long-term support and guidance for NNI [9]; (b) 10-year detailed vision for the field [1, 20, 37]; (c) a strategic planning process reported to Congress to repeat every 3 years by 2010 and every 5 years thereafter; (d) nanotechnology grand challenges for all participating agencies or for a group of agencies; (e) an annual NNI implementation and collaborative plan completed for WH and Congress; and (f) monthly or bi-monthly interagency meetings for agency coordination and program adjustments. A reverse mapping planning exercise of nanotechnology development was used for the first (2001–2010) [3] and second decade (2011–2020) [20].

The long view for specific goals has been coordinated either by NSET, by one of its working groups, or by a cluster of agencies most informed and with visionary expertise for the respective goals. For example, the NNI working group for Nanotechnology Environmental and Health Implications has prepared the long-view Environmental, Health, and Safety (EHS) Research Strategy for research with co-leadership from research and regulatory agencies in 2011 [48]. That perspective has been successively updated in 2014, 2017, 2022, and 2023.

The NNI governance approach has included periodic scientific evaluations of the program portfolios and the identification of opportunities for new research directions and grand challenges such as the grand challenges on energy in 2002, on computing in 2005, and on brain-like computing in 2015. Visionary challenges have been encouraged by the program such as in quantum mechanics, precision medicine, and nanocellulose [55–58].

Transformative, compelling development

This function includes the systematic selection of outcome-driven research and education projects and investments in infrastructure with high translational potential for increasing productivity and other benefits in society. One of the NNI goals is to “Foster the transfer of new technologies into products for commercial and public benefit.” To better address transformative and responsible development of nanotechnology, the NSET established several working groups on: Nanomanufacturing, Industry Liaison, and Innovation (NILI); Nanotechnology Environmental and Health Issues (NEHI); and Global Issues in Nanotechnology (GIN).

Nanomanufacturing was set up as a grand challenge in 2002, and NSF established a dedicated research program on the topic in the same year. Five Nanoscale Science and Engineering Centers (NSECs) on nanomanufacturing and the National Nanomanufacturing Network (NNN) were created by 2006.

The NNI agencies also formulated in 2003 a new approach for interaction with various industry sectors, called the Consultative Boards for Advancing Nanotechnology. Nanomanufacturing increasingly has been funded by mission-oriented agencies, partially in partnership with industry [59]. Examples of programs supporting translational research are SBIR/STTR for small business, Grant Opportunities for Academic Liaison with Industry (GOALI), Innovation-Corps, INTERN for student internships to industrial sites, and many others. Among the partnerships with translational goals, one may cite the SRC-NSF-NIST-DARPA collaboration for the Nanoelectronics Research Initiative NCORE and STAR for research “beyond CMOS/Moore’s Law and beyond,” the NIH’s National Cancer Institute Alliance for Nanotechnology in Cancer [50], and NIOSH-industry partnership, all beginning in 2005.

In another illustration, the Graphene Council [60] (https://www.thegraphenecouncil.org/) established a consortium platform for introducing graphene in the economy, with 45 targeted industry application sectors from additive manufacturing to concrete and plastics, plasmonics, and water filtration.

Another significant focus has been on creating an entrepreneurial culture in the nanotechnology community. The NNI-sponsored *Nanotechnology Entrepreneurship Network (NEN)*, for example, brings entrepreneurs together.

Nanotechnology development has been reflected in commercialization in many economy sectors [17–21], as well as in published patents and papers by

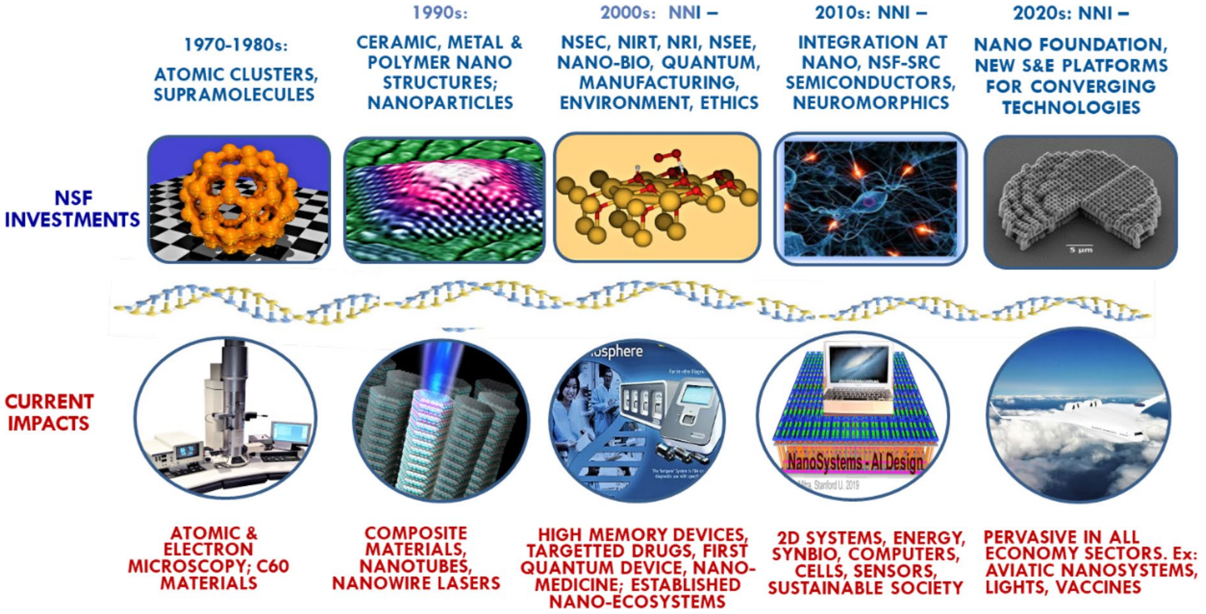


Fig. 10 Investment impact: examples of discovery-innovation DNA in nanotechnology [62]

nanotechnology related companies [61]. A schematic suggesting the pervasive impact of nanotechnology research is shown in Fig. 10 [62]. Several examples of new industries are nanostructured high-density batteries for cars and planes, optoelectronics systems, critical nanostructured materials and minerals, additive manufacturing for 3D printing, nanomedicine devices, products, and treatments such as T-cell trained treatment for chronic diseases and nanoliposomes for mRNA delivery.

Responsible

Responsible development of nanotechnology has been a core function of NNI with four main components: realizing balanced societal benefits, achieving responsible innovation and economic return, addressing risk management (nano-EHS, nano-ELSI), and supporting societal sustainability. The investments for nano-EHS research received special attention at the beginning of NNI; its budget increased from about 3% of the total initiative investment in 2003 to about 7% around 2010 and then decreased as the research data accumulated. This was the highest percentage allocation for environmental, health, and safety issues from all other national R&D programs in the US. A dedicated working group—Nanotechnology Environmental and Health Implications (NEHI)—was formally created in 2005 [63].

The concerns about the risks of nanotechnology, ethical aspects, benefits to society, public acceptance, and other ELSI aspects were addressed via meetings with stakeholders, studies addressing societal dimensions beginning from the first year of NNI [15, 53, 54], and funding research and outreach projects. The earlier perceptions such as "the transformative risks are too high," "applications too risky for food and cosmetic systems," "concerns on economic return," and "risks of terrorism" have been addressed upfront including mitigation solutions. It has been estimated that acceptance of many nanotechnology applications has improved on that basis. NSF established research networks focused on nanotechnology in society (two Centers for Nanotechnology in Society at University of Arizona and UCSB in 2005–2015), informal nanotechnology science education (the Nanoscale Informal Science Education Network in 2004–2014), nano-EHS (Center for Biological and Environmental Nanotechnology at Rice University in 2001–2011 and Centers for Environmental Implications of Nanotechnology at UCLA and Duke University in 2008–2018), and sustainability (Center for Sustainable Nanotechnology at University of Wisconsin in 2015–2025). These multidisciplinary, multimodal centers helped create communities of research in the US and internationally and supported interagency research, standards, and regulations on the respective topics.

New responsibilities are required to address the opportunities, outcomes, and risks of novel technologies originating from the nanoscale. Nano-EHS will need to address the new and more complex products and services that would be created. Higher risks are currently associated with nano-plastic pollution because of its volume (with bioaccumulation effects), with nanocomposites, and nano-metals because of their high toxicity, as well as with biological transformation of nanomaterials, tissue reactions, and neural effects that are not yet fully understood. Detection and measurement of exposure to nanomaterials in natural and working environments is a continuing challenge with increasing commercialization of nanoproducts. Nano-ELSI will grow in importance as the effects of new technologies deal with increasingly complex systems and have emerging health, legal, ethical, and other societal implications. Nano-ELSI must be adapted to be more anticipatory, inclusive, and integrative, addressing challenges in reaching diversity and inclusion. Overall, convergence will amplify the outcomes and implications to be addressed by society.

Several partnering organizations have been the Organization for Economic Cooperation and Development (OECD) on governance of nanotechnology (Biotechnology, Nanotechnology, and Converging Technologies working party) and nano-EHS (working party on Manufacturing Nanomaterials, WPMN [64]), US-EU community of research on nano-EHS, Technical Committee TC229 in International Standards Organization, and International Risk Governance Council (IRGC) on international governance of nanotechnology.

Inclusive

It refers to investigative methods, multidisciplinary communities, sectors of activity, sponsoring agencies, openness to new ideas, and contributors from all potential stakeholders, as nanotechnology is distributed in many domains. Diverse stakeholders, producers, and users of nanotechnology are included in the strategic and planning process: getting academic and industry input (from industrial groups such as SRC and NanoBusiness Alliance), requesting public comments at national level, holding workshops, and having dialogs with multiple partners in the process of producing the nanotechnology research direction reports and annual budget supplements, as well in preparation of various reports on societal implications [1, 37, 53, 54]. Partnering of interested federal agencies through the NSET Subcommittee has been collegial, collaborative, and synergistic. R&D programs require various disciplines and sectors of activity to work together. Funded projects are distributed across all 50 states. An example is support for a nanotechnology R&D network of 34 regional, state, and local nanotechnology alliances in the US in 2010 [3]. International collaboration began with the preparation of the visionary documents and workshops. It has included international dialogs on nanotechnology such as the first two in 2004 and 2006 with 25 nations and the EU in the US, and the third in 2008 with 49 countries and the EU in Europe. It also included US participation in key international fora for nanotechnology (ISO, OECD, International Risk Governance Council, etc.) that are focused on the development of collaborative research and education, appropriate international standards, terminology, and regulations. The International Risk Governance Council [51] has provided an independent international perspective for a framework for identification, assessment, and mitigation of risk. About 30% of NSF awards in nanoscale science and engineering have some form of international collaboration in 2020–2022. Inclusion of partnerships with industry has been cited earlier in the transformative function of nanotechnology governance.

Convergence

It includes the confluence of disciplines and communities, integrating tools and methods, creating a new system or framework for problem-solving and nanoproduct realization, and then diverging to a variety of new nanotechnology outcomes and applications. This function has been essential because of the multidomain nature of nanotechnology. NNI has become a model or scientific collaboration and an earlier model of S&T convergence. Convergence principles have been applied for the development of nanotechnology understanding and manufacturing [36, 65], for enhanced confluence with other science and technology fields [37, 45], and as a foundation for other emerging technologies [64, 66].

NSF nanotechnology programs have funded convergence awards since 2001. Dr. Cordova, NSF Director, wrote [67]: “I think of nano as quintessentially NSF:… The research crosses disciplines in science, engineering and the economy and is funded by NSF in coordination with twenty other NNI departments and independent agencies; … Nano research unifies concepts in science and engineering that fundamentally change our understanding of nature and the tools that can transform it.”

NNI actions in support of convergence have included advancing cross-field research and education, developing program announcements including convergence themes, supporting open collaborative networks (such as Network for Computational Nanotechnology), holding open webinars and meetings, creating groups and institutes across academic campuses, and cross-domain benchmarking of complex nanodevices (such as benchmarking of novel logic and memory devices by SRC-NSF-NIST Nanoelectronics Research Initiative). The convergence research and innovation culture in universities and research laboratories has been enhanced by supporting synergistic communities of interest, enabling remote collaboration, shared use of physical equipment and computational facilities, enabling distributed research, and preparing compelling collaborative and visionary plans before starting large projects.

The National Academies [68] have provided a model for convergence-driven research centers. In its 2020 evaluation of NNI initiative, NASEM [34] recommended a focus of nanotechnology research on convergence with other emerging technologies, extending the recommendations of the earlier convergence studies ([36, 37].

Overall, the NNI governance approach was subject of external evaluations:

- PCAST (1999) [23] highly recommended the proposed initiative to President Clinton: “The NNI is an excellent multi-agency framework to ensure US leadership in this emerging field that will be essential for economic and national security leadership in the first half of the next century.”
- Barbara Mikulski, Chair US Senate Science Committee, wrote “Now, at the beginning of the twenty-first century, we are on the verge of …the nanotechnology revolution. It is the science and technology that will drive the future” on June 12, 2000 [15].
- National Research Council (NRC, 2002), in the first evaluation of NNI by National Academies [31], wrote: “…The committee was impressed with the leadership and level of multiagency involvement in the NNI.”
- The Presidential Council of Advisors in Science and Technology (PCAST 2005) endorsed the governing approach of NNI: “(The Council) supports the NNI’s high-level vision and goals and the investment strategy by which those are to be achieved.”
- “NNI is a new way to run a national priority,” Charles Vest, president of the National Academy of Engineering, at the March 23, 2005, PCAST meeting reviewing the NNI for Congress.
- “NNI… has had ‘catalytic and substantial impact’ on the growth of the US nanotechnology industry” PCAST (2010) [26].
- David Rejeski, Director of the S&T Innovation program at the Woodrow Wilson International Center for Scholars: “The NNI story could provide a useful case study for newer research efforts,” in *Nature*, September 2, 2010 [58].
- NASEM report to Congress in 2020 [34]: “Impacts of NNI to date: Impressive, tangible outcomes that have emerged from these coordination efforts, including the recent formation of the NQI.” “Finding 1.2: The National Quantum Initiative (NQI) is, in large part, an important outgrowth of the National Nanotechnology Initiative (NNI).”
- David Guston, University of Arizona in 2010 [69]: “Nanotechnology has become a model and an intellectual focus in addressing societal implications and governance methods of emerging new technologies.”
- “The vision of NNI has been realized,” Arati Prabhakar, Assistant to the US President for Science and Technology, at the July 27, 2023, PCAST meeting reviewing the NNI for Congress.

Lessons learned (2000–2020)

Objectives that have not been fully realized after 20 years

- *General methods for achieving nanoscale* “materials and systems by design” with desired performance and their use in manufacturing, nanomedicine, quantum devices, and other fields have been delayed because reliable predictive tools have not been ready. In the last few years, hierarchical models, use of AI, and advanced handling of big data have made significant progress.

- *Establish large-scale academic nanomanufacturing capabilities with open-access Lab-to-Fab* for nanosystems and semiconductor technologies. The funding limitations for large projects did not allow this investment so far, but there is promise for progress particularly for semiconductor fabrication in the future.
- *Progress toward quantum computing and communication systems*. The expectation in 2000 of fast progress in quantum theory and devices to be incorporated in computing and communication systems was delayed because of conceptual, instrumentation, and modeling limitations. The first quantum device was prototyped in 2010. The first successful quantum internet and quantum computing experiments were completed only in the last couple of years. The National Quantum Initiative is an outgrown from NNI in 2018 [70] that promises faster outcomes.
- *Widespread public awareness of nanotechnology*. The public awareness figure has remained at about 30% despite significant outreach activities.
- *Institutionalizing* nanotechnology programs in academic institutions.

On target in 2020, even if doubted in 2000

- *Significantadvancement in interdisciplinary research, education, and innovation:* nanotechnology R&D has supported numerous scientific breakthroughs, multidisciplinary projects, organizations, and communities and led to the creation of other emerging areas. Nanotechnology has become a general-purpose technology for the material world and is increasingly incorporated in core research, design, and production programs. Molecular medicine at subcellular level and targeted drugs have become a reality.
- *A strong and flexible physical and cyber infrastructure* including new nanotechnology centers, integrated facilities, and networks.
- *The estimation that US nanotechnology R&D investment* will grow by an annual rate of about 20% in the first decade of NNI (2001–2010) to reach an established critical level of activity has been realized. The NNI budget increased from about \$270 million in 2000 to about \$1.9 billion in 2010, with an average growth rate of about 21.5%. The NNI investment has been relatively stable between 2010 and 2020, changing qualitatively in content.
- *Nano-EHS research* dealing with toxicity, exposure, and regulatory measures has become a key interagency task, with contributions for databases, epidemiological studies, and broader sharing of results. It has advanced to mechanistic explanations of underlying phenomena and proactive application of regulatory measures. ELSI-related investigations play an essential role.
- *A significant growth rate in scientific publications*: the average annual rate for nanotechnology publications has been about 13% for WoS papers and 19% of WIPO patents (15% for USPTO patents) in the first 20 years, at rates that are over three times higher than the average for papers and patents in all scientific fields.

Better than expected after 20 years

- *Earlier major industry involvement* beginning with 2002–2003. By 2009, more than 5400 US companies had research papers, patents, and products, and the use of nanotechnology in industry becomes prevalent around 2020 [19, 22]. Moore's law for improving performance of semiconductors has continued for the past 20 years, despite serious doubts raised in 2000.
- *Unanticipated discoveries* and advances in several science and engineering fields, including plasmonics, metamaterials, spintronics, graphene, cancer detection and treatment, drug delivery, vaccines, synthetic biology, neuromorphic engineering, nanocellulose, AI-designed semiconductors, and quantum biology. Self-powered nanodevices and self-healing polymers and metallic alloys have been produced.
- *It has inspired and enabled multiple new S&T domains*, rising horizons for the industries of the future and human development.
- The formation and growing strength of the *international nanotechnology community*, including nanotechnology EHS and ELSI: these developments have surpassed anticipated plans.

- *The long-view planning has proved essential*, and the main predictions have been realized. It has led to cultural change in interdisciplinary research in universities and rapid progress of converging technologies from the nanoscale.

Main lessons learned after 20 years

- *There is a continuum need for fundamental research pipeline*, with focused investments in theory, direct measurements, and simulation methods at the nanoscale.
- *Convergence of disciplines* and with other foundational fields has been essential for progress, and most of the future benefits reside in converging science, technology, and medicine.
- Besides R&D in new areas such as advanced computing devices, nanophotonics, and nanomedicine, excellent *opportunities for nanotechnology R&D exist in classical industries and economic sectors*, such as textiles, metallurgy, wood and paper, plastics, and agricultural and food systems. Improved mechanisms for public–private partnerships are needed to establish consortia or platforms for targeted development programs.
- Nanotechnology offers an opportunity to *better connect science and engineering* to translational research and the creation of jobs.
- There is a need for improving fundamental understanding and testing of scale-up nanotechnology in large-scale experiments.
- There is a need for increasing multistakeholder and public participation in nanotechnology research, education, and governance.
- Applying the five functions of nanotechnology governance (visionary, transformative, responsible, inclusive, convergence) has been essential in realizing the NNI investments. Societal implications have been addressed as an integral part of the core research and included in all large centers and networks.

Nanotechnology enables new science and technology horizons

Nanotechnology enables a bottom-up synergistic foundation for new horizons in science and technology as has been envisioned in earlier planning NNI studies [1, 20, 22, 36]. The progress in nanotechnology made in the last two decades has fundamentally changed how we think about nature and life and, consequently, how things are done in industry, medicine, energy, environmental protection, defense, and in most sectors of the economy. Addressing ethical, environmental legal, and other societal implications has been a key for the successful implementation of nanotechnology. Nanotechnology provides not only inspiration and new concepts but also building materials and tools for other technologies. Six "industries of the future" already are on fast-track funding in the US and other countries:

(i) Q*uantum information systems, including quantum materials, communication and computing, sensors, and biology*. It has grown by expanding nanotechnology research where quantum fluctuations are relevant and using nanomanufacturing to build quantum information systems. Theoretical quantum developments need the nanoscale multi-phenomena material context. The current efforts have moved to testing precursors of quantum computer systems and quantum internet. In 2020, NSF and DOE have established their Networks of Quantum Centers and research programs in the US as a part of the national strategy [71]. The contribution of the number of new quantum-related awards in the NSF nanotechnology portfolio is illustrated in Fig. 11, increasing from about 5% before 2015 to 40% in 2022.

(ii) *AI systems*. Nanotechnology provides critical, essential hardware for computing, sensing, communication, and dynamic realization of AI systems (Fig. 12). At its turn, AI helps design 3D nanostructures and nanosystems such as catalysts, molecular robots, neuromorphic circuits, and neural circuits. NSF and SRC co-sponsored the 2016–2020 "Energy-Efficient Components-Devices-Architectures" program including AI approaches. NSF and other agencies created the National AI Research Institutes and research programs after 2020 as part of a national AI strategy [72]. The confluence of NNI with AI in NSF awards is illustrated in Fig. 11; the proportion of the number of new AI awards in NNI portfolio rapidly increased from about 1% in 2015 to 14% in 2022.

Fig. 11 Number of quantum-related awards in NNI portfolio at NSF, which represents about 32% of all new nanoscale science and engineering (NS&E) awards made by NSF in 2020 and 40% in 2022

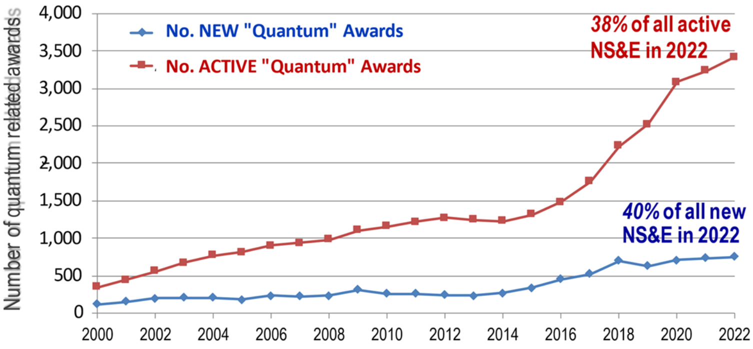
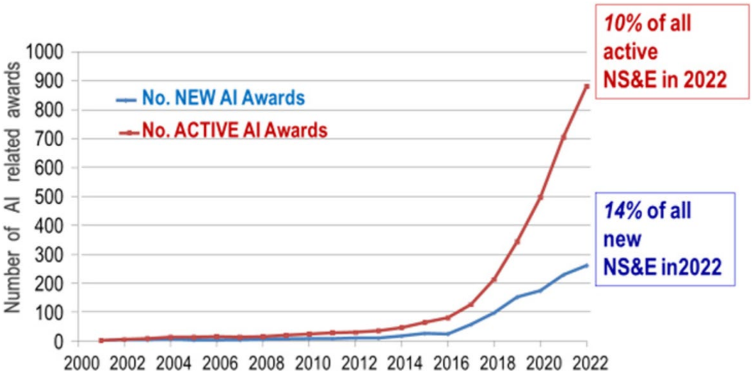


Fig. 12 Number of AI-related awards at NSF, which represents about 9.4% of all new NS&E awards made by NSF in 2020 and 14% in 2022



(iii) *Advanced computing elements and circuits* are based on semiconductors and neural networks. Current research areas include the transition from 2D to heterogeneous 3D nanostructures, DNA-based memory devices, incorporation of new nanomaterials and nanodevices and systems in CMOS, and computing element-neuro interfaces. NNI has played a lead role in nanoelectronics, magnetics, and photonics since 2001. "CHIPS and Science Act" of 2022 [73] provides new incentives for this field. The confluence of NNI awards with advanced computing (including semiconductors, neural networks, neuromorphic and quantum- and brain-like computing) is illustrated in Fig. 13.

(iv) *Advanced wireless*. Advanced emitters, antennas, and other nanoscale components and devices are developed for 5G and 6G wireless technology. An example of an interagency program is Resilient and Intelligent Next-Generation Systems (RINGS), which is supported in partnership with industry. Advanced wireless-related projects represent about 2% of all new NNI awards made by NSF in both 2020 and 2022.

(v) *Advanced bioeconomy*. It encompasses nano-enabled genomic, molecular, and cell biology in biotechnology, synthetic biology, and biomedicine. Examples are miniaturization of DNA sequencing devices and nanoengineering of DNA, proteins, and organisms. Bioeconomy-related projects represent about 37% of all new NNI awards made by NSF in 2022. This is the largest contribution from other emerging fields to the NNI portfolio.

(vi) *Advanced manufacturing*. It includes using NBICA in convergence production units, networked nanomanufacturing services, 3D printing with nanomaterials, and AI with machine learning for new nanomaterial and system architectures. Projects related to advanced manufacturing represent about 25% of new and all active NNI awards made by NSF in 2022 (Fig. 14).

In the future, nanotechnology will play an essential role in several other economic sectors:

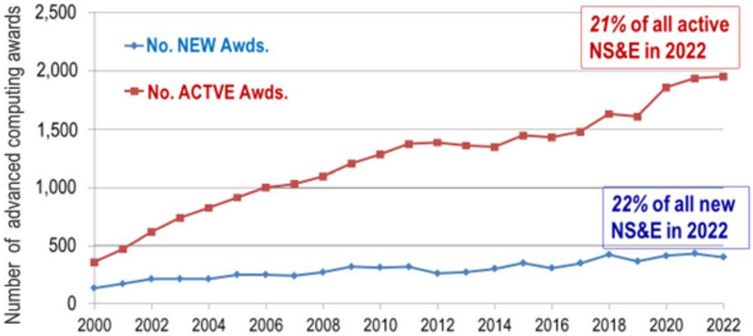


Fig. 13 Number of advanced computing awards at NSF, which represents about 21.7% of all new NS&E awards made in 2020 and 22% in 2022

(vii) *Sustainable society*, including a clean environment, a stable climate, and sustainable materials, water, energy, and food resources, by using a large variety of approaches such as nanostructured batteries and membranes, nano-enabled recycling and remediation, and cyber agriculture using nanosensor networks. The Climate Change National Nanotechnology Challenge was announced in 2022 as a priority for NNI (www.nano.gov/nano4EARTH). Sustainable society-related awards represent about 18% of all new NNI awards made by NSF in 2022 and about 14% of all active awards in the same year (Fig. 15). The growth of the number of sustainable society awards is more evident after 2020.

(viii) *Nanomedicine*, including diagnostics, therapeutics, nanostructured implantable materials, regenerative medicine, vaccines, treatment for chronic diseases, and prevention of pandemics. It represents about 26% of the number of new NNI awards in the interval 2020–2022.

(ix) *Cognition and brain* impacting economy and society, which includes nanoscale understanding of the brain, its interfaces, and neurotechnology. It represents 5.5 to 7% of the number of new NNI awards in the interval 2020–2022.

(x) *Flight and space exploration* including more efficient fuels, lighter nanomaterials for loads, bio-recycling, exploratory capabilities on nanoscale material synthesis, and controlled bio structuring.

(xi) *Reshaping education*, by adopting unifying nanoscale concepts, helping to learn via virtual and individualized programs using nanotechnology-enabled infrastructure.

(xii) *Support for independent aging* including advanced biomedicine, orthopedics, and robotics with nanosensors.

(xiii) *Increasing human capacity*, by enabling devices and systems for physical, mental, and collective improvements of human capabilities. This includes nanoscale understanding of the neural system and its interfaces.

(xiv) *Nanotechnology for quality of life*—a goal resulted from better using technology and convergence from the nanoscale for human development including "joy of living" goal as aimed at the beginning of the long-term view of nanotechnology R&D.

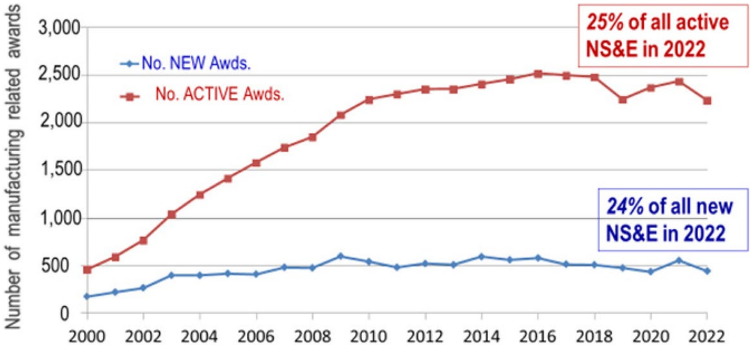
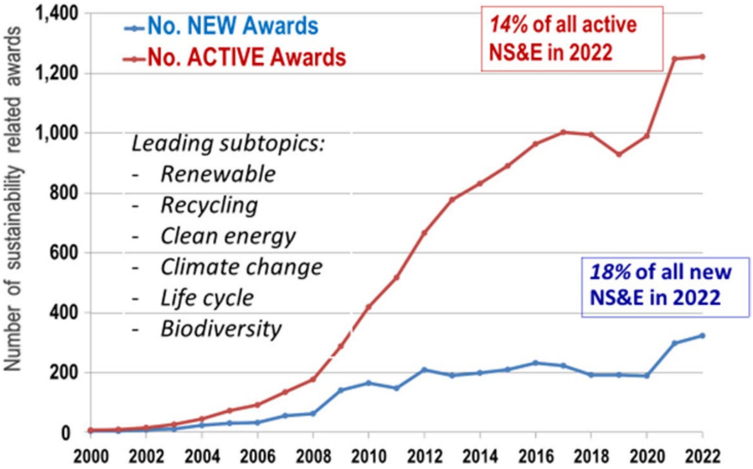


Fig. 14 Number of NBICA manufacturing-related awards at NSF, which represents about 23% of all new NS&E awards made by NSF in 2020 and 24% in 2022

Fig. 15 Number of sustainable society-related awards at NSF, which is about 10% of all new NS&E awards made by NSF in 2020 and 18% in 2022



Education and training evolve with the creation of new fields of knowledge, the need of synthesizing new knowledge, and the availability of emerging means to better communicate and learn. Education and training have to be across disciplines and areas of relevance for the material, digital, and logical world. Nanotechnology education preparing for the NBICA technology system should be included earlier at an age when the basic concepts are formed.

Several possible aspirational goals to consider are as follows:

- *Aspiration goal for the next 10–20 years*: economically produce by design suitable nanostructured components for emerging technologies. AI may change the design and use of nanotechnology significantly as simulations will increase in importance. An example of current opportunities is at the confluence between Chemistry and Quantum Information Science [[74].
- *Aspiration goal for the next 20–30 years*: a new theoretical framework for key phenomena at the nanoscale to include the essential nanoscale entities as variables instead of using variables that are best suited for much larger or much smaller scales. This would allow us more precisely and efficiently to understand and predict phenomena and processes at the nanoscale, for example, to describe the transition from quantum to classical physics, to simultaneously study co-current multimodal processes, and to make predictions at the nanoscale beyond what we can do in the current theoretical frameworks.
- *Aspirational goal for the next 50 years*: ability to control quantum biology and medicine and build on that basis advanced nanostructured materials, biosystems, and neuro architectures. Plants at room temperature show properties and functions we had only seen near absolute zero with hard materials in the laboratory and can perform complex processes such as photosynthesis [[55].
- *Aspirational goal for the next 100 years*: research will move closer to the true indivisible atoms through several hierarchical levels of subatomic particles, from where one may develop the ability to manipulate the current atomic building blocks known in the periodic table and eventually creating new nanoscale modules and structures on their basis. The last century's discoveries clearly show that the currently named atoms are just at a length scale where the structure of matter is more stable, but the real indivisible, indestructible "atoms" are at a smaller scale, and there is a possibility to increase control at the intermediate subatomic levels. Proper theories, tools, and system engineering will be developed.

Closing remarks

Nanotechnology has been defined based on specific properties, functions, and ability to control matter at the atomic, molecular, and macromolecular levels. It has become an essential foundation of the global S&T system for matter and energy, for industries of the future, and for human development. NNI has inspired and enabled new fields of research such as precision nanomedicine and quantum information systems. Nanoscience breakthroughs have continued during the last two decades, and the overall progress of knowledge is close to extraordinary. Chad Mirkin wrote, “NNI promised a lot. It has over-delivered” [57]. There is an increased need for scaling up engineering research experimentation, economic prototyping, and fabrication and for application to societal challenges.

This paper has examined NNI in the last two decades. The cumulative R&D investment in NNI is about $40 billion as of October 2023 [44]. It has become the second largest coherent initiative after the Apollo program [58]. An international community with more than 80 countries using a vision and programs similar to NNI at least for specific investment intervals has been formed. More than half of science discoveries and of nanotechnology benefits are realized at the confluence with other emerging technologies.

While the expectations of nanotechnology—both positive and negative—may have been overestimated in the short term, the impacts of nanotechnology in the long term on knowledge, innovation, productivity, healthcare, genesis of other technologies, and the entire S&T system appear now to be underestimated. The arguments are now stronger than in 2011 [3]. After two decades of NNI, nanotechnology already has penetrated and transformed almost all fields and disciplines of research, education, and innovation related to the material world from biology to aeronautics, becoming a model of scientific collaboration. Products incorporating nanotechnology are pervasive in daily life, from smart phone components to LEDs, solar panels, and vaccines. Furthermore, it has become the dominant technology in several production areas such as catalysts, semiconductors, advanced batteries, and new pharmaceutical products. Nanotechnology provides foundational knowledge, inspiration, enabling tools, and synergistic solutions for most industries of the future such as advanced computing, quantum, AI systems, 5G-6G wireless communication, and molecular bioeconomy. With proper consideration given to convergence methods, education, and safety aspects, it promises to form a core, unifying foundation for the entire emerging and converging S&T system in addressing societal needs and opportunities.

By advancing nanotechnology, one may paraphrase a quote of Louis Pasteur about the role of microbes in microbiology and declare about the developments in the material world: “Gentlemen, it is the atoms who will have the last word.”

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Compliance with ethical standards

Competing Interests The author is the Editor in Chief of JNR. Because of this, the peer review process of this manuscript and decision about suitability for publication were performed by the JNR Executive Editor.

Disclaimer The opinions expressed here are those of the author and do not necessarily reflect the position of NSTC/NSET or NSF.

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