



THE NATIONAL NANOTECHNOLOGY INITIATIVE

Supplement to the President's 2018 Budget



About the National Science and Technology Council

The National Science and Technology Council (NSTC) is the principal means by which the Executive Branch coordinates science and technology policy across the diverse entities that make up the Federal research and development enterprise. A primary objective of the NSTC is establishing clear national goals for Federal science and technology investments. The NSTC prepares research and development strategies that are coordinated across Federal agencies aimed at accomplishing multiple national goals. The work of the NSTC is organized under committees that oversee subcommittees and working groups focused on different aspects of science and technology. The National Nanotechnology Initiative (NNI) is managed by the Nanoscale Science, Engineering, and Technology (NSET) Subcommittee of the NSTC Committee on Technology. More information is available at www.whitehouse.gov/ostp/nstc.

About the Office of Science and Technology Policy

The Office of Science and Technology Policy (OSTP) was established by the National Science and Technology Policy, Organization, and Priorities Act of 1976 to provide the President and others within the Executive Office of the President with advice on the scientific, engineering, and technological aspects of the economy, national security, homeland security, health, foreign relations, the environment, and the technological recovery and use of resources, among other topics. OSTP leads interagency science and technology policy coordination efforts, assists the Office of Management and Budget with an annual review and analysis of Federal research and development in budgets, and serves as a source of scientific and technological analysis and judgment for the President with respect to major policies, plans, and programs of the Federal Government. More information is available at www.whitehouse.gov/ostp.

About this document

This document is a supplement to the President's 2018 Budget request submitted to Congress on May 23rd, 2017, and serves as the Annual Report for the National Nanotechnology Initiative called for under the provisions of the 21st Century Nanotechnology Research and Development Act of 2003 (Public Law 108-153, 15 USC §7501). The report also addresses the requirement for Department of Defense reporting on its nanotechnology investments, per 10 USC §2358. Additional information regarding the NNI is available on the NNI website at www.nano.gov.

About the cover

Outer Covers: Gold nanoparticles in the shape of two short pyramids attached at the base (250 nm on the long edge and 177 nm on the short edge) self-assemble into complex three-dimensional cages when coated with custom-made DNA. The DNA strands on the nanoparticles cross-link with each other, enabling the self-assembly. This approach has the potential to open up a new class of materials. These complex synthetic cages, with pores that can possibly hold cargo, have potential applications in sensing and storage, as well as medical diagnosis and drug delivery. The back cover shows a simulation of assembled gold nanoparticles, and the front cover depicts the same structure in a ball-and-stick layout to highlight the cage arrangement. This work was the result of a collaboration between researchers from the Mirkin laboratory at Northwestern University and the Glotzer laboratory at the University of Michigan. This research was supported in part by the Center for Bio-Inspired Energy Science, an Energy Frontier Research Center funded by the U.S. Department of Energy, as well as the Department of Defense and the National Science Foundation. See *Science* **355**, 931-935 (2017) for details (science.sciencemag.org/content/355/6328/931.full). Images courtesy of S. Lee and M. Spellings, The Glotzer Group, University of Michigan.

Inside Back Cover: The inside face of the back cover includes a collage of images illustrating examples of NNI educational outreach activities. See captions under the collage for additional information. Collage content and design by Quinn Spadola and Kristin Roy of the National Nanotechnology Coordination Office (NNCO).

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SUPPLEMENT TO THE PRESIDENT'S BUDGET FOR FISCAL YEAR 2018

THE NATIONAL NANOTECHNOLOGY INITIATIVE



Subcommittee on Nanoscale Science, Engineering, and Technology
Committee on Technology
National Science and Technology Council

November 2017

Report prepared by
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EXECUTIVE OFFICE OF THE PRESIDENT
NATIONAL SCIENCE AND TECHNOLOGY COUNCIL
WASHINGTON, D.C. 20502

November 30, 2017

Dear Members of Congress:

I am pleased to transmit the National Nanotechnology Initiative Supplement to the President's 2018 Budget. Under the National Nanotechnology Initiative (NNI), twenty Federal departments, independent agencies, and commissions work together toward the shared vision of 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.

This document is a supplement to the President's 2018 Budget Request and serves as the Annual Report for the NNI called for under the provisions of the 21st Century Nanotechnology Research and Development Act of 2003 (Public Law 108-153, 15 USC §7501). The document also addresses the requirement for Department of Defense reporting on its nanotechnology investments, per 10 USC §2358. It summarizes the progress made in achieving the goals of the NNI, research and development activities and plans of the participating agencies, and agency investments in each program component area. The President's 2018 Budget requests \$1.2 billion for the NNI, a continued investment in support of innovation promoting America's competitiveness, economic growth, and national security.

Thank you for your shared support of this important Federal initiative.

Sincerely,



Rachael L. Leonard

General Counsel

Office of Science and Technology Policy

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What is Nanotechnology?

Nanotechnology encompasses science, engineering, and technology at the nanoscale, which is about 1 to 100 nanometers. Just how small is that? A nanometer is one-billionth of a meter. For reference, a sheet of paper is about 100,000 nanometers thick. Nanoscale matter can behave differently than the same bulk material. For example, a material's melting point, color, strength, chemical reactivity, and more may change at the nanoscale.

Nanotechnology is affecting all aspects of life through innovations that enable, for example (some with images shown below), strong, lightweight materials for aerospace applications (a); clean, accessible drinking water around the world (b); superfast computers with vast amounts of storage; self-cleaning surfaces (c); wearable sensors (d) and health monitors; safer food through packaging and monitoring (e); regrowth of skin, bone, and nerve cells for better medical outcomes; smart windows that lighten or darken to conserve energy (f); and nanotechnology-enabled concrete that dries more quickly and has sensors to detect stress or corrosion in roads, bridges, and buildings (g).

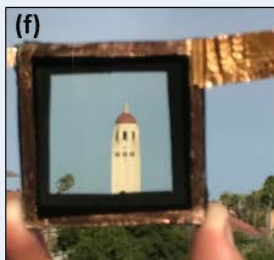
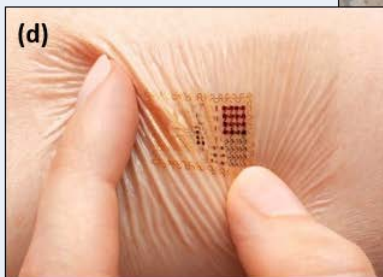
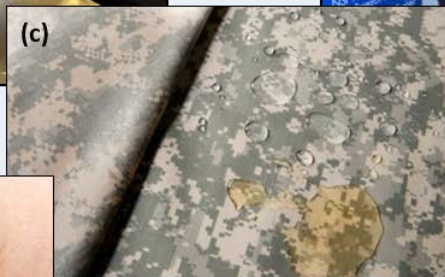
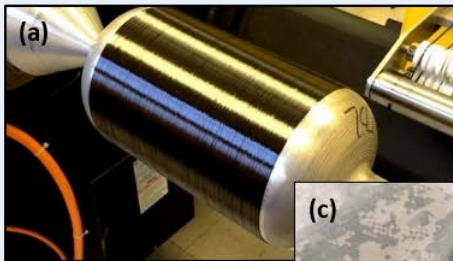


Image Credits: (a) National Aeronautics and Space Administration; (b) Paul Westerhoff, Nanosystems Engineering Research Center for Nanotechnology-Enabled Water Treatment; (c) David Kamm, U.S. Army Research, Development, and Engineering Command; (d) John Rogers, Northwestern University; (e) Joseph Walsh, Massachusetts Institute of Technology; (f) Tyler Hernandez, Michael Strand, Daniel Slotcavage, and Michael McGehee, Stanford University; (g) David Scaglione. For more information on nanotechnology benefits and applications, please visit www.nano.gov/you/nanotechnology-benefits.

1. INTRODUCTION AND OVERVIEW

Nanotechnology is broadly enabling, with applications that address this Administration’s highest priorities: national security, economic growth, and job creation. While still an emerging area of research and development, nanotechnology is already having a significant impact on the marketplace, with worldwide revenues of nanotechnology-enabled products projected to be \$3.7 trillion in 2018.¹ Nanotechnology is used in areas as diverse as consumer electronics, aerospace, water purification and monitoring, transportation and infrastructure, apparel and textiles, energy, agriculture and food safety, sporting goods, and medicine. Nanotechnology plays an increasingly important role in many sectors of the economy, especially in what is known as “High Tech” or “Knowledge- and Technology-Intensive” manufacturing industries (HT manufacturing)—a major driver of growth and job creation. In 2014, HT manufacturing accounted for 15% of the global manufacturing sector and added \$511 billion to the U.S. gross domestic product (GDP). The HT manufacturing industries also created 1.8 million high-paying U.S. jobs in 2014. Further, while only accounting for about three percent of U.S. GDP, HT manufacturing industries funded roughly half of all business research and development (R&D) in the United States.² Nanotechnology applications to HT manufacturing include the patterning of nanoscale devices in semiconductor manufacturing, multifunctional nanomaterial enhancements in sensors and communications equipment, nanoparticle formulations in pharmaceuticals and precision medicine, and nanomaterials used in enhanced-strength or multifunctional composites in the aerospace and automobile industries. The nanotechnology R&D underway today will provide the foundation for future applications enabling entirely new capabilities and products. From flexible electronics powered by our movements to nerve regeneration, nanotechnology has much more to offer.

Overview of the National Nanotechnology Initiative

The National Nanotechnology Initiative (NNI), established in 2001³ and authorized in 2003 in the 21st Century Nanotechnology Research and Development Act (“the Act”),⁴ is a U.S. Government R&D initiative. Twenty Federal departments, independent agencies, and commissions⁵ work together toward the shared vision of *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.*⁶

The NNI operates within the framework of the National Science and Technology Council (NSTC), the Cabinet-level council by which the President coordinates science and technology policy across the Federal Government. The Nanoscale Science, Engineering, and Technology (NSET) Subcommittee, chartered under the NSTC Committee on Technology, seeks to maintain the U.S. position as a world leader in nanotechnology; enhance national security; increase U.S. productivity and competitiveness and promote long-term economic

¹ www.luxresearchinc.com/content/nanotechnology-update-us-leads-government-spending-amidst-increased-spending-across-asia-0

² www.nsf.gov/statistics/2016/nsb20161/#/

³ General note: In conformance with Office of Management and Budget style, references to years in this report are to fiscal years unless otherwise noted.

⁴ 15 U.S.C. §7501(c)(4), P.L. 108-153: www.gpo.gov/fdsys/pkg/PLAW-108publ153/html/PLAW-108publ153.htm

⁵ Hereafter within this document the Federal departments, independent agencies, and commissions participating in the NNI are referred to collectively as “agencies.”

⁶ www.nano.gov/2016strategicplan, p. 3

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growth; achieve energy independence; improve the health and quality of life of the U.S. citizenry; and develop a future-focused workforce. The NSET Subcommittee, composed of representatives from the agencies participating in the NNI and from the Executive Office of the President, maximizes interagency coordination of nanotechnology R&D, enables agencies to avoid duplicative efforts, and establishes shared goals, priorities, and strategies that complement agency-specific missions and activities.

Table 1: Federal Departments and Agencies Participating in the NNI
Consumer Product Safety Commission (CPSC) [†]
Department of Commerce (DOC)
Bureau of Industry and Security (BIS)
Economic Development Administration (EDA)
National Institute of Standards and Technology (NIST)*
U.S. Patent and Trademark Office (USPTO)
Department of Defense (DOD)*
Department of Education (DOEd)
Department of Energy (DOE)*
Department of Health and Human Services (DHHS)
Food and Drug Administration (FDA)*
National Institute for Occupational Safety and Health (NIOSH)*
National Institutes of Health (NIH)*
Department of Homeland Security (DHS)*
Department of the Interior (DOI)
U.S. Geological Survey (USGS)*
Department of Justice (DOJ)
National Institute of Justice (NIJ)*
Department of Labor (DOL)
Occupational Safety and Health Administration (OSHA)
Department of State (DOS)
Department of Transportation (DOT)
Federal Highway Administration (FHWA)*
Department of the Treasury (DOTreas)
Environmental Protection Agency (EPA)*
Intelligence Community (IC)
National Reconnaissance Office (NRO)
Office of the Director of National Intelligence (ODNI)
National Aeronautics and Space Administration (NASA)*
National Science Foundation (NSF)*
Nuclear Regulatory Commission (NRC) [†]
U.S. Department of Agriculture (USDA)
Agricultural Research Service (ARS)*
Forest Service (FS)*
National Institute of Food and Agriculture (NIFA)*
U.S. International Trade Commission (USITC) [†]

* Denotes agencies (or organizations within agencies) with budgets dedicated to nanotechnology research and development

[†] Denotes an independent commission that is represented on NSET but is non-voting

1. Introduction and Overview

The NSET Subcommittee has previously identified areas that require focused interagency attention and activity, facilitated by subsidiary working groups or by other mechanisms. NSET currently has two working groups—the Nanotechnology Environmental and Health Implications (NEHI) Working Group and the Nanotechnology Innovation and Commercialization Ecosystem (NICE) Working Group. Four coordinators have also been designated, for global issues; standards development; environmental, health, and safety research; and education, engagement, and societal dimensions.

The agencies work together towards the four long-standing NNI goals:

1. Advance a world-class nanotechnology 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 a dynamic infrastructure and toolset to advance nanotechnology.
4. Support responsible development of nanotechnology.

For each of these goals, the NNI's strategic plan (last updated in 2016) identifies specific objectives aimed at collectively pursuing the NNI vision.

As directed by the 21st Century Nanotechnology Research and Development Act, the NSET Subcommittee has also identified R&D investment categories, known as Program Component Areas (PCAs). The five PCAs, listed below, include research and development activities that contribute to one or more of the NNI goals:

1. Nanotechnology Signature Initiatives and Grand Challenges.
2. Foundational Research.
3. Nanotechnology-Enabled Applications, Devices, and Systems.
4. Research Infrastructure and Instrumentation.
5. Environment, Health, and Safety.

Nanotechnology Signature Initiatives (NSIs) are designed to accelerate innovation in areas ripe for significant advances through close and targeted program-level interagency collaboration. The NSI portfolio is dynamic, with NSI topics retired when the additional focus afforded by this mechanism is no longer necessary, and new topics added when agencies identify a new area that would benefit from such focus. The NNI agencies review and update the technical content of each NSI on a regular basis to address emerging priorities and research progress in achieving program goals. NSI topics for 2016 through 2018 are as follows:

- Sustainable Nanomanufacturing: Creating the Industries of the Future (Nanomanufacturing NSI).
- Nanoelectronics for 2020 and Beyond (Nanoelectronics NSI).
- Nanotechnology Knowledge Infrastructure (NKI): Enabling National Leadership in Sustainable Design (NKI NSI).
- Nanotechnology for Sensors and Sensors for Nanotechnology: Improving and Protecting Health, Safety, and the Environment (Sensors NSI).
- Water Sustainability through Nanotechnology: Nanoscale Solutions for a Global-Scale Challenge (Water NSI).

A Nanotechnology-Inspired Grand Challenge (GC) is defined as an ambitious but achievable goal that harnesses nanoscience, nanotechnology, and innovation to solve important national or global problems and that has the potential to capture the public's imagination. To date, the NNI has established one such grand challenge, focused on future computing, which challenges the community to *create a new type of computer that can proactively interpret and learn from data, solve unfamiliar problems using what it has learned, and operate with the energy efficiency of the human brain*. Funding associated with this GC is reported for the first time in this budget supplement.

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NNI R&D activities are also guided by the 2011 Environmental, Health, and Safety Research Strategy, which agencies periodically review and remains relevant to current priorities.⁷ This strategy supports all four NNI goals but is most closely aligned with Goal 4 and PCA 5.

The NNI budget represents the sum of the nanotechnology-related investments allocated by each of the participating agencies (the “NNI budget crosscut”). Each agency determines its budget for nanotechnology R&D in coordination with the Office of Management and Budget (OMB), the Office of Science and Technology Policy (OSTP), and Congress. NNI agencies collaborate closely—facilitated through the NSET Subcommittee, its working groups and coordinators, and the National Nanotechnology Coordination Office (NNCO)—to create an integrated R&D program that leverages resources, including equipment and other infrastructure, and knowledge to advance NNI goals and meet individual agency mission needs and objectives. The NNI budget supplement this year details agency activities and plans based on the PCAs instead of by goal and objective, as structured in recent years, to better align with the required budget reporting as mandated in the Act. Chapter 1 provides an introduction and summary of progress towards the goals, and chapter 2 presents budget information. Detailed technical and programmatic highlights associated with each agency’s R&D activities under each PCA are included in Appendix A. Appendix B presents a list of abbreviations and acronyms used throughout this document, and contact information for representatives from the participating agencies, OSTP, OMB, and NNCO is listed in Appendix C.

The 21st Century Nanotechnology Research and Development Act codified the establishment of NNCO. The NNCO provides technical and administrative support to the NSET Subcommittee, including the preparation of multiagency planning, budget, and assessment documents; develops, updates, and maintains information about the NNI, including the NNI website www.nano.gov; serves as the point of contact on Federal nanotechnology activities; provides public outreach on behalf of the NNI; and promotes access to and early application of the knowledge, technologies, and innovations derived from NNI activities.

Progress towards the NNI Goals

Goal 1. Advance a World-Class Nanotechnology Research and Development Program

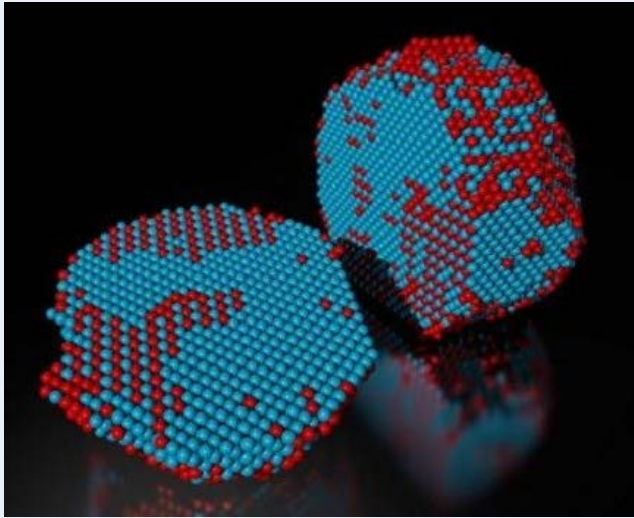
The frontiers of science are ever expanding, and the NNI agencies are committed to supporting basic and early-stage applied research at the leading edge, ensuring the development of next-generation nanotechnology-enabled innovations. Meanwhile, research results from past NNI investments are being broadly applied by the private sector in new commercial products. Continued Federal investments will enable future discoveries that build upon and expand the body of knowledge already developed under the auspices of the NNI, and ensure that the United States remains at the forefront of nanotechnology and realizes the benefits to our national and economic security. NNI agencies fund a diverse R&D portfolio that includes strategic and complementary research incorporating intramural and extramural programs consisting of single-investigator efforts, multi-investigator and multidisciplinary research teams, and centers and networks for focused research. Inherently interdisciplinary, nanotechnology research strengthens the intersections of traditional scientific disciplines, and agency investments facilitate convergence of knowledge, tools, and domains of nanotechnology with other areas of science and technology, including, but not limited to, biotechnology, information technology, and cognitive sciences. Nanotechnology R&D is benefiting from significant advances in analytical approaches that incorporate simulation, modeling, and data analytics to advance materials and device development, evaluation, and testing. The Nanotechnology Signature Initiatives and Nanotechnology-Inspired Grand Challenge encompass R&D activities that are more

⁷ www.nano.gov/2011EHSSStrategy

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closely coordinated based on the specific areas of focus identified by the participating agencies. Agency activities that support the NSIs and GC are reported under PCA 1, while agency activities supporting foundational research are reported under PCA 2. Goal 1 is interrelated with the other NNI goals because progress in R&D depends on a robust research infrastructure (availability of a skilled workforce, instrumentation, and tools, Goal 3), and on understanding potential implications of nanotechnology and laying the foundation for its incorporation into commercial products (Goals 4 and 2).

Scientists Map All 23,196 Atoms in a Nanoparticle



Visualization of atomic composition of an iron-platinum nanoparticle. Iron atoms are red and platinum atoms are blue. Image credit: Colin Ophus and Florian Niekie, Lawrence Berkeley National Laboratory.

Using one of the world's most advanced electron microscopes, researchers from Lawrence Berkeley National Laboratory, Oak Ridge National Laboratory, and two universities have determined the exact location and chemical identity of all 23,196 atoms in an 8.4 nm iron-platinum nanoparticle.

Mapping the nanoparticle in exquisite detail helps scientists understand grain structure and magnetic properties at the single-atom level, enabling potential future advances in magnetic data storage devices. Further, this technique can be applied to other nanoparticles of interest, revealing their precise atomic makeup and potentially enabling improvements in areas ranging from catalysis to disease diagnosis.

Goal 2. Foster the Transfer of New Technologies into Products for Commercial and Public Benefit

The science and technology advances supported under Goal 1 form the basis for new materials, devices, and systems. Early applications of nanotechnology can already be found in products throughout the marketplace, but there is significant potential for the novel properties that exist at the nanoscale to be used in entirely new devices and systems in a broad array of applications, from quantum computing to the treatment of disease. To realize this potential, the focus of Goal 2 is to facilitate the transfer of nanotechnology research and development breakthroughs into applications that the private sector can bring to market. Goal 2 encompasses four objectives that detail how the NNI aims to complement private sector investments and activities by sharing information, promoting access to user facilities, leveraging resources through public-private partnerships, and participating in international standards activities that are critical to commercialization.

As with any new technology, scalable, repeatable, cost-effective, and high-precision manufacturing methods are required to move nanotechnology discoveries from the laboratory into commercial products. The Nanomanufacturing NSI focuses on research needed to develop next-generation manufacturing processes and measurement technologies. NNI participating agencies also have a number of activities specifically supporting technology transfer and commercialization, including Small Business Innovation Research (SBIR) and Small Business Technology Transfer (STTR) programs.

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In addition to the NNI agency activities, NNCO conducts outreach activities to engage with and learn from the private sector about the barriers to commercializing nanotechnologies. Over the past several years, NNCO has also expanded the information available on nano.gov relevant to the business community, including links to funding programs, user facilities, best practices for safe handling of nanomaterials, and a list of frequently asked questions⁸ covering topics from intellectual property protection to regulation.

Collaborative Innovations Enable the Development and Deployment of Smart Fabrics



Image credit: iStock

Imagine if your jacket could charge your smartphone by harnessing the energy of your body's movements, or if sensors embedded in the fabric of your grandparents' clothes could detect a fall and notify a caregiver. These applications are among a host of possibilities that nanotechnology-enabled smart fabrics may make possible. Manufacturing USA institutes, including DOD-funded NextFlex and Advanced Functional Fabrics of America, have created a collaboration space for academic institutions, industry partners, and Federal agencies (including NIST) to develop relevant technologies, many of which rely on the unique properties of nanomaterials, and to accelerate the transition of these technologies from the bench to U.S. manufacturers.

Goal 3. Develop and Sustain Educational Resources, a Skilled Workforce, and a Dynamic Infrastructure and Toolset to Advance Nanotechnology

To advance a world-class nanotechnology research and development program (Goal 1) and foster the transfer of these new discoveries into useful applications (Goal 2), a strong ecosystem must exist that leverages the physical, cyber, and human infrastructure. The NNI continues to support the cyber and physical infrastructure for nanotechnology through its extensive network of research centers and user facilities that provide access to instrumentation for fabrication and characterization, as well as to modeling and simulation tools and data. A cornerstone of the physical research infrastructure is the NSF-funded National Nanotechnology Coordinated Infrastructure (NNCI), which is a network of university user facilities that provide access to state-of-the-art equipment for characterization and fabrication. This network of 16 nodes and their affiliated sites across the country leverages expertise in a vast array of disciplines and over 2,000 tools that support nanoscale science, engineering, and technology. The NNCI is also developing a skilled workforce, with student researchers working alongside experts, not only learning to operate the equipment, but also learning the methods and techniques needed to make the most of these tools. The NNCI complements the resources available at government laboratories, including the DOE Nanoscale Science Research Centers (NSRCs), DOD research laboratories, and NIST. In addition to these facilities, the NSF-funded Network for Computational Nanotechnology⁹ provides, through nanoHub, a cyber-platform for sharing simulation and education resources, and serves as the focal point for computational nanotechnology research, education, and collaboration.

Developing a future-focused workforce is a major objective of NNI-funded academic research. Traditionally, the focus has been primarily at the graduate and post-graduate levels, but there are increasing opportunities for undergraduates to participate in research through programs such as NSF's Research Experience for Undergraduates (REU) program or similarly structured programs funded by individual universities. In addition, community colleges across the country are collaborating with local industries to respond to the

⁸ www.nano.gov/bizfaqs

⁹ www.nanohub.org/groups/ncn

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increasing need for skilled workers who understand fundamental nanotechnology concepts. The community colleges are working together and leveraging their collective knowledge and facilities. For example, the Nanotechnology Applications and Career Knowledge (NACK) Network coordinates workforce development programs on behalf of the NSF Advanced Technological Education (ATE) program and partners with 25 community and technical colleges, 9 universities, and 5 other ATE centers. The network partners combine their resources and broaden impact with the Remotely Accessible Instruments for Nanotechnology (RAIN) program, in which students access and control equipment over the Internet with technical assistance via video conferencing.

NNCO supports and amplifies the NNI agencies' education and outreach efforts, including multimedia contests¹⁰ that encourage college students to communicate the value of their research ("EnvisioNano" and "Tiny Science. Big Impacts. Cool Videos."). "Generation Nano," a contest developed by NSF and NNCO, challenges high school students to explore how nanotechnology might give someone "superhero" capabilities. NNCO facilitates the Nano and Emerging Technologies Student Network of undergraduate clubs and the Teaching Nano and Emerging Technologies Network for K-12 teachers to share best practices and resources. Hundreds of resources for teaching nanotechnology, including lesson plans, demonstrations, and laboratory exercises—many of which were developed with NNI funding—are included in a searchable web portal as a result of a collaboration between NNCO and nanoHUB.¹¹

Generation Nano: Small Science, Superheroes



Image Credit: Amina Khan, NSF

NSF and NNI are collaborating for the third year to support a superhero contest. The "Generation Nano: Small Science, Superheroes" contest was designed to excite students who may not already be engaged with science, technology, engineering, and math (STEM) topics to learn more about nanotechnology. In 2018,

"Generation Nano: Superheroes Inspired by Science!" motivates students to imagine how applications of science, including nanotechnology, can save the day, and asks students to design science-powered gear for an original superhero. Students tell their heroes' stories in comics and videos explaining the technology behind the superhero gear. Cumulative submissions from the first two years came from 167 students representing 18 different states. In 2017, NSF brought the finalists to a comic convention in Washington, DC, and they toured the U.S. Capitol.

Goal 4. Support Responsible Development of Nanotechnology

The responsible development of nanotechnology has been a primary goal of the NNI since its inception. An understanding of the behavior of nanomaterials with respect to nanotechnology-related environmental, health, and safety (nanoEHS) considerations—in addition to potential ethical, legal, and societal implications (ELSI)—is essential for establishing public confidence and regulatory certainty so that companies can readily bring nanotechnology products to market. Considering the applicability of nanotechnology to a wide variety of market segments, well-coordinated nanoEHS research is vital to American innovation and to advancing manufacturing and economic competitiveness.

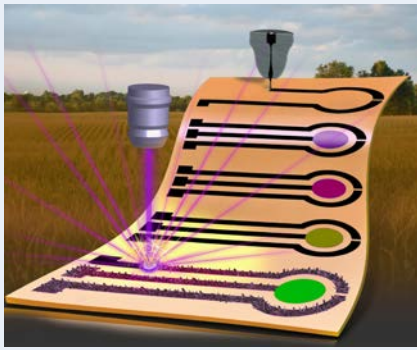
¹⁰ www.nano.gov/multimedia-and-contests

¹¹ nanohub.org/publications/118/

1. Introduction and Overview

The 2011 NNI Environmental, Health, and Safety Research Strategy continues to guide the extramural programs and intramural activities within the agencies focused on nanoEHS. The NEHI Working Group and the NNI Coordinator for Environmental, Health, and Safety Research provide extensive coordination for these efforts across the Federal Government.

Smart Technology for Food Production



Artist's rendering of the process in which a laser is used to weld graphene flakes together. Image Credit: Jonathan Claussen, Iowa State

The sensor technology incorporates graphene ink printed on paper, and the ink is welded with a laser to create a three-dimensional nanostructured surface. This graphene substrate provides a flexible, low-cost platform and potentially could be adapted for use beyond the agriculture community in the biomedical, environmental, and food safety arenas.

Since the end of World War II, pesticide use has fueled tremendous increases in crop yields. However, reducing the impact of these chemicals on agricultural and aquatic ecosystems is an ongoing priority. Researchers supported by USDA's National Institute of Food and Agriculture are developing a biosensor that can help farmers calibrate pesticide use. A team of university scientists has designed a graphene-based device to provide real-time, in-the-field measurements of pesticide levels in soil or water. The sensor technology incorporates graphene ink printed on paper, and the ink is welded with a laser to create a three-dimensional nanostructured surface. This graphene substrate provides a flexible, low-cost platform and potentially could be adapted for use beyond the agriculture community in the biomedical, environmental, and food safety arenas.

Over the years, considerable investments in nanoEHS research have resulted in significant advances in the state of knowledge and the development of characterization tools. Other regions in the world have also been making substantial investments in nanoEHS, and recent collaborations have enabled the sharing of data via a common format. This data sharing leverages resources and knowledge to accelerate progress in understanding the behavior of nanomaterials in the environment and biological systems. This shared knowledge also enables developers to design safe products and helps inform regulators, leading to greater certainty for companies commercializing nanotechnology. The U.S.–EU (European Union) Communities of Research (CORs)¹² activity is one vehicle for collaboration and information exchange among nanoEHS researchers. The CORs are researcher-led groups of experts who communicate via regular conference calls, a shared website, and annual workshops to develop technical work products such as white papers and database protocols. The annual COR workshops, which alternate between the United States and the European Union, bring participants together to report on scientific progress and plans. These meetings also provide a forum for U.S. and EU policy makers to exchange views about science-based regulation of nanomaterials.

External Reviews of the NNI

The 21st Century Nanotechnology R&D Act called for review of the NNI every two years by the National Nanotechnology Advisory Panel (NNAP)—historically designated as the President's Council of Advisors for Science and Technology (PCAST)—and every three years by the National Research Council, now referred to as the National Academies of Sciences, Engineering, and Medicine—National Academies. (Note that the

¹² www.us-eu.org

1. Introduction and Overview

American Innovation and Competitiveness Act,¹³ signed into law in January 2017, extended the reporting period to every four years for both bodies.) In 2017, both advisory bodies released reports on the NNI.

Triennial Review of the NNI

The National Academies convened a Committee on Triennial Review of the National Nanotechnology Initiative tasked to study (a) the mechanisms in use by the NNI to advance focused areas of nanotechnology and how those areas are chosen and (b) the physical and human infrastructure needed to realize the benefits of nanotechnology in the United States.

In its 2016 report,¹⁴ the Committee recognized the broad applicability of nanotechnology to many other areas of national importance and noted that success in these areas hinges upon further advancements in nanotechnology. It recommended that NSET strengthen engagement with the leadership in these other areas. NNI leadership, through the NSTC and other means, actively participates in synergistic committees and activities to strengthen engagement with and leverage efforts related to other national priorities. For example, NNCO and the National Coordination Office of the Networking and Information Technology Research and Development (NITRD) Program are collaboratively working to bridge their areas of focus related to future computing, including efforts in nanoelectronics and low-power cognitive computing.

With respect to manufacturing, the Committee recommended support for early-stage nanomanufacturing research and the formation of a working group to coordinate these efforts. One of the five NNI signature initiatives, Sustainable Nanomanufacturing: Creating the Industries of the Future, is focused on priority areas of nanomanufacturing, and agency representatives actively collaborate to identify the nanoscale research needs for advanced manufacturing. (See Appendix A for more details.) The team also engages with representatives from manufacturing centers and institutes where nanotechnology can play a key enabling role.

The Committee emphasized the importance of physical and computational infrastructure and encouraged agencies to identify funding mechanisms for the acquisition and maintenance of state-of-the-art equipment. The Committee also highlighted the value of facilities such as the National Cancer Institute's Nanotechnology Characterization Laboratory, which serves as a trusted source of information on the safety of nanomaterials under development for cancer treatment, and recommended the consideration of other areas where this mechanism could be useful. The NNI agencies are exploring the potential for this type of laboratory in a number of areas, including the characterization of exposure to nanomaterials from products.

Finally, the Committee encouraged the NNI to find ways to further share educational resources, including by incorporating them into the searchable web portal recently established by NNCO and nanoHUB. NNCO is actively distributing information about these educational resources, engaging teachers through a K-12 teachers network and science teachers associations at the state and national levels, and coordinating a webinar series for teachers.

¹³ P.L. 114–329, title II, §204(b)(1), Jan. 6, 2017, 130 Stat. 2999: www.gpo.gov/fdsys/pkg/PLAW-114publ329/html/PLAW-114publ329.htm.

¹⁴ www.nap.edu/catalog/23603/triennial-review-of-the-national-nanotechnology-initiative

Biennial Review of the NNI

In January 2017, the National Nanotechnology Advisory Panel released a brief letter report¹⁵ and reaffirmed the findings from its 2014 report. The Panel “observed that the NNI has spurred significant scientific discovery and understanding of nanoscale phenomena and has deeply integrated nanoscale science and technology into R&D portfolios across the Federal government.” It further recognized progress toward the 2014 report’s primary recommendation to focus efforts on specific technology goals with the launch of a Nanotechnology-Inspired Grand Challenge for Future Computing.¹⁶ The letter report also acknowledged and emphasized support for the recommendations regarding manufacturing and infrastructure from the National Academies triennial review of the NNI. The final recommendation—recognizing the recent statutory change to quadrennial assessments—was to have the next Panel review conducted in 2018. This schedule would result in an alternating release of NNAP and National Academies reviews every two years.

¹⁵ www.nano.gov/sites/default/files/pub_resource/pcast_2017_nni_review_final.pdf

¹⁶ www.nano.gov/futurecomputing

2. NNI INVESTMENTS

Budget Summary

The President's 2018 Budget provides \$1.2 billion for the National Nanotechnology Initiative (NNI), a continued investment in support of innovation promoting America's interests, including competitiveness, economic growth, and national security. The Budget supports investments in basic research, early-stage applied research, and technology transfer efforts that will lead to the breakthroughs of the future. Cumulatively totaling over \$25 billion since the inception of the NNI in 2001 (including the 2018 request), this support reflects the continued importance of investments that advance our fundamental understanding of and ability to control matter at the nanoscale, as well as the translation of that knowledge into technological breakthroughs that serve the American people. The NNI investments in 2016 and 2017 and those proposed for 2018 reflect a sustained emphasis on broad, fundamental research in nanoscience to provide a continuing pipeline of new discoveries that will enable future transformative commercial products and services. As the fundamental understanding of behavior at the nanoscale and the nanomaterial toolbox continue to grow, it is increasingly challenging to identify all of the relevant R&D programs, because in some cases nanotechnology may now be an enabling technology but is not called out as the focus of the overall program. Therefore, it is possible that some nanotechnology-enabled R&D investments at Federal agencies are not captured within the \$1.2 billion documented in this report.

Guided by this Administration's research and development priorities, agencies continue to prioritize investments in nanotechnology to meet their mission needs, including national, cross-agency needs for homeland security and defense; innovation in life sciences, medicine, and neuroscience; advanced manufacturing; information technology and high-performance computing; and energy conversion and storage. Nanotechnology has such a broad impact because it is one of several emerging "general-purpose technologies" that—like the steam engine, electricity, and the Internet—will have a universal impact on our economy and our society, with the ability to create entirely new industries, generate jobs, and increase productivity. The NNI also supports significant investments in research infrastructure and in STEM (science, technology, engineering, and mathematics) education, both of which are critical to the future prosperity and security of the United States.

The President's 2018 Budget supports nanoscale science, engineering, and technology R&D at 12 agencies. The five Federal organizations with the largest investments (representing 95% of the total) are:

- NSF (fundamental research and education across all disciplines of science and engineering).
- DHHS/NIH (nanotechnology-based biomedical research at the intersection of life and physical sciences).
- DOE (fundamental and applied research providing a basis for new and improved energy technologies).
- DOD (science and engineering research advancing defense and dual-use capabilities).
- DOC/NIST (fundamental research and development of measurement and fabrication tools, analytical methodologies, metrology, and standards for nanotechnology).

2. NNI Investments

Other agencies and agency components investing in mission-related nanotechnology research are CPSC, DHHS/FDA, DHHS/NIOSH, DHS, DOJ, DOT/FHWA, EPA, NASA, USDA/ARS, USDA/FS, and USDA/NIFA.¹⁷

Table 2 presents NNI investments for 2016 through 2018 for Federal agencies with budgets and investments for nanotechnology R&D. Tables 3–5 list the investments by agency and by NNI Program Component Area (PCA) for 2016 through 2018. Table 6 shows the NNI investments within Small Business Innovation Research (SBIR) and Small Business Technology Transfer (STTR) programs for 2012 through 2015. Figure 1 shows NNI annual funding by agency since the inception of the NNI in 2001. Figure 2 shows the breakdown of funding by PCA in the 2018 Budget.

Table 2: NNI Budget, by Agency, 2016–2018 (dollars in millions)			
Agency	2016 Actual	2017 Estimated*	2018 Proposed
CPSC	2.0	2.0	1.0
DHS	1.0	0.8	0.7
DOC/NIST	82.5	82.4	65.3
DOD	149.3	144.5	139.9
DOE**	333.5	327.5	227.1
DOI/USGS	0.0	0.1	0.0
DOJ/NIJ	1.3	1.4	1.4
DOT/FHWA	1.5	0.5	1.5
EPA	13.9	10.0	4.5
DHHS (total)	420.5	439.6	347.7
FDA	11.7	11.0	10.9
NIH	397.7	417.5	325.7
NIOSH	11.1	11.1	11.1
NASA	13.4	12.0	6.1
NSF	510.4	420.8	388.6
USDA (total)	28.4	28.2	23.7
ARS	3.0	3.0	3.0
FS	6.4	7.2	3.7
NIFA	19.0	18.0	17.0
TOTAL ***	1557.8	1469.7	1207.5

* 2017 numbers are based on 2017 enacted levels and may have changed under final operating plans.

** Funding levels for DOE include the combined budgets of the Office of Science, the Office of Energy Efficiency and Renewable Energy, the Office of Fossil Energy, the Office of Nuclear Energy, and the Advanced Research Projects Agency for Energy.

*** In Tables 2–6, totals may not add, due to rounding.

¹⁷ See Table 1 (p. 2) or Appendix B for explanations of the agency abbreviations used on this page and throughout the remainder of this report. DOI/USGS is also reporting investments in nanotechnology, but for 2017 only.

2. NNI Investments

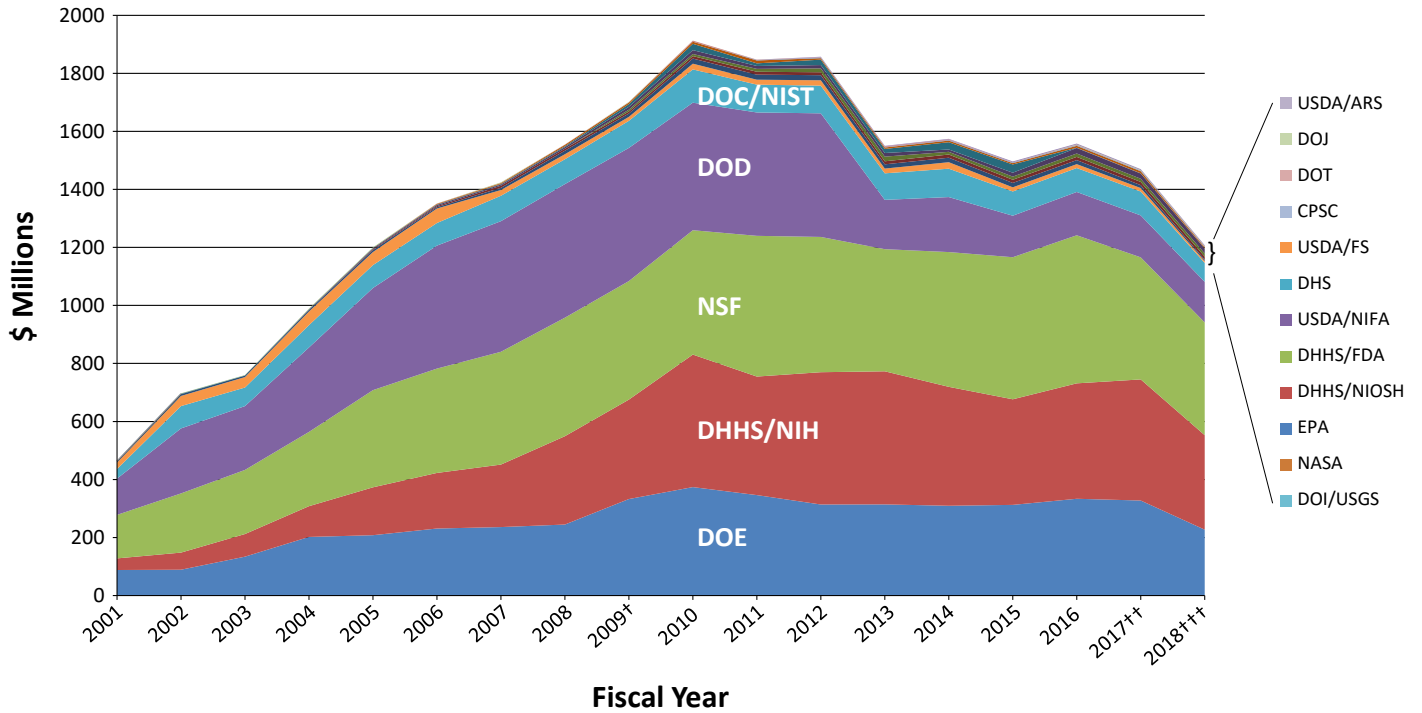


Figure 1. NNI Funding by Agency, 2001–2018.

- † 2009 figures do not include American Recovery and Reinvestment Act funds for DOE (\$293 million), NSF (\$101 million), NIH (\$73 million), and NIST (\$43 million).
- ** 2017 estimated funding is based on 2017 enacted levels and may have changed under final operating plans.
- *** 2018 Budget.

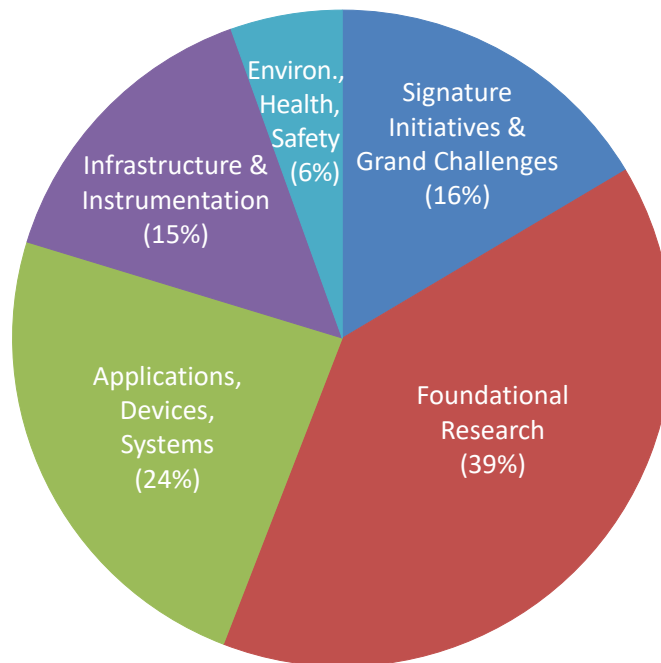


Figure 2. Breakout of NNI Funding by Program Component Area in the 2018 Budget.

2. NNI Investments

Table 3: Actual 2016 Agency Investments by Program Component Area
(dollars in millions)

Agency	1. Nanotechnology Signature Initiatives (NSIs) and Grand Challenges (GCs)*	1a. Nanomanufacturing NSI	1b. Nanoelectronics NSI	1c. NNI NSI	1d. Sensors NSI	1e. Water NSI	1f. Future Computing GC	2. Foundational Research	3. Nanotechnology-Enabled Applications, Devices, and Systems	4. Research Infrastructure and Instrumentation	5. Environment, Health, and Safety	NNI Total
CPSC	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	2.0	2.0
DHS	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	1.0	0.0	0.0	1.0
DOC/NIST	26.2	5.4	13.3	1.3	0.7	0.3	5.3	9.3	5.4	35.7	5.9	82.5
DOD	27.5	0.8	18.3	1.1	4.2	2.2	1.0	90.7	26.1	2.0	3.0	149.3
DOE	5.7	0.0	4.9	0.0	0.8	0.0	0.0	178.2	16.8	132.9	0.0	333.5
DOI/USGS	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0
DOJ/NIJ	0.2	0.0	0.0	0.0	0.2	0.0	0.0	0.0	0.9	0.2	0.0	1.3
DOT/FHWA	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	1.5	0.0	0.0	1.5
EPA	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	13.9	13.9
DHHS (total)	14.4	1.1	0.0	1.3	11.7	0.0	0.3	82.5	250.4	26.4	46.8	420.5
FDA	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	11.7	11.7
NIH	14.4	1.1	0.0	1.3	11.7	0.0	0.3	82.5	250.4	26.4	24.0	397.7
NIOSH	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	11.1	11.1
NASA	2.2	0.6	0.6	0.0	1.0	0.0	0.0	7.8	2.8	0.2	0.4	13.4
NSF	190.9	37.2	67.8	23.9	15.4	15.9	30.8	190.8	54.6	56.5	17.6	510.4
USDA (total)	10.5	5.4	0.1	0.0	4.0	1.0	0.0	4.0	9.0	2.6	2.3	28.4
ARS	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	3.0	0.0	0.0	3.0
FS	3.5	3.4	0.1	0.0	0.0	0.0	0.0	2.0	0.0	0.6	0.3	6.4
NIFA	7.0	2.0	0.0	0.0	4.0	1.0	0.0	2.0	6.0	2.0	2.0	19.0
TOTAL	277.7	50.6	104.9	27.5	38.0	19.3	37.3	563.3	368.5	256.4	91.8	1557.8

* Abbreviated titles for the Nanotechnology Signature Initiatives and Nanotechnology-Inspired Grand Challenges are used in Tables 3–5. See Chapter 1, p. 3, for full titles.

Key Points about the 2016–2018 NNI Investments

- Reductions in overall NNI investments for 2018 relative to 2016–2017 and previous years are consistent with the goal of the President’s 2018 Budget to prioritize Federal resources on areas that industry is not likely to support, over later-stage applied research and development that the private sector is better equipped to pursue.
- The actual NNI investments reported by the participating agencies for 2016 (\$1.56 billion) are significantly larger than 2016 estimated investments published in the 2017 Budget (\$1.43 billion) and 2016 requested investments published in the 2016 Budget (\$1.50 billion). This change is due largely to the fact that an increasing proportion of agencies’ nanotechnology investments are coming from “core” R&D programs, where the high success rate of nanotechnology-related proposals cannot be anticipated in advance.

2. NNI Investments

Table 4: Estimated 2017 Agency Investments by Program Component Area
(dollars in millions)

Agency	1. Nanotechnology Signature Initiatives (NSIs) and Grand Challenges (GCs)*	1a. Nanomanufacturing NSI	1b. Nanoelectronics NSI	1c. NNI NSI	1d. Sensors NSI	1e. Water NSI	1f. Future Computing GC	2. Foundational Research	3. Nanotechnology-Enabled Applications, Devices, and Systems	4. Research Infrastructure and Instrumentation	5. Environment, Health, and Safety	NNI Total
CPSC	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	2.0	2.0
DHS	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.8	0.0	0.0	0.8
DOC/NIST	26.0	4.9	10.7	1.3	0.7	0.3	8.2	10.3	4.4	35.7	6.0	82.4
DOD	24.1	0.6	14.9	0.7	4.7	2.3	1.0	89.7	26.0	1.4	3.4	144.5
DOE	0.3	0.0	0.0	0.0	0.3	0.0	0.0	180.9	11.4	134.9	0.0	327.5
DOI/USGS	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.1	0.1
DOJ/NIJ	0.2	0.0	0.0	0.0	0.2	0.0	0.0	0.0	1.0	0.2	0.0	1.4
DOT/FHWA	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.5	0.0	0.0	0.5
EPA	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	10.0	10.0
DHHS (total)	15.1	1.1	0.0	1.4	12.2	0.0	0.4	87.6	262.0	28.1	46.8	439.6
FDA	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	11.0	11.0
NIH	15.1	1.1	0.0	1.4	12.2	0.0	0.4	87.6	262.0	28.1	24.7	417.5
NIOSH	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	11.1	11.1
NASA	1.9	0.4	0.5	0.0	1.1	0.0	0.0	6.7	3.2	0.0	0.1	12.0
NSF	151.4	32.8	35.3	25.0	11.8	11.4	35.1	172.5	36.6	42.9	17.5	420.8
USDA (total)	12.8	7.6	0.1	0.0	3.0	2.1	0.0	3.0	8.0	2.0	2.4	28.2
ARS	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	3.0	0.0	0.0	3.0
FS	5.8	5.6	0.1	0.0	0.0	0.1	0.0	1.0	0.0	0.0	0.4	7.2
NIFA	7.0	2.0	0.0	0.0	3.0	2.0	0.0	2.0	5.0	2.0	2.0	18.0
TOTAL	231.8	47.4	61.4	28.4	33.8	16.1	44.7	550.6	353.7	245.2	88.3	1469.7

- Total funding for PCA 1, Nanotechnology Signature Initiatives and Grand Challenges, for 2018 (nearly \$200 million, representing over 16% of the NNI total) reflects the emphasis on focused investments in R&D that advances interagency cooperation and public/private partnerships in support of national priorities, as a key part of the overall NNI funding strategy.
- The NNI's Nanotechnology-Inspired Grand Challenge for Future Computing is a new investment category in the President's 2018 Budget, included for the first time under PCA 1. This challenge helps to address renewed international competition for U.S. leadership in semiconductor manufacturing and downstream information technology industries. For 2016, agencies are reporting over \$140 million in investments under the NNI budget crosscut (including related research under the Nanoelectronics NSI) in this sector, which is critical for both national security and economic competitiveness.

2. NNI Investments

Table 5: Proposed 2018 Agency Investments by Program Component Area
(dollars in millions)

Agency	1. Nanotechnology Signature Initiatives (NSIs) and Grand Challenges (GCs)*	1a. Nanomanufacturing NSI	1b. Nanoelectronics NSI	1c. NNI NSI	1d. Sensors NSI	1e. Water NSI	1f. Future Computing GC	2. Foundational Research	3. Nanotechnology-Enabled Applications, Devices, and Systems	4. Research Infrastructure and Instrumentation	5. Environment, Health, and Safety	NNI Total
CPSC	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	1.0	1.0
DHS	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.7	0.0	0.0	0.7
DOC/NIST	19.2	4.9	10.5	1.3	0.4	0.3	1.9	9.5	3.2	30.5	2.8	65.3
DOD	21.0	0.5	12.9	0.6	3.8	2.2	0.9	88.3	26.5	0.7	3.5	139.9
DOE	0.3	0.0	0.0	0.0	0.3	0.0	0.0	141.3	5.0	80.6	0.0	227.1
DOI/USGS	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0
DOJ/NIJ	0.2	0.0	0.0	0.0	0.2	0.0	0.0	0.0	1.0	0.2	0.0	1.4
DOT/FHWA	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	1.5	0.0	0.0	1.5
EPA	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	4.5	4.5
DHHS (total)	11.3	0.8	0.0	1.1	9.1	0.0	0.3	68.4	205.2	22.1	40.7	347.7
FDA	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	10.9	10.9
NIH	11.3	0.8	0.0	1.1	9.1	0.0	0.3	68.4	205.2	22.1	18.7	325.7
NIOSH	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	11.1	11.1
NASA	0.9	0.0	0.1	0.0	0.8	0.0	0.0	3.3	1.7	0.0	0.1	6.1
NSF	135.5	27.8	31.3	19.7	7.3	11.4	38.1	163.1	36.4	42.6	11.1	388.6
USDA (total)	10.2	5.2	0.0	0.0	3.0	2.0	0.0	2.2	7.0	2.0	2.3	23.7
ARS	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	3.0	0.0	0.0	3.0
FS	3.2	3.2	0.0	0.0	0.0	0.0	0.0	0.2	0.0	0.0	0.3	3.7
NIFA	7.0	2.0	0.0	0.0	3.0	2.0	0.0	2.0	4.0	2.0	2.0	17.0
TOTAL	198.6	39.3	54.7	22.7	24.9	15.9	41.1	476.0	288.1	178.7	66.1	1207.5

- The increase in the percentage of total NNI investments in PCA 2, Foundational Research (from 36% in 2016 to nearly 40% in the 2018 Budget) reflects the Budget's focus on supporting early-stage R&D, and is consistent with calls by NNI advisory bodies to maintain a pipeline of basic research that will lead to the innovations of the future.
- Proportional NNI investments in PCA 3 (Nanotechnology-Enabled Applications, Devices, and Systems) hold steady at about 24% of the total NNI investments for 2016–2018, down slightly from 25% in 2015.
- NNI agencies continue to provide consistent, proportional funding for PCA 4 (Research Infrastructure and Instrumentation) for 2016–2018, at 15–16% of the NNI total. The 2018 request (\$179 million, representing about 15% of the NNI total investment) includes sustained support for NSF's National Nanotechnology Coordinated Infrastructure network of university-based nanotechnology user facilities. The President's 2018 Budget for DOE requests continued support for three of the original five Nanoscale Science Research Centers. PCA 4 also includes research to

2. NNI Investments

develop novel or improved instrumentation, which is critical to continued progress in nanotechnology and to maintain U.S. competitiveness internationally.

- PCA 5 (Environment, Health, and Safety—EHS) investments are a key element of the NNI’s strategy to ensure responsible development of nanotechnology. For 2016–2018, the proportional research investments reported under PCA 5 (see Appendix A for definitions) are approximately 6% of the NNI total for 2016 and 2017, and 5.5% in the 2018 Budget. In addition to the PCA 5 investments, some research reported under other PCAs (e.g., PCA 1 and PCA 4) also contributes to the overall EHS research portfolio.
- The return of the Department of Justice’s National Institute of Justice (NIJ) to the NNI budget crosscut in the 2018 President’s Budget is another example of where nanotechnology innovations initially funded by basic research agencies are now coming to fruition in R&D programs focused on applications, devices, and systems that directly contribute to national priorities.
- Investments in SBIR and STTR funding by the participating agencies, reported outside of the formal NNI funding crosscut tabulated in the budget tables shown above, play a critical role in transitioning nanotechnology innovations into products for commercial and public benefit (NNI Goal 2), as discussed below.

Utilization of SBIR and STTR Programs to Advance Nanotechnology

As called for by the 21st Century Nanotechnology Research and Development Act, this report includes information on use of the Small Business Innovation Research and Small Business Technology Transfer programs to support nanotechnology development. Five NNI agencies—DOD, DOE, NASA, NIH, and NSF—have both SBIR and STTR programs. In addition, DHS, EPA, NIST, NIOSH, and USDA have SBIR programs that include funding for nanotechnology. Table 6 shows agency funding for SBIR and STTR awards for nanotechnology R&D from 2012 through 2015 (the latest year for which data are available).

Some NNI agencies (e.g., NSF and NIH) have included nanotechnology-specific topics in their SBIR and STTR solicitations. The NSF SBIR program has an ongoing nanotechnology topic included within its advanced materials, manufacturing, electronics, and biotechnology solicitations. Some agencies have had topical or applications-oriented solicitations for which many awardees have proposed nanotechnology-based innovations. SBIR/STTR data for 2004 through 2015 indicate that the NNI agencies have funded over \$1.1 billion of nanotechnology-related SBIR and STTR awards, in addition to the funding reported under the NNI PCAs. A complete listing by year (including data from 2004 through 2011) can be found at a download link in the Overview section of nanodashboard.nano.gov.

2. NNI Investments

Table 6: 2012–2015 Agency SBIR and STTR Awards (dollars in millions)												
	2012			2013			2014			2015		
Agency	SBIR	STTR	Total	SBIR	STTR	Total	SBIR	STTR	Total	SBIR	STTR	Total
DHHS/NIH	21.7	3.9	25.6	22.9	1.9	24.8	26.9	3.2	30.1	21.8	3.2	24.9
DHHS/NIOSH	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0
DHS	1.3	0.0	1.3	0.3	0.0	0.3	0.3	0.0	0.3	4.0	0.0	4.0
DOC/NIST	0.4	0.0	0.4	0.6	0.0	0.6	0.7	0.0	0.7	0.2	0.0	0.2
DOD	25.4	7.6	33.0	22.6	5.5	28.1	11.1	6.5	17.6	24.6	2.8	27.4
DOE	7.8	1.7	9.5	3.9	2.3	6.2	15.1	2.5	17.5	20.5	4.0	24.5
EPA	0.7	0.0	0.7	0.5	0.0	0.5	0.9	0.0	0.9	0.9	0.0	0.9
NASA	17.0	3.9	20.9	5.7	1.3	7.1	2.1	1.9	4.0	3.3	0.9	4.2
NSF	18.0	2.5	20.5	17.9	0.9	18.9	22.1	3.6	25.8	19.6	3.8	23.4
USDA	0.5	0.0	0.5	0.1	0.0	0.1	0.1	0.0	0.1	1.5	0.0	1.5
TOTAL	92.8	19.6	112.4	74.5	11.9	86.4	79.3	17.7	97.0	96.4	14.7	111.0

APPENDIX A. NNI RESEARCH BY PROGRAM COMPONENT AREA

The budget details presented in Chapter 2 encompass a broad array of National Nanotechnology Initiative (NNI) research and development activities. This appendix highlights examples of agency accomplishments and plans arising from the investments in each of the Program Component Areas (PCAs). For each PCA, 2016 and 2017 accomplishments are provided for individual agencies, as well as for collaborative activities among NNI agencies and with external entities. 2018 plans for individual agency and collaborative activities are also summarized for each PCA.

PCA 1. Nanotechnology Signature Initiatives and Grand Challenges

Nanotechnology Signature Initiatives (NSIs) serve to spotlight topical areas of national importance that exhibit particular promise for significant advances through close and targeted program-level interagency collaboration. The NSIs define the shared vision of the participating agencies for accelerating the advancement of nanoscale science and technology from research through commercialization in their respective areas. The NSI portfolio is intended to be dynamic, with topical areas rotating and evolving over time.

A nanotechnology-inspired grand challenge (GC) is an ambitious but achievable goal that harnesses nanoscience, nanotechnology, and innovation to solve important national or global problems and has the potential to capture the public's imagination. The current grand challenge topic was chosen based on extensive input from the private and academic research sectors, with the goal of stimulating additional public and private sector interest and collaboration in developing low-power cognitive computing capabilities far beyond what is currently possible.

These PCA 1 categories include both foundational research and nanotechnology-enabled applications, devices, and systems within each NSI or GC, as appropriate. Instrumentation that is specifically developed in support of a confined topical area covered by one of the NSIs or GCs is included here, but otherwise the development or acquisition of more broadly applicable instrumentation (as well as resources devoted to facilities) falls under the separate PCA on Research Infrastructure and Instrumentation. Most research on Environment, Health, and Safety falls within the separate Program Component Area (PCA 5) described below, but activities directly pertinent to specific NSIs or GCs are reported in this section instead. Note that the NSIs and GCs are focused on the thrust areas as described below, and that activity falling outside these areas is classified under other PCAs.

1a. Sustainable Nanomanufacturing: Creating the Industries of the Future

Overview

The Nanomanufacturing NSI supports R&D to establish advanced manufacturing technologies for integrating nanoscale building blocks into complex, large-scale systems. The initiative has two thrust areas: (1) design of scalable and sustainable nanomaterials (such as those derived from wood and other renewable resources), components, devices, and processes; and (2) nanomanufacturing measurement technologies.

The agencies participating in the Nanomanufacturing NSI continue to make progress toward the goals identified in the foundational white paper,¹⁸ and highlights of these accomplishments are provided in a summary document available on nano.gov.¹⁹ The National Nanotechnology Coordination Office (NNCO) continues to support interagency coordination and engagement among agency representatives and relevant entities in the private sector. For example, a Technology Pathways Workshop was held in November 2017, and provided case studies in nanotechnology commercialization from small and large companies for the benefit of current entrepreneurs seeking to scale up and commercialize their own nanotechnology businesses.²⁰

Agency Progress and Plans

DOD/Army: The U.S. Army Research Laboratory (ARL) is conducting a multiscale research program to investigate low-cost, high-performance reinforcement of transparent composites using cellulose-based nanomaterials derived from renewable bioresources. Target applications include lightweight films and composites for use in ballistic protection and structural applications, with particular interest in reducing mechanical failure of transparent laminates. Significant accomplishments include development of new processes for drying nanocellulose to increase surface area and processes for dispersing the nanocellulose particles in transparent engineering polymers. Epoxy nanocomposites have demonstrated significant reduction in optical haze and improved clarity with the new particles compared to standard freeze-dried nanocellulose, and a significant increase in tensile strain-to-failure providing greater toughness compared to the neat epoxy. Surface modifications were also developed; in one case they were used to change the failure mechanism in poly(methyl methacrylate) films and substantially increase elongation and toughness, and in another case to improve the strain-to-failure in bulk epoxy samples. ARL plans to continue to optimize formulations of nanocellulose in epoxy to validate and improve upon the results to date, and to elucidate the mechanisms for improved toughening. ARL will also be exploring alternative, non-particulate reinforcement architectures.

DOD/Army, USDA/FS, and academia: The Army has coordinated its nanocellulose activities with relevant leaders in preparation and processing, especially focusing on critical challenges in developing optimized nanocellulose-based fibers and composites. ARL has collaborated with the USDA Forest Service's Forest Products Laboratory in probing the effects of nanocellulose drying methods, surface chemistry, and microstructure on composite properties; and with several universities on better understanding and manipulating fundamental properties of cellulose nanocrystals as well as developing improved materials and techniques for secondary processing.

DOD/Army and academia: The Army Engineer Research and Development Center (ERDC) has initiated a new collaborative research program with a university focusing primarily on nanoscale modification of polymeric materials and cement-based materials with nanocellulose. The primary goal of this research is to produce structural materials for force protection and projection applications wherein the mechanical properties can be tailored by the addition of nanocellulose materials. Along with materials development, advanced nanoscale characterization methods will be applied to guide synthesis and material model development.

NASA: NASA continues to advance the technology maturation of structural carbon nanotubes (CNTs). Material property targets that guided the rapid advancement of CNT materials development drove the

¹⁸ www.nano.gov/sites/default/files/pub_resource/nni_siginit_sustainable_mfr_revised_nov_2011.pdf

¹⁹ www.nano.gov/sites/default/files/pub_resource/Nanomanufacturing_NSI_Highlight_Document.pdf

²⁰ www.nano.gov/TechPathwaysWorkshop

maturation of CNT composite processing and fabrication. The processing method was scaled up for implementation on a commercial filament winder, and a CNT composite overwrapped pressure vessel was flight tested in the summer of 2017.

Furthermore, NASA funded an effort to develop ultralightweight cores for efficient load-bearing structures and their applications. The project, supported by the Space Technology Mission Directorate's Game Changing Development Program, focused on the maturation and development of scalable methods to manufacture ultralightweight core materials as lower-mass alternatives to traditional honeycomb or foam cores in composite sandwich structures.

The processing method used to produce the CNT composites described above was developed in collaboration with an industry partner.

NASA, Air Force, academia, and industry: NASA has awarded a grant to a university to establish a Space Technology Research Institute focused on Ultra-Strong Composites by Computational Design (US-COMP).²¹ This grant will support efforts focused on enabling accelerated advancement of structural nanomaterials through computational guidance. Additional partners in US-COMP include several other universities, industrial partners, and the U.S. Air Force Research Laboratory (AFRL).

NIST: NIST continues to develop and deploy nanomanufacturing measurement technologies. The agency is developing accurate and precise nanoparticle measurement methods to be used as quality-control tools in manufacturing. Efforts include the development of quantitative, high-resolution tomography methods that can provide input data for nanocomposite models, and new fluorescence microscopy methods, using specially functionalized dyes, to elucidate failure mechanisms and identify particle-matrix interactions in nanocellulosic composites. NIST improved measurements of volume with the development of a validated fundamental measurement model for non-spherical nanoparticles, and NIST improved the production of well-controlled carbon nanotube populations through the demonstration of advanced separation and processing strategies. A patent was assigned to NIST on Fractionating Nanomaterials by a Liquid Multiphase Composition.²² These efforts will enable the research and industrial communities to optimize the design, processing, and application of nanomaterials for manufacturing applications.

NIST will continue to advance nanoparticle manufacturing by developing new measurement methods to enable high-throughput quality control at every stage of the manufacturing process, as well as specialized tools to elucidate the fundamental phenomena occurring during nanoparticle formation and functionalization. NIST intends to advance translational processing capabilities so that production bottlenecks for high-value populations of carbon nanotubes are eliminated.

NIST, academia, and industry: NIST has worked with collaborators at a university to build comprehensive models of carbon nanotube composites that predict mechanical, electrical, and thermal properties, using high-resolution tomography data obtained at NIST. NIST also will continue interactions with several companies for potential commercialization of a scalable separations technology for carbon nanotubes.

NSF: NSF is supporting research in novel processes and techniques throughout NSF directorates for continuous and scalable nanomanufacturing, directed (physical/chemical/biological) self-assembly processes leading to heterogeneous nanostructures with the potential for high-rate production, nanobiomanufacturing, modular systems, and principles and design methods. The NSF Nanomanufacturing (NM) Program and other ongoing core programs fund fundamental research projects and have contributions

²¹ www.nasa.gov/press-release/nasa-selects-proposals-for-first-ever-space-technology-research-institutes

²² US 20140174991 A1

in carbon-based nanomaterials, optical metamaterials, cellulosic nanomaterials, composite nanomaterials, and nanosystems. Examples include the following:

- The NM Program²³ in the Directorate for Engineering (ENG) supports fundamental research in novel methods and techniques for batch and continuous top-down (addition/subtraction) and bottom-up (directed self-assembly) processes leading to the formation of complex heterogeneous nanosystems. The program supports basic research in nanostructure, nanodevice, and process design principles; integration across length scales; and system-level integration. The program leverages advances in the understanding of nanoscale phenomena and processes (physical, chemical, electrical, thermal, mechanical, and biological), nanomaterials discovery, novel nanostructure architectures, and new nanodevice and nanosystem concepts. It seeks to address quality, efficiency, scalability, reliability, safety, and affordability issues that are relevant to manufacturing. To address these issues, the program encourages research on processes and production systems based on computation, modeling, and simulation; use of process metrology, sensing, monitoring, and control; and assessment of product quality and performance. NM focuses high-risk research on the discovery and invention of novel nanoscale processes, methods, and techniques that have the potential to translate into new manufacturing platforms. The NSF NM Program is a core basic research program that resides in ENG and is renewed every year. Other nanomanufacturing projects are supported by open competition in other NSF program areas.
- A program solicitation on scalable nanomanufacturing (SNM)²⁴ has had seven competitions from 2011 to 2017, where the expectations have changed and integrated systems have become an inherent part of the call. The emphasis of the SNM solicitation has been on multidisciplinary research to overcome the key scientific and technical barriers that prevent the production of useful nanomaterials, nanostructures, devices, and systems at an industrially relevant scale, reliably, and at low cost and within environmental, health, and safety (EHS) guidelines. SNM is a collaboration of multiple divisions in NSF's ENG and Mathematical and Physical Sciences (MPS) directorates. The current Scalable Nanomanufacturing for Integrated Systems (SNM-IS) solicitation has made awards in 2017 for projects that will continue for four years. The emphasis of SNM-IS is on research in new nanoscale manufacturing concepts and integration methods to realize complex integrated systems based on nanotechnology. The goal of the SNM-IS is to study and formulate the fundamental principles of scalable nanomanufacturing and integration for nanotechnology-based integrated systems towards the eventual manufacture of useful nanotechnology-enabled products. An additional goal is to investigate mass customization concepts for nanotechnology-enabled integrated systems. SNM-IS has synergy with the other activities focused on accelerated materials development, including the Designing Materials to Revolutionize and Engineer our Future (DMREF) program.²⁵
- Several nanotechnology Engineering Research Centers provide support for nanomanufacturing research and education in the areas of nanoelectronics, nanosensors, and energy applications. One example is the Nanosystems Engineering Research Center (NERC) for Nanomanufacturing Systems for Mobile Computing and Mobile Energy Technologies (NASCENT), which was funded in September 2012 for five years, renewable based on merit review for another five. The center develops high-throughput, high-yield, reliable, and versatile nanomanufacturing systems to take nanoscience discoveries from the lab to the marketplace. Its mission is to create these nanomanufacturing systems and associated processes through transformative research, education

²³ www.nsf.gov/funding/pgm_summ.jsp?pims_id=13347

²⁴ www.nsf.gov/funding/pgm_summ.jsp?pims_id=505265

²⁵ www.nsf.gov/funding/pgm_summ.jsp?pims_id=505073

of leaders, and global and industrial engagement that will revolutionize future generations of mobile computing and energy devices. NASCENT is a partnership between several universities and has strong industry engagement.

- The final report of the NSF-sponsored international study on Nanomodular Materials and Systems by Design (NMSD) was published in September 2016. Related activities will continue in 2018. NMSDs are materials and systems put together in a modular manner with nanoscale building blocks. The structures and functions of these nanoscale architectures are guided by design and computation. A suite of nanoelements such as quantum dots, CNTs, two-dimensional (2D) atomic layer materials, etc., and a range of precision methods, both top-down lithography and bottom-up self-assembly, are available to construct these multi-component units. These functional blocks are then used to form large-scale architectures and higher-order systems towards the design and production of high-performance devices.
- Additional activities are being organized for 2017 and 2018 in the Directorate for Biological Sciences and the ENG Directorate aimed at researching biology at the nanoscale for advanced manufacturing.
- NSF infrastructure investments also support nanomanufacturing. The NSF National Nanotechnology Coordinated Infrastructure (NNCI) user facilities are a resource for the nanomanufacturing community. A new node of the Network for Computational Nanotechnology for modeling and simulation research dedicated to nanomanufacturing was established at the end of 2017, for a five-year interval. More information is provided under PCA 4.

NSF, other NNI agencies, and Manufacturing USA: *Dear Colleague Letter (DCL): Advanced Manufacturing Research to Address Basic Research Enabling Innovation at Manufacturing USA Institutes (2017: NSF 17-030):*²⁶

On November 18, 2016, NSF announced interest in research proposals to address critical fundamental research needs in advanced manufacturing, including nanomanufacturing, especially proposals that will enable innovations in one or more of the Manufacturing USA institutes' focus areas, and that will leverage the facilities, infrastructure, and member companies of an institute. The resulting knowledge can, in turn, enable new technologies that feed into the innovation pipelines of one or more of the Manufacturing USA institutes. For example, the NextFlex manufacturing institute will develop manufacturing platforms for flexible hybrid electronics, where nanotechnology and nanomanufacturing will play a major role. This DCL signifies NSF's collaboration with Manufacturing USA, which is a multi-agency effort. Proposals to this DCL will be reviewed along with the regular unsolicited proposals.

USDA/FS: The USDA Forest Service continues to participate in Federal initiatives such as the National Nanotechnology Initiative, Manufacturing USA, and Bioeconomy to contribute to national goals with nanotechnology research, and will develop partnerships in nanotechnology research with other Federal agencies. A Forest Service expert-led International Organization for Standardization (ISO) cellulose nanomaterials terminology standard-development project was ballot-approved and published as *ISO Technical Specification TS 20477, Standard terms and their definitions for cellulose materials* in August 2017.

USDA/FS, public-private partnership, academia, and local governments: In 2016, the USDA Forest Service continued to collaborate with a public-private partnership named P³Nano to co-invest in cellulose nanomaterials research. To foster commercialization, P³Nano selects its projects with industry input, and the project teams require collaboration between Forest Service Forest Products Laboratory researchers and university researchers. A project review meeting took place at the Forest Service Forest Products Laboratory in Madison, Wisconsin, to review projects from past investments (\$4 million total, \$2 million from FS, \$2 million from the partner). Project teams at the review meeting reported several major accomplishments. The

²⁶ www.nsf.gov/pubs/2017/nsf17030/nsf17030.jsp

concrete performance-enhancement project team continued to identify the effectiveness of different types of cellulose nanomaterial for concrete strength improvement. The project team is exploring the possibility of collaborating with Yreka, California on a concrete bridge demonstration project. In bioplastics composites, the project team reported laboratory data showing that cellulose nanocrystals maintain their form in extrusion-blown cellulose nanocrystal-poly(lactic acid) composites and have improved barrier properties suitable for packaging applications. In fruit preservation, the research team has demonstrated that a cellulose nanocrystal coating can preserve the freshness of fruits. The team will continue to conduct research on post-application length of service. The non-formaldehyde-emitting wood adhesives team reported that it was able to produce laboratory-scale particleboard with cellulose nanofibril as the adhesive that meets industry standards. The team will continue to investigate the adhesion mechanism of cellulose nanofibril on wood substrate. In 2016, P³Nano issued a request for proposals for a new round of investment. The total amount of the new investment is \$2.25 million (\$1.5 million from FS, \$750,000 from the partner). P³Nano received 64 proposals totaling almost \$18 million in response to the request. The proposals have been reviewed and are awaiting final selection.

USDA/NIFA: NIFA's current focus in sustainable nanomanufacturing is on nanobiomaterials derived from crops, woods, and other biomass-based by-products. The Nanotechnology for Agricultural and Food Systems program in the Agriculture and Food Research Initiative (AFRI) Foundational area supports novel uses and high-value-added products of nano-biomaterials from agricultural and forest origins for food and non-food applications. There are ongoing research efforts in synthesis of carbon-based nanomaterials, development of cost-effective production methods, functionalization and characterization of nanobiomaterials, and exploration of applications such as piezoelectrics, renewable nanocomposite polymers, food packaging, barrier films, and energy and fuels. In addition, the Sustainable Bioenergy and Bioproducts program in the AFRI Challenge Area 2017 request for applications (RFA) invites research applications in nanocellulosic co-products from biomass feedstocks. This program intends to create, enhance, or optimize biological, chemical, and/or thermochemical processes to produce value-added products or industrial polymers through nanocellulosic technologies.

NIFA-supported research projects have advanced knowledge in novel applications of cellulosic nanomaterials. Nanocellulose and hyper-branched polymers (HBP) were covalently bound to make dendritic polymers. These hybrid nanostructures, of rod-spring elements (wherein rod refers to nanocellulose and spring refers to HBP) preserve the high stiffness and strength of nanocellulose while also providing impact energy absorbability through HBPs. This combination will transform the undervalued natural cellulosic nanomaterials into high-value advanced bio-renewable reinforcement materials for the automotive industry and beyond. Another significant development is to thermally transform lignocellulosic biomass into highly ordered mesoporous carbon (HOMC) using the natural plant cell structures as templates. HOMCs obtained have demonstrated a high capacitance and may become a promising material to fulfill the current needs of low-cost, facile, and renewable energy storage materials.

USDA/NIFA and USDA/FS: NIFA's plan in broad nanocellulose materials research complements well the USDA Forest Service's research plan in woody biomass-based nanocellulose.

1b. Nanoelectronics for 2020 and Beyond

Overview

The Nanoelectronics NSI supports R&D on discovery and use of novel nanoscale fabrication processes and innovative concepts to produce revolutionary materials, devices, systems, and architectures to advance the field of nanoelectronics. The initiative has five thrust areas: (1) exploring new or alternative "state variables"

for computing; (2) merging nanophotonics with nanoelectronics; (3) exploring carbon-based nanoelectronics; (4) exploiting nanoscale processes and phenomena for quantum information science; and (5) expanding the national nanoelectronics research and manufacturing infrastructure network.

There are considerable research and development activities across the participating agencies that support the goals of the Nanoelectronics NSI. A summary of recent accomplishments is provided in a highlights document available on nano.gov.²⁷ The agencies participating in this signature initiative are working together to identify future directions and focus areas in this rapidly evolving field. They are also coordinating closely with other Federal entities and activities, such as the Networking and Information Technology R&D (NITRD) Program and agencies engaged more broadly in future computing research.

Agency Progress and Plans

DOD/Air Force: AFRL is continuing to explore nanotechnologies related to fielding power for our soldiers, airmen, and sailors, including nanotechnology-enabled creasable and printable batteries. Flexible energy storage is a necessity to power the next generation of portable and flexible electronic devices such as sensors, smart skins for human performance monitoring, radio frequency ID tags, and wearable electronics. It was found that by replacing traditional metal foil current collectors with a porous, conductive, nonwoven, multi-walled carbon nanotube (MWCNT) mat, high-performance bendable and even creasable Li-ion batteries could be prepared without losing energy storage performance. The improvements in mechanical performance can be explained by the interwoven network of long MWCNTs. This network leads to better active material adhesion and electrolyte wetting. Additionally, the team has been able to develop both printable Li-ion battery electrodes and electrolytes centered around carbon nanofibers and nanoscale alumina, respectively. Printing is an enabling step toward direct integration of flexible power in confined areas and can potentially revolutionize the way flexible devices are manufactured. (This activity also supports the Nanomanufacturing NSI, PCA 1a.)

DOD/Navy: The U.S. Navy's Nanoscale Computing Devices and Systems (Nanoelectronics) program has pursued aggressively the bottom-up chemical synthesis approach to building carbon-based nanoelectronic devices and circuits with atomic precision. In the last few years, the Office of Naval Research (ONR) launched two major initiatives: an ONR internal Basic Research Challenge (BRC) program entitled "Carbon Molecular Electronics" is in its last year, and a 2016 Multi-University Research Initiative (MURI) project entitled "Synthetic Electronics" kicked off in October of 2016. ONR-funded researchers in these projects and other individual grants have succeeded in building a plethora of atomic-precision graphene nanoribbon (GNR) heterostructures, either by variation of widths or by atomic precision placement of heteroatoms such as nitrogen and boron into the pure carbon GNRs.

The ONR Power Electronics Program seeks to develop graphene nanoribbon-based power electronics. As part of this effort, a university team completed molecular dynamics simulations of different aspects in GNR chirality, studied the effect of stone-wall defects on the failure of armchair and zigzag GNRs, and studied the unravelling of armchair and zigzag GNRs. This work is important to lay an analytical foundation, including developing an understanding of failure mechanisms, for the application of these materials to power electronics applications with the potential to greatly improve power density.

The ONR Nanoelectronics Program will begin to design and synthesize functional devices and circuits that are amenable to atomic precision characterization, primarily with state-of-the-art scanning probe techniques. Naval Research Laboratory (NRL) plans in quantum systems include creating a new paradigm for manipulating quantum systems by trapping ultracold atoms in the evanescent field of SiN waveguides. This advancement will enable chip-scale quantum information systems. NRL also plans to use quantum

²⁷ www.nano.gov/sites/default/files/pub_resource/Nanoelectronics_NSI_Highlights_April2017.pdf

coherence and entanglement for improved measurement sensitivity using quantum dots in mechanical systems. In particular, this program will make use of an entangled spin system to perform sensitive measurements of mechanical motion at the quantum limit.

DOD/DARPA, NIST, NSF, academia, and industry: The Semiconductor Technology Advanced Research Network (STARnet) Program²⁸ has built a large, multi-university research community to explore beyond current evolutionary directions and make discoveries that drive technology innovation beyond what can be imagined for electronics today. This public-private partnership is organized into six multi-university centers, each focused in a specific challenge area. Researchers in these centers are advancing R&D in physics theory, materials, processes, circuits, and related areas (design, off-chip communications, etc.) for new devices that operate using unique information tokens due to physical phenomena that occur at the nanoscale. STARnet is jointly funded and managed by member companies and the Defense Advanced Research Projects Agency (DARPA). DARPA routinely shares the results with NSF and the other DOD component organizations.

A semiconductor industry technology research consortium has worked with NIST and NSF in a public-private partnership (called the Nanoelectronics Research Initiative—NRI—before December 2016 and nanoelectronic COmputing REsearch—nCORE—after January 2017) to address key national priorities. Through research investments in centers across the United States, NRI/nCORE seeks the next device that will propel computing beyond the limitations of current technology

Via the NRI and STARnet public-private partnerships, NIST, DARPA, NSF, and U.S. member companies continue to support nine major interdisciplinary research teams at academic institutions across the Nation. Benchmarking of new devices in order to optimize the selection of future technology is a component of these programs. The new nCORE program, with support from NSF beginning in 2018, has been developed based on learning from the NRI. A new DARPA program, Joint University Microelectronics Program (JUMP), is slated to begin in 2018, and is anticipated to include research in next-generation cognitive nanoelectronics.

NASA: Through the Space Technology Mission Directorate's Game Changing Development Program, NASA is currently funding an effort to develop methods to either coat or wrap carbon nanotube wires with polymer aerogels to replace the polymer dielectric layer. The project has successfully demonstrated flexible, uniform coating of CNT wires with polyimide aerogels with negligible loss in conductivity on the CNT conducting wires.

NASA is funding a Phase I Small Business Innovation Research (SBIR) project to develop lightweight, flexible cables for aerospace vehicles. The plan is to replace metal braids with carbon nanotube films and improve the performance of CNT electromagnetic interference shields to meet specifications.

NASA has done pioneering work in creating nanoscale vacuum field emission transistors (VFETs) on 200 mm wafers, by combining the best of vacuum electronics and silicon integrated circuit manufacturing. A record low drive voltage of 2 V gives a high current of 3 μ A and 35 μ S transconductance per emitter. These values can be increased by an array of emitters in the pad. The devices also showed immunity to gamma and proton radiation.

NASA and Air Force: NASA will continue the Si-based fabrication of the VFETs to explore further scaling, building circuits and potential applications in THz electronics. NASA will collaborate with AFRL to fabricate VFETs using other material systems with more favorable work functions and robustness.

²⁸ www.src.org/program/starnet/

NIST: NIST efforts underway that support the nanoelectronics NSI include the following:

- NIST is developing new measurements to elucidate the behavior of spin waves, new methods to control the interaction of magnetic multilayers in nanoscale devices, and new ways to image magnetic devices that will support the development of next-generation low-energy-consumption, nonvolatile electronics.
- Several NIST research teams are working on projects competitively awarded through the intramural Innovations in Measurement Science program. These efforts include a project to develop atom-based electronic devices that rely on precisely placed individual atoms for use in traditional and quantum information processing, and a team that is developing nanoscale superconducting devices (Josephson junctions) to extend quantum voltage standards into the microwave communications frequency range, laying the foundation for more energy-efficient computing.
- The NIST laboratories are enabling devices for classical and quantum information handling at the ultimate limits of today's silicon-based (Si-based) electronics by developing atomically precise manufacturing methods for single-atom-based electronic structures and by creating ultrapure, highly enriched nanomaterials for Si quantum electronics and ultrapure material standards. Furthermore, NIST is developing Si-based nanodevices for single-electron high-precision electrical current metrology.
- Research efforts to support future nanoscale memory device concepts, including resistive random access memory and an emerging effort in molecular (or DNA) memory, are aimed to take memory cell design to extreme nanometer scales and beyond to support the information economy.
- NIST's analytical metrology techniques help to assure the reliability and determine failure mechanisms in nanoelectronic devices; for example, NIST has demonstrated high-definition electron spin resonance (ESR) with a 10,000-fold improvement in sensitivity beyond previous cavity-based ESR.
- NIST intends to continue current efforts to support the measurement science needed by the U.S. nanoelectronics industry. For example, NIST is building an ultrafast coherent diffractive microscope that promises unprecedented lateral, depth, and time resolution and that will be capable of providing vital information about the performance of nanoscale semiconductor devices and magnetic memories.

NIST and industry: NIST, together with a magnetic data storage manufacturer, developed ways to image nanoscale magnetism in magnetic recording heads.

NIST spectroscopically measured magnetic spin dynamics in individual nanoelements to provide fundamental understanding of materials for computer memory applications and enable the development of new, ultralow-power computer memory.

NIST and leading U.S. semiconductor manufacturers: NIST is developing innovative high-resolution optical methods, working directly with industry to characterize and identify deep sub-wavelength defects critical to 14 nm node device fabrication and beyond.

NIST and academia: NIST is developing "lens-less," time-resolved, nanoscale imaging by use of ultrafast sources of extreme-ultraviolet radiation. Such an imaging system will be of great utility in the development of ultralow-power magnetic memory for "Internet of Things" applications. NIST plans to extend ongoing work on lens-less "coherent diffractive imaging" by developing imaging reference standards and a public database to facilitate quantitative applications of the technology, such as critical-dimension metrology needed to quantify and thus ensure performance of nanoscale semiconductor circuits and devices.

NIST discovered a material with extremely low dissipation of quantum-mechanical spin at microwave frequencies. The material is very effective in reducing the power consumption of a nanoscale magnetic memory replacement for silicon-based dynamic random-access memory (DRAM).

NSF: NSF-funded research in this area aims to discover and use novel nanoscale principles and processes to produce revolutionary materials, devices, systems, and architectures to advance the field of electronics. NSF's request will fund grants to advance semiconductor devices, computation, information processing, sensor technologies, and communications beyond the physical and conceptual limitations of current technologies.

The primary focus of the NSF Nanoelectronics NSI investment is on upstream, exploratory research in the following areas: new alternative "state variables" for logic and memory components and suitable computer architectures, computer-based research on new devices, integration of nanoelectronic and nanophotonic components into new systems, and new quantum information system components and systems.

Several core programs cover this thrust, including the Electronic and Photonic Materials Program and the Macromolecular, Supramolecular, and Nanochemistry Program within MPS's Division of Materials Research and Division of Chemistry, respectively; and the Electronics, Photonics, and Magnetic Devices Program within ENG's Division of Electrical, Communications, and Cyber Systems. Examples of center activities include the Materials Research Science and Engineering Centers (MRSECs), the Science and Technology Centers (STCs), the Engineering Research Centers (ERCs), and the Nanoscale Science and Engineering Centers (NSECs). Center efforts supported within the Division of Materials Research include: (1) the Center of Excellence in Materials Research and Innovation for Photonic and Multiscale Nanomaterials; (2) MRSEC: Polarization and Spin Phenomena in Nanoferroic Structures (P-SPINS); (3) MRSEC: Center for Precision Assembly of Superstratic and Superatomic Solids; and (4) MRSEC: Quantum and Spin Phenomena in Nanomagnetic Structures. One STC example is the Center on Quantum Materials and Devices.

The ENG Directorate supports two exploratory research areas in Advancing Communication Quantum Information Research in Engineering (ACQUIRE); and New Light, EM (Electronic) and Acoustic Wave Propagation (NewLAW): Breaking Reciprocity and Time-Reversal Symmetry.²⁹ (These also are in support of the Future Computing Grand Challenge—see PCA 1f, below.) NSF will also continue to support the new NNCI program with a diverse portfolio of capabilities for research, including in nanoelectronics (see PCA 4 section below for details).

NSF and industry: The Energy-Efficient Computing: from Devices to Architectures (E2CDA) program³⁰ has resulted in nine four-year awards made by the NSF Directorate for Computer and Information Science and Engineering (CISE), ENG, and industry partners in 2016. (This program is also directly in support of the Future Computing Grand Challenge, PCA 1f; see below.)

NSF, IARPA, and industry: Beginning in 2018, NSF will collaborate with a semiconductor industry technology research consortium and the Intelligence Advanced Research Projects Activity (IARPA) in supporting a three-year exploratory research program on "Semiconductor Synthetic Biology for Information Processing and Storage Technologies" (SemiSynBio).

USDA/FS: University researchers have successfully produced a working computer chip on a cellulose nanomaterial substrate using cellulose nanomaterials developed by FS scientists.³¹

²⁹ See www.nsf.gov/pubs/2016/nsf16612/nsf16612.htm for information on both ACQUIRE and NewLAW.

³⁰ www.nsf.gov/publications/pub_summ.jsp?ods_key=nsf17531

³¹ www.nature.com/articles/ncomms8170

1c. Nanotechnology Knowledge Infrastructure (NKI): Enabling National Leadership in Sustainable Design

Overview

The goal of the NKI NSI is to provide a stakeholder-driven, practical knowledge and data infrastructure to accelerate nanotechnology discovery and innovation. The NKI NSI has four thrust areas that focus efforts on cooperative interdependent development of: (1) a collaborative, multi-sector community of practice; (2) an agile modeling network coupling experimental basic research, modeling, and applications development; (3) a cyber-toolbox for nanomaterials design; and (4) a robust digital nanotechnology data and information infrastructure.

The nanoinformatics community—including the National Cancer Institute (NCI) National Cancer Informatics Program Nanotechnology Working Group, the European Union (EU) NanoSafety Cluster’s Databases Working Group, and the U.S.-EU Communities of Research—remains extremely active and vibrant. NNCO and agencies participating in the NKI NSI monitor and engage as appropriate in a variety of community-led nanoinformatics activities, such as the ongoing development of an international informatics roadmap and revisions to the ISA-TAB-Nano data templates. The NKI NSI released a document in March of 2017 highlighting progress towards the goals outlined in the white paper,³² as well as the expansion and maturation of the nanoinformatics community.³³ A significant recent advancement is the agreement by both U.S. and EU entities to utilize the ISA-TAB-Nano specification for data curation, enabling better comparisons between datasets. Data from EU programs are being entered into a university database, and U.S. data will be welcome in a new database being established by the European Chemicals Agency. Assess to commonly formatted data enables richer datasets for researchers and modelers. Future plans include renewed focus on use of these data in developing modeling and simulation tools, and development of stronger connections with the materials communities.

Agency Progress and Plans

DOD/Air Force: Researchers at AFRL are exploiting recent advances in robotics, artificial intelligence, data sciences, and high-throughput experiments to advance the production capabilities of so-called chiral-specific carbon nanotubes. Nanomaterials are an important contributor to the development of future capabilities, and yet the process of discovery and development for nanomaterials is slow. CNT materials and devices in particular suffer from availability of affordable and pure materials with the structure and quality needed for broad application. In general, current research is human-centered, where human researchers design, conduct, analyze, and interpret experiments, and then they decide what to do next. To accelerate this process, this program utilizes robotics, artificial intelligence, data sciences, and high-throughput *in situ* techniques to alleviate bottlenecks in experimental design, execution, and analysis. The Autonomous Research System (ARES)³⁴ represents a first-of-its-kind research robot that integrates these tools and is capable of closed-loop iterative autonomous materials experimentation. ARES leads to more efficient interpretation of experiments, scheduling, and resource allocation. For example, ARES recently studied the synthesis of CNTs and demonstrated that it is able to learn to grow CNTs at targeted growth rates. Furthermore, it helped researchers optimize growth conditions for chiral-specific CNT manufacturing, which is a crucial step to ultrapure CNTs for electronics and optics. Overall, ARES has broad implications for the roles

³² www.nano.gov/sites/default/files/pub_resource/nki_nsi_white_paper_-_final_for_web.pdf

³³ www.nano.gov/sites/default/files/NKI_NSI_Highlights_2017_FINAL.pdf

³⁴ www.wpafb.af.mil/News/Article-Display/Article/981505/disrupting-the-research-process-changing-materials-science-with-robotics-ai-and/

of human and research robots in the materials research process, where optimized human-machine partnering can accelerate progress in research and scientific understanding, and will be a valuable part of the nanomaterials production toolkit moving forward.

While ARES has proven itself in carbon nanotube growth, autonomous research robots have the potential for use in a number of scientific research areas. The ARES team at AFRL is working to program the AI software to allow ARES to be a generic research tool, enabling it to work on other materials research problems. In the future, the direction of ARES will be to explore chemical and physical phenomena autonomously.

DOD/Air Force, academia, and industry: AFRL will continue to partner on ARES efforts with industry and academic partners. The tools and analysis incorporated into ARES can assist a wide variety of materials science and nanomaterials research efforts, and further coordination is planned with the NNI and other activities focused on accelerated materials development.

DOD/Navy and academia: The Navy has worked with a research team at a university to develop DAEDALUS (DNA Origami Design Algorithm for User-defined Structures), which automatically computes the single-stranded DNA sequences needed to fold an arbitrary three-dimensional DNA nanostructure starting from a three-dimensional geometric representation of the final shape of the object. The software is now freely available online,³⁵ along with a synthesis strategy to self-assemble DNA nanostructures, offering the potential for numerous applications in biomolecular science and nanotechnology. Another Navy-sponsored team at the same university developed Matriarch (for “Materials Architecture”) for designing hierarchical protein materials. This computational tool allows users to combine and rearrange material building blocks, and it can be used in combination with molecular dynamics simulations for structure and function analyses, which then informs the design process, so biologically inspired materials can be designed based on their desired functionality.

NIH: Various NIH nanotechnology programs and projects address the goals of the NNI through data sharing. This data sharing includes continued NIH/NCI support for the cancer Nanotechnology Laboratory portal (caNanoLab), a web portal and data repository for annotating and sharing information on the physicochemical, *in vitro*, and *in vivo* characterization of nanomaterials relevant to cancer prevention, diagnosis, treatment, and control. The agency has a standardized data sharing policy that applies to all funded research, and has placed special terms and conditions on awards for IT infrastructure and modeling-specific initiatives, including NIH/NCI Alliance for Nanotechnology for Cancer grants. All Alliance awards have a designated data coordinator who has been trained to enter data into caNanoLab. NIH/NCI also supports continued development of the caNanoLab software and architecture. CaNanoLab Release 2.2 went live in January 2017.³⁶

Future strategies to enhance knowledge through greater data collection, sharing, and tool development include the establishment of policies and funding opportunity announcement (FOA) requirements that ensure the dissemination and reporting of results in databases such as caNanoLab and clinicaltrials.gov.

NIH, NIOSH, NSF, academia, and industry: NIH/NCI and NIH/National Institute of Environmental Health Sciences (NIEHS) are actively engaged in this NSI and jointly supported the Nanomaterial Registry with NIH/National Institute of Biomedical Imaging and Bioengineering (NIBIB) beginning in 2012. This registry is designed to become the definitive cross-disciplinary resource for nanoparticle characterization data for health, toxicity, and industrial concerns. It draws inputs from existing curated databases, including caNanoLab, and currently includes over 1,300 particle entries. Entries are populated on the web portal

³⁵ daedalus-dna-origami.org/about/

³⁶ wiki.nci.nih.gov/display/caNanoLab/caNanoLab+2.2+Installation+Guide

through curated data extraction using a Minimal Information About Nanomaterials (MIAN) characterization vocabulary architecture. MIANs capture the physicochemical characteristics, biological interactions, and environmental interactions of given particles. This homogenized vocabulary enables searches and comparisons based on MIAN similarity. The registry team is also working on integrating modeling and simulation tools through a portal between the Nanomaterial Registry and nanoHUB, an online simulation resource for nanotechnology supported by NSF.

NIH/NCI, NIOSH, academia, industry, and European partners: The NIH/NCI National Cancer Informatics Program (NCIP)³⁷ continues to support the Nanotechnology Working Group,³⁸ an NCIP interest group comprised primarily of external and academic researchers who develop and promote best practices in nanoinformatics. The working group remains active, and its members are participating in the development of a Nanoinformatics 2030 Roadmap through the U.S.-EU Communities of Research (CORs). The working group is also collaborating with NIOSH on a book, “Nanoinformatics Principles and Practices.”

NIST: In 2016, NIST released a prototype of the NIST Materials Resource Registry, an information tool to bridge the gap between existing resources and end users by allowing resources to be registered with associated metadata to aid in search and discovery. Also in 2016, the NIST-hosted Materials Data Repository, a concrete mechanism for the interchange and re-use of research data on materials systems, including nanomaterials, had reached approximately 150 gigabytes of highly heterogeneous data, spanning 25 individual research communities, with participation of 125 distinct organizations across academia, government, and industry.

NIST plans to continue to advance the availability of tools for predicting the physicochemical properties of nanomaterials. NIST efforts will include, for example, an upgrade of the NIST Materials Resource Registry and the development of new high-throughput methods to generate large quantities of processing-structure-properties data.

NIST, industry, and academia: In 2017 and 2018, NIST will continue to support the Center for Hierarchical Materials Design (CHiMaD), a NIST center of excellence led by a university in partnership with Argonne National Laboratory (ANL) and other contributing organizations. CHiMaD is integrating computation, data, and experiment for the design of new materials through an array of projects including many with a focus on nanotechnology, such as directed self-assembly for nanomanufacturing, 2D nanoscale materials, and organic electronics.

NSF: NSF supports modeling, simulation, and informatics projects in nanoscale science and engineering, including databases and networking. The Network for Computational Nanotechnology has been re-competed for five years in 2017, and has established three nodes dedicated to nanoelectronics, nanobiotechnology, and nanomanufacturing. Other efforts that are focused on targeted solicitations, Cyberinfrastructure Framework for 21st Century Science and Education (CIF21) and Software Infrastructure for Sustained Innovation (S2I2), have contributed significantly to data infrastructure, software advances, and high-throughput computation.

NSF’s future plans in support of the NNI NSI include investments in nanoscale modeling and simulation, database networking, nanoHUB, and Cyber-Enabled Discovery and Innovation initiatives within its Cyberinfrastructure Framework for 21st Century Science and Engineering—activities such as Software Infrastructure for Sustained Innovation. NSF will also contribute to the foundations of this NSI by means of specific databases for nanoscale materials and processes, transformative thinking about models for linkage

³⁷ cbiit.nci.nih.gov/ncip/ncip-home

³⁸ nciphub.org/groups/nanowg

of properties and behaviors at different scales, extension of computational and statistical techniques to support development and use of the nanotechnology cyber toolbox to accelerate discovery and manufacturing of nanomaterials and nanodevices, advances in fundamental theory and modeling, techniques across ranges of scales (from first principles to coarse-graining and phase-field modeling), and education by integrating the cyber toolbox into the fabric of next-generation science and the training of the next-generation modeling community.

NSF, NIOSH, other NNI agencies, industry, and academia: NSF and NIOSH will continue collaborations that started in 2014 and 2015 with the Nanoinformatics Consortium, which includes Federal partners NCI, NIH, NIST, Pacific Northwest National Laboratory (PNNL), and DOD, and many other university and industry partners.

1d. Nanotechnology for Sensors and Sensors for Nanotechnology: Improving and Protecting Health, Safety, and the Environment

Overview

The goals of the Sensors NSI are to support research on nanomaterial properties and the development of supporting technologies that enable next-generation sensing of biological, chemical, and nanoscale materials. The two thrust areas for the Sensors NSI are to: (1) develop and promote adoption of new technologies that employ nanoscale materials and features to overcome technical barriers associated with conventional sensors; and (2) develop methods and devices to detect and identify engineered nanomaterials across their life cycles in order to assess their potential impact on human health and the environment.

The Sensors NSI continues to focus on building community among agency representatives and with the research and development community in the academic and private sectors. Outreach to the community has included technical presentations at a variety of conferences and events in 2017. NNCO also hosted the Nanosensor Manufacturing: Finding Better Paths to Products workshop in June 2017.³⁹ Conversations at this workshop examined key research elements needed to achieve production-scale manufacturing of nanotechnology-enabled sensors. The workshop also surveyed the ecosystem for taking a nanosensor from the research lab to production and examined important issues related to manufacturing, such as fabrication, testing, and product performance. The report for the workshop is under development. Future plans include an internal assessment of key goals and objectives for the NSI and the development of a public document highlighting the key accomplishments and successful collaborations that were catalyzed by the Sensors NSI.

Agency Progress and Plans

DOD/Air Force: AFRL has established significant efforts to develop nano-bio reporters. These biosensors could be used *in vivo* to help detect and defeat a broad base of pathogens or other harmful chemicals. This new program is targeted to integrate sensing, targeting, payload delivery, and recovery into a single package. These nano-bio reporters will have applications from healthcare and geo-exploration to warfighter monitoring, para-rescue triage, and airbase monitoring. Key to this effort is the Air Force-funded Center of Excellence for Advanced Bioprogrammable Nanomaterials (C-ABN).⁴⁰

DOD/DTRA: The Defense Threat Reduction Agency (DTRA) has explored the use of nanowire/nanoribbon field-effect biosensors that could be used in a variety of nanoscale sensor applications. Recent DTRA-funded academic research has outlined the performance limitations for using these field-effect transistor based

³⁹ www.nano.gov/NanosensorManufacturing

⁴⁰ www.iinano.org/center-of-excellence-for-advanced-bioprogrammable-nanomaterials

systems, and introduced a universal performance metric that will ultimately enable these sensors to reach their full potential and bring them into clinical applications. Another DTRA-funded effort is examining how nanohybrid materials can be used for ultrasensitive radiation detection. Researchers at another university have shown improvements in the amount of light that is emitted in specific nanocrystals when exposed to gamma radiation, demonstrating the potential of such nanocomposite systems in the development of high-performance, low-cost spectroscopic gamma detectors.

DOD/Navy: NRL has demonstrated reconfigurable DNA structures that alter their conformation in response to the addition of biological processes such as enzymes. Dyes attached to the DNA provide a real-time read-out enabling monitoring of the system. Learning how to construct these responsive DNA systems will enable the future construction of "smart" nanomaterials able to sense, respond, and report from inside living systems. The long-term goals are centered on sensor applications, and especially the ability to monitor warfighter health *in vivo* in the field.

NRL has successfully achieved the development of a nanoparticle-based optical probe for imaging brain activity with substantially greater sensitivity than possible with currently available materials or techniques. The nanoscale optical probe visualizes the activity of neurons in the brain with 20- to 40-fold greater sensitivity than current brain imaging probes. The immediate impact of this accomplishment is the availability of value-added brain imaging probes for detecting/diagnosing brain conditions of critical interest to DOD, including traumatic brain injury, posttraumatic stress disorder, concussion, and depression.

NRL plans include creating bio/inorganic voltage-sensitive nanoprobes for the real-time imaging and control of neuronal signals, and using nanoprobes to detect cellular signaling in 3D-printed artificial wounds to better understand and control wound healing. NRL plans to construct "intelligent" molecular-scale machines that can sense, amplify, evaluate, and act on local, *in-situ* bioinformation, and to create and understand artificial enzymatic nanosystems with enhanced performance.

DOD/Army: The Army ERDC has developed a new research program (2017–2019) on development of environmental sensors called Chemical Collection, Refinement and Adsorption Beacon (ChemCrab) that will develop a sensor platform combining passive and active sensing capabilities to enable real-time detection of aqueous contaminants in the field. Current analytical capabilities are limited to field sampling and shipping to analytical labs, which is expensive and time-consuming at fixed Army facilities and impossible for real-time reconnaissance in the field. The program proposes using passive sampling and selective membrane materials to screen out interfering compounds, followed by functionalized nanomaterials (e.g., carbon nanotubes) adsorbing target contaminants to alter electrical circuit properties that can be measured using near-field communication technology from a cell phone. The ultimate intended Army impact and pay-off is a rapid chemical sampling platform at very low cost that could be used for a variety of sensing applications.

DOD/Navy and DOD/DTRA: Researchers at NRL, in conjunction with the DTRA, have shown that enzyme activity and long-term stability can be substantially enhanced by attaching the enzyme to nanoparticles. Working with phosphotriesterase, which is uniquely capable of degrading organophosphate nerve agents, they showed that catalysis could be enhanced four-fold by alleviating the enzyme's rate-limiting step. This approach is geared towards the development of new, more robust catalytic and bioremediation materials for protecting the warfighter in the field.

DOD/Air Force and academia: The Air Force C-ABN has funded efforts in three thrust areas, including: (1) Materials and Methods Development; (2) Functional Substrates; and (3) Advanced Bio Sensing. This effort, planned to run through 2021, will build collaborative, discovery-based research projects aimed at the development of bioprogrammable nanomaterials that will meet both military and civilian needs.

DOE: The DOE Office of Fossil Energy (FE) is supporting projects aimed at the development of nanotechnology-based fiber optic sensors for fossil energy applications. For example, FE-supported researchers have demonstrated that overlayers of silica or another suitable “filter layer” can substantially reduce the reactive evaporation of noble and precious metal nanoparticles typically used in high-temperature sensing, including Au and Ag. Through silica overcoating, reduced mass loss of Au nanoparticles in Au/TiO₂ and Au/SiO₂ functional sensing layers has been demonstrated, even in application-relevant fuel gas streams containing H₂S contamination for exposures of up to one week at 800 °C. This technique extends the expected useful temperature and chemical environment range for these nanoparticle-based gas sensors.

DOE/FE plans the continued support of projects aimed at the development of thin-film oxides and metal oxide nanocomposites for sensing in high-temperature harsh environments. Functional materials fabricated by sol-gel and sputter coating methods will be tested for durability at temperatures above 750 °C, and calculations will be performed of stability of various noble metals and noble metal nanoparticles under relevant fuel gas stream conditions.

NASA, DOE, and industry: NASA has developed several nanomaterials capable of selectively responding to 1 ppm levels of methane. The technology is currently being used by an industry partner in a joint effort to print the sensors for developing low-cost systems for detecting natural gas leaks from gas wells and pipes under an Advanced Research Projects Agency-Energy (ARPA-E) project.

NASA and industry: NASA has developed, in collaboration with industry, an acetone sensor using nanomaterials that can detect down to 1 ppm levels. The device is integrated into a breath analysis unit for healthcare diagnostics.

NIH: The NIH investment in sensors has not changed significantly in 2016–2017, due to the balance between ongoing and incoming awards. Sensor-related R&D is supported throughout the various NIH institutes and thus covers several disease areas (cancer, dental, cardiac, infections, etc.). Researchers have targeted the development of nanotechnology-enabled sensors in the form of *in vitro* devices and *in vivo* indicator materials that can be used for disease detection and diagnosis, including molecular profiling of disease sites to inform treatment choice and course. These sensors can also be used for basic studies of the biological processes and mechanisms underlying disease progression or therapeutic activity as illustrated below:

- NIH/NCI has supported university research on a magneto-nanosensor, which led to the development of an improved assay for interactions between the immune checkpoint receptor PD-1 and its ligands PD-L1, PD-L2, and B7-1. The PD-1 receptor is crucial to an important class of cancer immunotherapy, but its receptor-ligand interactions have not yet been fully elucidated.⁴¹
- NIH/National Institute of Dental and Craniofacial Research (NIDCR) reported significant advances in 2016–2017 due to a new RFA entitled “Biosensors in the Oral Cavity.” This program supports the development of biosensors aimed to assess and monitor health and disease states in the oral cavity and in the whole body. It also includes support for the development/adaptation of new and existing biosensors for noninvasive, dynamic, real-time monitoring of physiological processes in the human body using the oral cavity as the sensing site. Meritorious applications received in response to this RFA were awarded in 2017 for 2–5-year durations. The research proposals take advantage of recent progress in wireless technologies, dissolvable nanotechnology-based electronics, microfabrication, and nanofabrication, as well as improved sensing and drug delivery. These biosensors cover a broad range of areas in nanotechnology and nanomaterials to address mechanical, chemical, and microbial challenges imposed by the oral environment. Development of

⁴¹ www.ncbi.nlm.nih.gov/pmc/articles/PMC4961847/ (doi: 10.1038/ncomms12220)

these biosensors will include design verification and validation activities, as well as preclinical safety testing to facilitate the translation of the oral biosensors into clinical practice.

NIH will continue to support research on *in vitro* devices and materials for *in vivo* imaging and disease detection that address current needs. NIH is also planning a workshop devoted specifically to cancer applications for identifying opportunities in wearable sensors. The workshop, organized by NIH/NCI, is intended to bring together several NIH/NCI divisions, private sector developers, NIH-funded extramural investigators, and several Federal agencies—including DOD, DOE, NASA, and DHS—to identify common areas of scientific interest that may lead to further collaborations. NIH also plans to identify points of shared interest in wearable sensors (e.g., measures of disease/therapeutic fatigue) that could lead to co-funding of new initiatives or program announcements.

NIST: NIST is developing measurements toward the goals of this NSI. In 2016, NIST demonstrated measurement capabilities of graphene-modified nanoantenna structures for detection of gas-phase species of relevance to medical breath analysis. NIST studied the performance of polyaniline-gold interfaces for coupled electrochemical and surface-enhanced Raman biosensing. NIST is developing nanophotonic sensors on a chip that have maximum sensitivity for small temperature and humidity changes, and chip-scale optomechanical force sensors to improve optical power calibration and small mass determination. NIST research efforts are providing foundational measurements to allow sensor designers to determine performance-limiting phenomena and improve the reliability of monolithic three-dimensional (3D) integrated “More-than-Moore” devices in which sensors are co-integrated into 3D devices.

Future plans include design and fabrication of nanomaterials and platforms for chemical and biochemical sensors that use optical, spectroscopic, and electrochemical measurement methods for environmental, biomedical, and security applications. New nanoscale hole and pillar configurations will be developed for photonic sensing of gases and solution-phase biomolecules. Electrochemical microplatform prototypes will be further developed into array formats for efficient, stability-based studies of DNA and protein modification. NIST plans to develop methods for fabricating and measuring small-footprint, wearable, and flexible sensors based on semiconductor nanowires and 2D semiconductor layers that detect environmental pollutants and explosives.

NIST and industry: NIST will work with a small company to develop silver nanoparticle-containing, inkjet-printed sensor substrates for ultrasensitive detection of illicit narcotics and explosives. This work includes the establishment of optimal protocols for sensor production as well as nanometer-scale surface chemical characterization of the as-prepared sensor surfaces.

NIST will collaborate with a small company to scale up a NIST-developed, top-down process of dry and wet etching to fabricate gallium nitride (GaN) nanowire arrays for low-power, high-selectivity chemical and biochemical sensors.

NIST and NIH: NIST is developing and testing nanoscale sensor field-effect transistors made with two-dimensional materials for identifying and measuring biomolecule concentrations.

NSF: Directorate for Biological Sciences (BIO), ENG, and MPS (Division of Materials Research and Division of Chemistry) programs support fundamental research in developing nanoscience, including nanobiotechnology, for sensor applications. NSF is funding research on the creation of new nanobiosensors and novel uses of nanosensors for nanotechnology-related EHS research.

Through its Nano-Biosensing, Biophotonics, and other programs, NSF is supporting development of novel sensitive, discriminative, low-cost, and easy-to-operate biosensing systems; innovative ideas in the development of novel biorecognition strategies; multifunctional nanomaterials and interfaces with

predefined physical, chemical, or biological characteristics for biosensing applications; and fundamental studies of biomacromolecule confinement and orientation at the micro- and nanoscale interfaces for biosensing applications. NSF also supports the development of sensors to detect engineered nanoparticles in a variety of environmental matrices.

NSF, NIOSH, NIH, FDA, NIST, DOD, NASA, USDA/NIFA, and EPA: NIOSH and NSF participate with other agencies in an initiative to develop nanotechnology-enabled sensors and sensors for nanomaterials for EHS research applications. The objective of the initiative is to identify opportunities for the development and commercialization of sensors that will enable more specific tracking of engineered nanomaterials throughout their life cycles. This detection and measurement capability will support the efforts of private-sector companies to demonstrate responsible development. In 2018, NSF and NIOSH plan to continue their efforts in detection of airborne nanoparticles into specific applications in the areas of detection of nanomaterials in biologic systems to evaluate and predict biological behavior and translocation between organ systems.

USDA/NIFA: NIFA is utilizing multiple funding authorities to support development of nano-biosensors for more sensitive, specific, and robust detection of pathogens, toxins, and contaminants in food to ensure food safety and biosecurity. The Nanotechnology for Agricultural and Food Systems program in the AFRI Foundation area supports research projects in nanoscale sensing mechanisms and smart sensors for reliable and cost-effective early detection of pathogens, allergens, insects, diseases, chemicals, and contaminants in food, plant, and animal production systems, and in water, soil, and the agricultural production environment. The program also supports research in monitoring physiological biomarkers for optimal crop or animal productivity and health. The program seeks to develop cost-effective, distributed sensing networks for intelligent and precise application of agricultural inputs (e.g., fertilizer, water, and agrochemicals) using the Internet of Agricultural Things (i.e., cyber-physical systems). NIFA has also been providing leadership to a multistate research committee (NC1194: Nanotechnology and Biosensors),⁴² funded by the Hatch Multistate Formula Program, which has been effective in advancing nanoscale science and engineering for nanosensor development and commercialization.

Among the university grants funded in 2016, one project is developing a rapid, sensitive test to detect *Salmonella typhimurium* to enhance food supply safety. Previously funded grants include development of a low-cost and disposable biosensor that is made out of nanoparticle graphene and can detect pesticides in soil. The biosensor also has the potential for use in the biomedical, environmental, and food safety fields. NC1194 presented a special technical session at a 2017 international innovation conference to highlight a number of impressive accomplishments of its members in discovering novel sensing mechanisms, developing sensor prototypes, and exploring a global pathogen detection network to ensure food safety.

1e. Water Sustainability through Nanotechnology: Nanoscale Solutions for a Global-Scale Challenge

Overview

The goal of the Water NSI is to take advantage of the unique properties of engineered nanomaterials to generate significant breakthroughs in addressing our Nation's water challenges. The three thrust areas are

⁴² www.nimss.org/projects/17756

to: (1) increase water availability using nanotechnology; (2) improve the efficiency of water delivery and use with nanotechnology; and (3) enable next-generation water monitoring systems with nanotechnology.

In support of this NSI, NNCO organized a series of webinars to introduce the initiative and to engage with stakeholders on the technical thrusts of the activity.⁴³ “Water Sustainability through Nanotechnology: A Federal Perspective” was the first webinar in the series, and it included presentations from four Federal representatives on their agencies’ programs and priorities. The next two webinars, “Increasing Water Availability” and “Enabling Next-Generation Water Monitoring Systems,” featured technical presentations from Federal and non-Federal experts. The group is working with the stakeholder community to develop a series of case studies that outline the current capabilities and shortfalls of the current technologies used in the application areas described in the white paper.⁴⁴ Future plans include additional webinars and continued stakeholder engagement through appropriate technical meetings and conferences.

Agency Progress and Plans

DOD/Army: ARL has demonstrated the use of nanofiber liquid filtration membranes made from recycled polyethylene terephthalate (rPET) plastic bottles. PET nanofiber membranes were formed via solution electrospinning with fiber diameters as low as ca. 100 nm. Good filtration efficiency was shown, and to reduce biofouling, the mats were functionalized with quaternary ammonium and biguanide biocides. The biguanide-functionalized mats were effective against both gram negative and gram positive bacteria. The mats could be used in microfiltration applications such as a prefilter in a wastewater treatment system.

DOD/Army, NSF, industry, and academia: The Army ERDC is a board member and innovation partner with the NSF-funded Nanotechnology-Enabled Water Treatment Systems (NEWT) Engineering Research Center. ERDC is working with university partners and multiple industry members to develop nanotechnology water treatment solutions within the water-energy nexus.

NASA: There is a small NASA effort to look at whether boron nitride nanotubes can be used as ultrafast membranes for filtration.

NIST: NIST efforts to support this NSI focus on the detection, separation, and quantification of specific nanoparticles that are relevant to consumer and industry stakeholders, and on developing advanced broad-spectrum organic, inorganic, and biological measurement capabilities for assessing water quality. In 2016, NIST demonstrated surface complexation models to predict the reactivity of nanoparticles (e.g., graphene oxide) with heavy metal contaminants in groundwater. A workshop was held at a March 2016 professional society meeting to demonstrate these new tools to environmental chemists and identify data sets needed by the community to implement this approach in environmental remediation.

NIST models were successfully transferred to the environmental remediation community in 2016, and NIST intends to acquire chemical reactivity data for graphene and iron oxide nanoparticles to support the implementation and use of these tools.

NSF: Programs in BIO, ENG, and MPS (Division of Materials Research and Division of Chemistry) support basic research in advancing nanoscience to enable more efficient water filtration applications. One targeted area of investment for the ENG (particularly the Chemical, Bioengineering, Environmental, and Transport Systems Division); BIO; MPS; and Social, Behavioral & Economic Sciences (SBE) directorates is in the initiative: Innovations at the Nexus of Food, Energy, and Water Systems. The NSF NEWT NERC was launched in August 2015. The NEWT ERC aims to develop high-performance and easy-to-deploy water treatment systems that

⁴³ www.nano.gov/publicwebinars

⁴⁴ www.nano.gov/sites/default/files/pub_resource/water-nanotechnology-signature-initiative-whitepaper-final.pdf

will: (1) broaden access to clean drinking water from a variety of unconventional sources (briny well water, seawater, wastewater) for use on scales ranging from a household, to a neighborhood, to a remote town; and (2) enable industrial wastewater reuse at remote locations such as oil and gas fields. NSF plans to continue support for the NEWT ERC through 2020.

USDA/FS: In 2017, FS has been investigating if there is a role for nanotechnology on water issues in forests and watersheds.

USDA/NIFA: The Water for Food Production Systems program in the AFRI Challenge Area invited applications in 2017 to employ systems approaches that lead to solutions for water challenges in U.S. agricultural and food production. These solutions must be feasible and simultaneously take into consideration a broad spectrum of kinds of agricultural producers, competing industries, consumers, communities, and other relevant stakeholders. The impacts will be measured as appropriate changes that are needed by water users, consumers, and policy makers to improve resolution in conflicts over water supplies by reducing water use or increasing water use efficiency for the next several decades or more. The top priorities include use of transformative discoveries such as breeding, genomics, nanotechnology, sensors, modeling, microbiome manipulation, and data-driven decision tools to develop drought- and flood-tolerant cultivars, intensify food production, improve crop and livestock health, or reduce overall water use across food production systems.

With an AFRI grant, university researchers used engineered water nanostructures to inactivate pathogenic microorganisms on the surface of fresh produce. The potential of this new intervention technology for ensuring food safety has caught the attention of the global food industry for commercialization. NIFA has also supported research projects in water treatment and water quality monitoring. A project conducted by researchers at another university created a sponge that uses nanotechnology to quickly absorb mercury, as well as bacterial and fungal microbes, from polluted water. The sponge can be used on tap water, industrial wastewater, and in lakes. It converts contaminants into nontoxic waste that can be disposed in a landfill. Other academic researchers have developed a novel enzymatic bioelectrocatalytic device that is a highly sensitive and selective self-powered biosensor for detecting a variety of toxicants such as arsenic in crop production field and irrigation water.

1f. Nanotechnology-Inspired Grand Challenge for Future Computing

Overview

This grand challenge brings together scientists and engineers from many disciplines to look beyond the von Neumann computing architecture as implemented with transistor-based processors, and chart a new path that will continue the rapid pace of innovation beyond the next decade to enable low-power cognitive computing. Specifically, the challenge is to “create a new type of computer that can proactively interpret and learn from data, solve unfamiliar problems using what it has learned, and operate with the energy efficiency of the human brain.” It is a coordinated and collaborative effort across multiple levels of government, industry, academia, and nonprofit organizations. R&D focus areas for Federal R&D investments in support of this goal include: (1) materials; (2) devices and interconnects; (3) computing architectures; (4) brain-inspired approaches; (5) fabrication/manufacturing; (6) software, modeling, and simulation; and (7) applications.

In support of this grand challenge, NNCO organized a series of meetings and conference calls in 2016 to coordinate the development of a white paper⁴⁵ outlining the technical priorities shared by multiple Federal agencies, the challenges and opportunities associated with these priorities, and a guiding vision for the

⁴⁵ www.nano.gov/FutureComputingWhitePaper

research and development needed to achieve key near-, mid-, and long-term technical goals. Subsequent to the publication of the white paper, NNCO worked with the NITRD National Coordination Office to organize a meeting of representatives from the participating agencies to discuss and exchange ideas about relevant current and planned activities within their agencies and to identify areas for collaboration. Future plans will include technical Federal-only meetings to inform cooperation among the agencies as well as additional outreach to the broader computing and nanotechnology research communities and industry. NNCO will also continue to work with the participating agencies to help coordinate with other related national priorities and interagency initiatives, including NITRD, semiconductor manufacturing, strategic computing, research on the brain, and the NNI's Nanoelectronics NSI.

Agency Progress and Plans

NIST: NIST is developing measurement science to support future computing technologies in the “beyond complementary metal-oxide semiconductor (CMOS)” arena with a focus on the in-operando characterization of 2D heterostructure devices, and metrology for high-performance superconducting computing. NIST is also creating characterization techniques and measurement science for alternative computing paradigms including neuromorphic and quantum computing. NIST has developed high-speed, sub-micrometer, superconducting Josephson junctions and stacked Josephson junctions that will be used for future energy-efficient computer logic. NIST is advancing quantum information and communication technologies through activities such as fabrication of nanoscale superconducting devices and development of epitaxial semiconductor quantum dots.

Future research plans include demonstrating an integrated photonic circuit with both few-photon source and detector, which will serve as a foundational device for a photonic neuron for use in a prototype neuromorphic system.

NIST and international collaborators: NIST developed a theory of neuromorphic computing with nanomagnetic oscillators in partnership with researchers from France.

NIST and academia: In collaboration with university partners, NIST has developed measurements elucidating resistive switching mechanisms in memristor-based artificial synapses for neuromorphic computing applications. Future plans include developing neuromorphic circuits based on the integration of memristive artificial synapses with CMOS neurons to provide a test bed for new nanoscale neuromorphic-type measurements.

NIST research in partnership with a university is demonstrating early examples of perfect quantum state converters (quantum transducers) by using the quantum properties of microresonators, including the first cooling to the quantum ground state of a macroscopic object (microresonator consisting of 10^{19} atoms), the first electrical-optical-electrical signal conversion perfectly conserving quantum states, and the world's highest efficiency in quantum state conversion between electrical and optical signals.

NIST, IARPA, and industry: NIST is working with IARPA and industry partners in its Cryogenic Computing Complexity (C3) program in the development of spin-based nanoscale cryogenic memory and logic for energy-efficient exascale computing.

NIST, DARPA, industry, and academia: NIST and partners are developing nanoscale, high-frequency oscillators for rapid, low-energy processing of images in computer hardware instead of software.

NSF: The main NSF support for this GC is in three directions: highly energy efficient semiconductor devices aiming at “beyond Moore's Law,” neuromorphic engineering, and brain-like computing. The NSF Science and Technology Center on Integrated Quantum Materials (which involves several universities) is currently

working on graphene, topological insulators, and nitrogen vacancy centers in diamond, as well as their integration. Developing materials, techniques, and simulation methods for controlled evolution of quantum mechanical states of multiple to many qubit systems is one of the emphasized topics for the upcoming competition of the Materials Research Science and Engineering Centers.⁴⁶

Three ENG solicitations in support of this grand challenge in 2016 and 2017 are: Two-Dimensional Atomic-layer Research and Engineering (2-DARE);⁴⁷ Advancing Communication Quantum Information Research in Engineering (ACQUIRE); and New Light, EM (Electronic) and Acoustic Wave Propagation (NewLAW): Breaking Reciprocity and Time-Reversal Symmetry.

NSF and industry: NSF, in collaboration with a semiconductor industry technology research consortium, has supported two competitions (in 2016 and 2017) under the E2CDA program.⁴⁸ Nine four-year awards were made by CISE, ENG, and the industry consortium in 2016. Future plans for this collaboration include solicitations in 2018 that address grand challenges in biological computing and semiconductor synthetic biology for information processing and storage,⁴⁹ and will include continued funding under the E2CDA program.

NSF, DARPA, and industry: NSF sponsored the October 2016 workshop: “Intelligent Cognitive Assistants” with semiconductor industry groups. The report is available on the NSF website.⁵⁰ The goal is to create systems that are highly useful to humans, specifically on the topics of harnessing machine intelligence to augment human cognition and mimic human problem-solving capabilities—e.g., research that drives towards intelligent cognitive assistants. NSF has been participating in a working group together with industry consortia and 11 companies to explore opportunities for co-funding research on these topics beginning in 2018. DARPA has also begun to engage with NSF in this area, with the goal of determining potential areas for cooperation. Research will focus on exploring scenarios for developing the novel architectures, concepts, and algorithms that will be required for “assistants” to perceive, compute, and interact in an energy-efficient manner, and in this way to provide actionable information and informed advice to their human users. Further collaboration is planned with industry groups developing hardware (with a focus on a “beyond Moore” system architecture and corresponding devices) and software (with a focus on artificial intelligence).

PCA 2. Foundational Research

Overview

The foundational research under PCA 2 includes: (1) discovery and development of fundamental knowledge pertaining to new phenomena in the physical, biological, and engineering sciences that occur at the nanoscale; (2) elucidation of scientific and engineering principles related to nanoscale structures, processes, and mechanisms; (3) research aimed at discovery and synthesis of novel nanoscale and nanostructured materials and at a comprehensive understanding of the properties of nanomaterials ranging across length

⁴⁶ www.nsf.gov/pubs/2016/nsf16545/nsf16545.htm

⁴⁷ www.nsf.gov/pubs/2015/nsf15502/nsf15502.htm

⁴⁸ www.nsf.gov/publications/pub_summ.jsp?ods_key=nsf17531

⁴⁹ www.nsf.gov/pubs/2017/nsf17557/nsf17557.htm

⁵⁰ www.nsf.gov/crssprgm/nano/

scales, and including interface interactions; and (4) research directed at identifying and quantifying the broad implications of nanotechnology for society, including social, economic, ethical, and legal implications.

Agency Progress and Plans

DOD/Army: ARL has recently made significant progress in the science (and related processing) of stable nanocrystalline materials. ARL developed a divergent, bulk nanocrystalline copper–tantalum alloy that is able to achieve and retain high strength and creep resistance—a combination unexpected based on conventional wisdom. These published results⁵¹ will lead to advances in designing nanocrystalline alloys with many simultaneously enhanced high-temperature properties, similar to those exhibited by creep-resistant single crystals, but with the additional benefit of much higher strengths. Critical to the success of this work was the aim from the outset to design thermodynamically stable, nanoscale microstructures. It is this inherent stability of the nanoscale grain structure that ultimately results in these excellent properties. ARL also recently produced bulk samples of iron-based nanocrystalline alloys.

ARL plans to extend its work in stable nanocrystalline materials to new alloy systems for a variety of applications. Some alloys under consideration are directed towards high-strength applications, some toward high temperature resistance, and others towards unique portable energy applications. A key component is the establishment of world-class powder processing and consolidation facilities at ARL, targeted to a broad range of nanometallic systems.

ERDC has completed basic research studies that developed wet cell nanoindentation methods to determine mechanical properties of materials at the nanoscale in realistic states of hydration. This work is particularly critical to the successful investigation of properties of hydrous materials such as geomaterials, biomaterials, polymers, and cement-based materials. The project focused on measurements of a variety of Army-relevant hydrous materials to determine the impact of hydration state on measured properties, and these results are being used to modify inputs for nanoscale and microscale material modeling and simulation activities.

ERDC has initiated a new basic research project to study how flexible fabrics and coatings can incorporate electromagnetically active nanoparticles whose mechanical properties can be controlled through directed energy. These materials, while still at the basic research stage, have potential uses for adaptable/controllable materials for force protection and projection systems.

DOD/Navy: NRL has developed techniques to dope atomically thin crystals and to modify surface energies of atomically thin crystals to induce material phase changes. These accomplishments could impact the DOD if successfully implemented in advanced electronic devices, through reducing power consumption and increasing device performance.

NRL has also developed a fundamental understanding of surface phonon polaritons, which provide the means to confine light to nanoscale dimensions using polar crystals such as silicon carbide. NRL demonstrated that highly anisotropic (so-called “hyperbolic”) materials do not follow Snell's law; instead, the confined light will reflect at angles dictated by the anisotropic material properties. These results provide the basis for compact infrared optics that are desired for thermal imaging, sources, chemical and biological threat agent detection, and free-space communications.

DOD/Army, industry, and academia: The Institute for Soldier Nanotechnologies (ISN), an Army-sponsored University Affiliated Research Center, is structured as an alliance between academia, industry, and the Army. The Army, through ISN, is scaling up nanograin aluminum alloys produced through electroforming processes with a commercial partner. The lightweight alloys are also relatively thermodynamically stable, and have

⁵¹ www.nature.com/nature/journal/v537/n7620/abs/nature19313.html (doi:10.1038/nature19313)

excellent mechanical properties. Other recent accomplishments from the ISN include the detailed understanding of how to develop complex structures out of shape memory alloys to obtain superior superelasticity, advances in understanding effects of nanoparticle shapes and materials of construction on light extinction to achieve enhanced smoke obscuration, and new understanding of the dynamics of supersonic impact of microparticles on elastomers.

A unique ISN multimaterial optoelectronic fiber-devices technology became the basis for a university-led national partnership that resulted in the recently announced Advanced Functional Fibers of America, a new DOD-funded Manufacturing USA institute. Army, academic, and industry partners in ISN share their expertise on how to convert promising outcomes of fundamental research into practical products that work in harmony with other soldier technologies.

DOD/Army, academia, and international partners: ERDC has initiated new work through its International Research Offices with UK universities focused on developing advanced nanocomposite materials using ice templating methods to produce ceramic scaffolds, combined with chemical vapor deposition of carbon nanomaterials to produce toughened ceramic nanocomposites. University researchers are partnering with ERDC to perform characterization and mechanical measurements of developed materials. ERDC is also working with a U.S. university on research focused on advanced nanoscale simulation tools and materials development for metallic, cement-based, and polymeric materials. The goals of these studies vary, but largely focus in the long term on force protection and force projection systems.

DOD/Navy, DOD/Army, NSF, DOE, NIH, academia, and international partners: ONR has sponsored work at a university laboratory to use DNA origami to install fluorescent molecules into microscopic light sources using a novel technique. This technique allows for the precise positioning of DNA origami (within a margin of error of just 20 nanometers) on almost any surface used in the manufacture of computer chips, establishing that there is no longer a hurdle of large-scale integration of molecular devices on chips. While the initial work was focused on electronics, the findings facilitate the development of hybrid nanophotonic devices, hybrid nanoelectronic devices, and any heterogeneous fabrication wherein molecular or nanoparticulate components are integrated with microstructures. Other sponsors of work at this laboratory include the Army Research Office, NSF, DOE, NIH, and other domestic and international life sciences research partnerships.

DOD/Air Force, academia, and industry: The Air Force will continue to lead and work directly with the Nano-Bio Manufacturing Consortium.⁵² The mission of the consortium is to bring together leading scientists, engineers, and business development professionals from industry and universities in order to work collaboratively in a consortium, and to mature an integrated suite of nano-bio manufacturing technologies to transition to industrial manufacturing.

DOD/multiple services, industry, academia, and international partners: The Department of Defense has initiated a new program entitled “Synthetic Biology for Military Environments” as part of its Applied Research for the Advancement of S&T Priorities program. This program represents a joint-service DOD effort in synthetic biology that applies basic advances in synthetic biology and knowledge of how biological systems function to establish laboratory tools and systems tailored to meet unique defense needs. This effort will integrate existing and grow new foundational capabilities, leverage state-of-the-art academic and industrial innovations, and develop additional unique tools necessary to engineer microbes and components for DOD-unique materials, sensors, and warfighter health and performance monitoring. The team will use synthetic

⁵² www.nbmc.org/

biology approaches to create classes of nano/biomaterials. Collaborators include academic, industry, and international partners.

DOD/Navy and academia: ONR has initiated a BRC program on electrically assisted materials manufacturing of lightweight alloys (e.g., aluminum and titanium alloys) and ultrahigh melting point ceramics with increased hardness and low density (e.g., B₄C). This BRC supports two university-based multidisciplinary teams. This significant basic research effort will provide a comprehensive scientific basis along with predictive modelling tools of nanoscale phenomena defining macroscopic material properties.

DOE: The DOE Office of Basic Energy Sciences (BES) supports fundamental research in materials science, chemical science, geoscience, and bioscience, with the goal of understanding, predicting, and ultimately controlling matter and energy at the level of electrons, atoms, and molecules. This broad and diverse research provides the foundation for future new energy technologies and supports the DOE mission in energy, environment, and national security. For example, research on electron and atom displacement is increasing our understanding of both unusual and common mechanisms of energy transformation, and advanced instrumentation and innovative methodology are critical to achieving these insights, as demonstrated by the following projects:

- To generate electricity in organic solar cells, negative and positive charges must be separated over relatively large distances to avoid recombination. Using new terahertz microwave detection methods, researchers have found that the charges remained separated in a nanostructure only when the electron is delocalized over an ordered domain. These results suggest that ordered molecular nano-domains play an essential role in efficient organic solar cells.
- Scientists have confirmed experimentally and with high accuracy the long-held hypothesis that the structure of platinum catalyst nanoparticles, supported on alumina, changes during the catalytic conversion of ethylene to ethane. They designed a miniature reactor to collect nanoscale structural images simultaneously with synchrotron x-ray absorption spectra. This approach provides precise atomic-scale dynamic information to refine models and improve design of supported metal catalysts.

BES will continue broad support for fundamental nanoscience research in areas such as the following:

- Nanostructured materials for electron and ion transport in next-generation batteries and fuel cells.
- Nanoscale quantum materials for future energy technologies.
- Fundamental understanding of nanoscale defects that will enable predictive design of materials with superior mechanical properties and radiation resistance.
- Elucidation of the elementary steps of light absorption, charge separation, and charge transport in nanostructured materials and chemical systems for improved solar energy conversion.
- Atomically precise materials for molecular electrocatalysts that efficiently convert electrical energy into chemical bonds in fuels.
- Enhanced computational capabilities for the simulation of chemical and geochemical processes at the molecular- and nanoscales.
- Structural and dynamic studies of atoms, molecules, and predictive understanding at the nanoscale of the basic chemical and physical principles involved in chemical separations systems.

The DOE Fuel Cell Technologies Office (FCTO) in the Office of Energy Efficiency and Renewable Energy (EERE) has advanced the fundamental understanding of platinum group metal (PGM)-free catalysts at the atomic scale through the ElectroCat Consortium.⁵³

⁵³ www.electrocat.org/

Appendix A. NNI Research by Program Component Area

The DOE Vehicle Technologies Office (VTO) in EERE will support R&D on alloy anode materials for advanced batteries based on silicon nanowires, nanoflakes, nanorods, and nanoscale silicon oxide materials to reduce particle cracking during cycling and enhance power capability. VTO will support R&D on carbon nanotubes to improve cathode rate (power) capability and to enable higher voltage battery operation.

DOE's Advanced Manufacturing Office (AMO) in EERE will support kilogram-scale R&D on carbon covetic conversion processes at the National Energy Technology Laboratory and fundamental studies of structure and process physics at ANL for advanced conductors.

DOE and NIST: AMO has supported development of atomic-resolution images of carbon covetic nanomaterials through ANL, a university, and NIST, revealing the atomic-scale processes and behavior in advanced conductor applications.

DOE, DOD, NASA, and industry: AMO, ANL, and the National Energy Technology Laboratory plan to work with ARL, NASA Glenn Research Center, several companies, and a university on carbon covetic nanomaterials.

DOE and industry: DOE plans continuation of the ElectroCat Consortium involving FCTO, Los Alamos National Laboratory (LANL), ANL, Oak Ridge National Laboratory (ORNL), and the National Renewable Energy Laboratory, with funding for nanotechnology-centric catalyst projects at universities, PNNL, and two companies.

DOE will support the Hydrogen Materials Advanced Research Consortium,⁵⁴ involving FCTO, Sandia National Laboratory (SNL), Lawrence Livermore National Laboratory, Lawrence Berkeley National Laboratory (LBNL), and industry collaborators to advance nanomaterials for hydrogen storage.

NASA: There is funding from NASA's Internal Research and Development (IRAD) program to look into various ways of inducing bonding between carbon nanotube bundles in order to enhance load transfer between tubes. This work involves both modeling and experimental processing and testing.

NASA and Air Force: NASA currently funds grants under its Early Stage Innovation (ESI) program to look at mesoscale modeling of structural carbon nanotubes. This effort was co-funded by AFOSR. The grant completed its first year in March 2017.

NIH: NIH is reporting \$88 million in Foundational Research investments for 2017, the second-largest area within NIH's NNI investments. This investment reflects the discovery and understanding of scientific principles in medical research supported throughout the NIH institutes. NIH has provided funds for nanotechnology-related proposals covering all the major diseases (e.g., cardiac, cancer, diabetes, kidney, etc.). For example, the NIH/NCI Alliance for Nanotechnology in Cancer supported the Innovative Research in Cancer Nanotechnology (IRC�) U01 program⁵⁵ through 2017. The IRC� program supported multidisciplinary and transformative research in cancer biology and/or oncology, with each project expected to emphasize fundamental understanding of nanomaterial interactions with biological systems and/or mechanisms of their delivery. See below for a series of accomplishments that resulted in new insight or greater understanding at the nanoscale.

⁵⁴ energy.gov/eere/fuelcells/hymarc-hydrogen-materials-advanced-research-consortium

⁵⁵ grants.nih.gov/grants/guide/pa-files/PAR-14-285.html

Recent advances from NIH/National Heart, Lung, and Blood Institute (NHLBI)-supported research include the following:

- *Five-gene RNA interference (RNAi) reduce inflammatory response in post-MI mice.* Myocardial infarction (MI) leads to a systemic surge of vascular inflammation resulting in secondary ischemic complications and high mortality. As a potential therapy, researchers developed a nanoparticle-based RNA interference (RNAi) approach⁵⁶ that silences five cell adhesion molecules involved in recruiting inflammatory cells to the infarction site. This five-gene RNAi reduced the recruitment of inflammatory cells and breakdown of extracellular matrix after MI in mice.
- *Nanoparticle thrombin inhibitor treats atherosclerosis in mice.* Thrombin contributes to atherosclerosis by promoting inflammatory and coagulant pathways. To counteract these effects, researchers developed nanoparticles containing a powerful thrombin inhibitor.⁵⁷ Treatment of atherosclerotic mice with the nanoparticles for one month resulted in lower expression of pro-inflammatory and pro-coagulant markers, lower pro-coagulant activity, restoration of vascular endothelial integrity, and slower plaque progression.

Recent advances from NIH/NCI-supported research include a project in which scientists at a university medical school developed gold nanoparticles that mimic mutant Salmonella strains to limit membrane protein P-glycoprotein (P-gp) activity. P-gp, an ATP-binding cassette (ABC) transporter, is used by some cancer cells to expel chemotherapy agents. Researchers found that the nanoparticle could reduce P-gp levels in a human colon cancer cell line and plan to move forward with preclinical testing.

NIH plans to support R&D in this area through currently active, prearranged re-issuances, and new FOAs where nanotechnology is an integral component. Areas of ongoing interests include pediatric formulations and drug delivery, immunotherapy, and vaccine research, to name a few, including the Pediatric Formulations and Pediatric Drug Delivery Systems FOAs (PAR-17-191/192/193) at NIH's National Institute of Child Health and Human Development. In addition, NIH/National Institute of Allergy and Infectious Diseases held a second workshop on "Nanotechnology for HIV, RNA, Infectious Diseases, and Vaccine Delivery" in 2017.

NIST: NIST has made significant progress toward foundational measurements for a range of nanoscale systems and applications:

- A number of accomplishments in the area of 2D materials include the discovery of whispering gallery modes and Berry phase anomalies in circular graphene resonators, furthering the understanding of electronic properties of graphene using scanning tunneling microscopy, and foundational research exploiting the coupling of photons to phonons and electrons through nanoscale materials and devices.
- NIST has developed a number of new tools for improved microscopy and spectroscopy measurements of nanoscale materials of interest to areas such as high-performance computing, solid-state lighting, and compact power sources. These tools include environmental sample cells with atomically thin membranes for high-throughput measurements that enable the study of catalytic reactions in aqueous environments, and gallium nitride nanowire LEDs for non-destructive scanning probe microscopy that enables quantitative probing of optical and electrical properties.
- NIST has developed foundational measurements of nanoscale biological processes such as a unique technology to rapidly produce and characterize fluorescent proteins optimized to sense

⁵⁶ www.ncbi.nlm.nih.gov/pubmed/27280687

⁵⁷ www.ncbi.nlm.nih.gov/pubmed/26769047

chemical and biological processes within living cells, without disturbing or destroying those cells. NIST also developed the world's most stable atomic force microscope (AFM) to measure and research for the first time the complex folding and unfolding of individual biomolecules.

- NIST has demonstrated broadly applicable, quantitative, traceable, nanoscale measurement methods for applications of AFM in forensics on four types of evidence: trace evidence, questioned documents, impression and pattern evidence, and explosive materials. Overall, it was found that AFM addressed needs in forensic science as defined by several Federal agencies, in particular an improved ability to expand the information extracted from evidence and to quantify its evidentiary value.

In 2018, NIST will make available nanomechanical property reference materials (RMs) and standard reference materials (SRMs)—RM 8191 for measuring strain and SRM 3461 for calibrating cantilever stiffness in atomic force microscopes—that will enable accurate determinations of mechanical performance and reliability of nanodevices. NIST intends to extend nanoscale microscopy methods by developing a combined atomic force and scanning tunneling microscopy instrument that operates in an ultrahigh-vacuum, millikelvin environment to enable atomic-scale measurements for future electronic devices, and to demonstrate wafer-scale fabrication of scanning probe tips instrumented with GaN nanowire LEDs. In 2018, NIST will look to quantify the reproducibility of AFM nanoscale measurements to provide a measure of the probability that an AFM-measured quantity represents a particular material. Such quantification requires more detailed statistical studies on specific forms of evidence, and will be performed in concert with several Federal agencies and local forensics consultants. The first such in-depth study will focus on the physical properties of surface-modified cloth fibers.

NIST, DOE, and industry: In 2016, NIST and DOE worked with SBIR-supported companies to complete the infrastructure for two beamlines that will deliver photons to measurement instruments at the new DOE synchrotron facility, National Synchrotron Light Source II (NSLS-II),⁵⁸ which is designed specifically for nanoscale measurements. NIST has completed development of two novel synchrotron imaging instruments to be coupled to these beamlines: a large-area imaging near-edge x-ray absorption fine structure (NEXAFS) microscope that provides high-efficiency measurements of thousands of compositional samples in parallel, and an x-ray photoelectron spectroscopy (XPS) microscope that provides full 3D mappings of nanomaterials and nanodevices, combining nanometer-scale spatial resolution with chemical and electronic state specificity.

NIST will continue to work DOE and industry to couple the two novel synchrotron imaging instruments to the NSLS-II beamlines and commission these instruments. The resulting suite of synchrotron instruments will provide the capability to measure all elements in the Periodic Table. In addition, NIST is designing and developing an x-ray scattering capability on the NEXAFS instrument for simultaneous determination of average size, shape, and local molecular structure of carbon-based nanomaterials.

NIST and ORNL: In collaboration with ORNL, NIST developed a microwave-based method to image reactive and biological samples at nanoscale spatial resolution under realistic operating conditions.

NSF: Nanotechnology research is prevalent throughout core programs in the BIO, ENG, and MPS directorates at NSF. Research into quantum materials is essential for preparing future scientists to implement the discoveries of the next quantum revolution into technologies that will benefit the average consumer. There will be strong connections to industry, Federal agencies, and international partners. The Quantum Leap: Leading the Next Quantum Revolution topic in the NSF Big Ideas report⁵⁹ is NSF's approach to identifying

⁵⁸ www.bnl.gov/ps/nsls2/about-NSLS-II.php

⁵⁹ www.nsf.gov/about/congress/reports/nsf_big_ideas.pdf

and supporting research in this arena. It will address fundamental questions about quantum behavior and the manipulation of quantum systems. Investments will enable next-generation technologies for sensing, computing, modeling, and communicating that will be more accurate and efficient.

NSF supports a wide range of research aimed at gaining fundamental understanding of phenomena in nanoscale biosystems, including: (1) understanding of electron and bioenergy transfer in ubiquitous biological energy conversion systems, the thylakoid systems of plant chloroplasts, and the respiratory complex of mitochondria; (2) understanding of the relationship between structure and function of chromatin as it relates to epigenetic control of gene expression; and (3) development of technologies that take advantage of CRISPR/Cas9 genome editing discoveries that enable the facile engineering of synthetic organisms that will lead to applications in food, energy, healthcare and the environment that benefit the Nation.

The Division of Social and Economic Sciences in the SBE Directorate supports research on the social and ethical implications (SEI) of nanotechnology at four nodes of the recently formed NNCI. At a recent NNCI PI meeting, SEI researchers associated with these nodes developed plans to coordinate efforts, and to seek ways to include other nodes in SEI research on nanotechnology. The overarching goal is to foster the integration of social science research with nanoscale science and engineering (NSE) to promote socially responsible innovations at all nodes in the NNCI, and thereby serve as a national resource for all nanotechnology stakeholders seeking expert assistance with NSE/SEI issues.

In 2018, NSF will expand the current research in new areas in response to the NSF Big Ideas, including research related to human-technology co-evolution, quantum information systems, the rules of life, and convergence.

Chromatin and epigenetic engineering is a new area that will begin in 2018. It consists of modulating and control of chromatin and its nano-environment, leading to changes in cellular characteristics, with relevance to healthcare and biotechnology.

NSF will focus nanomanufacturing research on creating larger atomic structures, using modeling and simulation for design or manufacturing processes, and convergence with cybermanufacturing and biomanufacturing.

NSF, NIH, and AFOSR: NSF plans to collaborate with NIH and AFOSR in 2018–2019 on a research solicitation in the chromatin and epigenetic engineering topic discussed above.⁶⁰

USDA/Forest Service, DOE national laboratories, and academia: To accelerate innovations in new forest products development, Forest Service scientists, in collaboration with university and DOE national laboratory researchers, have been investigating ways to understand and control, at the nanoscale, mechanical properties, moisture-induced swelling, and chemical transport in wood. The collaborative research team has developed tools to study these nanoscale properties and phenomena in wood, including nano-indentation to study mechanical properties (Forest Service Forest Products Laboratory), small-angle scattering to study moisture-induced swelling (ORNL), and synchrotron micro x-ray fluorescence microscopy to study chemical transport (ANL). For the first time, these discoveries have provided researchers with specific nanoscale mechanisms in the effort to develop forest products with improved properties.

USDA/NIFA: NIFA continues to advance the frontiers of interdisciplinary nanoscale science, engineering, and technology for solving significant societal challenges facing agriculture and food systems. NIFA investments in nanotechnology research, education, and extension are reflected in multiple portfolios including sustainable agricultural production systems, the bio-based economy, food safety and quality,

⁶⁰ www.nsf.gov/pubs/2017/nsf17578/nsf17578.htm

human nutrition, environmental systems, natural resources, water quality, and climate variability. The Nanotechnology for Agricultural and Food Systems program in AFRI supports discovery and characterization of nanoscale phenomena, processes, and structures relevant and important to agriculture and food. It also encourages new platforms of nanotechnology in the area of higher-order assembled systems, and more complex systems that include the exploitation of bio-nano interfaces, hybrid bioinorganic systems, systems biology, and additive manufacturing technology. Public deliberation, social acceptability, and risk perception, management, and communication about nanotechnology and nanotechnology-enabled food or non-food products by agricultural stakeholders (including consumers) using appropriate social science tools are within the program scope.

PCA 3. Nanotechnology-Enabled Applications, Devices, and Systems

Overview

PCA 3 covers research and development that applies the principles of nanoscale science and engineering to create novel devices and systems, or to improve existing ones. It includes the incorporation of nanoscale or nanostructured materials and the processes required to achieve improved performance or new functionality, including metrology, scale up, manufacturing technology, and nanoscale reference materials and standards. To meet this definition, the enabling science and technology must be at the nanoscale, but the applications, systems, and devices themselves are not restricted to that size.

Agency Progress and Plans

DOD/Army: The Army Armament Research, Development and Engineering Center (ARDEC) has developed a nanothermite formulation to eliminate hazardous materials in many ammunition applications, and has demonstrated pilot-scale production methods of these compounds.

ERDC has completed development of a series of novel materials combining photocatalytic nanomaterials and toughening nanofibers in a biopolymer and synthetic polymer matrix as part of basic research studies. This work focuses on development of materials and coating systems with combined toughening capability for improving the high strain rate performance of brittle construction materials as well as imparting self-cleaning and integrated chem-bio defense capabilities.

DOD/Navy: ONR has developed a shipboard *in situ* repair tool for Cu-Ni piping in heat exchangers, fire suppression mains, etc., utilizing electrodeposited nanoalloys. This program adapted existing electroplating technology to produce a single-step nanostructured Cu-Ni repair coating for shipboard systems.

Another ONR-funded university program has examined the dielectric breakdown strength of nanoclay-filled epoxy. These nanostructured epoxies may be used on winding insulation for electric propulsion motors. Success to date includes improving alternating current dielectric strength by 50% and thermal conductivity by a factor of seven.

NRL has investigated nanoscale optical materials that include both transparent nanoceramics as well as nanolayered gradient-index (GRIN) materials. The transparent nanoceramics have shown considerable hardness improvements, and may find applications in radomes and armor materials. The nanolayered GRIN optics and design tools, developed in a collaboration with ARL, provide a unique way to control chromatic aberration in many optical systems.

DOD/Army, DOD/Navy, and academia: DOD has examined boron carbide at the nanoscale in several efforts. Researchers from the Army, Navy, and several universities are working to control the microstructure

and deformation processes of nanocrystalline boron carbide, at the nanoscale. The goals of these efforts are to improve the performance and reduce the cost of armor for soldier protection.

DOD/Army and NIST: ERDC has a new research program that will test several different nanotechnologies, advanced materials technologies, and additive manufacturing (3D printing) processes through collaboration with ARDEC (which will supply materials) and NIST (which will provide characterization and release methods). The technologies tested will include energetics, force protection, and construction materials applications.

DOD (multiple services), other NNI agencies, industry, and academia: DOD will continue to collaborate with a broad range of industrial and academic partners to address specific applications of nanotechnology. Many of these partners have been mentioned in prior sections of this report, and include the Institute for Soldier Nanotechnologies, the Advanced Functional Fibers of America Manufacturing USA institute, the Nano-Bio Manufacturing Consortium, the Center of Excellence for Advanced Bioprogrammable Nanomaterials, and a university laboratory, not to mention the other NNI participating Federal agencies.

DOE: The DOE Office of Nuclear Energy investments in nanotechnology-related experiments are executed via competitive Nuclear Science User Facilities Consolidated Innovative Nuclear Research facility access awards and Rapid Turnaround Experiment awards to researchers at U.S. universities and national laboratories, as well as through the Office of Nuclear Technology research and development programs. Recent research topics include radiation effects on engineered nanostructured features of cladding, structural component materials, and fuels towards increased performance, including advanced manufacturing techniques; understanding the effects of radiation-induced nanoprecipitate and nanocluster formation on the performance of cladding and structural component materials; and understanding the mechanical properties of cladding, structural component materials, and fuels employing nanoscale measurement technologies. Significant accomplishments have been made in designing and stabilizing nanostructured features in ferritic/martensitic alloys to enhance radiation resistance and mechanical properties. Advanced nanoscale material characterization techniques have also been developed to inform modeling and simulation efforts and to maximize utilization of small ion- or neutron-irradiated samples.

ARPA-E has supported a broad range of early-stage, potentially disruptive energy technology projects that involve both applications of current nanotechnology and applied R&D in new areas of nanotechnology. For example, the Integration and Optimization of Novel Ion Conducting Solids (IONICS) program was launched in 2016 to develop solid ion conductors with transformational potential for solid-state lithium batteries, low-cost chemistries for grid-scale flow batteries, and alkaline fuel cells. Across all applications, program teams are drawing upon recent advances in nanomaterials, including organic-inorganic composites and nanoporous polymer membranes, to develop and demonstrate high-performance, scalable components for electrochemical cells.

FCTO plans to advance the development of low-PGM catalysts and advanced electrode nanomaterials through the ElectroCat consortium. AMO plans to support the development of advanced conductor wire with carbon nanotubes.

DOJ/NIJ: The Department of Justice's National Institute of Justice (NIJ) has invested in research to apply nanotechnology to forensic science and in the development of nanoantennas for multi-band radios. These investments have the potential to make important contributions to criminal justice, the safety and effectiveness of our first responders, and national security.

DOT/FHWA: The Federal Highway Administration is pursuing nanotechnology-enabled solutions to enable a state of good repair for the Nation's highway system. Nanomaterials efforts focused on conventional and alternative cementitious materials have expanded the fundamental understanding of cement hydration kinetics by developing novel nanoscale interrogation and characterization techniques to complement

advanced models. Building on prior work on cementitious materials, multifunctionality for structural health monitoring, and advanced coatings, new investments in 2018 will seek to improve the performance, durability, and resiliency of transportation infrastructure.

NASA: NASA has developed an atmospheric pressure plasma jet printing technique, which is a dry alternative to inkjet printing of nanomaterials on flexible and 3D substrates. The technique does not need the post-deposition sintering or annealing steps commonly encountered in aerosol jet printing. Printing of conducting, semiconducting, dielectric, and other materials on paper, plastic, kapton, cotton, thin metal foils, and 3D objects has been demonstrated.

There is separate IRAD funding to investigate the application of boron nitride nanotubes for thermal protection systems needed in entry, descent, and landing for Mars entry.

There is an activity to explore the development of high-strength hybrid nanocomposites for lightweight space vehicle structures, including a Phase 2 SBIR to develop composites with enhanced interlaminar properties.

A collaboration between two NASA centers will demonstrate printable gas/vapor sensors, biosensors, ultracapacitors, and triboelectric power generators.

NIH: Nanotechnology-enabled applications, devices, and systems is the largest PCA within the NIH-reported NNI investment portfolio—\$262 million in 2017. Programs and projects in PCA 3 include medical devices, nanotherapeutics, drug delivery systems, and novel radiotherapeutics supported through several FOAs renewed in 2016–2017. Systems being studied in IRCN awards include nanoscale core-shell coordination polymers developed by university researchers, which are being used for synergistic chemo- and photodynamic therapy that stimulates the immune system and enhances response to immunotherapy. The combination therapy leads to regression of both treated and distant, untreated, tumors.⁶¹ Other systems and devices were developed through Image-guided Drug Delivery R01 awards⁶² and the Innovative Molecular Analysis Technology program.⁶³

In 2016, significant accomplishments in dental research were supported by NIH/NIDCR via the Design and Development of Novel Dental Composite Restorative Systems cooperative agreement program. The goal of this program is to enable design and development of novel dental composite materials that demonstrate superiority in material properties and durability in the oral environment over the currently utilized dental composites. Researchers demonstrated improvement in mechanical performance of dental materials by combining nanoparticle-based biomaterials with a variety of polymer resins. These newly developed dental materials exhibit valuable features such as self-healing and anti-microbial properties. Further development of these biomaterials is expected to generate dental composites with superior biocompatibility, ease of clinical handling, and durability.

Recent advances from NIH/NIBIB-supported research have shown that nanovaccines could enhance cancer immunotherapy. Researchers have created a nanovaccine that could make a current approach to cancer immunotherapy more effective while also reducing side effects. The nanovaccine helps to efficiently deliver a unique DNA sequence to immune cells—a sequence derived from bacterial DNA and used to trigger an

⁶¹ www.ncbi.nlm.nih.gov/pmc/articles/PMC4992065/

⁶² grants.nih.gov/grants/guide/pa-files/PAR-16-044.html

⁶³ imat.cancer.gov/

immune reaction. The nanovaccine also protects the DNA from being destroyed inside the body, where DNA-cutting enzymes are pervasive, as well as outside of the body when exposed to warm temperatures while being stored or transported. The researchers successfully tested the nanovaccine on melanomas in mice.⁶⁴

In 2017–2018, NIH/NCI is replacing the expired IRCN PAR with a FOA with similar goals and purpose. In 2018, NIH plans to host strategic workshops aimed at mapping future directions for cancer nanotechnology research, and also to identify emerging areas of research that are complementary to nanotechnology and likely to be areas of fruitful collaboration for nanotechnology researchers. The findings of these workshops will inform future funding opportunities and programs in nanotechnology. One of these workshops will be comprised entirely of researchers within 10 years of their terminal degree, and also will seek to establish mechanisms for supporting collaborative research among early career investigators.

In 2017, NIH/NIDCR launched Stage 2 of a three-stage effort to support establishing multidisciplinary Resource Centers (RCs) for the Dental, Oral and Craniofacial Tissue Regeneration Consortium (DOCTRC). This effort extends over a period of 8–9 years to include the Planning Stage (Stage 1), the RC Development Stage (Stage 2), and the Consortium Stage (Stage 3). Stage 2 of the DOCTRC will build on the activities of Stage 1, which was launched in 2015. By integrating the clinical, scientific, industrial, and regulatory expertise of the teams of investigators, the RCs will deliver technical support, research capacity, administrative infrastructure, and regulatory expertise for the DOCTRC. The RC also facilitates the advancement of promising strategies, including nanotechnology-based strategies, into clinical trials for regeneration and reconstruction of dental, oral, and craniofacial (DOC) tissues. The overall outcome of DOCTRC will be the development of tissue engineering and regenerative medicine products, including combination products, biologics, and/or devices and associated protocols ready for the initiation of Phase 1 clinical trials. It is expected that many individual DOCTRC projects will utilize nanotechnology-based strategies, thus facilitating introduction of nanotechnology into clinical practice. Examples of such products/devices include tissue regeneration-enhancing scaffolds, drug delivery systems, and “smart materials” that respond to cues from the tissue microenvironment, as well as nanomaterial-based imaging modalities and biosensors.

NIH and non-profit organization: The Startup Challenge in Cancer (NSC2) is an open innovation startup collaboration between a non-profit 501(c)(3) organization and NIH—including NCI, NIBIB, and NHLBI—to commercialize nanotechnology inventions originally conceived at NIH. Twenty-eight teams were accepted to participate in the cancer challenge at Phase 1.⁶⁵ Of those, the top 10 teams advanced past stage 2.⁶⁶ The final phase of the challenge will involve the NIH Office of Technology Transfer evaluating the startups’ licensing applications to determine the viability of commercialization and development plans.

NIH and NIST: An ongoing multi-year interagency agreement (IAA) between NIH/NIDCR and NIST supports development of performance-based, clinically relevant standards for dental materials, including nanomaterials for applications in the oral environment. Additionally, this IAA allows the design of new analytical instrumentation for characterization of nanomaterial-based dental composite restorative systems. In this collaboration, NIST develops measurement strategies, standard methods, and reference materials, while NIH/NIDCR provides funds and expert scientific and clinical advice. NIH/NIDCR also provides guidance to ensure that these materials and instrumentation are designed for routine and reliable use with adequate reproducibility and rigor.

Recent advances made under this NIH/NIDCR-NIST IAA have resulted in the development of the NIST Standard Reference Instrument 6005 Polymerization Stress Tensometer (SRI 6500 PST). This new instrument

⁶⁴ nibib.nih.gov/news-events/newsroom/nanovaccine-could-enhance-cancer-immunotherapy-reduce-side-effects

⁶⁵ www.prweb.com/releases/2016/04/prweb13312920.htm

⁶⁶ www.prweb.com/releases/2016/07/prweb13575946.htm

allows inter-comparability testing during development of nanomaterial-based dental composites. The SRI 6500 PST instrument is commercially available and has been procured by national and international stakeholders involved in dental materials research. Future work will involve broader research applications of the SRI 6005 PST instrument for the development of new dental composite materials. This new instrument is expected to be broadly applied across the dental materials research community and to receive ISO certification. Other accomplishments under this IAA include advances towards the development of a nanoscale carbonated apatite material mimicking human dental enamel that may find use as a standard reference material, and assessing the feasibility of using cellulose nanocrystals to restore bone volume to support teeth and dental implants. Results from this work suggest that cellulose nanocrystal-based scaffolds may offer a promising strategy for bone regeneration.

NIH, FDA, and NIST: NIH/NIDCR has been leading five participating NIH institutes on the “Forum on Regenerative Medicine,” organized under the auspices of the National Academy of Medicine of the National Academies. In addition, FDA, NIST, and other regenerative medicine stakeholders from academia, industry, patient advocacy groups, and private foundations are participating in this effort. Many of the regenerative medicine strategies that are currently being developed involve nanotechnology, and the forum aims to engage the different participating stakeholders in a dialogue about challenges, opportunities, and ethical aspects of translating regenerative medicine strategies to the clinic. In October 2016, NIH/NIDCR, along with the other forum partners, participated in a forum workshop entitled “State of the Science in the Field of Regenerative Medicine: Challenges and Opportunities for Cellular Therapies.” Plans are currently underway to define the goals and objectives of the next series of forum activities, where NIH/NIDCR will play a prominent role.

NIH, DOD, government laboratories, academia, and industry: In 2017 and 2018, NIH/NIDCR will continue to support and provide programmatic guidance for the Armed Forces Institute of Regenerative Medicine (AFIRM) in collaboration with two other NIH institutes (NIBIB and the National Institute of Arthritis and Musculoskeletal and Skin Diseases). AFIRM is a DOD-led interdisciplinary multi-institutional consortium that supports a network of academic institutions, Federal laboratories, and commercial partners to develop life-saving tissue/organ regeneration strategies for wounded warriors. AFIRM investigators have been utilizing numerous nanotechnology strategies from the inception of the AFIRM program in 2008. AFIRM research focus areas include projects in NIH/NIDCR mission areas geared toward craniofacial regeneration and reconstruction.

NIH and FDA: NIH/NIDCR investigators will continue to optimize the nanoscale properties of their candidate dental composites in 2017 and 2018, and will initiate interactions with FDA with a goal of bringing these restorative systems to market.

NIH, DOD, FDA, and industry: In 2017 and in the next 2–5 years NIH/NIDCR will be participating in a new trans-NIH RFA led by NIH’s National Center for Advancing Translational Sciences entitled “The Microphysiological Systems for Disease Modeling and Efficacy Testing.” This initiative will support studies to develop micro- and nanoscale *in vitro* microphysiological system platforms (also known as tissue chips) and to validate these platforms for their ability to mimic physiological functions of human tissues and organs. It will also support studies to demonstrate the functional utility of the tissue chips for disease modeling to understand disease mechanisms and to identify novel therapeutic targets and treatments to inform design of clinical trials. This nanomedicine effort leverages previous NIH investments in 2016 and in earlier years in this field that have been conducted in partnership with DOD, FDA, and the pharmaceutical industry. Technologies developed under the previous and the current 2017 initiatives utilize multidisciplinary approaches combining an array of nanotechnology-based strategies across fields of bioengineering, biology, microfluidics, materials science, “omic” sciences, and clinical science, among others. NIH/NIDCR

intends to support meritorious applications for development of tissue chip platforms relevant to the institute's mission areas.

NIST: NIST measurement science programs to support PCA 3 include efforts for photonic circuits, polymer membranes, energy-efficient electronics, and reliability for advanced microelectronics. NIST has continued to perform pioneering quantum optomechanics experiments that use quantum-correlated phonons as a means of realizing an absolute temperature scale, and is harnessing the unique properties of graphene to develop improved quantum resistance reference standards. The NIST Center for Nanoscale Science and Technology (CNST) user facility developed and introduced advanced nanofabrication techniques to medical and other bioscience researchers who were unaware of these techniques but can greatly benefit from them. By training bioscience and biomedical researchers in nanofabrication techniques and offering remote services when possible, NIST ensures that these researchers have access to tools and devices that are a catalyst for their existing projects and have helped inspire new innovative ideas.

Future plans include establishing a program to develop radiation-resistant, nanoscale calorimetric sensors based on photonic sensors that could eventually lead to direct realization of the SI (Le Système International d'Unités, or International System of Units) unit of dose (Gy) with unprecedented sensitivity and spatial resolution. NIST also plans to continue work to identify materials, architectures, and physical mechanisms for developing nanoscale sensors with a tunable radiation sensitivity that could be used as secondary standards or field-deployable cumulative dosimeters.

NIST and SNL: In collaboration with SNL, NIST demonstrated fast electrochromic switching devices enabled by plasmonic structures, offering a new technology opportunity for reflective and transmissive displays and sensors.

NSF: NSF invests in R&D that applies the principles of nanoscale science and engineering to create novel devices and systems, or to improve existing ones. This R&D includes the incorporation of nanoscale or nanostructured materials and the processes required to achieve improved performance or new functionality, including metrology, scale up, manufacturing technology, and nanoscale reference materials and standards. An example is the NEWT NERC, which has been investigating distributed water filtration methods.⁶⁷ Another example is the NERC, Center for Advanced Self-Powered Systems of Integrated Sensors and Technologies, focusing on using nanosensors for health and the environment.⁶⁸

The Division of Civil, Mechanical and Manufacturing Innovation in ENG plans to focus on the following areas for 2017–2018: processing-structure-property relationships in structural and functional nanomaterials; nanostructures; nanocomposites; metallic, ceramic, and polymeric materials; nanotribology; nanoscale routes to energy manufacturing and additive manufacturing using nanoparticles to make bulk shapes; nanomechanics and its implications for structural performance; and 3D nanoprinting.

USDA/ARS: The USDA Agricultural Research Service (ARS) has been researching a number of novel applications of nanotechnology in the agriculture and food sector. Examples include the following:

- *Food containers with antimicrobial surfaces.* Containers are used for harvesting fruits and vegetables in the field and for storage, display in stores, and during transportation; however, they can be easily contaminated with foodborne pathogens. When a contaminated container is in contact with food, pathogens transfer from the container to the food, hence, the importance of having a pathogen-free container. ARS researchers in Wyndmoor, Pennsylvania, developed methods and coating formulas to produce food containers with an antimicrobial surface. Scientists used

⁶⁷ See above under Water NSI (PCA 1e) for more details.

⁶⁸ assist.ncsu.edu/

titanium dioxide (TiO₂) nanopowders, which are ingredients in food coloring, with polymers to form an antimicrobial coating on the container surface. The surface coatings are activated by visible light to inactivate *E. coli* O157:H7, and in validation tests, reduced the pathogen by 99.7%. Studies further demonstrated that the developed methods and coating formula could be applied to different types of containers made of various materials such as metal, wood, plastics, or paperboard, and for a variety of foods, especially for fruits and vegetables. An invention disclosure and patent for the technology has been submitted to facilitate licensing by industry.

- *Value-added products from agro-industrial residues for sustainability and pollution reduction.* Industries such as textiles, leather, rubber, plastics, and food use synthetic dyes such as methylene blue (MB) to color their products, and discharge the ensuing colored wastewater into the environment. These effluents cause significant problems including increased chemical oxygen demand, toxicity due to their carcinogenic properties, and hindering light penetration (because they are highly colored, affecting the photosynthetic processes in aquatic plants). Removal of MB from wastewater, therefore, is very important to protect the environment and to reduce the dye hazard to biotic communities. ARS scientists from Bowling Green, Kentucky, utilized agro-industrial residues as a biomass source for silica extraction, and residual ash as a low-cost adsorbent for the removal of MB from an aqueous waste stream. The results show that a high percentage of pure amorphous nanosilica could be obtained from industrial waste via the acid dissolution–precipitation process, and residual ash is an effective adsorbent for dye removal from waste streams. The research team has found a potential eco-friendly and sustainable method to transform agro-industrial wastes to value-added starting materials for industrial applications, as well as adsorbent materials for treatment of chemical pollution from agricultural wastes. This new method of extracting adsorbent materials from renewable biomass, especially from agricultural wastes, will help farmers and producers to be more sustainable.
- *Plant starch nanoparticles for improved and lower-cost packaging films.* Currently, polyvinyl alcohol (PVOH) film has excellent properties that make it practical for use in food packaging, textile sizing agents, paper coatings, and fibers. However, it is expensive to manufacture and slow to decompose in landfills. ARS scientists in Peoria, Illinois, have blended PVOH film with starch nanoparticles prepared from inexpensive plant starch using the economical commercial process of steam-jet cooking. Studies determined that incorporating up to 50% of starch nanoparticles into PVOH films does not affect the breaking point of the films during stretching. Additionally, since starch biodegrades rapidly, incorporation of starch-based nanoparticles into PVOH films and other products prepared from PVOH will reduce the harmful buildup of these materials in the environment and reduce the cost of production by at least 30%.

For 2017–2018, ARS is planning a number of continuing and new research projects that involve nanotechnology. Topics covered by these projects include the following:

- *Integrated process and packaging technologies.* Development of novel food processing and packaging technologies to improve appearance, nutritional value, or product quality; antibacterial packaging to control pathogens and minimize loss of product quality and value; and evaluation of potential environmental, health, or safety concerns arising from novel non-thermal food processing interventions.
- *Technologies for value-added cotton-based products.* Development of new commercial cotton products, including cotton-containing nonwoven materials; cotton-based products with enhanced flame retardant and moisture control properties; body-contacting materials for use in biomedical, biosensor, and hygienic applications; and processes involving supercritical fluids, microwaves, ultrasound, or ionic liquids for production of cotton-based products.

- *Biophotonics in animal research and production systems.* Development of advanced imaging technologies (including use of nanoparticles) to improve understanding of health and fertility in food animal reproduction systems, and to track pathogens (e.g., Salmonella, Mycobacterium avian paratuberculosis) in avian and livestock hosts using photon-emitting sentinels in the animal system and/or environment; and development of pathogen mitigation strategies.
- *Bioproducts from agricultural feedstocks.* Use of biopolymers to develop sustainable technologies and bioproducts that will not negatively impact food reserves, and use of nonfood fibers and crop waste to create new bioproducts and to help improve efficiency in utilizing agricultural commodities. Plans include exploring the use of conventional and novel processing technologies to produce and characterize nanofibers from biopolymers and investigate potential applications, and the use of biopolymers to encapsulate/deliver beneficial soil microbes that improve crop production. This program also includes research to enable new commercial materials based on biopolymers and bio-based fillers, e.g., fiber-reinforced composite materials, and value-added bioproducts from torrefied crop waste and from almond, grape, and citrus waste.

USDA/NIFA: The NIFA nanotechnology program supports innovative, early-stage applied research to develop nanotechnology-enabled applications, devices, and systems for a wide range of national priorities. These priorities include improving global food and nutrition security and sustainability, adaptation and mitigation of agricultural production systems to climate variability, early detection and effective intervention for ensuring food safety and biosecurity, more effective therapies to improve animal health and wellness, development of the biology-based economy, and protection for natural resources, the environment, and agricultural ecosystems. Applications, especially those with potential near-term commercial impact, are encouraged to include socioeconomic analyses of anticipated benefits to agriculture, food, and society and to identify the factors that may contribute to, or hinder, adoption. For 2018, NIFA proposes to invest in the Sustainable Agricultural Systems programs⁶⁹ to support large integrative projects that address major outcomes of agricultural systems. This component of AFRI will build on the advances made in research, education, and extension priority outcomes through the former AFRI Challenge Areas such as water, resiliency and adaptation to climate variability, food safety, childhood obesity prevention, bioenergy, and food security. Sustainable Agricultural Systems will address these challenge topics comprehensively and collectively, rather than in isolation. This integration will enable NIFA's goal of advancing the convergence of agricultural sciences with engineering, nutritional and food sciences, social sciences, and other disciplines (including nanotechnology, computational sciences, and advanced manufacturing) to generate new scientific discoveries, new products, new markets, and consequently new high-skilled jobs.

The USDA SBIR program housed within NIFA has supported nanotechnology R&D aiming at commercialization. Topics of the NIFA SBIR projects have included nanotechnology-enabled sensor technologies for detection of microbial pathogens, insects, and crop environmental stresses; nanoscale delivery of antimicrobial agents; and nanocellulose composites to improve polymer functionalities.

PCA 4. Research Infrastructure and Instrumentation

Overview

PCA 4 supports the establishment and operation of user facilities and networks, acquisition of major instrumentation, workforce development, and other activities that develop, support, or enhance the Nation's physical, cyber, or workforce infrastructure for nanoscale science, engineering, and technology. It includes R&D pertaining to the tools needed to advance nanotechnology research and commercialization, including

⁶⁹ nifa.usda.gov/sustainable-agricultural-production-systems

informatics tools and next-generation instrumentation for characterization, measurement, synthesis, and design of materials, structures, devices, and systems. While student support to perform research is captured in other categories, dedicated educational efforts ranging from curriculum development to advanced training are included here as resources supporting the workforce infrastructure of the NNI.

Agency Progress and Plans

DOE: BES has continued to operate five Nanoscale Science Research Centers (NSRCs), which are national user facilities for interdisciplinary R&D at the nanoscale that serve as the basis for a national program that encompasses new science, new tools, and new computing capabilities. These are the Center for Functional Nanomaterials at Brookhaven National Laboratory, the Center for Integrated Nanotechnologies at LANL and SNL, the Center for Nanoscale Materials at ANL, the Center for Nanophase Materials Sciences at ORNL, and the Molecular Foundry at LBNL. The NSRC laboratories contain cleanrooms, nanofabrication resources, one-of-a-kind signature instruments, state-of-the-art electron microscopy, and other instruments not generally available except at major user facilities. Operating funds enable scientific staff that perform cutting-edge research and provide technical support through the user programs at these facilities, which are made available to academic, government, and industry researchers with access determined through external peer review of user proposals. The NSRCs provide training for graduate students and postdoctoral researchers in interdisciplinary nanoscale science, engineering, and technology research. Each center has particular expertise and capabilities in selected theme areas, such as synthesis and characterization of nanomaterials; catalysis; theory, modeling, and simulation; electronic materials; nanoscale photonics; soft and biological materials; imaging and spectroscopy; and nanoscale integration. Information about capabilities at all five centers is on the NSRC Portal.⁷⁰

In 2018, BES plans to continue support for three of the five NSRCs at 6% below the 2016 enacted level.

NASA: NASA currently supports student research in nanotechnology under the NASA Space Technology Research Fellowships. These graduate fellowships train students in technical disciplines related to nanotechnology and familiarize the students with capabilities in government laboratories that constitute some of the infrastructure that supports the advancement of nanotechnology. A total of about six students working in nanotechnology-related fields are usually supported every year, with maximum support being provided for four years if the student is in a PhD program. Six is a “rolling” number since students are at different phases of their graduate study, with about two students entering the pipeline, while two graduate, every year.

NIH: NIH provides funds for centers in cardiac, cancer, dental, and other clinical research areas. For instance, NIH/NCI has continued to support five Cancer Nanotechnology Training Centers dedicated to providing graduate and post-graduate training to researchers from diverse disciplinary backgrounds in the use of nanotechnology as an enabling tool for cancer biology and oncology research.

NIH, NIST, and FDA: NIH/NCI supports the Nanotechnology Characterization Laboratory (NCL) at the Frederick National Laboratory for Cancer Research, founded as an agreement between NIH/NCI, NIST, and FDA. NCL has developed a comprehensive assay cascade to characterize nanomaterials intended for use in cancer care, including protocols available on its website, and regularly publishes its findings on the physiological behavior of nanoparticles.⁷¹

⁷⁰ nsrcportal.sandia.gov

⁷¹ ncl.cancer.gov/resources

NIST: NIST has several facilities that support PCA 4, including CNST and the NIST Center for Neutron Research (NCNR) user facilities, serving industry, academic, and government researchers on NIST's Gaithersburg campus, and the MicroFabrication Facility located at NIST's Boulder campus, which houses nanofabrication tools for electronics and other applications. NIST continues to sustain and update the capabilities and capacity in these facilities, each providing essential resources for nanoscale measurements. CNST is NIST's dedicated nanotechnology user facility, providing rapid access to world-class nanoscale measurement and fabrication methods and technology. The CNST NanoFab provides users with access to a state-of-the-art commercial tool set at economical hourly rates, supported by a dedicated, full-time technical support staff. In 2016 NIST issued the CNST Nanolithography Toolbox,⁷² a platform-independent computer-aided design software package, to help users of the CNST NanoFab design their nanoscale devices. CNST also implemented a web-based digital knowledge base that disseminates the cumulative nanofabrication knowledge collected by the NanoFab staff and users to form a crowd-sourced means of sharing nanofabrication technologies and processes. The CNST NanoLab provides a collaborative research environment to create and use the next generation of nanoscale measurement instruments. The CNST NanoLab recently developed a new form of ion source for focused ion beams based on laser-cooled atoms, creating a new tool for nanoscale imaging, fabrication, and battery research.

Some planned developments include a multimodal measurement instrument combining electron microscopy with an atomic force microscope and a focused lithium ion beam. This CNST instrument will enable new research on battery materials and other ionic transport phenomena. Installation of two new NCNR instruments, VSANS (Very Small Angle Neutron Scattering)⁷³ and CANDOR (Chromatic Analysis Neutron Diffractometer or Reflectometer),⁷⁴ will finish in 2017 and 2018, respectively. VSANS will allow researchers to measure the characteristic size of material structures across five orders of magnitude, down to the nanoscale. This capability is critical to a broad range of real-world problems; for example, it can be used to measure the size distribution of voids that determine the shock resistance of explosives or the integrity of concrete used in nuclear waste storage. VSANS is a very small angle neutron scattering diffractometer that will collect data at rates 100 times faster than comparable instruments, making possible the study of nanoscale feature evolution in real time. Similarly, CANDOR is a reflectometer/diffractometer that will provide at least a ten-fold gain over existing instruments used to study nanostructured materials such as proteins, magnetic storage devices, and solar cells; it will enable kinetic studies as a function of temperature or magnetic field.

NIST and industry: In collaboration with a company, NIST developed a cold atomic beam ion source with twelve times the brightness of existing sources, enabling higher-resolution milling for applications such as next-generation circuit editing.

NIST and NSF: The CNST NanoFab collaborates with the NSF-funded Advanced Technological Education (ATE) centers in a program consisting of three 16-week terms per year that provides advanced training in nanofabrication. The program, open to two-year and four-year college graduates, has successfully provided nanotechnology companies with skilled workers.

⁷² www.nist.gov/services-resources/software/cnst-nanolithography-toolbox

⁷³ www.ncnr.nist.gov/expansion/individual_instruments/vSANS053007.html

⁷⁴ www.ncnr.nist.gov/expansion/individual_instruments/CANDOR053007.html

NSF: Nanoscale science and engineering often requires expensive equipment and specialized expertise, and user facilities alleviate the lack of these resources in smaller academic institutions, as well as in the small to medium-size commercial sector. NSF has supported a network of nanotechnology user facilities for the past forty years: initially, the National Nanofabrication Facility (1977–1993), followed by the National Nanotechnology Users Network (NNUN, 1993–2003), and then the National Nanotechnology Infrastructure Network (NNIN, 2004–2015). Recently, after rigorous competition, NSF established the National Nanotechnology Coordinated Infrastructure (NNCI) program⁷⁵ that consists of 16 university user-facility sites across the Nation, with a new coordinating office, and a diverse user facility portfolio for nanobiotechnology, nanoelectronics, nanomanufacturing, and other areas. The facilities for research and development support both academic research and product and process development. NNCI sites have experience supporting technology innovation and commercialization, for start-ups as well as larger and more established companies.

Research to develop the practical and computational tools to predict, design, and experimentally test the function of designed changes in the internal organization of cells, and to create the tools for building multicellular structures, is being supported through a new (2016) NSF-funded Center for Cellular Construction (annual award of approximately \$5 million). This center will create high-throughput and modular tools for nanoscale cell engineering, and will assemble a set of core resources and instruments for the community, including high-throughput and quantitative imaging systems, gene synthesis, and next-generation sequencing. Center researchers will work with counterparts in commercial companies to develop cellular machines with real-world applications, and to train a new generation of researchers at undergraduate, graduate, and postdoctoral levels.

In 2016, NSF also funded the Engineering Biology Research Consortium, a public-private partnership that brings together leaders in the field of synthetic biology from academia and industry. This consortium will provide leadership in development of workshops and strategic plans for the field as it applies engineering approaches of modular design, interoperability, and control theory to nanoscale biological systems, to enable the development of robust and reproducible biomanufacturing platforms.

NSF, NNCO, and media: In 2016 and 2017 NSF sponsored a series of videos: “Nanotechnology - Super Small Science” (together with a major commercial broadcasting network) in collaboration with NNCO.⁷⁶

NSF, NNCO, and high schools: In collaboration with NNCO, NSF sponsors a student competition, “Generation Nano,”⁷⁷ that challenges high school students to imagine novel superheroes who use the power of nanotechnology to solve crimes or tackle a societal technical challenge.

USDA/NIFA: NIFA provides funding to support universities to acquire research instruments, improve research facilities, and develop the future workforce. For example, NIFA’s 1890 Facilities Program supported a university to improve its agricultural and food sciences facilities and equipment, so the university can more effectively train students in the food and agricultural sciences and engineering. This program provides the state-of-the-art equipment critically needed for the university’s newly constructed and renovated laboratories. One of these laboratories focuses on research in nanotechnology applications in food crops and bioproducts development from biomass such as algae and agricultural waste byproducts. The equipment purchases for these laboratories help the school attract and retain faculty, and allow them to deliver up-to-

⁷⁵ www.nsf.gov/news/news_summ.jsp?cntn_id=136211

⁷⁶ www.nbclearn.com/nanotechnology

⁷⁷ www.nsf.gov/news/special_reports/gennano/

date instructional aides and hands-on experiential learning opportunities for students to prepare them for studies at the graduate and professional levels supporting agricultural needs in the region.

NIFA is proposing to invest in a new program focused on maximizing the value of data-driven research in specific foundational domains of agricultural science, as a part of the Food and Agriculture Cyberinformatics and Tools (FACT) initiative. The availability of big data provides unprecedented opportunities for synthesizing new knowledge, for making predictive decisions, and for fostering data-supported innovation in agriculture.

NIFA's Education and Literacy Initiative (ELI) program will continue to focus on building institutional capacity and enhancing the pipeline for producing more STEM graduates to meet the projected shortfall in agriculture-related fields. Intended outcomes are to enhance agricultural literacy in schools and to bridge the current 40% annual gap in available workforce with more graduates in agriculture or allied disciplines with skills and/or expertise needed for entering employment or higher education or both. NIFA's higher education programs support competitive grants to universities for developing nanotechnology curricula for undergraduate and graduate students in agriculture and food science and technology.

PCA 5. Environment, Health, and Safety

Overview

PCA 5 includes research and development primarily directed at understanding the potential environmental, health, and safety impacts of nanotechnology development, and at assessing, managing, and mitigating the corresponding risks.

Agency Progress and Plans

CPSC: The CPSC staff works to expand knowledge on the commercialization of nanomaterials and nanotechnology-enabled products (NEPs). Staff members are identifying new uses of nanomaterials in emerging technologies such as additive manufacturing, and are determining responsible utilization in these new technological areas.

CPSC is supporting a multi-investigator international research project on the risk of silver nanowires in touchscreen displays. This research consortium is not only addressing the risk of toxicity to human and environmental health, but also has a goal of determining how silver nanowires can be synthesized to minimize harm to people and the environment.

CPSC, other NNI agencies, and standards developing organizations (SDOs): The CPSC staff engages with Federal partners and voluntary standards groups to develop robust methods and tools for toxicity testing and exposure assessment research. CPSC has developed a number of interagency agreements with Federal partners, including EPA, FDA, NIOSH, and NIST, to conduct studies quantifying and characterizing the presence of nanomaterials in consumer products. These interagency collaborations have resulted in the development of methods, with one endpoint being incorporation of the methods into voluntary standards such that stakeholders can ensure the safety of their products. Areas of research include the release of nanosilver from treated textile products and nanoscale metals used in paint and floor finishes.

DOD/Army: ERDC is the DOD lead organization for understanding the EHS impacts of nanotechnology development. ERDC recently published methods and standard operating procedures for the preparation, characterization, release, fate, and hazards of nanomaterials. This information is critical to support robust

data generation for risk-informed management and regulatory decisions, including nanotechnology-specific EHS considerations.⁷⁸ Some of these methods were disseminated as video demonstrations on LabTube.⁷⁹

ERDC has published a tiered-based framework⁸⁰ for EHS testing and for assessing the potential for release of nanoscale materials from DOD and commercial NEPs with consideration to characterization, categorical testing exclusions, relevance, release potential, fate, and hazards. The framework is being integrated into the Office of the Secretary of Defense revised data collection guidance document to support DOD systems acquisitions. The framework also was developed into a beta version of a visual basic software program called NanoGRID (Nanomaterials Guidance for Risk Informed Deployment). Additionally, ERDC has developed and published a value of information framework for prioritizing risk research of nanomaterials. This approach utilizes control banding and decision analysis to quantify the contribution of different research strategies to hazard classification. This contribution, evaluated alongside the relative costs of each research strategy, serves as a basis from which to focus efforts to classify nanomaterial risk. This work provides DOD researchers with a mechanism to identify combinations of experiments that lead to the greatest improvement in hazard classification at the lowest cost.⁸¹

ERDC has developed a new research program (2017–2020) on Advanced and Additive Materials: Environmental Sustainability in Army Acquisitions that will support acquisition and fielding of advanced materials technologies, including nanotechnologies, by improving the science of and navigation through EHS requirements. The ERDC solution is to improve materials EHS assessment science, develop and standardize a transparent EHS assessment process, disseminate the enhancement of the EHS assessment science through decision support framework tools (such as Advanced Materials-GRID) and environmental models (such as NanoTrack), and develop novel analytical methods for detecting difficult to quantify materials in complex matrices. The ultimate intended DOD impact and pay-off is smoother technology acquisition and fielding due to reduced regulatory ambiguity for materials.

DOD/Army and academia: ERDC, with academic collaborators, published a methodology⁸² demonstrating the integration of life-cycle assessment (LCA) and multi-criteria decision analysis (MCDA) for assessing the sustainability of emerging photovoltaic technologies. The framework was validated in a hypothetical case study in which a Federal acquisition manager evaluates and decides between emergent photovoltaics that employ either nanoscale materials or conventional materials. Findings from the hypothetical case study demonstrated that a combination of LCA and MCDA increases the usability of LCA in assessing the sustainability of NEPs, and can help identify areas in which either engineering controls or further data collection may be necessary.

DOD/Army and NIOSH: ERDC is working with NIOSH to define and categorize advanced materials, nanomaterials, and additively manufactured materials in an EHS context to speed the reformed Toxic Substances Control Act prioritization process and foster technology acquisition by navigating through regulatory requirements.

DOD/Army, EPA, NIST, academia, OECD, and ASTM: These organizations are developing internationally recognized testing and assessment standards: ERDC is leading or participating in the development of five standardized guidance documents and methods to advance acquisition of consistent, high-quality data for

⁷⁸ pubs.acs.org/doi/abs/10.1021/acs.est.5b04173 (doi: 10.1021/acs.est.5b04173)

⁷⁹ www.labtube.tv/channel/ERDC-Nano-EHS

⁸⁰ link.springer.com/article/10.1007/s11051-015-2943-3 (doi:10.1007/s11051-015-2943-3)

⁸¹ www.nature.com/nnano/journal/v11/n2/full/nnano.2015.249.html (doi:10.1038/nnano.2015.249)

⁸² onlinelibrary.wiley.com/doi/10.1111/risa.2016.36.issue-10/issuetoc (doi: 10.1111/risa.12539)

nanomaterials and products. These standard methods were a joint collaboration with the government organizations listed above and with several universities. The methods are expected to begin review with the Organisation for Economic Co-operation and Development (OECD) and ASTM International, with anticipated completion by 2019.

DOD/Army, academia, and industry: ERDC, ARDEC, a university, and a company are organizing a series of workshops to define the decision process for evaluating potential EHS implications of nanomaterials, advanced materials, and additive manufacturing. Separate workshops will include DOD, regulatory, and international focus groups. The anticipated results will include a categorization regime for defining advanced materials, understanding constraints to technology acquisition/commercialization, and addressing regulatory and liability uncertainty in order to paint a clearer path forward for nanotechnology and other advanced materials technologies. The first workshop (EMERGE—Emergency Management of Emerging Technologies and Advanced Manufacturing) took place in 2017.⁸³

DOI/USGS: The U.S. Geological Survey (USGS) Columbia Environmental Research Center is supporting the development and implementation of a framework for evaluating the safety of advanced materials. Nanotechnologies have been extensively researched in the past two decades, with a wide variety of commercial applications on the horizon. However, the potential impacts and risks associated with these technologies, including EHS issues throughout their life, are not fully understood. The goal of USGS's work in this field is to address potential obstacles to commercializing nanotechnologies due to limited knowledge and/or misperceptions by the general population.

DOI/USGS, other NNI agencies, industry: USGS partners with private industry and Federal agencies by providing expertise in fate, toxicity, and risk analysis of advanced materials, including nanomaterials. USGS is providing technical expertise to support (1) sensor development; (2) risk analysis and life cycle assessment; (3) nanoparticle release testing; and (4) risk assessment tools for navigating regulatory and liability problems with nanotechnology innovation and commercialization. USGS is uniquely positioned to conduct this research because of the potential application of nanotechnology-enabled sensors within the USGS mission that includes collecting environmental data. USGS also has expertise in risk assessment, management, and communication of results through intergovernmental organizations such as the NNI.

EPA: Methods are required to characterize nanomaterials in simple and complex media and to evaluate the release of nanomaterials from consumer products, and alternative testing approaches are needed to evaluate adverse outcome pathways of nanomaterials. Accurately predicting impacts of engineered nanomaterials (ENMs) used in real-world conditions will depend on properties of both the ENMs and the matrices. EPA research evaluates nanomaterials across a life cycle of product use ranging from manufacture to use and end-of-life disposal and will consider the release, fate, transport, and transformations of nanomaterials as they age.

EPA research on ENMs is conducted within the agency's Chemical Safety for Sustainability research program. In 2015, EPA published the Chemical Safety for Sustainability Strategic Research Action Plan 2016–2019⁸⁴ describing new objectives and outputs for EPA research on implications of ENMs. A key scientific issue for EPA nanomaterials research is the complexity of relating nanomaterial features directly to risks. An important avenue of investigation focuses on identifying critical intermediate properties of ENMs that are predictive of potential risks. Another key issue is understanding the interactions between ENMs and biological or other complex media.

⁸³ www.ictas.vt.edu/EMERGE2017/schedule.php

⁸⁴ www2.epa.gov/research/chemical-safety-sustainability-strategic-research-action-plan-2016-2019

EPA also has funded the creation of the EPA Science to Achieve Results (STAR) Center for Organotypic Culture Models, a Predictive Toxicology Center for Organotypic Cultures and Assessment of AOPs (adverse outcome pathways) for Engineered Nanomaterials. The overall goal of this center is to develop innovative organotypic culture systems to better evaluate the potential for cellular and organ toxicity following exposure to ENMs within an AOP model. The funding period for this center is December 2014–November 2018.⁸⁵

In 2017, EPA researchers published a review article outlining a comprehensive framework for evaluating the health and safety implications of ENM releases into the environment, including purposeful releases such as for antimicrobial sprays or nanotechnology-enabled pesticides, and inadvertent releases as a consequence of other intended applications.⁸⁶ EPA plans for 2018 include development of decision support tools incorporating data on physiochemical transformations, exposure, and effects of ENMs.

EPA and CPSC: EPA and CPSC are nearing completion of a collaborative research project evaluating potential release of copper from pressurized copper-treated commercial wood products. The composition, particle size distribution, leaching, bioavailability, and exposure to micronized copper have been evaluated. Reports are now available to the public.⁸⁷ EPA has entered into a new research collaboration with CPSC on application and utilization of the CPSC wipe method for comparison across (product) matrices and with different emerging nanomaterials; characterization of the nanomaterial products either in development or currently available in the marketplace; evaluation of the potential for exposure from the use of the products identified through oral and inhalation exposure routes using *in vitro* assays; characterization of the aerosol formation from application of emerging nanomaterials to surfaces; and determining the pulmonary, cardiovascular, and neurological responses to inhalation of the emerging nanomaterials during applications and throughout the life cycle.

EPA and NSF: EPA and NSF have partnered in support of a 2014–2017 university grant entitled “Network for Characterizing Chemical Life Cycle: Life Cycle of Nanomaterials.” This project is evaluating the trade-offs between using nanomaterials to improve the functionality of consumer products and the potential risk to humans and the environment.⁸⁸

FDA: In 2016, FDA centers continued to provide research funding for regulatory science projects related to the products under their purview. This funding includes research projects for medical products such as devices, new drugs and generic drugs, foods, feeds, sunscreens, and food contact material. The FDA Office of the Chief Scientist funded several cutting-edge projects focused on cross-agency nanotechnology-related issues through the Collaborative Opportunities for Research Excellence in Science grants program. With funding beginning in 2006, over 36 research projects have led to the development of vital regulatory science tools such as biological and toxicological assays, assessment methodologies, and test protocols that FDA staff members use when reviewing the safety and efficacy of nanotechnology in FDA-regulated products.

Additionally, the Center for Drug Evaluation and Research supported over 20 individual projects on drug products containing nanomaterials in 2016. The projects encompassed characterization, pharmacology and toxicology, efficacy, manufacturing, quality assurance, and equivalence issues for drug products containing nanomaterials. Examples include the following:

- Establishing a robust particle counting technique to improve regulatory review of drug products containing nanomaterials.

⁸⁵ cfpub.epa.gov/ncer_abstracts/index.cfm/fuseaction/display.abstractDetail/abstract/10443/report/0

⁸⁶ www.ncbi.nlm.nih.gov/pubmed/28661217 (doi: 10.1080/10408444.2017.1328400)

⁸⁷ nepis.epa.gov/Exe/ZyPDF.cgi?Dockkey=P100LJWI.txt

⁸⁸ cfpub.epa.gov/ncer_abstracts/index.cfm/fuseaction/display.abstractDetail/abstract/10212/report/0

Appendix A. NNI Research by Program Component Area

- Advanced characterization and modeling of complex formulations and dosage forms for drug products containing nanomaterials.
- Continuous manufacturing of drug products containing nanomaterials.
- Bioequivalence of colloidal iron products.

FDA will continue to support agency-wide collaborative nanotechnology research in 2018.

FDA and CPSC: In 2014, FDA collaborated with CPSC through an interagency agreement on assessing whether current methods for determining migration of conventional additives are applicable to the evaluation of nanomaterial migration from solid and semi-solid materials used in consumer products that contact food. This work continued through 2017.

FDA, NIH, and SDOs: The NIH/NIEHS National Toxicology Program (NTP) and FDA are actively collaborating in toxicological research to understand the health hazards of nanomaterials (hazard assessment) and to develop novel methods and approaches for detection of nanomaterials in FDA-regulated products. This collaboration has included physicochemical characterization and standards development processes to enable responsible development of nanotechnology. The National Center for Toxicological Research-Office of Regulatory Affairs Nanocore at FDA's National Center for Toxicological Research (NCTR) is involved in collaborative consensus-based standards development with support from NTP, and is co-developing standards with SDOs. Examples of these collaborative activities include the following:

- In 2016, a cryo-transmission electron microscopy standard guide for liposome evaluation was proposed as a work item at the ASTM E56 subcommittee on Nanotechnology. Additional relevant standards are under consideration for co-development.
- Collaborative research with between NIEHS and NCTR/FDA led to the Global Summit on Regulatory Science (GSR516): "Nanotechnology Standards and Applications" that was held in collaboration with other governments, industry, and academic stakeholders to prepare a prioritized list of standards needed for regulation of nanotechnology-enabled medical products.
- NIH/NIEHS-FDA collaboration led to the development and validation of test methods for three assays from the "NCL assay cascade."

FDA, NIH, and NIST: FDA's Center for Biologics Evaluation and Research (CBER), in collaboration with the NIH/NCI NCL and NIST, is characterizing blood and vascular toxicity of engineered and biologic nanoparticles. This collaboration will continue with characterization of immunological properties of nanoparticles, with a focus on engineering biologic nanoparticles for optimum safety and efficacy profile.

NIH: EHS activities at NIH are led by NIH/NIEHS. NIH/NIEHS research efforts are designed to gain a fundamental understanding of the molecular and pathological pathways involved in mediating responses to engineered nanomaterials. Towards this goal, comprehensive biological response profiles are needed to gain detailed molecular understanding of the interactions between ENMs and biological systems.

To continue the success achieved with a small library of ENMs in the recently concluded NIH/NIEHS Centers for Nanotechnology Health Implications Research (NCNHIR) consortium, the Nanotechnology Health Implications Research (NHIR) consortium was established in September 2016 through two funding opportunities (RFA-ES-15-013 and RFA-ES-15-012, issued in October 2015). This consortium consists of nine academic research laboratories across the United States. The NHIR consortium had its first meeting and developed plans to prioritize the criteria for selection of sets of ENMs (present in consumer products as well as emerging 2D and 3D materials) to be investigated by using a wide range of test systems reflecting physiologically relevant models.

Appendix A. NNI Research by Program Component Area

The NHIR consortium investigators have started working on an initial set of ENMs, using diverse routes of exposure (inhalation, ingestion, and ocular). The engineered nanomaterials resource and coordination core at one of the participating universities is organizing a series of training sessions and webinars as an outreach program of the NHIR consortium.

The NIH/NIEHS NTP completed a short-term evaluation of the immune system impact of inhalation of multi-walled carbon nanotubes in rodent models to better understand the potential health effects from low-dose exposures in workers. This research complements exposure assessment of nanomaterial manufacturing facilities conducted in collaboration with NIOSH.

One example of recent advances from NIH/NIEHS-supported research is a project in which it was determined that aerosolized citrate-coated silver nanoparticles (Ag NPs) produce a delayed, short-lived inflammatory pulmonary response in rats. Ag NPs are increasingly being used to produce disinfectants due to their antimicrobial properties. New methods are being developed to produce more uniform Ag NPs through chemical reactions, and these reactants are present as contaminants or coatings on the Ag NPs. The responses peaked at day 7, and inflammation was resolved by day 56. Smaller Ag NPs persisted for longer and to a greater degree than the larger Ag NPs. While it is unclear whether Ag NPs or their coatings will adversely affect human health, this study provides information on the potential health effects of inhaling citrate-coated Ag NPs with consideration to recovery time and particle size.

In 2018, NIH/NIEHS is planning a FOA to initiate a program to develop tools for monitoring personal exposure to ENMs in the environment. The institute's small business program is also planning to invest in the development of high- to medium-throughput assay systems for toxicity testing of ENMs. Meanwhile, NTP has initiated a two-year chronic toxicity evaluation of MWCNTs in rodent models to better understand the potential health effects from low-dose "lifetime" exposures. This work will continue into 2018. The NHIR consortium will also be funded through 2021.

NIOSH: During 2016 NIOSH researchers published 132 peer-reviewed journal articles, published *Building a Safety Program to Protect the Nanotechnology Workforce: A Guide for Small to Medium-Sized Enterprises*,⁸⁹ released a draft Current Intelligence Bulletin (CIB), *Health Effects of Occupational Exposure to Silver Nanomaterials*,⁹⁰ and held a public meeting to discuss the CIB. One highlight of the 2016–2017 journal publications includes an update to the Nanoparticle Exposure Assessment Technique. NIOSH continues its efforts to develop more complete hazard and safety assessments using key classes of engineered nanomaterials, including the following types: carbon nanotubes; metal oxides; silver; the nanowire forms of silver, silica, and titania; graphene and graphene oxide; and cellulose nanocrystals and nanofibers. In 2017, NIOSH continued its efforts to develop "real world" evaluation of hazard and risk represented by various nanomaterials through their life cycles. In 2017, NIOSH published results from an *in vivo* toxicity assessment of occupational components of the life cycle of carbon nanotubes used in composites to provide context to potential health effects.⁹¹ In 2014–2016, NIOSH expanded its field investigation efforts to include a focused effort on developing risk management practices that support responsible development of nanotechnology.

⁸⁹ www.cdc.gov/niosh/docs/2016-102/pdfs/2016-102.pdf

⁹⁰ www.cdc.gov/niosh/docket/review/docket260a/pdfs/draft--niosh-cib-on-silver-nanomaterials-1_8_16.pdf

⁹¹ pubs.acs.org/doi/abs/10.1021/acsnano.7b03038 (doi: 10.1021/acsnano.7b03038)

In 2017, that particular element of the NIOSH field research effort is focusing on outputs that support the Sustainable Nanomanufacturing NSI along the life cycle of the nanomaterial.

NIOSH is considered to be a world leader in nanotoxicology. During 2016–2017, many NIOSH toxicology researchers received prestigious recognitions including publishing a paper that was ranked in 2017 as the most cited paper in the last ten years by a major peer-reviewed technical journal publisher.⁹²

One particle detection instrument has already been patented and licensed by NIOSH and is being manufactured by an instrument company. An advanced version of that instrument capable of elemental analysis is under development by NIOSH, and a prototype was created in 2016. During 2016–2017 NIOSH investigated the usefulness of a newly developed, direct-reading, aerosol multielement spectrometer (AMS) that measures size-selective elemental concentrations of aerosols, including airborne nanomaterials, bulk powders, and surface wipe samples in the workplace.

NIOSH is expanding its research activities that have direct connections to sustainable manufacturing. Many activities carried through 2016–2017 focused on safe and responsible development of nanomaterials, nanomanufacturing processes, and NEPs throughout the life cycle. In 2016, NIOSH continued to develop case studies that demonstrate the utility of applying Prevention through Design (PtD) principles to nanomanufacturing. NIOSH utilizes the best available evidence to develop occupational safety and health guidance. Worker health and safety principles and practice support the development of sustainable and advanced manufacturing.

NIOSH 2017 activities and plans for 2018 include the following:

- Release the draft CIB, *Approaches to Developing Occupational Exposure Limits or Bands for Engineered Nanomaterials*, that was cited as the basis for the framework described in ISO/TR 18637:2016. In addition, NIOSH plans to update the risk assessment and finalize the CIB on occupational exposure to silver nanomaterials. NIOSH will continue with foundational toxicological research and focus on the determinants of disease including biomarkers.
- Publish information on individual process-based control strategies (workplace design solutions) to promote effective and sustainable engineering controls.
- Continue efforts to apply PtD principles to the design of safer nanomaterials by identifying physicochemical properties of nanomaterials that could be modified to decrease adverse biological responses. NIOSH will continue to utilize the principles of research to practice in developing occupational safety and health guidance that can be incorporated into an organization's business plan in a way that worker safety is protected and, in turn, more rapid application development and commercialization can be realized.
- Sustain investment in the development, testing, and evaluation of direct-reading instruments capable of detecting and measuring airborne nanoparticles. NIOSH will field test the AMS at nanomaterial producer and user facilities.
- Continue efforts in detection of airborne nanoparticles into specific applications in the areas of detection of nanomaterials in biologic systems to evaluate and predict biological behavior and translocation between organ systems. An aligned effort is the reapplication of more sensitive and specific detection technology to evaluate worker exposures to nanomaterials, with an ultimate goal of real-time detection. Starting in 2016 and continuing into 2018, NIOSH has been evaluating the feasibility of applying advanced sensing technology to biomarkers as a means of evaluating nanomaterial exposure and possible early response in support of ongoing nanomaterial worker surveillance.

⁹² www.sciencedirect.com/science/article/pii/S0041008X12001263 (doi: 10.1016/j.taap.2012.03.023)

Appendix A. NNI Research by Program Component Area

- Conduct individual nanotoxicology research projects evaluating biomarkers, cardiovascular toxicity, pulmonary exposure to nanoclays and boron nitride nanotubes, copper nanoparticles in dust from treated wood, and the generation and characterization of aerosols from nanocomposites. The majority of NIOSH's foundational toxicology research continues to be conducted intramurally and is supplemented by strategic extramural collaborations (see collaborative examples, below).

NIOSH, other NNI agencies, industry, and SDOs: NIOSH participates with a number of other NNI agencies, industry, and with multiple SDOs on development of nanotechnology-related EHS (nanoEHS) protocols and standards. Some highlights include the following:

- Chaired ISO TC 229 Working Group 3 and developed ISO/TR 18637:2016, "Nanotechnologies — Overview of available frameworks for the development of occupational exposure limits and bands for nano-objects and their aggregates and agglomerates (NOAAs)," in 2016.
- Collaborated in developing an ASTM standard guide on detection and characterization of silver nanoparticles in textile products (published in 2016).
- Worked with international metrology institutes in developing protocols for determination of nanoparticle size and size distribution for numerous morphologies of industrially relevant metal and metal oxide nanomaterials that will be disseminated as ISO standards.
- In 2017–2018, continues leading the development of ISO/TR 12885, "Health and safety practices in occupational settings relevant to nanotechnologies," which aims to ensure that workers handling nanomaterials are protected not only in the United States, but also in countries around the world.

NIOSH, NIST, STPI, and academia: NIOSH, NIST, the Science and Technology Policy Institute (STPI), and two universities are collaborating on a Partnership to Advance Research and Guidance for Occupational Safety and Health in Nanoelectronics. This collaboration leverages an existing nanotechnology health and safety center at one of the participating universities and NIOSH's Nanotechnology Research Center to advance research and education, as well as to develop workplace safety and health recommendations. NIOSH and its partners plan to extend this collaboration into broader areas of advanced manufacturing during 2017–2018, and have identified private-sector organizations that have expressed interest in a public-private partnership to promote safe practices in nanotechnology and advanced manufacturing. A kick-off session was part of a 2017 international innovation conference, and an in-depth meeting is being planned for 2018.

NIOSH, other NNI agencies, and industry: To fully understand the potential health and safety impacts of nanotechnology, NIOSH utilizes field research teams that visit nanomaterial producers and users and conduct industrial hygiene evaluations. During 2016, NIOSH collaborated with 10 companies that extended invitations to the field team. NIOSH is also working with industry trade associations to promote education and training on risk management for nanomaterials. In 2017–2018, NIOSH continues its efforts to develop practical, "real world" evaluation of hazard and risk represented by various nanomaterials through their life cycles. NIOSH field research efforts will focus on outputs that support the Sustainable Nanomanufacturing NSI along the life cycle of the nanomaterial, including advanced manufacturing and evaluation of potential emissions from 3D printers.

NIOSH, NASA, academia, and industry: Historically, NIOSH funded a university in the development of a thermophoretic sampler for collection of nanomaterials directly on an electron microscope grid. This sampler has since been marketed by a company, and in 2016, NASA deployed the sampler to the International Space Station for collection of fine particles including nanomaterials. NIOSH will continue collaborations to evaluate the thermophoretic sampler at various nanomaterial producer and user facilities.

NIOSH, other NNI agencies, government laboratories, academia, and industry: NIOSH has worked with the Nanoinformatics Consortium (including other NNI agencies, government labs, universities, and industry) to plan a series of workshops, contributing NIOSH knowledge and expertise to the larger informatics effort.

NIOSH and international organizations: NIOSH has continued to partner with multiple European organizations on the Dustinano project. The project has been comparing “dustiness” (i.e., particle release with respect to inhalation exposure) evaluation methods for a limited set of nanomaterials, and is exploring the utility of dustiness as a metric for risk management decision making.

NIOSH, industry, and academia: NIOSH will use strategic partnerships with business and academia to develop and deploy effective nanoEHS practices, with emphasis on occupational safety and health, that can be incorporated into business and research plans. NIOSH will extend and reapply knowledge gained from sustainable nanomanufacturing into other areas of advanced manufacturing.

NIOSH and CPSC: NIOSH will work with CPSC in studying ENM emissions (CNTs, graphene) from 3D printers, and on *in vitro* and *in vivo* toxicology studies during 2018.

NIOSH and academia: NIOSH will continue collaborations with universities in the United States and abroad on studies of fabrication, characterization, transformation, and toxicology of a wide variety of nanomaterials of current and potential commercial interest.

NIST: In 2016, NIST reported novel validated methods and approaches for physico-chemical and biological measurements in complex environmental and biological media, and advanced the available metrology for a range of nanoscale materials:

- For broadly applicable methods, NIST demonstrated the capability of a hyphenated instrument (i.e., two commercial instruments coupled together) for simultaneously measuring the size and composition of nanoparticles and their agglomerates, developed a cloud point extraction approach to analyze metallic nanoparticles in a soil matrix, and used single-particle inductively coupled plasma mass spectrometry and microscopy methods to determine bioaccumulation and particle size distribution of gold nanoparticles ingested by whole organism *C-elegans* worms.
- NIST performed a number of studies on EHS-related measurements of carbon nanotube systems. For example, for CNT-epoxy nanocomposites, NIST reported a novel differential-charging x-ray photon spectroscopy method to detect carbon; the capability for 3D subsurface imaging of CNTs by scanning electron microscopy (SEM); and the use of multiple methods to determine the impact of ultraviolet (UV) radiation on the formation of an entangled, release-resistant network of CNTs on the surfaces of nanocomposites.
- NIST’s protocols for accelerating laboratory weathering and measurements of degradation of MWCNT polymer composites indicated that UV irradiation leads to a dense, entangled network structure on the polymer surface that appears to inhibit CNT release.
- NIST studies of performance and aging of graphene oxide/polyurethane composites revealed insights into the concentration of released graphene-based nanomaterials from aged composites as well as measurement challenges for these materials.
- After identifying flaws in a test historically used to determine single-wall carbon nanotubes (SWCNTs), NIST developed a new method that properly identifies the type and number of SWCNTs in a sample, to help researchers in isolating and characterizing SWCNTs to determine the health effects of each specific tube type and then ultimately remove those with adverse environmental or health impacts.
- For silver nanoparticles, several notable NIST accomplishments include a new SEM methodology to quantitatively determine the particle distribution in cotton threads simulating textile materials, *in*

situ methods to monitor nanoparticle sulfidation in simulated waters, and a method to detect and quantify the entire distribution of silver species in environmental media.

In 2017 and 2018, much of the work described above is expected to continue as NIST develops validated methods for physico-chemical and biological measurements. For example, NIST will develop methods to simultaneously measure nanoparticle size, mass, number concentration, and apparent density; broaden its cloud point extraction approach to include a wider range of nanomaterials and matrices; investigate transformations of silver nanoparticles released from textile materials; correlate the surface properties of a gold nanoparticle-based anti-tumor model to its drug loading, drug release, and stability for biomedical applications; and evaluate the applicability of an ISO standard method for *C-elegans* growth and reproduction inhibition using a broad range of nanoparticles.

NIST will continue to make nanotechnology-related reference materials available to academic, industry, and government stakeholders. For example, in 2017, NIST will make available Standard Reference Material 2843, a MWCNT soot with certified values for impurity metal fractions in the soot, and four new protocols will be added to NIST's publicly available website,⁹³ bringing the total number of protocols to 24.

NIST and FDA: In 2016, NIST and FDA developed reproducible methods to release silver nanoparticles from food containers by wear processes and to examine the container surfaces for free silver nanoparticles. This joint research will enable evaluation of potential risks of nanosilver in food applications.

NIST, EPA, NIOSH, CPSC, OSHA, Canada, industry, and non-governmental organizations: U.S. and Canadian federal agencies, including the U.S. Occupational Safety and Health Administration (OSHA), and industry completed two pilot interlaboratory studies (ILSs) to assess the potential release of CNTs from CNT-polymer-based composites by sanding and by weathering. Data and metadata from these two ILSs have been entered into the NanoRelease Data Repository hosted by NIST.

NIST and Canada: NIST and Canada's national metrology institute will develop and validate an asymmetric flow field-flow fractional method optimized for size separation and characterization of nanocrystalline cellulose.

NIST and international organizations: NIST, in partnership with a variety of international research and metrology institutes, determined the robustness of a NIST-developed *in vitro* nanocytotoxicology assay defined by nine quality metrics via an interlaboratory study.⁹⁴ Future plans for this partnership include developing two silica reference materials with certified values for zeta potential, a key characteristic that determines the stability of nanoparticles in solution.

NIST and EPA: In 2016, results of an investigation on bioaccumulation categorization of carbon nanotubes with ecological receptors were reported by NIST and EPA.⁹⁵

NIST and CPSC: NIST and CPSC are in the fifth year of a multi-year collaboration to develop testing and measurement protocols for determining the quantities and properties of nanoparticles released from floor coatings and paints induced by abrasion and/or weathering. Accomplishments to date include protocols and methodologies for characterizing particles released following rotary abrasion (both dry and wet), and for measurement of nanoparticle releases due to weathering, nanoparticle release by abrasion after weathering, and nanoparticle release from dry abrasion of coatings containing an antimicrobial agent in nanoparticle form.

⁹³ www.nist.gov/mml/nanoehs-protocols.cfm

⁹⁴ www.altex.ch/resources/altex_2017_2_201_218_Elliott.pdf (doi: 10.14573/altex.1605021)

⁹⁵ pubs.acs.org/doi/abs/10.1021/acs.est.6b01916 (doi: 10.1021/acs.est.6b01916)

NIST plans to continue work with CPSC on multi-year projects. For example, one project underway in 2017 is to detect and quantify CNTs released from CNT-polymer nanocomposite filaments used in 3D printing. In 2017 and 2018, NIST plans to develop reproducible and representative methods for air sampling around a 3D printer and for detecting and determining the concentration of CNTs in air samples. Methods will also be developed for evaluating CNTs released during abrasion and wear of hand tools fabricated from CNT-polymer composites by 3D printing. In a parallel effort to ongoing collaborations with CPSC, NIST researchers will engage with ASTM E56.06 on the development of test methods and guidelines.

NSF: The nanoEHS program within ENG was renamed Biological and Environmental Interactions of Nanoscale Materials, with a revised program description.⁹⁶ The program solicits proposals focused on exploring and understanding how, why, and under what circumstances nanomaterials interact and transform.

In 2017, NSF continued its funding for nanoEHS research at over 4% of its overall NNI investment. Requests for EHS research are primarily directed at understanding nano-bio phenomena and processes, as well as EHS implications and methods for reducing the respective risks of nanotechnology development. The NNCI plans to expand research on societal implications of nanotechnology at its nodes.

NSF and EPA: NSF and EPA are jointly sponsoring research on environmental implications of nanotechnology, including development of new measurement methods for nanoparticle characterization and toxicity of nanomaterials, under an interagency agreement that continues through 2018. This NSF/EPA collaboration supports the two dedicated multidisciplinary university Centers for Environmental Implications of Nanotechnology (CEIN); annual awards are approximately \$4 million each. Essential elements include research on methods and instrumentation for nanoparticle detection, characterization, monitoring, and environmental risk analysis, including interactions of nanomaterials with cellular constituents, metabolic networks, and living tissues; bioaccumulation and its effects on living systems; and the impacts of nanostructures dispersed in the environment. The CEIN centers also continue to increase dissemination of information to government regulators at state and Federal levels and to industry stakeholders, with a focus on decision support tools, nanosafety training, and consumer product safety.

USDA/FS, academia, and industry: In 2016, Forest Service researchers began participating in a project, as subject matter experts, to classify cellulose nanomaterials as “generally recognized as safe” (GRAS) through scientific procedures for use as food additives. Besides the Forest Service, several companies and academic experts are participating in this project.

USDA/NIFA: The NIFA nanotechnology programs support the EHS research targets that are most relevant to agricultural production and food applications. Appropriate EHS assessments of engineered nanoparticles applied in food and agricultural systems include characterization of hazards, exposure levels, and transport and fate of engineered nanoparticles or nanomaterials in crops, soils (and soil biota), and livestock. These assessments may also include animal feed formulations and processes that utilize novel nanomaterials or the development of new nanostructured materials or nanoparticles that are bio-persistent in digestive pathways. The AFRI Improving Food Safety program supports research applications dealing with the development and validation of concentration, purification, and detection methods for engineered nanoparticles as contaminants in foods; transport and fate of the engineered nanoparticles or nanomaterials associated with food production and processing; as well as control strategies.

AFRI research has focused on the fate and transformation of engineered nanomaterials in the human gastrointestinal tract (GIT). AFRI-funded university scientists have developed gastrointestinal tract *in vitro*

⁹⁶ www.nsf.gov/funding/pgm_summ.jsp?pims_id=505424

Appendix A. NNI Research by Program Component Area

models to investigate the behaviors of various nanoscale cellulosic materials in the GIT and their interaction with gut microbiome. A project elucidated absorption, accumulation, and toxicity mechanisms of titanium dioxide nanoparticles present in foods in the human GIT. The experimental results showed that TiO₂ NPs induced more pronounced adverse effects on mice fed with higher-fat diet in comparison with those fed with a lower-fat diet. If these effects also occur in humans, they could have significant implications for people with high-fat diets.

USDA/NIFA, NSF, and EPA: USDA/NIFA, jointly with NSF and EPA supported the fourth Gordon Research Conference on Environmental Nanotechnology held in the summer of 2017. The conference brought together academic, government, and industrial scientists and engineers from around the world for the exchange of ideas, analytical methods, and experimental approaches that balance the beneficial aspects of nanotechnology against the potential adverse risks to humans and the environment. Applications of nanomaterials for food and agriculture were discussed, as well as their potentially negative or positive implications for the environment.

APPENDIX B. ABBREVIATIONS AND ACRONYMS

AFOSR	Air Force Office of Scientific Research	EERE	Office of Energy Efficiency and Renewable Energy (DOE)
AFRI	Agriculture and Food Research Initiative (USDA/NIFA)	EHS	environment(al), health, and safety
AFRL	Air Force Research Laboratory	ENG	Engineering Directorate of NSF
AMO	Advanced Manufacturing Office (DOE/EERE)	ENM	engineered nanomaterial
ANL	Argonne National Laboratory (DOE)	EPA	Environmental Protection Agency
ARDEC	Armament Research, Development and Engineering Center (DOD/U.S. Army)	ERC	Engineering Research Centers (NSF)
ARL	Army Research Laboratory	ERDC	Engineer Research and Development Center (DOD/U.S. Army)
ARPA-E	Advanced Research Projects Agency-Energy (DOE)	EU	European Union
ARS	Agricultural Research Service (USDA)	FDA	Food and Drug Administration (DHHS)
BES	[Office of] Basic Energy Sciences (DOE)	FE	Office of Fossil Energy (DOE)
BIO	Directorate for Biological Sciences (NSF)	FHWA	Federal Highway Administration (DOT)
BIS	Bureau of Industry and Security (DOC)	FOA	Funding Opportunity Announcement
BRC	Basic Research Challenge (ONR program)	FS	Forest Service (USDA)
caNanoLab	cancer Nanotechnology Laboratory portal (NIH/NCI)	GC	grand challenge
CISE	Directorate for Computer and Information Science and Engineering (NSF)	IARPA	Intelligence Advanced Research Projects Activity (IC)
CNST	Center for Nanoscale Science and Technology (DOC/NIST)	IC	Intelligence Community
CNT	carbon nanotube	IRAD	Internal Research and Development (program)
COR	Community of Research	IRCN	Innovative Research in Cancer Nanotechnology (NIH program)
CPSC	Consumer Product Safety Commission	ISO	International Organization for Standardization
CRISPR	clustered regularly interspaced short palindromic repeats (short for CRISPR/Cas9 genome editing technology)	LANL	Los Alamos National Laboratory (DOE)
DARPA	Defense Advanced Research Projects Agency	LBNL	Lawrence Berkeley National Laboratory (DOE)
DHHS	Department of Health and Human Services	MPS	Mathematical and Physical Sciences Directorate of NSF
DHS	Department of Homeland Security	MRSEC	Materials Research Science and Engineering Centers (NSF)
DOC	Department of Commerce	MWCNT	multi-walled carbon nanotube
DOD	Department of Defense	nanoEHS	nanotechnology environment, health, and safety (research, etc.)
DOE	Department of Energy	NASA	National Aeronautics and Space Administration
DOEd	Department of Education	NCI	National Cancer Institute (DHHS/NIH)
DOJ	Department of Justice	NCL	Nanotechnology Characterization Laboratory (DHHS/NIH/NCI)
DOL	Department of Labor	NCTR	National Center for Toxicological Research (FDA)
DOS	Department of State	NEHI	Nanotechnology Environmental and Health Implications Working Group of the NSET Subcommittee
DOT	Department of Transportation	NEP	nanotechnology-enabled product
DOTreas	Department of the Treasury		
DTRA	Defense Threat Reduction Agency (DOD)		
E2CDA	Energy-Efficient Computing: from Devices to Architectures (NSF program)		

Appendix B. Abbreviations and Acronyms

NERC	Nanosystems Engineering Research Center (NSF)	PCA	Program Component Area of the National Nanotechnology Initiative
NEWT	Nanotechnology-Enabled Water Treatment Systems (NSF NERC)	PGM	platinum group metal
NHIR	Nanotechnology Health Implications Research consortium (NIH/NIEHS)	PNNL	Pacific Northwest National Laboratory (DOE)
NHLBI	National Heart, Lung, and Blood Institute (DHHS/NIH)	RFA	request for applications
NIBIB	National Institute of Biomedical Imaging and Bioengineering (DHHS/NIH)	SBE	Social, Behavioral & Economic Sciences Directorate (NSF)
NICE	Nanotechnology Innovation and Commercialization Ecosystem Working Group of the NSET Subcommittee	SBIR	Small Business Innovation Research Program
NIDCR	National Institute of Dental and Craniofacial Research (DHHS/NIH)	SDO	standards developing organization
NIEHS	National Institute of Environmental Health Sciences (DHHS/NIH)	SNL	Sandia National Laboratory (DOE)
NIFA	National Institute of Food and Agriculture (USDA)	STARnet	Semiconductor Technology Advanced Research Network (DARPA, industry, universities)
NIH	National Institutes of Health (DHHS)	STEM	science, technology, engineering, and mathematics
NIOSH	National Institute for Occupational Safety and Health (DHHS/CDC)	STTR	Small Business Technology Transfer Research Program
NIST	National Institute of Standards and Technology (DOC)	USDA	U.S. Department of Agriculture
NITRD	Networking and Information Technology R&D	USGS	U.S. Geological Survey
NKI	Nanotechnology Knowledge Infrastructure (Nanotechnology Signature Initiative)	USITC	U.S. International Trade Commission
nm	nanometer(s)	USPTO	U.S. Patent and Trademark Office (DOC)
NNCI	National Nanotechnology Coordinated Infrastructure (NSF)		
NNCO	National Nanotechnology Coordination Office		
NNI	National Nanotechnology Initiative		
NRC	Nuclear Regulatory Commission		
NRL	Naval Research Laboratory		
NSET	Nanoscale Science, Engineering, and Technology Subcommittee of the NSTC		
NSF	National Science Foundation		
NSI	Nanotechnology Signature Initiative		
NSRC	Nanoscale Science Research Centers (DOE)		
NSTC	National Science and Technology Council		
NTP	National Toxicology Program (DHHS/NIH/multiagency)		
OMB	Office of Management and Budget (Executive Office of the President)		
ONR	Office of Naval Research		
ORNL	Oak Ridge National Laboratory (DOE)		
OSHA	Occupational Safety and Health Administration (DOL)		
OSTP	Office of Science and Technology Policy (Executive Office of the President)		

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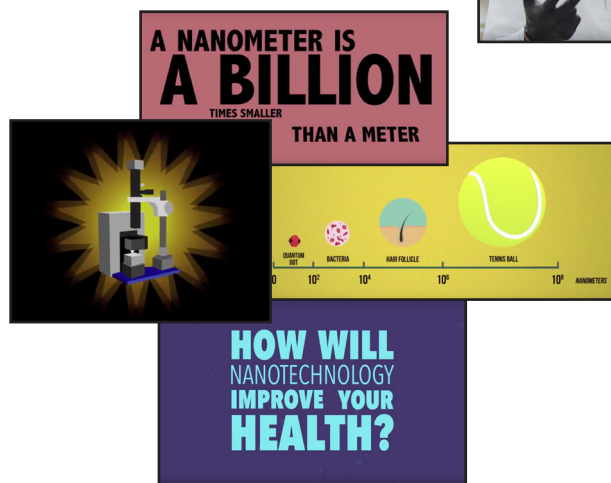
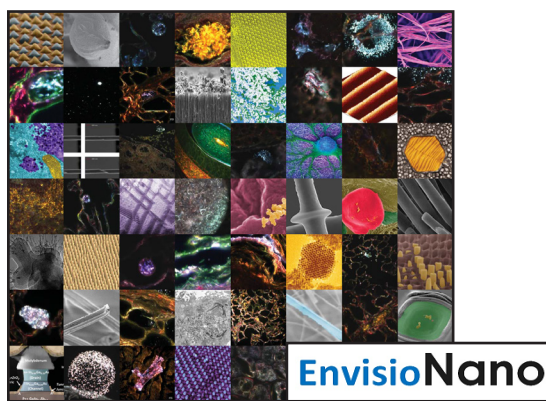
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Images Illustrating Examples of NNI Educational Outreach Activities

Clockwise from top left

- *Nano Nuggets* (www.nano.gov/nanotv) are short videos featuring experts, visionaries, and students sharing their thoughts on nanotechnology.
- *EnvisioNano* (www.nano.gov/envisioNano) and *Nano Film* (www.nano.gov/VideoContest) highlight the accomplishments of the NNI to help educate the general public about nanotechnology.
- The U.S. Nano & Emerging Technologies Student Network (www.nano.gov/StudentNetwork) raises awareness of current research and cutting edge technologies, promotes opportunities, and provides an interdisciplinary community for undergraduate students. This network organizes the annual Student Leaders Conference.
- *Generation Nano: Small Science, Superheroes!* (www.nsf.gov/news/special_reports/gennano/index.jsp), a competition presented by the NSF and the NNI, asks high school students to design nanotechnology-enabled gear for an original superhero and create a comic/video featuring their hero using the gear.
- Animations (www.nano.gov/TargetCancerCells) on nanotechnology are prepared by university graphic design students. The NNCO develops the scripts and provides technical guidance during the project.
- The Teaching Nano & Emerging Technologies Network (www.nano.gov/TeacherNetwork) connects teachers to facilitate access to classroom-ready resources and share best practices. The network hosts webinars featuring educators.



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