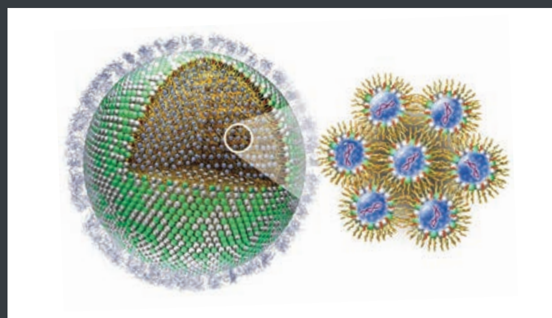
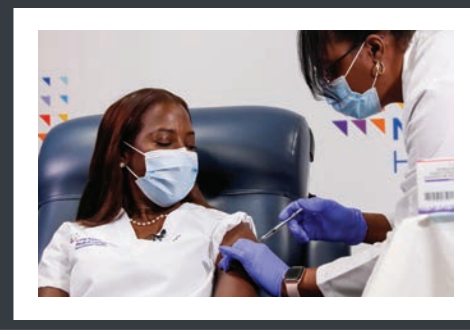
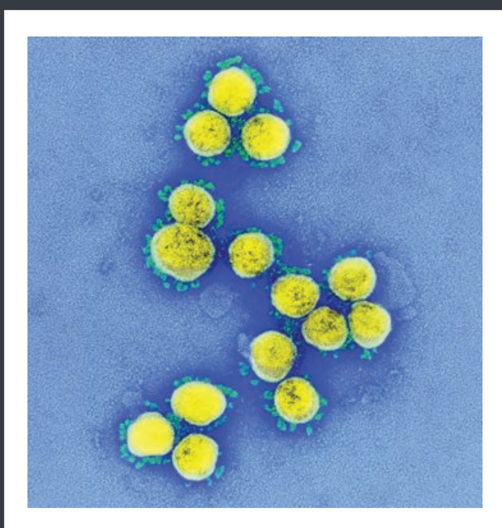
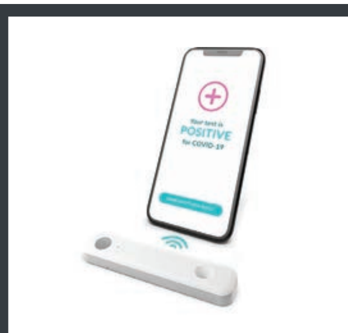
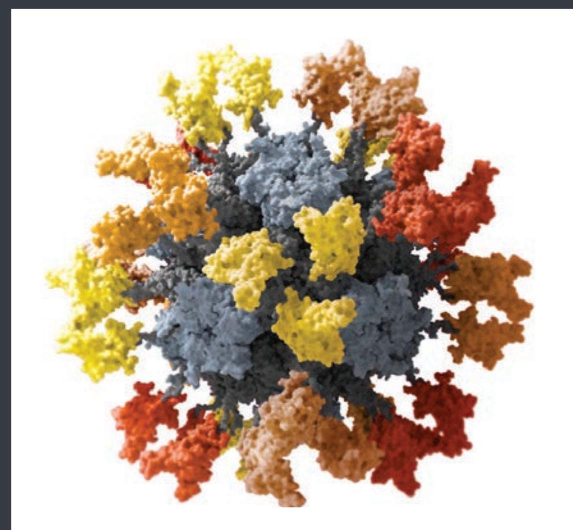
THE NATIONAL NANOTECHNOLOGY INITIATIVE SUPPLEMENT TO THE PRESIDENT'S 2022 BUDGET

Product of the

SUBCOMMITTEE ON NANOSCALE SCIENCE, ENGINEERING, AND TECHNOLOGY

COMMITTEE ON TECHNOLOGY

of the
NATIONAL SCIENCE AND TECHNOLOGY COUNCIL

MARCH 2022

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 to ensure that science and technology policy decisions are consistent with the President's stated goals. 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. 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 (OMB) 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 the Subcommittee on Nanoscale Science, Engineering, and Technology

The Subcommittee on Nanoscale Science, Engineering, and Technology (NSET) contributes to the activities of NSTC's Committee on Technology. NSET's purpose is to advise and assist the NSTC and OSTP on policies, procedures, and plans related to the goals of the National Nanotechnology Initiative (NNI). As such, and to the extent permitted by law, NSET Subcommittee defines and coordinates Federal efforts in support of the goals of the NNI and identifies policies that will accelerate deployment of nanotechnology. NSET also tracks national priority needs that would benefit from the NNI, identifies extramural activities that connect to NNI goals, and explores ways the Federal Government can advance the development of nanotechnology. More information is available at https://www.nano.gov/.

About this document

This document is a supplement to the President's 2022 Budget request submitted to Congress on May 28th, 2021, 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 (15 USC §7501). The report also addresses the requirement for Department of Defense reporting on its nanotechnology investments (10 USC §2358). Additional information regarding the NNI is available on the NNI website at www.nano.gov.

Cover, book design, and copyright information

Published in the United States of America, 2022.

About the Cover

Outer Covers: The front cover images highlight the role of nanotechnology in the coordinated U.S. Government effort to fight the COVID-19 pandemic. ***Top left:*** A roll of N95 filter material made and studied at the Department of Energy (DOE) Oak Ridge National Laboratory (ORNL) to determine efficiency against the SARS-CoV-2 virus. Neutron spectroscopy and advanced microscopy available at the Center for Nanophase Materials Sciences NNI user facility were used to analyze three different blends of the material to determine the characteristics necessary for enhancing filter efficiency. The research was part of the DOE COVID-19 manufacturing research response. The research was transitioned by industrial partners, supplying millions of masks throughout the United States. Image credit: DOE/ORNL; funded by DOE and the Department of Health and Human Services (HHS). ***Top center:*** Artist's (computerized) rendition of lipid nanoparticles used in the messenger RNA (mRNA) vaccine formulations to safely and efficiently deliver the fragile mRNA inside cells. Image credit: Genevant Sciences. ***Top right:*** Photograph of the first person to be vaccinated against SARS-CoV-2 in the United States using an mRNA-lipid nanoparticle vaccine, on December 14, 2020, less than a year after the SARS-CoV-2 virus was sequenced. Image credit: Northwell Health; funded in part by HHS/Biomedical Advanced Research and Development Authority. ***Bottom left:*** Transmission electron micrograph of SARS-CoV-2 virus particles, isolated from a patient. Image credit: captured and color-enhanced at the National Institutes of Health (NIH)/National Institute of Allergy and Infectious Diseases (NIAID) Integrated Research Facility; funded by NIH/NIAID. ***Center:*** A quantum-dot-based digital fluorescence immunoassay antigen home COVID-19 test, one of the many nanotechnology-enabled SARS-CoV-2 tests that were developed quickly after the onset of the pandemic. Image credit: Ellume; funded in part by the NIH Rapid Acceleration of Diagnostics (RADx) Initiative. ***Bottom center:*** A commercial nanotechnology-enabled air purifier that is FDA-cleared for the destruction of viruses and bacteria. Advanced filters are a critical tool for mitigating the spread of infection. Image credit: Molekule; funded in part by the Environmental Protection Agency. ***Bottom right:*** Computer-generated illustration of a nanoparticle (gray) holding several different versions of the viral spike protein. The different colors represent a spike protein from a different coronavirus. As more strains of SARS-CoV-2 emerge, scientists are working towards creating a pan-coronavirus vaccine that can protect against many coronavirus variants, even ones that have not emerged yet, at the same time. Image credit: (Illustration) V. Altounian/Science; (Data) David Veesler/University of Washington. From Cohen, *Science*, 15 April 2021, DOI: 10.1126/science.abi9939. Reprinted with permission from AAAS; funded by DOE and NIH.

Background image on both front and back outside covers: Computer-generated illustration of a SARS-CoV-2 viron being destroyed. Image credit: Shutterstock.

Inside Back Cover: The inside face of the back cover includes a collage of images illustrating examples of NNI outreach activities. Collage content and design is by Patrice Pages and Kristin Roy of NNCO. More information on NNI outreach activities is available on Nano.gov.

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Louise Lund

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

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Abbreviations and Acronyms[1]

2D	two-dimensional
3D	three-dimensional
AFRL	Air Force Research Laboratory
AI	artificial intelligence
AMO	Advanced Manufacturing Office (DOE)
ATE	Advanced Technology Education (NSF)
BES	[Office of] Basic Energy Sciences (DOE)
BIO	[Directorate for] Biological Sciences (NSF)
CISE	[Directorate for] Computer and Information Science and Engineering (NSF)
CNT	carbon nanotube
DARPA	Defense Advanced Research Projects Agency
DOCTRC	Dental, Oral and Craniofacial Tissue Regeneration Consortium (NIH)
EERE	Office of Energy Efficiency and Renewable Energy (DOE)
EHS	environment(al), health, and safety
ELSI	ethical, legal, and other societal implications
ENG	[Directorate for] Engineering (NSF)
ERC	Engineering Research Center (NSF)
ERDC	Engineer Research and Development Center (Army)
EU	European Union
HIV	human immunodeficiency virus
IDEA	inclusion, diversity, equity, and access
ISN	Institute for Soldier Nanotechnologies (Army)
ISO	International Organization for Standardization
LNP	lipid nanoparticle
MPS	[Directorate for] Mathematical and Physical Sciences (NSF)
mRNA	messenger RNA
MRSEC	Materials Research Science and Engineering Center (NSF)
nanoEHS	nanotechnology environment, health, and safety (research, etc.)
NCI	National Cancer Institute (NIH)
NCL	Nanotechnology Characterization Laboratory (NIH)
NCN	Network for Computational Nanotechnology (NSF)
NEHI	Nanotechnology Environmental and Health Implications Working Group of the NSET Subcommittee
NERC	nanotechnology ERC (NSF)
NIAID	National Institute of Allergy and Infectious Diseases (NIH)
NIDCR	National Institute of Dental and Craniofacial Research (NIH)
NIEHS	National Institute of Environmental Health Sciences (NIH)
NNCI	National Nanotechnology Coordinated Infrastructure (NSF)
NNCO	National Nanotechnology Coordination Office
NNI	National Nanotechnology Initiative
NRL	Naval Research Laboratory
NSE	nanoscale science and engineering
NSET	Nanoscale Science, Engineering, and Technology Subcommittee of the NSTC
NSRC	Nanoscale Science Research Center (DOE)
NSTC	National Science and Technology Council
OECD	Organisation for Economic Co-operation and Development

[1] See Table 1, p. 2, for abbreviations of NNI participating agencies not spelled out in this list.

OMB	Office of Management and Budget (Executive Office of the President)
ONR	Office of Naval Research
ORD	Office of Research and Development (EPA)
OSTP	Office of Science and Technology Policy (Executive Office of the President)
PCA	Program Component Area of the National Nanotechnology Initiative
PPE	personal protective equipment
RADx	Rapid Acceleration of Diagnostics (NIH)
R&D	research and development
RSV	respiratory syncytial virus
SBIR	Small Business Innovation Research Program
SGCID	Structural Genomics Centers for Infectious Diseases (NIH/NIAID)
STC	Science and Technology Center (NSF)
STEM	science, technology, engineering, and mathematics
STTR	Small Business Technology Transfer Research Program
US-COMP	Institute for Ultra-Strong Composites by Computational Design (NASA)
USP	United States Pharmacopeia
VOC	volatile organic compound

Executive Summary

The President's 2022 Budget requests $1.98 billion for the National Nanotechnology Initiative (NNI). Cumulatively totaling over $38 billion since the inception of the NNI in 2001[2] (including the 2022 request), this support reflects the importance of investments that advance the fundamental understanding of and ability to control matter at the nanoscale, as well as the translation of that knowledge into technological breakthroughs that benefit the American people. Past research has led to applications in areas as diverse as consumer electronics, energy, water purification, aerospace, automotive, infrastructure, sporting goods, textiles, agriculture, and medicine.

Despite the challenges posed by the ongoing pandemic, this document highlights significant progress toward the five goals of the NNI identified in the 2021 NNI Strategic Plan. Furthermore, the nanotechnology research community continues to leverage former NNI investments that have established a strong foundation of understanding at the nanoscale to combat COVID-19 and prepare for future pandemics. Example efforts, as highlighted on the cover, include vaccines, diagnostic tests, and preventative measures such as masks, filters, and antimicrobial coatings.

The NNI investments in 2020 and 2021 and those proposed in 2022 reflect a sustained emphasis on broad, fundamental research in nanoscience. Through this sustained support, the President's Budget includes nanotechnology investments that will further the progress of the NNI to advance a world-class research portfolio, facilitate commercialization of nanotechnology-enabled applications, support a dynamic infrastructure and skilled workforce, and ensure responsible development of nanotechnology.

This document serves as the annual report for the National Nanotechnology Initiative called for under the provisions of the 21st Century Nanotechnology Research and Development Act (15 USC §7501). The report also addresses the requirement for Department of Defense reporting on its nanotechnology investments (10 USC §2358).

[2] References to years in this report are to fiscal years unless otherwise noted.

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 materials 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 underpins key industries of the future such as artificial intelligence, quantum information science, and advanced manufacturing. Nanotechnology innovations are ensuring continued U.S. leadership in the semiconductor and strategic computing industries, and are advancing many other national priorities, including space exploration, energy, medicine, agriculture, and national security.

Examples of nanotechnology innovations are illustrated below: (a) a microneedle patch that uses fluorescent nanoscale labels to detect small amounts of antibodies in interstitial fluid; (b) a method to manufacture carbon nanotube transistors in commercial facilities that fabricate silicon-based transistors; (c) a nanomaterial (two-dimensional boron nitride substrate, blue, with imperfections that host tiny nickel clusters) that could help make hydrogen a viable energy carrier; (d) a technique that converts recycled plastic into graphene; (e) nanoscale sensors and fiber optics that measure elusive water levels in leaves; (f) an image from a detector that, when used with an electron microscope, enables the observation of atoms at unprecedented resolution; and (g) stretchable metal antennas integrated onto a conductive graphene material that can harvest energy from radio waves to power wearable devices.

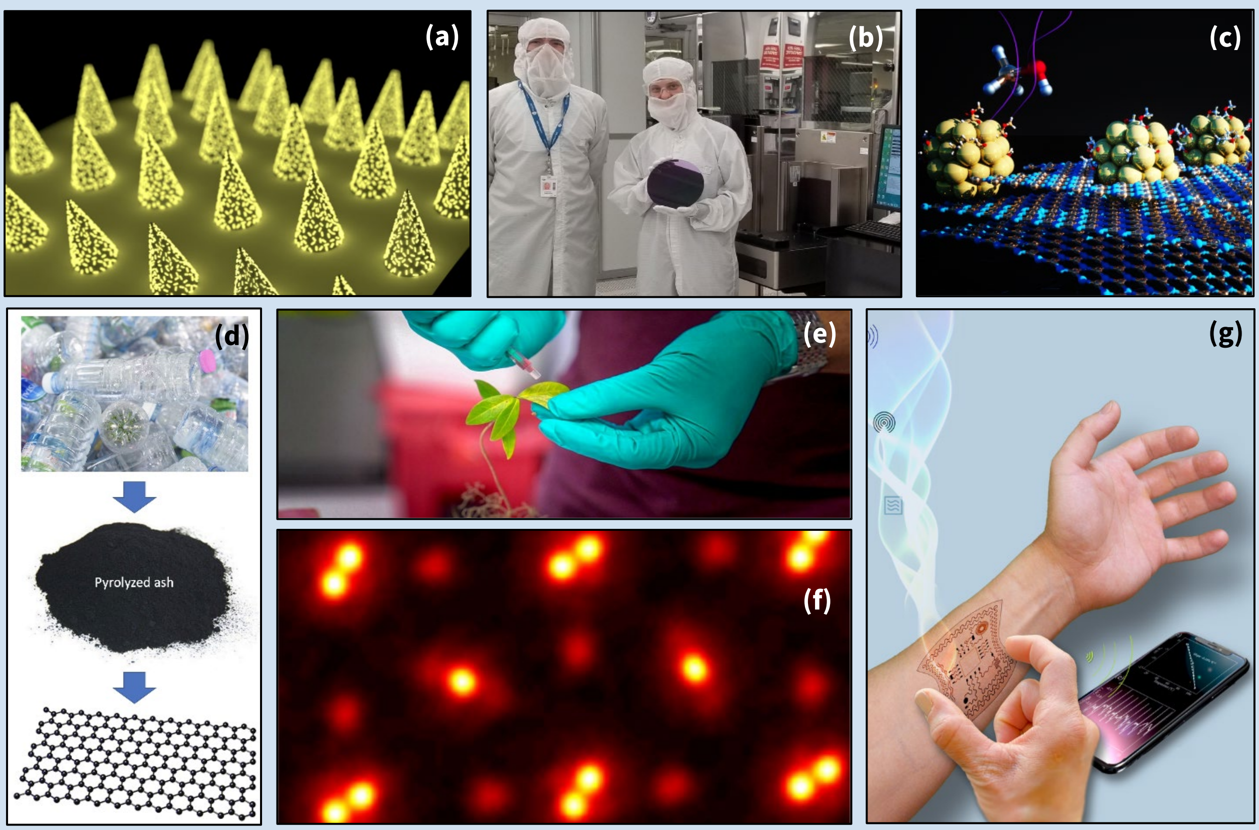

Image credits: (a) Sisi Cao, Washington University in St. Louis; (b) Max Shulaker Group/MIT; (c) Jeff Urban/Berkeley Lab; (d) James Tour Group/Rice University; (e) Cornell University; (f) David Muller Group/Cornell University; and (g) Larry Cheng, Penn State. For more information on nanotechnology benefits and applications, please visit https://www.nano.gov/about-nanotechnology/applications-nanotechnology.

1. Introduction

The National Nanotechnology Initiative (NNI) is a U.S. Government research and development (R&D) initiative. 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 ongoing revolutions in technology and industry that benefit society*. The NNI supports a shared infrastructure and establishes shared goals, priorities, and strategies to enhance interagency coordination of nanotechnology R&D that builds upon agency-specific missions and activities and leverages resources while avoiding duplication. Table 1 lists the agencies currently participating in the NNI. More information about the structure, goals, and priorities of the NNI can be found on Nano.gov.

The ability to understand and control matter at the nanoscale enables unique physical, chemical, and biological properties with broad applications across disciplines and industrial sectors. Past research has enabled current nanotechnology-enabled applications in areas as diverse as consumer electronics, medicine, clean energy, water purification, aerospace, automotive, infrastructure, sporting goods, textiles, and agriculture. The nanotechnology research underway today will enable entirely new capabilities and products and help address world challenges such as the climate crisis, food security, clean water, and future pandemics.

The NNI participating agencies work together to advance discovery and innovation across the nanotechnology R&D enterprise. The NNI portfolio ranges from early-stage fundamental science to applications-driven research and extends across many diverse fields of science and technology. The NNI brings together representatives from multiple agencies to leverage knowledge and resources and involve academia and the private sector as appropriate to promote technology transfer and facilitate commercialization. Strategic collaborations, including public-private-nonprofit partnerships, strengthen key aspects of the nanotechnology ecosystem. In addition to R&D efforts, the NNI is helping to build the nanotechnology workforce of the future, with efforts aimed across the spectrum from K-12 through postgraduate research training.

The NNI provides a focal point for engagement with a broad range of stakeholder groups including allies and partners with shared values. Nanotechnology remains an area of intense R&D activity worldwide. The National Nanotechnology Coordination Office (NNCO) and NNI agencies engage with international regulatory and research agencies and nanotechnology associations from around the world to share best practices, explore opportunities for collaboration, and promote science-based regulation. NNCO also facilitates international communities of research to exchange scientific information regarding nanotechnology-related environmental, health, and safety (EHS) matters and nanomanufacturing.

Despite the challenges posed by the ongoing pandemic, this document highlights significant progress toward the five goals identified in the 2021 NNI Strategic Plan.[3] Researchers quickly adapted to dynamic conditions and continued to advance their research. For example, many user facilities expanded remote access capabilities and prioritized research aimed to combat the pandemic. Furthermore, the nanotechnology research community made many noteworthy contributions to the pandemic response in areas including vaccines, diagnostic tests, and protective filters and masks.

[3] https://www.nano.gov/sites/default/files/pub_resource/NNI-2021-Strategic-Plan.pdf

Table 1: Federal Departments and Agencies Participating in the NNI	
Consumer Product Safety Commission (CPSC)*†	
Department of Agriculture (USDA)	
	Agricultural Research Service (ARS)*
	Forest Service (FS)*
	National Institute of Food and Agriculture (NIFA)*
Department of Commerce (DOC)	
	Bureau of Industry and Security (BIS)
	Economic Development Administration (EDA)
	International Trade Administration (ITA)
	National Institute of Standards and Technology (NIST)*
	Patent and Trademark Office (USPTO)
Department of Defense (DOD)*	
Department of Education (ED)	
Department of Energy (DOE)*	
Department of Health and Human Services (HHS)	
	Agency for Toxic Substances and Disease Registry (ATSDR)
	Biomedical Advanced Research and Development Authority (BARDA)*
	Food and Drug Administration (FDA)*
	National Center for Environmental Health (NCEH)*
	National Institute for Occupational Safety and Health (NIOSH)*
	National Institutes of Health (NIH)*
Department of Homeland Security (DHS)	
Department of the Interior (DOI)	
	Bureau of Reclamation (USBR)*
	Bureau of Safety and Environmental Enforcement (BSEE)*
	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 (State)	
Department of Transportation (DOT)	
	Federal Highway Administration (FHWA)*
Department of the Treasury (Treasury)	
Environmental Protection Agency (EPA)*	
Intelligence Community (IC)	
International Trade Commission (USITC)†	
National Aeronautics and Space Administration (NASA)*	
National Science Foundation (NSF)*	
Nuclear Regulatory Commission (NRC)†	

* Denotes agencies (or organizations within agencies) reporting funding for nanotechnology R&D in Table 5 below

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

Chapter 2 of this report presents budget information and highlights of agency plans and priorities by Program Component Area (PCA). Chapter 3 includes examples of progress toward the five NNI goals. Appendices include definitions of the NNI PCAs and contact information for agency representatives to the Nanoscale Science, Engineering, and Technology (NSET) Subcommittee of the National Science and Technology Council and for NNCO staff.

2. NNI Budget and Program Plans

Budget Summary

The President's 2022 Budget requests $1.98 billion for the NNI, with a continued investment in the foundational research that will fuel the discoveries necessary to advance industries of the future and address world challenges. Cumulatively totaling over $38 billion (including the 2022 request), NNI investments support research to understand matter at the nanoscale and to translate this knowledge into technological breakthroughs that benefit the American people. The NNI investments in 2020 and 2021 and those proposed for 2022 reflect a sustained emphasis on fundamental research in nanoscience; research to advance applications, devices, and systems; and the critically enabling infrastructure to support the research and development enterprise. The NNI budget represents the sum of the nanotechnology-related investments allocated by each of the participating agencies (the "NNI 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 group, communities of interest, coordinators, and strategic liaisons; and the NNCO—to create an integrated R&D program that leverages and amplifies resources and efforts to advance NNI goals and meet individual agency mission needs and objectives. NNI agencies support significant investments in research infrastructure, developing new research tools, and making these tools available through user facilities. The NNI also supports science, technology, engineering, and mathematics (STEM) education to inspire students and prepare the workforce of the future.

This document reports agency investments using existing appropriations as well as supplemental funding to address the COVID-19 pandemic, including major supplemental funding in both 2020 and 2021 by the Biomedical Advanced Research and Development Authority. Agencies are funding a variety of research and development activities as part of this effort, including many that utilize nanotechnology to detect, treat, and prevent the disease; and to understand the virus and how it spreads.

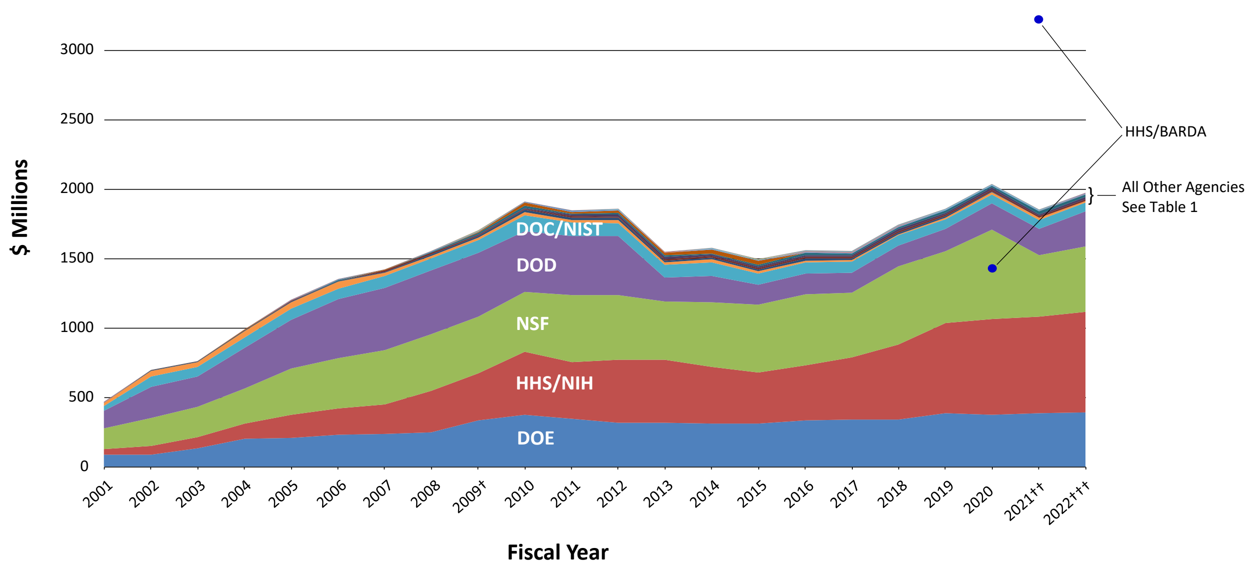

Figure 1. NNI Funding by Agency, 2001–2022.*

* 2020 and 2021 figures include supplemental funding. BARDA investments (blue dots) not included in line graph totals.
† 2009 figures do not include American Recovery and Reinvestment Act funds for DOE, NSF, NIH, and NIST.
†† 2021 numbers are based on appropriated levels.
††† 2022 Budget.

Table 2: Actual 2020 Agency Investments by Program Component Area
(dollars in millions)

Agency	1. Foundational Research	2. Nanotechnology-Enabled Applications, Devices, and Systems	3. Research Infrastructure and Instrumentation	4. Education and Workforce Development	5. Responsible Development	NNI Total
CPSC	0.0	0.0	0.0	0.0	0.4	0.4
DOC/NIST	16.3	11.1	34.6	0.0	3.9	65.9
DOD*	124.6	58.5	2.8	0.7	1.2	187.9
DOE	187.0	42.3	145.6	0.0	0.0	374.9
DOI/USBR	0.6	0.0	0.0	0.0	0.0	0.6
DOJ/NIJ	0.0	0.2	0.0	0.0	0.0	0.2
DOT/FHWA	0.0	0.5	0.0	0.0	0.0	0.5
EPA	0.0	0.0	0.0	0.0	2.4	2.4
HHS (total)	235.1	1839.6	31.3	0.0	36.9	2142.9
BARDA**	0.0	1431.1	0.0	0.0	0.0	1431.1
FDA	0.0	0.0	0.0	0.0	14.0	14.0
NCEH	0.0	0.0	0.0	0.0	0.1	0.1
NIH***	235.1	408.5	31.3	0.0	12.4	687.3
NIOSH	0.0	0.0	0.0	0.0	10.4	10.4
NASA	0.2	19.0	0.0	0.0	0.0	19.2
NSF****	401.6	119.0	43.8	31.7	50.6	646.7
USDA (total)	5.4	14.0	1.8	0.1	2.5	23.8
ARS	0.0	3.0	0.0	0.0	0.0	3.0
FS	0.4	3.3	0.9	0.0	0.0	4.6
NIFA	5.0	7.7	0.9	0.1	2.5	16.2
TOTAL[†]	**970.8**	**2104.1**	**259.9**	**32.5**	**98.0**	**3465.4**

* DOD FY '20 totals include $1.1 million in supplement funding (PCA 2 $0.2 million, PCA 3 $0.4 million, and PCA 5 $0.5 million).

** BARDA's FY '20 investment includes $1.399 billion in supplemental funding.

*** NIH FY '20 totals include $7.8 million in supplemental funding (PCA 1 $0.5 million and PCA 2 $7.3 million).

**** NSF FY '20 totals include $11.8 million in supplemental funding (PCA 1 $4.7 million, PCA 2 $3.9 million, PCA 3 $0.8 million, and PCA 5 $2.4 million).

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

The President's 2022 Budget supports nanoscale science, engineering, and technology R&D at 11 agencies. The five Federal organizations with the largest proposed 2022 investments (representing 96% of the NNI total) are:

- HHS/NIH (nanotechnology-based biomedical research at the intersection of life and physical sciences).
- NSF (fundamental research and education across all disciplines of science and engineering).
- 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).

Table 3: Estimated 2021 Agency Investments by Program Component Area (dollars in millions)*						
Agency	**PCA 1.**	**PCA 2.**	**PCA 3.**	**PCA 4.**	**PCA 5.**	**Total**
CPSC	0.0	0.0	0.0	0.0	0.4	0.4
DOC/NIST	15.5	10.1	32.9	0.0	4.0	62.5
DOD	138.2	49.8	1.4	0.7	1.2	191.3
DOE	193.3	44.1	145.9	0.0	0.0	383.3
DOI/USBR	0.3	0.0	0.0	0.0	0.0	0.3
DOJ/NIJ	0.0	1.2	0.0	0.0	0.0	1.2
EPA	0.0	0.0	0.0	0.0	2.7	2.7
HHS (total)	239.3	3642.1	32.3	0.0	36.7	3950.4
BARDA**	0.0	3225.8	0.0	0.0	0.0	3225.8
FDA	0.0	0.0	0.0	0.0	14.4	14.4
NCEH	0.0	0.0	0.0	0.0	0.1	0.1
NIH***	239.3	416.3	32.3	0.0	12.6	700.5
NIOSH	0.0	0.0	0.0	0.0	9.6	9.6
NASA	0.7	13.7	0.0	0.0	0.0	14.4
NSF	293.3	84.0	25.7	19.0	19.6	441.5
USDA (total)	5.5	18.3	1.8	0.1	2.5	28.2
ARS	0.0	4.0	0.0	0.0	0.0	4.0
FS	0.5	3.4	0.9	0.0	0.0	4.8
NIFA	5.0	10.9	0.9	0.1	2.5	19.4
TOTAL	**886.0**	**3863.3**	**239.9**	**19.8**	**67.0**	**5076.1**

Table 4: Proposed 2022 Agency Investments by Program Component Area (dollars in millions)						
Agency	**PCA 1.**	**PCA 2.**	**PCA 3.**	**PCA 4.**	**PCA 5.**	**Total**
CPSC	0.0	0.0	0.0	0.0	1.1	1.1
DOC/NIST	15.3	9.7	32.4	0.0	4.1	61.5
DOD	139.1	41.8	74.4	0.0	1.2	256.6
DOE	217.6	26.3	150.3	0.0	0.0	394.2
DOJ/NIJ	0.0	1.2	0.0	0.0	0.0	1.2
DOT/FHWA	0.0	1.0	0.0	0.0	0.0	1.0
EPA	0.0	0.0	0.0	0.0	2.6	2.6
HHS (total)	250.3	425.0	32.5	0.0	37.2	745.0
FDA	0.0	0.0	0.0	0.0	14.6	14.6
NCEH	0.0	0.0	0.0	0.0	0.1	0.1
NIH	250.3	425.0	32.5	0.0	12.9	720.7
NIOSH	0.0	0.0	0.0	0.0	9.6	9.6
NASA	0.7	11.9	0.0	0.0	0.0	12.6
NSF	306.3	97.0	25.7	20.5	21.1	470.5
USDA (total)	5.6	19.0	2.0	0.1	2.5	29.1
ARS	0.0	4.0	0.0	0.0	0.0	4.0
FS	0.6	4.1	1.1	0.0	0.0	5.7
NIFA	5.0	10.9	0.9	0.1	2.5	19.4
TOTAL	**934.9**	**632.9**	**317.3**	**20.6**	**69.7**	**1975.4**

* Headings in Tables 3 and 4 are abbreviated to PCA numbers.
** All of BARDA's FY '21 investment is from supplemental funding.
*** NIH FY '21 totals include $6.4 million in supplemental funding (PCA 1 $0.1 million and PCA 2 $6.3 million).

Table 5: NNI Budget, by Agency, 2020–2022
(dollars in millions)

Agency	2020 Actual	2021 Estimated*	2022 Proposed
CPSC	0.4	0.4	1.1
DOC/NIST	65.9	62.5	61.5
DOD	187.9	191.3	256.6
DOE**	374.9	383.3	394.2
DOI/USBR	0.6	0.3	0.0
DOJ/NIJ	0.2	1.2	1.2
DOT/FHWA	0.5	0.0	1.0
EPA	2.4	2.7	2.6
HHS (total)	2142.9	3950.4	745.0
BARDA	1431.1	3225.8	0.0
FDA	14.0	14.4	14.6
NCEH	0.1	0.1	0.1
NIH	687.3	700.5	720.7
NIOSH	10.4	9.6	9.6
NASA	19.2	14.4	12.6
NSF	646.7	441.5	470.5
USDA (total)	23.8	28.2	29.1
ARS	3.0	4.0	4.0
FS	4.6	4.8	5.7
NIFA	16.2	19.4	19.4
TOTAL	**3465.4**	**5076.1**	**1975.4**

* 2021 numbers are based on appropriated levels.

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

A significant proportion of agencies' nanotechnology investments now come from "core" R&D programs, which makes it difficult to predict the number of and success rate of nanotechnology-related proposals. As a result, the actual investments reported are often higher than the previously published estimates or proposed values. For example, the actual NNI investment for 2020 (nearly $3.5 billion, including $1.4 billion from BARDA for COVID diagnostics and vaccine research) is much higher than the 2020 estimated level ($1.84 billion) published in the NNI Supplement to the President's 2021 Budget, or the 2020 requested value published in the 2020 supplement ($1.47 billion).

Programmatic Plans and Changes by PCA

The budget details in the document represent NNI agency support for a vast array of nanotechnology R&D activities across scientific disciplines, application areas, and technology maturity levels. This section provides highlights of agency plans relating to each of the NNI Program Component Areas for 2022. The PCAs have changed for the 2022 Budget to align with the goals in the 2021 NNI Strategic Plan. PCA definitions are included in Appendix A. Additional details and examples can be found on Nano.gov.

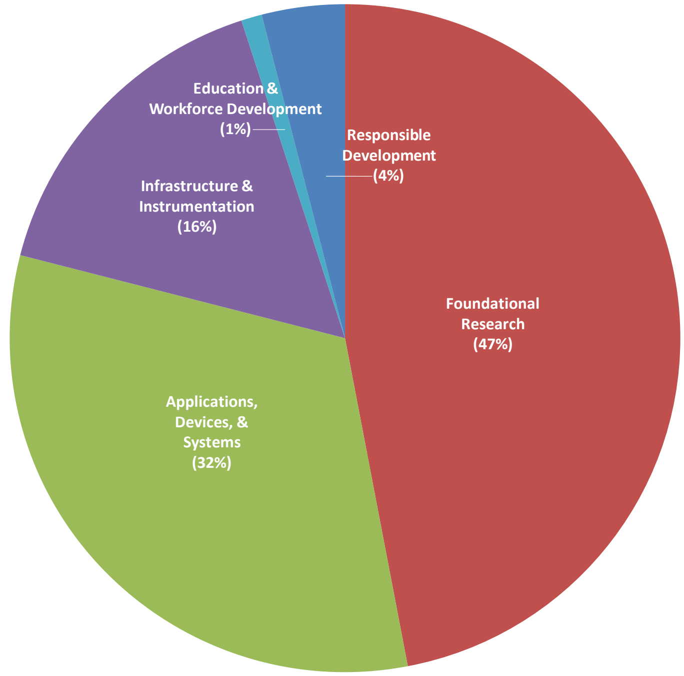

Figure 2. Breakout of NNI Funding by Program Component Area in the 2022 Budget.

PCA 1. Foundational Research

Foundational research continues to be the largest area of investment, accounting for 47% of the proposed NNI total for 2022. NSF is the largest contributor to this PCA, followed by NIH, DOE, and DOD. NSF, DOE, and DOD invest 65%, 55%, and 54% of their totals, respectively, in this category. Continued investment by NNI agencies in foundational research helps ensure new discoveries to seed the innovations of the future.

The NSF 2022 request includes funding for the discovery and development of fundamental knowledge pertaining to new phenomena in the physical, biological, and engineering sciences that occur at the nanoscale. Also included is funding for research aiming to understand scientific and engineering principles related to nanoscale systems, structures, processes, and mechanisms; research on the discovery and synthesis of novel nanoscale and nanostructured materials including biomaterials and modular structures; and quantum biology for understanding natural phenomena and interfaces. Most of the NSF-funded nanotechnology research is sponsored through individual and small group awards across NSF directorates. A subset of NSF's centers programs support various aspects of nanoscale science and engineering (NSE), including about 60 percent of the Materials Research Science and Engineering Centers (MRSECs).

NSF's Understanding the Rules of Life[4] priority area has a strong nanotechnology component, including support for efforts to understand the nanoscale machines that make up the nucleus of a cell and control cell function. NSF will expand its efforts in 2022 in nanobiotechnology associated with synthetic biology and synthetic cells through new solicitations on Designing Synthetic Cells Beyond the Bounds of Evolution[5] and Sentinel Cells for Surveillance and Response to Emergent Infectious Diseases,[6] and

4 https://www.nsf.gov/news/special_reports/big_ideas/life.jsp
5 https://www.nsf.gov/pubs/2021/nsf21531/nsf21531.htm
6 https://www.nsf.gov/pubs/2020/nsf20105/nsf20105.jsp

through core programs in the Directorate for Biological Sciences (BIO) and the Directorate for Engineering (ENG).

NSF will support research on foundational concepts for new nanomanufacturing methods at the confluence with digitization, biotechnology, artificial intelligence (AI), and cognitive sciences. NSF will support a new activity in Designing Synthetic Cells Beyond the Bounds of Evolution,[7] enabling novel nanomanufacturing applications, and Reproducible Cells and Organoids via Directed-Differentiation Encoding (RECODE).[8] NSF supports advanced nanoelectronics R&D across several directorates. Activities will focus on discovering and using novel nanoscale fabrication processes and concepts to produce revolutionary materials, devices, systems, and architectures to advance research into "brain-like computing" and "intelligent cognitive assistants." These investments also support the whole of government efforts in microelectronics research and development, including those authorized in the CHIPS for America Act.[9]

NIH supports foundational research in nanoscience across several institutes. For example, the National Human Genome Research Institute (NHGRI) supports research on nanotechnologies for direct single-molecule RNA and DNA sequencing. Research includes efforts to understand fundamental processes at the nanoscale to improve nucleic acid sequencing technologies (e.g., protein-based nanopores, precise measurements of nucleic acids stepping through an enzyme base-by-base, new electronic DNA sequencing methods, and the use of enzymes as conductors to determine individual base incorporations). Many of these novel approaches and technologies are supported by NHGRI's Genome Technology Program.[10] The most recent funding opportunities in this area are focused on the early stages of novel technologies that will enable improved DNA sequencing and direct RNA sequencing—Transformative Nucleic Acid Sequencing Technology Innovation and Early Development.[11]

Multiple programs at the NIH/National Institute of Allergy and Infectious Diseases (NIAID) support nanoparticle technology—including protein nanoparticle and messenger RNA (mRNA) packaged into lipid nanoparticle (LNP) platforms—for use in human immunodeficiency virus (HIV) vaccines. These programs include: HIV Vaccine Research and Design (HIVRAD),[12] Innovation for HIV Vaccine Discovery (IHVD),[13] Consortia for HIV/AIDS Vaccine Development (CHAVD),[14] Consortium for Innovative AIDS Research in Nonhuman Primates (CIAR-NHP),[15] and Integrated Preclinical/Clinical AIDS Vaccine Development (IPCAVD).[16] Also within NIAID the Advancing Vaccine Adjuvant Research for Tuberculosis (AVAR-T)[17] solicitation will further the development of preventive, including post-exposure, tuberculosis vaccines. Adjuvants tested in this program may include candidates containing nanomaterials. NIAID-funded Structural Genomics Centers for Infectious Diseases (SGCIDs) are

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7 https://www.nsf.gov/pubs/2021/nsf21531/nsf21531.htm

8 https://www.nsf.gov/pubs/2021/nsf21532/nsf21532.htm

9 Public Law 116-283, Creating Helpful Incentives to Produce Semiconductors (CHIPS) for America, Title XCIX of the William M. (Mac) Thornberry National Defense Authorization Act for Fiscal Year 2021, www.govinfo.gov/app/details/BILLS-116hr6395enr.

10 https://www.genome.gov/Funded-Programs-Projects/Genome-Technology-Program

11 https://grants.nih.gov/grants/guide/rfa-files/RFA-HG-21-006.html, https://grants.nih.gov/grants/guide/rfa-files/RFA-HG-21-007.html, https://grants.nih.gov/grants/guide/rfa-files/RFA-HG-21-008.html

12 https://grants.nih.gov/grants/guide/pa-files/par-21-024.html

13 https://grants.nih.gov/grants/guide/pa-files/PAR-20-158.html

14 https://grants.nih.gov/grants/guide/rfa-files/rfa-ai-18-001.html

15 https://grants.nih.gov/grants/guide/rfa-files/RFA-AI-15-022.html

16 https://grants.nih.gov/grants/guide/pa-files/PAR-20-120.html

17 https://sam.gov/opp/f87d60b154e44aaea4be8a12bfdd03bc/view

supporting development of nanoparticle vaccine technology for respiratory syncytial virus (RSV), SARS-CoV-2, and influenza.[18]

The NIH/National Cancer Institute (NCI) supports basic, applied, and translational research in the area of cancer nanotechnology. In particular, the funding opportunity PAR-20-284, Innovative Research in Cancer Nanotechnology (IRCN),[19] covers mechanistic studies contributing to design and refinement of next-generation nanosystem designs, to understanding of nanoparticle delivery mechanisms and implications of systemic distribution, and to the development of techniques and tools to overcome the failure of therapy and therapeutic resistance.

The NIH/National Institute of Dental and Craniofacial Research (NIDCR) has been supporting since 2015 a three-stage effort called Dental, Oral and Craniofacial Tissue Regeneration Consortium (DOCTRC),[20] which will extend until 2025. DOCTRC represents longstanding NIDCR support of nanotechnology development. The consortium is advancing promising technologies, include nanotechnology-based approaches for regeneration and reconstruction of DOC tissues, to Phase 1 clinical trials. Several dozen individual projects supported by DOCTRC are facilitating introduction of nanotechnology, such as tissue regeneration-enhancing scaffolds and drug and cell delivery systems, into clinical practice.

NIDCR and NIST have renewed an ongoing multi-year interagency agreement (IAA) to accelerate the development of measurement methods, standards, and reference nanomaterial-based composites for dental and biomaterials. Research under the IAA will advance dental nanomaterial-based composites and nanotechnology-based biosensing measurements in the oral environment. Projects will address three thrust areas: (1) Measurement Methods for Next Generation Dental Restoratives, (2) High-Throughput Screening of Selectivity Elements for Intraoral Electrochemical Sensors, and (3) Predictive Early-Stage Biocompatibility Testing of Dental Materials. Outcomes of these projects are expected to mitigate challenges in regulatory science and help to accelerate the lab-to-human and lab-to-market translation of novel nanotechnologies in dentistry. In addition, NIDCR, other NIH institutes, FDA, and NIST participate in the National Academy of Medicine Forum on Regenerative Medicine.[21] NIDCR participation in the Forum on Regenerative Medicine will continue at least through 2022.

DOE's Office of Basic Energy Sciences (BES) supports fundamental nanoscience research in the fields of 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 basic research is performed primarily at universities and DOE national laboratories through single-principal-investigator and small-group projects. BES also supports nanoscience as part of larger activities such as Energy Frontier Research Centers and Energy Innovation Hubs, with an emphasis on use-inspired basic research. These investments will continue in 2022, with a particular focus on foundational research in support of clean energy technologies. The Advanced Manufacturing Office (AMO) within the Office of Energy Efficiency and Renewable Energy (EERE) supports an atomically precise manufacturing portfolio, which includes efforts reported under PCA 1.

The planned Army investments at the Institute for Soldier Nanotechnologies (ISN) emphasize exploration of novel phenomena associated with fundamental processes at the nanoscale or arising from nanostructural features in materials and devices. Army relevancy and transitioning are important elements of ISN operations, with planned basic research supporting each of the Army Futures

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18 https://www.niaid.nih.gov/research/structural-genomics-centers

19 https://grants.nih.gov/grants/guide/pa-files/par-20-284.html

20 Dental, Oral and Craniofacial Tissue Regeneration Consortium, https://doctrc.org/; accessed 17 March 2022

21 National Academies of Science, Engineering, and Medicine; Forum on Regenerative Medicine, https://www.nationalacademies.org/our-work/forum-on-regenerative-medicine; accessed 17 March 2022

Command modernization priorities. The planned research program includes 16 projects within three Strategic Research Areas: (1) Soldier Protection, Battlefield Care, and Sensing; (2) Augmenting Situational Awareness; and (3) Transformational Nano-optoelectronic Soldier Capabilities.

The Office of Naval Research (ONR) supports bionanotechnology research with emphases on fabrication techniques for hierarchical, biologically based materials, DNA nanotechnology and applications, synthesis and patterning of materials by microorganisms, and bio-inspired and biomimetic materials and devices. ONR also supports programs to investigate scientific phenomena that define the unique properties of structural and multifunctional nanomaterials. There is special emphasis on identifying material systems and processes enabling the assembly of these materials at the mesoscale and beyond while preserving and potentially enhancing material properties initially defined at the nanoscale. In the area of nanoelectronics, ONR plans to foster high-risk nanoscience research that will enable revolutionary new electronic devices with a plausible route to either classical information processing with size/weight/power advantages over state-of-the-art, or robust quantum information processing. Research challenges that will be addressed include: the fundamental building block of classical information handling beyond transistors; “topologically protected” qubit designs; computing architectures that circumvent the von Neumann memory-compute information bottleneck; and reliable and cost-effective means to synthesize and fabricate electronic circuitry at atomic resolution. The MURI project, Topological Spin Qubits Based on Graphene Nanoribbons,[22] will leverage over a decade of graphene nanoribbon research supported by this program to enable the creation of carbon-backbone qubit circuits at the molecular level. In 2022, ONR will launch a MURI topic, Novel Routes to Majorana Qubits for Topologically-Protected Quantum Information, focused on realizing single-quasiparticle devices capable of two-dimensional (2D) particle exchange with non-commutative unitary transformation of degenerate ground states constituting a robust route to quantum computation. The Naval Research Laboratory (NRL) plans continued foundational research efforts in three main areas: materials/assembly, interactions, and nanosystems.

NIST’s foundational nanotechnology research portfolio includes the development of cutting-edge approaches to design and accurately measure the size, shape, quantity, and physico-chemical complexity of nanoparticles, nanostructured films, and nanocomposites in a variety of environments. NIST researchers are studying the impact of UV exposure and outdoor weathering on the scratch resistance of coatings using a NIST-developed nanoscratch test. This nanoscratch test will also be applied to UV-exposed photovoltaic backsheets and other polymer composites to investigate the interfacial properties of multilayer, multicomponent systems. NIST research is exploring optical metasurface technologies that enable virtually complete optical control in thin, easily manufactured elements that can replace traditional optics in many applications. NIST is developing high-performance optomechanical devices to localize and control the interactions of photons, phonons, and electrons in nanoscale structures to enable new measurements for biological, chemical, and physical sensing. NIST researchers are advancing ultrafast stroboscopic measurements of the sub-nanometer motion of mechanical resonators used in emerging high-impact technologies including 5G wireless communications. NIST is also developing new measurement methods and data analysis techniques that precisely and accurately determine the thermodynamics of DNA nanostructure assembly, as well as novel tools and models to study the ultrafast dynamics of biomolecules.

NASA supports nanotechnology R&D to advance space exploration and aeronautics research. Nanomaterials are being investigated for durability and system-level performance enhancements in extreme environments. For example, the Institute for Ultra-Strong Composites by Computational

22 https://www.cto.mil/wp-content/uploads/2021/02/FY21-MURI-press-release-03FEB21.pdf

Design (US-COMP) is promoting collaboration between NASA, other Federal agencies, industry, and academia, with a common goal of using computationally driven approaches to develop ultra-high-strength lightweight carbon nanotube (CNT) structural materials for space exploration.

NIFA supports foundational research in cutting-edge nanoscale science and engineering for solving significant agricultural and food system challenges. The scope covers discovery and characterization of novel nanoscale phenomena, processes, and properties that are relevant and important to agriculture and food; new platforms leading to novel applications; the exploitation of bio-nano interfaces; synthetic biology; and additive manufacturing technology.

PCA 2. Nanotechnology-Enabled Applications, Devices, and Systems

The agencies participating in the NNI support R&D on nanotechnology-enabled devices and systems across many applications, including biomedical innovations to address the COVID-19 pandemic and other health needs, improved infrastructure materials, nanoscale electronics and photonic devices, and nanomanufacturing. PCA 2 represents nearly a third of the total NNI 2022 request and is the largest category in the NIH NNI investment portfolio, accounting for 59% of its request.

The 2022 NIH request features investments in technology development to continue fighting the COVID-19 pandemic. For example, NIAID is investigating a self-assembling SARS-CoV-2 ferritin nanoparticle vaccine developed by intramural and extramural researchers that has shown neutralizing antibody response against bat-CoVs, SARS-CoV-1, SARS-CoV-2, as well as the widely circulating SARS-CoV-2 variants B.1.1.7, P.1, and B.1.351 in preclinical studies. Extramural researchers are developing a platform for ultrapotent structure-based nanoparticle vaccines that enables researchers to quickly and robustly create a candidate vaccine for a variety of pathogen-caused diseases, including SARS-CoV-2, RSV, influenza, and hepatitis-C. NIDCR is leading the Novel Biosensing for Screening, Diagnosis and Monitoring of COVID-19 From Skin and The Oral Cavity[23] initiative to support three years of advanced development of novel, non-traditional, nanotechnology-based approaches for detection of the SARS-CoV-2 virus and biomarkers of the COVID-19 disease, and to address future health emergencies. Projects funded through the Rapid Acceleration of Diagnostics-Radical (RADx-rad) initiative[24] will use nanotechnology and nanomaterial approaches to identify biomarkers in patients with symptomatic and asymptomatic COVID-19. A variety of nanotechnology-based designs are targeting detection of volatile organic compounds (VOCs) emanating from skin and exhaled breath in a passive and noninvasive manner, as well as other oral biosensing technologies targeting SARS-CoV-2 biosignatures sampled from exhaled breath/droplets, saliva, and tissues in the oral cavity. Planning is underway for follow-on funding of these technologies beyond the initial three-year cycle.

Other NIH investments include extramural NIAID projects that apply nanotechnology in diagnostics, vaccines, therapies, and improved structural biology understanding addressing HIV, hepatitis, tuberculosis, RSV, and influenza. NIAID is supporting the development of several nanoparticle-based candidates for a universal influenza vaccine. Intramural NIAID projects include research on targeted proteomics assays using nano-flow liquid chromatography; use of recombinant nano-platforms to aid in structure-assisted evaluation, prediction, and iterative optimization of conserved epitope; and improving understanding and correlating the disposition of conserved coronavirus epitopes on subunit vaccines and designed nanoparticles with immunogenicity.

[23] https://grants.nih.gov/grants/guide/notice-files/NOT-OD-21-035.html

[24] https://grants.nih.gov/grants/guide/rfa-files/RFA-OD-20-020.html, https://grants.nih.gov/grants/guide/rfa-files/RFA-OD-20-021.html

NIBIB-supported nanotechnology research includes the use of metal (e.g., gold) nanoparticles in optimizing sensitivity and image resolution of x-ray fluorescence computed tomography and three-dimensional (3D) printing of cell-seeded hydrogel matrices with conducting polymers infused with metal nanoparticles for tissue engineering and neural regeneration. NIBIB also supports the development of ultrathin, lightweight, and stretchable, bio-compatible nanogenerators that can harvest movement from the human body to power implantable biomedical devices such as pacemakers.

Several NCI-funded efforts have applied focus and are dedicated to developing new and improved diagnostics and therapeutics. The diagnostics efforts mostly emphasize high detection sensitivity and the ability of multiplexed detection, allowing for earlier cancer diagnosis and ability to stratify patients who have the best chance to respond to a given cancer treatment, as well as new intraoperative imaging techniques providing for improved surgery effectiveness. Nanotechnology-based cancer treatments, in addition to nanotechnology-based chemotherapeutics, have gradually migrated to gene therapies and immunotherapies and to combining different treatment modalities to enhance overall treatment efficacy.

NIDCR's investments leverage the promise of nanotechnology to produce novel structures that induce regeneration and repair of biological tissues, deliver biomolecules to tissues with pre-defined kinetics, and control tissue infection and inflammation. Additional research focuses on the development of oral biodevice technologies for the evaluation, monitoring, and management of oral and overall health and development of high-performing dental materials for the restoration, repair, and replacement of dental, oral, and craniofacial tissues. NIDCR also supports the development of clinically relevant standards for nanotechnology-based biosensing and nanomaterial-based dental composites, including reference materials and quality guidance to research and product manufacturing. NIDCR's nanotechnology investments include Enabling Technologies to Accelerate Development of Oral Biodevices[25] support for research in transformative engineering solutions that improve the evaluation, monitoring, and management of oral and overall health using multifunctional oral biodevices. Projects funded through this initiative will utilize nanotechnology and nanomaterial approaches that integrate electronic, physical, and biological systems into biodevices intended for detection, diagnosis, and treatment of oral and systemic diseases. Due to the coronavirus pandemic, this initiative has received increased attention by the scientific community looking to leverage the oral cavity for the design of biodevices to screen, monitor, and diagnose health and disease.

Core programs in the NSF ENG, Mathematical and Physical Sciences (MPS), and Computer and Information Science and Engineering (CISE) directorates support development of new principles, design methods, and constructive solutions for nanomaterials and nanodevices. A special focus is on smart, autonomous nanoscale-based devices and systems. NSF investments will include emphasis on sustainable nanomanufacturing, establishing manufacturing technologies for integration of nanoscale building blocks into complex, large-scale systems by supporting product, tool, and process design. A Dear Colleague Letter, Supporting Fundamental Research to Enable Innovation in Advanced Manufacturing at Manufacturing USA Institutes,[26] solicits proposals addressing critical fundamental research needs in advanced manufacturing, including nanomanufacturing and manufacturing across length scales, particularly projects that may enable innovations in the technical focus areas of one or more of the Manufacturing USA institutes. Engineering biology at the nanoscale for advanced

[25] https://grants.nih.gov/grants/guide/pa-files/PAR-20-232.html, https://grants.nih.gov/grants/guide/pa-files/PAR-20-233.html

[26] https://www.nsf.gov/pubs/2017/nsf17088/nsf17088.jsp

manufacturing activities are being organized in the BIO, ENG, and MPS directorates for 2021–2022. The Hierarchical Nanomanufacturing (NanoMFG) Node[27] of the Network for Computational Nanotechnology (NCN, nanoHUB) focuses on modeling and simulation of manufacturing processes. Exploratory research directions are manufacturing of nanomachines and nanobiostructures, cellular nanobiomanufacturing, atomically precise manufacturing, and nanomanufacturing for quantum devices and sensors. The Advanced Manufacturing (AM) program[28] includes support for nanoscale fundamental research to enable innovation in advanced manufacturing at universities exclusively or in collaboration with industry (Grant Opportunities for Academic Liaison with Industry, GOALI[29]). A new Future Manufacturing solicitation[30] was first announced in 2020 to support fundamental research and education of a future workforce to overcome scientific, technological, educational, economic, and social barriers to enable new manufacturing capabilities.

In the area of nanoelectronics, NSF plans ongoing collaboration with other agencies and industry in activities such as the Semiconductor Synthetic Biology for Information Storage and Retrieval (SemiSynBio II) program,[31] with awards continuing into 2023. The three-year NSF/CISE-ENG Real Time Machine Learning (RTML) program started in 2019 in collaboration with the Defense Advanced Research Projects Agency (DARPA) with a focus on chip design for AI. NSF will increase coordinated research on its Quantum Leap and Future of Work at the Human-Technology Frontier "Big Ideas" priority areas. The Addressing Systems Challenges through Engineering Teams (ASCENT) program[32] in ENG addresses research issues and engineering challenges associated with complex systems and networks that can only be achieved by interdisciplinary research teams. NSF continues active centers focused on future computing including the Science and Technology Center (STC) on Quantum Materials and Devices at Harvard University; the MRSEC on Quantum and Spin Phenomena in Nanomagnetic Structures at the University of Nebraska, Lincoln; and the Engineering Research Center (ERC) at the University of Arizona: Center for Quantum Networks. Further collaboration is planned with industry groups developing hardware (with a focus on a "beyond Moore" system architecture and corresponding devices), software (with a focus on artificial intelligence), and implementation in various applications. The research will be conducted in collaboration with other agencies (e.g., NIH, DARPA).

NSF plans continued support for projects in nanotechnology at the nexus of food, energy, and water systems. In addition to core nanoscience-related programs on water filtration and applications, the nanotechnology ERC (NERC) for Nanotechnology Enabled Water Treatment Systems (NEWT), funded through 2024, aims at developing high-performance water treatment systems that will broaden access to clean drinking water from a variety of unconventional sources (briny well water, seawater, wastewater), and enable industrial wastewater reuse at remote locations such as oil and gas fields.

DOD is supporting the AIM Photonics Manufacturing USA institute,[33] including the Hetero-Epitaxial Laser Integration on Silicon (HELIOS) project that will integrate quantum dot lasers and quantum dot semiconductor optical amplifiers into the 300 mm AIM Photonics platform. The HELIOS approach enables the densest integration of amplifiers and lasers within the most advanced silicon photonics platform in the world. Additional efforts will focus on lowering overall cost to enable uses of integrated photonics and hasten its adoption to a wider variety of applications. NRL is developing photonically

27 nanoHUB.org, nanomanufacturing node, https://nanohub.org/groups/nanomfg; accessed 17 March 2022
28 https://www.nsf.gov/funding/pgm_summ.jsp?pims_id=505572
29 https://www.nsf.gov/eng/iip/goali.jsp
30 https://www.nsf.gov/pubs/2021/nsf21564/nsf21564.htm
31 https://www.nsf.gov/pubs/2020/nsf20518/nsf20518.htm
32 https://www.nsf.gov/funding/pgm_summ.jsp?pims_id=505853
33 AIM Photonics Manufacturing USA institute, https://www.aimphotonics.com/; accessed 17 March 2022

coupled quantum dot lasers for ultralow-power, ultrahigh-speed neuromorphic computing. NRL research also is exploring new approaches to interface with and control biological systems, including the development of “protonic” devices for actuating cells and self-assembled nanoscale transducers that can photostimulate electrical activity in living neurons. In addition, NRL is developing dimensionally confined biological catalysts and multiscale architectures for chemical catalysts. Army Engineer Research and Development Center (ERDC) efforts focus on the use of advanced materials to support force protection systems. This work uses nanoscale graphene, carbon nanofibers, and other additives for modification of resins in composites, nanoceramic additive for hardening of metals, and nanoscale modification of asphalt and concrete materials.

DOE offices supporting research under PCA 2 include the Office of Energy Efficiency and Renewable Energy, the Office of Nuclear Energy (NE), and the Office of Fossil Energy and Carbon Management (FECM). EERE conducts nanoscience and nanotechnology related research through the Building Technologies Office, the Solar Energy Technologies Office, and the Advanced Manufacturing Office. Most of EERE’s nanoscience related efforts are in AMO’s Advanced Materials Manufacturing sector and support decarbonization/electrification and industrial greenhouse gas emissions reductions. AMO is planning a research program in ultra-energy-efficient microelectronics as part of the coordinated interagency effort to bolster U.S. competitiveness in microelectronics and semiconductor manufacturing. NE supports R&D projects across a wide field of science and engineering to investigate behavior and properties of nuclear energy-related materials that have been nanostructured or nano-modified, under various types of irradiation and other conditions; and lower-length-scale changes in materials used in nuclear applications. FECM supports nanoscale materials, modeling, and manufacturing projects in areas such as advanced sensors and separation membranes. The office plans investments to advance development of high-value, coal-derived solid carbon products/materials, including carbon fibers and nanomaterials (e.g., graphene, quantum dots, conductive inks, 3D printing materials, energy storage/battery anodes, carbon composites, and supercapacitor materials). FECM also plans to support research on sensors and controls with gap analyses to develop automated awareness technologies, data integration tools, and blockchain technologies to harden potential targets.

Successful integration of nanotechnology into NASA’s missions can enable humans to maintain a long-term, sustainable presence in space. Nanotechnology is also playing a more prominent role with advancing aeronautics research for rapid manufacturing of lightweight composites and the development of new materials to support electrified aircraft propulsion technologies. Examples of NASA research characterized as PCA 2 include the development of nanoplasmonic optical sensors; cost-efficient, compact, low-mass quantum-dot-based spectrometers; boron nitride electrical insulation materials; copper-CNT composite conductors; and CNT-enabled lightweight structural components. Examples of CNT-enabled lightweight structural components include next-generation linerless CNT composite overwrapped pressure vessels and net-shaped composites for extreme temperature applications.

USDA/NIFA support for innovative applied research under this PCA includes rapid detection and effective intervention technologies for ensuring food safety and biosecurity; treatments to improve animal health; novel value-added products; and utilization and protection of natural resources, the environment, and agricultural production ecosystems. NIFA proposes to invest in the Sustainable Agricultural Systems[34] programs to support large integrated projects that develop and apply technological solutions to major agricultural system challenges. NIFA also supports the development

[34] https://nifa.usda.gov/program/afri-sas

of nanotechnology-enabled sensors for food and agricultural applications such as food contaminant detection and intelligent precision agriculture, with particular emphasis on low-cost sensor technologies and manufacturing that can be translated to commercial markets. NIFA continues to explore nanotechnology applications for improving quality and quantity of agriculture water resources.

USDA Agricultural Research Service efforts in nanotechnology utilize sustainable agricultural-based feedstocks to develop value-added co-products that include pharmaceuticals, cosmetics, biodegradable plastics, rubber, and antibacterial textiles. Additional research involves efforts to detect peanut allergens through the potential use of single-chain antibodies from camelids in biosensors.[35]

The primary focus of Forest Service nanotechnology research is on producing cellulose nanomaterials and other nanoscale polymeric materials from wood, developing the science and technology for the application of cellulose nanomaterials in a broad range of products, and supporting the commercialization of forest-sourced nanomaterials. Other Forest Service research includes using nanotechnology techniques to understand the nanostructure of wood and wood properties, wood-water interactions, and adhesion of wood adhesives. A technology transfer team including multiple deputy areas and regions within the Forest Service, a university, and P^{3}Nano will work with the FHWA Emergency Relief for Federally Owned Roads program[36] to replace timber bridges destroyed by forest fire with cellulose-nanocrystal-enhanced concrete bridges. To accelerate commercialization of cellulose nanomaterials, Forest Service experts are leading and participating in international standards development projects.

The NIST 2022 request includes funds to establish a new research program to support the robust and reliable manufacture of future microelectronics. Research will focus on characterizing physical properties of complex material and processing interactions at the nanoscale. NIST will continue to advance research on nanoscale devices and systems for a variety of applications, from microelectronics to coatings and pharmaceutical products. For example, NIST is developing laser-based methods for the rapid measurement of the thermodynamics of single molecules that will provide a rapid assay for benchmarking nanopore biosensors. NIST is exploring applications to advance optical metasurface technologies for optical control in thin, easily manufactured elements, including photonic interfaces to atomic-scale quantum systems and ultrafast, quantum, and nonlinear optics. NIST is developing standards and calibrations for super-resolution optical microscopy, improving the accuracy of localization measurements by orders of magnitude, and is developing super-resolution optical microscopy and nanoparticle tracking methods to characterize microelectromechanical systems. NIST is working with FDA to develop nanoparticle tracking methods and microfluidic measurement devices to characterize complex liposomal products. NIST also is developing nanofluidic measurement devices and super-resolution optical microscopy methods to characterize nanoplastics, as well as single and multi-organ microphysiological systems that mimic the human body and can be used to evaluate the efficacy and toxicity of new drugs. NIST is also leading discussions of how to standardize microphysiological system designs so that data obtained can be compared across different platforms.

DOJ/National Institute of Justice sponsors nanotechnology research that provides objective, independent, evidence-based knowledge and tools to meet the challenges of crime and justice. New projects are awarded on a competitive basis; therefore, total investment may change each fiscal year. However, NIJ views nanotechnology as an integral component of its R&D portfolio.

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[35] https://doi.org/10.1021/acs.jafc.9b02388

[36] https://highways.dot.gov/federal-lands/programs/erfo

The FHWA Exploratory Advanced Research program supports materials research across multiple scales, starting from the nanoscale. One objective is to provide State departments of transportation and other agencies with choices of materials that can reduce the use of portland cement, a limited resource that requires substantial energy to produce. As part of this effort, FHWA is supporting research that applies machine learning to data from materials samples to understand the relationship between chemical and physical features of different mixes of supplementary cementitious materials and concrete performance attributes such as strength and permeability.

PCA 3. Research Infrastructure and Instrumentation

The research infrastructure, including physical facilities and cyber resources, is critical to support the entire NNI ecosystem, and agencies will continue to invest in these important areas. The NNI R&D infrastructure also supports quantum information science, microelectronics, the Materials Genome Initiative, and other priority areas. Agencies use a wide variety of mechanisms to support the research infrastructure, including center grants and instrumentation development or acquisition programs. The DOE Office of Basic Energy Sciences operates five Nanoscale Science Research Centers (NSRCs),[37] national user facilities for interdisciplinary R&D at the nanoscale, including synthesis, fabrication, characterization, and theory/modeling. The NSRCs contain cleanrooms, nanofabrication resources, one-of-a-kind instruments, state-of-the-art microscopy, and other capabilities 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.

The NIH National Cancer Institute continues to support the Nanotechnology Characterization Laboratory (NCL),[38] which conducts the characterization of nanomaterial formulations for imaging and therapeutic applications developed by researchers from academia, industry, and government. NCL receives a broad range of nanomedicine technologies through its Assay Cascade program,[39] and has experience with virtually all nanoparticle platforms, therapeutic agents, and applications employed in the pursuit of better treatments and diagnostics for cancer. NCL has expanded efforts towards the evaluation of nanomedicine bioequivalence and assessment of personalized vaccine strategies and immunotherapies. NCL also has started evaluation of nanotechnology strategies for the diagnosis and treatment of COVID-19.

NIST provides scientists from academia, industry, and other government agencies with access to unique, world-class facilities and research instrumentation that help advance emerging technology areas and advance understanding of nanoscale phenomena and systems. The NIST 2022 request includes support for a new equipment modernization fund for cutting-edge nanofabrication and advanced semiconductor characterization equipment on the NIST campuses in Gaithersburg, MD, and Boulder, CO, including the Center for Nanoscale Science and Technology (CNST) Nanofab and the Precision Imaging Facility. NIST will increase the research capacity to explore new electronic materials, devices, and process-structure-function relationships that accelerate lab-to-fab implementation. Facilities at NIST include the NIST Center for Neutron Research, a user facility on the NIST Gaithersburg

[37] https://nsrcportal.sandia.gov/
[38] https://ncl.cancer.gov/
[39] https://ncl.cancer.gov/resources/assay-cascade-protocols

campus that provides neutron measurement capabilities to the U.S. research community.[40] The CNST NanoFab on the NIST Gaithersburg campus provides researchers with rapid access to state-of-the-art, commercial nanoscale measurement and fabrication tools and methods.[41] The NIST Boulder Microfabrication Facility enables development of nanoelectronic devices for chip-based quantum standards, sensors, integrated and quantum photonics, and advanced computing.[42] NIST also supports capabilities at the National Synchrotron Light Source II (NSLS-II) located at Brookhaven National Laboratory, including beamlines based on "hard" x-rays, with two additional beamlines with "softer" x-rays. Nine end stations take advantage of the unique broad and brilliant spectrum at NSLS-II to provide a world-leading suite of measurements of the atomic, molecular, and electronic structure of materials.

NSF has funded the National Nanotechnology Coordinated Infrastructure (NNCI)[43] sites for 2015–2024, with a national coordination office added in 2016. NNCI provides access to over 2,000 tools at 29 sites across the country. Other STCs, ERCs, Centers for Chemical Innovation (CCIs), and MRSECs also provide important infrastructure that supports the nanotechnology research community, including the Center for Cellular Construction;[44] two NERCs, one each on nanobiotechnology and cell technology; and a CCI that investigates the fundamental molecular mechanisms by which nanoparticles interact with biological systems. NSF will increase coordinated research on its Mid-scale Research Infrastructure priority area. The Major Research Instrumentation (MRI) Program serves to increase access to multi-user scientific and engineering instrumentation, including instrumentation needed for NSE activities, for research and training in the Nation's higher education institutions and non-profit scientific/engineering research organizations.

NIFA invests in data science for food and agricultural systems to effectively utilize data, improve resource management, and integrate new technologies and approaches to further U.S. food and agriculture enterprises. This work addresses many challenges associated with data in agriculture and food production and processing systems.

PCA 4. Education and Workforce Development

The future of the NNI depends on a highly skilled workforce across the entire technology development pathway. In addition to targeted nanotechnology education, the novel properties at the nanoscale can provide a spark to excite students to pursue STEM careers and help build a robust domestic workforce. NNCO and the NNI agencies use a variety of mechanisms to support public outreach and education from "K to grey" and emphasize opportunities and access to resources, especially for people in traditionally underserved communities. Many R&D programs support important aspects of education and workforce development. A few examples of targeted programs are identified here.

NSF supports education and workforce development through a number of mechanisms, including fellowships and efforts related to single-investigator awards and centers. Several flagship programs are used by the nanotechnology community, including the Graduate Research Fellowship program,[45]

40 https://www.nist.gov/ncnr
41 https://www.nist.gov/cnst
42 https://www.nist.gov/programs-projects/boulder-microfabrication-facility
43 National Nanotechnology Coordinated Infrastructure, https://nnci.net/; accessed 17 March 2022
44 Center for Cellular Construction, https://centerforcellularconstruction.org/; accessed 17 March 2022
45 https://www.nsf.gov/funding/pgm_summ.jsp?pims_id=6201

Research Experiences for Undergraduates,[46] and Research Experiences for Teachers.[47] There are also focused efforts supported by the Education and Human Resources Directorate, including the Improving Undergraduate STEM Education program.[48] One example of a project supporting nanoeducation through this program is the development of a "Nano-Makerspace to Make and Explore the World of the Small" that exposes high-school students and teachers, undergraduate students, and the public to the nanoscale. To address the high demand for technicians in micro- and nanotechnology throughout the American Southwest, NSF is funding the "Supporting Micro and Nano Technicians through Hybrid Teaching Methods" project. The Advanced Technology Education (ATE) program[49] plays an important role in technician training and will continue to support nanotechnology education in 2022. NNCI also has devoted education and outreach efforts across the network.

NIFA supports curriculum development and future workforce training at educational institutions. The Agriculture and Food Research Initiative Education and Workforce Development (EWD) program[50] will focus on further enhancing the three distinct components of the pipeline for developing the workforce in the food and agricultural sciences: (1) Enhancing Agricultural Literacy and Workforce Training offers institutional grants for in-service training to provide K-14 educators increased knowledge of food and agricultural science career opportunities and help them develop improved curricula to train agricultural workforce for the future; (2) Developing Pathways offers undergraduates in food, agriculture, or allied disciplines the technical and leadership skills required for employment in the food and agricultural sectors or in graduate programs; and (3) Advancing Science supports graduate and post-graduate education in agriculture and related disciplines. NIFA Predoctoral and Postdoctoral Fellowship program areas support predoctoral candidates and postdoctoral trainees, respectively.

PCA 5. Responsible Development

The responsible development of nanotechnology has been an integral part of the NNI since its inception, and the initiative has proactively considered potential implications and technology applications at the same time. The responsible development framework articulated in the 2021 NNI Strategic Plan builds on concepts the NNI traditionally included in responsible development—such as nanotechnology-related EHS (nanoEHS) considerations to protect human health, the environment, and ethical, legal, and other societal implications (ELSI)—and embraces new ideas that have emerged, including an emphasis on inclusion, diversity, equity, and access (IDEA) and the responsible conduct of research.

Agencies continue to build on the rich body of nanoEHS knowledge and to collaboratively protect researchers, workers, consumers, and the environment. In 2022, NSF funding for nanoEHS research will be directed primarily at understanding nano-bio phenomena and processes, as well as EHS implications and methods for reducing the risks of nanotechnology development. Research in support of nanomaterials characterization, interfacial nanoscale phenomena, and exposure is performed in NSF's core programs, including the ENG Directorate's dedicated program, Nanoscale Interactions.[51] ENG will begin a program that supports quantum biology proposals in 2022 to better understand nano/bio quantum phenomena and control interfacial nanoEHS interactions. The Center for Sustainable Nanotechnology will continue its activities through 2025 with support from the MPS

46 https://www.nsf.gov/funding/pgm_summ.jsp?pims_id=5517
47 https://www.nsf.gov/funding/pgm_summ.jsp?pims_id=503658
48 https://www.nsf.gov/funding/pgm_summ.jsp?pims_id=505082
49 https://www.nsf.gov/funding/pgm_summ.jsp?pims_id=5464
50 https://nifa.usda.gov/program/afri-education-workforce-development
51 https://www.nsf.gov/funding/pgm_summ.jsp?pims_id=505696

Directorate. The NSF Directorate for Social, Behavioral and Economic Sciences addresses ethical, legal, and other societal implications related to nanotechnology.

FDA invests in nanotechnology research to help address questions related to the safety, effectiveness, quality, and/or regulatory status of products that contain engineered nanomaterials or otherwise involve the use of nanotechnology. FDA also invests in research to develop models for safety and efficacy assessment and to study the behavior of nanomaterials in biological systems and their effects on both human and animal health. FDA's Office of the Commissioner, in partnership with FDA's Nanotechnology Task Force (NTF), facilitates communication and cooperation on nanotechnology research, both within FDA and with national and international stakeholders. NTF provides the overall coordination of FDA's nanotechnology research efforts in the following programmatic investment areas: (1) scientific staff development and professional training, (2) laboratory and product-testing capacity, and (3) collaborative and interdisciplinary nanotechnology research. Most recently, NTF has increased its international efforts to strengthen global regulatory research activities aimed at developing novel characterization/measurement tools and consensus standards.

The nanoEHS efforts of NIH's National Institute of Environmental Health Sciences (NIEHS) are designed to provide a fundamental understanding of the molecular and pathological pathways involved in mediating biological responses to engineered nanomaterials. The Nanotechnology Health Implications Research Consortium is concluding in 2021, and new funding opportunities for extramural nanoEHS efforts are not expected at this time. The NIEHS Small Business Innovation Research (SBIR)/Small Business Technology Transfer (STTR) program continues to support research to develop tools for nanomaterials exposure monitoring. The NIEHS Superfund Research Program plans research that includes nanotechnology-enabled structures to enhance sustainable remediation and to enable rapid, accurate environmental monitoring. NIEHS efforts under the National Toxicology Program (NTP) will continue studies to better understand the impacts of inhalation of multiwalled CNTs on immune system function.

NIOSH will continue to develop occupational safety and health guidance that can be incorporated into business plans to both protect worker safety and promote safe application development and commercialization. NIOSH is evaluating biomarkers of exposure and disease using proteomic, metabolomic, and bioinformatic approaches; developing innovative *in vitro* methodology to better predict *in vivo* outcomes; and evaluating pulmonary and dermal exposure and toxicity, and systemic toxicity that may result from occupational exposures to wide variety of nanomaterials and nanotechnology-enabled products along the life cycle of the materials. These results will also be correlated with health studies conducted among workers at facilities where exposure evaluations are being conducted. NIOSH plans to develop, test, and evaluate direct-reading instruments capable of detecting and measuring airborne nanoparticles. Additional plans include continuing field tests of the portable aerosol multielement spectrometer developed by NIOSH, and efforts in detection of airborne nanoparticles to evaluate and predict biological behavior and translocation between organ systems. NIOSH will also explore the feasibility of applying advanced sensing technology and data analytics to biomarkers as a means of evaluating nanomaterial exposure and possible early response. NIOSH will collaborate with the America Makes Manufacturing USA institute and collaborators from industry and academia to promote safe practices in nanotechnology and advanced manufacturing. NIOSH plans to work with industry to develop practical, "real world" evaluations of hazard and risk represented by nanomaterials through their life cycles, focus the NIOSH field research effort on supporting sustainable nanomanufacturing, and collaborate with industry to assess the toxicology of carbon-based, metal-based, nanocellulose, and nanoclay-enabled materials. NIOSH plans to continue collaborations with non-profit organizations, trade unions, and industry to evaluate nanotechnology-enabled spray coatings, composites, and other nanotechnology-enabled materials in construction and manufacturing.

The NIST nanoEHS research portfolio includes projects focused on understanding and measuring incidental nanoplastics, development of reference materials, establishment of new measurement techniques for consumer products, and evaluations in real-world environments. For example, NIST researchers working in conjunction with FDA and academic scientists are investigating the degradation of polymers containing nanomaterials that exhibit barrier properties useful in many diverse applications, including outdoor coatings for corrosion-resistant infrastructure and food packaging for extended ingredient freshness. Efforts continue to develop metrics to assess changes in nanocomposite performance—including mechanical strength, gas permeability, corrosion resistance, and antimicrobial properties. Recently, NIST researchers have begun to investigate how different formulations of polyvinyl chloride (PVC, a key component of vinyl home siding) regulate the appearance, impact performance, and flammability of the resultant composite siding material before and after UV exposure. Chemical characterization and impact test analyses to simulate vehicle collision, hail, and debris during windstorms are ongoing.

EPA's engineered nanomaterials research is conducted as part of the Chemical Safety for Sustainability National Research Program within the Office of Research and Development (ORD). This research is focused on developing, collating, mining, and applying information on engineered nanomaterials to inform both exposure and hazard assessments and to support risk-based decisions related to the agency's implementation of the Toxic Substances Control Act (TSCA) and the Federal Insecticide, Fungicide, and Rodenticide Act (FIFRA). EPA's research activities have two objectives. The first objective is to evaluate the environmental release and assess human and ecological exposures to engineered nanomaterials. For example, EPA is conducting research to characterize the weathering, release, and transformation of nanomaterials from nanotechnology-enabled consumer products, and to characterize the transport, transformation, fate, and environmental impacts of nanotechnology-enabled pesticides.[52] The second objective of EPA's research activities is focused on integrating information and developing a user interface for ORD's existing nanomaterials database, NaKnowBase.

NIFA supports nanoEHS research relevant to agricultural production and food applications. Risk assessments of the use of engineered nanoparticles 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), livestock, and production environments. The program also supports research on transport and fate of engineered nanoparticles or nanomaterials and nanostructures for nutrient delivery in food production, processing, and interactions with microbiota in the human gastrointestinal tract. NIFA supports research on economic and social implications of food and agricultural technologies, including nanotechnology. The broad social, ethical, cultural, legal, and other potential impacts of emerging and disruptive technologies on society, agricultural markets, agricultural communities and rural prosperity, the food manufacturing industry, consumer preferences, and other domains will be investigated. Multidisciplinary and interdisciplinary approaches involving physical scientists, legal scholars, bioethicists, social scientists, and researchers from the humanities, the public, and other stakeholders are encouraged.

CPSC engages with Federal partners in projects intended to characterize and quantify exposures to engineered nanomaterials released from products. For example, CPSC and NIST continue to work on the optimization of *in vitro* test methods used to determine the toxic endpoints of nanomaterials. CPSC

[52] More information is available at https://www.epa.gov/chemical-research/research-nanomaterials.

and ERDC continue their collaboration, along with the Center for the Environmental Implications of NanoTechnology, to develop a model to predict the health effects of matrix-bound nanomaterials. The findings of this project, which uses novel and advanced techniques to capture toxicity and exposure data for a range of nanomaterials, and its resultant database will be released to the public.

The Federal nanotechnology community is proactively collaborating and leveraging existing nanoEHS knowledge and tools to understand and mitigate the potential risks of emerging concerns such as incidental nanomaterials (e.g., nanoplastics or particulate emissions from laser printers or 3D printers). The interagency nanoplastics interest group is facilitated by NNCO and convenes scientists from more than 20 Federal agencies to share interest, research, and resources available to advance the understanding of this emerging global issue. There are plans to continue and expand these conversations in international fora. Collaborative research efforts between NIEHS, FDA, and other Federal agencies on incidental nanoplastics are planned. The National Center for Environmental Health is supporting a research fellowship focused on understanding the environmental and health effects of micro- and nanoplastics. The Fellow is developing a scoping literature review and a plan to host a science symposium on microplastics.

CPSC, EPA, NIOSH, and NIST collaborative work is evaluating emissions, factors influencing emissions, and the potential toxicity from exposure to emissions from fused deposition modeling 3D printers. This interagency work is expanding to other types of 3D printers that are becoming more affordable to small businesses and the public. NIOSH and CPSC will continue collaborations to study the release of ultrafine particulate and engineered nanomaterials from polymer-based 3D printers. A study of metal-powder-based additive manufacturing will commence in 2022.

Consensus standards activities play an important role in developing confidence in the safety and efficacy of nanomaterials. Several Federal agencies contribute to efforts in the International Organization for Standardization (ISO) TC 229 Working Group 3: Health, Safety and Environmental Aspects of Nanotechnologies. NIOSH plans to continue collaborations with ISO 23151—Nanotechnologies—Particle Size Distributions for Cellulose Nanocrystals, and the Organisation for Economic Co-operation and Development (OECD) Test Guideline 110—Particle Size Distribution/Fibre Length and Diameter Distributions. CPSC staff are engaged in voluntary standards activities to create validated methods for quantifying and characterizing exposures from products, including an ISO project evaluating the release of nanomaterials from treated wood.

Use 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, as well as highlights of agency SBIR and STTR topics and other programs and activities that directly support the accelerated deployment and application of nanotechnology R&D in the private sector. Table 6 shows agency funding for SBIR and STTR awards for nanotechnology R&D from 2016 through 2019 (the latest year for which data are available). Even though few agencies specifically call out nanotechnology in their SBIR/STTR solicitations, it is enabling innovations in many R&D application areas.

Table 6: 2016–2019 Agency SBIR and STTR Awards
(dollars in millions)

	2016			2017			2018			2019		
Agency	**SBIR**	**STTR**	**Total**	**SBIR**	**STTR**	**Total**	**SBIR**	**STTR**	**Total**	**SBIR**	**STTR**	**Total**
DHS	0.0	0.0	0.0	0.0	0.0	0.0	0.3	0.0	0.3	2.0	0.0	2.0
DOC/NIST	0.3	0.0	0.3	0.7	0.0	0.7	0.5	0.0	0.5	1.1	0.0	1.1
DOD	41.9	7.3	49.2	61.5	14.5	76.0	38.3	23.3	61.6	63.5	22.5	86.0
DOE	26.2	4.7	30.9	25.1	5.4	30.5	36.6	5.2	41.8	31.2	3.4	34.6
EPA	1.7	0.0	1.7	0.3	0.0	0.3	0.5	0.0	0.5	0.7	0.0	0.7
HHS/NIH	18.2	5.7	24.0	27.2	7.1	34.3	34.9	7.1	42.0	42.6	5.5	48.1
NASA	3.5	1.1	4.6	12.2	2.6	14.8	4.7	1.5	6.2	7.7	1.6	9.3
NSF	22.9	3.5	26.5	18.2	5.5	23.7	17.4	3.1	20.5	16.2	3.4	19.6
USDA	0.0	0.0	0.0	0.3	0.0	0.3	1.6	0.0	1.6	0.8	0.0	0.8
TOTAL	**114.8**	**22.4**	**137.2**	**145.5**	**35.2**	**180.7**	**134.8**	**40.2**	**175.0**	**165.7**	**36.4**	**202.1**

Some of the topics supported by agency SBIR and STTR awards (and enabled by nanotechnologies) include the following:

- DNA nanostructure-based biosensing for rapid COVID-19 detection and monitoring from saliva samples (NIH).
- Silicon photonics lasers created from printed nanomaterial inks (DOD).
- Educational tool development and pilot deployment to facilitate adoption of advanced nanophotonics manufacturing technology (DOD).
- Nanoscale membranes for on-demand oxygen production and delivery (DOD).
- Nanosorbents for sensing and filtering contaminants in aircraft and spacecraft air supplies (DOD).
- Carbon nanotube-enabled nano-heaters for out-of-oven curing of aerospace composites (DOD).
- Nano-engineered heat exchanger surfaces to reduce energy and water usage of cooling systems (DOD).
- Ultra-lightweight carbon nanotube-lithium metal hybrid anodes to enable high-energy-density lithium-ion batteries (DOD).
- Direct bioelectronic detection of SARS-CoV-2 from saliva using a single-molecule field-effect transistor array (NIH).
- Nanoengineered (e.g., nanopore/nanochannel) devices for direct single molecule RNA and DNA sequencing (NIH).[53]
- Targeted liposomes to deliver inhalable drug therapy for pulmonary artery hypertension (NIH).
- Nanoparticle contrast agents to improve vascular CT imaging (NIH).
- Nanoparticle-based nano-warming of frozen banked vascular tissues (NIH).
- Nanodroplet technology for improved bacterial cell lysis in diagnosing infectious microorganisms (NIH).
- Nanoemulsion-adjuvanted and virus-like particle vaccines against RSV (NIH).
- Coupling fibrin-targeted superparamagnetic iron oxide nanoparticles and magnetic particle detection technology as a portable diagnostic test for high-risk plaques (NIH).
- Developing tools for nanomaterials exposure monitoring (NIH).

[53] Awards funded in response to "Novel Nucleic Acid Sequencing Technology Development" (https://grants.nih.gov/grants/guide/rfa-files/RFA-HG-18-003.html).

- Customized nanotechnology-based treatment of oral cancer (NIH).
- Nanoprobe-based infrared measurements, including the first instrument capable of providing chemistry and IR spectroscopy mapping with resolution of 10 nm in a tapping AFM (DOE).
- Increasing the frame rate of conventional TEM CCD cameras to yield video acquisition into the sub-MHz scale (DOE).
- Femtosecond-pulse EUV and soft x-ray tabletop sources, materials characterization tools enabling 3D, fast, element-sensitive, and high-resolution imaging (DOE).
- Advanced silicon and graphene composite materials for lithium-ion batteries (DOE).
- Long-lasting separation/water purification membranes based on graphene oxide (NSF).
- Manufacturing low-cost nano-metal functionalized materials for water purification (NSF).
- Detecting life in ocean worlds with solid-state nanopores (NASA, in collaboration with NSF).
- Tin oxide nanoclusters to enable extreme UV lithography and extend Moore’s Law (NSF).
- Developing and maturing technologies related to fabricating structural CNT composite components (NASA).
- Nanomaterials and nanosensors for spaceflight water systems (NASA).
- Bilayer nanofibers as wearable sensors for detecting fentanyl (DHS)
- Laser particle separation for sorting of nanoparticles by size (NIST).
- Nanoscale microbial polysaccharides for food and pharmaceutical applications (USDA).
- Inexpensive low-power nanosensor-based measurement of fugitive methane emissions (EPA).

3. Progress towards the NNI Goals

The following selected highlights illustrate progress toward each of the five goals of the NNI. For more information and additional highlights, please see Nano.gov.

Goal 1. Ensure that the United States remains a world leader in nanotechnology research and development.

At the heart of the NNI is support for nanotechnology R&D, from the fundamental discoveries that expand the boundaries of knowledge to the applied and translational breakthroughs that enable new products and help address societal challenges. The individual NNI agencies utilize a variety of mechanisms to conduct and fund research that supports their respective missions. Collectively, these efforts support a vibrant and dynamic nanotechnology R&D ecosystem that is making critical advances in areas as diverse as biomedicine, semiconductors, energy, agriculture, aerospace, and materials development. These continued investments will enable future discoveries that build on the strong foundation developed over the course of the NNI and ensure that the benefits to society and economy are realized.

Fighting COVID-19 and other infectious disease. NNI agencies have made substantial progress in applying nanotechnology advances to fighting immune and infectious disease for a wide variety of pathogens, including the virus that causes COVID-19 (SARS-CoV-2).[54] Key R&D highlights from the Federal response to the COVID-19 pandemic include work by NIH/NIAID investigators to create the first nanoscale resolution images of SARS-CoV-2[55] on February 11, 2020, with scanning and transmission electron microscopes. The NIAID-funded SGCID contributed to the structure-based design of a SARS-CoV-2 nanoparticle vaccine candidate that is currently in Phase I/II clinical trials.[56,57] Sensors were also a robust area of activity. For example, NIH/NIDCR-funded SBIR projects advanced saliva-based tests to detect COVID-19 using technologies such as DNA nanostructure-based biosensing and single-molecule field-effect transistor arrays (funded under the RADx initiative). NASA developed nanoplasmonic sensors for detection of SARS-CoV-2 in complex liquid samples. Efforts to understand and develop effective personal protective equipment (PPE) were also a priority. For instance, a study by NIST and the Smithsonian Institution on a variety of fabrics for masks showed that some of the most effective materials were cotton, and that multiple fabric layers further improve cotton’s effectiveness.[58]

Examples of research addressing other infectious and immune diseases include NIAID-supported development of a new nanoformulation of amphotericin B (CAmB) that facilitates oral absorption and prevents toxicity. This drug provides a treatment for *cryptococcus neoformans*, a global fungal pathogen that kills an estimated quarter of a million HIV-infected individuals yearly.[59] NIAID-funded researchers have also advanced a technology that combines FDA-approved HIV drugs with a nanoparticle platform as a long-acting injectable therapy for children with HIV. University researchers with support from NSF developed nanomaterial-based antimicrobials to combat bacteria resistant to conventional antibiotics.[60]

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54 See Goal 2 below for additional information on progress in nanotechnology-enabled vaccine development and other advances in response to the COVID-19 pandemic.
55 https://www.niaid.nih.gov/news-events/novel-coronavirus-sarscov2-images
56 https://clinicaltrials.gov/ct2/show/NCT04742738
57 https://clinicaltrials.gov/ct2/show/NCT04750343
58 https://www.nist.gov/news-events/news/2020/06/face-coverings-made-layered-cotton-fabric-likely-slow-spread-covid-19
59 https://doi.org/10.1128/mBio.00724-19
60 https://pubmed.ncbi.nlm.nih.gov/32975907/

Advancing cancer diagnostics and therapeutics. The NIH/NCI supports a breadth of research activities that utilize nanotechnology to fight cancer. For example, researchers elucidated *in vivo* mechanisms of nano-drug action with the goal to improve the efficacy of nanomedicines.[61] A university group designed and fabricated novel multifunctional contrast agent nanoparticles that exhibited long-term blood circulation time and high tumor uptake. The contrast agents were used for imaging breast and brain tumor xenografts with excellent tumor contrast to normal tissues.[62] Scientists developed a novel vaccine for a human papilloma virus (HPV-16) associated with cervical cancer. The vaccine uses a liposomal adjuvant based on cobalt–porphyrin-phospholipid and rejected a tumor challenge in a prophylactic setting and eradicated established tumors in local and metastatic settings.[63]

Addressing heart, lung, and blood disorders. Nanotechnology-based approaches are being used to address common heart, lung, and blood ailments with support from NIH/NHLBI. University researchers have developed a "nanotrap" therapy to improve survival in sepsis, employing telodendrimer nanotraps immobilized on hydrogel to efficiently adsorb septic molecules in blood. Nanotrap therapy in combination with antibiotic treatment resulted in 100% survival in severely septic mice.[64] Investigators developed systemically injected lipid polymer nanoparticles encapsulating small interfering RNA (siRNA) that regulate the release of stem cells and leukocytes from the bone marrow. In a mouse model of myocardial infarction, nanoparticle-mediated inhibition of cell release reduced leukocytes in the diseased heart, improved healing after infarction and attenuated heart failure.[65]

U.S. scientists and European collaborators developed nanotechnology-based immunotherapy to treat diseases characterized by excessive inflammation. The treatment increased allograft survival in a mouse model of heart transplantation.[66] Researchers developed a method for targeting liposomes to an inflamed brain in a mouse model using antibodies to vascular cell adhesion molecule 1 (anti-VCAM). VCAM-directed nanocarriers can normalize the integrity of the blood-brain barrier, potentially offering a path for treatment of a number of brain pathologies.[67]

Empowering vaccines and immunotherapies with improved adjuvants. Army-funded researchers are developing nanotechnology-based approaches to advance vaccine development for diseases such as malaria, tuberculosis, and HIV. Their technology uses self-assembled organic nanoparticles and targets vaccine adjuvants (immunomodulators) to lymph nodes, avoiding systemic exposure and potentially enhancing the potency and safety of vaccines. Efficacy studies in mouse and non-human primate models showed that this adjuvant is capable of inducing protective immune responses against HIV Env proteins as well as other antigens.

Developing microneedle coronavirus vaccines. NSF-funded researchers created a platform using cowpea mosaic virus (CPMV) as a nanotechnology scaffold to generate vaccine candidates for the novel coronavirus. The plant virus-based vaccine candidates can be quickly adapted if mutants or novel strains emerge and are especially suited for scalable manufacturing technologies. The CPMV vaccine candidates are blended into slowly degradable polymers and injection molded into microneedle patches. The patches can be shipped outside of the cold-chain and show efficacy when self-applied.

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61 https://www.ncbi.nlm.nih.gov/pmc/articles/PMC7244320/
62 https://pubmed.ncbi.nlm.nih.gov/31244043/
63 https://pubmed.ncbi.nlm.nih.gov/33605054/
64 https://doi.org/10.1038/s41467-020-17153-0
65 https://doi.org/10.1038/s41551-020-00623-7
66 https://doi.org/10.1126/sciadv.abe7853
67 https://doi.org/10.1073/pnas.1912012117

Completing genomes using nanopore technologies. NIAID-funded researchers are working to complete the genomic sequences of pathogens such as *Toxoplasma gondii* and other organisms with complex genomes. To date, many genome sequences remain incomplete due to difficult-to-sequence areas and limitations in the most widely used technologies. Nanopore sequencing is based on the changes in electric currents as DNA passes through nanoscale pores. The technology allows the generation of ultra-long sequences that overcome some of the current limitations.

Creating "smart" reusable bandages. NSF-supported scientists have developed carbon nanotube sensors that can be embedded within a bandage. These "smart" reusable bandages are capable of detecting infection in real time by monitoring hydrogen peroxide concentrations and communicating wirelessly. This approach could be extended to detecting other biomolecules in wounds or in sweat.[68] These bandages could have a significant impact on treatment of diabetic wounds or severe burns. The work is discussed in an episode of the NNI's Nano Matters podcast series.[69]

Exploring nanotechnology-based approaches to treating vision loss. NRL researchers have developed two nanoparticle-based platforms (gold nanoparticles and semiconductor quantum dots) to stimulate the retina in the eye. The platforms photostimulate electrical activity of living neurons. This work could lead to treatments for total or progressive vision loss.

Developing a bionic ear. Researchers supported by NIBIB engineered a functional bionic ear via 3D printing of a cell-seeded hydrogel matrix. The bionic ear included an intertwined conducting polymer consisting of infused silver nanoparticles. Cartilage tissue was cultured around an inductive coil antenna in the ear and then connected to cochlea-shaped electrodes, exhibiting enhanced auditory sensing for radio-frequency reception.

Understanding spinal injuries. NSF-funded researchers have developed scalable platinum nanorod microelectrode arrays on flexible substrates with excellent central nervous system recording and stimulation capabilities. This research will improve understanding of spinal injuries and inform potential treatments.

Developing stretchable and wearable electronics to monitor human health and performance. The Air Force Research Laboratory (AFRL) and an industry collaborator used liquid metal nanoparticles to develop printable inks for conductive circuits that can be stretched above 700%. These circuits are being integrated into textiles for body area networks, which connect to wearable sensors and haptic feedback for next-generation physiological monitoring and augmentation, and are being used in soft conformal robotics for confined space inspection.[70] Another project developed graphene transistors for wearable electronics to enable real-time sensing of neuropeptides in biofluids (e.g., sweat, saliva) for monitoring human health and performance.[71]

Using nanogenerators to power implantable devices. NIBIB-funded researchers have developed ultrathin, lightweight, stretchable, and bio-compatible nanogenerators that can harvest energy from body motion. The nanogenerators are being optimized to power implantable biomedical devices such

68 https://doi.org/10.1002/adfm.202006254

69 D. Roxbury, Exploring the promising applications of carbon nanotube-based biosensors, NNI *Nano Matters* podcast series (2021), https://www.youtube.com/watch?v=NniAegFX4JQ&list=PLy4wjGabGUTZsoVAFSJpGkV-4J_y3AzXB&index=5; accessed 17 March 2022.

70 https://doi.org/10.1002/adma.201903864

71 https://doi.org/10.1021/acsanm.0c00353

as pacemakers, artificial arteries for real-time blood pressure sensing and occlusion monitoring, a device that promotes hair regeneration, and a vagus nerve stimulation system for weight control.

Studying hopfions to advance spintronics. An international team co-led by researchers at DOE's Lawrence Berkeley National Laboratory has made a major advance in spintronics, a class of electronics that use an electron's spin to encode data. The team created and observed for the first time 3D magnetic quasiparticles called hopfions emerging from 2D skyrmions at the nanoscale in a magnetic system. The discovery is a significant step in realizing high-density, high-speed, low-power, yet ultrastable magnetic memory devices.[72]

Developing low-energy transistors. An NSF CAREER awardee has developed an energy-efficient transistor concept that leverages the unique properties of a new class of nanoscale materials called antiferroelectric oxides. Antiferroelectric negative capacitance field-effect transistors (NCFETs) can lead to reduced energy use in transistors, below the fundamental, thermodynamic limit. With support from DOE/AMO, Sandia National Laboratories developed an ultra-energy-efficient tunnel field-effect transistor (TFET) made with atomically precise advanced manufacturing (APAM). TFETs use ultra-low-power quantum tunneling to operate devices at 1/10th the power of leading-edge conventional transistors. This innovation uses APAM to enable abrupt ultra-doping and bring the TFET's low current up to CMOS-relevant levels while maintaining its energy efficiency.

Exploring applications of novel topological phenomena. Army-funded scientists identified a new mechanism for high-frequency rectification of terahertz waves using the intrinsic quantum properties of inversion-breaking materials. They proposed a skew scattering mechanism, predicting a much higher rectification efficiency than the previous Berry curvature dipole mechanism, using topological semimetals such as graphene and transition metal dichalcogenides. The team also designed an efficient rectifier and filed a patent for the device design.[73]

Discovering and exploring a new quasiparticle. An ONR-supported university group has reported a new type of quasiparticle, helical topological exciton-polariton, in a system of monolayer of tungsten sulfide strongly coupled to a photonic crystal. By creating a new type of topological insulator for polaritons, the group demonstrated propagation of polaritons around sharp bends with no backscattering losses. These polaritons provide a new platform for developing tunable polaritonic spintronic devices for classical and quantum information processing applications.[74]

Generating single-photon optical nonlinearities with a semiconductor platform. NRL scientists have developed a technique to tune individual nanoscopic photon sources, overcoming variability in the optical properties of the sources. The researchers generated giant optical nonlinearities at the single-photon level using multiple nanoscopic sources for the first time with a semiconductor platform. This work is a step toward on-chip quantum and neuromorphic computing.

Advancing semiconductor quantum dots as quantum bits and emitters. NRL scientists have discovered a way to perform quantum optical control of a spin in a semiconductor quantum dot while retaining the ability to optically measure the spin state. This development makes use of excited orbitals within the quantum dot in which motion of a hole is coupled to its spin state. These quantum dots, as quantum bits and emitters, may be useful for secure communications, quantum sensing, and quantum computing.

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[72] https://newscenter.lbl.gov/2021/04/08/spintronics-tech-a-hopfion-away/, https://doi.org/10.1038/s41467-021-21846-5
[73] https://doi.org/10.1126/sciadv.aay2497
[74] https://doi.org/10.1126/science.abc4975

Synthesizing novel nanocrystals for infrared devices. NRL scientists synthesized new core/shell colloidal nanocrystals with enhanced light-matter interactions. The nanocrystals combine ability of plasmonic $Cu_{2-x}S$ nanocrystals to focus infrared light at the nanoscale with excitonic PbS nanocrystals. This is a first step towards realizing enhanced optoelectronic properties of infrared colloidal nanocrystals for inexpensive, compact, lightweight, and low-power infrared devices such as detectors and single-photon emitters.

Enabling integrated quantum optics. NRL researchers developed an integrated quantum optics device comprising semiconductor quantum dots embedded in a photonic crystal waveguide. Using a laser-processing technique, several quantum dots can be tuned to the same emission wavelength, enabling quantum interactions, a critical test of an integrated quantum optics platform.

Facilitating high-speed, low-power optical computing. NSF-supported researchers are developing programmable photonic computation accelerators (PPCAs) that use controlled quantum symmetry to perform real-time programmable mathematical operations. Machine learning algorithms are being performed on the PPCA platform to demonstrate optical machine learning for the first time and test its corresponding speed and fidelity. These photonic computation accelerators could be applied in applications demanding extreme speed, energy efficiency, parallelism, complexity, and scalability on an ultra-compact footprint.

"Writing" electronic circuitry with lasers. AFRL scientists worked with an international team to pioneer a new nanomanufacturing technique that uses lasers to customize, design, repair and build electronics. This laser "writing" technique enables the precise placement of conducting, insulating, and semiconducting materials embedded within a nanoscale molybdenum disulfide thin film. By patterning the different structural or chemical modifications, researchers were able to directly write resistors, capacitors, sensors, and other circuitry using a simple laser setup in ambient conditions.[75] This technique subsequently was used to build inexpensive rapid-response sensors for SARS-CoV-2 spike proteins and influenza A hemagglutinin in saliva samples.[76]

Exploiting metamaterials for national security applications. An AFRL team is collaborating with industry to develop a hybrid metalens for compact optical systems. The effort has demonstrated hybrid optical system design and scaled nanomanufacturing. Another AFRL project developed dielectric metasurfaces for optical components using neural network AI/ML-based software to accelerate the discovery of materials with nanoscale metasurfaces. This software has sparked new cross-directorate and industrial collaborations to address mission-critical Air Force problems.[77,78]

Developing bio-inspired chromophore networks. Using an approach that mimics protein scaffolds used in photosynthesis, NRL researchers have shown that DNA nanostructures can be used to constrain the position and orientation of chromophore molecules. The work suggests that the control is sufficient to achieve highly efficient energy transfer between chromophore pairs. This advance is an initial step in developing DNA nanostructures to organize chromophore molecules into networks, with potential applications in energy harvesting and quantum technologies.

Understanding and enhancing lithium-ion batteries. Researchers at Argonne National Laboratory have developed a low-cost, high-performance, sustainable lead-based nanocomposite anode for

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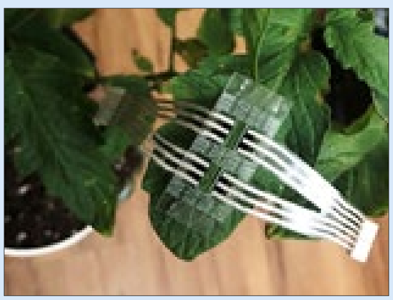
75 https://doi.org/10.1016/j.mattod.2020.09.036
76 https://doi.org/10.1101/2020.11.17.20233569
77 http://doi.org/10.1103/PhysRevB.101.195104
78 https://doi.org/10.1364/OE.400360

lithium-ion batteries.[79] Researchers at the DOE-funded Joint Center for Energy Storage Research Energy Innovation Hub[80] in collaboration with the Army Research Laboratory (ARL) developed new methods to study the formation and composition of the solid-electrolyte interphase (SEI) that forms on a battery's anode and often dictates performance.[81] The identification of LiF and LiH in the SEI sheds light on key amorphous components and can be used to enhance energy density.[82] Another team of researchers at the SLAC National Accelerator Laboratory have quantitatively profiled the nanoscale environment in layered oxide electrodes to better understand and control the development of holes that change the electrode's structure and degrade the battery's storage capacity.[83]

Reducing cable weight in high-voltage systems. NASA's Transformational Tools and Technology Project has developed lightweight Cu-CNT composite conductors via an electroplating process. Preliminary results revealed that the Cu-CNT wires produced by this method exhibited superior electrical properties compared to other Cu-CNT composite conductors. These materials can help reduce cable weight and increase mechanical strength and durability while maintaining electrical conductivity.

Improving water-responsive materials. Academic researchers supported by ONR, AFOSR, and NSF with international collaborators carried out mechanistic studies on biomimetic nanoporous tripeptide crystals to understand how these materials efficiently extract energy from evaporation and turn it into motion.[84] Potential applications include humidity-driven and water-driven actuators for robotics, adaptive textiles and architectures, and evaporation energy-harvesting devices.

Plant patch enables continuous monitoring for crop diseases



The flexible sensor continuously monitors plants to detect stresses and diseases. Image credit: North Carolina State University.

Low-cost sensors for agriculture and food safety are the next frontier in the fight for sustainable agriculture and food security. University researchers have developed a plant patch that enables continuous monitoring for crop diseases and other stressors such as extreme heat.[85,86] These small and flexible patches include graphene-based sensors and silver nanowire electrodes and detect the volatile organic compounds that are released when plants are exposed to certain stressors or diseases. The sensors alert farmers to the presence of the problematic VOCs, enabling interventions to protect the crop. This approach provides information more rapidly than sending samples to a laboratory for analysis. Further, the patch can test for multiple stressors and diseases concurrently, while laboratory-based tests provide one measurement at a time. Future work includes the expansion of detection capabilities to include other factors such as humidity, as well as the development of solar-powered device that can transfer data wirelessly. This work was partially funded by USDA and NSF.

79 https://doi.org/10.1002/adfm.202005362
80 Joint Center for Energy Storage Research, https://www.jcesr.org/about/, accessed 17 March 2022
81 https://doi.org/10.1038/s41565-019-0618-4
82 https://doi.org/10.1038/s41565-020-00845-5
83 http://dx.doi.org/10.1038/s41560-021-00832-7
84 https://doi.org/10.1038/s41563-020-0799-0
85 North Carolina State University, Plant patch enables continuous monitoring for crop diseases (7 July 2021), https://news.ncsu.edu/2021/07/patch-monitoring-crop-diseases/, accessed 17 March 2022.
86 https://doi.org/10.1016/j.matt.2021.06.009

Harvesting solar energy with nanobiomaterials. NIFA-funded researchers have developed nanobiomaterials for sustainable solar energy conversion utilizing two nanoscale protein complexes, Photosystems I and II, that are remarkably efficient in capturing light and transferring electrons across plant membranes. Both complexes can be extracted from green plants, including agricultural crops and residues, to supply the active nanoscale component. The team was the first to demonstrate that micrometer-thick films of the isolated protein yield tremendous enhancements in photoconversion as film thickness is increased.[87]

Generating electricity by mixing salt and fresh water. NSF-supported researchers, working with industry, have developed membranes with boron nitride nanotubes (BNNTs) that generate electricity when salt and fresh water are mixed, e.g., at river estuaries.[88] BNNT membranes show power densities up to 15,000 W/m^2 of open pore area, 1000x higher than other membranes. Solution-based fabrication techniques provide a path toward scale up and commercialization.

Bioprinting bionic coral to cultivate algae. NSF-supported researchers at UCSD and international collaborators have 3D printed optically tunable scaffolds containing cellulose-derived nanocrystals to mimic coral tissue for cultivating high-density algae. In the process they designed a new class of bionic materials capable of interacting with living organisms that could be used to design next-generation photobioreactors. The bionic coral has the potential to culture algae with reduced energy consumption, maintenance requirements, and water usage.[89] A provisional patent has been filed.

Developing high-performance nanocomposites for force protection. AFRL and academic researchers have collaborated to develop polymer composites containing polymer-grafted nanoparticles (PGNs) that can be used in multifunctional coatings, films, and monoliths. A second generation of PGNs optimizes toughness with optical, electronic, and transport performance.[90] One important application is lightweight nanocomposite films with extreme shock-induced deformation and kinetic energy dissipation, where nanoparticles with large numbers of strongly entangled grafted chains can lead to up to ~25% greater specific energy absorption over a comparable homopolymer.[91] These efforts complement work at ISN, where researchers have developed advanced multiscale modeling methods to guide the design and development of new ballistic testing media, as well as shock mitigating and reinforcing molecular nanocomposites and polymers for soldier protection.

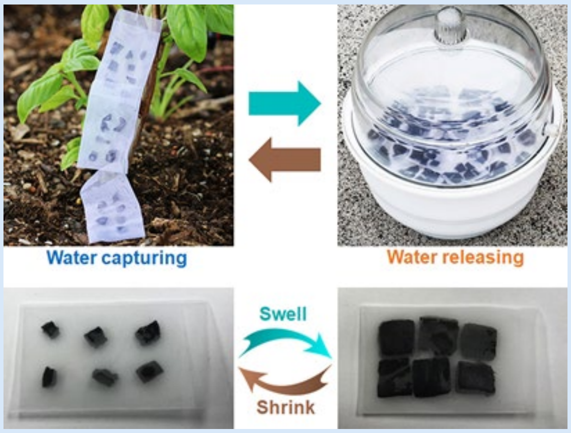
Exploring nanostructured fibers for smart textiles. ISN researchers have developed novel functional multimaterial fiber architectures and are exploring innovative fabrication technologies across a range of application areas. Recent advances include weaving and demonstrating acoustic fabrics with applications in selective hearing, sound communication, and heart monitoring; incorporating supercapacitor fibers into machine-woven fabrics for energy-storage textiles; and constructing a fiber with on-demand drug release for therapeutic intervention. Additional work has demonstrated a fabric capable of running a neural network that recognizes what the wearer is doing in real-time.

Exploiting nanomaterials as antimicrobials. ARS researchers have developed antimicrobials made from fish skin gelatin-based nanofibers that incorporate cinnamaldehyde.[92] Researchers have also conducted extensive characterization of antibacterial nanosilver on textiles after application and

87 https://doi.org/10.1002/adfm.201001193
88 https://www.doi.org/10.1126/science.aba4523
89 https://doi.org/10.1038/s41467-020-15486-4
90 https://doi.org/10.1021/acsnano.9b05001
91 https://doi.org/10.1021/acsnano.0c06146
92 https://doi.org/10.3390/ijms19020618

laundering.[93,94] Silver nanoparticles immobilized within cotton fiber exhibited persistent antibacterial activity after 50 home laundering cycles.[95]

Nanotechnology-enabled systems for atmospheric water extraction



Super moisture absorbent gels that can extract large amounts of water from ambient air, and quickly release it in the form of clean drinking water using only solar energy and enabled by nanostructures in the material. Image credits: University of Texas – Austin.

Properties at the nanoscale enable state-of-the-art materials such as hydrogels and metal-organic frameworks (MOFs) to swiftly adsorb water from the atmosphere and easily release it for use. Although technologies to collect water from the atmosphere have existed for centuries, they relied on humid environments or high energy inputs to function. Advances in nanotechnology have made it possible to create materials that extract atmospheric water in arid environments without a high energy trade-off.

Hydrogels, or gel-polymer hybrids, are highly absorbent. The polymers incorporate other molecules, nanoparticles, and nanostructures to induce thermal switching capabilities (hydrophilic at a certain temperature, hydrophobic with a temperature increase) permitting easy collection and release of water.

MOFs are highly porous materials composed of metal ions connected by organic molecules. While hydrogels are able to collect more water in humid temperatures, MOFs have an advantage in arid conditions.

Variations of these two technologies are currently making headway under DARPA's Atmospheric Water Extraction program. This program aims to create and scale up technologies that can meet the daily drinking water requirements of deployed warfighters and create a lightweight system that can meet the daily drinking water requirements of up to 150 people.[96]

Images from the Additively Manufactured Integrated Reservoir to Extract Water Using Adsorbents and Thermally-Enhanced Recovery (AIR2WATER) project, which aims to build a device that combines additive manufacturing and MOFs to deliver 500 L of water a day using the earth's atmosphere and a power source to start producing water. Image credits: UC Berkeley.

Developing high-value-added materials from agricultural feedstocks. ARS scientists investigated polymers made from canola protein as a potential alternative to synthetic plastics and found that incorporating cellulose nanocrystals (CNCs) improved the films' thermal and mechanical properties.[97] Researchers from academia and ARS developed a cost-effective copper iron magnetic bimetallic nanocatalyst supported on activated carbon. The catalyst converts an important biomass-derived compound into an industrial intermediate that can be used to make resins, fibers, foams, drugs,

93 https://doi.org/10.1007/s11051-019-4740-x
94 https://doi.org/10.1039/C9AY02545F
95 https://doi.org/10.1021/acs.jafc.9b07531
96 https://www.darpa.mil/news-events/2020-12-18
97 https://doi.org/10.1021/acsomega.9b02460

polymers, ketones, and ethers.[98] An international team led by ARS developed active packaging materials that incorporate CNCs and Pd nanoparticles in a polymer to scavenge oxygen.[99]

Innovating methods for multiscale materials growth. A university team supported by ONR and NSF has demonstrated a template-based bottom-up approach to guide hierarchical materials growth from disordered molecules all the way up to the macroscale using silk fibroin. Potential applications include information storage and encryption, surface functionalization, and printable 3D constructs with customized architecture and controlled anisotropy.[100]

Enabling rapid development and screening of peptoid nanostructures. Scientists at the DOE Molecular Foundry, with funding from DARPA, have developed a new method to synthesize and screen libraries of peptoid (artificial peptide) nanostructures. The data libraries enable researchers to design structures that can target bacteria, viruses, or other microorganisms. This approach provides the first rapid method for discovering and synthesizing compounds that can act like antibodies, selectively binding to pathogens or other targets. The ability to quickly design new "smart" materials has many potential applications, including in defense, environmental cleanup, and biomedicine.[101] These efforts also support the Materials Genome Initiative.

Harnessing enzymes for synthesis of food, fuel, and medicine. NRL scientists have developed a modular chemistry that allows enzymes to be brought into close proximity by nanoparticles and engage in highly efficient channeled biocatalysis. This technology harnesses the power of enzymes to make bulk precursor and specialty chemicals, including pharmaceuticals, from a common starting material. Kinetic rates in these nanoaggregates are hundreds of times more efficient than use of enzymes alone. Potential applications include on-site synthesis of foods, fuel, and medicine.

Advancing fabrication, design, and applications of DNA nanostructures. With support from ONR, a team of researchers from academia, industry, and NIST has developed a structural DNA nanotechnology fabrication technique called DNA bricks that they used to fold nanotrenches for confining DNA-hybridization-mediated carbon nanotube alignment. This scalable method for fabricating densely aligned, evenly spaced arrays was utilized to construct high-performance carbon nanotube field-effect transistors and may enable the production of biotemplated electronics.[102] Another ONR-supported team has developed and validated a new approach for autonomous design of all DNA staple sequences needed to fold any free-form 2D scaffolded DNA origami wireframe object from a long single-strand of DNA scaffold. Such nanostructures offer the ability to organize secondary molecules (e.g., dyes, nucleic acids, proteins, and semiconductor nanocrystals) for applications in fields such as photonics, nanoscale energy transport, and biomolecular sensing. The algorithm is available online as a stand-alone software tool.[103]

DOE-supported researchers developed a DNA-based molecular additive manufacturing process. The project demonstrated self-assembly of three independently moving layers of DNA origami and the

98 https://doi.org/10.1021/acssuschemeng.9b05575
99 https://doi.org/10.1007/s10570-019-02613-8
100 https://doi.org/10.1038/s41467-019-14257-0
101 https://www.energy.gov/science/bes/articles/new-data-libraries-open-new-chapter-designing-compounds-mimic-antibodies
102 https://doi.org/10.1126/science.aaz7440
103 https://doi.org/10.1126/sciadv.aav0655

control of motion in two dimensions with stepper motor positioning while printing a pattern at multiple sites simultaneously. The use of self-assembly methods makes this a highly scalable approach.[104]

Researchers supported DOE and NIH, using facilities at the Center for Functional Nanomaterials and National Synchrotron Light Source II at Brookhaven National Laboratory, have developed biocompatible molecular coatings that stabilize wireframed DNA origami cages to preserve the structural stability of the DNA cages in biological applications. They demonstrated that the coated cages can carry an anticancer drug with a slower release over time than is possible with the non-coated counterpart. The coatings also support targeted drug delivery and could advance DNA origami applications in drug delivery, bioimaging, and cellular targeting.[105]

Researchers supported by NIFA and NSF are exploring the use of DNA as building blocks. The team created the first tree-shaped DNA from which DNA-based nanobarcodes were engineered. Multiple pathogen DNA were detected simultaneously using the DNA nanobarcodes. They built an ultra-portable, all-in-one, smart-phone-based biosensor, as thin as and as small as an envelope, that can detect any pathogen DNA precisely with great sensitivity. Recently the team also used nanoscale DNA combined with microflows to create a dynamic DNA material with life-like properties: metabolism, self-assembly of shape, and hierarchical formation that autonomously regenerated and degraded. The team demonstrated biosensing of plant viruses with this material.[106]

Detecting food allergens and pathogens. ARS researchers screened for a single-chain antibody from camelids, also known as a nanobody, specific for the peanut allergen Ara h 3. One of the nanobodies, Nb16, showed promise for the development of biosensors because of its high stability, small molecular size, and ease of production.[107] Another ARS team used nanopore gene sequencing to achieve real-time identification of pathogens in food. They developed a universal nanopore sample extraction technique and a library of preparation protocols for identifying both gram-positive and gram-negative pathogenic bacteria.[108] FDA’s Center for Food Safety and Applied Nutrition has been developing nanotechnology-enabled sensors for contaminants, biological toxins, and pathogens in food products that will improve FDA’s ability to rapidly respond to foodborne disease outbreaks and other emerging threats.

Inventing a novel 2D material. University and Argonne National Laboratory scientists—with funding from ONR, NSF, and DOE and using facilities at Argonne’s Center for Nanoscale Materials—have created stable nanosheets containing boron and hydrogen atoms with potential applications in nanoelectronics and quantum information technology. The novel 2D nanomaterial called borophane, consists of a sheet of boron and hydrogen a mere two atoms in thickness. The 2D allotrope of boron, borophene, is unstable by itself. But when borophene is mixed with hydrogen, it is more stable, and should be easily integrated with other materials in the construction of novel optoelectronic devices.[109]

Paving the way for better GaN power electronics. AFRL and industry researchers have demonstrated heterogeneous integration of nanoelectronic films and radio frequency devices using 2D materials. The team developed a 2.2 nm hexagonal boron nitride on sapphire film that serves as a platform for wafer-

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[104] https://www.energy.gov/sites/prod/files/2019/09/f66/DNA%20Strand%20Displacement%20Driven%20Molecular%20Additive%20Manufacturing.pdf

[105] https://science.osti.gov/bes/Highlights/2021/BES-2021-03-f

[106] https://doi.org/10.1126/scirobotics.aaw3512

[107] https://doi.org/10.1021/acs.jafc.9b02388

[108] https://doi.org/10.3389/fmicb.2020.00514

[109] https://www.anl.gov/article/less-than-a-nanometer-thick-stronger-and-more-versatile-than-steel, https://doi.org/10.1126/science.abg1874

scale GaN and radio-frequency devices to be synthesized and transferred to any new substrate. This technology could enable GaN power electronics that can withstand higher power densities, be integrated into multifunctional platforms, and be used in flexible electronics.[110,111]

Growing a 2D superconductor. ONR-funded scientists grew a superlattice comprising alternating layers of hexagonal NbS_2 and Ba_3NbS_5, using the inert Ba_3NbS_5 layers to dissociate the superconducting NbS_2 layers from one another, resulting in high-carrier-mobility superconductivity. The structure of this material, which may have exotic quantum phases, could be extended to create a new class of systems based on transition-metal dichalcogenides (TMDs), including 2D superconductors, topological insulators, and excitonic systems.[112]

Synthesizing layered TMDs. AFRL researchers identified a mechanism for redox exfoliation of layered transition metal dichalcogenides (LTMDs), a class of two-dimensional inorganic nanocrystals with unique properties arising from confinement-induced effects. Integrating few-to-monolayer LTMDs into resins, inks, and polymers for industrial manufacturing processes such as flow coating, printing, and spray deposition could enable applications including composites, optical films, coatings, lubricants, catalysis, adhesives, energy harvesting and storage devices, and sensors. The group developed novel synthesis methods that are being applied for scaled-up production.[113]

Investigating magic-angle twisted bilayer graphene (MATBG). Scientists supported by ONR have been further exploring MATBG properties, including unexpected insulating phases. They developed a local spectroscopic technique using a scanning tunneling microscope to detect a sequence of topological insulators in MATBG. Their findings illustrate that many-body correlations can create topological phases materials such as MATBG beyond what was previously predicted.[114]

Understanding and controlling the properties of graphene. ONR-funded researchers have succeeded in synthesizing bow-tie-shaped graphene molecules first theoretically envisioned in 1972. Scanning tunneling microscopy and spin excitation spectroscopy of this material showed an antiferromagnetic order with an exchange-coupling strength exceeding the Landauer limit of minimum room temperature energy dissipation. The group demonstrated switching of magnetic ground states in molecules with quenched spins, using atomic manipulation. They showed for the first time direct evidence of carbon magnetism in graphene, which could enable room-temperature spintronic devices.[115] AFRL and academic researchers developed a mask-less, resist-free, and fully reversible process for patterned functionalization of graphene using electron beam chemistry. The method can be readily extended to other materials and types of functionalities, thereby enabling selective functionalization and doping for electronics and photonics applications.[116]

ONR-supported researchers have developed a method for on-surface synthesis of atomically precise graphene nanoribbons (GNRs) directly on semiconducting metal oxide surfaces, demonstrating the formation of planar armchair GNRs terminated by well-defined zigzag ends. The research suggests that the magnetic ground state of these open-shell GNRs was electronically decoupled from the substrate.[117]

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110 https://doi.org/10.1021/acsami.0c02818
111 https://doi.org/10.1021/acsaelm.0c01063
112 https://doi.org/10.1126/science.aaz6643
113 https://doi.org/10.1021/acs.chemmater.0c01937
114 https://doi.org/10.1038/s41586-020-3028-8
115 https://doi.org/10.1038/s41565-019-0577-9
116 https://doi.org/10.1016/j.carbon.2020.04.098
117 https://doi.org/10.1126/science.abb8880

Additional ONR-funded work has demonstrated a general technique for inducing metallicity in GNRs by inserting a symmetric superlattice of zero-energy modes into otherwise semiconducting GNRs.[118] These efforts, and other ONR-supported GNRs projects, may lead to carbon-based nanodevices with applications in next-generation electronics and quantum information science.[119]

Combining theory and modeling with experiment. In a project that is synergistic with the goals of the Materials Genome Initiative,[120] ONR-supported researchers have identified 130 enforced semimetals and topological insulators from a high-throughput search of the Magnetic Materials Database based on first-principles calculations. The results will inform future experimental studies and open-source code for diagnosing topologies of magnetic materials, and highlight several "high-quality" magnetic topological materials for further study.[121] FHWA-funded researchers developed theories and computational codes to better understand how materials behave over multiple lengths of time and at different scales. These theories dealt with modeling and simulations at the nanoscale. The goal was to provide a foundation to study how materials respond to environmental conditions and applied loadings over time.[122]

Goal 2. Promote commercialization of nanotechnology R&D.

Federal investments in nanotechnology R&D have led to thousands of products in the marketplace, and today's scientific discoveries serve as the foundation for the next generation of applications, from tissue regeneration to aerospace composites. The NNI fosters commercialization 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. In addition to these mechanisms, NNCO has a devoted industry liaison staff member who engages with industry and the development community by conducting outreach, sharing best practices, and suggesting collaborations as appropriate.

Supporting the entrepreneurial community. The NNI agencies and NNCO foster and support the entrepreneurial community through an array of activities such as SBIR and STTR programs (see the SBIR/STTR section above, p. 21), Innovation Corps (I-Corps), NIH's Concept to Clinic: Commercializing Innovation Program,[123] and entrepreneurship efforts associated with the DOE National Labs (e.g., Cyclotron Road[124]). NNCO facilitates the Nanotechnology Entrepreneurship Network to bring new and seasoned entrepreneurs together with the people and resources available to support them.[125] This network provides a forum for entrepreneurs to share best practices for advancing nanotechnology commercialization and lessons learned along the technology development pathway. The NSF SBIR program has an ongoing nanotechnology topic with subtopics for nanomaterials, nanomanufacturing, nanoelectronics and active nanostructures, nanotechnology for biological and medical applications, and instrumentation for nanotechnology.

The NSF I-Corps program helps researchers gain insight into entrepreneurship, including understanding requirements and challenges for starting a business.[126] The program includes

118 https://doi.org/10.1126/science.aay3588
119 https://doi.org/10.1002/adma.201906054
120 https://mgi.gov/
121 https://doi.org/10.1038/s41586-020-2837-0
122 https://www.fhwa.dot.gov/publications/research/ear/18067/
123 https://www.nibib.nih.gov/research-program/c3i-program
124 https://cyclotronroad.lbl.gov/
125 https://www.nano.gov/nanoentrepreneurshipnetwork
126 https://www.nsf.gov/news/special_reports/i-corps/

nanotechnology projects with DOE, NIH, and NASA. There are 99 sites and nine I-Corps nodes active nationwide. The NSF I-Corps Hubs Program,[127] initiated in 2020, forms the backbone of the National Innovation Network—a network of universities, NSF-funded researchers, established entrepreneurs, local and regional entrepreneurial communities, and other Federal agencies. The NSF Industry–University Cooperative Research Centers (IUCRC) program provides a structure for academic researchers to conduct fundamental, pre-competitive research of shared interest to industry and government organizations.[128] Examples of nanotechnology-related IUCRC awards include the Center for Atomically Thin Multifunctional Coatings[129] and the Center for Rational Catalysis.[130]

NASA's Technology Transfer Program focuses on taking technologies developed to support space exploration and aviation and making them available for public use. A monthly "Virtual T2 Webinar" series[131] promotes licensing opportunities of NASA-developed technologies, some of which include nanotechnology-enabled materials. The NIST Return on Investment Initiative Final Green Paper[132] includes 15 key findings to maximize U.S. innovation from government-funded research. NIST is continuing to explore legislative and regulatory revisions to address many of the proposals in the Green Paper, and is rebuilding the iEdison online system for reporting inventions.[133]

Technology transfer depends on effective mechanisms that protect new ideas and investments in innovation and creativity. USPTO provides intellectual property policy advice and guidance to the Executive Branch and grants patents on nanotechnology applications that meet the statutory requirements. To keep pace with rapid advances in nanotechnology, the USPTO provides in-depth nanotechnology-specific training events for patent examiners and fosters communication among examiners across multiple disciplines. In addition, USPTO has a subset of patent examiners across all technology disciplines who serve as points of contact to assist other examiners with nanotechnology issues. USPTO also collects a variety of patent data that can be used as a benchmark to analyze nanotechnology development and for trend analysis of U.S. and international nanotechnology patenting activity. USPTO also provides assistance on intellectual property issues to many stakeholders, including independent inventors and other entrepreneurs.

Leveraging research infrastructure to facilitate commercialization. The NNI user facilities and research centers are a key asset in the effort to foster technology transfer and commercialization. For example, the DOD-funded AIM Photonics manufacturing institute,[134] part of the Manufacturing USA network,[135] provides a state-of-the-art foundry enabling manufacturing of photonic crystals and other subwavelength photonic structures. These capabilities facilitate the transition of nanostructure engineering from R&D to advanced commercial manufacturing and enable new applications of integrated photonics. A university group tested the feasibility of wafer-scale production 2D photonic crystals in silicon nitride at AIM Photonics. The team was able to fabricate exceptionally high-quality devices at the AIM foundry, paving the way for using foundry processes in photonic crystal engineering.

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[127] https://www.nsf.gov/news/special_reports/i-corps/hubs.jsp
[128] https://iucrc.nsf.gov/about/
[129] https://iucrc.nsf.gov/centers/atomically-thin-multifunctional-coatings
[130] https://iucrc.nsf.gov/centers/center-for-rational-catalyst-synthesis
[131] https://technology.nasa.gov/virtual-events, https://technology.nasa.gov/virtual-events-archived
[132] https://nvlpubs.nist.gov/nistpubs/SpecialPublications/NIST.SP.1234.pdf
[133] https://www.nist.gov/tpo/bayh-dole/iedison-rebuild
[134] AIM Photonics Manufacturing USA institute, https://www.aimphotonics.com/; accessed 17 March 2022
[135] Manufacturing USA network, https://www.manufacturingusa.com/; accessed 18 March 2022

AFRL and the Cornell High-Energy Synchrotron Source developed high-throughput x-ray micro-scanning techniques to probe nanofiller alignment in complex-shaped nanocomposites. This work has direct impact on process optimization of 3D printing technologies developed by the additive manufacturing OEMs. The world-class speed and resolution of this technique is also used by the flexible electronics industry, through the NextFlex Manufacturing USA institute.[136] Previous bottlenecks in data analytics have been improved and enable industrial collaborators to obtain meaningful results within days.

Developing nanoparticle-enabled mRNA vaccines for COVID-19 and other diseases. The promise of nanotechnology for the future of health was demonstrated during the response to the COVID-19 pandemic. The stabilization of messenger RNA strands using novel lipid nanoparticle technology enabled their use as life-saving vaccines in the United States and across the world, and LNP-encapsulated messenger mRNA will continue to play a key role into the future as a novel vaccine platform. NNI participating agencies, including NIH, BARDA, FDA, and DOD, supported the development, validation, and commercialization of this technology through past and current support for Zika and COVID-19 mRNA vaccine development, and will continue to support development and commercialization of other uses of mRNA technology, including for vaccines to address existing and future viruses.

LNP mRNA vaccines are based on a novel approach that uses mRNA to produce the viral protein against which an immune response is mounted. Because RNA is rapidly digested by enzymes in the body, the mRNA cannot be injected as free nucleic acid but must be protected. The vaccines that were approved against COVID-19 in 2021 complex the mRNA with LNPs. Advantages over traditional vaccines include rapid vaccine development, particularly important in the current pandemic. Earlier versions of mRNA vaccines were developed to combat other infectious diseases, such as those caused by Zika virus, influenza virus, and cytomegalovirus, but the production of vaccines against COVID-19 has demonstrated the ability of this approach to generate vaccines rapidly.

The FDA Center for Drug Evaluation and Research (CDER) collaborated with the FDA Advanced Characterization Facility and the Nanotechnology Core Facility located in Jefferson, Arkansas. The goal of this collaboration was to perform physicochemical characterization and *in vitro* release testing of complex drugs to advance the development of product-specific guidance. FDA's Center for Biologics Evaluation and Research has seen an increase in lipid nanoparticle platform technologies, with 28 Investigational New Drug (IND) submissions since 2017. With the use of lipid nanoparticle platforms for COVID vaccines, CDER is identifying avenues that can accelerate product development on the basis of the growing understanding of these technology platforms.

Advancing universal flu vaccine candidates. Scientists at NIAID's Vaccine Research Center (VRC) investigated a self-assembling influenza ferritin nanoparticle vaccine in a clinical trial. The nanoparticle vaccine was safe, well-tolerated, and immunogenic in adults. The vaccine, which is based on H2N2 influenza, also induced broadly cross-reactive immune responses targeting the conserved part of the influenza hemagglutinin protein, providing a proof-of-concept for the ferritin nanoparticle-based vaccine platform.[137,138] VRC scientists and academic colleagues also have designed a self-assembling two-component nanoparticle vaccine and tested it in animals. The nanoparticle vaccine performed as well as or better than the commercial vaccine in eliciting antibody responses matched to the vaccine hemagglutinin (HA) components and was far better in eliciting protective antibody responses to viruses

[136] NextFlex Manufacturing USA institute, https://www.nextflex.us/; accessed 18 March 2022
[137] https://doi.org/10.1038/s41591-021-01660-8
[138] https://pubmed.ncbi.nlm.nih.gov/35115707/

Nanotechnology tools in the fight against COVID-19

Microneedle patches may provide a painless, hassle-free vaccine delivery, without the need for expensive cold-chain logistics. This BARDA-funded microneedle array delivers vaccine antigens and adjuvants at the same time, and the adjuvant is packaged in liposomes. Image credit: Vendari.

Vaccine developers leveraged decades of advances in lipid and polymer nanotechnology research to deliver the first mRNA vaccines, in less than a year.[139] *Meanwhile, viral vector nanotechnology was also utilized to develop nucleic acid vaccines, which deliver instructions to the cells.*[140] *Other vaccine formulations have leveraged proprietary multimeric nanoparticles to deliver recombinant S protein to the cells.*[141] *Nanotechnology-based vaccines have many advantages compared to traditional vaccines. For example, these formulations may prevent premature degradation, boost immune response, enhance control release kinetics, reduce adverse effects, deliver site-specific antigens, and facilitate intracellular uptake.*[142]

Current efforts to develop microneedle patches or plant viral nanoparticles for antigen delivery, which do not require a cold chain, could solve the vaccine distribution issues.[143] *Researchers are also working on pan-coronavirus vaccines, which would help protect from variant strains, even future variants, with a single formulation.*[144]

Nanotechnology also played an important role in testing strategies. Nanotechnology-enabled strategies for sensors and diagnostic devices include plasmonic-based colorimetric assays, antibody capture and antigen binding assays, paper-based biomolecular sensors, and thermoplasmonic chips.[145] *For example, the NIH RADx Tech program was created to rapidly expand COVID-19 testing capabilities and performance. An estimated 15-20% of total RADx investments has been in nanotechnology-based approaches, which translates to more than 100 million nanotechnology-enabled tests sold (as of September 2021). Nanotechnology-based approaches are providing better limits of detection, faster "design to product," and can be multiplexed with other pathogens and diseases to prepare for future pandemics. Nanotechnology-enhanced materials have been leveraged to prevent viral dissemination. These materials can be used for air filters and PPE and to coat or disinfect surfaces. Common nanomaterials for such tasks include silver or copper nanoparticles, graphene, and titanium dioxide.*[146]

Another opportunity is to create therapeutics that work on the scale of the SARS-CoV-2 virus (60–140 nm) by blocking binding sites and receptors.[147] *Reformulating existing drugs into nanoscale medicines can enhance or provide new therapeutic properties, saving development time.*[148] *Nanocarrier-based drugs can help increase aqueous solubility and bioavailability, enhance kinetics, reduce the dose needed, and decrease systemic toxicity.*[149] *For example, dexamethasone has emerged as a successful therapeutic for COVID-19, and researchers have recommended the use of a nanomedicine version of the drug to treat COVID-19.*[150]

[139] R. Cross, Without these lipid shells, there would be no mRNA vaccines for COVID-19, *Chemical and Engineering News*, **99**, 8 (8 March 2021), https://cen.acs.org/pharmaceuticals/drug-delivery/Without-lipid-shells-mRNA-vaccines/99/i8; accessed 18 March 2022.

[140] https://www.cdc.gov/coronavirus/2019-ncov/vaccines/different-vaccines/janssen.html

[141] https://www.ncbi.nlm.nih.gov/pmc/articles/PMC7553041/pdf/nn0c07197.pdf

[142] https://doi.org/10.3389/fnano.2020.588915

[143] https://doi.org/10.1038/s41565-020-0737-y

that were not included in the vaccine, such as avian H5N1 and H7N9 influenza viruses.[151] In related work, researchers have developed nanoparticle immunogens that display various combinations of HAs from seasonal subtypes and elicit similar or superior antibody responses compared to the commercial vaccine. A clinical trial for this vaccine began in 2021.[152]

Addressing regulatory hurdles for nanotechnology-enabled drugs and medical devices. FDA has worked to understand the properties of nanomaterials used in drug products to inform and ensure the development of a regulatory framework that appropriately assesses the impact of nanomaterials. To date, more than 970 drug product applications have been reviewed by FDA, resulting in over 70 new drug and generic drug approvals. The experience from these applications has guided research to support future drug development and understanding of regulatory hurdles that can be addressed proactively. In addition, FDA evaluated various complex drug products (e.g., emulsions, liposomes, and microbubbles) using advanced analytical methods such as cryo-electron microscopy to better understand their unique structural properties. This structural understanding advances the development of product-specific guidance that can be used for developing generic drug products.

FDA is developing test methods to evaluate medical devices that incorporate nanomaterials with functions ranging from antimicrobial properties to enhanced integration of implants with tissues. One investigation is exploring how nanoscale surface roughness of nanoscale coatings affects the interactions between implants and surrounding proteins, adhesion molecules, and blood platelets. FDA is also investigating how surface chemistries of ultrasmall superparamagnetic iron oxide nanoparticles (USPIONs) affect formation of the surrounding protein corona, which influences cell uptake of particles, cell injury, and other cellular responses. This will inform the development and safety profiles of USPION-enabled medical products. Proposed applications of USPION including contrast agents, tumor imaging, targeted drug delivery, and magneto-mechanical actuators to treat hyperthermia and thrombolysis.

Translating cancer diagnostics and therapeutics. NCI has been operating the Alliance for Nanotechnology in Cancer program since 2005. For 15 years, the pillars of this program were U54 Centers of Excellence (CCNEs), which were funded up to 2020.[153] CCNEs were very productive, both scientifically and translationally.[154] Entrepreneurial Alliance investigators established small companies to move technology developed in academia to translational and commercial stages, including human clinical trials.[155] These efforts demonstrated the potential of nanomedicine in the clinic, but also the need for ongoing support for maturing innovative technologies towards translation.

Developing nanotechnology for dental, oral, and craniofacial applications. The Dental, Oral and Craniofacial Tissue Regeneration Consortium is advancing nanotechnology-based approaches for

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144 K. Rempfer, Army's own vaccine that could fight COVID variants begins clinical trials, *Army Times* (April 7, 2021), https://www.armytimes.com/news/your-army/2021/04/07/armys-own-vaccine-that-could-fight-covid-variants-begins-clinical-trials/; accessed 8 March 2022.

145 https://doi.org/10.1038/s41565-020-0751-0

146 https://doi.org/10.1038/s41565-020-0751-0

147 https://www.ncbi.nlm.nih.gov/pmc/articles/PMC7123821/

148 https://doi.org/10.1038/s41565-020-0757-7

149 https://www.ncbi.nlm.nih.gov/pmc/articles/PMC7325519/

150 https://doi.org/10.1038/s41565-020-0752-z

151 https://doi.org/10.1038/s41586-021-03365-x

152 https://clinicaltrials.gov/ct2/show/NCT04896086

153 https://www.ncbi.nlm.nih.gov/pubmed/31442467

154 https://pubmed.ncbi.nlm.nih.gov/31257722/

155 https://www.nano.gov/sites/default/files/NCI%20Alliance%20Infographic.pdf

regeneration and reconstruction of DOC tissues to Phase 1 clinical trials. Several dozen individual projects are currently supported by the DOCTRC, facilitating introduction of nanotechnology into clinical practice, including tissue regeneration-enhancing scaffolds and drug and cell delivery systems. NIDCR also works with other agencies (e.g., NIST) and professional and scientific societies to promote progress in dental and craniofacial applications of nanotechnology. For example, NIDCR made an SBIR award to develop a customized nanotechnology-based treatment for oral cancer using a nanoengineered patch containing the chemotherapy drug cisplatin. The patch is placed directly onto the tumor, and has been shown to destroy cancer cells in the tumor and regional lymph nodes without systemic side effects. This patch is in Phase 2 clinical trials with additional NIDCR funding to support commercialization.

Commercializing bionanotechnology. Two start-up companies licensed patented technology developed under the ONR Biomaterials and Bionanotechnology program, including a company launched in March 2020 that licensed a university's patented poly(catechol-styrene) adhesive system that is based on the marine mussel. Another company, launched in July 2020, licensed technology for use in a highly multiplexed proteomics platform.

Promoting progress in manufacturing. NNI support for nanomanufacturing innovation is an essential enabler for commercialization across material and application areas. For example, university researchers funded by DOE developed nanometer-scale atomically precise metallo-catalysts with "molecular lego" to dramatically reduce the energy and environmental impact of plastic production. The "artificial enzyme" molecular lego catalysts are highly selective and will make biodegradable polyesters. The university is exploring potential licensing to industry, and the researchers have formed a spinoff company that is developing software to design molecular lego and therapeutic compounds for pharmaceuticals.[156]

FDA has been supporting the development of high-throughput continuous processes for manufacturing drug products containing nanomaterials. FDA and university scientists developed a commercial-scale manufacturing platform for continuous processing of nanomaterials such as liposomes and lipid nanoparticles. This advanced manufacturing system for liquid-injectable nanoparticles can produce a variety of pharmaceutical nanoparticles. The university has licensed this technology to a start-up company.

NASA's US-COMP Space Technology Research Institute—a collaboration between NASA, academia, Federal labs, and industry capitalizing on Phase 3 SBIRs—is enabling the parallel advancement of computational modeling tools, CNT manufacturing, composite processing, and component prototyping.[157] The collaboration enables process development while material quality and performance are still evolving. The industry performer has yielded a supply of commercial high-strength carbon nanotubes that are being used to prototype lightweight structures for aerospace applications.

ARL, in conjunction with a company, has successfully scaled up two nanoparticulate technologies, making them commercially viable products and establishing a manufacturing base. Two other companies have utilized ARL's iron-based nanotechnology to produce the first viable fully dense cobalt-free tungsten carbide materials. Such materials have potential advanced properties in applications such as commercial-grade cutting and machining tools.

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[156] https://www.energy.gov/sites/prod/files/2019/09/f67/Developing%20Nanometer%20Scale%20Atomically%20Precise%20Metallo-Catalysts%20with%20Mol....pdf

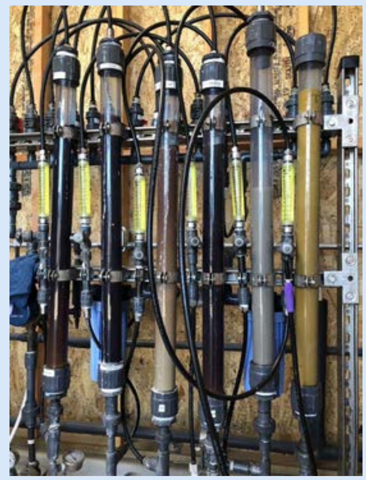
[157] Institute for Ultra-Strong Composites by Computational Design (US-COMP), http://us-comp.com/; accessed 18 March 2022

Generating hydrogen gas from water using nanoscale aluminum. The Army Research Laboratory developed a nanogalvanic aluminum alloy powder that has demonstrated the ability to generate large volumes of hydrogen gas when mixed with any liquid that contains water, a major breakthrough in the ability to generate power at the point of need. The technology was licensed for automotive and transportation power generation as well as power generation via generators and micro-grid equipment. The company has filed for international patent rights, on behalf of the Army.

Improving infrastructure materials. FHWA research on the nanoscale properties of cementitious materials has informed development of new industry guidelines for alternatives to portland cement for use in concrete,[158] which could reduce the energy and environmental impacts of cement production.[159] USDA/FS and FHWA are collaborating to replace wildfire-damaged bridges with cellulosic-nanomaterial-enhanced concrete bridges.

Small business tackles "forever chemicals"

Per- and polyfluoroalkyl substances (PFAS) are a group of over 8,000 synthetic organofluorine chemical compounds that do not degrade naturally due to the strong C-F bond. PFAS molecules bioaccumulate, posing many environmental and health concerns. The use of these chemicals was widespread in many products, including firefighting foam, and coatings, and they continue to be used in certain scenarios. Many NNI participating agencies have funded research to find ways to detect, track, collect, and remediate PFAS in the environment. A small company, funded in part by the National Institute of Environmental Health Sciences and the National Science Foundation, is commercializing an adsorbent that removes many different types of PFAS molecules (long-chained, short-chained, and branched) from water. The adsorbent is made of corn-derived cyclodextrins, and is composed of nanoscale cavities that can trap PFAS while resisting fouling by size exclusion of larger organic matter. The company conducted large-scale pilot studies at the Orange County Water District in California, and is also conducting pilot tests in NASA and DOD facilities, among other places. Once PFAS is adsorbed, it is destroyed using a mechanochemical process, and covalent changes are made to make sure any disposal is handled properly. The process, developed with funding from EPA, achieved >99% PFAS destruction and >95% flouride ion recovery. The material can be reused, and thus the solid waste created is minimal. For example, 5,000 kg of material can treat 365 million gallons of PFAS-contaminated water in one year, and decrease the PFAS concentration from 100 ppt to undetectable levels. After the "regeneration wash" only 140 g of solid waste is produced and the material can be reused with full capacity. After its initial success in large-scale projects and demonstrations, the company has begun to sell PFAS water testing kits for home use. Additionally, the company holds a U.S. patent for purifying fluid samples from micropollutants.



Column filtration system at the Orange County Water District pilot test; the far left column contains the adsorbent. Image credit: Cyclopure.

Synthesis of cylodextrin-based powder. Image credit: Cyclopure.

[158] American Concrete Institute, News Detail, ACI forms new committee to address alternative cements (5 May 2018), https://www.concrete.org/news/newsdetail.aspx?f=51702425; accessed 18 March 2022.

[159] https://www.fhwa.dot.gov/publications/research/ear/18031/

Supporting standards development. NNI agencies support standards activities to streamline development, regulatory approval, and market acceptance of nanotechnology-enabled products. For example, NIST leads and participates in several organizations developing voluntary consensus nanotechnology standards. The expertise NIST scientists contribute to the development of consensus standards helps ensure that they are technically robust, timely, and fit-for-purpose. NIST leadership and engagement in pre-standardization activities such as those being conducted under the Versailles Project on Advanced Materials and Standards (VAMAS) helps accelerate the development of consensus standards. NIST chairs ASTM International's Committee E56 on Nanotechnology, which also includes participation from several other NNI agencies, and leads nanotechnology-related efforts in Technical Committee 113 of the International Electrotechnical Commission (IEC). NIOSH chairs the U.S. Technical Advisory Group (TAG) to ISO TC 229, Nanotechnologies, which includes representatives from other Federal agencies, industry, academic, and nongovernmental organizations. FS leads the ISO TC229 cellulose nanomaterials terminology revision project and the TC 6 (paper, board, and pulps) cellulose nanomaterials working group.

The FDA Nanotechnology Task Force established a subcommittee on nanotechnology standards to prioritize standards based on FDA needs, assist in the development of standards, and consolidate FDA comments for nanotechnology standards under review. The subcommittee participates in ASTM E56 and ISO TC 229. Subcommittee members also serve as FDA liaisons to relevant working groups in the United States Pharmacopeia (USP) and OECD. In 2020, the FDA Center for Devices and Radiological Health added four ASTM E56 standards and ISO TC 229 standards to its list of recognized consensus standards for nanotechnology, bringing the total number of standards adopted for the use of nanotechnology in medical devices to 18. One *in vitro* test method was published as a standard through the ASTM E56-08 subcommittee on Nano-enabled Medical Products in early 2020. NIH/NIDCR worked with the Standards Committee on Dental Products of the American Dental Association to obtain approval of a proposed national standard method for determination of polymerization shrinkage stress of polymer-based restorative nanomaterials.

Goal 3. Provide the infrastructure to sustainably support nanotechnology research, development, and deployment.

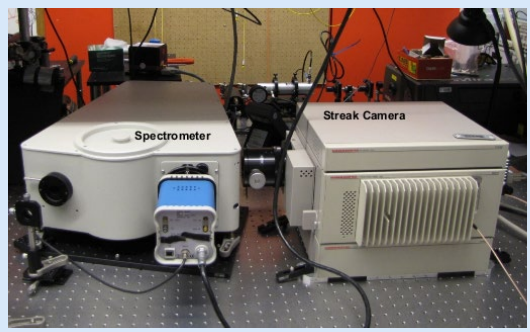
Research infrastructure includes physical equipment, digital models, simulations, and data, and is critical to all the NNI goals. The need for expensive, specialized tools remains a key requirement for much of nanotechnology R&D. One of the hallmarks of the NNI is the user facilities that provide researchers and developers access to the critically enabling tools required to create, characterize, and understand nanomaterials and nanotechnology-enabled components, devices, and systems. NNI agencies support advances in tool development, establishment of facilities, and creation and dissemination of cyber resources through mechanisms such as individual grants, collaborative centers, and networks of user facilities. The NNI user facilities have adapted operations to prioritize pandemic response and improve remote options to continue serving the nanotechnology community.

Sustaining and leveraging the NNI user facilities. NSF supports academic research infrastructure at more than 500 universities, including centers for research, education, and technology transfer, and the National Nanotechnology Coordinated Infrastructure and Network for Computational Nanotechnology user facilities. NNCI sites provide researchers from academia, small and large companies, and government with access to university user facilities with leading-edge fabrication and characterization tools, instrumentation, and staff expertise. The NNCI was able to rapidly adapt to the pandemic and provided a variety of online programs to support users. In 2020, the tools were accessed by over 10,000 users, including more than 2,800 new users, representing more than 200 U.S. academic institutions, nearly 800 small and large companies, ~30 government and non-profit institutions, as well as ~60 foreign entities. The existence of the NCN enabled the nanotechnology community to continue computational research and the number of visitors increased from 1.9 million in 2019 to 2.1 million in 2020. [160]

DOE operates five Nanoscale Science Research Centers, user facilities that provide open access to leading-edge synthesis, fabrication, characterization, and computational tools and scientific expertise for interdisciplinary research at the nanoscale. In 2020 the centers provided access to over 3,000 unique users from academia, industry, and government, based on a peer-reviewed proposal system.[161] With CARES Act funding in March 2020, DOE established the National Virtual Biotechnology Laboratory (NVBL).[162] The NVBL was enabled by the multiple national laboratories, user facilities, and strong industry interactions to commercialize the science. The NSRCs supported studies to understand the virus and develop novel detection methods, identify and synthesize promising vaccine candidates, and improve the effectiveness of personal protective equipment. For example, researchers at the Center for Integrated Nanotechnologies in collaboration with ARL developed a sensitive COVID-19 immune-detection lateral flow assay using giant quantum dots. Another team leveraged NSRC tools to verify face mask filtering efficacy. In response to the pandemic the NSRCs have revised operations to accommodate user/staff scientist needs with COVID-19 restrictions, including increased remote access.

Long term benefits of infrastructure investments

The instrumentation necessary to carry out cutting-edge nanoscience research is expensive. A hallmark of the NNI is the support for critical instrumentation that has driven new discoveries in nanoscale science and technology development for years. For example, the DOD Defense University Research Instrumentation Program (DURIP) supports university research infrastructure essential to high-quality Navy-relevant research. Ten years ago, DURIP provided funding for a streak camera that is still in use today. Recently, the streak camera enabled researchers to study valley properties and exciton transport in atomically thin materials, a research area that was not even envisioned when the original DURIP proposal was written.



The spectrometer (left) and streak camera (right) funded by DURIP that enabled researchers to study atomically thin materials. Image credit: Marko Loncar, Harvard University.

As nanoscale science and technology progresses, research and development infrastructure remains a critically enabling resource that will continue to serve research communities into the future.

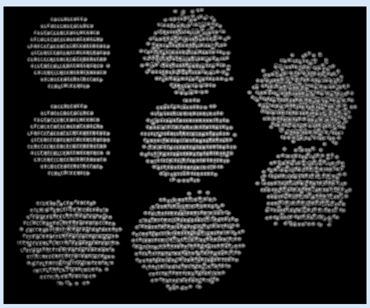
The National Cancer Institute, in collaboration with NIST and FDA, established the Nanotechnology Characterization Laboratory[163] to perform preclinical efficacy and toxicity testing of nanoparticles. NCL serves as a national resource and knowledge base for all cancer researchers to facilitate the regulatory review of nanotechnologies intended for cancer therapies and diagnostics. To-date, NCL has characterized over 400 different nanomaterials with a wide range of nanotechnologies and therapeutic loads; established a multitude of collaborations with academia, industry, and government labs; published over 200 peer-reviewed publications covering nanoparticle characterization, immunotoxicity, and safety; and established over 70 standardized protocols for various nanoparticle

160 nanoHUB.org, Usage, https://nanohub.org/usage; accessed 18 March 2022
161 https://science.osti.gov/User-Facilities/User-Statistics
162 https://science.osti.gov/nvbl
163 https://ncl.cancer.gov/

assays. Several of NCL collaborators have reached clinical trials with the aid of data produced at NCL. In the effort to help combat the global COVID-19 pandemic, NCL continues to accept applications for novel nanomaterials used for prevention and treatment of COVID-19.

Developing new tools to advance nanoscience. NIST developed a novel microresonator[164] to measure the properties of paramagnetic defects/dopants in nanostructured films. The device provides a rapid, scalable, and general technique to probe chemical properties at buried interfaces and in thin films, and detects electron spins at room temperature in a volume of about 0.1 nL, four orders of magnitude lower than state-of-the-art commercial systems. Researchers from a university, the Department of Energy's Argonne National Laboratory, and international collaborators built an electron microscope pixel array detector that set a new world record by doubling the resolution of state-of-the-art electron microscopes.[165] The detector enables researchers to locate individual atoms in all three dimensions. Thanks to this detector, the resolution of an electron microscope can be so fine-tuned that the only blurring that remains is the thermal vibration of the atoms themselves.[166] This cutting-edge tool is available to researchers through the university-based user facility. This technology has also been licensed to a microscope manufacturer and is being put into production.

Viewing the atomic composition of nanoparticles



3D images of platinum particles between 2–3 nanometers in diameter in liquid under an electron microscope. Image credit: Peter Ercius, Berkeley Lab.

Using one of the world's most powerful microscopes at the DOE Lawrence Berkeley National Laboratory Molecular Foundry, researchers have developed a technique that produces atomic-scale 3D images of nanoparticles tumbling in liquid between sheets of graphene.[167] The technique, called 3D SINGLE (Structure Identification of Nanoparticles by Graphene Liquid cell Electron microscopy), enables the measurement of atomic positions in three dimensions at a scale six times smaller than the diameter of hydrogen. The Molecular Foundry is one of the five DOE Nanoscale Science and Research Centers that serve as user facilities for the international science community to advance scientific and technical knowledge in areas of nanoscale science.

With support from the FHWA, researchers developed innovative analytical techniques that provide a more direct observation of reactions at the micro- and nanoscales. These techniques informed a deeper understanding of the chemical reactions that occur during and after concrete's hydration stage. Researchers used this knowledge to create computer models that will help guide the development of concrete that is more durable and cost-effective. ONR-funded scientists and international collaborators have developed a method for studying carrier transport through a single molecular junction. This method can be used to determine the distribution of hot carriers in a plasmonic nanostructure, which

[164] https://www.nist.gov/news-events/news/2020/11/new-twist-measuring-spin-nist-develops-microresonator-study-electron-spin; U.S. Provisional Patent Application serial number 62/982,879, filed March 2, 2020; Non-provisional patent docket #20-031US1 filed 2/22/21.

[165] https://doi.org/10.1038/s41586-018-0298-5, https://doi.org/10.1126/science.abg2533

[166] D. Muller, Improving electron microscopes to take a closer look at atoms, NNI *Nano Matters* podcast series (2021), https://www.youtube.com/watch?v=YI3n-Dj-ST8; accessed 18 March 2022.

[167] https://newscenter.lbl.gov/2020/04/09/3d-nanoparticles-atom-by-atom/

could in turn enhance the performance of plasmon-driven photochemistry, solar energy devices, and photodetectors.[168]

NSF-supported academic researchers and collaborators at Lawrence Berkeley National Laboratory developed an atomic electron tomography reconstruction method to experimentally determine the 3D atomic positions of an amorphous solid. The results provide experimental evidence supporting the efficient cluster packing model for metallic glasses and advance fundamental understanding of non-crystalline materials.[169]

Pushing the boundaries of science with nanotechnology-enabled tools. NRL is using nanoscale devices to build new tools that measure the flow of protons in biology. NRL researchers developed a protonics device using palladium to show the direct movement of protons in cable bacteria. Learning how to measure and control proton movement eventually could lead to prosthetics that are better-performing and tolerated. NIST researchers have demonstrated electronic measurements of neuronal spikes using cortical rat neurons cultured on electrodes. The measurements demonstrate the first steps for *in situ* chemical sensing within co-cultured systems for applications in biotechnology.

NASA-funded university researchers worked with the DOE Center for Integrated Nanotechnologies to develop a tiny high-power narrow-beam THz laser with potential imaging and scanning applications. While previous THz lasers required bulky laboratory equipment to stay cool enough to function, the new devices are the first to reach three key performance goals—high power, tight beam, and broad frequency tuning—in a design that can work outside a laboratory. NASA has selected lasers from this research to fly on the Galactic/Extragalactic Spectroscopic Terahertz Observatory, where they will help detect chemical emissions between stars.[170]

Bringing more accurate measurements directly to users. The NIST on a Chip (NOAC) program is focused on revolutionizing measurement services and metrology by bringing them out of the lab and directly to the user. NOAC leverages NIST's excellence in precision measurement with a focus on creating prototypes for a new generation of ultra-compact, inexpensive, low-power measurement tools. Many of the NOAC technologies are based on nanoscale measurements and devices. For example, NIST researchers have developed an optofluidic system[171] that accurately measures flow of liquid in nanoliters/min. Precisely measuring and controlling minuscule flow rates is critically important in the burgeoning field of microfluidics. Furthermore, the flow measurements are independent of the size and shape of the channel through which the fluid is traveling, which provides additional advantages in chip design over conventional techniques.[172] NOAC is creating industry and government collaborations to turn NIST innovations into commercial products.

Goal 4. Engage the Public and Expand the Nanotechnology Workforce.

The United States' position as a world leader in nanotechnology innovation relies on STEM talent and a highly skilled workforce for every aspect of the R&D continuum. The NNI has supported outreach, education, and workforce development activities as part of its primary goals for the past 20 years. Fostering the growth of a globally competitive and diverse nanotechnology workforce is a strategic objective of the NNI, as outlined in the 2021 NNI Strategic Plan. In recognition of the importance of

168 https://doi.org/10.1126/science.abb3457
169 https://doi.org/10.1038/s41586-021-03354-0
170 https://science.osti.gov/bes/Highlights/2020/BES-2020-12-e
171 https://doi.org/10.1021/acs.analchem.9b02056
172 http://dx.doi.org/10.1103/PhysRevApplied.11.034025

education, workforce development, and public engagement to the entire nanotechnology ecosystem, these efforts are now a stand-alone NNI goal.

NASA internships: Inspiring the next generation using space and emerging technologies

Remote interns at NASA Jet Propulsion Laboratory (JPL). The students are part of the fifth class of JPL's Historically Black Colleges and Universities/Underrepresented Minority Initiative called Maximizing Student Potential in STEM. Image credit: NASA.

Hands-on learning opportunities can inspire students to discover a passion for STEM. The NASA internship programs have consistently provided thousands of students, from the high school to graduate level, with the opportunity to contribute to the NASA mission, while learning how STEM tools and fields, such as nanotechnology and other emerging technologies, can help provide novel solutions to society's pressing technical needs. To increase equity, creativity, and innovation of the STEM pool in this country, NASA launched the "Maximizing Student Potential in STEM" program, which recruits and provides opportunities directly to underrepresented students pursuing undergraduate or graduate degrees in STEM. In addition to partnering students with a mentor, and having a designated project that provides educational experience and contributes to NASA's mission, the students also have the opportunity to participate in tours, lectures, and career mentorship sessions to help them better achieve their career goals. A NASA representative showcased these programs as part of the NextTech Student Network career development seminar services and is archived on the NextTech website.[173]

In addition to targeted nanotechnology education, the novel properties at the nanoscale can provide a spark to excite students to pursue STEM careers and help build a robust domestic workforce. NNCO and the NNI agencies use a variety of mechanisms to support public outreach and education from "K to grey" and emphasize opportunities and access to resources, especially for people in traditionally underserved communities.

Leveraging infrastructure for education and outreach. The NSF-funded National Nanotechnology Coordinated Infrastructure has education and outreach programs at each of the 16 sites. These programs were able to quickly adapt to challenges associated with the pandemic and were still able to reach more than 33,000 people between April 2020 and March 2021 through both in person and virtual programming including, for example, teacher workshops, webinars, and internships.[174] The nanotechnology education community was able to leverage the NNI cyberinfrastructure, Network for Computational Nanotechnology at nanoHUB.org, during the pandemic. NCN provides full academic and short courses, teaching materials, and a collection of lectures and seminars. The number of NCN users increased from an average of 1.9 million in 2019 to 2.1 million in 2020.[175]

[173] NextTech Student Network, https://nexttechnetwork.org/; accessed 18 March 2022

[174] National Nanotechnology Coordinated Infrastructure, NNCI Annual Report, https://nnci.net/nnci-annual-report; accessed 18 March 2022

[175] nanoHUB.org, Usage, https://nanohub.org/usage; accessed 18 March 2022

The Micro Nano Technology Education Center: A united effort to streamline micro and nano technician education

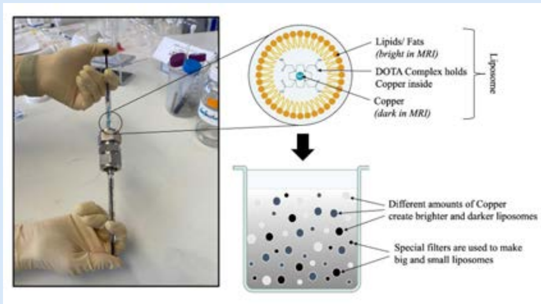
The Micro Nano Technology Education Center (MNT-EC) is working towards a coordinated national approach to advance micro- and nanotechnology education. The center has brought together over 30 educational institutions and industry partners with the goals of strengthening and fostering the creation of new education programs across the country. MNT-EC aims to develop a single curated online repository, remote education opportunities, and to engage with industry to identify needs in technical education. In addition, the new center is (1) delivering professional development opportunities to enhance knowledge, skills, and abilities, (2) conducting strategic outreach, recruitment and retention of traditional underrepresented faculty/students, and (3) creating a deep industry/education alliance that supports student success. MNT-EC has partners across the country. MNT-EC is funded by the Advanced Technological Education program at NSF. For more information go to: https://micronanoeducation.org/.

Undergraduate research experience used as a hands-on learning tool at MNT-EC. MNT student investigating the nanostructures that give blue morpho butterflies' wings their characteristic color. Image credit: ATE Central and the Internet Scout Research Group.

Training students through immersive educational experiences. NNI agencies employ internship, fellowship, and international exchange programs to provide immersive research and real-world experiences for students. For example, NSF provides both domestic and international research experiences for roughly 1,800 undergraduate students annually in all STEM disciplines, including nanotechnology-enabled research areas.[176] The NSF INTERN program[177] provides supplemental funding for graduate students to gain knowledge, skills, and experiences that will augment their career preparation through internships in industry, national laboratories, non-profit organizations, etc.; approximately 20% of the 288 INTERN awards in 2020 were in nanotechnology. In April 2021 NSF announced new supplemental funding opportunities for its Skills Training in Advanced Research & Technology program, which provides technical training for technicians, a critical segment of the STEM-capable workforce.[178] NASA's Established Program to Stimulate Competitive Research (EPSCoR) program facilitates industry internships to expose STEM students to business and commercialization pathways while also preparing them for high-quality jobs.[179] FDA's Office of Regulatory Affairs recruits and trains research fellows in development and validation of advanced analytical methods based on FDA, USP, and International Council for Harmonisation of Technical Requirements for Pharmaceuticals for Human Use (ICH) guidelines for characterization of nanomaterial constituents of FDA-regulated products. NCI provides several grant training mechanisms for students of different levels, post-doctoral researchers as well as mid-career scientists, through its Center for Cancer Training.[180]

176 https://beta.nsf.gov/funding/opportunities/research-experiences-undergraduates-reu
177 https://www.nsf.gov/pubs/2021/nsf21013/nsf21013.jsp
178 https://www.nsf.gov/pubs/2021/nsf21076/nsf21076.jsp?WT.mc_id=USNSF_25&WT.mc_ev=click
179 https://www.nasa.gov/stem/epscor/home
180 https://www.cancer.gov/grants-training/training/about

Summer Undergraduate Research Fellowships at NIST: Inspiring undergraduates to pursue careers in STEM



Virtual SURF intern making liposomes at her local university to ship to NIST for remote imaging. Image credit: E. Buchanan/NIST.

Every summer the NIST laboratories welcome a new cohort of students participating in the Summer Undergraduate Research Fellowship (SURF) program at their facilities in Boulder, Colorado; Gaithersburg, Maryland; and Charleston, South Carolina. The students work directly with a NIST research advisor, participate in seminar series and extramural group activities, and present their research results at the NIST SURF Colloquium. In 2021 the program was held virtually as a response to the global pandemic, but students still had the opportunity to learn about advanced microscopy and other nanotechnology tools available at NIST laboratories. Students and mentors devised innovative solutions to provide a rich learning experience while staying safe. Students were able to connect remotely to instrumentation and collect measurements, images, and other data points. Some students were able to conduct experiments at their local universities and send samples to NIST laboratories for further analyses. Others had the opportunity to learn advanced data analysis techniques and attend conferences around the world, which would not have been possible without the virtual environment.

SURF intern taking micro-MRI images remotely. Image credit: E. Buchanan/NIST.

Increasing participation of underrepresented groups. NNI participating agencies have numerous programs that support inclusion, diversity, equity, and access for people from communities that have been historically left behind, including, for example, NSF INCLUDES[181] and ADVANCE,[182] NIH's UNITE[183] effort, and NASA's Minority University Research and Education Project[184] and Mission Equity effort.[185] USPTO recently launched the National Council for Expanding American Innovation[186] to develop a comprehensive national strategy to increase participation in the innovation ecosystem by encouraging, empowering, and supporting all future innovators, including increasing involvement of women and other underrepresented groups. USDA/NIFA has encouraged proposals in its higher education programs to build capacity in minority-serving institutions and Tribal colleges and universities. NSF has developed programs to increase science and engineering efforts in HBCUs,[187] Hispanic-Serving Institutions,[188] and Tribal colleges,[189] encouraging them to establish and maintain close connections with existing cutting-edge research laboratories and institutions of higher education.

181 https://www.nsf.gov/funding/pgm_summ.jsp?pims_id=505289
182 https://www.nsf.gov/funding/pgm_summ.jsp?pims_id=5383
183 https://www.nih.gov/ending-structural-racism/unite
184 https://www.nasa.gov/stem/murep/home/index.html
185 https://www.nasa.gov/mission-equity
186 https://www.uspto.gov/initiatives/expanding-innovation/national-council-expanding-innovation/about-national-council
187 https://www.nsf.gov/funding/pgm_summ.jsp?pims_id=5481
188 https://www.nsf.gov/funding/pgm_summ.jsp?pims_id=505512
189 https://www.nsf.gov/funding/pgm_summ.jsp?pims_id=5483

These programs are available to support nanotechnology research and education activities.[190] In addition, DOD announced renewed funding for the Research and Education Program for HBCUs and the MSI program to enhance research and education programs and capabilities in scientific and engineering disciplines critical to the national security functions.[191]

Engaging with the public. The NNI recognizes that public trust in nanoscience and technology is critical for the potential of nanotechnology innovations to be realized. NNCO produces three podcast series—*Stories from the NNI*, *Nanotechnology Entrepreneurship Network*, and *NanoMatters*—that target researchers, entrepreneurs, and the general public. NNCO also organizes public webinars to share research, technological, and environmental health and safety information with the public. NNI agencies participate in celebrating National Nanotechnology Day (NND)[192] as an effort to spread the exciting world of nanotechnology with a broader audience. For example, as part of FDA's 2020 NND celebration, the FDA Nanotechnology Task Force organized a Virtual Research Symposium[193] to present guidances, research infrastructure, and research projects related to nanotechnology at FDA, with more than 350 participants. As another example, on October 8, 2021, DOE/AMO announced the Stage 1 winners of the Conductivity-enhanced materials for Affordable, Breakthrough Leapfrog Electric and thermal applications (CABLE) Conductor Manufacturing Prize. All the winning projects involved nanoscale carbon or a nanotechnology-enabled process. DOE's AMO office also shared a video showcasing how AMO is harnessing the power of nanotechnology to create a clean energy future. Overall, at least 90 organizations actively participated in the 2021 NND celebration, including Federal agencies, technical and professional societies, NNI-funded research centers and user facilities, universities, private companies, and international organizations. Activities included webinars, videos, image contests, publication of nanotechnology content online, and extensive social media engagement, which was amplified through NNI Twitter and LinkedIn. More than 700 unique Twitter users tweeted and retweeted about NND by using #NationalNanoDay, generating 9.23 million impressions.

Goal 5. Ensure the responsible development of nanotechnology

Since the beginning of the NNI, the responsible development has been an integral pillar of the initiative. The 2021 NNI Strategic Plan articulates an expanded framework for responsible development that includes long-standing considerations such as understanding ELSI and the nanoEHS implications of nanotechnology development. This new framework further embraces additional concepts, including an emphasis on inclusion, diversity, equity, and access and the responsible conduct of research. These efforts support the other NNI goals by helping ensure the integrity of nanotechnology R&D and fostering public confidence and regulatory certainty.

Sharing responsible development resources and information. The Federal community has created a breadth of responsible development information, training, and best practices, as well as approaches for improving IDEA across the STEM ecosystem. For example, NIST[194] and FDA[195] both have online IDEA

[190] For example, NSF award 2100402, Supporting Micro and Nano Technicians through Hybrid Teaching Methods
[191] https://www.arl.army.mil/wp-content/uploads/2020/05/FY-2021-DoD-HBCUMI-Equipment-FOA_Final-May-2020.pdf
[192] https://www.nano.gov/nationalnanotechnologyday
[193] https://www.fda.gov/media/142139/download
[194] https://www.nist.gov/diversity-equity-and-inclusion
[195] https://www.fda.gov/media/107939/download

resources while NIH,[196] NSF,[197] and NIFA[198] have information dedicated to responsible development. The responsible conduct of nanotechnology research applies across the research enterprise, and the NNI is coordinating related activities with other Federal efforts such as the Scientific Integrity Fast-Track Action Committee.[199] Information sharing in support of responsible development extends beyond sharing best practices to include sharing the state of nanoEHS science with the innovation community and transparently communicating the potential risks and benefits of new innovations with the public. In this effort the NNI has hosted a series of nanoEHS webinars to share progress and knowledge gained with the broader community. Finally, the long-term incorporation of responsible development principles and best practices is supported by widespread and easily accessible training opportunities. For example, NIH[200] and NSF[201] require grantees to participate in training on the responsible conduct of research.

Leveraging interagency nanoEHS expertise. NNI agencies have collaborated on nanoEHS research through interagency agreements, data sharing, and joint planning of research priorities facilitated by discussions in the NSET Subcommittee's Nanotechnology Environmental and Health Implications Working Group (NEHI) Working Group. For example, CPSC has collaborated with other Federal agencies to address the critical need for focused research on consumer product applications of nanomaterials and their potential risks to consumers. CPSC's collaborative activities have produced more than 72 reports and publications, in addition to voluntary standards that address nanomaterial hazards in consumer products. In 2020 and 2021 CPSC produced 12 publications on topics including toxicology of 3D printer emissions and method development.

Enhancing international nanoEHS research efforts. NNCO has established strong relationships with governments and organizations around the world and has supported a robust research dialogue through the U.S.-European Union (EU) nanoEHS Communities of Research (CORs).[202] There are currently seven CORs with topics including, for example, human toxicity and databases and computational modeling. They meet virtually throughout the year to discuss scientific advances and needs, identify collaborative activities, and plan an annual workshop, the last of which was hosted by NNCO in September 2020.[203]

Promoting international collaboration in nanotechnology regulatory science. FDA collaborates with domestic and international regulatory and research agencies to share information on the state of science, guidance documents, and regulatory research experience. Some of the venues for this dialogue include the Global Coalition for Regulatory Science Research Nanotechnology Working Group, the International Pharmaceuticals Regulators Program (IPRP) Nanomedicines Working Group, and the U.S.-EU CORs. During the pandemic, FDA also organized and participated in the 2020 Global Summit on Regulatory Science, Society of Toxicology (SOT), and SOT-FDA Colloquia to support scientific debate and data dissemination.

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196 https://oir.nih.gov/sourcebook/ethical-conduct/responsible-conduct-research-training
197 https://www.nsf.gov/od/recr.jsp
198 https://nifa.usda.gov/responsible-and-ethical-conduct-research
199 https://www.federalregister.gov/documents/2021/06/28/2021-13640/request-for-information-to-improve-federal-scientific-integrity-policies
200 https://oir.nih.gov/sourcebook/ethical-conduct/responsible-conduct-research-training
201 https://www.nsf.gov/bfa/dias/policy/rcr.jsp
202 U.S.-EU NanoEHS Communities of Research, https://us-eu.org/communities-of-research/; accessed 18 March 2022
203 U.S.-EU NanoEHS Communities of Research, 2020 NanoEHS COR Workshop, https://us-eu.org/2020-nanoehs-cor-workshop/; accessed 18 March 2022

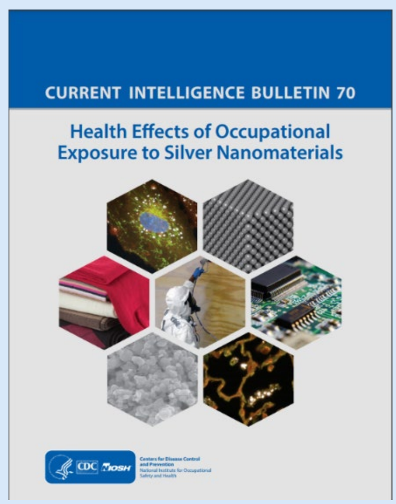
Developing analytical methods for regulatory science. FDA collaborates with other organizations to develop analytical methods and conduct regulatory science research. New analytical methods enable FDA to identify potential risks through pre- and post-market oversite and will provide guidance to sponsors/reviews for future products. FDA's regulatory science research on the advanced characterization, safety, and biodistribution of nanomaterials includes, for example, biochemical, genetic, and neurotoxicology effects and liposomal drug products. Results from this research help ensure the safety of FDA-regulated products containing nanomaterials and are used in capacity building and standards development. FDA scientists also are researching potential release of engineered nanomaterials from nanotechnology-enabled food contact materials. Data on nanoparticle migration and transformation within food systems will improve FDA's ability to make recommendations to manufacturers and will help regulatory scientists make informed decisions when reviewing future submissions.

Understanding and mitigating potential impacts in the workplace. NIOSH works with a variety of groups to understand the potential health and safety impacts of nanotechnology in occupational settings. NIOSH researchers develop hazard and safety assessments using key classes of engineered nanomaterials, including carbon-based nanomaterials, metals, metal oxides, and 2D materials. NIOSH researchers have performed "real-world" evaluations of hazard and risk represented by nanomaterials through their life cycles, including characterization of aerosols generated in spray coating of paints, sealants, and disinfectants. NIOSH published Current Intelligence Bulletin 70: Occupational Exposure to Silver Nanomaterials, in 2021 (see below).[204]

NIOSH is working with industry to develop a registry of workers who have worked with carbon nanotubes and nanofibers. This registry will form the basis of a longitudinal study that will evaluate the early health effects of exposure to carbon nanotubes or nanofibers. NIOSH field research teams visit nanomaterials producers and users to conduct industrial hygiene evaluations. The findings are used to develop guidance documents to protect workers from occupational injury and illness. NIOSH participated in numerous webinars and in-person seminars reaching hundreds of workers, providing them with information on how to work safely with nanomaterials and other advanced materials.

Applying what we know about nanoEHS to guidance documents and establishing exposure limits

In May 2021, after extensive review and public comment, NIOSH published the Current Intelligence Bulletin 70: Health Effects of Occupational Exposure to Silver Nanomaterials. Nanoscale silver is among the mostly widely used nanomaterials, and workers may be exposed during production or use of silver nanoparticles. The Bulletin reviewed 100 studies and made use of robust risk-assessment techniques built on more than a decade of research. These efforts supported advanced characterization tools and elucidated the role of factors such as dose metrics, particle size, and dissolution in observed responses. NIOSH concluded that it is prudent and reasonable to derive a recommended exposure limit (REL) for nanoscale silver. The CIB also sets out exposure control recommendations, identifies safe work procedures, training and education, and recommends the use of established medical surveillance approaches to protect workers.



[204] https://www.cdc.gov/niosh/docs/2021-112/default.html

Understanding the implications of incidental nanoplastics. NNI agencies are collaborating to address emerging issues associated with micro- and nanoplastics in the environment. Although these materials are not intentionally engineered nanomaterials, techniques developed and lessons learned from studying engineered nanomaterials can be used to investigate this emerging area of concern. The interagency nanoplastics interest group is helping to coordinate this work across the Federal Government and internationally. For example, an APEC workshop on nanoplastics in marine debris[205] is scheduled for December 2021, and NIST and the European Commission's Joint Research Centre are leading an effort to develop methods to collect nanoplastics from ocean water.[206] ATSDR and NCEH have been conducting research on incidental nanoplastics, presenting at national conferences, identifying and addressing data needs to evaluate human exposures to microplastics, and quantifying human exposure and risks.[207] NIST researchers developed measurement protocols that assess polymer nanocomposite degradation following accelerated moisture, heat, and UV exposure to simulate degradation of products. This work addresses challenges in distinguishing nanomaterials from polymer matrices during polymer nanocomposite degradation. It also evaluates how changes to the polymer nanocomposite morphology, including release of the nanomaterials, affects the potential exposure pathways of nanomaterials to their surroundings during use and disposal.

Investigating potential hazards of 3D printer emissions and aerosols. EPA in collaboration with CPSC and NIST investigated the potential risks from 3D printer emission.[208] These projects[209] demonstrated that exposure concerns may vary based on whether or not an additive is included in the 3D printing filament. Understanding the printing parameters that have the greatest influence on VOC emissions in a variety of filaments can lead to printer designs and/or containment measures that better limit exposure concerns. NIST researchers built the online Fate and Transport of Indoor Microbiological Aerosols (FaTIMA) tool that considers ventilation, filtration, and aerosol properties to estimate the concentration of aerosols in a room. [210] The tool can be used to evaluate options for reducing occupant exposure to SARS-CoV-2.

Developing and curating databases of nanoEHS research findings. EPA has been working in coordination with other Federal agencies to integrate information and develop a user interface for the NaKnowBase nanomaterials database. Recent updates facilitate the exchange of data with external data sources. The NNI community has been coordinating with the goal to make Federal nanoEHS databases interoperable.

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[205] APEC Workshop on Nanoplastics in Marine Debris, http://www.nanoplasticworkshop.org; accessed 18 March 2022

[206] https://www.nist.gov/news-events/news/2021/05/nist-collaborators-develop-new-method-better-study-microscopic-plastics

[207] https://doi.org/10.1016/j.scitotenv.2020.144010

[208] https://www.epa.gov/sciencematters/keeping-3d-printing-epa-researchers-build-new-plastic-emissions-study

[209] https://doi.org/10.1021/acs.est.9b00765

[210] https://www.nist.gov/news-events/news/2020/06/nist-airflow-model-could-help-reduce-indoor-exposure-aerosols-carrying

The role of data in the responsible development of nanotechnology

Data infrastructure—how data is gathered, used, disseminated, and curated—is an important element in the responsible conduct of research and a pillar in the NNI's evolving responsible development framework. In February 2020, participants in the NEHI Working Group came together as an informal interest group to facilitate collaboration and advance the NNI community's interest in integrating Federally managed and supported nanoEHS data. The group is focused on increasing the accessibility, integration, interoperability, and sustainability of these data, and aligning these outputs with FAIR (Findability, Accessibility, Interoperability, and Reusability) data principles.

EPA's Office of Research Development has led the effort to allow NNI data to be maintained in interoperable formats. To advance this goal, EPA/ORD has developed a python-based software application to automate the process of creating interoperable resource description frameworks (RDFs). These tools will allow data to be mixed and shared across databases and platforms. EPA has tested cutting-edge approaches on EPA databases such as NaKnowBase and on data from other agencies.

NaKnow Base
nanomaterials knowledge database

Appendix A. PCA Definitions

PCA 1. Foundational Research. The foundational research under PCA 1 includes: (1) discovery and development of fundamental knowledge pertaining to new phenomena in the physical, biological, chemical, and engineering sciences that occur at the nanoscale; (2) elucidation of scientific and engineering principles related to nanoscale structures, processes, and mechanisms; and (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 scales, and including interface interactions. This PCA encompasses basic research aimed at addressing national needs and priorities as well as undirected research aimed at expanding the frontiers of science and technology.

PCA 2. Nanotechnology-Enabled Applications, Devices, and Systems. PCA 2 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. This PCA includes 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.

PCA 3. Research Infrastructure and Instrumentation. PCA 3 supports the establishment and operation of user facilities and networks, acquisition of major instrumentation, and other activities that develop, support, or enhance the Nation's physical, data, and cyber infrastructure for nanoscale science, engineering, and technology. It includes R&D pertaining to the tools needed to advance nanotechnology research and commercialization, including informatics tools and next-generation instrumentation for characterization, measurement, synthesis, and design of materials, structures, devices, and systems.

PCA 4. Education and Workforce Development. PCA 4 supports research on and development of curriculum and other tools for effective training of students at all stages of education (from K-12, to community colleges and vocational schools, through doctoral and postdoctoral education) in the skills needed to succeed in the nanotechnology workforce. While student support to perform research is captured in other categories, dedicated educational efforts ranging from outreach to advanced training are included here as resources supporting the nanotechnology workforce. PCA 4 also includes support for programs, partnerships, or personnel exchanges among government, academia, and industry to develop the desired workforce skills and competencies. This PCA further encompasses mechanisms for public engagement and informal education.

PCA 5. Responsible Development. PCA 5 covers a broad range of activities to ensure responsible development of nanotechnology. Activities include research and development directed at understanding the potential environmental, health, and safety impacts of nanotechnology, and at assessing, managing, and mitigating identified risks. Research addressing the broad implications of nanotechnology for society is also captured in this PCA. Responsible development encompasses efforts to benefit society addressing topics such as social, economic, ethical, and legal considerations, as well as issues related to diversity, equity, inclusion, and access. Research integrity, safety, and reproducibility are also captured in PCA 5.

Appendix B. Contact List

Affiliations are as of October 2021.

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Examples of Engagement with the NNI Community

[The NNI Family of Podcasts]

[National Nanotechnology Day]

[Professional Development Webinars for Students]

Some of the panelists from the *What We Know About NanoEHS* webinar series.

[NNI Public Webinars]

Example keynote presentation at the January 2021 NNI Strategic Planning Workshop.

[Strategic Planning Workshop]

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