Highlights of the Sensors Nanotechnology Signature Initiative

October 2021

Introduction

Nanotechnology-enabled sensors (or nanosensors) continue to provide solutions in physical, chemical, and biological sensing that allow increased detection sensitivity, specificity, and portability for a wide variety of applications. The cross-cutting impacts of nanosensors intersect many areas of the economy, including the healthcare, pharmaceutical, agricultural, food, environmental, consumer products, and defense sectors. Unique properties of engineered nanomaterials, such as high surface area or enhanced chemical reactivity, in addition to advances in semiconductor technology, will ultimately pave the way for broader expansion of connected sensor systems (e.g., Internet of Things, IoT) due to their reduced form factors, cost, and facile component integration.

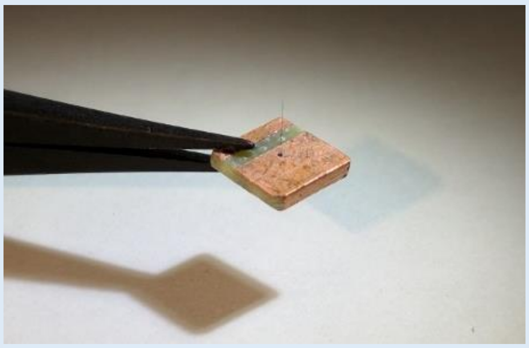
The National Nanotechnology Initiative (NNI) launched the "Nanotechnology for Sensors and Sensors for Nanotechnology: Improving and Protecting Health, Safety, and the Environment" Nanotechnology Signature Initiative (Sensors NSI) in 2012 to facilitate coordination and collaboration among participating agencies to accelerate the development and commercialization of nanotechnology-enabled sensors. The Sensors NSI white paper describes two thrust areas:

1. Develop and promote adoption of new technologies that employ nanoscale materials and features and the size-dependent properties of engineered nanomaterials to overcome technical barriers associated with conventional sensors.
2. Develop methods and devices to detect and identify engineered nanomaterials across their life cycles in order to assess their potential impact on health, safety, and the environment.

Participating agencies, collectively and individually, direct specific funding programs to accelerate nanotechnology-enabled sensor research, development, and deployment in support of their missions; select examples are highlighted throughout this document. The Sensors NSI leverages the connections and collaborations that comprise the nanosensors development community by drawing on interagency expertise as well as activities that convene participants from across the ecosystem. Agency representatives join regular teleconferences to discuss technical challenges and accomplishments, share information on plans and programming, and organize collaborative activities. Critical efforts have included external community engagement as well as internal collaboration and interagency coordination, as described in the sections below. The Sensors NSI is a dynamic community that adapts as science advances and the needs of the community evolve.

External Community Engagement

The exchange of information between the external nanosensor development community and the Federal Government is central to accelerating the development and deployment of nanotechnology-enabled sensors. A primary focus of interagency activities has been to foster an interconnected and engaged nanosensor development community. A key example of engagement was the release of a Request for Information (RFI) in 2013 to better understand the needs of the external community. The RFI focused on five areas: standards, testing, manufacturing, commercialization, and regulation. Respondents representing academia and the private sector highlighted specific challenges related to sensor development. Developers discussed a need for increased access to tools, testbeds, and standards to guide performance measurements, as well as facilities where researchers can evaluate sensors within environments representative of field use. Respondents also noted a scarcity of nanofabrication facilities for low-to-medium-volume production of prototypes. Lastly, a lack of understanding of the regulatory process, the implications of the use of nanomaterials in sensors technologies, and consumer safety considerations were identified as challenges. The RFI responses suggested that the community would benefit from enhanced support during the prototype-testing and scale-up stages of sensor development.



Artificial hairs composed of carbon nanotubes grown inside glass fiber capillaries. Credit: U.S. Air Force

Bringing nanotechnology to the aerospace market.

DOD researchers invented, patented, and demonstrated a bio-inspired artificial hair flow sensor that predictably measures the air flow in and above the boundary layer using the piezoresistive properties of carbon nanotube arrays grown between a single glass fiber and an electrode glass capillary.[1] The cantilevered hairs have successfully detected airfoil angle of attack, speed, coefficient of lift, moment, and flow separation. As small, agile fliers continue to join the fleet, lightweight, distributed sensors will increasingly be needed for "fly-by-feel" systems.

In response to the needs highlighted in the RFI feedback, the Sensors NSI developed a variety of community engagement efforts, including public workshops and webinars, participation in events organized by the broader community, and other information-sharing mechanisms. Outreach and engagement activities aimed to better understand nanosensor researcher and developer needs as well as to share information on Federal priorities, resources, and opportunities. Public workshops have convened representatives from the entire nanosensor development ecosystem, including experts from the Federal Government, academia, and the private sector. For example, in 2014, the NSI organized the *Sensors Fabrication, Integration, and Commercialization Workshop,* which focused on exploring the critical issues outlined in the 2013 RFI. Several key themes emerged, including the need for data security and guidance on how to best engage with appropriate contacts within regulatory agencies. As sensors become the backbone of the IoT and software development continues to play a vital role in sensor performance, data security is crucial for broad acceptance. Participants identified three main efforts to accelerate the early stages of sensor development: (1) leveraging the existing resources for testbed and foundries; (2) enhancing communication and engagement among researchers, developers, manufacturers, customers, and the Federal Government; and (3) encouraging developers to prepare for regulatory requirements early in the development process.

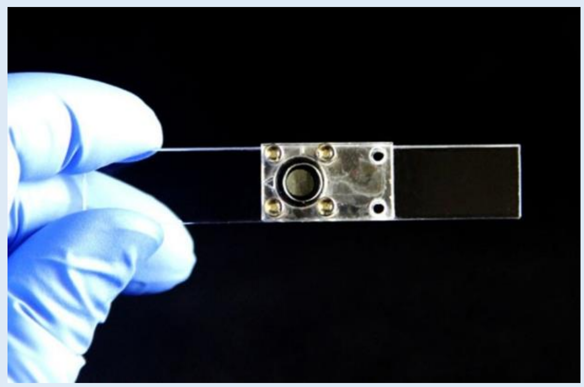
A follow-on workshop in 2017—*Nanosensor Manufacturing Workshop: Finding Better Paths to Products*—focused on bolstering the commercialization ecosystem by identifying the scientific challenges related to the development and deployment of nanotechnology-enabled sensors. Participants assessed the

[1] https://www.wpafb.af.mil/News/Article-Display/Article/1175838/bio-inspired-crickets-bats-inspire-afrl-researchers-to-develop-smart-hair-senso/

ecosystem for taking a nanotechnology-enabled sensor from the research and development stage to production stages. Several key considerations related to manufacturing emerged, such as fabrication, testing, and product performance. Agency representatives highlighted Federal resources and support mechanisms for companies and developers, including research centers, Small Business Innovation Research (SBIR) awards, public-private partnerships, business training programs, and research infrastructure such as characterization and fabrication tools and equipment. A tiered testing strategy that spans the entire development process and ensures access to appropriate testbeds was suggested to improve sensors testing. The critical role of performance and materials specifications in both guiding product development and facilitating communication of technical requirements between nanosensor developers and their suppliers, manufacturers, and customers was emphasized. Furthermore, the uncertainties around the availability and reliability of commercially sourced nanomaterials were highlighted as a unique challenge for developers that will likely diminish as nanomaterial production processes mature.

Detecting and monitoring cancer in blood.

University researchers funded in part by the National Cancer Institute have developed a diagnostic chip that detects biomarkers in blood, monitors how cancer patients respond to treatment, and can distinguish between indolent and aggressive tumors.[2] *The diagnostic chip is comprised of tunable magnetic* $\gamma\text{-}Fe_2O_3$ *nanoparticle tags, ultrasensitive magnetic sensor chips, and highly efficient magnetic sorters that harvest circulating tumor cells from lung cancer patients or ovarian cancer stem cells. The application of these advances in nanotechnology to pre-clinical models and clinical subjects may lead to better understanding and treatment of cancer.*



A MagSifter chip, shown here fastened to an acrylic holder, can purify circulating tumor cells from the blood of lung cancer patients. Credit: Seung-min Park

Insights from the Sensors NSI workshops guided the development of subsequent programming and information-sharing platforms to address the identified community needs. Periodic public webinars, such as *A Regulatory Case Study for the Development of Nanosensors*, have served to both highlight advances in nanosensor research and development as well as to share information regarding Federal resources and the regulatory process. The webinars have proven to be an effective and efficient method to share information between the Government and the broader nanosensors community and are an ongoing activity. The Sensors NSI also leverages events where the community already gathers. For example, agency representatives and the National Nanotechnology Coordination Office have provided summary presentations and hosted symposia and town hall sessions to exchange information directly with the broader nanosensor development community.

The Sensors NSI regularly explores new mechanisms to share information with the external community and digital resources have been created to help the community identify and access existing resources. Sensors NSI participants contributed to the development of the *Sensors Technology for the 21st Century* page on the

[2] https://www.pnas.org/content/pnas/105/52/20637.full.pdf

SBIR website, which was created to help the community locate SBIR and/or Small Business Technology Transfer Research (STTR) funding opportunities across Federal agencies. In addition, information was gathered on a wide variety of resources—including funding agencies and opportunities, Federally supported R&D infrastructure, regulatory guidance, and published standards—and a web portal was piloted to share these resources with the community. The portal was not widely accessed by the community, and the NSI continues to explore effective mechanisms to share information. Several NSI participants published a perspective piece in 2016, *Toward the responsible development and commercialization of sensor nanotechnologies*. This article outlined a nationally coordinated effort to support and advance nanosensor development and highlighted the Sensors NSI as a model for interagency collaboration.

Powering environmental sensors.

Researchers funded in part by USDA have developed a technique that harvests energy from tree branch movement to power a forest fire detection system.[3] The device monitors temperature and carbon monoxide and is powered by multilayered cylindrical triboelectric nanogenerators that harness small motions to produce energy. The device is both fireproof and waterproof, and because it has no batteries there is no risk of leaking harmful metals into the environment.

Credit: publicdomainpictures.net

Internal Collaboration and Interagency Coordination

Beyond the external community-building and engagement efforts undertaken, the Sensors NSI serves as an active platform for interagency coordination and collaboration. Through regularly occurring teleconferences and periodic in-person meetings, the Sensors NSI has fostered the development of a robust interagency community of interest focused on issues related to the development of nanosensors. The regular conversations have enabled Federal representatives to share information on planned and ongoing activities, discuss technical challenges and needs, and identify potential collaborators and persons to serve on agency review panels. These relationships and discussions have supported the agencies in the planning and execution of their programs in a wide range of tangible and intangible ways. The value of these interactions is illustrated by a few key examples. The FDA Center for Veterinary Medicine (CVM) was interested in rapid identification of species in food samples, to detect both counterfeiting and contamination in the food supply. Through the NSI, CVM researchers were connected with a USDA-support group that was developing a hand-held device with the ability to extract and amplify DNA to compare to reference libraries for species identification. In addition, a high-priority topic of interest is the appropriate use of standards and standardized methods when evaluating nanosensor performance. Sensors NSI-facilitated discussions led to the National Cancer Institute (NCI) sharing methods for characterizing nanoparticle surface properties with FDA scientists, in the context of biological sensing and the confounding effects of nanoparticles on optical protein assays.

Recently, wearable and implantable sensors have emerged as an area of common interest among participating agencies. This interest is due to the growing impact these devices have on agency missions and the important role that nanomaterials have in enabling the next generation of these devices. The Sensors NSI has hosted multiple day-long meetings to establish and strengthen a dialogue across the

[3] https://onlinelibrary.wiley.com/doi/epdf/10.1002/adfm.202003598

Federal agencies and seek opportunities for robust collaborations around wearable and implantable sensors. Agency representatives have shared information regarding R&D advances, programs, initiatives, and resources at their respective agencies. Discussions at these meetings also have identified key areas for interagency collaboration, such as the development and appropriate use of existing standards, the acceleration of energy-harvesting capabilities and/or smaller safer batteries to power wearable and implantable sensors, and the collection and analysis of meaningful data for identifying signals and biomarkers that lead to predictable outcomes. Conversations recently have shifted focus toward sensing technologies for future pandemics, ambulatory monitoring devices for telemedicine, and the regulatory and ethical challenges associated with wearable and implantable physiological sensors.

Researchers hold microfibrous materials embedded with carbon nanotube sensors. Credit: Negar Rahmani.

Wearable sensors to detect infections.

Researchers funded in part by NSF and NIH have developed a continuous, noninvasive way to detect and monitor an infection in a wound by embedding nanosensors in the fibers of a bandage.[4] The single-walled carbon nanotubes within the bandage are able to detect hydrogen peroxide, which indicates the presence of an infection. The team envisions this "smart bandage" being useful for treating diabetes, where the management of chronic wounds is crucial to providing critical healthcare.

Future Needs

Sensing technologies continue to play a key role in addressing priority topics such as healthcare, agriculture, and combatting climate change, and will require coordinated efforts across the community to more rapidly advance these technologies. Nanotechnology-enabled sensors are a critical component to achieve the sensing capabilities—sensitivity, rapid response, and portability—necessary in addressing these priorities. For example, advances in water and air sensors can be used for a myriad of applications ranging from pathogen detection for safe drinking water to environmental sensors for epidemiological studies. The occurrence of the novel corona virus, SARS-CoV-2, has emphasized the importance of the continued development of sensing technologies for infectious disease. Furthermore, the pandemic has forced the rapid adaptation of remote healthcare services to provide patient care while minimizing potential exposure to the virus. The development of nanotechnology-enabled physiological sensors will further enable remote healthcare services. These point-of-care services may be especially valuable to the aging population and those living alone.

As wearable and implantable physiological nanosensors continue to advance, broader questions around accuracy and precision, data management, regulation, and ethics also need to be addressed. The development and appropriate use of existing standards, as well as the generation of enough data to validate the signal to noise ratio, remain of critical importance to the development of sensing platforms. As sensors become widely distributed, the collection, storage, transmission, analysis, privacy, and security of data remain important considerations. The progression of artificial intelligence (AI) and machine learning (ML) will also have a significant impact on sensor development. Data generated from nanosensors will be used by AI/ML software to improve sensor performance, creating a feedback loop

[4] https://onlinelibrary.wiley.com/doi/epdf/10.1002/adfm.202006254

that ultimately leads to better, more accurate sensors. Physiological sensors will be used by the general population, raising questions about consumer education, appropriate use, and device calibration. Regulatory challenges also arise regarding how to delineate between a consumer device and a medical device. Furthermore, the ethical implications of continuously monitoring individuals are actively being discussed. To foster critical conversations around challenges, the Sensors NSI continues to organize public webinars, participate in broader community engagement activities, and facilitate dialogue and coordinated research efforts among participating agencies and with related organizations as appropriate.

Monitoring SARS-CoV-2 in wastewater.

A Virginia-based company funded by the NIH Rapid Acceleration of Diagnostics (RADx) program is developing a wastewater-based surveillance system for SARS-CoV-2.[5] The surveillance system is powered by magnetic virus nanoparticles that concentrate viruses rapidly from complex biological matrices for downstream analytical methods. This technology will be employed in a network of sites to monitor spatial and temporal trends in SARS-CoV-2 infection at a population level.

Researchers inspect an on-campus wastewater autosampler. Credit: Ceres Nanosciences.

The Sensors NSI has served as a valuable interagency platform to enhance community building and public engagement and improve government coordination in support of sensor technology development and deployment. Over the years, the Sensors NSI has evolved with respect to activities conducted, communication mechanisms employed, topical areas of focus, and increased agency participation. Agency representatives remain active participants in technical conferences and continue to communicate achievements, opportunities, and priority areas with the broader community. The evolution of the technical emphasis of the Sensors NSI, including the emergence of wearable and implantable sensors as a focus area, demonstrates the flexibility of the interagency community in identifying and responding to changes in needs and priorities. Building on lessons learned from the NSI mechanism, and in keeping with the 2021 NNI Strategic Plan,[6] in fiscal year 2022 the NSI communities transitioned to a "community of interest" model to support and build interagency engagements. As technology matures and new needs emerge, this interagency community serves as a key nexus for the internal government communities and external stakeholders to share critical information in support of the development of nanotechnology-enabled sensors.

[5] https://www.biospace.com/article/releases/ceres-nanosciences-receives-8-2m-nih-award-to-improve-wastewater-based-covid-19-surveillance/

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