Genesis Mission

GENESIS MISSION: NATIONAL SCIENCE & TECHNOLOGY CHALLENGES

THE WHITE HOUSE

WASHINGTON

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PREFACE

President Donald J. Trump's Executive Order on November 24, 2025, "Launching the Genesis Mission", established the Genesis Mission as a whole of nation effort, coordinated by the White House Office of Science and Technology Policy (OSTP), to harness the power of artificial intelligence to transform scientific discovery. The Genesis Mission brings together the world's most powerful supercomputers, experimental facilities, scientific datasets, AI capabilities, and research talent to address ambitious, mission-oriented national challenges at a scale no single laboratory, university, company, or Federal agency could achieve alone.

The National Science and Technology Challenges that follow give practical form to President Trump's mandate. Developed by over 15 Federal agencies, they identify consequential problems where artificial intelligence can change the speed and the nature of the questions American scientists are able to answer. These challenges represent the breadth of the American scientific enterprise, and reflect the nation's ambition to help Americans live longer, healthier lives, build American industrial strength, deliver reliable infrastructure and energy affordability, extend the frontiers of American discovery, and protect Americans from emerging threats.

Helping Americans Live Longer, Healthier Lives

Finding the Root Causes of Chronic Disease

Challenge: America faces a chronic disease crisis, with more than 40% of the nation's 73 million children living with at least one chronic condition and rising rates of obesity, diabetes, autism, ADHD, and pediatric cancer whose causes remain poorly understood. Tens of thousands of chemicals are in commercial use with little human safety data, and the cumulative effects of simultaneous exposures, especially during critical developmental windows, are largely uncharacterized because environmental, biological, and health-outcome evidence has never been integrated at scale. The Nation cannot yet trace how the environments in which Americans live, together with lifestyle and genetic variation, drive disease across the life course.

AI Solution: Researchers will leverage linked data sources, including data on genetic background, environmental exposure, biological response, and longitudinal health outcomes to move from associational epidemiology toward causal understanding of disease origins. Models will link environmental exposures and genetic background to molecular effects and to health trajectories across the lifespan, using causal-inference and multi-scale temporal methods to identify which exposures, at which developmental windows, drive which outcomes. Autonomous laboratories will screen environmentally prevalent chemicals at high throughput to generate the biological response data these models require, while physics-informed simulations estimate mixture effects for chemicals never directly tested.

Justification: Success requires assets no single agency holds. The Department of Health and Human Services contributes secure access to the Nation's longitudinal health cohorts, exposome and toxicology science, national biomonitoring, and the clinical and public-health expertise that connect exposures to disease endpoints while protecting patient privacy; the Department of Energy brings exascale computing, autonomous laboratories, and multi-scale modeling methods adapted from the physical and earth sciences; the Environmental Protection Agency contributes chemical characterization and monitoring data; and the National Science Foundation brings foundational research in AI, environmental science, and causal inference. The Make America Healthy Again Commission's designation of childhood chronic disease as a national emergency makes this a first-order national priority.

National Impact: Knowing the causes of disease is the precondition for preventing it. Understanding the environmental and biological origins of chronic disease will enable the healthcare system shift the Nation from disease management to disease prevention. Moreover, it will give regulators much needed evidence to make more informed decisions across thousands of poorly-understood exposures.

Accelerating Drug Discovery and Clinical Translation

Challenge: The Nation possesses the biomedical knowledge and clinical infrastructure to identify therapeutic relevance faster than it can turn these discoveries into treatments. Bringing new drug therapies to patients can still take over a decade and cost billions of dollars as many candidates fail late. This challenge intends to reduce the timeline by half in ten years, doubling the number of drug-based treatments we bring to patients as a nation. For example, in rare diseases, which impact 30 million Americans, 95% of 10,000 have no viable treatment options--small market size and the number of disparate conditions create economic barriers that standard drug development models cannot overcome. Thousands of approved and investigational drugs may hold untapped therapeutic value, yet the genomic, chemical, clinical, structural, and real-world evidence needed to find those uses sits in disconnected systems that cannot be queried together.

AI Solution: Researchers will leverage AI with integrated molecular, genomic, proteomic, phenotypic, clinical, and real-world evidence data sources from government and private partners to identify previously unrecognized relationships between drugs, targets, diseases, patient populations, and new surrogate endpoints. By aligning public-private datasets with predictive design models, the Nation can shift towards broad-spectrum, platform-based therapeutic discovery encompassing both repurposing of existing drugs and generation of new ones. Improved ability to evaluate drug and therapeutic candidates across new data sources will accelerate discovery by prioritizing safety profiles, biological plausibility, or potential to treat multiple indications simultaneously. Advanced capabilities running on DOE high-performance computing infrastructure and the DOW's high throughput screening and specialized validation infrastructure will enable rapid evaluation of therapeutic mechanisms, predict the effect of target engagement, and treatment-response predictions across diverse biological contexts. Autonomous laboratory platforms will be used to experimentally validate high-priority hypotheses while longitudinal cohorts, and clinical trial networks will provide downstream validation of repurposing candidates most likely to generate meaningful clinical and national security impact. This will substantially compress the time required to identify, evaluate, and validate new uses for existing therapies while improving the efficiency of clinical development.

Justification: AI will enable the Nation to rapidly identify high-confidence drug repurposing opportunities. Through leveraging the Department of Health and Human Services' biomedical knowledge, spanning decades of therapeutic development, translational pathways, and clinical trial networks, the Department of Energy's exascale computing resources, and the Department of War's end-use driven research, drug researchers will optimize development pipelines, thereby shortening the pathway from scientific discovery to patient benefit.

National Impact: Creating a scalable national infrastructure that continuously converts biomedical knowledge into actionable therapeutic opportunities can establish the United States as the global leader in AI-enabled translational science. Success would benefit patients across a wide range of diseases, including rare diseases, cancer, neurodegenerative disorders, infectious diseases, and chronic conditions, while providing a reusable framework for future biomedical discovery initiatives. The resulting capabilities would also strengthen national competitiveness in biotechnology, AI-enabled medicine, and precision health, potentially doubling the productivity and impact of American science and innovation.

Unlocking Cures for Pediatric Cancer

Challenge: Cancer is the leading cause of disease-related death for American children; roughly 15,000 are diagnosed each year, and those with relapsed, refractory, or rare cancers have few options. Unlike adult cancers, pediatric cancers are hundreds of rare, molecularly distinct diseases, producing small patient populations and fragmented data that defeat conventional approaches. Realizing AI's potential for these children requires secure, interoperable, AI-ready data and advanced computing at national scale, and will change lives and save thousands of children.

AI Solution: Researchers will leverage AI to integrate with linked genomic, multi-omic, imaging, pathology, clinical, and survivorship data into multimodal models that learn across distributed sources such as electronic patient and family health records, claims, and other data, using privacy-preserving federated learning and trusted-access methods. This overcomes the limits of small populations, enabling robust models even for ultra-rare cancers and revealing relationships among molecular alterations, tumor biology, therapeutic targets, and outcomes. Autonomous experimentation will screen priority pediatric molecular targets at high throughput, and patient-level digital twins will predict treatment response, progression, and toxicity to guide precision care and adaptive trial design. AI methods will be used to improve clinical trial design and execution, and AI models will advance the development of diagnostic, prognostic, and therapeutic biomarkers in pediatric cancer.

Justification: Executive Order 14355, sustained federal investment in a national pediatric cancer data ecosystem, and established laboratory collaborations provide the scientific and organizational foundation for this Challenge. The Department of Health and Human Services contributes the integrated pediatric cancer data ecosystem, the national network of designated cancer centers through which models can be trained and deployed, and clinical and regulatory expertise while protecting patient privacy; the Department of Energy contributes the computational scale required to train multimodal foundation models across hundreds of rare subtypes. Neither capability delivers impact without the other.

National Impact: This Challenge will accelerate biomarker discovery, target identification, precision medicine, and trial optimization for every child with cancer, while improving survivorship. It will establish the first national learning system that continuously integrates multimodal pediatric cancer data: a privacy-preserving model that is additionally usable across rare adult cancers and other diseases with small samples and distributed data.

Delivering Better Health Outcomes for Veterans

Challenge: The United States can develop more reliable ways to identify when a veteran's health or circumstances call for earlier care. Critical signals are distributed across years of clinical record, genetic background, and other health and social data, while existing risk models are static and difficult to validate across large and varied populations. Data integration and new medical and biological applications can advance discovery, diagnosis, and treatment of chronic diseases such as cancer, heart disease, neurologic disease, and mental health conditions. This challenge will expand ongoing efforts to improve risk prediction models in Department of Veteran Affairs (VA) priority areas such as homelessness, suicide, frailty, and chronic diseases prevalent among Veterans, leading to better preventive care and improved health outcomes for those who have served in our nation's military.

AI Solution: Bringing VA's vast electronic health record data (EHR) and one of the world's largest genomic datasets from the Million Veteran Program (MVP), together with DOE's exascale and supercomputing resources and expertise, provides a foundation for accelerated scientific discovery and the development of trusted biomedical AI models and applications to enable earlier disease detection, prevention, and treatment for Veterans. Secure data integration, large-scale training, and real-time application with continuous validation will ensure robustness, generalizability, and long-term reliability, allowing hypotheses to be generated, tested, and iterated upon to accelerate progress. Additional data from the Department of Health and Human Services (HHS), such as Centers for Medicare and Medicaid Services (CMS), will enhance predictive models.

Justification: VA and DOE have partnered since 2016 to apply secure computing practices to sensitive data, leading to improved health outcomes for Veterans. Copies of VA's clinical data and MVP genomic data reside in the secure computing enclave at DOE's Oak Ridge National laboratory (ORNL), with secure access to the Frontier supercomputer. This has enabled collaborative research projects advancing VA's priority areas, such as suicide prevention, prostate and lung cancers, schizophrenia and bipolar disorder, and heart failure, resulting in over 50 scientific publications and clinical translation of discoveries related to the risk of suicide and prostate cancer. Harnessing VA's data and Frontier, one of the world's fastest supercomputers, has produced novel and energy-efficient AI models pre-trained on 1.7 trillion tokens of clinical text and capable of handling contexts exceeding 1 million tokens.

National Impact: Building upon existing infrastructure, resources, and expertise across VA and DOE, this challenge will unlock precision medicine through accelerated scientific discovery, earlier disease detection, and consistent decision support to improve health outcomes for Veterans and, ultimately, all Americans. It will enable the VA to recognize changing needs earlier, connect Veterans with appropriate care and support, preserve independence as Veterans age, and reduce the rate of preventable crises and complications from chronic disease.

Building American Industrial Strength

Reenvisioning Advanced Manufacturing and Industrial Productivity

Challenge: Bridging the gap between scientific discovery and commercially viable products and processes, known as the "valley of death", remains the biggest challenge in industrial manufacturing. The scaling, modification, or deployment of innovative materials and processes depends on a vast and complex parameter space, requiring the uncovering and integration of underlying physical and chemical principles that hold the key to the next United States (U.S.) manufacturing revolution.

AI Solution: Recent advancements in agentic and generative artificial intelligence (AI) present opportunities to accelerate discovery and translational science. These new tools could navigate multi-scale and high-dimensional dynamic systems to find hidden relationships and uncover new manufacturing routes and products. AI can also enable end-to-end digital transformation of industrial manufacturing through integration of real-time data from machines, products, processes, and supply chains into digital twins for continuous human-in-the-loop automated decision support and deployment of emerging advanced manufacturing technologies.

Justification: The U.S. Department of Energy (DOE) National Laboratories co-locate world-leading expertise in the discovery, optimization, and scale-up of novel chemistry and materials for energy applications and in smart manufacturing, as well as operate cutting edge synthesis and characterization facilities and high-performance computing (HPC) resources. At the same time, DOE has a long history of partnering with industry, which has helped cultivate data from industrial facilities. This creates an ideal environment to advance AI-driven manufacturing for U.S. industries today and in the future.

National Impact: Delivering innovations through an efficient, distributed, and adaptive platform capable of real-time decision making and end-to-end intelligence will profoundly transform how we create chemicals and materials foundational to industrial products and advanced energy technologies while strengthening supply chain resilience and competitiveness of American industry to create jobs and economic growth.

Scaling Biology for American Industrial Leadership

Challenge: Bioindustrial manufacturing translates capability and advances in the biological sciences into industrial and economic power. The United States leads the world in scientific discovery but struggles to scale those discoveries into domestic industrial manufacturing. Living systems can synthesize unique molecules no chemical process can and they can also efficiently sequester elements such as critical metals from ores and wastes that conventional processing leaves behind. Securing domestic biomanufacturing of vital fuels, chemicals, and materials will contribute to the American industrial renaissance and build the commercial basis to move technology from the lab to everyday Americans.

AI Solution: AI will link biological design to manufacturing outcomes by connecting experimentation, structural analysis, models, discovery of biodiversity, and digital twins of organisms, bioreactors, and biochemical processes. AI can expand the design space available for bioprocesses, leveraging the diversity of feedstocks, organisms, and pathways, including cell-free biomanufacturing. Digital twins and process models can integrate organism design with process design. These digital representations can be extended beyond individual bioprocesses to model manufacturing networks and critical supply chains, enabling AI to identify vulnerabilities and forecast disruptions for essential products. Autonomous experimentation enables a virtuous cycle of hypothesis generation, wet-lab experimentation, and in-silico modeling to advance biological understanding and potential perturbations. Accelerated iteration speeds and improved simulations will decrease process and design uncertainty, driving higher yields, lower costs, and greater robustness.

Justification: The American science and technology enterprise operates the industrial infrastructure required to scale biological discovery. The Department of Energy brings extensive experience in the development of chemicals, materials, and processes such as mineral extraction, as well as bioreactor design and certification; the Department of Agriculture brings feedstocks, fermentation, and bioprocessing expertise; the Department of Health and Human Services advances foundational science in biochemistry, enzymology, and synthetic biology, supports roboticized biological experimentation, and oversees ARPA-H's biomanufacturing programs and FDA's AI-enabled supply chain analytics; the Department of War provides advanced research and development in microbial synthetic biology and anchors bio-industrial manufacturing scale-up and defense-critical supply; the Department of Interior's U.S. Geological Survey brings unique data and expertise on America's critical mineral assets; and the National Science Foundation contributes foundational research in synthetic biology and chemical, process, and metabolic engineering.

National Impact: A nation that can scale biology on demand can produce its own advantaged fuels, chemicals, materials, and minerals. Reshoring production and securing supply chains against disruption requires investing in biomanufacturing that turns discovery into industrial products.

Securing America's Critical Minerals Supply

Challenge: America's dependence on foreign supply chains for CMM threatens national security, economic competitiveness, and the deployment of technologies essential for energy independence. Domestic critical mineral production is expensive, complex, and time-consuming, in part because of the many steps to identify, extract, refine, and concentrate from complex, heterogeneous sources across critical mineral supply chains.

AI Solution: AI will revolutionize the entire critical minerals supply chain and development of alternative materials by integrating geophysical data, other fundamental science data, process optimization, cost estimation, and economic modeling into one connected system. Solving this challenge demands an AI that can reason scientifically, can understand complex structure-property relationships, and can design alternatives with different compositions. Physics-based AI offers advanced predictive capabilities to identify alternatives and understand processes underlying critical mineral availability, recovery, refinement, and replacement.

Justification: DOE's existing minerals characterization datasets (e.g., METALLIC, Critical Materials Innovation Hub), combined with DOE national laboratory expertise and DOE-supported efforts in materials science, chemistry, geosciences, biology, process engineering, and economic modeling, could enable acceleration from the years-long mineral development timelines to rapid resource assessment and production optimization. Further, use of AI could reveal new strategies to replace and/or eliminate the need for CMMs in some materials and chemical processes.

National Impact: This effort will reduce reliance on adversarial nations, expand America's mineral resource base, maximize production profitability, and strengthen supply chain resilience for technologies essential to national security and economic prosperity.

Recentering Microelectronics in America

Challenge: Microelectronics powers all aspects of our lives, including AI, but America faces intense global competition in critical microelectronics applications, including ultra-efficient semiconductors for AI computing, power electronics, and communication networks. At the same time, microelectronics in the national security enterprise must perform complex calculations across highly varied thermal, shock, vibration, electromagnetic, and radiation environments while meeting steep operational constraints that evolve with novel flight vehicle, terrain, and mission needs. Continued American leadership in microelectronics faces a tremendous scientific and technological challenge: designing and engineering the next generation of microelectronic devices and platforms that push the boundaries of miniaturization, processing speed, power consumption, thermal management, and operations environment.

AI Solution: An AI-driven full-stack co-design ecosystem will enable faster innovation cycles, de-risk new ultra-efficient manufacturing processes and component designs, and accelerate materials and manufacturing research and development (R&D), thereby leapfrogging foreign semiconductor technology. Frontier AI coupled with heterogenous and multiscale data that is accessible via federated learning techniques will accelerate microelectronics research by revealing the critical relationships and tradeoffs between materials, devices, and workflows. This co-design ecosystem will include AI/ML workflows that streamline the development of microelectronics in national security from design through certification, including applications such as radiation-hardened-by-design microelectronics, automated inspection of metallization, lithography, and epitaxial growth, and strengthened assurance processes to detect anomalous or tampered devices.

Justification: For decades, DOE has been at the leading edge of microelectronics research, both as a consumer and as an engine of scientific innovation with expertise in advanced materials, nanofabrication, and quantum-related technologies such as cryogenics, enabling many of the technological breakthroughs adopted by industry. DOE already possesses large fab and test datasets and emerging automated inspection efforts that can be expanded into broader AI-enabled workflows that spans both commercial and national security domains.

National Impact: Microelectronics continues to be at the heart of technological innovation, and every American will benefit from recentering leadership of the industry in the U.S. This effort will ensure sustained U.S. leadership in the global semiconductor landscape, enabling the rapid growth of domestic data centers, advancing beyond Moore's law for AI computing and national security applications, such as strengthening nuclear deterrent by accelerating the design, production, assurance, and certification of critical microelectronic components, and securing other technological advantages—such as global leadership in 6G communication networks essential for economic prosperity and national security.

Securing U.S. Leadership in Data Centers

Challenge: Winning the AI race will require accelerating the process of developing and deploying new data center technologies and energy management strategies to provide the extreme compute power for AI advancements, while ensuring secure, reliable, and affordable energy for consumers.

AI Solution: By leveraging AI/machine learning (ML), digital twins, and cyber-physical testbeds, we can rapidly de-risk advanced data center technologies and their grid integration, accelerating the time to deployment and supporting stakeholder needs including data center operators, equipment providers, communities, and utilities. AI/ML can accelerate physics-based models to enable real-time digital twins, explore millions of deployment scenarios, and optimize under a unique constraint surface.

Justification: This project leverages DOE's capacity to convene data center and utility stakeholders, the national laboratories' research expertise in both load flexibility and computing, and their unique cyber-physical testbed facilities. Specifically, the DOE already supports the Center of Expertise for Data Center Energy at LBNL, which can provide resources, including a variety of data sets on data center energy use, to aid this effort.

National Impact: By ensuring a robust capacity to develop cutting edge data center technologies and load management strategies, we will solidify U.S. intellectual and economic leadership in AI, driving prosperity and security while maintaining secure, reliable, and affordable energy for consumers.

Delivering Reliable Infrastructure and Energy Affordability

Reimagining the Lifecycle of American Infrastructure

Challenge: America's built infrastructure, including residential and commercial buildings roads, bridges, maritime ports, rail beds, rail track supports, runways, terminals, and transshipment warehouses that connect us, faces high costs and lengthy timelines at every stage of the lifecycle: design, materials, permitting, construction, operations, maintenance, and decommissioning. Developing stronger, longer lasting, and lower-cost materials remains slow, requiring years of laboratory testing and validation. When assets enter service, inefficient designs, unseen structural wear, and faulty controls can drive up costs and safety risks. New AI models and advanced simulations can reduce costs, accelerate the discovery of next-generation construction materials and improve the design, operation, and longevity of the Nation's physical infrastructure.

AI Solution: Physics-based machine learning, digital twins, and foundation models for materials science can lower costs and transform the lifecycle of physical transportation infrastructure and residential and commercial buildings. Simulations, digital twins, and models trained on validated physics can run structural, energy, and materials tests orders of magnitude faster than conventional methods, enabling breakthroughs in materials, automated design, predictive maintenance, and cost-effective decommissioning. AI can rapidly discover and optimize new materials with lower cost and improved strength, durability, and resilience, by predicting material properties and guiding experimental validation for high-stress environments. Federal agencies will partner with AI developers, materials manufacturers, academia, national laboratories, infrastructure owners, and other market participants who will provide the data to help validate models and accelerate development.

Justification: The Department of Energy's (DOE) building design expertise, materials science capabilities, integrated research infrastructure, and track record of public-private partnerships positions it well to modernize American buildings and optimize transportation efficiencies. The Department of Transportation's (DOT) expertise in infrastructure engineering, testing, and asset management enables it to innovate across transportation infrastructure. Both American buildings and transportation infrastructure rely on basic and use-inspired research from the National Science Foundation's (NSF) in advanced materials, which lead to new construction techniques and materials discovery that transform physical infrastructure design and operation across the full lifecycle. The DOT's relationships with states, localities, port authorities, and transit agencies will enable the integration of the diverse transportation network systems with the partnerships needed to accelerate breakthroughs in the design, materials, construction, and operational efficiencies and safety of the Nation's transportation infrastructure.

National Impact: This effort will accelerate the discovery and deployment of stronger, more resilient, and lower-cost materials, while reducing construction and maintenance costs, thus making physical infrastructure less expensive to build and operate, and safer to use. These advances will increase housing availability and affordability, shorten construction and maintenance time, extend the service life of infrastructure, and reduce operational costs through predictive maintenance. Together, this work will prolong the life and performance of the physical infrastructure that underpins the American economy.

Delivering Nuclear Energy That is Faster, Safer, Cheaper

Challenge: Nuclear power plants have historically been challenged by long development timelines and burgeoning costs, limiting America's ability to deliver affordable, resilient, and reliable energy as demand continues to grow—particularly from AI data centers.

AI Solution: This initiative will accelerate nuclear energy deployment by using AI to design, license, manufacture, construct, and operate reactors with human-in-the-loop workflows, enabling at least 2x schedule acceleration and greater than 50% operational cost reductions. To meet these goals, we are using a suite of explainable AI solutions including surrogate models, agentic workflows, autonomous labs, and digitals twins. For example, for reactor operations, we will use digital twin systems with AI components that will interpret complex operational data in real time.

Justification: DOE's combination of national laboratory nuclear expertise, test facilities (e.g., INL's Advanced Test Reactor, Transient Reactor Test Facility, Fuel Conditioning Facility, Hot Fuel Examination Facility, and Collaborative Computing Center; Oak Ridge National Laboratory's High Flux Isotope Reactor; Argonne National Laboratory's Mechanisms Engineering Test Loop Facility), decades of operational data, industry partners, and extensive computational ecosystem uniquely position it to accelerate reactor deployment. DOE's partnership with the Nuclear Regulatory Commission will enable workflows to drive design, licensing, manufacturing, construction, and operational excellence.

National Impact: This challenge will provide Americans more affordable energy while reducing human error, strengthening national security, and directly supporting U.S. energy dominance with multi-billion-dollar cost savings per gigawatt of generating capacity.

Accelerating Delivery of Fusion Energy

Challenge: Realizing fusion energy on the grid requires coordinated progress across six tightly coupled challenge areas defined in the Fusion Science and Technology Roadmap.[1] Isolated, device-specific trial-and-error approaches cannot manage these interdependencies at the scale, complexity, or pace required to meet national energy objectives.

AI Solution: AI enables physics-constrained digital twins that integrate plasma, nuclear, materials, and system behavior within a unified predictive framework, allowing performance and engineering trade-offs, failure modes, and design margins to be evaluated consistently in simulation and experiment. An AI-Fusion Digital Convergence Platform (DCP) will integrate novel algorithms in HPC codes, foundation models for plasma and materials science, physics- and chemistry-informed neural networks, surrogate models, and digital twins for whole-facility modeling and real-time control across the six Roadmap challenge areas. The DCP will accelerate infrastructure development, shorten innovation cycles, and support a competitive U.S. fusion ecosystem.

Justification: DOE uniquely brings together fusion facilities, national laboratories, leadership-class computing, data stewardship, and public-private partnerships to build and operate a trusted, national-scale AI platform that integrates data, models, and experiments across the fusion ecosystem. That platform will leverage large-scale domestic and international fusion facilities and fusion materials and technology infrastructure including high-heat-flux testbeds, tritium and blanket test stands and loops, irradiation facilities, and in situ and in operando materials characterization capabilities across both public and private sectors to meet fusion roadmap milestones.

National Impact: The DCP would accelerate delivery of fusion energy as a source of firm, scalable baseload power, strengthening U.S. energy security and competitiveness.

[1] The Fusion Science and Technology Roadmap is available at energy.gov/fusion-energy.

Transforming Nuclear Cleanup and Restoration

Challenge: DOE's environmental cleanup mission faces an estimated $540 billion liability over eight decades with ~90 million gallons of highly radioactive tank waste requiring treatment that impedes site remediation and restoration crucial for American energy, security, and innovation.

AI Solution: A multimodal AI foundation model will be trained on DOE Office of Energy Management's (EM) unparalleled 30+ years of operational data from unique nuclear processing facilities to predict scale-dependent behavior across lab, pilot, and full-scale systems. National laboratory experts will leverage Equinox supercomputing capabilities for accelerated simulation architecture in development of the AI models. The goal is to use AI to enable mission acceleration to meet EM's 2040 vision with significant liability reduction.

Justification: DOE EM's unique data assets from designing and operating large-scale facilities at complex sites (e.g., the Defense Waste Processing Facility and the Salt Waste Processing Facility at the Savannah River Site (SRS)), combined with the capabilities provided by the industry partners, will enable development of scale-bridging AI models that safely and efficiently address deployment challenges (e.g., the Waste Treatment and Immobilization Plant at the Hanford Site) no other institutions can leverage.

National Impact: This transformation will compress deployment timelines and accelerate nuclear remediation, thereby enabling renewed use of nuclear materials (for energy and medical applications) and infrastructure for American energy dominance.

Predicting U.S. Water for Energy

Challenge: Water availability is essential for expanding production and utilization of energy, as well as the nation's health and security. However, there are fundamental scientific gaps in our understanding of terrestrial and atmospheric systems that limit our ability to predict water resources, especially on the time scale of weeks to years.

AI Solution: AI capable of multi-scale temporal reasoning could tackle three inter-related grand challenges: cloud physics, surface and subsurface water flows, and the broader hydrologic cycle. AI could improve, accelerate, and couple exascale-class modeling systems through advances in model initialization, and develop surrogates trained on DOE's atmospheric and terrestrial observations and laboratory data, at a fraction of the computational cost of existing models. AI-based model diagnostics for enhanced analysis could refine a model-observational system aligned with decision-making needs.

Justification: DOE is the only agency with AI expertise, advanced computing, and integrated modeling capabilities (e.g., the DOE Energy Exascale Earth System Model, or E3SM), and infrastructure for field research necessary to meet the challenge of providing accurate information on surface and ground-water availability on the time scales of weeks to years.

National Impact: Solutions to these longstanding science challenges will radically improve America's ability to anticipate water supply in the context of changing water availability, demands, energy technologies, and ambitions for energy expansion.

Scaling the Grid to Power the American Economy

Challenge: The electric grid faces reliability challenges and infrastructure limitations to accommodate dramatic increases in electricity demand from data centers, manufacturing, and electrification while maintaining affordable power for Americans.

AI Solution: AI, using deep and reinforcement learning techniques on newly integrated big data sources, will reduce uncertainty, improve insights, and speed processes in grid planning, interconnection, operations, and security. This effort aims to enable 20-100x faster decision-making and at least 10% improvement in electricity cost and reliability.

Justification: The utility sector has critical grid data but a low risk tolerance, limited ability to develop new technology, and regional focus. DOE can bring integrated energy system expertise, computational facilities, and testbed infrastructure like the Critical Infrastructure Test Range Complex (CITRC) at INL and the Advanced Research on Integrated Energy Systems (ARIES) platform at NLR. The Department's strong partnerships with grid operators can bring utility data together with these DOE capabilities to develop validated, deployable AI solutions.

National Impact: This modernization will deliver lower-cost, more reliable power to American homes and businesses while strengthening energy security through faster deployment of grid capabilities and improved resilience against threats.

Unleashing Subsurface Strategic Energy Assets

Challenge: Delivering cost-effective energy from the Earth's subsurface entails the use of heterogeneous reservoirs, dominated by fractures. Tools capable of predicting reservoir behavior and the interactions of complex biogeochemical, mechanical, and hydrologic processes are critical to the development of innovative, cost-effective extraction of subsurface energy sources, including unconventional oil and gas, geothermal, and coal bed methane.

AI Solution: Developing AI capable of reasoning under extreme uncertainty, integrating heterogeneous data types (i.e., seismic, geochemical, biological, hydrologic), and building predictive models of systems that cannot be directly observed has broad applicability to any domain requiring inference from indirect evidence. For subsurface science, AI that connects molecular-scale mechanisms to field-scale resource availability will transform the field from descriptive to predictive. DOE's vast biological, geochemical, geomechanical, and hydrologic data sets can be combined with high performance modeling capabilities, laboratory analytics, and a suite of AI technologies, including surrogate models, physics-informed machine learning, and digital twins to enhance engineering evaluation and control of the subsurface during characterization, drilling, stimulation, and production.

Justification: DOE's laboratory complex includes a vast array of data, modeling, and analytical capabilities (e.g., Science-informed Machine Learning for Accelerating Real-Time Decisions in Subsurface Applications (SMART) Initiative suite of tools and machine learning-based surrogate models; National Energy Technology Laboratory's Energy Data eXchange (EDX) Discover; LBNL's Transport Of Unsaturated Groundwater and Heat (TOUGH) simulation suite; Los Alamos National Laboratory's (LLNL) GeoDTi design tool; LLNL's GEOS software; and PFLOTRAN and ATS models), that supports extensive research and operational activities in subsurface environments, and are uniquely positioned to apply AI to accelerate development of models that emulate microbial, mineral, and fluid interactions across molecular to field scales. Efforts will assemble, train, and analyze information from vast data libraries, experiments, and operational sensors, to produce subsurface transport models and digital twins to enhance reservoir characterization, enable real-time reservoir simulation, and address uncertainty to increase hydrocarbon resource recovery and unlock geothermal resources.

National Impact: Understanding subsurface complexities and stored energy sources is key to securing the nation's energy future and will reduce the costs of recovery for oil, gas, and heat, reduce costs of power to U.S. consumers, re-shore manufacturing, and enhance U.S. competitiveness.

Extending the Frontiers of American Discovery

Discovering Quantum Algorithms with AI

Challenge: Discovering new quantum algorithms is an exceptionally difficult challenge due to the number of potential quantum operations and is highly counter-intuitive for human researchers to navigate. U.S. leadership in the emerging quantum computing revolution will require accelerating the design and development of quantum algorithms (including those that capitalize on the convergence of classical HPC, AI, and quantum computers) that demonstrate scientific utility and a provable quantum advantage.

AI Solution: Novel AI could discover new quantum algorithms by automating and optimizing their design and translating them into applications without requiring prior domain knowledge. Furthermore, AI-powered platforms can translate high-level problem descriptions in natural language into executable quantum circuits, making algorithm design more accessible to researchers from various fields. AI could help establish scientific workflows that leverage the interplay of classical and quantum resources, managing data flow and executing complex computations across platforms.

Justification: There is strong evidence that quantum computers and algorithms will offer solutions to computational problems with high impact to the scientific community, beyond the limits of classical HPC and AI. DOE hosts the most complete suite of scientific computing capabilities and these advances in quantum capability will enable computations that are classically intractable.

National Impact: The discovery of new quantum algorithms will have broad applications to science domains, such as fusion sciences, high energy physics, nuclear physics, materials science, and chemistry, with proposed commercial applications for the acceleration of drug, material, and chemical discovery. This technological leap would not only bolster the nation's economy and security but also provide tools to address some of the most challenging scientific and societal problems.

Realizing Quantum Systems for Discovery and Use

Challenge: Quantum systems for quantum computing, quantum sensing, and quantum communication are poised to revolutionize discovery science by enabling unprecedented capabilities in modeling, simulation, and measurement. The use of current quantum systems is severely limited by their fragility, scalability, and integration into existing infrastructure. The inherent challenge is the lack of understanding and control of the complex cause-and-effect relationships within a quantum system. Quantum systems, both for computing and for sensing, rely on complex cause-and-effect relationships that are currently poorly understood. Sensors allow the ability to detect fundamental underlying features on the atomic scale, while computing allows numerous advancements in optimization and simulation.

AI Solution: AI has shown its ability to process vast amounts of multimodal data, to recognize complex patterns and relationships, and to learn adaptively how to handle dynamic and unpredictable environments. This ability makes AI uniquely suited to help understand and control the delicate nature of complex quantum systems. In quantum computing, AI will assist in real-time noise mitigation, adaptive error detection and correction, and system optimization and design. In quantum sensing, AI will optimize quantum entanglement, increase sensitivity, and control multi-sensor quantum networks. In quantum communication, AI will dynamically optimize multi-node quantum network design and control. New AI approaches are needed for making real-time decisions under quantum uncertainty, learning control policies when observation is costly and destructive, predicting behavior from incomplete information, and adapting to drift in real-time.

Justification: DOE is home to five National Quantum Information Research Centers in the U.S. working on overcoming limitations in quantum computing, quantum sensing, and quantum communication. The existing ecosystem is ideally suited to develop AI solutions to enable full quantum control. The Department of War, through its Quantum Science office, brings expertise in maturation and translation of quantum sensing and other applications of quantum materials and quantum information science.

National Impact: The AI enabled understanding and control of complex quantum systems will accelerate the deployment of quantum technologies and accelerate their utilization for currently intractable challenges in scientific discovery and technology development, while improved understanding of the cause-and-effect relationships that shape quantum system behavior will accelerate transition of sensors from the lab to more applied use cases, such as positioning, navigation, and timing.

Achieving AI-Driven Autonomous Laboratories

Challenge: The pace of scientific discovery is influenced by the traditional, human-driven experimental process and the availability of non-deterministic AI-driven control tools to implement complex experimental designs in combinatorially large design parameter spaces. These bottlenecks slow the cycle of hypothesis, experimentation, and discovery, leading to inefficient use of critical national assets and delaying scientific breakthroughs. Automating at least some parts of the scientific experimental scheme will both increase the volume of data produced for improved AI models and improve the repeatability of experiments.

AI Solution: Artificial intelligence will be integrated directly into the experimental workflow and data analysis, combining robotics, edge AI, real-time analysis and intelligent feedback, hypothesis generation, and data curation/sharing.

Justification: These AI-driven laboratories will allow scientists to explore complex phenomena at an unprecedented rate and scale and are critical to achieving the Genesis Mission goals. DOE's user facilities and long-standing national laboratories have the infrastructure, capabilities, and expertise to serve as the nucleus for innovation with this type of high throughput discovery.

National Impact: Accelerating discovery through AI-driven laboratories will directly advance U.S. scientific leadership and economic competitiveness. This capability will speed up the development of novel materials and molecules for energy, next-generation computing, national security, and biotechnology. Like other challenges, it will also solidify the nation's position at the forefront of AI and scientific innovation, create a new paradigm for 21st-century research, and train a future workforce fluent in the integration of AI, data science, and experimentation.

Predicting Living Systems

Challenge: The United States has cataloged life in extraordinary detail, but it lacks the ability to confidently predict the behavior of complex living systems from smaller, simpler building blocks, such as proteins or genes. We intend to change that by building a foundation for biology as predictable as the physical sciences by measuring and understanding the natural laws and causal mechanisms governing genomes, proteins, cells, tissues, systems, and eventually whole organisms.

AI Solution: By linking and integrating multiple inputs, such as nucleic acid sequences, protein structures, multi-omics analyses, imaging, and perturbation data into models and pipelines that connect molecular-scale components to broader system behavior and model biological features, functions, processes, pathways, and regulation at multiple size and temporal scales to better model and understand the complexity of biology. Mechanism-, biology- and physics-constrained AI models will improve our understanding of the fundamental rules of life. Automated, biological data-focused cloud labs will identify and gather data to fill critical gaps and compress the cycle of discovery, including bridging the genotype-to-phenotype gap.

Justification: The United States has built a vast corpus of biological data that spans the full range of biological complexity, from genomes and proteins, to cells, tissues, and whole organisms, positioning it to lead the development of AI-enabled solutions with enormous benefits for health, energy, agriculture, and the economy. The Department of Health and Human Services serves as the hub for some of the most comprehensive repositories for DNA, RNA, protein-sequence, and protein-structure data; the Department of Energy contributes microbial, plant, and environmental genomics paired with national-scale computing capabilities; the National Science Foundation brings foundational research in AI and biology, a National Ecological Observatory Network and Ocean Observatories, and shared data and computing resources; the Department of War provides applied research in AI, extensive computing resources and molecular biological data from model microbial systems and environmental matrices; and the Department of Agriculture brings plant, animal, and microbial datasets spanning decades. United through a common platform and connected with autonomous laboratories capabilities that will generate massive volumes of low and high-resolution biological data, these assets will transform the field of biology.

National Impact: A predictive foundation drives the bioeconomy's flywheel by accelerating every step of discovery. When progress becomes incremental and predictable rather than trial and error, achieving ambitious goals become a matter of direction and intent, not technical feasibility, turning 70 years of fragmented genomic, cellular, proteomic, imaging, and clinical data into one secure, integrated platform to accelerate scientific advancement.

Designing Materials with Predictable Functionality

Challenge: Accelerating materials innovation will enable rapid deployment of advanced energy and industrial technologies that are essential for American competitiveness, from structural materials to materials for energy storage to other functional materials for advanced technologies. The identification and commercialization of new materials with transformative properties that dramatically improve performance, energy efficiency, reliability, and resilience, however, is a time- and resource-intensive process due to the inherent complexity of materials science and the practical limitations of traditional simulations, synthesis, and characterization techniques that still require significant trial and error.

AI Solution: The convergence of current and emerging AI technology with the growing availability of large, curated datasets may be a tipping point for materials discovery, design, and qualification. The development of physics-aware AI frameworks that exploit the complementary strengths of foundation models, deep learning, computer vision, generative AI, and agentic AI will enable entirely new capabilities for materials design that iteratively couple prediction, synthesis, characterization, and analysis to yield closed-loop learning systems that are interpretable, trustworthy, and capable of bridging large scales in space and time. The ultimate goal of inverse design (designing materials for given property specifications) requires advanced experimental and simulation capabilities as well as AI reasoning and explainability.

Justification: DOE's suite of world leading and unique experimental and computational capabilities for materials research, including X-ray light sources, neutron scattering facilities (and their associated characterization equipment), nanoscale science research centers, materials databases, and exascale computers, is collectively the most comprehensive and performant in the world. These capabilities, along with the availability of very large materials data sets coupled with sustained investments in the development of AI-enabled physics-informed models, has positioned DOE to take a leadership role in implementing the materials by design vision.

National Impact: Tight integration of AI into the materials discovery-to-product workflow could significantly reduce time to market in manufacturing—from many years to decades down to months to a few years. This acceleration will dramatically reduce development timelines for critical technologies including batteries, energy systems, structural and functional materials, strengthening American technological leadership and enabling faster deployment of innovations that create jobs and strengthen economic and national security.

Enhancing Particle Accelerators for Discovery

Challenge: Modern particle accelerators are complex, requiring extensive human intervention that leads to high operating costs, operational variability, suboptimal experiment optimization, and inadequate data integration. Further, the physical limitations of existing accelerator technologies slow progress in pushing the limits of resolution in space, time, and energy. Transforming accelerator-based facilities into highly efficient, autonomous, and more productive capabilities requires a tight integration of AI with design and operation.

AI Solution: Predicting chaotic beam dynamics, in which small perturbations cascade into major problems, could push AI to develop new capabilities in multi-scale temporal reasoning, physics-constrained learning, and robust uncertainty quantification. AI-driven digital twins that simulate complete beam dynamics in real time could dramatically reduce tuning time. Collectively, facility-based AI will become adaptive and self-updating, significantly boosting performance, efficiency, and scientific output.

Justification: DOE stewards one of the largest suites of accelerator-based experimental facilities in the world, with extensive operational data and a large, highly skilled workforce. The optimization of the nation's large-scale scientific infrastructure through AI-enabled design and the elimination of operational bottlenecks and cost inefficiencies will maximize the nation's return on current and future infrastructure investments, revealing entirely new paradigms for scientific research through human-AI teaming and accelerating discovery.

National Impact: Accelerator-based facilities have been central to many of the most important discoveries of the 20th and 21st centuries. Integrating AI into accelerator design and optimization will increase the pace of future breakthroughs, enabling a deeper understanding of the universe, the development of new energy and computing technologies, and the creation of new techniques for the diagnosis and treatment of disease.

Unifying Physics from Quarks to the Cosmos

Challenge: The universe obeys only one set of rules, and scientists have hundreds of experiments targeting parts of that one set. Experiments range over distance scale (31 orders of magnitude), cost ($100k to $B), duration (fractions of a section to decades), and human investment (few to thousands). We need a way to integrate the disparate experimental results with theoretical knowledge to accelerate discovery.

AI Solution: High-energy physics and nuclear physics form a unique foundation to build AI reasoning models at unprecedented scale. Developing AI that simultaneously learns from particle collisions, nuclear decays, and cosmological surveys will require breakthroughs in multi-modal learning and the ability to derive insights rather than merely recognize patterns. An AI that internalizes the Standard Model could accelerate analysis by orders of magnitude, identify anomalies pointing to new physics, and propose theoretical extensions consistent with all data—a leap from pattern matching to physics reasoning.

Justification: DOE uniquely possesses the confluence of world-class scientific talent, stewardship of cutting-edge facilities, unparalleled access to experimental data, and a critical national mission to effectively address this challenge. These facilities, alongside a broad portfolio of programs that explore the fundamental constituents and forces of the universe and delve into the nature of atomic nuclei, underscore DOE's singular ability to conduct large-scale, long-term, and high-impact scientific research.

National Impact: The acceleration of discovery, particularly in areas involving vast datasets from cutting-edge experiments, means we could reach breakthroughs much faster than previously possible, impacting our technological capabilities and quality of life in unforeseen ways. Questions such as why is there more matter than antimatter, what is the nature of dark matter, and how do protons generate mass and spin address the nature of reality, and answering questions through advanced AI could have profound shifts in our philosophical and scientific understanding of the cosmos and our place within it.

Mining Decades of Space Mission Data for Discovery

Challenge: For over seventy years, NASA's telescopes, orbiters, landers, and satellites have returned more data about our planet and the cosmos than any institution in history. Only a fraction has been truly examined. These holdings now exceed a scale and complexity that traditional computational analysis methods cannot fully exploit; scientists have found planets, transient events, and physical phenomena in data previously thought fully analyzed. By processing and integrating more than 150 petabytes of heterogeneous data, scientists will connect observations, simulations, and models across disciplines, time scales, and physical regimes in ways that accelerate discovery.

AI Solution: Recent advancements in artificial intelligence, including agentic and generative approaches, physics-informed AI, multimodal AI, specialized AI models, and scientific AI workflows present an opportunity to accelerate analysis and discovery across NASA's research activities and science mission data. These tools will fuse observations, experimental data, simulations, and models from different instruments, missions, and scientific and physical domains, identify patterns and relationships across heterogeneous data sets, and improve prediction, interpretation, and hypothesis generation, particularly in areas such as space weather prediction, earth observation, and astrophysics.

Justification: NASA is uniquely positioned to contribute more than 150 petabytes of aeronautics research and science data, mission-driven research problems, and deep experience in data processing, data management, and scientific and engineering collaboration across aeronautics, astrophysics, heliophysics, planetary science, space weather research, Earth science, and biological sciences. The agency also brings fundamental expertise in developing foundation models based on scientific and engineering data. DOE is uniquely positioned to contribute complementary strengths in scientific data, high-performance computing, specialized AI models, scientific AI workflows, and methods emerging from existing DOE challenge areas. Together, these complementary assets can support AI-enabled scientific capabilities for integrating observations, simulations, and models to advance analysis, prediction, and discovery across NASA's research and science mission datasets.

National Impact: Turning America's mission archives into engines of discovery multiplies the return on every dollar the United States has ever spent in space. AI-enabled workflows which accelerate scientific and engineering discovery will improve the nation's ability to understand Earth and space systems and expand the value of one of the Federal government's most important science and engineering data resources. The resulting advances in AI-enabled scientific analysis will also support new approaches to prediction, modeling, and discovery across other data-intensive research domains.

Protecting the Nation from Emerging Threats

Early Detection and Attribution of Biological Threats

Challenge: Unlocking the full promise of biotechnology requires building and sustaining the technological means to identify and combat emerging biological threats, whether natural, accidental, or deliberate, across every stage: (i) early detection and characterization of enhanced and novel biological threats, including those that may not resemble known pathogens, (ii) synthesis screening tools robust enough to disrupt materials access at the point of acquisition, and (iii) the ability to rapidly and accurately discern the origin of a biological incident.

AI Solution: AI will fuse multi-omic, metagenomic, clinical, environmental, and open-source signals to detect anomalous biological signatures, characterize novel behavior from sparse data, accelerate countermeasure design, and sharpen attribution. This will enable new capabilities, including AI-guided automated sequencing of environmental samples to capture evolving biological threats, metagenomic next-generation sequencing and surveillance to flag unknown threats far faster and more cost-effectively than traditional methods, and robust, rapid screening for sequences of concern that safely broadens access to transformative scientific tools.

Justification: No Nation can match America's ability to build safe, secure scientific pipelines. The Department of Health and Human Services brings unique data and expertise in emerging epidemiological threats and the Centers for Disease Control and Prevention surveillance and biothreat radar initiatives, the Department of Energy's national laboratories contribute threat characterization, bioinformatics, and secure computing, alongside the National Nuclear Security Administration's experience embedding AI in extremely high-consequence environments; the U.S. Department of Agriculture guards American food and agricultural supply; the U.S. Department of Commerce's National Institute of Standards and Technology defines the methodology for verifiable synthesis screening; the Department of War and the Department of Homeland Security anchor threat detection, characterization, and response; and the U.S. National Science Foundation conducts foundational research in the evolution and ecology of infectious diseases.

National Impact: A predictive, verifiable, AI-enabled defense shrinks detection, response, and countermeasures timelines while ensuring superior capability to determine attribution. These capabilities protect Americans by deterring adversaries and shielding the bioeconomy from misuse.

Accelerating Design of Weapon Components and Systems

Challenge: Designing novel weapon components and systems using traditional, human-intensive methods is slow and costly, resulting in long timelines before new weapon systems reach national security missions and the American warfighter. The United States possesses exceptional modeling and simulation capabilities that could enable rapid virtual design, iteration, testing, and certification. In particular, large metal castings and forgings remain a key bottleneck.

AI Solution: The Department of Energy and the Department of War will develop, evaluate, and deploy highly efficient AI models and agentic workflows to rapidly decrease the timelines associated with the design of conventional and nuclear weapon components and full systems, including large metal castings and forgings. These AI workflows will automate or significantly streamline time-consuming steps associated with the design, simulation, testing, and certification of complex component and system designs; for example, translating requirements into parameterized simulation setups, generating and adapting meshes, designing high value-of-information tests and experiments, and triaging results to direct expert attention to the most important data. These workflows will be coordinated by an orchestration layer that enables component designers, physicists, and engineers to monitor and steer the process, integrating expert knowledge and feedback, ensuring accuracy, and providing traceability and interpretability for design choices, tradeoffs, and expert decisions.

Justification: The Department of War brings key data assets, model validation capabilities, and decades of validated data, while Department of Energy and NNSA contributes highly validated modeling and simulation tools, high performance computing, and physics-based machine learning expertise to drive each component of a design workflow. Design cycles for weapon components and systems today span many years, limiting the rate at which novel capabilities reach the theater and the warfighter. Given adversaries' clear intent to accelerate their own weapon development, the United States cannot risk falling behind.

National Impact: AI-accelerated design and certifications workflows will compress weapon component and system development from years to months, delivering conventional and nuclear capabilities much faster while preserving the rigor and validation standards essential to national security. By extracting greater capability from existing modeling, simulation, and test investments, the United States will sustain a decisive advantage in the pace of weapons innovation.

Accelerating Materials Discovery, Production, and Qualification for Strategic Deterrence

Challenge: The nuclear security enterprise faces significant hurdles in designing, manufacturing, and qualifying mission-critical nuclear and non-nuclear materials. This challenge will develop a digital, AI-accelerated workflow that connects the entire lifecycle of critical materials, from initial formulation to final production. This approach will incorporate real-time anomaly detection and in-process corrections to significantly reduce the need for extensive qualification testing and improve the safety and reliability of these critical materials. It will also expedite new technology development, enabling production acceleration opportunities to meet evolving military requirements.

AI Solution: This initiative will link material design, automated testing, and qualification into a single, data-driven process, using physics-based simulations on high-performance computers to screen and optimize material candidates, directing robotic labs and in-line sensors to accelerate certification processes, and feeding results back to production and iteratively refine hypotheses and inform new experiments. This workflow will invent and test new plutonium purification methods and deliver only the best options to scientists for review, compressing a months-long development process into just days.

Justification: The National Nuclear Security Administration (NNSA) uniquely combines supercomputing power, specialized test facilities, and decades of mission data. By uniting these assets in an AI-managed pipeline, we can shrink design-to-qualification times, improve manufacturing reliability, and build a stronger domestic supply of critical materials without sacrificing safety or oversight.

National Impact: Accelerating material development and certification for new materials and processes will ensure the rapid delivery of strategic components for deterrence, reduce reliance on fragile supply chains while lowering overall program costs, and provide a scalable model for safer, more efficient manufacturing in civilian sectors such as energy, chemicals, and aerospace.

Accelerating Nuclear Threat Assessment, Preparedness, and Response

Challenge: Rapid and effective response to nuclear and radiological events demands detailed analysis of vast and varied data, from radiation detectors and environmental sensors to intelligence reports and simulation outputs. Today, the NNSA Nuclear Emergency Support Teams (NEST) relies on manual review and static artificial intelligence (AI) models that cannot sufficiently adapt as new data streams in, creating delays in detection, assessment, and response. This leaves decision-makers without real-time situational awareness or clear risk metrics during threat assessment and event response.

AI Solution: The solution will deploy a continuously learning, multimodal AI fusion system that integrates radiation and environmental sensors, simulations, and intelligence reporting to deliver real-time decision support with scenario modeling and uncertainty-aware risk metrics on crisis timelines for nuclear threats. The system will include four capabilities to make it operational without sacrificing reliability: (i) cross-cutting data governance for secure, standardized data pipelines; (ii) AI-enhanced decision support for adaptive threat-mapping tools and operator dashboards; (iii) scalable AI agents for semi-autonomous drones and robotics to survey, sample, and report from contested areas; and (iv) real-time risk assessment models to process large datasets into automated visualizations and risk scores for nuclear sites.

Justification: NNSA brings unique nuclear science expertise, secure facilities, and high-performance computing resources, and it embeds physics-informed models for transparent, auditable AI in mission-critical environments. Deploying a continuously learning fusion system will replace brittle, hand-tuned workflows with a single, scalable solution that reduces development time and cost while leveraging existing archives and platforms for rapid deployment and scaling.

National Impact: The initiative will shrink detection-to-response times from days to hours, enhance public safety and national security, and improve decision confidence while reducing false alarms through clear, quantified risk assessments. It strengthens deterrence by embedding AI into critical decision loops and supporting interagency coordination, delivers cost-efficient capabilities that can be adapted by civilian emergency responders and international partners. Use of this data fusion system in training scenarios will build NNSA's capacity to identify signal through the noise during the most critical incidents.

Strengthening Deterrence Through Attribution of Nuclear Signatures

Challenge: Effective deterrence depends on credible accountability. Every nuclear material has a signature, and through a combination of radiation measurements and material characterization, the provenance of nuclear materials and detonated nuclear device designs can be determined. Attributing nuclear materials either outside of controlled environments or following a nuclear detonation of unknown origin to their source through forensic attribution will enable the credible commitment of American retaliation. This effort will dramatically improve the speed and accuracy of nuclear forensic assessments by leveraging AI-enabled workflows, data integration, and physics-based machine learning, thereby enhancing United States deterrence against potential nuclear threats.

AI Solution: The solution will further develop and use AI tools to rapidly characterize samples of special nuclear material and post-detonation nuclear debris, infer likely process history, and support device and material reconstruction. The Rapid Quantification of Nuclear Forensic Morphological Signatures focus area will use AI models to quickly analyze morphological features of nuclear materials, increase the speed and accuracy of signature interpretation, and improve understanding of material processing histories for effective nuclear forensics. The In-field Measurements of Nuclear Detonation Debris focus area will adapt AI tools for rapid quantification of nuclear debris in post-detonation scenarios, enabling real-time field analysis that significantly reduces debris diagnostic timelines. The Advances in Post-Detonation Device Reconstruction Modeling focus area will leverage AI, advanced simulations, and intelligent data interpretation to accelerate device reconstruction following a nuclear detonation and provide timely, actionable insights to decision-makers even in the early stages of an incident.

Justification: The project capitalizes on NNSA's unique resources and expertise to enhance the speed and accuracy of nuclear threat attribution. It builds on NNSA's combination of nuclear weapons design history, state-of-the-art laboratory capabilities, and subject matter experts; minimizes current bottlenecks in sample processing and reporting for more efficient use of existing resources; directly supports the deterrence of nuclear threats by enabling fast, credible attribution; and leverages existing infrastructure investment for rapid implementation without compromising quality.

National Impact: This initiative will significantly enhance national security and emergency response by accelerating threat assessment processes and shrinking the timeline from material collection to attribution, thereby accelerating policy and response decisions. It reinforces deterrence by showing adversaries that misuse of nuclear materials will be attributed swiftly, leading to decisive American retribution; improves the ability to quickly assess nuclear incidents and preserve public safety through real-time analysis; and creates AI-based forensic methods that can be adapted to other critical security and industrial domains.

Detecting, Locating, Identifying, and Characterizing Proliferation Threats

Challenge: It is central to America's security interest to be able to detect, locate, identify, characterize, and respond to or mitigate nuclear weapons development by our adversaries. This challenge is exacerbated by the surge in demand for civilian nuclear power, which will lead to many conflicting signals, making it harder to distinguish between civilian and military uses of nuclear power. AI-enabled tools can analyze large, complex data streams in real time, identifying anomalies that indicate potential proliferation activities and providing decision makers with faster, more actionable information.

AI Solution: Develop multimodal foundation models and analytic agents that fuse novel data types from research and development testbeds with data from across the U.S. government and commercial sources (e.g., intelligence information, satellite imagery, environmental sensing, and open-source data) to detect subtle proliferation-relevant anomalies in near-real time and to generate analyst-ready evidence packages with confidence scoring. To accelerate progress, we must build secure multi-network data sharing and data governance; domain-specific data ontologies and knowledge graphs for the nuclear fuel cycle; multimodal model and graph-based training and validation capabilities for new data types; and unique human-AI teaming interfaces tailored to nonproliferation analysis workflows across classified and unclassified environments.

Justification: The project leverages NNSA's unique capabilities to address the challenges of AI development in the nonproliferation domain. NNSA has the nuclear fuel cycle domain expertise required to aggregate global nonproliferation-relevant data sources. Manual analysis cannot keep pace with the volume and variety of modern data streams, whereas automated, trustworthy AI shortens detection timelines, increases efficacy of detection activities, and improves use of technical subject matter experts. This effort will leverage existing and planned NNSA platforms and partnerships for rapid transition and iteration.

National Impact: The outcomes of this initiative will significantly enhance U.S. national security, deterrence, and global nonproliferation efforts by accelerating threat detection and decision cycles. It will provide policymakers with timely, credible intelligence to guide diplomatic and enforcement actions, enhance global nonproliferation cooperation by sharing standardized, auditable insights, enhance the perceived and real value of cooperation with America on civilian nuclear activities, and establish a model for AI-driven monitoring in other critical security domains.

Accelerating Experimental, Design, Production, and Nuclear Deterrence Outcomes

Challenge: Deterring adversaries in a rapidly evolving threat landscape requires transforming experimental learning into fielded capabilities with greater speed, confidence, and agility. Today, high-consequence R&D campaigns, weapon design, qualification, production, and stockpile operations are slowed by limited-throughput experimental facilities, document-heavy workflows, fragmented data environments, and complex multi-site dependencies. These constraints delay risk-informed decisions and lengthen the path from novel idea to delivered deterrent capability.

AI Solution: Deliver a broad range of secure, human-supervised AI models, workflows, and tools for accelerating nuclear deterrence R&D campaigns, and connect experimental insights to downstream lifecycle decisions. Secure AI-enabled workflows would improve high-consequence experimental campaign planning, scheduling, execution support, diagnostic integration, modeling and simulation feedback, and data provenance so each experiment produces maximum mission-relevant knowledge. Targeted AI agents and decision-support tools will translate historical and acquired nuclear-stockpile relevant information into component and system design tradeoffs, producibility assessments, component qualification planning, manufacturing readiness, logistics and capacity planning, and stockpile evaluations, while keeping weapon professionals responsible for high-consequence technical judgment.

Justification: NNSA is uniquely positioned to address this challenge because it combines high-consequence experimental facilities, test sites, supercomputing, advanced simulation, secure production capabilities, and unmatched nuclear expertise. Its strategic advantage is not only the hardware it produces, but also the engineers, scientists, technicians, data, processes, and mission authority required to maintain a safe, secure, and effective nuclear deterrent.

National Impact: This initiative would create a more responsive nuclear weapons enterprise by compressing R&D learning cycles, improving the use of scarce experimental and research opportunities, increasing confidence in design and production decisions, and accelerating the application of advanced capabilities to national security missions. By transforming experimental campaign knowledge into better deterrence outcomes, NNSA can modernize at the pace of evolving threats and shift the strategic calculus of peer adversaries.

Software Understanding for National Security

Challenge: The United States faces extensive, unbounded risk to its national security and critical infrastructure (NS&CI) missions because of widespread dependence on largely inscrutable third-party and legacy software whose behavior cannot be verified. Assessing and mitigating this risk requires "software understanding," the ability to construct and assess software-controlled systems to verify their functionality, safety, and security across all conditions. The ability to create software greatly outstrips our ability to understand it, and current methods such as dynamic testing, digital signatures, software bills of materials, and attestation provide insufficient evidence for confidence in mission critical systems. The consequences are concrete and severe, from the Therac-25 radiation deaths to the SolarWinds and Log4j compromises to the PRC's Volt Typhoon prepositioning in U.S. critical infrastructure. Without a coordinated national capability, the nation accepts unknown and unbounded mission risk in the very systems on which deterrence, public safety, and economic prosperity depend.

AI Solution: Software understanding today is a largely manual, artisanal practice, with experts reverse-engineering systems by hand. Subject-matter experts estimate that a mature software understanding ecosystem would improve capabilities by 10x-100x but take decades to build using traditional, manual software engineering approaches. AI-enabled tools will compress that timeline into years and is already transforming the field into a science. By coupling agentic AI's inductive reasoning with rigorous, mathematically-grounded deductive tools, AI agents will orchestrate end-to-end analysis campaigns, autonomously decomposing high-level mission questions into focused sub-analyses, selecting and synthesizing analysis tools, and composing technical evidence packages. This ecosystem will revolutionize third-party and supply chain software assurance, enhance reverse engineering capabilities to recover meaning from stripped firmware, and enable entirely new analytical capabilities and fields of inquiry in formal methods, computer science, risk sciences, and cyber-physical modeling.

Justification: Verifying the software on which NS&CI systems run is core to the Department of Homeland Security's mission. DHS has led the national effort in software understanding, building the technical roadmap that defines the field and working directly with the analysts who confront inscrutable software daily. The Department of Energy's high performance computing, experience in high consequence environments, and coordination of the National Laboratories will enable a shared, federated ecosystem, unlocking new mission possibilities through interoperable software analysis capabilities. DHS' secure capabilities enable the use of unique, high-consequence datasets not otherwise accessible to commercially available models. The Department of War brings mission insight into how unclassified proxies align with its mission critical systems, as well as an initial path-finder activity exploring how agentic neuro-symbolic hybrid systems can reason about such software in energy-efficient ways.

National Impact: Accelerating software understanding will enhance cybersecurity of American critical infrastructure, speed the development and qualification of software systems for secure and high-consequence environments, and promote higher-quality software development. The economic stakes are immense, with the cost of poor software quality in the United States estimated to be at least $2.41 trillion in 2022. For national security, software understanding hardens critical infrastructure against state-sponsored activity and underpins every U.S. deterrent capability, from conventional and nuclear forces to economic tariffs and sanctions.

Ensuring American Space Superiority

Challenge: Superiority in space begins with the ability to see, predict, and safely maneuver within a domain that is growing more crowded, more contested, and more dynamic by the year. As American operations extend from low Earth orbit and out into cislunar space, the United States must develop, field, and sustain increasingly complex space capabilities on timelines that push beyond what traditional engineering and mission operations methods were designed to support. Across spacecraft, surface systems, communications, logistics, environmental forecasting, autonomous operations, and supporting infrastructure, NASA must be able to design, simulate, test, qualify, integrate, and operate tightly coupled systems at a speed, scale, and level of concurrency that was previously impractical. AI-enabled engineering capabilities will compress the path from concept to trusted operational readiness while preserving safety, performance, and mission assurance.

AI Solution: Recent advancements in artificial intelligence, including agentic and generative approaches, specialized AI models, and scientific AI workflows, present an opportunity to accelerate the development of complex space capabilities. These tools could help navigate high-dimensional design spaces, model tightly coupled system behavior, and uncover new approaches to spaceflight simulation, testing, qualification, mission design, and operations across NASA missions, including a Moon base. Tools will be used to unlock exploration deeper into space using more efficient propulsion technology, design and operation of processors in extreme environments, and faster calculation and analysis of mission-critical flight information.

Justification: NASA contributes science, technology, and mission data, operational experience, and high-consequence engineering problems associated with returning humans to the Moon, establishing an enduring presence, and supporting a broader set of scientific and technical objectives. DOE is uniquely positioned to contribute scientific data, high-performance computing, specialized AI models, scientific AI workflows, and methods emerging from existing DOE challenge areas, including materials science and other mission-relevant domains.

National Impact: The nation that can best see, predict, operate within, and sustain systems within the space environment will achieve an unmatched freedom of action, from protecting the satellites that anchor the American economy to safeguarding the astronauts and infrastructure of a permanent return to the Moon to unleashing the space economy.

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