U.S. Department of Energy

Secretary of Energy Advisory Board Report of the Task Force on Biomedical Sciences

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Acronyms

3D	Three-dimensional
ARPA-E	Advanced Research Projects Agency–Energy
BRAIN®	Brain Research through Advancing Innovative Technologies
CASL	Consortium for Advanced Simulation of Light Weight Reactors
Cryo-EM	Cryo-electron Microscopy
CT	Computerized Tomography
DOD	Department of Defense
DOE	U.S. Department of Energy
FDA	Food and Drug Administration
FY	Fiscal Year
HGP	Human Genome Project
MRI	Magnetic Resonance Imaging
NCBI	National Center for Biotechnology Information
NCI	National Cancer Institute
NIH	National Institutes of Health
OMB	Office of Management and Budget
ORNL	Oak Ridge National Laboratory
PET	Positron Emission Tomography
SEAB	Secretary of Energy Advisory Board
SPECT	Single Photon Emission Computed Tomography

Executive Summary

Progress in the biomedical sciences has crucial implications for the Nation's health, security, and competitiveness. Advances in biomedicine depend increasingly upon integrating many other disciplines—most importantly, the physical and data sciences and engineering—with the biological sciences. Unfortunately, the scientific responsibilities of the various Federal agencies are imperfectly aligned with that multidisciplinary need. Novel biomedical technologies could be developed far more efficiently and strategically with enhanced interagency cooperation. The Department of Energy's (DOE's) mission-driven basic research capabilities make it an especially promising partner for increased collaboration with the National Institutes of Health (NIH), the Nation's leading agency for biomedical research; conversely, NIH is well-positioned to expand its relationships with DOE. Particular DOE capabilities of interest include instrumentation, materials, modeling and simulation, and data science, which will find application in many areas of biomedical research, including cancer, neurosciences, microbiology, and cell biology; the analysis of massive heterogeneous clinical and genetic data; radiology and radiobiology; and biodefense.

To capitalize on these opportunities we recommend that the two agencies work together more closely and in more strategic ways to (a) define joint research programs in the most fertile areas of biomedical research and applicable technologies; (b) create organizational and funding mechanisms that bring diverse researchers together and cross-train young people; (c) secure funding for one or more joint research units and/or user facilities; (d) better inform the Office of Management and Budget (OMB), Congress, and the public about the importance of, and potential for, enhanced DOE-NIH collaboration.

Introduction

On November 21, 2015, Secretary of Energy Ernest J. Moniz requested that the Secretary of Energy Advisory Board (SEAB) constitute a task force to evaluate the prospects for increased collaboration between DOE researchers and biomedical scientists supported by other agencies, especially NIH. In particular, the Secretary asked that the Task Force identify "new areas of research by DOE investigators that could advance the pace of progress in biomedical sciences" and "new mechanisms for conducting research in coordination with scientists from government laboratories…universities, academic medical centers, and industry." He also enjoined the Task Force from addressing "funding arrangements to support this initiative." The Secretary's request (the full memorandum is reproduced in Appendix A) was endorsed by Francis S. Collins, Director of the National Institutes of Health, who asked Dr. Roderick Pettigrew, Director of the National Institute of Biomedical Imaging and Bioengineering, to serve as a liaison between NIH and the Task Force.

In response to the Secretary's request, SEAB assembled the Task Force on Biomedical Sciences, composed of four SEAB members and five other prominent scientists who were knowledgeable about multiple relevant subjects, including those listed in the Secretary's memo as possible collaborative areas. Biographical sketches of the Task Force members are provided in Appendix B.

Beginning in January 2016, members of the Task Force met by conference calls and at two workshops (March 10–11, 2016, at New York University's Center for Urban Studies and Progress in Brooklyn, New York, and July 18–19, 2016, at Lawrence Berkeley National Laboratory in Berkeley, California). In addition to the Task Force members and DOE support staff, other workshop participants included invited speakers and DOE and NIH program administrators. (The agendas and lists of participants are contained in Appendix C). Among the topics discussed at the workshops were DOE and NIH capabilities, potential areas for collaborative research, and possible research mechanisms. Following the second workshop, the Task Force developed this draft report, which is being submitted to SEAB for review and approval at its meeting on September 21, 2016, and will be subsequently submitted to the Secretary.

1 The Rationale for Stronger Interactions between DOE and NIH

The case for seeking new areas and mechanisms for collaboration between DOE-supported and NIH-supported researchers is based on several precepts, each of which is detailed in the following subsections:

- The importance of the biomedical sciences
- The confluence of diverse technologies and methodologies in the study of medicine and biology
- The imperfect alignment between national scientific goals and the domains of Federal science agencies
- The unique capabilities of DOE's national laboratories and their history of productive interactions with life science agencies, especially NIH
- The administrative flexibilities and goals of NIH.

Based on the history and operations of NIH and DOE, the Task Force became convinced during the course of these two workshops that the Nation's biomedical research efforts would be substantially augmented by closer communication and expanded collaboration between the two agencies and the researchers they support. The Task Force recognizes—and heard corroborating evidence during its workshops—that significant interactions already occur; some DOE laboratories have long-standing commitments to biomedical research topics, and some U.S. investigators receive support from multiple agencies, including DOE and NIH. The Task Force also came to appreciate the cultural and organizational differences between the two agencies that might impede more extensive collaboration. Nevertheless, we, the Task Force, are convinced that a collaborative effort to define and pursue selected scientific opportunities and to develop mechanisms that foster such collaborative work would accelerate progress in biomedical sciences.

1.1 Biomedical Sciences Are Vital to the Nation

The Federal Government's commitment to medical research and to a healthier nation is demonstrated tangibly by the $31 billion NIH budget, supplemented by biomedical research spending by other agencies; while DOE supports no biomedical sciences per se, it does

annually fund some $300 million of systems biology research. That level of public spending, unequalled elsewhere in the world, reflects the following:

- The importance that our Nation places on science that promises to improve the health of its citizens
- The recognition that U.S. leadership in the life sciences, especially the medical sciences, has promoted the prestige and economic success of the United States over many years
- The advocacy that often drives spending on specific diseases
- The concern about biological threats, both natural and anthropogenic, that pose risks to the Nation.

The competitive advantages that the United States enjoys from its investment in biomedical sciences result from prize-winning discoveries, immigration of talented individuals to our scientific programs and industries, and development of economically successful commercial products such as drugs and technologies. Fostering the growth and productivity of biomedical research through the work of multiple agencies, especially agencies working together effectively and efficiently, is obviously a worthy objective.

1.2 Biomedical Research Depends on Many Disciplines

Although medical progress is widely recognized as dependent on both fundamental research in biology and on clinical research (involving work with patients and human samples), history also documents the deep contributions made to medical sciences by physics (including radiology methods such as magnetic resonance imaging (MRI); computerized tomography (CT) and positron emission tomography (PET); crystallography; electrocardiography; and electroencephalography) by chemistry (including drug development and metabolic studies); and by engineering (the design of a wide variety of instruments and devices). More recently, computational and data sciences have become central to the creation, storage, and analysis of large data sets produced by new methods in genomics and proteomics, as well as by the traditional methods of clinical research, such as medical imaging. These information sciences are also affecting the planning and delivery of health care as providers increasingly depend on electronic health records, access to computerized clinical data, and medical systems for continuous learning, all of which are related to the President's Precision Medicine Initiative. At the same time, new technologies—nanotechnology, materials sciences, sensors, microfabrication, and microfluidics—have become essential features of the medical research landscape. The bulk of the Federal Government's programs and expertise in these rapidly evolving technologies does not reside in NIH.

1.3 U.S. Scientific Responsibilities and Federal Agencies Are Imperfectly Aligned

The programs of individual Federal agencies, including those with significant investments in science and technology, are directed by the interests and organization of the Executive and Legislative Branches; consideration of the substance of these programs is only one factor among many. This process has its benefits, including the distribution of important activities among components of the government that take different approaches to difficult tasks and will have variable success in the budget process. But, even the most casual inventory of agency

activities shows redundancies and, more intriguingly, opportunities for productive synergies in the governance of the Nation's science and technology programs.

The responsibility for monitoring these diverse efforts falls to the Office of Science and Technology Policy and its affiliated government-wide National Science and Technology Committees. But, individual agencies and departments are also expected to survey the research horizon for significant redundancies and potential synergies. Because biomedical research and its relevant technologies are broadly distributed among many Federal elements—most obviously NIH, but also DOE, the National Science Foundation, the Department of Defense (DOD), the Centers for Disease Control, and others—those organizations and the organizations that determine their programs—such as OMB and congressional committees—should be vigilant for opportunities to coordinate, if not collaborate, thereby acquiring useful scientific knowledge more efficiently and rapidly.

1.4 Novel Biomedical Technologies Could Be Developed More Efficiently and Strategically

The Task Force workshops demonstrated the rapid progress of many technologies that are newly important to biomedical research, including informatics, nanotechnology, materials research, and simulation.[a] Much of the fundamental technical work is being supported or conducted by non-NIH agencies (including DOE laboratories), often without recognition of the specific biomedical applications that might be envisioned. Conversely, NIH can and does support work in many of these areas (see section 1.6 below), but its efforts are necessarily limited by the perception that such technology development is not the agency's primary missions. As a result, the NIH programs do not encompass all or even a majority of the most promising technologies.

Although the NIH-funded research system offers some rewards for developing new technologies, there is no reward mechanism for making the technology robust and usable by others, so that the research group that invented a new method is likely to move on to the next problem. Students and engineers in the academic sector will be less inclined to advance such technologies beyond proof-of-principle as there is no glory or academic credit for making the technology practical and, in many cases, there isn't sufficient commercial incentive to strengthen new methods. Such "orphan technologies" may never get adopted broadly, and their potential impact will remain unrealized. DOE, on the other hand, has a tradition and a reward system for improving technologies, making them robust, and disseminating them to a larger community of users. That could play an important role in magnifying the impact of biomedical NIH-funded research.

There are other persuasive reasons to encourage collaboration in biomedicine among the U.S. scientific communities that receive support from different agencies. These reasons include the importance of the tasks, the need to conserve resources, and competition from a unified Europe and rising Asian nations whose biomedical programs are generally more mission-oriented. The

[a] These topics and others are individually addressed in section 2.

Task Force concludes that it is imperative to seek ways to better leverage expertise that currently might be focused on unrelated goals in the two organizations.

Such leveraging has occurred in the past, but in ways that have generally been serendipitous and episodic. Now, with a greater sensitivity to the importance of multi-disciplinary research—and with national commitments to accelerate progress in cancer and neurological sciences in the context of more broadly advancing biomedical sciences—it is time to become more deliberate in connecting biomedical sciences with promising areas of relevant technology. From the perspective of this Task Force, that means expediting greater collaboration between agencies such as DOE and NIH that work in closely related domains.

1.5 DOE Is an Especially Promising Partner for Collaboration with NIH

The breadth and quality of science supported by DOE and its history of accomplishments make it a prime candidate for expanded interaction with NIH. DOE is the largest Federal funder of physical sciences, particularly renowned for its mandated stewardship of basic research in high-energy and nuclear physics, as well as its mission-driven work on nuclear security, energy technologies, and environmental cleanup. To pursue those missions, DOE has combined the talents of natural scientists (including physicists and chemists), engineers, and computer scientists to develop extraordinary capabilities in materials research, instrumentation, modeling, and simulation.

DOE capabilities have long been leveraged by other Federal agencies, particularly the national security community (the Departments of Defense and Homeland Security, as well as the Intelligence Community). Those capabilities reside in the national laboratories and university communities that DOE supports, with funding for basic science and applied energy research amounting to some $12 billion in fiscal year (FY) 2016. DOE's culture is characterized by its traditional commitment to important national missions and its ability to form diverse, technical teams of scientists and engineers to pursue those missions with minimal delay. Indeed, DOE invented and continues to lead in "big" or "team" science. Today, it operates through a number of mechanisms, including the following:

- **National laboratories:**[1] DOE supports the operation of 17 national laboratories, 16 of which are government-owned, contractor-operated organizations.[b] Most of these are multi-purpose labs that host diverse teams of researchers focused on important national problems. A major role of these labs is the operation of facilities that serve large scientific communities.
- **User facilities:**[2] User facilities provide state-of-the-art scientific capabilities that would be too costly or complex for individual scientists or even individual universities to construct and operate. They range from particle and nuclear accelerators, powerful lasers, light sources, and neutron sources to high-performance computers and molecular-synthesis and -characterization facilities. Access to these facilities is based upon scientific merit, and users are not charged for non-proprietary projects.[3]
- **Energy Innovation Hubs:**[4] The Hubs advance promising areas of energy science and engineering from the earliest stages of research to the point of commercialization—

[b] Only the National Energy Technology Laboratory is government-owned, government operated.

technologies can move from the Hubs to the private sector by bringing together leading scientists to collaborate on critical energy challenges.

- **Energy Frontier Research Centers:**[5] These integrated, multi-investigator centers involve partnerships among universities, national laboratories, nonprofit organizations, and for-profit firms that conduct fundamental research focusing on one or more "grand challenges." The centers are intended to pursue "basic research needs" identified in major strategic planning efforts by the scientific community.
- **ARPA-E:**[6] The Advanced Research Projects Agency-Energy (ARPA-E) advances high-potential, high-impact energy technologies that are too early for private-sector investment. ARPA-E programs focus on developing entirely new ways to generate, store, and use energy.

Although most DOE missions are directed to goals outside the life sciences arena, some of the materials, tools, and methods that DOE generates are germane to biomedical science. For example, more than 30 percent of the users of DOE's synchrotron light sources are in the life sciences, and some 20 percent of users are NIH-supported investigators. Moreover, the Department also conducts a large amount of research in the life sciences, largely with non-human applications in mind. For example, basic biological methods similar to those of biomedicine are used to study plants and microbial organisms in pursuit of biofuels, bioremediation, and carbon cycle research.

DOE has also had direct impacts on biomedical sciences in selected areas. These include a major contribution to the Human Genome Project (HGP), during both the initiation of the project and the production of its finished product; provision of beam lines from DOE's national light sources for the conduct of structural studies of biologically important molecules; improvements of radiation therapies for cancer; and the development of an artificial retina. But these instances have generally been episodic and opportunistic, sometimes depending on the transient personnel leading the agency (or a partner agency such as NIH), rather than the result of deliberate efforts to exploit standing mechanisms that foster such collaborative, interdisciplinary work.

With increasing recognition of the utility of DOE-supported technologies in biomedical research and the announcements of national goals for biomedicine, this is an appropriate time to propose the kinds of mechanisms that would make synergistic interactions between the agencies more frequent, less complicated, and more productive. Furthermore, the Task Force is convinced that the benefits of greater collaboration would extend in both directions. Most obviously, NIH and the biomedical sciences would gain greater access to, and familiarity with, relevant technologies, but DOE researchers would also be helped by activities that focus technology development on specific novel questions. Indeed, there is a long tradition in the national laboratories of using unclassified problems such as astrophysics or climate modeling as venues to attract new talent and to develop methods relevant to classified work. In the present case, some problems in biomedicine (interpretation of cancer genotypes or mapping of neurological circuitry) could sharpen the skills of computational scientists in ways that might be applicable to problems in national security.

1.6 NIH Is Well-Positioned to Expand Its Relationships with DOE

NIH is a confederation of 27 Institutes and Centers, most of which receive direct appropriations, develop independent research programs, issue their own grants, and work within defined mission statements to pursue the purpose for which Congress created them. This structure might be a challenge for the coordination of NIH-wide efforts by the NIH director, but it offers a highly flexible system for making grants and issuing contracts with many kinds of institutions, including other Federal agencies. That flexibility is further enhanced by the multiple mechanisms available to support NIH research activities. Just more than 10 percent of the NIH budget is devoted to the support of intramural research, conducted by government scientists, mostly on the NIH campus in Bethesda, Maryland. The preponderance of the remaining budget supports grants and contracts for research and training at hundreds of institutions (universities, academic health centers, research institutes, colleges, and small industries) situated in all states and many foreign countries. Most of these awards are used for projects conducted by individual investigators and their laboratory groups; but, many are also given to small teams engaged in work on shared topics and sometimes awards are given to much larger teams, as illustrated by the HGP or The Cancer Genome Atlas project. In addition, the National Cancer Institute (NCI) funds the Frederick National Center for Cancer Research, a government-owned, contractor-operated facility in Frederick, Maryland, that resembles DOE's national laboratories. While most of the research funded by NIH can be viewed as biological or medical, the agency also provides significant support for studies in bioengineering (roughly $2.5 billion in FY15), chemistry ($2.8 billion in FY15), computational sciences ($1.5 billion in FY15) and materials research ($0.3 billion in FY15, including nanotechnology).

The variety of research modalities, scientific goals, and personnel at NIH offers many opportunities for collaboration with other agencies at several levels: the NIH Director's Office, individual Institutes or Centers, or specific programs within an Institute that are performed by intramural or extramural investigators. Interactions at these different levels have characterized past collaborations between NIH and DOE; despite the apparent complexity, they offer a diverse menu of components with which to propose and perform collaborative work at the grassroots level, as well as the leadership echelon.

As described briefly in the preceding section, NIH has a history of productive collaborations with DOE. In addition, many extramural NIH-supported scientists have grants or contracts from other Federal agencies, most commonly DOD or the National Science Foundation, but few of these entail the kind of coordinated partnerships between complementary capabilities and interests that can be envisioned for DOE-NIH interactions.

2 Opportunities for Expanded DOE-NIH Collaboration

During the workshops conducted for this report, the Task Force identified several significant opportunities to accelerate progress in biomedical sciences through collaborative activities between DOE and NIH researchers. Some of these are best discussed as relevant technology strengths that reside principally in DOE, while others are best described as biomedical challenges that mainly confront NIH. We consider the first group in this Section 2 and the second in the following Section 3.

2.1 Instrumentation

Modern biomedical research and clinical practice use increasingly sophisticated instrumentation in unusual circumstances—for example, measurements of neural activity in the brain of an awake, behaving animal. One of DOE's strengths is the development of instrumentation for sensitive measurements in exotic circumstances (e.g., deep underground during a nuclear explosion or high in the atmosphere above the North Slope of Alaska). This strength is an obvious opportunity for collaboration with NIH to build more sensitive and capable sensors. For instance, neural activity can now be modulated by the same devices that are used to measure it, adding a dramatic new dimension to this work. The potential for expanded joint efforts in neuroscience would be timely, given the current national Brain Research through Advancing Innovative Technologies (BRAIN)® initiative.

Another area for collaborative work would be the simultaneous analysis of the molecular activity in thousands of individual cells, made possible by recent advances in single-cell RNA sequencing. Systems for sampling single cells from tissue slices in a manner that records their initial three-dimensional (3D) configuration, while subjecting each cell individually to RNA sequencing, would provide an unprecedented window into the inner workings of our organs. That would be very useful in many areas of biomedical research, including cancer research, where it has become increasingly apparent that understanding the 3D cellular architecture of a tumor and its immediate environment plays a fundamental role.

We believe that if DOE-NIH teams assembled to devise more sensitive and multiplexed devices for measurement, perhaps using mechanisms for collaboration discussed later in this report, they could make progress that would not be possible in an individual laboratory. These projects would be akin to those that drove breakthroughs in earlier medical instrumentation, such as MRI, but are adapted now to the new reality of directly interrogating large numbers of single cells, both electrophysiologically and molecularly. The study of many other medical problems—metabolic, musculoskeletal, and cardiovascular diseases, as well as cancers and neurological disorders—would also benefit from new or improved instrumentation created by harnessing the combined abilities of NIH and DOE.

2.2 Data Sciences

Biomedical research and clinical practice already create an abundance of data. The genomic databases are of petabyte size, and imaging data sets are often far larger. Three-dimensional imaging (traditional tomography extended to single cells and whole organisms) will produce enormous amounts of raw data and impressive amounts of analyzed and compressed information. Data from clinical records are less plentiful but are growing, and they present the challenge of being far more heterogeneous; better storage, linkage, and analysis of such records will be critical for anticipated advances in the data-driven practice of medicine. New instrumentation will further enlarge biomedical research data by capturing continuous streams from sensors and imaging instruments and by monitoring more biochemical factors. That trend is driven in part by prodigious manufacturing capability allowing ever-denser sensor arrays. However, it is also driven by the fact that it is often cheaper to make the sensing device as simple as possible, to measure as long and as much as possible, and then to let the

downstream analysis sort out the meaning from the signal. This puts enormous burden on data-processing pipelines causing them to become the primary bottleneck.

Computing technologies that can handle data of such magnitudes and complexity and make them interpretable and appropriately accessible are still being developed. In some cases, sophisticated new machine-learning methods for both medical research and practice are required in conjunction with large-scale parallel computation, well beyond traditional methods or capabilities. These challenges are present in some of DOE's missions, but are also essential to the future of biomedicine.

DOE has impressive capabilities in mathematics (including applications to signal processing and machine learning), scientific software, security, and high-performance computing (both use and management). These have been applied with great success to the classic missions of the Department through high-fidelity modeling and simulation and have also been used to develop powerful new algorithms for assembling complete genomes from individual DNA reads. But, there are opportunities to expand the repertoire with new data-driven problems and techniques, inspired by, or in conjunction with, new kinds of instrumentation. By focusing more on discrete computing, machine learning, and advanced statistical analysis at enormous scale, DOE should be able to create the new technology required for all its missions to move forward. An excellent way to improve and gain acceptance of a new technology is to enable it to address an important problem, and biomedicine is replete with such problems. These provide great opportunities for building upon and broadening the scope of DOE expertise, expanding the frontiers of emerging fields, and simultaneously making progress on NIH's major subjects.

The importance of data management should not be ignored in these considerations. One of the repeated laments we heard from NIH researchers is that the large quantities of data now being generated in their fields are not shared, harmonized, coordinated, curated, or consistently interpreted to maximize utility. The ultimate experimental subjects of medicine—human patients—cannot all be sent to a centralized facility for data acquisition. To address this, especially within NIH's traditional mode of funding individual investigators, measurement devices should be made increasingly smaller and more portable, so that they can be used in hundreds or thousands of different settings. Ideally, all devices would be identical or inter-operable and linked online so that their output can be centrally aggregated for processing.

However, patient privacy considerations, which can vary by jurisdiction, often make such centralization of data impossible. A variety of geographically distributed approaches will be needed, wherein the computer code that is performing analysis and other tasks is moved to where the data reside, rather than the data moving to where the code resides. The availability and tuning of high-speed networking and strong approaches to data security and privacy will be needed to make this possible. Beyond the security and privacy issues, the development of more efficient access, sharing, and analysis of biomedical data sets will be increasingly essential as the amounts of data increase by orders of magnitude. DOE has great technical strengths and long experience in these areas (for example, in the high-energy physics data networks) and could contribute to the development of effective mechanisms for distributed data processing, analysis, curation, and result-sharing—mechanisms that will be critical both for research and more sophisticated modalities of individualized medical care.

While individual patient data may need to remain private, the aggregated results of statistical analysis should be automatically shared with the broadest possible community of experts. This is another area where collaboration between DOE and NIH might be fruitful, and also has broad applications in other sectors of society. The complexities of de-identification and re-identification, central when combining clinical and genetic data, are core to modern privacy research across the board.

2.3 DNA Technologies

DOE has continued to advance basic and applied aspects of DNA sequencing. As reading DNA becomes easier, there are more needs for sustained expertise in sequence analysis and annotation. For example, such capacities have proved essential for exploring, characterizing, and harnessing microbes for both health and energy applications (e.g., microbial conversion of biomass to fuels or understanding the role of soil microbes in the global carbon cycle).

More recently, significant reductions in the cost of DNA synthesis have captured the attention of DOE and NIH researchers. Companies now offer synthesis and assembly of up to 10,000 base pairs of DNA fragments at prices approaching $0.01 per base pair and turnaround times of about 4 weeks. So enabled, several research groups are now performing projects aimed to synthesize full microbial genomes. However, securing bulk orders (hundreds of millions of base pairs or more) from a few groups now drives development of leading-edge commercial DNA synthesis platforms. In contrast, most researchers need only a few specific sequences at a time, but they need them quickly (i.e., within a day), so they can rapidly iterate a process of discovery and design; imagine how limited computer science would remain if it took 4 weeks to compile and run a revised program.

DOE and NIH together have two specific opportunities to strengthen the commercial DNA synthesis sector while broadly enabling public research. First, they should collate latent demand for DNA synthesis via one or more “biofoundries,” so that individual researchers and small groups in government and academia can gain access to, and help drive development of, best-available commercial platforms. Second, they should help motivate, initiate, and sustain foundational and translational work to improve aspects of DNA synthesis beyond cost (e.g., turnaround time). We note that other countries and regions (the United Kingdom, China, and the European Union) now have standing planning capacities and road-mapping efforts focused on advancing and applying DNA synthesis; past U.S. Government efforts that ensured domestic leadership in computing and networking technologies should also be revisited as potential models for strategic framing and program development.

2.4 Materials Science

Functional biomaterials have become increasingly important to human health. Polymeric, colloidal, and biomolecular materials are critical to new technologies that will address many of the problems and needs of modern medicine. Among them are the following:

- Delivery systems capable of safely getting nucleic acids such as DNA, mRNA, and RNAi into the body and directed toward the target cells of interest for the treatment of medical disorders, including genetic diseases and cancers

- Effective and selective targeting of specific tissues within the body for therapeutic treatment, especially those parts of the body that present difficult barriers, such as systemic delivery across the blood-brain barrier, or targeted therapies that can effectively penetrate lung, gut, or other tissues
- Synthetic organs or organoids that replicate human function sufficiently for more effective in vitro drug testing
- Regenerative technologies that enable in situ healing of soft and hard tissues for wound repair, organ replacement, and bone regeneration
- Novel biosensors that are readily deployed, inexpensive, and highly accessible, thus enabling early detection of cancer and infectious disease
- Revolutionary imaging capabilities that can be used to detect and diagnose disease in humans in real time and with high depth and resolution.

Given the growing importance of materials science in biomedicine, it is important to harness and accelerate our understanding of structure-function-processing relationships and our abilities to synthesize and characterize new materials with desired biomedical properties. Understanding how materials interact with cells and tissues, in vivo as well as under artificial conditions, is also essential. A particular focus must be on the less-well-studied "soft matter," such as polymeric hydrogels and nanoparticles or self-assembled organic colloids, rather than inorganic crystalline materials commonly studied by DOE programs. The toolsets typically held by physicists and engineers in DOE's labs can be adapted or designed for these purposes by teams of chemists, materials scientists, physicists and engineers working in concert with biologists and clinicians.

The Molecular Foundry at Lawrence Berkeley National Laboratory is an especially potent example of how a national laboratory can bring together diverse materials expertise. The Foundry offers users capabilities for microfabrication, combinatorial synthesis, novel microscopy and spectroscopy, and state-of-the-art in situ structural imaging. While the emphasis has been on in situ studies in electrochemical, thermal, or other unusual conditions appropriate to energy storage, we can imagine a similar facility oriented to biomaterials that would, for example, allow the "seeing" of nanoparticle interactions inside the body or provide understanding of how differences in hydrogel or scaffold nanostructures promote different modes of cellular development. Such a facility would be very consistent with DOE's culture and capabilities and would greatly expand the range of tools and expertise available to traditional NIH investigators.

The Task Force heard about DOE's work on new 3D tissue-printing methods. Expanding the materials used in 3D printing to include living cells represents an opportunity with considerable potential in biomedical research, especially if scaffolding, infusion, sensing, and stimulatory networks can be printed in as well. Human cell culture methods used at present are too primitive to capture the molecular physiology of real human tissues, and model organisms such as mice are both expensive per experiment and often misleading as models of human tissues. Further, both present-day human tissue culture and mouse models are too crude in terms of single-cell interrogation and control. 3D-printed tissues, or even synthetic organoids, might offer a powerful new technology for biomedicine that overcomes these limitations.

Nanomedicine is a particularly important area of materials science that could benefit from DOE-NIH partnerships. Nanoparticles and other modes of nanomedicine show early promise in

lowering drug toxicity (including that of cancer therapeutics), enhancing drug biodistribution, and retarding drug clearance. There is also great potential for targeting drugs to specific regions of the body and for enhancing the synergy in combination therapies through greater control and specificity in delivery.

Achieving the full potential of nanomedicine will require surmounting both the physiological barriers to the delivery of nanoparticles and controlling nanoparticle homogeneity and reproducibility. The former requires better understanding of the mechanisms of nanoparticle targeting, the role of vasculature in diseased organs, the nature of non-cellular physiological barriers such as mucins and extracellular matrix, and the impact of different sizes, shapes, charge and chemical composition. For controlling the composition and shape of particles, NCI's Nanotechnology Characterization Lab, a cross-agency collaboration with the National Institute of Standards and Technology and the Food and Drug Administration (FDA), exemplifies the translation of nanoparticle systems to patients by focusing on the standardization and characterization of nanoparticle drug carriers. A broader and bolder approach would be for NIH and DOE to partner in establishing a nanoparticle "foundry" that would build large libraries of well-characterized nanoparticle and soft matter systems.

2.5 Modeling and Simulation

For more than 70 years, DOE has advanced the frontiers of high-fidelity simulation of complex physical systems. It has developed numerical algorithms to combine multiple physical phenomena (e.g., radiation and hydrodynamics) while bridging multiple two-dimensional and 3D spatial and temporal scales, methods to verify the codes and to validate such simulations against experiment or observation, and ways to quantify the uncertainties in simulations. It has also advanced the practicalities of such activities, from developing and fielding some of the world's most powerful hardware and the software systems through using them to manage and visualize enormous datasets. In addition, DOE is the lead Federal agency in the Government's exascale computing initiative.

These DOE capabilities were developed largely in service of the Department's nuclear weapons mission. But, over the decades, they have also been fruitfully applied to basic sciences (e.g., lattice gauge simulations, climate science, materials) and to energy-related problems (e.g., catalyst development, combustion, nuclear reactor operation, and the electrical grid). Such simulations integrate our understanding at more fundamental levels, are descriptive of emergent phenomena, and, at their best, are predictive of the consequences of interventions.

With the great growth of biomedical data and growing prowess in simulation, it is timely to apply simulation technologies to biomedical problems. The "sequence-structure-function" problem for proteins and the interaction of small molecules with biological macromolecules (i.e., drug design) are already prominent applications of simulation and are well-poised to benefit from future advances in computational hardware. But, successful simulations of other, more complex biological systems are further off, in part because they pose novel challenges. For example, a molecular-level description of the many functions of a single cell can be envisioned, but the stochastic nature of the structure and interactions of relatively small numbers of molecules will challenge deterministic methods. Similarly, the neuron-level description of cortex function is today, at best, schematic. And, in line with earlier comments about the importance of data

sciences for improving patient care methodologies, simulation technologies can be used to model strategies to improve the delivery of preventive measures and therapeutics, especially those based on complex molecular diagnostics.

DOE's Hub for simulating nuclear reactors, The Consortium for Advanced Simulation of Light Weight Reactors (CASL)[c] provides a recent example of how simulation can be applied to a complex problem. At CASL, a collaboration of reactor operators, nuclear engineers, and computer scientists has produced a validated simulation capability that improves the performance of operating light water reactors. We can imagine one or several similar "grand challenge" exercises in which DOE and NIH researchers collaborate to produce a predictive simulation of biomedical relevance.

3 Opportunities for Expanded DOE-NIH Collaboration: Biomedical Applications

Throughout the panel's deliberations, we were reminded of the many medical conditions that might be better studied by collaboration between NIH and DOE, and we reviewed many areas of biology in which DOE-NIH interactions have helped in the past or might help in the future to make progress against diseases. In this section, we highlight a few of the specific domains of biomedical research that show the greatest promise for closer working relationships between NIH and DOE researchers.

3.1 Cancer

Cancer research has long been a scientific domain of interest to both NIH and DOE because of the roles of radiation as a causative factor for some cancers (via mutation); as a means of imaging tumors and their spread; as part of cancer diagnosis and of monitoring therapeutic responses and cancer progression (see section 3.4 below); and as an important modality for cancer treatment (through cell killing). More recently, the agencies have perceived many other common interests in cancer research, most prominently as a result of the increasing use of DNA sequencing and other genomic technologies to make accurate diagnoses and to choose appropriate (especially, so-called "targeted") therapies. The large sets of genomic and clinical data arising from the new approaches to diagnosis and therapy have created another obvious common interest for two agencies: high-end data science. Two major initiatives of the current Administration have provided further impetus for DOE-NIH collaborative work that would advance both cancer research and cancer treatment: President Obama's Precision Medicine Initiative, about one-third of which is specifically directed to oncology, and Vice President Biden's Cancer Moonshot program.

Cancer research now addresses a wide variety of questions about biological systems—ranging from structural and cell biology to genetics and microbiology—and about medical practices—including radiological diagnoses, detection of early cancers, measurements of tumor response and recurrence, and improvements in drug delivery. Pursuit of these many topics involves methodologies that are especially well studied in DOE laboratories. Among them are nanotechnology and other materials sciences; printing organoids; radiation physics,

[c] http://www.casl.gov/

radiochemistry, and radiobiology; imaging methods that include X-ray diffraction and cryo-electron microscopy (cryo-EM) to discern molecular shapes and interactions, as well as methods for visualizing organs and whole organisms; and single-cell-based methods for monitoring cell physiology. Many of these capabilities at DOE labs offer powerful incentives for interagency collaboration, but the two most prominent cancer-related opportunities for DOE-NIH interactions lie in genomics and computational sciences.

As described earlier, DOE played several important roles in the HGP, which was managed largely by NIH, and the HGP has laid the groundwork for current studies of cancer cell genomes. Indeed, The Cancer Genome Atlas project—which has produced the largest available set of human genomic data, has transformed cancer research, and is gradually altering clinical practice of oncology—would not have been possible without the HGP and "next-generation" sequencing methods. DOE's engagement with DNA technologies (reviewed in section 2.3) might be a starting point for collaborative work to improve genome-based diagnostics, especially as the use of those methods diffuses through the clinical oncology community.

The resulting profusion of data about cancer genomes, with both somatic mutations and germline variations, is creating new demands for improved computational tools and for people with the requisite skills. Those demands are only increasing in response to efforts to incorporate heterogeneous clinical information into the evaluation of genomic data. Cancer advocacy groups and Vice President Biden's Moonshot team are also calling for improved management and analysis of such data, more widespread data sharing, and interoperability of data sets and the applications that manage them. NCI has embarked on a series of efforts to enhance its capacities to handle and learn from the rapidly enlarging data sets, with its pilot programs in cloud computing and its recently launched Genomic Data Commons. As the Task Force heard at its initial workshop, the head of NCI's bioinformatics program presented a proposal for a potential collaborative program with DOE on exascale computing to model the course of cancer treatment. These discussions have been strengthened, as we heard at the second workshop, by further conversations between the acting director of NCI and Secretary Moniz. It thus seems likely that such a joint effort to develop cancer-oriented computational methods might be a testing ground for some of the Task Force recommendations in section 4.

3.2 Neurosciences

Brain research is supported across many institutes of the NIH, but the opportunities for DOE involvement are perhaps best appreciated in the context of the recent BRAIN Initiative. Launched by President Obama in April 2013, BRAIN has begun a concerted effort to improve the methods available for brain research, both for experimental work and in the domain of theory and analysis. The ultimate goal is to understand large circuits of nerve cells: What are all the types of neurons involved? What is the structure and connectivity of the circuit? What are the signals flowing through the circuit? How do these circuit functions relate to behavior and cognition?

DOE laboratories clearly have expertise that relates to these goals, as described in section 2.1 above. Specific technologies of interest here include nano- and micro-fabrication, and simulation and data analysis. Modalities for possible collaboration include the following:

1. Small-scale collaborations with individual NIH-funded principal investigators
2. A large-scale project beyond the reach of individual groups
3. Fabrication and dissemination of cutting-edge tools
4. A user facility that offers access to cutting-edge technology

Modalities (1) and (2) are being or have been pursued successfully already. The artificial retina project is an example of technology development that was far out of reach of university or medical school laboratories. It involved six DOE labs and four universities over a decade and ultimately led to an FDA-approved device for implantation in humans. Small-scale collaborations occur at multiple sites, for example between Vanessa Tolosa (Lawrence Livermore National Laboratory) and Loren Frank (University of California, San Francisco) to design novel polymer-based electrodes. Modalities 3 and 4 remain to be implemented but possibilities relevant to neuroscience include the following:

- **A foundry for new electrode designs:** Methods of electrical recording and stimulation continue to provide superb access to neural signals in the brain, with high temporal resolution, access to deep structures, and proven clinical applications. Advances in nanofabrication are opening opportunities for fabricating electrode devices. For example, one can now plausibly envision arrays of electrodes with substantially increased density and number of sites that displace less brain tissue but integrate optical and chemical channels for stimulation and recording. To date, there has been no systematic development or testing of such devices. Commercial suppliers have failed to innovate in this area because the market is too small, while academic centers typically deliver one-of-a-kind devices with new capabilities, publish the accomplishment, but then fail to develop it for general use.

  DOE capabilities in nanofabrication and materials could be put to excellent use here in the form of a foundry that would play an enabling role comparable to that of the integrated circuits-prototyping facility MOSIS in the semiconductor revolution. The foundry could fabricate many copies of a prototype in a single run and perform basic testing. It would then ship functioning copies to external collaborators for evaluation in animal studies. Successful designs would then be produced in large numbers and made available to the research community. That would transform studies of dynamic processing in the brain. At some future date, 3D printing of artificial cortical tissue structures with built-in sensing and stimulation networks could become mature enough for widespread use in basic neuroscience research, with the benefits discussed above.

- **A user facility for connectomes:** The term “connectome” refers to the complete anatomical circuit diagram for a piece of brain, detailing every nerve cell and their synaptic connections. To date, this has been achieved for only a few circuits: the *C elegans* worm, portions of the fly visual system, and the vertebrate retina. In each of those cases, the available connectome enabled discoveries and was a crucial guide to interpreting function in the same circuit. Unlike the genome, the connectome is not a singular data set to be acquired once and for all. Instead we anticipate a great demand for small connectomes: diverse brain regions, multiple versions with specific cell types

labeled or for comparisons among mutant animals, etc. A user facility would facilitate acquisition of such data even as it researches new methods to analyze brain structure.

Three-dimensional electron microscopy currently offers the highest resolution. New electron microscopes are being introduced based on tools from the semiconductor industry; one such instrument has 61 electron beams that acquire data in parallel at previously unimaginable rates. This kind of equipment is far out of reach of individual laboratories.

A user facility could provide broad access to such equipment and the capabilities it enables. The primary output of the facility would be the 3D stacks of images. However, the facility would also be involved in the subsequent challenges of data analysis, developing the technologies that would allow users to reconstruct cell bodies, dendrites, axons, and synapses from the 3D image stacks. The challenges in creating and operating such a facility would be well-matched to DOE strengths.

In either of these modes (foundry or user facility), the lab would also act as a hub of activity, training, and scientific exchange. Visitors from NIH-funded groups will learn about instrumentation and receive training in data analysis. Conversely, lab investigators will learn about the details of biological systems so as to better integrate their technical approaches.

3.3 Microbiology and Cell Biology

Existing and proposed genomic capabilities (e.g., DNA sequencing and synthesis, multi-scale imaging, modeling, and others) allow us to envision routine understanding and reprogramming of entire cells—not just heterologous systems within microbial or therapeutic immune cells, but holistic cellular engineering at a full-genome scale. Properly developed, such capabilities would enable both the discovery of useful biochemistry and cellular control systems, as well as the deployment of cells for making medicines, materials, and fuels and for producing active diagnostic and therapeutic agents.

Three recent projects provide a sense of both the challenges and opportunities: (1) a single-investigator study at NIH identified more than 14,000 new biosynthetic gene clusters in genomes sampled from the human microbiota. While follow-on studies suggest these clusters encode many functional molecules, from new antibiotics to human immune system modulators, it is only practical to test a few clusters at a time; (2) another NIH-funded team realized the engineering of an approximately 30-enzyme biosynthesis pathway enabling yeast to brew an essential medicine traditionally sourced from plants, and (3) a third group, after 16 years of support from DOE and the Defense Advanced Research Projects Agency, revealed that their best-studied minimal microbial genome still encodes more than 100 genes of unknown function.

We recommend that DOE and NIH researchers work together to develop an integrated capability for moving directly from sequencing genomes, to high-throughput imaging, metabolomics, and biochemistry at molecular to cellular scales, and then to recapitulation and reprogramming of metabolism and cellular systems via synthesis of genes, pathways, and genomes. We imagine integrating and operating such capabilities so as to make routine the characterization of every molecule comprising any given cell. Realizing and operating such a facility would uniquely require sustained input and expertise from DOE scientists and engineers

to help invent, develop, integrate, and operate the multitude of genome-scale capacities required. But, the payoff would be enormous—any organism or human cell type that NIH, DOE, or the broader U.S. research community needed to understand or make use of could be fully characterized and made "engineerable" as quickly as possible.

3.4 Imaging and Radiobiology

Imaging provides the capacity to measure and monitor biological processes in real-time in living organisms in their native physiological context. For more than 70 years, DOE has leveraged unique capabilities in radiation chemistry, physics, engineering, computation, and radiation detection to support basic research in the use of radiation applied to biomedicine broadly, and imaging in particular. Indeed, the modern era of nuclear medicine is an outgrowth of the original charge of the Atomic Energy Commission to exploit nuclear energy to promote human health, morphing into DOE's Office of Biological and Environmental Research. In the broadest sense, imaging research is also supported by many institutions across NIH, including a legacy of robust investment in cancer molecular imaging, a program funded by NCI. These capabilities have yielded a vigorous history of DOE-NIH collaborations in biomedical imaging, radiotherapy, and radiobiology.

The Task Force's review included a broad overview of imaging, with examples in synchrotron radiation technology to visualize protein structure; development and recent exciting advances in cryo-EM, a form of transmission electron microscopy wherein the sample is studied at liquid nitrogen temperatures to determine protein structure and biological function; BRAIN imaging and the MR Brain Connectivity project; as well as biomedical isotope production. Other areas of discussion touched on super-resolution optical imaging, low-dose radiobiology, and advanced computational analytics.

Based on the presentations, a particularly noteworthy example of bridges between DOE (isotope production) and NIH (chemistry and imaging agents) focuses on applications in nuclear medicine. DOE's national laboratories have impressive capacities in producing medical isotopes that are useful in nuclear medicine and radiotherapy. The Isotope Development and Production for Research and Applications subprogram of the Office of Nuclear Physics in DOE's Office of Science is responsible for supplying stable and radioactive nuclei to a broad range of customers.[7] At Oak Ridge National Laboratory (ORNL), the Isotope Program has efforts in isotope production, research and development, material fabrication, and distribution. ORNL has pioneered many radiochemical separation processes, and continues to develop new production techniques and applications for isotopes. There are abundant established bridges between DOE (isotope production) and NIH (radiochemistry and medical imaging applications) for PET, single photon emission computed tomography (SPECT), and radiotherapy. As another example, a recent collaborative project involved studies of ^{229}Th (thorium) production reactions. This long-lived isotope is important as a precursor to ^{225}Ac (actinium) and ^{213}Bi (bismuth), which are relatively short-lived alpha-emitters that are of great interest in alpha-radioimmunotherapy procedures in medicine.[8] There is also the possibility for further research in the development of theranostic agents, compounds that combine the properties of diagnostic imaging and therapeutic agents in a single platform.

Radiomics and imaging genomics (also termed radiogenomics) are relatively new, evolving fields within the imaging community.[9] Radiomics is the automated extraction of high, multi-dimensional imaging features, not visible to the naked human eye, obtained from standard medical images. Radiogenomics refers to the linkage of imaging features (which can be qualitative, quantitative, or radiomic imaging features) to the underlying genomic composition of the tumor or tissue. With ever-increasing amounts of data and current efforts focused on developing large multiscale, high-computational platform capabilities, the merger of multiple types of data such as clinical, imaging, genomic, and other omic data is now possible, potentially providing robust, clinically relevant associations and predictions that may ultimately enhance patient outcomes. The vast amounts of genomic information provided by rapid next-generation sequencing and other large-scale genomic technologies, as well as the ability to extract thousands of radiomic features from conventionally obtained medical imaging, have the potential to allow for advanced diagnostics; they may also serve as predictive and prognostic biomarkers. Research conducted in data science and data harmonization has been successfully pursued at DOE labs and could be further advanced in biomedical imaging fields such as radiomics. Opportunities in advanced image analysis and radiomics could combine the computing power and computational expertise of DOE with advanced queries in NIH-sponsored biomedical imaging across cancer, radiobiology, neurosciences, and cardiovascular disease. Convergent teams of physical scientists and computational engineers could address areas of advanced imaging analytics, artificial neural networks, and automated image segmentation and feature extraction.

3.5 Biodefense

A vital national interest is the ability to anticipate, detect, and respond to biological threats, whether natural or man-made. While neither NIH nor DOE is a lead agency in these matters, their biomedical underpinnings are clearly within the biomedical scope of NIH, and DOE's national laboratories are involved through their work with other government agencies.

Essential capabilities are exploration of the nefarious potential offered by evolving biotechnologies, an understanding of the signatures that a bioweapons program might present, rapid and effective surveillance programs to detect the presence of a bioagent (whether natural or man-made), a rapid assessment of the nature of the agent, rapid deployment of countermeasures to the agent, and determination of origin. Clearly, NIH and DOE have much to offer in this enterprise, either individually or in collaboration.

4 Recommendations

From the outset of this study, the Task Force agreed that our goals were to seek areas of current and emerging science that would benefit from DOE-NIH collaboration and to identify mechanisms by which such collaborative efforts might be facilitated. In particular, we aimed to avoid being overly specific or directive about the kinds of cooperative science that should be undertaken, reflecting the Task Force's conviction that collaborative work proceeds most effectively through investigators working on specific problems at the grassroots level. Agency policies and enlightened leadership must, first and foremost, promote such activities. But, there

are also instances where user-facility or coherent multi-investigator efforts would be optimal, in which case leadership must catalyze grass roots support for their definition and inauguration.

That stance, together with our findings in sections 1–3, our own knowledge of past interagency collaborations, and our own research experiences lead us to make four broad recommendations to improve the substance and mechanisms of DOE-NIH interactions in the relatively near future that would also enhance the potential for even greater interaction in the longer term. In particular, we recommend that DOE and NIH work together to accomplish the following.

4.1 Define Joint Research Programs in the Most Fertile Areas of Biomedical Research and Applicable Technologies

Topic-oriented panels: DOE's Director of the Office of Science and the Office of the NIH Director, including the Offices of Intramural and Extramural Research and the Division of Program Coordination, Planning, and Strategic Initiatives should jointly charge working-level panels of researchers from both communities to explore and document opportunities for increased collaboration. Some of these panels will be problem-oriented, involving focused NIH researchers and a diversity of DOE technologists, while others will be technology-oriented, involving technology-focused DOE researchers and a diversity of NIH researchers. Problem-oriented topics might include cancer, neuroscience or low-dose radiation biology; technology-oriented topics might include informatics, imaging, materials, sensors and instrumentation, or modeling and simulation.

Annual review: The DOE Director of the Office of Science and the NIH Director's Office should convene an annual review of the substance and process of interagency collaboration, thereby providing regular guidance for promoting effective collaboration.

4.2 Define and Create Organizational and Funding Mechanisms that Bring Diverse Researchers Together and Cross-Train Junior People

The mixing of people with diverse backgrounds and skills is a crucial part of more productively bringing DOE technologies to bear on the biomedical problems addressed by NIH. This is particularly important for early-career researchers, who tend to be more catholic in their interests and more technically agile. Mechanisms for such mixing that could be instituted quickly and informally within current structures include:

- **Cross-agency assignments:** Immersion in the "other" culture is important. Sending a DOE researcher to an NIH lab (or vice versa) is an effective way of introducing investigators, especially junior investigators, to the practices used in the partner agency. Such stays should be multi-month in duration to allow the conception and inauguration of a joint project, which can then be pursued remotely and/or through repeated briefer visits.
- **Summer gatherings:** It is quite common in both DOE and NIH cultures for researchers to gather for multiple weeks for a summer workshop focused on a particular problem or technology. Training researchers in specific techniques can be another goal of such meetings. DOE and NIH program offices could work collaboratively to define, encourage participation, and fund several such gatherings through existing resources.

- **NIH grant supplements:** Many NIH Institutes make liberal use of their authority to rapidly issue supplementary funds to existing grants, contracts, or training awards; such uses could be targeted specifically to support favorably reviewed proposals for work by NIH-awardees in collaboration with DOE researchers. Such mechanisms are attractive and valuable means to act on appealing proposals for collaborative work—especially pilot projects that don't require large sums of money.
- **Training programs:** More formal, jointly funded training programs (e.g., NIH T32), perhaps initiated through NIH's Common Fund and DOE's Laboratory Directed Research and Development funds through its national laboratories, would take longer to establish but could involve much more substantial funding. Such programs might define a new pathway in "convergent post-doctoral training." For instance, it could be a sequential training experience wherein a career pathway is mapped to involve an NIH-funded biomedical post-doctoral experience focused on biomedical queries for perhaps 2–3 years, followed by a second post-doctoral experience in a quantitative DOE lab; the convergence pathway could be inverted for an individual who starts in a quantitative DOE lab. We expect that such cross-trained individuals would be very attractive candidates for faculty or permanent laboratory positions.

4.3 Define and Secure Funding for One or More Joint Research Units and/or User Facilities

"Big science" (structured, multi-researcher activities) and user facilities are characteristic (but not exclusive) features of DOE culture. The growing scale and complexity of biomedical research suggests that these organizational modalities will be more frequently used in addition to traditional single-investigator activities. Indeed, the DOE light sources, the HGP, the National Center for Biotechnology Information (NCBI), The Cancer Genome Atlas (at NCI and the National Human Genome Research Institute), many NIH clinical trials networks, and the RAS Initiative at the Frederick National Laboratory (under NCI) are examples of larger-scale activities that have been productive.

We recommend that NIH and DOE leaders routinely scan their research horizons for situations in which the creation of organizations that serve multiple users or focus on multi-investigator teams would significantly accelerate progress toward specific goals. Beyond securing broad community participation in the definition of such efforts (for example, through the mechanisms proposed in 4.1) effective implementation would demand negotiation with the heads of participating agencies and possibly with other Administration leaders and Members of Congress, as described in 4.4 below.

4.4 Better Inform OMB, Congress, and the Public about the Importance of and Potential for Enhanced Interagency Collaboration

Organizational and budgetary silos are endemic to government. While they do help decision makers understand and manage the work they oversee and keep agencies focused on their mission, they inhibit the kind of collaboration between DOE and NIH that currently seems so promising. We recommend that Task Force members and senior staff from NIH and DOE make joint presentations to OMB and to the relevant congressional authorization and appropriations

committees. These presentations will inform them about the advantages of and any obstacles to such collaborations, as well as their co-funding by the two agencies. An exploration of possible legal mechanisms for joint funding would also be appropriate.

In making these four broad recommendations, we are not unaware of the challenges to increasing cooperation between DOE and NIH. Simply making researchers and program managers aware of the capabilities and needs across two vast agencies is a challenge. Measures of research quality and impact are different in the two agencies. Moreover, the predominantly mission-driven culture of DOE, dominated by team science and by physics and engineering will not mix easily with the disease-oriented culture of NIH, dominated by grants to individual investigators. However, it is encouraging that the cultures of each agency are not monolithic. For example, DOE does (and will no doubt continue to) support some single-investigator work, and NIH does support multi-user capabilities like NCBI (part of the National Library of Medicine) clinical trials, and genomics projects. The recently announced national BRAIN and Cancer Moonshot initiatives provide valuable incentives and venues for greater interagency cooperation. And, then there will be the understandable pressure to keep the individual agencies focused on their separate historical missions. But, failure to address these challenges will, in our opinion, leave far too many opportunities unrealized in the national effort to accelerate progress in the biomedical sciences.

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Appendix A: Task Force Charge

The Secretary of Energy
Washington, DC 20585
November 21, 2015

MEMORANDUM FOR THE CHAIR
SECRETARY OF ENERGY ADVISORY BOARD

FROM: ERNEST J. MONIZ

SUBJECT: Establishing a New Task Force of the Secretary of Energy Advisory Board (SEAB) on Biomedical Sciences

I request that you form a new Secretary of Energy Advisory Board (SEAB) Task Force to identify:

- New areas for research by DOE investigators that could, over time, significantly advance the pace of progress in biomedical sciences, and
- New mechanisms for conducting research in coordination with scientists from government laboratories (both DOE and the National Institutes of Health [NIH]), universities, academic medical centers, and industry. The Task Force is not expected to address possible DOE and NIH funding arrangements to support this initiative.

This Task Force would be comprised of SEAB members and experts from, as examples, universities, the NIH intramural program, DOE National Laboratories, and various components of industry.

Purpose of the Task Force: For more than 60 years, the DOE and its predecessor agencies have used their potent and unique scientific capabilities to advance several facets of the biomedical sciences. These include, most notably, radiochemistry and nuclear medicine; instrumentation for diagnostic and therapeutic radiology; structural biology; and recently, genomics, as highlighted by the human genome project.

Advances in science and technology — particularly genomics, mass spectroscopy, informatics, and various forms of imaging — have led to widespread recognition today that biomedical sciences are poised to seize new opportunities that could vastly improve the health of Americans and other peoples of the world while significantly lowering risks and costs over time, maintaining U.S. leadership in the life sciences, and providing new knowledge for applications in the commercial sector.

Areas particularly ripe for the application of new technologies include:

(1) Precision medicine, in which diagnosis, prevention, and therapy are based on a description of disease at the molecular level;

(2) Brain science that promises to advance understanding of normal circuitry and its aberrations in neurological and psychiatric diseases;

(3) Bioinformatics for storage, retrieval, and analysis of enormous sets of molecular and structural data;

(4) Near real time imaging, fusion, and processing of molecules, cells, and tissues;

(5) New forms of therapy involving delivery and modification of genes and their functions; and

(6) Reengineering of biological systems for better understanding of cells and organisms and for more effective analysis and control of many diseases.

DOE has core competencies that could greatly accelerate progress in these areas, including:

— Sensors and high speed data acquisition from many sensors

— Imaging devices operating at a wide range of scales

— Instruments and methods for observing and measuring the functions and dynamics of large biomolecules, including multi-molecular complexes

— Material sciences and nanotechnology

— Multi-scale modeling and simulation

— Exascale computing

The NIH has a long history of using a variety of mechanisms to promote biomedically relevant work at DOE laboratories, taking advantage of DOE's unique capabilities in many fields of science, including several of those mentioned above. Presently, the NIH sponsors or helps to support over 150 projects in DOE laboratories at an annual cost of over $250 million. These activities result from direct collaborations between NIH-supported scientists and scientists at DOE laboratories, not from a top-down driven directive to cooperate.

Leaders at NIH and DOE have long recognized and publicly acknowledged the importance of such cooperation, and current leaders of both agencies want it to continue to prosper. Indeed, in October a joint DOE-NIH workshop was held to discuss the President's BRAIN initiative - a research effort into new ways to treat, prevent, and cure brain disorders - and seek ways in which the agencies might work together to achieve its goals.

Schedule: By September 2016, the Task Force should produce a report to identify new research areas for DOE in the area of biomedical sciences and proposals for DOE initiatives that would advance the Nation's progress in the health-related sciences. This report would be available to the public, Congress, and the current and next Administrations.

Liaisons to the Task Force: Sharlene Weatherwax, Associate Director, Biological & Environmental Research, Office of Science; and Dimitri Kusnezov, Chief Scientist and Senior Advisor.

Designated Federal Officer: Matthew Schaub, Deputy Director, Office of Secretarial Boards and Councils.

Appendix B: Task Force Member Biographical Sketches (* denotes SEAB member)

Steven E. Koonin* (Co-Chair) was appointed as the founding Director of New York University's Center for Urban Science and Progress in April 2012. That consortium of academic, corporate, and government partners pursues research and education activities to develop and demonstrate informatics technologies for urban problems in the "living laboratory" of New York City.

He previously served as the U.S. Department of Energy's (DOE's) second Senate-confirmed Under Secretary for Science from May 19, 2009 through November 18, 2011. As Under Secretary for Science, Dr. Koonin functioned as the Department's chief scientific officer, coordinating and overseeing research across DOE. He led the preparation of the Department's 2011 strategic plan and was the principal author of its Quadrennial Technology Review. Dr. Koonin particularly championed research programs in high-performance simulation; exascale computing; inertial fusion energy; and greenhouse gas monitoring, reporting, and verification. He also provided technical counsel on diverse nuclear security matters.

He joined the California Institute of Technology's (Caltech's) faculty in 1975, was a research fellow at the Niels Bohr Institute from 1976–1977, and was an Alfred P. Sloan Foundation Fellow during 1977–1979. He became a professor of theoretical physics at Caltech in 1981 and served as Chairman of the Faculty from 1989–1991. Dr. Koonin was the seventh provost of Caltech from 1995–2004. In that capacity, he was involved in identifying and recruiting one-third of the Institute's professorial faculty and left an enduring legacy of academic and research initiatives in the biological, physical, earth, and social sciences, as well as the planning and development of the Thirty-Meter Telescope project.

As the Chief Scientist at BP from 2004 to early 2009, Dr. Koonin developed the long-range technology strategy for alternative and renewable energy sources. He managed the firm's university-based research programs and played a central role in establishing the Energy Biosciences Institute at the University of California, Berkeley; the Lawrence Berkeley National Laboratory; and the University of Illinois at Urbana-Champaign.

Dr. Koonin is a member and past chair of the JASON Study Group, advising the U.S. Federal Government on technical matters of national security. He has served on numerous advisory committees for DOE, the National Science Foundation, and the Department of Defense, including the Defense Science Board and the Chief of Naval Operation's Executive Panel. He is a member of the Council on Foreign Relations and a Fellow of the American Physical Society, the American Association for the Advancement of Science, and the American Academy of Arts and Sciences, and a former member of the Trilateral Commission. In 1985, Dr. Koonin received the Humboldt Senior U.S. Scientist Award and in 1998 DOE's E.O. Lawrence Award for his "broad impact on nuclear many-body physics, on astrophysics, and on a variety of related fields where sophisticated numerical methods are essential; and in particular, for his breakthrough in nuclear shell model calculations centered on an ingenious method for dealing with the huge matrices of heavy nuclei by using path integral methods combined with the Monte Carlo technique."

Harold Varmus* (Co-Chair), co-recipient of the Nobel Prize for studies of the genetic basis of cancer, joined the Meyer Cancer Center of Weill Cornell Medicine as the Lewis Thomas University Professor of Medicine on April 1, 2015. He is also a senior associate member of the New York Genome Center. Prior to joining Meyer Cancer Center, Dr. Varmus was the Director of the National Cancer Institute for 5 years. He was also the President of Memorial Sloan-Kettering Cancer Center for 10 years and Director of the National Institutes of Health for 6 years. A graduate of Amherst College and Harvard University in English literature and Columbia University in medicine, he trained at Columbia University Medical Center, the National Institutes of Health, and the University of California, San Francisco (UCSF), before becoming a member of the UCSF Basic Science Faculty for more than two decades. He is a member of the U.S. National Academy of Sciences and the Institute of Medicine and is involved in several initiatives to promote science and health in developing countries. He is the author of more than 350 scientific papers and 5 books, including a recent memoir titled *The Art and Politics of Science*. In addition, he was a co-chair of President Obama's Council of Advisors on Science and Technology, a co-founder and Chairman of the Board of the Public Library of Science, and chair of the Scientific Board of the Gates Foundation Grand Challenges in Global Health.

Drew Endy is the Palmer Faculty Scholar of Bioengineering at Stanford University (Stanford) and President of the BioBricks Foundation. He is a voting member of the National Science Advisory Board for Biosecurity and the National Research Council Committee on Science Technology and Law; he serves as co-director of the Joint Initiative for Metrology in Biology, a partnership between Stanford and the National Institute of Standards and Technology. In 2013, Professor Endy was recognized by the White House for his contributions to open-source biotechnologies. He is a co-founder (retired) of the international genetically engineered machines competition (iGEM), a global competition now engaging about 4,000 undergraduates annually. Professor Endy helped develop and launch the new undergraduate majors in Biological Engineering at both the Massachusetts Institute of Technology and Stanford. He chaired the 2003 Defense Advanced Research Projects Agency study on synthetic biology and was a founding investigator of the National Science Foundation's Synthetic Biology Engineering Research Center. His academic teams demonstrated the first rewritable, non-volatile DNA memory registers, amplifying genetic logic gates, and pioneered the refactoring of natural genomes. He is a co-founder and director of Gen9, Inc., a high-throughput DNA construction company. Professor Endy earned a B.S. in Civil Engineering from Lehigh University in 1992, a M.S. in Environmental Engineering from Lehigh University in 1994, and a Ph.D. in Biochemical Engineering & Biotechnology from Dartmouth College in 1998.

Stuart Feldman is Head of Schmidt Sciences at The Eric and Wendy Schmidt Fund for Strategic Innovation, where he advises a number of scientific activities, arranges grants, and plans new fellowship and engineering programs. Feldman did his academic work in astrophysics and mathematics and earned his B.A. at Princeton University and his Ph.D. at the Massachusetts Institute of Technology. He was awarded an honorary Doctor of Mathematics by the University of Waterloo. He is former President of the Association for Computing Machinery (ACM) and former member of the board of directors of the Association to Advance Collegiate Schools of Business. He received the 2003 ACM Software System Award. He is a Fellow of the Institute of Electrical and Electronics Engineers, ACM, and the American Association for the

Advancement of Science. He serves on several diversity boards, university advisory boards, and government advisory committees.

Feldman was a computer science researcher at AT&T Bell Labs (where he wrote Make and the first Fortran 77 compilers), was a computer science research manager at Bell Communications Research (which included software engineering, as well as driving several large systems), was Vice President for Internet Strategy and Vice President for Computer Science Research at IBM Research, and was Vice President of Engineering at Google (where he was responsible for the New York engineering office and oversaw a dozen more in the Americas and Asia).

Paula T. Hammond* is the head of the Department of Chemical Engineering and David H. Koch Chair Professor in Engineering at the Massachusetts Institute of Technology (MIT). She is a member of MIT's Koch Institute for Integrative Cancer Research, the MIT Energy Initiative, and a founding member of the MIT Institute for Soldier Nanotechnology. She has recently been named the new head of the Department of Chemical Engineering (ChemE). She is the first woman and the first person of color appointed to the post. She also served as the Executive Officer (Associate Chair) of the Chemical Engineering Department (2008–2011). Professor Paula Hammond was elected into the 2013 Class of the American Academy of Arts and Sciences. She is also the recipient of the 2013 American Institute of Chemical Engineers Charles M. A. Stine Award, which is bestowed annually to a leading researcher in recognition of outstanding contributions to the field of materials science and engineering, and the 2014 Alpha Chi Sigma Award for Chemical Engineering Research. She was also selected to receive the Department of Defense Ovarian Cancer Teal Innovator Award in 2013. Professor Paula T. Hammond has been listed in the prestigious Highly Cited Researchers 2014 list, published by Thomson Reuters in the Materials Science category. This list contains the world's most influential researchers across 21 scientific disciplines based on highly cited papers in the 2002–2012 period. Professor Hammond is also included in the report, *The World's Most Influential Scientific Minds 2014*. Professor Hammond serves as an associate editor of the American Chemical Society journal, *ACS Nano*. She has published more than 250 scientific papers and holds more than 20 patents based on her research at MIT. She was named a Fellow of the American Physical Society, the American Institute of Biological and Medical Engineers, and the American Chemical Society Polymer Division. In 2010, she was named the Scientist of the Year by the Harvard Foundation.

Professor Hammond received her B.S. in Chemical Engineering from MIT in 1984, and her M.S. from the Georgia Institute of Technology in 1988 and earned her Ph.D. in 1993 from MIT.

David Haussler is the Scientific Director of the University of California, Santa Cruz (UCSC), Genomics Institute and a Distinguished Professor of Biomolecular Engineering at the University of California, Santa Cruz, He is also an Investigator for Howard Hughes Medical Institute, Vice Chair for the Global Alliance for Genomics and Health, Cofounder of the Genome 10K Project, and Scientific Co-Director for the California Institute for Quantitative Biosciences, UCSC. Haussler develops statistical and algorithmic methods to explore the molecular function, evolution, and disease process in the human genome, by integrating comparative and high-throughput genomics data to study gene structure, function, and regulation. As a collaborator on the international Human Genome Project, his team posted the first publicly available computational assembly of the human genome sequence on the Internet on July 7, 2000. They

subsequently developed the UCSC Genome Browser, a web-based tool that is used extensively in biomedical research and serves, along with the Ensembl platform, virtually all large-scale vertebrate genomics projects, including the National Human Genome Research Institute's ENCyclopedia Of DNA Elements (ENCODE) project, the 1000 Genomes Project, and the National Cancer Institute's (NCI's) The Cancer Genome Atlas (TCGA). In 2012, he developed the UCSC Cancer Genomics Hub (CGHub), the first trusted partner to manage data for all of the NCI's major cancer genomics projects, and joined the steering committee of TCGA project. CGHub became the first large, shared cancer genome database in the world, providing researchers more than 2 petabytes of cancer genomics data per month, on par with the entire output of the National Center for Biotechnology Information. In 2013, he co-founded the Global Alliance for Genomics and Health, an international organization with more than 400 member institutions from 40 countries dedicated to sharing genomic information so that scientists and clinicians can accelerate discoveries and develop new therapies. He co-leads the Data Working Group with Richard Durbin. His team at UCSC is developing and implementing new, more effective and more efficient methods to represent, exchange, store, and analyze genome information. In 2014, his team launched the Treehouse Childhood Cancer Project to enable international comparison of childhood cancer genomes. Building on Treehouse, in 2015, the team won the prestigious California Initiative to Advance Precision Medicine (CIAPM) grant competition, launched by Governor Jerry Brown. The CIAPM demonstration project, California Kids Cancer Comparison, aims to identify new treatment options for difficult-to-treat pediatric cancer patients through genome comparisons. The overall goal is to enable international comparison of childhood cancer genomes, and to develop and share infrastructure to support both research in and the clinical application of precision medicine.

Haussler is a member of the National Academy of Sciences, the American Academy of Arts and Sciences and a Fellow of the American Association for the Advancement of Science and the Association for the Advancement of Artificial Intelligence (AAAI). He has received a number of awards, including the 2015 Dan David Prize, the 2011 Weldon Memorial prize for application of mathematics and statistics to biology, 2009 American Society of Human Genetics Curt Stern Award in Human Genetics, the 2008 Senior Scientist Accomplishment Award from the International Society for Computational Biology, the 2006 Dickson Prize for Science from Carnegie Mellon University, and the 2003 Association for Computing Machinery/AAAI Allen Newell Award in Artificial Intelligence.

Markus Meister is the Anne P. and Benjamin F. Biaggini Professor of Biology at the California Institute of Technology (Caltech). Meister studies the function of large brain circuits, with a focus on the visual and olfactory systems. Early in his career, he pioneered the use of multi-electrode arrays for parallel recording from many nerve cells. Applying this to the retina, in combination with new approaches to data analysis, this helped reveal how much visual processing is accomplished already in the eye. In recent years, Meister has been exploring neural function in the mammalian superior colliculus to understand the next stage of visual processing. Meister studied physics at the Technische Universität München, Germany, then at Caltech, where he received a Ph.D. After postdoctoral research at Stanford University, he took a professorship at Harvard University in 1991, where he worked until his return to Caltech in 2012. Meister was named a Pew Scholar in 1993, won the 2009 Lawrence C. Katz Prize for Innovative Research in

Neuroscience, and received the Golden Brain Award for Vision and Brain Research from the Minerva Foundation. He serves on the advisory boards of research organizations and foundations including the Allen Brain Institute, the Howard Hughes Medical Institute, the Max Planck Institute for Neurobiology, the Pew Scholars Selection Committee, the Helen Hay Whitney Foundation, and the McKnight Fund for Neuroscience.

David Piwnica-Worms, M.D., Ph.D., is Professor and Chair, Department of Cancer Systems Imaging, and Deputy Head, Research Affairs, Division of Diagnostic Imaging at The University of Texas MD Anderson Cancer Center (MDACC). He earned his bachelor's degree in Mechanical Engineering from Stanford University, received his medical and doctorate degrees (Cell Physiology) as a Medical Scientist Training Program (MSTP) awardee at Duke University Medical School, completed residency training in diagnostic radiology and a fellowship at the Brigham and Women's Hospital, followed by his first faculty appointments at Harvard Medical School. For two decades, Dr. Piwnica-Worms was at Washington University School of Medicine in St. Louis, where he was Director of the BRIGHT (Bridging Research with Imaging, Genomics and High Throughput) Institute and the Molecular Imaging Center, driving interdisciplinary innovation in molecular imaging until 2013, when he was recruited to MDACC.

A pioneer and leader in the field of molecular imaging, Dr. Piwnica-Worms has created several innovative strategies to visually capture and measure biological processes in living animals, model systems, and humans at the molecular and cellular level using remote imaging detection methods. Dr. Piwnica-Worms has focused on genetically encoded bioluminescent and radiotracer reporter systems for imaging signal transduction, protein-protein interactions, and transcriptional regulation of gene expression at scales ranging from single cells to cell populations to live animals and humans in vivo. He was a Radiological Society of North America Scholar, an established investigator of the American Heart Association, a founding member and former president of the Society for Molecular Imaging and is a recipient of the Society for Molecular Imaging Lifetime Achievement Award. Dr. Piwnica-Worms has been honored with a Distinguished Alumnus Award from Duke University Medical School, the Gerald Dewey Dodd, Jr., Endowed Distinguished Chair in Diagnostic Imaging, is a recipient of the Texas STARs Faculty Award, an elected Fellow of the American Association for the Advancement of Science, and an elected member of the National Academy of Medicine.

Martha Schlicher serves as Mallinckrodt Pharmaceutical's Vice President for Specialty Generics. Prior to joining Mallinckrodt, Schlicher led Monsanto Company's bioenergy and sustainability efforts in the technology organization. These efforts focused on utilizing Monsanto's scientific expertise and capabilities to support the existing renewables industry, to develop Monsanto's sweet sorghum and sugarcane product pipeline in Brazil, and to identify and act upon new opportunities to create value for growers in the field of renewables. Most notably, Schlicher was the architect of Monsanto's commitment to carbon-neutral agricultural production. She has more than 25 years of direct pharmaceutical, agricultural, and bioenergy industry experience from roles at Mallinckrodt, Monsanto, leadership of the National Corn-to-Ethanol Research Center, and as the Head of Technology and Business Development for a London-based renewable company. Schlicher has held roles within Monsanto leading the Environmental and Regulatory Sciences and Regulatory Policy Groups, the Ag Biotech Crop Teams and Strategy, and the U.S. Western Corn Belt Commercial Business.

Schlicher has a B.S. in Chemistry from Indiana University, a Ph.D. in Bio-Organic Chemistry from the University of Illinois and an M.B.A. from the Kellogg Graduate School of Management at Northwestern University.

Schlicher serves as a trustee for the St. Louis Academy of Science, as a past-member of the Department of Energy Biological and Environmental Research Advisory Committee, the International Center for Advanced Renewable Energy Research at Washington University in St. Louis, the Department of Agricultural Economics at University of Missouri–Columbia, and the National Corn Growers Association.

Appendix C: Workshop Agendas and Participants

Agendas for the Brooklyn, New York, and Berkeley, California, workshops follow below. We are grateful for the assistance of the Department of Energy's Corey Williams-Allen and Karen Gibson in operation of the Task Force.

SEAB Task Force on Biomedical Sciences
New York University | Center for Urban Science and Progress
1 MetroTech Center, 19th Floor | Brooklyn, NY 11201

Meeting Participation by Invitation Only

March 10, 2016

Purpose: Outline the framework of current and past DOE-NIH collaborative efforts and key issues for action. Briefings cover imaging, materials, ultra-high performance computing and bioinformatics, instrumentation, and systems and synthesis.

Administrative Session (*Task Force Members Only)*

9:00 AM **Welcome and Review of Day:** Steven Koonin and Harold Varmus
- DOE Ethics Briefing: Susan Beard and Tina Hymer, DOE General Council
- Introductions, Orientation, Review of Charge
- Task Force Activities

General Sessions

10:00 AM **Past and Current Collaborative Efforts between DOE-NIH**
- Human Genome Project: Ari Patrinos, U.S. Department of Energy
- DOE beam lines: Sharlene Weatherwax, U.S. Department of Energy
- BRAIN initiative: Markus Meister, California Institute of Technology
- Computer modeling of cancer: Warren Kibbe, National Cancer Institute

12:00 PM **Lunch**

12:30 PM **Materials Session**
Session Co-Chair: Paula Hammond*
- Justin Hanes, Johns Hopkins University
- Angela Belcher, Massachusetts Institute of Technology
- Jennifer West, Duke University
- Monica Moya, Lawrence Livermore National Laboratory

2:30 PM **Systems and Synthesis**
Session Co-Chairs: Drew Endy* and Harold Varmus
- Peter Sorger, Harvard University

3:30 PM **Break**

3:45 PM **Imaging Session**
Session Co-Chair: David Piwnica-Worms
- Keith Hodgson, SLAC National Accelerator Laboratory
- Bridget Carragher, New York Structural Biology Center
- Rafael Yuste, Columbia University
- David Dean, Oak Ridge National Laboratory

5:45 PM **Adjourn**

6:00 PM **Dinner** (*Task Force Members Only*)

*Participating Remotely

SEAB Task Force on Biomedical Sciences
New York University | Center for Urban Science and Progress
1 MetroTech Center, 19th Floor | Brooklyn, NY 11201

Meeting Participation by Invitation Only

March 11, 2016

Purpose: Outline the framework of current and past DOE-NIH collaborative efforts and key issues for action. Briefings cover imaging, materials, ultra-high performance computing and bioinformatics, instrumentation, and systems and synthesis.

Administrative Session (*Task Force Members Only*)

8:00 AM **Review of Previous Day:** Steven Koonin and Harold Varmus (Task Force Only)

General Sessions

8:30 AM **Ultra-High Performance Computing and Bioinformatics Session**
Session Co-Chairs: Stuart Feldman and David Haussler
- Rick Stevens, Argonne National Laboratory
- Kathy Yelick, Lawrence Berkeley National Laboratory
- Folker Meyer, Argonne National Laboratory

10:00 AM **Break**

10:15 AM **Instrumentation**
Session Co-Chairs: Markus Meister and Steven Koonin
- Gyorgy Buzsaki, New York University
- Alan Litke, University of California, Santa Cruz
- Loren Frank*, University of California, San Francisco

11:45 AM **Lunch**

12:15 PM **Concluding General Discussion:** Steven Koonin and Harold Varmus
- Assignments and plan for future workshop(s) and report

2:00 PM **Adjourn**

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SEAB Task Force on Biomedical Sciences
New York University | Center for Urban Science and Progress
1 MetroTech Center, 19th Floor | Brooklyn, NY 11201

March 10–11, 2016

Meeting Participation by Invitation Only

Full Participants List

Task Force Members and DOE Staff

1. Drew Endy, Stanford*
2. Stuart Feldman, Google (Retired)
3. Paula Hammond, Massachusetts Institute of Technology*
4. David Haussler, University of California, Santa Cruz
5. Steven Koonin, New York University
6. Markus Meister, California Institute of Technology
7. David Piwnica-Worms, University of Texas MD Anderson Cancer Center
8. Martha Schlicher, Mallinckrodt Pharmaceuticals*
9. Harold Varmus, Weill Cornell Medicine
10. Corey Williams-Allen, Department of Energy
11. Karen Gibson, Department of Energy

Invited Participants

1. Angela Belcher, Massachusetts Institute of Technology
2. Steve Binkley, Department of Energy
3. Gyorgy Buzsaki, New York University
4. Bridget Carragher, New York Structural Biology Center
5. David Dean, Oak Ridge National Laboratory
6. Loren Frank, University of California, San Francisco*
7. Susan Gregurick, National Institutes of Health
8. Justin Hanes, Johns Hopkins University
9. Keith Hodgson, Stanford University
10. Warren Kibbe, National Institutes of Health
11. Dimitri Kusnezov, Department of Energy
12. Alan Litke, University of California, Santa Cruz/CERN
13. Betty Mansfield, Oak Ridge National Laboratory
14. Folker Mayer, Argonne National Laboratory
15. Monica Moya, Livermore National Laboratory
16. Aristides Patrinos, Department of Energy
17. Roderic Pettigrew, National Institutes of Health
18. Dave Rakestraw, Livermore National Laboratory
19. Peter Sorger, Harvard University
20. Rick Stevens, Argonne National Laboratory
21. Sharlene Weatherwax, Department of Energy
22. Susan Weiss, National Institutes of Health
23. Jennifer West, Duke University
24. Kathy Yelick, Berkeley National Laboratory
25. Rafael Yuste, Columbia University

* Participating Remotely

SEAB Task Force on Biomedical Sciences
Lawrence Berkeley National Laboratory
ALS User Support Building (Building 15) | 2nd Floor, Conference Room 253
1 Cyclotron Road | Berkeley, CA 94720

Meeting Participation by Invitation Only

July 18, 2016

Purpose: Consider topics and mechanisms for expanded and future DOE-NIH collaborative efforts.

Administrative Session (*Task Force Members Only)*

8:30 AM **Welcome and Preview of Workshop:** Steven Koonin and Harold Varmus
- Review Task Force timeline, agenda, drafting assignments

General Sessions

9:00 AM **Laboratory Welcome**
- Michael Witherell, Director, Lawrence Berkeley National Laboratory

9:05 AM **NIH Needs**
Session Chair: Harold Varmus
- Neuroscience: Walter Koroshetz, National Institute of Neurological Disorders and Stroke
- Computation: Philip Bourne, National Institutes of Health

10:35 AM **Break**

10:45 AM **Advanced Molecular and Cellular Technologies**
Session Chair: Drew Endy
- Panel Discussion on DNA Synthesis and Sequencing Applications:
  - Drew Endy, Stanford University
  - Eddy Rubin, Metabiota
  - Jay Keasling, Lawrence Berkeley National Laboratory
- Presentations on Single-Cell Biology
  - X. Sunney Xie, Harvard University
  - Aviv Regev*, Broad Institute and Massachusetts Institute of Technology

12:30 PM **Break/Lunch**

1:15 PM **Computation and Modeling**
Session Co-Chairs: Stuart Feldman and David Haussler
- Patrick Riley, Google
- Dan Rokhsar, University of California, Berkeley

2:15 PM **Break**

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2:30 PM **Organizations and Mechanisms for DOE/NIH Collaboration**
Session Chair: Steven Koonin
- Alex Lazelere, Council on Competitiveness
- Keith Yamamoto, University of California, San Francisco
- Group Discussion

3:30 PM **Materials Science**
Session Chair: Martha Schlicher
- Mark Davis, California Institute of Technology

4:00 PM **Adjourn**

Administrative Session (*Task Force Members Only*)

4:00 PM **Discussion of the Day:** Steven Koonin and Harold Varmus

5:30 PM **Adjourn; Depart for Hotel**

6:30 PM **Dinner** (*Task Force Members Only*)

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SEAB Task Force on Biomedical Sciences
Lawrence Berkeley National Laboratory
ALS User Support Building (Building 15) | 2nd Floor, Conference Room 253
1 Cyclotron Road | Berkeley, CA 94720

Meeting Participation by Invitation Only

July 19, 2016

Purpose: Consider topics and mechanisms for expanded and future DOE-NIH collaborative efforts.

Administrative Session (*Task Force Members Only*)

8:00 AM **Review of Previous Day:** Steven Koonin and Harold Varmus

General Sessions

8:30 AM **Materials Science (continued)**
Session Chair: Martha Schlicher
- Ron Zuckermann, Lawrence Berkeley National Laboratory

9:30 AM **NIH Needs (continued)**
Session Chair: Harold Varmus
- Cancer: Douglas Lowy, National Cancer Institute

10:15 AM **Break**

10:30 AM **Infectious Disease and Radiation**
Session Chair: Steven Koonin
- David Relman, Stanford University
- Duane Lindner, Sandia National Laboratories
- Gayle Woloschak, Northwestern University

12:00 PM **Adjourn**

Administrative Session (*Task Force Members Only*)

12:00 PM **Working Lunch:** Steven Koonin and Harold Varmus
- Outline of the report, writing assignments, report writing mechanics, future task force timeline and activities; individual writing time

3:00 PM **Adjourn**

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SEAB Task Force on Biomedical Sciences
Lawrence Berkeley National Laboratory
ALS User Support Building (Building 15) | 2nd Floor, Conference Room 253
One Cyclotron Road | Berkeley, CA 94720

July 18–19, 2016

Meeting Participation by Invitation Only

Full Participants List

Task Force Members and DOE Staff

1. Drew Endy, Stanford University
2. Stuart Feldman, Google (Retired)
3. David Haussler, University of California, Santa Cruz
4. Steven Kookin, New York University
5. Markus Mesiter, California Institute of Technology
6. David Piwnica-Worms, University of Texas, MD Anderson Cancer Center
7. Martha Schlicher, Mallinckrodt Pharmaceuticals
8. Harold Varmus, Weill Cornell Medicine
9. Corey Williams-Allen, Department of Energy
10. Karen Gibson, Department of Energy

Invited Participants

1. Teeb Al-Samarrai, Department of Energy
2. Paul Alivisatos, University of California, Berkeley
3. Philip Bourne, National Institutes of Health
4. Mark Davis, California Institute of Technology
5. Susan Gregurick, National Institutes of Health
6. Jill Heemskerk, National Institutes of Health
7. Jay Keasling, Lawrence Berkeley National Laboratory
8. Walter Koroshetz, National Institutes of Health
9. Dimitri Kusnezov, Department of Energy
10. Alex Lazelere, Council on Competitiveness
11. Duane Lindner, Sandia National Laboratories
12. Douglas Lowy, National Institutes of Health
13. Betty Mansfield, Oak Ridge National Laboratory
14. James Olds, National Science Foundation
15. Aristides Patrinos, Department of Energy
16. David Rakestraw, Livermore National Laboratory
17. Aviv Regev, Broad Institute and Massachusetts Institute of Technology*
18. David Relman, Stanford University
19. Patrick Riley, Google
20. Dan Rokhsar, University of California, Berkeley

* Participating Remotely