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Converging Questions, Emerging Answers: The Next Innovation Revolution

I'm always delighted to speak at the AAAS, but I'm particularly delighted to join you today, since we have something so important to celebrate. As you probably know, on Monday President Obama spoke at the National Academy of Sciences. In his speech he offered an endorsement of the value of science and engineering so broad, detailed and unwavering that it simply can't be dismissed as rhetoric. Let me read just one passage. Our President said,

> At such a difficult moment, there are those who say we cannot afford to invest in science. That support for research is somehow a luxury at a moment defined by necessities. I fundamentally disagree. Science is more essential for our prosperity, our security, our health, our environment, and our quality of life than it has ever been.

As we begin work with a new Administration, it is hard to imagine a more encouraging place to start. I am convinced that we can match the President's optimism and ambition because, quite apart from the prospect of better funding, this is a moment of exceptional scientific opportunities. I want to focus on just one source of that promise today, an area that the President actually called out in his speech: the historic convergence between the life sciences, and the physical and engineering sciences.

In academic labs and companies across the country, this accelerating convergence increasingly shapes this century's nascent technologies. It is marked by converging questions and animated by emerging answers. I believe the intellectual potential of this moment will pay off in many important ways: by furthering our understanding of some of the most fascinating systems in the universe; by generating striking new approaches to medical care and other great technical challenges, like clean energy; and by fostering a set of industries that will help fuel America's innovation economy.

To capitalize fully on this moment's potential, however, we need to recognize its promise, adapt our education and research strategies to capitalize on it, and build the understanding and support of those who set federal policy here in Washington. I want to take up each those topics today. First, however, I want to explore how this convergence has come about and why it will figure prominently in the 21st century's

R&D landscape.

The emergence of modern biology

As we all know, a fundamental group of discoveries in the middle of the 20^{th} century set the world of biology on an extraordinarily productive new path. Watson and Crick's elucidation of the structure of DNA in 1953 triggered a powerful new experimental direction that yielded an understanding of a set of fundamental building blocks, or, if you will, a "parts list," for the life sciences. The discovery of the structure of DNA laid the groundwork for two great revolutions in biology: the first was the development of the new science of molecular biology, which revealed how information encoded in DNA gets translated, through RNA, into the proteins that carry out biological functions. And molecular biology set the stage for the second revolution, the explosion of information through genomics.

For those of us who get excited by new scientific knowledge for its own sake, these developments were, and continue to be, incredibly exciting. But beyond their intellectual delight, these discoveries launched a host of practical outcomes that ranged from uniting the many different branches of biology through a common set of core building blocks, to remarkable medical advances such as targeted cancer therapies and the use of statins to lower cholesterol. What's more, the biotech industry, in addition to saving lives, now contributes billions of dollars to the nation's economy. In the health care biotech sector alone, revenues from publicly traded companies soared from $8 billion in 1992 to almost $60 billion in 2006.

Life science and engineering: a growing relationship

Unexpected new partnerships accelerated the growth of the biological knowledge base through these two life-science revolutions. At the inception of the new science of molecular biology, engineering and physical science technologies that had been developed during and after World War II increasingly found uses in the life sciences. Experiments to determine the structure and function of DNA, RNA and their protein products required new approaches, and as physicists turned to such questions, they swiftly commandeered their technologies for applications in biology. The adoption of new analytic tools, from centrifuges to chromatography, permitted life scientists to understand molecular and cellular processes at the level of individual genes and proteins. These discoveries sparked new approaches to drugs and clinical diagnostics.

Over the same period, the electron microscope and a range of powerful imaging technologies revealed the secrets of cellular and organ systems at higher and higher resolutions. Clinicians adopted these tools, too, for diagnostics and therapeutics, from CT and MRI to ultrasound and PET scanning, to mention just a few. This pattern of adopting and developing technologies from the physical sciences and engineering has led to stunning advances in biomedicine and far beyond.

For the avalanche of data pouring out of the genomics revolution, physical sciences-based engineering also offered up new strategies. The challenge of archiving and manipulating large data sets – a common problem in the physical sciences and engineering – is endemic to modern biology; now, the tools that engineers and physicists developed for their own work have a new life in the biology lab. The Human Genome Project drew on mathematics and computational science as much as on powerful new gene sequencing technologies.

In the life sciences, the birth of a third revolution

In recent years, the two revolutions in the life sciences, molecular biology and genomics, have triggered a third revolution. Initially, the connection between life scientists, and engineers and physical scientists, revolved around borrowing tools. It started very much as an arm's-length engagement, one that often cast engineers as service providers to biologists.

Today, what began as a relationship of proximity and convenience has evolved into a strong, fruitful new synthesis, a relationship of equal partners with converging questions. Both disciplines gain from the connection and emerge with potent new answers. In short, the seeds of the third revolution in the life sciences have certainly been sown, and in leading labs across the country, they are already beginning to bear fruit. At MIT, for instance, faculty and students in our School of Science and our School of Engineering are collaborating on projects in biomedical science and many other fields. To help illustrate the promise of this moment, I'll offer three MIT examples, but please note that comparable approaches are evolving nationwide.

1. **Cancer research**

   At MIT, we are capitalizing on the vast potential of this third revolution in the fight against cancer by designing both a new organization and a new building. The David H. Koch Institute for Integrative Cancer Research at MIT grew out of our Center for Cancer Research, established in 1974 during the War on Cancer.

   Look today along the frontier of cancer research, and increasingly you see biologists and engineers, computational experts and chemists. They bring together a mix of disciplines and perspectives that drive new strategies to diagnose, treat and prevent cancer. MIT's Koch Institute will house about a dozen cancer scientists as well as about a dozen engineers, along with their research groups. It will offer core facilities to the Koch investigators and to others on the MIT campus working at the interface of the life sciences with engineering.

   What can we expect to gain from this productive proximity? One example is new approaches in the long quest to focus chemotherapy on tumor cells alone. Labs at MIT and elsewhere have engineered nanoparticles that transport anti-cancer drugs directly to malignant cells. Designed to be internalized only by cancer cells, these particles can deliver high doses of chemotherapy, potentially including inhibitory RNAs and other novel cancer therapeutics, with minimal injury to normal cells. Several labs have demonstrated engineered nanoparticles that act as homing devices, or "smart bombs," with encouraging evidence of their efficacy. Our biologists and engineers anticipate that nano-smart bombs could become clinical tools against cancer within a decade.

2. **Energy**

The significance of this third revolution does not stop at the doors of the hospital. In fact, what makes this convergence so exciting is that the insights flow not only from engineering to biology, but both ways, and we find a prime example in new breakthroughs in the field of energy. For instance, MIT researchers have developed a new kind of battery. Improbably enough, it begins with benign viruses that are genetically engineered to incorporate battery materials, and which then self-assemble into both the positively and negatively charged sides of a lithium-ion battery. The result looks like plastic wrap, but has the same energy capacity and power performance as state-of-the-art rechargeable batteries designed for use in plug-in hybrid cars. Fabrication of these new bio-fab batteries occurs at room temperature and without generating toxic by-products. The first breakthrough, made a few years ago, was to synthesize the battery anode. But as the team reported recently in Science, they've now devised a method to virus-construct the cathode, too.

The team leading the research consisted of two materials scientists and two chemical engineers who brilliantly co-opted a biological process to create a high-performance battery, in a way that's both cheap and environmentally benign. The team's work now focuses on scale-up, seeking to increase the batteries' voltage and capacitance, at which point the technology could go into commercial production.

3. **Environmental science**

A third and final example comes from Environmental Science. Civil and environmental engineers at MIT are using genomics technology to decipher the microbial ecosystems of the ocean and monitor how they're responding to climate change. We know that ocean microbes play a role in vast natural cycles of water, carbon and energy, but we know surprisingly little about how they do it. Adapting tools developed for sequencing the human genome, MIT researchers devised a new way to analyze gene expression in complex microbial populations, a process that allows them to study which genes the bacteria actually use in their day-to-day activities and when they express them. This new strategy provides important new data on the effects of and responses to climate change and also makes it possible to consider using indigenous microbes much more broadly as *in situ* biosensors.

Seizing the potential of the moment: vital next steps

Describing these inspiring examples makes progress seem almost inevitable. Yet given the scale of the problems humanity faces, from pandemic disease, to a stumbling world economy, to an unsustainable global energy system, the pace of “inevitable” simply isn’t good enough. We need certain progress, soon, and that kind of progress demands immediate action. So let me close by suggesting four specific steps to accelerate this third revolution from questions and potential, to answers and applications:

First, Encourage young people to pursue work at the convergence.

I have to tell you how easy this seems, from my perspective at MIT. Every year in late August, I walk around campus, meeting the newly arrived freshmen. When I ask them what they think they might want to study, many talk about areas emerging at the convergence of disciplines. Whether they are interested in mechanical engineering or biology or computer science, they talk about the promise of work that crosses the disciplinary boundaries of science and engineering. I am confident we will have the soldiers to lead this revolution. Once we have captured their enthusiasm, however, we need to educate them to be “bilingual” across disciplines. We should also offer a broad education for biologists and engineers, computer scientists and mathematicians**,** so that the material they study has common elements, equipping them to talk and work fluently together.

Second, we must cultivate new academic organizations.

A number of universities have developed biomedical engineering activities, emphasizing the applications of engineering to medicine, fostered early on by visionary support from the Whitaker Foundation and other sponsors. At MIT, we’ve taken a somewhat different approach. Just as chemistry gave birth to chemical engineering, cellular and molecular biology have spawned the new discipline of biological engineering. Our department of Biological Engineering has established the intellectual framework of a new discipline, with sophisticated undergraduate and graduate curricula. It does more than put biologists and engineers in proximity; it produces individuals fluent in the language of engineering, in the language of the life sciences, and in the distinctive new language of biological engineering. With a very deep understanding of biology, biological engineers do what engineers do best: analyze complex systems, describe predictive mathematical models, derive fundamental design principles, and then design entirely new solutions.

We need to propagate models like these across the country. And even outside such focused departments, we need to make it much easier for faculty in all areas to work across disciplines, actively encouraging them to work with their colleagues from different fields.

Third, we should tune our funding mechanisms toward boundary-crossing work.

Several strategies can help here. For instance, if we fund our young investigators, they will be the nomads across disciplines. Young investigators often bring a cross-disciplinary perspective to their work. When I talk with the younger members of the MIT faculty, I am struck by how often their research engages more than a single area. However, research that crosses conventional fields and projects of young faculty with a shorter history of achievement often fall off the funding list, particularly when research funds are scarce. In 1990, the average age of first-time NIH (National Institutes of Health) RO-1 grantees was 39; by 2007, it had climbed to 43. In 1990, first-time applicants received 29 percent of the NIH's RO-1 grants. By 2007, it was 25 percent. Perhaps most troubling of all, the success rate on first submission dropped from 29% in 1999 to just 12% in 2007. NIH has programs designed to address the aging of the investigator population, and we must continue to make research open to young researchers. We simply cannot educate students for cross-disciplinary research careers and then fail to fund them.

We should also our current grant processes so that they foster projects that include investigators in different departments, different schools and different institutions. We need to simplify grant applications from multiple investigators and organizations. Our peer review system will require grant review committees with multi-disciplinary membership. Once we get the assessment process right, we will need monies set aside to ensure support for bold, crosscutting ideas.

Fourth, we need to build connections across stovepipe agencies.

We should consider funding structures that not only cut across internal NIH institutes and centers, but also across federal agencies. How do we unite a research environment historically funded separately by the National Science Foundation, the Department of Energy and the Department of Defense, with one funded primarily by the NIH? Our funding agencies, not just our scientists, should become collaborators. Beyond talking to each other, our funding agencies should together identify the great areas of opportunity and the set of top scientific challenges, and together develop common strategies across agencies. Our system of decentralized science agencies, each pursuing particular mission areas, has great advantages. However, crosscutting pursuits require a process that cuts across them.

The National Nanotechnology Initiative, which has already contributed crucial new science at the convergence, offers important lessons for organizing crosscutting science. As in the early stages of the Nanotechnology Initiative, the major scientific agencies should start to define and encourage coordinated agency funding and budgeting for this third revolution, perhaps through the power of the Office of Science and

Technology Policy to convene agencies around common goals.

A third revolution that will transform our lives

Let me sum up the potential of this third revolution in a simple way: In the early part of the 20th century, no one could have named the industries that would spring from the convergence of the physical sciences and engineering, yet the industries fueled by that convergence -- the electronics, computer and information industries -- have transformed life on earth. Today, we do not yet know the names of the industries that will grow from this century's convergence of the life sciences with the engineering and physical sciences, but those new industries will certainly transform our lives as powerfully.

Lest we feel too giddy with the opportunities before us, with newly emerging disciplines and the prospect of new funding, I will close on a note of caution, one born of the optimism inherent in the 21st century. During World War II, the U.S. developed a new kind of three-way, government-industry-academy collaboration that produced a huge number of remarkable technological accomplishments. After the war, we turned that three-way collaboration into the engine of a new kind of economy, one based on innovation. Economists now generally agree that in the decades following the war, more than half of America's economic growth came from technology. Because the war had not been fought on U.S. soil, for many years we had the field more or less to ourselves: as other nations rebuilt their cities, roads and governments, we reinvented our education and research enterprises and launched a half-century of innovation.

Needless to say, things have changed. Thanks to the 20th century's new technologies and to the extraordinary global progress that has propelled more people out of poverty more rapidly than at any other time in human history, we no longer have sole access to the economic benefits of innovation. Countries all over the world have built the foundation for their own innovation economies. I like competition; it makes everyone better. But we need to play if we want to compete. Investments in basic research are investments in that competition; they are not costs. Many analyses have demonstrated the remarkable return on investment that stems from funding basic research. It is now up to those of us who know the science, who know the engineering and who appreciate the nature of the challenges and their solutions to give policymakers and the public a picture of the results that sit only just beyond our reach today

In effect, with this convergence, the life and physical sciences expand beyond their questions of, "What, Why and How?" to take up, in the company of engineering, the potently practical question, "Why Not?" The emerging answers indeed constitute a Third Revolution. Today, with science back in its rightful place, it is our challenge to adapt our academic organizations and change federal practices to accelerate its potential: for human health, for national prosperity, and for the survival of the planet.