with polymers where both electrons and holes can be injected into the channel of the device. Localized electron trapping near one contact invalidated a key assumption of the gradual-channel approximation. The use of the simple transistor equations resulted in an overestimation of the hole mobility by a factor exceeding 20, 14 $cm^2 V^{-1} s^{-1}$, rather than a more likely value of 0.6 $cm^2 V^{-1} s^{-1}$ (*10*). Another type of nonideality occurs when non-ohmic injection from the electrodes generates a gate-bias dependence of the contact resistance. Single-crystal rubrene FETs with severely non-ohmic contacts also led to an overestimation of the mobility by more than an order of magnitude (*9*).

Without a robust and reliable method to determine carrier mobility as an intrinsic materials property, chemists dedicated to the synthesis of improved organic semiconductors can easily pursue erroneous design principles based on inaccurate literature values of mobility. For example, notable instances of these nonidealities are observed in the characteristics of recent polymers synthesized from a highly polar, electron-deficient diketopyrrolopyrrole (DPP) conjugated monomer (*12*). This repeat unit generates a high electron affinity that can facilitate electron injection in hole-based devices, thereby invalidating the use of formulas derived from the gradual-channel approximation to extract mobility. Molecular design principles for this class of polymers developed from these mobility values may thus be unsubstantiated and, in fact, impede an understanding of the fundamental structure-property relations. Furthermore, high mobilities obtained from nonideal characteristics may set erroneous benchmarks for device design. Until better models and solutions to eliminate nonidealities are found, the best prescription is conservatism on absolute metrics and trends, particularly with small differences in electrical properties, as suggested in a number of recent commentaries (*13*). ■


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BIOMEDICAL ENGINEERING

# Capitalizing on convergence for health care

## Integrate physical sciences, engineering, and biomedicine

*By* **Phillip Sharp, Tyler Jacks, Susan Hockfield***

POLICY

For decades, scientists have called for more collaboration between the life and physical sciences, and in the past 5 years, we have been among those calling for a new national research strategy—one we call "convergence"—that would integrate engineering, physical, computational, and mathematical sciences with biomedical science (*1*). Thanks to the accelerating pace of biological discovery, the expanding power of computation, and a new focus in engineering on biocompatible materials and nanotechnology, the potential of such a strategy for advances in health care is greater than ever (see the photo). Technologies emerging from such efforts have potential implications far beyond health care: creating jobs; speeding products to market; and improving everything from agriculture and the environment to defense, the economy, and energy production. It all adds up to a moment of unprecedented opportunity, if we choose to invest in it meaningfully. But so far we have not. We detail below, and in greater depth in a new report with colleagues from across the country (*2*), the stakes in the convergence revolution and what we should do to capitalize on it.

> *"The report recommends…an interagency working group on convergence with NIH, NSF, Department of Defense, FDA, and DOE…."*

Convergence and interdisciplinary research are closely allied, but convergence goes beyond collaboration. It involves integration of historically distinct disciplines and technologies into a unified whole that creates new pathways and opportunities. It is this integration that offers potentially revolutionary change for biomedical sciences. Consider the changes resulting from the 20th century's great convergence, which brought together physical sciences and engineering and which gave us tools that have reshaped our world—radios, telephones, cars, planes, computers, nuclear power, satellites, and the Internet. We can promote another era of transformational tools and technologies in health care if we invest in and commit our agencies, institutions, and ingenuity.

Yet only 3% of the principal scientists receiving research grants today from the U.S. National Institutes of Health, the major source of research funding for biomedical science, come from physics, biophysics, mathematics, engineering, or bioengineering (*3*). The National Institute of Biomedical Imaging and Bioengineering (NIBIB, NIH), which is primarily focused on convergence-related research, has a 2016 budget just short of $345 million (*4*). That amounts to only ~1% of the total NIH budget. Among federal agencies, the National Science Foundation (NSF) is the primary source of support for basic engineering and physical sciences, but the level of funding in the convergence of these disciplines with biomedical science is miniscule, because NSF has historically deferred to NIH on medical research (*5*, *6*). Although other federal agencies—such as the Department of Energy (DOE), Defense Advanced Research Projects Agency (DARPA), and Food and Drug Administration (FDA)—are beginning to recognize the promise of convergence, to date, no federal agency or office has the primary responsibility to promote the convergence of engineering, physical, and mathematical sciences with biomedical sciences. Difficulty in securing federal funding for projects that cross disciplines has impeded progress.

**HOW FAR HAVE WE COME?** Although investment has been far too modest in our view, we applaud efforts already under way that can serve as models and test beds for efforts to come. Several federal agencies have embraced convergence initiatives. The NIBIB has been awarding convergence-related grants since 2002. DARPA launched a Biological Technologies Office in 2014 to harness "the power of natural systems" as it develops smart prosthetics and strategies to combat brain disorders and infectious disease. The recently launched BRAIN Initiative (*7*), designed to revolutionize our

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**Convergence at work.** Microfabricated device by Stephen Quake, Stanford University, for sequencing DNA from one sperm.

understanding of the human brain, and the Precision Medicine Initiative (*8*), which aims to use big data analytics to evaluate information about disease at the level of individuals, both have built the interdisciplinary potential of convergence into their research models. The same is true for the recent National Microbiome Initiative (*9*). These initiatives have been encouraged by early support from foundations such as Kavli, Howard Hughes, Raymond and Beverly Sackler, and Simons and from the Burroughs Wellcome Fund.

Several academic institutions have made promising commitments to convergence in the recent past. Northwestern University's International Institute for Nanotechnology has brought together chemistry, bioscience, and engineering to develop tools for nanomedicine and nano-oncology. At the University of California, the California Institute for Quantitative Biosciences applies the techniques of physics, chemistry, and computer science to challenges of molecular biology. The Wyss Institute for Biologically Inspired Engineering at Harvard crosses disciplinary and institutional lines to develop innovative engineering solutions, commercial products, and therapies in multiple fields. At Massachusetts Institute of Technology (MIT), the David H. Koch Institute for Integrative Cancer Research has brought together engineers, biologists, and clinical oncologists to develop new insights and create tools to better diagnose, treat, and prevent cancer.

These programs, along with many others like them, are uncoordinated and modest in the big picture but have already generated impressive results (*2*). Dozens of companies have been spun out, many with products now in clinical trials: nanoparticles that home in on cancer cells to deliver chemotherapy directly, imaging technologies that allow surgeons to more accurately spot and remove cancer cells, and much more. These efforts have the important benefit of training a generation of scientists and engineers across disciplines to become facile and conversant in a range of fields in order to take full advantage of opportunities.

Many businesses have also moved into this space. Verily (formerly Google Life Sciences) is combining genomics with high-content and high-resolution imaging to develop individualized treatments based on biological, genetic, behavioral, and environmental data. Companies such as Apple, IBM, and Microsoft have invested and brought to market innovations that allow people and institutions to track and monitor individual health, fitness, and disease.

**HOW CAN WE GO FURTHER?** Despite these indicators of progress, there is reason for concern, and there are lessons to be learned. The new report makes several recommendations to improve and accelerate convergence: a substantial and sustained increase in federal funding for biomedical research that explicitly targets funds for convergence programs; a revision of grant-review mechanisms to include expertise from engineering, computation, and physical sciences; and, at colleges and universities, a realignment of academic structures to facilitate research and educational collaborations among biologists, clinicians, mathematicians, physicists, engineers, and computational scientists. The NIH will have a major role to play: It should aggressively develop convergence-technology strategies and recruit mathematicians, engineers, physicists, and computational scientists to apply their expertise to our biomedical challenges, in both fundamental and applied research. Although several federal agencies have already embarked on programs that embrace convergence, these efforts should expand. We are encouraged by NSF's new convergence-research emphasis and its planned changes to its grant reviews and new education models to support convergence models.

Big things will happen if we can align objectives across disciplines and provide funding and programs to foster working together. The report recommends creating an interagency working group on convergence with NIH, NSF, Department of Defense, FDA, and DOE, coordinated through the Office of Science and Technology Policy. In addition, a specific strategic plan for advancing biomedical science through convergence patterned on the Nanotechnology and Plant Genome initiatives should be developed. NIH's Common Fund mechanism should support convergence across multiple institutes and centers. Federal agencies should consider more traineeships with convergence research tracks and on a larger scale. Transformation of biomedical and health care by convergence depends on openness to change and the will to work together. This is clearly emerging but needs to be further strengthened. ■

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