Bionanoscience in Health and Medicine

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What is bionanoscience (or bionanotechnology)? It is the nexus where the worlds of solid state, chemistry, and biology unite—"to boldly go where no engineer, chemist, or biologist would have gone alone." Broadly defined as biomedical applications of nanotechnology, it is a highly interdisciplinary field that draws upon expertise and knowledge from a host of conventional subdisciplines within engineering, chemical, and biological sciences. It is the world of the nanoscale—at dimensions from a few nanometers to hundreds of nanometers where structures, devices, and materials are fabricated and constructed either using "top–down" fabrication methods with silicon manufacturing approaches, or the "bottom–up" self-assembly methods that are chemically or biologically inspired. Integration of these approaches can allow scientists and engineers to create devices with nanoscale features for detection or characterization of biological or chemical molecules, build new polymeric constructs for targeted drug delivery, construct hybrid materials interfacing semiconductor nanoparticles with DNA and other biomolecules with new properties, and many other possibilities yet to be realized. These new devices and materials offer many very exciting possibilities to tackle grand challenge problems facing health and medicine. Just as the last century was considered as the era of electronics and information technology, the current century could be regarded as that of biology, medicine, and health. Many grand challenge problems in health can benefit from the advancements in bionanosciences. Extensive research and development is taking place in diagnostics, therapeutics, and engineering of biological systems from molecular to tissue scale. The potential applications are many, ranging from "bench to bedside" (i.e., basic science to translational research) in cancer, infectious diseases, global health, tissue engineering and regenerative medicine, individualized medicine, synthetic biology, and many others.

Cancer, as one of the grand challenge disease, continues to take a huge toll on our society both in terms of lives and cost of disease management. Even though the average lifespan continues to be on the rise in the United States, the deaths due to cancer (about 190 deaths per 100 000) have decreased only negligibly over the last 50 years. One bold initiative is that undertaken by the National Cancer Institute Alliance for Nanotechnology in Cancer where researchers from a wide range of disciplines are funded to work together on applications of nanotechnology in cancer for diagnostics, therapeutics, and more, and to train the next generation of leaders to work in this critically important area for the nation and the world. As a matter of fact, according to reports from the World Health Organization, noncommunicable diseases, including cancer and heart diseases, are expected to become global epidemics and result in more death and suffering than communicable

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diseases. Advance in bionanosciences for early diagnostics and targeted personalized therapeutics can provide new solutions for management and eradication of cancer and other diseases.

The similarities in size of many biological entities to that of advanced human-made nanostructures provide exciting opportunities to interface the biological world and the synthetic world. The size of most viruses is the same or larger than the minimum feature size in today's modem integrated circuits. The diameter of a double stranded DNA at 2 nm is of the same order as the gate dielectric thickness in advanced silicon field effect transistors. Nanoscale pores and channels can be drilled with a focused electron beam in thin membranes on a chip to study the passage of single DNA molecules toward the goal of directly determining their sequence. These solid state nanopores, or their biological counterparts derived from components and machinery of viruses, are potential candidates for generation-4 sequencing devices potentially allowing the realization of the sequencing of entire human genome for less than 100$. Such low-cost sequencing could revolutionize individualized medicine and could have a similar impact on our society as did the invention of the transistor and integrated circuits.

Similarly, semiconductor nanowires with diameter of 10–20 nm could be used as highly sensitive detectors for just a few proteins or DNA molecules, without the need for fluorescent reporters enabling low-cost point of care sensors for monitoring of health. These nanowire sensors, originally demonstrated by chemical self-assembly methods, can now also be fabricated on highly integrated silicon chips, thanks to advancements by the semiconductor industry and the scaling of Moore's law. Perhaps use of highly integrated silicon chips for biosensing is a very promising area where the potential has yet to be fully utilized. Recent reports by the company Ion-Torrent on sequencing of Gordon Moore's genome using very large-scale integration (VLSI) silicon chips, where the individual transistors are acting as tiny pH sensors, demonstrates the potential of this approach.

Delivering specific drug molecules to specific sites of interest in the body is a goal of therapeutic applications of bionanotechnology. Polymeric nanoparticles can be synthesized, chemically loaded with cancer drugs, and conjugated with proteins to target these nanoparticles to cancer tumors or diseased sites. Also, the fate of the nanoparticles and how long they can stay in the circulatory system can determine their therapeutic efficiency and efficacy. If the nanoparticle was constructed from gold, the absorption of infra-red radiation can result in heating and localized inactivation or "killing" of the target cells. The transport of the nanoparticles across the cell membranes and into cells can also occur and it has been shown that specific sizes and shapes are preferentially taken up by cells; the mechanisms of these phenomena are still not clear. Toxicity, biodistribution, and the pharmacokinetics are important challenges to be addressed during the U.S. Food and Drug Administration (FDA) approval of any therapeutic approach, same as is the case for any new drugs molecules. Human testing of polymer nanoparticle for drug delivery in cancer has begun early this year by the company BIND Biosciences.

Much progress has also been made in design and engineering of molecular constructs from DNA, the basic building blocks of life. The general idea that information encoded in the sequence of the DNA can be utilized to perform programmable functions is still highly sought after. Just as the sequence of the DNA can be translated and transcribed to result in synthesis of proteins in cells, can DNA sequences be designed to subsequently result in programmed synthesis of new materials, crystals, or scaffolds, via self-assembly of complementary bases of DNA molecules? Researchers have made strides toward achieving this goal to create nanoscale constructs using such approaches for potential use in sensing and therapeutic applications.

Since bionanoscience is an enabling field, the applications can be crosscutting and many, and hence there is room for researchers from many fields to contribute. In these interdisciplinary fields of endeavors, research and graduate education occurs across many traditional departments and disciplines. This is "team science" in its true spirit, where working together with researchers from different backgrounds has the potential to result in major breakthroughs. The researchers have to not only be grounded in disciplinary excellence but also be able to work with colleagues from other disciplines. Interdisciplinary graduate training program grants from the National Science Foundation and the National Institutes of Health provide an excellent mechanism for training of this cadre of interdisciplinary researchers of tomorrow at the nexus of disciplines. Research in bionanosciences in academic institutions occurs in interdisciplinary labs and groups and not in any one department. The traditional departmental boundaries do not exist in this field, especially at the graduate level.

In summary, bionanoscience or bionanotechnology offers great excitement and great potential to address many grand challenge problems in health and medicine in the coming decades. Since 2000, many advances have been made in the first ten years of the national nanotechnology initiative and many more are expected in the next ten years. An increased focus on the potential adverse effects of nanotechnology on the body and the environment is already taking place and appropriately so, as an increased body of research is starting to make its way to commercial applications. Much more discoveries and applications await, adapting the famous words of Physicist Richard Feynman, "there is 'still' plenty of room at the bottom." ■